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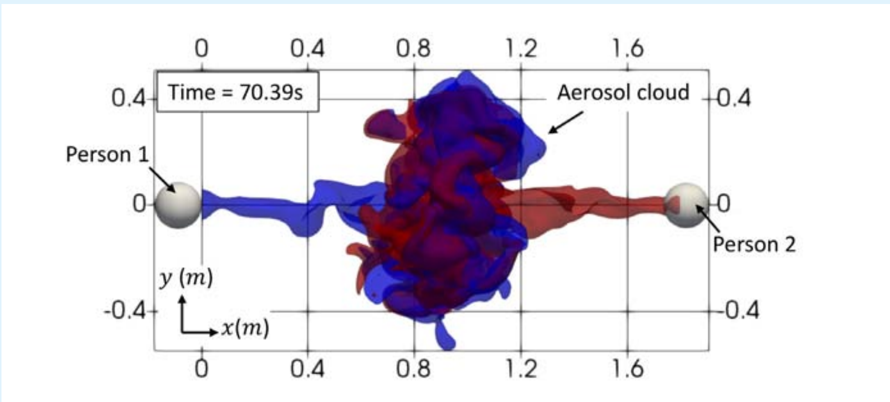
KERNEL

Editorial

Despite their limitations, models and simulations are useful for tracking the spread of a pandemic like COVID-19. In this issue of *Kernel,* read more about such tools developed by IISc researchers to gain deeper insights into disease transmission.

We also feature stories on how scientists have visualised ferroelectricity in nanomaterials and gauged how machine learning models match up to humans in "seeing" objects. Finally, our lab feature focuses on research in flexible electronics that can pave the way for novel materials capable of bending and folding.

MODELLING A PANDEMIC



Aerosol cloud formed between two people after 70 seconds of conversation (Image courtesy: Sourabh S Diwan)

PROJECTIONS AND SIMULATIONS HAVE HELPED PROVIDE A BETTER HANDLE ON UNDERSTANDING DISEASE SPREAD AND MANAGEMENT

In January 2020, India reported its first cases of COVID-19 caused by the now infamous SARS-CoV-2 virus. It was declared a pandemic by the World Health Organisation on 11 March 2020. A year and a half later, India is still struggling to escape from the clutches of this deadly disease. With a potential third wave lurking around the corner, how do we prepare for what's coming?

In this quest for better preparedness, modelling and simulations continue to play an important role. These models are built based on the current understanding of disease spread. Factors such as the pathogen's virulence, the number of people affected so far, the severity of infection, the mode of infection spread and so on are typically considered while building a model. Policy makers have relied on such models to devise suitable interventions that can prevent or reduce dangerous outcomes.

Many IISc researchers have also been involved in developing such models, simulations, and analysis tools for managing the response to COVID-19.

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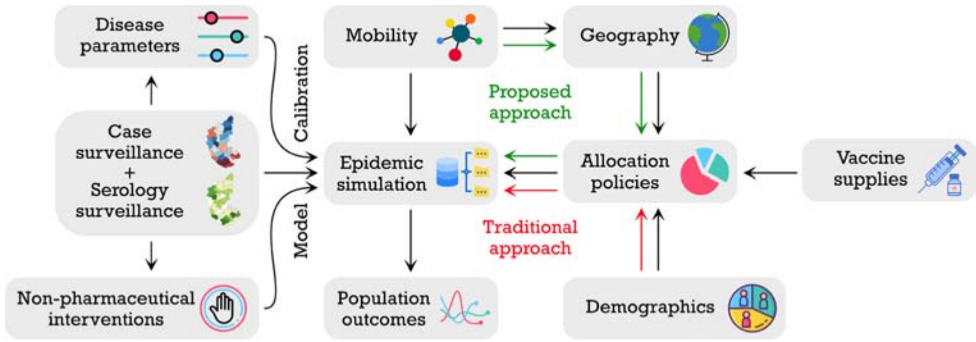
Modelling vaccination strategies (Image: Nihesh Rathod)



For example, during the first wave, a model and dashboard that projected the requirement of medical inventory like oxygen supply, masks, PPE kits and ventilators was developed. Other models studied the effectiveness of random testing, contact tracing, lockdown-like restrictions, and isolation on the spread of the disease.

