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Biochemistry Department
100 and counting

Anurag Kumar
An interview

Fighting COVID-19
IISc doctors speak

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IISc IN THIS ISSUE

Editorial

The Department of Biochemistry, which turns 100 next year, has stood witness to several watershed moments in India's history. In this issue, we bring you glimpses of the department's history and the evolution of its research. Read about the far-reaching work of Gilbert Fowler, its first head; the extraordinary versatility of M Sreenivasaya, whose work in fermentation technology spanned several fields; G Padmanaban's lifelong commitment to the battle against malaria; and the department's pioneering work on the now controversial legume – kesari dal. HS Savithri, the first woman Chair at Biochemistry, reminisces about her time at the department. And three alumni of the department, who are now faculty members at the Department of Molecular Reproduction, Development and Genetics, retrace the paths that brought them back to the Institute.

Look out for the second part of our profile of PR Krishnaswamy, another alumnus of the Department of Biochemistry, in which he talks about his journey from academia to industry, and back. Also featured in this issue is a unique MD-PhD programme that aims to take biomedical research from the bench to the bedside. In other features, we take a look at why glaciers in the Himalayas are melting, and at the trials and tribulations of conducting neuroscience research to understand human behaviour.

We also have interviews with Anurag Kumar, who recently retired as IISc's Director; alumnus Sethuraman Panchanathan, who has been appointed as the head of the US National Science Foundation; and AV Leelavathi, who spent 38 adventure-filled years at the Institute.

As we come to the end of 2020, a year overshadowed by the COVID-19 pandemic, we also hear from doctors at the Health Centre, who share their experiences of being at the frontlines.

Happy reading!

TEAM CONNECT

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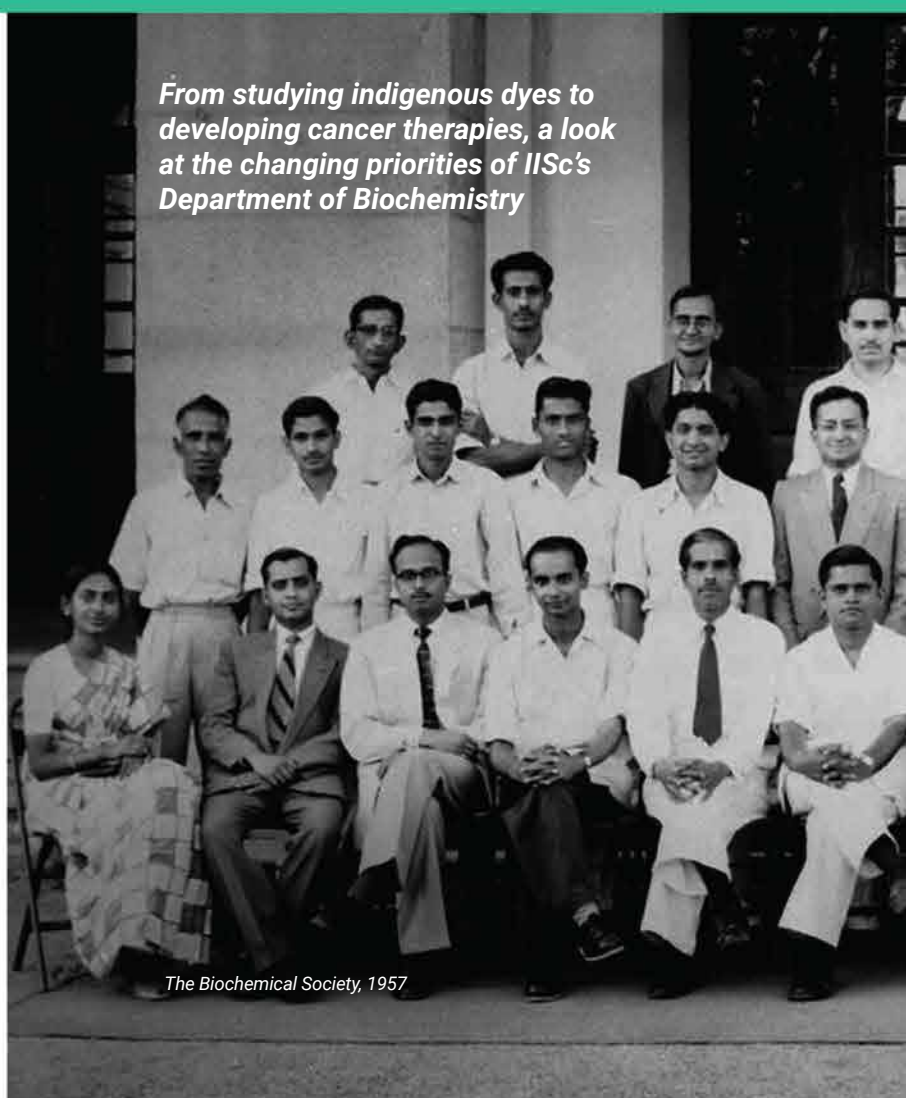
HOW **BIOCHEMISTRY RESEARCH EVOLVED** OVER A CENTURY

- Narmada Khare

From studying indigenous dyes to developing cancer therapies, a look at the changing priorities of IISc's Department of Biochemistry

The Department of Biochemistry at IISc turns 100 next year. It holds the distinction of being the first department dedicated to the studies of biological chemistry in India. In the century since it was established, the department has seen and responded to a world war; a few epidemics; India's struggle for independence; wars with neighbouring nations; and numerous governments with constantly changing ideologies and priorities. Add the myriad interests of the professors heading it to the mix, and what emerges is a rich tapestry of the history of life sciences in the Institute.

When tracing the evolution of the department, it becomes clear that the various changes that took place, particularly in the early years, were linked to the socio-economic transformations that the country underwent.



The Biochemical Society, 1957

Early years

When the Department of Biochemistry was set up in 1921, there were only three departments at the Institute: Electrical Technology, General and Organic Chemistry, and Applied Chemistry (which became Biochemistry).

The Department of Biochemistry was not just new, it was the first of its kind. There was no blueprint to follow. Older universities like Cambridge too had only recently accepted biochemistry as an independent area of science. A new syllabus had to be created for students wishing to join the Department, since no Indian universities taught bacteriology and biochemistry.

It started firing on all cylinders almost immediately. IISc's Annual Report for 1921-22 states: "The new activated sludge plant for dealing with a portion of the sewage from the western side of the estate has been completed during the year and should shortly be in operation. It will enable numerous researches on the biochemistry of the nitrogen cycle to be carried out." With the aim of increasing the production of lac (a resinous secretion by lac insects with several uses including as dye and varnish), the Government of Mysore gave land with 200 *Shorea talura* trees, which are favoured by lac insects. The Government of Madras supplied tamarind from Bezwada district, so that the department could investigate if it was a commercially viable source of tartaric acid. Several such requests came pouring in from across the country.

The approach of the scientists in the department illustrates their dedication to commissioned work as well as to the scientific curiosity that originally brought them to IISc. For instance, while studying the natural history of the lac insects, the same Annual Report (1921-22) records that the researchers observed "an extraordinary development of honey at certain stages of lac development." This 'honey' attracted ants that consumed it together with any potential parasites, thus protecting the lac insect. The department suggested that since honeybees were attracted to the 'lac honey', honey production from beehives could also be a by-product of a lac plantation.

Another section in the same Annual Report provides further proof of their commitment: a study on coconut retting, a practice in coastal areas, was conducted at the request of the Madras Government. Retting is a process in which coconuts are steeped in water, and the fibres are separated from the coconut by the action of microbes in water. It was observed that the binding material in the coconut fibres was being fermented very fast during the process. A number of water samples from the west coast were tested, but the analysis showed nothing unusual in the water. The scientists then carefully collected samples of coconut from all these areas and steeped their husks in a controlled retting process. Experimentation in aseptic conditions revealed the presence of at least two different hair-like bacteria in the husk, which seemed to affect the process adversely. Bacteriology of coconut retting became an important line of study after that.

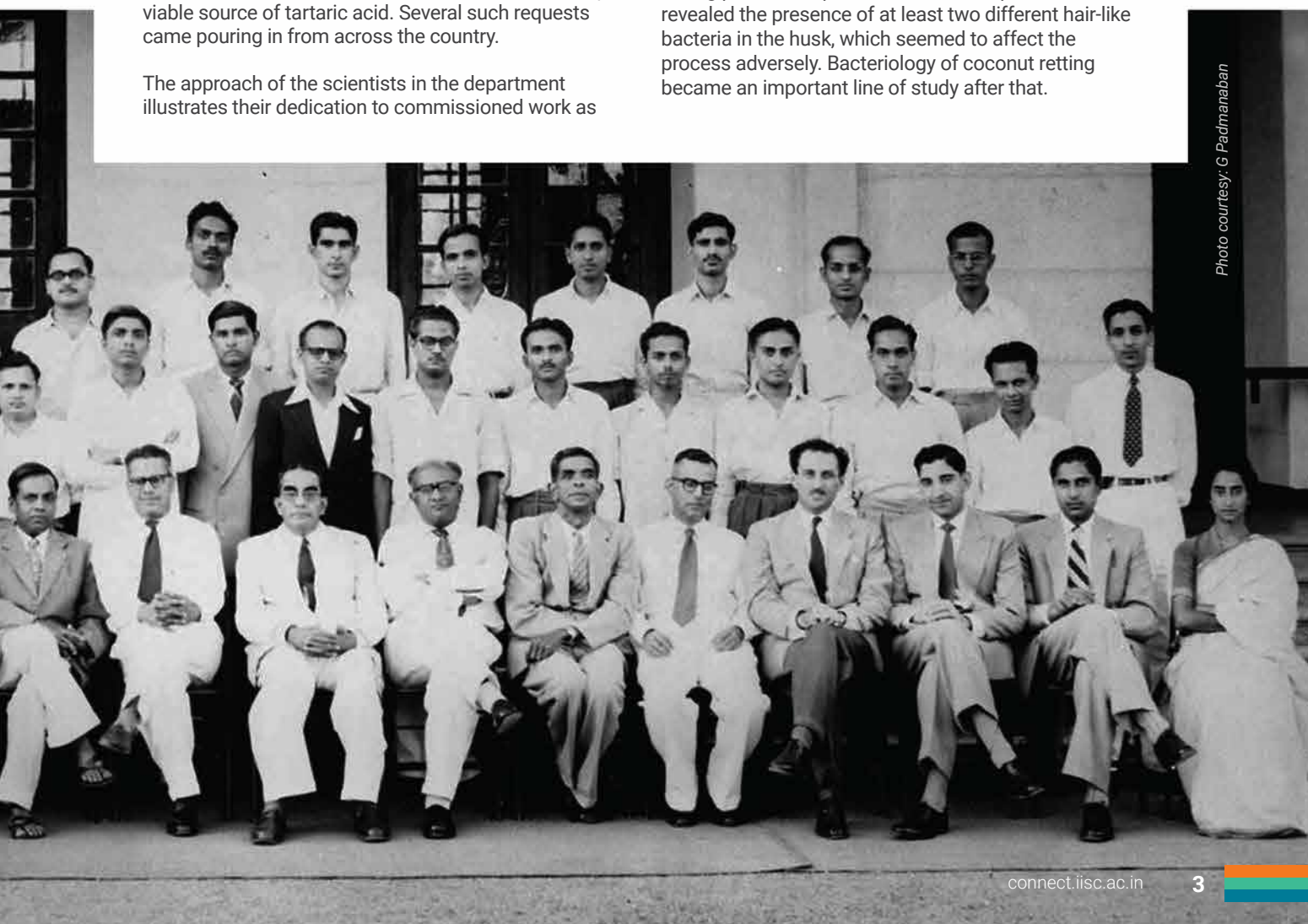


Photo courtesy: G Padmanaban

This was not science from the ivory tower, but at the grassroots. The problems to be solved were tangible and the material to be studied was in the neighbourhood.

Changing priorities

During the first few years, the structure of the department was simple. It had one professor, and the rest were students or assistants. Specialised sections like Fermentation Technology and Cytology were born later out of widening interests. In the years to come, these sections further branched out, merged, and emerged as independent departments such as Microbiology and Cell Biology (MCB) and Molecular Reproduction, Development and Genetics (MRDG) at the Institute.

Research in the first 50 years was largely influenced by national needs and by the scientists themselves. While the first Chair, Gilbert J Fowler (1921-24), introduced techniques for treating sewage, composting and waste management, the second Chair, Roland V Norris (1924-29), brought in the knowledge of microbiology. V Subrahmanyan (1930-49), the third Chair, introduced studies on nutrition. Subrahmanyan's tenure must have been tumultuous. It spanned the years of World War II, Indian Independence and the devastating Bengal famine of 1943. He had to gear up the department to meet the food and nutritional demands created by war and famine. Work on vitamins and antibiotics received a boost.

> ***Research in the first 50 years was largely influenced by national needs and by the scientists themselves***

By this time, several universities in the country had also initiated biochemical research. To provide the opportunity for researchers across India to interact and exchange ideas, the department started a group called 'The Society of Biological Chemists' in 1930. This was also the time when researchers started looking in their neck of the woods for microbes to produce medicine and foods with high nutritional value. Microbes adapted to the Indian climate were necessary for efficient fermentation of Indian fruits and flowers, and for the distillation of sugars to produce alcohol and acetone that were used in the manufacture of ammunition. In 1940, M Sreenivasaya, a researcher at the department, started a library of native microbes. Within 10 years, nearly 2,500 cultures were deposited in it. In the coming years, this 'National Collection of Type Cultures' was an extremely useful resource to screen for organisms that produced antibiotics and enzymes for specific chemical reactions.

Plant biochemistry

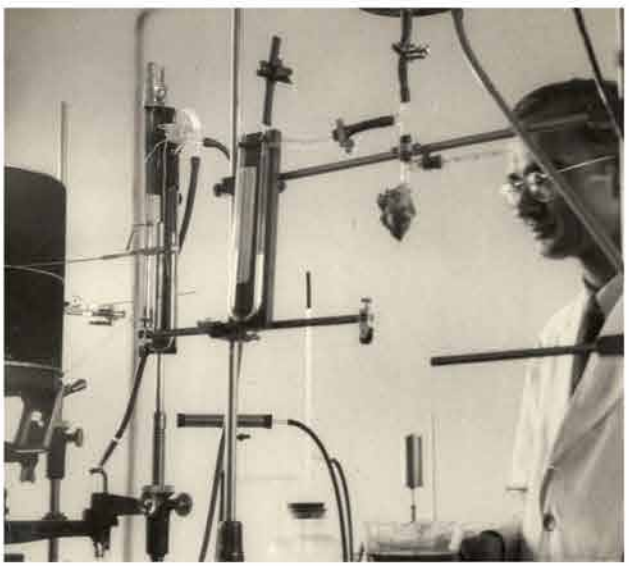


Photo courtesy: IISc Archives

The pharmacology laboratory in 1941

Though the focus of many in the department had now turned towards human health, work on plant physiology and biochemistry continued. KV Giri, the fourth Chair (1950-58), a plant biochemist as well as a nutritionist, developed effective methods for separation and quantification of specific compounds from plants. The effect of compounds from common plants like garlic on the tuberculosis bacterium was demonstrated for the first time in 1946.

In a pivotal contribution in 1969, the agent causing lathyrism, a crippling and sometimes lethal disease observed particularly in poor farmers and labourers, was identified. An easy method was devised to neutralise this neurotoxin from 'kesari dal', a cheap and hardy legume, in order to help thousands of families in famine-hit, poverty-stricken areas in central India where it was commonly consumed.

Certain plant compounds have motivated important research in the department. This was proven again more recently in the mid-2000s when curcumin, a compound found in turmeric, was shown to be effective in treating malaria, in combination with artemisinin. This treatment is set to undergo clinical trials.

Advent of molecular biology

It took a while before the focus of the department shifted from applied to pure biochemistry. SC Pillai and J Ganguly, in their overview of the department on its Golden Jubilee in 1971, suggested that the emergence of several institutes that practised biochemistry and trained biochemists in the years after Independence, lightened the burden on the department at IISc. The responsibility of being the scientific advisors for the agricultural and industrial sectors in the country was split between the many specialised institutes. This finally allowed the researchers in the department to move on to more fundamental questions in the field.

In the early 1950s, the structure of DNA and the sequence of insulin were discovered in Europe. It is unclear whether these discoveries created a stir at IISc at that time. It was only after PS Sarma took over as chair in 1959, that work on nucleic acids and on endocrine biochemistry began. During Sarma's tenure (1959-70), the department entered the age of modern biochemistry. He increased the number of students and staff, and acquired more current equipment. In 1968, the University Grants Commission acknowledged the department as a Centre of Advanced Study in Biochemistry.

In the last 50 years, classical biochemistry has made way for molecular and cellular biochemistry. J Ganguly, who became the chair in 1977, used his substantial Rockefeller Foundation grant to procure instruments like a refrigerated ultracentrifuge, a spectrophotometer, and a liquid scintillation counter. A wider net was cast in the field of public health in the 1980s, when inherited diseases were studied in infants born of consanguineous marriages, using biochemical approaches.

Today, proteins and nucleic acids have taken pride of place, and contributions are being made in transcriptional and translational regulation of genes, in chromosomal stability, and DNA damage and repair. Studies on abnormal recombination causing chromosomal breaks have led to identification of targets for cancer therapy. Today's researchers are also investigating mitochondrial DNA and its role in disease.

Current research also focuses on more affordable treatments and vaccines using indigenous strains of yeast. The vaccine for Hepatitis B, of which millions of doses have been sold, is an example of this. Research on the immunology of viruses and other infectious agents has helped save many lives.

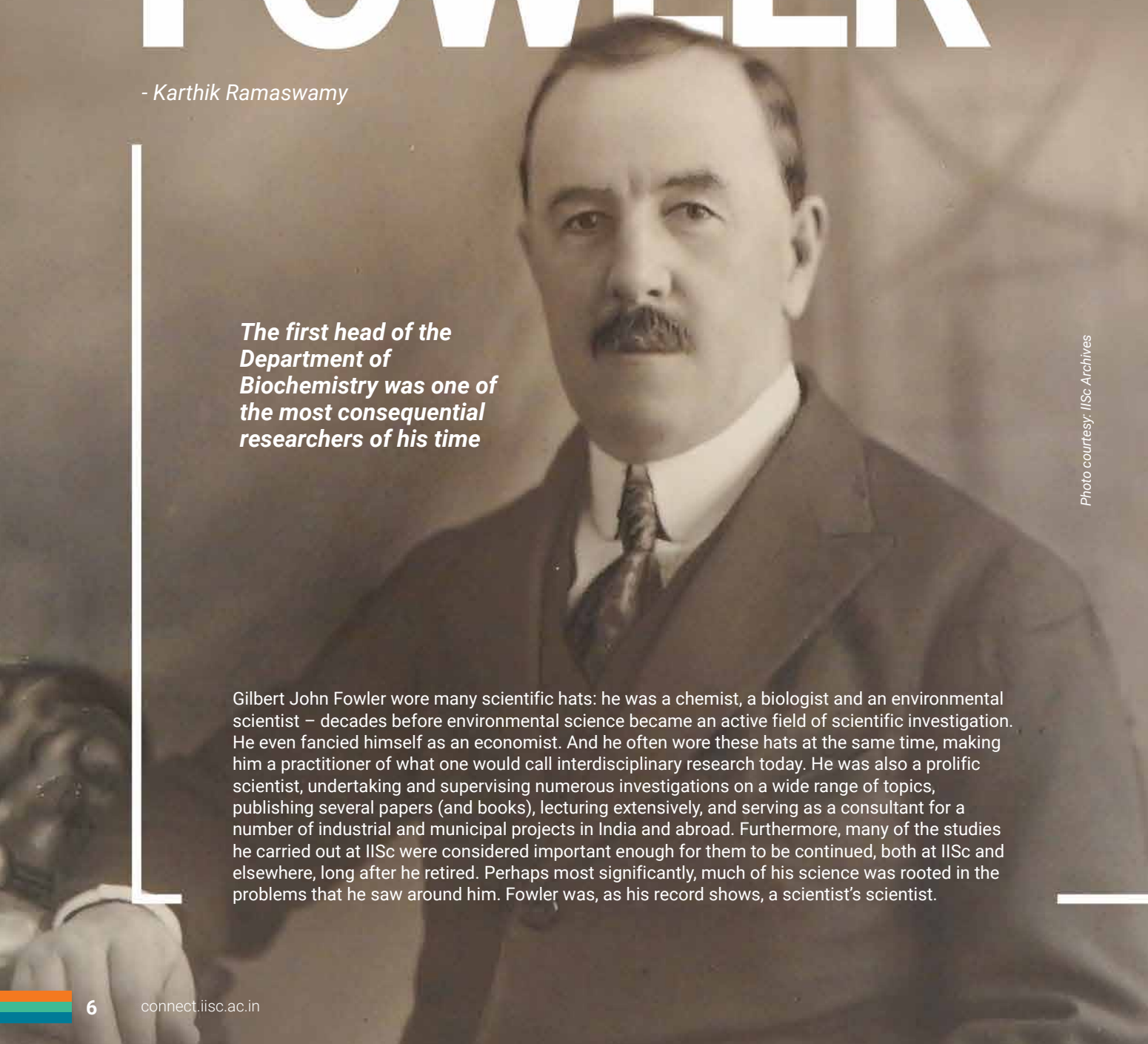
The Department of Biochemistry has undergone several transformations over many years. It has come a long way from the days of treating sewage and developing processes for making natural dyes to studying immune response and developing therapeutics for cancer. Many professors, whose stories have become legendary, have retired or moved on. Even the location of the department has changed from the beautiful colonial-era stone building to a more modern multi-storeyed one. Still, the ethos of the department remains the same.

Photo courtesy: I-imazine

A current lab at the Department of Biochemistry in the new Biological Sciences building

THE SCIENCE OF GILBERT FOWLER

- Karthik Ramaswamy



The first head of the Department of Biochemistry was one of the most consequential researchers of his time

Photo courtesy: IISc Archives

Gilbert John Fowler wore many scientific hats: he was a chemist, a biologist and an environmental scientist – decades before environmental science became an active field of scientific investigation. He even fancied himself as an economist. And he often wore these hats at the same time, making him a practitioner of what one would call interdisciplinary research today. He was also a prolific scientist, undertaking and supervising numerous investigations on a wide range of topics, publishing several papers (and books), lecturing extensively, and serving as a consultant for a number of industrial and municipal projects in India and abroad. Furthermore, many of the studies he carried out at IISc were considered important enough for them to be continued, both at IISc and elsewhere, long after he retired. Perhaps most significantly, much of his science was rooted in the problems that he saw around him. Fowler was, as his record shows, a scientist's scientist.

