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KERNEL

Editorial

Hidden inside rocks and fossils, isotopes have been helping scientists understand not just our planet's past, but also what the future could hold. Read more about how several students at IISc are using these isotopes to answer questions about the Earth's climate, in this issue of *Kernel.*

The DREAM lab, featured in this issue, seeks to tap into the power of distributed computing for socially-relevant applications. We also cover stories on an artificial protein shell that can mimic SARS-CoV-2, how fish bones are being used to estimate seawater temperature, and more.

CHASING ISOTOPES

Foraminifera (Image courtesy: Alain COUETTE/Wikimedia Commons)

CHEMICAL PROXIES HAVE PROVIDED SCIENTISTS A HANDLE ON UNDERSTANDING THE PLANET'S CHANGING CLIMATE

Over the last century, scientists have been keenly invested in quantifying the global impact of human activities on the environment. Of key concern is the reconstruction of the climate prior to large-scale human interference. This is where chemical proxies – such as isotopes – come in handy.

Isotopes are atoms of the same element with the same atomic number but a different mass number, owing to the different number of neutrons in their nuclei. Due to their differing properties in different environmental conditions, they have become an essential part of a climatologist's toolkit to understand the past and predict the future weather of Earth and other planetary bodies. Tiny differences in the stable isotope ratios in biological and abiotic archives have revealed more about the Earth's climate than most other methods. Perhaps the best example of this is the change in the ratio of carbon isotopes ($^{13}C/^{12}C$) present in the atmosphere. Since the Industrial Revolution in the mid-19th century, when humans started burning fossil fuels on a massive scale, there has been a significant decline in the atmospheric $^{13}C/^{12}C$ ratio. Plants prefer absorbing ^{12}C during photosynthesis, and increased human dependence on this fossilised plant matter has released tremendous amounts of ^{12}C in the atmosphere.

Several PhD students at the Centre for

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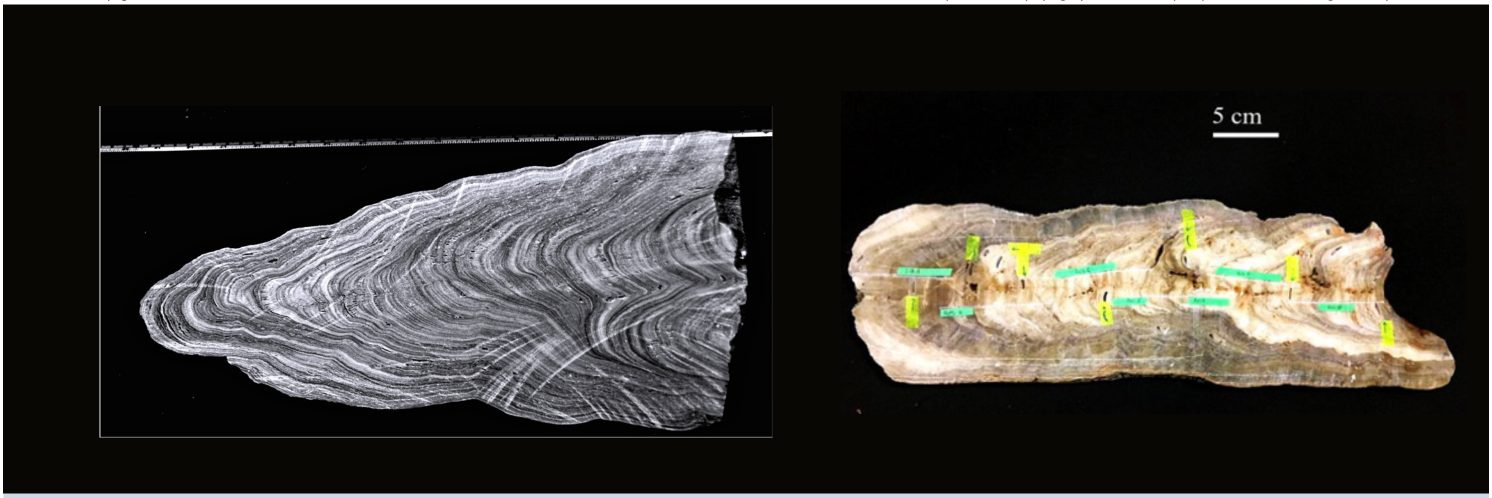
A cut speleothem displaying layers which have precipitated over time (Image courtesy: Rachana Subba)



Earth Sciences (CEaS) and the Divecha Centre for Climate Change (DCCC) at the Indian Institute of Science (IISc) are also harnessing the potential of isotopic signatures to answer questions about our planet's past as well as the present.

