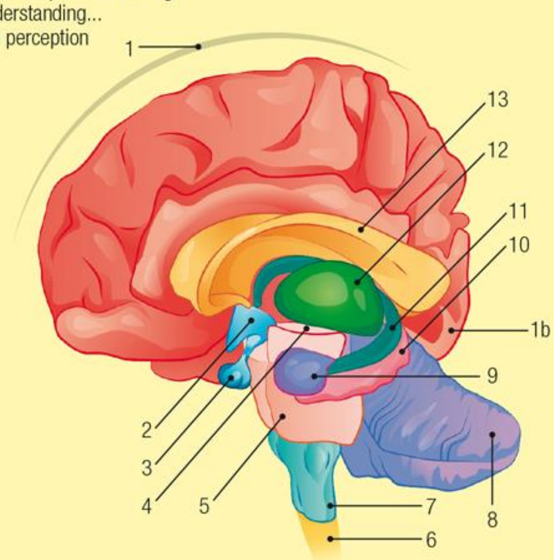
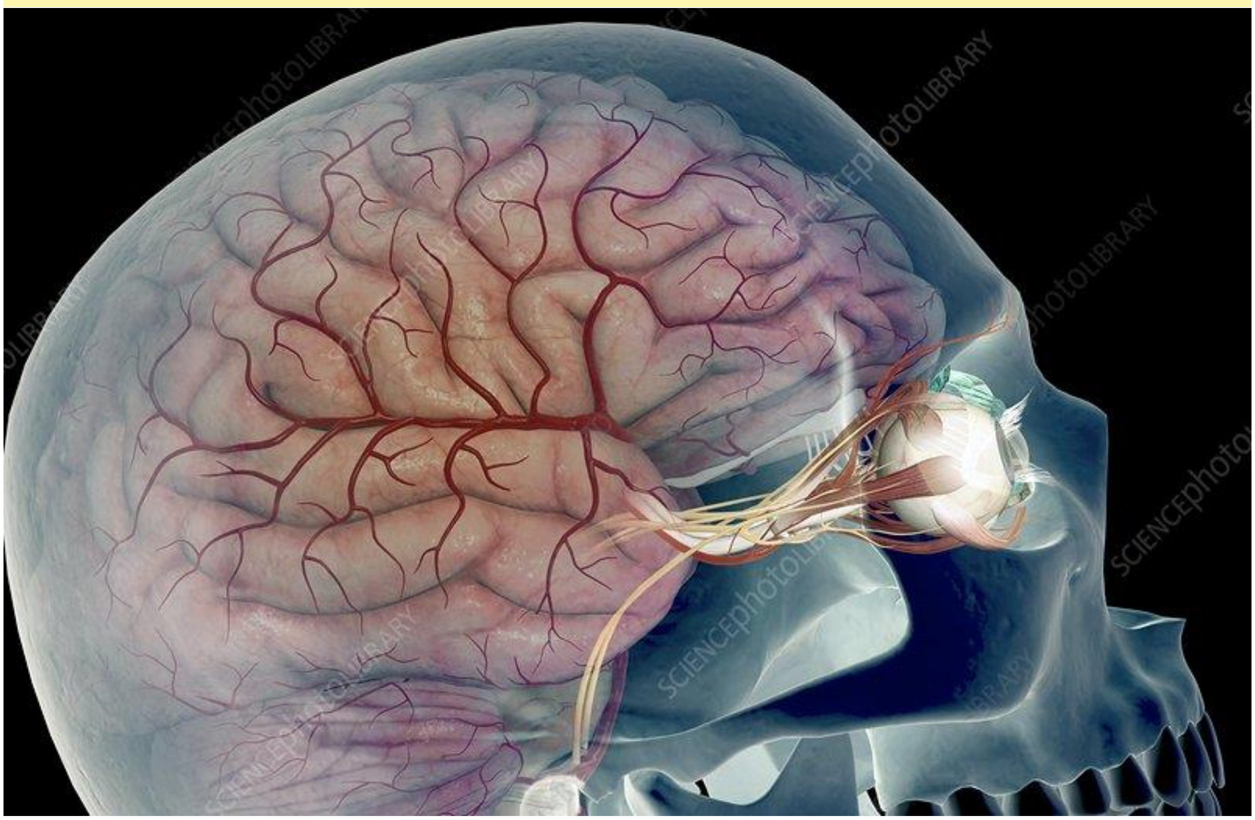
BRAIN INTRACRANIAL VOL 3

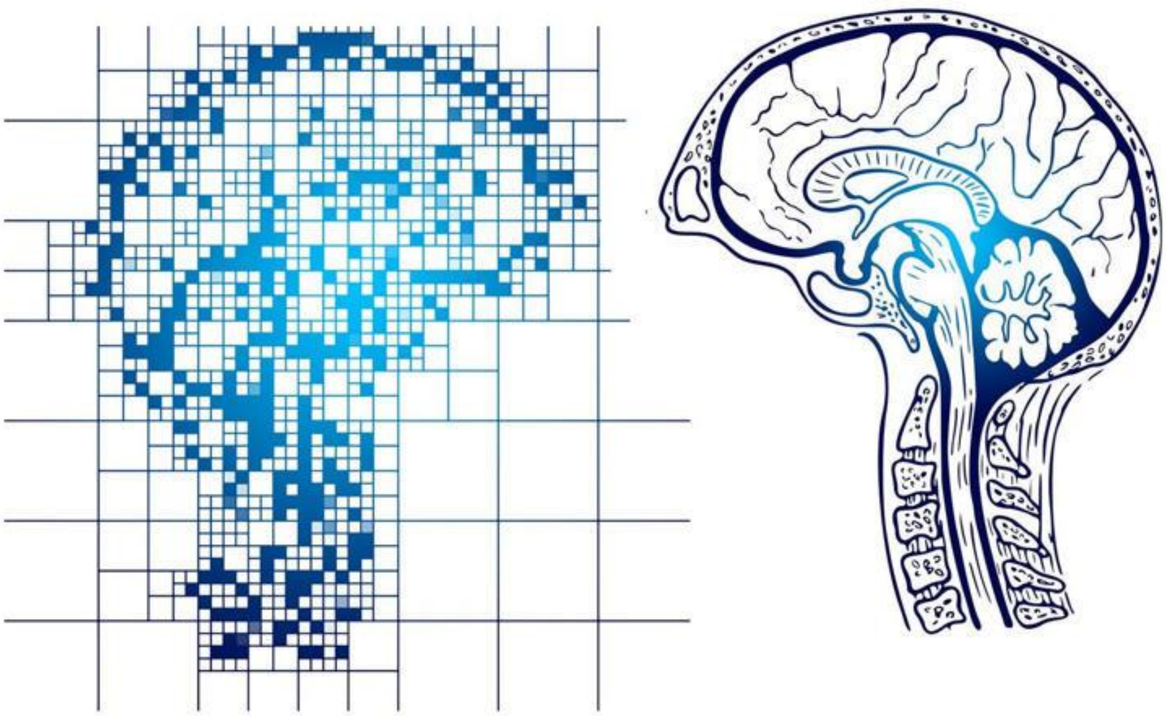
The brain consists of different parts and each part has its own functions

1 **Cerebral Cortex** the ultimate control and Information processing center: problem solving and planning, decision making, personality, attention, language, understanding...
- 1b **Visual Cortex** is part of the cerebral cortex and enables visual perception

2 **Hypothalamus** regulation of appetite and hormone production, emotions, reward system...
3 **Pituitary** master endorine gland, hormone production
4 **Midbrain** Movements, especially of the eyes, treatment of hearing and vision
5 **Pons** control of breathing, sensations such as hearing, taste and balance
6 **Spinal cord** pathway for neural fibres traveling to and from the brain. control of simple reflexes
7 **Medulla Oblongata** helps regulate breathing, heart and blood vessel function
8 **Cerebellum** coordinates voluntary movements and balance and supports motor memory
9 **Amygdala** linked to emotion (including fear)
10 **Hippocampus** linked to memory
11 **Fornix** behaviour, emotions, memory
12 **Thalamus** relays messages between the treatment areas and the decision-making cortex
13 **Corpus Callosum** link between the hemispheres







BOE Technology Group Co., Ltd is a leading company in the global semiconductor display industry and have a strong focus on innovative display solutions.

BOE Flexible AMOLED Display

Flexible display refers to the display technology designed for ultra-thin, ultra-light, and flexible products on the base of a flexible substrate. mobile phone can be worn on the wrist, tablet computer can be folded into a small pocket, and TV can also be rolled up like a scroll.

Active matrix organic light-emitting diode (AMOLED) is an organic light-emitting display device mainly consisting of a substrate, a TFT-driven array and OLED light-emitting device (metal cathode + organic light-emitting layer + anode). It is an ultra-thin device with fast response time, wide view angle, and high contrast， which is suitable for flexible display technology. AMOLED, with polymer plastic or metal foil as its flexible substrate material, has a strong anti-bending capability and can realize dynamic bending display or even folding display. It has broad application prospects in smart phones, wearable devices, and automotive devices. Through persistent technical innovation, BOE has made great breakthroughs in several key technologies such as flexible AMOLED display. BOE has now successfully developed foldable display, wrist display, flexible display with double fixed edges and other flexible AMOLED products, presenting unlimited potential of the innovation of smart display devices.

As China’ s first enterprise mastering flexible display technology, BOE has been actively building flexible AMOLED production lines in many regions, which will further enhance the global competitive power of China's display industry.

BOE Life Data Detection Technology

Life data detection is a technology that obtains the physiological information of human body by utilizing a special acquisition method, and evaluates the health conditions via data processing and analysis, which is mainly used for the detection of electrophysiological indexes (e.g. ECG, EEG, EMG, etc.), biochemical indexes (e.g. blood oxygen, blood glucose, etc.), image indexes (e.g. CT, PET, etc.), and other physiological indexes (e.g. body temperature, blood pressure, etc.), so as to comprehensively evaluate the health conditions of the user and provide a reliable basis for disease diagnosis and chronic disease management.

However, limited by the sensor technology and computing power of chips, the existing life data detection devices cannot completely satisfy users' demand for sport
health and chronic disease management due to such shortages as poor wearing ability of electrophysiological index detectors, impossibility of non-invasive detection of biochemical index detectors, and impossibility of continuous detection of physiological index detectors. Considering this, it is a major trend to transform life detection technologies from small to wearable, from invasive to non-invasive, and from random to continuous.

BOE integrates its years of experience in the four core technologies of display, sensor, AI, and big data with the medical and life science for cross-border innovation.
In the field of non-invasive vital sign detection device, BOE has launched MTX (noninvasive multi-parameter detector), with which, the patients can accurately measure and record 14 important physiological indexes such as blood pressure, oxyhemoglobin saturation, and hemoglobin within 1 minute by wearing MTX on the finger without blood sampling, so as to evaluate the user's health conditions based on the measurement results. In the field of continuous detection of life data, BOE has independently developed an undisturbed blood pressure measuring technology that is completely different from the traditional method of blood pressure measurement. It deduces the blood pressure by computing the transmission time with pulse signal and ECG signal without a cuff and air pump, and achieves wearable and continuous blood pressure monitoring.

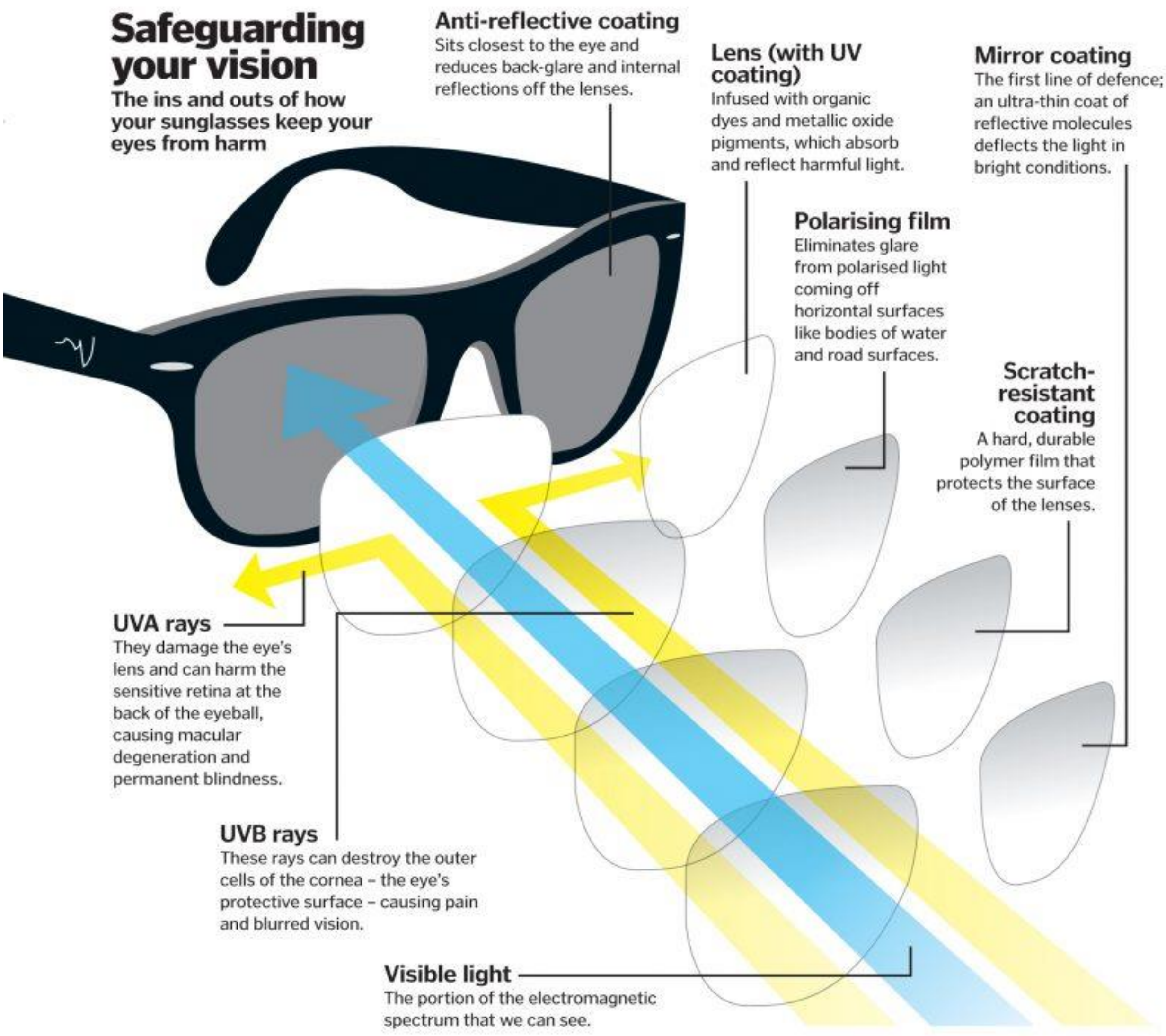
In the future, the company will continue to forge ahead in the field of life data detection, launch more high-end products and services, and make more contributions to the healthcare of human beings.

BOE ADSDS Ultra Hard Screen Technology

In the last century relatives and friends used to sit in front of a black-and-white TV to watch a program chosen from a very limited number of channels, which is now still a nice and unforgettable memory about sharing. In BOE, we seek to bring this happiness to a higher level. As one of the world’s leading Ultra Hard screen technologies, the unique ADSDS (Advanced Super Dimension Switch) technology owned by BOE provides higher transmittance, brightness, and contrast ratio, as well as a visual angle of about 180° to present a vivid image effect. Meanwhile, the ADSDS panel is featured by low power consumption and environmental friendliness, and can be used as the screen of smart phones, tablet PCs, laptops, displays, and TVs.

As for the traditional TN/VA display mode, the liquid crystal molecules are vertically arranged, with a relatively narrow visual angle. When an external force is exerted on the screen, the liquid crystal molecular structure will obviously sink in a herringbone pattern, and the recovery is slow, a phenomenon called VA. There will be an evident “water ripple” when it is touched, which may affect the user’s experience. ADSDS technology is a general name for core technologies invented by BOE independently, which is represented by the wide-view-angle technology. In the ADSDS mode, the liquid crystal molecules are arranged horizontally, with a much wider visual angle. When an external force is exerted on screen, the liquid crystal molecular structure only sinks slightly, but the overall molecular structure remains horizontal, without producing any water ripple. In addition, BOE’s ADSDS technology effectively solves the problem of low light transmittance, and achieves high light transmittance with a wide visual angle.

Currently, a series of high-end display technologies developed by BOE based on the ADSDS Technology Platform have been successively applied to the whole series of TV products from HD to 8K UHD, and from 32inch to 110inch, and have contributed a lot to the perfect integration of high definition and low power consumption, bridging China’s gap in large-sized high-end TFT-LCD display products and improving the competiveness of China’s display industry in the field of high-end displays worldwide.



What Are Augmented Reality (AR) Contact Lenses?

AR contact lenses are smart contact lenses embedded with microelectronics that overlay digital information onto a user's real-world view.

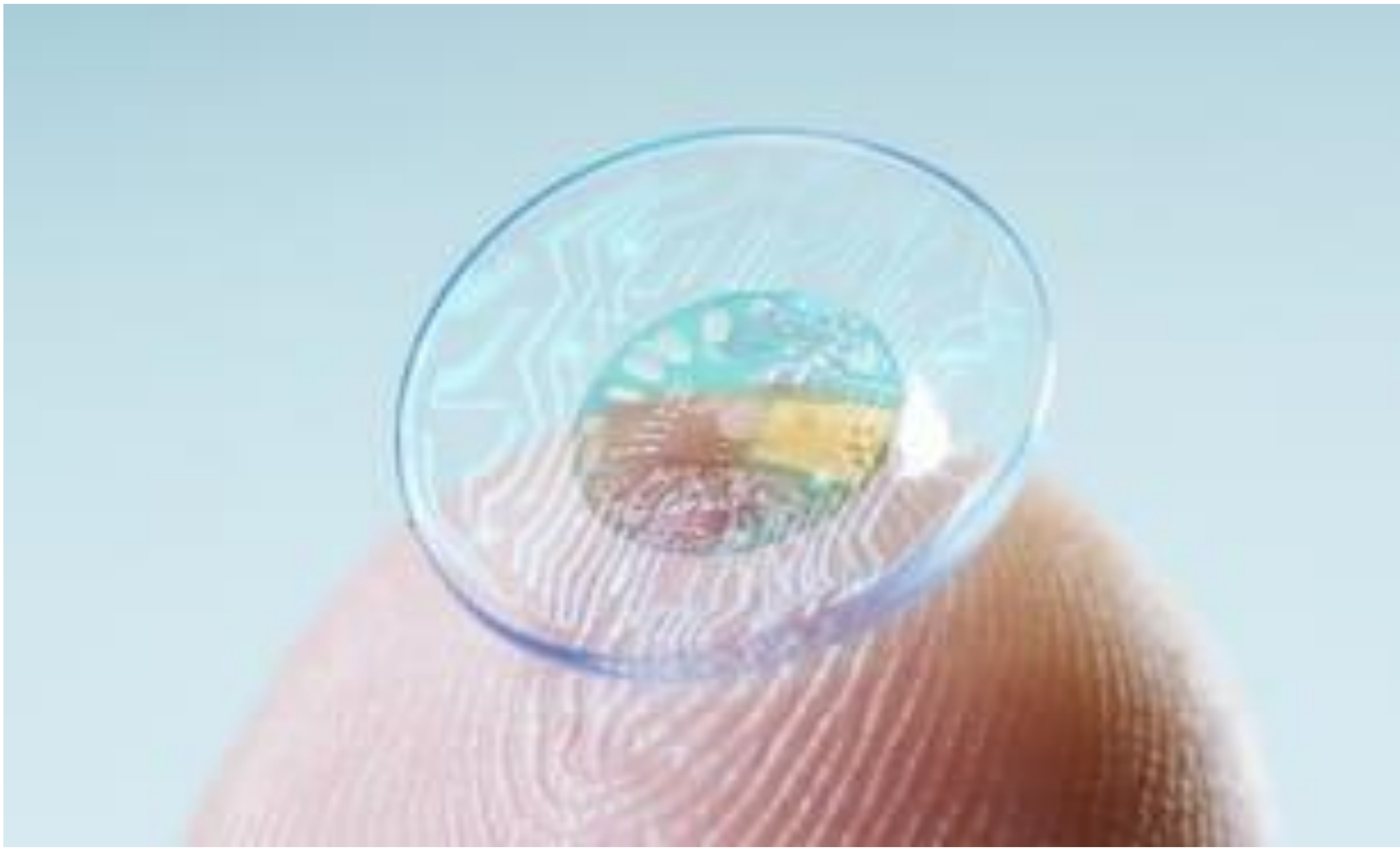


Image: Shutterstock

Does looking through a screen, rather than at one, still count as screen time?

AR contact lenses promise the immersiveness of augmented reality without having to wear a bulky headset or use your smartphone. These thin, curved lenses display digital information on top of your real-world view — and they're placed directly on the surface of your eye.

What Are Augmented Reality (AR) Contact Lenses?

Augmented reality contact lenses are wearable devices that overlay digital information onto a user's real-world view while applied directly to the eye. Like regular contact lenses, they're made out of hydrogels or silicone, but embedded with flexible microbatteries, tiny LED displays, microprocessors, sensors and wireless communication components.

Offering hands-free access to digital content in real-time, the idea is to project images, data or interactive elements directly onto a user's natural line of vision without obstructing it or disrupting social interaction. A user can control its interface with the flick of an eye or holding a prolonged glance thanks to built in eye-tracking technology.

Unlike bulky headsets and glasses that may have awkward and limited angles, smart contact lenses would provide a highly discreet and seamless AR experience with a natural field of view, including peripheral vision. Without the barriers posed by traditional AR devices, this innovation could revolutionize how users interact with digital information, impacting daily activities such as navigation and gaming while transforming workflows across a wide array of sectors, from medical and education to industrial and professional sports.

Do Augmented Reality Contact Lenses Exist?

Technically, yes. Prototypes of AR contact lenses exist, but none of them have made it out of the research lab.

The first prototype was developed by California-based startup Mojo Vision, which debuted the Mojo Lens in 2020. The project broke ground on smart lens technology, including preclinical testing and a live on-eye demonstration in 2022, but was indefinitely canceled the following year due to "significant challenges in raising capital."

Other AR contact lens and smart lens projects have emerged in its wake, many of which are geared toward medical applications. And while each new prototype brings AR contact lenses closer to consumer availability, reaching the mass market will require developers to successfully miniaturize electronics with sufficient battery life and display quality, in addition to undergoing rigorous clinical trials for regulatory clearance that ensures the product is biocompatible and ready for everyday use.

Examples of AR Contact Lenses

As augmented reality and virtual reality software, headsets and smart glasses establish a $40 billion market, stakeholders are eager to take part in the expanding space. So far, tech giants Sony, Google and Samsung have all filed for smart contact lens patents. But it's deep-tech startups that are leading the charge in AR-enabled and smart contact lens innovation. Consider the following projects that are establishing a proof of concept.

Mojo Vision's Mojo Lens

Mojo Vision's smart contacts, the Mojo Lens, was the first AR contact lens prototype. Now defunct, the device featured a 14,000 pixel-per-inch MicroLED display, eye-tracking and computer-vision image sensors and a micro-battery system. Measuring less than 0.5 millimeters in diameter, the smart contacts also included built-in, wireless radio communication antenna and a data-sorting ARM processor worn in a companion neck band device.

Innovega's eMacula system combines smart contact lenses with spectacles. | Video: eMacula

Innovega's eMacula System

Innovega is a smart AR/VR eyewear company developing a dual system that pairs disposable, daily smart contact lenses with high-tech glasses for those with moderate to severe visual impairments. In tandem, the "lens within a lens" picks up the images and media from the sunglasses display and projects them directly onto the eye, allowing a user to simultaneously view digital content transposed over the natural world. Innovega has filed over 80 patents, and is entering Phase III FDA clinical trials for its eMacula smart eyewear system.

InWith Corporation has made the first electronic soft contact lens capable of accessing AR. | Video: CNET

InWith Corporation's Soft Smart Lenses

InWith Corporation has the first claim to creating AR-enabled contact lenses of the soft variety. These lenses feature electronic circuits built directly into the hydrogel that are designed to work with a smartphone. The idea is that anything you can access on your smartphone would be cast directly into a user's line of vision, whether it be augmented or virtual reality. For those with a prescription to enhance sight, this feature would also be able to "tune" a user's vision for a sharper image.

XPANCEO's Smart Contact Lens Series

Dubai-based deep-tech company XPANCEO has developed a series of AR smart contact lenses, showcasing five different prototypes for various use cases. One uses its on-eye display to adjust lighting, contrast and enhance color perception for colorblind users. Another comes with optical verification tools that allows users to tackle digital tasks, such as making payments, transferring funds and gaining access to restricted areas, with intuitive gaze commands. Other features include night vision and zoom capabilities as well as app control.

Watch as Blink Energy's CTO tests their smart lens-powering eyelid patch. | Video: Vadoo AI

Blink Energy's BlinkIT Patch

Blink Energy developed BlinkIT, a device-agnostic patch that sits on the user's eyelid and is designed to wirelessly power and connect AR contact lenses, smart lenses and other smart ocular devices, like eye implants. Although this technology is not an AR-enabled lens itself, it makes the list for addressing one of the major pain points companies and startups are facing in the space — providing sufficient battery life within such a small footprint. External accessories like BlinkIT that accompany a smart lens could be the quickest way to actualizing autonomous ocular devices.

Azalea Vision's ALMA lens controls light exposure for users with light sensitivities. | Video: Andres Vasquez Quintero

Azalea Vision's ALMA Lens

Healthtech startup Azalea Vision developed a smart contact lens that offers a non-surgical option for users suffering from keratoconus, corneal irregularities, presbyopia and light sensitivities. While it's not specifically geared toward AR use, this device contains a microchip, micro battery, configurable light filter and radio frequency antennae and contributes to advances in on-eye electronic wearables.

In partnership with Novartis, Google set out to develop a smart contact lens in 2014 that could measure a user's glucose levels through their tears. Using tiny sensors, the device wirelessly transmitted data to an external source via RFID as a prick-free way for people with diabetes to monitor their blood sugar levels, generating a reading once per second. But the project shutdown in 2018 due to technical hurdles.

Sensimed Triggerfish Contact Lens Sensor

Swiss-based company Sensimed have developed a silicone soft contact lens, the Sensimed Triggerfish, that's designed to provide 24-hour glaucoma monitoring. Although the device doesn't have anything to do with augmented reality, its embedded sensors can track fluctuations in a user's intraocular pressure throughout the day, which may indicate a patient's risk factor for the chronic eye disease. In 2016, it became the first smart contact lens to receive FDA approval.

Challenges Creating AR Contact Lenses

As an emerging technology, AR contact lenses face a number of setbacks.

Working on the Nanoscale

Embedding electronics into a contact lens requires working on an extremely small scale with ultra-miniaturized components. This means that researchers have to figure out a way to embed tiny, wireless sensors and microbatteries into a thin, flexible material without interfering with the user's line of vision or blinking. Some aspects of creating a functioning AR contact lens rely on the entire nanotechnology field to advance and innovations that have yet to be discovered.

Biocompatibility

Any material used in an AR contact lens must be safe for prolonged exposure to the sensitive tissues of the eye. This means rethinking the typical build of electronic components. For example, making microLED displays and sensors without toxic metals and chemicals, batteries without lithium and processors without flame retardants. Figuring out a way to power these devices without overheating, losing connectivity, disturbing the eye's natural moisture and pH levels, triggering an allergic reaction or imposing on the user's line of sight prove to be significant challenges when working within the limited space of a contact lens.

Regulatory Approval

AR contact lenses are considered to be a medical device through the eyes of the FDA. Gaining regulatory clearance requires a product to pass a thorough, multi-step process — including preclinical research, animal testing and three clinical trial phases — that takes several years to complete, as its strict guidelines are designed to protect potential users. While no AR contact lenses have made it through the clinical trial stage, smart contact lenses with embedded electronics *have* achieved regulatory clearances: In 2016, Sensimed's Triggerfish device became the first smart contact lens to receive FDA approval.

Marketability

AR contacts have an obvious appeal to those who are visually impaired and other specified medical use cases, for sports enhancement, entertainment and technical training across sectors; however, a major disadvantage smart contact lenses have in comparison to AR glasses and headsets is that users may not actually be comfortable applying an electronically enhanced lens directly onto their eye. As beneficial as a smart contact lens may be for warehouse employees taking inventory or in-field construction workers, for example, it's unlikely that a company would be able to require its employees to wear AR contact lenses — limiting their viability to a certain degree.

Ethical Dilemmas

AR contact lenses pose several ethical dilemmas related to privacy, consent and information overload. If these devices are built with eye tracking technology, that means data is being collected in an extremely intimate way based on a user's behaviors as they glance around. This information could be used by companies to build a profile in order to generate targeted advertisements based on a user's interests and habits from information that wasn't necessarily gathered in a consensual way. Plus, there's something inherently dystopian about projecting ads directly onto a user's cornea. The advent of AR smart contact lenses also raises concerns about the device being used as a covert surveillance tool — of both the user and those in their line of sight — as well as a hazardous distraction, negatively impacting a person's ability to engage with the real world.

Contact lenses bring 3D holograms to life for augmented reality

A better way to fabricate metasurfaces allows scientists to create contact lenses capable of projecting 3D holographic images.

Scientists have developed contact lenses that project 3D holograms using specialized nanostructures embedded on them, known as metasurfaces. Metamaterials, in general, are engineered materials with properties not found in nature. A metasurface, as the name suggests, is a type of metamaterial simply applied to a surface. These structures are often smaller than the wavelengths of light, enabling them to manipulate electromagnetic waves, such as light and sound, in a unique way.

"[Metasurfaces] manipulate light […] with high precision," explained the *Advanced Science* study's author, Junsuk Rho at the Pohang University of Science and Technology in South Korea.

Why metasurfaces?

Metasurfaces have been useful in areas like biomedicine, speech recognition, and energy harvesting, but integrating them into contact lenses for virtual and augmented reality remains difficult. However, the potential they hold to surpass current technologies in significant ways makes them compelling.

“These augmented reality contact lenses [would] offer several significant advantages over existing technologies,” Rho explained. “Usually, there are gratings, prisms, or mirrors for delivering a virtual image from a display source located near the temple to the retina. At the same time, the light of the real-scene must be free from unwanted diffraction effects. Due to the complexity of these design requirements, the optical system is bulky.

“Because the lenses are worn directly on the eye, they preserve the natural field of view, providing an unparalleled level of immersion without the limitations imposed by external devices, like headsets or glasses.”

Outside of entertainment and gaming, there are boundless applications, from environmental monitoring, identity recognition, diagnosis, and real-time navigation, providing directions and contextual information directly in the user’s field of view.

“In settings, such as healthcare, the lenses could assist medical professionals by overlaying vital information during procedures,” Rho said. “Additionally, the lenses could serve personal health monitoring purposes, displaying real-time biometric data.”

But before any of this can come to fruition, barriers inherent in metasurface production need to be overcome. “First, ensuring the biocompatibility of the materials is critical, as contact lenses interact directly with the eye,” said Rho. “Traditional nanostructure transfer methods [for their production] often do not account for long-term biocompatibility, raising concerns about safety during extended wear.

“Second, maintaining structural stability is difficult due to the flexible and moist nature of contact lenses, which can lead to deformation or damage of the nanostructures. And finally, achieving precise pattern transfer on a flexible substrate like a contact lens is technically challenging.”

Producing metasurfaces for contacts

These hurdles only motivated Rho who has been working in this area since 2008. “I saw a news story about an ‘invisibility cloak’ being realized using metamaterials,” he said. From there, his research has expanded to include reality displays.

He and his team were motivated to overcome challenges around embedding metamaterials into contacts by developing a new production method. Their approach relies on hyaluronic acid, a naturally occurring molecule found throughout the body, particularly in the eyes, joints, and skin.

“We use it as a soft mold that allows for the gentle transfer of complex nanostructures onto the lens surface without compromising the structural integrity of the metasurface,” explained Rho. “It plays a crucial role in both the biocompatibility and functionality of the contact lenses.”

Metasurfaces are usually created using advanced fabrication techniques like photolithography or electron beam exposure. These methods involve coating a surface with a light-sensitive material, exposing it to light or electrons through a mask, and developing the pattern.

After this, additional desired materials, like semiconductors for electronics, are deposited onto the patterned substrate and etched away to form the final nanostructures that are small enough to alter or shape electromagnetic radiation. Once the metasurface is complete, it is transferred from the temporary substrate to the final material, such as a contact lens.

In the current study, the team’s fabrication process involved depositing gold onto a flexible, rubber-like material called polyurethane acrylate, which acts as the first mold for the fabricated surface. This 3D-patterned gold layer is then transferred from this initial mold to a second, hydrated hyaluronic acid film –for its final transfer onto the contact lens — that is then protected with a silicon capping layer.

“The SiO_2 capping layer, situated between the contact lens material and the gold patterns, prevents direct contact with the eye, thereby minimizing any potential risk of adverse effects,” wrote the team in their paper.

The silicon layer also acts as a waveguide that directs electromagnetic waves from one point to another, not only enhancing the lens’ stability, but overall performance.

Static holograms are just the beginning…

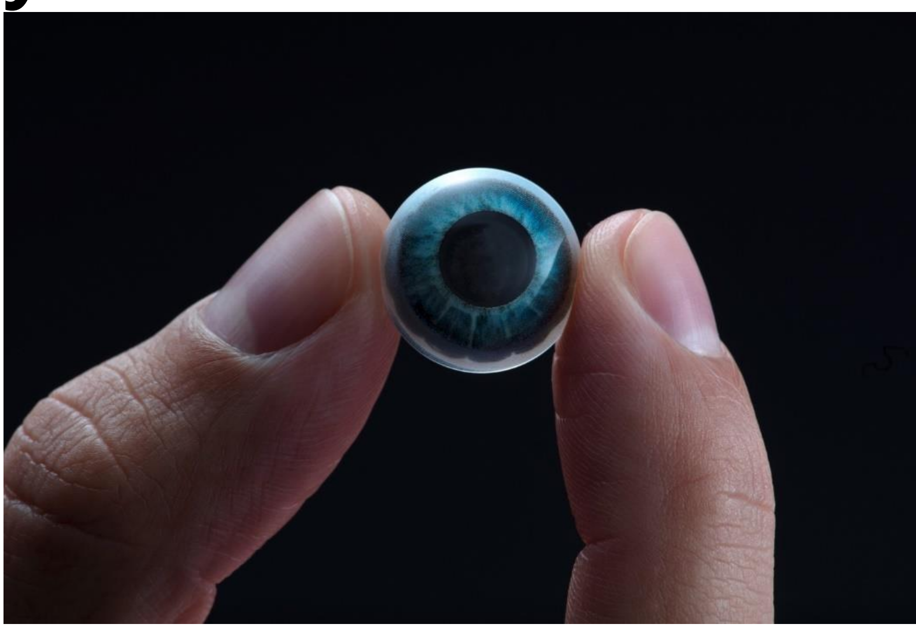
Now comes the fun part: creating holograms using the metasurfaces embedded in the new lenses. When light hits the metasurface — this could be from a controlled light source from a wearable device or perhaps even sunlight — each tiny, carefully crafted component changes the light’s intensity, angle, and direction to create the holographic image that you can see, explained Rho.

In this iteration of the technology, the images are static, but the team has plans to further develop this. Dynamic holographic videos could one day be generated by embedding a metasurface designed to function as a diffuser, and light source such as micro-LED into the contact lens, Rho said.

Before any of this, safety needs to be thoroughly assessed and the technology developed further. “Next steps include extensive live testing to assess the long-term safety and performance of the lenses in real-world conditions,” said Rho. “Additionally, we plan to refine the manufacturing process to ensure scalability and cost-effectiveness for commercial production,” he continued. |Regulatory approvals will also be a critical step, as we will need to demonstrate compliance with safety standards for medical devices.”

Reference: Jun-Ho Jeong, Inkyu Park, Junsuk Rho, et al.,Metasurface-Embedded Contact Lenses for Holographic Light Projection, Advanced Science (2024). DOI: 10.1002/advs.202407045

The Future of Vision: Augmented reality contact lenses will make you bionic



Augmented reality contact lenses have been “around the corner” for years. They’re finally set to arrive. Mojo Vision

Tech for Change

This story is part of Tech for Change: an ongoing series in which we shine a spotlight on positive uses of technology, and showcase how they're helping to make the world a better place.

Today (-ish): Long a dream, smart contacts are here, Tomorrow: Is infrared vision in your future?

Technology is reshaping every aspect of our lives. Once a week in The Future of series, we examine innovations in important fields, from farming to transportation, and what they will mean in the years and decades to come.

A decade ago, Google's ambitions seemed unchecked: The company would design self-piloting cars through Waymo, sponsor moonbases, and even conquer death. One of the company's plans: Smart contact lenses to measure the glucose level of your tears — and perhaps help reduce the damage caused by diabetes. "It's still early days for this technology, but we've completed multiple clinical research studies, which are helping to refine our prototype," wrote Google's Brian Otis and Babak Parviz back in 2014.

Seven years later, the company's ego remains just as inflated, but Verily's smart contact lenses are nowhere to be seen; the side project of Google parent Alphabet was officially abandoned in 2018. Yet smart lenses are finally becoming a reality, thanks to the efforts of countless scientists and engineers. And the future of this intriguing technology is nothing like what you might expect.

- FDA approves augmented reality surgery tool that gives surgeons 'X-ray vision'

Today (-ish): Long a dream, smart contacts are here

There have been many efforts to advance contact lenses, of course. Acuvue sells Oasys with Transitions lenses that automatically darken in sunlight, like tiny sunglasses for your pupils, and researchers have been working for years on smart lenses that zoom on demand, measure chemical levels in your body, and administer drugs (notably antihistamines). But smart ones? They've never really made it to market.

InWith Corp. is about to change that. At CES 2021, the company unveiled a method to place augmented vision display chips into the soft hydrogel contact lenses that millions of people wear daily. Smart contact lenses! In early 2020, the company announced a partnership with Bausch + Lomb, showing flexible electronic circuitry embedded directly into lenses. No, you can't buy 'em yet. But they're clearly almost here — and not just from InWith.

"It's closer than you'd think, but it's not tomorrow," Steve Sinclair, senior vice president of product at Mojo Vision, told me. Mojo's the big competitor to InWith, and has been secretly engineering lenses embedded with an enormous array of proprietary technology, including a nearly invisible Micro LED display under half a millimeter in size (think a grain of sand), tiny inertial sensors such as accelerometers and gyroscopes, a super-efficient image sensor to gauge the world around you, adorably tiny batteries, and more.

PreviousNext
Mojo Vision's contact lenses promise to enhance our vision. Image used with permission by copyright holder
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Mojo Vision's contact lenses promise to enhance our vision. Image used with permission by copyright holder

Like InWith's lenses, Mojo's are "just around the corner," Sinclair told me. About a dozen people in his company have worn the latest prototypes, and a new model this summer promises even more advancements. What can you do with them? Augmented reality applications probably leap to your mind, at least they do for me: Direction overlays that guide you through unfamiliar city streets, information about the people and buildings you pass by, and so on. But the power of a display in your eye is nothing like what you might expect. Sinclair offers different use cases, things that give you your mojo back (hence the name of the company): The text of a big speech, notes for a presentation, a checklist for a major repair project, and so on.

One area that will be important is performance athletics: Today's runners have a world of metrics on their wrists, but who wants to navigate a menu while sprinting at top speed? Imagine the power of biometric data directly in your field of view.

And as for AR? Eh, we'll get there.

Meanwhile, smart lenses hold huge immediate promise for people with low vision — glaucoma, macular degeneration, and so on. Mojo's chips will be able to take in the scene before a person and in real time add edges to buildings, boost the contrast around signs and people, and help those with dim vision navigate the world around them. This could be a game changer — but it's just the beginning.

Tomorrow: Is infrared vision in your future?

Vision is a complex dance between your hardware (meaning your retina, lens, the tiny rods and cones tucked away in there, and so on) and your brain, which interprets the electrical impulses sent from your eyes and translates them into images. Your brain accommodates for flaws in your hardware, to some extent. In the future, it may not have to.

Smart lenses could some day correct for an imperfect lens, or even replace it entirely, fixing those electrical impulses before your brain receives them for interpretation. Smart lenses could also interject different data before your lenses, giving you super-binocular vision, or infrared vision. Heck, researchers have already scienced up supermice with infrared vision. Why not you? The potential powers you could receive with a fresh pair of contacts is limitless, once the tech is perfected.

"We're just on the very precipice of figuring out what some of those things are," Sinclair told me. "The sky's the limit on what we can do with the information and the platform we've built."

"It's like talking to Siri 15.0."

Peer further down the road, into the post-smartphone era, and lenses like this could replace our very eyes. Futurist Gary Bengier, a former Silicon Valley technologist, writer, and philosopher, envisions a world 140 years from now, where displays aren't just worn in contact lenses but are actually part of you, thanks to a chip inserted behind your ear and connected to a corneal implant. In his new book *Unfettered Journey*, he describes how artificial intelligence and mind-machine interfaces combine with retinal implants to essentially build Wikipedia directly into your body:

“He picked out the distinctive towers of an occasional fusion plant. Joe hadn’t taken a long flight since grad school. The scene below him awakened his scientific curiosity. He let the keyword search fill his head, opening the NEST corneal connection, and images and words filled the viewer occupying the corner of his eye.”

Wild stuff, right?

“You basically use this to connect to the cloud, the net, whatever. It’s like talking to Siri 15.0,” Bengier told me recently. In the not-too-distant future, he believes, smarter artificial intelligence will combine with data about where you are and sensors that pick up on your every whim. You’ll be able to simply think about pizza and you’ll see a little map on your cornea showing where you can buy one.

Now *that’s* a vision for vision.

Huge milestone as human subject wears augmented reality contact lens for first time

For the very first time, an AR contact lens was worn on the eye of a human subject. And it has about 30 times the pixel density of an iPhone.

KEY TAKEAWAYS

- For the very first time, an augmented reality (AR) contact lens was worn on the eye of a human subject.
- AR contact lenses pose wildly difficult engineering challenges, the biggest of which is finding a way to provide these tiny devices with power. A company called Mojo Vision has done that.
- One day, we will look back at the years when people walked down the street, necks bent, staring down at little screens in their hands as an absurdly primitive way to interact with information.

Three decades ago, the first group of human subjects interacted with a mixed reality of real and virtual objects. They did this by climbing into a large upper-body exoskeleton, pressing their face to a vision system hanging from the ceiling, and manually performing tasks that required them to engage both physical and simulated objects. They were testing a prototype augmented reality system at Air Force Research Laboratory (AFRL) known as the Virtual Fixtures platform. The hardware filled half a room and cost nearly $1M, but it worked — showing for the first time that AR could boost human performance in real-world tasks.

Last week, an important new milestone was achieved in the field of AR, and it highlights how far the technology has come over the last 30 years: the first authentic test of an augmented reality contact lens. It was conducted in a research lab at Mojo Vision in Saratoga, California. No, it wasn't a crude bench test of oversized hardware with wires dangling. This was a genuine test of an AR contact lens worn directly on the eye of a human subject for the very first time.

A wildly difficult engineering challenge

As someone who has been involved in AR from the early days, I need to highlight the importance of this new milestone. Building a wearable augmented reality contact lens is a wildly difficult engineering challenge. When I say this, people usually ask about the display technology. Sure, the ability to put a high resolution display on a tiny transparent lens is difficult, but it's not the most challenging piece of the puzzle. The harder issue is that this tiny lens, which needs to sit comfortably on the human eye, has to communicate wirelessly with external devices and be fully powered without a physical tether of any kind. That is a daunting task, and yet it is what Mojo Vision achieved in their latest demonstration.

We will look back at the years when people walked down the street, necks bent, staring down at little screens in their hands as an absurdly primitive way to interact with information.

Louis Rosenberg

According to Mojo Vision, the prototype lens includes medical grade micro-batteries. It's unclear what the battery life is for the current prototype, but according to the company, their product goal is power management that enables all-day wear.

Of course, their display technology is impressive too. According to the company, the Mojo Lens has a 14,000 pixel-per-inch MicroLED display with a pixel pitch (the distance between adjacent pixels) of 1.8 microns. For context, an iPhone 13 with a Super Retina XDR Display has 460 pixels per inch resolution. In other words, the Mojo Lens hardware has about 30 times the pixel density of a current iPhone. In addition, these lenses include an ARM processor with a 5GHz radio transmitter, along with an accelerometer, gyroscope, and magnetometer to track eye movements. And all of this sits directly on the human eye.

AR contact lenses are the future

Still, many years of development will be required to get from today's prototypes to mass market consumer products that bring immersive AR capabilities to people around the world. I predict that AR eyewear, first as glasses and then as contacts, will eventually replace the mobile phone as our primary interface with digital content. Further, I believe augmented reality will completely change our relationship with information, transforming digital content from discrete artifacts we selectively access into seamless features of our physical world.

A few years ago, I wrote a futurist piece entitled "Metaverse 2030" that portrays what life will be like when AR contacts become commonplace — a world where mainstream consumers get fitted for new contacts whenever they sign up for a mobile subscription. When that day comes, we will look back at the years when people walked down the street, necks bent, staring down at little screens in their hands as an absurdly primitive way to interact with information. Will this happen in the next decade? Only time will tell, but the achievement from Mojo Vision takes us a large step closer.

Apple is crashing the smart glasses party, but Meta's Orion will be a tough act to follow

Apple is crashing the smart glasses party, but Meta's Orion will be a tough act to follow© Apple

Apple's Vision Products Group, the brilliant minds behind the ultra-deluxe Vision Pro, are reportedly working on several new VR/AR/Mixed reality projects, including a part of smart glasses that may arrive by 2027.

Following this year's Meta Connect event, smart glasses are the talk of the town (in no small part thanks to Meta's Orion frames) and even VR and AR are receiving some notable attention in the build-up to tomorrow's Meta Quest 3S release.

To that end, it's no surprise that Apple would put pedal to metal on its own projects — especially as Meta's holographic smart glasses aren't expected to face a consumer release until we near the end of the decade.

From Vision Pro fumble, to ready to rumble

According to *Bloomberg*'s Mark Gurman, Apple likely has four major projects in the works within its Vision Products Group: a lower-end Vision Pro, a second-generation Vision Pro, camera-touting AirPods, and a pair of high-tech glasses to go up against the Ray-Ban Meta smart glasses.

Sidestepping Apple's new Vision Pro models — which are no doubt destined to fall into the same price-tag punji pit that both the original Vision Pro and Meta Quest Pro fell into — Apple's smart glasses may have the most potential to perform, especially against Meta's smart glasses lineup. Apple will be late to the party on this one, but that's not to say it won't turn heads when entering.

As long as it shows up before Meta CEO Mark Zuckerberg sweeps everyone away to the private Orion after-party, anyway.

Apple: Late to the race, but often in first place

Apple has a long-standing tradition of showing up late to the party yet being credited for its inception — a feat they've managed to repeat ever since the iPod hit store shelves in 2001.

At the time, CEO Steve Jobs claimed that the iPod was a "Quantum leap" for portable MP3 players. If you forgot about the Nomad Jukebox offering the same features with more storage and a lower price tag, anyway.

Still, fittingly, there's no room for the Nomad in the history books, leaving its existence but a roaming memory in the minds of bitter tech fans like myself.

Being first through the door matters little when you have an adoring fanbase like Apple's behind you just waiting for the opportunity to blindly sacrifice their paychecks in lock-step unison at the altar of "different thinking."

This is something Apple may be able to bank on when going toe-to-toe with Meta in the smart glasses realm, especially as the next few generations of smart glasses become more advanced and more expensive, and Apple's history of delivering deluxe falls in their favor.

Outlook

Reportedly targeting a 2027 release, Apple smart glasses still have plenty of time to brew. However, when they do arrive it's unlikely that these will be the glasses to tackle Meta's Orion holographic glasses. Industry insiders claim that Apple's response to those hyper-advanced frames is likely five years off at least, placing them in the same end-of-the-decade release window as Meta.

In the meantime, we expect to see Meta release its third-generation smart glasses next year, the first to feature a heads-up display for visual feedback. These glasses will likely be paired with the company's neural wristband for control, which may find itself repurposed as a smartwatch.

With that in mind, if Apple is seeking to compete with Meta's glasses directly, we'd assume that the company's frames will offer similar features.

We've already seen the Apple Watch make use of gestures like double tap, and the device could be tweaked to capture more gestures in later models to better pair with the visual element of future smart glasses while strengthening the walls of Apple's tightly-knit eco-system.

Scientists Have Decoded the Secret History of the Mysterious 'Tree of Life'

How an iconic genus traveled from a single island to continents across the sea.© Martin Harvey - Getty Images

- The Baobab is one of the strangest-looking trees on Earth, and has been described as an "upside-down tree" and even the "tree of life" due to its nutrient-rich fruit.
- While six of the eight species of baobabs thrive on the island nation of Madagascar, scientists have never been 100 percent sure of their origin, as the trees don't appear in the fossil record.
- After immense genetic study of all extant species, a new study confirms that the 'tree of life' originated in Madagascar, and that one particular species made an incredible dispersal journey to Australia.

For 400 million years, trees have grown and diverged into some 73,000 species worldwide. There's the skyscraping enormity of the coastal redwoods (*Sequoia* *sempervirens*), the mind-boggling diminutive size of the dwarf willow (*Salix herbacea*), and nearly every imaginable size and shape in between. However, arguably the most *perplexing* genus in the plant kingdom is *Adansonia*, also known as the baobab tree.

Consisting of eight species spread across Africa, Madagascar, Asia, and Australia, this genus is usually defined by its chunky trunk and relatively small canopies, which together give it the overall impression of an "upside-down tree." It's also known as the "tree of life" for its ability to product nutrient dense fruit in the dry season.

This species of tree—found in dozens of African countries alone and first described by ancient Egyptians—is the subject of many tales and local folklore, and its prominence in human culture spurred a husband-and-wife research team to uncover the 21 million-year-long journey of this tree through its genetics. The results of the research were published in the journal *Nature* earlier this week.

"This project uncovered patterns of baobab speciation in Madagascar followed by the astonishing long-distance dispersal of two species, one to Africa and another to Australia," Queen Mary University of London's Andrew Leitch, a co-author on the study, said in a press statement. His wife, Ilia Leitch, a fellow co-author and expert at the Royal Botanic Gardens Kew, added that "this work has uncovered new insights into the patterns of speciation in baobabs and shows how climate change has influenced baobab distribution and speciation patterns over millions of years."

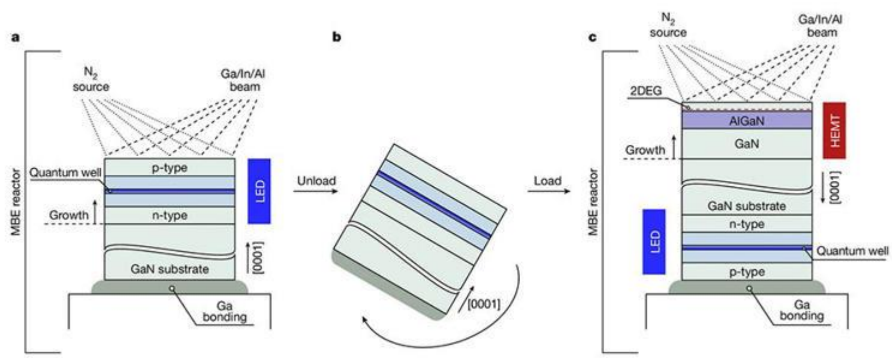
Apart from their almost otherworldly stature, baobabs have another strange attribute—their distribution. While most baobabs reside in Africa, and especially in the island nation of Madagascar, one species of a baobab (*Adansonia gregorii*) sprouts on the unlikely continent of Australia.

Andrew and Ilia Leitch, along with the rest of the research team, analyzed the genomes of the eight extant *Adansonia* species, including everything from the absolutely gargantuan *Adansonia grandidieri* to the Australia-based *A. gregorii*. Because *Adansonia* has no fossil record, scientists have been unsure of its place of origin, but this new study confidently states that the baobab evolved on what is now Madagascar some 21 million years ago.

Of course, this leads to another question: how did the tree somehow wind-up in Africa—and even more perplexingly, Australia, which is roughly 5,500 miles away? After all, the arrival of the baobab tree occurred *after* the break up of Gondwana, a supercontinent that contained two-thirds of today's landmass. The researchers theorize that the tree must've accomplished a long-distance dispersal event to the Land Down Under, which can be seen via evidence of a genetic bottleneck in the *A. gregorii* species.

After analyzing these baobabs, the researchers are also calling for stronger protections of these trees across the board and even theorize that the species *A. suarezensis* in northern Madagascar could even go extinct by 2080. While baobabs have inspired humans for millennia, it's now up to us to make sure they survive and inspire many more generations in the future.

Only 'limited by your imagination': Gallium Nitride breakthrough could make LED displays more affordable and convert your smartphone screen into an antenna



Only 'limited by your imagination': Gallium Nitride breakthrough could make LED displays more affordable and convert your smartphone screen into an antenna© Nature

Researchers at Cornell University, in collaboration with the Polish Academy of Sciences, have made a major breakthrough in semiconductor technology by developing the first-ever dual-sided chip - referred to as a "dualtronic" chip - that integrates both photonic and electronic devices on a single Gallium Nitride (GaN) wafer.

This innovation could shrink device sizes, improve energy efficiency, and reduce manufacturing costs.

The GaN wafer’s unique crystal structure is key to its dual functionality. Each side of the wafer has different properties, similar to how the poles of a magnet differ. The team utilized the metal-polar (Ga-polar) side to create light-emitting diodes (LEDs) and the nitrogen-polar (N-polar) side to construct high-electron mobility transistors (HEMTs). By doing so, they were able to achieve a configuration where the HEMT on one side powers the LED on the other - an accomplishment never before realized in any semiconductor material.

Limited only by the imagination

The research, led by Cornell professors Debdeep Jena and Huili Grace Xing, along with co-lead authors Len van Deurzen and Eungkyun Kim, has been published in the *Nature* journal.

"To our knowledge, nobody has made active devices on both sides, not even for silicon," noted co-lead author Len van Deurzen, emphasizing how this feat was possible only because of GaN's polarity-dependent properties. Traditional silicon wafers are cubic, making both sides nearly identical, which prevents such a design.

According to the researchers, this dualtronic approach could have immediate applications in making microLED displays more affordable and energy-efficient. By integrating photonic and electronic functions into a single chip, fewer components would be needed, leading to lower production costs and a smaller device footprint. This advancement could significantly impact display manufacturing, potentially making LED displays cheaper and more compact.

The technology’s potential goes even further. With the ability to use the same wafer for different functions, dualtronics could enable smartphone screens to be repurposed as antennas, supporting wireless communications directly through the display. The polarization properties of GaN and the dualtronic chip’s multifunctionality could transform not only displays but also radio frequency devices, lasers, and future 5G/6G technologies.

“A good analogy is the iPhone,” explained Debdeep Jena. “It is, of course, a phone, but it is so many other things. It’s a calculator, it’s a map, it lets you check the internet. So there’s a bit of a convergence aspect of it. I would say our first demonstration of ‘dualtronics’ in this paper is convergence of maybe two or three functionalities, but really it’s bigger than that.”

This breakthrough could reshape how semiconductor devices are designed and utilized. By eliminating the need for separate chips to handle different functions, dualtronics promises to optimize both performance and resource utilization across a variety of technologies. As the researchers point out, this development marks a significant step forward, and the potential applications are "limited only by the imagination."

Microsoft Co-Founder Bill Gates Says Everyone In Future Will Have A 'Utilitarian AI Agent' That Will Help You At Work

Microsoft co–founder Bill Gates has shared his insights on the future of workplace efficiency, emphasizing the transformative role of AI agents. In a conversation with Reid Hoffman and Aria Finger during Wednesday's episode of "Possible" podcast, Gates highlighted that AI will drastically change task execution.

What Happened

Gates elaborated on AI's potential to handle complex tasks, particularly in white-collar sectors, surpassing initial expectations. He noted the surprising sequence in which AI has affected job types, with the automation of white-collar tasks preceding that of blue-collar ones. Gates foresees AI robots performing tasks at construction sites and hotels within a decade.

Reflecting on his original vision of a PC on every desk, Gates predicted that AI would extend this concept. He envisions natural language becoming the primary programming language, enabling everyone to have a coding assistant. This shift will allow for more efficient data navigation and business operations without needing custom software.

AI’s Potential

Gates also mentioned the potential for AI to streamline software applications, suggesting that many current applications could be consolidated into comprehensive systems.

“You know we’ll all have an agent that is a utilitarian help you get things done…your agent can figure out okay which parts of that are important enough to to take your time to understand,” he said.

Why It Matters

The conversation aligns with ongoing discussions about AI’s impact on the workforce. In a recent podcast, Gates and Sam Altman, CEO of OpenAI, explored AI’s role in technological advancement, particularly in the workforce. Studies indicate that 37% of companies have already replaced staff with AI, with 44% predicting AI-driven layoffs in 2024.

Predictions for the Future

Furthermore, Hoffman has predicted the end of the traditional 9-to-5 job by 2034, attributing this shift to AI and the gig economy. This transformation offers increased productivity and flexibility but raises concerns about stable employment.

Additionally, billionaire Vinod Khosla has predicted that AI will replace most human jobs over the next 25 years. He suggests that AI could perform 80% of all jobs, including those of primary care doctors, salespeople, and engineers, more efficiently than humans.

Disclaimer: This content was partially produced with the help of Benzinga Neuro and was reviewed and published by Benzinga editors.

New memory chip controlled by light and magnets could one day make AI computing less power-hungry

New memory chip controlled by light and magnets could one day make AI computing less power-hungry© Brian Long, UCSB

Researchers have developed a new type of memory cell that can both store information and do high-speed, high-efficiency calculations.

The memory cell enables users to run high-speed computations inside the memory array, researchers reported Oct. 23 in the journal Nature Photonics. The faster processing speeds and low energy consumption could help scale up data centers for artificial intelligence (AI) systems.

"There's a lot of power and a lot of energy being put into scaling up data centers or computing farms that have thousands of GPUs [graphics processing units] that are running simultaneously," study co-author Nathan Youngblood, an electrical and computer engineer at the University of Pittsburgh, told Live Science. "And the solution hasn't necessarily been to make things more efficient. It's just been to buy more and more GPUs and spend more and more power. So if optics can address some of the same problems and do it more efficiently and faster, that would hopefully result in reduced power consumption and higher throughput machine learning systems."

The new cell uses magnetic fields to direct an incoming light signal either clockwise or counterclockwise through a ring-shaped resonator, a component that intensifies light of certain wavelengths, and into one of two output ports. Depending on the intensity of light at each of the output ports, the memory cell can encode a number between zero and one, or between zero and minus one. Unlike traditional memory cells, which only encode values of zero or one in one bit of information, the new cell can encode several non-integer values, allowing it to store up to 3.5 bits per cell.

Related: New 'petabit-scale' optical disc can store as much information as 15,000 DVDs

Those counterclockwise and clockwise light signals are akin to " two runners on a track that are running in opposite directions around the track, and the wind is always in the face of one and to the back of the other. One can go faster than the other," Youngblood said.. "You're comparing the speed at which those two runners are running around the track, and that allows you to basically code both positive and negative numbers."

The numbers that result from this race around the ring resonator could be used to either strengthen or weaken connections between nodes in artificial neural networks, which are machine learning algorithms that process data in ways similar to the human brain. That could help the neural network identify objects in an image, for example, Youngblood said.

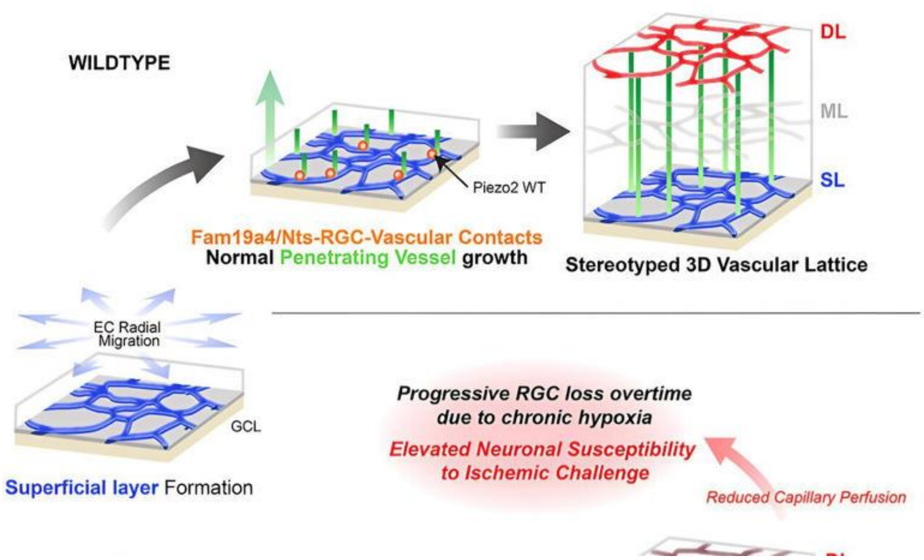
Unlike traditional computers, which make calculations in a central processing unit then send results to memory, the new memory cells perform high-speed computations inside the memory array itself. In-memory computing is particularly useful for applications like artificial intelligence that need to process a lot of data very quickly, Youngblood said.

The researchers also demonstrated the endurance of the magneto-optic cells. They ran more than 2 billion write and erase cycles on the cells without observing any degradation in performance, which is a 1,000-fold improvement over past photonic memory technologies, the researchers wrote.Typical flash drives are limited to between 10,000 and 100,000 write and erase cycles, Youngblood said.

In the future, Youngblood and his colleagues hope to put multiple cells onto a computer chip and try more advanced computations.

Eventually, this technology could help mitigate the amount of power needed to run artificial intelligence systems, Youngblood said.

How neurons build a 3D vascular structure to keep the retina healthy



Graphical abstract. Credit: Cell (2024). DOI: 10.1016/j.cell.2024.04.010© Provided by Medical Xpress

Scientists have known for years that a lattice of blood vessels nourishes cells in the retina that allow us to see—but it's been a mystery how the intricate structure is created.

Now, researchers at UC San Francisco have found a new type of neuron that guides its formation.

The discovery, described in *Cell*, could one day lead to new therapies for diseases that are related to impaired blood flow in the eyes and brain.

"This is the first time anyone has seen retinal neurons using direct contact with blood vessels as a way of guiding them to form these precise 3D lattices," said Xin Duan, Ph.D., an associate professor of ophthalmology and senior author of the study. "This brings us closer to the possibility of repairing them when they're damaged or rerouting them when they weren't built right in the first place."

A protein that senses the presence of nearby cells

The researchers worked with newborn mice, whose eyes still need several weeks to develop fully. Kenichi Toma, Ph.D., labeled the retinal neurons closest to the blood vessels with a protein that glows green under ultraviolet light so he could observe the lattice as it was forming.

The team then identified a subset of neurons, called perivascular neurons, which contact and then surround growing blood vessels, directing them to form the lattice. These perivascular neurons produce a protein called PIEZO2 that enables them to sense when they are touching another cell.

Perivascular neurons in mice that were unable to produce PIEZO2 could not maintain contact with blood vessels, and they grew in a tangled, disorganized way that disrupted blood flow.

Starved for oxygen, the surrounding nerve cells degraded, and the mutant mice were more vulnerable to stroke-like injuries.

Duan found that these neurons guide the formation of a similar network of blood vessels in the cerebellum, a part of the brain that is involved in coordination, language, and sense perception.

"The fact that we see this same pattern repeated in the brain means that damage to this lattice might have a role in multiple neurodegenerative diseases," Toma said.

The team collaborated with developmental biologist Arnold Kriegstein, MD, Ph.D., to confirm that perivascular retinal neurons also exist in humans.

3D view shows how the lattice forms

Most research to date on the connection between the vascular and nervous systems has been limited by technology that only allows scientists to take two-dimensional pictures.

But Duan and Toma benefited from a new technique, using multiphoton microscopy, that Tyson Kim, MD, Ph.D., an assistant professor of ophthalmology, had developed to make 3D images of retinal blood networks without disturbing the eye.

Kim helped Toma create revolving movies that captured the lattice from every angle and showed how it broke down in the absence of PIEZO2.

"We had been wanting to collaborate for some time, and this was the perfect opportunity," Kim said. "It was really a confluence of what we're each passionate about."

A new way to protect neurons

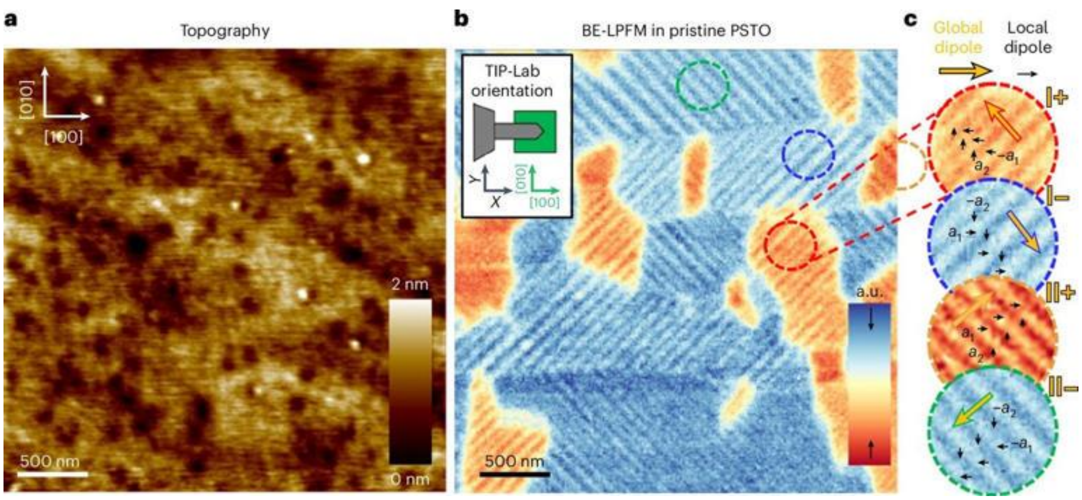
The discoveries could inspire new ways of treating neurodegenerative diseases by ensuring that neurons, which demand a lot of energy, maintain a healthy blood supply.

"There are lots of people trying to understand the ways we can grow neurons," Duan said. "But how in the world do we grow the intricate networks of blood vessels required to support them? That's the question we're trying to answer."

More information: Kenichi Toma et al, Perivascular neurons instruct 3D vascular lattice formation via neurovascular contact, *Cell* (2024). DOI: 10.1016/j.cell.2024.04.010

Provided by University of California, San Francisco

Nanoscale method boosts materials for advanced memory storage

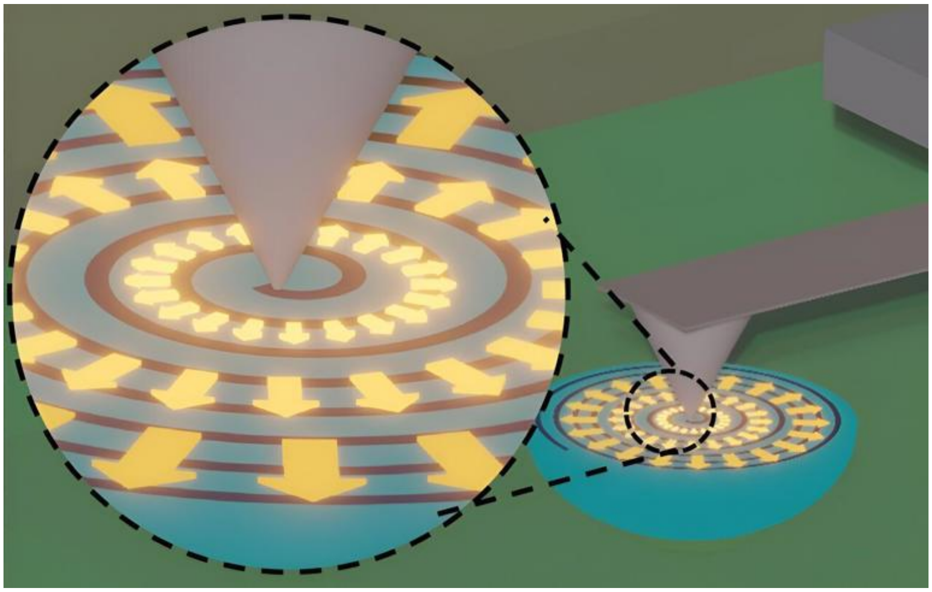


Pristine super-domain distribution in PSTO. Credit: Nature Nanotechnology (2024). DOI: 10.1038/s41565-024-01792-1

Next-generation technologies, such as leading-edge memory storage solutions and brain-inspired neuromorphic computing systems, could touch nearly every aspect of our lives—from the gadgets we use daily to the solutions for major global challenges. These advances rely on specialized materials, including ferroelectrics—materials with switchable electric properties that enhance performance and energy efficiency.

