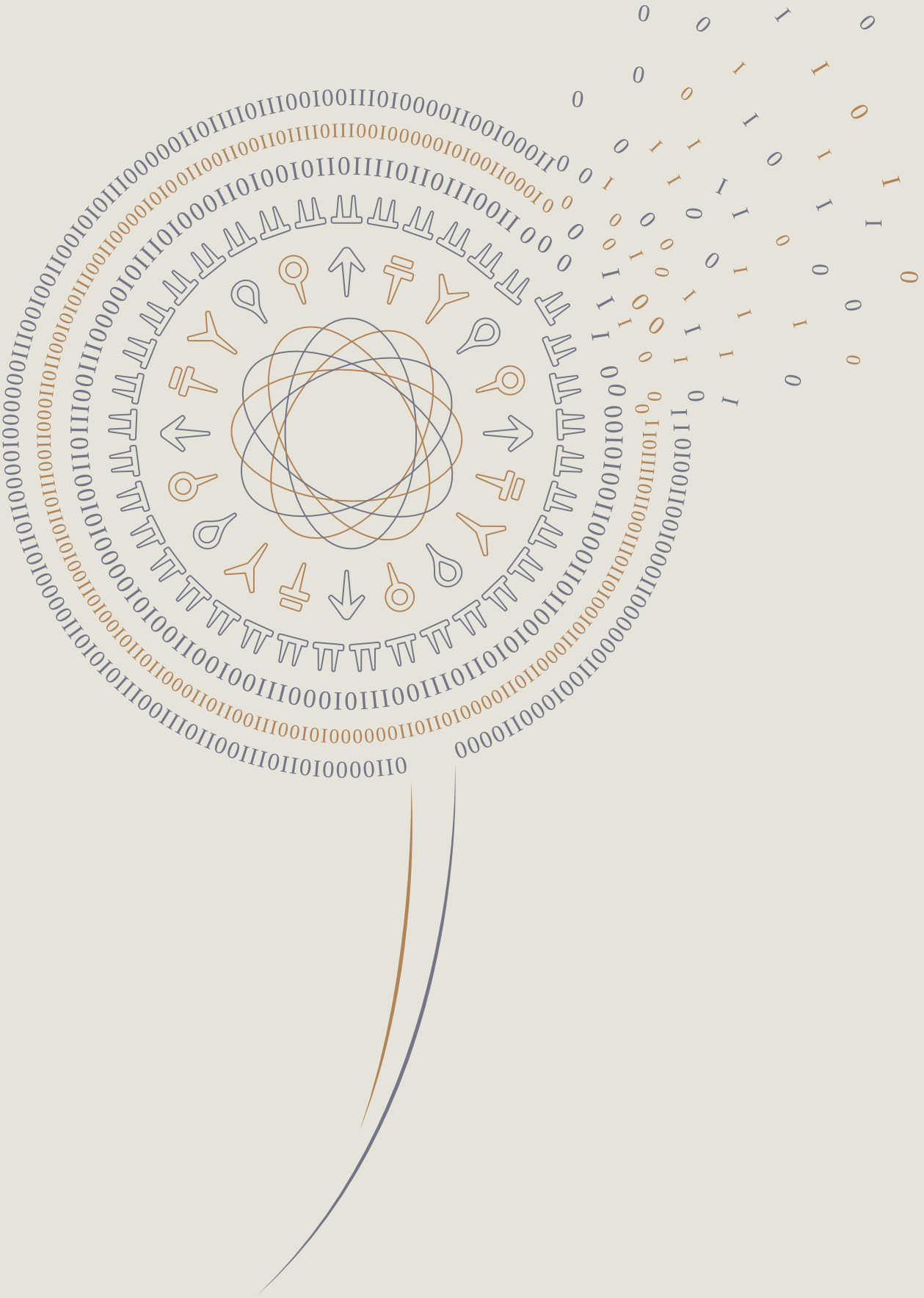

Making a Difference

NATIONAL CENTRE FOR BIOLOGICAL SCIENCES • ANNUAL REPORT 2019-2020

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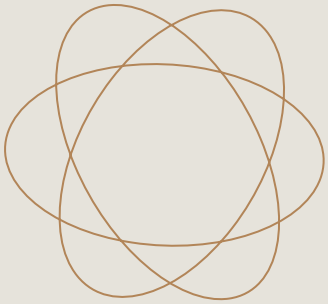
Making a Difference

NATIONAL CENTRE FOR BIOLOGICAL SCIENCES
ANNUAL REPORT 2019-2020

ncbs
National Centre for Biological Sciences
Tata Institute of Fundamental Research



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A Tumultuous Year: Trial by Virus

The year started on a high with the completion of the TIFR Council mandated Quinquennial Review in January 2020. I wish to place on record, my sincere and personal thanks—and thanks on behalf of NCBS-TIFR—for the tremendous effort and time invested by the eminent members of the committee, in collecting voluminous information, analysing, and meticulously reviewing the entire gamut of activities of NCBS. This culminated in the exhaustive Review Report (https://www.ncbs.res.in/five-year-report-2020).

As the report summarises, "NCBS has developed into an internationally renowned and competitive research centre in broad areas of the life sciences, whose excellence reflects the wisdom of TIFR in creating and nourishing this aspect of its broad portfolio. NCBS has created considerable value for the TIFR system, not only through its intramural research but also through its role in creating new institutes both within and outside of the TIFR system in Bengaluru, and elsewhere in India. NCBS is open in the best sense, collaborating widely, organising both user facilities and diverse training opportunities for scientists across India and taking an important role in national initiatives in which the life sciences and life science research are a major part. NCBS can be considered a, "national treasure" of which everyone at TIFR, indeed throughout India should be proud."

The high praise of such an eminent body of scientists is undoubtedly a consequence of the effort of all our colleagues, from our outstanding scientists, to our scientific and technical support staff, students, post-doctoral fellows, and the untiring set of administrators who make the wheels turn around day in and day out. I also wish to thank Upi Bhalla, the NCBS Dean and the steering committee, as well as scientific members of our management and scientific advisory boards whose constant encouragement and support has been invaluable over the years. Thanks are especially due to the members who are turning over, namely Utpal Banerjee, John Kuriyan, and Anjana Rao, as well as to those who are continuing to serve us. I hope that the points being raised by this report (and there are many) will serve to guide us for the next decade at least. In particular, we should pay attention to the suggested strategic directions where further growth can be effected.

COVID-19 interrupted our moment in the sun and soon challenged almost every element of the review. But I am happy to report that the reviewers had not erred in their judgement. During the entire span of the COVID-19 pandemic—both during lockdown and post lockdown periods thus far—NCBS (as part of the Bangalore Life Science Cluster i.e., BLiSC) has continued to

function. In the initial phase from March till June, we functioned exclusively in COVID-19 response mode without regular research activities. After this phase, gradually, we have opened up regular research and today we function at greater than 50% strength, and our research activities continue without much hitch on a day to day basis. This has been possible due to a series of procedures put in place to regulate entry attendance and movement within the campus. Further, the protocols for contact tracing and dealing with cases of possible infections of personnel on the campus were also prepared and operationalised. This year, we dedicate a separate section summarising our COVID-19 response from NCBS and BLiSC, and I will not belabour the same here, except to say that the campus has shown extraordinary resilience and cooperation.

Unfortunately, our finances were badly hit by the national shift in research priorities. Although core funds were extremely restricted, we raised substantial Corporate Social Responsibility (CSR) funds to support the much needed COVID-19 response. Working in a coordinated manner, NCBS and DBT-inStem set up testing facilities for RT-PCR testing supported by generous donations from Azim Premji Philanthropic Initiative, Nuclear Power Corporation of India, and Standard Chartered Bank. The Punjab National Bank and IQVIA joined these donors to support COVID-19-related technologies for diagnostics, protection, screening, therapy, computational modelling of drugs, as well as studying disease and virus spread. Along with C-CAMP, we now serve as sites to indigenise diagnostics in a Rockefeller Foundation-funded initiative called InDx (https://tinyurl.com/bliscindx).

We salute all our supporters and thank them for the faith they reposed in us and our science. I strongly believe that it is high quality science and its eventual application that has allowed us to see such a rapid response from the local to the global scale to this pandemic. There needs to be no better reason than this to continue to support scientific research in our country with the highest priority.

In 2016, as NCBS turned 25 years old, we recognised the need to create an institutional archive. Today we have come a long way, and thanks to the dedicated efforts of Venkat Srinivasan, our Head Archivist, we have an Archives at NCBS (http://archives.ncbs.res.in/). To cap this effort, we have been able to create an Obaid Siddiqi Chair in the History and Culture of Science, and a renewed vision for the Archives. This has been made possible due to generous CSR support from TNQ Technologies. I am particularly grateful to Mariam Ram (Chairperson, TNQ) for her tremendous support for science and also for believing in keeping the vision of Obaid alive and vital in these trying times. We hope to position the Archives at NCBS as one the premier centres in the country for the study of the contemporary histories and culture of science. The Chair in the History and Culture of Science will lead

the charge in a much-needed effort to bridge the sciences and humanities and foster a diverse and inclusive community of academics across disciplines.

As with any mature institute we are now approaching a steady state with retirements, liens, and renewals. Over the last three years, several of our founding faculty members have retired, Gaiti Hasan (2018), and this year Mathew K. Mathew and Sudhir Krishna. While Gaiti continues as SERB Distinguished Fellow at NCBS, Mathew takes on a guiding role at IISER Trivandrum and Sudhir moves to head up a School of Interdisciplinary Life Science at IIT Goa to drive a public health ecosystem that he has always dreamed about. We wish all our retirees success in their exciting endeavours and to Radhika Venkatesan who is on lien to IISER Kolkata. But steady state implies additions, and we are very happy to welcome Shaon Chakrabarti and Soumyashree Das to the campus and help mould the campus in the way they wish to see it grow.

We thank Ajith Kumar (Centre for Wildlife Studies) for guiding the MSc Wildlife Biology and Conservation programme at NCBS for the past 14 years and taking it to the exemplary programme that it has become. We wish him all the very best as he goes back to his true love, field biology. We look forward to Jayashree Ratnam taking over the directorship of this programme and building a consortium with Nature Conservation Foundation (NCF) and other partners, and acknowledge new support from the Habitats Trust, and continuing support from the Wildlife Conservation Trust. On behalf of the campus, I thank Mukund Thattai for his role as Head, Academics for the past six years and steering this vital part of our campus so effectively, and would like to welcome Raj Ladher as our new Head, Academics.

I congratulate our colleagues who have received awards and honours (see right), and in particular Vatsala Thirumalai for being awarded the Shanti Swaroop Bhatnagar Award for Life Science.

At the end of this decade, we must look to the new one with a renewed commitment to landing on our feet, with the nimbleness that will be needed, and with the backing of all those who support the potential of our science. In an environment of change and challenge we will get by with a little help from our friends!

Satyajit Mayor
Centre Director

NCBS Award List (2019–2020)

NCBS is host to a diverse set of faculty and NCBS researchers at every stage of their careers have received accolades in the last year for their work.

NATIONAL

Upinder S Bhalla
SASTRA-Obaid Siddiqi Award 2020
Sastra University
February 2020

Deepa Agashe
SERB Women Excellence Award 2020
Science and Engineering Research Board
February 2020

Vatsala Thirumalai
Shanti Swarup Bhatnagar Prize 2020
Council of Scientific and Industrial Research
September 2020

Mahesh Sankaran
Elected to INSA as a Fellow
Indian National Science Academy
October 2020

INTERNATIONAL

Gaiti Hasan
Gutenberg Chair
University of Strasbourg
March 2020

Deepa Agashe
Nominated as Vice President of the American Society of Naturalists (2021–2023)
American Society of Naturalists
May 2020

Sumantra Chattarji
Lifetime member of EMBO
European Molecular Biology Organization
July 2020

Smita Srinivas
Clarence E. Ayres Scholar 2021
Association for Evolutionary Economics
July 2020

Ben Wigley (ex post-doc at NCBS)
Julie S. Denslow Prize for the Outstanding Paper in Biotropica 2020
Biotropica
November 2020

Welcome Note for Dr Raj Ladher, the New Head of Academics at NCBS

Raj Ladher, takes over as Head of Academics, NCBS, from predecessor Mukund Thattai

Within academia, whether as freshman students or tenured professors, we are often thrown into the deep end with no road map. Research, by definition, pushes us to confront the unknown. But it is important to realise that we do not face this challenge alone. Over the past century, the natural sciences have moved from being a largely solitary pursuit to an intensely collaborative one. Science today is done by teams of researchers, connected across not just a single laboratory or institution but across the world. These teams are valuable sources of expertise, but more importantly, of support. When we get stuck there is always someone to turn to, someone who has been there before, someone who can share their experiences and give advice.

When people think of mentors in academia, they often think of the formal role of an advisor guiding a PhD student. But mentors come in many shapes and sizes: they could be your peers and colleagues, to share a coffee with and bounce ideas off; or they could be distant collaborators, whom you may have never met in person. The role of a mentor is not to instruct, but to help; not to judge, but to empathise; not to demand, but to inspire. Each of us needs many mentors, different ones at different times and places, as we go through life's failures and successes.

When young scholars come to NCBS to learn how to do science, they find sources of mentorship and support spread across the institution. Over the years our campus has developed a unique academic culture of interlocking parts: rotations, through which students choose host laboratories; journal clubs at which they learn how to read and critique papers; annual work seminars where they share their progress with peers; thesis advisory committees who are there to help at any stage of the PhD; and a host of courses, workshops, and meetings covering every aspect of biology. All these enrich the student experience, broadening their horizons beyond their own workbench and their particular research question.

When NCBS was founded nearly three decades ago, we were a blank slate. A fresh start is exciting but also daunting, because the systems one puts in place at the beginning must endure over the life of the institution. We owe much of our present academic culture to M. K. Mathew, our first Head of Academics, and Gaiti Hasan, his successor. By the time Apurva Sarin took over as the third Head of Academics, it was a time of rapid change. Our campus was getting larger in every way, expanding physically, expanding in student and postdoc numbers, expanding to new fields. We moved from being a small campus where everyone knew everyone else, to a much more complex enterprise. During Apurva's tenure, the role of Head of Academics expanded tremendously to keep up with these new circumstances. Assisting Apurva from the sidelines, I could see how easy she made her job look, but how hard it actually was.

Five years ago, when Apurva moved on to her role at DBT-inStem, I took over as Head of Academics. I was lucky: the systems my predecessors had put in place were robust, so I was able to focus on new and exciting opportunities. I worked to strengthen ties between NCBS and DBT-inStem, creating a seamless graduate programme across the two institutions, while navigating the changing landscape of UGC regulations and the new National Education Policy. I was happy to see the NCBS/TIFR entrance test grow into the JGEEBILS consortium, which now administers an online entrance examination accepted by dozens of participating institutions across the country, attracting nearly 10,000 candidates each year. I enjoyed working with colleagues at institutions across the world, including Cambridge University, the Max Planck Institutes, RIKEN, and Institut Curie, to set up joint postdoctoral programmes which led to a tremendous amount of exciting new science. None of this could have been done without the constant support of the Academic Office staff, particularly Vishalakshi and Valsala; the NCBS Research Development Office

(RDO) set up by Savita Ayyar and now ably run by Vineetha Raghavan; the Dean's Office; and many others across the entire NCBS administration. They did the hard work.

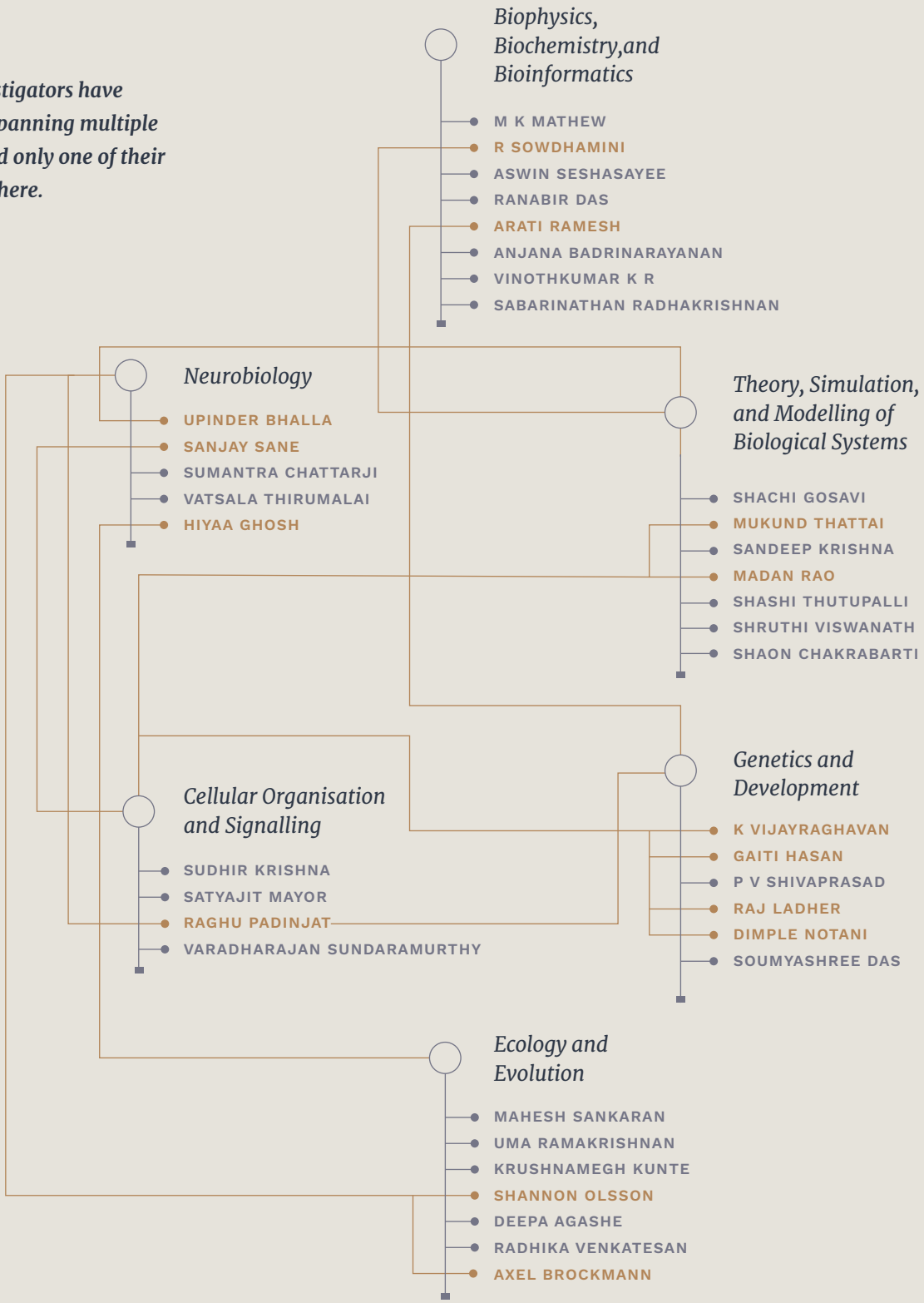
Each Head of Academics brings their own ideas, each has a chance to make a difference to the campus. As I planned to step down as Head of Academics, I could think of no better person to take over than Raj Ladher, because he always puts students' interests first. At the time Raj agreed to take over, we had no idea that 2020 would be the most challenging year our campus has ever faced. Raj was truly thrown into the deep end, but he took on the role with grace. In a time of great uncertainty for students and postdocs on campus, Raj has made himself fully accessible and deeply involved in all aspects of campus life. He has been instrumental in managing our response to the COVID-19 pandemic, setting up a campus contact tracing system. He has run our first ever online interviews, and welcomed our new batch of graduate students to our first ever virtual term, without a single hitch.

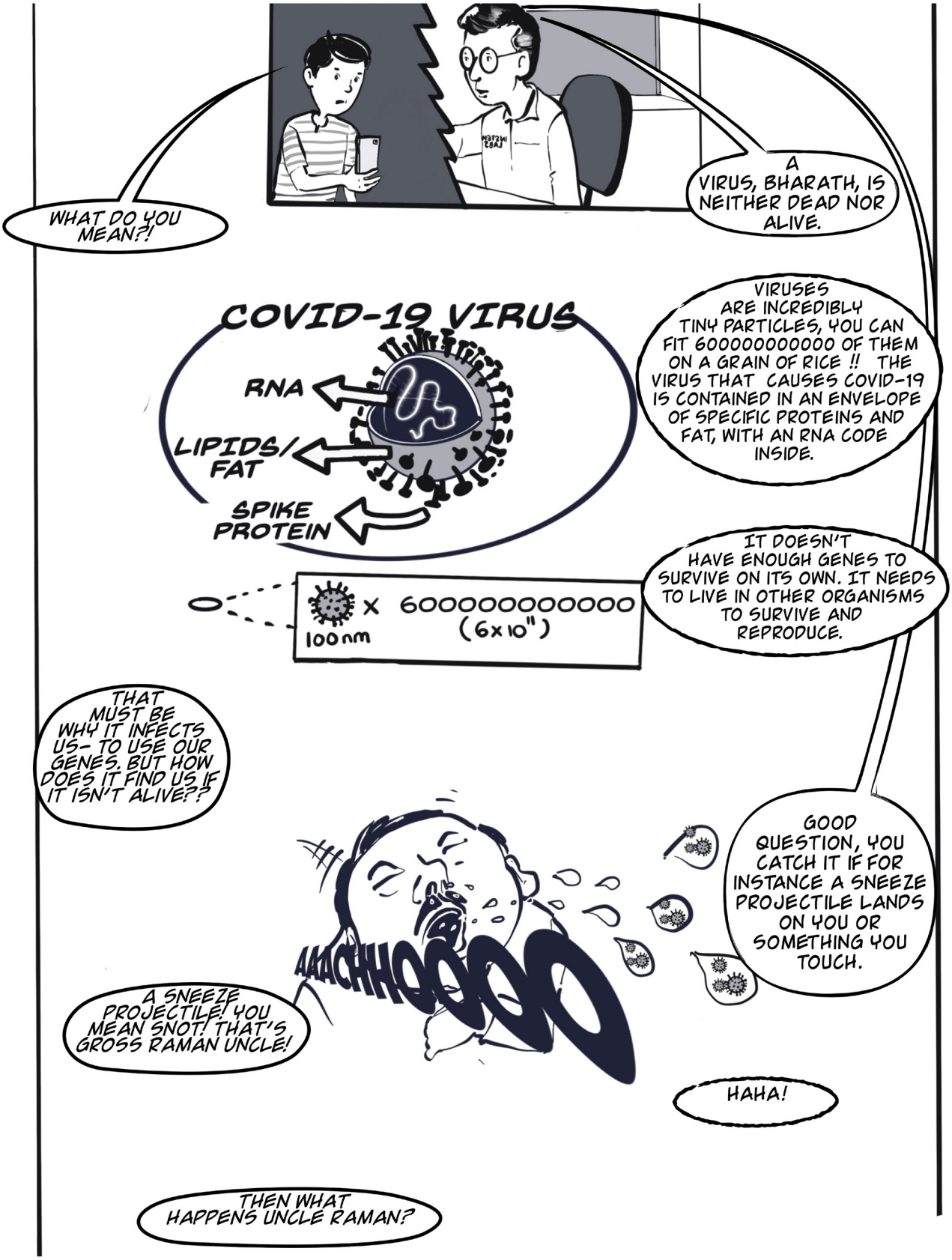
I know Raj has an ambitious vision for the campus. I have only one piece of advice. After years of exciting growth and change, of making national and international links, it is time to rededicate ourselves to the core activity of our campus: mentorship, and the health and well-being of our students. NCBS has grown from a village to a sprawling and often impersonal institution. At one time, students, staff, and faculty saw NCBS as an experiment whose success depended on their collective efforts. Today, they see a professional, functioning institution in which they can focus on their own interests. There is a real danger that the scale of the campus, and the diversity of research areas it hosts, could pull the campus apart, as if by a centrifugal force. But diversity and scale—while challenging—are also opportunities, as long as the centre holds and the foundation is strong. The task ahead is not easy, and Raj will need the support of all the faculty, students, postdocs, and staff on campus if he is to succeed.

Raj, I wish you luck, I know you will carry us through the present moment, to an even brighter future.

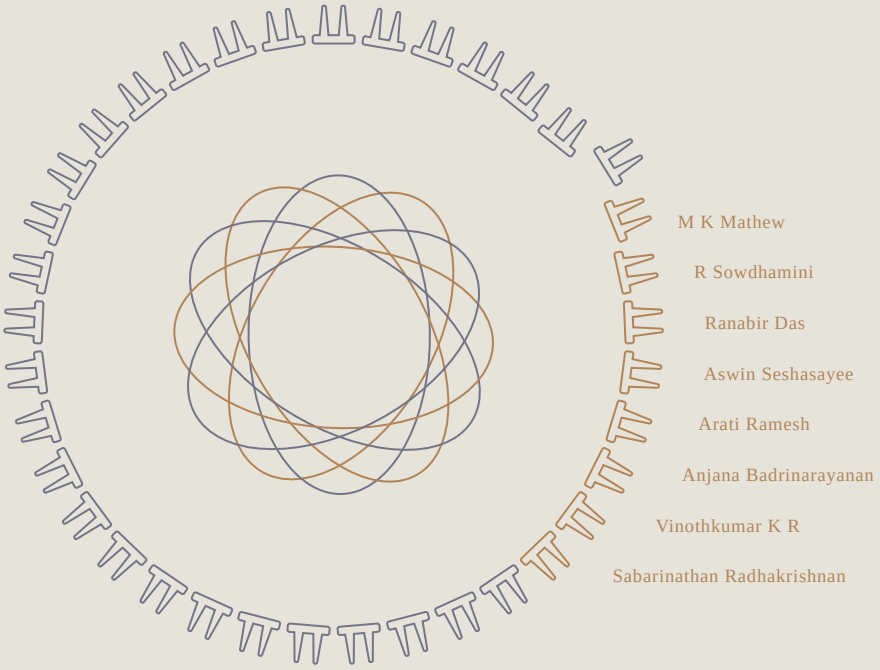
Mukund Thattai
Head of Academics, 2015-2020.

Several of our investigators have research interests spanning multiple areas of biology and only one of their affliations is given here.





These pages are excerpts from a series created, designed, and written, by Arvind Ramanathan of DBT-inStem and Sonia Sen from TIGS-CI. They are illustrated by Arvind Ramanathan as a part of the Cluster's COVID-19 Response Initiative. The work was originally published on www.covid-gyan.in



M K Mathew

R Sowdhamini

Ranabir Das

Aswin Seshasayee

Arati Ramesh

Anjana Badrinarayanan

Vinothkumar K R

Sabarinathan Radhakrishnan

Biochemistry, Biophysics, and Bioinformatics

Roots and Mechanisms of Salt Tolerance in Arabidopsis • M K Mathew
Computational Approaches to Protein Science • R Sowdhamini
Protein Modifications in Host–Pathogen Interactions • Ranabir Das
Adaptation, The Bacterial Way! • Aswin Seshasayee
Structure to Signalling: Insights into Bacterial Biology through RNA Structure • Arati Ramesh
Regulation of DNA Damage Response and Repair • Anjana Badrinarayan
Structure of Macromolecules and Dynamics • Vinothkumar K R
Deciphering Genetic and Molecular Alterations in Cancers • Sabarinathan Radhakrishnan

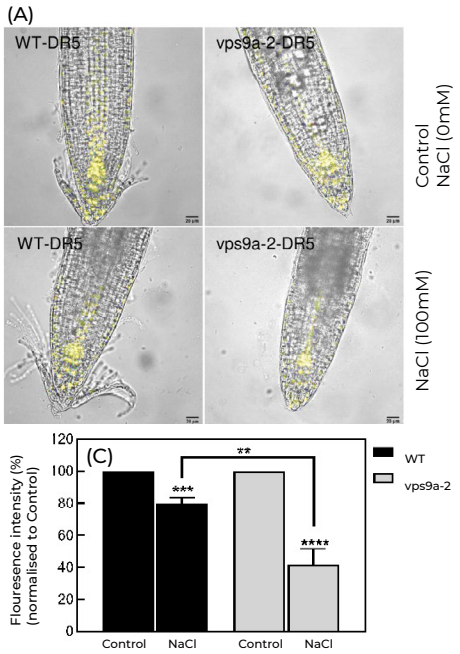
Roots and Mechanisms of Salt Tolerance in Arabidopsis

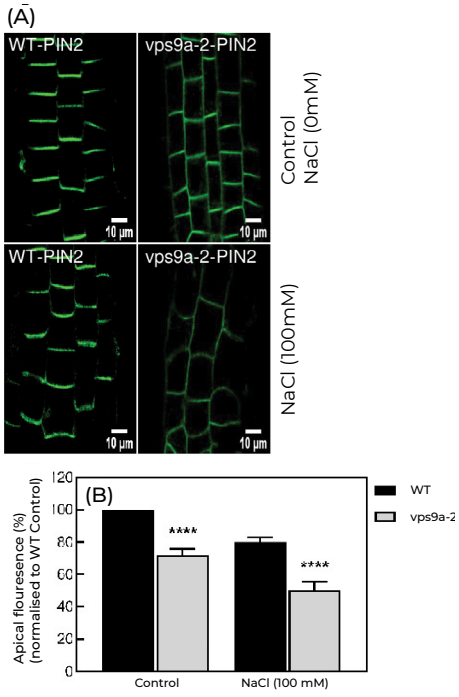
Salt stress induces enhanced endocytosis in plants and we have shown that it does so by turning on a novel endocytic pathway. In mutants that do not turn on this pathway, we now show proliferation of root hairs close to the elongation zone.

Salt stress is one of the major constraints impacting crop productivity worldwide. Plants achieve survival under salinity stress primarily by maintaining high cytosolic potassium/sodium ion (K+/Na+) ratios, preventing Na+ cytotoxicity and retaining osmotic balance. Ras-related protein 5 (Rab5) members are involved in trafficking of endosomes to the vacuole or plasma membrane (PM). The vacuolar protein sorting-associated protein 9 (vps9a) encodes the single guanine nucleotide exchange factor (GEF) that activates all three known Rab5 proteins in Arabidopsis thaliana.

Earlier work from our group has reported the critical function of vps9a for the operation of a salt-induced endocytic pathway, as well as expansion of endomembrane compartments under saline stress conditions. Our recent results show that roots from vps9a-2 mutant, subjected to 100 mM NaCl, display alterations in transcript levels of genes involved in K+ homeostasis pathway, and exposure to low K+ environments resulted in growth retardation and reduced rate of endocytosis. In addition, we find that imposed NaCl stress reduces the elongation capacity of cells in the root elongation zone of vps9a-2 mutant. Root elongation is dependent on the plant hormone, auxin. We have monitored the expression of auxin (using the auxin reporter Direct Repeat 5, DR5-YFP) and of an auxin efflux transporter PIN- FORMED2 (PIN2). NaCl stress attenuates the expression of DR5-YFP, and reduces the abundance and polarity of the auxin efflux carrier in the mutant line. Together our results indicate that alterations in K+ homeostasis and associated cellular changes contribute to diminished root growth and compromised survival of vps9a-2 mutants under conditions of salt stress.

