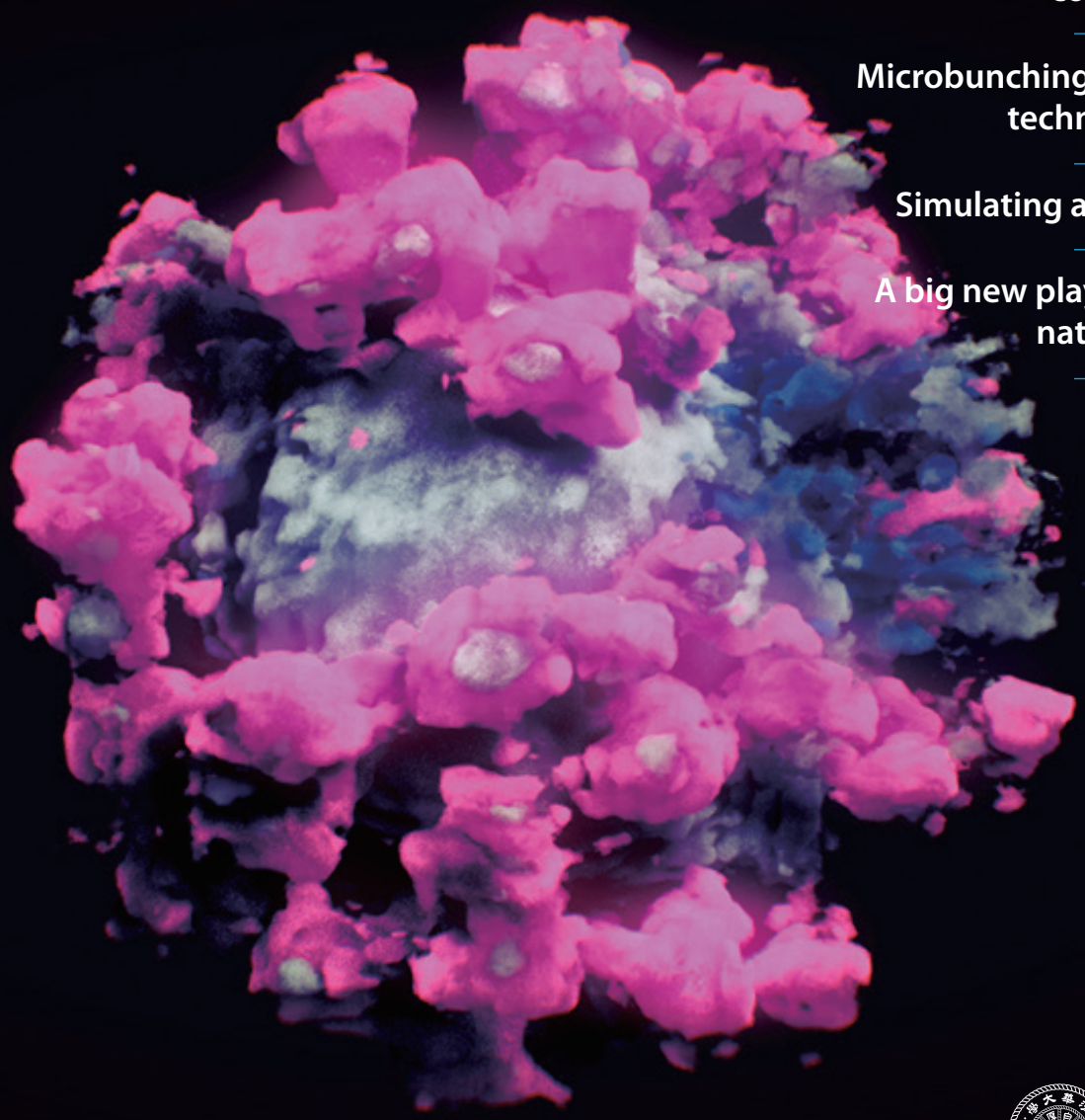
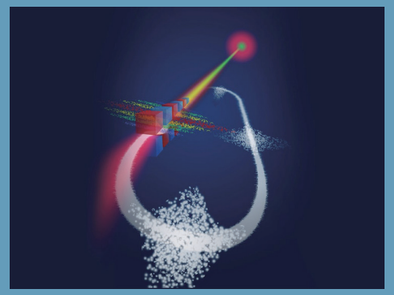
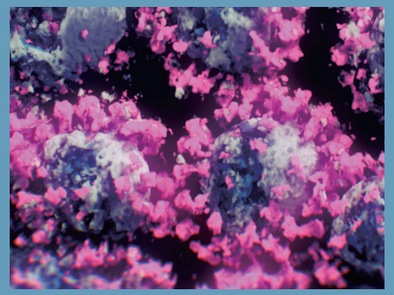
RESEARCH FEATURE 2021



清華大學
Tsinghua University





FOREWORD

As one of the world's leading universities, Tsinghua University stands at the forefront of high-quality scientific research and technological innovation. Tsinghua scientists and researchers have made major breakthroughs in a wide range of fields, constantly pushing the frontiers of science and technology and defining the future.

Take the flue gas treatment project at Tsinghua, for instance. Professor Junhua Li runs the flue gas treatment project through Tsinghua's School of Environment, and he is leading China's industrial emission-reduction effort. His group's focus has been selective catalytic reduction systems to remove ozone-depleting, smog-inducing and acid rain-causing nitrogen oxides, which are major air pollutants produced by several industries, including coal-fired power. Today, the flue gas treatment project at Tsinghua has 110 authorized patents, more than a dozen of software copyrights, and they have participated in shaping 25 environmental standards and technical specifications.

Another such breakthrough was the discovery of a new source of high-power extreme-ultraviolet (EUV) light, called steady-state microbunching (SSMB), by a group of researchers at Tsinghua in collaboration with two other prominent research institutions. This new source of EUV has the potential to redefine how semiconductor circuits, an essential component for the operation of electronic devices, are manufactured in the future as it can be used not just to etch more intricate patterns onto semiconductor circuits, but also to produce them in high volumes.

Likewise, early in the Covid-19 pandemic, a group led by Professor Sai Li at Tsinghua University detailed the molecular shape of SARS-CoV-2 at sub nanometer resolutions. The details on the molecular architecture of the COVID-19 virus were key for vaccine developers around the world in helping outline the shapes of its rich genome, flailing spikes, and sugar shields.

The groundbreaking discoveries made by Tsinghua University's faculty and researchers through their tireless hard work, perseverance and creativity have changed the way we see the world and beyond.

The Research Feature 2021 provides a closer look at some of their many outstanding accomplishments, and it showcases how innovation lies at the heart of Tsinghua's spirit of academic excellence as the University strives to become a leading world-class university.

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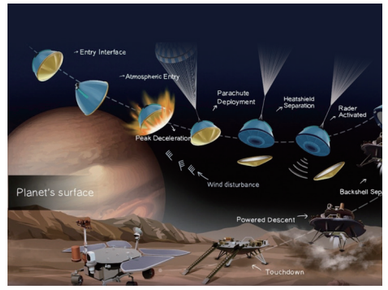
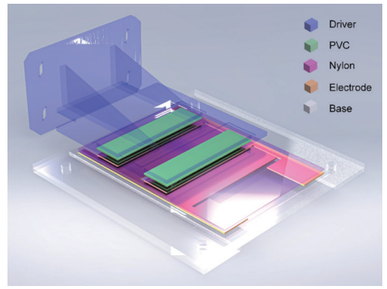
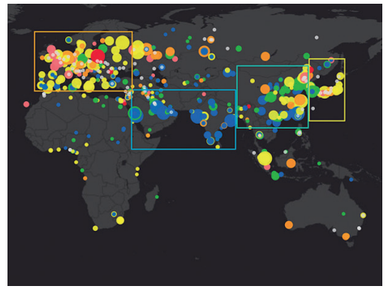
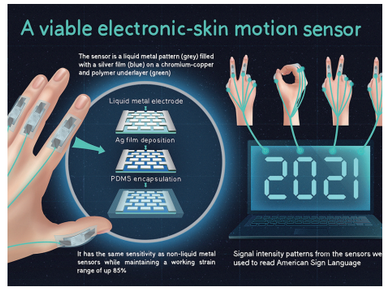








Psychology plan promotes positivity in a pandemic

Kaiping Peng designed much-needed social wellbeing support tools for those facing crises in the pandemic.

Early in the COVID-19 pandemic, social media was making 18 to 30-year-olds more anxious about the crisis. "We found the more people used social media, the more uncertain they felt, particularly in that age range," explains Kaiping Peng, an expert in positive psychology, a field that focuses on how to support psychological wellbeing across large groups. Peng, who was once the world's most cited social psychologist at his level, heads the Tsinghua Happiness Technology Laboratory (H+Lab), as well as a number of other departments at Tsinghua University.

His team's social media study was among a flurry from the lab that revealed that anxiety about the world's crisis was likely heightened by modern communication. At the apex of China's outbreak, a nationwide survey of roughly 53,000 people suggested more than a third of the Chinese population was experiencing symptoms of depression, anxiety, insomnia or acute stress.

In January 2020, on the first night of Wuhan lockdown, Peng was called in to discussions on preparations for a government-supported psychological assistance hotline. His experience working on post-traumatic relief efforts after the 2008 Sichuan earthquake, and SARS and MERS outbreaks in East Asia suggested that timely intervention is essential not just for those directly affected, but also the general public's sense of shared security and empathy. "In contrast to psychiatry for patients in need, positive psychology targets the general public," Peng explains.

Professor Kaiping Peng runs Tsinghua Happiness Technology Laboratory (H+Lab). He is also Dean of the School of Social Sciences.

Positive psychology, a field that focuses on how to support psychological wellbeing across large groups, is being used to help Chinese populations through the COVID-19 pandemic.

Within a fortnight, he had mobilized hotline volunteers with a background in psychological studies. This eventually included 23 clinical psychologists, 186 research supervisors and 2,836 research assistants. Alongside 3,453 volunteers, the group undertook training in counselling and how to support healthy individual strengths and behaviors.

The first hotline established was for medical staff in Wuhan hospitals, and it was later extended to their families, and then more widely to Chinese nationals and students. An English-language line was even established for foreigners in China. To date, Peng's team have received 14,322 hotline calls, and successfully counselled 154 people who expressed suicidal intentions. "These hotlines are part of our concerted efforts to identify and assist populations most susceptible to psychological risks, from native Wuhan citizens to the COVID-19 generation growing up in this pandemic," explains Peng.

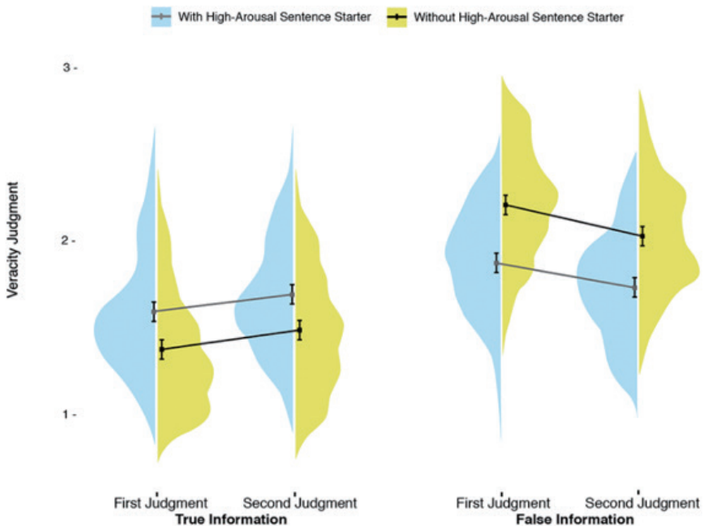
The rise of social psychology

Peng was tenured at the University of California, Berkeley, until he moved to Tsinghua to re-establish their Department of Psychology in 2008. Initially, he moved for a short stint, but was persuaded to make the move permanent. In 2014, Peng presented the findings of a study that canvassed 200-million people on their mood to the United Nations in New York. The study is possibly the largest of its kind ever conducted.

The results combined variables such as education levels and crime rates with big data on linguistic factors to identify the five happiest cities in China. According to Peng, each is traditionally rich in Chinese history and culture, has a government that follows 'happy city' policies that include concerted efforts at positive language in official communication, and is in a medium financial situation that is neither extremely rich nor poor.

More recently, Peng has focused on issues brought to the fore by the pandemic, assessing the effect of phenomena such as 'the sleeper effect', a theory on long-term cognitive vulnerability to fake news. First proposed by American psychologist, Carl Hovland, the sleeper effect describes how the persuasiveness of a poorly credible message increases over time. "Consistent with the sleeper effect, participants in a recent study exhibited a delayed but significant increase of arousal towards false information over the course of the pandemic, which was linked to increased anxiety," Peng explains. "This finding highlights the importance of timely intervention to clarify unscientific claims."

Both studies underline the importance of governance to a general sense of wellbeing across populations, Peng points out. Indeed, the pandemic has opened the door to the use of positive psychology as a large-scale crisis management tool. "Today we are



In one study, H+Lab found that when participants judged information after a time delay, their belief in true information decreased and their belief in false information increased. On the veracity judgment scale, 1 indicates participants think it's true, 2 indicates not sure, 3 indicates false.

focusing on putting social psychology theories into practice, including amassing volunteers to take part in arguably the biggest psychological campaign of Chinese history, with 13 hotlines working 24/7," notes Peng.

The hard science on feeling good

Peng and his team are also looking at the outcomes of the pandemic and asking key questions that include:

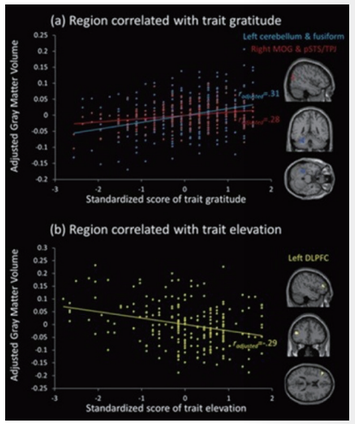
- how do we best evaluate human resilience to enclosure, isolation, and exposure long-term to negative information;
- how do cross-cultural responses to the pandemic differ, and what effect does this have on collective action;
- what have the effects been on child development and family relationships;
- how can we optimize employee health and teamwork while working remotely.

Based on these findings, the H+Lab are developing support technology that integrates bioengineering and big data on psychological indicators, including online platforms that provide psychological tests and positive psychology-based exercises.

Some exercises will stem from Peng's prior work on neural correlations. Specifically, brain scan studies that show how the activation of the dorsolateral prefrontal cortex in the prefrontal brain links to self-criticism. He has recently followed this up with studies that demonstrate how self-care interventions, such as meditation and guided writing exercises, can reduce the negative emotions and anxiety felt by study participants.

This research has also informed the ongoing development of a self-monitoring program to track facial expressions via selfies and videos, as part of a comprehensive self-assessment system to identify underlying emotional currents. "For these studies we ensure confidentiality," Peng emphasizes. "You have the right to withdraw any time without any consequences. The early detection of psychological distress using this type of technology could be game-changing," he adds. "People are often not consciously aware of their own changing outlook until a crisis point is reached."

"The government can play a big role in supporting a sense of wellbeing across its population," Peng concludes. While academic tenure in the United States is notoriously difficult to achieve, he made the move back to China because he felt that there was the support and scope for his work to make a huge difference. The pandemic has only further reinforced this belief, he says. "As we enter the post-pandemic new normal, our ongoing efforts to support public welfare will put our theories to good use."



MRI and questionnaires have been used to identify the common and distinct neuroanatomical correlates of the traits of gratitude and elevation (the uplifted feeling that people experience when they see unexpected acts of human goodness).

A clear view of industrial emissions control technology

Tsinghua researchers are at the forefront of industrial pollution mitigation, helping set emissions benchmarks and exporting their systems to the world.

This Baosteel plant in China must make sure its nitrogen oxides emissions comply with new 'ultra-low' 50 mg/m³ emission criteria by 2025.

For a hazy fortnight in 2013, China made global headlines when record air pollution levels around the country sparked major public health concerns. Today, Chinese technologies enable the enforcement of coal-fired power and industrial furnace emissions standards that are much more stringent than those in the United States or European Union. The country has also become a major exporter of emissions-reducing industrial flue gas treatment systems.

Professor Junhua Li runs a key flue gas treatment project through Tsinghua's School of the Environment, and he is leading China's industrial emission-reduction effort. His group's focus has been selective catalytic reduction systems to remove ozone-depleting, smog-inducing and acid rain-causing nitrogen oxides, which are major air pollutants produced by several industries, including coal-fired power.

Produced by the combustion of coal, petroleum, natural gas, and other fossil fuels, nitrogen oxides are being tackled with everything from vanadium pentoxide catalysts to specific performance parameters of ammonia escape, explains Li. Between 2013 and 2017, China moved to the point where denitrification systems were used in 92% of its coal-fired power plants.

"Our solutions have already helped both to set and fulfill very ambitious national targets," Li points out, "including lowering nitrogen oxides emissions by 17% between 2013 and 2017".

Since 2014, China has also required nitrogen oxides emissions of less than 50 mg/m^3 for newly built power plants, compared to 95 mg/m^3 in the United States and 150 mg/m^3 in the European Union.

With nearly half of the world's total installed capacity of coal-fired power, the size of China's industry makes it viable and expedient to develop and implement its own, sometimes tighter, environmental standards, explains Li. These, he says, can better adapt to the country's unique technical needs and conditions, such as the specificity of domestic coal.

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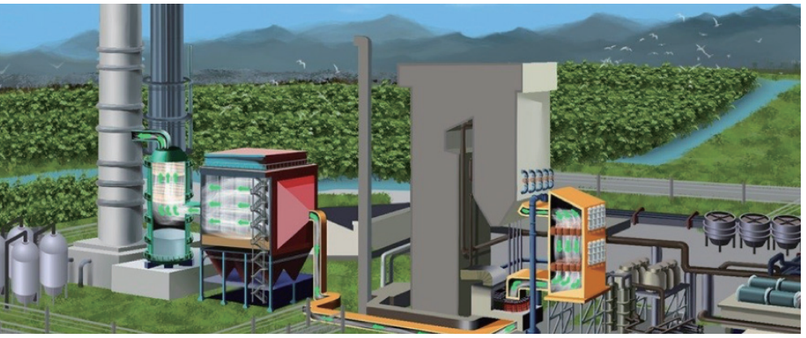
But coal-fired flue gas also contains hazardous substances other than nitrogen oxides, including particulate matter (PM), sulfur oxides (SOx), and heavy metals. The removal of these substances is relatively straightforward and the relevant scrubbing and filtering technologies are already established.

