CONNECT

WITH THE INDIAN INSTITUTE OF SCIENCE

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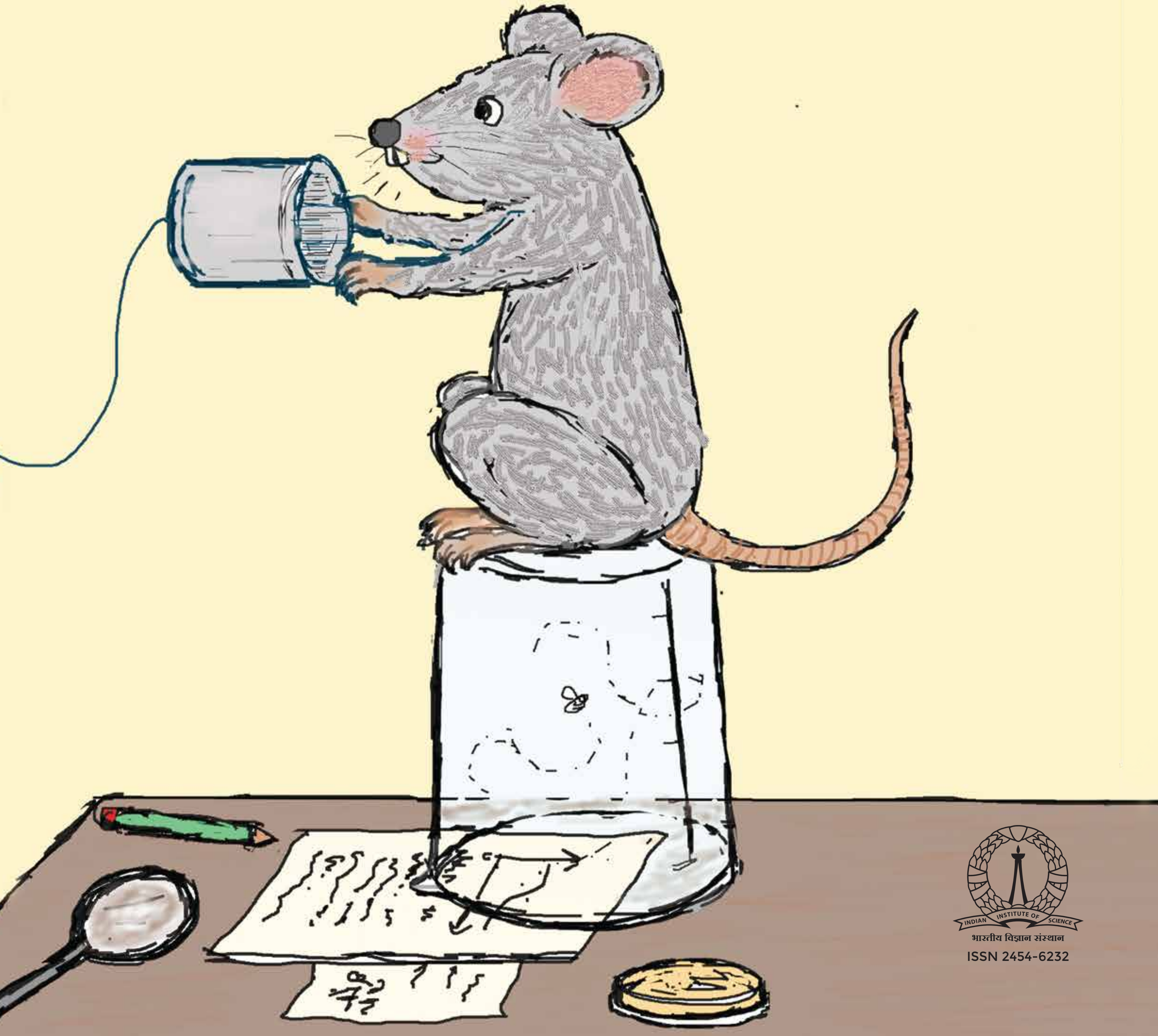
Model organisms
Why we study them

Kannada classes
Vocal for local

Mini-forest
A successful experiment



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IN THIS ISSUE

Editorial

In this issue of *CONNECT*, we explore aspects both mundane and exciting that are indispensable to the daily grind of research. For instance, whether they are Gregor Mendel's peas or Elon Musk's Neuralink monkeys, how does the study of model organisms help us discover what makes us tick? We take a closer look at some well-known lab animals, including mice, which have aided numerous advances – from the development of vaccines to the delivery of drugs – and monkeys, whose behaviour has enabled neuroscientists to unravel the intricacies of how the brain works. We also feature stories on how advances in microscopy are enabling deep dives into biological cells, and what it takes to build a research lab from scratch.

In addition, we look at how computational approaches are paving the way for innovations in materials research. Read about a long-term experiment that brought a sliver of the Western Ghats forests into IISc, and about self-organisation, a phenomenon in which global order emerges from local interactions in natural systems.

What connects us all more deeply than sharing a language and culture? In this issue, we speak to HG Srinivasa Prasad and his students, who share their thoughts on the spoken Kannada classes on campus that have been running full steam for almost 20 years.

And if you've ever wondered what counselling and therapy are all about, we have two of IISc's counsellors to break it down for you.

Happy reading!

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From Peas to Primates:

What models can tell us

- Narmada Khare

Photo courtesy: Harikumar RS

The study of model organisms is the key to unlocking mysteries about life on earth

Tardigrade, an upcoming model organism to study environmental stresses

When I first started working with the fruit fly *Drosophila melanogaster* after my Master's, many of my friends and family members were greatly amused. After 17 years of education, I had finally admitted that all I was doing was "mashya marne" or "killing flies", a saying in Marathi that suggests wasting time. Over the years, I was often asked when I was going to "evolve" to working with more complex organisms. One engineer friend was quite disappointed that instead of designing methods to eliminate these insects from our kitchens, I was trying to understand how cells in their wings organised themselves. I patiently explained to them that most cells in our bodies need to know their top from their bottom, and their left from right. Only then could they align in specific formations and perform functions correctly. Just like soldiers on a battlefield.

"But what's the point of studying this in flies?" they asked. "Shouldn't you study human cells?" A fair question. But here is the point: While researchers can perform non-invasive, observation-based studies using humans, they cannot perform invasive experiments on them. Besides, human bodies are often too complex to get clear answers purely by observation. In addition, for ethical reasons, researchers cannot change or mutate humans. Finally, and most importantly, what is biologically true for flies is often true for fishes and worms, and for mice and (wo)men.

Exploiting other species

Most organisms that scientists use for asking basic biological questions are found in their immediate surroundings: flies on their fruit, mice in their basement, bacteria in their gut and yeast in their bread. These are easy to acquire and economical to raise in labs. Their life-cycle is much shorter than ours, therefore several generations can be studied in a reasonable timeframe. They often grow fast (in number), allowing statistical analysis, and they are amenable to experimentation, albeit under some ethical regulations. This has resulted in scientists developing several tools and techniques for their study. A lot of their biology can be extrapolated to other life forms. They are our models, and give us a handle to understand complex phenomena associated with life on Earth.

Humans have historically exploited other species. The pharmaceuticals industry, for example, is almost entirely built upon microbial activities. We have used them to set our curd and ferment our beer, treat our oil spills and control our pests. However, sometimes this exploitation extends beyond direct benefits. They can become our windows into fundamental life processes and help us gain a deeper understanding of nature.

When scientists study certain species in depth to ask universal biological questions, they call these species 'model organisms'. Technologies develop around these organisms, like advanced microscopy and methods for molecular and genetic manipulation. These organisms are used to solve mysteries that may not be specific to the species to which they belong. For example, ecologists or organismal biologists may ask how honeybees foraging far away from their beehives find their way back, or how the lifestyles of birds affect the shapes of their eggs. But people using the frog *Xenopus* as a model organism may not necessarily be interested in the frog. They might be curious about how body axes are determined – head to tail, front to back – in the earliest stages of development, something that is easy to study in the frog where eggs are fertilised outside the mother's body. *Drosophila* biologists may not care as much for the fly, as they do for how genes control traits, the tools for which are available in the flies. "Worm people" study the nematode *C. elegans* for its almost glass-like body, making it easy to observe the development of organs, and may not care about its symbiotic relation with fig, the fruit in which they are often found.

Not every model organism is useful in understanding every process. For example, one cannot study gas exchange in lungs using the fruit fly, since it has a very rudimentary respiratory system, and the development of fingers from a limb-bud cannot be studied using fish. However, there is no denying the unbelievable insights into life on Earth that scientists have gained from studying such model organisms.

When scientists study certain species in depth to ask universal biological questions, they call these species 'model organisms'

Choosing the best model

For centuries, philosophers and naturalists have noticed fundamental similarities among life forms. This suggested a universality to life that was exploited by scientists, a notable example being Gregor Mendel.

Mendel, an Austrian monk and a mathematician, worked in an abbey in the mid-1800s. He was curious to know if it was possible to raise crops or breed cattle that consistently showed favourable traits in every generation. He had access to the abbey gardens and hence chose a pea plant, *Pisum sativum*, for his experiments. The plant grew fast, allowing him to cycle through multiple generations in one season. It had easily visible traits, and produced a large number of seeds. This was the beginning of genetics, the systematic study of inheritance.

Image courtesy: PICRYL

The pea plant, Mendel's model organism

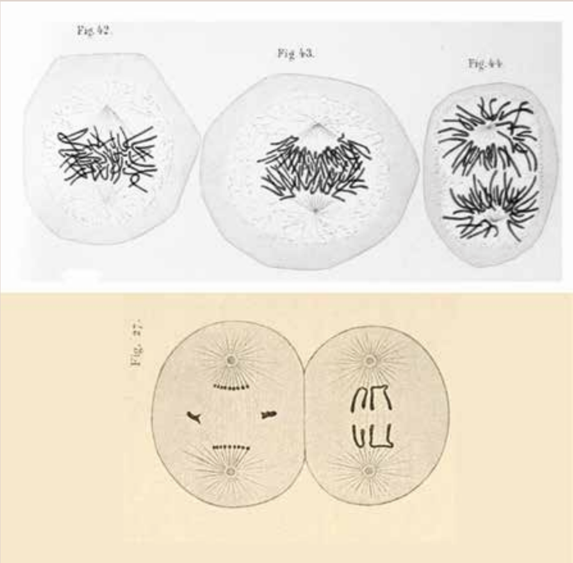
It is possible that the monk tried several other plants before zeroing in on the pea, but his choice turned out to be the right one. We know today that animals, with some exceptions, have two sets of chromosomes, the thread-like structures in the nuclei that contain the genetic material. The plant kingdom is more fluid, with some having multiple sets of chromosomes. But not the pea. It has just two copies. Mendel inadvertently chose a plant that not just gave him clear and interpretable results, but also allowed him to develop a theory that could be extrapolated to the animal world. He also realised that 'factors' for heritable traits (known today as genes) come in two copies, one from each parent. Any plant with more sets of chromosomes would have made Mendel's task unenviable.

Time and again, scientists have realised that some biological mysteries are impossible to solve until the right model organism comes along. Walther Flemming and several others had noticed chromosomes in the late 1800s, in stained samples of dividing cells of the salamander. Yet, nobody connected them to Mendel's genes, because salamander cells contained dozens of chromosomes, often tangled together. To prove that chromosomes carried hereditary information, it was important to be able to count them. It was almost 50 years after Mendel's discovery that Theodor Boveri made a crucial observation that added a new piece to this puzzle.

Boveri was working with the roundworm (*Ascaris megalocephala*), which had large, transparent cells with only two pairs of chromosomes. He noticed that when germ (reproductive) cells divided to create daughter cells (sperm in males and eggs in females), each daughter cell received only one pair of chromosomes (reduction division). He also found that the sperm and egg unite to create a zygote, a fertilised egg, with two pairs of chromosomes. When the zygote divided, the two daughter cells had the same number of chromosomes as the mother cell. Boveri realised that he had uncovered the physical basis for Mendel's laws of inheritance. He would then go on to publish beautiful drawings of equal and reduction cell divisions.

New models open new avenues

When a researcher realises that a model organism is easy to experiment on, many more researchers become drawn to it. They develop newer techniques and tools which make the study of that organism easier. *Drosophila* became a very attractive tool after TH Morgan, a revolutionary geneticist and embryologist in the early 1900s, and his students used it to make great strides in genetics. *C. elegans* became popular for those working on neural development. However, as the focus of scientists changes with new breakthroughs, the inherent limitations of established models become apparent.



Images: Wikimedia Commons

T: Illustrations of salamander chromosomes by Walther Flemming,
B: Illustrations of Sea urchin chromosomes by Theodor Boveri

For more than a century, scientists have looked to only a handful of species to decode biological mysteries. This is restrictive, because each model organism represents only one branch of the giant evolutionary tree of life. There are numerous interesting traits and biological phenomena that are not represented in it. Therefore, scientists often search for new species, hoping to overcome old impasses or find new mysteries to solve. These new species for which scientists are yet to establish experimental techniques are the 'non-model' organisms.

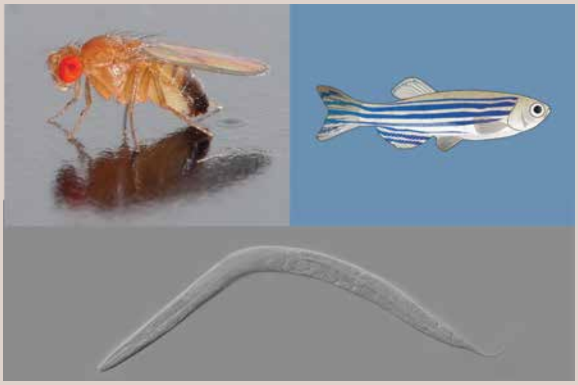
For example, Nipam Patel, a professor at the University of Chicago wanted to know how an organism with many pairs of appendages evolves a genetic programme where each pair is designed for a unique function. The lobster, for example, has one pair of legs for catching prey, some others for walking, some more for swimming and so on. Since working with lobsters is difficult and expensive, and because no conventional model fit the requirements, his team started looking for an alternative. One of his students found an ideal candidate, a tiny crustacean, *Parhyale hawaiensis*. It lived in the water filtration system in the lab, ate the garbage gathered there and was tolerant of a wide range of environmental conditions, making it quite easy to maintain in the lab. Soon, the team had identified genes that regulated the development of each appendage, found out where in the body they were active, and over a period of time, developed several experimental techniques suitable to work with this non-model species.

Model organisms at IISc

Researchers at IISc have a long history of using model and non-model organisms. The first primate centre in the country was set up here to house monkeys needed for research on reproduction. A repository of native microbes, the National Collection of Type Cultures (NCTC), was set up in what was then the Department of Fermentation Technology in 1941. Many species in the collection were used for commercial production of enzymes, fermenting sugars, and digesting different substrates to produce useful chemicals, vitamins and alcohols. The Annual Reports from 1944-45 state, "[the NCTC] has in its repository 275 bacteria, 156 fungi and 67 yeasts, making a total of 498. Microorganisms of scientific and industrial importance have been supplied to several research institutes and industrial concerns." In 1945-46, using the Feulgen technique, former faculty members MK Subramaniam and B Ranganathan stained the chromosomes of yeast for the first time, documenting their presence. The strain of yeast used for the study came from the NCTC.

A remarkable example of the use of an unconventional organism comes from the work of PS Sarma, a professor at the Department of Biochemistry, IISc, in the 1960s. Sarma tackled the mystery of a debilitating disease, neurolathyrism, caused by eating kesari dal. This dal was cheap and was an excellent source of several nutrients, but it contained a toxin that caused muscle spasms and paralysis of lower limbs in several people who had consumed it regularly. Researchers had tried to identify the toxin by testing extracts of kesari dal on mice and rats to no avail. Sarma decided to use a grain-eating insect, *Corcyra cephalonica*, instead, and was able to successfully isolate the toxin, a highly acidic amino acid, and show that it had neurotoxic effects on chicken and monkeys as well.

Today, there are several faculty members at IISc who use both conventional and unconventional model organisms, such as Sandeep Eswarappa, Associate Professor in the Department of Biochemistry. Inspired by Neil Degrasse Tyson's account of tardigrades – extremely hardy creatures that have survived five mass extinctions – he has started a project to study them in his lab. "They are not conventional model organisms, where we can manipulate their genomes or do genetic analysis," Sandeep explains. "Tardigrades are not ready yet for genetic studies. But if you are trying to understand strategies for overcoming environmental stresses like temperature or pressure, then they are good models for that."



Images courtesy: Wikimedia Commons

L-R: Drosophila, zebrafish and C. elegans – well-established model organisms

Another faculty member who relies on model organisms is Upendra Nongthomba, Professor at the Department of Molecular Reproduction, Development and Genetics, who studies the cellular basis of certain myopathies and neurodegenerative diseases. His lab uses two different model systems, the fruit fly *Drosophila* and zebrafish. Though maintaining zebrafish in a lab setting is not as easy as maintaining fruit flies, they are physiologically closer to humans. Newly developed molecular biology techniques are making it possible to use the fish for genetic studies as well. "Since our group is interested in modelling human diseases and genetic disorders, and screen drugs or formulations that alleviate the pathophysiology, the zebrafish serves as a much better model," says Upendra. "From the disease or pathological point of view, one model can be much better than another. For example, mice never develop Duchenne Muscular Dystrophy like humans do. However, the zebrafish shows a phenotype that almost mirrors human pathology, including death at a young age."

The search for new questions and model organisms is never ending. As Nipam Patel, in his 2019 lecture at the University of Chicago, puts it succinctly, "Biology has solved most problems. It is just a matter of finding the organism that has solved that problem, and then understanding *how* it has solved that problem."

