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This Could Be The World's Favorite Scent, No Matter Where You Are From

Odors people like or dislike tend to be common across individuals from different cultural backgrounds

Peter Dockrill

The kinds of smells people like or dislike tend to be common across individuals from distinctly different cultural backgrounds, which may suggest an evolutionary basis for our seemingly universal odor preferences, scientists say.

In a new study, researchers asked individuals from 10 distinct cultural groups – including a number of indigenous hunter-gatherer peoples and traditional farming communities, as well as modern city-dwellers – to sniff 10 unique scents and rank them in order of pleasantness.

"We wanted to examine if people around the world have the same smell perception and like the same types of odor, or whether this is something that is culturally learned," says neuroscientist Artin Arshamian from the Karolinska Institute in Sweden.

"Traditionally it has been seen as cultural, but we can show that culture has very little to do with it."

The researchers travelled far and wide, pooling data from field work in several cultural environments, representing diverse modes of subsistence across Thailand, Mexico, Ecuador, and the US, and encompassing deserts, tropical rainforests, highland climates, coastal regions, and more.

Participants included a number of hunter-gatherer groups (including the Semaq Beri people from the Malay Peninsula in Thailand), as well as several subsistence horticulturalist and agriculturalist communities (such as the Chachi people of Ecuador), and a cohort of subjects from New York City, representing a modern racially and ethnically diverse urban environment.

In each place visited, the participants – over 280 individuals in total – were presented with 10 randomly ordered pen-like odor dispensing devices. They were asked to smell each one and order the pens in a row, from most pleasant to most unpleasant.

The odor generally ranked as most pleasant was vanillin (the main component of vanilla extract), while the next most popular was ethyl butyrate (which has a fruity smell, and is often used as a flavor enhancer in fruit-flavored food). Third was linalool, which has a floral smell. The least popular smell in the study was isovaleric acid, which is known for having a pungent, unpleasant odor, associated with cheese, soy milk, and sweat.

While much prior research has examined this area – looking to see how odor perception is informed by cultural associations – the researchers here say that previous experimental approaches have failed to adequately study a diverse cultural spectrum.

Ultimately, we might expect people's ranking of odor pleasantness (odor valence) to reflect a mixture of their cultural tradition, personal sensibility, and universal preferences (ostensibly based on odorants' molecular features), but the extent of each of these influences has so far been unclear. Arshamian's team found the influence of cultural traditions plays only a small role in people's odor preference, with odor valence rankings correlating strongly and positively across all the cultures measured.

When people ranked individual scents differently to one another in terms of perceived pleasantness, the researchers say participants' culture only explained about 6 percent of the variance, whereas 54 percent was due to people's individual preference, and the scent chemical's molecular profile explained around 40 percent of the variance.

In other words, while people can and do rank different smells differently, most of the variation observed seems to be a matter of personal preference, not a reflection of culture; at the same time,

there is a lot of crossover between cultures in terms of what people like and don't like.

"There was a substantial global consistency," the researchers explain. "Taken together, this shows that human olfactory perception is strongly constrained by universal principles."

As for why the perception of odors appears to be at least somewhat universal across cultures – and is predicated upon the physicochemical properties of the odorants themselves – it's plausible that a preference for certain chemical scents may have served an evolutionary purpose in our history, somehow increasing our survival chances in times long forgotten.

If so, the findings here could help us to examine the possibility further, the researchers suggest. "Now we know that there's universal odor perception that is driven by molecular structure and that explains why we like or dislike a certain smell," Arshamian says. "The next step is to study why this is so by linking this knowledge to what happens in the brain when we smell a particular odor." The findings are reported in *Current Biology*.

https://bit.ly/3v9E0Yi

Revolutionary DNA Nanotechnology Speeds Up Development of Vaccines by More Than One Million Times

A new tool speeds up development of vaccines and other pharmaceutical products by more than one million times while minimizing costs.

In search of pharmaceutical agents such as new vaccines, industry will routinely scan thousands of related candidate molecules. A novel technique allows this to take place on the nano scale, minimizing use of materials and energy. The work is published in the prestigious journal Nature Chemistry.

More than 40,000 different molecules can be synthesized and analyzed within an area smaller than a pinhead. The method, developed through a highly interdisciplinary research effort in Denmark, promises to drastically reduce the amounts of material, energy, and economic cost for pharmaceutical companies.

The method works by using soap-like bubbles as nano-containers. With DNA nanotechnology, multiple ingredients can be mixed within the containers.

“The volumes are so small that the use of material can be compared to using one liter of water and one kilogram of material instead of the entire volumes of water in all oceans to test material corresponding to the entire mass of Mount Everest. This is an unprecedented save in effort, material, manpower, and energy,” illustrates head of the team Nikos Hatzakis, Associate Professor at the Department of Chemistry, University of Copenhagen.

“Saving infinitely amounts of time, energy and manpower would be fundamentally important for any synthesis development and evaluation of pharmaceuticals,” says PhD Student Mette G. Malle, lead author of the article, and currently Postdoc researcher at Harvard University, USA.

Results within just seven minutes

The work has been carried out in collaboration between the Hatzakis Group, University of Copenhagen, and Associate Professor Stefan Vogel, University of Southern Denmark. The project has been supported by a Villum Foundation Center of Excellence grant. The resulting solution is named “single particle combinatorial lipidic nanocontainer fusion based on DNA mediated fusion” – abbreviated SPARCLD.

The breakthrough involves integration of elements from normally quite distant disciplines: synthetic biochemistry, nanotechnology, DNA synthesis, combinational chemistry, and even Machine Learning which is an AI (artificial intelligence) discipline.

“No single element in our solution is completely new, but they have

never been combined so seamlessly," explains Nikos Hatzakis.

The method provides results within just seven minutes.

"What we have is very close to a live read-out. This means that one can moderate the setup continuously based on the readings adding significant additional value. We expect this to be a key factor for industry wanting to implement the solution," says Mette G. Malle.

Had to keep things hush-hush

The individual researchers in the project have several industry collaborations, yet they do not know which companies may want to implement the new high-throughput method.

"We had to keep things hush-hush since we didn't want to risk for others to publish something similar before us. Thus, we could not engage in conversations with industry or with other researchers that may use the method in various applications," says Nikos Hatzakis.

Still, he can name some possible applications:

"A safe bet would be that both industry and academic groups involved in synthesis of long molecules such as polymers could be among the first to adopt the method. The same goes for ligands of relevance for pharmaceutical development. A particular beauty of the method that it can be integrated further, allowing for direct addition of a relevant application."

Here, examples could be RNA strings for the important biotech tool CRISPR, or an alternate for screening and detecting and synthesizing RNA for future pandemic vaccines.

"Our setup allows for integrating SPARCLD with post-combinatorial readout for combinations of protein-ligand reactions such as those relevant for use in CRISPR. Only, we have not been able to address this yet, since we wanted to publish our methodology first."

The scientific article on SPARCLD will be published in the prestigious journal Nature Chemistry on April 4, 2022.

The technology

The SPARCLD method (single particle combinatorial lipidic nanocontainer fusion based on DNA mediated fusion) is a parallelized, multi-step and non-deterministic fusion of individual zepto-liter nano-containers. The research team has observed efficient (more than 93 %) leakage-free fusion sequences for arrays of surface tethered target liposomes with six freely diffusing populations of cargo liposomes, each functionalized with individual lipidated DNA (LiNA) and fluorescent barcoded by distinct ratio of chromophores. Stochastic fusion results in distinct permutation of fusion sequences for each autonomous nano-container. Real-time total internal reflection (TIRF) microscopy allowed direct observation of more than 16,000 fusions and accurate classification of 566 distinct fusion sequences using Machine Learning. The method allows for approximately 42,000 nano-containers per square millimeter.

Reference: "Single-particle combinatorial multiplexed liposome fusion mediated by DNA" 4 April 2022, Nature Chemistry. DOI: 10.1038/s41557-022-00912-5

https://bit.ly/3un7jaE

The Dream of Nuclear Fusion Is Now Closer to Reality. Here's Why

Scientists at a laboratory in England have shattered the record for the amount of energy produced during a controlled, sustained fusion reaction.

David Donovan & Livia Casali, The Conversation

The production of 59 megajoules of energy over five seconds at the Joint European Torus – or JET – experiment in England has been called "a breakthrough" by some news outlets and caused quite a lot of excitement among physicists.