Li's next aim is to develop integrated systems for the removal of two or more different pollutants in single-stage treatments. He has already worked with domestic companies to make this integrated technology viable, and hopes to pair this with domestication of the entire production chain – from raw material production to catalyst manufacture, and recycling of used catalysts.



Doubling Coal-fired power plants produce a number of dirty, smog-causing flue gas emissions. Of these, nitrogen oxides (NOx) can be mitigated using a process called selective catalytic reduction, which transforms NOx into water and nitrogen gas. Excess dust can be removed at the following precipitator. And finally, sulfur dioxide (SO_2) gas can be 'scrubbed' out through flue-gas desulphurization down on denitrification.

Greenfield for steel, cement, and glass

With the problem of air pollution from existing coal-fired power plants now being addressed, Li is now looking to score similar successes in other industries. "Over the years, we have changed gear from investigating pollutants from power plants to manufacturing industries," says Li.

Take steel, cement, and glass production as an example. China's total production capacity is half of the world's total, and the emission from these is about the same as from coal-fired power plants. But treating flue gas from these manufacturing plants is more difficult than emissions from coal-fired power plants and the specificity of emission ingredients makes it impossible to just simply modify existing technology.

In steelmaking, for example, it was found that higher concentrations of highly reactive alkali metals in the flue gas were 'poisoning and wearing' catalysts, deactivating desirable chemical properties. Li's research has looked at maintaining the potential of catalysts in terms of strength, anti-poisoning, and surface area – as well as maximizing selective catalytic reduction performance. For example, the project has developed integrated treatment systems that could pre-remove alkali metals, sulfur, and other pollutants from flue gas before they come into contact with any denitrification catalyst they might poison.

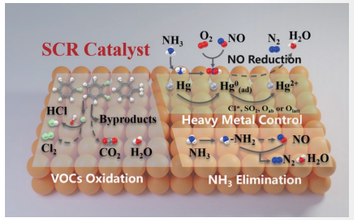
There is also a wider range of operating temperatures to consider in manufacturing. Flue gas from steel sintering, for example, is typically 150 °C; well below the 200 °C needed for existing catalysts to work. Novel low-temperature catalysts should in development help, says Li. He points particularly to the use of transition metals with rare earth elements. "We are conscious of taking full advantage of rich local resources from the vanadium titanium reserve in southwestern China to our coveted rare-earth ores dotted across the nation," he says.

In 2018, China's State Council ordered the Ministry of Ecology and Environment to draw up a plan to clean up the country's steel industry. Li has already worked successfully with Bao steel and other large manufacturers to demonstrate and then deploy high-performance flue gas treatment systems. He says this has paved the way for a new era. Hebei and Henan, two major provinces for steelmaking and air pollution, are now implementing strict new emissions standards.

"Consider the 600 m^2 treatment facility we designed for the Shanghai Baosteel Group in 2016. We encountered plenty of resistance from our users and the entire steelmaking industry as our flue gas treatment design was widely deemed as too difficult to realize," recalls Li. "We were under tremendous pressure given the million-dollar investments, but we always had the confidence to take it all the way, because we had been involved from theory proposal to final tests."

So far, in 32 Chinese provinces, autonomous regions, and municipalities, technologies from Li's group have been successfully applied to the manufacture of steel and building materials, and to petrochemicals, non-ferrous metals, and other industries. Outside China, they have been exported to 23 countries participating in the Belt and Road Initiative. Developed countries including the United States, Australia, South Korea, and Japan have become customers too. Over the past three years, sales revenue has totaled 14.9 billion yuan (US$2.3 billion).

Success depends on teamwork with other academic collaborators, including Senior Engineer Hengdi Ye and Professor Jiming Hao, President of Beijing-based environment protection body, the International Ecological Economy Promotion Association, and a member of the government consultation body, the Chinese Academy of Engineering, Li notes. "Whether the team is targeting the lowest possible temperatures for denitrification or enhancing the potential of recycling leftovers from catalytic processes, we are all trying to take these green technologies to a new level and charging forward with fresh ideas for overcoming existing limitations."



Redesigned novel catalysts from Li's group can realize the simultaneous removal of nitrogen oxides with one or more other emissions, such as volatile organic compounds, heavy metals, and ammonia.(Credit: Reprinted with permission from authors. Copyright © 2021, American Chemical Society. https://doi.org/10.1021/acs.est.0c07326)

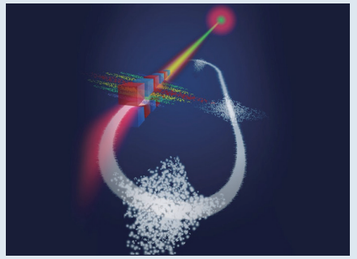
Microbunching illuminates new technological horizon

A scheme that causes electrons to form 'microbunches' could yield high power and coherent extreme-ultraviolet light, and perhaps the means to produce circuits faster.

Chuanxiang Tang is a Professor in Department of Engineering Physics at Tsinghua University. He is also Deputy President of Chinese Particle Accelerator Society, and on the panel on Advanced and Novel Accelerators (ANA) for the International Committee for Future Accelerators.

A new source of high-power extreme-ultraviolet (EUV) light, steady-state microbunching (SSMB), is peeking over the horizon, following a proof-of-principle experiment published in *Nature*[1]. Corresponding author, Chuanxiang Tang, says the potential power of SSMB EUV could be used to etch more-intricate patterns onto semiconductor circuits, which are used to store and transfer data in devices.

"A high-power EUV source is of crucial importance for high-volume manufacturing using EUV lithography," explains Tang, a professor in the Department of Engineering Physics at Tsinghua University. EUV lithography reduces the steps needed to manufacture circuits by bypassing multi-patterning, a multiple-exposure method currently used to get finer circuit pattern resolution. But power is the key to realizing viable EUV lithography, says Tang, since the optical system is reflective and the power loss of each of the 11 reflections exceeds 30%.



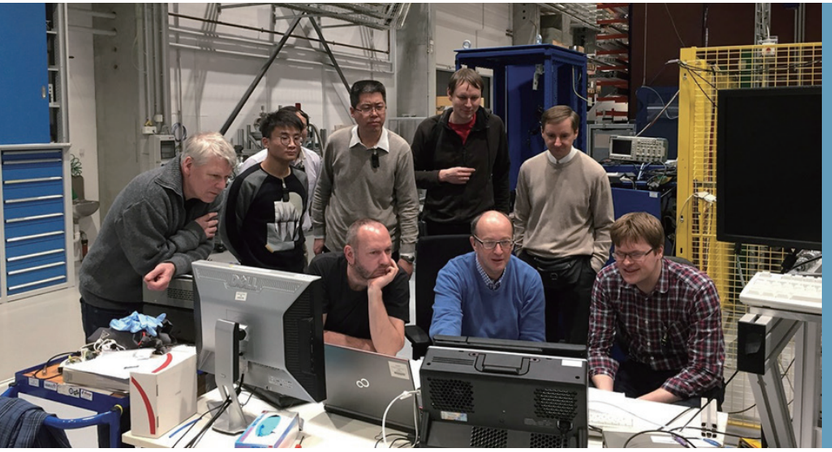
Stored electron bunches are modulated by a laser in an undulator. They become 'microbunched' after one complete revolution in the storage ring and produce coherent radiation at the laser wavelength and its higher harmonics.

Rolling with the bunches

The concept of SSMB was first proposed in 2010 by two scientists at Stanford University, Daniel Ratner and Alexander Chao. Published in *Physical Review Letters*[2], their idea was that electrons circulating in a synchrotron are organized into small bunches that support the emission of coherent light. However, the SSMB concept lay dormant for several years because its potential was not immediately recognized and it is difficult to perform experiments as most synchrotrons aren't suitable.

"After the paper was published in 2010, I was expecting some interest from the community, but nothing happened for five years," explains Chao. "In 2015, I finally realized that if there would be any response to this very interesting and promising idea, I would have to push for it. So, in 2015, I started to give talks about the idea."

In 2016, following a conference talk on SSMB from Chao, scientists from Tsinghua University and Helmholtz-Zentrum Berlin expressed interest, and a collaboration was born. A plan was devised to experimentally test SSMB at the Metrology Light Source, a synchrotron in Berlin owned by the Physikalisch-Technische Bundesanstalt, who became a third collaborator. The Metrology Light Source is one of the few synchrotrons at which SSMB could be experimentally investigated, as it operates in a 'low-alpha mode', in which the circulation times of the electrons are nearly independent of their energies.



A group from Tsinghua University, Helmholtz-Zentrum Berlin and Physikalisch-Technische Bundesanstalt experimentally tested steady-state microbunching at the Metrology Light Source, a synchrotron in Berlin.

In the experiment, a pulsed near-infrared laser is fired as electrons pass through a periodic arrangement of alternating magnets in the ring, causing them after one circulation to form localized spatial patterns of small bunches, separated on the scale of the laser wavelength. Importantly, these microbunches should emit light in a coherent manner, allowing higher power emission.

The key, says Tang, was to maintain phase correlation between the electron energies introduced by laser fields over a complete revolution in a storage ring. A precise, turn-by-turn phase correlation created steady-state microbunching.

Circuit maker

A completely operational SSMB source has still to be demonstrated. It will require using a special magnet lattice and a high-power optical enhancement cavity, according to Tang.

If realized in this way, the technique could also prove useful for fundamental experiments in condensed-matter physics that require high-flux, energy-tunable EUV photons, notes Tang. However, with the global EUV lithography market forecast to grow more than 20% between 2020 and 2021, Tang expects industry interest to be the driving force.

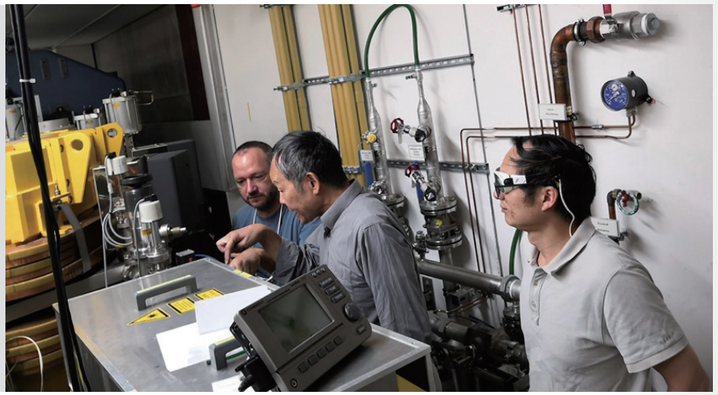
If funding is forthcoming, the Tsinghua team hope to construct a dedicated SSMB storage ring in Beijing, says Tang. "If things go well, we plan to build it in the following five to six years."

References

[1] Deng, X.et al. Experimental demonstration of the mechanism of steady-state microbunching. *Nature* 590, 576–579 (2021)

[2] Ratner, D. F. & Chao, A. W. Steady-state microbunching in a storage ring for generating coherent radiation. *Phys. Rev. Lett.* 105, 154801 (2010)

Dr Alexander Chao (centre), a co-author on the paper, works with colleagues to experimentally test steady-state microbunching (SSMB) in Berlin. He came up with the theory behind SSMB while at Stanford University, where he was a professor until he retired in 2019.



Building eco-friendly dams with rock-filled concrete

Using rock-filled concrete to make large dams means they are stronger, cheaper, and more environmentally friendly to build.

By most measures, China is the world leader in dam building. It leads the world in the number of extra high dams with a height of more than 200 m. China's dams also generate the most hydroelectricity – more than the next four countries combined.

It should be no surprise, then, that in recent years China has made several breakthroughs in the technology of dam construction. One of the most significant advances has been rock-filled concrete (RFC). Invented by Professors Feng Jin and Xuehui An at Tsinghua University, RFC is a material typically made of local rocks that are bound by a special concrete.

Since the two professors first conceived of their new material in 2003, it has been refined and used in scores of new projects, both in China and abroad. "An RFC dam is 10 to 20% less expensive than building a conventional concrete dam of the same size," explains Jin. "The use of local rocks reduces the amount of cement needed, and the nature of the material reduces or eliminates ongoing cooling, labour and construction costs." Importantly, RFC dams are also less likely to crack because less cement is in use.

Less cement

Air bubbles and cavities in dam concrete will compromise its strength and durability, so must be pushed out for conventional concrete by mechanical vibration or roller compacting after it has been poured. These processes add to the expense of pouring concrete and the difficulties of quality control, but without them the finished product may be seriously weakened.

Excess water added to improve malleability is also an issue. It will ultimately bleed out of the mixture, causing hardened concrete to shrink and crack. There is also 'heat of hydration', released by the chemical reaction of the cement in the concrete coming into contact with water. This again causes cracks as the hardening concrete cools. The standard way of dissipating it is to embed cooling pipes in the formwork before the concrete is poured and to supply cool water into the pipes during the harden process.

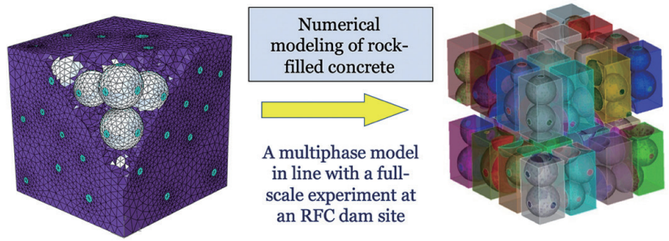
The use of rocks in RFC considerably reduces the demand for cement, explains Jin, thereby substantially lowering the temperature rise caused by hydration heat and reducing the shrinkage of concrete. "Because of this, RFC dams can completely eliminate temperature control measures such as cooling pipes," he says.

The Baijia RFC double curvature arch dam in Shaanxi Province has a maximum height of 69m.

The Dagutai RFC gravity dam in Guizhou Province has a maximum height of 41m.

RFC, however, does require a special concrete. In the 1980s, a Japanese professor, Hajime Okamura, solved some of the problems of conventional concrete when he invented self-compacting concrete (SCC). By using high-viscosity admixtures and more sand as an aggregate, he produced a mix with enough 'flowability' to fill every space in complex formwork, with no need for tamping or vibration after pouring. Further additives called superplasticizers allowed his concrete to be made with less water. "But SCC still faces high hydration temperature rise, significant shrinkage and is expensive, because it uses a high proportion of cement," explains Jin.

The insight of the Tsinghua professors was to further develop the Japanese wonder material to a point where it could be poured into formworks filled with medium-sized rocks. By tweaking the different ingredients, they arrived at a mixture – called high performance self-compacting concrete or HSCC – that can



A multiphase model for rock-filled concrete in parallel with an onsite full-scale test at the Lyutang RFC dam site.

flow around each and every rock in a space, to fill every last nook and cranny. The resulting RFC is dense and suitable to build a dam.

RFC as a dam-building material is significantly cheaper than the Conventional Vibrated Concrete or Roller Compacted Concrete it replaces. The use of HSCC does away with the need for mechanical compacting or vibration, which in turn reduces requirements for skilled labor and equipment.

Only about half as much concrete is needed to build RFC dams, which are often built in remote locations. Less cementitious material for mixing concrete needs to be trucked in from afar, replaced by rocks that can often be sourced locally. Less cement used also means less heat of hydration is released when RFC is made. So much so, that cooling pipes can be dispensed with.

Moreover, tests have shown that RFC has higher compressive strength than pure HSCC. The rocks in RFC, it turns out, restrict shrinkage in the concrete between them and limit the propagation of cracks.

Lastly, making cement creates the emission of a great deal of CO_2, so using RFC as a construction material is an environmentally friendly alternative. One 2013 study by An and two US-based collaborators puts this CO_2 reduction at 64% when compared to conventional concrete.

Global dam building force

Since they first created RFC 18 years ago, Professor Jin and his team have worked hard to make it better and easier to use. They have standardized and codified its use for designing and building dams. Several sector standards have been issued, and the technique has received more than 30 national patents. RFC has also been recognized by the International Commission on Large Dams (ICOLD), a significant international dam building industry association.

The efforts of the Tsinghua engineers have been paying off. Within China, more than 120 RFC dams have been completed or are under construction. RFC dam projects are due to break ground in other countries, including Pakistan, Burundi and Angola. The Songlin gravity dam now under construction in Yunnan province is one of the largest RFC dams so far, at 90m high and 230m long.

Moving on from gravity dams, Professor Jin's team has also made great progress with the use of RFC in arch dams, a graceful and efficient design that works by directing the force of the water it holds back into its abutments. Challenges normally arise in the design of the transverse joints between the dam sections that make up such structures, and the grouting used to fill them, but because RFC is less prone to thermal cracking, for example. Due to this, there is less need for separate sections to accommodate these changes, and consequently there are fewer joints between sections.

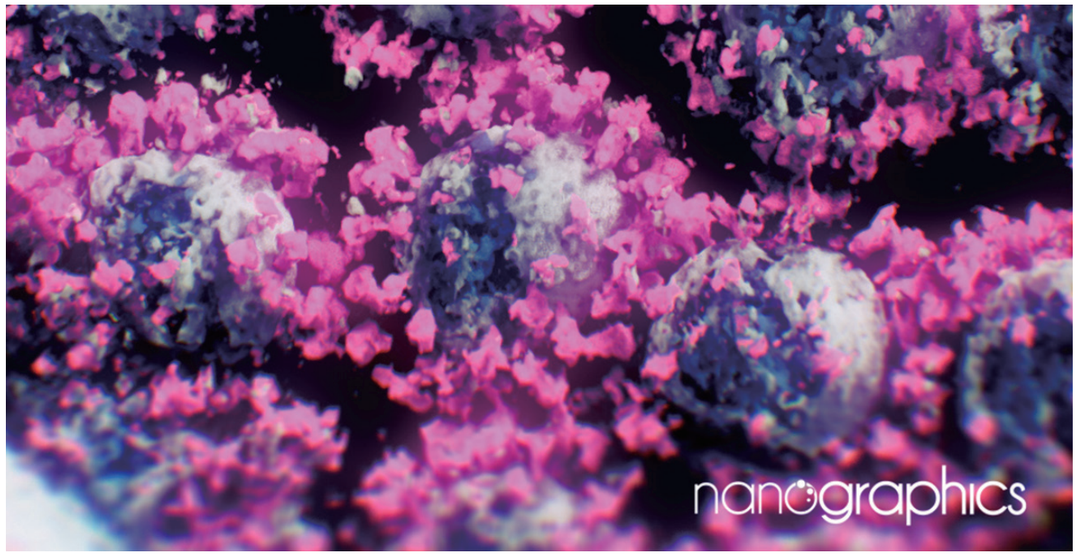
More than ten RFC arch dams have been completed or are under construction. Projects at Baijia, Shaqian, and Niudongkou in China are all above 60 m in height.

"We are also hoping to build RFC dams in several One Belt and One Road Initiative countries," notes Jin. "I believe in the future our technology will be used in dam projects all over the world."

