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ASIA PACIFIC

Australia Consults on Removing A Wrongly Listed Chemical from AIIC

2022-04-18

On April 8, 2022, the Australian Government issued a notice¹ to publicly solicit comments on removing a chemical (CAS No. 1428963-39-6) from the Australian Inventory of Industrial Chemicals (AIIC). The consultation will end on June 3, 2022.

According to the Draft Evaluation Statement - EVA000892, this chemical was wrongly listed on AIIC because of the misidentification of the chemical structure, of which the word "hydrolyzed" in the name is just a side reaction and should not be included in the polymer name. Instead, the chemical with CAS No. 1431957-88-8 is the one that should have been listed on AIIC.

Below are the details of the two chemicals to facilitate your understanding.

Table 1 - Chemical proposed to be removed from AIIC

CAS No.	Chemical Name
1428963-39-6	2,5-Furandione, telomer with ethenylbenzene and (1-methylethyl)benzene, hydrolyzed , 3- (dimethylamino) propyl imide, imide with polyethylene-polypropylene glycol 2- aminopropyl Me ether, 2-[(C10-16- alkyloxy)methyl]oxirane-quaternized, benzoates (salts)

Table 2 - Chemical proposed to be added to AIIC

CAS No.	Chemical Name
1431957-88-8	2,5-Furandione, telomer with ethenylbenzene and (1-methylethyl)benzene, 3- (dimethylamino)propyl imide, imide with polyethylene-polypropylene glycol 2- aminopropyl Me ether, 2-[(C10-16- alkyloxy)methyl]oxirane-quaternized, benzoates (salts)

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Read More

Chemlinked, 18-04-22

<https://chemical.chemlinked.com/news/chemical-news/australia-consults-on-removing-a-wrongly-listed-chemical-from-aiic>

South Korea notified a measure related to food additives G/SPS/N/KOR/749

2022-04-22

The Republic of Korea is proposing to amend the "Standards and Specifications for the Food Additives":

1) The standards for the use of nicotinic acid are revised. Nicotinic acid should be used only for Foods for particular nutritional uses, Foods for particular medical purpose, Food supplements and Nutrition-enriched wheat flour;

2) 22 active and inert ingredients for use in food-contact surface sanitizing solutions are deleted in the list:

Relevant documents:

(*) WTO Notification G/SPS/N/KOR/749

(*) Draft regulation

Read More

Chemycal, 22-04-22

https://chemycal.com/news/b51c1682-0f23-416b-b6a7-f617952c9217/South_Korea_notified_a_measure_related_to_food_additives_G_SPS_N_KOR_749

Australia Draft evaluations open for comments until 17 June 2022

2022-04-22

What is this about?

We have published 27 draft evaluation statements on 157 industrial chemicals that:

- we identified as having the potential to pose a risk to human health and/or the environment

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- are unlikely to require further regulation in Australia to manage human health risks

These evaluations are listed in our Rolling Action Plan and are part of the targets set in our evaluations roadmap. Please note, we have made some changes to the RAP.

We welcome your comments on any of these draft evaluations.

Read More

Australian Government Department of Health, 22-04-22

<https://www.industrialchemicals.gov.au/news-and-notice/draft-evaluations-open-comments-until-17-june-2022>

Call for information: chemicals that are unlikely to need further human health risk management controls - closes 17 June 2022

2022-04-22

We're seeking use and hazard information on chemicals that we believe are low concern and are unlikely to require further regulatory controls to manage risks to human health. We published a list of these chemicals in our draft evaluation statement.

Use the form on the linked page to tell us:

- If you have hazard information about any of these chemicals
- If you or your business are using any of the chemicals in an exposure category that is different to what we have described in our evaluation statement

Read more and download the draft evaluation statement

Read More

Australian Government Department of Health, 22-04-22

<https://www.industrialchemicals.gov.au/news-and-notice/call-information-chemicals-are-unlikely-need-further-human-health-risk-management-controls-closes-17-june-2022>

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AMERICA

Sodium cyclamate and cyclohexylamine

2022-04-08

These substances were identified for action under the Chemicals Management Plan (CMP).

Sodium cyclamate

Although a risk to human health or the environment has not been identified at current levels of exposure, sodium cyclamate has health effects of concern based on its potential to cause reproductive effects. Therefore, there may be a potential risk if exposure to this substance was to increase. An analysis of information related to current and potential future uses of sodium cyclamate suggest that it is unlikely that exposure will increase to levels of concern to human health. For this reason, follow-up activities to track changes in exposure and/or commercial use patterns for sodium cyclamate are not being considered at this time.

Cyclohexylamine

Although cyclohexylamine was not considered to be harmful to human health at levels of exposure considered in the assessment, it is considered to have a health effect of concern due to its potential to cause reproductive effects. Therefore, there may be a concern if exposures were to increase. The proposed follow-up activity for cyclohexylamine is to apply the SNAC provisions of the Canadian Environmental Protection Act, 1999 (CEPA 1999).

Background

Cyclohexylamine (CAS RN 108-91-8) was identified as being part of the Aliphatic Amines Group at the outset of the third phase of the CMP. This substance was subsequently moved to this assessment of sodium cyclamate, since cyclohexylamine is a metabolite of sodium cyclamate in mammals and cyclohexylamine data were used to assess the risk to human health of both substances.

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Read More

Government of Canada, 08-04-22

<https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan-3-substances/sodium-cyclamate-cyclohexylamine.html>

Op-Ed: FDA fails to protect the public from chemicals health risks

2022-04-21

The U.S. Food and Drug Administration (FDA) is responsible for protecting the public's health and ensuring the safety of our nation's food supply.

Sadly, as Politico reported this month, the agency "has repeatedly failed to take timely action on a wide range of safety and health issues the agency has been aware of for several years, including dangerous pathogens found in water used to grow produce and heavy metal contamination in baby foods."

Here, I focus on another critical agency mandate: To protect the public from harmful chemicals in food and cosmetics. Here too the agency is failing to protect consumers.

Chemicals in food and cosmetics—whether present as additives or contaminants—usually do not cause immediate or obvious health effects, but they pose a significant longer-term risk to public health. Consumers want to know that their food and products they use every day are safe and that neither individual chemicals nor their cumulative impacts will harm their health. Congress directed the FDA to do this more than 60 years ago.

Read More

Environmental Health News, 21-04-22

<https://www.ehn.org/fda-chemical-regulation-2657184101/fdas-2013-review-a-commitment-unfulfilled>

Product bans among panel's recommendations to rein in PFAS chemicals

2022-04-21

After almost a year of studying how "forever chemicals" touch nearly all aspects of life in Massachusetts, the PFAS Interagency Task Force released

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its final report Wednesday with recommendations that the state regulate PFAS chemicals as a class, restrict the sale of consumer products with intentionally-added PFAS and work to raise public awareness of the ubiquity of the problem.

Per- and polyfluoroalkyl substances (PFAS) are man-made chemicals that do not break down entirely in the environment, and exposure to their long-lasting presence has been linked to serious and negative health impacts like thyroid disease and kidney cancer.

PFAS chemicals are all around us; they are used in non-stick cookware, food packaging, children's products, carpets, leather goods, ski wax, firefighting foams and more, and they have leached into drinking water supplies and the soil.

"PFAS is present in the textiles, some of the clothing I bet each of us is wearing this morning, maybe is present in a pan you made your eggs in, is present in food packaging, in children's products, in you name it. There's a real ubiquity there," Sen. Julian Cyr, who co-chaired the task force, said. "As we get our hands around this issue, you just realize how widespread PFAS is."

The task force's report carries 30 specific recommendations that fall under eight general themes: funding PFAS detection and remediation, supporting environmental justice communities, phasing out PFAS from consumer goods, expanding the regulation of PFAS, encouraging private well PFAS testing and remediation, supporting firefighters and fire departments, addressing accountability for PFAS contamination, and enhancing public awareness of PFAS.

Read More

Wbur, 21-04-22

<https://www.wbur.org/news/2022/04/21/pfas-forever-chemicals-massachusetts-report>

Canada Plastics Pact develops packaging design rules

2022-04-21

Canada Plastics Pact publishes nine golden design rules for plastic packaging manufacturers; include using a single material per package, avoiding polyvinyl chloride (PVC), reducing headspace, and switching to reuse systems; more than 30 Canadian companies have already signed onto 50% or more of the rules.

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APR. 29, 2022

Read More

Canada Plastics Pact, 21-04-22

<https://goldendesignrules.plasticspact.ca/>

EUROPE

Reminder – upcoming GB active substance expiry dates

2022-04-21

The active substance/product type combinations listed below are due to expire under GB BPR on the following dates:

- 3-phenoxybenzyl-2-(4-ethoxyphenyl)-2-methylpropylether (Etofenprox) (CAS 80844-07-1 EC 407-980-2) in product type 8
31 October 2022
- Carbon dioxide (CAS 124-38-9 EC 204-696-9) in product type 18
31 October 2022

Once the approvals expire, the active substances can no longer be used in biocidal products of the relevant product types in Great Britain.

If you hold an affected GB BPR product authorisation or Control of Pesticides Regulations (COPR) product approval, we will contact you about cancelling or revoking your authorisation or approval. You will have an opportunity to submit comments or additional information and we will take account of these when finalising our decision.

If you are aware of any disproportionate negative effects that are likely to arise from the expiry of any of the active substance/product type combinations listed above, please contact us.

Read More

HSE, 21-04-22

<https://www.hse.gov.uk/>

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Reminder – upcoming GB active substance open invitation deadline

2022-04-21

HSE has published an open invitation (PDF) to provide an opportunity for a person, company, or task force/consortium to notify an intention to take up or take over the role of participant in the GB Review Programme for the following active substance/product type combination.

Anyone wishing to support one of the active substance/product type combinations listed below in GB will need to submit a notification (.docx) to HSE by the following deadline:

- Pyrithione zinc (Zinc pyrithione) (CAS 13463-41-7 EC 236-671-3) in product type 2
8 April 2023

If a notification to take over the role of participant is not received, this active substance/product type combination will be subject to a GB non-approval decision. Biocidal products containing active substances with GB non-approval decisions for the relevant product types will have to be removed from the GB market. HSE will provide separate updates on these where relevant.

If you are aware of any disproportionate negative effects that are likely to arise from the non-approval of any of the active substance/product type combinations listed above, please contact us.

Read More

HSE, 21-04-22

<https://www.hse.gov.uk/>

Exposure to cadmium: ANSES proposes limit values to better protect consumers and workers

2022-04-21

Cadmium, a substance that is omnipresent in the environment, can pose health risks to humans, who are exposed mainly through food. In order to limit the exposure of the population, it appears essential to control cadmium intakes from agricultural activities, in particular the application of fertilisers, including mineral phosphate fertilisers. Today, ANSES is publishing its expert appraisal work, whose results aim to further protect consumers and workers. To that end, the Agency has established a new

Submit a notification by the deadline to keep active substances in the GB Review Programme

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health-based guidance value (HBGV) by ingestion and recommends lowering cadmium levels in fertilisers in order to limit accumulation in soils, transfers to plants and ultimately consumer exposure to cadmium through food. ANSES reiterates that some population groups are overexposed to cadmium through food and therefore stresses the need to implement protective measures to reduce cadmium intakes.

Cadmium: a substance to be monitored

Cadmium is a trace metal element that is widespread in the environment in its natural state and as a result of human activity, particularly agriculture and industry. It is readily available for uptake by plants through their roots, by which it enters the food chain.

Cadmium is known to be carcinogenic, mutagenic and toxic to reproduction, and prolonged exposure causes kidney damage and bone fragility in humans, particularly from oral exposure via food and drinking water.

The main sources of exposure to cadmium in the general population are food, as well as tobacco for smokers. In 2011, following the second French Total Diet Study (TDS2), ANSES highlighted cases of the HBGV for cadmium being exceeded for some population groups; since this was likely to pose a health risk, it recommended reducing dietary exposure. To that end, the Agency advised acting at the source, in particular by targeting fertilisers, which were partly responsible for the increase in cadmium concentration in soils and ultimately the rise in levels of cadmium in food.

Read More

ANSES, 21-04-22

<https://www.anses.fr/en/content/exposure-cadmium-anses-proposes-limit-values-better-protect-consumers-and-workers>

INTERNATIONAL

Projects launched to support GHS implementation in Africa

2022-04-19

Kenya, Ghana, Cote d'Ivoire, Nigeria, and Rwanda implementing Globally Harmonized System of Classification and Labeling of Chemicals (GHS) in national policy; Sierra Leone and Malawi partner with the UN Environment

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Program (UNEP) to study chemical and waste management within the countries to design long term policies and projects

In early April, the International Council of Chemical Associations (ICCA) announced a new project with Kenya, Ghana, Cote d'Ivoire, and Nigeria to support the countries as they implement the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). The ICCA and other partners will support the nations as they develop legislation as well as provide training and tools to help implement and enforce the new rules. The United Nations Environment Program (UNEP) reported it is backing projects from Sierra Leone and Malawi as the two nations develop national chemicals and waste management plans. Currently, the majority of waste in the two countries is burned in the open.

Developed by the United Nations, the GHS is a way to standardize the management of chemicals and communicate their hazards, for international trade and safety. While many multinational corporations that operate in Africa use the GHS, currently only Mauritius, South Africa, and Zambia have the GHS implemented as part of national policy. Rwanda began the process in 2021 by informing the World Trade Organization of its intentions, and the comment period closed in March 2022.

The UNEP-backed projects in Sierra Leone and Malawi are focused on achieving comprehensive waste management systems for the countries. Nearly three-quarters of Malawi's waste "finds its way to open dump sites or is burnt," according to the UNEP, and 8.5% of that is plastic. The three-year-long initiative in Malawi "will focus on raising public awareness, piloting a plastics recycling project, and establishing an integrated information management system for chemicals and waste." An existing waste station will be retrofitted with a machine for turning plastics into pellets that can be sold to local plastics recycling facilities. Data gathering through the entire waste stream will enable the country to create long-term evidence-backed plans in the future.