RODENTS TO THE RESCUE

- *Arpit Omprakash*

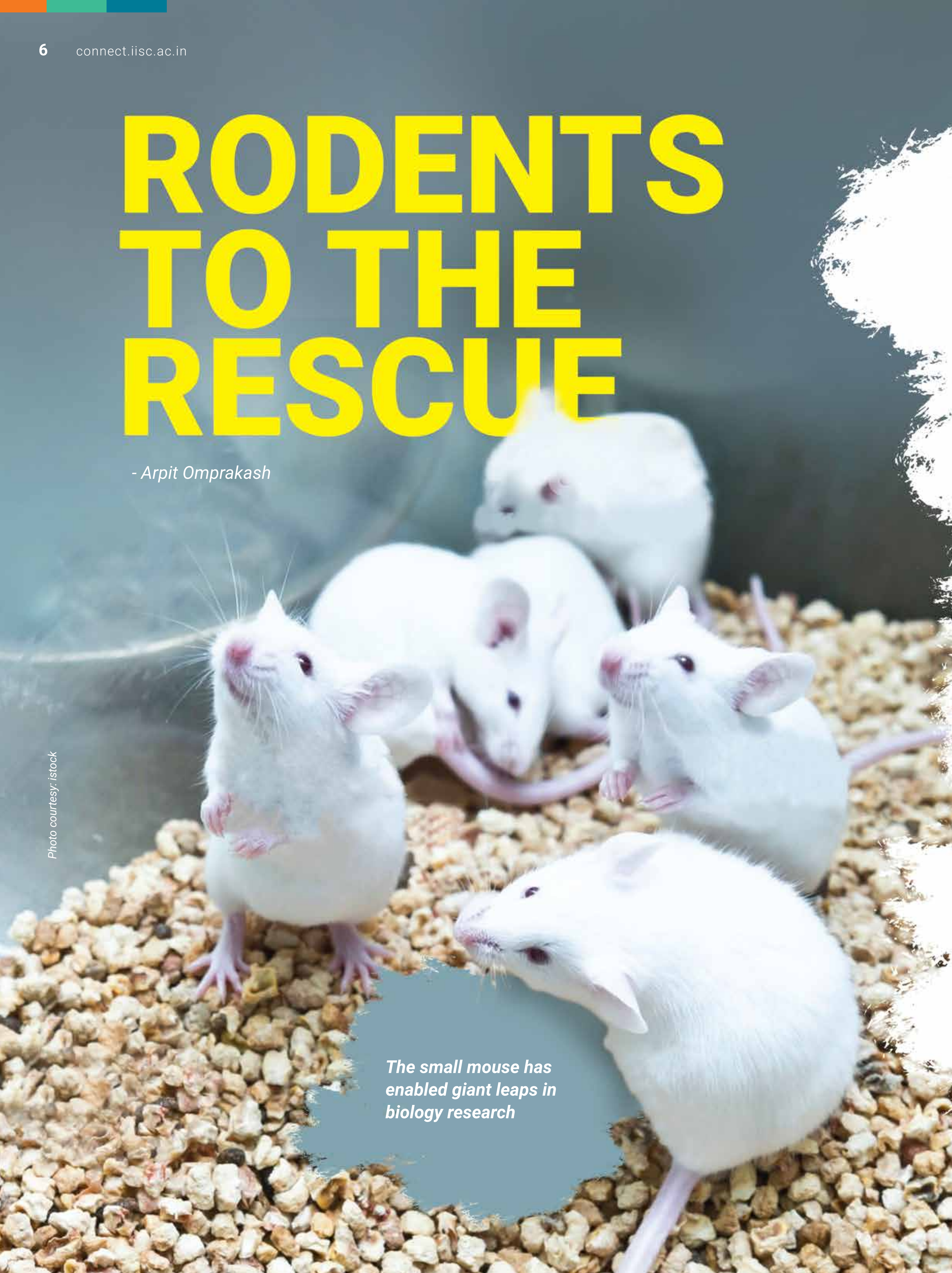


Photo courtesy: istock

The small mouse has enabled giant leaps in biology research

Claudius Galen (129-199 CE), a prominent physician in ancient Greece, obsessively studied anatomy – the science of how our bodies are structured and how our organs function. Since the ruling Roman government prohibited working with human cadavers, he dissected animals instead, to gain knowledge.

Even without human subjects, his investigations led to some remarkably accurate conclusions. One of the most important insights he gained was that the brain, and not the heart, controlled our actions. He deduced this when upon opening up the skull of a living cow and applying pressure to different parts of its brain, he could control its movements. He also found that muscles and nerves controlled our respiratory system, and kidneys produced urine.

Science has come a long way from the times of ancient Greece, and we have a deeper understanding of the human body. Still, there are many unanswered questions. Although now we can dissect corpses, researchers still need to work on live subjects to understand the normal functioning of the body. One of these subjects that has proved tremendously useful is the humble mouse.

A multifunctional model

Mice are magnificent model organisms. They are small, inexpensive to maintain, and easy to look after in a lab. Being mammals, they share considerable genetic similarities with humans.

According to the National Human Genome Research Institute in the US, on an average, the sequences of genes in the mouse and human genomes are 85% identical, with some genes being up to 99% identical. "Comparing mice to humans is complicated, but there are enough similarities to excite us to run experiments in these animals," explains Rachit Agarwal, Assistant Professor at the Centre for BioSystems Science and Engineering (BSSE) at IISc, who is working on developing innovative drug-delivery methods. "By virtue of their genetic similarities, organ systems like the respiratory system, the immune system and others and their functioning are quite similar in humans and mice," adds Ameya Dravid, a PhD student working with Rachit.

With the advent of new technologies to manipulate genes, researchers unlocked a potential game-changer in the development and use of mouse models. Mice with new genes or DNA introduced into their genome are generally called transgenic mice. This technology can reduce the gap between mouse models and human systems.

According to the Foundation for Biomedical Research, more than 90 percent of all medical research labs in the world rely on the mouse model. "The mouse model has been in use for a long time; a large body of literature, genetic tools, methods, and reagents are available, making it a well-researched and easy to use model," says Siddharth Jhunjhunwala, Assistant Professor at BSSE, who is interested in elucidating how our body reacts to foreign materials. A lot of knowledge can be gained from this model, especially now that we can engineer mice to express human genes.

But what is this knowledge, and how has it helped us?

Curbing contagion

Over the past couple of years, COVID-19 has wreaked havoc around the globe. Researchers everywhere have been working on understanding the disease and developing drugs and vaccines to counter the virus.

One of them, Raghavan Varadarajan, Professor at the Molecular Biophysics Unit (MBU), is interested in developing vaccines against major viral diseases, primarily influenza, HIV, and COVID-19.

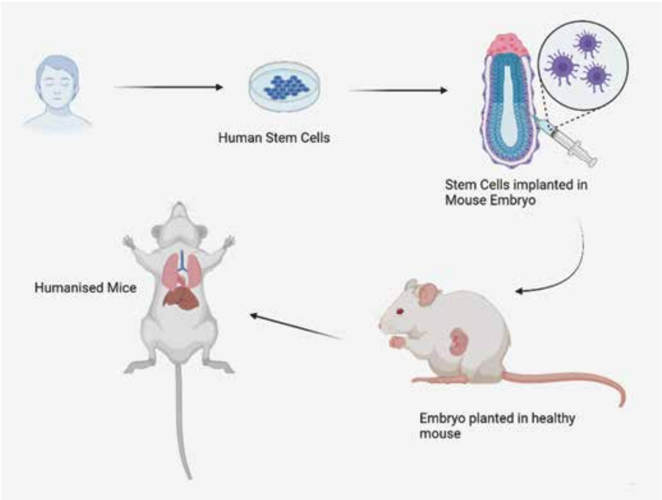


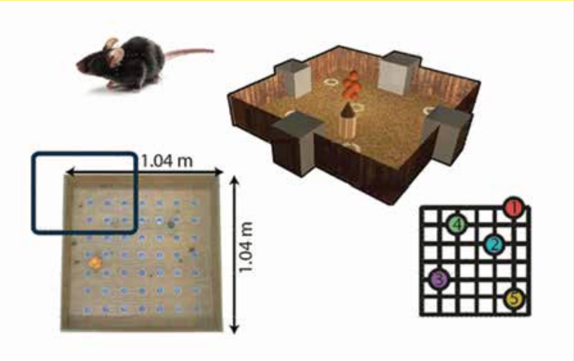
Illustration: Arpit Omprakash

How a humanised mouse is created

Influenza is a seasonal respiratory disease caused by viruses. Each year, the flu virus mutates, giving rise to new variants attacking the population. Current vaccine formulations target a viral surface protein with a highly mutable part. "That is why the vaccine needs to be updated annually," remarks Raghavan. Using a mouse model of influenza, his lab has developed a vaccine formulation that targets a less changeable part of the viral surface protein. This might offer protection against a wider range of influenza viruses and reduce the number of flu shots that an individual needs to take in their lifetime.

The first step in creating a vaccine is to understand the interactions between the virus and our body. The COVID-19 virus, for example, infects human cells by binding to a cell-surface protein called the 'ACE2 receptor'. Studying virus-ACE2 interactions in a test tube does not explain what actually happens inside our bodies. Using animal models like mice and guinea pigs has also been challenging since different animals have different versions of the ACE2 protein expressed in their cells. In addition, animal ACE2 proteins elicit different reactions to the virus compared to humans.

Image courtesy: Balaji Jayaprakash



Cue-location experiment. Clockwise from top: The mouse, the sandbox, location of cues and maze dimensions

"Our colleagues at the National Centre for Biological Sciences (NCBS) have developed transgenic mice which express the human ACE2 receptor and can be used to study COVID-19 infections in mice," says Raghavan. Transgenic mice that have human genes incorporated in them are called humanised mice, and they provide a great avenue to study interactions of virus and human proteins in the mammalian system.

Another issue with COVID-19 vaccines is refrigeration during transportation. It is likely that several batches of vaccines might be rendered unusable or unable to reach remote corners of the country due to a lack of refrigeration technology. Raghavan's lab has developed a "warm" COVID-19 vaccine that is not just effective against all the major variant strains tested to date, but also does not require refrigeration for storage or transportation. This has huge implications for a country like India as well as numerous other developing countries.

Training memory

Mice are also valuable in neuroscience research.

Balaji Jayaprakash, faculty member at the Centre for Neuroscience (CNS), studies how memories are formed and how they help us to carry out daily tasks. "We don't get to see inside the human brain at the microscopic scale, which makes it difficult to study the mechanistic causes of memory formation," he says. His lab uses mice as a model to elucidate the inner workings of the brain.

A recent study done in his lab suggests that our rodent cousins might be adept learners. In a related experiment, they investigate the effect of prior knowledge on problem-solving. The experiment involves presenting cues (flavour) to mice associated with specific locations in a sandbox. When presented with a certain flavour, the mice need to remember the associated hole and go to the correct location (one of the 5 white rings) to obtain the food reward.

They were able to show that the mouse can learn complex information – a set of five different flavour-place associations – but can learn faster when it is learning in relation to a prior experience or learning. If the second set is presented independently, many of them struggle to learn. On the other hand, when presented in relation to previously learned cues, they learn the new ones easily. Balaji says, "What would otherwise take them one and a half months to learn, they can learn in six days (if training is related to things they know)." More interestingly, they show that such learning is not only fast but also enables these mice to solve new problems. This may have implications in optimising the course structure in schools and colleges by emphasising and bringing out the relationships between concepts across the courses in adjacent semesters or adjusting the syllabus to build upon previous courses. On a smaller scale, this learning method can increase the amount of information one can learn in a short period of time.

Testing implants

When foreign particles enter our body, it assigns the immune system to fight against them. Although often life-saving, implants or prosthetic devices are also foreigners in the human body and elicit negative reactions from the immune system. Studies have shown that the first cells to attack an implant are neutrophils, which are the most abundant immune cells circulating in the body.

Image courtesy: Alakesh Singh

Microscopic section of 7-day old implants (pink) in mice abdomen surrounded by immune cells (blue, purple).

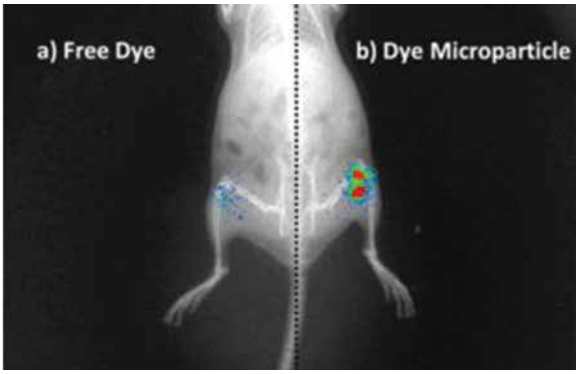
The initial interactions between implants and neutrophils attract other cells and molecules to the site of implantation. These aggregate on the surface of the implant, leading to the formation of a capsule around the implant. This process is called fibrosis. Alakesh, a PhD student in Siddharth's lab, studies this process in mice and is interested in quantifying the responses of the body towards different materials used to make implants.

Siddharth's work on mice has helped identify key processes and players in the immune response. The hope is that this will help in engineering implants that are more compatible and better at evading our immune system.

Delivering drugs

Similarly, Rachit and his student Ameya use the mouse to study osteoarthritis, one of the most common chronic diseases that affect the joints. Ameya uses liposomes, nanoscale lipid capsules, as carriers to deliver drugs to specific joints in the body of the mouse. Liposomes carrying the appropriate drug are injected near the affected joints where they slowly deliver the drug.

Image Courtesy: Kaamini M Dhanabalan



Mice knee joints on day 7 after injecting (a) dye and (b) dye with PLGA Microparticles.

The lab uses another molecule, poly lactic-co-glycolic acid (PLGA), to create nanoparticles that can deliver drugs via an inhalant for respiratory diseases like tuberculosis (TB). These polymeric particles gradually reduce in size. "Once they become small enough they are either excreted by the kidneys or metabolised – used up to produce energy – by the body," says Rachit. Such drug-delivery methods in humans, if successful, might revolutionise modern medicine. Instead of two or three pills a day, just one of these injections once in a while may suffice.

Treading cautiously

Although Galen's ancient experiments provided invaluable knowledge about the human body, they also produced or reinforced some misconceptions. He believed that blood is continuously produced by the liver and is used up by the body. His depictions of the human uterus were also more like a dog uterus. Galen probably discounted the differences in human and animal internal structures, and the lack of sophisticated technology might have played a significant role in amplifying his misunderstandings.

Today, researchers are aware of the risks as well as benefits of using animal models to study how the human body works. Scientists tread carefully by first establishing the similarities between humans and mice pertaining to their study, and then drawing conclusions based on insights from mice experiments. "The earliest experiments are to establish equivalence. Not equivalence in every aspect, but on a broad level," explains Balaji.

Some fundamental dissimilarities are challenging to overcome. For example, mice are tetrapods (four-legged organisms) while we humans are bipeds (two-legged organisms). This means that there is a higher load on our joints compared to those of mice. Thus, diseases like osteoarthritis are more debilitating for humans and their progression is different.

Perhaps the most significant disadvantage of the model is something that also plagued Galen. Insights gained from mouse models, while very useful, are not necessarily directly transferable to human systems. "They are very useful models, but eventually these animals are different from humans, and hence additional studies are required for translation," explains Siddharth.

Before any drug, device, or vaccine is certified for use, it often needs to go through an arduous process of testing in various animal models and human cells, starting often with the mouse. "Safety and toxicity studies in a couple of different animal models are needed to confirm that regardless of the protection a vaccine offers, the vaccine formulation is not toxic," explains Raghavan.

Lately, there has been a push to completely eradicate the use of the mouse model and shift to working with human cells in Petri dishes or organs grown in labs. But this is often impossible in fields like neuroscience, where scientists need to relate brain activity to behaviour.

At the same time, there are ethical concerns and heavy restrictions on experimenting on higher organisms like monkeys or humans.

Given its far-reaching applications and well-established protocols combined with the number of researchers invested in using it, the mouse model is here to stay, at least for the foreseeable future. As Rachit puts it, "...The mouse model remains our preclinical gold standard."

Arpit Omprakash is a PhD student at the Centre for Ecological Sciences and a former science writing intern at the Office of Communications, IISc

Monkeying Around

- *Anusha Rastogi*

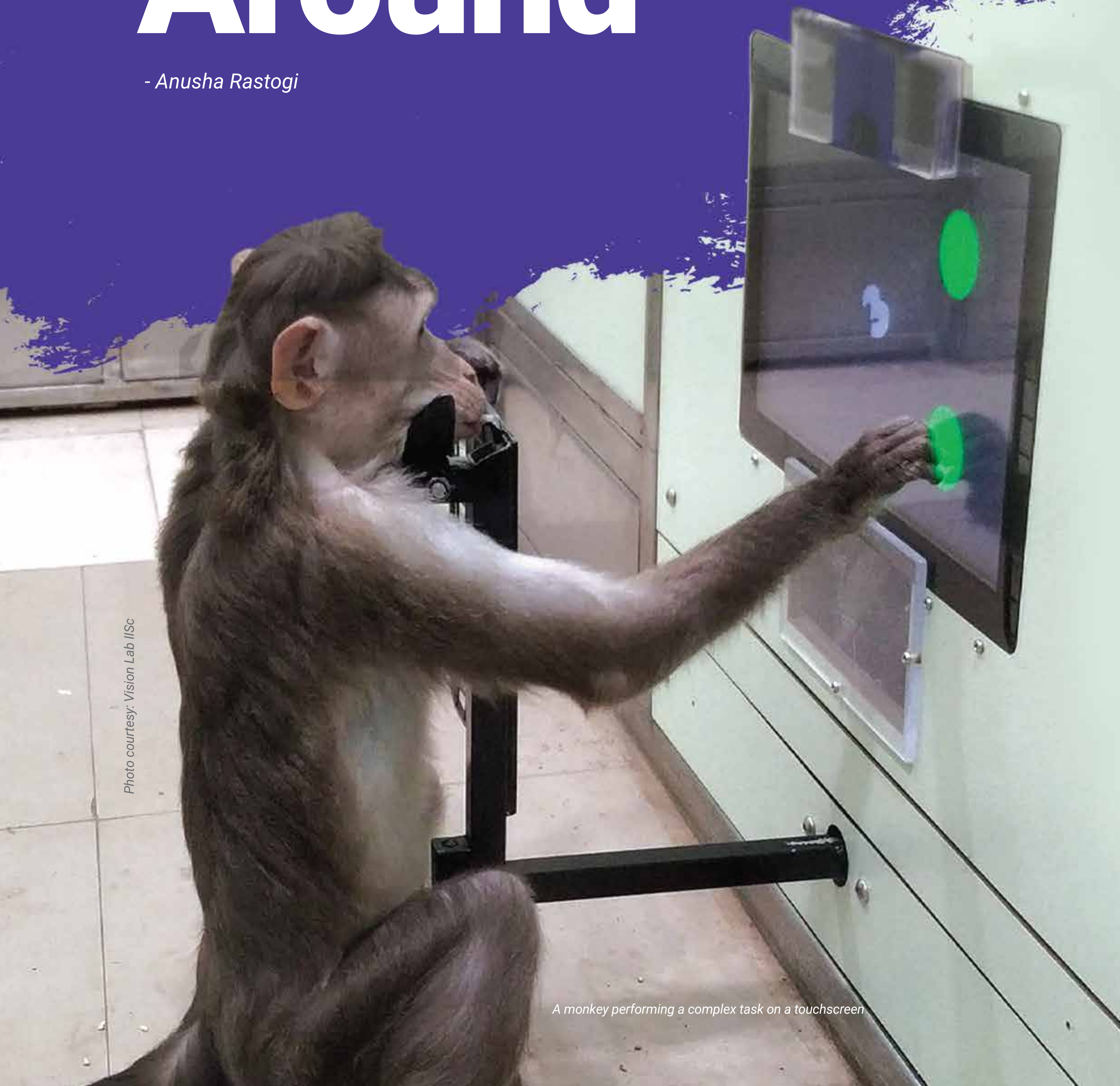


Photo courtesy: Vision Lab IISc

A monkey performing a complex task on a touchscreen

Neuroscientists at IISc study monkey behaviour to answer fundamental questions about brain function

In 2021, Elon Musk took the internet by storm with his video game-playing monkeys. Using technology that transmitted neural data from the monkey's brains directly to the computer screen, researchers from Musk's Neuralink Corporation created systems in which the monkeys could play the game on the basis of their thoughts alone, without needing any physical movement. Hailed as a potential means to assist people with paralysis, this threw the spotlight on the significant applications of neuroscience research that involves our ancestral cousins – primates.

For a long time now, the human brain – with its thousands of neurons sending out signals that span our body – has enthralled and intimidated scientists in equal measure. Demystifying these neural connections is a monumental undertaking, and studying primates as model organisms has spearheaded our understanding of a vast array of neurological phenomena such as vision, memory formation and attention. What makes monkeys attractive candidates for such research is that since they share ancestry with human beings, they are highly intelligent, social animals whose body, brain and behaviour closely matches ours.

But this also means that conducting research on monkeys is more challenging than that on mice or fruit flies. For starters, there are understandably more ethical regulations for large animal experimentation. Investigators have to obtain ethics clearance from not only the Institutional Animal Ethics Committee, but also another Central Government body, the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

The Indian Institute of Science has had a long history of primate research. Originally set up for biochemical research in 1965, the Primate Research Laboratory (PRL) housed hundreds of bonnet macaques (a species found in south India) at its peak. Ramesh V, who has been the Technical Officer-In-Charge of the Central Animal Facility for 36 years, recalls, "It was one of the largest facilities for bonnet monkeys in the world at the time, and was also used by other research institutes in the country." In those days, monkeys were specifically bred for research in diverse areas such as reproductive biology, physiology and endocrinology. With the retirement of many of these researchers, the number of monkeys at the facility has dropped considerably to less than 50 animals. These days, the monkeys in the facility are used mainly for neuroscience research, which requires only a few animals per study.

