CONNECT

WITH THE INDIAN INSTITUTE OF SCIENCE

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Space Bugs
Microbes on missions

'Junk' DNA
A genomic mystery

Quantum Cat
Dead or alive?

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EDITORIAL

Dear readers,

The human genome, shaped over millions of years of evolution, holds the key to our very existence. For decades, scientists believed that only a small fraction of this genome (~2%) – which coded for proteins – truly mattered, while the rest was labelled “junk.” But a landmark project in 2012 challenged this view, revealing that nearly 80% of our DNA was biochemically active. While some scientists rejoiced, critics pushed back, accusing the project of defining “function” too loosely. In our cover story, we explore both sides of this enduring debate, and ask: What does it even mean for DNA to “do” something?

Science is full of improbable questions with improbable answers. Take the case of the Schrödinger’s cat thought experiment in which the paradoxical feline is supposedly both alive and dead at once. Quantum mechanics, in theory, allows this to be true. But how? We unpack the many interpretations of this fascinating idea that underscores the strange nature of the quantum world.

In other stories, we explore how image manipulation can undermine biological research, how scientists are working hard to outpace drug-resistant cancer cells, the origins of the world’s first neural network, and the technological advances that might bring electric vehicles to the mainstream. We also explore how tiny microorganisms are adapting to life in space, teaching us how we could perhaps do the same one day.
On campus, we spent a day at DIGITS, the office that keeps the Institute’s digital processes running smoothly. We also spoke to students about their favourite campus events.

This issue also features two in-depth conversations – one with former Financial Controller Indumati Srinivasan and the other with alumnus Suhas Mahesh, a material physicist working on building self-driving labs using AI.

As always, don’t miss our crossword and student comic on the last page.

Happy reading!

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Behind the Screens

- Shravani Deoghare

A day at DIGITS

An exterior view of the DIGITS office at IISc

If IISc were a living organism, with the Main Building as its brain, then the DIGITS office (Digital Campus and Information Technology Services) would be its spine: positioned just behind the “brain”, tasked with carrying signals and coordinating responses across campus and beyond.

The office building stands at the intersection of Gulmohar Marg and Mahogany Marg, a modern structure crowned with a sloping rooftop and a garden decorated with Ashoka trees. Its central location is a sign of the office’s critical role on campus – holding up the Institute's growing digital footprint.

On the inside, cubicles stretch in neat rows, desks bearing the signs of long-term occupancy – sticky notes on monitors, notebooks with tasks and reminders, diagrams on soft boards alongside family photos and doodles.

By the time the clock hits 10 am, office noises – phones ringing, keyboards clacking, notifications pinging – envelop the room alongside murmured conversations about website bugs, fixes, and Wi-Fi outages.

But before anyone settles in, the day begins with a small ritual: a stop at an office room on the ground floor to mark their attendance. That room belongs to AY Naaraayani, the administrative assistant of the DIGITS office, and

Vinod Kumar, who manages office activities and procurement of all the departmental needs, including through the Government e-Marketplace and Naaraayani.

At the front desk

Naaraayani joined IISc in 2006, long before DIGITS existed, and worked across departments before assuming her current role. She has seen the office's evolution, not just in its technology but also in its very structure. What began as small, disconnected units for digitalising the campus – CCA (Committee for Computerisation and Administration), CCIT (Committee for Computerisation and IT) and TINA (Telecom and Internet Access) – eventually came together under one roof as DIGITS in 2016, under the chairmanship of Yadati Narahari (now Honorary Professor at the Department of Computer Science and Automation). Narahari handed over the DIGITS Chair role to Anil Kumar in January 2021, who still holds the position, in addition to his role as the Dean, Administration and Finance, at IISc.

The intention was to centralise all digital communication technology and to support the Institute's needs in this area. The department initially worked out of a single room in the erstwhile Choksi Hall, before finding its current home. "You can come here [DIGITS], get [all] your work done, and go. When new students join, they can easily get their email ID, network access, and SAP (Systems, Applications, and Products in Data Processing) ID set up, all in one place," Naaraayani notes.

Many calls related to SAP, HR queries, network complaints, email problems, vendor follow-ups, and more come first to the office and are routed by Naaraayani to the concerned person or section. "Some days, there are 20-30 calls and emails," she says. "Some days, there are very minimal. You cannot plan for it."

Additionally, Naaraayani oversees the building's day-to-day logistics, expenses, settling cash advances, and raising requests for hardware and other necessities. What would have been stacks of paperwork once is now easily handled digitally. Much of that shift has been enabled by SAP, the campus-wide system that connects workflows across departments.

Managing that system is the task of ISTAR (Implementation of SAP for Transforming the Administration and Research), located a few steps away from Naaraayani's office.

Inside project ISTAR

Before the advent of SAP, connections between departments were fragile. Systems did not communicate. A student leaving a programme might be marked inactive in one database while still receiving payments from another. These details had to be manually cross-checked; errors and delays were inevitable.

To address this, DIGITS launched Project ISTAR, under which SAP was introduced as a unified system to support students, faculty members, and staff through a single, shared database, or a "single source of truth," according to Anwesha Chakraborty, manager of the ISTAR core support team.

Implementation was a challenge. In its original form, SAP is a powerful but generic product. With CtrlS as a cloud service provider, Wipro was roped in to tailor it for the layered workflows of a research-intensive campus. The ISTAR team serves as the bridge between the campus, Wipro, and other support partners. "Departments often communicate their needs in business terms," Anwesha explains. "Wipro speaks in a more technical language. Somebody is needed in between who can speak both languages to connect the two sides – translating business requirements into technical inputs and explaining technical constraints back to the departments in a way that they can easily understand."

The rollout happened in two phases. The first, launched in June 2019, covered finance and accounts, sponsored projects, human resources and payroll, and stores and procurement. The second phase added academics, and hostel and mess management, which took more time as policies are prone to constant changes in these departments. It took nearly three years to complete campus-wide implementation.

Photo: Shravani Deoghare

The office for Project ISTAR under which SAP was introduced as a unified system to support students, faculty members, and staff through a single, shared database

Acceptance was not immediate. "The first thing that I heard from the user community was that it's not intuitive at all," Anwesha recalls. Over time, the ISTAR team reshaped the system – simplifying the interface and building an IISc-specific workflow, only to begin again as policies changed. "It is a constant cycle," Anwesha admits.

What often goes unnoticed is the continuous daily effort … staying alert, troubleshooting quickly, and anticipating issues before they grow

The team's job is to keep SAP's most routine functions running smoothly – from raising local purchase orders and foreign procurements to academic course registrations – and being on the lookout for complaints or service requests on the SolMan portal (Solution Manager for SAP). What often goes unnoticed is the continuous daily effort behind this stability: staying alert, troubleshooting quickly, and anticipating issues before they grow. Technical glitches here can quickly turn into panic for campus users. At the same time, the team remains focused on continuous improvement, adding new features and refining existing ones to meet evolving campus requirements.

"People would come with their frustration, and we [have to] accept it," Anwesha says. "We cannot be defensive." The ISTAR team puts this into practice by guiding users through the interface when they face difficulties. To strengthen this support, ISTAR is undertaking a major project: migrating from the 2017 version of SAP to the latest 2025 release, which promises a more intuitive interface and improved ease of use. This transition will be led directly by SAP rather than Wipro, an evolution expected to accelerate the rollout and testing.

But keeping departmental workflows running requires a more basic requirement: connectivity. Up a flight of stairs is the team responsible for keeping the campus online.

Staying connected

On the first floor, in the right wing of the building, sits TINA, the Telecom and Internet Access group. This unit predates DIGITS, quietly improving network infrastructure, centralising email databases, and adding layers of security on communication systems.

Walking into this wing, one can find a ring of cubicles with monitors surrounding a central workbench holding spare router switches, Wi-Fi devices, and cables. The staff are separated into two units within TINA: Network and Hardware Support, and Email Support.

The team is led by Rahul Nair, who is rarely found at his desk. Instead, he is walking with a phone pressed to his ear, diving in and out of meetings, or out for a site visit on campus.

On a day which Rahul considers calm, his to-do list involved visits to the Centre for Neuroscience to plan new optic fibre routes, the Department of Electrical Communication Engineering for Wi-Fi upgrades, and the Interdisciplinary Sciences building to inspect damaged optic fibre cables. This is in addition to his many meetings and tasks within DIGITS.

Photo: Shravani Deoghare

Rahul Nair (second from right), along with staff members from TINA and other vendors, inspecting a dug-out optic fibre cable outside the Division of Interdisciplinary Sciences building

At present, much of his attention is focused on a campus-wide Wi-Fi upgrade. The new routers being installed are expected to increase speeds from 70 Mbps to over 450 Mbps for older mobiles or laptops, and up to 1.3 Gbps for higher-end devices. Designing network infrastructure, Rahul insists, is not about planning for the average load but for peak traffic.

Currently, IISc has nearly 64 kilometres of optic fibre cables running underground, laid out in 12 interconnected rings with 24 termination points. On paper, it is robust. On the ground, it is constantly at odds with civil construction. Rahul notes how one of the underground fibres to the Division of Interdisciplinary Sciences building was cut during a dig-out and needed repair. In the same vein, the installation of new Wi-Fi routers becomes a challenge of optimisation. In the hostels, for example, the layout poses a problem – the placement of rooms in newer hostels, designed for improved privacy with staggered doors, has made them “not very Wi-Fi friendly.” The stone buildings are not helpful for Wi-Fi and 4G/5G mobile signals.

Network engineers at TINA monitor connectivity across the campus and respond when departments report internet or LAN failures, isolating issues that may stem from damaged cables, misconfigured switches, or deeper upstream problems.

Alongside network support, TINA’s email team manages another critical layer of infrastructure: user accounts. From creation and maintenance to shared mailboxes and extensions, the team supports over 22,000 active accounts along with alumni accounts, a task made manageable by centralising previously fragmented ERNET domains under Microsoft 365. Email support is also a frontline defence against security threats.

One of the most visible changes fronted by the team was the rollout of multi-factor authentication (MFA) for email accounts. Before MFA, in one incident, nearly 900 phishing emails were sent one morning from a hijacked account; by the time the system intervened, 22 recipients had already clicked malicious links. After MFA, when a faculty member clicked a phishing link, the account was immediately disabled. “Even if the hacker had the credentials, they couldn’t do anything,” says Rahul. “You won’t believe the number of brute-force attacks we see.”

For years, cybersecurity at IISc was handled within TINA, but the rise of cyberattacks in recent years made it clear that security needed undivided attention. Thus came the Information Security Office (ISO), led by Joy Kuri, Professor at the Department of Electronic Systems Engineering and the Chief Information Security Officer. This team works across the corridor, in the left wing of the first floor.

The ISO team continuously monitors the campus network, automated systems flag suspicious activity – connections to malicious websites, abnormal traffic, infected downloads – and every alert is checked manually. When needed, the team contacts users directly, cleans compromised systems, and, in rare cases, temporarily cuts off network access to contain risk.

A new website or service under the iisc.ac.in domain must first pass Vulnerability Assessment and Penetration Testing (VAPT) conducted by the ISO team. Weaknesses identified by thorough scans are reported and fixed, and only then is the website cleared to go live.

With security embedded into every new service before it goes live, the focus shifts from protection to creation. On the same floor, the software development team takes on the task of building the portals, websites and maintaining the cloud infrastructure that the campus depends on.

Custom portals

The software development team, hired from Integra Micro Software Services (an external technology partner), has worked with IISc for nearly a decade. The team is led by Robin T Daniel.

A wide range of campus processes that operate within departments require custom-built portals to formalise workflows or collect data digitally. For instance, the receipts portal serves as IISc’s payment gateway for all payment transactions. Earlier, departments hosting conferences, events or seminars had to coordinate separately with the finance office to create a debit head and rely on third-party websites to collect and track paid registrations. The receipts portal eliminates these steps by providing an interface that allows end users to make payments directly. The team maintains over 120 applications, some of them built by DIGITS.

One of the largest ongoing efforts is the new Admissions Management System. It is designed to manage admissions to all types of programmes centrally, eliminating the need to maintain multiple platforms for various sessions and applicant groups. The applicant-facing portal has gone live and is accessible globally, while internal portals support academic offices and departments in managing interviews, selections, and document verification.

"In projects like the Admissions Management System (AMS), clarity grows as we build. Requirements can evolve mid-way, so the real challenge is responding thoughtfully – absorbing new complexity without losing pace or quality," Robin says.

"The period before a go-live is when the team becomes most aligned – developers, testers, and the Committee working closely, double-checking every detail. That shared focus and responsibility is genuinely meaningful to me," he adds.

Moments like these reflect how DIGITS functions as a whole. From the ground floor, where requests first arrive and are routed, to the teams maintaining SAP, campus networks, security, and portals – the department is a linked system. Each team absorbs its own pressures, but the work only holds together through coordination.

Seated in the same left wing of the office is Harikrishnan Muthalanghat, a Senior Technical Consultant who has been working at DIGITS since July 2014. He is responsible for managing the ScholarOne Thesis Processing System. "The work includes maintenance, providing support to students, Deans, and caseworkers, and also generating periodic status reports," he shares.

He also handles maintenance and user support for Google Workspace (formerly known as G Suite), a cloud-based suite integrating multiple Google applications through a unified gateway system, and

Photo courtesy: DIGITS

The DIGITS team that keeps all campus digital processes running smoothly

manages the SharePoint-based intranet system, which functions as a centralised gateway to multiple information portals of IISc.

Keeping the spine aligned

At the centre of DIGITS' operations is the Chief Information Technologist, Srinivas Anand Rao. If individual teams keep systems running, Srinivas' responsibility is to ensure it all makes sense as a whole: technically, financially, and administratively.

Much of Srinivas' work involves navigating a rapidly shifting technology landscape. For instance, the campus is heavily dependent on Microsoft's services and large storage benefits. A recent change in Microsoft's storage policy dramatically reduced cloud space allocations (from 1 TB to 100 GB) and increased costs. What was once a predictable dependency is now a financial decision. "We cannot afford to continue in one domain blindly. We have to continuously look at alternatives," he says.

Srinivas also deals with vendor negotiations, license renewals, purchase orders, and committee approvals. Licensing models that were once life-long are now subscription-based, demanding frequent justification for renewal. Such procurements must pass through multiple levels of approval, including the DIGITS Purchase Committee. "If Microsoft changes a policy, I have to explain not just *what* changed, but *why* we are continuing with them, what alternatives exist, and what value the Institute is getting," he says.

Procedural delays are inevitable. Over time, trust and familiarity have enabled such approvals to move faster. "My biggest asset here is my relations with people now. For example, we were able to release the last Microsoft purchase order in two working days with a lot of changes," he admits.

Beyond managing the present, Srinivas emphasises on the long-term sustainability of the department. "Over the last couple of years, DIGITS has taken on many additional responsibilities, and the team has grown in size and capabilities," he says. There is a deliberate effort to build a better workplace culture, where staff welfare, engagement, and upskilling are essential. "Attrition is a concern," notes Srinivas, pointing to DIGITS' emphasis on bringing critical work in-house. "It may not give immediate benefits, but over time, we will be able to self-sustain."

Most of the work at DIGITS is unseen, although it is what keeps the Institute functioning smoothly. The campus population probably never thinks about DIGITS when things are working as they should be. That invisibility is the department's greatest success and its heaviest burden.

"It is a challenge for any support department to be noticed at all when things go smoothly, but it will be the first one to be noticed when something doesn't go well," Srinivas reflects.

And yet, every day, DIGITS holds these systems together, quietly keeping the Institute's digital spine aligned. Even when the lights dim and the last stragglers pack up for the day, the servers continue to run. Somewhere on campus, someone is always about to click 'submit' with near certainty that the system will work.

Almost always, it does.

Shravani Deoghare is a fourth year Bachelor of Science (Research) student at IISc and a science writing intern at the Office of Communications

(Edited by Sandeep Menon, Abinaya Kalyanasundaram)

Dark Side of the Genome

- Parth Kumar

Image courtesy: Theodore Palser/Publicdomainpictures

There's more than meets the eye when it comes to 'junk' DNA

In September 2012, as the final papers from the ENCODE (ENCyclopedia Of DNA Elements) project rolled out, the mood among many molecular biologists was triumphant. After more than a decade of coordinated experiments across dozens of laboratories, the consortium made a bold announcement: a whopping 80% of the human genome showed signs of biochemical activity. Long stretches of non-coding DNA, which had earlier been dismissed as 'junk', actually seemed to be humming with life – binding proteins, producing mRNAs, and shaping the behaviour of other genes. "Junk DNA is Dead!" claimed one of dozens of newspaper headlines around the world. Eric Lander, a luminary of the Human Genome Project, hailed ENCODE as the "Google Maps of the human genome."

But not everyone was celebrating. Dan Graur, an evolutionary biologist at the University of Houston, USA, read the claims with mounting disbelief. To him and many others, ENCODE had made the dangerous mistake of equating molecular "busy"-ness with real biological function and purpose. "We beg to differ," Graur shot back in a critique in 2013. "ENCODE is considerably worse than even Apple Maps."

What followed was not a quiet academic disagreement, but an open brawl: barbed blog posts, scathing papers laced with sarcasm, and a debate that spilled well beyond the pages of journals.

At the core of this brawl were two deeply different views of the genome. One side saw extensive biochemical activity as evidence that a large part of our DNA isn't 'junk' as widely believed before, and is extremely functional and finely regulated. The other side, however, envisioned a genome shaped largely by evolutionary accidents, where activity does not automatically mean importance or function.

The brawl also brought into sharp focus a debate that had been unfolding for decades: Can 'junk' DNA, that does not code for any protein, even be useful? At the same time, questions intensified after the Human Genome Project confirmed, in 2001, that barely 2% of human DNA encoded proteins. Was 98% doing 'nothing'?

More than two decades later, scientists in the field are still struggling to pin down the answer to a deceptively simple question: What does it even mean for DNA to 'do' something?

Shaped by evolution

The idea of 'junk' DNA emerged in the late 1960s from a group of evolutionary biologists who were grappling with a puzzle: Why do some organisms have vastly larger genomes than others – containing far more DNA base pairs – without the organism appearing any more complex?

To repeat a cliché, DNA is the "blueprint" of life. It instructs cells to make proteins that provide structure, catalyse reactions, transport molecules, send signals inside and outside the cell, and defend cells against pathogens. At a higher level, what proteins are made determines what the organism looks like and functions as a whole – its phenotype.

When cells divide, DNA is duplicated and distributed equally between the two daughter cells – but sometimes errors during this duplication can create mutations, which alter the sequence of DNA. If this happens in a sequence that codes for a critical protein, it could hamper the protein's function and, in effect, the organism's survival. Sometimes, a mutation could surprisingly make the protein more efficient at its job, boosting the organism's survival. Thus, random mutations create variations in a population on which natural selection can now act – mutations that are harmful don't stick around in the genome (because the organism dies), and those that are helpful stay around for a longer time, showing up in more and more organisms as they reproduce.

When scientists were studying 'simple' organisms like lungfish and salamanders, they were puzzled to find that these have genomes many times larger than that of humans. If DNA was mainly a set of instructions for building an organism, this made little sense. The complexity of an organism should scale with the length of the instruction manual, yet nature seemed to be handing out the longest manuals to some of its simplest characters. Something else had to be going on.

One of the first to articulate this mismatch was Japanese-American geneticist Susumu Ohno. In 1972, Ohno proposed that much of the DNA in large genomes was simply not doing anything useful. His argument was based on evolutionary logic, and the existing observations that organisms have large amounts of repetitive and highly variable DNA. If a DNA sequence does not affect an organism's survival or reproduction, natural selection has little reason to remove it. Over time, such 'neutral' sequences could accumulate, bloating the genome without adding new functions. Ohno famously referred to this excess as 'junk DNA.'

Over time, 'neutral' sequences could accumulate, bloating the genome without adding new functions. Ohno famously referred to this excess as 'junk DNA'

"The term 'junk' suggests a legacy of something that was of use, has no immediate use now, but may acquire a useful function in the future, which is what Ohno meant," explains Subhash C Lakhotia, Distinguished Professor at Banaras Hindu University. Meanwhile, around 1980, Francis Crick and others published a series of papers in *Nature* calling this "selfish" DNA. "They thought that although this DNA is of no use to the host cell in which it stays, it can't be thrown out. And because it's selfish, it just continues to replicate and stay in the genome," Subhash adds.

Imagine repeatedly copying a long document by hand, over generations. Glaring errors – a missing paragraph or a garbled sentence – would be corrected immediately. But tiny changes – an extra space or a duplicated word – slip through because they don't change much in the grand scheme of things.

In the late 1960s, Japanese biologist Motoo Kimura proposed his "neutral theory of molecular evolution," arguing that much of DNA evolves in exactly this way. Most mutations are neither beneficial nor harmful; they are effectively invisible to natural selection. Genomes accumulate these neutral changes simply because there is no

Image: Ryan Ray

Microscope image of dividing onion root tip cells with chromosomes visible as dark threads being pulled apart

The onion has feelings? (The C-value paradox)

"The onion test is a simple reality check for anyone who thinks they can assign a function to every nucleotide in the human genome. Whatever your proposed functions are, ask yourself this question: Why does an onion need a genome that is about five times larger than ours?"

– T Ryan Gregory, Canadian evolutionary biologist

For a long time, biologists naively assumed that the amount of DNA an organism has should roughly track how 'complex' it is – more moving parts should mean more DNA. Humans, with our big brains and existential crises, should be right near the top.

Enter the onion. When scientists began measuring genome sizes in the mid-20th century, they discovered that the common onion (*Allium cepa*) carries about five times more DNA than a human being. Not five times more genes, just more DNA. This discovery became a running joke in genetics, often called the 'onion test': if more DNA meant biological sophistication, then onions should be composing symphonies and filing tax returns.

This striking lack of correlation between genome size (called the C-value) and organismal complexity is known as the C-value paradox. It suggests that large portions of DNA could vary in the total amount between species without obvious consequences for complexity, anatomy, or intelligence. Salamanders, lungfish, lilies, and onions all seem to be hoarding DNA, while humans and other mammals make do with relatively streamlined genomes. Whatever all that extra DNA is doing, it clearly isn't turning onions into philosophers.

strong pressure to remove them. Duplicate copies of genes that lose function still continue to persist in the genome. Other sequences arrive as genomic hitchhikers inserted by viruses into our DNA. Special sequences called transposable elements copy and paste themselves across chromosomes. The result is a genome which looks less like a blueprint and more like a patchwork quilt, stitched together over time using scraps.

From this perspective, junk DNA is not a mistake. It is exactly what you expect when evolution works without a quality-control engineer. Natural selection is powerful, but it is not perfect – it does not work like an engineer; it works like a tinkerer, as French biologist François Jacob put it.

In organisms with low population sizes, where there is little competition for space and resources, even slightly deleterious mutations can be just as easily maintained over generations as neutral ones, increasing the amount of DNA that doesn't 'do' anything. "Most species with large genomes today have had low population sizes for much of their history, and that explains why they can have lots of slightly detrimental junk DNA," says Laurence Moran, Professor Emeritus at the University of Toronto.

For decades, this view was widely accepted because there was no way to systematically test what non-coding DNA was doing. The term 'junk' represented non-functional, not useless. But soon, that changed when new technologies started revealing something unusual across the genome.