Rachita Ghosh is studying ancient rock exposures from Badami, Karnataka, in order to reconstruct the climate in the past (palaeoclimate). This sedimentary rock locality that she focuses on primarily comprises limestone, dolostone and carbon-rich shale. Limestone and dolostone are made of calcite and dolomite respectively. The premise behind her work is simple. Lighter isotopes are always the first to move from the stable phase (here, liquid) to the unstable phase (here, gas). Rising surface temperatures lead to the evaporation of ocean water, and water molecules containing lighter oxygen isotopes evaporate faster. As a result, the water that is left is rich in heavier isotopes. And so, a carbonate rock with a greater quantity of heavier isotopes of oxygen indicates that the rock was formed or precipitated in warmer waters.

The same principles can be applied to other elements and other natural archives that capture these processes. Neha Tanwar is studying how the magnesium isotope ratios have changed in seawater over the last 70 million years as recorded in fossil foraminifera shells. Foraminifera are single-celled microorganisms that secrete a tiny shell made from calcium carbonate around themselves. Since each species dwells in different salinity and temperature conditions, and in different "habitats" (soil, mud, weed), their shells can be used to determine the age and environment in which foraminifera grew. The Mg/Ca ratio in foraminifera shells is used to determine the temperature of the aquatic environment in which they were formed.

On Earth and beyond

Each isotope gives a unique glimpse into Earth's history. This has enabled Utpalendu Haldar to see how the chemical composition of Earth's crust changed over time. He focuses on neodymium isotopes, which are released from rocks into surface waters by the erosion of the continental crust. As they carry the neodymium signature from nearby continents, marine archives offer an excellent palimpsest of past erosional processes. The movement of glaciers is one such process that cuts through mountains, revealing a record of the geophysical changes.

"Isotopic compositions of natural archives offer a great tool to understand processes going on, both on the Earth's surface as well as below," explains Sourav Ganguly. He examines the isotope ratios of strontium and calcium in the Sundarbans to study the movement of water between large rivers, ground water and sea water.

Isotopes can yield information about extraterrestrial phenomena as well. Thamizharasan Sakthivel works on how cosmic rays – high energy protons and nucleons that move as fast as light in space – impacted terrestrial biomes. Examining near-Earth explosions of stars (supernovae) that occurred 1.8 to 3 million years ago, one of his studies showed that this phenomenon triggered worldwide wildfires, effecting a vegetational shift from forests to grassland. "We are not the [first] ones [to have] proposed these hypotheses. These hypotheses have been well played in the hands of physicists since the 20th century but [were] not familiar among geoscientists. We substantiated the astrophysical theory with geological evidence," he explains.

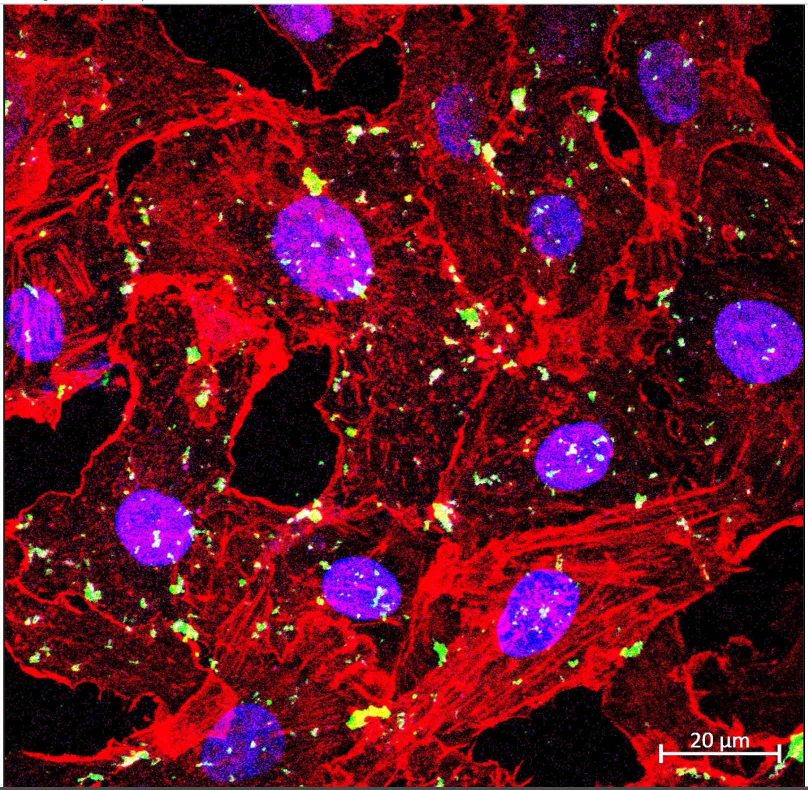
Finally, a key question in isotope-based reconstructions of climate change is the precision to which these chemical proxies are able to successfully record changes in parameters such as rainfall and temperature. To this end, Rachana Subba works on speleothems, which occur in caves and are formed as calcium carbonate aggregates over time, very much like ice cores and lake sediment cores. There are existing records of rainfall for the recent past, and Rachana is using chemical signatures found in speleothems as an analogy for rainfall. "The speleothem records form layer-by-layer, have a good resolution, sometimes at sub-annual levels as well," she explains. "Indian caves, having been subject to both south-west and north-east monsoon rains, serve as a natural rain gauge, helping detect past climate well before humans started measuring rainfall."