A research team led by scientists at the Department of Energy's Oak Ridge National Laboratory has developed a novel technique for creating precise atomic arrangements in ferroelectrics, establishing a robust framework for advancing powerful new technologies. The paper is published in the journal *Nature Nanotechnology*.

"Local modification of the atoms and electric dipoles that form these materials is crucial for new information storage, alternative computation methodologies or devices that convert signals at high frequencies," said ORNL's Marti Checa, the project's lead researcher. "Our approach fosters innovations by facilitating the on-demand rearrangement of atomic orientations into specific configurations known as topological polarization structures that may not naturally occur."



ORNL-led research demonstrated how an electric stylus can precisely pattern and measure the behavior of ferroelectric materials at the nanoscale, enabling scientists to create, understand and control the unique properties of promising new materials. Credit: Marti Checa/ORNL, U.S. Dept. of Energy

In this context, polarization refers to the orientation of small, internal permanent electric fields in the material that are known as ferroelectric dipoles.

To create complex structures that can be activated as needed, the team's technique uses an electric stylus that functions like a superfine pencil. The stylus can effortlessly alter electric dipoles in ferroelectrics by orienting them in selected directions, much like how children create images on magnetic drawing boards.

Just as a city's layout shapes the way people navigate it, designed topological structures impart distinctive properties to materials. The stylus presents exciting opportunities for creating materials with tailored characteristics ideal for low-power nanoelectronics and the high-speed broadband communications essential for the 6G era.

Transitioning from the 5G standard to the sixth generation of mobile communication technology will involve significant advances and transformations in the design and usage of communication networks. Broadband and computing technologies are intricately linked, each enhancing the performance of the other. Therefore, innovative materials will play a crucial role in broadening the possibilities for computing.

Upcoming nanoelectronic advances

Today's classical computers communicate in a straightforward language of "yes" and "no," represented by ones and zeros. This binary system relies on the flow of electricity through tiny circuits. However, this dual-choice framework is limiting and energy intensive because of the demands of writing and reading data.

By contrast, topological polarization structures can rapidly and effectively alter their polarization states, providing high stability with low energy consumption for switching. This swift change in polarization enhances the value of ferroelectrics, improving speed, efficiency and versatility across various devices. Furthermore, they allow for data retention without power, paving the way for the development of high-density, energy-efficient computing systems.

Scientists are exploring materials that can process information faster, as required by 6G-era broadband communications. These structures can also be exploited in devices that operate at high frequencies, thanks to intrinsic sub-terahertz resonances, which are natural oscillations or vibrations within a material or system that occur at frequencies below one terahertz—one trillion hertz.

Such progress could significantly enhance the processing power and efficiency of future computing systems, enabling them to solve more complex problems and perform tasks with greater adaptability and speed—capabilities that classical computers struggle to achieve.

Finally, these structures allow for the precise control of electronic and optical properties and thus could be used for tunable optoelectronic devices. A combination of unique electrical, mechanical and thermal properties makes ferroelectrics highly suitable for neuromorphic computing and other new technologies.

Swift polarization shifts, superdomain dynamics

The ORNL-led research unveiled how an advanced ferroelectric ceramic material commonly known as PSTO switches its polarization in a multistep process, guided by the electrical stylus. PSTO, or lead strontium titanate, is elementally composed of lead, strontium, titanium and oxygen.

A concept called the trailing field is commonly used to explain why ferroelectrics reorient their tiny electric dipoles—small positive and negative charges—in the plane of the material in response to an electric field moving along the surface.

However, the research team proposed as an alternative the existence of an intermediate out-of-plane state to describe the phase that occurs while the material is transitioning from one polarization state to another. This phase is a brief shift in polarization direction that occurs when the vertical part of an electric field momentarily orients the electric dipoles out of the plane of the surface when polarization changes in a thin layer of ferroelectric material.

The scientists' insight about the intermediate out-of-plane state has enabled the precise, on-demand manipulation of superdomain structures. Superdomain structures are large-scale patterns of tiny regions within ferroelectric materials such as PSTO, each with a different alignment of electric dipoles. Superdomain structures are important because they affect how well the materials perform in various applications by influencing their overall behavior and properties.

This study also demonstrated the ability to examine the delicate balance between elastic and electrostatic energy. Ferroelectrics have both mechanical (elastic) and electrical (electrostatic) energy interactions, which influence each other. For example, changing the shape of a ferroelectric can affect its electrical properties, and vice versa. Studying this balance helps researchers understand how to control the material's behavior more precisely.

Additionally, the researchers explored the accommodation of frustrated superboundaries—areas where different regions with dissimilar electric properties meet in the material. These boundaries cannot easily align or adjust to minimize energy expenditure because of conflicting forces or constraints and thus rarely occur in nature. However, the on-demand creation of new topological polarization structures enables researchers to stabilize these frustrated superboundaries and study their singular properties.

Prediction, control with nanoscale accuracy

By integrating structural and functional data about the ferroelectric material gathered from correlative microscopy techniques, the researchers created detailed phase-field models that predict how the material will behave under various conditions. This capability facilitates understanding and optimizing the stability and polarization of the material.

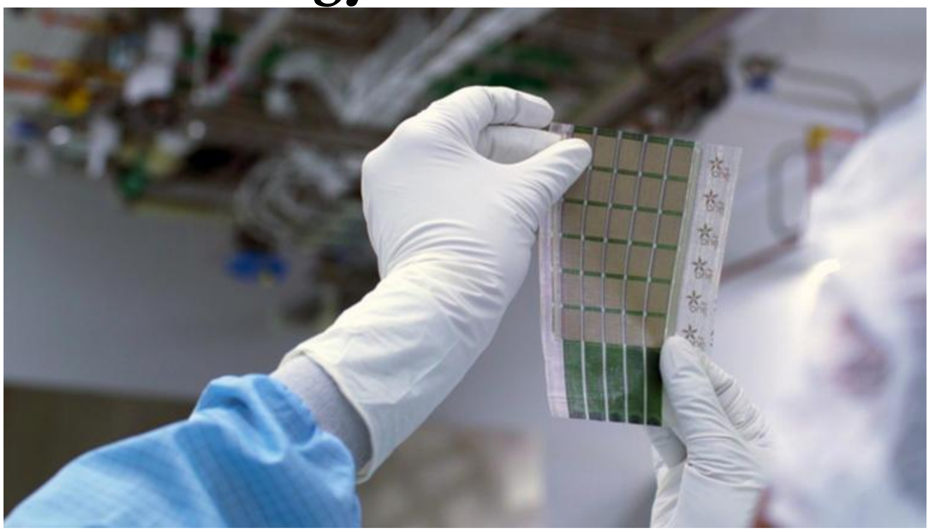
"Our project has developed advanced methods to precisely pattern materials at the nanoscale," Checa said.

"By combining specially designed electric stylus tip movements with automated experimental setups, we've demonstrated the ability to explore new and complex states of ferroelectric materials that weren't accessible before. A key aspect of this accomplishment is that it allows for a better understanding and control of these materials' unique properties."

More information: Marti Checa et al, On-demand nanoengineering of in-plane ferroelectric topologies, *Nature Nanotechnology* (2024). DOI: 10.1038/s41565-024-01792-1

Provided by Oak Ridge National Laboratory

Light trick helps super-thin solar panels absorb energy 10,000 times better



Light trick helps super-thin solar panels absorb energy 10,000 times better

Researchers have developed a new method for light and matter interaction, paving the way for the production of ultrathin silicon solar cells.

The University of California, Irvine (UC Irvine) team's study is based on previous work related to the transformation of pure silicon from an indirect bandgap semiconductor to a direct bandgap one by altering its interaction with light.

They transformed light interactions with silicon by trapping photons, enhancing absorption by 10,000 times, and improving device performance without changing the material's chemistry.

The team highlights that the discovery may contribute to the expansion of energy-converting technology into a wide range of uses, such as onboard car and device charging and thermoelectric apparel.

Innovative light manipulation

In the new study, researchers used a new method that involved changing the light instead of the material.

They trapped photons on very small bumps near the silicon, giving the light new properties that enhanced its interaction with the material. By modifying the surface of the silicon, they greatly improved how much light is absorbed and significantly boosted the devices' performance.

Photons lack the momentum needed to trigger indirect optical transitions in semiconductors like silicon, which means they rely on lattice phonons to maintain momentum. This characteristic makes silicon less desirable than direct bandgap semiconductors for many optoelectronic applications.

As an indirect bandgap semiconductor, silicon's limited optical properties hinder advancements in solar energy conversion and optoelectronics. This is a significant drawback, given that silicon is the second-most abundant element in Earth's crust and serves as the foundation for the global computer and electronics industries.

"Photons carry energy but almost no momentum, but if we change this narrative explained in textbooks and somehow give photons momentum, we can excite electrons without needing additional particles," said Eric Potma, professor of chemistry at UC Irvine and co-author of the study, in a statement.

This simplifies the interaction to just two particles: a photon and an electron, akin to what happens in direct bandgap semiconductors. This approach enhances light absorption by a factor of 10,000, fundamentally changing how light and matter interact without altering the material's chemistry.

Transforming energy conversion

The new phenomenon fundamentally alters the interaction between light and matter. According to researchers, traditionally, textbooks describe vertical optical transitions, where a material absorbs light, causing the photon to change only the electron's energy state.

However, momentum-enhanced photons can modify both the energy and momentum states of electrons, revealing new transition pathways previously unconsidered.

“Figuratively speaking, we can ‘tilt the textbook,’ as these photons enable diagonal transitions. This dramatically impacts a material’s ability to absorb or emit light,” said Ara Apkarian, distinguished professor emeritus of chemistry at UC Irvine and co-author of the study.

The researchers highlight that this development presents an opportunity to leverage recent advancements in semiconductor fabrication techniques at the sub-1.5-nanometer scale, which could significantly impact photo-sensing and light-energy conversion technologies.

With the increasing effects of climate change, transitioning from fossil fuels to renewable energy has become more urgent. Solar energy plays a crucial role in this shift, but current commercial solar cells are inadequate.

Silicon’s limited ability to absorb light necessitates thick layers—almost 200 micrometers of pure crystalline material—to capture sunlight effectively. This not only raises production costs but also reduces efficiency due to increased charge carrier recombination.

According to researchers, the thin-film solar cells made more feasible by this research are widely regarded as a solution to these issues.

The details of the team’s research were published in the journal *ACS Nano*.

'A mobile phone as thin as a credit card': How massless batteries, similar to the human skeleton, could give rise to the world's strongest power cell and change the future of our society forever

Researchers at Chalmers University of Technology in Sweden have made significant strides in developing a structural battery that could drastically reduce the weight and energy consumption of vehicles and electronic devices.

The structural battery, made from a carbon fiber composite, functions as both a power source and a load-bearing component, making it ideal for a range of purposes. "We have succeeded in creating a battery made of carbon fiber composite that is as stiff as aluminum and energy-dense enough to be used commercially. Just like a human skeleton, the battery has several functions at the same time," said Richa Chaudhary, lead author of a paper recently published in *Advanced Materials*.

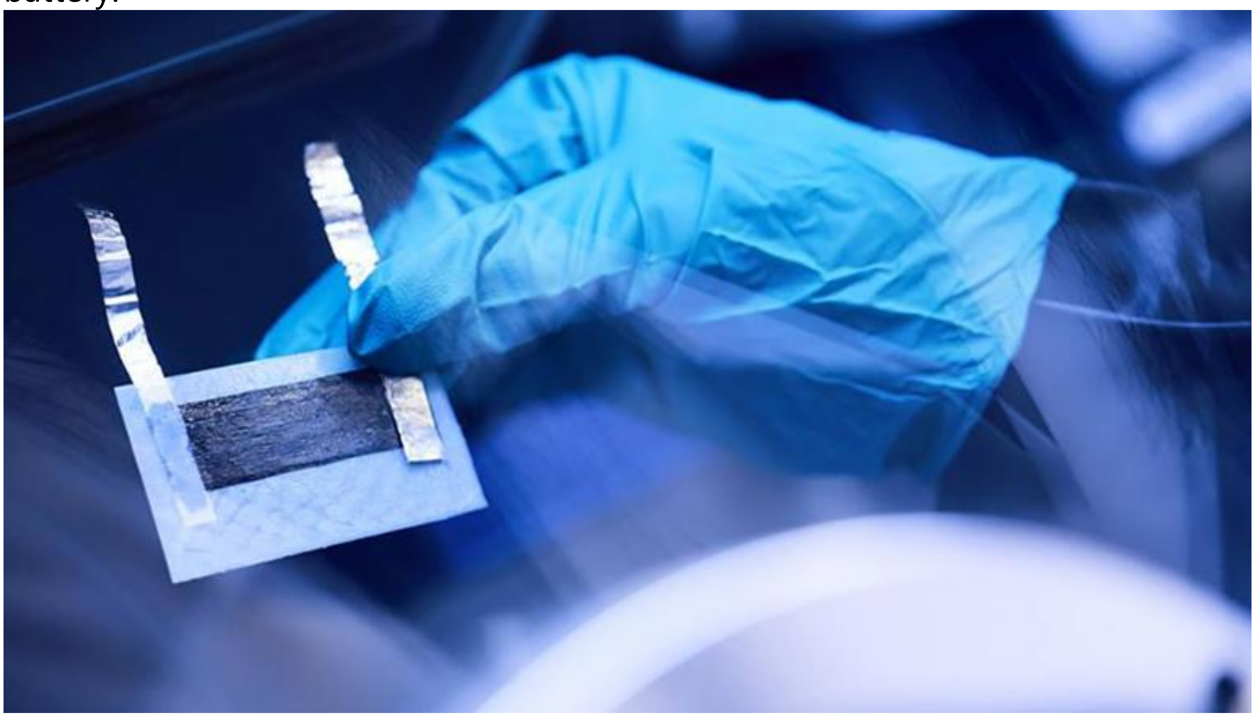
The battery offers an energy density of 30 watt-hours per kilogram (Wh/kg), which is lower than standard lithium-ion batteries but allows for a significant reduction in overall weight.

A huge boost for electric cars

Professor Leif Asp, who leads the research, explained that electric cars using this battery could see a huge boost in driving range. "Investing in light and energy-efficient vehicles is a matter of course if we are to economize on energy and think about future generations," said Asp. "We have made calculations on electric cars that show they could drive for up to 70 percent longer than today if they had competitive structural batteries."

The structural battery also has improved stiffness, now reaching 70 gigapascals (GPa), allowing it to carry loads as effectively as aluminum while being much lighter. Asp stated, "In terms of multifunctional properties, the new battery is twice as good as its predecessor – and actually the best ever made in the world."

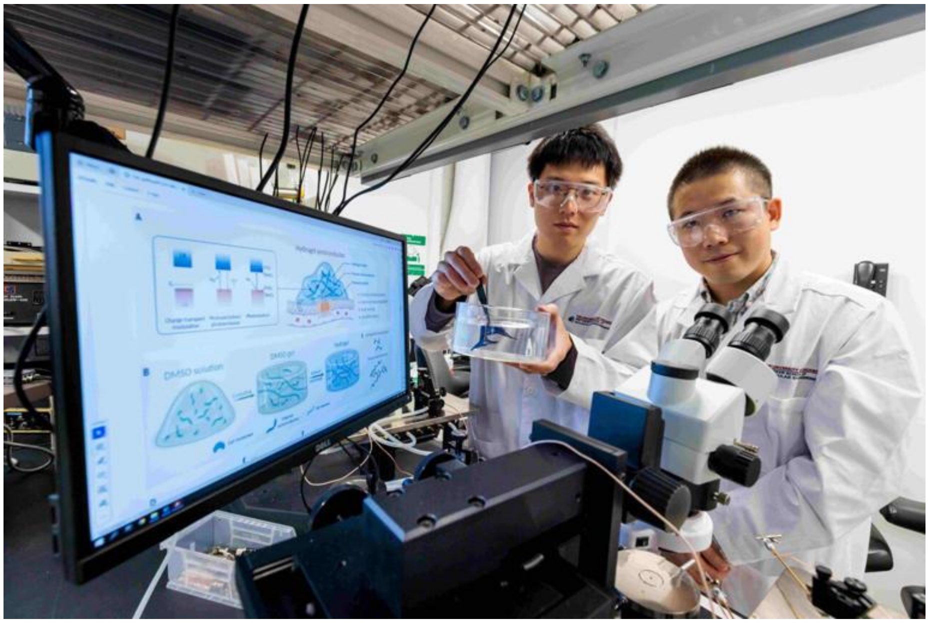
Although the technology is still under development, Sinonus AB, a spin-off from Chalmers Ventures, is working to bring this innovation to the market. Asp envisions that lightweight laptops, mobile phones, and electric vehicle components will be among the first products to benefit from the structural battery.



New hydrogel semiconductor could lead to better tissue-interfaced bioelectronics

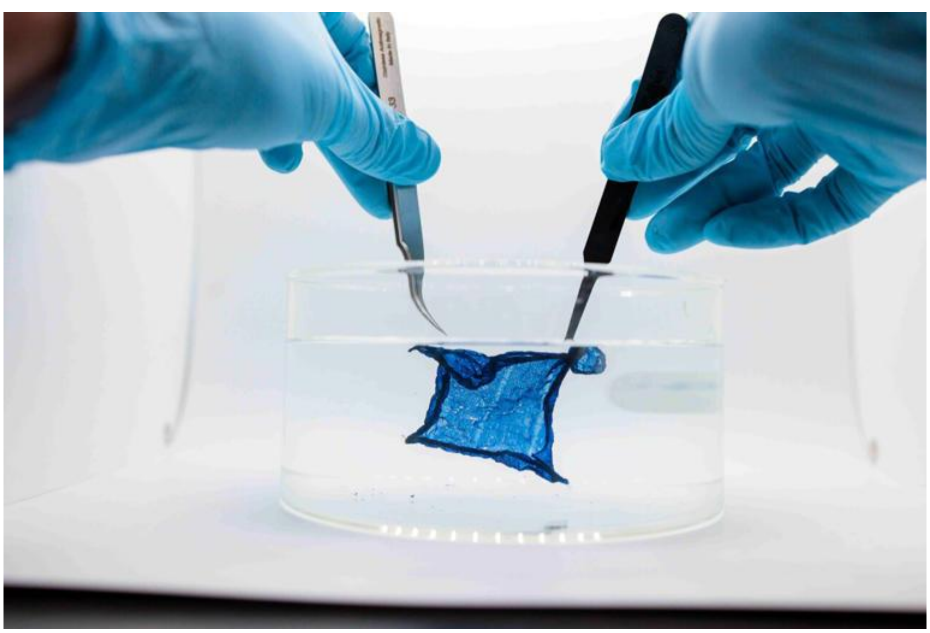
Researchers in the lab of UChicago Pritzker School of Molecular Engineering Asst. Prof. Sihong Wang have developed a hydrogel that retains the semiconductive ability needed to transmit information between living tissue and machine, which can be used both in implantable medical devices and non-surgical applications. Credit: UChicago Pritzker School of Molecular Engineering / John Zich

The ideal material for interfacing electronics with living tissue is soft, stretchable, and just as water-loving as the tissue itself—in short, a hydrogel. Semiconductors, the key materials for bioelectronics such as pacemakers, biosensors, and drug delivery devices, on the other hand, are rigid, brittle, and water-hating, impossible to dissolve in the way hydrogels have traditionally been built.



UChicago Pritzker School of Molecular Engineering Asst. Prof. Sihong Wang (right) and Ph.D. student Yahao Dai, first author of the new paper, with the newly developed hydrogel semiconductor. Credit: UChicago Pritzker School of Molecular Engineering / John Zich

A paper published today in *Science* from the UChicago Pritzker School of Molecular Engineering (PME) has solved this challenge that has long stymied researchers, reimagining the process of creating hydrogels to build a powerful semiconductor in hydrogel form. Led by Asst. Prof. Sihong Wang's research group, the result is a bluish gel that flutters like a sea jelly in water but retains the immense semiconductive ability needed to transmit information between living tissue and machine.



Researchers in the lab of UChicago Pritzker School of Molecular Engineering Asst. Prof. Sihong Wang have developed a hydrogel that retains the semiconductive ability needed to transmit information between living tissue and machine, which can be used both in implantable medical devices and non-surgical applications. Credit: UChicago Pritzker School of Molecular Engineering / John Zich

The material demonstrated tissue-level moduli as soft as 81 kPa, stretchability of 150% strain, and charge-carrier mobility up to 1.4 $cm^2 V^{-1} s^{-1}$. This means their material—both semiconductor and hydrogel at the same time—ticks all the boxes for an ideal bioelectronic interface.

"When making implantable bioelectronic devices, one challenge you must address is to make a device with tissue-like mechanical properties," said Yahao Dai, the first author of the new paper. "That way, when it gets directly interfaced with the tissue, they can deform together and also form a very intimate bio-interface."

Although the paper mainly focused on the challenges facing implanted medical devices such as biochemical sensors and pacemakers, Dai said the material also has many potential non-surgical applications, like better readings off the skin or improved care for wounds.

"It has very soft mechanical properties and a large degree of hydration similar to living tissue," said UChicago PME Asst. Prof. Sihong Wang. "Hydrogel is also very porous, so it allows the efficient diffusion transport of different kinds of nutrition and chemicals. All these traits combine to make hydrogel probably the most useful material for tissue engineering and drug delivery."

'Let's change our perspective'

The typical way of making a hydrogel is to take a material, dissolve it in water, and add the gelation chemicals to puff the new liquid into a gel form. Some materials simply dissolve in water, others require researchers to tinker and chemically modify the process, but the core mechanism is the same: No water, no hydrogel.

Semiconductors, however, don't normally dissolve in water. Rather than find new, time-consuming means of trying to force the process, the UChicago PME team re-examined the question.

"We started to think, 'Okay, let's change our perspective,' and we came up with a solvent exchange process," Dai said.

Instead of dissolving the semiconductors in water, they dissolved them in an organic solvent that is miscible with water. They then prepared a gel from the dissolved semiconductors and hydrogel precursors. Their gel initially was an organogel, not a hydrogel.

"To eventually turn it into a hydrogel, we then immersed the whole material system into the water to let the organic solvent dissolve out and let the water come in," Dai said.

An important benefit of such a solvent-exchange-based method is its broad applicability to different types of polymer semiconductors with different functions.

'One plus one is greater than two'

The hydrogel semiconductor, which the team has patented and is commercializing through UChicago's Polsky Center for Entrepreneurship and Innovation, is not merging a semiconductor with a hydrogel. It's one material that is both semiconductor and hydrogel at the same time.

"It's just one piece that has both semiconducting properties and hydrogel design, meaning that this whole piece is just like any other hydrogel," Wang said.

Unlike any other hydrogel, however, the new material actually improved biological functions in two areas, creating better results than either hydrogel or semiconductor could accomplish on their own.

First, having a very soft material bond directly with tissue reduces the immune responses and inflammation typically triggered when a medical device is implanted.

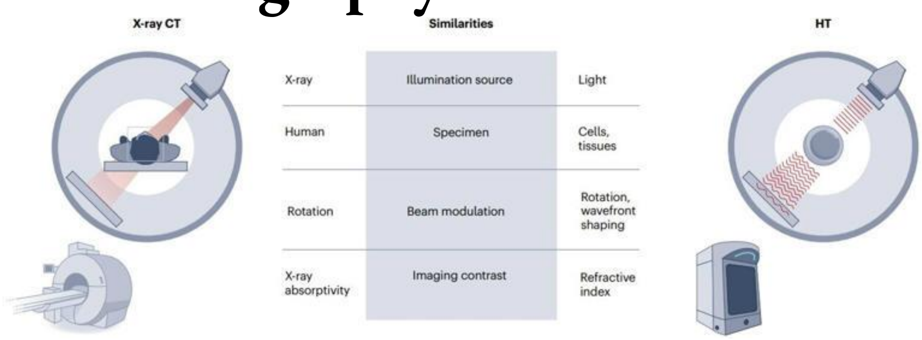
Second, because hydrogels are so porous, the new material enables elevated biosensing response and stronger photo-modulation effects. With biomolecules being able to diffuse into the film to have volumetric interactions, the interaction sites for biomarkers-under-detection are significantly increased, which gives rise to higher sensitivity. Besides sensing, the responses to light for therapeutic functions at tissue surfaces also get increased from the more efficient transport of redox-active species. This benefits functions such as light-operated pacemakers or wound dressing that can be more efficiently heated with a flick of light to help speed healing.

"It's a 'one plus one is greater than two' kind of combination," Wang joked.

More information: Yahao Dai et al, Ultrasoft hydrogel semiconductors with augmented biointeractive functions, *Science* (2024). DOI: 10.1126/science.adp9314. www.science.org/doi/10.1126/science.adp9314

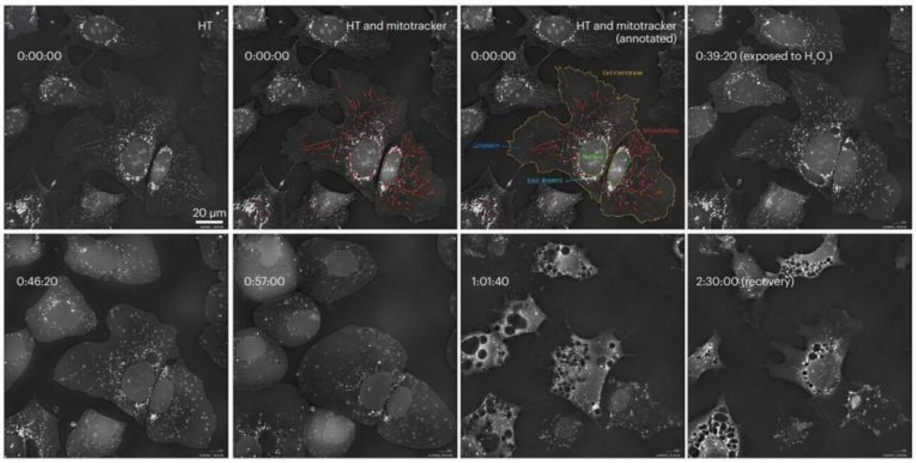
Provided by University of Chicago

Paper introduces strategies for holotomography in advanced bio research



Schematic illustration of holotomography compared to X-ray CT. Similar to CT, they share the commonality of measuring the optical properties of an unlabeled specimen in three dimensions. Instead of X-rays, holotomography irradiates light in the visible range, and provides refractive index measurements of transparent specimens rather than absorptivity. While CT obtains three-dimensional information only through mechanical rotation of the irradiating light, holotomography can replace this by applying wavefront control technology in the visible range. Credit: KAIST Biomedical Optics Laboratory

Measuring and analyzing three-dimensional (3D) images of live cells and tissues is considered crucial in advanced fields of biology and medicine. Organoids, which are 3D structures that mimic organs, are particular examples that significantly benefit 3D live imaging. Organoids provide effective alternatives to animal testing in the drug development processes, and can rapidly determine personalized medicine. On the other hand, active research is ongoing to utilize organoids for organ replacement.

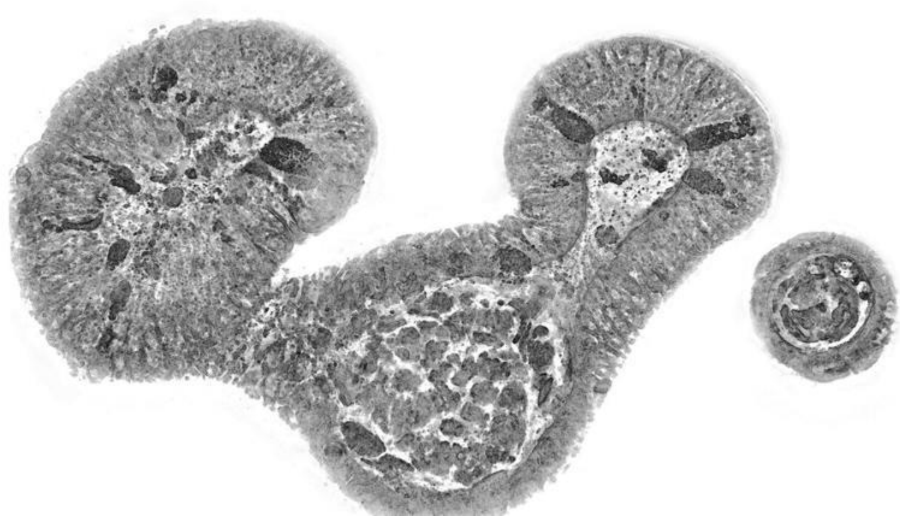


Label-free 3D imaging of diverse live cells. Time-lapse image of Hep3B cells illustrating subcellular morphology changes upon H2O2 treatment, followed by cellular recovery after returning to the regular cell culture medium. Credit: KAIST Biomedical Optics Laboratory

Organelle-level observation of 3D biological specimens such as organoids and stem cell colonies without staining or preprocessing holds significant implications for both innovating basic research and bioindustrial applications related to regenerative medicine and bioindustrial applications.

Holotomography (HT) is a 3D optical microscopy that implements 3D reconstruction analogous to that of X-ray computed tomography (CT). Although HT and CT share a similar theoretical background, HT facilitates high-resolution examination inside cells and tissues, instead of the human body.

HT obtains 3D images of cells and tissues at the organelle level without chemical or genetic labeling, thus overcoming various challenges of existing methods in bio research and industry. Its potential is highlighted in research fields where sample physiology must not be disrupted, such as regenerative medicine, personalized medicine, and infertility treatment.



Various types of cells and organelles that make up the imaging barrier of a living intestinal organoid can be observed using holotomography. Credit: KAIST Biomedical Optics Laboratory

This paper introduces the advantages and broad applicability of HT to biomedical researchers, while presenting an overview of principles and future technical challenges to optical researchers. It showcases various cases of applying HT in studies such as 3D biology, regenerative medicine, and cancer research, as well as suggesting future optical development.

Also, it categorizes HT based on the light source, to describe the principles, limitations, and improvements of each category in detail. In particular, the paper addresses strategies for deepening cell and organoid studies by introducing artificial intelligence (AI) to HT. The research is published in the journal *Nature Reviews Methods Primers*.

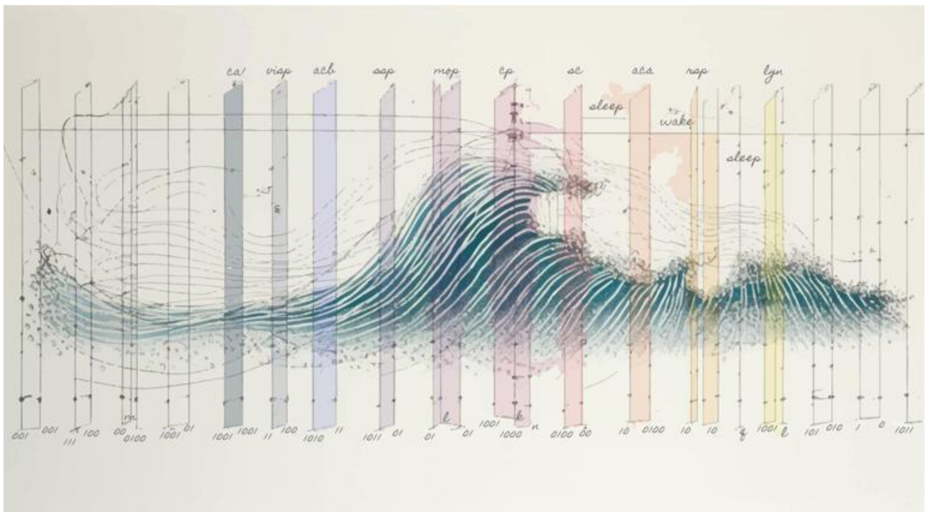
Due to its potential to drive advanced bioindustry, HT is attracting interest and investment from universities and corporates worldwide. The KAIST research team has been leading this international field by developing core technologies and carrying out key application research throughout the last decade.

This paper was co-authored by Dr. Geon Kim from KAIST Research Center for Natural Sciences, Professor Ki-Jun Yoon's team from the Department of Biological Sciences, Director Bon-Kyoung Koo's team from the Institute for Basic Science (IBS) Center for Genome Engineering, and Dr. Seongsoo Lee's team from the Korea Basic Science Institute (KBSI).

More information: Geon Kim et al, Holotomography, *Nature Reviews Methods Primers* (2024). DOI: 10.1038/s43586-024-00327-1

Provided by The Korea Advanced Institute of Science and Technology (KAIST)

Scientists find small regions of the brain can take micro-naps while the rest of the brain is awake and vice versa



Hengen's artistic interpretation of the varied brain wave patterns that produce the fundamental states of sleep and wake. Credit: Keith Hengen© Provided by Medical Xpress

Sleep and wake: They're totally distinct states of being that define the boundaries of our daily lives. For years, scientists have measured the difference between these instinctual brain processes by observing brain waves, with sleep characteristically defined by slow, long-lasting waves measured in tenths of seconds that travel across the whole organ.

For the first time, scientists have found that sleep can be detected by patterns of neuronal activity just milliseconds long, 1,000 times shorter than a second, revealing a new way to study and understand the basic brain wave patterns that govern consciousness. They also show that small regions of the brain can momentarily "flicker" awake while the rest of the brain remains asleep, and vice versa from wake to sleep.

These findings, described in a new study published in the journal *Nature Neuroscience*, are from a collaboration between the laboratories of Assistant Professor of Biology Keith Hengen at Washington University in St. Louis and Distinguished Professor of Biomolecular Engineering David Haussler at UC Santa Cruz. The research was carried out by Ph.D. students David Parks (UCSC) and Aidan Schneider (WashU).

Over four years of work, Parks and Schneider trained a neural network to study the patterns within massive amounts of brain wave data, uncovering patterns that occur at extremely high frequencies that have never been described before and challenge foundational, long-held conceptions of the neurological basis of sleep and wake.

"With powerful tools and new computational methods, there's so much to be gained by challenging our most basic assumptions and revisiting the question of 'what is a state?'" Hengen said. "Sleep or wake is the single greatest determinant of your behavior, and then everything else falls out from there. So if we don't understand what sleep and wake actually are, it seems like we've missed the boat."

"It was surprising to us as scientists to find that different parts of our brains actually take little naps when the rest of the brain is awake, although many people may have already suspected this in their spouse, so perhaps a lack of male-female bias is what is surprising," Haussler quipped.

Understanding sleep

Neuroscientists study the brain via recordings of the electrical signals of brain activity, known as electrophysiology data, observing voltage waves as they crest and fall at different paces. Mixed into these waves are the spike patterns of individual neurons.

The researchers worked with data from mice at the Hengen Lab in St. Louis. The freely-behaving animals were equipped with a very lightweight headset that recorded brain activity from 10 different brain regions for months at a time, tracking voltage from small groups of neurons with microsecond precision.

This much input created petabytes—which are one million times larger than a gigabyte—of data. David Parks led the effort to feed this raw data into an artificial neural network, which can find highly complex patterns, to differentiate sleep and wake data and find patterns that human observation may have missed. A collaboration with the shared academic computer infrastructure located at UC San Diego enabled the team to work with this much data, which was on the scale of what large companies like Google or Facebook might use.

Knowing that sleep is traditionally defined by slow-moving waves, Parks began to feed smaller and smaller chunks of data into the neural network and asked it to predict whether the brain was asleep or awake.

The team found that the model could differentiate between sleep and wake from just milliseconds of brain activity data. This was shocking to the research team—it showed that the model couldn't have been relying on the slow-moving waves to learn the difference between sleep and wake. Just as listening to a thousandth of a second of a song couldn't tell you if it had a slow rhythm, it would be impossible for the model to learn a rhythm that occurs over several seconds by just looking at random isolated milliseconds of information.

"We're seeing information at a level of detail that's unprecedented," Haussler said. "The previous feeling was that nothing would be found there, that all the relevant information was in the slower frequency waves. This paper says, if you ignore the conventional measurements, and you just look at the details of the high frequency measurement over just a thousandth of a second, there is enough there to tell if the tissue is asleep or not. This tells us that there is something going on a very fast scale—that's a new hint to what might be going on in sleep."

Hengen, for his part, was convinced that Parks and Schneider had missed something, as their results were so contradictory to bedrock concepts drilled into him over many years of neuroscience education. He asked Parks to produce more and more evidence that this phenomenon could be real.

"This challenged me to ask myself, 'To what extent are my beliefs based on evidence, and what evidence would I need to see to overturn those beliefs?'" Hengen said. "It really did feel like a game of cat and mouse, because I'd ask David [Parks] over and over to produce more evidence and prove things to me, and he'd come back and say, 'Check this out.' It was a really interesting process as a scientist to have my students tear down these towers brick by brick, and for me to have to be okay with that."

Local patterns

Because an artificial neural network is fundamentally a black box and does not report back on what it learns from, Parks began stripping away layers of temporal and spatial information to try to understand what patterns the model could be learning from.

Eventually, they got down to the point where they were looking at chunks of brain data just a millisecond long and at the highest frequencies of brain voltage fluctuations.

"We'd taken out all the information that neuroscience has used to understand, define, and analyze sleep for the last century, and we asked, 'Can the model still learn under these conditions?'" Parks said. "This allowed us to look into signals we hadn't understood before."

By looking at this data, they were able to determine that the hyperfast pattern of activity between just a few neurons was the fundamental element of sleep that the model was detecting. Crucially, such patterns cannot be explained by the traditional, slow and widespread waves. The researchers hypothesize that the slow-moving waves may be acting to coordinate the fast, local patterns of activity, but ultimately reached the conclusion that the fast patterns are much closer to the true essence of sleep.

If the slow-moving waves traditionally used to define sleep are compared to thousands of people in a baseball stadium doing the wave, then these fast-moving patterns are the conversations between just a few people deciding to participate in the wave. Those conversations occurring are essential for the overall larger wave to take place, and are more directly related to the mood of the stadium—the wave is a secondary result of that.

Observing flickers

In further studying the hyperlocal patterns of activity, the researchers began to notice another surprising phenomenon.

As they observed the model predicting sleep or wake, they noticed what looked at first like errors, in which for a split second the model would detect wake in one region of the brain while the rest of the brain remained asleep. They saw the same thing in wake states: For a split second, one region would fall asleep while the rest of the regions were awake. They call these instances "flickers."

"We could look at the individual time points when these neurons fired, and it was pretty clear that [the neurons] were transitioning to a different state," Schneider said. "In some cases, these flickers might be constrained to the area of just an individual brain region, maybe even smaller than that."

This compelled the researchers to explore what flickers could mean about the function of sleep, and how they affect behavior during sleep and wake.

"There's a natural hypothesis there; let's say a small part of your brain slips into sleep while you're awake—does that mean your behavior suddenly looks like you're asleep? We started to see that that was often the case," Schneider said.

In observing the behavior of mice, the researchers saw that when a brain region would flicker to sleep while the rest of the brain was awake, the mouse would pause for a second, almost like it had zoned out. A flicker during sleep (one brain region "wakes up") was reflected by an animal twitching in its sleep.

Flickers are particularly surprising because they don't follow established rules dictating the strict cycle of the brain moving sequentially between wake to non-REM sleep to REM sleep.

"We are seeing wake to REM flickers, REM to non-REM flickers—we see all these possible combinations, and they break the rules that you would expect based on a hundred years of literature," Hengen said. "I think they reveal the separation between the macro-state—sleep and wake at the level of the whole animal, and the fundamental unit of state in the brain—the fast and local patterns."

Impact

Gaining a deeper understanding of the patterns that occur at high-frequencies and the flickers between wake and sleep could help researchers better study neurodevelopmental and neurodegenerative diseases, which are both associated with sleep dysregulation. Both Haussler and Hengen's lab groups are interested in understanding this connection further, with Haussler interested in further studying these phenomena in cerebral organoid models, bits of brain tissue grown on a laboratory bench.

"This gives us potentially a very, very sharp scalpel with which to cut into these questions of diseases and disorders," Hengen said. "The more we understand fundamentally about what sleep and wake are, the more we can address pertinent clinical and disease related problems."

On a foundational level, this work helps push forward our understanding of the many layers of complexity of the brain as the organ that dictates behavior, emotion, and much more.

More information: David F. Parks et al, A nonoscillatory, millisecond-scale embedding of brain state provides insight into behavior, *Nature Neuroscience* (2024). DOI: 10.1038/s41593-024-01715-2

Provided by University of California - Santa Cruz

'Flow state' uncovered: We finally know what happens in the brain when you're 'in the zone'

any people know the feeling of being "in the zone": As they're fully immersed in a task, the background noise of the world fades and they may not notice time passing. Gymnasts may enter this all-consuming mental state as they're refining a floor routine, an artist might find "the zone" when adding delicate brushstrokes to a painting and a writer might enter it as they're crafting the climax of a chapter.

This state, known in psychology as a "flow state," is pursued by those who want to be more productive and creative in an enjoyable way. What happens in the brain during this state, however, has been under debate for more than four decades.

Now, in research published March 4 in the journal Neuropsychologia, scientists may have settled the debate. They conducted a new brain-scan study that has finally revealed which regions of the brain are activated in the midst of a creative flow state.

Their findings contradict one popular theory of flow while supporting another, and they seem to reveal the key ingredients needed to get "in the zone."

Related: What happens in our brains when we 'hear' our own thoughts?

The competing hypotheses of flow

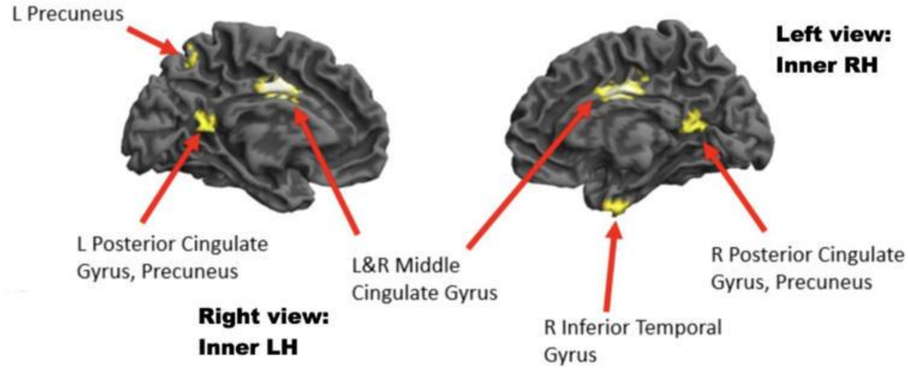
Two brain networks have historically been studied during tasks that could unlock flow. One is the default mode network (DMN), a circuit of connected brain areas associated with daydreaming whose activity spikes when people are not engaged in a specific task. The second is the executive control network (ECN), which supports complex cognitive processes, like problem-solving, and tunes out distractions.

Both networks can act independently, but they've also been shown to display certain levels of connectivity and to interact dynamically, especially during the creative process.

Researchers have proposed two main theories for how the flow state affects the brain. The first posits it's a state of hyperfocus in which ECN activity increases and guides the DMN to maintain focus on a task, to help generate relevant ideas, said Dmitri van der Linden, a professor of work and organizational psychology at Erasmus University Rotterdam who was not involved in the new study.

"It has been hypothesized that during flow, which is characterized by an intense task focus, DMN activity is relatively low," van der Linden told Live Science in an email. DMN activity is linked to "creative production," though, which is needed to generate ideas and improvise, he noted. With that in mind, this first hypothesis implies that both the ECN and the DMN are active and play off each other during flow, respectively contributing attention and creativity.

The alternative theory of flow, however, says that the expertise a person gains in a task through practice forges its own neural processing network that does not require ECN supervision or DMN involvement.



The researchers studied jazz guitarists in the study. This image highlights areas of reduced brain activity when experienced musicians were in a high-flow state, compared to a low-flow state. These areas include key nodes of the default mode network. (Image credit: Image provided by John Kounios, PhD, of Drexel University)© Provided by Live Science

If you don't know, you can't flow

To pit these hypotheses against each other, John Kounios, a professor of psychology at Drexel University and senior author of the study, and his team studied 32 jazz guitarists, some highly experienced and some less-experienced. Creative tasks like improvisational jazz lend themselves well to triggering a flow state.

The researchers scanned the musicians' brains using electroencephalogram caps, fitted caps studded with electrodes that track the brain's electrical activity. They examined activity in areas related to the DMN and the ECN and compared flow and non-flow states, which they evaluated with a questionnaire about the musicians' experiences while improvising.

Experienced musicians in a flow state showed decreased activity in the ECN and the DMN and increased activity in regions that process auditory, visual and movement information. This suggests that, during flow, individuals "let go" or switch into "autopilot" and experience less conscious control.

Moreover, experienced musicians in a flow state didn't seem to rely on the DMN to generate ideas, since its activity was down. Instead, they used the networks they had formed throughout their lives while honing their craft — in other words, networks involved in hearing and playing guitar, the researchers concluded.

Meanwhile, less-experienced musicians showed little change in the baseline activity of their ECNs, DMNs, or other processing centers while improvising in either low- or high-flow states. This suggests that only through gaining expertise and "letting go" can a person hope to achieve a high state of flow.

According to van der Linden, these findings address key questions in neuroscience and are especially impactful because they looked at brain activity during a real-life creative task rather than one invented for a study.

"This can be the basis for new techniques for instructing people to produce creative ideas," Kuonios said in a statement. In future work, the group hopes to confirm their theory with other creative tasks, such as drawing, while replicating the findings with higher-resolution brain-scanning techniques.

Unique Flow of Information Identified in The Human Brain

"What's new in our study is the use of multimodal data in a single model combining two branches of mathematics: graph theory, which describes the polysynaptic roadmaps; and information theory, which maps information transmission (or traffic) via the roads," says Alessandra Griffa, a biomedical engineer from EPFL.

"The basic principle is that messages passed from a source to a target remain unchanged or are further degraded at each stop along the road, like the telephone game we played as children."

To use another analogy, the information traffic moving around the brain is like traffic traveling down a road with multiple stops along the way. Our brains seem to be wired to simultaneously use multiple roads to get the convoy of signals to its destination.

What's more, the researchers discovered that these parallel pathways are as unique as fingerprints: studying the particular way that information flows around a brain can distinguish individual nervous systems.

"Such parallel processing in human brains has been hypothesized, but never observed before at a whole-brain level," says Griffa.

How these multiple channels affect thought processing, and why we have them when other animals don't, is beyond the scope of this study. However, the researchers think our larger brains have enabled more complex patterns of connectivity.

It might also add some level of resilience to the human brain, the researchers suggest. If one channel gets blocked or damaged, then it's possible that information can be rerouted through another channel instead.

Further down the line, the research could help us determine how damage from brain injuries could be repaired, or how we might be able to guard against the development of conditions such as dementia.

"We could hypothesize that these parallel information streams allow for multiple representations of reality, and the ability to perform abstract functions specific to humans," says Griffa.

"We looked at how information travels, so an interesting next step would be to model more complex processes to study how information is combined and processed in the brain to create something new."

The research has been published in *Nature Communications*.

Study provides first anatomical, functional representation of the ocular surface in the central nervous system

Nerve fibers on the eye surface are involved in many relevant physiological processes, from detecting and transmitting external stimuli to maintaining the integrity of the cornea. However, research on the sensory system of the ocular surface has focused mainly on the peripheral axons of the trigeminal ganglia neurons, leaving information processing in the central nervous system unknown.

Now, a new study carried out by the Institute for Neurosciences (IN), a joint center of the Miguel Hernández University (UMH) of Elche and the Spanish National Research Council (CSIC), together with the National Hospital for Paraplegics-SESCAM of Toledo, has characterized, for the first time, the neurons of the thalamus and cerebral cortex that respond to stimulation of the ocular surface.

The work, published in *The Journal of Physiology*, reveals that along the somatosensory pathway, there are neurons capable of responding to different types of stimuli applied to the eye surface and that their functional diversity increases as progress from the peripheral system to higher levels of the central nervous system.

The eye surface is sensitive to external stimuli that cause discomfort, such as irritation, dryness, or a feeling of sand in the eyes. Although these are the most relevant symptoms of many ocular pathologies, little is currently known about the central nervous system circuits involved in these perceptions.

"Until relatively recently, ocular sensitivity and pain had not been the subject of attention because these symptoms barely existed in the field of ophthalmology," explains Juana Gallar, co-director of the Ocular Neurobiology Laboratory at the IN together with Mª Carmen Acosta, who also has participated in the study.

"It has been the arrival of some social changes such as the habitual presence of air conditioning in many places, the high levels of environmental pollution or the introduction of refractive surgery, which has led to focusing on this issue," says the researcher.

The study shows the precise location of the thalamic and cortical neurons that receive information from the ocular surface and analyzes how the activity caused by stimuli of different types is integrated, which is transmitted from the trigeminal sensory neurons to the thalamus and, subsequently, the cerebral cortex.

"Until now, the primary sensory neurons have been characterized, which are those in the trigeminal ganglion, but this is the first time that it has been analyzed which stimuli activate the neurons of the thalamus and the cerebral cortex," says researcher Enrique Velasco, first author of the article.

Multimodal neurons

The peripheral nerves found on the ocular surface are composed of axons of unimodal neurons, which respond to a single stimulus modality, and polymodal neurons, which respond to stimuli from several modalities. As the authors describe, there are different degrees of sensory multimodality, so there are neurons that activate in response to multiple modalities of stimuli and others that respond to a smaller number.

Researchers have discovered that, although in the peripheral nervous system, some sensory nerves act as detectors of a single class of stimuli, this unimodality is practically non-existent in the brain.

"In the detectors of our eye, cold, heat and touch are totally separate," says Velasco. "However, in the central nervous system we find neurons that respond to various stimuli, which tells us that information from the periphery converges as it progresses through the nervous system and is compared one with another to give rise to conscious sensations that we perceive when we are exposed to a stimulus."

Furthermore, investigators have observed that both the degree of multimodality of neurons and the percentage of highly multimodal neurons increase along the somatosensory pathway: it is lowest in the trigeminal, intermediate in the thalamus, and maximum in the cerebral cortex.

This distribution implies that different stimuli can activate the same neuron, and conversely, the same stimulus can activate many different neurons, so the perceptions they produce are intermixed.

"In the case of the skin, we can clearly distinguish between a cold, hot, mechanical, or other type of stimulus. However, in the case of the cornea, we are not able to describe the sensations with that precision. This happens because most neurons that are part of the somatosensory pathway of the ocular surface are multimodal and, therefore, the information collected by these receptors on the eye surface converges and is intermixed along the pathway," explains Gallar.

To carry out this study, the researchers used electrophysiology techniques, which allowed them to explore the physiology of tissues and synaptic connections in living beings. To observe trigeminal, thalamic, and cortical activity in response to different stimulation modalities, the authors took recordings of rats while they administered eye drops of different temperatures, which allowed them to test five sensory modalities: intense cold, light cold, neutral temperature, light heat, and intense heat, the later capable of causing a sensation of pain.

Regarding the evolutionary significance of these results, experts consider that "the high functional diversity of these ocular neurons in the cerebral cortex guarantees that any kind of stimulus that we receive in the eyes produces a conscious perception," says Gallar.

"This allows us to be alert regarding our eyes to be able to react quickly in the case of harmful stimuli and, in addition, launch fundamental mechanisms to protect vision, such as increased tear production and blinking itself. The flip side is that we can not differentiate the types of stimuli with precision, or define their exact location on the ocular surface."

Along these lines, Gallar explains that this diversity of neurons constitutes the basis of the very characteristic sensations that are perceived on the surface of the eye.

"When we feel discomfort on the ocular surface we usually say that we have 'something' in the eye (the so-called foreign body sensation), grittiness, dryness, etc., but generally we do not use the word pain, although in reality what we are doing is using different terms to describe the different kinds of discomfort and pain that the neurons on our ocular surface are capable of processing," says the researcher. **More information:** Enrique Velasco et al, Ocular surface information seen from the somatosensory thalamus and cortex, *The Journal of Physiology* (2024). DOI: 10.1113/JP285008Provided by Miguel Hernandez University of Elche

Tiny eye movements are the key to making your vision sharper

BONN, Germany — Even when you think your eyes are perfectly still while reading these words, they're actually making tiny, unconscious movements. As it turns out, these seemingly random twitches serve a critical purpose: they help you see the world more clearly, according to new research from Germany.

The study, published in the journal *eLife*, reveals that these microscopic eye movements work in perfect harmony with the arrangement of light-sensing cells in our eyes, automatically adjusting to help us achieve the sharpest possible vision.

"Unlike a camera, our eyes are constantly and unconsciously in motion," explains Dr. Wolf Harmening, who leads the AOVision laboratory at the University Hospital Bonn's Department of Ophthalmology, in a media release.

These minuscule movements continue even when we're trying our hardest to stare at a fixed point.

How do our eyes create sharp vision?

At the center of each eye lies a tiny region called the fovea – a densely packed area of color-sensing cells known as cones. To put its size in perspective, this crucial region is about 200 times smaller than a quarter coin, yet it contains an astounding 200,000 cone cells per square millimeter. These cells are responsible for our ability to see fine details and vivid colors.

Unlike the uniform grid of pixels in your smartphone's camera, however, these cone cells aren't evenly distributed. Each person has their own unique pattern of cone density in their fovea, like a fingerprint for vision. What makes this new research particularly fascinating is how our unconscious eye movements – specifically, a type called "drift" – work in concert with this irregular arrangement of cells.

The research team used a specialized instrument called an Adaptive Optics Scanning Light Ophthalmoscope – the only one of its kind in Germany – to conduct their investigation. This high-tech device allowed them to observe both the precise arrangement of cone cells in participants' eyes and track their minute eye movements simultaneously.

The team studied 16 healthy volunteers, measuring their visual acuity during challenging vision tests while recording exactly how their eyes moved, and which photoreceptor cells were being used. What they found was remarkable: people could actually see finer details than what should have been possible based on the density of their cone cells alone.

The secret is in those tiny, drifting eye movements. Lead author Jenny Witten, a doctoral student at the University of Bonn, found that these movements weren't random at all.

"The drift movements repeatedly brought visual stimuli into the region where cone density was highest," explains Witten.

In other words, your eyes automatically drift in patterns that maximize the use of your highest-density cone regions, enhancing your ability to see detail.

The future of better vision

This discovery isn't just interesting for scientists and eye doctors – it could have important practical applications. Dr. Harmening's team suggests that understanding how these unconscious eye movements optimize vision could lead to better treatments for various eye disorders and improvements in artificial vision technologies, such as retinal implants.

The next time you find yourself marveling at your ability to read tiny print or appreciate the intricate details in a painting, remember: it's not just your eyes that are doing the work, but also those constant, invisible movements that help you see the world in crystal clarity.

Paper Summary

Methodology

This study explored how tiny movements of our eyes, called "fixational drift," influence how clearly we see very fine details. The researchers used special high-resolution imaging equipment to look closely at the center of participants' retinas (the area responsible for our sharpest vision). During the experiment, participants were asked to identify the orientation of a small letter "E" on a screen.

While they looked at the letter, the equipment recorded their eye movements and how different parts of the retina were involved in seeing the image. By analyzing these recordings, the researchers examined how eye movements could help us see even finer details than previously thought possible.

Key Results

The study found that small, controlled eye movements (fixational drift) helped participants see details smaller than a single photoreceptor cell (the tiny light-sensitive cells in the eye). The results showed that these eye movements are not random but are directed toward areas with the highest concentration of these photoreceptor cells. This adaptation allowed participants to see finer details than if their eyes remained still, suggesting that the human visual system uses both eye movement and retinal structure to enhance vision.

Study Limitations

One limitation is that the study was conducted under controlled laboratory conditions using specialized imaging technology, which may not fully represent natural viewing conditions. Additionally, the participants were limited in number, and all had normal vision without significant eye issues, which may not apply to those with vision impairments. Finally, the findings on eye movement patterns may vary among individuals and may not apply equally across different age groups or people with visual conditions.

Discussion & Takeaways

This research highlights how our eyes make subtle adjustments to enhance our ability to see fine details, especially during tasks that require high precision. These findings may help us better understand vision-related conditions and inform potential treatments, as they reveal that vision is a dynamic process involving not just our eyes' structure but also controlled eye movements. The study suggests that similar principles could apply in developing technologies to assist people with vision impairments or to enhance image quality in visual devices.

Funding & Disclosures

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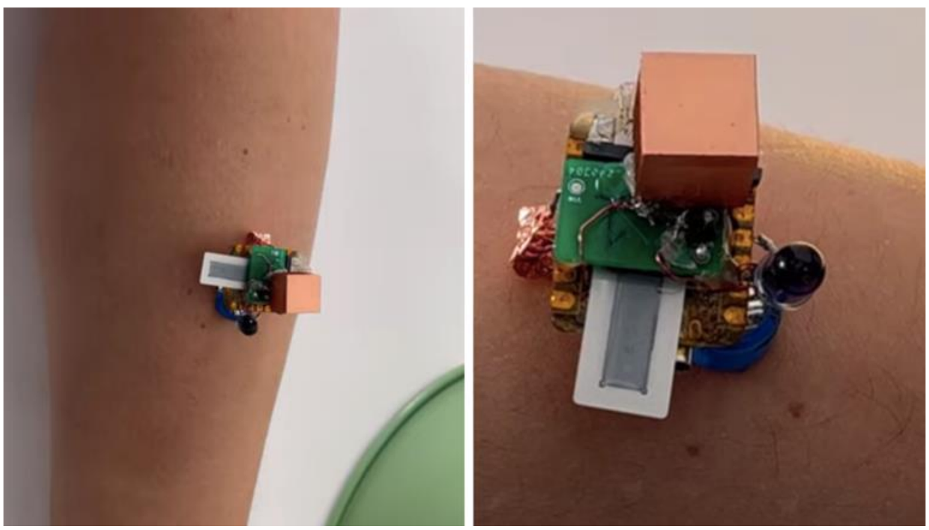
Human skin powers devices using intra-body RF energy, method eliminates battery needs



Human skin powers devices using intra-body RF energy, method eliminates battery needs

Researchers at Carnegie Mellon University have claimed that they have powered wearables using the human body. Called power-over-skin technology, the method used the human body to deliver power to many distributed, battery-free, worn devices.

Researchers claimed that they tested power delivery from on-body distances as far as from head-to-toe, with sufficient energy, to power microcontrollers capable of sensing and wireless communication.

Researchers stated that the human body could be modeled as a complex RC circuit.

Human body circuit

“Since we wish to have only one connection point to the body on the transmit and receive side, we must rely on the body’s capacitance and use high-frequency AC waves (RF) to conduct energy,” said researchers.

“Though the precise values of the human body circuit vary from person to person, this variation is negligible at the higher frequencies we need to use.”

The power-over-skin technology is claimed to be a refinement upon past intra-body power transfer (IBPT) systems for energizing battery-free receiver devices worn across the body.

More than a dozen experiments performed

This required improvements across every aspect of the system, including circuit design, component choice, and measurement apparatus.

Researchers documented over a dozen experiments to inform their system design, which they believe will be invaluable to future researchers. A key result was maintaining power delivery over a diversity of on-body locations and distances in spite of our small receiver board, according to researchers.

“This power was enough to run microprocessors and sensors, display output, and perform wireless communication at various worn locations. We believe this capability enables a wide range of new and interesting on-body applications.”

Researchers claimed that power-over-skin has the potential to increase the practicality and lifespan of many systems, as well as allowing for

novel body placements.

Several devices prove efficacy of technical approach

They created several example devices to convey the efficacy of their technical approach.

"As discussed previously, our transmitter can be comparatively large, as it contains the only battery in our system; the power-receiving devices can then be small and lightweight," said researchers.

They created an earring with a decorative ground and an LED.

"Blink rate is controlled by our power management IC, which discharges the storage capacitor across an LED when enough power is stored. The transmitter is contained in a hairband, which can accommodate the weight of batteries better than a small earring," added researchers.

Power-over-skin is particularly suitable for longitudinal health sensing

Researchers claimed that the power-over-skin is particularly suitable for longitudinal health sensing, since changes in bio-signals happen over minutes to hours (as opposed to real-time responsivity, e.g. ring joystick).

Their receiver can store plenty of energy, allowing us to power a microcontroller for an extended sensing operation (e.g., ECG heartrate) and perform a wireless transmission to another device which persists the data. This also means the transmitter can sit further away — for example, in a shoe or phone, according to researchers.

"As a simple example, we built a patch which senses body temperature and transmits the measurement over BLE to a laptop," said researchers.

Wearable ‘smart’ patch works with smartphone to detect health issues

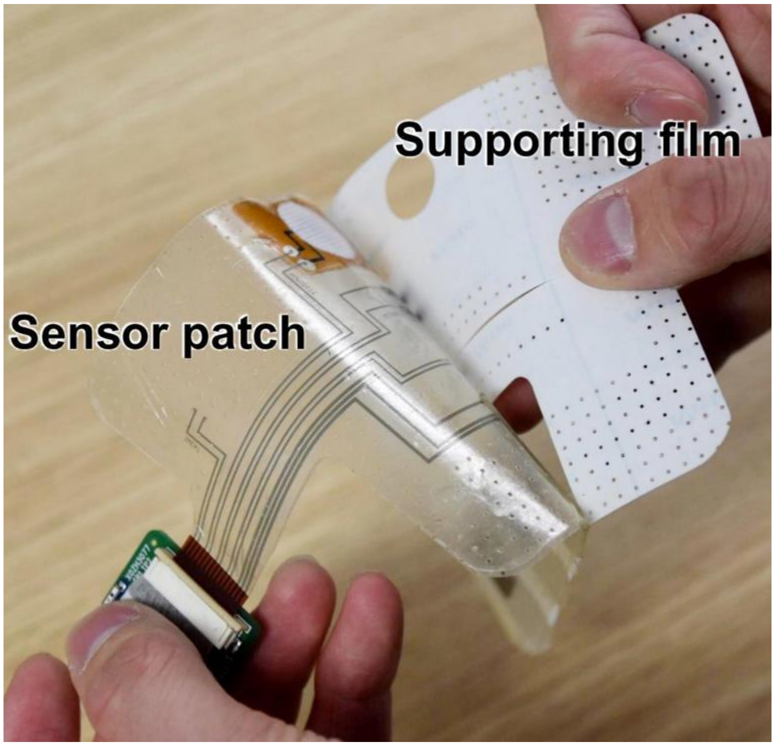
A new wearable "smart" sensor patch can detect health symptoms early via a smartphone.

The innovative device is able to spot an abnormal heart rhythm as well as coughs and falls, say Japanese scientists.

They explained that the sensors generate large amounts of data, and that data must be processed to be understood.

The field of computing dealing with processing the data on the sensor or a device that the sensor is connected to - rather than at a remote server on the cloud - is called edge computing.

The research team - led by Professor Kuniharu Takei at Hokkaido University and Associate Professor Kohei Nakajima at The University of Tokyo - says edge computing is a "key" element in wearable sensor technology.



The smart sensor patch is fabricated on a supporting film so that it may be peeled off and stuck onto the skin.

They have made a flexible wearable sensor patch and developed edge computing software that is capable of detecting arrhythmia, coughs and falls in volunteers.

The sensor uses a smartphone as the edge computing device.

Takei said: “Our goal in this study was to design a multimodal sensor patch that could process and interpret data using edge computing, and detect early stages of disease during daily life.”

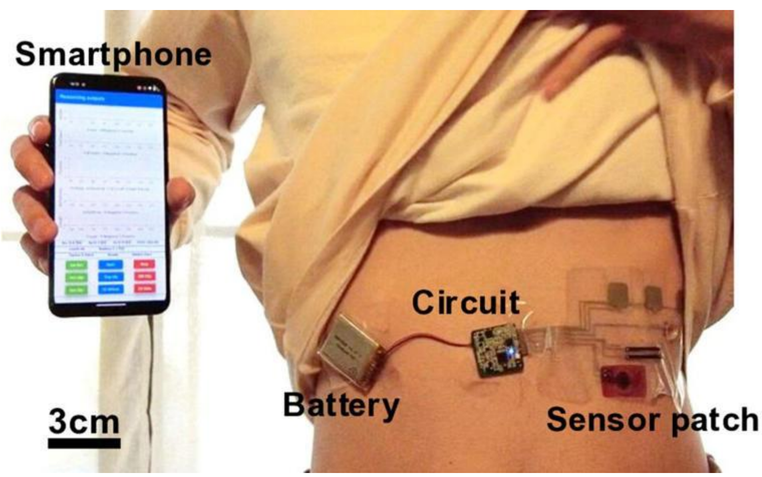
The team created sensors that monitor cardiac activity via electrocardiogram (ECG), respiration, skin temperature, and humidity caused by perspiration.

After confirming their suitability for long-term use, the sensors were integrated into a flexible film that adheres to human skin.

The sensor patch also included a Bluetooth module to connect to a smartphone.

The team first tested the capability of the sensor patch to detect physiological changes in three volunteers, who wore it on their chests.

The sensor patch, described in the journal Device, was used to monitor vital signs in the volunteers under wet-bulb globe temperatures - used to determine the likelihood of heat stress- of 22°C and over 29°C.



The sensor patch is connected to a processor (circuit) that includes a Bluetooth module and is powered by a battery.

Takei said: “Although our test group was small, we could observe their vital signs change during time-series monitoring at high temperatures.

"This observation may eventually lead to the identifying symptoms of early-stage heat stress."

The team developed a machine learning program to process the recorded data to detect other symptoms such as heart arrhythmia, coughing and falls.

Nakajima said: "In addition to performing the analysis on a computer, we also designed an edge computing application for smartphones that could perform the same analysis.

"We achieved prediction accuracy of over 80%."

Takei added: "The significant advance of this study is the integration of multimodal flexible sensors, real-time machine learning data analyses, and remote vital monitoring using a smartphone.

"One drawback of our system is that training could not be carried out on the smartphone, and had to be done on the computer.

"However, this can be solved by simplifying the data processing."

The post Wearable 'smart' patch works with smartphone to detect health issues appeared first on Talker.

What is wearable neurotech and why might we need it?

The wearables category already contains multitudes, from exercise-focused smart watches and sleep tracking smart rings to smart femtech and semi-invasive blood glucose monitors — to name a few of the gizmos we've tracked over roughly a decade of novel personal hardware launches. But the space is set to get even more active, with a new wave of neurotech: wearable devices targeting the brain.

The neurotechnology category tends to be associated with brain implants. But wearable neurotech refers to therapeutic medical devices that apply brain stimulation from outside the body — through the skin and skull — not via any physically invasive process as a treatment for a range of chronic health issues.

Think head-mounted wearables that allow the user to self-administer treatment for psychological conditions such as depression (Flow Neuroscience) or period pain & PMS (Samphire Neuroscience). Other target applications include anxiety, insomnia and even post traumatic stress disorder (PTSD). Metabolic disorders like obesity and Type II diabetes could even be treated using wearable neurotech.

Both are applications on the roadmap of Neurovalens, a U.K.-based startup that's been developing its non-invasive brain-stimulating technology for over a decade.

The market for wearable medtech remains small but it looks to be on the cusp of a growth spurt over the next few years as long-running efforts to commercialize R&D are poised to translate into a pipeline of products — assuming the necessary regulatory approvals flow.

Meet the "little zapper" for depression

TechCrunch spoke to a user of Flow about their experience of its wearable therapeutic. This person, who we'll call Alex (not their real name as they preferred to remain anonymous), has suffered from low mood for several years. This eventually led them to find out about Flow's device and get in touch with the company to ask to test it. They've been using the product since February 2024.

Flow's wearable, which has an RRP of €459, is designed to treat depression using a form of electrical brain stimulation called tDCS, or transcranial direct current stimulation. The device applies low current stimulation to the user's head via a pair of conductive pads that rest on the forehead. Daily treatments are suggested for an initial period of several weeks, after which Alex said they stepped down to a couple of sessions per week. They told us they continued to use Flow at a weekly cadence after that.

An FAQ on the company's website recommends that if the product is "helpful" for the first 10 weeks of treatment the user continue "for at least another 6 to 12 months, even if you have become symptom-free."

Discussing their experience with Flow, Alex said the wearable has been helpful and a lot less unpleasant than taking antidepressants.

They had previously been prescribed drugs several times but decided to stop medicating after it led to weight gain, low libido and feeling generally numb/dissociated. Even the process of getting off the drugs had been deeply distressing for them. But Alex said Flow's device provided a very different treatment experience, with none of the nasty side-effects.