One of these simulations looks at air flow patterns to understand how COVID-19 can spread from one person to another. Scientists have shown that COVID-19 is primarily transmitted via droplets from an infected individual. A research group led by Sourabh S Diwan, Assistant Professor at the Department of Aerospace Engineering (in collaboration with International Centre for Theoretical Sciences, Bengaluru and NORDITA, Sweden) has been studying the patterns of air ejected when a person coughs, sneezes or even speaks, using insights from the analysis of cumulus cloud evolution.

Over the past few months, the team has performed simulations on the SahasraT (CRAY XC40) supercomputer to examine COVID-19 transmission through transport of aerosols, which are tiny droplets that largely follow the air flow generated during speaking and can remain suspended in the air for hours even after the speech flow has died out. For instance, their simulations show that when two people of the same height are engaged in a short conversation, the jets coming out of their mouths face mutual opposition after travelling a certain distance, and therefore only a small fraction of aerosols released by one person reaches the other person's face. This considerably lowers the risk of infection. But if there is a certain height difference between the two people, the speech jets can slide over each other and reach the other person more easily, and therefore carry a higher risk.

Another way of decreasing risk of transmission, the team found, is lateral separation, where two individuals are not directly face-to-face. "[Tilting the] head away by about nine degrees can ensure that even when you're not wearing a mask, you are generally at a lower risk of infection than when you are looking directly in each other's faces, especially when you are separated by a distance shorter than six feet," explains Diwan. He warns, however, that such scenarios are more complex in real life, where factors like the exact phrases used during speaking, cross ventilation, and ambient humidity can also have a direct impact on disease spread.

Another model that has proved useful in policymaking is a partial differential equation (PDE)-based model developed by Sashikumar Ganesan, Professor at the Department of Computational and Data Sciences (CDS) and Deepak Subramani, Assistant Professor at CDS. Their model projects the potential number of infections in the medium-term (>6 weeks) based on the current caseload and multiple scenarios.

An important parameter it incorporates is the age distribution of the population, specifically the age distribution of the infected people, which largely determines the preparedness required from healthcare systems. It also includes parameters such as rate of testing, the loss of protective antibodies over time, and extent of interaction between individuals. The model then uses this information to predict the disease spread and its severity. Crucially, the model predicts how cases will rise or fall under different scenarios, such as no lockdown, complete lockdown, night or weekend curfew in some areas and so on. This capability is important for science-informed, data-driven policymaking. "The projections are good for the next 4-6 weeks, and once every 4-6 weeks, we update the parameters, introduce new scenarios and evaluate our model's performance since the last update," says Subramani.

Ganesan adds that they have discussed and shared their projections with authorities involved in COVID-19 management at both the local and national level.

Yet another recently developed model provides suggestions on how to manage vaccination strategies. Led by Rajesh Sundaresan from the Department of Electrical Communication Engineering, in collaboration with the Indian Statistical Institute and University of Virginia, this model incorporates seroprevalence (the extent of population exposed to the virus) and seroreversion (the extent of previously infected population which is now susceptible) while making decisions on different vaccination strategies. It evaluates the vaccination requirement and proposes three different roll-out plans, based on population size, seroprevalence, and number of cases – including active or recently recovered infections in a state or district.

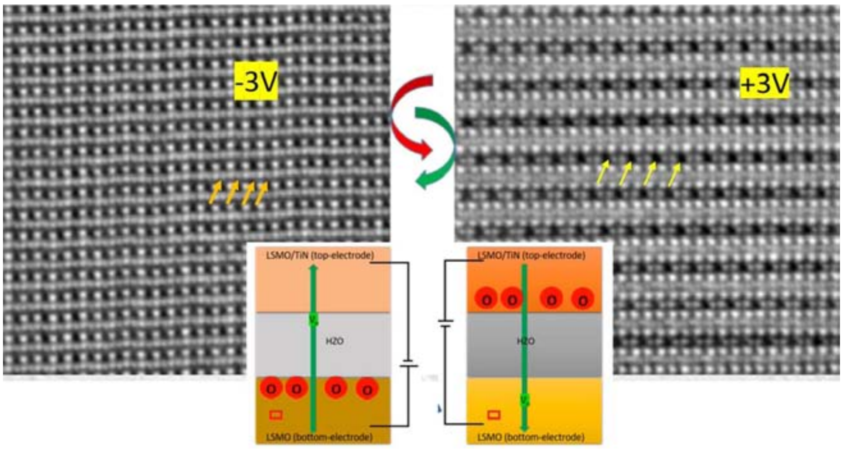
Their model shows, for example, that by increasing the number of vaccine doses to about 4 lakh per day in Karnataka (assuming an average of 1 lakh doses per day as the baseline), by 31 August 2021, the case load could be reduced by about 55%, when relatively strict non-pharmaceutical interventions (NPI), like lockdowns, are followed. On the other hand, when the NPIs are slightly relaxed, the case load could reduce only by 37%, and when there are no interventions at all, by 13.5%. "[This model] can help policy makers determine the level of non-pharmaceutical interventions needed to not overburden the healthcare system and come up with good strategies to prioritise vaccination across districts," says Sundaresan.