Harnessing the potential of carbon and oxygen isotopes, Bhanu Priya Thakur aims to reconstruct the palaeoclimate by tapping into vertebrate fossils, such as teeth or bones. Teeth offer a distinct advantage to such studies because of their preservation and abundance in the fossil record. Explaining the relevance of her work, she says that the Cretaceous Period (145-65 million years ago), was a fairly warm period in Earth's history. "The period I am examining was quite similar to future climate projections, and my studies could inform how biomes and their inhabitant communities are likely to shift should these projections become a reality," Bhanu explains.

Because they are highly sensitive to changes in water, land and air, isotopes serve as excellent indicators of ecological changes. However, the future holds some challenges for isotope research. Sampling of materials has to be well distributed across geography and time, in order to establish solid parameters that future isotope-based observations can be based on. Museums are also rapidly decommissioning their natural archives, which have served as a goldmine for all isotope researchers, making the hunt for isotopes a real race against time.

- Ritvik Chaturvedi

VLPs (visible as green dots) in cells (outlined by red colour) (Image courtesy: Raheja et al.)



ARTIFICIAL PROTEIN SHELL TO COMBAT COVID-19

During the first COVID-19 wave, when Saumitra Das and colleagues were sequencing thousands of samples every day to check for SARS-CoV-2 variants as part of INSACOG, they were racing against time to track mutations as they appeared. "If we wanted to predict whether one of these mutations was going to be dangerous from a public health perspective, we needed an assay system," says Das, Professor at the Department of Microbiology and Cell Biology (MCB), IISc.

The assay protocol widely followed involved isolating the virus from the samples, creating multiple copies, and studying its transmissibility and efficiency at entering living cells. Working with such a highly infectious virus is dangerous and requires a Bio Safety Level-3 (BSL-3) lab, but there are only a handful of these labs across the country.

To address this problem, Das and his team, along with collaborators, and with funding from DBT, have now developed and tested a novel virus-like particle (VLP) – a non-infectious nanoscale molecule that resembles and behaves like the virus but does not contain its native genetic material.

Such VLPs can not only be used to safely study the effect of mutations that may arise in SARS-CoV-2 – without requiring a BSL-3 facility – but can also potentially be developed into a vaccine candidate that can trigger an immune response in our bodies. Soma Das, DST Woman Scientist in the Department of Biochemistry and one of the authors of the study, adds that these VLPs can also be used to cut down the time taken to screen drugs that can fight the virus.

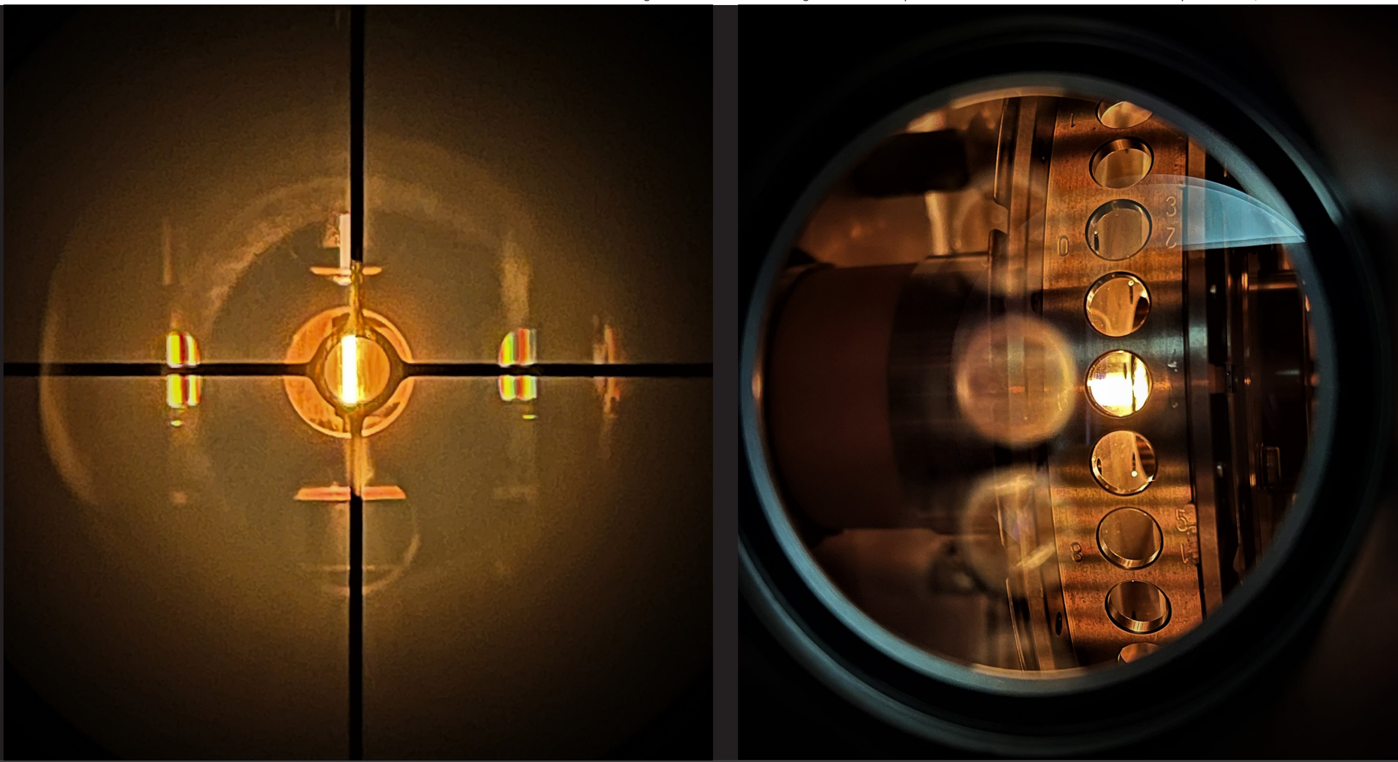
Das' lab has previously studied the Hepatitis C virus for 28 years, and shown that VLPs can be used as vaccine candidates. When the pandemic hit, they began working on a VLP for SARS-CoV-2. First, they had to artificially synthesise a VLP with all four structural proteins – spike, envelope, membrane and nucleocapsid. "The main challenge was to express all four structural proteins together," says Harsha Raheja, PhD student at MCB and first author.