Identical genomes, distinct cells

Around the same time as Ohno and Kimura, scientists started realising that genes were only a small part of what actually shapes a cell. After all, if all the cells of our body carry the same genes, how could they behave so differently across tissues, developmental stages, and environments?

The first semblance of an answer began to appear in the 1960s and 1970s, when geneticists began discovering that genes were surrounded by mysterious control regions. In 1961, François Jacob and Jacques Monod proposed the idea of gene regulation – certain DNA sequences outside the genome could turn genes on and off, controlling whether and when they made proteins. It was an early hint that some DNA elements could have roles beyond coding for proteins.

In the 1980s and 1990s, scientists began uncovering DNA elements scattered across the genome that act like switches. Enhancers, first identified in the 1980s, were often found to sit far from the genes they control, sometimes hundreds of thousands of base pairs away. These sequences loop through space to bind to genes and boost their activity in specific tissues. A single enhancer can control whether a gene is active in the brain but silent in the liver. Suddenly, vast stretches of non-coding DNA were revealed as a regulatory wiring system.

Parallely came the RNA revolution. For a long time, the only thing we knew (and believed) was that DNA is converted into mRNA, an intermediate messenger molecule, by a process called transcription in the nucleus of cells. mRNA then moves out of the nucleus and is translated to make proteins.

By the early 2000s, hundreds of non-coding RNAs were discovered in humans, plants, and animals, acting as molecular dimmer switches that fine-tune gene expression

But in the 1960s, scientists started finding RNA that stayed in the nucleus and never exited into the cytoplasm. "Since translation can only happen in the cytoplasm, the implication was that these RNAs don't get translated," explains Subhash. "But then the bigger question was: What are they even doing there?"

The question remained unanswered until 1993, when American scientists Victor Ambros and Gary Ruvkun studying tiny worms made the startling discovery that small RNA molecules – later called microRNAs – could control gene activity without ever becoming proteins. What had once been dismissed as transcriptional noise turned out to be a powerful regulatory system. By the early 2000s, hundreds of these non-coding RNAs were discovered in humans, plants, and animals, acting as molecular dimmer switches that fine-tune gene expression.

Non-coding DNA and RNA also shape the physical structure of the genome inside the cell. DNA isn't laid out like a straight line – it folds, loops, and packs into three-dimensional forms. "Some non-coding sequences act as anchors and scaffolds for this folding, helping

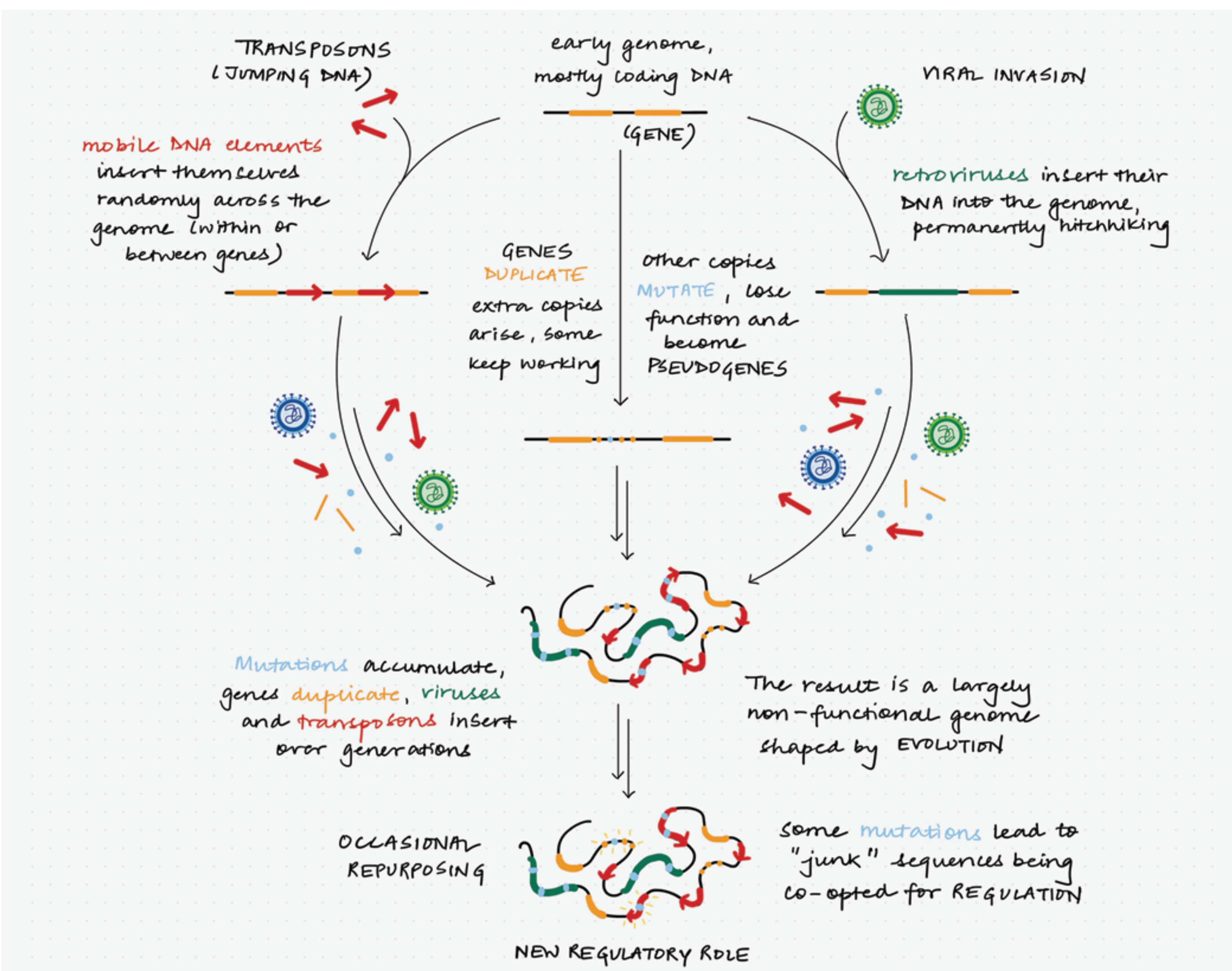
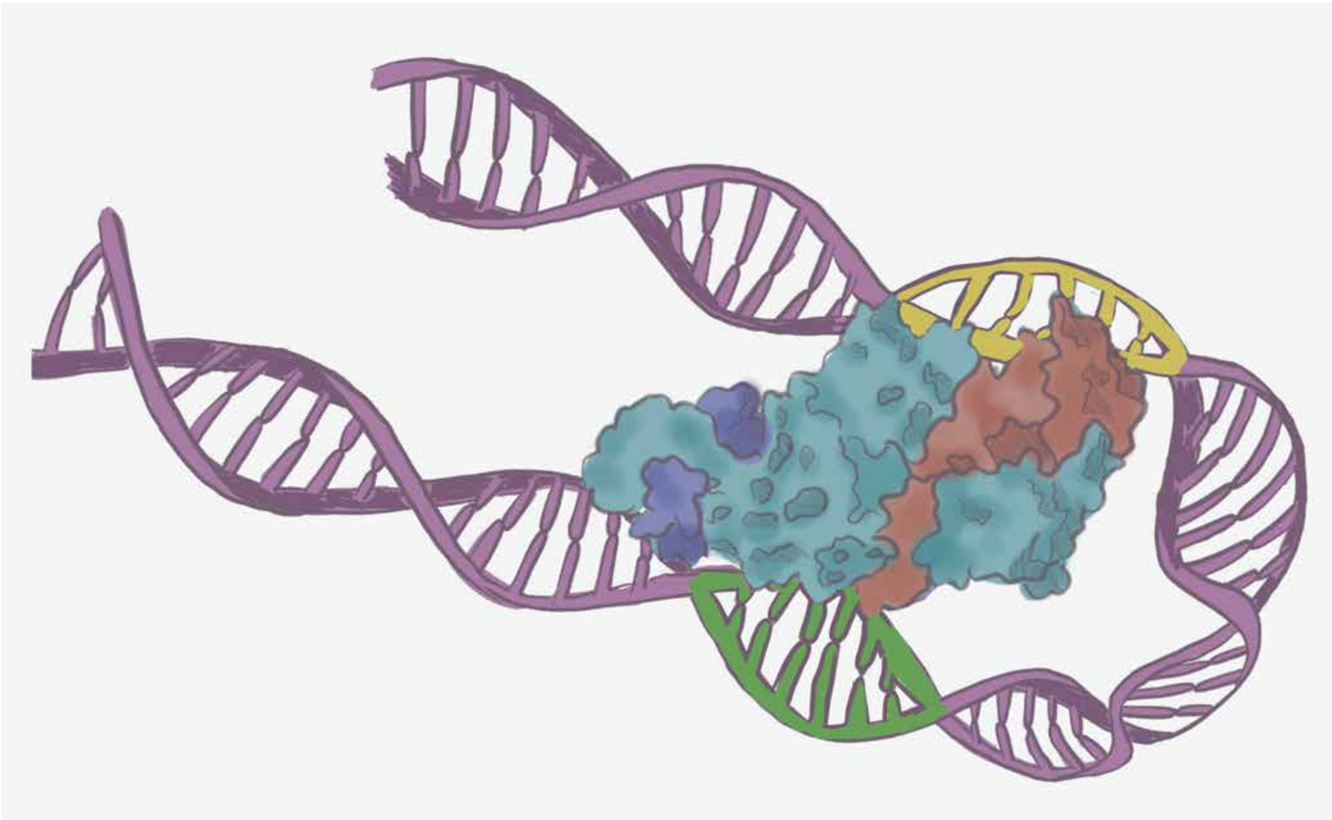


Illustration: Parth Kumar

Junk DNA accumulates in the genome passively, resulting in a genome which resembles a patchwork quilt. Some pieces may acquire function later, but most do not

Illustration: Ashmita Gupta



Enhancers (yellow) are non-coding DNA elements that bind the transcription protein complex and loop the DNA, bringing the complex into contact with the target gene (green), increasing the likelihood of transcription

organise the genome in space so that the right genes can interact with the right regulatory elements," explains Saumitra Das, Professor at the Department of Microbiology and Cell Biology, IISc. Other sequences can influence how tightly a DNA sequence is folded up.

These functions of non-coding DNA may seem intuitive today, but for a long time, they were anything but obvious, which made studying them harder.

Subhash underscores this with an example. Much of his earlier work was on a gene in the fruit fly *Drosophila* called *hsrω*. "I was looking for what protein it makes, and then it turned out it doesn't make a protein at all," he narrates. This was in the 1980s, around the same time that Crick first talked about selfish DNA, and *hsrω* seemed like it fit the brief. "But I didn't believe that this was a selfish gene, and I kept on pursuing it – and people kept asking me why," says Subhash. "My competitors abroad, who had started working on this gene because of our initial work, had to give up because they wouldn't get funding to work on this seemingly selfish gene. But fortunately, I did."

What Subhash found was that *hsrω* makes multiple long non-coding RNAs which could bind to a variety of RNA-binding proteins called hnRNPs, making these proteins unavailable for binding to their real targets and regulating whether or not they would be available to perform their functions. Over the next few decades, Subhash uncovered other functions of *hsrω* in development and stress responses.

But even though evolutionary biologists have never really denied that some non-coding DNA matters, they were still wary of attributing "usefulness" to it. And when the Human Genome Project announced its findings, things really came to a head.

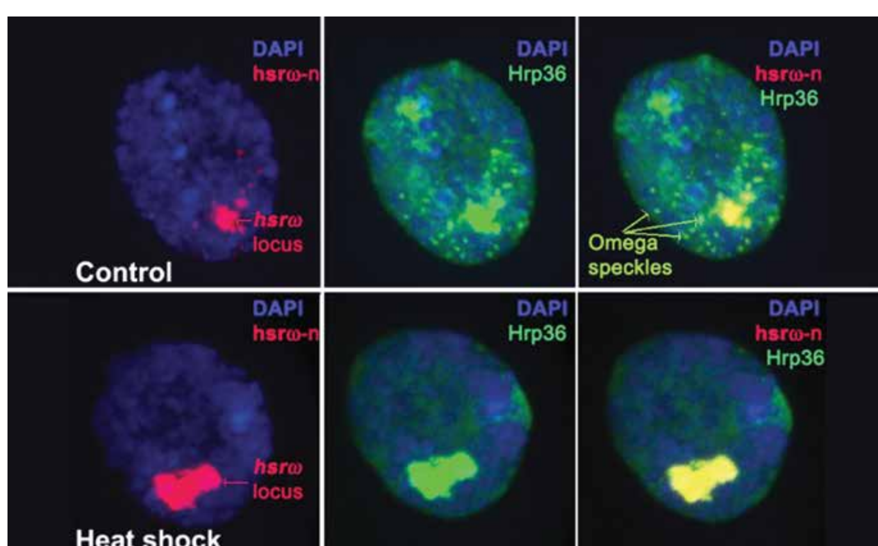


Image: Sanchari Ghorai, Subhash C Lakhotia's lab

Long non-coding RNAs produced by hsrω *bind to the protein Hrp36 and are visible as bright, dense spots called omega speckles in the nucleus of the fruit fly* Drosophila

Hunting for purpose

At the turn of the millennium, something changed dramatically. When the first draft of the human genome sequence was published in 2001 with a lot of fanfare, it was the first time scientists could see the genome as a whole. It was expected to settle long-standing questions about genetic complexity. Many anticipated millions of genes to exist. Shockingly, the number turned out to be closer to a mere 20,000 – not much more than in the genome of a worm or a fly.

The surprises didn't end there. Only about 2% of the genome, it seemed, coded for proteins. The remaining 98% was composed of repeated sequences, duplicated fragments, and vast stretches with no obvious role. Far from undermining the idea of junk DNA, the genome sequence seemed to confirm evolutionary predictions – large, complex organisms carried large amounts of DNA that did not appear to be under the influence of natural selection.

After the Human Genome Project, evolutionary biologists continued to be cautious, but molecular biologists began to push a bold narrative … they claimed that perhaps very little of the genome is truly junk at all

This abundance of ostensibly useless DNA created both opportunity and unease. Evolutionary biologists continued to be cautious, but molecular biologists began to push a bold narrative: as evidence mounted for the importance of non-coding DNA, they claimed that perhaps very little of the genome is truly junk at all.

Individual examples of non-coding function were already well established, but they were discovered piecemeal, one system at a time. What was missing was a genome-wide view. As new technologies made it possible to survey the entire genome at once, a new ambition to move beyond sequence, map activity, and probe regulatory and structural roles of non-coding DNA emerged.

From this excitement, ENCODE was born. Launched in 2003 by the US National Human Genome Research Institute, the project brought together hundreds of researchers across dozens of labs. It aimed to catalogue every detectable functional element in the human genome using a uniform experimental framework. ENCODE set out to annotate the DNA sequence that had come out of the Human Genome Project – mapping where proteins bind, where RNA is produced, and which regions act as regulatory switches. What they sought was clear proof of usefulness or "function" for non-coding DNA.

But the problem was that ENCODE's definition of function was somewhat vague. According to the researchers, for a DNA segment to be "functional," it needs to be either transcribed by RNA, bound by transcription factors (the proteins that control gene expression) or be marked by regulatory signals and modifications (like methylation). If a DNA segment binds to transcription factors, it is functional. So, other DNA segments that bind to transcription factors should also be functional. This is what they presumed.

Driven by these ideas, and after a decade of large-scale experiments, the ENCODE consortium published a coordinated set of more than 30 peer-reviewed research papers in *Nature, Science,* and *Genome Research* in 2012. Together, these studies mapped patterns of transcription, protein binding, chromatin modification, and DNA accessibility across dozens of human cell types.

Based on the prevalence of this biochemical activity, the consortium concluded that 80.4% of the human genome showed evidence of "function."

In an accompanying editorial, Stella Hurtley, a senior editor of the journal *Science* wrote, "No More Junk DNA."

The function wars

At the University of Houston, Dan Graur was upset. ENCODE's statement went against decades of evolutionary theory. According to the junk DNA model, it was the other way around: Only about 10% of the genome is evolutionarily conserved across species and selected for – which should be the functional portion – with the remaining 90% being 'junk'. "ENCODE's estimate of 80% [functional DNA] implied that at least 70% of the genome is invulnerable to harmful mutations," Graur wrote in a journal article in *Genome Biology and Evolution* in 2013. "Either because no mutation can ever occur in these so-called functional regions, or because no mutation in these regions can ever be deleterious."

Graur famously compared this to claiming that a television set left on and unattended will still be in working condition after a million years because no natural events, such as rust, erosion, static electricity, and earthquakes, can affect it.

This is absurd – clearly, there was a flaw in ENCODE's argument. A DNA segment

Evolution, the tinkerer

When biologists talk about the genome as messy or cluttered, they aren't really accusing nature of incompetence. They are describing how evolution actually works. In his 1977 essay titled *Evolution and Tinkering,* French biologist François Jacob argued that natural selection does not behave like a careful engineer working from a blueprint. Instead, it improvises with whatever happens to be lying around. "It works like a tinkerer … using pieces of string, fragments of wood, old cardboard – odds and ends – to produce something that merely works," he wrote.

This tinkering leaves behind a genome full of redundancies and long stretches of DNA that appear unnecessary. The result is not elegance or efficiency, but adequacy. Once something works well enough to pass on genes, there is little pressure to tidy up the rest – and the genome is inherited, patched, and passed on, piling up clutter over generations.

"Evolution is shaped by randomness and unpredictability," Moran wrote in his book *What's in Your Genome?* "Genomes reflect that – they are sloppy and not exquisitely designed like a Swiss watch."

can display a property without necessarily having the associated function. A random sequence may bind a transcription factor, but that may not result in transcription into RNA. Cells are noisy places; enzymes bind DNA promiscuously, RNA is transcribed and degraded without consequence. Just because a sequence *does something* does not prove a biological purpose, and it certainly does not mean that the organism would suffer if it were removed.

Thus began the function wars, marked by blunt critiques, sharply worded papers, and an unbridled willingness among scientists to be publicly, and unapologetically, combative.

Just because a sequence does something does not prove a biological purpose, and it certainly does not mean that the organism would suffer if it were removed

Don't shoot the gene, blame the switch

In the late 1990s, geneticists were puzzled by families in which children were born with extra fingers or toes – a condition known as polydactyly. Genetic tests came back clean. The *SHH* gene, which plays a crucial role in limb development, was completely normal. There was no broken protein, and no obvious culprit.

The actual culprit turned out to lie nearly one million DNA base pairs away from the *SHH* gene – in a stretch of non-coding DNA. This was the ZRS enhancer sequence, which acts like a remote switch and turns the *SHH* gene on at the right place and right time during embryonic development. In patients with polydactyly, tiny mutations in the ZRS enhancer caused *SHH* to switch on in the wrong place. The gene itself worked perfectly, but it was expressed where it shouldn't have been. The result was an extra signal telling the limb to grow additional digits.

This added weight to the growing recognition that a disease isn't always caused by a mutated gene making a broken protein. "In many cases, the protein itself is perfectly intact," explains Saumitra Das. "What goes wrong is when, where, or how much of it is made." In other words, the problem often lies not in the parts, but in the switches that control them – and this can have dramatic effects on the phenotype.

Similar regulatory mishaps are now being uncovered across medicine. In certain cancers, subtle changes in regulatory regions or non-coding RNAs can push growth genes into overdrive. In neurological and autoimmune disorders, genes may be activated too early, too late, or in the wrong cells altogether. "For patients and clinicians, this has expanded the diagnostic searchlight beyond genes alone," says Saumitra. This is also a stark reminder that junk DNA may or may not matter much, depending on which side of the debate you are – but when it matters, it can matter profoundly.

"In the absence of any solid evidence that a given sequence is functional, the default explanation has to be that it is not," believes Moran. This is why countless philosophers and experts in molecular evolution were upset with the 2012 ENCODE papers, and it is why they were retracted in 2014. Unfortunately, most scientists didn't read this retraction.

"A large part of the problem isn't about biochemical activity. It's about a misunderstanding of what the debate is about," explains Moran. "Dozens of papers that talk about non-coding DNA today say that scientists like Susumu Ohno and Motoo Kimura were really, really stupid."

According to this modern caricature, Ohno and Kimura – writing in the 1960s and 1970s – supposedly believed that the only functional DNA in the genome was protein-coding DNA, and therefore dismissed everything else as junk. Contemporary authors then show that a tiny bit of non-coding DNA has a function and claim that this disproves the entire concept of junk DNA.

"The ignorance of these modern scientists is frustrating," Moran says vehemently. "The original proponents of junk DNA were not stupid. They knew about all kinds of non-coding DNA that is functional. No knowledgeable scientist ever said that all non-coding DNA was junk, and anyone who makes such a false claim is simply demonstrating their ignorance of history."

When the ENCODE results were published in 2012, John Stamatoyannopoulos, a leading figure in the consortium, believed that their findings would necessitate the rewriting of textbooks. "We agree," Graur retorted in 2013. "Many textbooks dealing with marketing, mass-media hype, and public relations may well have to be rewritten."

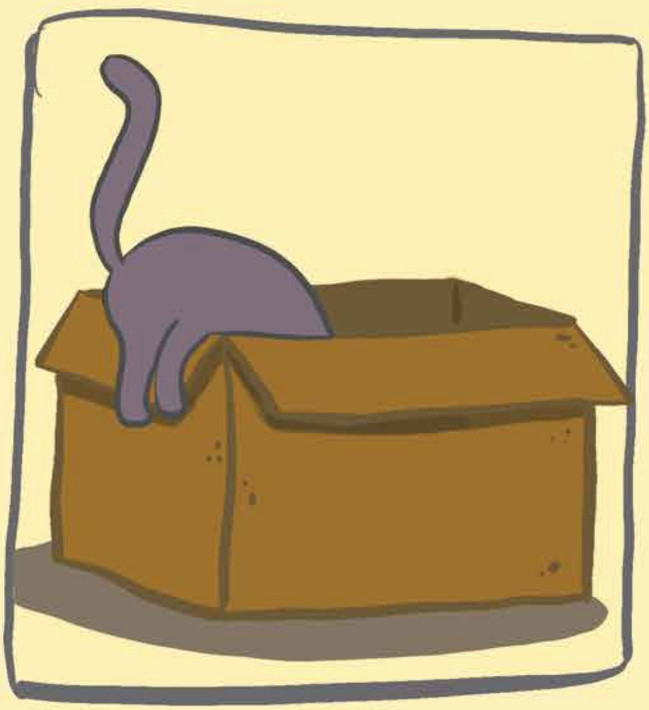
All of this matters because language shapes expectations. To the public, and even to young researchers, the idea that almost nothing in the genome is waste can smuggle in a comforting but misleading assumption: that biology is optimised, tidy, and intentional. Evolutionary biologists have long argued the opposite. The genome is not a masterpiece engineered from scratch, and is, in fact, full of redundancies and leftovers. When this messiness is flattened into a story of near perfection, something essential about how evolution works is lost.

"The general public and many scientists believe that humans are designed. But people should know that there's another worldview out there – composed of people like me who do not think the world looks designed," says Moran. "We think the world looks sloppy and inefficient, and that this is exactly what you would expect if life evolved."