But with any model, there are several challenges. A pandemic like COVID-19 is laden with uncertainties, partly driven by new variants and mutants. Any model should try to include the many underlying uncertainties at every step, points out Vishwesha Guttal, Associate Professor at the Centre for Ecological Sciences. He also says that incorporating the most recent data on disease spread, infectivity rates, target population, and so on, as well as genomic surveillance data – which could hint at the emergence of a new strain or variant – are crucial.

The time frame is also important, he says. "One must avoid long-term projections because, at the end of the day, there are many aspects of infectious diseases that are dependent on human behaviour, which in turn can be affected by policies."

- Sangeetha Devi Kumar

Image: Pavan Nukala



VISUALISING OXYGEN MOVEMENT IN FERROELECTRIC MATERIALS

STATE-OF-THE-ART MICROSCOPY HAS HELPED SCIENTISTS UNVEIL THE MECHANISM BEHIND AN UNUSUAL PHENOMENON

A new study by an international team of researchers, including those from IISc, reveals how an unusual form of ferroelectricity arises in certain nano-sized materials. The team includes Pavan Nukala, Assistant Professor at the Centre for Nano Science and Engineering (CeNSE), IISc, and former Marie Curie Research Fellow at the University of Groningen, Netherlands – where a large part of the work was carried out – as well as Tuhin Chakrabortty, PhD student at CeNSE.

Using state-of-the-art atomic resolution microscopy, the researchers show experimentally for the first time how ferroelectricity emerges in materials called hafnia-based oxides. It arises from the displacement and reversible movement of negatively charged oxygen atoms when an electric field is applied. Such materials are useful for low-power memory applications, according to Nukala, who is one of the corresponding authors of the study published in *Science.* “Hafnia-based ferroelectric memory devices are already in production, even though the mechanism behind their behaviour was not known,” he says.

Like magnets, ferroelectric materials show spontaneous polarisation – the separation of positive and negative charges – which can be reversed or switched using an electric field. However, they are generally unsuitable for miniaturisation because they lose their ferroelectric properties when the crystal is made smaller than a particular size. But in 2011, scientists showed that hafnia-based oxides could exhibit ferroelectricity even when they are nano-sized, and that this ferroelectricity in fact grows stronger as the material size gets smaller, opening up numerous opportunities for microelectronics. However, it wasn’t clear how ferroelectricity happens in these nano-sized materials. Some scientists have proposed compelling theories about why and how these materials switch, but they have not been experimentally proven so far.

Nukala and colleagues used an advanced electron microscopy technique that had recently been developed and earlier used by a research team at the University of Groningen to visualise a hydrogen atom, the lightest chemical element. In the new study, they imaged thin films of hafnium-zirconium oxide sandwiched between two electrodes. They were also able to track the movement of atoms, including oxygen, in real time when an electric field was applied.

The researchers found that charged oxygen atoms move from one electrode to another with the hafnia layer acting as a conduit. When the electric field was reversed, the direction of migration was also reversed. It was this migration that contributed significantly to the material’s ferroelectricity, they found. When the conduit size was reduced (as the device is made smaller), oxygen conduction became more robust. These findings were also confirmed by X-ray diffraction studies carried out in Sweden.

Oxygen migration occurs due to imperfections or “vacancies” in the crystal structure, explains Nukala. “These structural defects are the key to the ferroelectric behaviour, and in general give novel functions to materials.”