The team chose a baculovirus – a virus that affects insects but not humans – as the carrier to synthesise the VLPs, since it has the ability to produce and assemble all these proteins and replicate quickly. Under a transmission electron microscope, the VLP was seen to be just as stable as the native SARS-CoV-2. At 4 degrees Celsius, the VLP could attach itself to the host cell surface, and at 37 degrees Celsius, enter the cell.

When the team injected a high dose of the VLP into mice models, it did not affect the liver, lung, or kidney tissues. They also gave one primary shot and two booster shots to mice models with a gap of 15 days, after which they found a large number of antibodies generated in the blood sera of the mice. These antibodies were also capable of neutralising the live virus. "This means that they are protecting the animals," explains Raheja.

The researchers have applied for a patent for their VLP and hope to develop it into a vaccine candidate. They also plan to study the effect of the VLP on other animal models (using the expertise of SG Ramachandra, one of the inventors), and eventually humans. Raheja says they have also developed VLPs that might offer protection against more recent variants like Omicron and other sub-lineages.

- Pratibha Gopalakrishna



Images of salts of elements being ionised for isotopic measurements in a Thermal Ionisation Mass Spectrometer (Photos: Ramananda Chakrabarti)

USING FISH EAR BONES TO ESTIMATE SEAWATER TEMPERATURE

Researchers at the Centre for Earth Sciences (CEaS), IISc have identified a way to estimate ancient seawater temperature by probing tiny bones in the ears of fish.

Oceans cover three quarters of the Earth's surface and host many remarkable life forms. Earth scientists have been attempting to reconstruct the seawater temperature over time, but it is not easy to do so. "When you go back in time, you don't have any fossilised seawater," explains Ramananda Chakrabarti, Associate Professor at CEaS, and corresponding author of the study published in *Chemical Geology.* Therefore, he and his PhD student, Surajit Mondal, in collaboration with Prosenjit Ghosh, Professor at CEaS, turned to otoliths – tiny bones found in the inner ear of fish.

Like corals, otoliths are made of calcium carbonate and grow throughout a fish's lifetime by accumulating minerals from seawater. Similar to tree rings, these otoliths also hold clues to the fish's age, migration patterns, and the type of water that the fish lived in. For several years, Chakrabarti and his team have been tracking calcium carbonate deposits found in tiny animals like corals or foraminifera.

In the current study, they chose otoliths as scientists have discovered fossilised otoliths dating as far back as the Jurassic period (172 million years ago).

The researchers used six present-day otolith samples collected from different geographical locations along the east coast of North America. They analysed the ratio of different calcium isotopes in these otoliths with a Thermal Ionisation Mass Spectrometer (TIMS). By measuring the ratios of calcium isotopes in the sample, they were able to correlate it with the seawater temperatures from which the fish were collected. "We demonstrated that calcium isotopes are a powerful tracer of water temperature, and Surajit's efforts make our lab the only lab in the country that can actually measure these isotopic variations," says Chakrabarti.