Parth Kumar is a third year BSc (Research) student at IISc and a former science writing intern at the Office of Communications

(Edited by Ranjini Raghunath)

Quantum Cat



Text: Sayooj P
Illustrations: Ashmita Gupta

Is it dead? Is it alive? Surely it has to be either, right?

Consider a cat in a box – let's call him Meownstein. Along with him inside the box, there is a radioactive sample (which can decay to produce radiation) and a poison vial with a radiation sensor. If the sample decays, the sensor will break the vial open, killing Meownstein. If not, he lives for another day.

Radioactive decay, however, is not simple; it depends on the stability of the core of the atom, called the nucleus. The subatomic particles within the nucleus are not governed by the classical laws of physics, such as the intuitive Newton's laws of motion. Instead, their rules are set by quantum mechanics. Quantum laws are all about probabilities – they cannot predict how these particles will exactly behave, but they can suggest how they *could* behave.

Thus, quantum mechanics lets us precisely calculate the probability of the sample decaying, and hence our cat surviving. But it cannot say for sure if and when exactly it will happen. Until one opens the box, the sample could both have decayed and not decayed, and Meownstein could be both dead and alive.

This is not the physical reality that we are familiar with – last we checked, cats are usually either dead or alive, and often, hopefully, the latter. In 1935, in a letter to Albert Einstein, Austrian-Irish physicist

Erwin Schrödinger proposed this scenario as a thought experiment, to expose one of the many situations that are allowed mathematically by quantum mechanics but seem absurd in our classical view of the world. Since then, Schrödinger's cat has become one of the most popular thought experiments in theoretical physics, appearing in T-shirts, science fiction shows, and even smileys – ":):" looks both happy and sad at the same time.

Quantum laws are all about probabilities – they cannot predict how these particles will exactly behave, but they can suggest how they could behave

Over the years, physicists have tried hard to explain Meownstein's fate in a fashion that we can comprehend. Quantum laws apply to subatomic particles, but everything in this universe – including cats and humans – is made up of these particles. Surely then these laws should apply to the larger, macroscopic world as well? These attempts to reconcile quantum mechanics with our experience are known as "interpretations of quantum mechanics," but physicists still disagree on which interpretation is correct, or if they are even needed.

"All the interpretation problems of quantum mechanics arise from trying to convert the quantum theory to a classical description, while it is known from the outset that it cannot be done," says Apoorva Patel, Honorary Professor at the Centre for High Energy Physics, IISc. "Quantum theory only produces correlations (relations between variables) and not absolute results. Trying to convert [correlations] into absolute results causes problems of interpretation."

Nevertheless, the interpretations have endured, as they essentially attempt to answer the one question that quantum mechanics could not. Suppose you open the box and, luckily, find that Meownstein is alive, what was his state just before you opened the box?

Before closing the box

Before grappling with Meownstein's fate inside the unopened box, let's go back to the basics.

What do you picture when you hear the word "electron"? Till the 20th century, physicists thought of electrons, or other subatomic particles, as very tiny hard spheres hurtling through space. At any instant, these particles have a definite position and a velocity.

Quantum mechanics, however, provides a completely different picture. In 1924, French physics graduate student Louis de Broglie imagined that maybe, just maybe, particles behave like waves. Much like light, which behaves both like a hard sphere and like a wave, physicists describe electrons using an all-important mathematical quantity called the wavefunction. So, instead of a moving hard sphere, imagine a moving cloud that can constantly change its shape.

But what exactly is this electron cloud – described by the so-called wavefunction – made of? Schrödinger, who first formalised the idea, believed that it was a spread-out charge density. German-British physicist Max Born later corrected this, interpreting that a particle's wavefunction can tell you where the particle could be. It allows us to calculate the probability of finding the particle at a particular location, but it cannot accurately predict the particle's location. This is the probabilistic nature of quantum mechanics.

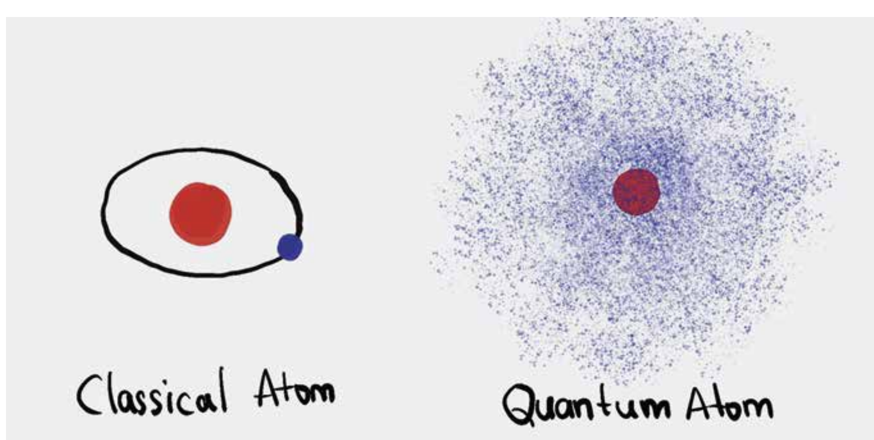
Thus, these clouds exist in a superposition of many positions – the particles are in a blend of all the states that they *could* be in. Multiple clouds can also be bonded via an invisible link, such that affecting one immediately affects the other, even at a distance. This is called quantum entanglement.

Now, back to the cat in the box. According to the most widely accepted interpretation of quantum mechanics, the radioactive sample's decay and the cat's fate are inextricably entangled – until we know about one, we cannot predict the other. And since we can never know for sure whether the radioactive sample decayed or not, we cannot predict the cat's exact fate before opening the box. This view was called the Copenhagen interpretation, the culmination of the philosophies of Niels Bohr, Werner Heisenberg, Max Born and others during 1924-27. Named after the city where Bohr and Heisenberg worked, the idea of this interpretation was to essentially give up on reality.

According to this, before you open the box, Meownstein's state has no classical, real-world analogue; only mathematics can help us comprehend it. As the sample is in a superposed state of decayed and not decayed, Meownstein is also in a superposed state of both dead and alive, but not entirely either.

"Every interpretation arises by adding something extra to the mathematical theory," says Apoorva. "And in the Copenhagen case, this is the observer."

According to the theory, when an observer opens the box, Meownstein's fate is immediately decided. They are the one bringing him to life, or if they're unlucky, the one who kills him. This is called quantum collapse – an ad hoc, instantaneous, destructive process that one triggers simply by opening the box and making a measurement. As long as one doesn't open it, the cat remains in a superposition.



The classical model of the Hydrogen atom (left), in which the electron (blue) revolves in a fixed orbit around the nucleus (red). In the quantum mechanical model (right), the one electron exists as a cloud around the nucleus. Studying the hydrogen atom was one of the most important problems that pushed forward the development of quantum theory

But how can something like Meownstein – a living, breathing furball of cuteness – be both dead and alive, and yet neither? Yet quantum mechanics, at least mathematically, allows for this to happen. This is the underlying reality of our world, according to the Copenhagen interpretation. "You just have to accept the extra features of quantum mechanics and live with it," says Apoorva.

According to the most widely accepted interpretation of quantum mechanics, the radioactive sample's decay and the cat's fate are inextricably entangled

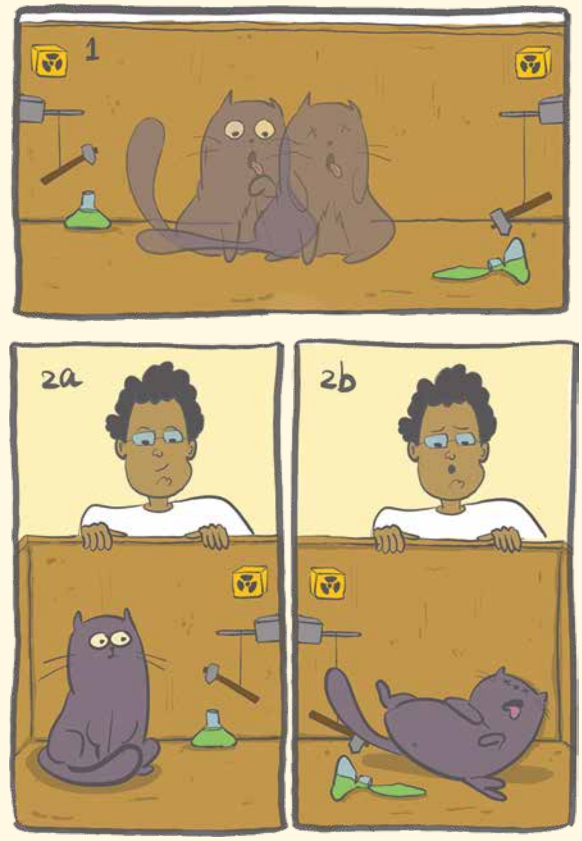
Schrödinger, however, did not fully agree with this interpretation. In fact, he devised the whole cat thought experiment to show how applying it to the macroscopic world leads to utterly absurd scenarios. A cat simply cannot be both dead and alive until an observer collapses its fate into one of them; hence, the interpretation must not be enough to explain the underlying reality of our world, he believed. Thus, the story continued.

A hidden variable

Albert Einstein, like Schrödinger, did not agree with the Copenhagen interpretation. In 1935, Einstein and Princeton colleagues B Podolsky and N Rosen published an article arguing that quantum mechanics itself does not provide a complete description of our reality. This was known as the EPR paradox. "According to Einstein, a physical theory is 'complete' only if every quantity in our physical reality can be explained by the theory," says Baladitya Suri, Associate Professor in the Department of Instrumentation and Applied Physics, IISc. "And any physical quantity in a system is called real if it can be measured or predicted with certainty, without disturbing the system."

But quantum mechanics thrives on uncertainty. The famous Heisenberg's uncertainty principle says that if you measure a particle's position exactly, you can never measure its momentum accurately. Due to this, Einstein believed that quantum mechanics was incomplete. With his famous slogan: "God does not play dice," Einstein strongly disagreed with the probabilistic nature of the universe. He believed that 'uncertainty' arose from the physicist's ignorance and that if the cat was found alive upon opening the box, it must have always been alive. Surely, the mere action of "seeing" cannot instantly give life or death to the cat. Then the question arises: Why can quantum mechanics not predict exactly that Meownstein was alive?

Some scientists believed that alongside the wavefunction, something else dictates the fate of Meownstein. However, this quantity or variable is hidden from the experimenter. Such theories are called the hidden variable theories, and Einstein believed that such a theory would predict everything in physical reality: a complete theory of everything.



According to the Copenhagen interpretation, the cat is in a superposed state (1) – both dead and alive – until an observer opens the box to check. It is thus the observer who causes the cat to be alive (2a) or dead (2b).

Physicists are still struggling to find a "Theory of Everything", but many hidden-variable theories have popped up over time. One example is Bohmian mechanics, first introduced by Louis de Broglie in the 1920s, and later modified by American physicist David Bohm in the early 1950s. In this, the hard, spherical (not cloud-like) particles are guided by a pilot wave – a hidden, immeasurable wavefunction that permeates all space. Further, just like Newton's laws, the dynamics of the particles and the pilot wavefunction are deterministic – knowing the present configuration lets us predict the exact future. Unfortunately, we do not know what the initial state of the universe was – the hidden variable – because of which we feel that outcomes of experiments are probabilistic. According to this or any other deterministic theory, all the particles of the universe follow fixed trajectories of motion that were decided since the beginning of their existence, implying that Meownstein's fate was pre-decided, but we only discovered it after opening the box.

Bohmian mechanics goes beyond Meownstein – it could apply to all of us (also made up of subatomic particles) as well. Metaphysically, this could mean that the story of all our lives has already been laid down since the beginning of the universe. We remain mere actors in a show that started with the Big Bang, and we simply act as the atoms dictate us to.

The Copenhagen interpretation, however, is not bound by this determinism. It suggests that the probabilistic nature of quantum mechanics, with all its absurdity, is perhaps what grants us all free will.

A universe of many worlds

Philosophical debates over free will aside, the Copenhagen interpretation had other dissenters as well. Some of them came up with a new idea that sounds even more like science fiction (if that were even possible). What if, instead of the observer collapsing the cat's fate into alive or dead by opening the box, the universe actually splits into two parallel possibilities when they open the box? One in which the cat is alive and one in which the cat is dead?

To understand, let's explore another thought experiment, a "meta" version of Schrödinger's cat.

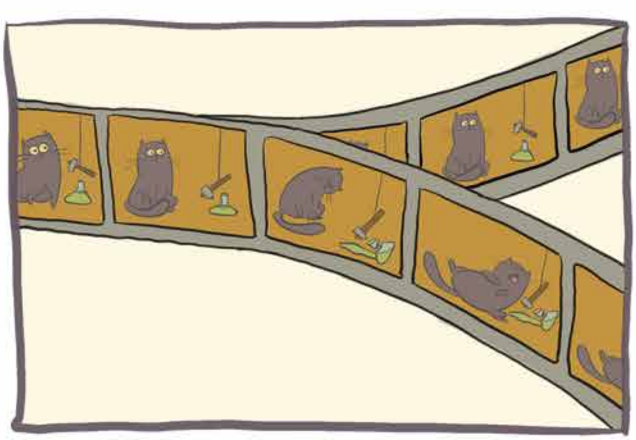
Suppose two reckless friends, Alice and Bob, experts in quantum mechanics, decide to test Meownstein's luck by performing Schrödinger's cat experiment. Alice performs the experiment in a closed room, with Bob standing outside, waiting for her results. After a while, she opens the box and finds that Meownstein is luckily alive and gladly writes this down in her notebook. Bob, however, does not know this. If he writes a wavefunction of the entire room, with Meownstein, Alice, and her notebook, it will be in a superposed state of "Meownstein alive; Alice happy" and "Meownstein dead; Alice mourning." To him, the entire room is Schrödinger's cat. He does not know which of these two states it is in until he opens the door and greets his friend. After, say, an hour, Bob opens the door and finds Alice's notebook. He then turns to Alice and says, "According to the Copenhagen interpretation, the cat has now collapsed into an alive state, and you have now collapsed into a happy state." Alice glares at him and replies, "What are you talking about? The collapse happened an hour ago."

The many-worlds interpretation ties the observer and the cat together, unlike in the Copenhagen interpretation

This is the Wigner's Friend paradox, first published by Nobel Laureate Eugene Wigner in 1961. He argues that, according to the Copenhagen interpretation, unless somehow the universe calls Alice the supreme observer, both she and Bob are equally correct. "The Copenhagen interpretation has this problem when you include multiple conscious experimenters," says Baladitya. "All of them will agree about the collapsed state of the system, but the question remains about when exactly the collapse happened. This is the context in which the many-worlds hypothesis gained popularity."

American physicist Hugh Everett conceived the many-worlds interpretation in 1957, proposing the idea of a wavefunction describing the entire universe. The modern version starts by removing the ad hoc idea of quantum collapse. A measurement is when the observer and the particle (or Meownstein in our case) together become entangled and branch out into each of its outcomes. When you open the box, the universal wavefunction splits into two non-interacting "branches" of "Cat observed alive" and "Cat observed dead". In a loose sense, two parallel worlds emerge. The entire universe exists in a superposition of two states – a universe where you find Meownstein alive, and one where you don't. The many-worlds interpretation ties the observer and the cat together, unlike in the Copenhagen picture, where the observer does an instantaneous measurement that collapses the cat.

Scientists hypothesise that using a setup similar to that of Alice and Bob, it might be possible to test between the Copenhagen interpretation and the many-worlds interpretation. But for this, we need to achieve a macroscopic superposition. Scientists have long since achieved the superposition of microscopic particles experimentally; many IISc physicists do this regularly in their research. Current technology, however, has not been able to achieve macroscopic superposition. Yet.



Based on the many-worlds hypothesis, the universe splits into two parallel worlds when the observer opens the box, with the cat dead in one and alive in the other

An absurd, beautiful universe

But why is that? If quantum mechanics were the underlying framework of the universe, why aren't such macroscopic superposition states found in real life? Theoretically, nothing is stopping us from making such exotic objects.

What if we made a cricket ball in a superposed state, existing in two different places, say Bengaluru and Delhi? Such a cricket ball will be defined by a wavefunction of more than 10^{24} atoms (roughly the number of atoms in a cricket ball), which is constantly interacting with the environment. At such large scales, it is believed that the "quantumness" of objects dies out and gives us the usual, familiar classical physics. This phenomenon is called quantum decoherence. "How exactly classical physics arises from the underlying quantum reality of its atoms is something we still don't know exactly. One of the pathways of explaining this is decoherence," says Baladitya.

Very recently, however, scientists have come one step closer to realising a macroscopic superposition. In a study published in *Nature* in January 2026, researchers constructed a superposition state of a cluster of around 7,000 sodium atoms that are in two different positions at once. This is the closest we have ever come to macroscopic superposition.

With all its weirdness, quantum mechanics, to this day, remains an experimentally undefeated theory. Not only has the human race learned to live with its absurdity, but also made use of it in real life. Quantum computers, which use quantum effects to store and process information, promise to solve problems with a much higher efficiency than current classical computers. "Quantum technology essentially uses superposition, and thereby entanglement, as a resource," says Baladitya, who works on quantum computation and superconducting qubits. Nanotechnology emerged as a field because of the exotic quantum behaviour observed in particles at such small scales.

Despite everything, we still do not know our beloved Meownstein's exact fate, and the quest to reconcile quantum mechanics with our classical reality continues. There is so much about our quantum cat and the quantum world that we do not know. All we know is that we continue to live and learn in this quantum universe, a beautifully absurd universe.

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(Edited by Rohini Subrahmanyam)

On Accounts and Arts

- Interview by Ashmita Gupta

Photo: Ashmita Gupta

Indumati Srinivasan has spent over three decades navigating some of India's most complex public institutions – from the vast system of the Indian Railways to the research-driven environment of the Indian Institute of Science. Trained as an economist and shaped by years in the Indian Railway Accounts Service (IRAS), she brought rigour and quiet resolve to her role as Financial Controller at IISc.

After retiring in August 2025, she is deeply engaged in the social sector, working closely with organisations focused on education, disability, and inclusion. In this conversation with CONNECT, she reflects on growing up across cities, learning music from her mother, managing public money in research institutions, and what brings her fulfilment.

Could you tell us about your early life?

I grew up in Bengaluru, where I did most of my schooling. We moved to Mysuru for a year and after that to Delhi, because my father, who worked in the Central Government, was transferred there. From the 10th standard until I entered service, all my education was in Delhi.

What did you major in college? What led you to pursue a career in the civil services?

I completed my Bachelor's with a major in Economics from Delhi University, and then I pursued a Master's at Jawaharlal Nehru University. I think the main persuasion [to pursue a career in civil services] came from my mother. Also, the environment in Delhi at that time played a role; there was a strong culture of preparing for competitive exams, particularly the civil services. So, I was naturally drawn in that direction.

How was your time in the IRAS?

I spent over 23 years in the IRAS. I joined in August 1987 and completed the foundation course at the Lal Bahadur Shastri National Academy of Administration (LBSNAA), Mussoorie. After my two-year probationary training at the Railway Staff College (now called the National Academy of Indian Railways) in Vadodara, I was assigned to the Southern Railway, with my first posting in Bengaluru.

Do you have any fond memories from Mussoorie or Vadodara?

Mussoorie was a nice experience. We went on a village trip in western Uttar Pradesh and also did a trekking expedition in the Himalayas. Beyond the classroom, it was really an introduction to the world of civil services.

Training in Vadodara was also very different from a conventional classroom experience. We were frequently sent to the field across various zonal railways, including to the Northeast. In many ways, the training felt like a 'Bharat Darshan' – we got to see a lot of the country during that period.

Eventually, it was nice to come back to Bengaluru. My parents were here – my father returned from Delhi in 1982 to serve at the Central Power Research Institute (CPRI) – and in many ways, coming back here felt inevitable.

Where were you posted when working with the Railways?

Several places. I was single at the time, and my parents were still independent, so I was open to moving. From Bengaluru, I went to Mysuru, then Madurai and Chennai, and later returned to Bengaluru. I also worked at the Rail Wheel Factory in Yelahanka.

From there, I had the opportunity to go to Mozambique for a year, through RITES (Rail India Technical and Economic Service Limited), a public-sector entity under the Ministry of Railways. That was a very special experience.

Photo courtesy: Indumati Srinivasan

Indumati Srinivasan with her mother

What was it like living and working in Mozambique?

Mozambique was particularly interesting. Its official language is Portuguese, not English. I did a crash course in Portuguese, but I think the locals learned more English from me than I learned Portuguese from them. They were extremely warm and respectful, addressing me as "Doctor," even though I'm not one. When I corrected them, they said, "For us, you are highly educated, so we call you that." That was probably the only time in my life I was addressed as a doctor.

I was provided with a flat and a new car, allowing me to drive to work. I cooked my own food, as I'm a vegetarian, and brought lunch to the office. It's definitely a poorer country than India, but what stands out is how kind and respectful the people were.

'The [IRAS] training felt like a 'Bharat Darshan' – we got to see a lot of the country during that period'

How did you transition from the Railways to IISc as Financial Controller?

Initially, I came on deputation from the Railways. Someone told me about the opening, and I was looking to settle down, as frequent transfers were becoming difficult with my parents growing older.

For the first five years, I was on deputation – my services were still with the Railways. At the end of those five years, the then Director of IISc, Prof Balram, asked me whether I would consider having my services absorbed by the Institute.

Can you describe your core responsibilities?

I was heading Finance and Accounts. There is a separate wing for sponsored schemes and projects (the Centre for Sponsored Schemes and Projects), which I was given additional charge of towards the end of my tenure, but for the larger part of my time, I handled only Finance and Accounts.

When I joined, I inherited a fairly difficult legacy. There had been a recent software change, and the system had not stabilised at all. Payroll processing was unpredictable, and every month brought new surprises. It took considerable effort, and about a year, for things to settle. I brought in a retired expert from the Railways to help stabilise the system, and that made a significant difference.

Photo courtesy: Indumati Srinivasan

Indumati Srinivasan, with retired faculty member KS Nanjunda Rao, on her last day at IISc

Culturally, it was a big shift as well. I came from an organisation of mammoth proportions: the Railways, with about 15 lakh employees. IISc is entirely different. It is a research institution, and there has to be freedom to pursue academic and scientific work. After about a year, I felt comfortable, both with the systems and the culture. By the time the absorption offer came, I had no hesitation in accepting it.

What role does the Finance and Accounts function play in core institutional decisions?

Administration serves as a support function at the Institute, which focuses on research and education. Our role is to maintain accounts of grants and projects, ensure compliance, and report utilisation accurately to funding agencies.

Most of our funding comes from government sources, though in recent years, private and CSR funding have increased. Because government grants come with mandates, expenditure must follow prescribed norms. Our responsibility is to maintain an efficient, transparent, and trustworthy accounting and reporting system.

Were there other challenges during your tenure?

Yes. Over time, staffing reduced significantly due to retirements. Recruitment had been frozen for nearly two decades, so while grants and expectations were growing, staff strength was shrinking. We had to rely heavily on contract staff, which brought its own challenges, such as a lack of continuity and uncertainty.

How did you find working on campus?