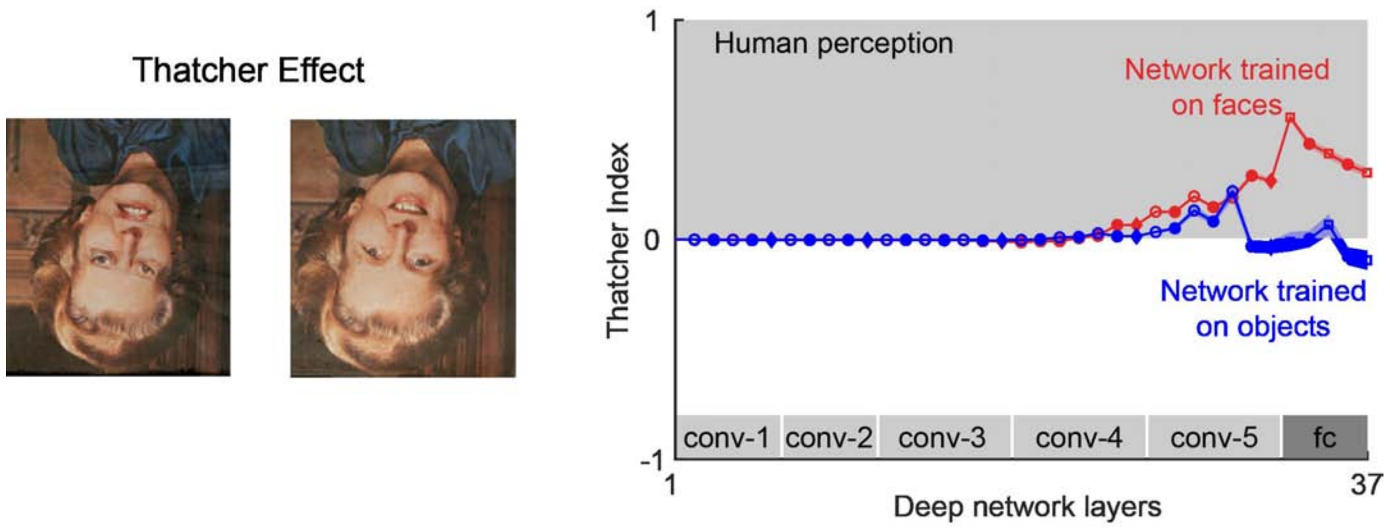
Directly imaging the dynamics of light elements using electron microscopy has not been attempted until recently. Among the many challenges was fabricating electron microscope-compatible capacitors made of hafnia. The task of designing these was successfully led by Nukala, who believes that the protocols they have developed could help researchers perform similar experiments on other materials.

Another challenge was accurate statistical analysis of the microscopy data. Nukala’s student Chakrabortty, who has been working on statistical inference in biological systems, used image processing tools to establish that the reversible oxygen migration is indeed statistically significant.

The insights offered by the study open up new avenues for designing oxygen-conducting ferroelectric materials that could be used for miniature memory and logic devices.

- Ranjini Raghunath

Tracking the Thatcher effect in deep networks trained on objects vs trained on faces (Image: Adapted from Jacob et al./*Nature Communications)*



DO DEEP NETWORKS "SEE" AS WELL AS HUMANS?

UNDERSTANDING HOW MACHINE LEARNING MODELS MEASURE UP TO HUMANS CAN HELP SCIENTISTS MAKE THEM MORE ROBUST

A new study from the Centre for Neuroscience (CNS) at IISc explores how well deep neural networks compare to the human brain when it comes to visual perception.

Deep neural networks are machine learning systems inspired by the network of brain cells or neurons in the human brain, which can be trained to perform specific tasks. These networks have played a pivotal role in helping scientists understand how our brains perceive the things that we see. Although deep networks have evolved significantly over the past decade, they are still nowhere close to performing as well as the human brain in perceiving visual cues. In a recent study, SP Arun, Associate Professor at CNS, and his team have compared various qualitative properties of these deep networks with those of the human brain.

Deep networks, although a good model for understanding how the human brain visualises objects, work differently from the latter. While complex computation is trivial for them, certain tasks that are relatively easy for humans can be difficult for these networks to complete. In the current study, published in *Nature Communications,* Arun and his team attempted to understand which visual tasks can be performed by these networks naturally by virtue of their architecture, and which require further training.

The team tested 13 different perceptual effects on the deep networks. An example is the Thatcher effect, a phenomenon where humans find it easier to recognise local feature changes in an upright image, but more challenging when the image is flipped upside-down. Deep networks trained to recognise upright faces showed a Thatcher effect when compared with networks trained to recognise objects. Another visual property of the human brain, called mirror confusion, was tested on these networks. To humans, mirror reflections along the vertical axis appear more similar than those along the horizontal axis. The researchers found that deep networks also show stronger mirror confusion for vertically-reflected images as compared to horizontally-reflected images.