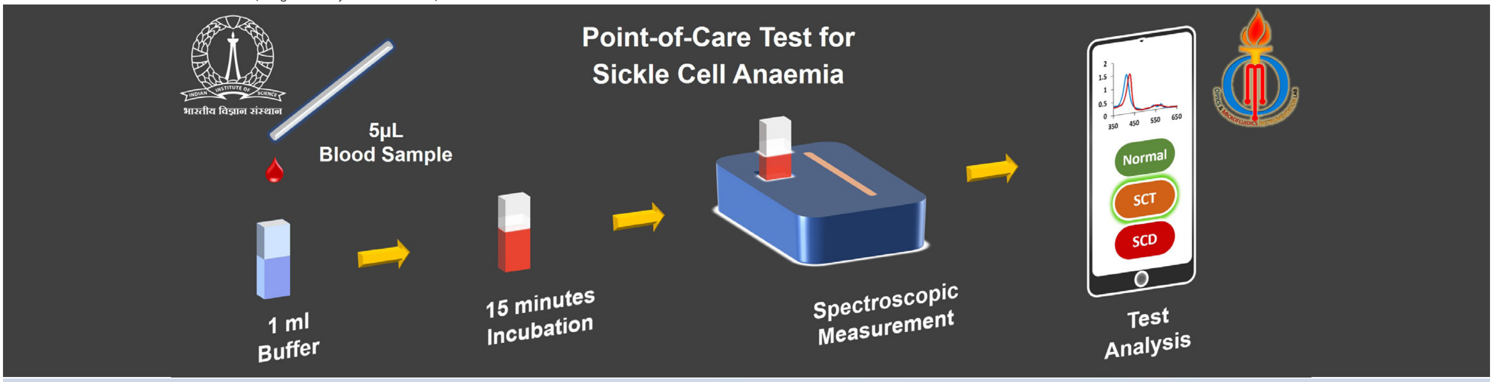
In addition to calcium isotopes, the team also analysed the concentration of other elements like strontium, magnesium, and barium, and their ratios in the same sample, and collated the data together to tease out a more accurate value for seawater temperature within a range of plus or minus one degree Celsius when compared to the actual value.

Organisms that live in the ocean are extremely sensitive to temperatures. A two-degree temperature rise could lead to the extinction of several species. In addition, because the atmosphere and the ocean are "on talking terms", says Chakrabarti, a lot of the carbon dioxide in the atmosphere eventually dissolves into the ocean, and this ability to dissolve carbon dioxide is also linked to seawater temperature – the lower the temperature, the more carbon dioxide is trapped. Just like a carbonated drink that loses its fizz as it warms up, the ocean loses its ability to hold carbon dioxide as it gets warmer.

Because of the close correlation they found between calcium isotope ratios and temperatures, the authors are confident that their approach can now be used on fossilised samples. Mapping early seawater temperatures is important to better understand Earth's history, they say. "What happened back in time," says Chakrabarti, "is key to our understanding of what will happen in the future."

- Pratibha Gopalakrishna

Schematic of the test for sickle cell anaemia (Image courtesy: Sai Siva Gorthi)



POINT-OF-CARE TEST FOR SICKLE CELL ANAEMIA

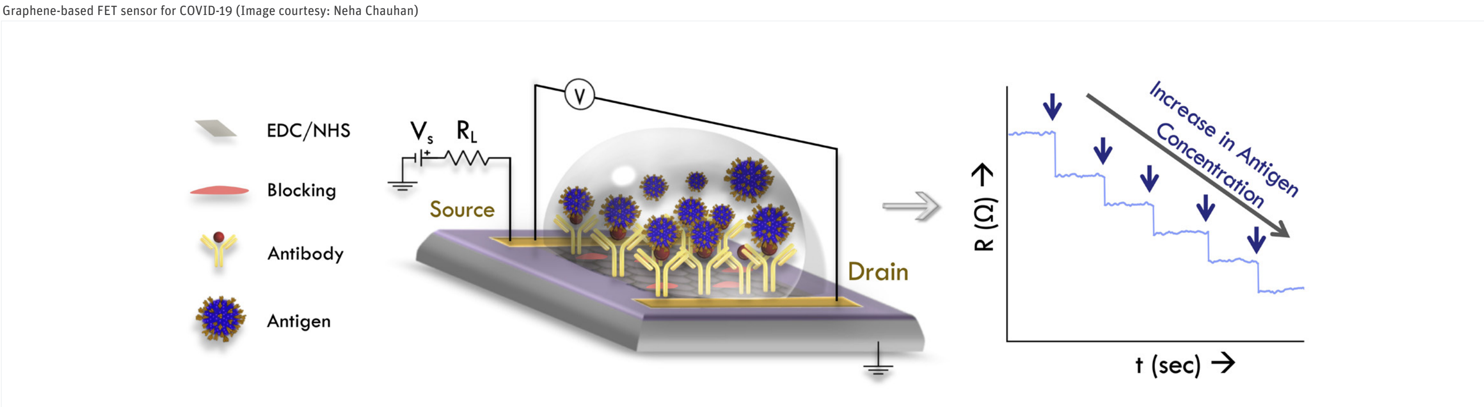
People with sickle cell anaemia (SCA) face life-threatening complications such as stroke and organ damage, and in some cases, premature death. SCA occurs due to a genetic mutation that makes the haemoglobin in red blood cells clump together, affecting their morphology, and damaging capillaries and other organs. The abnormal gene gets passed on either from one parent (Sickle Cell Trait or SCT), or from both parents (SCD). Existing diagnostic techniques are expensive, time-consuming and require specialised labs.