But a common line regarding fusion electricity production is that it is "always 20 years away." We are a nuclear physicist and a nuclear engineer who study how to develop controlled nuclear fusion for the purpose of generating electricity.

The JET result demonstrates remarkable advancements in the understanding of the physics of fusion. But just as importantly, it shows that the new materials used to construct the inner walls of the fusion reactor worked as intended.

The fact that the new wall construction performed as well as it did is what separates these results from previous milestones and elevates magnetic fusion from a dream toward a reality.

Fusing particles together

Nuclear fusion is the merging of two atomic nuclei into one compound nucleus. This nucleus then breaks apart and releases energy in the form of new atoms and particles that speed away from the reaction. A fusion power plant would capture the escaping particles and use their energy to generate electricity.

There are a few different ways to safely control fusion on Earth. Our research focuses on the approach taken by JET – using powerful magnetic fields to confine atoms until they are heated to a high enough temperature for them to fuse.

The fuel for current and future reactors are two different isotopes of hydrogen – meaning they have the one proton, but different numbers of neutrons – called deuterium and tritium. Normal hydrogen has one proton and no neutrons in its nucleus. Deuterium has one proton and one neutron while tritium has one proton and two neutrons.

For a fusion reaction to be successful, the fuel atoms must first become so hot that the electrons break free from the nuclei. This creates plasma – a collection of positive ions and electrons.

You then need to keep heating that plasma until it reaches a temperature over 200 million degrees Fahrenheit (100 million Celsius). This plasma must then be kept in a confined space at high densities for a long enough period of time for the fuel atoms to collide into each other and fuse together.

To control fusion on Earth, researchers developed donut-shaped devices – called tokamaks – which use magnetic fields to contain the plasma. Magnetic field lines wrapping around the inside of the donut act like train tracks that the ions and electrons follow.

By injecting energy into the plasma and heating it up, it is possible to accelerate the fuel particles to such high speeds that when they collide, instead of bouncing off each other, the fuel nuclei fuse together. When this happens, they release energy, primarily in the form of fast-moving neutrons. During the fusion process, fuel particles gradually drift away from the hot, dense core and eventually collide with the inner wall of the fusion vessel.

To prevent the walls from degrading due to these collisions – which in turn also contaminates the fusion fuel – reactors are built so that they channel the wayward particles toward a heavily armored chamber called the divertor. This pumps out the diverted particles and removes any excess heat to protect the tokamak.

The walls are important

A major limitation of past reactors has been the fact that divertors can't survive the constant particle bombardment for more than a few seconds. To make fusion power work commercially, engineers need to build a tokamak vessel that will survive for years of use under the conditions necessary for fusion.

The divertor wall is the first consideration. Though the fuel particles are much cooler when they reach the divertor, they still have enough energy to knock atoms loose from the wall material of the divertor when they collide with it.

Previously, JET's divertor had a wall made of graphite, but graphite absorbs and traps too much of the fuel for practical use.

Around 2011, engineers at JET upgraded the divertor and inner vessel walls to tungsten. Tungsten was chosen in part because it has the highest melting point of any metal – an extremely important trait when the divertor is likely to experience heat loads nearly 10 times higher than the nose cone of a space shuttle reentering the

Earth's atmosphere.

The inner vessel wall of the tokamak was upgraded from graphite to beryllium. Beryllium has excellent thermal and mechanical properties for a fusion reactor – it absorbs less fuel than graphite but can still withstand the high temperatures.

The energy JET produced was what made the headlines, but we'd argue it is in fact the use of the new wall materials which make the experiment truly impressive because future devices will need these more robust walls to operate at high power for even longer periods of time. JET is a successful proof of concept for how to build the next generation of fusion reactors.

The next fusion reactors

The JET tokamak is the largest and most advanced magnetic fusion reactor currently operating. But the next generation of reactors is already in the works, most notably the ITER experiment, set to begin operations in 2027.

ITER – which is Latin for "the way" – is under construction in France and funded and directed by an international organization that includes the US.

ITER is going to put to use many of the material advances JET showed to be viable. But there are also some key differences. First, ITER is massive. The fusion chamber is 37 feet (11.4 meters) tall and 63 feet (19.4 meters) around – more than eight times larger than JET.

In addition, ITER will utilize superconducting magnets capable of producing stronger magnetic fields for longer periods of time compared to JET's magnets. With these upgrades, ITER is expected to smash JET's fusion records – both for energy output and how long the reaction will run.

ITER is also expected to do something central to the idea of a fusion powerplant: produce more energy than it takes to heat the fuel. Models predict that ITER will produce around 500 megawatts of power continuously for 400 seconds while only consuming 50 MW of energy to heat the fuel.

This means the reactor produces 10 times more energy than it consumes – a huge improvement over JET, which required roughly three times more energy to heat the fuel than it produced for its recent 59 megajoule record.

JET's recent record has shown that years of research in plasma physics and materials science have paid off and brought scientists to the doorstep of harnessing fusion for power generation. ITER will provide an enormous leap forward toward the goal of industrial scale fusion power plants.

David Donovan, Associate Professor of Nuclear Engineering, University of Tennessee and Livia Casali, Assistant Professor of Nuclear Engineering, University of Tennessee.

https://wb.md/3raORQv

AI Systems Can Be Wrong and Not Admit It

Artificial intelligence systems are being built to help diagnose diseases, but before we can trust them with life-and-death responsibilities, AI will need to develop a very human trait: Admitting mistakes.

Tara Haelle

And the truth is: they can't do that … yet.

Today, AI can more often provide the correct answer to a problem than it can realize it made a mistake, according to researchers from the University of Cambridge and the University of Oslo.

This fundamental flaw, they report, is rooted in a math problem.

Some mathematical statements cannot be proven true or false. For example, the same math most of us learned in school to find answers to simple and tricky questions cannot then be used to prove our consistency in applying it.

Maybe we gave the right answer and perhaps we didn't, but we needed to check our work. This is something computer algorithms mostly can't do, still.

It is a math paradox first identified by mathematicians Alan Turing and Kurt Gödel at the beginning of the 20th century that flags some math problems cannot be proven.

Mathematician Stephen Smale went on to list this fundamental AI flaw among the world's 18 unsolved math problems.

Building on the mathematical paradox, investigators, led by Matthew Colbrook, PhD, from the University of Cambridge Department of Applied Mathematics and Theoretical Physics, proposed a new way to categorize AI's problem areas.

In the *Proceedings of the National Academy of Sciences* , the researchers map situations when AI neural networks — modeled after the human brain's network of neurons — can actually be trained to produce more reliable results.

It is important early work needed to make smarter, safer AI systems.

Source

Proceedings of the National Academy of Sciences: "The difficulty of computing stable and accurate neural networks: On the barriers of deep learning and Smale's 18th problem."

https://bit.ly/3unb2VF

The pleasant smell of wet soil indicates danger to bacteria-eating worms, researchers find

The smell of geosmin is made by certain kinds of bacteria that are known toxin producers

by Patrick Lejtenyi, Concordia University

The smell of geosmin is unmistakable: It's the odor that permeates the air after a summer rain squall or fills your nose while gardening. It's the smell of wet soil—an earthy, almost comforting scent.

But as a new study just published in the journal *Applied and Environmental Microbiology* points out, that smell also has a particular purpose. It is made by certain kinds of bacteria that are known toxin producers. This acts as a warning to C. elegans, a common type of worm, that the bacteria they are about to graze on is poisonous. The chemical is an aposematic signal that triggers the blind worm's sense of taste just like a caterpillar's bright colors or a pufferfish's spines tell a sighted predator to stay away.

Just a few millimeters long, nematodes like C. elegans are tiny but found all over the Earth, including Antarctica. Nematodes are also the most abundant animal on Earth, accounting for about four-fifths of the global animal population. Researchers often use C. elegans as a model organism in their studies because their biological systems are less complex but similar to those of humans.

"Through our study, we found that geosmin in Streptomyces coelicolor, a bacteria that is toxic to C. elegans, does not appear to have any role other than as a signal," says Brandon Findlay, associate professor in the Department of Chemistry and Biochemistry and the paper's supervising author. "It doesn't help the cells grow, eat or divide. It doesn't ward off predators directly. It just seems to be there as a warning." He says he is unaware of any other bacteria-produced chemicals that act in that fashion.