The project in Sierra Leone will run for two years and is focused on collecting the data necessary to create a national action plan. The plan will "bridge the gaps between the country's current practices on managing chemicals and waste and the best practices outlined under the chemicals and waste related conventions" to which it is a member, namely the Basel, Rotterdam, Stockholm, and Minamata Conventions.

Plastic waste was adopted into the Basel Convention in May 2019 (FPF reported) and places stricter controls on transporting plastic waste across borders. Despite that, the plastic waste trade continues to place the

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burdens of recycling and disposal on countries without the infrastructure to support it (FPF reported, also here). A report by the International Pollutants Elimination Network (IPEN) found that “toxic chemicals in plastic waste exports from wealthy countries are contaminating food in developing/transition countries” (FPF reported). In March, 175 nations agreed to create a plastic pollution treaty which should help to alleviate some of the problems associated with the international plastic waste trade (FPF reported).

[Read More](#)

Food Packaging Forum, 19-04-22

<https://www.foodpackagingforum.org/news/projects-launched-to-support-ghs-implementation-in-africa>

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REACH Update

APR. 29, 2022

Consultation opens on EU Cosmetics Regulation revision, including nanomaterials definition

2022-04-21

The European Commission has launched the stakeholder consultation process for the targeted revision of the Cosmetic Products Regulation. As for the REACH revision, this is part of the actions identified to bring chemicals legislation in line with the goals of the Chemicals Strategy for Sustainability. Stakeholders are invited to provide input on a new approach to risk management (from specific to generic); the introduction of a “combined exposure” measure to assess the combined effect of chemicals from different sources; a review of the definition of nanomaterial in the Regulation; the improvement of labelling information; and the streamlining of the scientific assessments of products. The consultation closes on June 21.

[Read More](#)

Nano News, 21-04-22

<https://nanotechia.org/news>

22 harmful chemicals added to PIC - exporters must notify from July

2022-04-21

EU exporters are now required to notify their intention to export 22 chemicals following an amendment to the PIC Regulation. The amendment also bans the export of four chemicals. The update was published on 20 April 2022 and will start to apply on 1 July 2022.

Helsinki, 21 April 2022 - The 22 additional chemicals include 15 pesticides and seven industrial chemicals, including all substances containing benzene as a constituent in concentrations above 0.1 % weight by weight.

As well as the export notification, most of these chemicals will also require an explicit consent from the importing country before exports can take place.

In addition, five chemicals that were previously only subject to export notification will also now require explicit consent.

The IT tool ePIC has been updated and companies can already start notifying their exports now.

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REACH Update

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Background

The European Commission updated PIC Annex I, which lists the chemicals subject to export notification and explicit consent from the importing country as well as Annex V which lists chemicals and articles banned from exporting. This amendment will enter into application on 1 July 2022.

Read More

ECHA, 21-04-22

<https://echa.europa.eu/pt/-/22-harmful-chemicals-added-to-pic-exporters-must-notify-from-july>

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Janet's Corner

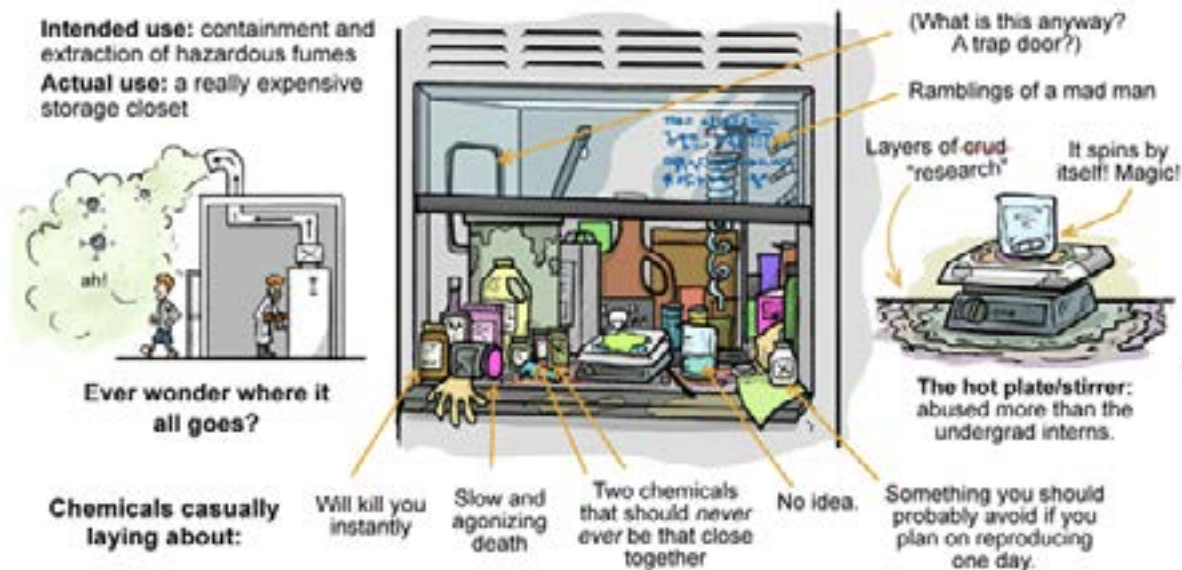
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Fume Hood Realities

2022-04-29

THE FUME HOOD: Where does it go??

WWW.PHDCOMICS.COM
JORGE CHAM © 2008



<https://phdcomics.com/comics/archive.php?comid=1023>

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Hazard Alert

APR. 29, 2022

Tartaric Acid

2022-04-29

Tartaric acid is a white crystalline dicarboxylic acid. It is the most water-soluble of the solid acidulants and is produced from potassium acid tartrate, which is a by-product of the wine industry from the press cakes, less and argols left behind. The acid is popular in major wine producing countries, including Spain, France, Germany and Italy. [1]

USES [1,2]

Tartaric acid is primarily used as an acidulant—additives that give a sharp (sour, tart or acidic) taste to foods. It is particularly effective in anything that is lime or grape flavoured, and as such, is often found in grape and lime flavoured beverages, gelatinous desserts, jams and hard boiled sweets. It is also used in baking in various applications, including as a leavening agent (when combined with baking soda), and to increase the stability of foods.

ROUTES OF EXPOSURE [2,3]

- People can be exposed to tartaric acid by inhalation, skin and eye contact and by ingesting the compound.
- Tartaric acid naturally occurs in fruit plants, including apples, bananas, apricots, avocados, grapes and tamarinds

Health Effects

Tartaric acid poisoning can affect a range of systems including the nervous, respiratory and cardiovascular systems.

Acute Effects [4]

Severity of symptoms depends on the level and type of exposure.

- In low doses, tartaric acid is an irritant.
- Skin contact can cause itching and a rash.
- Eye contact may result in lacrimation, redness and pain.
- Inhalation of the compound could result in coughing and irritation of the mucous membrane of the nasal passage.
- Due to the form of tartaric acid, high levels of ingestion are considered unlikely. However, if high levels are ingested, it may cause gastrointestinal (GI) irritation.

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Chronic Effects [5]

While chronic toxicity of tartaric acid is considered a low risk, it is still possible. Prolonged exposure to the compound can cause skin, upper respiratory tract and mucous membrane irritation. Ingestion of large quantities may result in irritation to the GI tract, which could result in nausea or vomiting.

SAFETY

First Aid Measures [3]

- Ingestion: If ingested, rinse mouth with water and DO NOT induce vomiting. Immediately call a doctor or a poison centre.
- Skin contact: In case of skin or hair contact, remove affected clothing and wash exposed skin with mild soap and water followed by a warm water rinse.
- Eye contact: Flush eyes out carefully with water for a few minutes. Remove contact lenses if easy to do so. Continue rinsing. Immediately call a poison centre.
- Inhaled: Take contaminated person to nearest fresh air source and monitor their breathing. Allow person to rest.

Exposure Controls/Personal Protection [3]

- Engineering controls: Safety showers and emergency eyewash fountains should be accessible in the immediate area of the potential exposure.
- Personal protection: Safety glasses and protective gloves.

REGULATION

United States [6]:

The Occupational Safety and Health Administration (OSHA) has set an 8-hour time-weighted average (TWA) concentration for tartaric acid of 15mg/m³.

Australia [7]

Safe Work Australia: Safe Work Australia has not set a specific TWA for tartaric acid. For dust limits that have not otherwise been specified, the TWA set for an 8-hour, 5-days-a-week is 10mg/m³. In industrial settings, it is recommended to keep exposure below the TWA levels. This can be

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Hazard Alert

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done by using local exhaust ventilation or by capturing substances at the source.

REFERENCES

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Gossip

APR. 29, 2022

COVID-19 breath tests could be the future of living with the virus, but this pandemic solution has a catch

2022-04-26

Whether it is a PCR test or the at-home variety, sending a swab up the nose to swirl around and test for COVID-19 has become a familiar but uncomfortable part of living through the pandemic.

However, what if there was an alternative?

For the first time, health authorities in the United States have given the green light to a COVID-19 breathalyser, a device promised to deliver results in less than three minutes.

As new sub-variants once again push up case numbers, some experts hope it will be the first of many new tools to diagnose and, therefore, improve the way we live with the virus.

There is even hope breath testing could eventually be used to detect and monitor other conditions, such as cancer.

So just how advanced is the technology? And could it actually replace the nasal swabs we have come to know and loathe?

Breath test with a catch

The US Food and Drug Administration (FDA) has granted emergency use authorisation for a breathalyser produced by small Texas-based company, InspectIR.

The test involves exhaling through a disposable straw into a device the size of a carry-on suitcase which then analyses so-called "volatile organic compounds" associated with the SARS-COV-2 infection.

"Essentially, when your body is fighting the illness, at a cellular level it creates off gas," co-founder and president John Redmond told the ABC.

"That gas is carried through your bloodstream to your lungs, and then is exhaled as waste. And, based on the sensitivity of our instrument, we can actually see that chemistry.

"And, based on analysis, we can determine if a person is sick or not."

The test has limitations. The FDA requires that it is conducted by a trained operator under the supervision of a healthcare provider and positive results are supposed to be confirmed by a PCR test.

For the first time, health authorities in the United States have given the green light to a COVID-19 breathalyser, a device promised to deliver results in less than three minutes.

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Gossip

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The cost of leasing the machines has not yet been made public, although the company insists it will be comparable to rapid antigen tests.

Either way, it is a major step forward according to Cristina Davis, a professor of mechanical and aerospace engineering at University of California Davis who is developing her own COVID-19 breath test.

“The way that there are dozens of at-home, over-the-counter COVID rapid antigen tests, I believe that there will be many [breath] devices that will come onto the scene at some point in the next year or year and a half,” she says.

Professor Davis wants to see them used as screening tools at crowded venues such as stadiums or airports, with guests asked to wait several minutes for their result before entering.

It is hoped they could also help to prevent so-called “superspreader” events, such as the exclusive dinner in Washington DC earlier this month where more than 70 people — including members of Joe Biden’s cabinet — are thought to have been infected.

Breath testing could be used for the flu, cancer as well as COVID-19

As it has done for other innovations — such as mRNA vaccines and telehealth — the pandemic has helped to focus attention and funding on breath research.

Perena Gouma, a professor of materials science and engineering, was working on a breath test to detect the flu when COVID-19 began.

“I received a phone call from the White House. They had read my flu breathalyser paper and they said, ‘Can you make a test for COVID-19?’” Professor Gouma says.

She and her team at Ohio State University have since developed a test that, she says, can be self-administered and return a result in less than 30 seconds.

Her test measures the make-up of various compounds in a person’s breath to determine whether or not they have COVID-19 and how severe it is.

Professor Gouma argues the test has a high accuracy rate and could “revolutionise” COVID-19 screening if it was rolled out widely.

However, her efforts to obtain emergency use authorisation from the FDA have so far been unsuccessful.

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“I’m a little bit furious because — after having spent two years really working on this technology day and night, and making everything so available to everybody, so transparent — then we got this result,” she says.

The FDA says it does not discuss the status of pending applications.

Professor Davis says the scientific community is only just scratching the surface of the field’s potential.

Eventually, she hopes breath testing could be used to diagnose or monitor conditions such as cancer.

“Breath research doesn’t have to just be about the lung, interestingly, because what we’re measuring from the exhaled breath is really representative of the entire body,” Professor Davis says.

“It’s not just about diagnostics, I think going forward we’re going to see monitoring as a key thing.

“If you’re taking a treatment for something, you could be monitoring, ‘OK, how’s that working?’

“It just gives more information to doctors so that they can help patients individually manage their own health conditions.”

At-home testing leads to COVID-19 blind spots

COVID-19 testing has come a long way since the start of the pandemic, with RATs now relatively widely available alongside the “gold standard” PCRs.

However, while access has improved, some experts fear an increasing reliance on at-home testing has also made it more difficult for authorities to track case numbers.

And that could mean they are less prepared for further waves.

“We are vastly under-counting what is going on in this country,” says Maureen Miller, an epidemiologist at Columbia University’s Mailman school of public health.

“I mean, it is great to have the technology so you can test at home, so you can protect yourself and those around you.

“But several recent studies have shown that people who test at home, [only] between 7 and 10 per cent report their results. Perversely, positive people tend not to report their results.”

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Case numbers are not the only measure used to track COVID-19, with hospital admission rates and wastewater surveillance also used to monitor its spread.

More than two years into the pandemic, the Centers for Disease Control and Prevention have set up a new forecasting headquarters, aimed at becoming “the equivalent of the National Weather Service for infectious diseases”.

However, as new Omicron sub-variants drive another increase in cases, Dr Miller is concerned that the US is not as prepared as it could be.

“Will it be this enormous bump? No,” she says, comparing it to Omicron’s peak at the beginning of this year.

“But will it prolong the pandemic longer than it has to? Yeah, it’s definitely going to do that.”

ABC News, 26 April 2022

<https://abc.net.au>

Researchers stimulate blind retinas using focused ultrasound technology

2022-04-18

The number of Americans with visual impairment or blindness is expected to jump to more than 8 million by the year 2050, according to research lead by the USC Gayle and Edward Roski Eye Institute conducted back in 2016.

With the youngest baby boomers reaching 65 years old by 2029, age-related eye diseases and conditions are expected to swell during what’s being called the “silver tsunami”.