The Maoxigou RFC gravity dam in Guizhou Province has a maximum height of 44.5m.

How SARS-CoV-2 packs its punch

Early details on the molecular architecture of the COVID-19 virus were key for vaccine developers in helping outline the shapes of its rich genome, flailing spikes, and sugar shields.



See SARS-CoV-2 in 3D with the help of cryo-electron tomography by Sai Li's team at Tsinghua University, graphics company Nanographics GmbH, and the King Abdullah University of Science and Technology in Saudi Arabia. (Credit: Nanographics GmbH/https://https://nanographics.at/projects/coronavirus-3d/ Creative Commons Attribution 4.0 International License: https://creativecommons.org/licenses/by/4.0/)

In late 2020, a group led by Associate Professor Sai Li at Tsinghua University detailed the molecular shape of SARS-CoV-2 at sub nanometer resolutions[1]. In the process, Li's team revealed more about the virus's exceptional infection and cloaking mechanisms, and added to the early series of structural studies supporting vaccine development.

To do this, Lanjuan Li's group from Zhejiang University, Hangzhou, first selected a viral strain isolated from a patient in her early 20s for advanced imaging. The strain made its way to Tsinghua's best electron microscope, after it propagated faster than any other strains in Lanjuan Li's lab. Li's team then flash froze millions of intact virions for imaging, 2,294 of which were eventually selected for structural work, producing what was perhaps the largest cryo-electron tomography (cryo-ET) dataset of SARS-CoV-2 at the time.

Infection advantage

Most structural studies focused on the 'spike' protein that studs SARS-CoV-2's envelope and helps the virus to fuse with healthy cell membranes, allowing the virus to enter and replicate, explains Li. This spike is the target of most vaccines, so the more vaccine developers know about how to create vaccines that bind effectively to its structure the better.

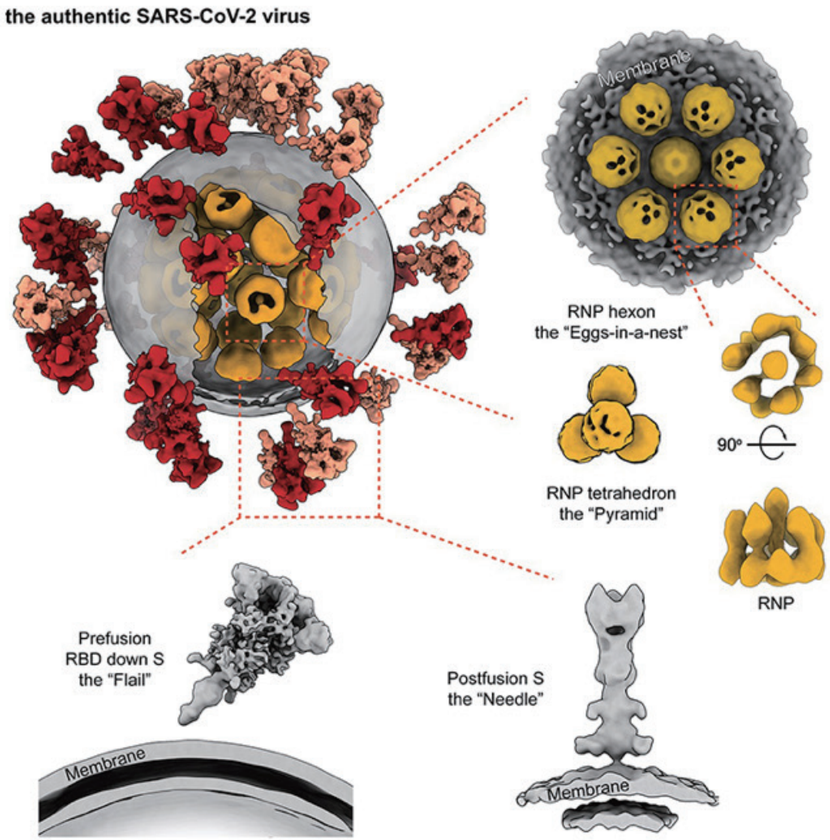
Li's team showed these spikes moving exceptionally flexibly around their 'stems' in their prefusion state, which precedes their interaction with a cell's receptor. The finding mirrored two other studies that came out at roughly the same time, says Li, who works within Tsinghua's School of Life Sciences.

The movement may be contributing to the coronavirus's exceptional infectiousness. "We suspect the spike benefits from mobility in exploring for another cell's receptor, which would help to make it exceptionally efficient at attaching to cells and spreading in the body," he explains. Most enveloped viruses, have a more stable prefusion spike that moves more like a 'loaded spring', he adds.

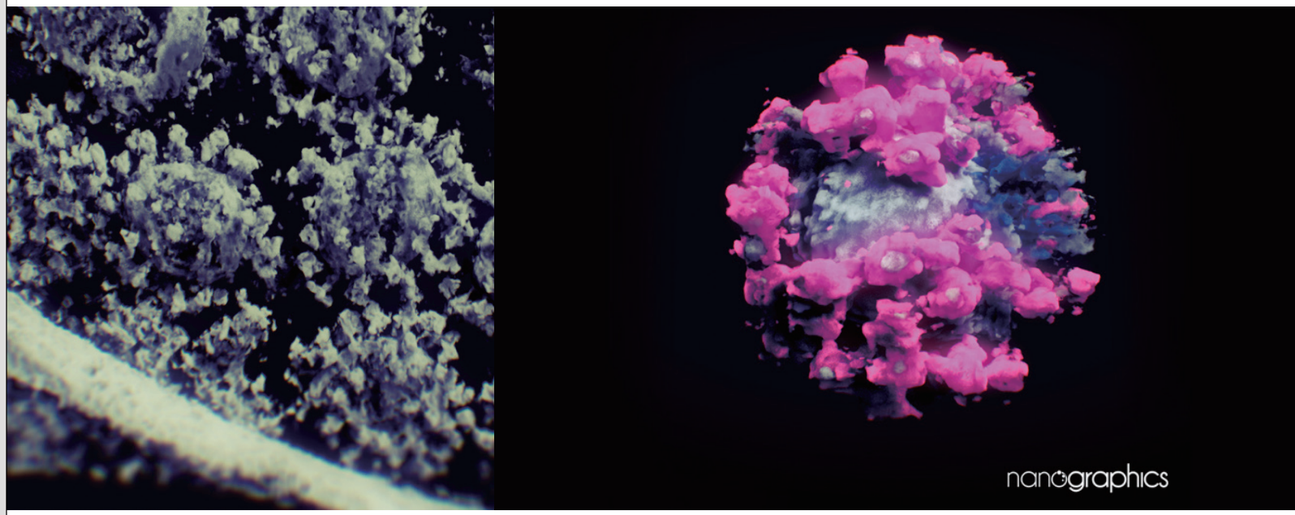
Mobility probably also means increased fragility, Li continues, and some virus purification methods used to make whole virus vaccines could lead to the snapping off of all or part of the spike. A so-called 'bald' virus particle wouldn't be effective as a vaccine, Li says, as it would stimulate low neutralising antibody activity.

Sugar shield and neat RNA

In addition, the team documented the spike's dense layer of sugars, called glycans. Li says these might be shielding the virus from recognition by the immune system. Mass spectrometry analysis showed that native glycans were similar to those seen in recombinant vaccines, such as the Moderna and Pfizer vaccines, which,



SARS-CoV-2 was shown by Tsinghua researchers to move to an up to 40-degree angle to the virus envelop (bottom left), which is an unusual amount of mobility. The ribonucleoprotein packaging of the virus was also the first to be documented of any positive-strand RNA virus, with hexagon and pyramid assemblies both revealed.



An image of SARS-CoV-2 created using cryo-electron tomography by Tsinghua, and cleaned up and colored by Nanographics GmbH and the King Abdullah University of Science and Technology in Saudi Arabia. (Credit: Nanographics GmbH/https://https://nanographics.at/projects/coronavirus-3d/ Creative Commons Attribution 4.0 International License: https://creativecommons.org/licenses/by/4.0/)

Sai Li is an associate professor in the School of Life Sciences at Tsinghua University.

using mRNA, create SARS-CoV-2 spike proteins within the body. Manipulation of these glycan layers could be a potential pathway to improvement, says Li.

The Tsinghua team also demystified how coronaviruses pack in the largest genome of all RNA viruses. And Li's study has also shed light on how positive-strand RNA viruses package their ribonucleoprotein in general.

Positive-strand RNA viruses release their genomes into healthy cells where the genetic information can also act as mRNA that the host cell translates into viral proteins. In SARS-CoV-2, Li's team was able to document how the hexagonal or pyramid-like tetrahedral assemblies of ribonucleoproteins are able to neatly nest inside the viral envelope. Li refers to the virus as "a genius architect".

Vaccines and validation

Structural studies have been key to vaccine development throughout the pandemic, says Li. But the speed of vaccines production has meant that rapid validation from teams such as his have been vital.

Luckily, Li's group already had expertise in inactivation and purification of coronaviruses alongside Lanjuan Li's group before the most recent outbreak began. Tsinghua was also quick to fund the time-sensitive work.

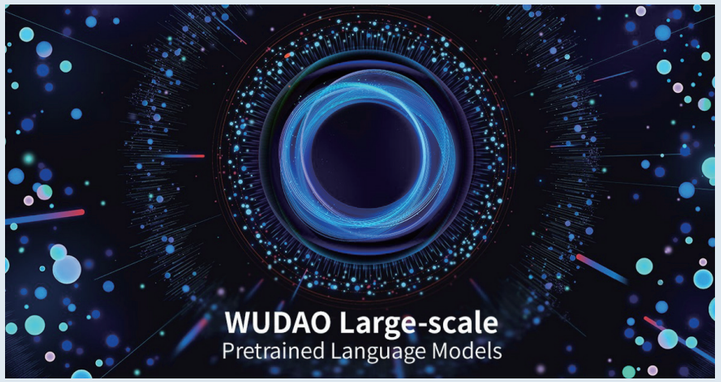
"The intact SARS-CoV-2 virus structures by many groups around the world provided vital structural and statistical references for major vaccines that went into development," Li says. "Happily, the conclusions about spikes are very consistent. I believe a series of 2020 papers together were able to confirm what the bona fide SARS-CoV-2 virus looks like."

Reference

Yao, H. et al. Molecular Architecture of the SARS-CoV-2 Virus, *Cell* 183(3), 730-738 (2020) DOI: 10.1016/j.cell.2020.09.018

A big new player in large-scale natural-language AI

Introducing the world's largest natural-language artificial intelligence model – the multi-lingual, multimedia-generating Wu Dao.



China's first super-scale natural-language AI was unveiled in early 2021, and an even larger version of 1.75 trillion parameters was released in June. It's currently the world's largest natural-language artificial intelligence (AI) model, able to understand and generate coherent text and images based on content and images in Chinese, as well as English and other mainstream languages.

Development of the AI, called Wu Dao, was led by Jie Tang, a professor in Tsinghua's Department of Computer Science and Technology and Vice Director of academics at the Beijing Academy of Artificial Intelligence (BAAI).

In essence, Wu Dao is an algorithm that studies datasets of images, video and natural-language text to reproduce statistical patterns that can generate coherent and relevant words and visuals, explains Tang.

It's thought that Wu Dao and similar tools could eventually help streamline paperwork, and generate video captioning and press releases, among other things. Tang and his team have created start-up Zhipu.AI to further develop these uses.

Wu Dao 2.0's creators point out that its number of parameters is ten times that of its most high-profile rival GPT-3, which was launched for beta testing in 2020 by San Francisco-based research laboratory OpenAI.

When GPT-3 was released, pundits were quick to explore its ability to come up with linguistically sound poems, memes and songs, although the meaning created by the AI was often nonsensical. Today, GPT-3's source code is licensed exclusively by Microsoft.

While Wu Dao 2.0 will undoubtedly improve upon this output, the ultimate hope, explains Tang, is that "the next generation of these tools will incorporate pretrained language models, large-scale knowledge graphs, and logical reasoning to produce meaningful content as well as, if not better, than humans".

In fact, at the same time that Wu Dao 2.0 was released, Tang's team also introduced China's first virtual student, who joined the Department of Computer Science and Technology at Tsinghua. It is a personification of the Wu Dao model, able to learn from all kinds of data to improve her cognition over time. Using Wu Dao, the virtual student is already able to compose music, reason, react to emotions, answer questions and even code, among other things. It was co-developed by the Beijing Academy of Artificial Intelligence, Tsinghua AI spin-off Zhipu AI and Microsoft-owned Asian chat bot pioneers, Xiaoice.

Making international AI

This isn't Tang's first attempt at counteracting the English-language bias of AI. In 2013, he and his team at Tsinghua created XLORE, the first large-scale cross-lingual knowledge graph to provide advanced knowledge linkages between Chinese and English text. The group used machine learning on Wikipedia in Chinese and English, as well as two Chinese-language encyclopedias to balance a discrepancy in language inputs due to the size of Wikipedia in English.

"XLORE was built to address the scarcity of non-English knowledge, the noise in the semantic relations, and the limited coverage of equivalent cross-lingual entities," explains Tang. XLORE, he says, has also been used to help train Wu Dao.

Before that, Tang's Tsinghua team had already created a researcher database using a multi-lingual data-mining tool. The database, AMiner, was launched in 2006. The mining algorithm collates academic profile and collaboration information in multiple languages, helps to resolve name ambiguity, offers social influence analysis and recommends research partners. So far, it has indexed more than 133 million researchers. The work was first presented in 2008 at annual international data-mining conference KDD'08. In 2020, it won the Association for Computing Machinery's SIGKDD Test-of-Time Award.

Professor Jie Tang from Tsinghua's Department of Computer Science and Technology is also Vice Director of Academics at the Beijing Academy of Artificial Intelligence (BAAI). He spoke about key eras in AI innovation at the launch of Wu Dao 1.0 in March 2021.

Four subsets of Wu Dao

Tang's Wu Dao team includes more than one hundred researchers, not only from Tsinghua, but also Peking University, Renmin University of China and the Chinese Academy of Sciences. In March 2021, BAAI unveiled four distinct branches of the AI.

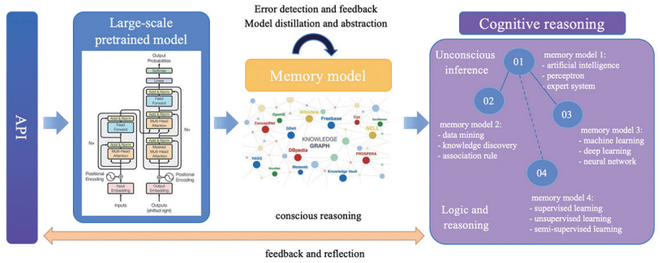
The first is Wen Hui, a model designed to explore cognitive ability of pretraining models. It can create poems, videos, and images with captions. Its potential uses include simplifying work for e-commerce retailers by creating product descriptions and facilitating product shots. BAAI says Turing tests show the model achieves near-human performance in poetry. Wen Hui was partly trained on the largest pretraining model to-date, featuring 1.75 trillion machine-learning parameters, and features complex reasoning, and text and image search functions.

Wen Hui showcases a series of core technical innovations:

FastMoE is the first Mixture-of-Expert (MoE) framework that supports PyTorch and native GPU acceleration, which is the foundation for the realization of a trillion-parameter model. It is easy-to-use, highly flexible, and runs 47 times faster than a naive PyTorch implementation.

GLM (General Language Model) is a general pretraining framework based on autoregressive blank filling, that unifies different pretraining models including BERT and GPT, and achieves state-of-the-art performance on natural language understanding, unconditional generation, and conditional generation at the same time.

The P-tuning 2.0 algorithm closes the performance gap between few-shot learning and fully-supervised learning.



CogView is a novel framework that achieves text-to-image generation via large-scale Transformers pretrained on aligned pairs of texts and images. It significantly outperforms OpenAI's DALL•E model on the MS COCO benchmark.

The Wen Lan model was trained on a Chinese-language dataset consisting of 650 million image-text pairs. It maps sentences and images into the same space and can be used for pure cross-modality searches between images and text. It will eventually be able to create images or videos given text, and caption videos, says Tang. Three applets have already been developed using Wen Lan: MatchSoul, which matches images with humorous, literary, and philosophical text; Soul-Music, which matches images with relevant song lyrics; and AI's Imaginary World, which matches sentences with relevant high-quality images.

Wen Yuan is the world's largest Chinese-language AI model and harnesses a suite of efficient, cost-effective and environmentally friendly techniques. Using Wen Yuan's framework, for example, one model with 198 billion parameters only required the processing power of 320 GPUs to run, while GPT-3, which has 175 billion parameters, uses 10,000 GPUs. The team working on Wen Yuan released several Cost-effective Pre-Trained Models (CPM-2), which achieve excellent performance in eight tasks in Chinese, including reading comprehension, summarization, and numerical reasoning.

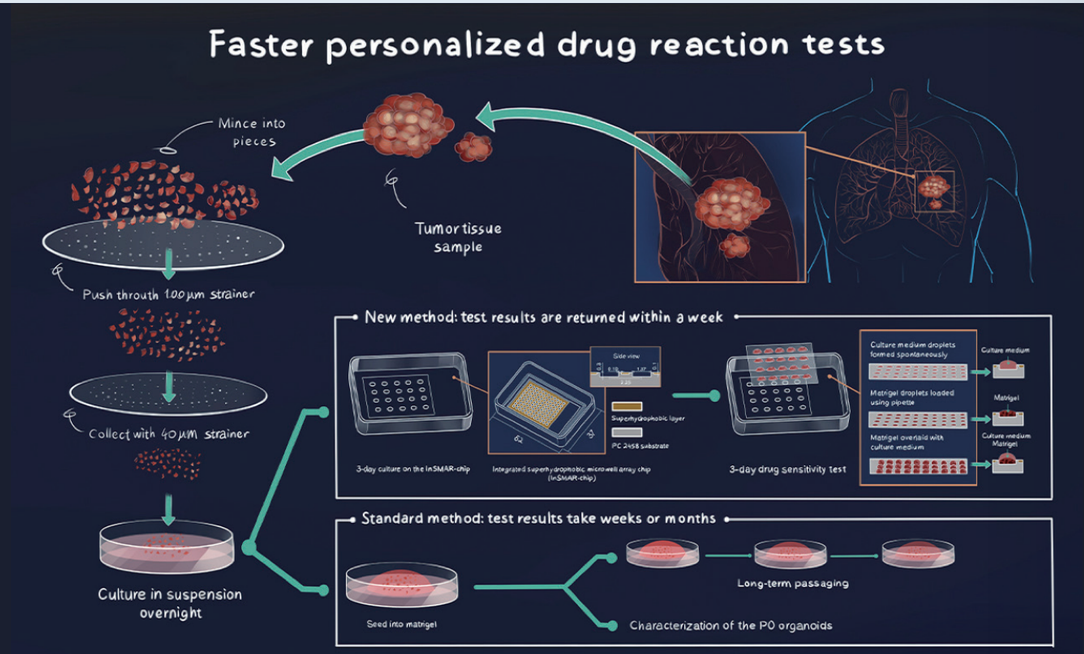
Finally, a tool called Wen Su has been built to predict ultra-long protein structures, and has already been trained on a variety of datasets.

