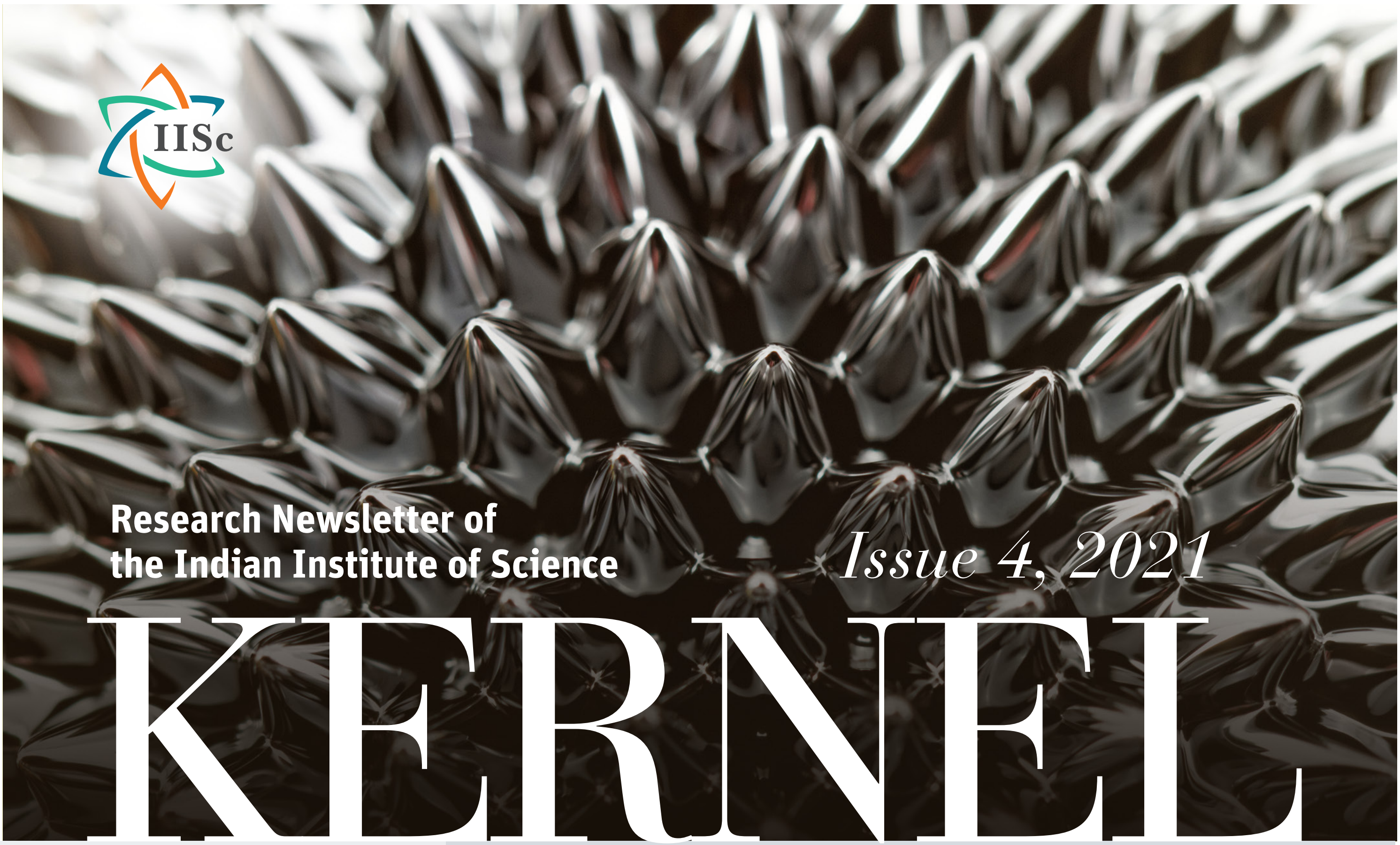

Research Newsletter of the Indian Institute of Science

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KERNEL

Editorial

Humans have always looked to the natural world to design more efficient devices, structures and materials that can improve the quality of our lives. In this issue of *Kernel,* read more about how researchers at IISc have applied their understanding of natural processes in diverse fields.

We also feature new research related to better understanding and diagnosis of the ongoing COVID-19 pandemic, and the work of a materials scientist who uses models and machine learning to understand how materials behave.