Initially, we were in the DIGITS office. In early 2017, we moved to the present building on the left near the main gate.

My social engagement on campus was limited. I lived outside the campus, and my parents were ageing. My mother was bed-bound for nearly four years with dementia, which demanded most of my attention.

Then, COVID-19 happened. For two years, everything changed. Managing work while dealing with the sudden disappearance of support systems was very challenging. A small core team in the office functioned extremely well during that period and supported me throughout.

You said the work environment here felt different from the Railways.

I wouldn't say I had greater freedom, but the environment here was more relaxed. In the Railways, you constantly feel like you're in a pressure cooker; there is continuous enforcement, accountability, and demand on your time.

At IISc, the challenges were different: software issues, staffing shortages, and so on. But there wasn't a daily, intense pressure.

Have you ever wanted to work at a different institution?

Not really. Coming to IISc was not something that I actively planned. I think I applied almost at the last moment. In those days, applications were not online – I remember coming to the Main Building in person and submitting my application by hand.

I was shortlisted and called for an interview. Dr K Kasturirangan was chairing the panel. Being interviewed by someone of his stature was a very special moment. I didn't recognise the other panel members then. I later realised that it included the Director, Associate Director, Registrar, and others.

I also remember that I was the only woman who appeared for the interview.

'Around the age of 11, I was introduced to the veena … It has always been part of me'

You are a veena player. How has music influenced your life?

My mother was a Carnatic vocalist, trained under stalwarts from a very young age. She had a very good voice and taught music to students. When I was four or five, she made me join her classes. Around the age of 11, I was introduced to the veena.

My musical training hasn't been consistent because of my professional life – I was transferred frequently. Obviously, the veena didn't travel everywhere with me. But whenever I got the opportunity, I went back to it. Even now, after retirement, I've returned to it. It has always been part of me.

When I was in Delhi, in the early 1980s, I successfully auditioned for the All India Radio (AIR) Yuvavani. I played regularly on AIR Delhi. They paid me Rs 40 for a 15-minute recording; not that the money mattered. What mattered was the exposure and the discipline. Every time, I wanted to do better than my last performance. I was competing only with myself.

After my mother passed away, I also took up painting. She herself had taken up painting – Tanjore-style art – at the age of 60 and continued until about 80, when her eyesight deteriorated due to macular degeneration, making intricate work impossible. One of the most meaningful moments for me was in August 2018, when I organised an exclusive exhibition of her Tanjore paintings, even when she was bed-bound.

Photo courtesy: Indumati Srinivasan

Indumati Srinivasan playing the veena at Seva Sadan, Malleshwaram, in 2025

Photo courtesy: Indumati Srinivasan

Tanjore art paintings by Indumati Srinivasan

While clearing my mother's things after her passing, I found all her painting materials. I couldn't bring myself to throw it away, and a thought struck me: Why not try it myself, if I could find a good teacher?

A cousin helped me find one, and I began learning. On weekends, I would sit and paint. Over time, I had enough work to hold exhibitions – one at Chitrakala Parishath and later at the Venkatappa Art Gallery.

Since retirement, you seem to be deeply engaged in the social sector. How did that begin?

After my mother passed away, I was introduced to the Swadha Foundation through a cousin. They were looking for mentors. I was assigned an underprivileged girl who was pursuing engineering in Anantapur. From October 2021, I mentored her over weekly phone calls. This led me to Social Venture Partners, a global philanthropic network with a Bengaluru chapter. Their model is not just about giving money – you engage with NGOs, help with capacity building, evaluate funding proposals, and understand their work closely.

Through this, I was exposed to many NGOs working in areas like solid waste management, human trafficking, child trafficking, and working with sex workers and transgender communities.

Eventually, I became actively involved with EquiBeing Foundation, a three-year-old organisation which focuses on empowering the visually impaired to live with dignity and independence. I am now deeply engaged with them, working across Karnataka, Kerala, and Maharashtra.

Why did blindness as a cause resonate so strongly with you?

Both my parents lost their vision towards the end of their lives. My father lost his sight to glaucoma due to neglect. He lived until 94, but in the last two years, after losing his vision, he also lost his will to live. He had always been independent and found dependency unbearable.

My mother didn't become blind, but she lost her focused vision. That frustration affected her deeply.

When I encountered EquiBeing through my philanthropic network, I felt I could meaningfully contribute to it.

'When I entered the social sector, I did not want to play a finance or accounting role. I wanted to work in operations'

What do you miss most about IISc?

I'm grateful for the opportunity to have served IISc. But today, I am in a space that feels more exciting and fulfilling to me.

Here [at IISc], as an administrator, you don't see the direct impact of your work on research or education. In the social sector, I see it immediately. I see a blind person being trained, skilled, and eventually placed in a job. I can see my contribution in that journey.

Just recently, I was in Mysuru for a soft skills programme for visually impaired participants. Initially, many of them didn't even have a white cane; they depended on someone else's shoulder to move. After mobility training, they walk independently with a cane. Being part of that transition – from dependency to independence – is deeply fulfilling.

Even in the Railways, unless you were on the construction side, you didn't always see the impact. But I was fortunate to work on projects like the Bengaluru-Mysuru gauge conversion and parts of the Bengaluru-Hubballi line. I saw things being built. I went to the field, interacted with engineers, learned civil engineering concepts, argued with them as a finance officer, and saw outcomes on the ground.

When I entered the social sector, I was very clear: I did not want to play a finance or accounting role. I wanted to work in operations. I wanted to see things happen. I said, "Give me the programmes, I'll manage them."

A friend from my JNU days once told me she wasn't surprised by where I ended up. She said I had spoken about wanting to do this kind of work even during our Master's programme. I don't remember saying it, but she does.

In some ways, it's the difference between doing a job and finding your passion. The latter is far more fulfilling.

Is there anything else you'd like to share about yourself?

I love animals. I have a dog and a cat: Coco and Molly. I had another dog Junie, a labrador I adopted when she was five and a half. Coco came to me as a six-week-old puppy from a friend's house. Molly, the cat, was rescued from a stormwater drain and made her way into my house through the garage. They are my children.

(Edited by Kavi Bharathi R, Abinaya Kalyanasundaram)

Photo courtesy: Indumati Srinivasan

Indumati Srinivasan with Equibeing CEO and founder, Ananthalakshmi

The Rebel Cell

- *Anjaney J Pandey*

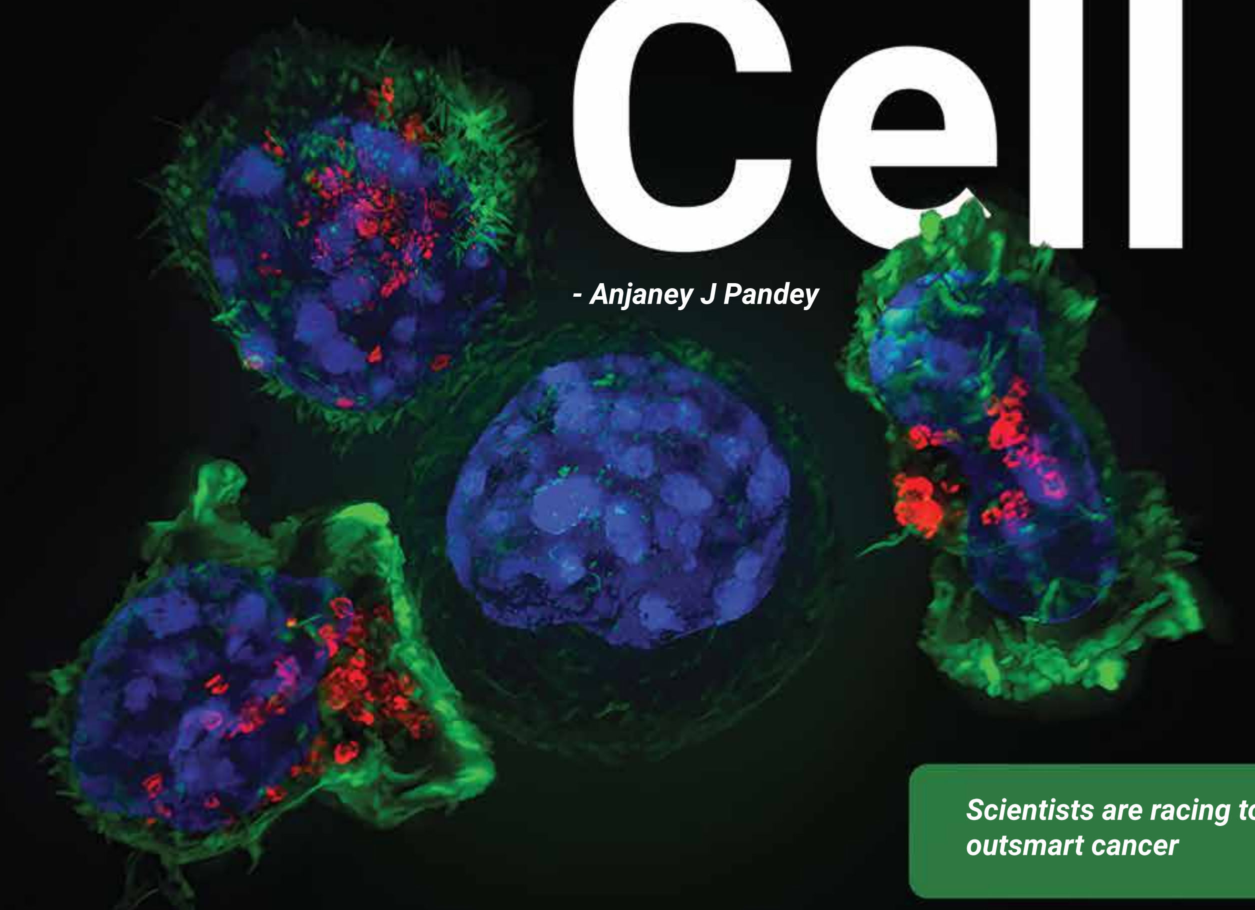


Image courtesy: Flickr/Alex Ritter, Jennifer Lippincott Schwartz and Gillian Griffiths, National Institutes of Health

Scientists are racing to outsmart cancer

Super-resolution image of a group of killer T cells (green and red) surrounding a cancer cell (blue, center)

Mohit Kumar Jolly was reading *The Emperor of All Maladies: A Biography of Cancer*, a popular science book by Siddhartha Mukherjee, when he became impressed by the idea of fighting against cancer. His interest grew exponentially after he started seeing cancer patients every day at the MD Anderson Cancer Research Centre in Houston, USA, where he was pursuing his PhD.

His aspiration to do groundbreaking work in systems biology led him to his current research, in which he uses an integrative approach to decipher how cancer drug resistance develops. "Cancer drug resistance," says Mohit, now Associate Professor at the Department of Bioengineering, IISc, "is the phenomenon where the same therapy [or drug] that was initially able to control tumour mass is now no longer effective."

In recent years, researchers like Mohit have taken on the formidable challenge of investigating how cancer cells develop this "superpower" of drug resistance. Scientists have already identified some strategies that cancer cells use, including altering drug-binding sites, ejecting cancer drugs using specialised proteins, or even changing how the human body metabolises a drug.

The human body has long-established mechanisms to keep the spurious growth of tumour cells under check. First in action are innate immune cells, such as natural killer (NK) cells and macrophages, that gobble up the abnormal tumour cells. They also release a barrage of cytokines (chemical messengers) that call other immune cells to the site of action. Dendritic cells are next – they capture the tumour-associated antigens (which act as "signatures" of tumour cells) and present them on their cell surface to alert the adaptive immune system, which comprises cells like T cells and B cells. The adaptive immune system recruits an entire army of cytotoxic killer T cells to fight against the tumour cells.

While all of this sounds organised, the reality is much more chaotic because tumour cells can evolve very quickly. This means that by the time the killer T cell army arrives at the site of action, some of the tumour cells have already changed their identity, and the T cells can't really recognise them anymore. Think of it as terrorists entering a foreign country being able to generate fake IDs on the fly to fool border security.

But what drives such tumour cells to evolve so rapidly?

Sabarinathan Radhakrishnan, Associate Professor at the National Centre for Biological Sciences (NCBS), reveals that genetic mechanisms could be a major factor. "The DNA in our body's cells undergoes constant damage and repair. [However], sometimes, the DNA replication machinery can introduce mutations, if the damage is left unrepaired, and if it happens in [cancer driver] genes, then those cells take advantage of that and divide rapidly," he explains.

But mutations are not the only factor. Instead, most tumours use a combination of genetic and non-genetic mechanisms for immune evasion.

"Mutations are not the only or even the major source of drug resistance," Shaon Chakrabarti, Assistant Professor at NCBS, explains. "[Some of it] has to do with what people call 'non-genetic' sources of drug resistance [such as] mRNA and protein levels in a cell, which can vary from cell to cell without any differences in the DNA of these cells." Think of it as two cells starting with the same raw material (DNA), but depending on their environment (epigenetics) and consequent choices they make at each step of their journey, they end up in different states. These choices are made at the levels of mRNA expression and proteins. Therefore, two cells having the same origin can evolve to show completely different behaviour, such as resistance or sensitivity to drug therapy.

By the time the killer T cell army arrives at the site of action, some of the tumour cells have already changed their identity

Mohit adds another level of complexity to our understanding of cancer as a dynamic process. He says, "Cancer is not one disease. Cancer is a set of diseases that may manifest very differently in different patients." This means that we need to start thinking of cancer as "a living system" with myriad evolutionary strategies, he adds.

A complex, dynamic system

Researchers are increasingly realising that tackling the current burden of drug resistance will require integrating cancer biology with multiple fields, including mechanical engineering and physics. For example, since biomolecules like mRNA and proteins are synthesised and degraded at some rate governed by the cell's internal and external states, physicists like to model these processes as problems of dynamics. A lot of foundational work has already been done in the field of dynamical systems. Thus, physicists and mathematicians, who work on fluctuations and stochasticity (the property of lacking any predictable order) in biological systems, can now test the validity of their theoretical predictions in the cancer drug resistance field.

Photo courtesy: Mohit Jolly lab

Vibishan B from the Cancer Systems Biology lab at IISc (led by Mohit Jolly) studies how competition and phenotypic plasticity influence cancer behaviour. His work focuses on their impact on the viability of adaptive cancer therapy

Mohit's group is taking such an integrative approach to tackle cancer drug resistance. Their central philosophy is to look at different possible outcomes of a perturbation given to cancer cells.

Mohit explains with an analogy of pulling strings in a network. "There are 20,000-30,000 types of molecules in a cell, and they are interacting with each other in complex manners across different length and time scales. When we pull one string out of that network, [assuming] that the string was certainly performing an important role, we might observe beneficial outcomes in terms of changing cellular behaviour," he says. "In the context of cancer, the expected outcome of pulling that string is that the cell dies. However, what is often not appreciated is that because that same molecule was impacting the behaviour of many others responsible for different functions, other unintended outcomes can also occur."

He cites the example of tamoxifen, the first targeted drug that came into the market in the 1970s for breast cancer. Tamoxifen can show a dual response: while it effectively kills certain breast cancer sub-populations by repressing estrogen receptor signalling, that same intervention can trigger pathways that make surviving cells more metastatic (easily spreadable to other parts of the body). The critical challenge is quantifying this trade-off – determining how the ratio of cell death versus increased malignancy shifts based on dosage, duration, and a patient's unique genetic profile.

There is also growing recognition of the need for personalised medicine – shifting from a "one-size-fits-all" approach to focusing instead on an individual's genetic makeup, lifestyle, and environment, in tailoring treatment regimes.

To build on this idea, Shaon's group is working on deciphering how our body's circadian rhythm (internal clock) plays a crucial role in an individual's response to chemotherapy. "The same drug given to an individual in the morning versus night can make a very big difference," he says. His group is also developing methods to extract data on sleep cycles using wearables such as smart rings or smart watches. He adds, "We are developing the maths for a lot of these technologies to personalise the measurement of the circadian time from, say, just a single skin sample. [Using that], can I make measurements and tell you what your body time is?" Their ultimate goal is to use the information about the body's internal clock to find the right timing to administer chemotherapy and targeted therapy.

Raghuraman Kannan, Professor of Radiology and Biological Engineering at the University of Missouri, has a different approach to tackling cancer therapy resistance. His background in chemistry has helped him develop targeted nano-therapeutics against resistant tumours. He proposes the idea of 'nanoparticles-as-a-platform' in which the precursor of a small RNA molecule called siRNA – pro-siRNA – can be attached to a nanoparticle carrier. The pro-siRNA sequence can be customised to silence the genes responsible for an individual's drug resistance. "The suitcase is going to be the same, but the pro-siRNA inside will be changed in such a way that it can work for personalised medicine," explains Raghuraman.

There is also growing recognition of the need for personalised medicine ... in tailoring treatment regimes

Despite advancements in producing such nanoparticles, a major bottleneck remains – delivering the drug in a targeted manner to tumour cells. There have been some developments in this area, Raghuraman says, but no unique formula is available yet.

Targeted therapies

There's a reason why chemotherapy and radiation therapy have remained popular strategies for so long, Sabarinathan points out.

"These [therapies] give more stress to the cell. Given that cancer cells have already lost some of the DNA repair pathways, they can't tolerate this stress and might undergo cell death. Normal cells – although they will receive some level of damage – because of their proficient DNA repair mechanisms, they would fix the damage," he explains.

But these therapies alone don't suffice, as they are quite generic and agnostic to whether a cancer cell or a normal cell receives the stress. Therefore, scientists have started using a targeted approach to specifically attack cancer cells. Sabarinathan adds, "For example, a protein might have a mutation which could change its conformation. Now, we can provide a drug that could directly bind to that altered protein or degrade that protein so that it can stop the function of that mutated protein."

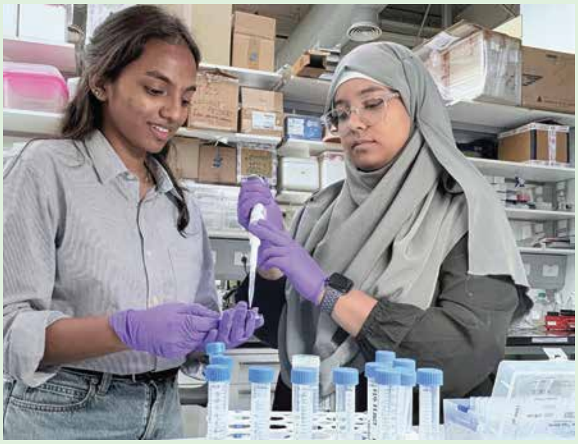


Photo: Adrian Alva

Anjoom Nikhat (right) and Divya Bandaru (left) in Shaon Chakrabarti's lab at NCBS, preparing cellular samples for RNA measurements

This approach can help overcome drug resistance in cases where certain proteins are responsible. For instance, a gain-of-function mutation in a protein called EGFR (epidermal growth factor receptor) – which promotes cell growth and division – or a loss-of-function mutation in BRCA1 (Breast cancer type 1 susceptibility protein) – which is involved in DNA repair – can promote tumour growth by altering different pathways of cell survival, growth, and repair. Targeting these mutated proteins specifically could slow down cancer growth.

But there's a catch. Because cancer cells have poor DNA repair, the few cancer cells that survive treatment will rapidly mutate and grow exponentially. And since DNA codes for mRNA, which is then translated into proteins, these mutated cancer cells can produce more protein variants, enabling them to survive and proliferate. For scientists to develop a clinically approved drug, it takes 10 to 15 years; for cancer cells to make a different protein, sometimes 10-15 days are sufficient.

Another promising route that many scientists are pursuing is boosting an individual's immune system to clear out most of the tumour cells. This is called immunotherapy. Immune cells are capable of rapidly making combinations of different antibodies, with minimal side effects. They are nature's mini-labs that can make effective and targeted therapies against cancer cells without harming the host.

The most popular immunotherapy techniques are the use of molecules called checkpoint inhibitors and CAR T-cell (chimeric antigen receptor T-cell) therapy.

Some well-known checkpoint inhibitors like PD-1 inhibitors and CTLA-4 inhibitors have shown promise in treating certain cancer types like lung cancer, malignant melanoma (skin cancer), and renal cell carcinoma (kidney cancer). These inhibitors are proteins found on the surface of T cells that help regulate the immune system's response to cancer. However, the incidence of immune-related side effects, such as fatal hypersensitivity and inflammation, along with exorbitant costs, has remained a barrier for wider adoption of this strategy.

CAR T-cell therapy, on the other hand, modifies a patient's T-cells to better target cancer cells. The US Food and Drug Administration (FDA) has approved its use for treating leukaemia and lymphoma. However, the limited success of CAR T-cell therapy is often because of the lack of specific targets on solid tumours, which are quite heterogeneous. In addition, the immunosuppressive environment of solid tumours can hinder T-cell function and proliferation.

Despite these challenges, scientists like Raghuraman are optimistic. "Now, immunotherapy works only for 20-30% of the patients, but these 30% of the patients have a very solid response. So, if we put all our energy into making it work for the [remaining] 70-80%, we will have a significant impact on the field."

Addressing cancer drug resistance will require more than better drugs alone – it will need integrating insights from genetics, systems biology, physics, engineering, and personalised medicine. "We are still not there as a community to be able to cater to all the different challenges that are being faced [by patients] in the clinic," Mohit says. "So that's the motivation that keeps [me going]."

Anjaney J Pandey is currently a research scientist at the National Centre for Biological Sciences, Bangalore, and a former science writing intern at the Office of Communications, IISc. He graduated from IISc in 2025 with a BS-MS degree in biology

(Edited by Ranjini Raghunath)

CONNECT ASKS

Which campus event or activity do you look forward to the most?

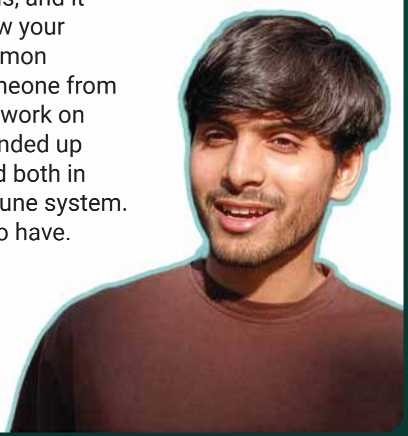
Recently, we have been busy with preparations for Open Day, and we'll be displaying a lot of cool experiments. I'm working with Ensemble (the UG Physics club), and I'll demonstrate the Meissner effect – making magnets float in air using superconductors in liquid nitrogen! So I'm really looking forward to the Open Day and to showing these experiments to the people visiting us and interacting with them. It'll be a very unique experience.

Chaudhari Kushal Manish
BSc (Research) student

I am really looking forward to Holi, which is one of my favourite festivals. It was really fun last year; we all gathered at the Tata Memorial Club (TMC) ground. It was very vibrant, and all of my friends were there. We played with colours, mud, water – everything we could possibly find – so it was pretty fun!

Shirin Kaushik
MTech student, Department of Electrical Communication Engineering

A lot of things, but I am most excited about the Open Day. You get to interact with people from diverse backgrounds, and it really makes you think about how your research connects with the common person. Last year, I spoke to someone from a finance background about my work on mathematical models, and we ended up discussing how models are used both in finance and in studying the immune system. Those are great conversations to have.



