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KERNEL

Editorial

With the world already reeling from catastrophes caused by climate change, many researchers – such as the ones in this issue's feature story – are turning to alternative and sustainable energy sources like biofuels. We also describe the work of a civil engineer who seeks to untangle the intricate web that is the city's transportation systems.

In other stories, we highlight how city lizards choose where they sleep, how modelling can help predict COVID-19 vaccine efficiency, and how hydrogen sulphide gas suppresses HIV reactivation.

THE ALTERNATIVE

Biomass gasification unit with throughput of more than 0.7 kg per hour of ultra-pure green hydrogen (Photo courtesy: Dasappa S)

RESEARCH ON BIOFUELS AND THEIR INTEGRATION INTO EXISTING VEHICLES IS PICKING UP STEAM

In a recent report, the Intergovernmental Panel on Climate Change (IPCC) declared that the adverse effects of climate change are far greater and vastly more disruptive to human life than previously understood. "Globally, heat and humidity will create conditions beyond human tolerance if emissions are not rapidly eliminated. India is among the places that will experience these intolerable conditions," it states. Mumbai is at great risk of severe flooding and sea-level rise; Ahmedabad is an extreme example of an urban heat island; Chennai, Bhubaneshwar, Patna and Lucknow are approaching dangerous levels of heat and humidity.

These grim implications of climate change have prompted scientists to hunt for alternative technologies to produce and utilise greener forms of energy, which can curtail the rising concentration of greenhouse gases in the atmosphere.

While futuristic green hydrogen and fuel cell-powered automotive and aviation technologies are being pursued, a more immediate solution would be to develop simpler alternatives that can be readily integrated into existing systems and machines. One such alternative is liquid biofuels – typically alcohols and their derivatives from renewable and green

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L: TVS engine on test bed at IISc (Photo courtesy: RV Ravikrishna). R: A project associate testing aviation fuel in a spray booth (Photo courtesy: D Sivakumar)

sources. However, there are two main challenges in adopting liquid biofuels as alternatives to conventional fuels like petrol and diesel: producing them efficiently and in sufficient quantities, and adapting them for use in existing vehicles or machinery. Several researchers at IISc are currently working on addressing these challenges.

Dasappa S, Professor at the Centre for Sustainable Technologies (CST), has been working on converting biomass – typically wood and agriculture residue, which are renewable and carbon-neutral energy sources – into a combustible gaseous fuel called syngas, conventionally obtained from reforming natural gas. During the gasification process, biomass is progressively subjected to high temperatures in the presence of controlled reactants (primarily air or oxygen and steam). The complex chemical structure of wood is thermally decomposed and reduced to form syngas which is rich in H_2, CO, CH_4 and CO_2.

Biomass gasification and the resulting fuel gas have various applications – from wood stoves at home to electricity generation through large-scale commercial gas engines. “The uniqueness of the fuel gas quality is its compatibility with the existing engines,” explains Dasappa. In the past two decades, over 100 biomass gasification units of various capacities (from kW to MW) have been commissioned in India and abroad. The technology transfer has saved 30 tons of fossil fuel per day, potentially avoiding the production of nearly 93 tons of CO_2 per day, he says.

In addition to gas engines, recent developments have paved the way to utilise H_2 and CO molecules in the syngas to generate liquid biofuels like kerosene and diesel using a cobalt-based catalyst developed and patented by the group. The flexibility that the technology offers to adjust the gas composition facilitates the generation of rich biofuels like high-purity hydrogen for fuel cell applications, as well as dimethyl ether and methanol.

Bio-methanol is widely recognised as a novel and promising fuel by technologists and policymakers. The government will soon mandate the use of petrol and diesel blends containing up to 15% methanol, reveals RV Ravikrishna, Professor in the Department of Mechanical Engineering. However, methanol’s properties and combustion characteristics differ from petrol and diesel, and different approaches are needed to adopt methanol in existing engines.

The energy generated on burning a unit mass of methanol is nearly half that of petrol, however, methanol burns faster than petrol, explains Ravikrishna. To address these challenges, he and his group have engineered fuel injection systems – based on an understanding of the fuel’s atomisation and its disintegration into droplets by electronically controlled injectors – and made changes to the engine control system to account for combustion properties of methanol. The technology is designed as a retrofit – it can be readily integrated into the existing engines. It has enabled the running of two-wheeler TVS engines and heavy-duty Ashok Leyland buses with 100% methanol, showing a 4-5% higher thermal efficiency than gasoline alone – a landmark achievement, according to Ravikrishna. “NITI Aayog has evinced keen interest in this work and has requested industry partners TVS Motors and Ashok Leyland to commercialise this technology at the earliest,” he adds.