Ramesh explains the efforts that go into ensuring that CPCSEA guidelines are followed to the letter, "We have dedicated staff for daily maintenance activities, such as cleaning the space, feeding animals and tending to any disruptions that break out. Even during the past three COVID waves, a smaller number of staff have come in daily so that the monkeys' needs don't go unattended." Monkeys involved in research studies are kept separately from the others and are housed in large, spacious cages. Monkeys that are not used for research studies such as aged or pregnant animals, are kept in the larger, outdoor runs.

Photo courtesy: Ramesh V

Ramesh V at the Primate Research Laboratory

To enable brain recordings, the monkeys undergo a surgical procedure to implant a chip into their brain. This involves removing a small portion of the skull and placing a chip that has numerous electrodes contained in it. Each of these electrodes picks up electrical impulses from nearby neurons. The surgery is performed under anaesthesia with the guidance of a vet, while graduate students observe and assist with the process. Once the monkey recovers, the neurosensory chip allows scientists to record from hundreds of neurons. Interestingly, because data from each neuron is normally treated as a single unit, the scientists only need to study two to three monkeys to have enough samples to validate their hypotheses. As a result, very few monkeys are under experimentation at any given point of time. Usually, the monkeys chosen for experiments are young adults between 8-14 years of age, as cognitive functions can be different in juvenile and aged animals.

Laying the foundation

Owing to their higher intelligence and enhanced social capabilities, working with monkeys can be a challenge. "One of the most important things when working with monkeys is to establish a sense of trust between the student and the animal," explains Supratim Ray, Associate Professor at CNS. Graduate students who choose to do primate research have to attend an orientation session where they are taught the basics of how to habituate the monkeys to their presence and the necessary precautions to take when working with monkeys. This includes wearing protective gear to maintain a sterile environment and prevent infections or injuries. Another key insight is to stay on guard and avoid eye contact, especially in the beginning, as monkeys often perceive it as a sign of aggression. New students initially approach the monkeys only with their seniors who are already acquainted with these animals.

Owing to their higher intelligence and enhanced social capabilities, working with monkeys can be a challenge

"Each monkey is unique," says Surya Prakash, a graduate student in Supratim's lab. "Some are very shy and retreat to the back of the cage when they see you coming, while others are more curious." Usually, every student's thesis starts with an outstretched arm holding out a treat for the assigned monkeys, hoping to entice the animals to come closer. Gradually, as the monkeys get used to the student's presence, researchers spend longer hours in the facility petting the animals and learning which fruits they prefer so they can reward them with their favourite juice. To forge a deeper connection and establish a sense of intimacy, students play games such as making the monkey guess which of their fists contains food. Depending on the monkey's inherent nature and the comfort level of the student, this can take anywhere from a few weeks to months.

But, as always, the proof is in the pudding. Once the students are reasonably certain of the bond they share with the monkeys, they start training them to engage in tasks that would lead them towards answering a research problem. "It is completely the choice of the monkey if he wants to perform the task." explains Sini Simon, a graduate student in SP Arun's lab at CNS, underlining the main hurdle in primate research. Both Arun's and Supratim's labs rely on the monkeys performing specific behavioural tasks to glean insights into different aspects of brain function. To induce monkeys to do their tasks, the researchers offer solid or fluid rewards to the animal for each step of training. They start small, initially encouraging the monkeys to open the researcher's hand to get treats. With time, the monkeys begin to sit on a specially designed chair, and learn to perform the task either by moving their eyes or touching a screen. Each of these steps is reinforced by rewarding the monkey with juice or fruit, and never through punitive measures.

Getting down to monkey business

Once the monkey is wheeled into the experiment room, students grapple with the herculean challenge of training the monkeys to perform the experiment. Supratim's lab studies neural mechanisms underlying the cognitive abilities of these primates by measuring a specific class of waves called "gamma". Using an elaborate setup involving an eye tracker, a computerised reward system and a dot on the computer screen, these scientists slowly piece together the neuronal activity that regulates their attention. In this process, the monkey is required to stare at a small dot on the screen without blinking, while the eye tracker (essentially, an infrared camera) monitors its movements and a reading of gamma oscillations is taken through the chip implanted earlier. Every time the monkey looks at the screen for the required length of time, the automated system releases a few drops of juice via a pipe located close to the monkey's mouth. While this process sounds pretty straightforward, training the monkeys to look at the screen for long durations can be cumbersome. "We usually increase the duration of time gradually, giving out the juice at longer intervals once the monkey starts adapting to the experiment." explains Supratim.

At Arun's lab, which studies the neural basis of vision and object recognition, the monkeys are trained to find differences between two objects. Known as the 'same-different' task, the experiments involve showing monkeys two images in rapid succession and training them to press a button if the two images are the same, and another button if the two images are different. Another task consists of displaying a series of photos on the screen and requires the monkeys to press the button if one of the images in the array is unrelated to others. Needless to say, because of the complexity that these processes demand, it takes a long time and a significant amount of effort (and, of course, juice) before the monkeys become proficient at these tasks and the researchers are able to record neuronal activity. Often, the monkeys understand the task, but have trouble touching the button with just one of their fingers, thereby generating faulty data by registering multiple touches at the wrong time. To circumvent such issues, scientists ease them into the process by starting with larger buttons and gradually scaling the button down to the desired size.

Recently, a new initiative by Arun's lab has been to create a naturalistic environment in which to record brain activity. Unlike the traditional approach wherein monkeys enter the artificial environment of a lab to be studied, this method emulates the wild by including trees and open areas, increased natural light and foraging opportunities. Bringing in a touchscreen workstation, a juice pipe and a chinrest that holds monkeys' heads immobile to enable gaze tracking, scientists at Arun's lab achieved remarkable success as the monkeys performed the same-different task of their own volition, coming to the setup as and when they desired, while obtaining highly accurate gaze signals. Incredibly, naive monkeys that were allowed to mingle with trained monkeys in this space also picked up on the experiment within a few weeks - a novel finding that enables the easy training of more animals.


Photo courtesy: Vision Lab IISc

A pair of animals in the novel naturalistic environment for studying behaviour

The road ahead

While results from research with primates have led to path-breaking discoveries across the world, training monkeys to perform any of these behavioural tasks is lined with difficulties. "Every monkey has its own challenges," reveals Surya. "Some might be easy to approach but won't get into the chair. Others will enter the lab in record time only to take a long time to figure out how the experiment works." Armed with juice and incredible amounts of perseverance, it is the researcher's job to patiently untangle these knots until the experiment is smoothly performed. Sini, from Arun's lab, reiterates this sentiment, "You can't just sit down and tell the monkey what the experiment is. We are at the mercy of the animals we record, so if the animal decides it is not going to come in for the recording, that's it. You're done. "

Despite the unpredictability of the animals' behaviours, Surya and Sini agree that the experience has been extremely rewarding. After five years of working in this area, Surya admits that he is enthusiastic about working with these animals for his long-term research goals. "The one advantage you have of working with monkeys is that you get access to the kind of recordings that you won't be able to get with humans. You can actually record at the single cell level. And you can also record from a population of neurons and examine how they communicate with another part of the brain," he explains.

The future is brimming with possibilities. Arun has high hopes for experiments in the naturalistic environment. He believes that this could be a gateway to identifying the mechanisms that link vision to natural movements, such as seeing a fruit and jumping to another tree to retrieve it. "We want to ultimately understand how the visual areas in the brain talk to other regions of the brain while animals engage in natural behaviours," he says. In tandem, Supratim's lab has discovered that the gamma waves generated in the monkey brain are colour sensitive. He plans to eventually expand to other behavioural tasks for the monkeys to understand which colour-identifying neural circuits induce gamma wave production. Since gamma waves are associated with higher-level cognitive processes such as memory and attention, this research could also help us understand the neural circuits in both health and disease.

Anusha Rastogi is an Integrated PhD student in the Division of Biological Sciences and a former science writing intern at the Office of Communications, IISc

To boldly see WHAT NO ONE HAS SEEN BEFORE

- Savyasachee Jha

Photo courtesy: Partha P Mondal

From simple combinations of lenses, microscopes have evolved into complex tools giving us unparalleled insight into cellular secrets

Classical single molecule super-resolution microscope built at the Mondal Lab, IAP, IISc. PhD research scholars (from left: Prakash Joshi, Neptune Baro, Aravinth S, Jigmi Basumatary) working on the system

January 1665 saw the publication of Robert Hooke's *Micrographia*. The beautiful illustrations of fleas, flies and other insects in it gave humanity an insight into the sheer beauty of the hitherto unobserved world of small creatures. The book sold more copies than any other scientific work published before it, earning it the sobriquet of "the first scientific bestseller".

Hooke had used a novel tool to look at these creatures: a microscope. But his most enduring legacy was something else he saw through its lens – tiny, repetitive structures in cork, resembling the small rooms which served as the homes of Christian monks. He named these structures *cells*.

The main themes of Robert Hooke's work have remained with biologists ever since. To use new and better techniques, and to get clearer and sharper images. And of course, to look at cells.

Towards ever sharper imaging

Since Hooke's time, the field of microscopy has become instrumental in understanding biological phenomena. And within this field, the technique of fluorescence microscopy stands out. This involves tagging proteins or subcellular components of interest with a "fluorophore" (usually a short protein) which will emit light when excited with light of a particular wavelength. When photons from the light source hit the electrons in the fluorophore, they gain energy and release it in the form of light at another, longer wavelength. This emitted light can then be captured and used to locate the object to which the fluorophore is bound.

"Biologists typically seek to understand two major challenges: Self-assembly of molecules, when they come together to create larger and larger structures, and the biological functions these structures are involved in or give rise to," explains Deepak Nair, Associate Professor at the Centre for Neuroscience (CNS), IISc. "Microscopy seeks to understand the locations where these functions manifest."

"This has been one of the greatest revolutions of our time," adds Rahul Roy, Associate Professor at the Department of Chemical Engineering, IISc. "Nowadays, you cannot publish a paper in biology without imaging the cells or animals you are studying under a microscope."

Fluorescence microscopy can be used on both stained and fixed cells as well as live cells. One can use it to understand how a cell was at a particular point in time, or to understand the dynamics of certain proteins as they move about inside a living cell.

Until recently, confocal microscopy was the cutting edge of fluorescence microscopy. Confocal microscopes use lasers to illuminate the sample and gather light from just the focal plane (the depth into the sample where the microscope's lens is focused), and not from other components behind or in front. This leads to an increase in the 'signal-to-noise ratio.'

Unfortunately, a typical confocal microscope is limited by the 'diffraction limit' of light. The resolving power of a microscope is inversely proportional to the wavelength of light being emitted. If fluorophores are closer than a certain distance from each other – the limit is typically 250-300 nm – the microscope is unable to resolve them as separate objects.

"Nowadays, you cannot publish a paper in biology without imaging the cells or animals you are studying under a microscope"

Can you super-res that?

But the limits of confocal microscopy have not deterred biologists from wanting greater resolution. A powerful new technique that aims to break through this limit is superresolution microscopy. In confocal microscopy, all the fluorophores of interest get excited at once. "But in superresolution microscopy, you can excite them stochastically, meaning only some of them can be active and fluoresce at a time. This allows for resolution of distances up to 20-30 nm," explains Partha Mondal, Professor at the Department of Instrumentation and Applied Physics, IISc.

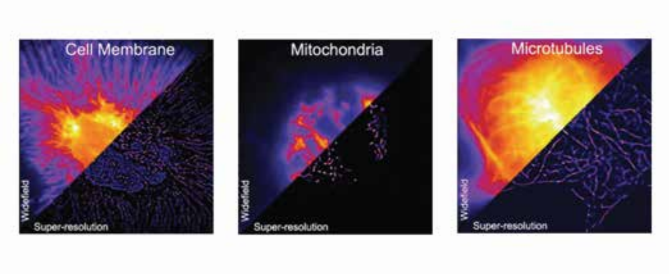


Image courtesy: Deepak Nair

Some examples of images captured using superresolution microscopy

In fact, these fluorophores blink, and using careful imaging techniques, one can figure out how many photons are being emitted by the molecule as well as the location of the blinks. Plugging this data into a mathematical formula enables one to get the centroid and size (enabling precision in localisation) of the blinking molecule. "At this stage," Partha remarks, "you are playing at the level of single molecules."

Partha's lab has worked on developing multiple superresolution techniques. Some examples are POSSIBLE (Probabilistic Optically-Selective Single Molecule Imaging Based Localisation Encoded) superresolution microscopy, which allows for resolving objects less than 10 nm in size, and SMILE (Simultaneous Multiplane Imaging-based Localisation Encoded) microscopy which allows for scanning the entire volume of a cell.

Another method for increasing resolution is a technique called DNA-PAINT, used by Mahipal Ganji, Assistant Professor at the Department of Biochemistry, IISc. "Our lab looks at the organisation of DNA in the cell," he explains. "The molecule is two metres long and compressed into a small volume. We look at events happening within this volume using DNA-PAINT."

DNA-PAINT works on the principle that two complementary DNA strands – constructed synthetically – will bind with each other. This binding is short-lived at room temperature, causing them to bind and unbind randomly. Mahipal and his team typically attach one DNA molecule to the protein they wish to study and later add a fluorophore-conjugated DNA molecule to the solution in which the cell is being imaged. Every time the fluorophore-conjugated DNA binds to its partner, a small flash of light appears as the attached fluorophore emits fluorescence. "This results in blinking," continues Mahipal, "which is essential to a lot of superresolution microscopy techniques."

One advantage of this technique is that the fluorophores do not "photobleach". In most types of fluorescence microscopy, the repeated activation of the same fluorophore makes it no longer fluoresce after a point. In DNA-PAINT, since the binding of fluorophore-conjugated DNA is completely random – the same molecule is not necessarily involved each time – the chances of photobleaching are low.

Unfortunately, DNA-PAINT imaging times tend to be very long. "It is not yet practical to use this technique on live cells," concedes Mahipal. "But the advantage is that once we're done with one protein, we can wash the fluorophores off and add a different strand of DNA which binds to another protein attached with corresponding partner DNA." Since the proteins are being imaged sequentially, one can use the same fluorophore for each protein. "We can add an imager for a protein, image it, then wash it off, and repeat this for as many proteins as we have prepared the cell for."

This is in stark contrast to most other techniques in which researchers must attach a different fluorophore emitting light at a different wavelength to each protein of interest. "You can only image around 2-3 different proteins in the conventional way, because that is the number of unique fluorophores you can practically image together," says Mahipal. "In contrast, DNA-PAINT can potentially image hundreds of proteins sequentially."

Mahipal uses a kind of microscope called a total internal reflection fluorescence (TIRF) microscope to perform DNA-PAINT. It works on the principle that light which hits glass at a particular angle does not get refracted at all, but gets completely reflected. The point at which light hits the glass produces an 'evanescent wave', an electromagnetic wave that remains localised at the point it is produced. This evanescent wave then goes on to excite fluorophores at the surface of the cell.

The same kind of microscope is also used by Rahul. "We employ TIRF or a light-sheet based method called HILO (Highly Inclined Illumination) to track single molecules," he explains. These methods allow a high signal-to-noise ratio during imaging of single molecules, and therefore enable capturing their motion in real-time. Rahul's lab uses it to examine the way in which molecules assemble into complexes by themselves.

Another technique he uses is single molecule Fluorescence Resonance Energy Transfer (smFRET) to study protein shapes and their interactions with each other. This technique involves a donor and an acceptor fluorophore. When the two fluorophores are very close to each other, the donor transfers energy to the acceptor, causing the acceptor to fluoresce. "This technique allows us to measure extremely short distances of around 1-10 nm, making this a very precise way of measuring interactions. So if two molecules come together to form a complex, this technique will report that."

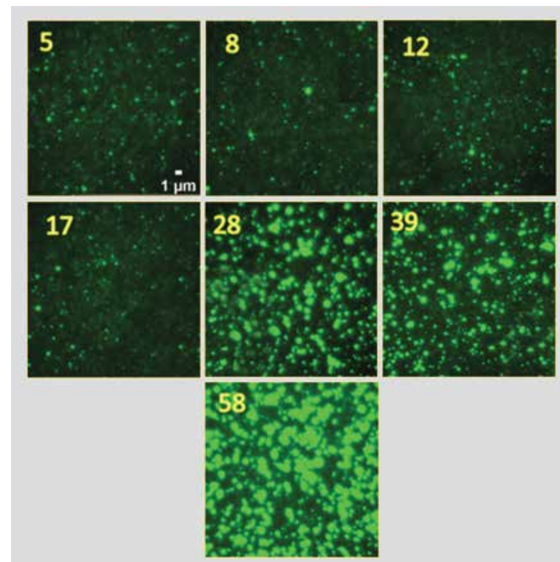


Image courtesy: Rahul Roy

Visualising assembly of lipid bilayer membrane at different times, indicated in minutes

"You can gain an unprecedented level of insight into the function of a cell through such techniques," explains Deepak. His lab works on understanding the organisation of neural synapses in the brain at extremely fine resolutions. They have built a modular microscope which allows them to perform different operations by merely switching out some parts. It is capable of being used for superresolution microscopy as well as other advanced techniques such as single-molecule tracking, optogenetics, and Fluorescence Recovery After Photobleaching (FRAP).

There are various other methods of getting to superresolution as well. "The past decade or so was the time of confocal microscopy," says Partha. "But the future is all superresolution and light sheet microscopy techniques."

Sheets of light

Despite being powerful techniques, confocal microscopy and superresolution microscopy have a major flaw: they tend to scan a plane point by point. This is often too slow to follow events happening in a live cell.

Light-sheet microscopy tries to solve this problem by illuminating an entire plane of light at once. "The illumination can be a rod or a lattice, depending on how the microscope is constructed," explains Rahul. "Either way, you image much more than one point at a time."

Partha's lab has worked extensively on light-sheet microscopy techniques. "The real advantage of light-sheets," he states, "is that you get amazing temporal resolution. Since a plane isn't being scanned point by point, you can get very good images at very short time intervals."

"Light-sheet microscopy also has a great advantage in areas where you wish to image a wide field of view at resolutions near the diffraction limit," he adds. "One can work with large samples such as zebrafish and *C. elegans*."

In 2013, Partha's lab demonstrated an integrated light-sheet imaging and flow-based enquiry (iLIFE) system. "We were able to integrate light sheets into microfluidic devices to carry out imaging cytometry," he says. "The channels in a microfluidic device are only wide enough for a single cell or organism (such as *C. elegans*) to flow through. The iLIFE system is able to scan them as they flow through, allowing the interrogation of a large population of cells. This is something which has never been done before."

Photon machine gunning

Some questions, however, require slightly different types of tools to answer. "Our lab is interested in understanding how information is stored in the brain," says Balaji Jayaprakash, faculty member at the Centre for Neuroscience, IISc.

His lab performs experiments on mice and track neuronal activity in the live brain. The typical tool at hand for such studies is the venerable MRI. "[However], the resolution we require is at an altogether different level," he explains. "We study synapses, which are of the order of microns. MRIs have a resolution of a few millimetres."

Which is why they use a technique called two-photon microscopy. "We open a window on the mouse's skull and image their brains," he continues. "Instead of using a photon with the exact energy needed to excite a fluorophore, we use two photons with half the energy required for excitation."

The realisation of this technique in practice was enabled by the development of ultrafast lasers which send a large burst of photons at once, like machine gun fire. This is key to building such microscopes, because the photons have to strike the fluorophore very quickly for the required energy transfer to take place.