Before IISc

Born in Paris on 23 January 1868, Fowler obtained an undergraduate degree in chemistry in 1896 from the Victoria University of Manchester, UK. Three years later, he received a Master's degree from the same institution, and for his thesis, which was in metallurgy, he was given the Dalton Prize. He continued at the varsity, where he was first appointed as a demonstrator and then a lecturer. During this period, he also served as a consulting chemist to the Rivers Committee of the Manchester Corporation. He remained a Mancunian until early 1916 and made a name for himself by helping to treat the sewage and trade effluents of Manchester, then the textile capital of the world. In 1904, he was awarded a DSc degree from the University of Heidelberg, Germany, for his work on sewage purification.

In 1915, Fowler applied for a vacant position in IISc. His application was successful, and in February of the following year, he arrived in IISc to take charge as a professor and the de facto head of the Department of Applied Chemistry, one of the only four departments in the Institute at the time (the others being the Departments of General Chemistry, Organic Chemistry, and Electrical Technology). In 1921, when IISc decided to start a department to focus on the relatively new field of biological chemistry, it did not have to look beyond Fowler to lead it.

Acetone

When Fowler joined IISc, the world was in the throes of an armed conflict that eventually came to be known as World War I. India was not untouched by the war. By virtue of being part of the British Empire, it sent over a million of its soldiers to the trenches. The imperial government also looked into other ways in which India could contribute to Britain's war effort. One of them, it believed, was in the manufacture of acetone, a colourless organic compound that most of us are familiar with as nail polish remover or white board cleaner. It was also the main ingredient in cordite, an explosive that was used by the British Army during WW I as a substitute for gunpowder. So the government decided to set up an acetone factory, and for the scientific expertise required to manufacture it in large quantities, it turned to IISc.

As soon as Fowler was hired by the Institute, he was tapped for the acetone project by the government – even before he left Manchester. So when he boarded the steamer to travel to India, he carried with him a stash of bacteria, the "Weizmann bacillus", for the fermentation of acetone (the bacterium, whose scientific name is *Clostridium acetobutylicum*, was first isolated by Fowler's colleague at Manchester, the Russian-born British biochemist Chaim Weizmann, who later renounced his British citizenship and became Israel's first President).

Photo courtesy: Forrest H Barfield/ Wikimedia Commons

Cordite filaments in a .303 British Rifle cartridge

Once Fowler arrived at IISc, he hit the ground running to make acetone. He, along with research scholars YD Wad and AG Gokhale, first set up an experimental unit that could be replicated on a larger scale at the Government Acetone Factory being built in Nasik in the Bombay Presidency. A temporary office for the factory was also established at IISc in Bungalow No. 9 and Fowler was appointed as a Consulting Advisor for the factory.

Until Fowler's work on acetone in IISc, it was made mostly by distilling wood. But this was an inefficient process. Fowler's team therefore began working on fermenting starch-rich substances like rice using the bacterial culture he brought with him. The bacteria degraded starch to produce organic solvents, which when distilled left behind pure acetone. However, they needed to find a cheaper source of starch. Initially, they spent a considerable amount of time and resources on fermenting the flowers of the mahua tree, but the amount of starch in them was not sufficient to make the huge quantity of acetone that was required.

> ***Much of Fowler's research was rooted in the problems that he saw around him***

Eventually they discovered an inexpensive raw material that could also produce an impressive amount of acetone: jowar. Following this discovery, the vats and other equipment were dismantled and the technology was transferred to the Nasik factory, where Wad and Gokhale were appointed as staff.

The acetone project was Fowler's main focus during his first two years at IISc. But when it ended, he had the time and freedom to pursue investigations on other natural products with greater vigour. One of them was on mahua, which had already been studied as a potential raw material for acetone fermentation.

Mahua

Mahua is a fast-growing tropical tree common in the plains of Central and North India. Its fruits and flowers have traditionally been used as food and for making medicines and country liquor by Adivasis. When Fowler began his studies on mahua, it drew the attention of the Nizam of Hyderabad who sponsored five research students to work with him at IISc. To carry out these studies, the Nizam would send flowers week after week to IISc. Within a year, however, Fowler's team found a few mahua trees in IISc's vicinity and the Lal Bagh Botanical Garden in Bangalore.

The most significant investigations into the mahua flower involved understanding the factors that determine the yield of alcohol when it is fermented. These included the composition of mahua decoction, kind of yeast used, temperature, and other growth conditions. One research student, Habib Hassan, also studied the possibility of making the decoction (which according to IISc's 1917 Annual Report has an "unpleasant" smell and taste) into a syrup for use in cooking and in jams. He succeeded in making it more palatable, says the Report, using lime and charcoal. Edal Behram, another student in the department, studied the developmental biology of the flower, and its biochemistry to understand how sugars are formed. Fowler's team also succeeded in extracting essential oils from the flower and even explored the possibility of using mahua sugar as an alternative to cane sugar.

Photo courtesy: Gypsypkd/Wikimedia Commons

Mahua flowers

Lac

Yet another natural product that interested Fowler was lac, produced by a group of scale insects. It is secreted by the larvae of these plant bugs after they feed on the sap of specific host trees. It has been used in India for centuries – as a seal, dye, and wood finish, and also to make cosmetics and bangles.

Lac became popular in Europe in the early 20th century because shellac, its processed form, became indispensable in the manufacture of gramophone records. It was also used in ammunition, paints and varnishes.

Photo courtesy: Nuberger13/Wikimedia Commons

Shellac varieties

Fowler worked with two gifted research scholars on lac at IISc: S Mahdihassan, an entomologist, and M Sreenivasaya, a biochemist. Several other students also became involved in the lac-related lab experiments and field studies that were carried out in and around Bangalore. Their research was enormously productive. In less than two years, IISc became the hub of lac research in India, as Debi Prosad Burma and Maharani Chakravorty note in their book *From Physiology* and *Chemistry to Biochemistry*. Research on lac at IISc not only resulted in several publications but also led to the setting up of the Indian Lac Research Institute in Ranchi by the government in 1924 (it still exists but has been renamed as the Indian Institute of Natural Resins and Gums). It was headed by Dorothy Norris who briefly taught chemistry at IISc. Burma and Chakravorty also write that the staff at the newly established institute was populated almost entirely by researchers who migrated from IISc.

The activated sludge process

Though Fowler had his fingers in many pies during his research career at IISc, which lasted for more than eight years, he never forgot his first love: the activated sludge process, which he is credited with developing. In 1912, he was invited to the United States to address the growing contamination of the East and Hudson rivers. During his visit, he had been shown some experiments which involved forcibly aerating wastewater to treat it. "These were not entirely successful, and it appeared to him that the correct type of bacteria was not present," writes HE Watson, his colleague at IISc, in an obituary for Fowler published in *the Journal of the Chemical Society*.

Back in Manchester, Fowler convinced Edward Ardern and William Lockett, engineers at the Rivers Committee of the Manchester Corporation, to carry out similar experiments. But in these studies, they retained the precipitated sludge. "This sludge proved to be the home of the missing bacteria, and the activated sludge process, perhaps the most important in the world today, became a commercial possibility," Watson adds. (In 1942, in a paper in *Nature*, SC Pillai and V Subrahmanyan from the department demonstrated the role of ciliated protozoans as well in the process.)

Photo courtesy: Wikimedia Commons

The Manchester lab where the activated sludge process was first developed

When Fowler moved to IISc, he continued his work on wastewater treatment. He was invited to several cities in India and around the world to help set up plants based on the technology developed at Manchester. Burma and Chakravorty write that, "Between 1925 and 1953, he [Fowler] was responsible for about a dozen activated sludge plants of different sizes in different parts of India."

In 1922, Fowler also designed and built an activated sludge treatment plant in IISc. Besides dealing with the sewage on campus, it allowed for many experiments to be carried out in the Biochemistry Department. The most valuable insight that Fowler obtained from these studies was that the sludge, rich in nitrogen, could be used as an organic fertilizer and a feed supplement for poultry. At IISc, he also developed a method to separate the solids and liquids in sludge in sewage treatment, a process he patented in 1935.

Towards the end of his research career in the Institute, a related area of study that Fowler became fascinated by was composting. Like the active sludge process, composting is a way of recovering nitrogen from waste for use in agriculture. "As time went on, it became clear to him that the activated sludge process could only deal with a small fraction of the available material, and his thoughts turned more and more to the possibility of conserving nitrogen in Indian villages," recounts Watson.

Other interests

After Fowler retired from IISc in 1924, he turned his attention to other subjects that interested him, though he continued to be an evangelist for the activated sludge process and composting. The titles of some of the articles he published after his retirement reveal the diversity of his interests: "The Multiplication of Scientific Societies", "The Rights of Man", "Land Management in the Punjab Foothills", "Industrial Possibilities of Some Research Work Done in India", "Arming for Peace", "Energy and Economics", and "The Relation of Universities and Scientific Institutes to Industrial Development".

However, a topic that Fowler considered to be of vital importance, Watson writes, was currency reform. In an article titled "Chemistry and Currency" in *Current Science*, Fowler argued that existing currencies did not represent the true work carried out to earn them. He therefore proposed a new currency called ERN. According to the proposal, each ERN would be equivalent to 10 g of nitrogen in the form of protein, or alternatively 300 calories, the heat produced in the body by this amount of protein. "The value of a commodity would thus be its food value or the amount of work expended in its production," explains Watson.

Fowler received many honours for his research, including being elected as a Fellow of the Royal Institute of Chemistry, the Chemical Society of England and the Royal Sanitary Institute. He was also chosen to be a member of the Industrial Research Council of the Government of India from 1937 to 1939.

Faith and country

Fowler was a devout Christian. Unlike many other scientists, he saw no conflict between religion and science. If anything, his faith seemed to motivate his research. "An ardent Christian Scientist," Watson writes, "he [Fowler] was profoundly distressed by the waste of combined nitrogen and the resulting loss of foodstuffs and the lowering of the standard of living for the poorest of the poor."

Even though Fowler did not explicitly write about his feelings towards India, his actions suggest that he felt a sense of belonging to his adopted country. He had been a regular visitor to India since 1906, ten years before he joined IISc. And when he did join the Institute in 1916, he chose to become a permanent resident of the country. After he moved to India, he favoured publishing in Indian journals – mostly in the *Journal of the Indian Institute of Science* during his active research career and *Current Science*, brought out by the Indian Academy of Sciences, after he retired. He and his wife Amy Hindmarsh decided to spend his post-retirement years in India (these were spent almost exclusively in Bangalore, except for two years between 1927 and 1929, when he was the Principal of Harcourt Butler Technological Institute in Kanpur).

Fowler also died in India – peacefully, according to Watson – on 21 March 1953 at the Central Hotel, Bangalore.

M Sreenivasaya's legacy

- Deepika S

Photo courtesy: PR Krishnaswamy

M Sreenivasaya

Having laid the foundations for fermentation technology research in India, he is remembered for the breadth and clarity of his scientific pursuits

In 1941, a new Fermentation Technology laboratory was set up at IISc. It was something of a travelling entity, having been founded at the Department of Biochemistry and transferred at different points between the departments of Biochemistry, Pure and Applied Chemistry, and Chemical Technology and Chemical Engineering. It was even established as a separate Section at the Institute for a few years until it eventually became a part of what is known today as the Department of Microbiology and Cell Biology. However, the work carried out in this laboratory in the early years contributed significantly to the kind of research pursued by the Department of Biochemistry. And the person responsible for shaping the work done here in the early years was M Sreenivasaya, who was in charge for over a decade.

Sreenivasaya was seen as someone whose work spanned several fields including biochemistry, microbiology, plant virology and enzymology, as an intrepid researcher with multiple scientific techniques in his arsenal, and as a skilled maker of instruments. Though he is remembered for the breadth and clarity of his scientific pursuits, he is also recalled fondly as a mentor who encouraged several younger women and men in his field. A sharp writer who believed in fostering science communication, he was involved with *Current Science* – published by the Indian Academy of Sciences – and went on to become its Editor.

Sreenivasaya spent most of his career at IISc. He first joined the Institute as a student in 1919. According to TN Ramachandra Rao (Sreenivasaya's former student, and a former Head of the Department of Microbiology of Fermentation Technology at the Central Food Technological Research Institute, who wrote a monograph in 1996 about Fermentation Technology at IISc), he had always been a brilliant student. Rao wrote that Sreenivasaya, who was born in Bangalore on 5 December 1895, had gone to high school in Kolar and stood first on matriculating with record marks in science subjects. But he didn't pursue science as a field of study straight away. In 1918 he received a BA degree from Bangalore's Central College, got married, and moved to Bombay to study law. There, he suffered a severe bout of influenza (during another large pandemic that swept through India – the Spanish Flu, which killed 50 million people across the world and an estimated 10-20 million in India) and had to give up his studies and return to Bangalore, where he lived through another tragedy – his family's home burned down due to arson. That was when he applied to IISc.

Initially, Sreenivasaya received a scholarship from the Government of Mysore to study biochemistry (though the Department of Biochemistry would only come into being at IISc in 1921), and in particular, to study indigenous dyes, especially shellac. Eventually, Sreenivasaya was appointed Research Assistant in the Department of Biochemistry in 1922, and earned an Associateship of IISc in 1924 and a Fellowship of IISc in 1933. While at IISc, he also worked for the Government of Mysore as a consultant on lac, as supervisor in its scheme for manufacturing ragi malt, and as investigator-in-charge of the scheme on the nutrition of the silk-worm. He was deputed to Europe from 1936 to 1938, to laboratories in Sweden, Denmark and the UK, and it was on his return, according to Rao, that he decided to work in the area of fermentation.

In 1940, the Board of Scientific and Industrial Research (precursor to the Council of Scientific and Industrial Research or CSIR, which came into being in 1942) was established, and JC Ghosh, IISc's Director, was appointed a member. It had no laboratories of its own at the time, and so it sponsored projects at IISc. Ghosh helped Sreenivasaya set up the Fermentation Technology laboratory, and CSIR funded its work in the following areas: molasses, production of industrial enzymes, production of yeasts and moulds that could serve as industrial sources of vitamin D and vitamin B complex, understanding conditions favouring the increase of alcohol concentration in fermented distillery washes, cytogenetics of yeast and fungi with the aim of evolving new races, and the creation of a National Collection of Type Cultures (NCTC).

The NCTC is said to have been created in 1941 (though according to TN Ramachandra Rao, it was in 1940) on the suggestion of Shanti Swarup Bhatnagar, an Indian colloid chemist who was the first Director-General of CSIR. Sreenivasaya headed this project, which in the span of a decade collected about 2,500 cultures of interest to researchers in the fields of microbiology and biochemistry. It was the main source of microorganisms for research in Fermentation Technology at IISc. Sreenivasaya was later nominated as a member of the Permanent Committee of the Commonwealth Collection of Type Cultures in London. In 1951, the collection was transferred to the Biochemistry Division of the National Chemical Laboratory, Pune, and in 1956, it was renamed the National Collection of Industrial Microorganisms (NCIM), which even today remains one of the largest culture collections in India.

In 1941, the same year that NCTC was set up, Sreenivasaya was appointed Lecturer in IISc's Department of Biochemistry. IISc's Annual Report for 1941-42 mentions the construction of "a small building consisting of four cubicles for work in Fermentation Technology", as well as the first "Lady-Students' Hostel", a significant development. Though the number of women students at the time was small, interestingly, a significant proportion of them studied fermentation technology or biochemistry, beginning with Kamala Sohonie (née Bhagvat), one of the first women students that Sreenivasaya supervised. She would go on to become a leading Indian biochemist herself and Director of the Royal Institute of Science, Bombay. Among the many other women to have worked in the Fermentation Technology lab were Violet Bajaj (née de Sousa, but spelled D'Souza in IISc's records) and Indira Bhatt (née Gajjar). Bajaj came to IISc as a Research Assistant funded by CSIR, and spent most of her subsequent career working in CSIR biochemistry laboratories in Pune and Delhi. Bhatt went on to head the Department of Biochemistry, Maulana Azad Medical College, Delhi.

Sreenivasaya was known for his skills in the laboratory. "He would come to the lab at 7.30 am, lecture for an hour, and then for an hour show us a lot of techniques including glass blowing to make our own pipettes," PR Krishnaswamy, a former student who joined the Fermentation Technology Laboratory in 1951, told Connect in February 2020. At a time when such equipment wasn't readily available, Sreenivasaya trained his students in a range of techniques including dilatometric, conductometric and manometric methods of studying the metabolism of microorganisms; ultra-micro technique to study single cells, and simple paper chromatographic methods to determine vitamin B12 in shark liver extracts, among others, and worked with his hands to create the instruments he needed for these tasks. He developed dilatometry as a method for assaying enzymes and measuring enzyme activity, and the dilatometer he made is still spoken of in the Department of Biochemistry today.

> ***JC Ghosh helped Sreenivasaya set up the Fermentation Technology laboratory, and CSIR funded its work in several areas***

Krishnaswamy had originally known of Sreenivasaya from reading *Current Science*. But as his student, he learnt about Sreenivasaya's pioneering work, beginning in the 1920s, across multiple fields. "I was thrilled to see the equipment he had used for his earlier classic experiments in these areas," said Krishnaswamy, "which he had carefully preserved." He found what he learned from Sreenivasaya to be exciting and contemporary. "They were beautiful experiments that gave me an insight into life, and remain so fresh in my mind." Krishnaswamy described his mentor as "an intellectual giant". "His knowledge and ability to perform experiments hands-on, his knowledge of instrumentation needed for these experiments and more importantly, his ability to put all these things together to articulate an idea and execute it, was incomparable," he said.

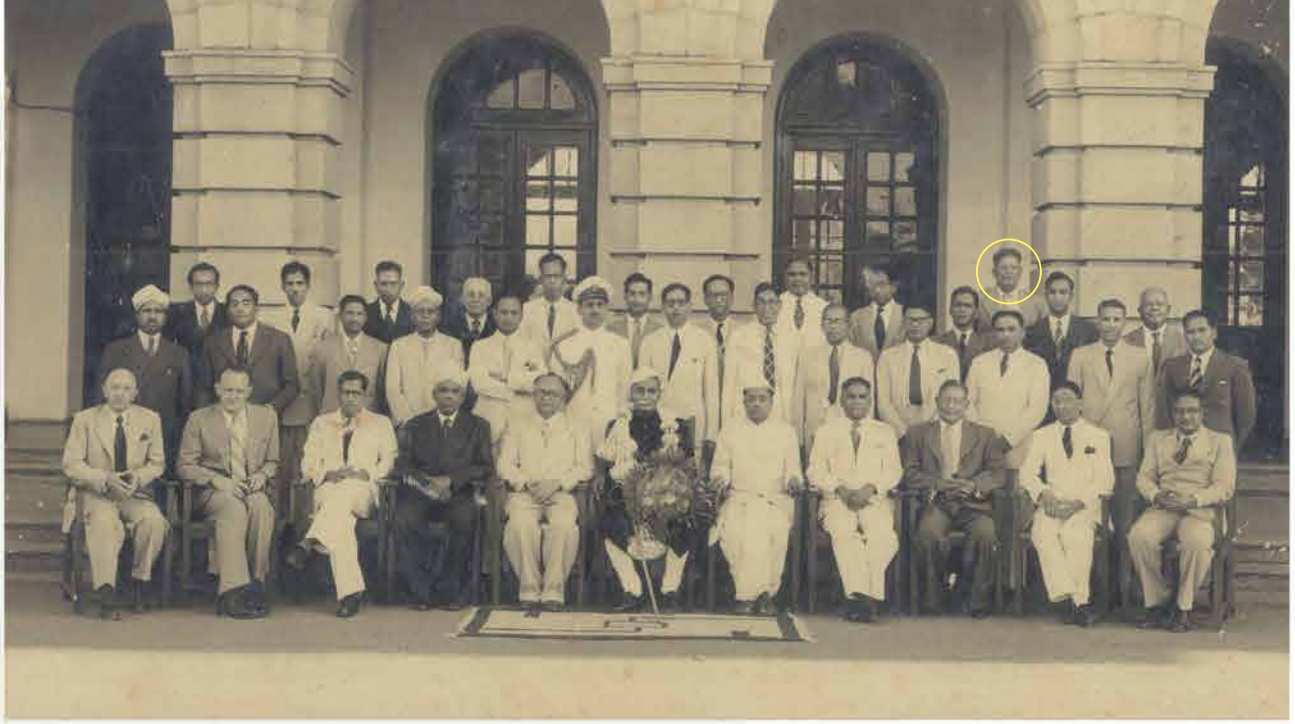


Photo courtesy: IISc Archives

M Sreenivasaya during a visit by the President of India, Rajendra Prasad, in 1951

Outside the laboratory, Sreenivasaya was associated with the South India Science Association and was deeply invested in *Current Science*, which, according to one of his former students, had an office situated in the Fermentation Technology and Pharmacology block. Rao wrote that he devoted himself to the task of "disseminating scientific information and news which is essential for educating the public mind to appreciate the methods, the possibilities, the blessings and the menaces of science." Sreenivasaya was its Editor from 1942 to 1950, handing it over to his successor, the physicist GN Ramachandran. But he continued to contribute to the journal as Secretary of the Current Science Association until 1952. Sreenivasaya also served on the advisory board of the journal *Biochimica et Biophysica Acta* alongside well-known scientists like the physicist JD Bernal and the biochemist and Nobel Laureate HA Krebs.

During his retirement, in contrast with the care he took to preserve his equipment, Sreenivasaya reportedly took the strange step of destroying his records. According to Rao, in 1954, Sreenivasaya was invited to work at CSIR's Central Drug Research Laboratory in Lucknow. As he planned to remain there for "a fairly long period", he took all of his research records with him. At the end of three years, however, he developed serious health problems and was advised to return to Bangalore, which caused him to be depressed. The night before he was due to return, in despair, he "gathered all his scientific records, put them into two gunny bags and descending alone to the banks of the river [Gomati, on which the laboratory was situated], lowered them into the flowing water." Rao continues, "We can only say 'Gomati, give us back those records'! Thus we have lost the most important documents related to his work." However, Rao suggests that he continued in research after this incident. Sreenivasaya passed away in 1969 at the age of 73.

Rao described his mentor as "essentially an intellectual, a clear thinker, a man of simple and frugal habits," and as someone who, at a crucial time in India's history, made it seem possible that Indians could be in the forefront of scientific research and give others a run for their money. He wrote that Sreenivasaya and his colleagues, "with a programme of persistent work for over a decade, ushered a new social force bent upon indigenous scientific and technological endeavour which could compete creditably with the challenge of the West."