Expression of a reporter for auxin in WT and vps9a-2 mutant lines. *4-day old plants were subjected to 0 mM NaCl (control) or 100 mM NaCl stress for 24h (as indicated). (A) Fluorescence pattern indicating auxin activity in root tissue from WT (A: left panel) and vps9a-2 mutant lines (A: right panel). Note the difference in lateral root emergence in the two cases. (C) Fluorescence intensity was normalised to respective control plants to quantify the effect of NaCl treatment and statistical significance of differences obtained between WT and vps9a-2 mutant lines. Statistical significance is denoted by *p<0.05,**p<0.01, ***p<0.001.*





Expression of auxin transporter PIN2 in WT and vps9a-2 mutant lines under control and NaCl conditions. *4-day old plants were subjected to 0 mM NaCl (control) or 100 mM NaCl stress for 24h (as indicated). (A) Fluorescence pattern of PIN2-GFP in root tissue from WT (A: left panel) and vps9a-2 mutant lines (A: right panel). Representative image showing PIN2-GFP signal intensity for the entire root (in pseudo-colour). (B) The GFP intensities were normalised with control plants and statistical significance of differences obtained between WT and vps9a-2 mutant lines, determined by non-parametric t-test, is denoted with asterisk. Error bars depict SEM (n = 30 cells from 3-4 plants). Statistical significance is denoted by,**p<0.01, ****p<0.0001.*

PUBLICATIONS

Rajagopal, D. and Mathew, M. K., 2020. ***Role of Arabidopsis RAB5 GEF vps9a im maintaining potassium levels under sodium chloride stress.*** *Plant Direct DOI: 10.1002/pld3.273*

Meena, M.K., Prajapati, R., Krishna, D., Divakaran, K., Pandey, Y., Reichelt, M., Mathew, M.K., Wilhelm, B., Axel, M., and Jyothilakshmi, V., 2019. ***The Ca2+ channel CNGC19 regulates Arabidopsis defense against Spodoptera herbivory****. The Plant Cell 31 (7), pp. 1539-1562.*

Computational Approaches to Protein Science

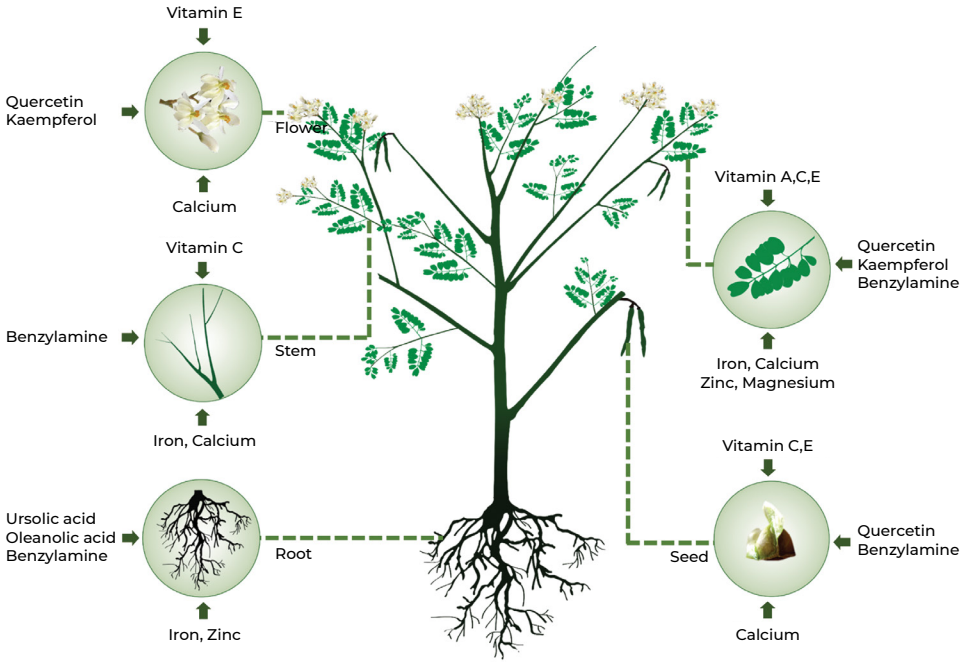
We employ computational algorithms to enable efficient annotation of functions to unknown gene products. Our ongoing and future projects are geared towards modelling protein/ligand interactions with applications in biomedical research and plant genomics, aided by in-depth, collaborative scientific ventures.

Genome sequencing projects have enormous potential to benefit human endeavours. However, just as acquiring a language's vocabulary does not enable one to speak it, databases that list the amino acid compositions of proteins do not directly tell us much about the higher-level structures and functions of these proteins. The most productive way to indirectly exploit the information in these databases has been to start with a small number of proteins that are fully-characterised, and to assume that other proteins with similar sequences will have related structures and functions. Proteins with very similar amino acid sequences are 'no-brainers', but the real test—which our group largely focuses on—is to detect the "essential" similarities in proteins whose non-critical sections have experienced random rearrangements during evolution.

In such cases, functionally similar proteins may have <25% sequence overlap. To enable more complete tracing of protein family trees, we have developed and improved upon a wide range of computational methods; some can be applied to all proteins, while others exploit characteristic features of specific protein types (e.g. the strong influence of disulphide bonds on the structures of extracellular proteins). Explicit computational pipelines have been devised to recognise parts of the genome that retain information for expression of protein families and to recognise genic regions. Such pipelines have been applied in DNA or RNA assemblies of select medicinal plants like the drumstick and Shankhpushpi. Applying these and other techniques, we have also carried out within and cross-genome surveys of several protein families and superfamilies to improve our understanding of their biological functions. Finally, we have identified families of enzymes—such as terpene synthases and cytochrome P450s in herbal plant genomes—to ascertain their roles in the biosynthesis of medicinally relevant secondary metabolites.

Reported biological activities

- *Quercetin/Kaempferol: Antidiabetic, antioxidant, hypolipidemic, hypotensive, anti-inflammatory, anticancer, neuroprotective, cardioprotective, and analgesic*
- *Benzylamine: Antidiabetic, antiobesity, antimicrobial, and cardioprotective*
- *Ursolic acid/Oleanolic acid: Hepatoprotective, anti-inflammatory, antiallergic, antiulcer, antimicrobial, cardioprotective, and analgesic*



Distribution of minerals, vitamins and secondary metabolites in different tissues of drumstick (Moringa oleifera) *Pasha et al., 2019.*

PUBLICATIONS

Ghosh, P., Joshi, A., Guita, N., Offmann, B., and Sowdhamini, R., 2019. ***EcRBPome: a comprehensive database of all known E. coli RNA-binding proteins.*** *BMC Genomics 20: 403.*

Pasha, S. N., Shafi, K. M., Joshi, A. G., Iyer, M., Harini, K., Mahita, J., Sajeevan, R. S., Karpe, S. D., Ghosh, P., Nitish, S., Gandhimathi, A., Mathew, O. K., Prasanna, S. H., Manoharan, M., Mutt, E., Naika, M., Ravooru, N., Rao, R. M., Shingate, P. N., Sukhwal, A., Sunitha, M. S., Upadhyay, A. K., Vinekar, R. S., Sowdhamini, R., 2019. ***The transcriptome enables the identification of candidate genes behind medicinal value of Drumstick tree (Moringa oleifera).*** *Genomics, https://doi.org/10.1016/j.ygeno.2019.04.014.*

Protein Modifications in Host-Pathogen Interactions

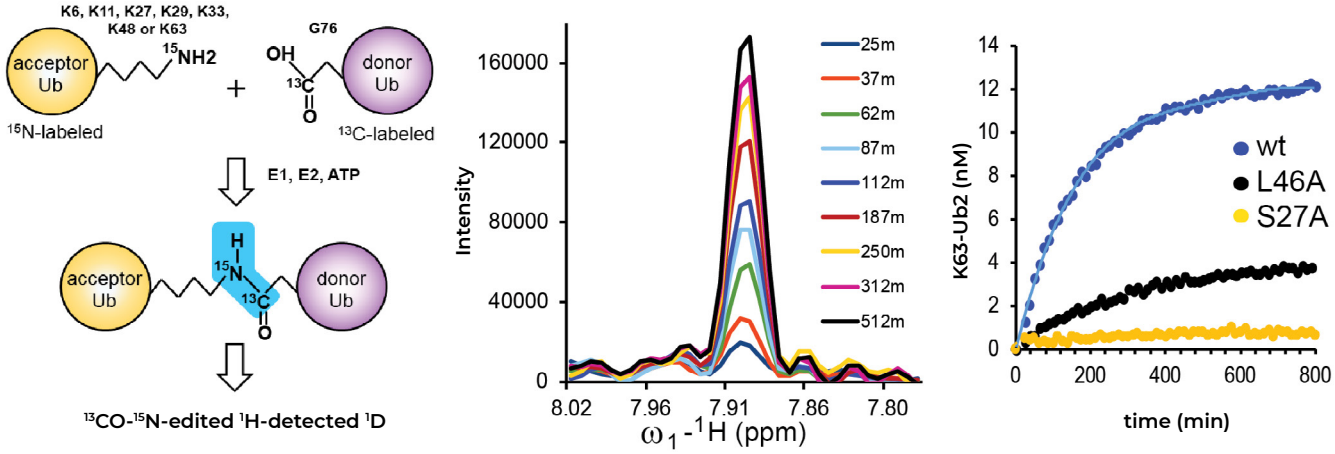
Protein post-translational modifications (PTM) regulate their function, localisation, or lifetime. How do pathogens exploit the cellular PTM signalling to suppress the host immune response? We address these questions by careful analyses of the molecular interactions between host and pathogen proteins.

Our group studies the role of post-translational modifications (PTMs) in host-pathogen interactions. Recent results from our lab provided the first structural insights into the mechanism where the collective action of Ubiquitination, SUMOylation, and phosphorylation enhances the activity of the herpes simplex virus protein ICP0 and depletes the host immune responses (Hembram et al 2020).

Crosstalk between PTMs was also invaluable for the life-cycle of the human cytomegalovirus, another member of the herpes virus family (Tripathi et al 2019). Few insect viruses encode a Ubiquitin variant—the central player in Ubiquitin signalling—to create unique Ubiquitin polymers that the host cannot regulate (Negi et al 2020). Methods were developed in the lab to measure the kinetics of protein post-translational modifications in real-time with high efficiency (Habibullah et al 2020, Tripathi et al 2020).

In a separate study, the lab uncovered an intriguing mechanism, where modification of the host Ubiquitin enzyme (UBC13 by Shigella) secreted deamidase OspI, creating a salt-bridge competition in UBC13 to perturb its interactions with Ubiquitin ligases and inhibit the host inflammatory response (Mohanty et al 2019). We have begun to scratch the surface regarding the repertoire of PTM crosstalk in host-pathogen interactions. It is of great interest to explore how they modulate the pathogen's life-cycle and the host immune response.

A new tag-free method detects Ubiquitination and SUMOylation of proteins in reaL time by NMR. *Habibullah BI, et al Chemical Communications, 56, pp. 6735–6738.*



PUBLICATIONS

Hembram, D. S. S., Negi, H., Biswas, P., Tripathi, V., Bhushan, L., Shet, D., Kumar, V., and Das, R., 2020. ***The viral SUMO-targeted Ubiquitin Ligase ICP0 is phosphorylated and activated by host kinase Chk2.*** *Journal of Molecular Biology, 432(7):1952-1977.*

Mohanty, P., Rashmi, A., Habibullah, B. I., Geetha, S. A., and Das, R., 2019. ***Deamidation disrupts native and transient contacts to weaken the interaction between UBC13 and RING-finger E3 ligases.*** *eLife 8: e49223.*

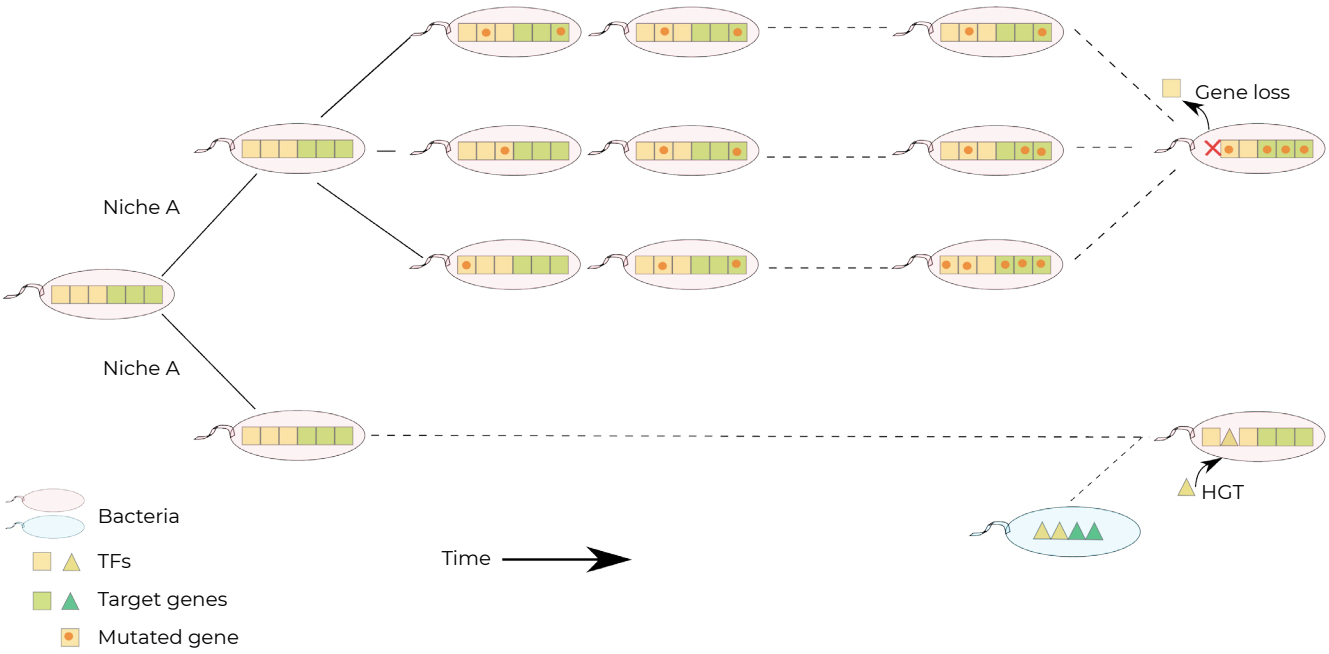
Adaptation, The Bacterial Way!

Bacterial adaptation to environments is complex and multi-pronged. Not only do they use combinations of regulatory players to determine what molecules to produce when, but they also adapt often by changing their genetic makeup in small steps. We ask how these phenomena operate using genetics and number crunching with computers.

Transcription factors (TF) are proteins that bind to DNA and affect the expression of proximal genes in response to environmental or cellular signals. These are central players in the establishment of gene expression states. Many TFs regulate a few genes, whereas a few TFs regulate a large number of genes. TFs and their targets together establish what is known as a transcriptional regulatory network. Regulatory networks evolve and cause phenotypic alterations. We studied sequence variation in TFs, relative to that in their target genes, over different time-scales in the bacterium Escherichia coli - from a few generations to a billion years, using publicly available genome sequence and regulatory network data.

Our results show the following: early adaptation to a novel environment favours mutations in TFs. But presumably, their pleiotropic nature selects against TF mutations at longer time-scales over which multiple mutations can fine-tune specific functions suitable for the prevailing circumstances. Across species, when extensive niche diversification takes effect, entire repertoires of TFs change by horizontal gene transfer and duplication (Figure 1). Using a short term evolution paradigm in the lab, we have shown how regulatory network evolution, adjusting the balance between growth and stress response, enables bacterial adaptation to prolonged periods of stasis.

FIGURE 1
A model of TF evolution over time. *Simplified from Ali and Seshasayee. Nucleic Acids Research, 2020.*



PUBLICATIONS

Nandy, P., Chib, S., and Seshasayee A. S. N.* ***A mutant RNA polymerase activates the general stress response, enabling Escherichia coli adaptation to late prolonged stationary phase.*** *mSphere 2020. 5:e00092-20.*

Ali, F. and Seshasayee* A. S. N.* ***Dynamics of genetic variation in transcription factors and its implications for the evolution of regulatory networks in bacteria.*** *Nucleic Acids Research 2020. 48: 4100-4114.*

Structure to Signalling: Insights into Bacterial Biology through RNA Structure

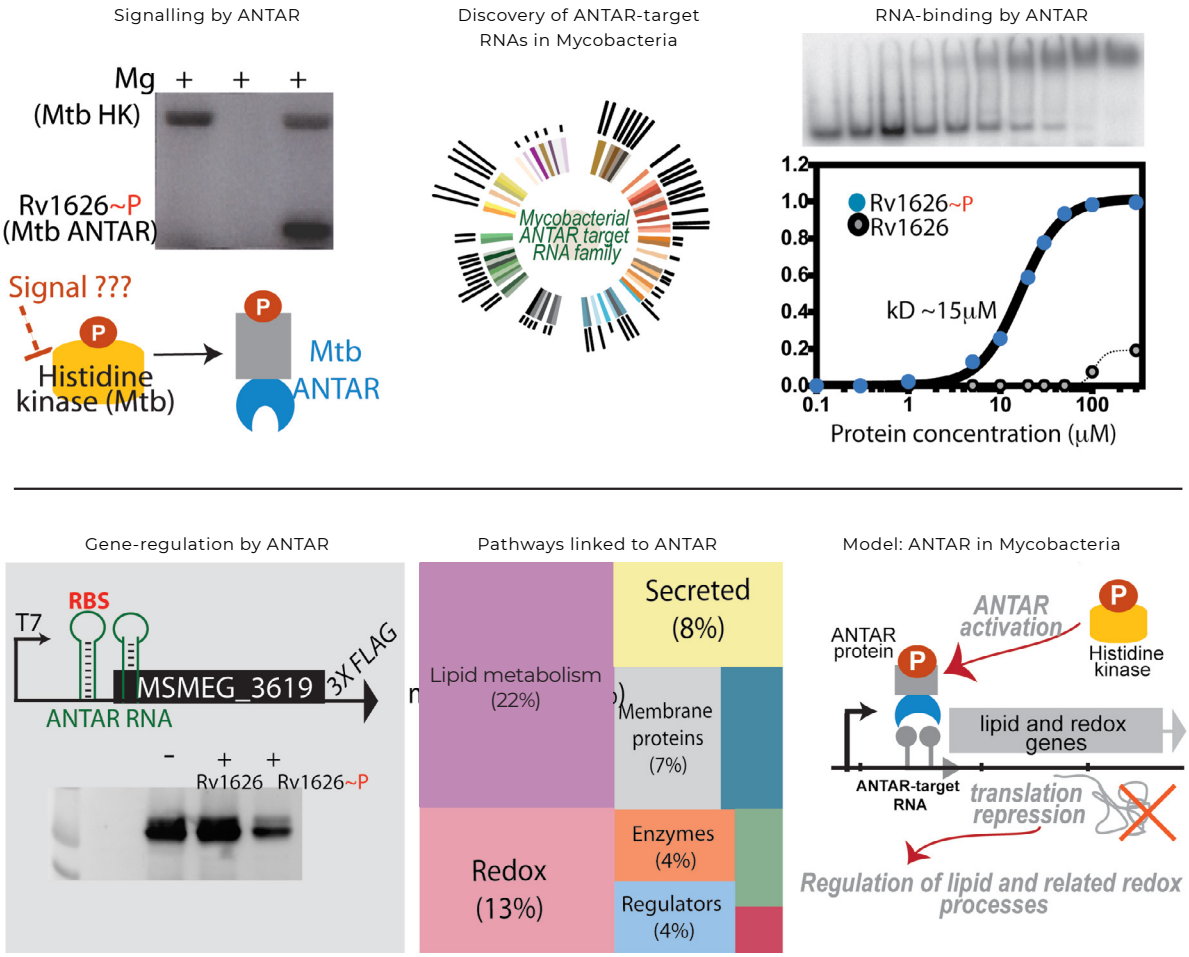
We are interested in RNA structure and RNA-mediated signalling. Using biochemical/structural approaches, we investigate how RNAs create the chemical complexities required to sense diverse molecules, how natural signal-sensing RNAs function, and how these molecules can be exploited to develop RNA-based biosensors.

My lab's programme addresses three broad areas centred around RNA structure:
(a) identifying signalling pathways mediated by metabolite-binding riboswitches and protein-RNA complexes
(b) designing RNA probes for cellular metabolites
(c) understanding the role of RNA structure in fundamental RNA-driven processes like transcription and translation

We are working towards identifying non-coding RNAs induced under infection-like conditions in pathogenic bacteria. Although crucial for bacterial signalling, RNAs from certain bacterial phyla remain elusive. By revamping computational approaches, we recently discovered a family of structurally-conserved RNAs in actinobacteria. These RNAs function by recruiting signal-sensing ANTAR proteins to select and regulate transcripts via translational repression. In mycobacteria, transcripts targeted by ANTARs encode important redox enzymes involved in lipid metabolism. The cellular response to ANTAR regulation is hierarchical, wherein the immediate metabolic changes induced by ANTAR–RNA binding are amplified through a global transcriptomic response. This response includes changes in gene activities of oxidative/reductive pathways, ultimately switching cells towards reductive metabolism. Our discovery of ANTAR RNAs and their associated regulatory mechanisms classifies RNAs as crucial players in controlling the metabolic flexibility of mycobacteria and indicates that ANTAR RNA regulation may play a prominent role in metabolic processes across actinobacteria.

From photosynthesis to energy (ATP) production via the electron transport chain, fundamental cellular processes use iron for its ability to participate in redox reactions. Given its role as a cofactor for enzymes, iron is critical for many pathogens to survive and colonise their hosts. Our understanding of how cells directly sense iron has been limited to protein-based mechanisms. In recent work from my lab, we have discovered iron-sensing RNAs (named Sensei). These RNAs are ubiquitous in bacteria and reside in the 5'UTRs or coding regions of mRNAs encoding iron-related proteins. Sensei act as riboswitches, specifically binding reduced iron (Fe2+) to undergo

conformational changes that alter the accessibility of conserved nucleotides. This results in increased translation of the riboswitch-associated mRNA in vivo, thus positioning Sensei as true metallo-regulators. Our work brings to the fore two very important ideas: a) that coding regions of mRNAs themselves can respond to basic cellular metabolites, and b) that RNA motifs residing in the coding regions of mRNAs can act as hubs that integrate metabolites with protein synthesis.



Discovery of the ANTAR RNA family and their mechanism of action in mycobacteria. *A graphical summary of our work. Mehta et al. JMB, 2020.*

PUBLICATIONS

Dolly, M., Anjali, K., and Arati, R. ***Discovery of ANTAR RNAs and their mechanism of action in mycobacteria.*** *J. Mol. Biol, 2020 Jun 26;432(14):4032-4048.*

HONOURS AND AWARDS

HFSP-Human Frontier Science Program Grant Awarded *(March 2019 to 2022)*

DST-SERB Early Career Award *(March 2017 to 2020)*

Wellcome Trust-DBT India Alliance Intermediate Fellowship *(2015 to 2021)*

Regulation of DNA Damage Response and Repair

Cells constantly face the threat of DNA damage. Incorrectly repaired or unrepaired damage can lead to mutations, loss of genetic information, or even cell death. We study how DNA damage repair is regulated in microbial systems to ensure the maintenance of genome integrity.

Successful DNA repair requires three steps to occur accurately
(a) regulation of cell cycle to ensure that cells do not divide before repair has been completed
(b) repair pathway choice to ensure that the right pathway is employed to repair damaged DNA
(c) modulation of activity of error-free and error-prone repair systems to maintain genome integrity while also increasing chances of survival under stress.

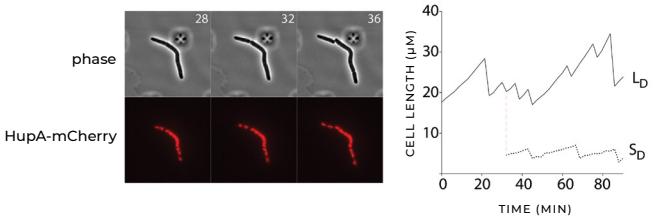
While repair pathways have been well studied in isolated contexts in vitro, little is known about their dynamics, mechanisms of action, and regulation in a living cell. To address these questions in an in vivo context, my lab employs live-cell imaging and novel genetic assays to introduce perturbations in the system. We primarily study genome integrity maintenance in bacteria, however, our recent work has also led us to investigate DNA damage response regulation in yeast mitochondria. Some questions we are currently working on are:

Damage response and cell cycle regulation
- *Understanding the bacterial adaptive response*
- *How is mitochondrial DNA damage sensed and DNA repair regulated?*

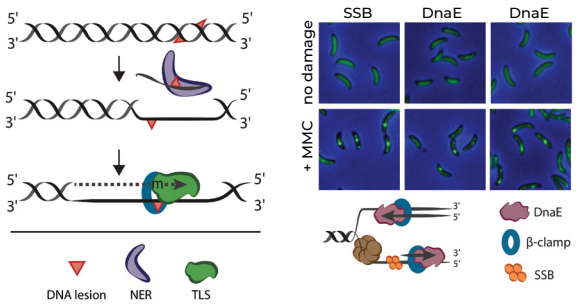
Repair pathway choice and regulation
- *Regulation of error-prone translesion synthesis and its crosstalk with other repair pathways in bacteria*
- *Mechanism of homology search: role of the SMC protein, RecN*
- *Bacterial stress responses in inter-microbial interactions - impact of DNA repair pathways*

Representative schematics and figures from some ongoing projects in the lab

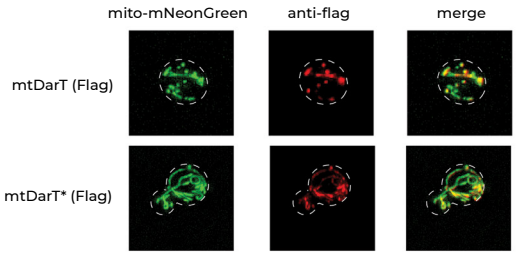
Regulation of DNA damage response:
asymmetric division during damage recovery



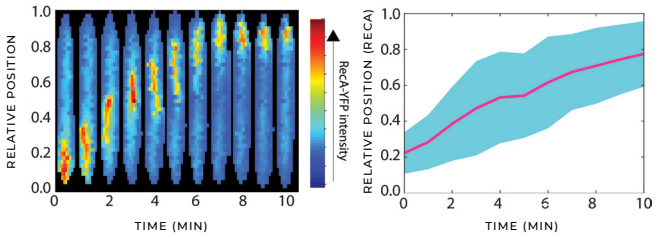
Regulation of cross-talk
nucleotide excision repair-mediated translesion synthesis



Tools to induce mitochondrial DNA damage



Mechanisms of homology search



PUBLICATIONS

Raghunathan, S., Chimthanawala, C., Vecchiarelli, A., Krishna, S., and Badrinarayanan, A.* ***Asymmetric chromosome segregation and cell division in DNA damage-induced bacterial filaments.*** *Mol Biol Cell (2020). mbc-E20-08-0547.*

Sharda, M., Badrinarayanan A., and Seshasayee*, A.* ***Evolution and conservation of the non-homologous end joining repair pathway in bacteria.*** *Genome Biol Evol (2020). gbe/evaa223.*

HONOURS AND AWARDS

Har-Gobind Khorana IYBA Award (DBT)

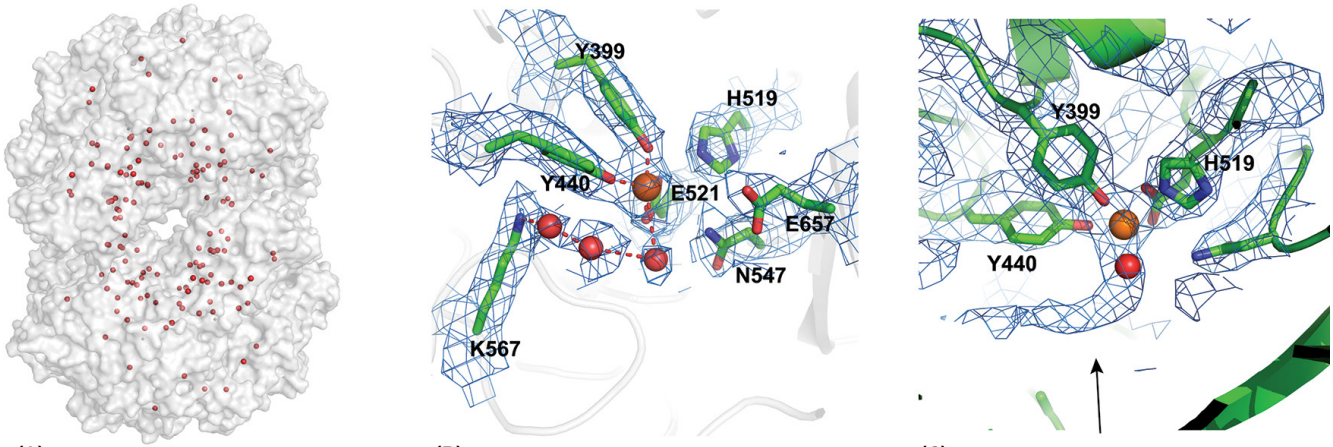
Structures of Macromolecules and Dynamics

In the crowded environment of the cell, macromolecules perform a wide range of functions and often are dynamic. We work on a wide range of biological problems to understand the function and dynamics of the macromolecules in the membrane, those that regulate translation and the enzymes that are involved in bioremediation.

Our broad interest lies in tackling challenging and interesting biological problems connected to membrane proteins and macromolecular complexes. We are currently working towards understanding the functioning of the rhomboid family of proteins, the mechanism of transport of molecules by ABC transporters (in particular, surfactants and retinal), the mechanism of peptide resistance in bacteria, mechano-transduction, and membrane junctions. We use a range of systems, from bacterial to eukaryotic cell lines, to express these proteins and characterise them biochemically and structurally using X-ray crystallography and electron cryo-microscopy (cryoEM).

Recent advances in cryoEM allow us to image macromolecules both in vitro and in many cases, in vivo within the cellular environment. To keep up with developments, we also employ proteins that are robust and easily amenable for testing in cryoEM with a focus on freezing and imaging. One such example is the enzyme, dimethylformamidase, which is produced by some bacteria to hydrolyse the environmentally hazardous compound, dimethyformamide. It is a robust enzyme with interesting properties and we have been able to achieve high-resolution with cryoEM (1) and are currently moving towards understanding the mechanism of how iron and water are used for catalysis (Figure 1).