The advantage of using low-energy photons is that they have greater penetrating power. For example, brains, when seen under the microscope, appear white, because the cells scatter all incident visible light. But infrared rays, which have lower energy than visible light, can penetrate some distance into a mouse's brain. This allows for the excitation of fluorophores at a greater depth. "The microscope we have built can image at depths up to 1 mm, and a few more adaptions can reach 1.5 mm," says Balaji.

Balaji explains that the microscope has enabled them to come up with a new kind of plasticity mechanism for how the brain integrates new memories. "Traditional explanations for memory formation focus either on the generation or the strengthening of synapses. We have been able to see that there is another mode for information storage: spatial rearrangement of synapses," he says.

Unfortunately, superresolution is not yet possible in multi-photon microscopy. "It is a trade-off," Balaji explains. "If you want to go deeper, you have to sacrifice some resolution. But people are working on it. It might not be here today, but it will come."

The path ahead

"The big thing about microscopy is that it is highly accessible," says Rahul. "Commercially available microscopes are becoming more and more powerful and accessible for researchers. People who work on microscopy also like to make their techniques more user-friendly so as to enable the wider community to benefit."

Deepak concurs. "Ever since the advent of confocal microscopy, the modularity of microscopes has been increasing. You can swap out one module for another depending on the functions you wish to access. This allows people who are not interested in instrumentation *per se* to also use extremely cutting-edge technology for their experiments. [Microscopy] has thus become one of the most democratised techniques in everyday research."

At the same time, the cutting edge of microscopy is also accelerating. Researchers are striving to combine light-sheet and superresolution techniques in a single setup. New reporter molecules are being developed that can tell scientists more than just the location of molecules. Tools to "bar-code" and distinguish individual neurons within a brain are also on the horizon. The advent of artificial intelligence (AI) and machine learning (ML) is transforming the way state-of-the-art microscopes acquire, store and evaluate large data sets.

Such developments will eventually allow instrument limitations to stop being an obstacle. "That truly is the dream," remarks Deepak. "Your work should only be limited by your ambition."

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Brick by Brick

- Sritama Bose

A behind-the-scenes look at the transformation of an empty space into a full-fledged research lab

Mugesh's team in 2015 when the new chemical biology lab was coming up

Setting up a new lab can be an exhilarating episode in the career of a faculty member. But it can also be a long and arduous journey, one that needs fellow travellers — often this caravan includes graduate students, research assistants, postdoctoral fellows, and other lab members.

All faculty members, particularly those doing experimental research, have to set up a new lab at the start of their careers. But some have to do it again later in their careers if the focus of their research changes or broadens.

The research agenda of Govindasamy Mugesh, Professor at the Department of Inorganic and Physical Chemistry (IPC), took such a turn a decade ago. The scope of his research was expanding into the discipline of chemical biology. Though he had a fully functional chemistry lab, a complementary biology lab had to be built from scratch.

The inception

Mugesh joined IISc in 2002. In the early years of his research career, though he was pursuing chemistry projects related to biological systems, he had no plans to set up a biology lab. "[But] as we progressed, we realised that to address a problem in biology, we need to apply our knowledge of chemistry and work with real biological systems. That is when we first thought of having our own chemical biology lab," he recalls.

"In 2008, we started by making a small cell culture room within our existing chemistry lab," says Mugesh. The intention at that time was to work with seleno-proteins — proteins containing selenium — which are difficult to obtain. Until then, the group had been working with small synthetic molecules containing selenium. Now, he wanted to study actual proteins. To do so, he and his team had to culture bacteria in the lab and engineer them to make seleno-proteins.

Photo: Manoj Sudhakaran

But soon, it became clear to Mugesh that he was constrained by the lack of infrastructure to make any meaningful headway in chemical biology research. "Since IPC did not have any extra space, I approached Prof Balaram, the then Director of IISc in 2011. He asked me to send a proposal of what work we intend to do." Fortunately, at around the same time, the Biochemistry Department was shifting to the new Biological Sciences building. After studying Mugesh's proposal, Balaram suggested that he could use one of the empty labs in the old Biochemistry building. By 2012, the new lab space was ready and the cell culture facility was shifted here. This was also the time I started working in the lab and had the opportunity to see an empty room transform into a fully functional, well-equipped biology lab.

The journey

However, in order to get there, Mugesh first needed funds to buy some basic equipment. "Biology work requires more funding as compared to chemistry [research]," he explains. The funds he had obtained for his chemistry research were grossly inadequate. So he had to raise money, but for Mugesh, the challenge was even greater. "Ours was neither a biology lab, nor did we have any facility in our department to carry out major biology work — it was difficult to convince funding agencies that we would be able to carry out what we propose," he says. But soon they started getting small grants from various sources — some from government agencies and some from industry. "Slowly the lab was being built," recalls Mugesh.

Another hurdle was finding students who could carry out biological experiments. Surendar Reddy Jakka, a graduate student and chemist by training, was the first to venture into the world of biological research. He visited a few labs in the Biological Sciences Division to learn new skills. By 2014, a couple of more members joined the biology bandwagon, but they too were chemists. It seemed impossible to convince trained biologists to work with chemists in a department which barely had infrastructure to do biology.

And what's more, even if students with a biology background wanted to work in the lab, they had to first get through the PhD interviews in IPC — not easy for a biology student to crack. "I realised that doing high quality chemical biology will be difficult with only chemistry students, and without having expertise in biology," says Mugesh. So he started looking for opportunities to work with hardcore biology labs. "We collaborated with Prof Patrick D'Silva's lab in the Department of Biochemistry, and Prof Amit Singh's lab in the Centre for Infectious Disease Research (CIDR)."

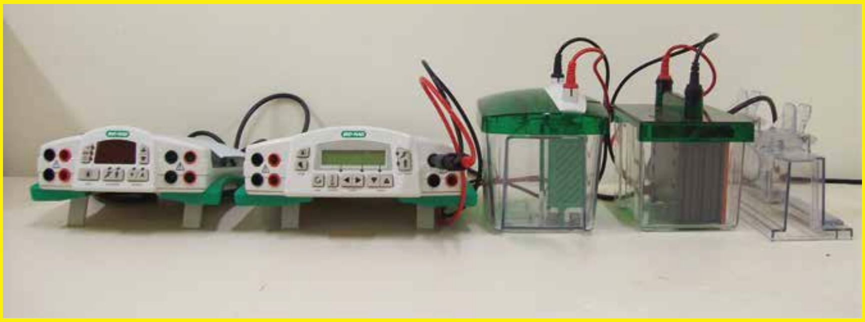


Photo courtesy: Mugesh lab

Some of the instruments from the first set procured in 2008

Changing fortunes

In 2015, Sharath BN, who had a Master's in biology, applied for a PhD in IISc and qualified for the interview. All aspiring PhD candidates are allowed to appear for an interview in three departments. Having chosen the Biochemistry Department and Molecular Biophysics Unit as his top two preferences, he was searching for a third department at which to interview, when he stumbled upon the webpage of Mugesh's group. He was intrigued and so selected IPC as his third choice. A few days before the interview, he met with Mugesh to learn about ongoing projects in chemical biology. "He attended the interview and the [interview] committee found him suitable," says Mugesh. An offer was made to Sharath, which he accepted. "I had offers from a few other good institutes, but I joined here because I found the work very interesting. Many people discouraged me from joining a chemistry group, but I took a chance," says Sharath.

By 2015, the biology lab became reasonably functional. In addition to having a graduate student with a biology background, the rest of the team was also well-trained in cell biology techniques by then. At around this time, the collaborations with other biology groups also began yielding results.

It was then that Mugesh decided to take a chance and embark on creating a full-fledged chemical biology lab. He, along with Sandeep M Eswarappa, Associate Professor at the Department of Biochemistry, submitted a joint proposal for a Science and Engineering Research Board grant to the Department of Science and Technology, Government of India. "After an elaborate peer review, within India and abroad, our project was accepted. We got significant funding for five years — generally funds are given for three years. This gave a huge boost and allowed us to establish a biology lab for studying endothelial dysfunction [a type of coronary artery disease]," says Mugesh about the pay-offs of his decision to apply for a grant, appropriately called the High-Risk High-Reward Grant.


Photo courtesy: IISc Archives

The old Biochemistry building where the new lab was set up

There was more good news. Mary Sarkar, a project assistant with more than 30 years of experience, joined the lab and took over the responsibility of maintaining the cell culture facility. "We bought new cell lines and started culturing them. With time, we added many types of cell lines. The challenge was to maintain the sterility and quality of the cell lines. We also started isolating cells from mammalian tissue — these are primary cell culture," says Mary.

Mugesh was pleased with the progress. "I think we got the right people." His vision of having a team of chemists and biologists was coming true. They started working on biologically important problems: the molecular mechanisms underlying disease conditions like endothelial dysfunction, neurodegeneration, and cardiac complications.

Mugesh illustrates the kind of questions his team began addressing with the example of their research on a class of molecules found in living cells known as reactive oxygen species (ROS). These molecules have both beneficial as well as harmful effects. It is therefore important that their levels are regulated. The crucial task of scavenging for excess ROS is performed by proteins known as antioxidant enzymes. The chemists in the group have synthesised antioxidant enzymes for the study. "We are looking at the molecular level mechanism of what roles ROS play during a pathological condition, say in neurodegeneration, and whether we can use our artificial enzymes to regulate the level of ROS in such cells," elaborates Mugesh.

Other pressures

But the journey to establish a new lab and research agenda has been far from easy. Besides the sweat and tears that went into raising money and building a new lab, there were several other emotionally taxing challenges lab members had to deal with.

For one, building the new biology lab required time. But time is also of essence for PhD students. The pressure of the ticking clock started mounting. They also encountered difficulties in executing experiments. At times, the experiments yielded counter-intuitive results. Because they spent a considerable amount of their time helping set up the new lab, these setbacks often felt overwhelming. As Surendar recalls, "All of it took more time than usual, but [my] scepticism started when I encountered failures in experiments. I started worrying about how I will finish my PhD, or whether I will finish it at all."

Sharath, a biologist pursuing his PhD from a chemistry lab, had a different concern, one that continues to bother him. "In India, at many places we still have a very traditional mindset. Most jobs seek subject specialists, and someone from an interdisciplinary background may not fit into either of the areas," fears Sharath.

Yet another aspect of research that the interdisciplinary group had to work on was to improve communication between the chemists and biologists. "The key to a successful interdisciplinary work is constant communication between people working on each aspect. Both should share knowledge, and both should respect and learn from each other," points out Vijayakumar Govindaraj, a biologist who is a senior postdoctoral researcher in the lab.

Fruits of labour

Nevertheless, the toil of setting up the biology lab, in spite of all the hurdles and setbacks, has paid rich dividends. There are several interdisciplinary projects in chemical biology underway and multiple important papers have already been published.

Mugesh elaborates on why he believes his lab has tasted success in just a few short years: "We decide the specific biological problem we want to address, then think back to identify what type of molecules will help us address it and make those. Even if the biology experiments do not produce expected results, they help gain insights — something the chemistry wing then uses to modify or redesign the molecules."

Surendar too credits the group's success to the nature of research it pursues. "We may not always get the results we wish for, but still there are many other clues." He believes that having expertise in both chemistry and biology allows them to explore such clues easily leading to novel findings.

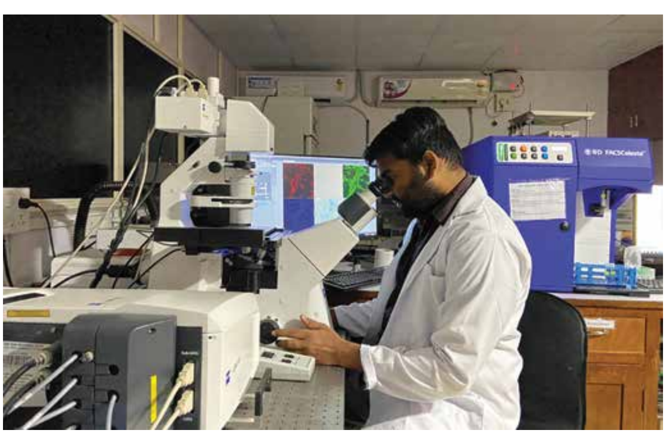


Photo: Ekta Chauhan

Sharath BN, a PhD student, using a confocal fluorescence microscope in the new chemical biology lab

Surendar's point is highlighted by a discovery made by the team in 2018. Researchers in the group observed how a simple chemical modification enhanced the cellular uptake of a species of small synthetic molecules. Surendar, who knew how to make bacteria express non-natural proteins, immediately decided to apply the idea to a biological system. He was able to induce the expression of a modified green fluorescent protein (GFP) by bacteria. The chemically modified GFP, unlike the wild type, could enter cells.

Sharath identifies yet another reason for the success of the team: having their own biology lab helps overcome some practical limitations associated with collaborating with another lab. "Doing biology work is both money and human resource intensive. Thus, if we approach another lab for collaboration, even if they are interested, they may not always have the resources to start working on our project immediately, leading to delay," he argues.

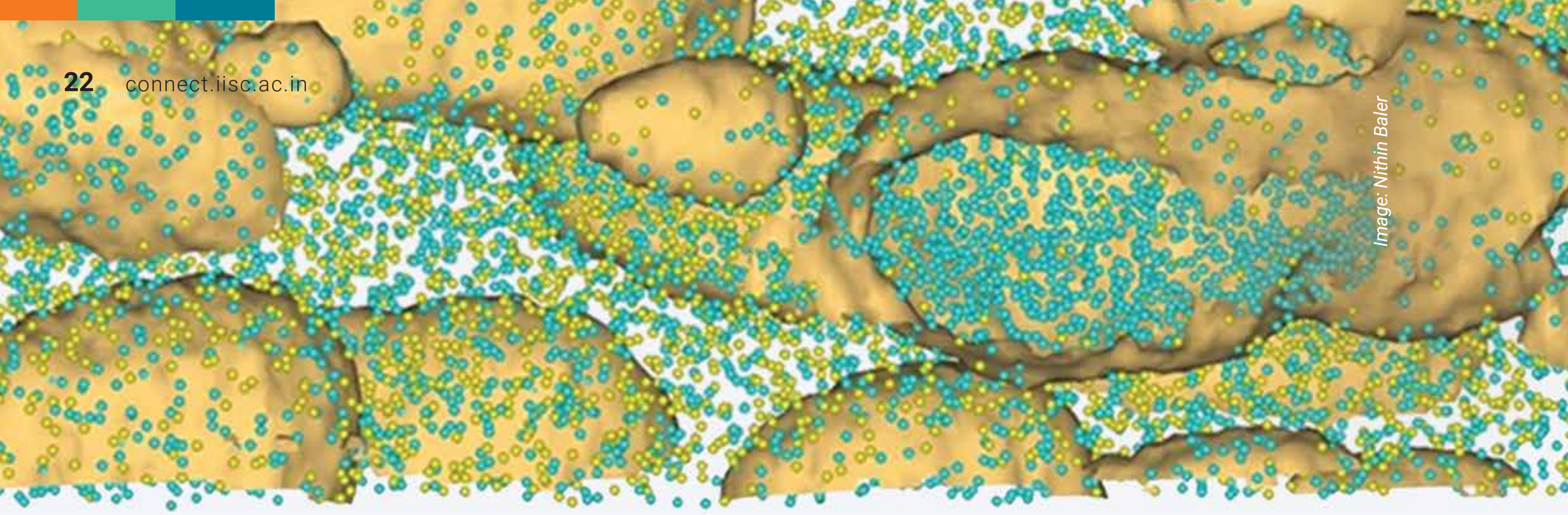
There have been other personal rewards for those who have been part of the journey. The biggest of them is experiencing the excitement of discovery, especially in a new field of scientific inquiry. "I get immense joy while exploring something new — I feel like I am the first person in this world observing such a phenomenon occurring in nature," Surendar says. "I got a lot of freedom to explore and come up with new ideas. This is how I envisioned doing research — this has made me confident and courageous," adds Sharath, who cherishes the unconventional career choice he made.

Lessons learnt

My inexperienced younger self used to harbour a misconception — all it takes to achieve a worthy scientific feat is a brilliant idea. When I read or heard a success story of scientific research, little did I realise that the *scientific* pursuits of curiosity, knowledge, creativity, or innovation are mostly built on a strong foundation of relatively *not-so-scientific* endeavours. These include procuring infrastructure, arranging funds, training people, and maintaining a functional laboratory. A good scientific publication is like the tip of an iceberg. But there is a lot of 'not-so-scientific' work that goes on behind the scenes in order to publish in a good quality journal, much like the big chunk of the iceberg that is hidden from our view.

My experience has taught me yet another important lesson. Some researchers may have been wary of spending time and energy to deal with the practical concerns of establishing new cross-disciplinary research projects. This, in their view, may come at the cost of keeping up with the fast pace of scientific publications, meeting the conventional standards of success in research, or future professional prospects. I learnt that all of these concerns are entirely legitimate. But I also learnt that all scientists have to make their own judgement call in these situations, one which will decide the course of their journey.

Sritama Bose completed her PhD at IPC in 2021 and was a science writing intern at the Office of Communications, IISc



Building alloys

Expanding the Material-verse

- Karthika Kaveri Maiappan

Researchers at IISc are using novel technologies to add to existing materials and to understand material properties

About 2.5 million years ago, our ancestors discovered that striking two pieces of rock against each other produces rough edges and stone chips that could be used to break animal bones and scoop flesh off carcasses. And thus, the first stone tools were made. But it was no mean task to shape them, especially as they became more sophisticated over time. It was only around 12,000 years ago that humans started to make tools with metals that could be heated and moulded with relative ease. The first metal tools were made from shiny copper bits found on riverbeds. Years later, humans discovered that mixing copper with tin makes for stronger tools. This marked the dawn of the Bronze Age; humans had now learnt the art of metal-working and alloying. The Bronze Age was followed by the Iron Age, which lasted until about 2,000 years ago. Each of these new technologies transformed our lives and are milestones in human history.

In the past few centuries, new materials have continued to shape the course of our progress. Thanks to modern materials like iron, steel, silicon, and plastics, descendants of hunter-gatherers now shop for groceries in supermarkets carrying smartphones and designer bags. The 21st century is again seeing a revolution, as researchers across the globe are in pursuit of novel materials for various applications using state-of-the-art technology.

Building new blends

Unlike in the past, the approach to developing new materials in the modern age is much more scientific. Among new materials, alloys are of particular interest because they find uses in areas as diverse as construction, transportation, defence, and energy. Researchers design new alloys by selecting elements and blending together based on their crystal structures and phase diagrams, according to Surendra Kumar Makineni, Assistant Professor at the Department of Materials Engineering, IISc. While the crystal structure describes the arrangement of atoms in a definite pattern, the phase diagrams are a graphical representation of the 'phases' or state of an alloy at different temperatures and compositions. The type of phases dictates alloy properties, and phase diagrams help researchers to find the compositions that yield desired properties.

Surendra's group works on the synthesis of new alloys for structural and high-temperature applications, like *superalloys* for gas turbines. Gas turbines provide thrust to aircraft by igniting fuel within them; as a result, temperatures within it could be as high as 1500°C. "The higher the operating temperature, the higher the operation yield," explains Surendra. Developing materials that can withstand high temperatures would enable us to improve the fuel efficiency – or how far the aircraft can travel per unit of fuel – of aircraft engines and reduce greenhouse gas emissions.

Traditionally, nickel-based alloys have been used in turbines because they are stable at high temperatures owing to their unique two-phase structure. But they contain dense and less abundant elements which are heavy and expensive. Surendra's lab is, therefore, working towards reducing dense elements without compromising the alloys' high-temperature properties.