But perhaps one of the most endearing accounts of Sreenivasaya remains that of his former student Violet Bajaj. In an interview with *Connect* in 2018, at the age of 101, she laughed as she remembered how she and Sreenivasaya, "a very orthodox Kannadiga Brahmin", would fight over the elaborate religious rituals he went through to purify himself after returning from abroad. Bajaj, an atheist from a Goan Catholic family, said, "We used to have terrific arguments about it," but – perhaps paradoxically, by the standards of today's times – also said that she and Sreenivasaya "got on wonderfully well". "In the end because I always stood up to him, he respected me," she said. She studied at IISc at a time when it was the norm for people on campus to eat in separate messes with members of their own caste and community. Bajaj, who passed away in May 2020, recounted that with time, Sreenivasaya's beliefs on caste and purity changed, and softened enough that he was willing to step out of his comfort zone. "Later, he even came to stay at my house and ate my food," she recalled.

‘I was fortunate to be the first woman to become chair of this great department’

- HS Savithri

HS Savithri graduated with a PhD from the Department of Biochemistry in 1976. After a short stint abroad, she returned to the same department, where she worked on the architecture, genome organisation and expression of plant viruses, before becoming the first and only woman to be Chair of the department. On the occasion of the department’s centenary, she penned her reminiscences – an edited version of which is reproduced here.

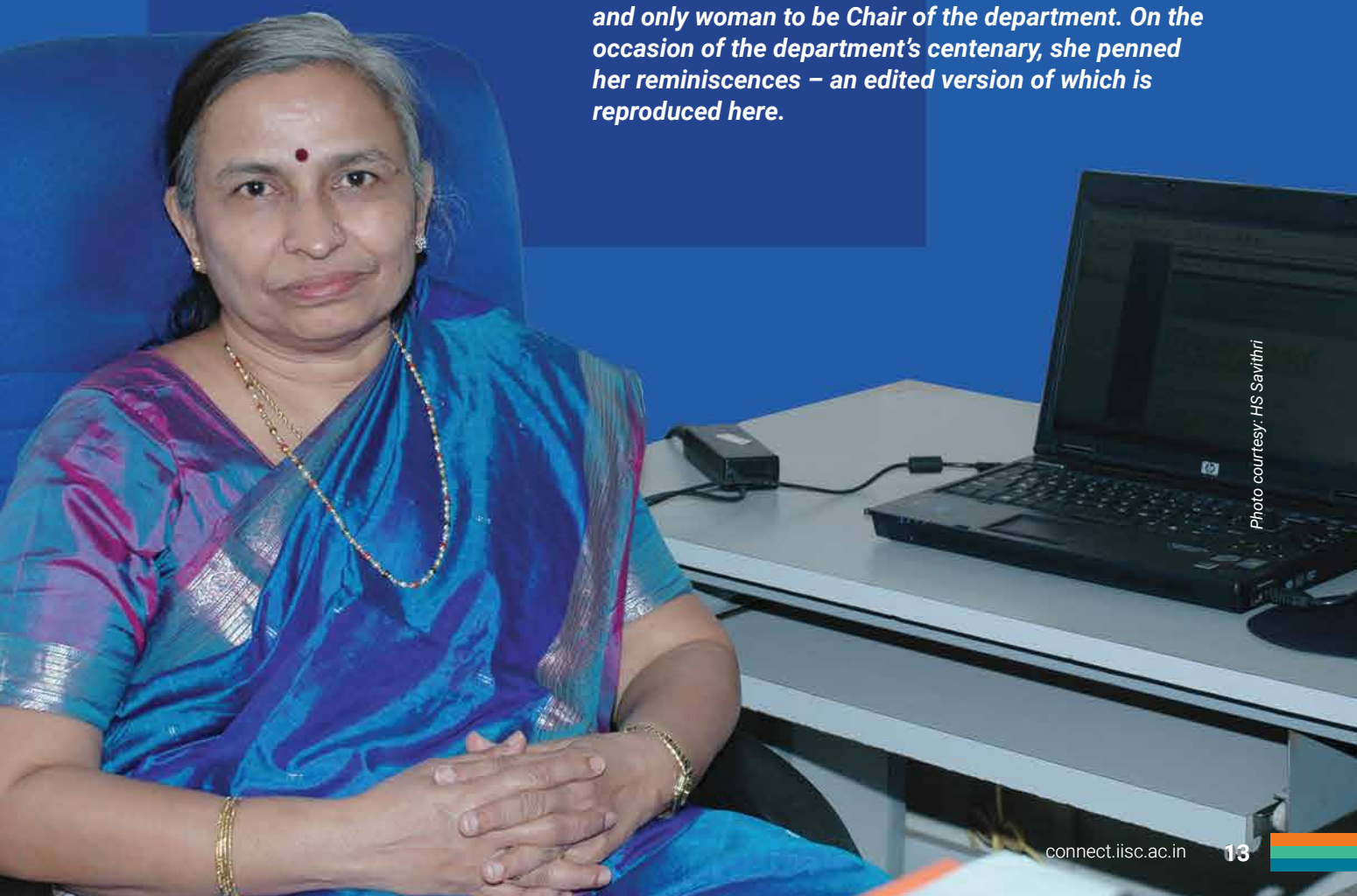


Photo courtesy: HS Savithri

After completing an MSc degree in Chemistry from Central College, Bangalore, about six of us joined the Department of Biochemistry in the year 1972. Prof N Appaji Rao was assigned as my research supervisor. This was a turning point in my career. I was fortunate to work with a distinguished enzymologist and a rare human being who made us all emulate his generosity, kindness to colleagues and passion for science.

My first experiment in the lab was to measure the activity of the enzyme aspartate transcarbomylase from mungbean seedlings. In fact, the very first assay I set up worked and I could show that the crude extract had activity. I was told that someone else had tried to establish the assay conditions for several months and had failed. This was beginner's luck!

It took me almost two years to standardise the purification protocol for this enzyme; it was difficult to purify plant enzymes by classical methods. I then began work on establishing the kinetic and regulatory mechanism of this enzyme. The purified enzyme would lose activity in less than 24 hours. The experiments had to be planned well before the enzyme was ready and executed without any delay. Since the yield of the enzyme was very low, I could use it only for activity measurements. Whenever I showed any data to Prof Rao, the first thing he would ask was, "Did you repeat the experiments?" This is indeed crucial in any experimental work.

Many of us used to have lunch together in the lab at a large table called the sweets table where we enjoyed celebrating every small event: a first paper, a birthday, someone joining the group or returning from home after a break. Even now, this legacy has continued in my lab.

> ***Many of us used to have lunch together in the lab at a large table called the sweets table where we enjoyed celebrating every small event***

There was a lot of self-learning to do and we used to go to the library every week to look at the new journals that arrived. There used to be a competition to see who would go there first – GP [G Padmanaban] or us – and invariably GP won! That culture has completely changed now, thanks to Google.

All of us used to go to a person called Sheshadri in Malleswaram for typing our theses and stencil cutting. He used to be very busy and would allot only two hours per day for each of us. We had to go through the handwritten draft very carefully as he would not repeat typing any page. His English was very good and he would make corrections by himself if there were any mistakes. For figures, we used to get them drawn by an artist on tracing paper and get ammonia prints. All these things are obsolete now.

After returning from an 18-month sabbatical in Japan, Prof Rao looked at the data I had generated and said that I could start writing my thesis. By that time, I was married to MRN Murthy [also an IISc alumnus], and he helped me analyse the data by writing a program that could estimate the kinetic constants accurately.

I submitted my thesis on 9 December 1976, and my son was born on 20 December.

Plant virology at Purdue

I worked as a postdoctoral fellow for a while and then we left for Purdue University in the US. There, I worked with Prof A Light from the Department of Chemistry and Murthy joined Prof Michael Rossmann's lab in the Department of Biological Sciences.

Four years later, we met Prof Ramaseshan, the then Deputy Director of IISc, at the International Union of Crystallography meeting in Canada. He verbally promised both of us permanent positions if we returned, and suggested that we should start work on virus crystallography in India – a highly ambitious proposition with no facilities. That was enough for us to decide to return. But before that, we wanted to identify a good problem.

Murthy and I went through the literature and realised that most of the work on plant viruses in India was done in plant pathology labs on epidemiology and disease control, with very little molecular characterisation. I moved to Prof Rossmann's lab to learn molecular virology. I worked with Dr John Erickson, and in less than three months we could get a paper in *Virology* on the assembly of the southern bean mosaic virus.

Murthy and I also took a course in plant molecular virology offered by Profs Lister and Jackson which really laid the foundation for future plant virus research in our labs. We decided to start work on a virus which was characterised reasonably well so that we could proceed with the structural work as soon as we returned.

Back to Biochemistry

At IISc, Murthy joined the Department of Physics as a Senior Research Fellow and then moved to the Molecular Biophysics Unit. I started to work as a CSIR pool officer with Prof Appaji Rao who very willingly accepted me into his lab once again. My job was to interact with and guide his students in addition to my own work that I initiated on plant viruses. I also had the task of mentoring short-term students from SV University. Some students who had already completed four years were desperate to get some data; we used to sit down together almost every day, and design experiments carefully and execute them.

One such student had come from Delhi. One day I asked him, "Did you have lunch?" He said, "No, since I do not have a fellowship, I do not want to ask my parents to give me money. I will go home and eat." This meant that he would fast during the day. Murthy and I used to get lunch from home and we shared with him the food that my mother-in-law generously packed for all three of us. This helped the student open up to me and together we designed activity-based experiments on the enzyme he was working with. He managed to get all the data required for his thesis submission in less than a year.

There was another student who, at the tail end of his work, somehow lost interest and would not complete the work and write his thesis. Prof Appaji Rao and Prof AN Radhakrishnan played a major role in bringing him back to normal. They used to pick him up from his room and bring him to the lab. I used to gently nudge him to finish the work. In the end, he submitted his thesis, got two very good papers published, went abroad and has done very well. These students really taught me how to be patient.

Photo courtesy: HS Savithri

HS Savithri, MRN Murthy and N Appaji Rao

Prof Appaji Rao was generous enough to grant two of his students to me under joint supervision even before I was a faculty member. We also had a lot of goodwill from Prof Rao's former students who sent us chemicals required from time to time.

Faculty and Chair

Seven years after I returned from abroad, I was offered a faculty position in the Department of Biochemistry. I was told not to ask for a separate lab but work with Prof Appaji Rao. This, in a way, turned out to be a blessing in disguise as I could use his lab facilities and add to them from my own grants. All his students became my students and vice versa. Similarly, all of Murthy's students were part of our lab and our students were part of his lab. We were one large family! The students had the unique opportunity to interact with all three of us.

I was lucky to have a large number of motivated students from whom I learnt more than what I taught them. Each one was different from the other and I have enjoyed mentoring them. Since we had a common lab, the students had to learn to share and work together. The senior students set the standards high and the juniors simply had to follow them. Once we had three students who had joined in the same year, and five years later, all of them had to go on pension. I had only one project assistant position available. I told them that one of them could take it and share the salary. Immediately they said that the position should go to the one who needed the money the most, and that the other two did not want any share in the salary.

When I joined as a faculty member, I was the only woman amongst 20-odd male faculty members who were quite aggressive and held diametrically opposite views. It took a lot of effort to make sure that my voice was also heard.

However, the department as such was highly congenial for doing research and my students could access not only the departmental facilities but also the facilities from individual faculty labs with or without the knowledge of the faculty member. Even now that tradition of sharing has continued in the department; students, postdocs and short-term workers from other departments and institutions come and use our facilities freely.

I was fortunate to be the first woman to become Chair of this great department. There were a lot of challenges, but the faculty members and the administrative staff of the department extended their full support. During my tenure as the Chair, we moved from the old building to the new building. It was indeed a mammoth exercise carried out with the complete cooperation of students and all the members of the department.

I have enjoyed working every single day at the department and I am proud to be a part of its centenary celebrations.

Photo courtesy: HS Savithri

HS Savithri, MRN Murthy and N Appaji Rao with students

NEUR

Photos courtesy: H Zell/Andrew Butko/Wikimedia Commons

The kesari dal plant and its seeds

For many years, the Department of Biochemistry at IISc worked extensively on nutrition. Its researchers have analysed the importance of vitamin B1 in our diet. They also recognised the nutritional benefits of "kanji", a type of rice gruel, and carried out various experiments in which students of a Bangalore-based school were fed kanji as part of their mid-day meals.

An important contribution related to nutrition was research on a disease caused by excess consumption of kesari dal (*Lathyrus sativus*). Kesari dal is a pulse crop that was at one point cultivated extensively in parts of Central India. Its hardy nature helps it survive the adverse conditions of drought, and it was more frequently consumed by people who were economically disadvantaged during these conditions. This crop is also rich in vitamin B1 and iron, and contains more protein than any other seed crop, making any food cooked with kesari dal a complete meal in itself.

However, this presumed life-saver had a downside too: excessive consumption of kesari dal seeds caused neurolathyrism, an upper motor neuron disorder characterised by muscular weakness, spasms, and paralysis of the lower limbs. Most of the people who experienced these symptoms were poor labourers who were given this dal as payment instead of their daily wages. In 1961, around 32,000 people were affected by this disease in Madhya Pradesh alone. This led to its ban in most Indian states. Cultivation of this crop was severely penalised by the government. But in June 1975, a severe drought brought this disease back when 1,00,000 men between the ages of 15 and 45 were affected in Madhya Pradesh and Bihar.

Around the same time, other scientists had already linked osteolathyrism, a form of lathyrism, with the excess consumption of seeds of a related plant: the sweet pea (*Lathyrus odoratus*). The culprit was identified as a toxic molecule in the seeds called β-amino propionitrile. PS Sarma, a nutritionist and faculty member at the Department of Biochemistry, was keen on identifying similar toxic molecules that could be responsible for the neurolathyrism linked to kesari dal.

The biggest challenge for Sarma's team was to find an ideal experimental organism to test the effects of kesari dal. The most commonly used model animals like rats and mice were not affected adversely by the dal. But then, in those days, insects were also used as experimental organisms for nutritional research. Therefore, Sarma and his team decided to use *Corcyra cephalonica*, an insect that feeds on rice and wheat flour.

OLATHYRISM: an unsolved mystery

- Sangeetha Devi Kumar

Experiments in PS Sarma's lab at the Department of Biochemistry in the 1960s explored a mystery disease caused by excess consumption of seeds of a controversial pulse crop

They first crushed the kesari seeds in different solvents to extract specific compounds. Each extract was tested on the insect larvae to identify which of them disrupted their neurophysiology. Among the extracts, the alcohol extract was the one found to inhibit the growth of the insect larvae.

Around the same time, in 1963, a research group at the National Institute of Nutrition, Hyderabad, published a study showing that the alcohol extract of kesari dal seeds was neurotoxic in day-old chicks. This exciting news led to a flurry of experiments by Sarma and his team. The alcohol extract was further analysed and was found to contain a highly acidic amino acid, β-N-oxalyl-L-α, β-diaminopropionic acid (ODAP),

Photo courtesy: IISc Archives

PS Sarma

which was indeed a neurotoxin. It was neurotoxic not just for chicks but also rats. Sarma, along with Dr KS Mani from NIMHANS, Bangalore, showed that ODAP causes paralysis of legs in monkeys when injected via the spinal cord. Surprisingly, oral feeding of ODAP or the dal itself did not produce the symptoms, suggesting a link to the blood-brain barrier, which regulates the flow of molecules from the blood to the brain.

Now that the causative compound was identified, Sarma wanted to develop ways to eliminate the toxin from the dal to make it safe for consumption. He observed that steeping seeds in hot water for an hour resulted in more than 90% of the toxin leaching into the water. The residual seeds could be sun-dried and ground into flour to make chapatis. Another method was to parboil the seeds, which removed most of the toxin. He and his team were also able to prepare a lysine-rich protein supplement from these seeds because they are a rich source of this amino acid, unlike other pulse crops. He also wanted to use it as baby food since it was rich in nutrients.

Unfortunately, with the untimely demise of Sarma in the year 1970, this promising endeavour was left unfinished.

Even today, neurolathyrism remains a disease without a cure. Many research groups have worked on ODAP because of its neurotoxic properties. Sadly, no one has been successful in reproducing the symptoms of neurolathyrism seen in the people of Central India. The infamous kesari dal still remains an enigma.

Sangeetha Devi Kumar is an Integrated PhD student in the Department of Biochemistry, IISc

Forty Years of Fighting Malaria

- Ranjini Raghunath

G Padmanaban has spent decades trying to understand the lifecycle of the malaria parasite and develop a cure

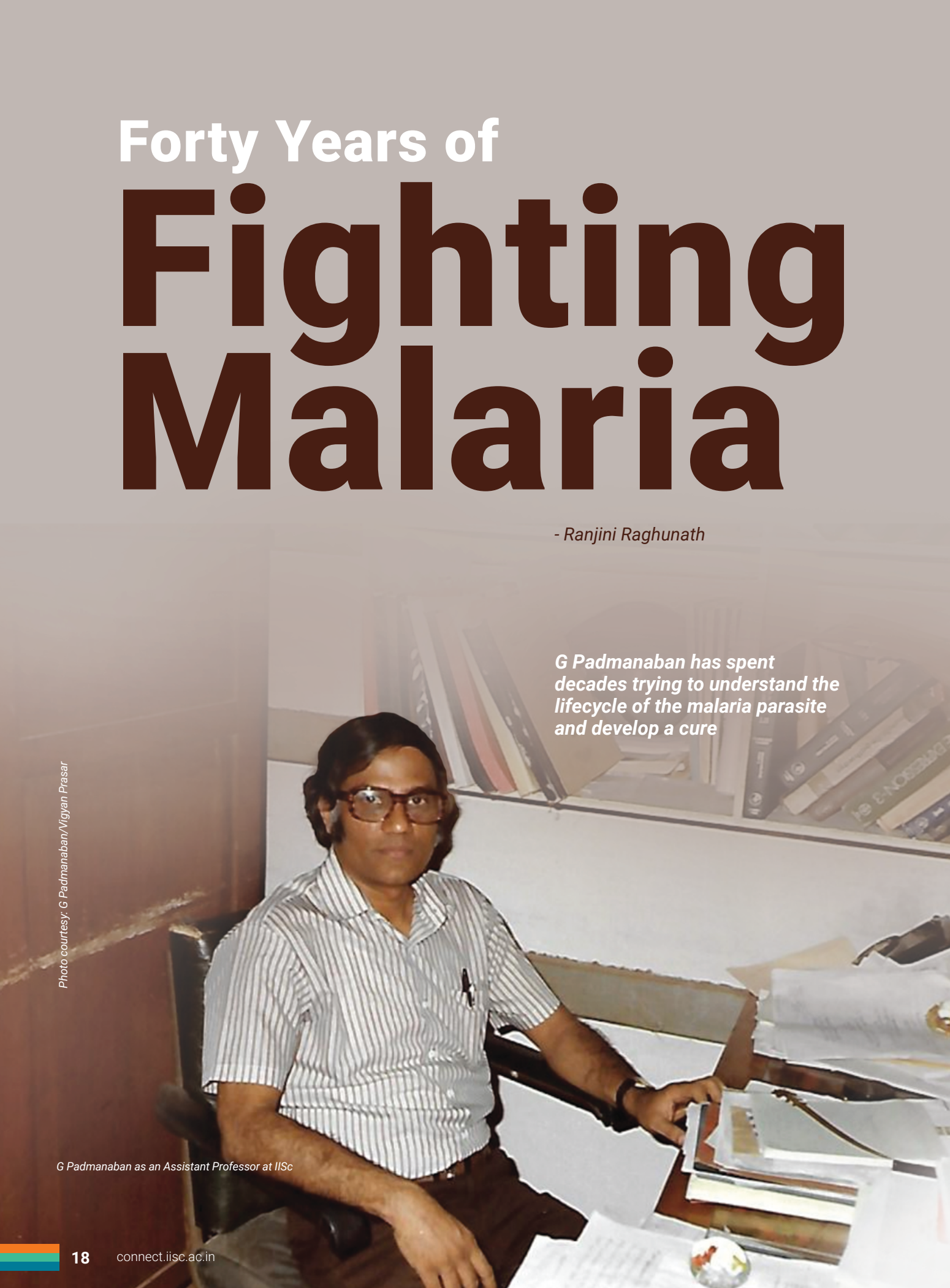


Photo courtesy: G Padmanaban/Vigyan Prasar

G Padmanaban as an Assistant Professor at IISc

A few years ago, researchers from Michigan State University tracking malaria in Malawi made a gut-wrenching discovery. The reason why many children with cerebral malaria were dying was because their brain was swelling up so much that it pushed out through the bottom of the skull and squeezed the brain stem, stopping their breathing.

A devastating complication arising from malarial infection, cerebral malaria kills thousands of children under the age of five in Africa, and leaves survivors suffering from long-term neurological problems.

The only effective treatment currently available for such severe forms of malaria is artemisinin – a compound found in a herb used for over 2,000 years in Chinese traditional medicine. It was first extracted in 1972 – an effort that earned a Nobel Prize – and its subsequent widespread use saved millions of lives. In order to prevent the malaria parasite from becoming resistant to artemisinin, the World Health Organisation declared in 2006 that it should not be given alone, and that combination therapies should be developed with other antimalarial drugs or compounds.

To G Padmanaban, who had by then been studying the disease for decades, this was an exciting proposition because he was already working on just that – trying to combine artemisinin with curcumin, another molecule having ancient roots.

By 1998, he had formally retired as the Director of IISc, but continued working as an Honorary Professor at the Department of Biochemistry. After delving deep into literature on the medicinal properties of curcumin, he became increasingly convinced that it had enormous potential for treating a variety of diseases.

Working with PN Rangarajan, now the Chair of the department, Padmanaban found that three oral doses of curcumin along with a single injection of an artemisinin derivative prevented malaria relapse in infected mice in the lab, and boosted their chances of survival. They also showed that the combination staved off neurological symptoms linked to cerebral malaria and completely cured infected mice.

Buoyed by these results, Padmanaban was eager to take the combination therapy to the market. He filed a patent in both India and the US. He also urged the Drug Controller General of India (DGCI) to carry out clinical trials to test its efficacy in patients.

But he hit roadblocks on both fronts. The National Biodiversity Authority (NBA) pulled him up for apparently not seeking clearance before filing the US patent because turmeric – the spice from which curcumin is usually extracted – is considered an endangered species. His arguments that they had not used turmeric extract but a commercially sold chemical form of curcumin fell on deaf ears. As the penalty could end up being a fine of Rs 10 lakh and a jail term, Padmanaban's patent attorney even advised him to withdraw the sanctioned US patent.