"Just the process of putting the thing on, feeling the little zapper, sitting quietly for half an hour, doing all the little things associated with it is also very calming," they told us. "It feels like little ants biting at your forehead… [or] one of those muscle stimulators for sports, where it kind of zaps your muscle.

"My experience was I went from a despondent situation, to moving through a more active depression which manifested itself as anger, into a fairly relaxed state at this point, which is unusual for me."

When we checked in a few months later to see how Alex was doing, they'd finally stopped using Flow. Why? "Feeling slightly better" came the quietly understated response.

A different kind of treatment

One big promise of non-invasive neurotech is that it could offer an alternative treatment for conditions like depression that don't always respond well to drugs. But how can an electronic device have a therapeutic effect on the human brain? The basic theory is that stimulating the brain's activity in a targeted way can influence how a person feels by changing the electric signals that brain cells use to talk to each other.

“Brain cells communicate with electrochemicals,” explains Cambridge University’s Dr. Camilla Nord, an assistant professor, head of the university’s Mental Health Neuroscience Lab and author of a book (The Balanced Brain) on the science of mental health. “So one way we can change activity in the brain — and thereby someone’s thoughts, mood [etc]… is by changing the chemistry. That’s what drugs like antidepressants, antipsychotics do.

“The second way we can change it is by changing their electrical signals — and that, in varying ways, is what brain stimulation does.”

While pharmaceuticals are a more established pathway for influencing mood and mental health, there are many drawbacks to taking medication — from ongoing cost; to not easily/being able to stop once you start; to a whole host of potential side-effects.

Drugs also aren’t equally effective for everyone, if they work at all. And, even if they do, no one wants to have to be taking any form of medication, even a painkiller, forever – unless they literally have no choice. So the case for neurotech wearables to expand treatment options looks strong — provided device makers can demonstrate that their products are safe and effective.

To the uninitiated, the idea of applying electricity to the brain might sound a bit scary. But, asked about potential risks, Nord says the amount of neurostimulation used in commercial devices is so mild it shouldn’t be a cause for concern.

“My understanding of the level of brain stimulation used in these commercial devices [is] they are not something to have safety concerns about,” she suggests. “These are very, very low levels of electrical brain stimulation – if they’re changing neuronal activity it’s likely to be at safe levels if you’re using them for a short amount of time, which is how they’re recommended for use.”

Whether there might be any risks related to usage duration – i.e. using non-invasive neurostimulators for long periods of time – is less clear. "To some degree, we can never fully know," she posits. But long term drug use may have its own risks, too.

Another big potential plus-point for neurotech vs pharmaceuticals is that a treatment that's lower risk can be tried earlier — before resorting to prescribing medication. Drugs may also require a full diagnosis before they can be dispensed. Whereas wearable neurotech could open up a market for earlier health interventions — allowing treatment to be applied sooner in a disease's progression with the chance of better outcomes for patients.

Technical & regulatory complexity

While neurotech has clear potential, there is a lot of complexity attached to this kind of medtech. Part of the reason the neurotech landscape is so complex is the variety of techniques that can be used to influence the brain's activity. Broadly speaking this includes transcranial magnetic stimulation (TMS), electrical current stimulation (CES), and even – research indicates – ultrasound (TUS).

So far, most commercial activity has focused on a form of CES called transcranial electrical current stimulation (aka tDCS). But there are several other electrical approaches being explored. Applications for non-invasive brain stimulation are also growing – but the main areas of interest so far are mental health and neurological issues.

Commercializing neurotech research into medical devices is far from simple due to a fragmented regulatory environment, too: In the U.S., the Food and Drug Administration (FDA) is an overloaded one-stop shop, while in Europe a decentralized system of private accredited bodies handle safety testing and audits. The rules for how medical devices are prescribed and reimbursed also differ between markets.

On top of that, there is some historical baggage to contend with – as a result of brain stimulation having a long but not always illustrious history. Legacy devices unsupported by science do explain some of the lingering scepticism about non-invasive neurotech therapy. But in recent years, the FDA has been looking to tighten up its rules for approving electrical neurostimulation for certain applications.

This is a course corrector for earlier waves of products that were brought to market in the U.S. from the late 1970s onwards under less rigorous standards. In 2019 the FDA finalized a reclassification of CES for treating insomnia and anxiety — moving these use-cases to a lower risk category (Class II) but also applying some special controls.

The 2019 FDA order also addressed CES devices targeting depression. These were maintained as Class III (high risk) under its revised rules but there's now a more involved pathway to get to market, known as Premarket Approval (PMA). Device makers must amass U.S. clinical evidence that will be reviewed, and ensure the hardware meets safety standards, before they can seek approval for a commercial launch.

A full PMA application process can take years. And while some devices targeting anxiety and insomnia have been cleared by the FDA since the 2019 rule changes, the regulator has yet to approve any CES devices for depression under its revised pathway.

Safe to say, the first depression-targeting neurotech wearable that gains FDA approval will be able to lay claim to a major credibility boost.

Modernized and strengthened rules for approving neurotech medical devices set the category up for a reputational reboot – provided startups can deliver to the upgraded standards.

Getting regulatory sign-off is not the end of the journey, though. Healthcare supply systems also assess novel treatments with a focus on costs — meaning they need to be able to demonstrate value for money. Again, different markets and healthcare systems may approach these cost-benefit assessments very differently, amping up the admin work for startups wanting to sell to multiple markets.

The U.K.'s publicly-funded National Health Service (NHS), for example, relies on a body called NICE (the National Institute for Health and Care Excellence) to evaluate both clinical efficacy and cost effectiveness of potential treatments. While the U.S. has a far more fragmented cost assessment process as a result of the larger role private healthcare plays.

Achieving reimbursement is the holy grail for a medical device maker as it unlocks the opportunity to reach serious scale. But there's no shortcut to get there.

Since March last year Flow's wearable has been made available to patients and clinicians in the U.K.'s NHS via a series of pilot programs. It's also started to have its hardware reimbursed in some European markets.

Co-founder and CEO Erik Rehn won't be drawn into predicting how long the next big step for Flow, of FDA approval, might take to obtain. But he credits the startup's initial B2C approach – of selling its wearable to interested consumers in Europe (where it has obtained a CE mark under regional medical device rules) – with giving it enough runway to work towards heading over the pond as a reimbursable medical device in the future.

"There's this big gap between getting regulatory approval and reimbursement," Rehn tells TechCrunch. "A lot of companies have a medical device idea, they develop it, they run the clinical trials to get approval, but then what? It can take years from that point to actually get it to a reimbursed state to actually earn money. And how do you survive that?

"We solved that by having a strategy where we could sell directly to consumers. But that's not possible in all cases. It might need to be a prescription device.... depend[ing] on the indication you're using it for – but also the technology, and also the regulatory framework on the market where you are."

“To have the really big impact in the long term we need to go B2B,” he adds. “We’d need to get reimbursement. We’d need to get this as a first line of treatment. And that’s much harder than just having the medical device approved.”

Flow’s strategy requires the startup to execute a long, slow switch from B2C to B2B – as it amasses usage data, traction and evidence for its novel wearable — to gain buy-in from healthcare systems far more accustomed to pushing pills on patients than head-mounted gadgets.

“It’s taken a long time,” admits Rehn. “I hoped it [would] be much faster. But I think, realistically, this is how long it takes to change how something is treated.”

Beyond placebo

Whether the sense of relaxation the person we spoke to earlier, Alex, was able to achieve within a few weeks of trying Flow’s non-invasive neurostimulation is a direct result of the therapeutic electricity the device applies or whether some kind of placebo effect could be involved — including as a result of mindful product design (Flow’s app encourages the user to get into a routine of reflective self-focus, for example) — is harder to determine.

Placebo is a phenomenon that refers to the brain’s ability to change a person’s experience with expectations.

Alex told us they believe Flow’s product worked for them. But they also wondered aloud whether it was placebo?

Rehn says Flow is able to demonstrate the product’s efficacy in trials that control for the placebo effect. And — specifically — he says it can demonstrate that it’s the electrical brain stimulation component which is having a therapeutic effect.

“So far we only looked at the brain stimulation — there’s no CBT [cognitive behavioral therapy], involved [in our clinical trials],” he stresses. “Because it’s the headset that we sell. So we want to be really sure that we have evidence for the treatment.

"That's the kind of evidence that we're going to the regulators with."

Discussing the role placebo might play in non-invasive brain stimulation, Dr Nord confirms there is no way for regular users to be sure. "These forms of brain simulation that are being used [commercially] – for the majority – they have a basis in science. They have the potential [to make] these changes in the brain. And then, therefore, a potential to have the effects that they claim to be having.

"But when you personally have experienced these effects – no, you can't say whether it has happened through that [placebo] pathway," she says.

A person experiencing relief from a debilitating condition like depression may not much care about the exact mechanism making it happen – whether it's their own neurons convincing them to shift perspective or a legit change in brain activity flowing from active neurostimulation. But for healthcare systems and regulators – and therefore for medical device builders – it obviously does matter.

Knowing a treatment is better than placebo is a standard clinical requirement that enables healthcare service providers to take decisions that properly consider risks and costs. So a direct-to-consumer strategy can only be a stepping-stone for any medtech startup.

Add to that, the really big prize this new wave of wearable neurotech builders are shooting for is to get their devices established as therapeutics within traditional healthcare supply systems where they can scale impact and have the chance to drive a more proactive approach to tackling complex concerns.

What about consumer neurotech?

There's another bundle of brain-targeting wearables to consider which sit outside the medtech category — in a broader but fuzzier wellness device space. These are lifestyle products, marketed and sold directly to consumers, typically with some brain training or tracking pitch. But with no regulatory oversight of claimed benefits it's harder to understand and verify impact.

While we've seen startups experimenting with consumer neurotech plays for years, there are signs the category might be heating up again – judging by recent device launches.

For example, Netherlands-based Alphabeats – which launched its first product in the U.S. in May – is combining an EEG (electroencephalography) brainwave detecting headband with music and other in-app visuals for a focus-tracking and focus-training pitch that's geared towards professional athletes and sportspeople.

The product is based on research originally conducted by the electronics giant Philips, along with researchers at the University of Tilburg in the Netherlands, according to co-founder Jorrit DeVries, who was also president & chief commercialization officer at the startup when we spoke to him (but has since taken over the CEO role).

Another consumer player that's set to launch its debut brain-targeting device in the U.S. shortly is Neurable. The Boston-based startup has actually been grinding away in the category for years – spinning out of the PhD research of founder and CEO, Ramses Alcaide.

After years developing algorithms to boost an EEG signal from brain-scanning hardware that's small enough to be housed in a standard-looking pair of headphone cups, Neurable's first consumer device is finally headed to market — via a partnership with premium audio brand, Master & Dynamic. The resulting product is a pair of premium smart headphones that will be marketed as an attention-tracking (and focus training) tool for information workers wanting to optimize their productivity.

Brain training itself isn't a new idea of course. Games claiming to up your mental agility have been touted and sold for years. But such apps don't have the best reputation, with limited evidence of utility beyond such stuff being good for improving users' ability to play brain training games.

Startups like Alphabeats and Neurable are hoping to reboot the category thanks to pulling in brain activity data via EEG. Their pitches push the notion that consumers can use their apps to track their brain activity in real-time and get feedback to support them to positively rewire mental habits.

Why does DeVries think the time is right to sell consumers on a wearable for training mental game?

"I think the stigma [around mental health and seeking support for it] is being removed quite rapidly," he suggests. "Role models like Simone Biles, for example, or Michael Phelps, or all these key athletes that that talk about mental performance and the importance of mental health – so that helps the market tremendously to be able to tap into to a bigger cohort of people that is not worried about what a lot of people think about it."

Another big change he flags vs earlier consumer neurotech plays is refinements to the wearable technology itself: Alphabeats is bundling a pretty slender headband with its app, which is made by a third party company (BrainBit), also helping it trim product costs.

"The form factor is getting smaller and smaller and more accessible. Prices are being driven down by competition," he says, adding: "Years ago there were headbands in the market that were at least $1,000 and now we're offering Alphabet for $499 including 12 months of the service."

"In five to 10 years from now, it will be very common to get EEG out of earbuds," DeVries also predicts. "So we want to focus on this platform to become the companion – the mental performance companion – for anybody that needs it."

In Neurable's case the U.S. startup kicked off with what Alcaide admits was a "bad strategy" – of focusing on targeting the tech at users of AR and VR. The new product positioning now has the startup leaning into the wellness trend.

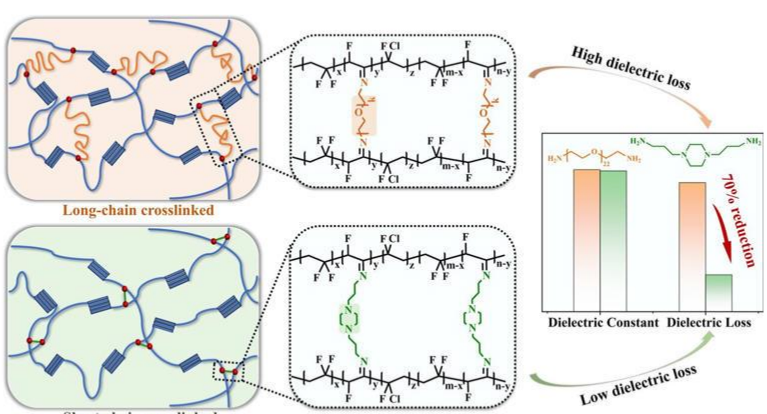
Neurable talks in terms of its smart headphones enabling users to take care of their "mental hygiene" – so there's a clear push to connect to the broader wearables space (which encompasses products like Apple's Watch, the Oura Ring or the Whoop band, to name a few), where health tracking has been a key selling point.

"We're definitely going to go the same path as Apple does," emphasizes Alcaide. "We're not going to make a medical device anytime soon – we're just going to help people better understand themselves and their data."

What else might brain-focused wearables end up targeting down the line? Research continues to turn up some tingling possibilities. A recent study suggested neurostimulation could even be used to dull the emotional pain of heartbreak. So maybe future consumers of neurotech wearables will be weighing the pros & cons of whether they want to give themselves a dose of *Eternal Sunshine of the Spotless Mind*.

A headband for heartbreak remains science fiction for now — but, well, it's quite a thought!

High-dielectric-constant elastomer with low dielectric loss improves performance of smart wearables



Intrinsic ferroelectric elastomer with a high dielectric constant and low dielectric loss. Credit: NIMTE

High-dielectric-constant elastomers possess outstanding softness and stretchability. They allow a fast response and have a high reliability, and thus have been widely applied to wearable electronics.

Prof. Hu Benlin's team at the Ningbo Institute of Materials Technology and Engineering (NIMTE) of the Chinese Academy of Sciences, has developed an intrinsic ferroelectric elastomer with a high dielectric constant and a low dielectric loss, which can effectively improve the performance and stability of smart wearables.

The study is published in *Advanced Materials*.

By introducing soft long-chain crosslinking structures into ferroelectric polymer materials with a "slight crosslinking" method, Hu's team had earlier achieved an intrinsic elastomer with high dielectric constants up to 35.4 at 1 kHz (54.2 at 100 Hz) that balances ferroelectricity and elasticity.

However, the dielectric relaxation and high mobility of the introduced soft long chains under alternating electric fields can trigger serious energy dissipation, leading to substantial dielectric loss.

In their new study, the NIMTE researchers integrated a rigid short-chain crosslinker with the relaxor ferroelectric P(VDF-TrFE-CFE). The obtained intrinsic ferroelectric elastomer showed a low dielectric loss of ~0.09 while maintaining a high dielectric constant of ~35 at 1 kHz and 25°C.

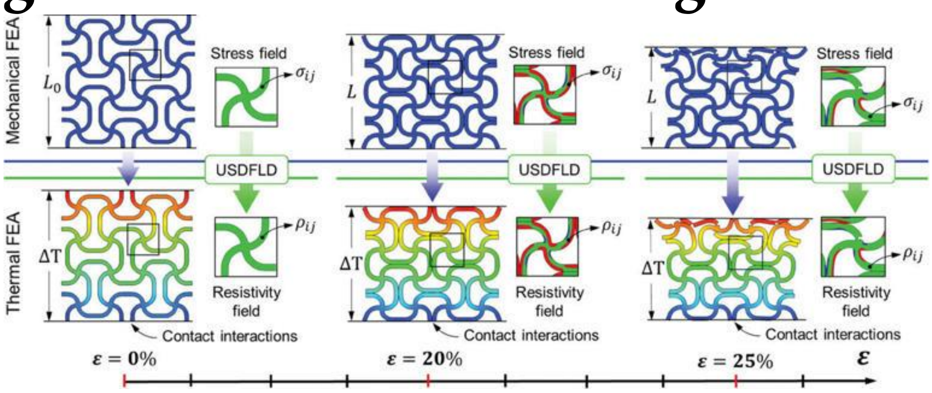
Compared with the soft long-chain crosslinking method, the rigid short-chain crosslinking approach reduced dielectric loss by more than 70%.

In addition to great ferroelectricity, piezoelectricity, and thermal stability, the obtained intrinsic ferroelectric elastomer achieved a high elastic recovery ratio exceeding 70% under 60% strain. The fabricated elastic devices based on the obtained intrinsic ferroelectric elastomer showed stable ferroelectric responses and relaxor characteristics even under 80% strain.

The study provides an effective approach to reducing the dielectric loss of high-dielectric-constant intrinsic elastomers, broadening their applications in wearable electronics, actuation, sensing, information processing, and energy storage.

More information: Fangzhou Li et al, Reducing Dielectric Loss of High-Dielectric-Constant Elastomer via Rigid Short-Chain Crosslinking, *Advanced Materials* (2024). DOI: 10.1002/adma.202411082

Modeling system could enable future generations of self-sensing materials



Methodology for the piezoresistive finite element analysis. Credit: Advanced Functional Materials (2024). DOI: 10.1002/adfm.202411975

Research that eliminates the guesswork in developing advanced 3D printed materials could help accelerate the development of new forms of "self-sensing" airplanes, robots, bridges and more.

A team of engineers led by researchers from the University of Glasgow have developed the first system capable of modeling the complex physics of 3D-printed composites capable of detecting strain, load, and damage using nothing more than a measure of electrical current.

By allowing material scientists to predict in advance for the first time how new structures can be fine-tuned to produce specific combinations of strength, stiffness, and self-sensing properties, it could help catalyze the development of revolutionary new applications for the technology.

In the aerospace and automotive sectors, new materials produced using the team's insights could enable real-time monitoring of structural integrity in aircraft, spacecraft, and vehicle components, enhancing safety and maintenance efficiency.

For civil engineering, these materials could enable developments in smart infrastructure by providing continuous assessment of the structures of bridges, tunnels, and high-rise buildings, highlighting problems long before they lead to collapse. They could offer similar benefits for robots at work in automated manufacturing, or even help soldiers on the battlefield keep tabs on the integrity of their body armor plates.

3D printing, also known as additive manufacturing, enables the creation of complex structures by building them layer by layer from materials like plastics, metals, or ceramics.

As technology has developed, researchers have been able to create increasingly complex materials with unique properties. Introducing a lattice of honeycomb-like chambers to the structure's interiors, for example, can allow materials to delicately balance weight with structural strength.

Weaving fine strands of carbon nanotubes throughout materials can allow them to carry an electrical current, imbuing them with the ability to monitor their own structural integrity through a phenomenon called piezoresistivity. When the readout of the current changes, it can indicate that the material has been crushed or stretched, allowing action to be taken to address the fault.

Professor Shanmugam Kumar, of the University of Glasgow's James Watt School of Engineering led the research, which is published in the journal *Advanced Functional Materials*. He said, "Imparting piezoresistive behavior to 3D-printed cellular materials gives them the ability to monitor their own performance without any additional hardware.

That means we can imbue cheap, relatively easy-to-manufacture materials with the remarkable ability to detect when they have been harmed and measure just how damaged they are. These types of lattice materials, which we call autonomous sensing architected materials, hold significant untapped potential to create advanced applications across various fields.

"While researchers have known about these properties for some time now, what we've not been able to do is provide a way to know in advance how effective new attempts at creating novel self-sensing materials will be. Instead, we have often relied on trial and error to determine the optimal approach for developing these materials, which can be both time-consuming and costly."

In the paper, the researchers describe how they developed their system through a rigorous set of lab experiments combined with modeling.

They used a plastic known as polyetherimide (PEI) mixed with carbon nanotubes to create a series of four different lightweight lattice structure designs. These designs were then tested for their stiffness, strength, energy absorption and self-sensing capabilities.

Using sophisticated computer modeling, they developed a system aimed at predicting how the materials would respond to a varied set of loads. They then validated their multiscale finite element model's predictions by subjecting the materials to intense analysis under real-world conditions, utilizing infrared thermal imaging to visualize electrical current flowing through the materials in real-time, leveraging the analogy between heat and current flow within these materials.

They found that their models could accurately predict how the materials would respond to various combinations of stress and strain, and how their electrical resistance would be affected. The results could help underpin future developments in additive manufacturing by providing insights into how proposed new materials will perform before the first real-world prototype is printed.

The research builds on previous developments from the team, who recently published a paper showcasing another approach to modeling which enables researchers to predict how additive manufacturing-induced flaws can affect the structural integrity of any new design.

Professor Kumar added, "With this study, we have developed a comprehensive system capable of modeling the performance of self-sensing, 3D-printed materials. Informed by rigorous experimentation and theory, it represents the first system of its kind that enables the modeling of 3D-printed materials across multiple scales and incorporates multiple types of physics."

"While we focused on PEI materials with embedded carbon nanotubes in this paper, the multiscale finite element modeling our results are based on could be easily applied to other materials which can be created through additive manufacturing too.

"We hope this approach encourages other researchers to develop new autonomous sensing architected materials, unlocking the full potential of this methodology in material design and development across a wide range of industries."

More information: Mattia Utzeri et al, Autonomous Sensing Architected Materials, *Advanced Functional Materials* (2024). DOI: 10.1002/adfm.202411975

Provided by University of Glasgow

LG's bizarre but impressive stretchable prototype display has the 'highest rate of elongation in the industry,' a measurement I had no idea existed

LG's bizarre but impressive stretchable prototype display has the 'highest rate of elongation in the industry,' a measurement I had no idea existed© LG Display

Flexibility could be the next bleeding edge for hardware to thread. Besides the bendy CPU whose performance leaves much to be desired outside its one party trick, monitor manufacturers are experimenting with pliable projects.

LG Display is the latest name to explore something with this technical twist, unveiling a stretchy screen prototype that can be expanded by up to 50% with a good tug (via Tom's Hardware). A prototype demonstration took place in Seoul at LG Science Park as part of a stretchable display national project during an event involving around 100 other South Korean tech stakeholders on November 8th.

This is far from the first bendy screen we've seen, with American company Corsair releasing the Xeneon Flex OLED Monitor a few years back. The big difference with LG's prototype is that it does a bit more than stretch; you can scrunch it, pull it, and twist it (though there's no word yet on whether you can bop it).

Dated reference aside (does Gen Z know the crushing low of flicking it when you mean to bop it?) LG's prototype is also a darn sight smaller than that Corsair monitor. LG's flexible display first presents RGB colour and 100 PPI at 12 inches, but can then expand up to 18-inches—which LG is quick to note in their press release exceeds "the original national project’s target of 20% elongation," and is "the highest rate of elongation in the industry."

As impressive as all of that is, I just can't get past how wrong the idea of scrunching up expensive tech feels; monitors may be hardware but they're historically not the hardiest of wares in the face of, say, a flung controller. Furthermore, in the case of the Corsair monitor, it's not just the fact you've really got to give it some welly to expand the display, but also the horrible sounds of protestation made by the frame that all contribute to the feeling of 'there's something wrong with this picture.'

Besides that, isn't the pliability of LG's prototype and its array of potential form factors just introducing heaps of new points of failure?

On the subject of durability, LG's press release states, "By using a micro-LED light source of up to 40 µm (micrometers), the new prototype's strengthened durability means it can be repeatedly stretched over 10,000 times, maintaining clear image quality even in extreme environments such as exposure to low or high temperatures and external shocks." That might be a bold claim but, if this prototype ever makes it to market in some form, it could mean cracked phone screens may one day be a thing of the past.

The LG Display prototype remains a ways off any kind of consumer environment, but the company also shared a handful of conceptual use cases. In a bid to further highlight both the prototype's durability and pliability, LG proposed a wearable application where a stretchable display panel attached to a firefighter's uniform could provide a real-time feed of information. While that could end up being a pipe dream, a wearable that actually achieves some real world good would certainly make a change.

How the brain structure that produces norepinephrine also helps control visual attention

The locus coeruleus (LC) is a small region of the brainstem that produces norepinephrine, a chemical with powerful effects on arousal and wakefulness which plays an important role in the body's response to stress or panic. Now, research from the University of Chicago shows it plays a specific role in visual sensory processing as well.

In a study, titled "Locus coeruleus norepinephrine selectively controls visual attention" and published in *Neuron*, neuroscientists artificially increased neuronal activity in the LC by briefly shining light on genetically modified neurons. They saw that this manipulation selectively enhanced performance in non-human primates performing a visual attention task, underscoring the crucial role that attention plays in sensory perception.

"We want to understand what changes in your brain when you pay attention to something in the environment, because attention greatly affects your ability to discern stimuli," said John Maunsell, Ph.D., the Albert D. Lasker Distinguished Service Professor of Neurobiology and Director of the Neuroscience Institute at the University of Chicago, and co-author of the study.

"Now we have found a brain structure that has strong signals related to whether the subjects are paying attention to a stimulus or not, and we see big differences in how its neurons respond depending on where that attention is directed."

Maunsell and co-author Supriya Ghosh, Ph.D., a postdoctoral researcher, focus their studies on how neurons in different areas of the brain change to represent sensory input when a subject is paying attention to a stimulus or not. For example, activity of neurons in the cerebral cortex may increase by 10–25% when a subject pays attention to the stimuli those neurons represent.

Previous research has shown that LC activation, coupled with its ensuing norepinephrine production, might improve performance on tasks that require attention to discern between visual stimuli.

Ghosh, who specializes in subcortical brain structures, suggested that the LC might be a good candidate to study for these effects. The team trained two monkeys to perform a visual task in which they paid attention to the left or right side of a screen. First, a sample image would appear on both sides of the screen.

Next, after a delay, a test image would appear on one side of the screen. The monkey would report if that image was oriented differently than the sample shown earlier on that side of the screen by moving its eyes to one of two targets. The researchers recorded neuron activity in the LC during the task and saw that activity increased greatly—and only—when the animal attended to the image that appeared on the side of the screen monitored by those neurons.

To see if there was a causal relationship between this increased activity and performance, they also used a method called optogenetics to increase activity in the LC while the animals were performing the task. Optogenetics allows researchers to selectively control the activity of norepinephrine-expressing cells via light.

First, they introduce a genetic modification that causes neurons to produce a light-sensitive protein called opsin, the same type of protein that photoreceptors in the eye use to detect light. When they shine a special light on these neurons, the opsin causes the neurons to fire.

Optogenetically boosting the responses of the neurons drastically improved the animals' ability to differentiate the shapes on the corresponding half of the screen, without affecting motor processing.

"This kind of artificial enhancement of that activity did not interfere with other cognitive factors either, such as motor actions or decision-related activities," Ghosh said. "So, it could selectively contribute to the perceptual sensitivity in a very precise way."

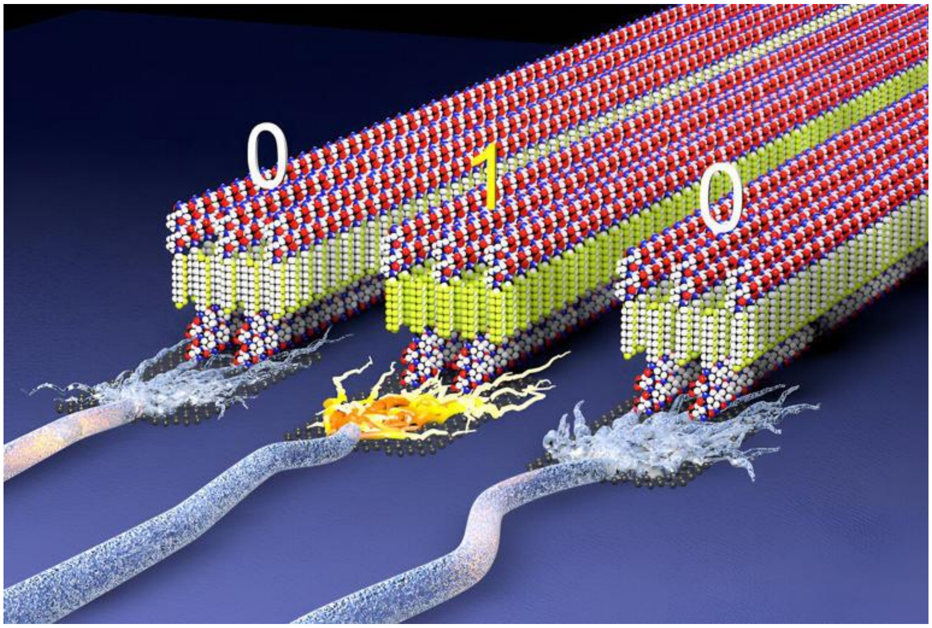
Distinguishing the effects of attention from other factors, like decision-making or motor movements, is crucial, Ghosh said. Those processes take place in other parts of the brain, and can contribute to performance independently. Understanding how a relatively small brain structure like the LC impacts such an important function as attention is also one step toward solving the overall puzzle of the brain.

"Every time we get more information about the likely contribution of a given brain structure, or how broad the range of functions of a given structure might be, that gives us much more power to understand the relationships among them," Maunsell said. "No one part of the brain does interesting behaviors by itself."

More information: Locus coeruleus norepinephrine contributes to visual spatial attention by selectively enhancing perceptual sensitivity, *Neuron* (2024). DOI: 10.1016/j.neuron.2024.04.001. www.cell.com/neuron/fulltext/S0896-6273(24)00239-3

Provided by University of Chicago

Peptides and plastics combine for energy-efficient materials



This illustration shows a future vision of assemblies of molecules formed by peptides and miniature molecular segments from a plastic material to create ferroelectric structures that switch polarity to store digital information or signal neurons. Credit: Mark Seniw/Center for Regenerative Medicine/Northwestern University

Step aside hard, rigid materials. There is a new soft, sustainable electroactive material in town—and it's poised to open new possibilities for medical devices, wearable technology and human-computer interfaces.

Using peptides and a snippet of the large molecules in plastics, Northwestern University materials scientists have developed materials made of tiny, flexible nano-sized ribbons that can be charged just like a battery to store energy or record digital information.

Highly energy efficient, biocompatible and made from sustainable materials, the systems could give rise to new types of ultralight electronic devices while reducing the environmental impact of electronic manufacturing and disposal.

The study, "Peptide programming of a supramolecular vinylidene fluoride ferroelectric phase," was published on Oct. 9 in the journal *Nature*.

With further development, the new soft materials could be used in low-power, energy-efficient microscopic memory chips, sensors and energy storage units. Researchers also could integrate them into woven fibers to create smart fabrics or sticker-like medical implants.

In today's wearable devices, electronics are clunkily strapped to the body with a wristband. But, with the new materials, the wristband itself could have electronic activity.

"This is a wholly new concept in materials science and soft materials research," said Northwestern's Samuel I. Stupp, who led the study.

"We imagine a future where you could wear a shirt with air conditioning built into it or rely on soft bioactive implants that feel like tissues and are activated wirelessly to improve heart or brain function.

"Those uses require electrical and biological signals, but we cannot build those applications with classic electroactive materials. It's not practical to put hard materials into our organs or in shirts that people can wear. We need to bring electrical signals into the world of soft materials. That is exactly what we have done in this study."

Stupp is the Board of Trustees Professor of Materials Science and Engineering, Chemistry, Medicine and Biomedical Engineering at Northwestern.

He has also served over the past decade as director of the U.S. Department of Energy-supported Center for Bio-Inspired Energy Science, where this research began. Stupp has appointments in the McCormick School of Engineering, Weinberg College of Arts and Sciences and Northwestern University Feinberg School of Medicine. Yang Yang, a research associate in Stupp's laboratory, is the paper's first author.

Peptides meet plastics for true innovation

The secret behind the new material is peptide amphiphiles, a versatile platform of molecules previously developed in Stupp's laboratory. These self-assembling structures form filaments in water and have already demonstrated promise in regenerative medicine. The molecules contain peptides and a lipid segment, which drives the molecular self-assembly when placed in water.

In the new study, the team replaced the lipid tail with a miniature molecular segment of a plastic called polyvinylidene fluoride (PVDF). But they kept the peptide segment, which contains sequences of amino acids. Commonly used in audio and sonar technologies, PVDF is a plastic with unusual electrical properties.

It can generate electrical signals when pressed or squeezed—a property known as piezoelectricity. It is also a ferroelectric material, which means it has a polar structure that can switch orientation by 180 degrees using an external voltage. The dominant ferroelectrics in technology are hard materials and often include rare or toxic metals, such as lead and niobium.

"PVDF was discovered in the late 1960s and is the first known plastic with ferroelectric properties," Stupp said.

"It has all the robustness of plastic while being useful for electrical devices. That makes it a very high-value material for advanced technologies. However, in pure form, its ferroelectric character is not stable, and, if heated above the so-called Curie temperature, it loses its polarity irreversibly."

All plastics, including PVDF, contain polymers, which are giant molecules typically composed of thousands of chemical structural units. In the new study, the Stupp laboratory precisely synthesized miniature polymers with only 3 to 7 vinylidene fluoride units. Interestingly, the miniature segments with 4, 5 or 6 units are programmed by nature's beta-sheet structures, which are present in proteins, to organize into a stable ferroelectric phase.

"It was not a trivial task," Stupp said. "The combination of two unlikely partners—peptides and plastics—led to a breakthrough in many respects."

Not only were the new materials equally ferroelectric and piezoelectric as PVDF, but the electroactive forms were stable, with the ability to switch polarity using extremely low external voltages. This opens the door for low-power electronics and sustainable nanoscale devices.

The scientists also envision developing new biomedical technologies by attaching bioactive signals to the peptide segments, a strategy already used in Stupp's regenerative medicine research. This offers the unique combination of electrically active materials that are also bioactive.

Just add water

To create the sustainable structures, Stupp's team simply added water to trigger the self-assembly process. After dunking the materials, Stupp was amazed to find that they achieved the highly sought-after ferroelectric properties of PVDF.

In the presence of an external electric field, ferroelectric materials flip their polar orientation—similar to how a magnet can be flipped from north to south and back again. This property is a key ingredient for devices that store information, an important feature for artificial intelligence technologies.

Surprisingly, the investigators found that "mutations" in the peptide sequence could tune properties related to ferroelectricity or even transform the structures into materials that are ideal for actuation or energy storage known as "relaxor phases."

"Peptide sequence mutations in biology are the source of pathologies or biological advantages," Stupp said. "In the new materials, we mutate peptides to tune their properties for the physical world.

"Using nanoscale electrodes, we could potentially expose an astronomical number of self-assembling structures to electric fields. We could flip their polarity with a low voltage , so one serves as a 'one,' and the opposite orientation serves as a 'zero.' This forms binary code for information storage. Adding to their versatility, and in great contrast to common ferroelectrics, the new materials are 'multiaxial'—meaning they can generate polarity in multiple directions around a circle rather than one or two specific directions."

Record-breaking low power

To flip their polarity, even soft ferroelectric materials like PVDF or other polymers typically require a substantial external electric field. The new structures, however, require incredibly low voltage.

"The energy required to flip their poles is the lowest ever reported for multiaxial soft ferroelectrics," Stupp said. "You can imagine how much energy this will save in increasingly energy-hungry times."

The new materials also have innate environmental benefits. Unlike typical plastics, which linger in the environment for centuries, the Stupp laboratory's materials could be biodegraded or reused without the use of harmful, toxic solvents or high-energy processes.

"We are now considering the use of the new structures in non-conventional applications for ferroelectrics, which include biomedical devices and implants as well as catalytic processes important in renewable energy," Stupp said.

"Given the use of peptides in the new materials, they lend themselves to functionalization with biological signals. We are very excited about these new directions."

More information: Samuel Stupp, Peptide programming of supramolecular vinylidene fluoride ferroelectric phases, *Nature* (2024). DOI: 10.1038/s41586-024-08041-4. www.nature.com/articles/s41586-024-08041-4

Provided by Northwestern University

The real science behind the billionaire pursuit of immortality

Jonathan An tries to ignore the hype about new life-extension treatments, but it's caught up to him anyway.

He has heard the gospel of the longevity influencers, including that one multimillionaire who has been on a media campaign for months claiming that the 111 pills he takes each day will help him live forever. An, an assistant professor of oral sciences at the University of Washington, doesn't buy it. But he recently found himself inadvertently ensnared by the fervor around anti-aging — thanks to his mice.

An has studied mice suffering from periodontal disease, a bacterial-induced inflammatory infection of the gums that can lead to tooth loss. Mice (and more than 60 percent of human adults over 65) have to deal with this uncomfortable oral illness — and they don't have much choice but to cope. When people's teeth fall out, dentists like An replace them. But he would rather not have to remove so many.

While studying for his doctorate in dentistry at the University of Washington, An pursued a joint PhD to research preventive dental measures. He experimented with giving mice chow infused with the drug rapamycin each day to see if it would improve their oral health.

It worked. Mice treated for eight weeks with the drug — traditionally used to help prevent organ-transplant rejection — not only experienced delayed symptoms of periodontal disease, but saw regrowth of their tooth-supporting jaw bones.

This year, An is planning to test rapamycin in humans. If it has the same effect in adults as it did in mice, people might eventually be able to pick up a drug at the pharmacy that helps them avoid unwanted trips to the dentist's office.

Better dental health would be a pleasant effect, but that's not why An's research drew an unusual amount of attention. Because the drug An chose to test was rapamycin, the longevity field took notice. In separate lab experiments over the past decade, rapamycin has been found to extend the lifespan of yeast, nematodes, fruit flies, and mice. It has helped mice delay or reverse immunity decline, muscle decline, cognitive decline, and cancer growth.

This string of successes for rapamycin, which belongs to a class of drugs that stifle one biological pathway for cell growth, has caught the eyes of renowned longevity researchers. It's also attracted the attention of wealthy lifehackers and the clinics, supplement companies, and biotech investors who — out of true belief, opportunism, or a combination — stand to make money from people seeking an elixir for longer life.

Since An's study was published in 2020, longevity clinics from across the country have asked him how they can incorporate rapamycin into their practices. Some scientists consider rapamycin a strong candidate for life-extension purposes both because it has helped lab species live longer and because it has already been approved as an immunosuppressant in humans. Today, doctors can and do prescribe rapamycin for off-label use — including for longevity.

An wants to believe that these clinics — part of a fledgling longevity industry that includes between 50 and 800 providers across the US, according to the Wall

Street Journal — are genuinely trying to improve their clients' health. But he suspects that may not always be the case.

He tells the longevity crowd what he does know, which is less exciting than they might hope. When it comes to human health, "I don't know what rapamycin does," he said. "But I always tell them to make sure to have a dentist on hand because some of the side effects are oral-related."

Other companies want him to help with their own studies, the results of which they plan to keep private. An says no. "I'm a dentist," An said. "Not a salesperson."

A longer, healthier life is one of the easiest products in the world to sell. According to a Deloitte report, the 50 biggest longevity companies raised more than $1 billion in venture capital funding as of 2020 — a number that the company said would rise "due to the growing conviction that the longevity market could outstrip the existing health care market." Altos Labs, a "rejuvenation" biotech whose investors include Jeff Bezos, announced in 2022 that it had raised $3 billion in funding.

An astronomer's discovery of a neutron star has much less commercial potential and therefore generates much less interest than a researcher's discovery that the micronutrient resveratrol helps yeast live longer — even if it's likely that neither ultimately affects human lifespan. The attention paid to billionaire-funded research risks obscuring whether the longevity field is genuinely on the verge of a breakthrough or whether a clinic is just saying that to promote their experimental blood transfusion.

In reality, longevity research is advancing — but slowly. Clinical trials are moving forward on select uses for longevity drugs, younger researchers are taking the field more seriously, and private organizations are pledging significant support to research: The Saudi-based Hevolution Foundation has promised up to $1 billion in funding annually for biotech startups and academic researchers.

But while there likely remain many promising treatment candidates that have yet to be identified, they would take decades to reach clinical trials. Even academics who are bullish on the promise of longevity research fear that, for all the fanfare, the field has become too fixated on a few drugs and lifestyle adjustments that have been under investigation for years, while neglecting the basic research that could reveal novel pathways to slow down human aging.

For now, the three best ways to extend your life remain boring: eating a healthy diet, exercising regularly, and sleeping well. We aren't going to add decades to human life any time soon; living to 150 or 200 remains in the realm of science fiction. But in decades to come, advancements in the science of aging may still lead to therapeutic breakthroughs that lengthen human healthspan — the period of life spent in good health. Perhaps a few more people will become centenarians, but the real success would be having more years when you can live well.

How longevity went mainstream in academia

Matt Kaeberlein, a longevity researcher at the University of Washington, remembers a time when few in academia took the study of aging — much less the idea of longevity — seriously.

"When I came into the field as a graduate student in 1998, there was nobody who went to graduate school to study aging," he said. "The perception among the broader scientific community was that it was mostly snake oil and crap. There's still a lot of snake oil and crap, but it is more accepted now than it used to be."

The field began gaining wider recognition in 1993 when Cynthia Kenyon, a pioneer in aging research who now works at the Alphabet-owned life sciences company Calico Labs, discovered that mutating a single gene of the roundworm Caenorhabditis elegans doubled its lifespan. Other scientists soon figured out why. Gary Ruvkun, a professor of genetics at Harvard Medical School, and his colleagues found that the altered gene regulated an insulin-signaling pathway similar to one in humans that might play a role in slowing cell growth and metabolism. Researchers like Andrzej Bartke found similar mechanisms in mice, which have been the subject of much of the relevant research so far.

"One of the key things that's happened is that the evidence that you can actually slow down and interfere with the aging process in mammals … has become so overwhelming that only the willfully blind can ignore it," Richard A. Miller, who leads the University of Michigan's Paul Glenn Center for Biology of Aging Research, told me.

In the last two decades, scientists have performed hundreds of lab experiments — mostly on animals — on drugs like rapamycin, canagliflozin, acarbose, empagliflozin, metformin, and on interventions like calorie restriction in diets and removal of nondividing senescent cells. Instead of testing the effects of these treatments on specific illnesses, many of these studies test whether certain interventions slow down animals' aging processes and help them live longer.

The expansion of longevity research has unearthed some potentially useful information about which biological mechanisms control aging and how to alter them. In mice and other species, changing a single pathway has the power to extend life by significant margins, raising hopes that if humans respond similarly, certain drugs could extend human lives by years.

"We just have a better understanding of what those pathways are," said Tom Rando, director of the UCLA Broad Stem Cell Research Center, "even if we don't have a complete understanding of why they work and why they extend lifespan."

Though most experiments with potential longevity drugs and other interventions like blood transfusions are still being tested on lab animals, two dozen candidate drugs have moved to clinical trials with human patients. Daniel Promislow, a University of Washington professor of medicine and pathology, told me that when he got into the field three decades ago, researchers talked hopefully about early developments someday making it to the lab. "Fast forward 25, 30 years, and many of these lab-based discoveries are now at the heart of a large number of clinical trials," he said.

The clinical trials could allow researchers to produce evidence for interventions — besides diet, exercise, and sleep — that might help people live longer. Coleen T. Murphy, professor of molecular biology at Princeton, wrote in her 2023 book *How We Age* that, "What drugs can I take to live longer?" is becoming an increasingly tangible goal.

"A few years ago I might have chuckled at the naivety of this question," she wrote, "but now it's not so crazy to think that we will be able to take some sort of medicine to extend our healthy lifespans in the foreseeable future."

The horizon for this future is still far off. Most researchers I spoke to didn't believe that humans were going to experience a rapid increase in life expectancy any time soon — or maybe ever. They believed progress would instead be made in healthspan, helping people stay healthier for longer and avoiding long periods of physical and cognitive decline as they get older.

Such results probably won't lead to someone living an extra decade. But they could make old age less burdensome. That would matter enormously for individuals, who could enjoy more years in good health, and society, by potentially reducing the high costs of late-in-life medical care.

"I can't fathom saying, 'Yeah, we're going to try to extend someone's lifespan by nine years,'" An told me. "There's really no way to do that."

Behind the hype, longevity research is moving — but slowly

In a way, some of the biggest improvements to human lifespans have already been made. Initiatives in public health — water sanitation, vaccination campaigns, sewage systems — have added decades to the average person's life over the past few centuries. Since 1900, the average lifespan of a newborn has more than doubled worldwide — from 32 years old to 71 years old.

But the very fact that humans already live far longer than a lab animal is part of the reason that longevity research is so slow and difficult. For experimental purposes, laboratory mice live less than three years. Researchers have tested rapamycin in both young and old mice at a range of doses and then waited for them to die. Doing the same in humans would be far more expensive and take much longer. It's also not strictly legal. The Food and Drug Administration doesn't classify aging as a disease, which means that clinical trials can't set out solely to test how much longer an intervention keeps someone alive. Instead, researchers must study age-related indicators like cardiovascular function and cognitive impairment instead of "aging" itself.

To compensate, longevity researchers are looking for other ways to measure aging that don't require a patient's death. They have identified several biomarkers that could serve as surrogate endpoints, but none have reached a scientific consensus. These include "aging clocks," predictive models that purport to measure biological age or the age of specific biological organs; Bryan Johnson, the multimillionaire tech founder who calls himself a "professional rejuvenation athlete," touts such data as proof that he has reversed his aging.

These tests are ostensibly based on the research of Steve Horvath, a former professor at UCLA who now works at Altos Labs. He has used age-related DNA methylation to determine biological age. Though most researchers I spoke to expressed cautious optimism about the potential of Horvath's findings, they were skeptical of the extant consumer tests.

"We're not really sure if the age we tell you is accurate and if it's going to be the same tomorrow and whether it has any value," said Tony Wyss-Coray, a Stanford professor of neurology who has found that elderly mice given the blood of younger mice see improvements in brain function. "And of course, no company wants to tell you that, but that's just a fact."

Most longevity researchers think about their research environment the same way: The flashiest stories are usually pretty removed from the actual state of the field. A drug that just helped mice live 50 percent longer is unlikely to do exactly the same for humans, no matter what a press release implies. Human bodies are much better at repairing their DNA than mice are, which makes them less susceptible to diseases like cancer. Plus, studies that would definitively prove a certain intervention would aid human life would take decades, and experts believe they could struggle to demonstrate their effectiveness to the FDA.

"You'll rarely find a scientist funded by the [National Institutes of Health] who's doing work in the biology of aging who would claim that their research could or will allow people to live to 140," Rando told me. "It's really coalesced around the idea that our main successes will be in reducing the burden of disease."

It reflects a realism among the real experts. In longevity, there is not going to be a moment when a chrysalis bursts and a butterfly flies out, Miller said, a sudden leap forward in people's life expectancy. "It's more like the evolution of land plants. Gradually, they creep up over the beach, and then onto the meadow and then into the meadows. This is sort of creeping through the scientific community — too slowly."

According to many researchers, part of the reason for the relatively slow progress in longevity treatments is lack of funding in the field. For all the flashy announcements about companies like Calico and Altos Labs, academic researchers struggle to find financial support. The National Institute on Aging, the NIH division that funds research on the aging process, projects that it will spend about 9 percent of its budget on the biology of aging in 2024 and just under 60 percent on neuroscience-specific research. (The NIA's total projected budget in 2024 is about $4.4 billion of the NIH's $47.1 billion.) Promislow and Kaeberlein, who co-run a long-term study on biological and environmental factors that could contribute to aging in dogs, are currently fighting to keep their project alive with their NIH funding expected to end in June.

"I think there's an assumption by a lot of people that there's a ton of money in aging research," Murphy told me. "If you're an academic trying to get funding from the NIH, it's actually not true."

The lack of funding also draws university researchers out of their scholarly institutions and to companies like Calico and Altos Labs. "The idea of working with very smart people with lots of resources, all that's really attractive," Miller told me.

But that drift to the private sector could actually slow down aging research, already a sluggish endeavor, even more in the long run. The field is trending toward investor-driven research, while the basic research studies necessary for the next generation of possible interventions languish because they depend on public or philanthropic funding.

Drugs like rapamycin have already taken decades to enter clinical trials, but it's possible that none of the current leading longevity candidates work. Researchers don't even agree on which of the current drugs and interventions is the most promising: Miller, for example, told me he thinks that rapamycin is "the wrong drug" and that more funding should go to canagliflozin, which has increased median survival age in male mice by 14 percent and for which human side effects are better known due to its use in treating type 2 diabetes since 2013. Still, he doesn't think it's easy, "from our limited amount of knowledge, to be confident as to whether rapamycin, or canagliflozin, or any other promising drug would produce major benefits in people with acceptably low side effects." Most aging-related biotechnology companies use investor money to test aging interventions already proven in mice. Few are conducting the basic research to find new possible pathways for future therapies.

The more aging-related pathways scientists can find, the more possible targets for longevity drugs they would have. Each discovery opens the possibility for new interventions. Kaeberlein said that though the field has expanded in terms of the number of studies on certain drugs and mechanistic pathways, it's also become in a sense more narrow.

"We think, 'This is how the system works. So we're going to test these parts of the model,' instead of the more exploratory science that was being done when I was a graduate student, which was, 'We have no frickin' clue how the system works. Let's go do some unbiased screens to figure out what's happening here,'" he said.

Longevity researchers may be playing in a tiny corner of the sandbox, investigating just a few pathways while ignoring other possibilities. Scientists blame such myopia for the long gap between breakthroughs. The most consistently effective intervention for extending animal lifespan has been known for decades: restricting the number of calories they eat.

"I think that shift in mentality has led to more incremental results and fewer big, exciting, new discoveries," said Kaeberlein, "and I think, personally, that's why nobody has done better than rapamycin in 15 years and no one has done better than caloric restriction in 50 years."

There's also the possibility that drugs that have worked consistently across different species will work for some humans but not others. "The vast majority of studies in our field are done in one genetically identical strain of mouse," Rando said. "It's sort of like running a clinical trial in humans and only using identical twins. … Even if something could work, it's likely to work in a subset of the population and not in everybody."

Oddly, even the most brazen of the (non-expert) anti-aging boosters have uninspiring perceptions of the current state of longevity research. I was surprised when Bryan Johnson explained to me that, despite having a team of doctors who track the age of his organs and feed him a daily canister of pills, his choices weren't really made based on today's advancements in health and wellness.

He instead puts his faith in the continued evolution of artificial intelligence capabilities, which has advanced greatly over the past few years. He sees AI continuing to develop at an exponential rate — and longevity research eventually progressing at a more rapid speed than human researchers could hope to replicate.

"It's an observation that we are baby steps away from super intelligence," Johnson told me, "and it's improving at a speed that we can't imagine."

It's that, he hopes, that will bring about eternal life. The mice studies are less relevant.

A more realistic future for the longevity field

Immortality is enticing, but it's not coming anytime soon. Neither is living to 150. Some people — hopefully more than now — will live to 100, but they will still be the exception. The way longevity research might push the field forward could look very similar to the treatments we already have. For people with a high risk of cardiovascular disease, statins are a sort of longevity drug. For those dealing with certain cancers, chemotherapy can be considered a longevity treatment.

The future of longevity likely looks more like the world where we discover that rapamycin — a drug that can extend the lives of mice and help humans accept a new organ — can also treat elderly patients for periodontal disease. It could mean that people take a blood sugar-regulating drug like canagliflozin and suffer from fewer heart attacks and cancers.

"I don't really care about life extension because there's no way to measure it," An said. "It's really about your health."

Even in slow motion, the field keeps advancing. Murphy told me she was excited to see trial results from the longevity company Unity Biotechnology back in 2020. The drug UBX0101, which interacts with a tumor-suppressing pathway, cleared a phase 1 clinical trial.

When it moved to phase 2, though, it failed to achieve its aim of helping patients with osteoarthritis of the knee. A success could have been a promising sign for treatments to get rid of non-dividing senescent cells. But even a failure was valuable. It might not have been the result that anyone wanted, but it was a result, and it was public.

“That’s progress for our field,” she told me. “This is moving forward.”

3,000 types of cells

Your brain has billions of cells, but they come in relatively few types: a little over 3,000 cells combine to build our brains and make us who we are.

Different wiring=different functions

However, the most critical difference between our brains and those of other primates is not in the cells but in the wiring between them.

The decade of the brain

That discovery has been part of many that researchers have done in the past decade, filled with breakthroughs on our path to understanding the human brain.

A detailed brain atlas

For that, an international team of scientists is creating the most detailed atlas of our brain, mapping the locations and functions of 170 billion cells.

The BRAIN project

The international research project is part of the BRAIN (Brain Research Through Advancing Innovative Neurotechnologies) Initiative, with laboratories across many disciplines.

Humans, primates and rats BRAIN researchers identify, characterize, and map the brain cells of humans, other primates, and rats, hoping to make critical discoveries about our brains as a base for new studies on diseases and brain function.

Mice, the basic plan

The researchers have fully mapped mice brains and found we have different cells. Humans, for example, have specialized cells for visual processing that mice don't.

What sets us apart

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However, the difference in other primates is much more subtle. Trygve Bakken, an assistant investigator at the Allen Institute, told PBS that the differences are in language processing.

Different conexions and proportions

Cell proportion sets us apart from other mammals in the area of the brain that processes language. We have similar cells but in different proportions.

Gene expression

However, in the case of other large primates, and particularly our closest relatives, Chimpanzees, the difference is not in the composition of the brain or the cells but simply in the genetic expression of those cells.

Long way to go

Those findings can lay a foundation for more research, but the BRAIN initiative still has a long way to go.

Intricate maps

Mapping the brain is a difficult task. Ed Lein, a neuroscientist at the Allen Institute for Brain Science, told The Washington Post that each part is as complex as a complete organ. From Stanford University, Henry Greely compared it to sending a spaceship to another planet.

Comprehensive data

The BRAIN initiative serves as a great source of data, but it is still not aimed at understanding the complexity of brain functions like memory or consciousness. Other studies are trying to tackle that.

A dictionary

For example, BRAIN developed a dictionary linking certain genetic changes to specific brain cell types, which could give researchers crucial data to study the mechanics behind brain diseases.

New techniques and tools

The BRAIN studies also helped develop techniques that will add to the advanced tools researchers already have to understand our brain, like MRI and EEG scans.

So do we understand the brain yet?

However, there is still much to learn about how our brain works. Brain expert and UC Berkeley Professor Doris Tsao told Cosmos Magazine: "What we know about the brain, including my work, is trivial."

The three-pound human brain is one of the most intricate organs, surpassing the most advanced supercomputer. It controls everything you do, from reading this sentence to dreaming up wild inventions. Despite being a small organ, the brain is packed with complexities scientists are still trying to understand. Ready to learn the astonishing truths about your brain? Click through our 15-slide gallery to explore its incredible capabilities and surprising facts!

Stores Massive Data

Our brains can reserve 2.5 petabytes of data, equivalent to roughly 3 million hours of TV shows. This immense capacity allows us to retain a lifetime of memories and experiences. Thanks to the intricate 100 trillion neural networks, we quickly and accurately remember information.

Consumes 20% of Total Body Energy

Are you aware that your brain uses about 20% of your body's energy despite accounting for only about 2% of your body weight? The high energy demand is necessary to support continuous electrical activity, which coordinates every thought, movement, and sensation.

A Fast Information Processor

Neurons in the brain can transmit information at high speeds of up to 268 miles per hour. The brain's rapid transmission facilitates quick reflexes, instant decision-making, and seamless body movement coordination.

A Lifetime Learning Machine

Human brains have the superpower to change and adapt throughout life. Neuroplasticity allows the brain to rearrange itself by creating fresh neural links whenever you learn or experience new things. A new lesson means a new connection.

Naps Fire Up Its Creative Potential

During naptime, the brain sometimes generates vivid, often surreal experiences that can inspire creativity and problem-solving. Nier Bohr, the physicist behind the atom's structure, credited this revelation with a dream. Scholars, linguists, and artists — across disciplines — report similar breakthroughs.

Powerful Emotional Processor

You're mistaken if you think your heart determines your emotions because that's the brain's job! The limbic system within the brain processes emotions using the amygdala, hippocampus, and hypothalamus to regulate all your emotional responses, including sexual stimulation, memory, and motivation.

It Has Two Areas Focused on Fluency

Our speech capability to understand and communicate is also part of the brain's functioning. The Wernicke's area controls word comprehension, and the Broca's area, working with the motor cortex, helps with speech production.

Directly Links to Your Gut

Have you ever felt happy or motivated after consuming certain foods? Coffee, chocolate, or berries? Well, that is because of the gut-brain axis. Specific foods interact with some neurotransmitters to influence mood, digestion, and overall well-being. The gut's network of neurons influences these changes.

Acts as a Memory Converter

The hippocampus, a small structure within the brain, forms and stores memories. After a while, the hippocampus converts short-term memories into long-term ones, helping the limbic system learn and recall better. Your brain makes remembering grade 2 math a piece of cake.

Powers Consciousness

Scholars — scientists, philosophers, and researchers — term consciousness as a state of awareness. When conscious, you can make decisions and solve problems faster because the brain's flexible response mechanism takes in information and reacts accordingly.

It Needs Sleep to Heal

As you sleep, your brain also takes a break and starts healing. It clears out toxins, consolidates memories, and supports learning and cognitive performance. This nightly restoration is crucial for maintaining mental health and overall well-being. Just make sure you sleep for 7-9 hours!

Stress Stresses the Brain

Chronic stress shrinks the hippocampus, affecting memory and learning. Stress also aggravates inflammation, spreading the damage to your heart. You can protect your brain from its demise by having a routine, getting enough sleep, exercising, and eating right.

Each Brain Hemisphere Has Specialized Jobs

The brain has two hemispheres: the left hemisphere handles all the logical reasoning and language tasks, and the right, creativity, non-verbal memory, and spatial awareness. The right side also controls muscles on the left side of your body and vice versa.

The Brain Dances to Music

When listening to your favorite jam, certain brain sections light up, evoking emotion, memory, and motor control. This incredible response shows how deeply music is wired into our neural circuitry. Music can also create new neural connections, keeping our brains healthy and young.

It Stores Scented Memories

Ever found a familiar scent instantly transporting you to a specific moment? That is because the brain stores all the memories and emotions associated with smells. The olfactory bulb links to the hippocampus and amygdala, making scents powerful triggers for emotional memories.

This Relatively Simple Device Completely Transformed Neuroscience

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Electroencephalography, or EEG, was invented 100 years ago. In the years since the invention of this device to monitor brain electricity, it has had an incredible impact on how scientists study the human brain.

Since its first use, the EEG has shaped researchers' understanding of cognition, from perception to memory. It has also been important for diagnosing and guiding the treatment of multiple brain disorders, including epilepsy.

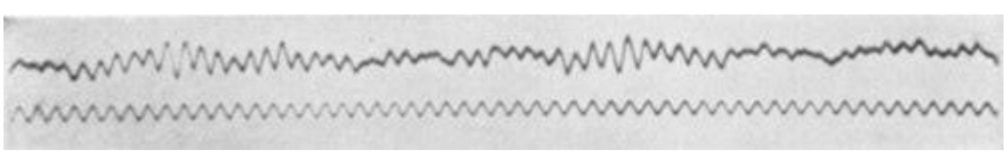
I am a cognitive neuroscientist who uses EEG to study how people remember events from their past. The EEG's 100-year anniversary is an opportunity to reflect on this discovery's significance in neuroscience and medicine.

Discovery of EEG

On July 6, 1924, psychiatrist Hans Berger performed the first EEG recording on a human, a 17-year-old boy undergoing neurosurgery. At the time, Berger and other researchers were performing electrical recordings on the brains of animals.

What set Berger apart was his obsession with finding the physical basis of what he called psychic energy, or mental effort, in people. Through a series of experiments spanning his early career, Berger measured brain volume and temperature to study changes in mental processes such as intellectual work, attention, and desire.

He then turned to recording electrical activity. Though he recorded the first traces of EEG in the human brain in 1924, he did not publish the results until 1929. Those five intervening years were a tortuous phase of self-doubt about the source of the EEG signal in the brain and refining the experimental setup. Berger recorded hundreds of EEGs on multiple subjects, including his own children, with both experimental successes and setbacks.



This Relatively Simple Device Completely Transformed Neuroscience© Provided by Inverse

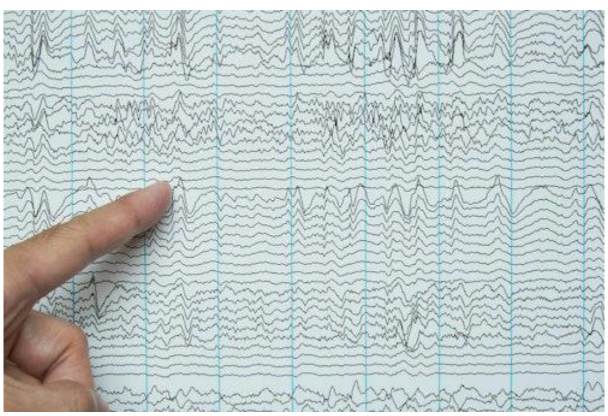
Finally convinced of his results, he published a series of papers in the journal Archiv für Psychiatrie and had hopes of winning a Nobel Prize. Unfortunately, the research community doubted his results, and years passed before anyone else started using EEG in their own research.

Neural oscillations

When many neurons are active at the same time, they produce an electrical signal strong enough to spread instantaneously through the conductive tissue of the brain, skull, and scalp. EEG electrodes placed on the head can record these electrical signals.

Since the discovery of EEG, researchers have shown that neural activity oscillates at specific frequencies. In his initial EEG recordings in 1924, Berger noted the predominance of oscillatory activity that cycled eight to 12 times per second, or 8 to 12 hertz, named alpha oscillations. Since the discovery of alpha rhythms, there have been many attempts to understand how and why neurons oscillate.

Neural oscillations are thought to be important for effective communication between specialized brain regions. For example, theta oscillations that cycle at 4 to 8 hertz are important for communication between brain regions involved in memory encoding and retrieval in animals and humans.



This Relatively Simple Device Completely Transformed Neuroscience© Provided by Inverse

Researchers then examined whether they could alter neural oscillations and, therefore, affect how neurons talk to each other. Studies have shown that many behavioral and noninvasive methods can alter neural oscillations and lead to changes in cognitive performance. Engaging in specific mental activities can induce neural oscillations in the frequencies those mental activities use. For example, my team's research found that mindfulness meditation can increase theta frequency oscillations and improve memory retrieval.

Noninvasive brain stimulation methods can target frequencies of interest. For example, my team's ongoing research found that brain stimulation at theta frequency can lead to improved memory retrieval.

EEG has also led to major discoveries about how the brain processes information in many other cognitive domains, including how people perceive the world around them, how they focus their attention, how they communicate through language, and how they process emotions.

Diagnosing and treating brain disorders

EEG is commonly used today to diagnose sleep disorders and epilepsy and to guide brain disorder treatments.

Scientists are using EEG to see whether memory can be improved with noninvasive brain stimulation. Although the research is still in its infancy, there have been some promising results. For example, one study found that noninvasive brain stimulation at gamma frequency – 25 hertz – improved memory and neurotransmitter transmission in Alzheimer's disease.

A new type of noninvasive brain stimulation called temporal interference uses two high frequencies to cause neural activity equal to the difference between the stimulation frequencies. The high frequencies can better penetrate the brain and reach the targeted area. Researchers recently tested this method in people using 2,000 hertz and 2,005 hertz to send 5-hertz theta frequency at a key brain region for memory, the hippocampus. This led to improvements in remembering the name associated with a face.

Although these results are promising, more research is needed to understand the exact role neural oscillations play in cognition and whether altering them can lead to long-lasting cognitive enhancement.

The future of EEG

The 100-year anniversary of the EEG provides an opportunity to consider what it has taught us about brain function and what this technique can do in the future.

In a survey commissioned by the journal Nature Human Behaviour, over 500 researchers who use EEG in their work were asked to make predictions on the future of the technique. What will be possible in the next 100 years of EEG?

Some researchers, including myself, predict that we'll use EEG to diagnose and create targeted treatments for brain disorders. Others anticipate that an affordable, wearable EEG will be widely used to enhance cognitive function at home or will be seamlessly integrated into virtual reality applications. The possibilities are vast.

Magnetically regulated gene therapy tech offers precise brain-circuit control

A gene therapy allows precise magnetic field control of specific brain circuits without implanted devices. The image shows restricted mRNA expression of the genetically encoded magnetic sensor (red) in dopaminergic neurons type 2 (green) in the mouse striatum that regulate initiation of movement. Dopaminergic neurons type 1 (cyan) and cell nuclei shown with dapi staining (blue). Credit: Dr. Santiago Unda.

A new technology enables the control of specific brain circuits non-invasively with magnetic fields, according to a preclinical study from researchers at Weill Cornell Medicine, The Rockefeller University and the Icahn School of Medicine at Mount Sinai. The technology holds promise as a powerful tool for studying the brain and as the basis for future neurological and psychiatric treatments for conditions as diverse as Parkinson's disease, depression, obesity and complex pain.

The new gene-therapy technology is described in a paper published Oct. 9 in *Science Advances*. The researchers performed experiments in mice showing that it can switch on or off selected populations of neurons, with clear effects on the animals' movements. In one experiment, they used it to reduce abnormal movements in a mouse model of Parkinson's disease.

"We envision that magnetogenetics technology may someday be used to benefit patients in a wide range of clinical settings," said study senior author Dr. Michael Kaplitt, professor and executive vice-chairman of neurological surgery at Weill Cornell Medicine and director of Movement Disorders Surgery at NewYork-Presbyterian/Weill Cornell Medical Center.

The study was a collaboration between Dr. Kaplitt's laboratory and the laboratories of Dr. Jeffrey Friedman, the Marilyn M. Simpson Professor in the Laboratory of Molecular Genetics at The Rockefeller University; and Dr. Sarah Stanley, an assistant professor in the Department of Medicine at the Icahn School of Medicine at Mt. Sinai. The study's first author was Dr. Santiago Unda, a postdoctoral researcher in Dr. Kaplitt's laboratory.

Controlling brain circuits in real-time, in a way that allows animals—or humans—to move around normally, has been a major goal for neuroscientists, but a very challenging one. In the laboratory, optogenetics technology, for example, can make selected neurons switch on or off immediately with light pulses, but requires an invasive apparatus for delivering those light pulses to the brain. In the clinic, deep brain stimulation permits modulation of brain regions, but this also requires a permanently implanted device and greater precision also remains a goal.

After doing early work on magnetogenetic technology as an alternative to other approaches, Dr. Friedman and Dr. Stanley joined forces with Dr. Kaplitt, a pioneer of brain-targeted gene therapies, to develop a method of this type with the potential for clinical applications.

The resulting approach uses gene therapy techniques to deliver an engineered ion-channel protein to a desired type of neuron. The ion channel protein essentially works as a switch to turn affected neurons on or off, and is sensitive to a magnetic field because it includes an antibody-like protein that sticks to a natural iron-trapping protein called ferritin.

While the gene therapy is delivered to precise brain regions through a minimally invasive surgery, a sufficiently strong magnetic field can then exert enough force on the ferritin-trapped iron atoms to open or close the channel—activating the neuron or inhibiting it, depending on the design, without the need for an implanted device or drug.

In one proof of concept, the team injected the gene therapy for the magnetically sensitive channels into specific neurons within a movement-controlling region called the striatum in mice; they then used the magnetic field from a magnetic resonance imaging machine to activate the neurons and markedly slow, even freeze, the mice's movements. In another experiment, they reduced neuronal activity in a brain region called the subthalamic nucleus to ameliorate movement abnormalities in a parkinsonism mouse model.

The researchers showed that their method can work even when using a much smaller and less expensive "transcranial magnetic stimulation" device, which is often used currently in the clinic to treat patients with depression, migraine and other conditions.

The experiments uncovered no safety issues, and the researchers note that normal ambient magnetic fields would be far too weak to trigger magnetogenetic switches inadvertently.