“While methanol blends easily with petrol, when it comes to diesel, there’s a big challenge. It does not mix with diesel at all,” explains Ravikrishna. Efforts by his group on emulsions (mixtures of two or more immiscible liquids) have resulted in highly stable methanol-in-diesel macroemulsions containing up to 10% methanol, and methanol-dodecanol-diesel microemulsions containing even up to 30% methanol, which can be directly used in current engines. In addition, Ravikrishna’s lab is working on using hydrogen in engines as a step toward zero-carbon energy utilisation.

Just like the automotive industry, the global aviation industry aims to achieve net-zero carbon emissions by 2050.
D Sivakumar, Associate Professor in the Department of Aerospace Engineering, works in the niche area of using biofuels in the aviation sector. With advancements in technology, batteries could one day replace internal combustion engines in automobiles, but they don’t store enough energy to fuel a commercial airliner, says Sivakumar. In this context, biofuels emerge as one of the most promising alternatives in aviation. However, the aviation sector has its own set of challenges.

Unlike the automobile sector, modifications or retrofits to the aviation gas turbine could have significant implications for their performance and safety. Biofuels need to be chemically configured to reflect properties similar to conventional aviation fuels. Sivakumar and his collaborators have examined the properties of biofuels derived from plants (such as *Jatropha* and *Camelina*) and their flow properties when blended with conventional aviation fuels.

Such blended fuels (also called ‘drop-in’ fuels) need dedicated research on several topics to make them compliant with engine infrastructure and operation, explains Sivakumar. He and his group are working on understanding the atomisation and injection characteristics of biofuel blends. A promising result from their studies is the potential to use blends containing up to 70% biofuels as drop-in fuels.

Efforts to develop alternative fuels have been progressing rapidly in recent years. However, to bring these technologies and their benefits to the common person, collaborations between industry and academic institutions are crucial, remarks Sivakumar. “This is not a single laboratory’s work,” he says. Dasappa adds that policy decisions by the government will also determine the future of such alternative fuels.

- Mohammed Asheruddin

L: Hot and cold – thermal image of a sleeping rock agama. R: A juvenile rock agama sleeping in rural Bangalore (Photos: Nitya Mohanty and Mihir Joshi)

HOW ROCK AGAMAS CHOOSE THEIR SNOOZING SPOTS

Sleep is fundamental for all animals; when an animal sleeps, the brain sorts and categorises memories, and restores its energy. Urban habitats like cities, however, can hamper an animal's sleep quality and patterns due to higher temperatures, the presence of artificial structures like walls and buildings built by humans, and artificial light at night.

To adapt to these unusual conditions, urban peninsular rock agamas choose sleep sites that resemble their rural counterparts in the type of surface and the amount of light and heat received, a recent study by researchers at the Centre for Ecological Sciences (CES) at IISc has found. This study was published in *Behavioral Ecology and Sociobiology.*

While scientists have a reasonably good understanding of how animal brains work during sleep, how they sleep in the real world is not well known, says Maria Thaker, Associate Professor at CES and senior author of the study. "We know from human literature that certain conditions allow us to sleep better than others, and some disrupt our sleep. But animals live in the real world with all these conditions … and we wanted to understand where and how they sleep in the wild."

The researchers compared lizard sleep sites in urban and rural habitats to look for differences in the types of surfaces the lizards were sleeping on, the extent of cover, temperature, and amount of light received.

"In the rural areas that are undisturbed, we scanned all the rocks, boulders, the ground, and shrubs to look for sleeping lizards. But in [urban] Bangalore, we would go into people's backyards, because these lizards occupy empty lots or undeveloped plots, where there would be some concrete blocks that they use," says Nitya Mohanty, first author of the study. Poking around in neighbourhoods at night with headlights and fancy camera equipment often drew a lot of attention from people and the police, and the team had to explain what they were doing to the public on several occasions, he adds.