Structure and mechanism of dimethylformamidase
(A) The resolution and quality of EM maps are now sufficient to build solvent molecules and thereby explain their function. The enzyme DMFase is shown in surface representation and the water molecules as red spheres. A clear symmetry in the modelled water molecules reflecting the enzyme can be observed (Vinothkumar et al 2020).
(B) The current best resolution of DMFase is ~2.4 Å and in this panel, the active site residues are shown in stick representation and iron and water molecules as spheres. Such networks are often essential for catalysis.
(C) In many maps of DMFase, extra density is observed in the active site. Shown here is a mutant that is inactive but with an intact iron-bound active site. The extra long density, marked with a black arrow, is seen in the EM map, an interesting feature but difficult to model at the moment.



(A) (B) (C)

PUBLICATIONS

Arya, C. A., Yadav, S., Fine, J., Casanal, A., Chopra, G., Ramanthan, G., Vinothkumar, K. R., and Ramaswamy, S., 2020. ***A 2-Tyr-1-Carboxylate Mononuclear Iron Center is the active site of Dimethylformamidase****. Angew.Chem.Int.Ed.Engl. V47, 868. DOI: 10.1002/anie.202005332*

Kumari, A., Kesarwani, S., Javoor, M. G., Vinothkumar, K. R., and Sirajuddin, M., 2020. ***Structural insights into actin filament recognition by commonly used cellular actin markers.*** *Embo J V10 3058.*

HONOURS AND AWARDS

EMSI Award for Excellence in Science (Life Science/Medicine), India

Deciphering Genetic and Molecular Alterations in Cancers

We are interested in understanding the genetic and molecular alterations responsible for cancer development and resistance to treatments, using computational and functional genomics approaches.

The DNA in the cells of our bodies contains all the information required to ensure correct cellular functioning. However, the accumulation of DNA alterations or mutations can cause cells to grow and divide in an uncontrolled manner to form tumours that may also metastasise. In order to prevent and treat any cancer, it is of paramount importance to fully understand the genetic and molecular basis of the disease; this includes identifying and understanding what gene(s) are affected by mutations and how they alter cellular functions.

We address these questions through the analysis of large-scale cancer genomics datasets (whole genomes, exomes, and transcriptomes) generated by national and international cancer genome projects, with a particular focus on the Indian population. We develop computational methods to integrate different levels of genomic information to identify genes and pathways that are altered due to mutations and may be likely drivers of cancer in individual patients (Figure 1).

In addition, we are also interested in understanding how three-dimensional chromatin architecture influences the somatic mutational processes and gene regulation in cancer. In particular, we aim to study why the boundaries of local chromatin structures, such as topologically associating domains (TADs) and chromatin-loops, are vulnerable to somatic mutations and whether those mutations can affect local chromatin structures and gene regulation that lead to cancer development (Figure 2).

FIGURE 1
The schematic diagram represents the multi-omics approach to identify cancer driver mutations in individual patients

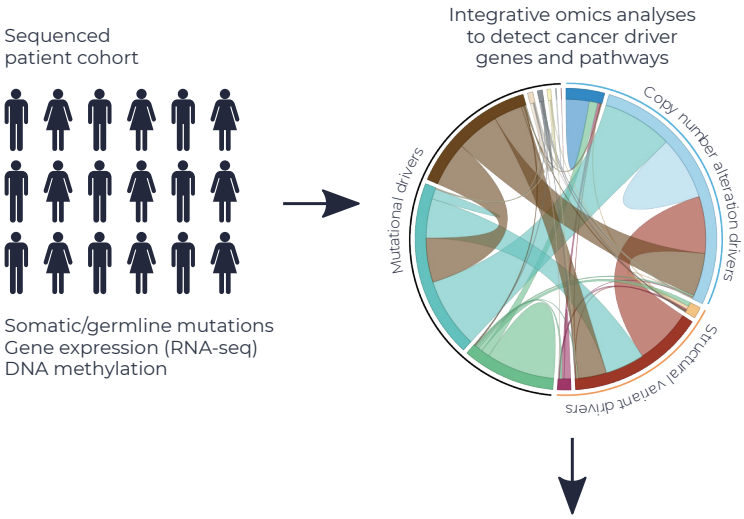
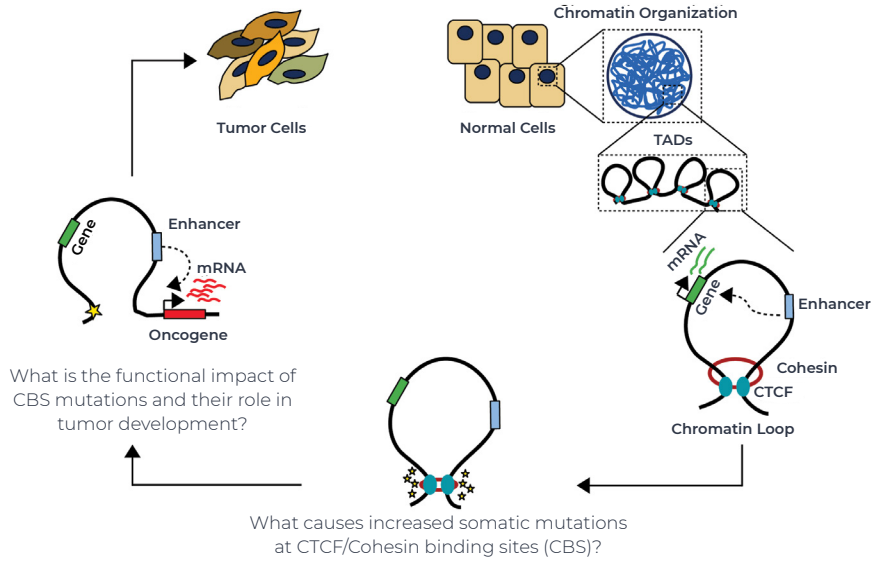


FIGURE 2
Understanding the impact of chromatin architecture on somatic mutational processes and gene regulation in cancer



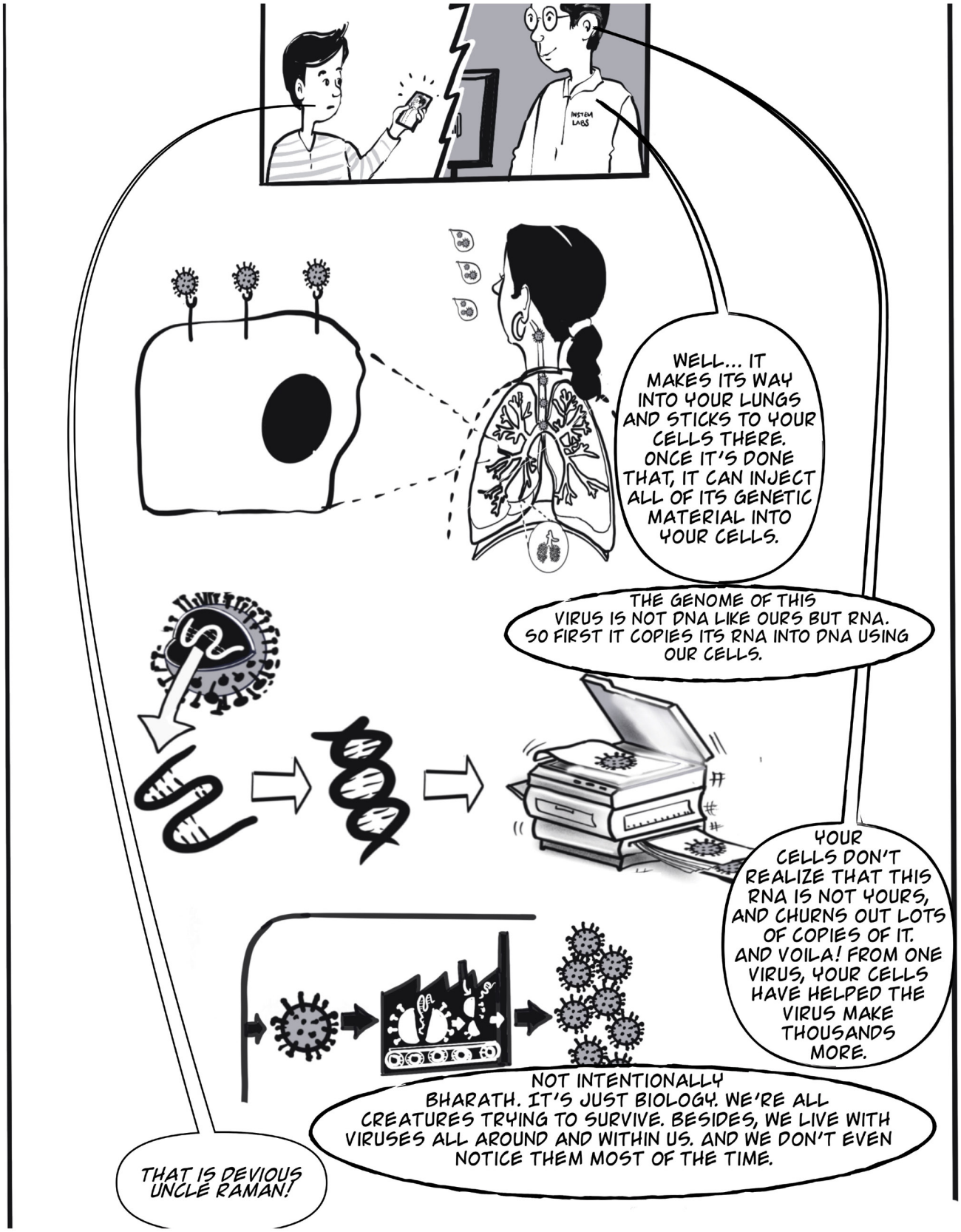
PUBLICATIONS

ICGC/TCGA pan-cancer analysis of whole genomes consortium. Pan-cancer analysis of whole genomes. *Nature, 578(7793):82-93, 2020. PMID: 32025007*

Walavalkar, K., Saravanan, B., Singh, A. K., Jayani, R. S., Nair, A., Farooq, U., Islam Z., Soota, D., Mann, R., Shivaprasad, P. V., Freedman, M. L., Sabarinathan, R., Haiman, C. A., and Notani, D. ***A rare variant of African ancestry activates 8q24 lncRNA hub by modulating cancer associated enhancer.*** *Nature Communications, 11(1):3598, 2020.*

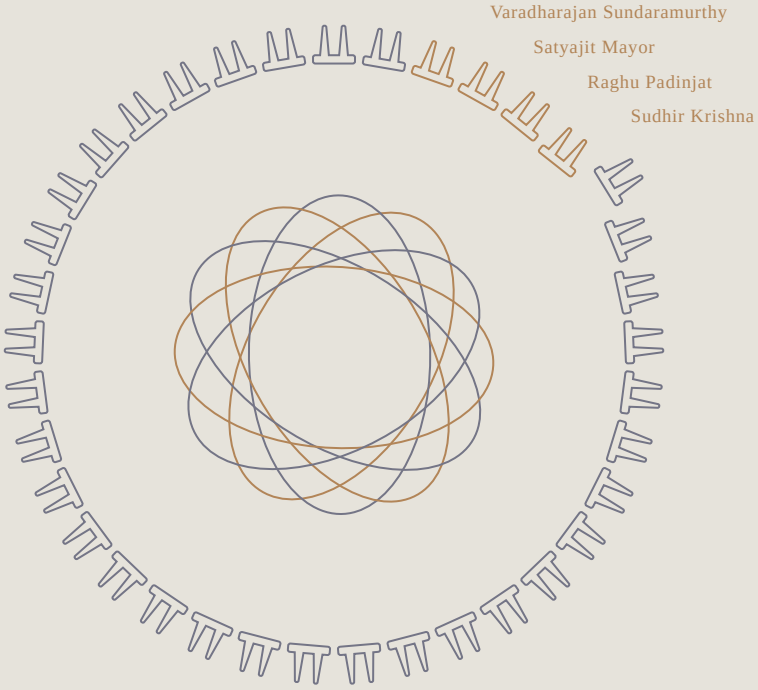
HONOURS AND AWARDS

DBT/Wellcome-Trust IA Intermediate Fellowship *(2020)*



These pages are excerpts from a series created, designed, and written, by Arvind Ramanathan of DBT-inStem and Sonia Sen from TIGS-CI. They are illustrated by Arvind Ramanathan as a part of the Cluster's COVID-19 Response Initiative. The work was originally published on www.covid-gyan.in

Varadharajan Sundaramurthy
Satyajit Mayor
Raghu Padinjat
Sudhir Krishna



Cellular Organisation and Signalling

Understanding Human Cervical Cancer Progression and Building a Biology–Medicine Interphase • Sudhir Krishna
Mechanisms of Membrane Organisation and Endocytosis • Satyajit Mayor
Phosphoinositide Signalling in Cell Biology • Raghu Padinjat
Biology of Host–Pathogen Interactions during Intracellular Infections • Varadharajan Sundaramurthy

Understanding Human Cervical Cancer Progression and Building a Biology-Medicine Interphase

Our group has two interests: (a) understanding the nature of human cervical cancer progression with a particular focus on notch signalling and therapeutic strategies for cancers, and (b) enabling inter-campus bio-medical efforts spanning diverse areas such as haematology, dengue vaccines, etc.

Human cervical cancers constitute a major part of malignancies in women in our country, and are caused by papillomaviruses of a highly oncogenic type. Our cumulative data over decades has led us to suggest that ligand-dependent notch pathway activation acts as a 'second signal' in human cervical cancer progression (Figure 1a) (reviewed in Maliekal T. et. al., Oncogene 2008). Subsequently, we have identified a subset of CD66+ cells with distinctive tumour-promoting properties that are dependent on notch signalling (Bajaj J. et al., Cancer Research 2011 and Pattabiraman C. et al., Cancer Research 2014). An analysis of recently published literature and available information on genetic changes in cervical cancers are consistent with notch pathway activation and amplification (Rodrigues et al., 2019). At present Sasikala P. (working on notch signalling) and PhD student Leanna Rose Joy's focus is to understand the role of cell extrusion. Nayim Paul is a PhD student supported by the DBT-TWAS Fellowship. He is working on natural products as a source of anticancer agents.

The group has also received a dengue-focused philanthropic grant from Shri Narayana Murthy. Under this project, we are investigating the genetic diversity profile of dengue viruses across India in order to integrate viral diversity and sequence information to build a novel vaccine against dengue. Taking forward the sequencing effort in developing vaccines against dengue, the team is also involved in DNA (Arun Sankaradoss, Junaid Nazir, and Meenakshi Iyer) and RNA (Swetha Raghavan and Pratik Lakhani) based vaccine development against dengue. Abhishek is a joint integrated PhD student between myself and Prof. R. Sowdhamini. His aim is to understand the effect of mutational landscape on dengue non-structural protein stability and functionality (Figure 1b).

Additionally, in our group several independent post-doctoral researchers are driving their own projects. Reety Arora developed an in vitro molecular diagnostic tool for MCV-positive MCC using a guided molecular scissors based-DNA Endonuclease Targeted CRISPR Trans Reporter (DETECTR) technique (Arora et al., 2020) (Figure 2a).

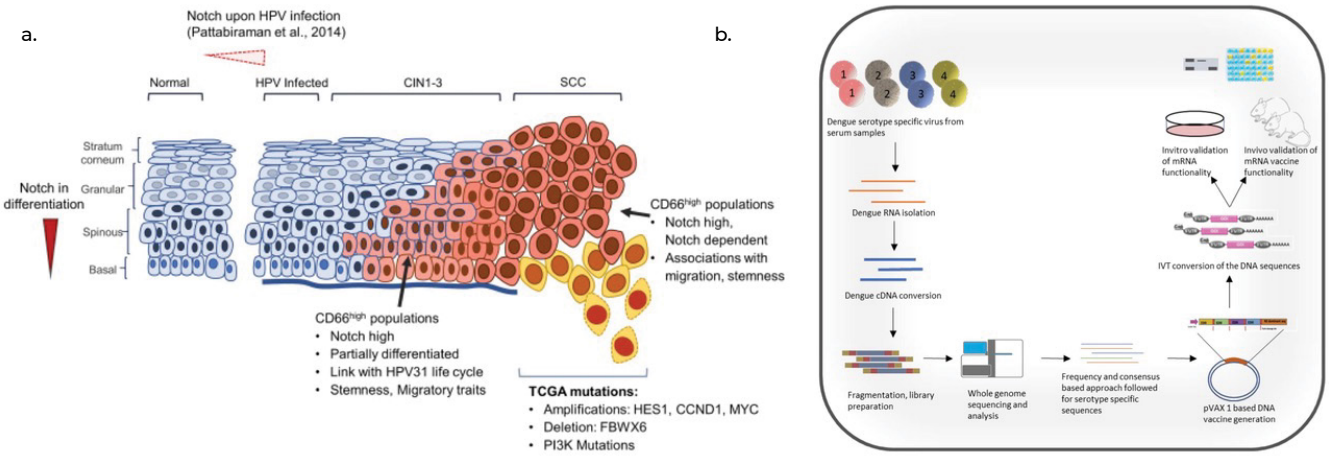


FIGURE 1
(a) Expression of notch and its targets during cervical cancer progression
(b) Vaccine strategy for dengue

Sanjukta Mukherjee in our group is developing RNA-targeted, small molecular therapeutics. She identified a small molecule that inhibits cervical cancer cell migration by targeting miRNA biogenesis. Her recent work analyses the effect of the ligand on cancer cell migration in vivo and elucidation of underlying molecular mechanism of regulation (Figure 2b).

Swetha Raghavan has two research interests; one is focused on exploring therapeutic resistance in gynaecological cancers and the other is to aid in the development of a potential nucleic acid-based vaccine platform (Figure 1b).

Anshika's research focus is (a) how filter-feeder marine sponges survive in the presence of deadly pathogens and environmental pollutants (such as microplastics), (b) how the sponge filtering system removes pathogens and microplastics from water thereby inspiring filter-making for water purification and, (c) to understand mechanistic effects of pathogen and microplastics pollution on different species of marine sponges, to establish them as the biomonitors of overall health of the marine environment (Figure 2c).

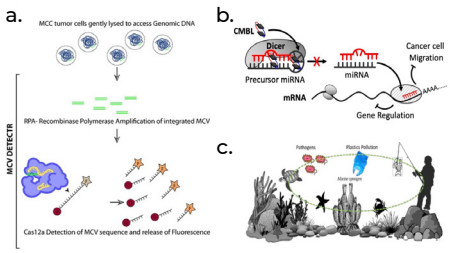


FIGURE 2
(a) Schematic summarising MCV DETECTR
(b) Schematic representation of CMBL mediated regulation of miRNA biogenesis for development of miRNA targeted cancer therapy
(c) Sponge Watch Programme: An initiative towards one ocean, one health concept

PUBLICATIONS

Arora, R., Gupta, K., Vijaykumar, A., and Krishna, S., 2020. ***Detecting Merkel cell polyomavirus in Merkel tumors.*** *Frontiers in Molecular Biosciences, 7, Article 10.*

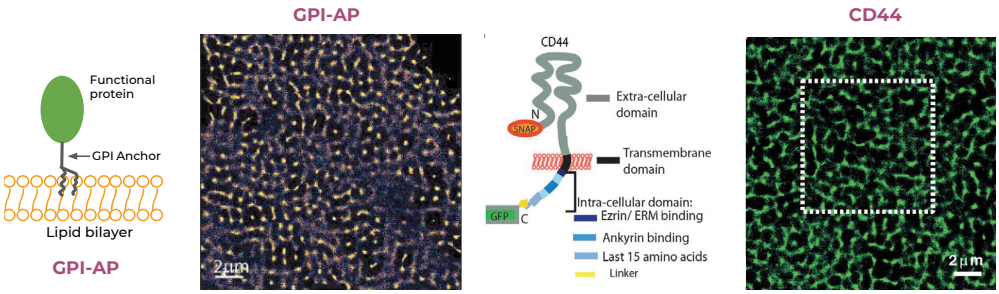
Rodrigues, C., Joy, R. S., Sasikala, P. S., and Krishna, S., 2019. ***Notch signaling in cervical cancer.*** *Experimental Cell Research (Review), 385, 111682.*

Mechanisms of Membrane Organisation and Endocytosis

The principal focus of our laboratory is to uncover the physico-chemical rules that govern local organisation of the cell membrane in a living cell, and connect this to cellular and organismal physiology. Specifically, we ask: How does the cell build functional signalling complexes at the plasma membrane? What are the requirements to create a responsive endocytic platform?

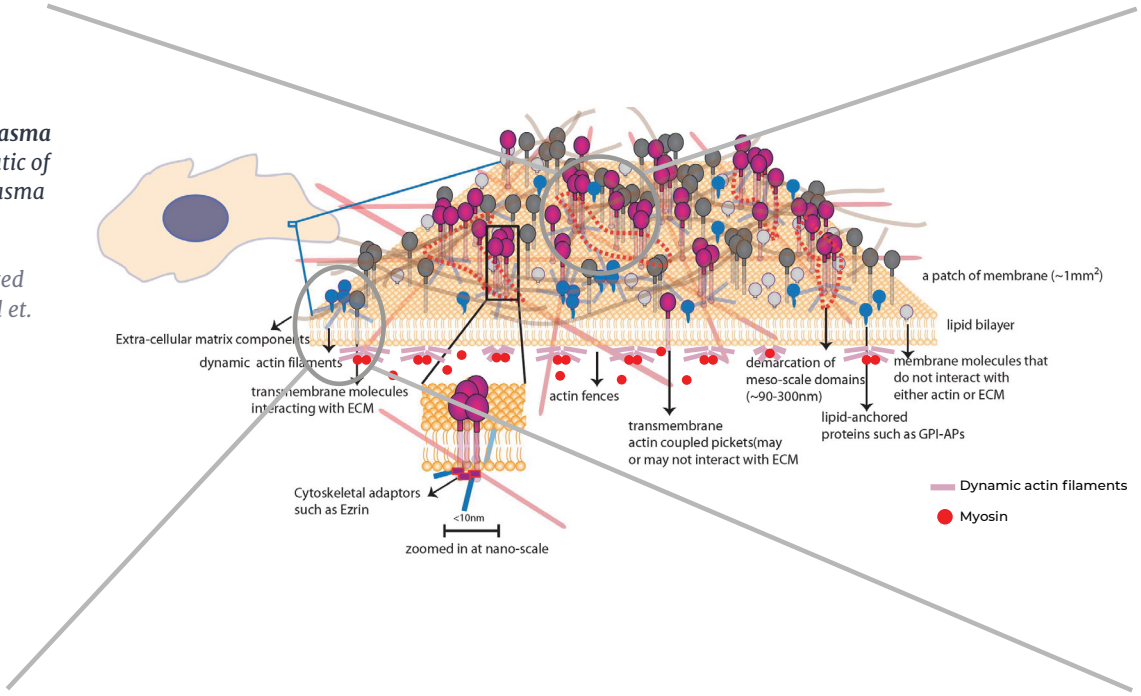
The plasma membrane is not a homogeneous, passive boundary of a cell, but a macromolecular assembly teeming with activity and local heterogeneities. It is the hub of signalling processes mediating bilateral information transfer and endocytic activities. Our laboratory studies how local membrane heterogeneities arise and how endocytic trafficking is regulated. Our studies provide a compelling picture of the cell membrane as an active composite of the lipid bilayer with a dynamic cortical actin layer beneath, wherein, dynamic actin filaments help in controlling the local composition of the membrane, and endocytic processes help to regulate global composition and tension in the membrane.

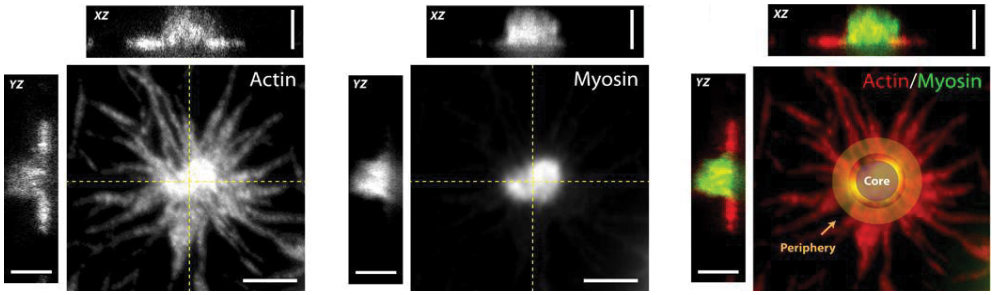
While working towards understanding the physiological functions of the membrane we study organising principles of membrane components at different length scales. We have investigated the organisation and dynamics of a transmembrane cell adhesion protein CD44, using various super-resolution microscopy techniques. We found that the dynamic actin cytoskeleton patterns CD44 at both the nano (~10 nm) and the mesoscale (100-300nm), arising from the interplay between diffusion and clustering behaviour of the protein [1]. We have also utilised a combination of theoretical approaches and in vitro reconstitution to study the role of the actomyosin cortex that leads to clustering of membrane components. Using STED microscopy, we found that actin filaments and myosin II mini-filaments are stratified in a quasi 3D environment. This arrangement of cytoskeletal components relieves steric constraints imposed by the physical size of components and permits tight actomyosin based asters at the membrane cortex [2].



Actomyosin mediated mesoscale organisation of CD59 (GPI-AP) and CD44 (TM protein) visualised using Single Particle tracking. *Adapted from Sil, P., Mateos, N., et. al. 2020.*

Active composite plasma membrane. *Schematic of active composite plasma membrane model and its hierarchical organisation. Adapted from Kalappurakkal et. al. 2020.*





Actin and myosin themselves are organised in a stratified manner. *STED Microscopy imaging reveals the stratified arrangement of actin and myosin II filaments in a quasi 3D environment. Adapted from Das, A., Bhat, A., et. al. 2020.*

PUBLICATIONS

[1] Sil, P., Mateos, N., et al. 2020. ***Dynamic actin-mediated nano-scale clustering of CD44 regulates its meso-scale organization at the plasma membrane.*** *Mol Biol Cell, Vol. 31, No. 7.*

[2] Das A., Bhat A., et al. 2020. ***Stratification relieves constraints from steric hindrance in the generation of compact actomyosin asters at the membrane cortex.*** *Sci Adv, Vol. 6, no. 11, eaay6093. DOI: 10.1126/sciadv.aay6093*

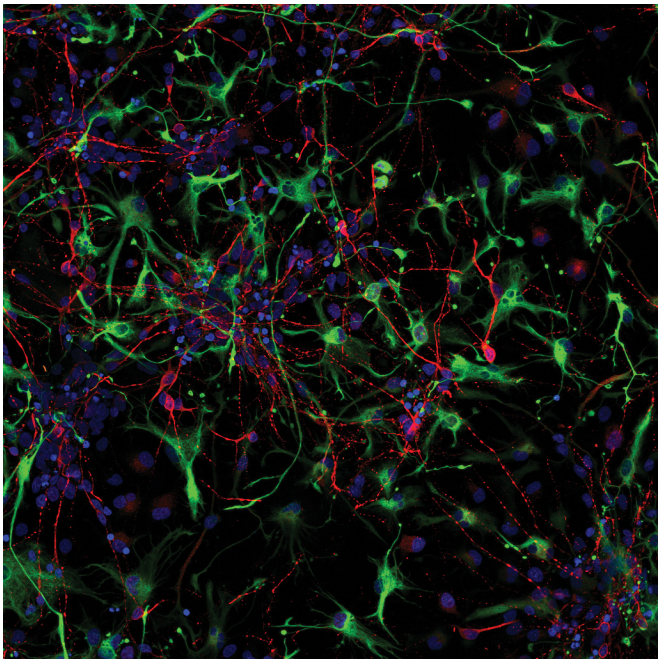
Phosphoinositide Signalling in Cell Biology

Chemical messengers derived from the lipid phosphatidylinositol are part of an evolutionarily conserved mechanism of cell signalling. These molecules regulate key cellular and biological processes in eukaryotes. We study the logic underlying lipid signalling and its relevance to biomedical science.

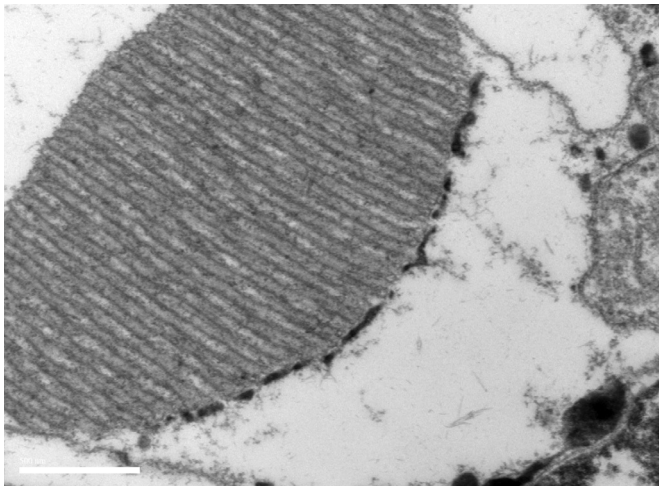
Our long-term scientific interest is to understand cellular communication mediated by lipid molecules generated by the metabolism of phosphatidylinositol. Phosphoinositide signals provide molecular control for key subcellular processes such as membrane remodelling, cytoskeletal function, transcription, and translation. Through these processes, this signalling pathway orchestrates basic cellular behaviours such as cell division, shape changes, polarised movement, and cell death; and these behaviours play key roles in a number of physiological processes including early embryogenesis, lymphocyte development and function, as well as neuronal activity.

The overall goal of our work is to understand how the architecture in this signalling cascade is designed to optimally deliver physiological outputs. The work is multidisciplinary and done using a combination of Drosophila and human disease models. Over the last year, we have uncovered the function of key enzymes that regulate lipid signalling and provided a molecular mechanism by which they control cellular processes. These include the mechanism by which lipid molecules are exchanged between cellular compartments, the control of membrane turnover and receptor activity by lipids, and a quantitative model of the turnover of lipids during critical cell signalling reactions important for brain function.

We also study the function of phosphoinositides in neuronal cell biology and brain disorders using human iPSC-derived neural cells in cell culture. The goal of this work is to uncover the function of altered phosphoinositide signalling in brain disorders.