The DGCI, for its part, dragged its feet on the clinical trial application for over a decade. Last year, after a relentless battle, it finally gave approval for the trials to be carried out in two hospitals in Chhattisgarh and Rourkela by the National Institute of Malaria Research (NIMR), New Delhi. A tablet made from curcumin and an artemisinin derivative called artesunate was to be tested in patients with simple malaria. The clinical trial project was approved by the Department of Biotechnology. Everything was set. Then, COVID-19 struck. Now, NIMR is waiting for the hospitals to return to their normal routine.

"Sometimes I feel like [the mythological king] Bhagiratha trying to bring the river Ganges down to Earth," chuckles Padmanaban, now 82.

The haem connection

By the time Padmanaban applied to IISc for a PhD in late 1960, all formal admissions for that year had closed. Luckily, he was selected as a Junior Research Fellow in a sponsored project under PS Sarma at the Department of Biochemistry. Sarma's lab was working on kesari dal, a controversial pulse whose excess consumption was linked to neurological disorders. Padmanaban was able to isolate the amino acid from kesari dal that turned out to be a neurotoxin. But then, he was asked to work on trace element metabolism as that was the goal of the sponsored project.

While carrying out experiments on a type of mould under iron-starved conditions, he stumbled upon the synthesis of haem, an iron-containing molecule also found in haemoglobin, the oxygen-carrying protein of red blood cells. He developed a keen interest in this molecule, which would serve him well years later.

After completing his PhD in 1966, he continued working in Sarma's lab, giving up the chance to go abroad. In 1969, he was appointed as an assistant professor in the same department. "Everybody was working on molecular biology in prokaryotes. But I wanted to work on animals, and humans, which was considered a 'black box'," he says. He learnt all the techniques needed in the lab of Murray Rabinowitz at the University of Chicago, which he visited 10 times between 1973 and 1986.

Around the early 1980s, the Swedish pharmaceutical firm Astra – now AstraZeneca – approached Padmanaban and asked for his help to set up a research centre in Bangalore. With support from the Department of Science and Technology (DST), Government of India, the company acquired a building close to IISc campus. Padmanaban opened up his own lab to the Astra team. "It was one of those old labs, with cockroaches and all," he reminisces. "But still research went on." He also convinced about half a dozen students, who were planning to go abroad for their PhD, to stay back and work on joint projects with Astra.

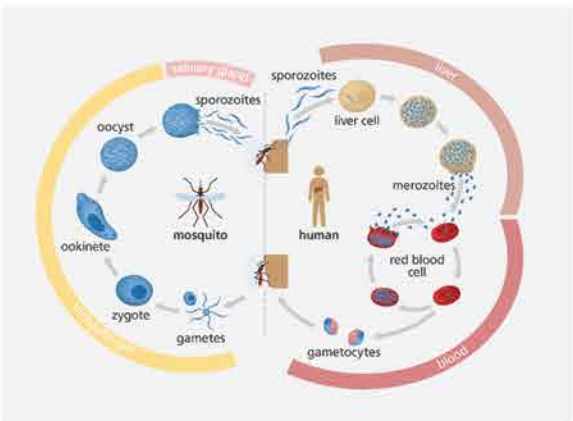


Image courtesy: Genome Research Limited/Wellcome Trust

Life cycle of the malaria parasite

The company was keen on carrying out research on infectious diseases in India and provided generous funding. "We built the entire north wing of the department with Astra money," he recalls. Spurred by their interest, he began projects on four diseases, one of which was malaria. Eventually Astra moved out to Hebbal in the city and was later shut down, but Padmanaban continued working on malaria, which soon consumed his entire attention.

"It was the haem connection," he explains. The malaria parasite, *Plasmodium*, breaks down the haemoglobin in our red blood cells to release haem and amino acids, which are vital for its survival. But free haem can kill the parasite, so it converts the haem into a safer form called haemozoin. Drugs such as chloroquine work by blocking this conversion.

However, as Padmanaban discovered, the parasite was also able to synthesise haem by itself. If it was getting plenty of haem from our blood, why would it need to make its own? "We were more or less the only group in the world looking at this question," he says.

Shortly after Padmanaban formally retired, Arun Nagaraj, now a scientist at the Institute of Life Sciences, Bhubaneswar, joined him and continued investigations into the parasite's life cycle, using lab mice infected with a related species called *Plasmodium berghei*.

First, they tried to see if knocking out genes involved in haem synthesis stopped the parasite from growing. "But it didn't do anything. The parasite continued to grow merrily," explains Padmanaban.

Then, they wondered if they were looking in the wrong place. So far they were only looking at one host – the human. But the parasite's life actually cycles between the human and another host – the female *Anopheles* mosquito. When the mosquito bites us, it injects larvae-like forms of the parasites (sporozoites) into our body. Inside our liver, these sporozoites grow and transform into merozoites, which burst out into the bloodstream. These merozoites then develop into male and female sexual forms, which are sucked back into another mosquito that bites us the next time. Inside the newly infected mosquito, the sexual forms fuse to eventually give rise to more sporozoites, thus completing the cycle.

Perhaps the parasite didn't need to make haem to grow inside the human red blood cells, but needed it inside the mosquito.

To test this theory, the team had to breed infected mosquitoes, slice them open and study them. "At that time, we didn't have an insectary to grow the mosquitoes," says Nagaraj. He had to travel 40 km from IISc to an ICMR lab close to the airport, where they could breed the infected mosquitoes, and carry them back to campus to test them on mice models. Each experiment would take 40 days, and frequent power disruptions in the ICMR lab meant entire experiments had to be scrapped, because the mosquitoes needed steady environmental conditions to survive.

> ***Nagaraj had to travel 40 km to an ICMR lab where they could breed the infected mosquitoes, and carry them back to campus to test them on mice models***

Their perseverance eventually paid off. In 2013, they published a study showing that the parasite absolutely needs to make its own haem inside the mosquito and in the human liver. Parasites that could not make haem were unable to sexually reproduce. "They can survive in the [human] blood stage, but when they go back into the mosquito, you will not find development of sporozoites," explains Nagaraj.

But the mystery wasn't completely solved yet. Yes, the parasite needed to make haem inside the mosquito and yes, it also had access to haem from haemoglobin. Then why would it continue to make haem inside human blood cells?

"Finally, we have an answer for that now; we have not yet published the data," says Nagaraj. "The parasite makes haem to sustain virulence." He says that they have also identified a drug already in use that can be repurposed to block haem synthesis and abolish parasite virulence.

Photo courtesy: G Padmanaban/IISc Press

Arun Nagaraj (second from left) with malaria research group at IISc

Curcumin as a cure

The problem with developing new drugs to treat malaria is that the parasite can quickly become resistant to them. Its genetic material is rich in a specific DNA base pair combination that makes it unstable and easily mutable. "You develop a drug or vaccine, it will develop resistance. If [the drug or vaccine] works one year, it may not work the next year. And what works in India may not work in Africa," explains Padmanaban.

Plasmodium falciparum, the deadliest malarial parasite species, has already become resistant to many of the partner drugs used with artemisinin. Alarming reports of artemisinin resistance are also emerging across Southeast Asia, and more recently in Africa. "There is no alternative drug, really speaking, although there are drugs in the pipeline, in clinical trials," says Padmanaban.

This is where he believes a molecule like curcumin can make a difference, at least as an adjunct drug. It is not a newly developed compound, but a food molecule that has been consumed by humans for millennia. The parasite is therefore unlikely to become resistant to it, he says.

Initially when his team tested the effect of curcumin, they found that it could only delay parasite growth in culture. Then, they decided to combine it with an artemisinin derivative called arteether and the results were more encouraging. Giving three oral doses of curcumin with a single shot of arteether was especially helpful in preventing the infection from relapsing, a common problem with some drug combinations. Weeks after giving the combination therapy, the team could detect antimalarial antibodies circulating in the blood of infected mice.

In another experiment, this time on cerebral malaria, the team found that curcumin alone could prevent the onset of neurological symptoms. It prevented the breakdown of the blood-brain barrier – which regulates the flow of molecules from the blood into the brain – and clumping of red blood cells in the brain, and therefore reduced inflammation. The mice still ended up dying because of anaemia. But when curcumin was given along with arteether, the combination once again saved the mice from death.

Inspite of these promising results, Padmanaban had a hard time convincing the DGCI to approve the clinical trials. Their argument, he says, was that a naturally occurring molecule like curcumin should not be combined with a chemical artemisinin derivative.

Another issue, as Padmanaban writes in his book *Doing Science in India: My Second Innings*, is that curcumin "does not act like a drug in a way that is understood by medicinal chemists." Some believe that it won't be as effective as other drugs because it gets broken down within minutes of entering the bloodstream. "Then, how is it that the protective effects of curcumin are seen after several days?" he writes. "We could detect copious amounts of anti-parasite antibodies in the blood at the time of parasite recrudescence [recurrence] only in curcumin-treated animals." He speculates that curcumin likely activates memory cells of the immune system to respond to the parasite, although those mechanisms are yet to be understood.

Photo courtesy: G Padmanaban/IISc Press

G Padmanaban (right) with PN Rangarajan (centre) and former student Sendurai Mani in the old Biochemistry building

Despite the delays due to COVID-19, Padmanaban is optimistic about the success of the clinical trials testing the combination therapy. "This will be the first powered trial to establish that it works," he says. "It will take another 4-5 years. But it will be worth it." His patent battle also thankfully ended last year. "The government said that the NBA should reinvent itself and settle all cases before 2019. In that process, ours was dropped."

Homecoming:

Biochemistry Alumni who Returned to the Institute

- Joel P Joseph

Photo courtesy: PB Seshagiri

PB Seshagiri, Sandhya S Visweswariah and Varsha Singh talk about their academic journeys

From left to right - Vani, Sandhya Visweswariah, and PB Seshagiri in 1986

There is no doubt that IISc attracts some of the best students in the country. But a few of them have come full circle, returning to the Institute – some even to the same building – where they took their baby steps into the world of research. As the Department of Biochemistry at IISc celebrates its centenary year, it is only fitting to turn the spotlight on the alumni who are now faculty members at other departments in the Institute.

The Biochemistry Department has come a long way since its inception in February 1921. It has moulded and nurtured some of the finest scientists in the country, many of whom have gone on to become institution builders, entrepreneurs, and industry leaders. And some of them have found their way back home – to the place where it all began.

Three of them, currently faculty at the Department of Molecular Reproduction, Development and Genetics (MRDG), obtained their PhDs from the Biochemistry department – Polani B Seshagiri (Professor), Sandhya S Visweswariah (Professor), and Varsha Singh (Associate Professor). They are the only Biochemistry alumni among the current faculty members of the institute outside of the Biochemistry Department.

From student to supervisor

The academic journeys of Seshagiri and Visweswariah are remarkable. They completed their PhD from the same lab as contemporaries, returned to the Institute as faculty around the same time, and went on to become Chairs – a position that their PhD advisor held when they were recruited. Singh's story is equally interesting. Academically speaking, she is a second generation alumnus of the Biochemistry department – her advisor, Utpal Tatu, who is still a professor in the Biochemistry Department, also did his PhD there.

Seshagiri and Singh only have words of appreciation and gratitude as they recall their student life in the department. The lectures hosted at the Biochemistry Lecture Hall, resource-sharing among peers and informal scientific discussions among students are themes that stand out in their reminiscences.

After his MSc in Clinical Biochemistry from the Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry, Seshagiri joined PR Adiga's lab for his PhD in 1980. It was his keen interest in endocrinology (the study of hormones and the glands that secrete them) that led him to join the lab. As a student, he learnt many experimental techniques from his seniors. He also had much to offer to his peers: animal handling techniques, injections and surgeries – some skills he had gained from his anatomy and physiology background at JIPMER.

Photo courtesy: PB Seshagiri

PB Seshagiri as a PhD student in 1981

Seshagiri remembers his peers in the department as a bunch of dedicated and enterprising students. "We worked very hard and shared resources and research workload. We had a feeling of togetherness, discussed ideas, and knew how to troubleshoot problems in experiments," he says. "Most of all, we enjoyed great academic freedom."

About halfway through his PhD, Seshagiri attended the Indo-US conference on Blastocyst Research organised by NR Moudgal, a professor in the Department of Biochemistry at the time. And this would be a turning point in his career. "The workshop featured amazing demonstrations of sperm culture, embryo culture, embryo transfer etc, and fantastic lectures were delivered by stalwarts in the field," says Seshagiri. "At that time, the most profound lecture was the one by BD Bavister, the architect of the first IVF-test tube monkey, *Petri*."

Photo courtesy: PB Seshagiri

Indo-US Conference on Blastocyst Research at the Faculty Hall in 1983. First row (from right): AJ Rao (Faculty, Biochemistry Dept from 1982 to 2004), PR Adiga (Faculty, Biochemistry Dept from 1969 to 1995). Third row, third from right: PB Seshagiri

In 1987, a year after obtaining his PhD, Seshagiri joined Bavister as a postdoctoral fellow at the University of Wisconsin, Madison. Three years later, he became an Assistant Scientist at the Wisconsin National Primate Research Centre (WNPRC). But all this while, he longed to return to India. "So, when the faculty recruitment for the newly founded Centre for Reproductive Biology and Molecular Endocrinology (CRBME) – which is now called MRDG – started, I applied and was selected," he says.

Visweswariah's experience with the department was quite different. After her Master's in Chemistry from IIT-Kanpur, she moved to Bangalore with her husband who got posted here, and applied for a PhD in the Biochemistry Department in 1980. "The Department of Biochemistry at IISc was perhaps the most well-known biochemistry department in the country. A lot of students aspired to do their PhD [there]," she says. Looking back, Visweswariah considers herself fortunate to have been selected there for a PhD, coming from a pure chemistry background. On G Padmanaban's suggestion, she joined PR Adiga's lab.

As she was married, Visweswariah lived outside the Institute and only spent her work hours on campus. "I used to come in the morning, do my work, and leave in the evening," Visweswariah says. "But as a result, I could stay quite focused. I knew what I had to do, and I knew I had exactly so many hours to do it."

Visweswariah remembers fondly that she found a great friend in Anjali A Karande, a postdoctoral fellow in Adiga's lab at the time, who would go on to become a faculty member at the Biochemistry Department. "She lived very close to where I lived. So, we would come to the lab together every day and go back home together. She was also married and with children. So, you know, there was a companionship there and an understanding of each other's difficulties – trying to do some science as well as run a family," says Visweswariah.

Unlike Seshagiri and Visweswariah who directly joined the department for their PhD, Singh joined the Division of Biological Sciences as an integrated PhD student in 1997 – when Seshagiri and Visweswariah were faculty at MRDG. After trying out different labs across departments in the biological sciences during her lab rotations, Singh decided to join Tatu's lab in the Department of Biochemistry. It was her interest in host-pathogen interactions, in understanding how disease-causing organisms interact with the organisms they infect, that led her there.

Singh recalls the time she spent in the department and the academic freedom she enjoyed there. "We had the freedom to perform different experiments – some of which our advisors knew, and some that they didn't. We could work in the lab at any time, night or day," she says.

In 2002, when Tatu had procured a MALDI-TOF machine (an instrument that is used to analyse different proteins) for the lab, it gave Singh more access to the coveted instrument and the flexibility to use it at any time. "I remember spending a long time, even in the night, chopping proteins into fragments using the enzyme *Trypsin* and analysing them," she says. "This wouldn't have happened if this was a department or institute facility." Her face lights up when she says that some of the coolest outputs she got using the instrument were past dinner time. She describes how one night, around 9.45 pm, she predicted an unknown protein in *Plasmodium* to be a chaperone (a class of proteins that serve as quality control to check whether the proteins in the cell get folded into the right shape). "As a graduate student, it was an exciting experience," Singh says.

> ***"We had a feeling of togetherness, discussed ideas, and knew how to troubleshoot problems in experiments. Most of all, we enjoyed great academic freedom"***

She also recalls the magnanimity of students in the department. She narrates how she and a few others in the lab had to collect O+ blood to cultivate *Plasmodium* for their research. "Every three weeks we would get hold of a person whose blood group was O+, take them to the Health Centre, and collect their blood," Singh says. "It's amazing how we drew blood from some people a dozen times, and I now realise we didn't even take them out for dinner! It was such a selfless thing they did." She adds that they eventually also became friends with the people in the Health Centre who used to draw blood for them.

However, as is the case with any graduate student, Singh's PhD was not a smooth sail. She had her own share of struggles. Once working on an important experiment with *Plasmodium* cultures, she had set the incubator temperature to 37°C, but it failed to work, and the temperature rose to 42°C. "All the cultures I was maintaining died," she says. After this incident, Singh embarked on a lookout for model systems whose genetics can be easily manipulated for experiments. Eventually, she went on to do her postdoctoral research on another organism called *C. elegans*, and now studies interactions between *C. elegans* and bacteria.

Photo courtesy: Varsha Singh

From left to right: Banumathy, Pavithra S, Varsha Singh, Yadunanda Kumar on the roof of the old Biochemistry building in 2002

Photo courtesy: PB Seshagiri

PB Seshagiri in front of the old Biochemistry building

After her postdoctoral research abroad, personal and professional reasons led Singh to return to India. She had applied for a faculty position at nine institutes in India, and received offers from six including IISc. "IISc is an amazing place, and Bangalore is very open to people who are not Kannadigas. And I liked MRDG for the diversity in terms of the questions they address and the model systems they use," she says. These factors, and her conversations with Visweswariah, who was by then a faculty at MRDG, influenced her decision to join IISc.

These and many other experiences from the Biochemistry Department shaped Singh, in some ways, to be the scientist she is today. When she joined Tatu's lab, it was relatively new – she was the third PhD student in the lab. "When I joined the lab, we were still trying to set up a lab. So, I [gained experience in] how to start a new lab," she says. Seshagiri and Visweswariah also agree that the training in the department came in handy while setting up their own labs. It gave them essential lessons on the "how-tos and how-not-tos" of running a lab. Seshagiri says that his responsibilities in Adiga's lab, having to procure chemicals and equipment, helped him later on. He adds that the qualities he had imbibed from the PhD training in the department – interpersonal skills, a hardworking nature, and the self-confidence to do things in the face of difficulties – also helped.

From mentee to mentor

Some of the professors at the department, and the Institute, left a lasting impact on the students. "Academically, I grew up among a super-class of professors and teachers," Seshagiri says. He is all praise for his advisor's intelligence and commitment to research. "Adiga was a great mentor; very time-conscious and work-conscious," he says. Visweswariah also describes Adiga as a strict mentor. NR Moudgal and G Padmanaban were two other professors who strongly influenced Seshagiri. Moudgal's courteous nature, generosity, and incessant efforts to stay connected with the western world and bring Indian molecular reproductive research infrastructure on a par with the USA, left a deep impression on Seshagiri. "Moudgal is one of the finest reproductive endocrinologists the country has seen," he says. He still admires how Moudgal "singularly established the primate research facility in IISc, which was one of the first in the country, and is still functional." Seshagiri also served as the convenor of the facility for about six years.

Padmanaban comes across as a professor who influenced many students. "He was somebody who everybody looked up to," Visweswariah says. There is a sense of respect and admiration in their voice as they talk about GP (as they call him affectionately). "GP was one person who strongly influenced me indirectly," Singh says. "He asked fundamental questions which reminded me why I was doing what I was doing." In addition to his intense commitment to research, Seshagiri also remembers how humble, self-disciplined and humane GP was. "Most of all, GP was a very approachable person, be it for research advice or social events," he says, remembering the days when they played cricket together.

Singh also describes how her advisor was very critical of his students, and in hindsight, how that helped her think things through before verbalising them. She now tries to apply that to her own research to ensure that there are no gaps. She adds that IISc has this amazing ability to bring that out of certain people – the confidence that they can do it.

In many ways, these alumni have passed on some of the qualities they absorbed as students, from their seniors and professors. Visweswariah says that MRS Rao, who was a postdoctoral fellow when she was a PhD student but a faculty member in the Biochemistry Department when she joined MRDG, was another person she looked up to. Rao went on to chair the department and later became the President of the Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR).

Visweswariah herself has been an inspiration for the next generation of scientists, including Singh. "Sandhya has always been a mentor since I came back. She's the kind of mentor that I can disagree with, and let her know that I disagree with her views," Singh says.

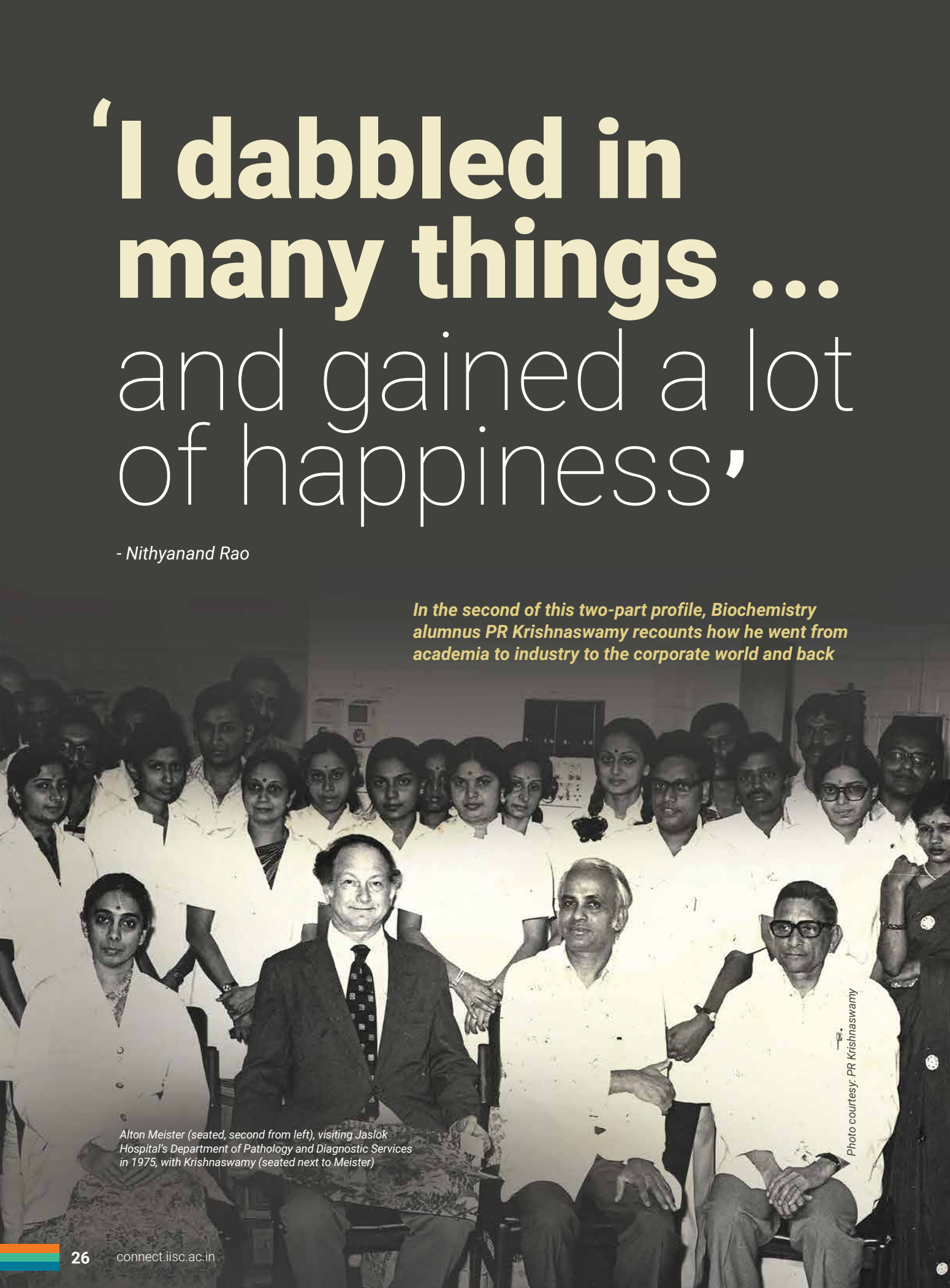
This nature of paying it forward is essential to build a great legacy. Which is what these alumni have been doing since they came home, giving back to their alma mater while moving ahead in their academic journeys.