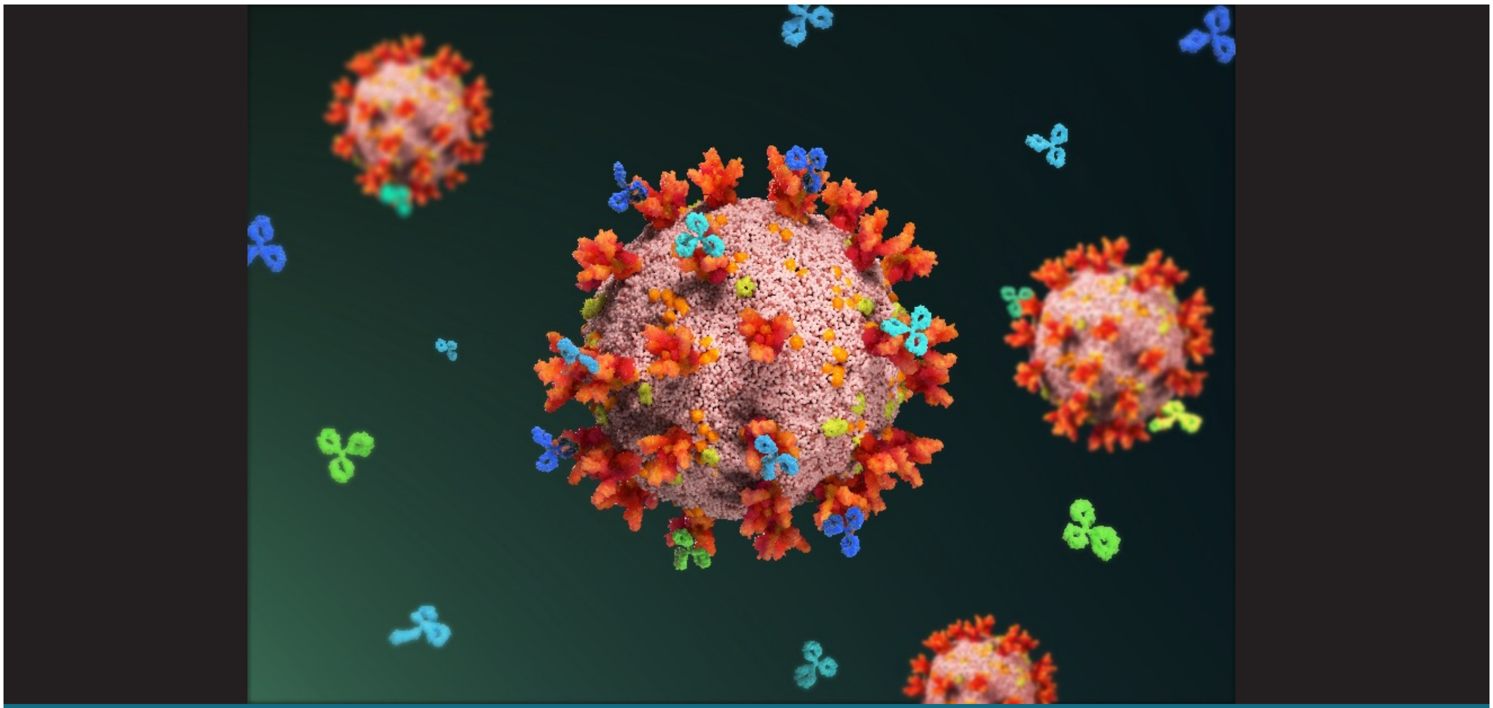
Since urban habitats pose differences in terms of structure and more illumination at night as compared to rural areas, lizards would have to cope somehow, points out Thaker. "One way is to just sleep under these conditions. Or they can cope in another way, by finding conditions that closely match the wild as much as possible. What we found is somewhere in between the two."

The team found that the lizards tend to pick structures that mimicked those in their natural habitat – they were more likely to sleep in rough concrete blocks that resembled their rocky sleep sites in the wild. The temperatures of both urban and rural sleep sites were also found to be similar. Urban sleep sites, however, were nine times more likely to be sheltered and covered as compared to rural sites, and this helped address the light problem in urban areas. This indicates that the lizards try to mitigate urban stressors by being flexible in their sleep site choices, and end up picking sites that resemble their rural sites.