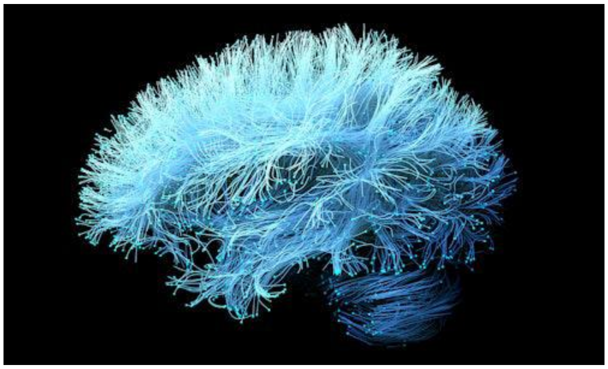
The team now intends to explore potential clinical applications including treatments for psychiatric disorders and even chronic pain in peripheral nerves. They also will continue to explore and optimize the magnetogenetics technology itself.

"Being able now to do directional manipulations of brain activity with this relatively simple system is going to be very important in helping us better understand the underlying principles to help further advance this new technology," Dr. Unda said.

More information: Santiago R. Unda et al, Bidirectional regulation of motor circuits using magnetogenetic gene therapy, *Science Advances* (2024). DOI: 10.1126/sciadv.adp9150

Provided by Weill Cornell Medical College

Brain Scans Of Jazz Musicians Could Unlock The Mystery Of Creative Flow



Flow, or being "in the zone," is a state of amped-up creativity, enhanced productivity, and blissful consciousness that, some psychologists believe, is also the secret to happiness. It's considered the brain's fast track to success in business, the arts, or any other field.

However, in order to achieve flow, a person must first develop a strong foundation of expertise in their craft. That's according to a new neuroimaging study from Drexel University's Creativity Research Lab, which recruited Philly-area jazz guitarists to better understand the key brain processes that underlie flow. Once expertise is attained, the study found that this knowledge must be unleashed and not overthought in order for the flow to be reached.

As a cognitive neuroscientist who is the senior author of this study and a university writing instructor, we are a husband-and-wife team who collaborated on a book about the science of creative insight. We believe that this new neuroscience research reveals practical strategies for enhancing, as well as elucidating, innovative thinking.

Jazz musicians in flow

The concept of flow has fascinated creative people ever since pioneering psychological scientist Mihály Csíkszentmihályi began investigating the phenomenon in the 1970s.

Yet, a half-century of behavioral research has not answered many basic questions about the brain mechanisms associated with the feeling of effortless attention that exemplifies flow.

The Drexel experiment pitted two conflicting theories of flow against each other to see which better reflects what happens in people's brains when they generate ideas. One theory proposes that flow is a state of intensive hyperfocus on a task. The other theory hypothesizes that flow involves relaxing one's focus or conscious control.

The team recruited 32 jazz guitarists from the Philadelphia area. Their level of experience ranged from novice to veteran, as quantified by the number of public performances they had given. The researchers placed electrode caps on their heads to record their EEG brain waves while they improvised chord sequences and rhythms that were provided to them.

Jazz improvisation is a favorite vehicle for cognitive psychologists and neuroscientists who study creativity because it is a measurable real-world task that allows for divergent thinking – the generation of multiple ideas over time.

The musicians themselves rated the degree of flow that they experienced during each performance, and those recordings were later played for expert judges who rated them for creativity.

Train intensively, then surrender

As jazz great Charlie Parker is said to have advised, "You've got to learn your instrument, then, you practice, practice, practice. And then, when you finally get up there on the bandstand, forget all that and just wail."

This sentiment aligns with the findings of the Drexel study. The performances that the musicians self-rated as high inflow were also judged by the outside experts as more creative. Furthermore, the most experienced musicians rated themselves as being in flow more than the novices, suggesting that experience is a precondition for flow. Their brain activity revealed why.

The musicians who were experiencing flow while performing showed reduced activity in parts of their frontal lobes, which are known to be involved in executive function or cognitive control. In other words, flow was associated with relaxing conscious control or supervision over other parts of the brain.

When the most experienced musicians performed while in a state of flow, their brains showed greater activity in areas known to be involved in hearing and vision, which makes sense given that they were improvising while reading the chord progressions and listening to rhythms provided to them.

In contrast, the least experienced musicians showed very little flow-related brain activity.

Flow vs. nonflow creativity

We were surprised to learn that flow-state creativity is very different from nonflow creativity.

Previous neuroimaging studies suggested that ideas are usually produced by the default-mode network, a group of brain areas involved in introspection, daydreaming, and imagining the future. The default-mode network spews ideas like an unattended garden hose spouts water without direction. The aim is provided by the executive-control network, residing primarily in the brain's frontal lobe, which acts like a gardener who points the hose to direct the water where it is needed.

Creative flow is different: no hose, no gardener. The default mode and executive control networks are tamped down so that they cannot interfere with the separate brain network that highly experienced people have built up for producing ideas in their field of expertise.

For example, knowledgeable but relatively inexperienced computer programmers may have to reason their way through every line of code. Veteran coders, however, tapping their specialized brain network for computer programming, may just start writing code fluently without overthinking it until they complete – perhaps in one sitting – a first-draft program.

Coaching can be a help or hindrance

The findings that expertise and the ability to surrender cognitive control are key to reaching flow are supported by a 2019 study from the Creativity Research Lab. For that study, jazz musicians were asked to play “more creatively.” Given that direction, the nonexpert musicians were indeed able to improvise more creatively. That is apparently because their improvisation was largely under conscious control and could, therefore, be adjusted to meet the demand. For example, during debriefing, one of the novice performers said, “I wouldn’t use these techniques instinctively, so I had to actively choose to play more creatively.”

On the other hand, the expert musicians, whose creative process was baked in through decades of experience, were not able to perform more creatively after being asked to do so. As one of the experts put it, “I felt boxed-in, and trying to think more creatively was a hindrance.”

The takeaway for musicians, writers, designers, inventors, and other creatives who want to tap into flow is that training should involve intensive practice followed by learning to step back and let one’s skill take over. Future research may develop possible methods for releasing control once sufficient expertise has been achieved.

Fascinating Facts About the Human Brain

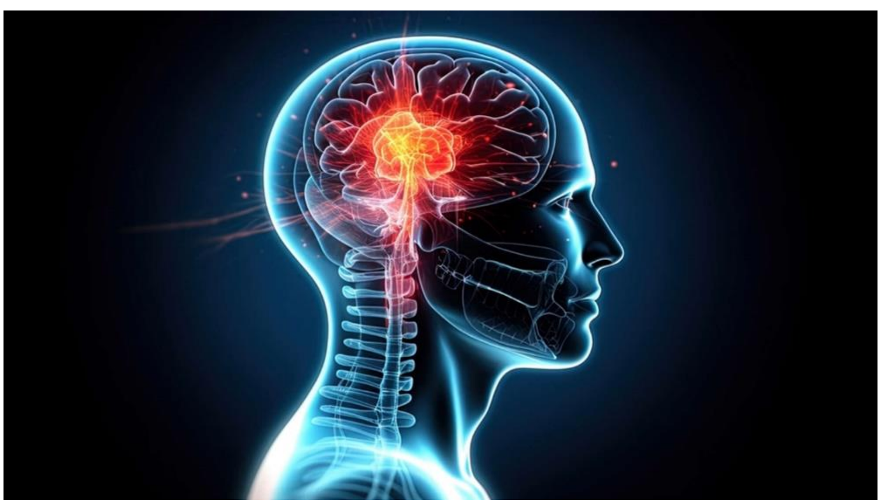
Prepare to be amazed as we delve into the extraordinary world of the human brain! This incredible organ not only orchestrates our thoughts, emotions, and behaviors but also holds secrets that are as fascinating as they are vital to understanding ourselves. From its astonishing capacity to generate electricity to its ability to adapt and heal, join us as we explore some of the most interesting and surprising facts about the human brain that will surely captivate your curiosity.

The Brain’s Water Content

The human brain is approximately 75% water. This high water content is crucial as it helps maintain chemical processes, delivers nutrients to brain cells, and removes waste. Dehydration, even in small amounts, can affect cognitive function and the ability to think clearly.

Neuron Count

There are roughly 86 billion neurons in the human brain. Each neuron is capable of forming thousands of connections with other neurons, leading to an almost infinite number of potential neural pathways. This vast network is what allows for the complexity of human thought, memory, and emotion.



Electrical Power

The brain operates on the same amount of power as a 10-watt light bulb, even when you’re sleeping. The electrical activity generated by the brain is enough to power a small light bulb, highlighting the organâ€s efficiency and energy management.

Blood Vessels Length

If stretched out, the blood vessels in the brain would be about 100,000 miles long. This extensive network ensures that brain cells receive a constant supply of oxygen and nutrients essential for optimal function.

New Neurons

The adult human brain can grow new neurons, a process known as neurogenesis. Primarily occurring in the hippocampus, this phenomenon is vital for learning and memory. It challenges the old belief that adults cannot grow new brain cells.

Brain Weight

The average adult human brain weighs about 3 pounds, which is about 2% of total body weight. Despite its weight, it uses about 20% of the body’s energy and oxygen intake, emphasizing its importance and metabolic demand.

Synapses

For each neuron, there can be between 1,000 to 10,000 synapses, amounting to over 100 trillion in total. This immense network of connections is what allows for complex thought, learning, and the formation of memories.

Speed of Information

Information in the brain travels at different speeds but can be as fast as 270 miles per hour. This fast processing speed enables quick reflex responses and seamless coordination of physical actions.

Oxygen Usage

The brain consumes about 20% of the oxygen we breathe in. Its high oxygen use reflects its intense metabolic activity, required for maintaining normal cognitive and neurological functions.

The Visual Brain

Around 30% of the brainâ€s cortex is devoted to visual processing, more than any other sense. This extensive area highlights the importance of vision in human evolution and function.

Memory Capacity

The storage capacity of the human brain is considered to rival about 2.5 petabytes of binary data, which is equivalent to about three million hours of TV shows. This vast capacity allows humans to store a tremendous amount of information over a lifetime.

Protective Blood-Brain Barrier

The brain is protected by a selective barrier called the blood-brain barrier, which prevents most substances in the blood from entering the brain. This feature is essential for protecting the brain from pathogens and toxins.

The Brain's Clock

The suprachiasmatic nucleus in the brain acts as the master clock, coordinating all the biological clocks in a human body, regulating circadian rhythms, and ensuring timely hormone release for sleep and other body functions.

Processing Power

The human brain can process images the eye sees for as little as 13 milliseconds much faster than a blink, which takes about 100 to 400 milliseconds. This rapid processing ability is critical for quick reactions and seamless visual understanding.

Language and the Brain

The brain's left hemisphere is predominantly responsible for language abilities in right-handed individuals. This lateralization shows how certain high-level functions are compartmentalized within the brain.

Brain Growth

The human brain continues to grow until about the age of 25. This extended period of development is crucial for the maturation of advanced cognitive functions and emotional regulation.

Neural Plasticity

The brain has the remarkable ability to reorganize itself by forming new neural connections throughout life. This plasticity allows for learning new skills, adapting to new environments, and recovering from injuries.

Gamma Waves

The brain can produce gamma waves, which have a frequency of about 25 to 100 Hz and are associated with higher mental activity, including perception, problem-solving, and consciousness.

Fascinating neuroscience research reveals a key mechanism underlying human cognition

How does the brain adapt to different levels of mental challenge? A new neuroimaging study reveals that when we engage in more complex cognitive tasks, our brain activity becomes not only richer in detail but also more streamlined. The findings suggest that the brain adjusts its patterns of activity to match the demands of the task, allowing for more efficient processing during mentally challenging activities.

The study, published in the *Proceedings of the National Academy of Sciences*, was driven by a desire to understand how the brain manages different cognitive demands. Previous research by the same team had revealed the brain's remarkable ability to reconstruct missing data from minimal measurements, raising questions about why the brain can generate such detailed and efficient activity patterns with limited input.

"Several years ago, my co-author and graduate student at the time, Lucy Owen, and I came out with a precursor to this study, where we found something very surprising," explained study author Jeremy Manning, an associate professor of psychological and brain sciences at Dartmouth College and director of the Contextual Dynamics Lab.

"At the time, we were working with neurosurgical patients who had electrodes implanted in their brains to monitor for seizure activity. A challenge with working with those recordings is that our brains contain roughly a hundred billion neurons, but we can only safely implant around a few hundred wires into someone's brain. So there is a massive undersampling problem: for every measurement we take, we miss roughly a billion others! We wanted to understand how much of that ‘missing’ data we could reliably and accurately reconstruct using statistical ‘hacks.'”

“We were very surprised to find that just a few hundred measurements from an essentially random sampling of locations throughout someone’s brain could give us enough information to fill in an accurate guess about activity patterns throughout their entire brain, at millimeter-scale resolutions (roughly on par with the best fMRI available today), but at millisecond-scale sampling rates (roughly 1000 times faster than fMRI),” Manning said. “If human language was similarly efficient, I’d be able to tell you the details of every Wikipedia article just by speaking a dozen or so words.”

“In that initial study, we were primarily concerned with the ‘how’ and ‘what’ aspects of our approach: in other words, we reported how we built our model and generated guesses, how we validated the guesses, and the circumstances that affected accuracy, and so on. But it left us with a much deeper question that we weren’t able to answer back then: why is it possible to reconstruct what nearly our entire brain is doing at a given moment, using a comparatively miniscule number of measurements? That led us down a rabbit hole of additional questions about the fundamental properties of brain activity patterns. Our findings are reported in this new study.”

To answer these deeper questions about how the brain adjusts its activity to match cognitive demands, the researchers examined a dataset collected from previous neuroimaging experiments. These experiments involved functional magnetic resonance imaging (fMRI) scans of participants as they listened to different audio recordings.

Some participants listened to a coherent, seven-minute story, while others listened to a scrambled version of the story, in which either the paragraphs or individual words were randomly ordered. A final group underwent a resting state scan with no auditory stimulus, meant to simulate a condition of minimal cognitive engagement.

The goal was to analyze how the brain’s activity changed under these varying levels of cognitive demand. In a high-demand task—following a coherent story—the brain has to actively process and organize information to make sense of the narrative. In contrast, during the scrambled story conditions, the brain’s task is less cognitively challenging because the information is less meaningful. The resting state condition provided a baseline measure of brain activity in the absence of any specific cognitive task.

The authors sought to investigate two properties of brain activity: informativeness and compressibility. The authors hypothesized that these properties might shift depending on the complexity of a task, allowing the brain to strike a balance between flexibility and efficiency.

To assess the informativeness and compressibility of brain activity, the researchers used advanced computational techniques. They measured informativeness by analyzing how much specific information about the task was reflected in participants' brain activity. Compressibility, on the other hand, was evaluated by examining how efficiently the brain's activity patterns could be represented using fewer components or data points. A highly compressible brain pattern is one in which fewer pieces of information are needed to reconstruct the full activity.

"In the world of machine learning, the ability to reconstitute a detailed pattern from its parts is called 'compression,'" Manning told PsyPost. "Highly compressible patterns can be accurately rebuilt from just a tiny sliver, like reconstructing the complete text of a novel from just a single word. Another related property is called 'informativeness.' This refers to how 'expressive' a sequence of patterns is– akin to the length of a novel."

The researchers uncovered two key findings. First, brain activity was more informative and compressible when participants engaged in the more demanding task of listening to a coherent story compared to the scrambled story or resting conditions. This suggests that during higher-level cognitive tasks, the brain produces detailed, information-rich activity that is also organized efficiently. In simpler tasks, or during rest, the brain's activity is less organized and contains less specific information.

Second, the study found that these brain patterns became more informative and compressible over time as participants continued to listen to the coherent story. As the narrative unfolded, the brain seemed to adapt by refining and optimizing its activity patterns. This pattern was less pronounced in the scrambled conditions, where the lack of a coherent structure in the story likely led to less mental engagement and, consequently, less organization in the brain's activity.

“Going into this study, we would have guessed that ‘compression’ and ‘informativeness’ would have changed in opposite directions,” Manning said. “That would be analogous to either being able to reconstruct short novels from just a few words (perhaps under certain cognitive circumstances — representing high compressibility but low informativeness), or being able to reconstruct longer novels from more words (perhaps under different circumstances — representing low compressibility and high informativeness). Finding that compression and informativeness change in the same direction helped us to understand that these two aspects of how our brains respond can vary independently from each other.”

The researchers also took a closer look at different brain networks to see if certain regions were more affected by task complexity than others. They found that higher-order brain networks, which are typically associated with complex functions like decision-making and memory, showed more pronounced changes in informativeness and compressibility than lower-order networks, which are primarily involved in basic sensory processing. This supports the idea that the brain’s ability to adjust its activity is not uniform across all regions; instead, areas involved in more complex cognitive functions are especially responsive to task demands.

“We have known for a long time that our ‘thoughts’ come from patterns of electrical activity in our brains,” Manning told PsyPost. “What we found is that our brains seem to change the ‘language’ that those patterns are expressed in according to what we are doing. When we are highly engaged or thinking ‘deeply’ about what we are doing, our brains move into a mode where the activity patterns become both highly compressible and highly informative.”

“In other words, our brains start representing what we are doing or thinking about in a very efficient way that is also incredibly robust to data corruption. That helped us understand why, under the right circumstances, it becomes possible to accurately guess what someone’s entire brain is doing from just a few hundred measurements.”

“When we stop being engaged, or when we think more ‘shallowly’ about what we are doing, our brains switch into a much less efficient mode, where the activity patterns become less structured, less informative, and more idiosyncratic,” Manning continued. “We’re not totally sure why this happens, but we go through some speculations in our paper.”

The research provides valuable insights into the fundamental mechanisms of human cognition. But the study, like all research, has limitations. The study only examined a specific set of tasks and stimuli, which means that the results may not apply to all types of mental activities. Additionally, the researchers used one method of measuring brain activity—fMRI—which provides a detailed view of brain activity but is limited by its relatively slow sampling rate compared to other techniques.

"We looked at data from a little over 100 participants, using one set of experimental conditions, and using one method for measuring brain activity," Manning noted. "Although it is tempting to generalize to 'all humans and circumstances,' the true test of these findings, as with any study, will be in how well they replicate and generalize."

The researchers suggest that future studies could examine how the brain's ability to adjust informativeness and compressibility might apply to other cognitive processes, such as decision-making, problem-solving, or creativity. Understanding how these brain properties change in different contexts could offer new insights into the nature of cognition and how the brain adapts to a wide range of mental challenges.

Despite its limitations, the study provides a compelling look at how the brain organizes itself to meet the demands of complex tasks. The findings suggest that the brain's ability to adapt is not just a matter of activating more areas or working harder, but rather involves fine-tuning its activity patterns to balance flexibility and efficiency.

In the long term, this line of research could help scientists better understand how the brain supports higher-level cognitive functions and what happens when these processes break down, such as in conditions like dementia or traumatic brain injury. By identifying the mechanisms that allow the brain to optimize its activity for different tasks, researchers may eventually develop new interventions or treatments to support cognitive health and recovery.

"We are deeply curious about understanding fundamental questions about how our brains work, and what makes us 'us.' This line of work is a tiny part of a much broader literature aimed at uncovering the neural basis of thought," Manning said. "My website is www.context-lab.com. It has links to all of my lab's publications, data, and software, along with some open courses that could be of interest to people who want to learn more about this stuff."

The study, "High-level cognition is supported by information-rich but compressible brain activity patterns," was authored by Lucy L. W. Owen and Jeremy R. Manning.

Beyond reward: A new study offers a glimpse into how the brain learns

- Learning involves acquiring knowledge through experiences and adapting behaviors based on rewards or consequences.
- Dopamine plays a pivotal role in the brain's learning and decision-making processes.
- A new study in animals uses light to peer into cells, linking specific mouse actions to real-time dopamine release.

Learning is essential for survival and intelligence. It enables living things to navigate their world, make wise choices, and adjust their behaviors based on past experiences.

Learning is, among other things, about getting new information, abilities, or behavior patterns using experiences, research, or teaching. Trial and error helps organisms learn which behaviors get rewarded and which do not.

A critical part of learning is how our brains give value or importance to particular actions or behaviors based on their outcomes. This process is known as credit assignment and is a critical part of learning.

Understanding credit assignment is crucial for comprehending how organisms learn from their experiences, make decisions, and adapt their behavior to maximize positive outcomes.

A new study published in *Nature* by a group of scientists from Allen Institute, the Champalimaud Centre for the Unknown, Columbia University's Zuckerman Mind

Brain Behavior Institute, and Seattle Children's Research Institute explores this phenomenon in mice.

The researchers conducted a comprehensive study to understand how dopamine influences credit assignment in mice. In particular, they wanted to explore how the neurotransmitter shapes learning and behavior by reinforcing specific actions.

Understanding credit assignment in behavioral psychology is vital for understanding how organisms adapt, learn, and optimize behavior based on experiences. This process has implications for decision-making, skill acquisition, and potential clinical applications.

The role of dopamine

Dopamine, often referred to as the "feel-good" neurotransmitter in the brain, contributes to mood changes when its levels vary.

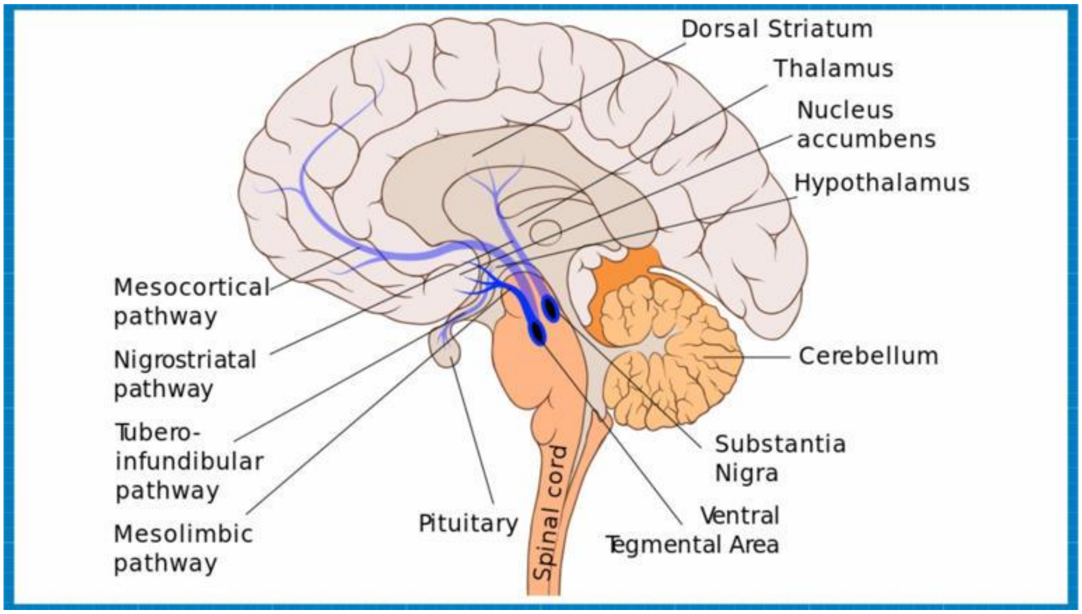
Dopamine originates in various parts of the brain, such as the substantia nigra and the ventral tegmental area. It is linked to motivation and pleasure and plays a major role in the brain's reward system.

For instance, when encountering pleasurable or rewarding experiences, like savoring a delightful meal or accomplishing a goal, dopamine is released. This release of dopamine reinforces the behaviors or actions that led to the positive experience, encouraging the individual to repeat those actions.

Dopamine is also involved in various cognitive processes, including learning, memory, and decision-making.

In the context of learning, the attribution of credit is fundamental for organisms to adapt their behavior and optimize their chances of experiencing favorable outcomes.

For example, when learning to play the guitar, actions like pressing the correct strings lead to positive outcomes, creating an association. The brain recognizes and reinforces these actions linked to favorable results through credit assignment.



The dopaminergic mesolimbic pathway in the brain. (Source: Slashme/Patrick J. Lynch/Fvasconcellos)© Provided by Interesting Engineering

Now that we have established what credit assignment is, let's go back to the research question: How does dopamine contribute to the assignment of credit for specific actions?

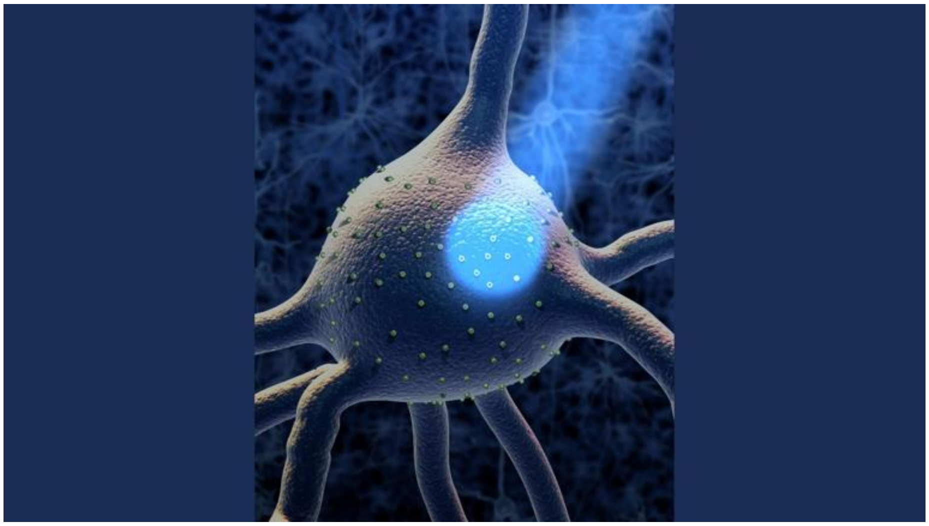
You might assume this is a purely academic pursuit. However, assigning credit accurately to actions allows organisms to learn from their experiences, make informed decisions, and modify their behavior to maximize positive outcomes.

What is closed-loop optogenetics?

To observe and manipulate the mice, the researchers used a closed-loop system that linked specific actions to dopamine release in real time. These mice were equipped with wireless sensors to monitor their behavior or movement.

The researchers used a technique called optogenetics to stimulate the dopamine neurons in mice. In simple terms, they used light to control the neurons.

By stimulating the dopamine neurons, the researchers were able to observe the mice's responses to the release of dopamine triggered by specific "target actions" (or specific outcomes).


Optogenetics involves controlling neurons with light. (Source: statenews website / hayadan website)© Provided by Interesting Engineering

The researchers used two distinct target actions (A and B) to study how the mice adjusted their behavior based on changes in the contingency between actions and closed-loop dopamine stimulation.

Closed-loop optogenetics gave the researchers a distinct edge by giving real-time feedback and control to them. This provided a more detailed understanding of how the brain refines behavior in response to reinforcement.

Reward and behavior

Learning action-reward contingencies

The researchers observed that the mice adapted to changes in action-reward contingencies by refining their behavioral repertoire. This means that in response to altered circumstances or learning experiences, the mice adjusted and improved their range of behaviors to optimize the likelihood of receiving rewards, especially dopamine release.

Temporal dynamics of reinforcement

The time between the mice's actions and dopamine release was crucial in shaping their behavioral repertoire dynamics. This means that the specific time relationship between actions and rewards significantly influenced how mice adjusted their behavior.

Furthermore, the study found that behavioral similarity and baseline temporal proximity were the main factors in predicting the type of action dynamics observed after reinforcement.

Behavioral similarity refers to the likeness or resemblance between different actions, and baseline temporal proximity relates to the time intervals between actions.

Overall, this emphasizes the importance of time-related factors in how mice adapt their behavior to dopamine stimulation.

Individual learning differences

Among the mice in the study, there were differences in how quickly they learned. The speed of learning was correlated with the initial time gap between triggers (stimuli that led to dopamine release).

Mice with different learning speeds also showed distinct patterns in their behavioral response refinement.

Credit assignment for action sequences

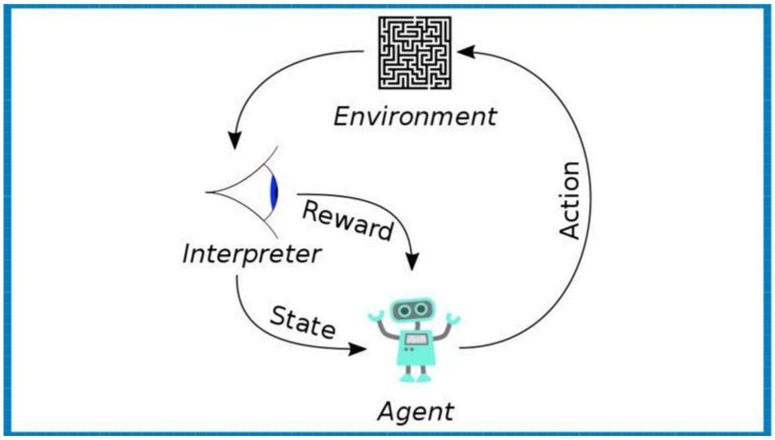
The researchers found that the mice could learn sequences of actions, which led to dopamine stimulation.

This finding emphasizes the complexity of learning action sequences and the influence of dopamine in reinforcing specific behavioral patterns.

Retrospective reinforcement

The study supported the concept of retrospective reinforcement, where behavior leading to dopamine stimulation was reinforced even if it was delayed.

Retrospective reinforcement contributed to the gradual refinement of behavioral repertoires over time.



A typical reinforcement learning system. (Source: Megajuice)© Provided by Interesting Engineering

"When you reinforce behavior, we often think it's just that action. But no: you're changing the entire behavioral structure. And what was really surprising was how rapid it was," said Dr. Rui Costa, the President and CEO of the Allen Institute, in a press release.

Conclusion

So there we have it; rewards don't just reinforce certain actions; they completely change how we behave, and quickly so!

The observed dynamic adaptation to changing action-reward dependencies provides a peek into neural plasticity. This prompts further investigation into the cellular and synaptic mechanisms at play.

Beyond the lab setting, these findings could have wide-ranging implications in behavioral psychology. They offer a valuable perspective on human and animal behavior in reward-based learning.

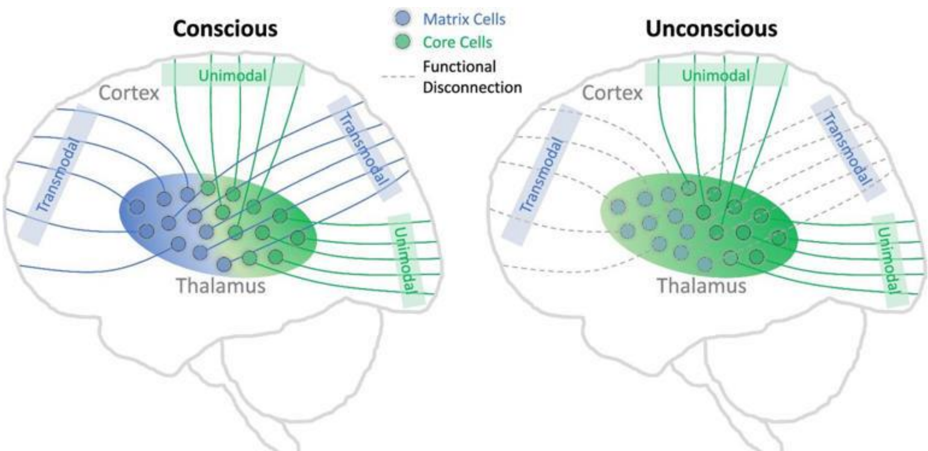
The use of closed-loop optogenetics introduces a new approach, providing unmatched control over neural circuits. Looking forward, this technology invites further exploration into various aspects of neural modulation and behavior.

On the clinical front, the study has revealed promising insights into dopamine-mediated reinforcement. They could contribute to a better understanding of neurological and psychiatric disorders linked to dopamine dysregulation, potentially guiding future research on therapeutic interventions.

The researchers suggest a potential impact on education by emphasizing exploration and gradual refinement aligned with natural learning processes.

Additionally, replicating biological learning could enhance the adaptability of artificial intelligence systems to new data and situations, fostering more sophisticated learning mechanisms.

How the brain's inner chamber governs our state of consciousness



Schematic illustration of the primary conclusion. Credit: Nature Communications (2024). DOI: 10.1038/s41467-024-51837-1

In hospital operating rooms and intensive care units, propofol is a drug of choice, widely used to sedate patients for their comfort or render them fully unconscious for invasive procedures.

Propofol works quickly and is tolerated well by most patients when administered by an anesthesiologist. But what is happening inside the brain when patients are put under and what does this reveal about consciousness itself?

Investigators at U-M who are studying the nature of consciousness have successfully used the drug to identify the intricate brain geometry behind the unconscious state, offering an unprecedented look at brain structures that have traditionally been difficult to study.

"Consciousness has been the subject of study from various perspectives and understanding the neurobiological foundations of consciousness carries major implications of multiple medical disciplines such as neurology, psychiatry and anesthesiology," said Zirui Huang, Ph.D., Research Assistant Professor in the Department of Anesthesiology at U-M Medical School.

To date, researchers have debated about how anesthetics suppress consciousness. Specifically, whether the site of action lies primarily in the thalamus, an egg-shaped structure deep within the brain, which receives information from what we see, touch and hear, or in the cerebral cortex, which processes that information in complex ways.

A study published in the journal *Nature Communications* and led by Huang, George Mashour, M.D., Ph.D. and Anthony G. Hudetz, Ph.D., of the U-M Center for Consciousness Science, outlines for the first time in humans how the connections among brain cells within those two important areas are modified by propofol. The paper is titled "Propofol Disrupts the Functional Core-Matrix Architecture of the Thalamus in Humans."

In healthy volunteers, they mapped changes in the brain's architecture before, during and after propofol sedation, guided by functional magnetic resonance imaging (fMRI). This enabled them to monitor blood flow to areas of the brain as the study participants entered and exited an unconscious state.

At baseline, explained Huang, the thalamus has a balanced level of activity of both specific nuclei (clusters of brain cells) that send sensory information to highly defined areas of the cortex—known as unimodal processing—and nonspecific nuclei that send information more diffusely throughout a higher layer of the cortex, known as transmodal processing.

The team found that, under deep sedation, the thalamus showed a drastic reduction in activity in clusters of brain cells responsible for transmodal processing, leading to a dominant unimodal pattern—suggesting that while sensory inputs are still received, there is no integration of those inputs.

"The field has been focusing on anesthetic effects in the thalamus and cortex for more than two decades—I believe this study significantly advances the neurobiology," said George Mashour, M.D., Ph.D., Professor of Anesthesiology and Pharmacology, and founder of the U-M Center for Consciousness Science.

Next, they discovered the specific cell types that played a role in the shift to an unconscious state and their relationship to the change in thalamic processing. The thalamus contains at least two distinct cell types, said Huang, core cells and matrix cells.

"We now have compelling evidence that the widespread connections of thalamic matrix cells with higher order cortex are critical for consciousness," says Hudetz, Professor of Anesthesiology at U-M and current director of the Center for Consciousness Science.

Imagining that the cortex is layered like an onion, core cells connect to lower layers while matrix cells connect to higher layers in a more spread-out manner.

By measuring mRNA expression signatures—like I.D. badges for the cells—they were able to see that a disruption in the activity of matrix cells played a greater role in the transition to unconsciousness than core cells. An additional surprise was that GABA, a major inhibitory transmitter in the brain usually thought to be key to propofol's actions, did not appear to play as prominent a role as expected.

"The results suggest that loss of consciousness during deep sedation is primarily associated with the functional disruption of matrix cells distributed throughout the thalamus," said Huang.

More information: Huang, Z., et al. Propofol disrupts the functional core-matrix architecture of the thalamus in humans. *Nature Communications* (2024). DOI: 10.1038/s41467-024-51837-1

Provided by University of Michigan

NASA says that warp drive is getting closer to reality

he sci-fi TV series Star Trek has captivated audiences since it first aired, blending real-life science with fiction in ways that have sparked technological innovations. One of the most fascinating concepts presented in the series is warp drive, an idea that has challenged Einstein's Theory of Relativity by proposing travel at speeds exceeding that of light.

Theoretical physicist Miguel Alcubierre developed the Alcubierre drive in 1994, a theory suggesting that a bubble within space-time could twist distances, making faster-than-light travel possible. This idea, while theoretically sound, was deemed impractical by many.

However, Joseph Agnew, an undergraduate from the University of Alabama, aimed to test this theory. "Mathematically if you fulfill all the energy requirements, they can't prove that it doesn't work," Agnew stated in a university press release.

He explained, "Suppose you have a craft that's in the bubble. What you would do is, you'd compress space-time ahead of the craft and expand space-time behind it."

A ring-shaped warp drive device could transport a football-shape starship (center) to effective speeds faster than light. The concept was first proposed by Mexican physicist Miguel Alcubierre. (CREDIT: Harold White)© The Brighter Side of News

Einstein's theory, however, presents a significant challenge. According to relativity, as objects travel faster, they gain mass, making it increasingly difficult to achieve acceleration. Essentially, reaching the speed of light is impossible because it would require infinite energy.

So, what exactly is warp drive? Often referred to as the holy grail of space exploration, warp drive is a propulsion system concept that would allow travel faster than light. With such a system, humanity could theoretically reach any corner of the galaxy.

Despite the constraints of Einstein's Theory of Relativity, the idea of warp drive remains compelling. While traditional views on interstellar travel at light speed seem absurd, science fiction writers have fueled our hopes with imaginative depictions of such journeys.

Einstein's theory explains that nothing can travel faster than light due to the infinite energy required to accelerate an object to that speed. Photons, the particles of light, avoid this problem because they have no mass. Consequently, a spacecraft traveling at light speed is currently impossible.

There are, however, two potential loopholes. First, the focus could shift from achieving light speed to approaching it as closely as possible. Second, the Alcubierre warp drive theory proposes bending the laws of physics to circumvent the universal speed limit. By warping space-time, this drive could enable travel at ten times the speed of light without violating general relativity.

The theory posits that a spacecraft could sit within a warp bubble surrounded by a ring of negative mass. This ring would compress space-time ahead of the ship and expand it behind, allowing for faster-than-light travel. Within the bubble, the spacecraft would still adhere to the universal speed limit while moving at extraordinary speeds relative to outside observers.

The Alcubierre Warp Drive Model. The blue area below the plane represents contracted space while red and raised area represent expanded space. (CREDIT: Harold White)© The Brighter Side of News

A significant challenge to this theory is the enormous amount of mass-energy required. To propel a spacecraft using the Alcubierre drive, one would need mass equivalent to that of Jupiter. According to Einstein's equation, $E=mc^2$, this represents an immense amount of energy, far beyond what the universe can currently provide.

Dr. Harold "Sonny" White, a NASA mechanical engineer and physicist, is working to address this issue. He believes it might be possible to reduce the mass-energy requirement by altering the shape of the negative mass ring. This could potentially lower the mass needed to around 700 kg.

White leads a team of physicists and engineers at NASA in building the White-Juday Warp Field Interferometer, a device designed to detect and generate the tiniest warp bubbles. While this technology might not immediately enable travel to distant galaxies like Andromeda, it represents a significant step toward making warp drive a reality.

Despite these advancements, we remain far from achieving interstellar travel and warp drive. Yet, ongoing technological progress brings us closer to finding the answers. Star Trek predicted the invention of warp drive in 2063. While that date remains in the future, continued research and innovation may one day turn this science fiction concept into science fact.

Other theories for the development of warp drive

Aside from Joseph Agnew's Alcubierre model theory, here are some other warp drive theories and concepts currently being explored:

White-Juday Warp Field Interferometer Harold "Sonny" White, a NASA scientist, proposed adjustments to the Alcubierre model to make the concept more feasible. He suggested that shaping the warp bubble into a torus could reduce the energy requirements by orders of magnitude, theoretically making it possible to create a smaller warp bubble around a craft. Challenges: Despite energy reductions in theory, creating even this smaller warp bubble still demands technologies and materials that are currently beyond our reach. Casimir Effect and Negative Energy The Casimir effect demonstrates how quantum fluctuations between two closely spaced objects can create negative energy, which may contribute to warp drive development. This approach is still in the early stages and primarily focuses on understanding if and how we can harness negative energy on a larger scale. Challenges: Controlling and generating enough negative energy is currently beyond our technological capabilities, and more research into quantum field theory is needed. Manipulating Extra Dimensions (Brane Cosmology) Some theories in string theory and brane cosmology propose that our universe may have extra spatial dimensions. If this is true, it might be possible to "shortcut" through these dimensions, effectively enabling faster-than-light travel without violating relativity. This idea is closely related to the concept of wormholes, another theoretical method for FTL travel. Challenges: This theory is still highly speculative and lacks empirical support, as no direct evidence of extra dimensions or brane structures has been found.

Warp Drive with Quantum Field Theory Adjustments Some researchers have explored modifications to quantum field theory that could make warp drives more feasible. This approach involves exploring how quantum fields interact with spacetime and whether these interactions can be controlled or utilized to create stable warp bubbles. Challenges: Current quantum field theory modifications remain largely theoretical, and experimental methods to test these ideas are not yet available. Dark Energy Manipulation Since dark energy is thought to drive the accelerated expansion of the universe, some have theorized that manipulating dark energy could enable us to create similar expansion and contraction effects in local space around a spacecraft. Challenges: Dark energy is one of the least understood aspects of physics, and manipulating it remains speculative. Researchers would first need to identify a way to harness dark energy in controlled settings.

Each of these theories faces significant obstacles due to the requirement for exotic matter, negative energy, or extremely advanced technologies that we do not yet possess. However, advances in quantum field theory, energy manipulation, and fundamental physics could potentially make warp drive—or something like it—more feasible in the far future.

MIT researchers have developed a new type of 3D transistor that could be more energy-efficient and powerful than current silicon-based transistors.

The novel 3D transistors have been designed using ultrathin semiconductor materials.

“This is a technology with the potential to replace silicon, so you could use it with all the functions that silicon currently has, but with much better energy efficiency,” said Yanjie Shao, an MIT postdoc and lead author.

The transistors harness quantum mechanics to achieve high performance at low voltage within a nanoscale area.

Their minuscule size paves the way for a new era of ultra-dense, high-performance, and energy-efficient electronics.

Overcoming limitations

Silicon transistors function as electronic switches. A simple voltage application triggers a dramatic state change in the transistor, from off to on. This on/off state represents binary digits, enabling computation.

The efficiency of a transistor is linked to its switching slope. A steeper slope directly correlates to lower energy consumption. This means that the transistor can be switched on and off quickly, requiring less time and, consequently, less energy.

However, a fundamental limitation known as Boltzmann tyranny imposes a minimum voltage requirement for transistor operation at room temperature.

This limit is generally found in silicon transistors.

To overcome it, these new transistors use ultrathin semiconductor materials and quantum mechanics to achieve high performance at low voltage.

MIT researchers turned to gallium antimonide and indium arsenide semiconductor materials.

Furthermore, they incorporated quantum tunneling principles into their device architecture. In this phenomenon, electrons can penetrate potential barriers.

“Now, you can turn the device on and off very easily,” Shao added.

The transistor’s unique geometry

However, tunneling transistors often suffer from low current output. This limitation hinders their performance in demanding applications that require high currents for efficient operation.

To address this, the engineers worked on the 3D geometry of the transistors. For this, they fabricated nanowire heterostructures with a diameter of only 6 nanometers.

This led to the creation of the “smallest 3D transistors reported to date.”

Thanks to quantum confinement, this technique helped them achieve sharp switching slopes and high current. Quantum confinement occurs when electrons are restricted to tiny spaces.

This confinement unlocks the potential for enhanced tunneling, revolutionizing device performance.

“We have a lot of flexibility to design these material heterostructures so we can achieve a very thin tunneling barrier, which enables us to get very high current,” Shao said.

During testing, the devices exhibited sharper switching slopes than conventional silicon transistors. This means they can switch states more rapidly and efficiently, opening the door to faster and more energy-efficient electronic devices.

According to the press release, the MIT devices demonstrated a 20-fold performance improvement compared to similar tunneling transistors.

“This is the first time we have been able to achieve such sharp switching steepness with this design,” Shao noted.

The researchers are working to improve the fabrication process to ensure consistent transistor performance across the entire chip.

To further enhance uniformity, they are investigating alternative 3D transistor designs, such as vertical fin-shaped structures.

The findings were published in the journal *Nature Electronics.*

Researcher explores how you can stretch your mind to grasp quantum entanglement

My new article, "Quantum Entanglement of Optical Photons: The First Experiment, 1964–67," is intended to convey the spirit of a small research project that reaches into uncharted territory. The article breaks with tradition, as it offers a first-person account of the strategy and challenges of the experiment, as well as an interpretation of the final result and its significance. In this guest editorial, I will introduce the subject and also attempt to illuminate the question "What is a paradox?"

Let's begin with the gyroscope that I bought when I was eight, from a store that sold novelties and magic tricks. The spinning disk, supported at one end of its shaft, did not fall, but moved slowly around in a horizontal plane. This behavior seems mysterious or paradoxical in the context of common experience that excludes gyroscopes, but makes complete sense in the context of Newtonian mechanics, which resolves the paradox by predicting precisely how gyroscopes will behave.

Quantum theory, conceived in the mid-1920s, has been impressively successful in accounting for the properties and interactions of atoms and molecules. In 1935, Einstein, Podolsky, and Rosen stirred controversy with a thought experiment in which two particles of common origin move apart, noting that quantum theory predicts correlations in subsequent measurements of their spins. The correlation may seem quite puzzling, as a measurement on one of the particles appears to influence a subsequent measurement on the other, even if the particles do not interact.

In current terminology, these correlations are an example of entanglement, and the correlation phenomenon is known as the EPR paradox. The puzzle has become a subject for much discussion and analysis, especially because there was (and is) no known mechanism for measurements to communicate with each other.

Disentangling entanglement

In 1964, I was intrigued by this unfamiliar effect and began to think of a way to actually perform the EPR experiment—or at least a version of it— by observing the correlation and entanglement. It would be a low-energy experiment that could be set up in a small laboratory.

For the experiment outlined here, the particles of interest are visible-light photons, which are noninteracting, emitted by excited calcium atoms in a two-stage spontaneous emission process. The polarization states of the photons, which are related to their spins, can be measured simply, with ordinary linear polarizers. Photomultiplier detectors count the individual photons, #1 (green) and #2 (violet), and timing circuits enable the identification of photon pairs from the same atom. A rotatable linear polarizer is mounted in front of each detector.

In the simplest terms, the experiment involves counting the rate at which photon pairs are detected, as a function of the orientation of the polarizers. A photon pair detected from the same atom is recorded as a "coincidence count."

Quantum theory makes the following predictions:

1. Each photon, taken separately, has a 50% chance of being transmitted by its polarizer, regardless of its angle of orientation.
2. If the polarizer axes are parallel, both photons from the same atom can pass through their polarizers and be counted. Coincidence counts will be observed.
3. If the polarizer axes are perpendicular, it never happens that both photons pass through their polarizers. Therefore, no coincidence counts will be observed.

Predictions #1 and #2 are not surprising, as the green and violet beams of light are unpolarized.

Prediction #3, discussed further in my article, is a quantum entanglement effect with no analog in classical (non-quantum) physics. It is especially interesting because it can be tested experimentally. I designed the experiment specifically for this purpose.

The results of the experiment, after nearly three years of effort in the laboratory, clearly demonstrate that coincidence counts are recorded if the polarizer axes are parallel, and that no coincidences are recorded if the polarizers are perpendicular. The agreement between theory and experiment is unequivocal and striking.

So, is there a paradox?

In our brief discussion of the gyroscope, no paradox was acknowledged because Newton's theory (classical dynamics) fully explains how a gyroscope moves. Furthermore, both the theory and the observed gyroscopic behavior are compatible with our life experience and intuitive ability to grasp natural processes in the classical realm.

In the entanglement case, quantum theory accounts for the observed correlation of the photon polarizations. But even when a theory predicts experimental results, a paradox may remain if the intuition cannot reach out to connect with it.

Take another look at predictions #1 and #3 above. If we draw on our experience of life in a non-quantum world, we may notice something very strange when the polarizers are "crossed" at 90 degrees. If each photon has a 50% chance of transmission through its polarizer, why don't we get coincidences 25% of the time? Instead, we observe none at all.

On first consideration, this does seem to qualify as a paradox. One possible explanation could involve a missing component of quantum theory—perhaps a causal mechanism that could allow one photon, or one measurement, to communicate with the other. However, despite extensive research, no evidence has been found for such a mechanism.

As we do not live in an overtly quantum world, classical phenomena may influence our thought processes—even when we venture into the quantum realm. It may therefore remain a challenge to assimilate entanglement into the intuition. I believe that the paradox can be at least partially resolved when further thought and experience, such as the experiment considered here, 'stretch the mind' to more fully embrace entanglement and other quantum phenomena.

I have come to view these aspects of nature as "strangely wonderful."

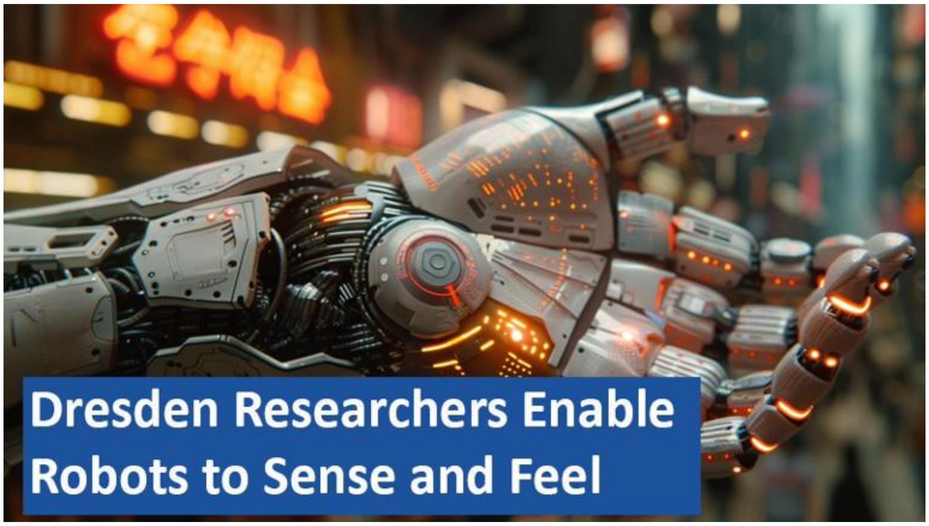
More information: Quantum Entanglement of Optical Photons: The First Experiment, 1964-67, *Frontiers in Quantum Science and Technology* (2024). DOI: 10.3389/frqst.2024.1451239

Provided by Frontiers

Dresden Researchers Enable Robots to Sense and Feel

To expand the capabilities of robots, scientists in Dresden have developed robotic hands with advanced sensing abilities. Inspired by nature, these robotic hands use sensor integration and 3D printing to replicate the delicate touch of a human hand. This breakthrough could pave the way for robots that harvest crops, assemble products, or explore remote terrains with greater dexterity and control.

Nature-Inspired Robotics for Enhanced Dexterity



Dresden Researchers Enable Robots to Sense and Feel© Provided by Ever-Growing

Researchers from Dresden's Fraunhofer Institute for Material and Beam Technology (IWS) have developed robotic grippers that "feel" by mimicking natural systems. Using a combination of 3D and dispensing printing, they've engineered grippers equipped with sensors that gauge force, allowing robots to grip objects with precision. These enhanced robots could soon be used in agriculture to pick delicate produce or in planetary exploration to handle unknown objects carefully. Projects like "BioGrip" and "Nature4Nature" aim to replicate biological principles to build robotic grippers that act similarly to human hands.

Borrowing Abilities from Aquatic Life

In designing these sensitive grippers, scientists drew inspiration from fish, whose fins naturally respond to pressure by moving inward rather than away from it. This adaptive response, known as the "Finray effect," allows fish to move more efficiently by creating an opposing force to external pressure. Applying this principle, engineers have designed grippers that use sensors and Finray-inspired movement to hold objects securely without exerting damaging force. This technology was developed and tested extensively through the BioGrip project between mid-2021 and early 2023.

Advanced Sensors Mimic Human Touch

The team’s work centers on sensors that enable robots to recognize exactly how much pressure is needed for different objects, preventing damage to fragile items. With this technology, robotic grippers can “sense” texture and firmness, adjusting their grasp accordingly. These advancements open up applications in agriculture, where robotic harvesters could gently pick fruit, and in underwater exploration, where robotic arms can handle sensitive marine samples. The combination of biological principles and modern technology is transforming robot interactions with their environment.

The Future of Responsive Robotic Applications

As robotic technology advances, the use of nature-inspired designs could revolutionize machine function in numerous fields. Responsive grippers are being tested across different industries, from food processing to space exploration, enhancing the potential of robots to operate autonomously. Engineers hope that continued advancements in bionic technology will create machines capable of performing increasingly complex tasks with minimal human intervention. This fusion of sensor technology with biological inspiration marks a significant step toward more adaptable and self-sufficient robotic systems.

This latest research highlights the promise of biologically inspired technology to transform robotics, offering an exciting glimpse into future applications.

Neuroscientists explore how the brain makes decisions

Scientists have gained new insights into how neurons in the brain communicate during a decision, and how the connections between neurons may help reinforce a choice.

The study—conducted in mice and led by neuroscientists at Harvard Medical School—is the first to combine structural, functional, and behavioral analyses to explore how neuron-to-neuron connections support decision-making.

The findings are published in the journal *Nature*.

"How the brain is organized to help make decisions is a big, fundamental question, and the neural circuitry—how neurons are connected to one another—in brain areas that are important for decision-making isn't well understood," said Wei-Chung Allen Lee, associate professor of neurobiology in the Blavatnik Institute at HMS and professor of neurology at Boston Children's Hospital.

Lee is co-senior author on the paper with Christopher Harvey, professor of neurobiology at HMS, and Stefano Panzeri, professor at University Medical Center Hamburg-Eppendorf.

In the research, mice were tasked with choosing which way to go in a maze to find a reward. The researchers found that a mouse's decision to go left or right activated sequential groups of neurons, culminating in the suppression of neurons linked to the opposite choice.

These specific connections between groups of neurons may help sculpt decisions by shutting down neural pathways for alternative options, Lee said.

A fruitful collaboration is born

It was a chance meeting on a bench outside their building during a fire drill that led Harvey and Lee to realize the complementary nature of their work. On that day, they forged a collaboration that propelled the new work.

The Harvey lab uses mice to study behavioral and functional aspects of decision-making. Typical experiments involve placing a mouse in a virtual reality maze and recording neural activity as it makes decisions. Such experiments have shown that distinct, but intermingled, sets of neurons fire when an animal chooses left versus right.

Lee works in a new field of neuroscience called connectomics, which aims to comprehensively map connections between neurons in the brain. The goal, he said, is to figure out "which neurons are talking to each other, and how neurons are organized into networks."

By combining their expertise, Harvey and Lee were able to delve deeper into the different types of neurons involved in decision-making and how these neurons are connected.

Choosing a direction

The new study focused on a region of the brain called the posterior parietal cortex—what Lee describes as an "integrative hub" that receives and processes information gathered by multiple senses to help animals make decisions.

"We were interested in understanding how neural dynamics arise in this brain area that is important for navigational decision-making," Lee said. "We're looking for rules of connectivity—simple principles that provide a foundation for the brain's computations as it makes decisions."

The Harvey lab recorded neural activity as mice ran a T-shaped maze in virtual reality. A cue, which happened several seconds beforehand, indicated to the mice whether a reward would be in the left or right arm of the T. The Lee lab used powerful microscopes to map the structural connections between the same neurons recorded during the maze task.

By combining modalities, the researchers distinguished excitatory neurons—those that activate other cells—from inhibitory neurons, which suppress other cells. They found that a specific set of excitatory neurons fired when a mouse decided to turn right, and these "right-turn" neurons activated a set of inhibitory neurons that curbed activity in "left-turn" neurons. The opposite was true when a mouse decided to turn left.

"As the animal is expressing one choice, the wiring of the neuronal circuit may help stabilize that choice by suppressing other choices," Lee said. "This could be a mechanism that helps an animal maintain a decision and prevents 'changes of mind.'"

The findings need to be confirmed in humans, although Lee expects that there is some conservation across species.

The researchers see many directions for future research. One is exploring the connections between neurons involved in decision-making in other brain regions.

"We used these combined experimental techniques to find one rule of connectivity, and now we want to find others," Lee said.

More information: Wei-Chung Lee, Synaptic wiring motifs in posterior parietal cortex support decision-making, *Nature* (2024). DOI: 10.1038/s41586-024-07088-7. www.nature.com/articles/s41586-024-07088-7

Provided by Harvard Medical School

Humans have a magnetic sensor in our eyes, but can we detect magnetic fields?

Many birds have a compass in their eyes. Their retinas are loaded with a protein called cryptochrome, which is sensitive to the Earth's magnetic fields. It's possible that the birds can literally *see* these fields, overlaid on top of their normal vision. This remarkable sense allows them to keep their bearings when no other landmarks are visible.

But cryptochrome isn't unique to birds – it's an ancient protein with versions in all branches of life. In most cases, these proteins control daily rhythms. Humans, for example, have two cryptochromes – CRY1 and CRY2 – which help to control our body clocks. But Lauren Foley from the University of Massachusetts Medical School has found that CRY2 can double as a magnetic sensor.

Foley worked with *Drosophila* flies, which can normally sense magnetic fields using cryptochome. You can show this by placing them in an artificial magnetic field and training them to head in a specific direction in search for food. Normal flies can do this easily. Mutants that don't have the *cry* gene, which makes the cryptochrome protein, lose their ability to find their meal.

To restore their internal compass, Foley simply has to give the mutant flies extra copies of *cry*. But she found that the human version of the gene works just as well. When she loaded her mutants flies with human CRY2, she found that they could sense magnetic fields like their normal peers. Foley also found that human cryptochrome is sensitive to blue light. It only managed to restore the magnetic sense of flies when they were bathed in this colour.

These simple experiments show that human cryptohrome *can* act as a magnetic sensor. This doesn't mean that it does, much less that humans can sense magnetic fields. Plugging human cryptochrome into an alien environment like the body of a fly tells you very little about what it does in its native surroundings.

Roswitha Wiltschko, one of the scientists who first discovered the magnetic sense of birds, says, "To sense the magnetic field, one does not only need a molecule like cryptochrome, but also an apparatus that picks up the changes in that molecule and mediates it to the brain. *Drosophila* obviously has this apparatus, but humans? I have my doubts." Steven Reppert, who led the new study, is also cautious. However, he notes that Cry2 is heavily active in the human retina. "It's beautifully poised to sense light but we don't know if it has the downstream pathways that communicate magnetic information to the brain. The possibility exists."

A radical idea

The connections between light, cryptochrome and a magnetic sense were laid out by Klaus Schulten and Thorsten Ritz in 2000, in a bravura paper that united biology and quantum physics. They suggested that when cryptochrome is struck by blue light, it transfers one of its electrons across to a partner molecule called FAD. Electrons normally waltz around in pairs, but thanks to the light, cryptochrome and FAD now have lone electrons. They are known as a "radical pair".

Electrons also have a property called "spin". In a radical pair, the spins of the two solo electrons are linked – they can either spin together or in opposite directions. These two states have different chemical properties, the radical pair can flip between them, and the angle of the Earth's magnetic field can influence these flips. In doing so, it can affect the outcome or the speed of chemical reactions involving the radical pair. This is one of the ways in which the Earth's magnetic field can affect living cells. It explains why the magnetic sense of animals like birds is tied to vision – after all, cryptochrome is found in the eye, and it's converted into a radical pair by light.

Several experiments in the past few decades have support Schulten and Ritz's theory. Foley's work also seems to fit – human cryptochrome can support a magnetic sense in flies, in a way that depends on blue light. But Wiltschko thinks that using the human protein is a red herring. "All cryptochromes should be light-sensitive and since they form radical pairs, they should be sensitive to magnetic fields. The authors are describing intrinsic properties of cryptochrome. Using human cryptochrome is a nice gag!"

Indeed, Reppert says, "Of all the cryptochromes one could think of, the human one seemed the most interesting. We thought that if it did work, it might reignite some interest in magnetoreception in humans, which has waned down to virtually nothing."

Can humans sense magnetic fields?

The current consensus is that humans cannot sense magnetic fields. Birds can do it, as can bats, turtles, ants, mole rats, sharks, rays, and more. Recently, Czech scientists have suggested that foxes, cows and deer also have the same ability. But look at all the recent reviews in this field, and you'll see very little mention of our own species. A decade ago, a German group showed that our vision is slightly more sensitive in some directions than in others, but the results have not caught on.

It wasn't always like this. In the 1980s, Robin Baker from the University of Manchester carried out a series of experiments which seemed to show that humans could sense magnetic fields. He took busloads of blindfolded volunteers on winding journeys for several kilometres before asking them to point their way back home. They did so more often than expected, and if they wore magnets on their heads, their accuracy dropped.

The results were published in *Science*were published in *Science* and you can read Baker's own description of his study in this 1980 issue of New Scientist. He even wrote a book about it. At the time, Baker said, "Whatever the repercussions, we have no alternative but to take seriously the possibility that Man has a magnetic sense of direction."

Unfortunately, the main repercussion was a fierce series of rebuttals. Over the next decade, several groups around the world failed to repeat Baker's results, even though Baker himself had no problems in doing so. He argued that their failure could have been due to local magnetic anomalies or brief changes in the strength of the magnetic field due to solar activity.

An American duo – Gould and Able – charitably suggested that Baker's British students "either had cues available to them which were absent in our experiments, or are dramatically better than Americans in using whatever cues may be involved." Max Westby and Karen Partridge, who failed to replicate Baker's results in Sheffield, were less kind. "Perhaps it depends on which side of the Pennine Hills the experiments are conducted?" they asked. "It is obviously extremely difficult to counter all conceivable explanations for a negative result but we are forced to wonder about the ecological importance of a magnetic sense, the existence of which is so difficult to demonstrate."

In the end, Baker relented and he moved on to the science of sperm. When I talked to him about the new study, he confesses that he hasn't kept up with the field. "I'd spent nearly a decade, tested thousands of people under all sorts of conditions, and had absolutely no doubt. Then people did a few tests here and there and claimed the experiments didn't replicate," he says. "Even after I'd collected everybody else's results and published that taken together, they did in fact constitute successful replication, nobody wanted to know. There was an element of 'Sod them, then'."

Reppert thinks that Baker's story was an unfortunate one, especially since he stopped just when others were starting to discover light-based magnetic sensors. "I think Baker's work was very good work but a lot of people had trouble reproducing aspects of it," says Reppert. "It's just very hard to do these sorts of behavioural experiments in humans."

The hardest sense

Magnetoreception has to be one of the hardest of all animal senses to study. Thorsten Ritz says, "Basic things that you do in other senses don't make sense when it comes to magnetoreception. Almost every other sense is linked to an opening in bone structure – eyes, ears and so on. The magnetic sense could sit anywhere in the body because the magnetic field penetrates the body."

To complicate matters, we don't really know what a magnetic sense would be used for. For birds and turtles, it seems obvious that an internal compass would help them to navigate over long migrations. But that doesn't really apply to humans, and we know that lost humans tend to go round in circles when other landmarks are unavailable.

But navigation isn't the only use for a magnetic sense. Recently, John Philips has suggested that animals could use magnetic fields to estimate distances over much smaller scales. Indeed, it's possible that foxes could use a magnetic range finder to gauge the distance of their pounces, when their prey is hidden by snow.

It's clear that magnetic senses will remain alluring and controversial for many years to come. Baker has left the field behind, but he is still intrigued by it. "I would be really thrilled if somebody managed to vindicate those ten years of work, because I still have no doubt that there is a real phenomenon there," he says. "This new paper is a very long way from being vindication, but just to read somebody saying that human magnetoreception deserves another look did give me a brief surge of satisfaction."

Reference: Foley, Gegear & Reppert. 2011. Human cryptochrome exhibits light-dependent magnetosensitivity. Nature Communications http://dx.doi.org/10.1038/ncomms1364

Scientists discover a framework in the brain for organizing the order of things

Scientists at NTNU's Kavli Institute for Systems Neuroscience in Norway have discovered a pattern of activity in the brain that serves as a template for building sequential experiences.

"I believe we have found one of the brain's prototypes for building sequences," says Professor Edvard Moser. He describes the activity pattern as "a fundamental algorithm that is intrinsic to the brain and independent of experience."

The breakthrough discovery was published in *Nature*.

The ability to organize elements into sequences is a fundamental biological function essential for our survival. Without it, we would not be able to communicate, keep track of time, find our way, or even remember what we are in the process of doing. The world would cease to present itself to us in meaningful experiences, as every event would be fragmented into an erratic series of random happenings.

The NTNU researchers' discovery of a rigid sequence pattern in the brain provides new insights into how we organize experiences into a temporal order.

The sequential nature of memory

Have you ever heard memories described as snapshots? That is not a very faithful description, according to Professor Edvard Moser. "It is more helpful to think of memories as videos," he says.

"All your experiences in the world extend over time," says Professor May-Britt Moser. "One thing happens, then another thing, then a third."

Your brain has the remarkable ability to mentally capture and organize selected events into the chronological order in which they occurred, and to link them together as meaningful experiences. This sequence-building activity takes place on the timescale in which you interact in the situation. When you recall this memory, the process of reliving the sequence of events in your mind also takes time.

"How is the brain able to generate and store all these unique and lengthy sequences of information on the fly?" asks Edvard Moser.

"There has to exist a foundational mechanism for sequence formation there."

"There is a mismatch in neuroscience between the timescales at which brain activity is typically studied, in the millisecond regime, and the timescales at which many of our most important brain functions occur, in the tens of seconds to several minutes range," says Soledad Gonzalo Cogno, Kavli Research Group Leader and first author of the paper, expanding on the motivation behind this study.

The team set out to identify this fundamental mechanism for sequence formation, which occurs on very slow timescales as most of our brain functions do.

The experiment

To uncover how neurons coordinate at the slow timescales at which many of our brain functions unfold, the Kavli researchers focused on the medial entorhinal cortex (MEC), a brain area that supports brain functions that depend on sequence formation, such as navigation and episodic memory, which unfold very slowly in time.

The sheer volume of information about the outside world being processed in the brain at any one time posed a challenge to the pursuit. Any baseline signal from structured and recurrent neural algorithms would risk drowning in the "noise" of incoming experience.

To get around this, the researchers created an experimental environment that was almost devoid of sensory inputs. They let a mouse run in complete darkness, with no task to complete and no reward to earn. The mouse could run or rest as it pleased for as long as the session lasted.

At the same time, the researchers recorded what was happening in the entorhinal cortex of the mouse's brain while its orchestra of nerve cells remained in this soft-spoken standby position.

A fundamental brain mechanism for sorting information into sequences

"This is what we found," says Soledad Gonzalo Cogno, pointing to a zebra-striped figure before her.

The pattern is made up of thousands of dots clustered together. Each dot is a neural signal. We can see that the neural activity moves through all the cells from bottom to top along the Y-axis as time progresses along the X-axis. The clustering tells us that the activity is coordinated as waves running through the network, like rhythms in a symphony.

The sequences are ultra-slow, meaning that it takes two minutes for the wave to travel through the neural network, before the whole process repeats again, sometimes for as long as the duration of the test session, over periods of up to an hour.

The figure shows several hundred mouse entorhinal cortex neurons oscillating at ultra-slow frequencies, spanning time windows ranging from tens of seconds to several minutes. The dynamic that excited the researchers, even more, is that as each cell oscillates, the cells also organize themselves into sequences, with cell A firing before cell B, cell B firing before cell C, and so on, until they have completed a full loop and return to cell A, where the cycle repeats.

This highly structured activity overlaps with the timescale of events that we encode into our memories and provides the perfect template for building the sequential structure that forms the basis of episodic memories.

These waves of coordinated activity did not travel straight from one end of the brain tissue to the other. Instead, the waves travel along the thin synaptic connections between cells that talk to each other in the network. Cells can talk to other cells far away and to their nearest neighbors. The anatomical tangle makes it difficult to see coordinated activity with the naked eye without first locating the cells from the raster plot.

Zebra-stripes, spiral, and ring

The zebra-striped raster plot shows the slow waves of activity through the whole network over a period of time. "If you fold the raster plot into a tube so that the top and the bottom of the figure overlap, you will see that the diagonal stripes connect to form a coherent spiral," explains May-Britt Moser. "The spiral represents the network activity over time."

You will see a ring if you rotate the spiral by 90 degrees. All the cells in the network have their set time to fire, distributed across the surface of this ring. The signal travels through the entire ring structure before returning to the same cell.

"This ring is a signature for coordination patterns in the form of repetitive sequences, which is what we found in the MEC," says Soledad Gonzalo Cogno. "Other brain areas have different coordination patterns."