Another feature peculiar to the human brain is that it first focuses on coarser details. This is known as the global advantage effect. For example, when we are shown an image of a tree, our brains would first see the tree as a whole before noticing the details of the leaves in it.

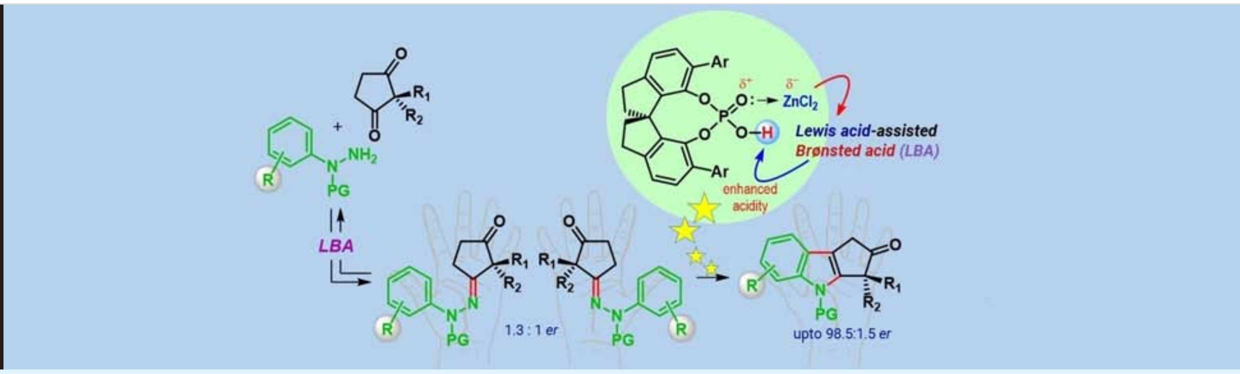
Similarly, when presented with an image of a face, humans first look at the face as a whole, and then focus on finer details like the eyes, nose, mouth and so on, explains Georgin Jacob, first author and PhD student at CNS. "Surprisingly, neural networks showed a local advantage," he says. This means that unlike the brain, the networks focus on the finer details of an image first. Therefore, even though these neural networks and the human brain carry out the same object recognition tasks, the steps followed by the two are very different.

"Lots of studies have been showing similarities between deep networks and brains, but no one has really looked at systematic differences," says Arun, who is the senior author of the study. Identifying these differences can push us closer to making these networks more brain-like.

Such analyses can also help researchers build more robust neural networks that not only perform better but are also immune to adversarial attacks that aim to derail them.

- Sangeetha Devi Kumar

Image: Santanu Mukherjee



NOVEL SYNTHESIS OF DIFFICULT-TO-MAKE INDOLE DERIVATIVES

Indoles and compounds derived from indoles are found in many natural substances. These compounds have extensive applications in pharmaceuticals and agrochemicals.

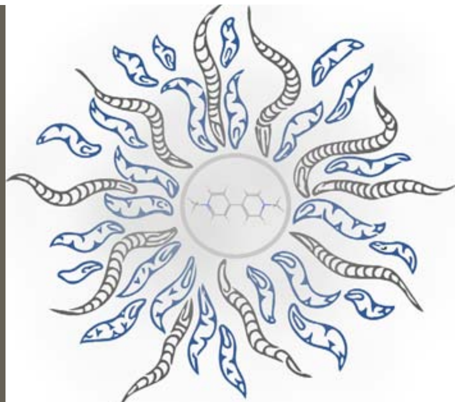
A research team from the Department of Organic Chemistry led by Santanu Mukherjee has now developed an efficient method to synthesise cyclopenta[b] indolones – an important class of indole derivatives. These molecules are 'chiral' in nature which means they can exist in two distinct forms whose 3D structures are non-superimposable mirror images of each other, called enantiomers. Often, only one enantiomer is biologically relevant, but it is extremely difficult to selectively synthesise just one of them individually in the lab – most existing methods produce a mixture of both.

The IISc team has overcome this hurdle using a catalyst which is also chiral in nature, and by carrying out a modified version of a century-old reaction called Fischer indolization. Computational studies through Density Functional Theory (DFT) calculations, led by Garima Jindal, helped in shedding light on the mechanism of this reaction.