The study was led by Liana Zaroubi, one of Findlay's students who is now pursuing her Ph.D. at Simon Fraser University.

A scent of danger

Zaroubi acknowledges that it took her some time to arrive at the idea that geosmin was aposematic.

"It was definitely not obvious," she says. "I eliminated many hypotheses before finding that geosmin acted as a warning signal. However, each ruled-out experiment revealed important clues that helped elucidate the mystery that is geosmin. We followed the science and I believe that was key to this discovery."

The researchers used several strains of C. elegans to test their hypothesis. First, they observed the movement and behavior of worms on agar plates where geosmin was present but bacteria was absent. In this instance, the worms reacted adversely to the presence of the compound, moving rapidly with frequent changes in direction. However, mutant nematodes without the chemosensory

ASE neuron, which is dedicated to taste, were observed to behave normally. Geosmin itself appeared to be non-toxic to C. elegans.

A separate experiment was designed that included Streptomyces coelicolor bacteria. The researchers observed the worms avoiding their prey when they could taste the presence of geosmin. But those without the ASE neurons devoured the toxic bacteria, with predictably fatal consequences for both predator and prey.

A taste of evolution

Geosmin is a very pungent compound, detectable by humans at five parts per trillion. While many find its odor pleasant, it is also a common bacteria-created contaminant in human drinking water that can cause water to taste like dirt.

The extent of geosmin's biological uses is still not completely understood. However, the researchers believe the compound offers insight into how bacteria and their predators interact and how complex behaviors like toxin avoidance evolve.

More information: *Liana Zaroubi et al, The Ubiquitous Soil Terpene Geosmin Acts as a Warning Chemical, Applied and Environmental Microbiology (2022). DOI: 10.1128/aem.00093-22*

https://wb.md/3DVAVyF

About 19% of COVID-19 Headaches Become Chronic

1/5 of patients presenting with headache during acute COVID-19 developed chronic daily headache

Javier Cotelo, MD

Madrid — Approximately 1 in 5 patients who presented with headache during the acute phase of COVID-19 developed chronic daily headache, according to a study published in the journal *Cephalalgia.* The greater the headache's intensity during the acute phase, the greater the likelihood that it would persist.

The research, carried out by members of the Headache Study Group of the Spanish Society of Neurology (GECSEN), evaluated the evolution of headache in more than 900 Spanish patients. Because they found that headache intensity during the acute phase was associated with a more prolonged duration of headache, the team stressed the importance of promptly evaluating patients who have had COVID-19 and who then experience persistent headache.

Long-term Evolution Unknown

Headache is a common symptom of COVID-19, but its long-term evolution remains unknown. The objective of this study was to evaluate the long-term duration of headache in patients who presented with this symptom during the acute phase of the disease.

Recruitment for this multicenter study took place in March and April 2020. The 905 patients who were enrolled came from six Level 3 hospitals in Spain. All completed 9 months of neurologic follow-up.

Their median age was 51 years, 66.5% were women, and more than half (52.7%) had a history of primary headache. About half of the patients required hospitalization (50.5%); the rest were treated as outpatients. The most common headache phenotype was holocranial (67.8%) of severe intensity (50.6%).

Persistent Headache Common

In the 96.6% cases for which data were available, the median duration of headache was 14 days. The headache persisted at 1 month in 31.1% of patients, at 2 months in 21.5%, at 3 months in 19%, at 6 months in 16.8%, and at 9 months in 16.0%.

"The median duration of COVID-19 headache is around 2 weeks," David García Azorín, MD, PhD, a member of the Spanish Society of Neurology and one of the co-authors of the study, told *Medscape Spanish Edition.* "However, almost 20% of patients experience it for longer than that. When still present at 2 months, the headache is more likely to follow a chronic daily pattern." García Azorín is a neurologist and clinical researcher at the Headache Unit of the Hospital Clínico Universitario in Valladolid, Spain.

"So, if the headache isn't letting up, it's important to make the most of that window of opportunity and provide treatment in that period

of 6 to 12 weeks," he continued. "To do this, the best option is to carry out preventive treatment so that the patient will have a better chance of recovering."

Study participants whose headache persisted at 9 months were older and were mostly women. They were less likely to have had pneumonia or to have experienced stabbing pain, photophobia, or phonophobia. They reported that the headache got worse when they engaged in physical activity but less frequently manifested as a throbbing headache.

Secondary Tension Headaches

On the other hand, Jaime Rodríguez Vico, MD, head of the Headache Unit at the Jiménez Díaz Foundation Hospital in Madrid, told *Medscape Spanish Edition* that, according to his case studies, the most striking characteristics of post-COVID-19 headaches "in general are secondary, with similarities to tension headaches that patients are able to differentiate from other clinical types of headache. In patients with migraine, very often we see that we're dealing with a trigger. In other words, more migraines — and more intense ones at that — are brought about."

He went on to say, "Generally, post-COVID-19 headache usually lasts 1 to 2 weeks, but we have cases of it lasting several months and even over a year with persistent daily headache. These more persistent cases are probably connected to another type of pathology that makes them more susceptible to becoming chronic, something that occurs in another type of primary headache known as new daily persistent headache."

Primary Headache Exacerbation

García Azorín pointed out that it's not uncommon that among people who already have primary headache, their condition worsens after they become infected with SARS-CoV-2. However, many people differentiate the headache associated with the infection from their usual headache because after becoming infected, their headache is predominantly frontal, oppressive, and chronic.

"Having a prior history of headache is one of the factors that can increase the likelihood that a headache experienced while suffering from COVID-19 will become chronic," he noted.

This study also found that, more often than not, patients with persistent headache at 9 months had migraine-like pain.

As for headaches in these patients beyond 9 months, "based on our research, the evolution is quite variable," said Rodríguez. "Our unit's numbers are skewed due to the high number of migraine cases that we follow, and therefore our high volume of migraine patients who've gotten worse. The same thing happens with COVID-19 vaccines. Migraine is a polygenic disorder with multiple variants and a pathophysiology that we are just beginning to describe. This is why one patient is completely different from another. It's a real challenge," he added.

Infections are a common cause of acute and chronic headache. The persistence of a headache after an infection may be due to the infection becoming chronic, as happens in some types of chronic meningitis, such as tuberculous meningitis. It may also be due to the persistence of a certain response and activation of the immune system or to the uncovering or worsening of a primary headache coincident with the infection, added García Azorín.

"Likewise, there are other people who have a biological predisposition to headache as a multifactorial disorder and polygenic disorder, such that a particular stimulus — from trauma or an infection to alcohol consumption — can cause them to develop a headache very similar to a migraine," he said.

Providing Prognosis and Treatment

Certain factors can give an idea of how long the headache might last. The study's univariate analysis showed that age, female sex, headache intensity, pressure-like quality, the presence of photophobia/phonophobia, and worsening with physical activity

were associated with headache of longer duration. But in the multivariate analysis, only headache intensity during the acute phase remained statistically significant (hazard ratio, 0.655; 95% CI: 0.582 – 0.737; $P < .001$).

When asked whether they planned to continue the study, García Azorín commented, "The main questions that have arisen from this study have been, above all, 'Why does this headache happen?' and 'How can it be treated or avoided?' To answer them, we're looking into pain: which factors could predispose a person to it and which changes may be associated with its presence."

In addition, different treatments that may improve patient outcomes are being evaluated, because to date, treatment has been empirical and based on the predominant pain phenotype.

In any case, most doctors currently treat post-COVID-19 headache on the basis of how similar the symptoms are to those of other primary headaches. "Given the impact that headache has on patients' quality of life, there's a pressing need for controlled studies on possible treatments and their effectiveness," noted Patricia Pozo Rosich, MD, PhD, one of the co-authors of the study.

"We at the Spanish Society of Neurology truly believe that if these patients were to have this symptom correctly addressed from the start, they could avoid many of the problems that arise in the situation becoming chronic," she concluded.

García Azorín and Rodríguez have disclosed no relevant financial relationships.