During his PhD at IISc, Surendra also helped develop a new class of low-density cobalt-based alloys. The advantage of cobalt is that it has a melting point that is higher than nickel by 40°C and can form a two-phase structure similar to that of nickel-based alloys, he points out. "We have shown that some of the [cobalt-based] alloys have better properties than nickel-based ones," he says, making them an attractive option for building turbine components. His group is also exploring ways to increase their performance at higher temperatures by adding other elements.

Modelling material properties

In 2011, the then US President Barack Obama launched the Materials Genome Initiative (MGI), with an aim to accelerate the discovery and development of new materials at lower costs. This provided a major thrust to the field of computational materials sciences, according to Abhishek Singh, Professor at the Materials Research Centre, IISc.

Abhishek's lab specialises in using machine learning tools to advance materials science and development. These tools help develop new materials faster, according to him. "When you search for a new material with traditional science, it will take you 20 to 30 years. Now, you can do it in one to two years for database development, and another six months of model development. Nowadays, there are many databases already [available]; so you could use them directly," he says.

Machine learning is particularly useful for correlating material properties that are not connected through underlying theory, or connecting experimental data to material properties – an application Abhishek's group has been exploring. They recently developed a model that predicts the hardness of a superalloy using scanning electron microscope (SEM) images. This would greatly reduce the time and cost required to experimentally develop the alloy and determine its hardness, which would enable experimentalists to test alloys for various applications easily.

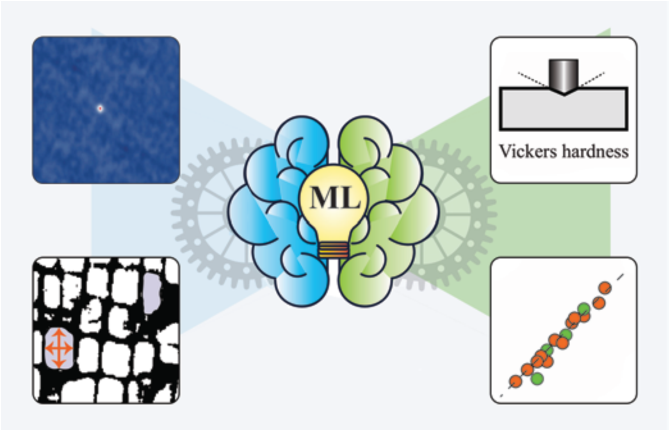


Image: Abhishek Singh lab

Mapping of microscopic images for prediction of Vickers hardness in superalloys using machine learning

Abhishek and his group reduced SEM images to binary data, and processed this data using statistical tools to choose only those 'features' or image parameters that were sufficient to encapsulate the data accurately. These features, along with material composition and information regarding material processing, were used to generate a model that could predict the hardness of the material. They also developed a second model using geometrical attributes of the materials extracted from the SEM images and processing information and found that the hardness predicted by both these models was very similar. These models for predicting hardness can be extended to any material, says Abhishek. His lab now has ambitious plans for this in the near future. "[We are working on] an app [where] if you upload your SEM image and give the compositions of your alloys and some processing information, it will predict the hardness for you from these two approaches," he spells out.

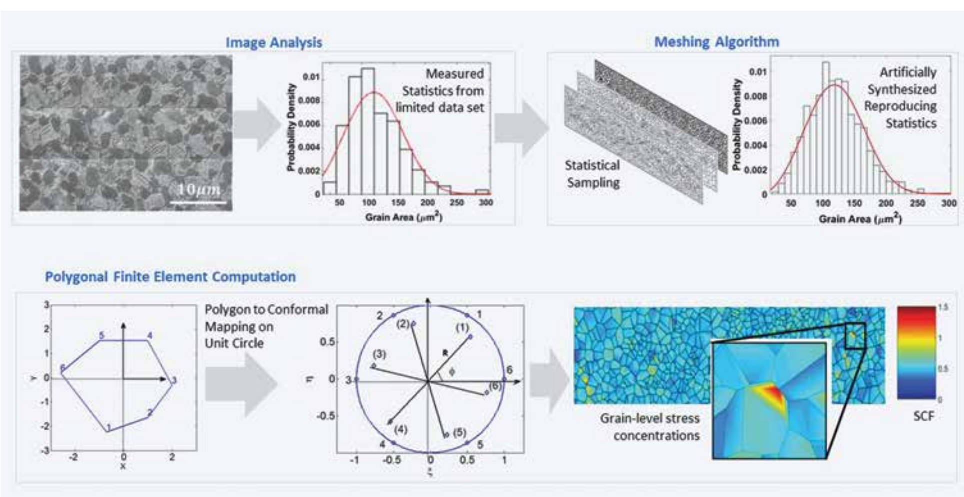
Little things matter

Often, designing materials for engineering applications requires researchers to understand how events at a molecular or crystal level contribute to the properties of the whole material, and this cannot be done using experimental methods. This gap can be bridged using a suitable modelling approach, according to Debiprosad Roy Mahapatra, Associate

Professor at the Department of Aerospace Engineering, IISc. His group recently modelled material microstructures – material structures that appear at a small scale – to help predict mechanical and fracture-related properties of bulk materials.

Since metal surfaces appear uniform to the naked eye, it is easy to assume that they show similar properties along different directions; yet, when exposed to a load, cracks appear at specific locations and in different directions. It is often difficult to predict when and where they will initiate, and in which direction they will grow, but this information is hidden in material microstructures, says Debiprosad. SEM images of metals reveal crystals in different orientations – or 'grains' – and their boundaries; some of these crystals have defects, and these defects tend to arrange themselves along certain planes in the material. This can create excessive stresses in certain regions when loaded, leading to material failure along certain directions, he explains.

Image: Mahapatra lab



Modelling material microstructures

With the help of SEM images, Debiprosad and his team determined the probability distributions of certain parameters like grain size by analysing different regions of metals, like in titanium alloys used in aerospace applications. Using these, they synthetically created an artificial mesh that simulated the original image. They then used a mathematical technique – the polygonal finite element method – to model the grains and grain boundaries accurately in order to predict crucial properties of the material. They computed the stress concentrations at different regions of the mesh, and were able to predict where cracks are more likely to develop in the material. "Further work is in progress where we are linking this information to molecular dynamics. We hope to be able to predict molecular level fatigue nucleation sites from this information," Debiprosad says.

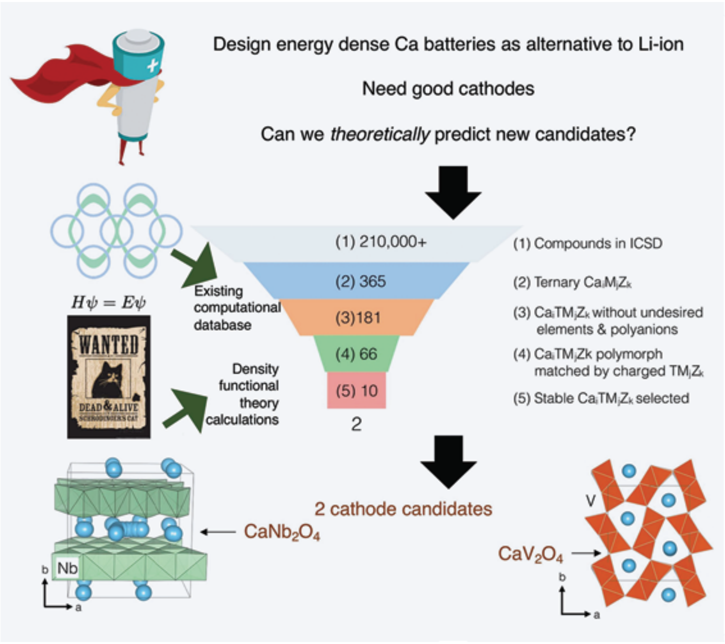
'Transition'ing to efficient

Lithium-ion batteries have wide-ranging applications in devices like mobile phones, and in electric vehicles. These batteries are powered by the flow of lithium ions from the negatively charged electrode (the anode, typically graphite) to the positively charged cathode through a liquid electrolyte. However, with this architecture, we are approaching the limits on the energy that can be stored per unit mass or volume of the cell – or its energy density – says Sai Gautham Gopalakrishnan, Assistant Professor at the Department of Materials Engineering, IISc. "If we can improve the energy density, we can use our batteries for longer; this could make our portable electronics last longer, and increase the driving range for electric vehicles," he suggests. The promise of more efficient batteries drives his interest in exploring calcium-based batteries as possible alternatives to lithium-based ones.

Calcium batteries offer several advantages as compared to lithium ones; unlike the latter, which have graphite-based anodes, calcium batteries can use metal anodes. "Graphite occupies a lot of space, and it's dead-weight; it doesn't contribute to the electrochemical process. It's just a place to store lithium, because metallic lithium is very reactive," Sai explains. He argues that replacing the anode with a metal would improve the energy density of the cell. Calcium is also much more abundant as compared to lithium, and has similar electrochemical properties. Calcium, therefore, promises to be an attractive replacement for lithium in batteries.

Sai and his team recently adopted a computational approach to identify candidates to serve as cathodes in calcium batteries. "The approach that we take is what I call the Iron Man approach; Iron Man basically runs simulations on J.A.R.V.I.S., which is his AI, and he comes up with [new] things. So that's the approach we want to take. We don't want to necessarily go into the lab to find a new candidate, but run calculations and simulations and be able to robustly predict new candidates," says Sai. This helps reduce the time to innovate, and allows researchers to test a large number of materials, he adds.

Image: Gopalakrishnan lab



Screening process for identifying cathode materials

The team screened for materials across all possible three-element systems with calcium – compounds composed of calcium, another redox-active transition metal, and an element from the oxygen series as a counter-ion. They found that only ten candidates were thermodynamically stable, and could potentially function as cathode materials. They then calculated some essential parameters that would govern the energy density and power of the battery, and zeroed in on two compounds, namely calcium vanadium oxide and calcium niobium oxide, that would make good cathode materials. "This is how screening studies work; there is some chemical intuition, some prior work that you use, and the new work you add to find new candidates," says Sai.

Abhishek's lab is also involved in developing better thermoelectric materials – those that can convert waste heat to voltage – for more efficient energy generation. Recently, they developed a model that correlated thermal transport and electronic transport in a lattice, properties that were hitherto considered unconnected. "Electronic transport is much easier to calculate; we can do it in five to twenty minutes. But if you want to calculate the thermal conductivity of the material, it can take you one week easily," he says. "Using electronic transport, now we can calculate the thermal transport easily." This would be especially beneficial for computing some properties of thermoelectric materials which require both these parameters, and could accelerate the pace at which new thermoelectrics are discovered.

Abhishek is also interested in a class of transition metal-based compounds known as MXenes – these are two-dimensional transition metal carbides or nitrides that are popular candidates for making batteries and sensors. His group developed "aNANt", India's first computational database for materials, with electronic and structural properties of nearly 25,000 MXenes in 2018. This could help researchers develop models for various applications, and help experimentalists pick the right materials for their specific applications, according to him.

Not all a bed of roses

Using computational tools and modelling to develop materials is not without limitations. Abhishek believes that the lack of high-quality reproducible data remains the biggest challenge in applying machine learning to the field of materials design. It is extremely important that we develop the infrastructure required to document and share the massive amount of data generated across the world, he says.

Moreover, the theoretical framework used for calculations at times comes with its own challenges. For instance, Sai's group uses the density functional theory, a well-known quantum mechanical computational method, for their calculations. It is used to obtain an approximate solution to Schrödinger's equation, a partial differential mathematical equation. "When we solve Schrödinger's equation accurately, the properties you get are also very accurate. But here we're solving it approximately; so the properties you get are also approximate, and there are limits to this approximation," he admits. This theory is also scalable only for systems with a few hundred atoms, making it harder to study properties that emerge at a larger length scale. Moreover, knowing the properties of materials at the molecular level is even more challenging due to the quantum mechanical effects involved, adds Debiprosad. "If one really has to solve this problem, one would probably need quantum computers," he adds, underscoring the importance of coupling quantum computing with solid mechanics for advancing computational materials science in the future.

In spite of these constraints, researchers across the globe continue to expand their toolkit with more powerful and multidisciplinary approaches, and we may very well be witnessing the green shoots of the next materials revolution. From discovering transformational materials once every few centuries or even millennia, we are now in a position to develop such materials in just a matter of months.

Karthika Kaveri Maiappan is a Master of Science student and a former science writing intern at the Office of Communications, IISc

Photo: Subash Chandra NS

A MINI FOREST IN AN URBAN JUNGLE

- Joel P Joseph

A panoramic view of the old CES building and the location of the mini-forest shot at the Silver Oak Marg in IISc

In the heart of Bangalore, a city known for its beautiful gardens and majestic trees – now dwindling – lies the lush green campus of IISc. Within it is a small patch of unmanicured woods, populated by over 49 tree species, many of them from the Western Ghats, besides several animals, including a variety of birds, butterflies, reptiles and primates.

The origin of this woodland, popularly known as the *mini-forest*, dates back to 1985 when CNR Rao assumed office as the Director of the Institute and Madhav Gadgil was the Convenor of the Centre for Ecological Sciences (CES), established in 1983.

Before the beginning

For a few years then, Madhav, who was initially part of the Centre for Theoretical Studies at IISc, and his colleagues had been studying the ecology of the Western Ghats. He ran a field station in Dandeli, which was shifted to Sirsi, also in the Uttara Kannada district of Karnataka, in 1980.

The nursery in the field station had become the centre of a thriving ecodevelopment project. Madhav and others were helping villagers replant the hills with native trees, trying to save the local vegetation that was soon disappearing because of arecanut monocultures.

DM Bhat, then a Scientific Assistant at CES who was working at the field station grew indigenous plant saplings for the revegetation programme with the help of his staff. The saplings from the field station, including bamboo from Dandeli, and plants from the forest department, would eventually make their way into the mini-forest.

From a scrubland to a forest

In 1985, the Institute proposed the construction of two buildings located close to each other: one for CES and another for the Centre for Electronic Design and Technology (now the Department of Electronic Systems Engineering). But Rao insisted that the buildings be spaced apart to make room for some greenery on the campus.

“So, we proposed the idea of planting tree species of the Western Ghats,” says TV Ramachandra, a Scientific Officer at CES, who heads the Energy and Wetlands Research Group. The Institute allocated a 1.75-hectare plot right opposite the place where the CES building was to come up. Ramachandra, along with CJ Saldanha, a Professor at CES, and Madhav implemented the project. Two workers, Venkatiah and Venkatalakshmi, helpers at CES, watered the plants and removed the weeds in the initial stages. Raghavendra Rao and Manjunath, field assistants at CES, Venkatappa, Mechanic, and Murugeshachar, helper, fenced off the area and monitored it.

During the implementation of the project, there was one mishap. "Regretfully, it [the mini-forest] has some admixture of exotics because one of the daily wage workers in the nursery, without checking with us, brought some exotics from the forest department's nursery, where the husband of a friend of hers was employed," Madhav recollects.

In addition to its primary goal of preserving the green cover on the campus, the mini-forest was planted to understand important questions about ecological dynamics: how adaptable are rainforest trees in a novel habitat and what is the nature of the relationships they develop in the new environment? The performance of these trees was monitored for 23 years and was reported in a research paper authored by Sankara Rao (a retired professor from the Biochemistry Department now in charge of the CES herbarium), along with CES researchers Harish Bhat, Varsha Kulkarni and Ramachandra.

The mini-forest, according to its authors, has been a successful experiment, one which showed that many plant species from wet evergreen forests can survive and thrive in a foreign habitat. As Rao and his colleagues put it in their paper, the trees grew "as good as they would in their native habitat" despite the difference in the annual rainfall.

Photo courtesy: TV Ramachandra

Venkatiah and Venkatalakshmi, helpers at CES, planting saplings in the mini-forest in 1988

The gigantic climber, *Entada rheedei* Spreng, planted opposite the mini-forest, in front of the old CES building at the Silver Oak Marg, stands as a great testimony to this. The liana, which is extremely difficult to grow in a habitat other than its natural one, has flourished, climbing into the mini-forest across the road.

The mini-forest has had other ecological benefits. In the same paper, the authors reported that the mini-forest area was cooler than other parts of the campus by as much as 2°C. It has also helped recharge the groundwater. "The water table at this location was in the range of 60 – 70 m depth before creating the mini-forest. Present monitoring of the water table shows the level of water is at about 3 to 3.5 m below the ground," they write.

Photo courtesy: TV Ramachandra

The gigantic woody climber in front of the old CES building, opposite the mini-forest, at Silver Oak Marg

Conserving urban ecology

In a bustling city like Bangalore, which has lost over 95% of its tree cover to construction projects in the last five decades, the mini-forest is one of the few spaces conserving biodiversity. Such a model of conserving biodiversity in patches that preserve the natural biota spread across the country is far better than just having pockets of wilderness like wildlife sanctuaries and national parks in a few places, explains Madhav. "This is consistent with ecological theories and is rooted in our traditional methods of conservation," he says.

Anindya Sinha, Professor at the National Institute of Advanced Studies (NIAS), who studies behavioural ecology and has always been deeply interested in the flora and fauna of the campus, speaks about the dichotomy of thought associated with urbanisation – of maintaining natural existence before urbanisation vis-à-vis creating aesthetic, green, exotic spaces. "Manicured spaces are impositions on nature," he says. "Such cultivated spaces lose the flora and fauna of the region. But we urbanites have an exclusionary outlook: us as space-makers who assign spaces for species, rather than enabling them to establish their own."

In contrast to this exclusionary view, the mini-forest has become a home for animals that are soon disappearing from the city due to habitat loss. Take for instance the slender loris: a small, nocturnal primate that inhabits this forest. An adult slender loris is about 25 cm long, weighs about 275 g and has large brown eyes with reflective membranes. These animals, who once inhabited the shrubs and bamboos of Bangalore, are now rarely seen.

The mini-forest is now one of the few green covers in the city with a healthy loris population. "I am proud of the mini-forest in that we could demonstrate the conservation of slender loris," Madhav says.

These lorises have also proved helpful in understanding urban ecology, adaptation of wildlife to human habitation, and animal behaviour by researchers like Kaberi Kar Gupta. In 2014, Kaberi, then a Visiting Scientist at CES, founded a citizen science initiative called the *Urban Slender Loris Project* to study the dwindling loris population in urban spaces, a project that continues to this day.

Photo courtesy: TV Ramachandra

A slender loris at the woodland in IISc

Sindhu Radhakrishna, Professor at NIAS, has also spent a lot of her time studying lorises in the mini-forest. Her research has ranged from understanding vocal communication in the lorises to how these shy, nocturnal primates adapt their food habits in new habitats.

In the early 2000s, when she first started studying the lorises on the campus, Sindhu asked people of this part of the city about the last time they spotted a loris. While some described their parents' memories of growing up with lorises, the current generation did not remember them – some had not even heard of them. "I think it correlates with our consistent loss of green patches," Sindhu says. "Only large educational campuses like IISc can still afford to keep these patches of greenery that are crucial for the species that have quietly co-existed alongside us for years. They can continue to exist only because of these small patches."

The butterflies of the mini-forest have also been of interest to ecologists. Nitin Ravikantachari, a PhD candidate at the University of South Carolina in the US, monitored butterflies in Bangalore from 2012 to 2017. This study of seasonal fluctuations in species abundance and diversity brought him to the mini-forest.

"I used to visit the IISc campus and the mini-forest for about three hours every alternate Sunday to monitor butterfly species diversity and abundance," Ravikantachari says. He recalls how Suman Attiwilli, then a PhD student at IISc, showed him the place around the mini-forest. Monitoring these butterflies has helped him learn a lot about their life histories. "This has definitely influenced a lot of the research that I conduct now," he says.