LESSONS FROM LIFE

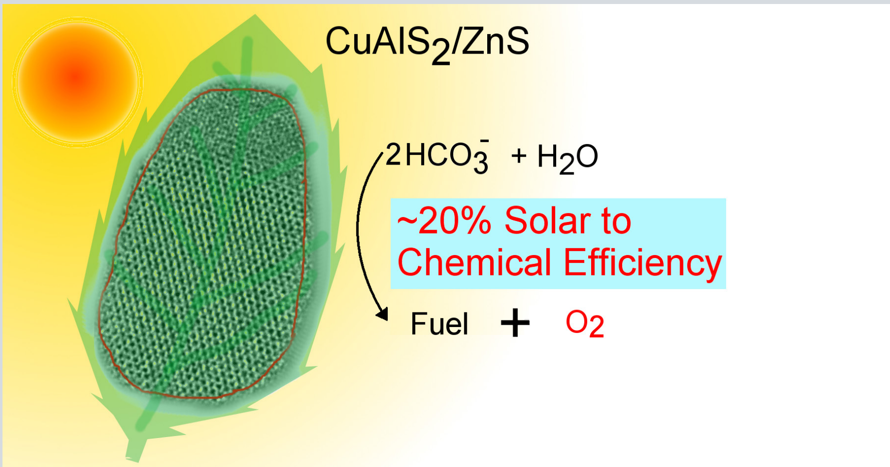

Image courtesy: Anshu Pandey

Be it the inventor of the Velcro fastener, who noticed clingy burdock seeds on his pants, or the makers of more recent ant-inspired robots that navigate better than GPS, when it comes to building things, humans have always looked to nature for inspiration. From nanomaterials to machines and architecture, scientists have long used their knowledge of biological processes to improve upon and build diverse devices and materials. Researchers at IISc too have applied their knowledge of biological processes to fields such as materials and bioinorganic chemistry, in ways that could potentially improve our understanding of biology as well.

Take photosynthesis, for example. Anshu Pandey, Associate Professor at the Solid State and Structural Chemistry Unit (SSCU), who specialises in the study of nanocrystals called quantum dots, has devised a novel way to perform artificial photosynthesis by creating a 'quantum leaf', along with collaborators in SSCU and the Department of Organic Chemistry. These nanocrystals can convert an inorganic carbon dioxide salt to organic fuel

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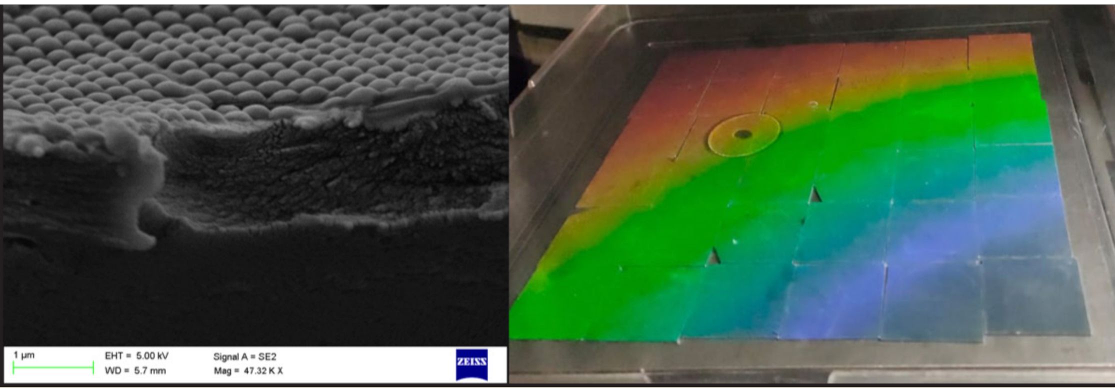


Enhancing solar cell performance through biomimetics (Image courtesy: Praveen Ramamurthy)

in the presence of visible light. Crucially, the researchers synthesised the quantum dot material ($CuAlS_2/ZnS$) from scratch. The material has an optimal bandgap for photocatalytic light harvesting, which means that electrons can jump easily from the catalyst to nearby molecules. This property enables the material to act as a superior photocatalyst for the main reaction that produces organic carbon (in the form of formate salt) efficiently.

"The field of artificial photosynthesis has been active since the 1980s, but the real challenge has been to make a system that is efficient enough to actually be useful. Our 'quantum leaf' is roughly 100 times more productive than natural leaves, and the solar-to-chemical energy conversion rate is very high, at 20%," he says. "Nature does photosynthesis in one way and does it pretty well. The goal is not simply to mimic the efficiency of living processes, but to try to exceed it through a different route. We wanted to ask if there was any other, more efficient way we can devise that serves the same utility." The quantum leaf is currently being developed into a device for industry-level use that can produce organic feedstock and fuel at a large scale.

The sun's energy can also be harnessed through the use of solar cells. However, developing efficient solar cells is challenging, explains Praveen Ramamurthy, Professor at the Department of Materials Engineering. "There are many challenges in developing solar cells, like choosing the appropriate material and optimising device architecture. Secondly, the efficiency of such cells varies with many factors such as the angle of the incident light," he says.

By chance, Ramamurthy and his team (comprising Jagadeesh AK, Varun A, G Hegde, and R Mahapatra) stumbled upon a discovery that biologists had made in fruit flies. These flies, which rely on sunlight for navigation like many other insects, had solved the problem quite exquisitely. Their eyes have intricate nanoscale patterns that allow them to adapt well to light-starved conditions. The grating structure of the insects' eyes has a multiscale arrangement that absorbs light optimally by reducing the portion that is reflected in a particular wavelength.

Inspired by this design, Ramamurthy and his colleagues fabricated a silicon-polystyrene architectured solar cell that performs efficiently due to the lower reflectance and the easier charge separation which is a characteristic of the material used to build the array. The team has thus built large-area solar cells with a superior and robust performance by combining biomimetics and novel material engineering. This design has made the solar cell angle of incidence agnostic, enhancing the cumulative power harvesting by about 25%.