Studying animals coping with anthropogenic environments is very important, according to Thaker. "The world is changing, and it is going to continue to change. So, if we know what it is that [other organisms] require to live here, then we can make some choices of our own to help keep them here."

- Karthika Kaveri Maiappan

Artist's rendition of SARS-CoV-2 viral particles with their spike proteins (orange) blocked by different antibodies (smaller floating objects of different colours) generated in an individual following vaccination (Image courtesy: https://www.lensmedical.com)



MATH MODEL TO PREDICT COVID-19 VACCINE EFFICACY

COVID-19 vaccines have been a game-changer in the current pandemic. Several vaccine candidates have conferred a high degree of protection, with some reducing the number of symptomatic infections by over 95% in clinical trials. But what determines this extent of protection vaccines confer? The answer to this question would help optimise the use of available vaccines and speed up the development of new ones.

Researchers at IISc and Queensland Brain Institute (QBI) in Australia have now addressed this question by developing a mathematical model that predicts how antibodies generated by COVID-19 vaccines confer protection against symptomatic infections. The study was published in *Nature Computational Science.*

The researchers first analysed over 80 different neutralising antibodies that are known to be generated after vaccination against the surface spike protein of SARS-CoV-2, the virus that causes COVID-19. These antibodies are typically present in the blood for months and prevent the entry of viruses by blocking the spike protein. The researchers hypothesised that these 80 antibodies constitute a 'landscape' or 'shape space', and each individual produces a unique 'profile' of antibodies which is a small, random subset of this landscape.

The team then developed a mathematical model to simulate infections in a virtual patient population of about 3,500 people with different antibody profiles, and to predict how many of them would be protected from symptomatic infection following vaccination.

"The reason predicting vaccine efficacies has been hard is that the processes involved are complex and operate at many interconnected levels," says Narendra Dixit, Professor at the Department of Chemical Engineering, IISc, and the senior author of the study. "Vaccines trigger a number of different antibodies, each affecting virus growth in the body differently. This in turn affects the dynamics of the infection and the severity of the associated symptoms. Further, different individuals generate different collections of antibodies and in different amounts."

"This diversity of antibody responses was a challenge to comprehend and quantify," adds Pranesh Padmanabhan, Research Fellow at QBI, the first author of the study.

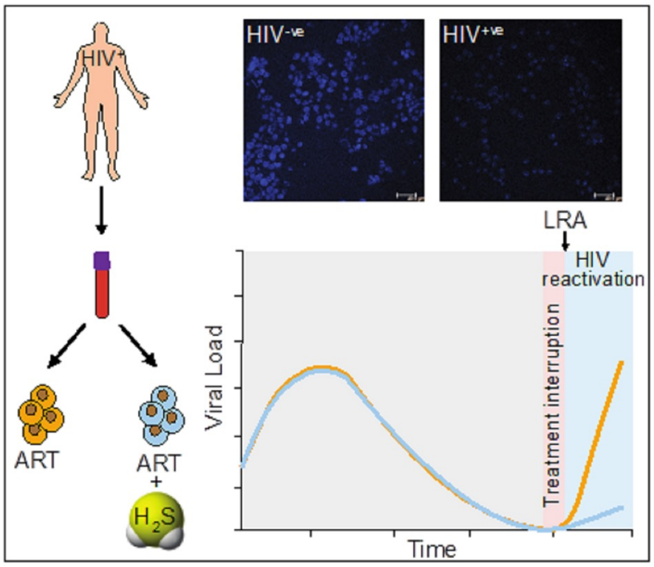
The model developed by the team was able to predict the level of protection that would be conferred after vaccination based on the antibody 'profile' of the individual, and the predictions were found to closely match efficacies reported in clinical trials for all the major approved vaccines.

The researchers also observed that vaccine efficacy was linked to a readily measurable metric called antibody neutralisation titre. This opens up the possibility of using such models to test future vaccines for their efficacies before elaborate clinical trials are launched, the authors suggest.

Dixit, however, cautions that the study is based on current vaccines which have been designed to work on the original SARS-CoV-2 strain. "Our formalism is yet to be applied to the new variants, including Omicron, where other arms of the immune system and not just antibodies appear to be contributing to vaccine efficacies. Studies are ongoing to address this."