Talks are underway about deploying these tools for e-commerce giant Alibaba, search engine Sogou, and Xinhua News Agency, among others.

The aim is to keep developing Wu Dao with more cognitive AI functions to instill it with powerful reasoning and sense-making abilities.

A new rapid lung-cancer drug sensitivity test

An organoid-based test to predict drug effectiveness returns individualized results within a week for the world's deadliest cancer.



Hundreds of miniature organs, or 'organoids', grown in a nanoliter-scale microwell array system designed by Tsinghua researchers and their collaborators could soon be used to speed up decisions about personalized lung cancer drug treatment.

In *Nature Communications* in May 2021, Tsinghua's Peng Liu and his collaborators showcased how their new drug sensitivity testing system could produce results on lung cancer tumor tissue samples within a week.[1]

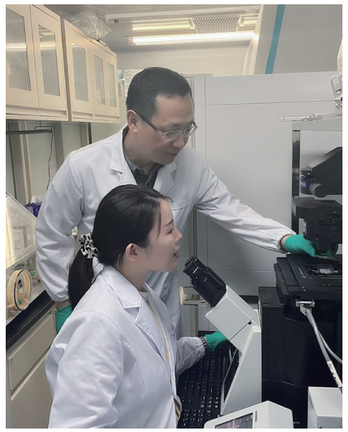
A long wait for personalized prediction

Patient-derived organoids (PDO) are useful for personalized drug testing because they reflect the basic structural and functional characteristics of the original cancer tissue. The three-dimensional cellular structures are grown from a patient's biopsy or from surgically removed tissue samples.

Previous clinical studies on colorectal and gastroesophageal cancer suggest that tests with PDOs could be highly successful in predicting whether a given drug will be effective for certain patients.

Culturing enough PDOs to run a test to determine which drugs will be most effective usually takes weeks or even months. "The initial number of PDOs generated from lung cancer tissue ranges from several to thousands, but the number of PDOs required to complete drug screening in a typical well plate is in the order of millions," explains Liu, a professor in Tsinghua's Department of Biomedical Engineering.

For lung cancer this is particularly problematic as the diagnosis is often late. The world's deadliest cancer has broad symptoms, such as coughing and wheezing, and as a result, in the United States, more than two-thirds of lung and bronchial cancer cases between 2010 and 2016 were found at a late stage. "Patients are reluctant to wait until they receive drug sensitivity test results," says Liu. "So shortened testing times will be significant to lung cancer patients in particular."



Peng Liu and his team have come up with a new drug sensitivity testing system that can produce results from organoids derived from lung cancer tumor tissue samples within a week.

In the May paper, the researchers were able to create a tiny and fast PDO production, isolation, and drug reaction testing system by processing lung cancer tumor tissues in a special integrated superhydrophobic microwell array called the 'InSMAR-Chip'.

Reactions at the nanoscale

In creating a sample processing method that increased the number of organoids derived from patients, a key component was to culture the organoids at the nanoliter scale on the InSMAR-Chip, which contains 108 miniature-sized wells for measuring drug reactions.

Conventional cell culture techniques at microliter-scale volumes require prolonged *in vitro* expansion to generate enough quantities of PDOs to take meaningful measures in that sized well. The nanoliter-scale wells on InSMAR-Chip make it possible to evaluate responses to anticancer drugs from just hundreds of organoids.

The InSMAR-Chip builds on Liu's previous development, the SMAR-Chip, and includes enhancements such as the use of new, water-repellent materials that help create uniform droplets in each of the wells.

Tests with the InSMAR-Chip can also flag acquired drug resistance; the team verified that lung cancer organoids derived from a patient with resistance to tyrosine kinase inhibitor therapy also showed greater resistance to the drug in the InSMAR-Chip test. "The drug responses reported using our method correlated strongly with genetic mutations and clinical outcomes," concludes Liu.

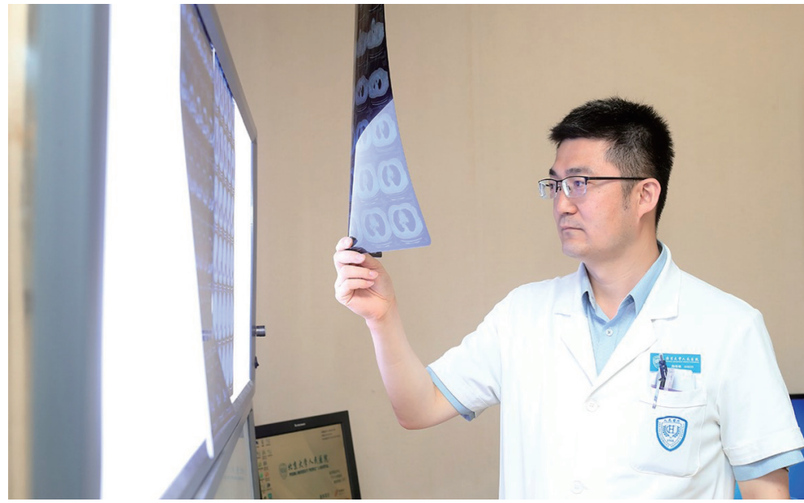
Towards universal use

While the team conducted the current study on lung cancer, they have since applied the technology to colorectal, ovarian, liver, and pancreatic cancer.

But a challenge remains with the number of PDOs that can be generated from middle- and advanced-stage patients. "Many such samples are obtained through punctures, and the number of PDOs generated from these samples is very limited. The success rate of establishing organoids is low," says Liu. "We will continue to optimize the sample processing method and organoid culture conditions, with the aim of making this technology more universal."

Reference

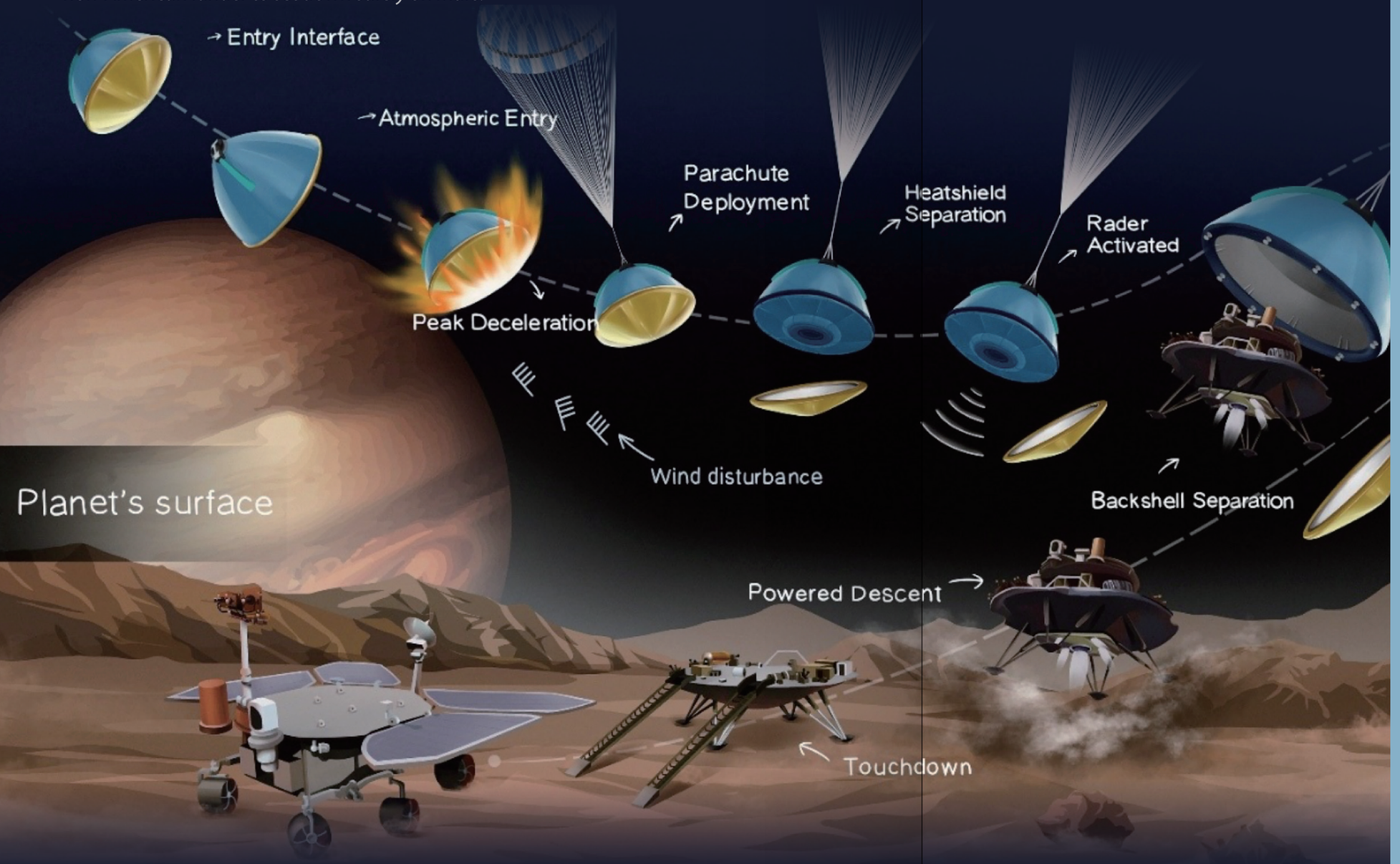
1. Hu, Y. et al. Lung cancer organoids analyzed on microwell arrays predict drug responses of patients within a week, *Nature Communications* 12, 2581 (2021) DOI: https://doi.org/10.1038/s41467-021-22676-1



Xinzhao Sui assesses the clinical efficacy of drugs by comparing changes in lung cancer lesions before and after treatment.

Simulating a Martian landing

A cable system replicating the rough descent through another planet's atmosphere helped the Tianwen-1 lander become the first non-American lander to set down safely on Mars.



In May 2021, China's Tianwen-1 lander completed the process of atmospheric entry, descent and landing on Mars, a feat only ever successfully achieved by NASA previously. It's a famously perilous part of the mission that Tsinghua's Xiaoqiang Tang, Senhao Hou, Haining Sun and Jinhao Wei had already helped simulate hundreds of times using cable-driven parallel robots.

Such are the challenges of the Martian atmosphere that China was only the second country, after the United States, to have landed a working lander on Mars' surface. As NASA's former chief historian Roger Launius put it, "This is a really big deal."

A team led by Tsinghua's Xiaoqiang Tang was instrumental to this milestone. The researchers had developed systems for simulating the Martian environment to test the trickiest and most essential components, the landing equipment. So when Tianwen-1 took off in July 2020, its atmospheric deceleration system had been thoroughly vetted by Tang's team.

Landing logistics

The Tianwen lander had to follow the same sequence as most space missions landing on other planets (or back on Earth), a process known as Entry, Descent and Landing (EDL).

Initially, China's lander was allowed to fall freely into Mars's atmosphere at 4.8 km/s. The protective capsule preventing the lander from burning up due to atmospheric friction was blown off with explosive bolts. After the atmosphere became sufficiently dense, parachutes were deployed to slow the lander to subsonic speed. These were jettisoned. Thrusters provided upward force for a gentle touchdown for the last meters of the lander's journey.

NASA engineers have described the descent phase of Mars landing missions as 'seven minutes of terror' as it's the most unpredictable. About 20 attempts to land on Mars have been made by different countries so far. For most, the harrowing interval has been followed only by silence. Among six Russian efforts, for example, the best result was a 1973 landing, with which all contact was lost 130 seconds after touchdown.

Tang was researching cable-driven parallel robots (CDPRs) before he became involved in China's space program. These systems use wires, attached to a tested object at different points, to pull it in different directions, thus simulating the forces that will push it around under real conditions. These would eventually be used to bring China success by simulating a landing on Mars hundreds of times, rather than using far fewer expensive aircraft drop tests.

But adjusting for Mars conditions is difficult, says Tang. The planet's atmosphere is about a hundred times thinner than Earth's, with about one percent of its density. It therefore provides more than enough friction to unpredictably disintegrate the lander's heat shield capsule, but does little to slow its speed.

Unpredictability is inherent in the ejection forces during the heatshield separation process. The first, when explosive bolts blow off the front heatshield so that landing struts could pop out together with ground scanning sensors to select a suitable surface spot to land. And the second, when the backshell is separated in parallel almost immediately afterwards, with a peak acceleration of 20 m/s^2. The lander could also have been buffeted by winds in the Martian atmosphere, about which little is known. Under an extreme scenario, the front heat shield might have been blown backwards after it was ejected, to smash into the lander's emerging landing gear and permanently disable it.

Simulation efficiencies

Tang had previously used eight and nine-cable CDPRs to test the landers of China's Chang'e lunar missions. Last year, Chang'e 5 returned samples of lunar rock to earth. However, Mars is a unique challenge. Due to its distance, communication with landers is harder and knowledge of the planet is sparser.

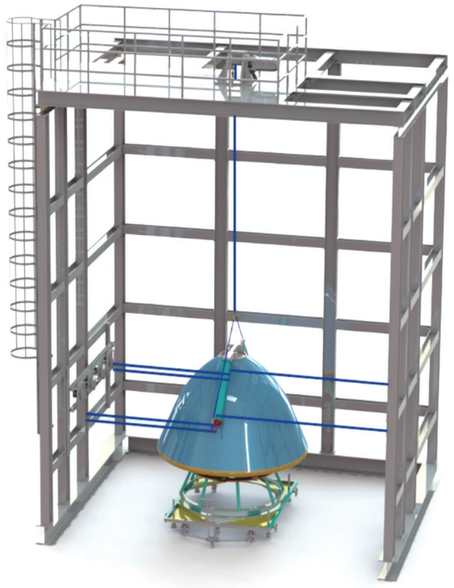
There was never disagreement that a soft landing on Mars would be Tianwen-1's biggest challenge. While the Zhurong rover, carried by the lander, is now traversing the red planet's surface with six scientific payloads, its engineering never received the same level of attention.

In the 1970s, Americans tested their two successful 1976 Viking lander missions to Mars in nine separate aircraft drops in the Earth's atmosphere.

China's space agency, the China Aerospace Science and Technology Corporation (CASC), decided against this approach for several reasons. In addition to its high cost, the individual atmospheric conditions surrounding each test could not be controlled, and would take a long time. If they missed the most favorable time window for launch, they would have had to wait two years before they could try again. A method that allowed as much testing as necessary, within a given time, was therefore desirable.

CDPRs have the advantage of being low cost, with short experiment cycles. They can be assembled indoors to test large objects like Tianwen-1's 720 kg lander. If they are adequately engineered, they can accurately deliver a preprogrammed sequence of yanks and shocks, for exhaustive testing within conceivable parameters.

Before testing for the Moon missions, Tang developed a six-cable CDPR to test a scale model of China's giant Five-hundred-meter Aperture Spherical Radio Telescope, before it was rigged up in a Guizhou karst depression in 2016. The size of 30 soccer pitches, it's the world's largest single-dish radio telescope, and it needed to be tested for use during buffeting winds. The telescope became fully operational in 2020.



Cable-driven parallel robots (pictured), developed by Xiaoqiang Tang, Senhao Hou, Haining Sun and Jinhao Wei, helped simulate the atmospheric entry, descent and landing conditions on Mars to test China's Tianwen-1 lander (pictured).

Red planet replica

Unlike the Moon, Mars has no atmosphere to simulate. When Tianwen's heatshield exploded off with an acceleration of 17 units of g-force, the cable delivering force to it had to keep up without going slack. Tang's machine is a special CDPR, which can simulate axial separation and wind disturbance.

The moon landing was tested by CDPR powered by motors, and while the Mars lander was tested powered by gas springs, which are simpler and more reliable. Researcher, Senhao Hou, worked with Tang to test the Tianwen lander.

In addition to having a much thinner atmosphere, Mars's gravitational field is weaker than Earth's. On average it delivers 38% as much downward acceleration. Researchers, Haining Sun and Jinhao Wei therefore built a second machine for simulating the lander's last, powered descent phase.

Their large-scale gravity compensation system used a vertical cable, attached to the top of the lander, to deliver precisely the amount of upward force needed to reduce the Earth's downward pull to that of Mars.

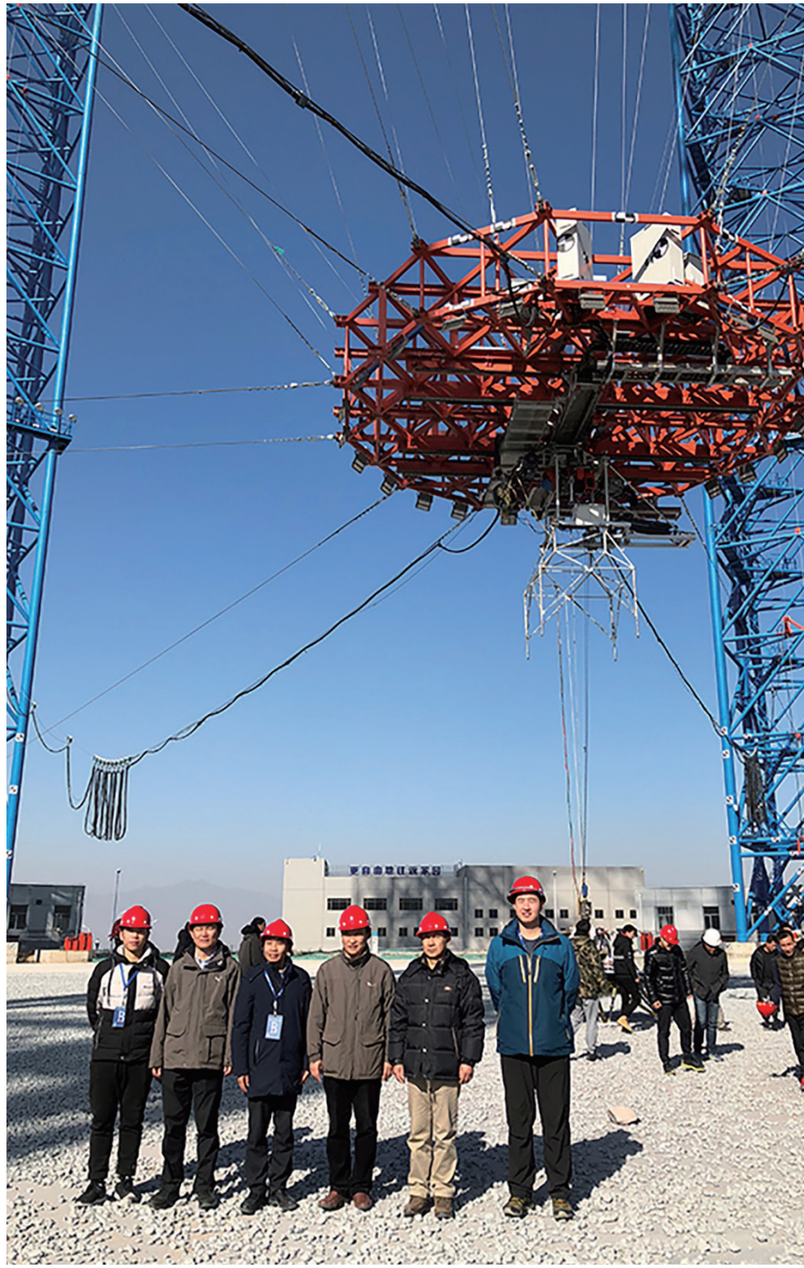
To achieve this, it relied on three force-delivering mechanisms. A 'big drive system' (BDS) did the job when the falling lander was between 70 m and 0.8 m from the ground. Below this range, upward force delivered by the lander's collision with the ground would act against the pull of gravity, so a different, constant force mechanism (CFM) was brought into play. To allow a smooth handover between the two mechanisms, a third' small drive system' (SDS) was used.