Cephalalgia. Published online February 15, 2022. Abstract

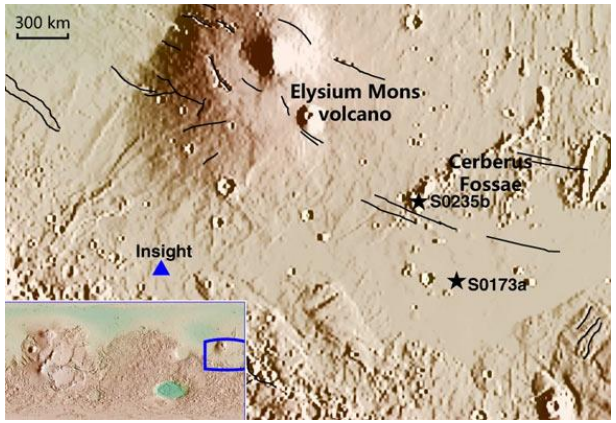
https://bit.ly/3NYqnDC

Volcanic Activity Could Be Responsible for Triggering Marsquakes in Cerberus Fossae

Planetary researchers have discovered 47 previously undetected marsquakes, >90% associated with the two previously known events beneath Cerberus Fossae

Using seismic data from NASA's Interior Exploration using Seismic Investigations, Geodesy and Heat Transport (InSight) lander, planetary researchers from Australia and China have discovered 47 previously undetected marsquakes, >90% of which are associated with the two previously known events located beneath Cerberus Fossae, a seismically active region on Mars that is less than 20 million years old.

In the study, Australian National University's Professor Hrvoje Tkalčić and Dr. Weijia Sun from the Institute of Geology and Geophysics at the Chinese Academy of Sciences analyzed data from a seismometer attached to NASA's InSight lander, which has been collecting data about marsquakes, Martian weather and the planet's interior since landing on Mars in 2018.



The landing site of InSight is marked by a blue triangle, while black stars denote the two identified marsquakes. The solid black lines demonstrate the Graben faults. The lower left inset map shows the global Martian topography, and the blue rectangular illustrates the research region. **Image credit: Sun & Tkalčić, doi: 10.1038/s41467-022-29329-x.**

Using a unique algorithm, they were able to apply their techniques to the InSight data to detect the 47 previously undiscovered marsquakes.

While the marsquakes would have caused some shaking on Mars, the events were relatively small in magnitude and would barely be felt if they had occured on Earth. They were detected over a period of about 350 Sols — a term used to refer to one solar day on Mars — which is equivalent to about 359 days on Earth.

The authors speculate that magma activity in the Martian mantle, which is the inner layer of Mars sandwiched between the crust and

the core, is the cause of these newly detected marsquakes.

Their findings suggest magma in the Martian mantle is still active and is responsible for the volcanic marsquakes, contrary to past beliefs held by scientists that these events are caused by Martian tectonic forces.

"The repetitive nature of these quakes and the fact they were all detected in the same area of the planet suggests Mars is more seismically active than scientists previously thought," Professor Tkalčić said. "We found that these marsquakes repeatedly occurred at all times of the Martian day, whereas marsquakes detected and reported by NASA in the past appeared to have occurred only during the dead of night when the planet is quieter."

"Therefore, we can assume that the movement of molten rock in the Martian mantle is the trigger for these 47 newly-detected marsquakes beneath the Cerberus Fossae region."

"The continuous seismicity suggests the Cerberus Fossae region on Mars is seismically highly active," he added.

"Knowing that the Martian mantle is still active is crucial to our understanding of how Mars evolved as a planet."

"It can help us answer fundamental questions about the Solar System and the state of Mars' core, mantle and the evolution of its currently-lacking magnetic field."

The study was published in the journal *Nature Communications*.

W. Sun & H. Tkalčić. 2022. Repetitive marsquakes in Martian upper mantle. Nat Commun 13, 1695; doi: 10.1038/s41467-022-29329-x

https://bit.ly/3E31ty0

Can Mushrooms "Talk" to Each Other?

Forest floor-dwelling fungi can send one another electrical signals to form word-like clusters, according to a computer scientist, but whether that represents something akin to language isn't clear.

Natalia Mesa

Have mushrooms been chatting with each other this whole time? Maybe so. An analysis of the electrical spike-based "language" fungi use to communicate, reported today (April 6) in *Royal Society Open Science*, finds that the patterns in these spikes are strikingly similar to human speech.

Fungi send electrical signals to one another through hyphae—long, filamentous tendrils that the organisms use to grow and explore. *The Guardian* reports that previous research shows that the number of electrical impulses traveling through hyphae, sometimes likened to neurons, increases when fungi encounter new sources of food, and that this suggests it's possible that fungi use this "language" to let each other know about new food sources or injury.

In the new study, Adam Adamatsky, a computer scientist at the Unconventional Computing Laboratory at the University of West of England, focused on four species of mushrooms: enoki, split gill, ghost, and caterpillar fungi. He inserted tiny electrodes into substrates colonized by the mushroom's hyphae and recorded their electrical activity.

The data showed that the electrical spikes often occurred in clusters, which Adamatsky says resemble a human vocabulary of up to 50 words. "We demonstrate that distributions of fungal word lengths match that of human languages," he writes in the paper. Split gills—mushrooms that grow on rotting wood—seemed to have the most complex speech patterns, he adds.

Adamatsky tells *Newsweek* that the fungi in a network may use these spike trains to indicate their presence, akin to a wolf's howl.

"There is also another option—they are saying nothing," he tells *The Guardian*—that is, the spikes could be meaningless byproducts of physical processes. But countering this idea, the "spiking events" don't appear to be random, he adds.

Other scientists are skeptical that these spikes are a form of fungal language. Pulsing behavior has been recorded previously as fungi

transport nutrients, which might cause the spikes seen in the new study. “This new paper detects rhythmic patterns in electric signals, of a similar frequency as the nutrient pulses we found,” University of Exeter mycologist Dan Bebber, a coauthor on previous studies on the phenomenon, tells *The Guardian*. “Though interesting, the interpretation as language seems somewhat overenthusiastic, and would require far more research and testing of critical hypotheses before we see ‘Fungus’ on Google Translate.”

https://bit.ly/38HmFhI

Doctors fish out more than a dozen tiny maggots from man’s eye

Here's what happens when sheep bot fly larvae sink their mouth hooks into your eyeball.

Beth Mole

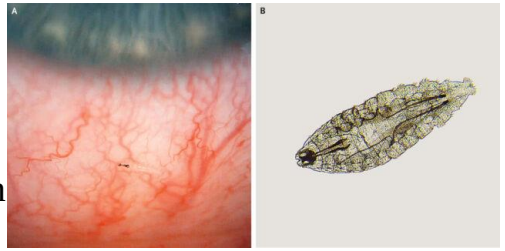
On Wednesday, doctors in France reported a rare case of tiny sheep bot fly larvae—aka maggots—infesting the outer surface of a man's eyeball.

The small, spiky larvae were seen slithering around the man's peeper, which explained the redness and itchiness he was experiencing. Doctors counted more than a dozen of the disturbing grub-like critters outside the eyeball and surrounding tissue. Doctors had no choice but to pluck the bloodsuckers out, one by one, using forceps. The doctors also prescribed topical antibiotic treatments in case they missed any bugs.

Sheep bot flies, or *Oestrus ovis*, are found worldwide in areas with sheep. They typically deliver their squirmy offspring to the nostrils of sheep and goats. The larvae mature in their nasal nurseries, then fall to the ground and pupate in the environment before transforming into parasitic pests. But, on rare occasions, adult female flies become bleary-eyed and lay festering broods in a human eyeball, causing a disease called ophthalmomyiasis. This is typically a dead end for the flies; the larvae generally don't survive to adulthood in the human eye. But if you think the unfortunate infestation is nothing to wince at, you'd be incorrect.

Eye-opening

Oestrus ovis larvae have bands of thick spikes around the outside of their bodies and piercing hooks in their mouth. The spikes can cause irritation and abrasions on the outer membrane of the eye as they wriggle around. This can lead to redness, itchiness, swelling, watering, and a feeling of a foreign body in the eye.



***Enlarge* / External ophthalmomyiasis (left, showing larvae present in eye) due to Oestrus ovis larvae (right). NEJM**

In rare cases, the larvae can also burrow their way inside the eyeball. Once inside, they can cause more severe damage, including to vision. Symptoms can manifest as floaters in vision, flashes of light, lines through vision, and eye pain. Even if the maggots die inside the eyeball—whether by laser treatments or natural causes—the lingering larval corpses can cause serious inflammation, which can further imperil vision. Overall, the outcomes of ophthalmomyiasis, which can be caused by a variety of flies, can range from mild, short-lived discomfort to blindness.