According to medical experts, it’s safe to say many of those cases will be caused by retinal degenerative diseases, the progressive degeneration of the light-sensitive photoreceptors in your retina.

Based on these estimates, there is an unmet need for new technologies that treat vision loss due to diseases of photoreceptor degeneration.

While there are no successful non-invasive therapeutics currently available for the treatment of vision loss, researchers at USC have come up with a new idea to address this growing problem.

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Currently, ophthalmologists use electronic technology to directly stimulate retinal neurons by implanting electrode devices inside the eye, a technique that requires expensive and invasive surgery.

The research team in the USC Viterbi School of Engineering’s Department of Biomedical Engineering is exploring a non-surgical solution that could restore sight by using another of the five senses.

Sound.

Ultrasound Technology

“This is innovative technology,” said Qifa Zhou, professor of biomedical engineering and ophthalmology at USC. “Right now, we are doing animal studies trying to use ultrasound stimulation to replace electric stimulation.”

The research group is led by Zhou, and Mark S. Humayun, professor of ophthalmology and biomedical engineering at USC, and one of the inventors of Argus II—the world’s first artificial retina.

“The technology is advantageous since no surgery is required and no device will be implanted inside the body,” said Gengxi Lu, a Ph.D. student in Zhou’s lab. “A wearable ultrasound device will generate ultrasound waves to stimulate the retina”.

Similar to how shapes and bright spots appear when you gently push on your eyeball with your eyes closed; researchers realized that applying pressure to the eye can activate neurons and send signals to the brain.

Unlike a normal eye that is activated by light, the blind eyes were stimulated by mechanical pressures generated by ultrasound waves in this study.

“The neurons present in the retina of the eye possess mechanically sensitive channels that respond to mechanical stimulation,” Lu explained. “These neurons are activated when we use ultrasound to generate mechanical pressure.”

How It Works

To test this ultrasound approach, in pre-clinical studies the team at USC stimulated a blind rat’s eyes using high-frequency ultrasound waves that are inaudible to humans.

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The technology used in this research is comparable to the ultrasound probe used for baby imaging that sends and receives sound waves through a pregnant woman's stomach.

In this case, for retinal stimulation the research group created a small ultrasound device that can be directed at a specific region of the eye to send sound waves to the retina, which is located in the back of the eye.

Using these high-frequency sounds that can be manipulated and focused on a specific area of the eye; the study demonstrated that when the ultrasound waves are projected as a pattern—for example, the letter 'C'—the rat's brain was able to pick up a similar pattern.

Unlike in humans, researchers are unable to get direct answers about the rat's visual experiences during the ultrasound stimulation.

To answer these questions of what exactly the rat was able to visualize from the ultrasound waves, the team measured visual activity directly from the rat's visual brain area known as the visual cortex by attaching a multi-electrode array.

Based on the visual activities recorded from the brain, researchers found the rat was able to perceive visualizations comparable to the ultrasound stimulation pattern projected to the eye. This work was just published in *BME Frontiers*.

The Future

The research is currently funded by a four-year, \$2.3 million grant from the National Eye Institute (NEI). The team recently applied for another NEI translational grant to take their studies to the next level.

Current studies are conducted mostly using rodent models. However, the team plans to test this approach using non-human primate models prior to conducting human clinical trials.

"Right now, we are using a transducer placed in front of the rat's eyeball to send the ultrasound signals to the retina, but our final goal is to create a wireless lens transducer" said Dr. Zhou.

While the team is currently analyzing the capabilities of ultrasound technology for vision study, their future goal is to generate sharper images and install the ultrasound transducer on a wearable contact lens for next generation.

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There is also a pending patent for this novel ultrasound technology that hopes to change the way visual impairment is treated years down the road.

Tech Xplore, 18 April 2022

<https://techxplore.com>

Newly developed genetic risk scores could help patients, physicians make health decisions

2022-04-18

A person's risk of developing diseases such as type 2 diabetes or breast cancer may be influenced by thousands of genetic differences. Looking at a single DNA difference that has a small effect on risk may not be clinically useful, but when hundreds or thousands of these small risks are added up into a single score, often called a polygenic risk score (PRS), they might offer clinically meaningful information about a person's disease risk. In a new paper published in *Nature Medicine*, researchers from Brigham and Women's Hospital, Veterans Affairs (VA) Boston Healthcare System, and Harvard Medical School developed and validated polygenic risk scores for six common diseases. The team also developed informational resources for each disease to help physicians and patients discuss how to incorporate PRS when making medical decisions about screening and prevention.

"As a primary care physician myself, I knew that busy physicians were not going to have time to take an entire course on polygenic risk scores," said corresponding author Jason Vassy, MD, MPH, of the Brigham's Division of General Internal Medicine & Primary Care, the Brigham's Precision Population Health at Ariadne Labs and VA Boston. "Instead, we wanted to design a lab report and informational resources that succinctly told the doctor and patient what they need to know to make a decision about using a polygenic risk score result in their health care."

Vassy and colleagues developed the risk scores as part of the Genomic Medicine at VA (GenoVA) Study, a randomized clinical trial of PRS testing among generally healthy adults. The study team developed and validated a laboratory test at the Mass General Brigham Laboratory for Molecular Medicine (LMM) for polygenic risk scores for atrial fibrillation, coronary artery disease, type 2 diabetes, breast cancer, colorectal cancer, and prostate cancer.

The GenoVA Study is currently enrolling patients at the VA Boston Healthcare System, and the investigators reported the results from the

"Researchers must continue working to increase the diversity of patients participating in genomics research"

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first 227 patients, among whom 11 percent were found to have a high polygenic risk score for atrial fibrillation, 7 percent for coronary artery disease, 8 percent for type 2 diabetes, and 6 percent for colorectal cancer. Among men, 15 percent had a high score for prostate cancer, while 13 percent of women had a high score for breast cancer. The GenoVA Study will ultimately enroll more than 1,000 patients and follow them for two years to observe how they and their primary care providers use the polygenic risk scores in clinical care. For example, high-risk patients might choose to undergo screening tests more frequently or take preventive medications that can lower their risk.

The researchers had to address many challenges in implementing a clinical laboratory PRS test. Most importantly, their own observations confirmed a problem that was already known about these scores: they are less accurate in individuals of non-European descent. Most genomic research to date has been conducted in European populations, thus the scores resulting from this research have a weaker ability to predict disease risk among non-European populations. Implementing a polygenic risk score into clinical care that is only accurate for people of European descent would exacerbate existing health disparities. To address this important limitation, the researchers applied additional statistical methods to enable PRS calculation across multiple racial groups.

“Researchers must continue working to increase the diversity of patients participating in genomics research,” said Matthew Lebo, Ph.D., Chief Laboratory Director at the LMM. “In the meantime, we were heartened to see that we could generate and implement valid genetic scores for patients of diverse backgrounds.”

To date, 52 percent of GenoVA Study enrollees report non-white race and/or Hispanic/Latinx ethnicity.

Another key challenge in bringing polygenic risk score to clinical medicine is that physicians and patients will need support to understand them and use them to make medical decisions. Clinical guidelines do not yet exist to help a physician know whether and how they should treat a patient with a high-risk score differently than an average-risk patient, but the study provides physician- and patient-oriented educational materials to help them incorporate the results. In addition, patients and primary care physicians can seek support from a genetic counselor in the study.

The researchers hope that this first report from the GenoVA Study will be a useful guide for other laboratories and health care systems looking to implement polygenic risk score testing in patient care. “It’s still very early

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days for precision prevention,” says Vassy, “but we have shown it is feasible to overcome some of the first barriers to bringing polygenic risk scores into the clinic.”

Medical Xpress, 18 April 2022

<https://medicalxpress.com>

Plant-based patties, lab-grown meat and insects: how the protein industry is innovating to meet demand

2022-04-18

As demand for alternative protein sources grows, Australians are increasingly looking for options that are healthy, sustainable and ethically made.

At CSIRO, we have produced a “protein roadmap” to guide investments in a diverse range of new products and ingredients. We believe plant-based patties, lab-made meat and insects are just some of the foods set to fill Australian fridges by 2030.

The roadmap sketches out the foundations for a future with greater choice for consumers, and better outcomes for Australian producers across all types of protein.

Changing protein preferences

Australia is one of the world’s largest per-capita beef consumers, but there has been a steady decline in consumption over the past two decades.

The most common reason for eating less red meat is cost, followed by concerns related to health, the environment, and animal welfare.

At the same time, meat consumption among the middle class in countries such as China and Vietnam has been rising.

This shift in demand is creating an opportunity for protein producers to expand and diversify.

Producing plant-based protein locally

The plant protein industry is still small in Australia. However, it is ramping up rapidly.

The total number of plant-based protein products on grocery shelves has doubled over the past year to more than 200. Recent data from the

Plant-based food products are made by processing various plant ingredients (such as wholegrains, legumes, beans, nuts and oilseeds) into food products, including breads, pasta, and alternatives to meat and dairy.

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Australian Bureau of Statistics shows demand for these products has increased by about 30% in the past two years.

Plant-based food products are made by processing various plant ingredients (such as wholegrains, legumes, beans, nuts and oilseeds) into food products, including breads, pasta, and alternatives to meat and dairy.

Lupins, chickpeas and lentils can be turned into plant-based burgers, while protein powders can be made from faba or mung beans.

Most plant-based products available now are either imported or made in Australia using imported ingredients, so there is plenty of room for Australian producers to enter the industry.

The story behind the steak

Meat will continue to be a staple in many people's diets for years to come.

When we do eat meat, Australian consumers are increasingly asking questions about where their meat came from. On this front, "digital integrity" systems can be a useful solution.

These systems track everything from the origin of ingredients, to nutrition, sustainable packaging, fair trade and organic certifications. They also keep a record of associated labour conditions, carbon footprint, water use, chemical use, animal welfare consideration, and impacts to biodiversity and air quality.

One example is made by Sydney-based firm NanoTag Technology: a unique micro-dot matrix pattern printed on the packaging of meat products which, when scanned with a pocket reader, verifies the authenticity of the product. Buyers can see the product's pack date, batch number and factory of origin.

Seafood is also an important source of healthy and low-fat protein. Demand is growing for local, inexpensive white-flesh fish such as barramundi and Murray cod.

While Australia produces 11,000 tonnes of white-flesh fish annually, it also imports almost ten times this amount to help meet annual demand.

Responding to this demand, the Australian aquaculture industry has ambitions to reach 50,000 tonnes of homegrown produce by 2030.

Fermented foods

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Precision fermentation is another technology for creating protein-rich products and ingredients – potentially worth A\$2.2 billion by 2030.

Traditional fermentation involves using microorganisms (such as bacteria and yeast) to create food including yoghurt, bread or tempeh.

In precision fermentation, you customise the microorganisms to create new products. The US-based Every Company, uses customised microorganism strains to create a chicken-free substitute for egg white. Similarly, Perfect Day has created a cow-free milk.

Man made meats

Still want to eat meat, but are concerned about animal welfare or environmental impacts? Cultivated or cell-based meat is biologically similar to the regular variety, but the animal cells are grown in a lab, not a farm.

Australian company Vow is making pork and chicken, as well as kangaroo, alpaca and water buffalo meat using cells from animals. These products are not yet commercially available, though chef Neil Perry did use some of them to create a menu in 2020.

Edible insects

Edible insects, such as crickets and mealworms, have been part of cuisines around the world for millennia, including Australian First Nations Peoples.

Insects have a high nutritional value, are rich in protein, omega-3 fatty acids, iron, zinc, folic acid and vitamins B12, C and E.

Insect farming is also considered to have a low environmental footprint, and requires less land, water and energy.

Australian company Circle Harvest sells a range of edible insect products including pastas and chocolate brownie mixes enriched with cricket powder.

Protein is vital to our health. However, until now its production has placed strain on the health of most other ecosystems. CSIRO's protein roadmap offers not only sustainability, but also more choice for consumers and opportunities for Australian producers.

The Conversation, 18 April 2022

<https://theconversation.com>

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New inexpensive and nontoxic method for creating benzene rings

2022-04-14

Chemical syntheses in liquids and gases take place in three-dimensional space. Random collisions between molecules have to result in something new in an extremely short time. But there is another way: on a gold surface under ultrahigh vacuum conditions, molecules lying still next to each other can be made to combine—even those that would never want to react with each other in a liquid. Researchers at Empa have now discovered such a reaction. Best of all, the experts can “take pictures” and watch every step of the reaction.

In chemistry, there are structures that are particularly stable, such as the so-called “benzene ring” consisting of six interconnected carbon atoms. Such rings form the structural basis for graphite and graphene, but they also occur in many dyes—such as the jeans dye indigo and in many drugs such as aspirin.

When chemists wanted to build such rings in a targeted manner, they used so-called coupling reactions, which usually bear the name of their inventors: for example, the Diels-Alder reaction, the Ullmann reaction, the Bergman cyclization or the Suzuki coupling. Now there is another one that does not yet have a name. It was discovered by a team from Empa together with the Max Planck Institute for Polymer Research in Mainz. Their related research has been published in *Nature Synthesis* and *Nature Reviews Chemistry*.

Everything in the dry

The Empa researchers omitted liquids in their chemical synthesis and instead attached the starting materials to a gold surface in an ultra-high vacuum. The starting material (diisopropyl-p-terphenyl) can be observed resting calmly in the cooled-down scanning tunneling microscope before the researchers turn up the heat.

Turn up the heating—movement on the dance floor

At room temperature, nothing happens yet, but at about 200 degrees Celsius, an amazing reaction occurs that would never happen in liquids: the two isopropyl groups—which are normally completely inactive from a chemical point of view—combine to form a benzene ring. The reason: due to the firm “adhesion” on the gold surface, a hydrogen atom is first loosened and then released from the molecule. This creates carbon

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radicals that are waiting for new partners. And there are many partners on the gold surface. At 200 degrees Celsius, the molecules vibrate and perform rapid pirouettes—there is a lot of movement on the golden dance floor. So what belongs together soon gets together.

And once again everything in slow motion

Matchmaking on the golden surface has two advantages. First, there is no need for coercion: the reaction takes place without mediating boric acids or halogen atoms flying away. It is a coupling involving only saturated hydrocarbons. The starting materials are cheap and easy to obtain, and there are no toxic byproducts.