More Martian missions

Tianwen-1 orbited Mars for nearly three months before releasing its lander. The descent lasted about nine minutes rather than seven, because it went in at a shallower angle than NASA's landers. "Although I was nervous, I was also confident because we had done so many experiments and tests to verify our system," says Tang, who was monitoring the process with his teammates.

On top of this stunning success, Tang wants to further refine his CDPRs to deliver forces even more precisely and flexibly, across a wider range of parameters. "Different landers are being designed for different planetary environments with more diverse landforms," he says. "There is an urgent need for a simulation system with more comprehensive functionality, that can be quickly adjusted to suit a target planet."

China is planning more Mars missions, including one that will return samples to Earth. Doing so will require a much bigger lander, able to achieve lift off from Mars and survive second EDL to get back to Earth. Given that this is far ahead of anything the United States has yet achieved, a race could soon be on to do it first.



Xiaoqiang Tang's team in front of the scaffolding that helped frame their cable-driven Mars simulator.

Multiple moves for malaria

Starving malaria parasites by blocking their sugar uptake could be the key to combating the looming threat of drug resistant strains.

In June 2021, for the first time the World Health Organization (WHO) certified China as malaria-free after it reported zero indigenous cases since 2017. In the same summer, Tsinghua researchers detailed a new anti-malarial avenue, a small molecule that blocks sugar uptake in the malaria parasite.

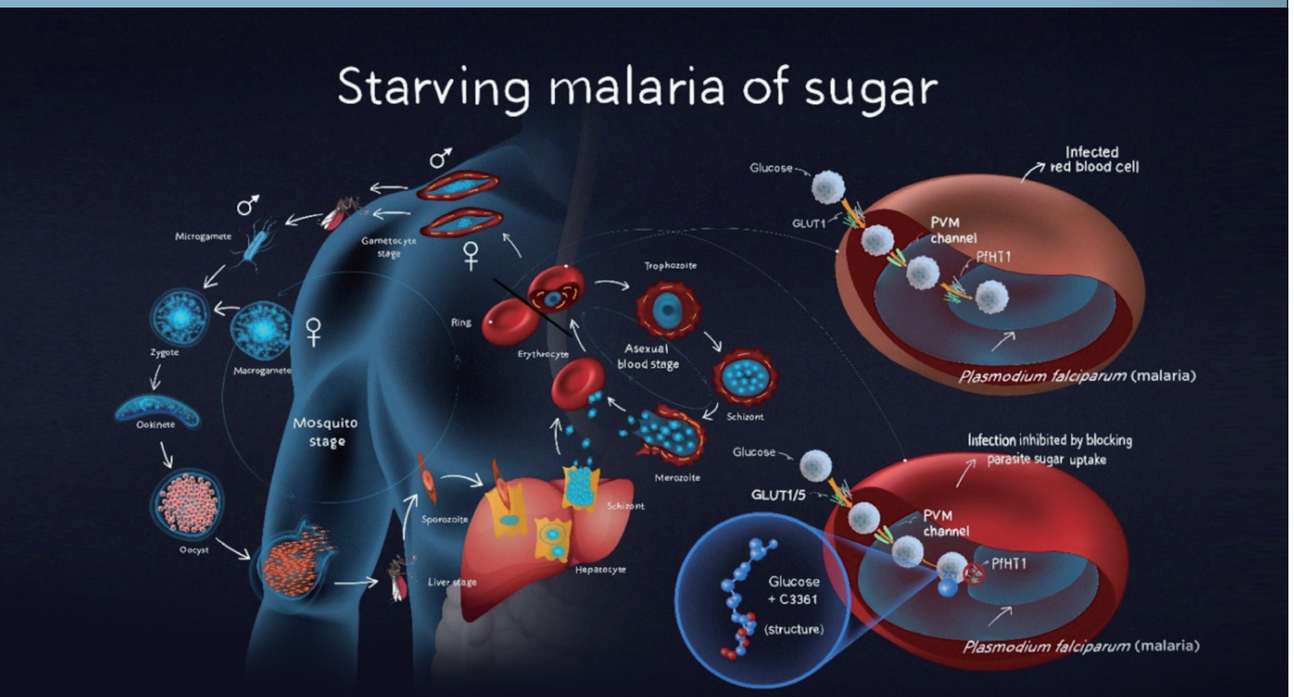
If China and other parts of the world wish to keep malaria at bay there is an urgent need for new treatments to battle emerging drug resistant strains, says Hang Hubert Yin, Deputy Dean of the School of Pharmaceutical Sciences at Tsinghua.

While artemisinin-based therapies, which emerged in the 1990s, have almost halved malaria's enormous death toll since the 2000s, resistance to first-line defence artemisinin-based combination therapies have recently emerged in both South America and parts of Southeast Asia, just south of China. So Yin's team have continued to work hard toward a solution.

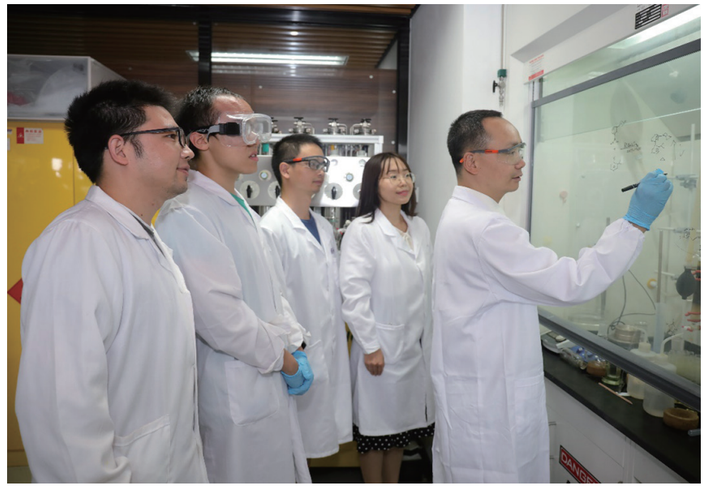
Like most animal cells, malaria cells use sugar as their main source of energy, explains Yin. "Unlike previous methods to perturb the membranes or target the parasite's DNA, this new approach attempts to selectively limit the parasite's sugar intake."

The key to the new strategy is to block the parasite's sugar uptake without compromising the same physiological process in the host, explains Yin. The team hopes to do this by exploiting structural differences between the proteins mediating the transport of sugar across cell membranes in humans and *Plasmodium falciparum*, the deadliest of the four species of malaria.

P. falciparum has already developed resistance to most first-line antimalarial drugs currently in use.



A Tsinghua team has designed a small molecule that inhibits the Plasmodium falciparum hexose transporter 1, the main sugar-uptake protein of the deadliest species of malaria, without depriving host cells of sugar. The possibility that this could slow malaria's replication process in human blood is an important new avenue for development given the rise of drug resistant strains of the deadly parasite across the world, says lead researcher Hang Hubert Yin.



Hang Hubert Yin's team is developing next-generation antimalarial strategies that exploit the structural differences between proteins that mediating sugar transport across cell membranes in humans and malaria.

Structural sweet spot

In 2020, Yin and his colleagues resolved the atomic structure of PfHT1(*Plasmodium falciparum* hexose transporter 1), the parasite's main sugar-uptake protein.

They found that when PfHT1 was bound to a moderately selective inhibitor, C3361, its structure re-arranged affecting the protein's function. This discovery suggested that it could be possible to design more potent and selective agents that target both the protein's orthosteric site, where the sugar substrate binds, and a newly identified site induced by the C3361 binding, also known as an allosteric site.

In their latest 2021 paper published in *Proceedings of the National Academy of Sciences (PNAS)*, Yin's team, in collaboration with researchers at Princeton University in the United States and the Global Health Drug Discovery Institute (GHDDI) in Beijing, described the effects of a series of rationally designed, novel small molecules that bind to both the orthosteric and allosteric sites of PfHT1 simultaneously.

These compounds selectively inhibit PfHT1 more than the human glucose transporter 1 (hGLUT1) and effectively limit the growth of multiple strains of *P. falciparum* in human red blood cells.

"To the best of our knowledge, this is the very first successful case for simultaneously targeting both the allosteric and the orthosteric sites of a transporter," says Yin. "Our findings demonstrate that PfHT1 is a druggable target and establish the basis for the rational design of next-generation antimalarial drugs."

China's gatekeepers

China's malaria free certification requires it to demonstrate the capacity to prevent the re-establishment of transmission.

Effective prevention and monitoring efforts are already reducing the risk of importing cases from neighbouring countries in which the disease is endemic, but work like Yin's is necessary to ensure the looming threat of drug resistant strains is kept at bay too.

Yin says that there's no room for complacency and his team looks forward to continuing to work with world-leading institutions such as GHDDI and Princeton University to validate their compounds' clinical efficacy, and to develop new drugs against other infectious diseases using structure-based drug design.

Reference

Huang, J. et al. Orthosteric–allosteric dual inhibitors of PfHT1 as selective antimalarial agents. *PNAS* 118 (3), e2017749118 (2021) DOI: 10.1073/pnas.2017749118

Hang Hubert Yin is a Deputy Dean of the School of Pharmaceutical Sciences at Tsinghua University. Yin arrived at Tsinghua after receiving a Ph.D from Yale University, working as a post-doctoral researcher at the University of Pennsylvania and gaining tenure at the University of Colorado Boulder. He has received numerous awards including, among others, the American Chemical Society's David W. Robertson Award for Excellence in Medicinal Chemistry and the American Association for Cancer Research's Gertrude B. Elion Cancer Research Award.

Backpack makes walking a power trip

A backpack that generates electricity while reducing the wearer's load.

A prototype backpack that can generate electricity as well as reduce load on the wearer has been designed by Jia Cheng, Zhonglin Wang and their team.

The backpack uses a triboelectric nanogenerator to convert mechanical energy from walking or running into electrical energy via the coupling effects of triboelectrification and electrostatic induction — a generation and redistribution of charges in an object caused by the changeable electrostatic field.

Movement power

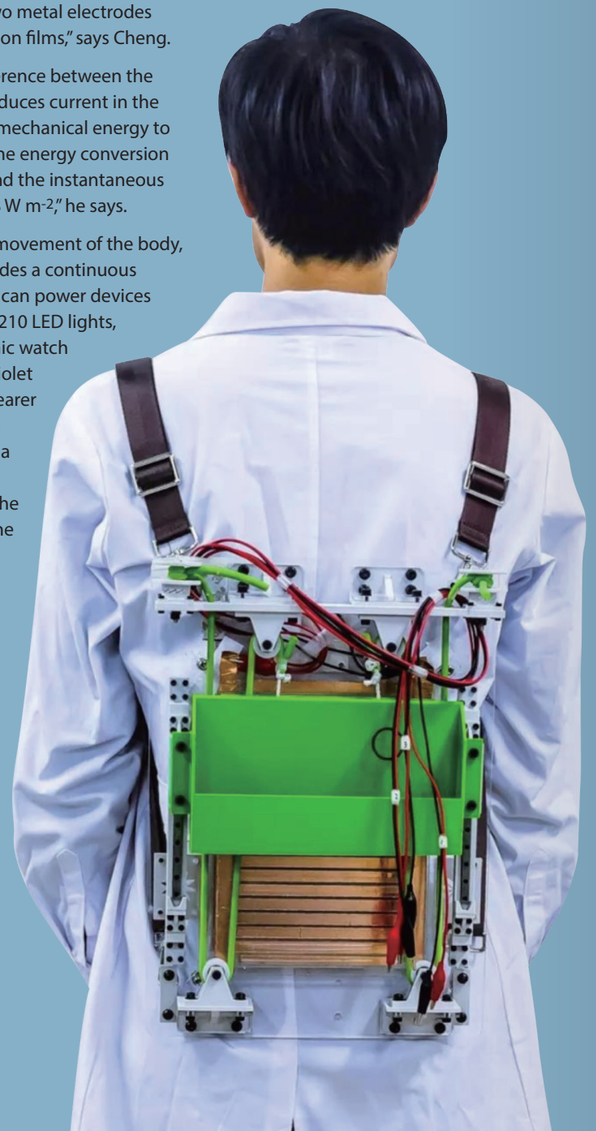
But first, the design of the backpack, detailed in *ACS Nano* in 2021[1], had to optimize the effect of natural walking movement, says Cheng. "Our backpack decouples the synchronous movement between the backpack and the body," he explains.

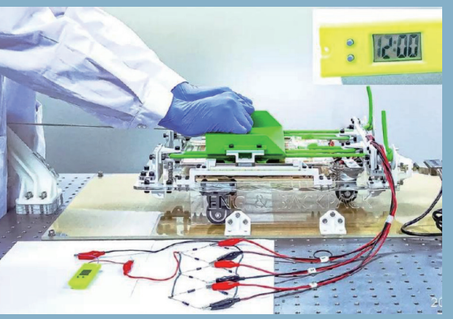
This was achieved by a plate that slides on two rails fixed on the backpack's frame. One end of an elastomer is attached to the top plate, and the other end is attached, through two fixed pulleys, to the frame. During walking or running, the frame of the backpack moves up and down, causing the two elastomers to stretch and shrink.

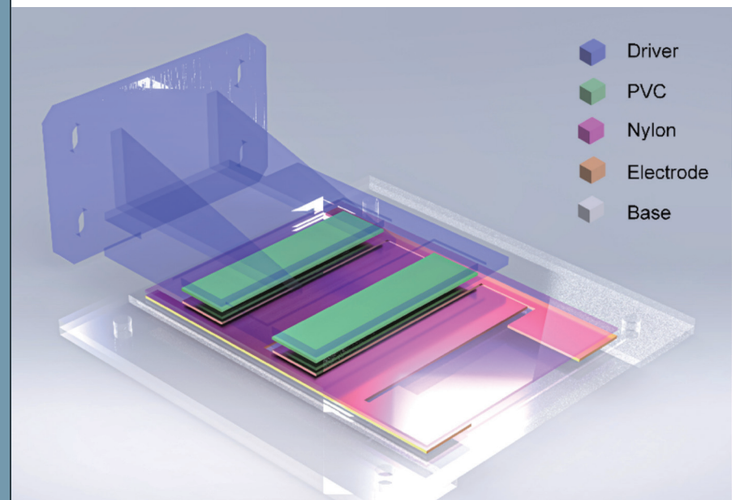
As well as acting as shock absorbers, the movement triggers the generation of electricity by using a triboelectric nanogenerator, which comprises polyvinyl chloride films, nylon films and metal electrodes. "The polyvinyl chloride films slide on the surface of the nylon films and, as a result, induce charges of different polarities on the two metal electrodes underneath the nylon films," says Cheng.

"The potential difference between the two electrodes produces current in the circuit, converting mechanical energy to electrical energy. The energy conversion efficiency is 14% and the instantaneous power density is 58 W m^{-2}," he says.

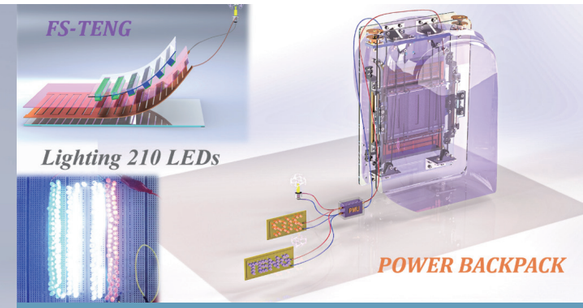
By harnessing the movement of the body, the backpack provides a continuous energy supply that can power devices such as an array of 210 LED lights, a low-watt electronic watch or a series of ultraviolet tubes. When the wearer with the LED-laden backpack walks on a treadmill, the light shines brighter as the walking speed of the wearer increases.







The triboelectric nanogenerator comprises polyvinyl chloride films (green) that slide against the nylon films (pink) and induce charges on the metal electrodes (orange).

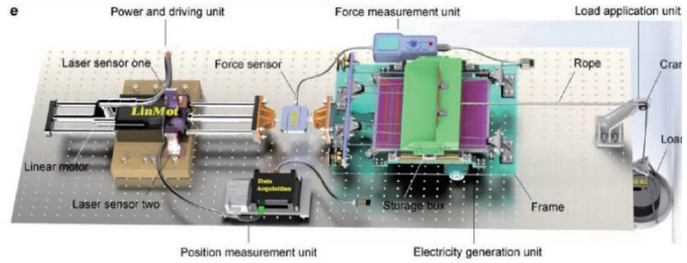


A triboelectric nanogenerator (TENG) attached to a load-suspended system within a backpack can help convert mechanical energy into power for LEDs. It has great potential to create enough electricity to support a phone and/or navigation device.

Controlling the rhythm, decreasing the load

The vertical oscillation of the load on the wearer can be reduced by roughly 29% and the vertical force declines by roughly 21%. Within the allowed weight for the elastomer, the faster the wearer walks, the greater the wearing force is reduced and hence, the lighter the backpack feels.

In future modifications, the researchers aim to improve the backpack's performance by changing the stiffness of the suspension system to adapt to different loads and motion frequencies, as well as using stronger elastomers that can withstand heavier loads. "The weight of the backpack is about 3 kg, which is a little heavy for wearers," says Cheng. "In the next-generation backpack, we would like to incorporate more lightweight materials."