Some of these findings have culminated in a book, *Butterflies of Bengaluru*, which he co-authored with Krushnamegh Kunte, Associate Professor at the National Centre for Biological Sciences (NCBS).

Over the years, the mini-forest has also become a refuge for animals rescued from other places, where their lives would have been under threat. In 2011, Rahmath Ataz, a wildlife enthusiast, helped rescue an ailing slender loris found in the Chamundinagar area of Bangalore. The loris was released into the mini-forest. Ramachandra also mentions that snakes captured at different parts of the campus have been released into the mini-forest.

Inspiring the next generation of ecologists

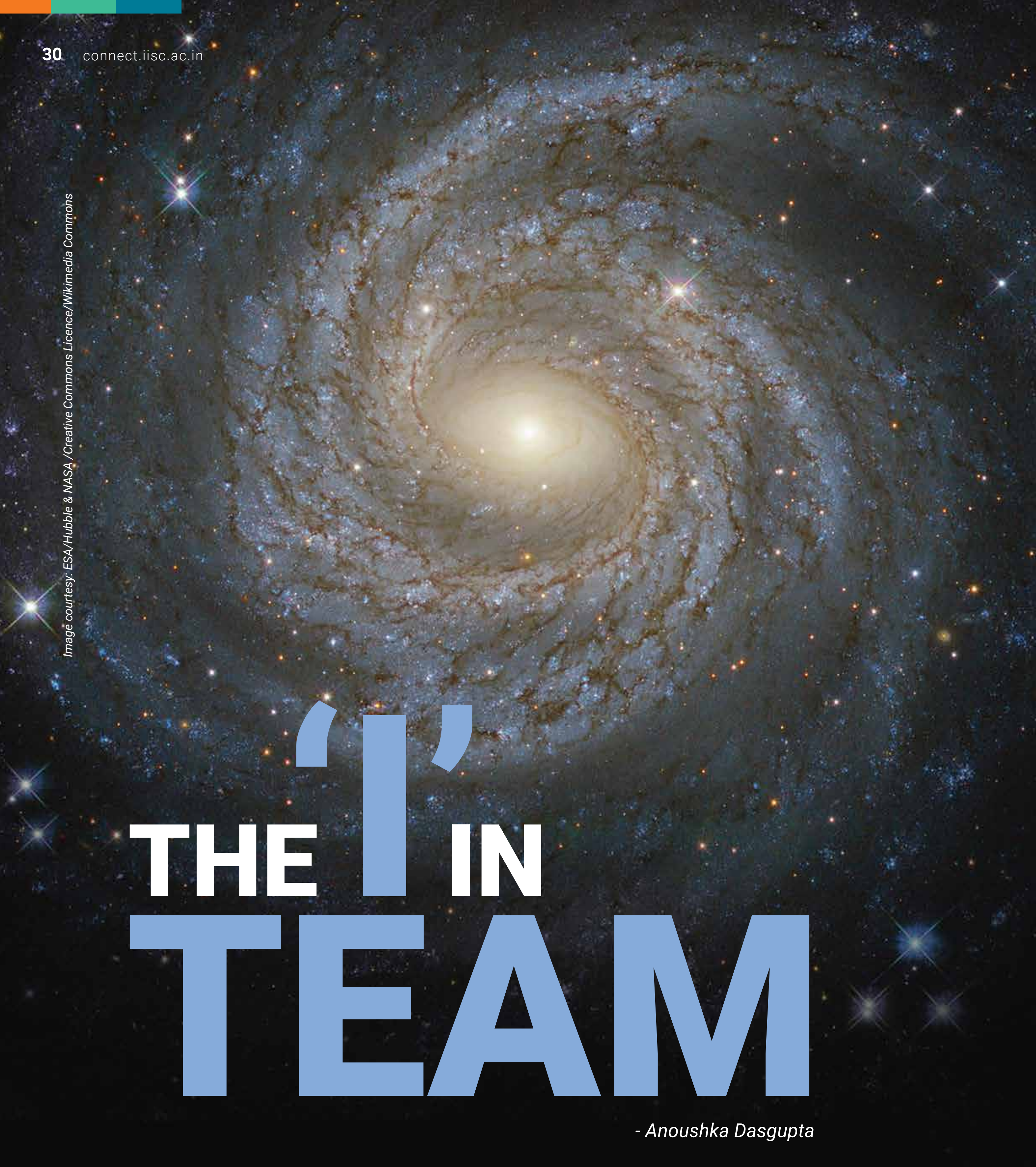
The mini-forest has thus become a source of inspiration for the next generation of ecologists like Nitin.

Photo courtesy: TV Ramachandra

TV Ramachandra working in the mini-forest as his colleagues look on

Ramachandra and his colleagues are making efforts to inspire many more. "We have the environment education program where the school children visit the campus, monitor the biomass of the trees and identify the species," Ramachandra says. In one such programme held on 30 November 2017, a group of school kids planted about 500 saplings of five different varieties of ficus trees in Jubilee Gardens at IISc. He hopes that many more will take it upon themselves to plant more trees.

Joel P Joseph is a PhD student at the Centre for BioSystems Science and Engineering (BSSE), and a former science writing intern at the Office of Communications, IISc



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THE ‘I’ IN TEAM

- *Anoushka Dasgupta*

Self-organisation is the emergence of order in an initially disordered system and is observed from microscopic to astronomical levels

Spiral galaxy NGC 6814

Spiral galaxies. Honey bees. *Proteus mirabilis*, the urinary-tract-infection-causing bacteria. What do they all have in common? A phenomenon called self-organisation. It transcends scale – from the formation of galaxies to the arrangement of lipids in cell membranes. Self-organisation is the phenomenon by which order is established in a system by the co-ordinated action of the smaller members of that system.

Self-organisation – an emergent phenomenon

Self-organisation exists in all fields. Nirupam Roy, Assistant Professor at the Department of Physics, who studies the formation of stars and galaxies, gives the example of the emergence of spiral patterns in galaxies. A galaxy is a collection of stars moving in their own orbits. All these orbits are oriented in a particular way determined by the large-scale gravitational forces among the stars. While the galaxies appear as spirals, the stars themselves aren't arranged in a spiral pattern, as one would assume. Nirupam explains that every star takes a specific amount of time to travel in its orbit. If we consider separate times of revolution and orientations of orbits, then certain regions of the galaxy show higher density of stars at a time, giving it a spiral appearance. The formation of galaxies and their patterns follow a bottom-up or hierarchical approach, with smaller structures, like stars coming together to form larger patterns like spirals and ellipses.

The bottom-up approach is seen even in the regulation of societies of social insects like bees, wasps and ants. Raghavendra Gadagkar, the DST Year of Science Chair Professor at the Centre for Ecological Sciences (CES), has studied social insects for nearly 50 years. He differentiates between the two types of control seen in these insect colonies – bottom-up and top-down. In top-down control, there is one leader who knows how a particular task must be carried out and not only communicates it to the others, but also makes sure that everybody fulfils their role. On the other hand, bottom-up control involves no leader. The tasks of the colony are regulated in a decentralised manner. In his article *More Fun Than Fun: The Exquisite Wax Palace of the Honey Bees*, Raghavendra throws light on how a large number of bees perform simple tasks following basic local rules, ultimately leading to completion of complex tasks like building the hive. This is an example of self-organisation.

Self-organisation leading to collective animal behaviour depends on the balance between the costs and benefits to the members of the system. Vishwesha Guttal, Associate Professor at CES, highlights the case of predators. "While a predator can easily spot groups of prey, and may manage to hunt some individuals, the chance of each individual getting caught reduces as the group grows larger." Community living is advantageous for unicellular organisms too. Varsha Singh, Associate Professor at the Molecular Reproduction, Development and Genetics department works on swarming bacteria. She explains, "If bacteria want to punch holes in a eukaryotic cell, a single bacterium may keep trying to punch holes, yet not succeed. But when they unite, they are more likely to succeed and receive nutrition [and propagate]."

Image credits: Anoushka Dasgupta

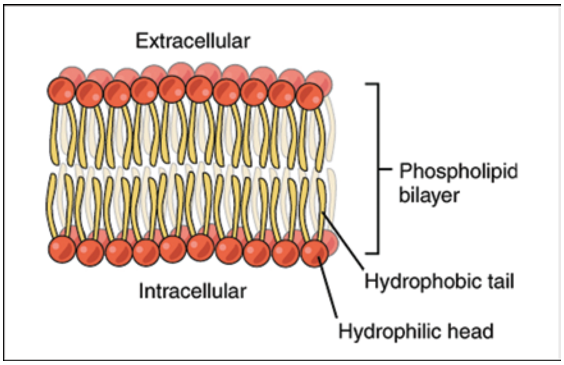
*A paper wasp (*R. marginata*) colony at the Centre for Society and Policy, IISc*

Driving forces behind self-organisation

We know some of the driving forces behind self-organisation in several systems. In social insects, the complexity of the tasks and the cognitive ability of individuals determine whether the top-down or bottom-up approach is used. For example, termites make large, complex mounds. "It's very hard to imagine that a queen termite has a detailed architectural map in her brain, or be able to communicate to the workers exactly what to do. They have tiny brains – the size of a pinhead – but they accomplish very complex tasks," elucidates Raghavendra, concluding that self-organisation is at play in such cases.

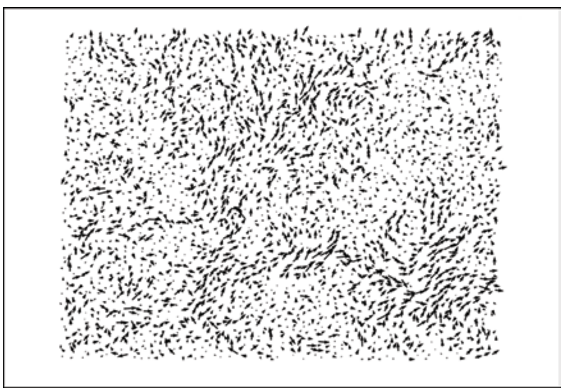
The complexity of the functions to be carried out by certain structures like the plasma membrane also dictates self-organisation. The plasma membrane has more than 800 species of lipids. Lipid molecules are asymmetric, with a distinct water-loving head and a water-repelling tail. Prerna Sharma, Associate Professor at the Department of Physics, who works on membrane biophysics, explains that the tails of lipids are always oriented away from water, and their heads always face water, making the system energetically stable.

Image courtesy: Creative Commons Licence/Wikimedia Commons



The lipid bilayer of the plasma membrane

Image courtesy: Harini Sureshkumar, Molecular Biophysics Unit, IISc



Tracking movements of lipids in a membrane over time using molecular simulations

While this orientation of lipids is uniform, the composition of the species of lipids in different regions of the membrane may vary. "Since there are so many different kinds of lipids, there is also a huge number and types of interactions among them, leading to a complex organisation," describes Anand Srivastava, Assistant Professor at the Molecular Biophysics Unit. This raises questions like what determines the composition and organisation of lipids in the plasma membrane, and how their organisation affects their functions.

Other than the forces that drive self-organisation in complex systems, there are also forces that hold several systems together. At the gargantuan scale of space, stars emerge from dense molecular clouds. "At an intermediate scale, there is an interplay of thermodynamic processes like heating and cooling, which depend on the density and temperature inside the cloud. These in turn are affected by magnetic forces and large-scale gravitational forces," explains Nirupam.

Studying the physics behind self-organisation

Lipids are the building blocks of the cellular plasma membranes, but they are hard to visualise and work with. So instead, Prerna's lab uses rod-shaped M13 viruses mixed with polymers like polyethylene glycol. In such a mixture, as reported by *The Life of Science*, the viruses that Prerna studies organise themselves into a single layer, with physical properties similar to that of plasma membrane. "There is an attraction between the rods in a way that the alignment of the rods is preferred over random orientation," says Prerna. This system is larger, and easier to visualise and tweak to study membrane biophysics. Her breakthrough work is in the area of stability of the plasma membrane.

Another researcher using asymmetric particles to study self-organisation is Ajay Sood, Year of Science Professor at the Department of Physics, in collaboration with Sriram Ramaswamy, Professor in the same department. Unlike Prerna, they use inanimate particles – brass rods, around four mm long with a physically distinct head and a tail region. These particles are placed on a vertically vibrating plate. The vibrations from the plate act as the 'fuel' for the particles to move. Systems whose individual particles use energy and move are called 'active matter'. The direction of the movement of the brass rods is determined by their orientation. Over the past 10-15 years, Ajay's lab has made several important discoveries about the collective behaviour in this non-living system. They found that a minimum number or quorum was required for the rods to show cooperative movements. Also, a coordinated movement was observed when inactive spherical beads were interspersed between them, which act as a medium of communication. Expanding on the concept of active matter, Ajay adds, "Systems like insects, birds, fish, etc, are all examples of active matter."

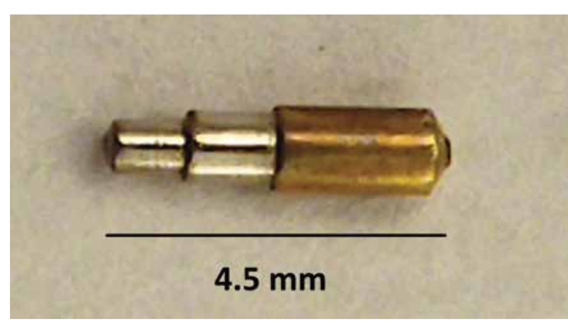


Image courtesy: Raushan Kant, Department of Physics, IISc

Asymmetric brass particles like this one display flocking behaviour under certain conditions

Active matter is governed by nonequilibrium physics. The vastness of this concept is beautifully explained by Sriram. "Anything you see around you that's alive is in a nonequilibrium state," he explains, adding, "By nonequilibrium, I mean a thermodynamic parameter, like temperature, or chemical potential is maintained at different values for different components or locations. This will always result in a flux of energy through the system. And all life [is maintained by] converting this flux of energy into work."

Sriram, a condensed matter physicist, studies the organisation of different states of matter and the rules governing them. His journey into biological physics and the formation of flocks in organisms stems from observing common properties between living systems like bacterial or locust swarms, and liquid-crystalline states. One of his research interests is finding the rules at the heart of the behaviour of motile organisms moving through a viscous fluid medium.

The plasma membrane is also in a state of nonequilibrium. Anand explains, "While a complex system tends to go towards an equilibrium level, the constant disturbances in the plasma membrane do not let it stabilise. Therefore, there is always a state of flux."

'Phone a friend' in case of disturbances

Self-organisation depends on a feedback system as observed in fish schools and blackbuck herds by Vishwesha's group. He gives the example of predator attacks as an external stimulus in blackbuck herds. At first, a few members of the herd may spot a predator and start moving to avoid it. Due to an intrinsic feedback mechanism, their neighbours start to copy their movement. In this way, the reaction to move away from the predator is amplified through the herd and they are able to escape the predators with minimum damage. Thus, the interplay between the external stimulus and internal feedback helps the herd escape.

Communication and feedback are key to every activity of cooperative insects like honey bees and wasps too. Colonies of the paper wasp, *Ropalidia marginata*, show a division of labour based on factors like age and dominance. Different members perform specific tasks like foraging, looking after the larvae and building their nest. Raghavendra says, "My students have shown that in *R. marginata*, if the workers in the nest receive food from the forager without showing dominance behaviour [like biting], then she knows she doesn't need to bring any more food. Whereas if they bite her and snatch the food, it means that more food is required." This communication is a feedback for the foragers. Honeybees use a less aggressive feedback system. "Foragers bring food and nectar and have to wait in a queue for the food to be unloaded. If they wait very long, they understand that not much food is required. But if they are mobbed and the food grabbed from them, they know more food is required. So, the longer the queue, the less the food requirement," says Raghavendra.

Not only animal systems, but plants growing in clumps in semi-arid areas or grasslands also show cooperative behaviour and a feedback system. Self-organisation in in plants is in the form of collective growth. Vishwesha says, "The presence of one plant facilitates the other plants nearby to grow better."

Perturbations in these self-organised systems are usually short-lived. Be it in the ephemeral disturbances seen in stars and galaxies, or be it predator attacks on blackbuck herds; complex systems go back to their original order. Sometimes there are obstacles in the path of collectively moving groups. Swarming bacterial colonies spread in different patterns on a moist and nutrient-rich surface. They swarm around obstacles, as seen by Varsha's work on *Pseudomonas aeruginosa*. "We believe that the bacteria produce a chemical signal, which helps them realise that there's an obstacle close to their moving end, and they should change direction," says Varsha. Her team thinks that the signal might be a chemical molecule that diffuses from bacteria through the surface, and is recognised by sensors on the other bacteria.

Sriram's team of physicists has also modelled the movement of 'swimmers' in a viscous medium. One of his key findings is that it is impossible for large numbers of slowly swimming creatures, like bacteria, to align in the same direction. They dissolve into a chaotic state called 'bacterial turbulence'. Purely physics-based modelling of collective behaviour, however, gets increasingly difficult with increasing complexity of the organisms and the motivation behind their actions.

Some kinds of obstacles can cause more long-lasting disturbances in flocks. Ajay's group studies what would happen if you mix active matter, in the form of self-driven brass rods that are prone to flocking, with other moving particles that are averse to flocking. He equates it to putting moving pillars in a crowded space with humans, which compels them to break the 'flock'. These anti-flocking particles, called 'dissenters', disturb the flocking of the other particles as well. "It's a case where birds of different feathers don't flock together," he quips.

Self-organisation of living and non-living matter and their constant state of flux is evident everywhere. Deciphering the rules governing it is vital to understanding how the very fabric of the universe works in a constantly changing state. The study of active materials is as dynamic as these systems themselves. The essence of this is captured by the American biophysicist Rob Phillips when he explained the clever title of his review from 2015, *Napoleon is in equilibrium*, which implied that only dead things are in complete equilibrium.

Anoushka Dasgupta is a freelance science writer and former intern at the Office of Communications, IISc. She has a Master's in Biotechnology from Savitribai Phule Pune University

Found in Trans

How the non-Kannadigas of IISc learn the local lingo

In a country like India, which is home to hundreds of languages and dialects that can vary drastically across the subcontinent, language can be a barrier to communication across regions. In an institute like IISc, students, faculty, and non-teaching staff come from all over India and even abroad, bringing in different cultures and languages. Although English is the language of communication inside the Institute, it often falls short when one wants to communicate with people who only speak Kannada, especially outside the campus.

Many of us cannot converse in Kannada when we join IISc. For those who want to learn, the Kannada Sangha at IISc organises spoken Kannada classes every year. These are taught by HG Srinivasa Prasad, whose vast experience and innovative methods for the classes are much sought after at IISc.

Prasad recalls a student's experience when the latter tried to speak in Kannada. Exams were going on, and the student had gone for dinner to the mess. As always, fruits were being served after dinner, but the distribution was delayed. As he was getting late for his studies while standing in the queue, he went up to the distributor and asked, "*Nanage bega bega hennu kodi; nanage tumba kelasa ide*" (Please give me a lady

lation

- Debraj Manna

HG Srinivasa Prasad in his element

Photo courtesy: HG Srinivasa Prasad

quickly; I have got a lot of work). The distributor was stunned. Upon further conversation, he realised that what he should have asked for was *hannu* (fruit) and not *hennu* (lady)! Another incident that happened many years back was with a pupil who was buying a dosa. The seller asked him to pay *hanneradu rupayi*, and the customer was shocked and started quarrelling with the seller as he thought he had to pay Rs100. He was relieved to know that it was just Rs12.

Anecdotes like these remind us of the importance of language. Knowing the local lingo can not only make life much easier, but it can also open doors to understanding another culture.