Joel P Joseph is a PhD student at the Centre for BioSystems Science and Engineering (BSSE) at IISc

‘I dabbled in many things … and gained a lot of happiness’

- Nithyanand Rao

In the second of this two-part profile, Biochemistry alumnus PR Krishnaswamy recounts how he went from academia to industry to the corporate world and back



Alton Meister (seated, second from left), visiting Jaslok Hospital’s Department of Pathology and Diagnostic Services in 1975, with Krishnaswamy (seated next to Meister)

Photo courtesy: PR Krishnaswamy

It was a rainy day in July 1973 when Prime Minister Indira Gandhi arrived to inaugurate the Jaslok Hospital in Mumbai. After her speech, she was taken on a tour of the 20-floor hospital by its Director, the surgeon Dr Shantilal Mehta. With them was PR Krishnaswamy, who had set up the most striking feature of the facility, the pathology laboratory and research space which occupied one-and-a-half floors.

"She was astonished," says Krishnaswamy. Having been given a free hand by Dr Mehta, he says he had filled the laboratory with the latest equipment and trained clinicians, creating a research facility unique among private hospitals in India at that time.

It was quite a turnaround for Krishnaswamy. After completing his DSc with KV Giri at the Department of Biochemistry in IISc, with many notable publications to his credit, he went abroad to work with Alton Meister at the Tufts University School of Medicine. But when he returned to India in 1963, he did not have a job. He initially worked at the Central Food Technological Research Institute (CFTRI) in Mysore but could not get a permanent appointment despite his research record. Good advice led him to join the Protein Foods Association of India (now the Protein Foods and Nutrition Development Association of India) as its first Director. And now, he was giving the Prime Minister a tour of the research space he had put together at Jaslok Hospital.

He had joined CFTRI initially in an honorary position, and began work on child malnutrition, collaborating with the CSI Holdsworth Memorial Mission Hospital nearby. They found that the nutritional deficiencies in malnourished children rendered their body unable to utilise even the meagre amounts of proteins that were available in their food. They excreted significant amounts of unutilised amino acids in their urine. Among them was the cyclic form of glutamic acid, 5-oxoproline.

Krishnaswamy was familiar with glutamic acid, having worked on it at Tufts. Its cyclic form, 5-oxoproline, is not usually found in blood or urine to any great extent, as he found by analysing his own. "But in malnourished children, I found it in their urine in large amounts," he says. It had always been considered to be a compound without metabolic significance, but Krishnaswamy, in collaborative experiments with a colleague at CFTRI, D Rajagopal Rao, was able to prove otherwise. Their publication on the metabolic significance of 5-oxoproline set the stage for further discoveries and studies on medical applications.

During this period, M Sreenivasaya, his mentor at IISc, came to visit him at CFTRI. "I told him about our oxoproline work," he says. "The most satisfying moment for me was his extraordinary exhilaration. It was my tribute to his mentoring me in the early part of my career."

His initial honorary position at CFTRI had led to a CSIR Pool Officers' fellowship after six months, but it proved to be a dead end. He couldn't get a permanent position even after three years, and decided to leave. "This was a crisis in my career," he recalls. Fortunately, through contacts, he soon took up a more challenging assignment, on a national level.

This period, 1966-67, saw a famine in Bihar, and the country experienced a food shortage. The grim situation, says Krishnaswamy, galvanised some of the leading players in the food industry, such as Hindustan Unilever, Amul, Nestle and Brooke Bond, among others, to work together, leading to the formation of the Protein Foods Association of India with the help of USAID (United States Agency for International Development). The Association offered him the role of Executive Director. "What I had to do was to advise the government, advise the industry, set up programs, work with UNICEF [the United Nations Children's Fund] and the WHO [World Health Organisation], and other organisations on practical implementation; get everyone interested. This was a job I had to do single-handedly," he says.

He initiated nationwide surveys that showed that protein and caloric deficiencies were prevalent in the middle class too, and worked on campaigns to raise awareness about these deficiencies. Among these was a 20-minute documentary film, "Your Child's Plate is His Horoscope," starring the late actor Smita Patil and made by a team involving actor and author Gerson da Cunha and filmmakers Shyam Benegal and Mrinal Sen. It was produced by the Films Division of the Government of India and shown before movie screenings in all cinema theatres across the country. "The experience of working with all of them on this film was a most memorable one," says Krishnaswamy.

The Association also facilitated food companies developing products that could ameliorate nutritional deficiencies – such as weaning foods, and wheat flour fortified with lysine, an amino acid – and used existing distribution networks to make these available even in remote areas.

Photo courtesy: PR Krishnaswamy

At the Annual General Meeting of the Protein Foods Association of India in Mumbai, 1971. L to R: Wadud Khan (Director, Tata Sons, and MD, Tata Oil Mills); V Ramalingaswami (Director, AIIMS); and PR Krishnaswamy

Before joining the Association, Krishnaswamy had informed them that he did not intend to stay beyond three or four years. In the meantime, he had been visiting medical colleges to give occasional lectures to students and interact with faculty. "This contact with the medical profession opened a few doors for me," he says. This eventually led him to meet Dr Mehta, who offered him the position of the Chief of Laboratories of Pathology and Head of Research at Jaslok Hospital that was then being built. "It was the most premier hospital in the country," says Krishnaswamy. "Though it was a private institution, it was shaped in the first decade by one of the most outstanding doctors, surgeons, teachers and visionaries in this country – Shantilal Mehta put it together with a lot of idealism."

A fourth of the beds at Jaslok would serve the poor, free of charge, and another fourth were available at subsidised rates. Jaslok became well-known after Jayaprakash Narayan was admitted for renal failure during the Emergency, and stayed for many months. "By turns we would go and sit with him and talk to him, listen to his stories," says Krishnaswamy. "JP's presence made Jaslok a household name in the country. Famous and influential people, including chief ministers, would come for treatment there."

But Jaslok also earned its reputation through its research efforts. The equipment at Jaslok's laboratories, recalls Krishnaswamy, included many new technologies such as an electron microscope, spectrophotometers, cold centrifuges and amino acid analysers. One of the studies he undertook during this period was on the pathophysiology of diabetes. Krishnaswamy knew that increased blood sugar levels oxidise and modify the structures of proteins, including haemoglobin, through a process called glycosylation. Working with Dr HB Chandalia (professor of endocrinology at Grant Medical College), he developed a method to estimate the levels of glycosylation of haemoglobin in diabetic patients. This "HbA1c test", as it came to be known, was a useful method for monitoring diabetes treatment, a novel approach at that time in India. Its introduction at Jaslok was an early innovation, and brought the hospital to the attention of endocrinology researchers and clinicians in the country.

> ***This "HbA1c test", as it came to be known, was a useful method for monitoring diabetes treatment, a novel approach at that time in India***

Such a research culture was enabled by weekly meetings where clinicians would present interesting cases. "That's not done even in most corporate hospitals nowadays. People don't have the time because it's so practice-oriented," says Krishnaswamy. Jaslok also ran its own journal which he edited for a while.

At Jaslok, Krishnaswamy worked on other research problems too. In the late 1970s, he found that seminomas, germ-cell tumours of the testes, express a protein, a membrane enzyme called gamma-glutamyl transpeptidase. "I suspected we should look at it in all germ-cell tumours as a marker. That, I couldn't do in Jaslok fast enough because we don't get so many cases of that kind of cancer." So he applied for and obtained an International Cancer Union fellowship to visit the La Jolla Cancer Research Foundation (now the Sanford Burnham Prebys Medical Discovery Institute) to work on biomarkers for testicular tumours. "It was preliminary work but later on people took it to other levels."

Then, in 1983, Krishnaswamy had a visitor at Jaslok. "I had thought he had come for a blood test or to have some investigations done. He said, 'I want to ask you whether you would consider a very senior position in the UB [United Breweries] Group board and as head of research for the whole Group.' I said, 'Are you kidding me?'" The man turned out to be a headhunter for the UB Group who had zeroed in on him.

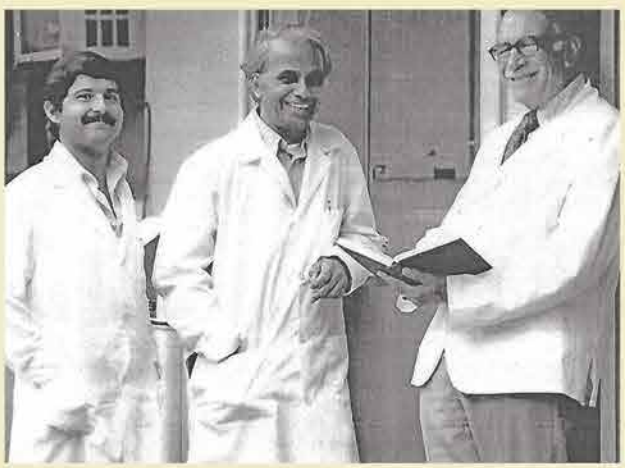


Photo courtesy: PR Krishnaswamy

At La Jolla Cancer Research Foundation, 1976. L to R: José Luis Millán, Krishnaswamy, and William Fishman (Founder-Director)

Krishnaswamy flatly declined and sent him away with a list of suggested names. But four months later, the recruiter returned, saying that all of the suggested people had pointed him back to Krishnaswamy as the most suitable person. He mulled over it for many months, and eventually met Vijay Mallya in Bangalore. "I was astonished," says Krishnaswamy of Mallya. "He was about 28 then; I had not met many at his age who were as composed, articulate, effectively communicating, clear in his thoughts and goals, and convincing. I was impressed with what he was made up of," he says. "My apprehension was whether I could do what was needed and what would be enjoyable for me."

He had known Vijay's late father, Vittal Mallya, from his visits to Jaslok. The UB Group had about 30 companies, and Vijay wanted to transform them and expand the Group's operations. He also wanted to invest in research that could support these goals. "He said, 'liquor is our main business' but he wanted to diversify," says Krishnaswamy. "He wanted to become a technology-oriented, well-diversified group in a changing world, where new technologies were emerging."

In 1984, after 12 years at Jaslok, Krishnaswamy decided to leave and join Mallya as President of Group Research and Development, on the condition that he would be allowed to engage in research in the rapidly developing field of biotechnology. This, he proposed, was to be done through a standalone not-for-profit foundation which the Group would have to support, but which would eventually generate its own funds. "He readily agreed," says Krishnaswamy. "But he put one rider. He said, 'You set up a hospital in my father's name in Bangalore.' I said I'll do it."

This became the Mallya Hospital. Krishnaswamy also worked as a president of the UB Group, on its supervisory board. In parallel, he recruited people for what was named the Vittal Mallya Scientific Research Foundation (VMSRF). He even set up a separate technical centre which did research on developing and improving the Group's products, or, as he puts it, their core "spiritual" business. "I didn't want to mix the science part of the operation with the business-oriented research," says Krishnaswamy. "I think, for new ideas, the creative thing must be separate but integrated when needed."

He organised research at VMSRF, with more than two dozen researchers and PhD students, at a time when biotechnology in India was at a nascent stage. One of the achievements of the research efforts at VMSRF was to synthesise recombinant insulin, a project that took four years. "Without any vanity, I can say that it was perhaps the first attempt in the corporate sector to undertake research," says Krishnaswamy. "Mallya was very proud of it; I wish he had stayed on that track. He gave us every support for basic research and academic excellence."

Krishnaswamy's move from Mumbai to Bangalore had meant that his wife, Rukmini, had to leave the SPJ Sadhana School for children with special needs, where she was the Principal. In Mumbai, she taught at various other schools and worked with kids in Dharavi. "I would start my day with preschoolers," she says, "and end it with teaching postgraduates in developmental psychology." Having trained in the subject at Harvard, she pursued her calling by starting a school on the CFTRI campus in Mysore, where she developed her methods in inclusive education by having children of faculty and staff learn together. After moving to Bangalore, she became one of the founders of the Spastics Society of Karnataka, and has now spent more than six decades working with children, particularly those with special needs, and training teachers and parents. "We now serve over 4,000 children in all our institutions, mostly in rural areas. We work in district hospitals, community medical centres, various hospitals," she says.

Photo courtesy: PR Krishnaswamy

Rukmini Krishnaswamy (front row, second from right), with Mother Teresa at SPJ Sadhana School in December 1980. Also in the photo are Sister Mary Braganza (first from left), Principal of Sophia College, and Sister Eileen Gaitonde (between Mother Teresa and Rukmini), who later became Principal of SPJ Sadhana School

Krishnaswamy left VMSRF after 12 years, in 1996. But this did not imply retirement. As Director, he headed the Diagnostic Division – the Pathology Laboratories and the imaging facilities – at Manipal Hospital, where he continued to mentor PhD students working on disorders such as thalassaemia, and investigating biochemical changes in renal patients. "I was also an Honorary Director [of the hospital], the only condition of engagement being that I would be free to pursue my research interests, 'translational' in nature, on clinical problems."

Around this time, he started collaborating with P Balaram, the former Director of IISc. "He's tremendously interested in haemoglobin as a protein molecule," says Krishnaswamy. More recently, he has also worked with Navakanta Bhat at the Centre for Nano Science and Engineering, and the team behind PathShodh, a start-up that has developed diabetes monitoring devices. In parallel, he has advised students at Sri Devaraj Urs Medical College in Kolar.

"One of the things which added real value to my career," says Krishnaswamy, looking back over his decades straddling academia, industry, and the corporate world, "is that I dabbled in many things. Not by choice, but I made the most of what I could do. And I gained a lot in terms of my own happiness."

Nithyanand Rao is a graduate student at the University of California, San Diego and former Consultant Editor at the Office of Communications (OoC), IISc

What IISc Needs to Become World-Class: Interview with Anurag Kumar

- Ranjini Raghunath

Photo: Manoj Sudhakaran

In July 2020, Anurag Kumar completed his tenure as the Director of IISc. He began his journey in engineering with a bachelor's degree from IIT Kanpur and a PhD from Cornell University, and then worked at Bell Labs, New Jersey, USA, before joining IISc in 1988. After serving as the Chair, Department of Electrical Communication Engineering, and later the Chair, Division of Electrical Sciences, he was appointed Director in 2014.

During his tenure, he introduced initiatives to modernise IISc's administration and infrastructure, improve faculty recruitment, increase support from non-government sources, and enhance IISc's visibility abroad. In 2018, IISc was also recognised as an Institution of Eminence (IoE) by the Government of India.

Kumar spoke to CONNECT about his vision for the Institute and what it would take to make IISc a world-class institution.

How did you come to join IISc?

After completing my PhD at Cornell, my desire was to enter academics, but, being an engineer, I also wanted to see how industrial labs work. So, I joined Bell Labs and was there for about seven years. My wife and I had decided that after our Bell Labs stint, we would return to India.

In 1986, I began to apply for positions in India. Apart from a couple of government positions, I got offers of Assistant Professorships from IIT Kanpur and IISc. Frankly, I knew very little about "the Institute" at that time. My father-in-law, Prof Ravindra Nath, had been a PhD student in the Department of Biochemistry at IISc in the 1950s. He knew IISc well, due to his many continuing connections there. It was he who encouraged me to accept the IISc offer. It turned out well for me, and for my wife too, for whom, being an electronics engineer, Bangalore was the ideal place to move to.

Are there any experiences during your time at IISc that stand out?

The experience of building my academic career at IISc, in an area that was still emerging at that time, was itself a remarkable experience. The experience of participating in the national ERNET project was very special, and one that I would not replace with anything else. From 2007, I was asked to join the higher level of administration in the so-called "Tower Building." This aspect of my career at IISc has been full of new experiences on a daily basis.

What was it like working on the ERNET project, which established India's first nationwide internet?

I took charge of the ERNET project, hesitatingly, just a few months after coming to IISc. ERNET was a collaboration between eight sites in India (five IITs, IISc, the National Centre for Software Technologies, Mumbai, and the Department of Electronics, Delhi). The objective was for these sites to collaborate in setting up India's academic and research network, based on the emerging technology of packet networking.

It must be noted that, at the time, the so-called "Internet" was not necessarily the technology of choice. Thus, the emerging alternatives had to be understood and decisions made about which technology and hardware to adopt. Many mundane issues had to be addressed, but it was a huge learning experience. The model of eight organisations cooperating to implement a national project, learning the principles and the evolving technology as they did so, meeting regularly, brainstorming, running conferences and workshops, and training hundreds of young people was quite remarkable. It helped me in my teaching and in selecting research problems, and gave me the opportunity to work with a large number of young people who were flocking to the area of networking in those days. This is a national project model that needs to be learnt from and adopted again and again in other domains.

Photo courtesy: Network Engineering Lab, IISc

The ERNET team at IISc in 1988

When you took over as the Director in 2014, what was your vision for the Institute? What areas did you feel needed attention?

In my 2014 interview for *Connect*, I had mentioned that it would take a few months for me to get a feel for the system and the challenges, and for my vision to develop. And it did.

My vision was that IISc should be among the top 50 institutions for higher education and research in the world. For this, its infrastructure and campus needed to be modern and efficient, and the administration needed to be much more digital. This would help faculty members and students conduct their research without any hindrance.

Administrations today are modernised to a large extent by the amount of technology they adopt, whether it is the way we handle our finance and payments or the way we facilitate the flow of administrative work within the organisation. DIGITS (IISc's Office of Digital Campus and IT Services) was formed around 2015 to essentially drive this digitalisation.

We now use much less paper. All meetings are conducted on WiFi-connected tablets. Practically all interactions with the outside world such as admissions and faculty applications are conducted online. Today, due to the digitalisation, there is substantially more transparency about what is happening in the administration. But we still have a long way to go.

What were the biggest challenges you faced as you went about implementing your vision?

The biggest challenges were the lack of speed in the system, outdated practices, and the lack of a command and control structure that worked day after day, efficiently, and according to a consistent and transparent set of rules.

Are there any initiatives that you had in mind, but could not implement?

Many initiatives have been started under the Institution of Eminence (IoE) programme, and will, hopefully, be completed in the next two to three years.

One of the things that I am unhappy about is the way we construct buildings. We have big plans to expand infrastructure under the IoE grant. But it has taken too much time to sort the processes out, even when funds are available. When I travel to other countries, they talk about building a massive infrastructure project one year, and the next year, the buildings are already up. But we can't do that here, and that bothers me.

How has support for the Institute from the government and other stakeholders changed over the last few years?

The support from the Government of India has been consistent, and growing at a steady pace. The big change has been with respect to support from non-government sources.

The Office of Development and Alumni Affairs (ODAA) was set up in 2015. We had begun to see more non-government organisations and donors who were willing to support us, such as Kris Gopalakrishnan and the Robert Bosch Foundation. That gave us the motivation to look for more funds. We now have a lot more donors, and several Chairs and endowments have been set up.

Photo courtesy: PRO, IISc

PM Narendra Modi unveiling the Foundation Stone of the Centre for Brain Research set up with a Rs 225 crore endowment from Kris and Sudha Gopalakrishnan

We are also putting a lot of emphasis on sponsored research under the Society for Innovation and Development at IISc. Overheads from such sponsored research contribute directly to IISc's internal earnings, which are relatively less controlled by the government. If sponsored research grows, we will get these extra internal funds, and will be able to execute projects that will further strengthen IISc's infrastructure, research output, and visibility.

IISc was declared an IoE in 2018. How will this recognition help the Institute?

The IoE programme has been conceived to support many things: limited and calibrated growth, additional research and innovation, maintaining lab equipment and supplies, increasing international interactions, maintaining the campus better and expanding infrastructure.

The money that we get from the government is spent on salaries, pensions, utilities, maintenance and scholarships. So where do we get money for international activities, or for increasing the number of postdocs? Some departments may also need more money for consumables or for strengthening their research equipment.

I also believe that we should have an excellent campus. A small part of the IoE grant is to make the campus smarter and better-looking. We also need an international house, postdoc housing, and more hostels.

The existing pattern of government funding does not permit substantial growth [in number of faculty members and students]. On the other hand, in the IoE programme, we have projected for calibrated growth over 5 years, 10 years and so on.

IoE money is still government money. Further, as part of the grant conditions, we have to raise funds to match every rupee the Government of India gives.

What would it take to make IISc a truly world-class institution?

IISc needs to have a world-class campus where the best and brightest in the world would like to come to stay, study, and work. Administrative support must be efficient and professional, and the digital infrastructure needs to be on a par with the best.

IISc recruits excellent faculty members, and gets some of the best students in India. There is a lot of good research happening, but it seems that we are missing the peaks, either due to lack of risk-taking in problem selection, or lack of early engagement with the really "hot" problem areas.

Recently, when we analysed IISc's rankings data, we found that we publish a lot and many papers get decent citations. But there are many institutions around the world that publish fewer papers, yet are cited more often. Clearly, they are working on some problems that other researchers really care about. I think we are missing out on areas where we can be leaders, areas that people will say that IISc is the "go-to" place for.

What more can IISc do to attract the best researchers?