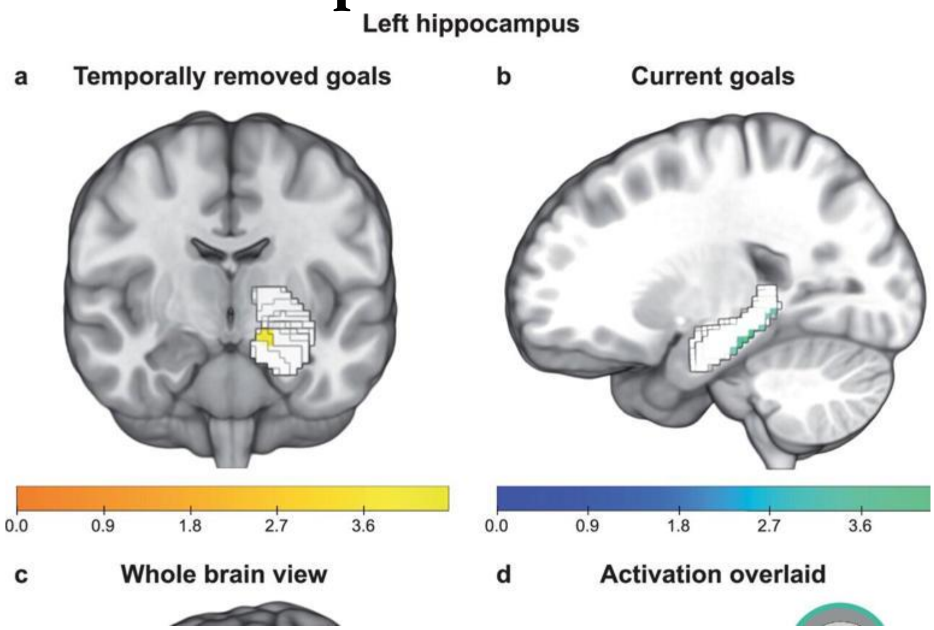
Your brain may already be equipped with this ring before you experience anything in this world. It is acquired through evolution and may be specified in our genes.

"What excites me most about this discovery is the prospect that these sequences may open up for new ways of understanding the brain," says Gonzalo Cogno. "The discoveries that follow may challenge the way we think about coordination throughout the brain. Cells that are so different still seem to be coordinated and work together on different timescales."

More information: Edvard Moser, Minute-scale oscillatory sequences in medial entorhinal cortex, *Nature* (2023). DOI: 10.1038/s41586-023-06864-1. www.nature.com/articles/s41586-023-06864-1

Provided by Norwegian University of Science and Technology

Scientists show how the hippocampus is activated to prioritize our activities



Temporally removed goals activated the left anterior hippocampus and current goals activated the left posterior hippocampus. a Activation maps for the contrasts comparing the remote (distant future + near future + distant past + near past) > current are overlaid in yellow. b Activation maps for the contrasts comparing the current > remote are overlaid in green. c Activation for the temporally removed goals (yellow) and the current goals (green) shown concurrently on the brain. d The same goal, for instance fixing the space helmet, was anatomically dissociated along the longitudinal axis based on whether it was currently relevant, or relevant at a point removed in time. The left hippocampal region of interest (ROI) is displayed in white. Credit: Nature Communications (2024). DOI: 10.1038/s41467-024-48648-9© Provided by Medical Xpress

How does our brain distinguish between urgent and less urgent goals?

Researchers at the University of Geneva (UNIGE) and the Icahn School of Medicine in New York have explored how our brain remembers and adjusts the goals we set for ourselves on a daily basis.

Their study reveals differences in the way we process immediate and distant goals, at both behavioral and cerebral levels. These discoveries, published in the journal *Nature Communications*, could have significant implications for understanding psychiatric disorders, particularly depression, which can hamper the formulation of clear goals.

Throughout the day, we set ourselves goals to achieve: picking up the children from school in an hour, preparing dinner in three hours, making a doctor's appointment in five days or mowing the lawn in a week. These goals, both urgent and less urgent, are constantly redefined according to the events that occur throughout the day.

Researchers from the UNIGE and the Icahn School of Medicine at Mont Sinai Hospital in New York have studied how the brain memorizes and updates the goals to be achieved. More specifically, how the brain sorts out which goals require immediate attention and which do not.

Their study focused on a particular region of the brain, the hippocampus, because of its established role in episodic memory. This is responsible for encoding, consolidating and retrieving personally experienced information, integrating its emotional, spatial and temporal context.

An imaginary mission to Mars, in the time of an MRI scan

Neuroscientists asked 31 people to project themselves into an imaginary 4-year space mission to Mars, requiring them to achieve a series of objectives crucial to their survival (taking care of their space helmet, doing exercise, eating certain foods, etc.). The mission objectives varied according to when they had to be achieved, with different tasks for each of the four years of the journey.

As participants progressed through the mission, they were presented with the same objectives. They were then asked to indicate whether these were past, present or future goals.

As the participants moved forward in time, the relevance of these objectives changed: Objectives initially planned for the future became current needs, while current needs became past objectives.

In this way, participants had to manage several objectives at different distances in time and update their priorities as their mission progressed.

Prioritizing immediate objectives

The team observed the reaction times of each individual to determine whether the task was to be achieved in the present, the past or the future. "Goals to be achieved immediately are recognized more quickly than those to be achieved in the distant future. This different processing of stored information reveals the priority given to needs in the present over those in the distant future.

"It takes extra time to mentally travel back in time to retrieve past and future goals," explains Alison Montagrin, research and teaching fellow in the Department of Basic Neurosciences at the UNIGE Faculty of Medicine, former post-doctoral fellow at the Icahn School of Medicine, and first author of the study.

The scientists also investigated whether differences were also apparent at the cerebral level. Images obtained using very high-resolution MRI revealed that, when retrieving information about the present, the hippocampus is activated in its posterior region. On the other hand, when recalling past goals or goals to be achieved in the future, the anterior region is activated.

"These results are particularly interesting because previous studies have shown that when we call on our episodic memory or our spatial memory, the anterior region of the hippocampus is involved in retrieving general information, while the posterior part deals with details.

"It will therefore be interesting to explore whether—unlike immediate goals—projection into the future or recall of a past goal do not require specific details, but a general representation is sufficient," concludes the researcher.

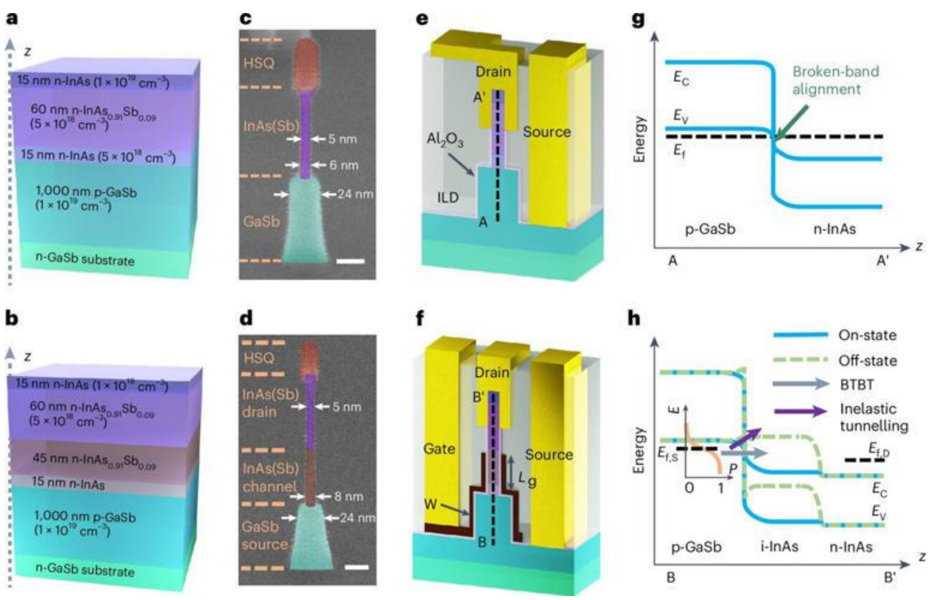
This research shows that the time scale plays a crucial role in the way people set personal goals. This could have important implications for understanding psychiatric disorders such as depression. Indeed, people suffering from depression may present difficulties in forming specific goals and envisage more obstacles in reaching their objectives.

Investigating whether these people perceive the distance to their goals differently—which could make them pessimistic about their chances of success—could open up a therapeutic avenue.

More information: Alison Montagrin et al, The hippocampus dissociates present from past and future goals, *Nature Communications* (2024). [DOI: 10.1038/s41467-024-48648-9](https://doi.org/10.1038/s41467-024-48648-9)

Provided by University of Geneva

Nanoscale transistors could enable more efficient electronics



Ultra-scaled vertical-nanowire device design. Credit: Nature Electronics (2024). DOI: 10.1038/s41928-024-01279-w

Silicon transistors, which are used to amplify and switch signals, are a critical component in most electronic devices, from smartphones to automobiles. But silicon semiconductor technology is held back by a fundamental physical limit that prevents transistors from operating below a certain voltage.

This limit, known as "Boltzmann tyranny," hinders the energy efficiency of computers and other electronics, especially with the rapid development of artificial intelligence technologies that demand faster computation.

In an effort to overcome this fundamental limit of silicon, MIT researchers fabricated a different type of three-dimensional transistor using a unique set of ultrathin semiconductor materials. The research appears in *Nature Electronics*.

Their devices, featuring vertical nanowires only a few nanometers wide, can deliver performance comparable to state-of-the-art silicon transistors while operating efficiently at much lower voltages than conventional devices.

"This is a technology with the potential to replace silicon, so you could use it with all the functions that silicon currently has, but with much better energy efficiency," says Yanjie Shao, an MIT postdoc and lead author of a paper on the new transistors.

The transistors leverage quantum mechanical properties to simultaneously achieve low-voltage operation and high performance within an area of just a few square nanometers. Their extremely small size would enable more of these 3D transistors to be packed onto a computer chip, resulting in fast, powerful electronics that are also more energy-efficient.

"With conventional physics, there is only so far you can go. The work of Yanjie shows that we can do better than that, but we have to use different physics. There are many challenges yet to be overcome for this approach to be commercial in the future, but conceptually, it really is a breakthrough," says senior author Jesús del Alamo, the Donner Professor of Engineering in the MIT Department of Electrical Engineering and Computer Science (EECS).

They are joined on the paper by Ju Li, the Tokyo Electric Power Company Professor in Nuclear Engineering and professor of materials science and engineering at MIT; EECS graduate student Hao Tang; MIT postdoc Baoming Wang; and professors Marco Pala and David Esseni of the University of Udine in Italy.

Surpassing silicon

In electronic devices, silicon transistors often operate as switches. Applying a voltage to the transistor causes electrons to move over an energy barrier from one side to the other, switching the transistor from "off" to "on." By switching, transistors represent binary digits to perform computation.

A transistor's switching slope reflects the sharpness of the "off" to "on" transition. The steeper the slope, the less voltage is needed to turn on the transistor and the greater its energy efficiency.

But because of how electrons move across an energy barrier, Boltzmann tyranny requires a certain minimum voltage to switch the transistor at room temperature.

To overcome the physical limit of silicon, the MIT researchers used a different set of semiconductor materials—gallium antimonide and indium arsenide—and designed their devices to leverage a unique phenomenon in quantum mechanics called quantum tunneling.

Quantum tunneling is the ability of electrons to penetrate barriers. The researchers fabricated tunneling transistors, which leverage this property to encourage electrons to push through the energy barrier rather than going over it.

"Now, you can turn the device on and off very easily," Shao says.

But while tunneling transistors can enable sharp switching slopes, they typically operate with low current, which hampers the performance of an electronic device. Higher current is necessary to create powerful transistor switches for demanding applications.

Fine-grained fabrication

Using tools at MIT.nano, MIT's state-of-the-art facility for nanoscale research, the engineers were able to carefully control the 3D geometry of their transistors, creating vertical nanowire heterostructures with a diameter of only 6 nanometers. They believe these are the smallest 3D transistors reported to date.

Such precise engineering enabled them to achieve a sharp switching slope and high current simultaneously. This is possible because of a phenomenon called quantum confinement.

Quantum confinement occurs when an electron is confined to a space that is so small that it can't move around. When this happens, the effective mass of the electron and the properties of the material change, enabling stronger tunneling of the electron through a barrier.

Because the transistors are so small, the researchers can engineer a very strong quantum confinement effect while also fabricating an extremely thin barrier.

"We have a lot of flexibility to design these material heterostructures so we can achieve a very thin tunneling barrier, which enables us to get very high current," Shao says.

Precisely fabricating devices that were small enough to accomplish this was a major challenge.

"We are really into single-nanometer dimensions with this work. Very few groups in the world can make good transistors in that range. Yanjie is extraordinarily capable to craft such well-functioning transistors that are so extremely small," says del Alamo.

When the researchers tested their devices, the sharpness of the switching slope was below the fundamental limit that can be achieved with conventional silicon transistors. Their devices also performed about 20 times better than similar tunneling transistors.

"This is the first time we have been able to achieve such sharp switching steepness with this design," Shao adds.

The researchers are now striving to enhance their fabrication methods to make transistors more uniform across an entire chip. With such small devices, even a 1-nanometer variance can change the behavior of the electrons and affect device operation.

They are also exploring vertical fin-shaped structures, in addition to vertical nanowire transistors, which could potentially improve the uniformity of devices on a chip.

More information: Yanjie Shao et al, Scaled vertical-nanowire heterojunction tunnelling transistors with extreme quantum confinement, *Nature Electronics* (2024). DOI: 10.1038/s41928-024-01279-w

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Provided by Massachusetts Institute of Technology

Brain waves found to travel in one direction when memories are made and the opposite when recalled

Traveling wave propagation directions in the memory task reveal how the brain quickly coordinates activity and shares information across multiple regions. Credit: Honghui Zhang© Provided by Medical Xpress

In the space of just a few seconds, a person walking down a city block might check their phone, yawn, worry about making rent, and adjust their path to avoid a puddle. The smell from a food cart could suddenly conjure a memory from childhood, or they could notice a rat eating a slice of pizza and store the image as a new memory.

For most people, shifting through behaviors quickly and seamlessly is a mundane part of everyday life.

For neuroscientists, it's one of the brain's most remarkable capabilities. That's because different activities require the brain to use different combinations of its many regions and billions of neurons. How it manages to do this so rapidly has been an open question for decades.

In a paper published March 8 in *Nature Human Behaviour*, a team of researchers, led by Joshua Jacobs, associate professor of biomedical engineering at Columbia Engineering, shed new light on this question. By carefully monitoring neural activity of people who were recalling memories or forming new ones, the researchers managed to detect how a newly appreciated type of brainwave—traveling waves—influences the storage and retrieval of memories.

"Broadly, we found that waves tended to move from the back of the brain to the front while patients were putting something into their memory," said the paper's co-author Uma R. Mohan, a postdoctoral researcher at NIH and former postdoctoral researcher in the Electrophysiology, Memory, and Navigation Laboratory at Columbia Engineering.

"When patients were later searching to recall the same information, those waves moved in the opposite direction, from the front towards the back of the brain," she said.

In the brains of some of the study's 93 participants, waves traveled in other directions.

"There was a lot of diversity across patients, so we implemented a framework based on the direction an individual's oscillations 'preferred' to travel," Mohan said.

The researchers say these findings advance fundamental neuroscience research and point toward diagnostic and therapeutic approaches for memory-related disorders.

"We think the work may lead to new approaches for interfacing with the brain. By measuring the direction that a person's brain waves move, we may be able to predict their behavior," Jacobs said.

Brain waves are patterns of electrical oscillations that reflect the state of hundreds or thousands of individual neurons at a particular moment. One major question, which remains unsettled, is whether brain waves drive activity or simply occur as a byproduct of neural activity that was already happening. Researchers who study brain waves have tended to treat them as a stationary phenomenon that occurs in a particular region, noting when oscillations in multiple regions seem synchronized.

In this study, Mohan and her colleagues contribute to a growing understanding of these oscillations differently, as "traveling waves" that spread across the brain's cortex, the outermost layer that supports higher cognitive processing. Mohan compares the traveling waves to the ripples that would spread outward after a pebble was thrown into a pond.

"We're looking at neural oscillations not as independent stationary things but as things that are constantly and spontaneously moving across the brain in a dynamic way," Mohan said.

This relatively new way of understanding brain waves is an exciting step in neuroscience because it offers a pathway to explaining how the brain quickly coordinates activity and shares information across multiple regions.

The study drew on data from participants who were being treated for drug-resistant epilepsy at hospitals across the United States. The experiments occurred while the participants had grids or strips of electrodes temporarily implanted on the surface of the brain, beneath the skull, to determine where the patients' seizures arise. For the researchers, these electrodes offer the chance to perform experiments that wouldn't otherwise be feasible.

"It's a rare opportunity to be able to see what's going on directly from the brain while the participants are engaged in different cognitive behaviors," Mohan said.

During the experiments, researchers recorded the participants' brain activity while they performed tasks that required memorizing and recalling lists of words or letters.

After the experiments, the researchers analyzed the brain activity from each participant in the context of what they were doing in the memory task and how well they performed.

"I implemented a method to label waves traveling in one direction as basically 'good for putting something into memory." Then we could see how the direction switched over the course of the task," Mohan said. This method builds on previous research from the Jacobs lab by expanding the mathematical framework used to make sense of the vast quantities of data these experiments produced.

"The waves tended to go in the participant's encoding direction when that participant was putting something into memory and in the opposite direction right before they recalled the word," she said. " Overall, this new work links traveling waves to behavior by demonstrating that traveling waves propagate in different directions across the cortex for separate memory processes."

The data also showed that participants tended to perform the memory task more accurately when the traveling waves were moving in the appropriate direction for memory storage and recall.

"These findings shed light on the mechanisms that underlie memory processing. More broadly, they help us better understand how the brain supports a wide range of behaviors that involve precisely coordinated interactions between brain regions," Mohan said.

Potential impact and future directions

As traveling waves are increasingly well understood, they could be the basis for a new class of diagnostic tools that recognize abnormal patterns in brain activity.

There is also significant therapeutic potential.

"If someone's waves are moving in the wrong direction when they're about to try to remember something, that might put them in a poor memory state," Mohan explained. "If you could apply stimulation in the right way, you could maybe push those waves to move in a different direction, bringing about a fundamentally different memory state."

Advances in understanding traveling waves offer significant potential for human-computer interaction.

In terms of both research and application, Mohan notes that memory is just the starting point.

"I am interested in how characteristics of cortical traveling waves change to support a wide range of cognitive functions, including attention and associative memory," she said.

"The direction of traveling wave propagation may tell us where information is moving across the brain at each moment, showing us how different parts of the brain transfer information during behavior," Jacobs said.

More information: The direction of theta and alpha travelling waves modulates human memory processing, *Nature Human Behaviour* (2024). DOI: 10.1038/s41562-024-01838-3. www.nature.com/articles/s41562-024-01838-3

Provided by Columbia University School of Engineering and Applied Science

Imagine using a computer with your thoughts. No more typing and scrolling, you just think about sending an email and off it goes.

This kind of technological telepathy is the broad idea behind the brain-computer interface (BCI).

Also known as a brain-machine interface, these devices are intended to bypass our typical modes of interacting with computers – hands, fingers, and voices – in favour of capturing and interpreting signals directly from the brain.

The possibilities of this technology are so wide-reaching to the point where we could have near-instant communication with anyone on Earth using just our minds.

These devices could also let you control robotic limbs or pilot drones and, as virtual reality continues to develop, you may be able to move around digital worlds without lifting a finger.

In scientific literature, the concept of BCIs goes back at least as far as a 1973 paper from Jacques Vidal of the University of California's Brain Research Institute who pondered whether brain signals captured by an electroencephalogram (EEG) could be used "for the purpose of controlling such external apparatus as prosthetic devices or spaceships".

Vidal described an early BCI built on the "conviction" that EEG signals "contain usable concomitances of conscious and unconscious experiences" that – though largely consisting of noise – still "reflects underlying neural events".

BCIs could do more than read brainwaves – they may be able to write them as well, letting you 'see' a user interface where there is none, or even giving you a consistently calm mental state with the kind of direct brain access pharmaceutical companies could only dream of achieving.

These are just some of the potential future use-cases for BCIs. They may sound like fantastical ideas ripped from the pages of science fiction novels, and that's because much of this technology lies at the bleeding edge where science fiction meets science fact.

At the heart of modern BCI research and development is a striving for greater inclusivity. People living with disabilities and chronic health conditions are the immediate beneficiaries of this technology as they find new ways of communicating and interacting with the world and other people.

The foundations being laid in the name of creating a more inclusive world could one day lead to a general computing revolution that has implications for how we define autonomy and free will, how we preserve the privacy of our inner-most thoughts and feelings, and what it means to be human.

An unreal vision

It's a technology that, like much of the bleeding edge, involves billionaire Elon Musk and his outrageous, sci-fi promises.

In March 2017, early reports of Musk's company Neuralink surfaced. When he began to speak publicly about the idea behind Neuralink, Musk mentioned the devices as a way of creating "symbiosis with artificial intelligence" in order to give people "superhuman cognition" and mitigate the "existential risk" Musk and other long-termist adherents believe is inherent in AI development.

Neuralink's soft launch was nudged along with a long explainer from blogger Tim Urban about how BCIs could usher in a future where humans collectively and telepathically make decisions – something Musk insists is necessary lest humans become "effectively useless or like a pet" to AI.

"If we achieve tight symbiosis [with AI through BCIs], the AI wouldn't be 'other'," Musk said. "It would be you and with a relationship to your cortex analogous to the relationship your cortex has with your limbic system."

To get to this point, Musk wants to implant Neuralink devices into willing customers in order to both "report from and stimulate spikes in neuron activity".

"It will be safe enough that it's not a major operation and will be equivalent to LASEK surgery," Musk previously said.

One day, Musk claims, the device will even let people "save and replay memories".

As with many of his business ventures, Musk's intended future state of Neuralink is as ambitious as it is divorced from the current technological reality.

Neuralink has yet be approved for human trials and has been plagued by reports of animal cruelty during testing.

One of the few glimpses we have seen of Neuralink involve a monkey playing the video game Pong with its mind which, while impressive in its own right, failed to demonstrate new developments in the BCI space.

In mid-2004, researchers with the BrainGate project conducted human trials of its technology that gave a handful of patients who had spinal cord injuries or motor neurone disease. They were able to control a computer cursor and even issue simple commands to a prosthetic hand using their minds.

Leaving the lab

Today, much of the effort in BCI development is about taking the technologies out of the lab, according to Professor David Grayden, Clifford Chair of Neural Engineering at the University of Melbourne.

He told *Information Age* there has "been a lot of work trying to understand the [brain] signals, decode them, and use AI to interpret the signals, but with systems that are sort of unusable in the home".

Moving BCI technologies into people's homes will be a game changer for the people who use them and is part of a gradual adoption curve.

There are a few different ways for extracting your thoughts, Professor Grayden said, including the EEG technology explored 50 years ago by Jacques Vidal.

"[The electrodes] don't need surgery to put on so it's about trying to get the best possible signal from those," he told *Information Age*.

"This is really difficult because the signal is attenuated a lot by the skull and the scalp so you really only get the low frequencies."

Maximising the fidelity and interpretation of brain signals using EEG could be an important step toward broader BCI adoption and use because of its non-invasive nature.

You could imagine buying a consumer-grade headset with powerful enough electrodes to read signals via processing that happens on-board or on a nearby device.

Back in 2019, Meta (then Facebook) told the world about its own experiments with BCI technology in a blog post that described its research into decoding words and phrases captured from invasive electrocorticography (ECoG).

Meta's researchers used this data to train a neural network that could interpret a "sentence-length sequence of neural activity" into language.

Incredibly, the researchers claimed in an article subsequently published in *Nature Neuroscience*, that the model could decode brain activity "with high accuracy and at natural-speech rates".

Meta posed a possible future in which you could have the "hands-free convenience and speed" of using your voice to control your phone, tablet, laptop "with the discreteness of typing".

Aside from EEG, Meta also spoke about how it tested measuring changes in oxygen levels in the brain that correspond to activity.

Combined with its research on decode brain activity, Meta suggested that the ability "to recognise even a handful of imagined commands, like 'home,' 'select,' and 'delete' would provide entirely new ways of interacting with today's VR [virtual reality] systems – and tomorrow's AR [augmented reality] glasses".

Here you can see the potential for consumer-grade BCIs with rudimentary mind-reading technology for walking around virtual worlds or controlling AR glasses.

But so far, the best way to control a computer with your mind is to have electrodes placed directly onto brain tissue.

"If you're inside the skull, you can get higher frequencies and a better localisation of the signal," Professor Grayden said.

"This involves putting penetrating electrodes down into people's heads, kind of like a bed of nails that just gets pushed into the brain.

"Those electrodes are so small and they're so close to the neurons that they can record even individual neuron activity."

Localisation is important given how our brains process different information in different areas of tissue.

It's an imperfect description of how brains work – there is plenty of overlap with activity that activates neurons in different sections of the brain – but is nonetheless useful when trying to target specific areas or functions like in the motor cortex, which controls voluntary movements.

The more invasive the BCI technology, the better the signal and localisation – but implanting anything onto the brain is fraught with difficulty.

In part two of this series, we will look at the limitations for the development of BCIs, an Australian company that has taken a novel approach, and some of the real-world uses of BCIs today.

Scientists Prove That Telepathic Communication Is Within Reach

An international research team develops a way to say “hello” with your mind

In a recent experiment, a person in India said “hola” and “ciao” to three other people in France. Today, the Web, smartphones and international calling might make that not seem like an impressive feat, but it was. The greetings were not spoken, typed or texted. The communication in question happened between the brains of a set of study subjects, marking one of the first instances of brain-to-brain communication on record.

The team, whose members come from Barcelona-based research institute Starlab, French firm Axilum Robotics and Harvard Medical School, published its findings earlier this month in the journal *PLOS One*. Study co-author Alvaro Pascual-Leone, director of the Berenson-Allen Center for Noninvasive Brain Stimulation at Beth Israel Deaconess Medical Center and a neurology professor at Harvard Medical School, hopes this and forthcoming research in the field will one day provide a new communication pathway for patients who might not be able to speak.

“We want to improve the ways people can communicate in the face of limitations—those who might not be able to speak or have sensory impairments,” he says. “Can we work around those limitations and communicate with another person or a computer?”

Pascual-Leone's experiment was successful—the correspondents neither spoke, nor typed, nor even looked at one another. But he freely concedes that the test was more a proof of concept than anything else, and the technique still has a long way to go. "It's still very, very early," he says, "[but] we can show that this is even possible with technology that's available. It's the difference between talking on the phone and sending Morse code. To get where we're going, you need certain steps to be taken first."

Indeed, the process was drawn out, if not downright inelegant. First, the team had to establish binary-code equivalents of letters; for example "h" is "0-0-1-1-1." Then, with EEG (electroencephalography) sensors attached to the scalp, the sender moved either his hands or feet to indicate a 1 or a 0. The code then passed to the recipient over email. On the other end, the receiver was blindfolded with a transcranial magnetic stimulation (TMS) system on his head. (TMS is a non-invasive method of stimulating neurons in the brain; it's most commonly used to treat depression.) The TMS headset stimulated the recipient's brain, causing him to see quick flashes of light. A flash was equivalent to a "1" and a blank was a "0." From there, the code was translated back into text. It took about 70 minutes to relay the message.

Grau, C., et al. PLOS ONE 2014

There is a bit of contention about the degree to which this approach was actually novel. *IEEE Spectrum* reports that this recent study is quite similar to one conducted at the University of Washington last year. In that study, researchers used the same EEG-to-TMS setup, but rather than pulsed light, stimulated the brain's motor cortex to subconsciously cause the recipient to strike a key on a keyboard. Pascual-Leone contends, however, that his work is notable because the recipient was conscious of the communication.

Both studies represent only a small step toward engineering telepathy, which might take years—or decades—to perfect. Ultimately, the goal is to remove the computer middleman from the transmission equation and allow direct brain-to-brain communication between people. "We're still a long way from that," Pascual-Leone admits, "but in the end, I think it's a pursuit worthy of the effort."

Outside of medicine, brain-to-brain communication could find applications across many disciplines. Soldiers, for instance, could use the technology on the battlefield, sending commands and warnings to one another. Civilians might benefit, as well; businesspeople could use it to send cues to partners during negotiations, or pitchers and catchers could avoid sign-stealing during baseball games.

Still, telepathic communication that works like a sort of futuristic walkie-talkie will involve major advances in sensing, emitting and receiving technologies—and perhaps even a slight retraining of the human brain. At the same time, Pascual-Leone cautions that scientists must also keep in mind the ethics of telepathy.

“Could there be potential for sending someone a thought that’s not desirable to them?” he says. “Those kinds of things are theoretically in the realm of possibility."

Old people can produce as many new brain cells as teenagers

Research contradicts decades-old theory that humans stop producing neurons in adulthood

Elderly people grow as many new brain cells as teenagers, according to a new study which counters previous theories that neurons stop developing after adolescence.

Healthy men and women continue to produce new neurons throughout life, suggesting older people remain more cognitively and emotionally intact than previously believed, researchers found.

For decades it was thought that adult brains were hard-wired and unable to form new cells.

But a Columbia University study found older people continued to produce neurons in the hippocampus – a part of the brain important for memory, emotion and cognition – at a similar rate to young people.

Researchers examined the brains of 28 previously healthy people who died suddenly between the age of 14 and 79.

“We found that older people have similar ability to make thousands of hippocampal new neurons from progenitor cells as younger people do,” said the study's lead author Maura Boldrini, associate professor of neurobiology.

"We also found equivalent volumes of the hippocampus across ages."

The ability to generate new hippocampal cells, a process known as neurogenesis, declines with age in rodents and primates.

Declining production of neurons and shrinkage of parts of the brain which help form of new episodic memories were believed to occur in ageing humans as well, explaining why younger people find it easier to learn skills and languages.

But the Columbia University study found similar numbers of newly formed cells in old and young brains.

However, the researchers also noted fewer blood vessels and connections between cells in the older brains, which Ms Boldrini said "may be linked to compromised cognitive-emotional resilience" in the elderly.

The findings, published in the journal *Cell Stem Cell*, are likely to be hotly debated.

They come just a month after a University of California study suggested adults do not develop new neurons.

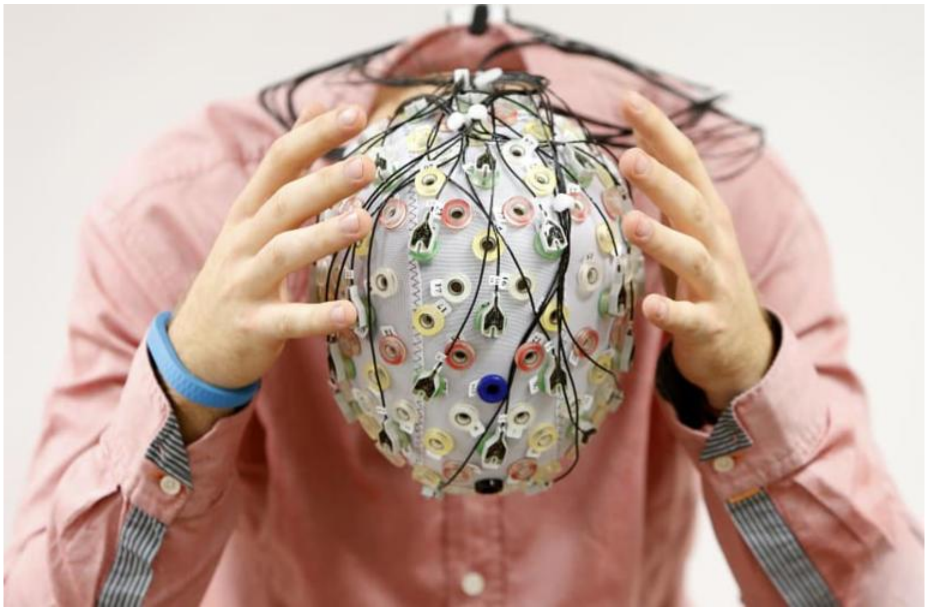
Shawn Sorrells and Mercedes Paredes, who co-authored that research, said: "For now, we do not think this new study challenges what we have concluded from our own recently published observations: if neurogenesis continues in the adult human hippocampus, it is an extremely rare phenomenon."

However, other scientists said the Columbia University findings were promising and could be helpful in developing new treatments for neurological conditions such as Alzheimer's Disease.

Written by: Chris Baynes

This article was originally published on Independent.

Two-stage brain coding explained by University of Haifa study



Test person Niklas Thiel poses with an electroencephalography (EEG) cap which measures brain activity, at the Technische Universitaet Muenchen (TUM) in Garching near Munich© (photo credit: REUTERS/Michaela Rehle)

Understanding how the brain encodes information is important to understand how parts of the body "communicate" with the brain – for example, if doctors want to connect a prosthetic hand or leg to the brain and let the brain operate it.

"Understanding the language that the brain uses to speak to itself will enable us to better understand how to transfer information to and from the brain with a high degree of precision," according to Prof. Eran Stark of the Sagol neurobiology department at the University of Haifa who led a study just published in the prestigious journal *Science* under the title "Local activation of CA1 pyramidal cells induces theta-phase precession."

To encode new information, brain cells in the hippocampus – a complex brain structure embedded deep into the temporal lobe that has a major role in learning and memory – activate a mechanism that triggers an increase in the firing rate and influences the precise timing of the firing.

The importance of understanding the brain

"The new study shows us that local circuits in the brain are more sophisticated than we might have thought. The brain can encode information in two different ways, one of which causes the other," Stark explains.

The question of how the brain encodes new information it receives is one of the most important and complex issues in understanding processes of learning, memory, and more.

One of the main problems involved in understanding coding mechanisms concerns the difficulty in "controlling" neurons and making them act in a particular manner.

Until now, neurobiologists knew that during the encoding of new information (specifically, the identification by mice of new places within space), neurons in the hippocampus participate in two processes.

What are the two processes that occur?

The first process entails an increase in the firing rate of the individual cell.

In simple terms, the cell fires more times within a given period of time. The second process is a change in the timing mechanism. Theta waves with a frequency of 8 Hertz occur in the hippocampus, and it is possible to measure precisely when within the shape of the theta wave the cell fires – at what timing (phase) "along the wave."

In the second process, when entering a new place in space, the neurons initially fire at the peak of the wave, then at an earlier phase, and on leaving the new place, they again fire close to the peak of the wave – a process known as phase precession.

According to the current state of knowledge, both of these processes occur simultaneously in the same cell in mice during the encoding of new information concerning spatial location.

Until now, however, it was not known whether there is a causal relationship between the two processes – does one cause the other or do they operate independently? In addition, if there is a causal dependence between the two processes, it has been unclear what mechanism promotes the conversion of the code for the firing rate into a temporal code for phase precession, causing the two to operate simultaneously.

Over the years, six groups of mathematic models were proposed, each assuming a different mechanism for the relationship between the two processes.

A new study at Tel Aviv University

In the new study – which was headed by Stark while he was the head of the Center of Excellence for the Study of the Neural Code underlying Cognition at Tel Aviv University TAU, the researchers used optogenetic technology that uses a special protein channel that reacts to light: each time the protein is exposed to blue light, the electric potential inside the neuron changes and it fires.

The researchers implanted miniaturized optoelectronic devices in the brains of freely moving mice and, using closed-loop feedback methods, caused an individual cell in the hippocampus to increase its firing rate artificially – the condition for the first process of information encoding.

The researchers monitored the mouse as it moved back and forth along a track – as it used coding mechanisms for spatial recognition.

In some track crossings, the researchers caused an increase in the firing rate of the examined cell in the hippocampus, and in others, they did not.

This allowed them to examine the effect of the artificial constraint on the firing rate at different points and times and under different conditions and thereby compare their results to “control” instances.

The findings showed that when the researchers increased the cell firing rate and created a new rate code, a change occurred in the precise timing of firing, and a phase code emerged. When the firing rate was not increased, no change in timing was observed. Thus, a clear causal relationship could be seen, whereby increasing the rate causes a change in timing.

“Firstly, it is important to clarify that although we examined the six existing model groups, there may, of course, be additional explanations we did not consider that are correct,” Stark stressed.

“If we wish to elaborate the model that explains the observations, we need to understand where the additional wave that causes interference comes from. For there to be a new wave, there must be an additional oscillator – something that creates the oscillations that form the faster waves," Stark added.

"Regarding the practical ramifications of understanding the brain mechanism for the first time, Stark said that for us to communicate effectively with the brain, we need to use its own language (code). Before our study, it might have been assumed that the brain uses several separate systems to operate the two codes simultaneously –that the brain uses several languages. But now we know that at least in one area of the brain, one code – the rate code – can be automatically converted into a code for precise timing that may be better suited to the transmission of information between the cells but is harder to implement artificially. So, if we want to elaborate the model that explains the observations, we need to understand where the additional wave that causes interference comes from,” he concluded.

New state of mind: Rethinking how researchers understand brain activity

Understanding the link between brain activity and behavior is among the core interests of neuroscience. Having a better grasp of this relationship will both help scientists understand how the brain works on a basic level and uncover what specifically goes awry in cases of neurological and psychological disease.
One way that researchers study this connection is through what are known as "brain states," patterns of neural activity or connectivity that emerge during specific cognitive tasks and are common enough in all individuals that they become predictable. Another, newer, approach is the study of brain waves, rhythmic, repetitive patterns of brain cell activity caused by synchronization across cells.

In a new paper, two Yale researchers propose that these two ways of thinking about brain activity may not represent separate events but two aspects of the same occurrence. Essentially, they suggest that though brain states are traditionally thought of as a snapshot of brain activity while waves are more like a movie, they're capturing parts of the same story.

Reconsidering these two approaches in this context, the researchers say, could help both fields benefit from the methods and knowledge of the other and advance our understanding of the brain.

Inspired by ecological, conservation, and Indigenous philosophies, Maya Foster, a third-year Ph.D. student in the Department of Biomedical Engineering, began pursuing this idea once she joined the lab of Dustin Scheinost, an associate professor in the Department of Radiology and Biomedical Imaging at Yale School of Medicine.

They are co-authors of the new paper, published in the journal *Trends in Cognitive Sciences*.

"We're arguing that rather than a brain state being one single thing, it's a collection of things, a collection of discrete patterns that emerge in time in a predictable way," she said.

In an interview with Yale News, Foster and Scheinost describe their proposal, and discuss how they might help researchers better understand the mysteries of the brain. This interview has been edited and condensed.

When did you start to consider these might be two aspects of the same occurrence?

Maya Foster: This has been on my mind even before I came to this lab. I was reading a book—"Erosion: Essays of Undoing" by Terry Tempest Williams—and she talks about how human-made machinery like helicopters cause vibrations that interrupt the natural pulse of things and cause things like rock formations to fall apart. Relatedly, there are a lot of Indigenous populations that believe everything has a pulse. And that got me thinking of the brain and whether we have some type of resonance or vibration that can be disrupted.

Then I joined this lab and Dustin let me experiment with a lot of different things. During one of those experiments, I input some data into a particular analysis and the outputs looked wave-like, and patterns emerged and then repeated. That took me down a whole rabbit hole of research literature and there was a lot of evidence for this idea of wave-like patterns in brain states.

What are the benefits of considering brain states as wave-like?

Foster: I think it creates a synergy where both sides—the brain state folks and the brain wave folks—benefit by learning from each other. And maybe the gaps in knowledge we have now when it comes to how brain activity relates to behavior might be filled by both groups working together.

Dustin Scheinost: Brain waves are newer in this field and they're complex. And any time you can take something new and relate it to something old—brain states in this case—it gives you a natural jumping off point. You can bring along everything you've learned so far. It's kind of like not throwing the baby out with the bath water. We don't need to drop brain states. They've informed us, but we can go in a different direction with them too.

How are you proposing researchers consider brain states and brain waves now?

Foster: Borrowing from physics, when you analyze light, it can be a discrete point—a photon—or it can be wave-like. And that's one way we're thinking about this. Similarly, depending on how you analyze brain states you can get static patterns, much like a photon, or you if you look at activity more dynamically, certain patterns start to occur more than once over time, kind of like a wave.

So we're arguing that rather than a brain state being one single thing, it's a collection of things, a collection of discrete patterns that emerge in time in a predictable way.

For example, if we measured four distinct patterns in brain activity as someone completed a cognitive task, a brain state could be that pattern one emerges, then pattern three, then two, then four, and that series might repeat over time. And when that repetition stops, that would be the end of that particular brain state.

You also draw comparisons to the musical technique known as 'fugue.' How does that fit with how you're visualizing these phenomena?

Foster: I'm a music person, so that's where this came from. In a fugue, you have a basic melody and then that melody emerges later in the music in different forms and formats. For instance, the melody will play, then some other music comes in, then the melody returns with the same rhythm and time sequence but maybe it's in a different key.

Fugues are cyclical and wave-like, they have distinct groups of notes, and there's a systematic repetition and sometimes layering of the main melody. We're arguing that brain states are also wave-like, have distinct patterns of brain activity, and display systematic repetition and layering of sequential patterns.

How are you hoping other researchers respond to your argument?

Foster: I would love feedback, honestly. There is evidence for what we're proposing but when it comes to implementing these ideas going forward, it would be helpful to have a conversation about how that might work. There are a lot of different strategies and I'm interested in a broader conversation about how we as researchers might go about studying this.

What's it like as someone who has been in this field for a while to have a student come in with a new idea like this?

Scheinost: You can get set in your ways as a researcher and you need new ideas, new creativity. Sometimes they may sound outlandish when you first hear them. But then you ruminate, and they start to take form. And it's fun. That's really where the fun of this job is, to hear new ideas and see how people discuss and debate them.

More information: Maya Foster et al, Brain states as wave-like motifs, *Trends in Cognitive Sciences* (2024). DOI: 10.1016/j.tics.2024.03.004

Provided by Yale University

Early genetic development of the brain mapped

In an article published in *Nature*, researchers from Karolinska Institutet present an atlas of the early development of the brain. The atlas can be used, among other things, to find out what went wrong in the development of brain tumors in children and also to find new treatments.

An international research team led by Karolinska Institutet has mapped the early genetic development of the brain and can now present an atlas of embryonic development between weeks six and 13.

"This is the first comprehensive study of brain development with a focus on gene regulation. Previous studies have almost always focused on the cortex, or cerebral cortex. Our study is a systematic mapping of the entire brain so that all regions can be compared with each other," says Sten Linnarsson, Professor of Molecular Systems Biology at the Department of Medical Biochemistry and Biophysics at Karolinska Institutet and research leader of the study.

When the brain begins to develop in the early embryo, it starts with something like a tube, where the walls of the tube will develop into the brain and the fluid-filled center of the tube becomes the ventricles, the cavity of the brain.

Rapid specialization early in pregnancy

Between weeks six and 13 of pregnancy, there is a rapid specialization of the cells in the walls of the tube. This happens through a very complex cascade reaction where substances are secreted that induce the first cells to develop in a certain way. These cells then secrete additional signals that control the next stage of cell development and so on.

The signals activate genes that produce proteins that specialize the different cell types and also act as new signals.

"It is this process, how, in which order and in which cell types genes are activated during this process of brain formation that we have been studying. We wanted to follow the process from DNA to RNA, to the protein at each step," says Linnarsson.

The research has been carried out using a method that can measure both active regions on DNA and formed RNA strands in individual cells. The researchers have then put the puzzle together and can now present a map of how it works.

The research is part of the larger Swedish project "Human Developmental Cell Atlas" where several research groups have studied the genetic development of the brain, heart, lungs, and so on. The research in the project is now moving forward and the researchers are using the maps to find answers to what went wrong in disease.

"We are now studying the onset of brain cancer in children. Fortunately, it is a rare disease, but of the various diseases that lead to death in children, it is one of the more common. We are studying the tumors that arise during embryonic brain development and using the atlas to try to understand the mechanisms of normal development that have gone wrong and how this drives tumor formation and tumor growth," says Linnarsson.

More information: Camiel C. A. Mannens et al, Chromatin accessibility during human first-trimester neurodevelopment, *Nature* (2024). DOI: 10.1038/s41586-024-07234-1

Provided by Karolinska Institutet

Neuroscientists Reveal How Magic Mushrooms Work on the Brain

Scientists have figured out why magic mushrooms make you have weird and wacky hallucinations.

Psilocybin, one of the psychoactive ingredients in magic mushrooms, impacts a region of the brain associated with daydreaming, remembering and other introspective thinking, according to a new paper in the journal *Nature*.

The effects it has on the brain may last for weeks, the paper reveals. The discovery helps to explain why the drug causes such strange psychedelic experiences, and it may pave the way for psilocybin to be used to help with mental health conditions.

"Siegel (the study author) et al. provide compelling evidence that desynchronized brain activity underlies the acute psychedelic state and might contribute to persistent changes in neural activity in brain regions that are responsible for controlling a person's sense of self, emotions and life-narrative," Petros Petridis, a psychedelics researcher at NYU Langone Center for Psychedelic Medicine, said in an accompanying News & Views article also published in Nature.

"This has significant clinical implications because it suggests that psilocybin could make the brain more malleable, which could be beneficial for people who suffer from rigid maladaptive patterns of thought and behaviour."

There are several species of magic mushrooms, all of which contain the active compounds psilocybin and psilocin, which can alter perception, mood and thought processes. The effects of magic mushrooms can vary widely based on the species, the amount consumed and the individual's mental state and environment, but common effects include visual and auditory hallucinations, an altered perception of time and space, euphoria and increased introspection. The effects typically begin 30 to 60 minutes after consuming the mushrooms, and can last between four to six hours.

Recent years have seen a spike in research into the potential therapeutic uses of psilocybin, with several studies showing promise in using psilocybin-assisted therapy for conditions such as depression, anxiety, PTSD and even substance abuse.

"These days, we know a lot about the psychological effects and the molecular/cellular effects of psilocybin," study author Joshua S. Siegel, a psychiatry researcher at Washington University School of Medicine in St. Louis, said in a statement. "But we don't know much about what happens at the level that connects the two — the level of functional brain networks."

According to the new paper, the researchers tracked changes in the brains of seven adults aged between 18 and 45 using MRI scans before, during, and three weeks after taking psilocybin. The researchers discovered that the drug desynchronized various areas of the brain, changing connectivity between these regions.

"The idea is that you're taking this system that's fundamental to the brain's ability to think about the self in relation to the world, and you're totally desynchronizing it temporarily," Siegel said. "In the short term, this creates a psychedelic experience. The longer-term consequence is that it makes the brain more flexible and potentially more able to come into a healthier state."

Some small effects of the drug were seen to persist for weeks after taking it, which the scientists say makes it ideal for therapeutic use.

"There's a massive effect initially, and when it's gone, a pinpoint effect remains," co-author Nico U. F. Dosenbach, professor of neurology at at Washington University, said in the statement. "That's exactly what you'd want to see for a potential medicine. You wouldn't want people's brain networks to be obliterated for days, but you also wouldn't want everything to snap back to the way it was immediately. You want an effect that lasts long enough to make a difference."

Interestingly, the researchers found that while each person's brain signals were unique to them and easily distinguished from one another while sober, after taking psilocybin, their brain networks appeared very similar and could not be identified until they finished their trip.

"The brains of people on psilocybin look more similar to each other than to their untripping selves," Dosenbach said. "Their individuality is temporarily wiped out. This verifies, at a neuroscientific level, what people say about losing their sense of self during a trip."

By asking the participants to rate their feelings during the trip using something called the Mystical Experience Questionnaire, the researchers could compare their experiences to their brain signals.

"We were able to get very precise data on the effects of the drug in each individual," Ginger E. Nicol, an associate professor of psychiatry at Washington University, said in the statement. "This is a step toward precision clinical trials. In psychiatry, we often don't know who should get a particular medicine and how much or how often. As a result, we end up prescribing one medicine after another, tinkering with the dosage, until we find something that works. By using this approach in clinical trials, we can identify the factors that determine who benefits and who doesn't, and make better use of the medicines we have."

However, the researchers note that this research is in its earliest stages, and people should not use their findings as a reason to self-medicate for any mental health conditions with psilocybin.

"Verification of the proposed antidepressant mechanism of psilocybin will require precision patient studies. New methods to measure neurotrophic markers in the human brain will provide a critical link between mechanistic observations at the cellular, brain networks and psychological levels," they wrote in the paper.

First 3D images of complete human thymus illuminate its structure and function

The first 3D images of a whole human thymus have been created using a specialized X-ray technique by researchers from University College London (UCL) and the Francis Crick Institute. The highly-intricate images showed that structures called Hassall's bodies occupy a large fraction of thymic medulla, suggesting they might play a role in regulating thymic microenvironment and immunity.
In research published in *Communications Medicine*, the team used phase contrast computed tomography (PC-CT) to take detailed 3D images of thymi from developing fetuses or babies aged under one year. The images were created at the cutting-edge European Synchrotron Radiation Facility (ESRF) in Grenoble, France.

The thymus is responsible for programming the immune system to respond to external threats, such as viruses and bacteria. It begins producing T cells, a type of immune cell, 12-13 weeks into a pregnancy, which then go on to colonize other areas of the body.

But there remain many unanswered questions about the structure and function of the thymus, both in health and disease, which more detailed imaging may help to address.

The new images reveal the inner structure of the thymus and shed light on the size and evolution of areas called Hassall's bodies, which form around 15 weeks into pregnancy. Until recently they were considered onion-like structures defined as the "graveyard of thymocytes."

Professor Paola Bonfanti, an author of the study from UCL Institute of Immunity & Transplantation and the Francis Crick Institute, said, "The thymus is often neglected in research, but it can tell us a lot about how our immune system works. Key to this is how the organ changes during the first few years of life and throughout adulthood.

"New methods like PC-CT can start to unravel the thymus's functions by preserving the overall integrity of the organ structure without having to slice it, which can help us understand what happens during disease where the organ architecture is compromised."

The imaging method, which exploits the fact that X-ray trajectories bend slightly when they travel through different types of tissue, showed how the ratio of compartments in the thymus—known as the cortex and the medulla—changes with age. The researchers showed that structures called Hassall's bodies appear early during organ development and occupy about a quarter of the medulla in the thymus in children when the thymus is most active, suggesting that they play a role in immune regulation.

Given that access to synchrotron facilities is limited and expensive, the team then investigated whether a smaller-scale version of the X-ray technique could be used in a standard lab. The method, called edge-illumination, exploits the same trajectory-bending principle in a standard lab space, while maintaining comparable quality to the synchrotron images.

The team confirmed that both the synchrotron and the edge-illumination system were able to distinguish between the cortex and medulla, as well as show Hassall's bodies, in images of a 19-day-old thymus.

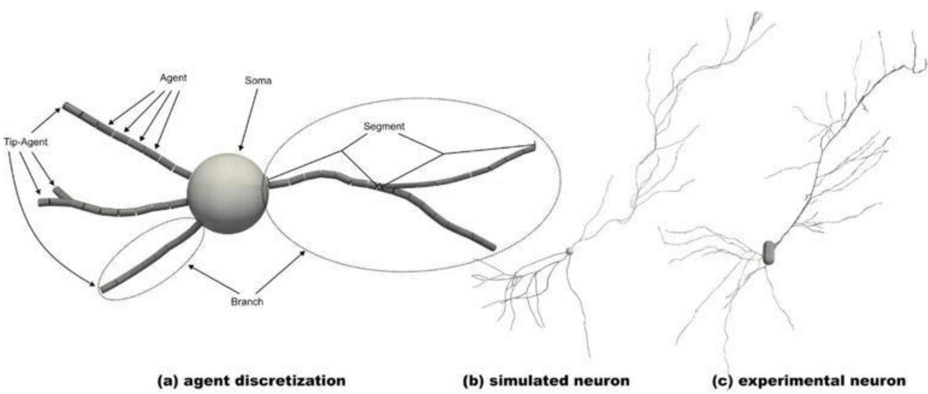
Professor Sandro Olivo, an author of the study from UCL Medical Physics & Biomedical Engineering, said, "The lab-based X-ray system provides a more accessible way to study the 3D makeup of organs without having to disrupt or destroy tissues. It also avoids having to use a small part of a sample to represent the whole organ, which can be biased. In bringing the synchrotron to the lab, we hope the technique can be used by more researchers and applied to new challenges."

The scientists believe the method could be used to study how the thymus changes in medical conditions, like the presence of tumors, or how it shrinks with age.

More information: Savvas Savvidis et al, Advanced three-dimensional X-ray imaging unravels structural development of the human thymus compartments, *Communications Medicine* (2024). DOI: 10.1038/s43856-024-00623-7

Provided by University College London

Computer simulation mimics how the brain grows neurons, paving the way for future disease treatments



3D Mechanistic ABM for neuronal growth. Panel a shows the agent-based discretization and the early stage of a neuron simulation (pyramidal cell). The center is the spherical soma (cell body). The dendrites are discretized with small, cylindrical agents. Typically, the tips drive the growth (Shree et al. 2022); hence, we differentiate between the general and tip agents. The agents define a tree-like structure with different segments and branches. b Pyramidal cell at the end of the simulation. c Experimental pyramidal cell in the mouse hippocampus observed by Benavides-Piccione et al. (2019) (NMO_147071). Credit: Journal of Mathematical Biology (2024). DOI: 10.1007/s00285-024-02144-2

A new computer simulation of how our brains develop and grow neurons has been built by scientists from the University of Surrey. Along with improving our understanding of how the brain works, researchers hope that the models will contribute to neurodegenerative disease research and, someday, stem cell research that helps regenerate brain tissue.

The research has been published in the *Journal of Mathematical Biology*.

The research team used a technique called Approximate Bayesian Computation (ABC), which helps fine-tune the model by comparing the simulation with real neuron growth. This process ensures that the artificial brain accurately reflects how neurons grow and form connections in real life.

The simulation was tested using neurons from the hippocampus—a critical region of the brain involved in memory retention. The team found that their system successfully mimicked the growth patterns of real hippocampal neurons, showing the potential of this technology to simulate brain development in fine detail.

Dr. Roman Bauer from the University of Surrey's School of Computer Science and Electronic Engineering said, "How our brain works is still one of the greatest mysteries in science. With this simulation, and the rapid advancements in artificial intelligence, we're getting closer to understanding how neurons grow and communicate. We hope that one day this work could lead to better treatments for devastating diseases like Alzheimer's or Parkinson's—changing lives for millions."

The accuracy of the model is closely tied to the quality of the data used to calibrate it. If the real-life neuron data is limited or incomplete, the precision of the simulation may decrease. While the current model has shown impressive results in replicating the growth of specific neurons, such as hippocampal pyramidal cells, further adjustments may be needed to accurately simulate other types of neurons or regions of the brain.

The computer simulation is built from the BioDynaMo software, which Dr. Bauer co-developed. The software supports scientists to easily create, run, and visualize multi-dimensional agent-based simulations, be they biological, sociological, ecological or financial.

More information: Tobias Duswald et al, Calibration of stochastic, agent-based neuron growth models with approximate Bayesian computation, *Journal of Mathematical Biology* (2024). DOI: 10.1007/s00285-024-02144-2

Provided by University of Surrey

New techniques shed light on how the brain's landscapers prune unnecessary synapses

Oligodendrocyte Precursor Cells, or OPCs (the purple and green blobs above), prune unneeded synapses (the silver streaks) in the brain's visual cortex in response to new information and experiences. Credit: Cheadle lab/Cold Spring Harbor Laboratory

Imagine yourself sometime in the far future aboard a routine rocket to Mars.

Someone just spilled their drink. Without gravity, it collects in floating blobs that ripple right before your eyes. Now freeze.

What you see might look something like the above image from Cold Spring Harbor Laboratory's (CSHL's) Cheadle lab. But those purple and green blobs aren't the floating remains of somebody's drink. They're mysterious cells in the brain's visual cortex called oligodendrocyte precursor cells (OPCs). The findings are published in the journal *Nature Protocols*.

The visual cortex processes everything we see. Incoming visual information is relayed to this outer layer of the brain via synapses—the silver streaks above. When the brain's neural circuits are first wired up, more connections, or synapses, are created than needed. As the brain accumulates new experiences and information, OPCs shape neural circuitry by pruning unnecessary synapses.

"OPCs are doing all sorts of things in the brain that help it to function in a normal, healthy way," CSHL Assistant Professor Lucas Cheadle says. OPCs are a specialty of the Cheadle lab. He and his team discovered OPCs' function as neural landscapers in 2022. Before that, they were thought only to produce oligodendrocytes, cells that sheath and support neurons. Now, Cheadle has developed new ways to zoom in and see OPCs in action.

"We're able to see what thousands of OPCs, and even smaller groups of 30–50, are doing," he explains. "From there, we can figure out which synapses are fully engulfed by an OPC, which are in the process of being pruned, and which have maybe just been checked on by an OPC but not processed."

The new techniques used to produce the image above have become essential tools in Cheadle's ongoing work. He and his team are now building on their 2022 discovery to help paint a complete picture of OPCs' role in health and disease.

Cheadle explains, "These mysterious cells are one of the primary sources of glioma," a deadly brain cancer. "They're potentially involved in Alzheimer's disease as well."

It'll take more research to illustrate these connections in detail. In the meantime, Cheadle is eager to share his lab's new tools with researchers around the world.

"The brain is constantly changing, and the same approaches you'd use to look at one type of cell can't just be applied across the board," he says. "We're adapting and innovating to keep up with it—to better understand how the brain works."

More information: Jessica A. Kahng et al, High-confidence and high-throughput quantification of synapse engulfment by oligodendrocyte precursor cells, *Nature Protocols* (2024). DOI: 10.1038/s41596-024-01048-1

Provided by Cold Spring Harbor Laboratory

The Hunt For The Laws Of Physics Behind Memory And Thought

One of the curious features of the laws of physics is that many of them seem to be the result of the bulk behavior of many much smaller components. The atoms and molecules in a gas, for example, move at a huge range of velocities. When constrained in a container, these particles continually strike the surface creating a force.
But it is not necessary to know the velocities of all the particles to determine this force. Instead, their influence averages out into a predictable and measurable bulk property called pressure.

This and other bulk properties like temperature, density and elasticity, are hugely useful because of the laws of physics that govern them. Over one hundred years ago, physicists like Willard Gibbs and others determined the mathematical character of these laws and the statistical shorthand that physicists and engineers now use routinely in everything from laboratory experiments to large scale industrial processes.

The success of so-called statistical physics raises the possibility that other systems that consist of enormous numbers of similar entities might also have their own "laws of physics". In particular, physicists have long hoped that the bulk properties of neurons might be amenable to this kind of approach.

Neural Physics

The behavior of single neurons is well understood. But put them together into networks and much more significant behaviors emerge, such as sensory perception, memories and thought. The hope is that a statistical or mathematical approach to these systems could reveal the laws of neural physics that describe the bulk behavior of nervous systems and brains.

"It is an old dream of the physics community to provide a statistical mechanics description for these and other emergent phenomena of life," say Leenoy Meshulam at the University of Washington and William Bialek at Princeton University, who have reviewed progress in this area.

"These aspirations appear in a new light because of developments in our ability to measure the electrical activity of the brain, sampling thousands of individual neurons simultaneously over hours or days."

The nature of these laws is, of course, fundamentally different to the nature of conventional statistical physics. At the heart of the difference is that neurons link together to form complex networks in which the behavior of one neuron can be closely correlated with the behavior of its neighbors.

It is relatively straightforward to formulate a set of equations that capture this behavior. But it quickly becomes apparent that these equations cannot be easily solved in anything other than trivial circumstances.

Instead, physicists must consider the correlations between all possible pairs of neurons and then use experimental evidence to constrain what correlations are possible.

The problem, of course, is that the number of pairs increases exponentially with the number of neurons. That raises the question of how much more data must be gathered to constrain the model as the number of neurons increases.

One standard system in which this has been well measured is the retina. This consists of a network of light sensitive neurons in which activity between neighbors is known to be corelated. So if one neuron is activated there is a strong possibility that its neighbor will be too. (This is the reason for the gently evolving, coral-like patterns in vision that people sometimes notice when they first wake up.)

Experiments in this area began by monitoring the behavior of a handful of neurons, then a few dozen, a few hundred and now approach thousands (but not millions). It turns out that the data helps constrain the model to the point where they give remarkably accurate predictions of neural behavior when asked, for example, to predict how many neurons are active out of any given set of them.

That suggests the system of equations accurately captures the behavior of retinal networks. In other words, "the models really are the solutions to the mathematical problem that we set out to solve," say Meshulam and Bialek.

Of course, the retina is a highly specialized part of the nervous system so an important question is whether similar techniques can generalize to the higher cognitive tasks that take place in other parts of the brain.

Emergent Behavior

One challenge here is that networks can demonstrate emergent behavior. This is not the result of random correlations or even weak correlations. Instead, the correlations can be remarkably strong and can spread through a network like an avalanche.

Networks that demonstrate this property are said to be in a state of criticality and are connected in a special way that allows this behavior. This criticality turns out to be common in nature and suggests networks can tune themselves in a special way to achieve it.

"Self-organized criticality" has been widely studied in the last two decades and there has been some success in describing it mathematically. But exactly how this self-tuning works is the focus of much ongoing research.

Just how powerful these approaches will become is not yet clear. Meshulam and Bialek take heart from the observation that some natural behaviors are amenable to the kind of analysis that physicists are good at. "All the birds in a flock agreeing to fly in the same direction is like the alignment of spins in a magnet," they say.

The fact that this is merely a metaphor concerns them - metaphors can help understanding but the real behavior of these system is often much more complex and subtle.

But there are reasons to think that mathematical models can go further. "The explosion of data on networks of real neurons offers the opportunity to move beyond metaphor," they say, adding that the data from millions of neurons should soon help to inform this debate.

"Our experimentalist friends will continue to move the frontier, combining tools from physics and biology to make more and more of the brain accessible in this way," conclude Meshulam and Bialek. "The outlook for theory is bright."

New study tries to decode how brains convert sounds into actions

Researchers from the Champalimaud Centre for the Unknown have discovered how the brain converts sounds to actions. These discoveries could someday help us unravel how the brain translates perceptions into actions. The study's foundation is to question how we make many daily decisions based on sounds without realizing it. The study helps us understand better how sensory information and behavioral choices are connected within the cortex.

This is the brain's outer layer responsible for shaping our conscious perception of the world. The cortex is a part of the brain divided into different regions, each responsible for specific functions.

The sensory areas in the cortex process information from our surroundings, while the motor areas manage our actions. Interestingly, even though signals related to future actions are expected to be found only in motor areas, they also appear in sensory areas.

How do we perceive sound?

This raises the question of why movement-related signals are present in regions dedicated to sensory processing and when and where these signals emerge. By exploring these questions, the study authors sought better to understand the origin and role of these signals.

To achieve this, they conducted a study using mice.

The study's lead author, Raphael Steinfeld, explained that they carefully designed a task for the mice to perform. In previous studies, the "Go-NoGo" task was often used, but it mixed signals related to specific movements with those related to general movements.

The mice were trained to decide between two actions to isolate signals for specific actions. They had to determine if a sound was high or low compared to a set threshold and indicate their decision by licking one of two spouts on the left or right side.

However, this wasn't enough on its own.

"To separate brain activity related to the sound from that related to the response, we introduced a critical half-second delay. During this interval, the mice had to withhold their decision," Steinfeld explained.

What is going on?

"Crucially, this delay allowed us to temporally separate brain activity linked to the stimulus from that linked to the choice and track how movement-related neural signals unfolded over time from the initial sensory input," he added.

"We found that sensory- and choice-related signals displayed distinct spatial and temporal patterns," Renart continues.

“Signals related to sound detection appeared quickly but faded fast, vanishing around 400 milliseconds after the sound was presented, and were distributed broadly across all cortical layers,” he stressed.

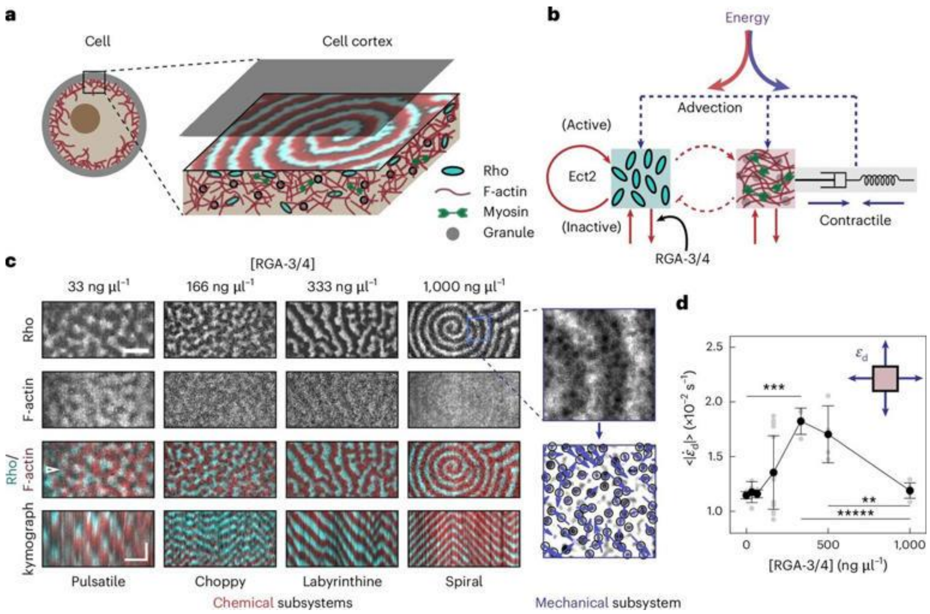
“In contrast, choice-related signals, which indicate the movement the mouse is about to make, emerged later, before the decision was executed, and were concentrated in the cortex’s deeper layers.”

“So, what might the origin of these choice signals in the auditory cortex be?,” notes explains Alfonso Renart, principal investigator and the study’s senior author.

“The early sensory signals in the auditory cortex don’t seem to predict the mice’s eventual choice, and the choice signals emerge significantly later,” added Renart. “This suggests that the sensory signals in the auditory cortex don’t directly cause the mice’s actions and that the choice signals we observe are likely computed elsewhere in higher brain regions involved in planning or executing movements, which then send their feedback to the auditory cortex.”

You can read the study for yourself in the journal *Current Biology*.

Scientists decipher the energy patterns in our cells



RGA-3/4 expression drives diverse mechanochemical patterns in the cell cortex. Credit: Nature Physics (2024). DOI: 10.1038/s41567-024-02626-6

Our cells harness energy for essential functions such as division, wound healing, and our immune response to diseases including cancer. But until now, the mechanics of how that energy affects cell behavior—and how this relates to health outcomes—have remained elusive.

Scientists at the Yale Systems Biology Institute have discovered the thermodynamic principles underpinning energy use in our cells. Published in *Nature Physics*, the discovery comes from the lab of Michael Murrell, associate professor of Biomedical Engineering and Physics.

For the first time, the scholars measured how energy is arranged into different wave patterns formed in the cell's external membrane and its internal structure, or "cytoskeleton"—both components of the cell "cortex."

Before our cells divide, they generate protein "wave patterns" in two distinctive forms—one pulsing like a heartbeat and the other displaying seemingly jumbled spiral patterns.

To understand how energy is arranged and consumed by both wave types, and how this relates to the laws of energy dissipation and distribution—or thermodynamics—postdoctoral fellow and first author of the study Sheng Chen measured the energy consumption of mechanical and chemical waves moving in different cells.

Far from being jumbled, the scholars were surprised to reveal an organized energy system dependent on distance from thermodynamic equilibrium. They found that cells displayed an optimal advantageous state—a sweet spot between the two wave types yielding maximum energy to drive cell functionality.

Discovering the principles of how energy is arranged inside our cells enhances our understanding of the physics governing cell energy dynamics and its crucial role in essential cell behavior.

From their labs at Yale's West Campus, the scientists plan to use mathematical modeling and machine learning to further quantify the relationship between different wave patterns and specific cell functions related to the spread of disease.

More information: Sheng Chen et al, Energy partitioning in the cell cortex, *Nature Physics* (2024). DOI: 10.1038/s41567-024-02626-6

Provided by Yale University

Neuroscience sheds light on brain mechanisms underlying exceptional creativity

A new study sheds light on how highly creative individuals, such as visual artists and scientists, may have brains that function differently compared to others. The research, published in *Psychology of Aesthetics, Creativity, and the Arts*, reveals that people who exhibit exceptional creativity—referred to as "Big C" creative individuals—demonstrate more random patterns of connectivity in their brains. By using functional MRI (fMRI) technology, the researchers observed that highly creative brains bypass typical neural hubs, making distant connections between different regions of the brain more quickly and efficiently.

The purpose of the study was to explore the biological foundations of exceptional creativity. Despite over seventy years of research on creative achievement, there has been limited data to support the biological mechanisms that differentiate highly creative individuals from others. Most studies of brain function in creativity have focused on everyday or professional-level creativity.