The second advantage is that the researchers can watch every step of the reaction—another thing that is not possible with classical, “liquid” chemistry. The Empa team simply turns up the heating of the gold surface gradually. At 180 degrees Celsius, the molecules have only connected one arm with their neighbors, the second still protrudes freely into the dance floor. If one now cools down the gold surface inside a scanning tunneling microscope, one can view and “photograph” the molecules just before they are “married off.” This is exactly what the researchers did. Thus, the reaction mechanism can be followed in the form of “snapshots.”

Opportunities for a ‘new’ chemistry

The researchers and their colleagues expect two kinds of effects to emerge from the current work. First, the “snapshot method” could also be suitable for elucidating completely different reaction mechanisms. At Empa, instruments are being developed that use ultrashort laser pulses in a scanning tunneling microscope to elucidate such chemical reactions step by step. This could provide additional insights into chemical reactions and soon shake up many an old theory.

However, the research results “from the dry” could also be useful to further develop “liquid” chemistry. So far, most of the reactions documented in the literature have come from classical liquid chemistry, and scanning probe researchers have been able to recreate these experiments. In the future, certain reactions could also be designed in the scanning tunneling microscope and later transferred to liquid or gaseous chemistry.

Phys Org, 14 April 2022

<https://phys.org>

[Benzene] rings form the structural basis for graphite and graphene, but they also occur in many dyes—such as the jeans dye indigo and in many drugs such as aspirin.

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Tumors partially destroyed with sound don't come back

2022-04-18

Noninvasive sound technology developed at the University of Michigan breaks down liver tumors in rats, kills cancer cells and spurs the immune system to prevent further spread -- an advance that could lead to improved cancer outcomes in humans.

By destroying only 50% to 75% of liver tumor volume, the rats' immune systems were able to clear away the rest, with no evidence of recurrence or metastases in more than 80% animals.

"Even if we don't target the entire tumor, we can still cause the tumor to regress and also reduce the risk of future metastasis," said Zhen Xu, professor of biomedical engineering at U-M and corresponding author of the study in *Cancers*.

Results also showed the treatment stimulated the rats' immune responses, possibly contributing to the eventual regression of the untargeted portion of the tumor and preventing further spread of the cancer.

The treatment, called histotripsy, noninvasively focuses ultrasound waves to mechanically destroy target tissue with millimeter precision. The relatively new technique is currently being used in a human liver cancer trial in the United States and Europe.

In many clinical situations, the entirety of a cancerous tumor cannot be targeted directly in treatments for reasons that include the mass' size, location or stage. To investigate the effects of partially destroying tumors with sound, this latest study targeted only a portion of each mass, leaving behind a viable intact tumor. It also allowed the team, including researchers at Michigan Medicine and the Ann Arbor VA Hospital, to show the approach's effectiveness under less than optimal conditions.

"Histotripsy is a promising option that can overcome the limitations of currently available ablation modalities and provide safe and effective noninvasive liver tumor ablation," said Tejaswi Worlikar, a doctoral student in biomedical engineering. "We hope that our learnings from this study will motivate future preclinical and clinical histotripsy investigations toward the ultimate goal of clinical adoption of histotripsy treatment for liver cancer patients."

Liver cancer ranks among the top 10 causes of cancer related deaths worldwide and in the U.S. Even with multiple treatment options, the prognosis remains poor with five-year survival rates less than 18% in the

Noninvasive sound technology breaks down liver tumors in rats, kills cancer cells and spurs the immune system to prevent further spread -- an advance that could lead to improved cancer outcomes in humans.

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U.S. The high prevalence of tumor recurrence and metastasis after initial treatment highlights the clinical need for improving outcomes of liver cancer.

Where a typical ultrasound uses sound waves to produce images of the body's interior, U-M engineers have pioneered the use of those waves for treatment. And their technique works without the harmful side effects of current approaches such as radiation and chemotherapy.

"Our transducer, designed and built at U-M, delivers high amplitude microsecond-length ultrasound pulses -- acoustic cavitation -- to focus on the tumor specifically to break it up," Xu said. "Traditional ultrasound devices use lower amplitude pulses for imaging."

The microsecond long pulses from UM's transducer generate microbubbles within the targeted tissues -- bubbles that rapidly expand and collapse. These violent but extremely localized mechanical stresses kill cancer cells and break up the tumor's structure.

Since 2001, Xu's laboratory at U-M has pioneered the use of histotripsy in the fight against cancer, leading to the clinical trial #HOPE4LIVER sponsored by HistoSonics, a U-M spinoff company. More recently, the group's research has produced promising results on histotripsy treatment of brain therapy and immunotherapy.

The study was supported by grants from the National Institutes of Health, Focused Ultrasound Foundation, VA Merit Review, U-M's Forbes Institute for Discovery and Michigan Medicine-Peking University Health Sciences Center Joint Institute for Translational and Clinical Research.

Science Daily, 18 April 2022

<https://sciencedaily.com>

Engineers develop new kind of 3D printing

2022-04-20

While 3D printing techniques have advanced significantly in the last decade, the technology continues to face a fundamental limitation: objects must be built up layer by layer. But what if they didn't have to be?

Dan Congreve, an assistant professor of electrical engineering at Stanford and former Rowland Fellow at the Rowland Institute at Harvard University, and his colleagues have developed a way to print 3D objects within a stationary volume of resin. The printed object is fully supported by the

While 3D printing techniques have advanced significantly in the last decade, the technology continues to face a fundamental limitation: objects must be built up layer by layer. But what if they didn't have to be?

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thick resin—imagine an action figure floating in the center of a block of Jell-O—so it can be added to from any angle. This removes the need for the support structures typically required for creating complex designs with more standard printing methods. The new 3D printing system, which was recently published in *Nature*, could make it easier to print increasingly intricate designs while saving time and material.

“The ability to do this volumetric printing enables you to print objects that were previously very difficult,” said Congreve. “It’s a very exciting opportunity for three-dimensional printing going forward.”

Printing with light

At its surface, the technique seems relatively straightforward: The researchers focused a laser through a lens and shone it into a gelatinous resin that hardens when exposed to blue light. But Congreve and his colleagues couldn’t simply use a blue laser—the resin would cure along the entire length of the beam. Instead, they used a red light and some cleverly designed nanomaterials scattered throughout resin to create blue light at only the precise focal point of the laser. By shifting the laser around the container of resin, they were able to create detailed, support-free prints.

Congreve’s lab specializes in converting one wavelength of light to another using a method called triplet fusion upconversion. With the right molecules in close proximity to each other, the researchers can create a chain of energy transfers that, for example, turn low-energy red photons into high-energy blue ones.

“I got interested in this upconversion technique back in grad school,” Congreve said. “It has all sorts of interesting applications in solar, bio, and now this 3D printing. Our real specialty is in the nanomaterials themselves—engineering them to emit the right wavelength of light, to emit it efficiently, and to be dispersed in resin.”

In this 3D printing process, the little dot of blue light triggers a chemical reaction that makes the resin harden into plastic. Credit: Tracy H. Schloemer and Aryn O. Gallegos

Through a series of steps (which included sending some of their materials for a spin in a Vitamix blender), Congreve and his colleagues were able to form the necessary upconversion molecules into distinct nanoscale droplets and coat them in a protective silica shell. Then they distributed

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the resulting nanocapsules, each of which is 1000 times smaller than the width of a human hair, throughout the resin.

“Figuring out how to make the nanocapsules robust was not trivial—a 3D-printing resin is actually pretty harsh,” said Tracy Schloemer, a postdoctoral researcher in Congreve’s lab and one of the lead authors on the paper. “And if those nanocapsules start falling apart, your ability to do upconversion goes away. All your contents spill out and you can’t get those molecular collisions that you need.”

Next steps for light-converting nanocapsules

The researchers are currently working on ways to refine their 3D-printing technique. They are investigating the possibility of printing multiple points at the same time, which would speed up the process considerably, as well as printing at higher resolutions and smaller scales.

Congreve is also exploring other opportunities to put the upconverting nanocapsules to use. They may be able to help improve the efficiency of solar panels, for example, by converting unusable low-energy light into wavelengths the solar cells can collect. Or they could be used to help researchers more precisely study biological models that can be triggered with light or even, in the future, deliver localized treatments.

“You could penetrate tissue with infrared light and then turn that infrared light into high-energy light with this upconversion technique to, for example, drive a chemical reaction,” said Congreve. “Our ability to control materials at the nanoscale gives us a lot of really cool opportunities to solve challenging problems that are otherwise difficult to approach.”

Additional Stanford co-authors of this research are postdoctoral scholar Tracy Schloemer; former visiting researcher Michael Seitz; and graduate student Aryn Gallegos. Other co-authors, including a co-lead author, are from the Rowland Institute at Harvard University.

Tech Xplore, 20 April 2022

<https://techxplore.com>

Uranus should be NASA’s top planetary target, influential report finds

2022-04-19

After decades in the shadow of the other planets, Uranus should become NASA’s focus of exploration, a panel of planetary scientists reported today

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in the field's long-awaited "decadal survey," a priority-setting report the agency will use to make its case to congressional funders. If the scientists get their wishes, NASA in the early 2030s will launch a \$4.2 billion orbiter and atmospheric probe to Uranus, seeking to understand the formation and composition of this ice giant. Intermediate between the rocky planets and gas giants in size, Uranus and its neighbor Neptune "represent a unique planetary type that we poorly understand," says Ravit Helled, a planetary scientist at the University of Zürich, one of 130 scientists who contributed to the survey.

The decision to favor Uranus over Neptune ultimately came down to celestial opportunism, says Robin Canup, a planetary scientist at the Southwest Research Institute and co-chair of the report, which was overseen by the National Academies of Sciences, Engineering, and Medicine. If launched on a Falcon Heavy rocket in 2031 or 2032, the orbiter could get a gravity assist from Jupiter and arrive in 13 years; Neptune would take far longer. "This mission is technically ready to go," Canup says. "We advocate that it be started right away." But whether that can happen depends on NASA figuring out a budget that has been strained by the pandemic and soaring mission costs.

It was Uranus's turn. The last decadal report, in 2011, ranked an ice giants mission third, following a set of missions to return rock samples from Mars and a visit to Europa, Jupiter's icy moon—missions that are now underway or in development. So perhaps the survey's biggest surprise is its recommendation for what comes after Uranus: a \$4.9 billion mission to Enceladus, the tiny moon of Saturn that spews organic-rich plumes of water out of fissures in an icy cap—ready-made samples of a subsurface ocean that might host microbes. "Enceladus is probably the best place to look for evidence of life that we can do today," says Philip Christensen, a planetary scientist at Arizona State University, Tempe, and the report's other co-chair. (The recommendation will mark an end for plans to put a lander on Europa's surface, which had previously been advanced as a top future mission.)

The report also lists targets for a set of competitive missions, called New Frontiers. Some concepts are familiar from past surveys: a Saturn probe, a comet sample return, a lunar geophysical network. Others are new: sample return from Ceres, the water-rich dwarf planet in the asteroid belt; an orbiter and lander to a Centaur, one of the small bodies between Jupiter and Neptune believed to capture the composition of the early Solar System; a Titan orbiter; a Venus lander; and an Enceladus plume

"Decadal survey" recommends \$4.2 billion flagship mission to the ice giant

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sampler. (Enceladus's inclusion in two different mission categories stresses its importance, Christensen says.)

NASA should also continue programs dedicated to exploring the Moon and Mars, the panel recommends. After the agency builds the Mars sample return missions, the panel calls for it to develop a \$1.1 billion robotic lander, called the Mars Life Explorer, that would drill 2 meters into midlatitude ice deposits.

For the Moon, the panel endorses the Artemis program, funded by NASA's human spaceflight division, which plans to return astronauts to the surface. But it suggests science should drive the choices of what to do, rather than being an afterthought. "It's not just flags and footprints," says Bethany Ehlmann, a planetary scientist at the California Institute of Technology and co-author of the report. The report calls for a \$1.5 billion long-range large robotic rover called Endurance-A that could cover 1000 kilometers, drill 100 kilograms worth of samples, and return them to astronauts who would eventually bring them back to labs on Earth.

Those ambitions will strain NASA's planetary science budget, now \$3.1 billion per year—the highest since the Viking missions to Mars in the 1970s. The Mars sample return campaign, which will retrieve rocks collected by the Perseverance rover, will cost more than \$7 billion and consume one-fourth of the planetary budget in the next few years. The cost of Europa Clipper, which after launch in 2024 will swoop past the moon nearly 50 times, has grown from \$4.25 billion to \$5 billion. And several cost-capped competitive missions have seen their budgets more than double because of the time needed to reach their remote destinations, a factor not included in their spending limits.

The budget overruns have led NASA to postpone missions: The ambitious Dragonfly rotocopter to Titan, Saturn's methane-rich moon, will now launch in 2027 instead of 2025, and the next New Frontiers selection will be delayed by several years. To stop this cycle, NASA needs to face reality and raise the cost caps for the two competitive mission lines, New Frontiers and Discovery, to \$1.65 billion and \$800 million, respectively, while also forcing those missions to fully account for lifetime costs. Those measures should still allow NASA to select five Discovery missions over a decade, but only one New Frontiers mission.

Although the planetary science budget has grown to accommodate big missions, the scientists who advance that work have not seen the same gains, the report stresses. The share of the budget spent over the past decade on research grants has fallen from 14% in 2010 to 7.7%.

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Progress has been made in recruiting more women to the field, but underrepresented racial and ethnic groups, notably Latino and Black scientists, make up just 5% and 1% of its workforce, respectively. “We have untapped talent and we’re missing out on great people and great ideas,” Canup says. The report recommends collecting better demographic data and expanding predoctoral programs that support students from underrepresented communities.

Students entering the field now could constitute the scientific heart of the mission targeting Uranus, which humanity first saw up close with the Voyager 2 flyby in 1986. That survey prompted many scientists to think of the ice giants as anomalies: stunted gas giants that accumulated only a couple Earth masses’ worth of hydrogen and helium before stopping, either because of a lack of gas or late formation. But since Voyager, astronomers have found thousands of planets around other stars, and many are Uranus-size, says Jonathan Fortney, a planetary scientist at the University of California, Santa Cruz. “Nature loves to make planets of this size.”