Sumedh Chipde
MTech student, Department of Chemical Engineering

I am really looking forward to Spectrum. Sports makes us physically and mentally sound – it helps in building social skills and transform us into community beings, rather than just isolated beings. And I feel that would help us in our research careers, too. I like being active – I've been coming to the Gymkhana for a run at least three times every week, and I'll also be representing my department in the Inter-Departmental Cricket Cup (IDCC). So, I think it should be great fun!

Ritesh Tandon
MTech (Research) student, Department of Materials Engineering

I look forward to Pravega and Rhapsody because they arrange events so that everyone enjoys them. Everyone looks forward to the events because they bring together all the tech and cultural events. I attended it this year, and I enjoyed it! But just a suggestion: they should increase the auditorium's capacity so more people can attend.

Pratima Jhanwar

PhD student, Department of Biochemistry

My favourite organised activity on campus would have to be the various nightwalks organised, especially during the rains. I particularly enjoy the 'firefly walks' at night. It is just magical. During the monsoon, parts of the road light up with these glimmering orbs, floating all around us. At night, the forested quadrangle in front of the main building is illuminated by the light of the hundreds of fireflies. Most people spend most of their time in labs or other workspaces, and we miss out on the magic around us. However, during those few rainy weeks, everyone I know tries to catch a glimpse of the fireflies. A lot of us come from places where we don't see fireflies as much. Experiencing this beautiful haven created by these creatures in the middle of the campus is really something I look forward to every year.

Gauravya Mohan

MSc student, Centre for Ecological Sciences

One event I eagerly look forward to on campus is the Pronites, be that Pravega or Rhapsody. For people working in labs day in and day out, these two-three days provide us with the energy and the motivation to keep working. Everything – from the planning and excitement building up to the day, the DJ nights, the amazing artist performances – all of it becomes an unmissable part of campus life. Friends and the campus, with all the lights and decorations, make it better. Even the most serious people I know let loose and have a good time. We had heard from seniors but didn't know the scale of this event. These events are basically the perks of being a student at IISc.

Sreenjoy Saha

MSc student, Department of Microbiology and Cell Biology

I look forward to the Durga puja at IISc. I am Bengali, and that is my favourite festival. I look forward to the decorations and the dinner that they provide at SAC!

Debarthi Pal

MTech student, Department of Instrumentation and Applied Physics

(Compiled by Amrapali Datta, Shreya Vashista, Kritika Gaur, Souptika Das, Manauv Vyas Hemakumar)

Teeny Tiny Voyagers

- Rohini Subrahmanyam

What microbes are teaching us about life in space

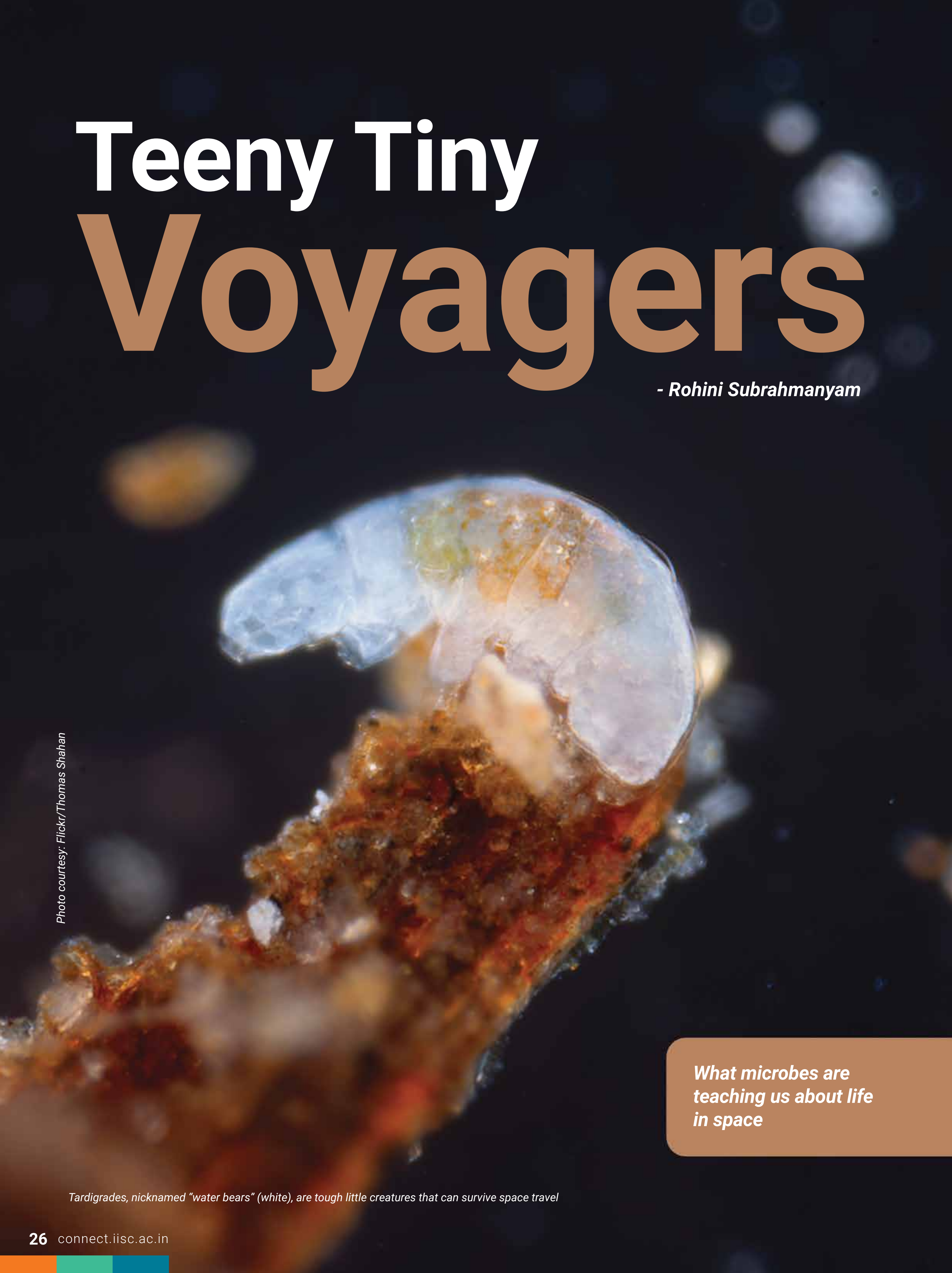


Photo courtesy: Flickr/Thomas Shahan

Tardigrades, nicknamed "water bears" (white), are tough little creatures that can survive space travel

In Andy Weir's fiction novel *The Martian*, NASA astronaut Mark Watney is stranded alone on Mars after his crew is forced to evacuate. To survive, he begins growing potatoes in his crew's Martian habitat. Soon, however, he develops a new priority – ensuring the survival of beneficial bacteria in the soil. So much so that after a small accident, the bacteria's fate concerns him more than the potatoes'. He realises that the potatoes' and his own survival are at the bacteria's mercy; it is they who provide key nutrients to the crop.

Mark's actions may be fictional, but they offer real lessons for how humans might survive on Mars, according to Aloke Kumar, Associate Professor in the Department of Mechanical Engineering, IISc. "Humans are not going to go to Mars alone; we have to take these smaller companions with us – bacteria, fungi, even viruses, everything together," he says.

Living on Mars would be impossible without a supporting ecosystem, and for that, we need to first know whether small organisms can survive in space

The idea of life on Mars, and in space, has intrigued us for ages. But living on Mars would be impossible without a supporting ecosystem, and for that, we need to first know whether small organisms have what it takes to survive in space. At IISc, researchers have been investigating whether microorganisms – like bacteria, yeast, or tardigrades (water bears) – can deal with alien conditions. Studying this can shed light on a millennia-old mystery – whether life could evolve on other planets. It can also simplify space travel and guide future missions to build extraterrestrial colonies.

"Life has amazing ways of adapting to and shaping the environment around it," says Swati Dubey, former Project Associate at the Centre for Earth Sciences, IISc. "We need to be vigilant of that and use it for our own benefit – not just for humanity, but for the [whole] ecosystem."

Unbreakable bears

A known expert at adapting to adverse environments is the tardigrade – one of the tiniest but toughest creatures on Earth. These alien-like creatures are about a millimeter long and are extremotolerants – some of them can survive at extreme temperatures of Change this to 100°C or -272°C and tremendously high pressures of 7.5 giga pascals (atmospheric pressure is a tiny fraction of a giga pascal). Intrigued by their extreme tolerance, Sandeep Eswarappa, Associate Professor at the Department of Biochemistry, IISc, began exploring whether they could survive the final frontier – space.

The idea of sending tardigrades to space was seeded more than 60 years ago, when a 1964 paper in *Bulletin biologique de La France et de La Belgique* suggested that their extraordinary radiation tolerance makes them ideal space travellers. But it wasn't until 2007 that astronauts took tardigrade specimens on a low Earth orbit mission (about 258-281 kilometres above sea level), proving that the creatures could indeed survive the vacuum in space (the solar radiation, however, killed most of the specimens).

In 2016, Sandeep and his team found some tardigrades on the IISc campus, hiding in the moss covering an abandoned concrete wall, at the old building of the Department of Aerospace Engineering. Despite existing

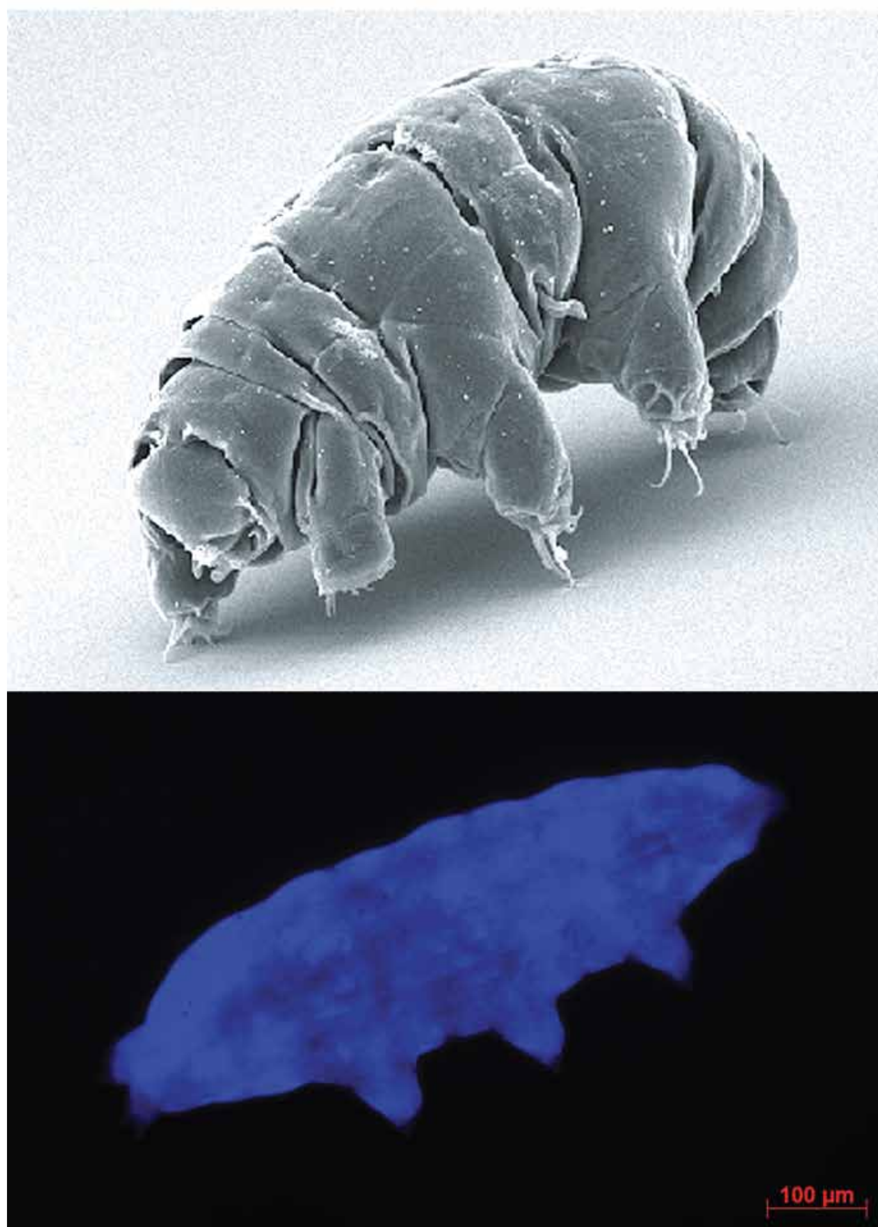


Photo courtesy: Wikimedia Commons/PLoS One (top), Harikumar R Suma (bottom)

Tardigrades (top) emit blue fluorescence (bottom) when they are exposed to UV radiation evidence of the tardigrades' almost indestructible nature, the team wanted to test it for themselves. To start with, they zapped the water bears with ultraviolet (UV) radiation. The DNA-damaging, cancer-causing radiation usually kills unwanted bacteria, but it did nothing to the tardigrades. "To our surprise, even after 30 minutes of exposure, they were surviving," says Sandeep. Strangely, the UV rays made them glow bright blue, which they later found was key to their UV tolerance.

It turns out that these tardigrades have a fluorescent pigment that absorbs lethal UV radiation, emitting blue light and shielding their bodies. "It acts like a natural sunscreen," Sandeep says.

To systematically test the limits of the tardigrades, Sandeep collaborated with the Indian Space Research Organisation (ISRO), with the ultimate aim of sending them into space. They first tested for tolerance to gamma radiation – high-energy electromagnetic radiation prevalent in space. "Humans die if exposed to five grays of gamma radiation," says Sandeep. Tardigrades, however, survived even up to 4,000 grays of radiation, and were still able to reproduce.

'So far, no one has tested this idea: that a dormant organism can be reactivated outside the Earth'

The next test was survival without water. The team placed tardigrades on filter paper inside a dessicator – a sealable enclosure with no moisture. After 10 days, they took the tardigrades out – the creatures were very still. When water was added, the dormant tardigrades came right back to life.

Finally, the tardigrades were put through the ultimate test – a near-vacuum chamber at a freezing -272.99℃ (~ 10 milli Kelvin), a few degrees colder than space itself. The chamber was provided by Vibhor Singh, Associate Professor in the Department of Physics, IISc, who uses it to test quantum properties of materials. The dormant tardigrades easily survived for even up to 21 days. "When we revived [them], they were fine," says Sandeep. "They behaved as if nothing had happened."

This remarkable capacity for long-term dormancy raised an intriguing possibility – could tardigrades inspire a new way to travel to space? Long-term space travel is expensive and physically demanding, requiring a constant supply of food, oxygen, and stimulation. But if organisms could be sent in a dormant state, to be awakened only after reaching their destination, the energy requirement would be minimal, says Sandeep. "So far, no one has tested this idea: that a dormant organism can be reactivated outside the Earth," he says.

In collaboration with ISRO and NASA, Sandeep and his team sent dormant tardigrades to the International Space Station (ISS) via the Axiom-4 mission. ISRO astronaut Group Captain Shubhanshu Shukla, who is pursuing his MTech at IISc, was asked to try and reactivate them on board. On D-Day, the team held their breath as they watched a live broadcast of the microscope. Shubhanshu added water to the plate, and after a few seconds, slowly but surely, the water bears wiggled back to life.

"Seeing them coming back to life ... we were very happy and relieved," says Sandeep.

Shubhanshu then put the tardigrades back into a dormant state for the return journey to Earth. About 45% of them were successfully revived in Sandeep's lab; they eventually even reproduced normally.

The team was ecstatic; these findings confirmed that tardigrades remain unfazed in the most extreme and even extraterrestrial situations. "Life has the potential to tolerate [even] the harsh conditions of space," says Sandeep. Understanding the mechanisms of such survival, he adds, could potentially make space travel, even for us humans, much easier.

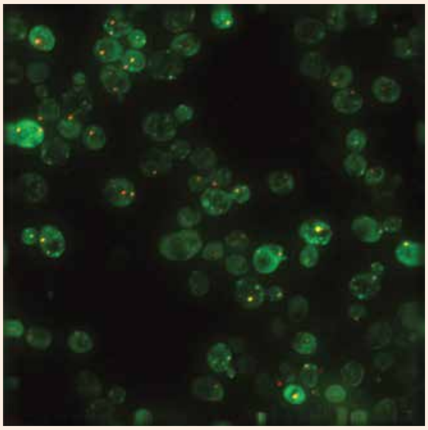
Resilient yeast

Another potential space survivor that has caught scientists' attention is a microbe much closer to home – the humble baker's or brewer's yeast, *Saccharomyces cerevisiae*.

Photo courtesy: Bhalamurugan Sivaraman

High-Intensity Shock Tube for Astrochemistry (HISTA) tubes were used to simulate meteor-impact shockwaves and test whether yeast could survive

Photo: Chitra Togra



Yeast cells (green) make different RNP condensates (red, green, and yellow dots) when they are stressed, which allowed them to survive simulated Mars conditions such as shockwaves and the presence of toxic perchlorate

Purusharth I Rajyaguru, Associate Professor in the Department of Biochemistry, IISc, has loved working with yeast since his postdoctoral studies. His lab investigates how translation – mRNA molecules getting converted into proteins – is regulated inside the cell. Not all mRNAs leaving the nucleus get translated immediately; depending on the cell's situation, some are stored safely in the cytoplasm. Under stress, these untranslated mRNAs can clump together with proteins to form RNA-protein (RNP) complexes, and when protein concentrations rise, they phase separate – "condensing" into structures called RNP condensates. Cells in organisms ranging from yeast to humans form RNP condensates. For the past decade, Raj has been investigating how yeast cells make these condensates under regular lab stresses such as nutrient deprivation or excess oxygen.

Yeast managed to survive both massive shockwaves and exposure to toxic perchlorate found in Martian soil

More recently, he became curious about how yeast cells would react to Mars-like conditions. "This is a different kind of stress, right? Going to a planet like Mars or the moon … temperature, UV radiation, and salt conditions are going to be different," says Raj.

Mars is regularly bombarded by meteors, producing massive shockwaves. Working with Bhalamurugan Sivaraman at the Physical Research Laboratory, Ahmedabad, Raj and his team exposed yeast cells to such shock waves in a High-Intensity Shock Tube for Astrochemistry (HISTA) – tubes usually used for non-living materials like gases. They also exposed yeast to perchlorate – a toxic, chlorine-containing chemical found in Martian soils at levels up to 1%. A combination of these two stresses was also tested.

Not only did the yeast manage to survive the two stresses, separately and together, but they also responded by making more RNP condensates, as the scientists had predicted. In fact, the RNP condensates were necessary for mounting the stress response – lab-made mutant yeast that could not form condensates were unable to survive the stresses. "When you expose yeast cells to a stress they have never seen, they are still able to deploy their typical stress response," explains Raj. "Which means that if there is a life form [on Mars], then perhaps it could be using similar mechanisms."

The researchers also observed that immediately after stress exposure, the yeast entered a long lag phase, becoming dormant for 18-20 hours before dividing again. Raj hypothesises that this pause allows the cells to make condensates, to hoard mRNAs, and make the right proteins at the right time. "Once [the cell] has the necessary repertoire to deal with the stress, that is when the cell resumes growing."

Similar condensates also form during starvation, when cells avoid the energy-consuming process of translation. Instead, they temporarily store mRNAs in condensates until conditions improve. Raj suspects that yeast use a similar strategy to cope with Mars-like stress.

Related RNP condensate responses in human cells could even serve as potential markers of stress response during space travel, Raj says. Potential space travellers can be screened under space-like conditions to measure their RNP condensate response. "That could be one way of knowing whether these people will respond well to space travel or are more likely to have complications," he adds.

Brick-building bacteria

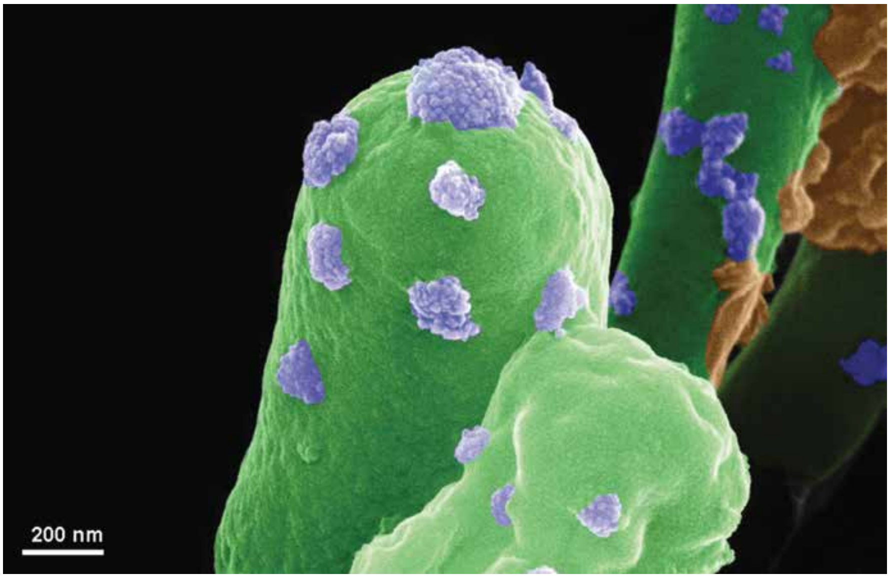
Among microscopic life that could survive in Martian soil, bacteria are ahead of the game – they can even help humans build potential habitats on Mars. The bacterium *Sporosarcina pasteurii* has naturally evolved to use urea and calcium in Earth's soil to produce calcium carbonate crystals or precipitates, in a process called biocementation. Using this skill, the microbe can also help mould Martian soil into strong bricks.

Aloke and his team had been interested in microbes that could survive on Mars for some years when they started working with *Sporosarcina pasteurii*. They initially used it to build "space bricks" made from synthetic lunar or Martian soil that can potentially be used to set up extraterrestrial habitats. Just like it could in Earth's soil, the bacteria could glue the Martian or lunar soil particles together into bricks, though it also needed the natural adhesive guar gum, a powdery polymer extracted from guar beans.

More recently, Swati, Aloke, Shubhanshu, and other researchers used a more robust, native strain of the bacterium that they discovered in Bengaluru. After confirming its precipitate-forming skills, they wondered if this strain could also survive in the presence of the toxic chemical perchlorate of Martian soil, as the yeast in Raj's lab did.

Collaborating with Punyasloke Bhaduri, Professor at the Indian Institute of Science Education and Research, Kolkata, the team first studied how the bacteria respond to perchlorate in isolation, in the absence of synthetic Martian soil. They found that perchlorate stresses out the bacterial cells – they grow slowly, become more circular in shape, and start clumping together into multicellular-like structures. The stressed bacterial cells also release more proteins and molecules in the form of extracellular matrix (ECM) into the environment. Using electron microscopy, the researchers found that more calcium carbonate-like precipitates were formed, and that the ECM formed little "microbridges" between the bacterial cells and the precipitates.