Researchers led by Sai Siva Gorthi in the Department of Instrumentation and Applied Physics (IAP) and collaborators have now designed a rapid, low-cost, point-of-care method to screen individuals for sickle cell anaemia.

The system relies on the characteristic property of haemoglobin in a solution to absorb and transmit light. The team observed differences in the light absorption capacity between deoxygenated blood samples taken from people with SCT and SCD, and healthy volunteers. In preliminary clinical trials with 438 patient samples, the test showed high sensitivity (96.9%) and specificity (98.6%). According to the researchers, the test takes only 15 minutes and is expected to cost less than Rs 100. A technology patent has been filed and licensed by ShanMukha Innovations, an IISc-incubated startup.

- Seemadri Subhadarshini

Graphene-based FET sensor for COVID-19 (Image courtesy: Neha Chauhan)



RAPID METHOD TO DETECT SARS-CoV-2 SPIKE S1 ANTIGEN

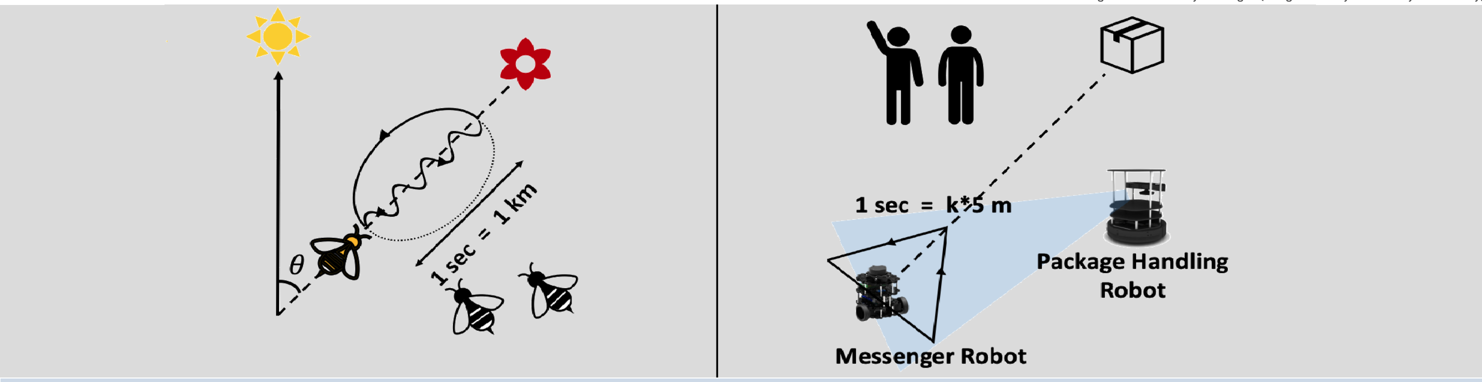
COVID-19 has posed an enormous global health challenge for the past few years. Currently, the most widely used diagnostic techniques such as chest computed tomography (CT) scans and RT-PCR tests are costly and time-consuming. To address this issue, a team led by Sonu Gandhi, Scientist D at the National Institute of Animal Biotechnology (NIAB), Hyderabad and Arindam Ghosh, Professor at the Department of Physics, IISc, has developed a highly sensitive graphene-based immunosensor for rapidly detecting the SARS-CoV-2 Spike S1 antigen.

The team built the sensor using a chemically modified graphene-based field-effect transistor (FET). To the graphene channel, they attached antibodies that specifically bind to the virus' spike S1 antigen – the attachment was confirmed using optical spectroscopy and enzyme assays. Real-time change in channel resistance was monitored for detecting the antigen. The lowest concentration that the sensor could detect was 10 femtomolar.

A major advantage of FET sensors is their rapid detection and ultra-high sensitivity. The team reduced the fabrication cost by generating the spike S1 antibodies in-house. According to them, in the future, the sensor could also be miniaturised to develop a portable device for the diagnosis of COVID-19.

- Faizan Bhat

Schematic of how robots mimic bees' dancing action to convey messages (Image courtesy: Abhra Roy Chowdhury)