Uranus also holds its own individual appeal. Its spin axis lies nearly horizontal—likely the result of a giant impact early in its history that tipped it over. Compared with the other planets, it is also surprisingly cold, suggesting it either cooled quickly or that its atmosphere has put a lid on any heat escape. It has two sets of rings, along with a densely packed set of primordial moons and oddball objects, likely trapped comets or objects from a region beyond Neptune called the Kuiper belt. “Some may still have water on the inside,” says Kirby Runyon, a planetary scientist at the Johns Hopkins University Applied Physics Laboratory (APL).

For the lure of an ocean, however, it’s hard to top tiny Enceladus, just 504 kilometers wide. In 2005, NASA’s Cassini spacecraft spotted plumes of saltwater erupting from rifts in its icy surface. Subsequent flights through those plumes revealed abundant organic molecules, necessary to build life, along with silica and hydrogen gas, a sign that the ocean feeding the plumes probably has hydrothermal vents in its depths, a potential energy source for microbes.

The survey endorsed a hybrid “orbilander” mission to Enceladus, which would sample the plume and survey the moon’s surface for a couple of years before turning on its side and landing, a relatively easy task in a place with weak gravity and no appreciable atmosphere. It would target a place where the erupting water falls as snow, which its instruments could sample. Two would explicitly be aimed at detecting life: a DNA sequencer

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and a microscope. Enceladus has checked off all the requirements for habitability, says Shannon MacKenzie, a planetary scientist at APL who led a study developing the idea. “The next question is: Is Enceladus inhabited?”

Science, 19 April 2022

<https://science.org>

Scientists build microporous MOF traps for mitigating toxic gases

2022-04-20

Nitrogen dioxide and sulfur dioxide (NO₂ and SO₂) are toxic gases harmful to the environment and human health. Once they enter the atmosphere, they can travel hundreds of miles, polluting the air and causing acid rain which in turn damages buildings, trees, and crops. Exposure to the toxic gases can also lead to respiratory infections, asthma, and chronic lung disease.

For those reasons, the so-called acid gases are high on the list of pollutants targeted by the Clean Air Act, which requires the Environmental Protection Agency to regulate and set limits on NO₂ and SO₂ emissions with the goal of improving air quality and preventing widespread illnesses.

Scientists are developing materials that can detect and trap acid gases, an effort among some of the leading innovative strategies to mitigate air pollution and combat climate change. The approach consists of various technological solutions designed to filter the air by capturing or trapping toxic gases from emissions. In some cases, captured molecules can also be stored and reused—carbon dioxide, for example, can be reused in certain applications to promote photosynthesis and plant growth.

Materials called metal organic frameworks, or MOFs, could take acid-gas sequestration to the next level, making it a more viable, practical approach to improving air quality on a global scale. MOFs are essentially a microscopic matrix of metal atoms attached to each other by organic molecules that form a repeating pattern of tiny, interconnected metal cages. They act like a sponge that can adhere, or soak up, molecules to its surface. In fact, MOFs are so highly porous that the amount that would fit inside someone’s pocket, if stretched out, would cover the surface of an entire football field.

In a recent study published in the journal ACS Applied Materials and Interfaces, researchers searching for candidate materials to remediate

Scientists are developing materials that can detect and trap acid gases, an effort among some of the leading innovative strategies to mitigate air pollution and combat climate change.

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NO₂ and SO₂ investigated a series of MOFs that can be made from the entire family of rare-earth metals. They used computer simulations and a combination of neutron and X-ray scattering experiments to help them determine the optimal conditions for synthesizing the materials. In the process, they also uncovered important details about an interesting defect that forms in the MOFs that they say could be useful in building devices for capturing emissions or sensing dangerous levels of toxic gases.

“Metal organic frameworks are really novel in their flexibility, their chemistry, and how you can tailor their structure. If you swap out organic molecules, you can tune the structure to target different gases,” said Sandia National Laboratory’s Susan Henkelis, the study’s lead author. “Acid gases typically come from combustion processes, so this research could be useful in developing devices to help limit emissions from large-scale industrial facilities like oil refineries and fossil fuel-based power plants.”

The team includes researchers from the Department of Energy’s (DOE) Sandia and Oak Ridge national laboratories (ORNL) and the University of Tennessee, Knoxville (UTK). The researchers are part of the Center for Understanding and Control of Acid Gas-Induced Evolution of Materials, or UNCAGE-ME, a program developed specifically to understand the interactions between acid gases and solid materials. UNCAGE-ME is part of a broader research effort supported by DOE’s Energy Frontier Research Center (EFRC) program, which brings together the research capabilities of universities and national laboratories to provide atomic-scale insights into tackling some of the world’s biggest energy challenges that can only be achieved through large collaborations.

“The fundamental science objective of this work was aimed at understanding how the chemistry and the synthesis process creates these defects, because we want to know how the defects can be controlled and what their affect is on adsorption of acid gases,” said Peter Metz, a postdoctoral researcher at UTK who worked in Neutron Sciences at ORNL during the time of the study. “To do that, we need to understand how the atomic bonds in the MOFs form and how the atoms are arranged.”

Ideally, the cages inside each synthesized MOF form a cube. Each corner contains a cluster of six rare-earth metal ions with another cluster in the center of the cube. Each pair of metal ions in the cluster connects to another pair in another cluster by a single link, or linker molecule.

But sometimes a defect occurs, especially in MOFs made of europium ions, where the linker kinks and exposes the rare-earth ion, which increases the likelihood a pollutant molecule will become trapped within the structure.

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To find out why this happens, the researchers used a combination of neutron and X-ray scattering experiments to map the materials’ atomic structures.

They used X-rays to find the heavy metal elements, which provided an outline of the overall structure. And, to better understand how the organic molecules are arranged, they bombarded the materials with neutrons using the POWGEN instrument at ORNL’s Spallation Neutron Source (SNS), which helped them track the positions of the hydrogen, carbon, and oxygen atoms that form the molecular bonds between the metal ion clusters.

From the experiments, the team was able to determine that the materials with the defects actually formed more rapidly than their defect-free counterparts. They also discovered the defects could be intentionally induced by adjusting the temperatures and the time it takes to grow the crystalline materials.

The team then used the structural data obtained from the experiments to run computer simulations to see how each of the materials—with and without the defects—interacted with the toxic gases NO₂ and SO₂.

“While these new insights are on the basic research side of things, they could have a big impact down the road,” said Sandia’s Tina Nenoff, the study’s corresponding author. “We learned new information about how these materials form, which we can use to control and design MOFs with more specificity. And furthermore, we developed a comprehensive approach to evaluating large series of MOFs, which will help expedite the pace of finding new candidate materials and developing them in useful technologies.”

Phys Org, 20 April 2022

<https://phys.org>

Neural network can read tree heights from satellite images

2022-04-20

Using an artificial neural network, researchers at ETH Zurich have created the first high-resolution global vegetation height map for 2020 from satellite images. This map could provide key information for fighting climate change and species extinction, as well as for sustainable regional development planning.

Researchers at ETH Zurich have developed a world map that for the first time uses machine learning to derive vegetation heights from satellite images in high resolution.

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Last year marked the beginning of the UN Decade on Ecosystem Restoration. This initiative is aimed at halting the degradation of ecosystems by 2030, preventing it going forward and, if possible, remedying the damage that has already been done. Delivering on these kinds of projects calls for accurate foundations, such as surveys and maps of the existing vegetation.

In an interview, Ralph Dubayah, the Principal Investigator of NASA's Global Ecosystem Dynamics Investigation (GEDI) mission, explains: "We simply do not know how tall trees are globally. [...] We need good global maps of where trees are. Because whenever we cut down trees, we release carbon into the atmosphere, and we don't know how much carbon we are releasing."

Analyzing and preparing precisely this kind of environmental data is what the EcoVision Lab in the ETH Zurich Department of Civil, Environmental and Geomatic Engineering specializes in. Founded by ETH Zurich Professor Konrad Schindler and University of Zurich Professor Jan Dirk Wegner in 2017, this lab is where researchers are developing machine learning algorithms that enable automatic analysis of large-scale environmental data. One of those researchers is Nico Lang. In his doctoral thesis, he developed an approach—based on neural networks—for deriving vegetation height from optical satellite images. Using this approach, he was able to create the first vegetation height map that covers the entire Earth: the Global Canopy Height Map.

The map's high resolution is another first: thanks to Lang's work, users can zoom in to as little as 10x10 meters of any piece of woodland on Earth and check the tree height. A forest survey of this kind could lead the way forward particularly in dealing with carbon emissions, as tree height is a key indicator of biomass and the amount of carbon stored. "Around 95 percent of the biomass in forests is made up of wood, not leaves. Thus, biomass strongly correlates with height," explains Konrad Schindler, Professor of Photogrammetry and Remote Sensing.

Trained with laser scanning data from space

But how does a computer read tree height from a satellite image? "Since we don't know which patterns the computer needs to look out for to estimate height, we let it learn the best image filters itself," Lang says. He shows his neural network millions of examples—courtesy of the images from the two Copernicus Sentinel-2 satellites operated by the European Space Agency (ESA). These satellites capture every location on Earth every

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five days with a resolution of 10x10 meters per pixel. They are the highest-quality images currently available to the public.

The algorithm must also have access to the correct answer—that is, the tree height derived from space laser measurements from NASA's GEDI mission. "The GEDI mission delivers globally distributed, sparse data on the vegetation height between the latitudes of 51 degrees north and south, so the computer sees many different vegetation types in the training process," Lang explains. With the input and answer, the algorithm can acquire the filters for textural and spectral patterns itself. Once the neural network has been trained, it can automatically estimate the vegetation height from the more than 250,000 images (some 160 terabytes of data) needed for the global map.

In specialist jargon, Lang's neural network is known as a convolutional neural network (CNN). The "convolution" is a mathematical operation in which the algorithm slides a 3x3 pixel filter mask over the satellite image to obtain information on brightness patterns in the image. "The trick here is that we stack the image filters. This gives the algorithm contextual information, since every pixel, from the previous convolution layer, already includes information about its neighbors," Schindler says. As a result, the EcoVision Lab was the first to successfully use satellite maps to also reliably estimate tree heights of up to 55 meters.

Because their many layers make these neural networks "deep," this method is also called "deep learning." It heralded a major revolution in image processing around ten years ago. However, dealing with the sheer amount of data remains very challenging: calculating the global vegetation height map would take a single powerful computer three years. "Fortunately, we have access to the ETH Zurich high-performance computing cluster, so we didn't have to wait three years for the map to be calculated," Lang says with a laugh.

Transparency by estimating uncertainties

Lang didn't prepare just one CNN for this task, but several. This is known as an ensemble. "An important aspect for us was also letting users know the uncertainty of the estimate," he says. The neural networks—five altogether—were trained independently of each other, with each one returning its own estimate of tree height. "If all the models agree, then the answer is clear based on the training data. If the models arrive at different answers, it means there is a higher uncertainty in the estimate," Lang explains. The models also incorporate uncertainties in the data itself: if a

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satellite image is hazy, for instance, the uncertainty is greater than when atmospheric conditions are good.

Foundation for future ecological research

Thanks to its high resolution, Lang's global map provides detailed insights: "We have already discovered interesting patterns," Schindler says. "In the Rocky Mountains, for example, forests are managed in fixed sections, and the rainforest also forms interesting structures that can't be coincidental." Now ecologists can interpret these captured patterns and data globally.

To allow this research to continue, the map and its source code will be made publicly accessible (see link). The first interested parties have already been in touch: Walter Jetz, a professor at Yale University, wants to use the Global Canopy Height Map for biodiversity modeling. However, the map could also be of interest to governments, administrative bodies and NGOs. "Thanks to Sentinel-2, vegetation height can be recalculated every five days, making it possible to monitor rainforest deforestation," Lang says.

In addition, he adds, it is now also possible to globally validate regional findings, such as the way tropical leaf canopies act as a climate buffer. Coupled with the High Carbon Stock Approach, which classifies forests according to their carbon storage and biodiversity value, the vegetation height map is an important foundation for maintaining and strengthening ecosystems. According to Lang's calculations, vegetation with a height of more than 30 meters is found on only 5 percent of the landmass, and only 34 percent of it is located in protected areas.

With the GEDI mission set to end in 2023, Lang's newly developed approach offers the possibility to continue mapping vegetation height in future. However, getting the GEDI mission extended—something that is currently also being discussed in the media internationally—is key to comparing its data with future satellite missions such as the ESA Biomass mission and calibrating the model for changes.

Tech Xplore, 20 April 2022

<https://techxplore.com>

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Scientists resurrect ancient enzymes to improve photosynthesis

2022-04-18

A Cornell study describes a breakthrough in the quest to improve photosynthesis in certain crops, a step toward adapting plants to rapid climate changes and increasing yields to feed a projected 9 billion people by 2050.

The study, "Improving the Efficiency of Rubisco by Resurrecting Its Ancestors in the Family Solanaceae," was published April 15 in *Science Advances*. The senior author is Maureen Hanson, the Liberty Hyde Bailey Professor of Plant Molecular Biology in the College of Agriculture and Life Sciences. First author Myat Lin is a postdoctoral research associate in Hanson's lab.

The authors developed a computational technique to predict favorable gene sequences that make Rubisco, a key plant enzyme for photosynthesis. The technique allowed the scientists to identify promising candidate enzymes that could be engineered into modern crops and, ultimately, make photosynthesis more efficient and increase crop yields.

Their method relied on evolutionary history, where the researchers predicted Rubisco genes from 20–30 million years ago, when Earth's carbon dioxide (CO₂) levels were higher than they are today and the Rubisco enzymes in plants were adapted to those levels.

By resurrecting ancient Rubisco, early results show promise for developing faster, more efficient Rubisco enzymes to incorporate into crops and help them adapt to hot, dry future conditions, as human activities are increasing heat-trapping CO₂ gas concentrations in Earth's atmosphere.

The study describes predictions of 98 Rubisco enzymes at key moments in the evolutionary history of plants in the Solanaceae family, which include tomato, pepper, potato, eggplant and tobacco. Researchers use tobacco as the experimental model for their studies of Rubisco.