Being a Bengali, I grew up speaking Bangla with my schoolmates. I started speaking Hindi during my high school and college days, as I did not want to restrict my friends circle to the few who understood Bangla. I was overwhelmed to find out how much I had been missing out on by not conversing with people in their native tongue. Sure, English can always help one speak to others from different states, but in my case, it was Hindi that helped me bridge the conversation gap. Some thoughts are just better expressed in the vernacular than in English. Similarly, when I visit Bengali restaurants here in Bangalore, I find the waiters giving me more detailed information about the dishes they have than what they normally tell my non-Bengali friends. This is how multilingualism can work wonders in connecting with diverse people on a daily basis.

Through Prasad's course, close to 4,000 members of the IISc community have learnt to speak Kannada over the past 19 years. Several faculty members have also taken part in these classes, including former Director Anurag Kumar. GV Satisha, a Junior Scientific Assistant at the Department of Electronic Systems Engineering, and the General Secretary of the Kannada Sangha, muses on the next steps that they wish to take for the course. "We have plans to get a dedicated auditorium and to start a regular course like many other courses of the Institute. And if people are interested, we want to have advanced courses as well, in the future. Say, if somebody wants to learn how to read and write Kannada, then they will be offered an advanced course," he says.

Kannada classes: the conception

Back in 1975, Prasad completed his Master's degree in Kannada from the University of Mysore. Although he became an employee of the Reserve Bank of India (RBI), his heart was always in teaching. In the late 1980s, as Karnataka started seeing an influx of numerous IT firms and other companies, people from all around the nation and foreign lands conglomerated in the state. The need of the hour for them was to learn Kannada. The Department of Kannada and Culture, which is part of the Government of Karnataka, in collaboration with the Central Institute of Indian Languages, Mysore, offered to train people to teach Kannada specifically to non-Kannadigas. After undergoing this training, from 1982, Prasad started teaching in various companies and banks, including the Reserve Bank of India, Nrupathunga Road branch, where he worked. Soon, he became the go-to person for non-Kannadiga bank employees when they needed to communicate with their local customers. After a few years, Prasad felt the need to change careers when he realised how much he could help people by teaching them to speak the language. He quit his secure government job in the RBI despite several warnings from colleagues about the 'wrong' decision he was planning to take. His determination helped him to start teaching at various engineering and medical colleges, banks, NGOs, IT organisations, and some governmental organisations. That is when he was introduced to the Kannada Sangha in IISc by Baraguru Ramachandrappa, the then Chair of the Kannada Development Authority. Ramachandrappa inaugurated the first Kannada classes in the Institute in 2004. Since then, every Tuesday and Thursday, Prasad keeps his calendar booked for the Institute community.

Photo courtesy: The IISc Kannada Sangha

Prasad's classes are much sought after

Prasad's classes do not start with ABCs like a typical language class. He teaches the first class in the 24-class course in English. He keeps using both Kannada and English in the initial classes. Shubham Lochab, an Integrated PhD student at the Materials Research Centre, explains how Prasad keeps his pupils engaged. “He likes to tell stories. Initially, he starts in English, and then in between, he will switch to Kannada. If he has to introduce 20 new words in a lesson, he will use these 20 words in his stories. He comes, tells us stories, and goes, but in between, we learn a lot. He also focuses on making connections between different cultures, and, like that, he can form bridges between languages.” While it’s important to start teaching in English since it is the language that most people who come to IISc are fluent in, Prasad believes that the best way to learn Kannada is through one’s mother tongue. “I ask my students to learn Kannada through Hindi, Bengali, Marathi, and so on because there are some common words, and most of these Indian languages have a similar overall sentence structure. This makes learning the language easy,” he elaborates.

Another interesting aspect of the classes is that they are not bound by grammar rules. He encourages people to speak in Kannada before understanding the grammar. “He asks every student to speak. He makes the class very interactive and pushes us to speak even if we are wrong. Because the first threshold that anybody faces in any language, in the beginning, is that you might know the word, but you have a fear from within that you might end up speaking the wrong word or something you don’t mean. He helped me overcome my fear and speak up in the class,” adds Nupur Bhatter, a former PhD student at the Department of Biochemistry.

TN Manjari, who works as the Secretary to the Chair of the Department of Organic Chemistry, is a regular attendee of these classes along with her husband, Unni Krishnan. Although Manjari speaks Kannada fluently, Unni did not, and would often take her help to talk to people outside his professional life, where English or Hindi were the norm. She wanted to give Unni some company in getting started with the language in these classes. Manjari, who speaks Kannada, Telugu, Tamil, Hindi, and English, believes that once we consistently show interest in a language, we eventually start speaking it. “Previously, I used to sit between two Tamil ladies in my workplace, and they would speak in Tamil. For almost 7-8 years, I continued hearing the language and started speaking Tamil. When you keep on listening to how people speak, automatically you pick up their language,” elaborates Manjari.

Marcus Lehmann, a postdoctoral fellow at the Department of Civil Engineering, is an international researcher at the Institute. After coming to IISc, he realised that Indians spoke many languages. He was also confused by the Indian accent when people spoke English here. As a foreigner starting with the Kannada classes, his experience differed from others. “In the first 2-3 classes I attended, I couldn’t recognise any differences between the teacher speaking in Kannada or English. For me, all of that sounded exactly the same. I did not have any ability to hear the difference … But this changed suddenly, in the fourth class I went to. I could understand: ‘hey, that was an English word, this was a Kannada word.’ Then I could distinguish. That was the first big step, and now when I am out at Mysore, Hampi or sitting in a bus, I can sense if this guy is speaking Kannada or English or something else,” exclaims Marcus.

Why learn Kannada?

Even after more than 18 years since he first taught in the Institute, Prasad continues to come back to IISc to help people learn how to share their thoughts with others in the vernacular. He says, “At some other places wherever I go, like banks, it is mandatory to learn Kannada. Without knowing the language, they cannot do their business. Even in the engineering colleges where I teach, it is mandatory – they have some credits allotted for the course which they must complete. But in IISc, it is not mandatory, there are no compulsions, yet people are learning only based on their interest. That’s why I am interested. Where they want to learn *swayam preritavagi* (on their own), definitely they’ll learn it. This is the plus point! Two or three years back, one professor told me that they wanted to translate some Bengali novels to Kannada. I felt so happy.” Nupur agrees with this sentiment, saying that she joined the classes towards the end of her PhD, despite knowing that she would soon leave the Institute and go out of India for her postdoctoral research where she would not need to speak Kannada. She wanted to take back something with her, and the local language and culture seemed like the perfect keepsake.

Finally, Prasad answers a question that we might all have: Why should we make the effort to learn the native language when we come to a new place? He shares the words of the famous Kannada poet, SR Ekkundi: “When we visit someone's house and they offer coffee, we can't just sip the coffee and leave; we would indeed say that the coffee was very nice and that we would love to visit again. Similarly, how do we show gratitude when we come to a new place? By learning the language, respecting the culture and mingling with the people.”

Debraj Manna is a PhD student at the Department of Biochemistry and a former science writing intern at the Office of Communications, IISc

Balancing

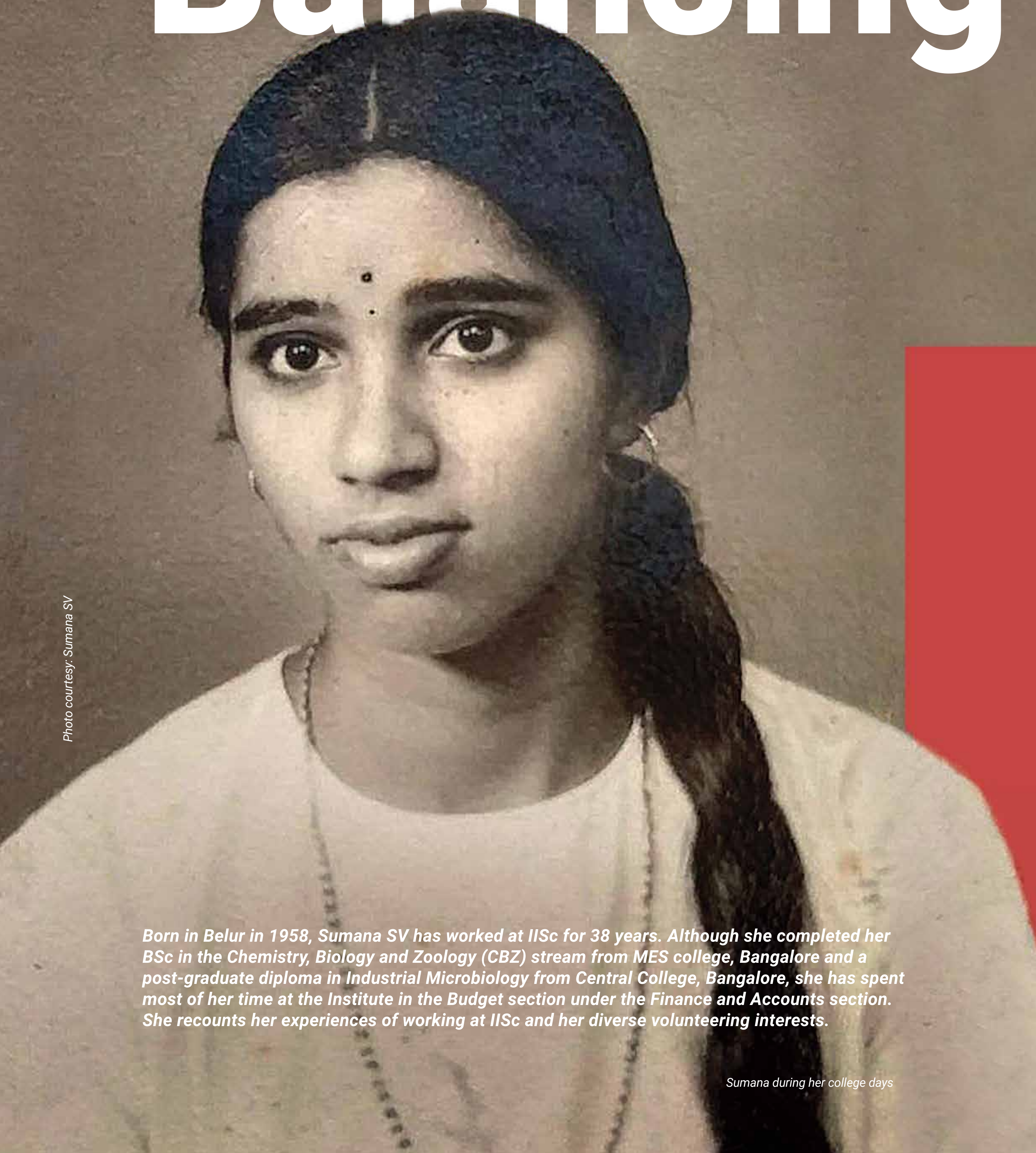


Photo courtesy: Sumana SV

Born in Belur in 1958, Sumana SV has worked at IISc for 38 years. Although she completed her BSc in the Chemistry, Biology and Zoology (CBZ) stream from MES college, Bangalore and a post-graduate diploma in Industrial Microbiology from Central College, Bangalore, she has spent most of her time at the Institute in the Budget section under the Finance and Accounts section. She recounts her experiences of working at IISc and her diverse volunteering interests.

Sumana during her college days

Budgets & Bills

- *Sumana SV*

Early life

IISc has felt like my home ever since I was young. Right from when I was eight years old, I have spent time walking and playing on campus, attracted to its atmosphere. I always dreamed of working at the Institute so that I could spend more time here.

At home, we were eight children, six boys and two girls. All of us were technically qualified, as my parents always valued education. My father worked as a superintendent engineer in the Military Engineering Services, and served in military bases all over India. While he was travelling for his job, my mother stayed with us in Bangalore. Both of them supported our education and encouraged us to study well. I remember my mother once pledging her jewellery at the end of the year to pay our fees. My brother pursued his MSc in Civil Engineering at IISc, under Prof Shiva Reddy (sadly, my brother passed away a few months ago). I recall that we both used to come together to the Institute and go home for lunch as our house was on 15th cross, Malleswaram.

Although I got permanent job offers in government organisations such as PNT, I opted to join the Institute because of my technical qualifications. Initially, I joined as a lab assistant on a temporary, contract basis, in the Department of Biochemistry, from 1980 to 1985. I applied for the position after seeing an advertisement in the newspaper. More than 150 candidates were present for the written test, 50 qualified for the first round of interviews, 16 for the second, and finally, I got selected with five other candidates.

I have worked with Prof PS Sastry, Prof T Ramasarma, Prof PV Subba Rao and Prof Kurup in the Department of Biochemistry. My job was mainly in the 'allergy lab' with Prof Subba Rao where I was doing allergy tests – even for outsiders – when needed. Prof Subba Rao provided me the opportunity to get trained at the Health Centre for doing the allergy tests. During the Platinum Jubilee celebrations of the Institute, I recall doing allergy tests in the lab for visitors.

From lab assistant to lower division clerk

Since mine was a temporary position, I applied for the 'Lower Division Clerk (LDC)' position, which was an administrative and permanent position at the Institute. Prof Ramasarma instructed me to undergo the required training, and so, I took courses in English Senior Typing. When I was in Prof Subba Rao's lab, he had given me the opportunity to take a clinical lab technician course.

I remember typing up publications for Prof Subba Rao, Prof Ramasarma and Prof Kurup, and also the thesis drafts and papers for students like Nandini, Vipin Chakravorthy, Usha, Lalitha, Patoudi and many more. I was happy to be assisting technically in the lab and at the same time helping with administrative work.

In 1985, I applied for the LDC position and got selected. Initially I had some regrets about not continuing in my qualified profession, but later, after I realised that I could stay and work at IISc – my favourite place since childhood – until the age of 60, I had no regrets. I learned to enjoy my job in the Finance and Accounts section where I spent the next 33 years.

Photo courtesy: Sumana SV

Sumana (fourth from left) with other staff members in Finance and Accounts. L-R: Veena, Sunitha, Indira, Chitra, Padmini and Girija

When I reported to my first supervising officer, Mr Sheshagiri Rao, Deputy Financial Controller in the Finance and Accounts section, he saw me and said, "A scientific staff member posted to the Accounts section? It is very difficult to train you people as you don't understand anything, and by the time we train you, it takes a lot of time." I was surprised by his concern. Since I had no clue what to do, I immediately asked if he could send me to another department. He was in turn surprised by my reply, and then smiled and asked me to report to the Budget section. I learnt all about the Institute's accounts from my senior colleagues, who were very helpful and enthusiastic in teaching me. Mr Gangadhar in the Budget section was especially helpful; he taught me each and every thing that the section does.

When computerisation was first introduced in the Finance and Accounts section, all of us were curious and passionate to learn how to use the computers. The first programme installed in our Finance and Accounts section was COBOL in 1987.

My job involved receiving project proposals from the faculty members and departments, getting the sanctions from the funding agencies such as UGC, MHRD, DST, DBT, CSIR and ICMR for development projects, bifurcating the funds as mentioned in the proposals, creating a debit head for each grant, and finally submitting the utilisation certificates to the agencies. Almost all the employees in the Finance and Accounts section were permanent employees.

I was frank and bold in expressing my views if we had any issues in the section, and initiated discussions with the officers to get the work done. Sometimes, I was branded as "straightforward" which was not seen as good, but later when the issue was resolved, the officers formed a good opinion of me, which encouraged me to do more work.

I was grateful for being involved in projects worth Rs 100 crore which were given to IISc, as the work was challenging. We used to do stencil cutting and making copies of the Annual Accounts for the Council meetings; working extra hours and on Saturdays, we all became friendly with senior colleagues. In the Bills section, the work was different; the nature of the bills was payments for building works, travel of faculty members, journals and conferences, visitors, even confidential bills. I was processing an average of 300 travel bills each month. I never sat without work for even a single day during my tenure in the Budget and Bills sections from 1985 to 2018. I don't remember anybody asking me for their pending bills; I had the habit of completing all the work on a day-to-day basis.

In those days, faculty members and officers were very friendly with the administrative staff, but by the end of my career, I felt that was missing.

Photo courtesy: Sumana SV

Sumana with TMC committee members and Ratan Tata

Work-life balance

When the crèche was opened on campus, it was a boon for working women. Maternity leave was only for three months in those days. Since I had no help at home, I was forced to bring my three-month-old baby to the campus. She grew up until the age of 14 in the crèche, and even used to assist the caretakers and younger children as she grew older. When she got a job, she went and met the caretakers there, Uma and Lalithamma, and shared sweets with everyone. My office staff also supported me a lot in taking care of my daughter whenever needed.

I worked as a committee member in the Kannada Sangha, the Union Office, the Tata Memorial Club (TMC), the Women's Forum and also in the Employees Housing Society. I also served in the Board of Directors of the IISc Housing Society for two terms. Working in these associations gave me the opportunity to meet people from varied fields and backgrounds. It helped me with my personal growth as I evolved into a more confident person with a thirst to explore and learn new things. My most favourite memory was being part of the drama group where I got the opportunity to bring various characters to life.

Photo courtesy: Sumana SV

Sumana (rightmost) with college lecturers during a Ranger training session

Photo courtesy: Sumana SV

Sumana (right) with Udaya (left) performing in a play on the occasion of International Women's Day

With the Kannada Sangha, I helped in organising many programmes and competitions. I also won several prizes in debates, 'pick-and-speak' and games. We arranged Kannada classes to teach Kannada to the campus community. Due to this initiative, staff members and students developed a very close friendship with us. As a member of the Tata Memorial Club, I have volunteered for the Science and Technology Day quiz programme every year during the month of February. I helped to select books for the club library, start a gym room for staff, and arranged *sloka* classes for employees and their family members. I was the President of the Women's Forum for two terms, and helped to arrange several cultural programmes.

During my tenure at IISc, I had the honour and privilege of meeting late Dr Abdul Kalam and discussing women's empowerment with him. I also feel honoured to have met Mr Ratan Tata during my time as a committee member of TMC. These are some memorable events that I will cherish for the rest of my life.

Apart from these, I have also volunteered in many organisations like the Bharat Scouts and Guides, Vedanta Bharathi, and in many temples as well. I joined the National Social Service (NSS) in my college days. In 2006, I completed the basic course and qualified as a Ranger Leader in the Bharat Scouts and Guides, and started my Ranger team with the name 'Spoorthy Ranger team'. I used to train Rangers (girls between 16-25 years). For nearly 16 years, our team performed voluntary service at the Tirumala Tirupati temple. I also completed the advanced courses, became a Leader Trainer and I am presently working as a Head Quarters Commissioner for Karnataka. In 2019, I represented Karnataka at the World Jamboree in West Virginia, US, through the Scouts and Guides programme.

In 2006, I also became a life member of the Indian Association of Secretaries and Administrative Professionals (IASAP). I have attended both national and international conferences, which helped me tick off a lot of places from my travel list and explore new places. This organisation has provided me with a holistic development and pushed me to achieve higher. I am also a volunteer with the Rashtriya Swayamsevak Sangh (RSS) and helped with the distribution of groceries to the needy during the pandemic.

I always like to keep busy and multi-task. Whichever group I joined, when I say I am from IISc, I have been recognised and respected. The Institute feels like my home. It has supported me, and I have cherished my life here.

As told to Kavitha Harish

Kavitha Harish is Personal Assistant to the Assistant Registrar (HR, Council)

“People often think that A THERAPIST GIVES ADVICE, BUT THAT ISN’T TRUE”

- Deepika S

Image courtesy: Pixabay

With four new consulting psychologists as of March 2022, IISc's team of counsellors has expanded significantly. We spoke to Shridhar BG and MS Savitha, both clinical psychologists who have been counselling IISc students on campus since 2018, and are part of the team of mental health professionals (including psychiatrists and wellness coordinators trained in crisis intervention) who make up IISc's Wellness Centre. In this interview, they explain what counselling and therapy are, and bust some misconceptions about addressing problems with mental health.