ROBOTS TAKE CUES FROM DANCING BEES AND HUMAN GESTURES TO DELIVER PACKAGES

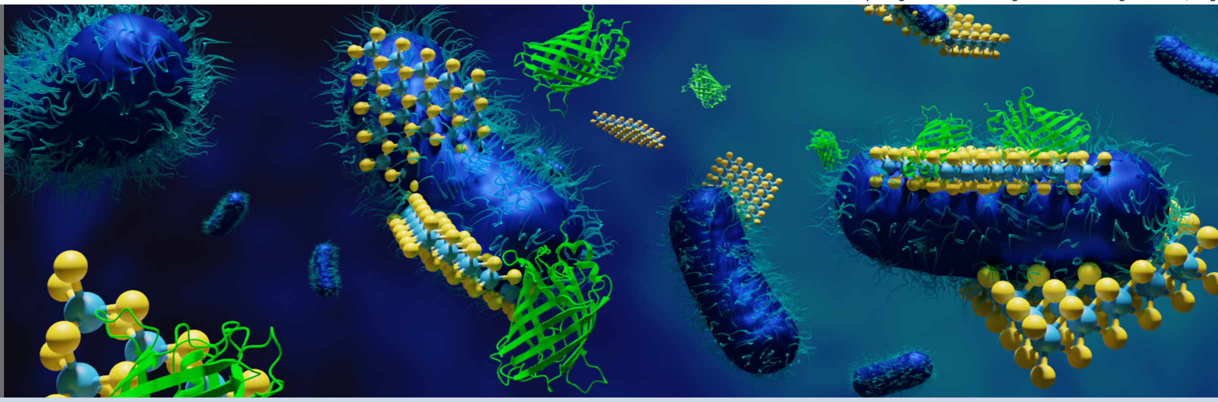
Have you ever had to navigate a noisy room in search of a friend? Your eyes scour the room in the hope of catching sight of them, so that you can walk quickly in that direction. Now picture the same thing, but with robots instead. In recent work by Abhra Roy Chowdhury at the Centre for Product Design and Manufacturing, IISc, and Kaustubh Joshi at the University of Maryland, robots can now use visual cues, instead of network-based communication, to not only navigate but also deliver a package, with the aid of a human.

A human first signals a messenger robot via hand gestures about the destination to which a package must be delivered. The messenger robot then signals a package handling robot, by moving along paths in specific geometric shapes, such as a triangle, circle or a square, to communicate the direction and distance towards this destination. This is inspired by the 'waggle dance' that bees use to communicate with one another. The robots use an object detection algorithm and depth perception to detect and react to the gestures.

Such interactive robots can be deployed for search and rescue operations, package delivery, and in industrial settings where multiple robots talk to one another.

- *Ullas A*

Illustration depicting nanosheets binding to disease-causing microbes (Image courtesy: Mrinmoy De)



USING NANOSHEETS TO IDENTIFY BACTERIAL STRAIN AND DRUG RESISTANCE

Researchers from the Department of Organic Chemistry and Department of Molecular Reproduction, Development and Genetics in IISc have developed an optical nanosheet sensor to identify disease-causing microbes from urine samples.

Optical sensors are faster and simpler than culture-based methods and PCR. Nanosheet sensors such as those made of Graphene Oxide (GO) have a high surface area to volume ratio, but have been largely unsuitable for biological applications so far because of their poor stability in aqueous media such as urine or blood.

To overcome these limitations, the researchers led by Mrinmoy De designed chemically modified Molybdenum Disulfide nanosheets, which are water soluble and positively charged, and bind to the negatively-charged cell membrane of microbes. They coupled Green Fluorescent Protein (GFP) to the nanosheet to visualise the interaction between the microbe and the nanosheets.

The difference in intensity of the GFP signal after adding the microbe sample was used to differentiate bacterial strains. In addition, the sensor can be used to identify whether the strain is resistant to antibiotics or not. The researchers say that the sensor can be also used to study the effect of drugs on diseased cells.

- *Sindhu M*

Photo: Yogesh Simmhan

MAKING DREAM A REALITY

DRONES, SMART CITIES, OBJECT TRACKING – THESE ARE SOME OF THE FASCINATING IDEAS THAT THE DREAM LAB HEADED BY YOGESH SIMMHAN WORKS ON

Have you ever wondered how companies like Facebook and Google manage the large amount of user data that only keeps growing by the day? Such voluminous data can't be processed or stored within a single computer or even a handful of computers. Tackling this problem requires the power of Distributed Computing, a model in which processing power is distributed among dozens of machines that work independently to solve the same problem. And with advances in technology today, Distributed Computing has become so pervasive that its principles and core concepts can be applied in many critical scenarios – querying complex data, analysing video feeds from security cameras, and training machine learning models. These are the kinds of applications that the DREAM Lab, headed by Yogesh Simmhan, Associate Professor at the Department of Computational and Data Sciences (CDS), is keenly interested in.

Yogesh gives an example of a crucial application that his team used Distributed Computing for. When the country went into lockdown during the first wave of COVID-19, he and his collaborators worked on developing a contact-tracing app. This app collects anonymised data of people testing positive for COVID-19 and uses that to build a graph or a network, which can subsequently be probed using graph algorithms to detect primary, secondary and tertiary contacts. The app, called GoCoronaGo, predated Arogya Setu, the Government of India's own contact-tracing app, and had several important privacy-protecting features built into it.

Although GoCoronaGo is a recent example, Yogesh's lab has been working on Distributed Computing for many years now. "Everything that you touch today is really a Distributed System," he explains.