"We were able to identify predicted ancestral enzymes that do have superior qualities compared to current-day enzymes," Hanson said. Lin developed the new technique for identifying predicted ancient Rubisco enzymes.

Scientists have known that they can increase crop yields by accelerating photosynthesis, where plants convert CO₂, water and light into oxygen and sugars that plants use for energy and for building new tissues.

The authors developed a computational technique to predict favorable gene sequences that make Rubisco, a key plant enzyme for photosynthesis.

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For many years, researchers have focused on Rubisco, a slow enzyme that pulls (or fixes) carbon from CO₂ to create sugars. Aside from being slow, Rubisco also sometimes catalyzes a reaction with oxygen in the air; by so doing, it creates a toxic byproduct, wastes energy and makes photosynthesis inefficient.

Hanson's lab had previously tried to use Rubisco from cyanobacteria (blue-green algae), which is faster but also reacts readily with oxygen, forcing the researchers to try to create micro-compartments to protect the enzyme from oxygen, with mixed results. Other researchers have tried to engineer more optimal Rubisco by making changes in the enzyme's amino acids, though little was known about which changes would lead to desired results.

In this study, Lin reconstructed a phylogeny—a tree-like diagram showing evolutionary relatedness among groups of organisms—of Rubisco, using Solanaceae plants.

"By getting a lot of [genetic] sequences of Rubisco in existing plants, a phylogenetic tree could be constructed to figure out which Rubiscos likely existed 20 to 30 million years ago," Hanson said.

The advantage of identifying potential ancient Rubisco sequences is that carbon dioxide levels were possibly as high as 500 to 800 parts per million (ppm) in the atmosphere 25 million to 50 million years ago. Today, heat-trapping CO₂ levels are rising sharply due to many human activities, with current measurements at around 420 ppm, after staying relatively constant under 300 ppm for hundreds of millennia until the 1950s.

Lin, Hanson and colleagues then used an experimental system developed for tobacco in Hanson's lab, and described in a 2020 *Nature Plants* paper, which employs *E. coli* bacteria to test in a single day the efficacy of different versions of Rubisco. Similar tests done in plants take months to verify.

The team found that ancient Rubisco enzymes predicted from modern-day Solanaceae plants showed real promise for being more efficient.

"For the next step, we want to replace the genes for the existing Rubisco enzyme in tobacco with these ancestral sequences using CRISPR [gene-editing] technology, and then measure how it affects the production of biomass," Hanson said. "We certainly hope that our experiments will show that by adapting Rubisco to present day conditions, we will have plants that will give greater yields."

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If their method proves successful, these efficient Rubisco sequences could be transferred into crops such as tomatoes, as well as those from other plant families, such as soybeans and rice.

Phys Org, 18 April 2022

<https://phys.org>

Could gut microbes regulate appetite and body temperature?

2022-04-14

With more microbes than cells in our body, it's not surprising that bacteria and other invisible "guests" influence our metabolism, immune system, and even our behavior. Now, researchers studying mice have worked out how bacteria in the mammalian gut can ping the brain to regulate an animal's appetite and body temperature—and it involves the same molecular pathway the immune system uses to detect bacterial pathogens.

"It's quite an important finding," says Antoine Adamantidis, a neuroscientist at the University of Bern who was not involved with the work. "Our life depends on food intake, and this is one more [thing] that bacteria can [influence]."

Over the past 20 years, researchers have uncovered connections between the human gut and the rest of the body. They have linked certain intestinal microbes to conditions such as depression, multiple sclerosis, and immune system disorders; they have also documented nervous system connections between the gut and the brain. But researchers have been hard pressed to understand exactly how gut microbes—or the molecules they make— influence the brain.

When certain gut bacteria infiltrate the rest of the body, our immune system picks up on them by sensing fragments of their cell walls, known as muropeptides. Our molecular detectors for these muropeptides, proteins called Nod2, coat the surfaces of cells involved in the body's first line of defense. Ilana Gabanyi, a neuroimmunologist at the Pasteur Institute, wanted to know whether these molecular detectors also exist in the brain's nerve cells.

Gabanyi and colleagues started with genetically engineered mice: Some were designed to lack Nod2, and others were engineered to produce a fluorescent tag that marked wherever the molecular detector was

Bacterial cell wall molecules that travel to the brain could trigger a host of behaviors

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made. The first evidence that mucopeptides influence appetite came from the mice without Nod2. Compared with regular mice, these rodents gained extra weight as they aged. That suggested, Gabanyi says, that the mucopeptides may provide a “full” signal to the brain that is absent in Nod2-free mice. Because food can stimulate microbes in the gut, eating likely induces the release of mucopeptides, she adds.

Next, she and colleagues fed other mice slightly radioactive mucopeptides. Four hours later, they checked to see where the mucopeptides traveled in the rodents’ bodies. By monitoring for radioactivity, they found that the mucopeptides had traveled to the brain. Together, the experiments reveal Nod2 is indeed produced in the mouse brain, and that mucopeptides can get there within hours of reaching the gut, Gabanyi and her colleagues report today in *Science*.

“I had no idea that these [fragments] make it into the brain,” says Christine McDonald, a molecular biologist who studies the body’s bacterial sensors at the Cleveland Clinic.

The experiments also showed radioactive mucopeptides build up more in female mouse brains than in male brains, and have stronger effects on females, Gabanyi says. Older female mice lacking Nod2 in the brain ate more per meal than mice that had not been genetically modified. They also maintained a higher body temperature and tended to spend less time building nests to stay warm—indicating that Nod2 might have other physiological roles.

There were other downsides of disrupting this gut-brain communication pathway: Female mice without a normal complement of Nod2 tended to develop diabetes and did not live as long as typical mice. And mice given antibiotics to kill off their gut bacteria had similar problems; researchers think this is because mucopeptides never got into the brain to help regulate appetite and body temperature.

Together, the new experiments identify a direct mechanism by which bacteria can control the brain, says Livia Hecke Morais, a neurobiologist at the California Institute of Technology. Until now, demonstrations of such direct connections “have been lacking,” adds Margaret McFall-Ngai, a developmental biologist at the Carnegie Institution for Science.

Unclear is whether Nod2’s role in the brain, or its immune function, came first. “The same molecule that alerts our immune system that something is wrong could be used by our nervous system as a signal to regulate key survival processes” such as eating and temperature control, says Juan

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Escobar, an evolutionary biologist studying gut microbes at the Vidarium Nutrition, Health, and Wellness Research Center who was not involved with the work.

Based on the findings in the older, female mice, Gabanyi and her colleagues speculate that the mucopeptide control system gains importance as hormone-driven regulation of appetite and body temperature declines with age. Similar hormonal changes in women entering menopause are associated with weight gain and hot flashes, making researchers wonder whether the mucopeptide-Nod2 system could provide a nonhormonal target for treating those problems. If this system also exists in humans, “there’s a lot of potential [for treatment],” Morais says.

Still other scientists stressed that the findings were in mice—and therefore need much further study. But McFall-Ngai notes that in squid, Nod2 also senses bacterial cell wall fragments and helps controls the animal’s development. So she is convinced this communication system is an ancient one, likely to be found in all vertebrates.

Science, 14 April 2022

<https://science.org>

Time might not exist, according to physicists and philosophers — but that’s okay

2022-04-17

Does time exist? The answer to this question may seem obvious: of course it does! Just look at a calendar or a clock.

But developments in physics suggest the non-existence of time is an open possibility, and one that we should take seriously.

How can that be, and what would it mean? It’ll take a little while to explain, but don’t worry: even if time doesn’t exist, our lives will go on as usual.

A crisis in physics

Physics is in crisis. For the past century or so, we have explained the universe with two wildly successful physical theories: general relativity and quantum mechanics.

Physicists want to produce a theory of “quantum gravity” that replaces general relativity and quantum mechanics, while capturing the extraordinary success of both.

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Quantum mechanics describes how things work in the incredibly tiny world of particles and particle interactions. General relativity describes the big picture of gravity and how objects move.

Both theories work extremely well in their own right, but the two are thought to conflict with one another. Though the exact nature of the conflict is controversial, scientists generally agree both theories need to be replaced with a new, more general theory.

Physicists want to produce a theory of “quantum gravity” that replaces general relativity and quantum mechanics, while capturing the extraordinary success of both. Such a theory would explain how gravity’s big picture works at the miniature scale of particles.

Time in quantum gravity

It turns out that producing a theory of quantum gravity is extraordinarily difficult.

One attempt to overcome the conflict between the two theories is string theory. String theory replaces particles with strings vibrating in as many as 11 dimensions.

However, string theory faces a further difficulty. String theories provide a range of models that describe a universe broadly like our own, and they don’t really make any clear predictions that can be tested by experiments to figure out which model is the right one.

In the 1980s and 1990s, many physicists became dissatisfied with string theory and came up with a range of new mathematical approaches to quantum gravity.

One of the most prominent of these is loop quantum gravity, which proposes that the fabric of space and time is made of a network of extremely small discrete chunks, or “loops”.

One of the remarkable aspects of loop quantum gravity is that it appears to eliminate time entirely.

Loop quantum gravity is not alone in abolishing time: a number of other approaches also seem to remove time as a fundamental aspect of reality.

Emergent time

So we know we need a new physical theory to explain the universe, and that this theory might not feature time.

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Suppose such a theory turns out to be correct. Would it follow that time does not exist?

It’s complicated, and it depends what we mean by exist.

Theories of physics don’t include any tables, chairs, or people, and yet we still accept that tables, chairs and people exist.

Why? Because we assume that such things exist at a higher level than the level described by physics.

We say that tables, for example, “emerge” from an underlying physics of particles whizzing around the universe.

But while we have a pretty good sense of how a table might be made out of fundamental particles, we have no idea how time might be “made out of” something more fundamental.

So unless we can come up with a good account of how time emerges, it is not clear we can simply assume time exists.

Time might not exist at any level.

Time and agency

Saying that time does not exist at any level is like saying that there are no tables at all.

Trying to get by in a world without tables might be tough, but managing in a world without time seems positively disastrous.

Our entire lives are built around time. We plan for the future, in light of what we know about the past. We hold people morally accountable for their past actions, with an eye to reprimanding them later on.

We believe ourselves to be agents (entities that can do things) in part because we can plan to act in a way that will bring about changes in the future.

But what’s the point of acting to bring about a change in the future when, in a very real sense, there is no future to act for?

What’s the point of punishing someone for a past action, when there is no past and so, apparently, no such action?

The discovery that time does not exist would seem to bring the entire world to a grinding halt. We would have no reason to get out of bed.

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Business as usual

There is a way out of the mess.

While physics might eliminate time, it seems to leave causation intact: the sense in which one thing can bring about another.

Perhaps what physics is telling us, then, is that causation and not time is the basic feature of our universe.

If that's right, then agency can still survive. For it is possible to reconstruct a sense of agency entirely in causal terms.

At least, that's what Kristie Miller, Jonathan Tallant and I argue in our new book.

We suggest the discovery that time does not exist may have no direct impact on our lives, even while it propels physics into a new era.

Sam Baron is an associate professor at Australian Catholic University. This piece first appeared on The Conversation.

ABC News, 17 April 2022

<https://abc.net.au>

How do I improve my motivation to exercise when I really hate it? 10 science-backed tips

2022-04-14

We've all heard those people who say "running gives you a high" or "exercise is addictive," but for many of us, it's hard to love exercise. Some might even say they hate it, dread it, or the thought of going to the gym gives them anxiety.

Why do some of us hate exercise? And how can we overcome this to reap the lifesaving benefits of getting the body moving?

Humans didn't evolve to 'exercise'

Throughout most of human history, food was scarce and being active wasn't a choice. For millennia, humans had to move to find food, and once they were fed, they rested to conserve energy, because they didn't know where their next meal was coming from.

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So, if you have the urge to sit down and watch Netflix rather than going to the gym, you might take solace in the knowledge resting is a natural human tendency.

Having said that, our 21st-century lifestyles involve far too much sitting and resting. With technology, cars, and other labour-saving devices, moving is no longer necessary for daily survival.

Yet, being physically inactive is terrible for our health. A meta-analysis published in prestigious medical journal The Lancet found physical inactivity is associated with a 30-40% increased risk of colon cancer, 30% increased risk of breast cancer, 20-60% increased risk of type 2 diabetes, and a 30-50% higher risk of premature death, compared with being physically active.

So how much physical activity do you actually need?

It's recommended Australian adults (aged 18-65) get at least 150 (though preferably 300) minutes of moderate-intensity physical activity each week. Moderate intensity exercise might be a brisk walk, light cycle or mowing the lawn.

If you are willing to do vigorous physical activity, you only need half that (75-150 minutes per week). Vigorous activity is anything strenuous enough you would struggle to have a conversation: jogging, or running around playing a sport like footy or tennis.

A variety of activity types are encouraged since different physical activities entail different benefits. Muscle-strengthening exercises, like lifting weights or doing push ups, are encouraged twice a week, to keep bones and muscles strong.

If that is all starting to sound too complicated, rest assured ANY exercise is good for you. You don't have to achieve the physical activity guidelines to benefit from physical activity.

What are some science-backed tips for getting motivated?

According to psychologists there are two main types of motivation: extrinsic and intrinsic motivation. Intrinsic motivation arises from within – doing something for the personal reward or challenge of it. Extrinsic motivation comes from external factors, like trying to earn a reward or avoid a punishment.

You can boost your *intrinsic* motivation by identifying why exercising is important to you.

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1. Identify your “why” – do you want to exercise for your health? Is it for your kids? Is it for how working out makes you feel? Exercise has long-term benefits for health and function, flow-on benefits for your children, and immediate effects on mood and vitality. Being clear in your mind about what you want to gain from exercising, can help prompt you into action.

Extrinsic motivators can also help you get started with exercise.