Photo : Tanushree Ghosh



Under the right conditions, Sporosarcina pasteurii *(green) induces the precipitation of calcium carbonate (blue); this skill could be used to build bricks using Martian soil*

The bacteria's biocementation abilities also hint towards what life on the alien planet – if even present – could look like. Recent findings from the Sapphire Canyon sample, collected by NASA's Perseverance Rover on Mars, revealed one of the strongest signs of life on the planet – not cells, but evidence of biomineralisation, a process akin to *S. pasteurii's* biocementation. "Maybe these kinds of microbes lived on Mars one day, and these minerals shaped its soil texture," suggests Swati.

'Maybe these kinds of microbes lived on Mars one day, and these minerals shaped its soil texture'

The team then tested the effect of perchlorate on the bacteria in the presence of synthetic soil. Although synthetic Martian soils usually exclude perchlorate because it is flammable, the researchers carefully added it in the lab. To their surprise, they found that the presence of perchlorate made the bacteria better at glueing the soil together in the bricks, but only if guar gum – essential for bacterial survival – and the catalyst nickel chloride were also present.

"When the effect of perchlorate on just the bacteria is studied in isolation, it is a stressful factor," says Swati, currently a PhD student at the University of Florida. "But in the bricks, with the right ingredients in the mixture, perchlorate is [actually] helping."

Swati suspects that the ECM microbridges could be enhancing the bacteria's biocementation skills by funnelling nutrients to the stressed cells – a theory that the team plans to explore further. They also want to test the bacteria's performance in a more Mars-like high-CO_2 atmosphere.

Ultimately, the goal is to deploy biocementation as a sustainable building strategy, to rely less on carbon-intensive cement – both on Earth and Mars. Such technologies can also make future landing missions smoother by helping build better roads, launch pads and rover landing sites, says Shubhanshu. The Moon's uneven topography, for instance, has caused some landers to topple over.

"The idea is to do in situ resource utilisation as much as possible," Shubhanshu says. "We don't have to carry anything from here, which will make it a lot easier to do sustained missions over a period of time."

Understanding how organisms like bacteria and yeast survive in Mars-like conditions can also help future colonisation efforts. After all, just like Mark needed the bacteria in *The Martian* (which thankfully survived the accident), we humans will need microbes to survive on the Red Planet. "Colonisation is not going to happen by us just landing there one fine day and starting to live," says Raj. "It has to start from looking at how simpler life forms survive, which could give us an indication of how we might be able to survive."

(Edited by Abinaya Kalyanasundaram)

Photo: Amogh Jadhav

Slurry containing S. pasteurii *was found to be able to repair flawed bricks, which could come in handy for easy repairs in extraterrestrial habitats*

Is Seeing Really Believing?

- Kedhar R Thyagarajan

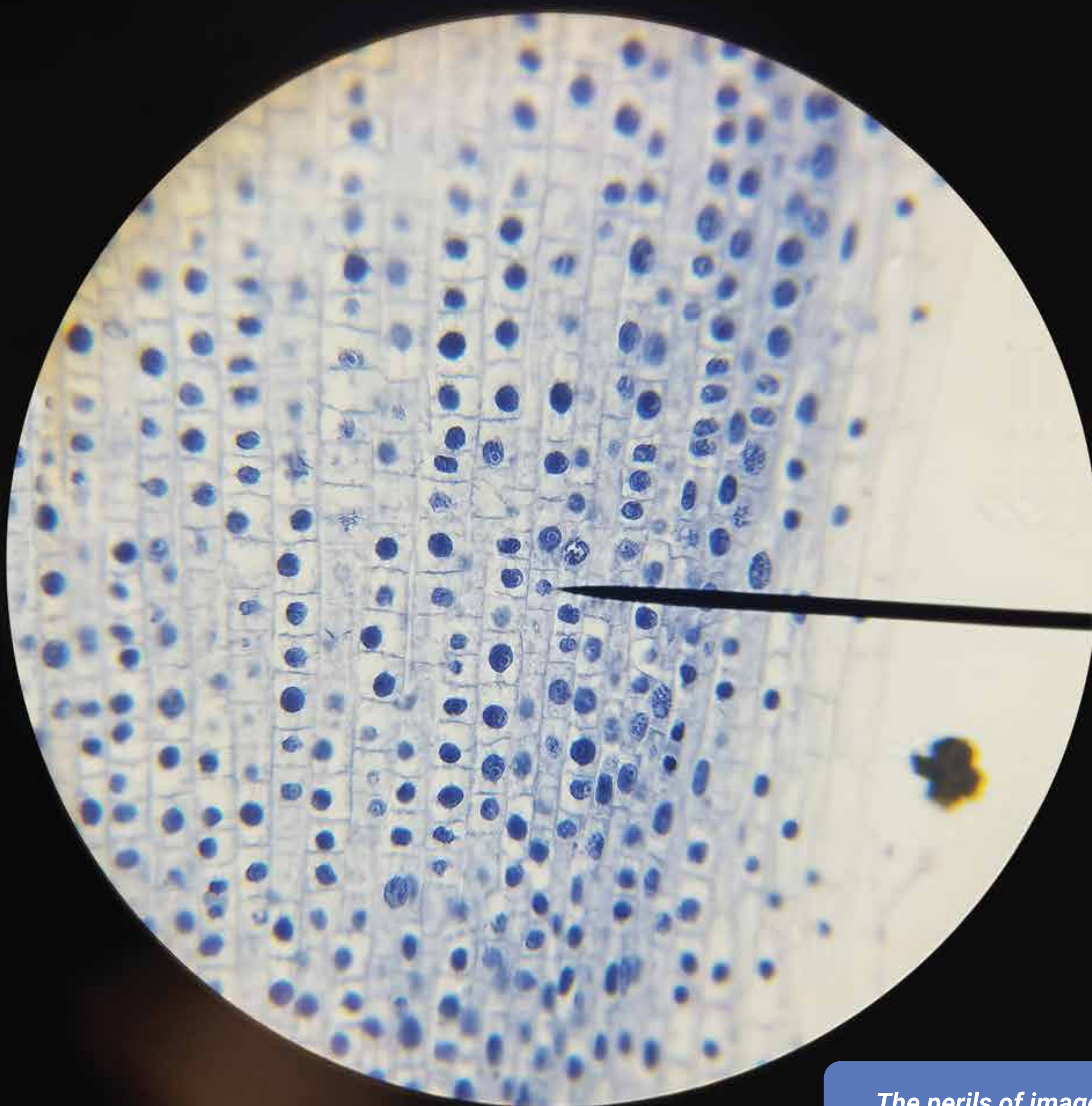


Image courtesy: Isisrichardson13/Wikimedia Commons

The perils of image manipulation in science

Microscopic image of an onion cell during mitosis. This image is used for representation only

Volume 119, No 38, Figure 1. To most people, this is just a set of incomprehensible scientific data. But this figure, along with those from 13 other papers, is special. They lie at the heart of a high-profile scientific scandal: the downfall of a Nobel Laureate.

Studies claim that over 6% of biomedical studies contain plagiarised, falsified or manipulated images

Unlike many other scientific fields, biology, and especially sub-cellular biology, is uniquely dependent on captured images as a primary form of data. A lot of techniques used daily in labs rely on cameras to take snapshots, whether that be of cells under the microscope, or of 'blots' to quantify protein levels in cells. This dependence exposes the field to a pressing problem – image manipulation.

Studies claim that over 6% of biomedical studies contain plagiarised, falsified or manipulated images. Included in this statistic are the many papers by American paediatrician and scientist Gregg Semenza, who shared the 2019 Nobel Prize in Physiology or Medicine.

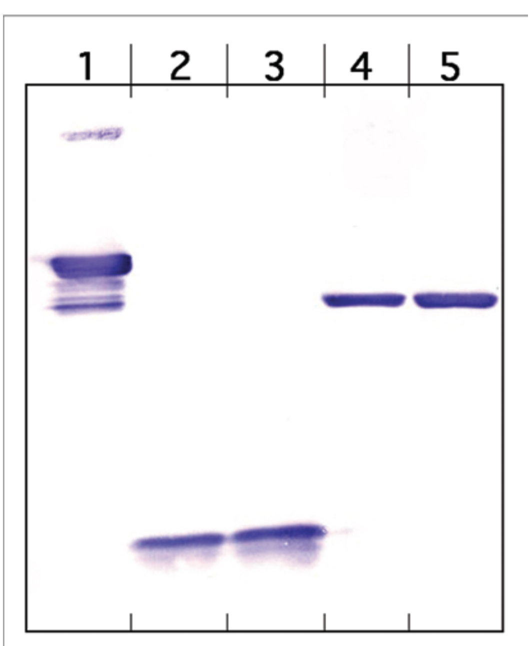


Image courtesy: Magnus Manske/Wikimedia Commons

An example of a protein blot: each numbered column represents a different sample, and individual 'bands' within the columns are different proteins. How dark a band appears indicates the amount of protein present

Semenza's research focused on understanding how cells sense and react to oxygen availability. Proteins are the workhorses of the cell, with different types of proteins (of which there are thousands) performing different tasks. To understand a cellular process, such as oxygen response, one needs to identify the proteins responsible. Blots are a common technique used in this endeavour. The contents of cells are passed through a membrane which separates the proteins into various "bands". The intensity of a band in the picture of a blot indicates the level of protein. This is a simple approach in theory, but one often encounters many challenges while running and analysing a blot – for instance, a band which should be bright may be absent, or may look deformed. The complexity arises from the large number of steps leading to the final image.

By the time he received his Nobel in 2019, Semenza had been leading his research group for over two decades. In this time, paper after paper was released from his group – *PubMed*, an online scientific literature tracker, reports over 300 publications between 1999 and 2019 alone. In the midst of this publishing spree came his first retraction in 2011. This could easily be dismissed as a genuine error. Four years after the Nobel was awarded, however, began the run of retractions that he is now (in)famous for. Between 2022 and today, 12 more of Semenza's papers have been withdrawn due to image manipulation.

These retractions followed after brewing suspicions on Semenza's research were made public on *PubPeer*, an online forum created to discuss published literature. Multiple users of the website, some anonymous, reported multiple irregularities in published images across a number of publications. The 13 retractions awarded to Semenza were primarily because individual bands were modified, cut out, or photocopied between different blot images. Such changes meant that the resulting images are no longer a truthful reflection of the reality in cells. In essence, this is tantamount to fraud. It is still unclear who was directly responsible for these shenanigans, since other co-authors were commonly listed on the retractions. Semenza, being the primary corresponding author, however, bears primary responsibility.

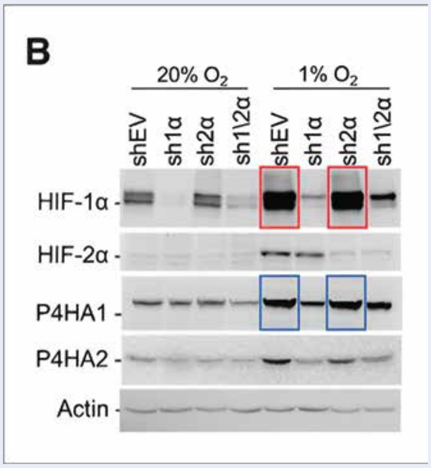
Improper manipulation extends beyond just blots. Microscopic images of cells, tissue sections, and other lines of evidence also fall prey. An example of this is a (formerly) pivotal study in the field of stem cell research, published in *Nature* in 2002. The paper showed that cells derived from an adult human's bone marrow can transform into any cell type, with huge implications for treating many diseases.

The only problem? Two microscopy images of cells in the study, which were supposed to be from entirely different mice, clearly overlapped – one region of the first image was identical with another region of the second image, even though they were purportedly separate animals. Another image of a tissue section had two regions that looked duplicated. The paper was retracted in 2024, 22 years after its publication, after these concerns were pointed out on *PubPeer*. This makes it the most cited retracted paper of all time, with 4,491 citations before the retractions. Hundreds of research groups referred to this paper in their own research, without knowing about the problems that lay within.

Untrustworthy data poses a bigger risk than just casting doubt on a single set of conclusions

Untrustworthy data poses a bigger risk than just casting doubt on a single set of conclusions. Any study in the making necessarily draws on previous research, and when this previous research is faulty, an ocean of subsequent research suddenly looks murky. Image manipulation is a huge problem in biology particularly, but shoddy science is not limited to this one field. A 2009 study reported that close to 2% of surveyed scientists admitted to falsifying data, and many consider that to be a low estimate.

Image courtesy: American Association for Cancer Research



A blot from one of Semenza's retracted papers. The red and blue boxes show identical bands, clearly duplicated, even though they are supposed to be from completely different samples

The sheer volume of such data has given birth to entire organisations dedicated to uncovering falsification in research. Sites such as Retraction Watch are chock-full with reports of suspicions and retractions. Amidst all this commotion, however, the simplest questions remain the hardest to questions remain the hardest to answer: *Why* are images falsified in the first place?

Not all that lustres red is blood ...

Getting things to work in biological research is complex. Talk to any person who works in a lab, and you're guaranteed to hear about an experiment not working for some or other reason. Weeks are spent in optimising protocols and making changes. After an experiment does work, it must be repeated a few times, to ensure that what one sees is true and not just a fluke. Researchers thus end up generating a huge amount of data, sometimes up to terabytes of images, of which only a small fraction is usable.

Keeping track of which image was from which experiment is thus a momentous task in and of itself. When it's time to frame the results and write a manuscript, mistakes are understandably made. After images are generated, they need to be processed and edited to make them more facile to interpret and ready for publication. This step is where it is easiest to mess up.

"A common mistake is that students contrast images corresponding to a control group and a study group differently. This just comes naturally to us – we all have mobile phones, we take pictures, and we enhance pictures to make them look pretty. Scientifically, however, doing this to an image changes its properties, which one will [improperly] quantify later," says Shova Maharana, Assistant Professor at the Department of Microbiology and Cell Biology, IISc.

Images are often used to infer changes in a biological system. For instance, if a drug is meant to reduce the levels of a specific protein in the cell, one can simply image cells treated with the drug and compare the intensity of the protein against untreated cells to check its function. However, since the treated and untreated cells need to be compared directly with each other, care must be taken to ensure they are processed the same way. Otherwise, the intensity from one set may falsely be increased.

What can be attributed to blunder must not be attributed to malice. Papers can be published with genuine errors, which may be flagged for suspicion down the line. These can be corrected, since almost all journals offer authors an option to submit corrections. But to say that all faulty data in the literature is simply a result of errors would be ignorant.

... but blood has a distinct taste

Contrast is a powerful tool for editing images. It can be used to simply make an image look clearer. But contrast can be used to play detective too. By playing with the colour levels of an image, one can analyse if an image has been altered substantially. A cell pasted in from another image, for instance, may not have the same background properties as the rest of the image – so when contrast is increased, it looks obviously different. And this kind of manipulation cannot simply be attributed to error.

It is easy to frame a researcher who indulges in this kind of fabrication as just another bad apple. The scale of the problem, however, suggests a more systemic issue.

"We currently live in a 'publish or perish' world," says Meetali Singh, Assistant Professor at the Department of Developmental Biology and Genetics, IISc. "A huge pressure exists to publish a certain number of papers every year. Instead of focusing on numbers, we need to focus on quality."

Universities often have publication requirements for lab heads to continue in the institute or be promoted, which can be extremely stressful, especially in labs which experiment with novel and volatile ideas. This pressure is transmitted to students and scientists in the lab, who must also publish more to earn scholarships and positions. Even though it may be argued that pressure is necessary to ensure good science, this severe focus on metrics is unsustainable, and leads to stress, conflict, and potentially fraud.

Academic stress is often not the only source of tension. "A lot of it boils down to lab culture. Manipulation happens when the environment in the lab is not supportive, or if one is under pressure [from the lab head] to get a certain specific result," says Shruthee*, PhD student in the Division of Biological Sciences, IISc.

While pressure is shared amongst those in a lab, so is responsibility. Technically, all co-authors of a paper share the duty of ensuring the veracity of the data, including foremost the corresponding author – usually, the head of the lab. It is extremely difficult, however, for every person involved to check all the data, due to the number of different experiments a modern biological paper usually includes.

Modern papers are also often co-authored by a large number of researchers (depending on the subfield and journal, seeing publications with 20-25 contributors is not unusual). Collaborations between specialists in different fields is the bread and butter of science today. But when misconduct takes place, the source of it becomes difficult to pinpoint.

Cleaning up the scene

Faults at multiple points – experimentation, supervision, publishing, and administration – result in unsound data and untrustworthy results. Changes, both incremental and systemic, are necessary to ensure integrity in the scientific process. This, no doubt, must start in the lab. Rigorous practices, tolerance for genuine mistakes, and harsh consequences for malpractice are essential. Early career researchers must also be trained in the ethics of research.

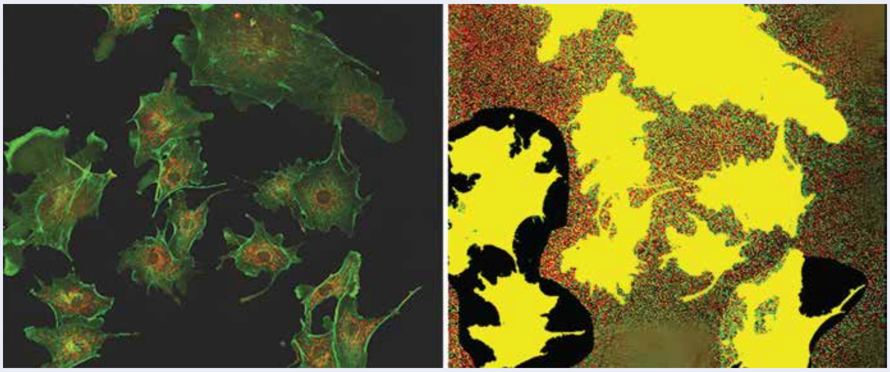


Image: Reproduced with permission from the Journal of Chemical Biology/Rossner and Yamada, JCB (2004)

(Left) A manipulated image in which cells from different images have been placed in a single image, giving the impression that they were present together. (Right) When the contrast is adjusted, however, the manipulation is revealed

"As lab heads, we should not hurry students up in generating data. We must invest time in ensuring that lab members learn techniques properly, and proper mentoring is really important," says Shova. A healthy culture at work is probably the most effective deterrent to scientific malpractice. In addition, a proactive effort must also be taken to ensure that the data published by a lab is authentic. "Before publishing, the raw data and analysis pipelines must be checked. One must be able to vouch for the data published," she says.

'Researchers are judged based on the number of publications and citations. Chasing such metrics results in [falsification]'

While incremental improvements are imperative, they can only hold ground when accompanied by systemic reform. At the forefront of this are organisations such as India Research Watch (IRW).

"Researchers are judged based on the number of publications and citations. Chasing such metrics results in [falsification]," says Achal Agrawal, founder of IRW. "We have to stop being lazy. We have to move away from the convenience of simple metrics if we want to incentivise quality work." Pressure from IRW and other groups led to the NIRF rankings, published by the Government of India, penalising universities with many retractions.

It is clear that this is not enough. As more money continues to pour into technology and artificial intelligence, generating falsified images is easier than ever. Bands in a Western blot, images of bacterial plates, and even entire microscopic images can be generated just by submitting a prompt.

Even then, a sense of cautious optimism prevails. "If we can use AI to make images, we can use AI to detect fraudulent images. And I'm sure that technology will come soon," says Shova.

The future tests the past

The trustworthiness of science depends on the belief that even if faulty conclusions are drawn, they will be tested by future research in the field. For particularly exciting results, scientists often jump on the case immediately, trying to replicate the results in their own lab. If it works, confidence is built in the result. If not, eyebrows are raised.

A well-known case of this kind of sleuthing paying off happened in stem cell research. Stem cells are cells that can become any type of cell in the body, a capability that does not exist in most cells of an adult. Obtaining stem cells from a grown human is the holy grail of regenerative medicine, since they can technically be used to treat defects in any organ, without dealing with the complications of transplants and other procedures. The field of stem cell therapy often makes headlines. A lot of the time, however, this is for the wrong reasons. Fraud is exceedingly common in this line of research.

In 2014, two papers were published in *Nature*, both from a lab in the Riken Center for Developmental Biology (CDB) in Kobe, Japan. The papers essentially claimed that an acid bath is enough to convert normal cells into stem cells. This was monumental, and biologists from across the world rushed to replicate this. Worryingly, no one was able to. Along with allegations of plagiarism and image manipulation, this prompted both papers to be withdrawn within just a few months, sending the institute and field into disarray.

It is often argued that this incident is proof of science working as intended, with fraud being revealed as a result of more research. This obfuscates the fact that only the most exciting results ever get looked at again. Most scientific results do not get validated for reproducibility, and this has led to what is called a "replication crisis".

Solving this crisis only requires simple solutions. For instance, more roles aimed specifically at ensuring the authenticity of previous experiments, through data validation and reproducing them, must be established. However, bringing these changes to fruition necessitates political will and funding.

"We do not have a dearth of talent. There are currently more qualified individuals than there are positions available in academia. If the funding becomes available, I'm sure people would be interested in taking such positions," explains Meetali.

Scientists who have their data retracted do not have it easy. Any future research conducted by the lab will be surrounded by a cloud of suspicion, even if it is scientifically sound. Retractions have a ripple effect – other related articles are cited less when a retraction occurs, and the entire field of study may receive less funding.

In an era of increasing scepticism, decreased funding, and more opportunity to do the wrong thing, one can only hope that these repercussions are not outweighed by a growing pressure to perform.

As the old adage goes, science is self-correcting. Only time can tell if this saying is dead in the water.

**The name of the student has been changed to protect their privacy.*

Kedhar R Thyagarajan is a fourth year Bachelor of Science (Research) student at IISc and a science writing intern at the Office of Communications

(Edited by Abinaya Kalyanasundaram)

Transforming Mobility

- Kavi Bharathi R

Designing an electric future

Photo courtesy: ESE Lab, with enhancements using Nano Banana

Tabby, an electric vehicle chassis (vehicle's supporting structure) obtained from an open-source design, modified with in-house electronics and controls built by students in EECS, IISc, in 2020

A quiet hum is redefining mobility. More than a century ago, the rhythm of modern travel was measured by hoofbeats – the rhythmic sound of iron shoes on cobbled streets. Then came the gas-chugging Internal Combustion (IC) engines, whose roars marked a revolution of speed and power. Now, mankind stands at the crest of the latest mobility transition – electric vehicles (EVs).

Though often perceived as a 21st-century innovation, the earliest efforts to design electric vehicles date back well over a hundred years, the same time when horses were relieved of their carriage duties. The first EV was built in the 1830s using non-rechargeable batteries. It took nearly half a century to commercialise EVs with rechargeable batteries, and only by the end of the 19th century did EVs gain widespread use. However, at that time, the electricity supply was limited, while gasoline was cheaper and more readily available. This led to IC engines winning the automotive race and rapidly gaining popularity.

The dominance of fossil fuel-powered vehicles lasted for decades, until the world finally looked around and realised the damage they were causing. This awareness forced us to search for alternatives to reduce emissions and increase efficiency. Now, a century after its initial conception, EVs are making a comeback. Over the years, the engines have become quieter; with EVs, it is barely a hum.

Despite all the excitement surrounding the billion-dollar EV economy, there is still a long way to go before EVs rule the roads. "The transition to EV penetration presents serious challenges ranging from fundamental issues with battery design to large-scale charging infrastructure," notes Kaushik Basu, Associate Professor at the Department of Electrical Engineering (EE), IISc.