In vitro culture of neural cells differentiated from a human induced pluripotent stem cell line (hiPSC). *Astrocytes are marked with an antibody to the glial cell marker (GFAP-green) and neurons are marked with an antibody to the neuron specific MAP2 protein (red). Nuclei stained blue with DAPI.*



Scanning electron micrograph of a photoreceptor from the adult Drosophila eye. *The apical domain plasma membrane is shown expanded into microvillar folds collectively called the rhabdomere. The sub-microvillar endoplasmic reticulum stained in black is shown in close apposition to the rhabdomere membrane forming a membrane contact site.*

PUBLICATIONS

Nath, V. R., Basak, B., Mishra, S., Trivedi, D., and Raghu, P., 2020.* ***Extended synaptotagmin regulates membrane contact site structure and lipid transfer function in vivo.*** *EMBO Reports. 27 July. e50264. https://doi.org/10.15252/embr.202050264*

Sharma, Y., Saha, S., Joseph, A., Krishnan, H., and Raghu P., 2020.* ***In vitro human stem cell derived cultures to monitor calcium signaling in neuronal development and function.*** *Wellcome Open Res. 2020 Feb 3;5:16. doi: 10.12688/wellcomeopenres.15626.1. eCollection 2020. PMID: 32195361*

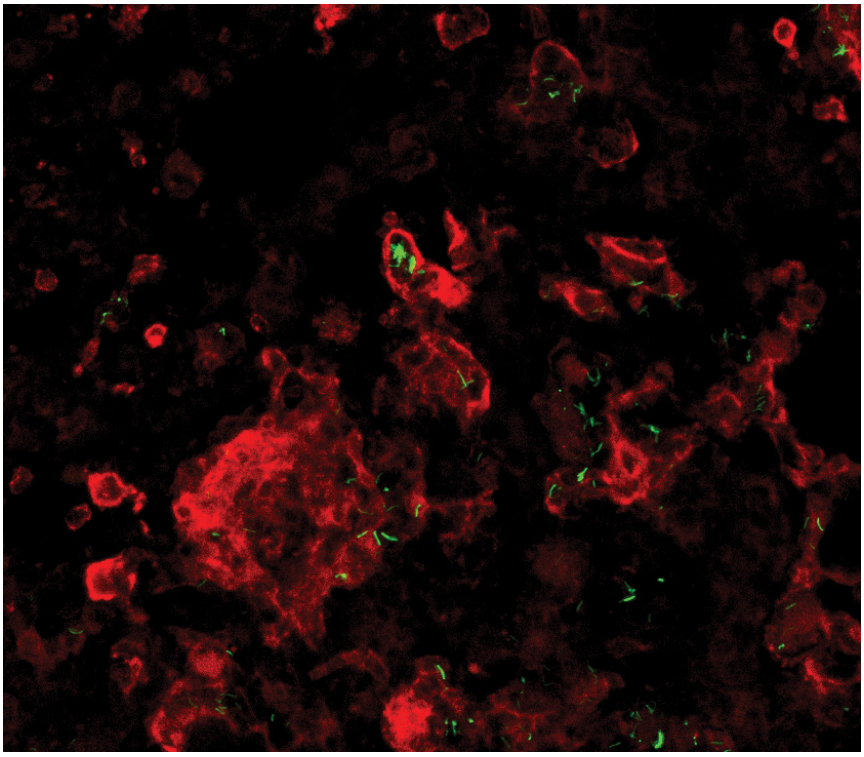
Biology of Host-Pathogen Interactions during Intracellular Infections

The broad goal of our lab is to understand the interactions between intracellular pathogens and host cells, with particular interest in the modulation of host trafficking pathways. We combine cell biological methods, high content imaging, and computational approaches with conventional cell and molecular biology to address these questions.

My lab works on host-pathogen interactions, specifically, on how fundamental host cellular processes such as endocytosis, autophagy, and polarity are modulated by intracellular infections. The lab focus is on two distinct pathogens: (a) M. tuberculosis, which causes tuberculosis, and (b) the liver stage of Plasmodium spp., that cause malaria.

Our aim is to combine quantitative image analysis from 2D, 3D, and live-cell imaging with conventional tools of cell and molecular biology to explore the relationships between the two pathogens with their host systems at molecular, cellular, and tissue levels. Recent results show that both pathogens cause global alterations in the organisation and dynamics of the host cell endocytic network. These alterations include sub-cellular redistribution of specific endosomal pools and an increase in the numbers and contents of distinct endosomal populations specifically in the infected cells. In case of M. tuberculosis infections, the endosomal system influences the infectivity of the pathogen, and lysosomes distinctly modulate the intracellular survival of the pathogen.

In some cases, abrogation of these alterations by chemical treatment results in killing of the pathogen, suggesting the importance of these changes in pathogenesis mechanisms. These results provide further support for host-directed therapeutics against infectious diseases. Alternatively, modifying the endolysosomal pathways in different ways results in elevated levels of pathogens in cells. Thus, the host-pathogen interface represents a finely nuanced space where two dynamic systems reciprocally influence each other. Current work in the lab is centred in addressing specific examples of these interferences.

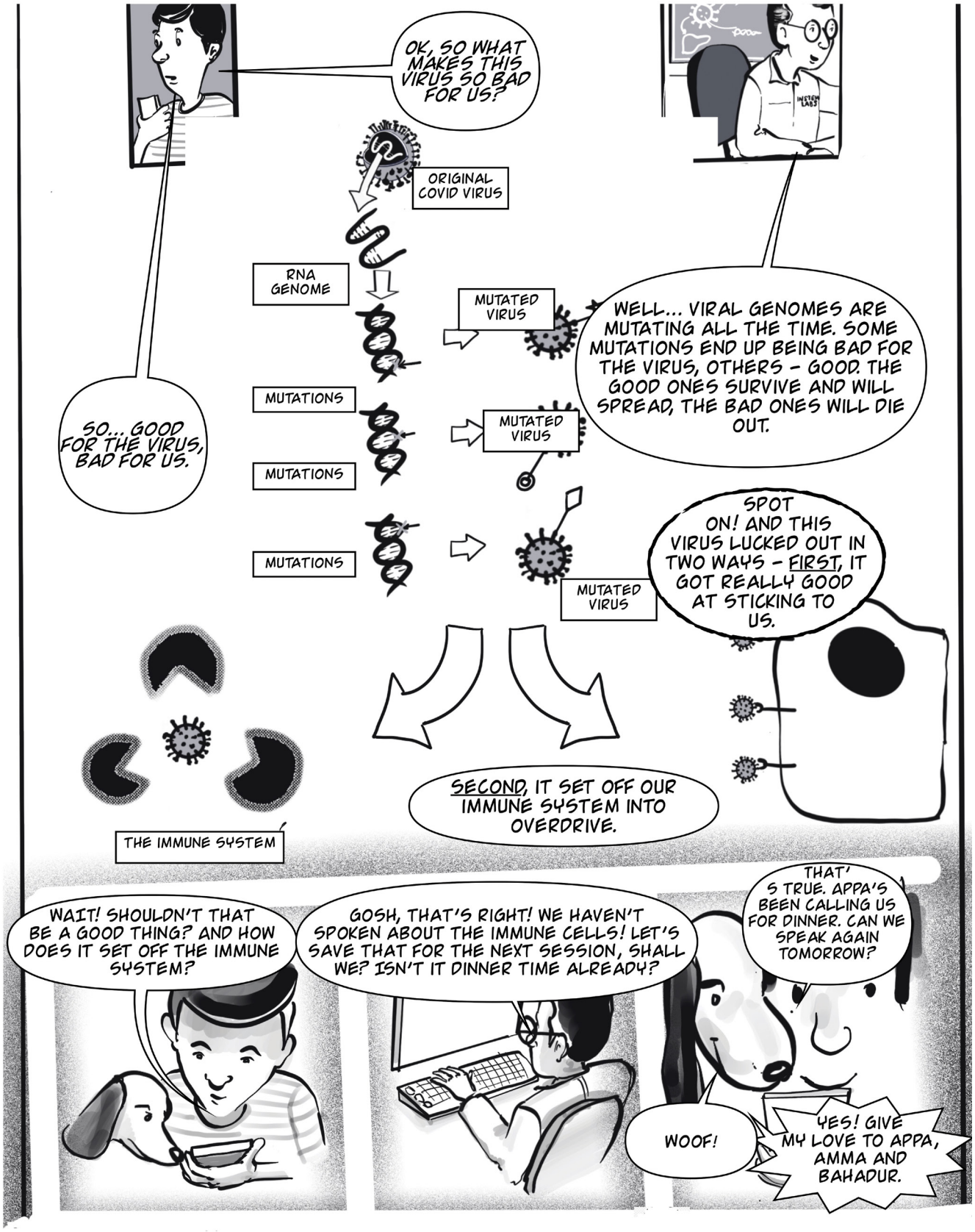


Tissue section from mice infected with M. tuberculosis expressing GFP and immunostained for the macrophage surface marker CD11b (red)

PUBLICATIONS

Sachdeva, K., Goel, M., and Sundaramurthy, V. ***Heterogeneity in the endocytic capacity of individual macrophage in a population determines its subsequent phagocytosis, infectivity and subcellular trafficking.*** *Traffic. 2020 Aug;21(8):522-533.*

Sachdeva, K., Goel, M., Sudhakar, M., Mehta, M., Raju, R., Raman, K., Singh, A., and Sundaramurthy, V. ***Mycobacterium tuberculosis (Mtb) lipid mediated lysosomal rewiring in infected macrophages modulates intracellular Mtb trafficking and survival.*** *J Biol Chem. 2020 Jul 3;295(27):9192-9210.*



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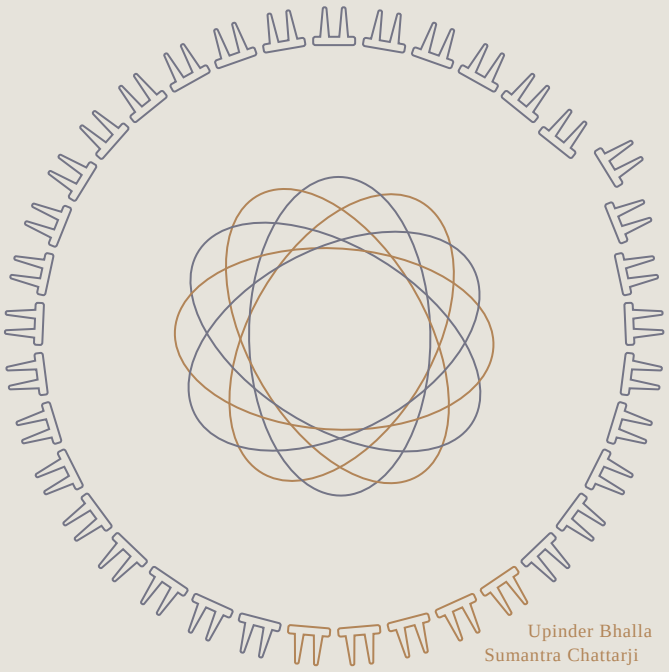


Upinder Bhalla
Sumantra Chattarji
Sanjay Sane
Vatsala Thirumalai
Hiyaa Ghosh

Neurobiology

Multiscale Signal Flow in Brain Computation and Memory • Upinder Bhalla
Effects of Stress Distributed across Neural Networks: The Amygdala and Beyond • Sumantra Chattarji
The Physics, Neurobiology, and Ecophysiology of Insect Flight • Sanjay Sane
Development, Modulation and Function of Motor Systems • Vatsala Thirumalai
Cellular Mechanisms Governing Brain Homeostasis and Neuroinflammation • Hiyaa Ghosh

Multiscale Signal Flow in Brain Computation and Memory

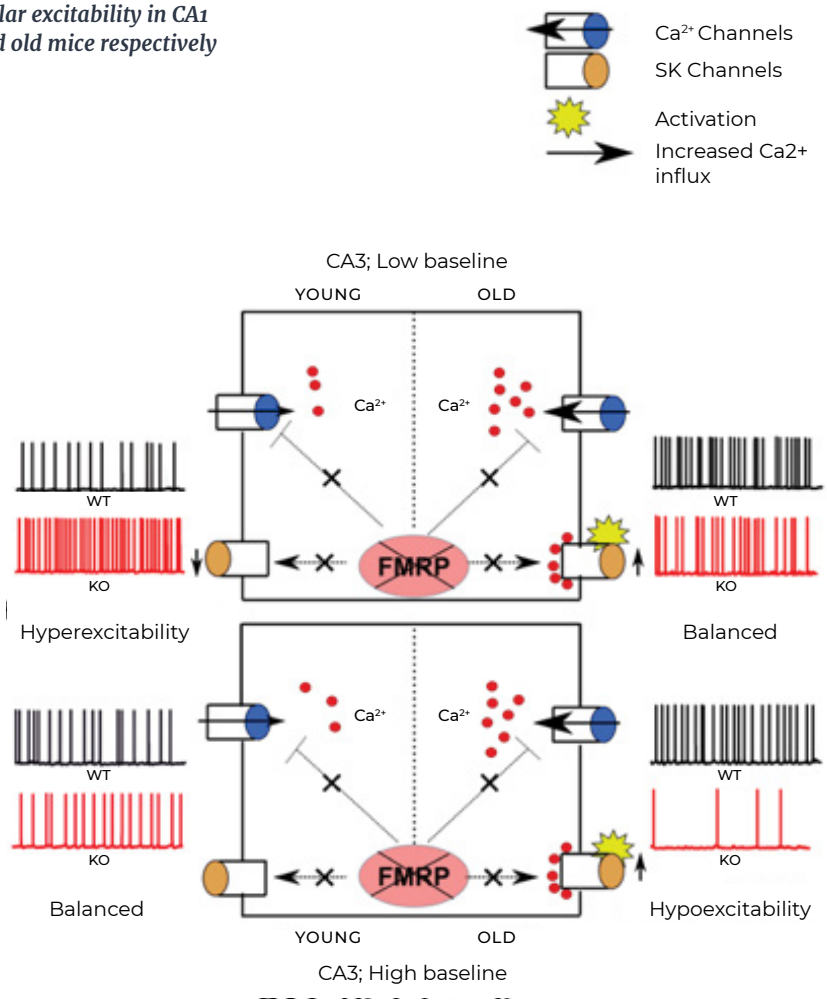
We use in vivo and in vitro optical and electrical recordings as well as multiscale computer models to understand sequence recognition and memory as fundamental computations in the brain. We develop tools for rigorous, experiment-driven neural models in health and disease.

In vivo, we use 2-photon imaging to monitor hippocampal activity from hundreds of neurons to watch how sequences form when mice learn to associate stimuli separated in time. This provides a window into brain computation and memory.

In vitro, we use optogenetics to deliver precise patterned stimuli to the hippocampal network to analyse how background activity influences synaptic plasticity. We perform single-cell patch recordings to study plasticity, summation, and balance between excitatory and inhibitory inputs. We also analyse the physiological differences that arise due to the Fragile-X mutation.

In silico, we have developed an array of tools for building data-driven models of brain function in health and disease. Together, these provide a resource for codified primary data, for models, and for the entire parameter analysis and optimisation pipeline that connects data to models (https://findsimweb.ncbs.res.in). All our tools and data are open sourced and use standard formats such as SBML and NeuroML. We have used these tools to develop detailed models of synaptic plasticity, subcellular sequence recognition, and activity-triggered protein synthesis in synapses with particular relevance to autism. We have specific projects on the mechano-chemical basis for dendritic spine formation, sequence propagation in networks (with Arvind Kumar, KTH) and on the robustness of bistable chemical switches.

Schematic of effects of Fragile-X mutation on cellular excitability in CA1 and CA3 regions of hippocampus, and in young and old mice respectively



PUBLICATIONS

Dwivedi, D., Chattarji, S., and Bhalla, U. P., 2019. ***Impaired reliability and precision of spiking in adults but not juveniles in a mouse model of Fragile X Syndrome.*** *Eneuro 6 (6).*

HONOURS AND AWARDS

SASTRA Obaid Siddiqi Award in Life Science

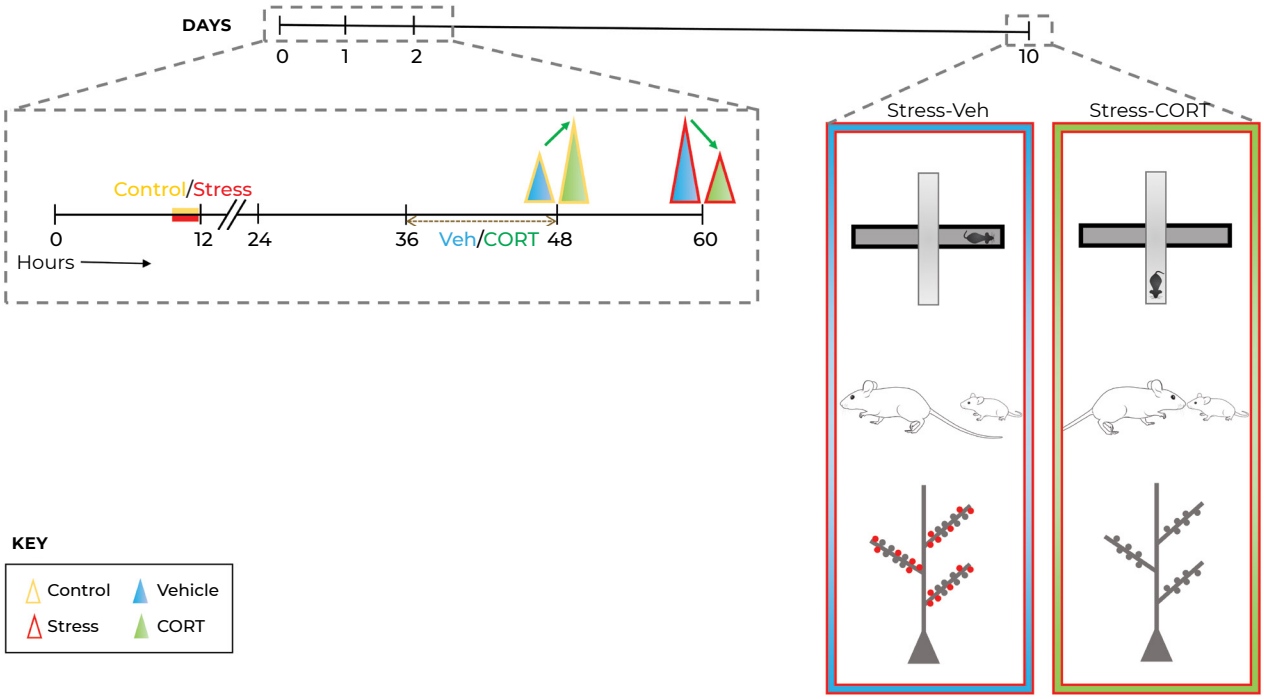
Effects of Stress Distributed across Neural Networks: The Amygdala and Beyond

Debilitating emotional problems are a hallmark of stress-related psychiatric disorders. We use animal models to explore the neural basis of these phenomena in the brain's emotional hub, the amygdala, from molecular and synaptic mechanisms at one end, to their behavioural consequences at the other.

All memories are not created equal – some are more equal than others. For instance, emotionally salient experiences tend to be well-remembered, and the amygdala plays a central role in this process. But the rapid and robust encoding of emotional experiences, such as aversive memories, can become maladaptive; traumatic or prolonged stress often turns them into a source of debilitating anxiety. What are the neural mechanisms underlying these powerful emotional symptoms? To answer this question, we combine a range of behavioural, morphometric, molecular, and electrophysiological techniques to analyse stress-induced modulation of neuronal structure and function in the amygdala. We have identified unique features of stress-induced plasticity in the amygdala, which are strikingly different from those seen in the hippocampus, and could have long-term consequences for behavioural symptoms seen in affective disorders.

In earlier studies, stress-induced plasticity in different brain regions was viewed as a stand-alone effect, manifested as properties intrinsic to individual structures. Further, function was inferred from analysis at the cellular and behavioural levels without any online readout of dynamic changes in neuronal activity in the intact animal. However, neuroanatomical data also points to extensive interconnections between the hippocampus and amygdala. This raises the intriguing possibility that some of the structural and physiological changes triggered by stress in one brain area may, at least in part, influence changes in other areas. Therefore, we are using in vivo recordings in freely behaving animals to investigate the potential interdependence and interactions between brain areas differentially affected by stress.

Previous work from our laboratory showed that when rats are exposed to a brief 2-hour immobilisation stress, it triggers enhanced anxiety-like behaviour and the formation of new synapses in the basolateral amygdala, not one day, but 10 days later. This delayed build-up of morphological and behavioural effects offers a stress-free time window of intervention after acute stress, which we used in a recent study (Chakraborty et al., Neuropsychopharmacology 2020). We show that administration of corticosterone (CORT) via drinking water 24 h after stress (H36–48) decreases stress-induced increase in systemic CORT concentrations measured 24 h later (H60), and importantly, blocks the delayed behavioural and synaptic changes 10 days after acute stress. On the other hand, in non-stressed rats, the CORT administration paradigm increases CORT to levels comparable to those observed after stress, relative to vehicle-treated non-stressed rats (H48). Triangles depict systemic CORT concentrations. These findings are relevant to clinical observations wherein human subjects given cortisol infusions immediately after traumatic stress show a significant reduction in symptoms of post-traumatic stress disorder (PTSD). Adapted from Yasmin & Patel, doi.org/10.1038/s41386-020-00796-4



PUBLICATIONS

Yasmin, F., Colangeli, R., Morena, M., Filipski, S., van der Stelt, M., Pittman, Q. J., Hillard, C. J., Teskey, G. C., McEwen B. S., Hill M. N., and Chattarji, S., 2019. ***Stress-induced modulation of endocannabinoid signaling leads to delayed strengthening of synaptic connectivity in the amygdala.*** *Proc. Natl. Acad. Sci. USA DOI: 10.1073/pnas.1910322116.*

Chakraborty, P., Datta, S., McEwen, B. S., and Chattarji, S., 2020. ***Corticosterone after acute stress prevents the delayed effects on the amygdala.*** *Neuropsychopharmacology org/10.1038/s41386-020-0758-0.*

HONOURS AND AWARDS

Elected Associate Member of European Molecular Biology Organization (EMBO) *(2020)*

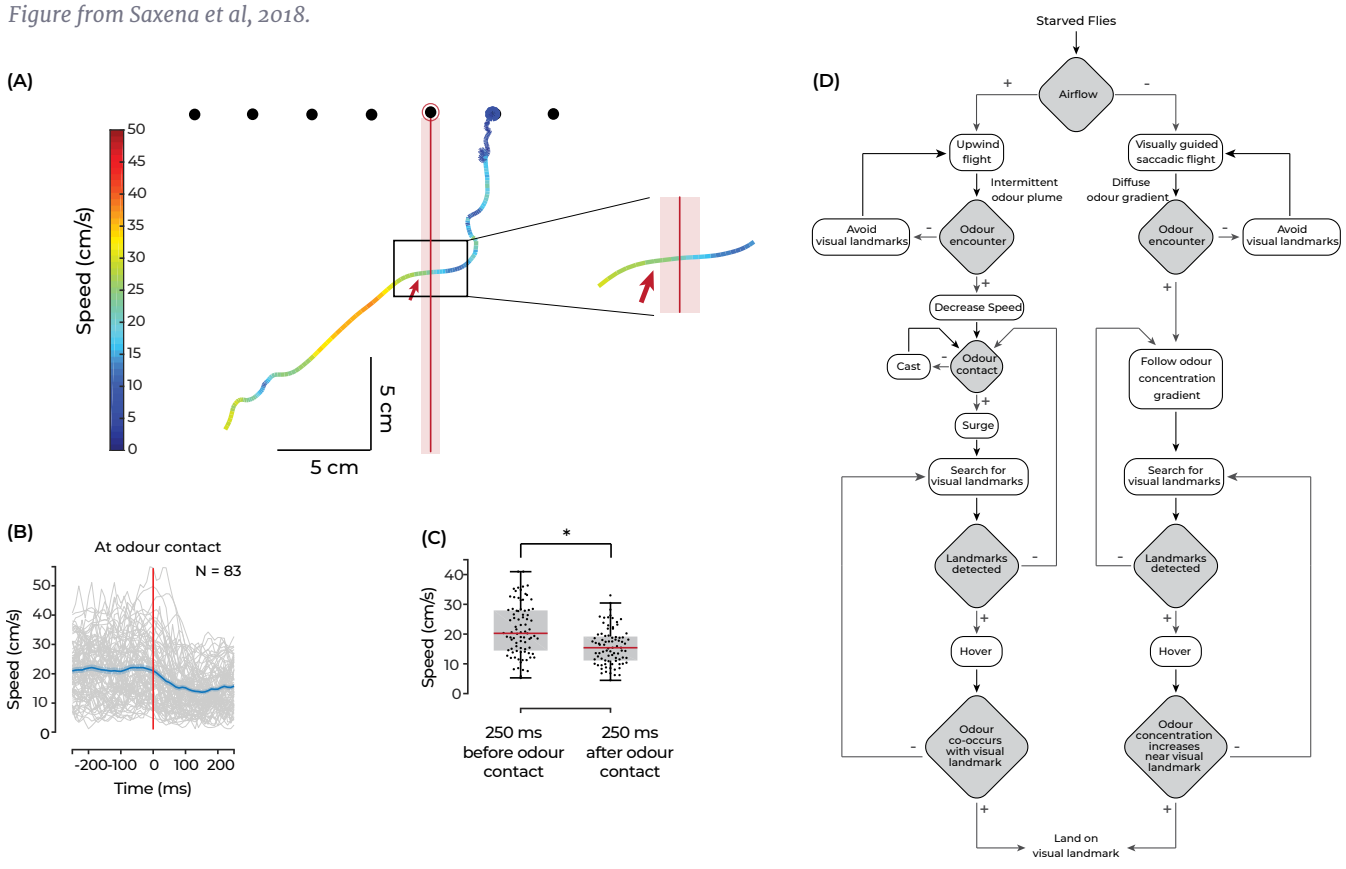
The Physics, Neurobiology, and Ecophysiology of Insect Flight

My laboratory studies the physical, neural, and ecological basis of insect flight and insect architecture. We study diverse flight-related behaviours including fast aerial manoeuvers, territorial chases, short-distance navigation tasks (such as foraging or odour-source localisation), long-distance migration, and also the fascinating intricacies of individual and collective insect nest-building.

Insect flight is an extraordinary feat of evolution. Insects were the first animals to evolve flight and have maintained their mastery over the aerial habitats. Across various scales of size and neural complexity, insects fly with exquisite speed, control, and maneuverability. Their wings flap rapidly—often at frequencies of several hundred beats per second—each wing stroke finely controlled by a sensorimotor system that acquires and processes information at similarly rapid rates. Sensory input is acquired by visual, olfactory, mechanosensory, hygro-, and thermo-sensory organs, and is communicated to the central nervous system, which then generates appropriate motor responses in the form of head, leg, and wing movements. To understand the mechanistic details of even the most mundane observations about flying insects (e.g. flies chasing other flies, moths hovering on flowers, dragonflies or hoverflies guarding territories, etc.), we must conduct a multi-disciplinary study of the entire chain of events from sensory input to motor output and flight force generation.

My laboratory combines inputs from physics, engineering, biomechanics, neurobiology, muscle mechanics, and behavioural biology to address diverse flight-related phenomena. We are also interested in how the flight system of insects adapts to the miniaturisation of their body size. In addition to flight, we study complex nest-building behaviour in insects, which involves intricate coordination of their movements at the individual and collective levels.

Odour encounter modulates the speed of flies
(A) Sample trajectory of a fly following an odour contact with the plume (red bar of 1.6 cm width), and an enlarged view (inset). Colours represent speed (see colour bar). (B) Speed at first odour contact shown in a 500 ms window centered on the likely odour contact (250 ms before and 250 ms after odour contact). N=120. Individual speed–time curves (gray) are overlaid by mean (blue) and s.e.m. (light blue) (N=83). To avoid confounding effects of speed changes due to landing responses, only flies that encountered the odour at least 4 cm before landing were used in the analysis. A decrease in flight speed was observed less than 100 ms after the first odour encounter, but not in regions before or after the first odour encounter. (C) Mean speed after the first odour encounter was significantly lower than speed before the encounter. (D) Flowchart of odour-tracking strategies in flies. A flowchart synthesised from previous literature and the current study showing distinct strategies employed by flies in the presence (left) or absence (right) of airflow. + signifies the presence and – the absence of the associated cue. Gray diamonds show sensory cues and open rectangles show motor responses. Figure from Saxena et al, 2018.



PUBLICATIONS

Natesan, D., Saxena, N., Ekeberg, O., and Sane, S.P., 2019.* ***Tuneable reflexes control antennal positioning in flying hawkmoths.*** *Nature Communications 10 (1), 1-15*

Balebail, S., Raja, S. K., and Sane, S. P., 2019.* ***Landing maneuvers of houseflies on vertical and inverted surfaces.*** *PloS one, 14(8), e0219861.*

HONOURS AND AWARDS

Selected for the Japan Society for Promotion of Science Invitational Fellowship *(2020)*

Selected as an Editor of the Journal of Experimental Biology *(2020)*

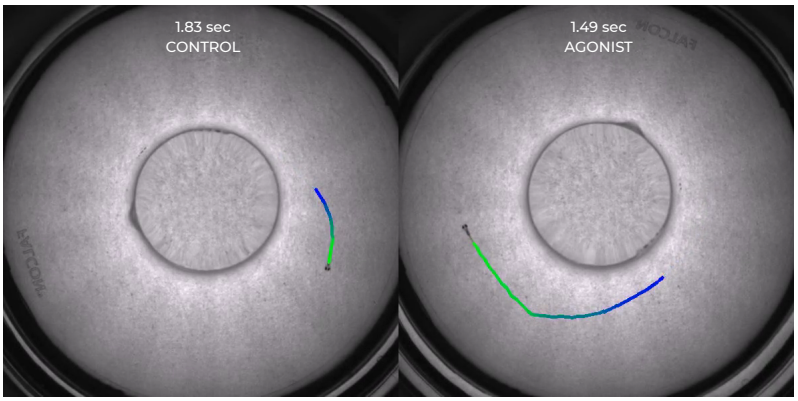
Development, Modulation, and Function of Motor Systems

In vertebrates, locomotion is generated by multiple circuits in the brain and spinal cord acting in a coordinated fashion. We study how these circuits assemble and how they function at all stages of life.

In vertebrates, the circuits that control movement are found in the spinal cord and in the brain. My lab focuses on the function and development of brain circuits that control locomotion. We use zebrafish, a small freshwater tropical fish endemic to the Ganges, as our model system. The embryonic and larval stages of these fish are transparent, allowing for direct visual observation of developing internal organs including the brain. We employ a suite of techniques to tease out the circuitry responsible for generating swimming in developing and more mature zebrafish. We record electrical activity from individual neurons using extracellular and whole-cell patch clamp techniques. We record activity from populations of neurons simultaneously using calcium imaging. We generate transgenic zebrafish to express proteins of interest in particular neurons. This allows us to selectively ablate and also to electrically activate/inactivate specific populations at will. Our work aims to understand how sensory inputs are integrated by disparate circuits in the optic tectum, cerebellum, hindbrain, and spinal cord to generate appropriate locomotor behaviour.

Using these cutting-edge tools, we have begun studies looking at circuits in the cerebellum. We have discovered dynamical properties of cerebellar Purkinje neurons and demonstrated the significance of these properties for locomotion. We have established that gap junctions are crucial for cerebellar circuit assembly. Currently, we are exploring the synaptic information transfer and neuromodulation of this circuit. Further, we are also probing the properties of eurydendroid cells, which are downstream targets of Purkinje neurons. Additionally, we are exploring how spinal motor circuits control the speed of locomotion. We showed that activation of D1-like dopamine receptors increases the speed of swimming in larval zebrafish by recruiting additional motor neurons (Figure 1). Previously it has been shown that sensory feedback and locomotor drive from the brain can increase or decrease speed by acting on spinal central pattern generating circuits (CPGs). Our study adds to this framework by conclusively proving that speed can also be controlled at the level of motor neurons, which are the final relay station of the nervous system (Figure 2).