2. Arrange to meet a friend to exercise together. You’ll be more likely to follow through, as you won’t want to let your friend down. Also, research suggests people exercise for longer when they exercise with family members and friends compared with those who exercise alone

3. Reward yourself with a new piece of clothing or shoes you’ll enjoy exercising in. Be sure to make the reward conditional on doing a certain amount of exercise, so you have to earn it

4. Get an activity tracker. Fitness trackers have a host of features designed to boost motivation, such as prompts, self-monitoring and goal-setting. There is a plethora of research suggesting activity trackers increase physical activity

5. Exercise at the same time each day, so it becomes a habit. Research suggests exercising in the morning leads to faster habit formation compared with evening exercise

6. Do an activity you enjoy. Starting a new exercise habit is hard enough. Increase your chances of sticking with it by doing an activity you find enjoyable. Also, you may exercise at a higher intensity without even realising it, if you are doing a form of exercise you enjoy. If you hate running, don’t do it. Go for a long walk in nature

7. Start small. Leave yourself wanting more, rather than overdoing it. You’re also less likely to feel sore or injure yourself

8. Listening to up-beat music improves mood during exercise, and reduces perceived exertion, leading to increased work output. These benefits are particularly effective for rhythmic, repetitive forms of exercise, such as walking and running

9. Take your dog for a walk. Dog-walkers walk more often and for longer than non-dog walkers, and they report feeling safer and more socially connected in their neighbourhood

10. Make a financial commitment. Behavioural economic theory recognises humans are motivated by loss aversion. Some commercial

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websites have harnessed this for health by getting people to make a “commitment contract” in which they pay a financial deposit that is forfeited if the health behaviour commitment is not met. This approach has been shown to improve physical activity, medication adherence and weight loss.

Be patient with yourself, and keep the long game in mind – it takes around three to four months to form an exercise habit. After that, the intrinsic motivators take over to keep your exercise routine going. Who knows, maybe you’ll be the one hooked on exercise and inspiring your friends and family a few months from now.

The Conversation, 14 April 2022

<https://theconversation.com>

Anti-aging technology is coming. Here’s how you can be ready for it

2022-04-15

The world’s billionaires are pouring money into age-reversal investments.

Last September, it came out that Jeff Bezos had invested in Altos Labs, a company pursuing biological reprogramming technology. “Reprogramming” is the scientific term for turning old cells young again. It was discovered in 2012 by Japanese scientist Shinya Yamanaka, who called it a potential “elixir of life.” The Nobel Prize in Medicine Committee seemed to agree.

Bezos—and Altos—aren’t the only ones.

There’s Google-backed Calico Labs, also focused on longevity via reprogramming. And Lineage Cell Therapeutics, backed by BlackRock, Raffles Capital Management, Wells Fargo, and others.

Coinbase Co-founder and CEO Brian Armstrong recently invested in a company working to radically extend human healthspan using epigenetic reprogramming therapies. Altogether, the anti-aging industry is expected to grow to over \$64 billion by 2026, a 45% increase from its 2020 value (\$44 billion).

So, why are billionaires like Jeff Bezos investing in age-reversal or “anti-aging” tech?

Because they have a Longevity Mindset.

Billionaires like Jeff Bezos believe that aging is a disease that can be slowed, stopped, even reversed. But you have to be ready to receive its benefits.

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WHAT EXACTLY IS A LONGEVITY MINDSET?

One way to understand the Longevity Mindset is by looking at its opposite.

Most people take the aging process for granted. If they're disciplined, healthy, and lucky, they'll get 20 or so years of youth, start declining in their 40s, and die sometime between 60 and 80.

They accept that life expectancy is 81.2 years for females and 76.4 years for males—nothing they can do, just take the lemons and make lemonade.

And who can blame them? Nearly every human institution—governments, the insurance industry, medicine, religion—is organized around this mindset.

The anti-Longevity Mindset is: mortality is inevitable, youth is fleeting.

So, the Longevity Mindset is: mortality is avoidable, youth is extendable.

If that sounds shocking to you, you're not the only one. For years, scientists supporting a Longevity Mindset were shunned, and as a result longevity studies were tabled for fear of losing grant funding.

But medicine has evolved.

We've entered a period of exponential medicine: Innovations like genome sequencing, RNA transcriptomics, Wnt pathway modifiers, vaccines, CRISPR, liquid biopsies, CAR-T cells, Gene Therapy, exosomes, and stem cells are just a sampling of the technologies that the world's billionaires are fast-tracking.

Free from the narrow paradigm of academia, these scientists earn as much as five to ten times a top professor's salary by working for Altos and others.

Ultimately, aging is a disease—a disease that many of the most powerful people on the planet believe can be slowed, stopped, even reversed.

That's the spirit of the Longevity Mindset.

HOW TO DEVELOP YOUR OWN LONGEVITY MINDSET

Examine and assess the six basic areas of life that everyone, whether you live on the margins or in a mansion, must negotiate.

- Beliefs. At one end of the spectrum are people who see age 75 as the end. At the other end are people who see aging as a disease, and who

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actively track breakthroughs in biotech that have the potential to slow or even reverse aging. Which are you?

- Media diet. The films, books, articles you consume have a deep, direct impact on how you think. Does your media diet reinforce the anti-longevity mindset? Or are you reading books like David Sinclair's *Lifespan*, blogs like mine, newsfeeds like www.LongevityInsider.org?
- Community. The people we spend time with also shape our mindset. Do you spend time with people who constantly worry about death? Or do you hang out with a younger, more vital crowd who surround you with optimism and a youthful vision of the future?
- Sleep habits. We physiologically need eight hours of sleep per night. Do you burn the candle at both ends? Or do you prioritize this most valuable resource, using the best techniques to help you?
- Your diet. You very literally are what you eat. The nutrients (or non-nutrients) you consume become your body, your mind, your spirit. Do you overindulge in good-tasting (sugar-rich) but destructive foods? Or do you craft a sensible diet and practice intermittent fasting to maximize your energy and longevity?
- Exercise habits. Exercise—especially that which increases muscle mass—is crucial to longevity. Do you exercise a minimum of three times a week—perhaps taking peptides to maximize growth hormones and increase muscle mass?
- Mindset. Do you cultivate your Longevity Mindset? Do you see your future as bigger than your past?

Laying the foundation of a Longevity Mindset doesn't take any capital investment. Everyone has beliefs, a media diet, and a community. Everyone has to sleep, eat, and move around.

In the background, billionaires like Bezos are accelerating the industry, working to bring cutting-edge longevity tech to human beings.

When they do, will you be ready?

Fast Company, 15 April 2022

<https://fastcompany.com>

Company's limited data release backs promise of new, lower dose vaccine designed to be easier to distribute and cheaper

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An mRNA vaccine with a twist—it copies itself—protects against COVID-19

2022-04-18

A third messenger RNA (mRNA) vaccine appears to have proved its worth against COVID-19. And although it is more than a year behind the Moderna and Pfizer-BioNTech vaccines now seen as gold standards, the new vaccine may come with significant advantages: easier storage, along with lower cost because its “self-amplifying” design allows for smaller doses.

Arcturus Therapeutics of San Diego, which staged a placebo-controlled trial of its candidate in more than 17,000 participants in Vietnam, announced yesterday in a press release that the vaccine had 55% efficacy against symptomatic COVID-19 and provided 95% efficacy against severe illness and death. “It’s a huge accomplishment that for the first time a self-amplifying RNA vaccine has been shown to be safe and effective,” says Deborah Fuller, a vaccinologist at the University of Washington School of Medicine who is an adviser to HDT Bio, which has its own self-amplifying COVID-19 mRNA vaccine in human studies.

Arcturus’s success may also help make mRNA vaccines more broadly accessible. Its candidate incorporates a freeze-drying process to transform the mRNA-filled solution into a powder that can be stored at room temperature, then rehydrated. This has far simpler cold-chain requirements than the conventional, liquid mRNA vaccines in use. And Vietnam’s Vinbiocare Biotechnology, which collaborated with Arcturus on the trial and has submitted the efficacy data to the country’s regulators for emergency use authorization, hopes to manufacture the product there.

The Pfizer-BioNTech and Moderna vaccines contain mRNA that codes for the SARS-CoV-2 spike protein. When the vaccines are injected, they deliver the mRNA to cells, which make copies of spike and then clear the foreign genetic material within a few days. Arcturus’s self-amplifying vaccine and others in development include enzymes from alphaviruses to repeatedly copy the genetic strand inside a cell and stay in the body for more than twice as long.

Some researchers have cautioned that self-amplifying vaccines cannot use an mRNA modification that is key to the Moderna and Pfizer-BioNTech vaccines: the replacement of the natural RNA building block uridine with pseudouridine. Studies have shown the swap leads to higher levels of the spike protein and lower production of immune chemicals called cytokines

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that can cause side effects. A conventional mRNA vaccine made by CureVac failed in an efficacy trial last year, and some scientists suggested this may have been because it didn’t use pseudouridine. But Arcturus says the efficacy findings refute those concerns. “It’s a big deal for the field,” says Pad Chivukula, the company’s chief scientific officer.

The trial, which began in August 2021, gave participants two doses, each containing 5 micrograms of the self-amplifying mRNA, spaced 28 days apart. The Pfizer-BioNTech and Moderna vaccines use 30-microgram and 100-microgram doses, respectively, for the first two shots.

Like most COVID-19 vaccinemakers with fresh efficacy trial results, Arcturus only released a peek at the findings. The bottom line against symptomatic infection—55% efficacy—is below the 90% to 95% seen in trials of the first two mRNA vaccines. But those vaccines faced the original SARS-CoV-2 virus. The Arcturus candidate, based on a similar strain, had to protect against the Delta and Omicron variants that were circulating in Vietnam during the trial, which have evolved dramatically from the ancestral strain, decreasing the power of vaccine-triggered antibodies. Fuller says the current real-world effectiveness of existing mRNA vaccines may be in the same ballpark. Of the 43 severe cases of COVID-19 recorded by Arcturus during the trial, only two were in the vaccinated group, and nine of the 10 people with COVID-19 who died received the placebo.

“These are indeed exciting results,” says chemist Benjamin Pierce, who is helping run a Ugandan trial of a self-amplifying mRNA COVID-19 vaccine made by Imperial College London. “The low dose used here—six to 20 times lower than approved RNA vaccines—further indicates that self-amplifying RNA technology has such potential. I look forward to seeing more of the data from the trial.”

Fuller says a self-amplifying mRNA COVID-19 vaccine ideally would replace the two primary doses, giving it an even clearer benefit over its conventional relatives. A booster months later might still be warranted, as is encouraged now for the current mRNA vaccines. But self-amplifying mRNAs could also lead to more durable immune responses, Fuller suggests.

When the Arcturus trial began, less than 15% of the eligible Vietnamese population had received even a single shot of a COVID-19 vaccine. Now, the figure is 80%, which raises the question of how the vaccine will perform in the vast majority of people who have already been vaccinated or naturally exposed to SARS-CoV-2. Arcturus hopes to soon launch a 2400-person trial to assess its value as a booster shot. This trial will aim

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to show the vaccine boosts antibody responses that other studies have shown correlate with protection—though no new COVID-19 vaccine has yet received authorization from strict U.S. or European regulators based on “immunobridging” data.

The Pfizer-BioNTech collaboration and Moderna have received intense criticism for not quickly sharing their manufacturing skills and intellectual property with developing countries, which have had relatively little access to their mRNA vaccines. Arcturus, in contrast, in August 2021 agreed to a technology transfer deal with Vinbiocare, which is building a plant in Hanoi to manufacture the vaccine.

But with much of the world vaccinated, the Arcturus vaccine may be making its debut too late, at least for primary vaccination. Chivukula is confident it will find a market in countries that have far lower vaccination rates than Vietnam and stresses it will be at “a price point that everyone can afford.”

Science, 21 April 2022

<https://science.org>

There's more than one way to grow a baby

2022-04-20

In his 1989 book *Wonderful Life*, evolutionary biologist Stephen Jay Gould famously argued that, if we could “replay the tape”, life on Earth would evolve to be fundamentally different each time.

Was he right? Convergent evolution, in which similar features evolve to perform similar functions in distantly related organisms, offers an excellent model in which to run Gould's thought experiment.

One classic example of convergent evolution is the independent evolution of wings and flight in insects, birds, pterosaurs, and bats. Another is live birth (or “viviparity”), which has evolved independently from egg-laying more than 150 times in vertebrates (animals with backbones).

To understand how this happened, we studied the genes involved in pregnancy and live birth in six different live-bearing species. We discovered that, despite broad similarities in the anatomy and physiology involved, each species used a completely different set of genetic tools to give birth to live young.

Is live birth controlled by a universal set of genes?

The changes that occur during pregnancy and birthing must be mainly controlled by genetics, and we know that the expression of genes changes during pregnancy in different live-bearing animals.

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In nearly all live-bearing vertebrates examined so far, changes to the gestational tissues and biophysical processes during pregnancy appear remarkably similar.

Some common elements of the process are:

- tissues in the bodies of the mother and fetus which grow more blood vessels to exchange gases and water with each other
- protection of the fetus from the mother's immune system
- allocation of nutrients to the fetus.

The changes that occur during pregnancy and birthing must be mainly controlled by genetics, and we know that the expression of genes changes during pregnancy in different live-bearing animals.

However, the generality of these changes is less clear. For example, are the same genes used during pregnancy in mammals and fish? Or are similar outcomes driven by entirely different genes?

That's what we set out to discover in our study, newly published in *Molecular Biology and Evolution*, in collaboration with researchers from the University of Queensland and James Cook University.

Measuring gene activity during pregnancy

An animal's development is controlled by its genes, its environment, and an interaction between the two.

Not every gene within an animal is always active. Genes are switched on (or “expressed”) when needed, and then switched off again when no longer needed.

Gene expression levels naturally vary over time as an animal interacts with the environment and undergoes physiological changes, such as those associated with pregnancy. Using a technique called “transcriptomics”, we can take snapshots of these changes in gene expression as they occur.

To investigate the genetic changes occurring in the uterus during pregnancy in different species, we collected samples or used existing data from six live-bearing animals: the Australian sharpnose shark, three species of Australian lizards, the gray short-tailed opossum, and the brown lab rat.

Sampling this wide range of animals allowed us to determine whether the same gene expression changes occur during pregnancy across species in which live birth evolved independently.

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Our work is the first quantitative study into the genetic basis of live birth at such a broad evolutionary scale.