The vivid variety of living organisms around us catches our eye easily. However, there is also an invisible world at the level of cells and molecules inside our body. At this level, biological processes are built on a foundation of similar structures and biochemical reactions. All these reactions depend on catalysts called enzymes; their absence or failure could potentially lead to diseases. In recent times, researchers have been able to design enzymes in the lab tailored to perform a desired function.

But going one step further, imagine something unquestionably non-living serving a living function. Enter nanozymes – bioinorganic catalysts that are small enough to pass into our cells and mimic the activity of real enzymes. G Mugesh's group at the Department of Inorganic and Physical Chemistry works on engineering nanoscale materials that can supplement the catalytic actions of normal or dysfunctional enzymes inside our body. These actions are crucial to the smooth functioning of our tissues and organs. However, it is not an easy task to introduce any foreign substance into our body or even into single cells. It is likely that the foreign material will be rejected, either blocked by cell membranes or inactivated by chemicals secreted by our immune system.

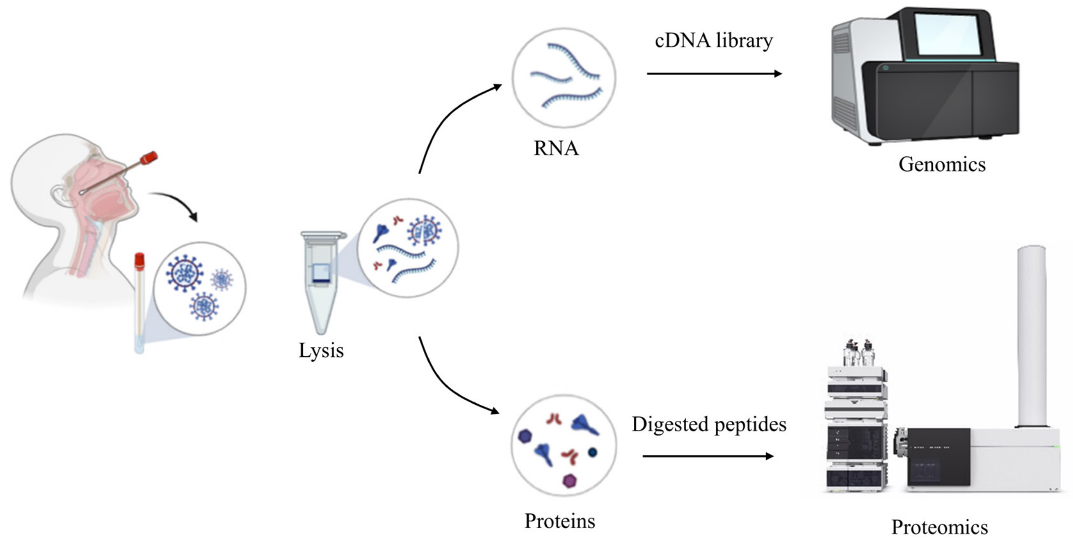
In living cells, oxidative stress due to the presence of excess reactive oxygen species such as superoxide can damage the mitochondria and cause premature aging. Mugesh's group has developed a cerium vanadate nanozyme which can entirely substitute the function of a metal-containing enzyme called Superoxide Dismutase. It works to keep the superoxide levels in control, thereby regulating mitochondrial function in neuronal cells, and leading to an increase in the levels of a critical energy-carrying molecule called ATP. In a recent interdisciplinary study, Mugesh and collaborators also discovered that vanadium pentoxide nanosheets may successfully counter HIV-1 infection by undoing oxidative damage caused by the virus.

Some artificial enzymes even serve to fight serious infection-causing bacteria. Cerium-oxide-based nanozymes synthesised via a chemical method can disrupt a process essential to cause infection: the formation of biofilms by many disease-causing bacteria like *E. coli, Vibrio cholerae* and *Kleibsiella pneumoniae.* This finding was also a collaboration between chemistry and microbiology labs. The nanozyme has been tested on urinary catheters which are susceptible to biofilm contamination in hospitals.

All these examples – the quantum leaf for photosynthesis, the fruit fly-inspired solar cell, and the artificial bioinorganic enzymes – are testimony to how knowledge can be transferred across conventional research fields and lead to unique innovations. As Ramamurthy says, "It is always a good idea to look at nature for inspiration and to not think of any problem as belonging to a specific field."

- Sunreeta Bhattacharya

Image: Sheetal Tushir



NEW MUTATIONS AND PROTEINS OF NOVEL CORONAVIRUS REVEALED BY IISc TEAM

A recent study from the IISc, published in the *Journal of Proteome Research,* has identified multiple mutations and unique proteins in isolates of SARS-CoV-2, the virus that causes COVID-19. It has also shown that the host produces several proteins of their own as their body launches an immunological defense in response to the viral attack.

COVID-19 has claimed over 2.5 million lives in just over a year. Humanity continues to face new challenges with novel strains – or genetic variants – of the virus being reported from around the world. To better understand how the virus is mutating and its protein biology (proteins are made using genetic information), an IISc team led by Utpal Tatu, Professor in the Department of Biochemistry, has carried out a comprehensive "proteo-genomic" investigation – a series of analyses of SARS-CoV-2 isolates. The isolates or viral samples were recovered from nasal secretions of consenting COVID-19 positive individuals in Bengaluru.