Though often perceived as a 21st-century innovation, the earliest efforts to design electric vehicles date back well over a hundred years

India's biggest challenges in scaling electric mobility include expanding charging infrastructure, strengthening grid capacity, and improving energy management. But the problems lie beyond wires and watts. Researchers at IISc are now exploring multiple avenues to solve these issues, all with the goal of achieving an electric future.

The instant kick

Driving an EV feels starkly different from driving a conventional IC engine vehicle. Press the accelerator, and the response is immediate and silent; it takes drivers a while to adjust to this unfamiliar feeling, which reflects a fundamental difference in how the vehicle operates.

Conventional vehicles burn fuel, converting chemical energy into heat and then into mechanical motion through combustion. EVs bypass these steps entirely. Electrical energy in batteries is delivered directly to the electric motors, which then drive the wheels, eliminating the need for an engine, tailpipe, and combustion. The power delivery is immediate; there is no delay caused by the motion of fuel and levers. An inverter determines how much energy to draw from the battery and controls the speed at which the motor rotates. Speed, torque, and braking are all managed electronically by circuits, resulting in smooth acceleration without gears, noise, or emissions.

"Energy is stored in batteries, motion comes from an electric motor,

Photo courtesy: Washington Libraries digital collection/Public domain

An advertisement for a Fritchle electric automobile, the Model A Victoria Phaeton. After patenting a lead-acid battery in 1903, Oliver Fritchle established the Fritchle Electric Storage Battery Company in Denver, Colorado, which produced its first electric car in 1905 controlled by a power electronic motor drive – the three main components which differentiate an EV," explains Harisyam PV, PhD student in EE.

Designing motor drives and battery chargers, however, is not trivial. "This is where power electronics – conversion of one form of electrical energy to another – becomes critical. It controls energy flow with precision and efficiency. It happens at a smaller scale in a mobile charger and a larger scale in a home inverter," explains Harisyam. It is a fundamental change in how energy is stored and motion is generated in electric vehicles.

Electric motors also differ fundamentally from how engines operate. Unlike an engine, which operates efficiently over a narrow speed range, a power electronics-controlled electric motor can smoothly operate over a wide speed range. It can even reverse its role, acting as a generator during braking and converting mechanical energy (associated with motion) back into electrical energy. This process is called regenerative braking – "recovering energy that would otherwise be lost as heat," explains G Narayanan, Professor in EE.

'Energy is stored in batteries, motion comes from an electric motor, controlled by a power electronic motor drive – the three main components which differentiate an EV'

Photo courtesy: ESE lab

An electric three-wheeler with a chassis from Scooters India Limited. The superstructure, electronics and controls were built in-house at the ESE workshop, IISc, in 2003

Elemental design

Building an efficient EV motor requires a material that enables a lightweight, compact design without compromising strength. Most EVs today use permanent-magnet motors, like Neodymium-iron-boron (NdFeB) magnets. These, unfortunately, are scarce elements found only in some parts of the world. This raises concerns about technological dependence.

"This creates a reliance on imports. Instead, using induction motors will be an indigenous choice that is self-sufficient," says Umanand L, Professor at the Department of Electronic Systems Engineering.

Umanand's research focuses on identifying suitable alternatives that could support homegrown electric mobility solutions. His team is developing induction motors for hybrid electric vehicles. Unlike permanent-magnet motors, induction motors operate by passing current through coils rather than rare-earth metals, reducing dependency on these imported materials.

Furthermore, Umanand explains, since hybrid vehicles combine a fuel engine with electric motors, this combination allows the electric motors to handle low-speed, high-dynamic, everyday city driving while retaining the fuel engine to supply the average power. This makes them a practical and efficient solution for transitioning to electric mobility, addressing the current constraints in charging infrastructure.

EV batteries, too, require a scarce element as the key component. Lithium-ion and lithium-polymer batteries dominate the EV market today, offering high energy density and reliable performance. However, lithium resources are geographically limited. So, battery technology needs to evolve. A promising alternative in the global limelight is the sodium-ion battery. Unlike lithium, sodium is an abundantly available resource and can be extracted easily. "Since most countries have access to coastlines or sodium reserves, sodium-ion batteries are being explored as a more globally accessible and potentially affordable energy-storage solution," notes Umanand. Researchers believe that, in the long term, sodium-ion technology could complement or even partially replace lithium-based batteries. However, the technology and the ecosystem for sodium-ion batteries are still in a nascent state.

Another major concern with batteries is safety – particularly battery fires, which have been a frequently reported issue in recent years. These incidents are typically linked not to the motor or electronics, but to poor battery design and inadequate protection systems. In response, according to Umanand, India introduced stricter battery safety norms, such as the Automotive Industry Standard (AIS 156) certification. Improved battery management systems and stricter regulations are now helping reduce such risks.

Charging the future

Electric vehicles are no longer a rare sight in Indian cities. Electric scooters glide past traffic signals, delivery e-bikes navigate through narrow lanes, and electric autos line up at street corners.

"By 2030, the country aims to ensure that 30% of all vehicles on roads are electric. The goal is ambitious. It raises a practical question – where will all these vehicles charge?" states Vishnu Mahadeva Iyer, Assistant Professor in EE. "Recent reports in national dailies have pointed out that, in some regions, a single public charger is overburdened – serving more than a hundred electric vehicles. For users, this imbalance creates uncertainty."

The challenge becomes more complex with two-wheelers, which are currently the most prevalent EVs in India. Unlike electric cars, electric two-wheelers do not follow a unified charging standard. Battery voltages vary widely, from 48 volts to 72 volts and beyond. As a result, one charger cannot charge all vehicles. Most manufacturers sell proprietary chargers, designed only for their own scooters. This works at a personal level, but in public spaces, it fragments the charging ecosystem.

"This brand-locked approach limits EV adoption and raises important safety and interoperability concerns," states Himanshu Bhusan Sandhibigraha, PhD student in EE. For India's EV transition to truly scale, charging must become brand-agnostic, much like fuel stations today.

Vishnu's team has developed interoperable, multiport chargers that can adapt to a wide range of battery voltages and charge multiple vehicles using a single platform

To this end, Vishnu's team has developed interoperable, multiport chargers that can adapt to a wide range of battery voltages and charge multiple vehicles, both two-wheelers and three-wheelers, using a single platform.

Like any power converter, the charger went through multiple rounds of design and testing before it was finalised. While it is built on a new circuit topology, the bigger challenge was transforming a lab prototype into a reliable field-deployable system. This meant adding automation, incorporating metering and protection features, and ensuring that the charger could operate continuously for long hours. Thermal design and system integration were especially important to guarantee dependable performance.

The team also acknowledged Gurunath Gurrala, Associate Professor in EE, for supporting the development of the user interfaces for the chargers and Zakir Rather, Professor at the Indian Institute of Technology Bombay (IITB), for facilitating field trials at IITB. "Because this is a new circuit topology and intended for real-world deployment, we had to design and integrate everything from scratch, making sure that each part worked seamlessly together and could operate reliably in the field," adds Himanshu.

After two years of painstaking research and experimentation, the team successfully designed a single charging unit that charges scooters from different manufacturers with varied specifications. "I would like to acknowledge the efforts of my team members for their support with hardware development and field demonstration: Manas, Neha, Siddhi, Shiv, and Shahrukh," notes Himanshu.

They further extended the concept and devised another platform that allows the same multiport charger to charge a single electric four-wheeler or multiple electric two- and three-wheelers.

These multiport chargers are also designed to comply with grid standards. "Scaling charging infrastructure is not just about installing more chargers; it is also about ensuring that higher-power systems remain compliant with grid standards. Simply deploying multiple low-power proprietary chargers does not solve this problem," notes Himanshu.

Photo courtesy: Himanshu Bhusan Sandhibigraha

Neha Rajput (left) and Siddhi Kadam (right), PhD students in EE, IISc, performing routine tests on the multiport chargers during field trials at the Department of Energy Science and Engineering, IITB

Photo courtesy: Himanshu Bhusan Sandhibigraha

Three different batteries (left to right – Kinetic Green, 60V, 23Ah; Hero Electric, 51.2V, 30Ah; Okinawa R30, 48V, 30Ah) are being charged using the multiport charger during field trials at IITB

Turning this vision into reality, however, will need more than technology. Standards, regulations, and industry cooperation must align. "The charging ecosystem in India is rapidly evolving. We must think of building future-proof charging systems that are universally compatible and interoperable across vehicle segments. It's encouraging to see some of the recent policies moving in this direction," adds Vishnu.

The facility is being designed to test 500-kW power converters – large enough to fast-charge two heavy-duty electric buses simultaneously

The success of electric mobility will not be decided by how many EVs we build, but by how easily we can charge them. And this is not just limited to small vehicles. "As electric vehicles scale up in India, charging technology must scale with them – not just for two wheelers, but for four wheelers and heavy-duty vehicles that demand enormous power," notes Harisyam, whose research focuses on developing novel fast charging solutions for electric vehicles.

This is where his team's collaboration with Delta Electronics, one of India's leading EV charger manufacturers, started. Led by Kaushik Basu, the team is focusing on setting up a 2,000-square-foot high-voltage laboratory within the department. This facility is being designed to test 500-kW power converters – large enough to rapidly charge two heavy-duty electric buses simultaneously. This is a crucial step toward establishing a reliable, high-power charging infrastructure.

Photo courtesy: Sustainable Power Electronics Lab, IISc

Upcoming 2,000 sq ft lab (11kV, 500-kW) under development at the Department of EE, IISc, in collaboration with Delta Electronics, which is being designed to test 500-kW power converters

"This project is part of a national effort to implement fast EV charging technology across India within the next five years," notes Basu.

The future of electric mobility also involves rethinking how energy flows – between the grid, charger, battery, and motor. Addressing this fundamental problem may be what finally makes EVs truly effortless for Indian users. Looking ahead, researchers see charging stations evolving into something more powerful – two-way energy systems with bidirectional charging. Harisyam says, "Parked EVs could one day support homes during power cuts, send electricity back to the grid, or even store solar energy during the day and release it at night."

While the long-term trajectory of mobility is clearly moving towards EVs, the path to that future is unlikely to be linear. Widespread EV adoption raises important questions that remain unresolved – from the massive scale of power grids required to whether the electricity used to charge vehicles is truly green. Umanand states, "The greatest gains come when electric mobility is combined with clean energy – and ultimately, with reduced dependence on motorised travel itself."

(Edited by Sandeep Menon, Abinaya Kalyanasundaram)

The Perceptron

- Aishwarya Segu

Tracing the history of the earliest neural network

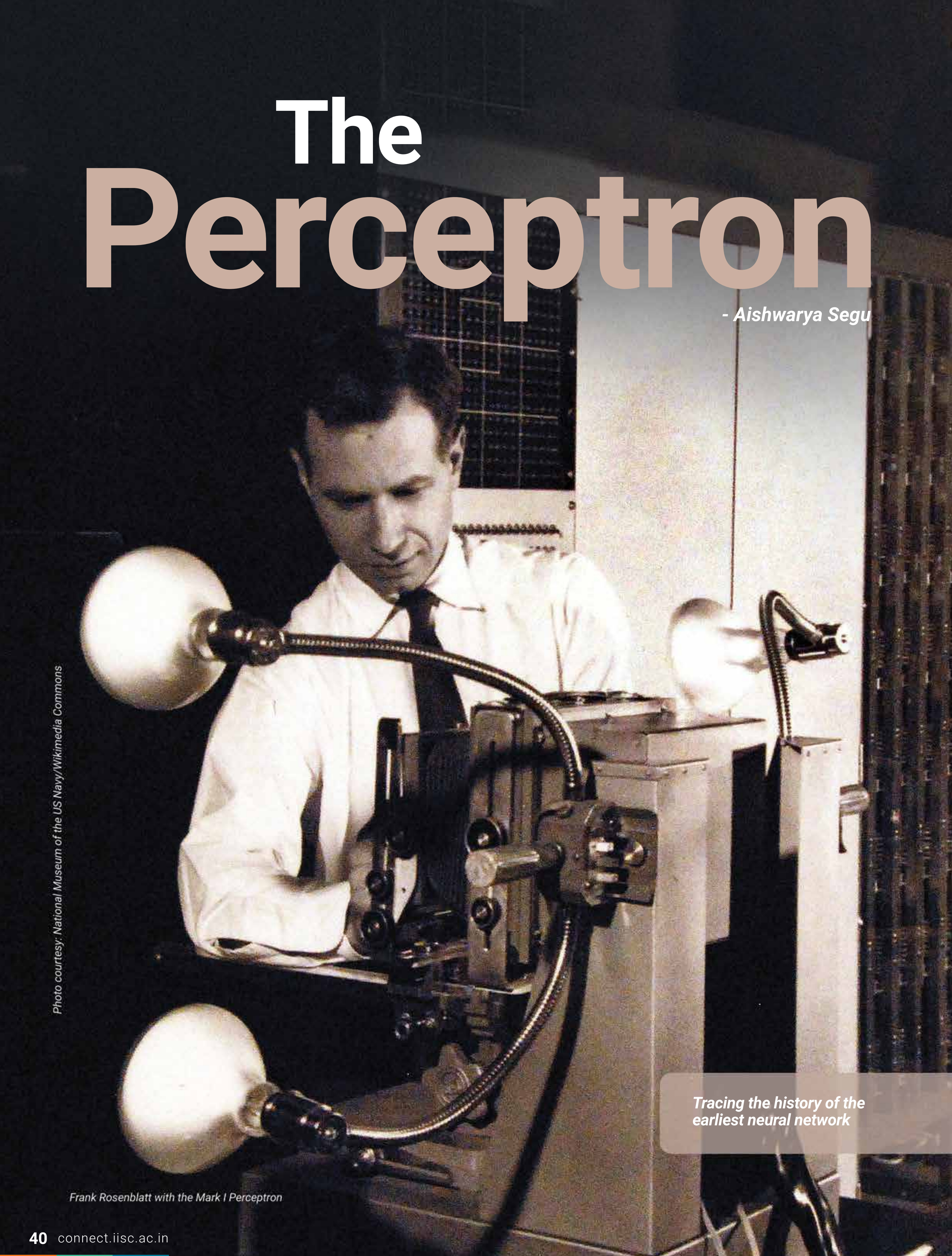


Photo courtesy: National Museum of the US Navy/Wikimedia Commons

Frank Rosenblatt with the Mark I Perceptron

The year was 1958 when the United States Navy unveiled what they called a thinking machine – a perceptron. It was an IBM 704 equipped to "react" to and learn from its inputs. The giant computer simulator was the brainchild of Frank Rosenblatt, a scientist at Cornell University. In an interview with *The New Yorker*, Rosenblatt said, "Simply put, the perceptron is a self-organised machine that can learn." He felt that the perceptron would become the technology closest to resembling the human brain. It laid, in some sense, the foundation for the era of artificial intelligence (AI).

But why did it take nearly half a century after Rosenblatt's perceptron to unleash the true power of AI? A key reason is an age-old tale of scientific rivalry. American scientists Seymour Papert and Marvin Minsky, who were sceptics in the field, questioned Rosenblatt's claims about the perceptron's learning abilities, and even came up with alternative proofs for the limitations of the perceptron's functionality. All of this diluted the hype around the perceptron's development.

Today, AI has changed the way we perceive the world. AI tools can now flawlessly transcribe text in native languages, break down a dense scientific paper in seconds, create artificial art, and compose a poem. To understand the origins of this marvellous modern technology, let us rewind to six decades ago.

The first "learning" machine

In the 1940s, English mathematician and computer scientist Alan Turing was working on building a machine that could "think" – a feat that remained unachievable in his time. From that time, scientists have been drawing inspiration from the human brain to design a machine that could exhibit signs of learning.

A key insight from the human brain was the functioning of neurons. "Biological neurons have an all-or-none property; they either fire or do not fire," explains Sitabhra Sinha, Professor at the Institute of Mathematical Sciences, Chennai. This meant that every neuron has just two states, an ON and an OFF state. Thus, the simplistic model of a neuron could be depicted as an electrical switch. American scientists Warren McCulloch and Walter Pitts used this logic and constructed the very first 'switch neuron', a simulated computer model in 1943, using the binary code of ON (firing neuron) and OFF (non-firing neuron) states.

McCulloch and Pitts demonstrated the simplest logic behind the functioning of the biological neuron. However, just switching on the neuron was not enough to achieve learning. In 1958, Frank Rosenblatt finally achieved this triumph by building a computer called the Mark I Perceptron, with a built-in programme functioning as a pattern classifier – it could learn to distinguish between different patterns.

The perceptron became the first supervised learning machine

The perceptron became the first supervised learning machine. Rosenblatt created a series of neurons that switched ON and OFF. He connected them using a binary logic gate (AND and OR gate). Then, to achieve learning, each of the switch neurons was given a random value (an activation energy, also called weight) which determined when it would switch ON, similar to how biological neurons require a certain activation energy to fire. "The activation energies have a threshold value beyond which they activate, directing the firing properties of the network," adds PS Sastry, Honorary Professor at the Department of Electrical Engineering, IISc.

This allowed the series of switch neurons to store the learned pattern. And the series came to be called the single-layered neural network. "The perceptron is the basis of most artificial neural networks that we see today," emphasises Rishikesh Narayanan, Professor at the Molecular Biophysics Unit, IISc.

Rosenblatt's innovation wasn't in the development of the neural network structure, but in the implementation of the learning rule. When the neural network encounters a pattern (input), it attempts to learn it. This results in the alterations of the activation energies associated with each subunit of the network. "By iteratively tuning these weights (activation energies), the perceptron was able to classify data, which is represented as the output," says Sastry. Whenever the network was shown a particular pattern, it recognised it, and as an output produced a YES or NO answer.

"The perceptron could only solve linear equations," explains Sitabhra. "[But] it failed to solve the infamous XOR [Exclusive OR] problem, whose solutions are non-linear," adds Sastry. The single-layer perceptron could learn the difference between simple logic gates (simple linear function). But its limitations arose when the logical reasoning was not bound by AND and OR gates.

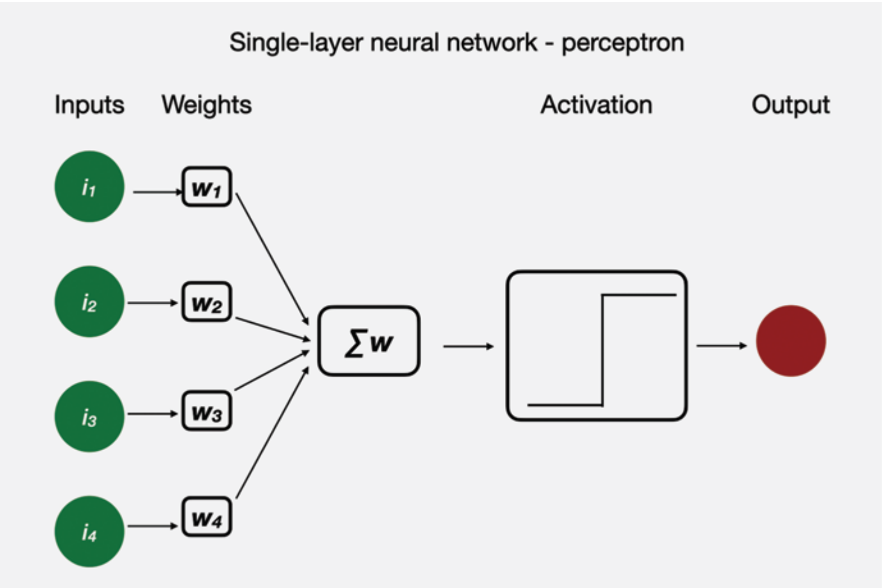


Image: Aishwarya Segu

A simplistic schematic representation of a single-layered neural network

The XOR problem was a classic example of this. In XOR, the answer is YES only when two inputs are different [such as (0, 1); (1, 0)]. However, it is a NO when the inputs are similar [such as (0, 0); (1, 1)]. If we plot the four possible input combinations on a 2D graph, the YES outputs (0, 1 and 1, 0) and the NO outputs (0, 0 and 1, 1) are diagonally opposed, and the solution for this can never be a straight line. The Mark I Perceptron, the single-layered neural network, could never solve this.

Marvin Minsky, co-founder of the AI lab at the Massachusetts Institute of Technology (MIT), and Seymour Papert, a mathematician from MIT, critiqued this flaw of the single-layered perceptron with a sharp mathematical argument in their book titled *Perceptrons: An Introduction to Computational Geometry*, published in 1969.

This critique of perceptrons triggered the first AI winter – a long hiatus in neural network research – which simultaneously resulted in a reduction in monetary funding for neural network research. Unfortunately, the untimely death of Rosenblatt in 1971 further stalled developments in the field.

"Like the phoenix, I rise"

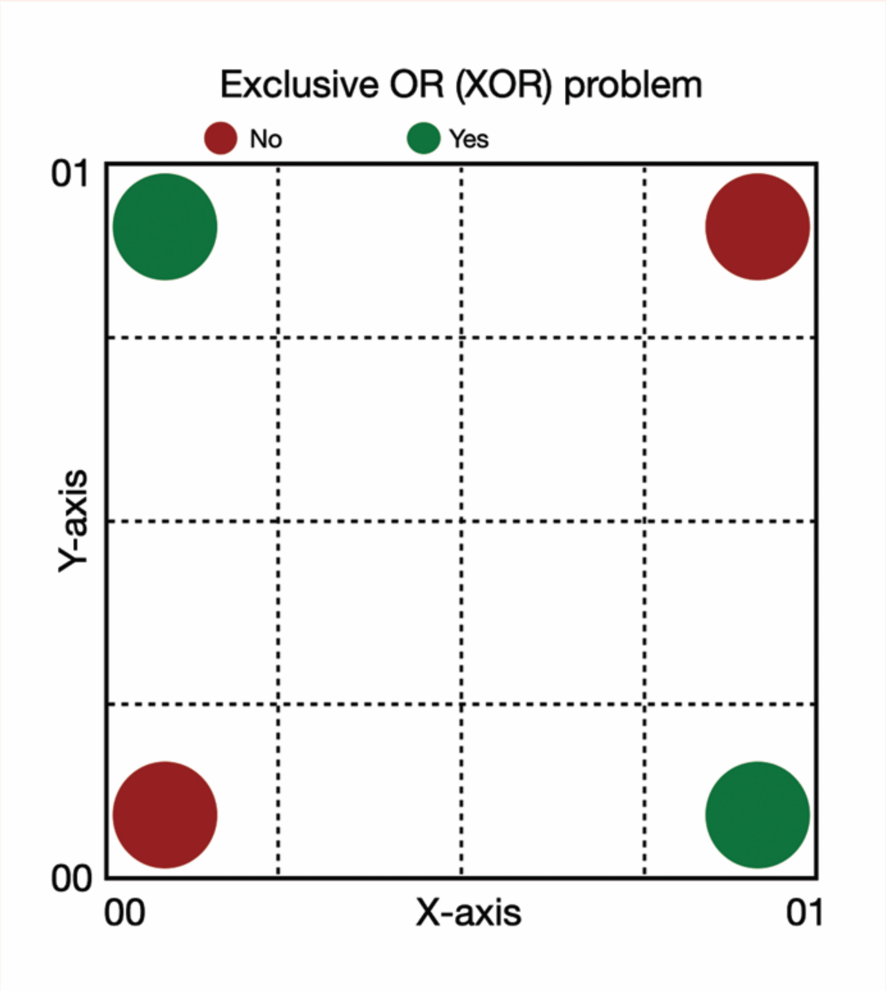
Fifteen years after Rosenblatt's death, the AI winter turned when scientists finally modified neural networks to solve the XOR problem. For this, they added a second, hidden layer of inputs to Rosenblatt's single-layer neural network.