Over the past three years, several senior faculty members and I visited top universities around the world to talk to post-doctoral researchers about career opportunities at IISc [called Young Researchers Meetings or YRMs]. The careers of the young people who come to these meetings need to be tracked, in particular women and those from reserved categories, so that they can be encouraged to apply to IISc.

What we are also not doing is tracking the careers of good young researchers in India. For example, if we know that a good PhD student is graduating from one of the IITs and if we don't track them, they just disappear [abroad], because they don't even know that they are wanted back in India. We should have a way to attract them.

What would be your advice for young researchers as they embark on their careers?

My advice would be to not straightjacket oneself into a way of thinking and working only because it is yielding a stream of publications. If things have become routine, the researcher should switch to a new challenge, even if it means a decrease in productivity for some time. It is important to take risks, particularly when one is in a premier institute such as IISc. One should also pursue many modes of working during one's career: follow, collaborate, and find opportunities to lead.

COVID-19 was an unprecedented crisis that struck during the last few months of your tenure. What measures did you and the Institute administration have to take to address this?

The experience with COVID-19 has been remarkable in many ways. The sudden closure of the Institute (almost overnight), the students going away, and the faculty and staff retreating to the safety of their homes left the offices and the labs deserted over several weeks. This was unprecedented, but an experience that was repeated in many campuses and research labs around the world.

We began daily meetings to ensure that the situation was constantly monitored, in light of the many government orders and advisories. Some said that it was a "war-like" situation.

In this challenging period, many faculty members turned their knowhow, their inventive and innovative sides to address many COVID-19 related problems. Whenever we got a request for supporting such activities (in terms of funds or connections), we ensured that the teams got it.

What impact has the crisis had on the Institute's functioning and plans for the future?

The COVID-19 crisis has considerably disrupted the current academic year, and will affect at least one more semester. Most importantly, the crisis has underlined the vulnerability of modern human society, and given some insights into new directions for research that could lead to better preparedness as a nation.

What will you miss most about being the Director of IISc?

IISc needs to constantly drive initiatives so that it can become a world-class institution for higher education and research. The Director is in a unique position to drive these initiatives, and has the opportunity to make a difference.

On a more personal level, I will miss getting to know everybody in the Institute, and being able to go to every corner of the campus and seeing what they are working on.

Photo courtesy: Ashish Verma

Anurag Kumar and S Ramakrishnan (former Deputy Director) inaugurating PEDL, a smart cycle-sharing initiative on campus

What are your plans now? What's next?

I like to be busy; I think the only time I really do nothing is when I go to sleep. For the next five years, I will be back in my academic department, as an Honorary Professor. I also need to focus on managing my health, and spend more time with my family. I will try to find more time to read other than what is required for my academic work; there is so much of such reading piled up. On my 60th birthday, my current and former students gave me the entire collection of Calvin and Hobbes; I look forward to cracking those volumes open! But what I will enjoy most is getting back to my research, teaching, and consultancy, for as long as I can. Our kids are abroad; we will travel more.

Is there any message that you would like to share with the Institute community?

The Indian Institute of Science is a remarkable place for an academic career. It enjoys a high reputation with the government and with national organisations. Its faculty and students are held in high esteem. Faculty members are carefully selected and given tremendous freedom to define their research areas and objectives. They are driven by a quest for deep understanding, an aspect that is also brought to bear on their teaching and research. With this background, I would like to leave two messages:

The Institute needs to be world-class in its academics, its research, its infrastructure, its hospitality, in fact, in every possible way.

The Institute needs to continue to serve the needs of the nation, by contributing the knowhow and expertise of its faculty to the government and the industry.

The Curious Case of the Disappearing Himalayan Snow

- Gouri Patil

With its myriad colours and the imposing mountains in the background, the confluence of two Himalayan rivers in Ladakh, Zanskar and Indus, is a sight to behold. Not surprisingly, the valley where the rivers meet is thronged by tourists. But Rizwan, a local chauffeur, seems less than amused by the sight of the large number of visitors, even though his livelihood depends on them. He hails from a small village in the Leh valley, and like many others in his village with a farm, he has been forced to take up an alternative career because water, he says, is becoming scarce here, particularly in the summer. His complaint is not unfounded – Ladakh has been facing a drought-like situation in recent years. So how did an area nestled among the snow-capped mountains of the Himalaya with its glaciers and a promise of perennial streams get to this point? While unsustainable tourism is of serious concern and has exacerbated Ladakh's dry spell, the real culprit is the changing climate, and its effects on glaciers.

Climate change is wreaking havoc on our glaciers

Photo: Gouri Patil

The Sind river flowing through Sonamarg glacial valley in Kashmir

Our lifeline

The Himalayan mountain range, stretching from Bhutan in the east to Pakistan in the west, is home to 52.7 million people. It also provides indirect sustenance to the nearly 2 billion people who live in South Asia. The Himalaya blocks the cold winds from the north during winter and warms the land to its south, drawing the moisture-laden monsoon winds from the Indian Ocean every summer. It also serves as a barrier to these monsoon winds which empty much of their water in the subcontinent. It has another crucial role: it stores freshwater in the colder months in its glaciers, some of which is released in the summer to all the major river systems in the northern part of the subcontinent. These glaciers contain the largest freshwater reserve in the world outside of the polar regions. The Himalaya are bordered in the north-west by the Hindu Kush mountain ranges of Central Asia, and together they are popularly known as The Third Pole.

A glacier is a perennial body of dense ice which constantly moves under its weight. Mountain glaciers, like the ones in the Himalaya, are different from the continental glaciers in Antarctica or Greenland, which are thin slow-moving ice sheets where the freshwater usually flows into the oceans. In the colder months every year, the nearly 56,000 Himalayan glaciers are replenished by snowfall, and in the summer, the glaciers melt. The water from the melting ice flows down the valleys quickly, feeding some of the great rivers of the world along the way: the Ganga, Yangtze, Indus, Brahmaputra and the Mekong. The glaciers are the primary source of their waters, though, for a few months during the monsoon, the rains also provide them with fresh water. These rivers are vital for irrigating the vast agricultural areas in the northern and northwestern plains of the subcontinent, where many crops, including wheat and rice, the staple food grains of the region, are grown. The water from these rivers is also used to produce a huge amount of hydroelectricity. But despite the importance of these glaciers, they have not been studied as well as their polar counterparts. That, however, is changing.

Studying glaciers

How do scientists study glaciers? Apart from staking out in the glaciers to estimate the volumetric snow loss, they also resort to other modern methods like remote sensing via digital aerial photography and the use of satellite images. These monitoring techniques map the perimeter of snow cover. Satellite images help in recording the snowline at the end of each summer which becomes the equilibrium line. Above this line, snow accumulation is more than the loss, and hence the ice remains all through the year. And below this line, there is more loss than accumulation, and therefore the snow has melted at the end of summer.

Field studies continue to be crucial for scientists investigating glacial dynamics. However, they are not easy to carry out. "Glaciology demands a lot of personal sacrifices as well as personal efforts. It needs perseverance," says Anil Kulkarni, a renowned glaciologist, currently Distinguished Visiting Scientist at the Divecha Centre for Climate Change in IISc.

Kulkarni was one the authors of an influential paper titled "The State and Fate of Himalayan Glaciers", published in *Science* in 2012. In the article, the authors discuss the challenges of working in the Himalayan glaciers. "There are few high-elevation weather stations and no long-term field measurement programs on glaciers, and information about the current ice extent is non-uniform and unsatisfactory in places. This can be attributed to the remote location of glaciers, the rugged terrain, and a complex political situation, all of which make physical access difficult," they write.

Despite these challenges, scientists have been able to collect the data required to study glaciers and how they are changing. Kulkarni recalls that when he started his career back in the 1980s, climate change or snow retreat was not a matter of concern to Indians. He nonetheless continued his quest to study them and even trained in a mountaineering institute. The missions that he has undertaken have presented him with many deadly threats: snowstorms, crevices in the mountains, low oxygen levels and harsh temperatures.

Image courtesy: Anil Kulkarni

Retreat of Samudra Tapu Glacier, a large glacier in the Chandra basin of Himachal Pradesh. The satellite image is marked with receding snowline from 1962 to 2006

Kulkarni's expeditions are usually a result of the combined efforts of researchers, porters, cooks and even mules. These days, he says, access to the Himalaya has improved considerably due to better road connectivity. But some struggles remain the same. "You're sitting at a 5,000 m altitude, and for 100 km around you, there is no habitat. If you face some problem, there is no one to help you, and you're on your own. And you're there for weeks or months," he says. "So, you've to be physically fit, mentally tough and resourceful, and should be able to do whatever you came to do by yourself." It is challenging, but to Kulkarni, to be able to see the beautiful Milky Way in the night sky in the snow-covered mountains seems worth the trouble. "It can be really rewarding," he adds.

Disturbing a delicate balance

Scientists like Kulkarni who study glaciers are interested in a critical concept called the *mass balance* of a glacier. It is the difference between how much ice mass is gained and how much is lost. Glaciers can have a positive or negative mass balance. But typically, in the short term (in geological time scale), glaciers remain in a state of equilibrium, in which the accumulated snow mass is equal to the dissipated snow mass.

But the glaciers in the Himalayan region have shown a negative mass balance since the middle of the 19th century. A study carried out by Kulkarni and his team, using a combination of satellite images and field studies, tracked 1,868 glaciers in the Himalaya between 1962 and 2002. It showed that the total glacial area had reduced by a whopping 16%. The retreat of glaciers has been documented by several other studies as well.

In the past few decades, however, the rate of glacial retreat at the Himalaya has accelerated. In a recent study, researchers from Columbia University, USA, found that the rate of snow loss increased more rapidly between 2000 and 2016 than between 1975 and 2000. Published in 2019 in *Science Advances*, it used data from Cold War-era spy satellite images as well as more recent ones.

A warming planet

The cause of glacial retreat has also been the subject of much scientific investigation. The Earth goes through periods of warming and cooling. This fluctuation between greenhouse and icehouse periods has been occurring for millions of years and has played a crucial role in the evolution and distribution of life on the planet. The former is characterised by more carbon dioxide and other greenhouse gases like methane and water vapour, whereas lesser amounts of greenhouse gases in the atmosphere mark the latter. The colder temperatures of an icehouse period result in the formation of both mountain and continental glaciers. The Earth is currently in the midst of an ice age called Quaternary glaciation.

In spite of going through an ice age, our planet has been experiencing warmer than expected temperatures since the beginning of the 20th century. This warming has coincided with the release of vast amounts of carbon dioxide and other greenhouse gases due to rapid industrialisation. According to the Intergovernmental Panel on Climate Change (IPCC), the global average surface temperature of Earth has increased by 1.1°C from 1880 to 2013. An important consequence of human-induced warming is the rapid melting of glaciers, including in the Himalaya. Even more worryingly, the surface air temperature in the Himalaya has increased by 0.65°C during the 1991–2015 period, more than the mean global temperature rise of 0.47°C seen during the same period.

Photo: Gouri Patil

A glacial lake in Sikkim

Impact

Discussing the more immediate impact of the melting glaciers, Kulkarni explains, "As the glaciers retreat, they erode the space and depression is created and eventually lakes are formed. The glacial flow carries rocks and debris and keeps dumping them here." He says that if there is an avalanche, a landslide or earthquakes, these lakes burst resulting in flash floods. Kulkarni and his colleagues at the Divecha Centre have modelled glacial retreats in an attempt to predict lake bursts and the consequences of these floods to the local communities.

What is counterintuitive, however, is that glacial retreat is also leading to droughts in some parts of the Himalaya. Due to the decrease in snow cover, the summer melt-off is no longer an adequate source of water. In places like Ladakh, even the summer showers are not helping as the rocky region is unable to soak up the water. Instead, it is leading to both droughts and floods. The erratic weather has made the traditional farming practices obsolete, and farmers like Rizwan are being forced to either abandon the farms or try to grow different crops. Agriculture which used to be the main livelihood of people in the hill communities, is no longer a viable option for many.

> ***The rate of snow loss increased more rapidly between 2000 and 2016 than between 1975 and 2000***

In the not-too-distant future, the plains of North India are also likely to suffer due to glacial melting. “These [glacial] changes vary across the Indus, Ganges, and Brahmaputra river basins: in the Indus, the marked effect is on meltwater; for the Ganges, the effect is on runoff that is expected to increase; and for the Brahmaputra, climate change may result in enhanced flood risk,” says a report by the think tank Observer Research Foundation. It further states, “.... there would be a decrease in snow and a rise in glacier melt by the middle of the century. Initially, there will be an increased amount of meltwater available, but this quantity will decline abruptly as the glacier storage is reduced.”

Not all the short-term impacts of melting ice in the Himalaya are detrimental to the region. Kulkarni describes an ongoing project between the Divecha Centre and government agencies in the Manali basin to understand the impact of retreating glaciers on the generation of hydroelectricity. They predict that by the end of the century, small glaciers at lower altitudes are going to be significantly affected, and the snow will start melting early. This will lead to a change in seasonality in water availability. The water now available during summers will be accessible during winters, resulting in an increase in power generation in the colder months. Interestingly, due to monsoon rains in the summers, the power generation will not be affected in the warmer months. Climate change, in this instance, can become our ally in increasing power generation. But this is merely a silver lining. The dark clouds have to be dealt with.

The Future

In order to mitigate global climate change, countries around the world will have to cut greenhouse gas emissions and live up to the promises that they have made as part of the Paris Accord on Climate Change, which they signed in 2015. But even if that does happen, many parts of the world are already facing the consequences of a warming planet, and will continue to do so for many decades. Ironically, the communities nestled in the remotest places of the Himalaya, which have almost zero carbon footprint, are paying a hefty price. So is there anything that can be done at the local level to reduce the impact of climate change?

Ladakh may show us the way forward. Already, several projects which seek to address problems arising from the retreating glaciers are being initiated here. For instance, Chewang Norphel, an engineer, is building glaciers. He uses a network of pipes to divert meltwater on the shaded side of the mountain and slow its flow by constructing barriers. This water would freeze at night, creating glaciers that grow each day as new water flows into the basin. So far, he has made 12 such glaciers. These glaciers are helping at least a thousand people living in the lower altitudes. Similarly, Sonam Wangchuk, who inspired Aamir Khan’s character in the movie *3 Idiots*, has built “ice-stupas”, artificial glaciers in the shape of a stupa. During summers, these release water steadily, about 5,000 litres each day. The conical shape maximises the amount of ice it can hold while decreasing the area exposed to the sunlight.

In spite of these measures, glaciers will continue to recede if climate change goes unchecked. The good news for them, however, is that they will be restored to their original glory at some point in the distant future, possibly in a few thousand years. But on a time scale that is more meaningful for us, the melting glaciers pose an existential threat to the current and future generations. As Sir David Attenborough reminds us, "However grave our mistakes, nature will ultimately overcome them. The living world will endure; we humans cannot presume the same."

Gouri Patil, a science writing intern in the Office of Communications (OoC) at IISc, is an Integrated PhD student in the Department of Physics

‘The fact that my patients needed me kept me motivated’

- Connect Staff

Healthcare professionals across the world have been working relentlessly during the pandemic. With dozens of cases reported from IISc.* CONNECT *spoke to doctors at the Institute’s Health Centre about their experiences during these challenging times.

Photo: KG Haridasan

The outdoor Out-Patient Department at the Health Centre

What changes did the Health Centre have to make, in order to deal with the pandemic?

Dr R Nirmala: Several changes have been made at the Health Centre during the ongoing pandemic. We set up our own COVID-19 sample collection and Rapid Antigen Test (RAT) centre, and had to hire extra personnel such as a swab technician, to handle the increasing workload. These personnel were also involved in the follow-ups on all COVID positive patients on campus. We now have 63 staff members.

Shanmukha Innovations set up a sample collection kiosk, and provided an ambulance that has been specifically assigned to transport COVID-19 patients. Suspected COVID-19 patients were examined at a separate flu corner. The current flu corner has two isolation beds to manage patients till the point that they are shifted to a hospital.

We also invited specialists to talk about COVID-19, and conducted Q&A sessions for the students and campus community.

The Health Centre issues regular advisories for the campus community about quarantine and testing norms, and also conducts COVID-19 screening tests for hostel dwellers.

Dr Apoorva Nagarajan: We started seeing patients outside the Health Centre, near the entrance, to reduce patient crowding and interactions inside. We also use protective gear like respirators, Personal Protective Equipment (PPE) kits, gloves, N95 masks and face shields.

We established our own sample collection centre for prompt diagnosis and treatment of patients, and created an isolation centre for mildly symptomatic students who were kept under observation.

Photo: KG Haridasan

Swab sample being collected for COVID-19 testing at one of the kiosks at the Health Centre

What brought about the setting up of a COVID-19 sample collection and testing centre at the Health Centre?

Dr R Nirmala: At the start of the pandemic, when we slowly started getting more symptomatic cases, we found that getting a COVID-19 test took considerable effort. Most tests then were done only in government hospitals, and patients were hesitant to go and get themselves tested there. The few private institutions that were doing the tests were very expensive, and retired employees could not afford them. Hence, we felt that we needed to start our own testing facility. It would give us the necessary freedom to test and isolate COVID positive persons, and at the same time would be easy to access, economically feasible and reliable. The testing centre was set up in collaboration with the Bruhat Bengaluru Mahanagara Palike (BBMP) and the Centre for Infectious Diseases Research (CIDR) at IISc. Since the setting up of the sample collection centre on 5 September 2020, we have collected around 500 samples. These samples are processed at CIDR. Needless to say, this has helped us to keep the COVID-19 infections under control in the hostels, and on campus.

Photo: KG Haridasan

The COVID-19 ambulance, with the driver in personal protective equipment

How has the Health Centre been managing regular appointments/non-COVID-19 emergencies or cases?

Dr R Nirmala: The Health Centre was fully functional during the days of lockdown. Patients were seen as usual for non-COVID-19 infections and emergencies. The Out-Patient Department (OPD) functioned as usual. The only difference was that the waiting area for patients was moved to the open area outside of the main building, to reduce the chances of cross-infection. All patients and patient attenders were thermally scanned before being allowed inside for examination.

Dr Apoorva Nagarajan: Non-COVID-19 cases are seen in the OPD and on an emergency basis on holidays. We evaluate them outside the Health Centre and issue medicines. Telephone and video consultations are also encouraged.

How does the Health Centre liaise with doctors and hospitals outside campus to find hospital beds for IISc's COVID-19 patients? What is this process like? Has there been any situation in which the Health Centre struggled to place a patient?

Dr R Nirmala: It has been a challenge to find beds for patients, especially during the initial days of the pandemic when BBMP was not well prepared. We have encountered many situations where we found it difficult to find beds for patients. As time passed, we were able to identify and liaise with doctors and management personnel at different hospitals in the city. On several occasions, we have made personal calls to hospitals and explained the case summary of the patient, and requested them to arrange for a bed. Meanwhile, BBMP also came up with the centralised bed allotment facility which has now eased the burden to a great extent. IISc has also entered into an MoU [Memorandum of Understanding] with MS Ramaiah Hospital for COVID beds, which has helped us a lot.

Photo: KG Haridasan

A patient being evaluated at the outdoor OPD

Does the Health Centre have a system to monitor the health of patients on campus?

Dr R Nirmala: All COVID-19 positive patients on campus are contacted by the Health Centre two times a day, to check on them till they clear their quarantine period. A WhatsApp group which includes all doctors and all students in isolation has been set up as a channel for communication. Regular phone and video consultations are also permitted on a needs basis.

Dr Apoorva Nagarajan: Yes, each doctor calls and checks on their patients regularly. We support them not just by issuing medicines, but try to help them recover in every way possible by providing emotional and moral support also.

The Health Centre had to be shut down for disinfection in July, after a staff member tested positive. What was it like to come back to work after that?

Dr R Nirmala: When we had to shut down due to a staff member testing positive, my morale was down. The general feeling was, "Who will be next?" Returning to work was scary, especially with an elderly parent at home. As I started seeing more COVID positive patients, I used to wait restlessly to see if I would start showing symptoms too, but over time, I realised that following ground rules, using appropriate PPE and maintaining hand hygiene (health care workers cannot maintain social distance with a patient) go a long way in keeping a healthcare worker safe.

Dr Anusha Narayanan: The unfortunate incident of our staff testing positive showed that the infection had, indeed, come closer to us. The possibility of the Health Centre being a point of contact for others to acquire the infection mandated the decision to alter our functioning, while making sure that regular services were not hindered. The protective gear provided to us has also helped a great deal!

Dr Aditya Malladi: It was quite a challenge to come back. We took all the necessary precautions. The fact that my patients needed me kept me motivated.

What is it like to work as a healthcare provider during a pandemic, and to interact with people who may be infected?

Dr R Nirmala: Initially, when I had to go to the Centenary Visitors Housing (CVH) to see and refer a couple of COVID positive patients to a hospital (it was the first case on campus), I was frightened to even go near them, because I was not sure whether the PPE I was using would protect me. I maintained distance and was not happy about it because as a doctor we need to see patients up close. After some research, all doctors were given a 3M respirator, and now I go near COVID positive patients with confidence. Also, as the number of cases increased, I could see that even basic PPE like surgical masks and hand gloves keep healthcare professionals safe. Earlier on during the pandemic, I was experiencing constant internal turmoil – on one side with my duty as a doctor, and on the other side with the fear of carrying the infection home. This turmoil has now eased a little with the knowledge that has been gained after seeing several COVID positive patients. The pandemic has shown me how valuable life is, and now I find myself very happy doing small things such as completing kitchen chores, cooking something good for the family, spending time with my son and sometimes just sitting idle!

Dr Anusha Narayanan: The very first lesson we were given in medical school was to never fear a disease. Fear clouds the mind and interferes with our thinking. That being said, the risk of acquiring the infection from the workplace for a healthcare provider is very real. Most of us have had to make a lot of changes in our working routines as well as our lifestyles to protect our patients and families from the virus. For example, I have an 'unclean corner' at home where I leave my work-related things. I am very careful when I meet friends or family, knowing that I could always be potentially infected, and do not want to pass it on to others. At work, just to drink water takes a whole lot of effort and time, in taking off PPE the correct way, washing up and making sure there is no one else in the room while my mask or respirator is off.

Photo: KG Haridasan

The Health Centre staff

Dr Apoorva Nagarajan: It is intimidating, but the satisfaction when someone gets cured and thanks you and blesses you is truly gratifying.

Dr Aditya Malladi: Even if I'm aware that a patient is infected, I perform all that is necessary. To relieve the pain and anxiety of a patient gives a lot of satisfaction. A lot of precautions are needed to withstand an unknown and invisible enemy. It is even more frightening when I think that I might carry the virus to my home.