FIGURE 1



Activation of D1 receptors increases swim speed during an innate behavioural reflex in larval zebrafish. *(top) A freely swimming larva placed in normal water responds to radially moving gratings by executing slow swims. The same larva, placed in water containing D1 receptor agonist increases swim speed dramatically. (bottom) Fictive swim rhythms recorded in larvae under similar conditions, show the frequency of the swim rhythm to be unaltered, but the amplitude, reflective of motor neuronal firing intensity, has significantly increased.*

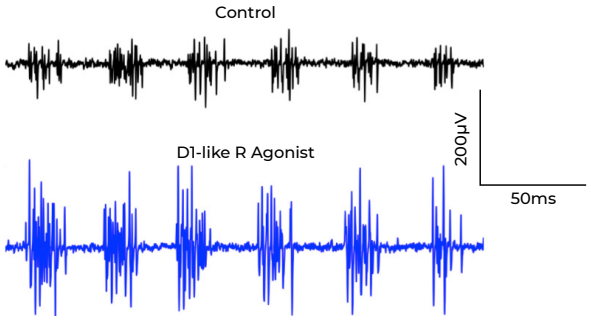
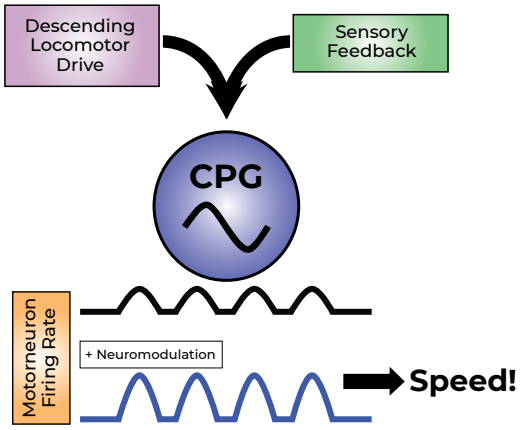


FIGURE 2

A general principle for speed control. *Previous studies show that descending locomotor drive and sensory feedback can control speed by modulating the frequency of the locomotor rhythm generated by central pattern generator circuits (CPGs). Our work on dopaminergic regulation of swim speed in larval zebrafish shows that neuromodulators can alter speed independent of CPG frequency by modulating motor neuronal recruitment and firing.*



PUBLICATIONS

Jha, U. and Thirumalai, V.* ***Neuromodulatory selection of motor neuron recruitment patterns in a visuomotor behavior increases speed.*** *Current Biology. 2020 Mar 9;30(5):788-801.e3.*

Wyart, C. and Thirumalai*, V.* ***Building behaviors, one layer at a time.*** *Elife. 2019 Apr 4;8. pii: e46375. doi: 10.7554/eLife.46375.*

HONOURS AND AWARDS

Senior Fellow, Wellcome Trust DBT India Alliance *(2018-2023)*

Shanti Swarup Bhatnagar Award for Biological Sciences *(2020)*

Program Committee, Society for Neuroscience *(2020-2023)*

Editorial Board, eLife *(since 2017)*

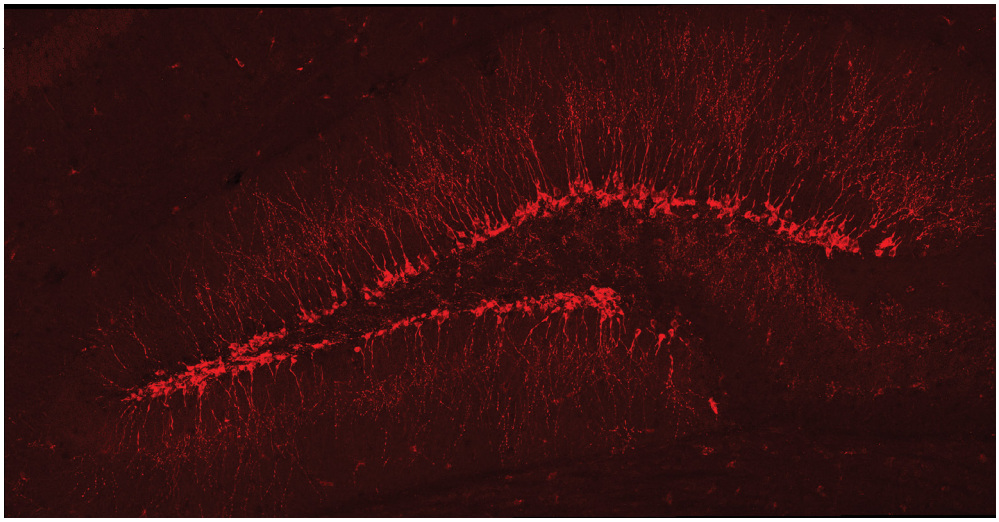
Editorial Board, Journal of Physiology *(since 2019)*

Editorial Board, Journal of Neurophysiology *(since 2014)*

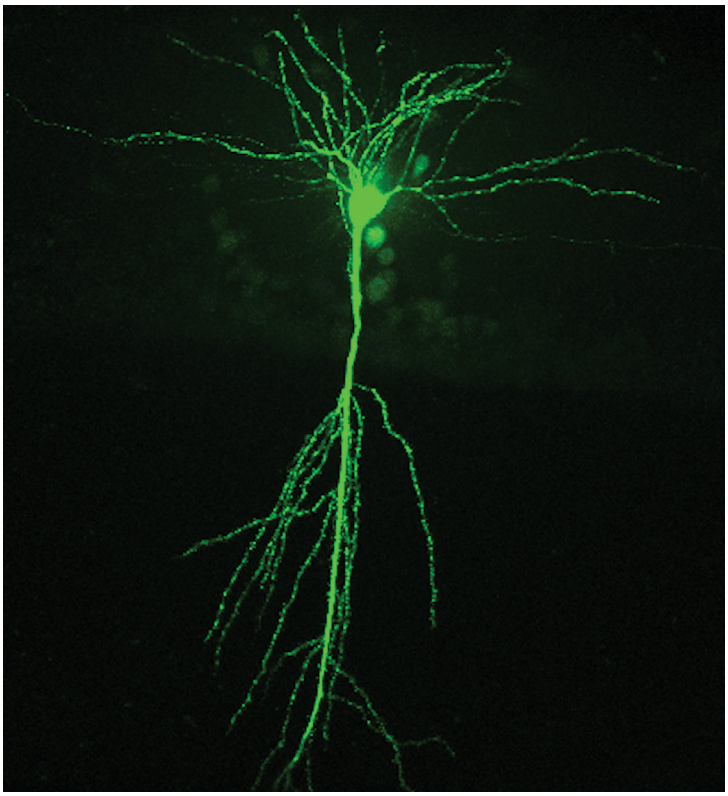
Cellular Mechanisms Governing Brain Homeostasis and Neuroinflammation

My lab seeks to understand molecular actions that underlie cell-specific processes and intercellular interactions influencing normal functionality of the brain. Broadly, we are investigating the molecular control of adult neurogenesis, mature neuronal maintenance, and microglial functions in the adult brain.

The brain consists of neuronal and non-neuronal cells, which function in an interdependent manner contributing toward normal functioning of the nervous system. Research in my lab is focused on three cell-types of the adult brain: the neural stem cell, the neuron, and the microglia, probing the genetic and molecular regulations that underlie their homeostatic functioning. The discovery of neural stem cells in the adult brain has ignited new hopes for regenerative medicine in the context of brain pathologies. However, we don't yet fully understand the full spectrum of fate-potential and the molecular mediators of environmental responsiveness of the adult neural stem cells (aNSC). Our investigations seek to gain insights into the fundamental principles of fate-regulation of the aNSC. The second major interest in the lab is in mature neuronal maintenance. The neuron is one of the longest-living cell-types of our body, yet has little capacity for regeneration or repair. While neurodegenerative diseases are a big health burden to our society, the late onset of these disorders also indicate the resilience of the nervous system. We investigate molecular mechanisms that govern the homeostatic functioning of mature neurons and seek to understand how neurons adapt to dysfunctionalities or loss of individual neurons. Finally, as yet another interest in the lab, we investigate microglial homeostasis and heterogeneity. Although known as the resident immune cell of the brain, microglia perform a myriad of non-immune functions during development and in the adult brain. We seek to uncover the transcriptional programmes that could govern a, "specialised" versus, "generic" functional manifestation of microglia in a context-dependent manner. Our overall goal is to decipher fundamental principles of cellular homeostasis in the brain, to better correlate conditions of impaired or aberrant functionalities underlying genetic and neuro-inflammatory pathologies.



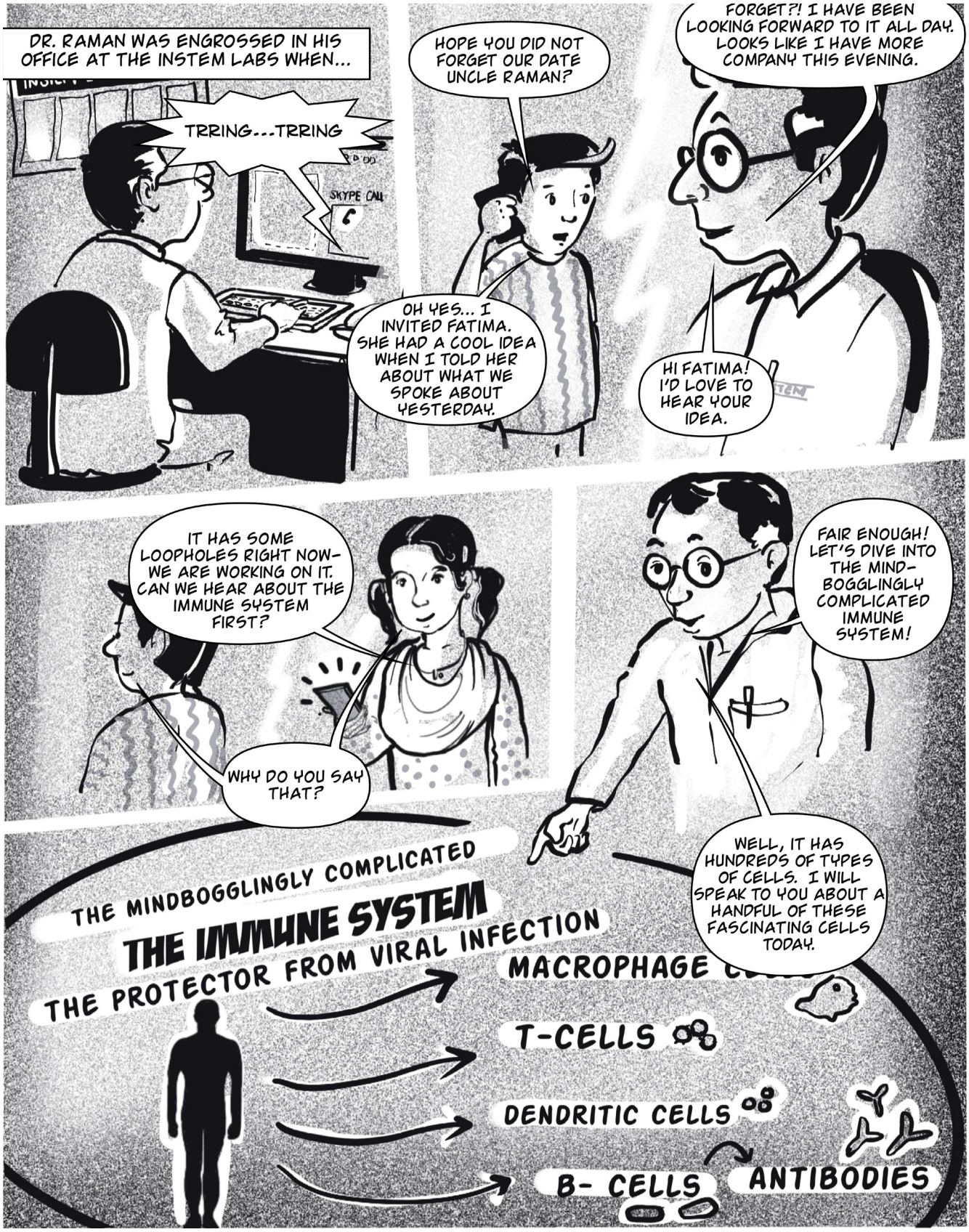
Adult born immature neurons labelled with doublecortin in the dentate gyrus of the adult mouse brain



Dye-filled pyramidal neurons in the adult brain hippocampus demonstrating the elaborate morphology of mature neurons

PUBLICATIONS

Ghosh, H. S. ***Adult neurogenesis and the promise of adult neural stem cells.*** *J Exp Neurosci. 2019 Jun 27;13:1179069519856876.*



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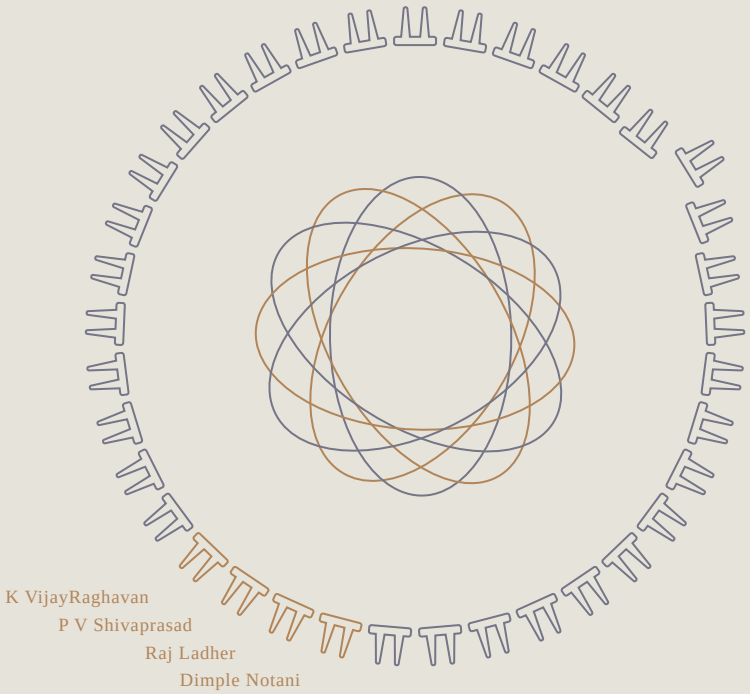


K VijayRaghavan
P V Shivaprasad
Raj Ladher
Dimple Notani

Genetics and Development

Development of Neural Circuits, Muscles, and the Emergence of Behaviour • K VijayRaghavan
RNA Silencing and Regulation of Epigenetics • P V Shivaprasad
Development and Morphogenesis of the Inner Ear • Raj Ladher
Chromatin Dynamics in Gene Regulation • Dimple Notani

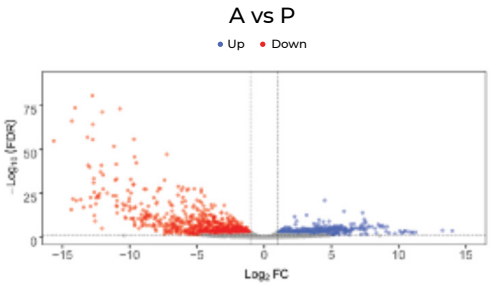
Development of Neural Circuits, Muscles, and the Emergence of Behaviour

Our laboratory studies how the birth, morphogenesis, and connectivity of neurons and muscles translate into behaviour. We pare this complex problem to tractability by focusing on the olfactory and motor system of drosophila melanogaster.

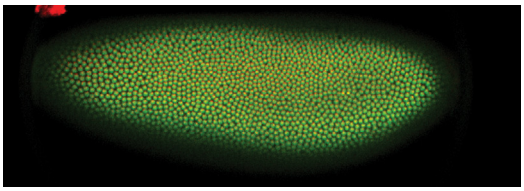
The lab primarily employs Drosophila to investigate the emergence of animal behaviour at the interface of neural and muscular development, from the molecular to the behavioural.

In collaboration with the Ramaswami group we have long studied the neural basis for critical periods in development of long-term habituation to specific odours in young adult flies. The molecular processes and proteins underlying olfactory habituation have had particular attention. As part of our studies on muscle development and repair we find significant heterogeneity in mRNA distribution across the muscle fibre, breaking the stereotype of skeletal muscles being uniform contractile tubes.

Neurons, muscles and their precursors depend extensively on cells they contact for development and function. To further study cell to cell communication in neural and muscle development, we are exploring how a family of junctional channel proteins impinges on signalling pathways. In a significant departure from our usual research, a colleague and expert has been exploring reptiles in Arunachal Pradesh.



The front and back of the same flight muscle show significant differences in mRNA distribution



Putzig expression in the early syncytial blastoderm

Trimeresurus salazar, a pit viper discovered by Zeeshan Mirza and team in Arunachal Pradesh

PUBLICATIONS

Chodankar, A., Sadanandappa, M. K., VijayRaghavan, K., and Ramaswami, M. ***Glomerulus-selective regulation of a critical period for interneuron plasticity in the Drosophila antennal lobe.*** *Journal of Neuroscience 40 (29), pp. 5549-5560*

Chaturvedi, D., Prabhakar, S., Aggarwal, A., Atreya, K. B., and VijayRaghavan, K., ***Adult Drosophila muscle morphometry through microCT reveals dynamics during ageing.*** *Open biology 9 (6), 190087*

RNA Silencing and Regulation of Epigenetics

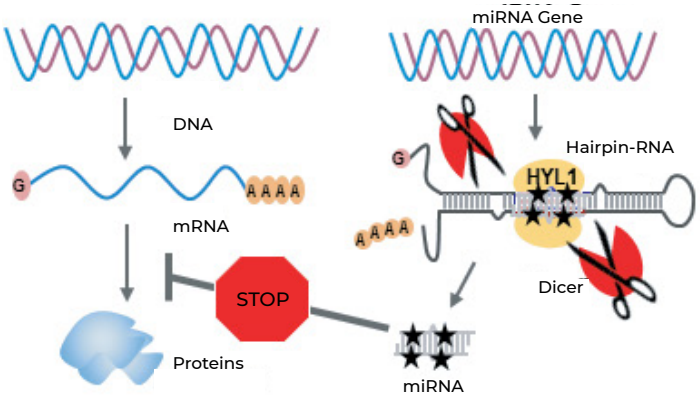
Small RNA regulators play a major role in the establishment and maintenance of epigenetic marks thereby influencing growth and development. We are interested in understanding the mechanism of small RNA biogenesis, their functions, and their role in the establishment and maintenance of epigenetic information.

Micro (mi)RNAs are 20-22nt long non-coding RNA molecules involved in post-transcriptional silencing of targets having high base-pair complementarity. Plant miRNAs are processed from long Pol II-transcripts with specific stem-loop structures by Dicer-like (DCL) 1 protein. How a specific region in the long dsRNA structure is selected for miRNA biogenesis was unknown. We showed that the presence of a specific GC-rich sequence signature within miRNA/miRNA region is required for the precise miRNA biogenesis (Fig. 1). Consistent with the presence of the miRNA-specific GC signature, target RNAs of miRNAs also possess conserved complementary sequence signatures in their miRNA binding motifs. The selection of these GC signatures was dependent on an RNA-binding protein partner of DCL1 named HYL1 (Anushree et al., 2020). We also demonstrated a direct application of this discovery for enhancing the abundance and efficiency of artificial miRNAs that are popular in plant functional genomic studies.*

RNA silencing is a defense mechanism operating against invading and unruly nucleic acids such as those of viruses. Many steps in RNA silencing were elucidated by studying plant-virus interactions. Plant ssDNA viruses of Geminiviridae family infect commercially important crops to cause huge crop losses. We described a novel mechanism by which the host and the pathogen indulge in a defense and counter-defense arms race through post-translational modifications (PTM) of a viral pathogenicity determinant protein.

We identified several previously unknown aspects of plant-virus interaction, for example, we showed how viral pathogenicity protein βC1 gets SUMOylated by host defense machinery (Fig. 2) to promote its Ubiquitin-mediated degradation (i); how βC1 has evolved SUMO-Interacting Motifs (SIM) to counter this modification (ii); how both these modifications are important for viral systemic movement, protein localisation, interaction with host proteins, and in augmenting viral replication (iii); and finally, how βC1 induces global SUMOylation of host proteins. These findings indicate the presence of previously unappreciated layers of defense and counter-defense operating between hosts and viruses.

FIGURE 1
miRNAs stop specific mRNAs from making proteins. *It was not known how they are made in plants. This study showed how specific sequences (shown in black stars) in the hairpin loops from which miRNAs originate are essential for the selection of miRNA regions.* *Adapted from Anushree et al., 2020.*



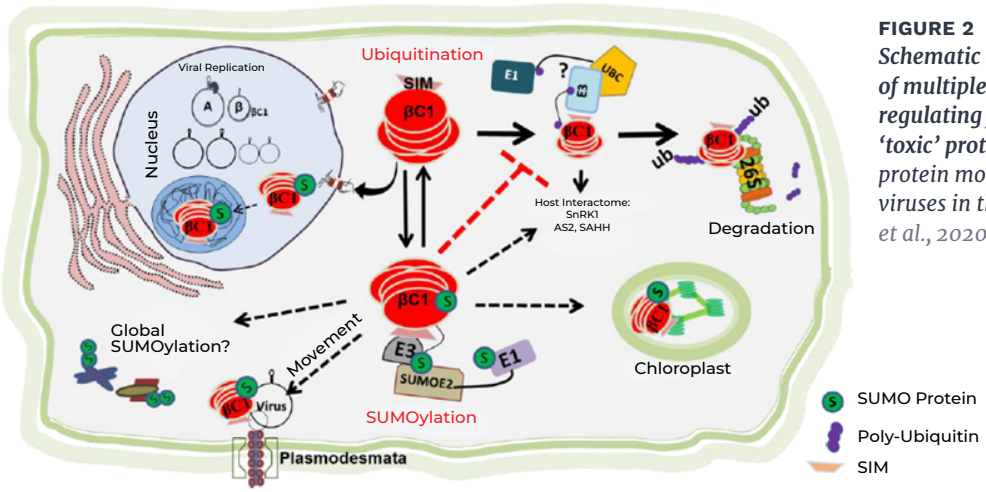


FIGURE 2
Schematic representation showing interplay of multiple post-translational modifications regulating function of viral pathogenicity 'toxic' protein βC1. *We identified how these protein modifications are used by plants and viruses in their arms race.* *Adapted from Nair et al., 2020.*

PUBLICATIONS

Anushree, N., Nair, A., Sundar, V. H., Tirumalai, V., and Shivaprasad, P. V., 2020. ***A conserved sequence signature is essential for robust plant miRNA biogenesis.*** *Nucleic Acids Res. 48:3103–3118.*

Nair, A., Chatterjee, K., Jha, V., Das, R., and Shivaprasad, P. V., 2020. ***Stability of Begomoviral pathogenicity determinant βC1 is modulated by mutually antagonistic SUMOylation and SIM interactions.*** *BMC Biology. 18:110.*

HONOURS AND AWARDS

Sir C V Raman Young Scientist Award *(2020)*

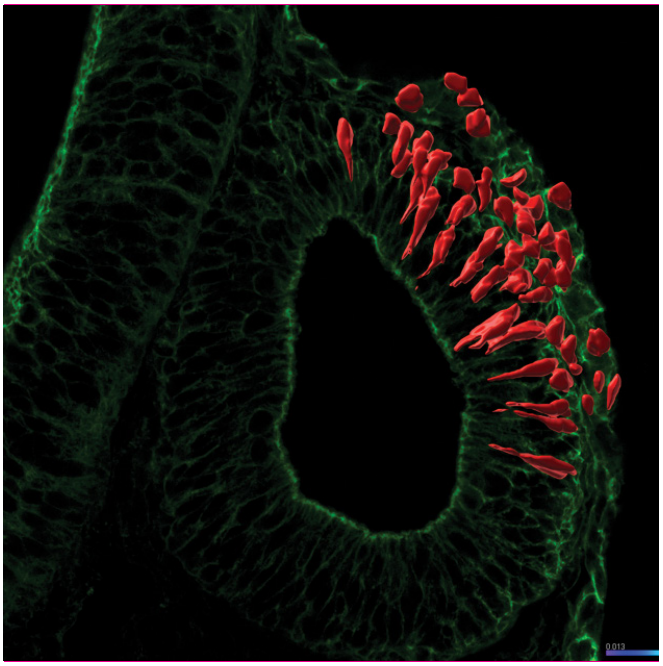
Development and Morphogenesis of the Inner Ear

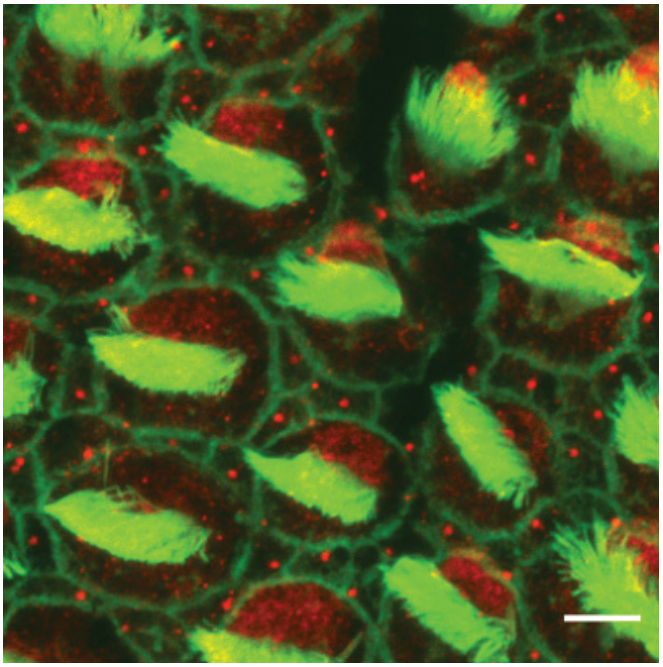
We want to understand the blueprint for making an inner ear, with particular emphasis on how cells integrate extrinsic instructions, the genes that they control, and the cellular and subcellular changes that drive morphological adaptation to mechanosensory function.

The specialisation and organisation of cells to form organs that effectively carry out functions vital to life, is a fascinating problem. We investigate the formation of the inner ear as a model for cellular and tissue-level differentiation. The inner ear is a complex structure that is actually generated from a relatively simple group of cells. These cells should have become skin, yet receive a series of instructions that change their potential and their shape. Over time, a subset of these cells form inner ear hair cells. These are the sensors of the vertebrate inner ear, converting the mechanical vibrations associated with sound and balance into electrochemical impulses that are sent to the brain. These cells possess sub-cellular adaptations in the form of fine hair-like protrusions from the top of the cell, that enable the sensitive and precise detection of these vibrations.

The formation of these cells is also a consequence of instructions. How do inner ear cells receive these instructions and then decode and implement them? What are the physical and molecular responses of cells to these dynamic genetic and epigenetic cues? How can variation be introduced into the development of cells and tissues to enable fine-level functional tuning? Using a variety of molecular, cellular, imaging, and computational techniques, our aim is to generate a blueprint of the inner ear, that we can interrogate to understand congenital hearing impairment in particular, and developmental morphogenesis in general.

Closing Otic Vesicle
Cells change shape during the formation of the otic vesicle, the precursor of the inner ear. Some cells are false coloured in red to mark their shape. Green marks actin.





Chick Auditory Epithelium
The hair cells of the chick inner ear. Green marks actin bundles which are the mechanosensitive filaments that respond to sound.

PUBLICATIONS

Honda A., Kita T., Seshadri S. V., Misaki K., Ahmed Z., Ladbury J. E., Richardson G. P., Yonemura S., and Ladher R. K., 2018. ***FGFR1-mediated protocadherin-15 loading mediates cargo specificity during intraflagellar transport in inner ear hair-cell kinocilia.*** *Proc Natl Acad Sci USA. doi: 10.1073/pnas.1719861115.*

Ladher R. K., 2017. ***Changing Shape and Shaping Change: Inducing the Inner Ear.*** *Semin Cell Dev Biol. doi:0.1016/j.semcdb.2016.10.006.*

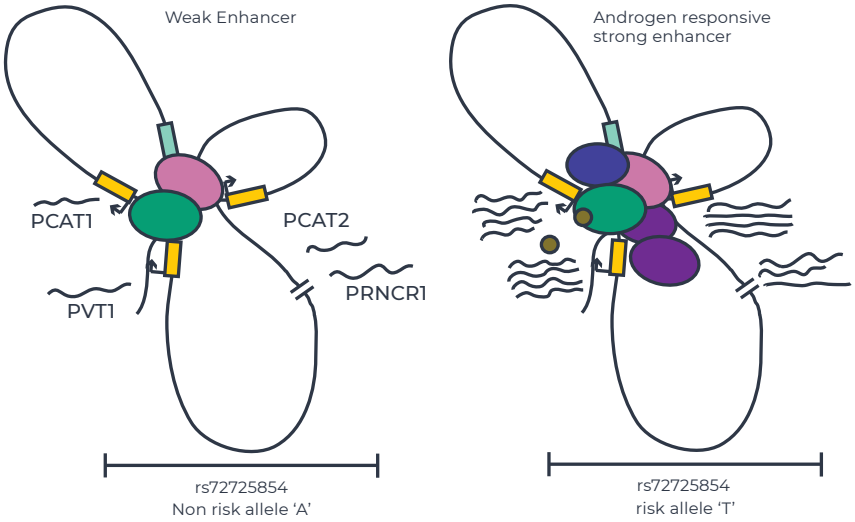
Chromatin Dynamics in Gene Regulation

My group is interested in understanding the dynamic interplay between regulatory elements, non-coding RNAs, and chromatin-architecture in gene regulation.

Gene regulation is often governed by distal regulatory elements such as enhancers, which regulate the target gene transcription by delivering important protein cargos to the promoter. While the biological importance of enhancers has long been appreciated, a mechanistic understanding of how enhancers regulate genes dynamically during short bursts of signalling remains unsolved.

Using oestrogen signalling that peaks at 1h and declines at 3h after ligand stimulation, we show that unliganded ERα (Estrogen Receptor alpha) binds to specific sites in the genome, thereby marking them as future enhancers. Upon ligand exposure, ERα binds to several EREs relatively proximal to these pre-marked or persistent ERα-bound sites. Interestingly, the persistent sites interact extensively, via chromatin looping, with the proximal transiently bound sites, forming ERα-clustered enhancers in 3D. The clustered enhancers regulate the target gene expression in a transient but robust fashion, where the loss of target gene expression coincides with the disappearance of clustered enhancers and concomitant loss of total ERα protein levels. Our work thus establishes the role of persistent unliganded ERα binding in priming enhancer clusters and transient but robust gene regulation in a ligand-dependent fashion (Saravanan et al., 2020).