There are many different ways to grow a baby

We expected to find many of the same genes used during pregnancy to support the growth and survival of embryos in each of the live-bearing species we sampled.

This hypothesis seemed logical, given the many similarities in anatomical changes during pregnancy across live-bearing vertebrates, along with qualitative findings from previous research.

Instead, we found there was no one set of “live-bearing genes” utilised during pregnancy across our sampled range of animals. In other words, evolution has converged on similar functions for successful pregnancy but those functions have been achieved by recruiting different groups of genes.

Despite not being what we expected, this finding also makes sense. Different animal lineages may have different “toolboxes” of genes to draw from, due to their unique evolutionary histories.

A genetic “toolbox” can be thought of as a broad class of genes that perform similar basic functions. Over the long timescales of evolution, different genes from this ancestral toolbox can be recruited to carry out the same physiological functions in different animals.

For example, developing babies require access to a supply of amino acids for successful development. In many species these amino acids are transported from the mother to the fetus across the placenta via “solute carrier” genes.

We identified more than 75 different solute carrier genes in the combined genetic toolbox of our study species. However, each species recruited different genes from the toolbox to transport amino acids during pregnancy.

Rethinking live birth

Our findings force us to rethink the idea that the cross-species similarities in live birth are controlled by the same genetic changes.

We can also consider our results in the context of Gould’s thought experiment about “replaying the tape of life”.

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Was the evolution of live birth predictable? It depends on how you look at it.

Large-scale similarities, such as the anatomy and functions of the uterus, seem predictable. They appear to have evolved repeatedly to solve the biophysical challenges of successful pregnancy.

However, our results show this predictability does not extend to the underlying genes.

The Conversation, 20 April 2022

<https://theconversation.com>

Surprising strategy would fight mutant cancer cells by making more mutations

2022-04-19

Researchers are devising ways to paint targets on cancer cells. Drugs that unleash the immune system against cancer can be powerfully effective, but they appear to work best on the subset of tumors that are most riddled with mutations. Enter a controversial solution: Use chemotherapy to deliberately create new mutations in tumors and thereby make them more vulnerable to an immune system attack.

Lab studies and several small clinical trials already hint the strategy may help. “There might be an opportunity to begin to remodel the genetics of the tumor in such a way” that immunotherapy works better, a leader of one trial, cancer geneticist Luis Diaz of Memorial Sloan Kettering Cancer Center, said at a plenary session here at the annual meeting of the American Association for Cancer Research (AACR).

Still, some cancer researchers are leery of purposely inducing mutations and say animal experiments suggest doing so could cause more harm than good. “I question the rationale,” says melanoma immunotherapy researcher Antoni Ribas of the University of California, Los Angeles.

Drugs called checkpoint inhibitors remove a molecular brake that keeps immune sentries called T cells from attacking tumors. They work best on cancers such as lung tumors triggered by smoking-induced DNA damage and melanomas, which accumulate mutations from ultraviolet (UV) light. Many of these genetic changes cause cells to make “neoantigens,” novel protein fragments on tumor cells that flag them to T cells.

Chemotherapies that induce new DNA errors may help unleash the immune system on tumors

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The notion that forcing cancer cells to make more neoantigens might bolster immunotherapy traces back to studies of tumors with defects in certain mechanisms that repair DNA. These cancer cells accumulate many mutations, and in 2015 a team led by Diaz, then at Johns Hopkins University, reported that checkpoint drugs work well on multiple tumor types with these “mismatch” DNA repair defects.

Cancer geneticist Alberto Bardelli of the University of Turino and colleagues went further by deliberately inactivating a mismatch repair gene in tumor-bearing mice. They reported in *Nature* in 2017 that the change resulted in a buildup of DNA errors in the cancer cells and boosted the effectiveness of checkpoint drugs.

Since then, two Italian trials have documented similar effects in people. One study gave the standard chemotherapy drug temozolomide, which disables mismatch repair genes, to 33 people with advanced colon cancer, which normally does not respond to checkpoint inhibitors because it has too few mutations. The chemotherapy alone shrank tumors in eight people but another seven people similarly responded after all later received two checkpoint inhibitors. Tumor growth halted in the overall group for an average of 7 months, the team reported last month in the *Journal of Clinical Oncology*.

In four patients who had tumor biopsies analyzed, as well as in 14 of 16 patients in a trial described in a poster at the AACR meeting, the team showed that temozolomide had induced mutations. Bardelli says the preliminary data offer a “proof of concept.”

Diaz wondered whether inducing a specific kind of mutation would work even better. His team was particularly interested in a type that shifts how a cell’s proteinmaking machinery reads a gene’s messenger RNA. Such a “frameshift” mutation can change many of the amino acids of a gene’s protein, making it more foreign to the immune system.

Postdoc Benoit Rousseau and others in the Diaz lab tested temozolomide and another chemotherapy drug, cisplatin, on cancer cells and found the combination produced 1000 times more frameshift mutations than either drug alone. When cancer cells treated with the drug combination were injected into mice, the resulting tumors vanished in response to a checkpoint drug.

Diaz’s team is now giving the combination to people with metastatic colon tumors before they receive a checkpoint drug. In two of the first 10 patients, tumor cell DNA shed into their blood showed they had

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developed relatively high levels of frameshift mutations—and their tumors stopped growing. “It’s early days,” Diaz cautions, but the results give “a flavor of what we’re expecting.”

Still, there’s an obvious safety concern: The chemotherapy drugs might also create mutations in a patient’s healthy cells. Diaz says his group has not seen new tumors in mice treated with the drugs.

Some researchers worry the approach will be counterproductive. They say tumors made up of one or just a few genetically identical cell lineages, or clones, respond better to checkpoint inhibitor drugs than highly heterogenous masses do. Ribas fears that inducing more mutations creates new clones in a tumor and dilutes the impact of any T cells unleashed. He points to a 2019 study in which an Israeli group used UV light to create mutations in melanoma tumors in mice and found the increased diversity of cancer cells actually hampered the checkpoint inhibitor response.

Bardelli, now also at the FIRC Institute of Molecular Oncology, Milan, says UV light induces a less immunogenic type of mutation than temozolomide. And Diaz and Rousseau argue that their team’s two-drug approach will spin out so many potent neoantigen targets for T cells that any harm from greater genetic heterogeneity within the tumor will be minimal.

“What we are doing is different,” says Bardelli, who founded a company, with Diaz as an adviser, to develop cancer drugs that will block mismatch repair enzymes—and, the team hopes, turn cancer cells into sitting ducks.

Science, 19 April 2022

<https://science.org>

Astronomers discover micronovae, a new kind of stellar explosion

2022-04-20

A team of astronomers, with the help of the European Southern Observatory’s Very Large Telescope (ESO’s VLT), have observed a new type of stellar explosion—a micronova. These outbursts happen on the surface of certain stars, and can each burn through around 3.5 billion Great Pyramids of Giza of stellar material in only a few hours.

“We have discovered and identified for the first time what we are calling a micronova,” explains Simone Scaringi, an astronomer at Durham

“The phenomenon challenges our understanding of how thermonuclear explosions in stars occur. We thought we knew this, but this discovery proposes a totally new way to achieve them”

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University in the U.K. who led the study on these explosions published today in *Nature*. "The phenomenon challenges our understanding of how thermonuclear explosions in stars occur. We thought we knew this, but this discovery proposes a totally new way to achieve them," he adds.

Micronovae are extremely powerful events, but are small on astronomical scales; they are much less energetic than the stellar explosions known as novae, which astronomers have known about for centuries. Both types of explosions occur on white dwarfs, dead stars with a mass about that of our sun, but as small as Earth.

A white dwarf in a two-star system can steal material, mostly hydrogen, from its companion star if they are close enough together. As this gas falls onto the very hot surface of the white dwarf star, it triggers the hydrogen atoms to fuse into helium explosively. In novae, these thermonuclear explosions occur over the entire stellar surface. "Such detonations make the entire surface of the white dwarf burn and shine brightly for several weeks," explains co-author Nathalie Degenaar, an astronomer at the University of Amsterdam, the Netherlands.

Micronovae are similar explosions that are smaller in scale and faster, lasting just several hours. They occur on some white dwarfs with strong magnetic fields, which funnel material towards the star's magnetic poles. "For the first time, we have now seen that hydrogen fusion can also happen in a localized way. The hydrogen fuel can be contained at the base of the magnetic poles of some white dwarfs, so that fusion only happens at these magnetic poles," says Paul Groot, an astronomer at Radboud University in the Netherlands and co-author of the study.

"This leads to micro-fusion bombs going off, which have about one millionth of the strength of a nova explosion, hence the name micronova," Groot continues. Although "micro" may imply these events are small, do not be mistaken: just one of these outbursts can burn through about 20,000,000 trillion kg, or about 3.5 billion Great Pyramids of Giza, of material.

These new micronovae challenge astronomers' understanding of stellar explosions and may be more abundant than previously thought. "It just goes to show how dynamic the Universe is. These events may actually be quite common, but because they are so fast they are difficult to catch in action," Scaringi explains.

The team first came across these mysterious micro-explosions when analyzing data from NASA's Transiting Exoplanet Survey Satellite (TESS).

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"Looking through astronomical data collected by NASA's TESS, we discovered something unusual: a bright flash of optical light lasting for a few hours. Searching further, we found several similar signals," says Degenaar.

The team observed three micronovae with TESS: two were from known white dwarfs, but the third required further observations with the X-shooter instrument on ESO's VLT to confirm its white dwarf status.

"With help from ESO's Very Large Telescope, we found that all these optical flashes were produced by white dwarfs," says Degenaar. "This observation was crucial in interpreting our result and for the discovery of micronovae," Scaringi adds.

The discovery of micronovae adds to the repertoire of known stellar explosions. The team now want to capture more of these elusive events, requiring large scale surveys and quick follow-up measurements. "Rapid response from telescopes such as the VLT or ESO's New Technology Telescope and the suite of available instruments will allow us to unravel in more detail what these mysterious micronovae are," Scaringi concludes.

This research was presented in a paper titled "Localized thermonuclear bursts from accreting magnetic white dwarfs" to appear in *Nature*. A follow-up letter, titled "Triggering micronovae through magnetically confined accretion flows in accreting white dwarfs" has been accepted for publication in *Monthly Notices of the Royal Astronomical Society*.

Phys Org, 20 April 2022

<https://phys.org>

Global warming is speeding up ocean currents. Here's why

2022-04-20

Two years ago, oceanographers made a surprising discovery: Not only have oceans been warming because of human-driven climate change, but the currents that flow through them have accelerated—by some 15% per decade from 1990 to 2013. At the time, many scientists suspected faster ocean winds were driving the speedup. But a new modeling study fingers another culprit: the ocean's own tendency to warm from top to bottom, leading to constricted surface layers where water flows faster, like blood in clogged arteries. The study suggests climate change will continue to

Excess heat constricts water flow in shallow surface layers

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speed up ocean currents, potentially limiting the heat the ocean can capture and complicating migrations for already stressed marine life.

“This mechanism is important,” says Hu Shijian, an oceanographer at the Chinese Academy of Sciences’s Institute of Oceanology, who was the lead author on the 2020 paper. “[The new paper] links directly the surface warming and acceleration of upper ocean circulation.”

Currents like the Atlantic Ocean’s Gulf Stream are highways for marine life, ushers of heat, and drivers of storms. Driven in large part by wind, each of them moves as much water as all the world’s rivers combined. And, despite the fact that the ocean absorbs more than 90% of the heat caused by global warming, until 2020, there had been little evidence that these currents were changing.

When Shang-Ping Xie, a climate scientist at the Scripps Institution of Oceanography, saw Hu’s study, he immediately suspected that the structure of the ocean—not winds—played a leading role in the speedup. He knew the excess warmth from climate change is not distributed evenly through the ocean but is instead concentrated at its surface. This causes surface waters to grow more buoyant—and more reluctant to mix with waters below. The shallower surface layers created by this process have been seen across the world’s oceans.

Xie and his colleagues also realized that, in shallower layers, currents would naturally have to speed up: In effect, the winds were pushing the same amount of water through a narrower pipe. “If you assume the total transport can’t change, your stuff is going to accelerate,” Xie says.

To test that hypothesis, Xie’s team turned to a climate model of all the world’s oceans. The researchers increased either winds, saltiness, or surface temperatures, while holding all other variables steady. Increasing temperatures alone caused currents to speed up more than 77% of the ocean’s surface. That was by far the largest increase, they found in a new study published today in *Science Advances*. One notable exception was the Gulf Stream, which is likely slowing for an unrelated reason: As Arctic ice melts, it dilutes the sinking, salty water in the North Atlantic that pulls the current northward.

“This is an interesting study with a provocative finding,” says Sarah Gille, a physical oceanographer at Scripps. “We usually assume that if you uniformly warm the ocean, there will be no major impact on ocean circulation.” Accounting for the top-down nature of ocean warming changes that picture, she adds.

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The new findings also suggests that in much of the ocean, lower waters, some 400 meters or so down, would slow as warm upper waters take up more and more of the movement, Xie says. Hu is not so certain of that, however. Unpublished measurements of the speed of Argo floats, a fleet of robotic instruments that have been drifting through the ocean for nearly 20 years, show a significant acceleration in surface currents—and a modest increase at lower depths. “I trust what the observations tell us,” Hu says. The new finding, he adds, “might not be the total story.”

But if ocean currents are indeed becoming faster and shallower, there are many implications for the planet. For example, the shallow, speedy currents could ultimately limit how much heat the ocean can absorb, causing more of that excess heat to remain in the atmosphere. Marine microbes and wildlife could be subjected to shallower, hotter, and faster surface waters. And given that the speedup is driven by the steady drumbeat of warming, it means these trends are likely to continue in the future—as long as human emissions of greenhouse gases continue.

Science, 20 April 2022

<https://science.org>

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Technical Notes

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[Environmental Co-Exposure to Potassium Perchlorate and Cd Caused Toxicity and Thyroid Endocrine Disruption in Zebrafish Embryos and Larvae \(*Danio rerio*\)](#)

[Comprehensive interpretation of in vitro micronucleus test results for 292 chemicals: from hazard identification to risk assessment application](#)

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