Using this method, the team synthesised a range of enantioenriched cyclopenta[b] indolones which are challenging to make. Their method, therefore, increases the scope of making indole derivatives.

- *Sritama Bose*

Image: Kaling Danggen, Shivangi Mishra and Varsha Singh



USING ROUNDWORMS TO STUDY SKIN DISEASES

Collagen proteins in our skin play an important role in preventing environmental toxins from entering our body. Defects in this collagen barrier can cause several diseases like Gaucher's disease, atopic dermatitis and psoriasis.

A new study from Varsha Singh's lab at the Department of Molecular Reproduction, Development and Genetics proposes that *Caenorhabditis elegans,* a soil-dwelling roundworm, may be used as a model organism to understand how our skin responds to environmental toxins. Throughout its lifetime, it produces 177 different types of collagens and some of these are important for maintaining its skin shape and structure. But little is known about the function of a majority of these 177 proteins.

In the study, the researchers found that at least six of these proteins are responsible for determining what can pass through the skin. Genetically modified worms lacking even one of these proteins were found to be more susceptible to herbicides and deworming drugs like ivermectin. The loss of four out of the six crucial proteins led to physical changes in the skin structure, making it look discontinuous and wrinkled under a high resolution electron microscope. They also found that when skin permeability was compromised, it led to increased accumulation of toxins, greater tissue damage and accelerated death.

- *Debayan Dasgupta*

Photo: Roshan R Rao

TRADITIONAL DWELLINGS ARE BETTER SUITED FOR CHANGING CLIMATE

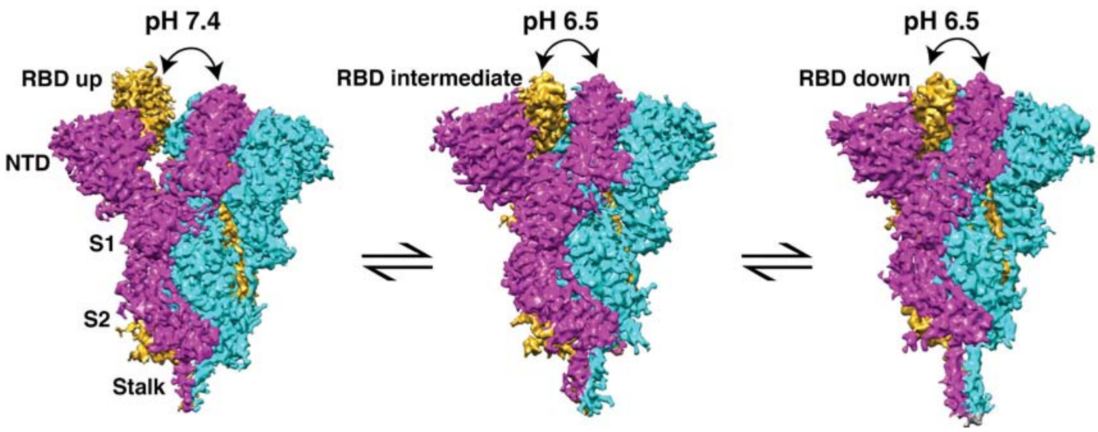
Many people have gradually shifted from traditional houses – which rely on locally available building materials and knowledge – to modern dwellings, even in rural areas. Khadeeja Henna, Aysha Saifudeen and Monto Mani from the Centre for Sustainable Technologies recently studied which of the two were more resilient to climate change.

They evaluated houses in three different Indian villages that had temperate, warm-humid and cold climates. Using data loggers, they recorded temperatures inside the houses every 30 minutes for almost a year, and built a mathematical model to predict how indoor temperatures would be in the future. The team then simulated three future global warming scenarios with different levels of greenhouse gas emissions, and estimated how the houses fared.

In all three climates, traditional houses – such as ones with timber walls or slate roofing – were less affected by climate change than modern houses. In the cold climatic zone, traditional dwellings were warmer indoors, making them more suitable for residence. In the warm-humid and temperate climatic zones, modern houses had relatively higher indoor temperatures. This would make them more dependent on artificial air conditioning, fuelling global warming further. The study suggests that traditional dwellings have design solutions that can help adapt better to climate change.

- Joel P Joseph

Image: Ishika Pramanick and Nayanika Sengupta



NOVEL INSIGHTS INTO THE STRUCTURE OF SARS-CoV-2 SPIKE PROTEIN

The SARS-CoV-2 S proteins, which appear as crown-like spikes on the viral surface, mediate the entry of the virus into the host cell. They are also the site where neutralising antibodies produced by the host cells bind to the virus to inactivate it. Understanding the protein's detailed structure is therefore important.