Do you have any personal anecdotes from these trying times that you would like to share?

Dr R Nirmala: The most challenging event was when I could not find a hospital bed for a sick student. This happened during the start of the caseload spike when the testing facility was not yet established. The student presented to the flu corner with a mild cold and loss of taste and was isolated and tested in a private lab. The test results came on the fourth day, by which time she had a severe dry cough and was very sick. A private hospital promised a bed for her over the phone, but when she went there in the ambulance they refused. This sick student was out in the ambulance without help. I desperately started calling all the hospitals but there were no beds available. This was a time when nobody knew how to get beds in hospitals for COVID-19 patients. The student was getting sicker by the minute in the ambulance, to the point where I was worried that she would collapse. Finally, Dr Sridhar from St Theresa's Hospital understood my dilemma and offered a bed, but wanted someone to come and sign forms on her behalf. I had to convince a friend to go to the hospital and sign the forms, and the student was finally admitted. Dr Sridhar still answers my phone promptly, and has helped me many times over the past months when I had difficulty finding beds. Though I never knew him before the pandemic, he helped me that day. I think that I have been able to manage so far with the help of so many helpful people: Dr Satyavathi from BBMP, Sriramapuram who helped us screen all the Health Centre staff when we were closed due to a positive case as well as in the screening of 129 students from the New Girls Hostel, and also helped IISc to establish a COVID-19 testing facility; Dr Sridhar from St Theresa's; Mr Arun, Ms Vidya and Mr Naveen from BBMP; Mr Praveen from Sparsh Hospital; Mr Shanmugam from Vikram Hospital and Mr Pranam from Columbia Asia Hospital.

Dr Anusha Narayanan: It is definitely not easy being a doctor during a pandemic! We need to make sure that patients who do acquire the infection get treated while others do not get infected. At the same time, we cannot afford to miss diagnosing or treating other diseases, especially during health emergencies. I have seen a few patients succumb to the virus. Seeing a patient die is more painful to a doctor than anyone can possibly understand. There also have been instances where patients have miraculously survived the infection, even after having moderate to severe illnesses. These heartening moments reinforce the commitment we made to our community as medical professionals.

Dr Aditya Malladi: A funny thing happened initially – people were unable to recognise me in my full PPE kit. I still have to keep introducing myself.

Dr Apoorva Nagarajan: I would like to say that it is definitely a difficult task to interact with suspected COVID-19 patients on a daily basis, and then go back home and hope not to infect your family members. But of course, the pandemic has taught us so much about handling tough situations with a clear head, and to trust our decision making above all.

It was extremely hurtful when it was brought to our notice that there were some hate messages circulating on WhatsApp and social media, about the doctors and the Health Centre. We reported this to our superiors, who informed the Director, and an inquiry is currently underway.

We are only trying to help the IISc community fight this virus as strongly as possible. We want to be a community of self-sufficient, smart individuals who adhere to norms and contain this infection as soon as possible.

Bridging the technology gap

- Mahatabb Nundy

Technology plays a key role in healthcare – in diagnostics, therapeutics, as well as in rehabilitation. Though technology has progressed considerably in the last few decades, innovations in healthcare, compared to other fields, have been limited. The lacunae exist partly due to a paucity of a meaningful dialogue between clinicians and scientists. And when technology is available, it comes at a crippling cost. This calls for a proactive, concerted effort from both the medical establishment and the scientific community to ensure a fruitful exchange of ideas and multidisciplinary collaborations, especially in a country like India which lacks quality medical infrastructure that is affordable and sustainable.

One way to take research from the bench to the bedside is to involve physicians in research, in both the sciences and engineering, a need that was recognised over half a century ago in the United States. In 1964, the National Institute of General Medical Sciences (NIGMS), a branch of the National Institutes of Health (NIH), established the Medical Scientist Training Program (MSTP), an MD-PhD training programme that involves several universities. Its goal, according to the mission statement of Yale University, is to "cultivate the characteristics of curiosity, creativity, compassion and service." But despite the success of the programme, it is less widespread than one would expect.

India too did not have such an initiative until 2019, when the Centre for BioSystems Science and Engineering (BSSE) at IISc and CMC came together to start an MD-PhD programme. The brainchild of Sandhya S Visweswariah (Co-Chair, BSSE) and GK Ananthasuresh (Chair, Mechanical Engineering and former Co-Chair, BSSE), its genesis was closely related to the idea of BSSE itself, which was established in 2015. "Prof GK Ananthasuresh and I were very clear that what would distinguish BSSE from other departments is fostering a very close interaction with clinicians," points out Visweswariah. "This interaction should not just be in terms of clinicians being sample providers," she explains, "but actually engaging [them] in formulating the research question." The programme

Photo courtesy: Lubap/Wikimedia Commons

Christian Medical College, Vellore

The MD-PhD programme is a unique collaboration between IISc and Christian Medical College (CMC) at Vellore to improve healthcare in India

was supported by Visweswariah's Margadarshi fellowship, funded by the DBT/Wellcome Trust India Alliance. When she defended her proposal, there were concerns that the physical distance between the two institutions could hinder interactions. "I allayed their fears by explaining that it is the distance between minds that is more of an issue. If people are on the same page, physical distance does not mean much in this age of technology," she says.

When the initiative was being conceived, both Visweswariah and Ananthasuresh felt that if IISc was to have a successful biomedical research programme, it would have to collaborate with an acclaimed medical college hospital which is serious about research. Ananthasuresh also believed that the programme would work only if doctors stayed on the campus of IISc as full-time researchers.

It was during this time that Visweswariah met Gagandeep Kang, the well-known clinician-scientist and a professor of Gastrointestinal Sciences at CMC, at a DBT Wellcome Trust meeting. Kang suggested that they approach Nihal Thomas, Associate Director and former Vice-Principal for Research of CMC. Visweswariah adds, "Prof Nihal Thomas then visited IISc and spent a day here. That convinced us that we should try to foster interactions with CMC Vellore." So Visweswariah and Ananthasuresh too went to Vellore and were impressed with what they saw. Students at CMC, a premier medical institute, were trained not only in medicine but also in clinical research. "In CMC, the atmosphere is very research-oriented … and we thought that it is the right place to start the MD-PhD programme," Ananthasuresh recalls.

Once the proposal from IISc for the programme was made, it was welcomed by Anna B Pulimood, Professor (Clinical Pathology) and Principal of CMC. Soon after, Visweswariah, Pulimood, and Sathya Subramani, (Professor and former Head, Physiology, CMC) worked towards getting the programme up and running. "It took a group of committed women, who were keen to get this off the ground, both in CMC Vellore as well as in IISc, which took almost two years of leg work," says Visweswariah, who is the chief coordinator of the programme along with Subramani.

> ***"This interaction should not just be in terms of clinicians being sample providers," she explains, "but actually engaging [them] in formulating the research question"***

"There are physician-scientist programmes in other countries also, and they form a very good interface between medicine and science. They have the right questions towards healthcare and know the right tools as well," says Subramani, elaborating on the rationale behind the programme.

Pulimood is excited about the collaboration because she believes that both the partner institutions share similar attributes and a common vision: to improve healthcare. "IISc is looking to promote excellence in training and research, they give importance to innovation and technology, they give importance to social welfare as well. At CMC, we also aim for excellence in healthcare, education, and research." She adds that the collaboration is in line with CMC's commitment to the use of appropriate cost-effective technology to help marginalized and disadvantaged people.

The first student to enrol in this programme was Farhan Adam Mukadam, who has an MD in Physiology from CMC. He is supervised by KVS Hari (Professor, Electrical Communication Engineering, IISc) and K Subramani (Professor and Head, Division of Critical Care, CMC). Mukadam's research seeks to foster a culture of data-driven critical care and to design the next generation of intensive care units (ICU). His dream is to eventually build an intelligent system, like a medical JARVIS – the fictional AI from the Marvel Universe – capable of near real-time patient monitoring and care.

The relationship between IISc and CMC goes beyond just the MD-PhD programme. Several faculty members at IISc have collaborations with their counterparts at CMC: Ananthasuresh works with the Department of Hepatology at CMC; Visweswariah collaborates with the Department of Gastroenterology at CMC on pancreatitis; Bhushan Toley (Assistant Professor, Chemical Engineering, IISc) and Joy Michael (Professor and Head, Microbiology, CMC) have devised a paper-based technique for point of care diagnostics of tuberculosis. A symposium is conducted every year in IISc, where doctors and scientists from both institutions exchange ideas with each other. Burning issues in healthcare are discussed and research questions are formulated in these brainstorming sessions. Furthermore, about 12 medical undergraduates from CMC attend a three-week summer internship programme in IISc called the BEST+ programme, where they are exposed to the research ecosystem.

Besides engaging doctors in biomedical research, IISc has developed an ambitious digital healthcare initiative that is being coordinated by Ananthasuresh. The blueprint for the plan includes digital hospitals networked by 5G, a centralised health data centre, and a greater emphasis on research in bioengineering interventions in medicine. He also envisages an MD programme in digital health and even an MBBS programme with a specialisation in technology.

Mahatabb Nundy, an MD in Physiology from CMC, joined the MD-PhD programme at IISc earlier this year

Behind the Scenes of Behavioural Experiments

- Rohini Murugan

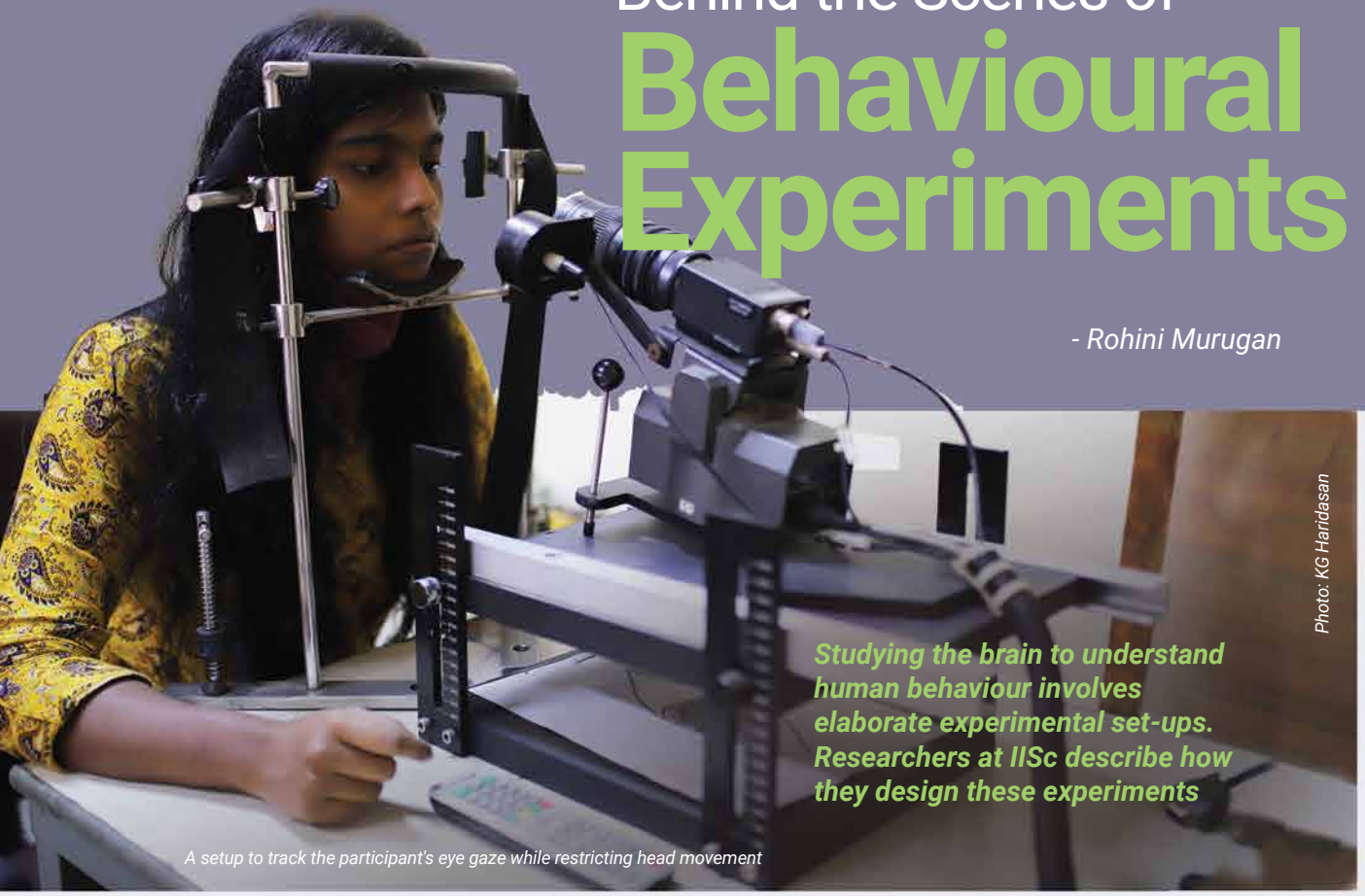


Photo: KG Haridasan

Studying the brain to understand human behaviour involves elaborate experimental set-ups. Researchers at IISc describe how they design these experiments

A setup to track the participant's eye gaze while restricting head movement

Ever walked into a room and forgot why you went in there? Or struggled to keep your New Year's resolutions? We have all shown such behaviours at some point or the other. The field of psychology tries to understand this: why we behave the way we do.

While psychology deals with the mind and behaviour, the study of the underlying biological components and processes comes under the realm of neuroscience. Though it borrows some experimental techniques from psychology, neuroscience investigates the activity of brain cells (called neurons) when we display certain behaviours.

Scientists have known for decades that neurons are specialised for transferring information to other neurons, as well as to other cells of the body. One might think that, if we know what a cell does, how hard would it be to figure out the function of an organ that is made up of those cells? When it comes to the brain, it is especially hard. And it gets harder when you move from the level of neurons to behaviour, which arises from a complex interplay of different neuronal networks in the brain. However, scientists have found a way around this problem: through behavioural experiments, which form the basis for much of neuroscience research.

What is a behavioural experiment?

A behavioural experiment is one of the tools that both neuroscientists and psychologists use to study behaviour. "There is a task that you tell or train the participant to do. Typically, you show them a stimulus and you get a response," explains SP Arun, an Associate Professor at IISc's Centre for Neuroscience (CNS).

In fact, behavioural experiments are not very different from what most of us do in our daily lives. For example, if you have ever tried to guess your dad's mood from the pitch of his voice – especially when you need him to sign your report card – by asking him a trivial question like how his day was, then you have successfully conducted a behavioural experiment.

Neuroscientists, however, study much more than someone's mood. They also study how the brain perceives the five senses (sight, sound, taste, touch and smell), higher level cognitive processes like attention and emotion, and motor control, or the ability of the brain to control our voluntary movements.

But how do they study these behaviours? What goes into designing a successful behavioural experiment?

Chalk out a plan

Just like an architect begins with a basic blueprint before building a house, a behavioural scientist starts by designing an experiment. A lot of thought goes into this part.

Let us say we want to study how long it takes for people to see the colour difference between two objects. How would one go about designing an experiment to study this? We could show people images of apples and oranges and ask if the two images are the same or different. By analysing their response time, we could get a fair estimate of how long people take to perceive colour difference.

But there is a major flaw in this theory.

When a person sees apples and oranges, how do we know that they are seeing the difference only based on colour? It could be based on size difference. Or, on the categorical difference - that they are two different fruits. Thus, if we want this experiment of ours to truly test for colour perception, we should show two identical circles, similar in every possible way other than their colour.

"Usually you're trying to make sure that the participant is using the clues or the criteria that you want them to use. Just because you ask them to use a strategy, it doesn't guarantee that they are going to use it. So, to really make sure that your participant is solving the task in the way that you intended, you should have a lot of controls," explains Arun.

The controls that Arun talks about are the variables that might differ, like the size and category of the images in our experiment. These major variables are checked off during trial runs or 'piloting', when the experiment is done with a small set of people. Other trivial variables like the brightness of the screen or in the room are accounted for, and maintained constant across trials. The experiment is perfected through careful repeated trials to ensure that all possible gaps are accounted for.

Recruit participants

Once a perfect behavioural experiment is designed, the next step is to seek out participants. Posters and emails are circulated, mostly within the university, calling for willing participants, who are usually paid a fee for their participation.

Sometimes, behavioural experiments are complemented by modern techniques like functional Magnetic Resonance Imaging (fMRI), Electroencephalography (EEG), Magnetoencephalography (MEG) or Transcranial Magnetic Stimulation (TMS). These additional methods help researchers observe and record the activity of the brain while a person is doing the experiment. This allows the researcher to determine which part(s) of the brain is responsible for a particular behaviour.

Photo courtesy: CNS, IISc

The JN Tata MRI facility established at IISc with support from the Tata Trusts

It is not always easy to recruit participants. For instance, fMRI experiments need people who do not have any kind of metal implants and are not claustrophobic. Some behavioural experiments recruit people who are not under any kind of medications, to eliminate the effects of drug interference. Other times, the experiment requires participants with specific neurological disorders in order to study how their behaviour differs from those without the disorder. This helps researchers come up with effective diagnostic tools for that disorder.

In a university, participants are mostly recruited from among the students. In a 2010 study, scientists criticised this practice by arguing how most research revolves around WEIRD – Westernised, Educated, Industrialised, Rich and Democratic – people. The study cautions against making sweeping claims based on a small and specific sample of participants.

But there is a way to reduce this bias. "One good thing is that we go outside the Institute and recruit people who are not just students, and are naive to the research," explains Lakshman Chakrav, a Research Assistant in the Emotion and Cognition Lab at CNS. "This is to have generalisability to the research that we do. We can do a study [with a limited number of participants] and publish it, but two years from now, if no one can reproduce it, there's no point in wasting public money."

Once the participants are recruited, they are asked to fully understand the study before giving their written consent. A core tenet of human ethics policies is that participants' refusal should not have any adverse consequences for them – this can be important in hospital settings where they receive care, or in university settings where they might receive grades.

Experiment begins

Different neuroscience questions call for different kinds of experiments. A lab that studies how our vision works, for example, would do something similar to the colour perception experiment. Whereas a lab that studies how our brain controls our muscles and joints for movement would require its participants to move their eyes, hands or head during the experiment.

Various metrics are used to measure the outcome of the experiment. For example, in the colour experiment, the

time taken for the participant to respond would be a good metric that would answer our question on colour perception. Similarly, a lab that studies eye movement would use eye trackers to see how fast our eyes move or which way they move. Software tools enable these metrics to be recorded by computers for further analysis.

Experience of an experimenter

From a participant's point of view, an experiment may just be a fun way to spend time, or perhaps an exciting game that also helps them earn money. But for the experimenter, it may lead to some nail-biting moments, as they can see how each participant's response becomes a data point in support of, or against, their hypothesis.

These trials can also test the experimenter's patience. Surprisingly, the most common problem they face during an experiment is that participants sometimes doze off!

"I can usually see that after the first 100 trials, people get tired and their eyes begin to droop. Many people end up sleeping with their head at the chin rest," says Kavya Rajendran, a PhD student at the Cognition Lab in CNS. Jana, too, recalls a particular participant who came in for the task and went on to sleep for two uninterrupted hours. fMRI experiments have it worse, as many people find the dull monotonous sound of the magnet soporific, and end up falling asleep comfortably inside the MRI chamber, rendering the data that was collected until then completely useless. Who knew that the fringe benefits of research life would include acquiring such essential life skills as patience and fortitude?

A behavioural experiment, apart from its academic significance, also helps make new acquaintances. Experimenters often meet interesting people, and these acquaintances lead to stimulating and interesting discussions.

"You get to meet so many people. It's nice to get to know a little about the story behind a person. I learn about people's families, why they came into this field, their pets and the books they read. I sometimes get good recommendations too. The interaction also helps people [participants] to become more engaged and motivated," Priyanka Gupta, another PhD student at the Cognition Lab, says excitedly.

Photo: Atul Gopal

An EEG experiment underway in Supratim Ray's lab at CNS, IISc

Experiments in the time of COVID-19

While behavioural experiments may lead to invigorating conversations and connections – and hopefully important scientific insights – they also involve close human contact. But that isn't possible during the current pandemic. Many labs, including at IISc, were either designing experiments, recruiting participants or in the middle of conducting experiments when the pandemic hit, forcing them to shut down their research.

The experiments conducted at the Cognition Lab, for example, focus specifically on attention, and were significantly impacted by the pandemic-related lockdown. Priyanka says, "It was all of a sudden, and our contingency plan was to work with the data we had already collected till then. We closed in March and I haven't run a single human experiment since then."

However, as the world is waiting to recover from this viral onslaught, cognitive research too is slowly waking up from its pandemic-induced slumber. With labs slowly re-opening, work is resuming steadily. New rules are in place, ensuring reduced risk of infection while conducting behavioural experiments. These include using ultraviolet lamps that kill viruses and disinfection sprays, ventilating rooms before and after each participant does an experiment, and wearing masks and gloves.

Learn, adapt and overcome

Some of Priyanka's colleagues have also turned to other possible ways to plough through during the pandemic. As classrooms go live and virtual meetings replace physical conferences, unsurprisingly, even behavioural experiments are going online. Though sophisticated tasks using techniques like fMRI cannot be done online, researchers are adapting to the new normal by designing simple experiments that can be done from the comfort of the participant's home.

But there is a catch to this as well. Arun explains, "It is a much more controlled setup because the same set of participants use the same computers. But now with experiments going online, there is this extra variability – whether they are using a big or a small laptop; sitting in a bright or a dark room." It's not all bad, he adds. "We have run some experiments online and are happy to find that the results are very similar to what we get in a lab-based set-up." Another limitation is that only a small percentage of those that can afford to access the Internet can participate.

When asked if he thinks online experiments would be prevalent post the pandemic, Arun says yes. "There is certainly a range of experiments one can do online. Doing it online means you can send it to 100 people and they would do it from the safety of their homes. There is potential to collect data really, really quickly. In [the] online mode, one can also reach out to a more diverse set of people. I think it certainly allows us to do more interesting things."

Rohini Murugan, a science writing intern in the Office of Communications (OoC) at IISc, is an Integrated PhD student in the Centre for Neuroscience

‘I no longer call IISc Tata Institute, but Thaatha mane’

- Kavitha Harish

When AV Leelavathi joined IISc in 1964, her entry to the Institute was quite unplanned.

While studying at a friend’s house one day, the friend received a visit from someone who had gone to IISc to pick up an application form for the post of Stenographer for his sister. He had been given three forms, and so passed two of them on to Leelavathi and her friend. She filled out the form, and eventually she got a letter asking her to appear for a written test and was selected after an interview. Her father insisted that she join – and that was how her career at the Institute began.