The genomic analysis was done using what molecular biologists like Tatu call next generation sequencing (NGS), a technology that allows for rapid sequencing of the entire genome. He says that sequencing the genomes of viral strains from around the world is important because it helps keep track of mutations that are arising constantly. His team's analysis suggests that the virus is now mutating faster than before – the three Bengaluru isolates had 27 mutations in their genomes with over 11 mutations per sample, more than both the national average (8.4) and global average (7.3).

To understand the spread and evolutionary history of the virus, the team constructed a global phylogenetic tree, or a tree of relatedness, of viral isolates using the sequence data. The phylogenetic analysis found that the Bengaluru isolates are most closely related to the one from Bangladesh. It also showed that the isolates in India have multiple origins rather than having evolved from a single ancestral variant.

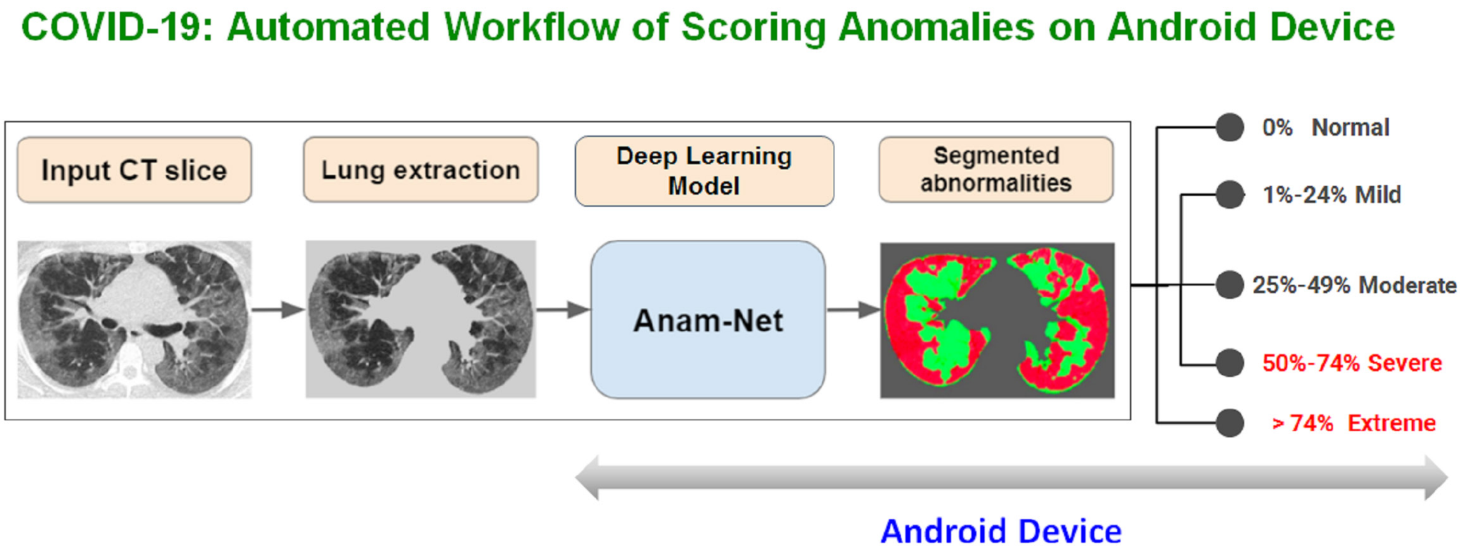
The SARS-CoV-2 genome codes for more than 25 proteins, but only a handful of these proteins have been identified so far. "Studying viral proteins provides functional information which is currently not well represented," says Tatu. In the proteomic analysis, his team detected 13 different proteins – most of them previously unidentified – from clinical samples. One such protein called Orf9b, which suppresses the host's immune response, had been predicted, but the IISc team provided the first evidence of its expression.

"Just knowing how the virus functions will not be enough. We need to put it in the context of the host," Tatu says. Therefore, in the third analysis, his team explored how our bodies respond to the virus by examining host proteins. They discovered as many as 441 proteins unique to COVID-19 positive patients, many of which are speculated to play a key role in the body's immune response.

The proteomic analyses were carried out using a technique called high resolution mass spectrometry. The team is upbeat about the potential that this method has for large-scale testing. Proteins can be reliable markers of infections like COVID-19 because they are more abundant and stable as compared to RNA molecules on which the prevalent RT-PCR tests rely. Sheetal Tushir, a PhD student and the paper's first author says, "The best thing we can [hope to] see in this century is the use of mass spectrometry as a basic technique for diagnostics."

- Sidrat Tasawoor Kanth

Image courtesy: IEEE



AI-BASED TOOL FOR AUTOMATED DIAGNOSIS OF COVID-19 LUNG INFECTION

A new software tool that reveals the severity of lung infections in COVID-19 patients has been developed by researchers from the Departments of Computational and Data Science (CDS) and Instrumentation and Applied Physics at IISc, in collaboration with colleagues from the Oslo University Hospital and the University of Agder in Norway. It has been described in a recent study published in the journal *IEEE Transactions on Neural Networks and Learning Systems.*

COVID-19 can cause severe damage to the respiratory system, especially the lung tissues. Image-based methods such as X-ray or CT scans can prove helpful in determining how bad the infection is.