This hidden layer was the key to breaking the linearity barrier. "It laid the foundation for modern deep-learning tools," says Sastry. The problem with the single-layer neural network was the absence of a method to identify failures and errors when the solution was not linear. One way to solve this problem was by developing a method to convey the error back to the initial input layer for correction. To evaluate this error, scientists built a step-by-step computer programme or algorithm.

"This was called the backpropagation algorithm," explains Sitabhra. It first identifies the error in the output stage and backtracks the error to the input layer through the hidden layer. This process results in precise adjustments to the initial weights, which ultimately can produce the desirable solution for nonlinear functions.

Seppo Linnainmaa, a Finnish mathematician, first postulated the mathematical proof for backpropagation using calculus in 1970. But it was Paul Werbos, a PhD student at Harvard University in 1974, and Shun'ichi Amari, a Japanese neuroscientist in the 1980s, who independently described the application of backpropagation as a training method for multi-layered perceptrons.It is possibly the most influential work on modern-day multi-layered neural networks.

Image: Aishwarya Segu



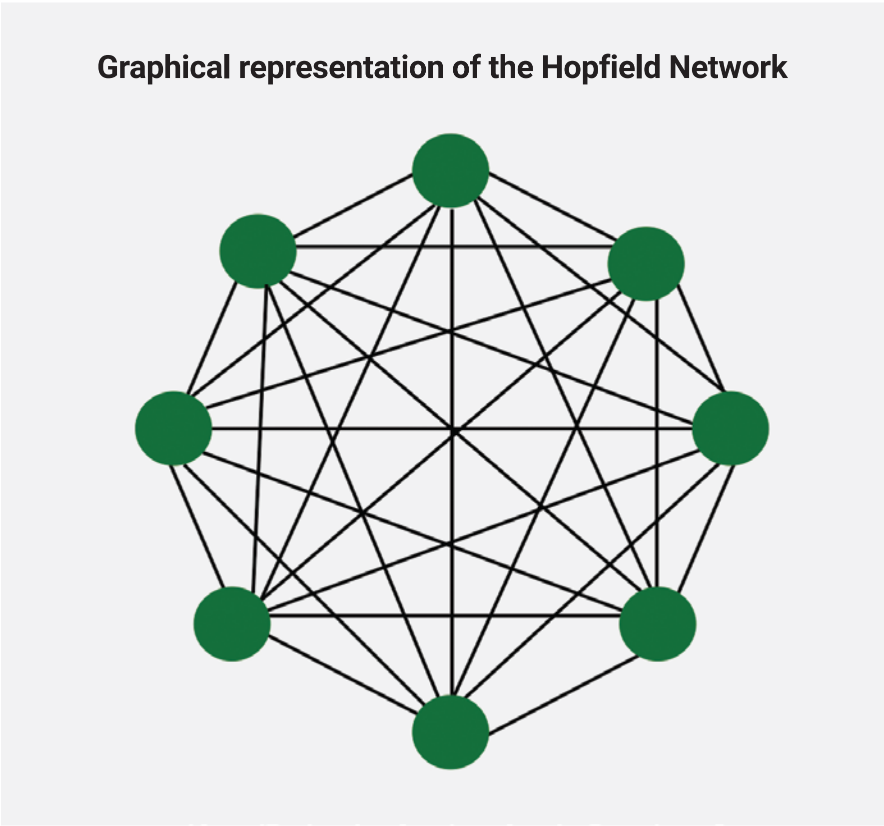
Graphic depicting the XOR problem

Finally, in a 1986 paper titled 'Learning representations by back-propagating errors,' American scientists David Rumelhart and Ronald Williams, and British-Canadian scientist Geoffrey Hinton provided the compelling experimental and mathematical proof of multi-layered perceptrons. It is possibly the most influential work on modern-day multi-layered neural networks.

Simultaneously, in 1982, American physicist John J Hopfield developed an alternative approach to solving complex problems using neural networks. Multi-layered networks are feedforward networks – information moves in only one direction, from input to output. In contrast, Hopfield built a recurrent neural network, which was still single-layered. In a recurrent network, all neurons are connected to all other neurons at all times, with symmetric activation energies, instead of random as seen in Rosenblatt's design. The neurons still behaved as switches.

As the neurons were all connected, a change in the activation energies during learning results in overall changes in the network. This also means that the energy of the network changes. Thus, the network can have

Image: Aishwarya Segu



A schematic representation of Hopfield's recurrent neural network. Green circles depict switch neurons

multiple energy states, resulting in hills and valleys corresponding to high and low energy states. When a pattern is recognised by the network, it attains the lowest energy function (a valley). Because this is a stable state of energy, it can learn and memorise it. The Hopfield network became a key to visualising associative memories and patterns.

Hopfield and Hinton received the 2024 Nobel Prize in Physics for their contribution to neural networks. By adding a third layer, perceptrons could now solve non-linear functions, and by developing recurrent neural networks, scientists were able to write algorithms capable of modern pattern recognition.

The power of computation

The idea of building thinking machines did not begin with the invention of the computer but with a fundamental question: Can human thought be reduced to a logical process? But with the advent of the multi-layered neural networks, the field required greater computational power to achieve the possible computations.

"In our times [in the 1990s], we largely had 3-4 layers, and to add even a single neuron in the layer – forget about a layer – we thought 100 times, only because of the number of computations it increased, for which machines were not available," recalls Rishikesh.

The next essential step in neural network research was to achieve the computational power required to run the algorithms. This became possible because of Parallel Distributed Processing (PDP), developed during the mid-1980s. Until then, computers ran neural networks sequentially; PDP changed that notion. It allowed operations to be performed concurrently, distributing computations across multiple processors. This exponentially enhanced the computational abilities of the machine learning models.

In the late 1990s, scientists realised that Graphics Processing Units (GPUs) – originally designed to perform thousands of parallel matrix multiplications for rendering video game graphics – were best suited for the parallel computations required by backpropagation. The use of GPUs to train artificial neural networks began in the early 2000s, officially lifting the AI winter. Simultaneously, the rapid growth of the semiconductor industry enabled cheaper hardware components needed for the processors.

Artificial neural networks could now recognise patterns including alphabets, pictures, and even voices. The true inflection point came in the early 2020s, when widespread development and access to AI models and applications unleashed its full power, making AI a household term overnight.

The journey of the perceptron is a testament to the complex, non-linear nature of scientific progress

The journey of the perceptron is a testament to the complex, non-linear nature of scientific progress. It wasn't without conflict. "Minsky and Papert were excellent critics of the field," says Rishikesh. But some scientists think that they may have tried to kill perceptron research during the late 1970s and perhaps delayed the timeline of AI's evolution.

Sitabhra adds that such a debate is ultimately a "chicken and egg problem" where the contributions of both theories have equal merit. "Without Minsky's critique, we would not have maybe developed transformers, an essential part of neural engines," he adds. Today's AI tools use both Rosenblatt's and Minsky and Papert's approaches. "The vast, powerful networks learn patterns from data, while symbolic methods provide structure," explains Sastry.

Rishikesh cautions that while AI can do a lot, its use as a "mimicry of biological intelligence is falsification." As Papert once pointed out in his essay published in the journal *Daedalus*: "Artificial intelligence should become the methodology for thinking about ways of knowing."

Aishwarya Segu is a PhD graduate from IISER Thiruvananthapuram and a former science writing intern at the Office of Communications, IISc

(Edited by Ranjini Raghunath)

Bridging Worlds

- Interview by Sandeep Menon

Photo courtesy: Suhas Mahesh

Suhas Mahesh is a man of many talents. He is a material physicist working on building self-driving labs using Artificial Intelligence (AI) to accelerate materials discovery. A Rhodes Scholar currently working with Schmidt Sciences in New York, he also nurses a love for languages, particularly ancient ones like Sanskrit and Prakrit. He has published a translated collection of Sanskrit love poetry,* How to Love in Sanskrit, *bringing together verses and short prose pieces by some of the tradition's greatest writers.

A former undergraduate student at IISc (batch of 2012-2016), Suhas speaks to* CONNECT *about his journey in academia, his memories of IISc, and his efforts to make Sanskrit more accessible.

You were an undergrad at IISc. What was the impact that the institution had on you?

An enormous impact! I grew up in Bengaluru, and from the time I was about 10, I would come for Open Day every year. I particularly remember seeing superconductors levitating on neodymium magnets; that was absolutely thrilling. I had it in my mind very early that this was a place I wanted to be. Fortunately, when it was time to start university, IISc had just started the undergraduate programme. So, it was a no-brainer.

I was so excited that I started a research project just three months in, with Prof GK Ananthasuresh at the Robert Bosch Centre for Cyber Physical Systems. That led to a string of research projects with different faculty members at IISc, which is not something you usually get at other places. I've been at multiple institutions now and I have never seen more concentrated talent than in my IISc undergraduate class. Ten years later, that class has gone on to do truly amazing things.

IISc has been a formative experience in my life. And I'm very proud to be an alumnus.

Can you talk about your journey since leaving IISc?

It was a journey that involved hopping from field to field. I got the Rhodes Scholarship and went to Oxford. I did my PhD in physics, studying semiconductors. At some point, I realised that the computational methods that we have today have plateaued over the last 20-30 years. And then, there was a new kid on the block.

The great advances in science have often come not from discovering new phenomena but from building new instruments that let you see the world differently

The new kid on the block was Artificial Intelligence (AI)?

Yes. The great advances in science have often come not from discovering new phenomena but from building new instruments that let you see the world differently. AI struck me as exactly that kind of instrument – one that could be applied across virtually every scientific field. I was very keen to start using AI to see what difference it could make in research. This was before it became cool.

At that point, Eric Schmidt (former CEO of Google) sponsored me to go to the University of Toronto and re-train as a computer scientist, so that I could work natively in both computer science and physics. I spent three years there and built automated labs for doing catalyst synthesis and for semiconductor discovery, all driven by AI.

At the end of that, Schmidt had a new organisation called Schmidt Sciences in New York, which supports cutting-edge science. And Schmidt Sciences asked me if I wanted to lead the AI for Science programme there. I'm setting that up in New York now.

You enjoy working at the cutting edge of science, then?

Yes, absolutely. There is no greater pleasure than being able to stand at that edge, punch forward, and make that dent at the edge of human knowledge. It also excites me that this field is profoundly interdisciplinary right now. You have multimodal AI ingesting images, audio, and text to make predictions. Meanwhile, more mathematical researchers are developing tricks such as neural operators to handle different resolutions of data. My job allows me to work at the interface of many fields and bring ideas across them. It's not often that you get to be in the middle of a revolution like this.

It seems like you have jumped across a lot of fields. Is that something you always wanted to do or something that just happened?

Mostly accidental. You chase good ideas no matter where they come from. And it seems like the nature of good ideas is

Photo courtesy: Suhas Mahesh

Suhas Mahesh (top right) with friends during the IISc convocation in 2016 that they are not localised. You have to become interdisciplinary.

You are working in material physics now, or have you shifted away from that?

Materials remain my core, but it's a little broader than that right now.

Your website says that you are working on self-driving labs using AI to accelerate material discovery. What does that work entail?

The idea is to use AI to find new materials. So far, if we wanted to do materials discovery on the computer, we were sort of at the mercy of the theorists. There hasn't really been any fundamental progress in theory for a long time now. So, how do you make progress? We finally have a way because with AI, you can learn from data. You don't really have to know what the data is doing or what it's saying, but you can learn from it. And that is what we are trying to exploit – generate large amounts of data and make these predictions better, even without having any theory behind it.

How do you use AI to come up with new things?

Picture an autonomous laboratory – a robot, guided by an AI algorithm, carries out synthesis and characterisation, then fabricates the material. Then, it sees what it has made and makes decisions about whether it did the right thing and got what it wanted. If not, it does the loop again and loops back and says that these are probably the things that went wrong. It keeps iterating, tightening the error bar until, ideally, it converges on the material that you're after.

What is the scientist's input with this AI?

I should be honest: I'm making it sound more automated than it currently is. The field is still nascent. You need a lot of human input to keep this running. A material is a three-dimensional arrangement of atoms. How do you represent that for a computer? It's a harder question than it sounds. Atoms may be disordered in various ways. They vibrate and rotate. All of this must be explained to the AI algorithm. That's what we call featurisation.

Photo courtesy: Suhas Mahesh

Suhash Mahesh (left) working on an AI-Driven Crystal Growth Robot at the University of Toronto

And then, there's the problem of competing products. You try to make one thing and end up making 10 others. The decision tree is something a scientist has to manage because, as you pursue a particular goal, the possibilities explode exponentially.

Now, can I ask you about your interest in Sanskrit and Prakrit? Where did that come from?

Strangely enough, from the failings of the Karnataka state board education system *(laughs)*.

My languages in school were English, Kannada, and Sanskrit. The English and Kannada syllabuses were uninspiring – lessons on rainwater harvesting, pollution, global warming. Language textbooks should present a cross-section of the finest literature. The Sanskrit textbook, by contrast, was just the purest, highest-quality literature thrown at us with absolutely no mediation. Direct extracts from Kalidasa's *Raghuvamsha* and Banabhatta's *Kadambari*. Very early on, I realised that this was real, incredible literature. Every day I'd do my science work, and around 7 pm. I'd start reading Sanskrit. That would go on until 10 pm. Sustained effort over many years led to this.

'The question was: Can you write a book that people will actually read? Coming up with the right idea was the hard part'

How did you get the material to keep reading? Because most Sanskrit students never read anything more than their textbooks.

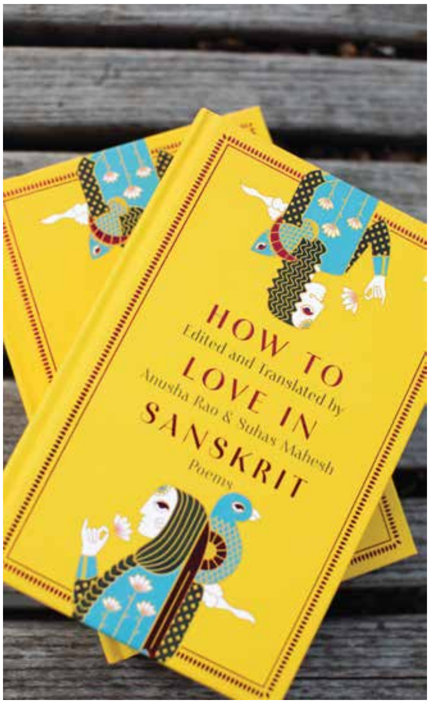
The materials are generally out there. You can go to Vedanta Book House in Basavanagudi or any public library in Bengaluru. I was lucky to get in touch with many Sanskrit scholars in the city.

Oxford has one of the largest Sanskrit departments outside India, which gave me training in Western philological methods. I also took classes in Greek and Latin there. That connection to a related language family gave me more insight into the nature of ancient languages. It kept building that way.

When did you think that you had the proficiency to write a whole book, *How to Love in Sanskrit*?

Proficiency was not the issue. The question was: Can you write a book that people will actually read? Coming up with the right idea was the hard part. The book has about 200 verses in it. My co-author is my wife, Anusha. We read roughly 10,000 poems and felt that only 200 could be appreciated by a modern reader without a thicket of footnotes. The age gap with these poems is just too large otherwise.

Photo courtesy: Suhas Mahesh



How to Love in Sanskrit, *a book co-written by Suhas Mahesh and his wife Anusha Rao*

Your wife is also interested in Sanskrit then?

Yes, my wife is doing a PhD in Sanskrit at the University of Toronto. She's just about to finish. We met while I was at IISc. She used to live in Malleswaram, and a common friend introduced us. And then, I went to the UK and she went to Canada. After I finished my PhD, I moved to Canada and now we live in New York.

I saw a post of yours. Somebody had written that Sanskrit was for elites and Prakrit was for normal people, and you said that was false. As I understand, Prakrit is the language that links us to ancient Sanskrit and the present languages. Is that right?

That's a great question. Prakrit is essentially the language that Sanskrit evolved into. Sanskrit was spoken by people in Punjab about 3,000 years ago, and that evolved into many Prakrits across India.

When people point to a Prakrit literary work and claim that it was written by commoners, that's simply not true; by the time those works were composed, Prakrit had long ceased to be a spoken language and had become a language of elites. The way literature has always worked in India is that there's a language which is spoken, then it stops being spoken and becomes an elite literary vehicle. People use it for hundreds of years to write things, but nobody speaks it in the kitchen or the bedroom.

Like Latin.

Yes, exactly. Like Latin 300 years ago in Europe, a language of scholars and kings, not of daily life. That was the case with Prakrit and Sanskrit as well.

What would you attribute Sanskrit's longevity to? Because Sanskrit is still something that people hear about or know and is taught in schools.

Several things. It was adopted by very prominent religious traditions – Hindu, Buddhist and Jain – and remains integral to them. Because it attached itself to flourishing religious systems, all the ancillary sciences that come along with that – logic, Indian linguistics, mathematical texts and so on – got preserved and studied. Quantity is a quality of its own. The entire output of a civilisation has been preserved in the language.

Prakrit, by the way, is still used too. The Jains still memorise prayers in Prakrit. Because they're a small minority in India, you don't hear about it as much, but it retains some force in the Jain context.

You started Ambuda.org, a library for Sanskrit. How important was it for you to do that?

It takes about 10 years of dedicated effort before you can pick up a Sanskrit book like it's a storybook and just start reading. My friend Arun Prasad and I wanted to help accelerate that process. The site lets you take a text, click on the verses, and it will auto-segment them – split the words apart, do a grammatical analysis, and link to dictionaries. I'm hoping that tools like this can shorten the journey from 10 years to three.

You have also written for *CONNECT* before. Have you continued doing science communication?

When I was a PhD student at Oxford, I'd organise multiple outreach events every year. One that I particularly remember: there was a big astronomy festival, and they sent out a call for exhibits. I had nothing to do with astronomy, but I was determined to bulldoze my way in because it seemed too interesting to miss. My PhD was in solar cell physics, so I named my exhibit "Powering the World with Starlight," the sun being the star in question.

I didn't get much of a chance to do that in Toronto; there wasn't the same atmosphere for it. But I'm in New York now, and the city is big on science communication. I'm looking forward to getting that engine running again.

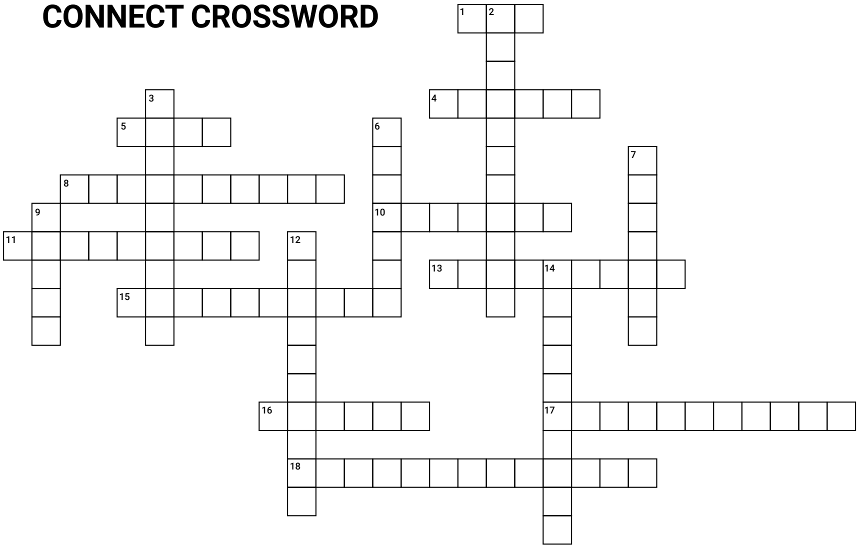
(Edited by Ashmita Gupta)

Photo courtesy: Suhas Mahesh

Suhas Mahesh at a science outreach event at Oxford University during his PhD days

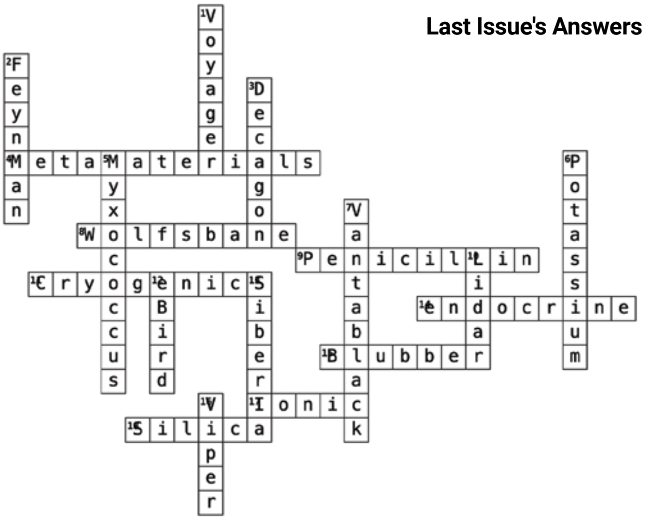
Fun Corner

CONNECT CROSSWORD



Send your completed puzzles to **connect.ooc@iisc.ac.in**
The top 3 winners will be announced in the next issue!

Last Issue's Answers



ACROSS

1. Particulate matter ejected from erupting volcanoes
4. Test designed to determine if a machine can think
5. A large ocean current that spins in place like a giant vortex
8. The fear of dogs
10. Nobel prize laureate who was later found to have manipulated scientific images
11. First targeted drug for breast cancer released in the 1970s
13. Type of machine containing or operated by pressurised air or gas
15. First "learning machine" that became the building block of artificial neural networks
16. The complete set of genetic instructions (DNA) found in an organism
17. Organisms that can survive in space, also called water bears
18. State of being in multiple states simultaneously

DOWN

2. Proposed the question of a cat being both dead and alive
3. Chemical messengers which initiate, amplify, or suppress immune responses
6. Chemical compound responsible for petrichor
7. Commonly used element in EV batteries
9. Highest-energy, shortest-wavelength, and most intense radiation abundant in space
12. Red supergiant star in the Orion constellation, expected to soon explode as a supernova
14. Type of tumour that spreads to other parts of the body

LAST ISSUE'S WINNERS!

1. Suhas Kamath, MTech student, Department of Computational and Data Sciences
2. Shreoshee Mukherjee, Project Research Scientist, Department of Design and Manufacturing
3. Shivaprasad L Kulkarni, System Engineer, Supercomputer Education and Research Centre

CAMPUS CARTOONS

Seeds of friendship

By **Kruthika Eswaran**, PhD student (2017), Centre for Atmospheric and Oceanic Sciences

Submit entries to Campus Cartoons to **connect.ooc@iisc.ac.in**

Abstracts | Rishabh Maurya | IISc Photography Club