The researchers envisage self-powering more energy-demanding devices such as BeiDou or GPS systems, sensors for healthcare applications, and a cell phone, by incorporating a power management circuit into the electricity generation unit of the backpack.

Reference

Yang, Z. et al. Power Backpack for Energy Harvesting and Reduced Load Impact, *ACS Nano*, 15, 2611-2623 (2021). https://doi.org/10.1021/acsnano.0c07498

Untangling the mystery of ultrasonic hearing in mice

A separate biomechanical pathway allows mice to communicate at high frequencies.

Like many mammals, mice can hear and communicate with sounds well outside the range audible to humans. In addition to their familiar squeaks, mice also use much higher frequency ultrasonic sounds for social communication, between mothers and pups, and during courtship or aggressive interactions.

For a long time, it was thought that animals use the same biomechanical pathways and molecules to hear ultrasonic frequencies, those higher than 20 kHz, that they use to hear lower-frequency sounds.

However, in July a team from Tsinghua showed that mice lacking a mechanosensitive ion channel found in cochlear hair cells, *Piezo2*, weren't as sensitive to ultrasonic sounds, but remained sensitive to lower- frequency sounds[1].

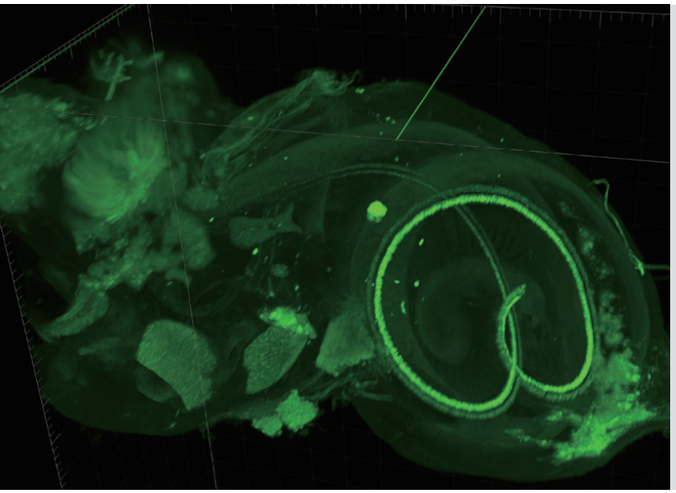
"We thus hypothesized that *Piezo2* may play a role in transducing higher frequencies," says Wei Xiong, an assistant professor in the School of Life Sciences at Tsinghua University.

Xiong and his colleagues bred knockout mice that did not express *Piezo2*, which is involved in the somatosensory system, in their cochlear outer hair cells for the experiment.

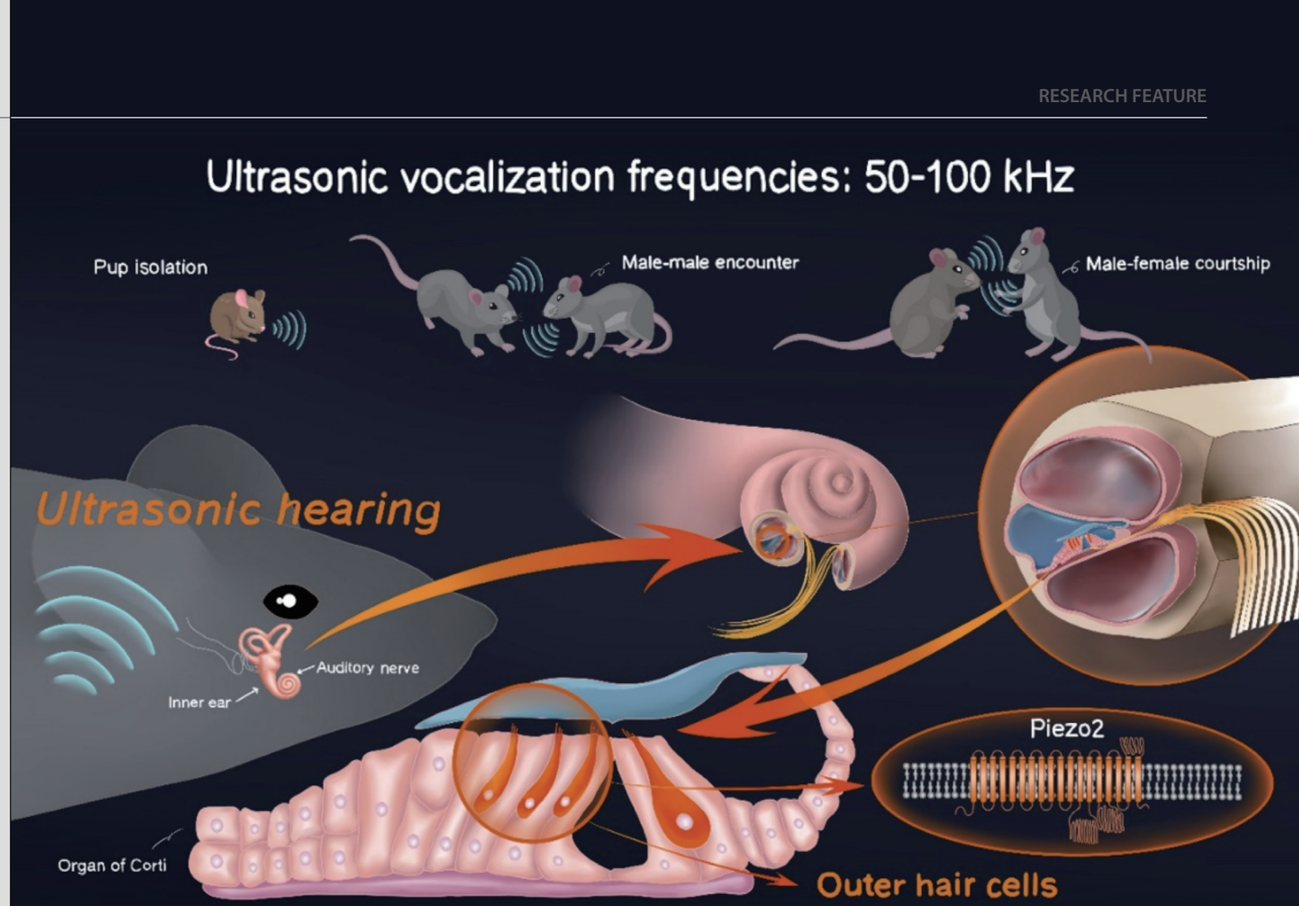
Ultrasonic responses

Recordings of the auditory brainstem response, measured with an electrode attached to their skull, showed that the knockout mice were significantly less sensitive to ultrasonic sounds compared with controls. In a behavioral test, in which the mice learn to freeze when they hear certain sounds, the knockout mice did not learn to freeze in response to an ultrasonic cue. This indicates that *Piezo2* is essential for mice hearing ultrasonic frequencies within the range necessary for social communication. The results were published in *Proceedings of the National Academy of Sciences (PNAS)*[2].

How, exactly, *Piezo2* detects ultrasonic frequencies, and what specific part it plays in ultrasonic hearing, is not yet determined, says Xiong. It appears that *Piezo2* is involved in detecting ultrasonic sounds specifically in the outer hair cells, and that it somehow coordinates with the hair-bundle mechanotransduction machinery to achieve ultrasonic transduction, but the details are still to be worked out. "These questions are exactly what we are investigating now," he says.



The researchers doubled checked that the loss of ultrasonic hearing in mice bred not to express ion channel Piezo2 in their outer hair cells was not due to a loss of hair cells at the basal coil of the cochlea by imaging mouse ears. The whole structure of the inner ear appeared intact with hair cells remaining in normal allocation and abundance in the above video, they wrote.



Mice vocalize at frequencies higher than 25 kHz during certain social behaviors, including mother–pup interactions, male–male encounters, and male–female courtship. Mice without Piezo2 ion channels, which are mostly found in the membranes of outer cochlear hair cells, weren't as responsive in ultrasonic behavioural tests, suggesting that this channel may be key to their ultrasonic hearing.

Wei Xiong is an associate professor in the School of Life Sciences at Tsinghua University.

Understanding hearing loss

The studies demonstrate that hearing uses a more complicated set of mechanisms than was thought, says Xiong. And it raises new questions about the diversity of hearing across different species. Some animals, such as insects and frogs, lack a cochlear structure, but are still able to sense and make ultrasonic vocalizations. Whether *Piezo2* is involved in their hearing needs to be examined.

This will also help understand the genetic mechanisms underlying human hearing. People gradually lose their higher-frequency hearing. Further studies of *Piezo2* may shed light on the genetic basis of auditory function disorders and bring potential solutions to address age-related hearing loss.

References

1. Wu, Z., et al. Mechanosensory hair cells express two molecularly distinct mechanotransduction channels. *Nature Neuroscience* 20, 24-33 (2017) doi: https://doi.org/10.1038/nn.4449

2. Li, J. et al. PIEZO2 mediates ultrasonic hearing via cochlear outer hair cells in mice. *PNAS* 118, e2101207118 (2021) doi: 10.1073/pnas.2101207118

Recycling electric vehicle batteries sustainably

Researchers at Tsinghua have demonstrated a greener way of recovering lithium from batteries to pave the way for a more sustainable electric vehicle market.

Jinhui Li and his team at the School of Environment at Tsinghua University seek to use chemistry to create more sustainable battery consumption systems.

Electric vehicles will be instrumental to reduce carbon dioxide emissions in order to reach carbon neutrality. With more than 3 million electric vehicles sold worldwide in 2020, the question of how to recycle the lithium-ion batteries that power them is pressing, in particular, because lithium mining requires the use of large amounts of chemicals.

For green technologies such as electric vehicles to be sustainable, it's important to quickly identify environmentally friendly ways to recover lithium from spent batteries. Now, Jinhui Li and his team, writing in *Green Chemistry*, present a fast and sustainable process for the rapid extraction of lithium from the cathode of lithium iron phosphate batteries.

At present, there are two main types of lithium-ion batteries for electric vehicles: ternary nickel-cobalt manganese ($LiNixCoyMnzO_2$) and lithium iron phosphate ($LiFePO_4$) batteries.

"In May 2021, the monthly output of lithium iron phosphate batteries in China exceeded that of ternary batteries for the first time," observes Li. "This means that the market share occupied by lithium iron phosphate batteries will continue to increase and become the mainstream in the future, and that the development of a suitable recycling technology is urgently needed."

Mechanochemical extraction

Because spent $LiFePO_4$ batteries do not contain precious metals, the economic drive for material recovery is weak. Lithium can currently be recovered from such batteries using technologies based on hydrometallurgy, which uses aqueous solutions to recovery metals from the spent material, but the process is inefficient and involves the use of strong acid reagents, which are cause for serious environmental concerns.

In the new study, the researchers introduce a more environmentally friendly process based on a mechanochemical method, which uses mechanical energy as a driving force to induce a solid-phase chemical reaction to selectively and quickly extract lithium without the need to use acids or the generation of waste water.

"Mechanochemistry is a widely used green technology," explains Li. "Compared with direct hydrometallurgy, the advantages of mechanochemistry are that the reaction space is closed, reducing environmental pollution; a mechanical force accelerates the chemical reaction, which is 3-4 times faster; and, finally, the use and waste of water are reduced."

Practical process

In practice, the researchers put the spent cathode lithium iron phosphate material and a solid-phase oxidant, sodium persulfate, into a ball mill tank, in which the mechanical force generated by the collision of the grinding balls accelerates the oxidation reaction. The iron in lithium iron phosphate is oxidized, and the lithium is released and converted into lithium sulfate. The lithium sulfate is then precipitated and recovered in the form of lithium phosphate.

Using this method, 99.7% of the lithium in $LiFePO_4$ cathodes can be recovered. And the reaction is fast – as quick at five minutes – highly selective, avoids the use of acids and bases, and results in three new chemical products: iron phosphate, sodium sulfate and lithium phosphate.

"We are still trying more solid oxidants and other types of co-milling solid-phase reaction reagents," concludes Li. "We look forward to finding a solid-phase oxidant with a faster reaction rate, or to obtaining a higher value-added lithium product, so as to further broaden the profit margin of lithium recovery."

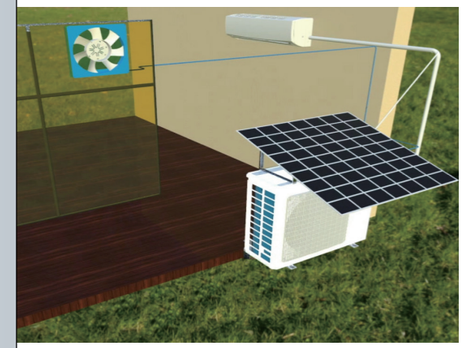
Demand for lithium iron phosphate batteries (pictured) in electric vehicles is growing, and so too is the need for recycling technologies.

Reference

Liu, K. et al. Selective extraction of lithium from a spent lithium iron phosphate battery by mechanochemical solid-phase oxidation. *Green Chem*. 23, 1344 (2021) Doi: 10.1039/D0GC03683H

Could we reduce aircon's climate impact by more than 80%?

Systems that make use of evaporative cooling and ventilation, as well as optimized vapor compression refrigeration, are on their way to the market, thanks to new research.



An efficient vapor compression air conditioner (white) works in tandem with an evaporative membrane installed within an environmentally responsive ventilator and photovoltaic power.

It's an irony of global warming that the more humans do to keep themselves cool against rising temperatures, the more they will probably be adding to the problem by burning fossil fuels to power air conditioners. But, because conventional air conditioning technology now only achieves roughly 35% of theoretically maximum efficiency, there is still room to improve the situation.

Recently, researchers from Tsinghua, supervised by Doctor Baolong Wang and Professor Wenxing Shi, have developed a series of intelligent hybrid systems, one of which can achieve a peak 85.7% reduction in climate impact. This work has been done in partnership with one of the largest residential air conditioner manufacturers in the world, Gree.

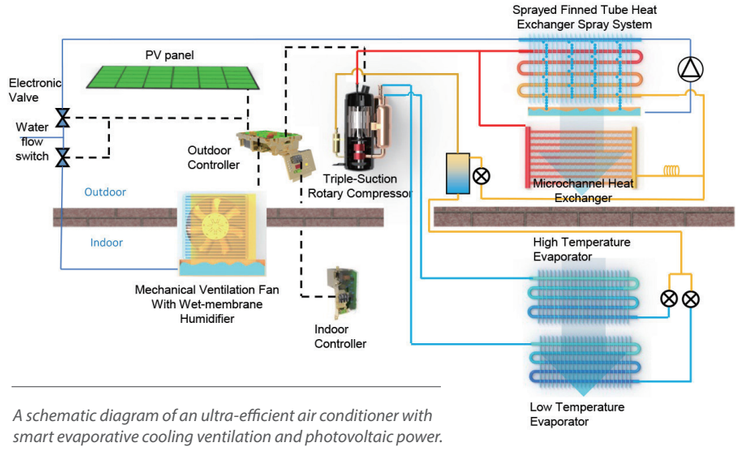
The system combines improvements to the energy intensive process of conventional vapor compression refrigeration technology, with calibrated input from less energy intensive water evaporation and ventilation cooling, as well as solar power.

"An environmentally responsive fresh air ventilator with evaporative cooling was developed to diminish the operating hours of the vapour compression air conditioner," explains Shi. When the air outside is humid, for example, then conventional vapor compression refrigeration is the best option. But when the conditions are hot and dry, water evaporation can remove heat from the air by using heat energy to turn water into vapor. The Tsinghua/Gree system uses a wet membrane to do this, although spraying water mist into hot air or onto fine pipes through which hot air passes can achieve the same result.

When the air outside is cool and dry, using a fan to bring in outside air can also be an efficient means to cool a room than recycling the air inside it via a conventional air conditioning system. In the early morning or in the evening, for example, the air outdoors is sometimes cooler. Even if the air is warmer, it may still have a cooling effect as long as the air is dryer and can create an evaporative effect with more humid air inside, adds Shi.

In April, 2021, one design by the team was selected from more than 2,100 entries as the winner of the Global Cooling Prize.

To achieve the gains needed to win the Global Cooling Prize, the team not only used solar power for their system, but also a super-efficient vapor compressor. This utilized a gas-injected compression cycle with relay cooling, a rotary compressor with triple suction ports and two condensers and evaporators.



A schematic diagram of an ultra-efficient air conditioner with smart evaporative cooling ventilation and photovoltaic power.

Local climate-aware cooling

The elegance of the Tsinghua/Gree team's innovation comes from its integration of the three cooling methods with intelligent control of the input from each to suit outdoor conditions, says Shi.

However, outdoor conditions will vary by season, time of day and of course local climate, so a hybrid system featuring smart evaporative cooling ventilation, alongside a conventional air conditioner, was tested in three cities; Nanjing (in a wet climate zone), Beijing (semi-wet) and Lanzhou (semi-dry/dry).

The system achieved the biggest energy efficiency improvement in arid Lanzhou (221.9%), and the least in humid Nanjing (12.3%).

"Different versions of our systems could be manufactured to suit different climates and economic conditions," explains Wang. "A simplified version may be suitable for hot and dry underdeveloped areas, while a system incorporating a hybrid heat pump might be developed for regions with heating demands. It also accords with the goal of "Providing Sustainable Cooling for All" proposed by the UN."

The Global Cooling Prize was a one-off contest launched in November 2018. It was sponsored by the Government of India and sustainability advocacy groups, the Rocky Mountain Institute and Mission Innovation. It attracted entries from 96 countries. At the award ceremony in April, organizing committee chairman Iain Campbell said he believed the Tsinghua/Gree system has "become an important part of the global climate change solution."

It may well help China meet its emissions targets, agrees Shi, who points out that China is the largest country in regards to the manufacturing of room air conditioners, exceeding 150 million units in 2019. Hybrid air conditioning units are currently being commercialized with Gree.