The software tool developed by the IISc-led team, called AnamNet, can 'read' the chest CT scans of COVID-19 patients, and, using a special kind of neural network, estimate how much damage has been caused in the lungs, by searching for specific abnormal features. Such a tool can provide automated assistance to doctors and therefore help in faster diagnosis and better management of COVID-19.

AnamNet employs deep learning and other image processing techniques, which have now become integral to biomedical research and applications. The software can identify infected areas in a chest CT scan with a high degree of accuracy.

The researchers trained AnamNet to look for abnormalities and classify areas of the lung scan as either infected or not infected – this is called 'segmentation'. The tool can judge the severity of the disease by comparing the extent of the infected area with the healthy area. "It basically extracts features from the chest CT images and projects them onto a non-linear space [a mathematical representation], and then recreates the [segmented] image from this representation. This is called anamorphic image processing," explains Naveen Paluru, first author and PhD student in the lab of Phaneendra Yalavarthy, Associate Professor at CDS.

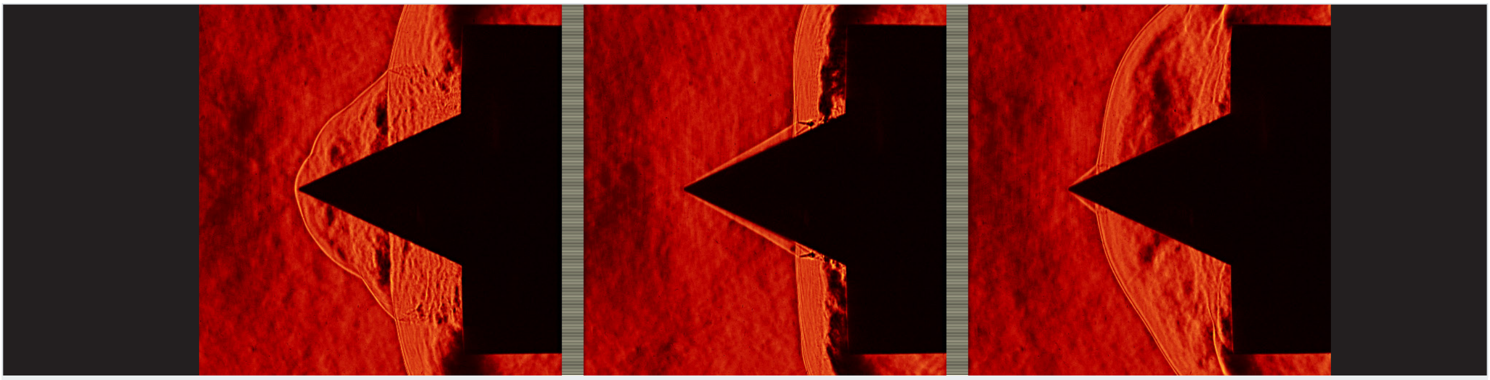
The study also compared AnamNet's performance with other state-of-the-art software tools which perform similar tasks. It not only matched its peers in its accuracy, but also performed just as well using fewer parameters. The neural network was also computationally less complex, which allowed the researchers to train it much faster to detect anomalies. Another significant advantage of AnamNet is that the software is lightweight with a small memory footprint. This has enabled the team to develop an app called CovSeg that can be run on a mobile phone and hence potentially be used by healthcare professionals. "We felt the need for a lightweight framework that could be deployed as a point-of-care diagnostic device on smartphones or a Raspberry Pi," says Paluru. He adds that this feature is missing from currently available state-of-the-art technologies such as UNet, which requires specialised hardware.

According to the authors, AnamNet holds promise beyond merely identifying lung infections in COVID-19 patients. "We are currently focusing on making our software more robust to handle COVID-19 scans, but we are also looking to diversify to other common lung diseases like pneumonia, fibrosis and even lung cancer in the near future," Yalavarthy says. He suggests that with some changes to the present design, the software could even be used to read brain scans.

The software tool is freely available to the public. The researchers caution, however, that it has not yet been clinically proven or evaluated.

- Sunreeta Bhattacharya

Image: Vaisakh Sasidharan and Duvvuri Subrahmanyam



UNSTEADY SHOCK WAVES AT HYPERSONIC SPEEDS

When rockets and aircraft move faster than the speed of sound, strong disturbances called shock waves are created around the flight body. Under certain conditions, shock waves can exhibit periodic oscillatory motion relative to the body. Such behaviour is of fundamental interest, and was previously studied for simple bodies that can be described by a single geometric parameter.

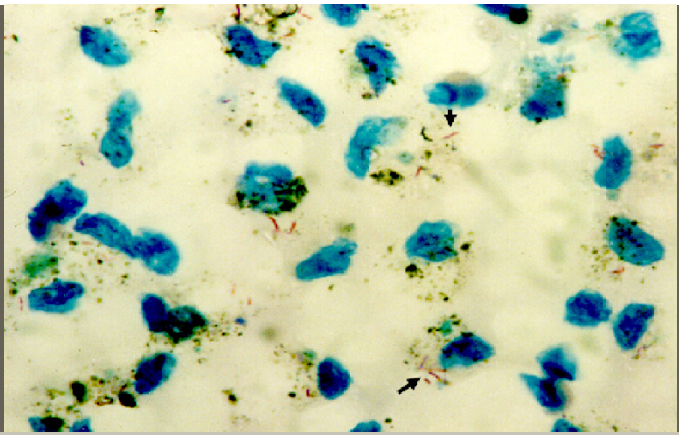
Now, researchers in the Department of Aerospace Engineering, led by Duvvuri Subrahmanyam, have uncovered new and interesting dynamics that govern unsteady shock-wave motion when two geometric parameters are at play. Their moving object is a cone set on a cylinder – the cone angle and the ratio of cone base and cylinder diameters constitute the two parameters. It was subject to air flow at six times the speed of sound in a hypersonic wind tunnel. An optical imaging technique called Schlieren was used to study the shock-wave behaviour.