Similar to ERα, we observe that an enhancer in the 8q24 region engages in the long range interactions with multiple genes, forming a hub in prostate cancer cells. The genetic variant in this enhancer causes gain of Androgen receptor (AR) binding and therefore, activates the enhancer causing the rampant cell growth (Walavalkar et al., 2020).



Schematic showing the chromatin architecture around enhancer carrying risk (right panel) and non-risk (left panel) rs72725854 variant. *Walavalkar et al., 2020.*

PUBLICATIONS

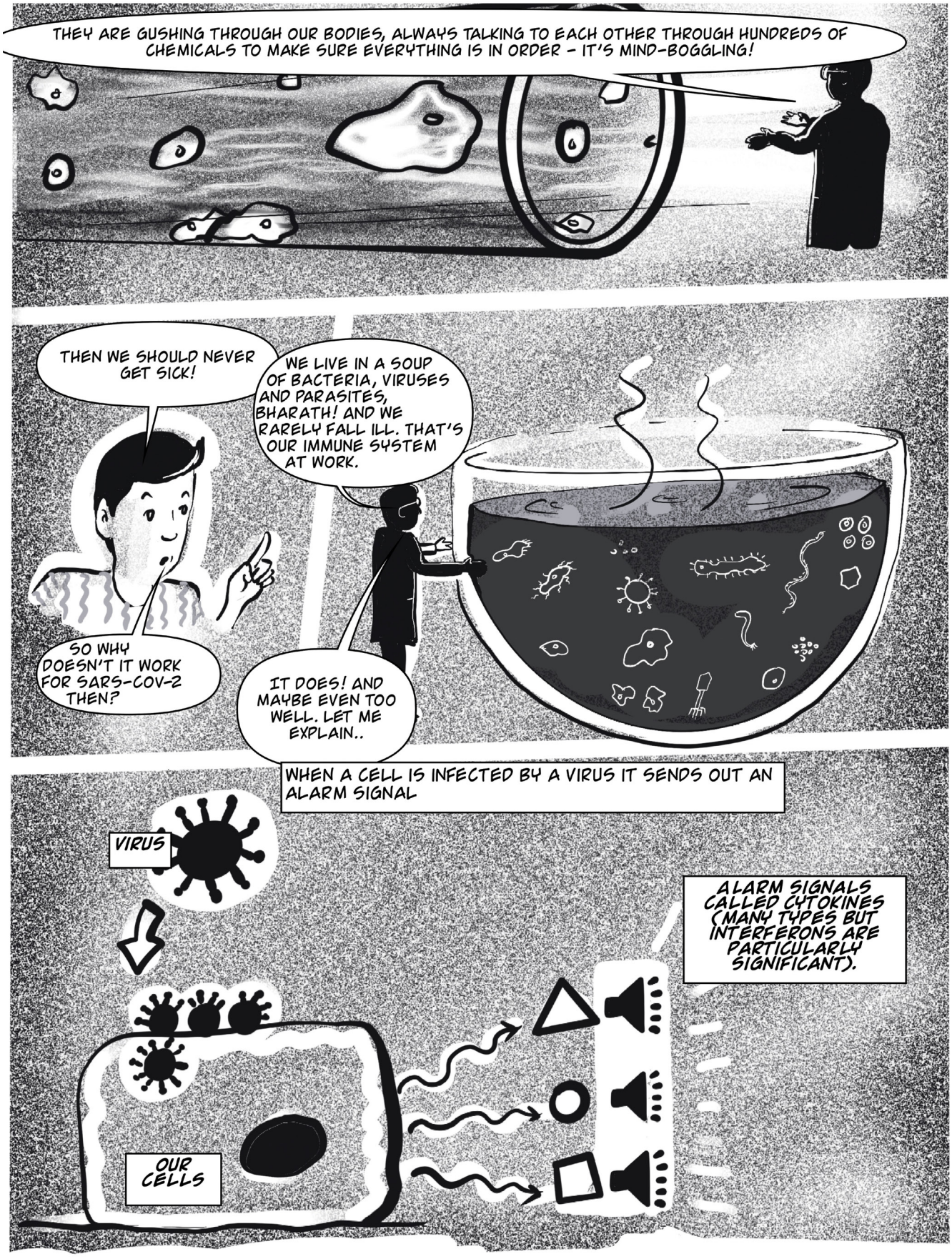
Walavalkar, K., Saravanan, B., Singh, A. K., Jayani, R. S., Nair, A., Farooq, U., Islam, Z., Soota, D., Mann, R., Shivaprasad, P. V., Freedman, M. L., Sabarinathan, R., Haiman, C. A., and Notani, D. ***A rare variant of African ancestry activates 8q24 lncRNA hub by modulating cancer associated enhancer.*** *Nat Commun. 2020.11(1):3598.doi: 10.1038/s41467-020-17325-y*

Saravanan, B., Soota, D., Islam, Z., Majumdar, S., Mann, R., Meel, S., Farooq, U., Walavalkar, K., Gayen, S., Singh, A. K., Hannenhalli, S., and Notani, D. ***Ligand dependent gene regulation by transient ERa clustered enhancers.*** *PLoS Genetics. 2020 Jan 6;16(1):e1008516.*

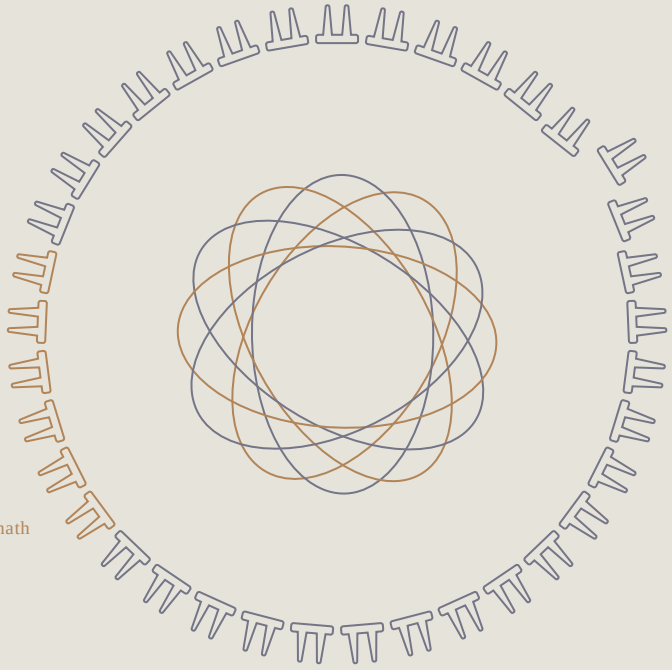
HONOURS AND AWARDS

EMBO Global Investigator
(2020-2025)

Wellcome-IA Intermediate Fellowship
(2016-2021)



These pages are excerpts from a series created, designed, and written, by Arvind Ramanathan of DBT-inStem and Sonia Sen from TIGS-CI. They are illustrated by Arvind Ramanathan as a part of the Cluster's COVID-19 Response Initiative. The work was originally published on www.covid-gyan.in



Madan Rao

Mukund Thattai

Sandeep Krishna

Shachi Gosavi

Shashi Thutupalli

Shruthi Viswanath

Theory, Simulation, and Modelling of Biological Systems

Theoretical Approaches in Cell Biology: Physics of Active, Evolving Systems • Madan Rao
The Origins of Complex Cells • Mukund Thattai
Dynamics of Biological Systems across Scales • Sandeep Krishna
Computational Protein Folding, Design, and Assembly • Shachi Gosavi
Origins and Organisation of Living Systems • Shashi Thutupalli
Integrative Structural Biology of Protein Assemblies • Shruthi Viswanath

Theoretical Approaches in Cell Biology: Physics of Active, Evolving Systems

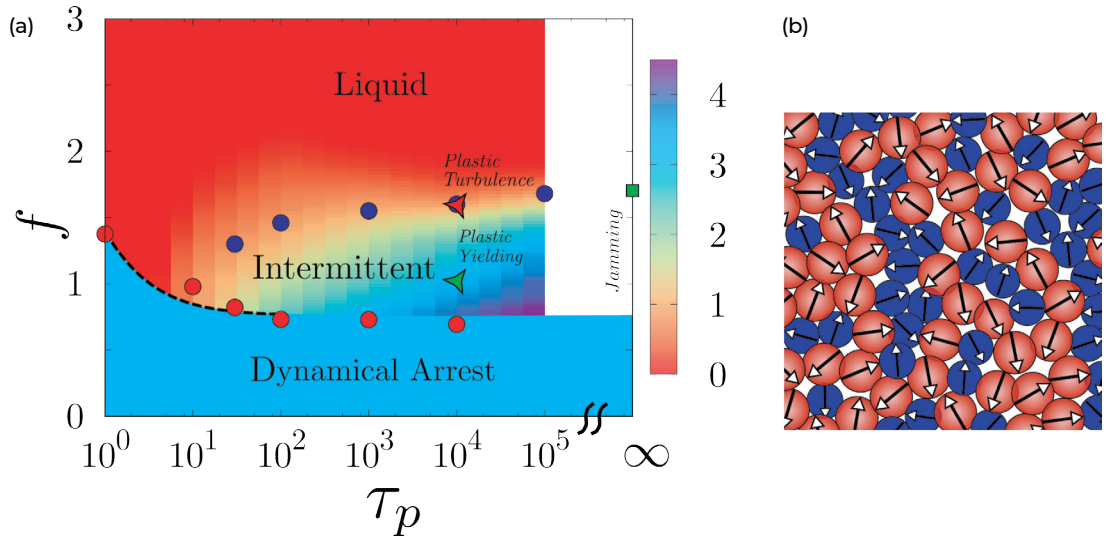
Our group studies the interplay between active mechanics, molecular organisation, geometry, and information processing in a variety of cellular contexts such as cell surface signalling and endocytosis, packing of chromatin within the nucleus, organelle biogenesis, and tissue morphogenesis.

We are interested in how living systems, composed of physical entities such as molecules and molecular aggregates, driven far from equilibrium, have self-organised (evolved) to perform, "engineering tasks", such as efficient processing of information, computation, and control. This potentially brings together many fields of research, including non-equilibrium statistical physics, soft active mechanics, information theory, and control theory, to the study of biology.

We explore new physical and chemical principles underlying biological organisation across scales, from functional biomolecules, to subcellular organelles, to the cellular and tissue scale. We are interested in the folding and packaging principles that govern the three-dimensional functional organisation of large biomolecular assemblies, such as proteins and chromatin, and their interactions with other cellular components. At a larger scale—at the subcellular, cellular, and tissue level—organisation is often driven by active mechanisms fueled by energy.

Typically these active forces arise from: (a) the coupled dynamics of the cytoskeleton, motors, and cytoskeletal regulatory proteins, and (b) the active dynamics of fission and fusion of organelles, and regulate the flux of mass, stress, energy, and information. Using the framework of active hydrodynamics, we study the mechanical response, pattern formation, symmetry breaking, hydrodynamic instabilities, and information flows in both in vivo and in vitro reconstituted active systems.

(a) Dynamical phase diagram as a function of the active force (f) and activity decorrelation time (tp) at fixed density, showing a transition from an active liquid to a dynamically arrested phase, via a novel intermittent phase. This intermittent phase is characterised by bursts of plastic yielding and plastic turbulence, close to the transition to the liquid phase. At tp = 1, the assembly shows a sudden transition from a liquid to a jammed configuration at a force threshold, where the elastic stresses assemble along force chains which are mechanically stable. (b) Schematic of a dense assembly of active particles interacting via soft Lennard-Jones potentials. The arrows mark the instantaneous direction of the active force.



PUBLICATIONS

Vishen, A. S., Prost, J., and Rao, M., 2019. ***Breakdown of effective temperature, power law interactions and self-propulsion in a momentum conserving active fluid.*** *Phys. Rev. E 100, 062602.*

Mandal, R., Bhuyan, P. J., Chaudhuri, P., Dasgupta, C., and Rao, M., 2020. ***Extreme active matter at high densities.*** *Nat. Comm. 11, 2581.*

The Origins of Complex Cells

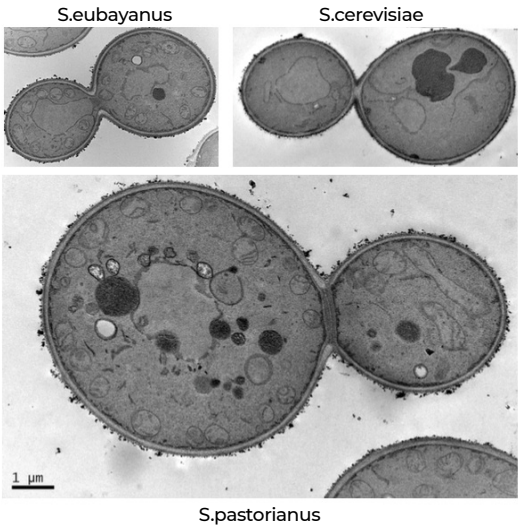
We use the eukaryotic membrane traffic system as a window to study the evolution of eukaryotes from prokaryotic ancestors, over two billion years ago. This effort combines population genetics, dynamical systems, and graph theory, with genomics data and quantitative experiments.

As a physicist practising biology, I am interested in how cellular complexity emerges from microscopic disorder. My group, based within the Simons Centre for the Study of Living Machines at NCBS, has pioneered the application of mathematical models and biophysical principles to the study of cell biology, particularly focusing on the dynamic membrane traffic network that couples eukaryotic endomembrane organelles. We collaborate extensively: we work with computer scientists to develop rigorous mathematical formulations of cell-biological hypotheses, and with experimental cell biologists to test the predictions of our models.

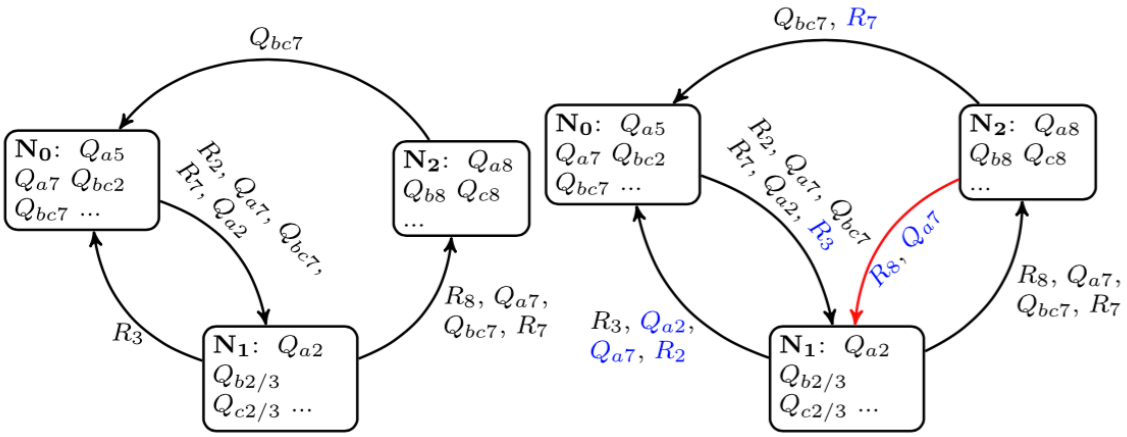
We ask:

- *What genomic variations drive the diversity of membrane traffic across species?*
- *How do organelles maintain their identity despite constant molecular exchange?*
- *How do cells use membrane traffic to regulate distributed biochemical activities?*

For the past decade, we have been deeply involved with the development of the field of evolutionary cell biology, combining molecular data and phylogenetics to answer questions about key stages of eukaryotic evolution. Our most recent work focuses on the role of interspecies hybridisation as a source of genetic novelty in cellular evolution, on the evolution of molecular information exchange in eukaryotic mating strategies, and on questions of optimal error correction in metazoan cell fate specification.



The lager brewing yeast Saccharomyces pastorianus is the result of a 500-year-old interspecies hybridisation event between two other yeast species, S. eubayanus and S. cerevisiae. We have demonstrated that hybridisation events are a potent source of genetic novelty, which have played key roles in the evolution of vesicle traffic networks over hundreds of millions of years of eukaryotic evolution.
EM image credit: Ramya Purkanti.



The eukaryotic vesicle traffic network uses local rules governed by molecular interactions (here, the interactions between Q and R SNARE proteins that regulate vesicle fusion) to generate the global structure of transport between organelles (arrows between boxes). We use formal methods from theoretical computer science to explore the constraints such transport systems must obey. Figure from Bhattacharyya et al., 2019.

PUBLICATIONS

Bhattacharyya, A., Gupta, A., Kuppusamy, L., Mani, S., Shukla, A., Srivas, M. and Thattai, M., 2019. ***A formal methods approach to predicting new features of the eukaryotic vesicle traffic system.*** *Acta Informatica, pp.1-37.*

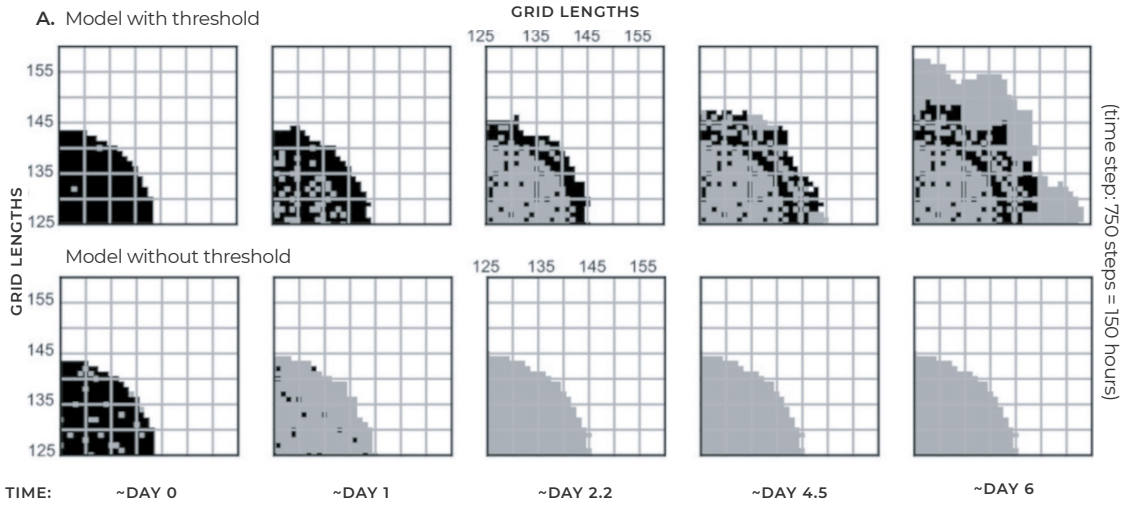
Biswas, A. and Thattai, M., 2020. ***Promiscuity and specificity of eukaryotic glycosyltransferases.*** *Biochemical Society Transactions, 48(3), pp.891-900.*

Dynamics of Biological Systems across Scales

I am interested in a theoretical understanding of dynamical patterns in biological systems ranging from molecules to cells to populations.

At the molecular level, I am interested in using a combination of experimental data and mathematical models to study the dynamics of different mechanisms of protein regulation and their roles in feedback loops. At the cellular level, I have been interested in oscillatory behaviour, synchronisation, and entrainment in signalling pathways. Finally, at an ecosystem level, I have been studying microbial communities to understand issues related to the spontaneous emergence of heterogeneity in isogenic populations, and the long-term coexistence and coevolution of multiple species.

Figure extracted from reference [2] compares simulations (A) with experimentally observed (C) patterns in yeast colonies growing under low glucose conditions. We observe the spontaneous emergence of metabolic specialisation into gluconeogenic (dark) and glycolytic (light) cell states. The light cells grow by consuming a resource that is secreted by the dark cells. The simulations demonstrate that a necessary condition for the observed patterns to emerge is that the dark-to-light cell state switching rate is a sharp, threshold-like function of the concentration of the secreted resource.



PUBLICATIONS

Juul, J. S., Jensen, M. H., and Krishna*, S., 2019.* ***Constraints on somite formation in developing embryos.*** *J. Royal Soc. Interface 16, doi: http://doi.org/10.1098/rsif.2019.0451 (*Co-corresponding authors).*

Varahan, S., Sinha, V., Walwekar, A., Krishna, S., and Laxman, S., 2019. ***Metabolic constraints drive self-organization of specialized cell groups.*** *eLife 8, e46735.*

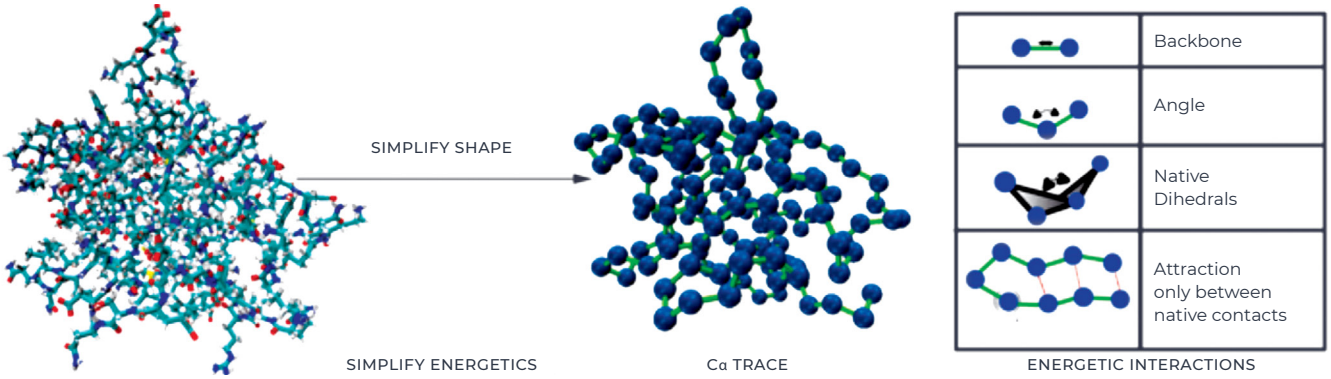
Computational Protein Folding, Design, and Assembly

My group uses computational methods to understand the architecture of proteins. We are specifically interested in understanding how protein function and conformational dynamics affect the folding of proteins and how folding simulations can, by themselves, impart information on protein function.

Natural proteins fold robustly because of a funnel-shaped energy landscape. This funnel shape arises because native interactions dominate the folding landscape, while interactions not present in the native state (i.e. non-native interactions) contribute only in an average way. Structure based models (SBMs) of proteins ignore non-native interactions by encoding only the folded structure of the protein into the energy function. This energy function can then be used to perform molecular dynamics (MD) simulations. SBMs have been successfully used by us and others to understand the folding routes and folding rates of several proteins. The advantage of using SBMs is that they simplify the energy function such that large proteins can be folded and unfolded. In my group, we use and develop SBMs and variants to understand the folding and conformational dynamics of natural and designed proteins.

Natural proteins have evolved to fold on a biologically reasonable timescale and to be as stable as is necessary to perform their function. However, selection directly acts only on the functional residues (where function could be binding, catalysis, cellular localisation, etc.). These functional residues cannot be mutated to make protein folding more efficient or protein stability greater. Given the choice of only twenty amino acids at each position, it has become apparent that parts of the protein which function are likely to be the least foldable or stable. Functional regions thus perturb folding from the "ideal" and we use SBMs to understand both, what ideal folding is, and how functional regions perturb it.

Cartoon of a coarse-grained structure based model
The protein shape is simplified by coarse-graining it to a Cα level. The energetic terms that contribute to the potential energy function are listed in the table. The parameters for these terms are all derived from the folded state of the protein. All Cα atoms not in contact in the folded state of the protein interact through a purely repulsive interaction.



PUBLICATIONS

Gershenson, A., Gosavi, S., Faccioli, P., and Wintrode, P. L. ***Successes and challenges in simulating the folding of large proteins.*** *Journal of Biological Chemistry 295 (1), pp. 15–33.*

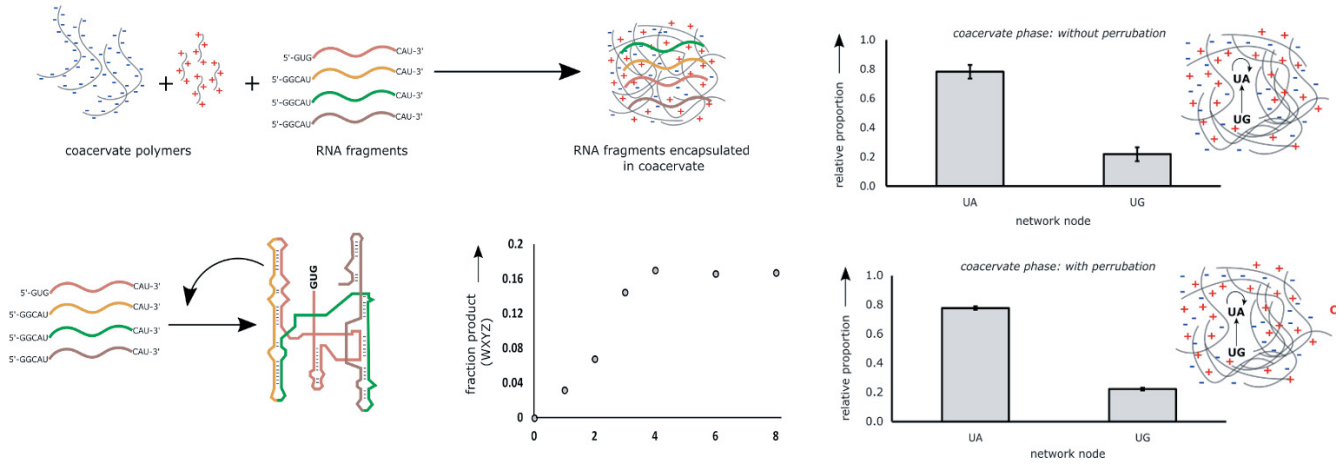
Jayanthi, L. P., Mascarenhas, N. M., and Gosavi, S. ***Structure dictates the mechanism of ligand recognition in the histidine and maltose binding proteins.*** *Current Research in Structural Biology 2, pp. 180–190.*

Origins and Organisation of Living Systems

Our research programme aims for a broad understanding of the origins and organisation of living systems. We are an interdisciplinary group combining experimental and theoretical techniques drawn from physics, engineering, and biology.

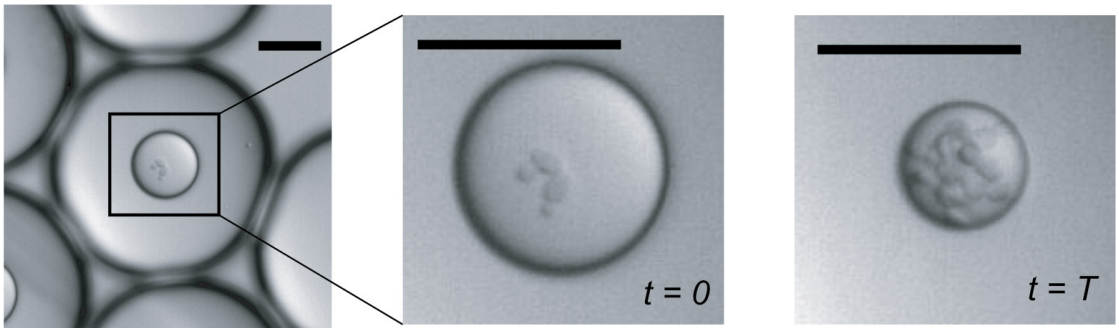
(i) Construct de novo, synthetic mimics of living matter: *These studies serve as a kind of synthetic biology from a physical perspective and are likely to shed light on early evolution and the transitions therein. We study the minimal ingredients for self-assembly, replication, feedback, and evolvability. This year, we have demonstrated the encapsulation of a self-reproducing RNA system in compartments where catalytic RNAs are synthesised from the self-assembly of smaller RNA fragments. Using a cross-catalytic network of such RNA self-reproducers, a unique chemical compositional identity, robust against perturbation by other RNA catalysts, is established in compartments. This is a first step towards constructing a synthetic, information carrying self-replicating compartment.*

(ii) Probe the physical basis of organisation in cells: *This represents a kind of physical biology which will allow us to quantitatively identify the broadly universal features of cellular organisation. We study cellular material properties and energetics during growth, dormancy, and death. We have been focused on developing techniques for precision measurements of such properties as single cell growth rates, cytoplasmic crowding/viscoelasticity, and metabolic rates. A particular highlight of the work from this year was the development of a microfluidic technique to measure glucose uptake rates in single cells.*



(Top) Encapsulation of a self-replicating RNA chemistry into a polymer coacervate compartment. RNA fragments self-assemble in an autocatalytic manner inside the compartment. An autocatalytic reaction network establishes a chemical compositional identity inside the compartment which provides protection from parasitic perturbation.

(Bottom) A droplet microfluidic technique to measure nutrient uptake in reproducing systems, here glucose uptake in single cells of yeast; encapsulating droplets shrink at a rate proportional to concomitant glucose uptake by the cells. The scale bars represent 50 microns.