Regarding the case in France, published Wednesday in The New England Journal of Medicine, the man was lucky. The infestation was only external ophthalmomyiasis, meaning the larvae didn't get inside his eyeball. The 53-year-old man went to an emergency department after dealing with itchiness in his right eye for several hours. He told doctors he was gardening earlier in the day near a sheep farm and felt something get into his right eye, though he didn't know what it was.

Doctors noted that the man had 20/20 vision in both eyes, but his right eye was red and irritated. A closer look revealed the squirmy

interlopers. After the maggots were manually removed, the man was given topical treatment. At a 10-day follow-up, the man's eye was back to normal with no other symptoms.

https://bit.ly/37cRFFL

'Magnetic anomalies' may be protecting the moon's ice from melting

The moon lost its magnetic field billions of years ago. What are these strange pockets of magnetism on its surface?

By Brandon Specktor

In 2018, NASA astronomers found the first evidence of water ice on the moon. Lurking in the bottom of pitch-black craters at the moon's north and south poles, the ice was locked in perpetual shadow and had seemingly survived untouched by the sun's rays, potentially for millions of years.

The discovery of water ice came with a fresh mystery, however. While these polar craters are protected from direct sunlight, they are not shielded from solar wind, waves of charged particles that gush out of the sun at hundreds of miles a second.

This ionized wind is highly erosive and should have destroyed the moon's ice long ago, Paul Lucey, a planetary scientist at the University of Hawaii, told Science. And unlike Earth, the moon no longer has a magnetic shield to protect it from the brunt of these charged particles.

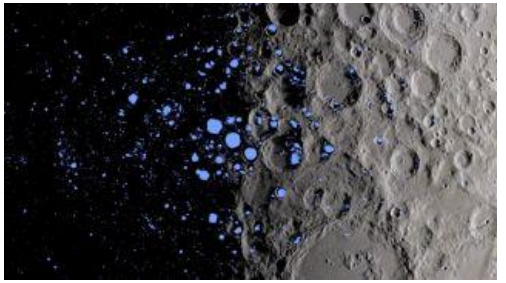
How, then, had the moon's polar ice survived? A new map of the moon's south pole — and the strange pockets of magnetic field that lie there — may provide an answer.

In research presented at the Lunar and Planetary Science Conference last month, scientists from the University of Arizona shared their map of magnetic anomalies — regions of the lunar surface that contain unusually strong magnetic fields — sprinkled across the moon's south pole.

These anomalies, first detected during the Apollo 15 and 16 missions in the 1970s, are thought to be remnants of the moon's ancient magnetic shield, which likely disappeared billions of years ago, according to NASA.

The magnetic anomalies overlap with several large polar craters that sit in permanent shadow and may contain ancient ice deposits. According to the researchers, these anomalies may be serving as tiny magnetic shields that protect lunar water ice from the constant bombardment of solar wind.

"These anomalies can deflect the solar wind," Lon Hood, a planetary scientist at the University of Arizona, told Science. "We think they could be quite significant in shielding the permanently shadowed regions."



A map showing the permanently shadowed craters (blue) near the moon's shouth pole **(Image credit: NASA Goddard)**

In their research, the authors combined 12 regional maps of the lunar south pole, originally recorded by Japan's Kaguya spacecraft, which orbited the moon from 2007 to 2009. Included among the spacecraft's science tools was a magnetometer capable of detecting pockets of magnetism across the lunar surface.

With their composite map in hand, the researchers saw that magnetic anomalies overlapped with at least two permanently shadowed craters — the Shoemaker and Sverdrup craters — at the lunar south pole. While these anomalies are only a fraction of the strength of Earth's magnetic field, they could still "significantly deflect the ion bombardment" of solar wind, the researchers said in their presentation. (The team's research has not been published in a peer-reviewed journal.) That could be the key to the moon's long-lasting water ice.

No one is certain where the moon's magnetic anomalies came from.

One theory is that they date back about 4 billion years, to when the moon still had a magnetic field of its own, according to a 2014 paper written by Hood in the Encyclopedia of Lunar Science (opens in new tab) reference book. When large, iron-rich asteroids crashed into the moon during this era, they may have created magma surfaces that slowly cooled over hundreds of thousands of years, becoming permanently magnetized by the moon's magnetic field in the process.

Upcoming lunar missions could shed light on the lunar south pole's pitch-dark ice deposits. The Artemis missions, which will ultimately return humans to the lunar surface for the first time since 1972, plan to land astronauts at the lunar south pole and establish a permanent base there. Studying the ice deposits in this region could reveal how they were created and why they've lasted so long.

Read more about this ancient magnetic field at Science.

https://bit.ly/3LYVb5B

Scientists Discover Fish-Like Marine Reptile Buried in Its Own Blubber 150 Million Years Ago

A new study published in PeerJ uses modern methods to understand the preservation of unique ichthyosaur fossils. One complete animal and one tail are the first to preserve outer body shape in the last, large group of ichthyosaurs.

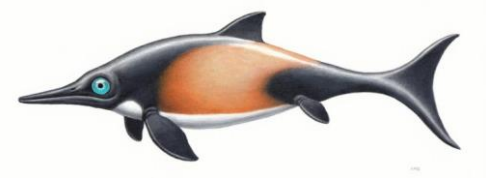
Two important terms:

Ichthyosaurs *were marine reptiles living in the Age of dinosaurs. Their fossils are found all over the world, and they are famous for having a fish-like shape resembling today's dolphins.*

The ***Solnhofen*** *area in Southern Germany is famous for its fossils from the Late Jurassic, which includes* Archaeopteryx, *usually recognized as the first bird, and numerous other animals, many of them preserved with soft tissues in addition to skeletons and teeth, which is rare in the fossil record.*

The new peer-reviewed paper describes two ichthyosaur specimens from the Solnhofen area, approximately 150 million years old. They are housed in the Jura-Museum, owned by the Bishops Seminar Eichstätt.

One ichthyosaur is a complete specimen, with the internal skeleton and an outline of the soft tissue around the body. The other is a complete tail fin. It is preserved with the tail vertebrae and the soft tissues around, confirming that ichthyosaurs also in this group had a moon-shaped tail, like their ancestors.



Ichthyosaur ill. **Credit: Esther van Hulsen**

The research was carried out by a cross-disciplinary team of scientists. Lene Liebe Delsett, the lead author, and Jørn Hurum, have worked with marine reptiles for several years at the Natural History Museum in Oslo, Norway. Martina Kölbl-Ebert is a specialist on the Solnhofen area and its fauna. They worked with mineralogist Henrik Friis, who analyzed the soft tissue samples in order to see what it contained.

The complete specimen is really what makes this project unique because it tells a complete story. Ichthyosaurs are not common as fossils in Solnhofen, which at the time was a relatively shallow area with many islands, whereas ichthyosaurs were open ocean dwellers. We do not know why this one entered the lagoons, but it might be the reason why it died. Seeing the specimen makes an impact because it is so obviously a complete, dead animal body, where we can see its shape because of the unique preservation, Delsett says.

During or after death, the ichthyosaur landed on its back and side on the seafloor, and was covered in fine sediments. Little oxygen and quite a lot of luck preserved it until it was found and excavated in 2009.

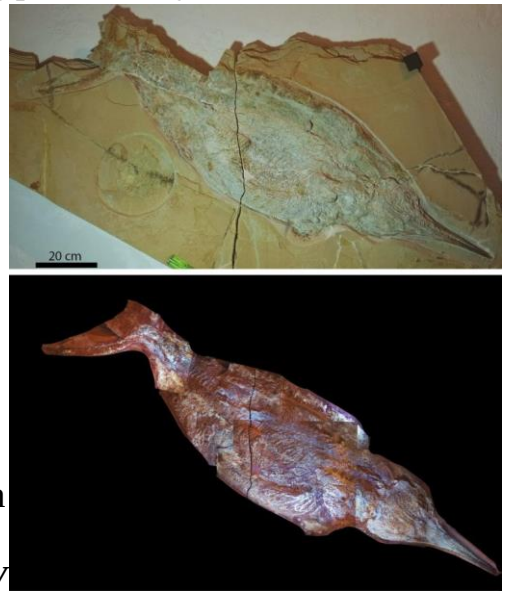
In the paper, the scientists do a first description of the specimen and

start the process of understanding its soft tissue. In order to do so, they took small samples from the soft tissue in the tail and looked at it via X-ray crystallography and a scanning electron microscope.