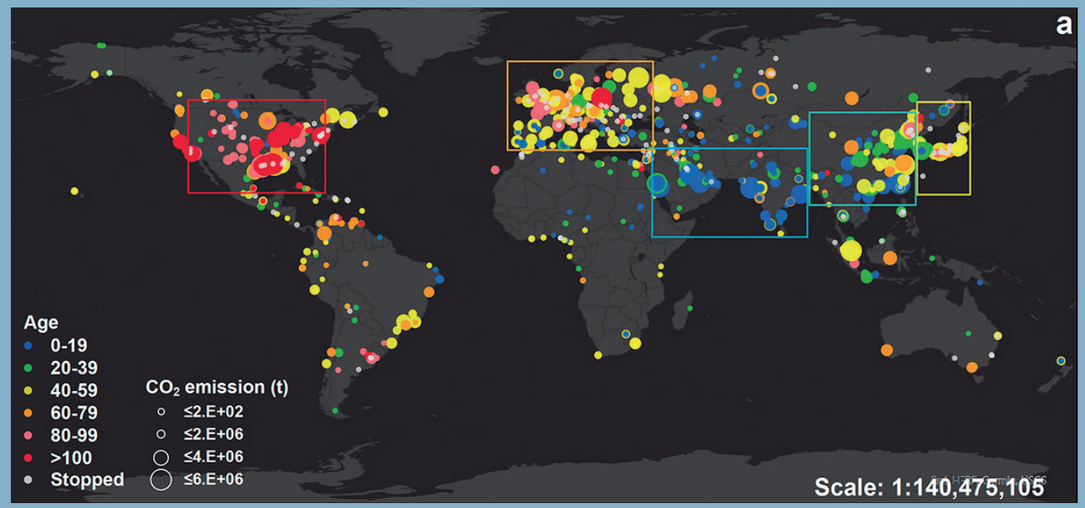
Reference

Yang, Z., Zhao, J.,Wang, B., Zhuang, R., Li, X. et al Experimental performance analysis of hybrid air conditioner in cooling season. *Building and Environment* 204, 108160 (2021)

(L-R): Mengdi Cui, Zixu Yang, Baolong Wang, Yi Jiang, Wenxing Shi, Hansong Xiao and Jiaan Zhao.

Oiling the wheels of emissions reduction

A global inventory of oil refineries reveals an expansion of high emission new facilities in Asia and the Middle East.



A heatmap of oil refinery age and emissions shows a clear concentration of older refineries in North America and a much younger cohort across Asia and the Middle East.

The oil refining industry contributes to 4% of global emissions, and an audit of its status is overdue. In 2021, an international team published a thorough review called the Carbon Emission Accounts and Datasets-Global Refinery Emission Inventory (CEADs-GREI).

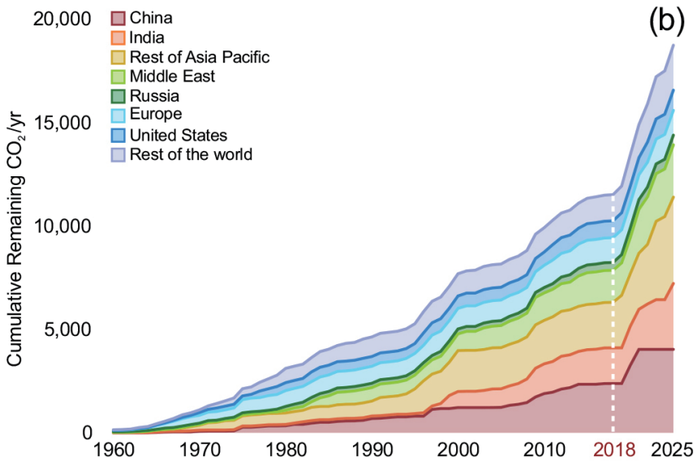
The researchers, led by distinguished professor of climate change economics at Tsinghua, Dabo Guan, and PhD candidate, Tianyang Lei, based CEADs-GREI on 1,056 refineries in operation between 2000 and 2018. In a paper published in August 2021, they revealed a continued growth in oil refinery emissions in the last two decades, as well as a trend, since the 2008 financial crisis, towards an increase in the number and intensity of new refineries in Asia and the Middle East.

After considering future output as well as planned additional plants, they have concluded that a 10% reduction in CO_2 emissions can be achieved by 2030 via more efficient petrochemical processing integration at new facilities, upgrading catalytic cracking units at old facilities to cleaner hydrocracking units, renewable fuels and the installation of carbon capture and storage devices.

"The remaining carbon budget for 1.5°C and 2°C from the beginning of 2020 is 400 and 1,150 gigatonnes of CO_2 respectively," Guan points out. "If all the existing and proposed refineries operate as usual, without adopting any low-carbon measures, we estimated the cumulative CO_2 emissions of global oil refineries from 2020 to 2030 will be 16.5Gt, accounting for 4% of the remaining 400Gt carbon budget. Coordinated action in this space could have a huge impact."

Oil refineries move east

In addition to mapping geographical distribution of refineries, CEADs-GREI looked closely at their age. In the developed regions of the United States, Europe and Japan for example, older refineries (40 years or older) tend to dominate, while most facilities in the Middle East, China and India are relatively new (less than 40 years). This reflects the origins of the industry in the United States in the 1930s, followed by its spread to other regions.



The committed emissions and regional distribution of the global oil refining industry in 2018 and 2025.

The study also looked at whether plants were shallow processing refineries, meaning simple configuration without conversion units, or more complex deep processing refineries, with catalytic cracking and hydrocracking units. Unlike shallow processing refineries, deep processing refineries can convert heavier, cruder oil into lighter products, such as petrol. They tend to be much larger, and their emissions per unit of throughput are four times higher.

The study found global refining and emissions generally rose steadily over the 20-year period it surveyed. The increase was reversed briefly by the 2008 financial crisis. Since then there has been a clear shift in capacity towards Asia.

The shift towards Asia should continue over the coming years, adds Guan, with 85% of new capacity built in emerging regions. CO_2 emissions will thus continue to rise, from 1,242 million tonnes in 2018 to 1,343Mt in 2025, but not only because of greater throughput. Heavier and lower quality crude oil supply and increasing demand for light refined oil products, will drive a configuration shift from shallow processing refineries to deep processing ones. This was one of the study's important findings, and it will work against emissions reduction.

Foundation for lower emission strategies

Lei is hoping the study will form a basis for global coordinated action. "Our time-series, global oil refining CO_2 emissions inventories at the plant-level will provide a firm basis for the analysis of technology-driven carbon mitigation pathways worldwide," she says.

As for how reduction can be achieved, the study indicated that the best way will be to improve the efficiency and technology of existing plants without adding new refineries and refining equipment against the backdrop of growing demand for light refined oil products and heavier crude oil supply.

Efficiency improvements will yield the biggest gains in Asia's newer and less well-run refineries, where, for example, the addition of petrochemical processing units for value added production could lead to greater output without the need to increase emissions hugely. "We hope to see more oil refining-petrochemical integrated facilities in the future," says Guan. Technical improvements, including the upgrading of fluid catalytic cracking units – which convert crude oils into gasoline, olefinic gases, and other petroleum products – to cleaner hydrocracking will make the most difference in the older plants of the United States. In the long run, carbon capture and storage technology should also be added, says Guan.

CEADs-GREI will certainly inform the policy of China, which has been the world's largest greenhouse gas emitter since 2005. Its oil refining industry, which has been the fastest growing, is currently the second largest. Two of its state-owned oil companies – China National Petroleum Corporation and China Petrochemical Corporation – control about 10% of global distillation throughput.

"In the face of these pressures, China is still the first developing country to have committed to carbon neutrality before 2060," notes Guan. "To achieve carbon mitigation and sustainable development, more vigorous measures will be taken."

Reference

Lei, T., Guan, D., Shan, Y., Zheng, B., Liang, X. et al. Adaptive CO_2 emissions mitigation strategies of global oil refineries in all age groups. *One Earth* 4(8), 1114-1126 (2021) doi: https://doi.org/10.1016/j.oneear.2021.07.009

An ultrasensitive, liquid metal-based e-skin motion sensor

An electronic skin with cutting-edge sensitivity tracking a broad range of body motion has been created using liquid metal and a rigid nacre-inspired chromium-copper and silver underlayer.

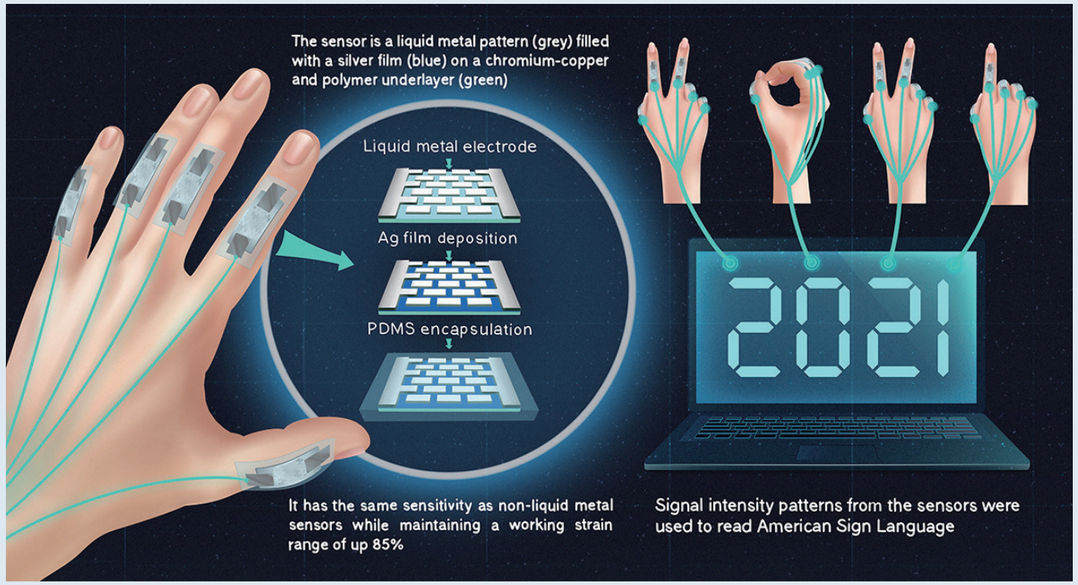
Electronic skins are flexible, stretchable and self-healing devices that may one day form the basis of wearable and implantable sensors that monitor motion and physiological data, or give sensation feedback to prosthetics or robotics.

In May 2021, Tsinghua's Lei Liu, Hongwei Zhu, Guisheng Zou, and their colleagues, described an exceptionally strain tolerant and sensitive electronic skin based on liquid metal and a shell-inspired chromium-copper and silver supporting structure.

"We improved the sensitivity of liquid metal-based strain sensors by two orders of magnitude while maintaining a wide (>85% strain) working range," explains Liu. The team tested their device by accurately interpreting sign language in English and Chinese, by sensing finger motions. It's the first time, to Liu's knowledge, that a sensor based on a liquid metal or a liquid metal composite has achieved comparable sensitivity as other state-of-the-art sensors.

Cracking e-skin

Liquid metals are popular electronic skin materials because they have strong electrical and thermal conductivity, stretchability and biocompatibility. But liquid metal-based electronic skins haven't typically been able to achieve great sensitivity as electromechanical sensors, because their resistance change



A laser forms a pattern in liquid metal (grey) coated over a chromium-copper underlayer on a polymer base (green). A silver film (blue) is deposited within the pattern. This sensor is then encased in polydimethylsiloxane (PDMS), a polymer containing carbon and silicon widely used for the fabrication of microfluidic chips.

is normally insensitive during mechanical stimuli due to the fact that cracks form much less often in liquid metals.

Solid metal film cracking has been an established strategy to achieve high-sensitive electrochemical sensors. Although it appears a promising way to improve the sensitivity of liquid metal-based sensors by incorporating crack-sensitive films, it typically only works for limited strains, beyond which the cracking becomes so extensive that the sensor is not able to conduct a current.

"In our work, we propose a unique brick-and-mortar architecture to cope with this issue," explains Liu. "This architecture consists of a biphasic pattern, which is the liquid metal with a chromium-copper underlayer as the 'bricks', and a silver film as the 'mortar'". The researchers took inspiration from the natural material nacre, also known as mother-of-pearl, which has a very high fracture toughness due to a combination of calcium carbonate platelets (the 'bricks') and a polymer (the 'mortar').

Strong, flexible foundation

The liquid metal was first coated over a chromium-copper underlayer supported on a flexible polymer, and then removed with a laser to form a pattern around which the silver film was deposited.

The rigid chromium cells regulate local strain, avoiding the formation of cut-through cracks in the silver film and instead promoting the formation of small cracks and buckling, which maintains electrical conductivity and ensures a wide working range. In a simple silver layer, cut-through cracks appear already at a strain of 20% and induce electrical disconnection. In the engineered structure, even at 50% strain, cut-through cracks barely started appearing. The separation between the liquid metal pockets prevents the formation of continuous liquid metal paths, while letting the liquid metal create crack-free regions during strain.

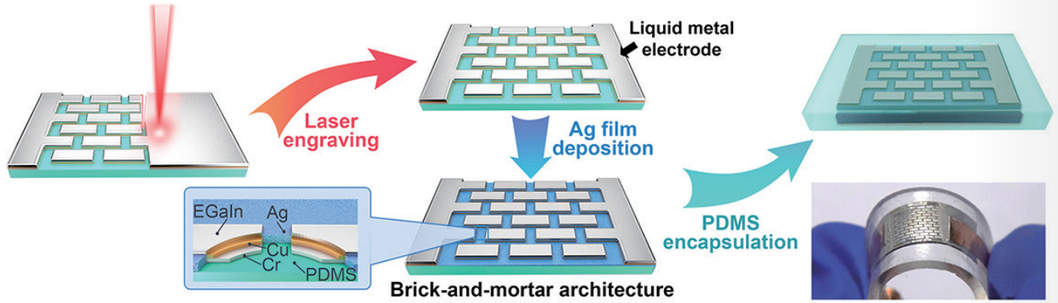
To test the sensor, the researchers used it to detect hand gestures to identify a phrase in American Sign Language, and English and Chinese sentences in Morse code.

"The sign language test is a good demonstration of the applicability of electronic skins," remarks Liu. "By sensing finger motions, different signs can be distinguished, and thanks to the connection with information processing terminals their meaning can be extracted."

The next steps in the development of this type of sensors include the ability to distinguish between different types of movement, such as bending and stretching, which often co-exist. Because the device uses low-cost materials that are already commonly used in flexible electronics and standard processing methods, there is potential for scalable and economical fabrication of sensors based on this design.

Reference

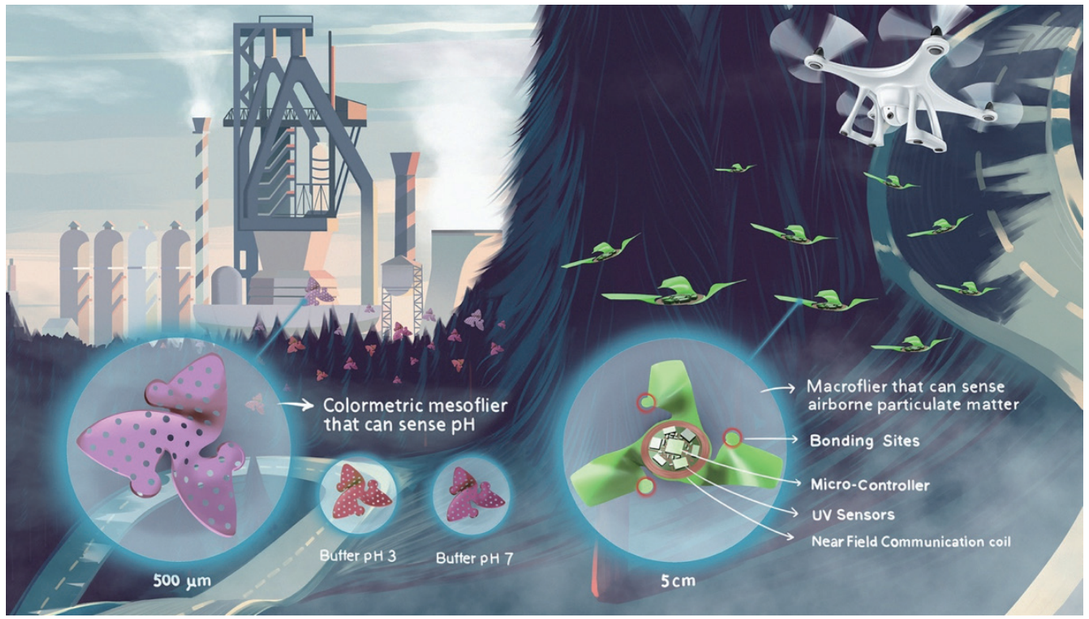
Feng, B., Jiang, X., Zou, G., Wang, W., Sun, T. et al. Nacre-Inspired, Liquid Metal-Based Ultrasensitive Electronic Skin by Spatially Regulated Cracking Strategy *Advanced Functional Materials* 31(29), 2102359 (2021) doi: 10.1002/adfm.202102359



To make the sensor a laser forms a pattern in liquid metal (grey) coated over a chromium-copper underlayer on a polymer base (green). A silver film (blue) is deposited within the pattern. This sensor is then encased in polydimethylsiloxane (PDMS), a polymer containing carbon and silicon widely used for making microfluidic chips.

Airborne sensors inspired by seeds

Imagine floating fleets of small-scale, low energy fliers that can monitor pathogens or particulate matter in the air.



The researchers modeled a number of fliers with geometries inspired by seeds that were designed to carry out environmental monitoring. These included helicopter style 'mesofliers' (usually about 1 mm) with polycarbonate surfaces that respond with different colours based on local pH and 'macrofliers' (>1 mm) that use UV sensors to identify airborne particulate matter.

Seeds have planted new inspiration for scientists who are trying to emulate their ability to travel long distances in freefall.

The geometries of seeds combine high drag forces and significant uplift, relative to the downward force of gravity, which results in the very slow descent speed or 'terminal velocity', explains Yihui Zhang, who works in Tsinghua's Engineering Mechanics Department and Center for Flexible Electronics Technology.

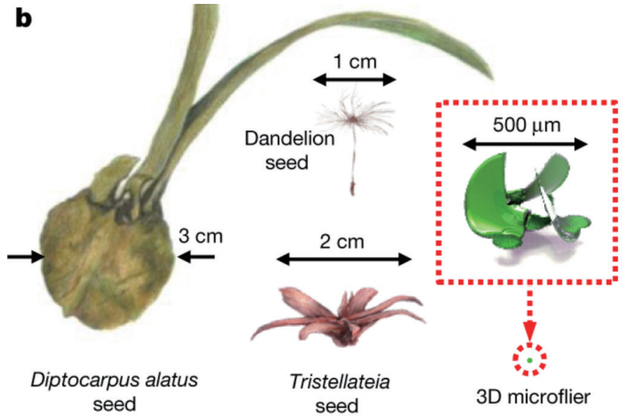
In *Nature* in September 2021, Zhang and his collaborators described a framework to explore some of the possibilities seed-inspired fliers bring to environmental monitoring. To do so, they created and tested a number of shapes, the most complete version of which was a 5 cm battery-free wireless flier capable of detecting airborne particles.

Why are these shapes being examined now? Very small objects tend to have advantages in the aerodynamic behaviour that makes passive 'flight' possible, explains Zhang. Recent developments in 3D mesostructure manufacturing and miniaturized electronic, optoelectronic, microfluidic and microelectromechanical technologies make the fabrication of seed-inspired 3D electronic devices practical.