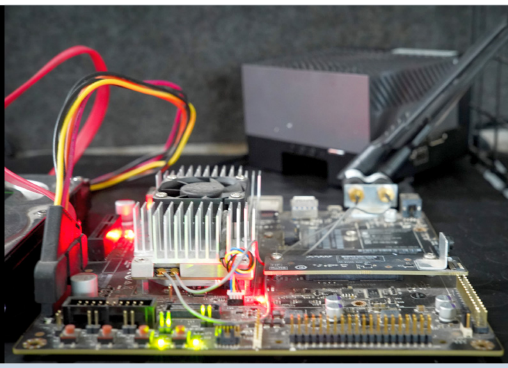
Today's computers are much more powerful than we could have imagined decades ago, but they are still unable to keep pace with the enormous amount of data being generated. Processing this kind of data requires a paradigm shift from the typical personal computer (PC) setup that many of us are familiar with. Distributed Computing is an answer to this problem: using the processing power of multiple, network-connected systems operating in tandem.

"To me, bringing multiple machines together has always been interesting. It shows you that the sum is greater than the parts," says Yogesh, who became fascinated by the vast web that is Distributed Systems during his undergraduate days at SRM College of Engineering in Chennai. He recalls that he chose to work on a Distributed Systems project as his final year project, as it was a relatively new field at the time. Since then, there has been no looking back, and even though the projects he works on have diversified, there is always an underlying thread that connects them to the motif of Distributed Systems. After his bachelor's degree, he went on to Indiana University to complete an MS and PhD in Computer Science. His PhD dissertation focused on developing a framework for the collection of metadata during the execution of distributed workflows. After his PhD, he worked as a Postdoctoral Researcher at Microsoft Research and a Research Assistant Professor at the University of Southern California (USC) for a brief stint, before joining IISc in 2013.

Distributed Computing is a continuously evolving field because when someone develops a solution to a problem, it might no longer be sufficient soon after, if the computing or networking hardware changes. And so one will need to solve the same problem again from scratch, developing new algorithms, software or tools that can adapt to the evolving hardware. This is what keeps the field alive and kicking even after so many decades, according to Yogesh.

In recent years, the DREAM Lab has worked on projects to optimise graph

Edge GPU Accelerators used by the DREAM:Lab (Photo: Aakash Kochare)



algorithms, in particular, those that can operate on large temporal graphs. Temporal graphs, unlike regular mathematical graphs, are like networks where the set of vertices and edges change with time. For instance, if we consider a contact-tracing app like GoCoronaGo, each person would be a node in the graph, and their contacts would have edges connecting them to this person. And what makes this graph temporal would be how the primary, secondary and tertiary contacts keep changing with time.

Drones have also been an active area of exploration at the DREAM Lab. Yogesh's team has been collecting data from drones – such as video camera feeds – to perform real-time analytics. One ambitious project, for example, is aimed at helping the visually challenged, almost like a seeing-eye dog. The idea is to use the camera feeds from drones in order to provide continuous and real-time instructions to visually challenged people so as to aid them in navigating their environment. Another project of his, called *Anveshak*, recently won the IEEE TCSC SCALE challenge. In this project, his lab developed a robust software platform that uses data from camera feeds across a city to track an object in real time, such as a stolen car. In a simulated setting, the team also demonstrated the platform's ability to control traffic signals and create a "green corridor" for the rapid movement of ambulances.

Apart from these individual projects, Yogesh has worked on several collaborations that extend beyond the campus. "In an institute like IISc, where funding isn't that hard a problem, we have the freedom to open our minds up a bit and see what's interesting out there," he explains. He has worked on projects related to the Smart Cities initiative launched by the Government of India, leveraging his experiences from similar work he had done at USC. A smart city is a technologically advanced city that uses many sensors to collect data about various operations and uses this data to improve the functioning of the city. Yogesh worked on a project called EqWATER with other collaborators from IISc, the goal of which was to collect and analyse the data from water management systems in a city like Bangalore so as to ensure fair and equitable distribution of water.

Yogesh also collaborates closely with the industry, and is currently heading the IBM-IISc Hybrid Cloud Lab, a venture to foster ties between academia and industry. He explains that at least in the area of systems research, the industry has clearly overtaken academia, given the enormous scale of data that they handle. He says that collaboration with industry is therefore beneficial for academics to get a glimpse into future possibilities, and also to take a plunge into tackling real-life problems.

In addition, Yogesh likes to keep an eye out for new research ideas from offbeat sources. Recently, when the DREAM lab conducted a Quantum Computing workshop at IISc, it turned out to be a light-bulb moment. The conversations with some of the participants made him realise that there are many unexplored questions at the intersection of cloud computing and quantum computing. "Having an open mind to such ideas is a prerequisite for research," he says.

His advice to budding research students is to work hard and to be curious. "It doesn't matter which path you take in life," he says, "for as long as you work hard, you can achieve what you want to achieve. And one should never underestimate the importance of curiosity in research, for research is not about saying 'What can I do?' but rather 'Why can't I do something?'"

- Ullas A

DREAMers from Yogesh Simmhan's lab (Photo: Aakash Kochare)

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