Starting in administrative work, she says, was a challenge because it was “a male world” in which she was the only woman. Over the next 38 years, she worked in the Central Office (Student Section), the Department of Applied Mathematics, the Centre for Theoretical Studies, the Microbiology and Cell Biology Laboratory, and the Department of Electrical Communication Engineering before retiring in 2002. Here is an edited excerpt from an interview with her, in which she talks about attending a party at Nalini Dhawan’s house, lunchtime adventures on IISc’s campus, and more.

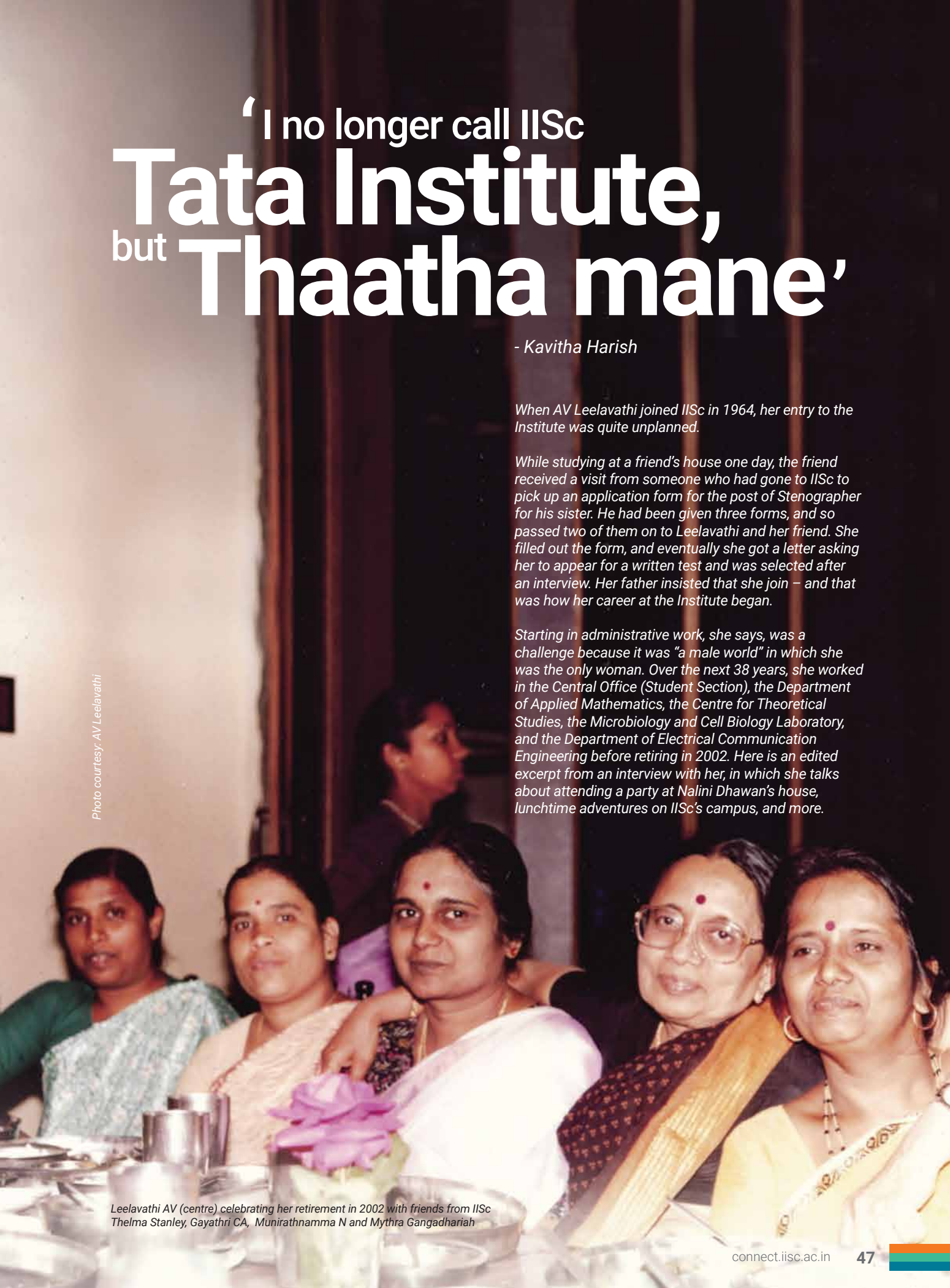


Photo courtesy: AV Leelavathi

Leelavathi AV (centre) celebrating her retirement in 2002 with friends from IISc Thelma Stanley, Gayathri CA, Munirathnamma N and Mythra Gangadhariah

What was your role at the Institute?

I started my career as a Stenographer. To start with, I was in the Student Section, and my work was related to thesis submission by students for MSc and PhD degrees. I had to co-ordinate with students, faculty, examiners, and IISc's Senate and Council. This meant direct contact with the Assistant Registrar, the Registrar, the Director's Office, and the Finance Officer.

After that, I was transferred to the Department of Applied Mathematics.

What was the Department of Applied Mathematics like at the time?

When I was first transferred, the Registrar called and said, I am sending you there as my representative to look after the office work, don't take sides. I did not know why he was telling me this. But as I entered the department building, a senior faculty member said, "What can we do with a lady here?" Then one more faculty member advised me to go back, because I would not survive here. I learned that things had gone wrong in the department and the Director at the time, Prof Dhawan, had taken over. I found the office empty, because they had transferred out all three people who had been there, and I was posted in their place.

I started from scratch and built up the office. Proof of this is that Prof Dhawan recommended me for – and got me – an advance increment, which was unheard of in those days. In the end when I was transferred, the whole department was against my transfer. I was given a very warm and grand party with a gift. The chairman said, "We are waiting to give you a welcome [back] party."

Where were you transferred to?

I was transferred to the Centre for Theoretical Studies (CTS). This department was mainly involved with visitors programmes. Prof ECG Sudarshan had come as a visiting professor. There were other visiting faculty such as Dr AM Verma, who was in NIMHANS, and other eminent scientists from abroad.

Then I was transferred to the Department of Microbiology.

My time in Microbiology was the peak of my service at the Institute. I helped organise a number of international seminars and conferences. When Prince Charles visited the department, I had an important role in organising it. After visiting the silkworm lab, he wanted some sarees which he took with him.

Faculty, students, workshop staff, laboratory staff and office staff were like a joint family. We used to arrange two picnics a year – one included our actual family members, and we would prepare our own food.

Then I moved to the Department of Electrical Communication Engineering (ECE), one of the biggest departments. It was here that I was introduced to the world of computers. I learned the basics from students, and account-keeping from one of the faculty members. Though I started my career with manual typewriters, I went on to electronic typewriters and ended with electronic mail and a fully computerised office (Professor Anurag Kumar ran the ERNET project, through which computers and email were introduced). Actually the Chairman at the time had doubts about whether I would learn how to use a computer, but I did it!

Photo courtesy: AV Leelavathi

AV Leelavathi with Anurag Kumar at her retirement send-off hosted by the Department of Electrical Communication Engineering

You were also involved in several activities that helped people at IISc in many ways. Could you say more about them?

While in Applied Mathematics, some faculty member had once worked out a big mathematical calculation on the blackboard. In one corner they had written, "Please do not erase". But the office had instructed the attender, who was illiterate, to clean all the blackboards while cleaning the rooms and lecture halls, and he cleaned this one too. The next day the faculty members were naturally furious. So I told all faculty members to use coloured chalk to write "Please do not erase", and instructed the attender not to clean the black board when it had coloured writing.

But I realised this was not the solution. I asked the attender whether he would like to learn English. He said "yes". So with waste paper and gifted pens, I started teaching him the alphabet and he learned how to write and read. I am happy to report that he became very thorough and used to help his colleagues write applications and so on, and even learned Hindi from my colleague. Each one teach one. Even now the Institute can do this by introducing an adult education programme to make 100 percent of people on this campus literate. I am sure we retired people will volunteer to help.

When I was in the Department of Microbiology, I helped start a fund for lab helpers and attenders, and took responsibility for collecting contributions for the families of supporting staff when they died. I also joined others in petitioning for a creche at IISc as I found it difficult to look after my young son and I am happy to see that there is now more than one.

Can you tell us about your adventures exploring IISc's campus?

Here is my experience of the height, width and depth of the Main Building. After I had been at IISc for some time, one day I noticed how high the tower of the Main Building was, and I wanted to explore it. During my lunch hour, I went with a few of my colleagues, took the key from the person in charge, opened the door leading to the tower and climbed up. I saw not only steps but ladders – shaky ones – that we needed to climb. After reaching almost to the top, there was a water tank and a very shaky ladder at the side of it, and as we climbed up, the pigeons who had made nests there started flying away. Imagine our plight on a shaky ladder, trembling – somehow we got up, opened the door and came out onto the balcony. We felt the whole tower was shaking and floating, and holding the railing with all our might, we looked out at the landscape of the city from that height. As the pigeons started flying away in large numbers, the people who were on the ground started looking up and saw us. Among them was the Registrar, who was returning after the lunch hour. We waved at him and he reciprocated. And we came down, exhausted but with the full satisfaction of achieving something huge, as if we had climbed Mount Everest. I received a message asking me to meet the Registrar, and when I went he asked how it was (of course I explained with full enthusiasm exactly how it was). Cool and calm, he said, "Don't ever repeat this adventure." Needless to say, the entrance to the tower stayed locked after that and the key was put in safe custody.

Another time, as usual after lunch, a colleague and I started exploring the Institute's border. It took nearly two hours – there was no wall all around at the time, and I came back to the office very late. I had to pass through the Assistant Registrar's room to get to my desk, so I entered his room and naturally he was not happy to see me coming so late. But immediately he noticed I was exhausted and sweating, and he offered me a seat and a glass of water and asked what happened. When I told him, he was speechless. After some time, he advised me not to venture around campus as it was not safe, and full of snakes, and so on.

Once I had the chance to visit the cellar of the main building, to get some records from there. It is huge, running the length and breadth of the main building.

What are your best memories of your time at IISc?

For me, it has been special to have served the former Director Prof Bhagavantam, a serving Director, Prof Dhawan, and a future Director, Prof Anurag Kumar. And I am happy that I was not the first person from my family to serve the Institute. My maternal uncle, Cheluvaraja Moduliar, was here as an artist. He used to write the degree certificates, has painted the scenes from the Founder's Day celebrations, and performed a few more tasks at ECE. My brother AV Kumar joined ECE as a student, but as he got an opportunity to go to Germany he discontinued his course. My sister AV Asha Jayanthi did her research at IISc's School of Automation and joined ISRO.

Let me tell you about life on campus outside the office.

I used to walk with Ms Sudha Murthy of Infosys when she was a student at ECE. And as the ladies' hostel was next to our house, those students used to visit us as they used to miss their families and they enjoyed my cooking.

As I used to live on campus and would walk up and down, Mrs Nalini Dhawan became friendly with me as both of us were interested in the plants, trees and even weeds on campus. Before the Dhawans left the campus, she hosted a party for all the women faculty and wives of faculty in their bungalow. I was the only one among them who fit neither category, but she introduced me so nicely to them.

In 1964, a few women started assembling during the lunch hour under the tree at the back of the main building. Slowly women on campus from other departments and some women students joined us. We used to go to movies, mostly at Lido Theatre, on Saturdays as we had only half a day of work, and also organised some picnics to nearby places. I think this was the beginning of what is now the Ladies' Club.
I not only worked at the Institute, I lived and breathed it all through the 38 years of my service. When I joined I was the only woman in the Administrative Section. Though one more woman joined soon after, she left in a little while. But now, I see ladies everywhere. Proof of women power. 'His-story' is always there but 'Her-story', the lady stars, should always shine bright and show the way.

How have you been spending time after retirement?

This was the big question I had. But one of my friends at church suggested that I do social service. I take a very active role in this. I attended Bible classes at St Peter's Pontifical Seminary and one of the priests there asked me, you are from a nearby institute, how is religion practised there? I said, "There is no religion there, people are there from all over the world. All are one." He was astonished.

Once again I am thankful. The Institute is taking care of my health and wealth. I no longer call IISc 'Tata Institute', but 'Thaatha mane' [grandfather's house].

Meet NSF's New Director

- Connect Staff

An IISc alumnus, Sethuraman "Panch" Panchanathan, was appointed as the 15th Director of the National Science Foundation (NSF), USA. Before being chosen to head NSF, he was at Arizona State University (ASU), where he founded the Center for Cognitive Ubiquitous Computing (CUbiC) which is focused on designing technologies and devices for assisting individuals with disabilities. He has also served as the Chief Research and Innovation Officer at the university. For his many achievements, Panchanathan has received the IISc Distinguished Alumnus Award 2020. Following the announcement of the award, he did an email interview with *Connect* about the recognition from his alma mater and his vision for NSF.

Photo courtesy: NSF

You received your engineering degree from the Department of Electrical Communication Engineering at IISc in the early 1980s. What is your favorite memory from your time at the Institute?

There are so many favourite memories from my time at the Institute, including spending time with amazing friends (fellow students), engaging with inspiring faculty, playing cricket for IISc, and enjoying the awesome food in the A mess.

After having gone through the rigour of the North American education system – first in Canada and then in the US – what do you think was good about the education you received in India (in IISc and then in IIT Madras)? And what do you think was lacking?

India provided me a strong foundation with high-quality education enabled by selfless and dedicated faculty members. I credit my fellow students and the outstanding faculty at both IISc and IIT Madras for creating an environment of excellence and motivating me to do my best.

What has been NSF's role in fighting the COVID-19 pandemic?

The role of NSF and other science agencies is to unleash talent and ideas by providing support to the scientific community to find solutions to the challenges presented by the pandemic. NSF reacted right away to the pandemic through its Rapid Response Research grants by funding non-medical research to understand the spread of COVID-19, educate about the science of virus transmission and encourage the development of actions to address this global challenge. To date, we have funded more than 1,000 coronavirus research projects totaling more than $197 million.

The research community continues to display resilience under tremendous pressure. It makes me proud to be a scientist and an engineer at this time. We are facing new and unique challenges as we deal with COVID-19, and NSF is prioritising the health and safety of our community. NSF recognises the multiple concerns related to the effects this will have on NSF-funded research and facilities and is committed to providing the greatest flexibility to support researchers' health and safety. NSF is consistently updating guidance and resources to keep the scientific community informed. This information is available on our website at: nsf.gov/coronavirus

When you were confirmed as the Director of NSF, you said in a statement, "My personal mission is to inspire, empower and serve humanity through life-changing innovations that have the potential to alter the face of how we view 'different abilities' on a global scale." How does that align with NSF's traditional emphasis on fundamental research?

At a young age, I was privileged to have the opportunity to teach math and English to disadvantaged middle and high school students in underserved areas in Chennai. I had a special affinity for those with different abilities in my community, and I wanted to find ways to empower those that were disadvantaged in society. I believe that every human being has raw, untapped potential that can be realised with the right support and opportunity.

My personal research in designing technologies and devices for empowering individuals with a range of abilities opened my eyes to the importance of inspiring, motivating, and nurturing talent across the socio-economic spectrum. All of these experiences have helped prepare me for my current role as NSF director and have deeply shaped my vision for the agency's future, which hinges on things like ensuring inclusivity and accessibility in STEM as well as expanding the agency's partnerships. We need to inspire new generations across all communities to explore the wonders waiting to be discovered.

As an engineer and an innovator – you previously served as the Chief Research and Innovation Officer at ASU – what do you bring to the table as the head of NSF?

Working in academia has inspired me to pursue exploratory and translational research, mentor outstanding talent, and engage with industry and other collaborators across the globe through a range of partnerships. My leadership roles at Arizona State University enabled me to envision programmes that encouraged the scientific and innovative spirit to permeate, prosper and advance among faculty, researchers, and students. These experiences provided me with an opportunity to enhance my understanding of the importance of higher education for national prosperity and competitiveness.

As a former member of the National Science Board, I had the opportunity to contribute to policies that advance science and engineering. I personally believe in seeding bold, large-scale foundational research with meaningful societal impact. As NSF director, I want to work to ensure that the agency is strengthening its mission working at speed and scale.

Science published a profile about you, describing you as an optimist. Do you think that will remain unchanged as you navigate your way through the beltway politics of Washington DC?

I am an eternal optimist. We cannot have innovation in science without optimism, hope and confidence about the future. Yes, we are facing a global pandemic, but this is the greatest time in the history of the human race for innovation and discovery. I am a strong believer that challenges can be turned into opportunities. My unanimous confirmation by the [US] Senate is good proof that people feel very bullish that science and technology has got a great future in our country and, more importantly, that we can be a global leader.

This year, the White House Office of Science and Technology Policy announced a nationwide focus on driving new developments in "Industries of the Future" (artificial intelligence, advanced manufacturing, quantum information science, advanced wireless, and synthetic biology). NSF can be a huge player in terms of moving these initiatives into the future. I believe we have all the support essential to moving this agenda forward.

In the coming years, what are the new frontiers of research that NSF will focus on?

NSF plays a critical role in US science and engineering because it supports basic research in all fields. We enable researchers to explore fundamental scientific questions about everything from the forces that govern the universe around us to the biological, chemical and social systems that make us who we are. I believe in seeding bold, large-scale foundational research with meaningful societal impact. Science is extremely important if you want to address societal problems in a constructive and an outcome-oriented way.

I have identified three pillars for my vision: advancing research into the future, ensuring inclusivity, and expanding global leadership in science and engineering. I am looking to focus on strengthening at scale and speed. I would like to see NSF's investments amplified through partnerships with industry, non-profits, agencies, and other entities. Finding partners who share our values, aspirations and approach and then leveraging each other can benefit the country both economically and societally.

The New Education Policy (NEP 2020) announced by the Government of India envisages a National Research Foundation (NRF) to fund research in science and technology in the country. With the benefit of hindsight, what are the lessons that it can learn from NSF?

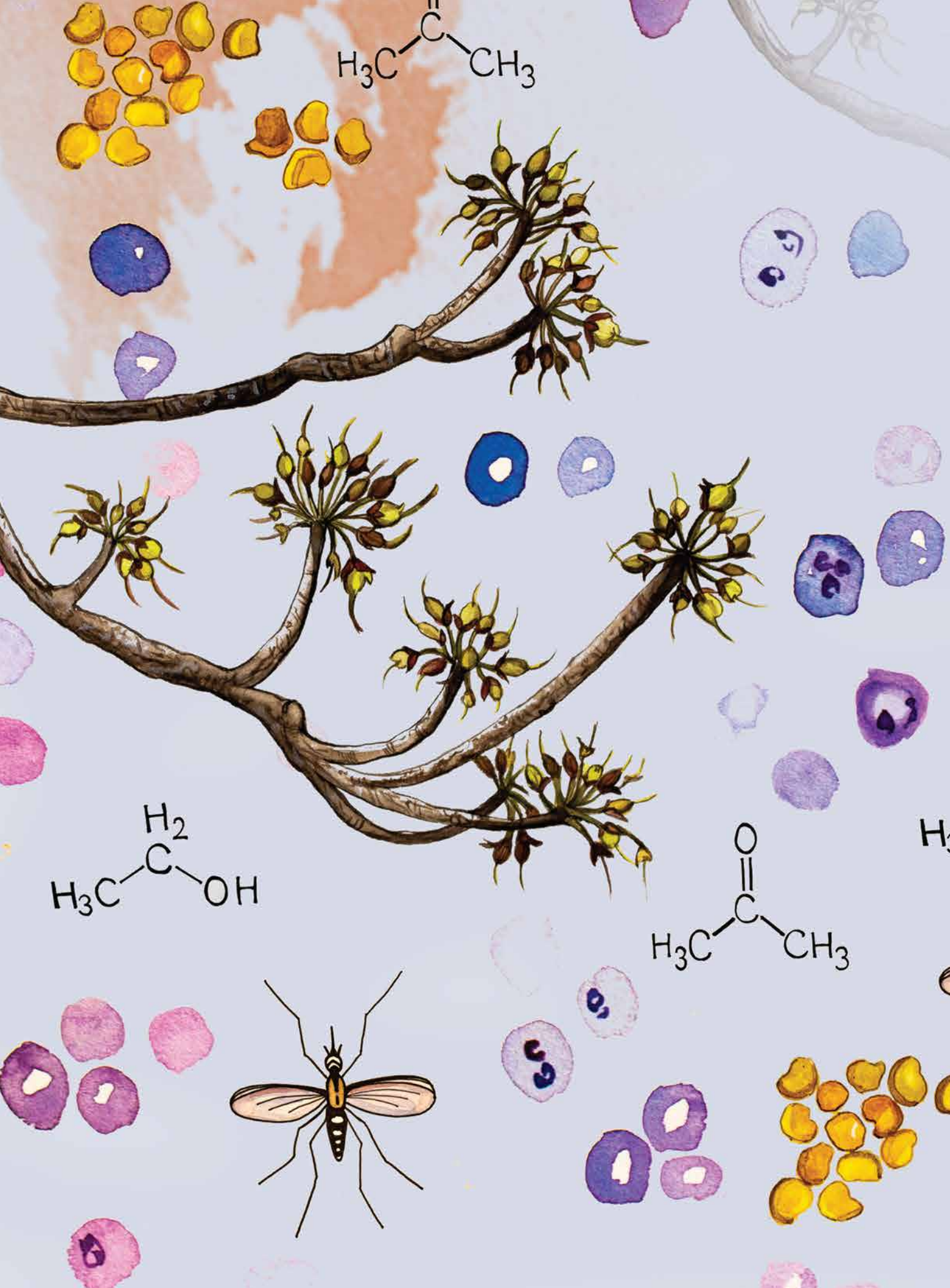
From the very beginning, NSF's integrity has been its most important feature. This agency was created to support basic research to expand what we know and benefit our country's population. We work with research communities to determine the highest priority areas to advance, and also created a review process that serves as the global gold standard – and we have never stopped working to improve ourselves. We have earned the trust of the research community and the public. What we have done over the decades has been profound, ranging from building telescopes to explore the universe to helping establish the foundations of the Internet to connect everyone here on planet Earth, all enabling breakthroughs in every field. But we could not have done that without a strong backbone of openness, transparency and integrity from the outset that guides our activities everyday.

IISc has announced that you have received the Distinguished Alumnus Award for 2020. Congratulations. What does it mean to you?

I am extremely honoured to receive this recognition. It is always a delight to be recognised by your alma mater. The fact that this celebrates the work on empowering individuals with disabilities makes it even more special. I am indeed grateful for this award.

ABSTRACTS

IISc Photography Club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