Most previous studies on the S protein structure have been carried out either at pH 8.0 or pH 4.0 to pH 5.0. But the structure of the S protein at physiologically relevant conditions – at which the virus actually infects the host cells – remains poorly understood.

Researchers in the Molecular Biophysics Unit led by Somnath Dutta have now successfully visualised the different conformations or forms of the S protein at physiological pH (7.4) and near physiological pH (6.5 and 8.0) using a technique called single-particle cryo-electron microscopy.

The team observed that around 68% of the S proteins exist in open conformation at physiological pH 7.4, but their proportion decreases when the pH is slightly higher or lower.

They also detected many intermediate conformations between fully open and closed, and showed that distinct states of both conformations have different binding affinities towards neutralising antibodies.

- Sritama Bose

Photo courtesy: Sanjiv Sambandan

WHEN ELECTRONICS FLEXES ITS MUSCLES

SANJIV SAMBANDAN'S RESEARCH PROMISES NOVEL ELECTRONIC DEVICES THAT CAN BEND AND FOLD

During Sanjiv Sambandan's undergraduate days as an electrical engineering student at IIT Kharagpur, he was introduced to the world of flexible electronics, especially the work being done at the University of Waterloo in Canada, where he would eventually pursue his PhD. His research was on flexible electronics on plastic substrates, an idea that he thought was "very cool." Following his doctoral studies, he worked at Xerox PARC in California, where he explored a diverse range of research, paving the way for a genuinely interdisciplinary academic career.

In 2010, he decided to return to academia and applied for a faculty position at IISc. "At some point, the academic bug begins to bite," recalls Sanjiv, who got the job and returned to his hometown, Bangalore, as an Assistant Professor in the Department of Instrumentation and Applied Physics (IAP).

Sanjiv's IAP lab attempts to solve fundamental problems of flexible electronics and semiconductor physics. His group uses this research to build thin-film transistor-based integrated systems. Flexible electronics does not use wafers like silicon or gallium arsenide, commonly employed in conventional electronics. Instead, the main focus here is to make thin-film transistors by depositing a layer of patterned semiconductor on flexible materials like textiles and plastics that can bend and fold. Electronic circuits printed on such flexible substrates hold enormous promise: they have the potential to enable futuristic devices with rollable displays, e-paper, smart wearable sensors and transparent Radio-frequency ID tags.

In the quest for flexible electronic systems, Sanjiv's lab tries to take advantage of the impact of geometrical, mechanical and electrical stresses on thin film devices, a phenomenon that other engineers usually regard as a problem in flexible systems. He and his team have been exploring how this handicap can be turned into an advantage. In this process, they have invented devices and circuit techniques for flexible electronics, including the adaptive dielectric thin film transistor, corrugated thin-film transistor and self-compensating circuits.

Another aspect of Sanjiv's lab involves interdisciplinary research that studies the behaviour of dispersions in electric fields, biodegradable electronic materials and so on. This research has led to innovations such as self-healing circuits and self-assembled sensors and actuators. Such interdisciplinary research has also led to technology translation. A shining testament to this is the lab spinoff that aims to treat wastewater.

One of Sanjiv's students, Aswathi Nair, explored how dispersions behave in an electric field for her MTech thesis. These questions led to the genesis of Openwater.in, a startup that specialises in treating wastewater. It employs a technology that builds on electrocoagulation, a well-known technique used to treat waste suspended in water. Electrocoagulation involves changing the particle surface charge, causing the suspended particles to agglomerate, which can then be separated. Using insights from this research, Sanjiv's lab came up with a cost-effective process of enhancing electrocoagulation, ensuring that agglomerates are formed more aggressively and at lower power.

Since 2017, Openwater.in, supported by grants from the Government of India's Department of Biotechnology, has been able to build systems that treat up to 10,000 L of wastewater per day. The startup is currently involved in several government projects and has plans to set up several groundwater, industrial discharge and grey water treatment plants across the country, including one at Mavallipura that can generate 25,000 L of potable water per day. Although Openwater.in is working exclusively with the government, several apartment complexes have also sought the help of the startup to treat their grey water.