However, few have investigated what happens in the brains of those who make transformative, world-changing contributions in the arts and sciences—people often referred to as "Big C" creative types. These individuals are not only distinguished by their high levels of creative achievement but also by their ability to think in novel and non-linear ways.

The new study sought to fill the gap in understanding how the brains of these exceptional individuals work differently from both typical people and those who are merely highly intelligent. The researchers were specifically interested in how brain regions responsible for creativity, problem-solving, and artistic or scientific invention interact during tasks that demand creative thinking.

"I became interested in the topic of creativity because creativity is elusive," said study author Ariana Anderson, an assistant research professor at the Semel

Institute for Neuroscience and Human Behavior at UCLA. "People can be highly creative without being highly educated, yet most studies of creativity have compared highly intelligent and creative individuals with 'garden variety' average people."

"This confound suggests that the studies might be identifying what makes some individuals more clever than others, but not necessarily more creative. Our study compared creative people, who tend to be smarter than average, with garden variety smart people with equal intelligence."

To investigate the neural basis of exceptional creativity, the research team recruited highly creative visual artists and scientists, as well as a comparison group of individuals matched for intelligence but not necessarily known for creative accomplishments. The study's sample consisted of 66 participants: 21 Big C visual artists, 21 Big C scientists, and 24 "smart" individuals from the general population who served as a control group.

Each participant underwent brain scanning using fMRI technology, which measures brain activity by detecting changes in blood flow. The researchers captured brain connectivity both while participants were at rest and while they completed tasks designed to test their creative thinking. These tasks included:

- **The Alternative Uses Test**, which required participants to think of as many different uses as possible for a common object (for example, an umbrella).

- **The Remote Associates Test**, which presented three seemingly unrelated words and asked participants to find a fourth word that connected them (for example, the word "horse" connects the words "sea," "rocking," and "shoe").

The researchers used a mathematical approach called graph theory to analyze the brain's connectivity patterns. In this context, the brain's regions were treated as "nodes," and the connections between them as "edges." The goal was to see how efficiently information flowed through these networks and whether Big C individuals exhibited distinct connectivity patterns compared to the control group.

During the resting-state scans, when participants were not engaged in any specific task, the Big C individuals showed more random patterns of brain connectivity compared to the control group. Specifically, they exhibited less "small-worldness", a feature of brain networks that indicates an efficient balance between local and global connections. Instead of maintaining a highly organized structure, their brains displayed less clustering of connections between nearby regions, with more randomness overall.

However, locally, the creative individuals had increased clustering and efficiency, meaning certain brain areas were more specialized or active at rest. This suggests that while their overall brain network was more random, specific regions were more densely connected, potentially preparing them for creative thinking.

During the Alternative Uses Test, the Big C individuals had lower local efficiency and clustering compared to the control group. In other words, their brain activity was less organized and efficient while performing the task, which aligns with the idea that their brains may function in a more exploratory and less constrained manner during creative tasks. This reduced local connectivity suggests that, instead of focusing on specific brain regions, the creative individuals' brains may adopt a more flexible approach, allowing for the generation of diverse and novel ideas.

"Our study found that creative individuals exhibited more random connectivity in their brains," Anderson told PsyPost. "This suggests that to be creative, we need to focus less and relax more. However, relaxing doesn't mean watching TikTok—it means resting our brains so they can generate their own internal content, rather than being influenced by external sources. In fact, our study showed the greatest differences in brain activity when creative individuals were doing nothing—not when they were actively trying to be creative or clever. Mind-wandering can be the optimal time for our creative brains to shine."

Interestingly, no significant differences in brain connectivity were found during the Remote Associates Test. The lack of differences during this task suggests that while the Big C individuals excel in making broad, random connections during divergent thinking, their brain connectivity during tasks that require finding one correct solution may be similar to that of non-creative individuals.

"The creative group did not show significant differences in verbal word-play tasks compared to the IQ-matched group," Anderson explained. "For example, if given the words 'house, horse, dragon,' both a creative and non-creative person would display similar brain activity when identifying the common word that links them ('fly')."

Despite these intriguing findings, the study has some limitations. One challenge in studying exceptional creativity is that it is difficult to recruit large samples of individuals who have achieved such high levels of success in their fields. As a result, the sample size in this study was relatively small, which limits the ability to detect more subtle differences between groups.

"Major caveats of our study include that we compared individuals already well-known for their creativity," Anderson noted. "It doesn't address the question of what makes some people highly creative, nor whether creativity is an inherent trait, or something that can be acquired *or* diminished. Many studies have shown that creativity rapidly diminishes in early childhood, so it's crucial to explore how cultural shifts in parenting and screen time may be stifling the creative potential of children."

"My long-term goals for this research are to determine how we can foster creativity in children. Do we become more creative through exposure to the arts or nature, or do we merely learn to mimic others' styles, thus limiting originality? How does screen time affect children's ability to generate new ideas, given that they are constantly exposed to repetitive content?"

"A 2019 study showed that today's children are much less creative than previous generations of children," Anderson added. "With post-COVID education being highly dependent on screens, it's likely this trend is worsening. This will inevitably result in decreased innovation from future generations, which could have economic consequences."

The study, "Big-C Creativity in Artists and Scientists is Associated With More Random Global but Less Random Local fMRI Functional Connectivity," was authored by Ariana Anderson, Kevin Japardi, Kendra S. Knudsen, Susan Y. Bookheimer, Dara G. Ghahremani, and Robert M. Bilder.

Therapy using a digital avatar could help patients suffering from psychosis, study says

Therapy using a digital avatar could help patients suffering from psychosis, study says© Canva

Therapy involving computer-generated avatars may show promise in easing symptoms for people with psychosis, a new study suggests.

The research involved 345 participants who experienced auditory hallucinations, a common symptom of psychosis.

Tested across multiple UK centres, the therapy uses virtual representations akin to an avatar, to help patients engage directly with the voices they hear.

During sessions, participants design an avatar with their therapist to represent the voice they hear.

The therapist speaks both as themselves and as the avatar, using software to mimic the voice's tone.

Participants were assigned to either six sessions of therapy or to an extended 12 sessions.

Both versions were combined with standard care and compared against people who only received their usual care.

“The results of this trial confirm the value of AVATAR therapy for the reduction in the frequency and the distress of persecutory voices in psychosis, and open the door to providing the therapy within clinical practice,” Mark Huckvale, an emeritus professor of speech, hearing, and phonetic sciences at University College London (UCL) who built the voice conversion system, **said in a statement**.

From hearing 50 voices to fewer than five

At 16 weeks, both therapy groups reported lower levels of distress compared to those in the standard support group, according to the findings published in **Nature**.

By 28 weeks, the group in extended therapy showed a “sustained reduction in the frequency of the occurrence of voices”.

“To our knowledge, this is the first therapeutic intervention that has a direct and sustained impact upon the frequency with which people hear voices,” said Philippa Garety, a professor at King’s College London and the study’s lead author.

“This is an extremely important finding, as it is a clear priority for voice hearers, and hearing fewer voices, less often, or voices going away altogether can have a hugely positive impact on their day-to-day lives," Garety added.

Nick, a trial participant who experienced significant relief, described hearing up to 50 abusive voices a day before the therapy, which sessions helped reduce to fewer than five.

“I felt like I was taking back control of my life,” he said.

Building on these results, researchers are investigating how AVATAR therapy could be introduced in clinical practices nationwide.

“We hope to see AVATAR therapy available in several NHS Trusts in 2025,” said Dr Thomas Ward, the therapy’s lead and one of the study’s authors.

However, Alberto Ortiz Lobo, a psychiatrist at the Carlos III Day Hospital, who didn't take part in the study noted **in a statement** that the research wasn't comparing the intervention to other types of intervention or technique except standard care.

"The results are unpromising because they find a significant difference in improvement at 16 weeks that is lost when the results are measured at the end of the study, at 28 weeks," he said.

Quantum Entanglement Communicator

The Quantum Entanglement Communicator represents a monumental leap in global communication technology, inspired by the advanced systems featured in *Ender's Game*. This groundbreaking device harnesses the principles of quantum entanglement to enable instantaneous communication across vast distances, eliminating the delays associated with traditional systems.

By utilizing entangled particles, this communicator ensures that messages are transmitted instantly, regardless of physical barriers. Its secure, nearly unhackable nature provides a significant tactical advantage, allowing for strategic discussions without the risk of interception.

As the Quantum Entanglement Communicator bridges the gaps of time and space, it transforms not only military operations but also the very fabric of global connectivity, paving the way for a future where communication knows no bounds.

Jarvis AI is real – Google accidentally leaks its AI agent that browses the web for you

- **Google has accidentally leaked its Jarvis AI**
- **Jarvis AI browses Chrome for you**
- **It's expected to be officially unveiled in December**

Google has accidentally leaked its upcoming AI agent, Jarvis AI, which will browse the web for you in Chrome.

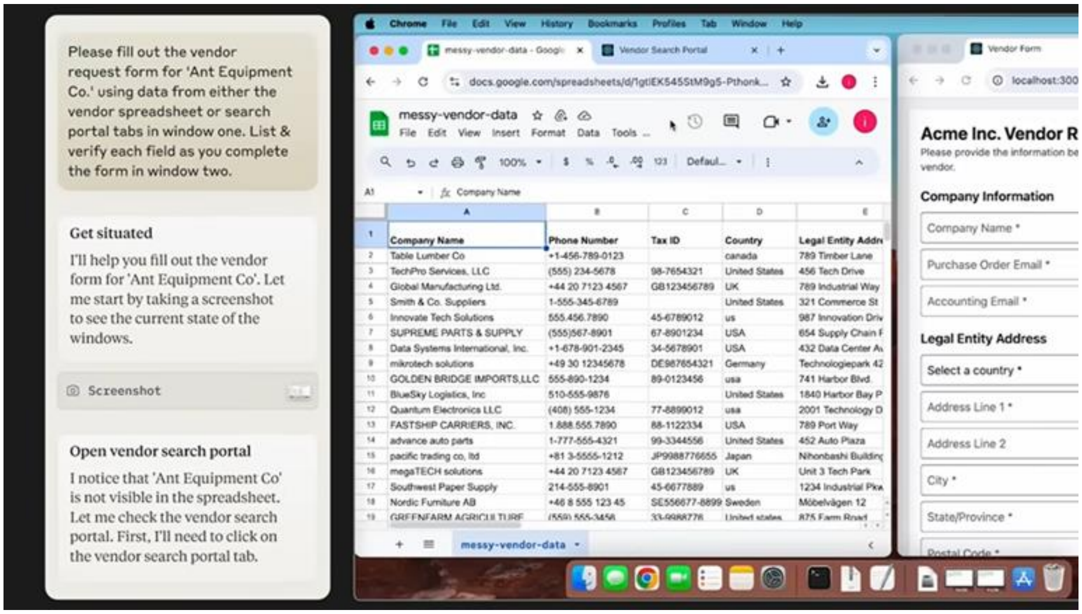
According to The Information, Google posted an internal preview of the product, codenamed Jarvis, on the Chrome extension store but was quick to remove the prototype before too many users noticed.

The listing read "a helpful companion that surfs the web with you." which lines up with the news from October that Google was developing Jarvis, the AI agent that would help you shop online and even be able to book your next vacation.

Those who managed to download the Jarvis AI prototype before it was pulled from Chrome's extension store were unable to use it as the program required specific access permissions.

With The Information reporting Google plans to officially unveil Jarvis in December, this leak confirms that we won't have long to wait.

Christmas shopping for me



Anthropic released the 'computer use' feature (above) for its Claude AI, which similarly lets it interact with your computer. (Image credit: Anthropic)

Jarvis AI is expected to allow users to automate web browsing tasks from within Google Chrome so they can focus on more important things while the AI agent shops or even books flights for you.

For example, think of how great this could be for mundane Christmas shopping – after all, nothing says 'I love you' more than a gift purchased by AI.

AI agents, which are systems that can complete tasks without your supervision, are starting to pop up increasingly with companies like Anthropic releasing a product similar to Jarvis last month. It's also reported that OpenAI could be working on an agent too, although we're yet to see how that would differ from Google's upcoming product.

AI development is booming with companies releasing new tools almost daily. Just last week ChatGPT Search became available to Plus subscribers ushering in a new era for AI search engines. With Jarvis AI, however, we might not even need to do the searching ourselves.

Memories are not only in the brain, human cell study finds

An NYU researcher administers chemical signals to non-neural cells grown in a culture plate. Credit: Nikolay Kukushkin

It's common knowledge that our brains—and, specifically, our brain cells—store memories. But a team of scientists has discovered that cells from other parts of the body also perform a memory function, opening new pathways for understanding how memory works and creating the potential to enhance learning and to treat memory-related afflictions.

"Learning and memory are generally associated with brains and brain cells alone, but our study shows that other cells in the body can learn and form memories, too," explains New York University's Nikolay V. Kukushkin, the lead author of the study, which appears in the journal *Nature Communications*.

The research sought to better understand if non-brain cells help with memory by borrowing from a long-established neurological property—the massed-spaced effect—which shows that we tend to retain information better when studied in spaced intervals rather than in a single, intensive session—better known as cramming for a test.

In the research, the scientists replicated learning over time by studying two types of non-brain human cells in a laboratory (one from nerve tissue and one from kidney tissue) and exposing them to different patterns of chemical signals—just like brain cells are exposed to patterns of neurotransmitters when we learn new information.

In response, the non-brain cells turned on a "memory gene"—the same gene that brain cells turn on when they detect a pattern in the information and restructure their connections in order to form memories.

To monitor the memory and learning process, the scientists engineered these non-brain cells to make a glowing protein, which indicated when the memory gene was on and when it was off.

The results showed that these cells could determine when the chemical pulses, which imitated bursts of neurotransmitter in the brain, were repeated rather than simply prolonged—just as neurons in our brain can register when we learn with breaks rather than cramming all the material in one sitting.

Specifically, when the pulses were delivered in spaced-out intervals, they turned on the "memory gene" more strongly, and for a longer time, than when the same treatment was delivered all at once.

"This reflects the massed-space effect in action," says Kukushkin, a clinical associate professor of life science at NYU Liberal Studies and a research fellow at NYU's Center for Neural Science. "It shows that the ability to learn from spaced repetition isn't unique to brain cells, but, in fact, might be a fundamental property of all cells."

The researchers add that the findings not only offer new ways to study memory, but also point to potential health-related gains.

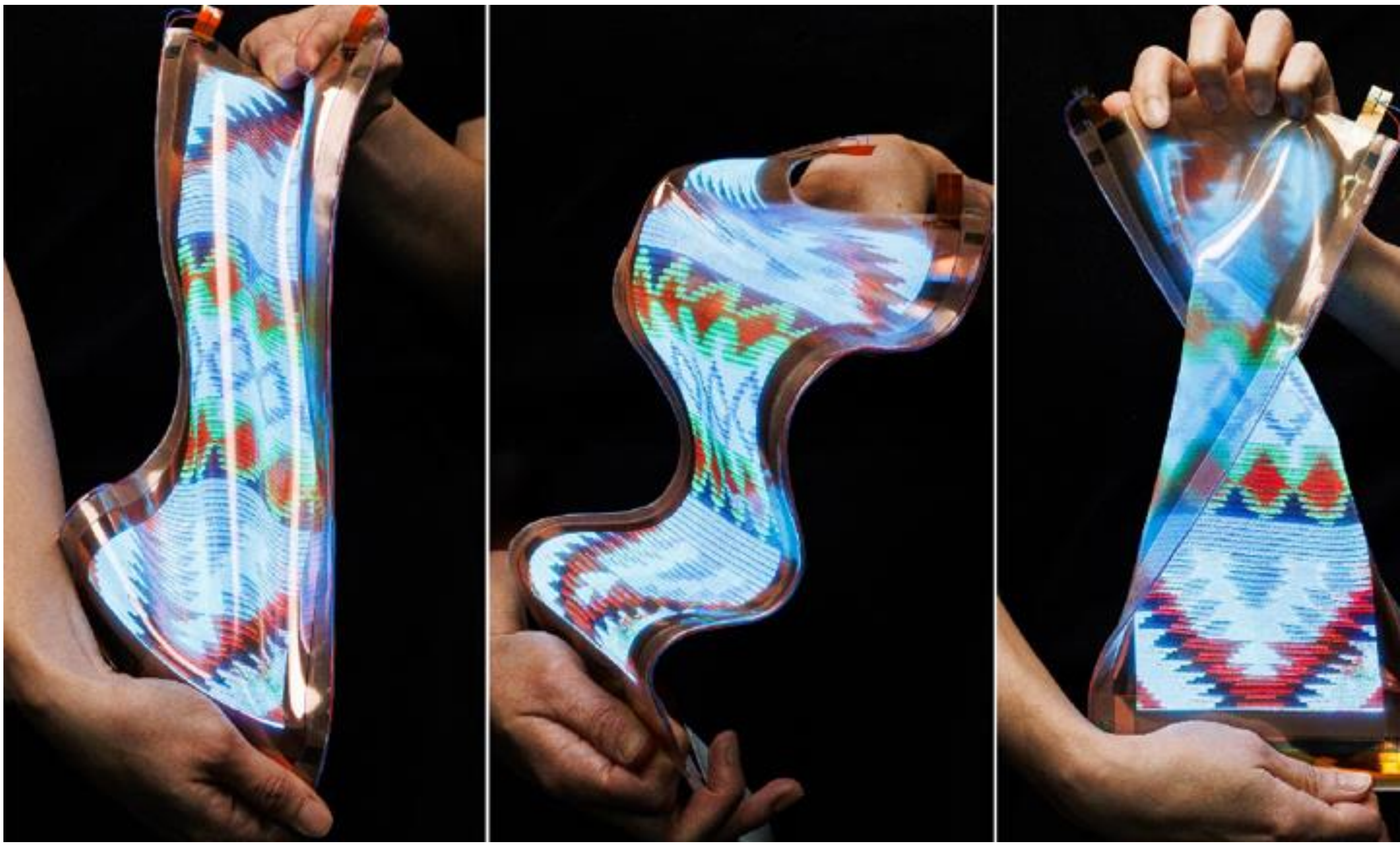
"This discovery opens new doors for understanding how memory works and could lead to better ways to enhance learning and treat memory problems," observes Kukushkin.

"At the same time, it suggests that in the future, we will need to treat our body more like the brain—for example, consider what our pancreas remembers about the pattern of our past meals to maintain healthy levels of blood glucose or consider what a cancer cell remembers about the pattern of chemotherapy."

The work was jointly supervised by Kukushkin and Thomas Carew, a professor in NYU's Center for Neural Science. The study's authors also included Tasnim Tabassum, an NYU researcher, and Robert Carney, an NYU undergraduate researcher at the time of the study.

More information: N. V. Kukushkin et al, The massed-spaced learning effect in non-neural human cells, *Nature Communications* (2024). DOI: 10.1038/s41467-024-53922-x Provided by New York University

LG's bizarre but impressive stretchable prototype display has the 'highest rate of elongation in the industry,' a measurement I had no idea existed



LG's bizarre but impressive stretchable prototype display has the 'highest rate of elongation in the industry,' a measurement I had no idea existed© LG Display

Flexibility could be the next bleeding edge for hardware to thread. Besides the bendy CPU whose performance leaves much to be desired outside its one party trick, monitor manufacturers are experimenting with pliable projects.

LG Display is the latest name to explore something with this technical twist, unveiling a stretchy screen prototype that can be expanded by up to 50% with a good tug (via Tom's Hardware). A prototype demonstration took place in Seoul at LG Science Park as part of a stretchable display national project during an event involving around 100 other South Korean tech stakeholders on November 8th.

This is far from the first bendy screen we've seen, with American company Corsair releasing the Xeneon Flex OLED Monitor a few years back. The big difference with LG's prototype is that it does a bit more than stretch; you can scrunch it, pull it, and twist it (though there's no word yet on whether you can bop it).

Dated reference aside (does Gen Z know the crushing low of flicking it when you mean to bop it?) LG's prototype is also a darn sight smaller than that Corsair monitor. LG's flexible display first presents RGB colour and 100 PPI at 12 inches, but can then expand up to 18-inches—which LG is quick to note in their press release exceeds "the original national project’s target of 20% elongation," and is "the highest rate of elongation in the industry."

As impressive as all of that is, I just can't get past how wrong the idea of scrunching up expensive tech feels; monitors may be hardware but they're historically not the hardiest of wares in the face of, say, a flung controller. Furthermore, in the case of the Corsair monitor, it's not just the fact you've really got to give it some welly to expand the display, but also the horrible sounds of protestation made by the frame that all contribute to the feeling of 'there's something wrong with this picture.'

Besides that, isn't the pliability of LG's prototype and its array of potential form factors just introducing heaps of new points of failure?

On the subject of durability, LG's press release states, "By using a micro-LED light source of up to 40 µm (micrometers), the new prototype’s strengthened durability means it can be repeatedly stretched over 10,000 times, maintaining clear image quality even in extreme environments such as exposure to low or high temperatures and external shocks." That might be a bold claim but, if this prototype ever makes it to market in some form, it could mean cracked phone screens may one day be a thing of the past.

The LG Display prototype remains a ways off any kind of consumer environment, but the company also shared a handful of conceptual use cases. In a bid to further highlight both the prototype's durability and pliability, LG proposed a wearable application where a stretchable display panel attached to a firefighter's uniform could provide a real-time feed of information. While that could end up being a pipe dream, a wearable that actually achieves some real world good would certainly make a change.

Study discovers a 'brain thesaurus' that lets neurons derive meaning from spoken words

Using a novel technology for obtaining recordings from single neurons, a team of investigators at Massachusetts General Hospital, a founding member of the Mass General Brigham health care system, discovered a microscopic "thesaurus" that reflects how word meanings are represented by neurons in the human brain.

The research, which is published in *Nature*, opens the door to understanding how humans comprehend language and provides insights that could be used to help individuals with medical conditions that affect speech.

"Humans possess an exceptional ability to extract nuanced meaning through language—when we listen to speech, we can comprehend the meanings of up to tens of thousands of words and do so seamlessly across remarkably diverse concepts and themes," said senior author Ziv Williams, MD, a physician-investigator in the department of Neurosurgery at Massachusetts General Hospital and an associate professor of Neurosurgery at Harvard Medical School.

"Yet, how the human brain processes language at the basic computational level of individual neurons has remained a challenge to understand."

Williams and his colleagues set out to construct a detailed map of how neurons in the human brain represent word meanings—for example, how we represent the concept of animal when we hear the word cat and dog, and how we distinguish between the concept of a dog and a car.

"We also wanted to find how humans are able to process such diverse meanings during natural speech and through which we are able to rapidly comprehend the meanings of words across a wide array of sentences, stories, and narratives," Williams said.

To start addressing these questions, the scientists used a novel technology that allowed them to simultaneously record the activities of up to a hundred neurons from the brain while people listened to sentences (such as, "the child bent down to smell the rose") and short stories (for example, about the life and times of Elvis Presley).

Using this new technique, the investigators discovered how neurons in the brain map words to particular meanings and how they distinguish certain meanings from others.

"For example, we found that while certain neurons preferentially activated when people heard words such as 'ran' or 'jumped,' which reflect actions, other neurons preferentially activated when hearing words that have emotional connotations, such as 'happy' or 'sad,'" said Williams.

"Moreover, when looking at all of the neurons together, we could start building a detailed picture of how word meanings are represented in the brain."

To comprehend language, though, it is not enough to only understand the meaning of words, but also to accurately follow their meanings within sentences. For example, most people can rapidly tell the correct meaning of words such as "sun" and "son" or "see" and "sea" when used in a sentence, even though the words sound exactly the same.

"We found that certain neurons in the brain are able to reliably distinguish between such words, and they continuously anticipate the most likely meaning of the words based on the sentence contexts in which they are heard," said Williams.

Lastly, and perhaps most excitingly, the researchers found that, by recording a relatively small number of brain neurons, they could reliably predict the meanings of words as they were heard in real-time during speech. That is, based on the activities of the neurons, the team could determine the general ideas and concepts experienced by an individual as they were being comprehended during speech.

"By being able to decode word meaning from the activities of small numbers of brain cells, it may be possible to predict, with a certain degree of granularity, what someone is listening to or thinking," said Williams.

"It could also potentially allow us to develop brain-machine interfaces in the future that can enable individuals with conditions such as motor paralysis or stroke to communicate more effectively."

More information: Mohsen Jamali et al, Semantic encoding during language comprehension at single-cell resolution, *Nature* (2024). DOI: 10.1038/s41586-024-07643-2

Provided by Massachusetts General Hospital

Our brains trick us into thinking consciousness can reside outside the body, research argues

Psychology professor Iris Berent says perceiving minds and bodies as separate has evolutionary roots. Credit: Matthew Modoono/Northeastern University© Provided by Medical Xpress

The origins of consciousness have been debated by philosophers for centuries. Each conscious person has a sense of "being me," which invariably gives rise to the question of where that sense originated—from within or outside the body, says Northeastern University psychology professor Iris Berent.

"How do human brains give rise to this experience? That's the big mystery, right?" she says.

Influential philosopher David Chalmers famously won a bet in 2023 for claiming consciousness exists beyond the merely physical, Berent says.

But she says the question of where consciousness exists is a false one—and she has a new paper that presents her position.

In an article published in the *Neuroscience of Consciousness*, she argues that the debate stems from the delusional—albeit natural—biases in the way humans think about the separation, or lack thereof, between body and mind.

"One of the biases is dualism, intuitive dualism—the fact that we perceive minds as separate from our bodies."

"The extent to which we look at consciousness and think that it is this really mysterious thing could very well arise from how we see it rather from what consciousness really is," Berent says.

"Consciousness isn't hard. Psychology is," she says.

Mary and the zombie

Berent points to an experiment in perception she conducted in her lab that used the well-known Mary and the zombie hypothetical exercise, but with a twist.

According to the experiment, when people are asked to think of a zombie twin of themselves, they describe a creature with their physical features but without their thoughts or feelings.

"They intuit that the mind, consciousness included, is really separate from the physical," Berent says.

In the other thought experiment, Mary is a neuroscientist who knows everything about color and how the brain perceives color, even though she lives in a black-and-white world.

When Mary sees a red rose for the first time, people participating in the experiment say she learns something outside the bounds of physical, scientific explanation.

Berent says she decided to challenge these conclusions with two additional questions.

"The first question is kind of a reality check question, which is do they think Mary's case is significant? Is it transformative? And everybody said, 'Sure, it's super transformative,'" Berent says.

"We also asked how likely is it that this experience will actually show up in her brain? If we scan her brain, will it light up? And it turns out that that's exactly what people said. It will significantly register in the brain."

"The point being, in the condition of the zombie people say, 'no,' (consciousness) is not physical," Berent says. "And in Mary's condition, people say it's physical."

"If people change their mind in this way, it can't possibly be that in reality consciousness has changed. It must be that there is something within the human psyche that colors how we see consciousness."

"For me, this means that we need to be really careful before we assume that there is any real mystery going on."

The evolutionary roots of dualism

Berent blames what she calls "delusional attitudes about bodies and minds" to "the same old psychological biases that I've been studying in my lab for years."

She calls the separation of mind and body dualism Previous research by Berent shows that autistic people are less dualistic than neurotypical people and that males are less dualistic than females.

Evolution is responsible for the fact people hold two different systems of perception in their mind, Berent says.

"Animals have an evolutionary advantage to be able to perceive objects, say, the bodies of their mothers," she says.

It's also important to be able to perceive objects that have agency as separate from other objects, Berent says. "You want to follow the mother and not a body that is inanimate" to receive nurturance and protection.

This type of dualism, she says, "primes us to think about people and their minds and bodies as separate from each other. That's one reason we think about consciousness as this ethereal thing separate from the body."

"The point is that our perception of consciousness changes depending on the situation. And if that's the case, there's no way that we can trust it to reflect what our consciousness really is. It must be that our brain plays tricks on us."

An intimate understanding of who we are

"Every psychology student that has ever come into my class asks if we're going to talk about consciousness," Berent says.

"This is considered to be super important. This is our intimate understanding of who we are."

Berent says the thought experiment outlined in her paper provides "the smoking gun" that intuitions about consciousness existing outside the body are manufactured by humans' dualistically inclined brains.

Consciousness likely comes down to electrochemical functions in the brain, she says. "It's hard for psychological reasons."

More information: Iris Berent, Consciousness isn't "hard"—it's human psychology that makes it so!, *Neuroscience of Consciousness* (2024). DOI: 10.1093/nc/niae016

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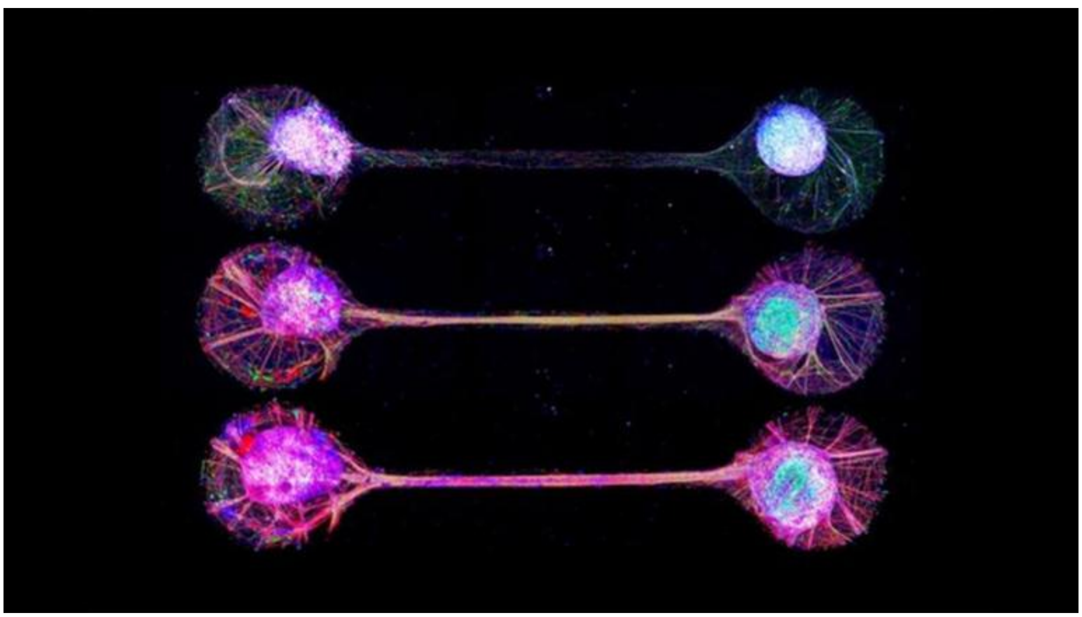
Provided by Northeastern University

Mini brains wired: Scientists grow brain-like thinking tissues in lab



Mini brains wired: Scientists grow brain-like thinking tissues in lab© Provided by Interesting Engineering

A Japanese and French research team has developed a technique for connecting lab-grown brain-imitating tissue. The most interesting part is that it has been done in a way that resembles circuits in our brains.

The idea of growing functioning human brain-like tissues in a dish has always sounded far-fetched.

It is challenging to study the exact mechanisms of brain development and functions. For example, brain cells grown in the lab tend to lack the characteristic connections of cells in the human brain. Researchers are realizing that these interregional connections and the circuits they create are important for many brain functions.

Physiological connections between lab-grown brain tissue

Researchers from The University of Tokyo have found a way to create more physiological connections between lab-grown “neural organoids.” That is an experimental model tissue in which human stem cells are grown into three-dimensional developmental brain-mimicking structures.

Scientists from The University of Tokyo have discovered a way to make better connections between lab-grown “neural organoids.” These special tissues are created in experiments where human stem cells are grown into 3D structures to mimic brain development. They connected these organoids using axonal bundles, which are like bridges connecting different areas in a living human brain.

As co-lead author of the study, Tomoya Duenki said in single-neural organoids grown under laboratory conditions, the cells start to display relatively simple electrical activity.

How they did it?

First, they connected two neural organoids with axonal bundles. Then they observed how these connections contributed to generating and synchronizing activity patterns between the organoids. That demonstrated some similarity to connections between two regions within the brain.

The cerebral organoids that were connected with axonal bundles showed more complex activity than single organoids. So the team stimulated the axonal bundles using a technique known as optogenetics. The organoid activity was altered accordingly and the organoids were affected by these changes. That lasted for some time and in a process that is known as plasticity. For example, plasticity is important because it helps researchers understand how brain-like structures respond and adapt to changes. This means learning more about how these artificial brain tissues function.

Light detection for better treatments

Optogenetics is a method used to control and study the activity of cells in living organisms. It was introduced in 2006. It uses genetic engineering and optical technology to control and monitor biological functions. For example, defined light stimulation and efficient light detection systems has enabled optogenetics to disrupt and observe biological functions.

"These findings suggest that axonal bundle connections are important for developing complex networks," explained Yoshiho Ikeuchi, senior author. "Notably, complex brain networks are responsible for many profound functions, such as language, attention, and emotion."

Alterations in brain networks have been associated with various neurological and psychiatric conditions. The ability to study lab-grown human neural circuits will improve knowledge of how these networks both form and change. With the main focus on how they do that over time in different situations. That can lead us to improved treatments for these conditions.

The article, "Complex Activity and Short-Term Plasticity of Human Cerebral Organoids Reciprocally Connected with Axons," was published in Nature Communications.

Neuroscience research leverages stem cells to understand how neurons connect and communicate in the brain

Human neurons derived from stem cells by Assistant Professor Soham Chanda and his team at Colorado State University. Credit: Colorado State University© Provided by Medical Xpress

Newly published research from Colorado State University answers fundamental questions about cellular connectivity in the brain that could be useful in the development of treatments for neurological diseases like autism, epilepsy or schizophrenia.

The work, highlighted in the *Proceedings of the National Academy of Sciences,* focuses on how neurons in the brain transmit information between each other through highly specialized subcellular structures called synapses. These delicate structures are key to controlling many processes across the nervous system via electrochemical signaling, and pathogenic mutations in the genes that impair their development can cause severe mental disorders.

Despite their important role in linking neurons across different brain regions, the way synapses form and function is still not well understood, said Assistant Professor Soham Chanda.

To answer that fundamental question, Chanda and his team in the Department of Biochemistry and Molecular Biology focused on a specific and important type of synapse called GABAergic. He said neuroscience researchers have long hypothesized that these synapses might form because of a release of GABA and the corresponding sensing activity between two neurons in proximity. However, research in the paper now shows that these synapses can begin to develop autonomously and apart from that neuronal communication, mainly due to the scaffolding action of a protein called Gephyrin. These findings clarify the key mechanisms of synaptic formation, which might allow researchers to further focus on synapse dysfunction and health treatment options.

Chanda's team used human neurons derived from stem cells to develop a model of the brain that could rigorously test these relationships. Using a gene-editing tool called CRISPR-Cas9, they were able to genetically manipulate the system and confirm the role of Gephyrin in the synapse formation process.

"Our study shows that even if a pre-synaptic neuron is not releasing GABA, the post-synaptic neuron can still put together the necessary molecular machineries prepared to sense GABA," Chanda said. "We used a gene-editing tool to remove the Gephyrin protein from neurons, which largely reduced this autonomous assembly of synapses—confirming its important role irrespective of neuronal communication."

Using stem cells to advance understanding of neuron and synapse formation

Neuroscientists have traditionally used rodent systems to study these synaptic connections in the brain. While that provides a suitable model, Chanda and his team were interested in testing synapse properties in a human cellular environment that could eventually be more easily translated into treatments.

To achieve this, his team cultivated human stem cells to form brain cells that could mimic the properties of human neurons and synapses. They then conducted extensive high-resolution imaging of these neurons and tracked their electrical activities to understand synaptic mechanisms.

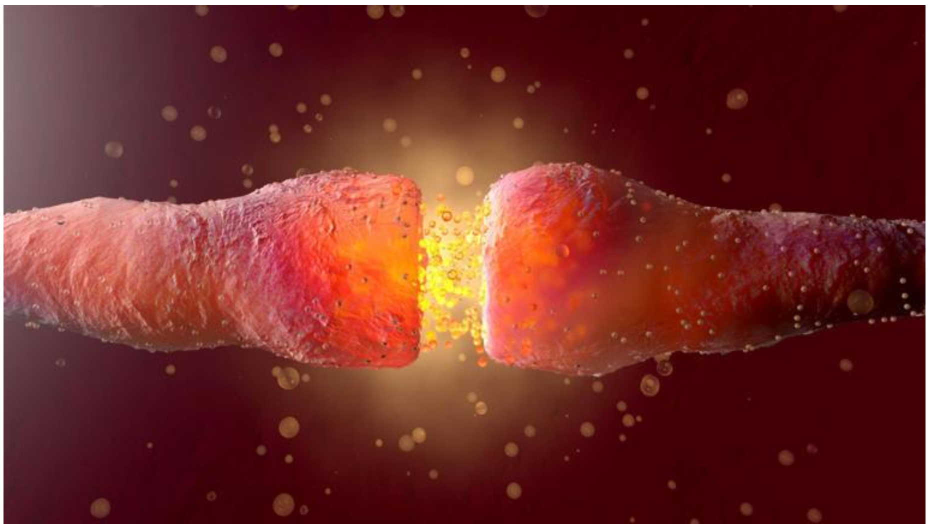
Chanda said that several mutations in the Gephyrin protein have been associated with neurological disorders like epilepsy, which alters neuronal excitability in the human brain. That makes understanding its basic cellular function an important first step towards treatment and prevention.

"Now that we better understand how these synaptic structures interact and organize, the next question will be to elucidate how defects in their relationships can lead to disease and identify the ways one can predict or intervene in that process," he said.

More information: Etta Carricaburu et al, Gephyrin promotes autonomous assembly and synaptic localization of GABAergic postsynaptic components without presynaptic GABA release, *Proceedings of the National Academy of Sciences* (2024). DOI: 10.1073/pnas.2315100121

Provided by Colorado State University

Secret to lifelong memories sticking is molecular 'glue'



Scientists have discovered that a particular protein is responsible for guiding an enzyme needed to maintain long-term memory to the correct region of the brain. Specifically, this is to particular synapses, or connections between neurons, as illustrated above.© Westend61 via Getty Images

Some memories last a lifetime — and now, scientists have revealed a type of molecular "glue" that helps those memories stick around.

Memories form when collections of neurons in a region of the brain called the hippocampus activate in response to a particular experience. Each time you recall that experience, the same set of cells activates. When one neuron repeatedly activates another, the connection between those neurons strengthens.

Over time, this process in the hippocampus, along with related activity in other regions of the brain, solidifies a short-term memory into a long-term one.

To maintain these long-term memories, brain cells make proteins that help strengthen the connections, or synapses, between neurons. One critical protein is the enzyme PKMzeta, which is continually made by neurons. However, an outstanding question is how this enzyme "knows" to go to the right synapses to ensure that certain memories stay with us forever.

In a new study, scientists think they've found the answer: an unsung molecule called KIBRA glues the enzyme to strong synapses and also summons new PKMzeta to replace that enzyme when it degrades. The researchers published their findings Wednesday (June 26) in the journal Science Advances.

Related: The brain has a 'tell' for when it's recalling a false memory, study suggests

Previous research in humans suggested that different versions of the KIBRA molecule are associated with differences in memory performance, either better or worse. KIBRA was also already known to interact with the PKMzeta enzyme in the hippocampus of mice. So, the scientists behind the new study decided to delve further into that interaction.

In lab experiments, the team investigated whether blocking the interaction between KIBRA and PKMzeta influenced how well mice performed in long-term memory tests. These tests included seeing whether the mice could remember to avoid entering an area where they had previously been shocked with electricity.

Blocking the interaction between KIBRA and PKMzeta impaired the mice's long-term spatial memory — in other words, their ability to avoid the shock zone.

In a separate experiment, when the KIBRA-PKMzeta interaction was left undisturbed, the team found that even when PKMzeta degraded as expected, new complexes of KIBRA and PKMzeta formed in the hippocampus. This, in turn, helped maintain the mice's memory of the shock zone for a month.

Earlier work by the same team showed that if researchers increase the amount of PKMzeta in a rodent's brain, it appears to enhance weak long-term memories that have faded over time. This initially surprised the scientists, as the team expected PKMzeta to boost the strength of synapses at random, rather than specifically acting on those involved in long-term memory.

Instead, the new findings suggest that KIBRA acts like a "glue," sticking to these strong synapses and also guiding PKMzeta to them, which would explain this phenomenon, the team said.

The research is only in its infancy. However, eventually, it may be possible to someday use this knowledge to treat brain disorders that cause memory loss, such as Alzheimer's disease, said study co-senior author André Fenton, a professor of neural science at New York University. Such treatments could work by using KIBRA to deliver PKMzeta or similar molecules to weakened synapses.

However, with neurodegenerative diseases such as Alzheimer's, the conditions damage and eventually kill off neurons in the brain. That means that this kind of therapy would theoretically only work for as long as there are still synapses left to enhance.

For now, more research is needed to understand how the interaction between PKMzeta and KIBRA actually translates into people's experiences of memory.

"We have quite a way to go to turn the description of these molecules into that experiential thing that we cherish — what we call memory, belief, intention and so forth," Fenton said.

Scientists find the reason why people with schizophrenia hear voices — and maybe how to stop them

Credit: Gregory Nemec/Yale Alumni Magazine.© ZME Science

For those who live with schizophrenia, the sound of voices — voices that no one else can hear — can be an overwhelming and persistent part of daily life. But the mystery of why these hallucinations happen has stumped scientists for decades. Now, researchers believe they may be closer to solving this riddle.

A new study suggests that the cause of these phantom voices lies in the brain's inability to recognize its own speech signals. The findings could open the door to treatments that go beyond medications, offering new hope to the millions of people who struggle with schizophrenia worldwide.

Scientists are finally beginning to understand the specific brain mechanisms that cause auditory hallucinations. And this could change the way we think about the disorder and how we treat it.

When the Brain Can't Hear Itself

People with schizophrenia often report hearing voices that seem to come from somewhere outside themselves. These auditory hallucinations affect up to 80% of patients and are one of the hallmarks of the illness. But what's happening in the brain to create this experience?

The answer may lie in the way the brain processes its own speech signals. Normally, when we prepare to speak, our brain generates a copy of the motor commands it uses to move our mouths and tongues. This copy, known as a "corollary discharge," is sent to the auditory system to let it know that the sounds we are about to make are coming from us — not the outside world.

In people with schizophrenia, however, this system seems to malfunction. Using EEG monitors, the research team tracked brain activity in three groups of people: those with schizophrenia who experience auditory hallucinations, those with schizophrenia who don't, and a control group of healthy individuals. The results were telling.

Both groups of patients with schizophrenia showed a disruption in their brain's ability to predict the sound of their own voices before speaking. But for those who heard voices, something else was happening: a hyperactive efference copy — the signal that tells the body to vocalize. This overactive signal, researchers suggest, floods the auditory system, creating a chaotic jumble of internal sounds that the brain can't properly filter out.

"People who suffer from auditory hallucinations can 'hear' sounds without external stimuli," explained neuroscientists led by Fuyin Yang from Shanghai Jiao Tong University, who co-authored the study. "Impaired functional connections between motor and auditory systems in the brain mediate the loss of ability to distinguish fancy from reality."

In short, the brain of someone experiencing hallucinations is overwhelmed by its own noise.

Voices from Within

It may seem abstract, but the mechanisms behind these hallucinations are something we all experience on a much smaller scale. Think about tickling. No matter how hard you try, you can't tickle yourself. That's because your brain predicts the sensation and dampens your response.

For people with schizophrenia, however, this internal suppression breaks down. Without the ability to filter out their own speech signals, their brains treat their inner thoughts as if they were external sounds — leading to the sensation of hearing voices.

The research builds on decades of work trying to explain why schizophrenia patients experience such profound distortions of reality. Earlier studies have pointed to disruptions in the brain's motor systems, suggesting that misfired signals may be at the root of auditory hallucinations. But this new study goes a step further, identifying the specific signals that go awry.

These insights could be a game-changer for treating schizophrenia as they add a level of nuance to the condition that wasn't available before.

"You can't treat what you don't understand," Tom Whitford, a psychology professor at the University of New South Wales in Australia who was not involved in the research, told STAT. "It's very worthwhile knowing exactly what aspect of that mechanism is not normal in people with schizophrenia," he added.

A Future Without Medications?

Currently, schizophrenia is treated primarily with antipsychotic medications, which can have severe side effects and don't work for everyone. Many patients are resistant to drug treatments, leaving them with few options for managing their symptoms.

But if the brain's faulty signals are to blame for auditory hallucinations, there may be other ways to address the problem. Xing Tian and his colleagues believe that non-invasive treatments, such as transcranial magnetic stimulation (using a magnetic coil to influence the brain's natural electrical activity), could help regulate brain activity and potentially silence the voices in patients who don't respond to medication.

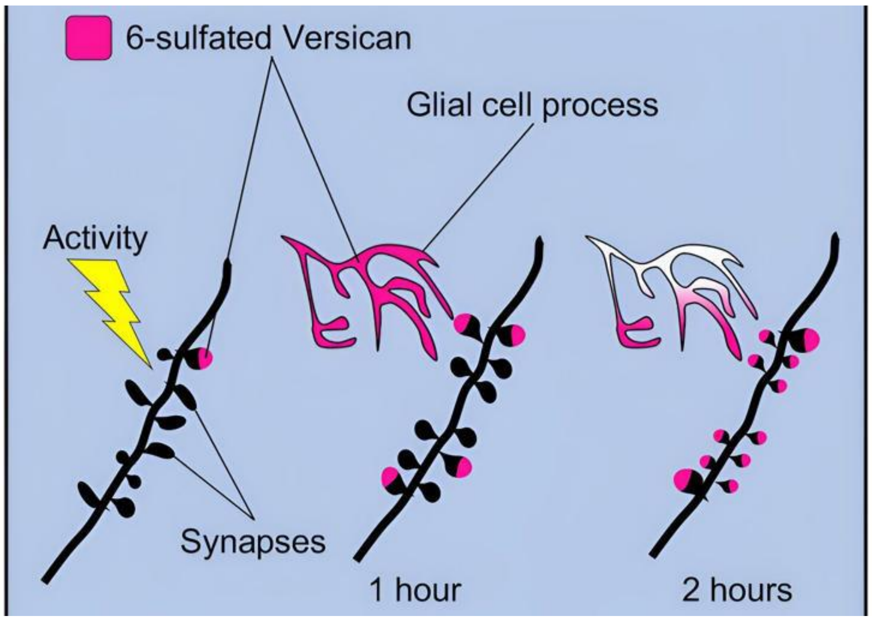
"Some patients are really resistant to drugs — maybe that's because it's hard to modulate the function network [with them]," said Xing Tian, the study's lead author and an associate professor of Neural and Cognitive Sciences at NYU Shanghai. "If our theory is right, then using a non-invasive neuromodulation technique can alleviate the hallucinations."

This research comes at a pivotal time for schizophrenia treatment. In recent months, the FDA has approved a new drug that could change how the disorder is treated, marking the first major advancement in decades. Coupled with these new insights into the brain's role in hallucinations, the future for schizophrenia treatment may be brighter than it has been in years.

For the nearly 4 million people living with schizophrenia in the United States alone, that future can't come soon enough. As researchers continue to peel apart the secret layers of the brain, the hope is that one day, those voices will finally fall silent.

The findings appeared in the journal *PLOS Biology*

Researchers demonstrate a new mechanism of neural plasticity underlying learning and memory processes



Graphical abstract. Credit: Cell Reports (2024). DOI: 10.1016/j.celrep.2024.114112© Provided by Medical Xpress

Neurons are important, but they are not everything. Indeed, it is "cartilage," in the form of clusters of extracellular matrix molecules called chondroitin sulfates, located in the outside nerve cells, that plays a crucial role in the brain's ability to acquire and store information.

A study published in *Cell Reports* describes a new mechanism of brain plasticity, or how nerve connections change in response to external stimuli. The paper is titled "Focal clusters of peri-synaptic matrix contribute to activity-dependent plasticity and memory in mice."

The work stems from a collaboration between the Harvard Medical School, the University of Trento, and the German Center for Neurodegenerative Diseases (DZNE) in Magdeburg.

"Sensory skills and the ability to understand our surroundings depend on the activity of the brain, which enables us to perceive and process stimuli that come from the outside world. Through our brains we are able to acquire and store new information, and to remember information we have already acquired," say Yuri Bozzi and Gabriele Chelini.

"This fascinating phenomenon is made possible by the brain's ability to continuously change the structure and effectiveness of neuronal connections (synapses) in response to external stimuli. An ability that goes by the name of synaptic plasticity. Understanding how synaptic modifications occur and how they contribute to learning and memory is one of the great challenges in neuroscience."

Yuri Bozzi is a professor at the University of Trento and co-senior author. Gabriele Chelini is the first author of the study. Chelini worked on this project starting in 2017, as a postdoctoral fellow in a lab directed by Sabina Berretta (McLean Hospital and Harvard Medical School, Boston), and completed the scientific publication during his years as a postdoctoral fellow in Bozzi's lab at the University of Trento.

At the center of the research are chondroitin sulfates, molecules well known for their role in joints, which also play a crucial function in brain plasticity, being an integral part of the brain's extracellular matrix, as was originally discovered in 2001 by Dr. Alexander Dityatev's group.

In 2007, a Japanese study described the presence of clusters of chondroitin sulfates, circular in shape, scattered seemingly randomly in the brain. This work had slipped into oblivion, however, until Sabina Berretta's translational neuroscience laboratory brought these structures back to the attention of the scientific community, renaming them CS-6 clusters (from chondroitin sulfate-6, which identifies their precise molecular composition) and demonstrating how these structures were associated with glial cells and were severely reduced in the brains of people with psychotic disorders.

Then in 2017, Gabriele Chelini, newly hired in Berretta's lab, was tasked with revealing the function of these clusters.

"First we went to explore these structures in detail, visualizing them at very high resolution. We found that they are essentially clusters of synapses coated with CS-6 and organized in a clearly recognizable geometric shape. We then highlighted a new type of synaptic organization," the scholars recount.

"At this point, we had to use some 'experimental creativity'; with a combination of behavioral, molecular and refined morphological approaches, we realized that these connections encapsulated in CS-6 clusters change in response to electrical activity in the brain."

"Finally, through collaboration with Alexander Dityatev at DZNE Magdeburg, and the efforts of Hadi Mirzapourdelavar from his group, we attenuated the expression of CS-6 in the hippocampus (the region of the brain responsible for spatial learning), and demonstrated that the presence of CS-6 is necessary for synaptic plasticity and spatial memory," Bozzi and Chelini point out.

"This work paves the way for a new way of thinking about brain functioning. It is possible that all synapses formed on different neurons within CS-6 clusters have the ability to respond chorally to specific environmental stimuli, and are involved in a common function aimed at learning and memory processes," they note.

"They seem to represent a new substrate of information integration and association formation at the multicellular level," add Dityatev and Berretta.

The work is the result of a collaboration between several laboratories, including the translational neuroscience laboratory (Sabina Berretta; McLean Hospital—Harvard Medical School, Boston), the neurodevelopmental disorders research laboratory (Yuri Bozzi; CIMeC—Centro Interdipartimentale Mente/Cervello, University of Trento) and the Molecular Neuroplasticity laboratory (Alexander Dityatev; DZNE Magdeburg).

More information: Gabriele Chelini et al, Focal clusters of peri-synaptic matrix contribute to activity-dependent plasticity and memory in mice, *Cell Reports* (2024). DOI: 10.1016/j.celrep.2024.114112

Provided by University of Trento

Minds that don't conjure images: How a brain with aphantasia works

Imagine a Christmas tree. Or try to visualize in your mind the last meal you ate yesterday. Recall the face of a family member you haven't seen in a while. Surely, the majority of us are able to evoke these mental images without a problem, perhaps to varying levels of precision and detail, but with the same fluidity with which we recall objects, people and lived experiences every day of our lives. But a certain percentage of us, around 1% of the total population, can't carry out such exercises: these are the people living with aphantasia, a neurological condition that prevents the creation of conscious mental images. A scientific review has dug into our still-limited understanding of the characteristic, concluding that it is associated with reduced autobiographical memory and facial recognition. Also, that it is more common among autistic individuals and people in scientific professions.

Typically, our imagination hangs onto the sensory properties of objects and activities when they are absent, such as what the color orange looks like or the sound of thunder. Through an intricate neurological process, we are able to mentally call up these images. However, people with aphantasia are unable to build these internal images, to visualize them through thought. That doesn't mean they have no imagination, qualifies Adam Zeman, professor at the University of Exeter and author of the aforementioned scientific review. "It indicates a lack of visual imagery and oftentimes, also sensory imagery, but people with aphantasia can be imaginative in the sense of creativity," says the scientist, who published the article in the journal *Trend in Cognitive Sciences*.

First of all, it's important to establish that aphantasia is not an illness. It's more accurately classified as a characteristic that explains how an individual process information and that, "occasionally, can be a symptom of a neurological or psychological disorder," says Zeman. A cerebral lesion or the evolution of a pathology can cause a loss of the ability to call up visual images in the mind, but the characteristic can also be hereditary and lifelong. The healthy people who experience it are completely functional.

In this sense, Saul Martínez-Horta, neuropsychologist at Barcelona's Hospital Sant Pau who did not participate in the review, emphasizes that "normality in human cognition is diverse" and can function in very different ways. With aphantasia, he points out, "the way the neurological systems that process visual information are organized will probably be different," but that doesn't mean a person is incapacitated. "When something has always took place without any effect on our day-to-day life, that doesn't mean much. But if something appears suddenly, like an inability to project images in the mind, that could be an indication that something has happened," he says. Psychiatrists have reported the appearance of aphantasia in the context of depression, depersonalization and psychosis, among other conditions.

Zeman's scientific review found that 1% of the population experiences pronounced aphantasia, but the spectrum is varied, and 2% to 6% of people were found to have "vague and tenuous" visual imagination. There's also the other side of the coin, which is that around 3% of the population tends in the opposite direction and displays signs of hyperphantasia, the ability to generate hyperrealistic images in the mind. "There's an entire spectrum of ability to evoke, but there is no standard value and it's very difficult to quantify. Probably, it's what one is born with," says Javier Camiña, spokesperson for the Spanish Neurology Society, which did not participate in the investigation.

According to scientists, aphantasia is overrepresented among people who work in mathematics, computations and the sciences, a phenomenon that Martínez-Horta associates with convergent thinking. "In convergent thinking, when you consider the uses of a pen, your thoughts will be rigid and methodical: it is used for writing. On the other hand, divergent thinking is more childish: the pen can be a weapon or used to put up your hair. Aphantasia is associated with a convergent pattern, that is more bound by the predictable," he says. In traditionally more creative industries, there is a greater likelihood of finding individuals with hyperphantasia.

Less autobiographical memory

When it comes to experimental memory measurements, people with aphantasia have also shown mild to moderate impairment. “Consistent with the close relationship between remembering the past and imagining the future, the richness of descriptions of imagined scenes is also reduced in aphantasia. Aphantasia similarly reduces the detail of eyewitness testimony,” Zeman points out in the article. Autobiographical memory, which refers to memory of a person’s own life, is also reduced among these individuals, to the point of being linked to a syndrome in which the individual lacks vivid first-person memories of his or her life history, even though he or she is able to function normally in day-to-day life.

Scientists are still trying to ascertain how a brain with aphantasia works. “The key difference probably lies in connectivity, with a stronger connection between the regions of thought and sensory areas among people who have more vivid mental images,” says Zeman. Camiña agrees that there likely are “differences in the modulation of certain processes” that play a role in the brain’s powers of perception. “In the absence of a stimulus, cerebral structures like the prefrontal cortex play a role; also, the limbic system, because we have to evoke past memories; and the fusiform gyrus, which is involved in facial recognition. Rather than structurally altered areas, there’s may be abnormal regulation of connectivity between these areas.

Indeed, another peculiarity of aphantasia is difficulty in recognizing faces: about 40% of people who experience this neurological feature say they have difficulties with facial recognition, more than twice as often as people who do not have the trait. The studies analyzed by Zeman also indicate that people with aphantasia score higher on questionnaires that measure the autistic spectrum.

Zeman also suggests that aphantasia “can offer certain protection against some mental health conditions,” because some studies have pointed to an elevated ability to create mental images as a risk factor for hallucinations caused by schizophrenia and Parkinson's, as well as visual intrusions caused by post-traumatic stress. Still, the experts consulted for this article wanted to be prudent, and suggested that the issue is complex. "Likely, if that person has schizophrenia or Parkinson's, they are going to have different hallucinations, possibly less symptoms. But it's not the deciding factor. A person who starts out with hyperphantasia, if they suffer from post-traumatic stress, they will have the ability to recall a traumatic episode and it will show up with more frequency, intensity and duration of symptoms," says Camiña.

Ability to dream

Paradoxically, although aphantasia prevents evoking conscious images, people with the neurological characteristic can dream. "This is probably explained by the fact that the path to the imagination in the brain is very different when it comes to voluntary imagination in a wakened state versus the imagination of dreams," says Zeman. People with aphantasia are able to have dreams with visual qualities, although some studies describe avisual dreams "with variable narrative, textual, conceptual, auditory and emotional content" more frequently than among participants who do not have the characteristic, states the scientific review.

Experts admit that identifying aphantasia is complex because there are no infallible tests for its diagnosis and there is a high level of subjectivity in its perception. "Explaining how I see my internal world is very difficult. A person who has challenges in constructing internal images doesn't know it. The majority discover what aphantasia is when they read about it somewhere," points out Martínez-Horta. But that complexity doesn't mean that it doesn't exist or that everything is a product of our own perception. Zeman says that behavioral, physiological and neural data exists that unpacks differences in the aphantasia spectrum. He gives one such example in the article itself: "Whereas normal participants listening to (extremely) scary stories show a hike in their galvanic skin response (GSR) (they sweat!), people with aphantasia do not. The natural interpretation is that, in the absence of imagery, the impact of emotive language is reduced because imagery typically mediates between verbal description and emotional response."

People with aphantasia also have reduced brain activity in response to sounds, finds study

Credit: Pixabay/CC0 Public Domain

People with aphantasia—individuals who report experiencing no visual imagery at all—also showed reduced activation of the brain's visual cortex in response to sounds, according to a new study.

The research, led by the University of Glasgow, uncovers new insights into the relationship between visual imagery and multisensory integration in people with "blind imagination," or aphantasia.

The study, "Decoding sound content in the early visual cortex of aphantasic participants," is published in the *Journal of Vision*.

When we look at something, information is transmitted from our eyes to a part of our brain called the visual cortex. Aside from its input from the outside world, which is called feedforward information, the visual cortex also receives feedback information from other parts of the brain.

This feedback information is crucial to help us contextualize and understand what we're seeing, but it can also allow us to experience things which are not in the external world, as it happens with visual imagery.

The causes of aphantasia are debated, with evidence showing that it might be caused by a reduction of feedback to the visual system, which is what the researchers investigated in this study.

For the research, blindfolded aphantasic participants listened to auditory scenes. Previous work from the researchers has shown that auditory scenes are not only processed in auditory cortex but are also represented in the visual areas of the brain in blindfolded and congenitally blind participants.

However, aphantasic participants report a reduced representation of sound content in their visual areas. This pattern of results suggests that feedback signals to the visual system could be weaker in aphantasia, which in turn may be linked to the absence of visual imagery.

Professor Lars Muckli, from the University's School of Psychology and Neuroscience, said, "Visual imagery comes naturally to me—If I am asked to describe a beautiful landscape I would picture it in my mind and then describe it with my mind's-eye.

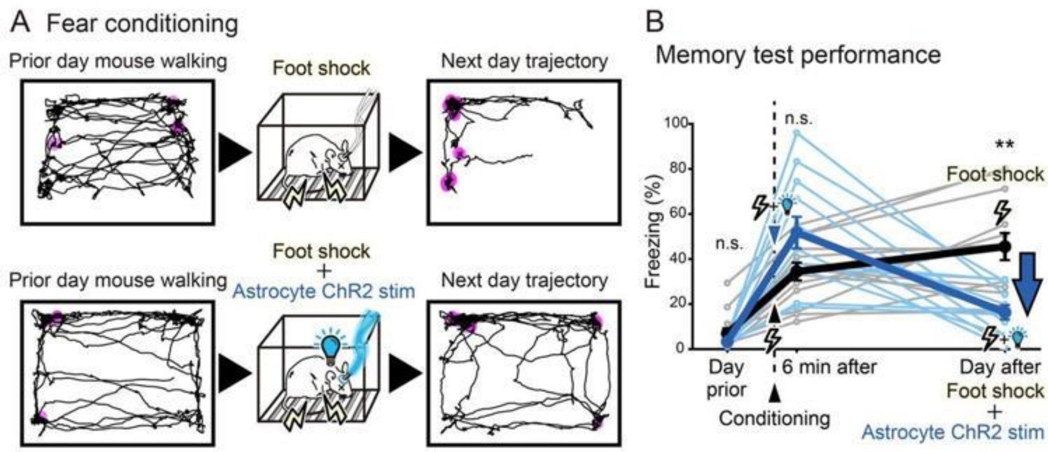
"Understanding that subjects with aphantasia are blind to the mind's-eye is intriguing to me. Our study helps to uncover that Aphantasia might go along with reduced feedback to the early visual cortex.

"One of the co-authors of the study has aphantasia, and it is fascinating to discuss subjective experiences with him to better understand how they differ."

More information: Belen M. Montabes de la Cruz et al, Decoding sound content in early visual cortex of aphantasic individuals, *Journal of Vision* (2024). DOI: 10.1167/jov.24.10.1347

Provided by University of Glasgow

Manipulating astrocytes affects long-term memory, researchers discover



Selective suppression of long-term memory formation through ChR2 photoactivation of amygdala astrocytes. The experiments suggest the presence of parallel processes governing short-term and long-term memory formation, respectively. Credit: Hiroki Yamao, Ko Matsui

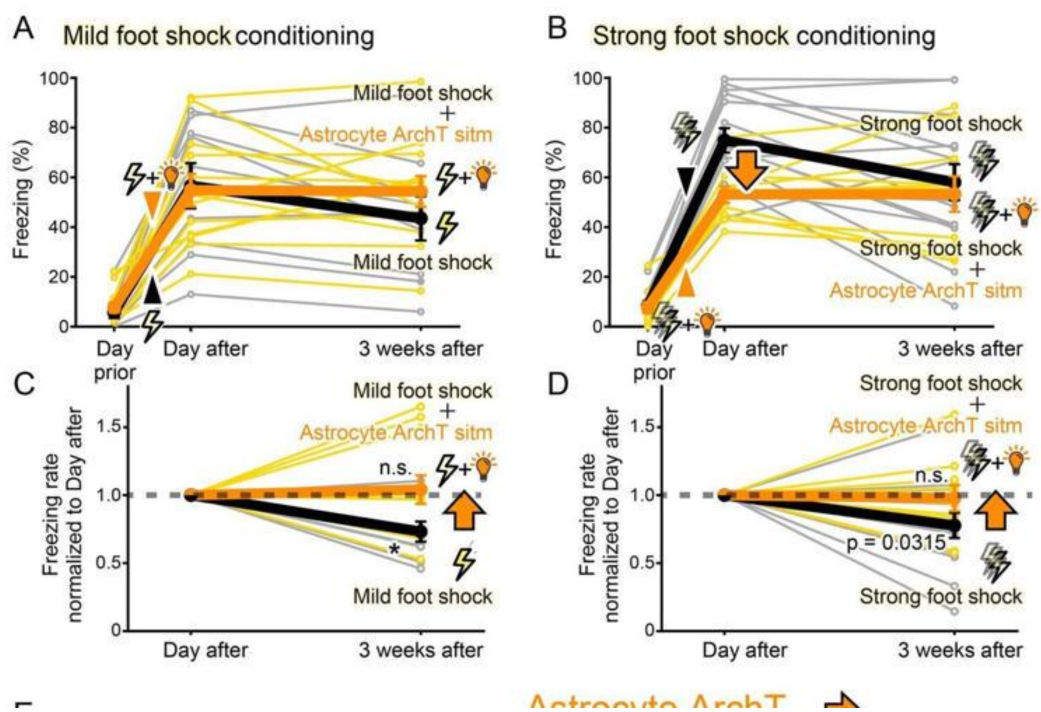
One of the most powerful assets of the brain is that it can store information as memories, allowing us to learn from our mistakes. However, some memories remain vivid while others become forgotten. Unlike computers, our brains appear to filter which memories are salient enough to store.

Researchers from Tohoku University have discovered that part of the memory selection process depends on the function of astrocytes, a special type of cell that surrounds neurons in the brain. They showed that artificially acidifying the astrocytes did not affect short-term memory but prevented memories from being remembered long-term.

The findings are published in the journal *Glia*.

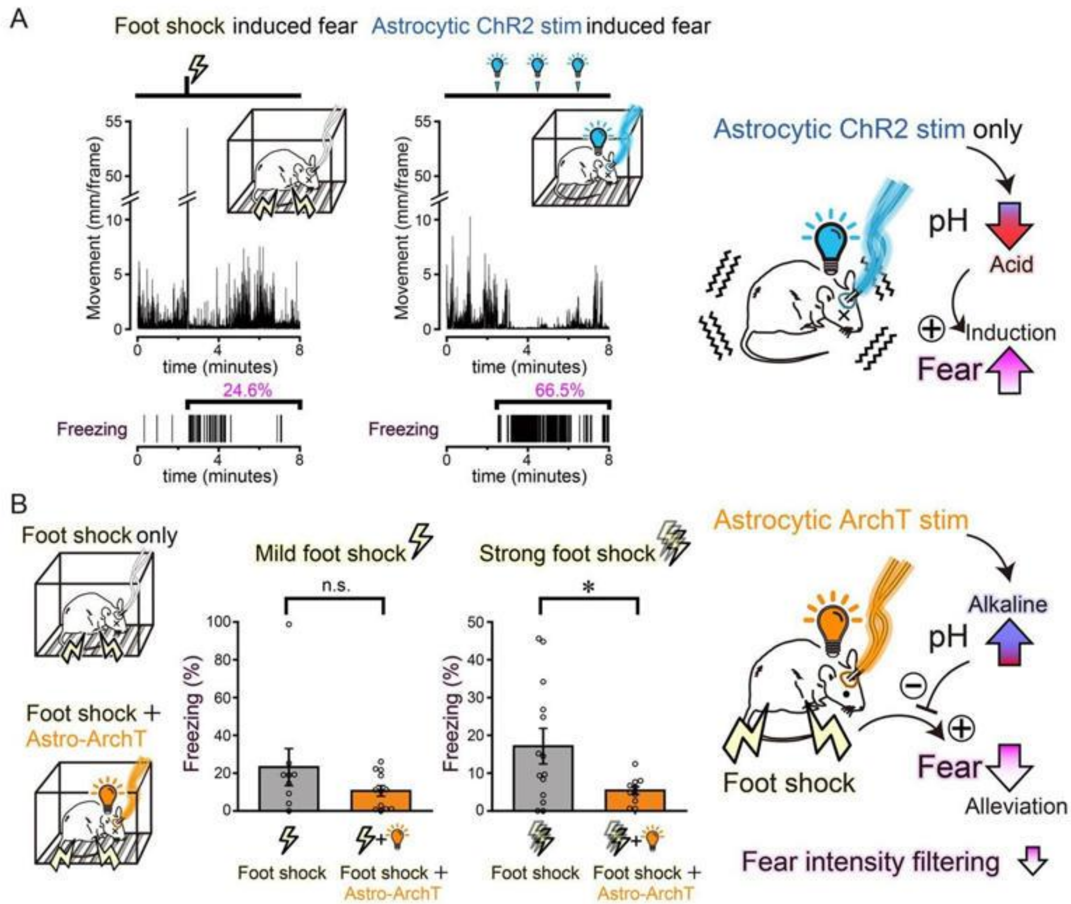
The researchers implemented a technique called "optogenetics" to manipulate the astrocytes by shining light onto them through optical fibers inserted in the mice's brains. This enabled the team to directly stimulate and either acidify or alkalinize the astrocytes in that area. They focused on the functions of astrocytes in the amygdala, a brain region known to be crucial for regulating emotion and fear.

A mild electrical shock was delivered to mice in an experiment chamber. When placed back in the same chamber, the mice remembered the shock and froze as a natural response. In comparison, the mice who had their astrocytes acidified immediately after the mild shock were able to temporarily hold onto the fear memory, but they forgot it by the next day. This shows that acidifying the astrocytes did not affect short-term memory but prevented the memories from being remembered long-term.