Because the skeletons and the rock they are preserved in, have almost the same colour, UV light was used for studying the shape of the bones to understand which type of ichthyosaur these are.

They found that phosphate found in the tissues of the ichthyosaurs likely contributed to the preservation.

It is not yet possible to identify all of the fossilized tissue types in the ichthyosaur, but the new study confidently confirms the preservation of skin and possibly connective tissue. However, the major part of the matter that surrounds and covers the specimen is probably decomposed blubber.



Large ichthyosaur in normal and UV light. **Credit: Lene L Delsett**

We know from earlier research that ichthyosaurs likely had a blubber, like whales have today. Our research confirms this, for a group of ichthyosaurs where this has not been certain. The blubber is another strong similarity between whales and ichthyosaurs, in addition to their body shape.

In the future, I hope that these two ichthyosaurs from Solnhofen can be used to enhance our understanding of swimming, as they preserve tail and body shape, Delsett says.

Reference: "The soft tissue and skeletal anatomy of two Late Jurassic ichthyosaur specimens from the Solnhofen archipelago" by Lene L. Delsett?, Henrik Friis, Martina Kölbl-Ebert and Jørn H. Hurum, 7 April 2022, PeerJ. DOI: 10.7717/peerj.13173

https://bit.ly/3LWzW48

New Cell Type Discovered Deep in Human Lungs – With Regenerative Properties

Findings shine light on underpinnings of COPD, pave new direction for future research on treatments.

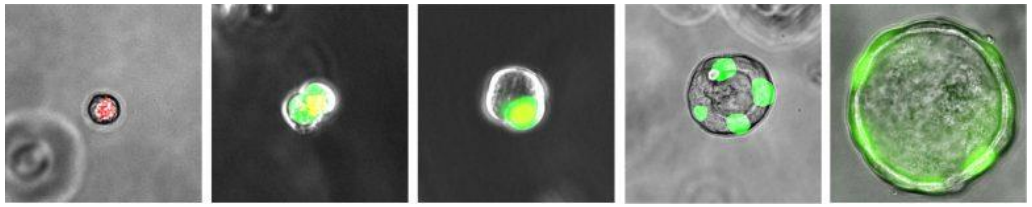
A new type of cell that resides deep within human lungs and may play a key role in human lung diseases has been discovered by researchers at the Perelman School of Medicine at the University of Pennsylvania.

The researchers, who report their findings today in *Nature*, analyzed human lung tissue to identify the new cells, which they call respiratory airway secretory cells (RASCs). The cells line tiny airway branches, deep in the lungs, near the alveoli structures where oxygen is exchanged for carbon dioxide. The scientists showed that RASCs have stem-cell-like properties enabling them to regenerate other cells that are essential for the normal functioning of alveoli. They also found evidence that cigarette smoking and the common smoking-related ailment called chronic obstructive pulmonary disease (COPD) can disrupt the regenerative functions of RASCs—hinting that correcting this disruption could be a good way to treat COPD.

"COPD is a devastating and common disease, yet we really don't understand the cellular biology of why or how some patients develop it. Identifying new cell types, in particular new progenitor cells, that are injured in COPD could really accelerate the development of new treatments," said study first author Maria Basil, MD, PhD, an instructor of Pulmonary Medicine.

COPD typically features progressive damage to and loss of alveoli, exacerbated by chronic inflammation. It is estimated to affect approximately 10 percent of people in some parts of the United States and causes about 3 million deaths every year around the world. Patients often are prescribed steroid anti-inflammatory drugs

and/or oxygen therapy, but these treatments can only slow the disease process rather than stop or reverse it. Progress in understanding COPD has been gradual in part because mice—the standard lab animal—have lungs that lack key features of human lungs.



Human ES cell derived RASC (respiratory airway secretory cell transitioning to an Alveolar type 2 cell over time in culture. **Credit: Penn Medicine**

In the new study, Morrisey and his team uncovered evidence of RASCs while examining gene-activity signatures of lung cells sampled from healthy human donors. They soon recognized that RASCs, which don't exist in mouse lungs, are "secretory" cells that reside near alveoli and produce proteins needed for the fluid lining of the airway.

"With studies like this we're starting to get a sense, at the cell-biology level, of what is really happening in this very prevalent disease," said senior author Edward Morrisey, PhD, the Robinette Foundation Professor of Medicine, a professor of Cell and Developmental Biology, and director of the Penn-CHOP Lung Biology Institute at Penn Medicine.

Observations of gene-activity similarities between RASCs and an important progenitor cell in alveoli called AT2 cells led the team to a further discovery: RASCs, in addition to their secretory function, serve as predecessors for AT2 cells—regenerating them to maintain the AT2 population and keep alveoli healthy.

AT2 cells are known to become abnormal in COPD and other lung diseases, and the researchers found evidence that defects in RASCs might be an upstream cause of those abnormalities. In lung tissue from people with COPD, as well as from people without COPD who have a history of smoking, they observed many AT2 cells that were altered in a way that hinted at a faulty RASC-to-AT2 transformation.

More research is needed, Morrisey said, but the findings point to the possibility of future COPD treatments that work by restoring the normal RASC-to-AT2 differentiation process—or even by replenishing the normal RASC population in damaged lungs.

Reference: "Human distal airways contain a multipotent secretory cell that can regenerate alveoli" by Maria C. Basil, Fabian L. Cardenas-Diaz, Jaymin J. Kathiriya, Michael P. Morley, Justine Carl, Alexis N. Brumwell, Jeremy Katzen, Katherine J. Slovik, Apoorva Babu, Su Zhou, Madison M. Kremp, Katherine B. McCauley, Shanru Li, Joseph D. Planer, Shah S. Hussain, Xiaoming Liu, Rebecca Windmueller, Yun Ying, Kathleen M. Stewart, Michelle Oyster, Jason D. Christie, Joshua M. Diamond, John F. Engelhardt, Edward Cantu, Steven M. Rowe, Darrell N. Kotton, Harold A. Chapman and Edward E. Morrisey, 30 March 2022, Nature. DOI: 10.1038/s41586-022-04552-0

The research was supported by the National Institutes of Health (HL148857, HL087825, HL134745, HL132999, 5T32HL007586-35, 5R03HL135227-02, K23 HL121406, K08 HL150226, DK047967, HL152960, R35HL135816, P30DK072482, U01HL152978), the BREATH Consortium/Longfunds of the Netherlands, the Parker B. Francis Foundation, and GlaxoSmithKline.

https://bit.ly/3KMSfIM

Lightning Had Difficulty Forming in Early Earth's Atmosphere

Lightning could have sparked the beginnings of life, but the primordial atmosphere might have made it more difficult for lightning to initiate.

by Rebecca Dzombak

The composition of Earth's primordial atmosphere likely made it harder to generate lightning, which may have increased the time it took to create and accumulate prebiotic molecules like amino acids, the building blocks of life. **Source: *Geophysical Research Letters***

In 1952, Stanley Miller and Harold Urey made sparks fly in a gas-filled flask meant to reflect the composition of Earth's atmosphere around 3.8 billion years ago.

Their results suggested that lightning could have led to prebiotic molecules necessary for the evolution of life, such as amino acids. At the time, scientists thought the early atmosphere would have been primarily methane and ammonia, but by the 1990s, experts argued for an atmosphere filled with carbon dioxide and molecular nitrogen.

Now, a new study suggests that the composition of Earth's primordial atmosphere likely made it harder to generate lightning, which may have increased the time it took to generate and accumulate prebiotic molecules important for life.

Lightning Behavior in Different Atmospheric Compositions

Electrons behave differently in an atmosphere composed of methane and ammonia versus one made mostly of carbon dioxide and molecular nitrogen.

It stands to reason lightning discharges would behave differently, too, which could affect the likelihood of prebiotic molecules forming on early Earth. Yet few people have modeled how lightning discharges vary in different atmospheric environments.