- Ranjini Raghunath (with inputs from authors)

Hydrogen sulphide donor (GYY4137) subverts HIV reactivation from latently infected human T-cells derived from ART-treated HIV patients. Upper panel: Fluorescent indicator detecting diminished endogenous H_2S levels inside HIV-infected cells (Image: Virender Kumar Pal)



HYDROGEN SULPHIDE GAS SUPPRESSES HIV INFECTION

Researchers at IISc and their collaborators have identified a key role played by hydrogen sulphide (H_2S) gas in suppressing the Human Immunodeficiency Virus (HIV). Increased H_2S was found to have a direct effect on reducing the rate at which the virus multiplies in HIV-infected human immune cells. The finding paves the way for developing a more comprehensive antiretroviral therapy against HIV.

The team included researchers from the Department of Microbiology and Cell Biology (MCB) and the Centre for Infectious Disease Research (CIDR) at IISc, along with collaborators from the Bangalore Medical College and Research Institute. The results are published in the journal *eLife.*

Current state-of-the-art combined antiretroviral therapy (cART) is not a cure for HIV. It can only suppress the virus and cause it to become latent. Unfortunately, in some cases, cART is known to fail even when patients follow their drug regimen fully. Certain negative effects are also associated with cART, such as the build-up of toxic molecules leading to 'oxidative stress' and loss of function in the mitochondria, the cell's powerhouse. These effects can contribute to inflammation and organ damage. Stopping cART is also not an option because the virus can reactivate – emerge from its latent state – in the absence of therapy.

Scientists have recently begun exploring the beneficial effects of the presence of H_2S in HIV-infected cells on both oxidative stress and mitochondrial dysfunction, according to Amit Singh, Associate Professor in MCB/CIDR and corresponding author of this study.

In a previous study, Singh's lab developed a tool to measure oxidative stress in cells infected with HIV. "In that work, we showed that the chemical agent N-acetylcysteine was able to suppress HIV reactivation from latently infected cells," he explains. "A German study later showed that N-acetylcysteine partly acts by releasing H_2S molecules, which is when we began examining its role." Previous work from Singh's lab has also looked at the effects of counteracting oxidative stress by an antioxidant nanozyme during HIV infection. "Since H_2S also functions as an antioxidant molecule, we wished to see whether our prior insights on oxidative stress and HIV could be translated to show the contribution of H_2S on HIV infection."

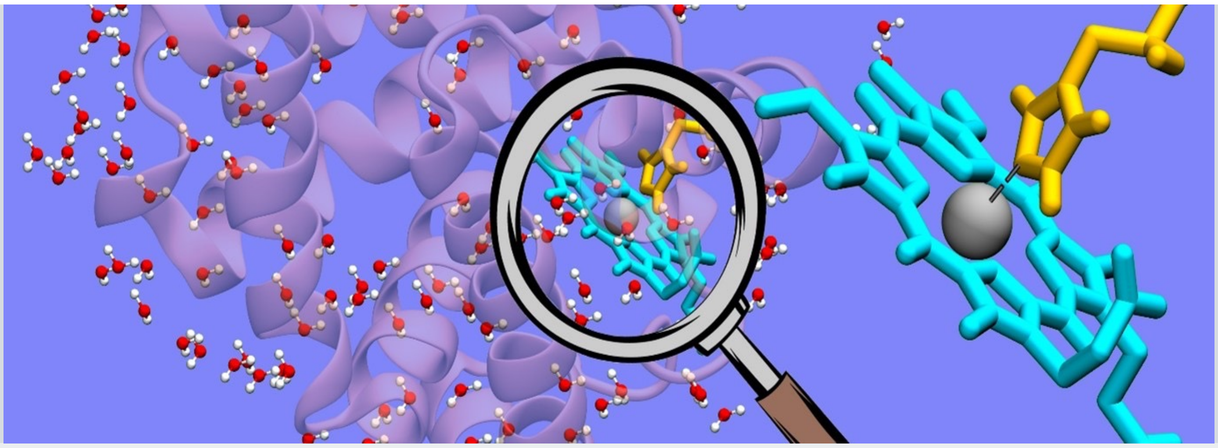
As the role of H_2S in HIV has not been explored before, the authors had to set experiments up from scratch. "Studying the effects of a gaseous molecule on HIV required us to build and validate new model systems," says Virender Kumar Pal, a PhD student in MCB and the first author of this study. "We started with experiments on established cell lines before moving on to cells donated by HIV patients in 2019. Our collaborators in the Bangalore Medical College and Research Institute, and Prof Annapurna Vyakarnam's group at CIDR were of great help." Detecting H_2S inside the cells was also not a straightforward task. "Since H_2S cannot be detected using conventional biochemical techniques, we had to use colorimetric and fluorometric techniques," he recalls.