What is counselling?

Shridhar: For me, counselling is more about helping someone build themself from within when they are facing a conflict or a problem. People often think that a therapist or a counsellor gives advice, but that isn't true – that's the last thing we do. We try to get them to look within, so that they can start looking at this problem with a different perspective and find a solution. Most of the time the individual will have their own solutions, but sometimes, in a particular scenario, they may not be able to find it themselves because they might be stressed, or anxious, or depressed. So in counselling, we try to pose questions that can make them examine and rethink their perspective, and help them figure out a workable solution.

Is therapy the same as counselling?

Shridhar: It is different. In counselling, we ask questions and try to dive within. Counselling is useful in dealing with conflicts that come up in our day-to-day activities, where there may be difficult choices to be made. Therapy is slightly more complicated, and is used when there is some deeper trouble. In therapy, we might follow a particular school of psychology and use certain techniques to help someone modify certain behaviours or thoughts. Behaviour is learned – and anything you learn, you can unlearn. We might give our clients a bit of homework (in the form of recommendations for behavioural changes, or maintaining a diary) when it comes to therapy.

Savitha: In counselling, someone might be trying to work through a problem and we help them resolve that problem. In therapy, we go a little deeper. We chat with the client to get a sense of their case history, and we might suggest some steps they can follow, based on the schools of psychology we use. It depends on the severity of the issue. If they are facing a situation to which they have a specific response such as mild anxiety, without a history of it, then we might use counselling. But if it seems like the client has had similar experiences in the past to which their response has been to feel very anxious, and if the impact on them is severe, then we might shift to using therapeutic techniques to help them.

Photo: KG Haridasan

MS Savitha, a full-time counsellor on campus, can be found at the Psychology Unit in the Faculty Club building

What happens in a typical counselling session?

Shridhar: The first session usually starts with a greeting, and we introduce ourselves. We gather information about the individual and try to build a rapport. Building that rapport is very important in order to get a person to open up to us. Then we ask about the reason that they have come to us, and try to see – based on the severity of their issue, and their ability to perform day to day activities – whether to go in for counselling, therapy, or refer them to a psychiatrist. If we do feel a psychiatrist needs to chip in, we let them know why we are referring them to one.

What is the difference between a counsellor and a psychiatrist?

Shridhar: As counsellors and therapists, we try to deal with problems or certain behaviours with counselling methods and therapeutic modules. We do not prescribe medication. Psychiatrists deal with these by prescribing medication if it is required.

How long does a course of counselling usually last?

Savitha: There is no time limit as such, it depends on the severity of the issue. Sometimes things may get resolved with 3-4 sessions of counselling. But when it comes to therapy, it can take a little longer as they usually involve a few structured sessions. Sometimes we have an assessment between the sessions. Based on the client's improvement, we decide whether to continue with therapy or not.

Who needs counselling or therapy?

Savitha: Any person facing a situation that is impacting them adversely, affecting their daily activities, affecting their relationships, or affecting their decision-making skills. Sometimes the impact of these situations is severe, and sometimes not. Often the person is able to handle the situation and take care of most aspects, but there may be one that they might need help with.

Shridhar: Any normal person needs it. To be very frank, we cannot counsel a person who is not sane. Counselling is for a person who has to navigate a difficult scenario, and might be feeling stuck.

In your experience, what are some of the most common reasons why people seek counselling on campus?

Shridhar: To start with, it is usually academic issues, and stress related to academic issues. We also see people with anxiety, depression, and relationship issues. When I say relationship, this can be with their academic advisor, their parents, their friends, or their partner. But the most common ones are academic situations.

Savitha: In my experience it is the same – I mostly see issues with academics, anxiety, depression and interpersonal relationships.

Are these issues the same for most people, irrespective of gender?

Savitha: Yes, these are the most common issues for people that we are seeing.

Photo: KG Haridasan

Shridhar BG, a full-time counsellor on campus, can be found at the Psychology Unit in the Faculty Club building

Some people think that seeking counselling is unnecessary because they have already spoken to their friends about their problems. What do you think counselling brings to the table that is different from sharing with friends and family?

Shridhar: Usually, when a family member or friend shares something with us, we are so emotionally attached that we are just looking for ways to protect the person in whatever way possible. It is an emotional and subjective approach, rather than an objective one. With a counsellor or a therapist, it's about you looking into things in a more objective way, choosing the most workable solution, and getting started with it.

Savitha: A counsellor's approach is a more objective one. To friends or family we may not be able to say what we truly feel, or we might say what we think the other person wants to hear. As professionals, we don't give advice. We guide people to find their own solutions.

What do you think are some of the biggest reasons that people are hesitant to reach out to a mental health professional?

Shridhar: Even though a psychiatrist is different from a therapist, people often confuse the two. They feel that if they meet a therapist they will have to take medication. They are not okay with taking medication, but are fine with attending counselling sessions. So, I think it is mostly related to the taboo attached to taking medication for mental health issues. Also, it could be that they had a prior negative experience with a mental health professional, or just a case of judging the process too quickly.

The stigma around mental health means that students sometimes do not wish to engage with us. Sometimes they are referred to us by their friends and when we reach out to the student, they are not receptive to us. The moment they hear the term psychology or psychiatry, they shut down.

Savitha: Many people assume that psychiatric medication is addictive. They may also believe that seeking counselling would mean they are weak-minded, or "mad" or "crazy". Perhaps they worry that people around them will begin to look at them differently. Or they think, if I have any kind of emotional outburst, people will say, oh, now she needs to be admitted in a hospital, or something to that effect.

Another thing I have observed is that most of the time students don't tell their faculty advisors that they are seeing a psychiatrist or a counsellor, as they are worried that they will be treated differently from their colleagues. They are worried that they won't be given important tasks, or that the professor will complain that they can't shout at them because then that will make them anxious. They are very scared that if their professor finds out, it will not be kept confidential and their reputation in the lab will go down, and their friends will look at them differently. Some of the students even hide it from their family members, because they are scared their parents will think that they haven't been raised properly. There is still a huge stigma around mental health, even among so-called educated people, and we see it in IISc too.

Since you joined the Institute, have you seen students more willing to reach out over time?

Shridhar: I've been here for almost three and a half years now. At the start, we hardly had any sessions, but now the numbers speak. On an average we have around 8 to 10 between us each day. That's a huge number for an educational institute. So yes, students are reaching out. That's a wonderful thing.

However, one concern we have is that people might have had a negative experience with a therapist in the past, and because of this they give up on therapy or counselling altogether. We just want them to give it another chance, even if it is not with us. It's not like therapy involves medication, and there is free will here – you can always back out if you are not okay with the therapist. I am very sure there is no therapist or counsellor who can deal with all issues. It depends on the rapport that is built, and if the person is not comfortable with the therapist, they can always find someone else that they are comfortable with. Sometimes if we ourselves feel that the counselling or therapy is not working, we let the individual know this. I hope people give it another chance and use the facilities available to them – there are other means of accessing mental health services at IISc [such as the online portal YourDost, or reimbursements for counselling or psychiatry sessions off campus] than coming to us.

We also see very little participation from students when we run surveys, and that doesn't help us get an accurate picture. More student participation will help us come up with new modules based on this information, something we are looking forward to creating.

If there was someone who is considering seeking counselling but might be scared to reach out, what would you say to them?

Shridhar: I would say, please reach out to us, and if you are worried about confidentiality, rest assured. We are bound by a code of ethics to maintain confidentiality, unless instructed by the client. We would also like your feedback on the process, and ask if your expectations are being met. Together, I think we can build a stronger community. It's about working together, no matter what we do.

Savitha: To add to that, I want to say, you might have some thoughts about therapy – you might think this therapy or this medication is for weak-minded people. Or maybe you might have heard from others that going to a psychologist or a psychiatrist is not a good thing, and that you have to deal with your problems yourself. Honestly, sometimes we cannot deal with certain problems, sometimes the situation is overpowering, and we are unable to overcome it without a little help. When you come to a mental health professional, it is not like we force you to do something. We will only discuss the best way to solve your problem, or suggest coping mechanisms to handle certain situations, so that next time you face something similar, you will be able to handle it well. It's about identifying the problem and understanding yourself, in a space where no one will judge you.

Shridhar, Savitha and four more consulting psychologists can be contacted through IISc's Wellness Centre (https://wellness.iisc.ac.in/index.php/committee/consulting-psychologists/)

A Clique that Clicks

- Karthik Ramaswamy

The Photography Club is a forum for students to learn the craft from their peers

During the orientation programme marking the start of the 2012–13 academic year at the Department of Computer Science and Automation (CSA), faculty member Chiranjib Bhattacharyya spoke to the incoming PhD students. In the course of this interaction, he told them why it was important for research students to also pursue extracurricular activities. One of the students in the audience was Abhiruk Lahiri, now a postdoctoral researcher at Charles University in the Czech Republic. Already a passionate amateur photographer, the new PhD student took the words of Chiranjib, currently the Chair of the Department, to heart.

Abhiruk soon learnt that IISc used to have a photography club back in the 1990s and early 2000s — the webpage still existed on the Physics Department website. One of the members of the club had been Chiranjib himself, who was then doing his PhD in the CSA Department. The club, however, was defunct by the time Abhiruk joined IISc. What remained were some pieces of photography equipment from the pre-digital era and a darkroom in the old Physics building (which now houses the undergraduate labs).

It was then that Abhiruk stumbled upon a Facebook group called "Photography Lovers @ IISc Bangalore" where photographs were being shared by IISc students. "I started contributing to their page. That's how I met some people, including two accomplished photographers who joined as PhD students soon after I did: Manuj Mukherjee, from the Department of Electrical Communications Engineering, and Shounak Roy, from the Department of Electronic Systems Engineering." Abhirukh and Shounak were already acquainted with each other — their paths had crossed during their photography days in Kolkata.

By the time Abhiruk met Shounak and Manuj in IISc, the two new students had run into each other and were bonding over their shared passion. "Manuj used to shoot a lot of landscape photographs and I was into street photography," recalls Shounak, who now works for a tech firm in Bangalore.

Photo courtesy: Photography Club

Spiti Valley, Himachal Pradesh

A new avatar

Though they were sharing their photographs on the online group, Abhiruk, Manuj and Shounak felt that it did not provide them with an opportunity to work on their skills. "There was not much knowledge exchange," says Abhiruk. "I too was disappointed with the Facebook group," laments Shounak.

"In 2015, the three of us, along with a couple of our juniors — Sangram Biswas and Subham Dutta Chowdhury [both PhD students from the Physics Department] — started thinking more seriously about photography," says Shounak. "We decided to start our own Photography Club."

Photo courtesy: Photography Club

Photography exhibition on theme of light and shadows in 2019

And so, they did. The new club included the five of them as well as a few members from the Photography Lovers group like Chirantan Pramanik and Ruby Saha, who were then PhD students at the Centre for Earth Sciences. The club soon expanded as they organised more activities on campus (the conveners of the newly formed club also eventually started managing the Facebook group).

Exhibitions

Before the club was established, photography exhibitions were held now and then. "But the choosing of photographs was a bit ad hoc," says Abhiruk. Shounak also remembers not being too impressed by these exhibitions. "They were not particularly well-curated."

"We therefore decided that we'll have our own members shoot over a year and then exhibit their work," says Abhiruk. This, however, meant excluding people who were not part of the club from showcasing their photography skills. So the club decided to have two week-long exhibitions during the course of the year: the first would be exclusively for their members, and the second would be open to all members of the IISc community (in recent years, the second exhibition has also been thrown open to students from the National Centre for Biological Sciences and the Jawaharlal Nehru Centre for Advanced Scientific Research). While the first exhibition was to be curated internally by the members of the club, the second would have external judges.

But money was an issue – the fee collected from members of the club was not sufficient to cover the cost of organising exhibitions. "So participants whose photographs were selected to be exhibited in the open exhibition pay a fee. But we didn't collect any money from the Photography Club members since they already pay the membership fee," says Shounak.

Once the first set of exhibitions was held successfully, it became a regular feature in the calendar of the Photography Club. And so too did workshops to help students learn the art and science of photography.

Workshops

"Many of them who attended the exhibitions were keen to learn photography," says Abhiruk. So the club decided to have a photography workshop. "Fortunately, Manuj already had this experience — he was part of the Jadhavpur University Photography Club before he came to IISc."

According to Abhiruk, in the early days, the club was a bit ambitious with the workshops. "We tried to dump all our knowledge on the workshop participants." The senior members eventually decided on having practical sessions to complement the theory classes. And to end with a post-processing class using photographs shot by the workshop participants during the practical sessions.

Anindya Datta, a PhD student at the Department of Aerospace Engineering and a member of the Photography Club, fondly recalls the workshop he attended in 2020-21, just before the COVID-19 pandemic struck. "In the first theory class, we talked about the evolution of cameras and the technical aspects of photography — shutter speed, aperture, etc." Anindya says that in the class that followed, the discussion was on the aesthetic aspects of photography like composition and the dissection of popular photographs of well-known photographers.

Photo courtesy: Photography Club

Abhiruk Lahiri sharing his insights on post-processing

The goal of the first practical session, usually held on the IISc campus, was to make those who were new to photography comfortable with a DSLR (Digital Single-lens Reflex) camera and give them an opportunity to "play around with technical specifications." "We were told not to use the automatic mode," Anindya says. The second practical session which focused on composition was held at Cubbon Park for Anindya's batch. After the two practical sessions, Anindya and the rest of the participants were introduced to the idea of editing photographs. Following this class, members of the club organised a landscape photography session in Skandagiri hills outside Bangalore and street photography sessions within the city. Places like Shivajinagar, Pottery Town and KR Market are popular destinations among members of the club to practice this style of candid photography, according to him.

Growing as photographers

Atanu Dolai, who joined IISc as a Master's student in 2015 and is now a PhD student in the Mechanical Engineering Department, says that he is one of those people whose photography skills benefited enormously by being part of the club. "When I came to IISc, I had a DSLR, but did not know much about composition or other artistic aspects of photography. Then I started following the work of people like Manuj and Abhiruk." Atanu officially joined the club only in 2017 after he started his PhD. He began to travel around Karnataka to places like Kudremukh and Hampi to practice his skills. "When I returned, we would discuss my photographs — is it good, is it bad, how to improve it. And then I learnt post-processing techniques from Sangram. So I started as a novice and grew into a much better photographer," says Atanu, who went on to become the convener of the club in 2020-21.

Like Atanu, Sayan Sen Gupta, a PhD student from Electrical Communications Engineering, developed his skills as a photographer after he joined the club. But unlike Atanu, Sayan joined the club because of peer pressure. "I used to hang out with people who were part of the club and I used to get left out of their activities. So because of that motivation, I started attending the training sessions," he says in jest. Sayan, who "doesn't like to travel much," would however go to KR Market, a large wholesale market in the city, early in the mornings to develop his street photography skills. "Another hobby I picked up was taking macro photographs of insects." Sayan too went on to become a convener of the club.

Photo courtesy: Photography Club

Learning landscape photography at Cubbon Park, Bangalore, in 2019

Abhiruk is happy for the success of the alumni and current members of the club, many of whom had not held a DSLR before joining it. "After learning from us, they reached a stage when they could actually teach us things. Quite a few of them have won awards and received recognition for their photography outside IISc as well. This gave us a lot of satisfaction."

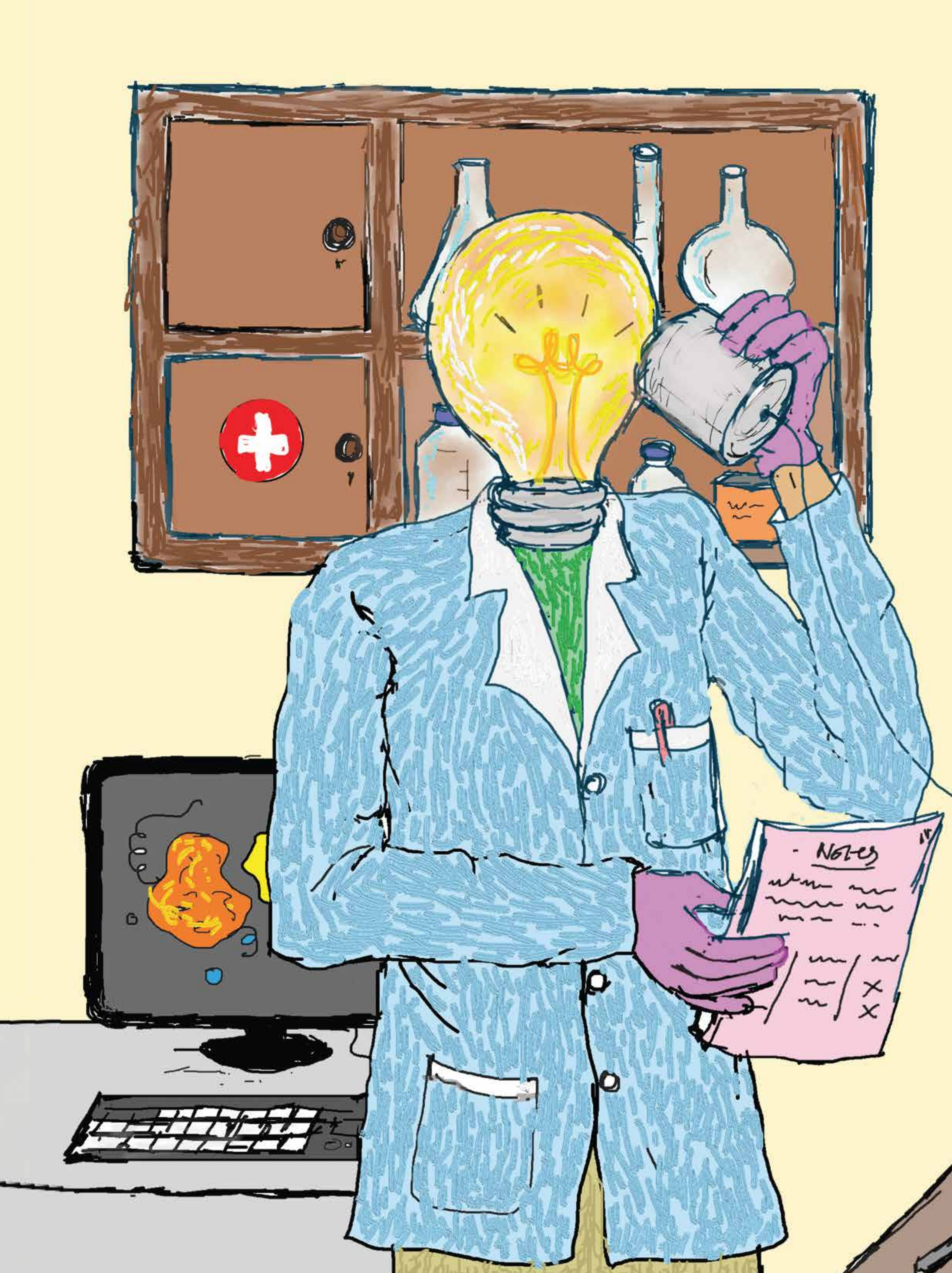
Mental wellbeing

Besides helping him and others become better photographers, Abhiruk believes that being part of the club gave him mental and emotional support, particularly when he felt that his research was not moving forward. "When I did photography, even for an hour or two, it gave me results and gave me positive feedback immediately unlike my research. This really helped me continue my regular work."

Abhiruk recalls the words of Chiranjib at the 2012-13 orientation for new students. "Chiru said that inculcating hobbies outside our research was important for our mental health. When I look back now, I think he was right — photography helped me keep going. I guess this is true for many others as well whether they pursued photography or some other art."

ABSTRACTS

IISc Photography Club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