The researchers found that the different air flow patterns created by variation in the governing parameters resulted in two disparate states of shock-wave unsteadiness.

In a certain parameter regime, the shock waves were highly disturbed, resulting in 'pulsations', which have much higher amplitude of unsteadiness than the relatively low-amplitude 'oscillations' that occurred in a different regime.

- *Sidrat Tasawoor Kanth*

Image courtesy: S Vijaya



TB DIAGNOSIS USING IMMUNE SYSTEM BIOMARKER

Tuberculosis (TB), particularly in forms that affect body parts other than the lungs, can be tricky to diagnose. Researchers led by S Vijaya in the Department of Microbiology and Cell Biology have found a new, faster and more efficient way to use a host's immune response to certain proteins unique to the bacilli to detect whether they have active TB.

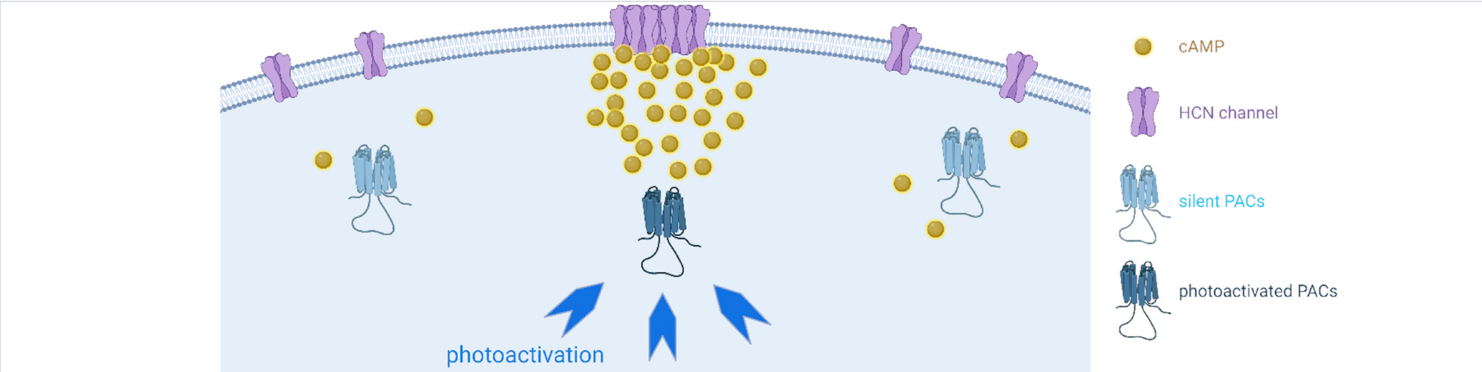
Immune cells in our blood have different sets of molecules on their surface – proteins, sugars, small compounds – depending on whether they are inactive as in healthy people, fighting a current infection, or remembering a past infection. The presence or absence of a certain unique combination of such molecules (called a biomarker) makes it possible to detect current disease in the body.

The team has discovered that active TB can be diagnosed if blood samples have immune cells with the following signature – having the biochemicals CD38 and CD4 but lacking CD27, while releasing a messenger molecule called Tumor Necrotic Factor (TNF-α). They added TB antigens to a blood sample to trigger an immune reaction.

By analysing the presence or absence of marker proteins on T cells in the sample using flow cytometry, they were able to accurately diagnose TB.