The researchers studied the effects of natural generation of H_2S in HIV-infected cells as well as supplementing this with a chemical donor. "We observed a direct effect of H_2S on suppressing HIV reactivation and replication along with all its other beneficial effects, such as maintenance of mitochondrial health and dissipation of oxidative stress in our [cellular] models," says Singh. "Our results suggest that maintenance of HIV latency and reactivation are closely linked to the H_2S levels in infected cells."

Singh adds, "This opens the door to supplementing cART with chemical donors of H_2S to lock HIV in a state of deep latency, potentially improving the lives of millions infected with the virus. Since H_2S donors are already undergoing clinical trials for other diseases, they can quickly be repurposed for HIV treatment."

- Savyasachee Jha

Image courtesy: Mukherjee et al.



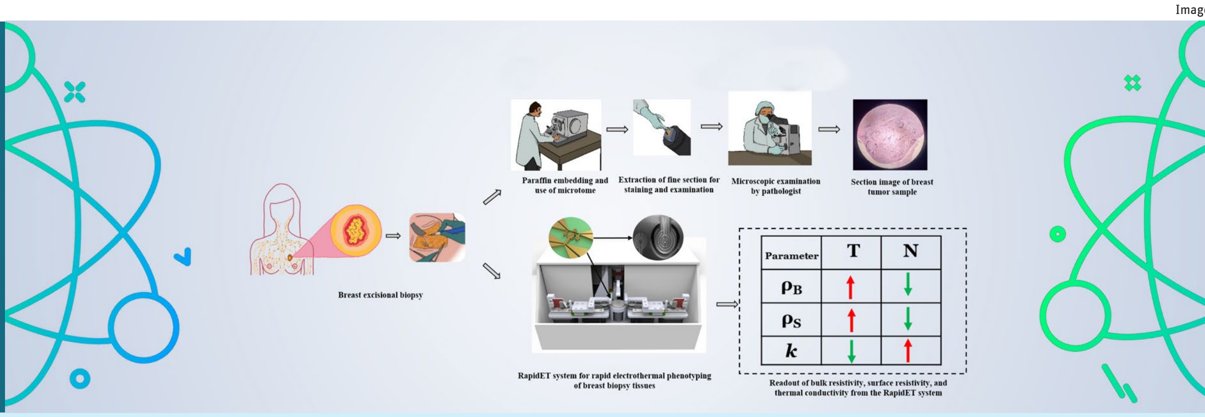
USING PROTEIN DYNAMICS TO STUDY ROLE OF WATER IN BIOLOGICAL REACTIONS

Water is generally regarded as the "matrix of life". But how exactly does water help in biological reactions? This question has perplexed researchers for years. In recent work led by Biman Bagchi at the Solid State and Structural Chemistry Unit (SSCU), researchers have attempted to understand this issue by focusing on three different proteins: myoglobin, GB1 and dimeric insulin. In each of these systems, they considered a single reaction coordinate (hydrogen bond or coordination) and studied the effect of water on its dissociation. More specifically, they calculated the fiction components on the bond, separately from protein and water.

Their investigation reveals that the cross-correlation between the forces from these two domains results in a negative friction term at the reaction coordinate, which reduces the total friction and effectively increases the reaction rate. The action-at-a-distance of water on protein function and dynamics is shown to lead to a tug-of-war between internal (due to protein) and external (due to water) frictions, revealed clearly by considering the three different proteins.

The researchers demonstrate that such out-of-phase behaviour in protein-water interactions, pointed out here for the first time, facilitates reactions through reduction of the friction on the reaction coordinate.

Image courtesy: Hardik J Pandya



RapidET: A MEMS-BASED PLATFORM FOR RAPID DIAGNOSIS OF BREAST CANCER

Conventional diagnosis of breast cancer involves the histological and immunohistochemical analysis of tissue sections obtained through clinical biopsy. For surgical margin assessment within the operating room, the standard technique is frozen section examination, which takes between 30 minutes to two hours to give results. Technologies for rapid and label-free diagnosis of malignancies from breast tissues thus have significant potential for application in pathology labs and operating rooms. An IISc team led by Annapoorni Rangarajan and Hardik J Pandya along with researchers from Assam Medical College, reports the design, development, and clinical validation of a MEMS-based platform for characterisation of ex vivo breast biopsy tissues to classify them as either tumour or normal.