Mice inherently possess a selective filtering mechanism that enhances the memory of intense experiences; however, this filtering function was inhibited by ArchT photoactivation of astrocytes in the amygdala. Additionally, the natural forgetting process over three weeks was suppressed by the light stimulation of ArchT-expressing astrocytes. Credit: Hiroki Yamao, Ko Matsui

A different effect was seen for mice who had their astrocytes alkalinized. When tested three weeks later, control mice typically showed signs of forgetting, demonstrated by a decrease in freezing responses. However, mice whose astrocytes were alkalinized immediately after a strong shock still displayed strong fear responses even after three weeks.



Astrocytes are capable of triggering fear. Astrocyte ChR2 photoactivation alone induced freezing responses akin to those observed after receiving an electric foot shock. In contrast, astrocyte ArchT photoactivation suppressed the freezing responses following a footshock. Credit: Hiroki Yamao, Ko Matsui

This suggests that astrocytes play a key role in determining whether memories are erased or preserved for a long time, immediately after a traumatic event.

While it is generally believed that memories are formed in a continuous process whereby short-term memories gradually solidify and become long-term memories, this research suggests they may actually develop in parallel.

"We believe that this could change the way we understand memory formation," says Professor Ko Matsui of the Super-network Brain Physiology lab at Tohoku University, who led the research. He added, "The effect of astrocytes on memory likely also depends on various contexts, including mental, social, or environmental factors."

Lead investigator Hiroki Yamao believes astrocytes could hold the key to understanding emotional changes and memory formation. "This may be just a glimpse of how astrocytes affect emotional information processing," Yamao explains.

"Our next goal is to uncover the mechanisms by which astrocytes regulate emotional memory. Understanding these processes could pave the way for therapies that prevent traumatic memories from forming, offering a valuable approach to treating disorders like post-traumatic stress disorder (PTSD) by intervening in memory formation," says Yamao.

More information: Hiroki Yamao et al, Astrocytic determinant of the fate of long-term memory, *Glia* (2024). DOI: 10.1002/glia.24636

Provided by Tohoku University

Brain creates multiple copies of single memory for robust storage

Brain creates multiple copies of single memory for robust storage

Aiming to comprehend the dynamics of memory in brains, scientists conducted a new study on mouse models and examined how memories are stored and modified in the hippocampus.

The hippocampus is a tiny, complex structure of the brain that plays an important role in learning, memory, and emotions.

Researchers from the University of Basel in Basel, Switzerland, found that memories of specific experiences are stored in the brain as multiple parallel copies distributed across a minimum of three different clusters of neurons.

These clusters emerge at different stages during embryonic development. The copies vary in terms of their duration, modifiability, and susceptibility to deletion over time.

Dynamics of memory preserves in the brain

Scientists sought to learn the dynamics of the brain, which preserves and adapts memories, to understand how these processes contribute to learning from past experiences and decision-making in changing environments.

The research team showed that the activation and timing of specific memory copies can significantly impact how we recall, modify, and utilize our memories.

Flavio Donato from the University of Basel explained in an official statement that the brain faces impressive challenges concerning memory.

"On one hand, it must remember what happened in the past, to help us make sense of the world we live in. On the other, it needs to adapt to changes happening all around us, and so must our memories, to help us make appropriate choices for our future," says Donato.

Understanding how past experiences impact decision-making could be vital because memories help living beings learn from the past and adapt to changing circumstances, thus influencing future decisions and behavior.

Scientists also note that until the discovery of multiple memory copies, the mechanism behind the brain regulating a memory's dynamics remained a mystery.

Parallel copies of stored memories

Upon studying the hippocampus in mice, the team observed that parallel copies of stored memories in neuron clusters emerged at different phases during embryonic development.

These copies vary in their accessibility over time, with early-born neurons maintaining long-term memories that become accessible only after some time, while late-born neurons store memories that are strong initially but fade over time. Middle-stage neurons store more stable memories.

“How dynamically memories are stored in the brain is proof of the brain’s plasticity, which underpins its enormous memory capacity,” stated first author Vilde Kveim.

This flexibility in memory storage explains how our brain can adapt memories over time, helping us learn from new experiences while still holding on to important long-term memories.

A statement by the researchers emphasizes that persistence through dynamics is a delicate act to balance, one for which they might now have an entry point to fully understand.

This finding could potentially help scientists treat issues such as traumatic memories that might be too overwhelming or intense for an individual to manage.

It could also aid in recovering memories that have faded or seem lost, offering new ways to manage and improve mental health.

Researchers are now aiming to understand the driving force behind how memories are encoded and modified in the brain, potentially leading to ways to alleviate the impact of intrusive memories.

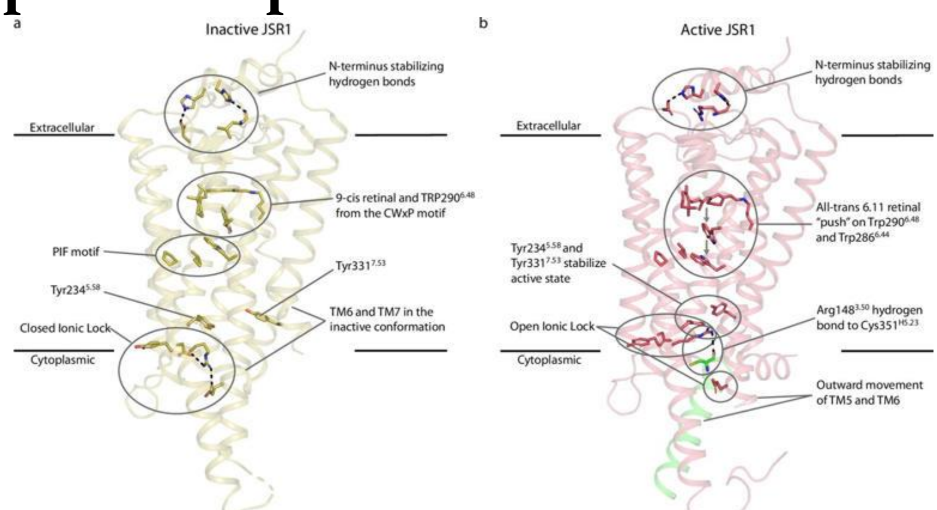
MindSpeech: Continuous Imagined Speech Decoding using High-Density fNIRS and Prompt Tuning for Advanced Human-AI Interaction

Suyi Zhang, Ekram Alam, Jack Baber, Francesca Bianco, Edward Turner, Maysam Chamanzar, Hamid Dehghani

In the coming decade, artificial intelligence systems will continue to improve and revolutionise every industry and facet of human life. Designing effective, seamless and symbiotic communication paradigms between humans and AI agents is increasingly important. This paper reports a novel method for human-AI interaction by developing a direct brain-AI interface. We discuss a novel AI model, called

MindSpeech, which enables open-vocabulary, continuous decoding for imagined speech. This study focuses on enhancing human-AI communication by utilising high-density functional near-infrared spectroscopy (fNIRS) data to develop an AI model capable of decoding imagined speech non-invasively. We discuss a new word cloud paradigm for data collection, improving the quality and variety of imagined sentences generated by participants and covering a broad semantic space. Utilising a prompt tuning-based approach, we employed the Llama2 large language model (LLM) for text generation guided by brain signals. Our results show significant improvements in key metrics, such as BLEU-1 and BERT P scores, for three out of four participants, demonstrating the method's effectiveness. Additionally, we demonstrate that combining data from multiple participants enhances the decoder performance, with statistically significant improvements in BERT scores for two participants. Furthermore, we demonstrated significantly above-chance decoding accuracy for imagined speech versus resting conditions and the identified activated brain regions during imagined speech tasks in our study are consistent with the previous studies on brain regions involved in speech encoding. This study underscores the feasibility of continuous imagined speech decoding. By integrating high-density fNIRS with advanced AI techniques, we highlight the potential for non-invasive, accurate communication systems with AI in the near future.

On the way to light-controlled medicine: Researchers elucidate the structure of specific photoreceptors



Activation of JSR1 by the agonist all-trans 6.11 retinal. Credit: Nature Communications (2024). DOI: 10.1038/s41467 024-53208-2

Researchers in biology and medicine have long dreamed of controlling the activities of cells without, for example, having to use chemicals. After all, in a structure as complex as an entire organism, unwanted side-effects can often arise.

The ideal solution would therefore be a type of remote control for cells, which would allow the functions of individual organs to be better examined and understood, and could even be used for therapeutic purposes. Remote control using light would be ideal for this, as it would enable organs and tissues deep inside the body to be influenced in a very selective and non-invasive way.

However, such a process also requires a cellular light receiver in the relevant organs. The receptors that receive light impulses in the retina of our eyes—called rhodopsins—could be suitable for this. With such photoreceptors, it might be possible to switch certain cell functions on and off using a light impulse.

This would work more rapidly and in a more targeted manner than drugs, which take a long time to take effect and often have unwanted side-effects because they cannot simply be activated in just one specific organ.

In the neurosciences, something similar is already working and is currently being tested in animal models to investigate brain diseases such as Parkinson's and epilepsy: Light-controlled ion channels from single-celled organisms are being incorporated into neurons using genetic engineering.

In the animal model, these ion channels in the cell membrane open when exposed to blue light, for example, and allow positively charged ions to flow into the neuron. In a chain reaction, further channels open, creating an electrical signal—the neuron becomes active.

A new kind of optogenetics

But such light-controlled ion channels only work in nerve cells. The goal of this research, however, is to stimulate other cells and organs in the organism to control a variety of bodily functions. For example, one could investigate the heart's natural pacemaker, or the mechanisms of chronic pain, anxiety, depression, and other mental illnesses.

It might be possible to develop effective cell therapies for hormonal malfunctions as well as immune, heart, and other diseases, including cancer.

To this end, researchers led by Gebhard Schertler of the PSI Center for Life Sciences are working on a new kind of optogenetics. In this approach, it is light receptors similar to the rhodopsins in our retina that become active: Triggered by a light pulse, they couple to proteins in the cell and thus initiate specific cellular signaling processes that take place in all organs.

The PSI researchers have joined forces with leading colleagues in Germany and England. Their project, Switchable rhodOpsins in Life Sciences (SOL), has three goals:

1. Find rhodopsins that can do this and elucidate their structure to better understand how they work.
2. Modify such rhodopsins, using molecular biological methods to optimize them for switching processes in various bodily functions.
3. Use the switches to better understand the signaling mechanisms of the proteins; use them as a tool in research and, on that basis, develop gene therapeutics.

The structural elucidation of proteins is a core competence of PSI, thanks to its high-resolution large research facilities. And PSI researchers have now made two significant steps towards SOL's first goal, as they report in two new studies.

First, they succeeded in finding a suitable rhodopsin and modifying it in such a way that it remains stable in the active state and thus can be examined. And second, the structure of this active state was clarified using a cryo-electron microscope at ETH Zurich.

A switch that bends and stretches

Rhodopsins are proteins. They are among the most important photoreceptors in the animal world. They have an elongated molecule in the middle, called retinal, that is derived from vitamin A. When a light pulse hits this molecule, it absorbs the energy and changes its shape within a quadrillionth of a second. A curved molecule—called the 11-cis form—becomes an elongated one—called the all-trans form. Through this transformation, the retinal also changes the structure of the entire rhodopsin so that it can now bind to other proteins in the cell membrane, so-called G proteins.

Therefore these light-sensitive rhodopsins also belong to the GPCRs (G protein-coupled receptor) family, as rhodopsin-G protein complexes stimulate other proteins to react, triggering a whole series of biochemical processes leading, for example, to the transmission of a visual signal to the brain.

The human body possesses hundreds of different types of GPCRs, which are located in the cell membranes, receive signals from the outside, and pass them along to the inside of the cell. In this way, they control many bodily functions. That's why roughly 40% of all medications target GPCRs with active ingredients that dock onto their receptors.

The advantage of simple photoreceptors

Rhodopsins are found in the retina of the human eye. In the rod cells, for example, they are responsible for distinguishing between light and dark at night. However, like those of most vertebrates, these rhodopsins are monostable.

This means that once the retinal is changed by light, it leaves the protein and has to be regenerated. Only then is it available for the next switching process. This is too complicated to allow this molecule to be used effectively as an optogenetic switch, since enzymes would also have to be used to regenerate it.

Many invertebrates, such as squid, insects, and spiders, have bistable rhodopsins. "From an evolutionary perspective, these are actually a more primordial form of rhodopsins, and less sensitive," says Gebhard Schertler. They offer advantages for optogenetics, however: The retinal remains in the protein after being switched on, and with a second light pulse it can immediately return to its original form and switch the cellular process off again.

The rhodopsin of a jumping spider species, for example, proved to be robust and easy to produce, unlike other bistable rhodopsins. This qualified it as a possible optogenetic switch.

With the Swiss Light Source SLS at PSI, it was possible to determine the molecular structure of this spider rhodopsin in its inactive ground state. But before it could be used as an optogenetic switch, its structure in the active form also had to be known precisely. This state, however, when the retinal is stretched and the rhodopsin binds to the G protein, is extremely short-lived.

How to make proteins happy

In one study, which was recently published in the *Proceedings of the National Academy of Sciences*, lead author Matthew Rodrigues now reports how they managed to stabilize the active state to be able to elucidate its structure: by making a tiny modification to the retinal.

"The properties of the retinal remain the same, but the modification—one small additional molecular ring—ensures that it apparently fits better into the binding pocket of the protein," reports Rodrigues. "It stays there for hours. As we structural biologists say, it's happy." Now the conditions were in place to examine the structure of the active rhodopsin in conjunction with a G protein.

A mixed protein

In a second study, now published in *Nature Communications*, first author Oliver Tejero and last author Ching-Ju Tsai did exactly that. "However, as expected, it was found that a spider protein (rhodopsin) naturally never fits optimally with a human protein (the G protein)," says Tsai. "So we compared spider G proteins with those of humans and assembled a chimera from both forms."

The researchers replaced the end part of the gene sequence of the human protein, which contains the code for the docking site, with that of the spider.

With additional genetic modifications in the actual light receptor, they addressed another problem: The spider rhodopsins are both activated and deactivated by light of the same wavelength.

"This means that a light pulse produces a hopeless hodgepodge of activated and deactivated states in a cell sample," says Tsai. Naturally, this is bad for a switch that is intended to turn on or off in a targeted manner. "With our modifications, we have ensured that switching on and off now takes place with different colors of light."

However, such "color tuning" by means of genetic engineering is only just beginning. The next step in the fundamental research into these new optogenetic switches will now be to find out how the proteins involved need to be designed to enable control using other colors of light.

This would then make it possible to selectively switch different cell functions on or off. It is also a matter of constructing the switches so that they are not only sensitive to blue, orange, and green light, but also, for example, to infrared light.

"The big question remains, if optogenetics is actually to be used in everyday medical practice, how the light will get to the rhodopsin," says Rodrigues. "You could implant the light source into the body. But the much more elegant and gentler method would be to work with infrared light. This can penetrate body tissue."

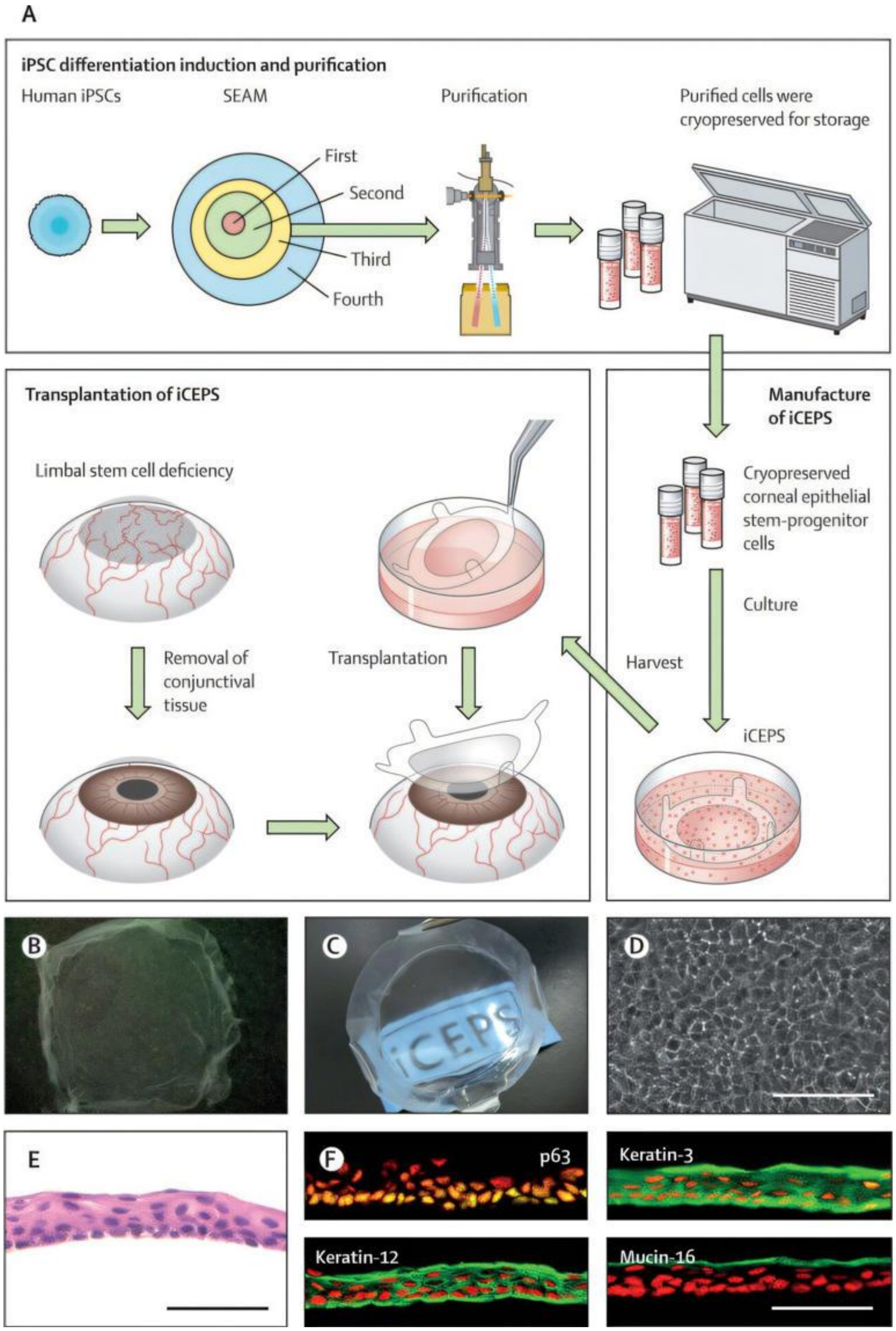
The largest part of the protein engineering, project leader Schertler confirms, is still to come, now that the structural basics are known. Ultimately, the goal is to put together a whole assembly kit of light-activated GPCRs that can be used for various purposes in the organism.

More information: Matthew J. Rodrigues et al, Activating an invertebrate bistable opsin with the all-trans 6.11 retinal analog, *Proceedings of the National Academy of Sciences* (2024). DOI: 10.1073/pnas.2406814121

Oliver Tejero et al, Active state structures of a bistable visual opsin bound to G proteins, *Nature Communications* (2024). DOI: 10.1038/s41467-024-53208-2

Provided by Paul Scherrer Institute

Human vision restored by stem cell replacement in regenerative medicine breakthrough



Fabrication and transplantation of human iCEPSs. Credit: The Lancet (2024). DOI: 10.1016/S0140-6736(24)01764-1

Researchers led by Osaka University in Japan have conducted the first human trial using induced pluripotent stem-cell-derived corneal epithelium to treat limbal stem cell deficiency, offering a potential new avenue for restoring vision.

Limbal stem cell deficiency (LSCD) is a severe ocular condition where the loss of functioning adult stem cells at the cornea's edge leads to vision impairment due to the invasion of fibrotic conjunctival tissue over the cornea. Limbal stem cells normally perform repair functions by differentiating into corneal epithelium. Without them, the integrity and transparency of the corneal surface becomes compromised, leading to fibrotic tissue buildup, and ultimately, vision loss.

Traditional treatments often involve grafts from the patient's healthy eye or donors, but these methods carry risks like immunological rejection, or require the removal of healthy tissue.

In a study titled "Induced pluripotent stem-cell-derived corneal epithelium for transplant surgery: a single-arm, open-label, first-in-human interventional study in Japan," published in *The Lancet*, researchers conducted transplants of pluripotent stem cell (iPSC)-derived corneal epithelial sheets (iCEPS) as a potential treatment for LSCD.

Four patients with LSCD participated in the study. After removing any fibrotic tissue, the team transplanted allogeneic iCEPS onto the affected eyes. All surgeries were performed without human leukocyte antigen (HLA) matching. Half the patients received low-dose cyclosporine (typically used to mitigate organ rejection after a transplant), while the other half received no immunosuppressive agents beyond corticosteroids.

Two years of monitoring revealed no severe adverse events. Minor adverse events were managed effectively and without lasting effects.

All four patients experienced significant improvements in vision. Disease stages advanced to less severe classifications in three patients. One patient, with a more severe underlying condition, initially improved to a less severe stage by 32 weeks, but later regressed to baseline after one year. Quality-of-life assessments aligned with visual improvements, with three of the four patients reporting enhanced scores.

Overall, the study demonstrated that iCEPS transplantation not only stabilizes the corneal surface but also restores functional vision, significantly enhancing the daily lives of patients with limbal stem cell deficiency. Beneficial outcomes were more pronounced in patients who received low-dose cyclosporine, suggesting that non-use might have triggered subclinical immunological rejection.

The iCEPS were cultivated using a method that replicates aspects of natural eye development to produce functional corneal cells. This technique not only ensures the structural integrity of the grafts but also reduces immunogenicity, potentially eliminating the need for HLA matching and extensive immunosuppression typically required in traditional grafts.

The successful result is a major therapeutic advancement, building on earlier successes in regenerative medicine while overcoming the limitations of existing LSCD surgical treatments. The Osaka team plans to initiate a larger multicenter clinical trial to further validate the findings and explore the broader applicability of iCEPS transplantation.

More information: Takeshi Soma et al, Induced pluripotent stem-cell-derived corneal epithelium for transplant surgery: a single-arm, open-label, first-in-human interventional study in Japan, *The Lancet* (2024). DOI: 10.1016/S0140-6736(24)01764-1

Laser eye op that can give patients 'super-vision': better than 20/20

- **READ MORE: Risks of laser eye surgery may be MUCH higher than clinics claim**

Patients with poor eyesight can achieve 'super-vision' thanks to the first ever personalised eye surgery.

The groundbreaking technology, performed for the first time in the UK today, creates a 3D digital clone of a patient's eyes.

Treatment is then tailored to meet their specific needs, achieving better results than with current standard prescriptions for glasses laser eye surgery.

Experts believe it could become the standard treatment for thousands of patients treated for sight loss every year.

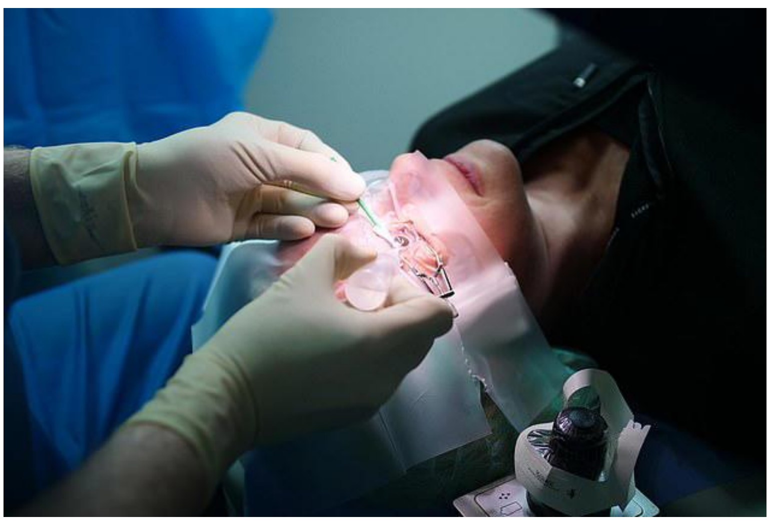
The digital clone, called an 'Eyevatar', duplicates how an individual sees.

This allows surgeons to operate virtually 'many times over to perfect the results' before it is performed on the patient.

Astonishingly, trials have suggested the treatment — which costs £6,500 for both eyes — can result in better-than-20/20 vision.

Trials found it had a 100 per cent success rate in achieving 20/20 or 'normal vision', stopping the need for glasses.

Patients with poor eyesight can achieve 'super-vision' thanks to the first ever personalised eye surgery



Rebecca Hackworth, 50, underwent new laser surgery using the new technology - pictured above - that leaves some patients with better than 20/20 vision

But half achieved 20/12.5 vision, according to the findings published in the Journal of Cataract & Refractive Surgery.

This means they can they can see at 20ft what a person with normal vision needs to be 12.5ft away to see.

Some eight per cent scored 20/10 or 'perfect vision', generally only seen in one per cent of the population.

Early results suggest it may also boost night vision — something never seen in laser eye surgery before.

Ophthalmologist David Allamby, who carried out the procedure on six patients at London's Focus Clinic yesterday, said it had the potential to 'transform' corrective eye surgery.

One of the first patients to benefit is Rebecca Hackworth, who needed reading glasses to see text clearly.

The communications director, 50, was also short-sighted which made things in the distance blurry.

Mr Allamby said he expects the results will mean she can now see perfectly.

Patient Rebecca Hackworth, 50, pictured with David Allamby, ophthalmologist and director of Focus Clinics, London, who performed her surgery

He said: 'I think it went really well. I treated her right eye only with ray-tracing-guided LASIK to give her what we call blended vision.

'Her right eye will see very clearly for distance, and her left eye is left alone with mild myopia, which allows her to read without glasses.

'The result is clear distance and reading without any glasses.'

He added: 'The technology has been nearly 20 years in development and is a major leap forward.

'It means we can now perform the surgery virtually and treat your eye many times over inside the computer to refine and remove aberrations.

'The new ray-tracing procedure understands these optical imperfections and is able to adjust the laser treatment pattern to correct them.

'The implication is that this raises the bar on what we can achieve with laser eye surgery and will become the new standard for what patients expect from treatment.'

The technology is used as part of laser-assisted in situ keratomileusis (LASIK), the most common type of laser eye surgery in the UK.

Some patients achieved 20/12.5 vision, meaning they can they can see at 20ft what a person with normal vision needs to be 12.5ft away to see

The groundbreaking technology, performed for the first time in the UK today, creates a 3D digital clone of a patient's eyes

This uses lasers to reshape the cornea to correct vision problems like short-sightedness and astigmatism, using a uniform prescription in the same way glasses do.

With this precision treatment, a new Sightmap scanner first creates an 'eyevatar' of a patient's eye.

The digital twin then traces up to 2,000 rays of light to determine their path as they are refracted and focused by the cornea and lens inside the eye.

The laser eye treatment can then be customised so that all rays are focused properly onto the retina, achieving the best sight possible.

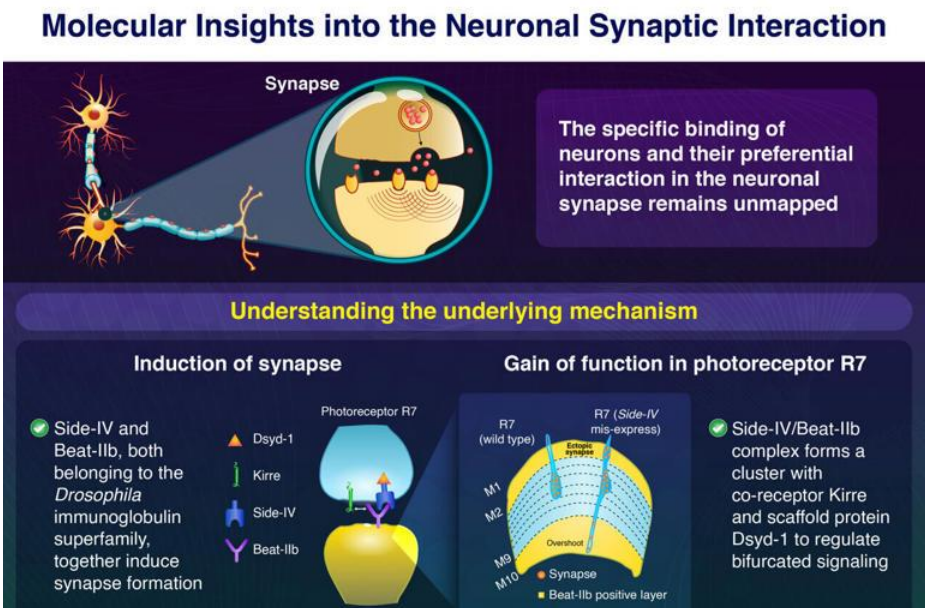
Today, the UK became the first country in Europe to routinely offer the procedure, at the clinic which is popular with celebrities.

Mr Allamby added: 'It is really exciting technology. If it works how it has in the studies, it really well make a huge difference to a lot of people.

'I expect around three-quarters of patients to achieve 20/12, and around 20 per cent will achieve 20/10, binocularly.

'That's amazing, considering less than one per cent of humans can see this well.'

A molecular route to decoding synaptic specificity and nerve cell communication



This study provides insights into the molecular mechanisms underlying the neuronal synaptic interaction. Credit: Tokyo Tech© Provided by Medical Xpress

Neurons or nerve cells are the fundamental components of the central nervous system and are critically involved in signal transduction pathways. Transmission of information or signal from one neuron to another requires the establishment of a neuronal synapse: either chemical (neurotransmitters) or electrical (protein channels and ions). However, little is known about the underlying mechanism regarding the binding specificity and the ability to form preferential interactions between neuronal pairs.

In this regard, a team of researchers from Japan, led by Associate Professor Takashi Suzuki from the School of Life Science and Technology at Tokyo Institute of Technology (Tokyo Tech), recently attempted to unravel the molecular mechanisms behind the complex neuronal communication circuit.

Dr. Suzuki explains, "Take, for example, a person driving an automobile. The precise and rapid communication between the driver's perception and the locomotor system can be the difference between life and death. The appropriate functioning of the nervous system ultimately comes down to a precise synaptic interaction between different types of neurons.

"Hence, our group focused on studying the molecular mechanisms of synaptic specificity using Drosophila, which allowed a genotypic as well as phenotypic assessment."

The researchers employed a combination of genomic and interactome (protein–protein interactions) analyses to identify the molecular mechanisms involved in synaptic communication.

The results revealed that the specific interaction of Side-IV/Beat-IIb immunoglobulin superfamily protein molecules was responsible for inducing the formation of synapse. This combination of Side-IV/Beat-IIb was central to the synaptic specificity between neurons. Side-IV/Beat-IIb, along with Side-IV's co-receptor, Kirre, and Dsyd-1, a synaptic scaffold protein, formed a cluster to regulate a preferential signaling mechanism among neuron pairs.

The research findings were published in *Cell Reports*.

Knockdown studies of synaptic scaffold protein Dsyd-1 and Liprin-α revealed the suppression of synapse formation. Moreover, Side-IV protein interaction with Dsyd-1 led to the formation of an active zone and resulted in a higher preference for synapse formation between specific neurons, thereby preventing miswiring.

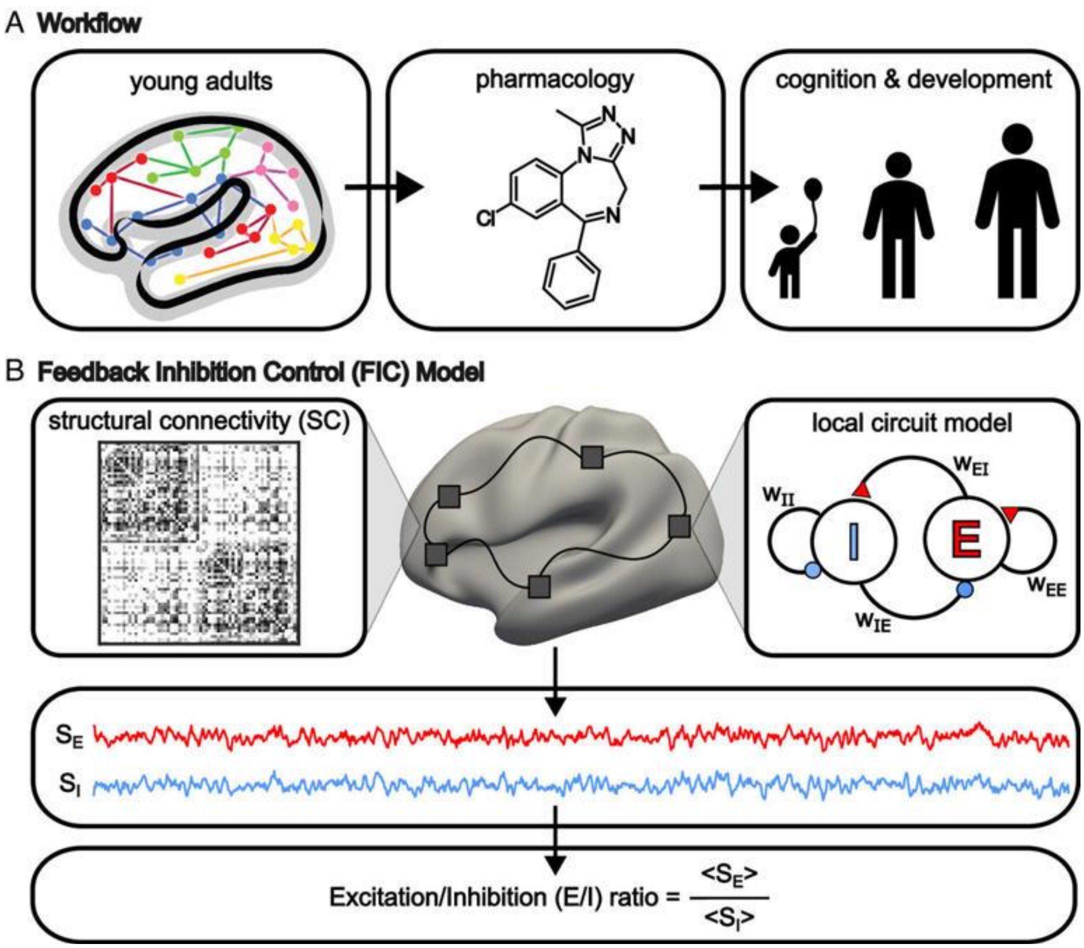
Dr. Suzuki says, "We believe that our study can contribute to our current understanding of neuronal synapse and hierarchical ranking interactions among neuronal pairs. Future research involving higher order mutant species can build on our study to address the neurodegenerative disease landscape and aid in developing therapeutic strategies in the long term."

Overall, this study sheds valuable light on the molecular intricacies of neuronal communication.

More information: Jiro Osaka et al, Complex formation of immunoglobulin superfamily molecules Side-IV and Beat-IIb regulates synaptic specificity, *Cell Reports* (2024). DOI: 10.1016/j.celrep.2024.113798

Provided by Tokyo Institute of Technology

Neural balance in the brain is associated with brain maturity and better cognitive ability, study finds



Workflow and schematic of the pFIC model. Credit: Proceedings of the National Academy of Sciences (2024). DOI: 10.1073/pnas.2318641121© Provided by Medical Xpress

In a world where external and internal stimuli can throw our entire body system off balance, how does our brain prevent itself from becoming overly stimulated?

The answer lies in our brain's ability to maintain the balance of neural excitation (E) and inhibition (I), known as the E/I ratio. By regulating the E/I ratio, the brain prevents over-stimulation and under-stimulation.

The E/I ratio of children decreases with healthy development. Children with a lower E/I ratio were observed to have better performance than their peers in cognitive tests such as memory and intelligence, according to studies by researchers from the Centre for Sleep and Cognition at the Yong Loo Lin School of Medicine (NUS Medicine).

With the aim of drawing meaningful connections between E/I ratio and brain maturation, the study team, led by fourth-year Ph.D. student Zhang Shaoshi, Associate Professor Thomas Yeo from the Centre for Sleep and Cognition at NUS Medicine, Assistant Professor Bart Larsen from the University of Minnesota and Associate Professor Theodore Satterthwaite from the University of Pennsylvania, looked at how E/I ratio changes in youths, by studying the MRI brain scans of 885 children, adolescents and young adults from the United States of America and 154 children from Singapore.

E/I ratio is an aspect that is continually changing and developing throughout childhood and adolescence. The Singaporean data cohort were obtained from GUSTO, Singapore's largest and most comprehensive birth cohort study that seeks to help the next generation become healthier.

Described as the Yin and Yang of the brain, researchers have found that too much excitation or excessive inhibition can be harmful, leading to a higher risk of developing brain disorders, such as autism, Alzheimer's disease and schizophrenia.

In less severe situations, someone with too much excitation might overthink in social situations, resulting in anxiety. Indeed, a common drug for reducing anxiety symptoms is Xanax, which increases neural inhibition, thus reducing neural excitation. In more severe scenarios, over-excitation can cause an epileptic seizure.

On the opposite end of the spectrum, too much inhibition indicates an absence of brain activity, effectively putting the person in a vegetative state. Therefore, inhibition is needed to balance excitation. Overall, a balanced E/I ratio is important for a well-functioning brain.

Despite E/I's importance for brain health, it is hard to measure its ratio in the human brain without using invasive techniques. Therefore, the team developed a technique, combining artificial intelligence and biophysical modeling to infer E/I ratios from non-invasive, non-radioactive MRI scans. The team demonstrated the validity of their estimated E/I ratios through an experiment, during which participants ingested anti-anxiety medication (Xanax) or a placebo.

The team's hypothesis is that once Xanax is ingested, inhibition will increase, so the overall E/I ratio decreases. To test this hypothesis, the research team scanned healthy individuals on two separate occasions. A participant is given Xanax before one MRI session and placebo in another MRI session. For some participants, Xanax might be administered in the first session, while for others Xanax might be administered in the second session.

All parties involved in this experiment were not privy to whether an MRI session involved the placebo or the anti-anxiety drug. The team found that estimated E/I ratio markers were indeed lower after participants had ingested Xanax, compared with the placebo, and thus validating their technique.

The study team then proceeded to use MRI brain scans to study brain development in a large sample of more than 1000 children, adolescents and young adults from Singapore and the United States of America. They discover that E/I ratios decrease with healthy development.

Next, to establish the link between E/I ratios and cognitive function, the team divided participants, ranging from age 7 to 23, into high and low-performance groups based on their scores on certain cognitive tests. They found that the high performing groups had lower E/I ratios than their peers of the same age, suggesting that cognitive abilities improve as the E/I ratio matures during development.

Beyond their study on neurodevelopment, the team is keen on applying their approach to gain mechanistic insights into various brain disorders, by studying how the E/I ratio differs between healthy participants and patients battling mental disorders. The team also aims to study how the E/I ratio changes as people age, to gain insights into neurodegenerative disorders, such as Alzheimer's Disease.

Assoc Prof Yeo, who is also from the NUS College of Design and Engineering and Principal Investigator of this study, adds, "Our findings enhance our understanding of brain development and highlight potential avenues for understanding the emergence of psychopathology in youth.

"Hopefully, these findings will lead us to figure out which brain circuits get over-excited or over-inhibited easily, or pinpoint certain abnormal brain regions specific to an individual patient. This could shed more light on how medication or brain stimulation can be customized according to individuals, that would shape the course of treatment of brain disorders in the long run."

This study is published in *Proceedings of the National Academy of Sciences* titled "In vivo whole-cortex marker of excitation-inhibition ratio indexes cortical maturation and cognitive ability in youth."

More information: Shaoshi Zhang et al, In vivo whole-cortex marker of excitation-inhibition ratio indexes cortical maturation and cognitive ability in youth, *Proceedings of the National Academy of Sciences* (2024). DOI: 10.1073/pnas.2318641121

Provided by National University of Singapore

How much of our brains do we actually use?

The human brain, often regarded as one of the most complex and mysterious organs, has long been the subject of fascination and myth. One of the biggest misconceptions is the idea that we only use 10% of our brains. Modern neuroscience has debunked this claim, showing that nearly all parts of the brain are active and play essential roles in our daily lives.

The 10% myth

The widely spread myth that humans only use 10% of their brains is entirely false. In reality, brain activity is far more complex, involving nearly all regions during different tasks.

Brain imaging reveals truth

Neuroimaging technologies like fMRI and PET scans have debunked the 10% myth. These scans show that even during simple tasks, large portions of the brain are simultaneously active.

Continuous brain activity

Even when we're not consciously doing anything, our brains remain active. This resting activity helps maintain essential functions such as breathing, heartbeat, and subconscious mental processes like daydreaming.

Task-specific brain regions

Different areas of the brain activate for specific tasks. For instance, the occipital lobe processes visual information, while the temporal lobe handles auditory input.

The role of the prefrontal cortex

The prefrontal cortex, located at the front of the brain, is responsible for complex processes like decision-making, planning, and problem-solving.

Neural networks and connectivity

The brain operates as an interconnected system, with its regions linked by extensive networks of neurons. These networks allow different brain areas to communicate and work together to complete complex tasks.

Energy consumption

Despite its relatively small size, the brain accounts for about 20% of the oxygen and calories consumed by the body. This high energy demand reflects the constant communication between neurons and overall brain activity.

Motor and sensory functions

The brain's motor cortex controls movement, while the sensory cortex processes touch, pain, and temperature.

Emotions and the limbic system

Emotional processing involves the limbic system, which includes the amygdala and hippocampus. These areas regulate our emotional responses, mood, and memory.

Subconscious processing

A significant portion of brain activity happens without our conscious awareness. Subconscious processes manage everything from breathing and heartbeat to forming automatic responses and implicit memory.

Plasticity and brain adaptation

Neuroplasticity is the brain's ability to reorganize itself by forming new neural connections. This adaptability allows us to learn new skills, recover from injuries, and improve cognitive functions over time.

Learning and brain usage

When we learn something new, multiple brain regions collaborate to process, store, and retrieve the information. This process strengthens neural connections, boosting brain activity in areas specifically linked to the task at hand.

Memory systems

Memory is distributed across multiple brain regions. The hippocampus forms new memories, while the cortex stores long-term ones, ensuring efficient learning and recall.

Brain activity during sleep

Contrary to what many think, the brain remains active during sleep. Sleep has been proven to improve memory recall, regulate metabolism, and reduce mental fatigue.

Creativity and brain integration

Creativity involves multiple regions working together. The prefrontal cortex, temporal lobes, and other areas collaborate to blend existing knowledge in innovative ways, emphasizing the brain's interconnectedness.

Reflexive and automatic responses

Some brain functions are reflexive and automatic, like the body's response to danger. These fast reactions are controlled by the brain stem and spinal cord, allowing for quick action without conscious thought.

Sensory integration

The brain continuously processes sensory input from the environment. The occipital, parietal, and temporal lobes handle vision, touch, and sound, respectively, integrating these inputs for a cohesive understanding of surroundings.

Brain regions and language

Language processing requires the activation of specific areas like Broca's area for speech production and Wernicke's area for language comprehension. Both regions work together to facilitate communication and understanding.

The brain's role in attention

Attention is a complex process that involves the activation of various brain regions, particularly the parietal and prefrontal cortex. These areas help focus our thoughts on relevant information, while filtering out distractions.

Coordination and the cerebellum

The cerebellum, located at the back of the brain, is responsible for coordination, balance, and motor control. It plays a crucial role in fine-tuning movements and ensuring smooth, coordinated physical activity.

Brain function in social interaction

Social interactions involve multiple brain regions. The prefrontal cortex, for instance, helps us understand social cues, make judgments, and regulate behavior, allowing us to interact with others.

Brain stem's vital functions

The brain stem controls basic life functions like breathing, heart rate, and blood pressure. It works automatically, ensuring our body's survival without needing conscious thought from other areas.

Multitasking and brain efficiency

When multitasking, the brain switches between tasks rapidly, activating different regions for each task. However, multitasking can reduce efficiency, as the brain is less effective at managing multiple tasks simultaneously.

Stress and brain activity

Stress significantly affects brain activity, particularly in areas like the amygdala, which regulates emotional responses. Prolonged stress can hinder memory, learning, and decision-making by overstimulating specific brain regions.

Cognitive reserve and brain health

Cognitive reserve refers to the brain's resilience in coping with damage. Engaging in mentally stimulating activities, like puzzles or learning, can build cognitive reserve and protect against cognitive decline.

Synaptic connections and learning

Learning new skills strengthens synaptic connections between neurons, laying the foundation for memory and cognitive growth.

Focused attention and brain regions

Focused attention, such as during meditation or deep work, activates the brain's prefrontal cortex and thalamus. This sustained concentration helps improve cognitive function and mental clarity over time. Even when we're distracted, our brain remains active. The default mode network, a set of brain regions, becomes active during idle or wandering thoughts, showing constant brain activity even while distracted.

In conclusion, we use almost all of the brain over the course of daily life. Different regions activate for various tasks, debunking the myth that only 10% of the brain is utilized.

Perfect balance: How the brain fine-tunes its sensitivity

Inhibitory neurons (magenta) and their synapses (green) in the mouse neocortex. Credit: Biozentrum, University of Basel© Provided by Medical Xpress

A sensitive perception of he environment is crucial for guiding our behavior.

However, an overly sensitive response of the brain's neural circuits to stimuli can lead to neurodevelopmental disorders such as epilepsy. University of Basel researchers report in the journal *Nature* how neuronal networks in the mouse brain are fine-tuned.

We are constantly exposed to a wide range of sensory stimuli, from loud noises to whispers. In order to efficiently process these diverse stimulus intensities, the brain needs to strike a balance in its responsiveness. An excessive sensitivity triggers an over-activation of nerve cells in response to a stimulus, leading to epileptic seizures. Conversely, insufficient sensitivity results in a reduced ability to perceive and discriminate stimuli.

But how does the brain manage to be highly sensitive without becoming over-activated? "The key lies in maintaining a balance between neural excitation and inhibition," explains Professor Peter Scheiffele from the Biozentrum, University of Basel.

"In mouse models, we have now discovered how this balance is maintained to ensure stable brain function." The study particularly focused on the neocortex, a brain area responsible for perception and a range of complex functions such learning.

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Our brain consists of billions of interconnected nerve cells that interact through so-called synapses and process sensory stimuli such as sounds, touch, and sights. While excitatory neurons pass on the input signal, inhibitory neurons control the timing and intensity of the information flow. This internal control system ensures that the nervous system responds appropriately to stimuli.

Neurons are able to detect an elevated neuronal network activity and subsequently reduce the system's sensitivity to stimuli. But how the cells are instructed at the molecular level was poorly understood.

"We have now revealed that highly activated excitatory neurons release a protein called BMP2," says lead author Dr. Zeynep Okur. "BMP2 signals to the inhibitory neurons, initiating a genetic program that leads to the formation of new synapses." These additional synapses increase the impact of inhibitory neurons and dampen network activity.

This feedback mechanism is critical for tuning the sensitivity of neuronal networks, preventing over-activation and thus excessive responses to stimuli. "Switching-off the BMP2-induced genetic program in inhibitory neurons triggers epileptic seizures in mice, but only when they are older," explains Okur. Thus, this process is involved in long-term adaptations of cortical networks.

The BMP2 signaling pathway has been known for its role in early brain developmental, particularly in nerve cell differentiation. "We have been able to show that this pathway is re-purposed to stabilize neuronal circuits in the adult brain," emphasizes Scheiffele. This plays an important role for brain plasticity in adulthood—the basis for learning and memory.

"We now understand at the molecular level how neural networks balance excitation and inhibition," says Scheiffele. "With our work, we are expanding the repertoire of options to treat epilepsy and other neurodevelopmental disorders." Targeted interventions in the BMP2 signaling pathway could help to fine-tune and re-adjust brain sensitivity.

More information: Zeynep Okur et al, Control of neuronal excitation–inhibition balance by BMP–SMAD1 signalling, *Nature* (2024). DOI: 10.1038/s41586-024-07317-z

Provided by University of Basel

Study pinpoints origins of creativity in the brain

Electrodes at multiple brain regions reveal brain activity in real time. Colored dots show the locations of all of the electrodes across all patients, color-coded by brain region. Red dots in the lower images show the locations of the electrodes in the DMN. Credit: Brain (2024). DOI: 10.1093/brain/awae199© Provided by Medical Xpress

Have you ever had the solution for a tough problem suddenly hit you when you're thinking about something entirely different? Creative thought is a hallmark of humanity, but it's an ephemeral, almost paradoxical ability, striking unexpectedly when it's not sought out.

And the neurological source of creativity—what's going on in our brains when we think outside the box—is similarly elusive.

But now, a research team led by a University of Utah Health researcher and based in Baylor College of Medicine has used a precise method of brain imaging to unveil how different parts of the brain work together in order to produce creative thought.

Their findings published in *Brain* on June 18.

The new results could ultimately help lead to interventions that spark creative thought or aid people who have mental illnesses that disrupt these regions of the brain.

Outside the box

Higher cognitive processes like creativity are especially hard to study. "Unlike motor function or vision, they're not dependent on one specific location in the brain," says Ben Shofty, MD, Ph.D., assistant professor of neurosurgery in the Spencer Fox Eccles School of Medicine and senior author on the paper. "There's not a creativity cortex."

But there's evidence that creativity is a distinct brain function. Localized brain injury caused by stroke can lead to changes in creative ability—both positive and negative. That discovery suggests that narrowing down the neurological basis of creativity is possible.

Shofty suspected that creative thought might rely strongly on parts of the brain that are also activated during meditation, daydreaming, and other internally focused types of thinking. This network of brain cells is the default mode network (DMN), so called because it's associated with the "default" patterns of thought that happen in the absence of specific mental tasks.

"Unlike most of the functions that we have in the brain, it's not goal-directed," Shofty says. "It's a network that basically operates all the time and maintains our spontaneous stream of consciousness."

The DMN is spread out across many dispersed brain regions, making it more difficult to track its activity in real time. The researchers had to use an advanced method of brain activity imaging to understand what the network was doing moment-to-moment during creative thought. In a strategy most commonly used to pinpoint the location of seizures in patients with severe epilepsy, tiny electrodes are implanted in the brain to precisely track the electrical activity of multiple brain regions.

Participants in the study were already undergoing this kind of seizure monitoring, which meant that the research team could also use the electrodes to measure brain activity during creative thinking. This provided a much more detailed picture of the neural basis of creativity than researchers had been able to capture before.

"We could see what's happening within the first few milliseconds of attempting to perform creative thinking," Shofty says.

Two steps toward originality

The researchers saw that during a creative thinking task in which participants were asked to list novel uses for an everyday item, like a chair or a cup, the DMN lit up with activity first. Then, its activity synchronized with other regions in the brain, including ones involved in complex problem-solving and decision-making. Shofty believes this means that creative ideas originate in the DMN before being evaluated by other regions.

What's more, the researchers were able to show that parts of the network are required specifically for creative thought. When the researchers used the electrodes to temporarily dampen the activity of particular regions of the DMN, people brainstormed uses for the items they saw that were less creative. Their other brain functions, like mind wandering, remained perfectly normal.

Eleonora Bartoli, Ph.D., assistant professor of neurosurgery at Baylor College of Medicine and co-first author on the paper, explains that this result shows that creativity isn't just associated with the network but fundamentally depends on it.

"We moved beyond correlational evidence by using direct brain stimulation," she says. "Our findings highlight the causal role of the DMN in creative thinking."

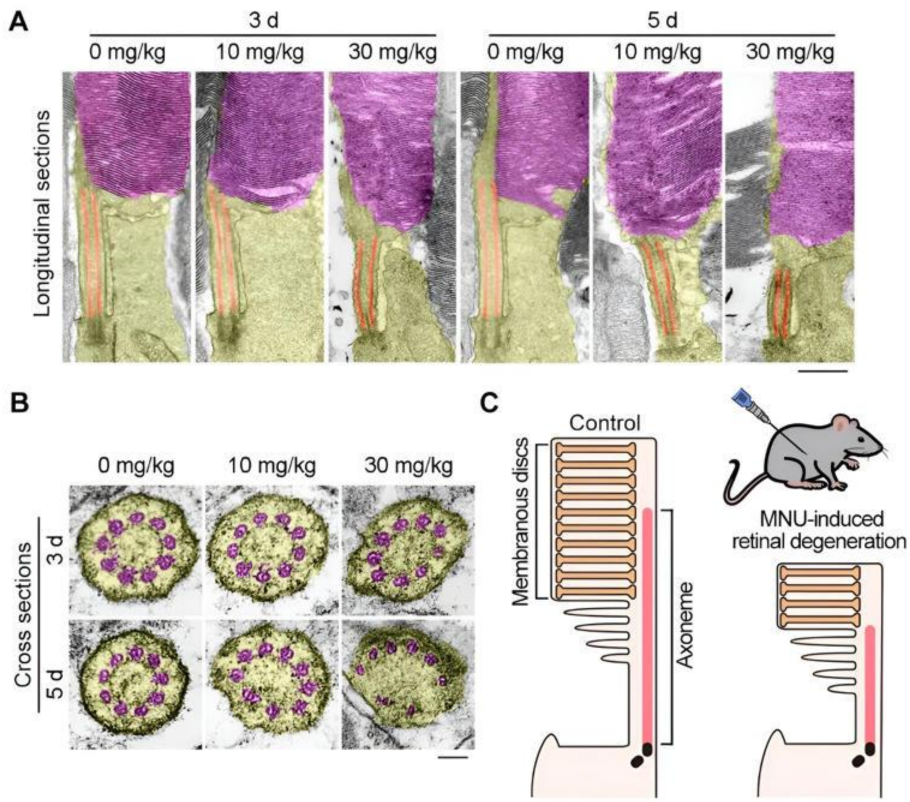
The activity of the network is changed in several disorders, such as ruminative depression, in which the DMN is more active than normal, possibly related to increased dwelling on negative internally directed thoughts. Shofty says that a better understanding of how the network operates normally may lead to better treatments for people with such conditions.

By characterizing the brain regions involved in creative thought, Shofty hopes to ultimately inspire interventions that can help spark creativity. Shofty says, "Eventually, the goal would be to understand what happens to the network in such a way that we can potentially drive it toward being more creative."

More information: Eleonora Bartoli et al, Default mode network electrophysiological dynamics and causal role in creative thinking, *Brain* (2024). DOI: 10.1093/brain/awae199

Provided by University of Utah Health Sciences

Novel mechanism of retinal degeneration



(A) Transmission electron microscopy images of longitudinal sections of photoreceptors in controls or RD mice. Scale bar, 1 µm. (B) Transmission electron microscopy images of cross sections of ciliary axonemes in RD or control mice. Scale bar, 0.1 µm. (C) Schematic illustration of photoreceptors in control or RD mice. Credit: Science China Press

Photoreceptors, like polarized sensory neurons, are essential for light sensation and phototransduction, which are highly dependent on the photoreceptor cilium. Disruption of photoreceptor cilia has been implicated in a variety of retinal diseases, collectively called retinociliopathies, such as Leber congenital amaurosis and retinopathy of prematurity.

Recently, teams led by Prof. Jun Zhou and Assoc Prof. Jie Ran from Shandong Normal University revealed that ciliary disassembly in photoreceptors is a significant event in the pathogenesis of retinal degeneration (RD). The work is published in the journal *Medicine Plus*.

Their work demonstrated a significant reduction in retinal electrophysiological a-wave and b-wave responses and a marked decrease in the thickness of the outer nuclear layer (ONL) in RD mice, indicating severe damage to photoreceptors.

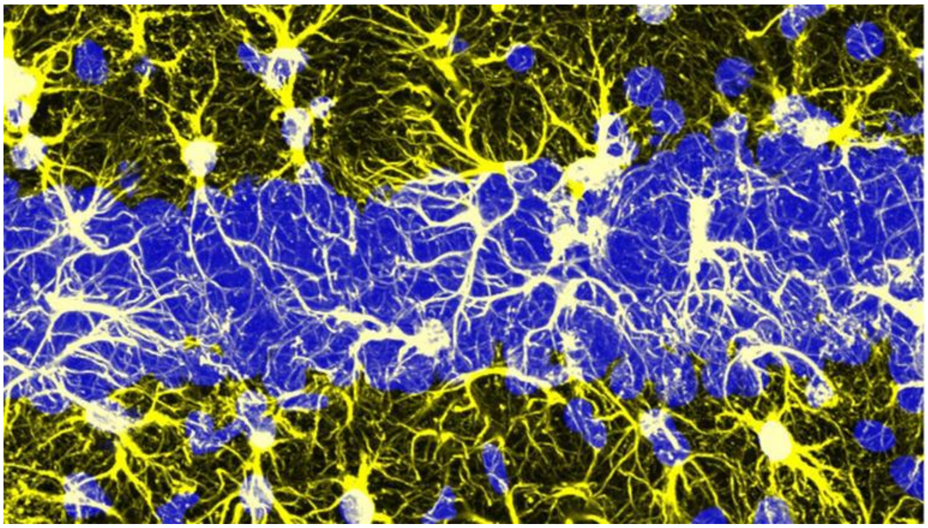
Transmission electron microscopy and immunofluorescence microscopy analyses revealed varying degrees of damage to photoreceptor membrane disks and ciliary axonemes. These results indicate that photoreceptor ciliary disassembly is a key event triggering photoreceptor dysfunction and retinal damage in the pathological process of RD.

In general, their study elucidates the significant role of photoreceptor cilia in RD and provides novel targets for clinical intervention in RD. Graduate students Guizhi Guo and Runa Wang from Shandong Normal University are the first authors of this work, with Assoc Prof. Jie Ran as the corresponding author.

More information: Guizhi Guo et al, Disruption of photoreceptor cilia is a critical event in the pathogenesis of retinal degeneration—Insights from N-methyl-N-nitrosourea-induced mouse model, *Medicine Plus* (2024). DOI: 10.1016/j.medp.2024.100040

Provided by Science China Press

Study shows that astrocytes integrate information about past events in their soma



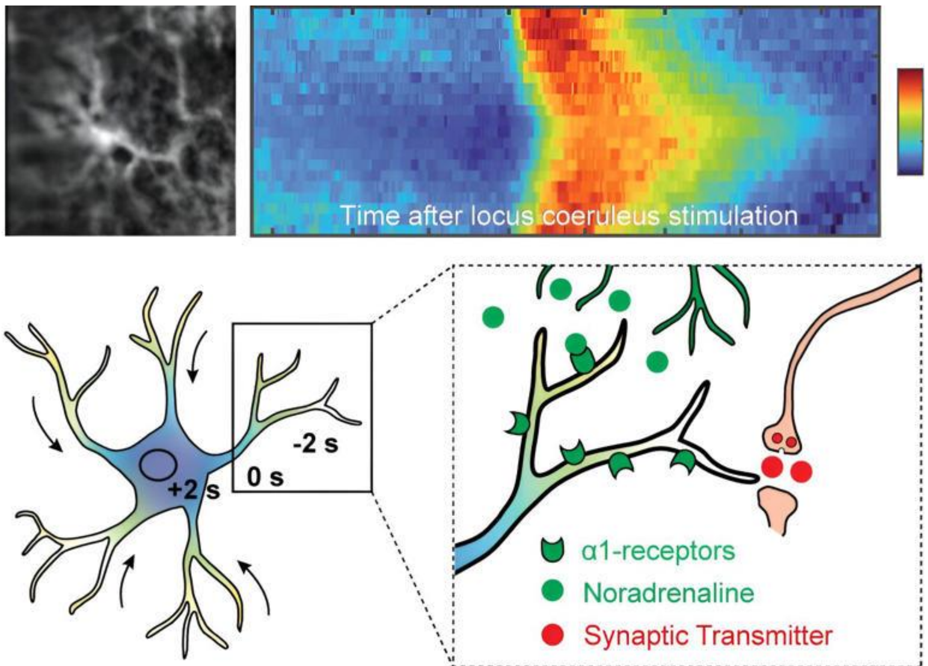
Fluorescence image of astrocytes and their processes in the hippocampus (yellow), with co-staining of cell bodies (blue). Credit: Peter Rupprecht© Provided by Medical Xpress

Neurons are known to communicate and integrate information they receive from their dendrites, branch-like structures extending from their body. In contrast, the activity in astrocytes, a class of star-shaped glial cells found in the central nervous system (CNS), has so far been assumed to be largely uncoordinated, thus lacking the central integration of information.

Researchers at University of Zurich and ETH Zurich recently gathered evidence suggesting that this widespread description of astrocytes might be false or at least incomplete, as they do in fact integrate information about past events.

Their findings, published in *Nature Neuroscience*, specifically reveal the conditional integration of calcium signals in processes taking place in the astrocytes' soma (i.e., cell body).

"Our research was originally aimed at testing a specific hypothesis about the function of astrocytes," Fritjof Helmchen, co-author of the paper, told Medical Xpress. "During in-depth analysis of calcium imaging data, however, we made an unrelated and intriguing observation about calcium signals in astrocytes: We observed that calcium signals propagated from fine cellular processes to the soma on a timescale of seconds. This turned out to be a highly robust and fundamental effect."



Top: Calcium image of a single astrocyte in the living animal (left), with its activation upon stimulation of the locus coeruleus. Bottom: Schematic of earlier activation of processes and later activation of cell bodies of astrocytes, mediated by noradrenaline release. Credit: Peter Rupprecht© Provided by Medical Xpress

The results that Helmchen and his colleagues gathered in their experiments do not answer the research question they were originally trying to address. Nonetheless, they led to an unexpected observation that could open a new avenue for neuroscience research.

In contrast with neurons, astrocytes are not electrically excitable, which means that they do not generate and transmit electrical signals (i.e., action potentials). The only way to observe the activity of astrocytes is thus to image signaling molecules, such as calcium, inside of them.

"We performed two-photon imaging of calcium signals in the hippocampus of mice that were running on a treadmill and carefully analyzed the recordings," Peter Rupprecht, co-author of the paper, told Medical Xpress. "Our main technique was therefore centered on pure observation and in-depth analysis."

Helmchen, Rupprecht and their colleagues were only able to gather evidence of the integration of past events in astrocytes using advanced analysis methods based on so-called correlation functions. In their experiments, they also used optogenetics techniques to activate the locus coeruleus, a small nucleus in the brainstem that regulates arousal and attention processes.

"With these methods, we demonstrated that the astrocytic events are regulated by the neuromodulator noradrenaline," Rupprecht said. "We hope that our study will encourage other astrocyte researchers to apply our methods and analysis techniques also to their research."

This team of researchers was the first to systematically show how astrocytes slowly integrate information in their soma. Interestingly, the integration process they observed resembles the somatic integration that has been extensively documented in neurons.

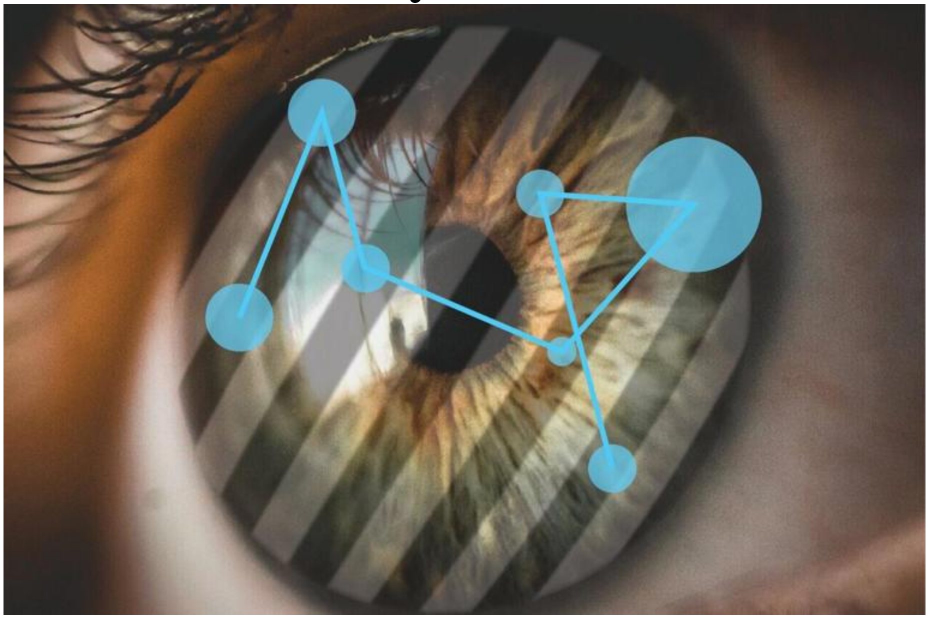
"We also showed how this integration is regulated by arousal and the locus coeruleus, a small nucleus in the brain stem," Rupprecht said. "We believe that this mode of information processing is very likely fundamental for the function of astrocytes as computational units in hippocampus and cortex."

The findings gathered by Helmchen, Rupprecht and their collaborators could have profound research implications, as they suggest that astrocytes play a greater role than expected in the processing and integration of incoming signals. In the future, they could pave the way for more ground-breaking discoveries about the function of astrocytes in health and disease.

"In this study, we investigated how astrocytes integrate signals in their soma, but what do they do once their soma is activated and how do they act upon neurons?" Helmchen added. "We hypothesize that they contribute, in one or the other way, to information processing in the neuronal networks. Our study raises many questions that will require the joint effort of many labs in the future."

More information: Peter Rupprecht et al, Centripetal integration of past events in hippocampal astrocytes regulated by locus coeruleus, *Nature Neuroscience* (2024). DOI: 10.1038/s41593-024-01612-8

Neuroscientists reveal how brain coordinates attention and eye movements



Exploring the link between attention and eye movements. Credit: Priyanka Gupta/Pixabay© Provided by Medical Xpress

Two new studies from the Center for Neuroscience (CNS), Indian Institute of Science (IISc) explore how closely attention and eye movements are linked and reveal how the brain coordinates the two processes.

Attention is a unique phenomenon that allows us to focus on a specific object in our visual world, and ignore distractions. When we pay attention to an object, we tend to gaze towards it. Therefore, scientists have long suspected that attention is tightly coupled to rapid eye movements, called saccades. In fact, even before our eyes move towards an object, our attention focuses on it, allowing us to perceive it more clearly—a well-known phenomenon called pre-saccadic attention.

However, in a new study published in *PLOS Biology*, the researchers at CNS show that this perceptual advantage is lost when the object changes suddenly, a split second before our gaze falls upon it, making it harder for us to process what changed.

"Our study provides an interesting counterpoint to many previous studies which suggested that pre-saccadic attention is always beneficial," explains Devarajan Sridharan, Associate Professor at CNS and corresponding author of the study.

In the study, Priyanka Gupta, a Ph.D. student in Sridharan's lab, trained human volunteers to covertly monitor gratings (line patterns) presented on a screen, without directly looking at them, and to report when one tilted slightly. "Importantly, the participants did this task just before their eyes moved, in the pre-saccadic window. So, we were able to study the relationship between pre-saccadic attention and the detection of changes in the visual environment," explains Gupta.

A tracker was used to monitor their eye movements before, during and after their gaze fell on the object. "To our surprise, participants found it harder to detect the changes in the pre-saccadic window," Gupta adds.

In a follow-up experiment, they made the participants monitor two gratings presented one after the other quickly, again, just before their eyes moved. What the team found was that if the orientation of the second grating suddenly changed during this time, the participants tended to mix up the orientations of the two gratings—explaining the loss of the attentional advantage.

"This is essentially a basic science study," says Sridharan. But such insights, he adds, can be useful for how we track multiple objects in rapidly changing environments—in driving or flight simulators, for example.

In the other study, published in *Science Advances* and carried out with collaborators at Stanford University, the researchers devised an unusual experiment—this time, to decouple attention from eye movements—in monkeys. Their goal was to tease out what is happening in the brain while these processes play out.

The monkeys had been trained on a counter-intuitive task called an "anti-saccade" task. Like the human study, the monkeys covertly monitored several gratings on a computer screen without directly looking at them. But when any one grating tilted slightly, the monkeys had to look away from it instead of focusing more sharply on it. This helped the researchers delink the location of the monkey's attention, from the location where its gaze ultimately fell.

Using a special kind of electrode called a "U-probe," they also recorded signals from hundreds of neurons across different layers of a specific region in the monkey's brain called the visual cortex area V4. What they found was that neurons in the more superficial layers of the cortex generated attention signals, while neurons in deeper layers produced eye movement signals.

Interestingly, these neurons also showed different activity patterns. "The superficial neurons increased their firing rates, to signal the object that needs to be attended to and prioritized for decision-making," says Adithya Narayan Chandrasekaran, first author of the *Science Advances* study and a former research assistant in Sridharan's lab at CNS. On the other hand, the deep neurons were tuning down their "noise," possibly to allow the animal to perceive the object better.