To look at how often electrons and gas molecules would have collided in the two versions of early Earth atmospheres, *Köhn et al.* modeled the probability of discharge sparking—the first step to a lightning strike. They found that in the carbon dioxide–nitrogen atmosphere, it's harder to get lightning to spark.

"Basically, in the nitrogen- and carbon-rich atmosphere, you need stronger electric fields for a discharge to initiate," said Christoph Köhn, a scientist at the National Space Institute at the Technical University of Denmark, who led the study.

The models revealed that the carbon dioxide and nitrogen atmosphere needed about a 28% stronger electric field for streamers—the precursors of lightning—to discharge, because gas molecules and electrons are less likely to collide and build up electrical charges that can generate lightning strikes.

Scaling up over space and time suggests there may have been fewer lightning strikes early in Earth's history, therefore shrinking the odds of generating prebiotic molecules.

"If lightning discharges were responsible for the production of prebiotic molecules, it's important to get a very good theoretical understanding of what happened," said Köhn. "The big question is still, Where do all these prebiotic molecules come from?"

The study strictly modeled the earliest stages of a lightning strike—the sparks that start strikes—so for Köhn and colleagues, the next steps are to model whole lightning strikes and couple that with models of atmospheric chemistry.

Together these studies could give a more complete look into how lightning may have been linked to prebiotic molecules.

(*Geophysical Research Letters*, https://doi.org/10.1029/2021GL097504, 2022)

https://bit.ly/37FWBCS

COVID Can Infect Pacemaker Cells That Maintain the Heart's Rhythm, Setting Off a Self-Destruction Process

Are COVID-19-linked arrhythmias caused by viral damage to the heart's pacemaker cells?

The SARS-CoV-2 virus can infect specialized pacemaker cells that maintain the heart's rhythmic beat, setting off a self-destruction process within the cells, according to a preclinical study co-led by researchers at Weill Cornell Medicine, NewYork-Presbyterian and NYU Grossman School of Medicine.

The findings offer a possible explanation for the heart arrhythmias that are commonly observed in patients with SARS-CoV-2 infection.

In the study, reported on March 8, 2022, in *Circulation Research*, the researchers used an animal model as well as human stem cell-derived pacemaker cells to show that SARS-CoV-2 can readily infect pacemaker cells and trigger a process called ferroptosis, in which the cells self-destruct but also produce reactive oxygen

molecules that can impact nearby cells.

"This is a surprising and apparently unique vulnerability of these cells—we looked at a variety of other human cell types that can be infected by SARS-CoV-2, including even heart muscle cells, but found signs of ferroptosis only in the pacemaker cells," said study co-senior author Dr. Shuibing Chen, the Kilts Family Professor of Surgery and a professor of chemical biology in surgery and of chemical biology in biochemistry at Weill Cornell Medicine.

Arrhythmias including too-quick (tachycardia) and too-slow (bradycardia) heart rhythms have been noted among many COVID-19 patients, and multiple studies have linked these abnormal rhythms to worse COVID-19 outcomes.

How SARS-CoV-2 infection could cause such arrhythmias has been unclear, though.

In the new study, the researchers, including co-senior author Dr. Benjamin tenOever of NYU Grossman School of Medicine, examined golden hamsters—one of the only lab animals that reliably develops COVID-19-like signs from SARS-CoV-2 infection—and found evidence that following nasal exposure the virus can infect the cells of the natural cardiac pacemaker unit, known as the sinoatrial node.

To study SARS-CoV-2's effects on pacemaker cells in more detail and with human cells, the researchers used advanced stem cell techniques to induce human embryonic stem cells to mature into cells closely resembling sinoatrial node cells.

They showed that these induced human pacemaker cells express the receptor ACE2 and other factors SARS-CoV-2 uses to get into cells and are readily infected by SARS-CoV-2. The researchers also observed large increases in inflammatory immune gene activity in the infected cells.

The team's most surprising finding, however, was that the pacemaker cells, in response to the stress of infection, showed clear signs of a cellular self-destruct process called ferroptosis, which involves accumulation of iron and the runaway production of cell-destroying reactive oxygen molecules. The scientists were able to reverse these signs in the cells using compounds that are known to bind iron and inhibit ferroptosis.

"This finding suggests that some of the cardiac arrhythmias detected in COVID-19 patients could be caused by ferroptosis damage to the sinoatrial node," said co-senior author Dr. Robert Schwartz, an associate professor of medicine in the Division of Gastroenterology and Hepatology at Weill Cornell Medicine and a hepatologist at NewYork-Presbyterian/Weill Cornell Medical Center.

Although in principle COVID-19 patients could be treated with ferroptosis inhibitors specifically to protect sinoatrial node cells, antiviral drugs that block the effects of SARS-CoV-2 infection in all cell types would be preferable, the researchers said.

The researchers plan to continue to use their cell and animal models to investigate sinoatrial node damage in COVID-19—and beyond.

"There are other human sinoatrial arrhythmia syndromes we could model with our platform," said co-senior author Dr. Todd Evans, the Peter I. Pressman M.D. Professor of Surgery and associate dean for research at Weill Cornell Medicine.

"And, although physicians currently can use an artificial electronic pacemaker to replace the function of a damaged sinoatrial node, there's the potential here to use sinoatrial cells such as we've developed as an alternative, cell-based pacemaker therapy."

Reference: "SARS-CoV-2 Infection Induces Ferroptosis of Sinoatrial Node Pacemaker Cells" by Yuling Han, Jiajun Zhu, Liuliu Yang, Benjamin E. Nilsson-Payant, Romulo Hurtado, Lauretta A. Lacko, Xiaolu Sun, Aravind R. Gade, Christina A. Higgins, Whitney J. Sisso, Xue Dong, Maple Wang, Zhengming Chen, David D. Ho, Geoffrey S. Pitt, Robert E. Schwartz, Benjamin R. tenOever, Todd Evans and Shuibing Chen, 8 March 2022, Circulation Research. DOI: 10.1161/CIRCRESAHA.121.320518

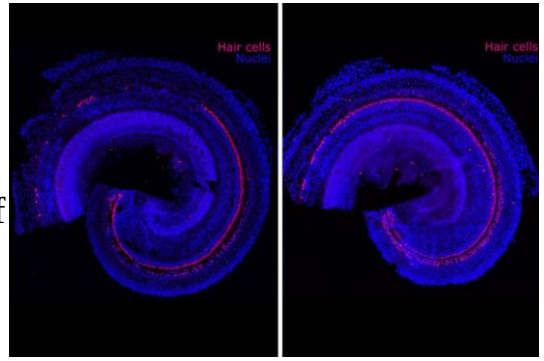
https://bit.ly/3v9IUV3

MIT Scientists Develop New Regenerative Drug That Reverses Hearing Loss

MIT spinout Frequency Therapeutics' drug candidate stimulates the growth of hair cells in the inner ear.

By Zach Winn, Massachusetts Institute of Technology

The biotechnology company Frequency Therapeutics is seeking to reverse hearing loss — not with hearing aids or implants, but with a new kind of regenerative therapy. The company uses small molecules to program progenitor cells, a descendant of stem cells in the inner ear, to create the tiny hair cells that allow us to hear.



These images show cellular regeneration, in pink, in a preclinical model of sensorineural hearing loss. The control is on the left and the right has been treated. **Credit: Hinton AS, Yang-Hood A, Schrader AD, Loose C, Ohlemiller KK, McLean WJ.**

Hair cells die off when exposed to loud noises or drugs including certain chemotherapies and antibiotics. Frequency's drug candidate is designed to be injected into the ear to regenerate these cells within the cochlea. In clinical trials, the company has already improved people's hearing as measured by tests of speech perception — the ability to understand speech and recognize words.

"Speech perception is the No. 1 goal for improving hearing and the No. 1 need we hear from patients," says Frequency co-founder and Chief Scientific Officer Chris Loose PhD '07.

In Frequency's first clinical study, the company saw statistically significant improvements in speech perception in some participants after a single injection, with some responses lasting nearly two years.

The company has dosed more than 200 patients to date and has seen clinically meaningful improvements in speech perception in three separate clinical studies.

Another study failed to show improvements in hearing compared to the placebo group, but the company attributes that result to flaws in the design of the trial.

Now Frequency is recruiting for a 124-person trial from which preliminary results should be available early next year.