Sanjiv's research on flexible electronics has also received widespread attention, Waste water treatment unit developed by Openwater (Photo courtesy: Openwater.in)

particularly his recent work on developing "self-healing" circuits. In flexible materials, stretching causes circuits to break, thus reducing the lifespan of wearable electronics. To help address the problem, he mooted the idea of electronic circuits which repair themselves. The self-healing mechanism kicks in to repair open circuit faults by using dispersions of oil and metallic microparticles smeared over connections between various circuit elements. If a fault occurs in the connections in the circuit, the electric field polarises the metallic particles and forces them to bridge the gap. The particles are fixed in place by sintering once the flow of current is restored.

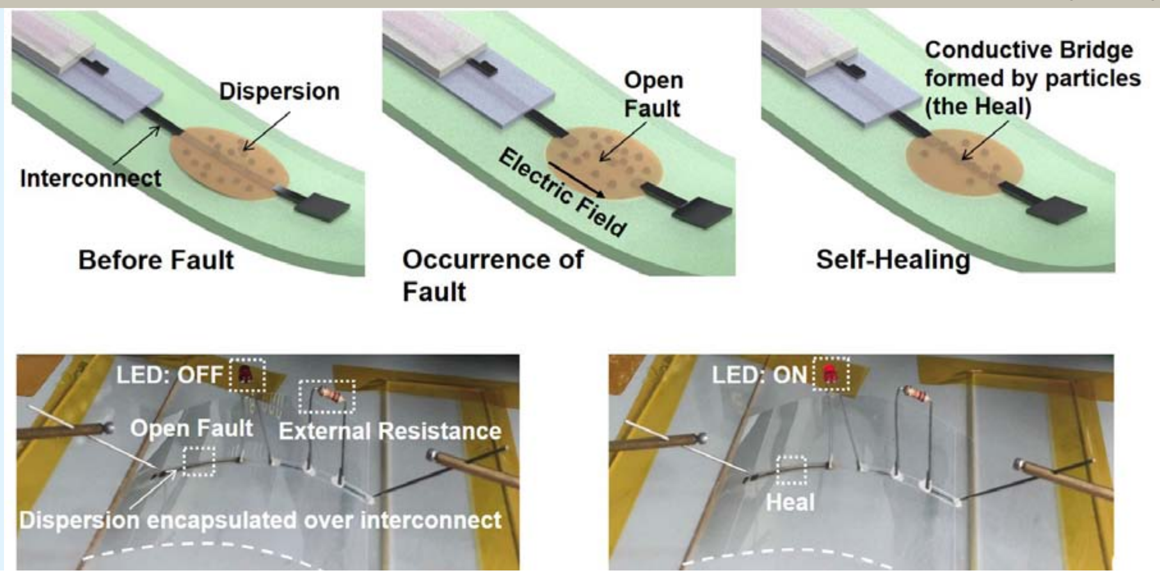
Another fascinating foray for Sanjiv's lab has been in, believe it or not, edible electronics. Edible electronics uses benign, and often food-grade, materials like sugar, proteins and silver thin films to form circuits. His team aims to use this technology to make edible pills that can perform diagnostic tests to yield a 'yes' or a 'no' answer, without supervision from a doctor. Sanjiv believes that this will serve a niche area of diagnosis between traditional invasive tests that need a doctor's precious time and wearable fitness gadgets that are often inaccurate in their diagnosis. However, the challenge for his lab in the coming years will be to integrate sub-systems and make these pills safe for humans to ingest.

Sanjiv, now Associate Professor, is delighted with what he has achieved as a researcher at IISc. "I have been an electrical engineer doing interdisciplinary work. All of it has been encouraged and taken positively here."

A decade-long career as a researcher at IISc has also seen Sanjiv mentor several students from all over India. Based on his experience as a mentor, he has a message for those just starting their research careers: "Explore a lot. Do not restrict yourselves. Be creative like a child." He also urges students to go back to the basics of their subject of interest. "Focus strongly on the fundamentals."

- Debayan Dasgupta

Self healing circuits (Image courtesy: Sanjiv Sambandan)



Office of Communications (OoC)
Indian Institute of Science (IISc)
Bengaluru - 560012
kernel.ooc@iisc.ac.in
https://kernel.iisc.ac.in/

भारतीय विज्ञान संस्थान

EDITORIAL TEAM
Deepika S
Karthik Ramaswamy
Narmada Khare
Ranjini Raghunath (Coordinator)
Samira Agnihotri

DESIGN
TheFool.in