Their RapidET system integrates silicon microchips with interdigitated electrodes, a microheater, resistance temperature detectors, and onboard electronics for control, actuation, and data acquisition. Measurements performed on deparaffinised and formalin-fixed breast biopsy tissues show a higher surface and bulk electrical resistivity and lower thermal conductivity for tumours compared to the adjacent normal tissues. The study also presents a novel method of using changes in electrical resistivity with temperature and combining it with thermal conductivity measurements as a metric for classifying tissues as tumour or normal.

Photo courtesy: Mehek Biswas

WHERE THERE'S TRAFFIC, THERE IS A WAY

ABDUL RAWOOF PINJARI, A CIVIL ENGINEER, STUDIES HUMAN BEHAVIOUR PATTERNS FOR SOLUTIONS TO THE CITY'S CONGESTION

Bangalore is infamous for its congested roads. But it wasn't always like this. Even now, not all roads are congested, and not at all hours. But travelling to certain parts of the city during certain times of the day can be a nightmare. Some modes of transport are more uncomfortable than others. What travel patterns emerge if systematic data is collected from the city? Which seasons, which roads and what modes make traffic better or worse? These are the questions that interest Abdul Rawoof Pinjari, a civil engineer who studies how city infrastructure can be planned to accommodate the lifestyles of its citizens.

Two unusual aspects of civil engineering fascinated Abdul during his undergraduate studies at IIT Madras: the social and human aspect of infrastructure systems, and a scientific and mathematical approach to understanding cities. He wanted to determine what infrastructure is necessary for the smooth running of a city, and if, in frequently changing conditions, one can predict these requirements and manage the city using mathematical modelling.

As a Master's student at the University of South Florida, the connection between socio-economic systems and transportation infrastructure became clear to him. "How much we travel, how we travel, and where we travel have implications on how much infrastructure is needed," says Abdul. As a PhD student at the University of Texas at Austin, he modelled travel behaviour of people in the city of Dallas. Such mathematical models try to mimic people's choices and decisions pertaining to travel, and are then applied to city-wide complex transportation systems to simulate the travel patterns inside a city.

Later, as a faculty member at the University of South Florida, he worked on modelling not just passenger travel, but also freight movement, which depended on behaviours of suppliers and distributors. In 2017, he moved to IISc and joined the Department of Civil Engineering and the Centre for Infrastructure, Sustainable Transportation and Urban Planning (CiSTUP) as an Associate Professor.

Compared to the cities in the US that he had studied, travel patterns in Indian cities are more diverse in terms of the types of vehicles, travellers and travel behaviours, orderliness of traffic streams and so on. Infrastructure is insufficient. There is little coordination between long-haul public transit systems like buses and potential last-mile providers like taxis. Though internet and mobile connectivity is much better now in urban India, transportation systems are not yet organised well enough to take full advantage of it.

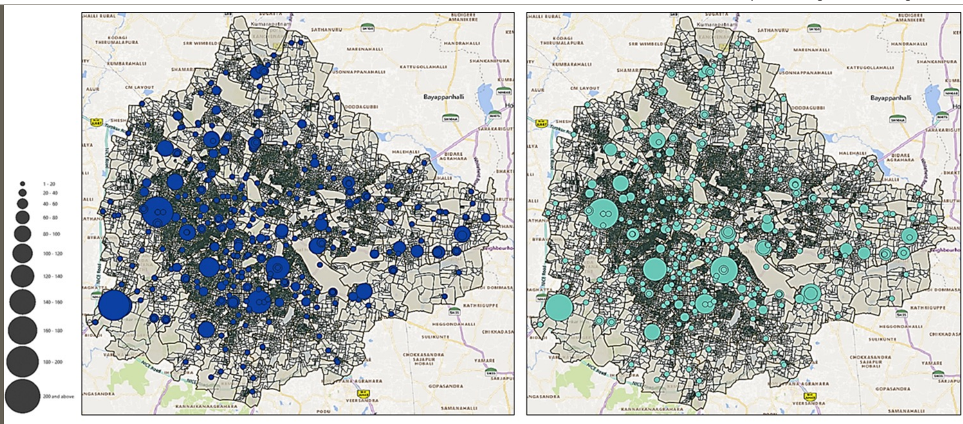
Studies have shown that it is not advisable to provide transportation infrastructure to meet the demand before assessing the nature of the need. Abdul explains, "There is a tendency that more infrastructure leads to increased personal vehicle travel. And that leads to even more infrastructure need, and it just becomes a vicious circle." Instead, it is better to first understand which travel choices of commuters are putting strain on the transportation systems.