The researchers believe that uncovering such brain signatures can eventually point to what fails in attention disorders. Sridharan says, "Discovering such mechanisms is vital for developing therapies for disorders like ADHD."

More information: Priyanka Gupta et al, Presaccadic attention does not facilitate the detection of changes in the visual field, *PLOS Biology* (2024). DOI: 10.1371/journal.pbio.3002485

Adithya Narayan Chandrasekaran et al, Dissociable components of attention exhibit distinct neuronal signatures in primate visual cortex, *Science Advances* (2024). DOI: 10.1126/sciadv.adi0645

Provided by Indian Institute of Science

Exploring the origins of excitatory and inhibitory neuronal tuning in the postsubiculum

Action potentials from dozens of individual neurons recorded in mouse postsubiculum. Credit: Adrian Duszkiewicz.© Provided by Medical Xpress

Brain cells can be broadly divided into two categories: inhibitory and excitatory neurons. Excitatory neurons are cells that support the generation of electrical impulses in postsynaptic neurons, thus prompting the activation of cells in specific brain regions. Inhibitory neurons, on the other hand, contribute to inhibiting these electrical impulses and thus reducing activity in specific brain regions.

The balance between inhibition and excitation contributes to the healthy functioning of the brain. While the neurobiological processes underpinning the fine-tuning of excitatory neurons are now well understood, those underlying the fine-tuning of inhibitory neurons remain elusive.

Researchers at McGill University and University of Edinburgh carried out a study aimed at better understanding the principles governing the fine-tuning of both excitatory and inhibitory neurons in the mouse postsubiculum, a region in the brain's medial temporal lobe known to support spatial navigation and memory.

Their findings, published in *Nature Neuroscience*, validate the hypothesis that the equivalent tuning of excitatory and inhibitory neurons is an intrinsic property of local cortical networks.

"Our laboratory is interested in how information about the outside world is reflected in the activity of individual brain cells," Adrian J. Duszkiewicz, lead author of the paper, told Medical Xpress.

"The mammalian brain is made of millions of brain cells, called neurons, forming billions of connections, and cracking its code knowing the activity of only a fraction of those brain cells is a challenging task. Still, in some parts of the brain activity of individual neurons is relatively straightforward to interpret, and if we study such circuits in detail we may discover some more general principles of how activity of individual brain cells relates to the outside world."

Cells that engage in fairly straightforward patterns of activity include neurons in the primary visual cortex, which become active in response to visual stimuli. Other examples of these cells are place cells in the hippocampus and grid cells in the medial entorhinal cortex, both of which exhibit patterns of activity that are closely related to an animal's location in its surrounding environment.

The existence of grid cells was first unveiled almost two decades ago and the team who discovered them received the 2014 Nobel Prize in Physiology/Medicine.

"Both place cells and grid cells belong to the class of 'excitatory' cells, that is, brain cells that activate other brain cells they connect to," Duszkiewicz explained. "Such cells constitute a majority of neurons in the cerebral cortex (~85%), while remaining neurons largely belong to another cell class, called 'inhibitory' cells, which decrease the activity of cells they connect to."

Past studies have found that the activity of excitatory cells, including neurons in the primary visual cortex and place cells, is closely connected to environmental features. Inhibitory cells, on the other hand, tend to be permanently active and their activity can only be slightly modulated by external/environmental events.

The primary objective of the recent work by Duszkiewicz and his collaborators was to better understand the origin of inhibitory cell activity. Specifically, the team set out to determine whether the activity of these cells is really random, or whether it follows a particular pattern.

"To do this, we turned to another part of cerebral cortex—a brain area called postsubiculum, that is dedicated to the sense of orientation in space," Duszkiewicz said. "Excitatory cells in postsubiculum are called 'head-direction cells' because each of them is active when the animal is facing a particular direction, and together they form the brain's equivalent of a compass, accurately tracking the animal's orientation in the environment."

The researchers decided to focus their efforts on the mouse postsubiculum because this brain region is known to have a very simple neural code. The simplicity of its code allowed them to map out the activity patterns of individual neurons simply by tracking the direction in which a mouse was moving while it was exploring a box.

"We used miniature electrode arrays that we implanted into the brains of mice and aimed at the postsubiculum," Duszkiewicz said. "This technique allowed us to track activity of dozens of individual neurons, up to 180 at a time, while the mice were foraging for cereal in a large box."

Most of the neurons examined by the researchers, namely the mice's excitatory head-direction cells, were only active when the mice were facing a specific direction. The team also observed some inhibitory neurons that were active all the time and yet appeared to prefer seemingly random sets of directions.

"When we took a closer look at activity patterns of neurons in postsubiculum, or their 'tuning' to the animal's direction, we realized that tuning of inhibitory neurons was not exactly random," Duszkiewicz said. "By looking at their activity alone we were able to determine which way the mouse is currently looking, with similar accuracy to excitatory cells, which means that their activity was meaningful. But more importantly, their activity patterns looked as though they summed the activity of all neighboring excitatory neurons—the canonical head-direction cells."

Interestingly, the researchers found that the patterns of activity of inhibitory neurons did not appear to be at all influenced by inputs originating from other brain areas. In contrast, they appeared to be entirely determined by the tuning of nearby excitatory neurons.

Duszkiewicz and his colleagues defined this interplay between the tuning patterns of excitatory and inhibitory activity as "excitatory/inhibitory equivalence." Specifically, their findings show that the tuning patterns of excitatory and inhibitory cells are comprised of the same components and inhibitory patterns are the sum of excitatory patterns.

"We think that this finding brings us closer to understanding how the two neuron classes, the excitatory and inhibitory cells, work together to create a mental map of the outside world inside the brain," Duszkiewicz said. "This could be particularly important in the age of artificial neural networks, as it puts some constraints on how individual nodes of artificial neural networks should map to the external world if those networks are to model the activity inside real brains."

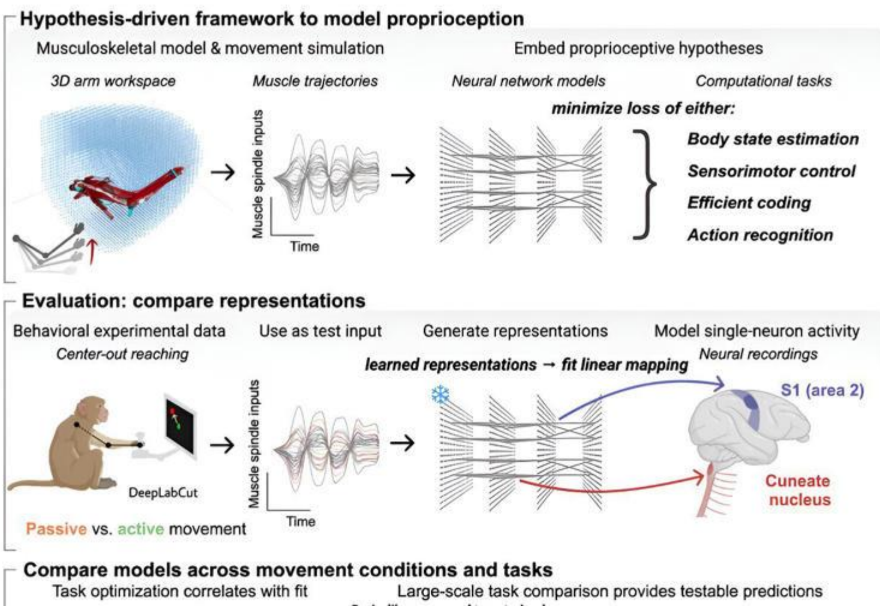
The results gathered by Duszkiewicz and his collaborators shed some new light on the local origins of excitatory and inhibitory tuning in the mammalian brain. While their recent study focused on the postsubiculum, the team hopes to soon broaden their investigation and examine other brain regions.

"Up until now, we have only focused on one neural circuit, the postsubiculum, because its activity patterns are relatively easy to understand," Duszkiewicz added.

"Yet now that we know what to look for, we want to confirm that this excitatory/inhibitory tuning equivalence can be observed in brain areas with more complex activity—such as the grid cells in the medial entorhinal cortex. Another avenue we will pursue in our future work is looking more closely at different sub-classes of inhibitory neurons (of which there are many), to see if they show any differences in their tuning to the animal's orientation."

More information: Adrian J. Duszkiewicz et al, Local origin of excitatory–inhibitory tuning equivalence in a cortical network, *Nature Neuroscience* (2024). DOI: 10.1038/s41593-024-01588-5

Unraveling the 'sixth sense': New study explores how the brain senses body position and movement



Graphical abstract. Credit: Cell (2024). DOI: 10.1016/j.cell.2024.02.036© Provided by Medical Xpress

How does your brain know the position and movement of your different body parts? The sense is known as proprioception, and it is something like a "sixth sense," allowing us to move freely without constantly watching our limbs.

Proprioception involves a complex network of sensors embedded in our muscles that relay information about limb position and movement back to our brain. However, little is known about how the brain puts together the different signals it receives from muscles.

A new study led by Alexander Mathis at EPFL now sheds light on the question by exploring how our brains create a cohesive sense of body position and movement. Published in *Cell*, the study was carried out by Ph.D. students Alessandro Marin Vargas, Axel Bisi, and Alberto Chiappa, with experimental data from Chris Versteeg and Lee Miller at Northwestern University.

"It is widely believed that sensory systems should exploit the statistics of the world, and this theory could explain many properties of the visual and auditory system," says Mathis. "To generalize this theory to proprioception, we used musculoskeletal simulators to compute the statistics of the distributed sensors."

The researchers used this musculoskeletal modeling to generate muscle spindle signals in the upper limb to generate a collection of "large-scale, naturalistic movement repertoire." They then used this repertoire to train thousands of "task-driven" neural network models on sixteen computational tasks, each of which reflects a scientific hypothesis about the computations carried out by the proprioceptive pathway, which includes parts of the brainstem and somatosensory cortex.

The approach allowed the team to comprehensively analyze how different neural network architectures and computational tasks influence the development of "brain-like" representations of proprioceptive information. They found that neural network models trained on tasks that predict limb position and velocity were most effective, suggesting that our brains prioritize integrating the distributed muscle spindle input to understand body movement and position.

The research highlights the potential of task-driven modeling in neuroscience. Unlike traditional methods that focus on predicting neural activity directly, task-driven models can offer insights into the underlying computational principles of sensory processing.

The research also paves the way for new experimental avenues in neuroscience since a better understanding of proprioceptive processing could lead to significant advancements in neuroprosthetics, with more natural and intuitive control of artificial limbs.

More information: Alessandro Marin Vargas et al, Task-driven neural network models predict neural dynamics of proprioception, *Cell* (2024). DOI: 10.1016/j.cell.2024.02.036

Provided by Ecole Polytechnique Federale de Lausanne

Often seen, never studied: First characterization of a key postsynaptic protein

A Kobe University research team identified a protein, called "FAM81A," that has been showing up in the majority of studies on the "postsynaptic density" but has remained uncharacterized so far. In a series of analyses, they now found that the protein probably is a major regulatory factor. The picture shows a cultured mouse hippocampal neuron. The small white dots are postsynaptic densities containing labelled FAM81A. Credit: Kaizuka Takeshi© Provided by Phys.org

A protein that appears in postsynaptic protein agglomerations has been found to be crucial to their formation. The Kobe University discovery identifies a new key player for synaptic function and sheds first light on its hitherto uncharacterized cellular role and evolution.

What happens at the synapse, the connection between two neurons, is a key factor in brain function. The transmission of the signal from the presynaptic to the postsynaptic neuron is mediated by proteins and their imbalance can lead to neuropsychiatric conditions such as severe depression, autism, or alcohol dependence.

However, due to the vast diversity of proteins present at this junction, many have not yet been studied and often it is not even clear whether those previously found actually belong there or whether they are just impurities resulting from the analysis process.

A particularly conspicuous structure directly underneath the postsynaptic membrane is the so-called "postsynaptic density," an agglomeration of possibly thousands of different proteins.

To shed some light on the postsynaptic density, Kobe University neurophysiologist Takumi Toru and his group first compared 35 datasets of previous studies on the phenomenon to find out which uncharacterized proteins appear consistently. Their paper has been published in *PLoS Biology*.

Kaizuka Takeshi, the first author of the paper, explains, "We established an analytical pipeline to unify and align protein structures in different datasets. This resulted in the identification of a poorly characterized synaptic protein that has been detected in more than 20 of these datasets."

This suggested that the protein, which goes by the label FAM81A, is probably relevant to the function of the whole structure, so the team analyzed its interactions with other proteins, its distribution in and around neurons and its effect on neuron shape and function, the mechanism of its function, and its evolution. In short, they gave this protein a full first characterization.

Takumi summarizes, "The important finding is that FAM81A interacts with at least three major postsynaptic proteins and modulates their condensation. This suggests that FAM81A is a major regulatory factor in the postsynaptic density."

The group could confirm that FAM81A facilitates the condensation of key proteins into a membrane-less organelle through liquid-liquid phase separation, a process in which strongly interacting molecules exclude elements of the surrounding medium, and that the absence of the protein leads to a significant decrease of activity in cultured neurons.

Humans have two related copies of the gene, FAM81A and FAM81B. However, while FAM81A is expressed in the brain, FAM81B is expressed only in the testes. Furthermore, birds and reptiles also have two copies of the gene, but amphibians, fish and invertebrates have only one, and its expression is not localized to one tissue.

"Interestingly, it seems that the evolutionary conservation of FAM81A function in the synapse is limited compared to other synaptic molecules, as the FAM81A homolog in fish is not detected in the synapse. This suggests that FAM81A could be a key protein in understanding the cognitive functions of higher vertebrate brains," says Kaizuka.

But their work was only the first step. To really understand the role of the protein, it is necessary to study its function in the complex environment of the brain. The Kobe University research team thus wants to create mouse models that lack the gene for FAM81A and study what this means both for the function of the synapses and the behavior of the organism.

More information: FAM81A is a postsynaptic protein that regulates the condensation of postsynaptic proteins via liquid-liquid phase separation, *PLoS Biology* (2024). DOI: 10.1371/journal.pbio.3002006

Provided by Kobe University

Scientists uncover new hormone in unusual discovery

The newfound hormone is made in the brain and then sent out to the body via the bloodstream, studies in mice and human cells suggest.© SCIEPRO via Getty Images

Scientists just discovered a hormone that may solve a long-standing biological mystery.

It's difficult to prove you've identified a new hormone — a chemical signal that directs behavior in distant cells, often by traveling through the bloodstream. To be sure, you need to confirm where it's made, which tissues it affects and that it can be found in the bloodstream, senior study author Holly Ingraham, a professor and vice-chair of cellular and molecular pharmacology at the University of California, San Francisco, told Live Science.

"Most have been discovered, so it's pretty novel to actually uncover a new hormone," said Dr. Sundeep Khosla, a physician-scientist at Mayo Clinic in Rochester, Minnesota, who was not involved in the research. "They make a pretty convincing case that this is really a hormone."

Scientists had previously found the substance in mammals, including humans, Khosla noted, but they didn't know it was a hormone. The new study shows that the chemical — which the researchers have dubbed "maternal brain hormone" — travels from the brain to bone-forming cells, where it helps build bone, according to the new study, published Wednesday (July 10) in the journal Nature.

Related: New drug could prevent bone loss on lengthy space missions, study in space-faring mice suggests

This bone-building comes into play after pregnancy, when estrogen levels plummet and the demand for calcium skyrockets as the body starts making milk. Normally, estrogen strengthens bones and prevents their calcium from being stripped away. Thus, it's been unclear how bones retain much of their strength during breastfeeding and then recover soon after weaning.

The new hormone "adds an important piece to that whole biology that we didn't know before," Khosla told Live Science. What's more, although it's important in the postpartum period, the new hormone can also boost bone growth in males, the researchers showed.

"This is an equal-opportunity hormone — it works in both males and female bones and skeletal stem cells," Ingraham said. "If we can develop it into a therapy, [it] will work in both males and females." The hormone could theoretically help speed up fracture repair, treat osteoporosis and prevent premature bone loss triggered by medical treatments.

Hunting for a hormone

The new study builds upon research in mice published in 2019, in which Ingraham and colleagues found a way to boost bone density and strength by up to 800%. This dramatic effect was mediated by cells in the brain's hypothalamus, a hormone-making structure. Blocking estrogen in specific cells in the hypothalamus supercharged bone growth. However, this trick only worked in female mice, not in males, suggesting this particular pathway only exists in females.

The researchers theorized that, when estrogen is switched off, these cells in the female brain somehow prompt the body to channel energy into growing bone.

The question was, how do these cells get the word out? So in the new study, they looked for a blood-borne molecule that would relay the message.

This quest was like hunting for a needle in a haystack, because hormones present in the blood exist in only "miniscule amounts," Ingraham told Live Science.

The team first confirmed that their culprit was in the blood using mice with blocked estrogen signaling, and thus, extra-thick bones. Normal mice infused with blood from these modified mice showed dramatic bone growth. The team also transplanted bone-growing stem cells and whole bones into different parts of the modified mice; these transplants too showed enhanced growth, suggesting the hormone was both potent and in widespread circulation.

Related: What is bone density?

The team then looked at gene activity in the hypothalamus and found that, in the big-boned mice, a specific gene in these cells was very active: CCN3, which encodes instructions for a protein. (This is the protein that the researchers propose should now be called "maternal brain hormone.")

Not much is known about the CCN3 protein, but historically, people didn't think it was a hormone. It was thought to do its job locally, rather than entering circulation, Ingraham said. Nonetheless, the group's experiments pointed to this protein as the hormone they sought.

It's particularly novel because hormones made in the hypothalamus normally talk to the pituitary gland — a master hormone-maker attached to the base of the brain. The pituitary gland would then pass messages from the hypothalamus on to the body, but in this case, the hypothalamus-made hormone "talks directly to bone," Khosla said.

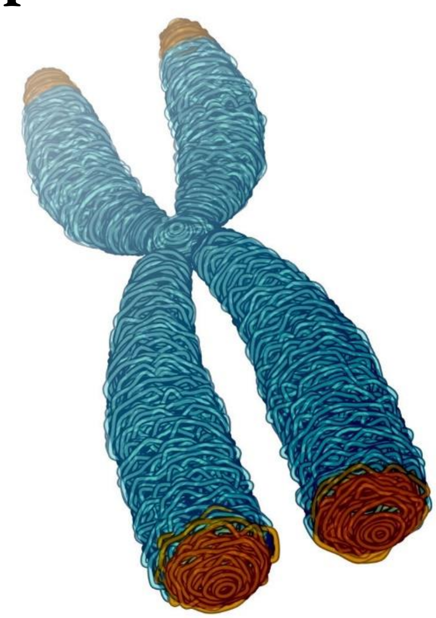
The team even showed that, in elderly mice, the bone-boosting hormone can accelerate the healing of fractures.

"When I saw that fracture repair data, I knew that this absolutely had to be real," Ingraham said. "It's just so phenomenal that you can take these 2-year-old male mice ... and see that sort of repair."

Finally, the scientists revealed that, in the postpartum period, CCN3 naturally goes up in female mice's brains. If you block that increase, the mice's bones rapidly grow weaker as they continue to lactate. This uptick in CCN3 still needs to be confirmed in humans, Khosla said, but the mouse data suggest that the hormone is key to keeping bones strong during breastfeeding. For now, though, it's unclear how that switch actually gets flipped in the brain.

"What is it about this [postpartum] period that turns this thing on in the brain, in those neurons?" Ingraham said. "We don't know." That mystery will take much more work to solve — and it may just reveal additional hormones in the process, she said.

New study finds potential targets at chromosome ends for degenerative disease prevention



Telomeres are found at the ends of chromosomes and play a critical role in the cell-renewal process. Credit: National Human Genome Research Institute© Provided by Phys.org

We depend on our cells being able to divide and multiply, whether it's to replace sunburnt skin or replenish our blood supply and recover from injury. Chromosomes, which carry all of our genetic instructions, must be copied in a complete way during cell division. Telomeres, which cap the ends of chromosomes, play a critical role in this cell-renewal process—with a direct bearing on health and disease.

The enzyme telomerase plays a key role in maintaining the length of telomeres as chromosomes replicate during cell division. UC Santa Cruz professor Carol Greider has been studying telomeres and telomerase for over 30 years. The impact of the discoveries she has made over that time are why she, along with two colleagues, won the Nobel Prize in Physiology or Medicine in 2009.

So, the findings of Greider's latest study on telomeres shouldn't have surprised her. And yet, they did.

Published today in *Science*, a new study finds that telomere lengths follow a different pattern than has thus far been understood. Instead of telomere lengths falling under one general range of shortest to longest across all chromosomes, this study finds that different chromosomes have separate end-specific telomere-length distributions.

According to Greider, this discovery means we don't fully understand the molecular process that regulates telomere lengths. That's important because of how telomere lengths affect human health: "When telomeres get to be too short, you have age-related degenerative diseases like pulmonary fibrosis, bone-marrow failure, and immunosuppression," Greider said. "On the other hand, if telomeres are too long, it predisposes you to certain types of cancer."

Kayarash Karimian, the lead author on the paper, is a former Ph.D. student in Greider's lab at the Johns Hopkins University School of Medicine. Other co-authors of this study include researchers at the Dana-Farber Cancer Institute, Harvard Medical School, and University of Pittsburgh. Greider, a distinguished professor of molecular, cell, and developmental biology at UC Santa Cruz, and a University Professor at Johns Hopkins, was the senior author on the paper and led the work.

Why length matters

Without telomerase, telomeres would get shorter and shorter as a cell divides over and over again. Over the past 30 years, research by Greider and others have confirmed that short telomeres lead to degenerative disease—as well as shown that telomere lengths fall within a certain range.

But this paper challenges scientific consensus by showing that a singular telomere-length range is too broad. Measuring the telomeres of 147 people for this study, the researchers found in one individual that the average telomere length across all chromosomes was 4,300 bases of DNA. Then when they isolated specific chromosomes, they found most telomere lengths differed significantly from this average. In one case, lengths differed as much as 6,000 bases, which Greider describes as "jaw-dropping."

Further, they found across all 147 individuals the same telomeres were most often the shortest or longest, implying telomeres on specific chromosome ends may be the first to trigger stem-cell failure.

Innovating on nanopore sequencing

To make such precise measurements at the molecular level, Greider's team used a technique invented at UC Santa Cruz called "nanopore sequencing," a revolutionary method for reading DNA and RNA that has had an immense impact on genomics research since its 2014 debut on the market as the commercial product MinION.

Nanopore technology has enabled some of the most significant advances in the genomics field, such as the completion of a gapless human genome, and sequencing of COVID-19 genomes—making it crucial in the fight to end the pandemic. UC Santa Cruz licensed the concept for nanopore-sequencing technology to the UK-based company Oxford Nanopore Technologies, which made MinION, the first hand-held DNA sequencer.

Notably, in the eyes of nanopore sequencing's inventors, Greider's study proves that the technique's ability to advance scientific research continues to unfold.

Mark Akeson, emeritus professor of biomolecular engineering at UC Santa Cruz, notes that two preprint studies that corroborate the basic findings of Greider's paper have also been posted online.

"In my opinion, this is the most important nanopore-based paper focused on human biology since the MinION was introduced," Akeson said. "It is easy to envision broad use of their telomere-length assay in the clinic."

Akeson and David Deamer, also an emeritus professor of biomolecular engineering at the Baskin School of Engineering, were honored at the Library of Congress last year for inventing nanopore sequencing. Their colleague and friend Daniel Branton, a Havard biologist and co-inventor of the technology, was honored as well.

Implications for disease prevention

Such precise DNA reads allowed Greider's team to pinpoint the sequences adjacent to telomeres and hypothesize that those areas are where telomerase is regulating length. And if that's true, Greider said those regions, and the proteins that bind there, could serve as potential targets for new drugs for preventing disease.

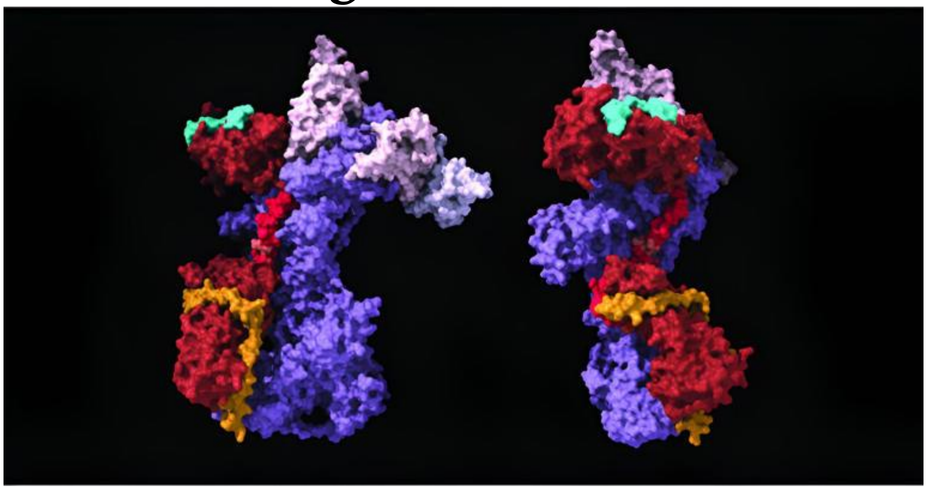
In addition, their process of "telomere profiling" via nanopore sequencing could serve as a model for the development of additional MinION-based assays for high-throughput drug screening.

"This accessible technique has widespread potential for use in research, diagnostics, and drug development," Greider said. "This work indicates that there are yet undiscovered mechanisms for telomere length regulation; probing these mechanisms will inform new approaches to cancer and certain degenerative diseases."

More information: Kayarash Karimian et al, Human telomere length is chromosome end–specific and conserved across individuals, *Science* (2024). DOI: 10.1126/science.ado0431

Provided by University of California - Santa Cruz

Key mechanism for maintaining proper telomere length identified



CST (purple/lavender) bound to POT1 (red). Phosphorylation of the crimson-highlighted region in POT1 regulates the recruitment and activity of CST–Polα-primase at telomeres. Credit: Laboratory of Cell Biology and Genetics at The Rockefeller University© Provided by Phys.org

The length of telomeres that protect the ends of our chromosomes should be tightly regulated. Those that are too long predispose to cancer, and those that are too short lose their protective ability, resulting in telomere disorders with serious health consequences.

Our cells prevent this excessive shortening by adding telomeric DNA to the ends of chromosomes. Researchers at Rockefeller showed that this process is mediated by two enzymes: telomerase and the CST–Polα/primase complex. Having determined how telomerase is recruited, scientists were left with a fundamental question: how does CST–Polα/primase find its way to the telomere?

Now, a new study published in *Cell* demonstrates that CST is recruited to the end of the telomere and regulated by subtle chemical changes made to POT1, a protein in the shelterin complex involved in telomere maintenance and implicated in cancer risk. The findings provide new insight into how human telomeres function at the molecular level, with implications for numerous diseases and disorders.

"After the discovery of telomerase, it took decades to figure out how it gets to the telomere. Now, just months after discovering that CST–Polα/primase is the second critical enzyme required for telomere maintenance, we understand the details of how it is recruited," says Titia de Lange, the Leon Hess professor. "Moreover, we've found out how this process is regulated."

Recruiting and regulating CST

Telomeres have two different types of strands, G-rich and C-rich. Scientists have long known how telomerase maintains the length of the G-rich strand, but only recently was it recognized that the same problem also exists for the C-rich strand. A recent study from the de Lange lab identified the CST–Polα/primase complex as the key regulator responsible for keeping that strand intact.

What remained to be seen was how CST, and its associated enzyme Polα-primase, travels to telomere to facilitate C-strand maintenance across replication cycles. Sarah Cai, a Ph.D. candidate at Rockefeller, began investigating this piece of the telomere puzzle.

Building on a decade of the de Lange lab's groundwork on CST, Cai added cryo-EM to the techniques used in this study while being co-advised by Rockefeller's Thomas Walz.

"The interdisciplinary nature of the study is one of the most exciting parts," Cai says. "It was a very successful double-lab effort, making use of many different technologies." Walz, whose research focuses on cryo-EM, noted how Cai incorporated AlphaFold, a deep-learning algorithm that can predict the unique 3D structures of proteins, into her work.

With the combined power of biochemistry, structural biology, and cell biology, the team ultimately confirmed that CST is recruited to telomeres by the POT1 protein. Once CST–Polα/primase is onsite, the addition and removal of phosphate groups from POT1 appears to function as an on/off switch that coordinates the final steps of telomere replication.

Phosphorylated POT1 ensures that CST–Polα/primase remains inactive until telomerase has finished its job, upon which the dephosphorylation of POT1 activates CST–Polα/primase to add the finishing touches to the telomere.

Telomere disorders and cancer

Next, the team will look for specific enzymes that attach and remove phosphates during this process, controlling the on/off switch on POT1, and determining their role in regulating CST–Polα/primase recruitment and activity.

A better understanding of how CST is recruited to the telomere cannot come fast enough for patients suffering from telomere disorders, such as Coats plus syndrome, a severe multi-organ disease characterized by abnormalities in the eyes, brain, bones, and GI tract.

"For a long time, we didn't know why mild alterations in single amino acids would cause such a devastating disease," Cai says. "We now have a better idea of how these mutations affect the recruitment of this critical telomere maintenance machine and lead to Coats plus syndrome."

The findings will also impact their cancer research. The de Lange lab has spent decades studying how telomere shortening contributes to tumor suppression and genome instability in cancer, and the present research may ultimately help answer questions that lie at the heart of tumor development.

"Anything critical to telomere length regulation may well be critical to cancer prevention too," de Lange says. "This is a major focus of our lab, and one of the reasons we'll be looking into the interplay between CST–Polα/primase and telomerase more closely in the future."

More information: Sarah W. Cai et al, POT1 recruits and regulates CST-Polα/primase at human telomeres, *Cell* (2024). DOI: 10.1016/j.cell.2024.05.002

Provided by Rockefeller University

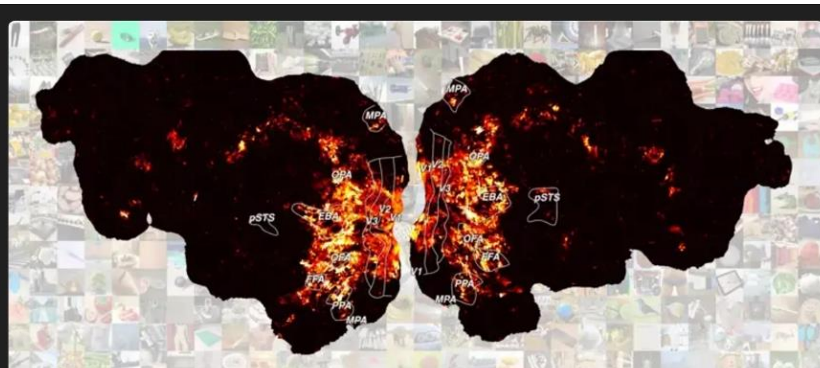
People think in many dimensions at the same time, study finds

Seeing the world around you may feel effortless. You open your eyes and can quickly distinguish people, animals, and objects in your surroundings.

Traditionally, scientists believed that the main goal of perception was to recognize and categorize these objects. However, new research suggests that the process might be more complex than previously thought.

A study led by the Max Planck Institute for Human Cognitive and Brain Sciences, the Justus Liebig University in Germany, and the National Institutes of Health in the USA indicates that brain activity during object recognition is influenced by various behaviorally important factors, not just categorization.

The traditional view of the brain's visual system suggested that when you see an object, your brain breaks it down into basic features—such as color, shape, and texture—and then reassembles these features to help you recognize and categorize it.



The brain activity of study participants was measured in the MRI scanner over 15 sessions while they saw over 8,000 different images of 720 objects. (CREDIT: MPI CBS)

According to this view, the ultimate aim is to assign an object to a specific category, like recognizing that a dog is an animal. However, Martin Hebart, a group leader at the Max Planck Institute and professor at Justus Liebig University, explains that their findings challenge this idea.

He states, "Our results have shown that recognition and categorization are important goals of our vision, but by no means the only ones." Hebart adds that behaviorally relevant signals are found at all stages of visual processing, and these signals extend beyond mere recognition.

The researchers used a computational model to explore the way objects are represented in the brain. They identified 66 different dimensions based on behavioral data gathered from more than 12,000 participants.

These dimensions do more than just help categorize an object as, for example, a dog or an animal. They also explain various attributes like color, shape, and the typicality of an object—such as how typical a dog is as a representative of the animal category.

This broader set of dimensions allows a deeper understanding of how the brain perceives and makes sense of the environment. Hebart notes, "This allowed us to explain much better how our brain enables us to perceive the objects in our environment and understand their meaning."

The study examined the brain activity of three participants, who were shown over 8,000 different images of 720 objects while in an MRI scanner.

An fMRI encoding model of object dimensions underlying human similarity judgements. (CREDIT: MPI CBS)© The Brighter Side of News

First author Oliver Contier describes the results: "When the participants saw a rocket, for example, we were able to measure from the brain activity that their visual system not only recognized that it was a rocket or that a rocket is a vehicle, but also that it is grey and elongated, has to do with fire, can fly, or sparkles."

This demonstrates that the brain does not only recognize and categorize objects; instead, it processes a wide array of characteristics, engaging all perceptual processing stages.

This richer, multidimensional approach to understanding visual perception offers insights into how people make sense of what they see. Martin Hebart explains that their work reveals a "multidimensional framework that is consistent with the rich and diverse behavioral relevance of objects."

Regional tuning profiles across 66 object dimensions and representative images for selectivity of each region of interest in visual cortex. (CREDIT: MPI CBS)© The Brighter Side of News

Unlike a focus purely on categorization, this approach better captures the broad spectrum of human behavior and the complexity of interacting with the visual world. By considering multiple dimensions, the study shows how perception is not just about knowing "what" something is, but understanding a broader array of attributes that give it meaning in a variety of contexts.

Ultimately, this new perspective on vision can help explain human behavior more effectively than the traditional categorization-focused view. Whether recognizing an object, understanding its properties, or predicting how it might interact with its surroundings, the human visual system is far more dynamic than previously thought.

The findings underline the importance of behaviorally relevant features, which include not just the identity of objects but also qualities like form, function, and context.

Representational sparseness of behaviour-derived object dimensions in object-category-selective brain regions. (CREDIT: MPI CBS)© The Brighter Side of News

This approach provides a clearer understanding of how people navigate the visual complexities of everyday life. Instead of the brain working purely to sort objects into categories, each visual experience involves interpreting numerous dimensions simultaneously.

This insight offers a more complete picture of how perception works, shedding light on how individuals perceive, interpret, and respond to their environment.

Scientists take huge step forward in mapping all 37 trillion cells in the human body

The human body contains around 36 trillion to 37 trillion cells, and researchers are mapping out where every one of those cells lives.

Scientists with the Human Cell Atlas (HCA), an international research consortium, have profiled 100 million cells from more than 10,000 people around the world. Working in over 100 countries, the researchers aim to pinpoint similarities and differences in the cells of people from different demographics and genetic backgrounds.

By 2026, the team plans to unveil an atlas of the whole human body that details the location, identity and function of each cell at different stages of life. That atlas will just be a first draft; later iterations could include data from billions of human cells, the scientists project.

Now, HCA scientists have just dropped more than 40 papers that will aid in the construction of the groundbreaking first draft of their atlas. The research trove, published Wednesday (Nov. 20) in several Nature journals, charts cells in many organs and organ systems — including the lungs, brain and skin — and describes the advanced computational tools needed to crunch all those data.

Aviv Regev, a founding co-chair of the HCA, compared the advance to leaps in traditional cartography. Imagine going from having only 15th-century maps of the world to having Google Maps, complete with detailed topographies, street views and dynamic traffic patterns.

"So that is the leap that we have done — moving from maps that look as crude as that to maps that are the resolution of the Google Map," Regev said at a news conference Tuesday (Nov. 19). "But we still have work to do."

The new research includes a detailed map of the digestive tract, running from the esophagus to the colon. The researchers mapped a healthy digestive tract based on 1.1 million cells sampled from nearly 190 people. They also compiled data from people with different gastrointestinal conditions, including ulcerative colitis and Crohn's disease. Through this work, they uncovered a type of cell that seems to contribute to the inflammation in these diseases, likely by summoning immune cells.

"Intestinal inflammation can cause cells to undergo metaplasia, a shift from one cell type to another," Itai Yanai, scientific director of the Applied Bioinformatics Laboratories at NYU Langone Health, wrote in a commentary. With data from both healthy and diseased guts, the researchers were able to pinpoint which stem cells gave rise to the "metaplastic" cells, Yanai said. After transforming, the metaplastic cells then spurred more inflammation, the research suggested.

In other papers, researchers opened a window into early human development, revealing how the placenta develops and the skeleton starts to form in the first trimester of pregnancy. The latter study revealed never-before-seen states that cells enter as they prepare to form the skull. The researchers also investigated genes that might be involved in craniosynostosis, a birth defect in which the soft spots of the skull fuse too soon.

Other papers focused on "organoids," miniature versions of human organs grown in the lab. One looked at brain organoids, which mimic developing brains. Different labs use various strategies to grow organoids, but that raises questions about which method produces the best model — which brain organoid best mimics an actual brain? The scientists compared maps of human brains to those of organoids, finding that, at least up to the second trimester, the organoids match fetal brains fairly closely. Open questions remain about the third trimester.

Another lab ran a similar study looking at skin organoids, to see how closely they resembled real skin.

The atlas helps researchers come up with "better recipes" for organoids, Muzlifah Haniffa, a member of the HCA organizing committee, said at the news conference.

But "the information kind of flows both ways," Sarah Teichmann, an HCA co-chair, added, because the organoids also reveal subtle details of what's happening inside the body. Scientists can "poke the cells, perturb the cells" in ways that wouldn't be possible in human subjects, she said. Thus, making true-to-life organoids can help reveal how diseases arise and which drugs might effectively treat them.

Taken together, the more than three dozen HCA papers represent a major step forward. Meanwhile, data previously published by the consortium have already fueled new discoveries: Work published in 2020 helped reveal unexpected tissues that were vulnerable to COVID-19, and a map of the human lung revealed a new type of cell — the ionocyte — that may play a key role in cystic fibrosis.

"Collectively, the atlases have the potential to constitute a resource that others might be inspired to explore and compare with other biological contexts, such as different species and rare diseases," Yanai wrote. "Researchers might then discover aspects of the human body that cannot yet be imagined."

How 36 Trillion Cells Work to Keep Us Alive

When Walt Whitman wrote that he contains "multitudes," he was probably referring to personal potential. But the 19th-century American poet may just as well have been referring to cells.

Cells are both the smallest biological unit that can survive on their own, as well as the building blocks that construct all living organisms. They contain instructions that can produce over 200 different types - each with their own function. Those instructions contain rules about what kind of cells they can divide into.

Understanding the Basics: What Are Cells?

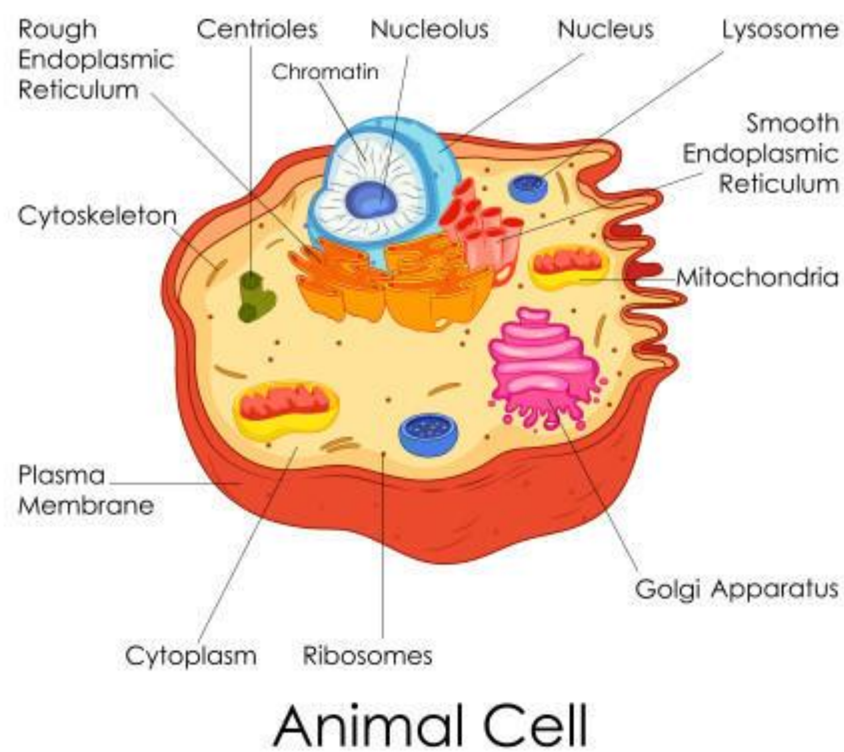


Diagram of Animal Cell showing cytoplasm and cytoskeleton

The comparison is apt because the youngest cells in a fertilized egg can, indeed, become multitudes - both in terms of numbers and types. They are often referred to as the building blocks of life.

However, that description may be a bit too simplistic, says Quyen Aoh, Associate Professor of Biology at Gannon University in Erie, Pennsylvania. She prefers to refer to them as robots.

Like robots, all cells contain a membrane - an outer layer that defines the cell and contains its pieces. That layer is porous, allowing nutrients to feed the cell and waste to leave it.

Inside the skin is the cytoplasm, an area that contains parts that keep the robot running. This includes a framework called the cytoskeleton that gives the cell its shape.

The center of the cell contains the nucleus, which acts like the robot's hard drive. That hard drive holds DNA, the genetic code that tells each cell what to do or become.

How Many Cells Are in the Human Body?

We all start as a single cell, called a zygote that is created after sperm fertilizes an egg.

The zygote is the first embryonic stem (ES) cell. This cell is considered "totipotent"-meaning that it can produce any kind of cell. Initially, it gives rise to more of the same. "When the robot is turned on, it figures out that it'd probably have a better chance of survival if it had some buddies, and so makes more of itself," says Aoh.

Once the embryo grows to about 32 ES cells, they begin to differentiate - or produce more diverse cell types, each with their own specialty. "As the robot population grows, they figure out that they'd survive even better if different groups of robots did different things instead of doing all the same things," Aoh says.

As the embryo grows, it produces more and more specialized cells - like blood, tissue, and neurons. Once the embryo grows into an adult, it will max out at about 36 trillion cells in men and 28 trillion in women.

What Does a Cell Do?

Each cell is alive but depends on both itself and its neighbors for survival. A cell has many of the basic needs of a larger, more complicated living organism.

"It's got to take in nutrients, it's got to build things, it's got to maintain things, it's got to get rid of waste," says Aoh. "It has to be able to communicate both inside of the cell and outside the cell."

The cell's other main job is to make more cells. The question is when, what kind, and how many.

Exploring the Different Types of Cells in the Body

That's where the "software" in each cell's DNA comes into play. The genes - individual pieces of "code" in the hard drive - contain rules about how and what each can become. For instance, once a cell becomes more specialized, it can no longer produce an ES cell.

Also, broad categories of cells cannot change their developmental trajectory. For example, a category of cell that makes blood cells can produce red or white blood cells - but cannot arbitrarily divide into skin cells or neurons. This is true further down the line as well. A red blood cell can't divide and form white blood cells, for instance.

The differentiation into specific cell types is akin to robots creating a society with a variety of specialized workers. Some stick together to do one job. That's how a particular tissue is formed.

Others break off and choose a different job. "Soon enough, they've created a self-sustaining robot civilization," Aoh says. "The amazing thing is that they never really had to change the information in their hard drive to do all this. They just altered their programming as their civilization grew to use it more effectively."

Eventually, this "civilization" will include over 200 specialized cell types. Depending on the type, some "turn over" faster than others - essentially dying off and being replaced by substitutes. The rate of turnover differs by cell type and function. For instance, cells that line your gut are being almost constantly replaced since they battle "invaders" like gut microbes in a hostile environment. Skin cells, too, turn over - but not as quickly as stomach cells, because the level and intensity of "attack" from the environment is neither as frequent nor as severe.

In general, the number of cells in each type grows as we move from childhood to adulthood. There are some counter-intuitive exceptions, though. For instance, we are born with more neurons than we have when we reach adulthood.

"That might sound like a really scary thing," says Aoh. "But one thing that's really amazing about the neurons in our brain is that our brains figure out more efficient ways to make connections between neurons."

At some point, cells stop being able to differentiate into other cell types and eventually lose the ability to divide.

When Cells Go Rogue

There are exceptions, though. "Occasionally, you've got a malfunctioning robot that decides it'd be better on its own than with its robot buddies," says Aoh. "But because it's no longer working with everyone, it becomes a drain on all the other robots as it replicates more of itself. And soon, those defunct robots start causing the good robots to malfunction more often than they're supposed to. This is cancer."

Cancer is essentially cell division that is out of control. Cells that SHOULD be done dividing and creating more of their own type instead start creating a different cell type. "Cancer cells somehow or other are able to switch on a program that they should have had turned off," says Aoh. Instead, their software has essentially become corrupted and the new cell types divide out of control.

Each type of cancer is caused by a different combination of glitches. Those glitches could include damage to the DNA or mutations in genes that are supposed to tell cells to stop dividing, among others. That is why there is no unified cure for cancer. Instead, scientists are finding ways to combat each type, using different weapons and approaches.

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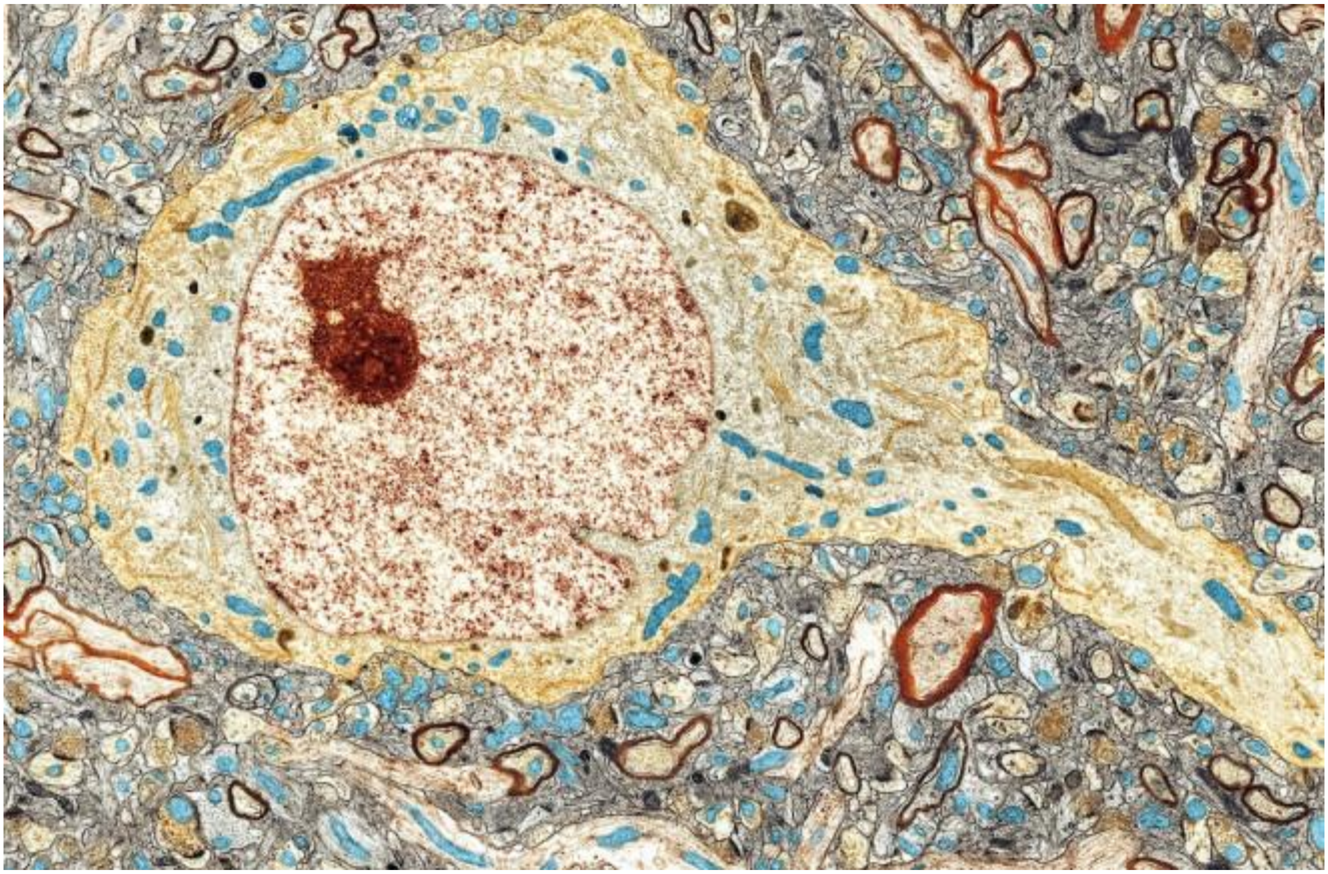
An Atlas of Our Cells

Hundreds of researchers team up to map the human body's trillions of cells, and how they all get along.



Hippocampus neuron (Credit: Thomas Deerinck/NCMIR/Science Source)

When Robert Hooke peered through a primitive microscope in the mid-17th century, he set in motion a revolution. Today's understanding of the fundamental structure of living organisms began when he examined thin slices of cork and saw tiny walled compartments that looked like a monk's dwelling: He called them cells.

Subsequent advances over the centuries deepened our understanding of these structures, which we now know to be the basic unit of life. In the past decade alone, quantum leaps in technology have enabled scientists to explore the Lilliputian universe of the cells with unprecedented precision. The developments have sparked the creation of a massive scientific juggernaut that rivals the Human Genome Project in scope and importance.

Called the Human Cell Atlas (HCA), the international research effort aims to create a comprehensive 3D reference map of how genes are expressed, or activated, in different cell types and their states in every organ system of the human body. The global consortium includes more than 1,000 scientists from 584 institutes in 55 countries. While they won't attempt to plumb all 37 trillion cells in the human body, initial research is zeroing in on five main areas, including cancer; the brain and nervous system; the immune system; the epithelial tissues that serve as a protective layer throughout our body; and human development, starting with cell differentiation in the womb.

The work has the potential to usher in a new era of precision medicine that will transform our understanding of health and disease, leading to better detection, monitoring and treatment of the ills that plague humanity. "There's much more diversity in the cells than we previously imagined, and there has been an explosion in technology that is shedding light on that," says Sarah Teichmann, head of cellular genetics at the U.K.'s

The Universe of the Cell

Our cells are complicated creatures. Each one is composed of many millions of molecules, which continuously transmit messages to each other to complete the cell's basic work, whether that particular cell's job is to repair tissue damage, mop up debris or send messages along the brain's neural circuitry. Coiled inside the nucleus of each cell is the double helix of DNA, two intertwined strands of chemicals dotted with more than 20,000 genes that provide the basic blueprint of life. As each gene is expressed, it produces RNA, which then produces proteins, the workhorses of the cells. Proteins also sit on the cell's surface, like tiny periscopes scanning the immediate surroundings for food or hazards or foreign invaders. They relay that information to the proteins inside, which use that data to begin anew the process of cell turnover and regeneration that starts with messages from the genes.

But while each cell carries the same genes, every cell only uses some of these instructions, like a sonata that only uses some of the keys on the piano. The consortium's lofty goal, in their quest to categorize the 37 trillion cells in the human body, is to understand which specific genes are activated in each cell type — or in scientific parlance, the patterns of gene expression.

They plan to decipher how genes inside healthy cells are properly expressed. Taking this information and using it as a point of reference will allow them to immediately see where gene expression deviates from normal. It illuminates when genes are being expressed at the wrong time, in the wrong cell type or in the wrong amount, says Dana Pe'er, a leading member of the consortium and chair of the computational and systems biology program at Memorial Sloan Kettering Cancer Center in New York. "We're looking at a host of complex questions," she says. "These range from how an ensemble of cells function together to fight pathogens or how a cell's regulatory circuits go awry in disease."

Eventually, this massive library of cell types — indexed by their states, their locations and their gene expressions — could help scientists make countless new discoveries. One of the more immediate applications: identify how gene signals go wrong in diseases such as cancer or hereditary disorders, which are triggered by mutant DNA. Researchers also could gain a better understanding of brain cells to help treat neurodegenerative diseases like Alzheimer's, Parkinson's and ALS. And the cell atlas might tease out which medicines an individual patient's genes will respond to best. The same goes for treatments to which their body might already have resistance.

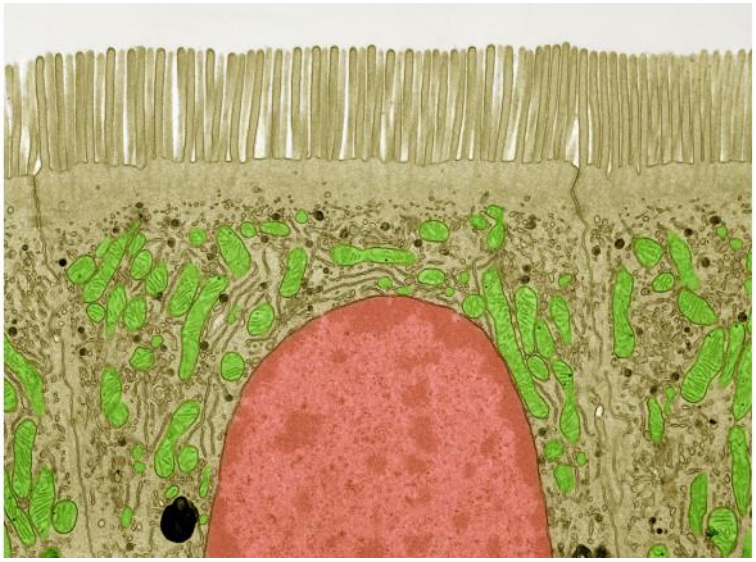
The research could also help a doctor know which medicines to avoid giving patients altogether. Drugs can often be unexpectedly toxic. That's because treatments may target a specific protein, but we don't realize that said protein may serve a useful function in another part of the body. "These are things we can spot quickly once we have a good reference tool," says Aviv Regev, a computational and systems biologist at the Broad Institute of MIT and Harvard who helped spearhead the creation of the HCA and now co-chairs its organizing committee.

A Cellular Smoothie

Scientists had long wanted to understand how the complex array of genes works its magic inside each individual cell, but the technology just wasn't there until the past decade. By about 2012, a technique called single-cell genomics had grown in popularity and provided a new way to categorize individual cells. Scientists could pluck a single cell out of a test tube and sequence its genetic information. But that meant hundreds of thousands, sometimes millions, of cells didn't get sequenced. To get around this, scientists blended the results of various cells to stand in for the entire cell population — a process that Regev compares to making a fruit smoothie.

The technique missed the range of variation in individual cells or, to extend the smoothie metaphor, failed to distinguish between the taste of strawberries and blueberries and kiwis. "By the end of the smoothie preparation process, it might look pink," says Regev. "But if there were a few kiwis inside, you might not recognize that.

And we knew that the cells are probably different from each other — and these differences matter because they all reflect on what the cell can be or will be doing."



An epithelial cell. (Credit: Thomas Deerinck/Science Source)

Scientists can now simultaneously sequence thousands of individual cells thanks to the development in 2015 of a microtechnology that Regev helped invent. The new technique encapsulates each cell inside tiny droplets. A process then breaks the cell apart, during which pieces of its RNA are captured inside tiny beads for analysis. This led to a host of discoveries that revealed there may be thousands — not just hundreds — of different cell types, according to Teichmann. In the immune system alone, we now know there are more than 200 cell types, and even the tiny retina that coats the surface of the eye has about 100 different types of cells.

Energized by these findings, scientists around the world began talking about the tantalizing prospect of peering deep inside each cell and mapping their constituent parts. By 2014, Regev had started "evangelizing" about creating a Human Cell Atlas and eventually got interest from Teichmann that pushed them both to make the big leap to actually doing it.

Big Funders Step In

> The HCA has already generated strong institutional support that includes $200 million from the National Institutes of Health and

about $9 million from the Wellcome Trust, a London-based biomedical research charity. It also has landed a $15 million grant from the Chan Zuckerberg Initiative, which is underwriting the open-source data coordination platform that will store the terabytes of data generated by researchers.

Early Successes

The HCA, which kicked off in 2017, has already notched some intriguing discoveries. In 2018, Regev and researchers from the Broad Institute and Massachusetts General Hospital discovered that the lining of the trachea has seven cell types — one more than expected. That new type of cell is especially important in the expression of a specific gene that, when mutated, causes cystic fibrosis, and could prove crucial for understanding and eventually developing a cure for the genetic disease. The discovery also could lead to a better treatment for asthma.

In another 2018 study, Teichmann's team, along with collaborators from the University of Cambridge and the Newcastle University, characterized the cancer cells behind the most common childhood and adult kidney cancers. Specifically, they found that childhood kidney cancer cells appear just as they did while they were still developing in the womb, indicating that the cells are trapped in an immature fetal state. "We found which cells are driving the tumor," says Teichmann, "which is a tremendously important finding." She believes it can lead to more precisely targeted therapies.

Recent research by Regev's team also provided some clues as to why a new class of cancer drugs known as checkpoint inhibitors, which prompt the immune system to attack malignant cells, only work for a handful of patients. In a study that looked at how genes were activated in melanoma cells, her team found that some tumors have a subset of cells that simply don't respond to immunotherapy, preventing immune system cells from thwarting the cancerous cells. The researchers are now looking at ways to reverse this resistance. Now that they can drill down to see what cells are doing, says Regev, "you can listen to the chatter between these different cells" to understand where the wrong signals are being sent and which ones halt tumor growth or restore the efficacy of the therapy.

There are many technological hurdles ahead for the HCA — just establishing platforms to share data between all the labs will be a challenge. But Regev is undaunted and predicts they'll have a complete map within a decade.

More than 3,600 scientists are building a manual of all human cells: 'A Google Maps of biology'

In science fiction films, we often see characters entering machines that scan their cells to detect illnesses and cure them. While the concept of a robot doctor may belong to dystopian visions, science is working toward a technology that could help real-life medical professionals diagnose diseases early and accurately, and prescribe personalized and precise treatments. Though this goal remains distant, it is one step closer today. A series of over 40 studies published on Wednesday brings us closer to building a 3D atlas of all human cells — a detailed and complete digital manual of the body.
As with any major scientific endeavor, the announcement of the Human Cell Atlas (HCA) in 2016 wasn't the headline of the day. It began as an ambitious but relatively modest project, introduced in London by a group of about a hundred scientists led by two biologists, Aviv Regev — now at Genentech — and Sarah Teichmann — now at the Cambridge Stem Cell Institute. Over the years, the HCA has expanded to include over 3,600 members from around the world, supported by more than a hundred institutions. Today, it is one of the largest global consortia in the field of Big Science, surpassing even the size of the Human Genome Project at its peak.

The HCA is divided into 18 networks, each focused on a specific organ, tissue, or system. Researchers have already analyzed over 100 million cells from approximately 10,000 individuals, ensuring a broad representation of human diversity. Applying precision genomic techniques to each individual cell, together with powerful bioinformatics and artificial intelligence (AI) tools, they are mapping which of the 20,000 genes in the human genome are active in different cell types. The idea is to create a kind of "cellular ID" for each profile, identifying the proteins they produce, how they function, and how cells communicate within tissues, all captured in intricate, navigable spatial maps. As Teichmann explains, the HCA will be "a kind of Google Maps of cellular biology."

The HCA has contributed more than 440 studies, and its data portal already offers atlases of the nervous system, the lungs and the eye. These atlases will be superimposed to form a "complete reference map of the healthy human body," says Teichmann. The atlas not only covers the adult organism, but also the development of organs and tissues from the embryonic and paediatric stages, which are often the cause of ailments.

Causes of the disease and new drugs

The more than 40 studies published on Wednesday in various journals of the *Nature* group mark "a crucial moment for the HCA community," according to Regev. This major collaborative effort spans multiple areas, including the development of the placenta, skeleton, and nervous system, as well as the impact of genetic variations on cell diseases. The studies also explore the effects of Covid-19 on the lungs and the function and alterations of the digestive system, among other topics.

These findings will be incorporated into the first draft of the Human Cell Atlas, which is set to be published in 2025-26. The atlas will be made available online with open access and will continue to grow, ultimately encompassing billions of cells from every organ and tissue in the human body, which is made up of around 37 trillion cells.

According to Regev, "the main future — and current — benefit is the progress in discovering the causes of diseases and the development of medicines." Scientists are already using the atlas daily for these purposes. As the HCA co-founder explains, researchers compare cells from diseased tissues — such as biopsies from tumors or patients with autoimmune conditions — with healthy reference cells. The differences in their composition and gene expression offer valuable insights into the origins of the disease and potential treatments. "At Genentech, we have a clinical trial for inflammatory bowel disease that we have undertaken in part thanks to the large-scale data analysis from the atlas," says Regev.

The study cited by Regev is part of one of the studies published on Wednesday, which identifies a specific type of cell involved in inflammatory bowel diseases such as ulcerative colitis and Crohn's disease. Co-led by Teichmann and published in *Nature*, this study is the result of a collaboration between scientists from the Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) — based at the Hospital Clínic de Barcelona — and Spain's Center for Biomedical Research Network on Liver and Digestive Diseases (CIBEREHD).

The researchers compiled existing RNA sequences — the product of genes that are used to create proteins — from single cells, as well as new samples, bringing the total to 1.1 million healthy cells of 137 different types from across the entire digestive tract, both in adults and during development. The digestive atlas also includes an additional half million cells affected by diseases such as stomach and colorectal cancer, celiac disease, ulcerative colitis, and Crohn's disease.

Misguided cells in intestinal inflammation

By comparing the transcriptional profiles — the RNA present in the cells — the scientists identified certain cells in the large intestine of patients that resembled cells found in the stomach or small intestine. "The presence of cells corresponding to another tissue is common in the context of chronic inflammation," explains Azucena Salas, the director of the Spanish group. While this phenomenon had previously been attributed to the healing of wounds in the intestinal wall, the study revealed a new insight: these misdirected cells, generated from stem cells during tissue repair, actually contribute to the inflammation itself. "They are not mere spectators, but actively participate in the intestinal damage," says Salas.

Rasa Elmentaite, co-director of the study at Ensocell Therapeutics, suggests that processing the findings from the digestive atlas using AI platforms will facilitate the design of a new generation of therapies. "Despite the critical role of epithelial cells in the progression of inflammatory bowel disease, available treatments do not effectively target them," she says.

Organoids — miniature, lab-grown versions of organs and tissues — are already being used in research to better understand organ functions, diseases, and to test potential new drugs. These organoids will play a central role in the development of new therapies.

“To ensure that an organoid correctly represents the organ, we need to compare its cells to a reference atlas of the organ, which is what the HCA provides us,” explains Regev. Looking ahead, regenerative medicine’s long-awaited promise is also on the horizon: “Understanding normal cell development will help biomedical engineering create cells that can be introduced into the body as therapy.”

How do you see pictures in your brain?

Why are some people able to visualize scenarios in their minds, with colors and details, and some people are not?

–Luiza, age 14, Goiânia, Brazil

Imagine you are in a soccer match, and it's tied. Each team will begin taking penalty kicks. The crowd is roaring, and whether or not your team wins the game depends on your ability to hit the shot. As you imagine this scene, are you able to picture the scenario with colors and details?

Scientists are hard at work trying to understand why some people can visualize these kinds of scenarios more easily than others can. Even the same person can be better or worse at picturing things in their mind at different times.

As neuroscientists in the fields of physical therapy and psychology, we think about the ways people use mental imagery. Here is what researchers do know so far.

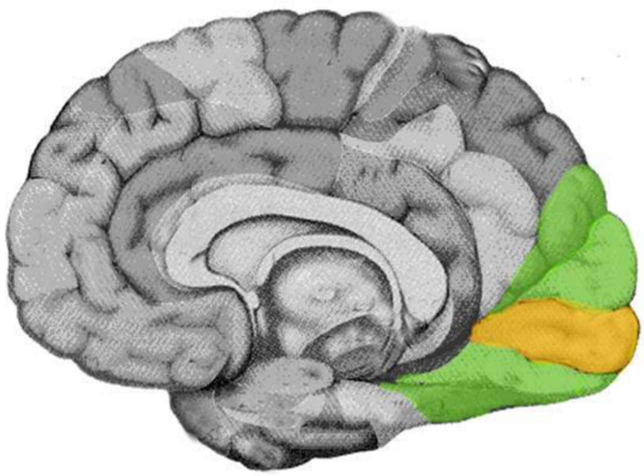
The brain and mental imagery

Mental imagery is the ability to visualize things and scenarios in your mind, without actual physical input.

For example, when you think about your best friends, you may automatically picture their faces in your head without actually seeing them in front of you. When you daydream about an upcoming vacation, you may see yourself on the sunny beach.

People who dream about taking a penalty kick could visualize themselves like they are watching a video of it in their mind. They may even experience the smell of the turf or hear the sounds that fans would make.

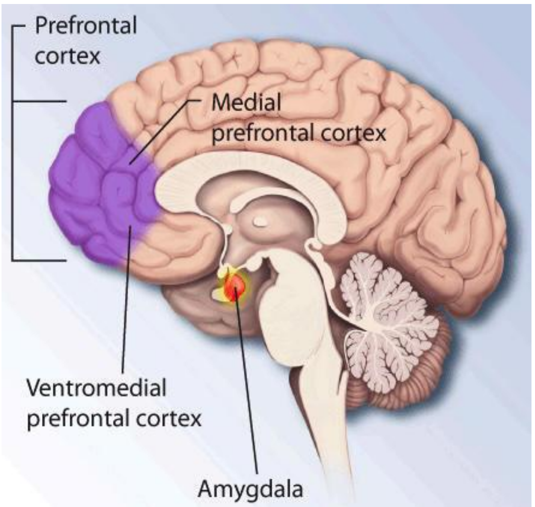
Related: Optical illusion reveals key brain rule that governs consciousness



The visual cortex influences both visual and mental imagery. (Image credit: Coxer via Wikimedia Commons)

Scientists believe your primary visual cortex, located in the back of your brain, is involved in internal visualization. This is the same part of the brain that processes visual information from the eyes and that lets you see the world around you.

Another brain region, located in the very front of the brain, also contributes to mental imagery. This structure, called the prefrontal cortex, is in charge of executive functions — a group of high-level mental skills that allow you to concentrate, plan, organize and reason.



The prefrontal cortex controls executive functions. (Image credit: The National Institute of Mental Health via Wikimedia Commons)

Scientists have found such skills to be, at least to some extent, related to one's mental imagery ability. If someone is good at holding and manipulating large amounts of information in mind, this person can play with things like numbers or images in their mind on the go.

Experiencing and remembering

Most of the same brain areas are active both while you're actually experiencing an event and also when you're visualizing it from a memory in your head. For example, when you behold the beauty of the Grand Canyon, your brain creates a memory of the image. But that memory is not simply stored in a single place in the brain. It's created when thousands of brain cells across different parts of the brain fire together. Later, when a sound, smell or image triggers the memory, this network of brain cells fires together again, and you may picture the Grand Canyon in your head as clearly as if it were in front of you.

Benefits of mental imagery

The ability to mentally visualize can be helpful.

Notice the look of concentration on a gymnast's face before competition. The athlete is likely visualizing themselves executing a perfect rings routine in their mind. This visualization activates the same brain regions as when they physically perform on the rings, building their confidence and priming their brain for better success.

Athletes can use visualization to help them acquire skills more quickly and with less wear and tear on their bodies. Engineers and mechanics can use visualization to help them fix or design things.

Mental visualization can also help people relearn how to move their bodies after a brain injury. However, with additional practice, those who do not use visualization will eventually catch up.

Nature-nurture interactions

All is not lost if you have difficulty visualizing. It is possible that the ability to visualize in your mind is a combined effect of both how your individual brain works and your life experiences.

For example, taxi drivers in London need to navigate very complicated streets and, scientists found, experience changes to their brain structures over the course of their careers. In particular, they develop larger hippocampuses, a brain structure related to memory. Scientists believe that the training the taxi drivers went through — having to visualize a map of complex streets across London in daily driving — made them better at mental imagery via changes in their hippocampus.

And watching someone else do a physical action activates the same brain areas as creating your own internal mental imagery. If you want to be able to do something, watching a video of someone else doing it can be just as helpful as visualizing yourself doing it in your head. So even if you struggle with mental visualization, there are still ways to reap its benefits.