The paper's authors identified promising forms and fabrication techniques, but they also note the challenges of wind and biodegradability. Nonetheless, Zhang estimates that it could take as little as "three to five years to realize useful environmental monitoring via seed-inspired fliers".

Seeds of innovation

There are many potential uses for fliers. Chinese researchers have been working hard to understand the sources of airborne particulate matter from pollution, for instance.



Shown to scale: the helicopter shaped seeds of Diptocarpus alatus and Tristellateia, a parachute type seed from a dandelion, and a 3D microflier.

After a series of weather events, exacerbated by pollution, caused widespread health problems across the country in 2013, the Chinese government's 2013 Air Pollution Action Plan put in place reforms that helped make significant improvements to air quality. Atmospheric particulate matter (PM) 2. 5 levels in Beijing reduced by 33% between 2013 and 2017, for example.

So far, these reductions have come about largely due to stringent regulation of industry, but to understand smaller sources of airborne particulate matter is complex. Plane, drone or weather balloon measurements are limited by the cost implications, while tracking by satellite can only show detail at a resolution down to 3 km. Fliers could provide much more detailed data than stationary ground monitors. This detailed data could also help build algorithms to improve satellite pollution assessments, says Zhang.

Tiny seed-inspired fliers could be deployed by plane or drone, he suggests. "Even releasing the fliers by hand at the ground level is possible, as the fliers can be carried far away by the wind," he speculates.

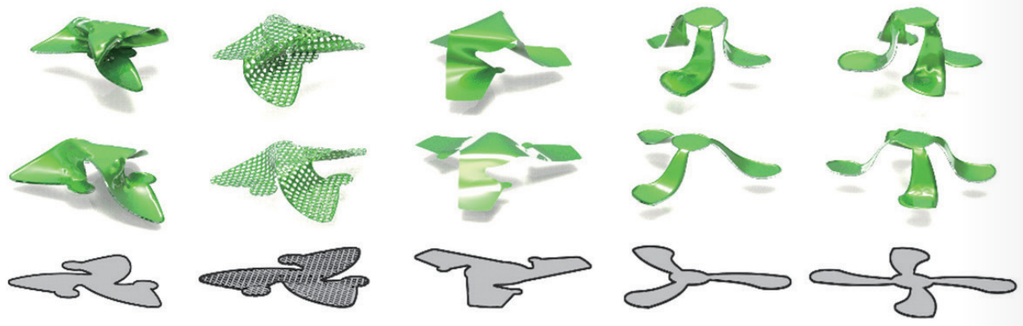
Size does matter

In their study, Zhang and his collaborators set out to look specifically at the possibilities of passive structures designed for controlled, unpowered flight across natural environments or city settings.

Seed geometries, they note, fall broadly into four categories: parachutes, gliders, helicopters and flutterers, all of which are of a large area relative to their mass, slowing their descent.

Using theoretical, experimental and numerical methods, the international group determined that helicopter fliers exhibited the most stable falling behaviours. They also noted that small micro-fliers were typically more aerodynamically effective. "But a trade-off is that the small scale microfliers cannot carry large payloads, such as electronic components for targeted missions," says Zhang. "Therefore, practical applications will need balance terminal velocity and capability to carry payloads."

The team examined the effect of scale, porosity, number of wings and aspect ratio

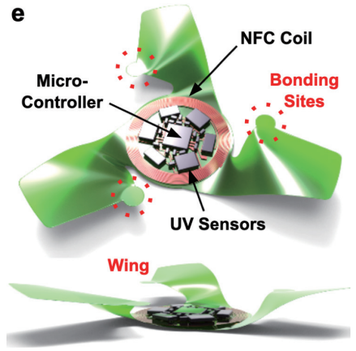


The geometrical transformation of different 2D precursors (bottom row) into corresponding 3D structures with modest (middle row) and large (top row) aspect ratios.

for helicopter style microfliers (<1 mm), mesofliers (about 1 mm) and macrofliers (>1 mm). "At small scales, shapes composed of fibers, or with porosity, can help create more drag and lower terminal velocity. At relatively larger scales, chiral design and improved blade design such as curved blades can help to reduce terminal velocity," explains Zhang.

While the team hopes to focus more on IoT enabled fliers, they also looked into an example that used electronic alternatives – pH-responsive 3D mesofliers that use a color indicator based on anthocyanin infiltrated into a polycarbonate membrane. Aerial photographs of these sensors could be analyzed for monitoring purposes.

Other options for non-electrical sensors, says Zhang, include ultraviolet light intensity sensors, temperature/humidity-triggered sensors and chemically driven Volatile Organic Compounds (VOC) gas sensors.



A 3D IoT macroflier with a circuit to measure fine dust pollution through a light dosimetry method.

This 'planar-fabrication-based process' is intrinsically compatible with the well-developed fabrication techniques of conventional silicon-based electronics, Zhang points out.

Particulate matter sensing

Polymer films were used to form each of the fliers the group tested via shape material memory effects. Specifically, after etching, heating the assembled flier to 70 °C for one minute in an oven and cooling it to room temperature created the 3D shape. Immersing the structure into chemical solutions to eliminated bonding site layers then helped further release the structures as free-standing objects.

To make their largest test flier, the electronics-carrying particulate matter sensing flier, Zhang and his team layered 12 micrometre shape memory polymer and 18 micrometre copper foils.

The copper foils can serve as reliable metal interconnections for electronic components after wet etching, explains Zhang. Transfer printing the individual components and soldering yielded a wireless sensing system of particulate matter.

Flight path forward

There are other possible uses for the fliers, of particular interest, in disease management. "Some biochemical sensors can sense the metabolites of certain pathogens," explains Zhang. "In combination with the spatiotemporal monitoring of temperature and humidity, it is possible to judge the spread of pathogens in the air."

But there are still a number of challenges to be addressed — including how to effectively account for wind. "In future works, dynamic modelling methods will be applied to simulate the flier in wind, and dynamic theoretical models will help to understand the underlying mechanisms," says Zhang.

This melds into future plans to make the fliers slightly less passive. "For example, we plan to integrate the flier with actuation and control modules so that they can self-adjust the tilt angle of their blades to change the flight path, according to local wind strength and direction sensed by the flier," explains Zhang.

Other commentators have noted that researchers will need to create biodegradable components as the largely passive devices will likely not be easily retrievable. This important advance will take a coordinated international effort and is still some way off, says Zhang.

"As far as I am concerned, it will probably take 10 years to realize fully-degradable integrated smart fliers," he says. "The connections and the substrates can already be made degradable. But to make the chips also degradable, enormous efforts are still needed."

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Kim, B.H., Li, K., Kim, JT., Park, Y., Jang, H. et al. Three-dimensional electronic microfliers inspired by wind-dispersed seeds. *Nature* 597, 503–510 (2021) doi: 10.1038/s41586-021-03847-y

Lessons in low-light photosynthesis

Understanding antennae-like phycobilisomes, and the complex mechanisms of photosynthesis in organisms such as red algae may be key to low-light artificial photosynthesis.

If artificial photosynthesis is ever realized, the unique light harvesting abilities of organisms that live in low light could inspire super-efficient solar conversion systems that could be stored under the vast ocean surface, says Sen-Fang Sui, a professor at Tsinghua's School of Life Sciences.

Sen-Fang is using advanced cryogenic electron tomography to study the macromolecular structures of a uniquely efficient group of light-converting organisms, including cyanobacteria and red algae.

These organisms all use photosynthesis enhanced by antenna-like structures that capture and transfer light energy known as phycobilisomes. "Most organisms using phycobilisomes are adapted to habitats with low light and blue-green light 20 meters or more below the ocean surface," he explains. "Thus, they need the large and high-efficient phycobilisome light harvesting antenna to capture limited light energy."

Significant structures

Phycobilisomes, Sen-Fang's group are revealing, have an orderly efficiency. In photosynthesis, light is absorbed by chromophores and in red algae. Energy transfer is then mediated by chromophores that covalently bind to phycobilisomes composed of phycobiliproteins and linker proteins. These phycobilisomes contain hundreds to thousands of chromophores that ensure a vast absorption of light energy.

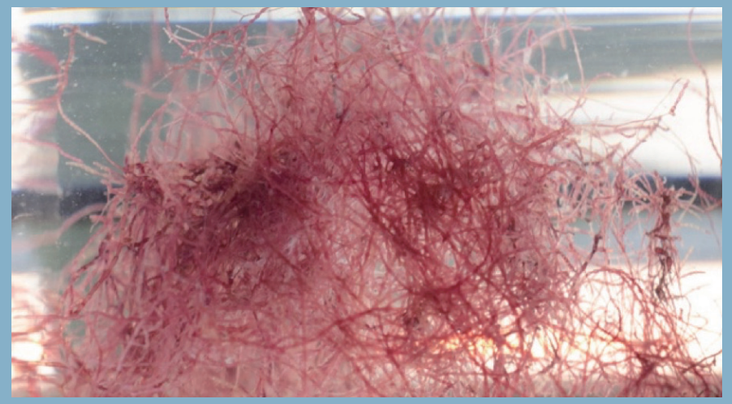
The energy they absorb is then used by photosystem II, a pigment-protein complex, to catalyze water oxidation and release oxygen.

Recently, Sen-Fang's group have been using *in situ* cryogenic electron tomography in combination with cryogenic focused ion beam milling to directly dissect key macromolecular structures involved in photosynthesis in the undisturbed cellular environment at molecular resolution. By using this approach, they are able to study native phycobilisome-photosystem II complexes by bypassing the most difficult isolation step usually needed for *in vitro* study.

"Phycobilisomes are water-soluble, while photosystem II is a transmembrane protein complex that needs detergent to remain soluble *in vitro*," explains Sen-Fang. "We usually use detergent to purify a phycobilisome-photosystem II complex. However, detergent can affect the binding between phycobilisomes and photosystem II and lead to the disassembly of the complex, which previously made it difficult to obtain intact complexes."

The group's recent high-resolution cryo-electron microscopy imaging of intact phycobilisome structures has revealed that their most striking feature is a scaffold formed by the linker proteins. Phycobiliproteins are assembled on the scaffold in a well organized manner. Thus, all chromophores are also kept in order[1].

Importantly, an analysis by the team published in 2020 in *Nature* demonstrated that the linker proteins not only control the assembly of phycobiliproteins into phycobilisomes, but are extensively involved in the modulation of the energy states of the chromophores through various dispersion forces that ensure the efficient unidirectional energy transfer[2].



Red alga Griffithsia pacifica

Light adjustable

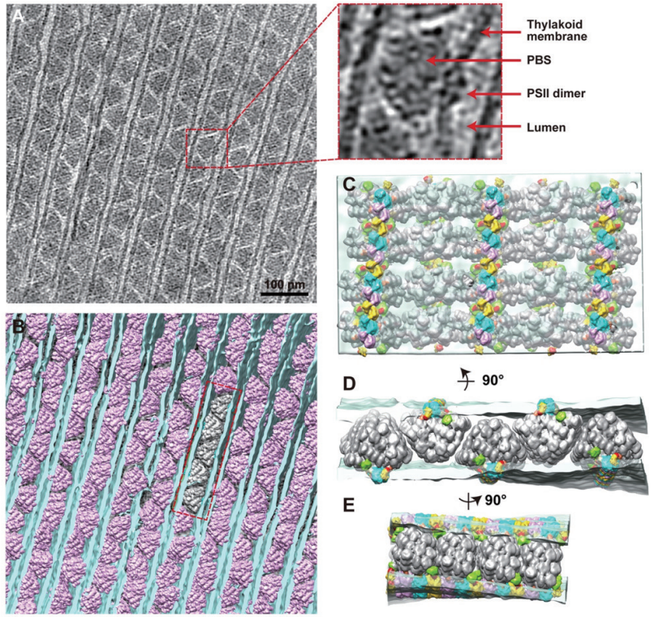
The group has also looked closely at the biogenesis and repair of photosystem II. In a study published in *PNAS* in 2021, Sen-Fang's group looked at binding sites of assembly factors cyanobacteria at the luminal surface of photosystem II.

They found that the binding sites of Psb27, an assembly factor that plays important roles in the repair of photosystem II, largely overlaps with that of PsbQ or PsbQ' proteins[3]. These proteins help plants to grow under ever-changing environmental conditions.

"Based on this observation, we speculated that this binding site may bind to different subunits with similar 3D structures at different stages, for instance, binding to Psb27 during the repair cycle and binding to PsbQ to maintain high activity at a more mature stage," says Sen-Fang.

The better researchers understand these complex living systems, says Sen-Fang, the easier it is for those pursuing artificial photosynthesis, an emerging technology, inspired by natural photosynthesis, that aims to produce hydrogen or other industrially useful compounds using CO_2, water, and sunlight.

Not only could highly sensitive artificial photosynthesis technology make use of the planet's vast water-covered surface area, but it could absorb large quantities of carbon at the same time.



(A) A tomogram cross-section of phycobilisome–photosystem II supercomplexes. (B) Spatial mapping of phycobilisomes (purple) attached to photosystem II dimers in the thylakoid membrane (blue). (C–E) Insets from (B) at different angles. Thylakoid membrane (light blue) and phycobilisome (grey).

(A) The structure of a double phycobilisome–photosystem II supercomplex at a resolution of 15.6 Å. (B) The structure of a single phycobilisome–photosystem II supercomplex at a resolution of 14.3 Å. (C) Photosystem II dimers A and B, and (inset) two PsbO subunits bind with each other at the interface of adjacent photosystem II dimers.

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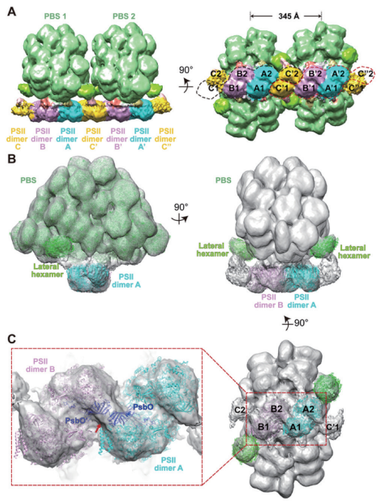
2. Ma, J., You, X., Sun, S., Wang, X., Qin, S. et al. Structural basis of energy transfer in *Porphyridium purpureum* phycobilisome. *Nature* 579(7797), 146-151 (2020) doi: 10.1038/s41586-020-2020-7

3. Huang, G. Xiao, Y., Pi, X., Zhao, L., Zhu, Q. et al. Structural insights into a dimeric Psb27-photosystem II complex from a cyanobacterium *Thermosynechococcus vulcanus PNAS* 118, (2021) doi: 10.1073/pnas.2018053118



Robotic lab on wheels offers safe, fast and accurate COVID-19 testing

A state-of-the-art diagnostic van can test up to 2,000 people a day, return results within 45 minutes with a very high sensitivity (limit of detection of 150 copies/mL), and reduces contact risks.

A new laboratory-on-wheels developed by Tsinghua University scientists allows for fast-turnaround and highly-accurate COVID-19 testing, without the stress and risk of people with suspected coronavirus infections having to travel and wait long for a diagnosis.

Equipped with oropharyngeal (middle throat) swap sampling robots, a new type of virus inactivation device, integrated microfluidic nucleic acid analyzers, and a 5G communication system for automated result reporting, the small-footprint mobile testing van can deliver results in under 45 minutes, with almost 100% accuracy and minimal human involvement.

At this point in the COVID-19 pandemic, the coronavirus is largely under control in China and in parts of the world that adopted aggressive containment measures, notes Jing Cheng, who headed the development of technology at Tsinghua. But outbreaks still flare up occasionally, demanding quick, accurate local testing responses — which is where the COVID-19 Mobile Laboratory comes in.

Biosafety first

Technologies that streamline and contain the complete workflow of the molecular diagnostic assays set the laboratory apart from others like it. "Unlike conventional systems that simply adopt the layout and instruments of typical biological laboratories to construct a 'laboratory-on-a-truck', our mobile laboratory uses state-of-the-art robotics and microfluidic technologies to create a system of automated and contained sample acquisition and processing," explains Cheng.

The COVID-19 Mobile Laboratory is equipped with a six-axis robotic arm, a biosafety cabinet, quick pathogen inactivation device, microfluidic nucleic acid analyzers, and a 5G enabled information system to report results.

"The industrial design takes biosafety and functionality into consideration, enabling highly automated and self-sustained nucleic acid testing within a compact footprint," explains Cheng, who is a member of the Chinese Academy of Engineering, director for National Engineering Research Center for Beijing Biochip Technology, and CEO for CapitalBio Corporation, a company that helped with the van's development.

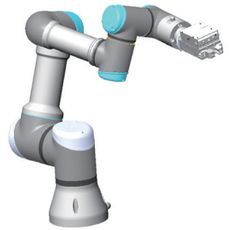
The microfluidic component of the van, for example, can extract and amplify coronavirus RNA much quicker than other genetic analysis instruments. The thermoelectric inactivation device, which relies on infrared radiation to precisely control sample temperatures, ensures biosafety without compromising the integrity of pathogen nucleic acids. And the six-axis sampling robot arm, guided by a digital camera with a force feedback system, can swab the oropharynx with minimal discomfort for test participants.

The mobile laboratory is also equipped with cables for plugging into a municipal electric supply, along with a power generator capable of delivering backup power. Plus, there are ventilation systems for both the biosafety cabinet and the laboratory cabin, and a water distribution system to avoid cross-contamination. In total, it can provide on-site tests for up to 2,000 people daily, requiring only two lab technicians and a driver for its operations.

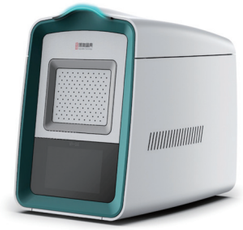
Validated design

Cheng and his colleagues clinically validated their mobile testing set-up on more than 700 clinical samples collected from patients across China. Compared to the gold standard PCR testing platform, the Tsinghua system yielded the same result roughly 99% of the time, demonstrating the feasibility and accuracy of the approach. The researchers detailed their findings and experimental design in the journal *Clinical Chemistry*.

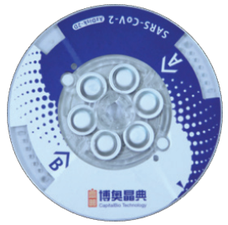
"The small footprint mobile testing facility enables molecular diagnostics outside people's homes," Cheng says. "In this way, not only can we save the time and identify potential patients on-site, but also reduce the risk of contamination during sample transportation to central laboratories."



Robot arm



Quick inactivation device



Microfluidic chip

Microfluidic nucleic acid analyzer

Reference

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