- *Sunreeta Bhattacharya*

Image courtesy: Mini Jose Deepak

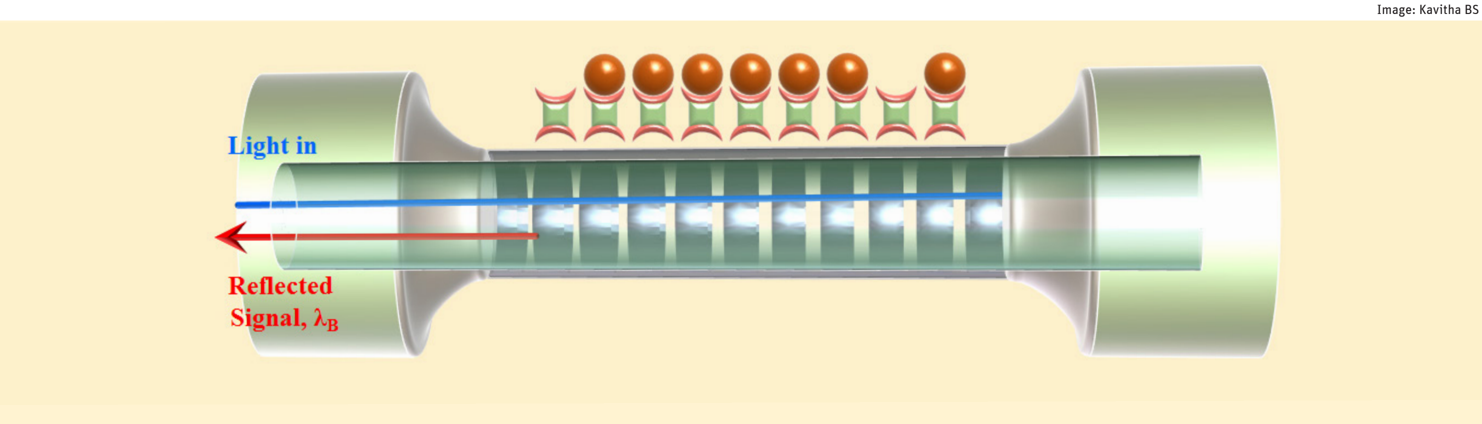


CONTROLLING MOLECULAR SIGNATURES IN LIVE CELLS USING LIGHT

Molecules called secondary messengers convey information from the surface of the cell membrane to the target inside living cells. cAMP is a major secondary messenger in the brain, important for modulating processes ranging from learning and memory to contraction and relaxation of heart muscles. Alteration in cAMP levels regulates various biomolecules involved in near-membrane signalling. Among the prominent molecules altered by cAMP are ion channels called HCN channels, involved in rhythmic pacemaker activity in heart cells and communication between neurons. Enzymes called photoactivated adenylyl cyclases (PACs) control cAMP levels within the cells by controlling the amount of blue light falling on them ("photoactivation").

A research group from the Centre for Neuroscience led by Mini Jose Deepak shows how global and local photoactivation of cAMP by PACs controls the organisation and random movement of individual HCN channels in live cells. Different classes of PACs change intracellular cAMP in different ways, which in turn alters the movement of HCN channels. This study opens up new ways of altering the organisation and movement of biomolecules in live cells using a non-invasive, light controlled approach. It also provides new ideas for therapeutic interventions to alter molecular pathways.

Image: Kavitha BS



SENSORS THAT DETECT TOXIC MERCURY IN DRINKING WATER

Access to clean and safe drinking water is a fundamental human right. Since contamination of drinking water sources is a serious public health hazard, the World Health Organisation (WHO) has set specific limits for the presence of toxic pollutants in water. If the pollutant levels exceed this limit, water is considered unfit for consumption. Mercury is one such heavy metal pollutant that can damage the kidneys and the brain.

Although traditional spectroscopy techniques can accurately determine mercury concentration at the WHO's guideline value (6 mg/litre), they require sophisticated equipment and handling by trained experts. Researchers at IISc and Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR) have worked to develop a sensitive, portable and cost-effective etched Fiber Bragg Grating sensor (eFBG) which can be used in practical settings. The surface of this sensor was coated with cysteine-conjugated naphthalene diimide (CNC) bolaamphiphile molecules.

The interaction between CNC and mercury gives the specificity to the sensor for it to be capable of detecting minute mercury concentrations (up to 0.0000003 mg/litre or 10 million times less than the hazardous limit) in test samples. The sensor gave promising results for regular tap water samples too. It has the potential for real-time testing of mercury contamination in water sources.

- Sukriti Kapoor

Abhishek Singh (Photo: KG Haridasan)

MATERIALISM IS GOOD

ABHISHEK SINGH'S LAB STUDIES THE PROPERTIES OF MATERIALS USING THEORETICAL SIMULATIONS AND MACHINE LEARNING

Abhishek Singh, Associate Professor at the Materials Research Centre (MRC) in IISc, is in a hurry to make a difference. "I just didn't want to do research in an area where applications may come after 20-30 years. I wanted to work in an area in which [my research] can be utilised right away," says Singh, explaining why he chose to become a materials scientist.

Singh's journey as a researcher in this field began during his PhD at Tohoku University in Japan, which he did after a Master's at the Indian Institute of Technology, Delhi. For his PhD, he studied silicon-based nanostructures. He then had two postdoctoral stints in the US – first at the University of California (UC), Santa Barbara, where he studied semiconductor devices, and the second at Rice University, which involved optimising graphene nanomaterials for hydrogen storage.

Singh joined IISc as Assistant Professor in 2010. At MRC, he heads a lab called the Materials Theory and Simulation Group, where he and his students use computational methods to identify materials that can be used in research and in devices to improve the quality of our lives. He says, "Most of the time, I try to solve problems of relevance. I also like to challenge myself."

One of the first challenges that Singh took on when he started his lab was to study thermoelectric materials, which convert heat energy into electricity, and are used in engines and for refrigeration. According to him, in spite of their enormous potential, these materials have not been well-studied, at least in India. Singh has been on a quest to find suitable thermoelectric materials to replace traditional materials, such as lead based materials and silicon-germanium alloys, which have limited efficiency. For instance, the use of a thermoelectric material in a car engine could harvest up to two-thirds of the energy that is wasted as heat.