PUBLICATIONS

Samhita, L., Raval, P. K., Stephenson, G., Thutupalli, S., and Agashe, D. ***The impact of mistranslation on phenotypic variability and fitness.*** *bioRxiv, 2020.05.19.104141*

Davis, J., Bisson-Filho, A., Kadyrov, D., De Kort, T., Biamonte, M., Thattai, M., Thutupalli, S., and Church, G. ***In vivo multi-dimensional information-keeping in Halobacterium salinarum.*** *bioRxiv, 2020.02.14.949925*

Integrative Structural Biology of Protein Assemblies

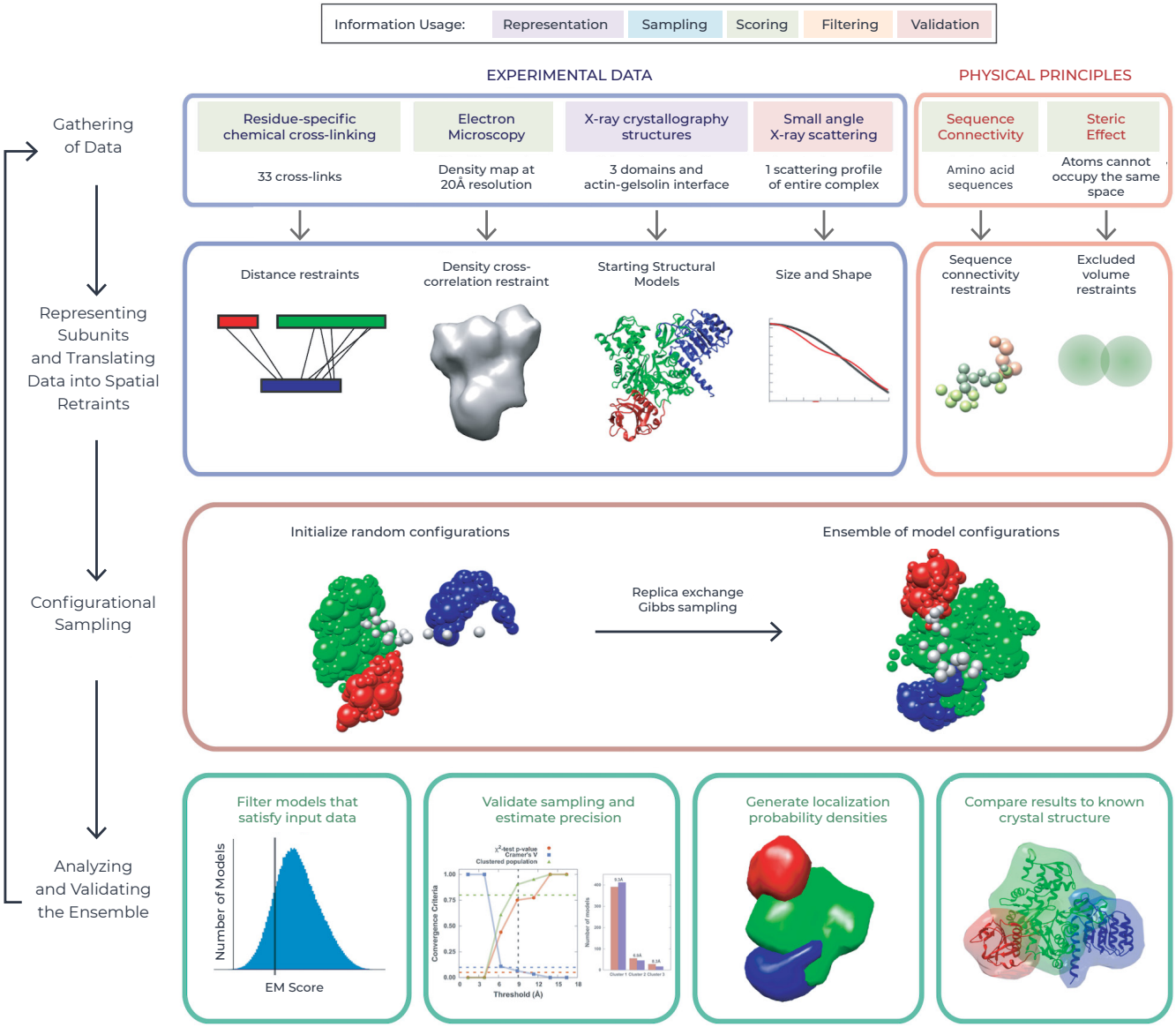
We are interested in understanding cellular organisation at the nanoscale. We determine structures of large multi-protein assemblies using an integrative approach, combining data from biophysical, biochemical, genetic, and cell biology experiments, along with statistical inference and physical principles.

Large protein assemblies, such as the ribosome or proteasome, contain tens to hundreds of proteins, and act as molecular machines in the cell. The structures of these assemblies are key to understanding mechanistic details of biological function in both normal and diseased states. We seek to understand the organisation of these molecular machines from an engineering perspective: How did they evolve? How are they assembled and regulated in the cell? What do these structures inform about basic architectural design principles in biology?

Determining the structures of these assemblies using a single experimental method is challenging. Therefore, we use an integrative approach, combining data from biophysical, biochemical, genetics, and cell biology experiments, along with statistical inference, physical principles, and prior models to obtain the structure. Along with collaborators, we are currently characterising assemblies in cell-cell junctions and transcriptional co-repressor complexes using an integrative approach.

We also develop software for computational modelling of protein organisation at the nano-scale. Our current efforts include (a) optimising coarse-graining of integrative models based on information theoretic considerations, (b) machine learning for validating ensembles of integrative models, and (c) automatically annotating organelles in cryo-electron tomograms.

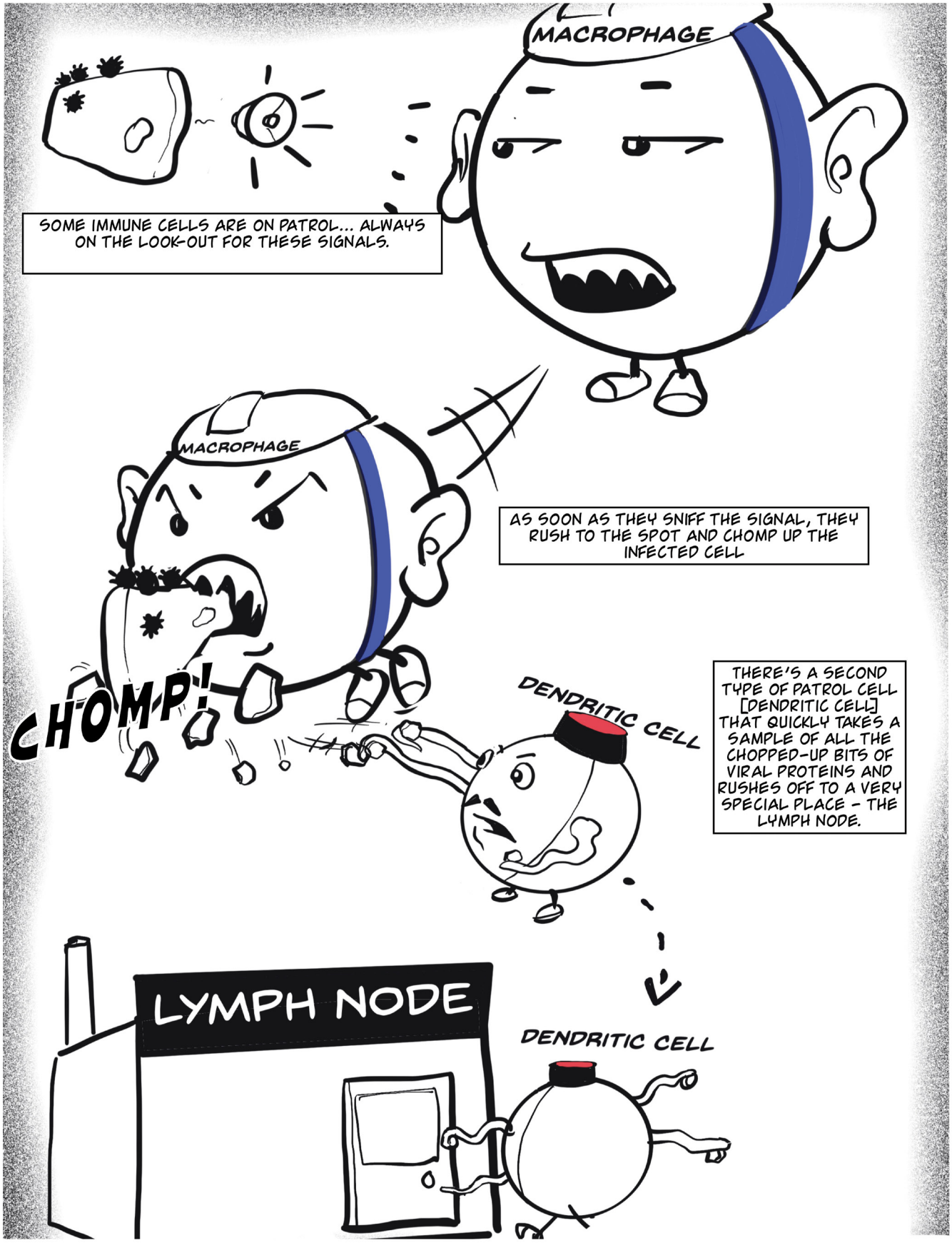
Schematic showing the four stages of integrative structure determination
The first row details the information used in modelling. The background colour of each information source indicates where the information is applied in modelling, as detailed in the key at the top. The second row describes how each information source is converted into spatial restraints. The third row details the sampling protocol. The last row details the steps for analysis and validation of the modelling.



PUBLICATIONS

Viswanath, S. and Sali, A., 2019. ***Optimizing model representation for integrative structure determination of macromolecular assemblies.*** *Proc Natl Acad Sci USA, 116 (2), pp. 540–545.*

Saltzberg, D., Greenberg, C.H., Viswanath. S., Chemmama, I., Webb, B., Pellarin, R., Echeverria, I., and Sali, A. ***Modeling biological complexes using integrative modeling platform. Biomolecular simulations.*** *Humana, New York, NY. pp. 353–377.*



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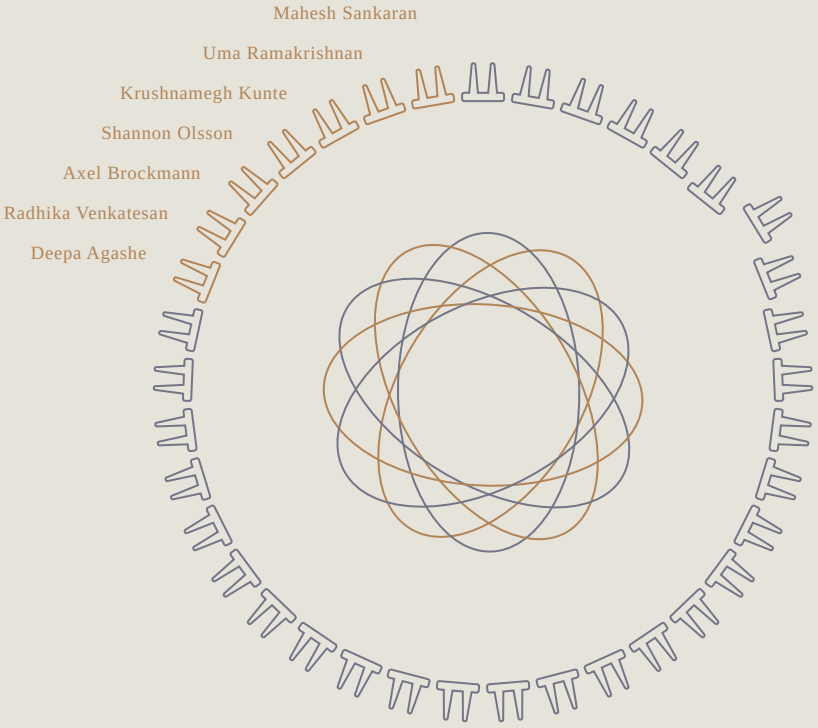


Ecology and Evolution

Terrestrial Ecosystems and Community Ecology • Mahesh Sankaran
Understanding Human Impacts on Biodiversity and Facilitating Future Survival through a Genetic Lens • Uma Ramakrishnan
Speciation, Adaptation and Morphological Diversification in the Tropical Region • Krushnamegh Kunte
Tracking the Objects of Insect Affections across Species and Continents • Shannon Olsson
The Honey Bee Lab • Axel Brockmann
Genetic and Ecological Factors Underlying Adaptive Evolution • Deepa Agashe
Chemical Ecology of Tritrophic Interactions • Radhika Venkatesan

Terrestrial Ecosystems and Community Ecology

Can our ecosystems cope with the challenges of ever-expanding human activities? We work on understanding the dynamics of grasslands and mixed tree-grass ecosystems, their responses to changes in climate—particularly drought—and what this means for their future distribution and functioning.

Current research in the lab is grouped around the following broad themes that examine: (a) how interactions and feedbacks between climate, biogeochemistry, fires, and herbivory influence the structure, composition, and stability of ecosystems and the cycling and sequestration of nutrients; and (b) how projected changes in climate, such as increasing variability of rainfall, frequency of droughts, aridity in the tropics, nitrogen and phosphorus deposition, and rising CO2 levels will impact ecosystem function, stability, and services.

Most of our research is carried out across a range of systems, from savannas and grasslands to tropical forests, in India and Africa. Our current and planned future work will employ both long and short-term experiments, as well as targeted field surveys to address the above questions across the gamut of natural ecosystem types of the Indian subcontinent, with the goal of bringing a comprehensive understanding of biome-scale vegetation and nutrient dynamics in the Indian subcontinent.

Photo of a semi-arid savanna site

Quantifying soil carbon fluxes at one of our study sites

PUBLICATIONS

Wigley, B. J., Augustine, D. J., Coetsee, C., Ratnam, J., and Sankaran, M., 2020. ***Grasses continue to trump trees at soil carbon sequestration following herbivore exclusion in a semiarid African savanna.*** *Ecology, 101(5), e03008. https://doi.org/10.1002/ecy.3008*

Sriramamurthy, R. T., Bhalla, R. S., and Sankaran, M., 2020. ***Fire differentially affects mortality and seedling regeneration of three woody invaders in forest–grassland mosaics of the southern Western Ghats, India.*** *Biological Invasions, 22, pp. 1623–1634.*

HONOURS AND AWARDS

Fellow of Indian National Science Academy (INSA)

Understanding Human Impacts on Biodiversity and Facilitating Future Survival through a Genetic Lens

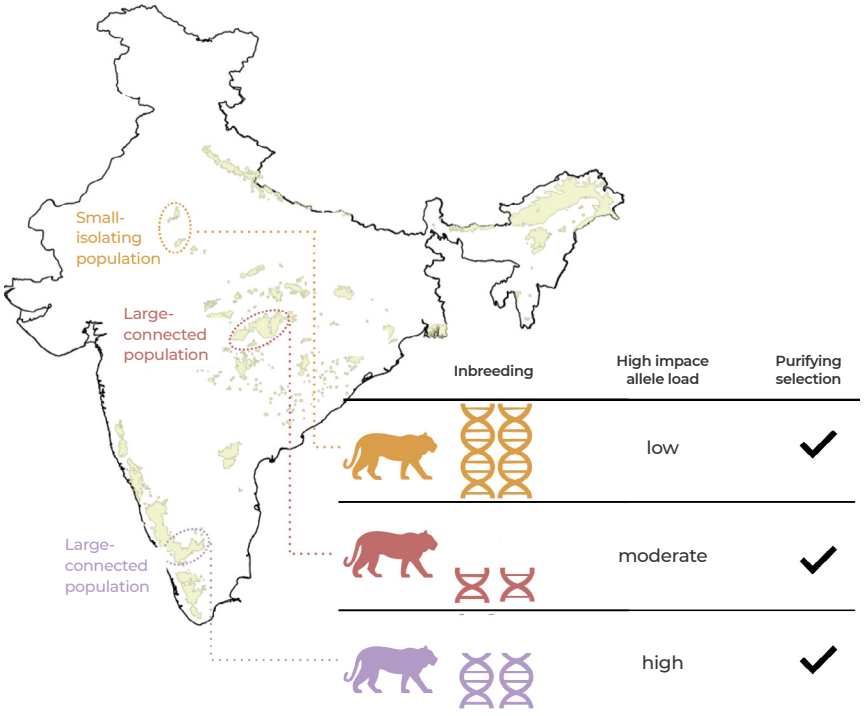
India has a population of over a billion people with only 4% of its area protected as wildlands. Yet the Indian subcontinent harbours incredible biodiversity. How are we impacting this diversity, and can we facilitate its survival? My research attempts to address these questions. We conduct fieldwork to sample behavioural, ecological, and genomic data from wild animal populations and analyse this data in population genomic and phylogenetic contexts to better understand the evolution, population ecology, and conservation of animal populations.

Indian biodiversity: tracking its history, conserving its future.

An individual's genome defines it, reflects its evolutionary journey, and could be used to predict future survival. Today, we are able to completely read the genome of an individual, thanks to novel, cutting-edge genomic sequencing methods. Genomes from several individuals provide information about a species' population history, and recent human impacts including population isolation and potential inbreeding. In my group, we use genetic information to better understand the evolutionary history of Indian biodiversity and human impacts. Then, we devise strategies for the conservation of threatened species in the Indian subcontinent.

How isolated are populations of endangered species today? What determines connectivity? Are individuals in isolated populations inbred? How has human-induced fragmentation impacted the probability of zoonoses? We use field collected samples (invasive at times, but mostly non-invasive), generate genomic (or genome-wide) data, and use computational tools to analyse this data and make inferences. Ongoing conservation efforts must be informed by genetic analyses to establish if threatened populations have sufficient heterogeneity for unaided survival. If not, what are the possible management actions that can be taken? Similarly, understanding the impacts of land-use change in facilitating zoonotic disease spillover will allow us to suggest land use management to minimise such effects. We are already working with on-the-ground teams around the country to support action-oriented programmes for tigers and vultures. We hope to continue and enhance such engagement in conservation and the emerging infectious disease space.

In order to investigate the effect of population isolation, we sequenced 57 whole genomes of tigers from across India and measured inbreeding, deleterious allele load, and site frequency spectra. We find that tigers from a small isolated population are the most inbred but have low high impact deleterious allele load, while the large and connected population from central India has the least inbred individuals and moderate load of high impact deleterious alleles. The large population from southern India has intermediate inbreeding and intermediate load. Surprisingly, all populations show signatures of purifying selection.



PUBLICATIONS

Natesh, M., Taylor*, R. W., Truelove, N., Palumbi, S. A., Hadly, E. A., Petrov*, and Ramakrishnan*, U., 2019.* ***Empowering conservation science and practice with efficient and economical genotyping from poor quality samples.*** *Methods in Ecology and Evolution. https://doi.org/10.1111/2041-210X.13173 *Equal contribution*

Dovih, P., Laing, E. D., Chen, Y., Low, D. H. W., Ansil, B. R., Yang, X., Shi, Z., Broder, C. C., Smith, G. J. D., Linster, M., Ramakrishnan, U., and Mendenhall, I. H., 2019. ***Filovirus-reactive antibodies in humans and bats in Northeast India imply zoonotic spillover.*** *PLoS Neglected Tropical Diseases 13(10): e0007733.*

Speciation, Adaptation, and Morphological Diversification in the Tropical Region

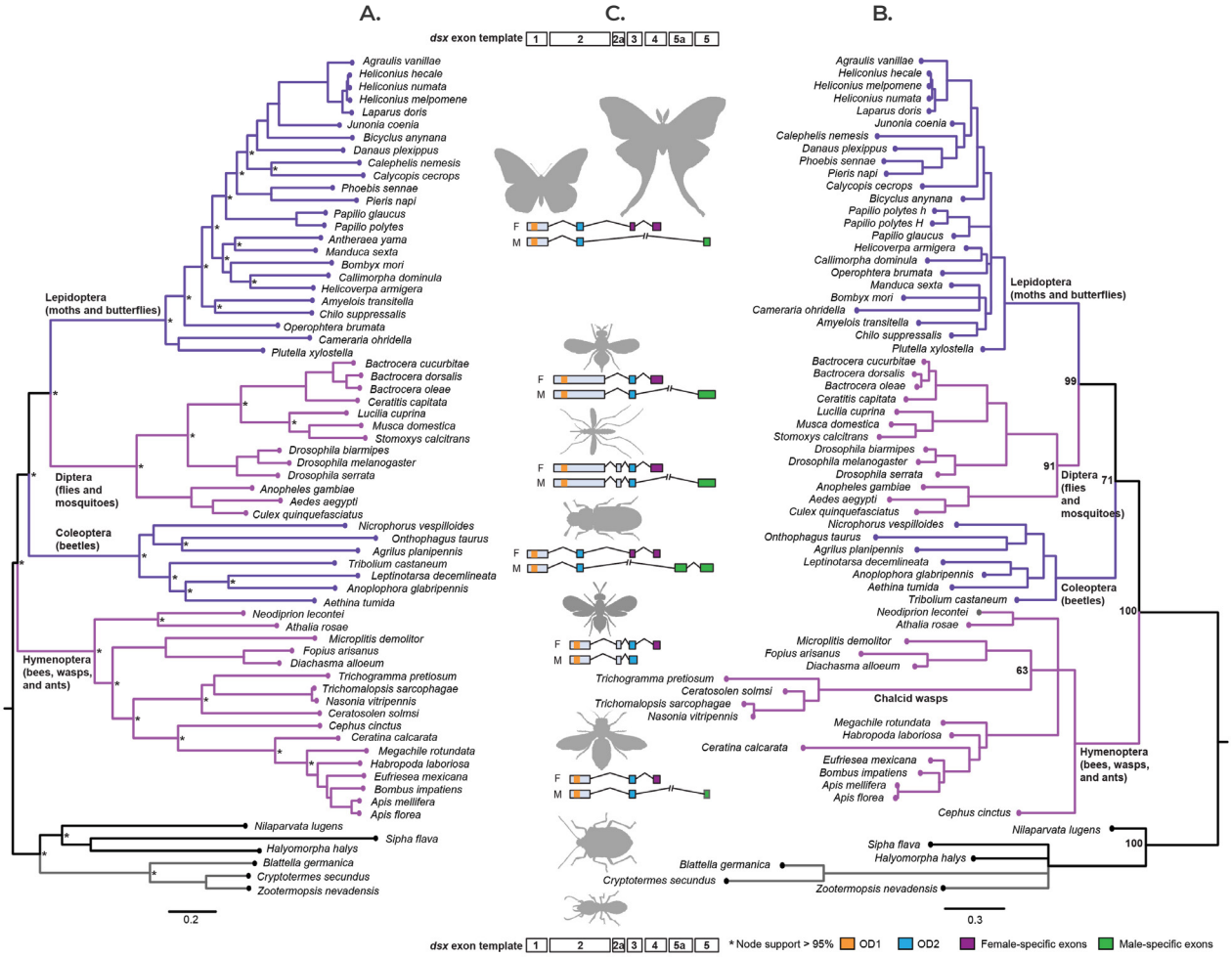
Diversity is the cornerstone of life on earth. We are evolutionary biologists who study biodiversity, its organisation and complexity, the selective processes that shape it, and the means to preserve it in tropical regions such as India.

I have a broad interest in biology encompassing the fields of natural selection theory, genetics, population and community ecology, and conservation biology. The long-term goal of my lab is to study the organisation of biological diversity, the selective processes that shape its evolution, and the means to preserve it in India. We use two systems as microcosms to study a range of phenomena that fascinate us, such as morphological evolution, sexual dimorphism and polymorphism, geographical distribution of animals, and speciation.

Our first study system is Batesian mimicry, which is a phenomenon in which unprotected prey species (called 'mimics') gain protection from predators by mimicking toxic or otherwise protected species (called 'models'). Predators learn to avoid models based on prior experience, and subsequently avoid eating mimics due to misidentification. Hundreds of mimetic insects (especially butterflies) are known to be from tropical forests. There is tremendous variation in Batesian mimicry: mimicry can be sexually monomorphic, polymorphic, or sex-limited within and across species. Our research aims to understand selective pressures that favour such variations in mimetic colour patterns, and uncover its genetic basis.

Our second study system is focused on Indian butterflies. India's butterfly diversity is spread across four globally-recognised biodiversity hotspots and offers virtually unlimited opportunities to study biogeography, community ecology, population biology, and conservation issues. Some Indian butterfly species also exhibit seasonally variable wing patterns, large-scale annual migrations, and phenomenal boom-and-bust population cycles, which make them excellent model organisms to address a wide variety of scientific questions. We study all these phenomena as part of our various ongoing projects.

Hylogenetic relationships and exon usage among insect orders in relation to DSX evolution. *(A) A mito-nuclear phylogeny of the four orders sampled. (B) dsx gene tree based on its coding sequence. In (A) and (B), adjacent clades are coloured pink and purple, and the outgroups are coloured gray and black, for contrast. (C) Exon usage of dsx across insect orders. Exons are numbered arbitrarily on the basis of mRNA initiation as per scientific convention and indicate a generalised exonic organisation of dsx in holometabolous insects. Order-wise exon organisation of the translated product of dsx is depicted in the center with domains and sex-specific regions coloured based on sequence homology. Only those exons that are translated are shown, but 5′ and 3′ untranslated exons (not shown) may have poorly understood regulatory functions. OD1 is a DM DNA-binding domain, and OD2 is a DSX dimerisation domain. Exon 5a, unique to Coleoptera, is homologous to OD2.*



PUBLICATIONS

Baral, S., Gandhimathi A., Deshmukh, R., and Kunte, K., 2019. ***Genetic architecture and sex-specific selection govern modular, male-biased evolution of doublesex.*** *Science Advances, 5:eaau3753.*

Yang, L., Ravikanthachari, N., Mariño-Pérez, R., Deshmukh, R., Wu, M., Rosenstein, A., Kunte, K., Song, H., and Andolfatto, P., 2019. ***Predictability in the evolution of Orthopteran cardenolide insensitivity.*** *Philosophical Transactions of the Royal Society B, B374:20180246.*

HONOURS AND AWARDS

Earthwatch Institute's Conservation of Species Fellowship *(2020-2021)*

Tracking the Objects of Insect Affections across Species and Continents

The Naturalist-Inspired Chemical Ecology (NICE) group studies how animals—and especially insects—identify objects in nature. We take field trips, record neurons, generate models, and even build virtual worlds to understand how insects have evolved to detect relevant cues and make decisions.

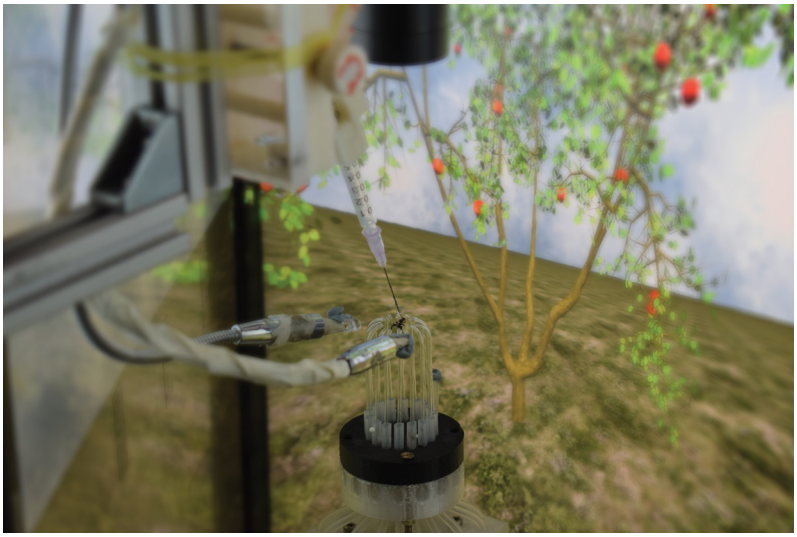
The NICE group listens to nature's chemical conversations across India's diverse ecosystems. This past year saw the publication of several major projects, including the COVID-19 response efforts.

First, we published a study to understand long-range search behaviour in tethered flying insects using virtual reality. These results provide the foundation for studies that aim to elucidate search processes for applications ranging from pest management to robotics.

Second, in collaboration with Dr. Axel Brockmann of NCBS and Dr. Dhandapany Perundurai of DBT-inStem, we found that field-collected Giant Asian honey bees and lab-reared Drosophila fruit flies exposed to increased air pollution in the city of Bangalore, exhibit differences in behaviour, physiology, gene expression, and survival. This is the first quantitative analysis on the current impacts of air pollution on wild pollinators, and indicates the urgency for more non-human studies to accurately assess the effects of pollution on our natural world.

Finally, we have been part of a global consortium for Chemosensory Research (https://gcchemosensr.org/) who are a group of over 500 scientists, clinicians, and patient advocates around the world dedicated to assessing the relationships between respiratory illnesses (including COVID-19) and their effects on smell and taste. We have published multiple studies regarding COVID-19 and its connection to smell and taste loss.

Cover of PNAS Volume 117 issue 34 featuring our study on the impact of air pollution on pollinators



A tethered apple fly (Rhagoletis pomonella) approaching a tree-like virtual object in our multimodal virtual reality arena. *Photograph courtesy of Shoot for Science: Deepak Kakara, Dinesh Yadav, Sukanya Olkar, and Parijat Sil.*

PUBLICATIONS

Geetha, G. T., Sharma, A., Mullen S., Sottilare, K., Saptarshi, S. M., Brockmann, A., Perundurai, D., and Olsson, S. B., 2020. ***A field-based quantitative analysis of sublethal effects of air pollution on wild pollinators.*** *Proc. Natl., Acad. Sci. USA, 117 (34) pp. 20653-20661.*

Kaushik, P. K., Renz, M., and Olsson, S. B., 2020. ***Characterizing long-range search behavior in Diptera using complex 3D virtual environments.*** *Proc. Natl., Acad. Sci. USA, 117 (22) pp. 12201-12207.*

HONOURS AND AWARDS

Director, the echo network, steered by the Principal Scientific Adviser GOI

Associate Editor, Ecology, Economy, and Society (INSEE)

Counsellor, Asian-Pacific Society of Chemical Ecologists

Member, Sigma Xi Research Honor Society

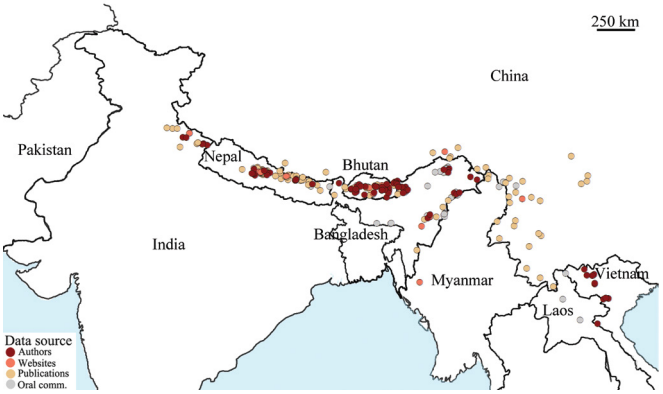
The Honey Bee Lab

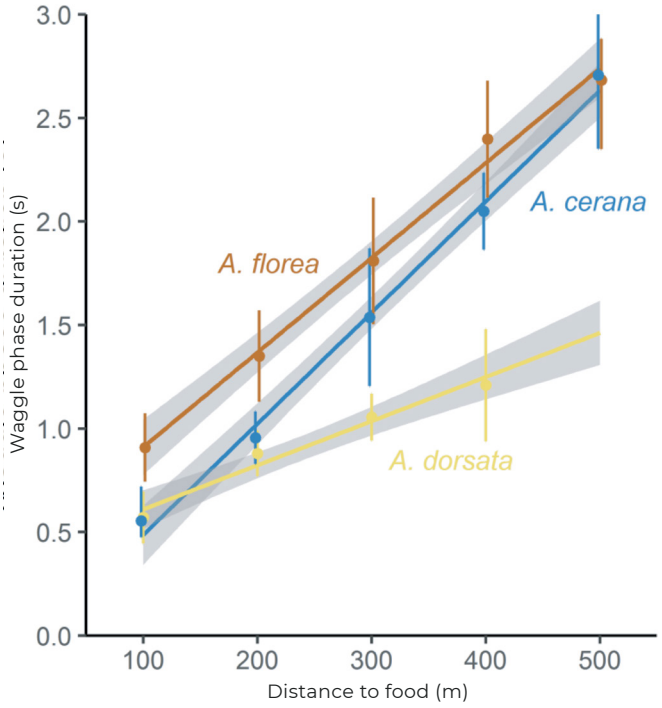
The research in the Honey Bee Lab focuses on two broad themes: (a) identifying molecular processes underlying complex behavioural capabilities like time-memory and communication of navigational information, and (b) comparative studies on the biology and ecology of Asian honey bees.