The company's founders, including Loose, MIT Institute Professor Robert Langer, CEO David Lucchino MBA '06, Senior Vice President Will McLean PhD '14, and Harvard-MIT Health Sciences and Technology affiliate faculty member Jeff Karp, are already gratified to have been able to help people improve their hearing through the trials. They also believe they're making important contributions toward solving a problem that impacts more than 40 million people in the U.S. and hundreds of millions more around the world.

"Hearing is such an important sense; it connects people to their community and cultivates a sense of identity," says Karp, who is also a professor of anesthesia at Brigham and Women's Hospital. "I think the potential to restore hearing will have enormous impact on society."

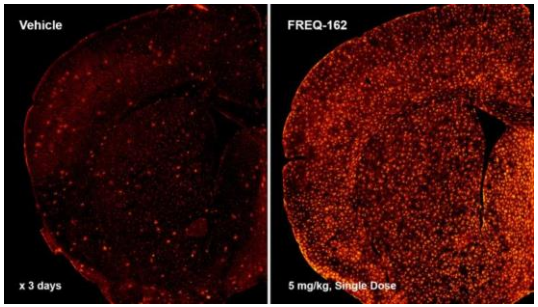
From the lab to patients

In 2005, Lucchino was an MBA student in the MIT Sloan School of Management and Loose was a PhD candidate in chemical engineering at MIT. Langer introduced the two aspiring entrepreneurs, and they started working on what would become Semprus BioSciences, a medical device company that won the MIT $100K Entrepreneurship Competition and later sold at a deal valued at up to $80 million.

"MIT has such a wonderful environment of people interested in

new ventures that come from different backgrounds, so we're able to assemble teams of people with diverse skills quickly," Loose says.

Eight years after playing matchmaker for Lucchino and Loose, Langer began working with Karp to study the lining of the human gut, which regenerates itself almost every day.



These two images show that one of Frequency's lead compounds, FREQ-162, drives progenitor cells to turn into oligodendrocytes. The control is on the left and the right has been treated. **Credit: Frequency Therapeutics**

With MIT postdoc Xiaolei Yin, who is now a scientific advisor to Frequency, the researchers discovered that the same molecules that control the gut's stem cells are also used by a close descendant of stem cells called progenitor cells. Like stem cells, progenitor cells can turn into more specialized cells in the body.

"Every time we make an advance, we take a step back and ask how this could be even bigger," Karp says. "It's easy to be incremental, but how do we take what we learned and make a massive difference?"

Progenitor cells reside in the inner ear and generate hair cells when humans are in utero, but they become dormant before birth and never again turn into more specialized cells such as the hair cells of the cochlea. Humans are born with about 15,000 hair cells in each cochlea. Such cells die over time and never regenerate.

In 2012, the research team was able to use small molecules to turn progenitor cells into thousands of hair cells in the lab. Karp says no one had ever produced such a large number of hair cells before. He still remembers looking at the results while visiting his family, including his father, who wears a hearing aid.

"I looked at them and said, 'I think we have a breakthrough,'" Karp says. "That's the first and only time I've used that phrase."

The advance was enough for Langer to play matchmaker again and bring Loose and Lucchino into the fold to start Frequency Therapeutics.

The founders believe their approach — injecting small molecules into the inner ear to turn progenitor cells into more specialized cells — offers advantages over gene therapies, which may rely on extracting a patient's cells, programming them in a lab, and then delivering them to the right area.

"Tissues throughout your body contain progenitor cells, so we see a huge range of applications," Loose says. "We believe this is the future of regenerative medicine."

Advancing regenerative medicine

Frequency's founders have been thrilled to watch their lab work mature into an impactful drug candidate in clinical trials.

"Some of these people [in the trials] couldn't hear for 30 years, and for the first time they said they could go into a crowded restaurant and hear what their children were saying," Langer says. "It's so meaningful to them. Obviously more needs to be done, but just the fact that you can help a small group of people is really impressive to me."

Karp believes Frequency's work will advance researchers' ability to manipulate progenitor cells and lead to new treatments down the line.

"I wouldn't be surprised if in 10 or 15 years, because of the resources being put into this space and the incredible science being done, we can get to the point where [reversing hearing loss] would be similar to Lasik surgery, where you're in and out in an hour or two and you can completely restore your vision," Karp says. "I think we'll see the same thing for hearing loss."

The company is also developing a drug for multiple sclerosis (MS),

a disease in which the immune system attacks the myelin in the brain and central nervous system. Progenitor cells already turn into the myelin-producing cells in the brain, but not fast enough to keep up with losses sustained by MS patients. Most MS therapies focus on suppressing the immune system rather than generating myelin.

Early versions of that drug candidate have shown dramatic increases in myelin in mouse studies. The company expects to file an investigational new drug application for MS with the FDA next year.

“When we were conceiving of this project, we meant for it to be a platform that could be broadly applicable to multiple tissues. Now we’re moving into the remyelination work, and to me it’s the tip of the iceberg in terms of what can be done by taking small molecules and controlling local biology,” Karp says.

For now, Karp is already thrilled with Frequency’s progress, which hit home the last time he was in Frequency’s office and met a speaker who shared her experience with hearing loss.

“You always hope your work will have an impact, but it can take a long time for that to happen,” Karp says. “It’s been an incredible experience working with the team to bring this forward. There are already people in the trials whose hearing has been dramatically improved and their lives have been changed. That impacts interactions with family and friends. It’s wonderful to be a part of.”

https://bit.ly/3v4OoQU

A Strange Genetic Link Between Humans And Sea Anemones Was Just Confirmed

A gene linked to the development of hearing in humans has just been linked to sensory development in sea anemones, too.

Michelle Starr

Called *pou-iv* (pow-four), the gene can be found in the tentacles of the starlet sea anemone (*Nematostella vectensis*), where it plays a crucial role in the animal's sense of touch.

Cnidaria, the phylum to which sea anemones belong, is the closest relative to Bilateria, animals with bilateral symmetry such as humans, diverging from their last common ancestor that lived around 748 to 604 million years ago.

The discovery of the gene's role in the starlet sea anemone suggests that it was present in their common ancestor and likely played a role in sensory development then, too.

"This study is exciting because it not only opened a new field of research into how mechanosensation develops and functions in a sea anemone .. but it also informs us that the building blocks of our sense of hearing have ancient evolutionary roots dating back hundreds of millions of years into the Precambrian," said biologist Nagayasu Nakanishi of the University of Arkansas.

In humans and other vertebrates, the sensory receptors of the auditory system are called hair cells. These cells have bundles of finger-like organelles called stereocilia that sense mechanical stimuli; namely, the vibrations we hear as sound. In mammals, *pou-iv* is required for the development of hair cells; we know this because mice that have had *pou-iv* knocked out are deaf.

The starlet sea anemone has similar mechanosensory hair cells on its tentacles, used for sensing movement. Little, however, was known about the anemone's *pou-iv* gene and what role, if any, it played in sensory development.

A team of researchers led by biologist Ethan Ozment of the University of Arkansas wanted to figure out what the gene was doing. The best way to do this is to disable the gene using the CRISPR-Cas9 gene-editing tool and observe what changes. So this is what the team did.

They injected a cocktail containing Cas9 protein into fertilized starlet sea anemone eggs to cut out the *pou-iv* gene, and studied the developing embryos, as well as the grown, mutated anemones.

Compared to wild-type control anemones, the mutant animals

showed abnormal development of the tentacular hair cells, and showed no response to touch. Without *pou-iv*, the anemones were unable to sense mechanical stimuli via their hair cells.

In addition, knocking out *pou-iv* in the anemones significantly suppressed a gene very similar to the one which makes *polycystin 1* that is found in vertebrates, where it is required for the sensing of fluid flow in kidneys. Sea anemones may not have kidneys, but sensing fluid flow would be a useful ability for marine animals.

Together, the researchers said, the results suggest that *pou-iv* played a role in the development of mechanosensory cells in the common ancestor between Cnidaria and Bilateria. To trace the gene back even further, however, will require data from other phyla with earlier divergence points.

"Our results indicate that the role for *pou-iv* in mechanoreceptor development is broadly conserved across Cnidaria and Bilateria," the researchers wrote in their paper.

"How early the role of *pou-iv* in mechanoreceptor differentiation emerged in animal evolution remains unresolved, and requires comparative data from placozoans and sponges, which are wanting."

The research has been published in *eLife*.