Another active area of research in Singh's lab is using computational methods to identify the properties of two-dimensional (2D) materials and finding ways of enhancing their useful properties. 2D materials have wide-ranging applications in nanoelectronics, optics, and flexible devices. Because Singh's lab is involved largely in theoretical research on such materials, they collaborate extensively with experimental labs around the world to validate their findings.

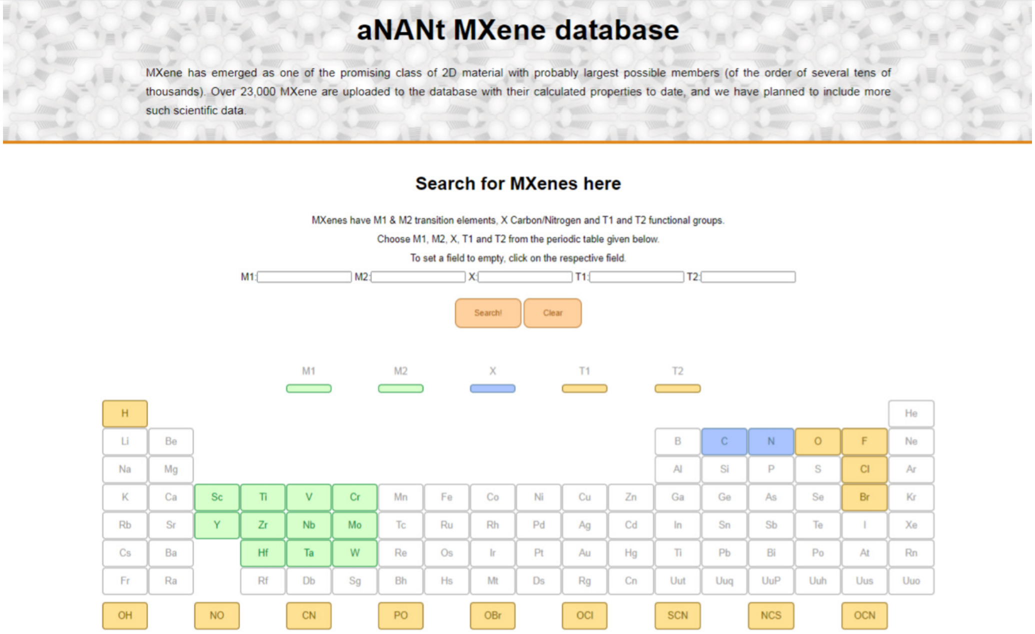
For instance, in a significant theoretical breakthrough, Singh's group found that the semiconductor molybdenum disulphide (MoS_2) transitions into a metal when pressure is applied to it. Their results were independently validated by an experimental lab at the University of Texas at Austin in the US. This was followed by a fruitful collaboration between the two labs that explained the observed phenomenon. This joint effort could lead to the development of improved pressure switches and sensors.

MXenes, another class of 2D materials, has several applications in ion batteries, gas storage, sensors, and catalysis. MXenes are composed of several layers that are bonded through chemical interactions. One can control the process of separating the individual layers and in the process generate a huge array of MXene-derived structures. The individual structures differ in their functional groups and/or metals and therefore possess different material properties, thus broadening the scope of the utility of these materials.

In addition to fine-tuning interesting properties of individual materials, Singh's group has built the world's largest 2D materials open-access database on MXenes called aNANt. Released in 2018, it describes the material properties of up to 23,000 MXenes. Singh and his team began the process of creating the database from scratch four to five years ago. They have used aNANt to develop several powerful machine learning (ML) models, which could predict the properties of a material within a few seconds, giving a fair assessment of the suitability of a material for a target application.

ML allows the team to visualise unknown patterns in material properties and

Screenshot of the aNANt web database for MXenes (Image courtesy: Materials Theory and Simulation Group)



to make connections among seemingly disparate behavioural parameters, a process that would have taken them decades had they used more traditional approaches. The use of ML has also led to a recent publication that describes the relationship between thermal and electronic properties, previously unknown to materials science. The results of the study, which Singh describes as “one of his favourites”, are useful in thermoelectrics, where both these properties would have to be simultaneously optimised.

In line with his long-term motivation of extracting real-life applications from his research, Singh’s lab has also contributed to research on superalloys, which are used in aerospace, marine, chemical, and petrochemical industries because they have a set of unique properties: superior mechanical strength, creep resistance (resistance to deformation) at high temperatures, surface stability, and corrosion resistance. The group has also created a tool, again using ML, to predict the hardness of superalloys using only a few images of the material taken on a scanning electron microscope (SEM) and its composition. The lab is now working towards extending the use of this tool to predict other properties of materials.

Singh expects that in the coming years, his lab will focus on the design of new materials based on properties predicted using machine learning. “We would like to tell them [experimentalists] the parameters they should use in their experimental setup to get a material with desired properties,” he elaborates. One drawback of making computational predictions about material properties is that the material does not always perform as expected when it is integrated into a device. Therefore, Singh wants to simulate the process of designing materials as well. This, he says, will help standardise parameters for manufacturing the material, such that it does not lose its superior properties.

Singh believes that his curiosity about the world is key to his scientific success. He says that he always tells young students that they should take up research only if their goal is to learn. “I entered research because this is the only profession which pays me to learn.”

- Sukriti Kapoor

Abhishek Singh with his lab members (Photo: KG Haridasan)

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