This is easier said than done. While it is possible to observe people's choices, the reasoning behind them is often obscure. Therefore, Abdul and his team have developed ways to first observe the commuters' choices, and then infer which preferences, perceptions and constraints may have resulted in those choices. For this, they borrow statistical models from microeconomics and psychology, known as "econometric" and "choice" models.

The team uses household surveys to ask people the travel choices they make and why. Then there are indirect methods, like collecting data from GPS or sensors in mobile phones – strict ethical norms of anonymity are followed when using such data. The team also presents users with hypothetical situations, and asks them to choose from a set of actions as well as about how users perceive risk in such scenarios.

Several studies suggest that three major factors affect commuters' choices: travel time, cost of travel, and how reliable the timing and safety measures are. Yet, to build a model, other parameters affecting choices also have to be considered. Known measurable factors like travel times and

Ridership forecasting model for Bangalore's bus transit system (Image courtesy: Abdul Pinjari)



Observed bus transit boardings in Bangalore, India

Predicted boardings using direct demand model of bus transit ridership

costs can be incorporated directly into models. Then there are factors that cannot be quantified; for example, there is no tool to easily measure human perceptions. How can one assign a value to how risky someone thinks taxi travel is during the pandemic? To tackle this problem, the team uses comparisons between choices. For example, during the pandemic, the proportion of commuters who believe an autorickshaw is safer than a taxi might be higher. Or, a certain proportion of commuters might prefer cycling over short distances to using a motorised vehicle. These comparative values can then be incorporated in a model.

Since most of his projects are deeply multidisciplinary, Abdul has collaborations with people from diverse backgrounds.

For example, he and Rajesh Sundaresan, Dean of the Division of Electrical, Electronics and Computer Sciences, co-advise a PhD student, Vishal Kushwaha, who studies the benefits of possible collaborations between public transit systems like BMTC buses or the Bengaluru Metro and app-based services like Ola and Uber.

Abdul's team also collaborates with economists, who help in estimating the economic benefits of certain improvements to transportation systems and infrastructure. Some benefits are relatively easy to assess, like increased revenue, while others like travel time reductions, improved environmental conditions and water quality cannot be easily assigned a monetary value.

While Abdul's core research interests lie in analysing and modelling travel behaviours, the insights gained from these studies need to be implemented at the policy level, which is why he also frequently collaborates with government agencies and departments. In his experience, they have always been eager to get help. "At the same time, they understand that these problems have been built over decades, not overnight, and cannot be solved overnight," he says.

Currently, his team is working together with the Directorate of Urban Land Transport (DULT), a Karnataka Government department, and Robert Bosch, the technology and services company. "It's a true academia-government-industry collaboration, where we put all our understanding into these city-scale systems to simulate travel demands," says Abdul. They are developing models that can be used to answer the "what-if" questions, such as: What if the Metro line phase 2 comes to the airport? How much congestion will it reduce and where? Abdul expects that it may take a couple of years to develop such model systems. In the meantime, his team is also working on intermediate strategies for improvement. Deepa L, a PhD student, is creating a 'transit ridership forecasting tool' that will predict how many people use a specific mode of public transport. It is expected to answer questions like: If an extra bus line is provided from location A to location B, how much will the ridership increase? Will it compete with the Metro for ridership, or complement it? This tool will be ready in five to six months.

Understanding and modelling a system as complex as transportation can be quite challenging, Abdul acknowledges. "So, it helps to have humility, and accept that we may not be able to model every single detail. We may not be able to predict it accurately and precisely. Still, there is value to doing that, because otherwise it is like shooting in the dark."

- Narmada Khare

Abdul Pinjari and lab members (Photo: Ajith Yadati)

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

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

DESIGN
TheFool.in