Starting with Karl von Frisch, many scientists have made honey bees (Apis mellifera) the insect species of choice in studies to identify and study complex sensory and behavioural capabilities in the natural context. In the last few years, we have established different behavioural paradigms and technical procedures to identify molecular and neural mechanisms involved in the cognitive capabilities of honey bees. For example, by training honey bees to visit a feeder at a specific time of day, we have demonstrated that the expression of the transcription factor Egr-1 (early growth response protein-1) in the mushroom bodies likely plays an important role in time-memory. Recent manipulation experiments suggest that Egr-1 expression is regulated by the circadian clock.

In addition to our work on Apis mellifera, we have also started behavioural and molecular studies on Asian honey bees. We conducted a revision of the geographic distribution of the unique Himalayan giant honey bee, Apis laboriosa (Figure 1). Further, we were able to demonstrate that honey bee species really show distinct distance dialects in the dance communication (Figure 2). We will continue this research on dance dialects comparing Apis cerana populations from tropical and temperate climate zones.

Revised geographical distribution of Apis laboriosa. *Each circle indicates a locality at which a nest of A. laboriosa or workers foraging on flowers were found. The colour indicates the source of information. Dark red: information collected by one or several of the authors; orange: photos published on websites; tan: information from published papers; and grey: oral reports by colleagues or local people. Scale bar: 250 km*





Flight distance/Waggle run duration calibrations curves of the three major Asian honey bee species Apis florea, Apis cerana, and Apis dorsata. *Differences in the slope of the calibration curves have been interpreted as dance dialects.*

PUBLICATIONS

Kohl, P.L., Thulasi, N., Rutschmann, B., George, E.A., Steffen-Dewenter, I., and Brockmann, A., 2020. ***Adaptive evolution of honeybee dance dialects.*** *Proceedings of the Royal Society London B 287:20200190. doi: 10.1098/rspb.2020.0190*

Kitnya, N. , Prabhudev, M.V., Bhatta, C.P., Pham, T.H., Nidup, T., Megu, K., Chakravorty, J., Brockmann, A., and Otis, G.W., 2020. ***Geographical distribution of the giant honey bee Apis laboriosa Smith, 1871 (Hymenoptera, Apidae).*** *ZooKeys 951: 67–81. doi: 10.3897/zookeys.951.49855.*

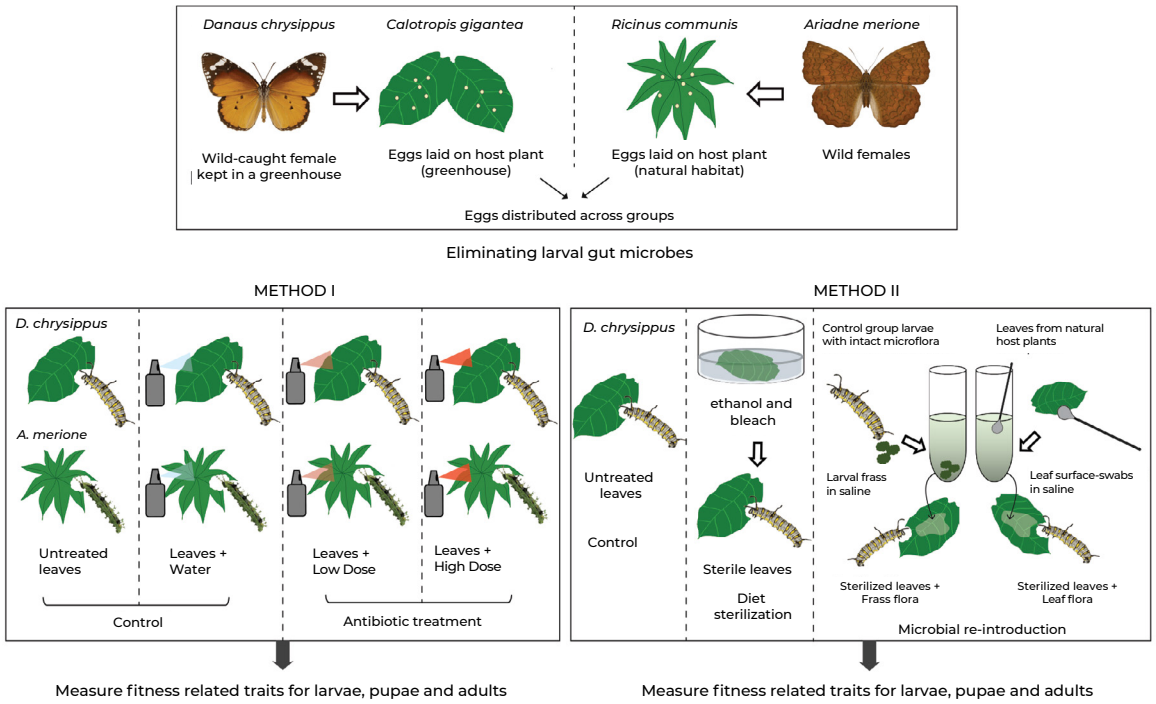
Genetic and Ecological Factors Underlying Adaptive Evolution

We aim to understand evolutionary processes and constraints acting at three levels:
1. Genetic and genomic features that limit cellular growth
2. Phenotypic and genetic tradeoffs that constrain adaptation
3. Inter-species associations that may either limit or facilitate population growth

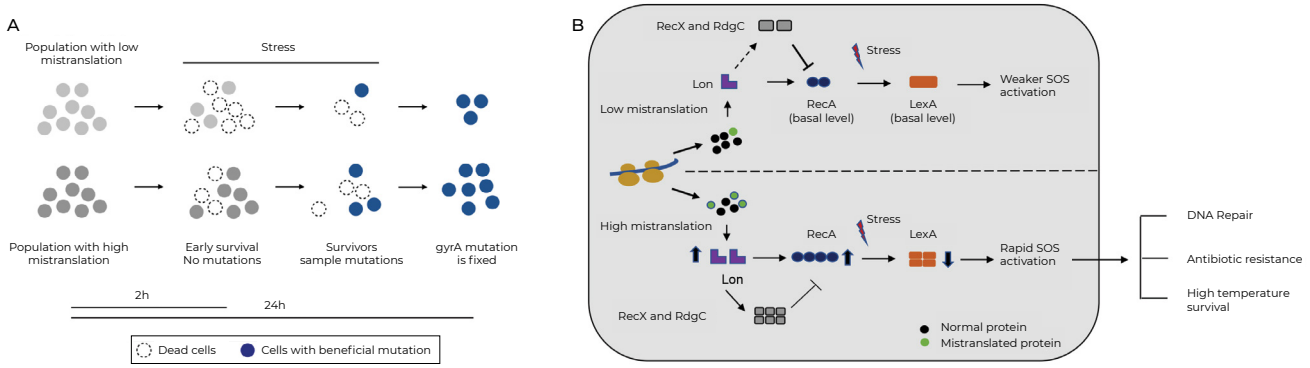
In the past year, we analysed host-bacterial interactions in natural populations of different species, to determine their impact on host ecology and evolution. We found that variation in immune memory across flour beetle populations is driven by differential susceptibility to bacterial pathogens, as well as varying costs of immune memory (Prakash et al 2019, Journal of Animal Ecology). Contrary to results from a large body of work on insects, we found that host-associated bacterial communities of dragonflies are probably not shaped by selection (Deb et al 2019, PeerJ). Similarly, manipulating the bacterial communities of butterflies had no effects on host development and survival (Phalnikar et al 2019, Proceedings B). On the other hand, Methylobacterium strains inhabiting the leaves of traditionally grown rice varieties in north east India are shaped by their association with the rice host (Sanjenbam et al 2020, PLoS One). Together, these results highlight the diverse effects of host-bacterial associations on interacting partners.

For a separate research theme, we found that a high level of global mistranslation is beneficial under stress, because it increases early cell survival via rapid activation of key stress response pathways (Samhita et al 2020, PLoS Genetics). Thus, global mistranslation levels could potentially evolve under selection.

Schematic illustrating the methods used to eliminate gut microbes from host butterfly larvae. *Figure from Phalnikar et al, 2019.*



Summary of the effect of global mistranslation on cell survival under stress. *(A) Proposed model for how mistranslation leads to increased sampling of beneficial mutations by enhancing early survival (B) Proposed model for stress resistance mediated by faster SOS activation in mistranslating strains.* *Figure from Samhita et al, 2020.*



PUBLICATIONS

Samhita, L., Raval, P. K., and Agashe, D., 2020. ***Global mistranslation increases cell survival under stress in Escherichia coli.*** *PLoS Genetics 16(3): e1008654*

Phalnikar, K., Kunte, K., and Agashe, D., 2019. ***Disrupting butterfly microbiomes does not affect host survival and development.*** *Proceedings of the Royal Society of London B 286: 20192438*

HONOURS AND AWARDS

Elected Vice President of the American Society of Naturalists *(2021–2023)*

Women Research Excellence Award, Science and Engineering Research Board (SERB), India

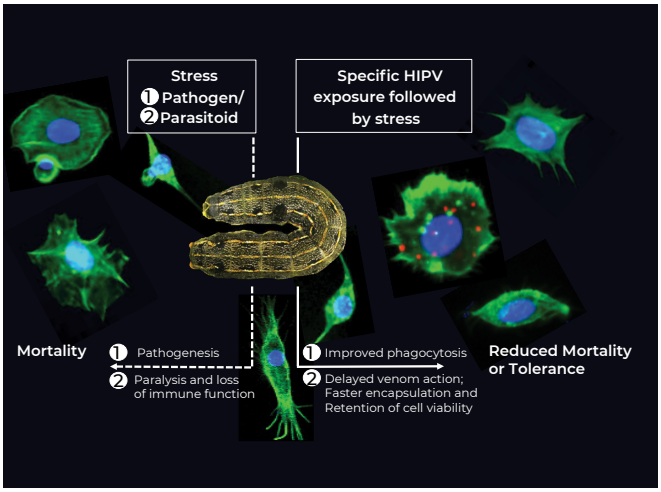
Chemical Ecology of Tritrophic Interactions

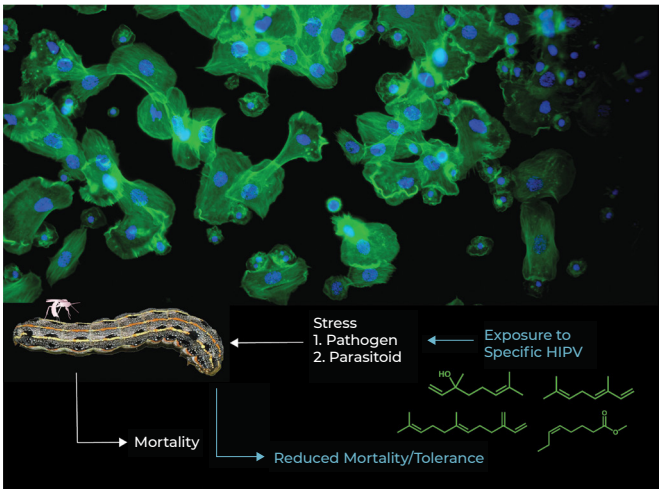
Chemical ecology is the study of chemically mediated interactions in nature. We study such interactions across a broad range of levels, from those involving biochemistry to those spanning ecosystems. Specifically, we investigate plant defence responses and their regulation by phytohormones, insect detoxification mechanisms, and the evolutionary origins of plant defence responses.

Plants possess many defences against herbivores that can be direct or indirect. Indirect defences include the production of herbivore-induced plant volatiles (HIPVs) that attract predators and parasitoid wasps. HIPVs thus function as information conduits between plants and insects. We study the roles of HIPVs in regulating insect adaptation, parasitoid attraction, as well as their effects on insect physiology and behaviour.

We investigate HIPV-mediated tri-trophic interactions between plants, insect herbivores, and the parasitoid wasp: how do wasps select their host? Does the host suitability change with plant quality? Can insect herbivores resist parasitisation? Insects lack adaptive immunity, but harbour effective innate immune systems to combat parasites; however, parasitoid wasps have strategies such as injection of maternal factors to suppress insect immune responses. Since survival of parasitoid progeny strictly depends on the host, we examine the roles of plant secondary metabolites in how parasitoids choose their insect hosts. We have found that parasitoid choice is affected by certain plant metabolites. We are working on further studies to reveal the exact nature of these compounds and their roles in parasitoid survival.

We study these questions in the lab using various imaging and analytical tools such as gas and/or liquid chromatography coupled to mass spectrometry. Taken together, our lab attempts to understand ecological interactions mediated by chemistry, and elucidates the role of various plant defensive metabolites in shaping these interactions.



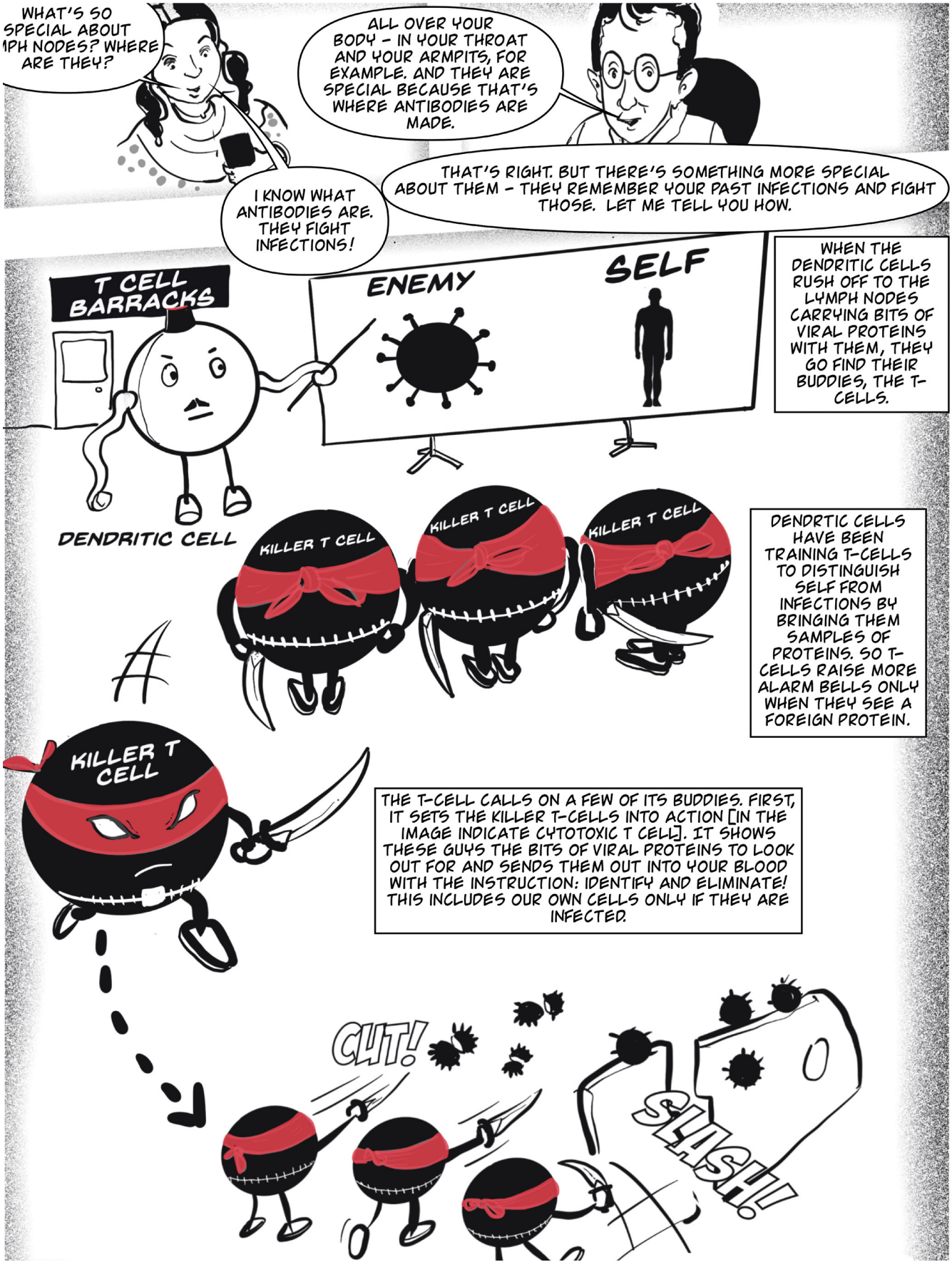


Schematic shows the effect of a specific HIPV in enhancing the innate immunity of Spodoptera litura, a polyphagous insect herbivore. The enhanced immune responses translated into better survival against natural enemies. Ghosh & Venkatesan, 2019.

PUBLICATIONS

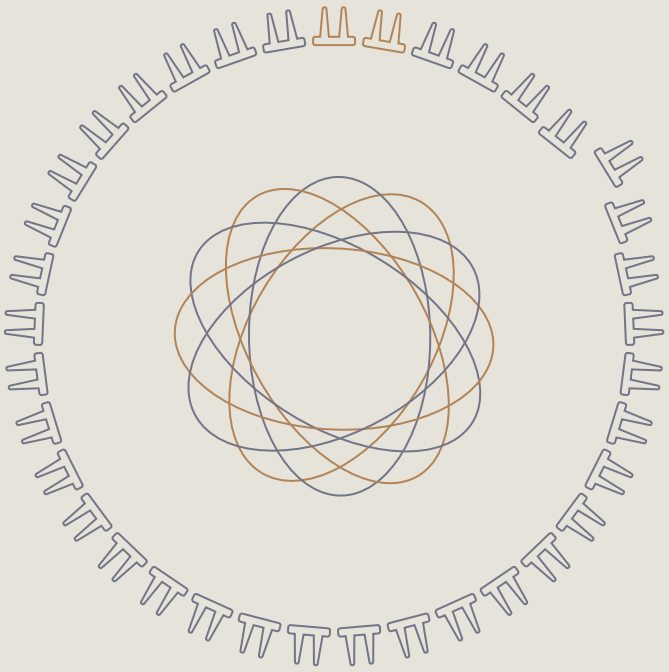
Kalmankar, N., Venkatesan, R., Balaram, P., and Sowdhamini, R., 2020. ***Transcriptomic profiling of the medicinal plant, Clitoria ternatea: Identification of potential genes in cyclotide biosynthesis.*** *Scientific Reports. 10: 12658. https://doi.org/10.1038/s41598-020-69452-7*

Ghosh, E., and Venkatesan, R., 2019.* ***Plant volatiles regulate immune responses in Spodoptera litura.*** *Journal of Chemical Ecology 45:715-724*



These pages are excerpts from a series created, designed, and written, by Arvind Ramanathan of DBT-inStem and Sonia Sen from TIGS-CI. They are illustrated by Arvind Ramanathan as a part of the Cluster's COVID-19 Response Initiative. The work was originally published on www.covid-gyan.in

Shaon Chakrabarti
Soumyashree Das



New Faculty

Quantitative Cell Biology: Cellular Proliferation in Development and Disease • Shaon Chakrabarti
Investigating the Role of Endothelial Cells in Cardiovascular Regeneration • Soumyashree Das

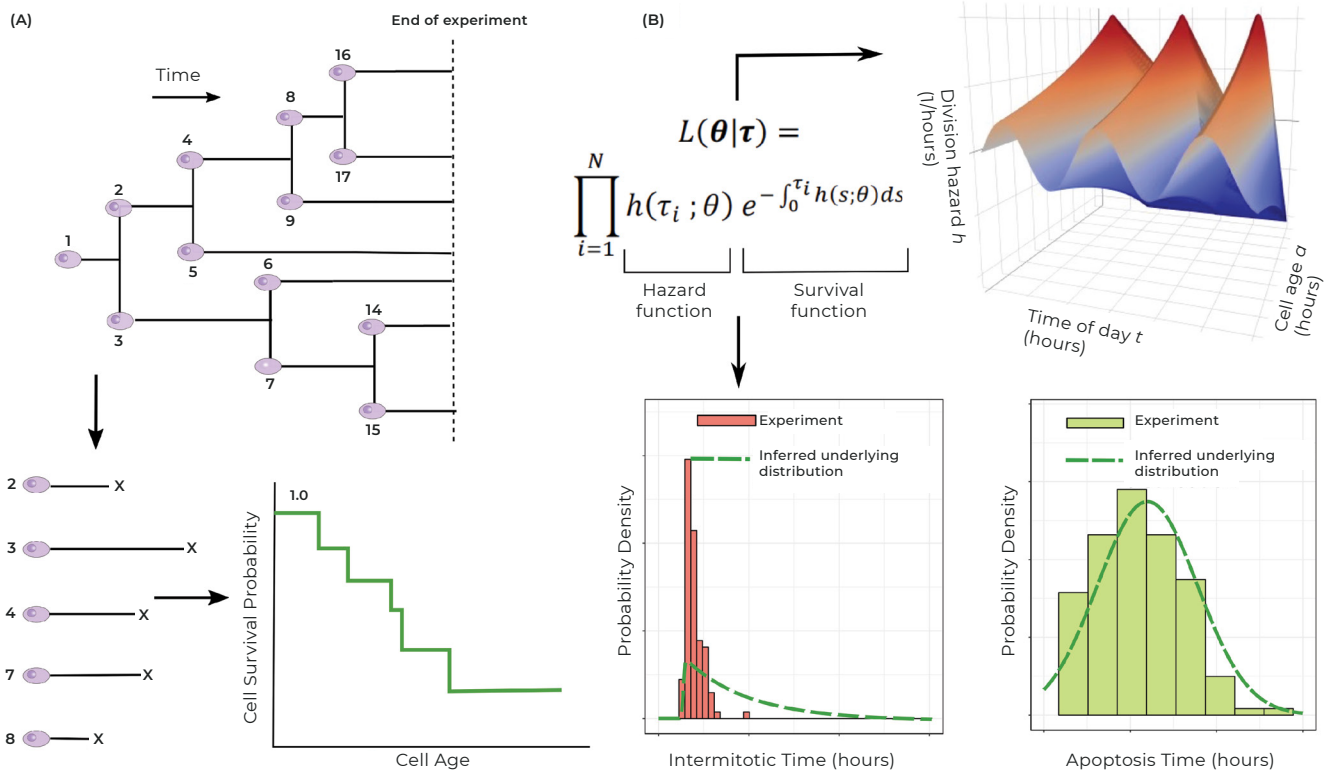
Quantitative Cell Biology: Cellular Proliferation in Development and Disease

My research combines theory and experiments to study cellular proliferation at the single cell level: its underlying physical principles, control mechanisms, and consequences in development and disease.

A fundamental challenge in cell biology is to understand and quantitatively predict how population growth of cells results from heterogeneous single cell division kinetics. This is particularly important in understanding the response of cells to drugs, for example in the treatment of diseases like cancer. Fluctuations in various cellular components drive divergent fates of single cells in response to drugs. Recent advances in microscopy and theoretical/computational tools are beginning to allow quantitative characterisation of these fluctuations, which can be leveraged to probe fundamental questions on the control of cellular decision-making.

Our lab combines theory with experiments to study cellular proliferation at the single cell level; uncover its underlying physical principles, control mechanisms, and consequences in development and disease. We use a variety of live and fixed cell imaging techniques on the experimental side, and methods borrowed from statistical physics, stochastic modelling, biostatistics, and machine learning on the theoretical end in this endeavour. Our lab's ultimate goal is to develop novel ways of bringing together theory and experiment to translate a basic understanding of cellular proliferation and its control to more clinically relevant settings.

Stochastic modelling of single cell divisions
A schematic showing how cellular proliferation as observed using live cell microscopy can be described using the language of survival analysis, where every cell division is considered an 'event' denoted by an 'x'. (B) A schematic of the basic approach to inference using survival analysis. The likelihood of observing a dataset comprising division (and/or apoptosis) times of all the N cells is written down in terms of hazard functions. The underlying parameters are then inferred, often using Markov Chain Monte Carlo methods. The hazard for division can be modelled as a function of the various measured covariates such as the circadian phase, and the parameters inferred computationally (top). Red denotes larger hazard for division, while blue represents lower hazard. In experiments performed in the presence of drugs, multiple cell fates such as cell division, death, and arrest can be induced (bottom). "Competing risks" survival analysis can be used to infer the unbiased underlying division and apoptosis time distributions (bottom; green dashed lines). The experimentally observed distributions (bottom; red and green histograms) may be highly skewed and different from the underlying distributions depending on the drug concentration used. Figure taken from Chakrabarti and Michor, Current Opinion in Cell Biology, 2020.



PUBLICATIONS

Chakrabarti and Michor, 2020. Current Opinion in Cell Biology 67, pp. 17-26.

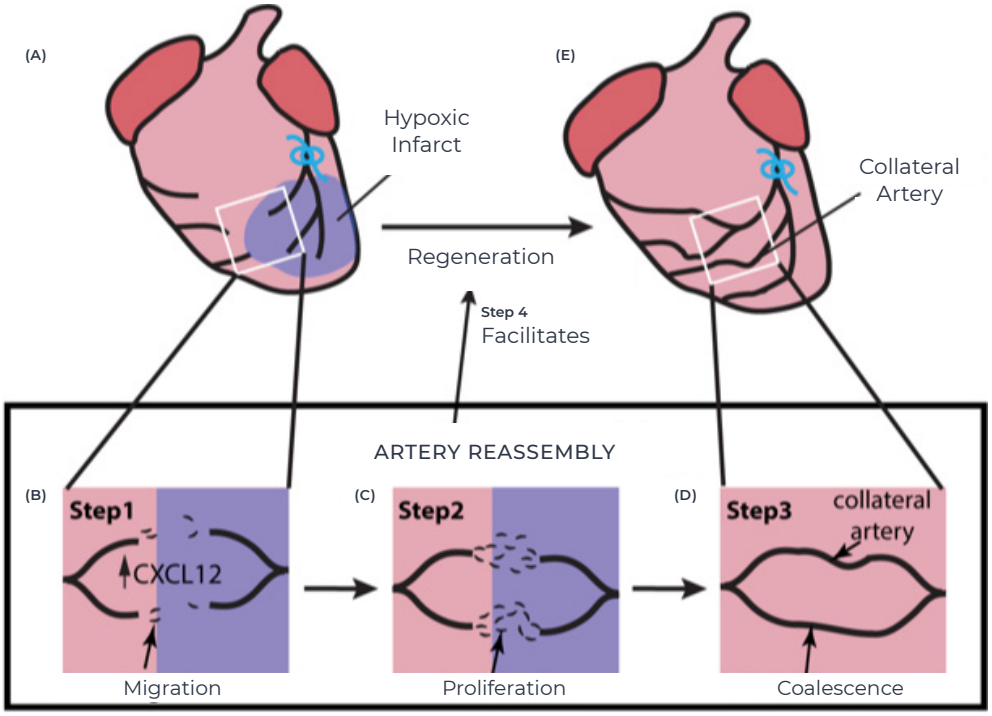
Investigating the Role of Endothelial Cells in Cardiovascular Regeneration

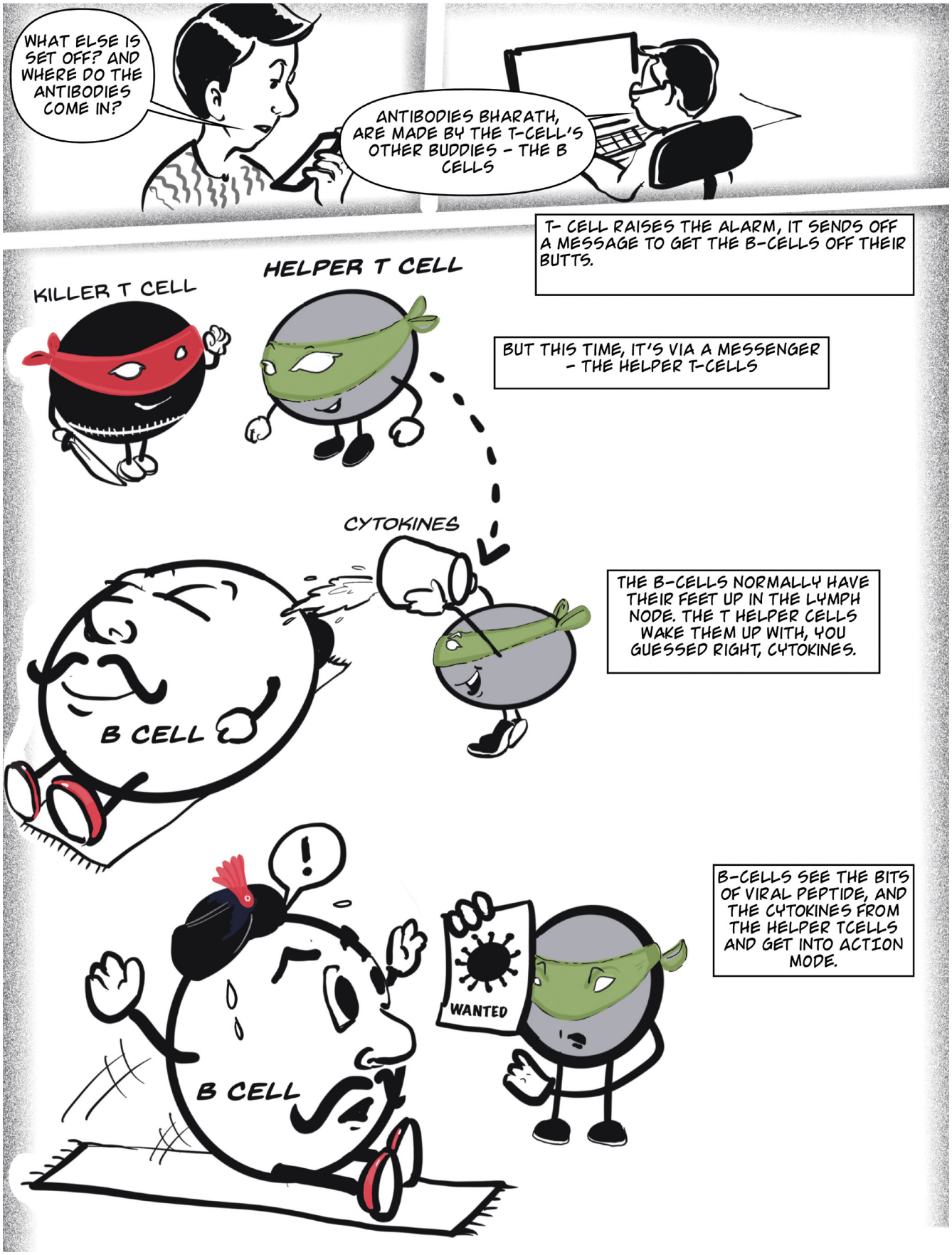
We investigate the cellular and molecular mechanisms utilised by endothelial cells (ECs) during coronary vascular remodelling, in development and disease. We use genetic mouse models, whole organ imaging, and cardiac functional assays to understand how ECs contribute to cardiac regeneration.

Management of occlusive heart disease, with angioplasty/bypass grafting can treat very few eligible patients. An alternate solution is to grow new coronary arteries in the heart. A special subtype of coronary arteries—collateral arteries—connect occluded vessels with healthy vessels and create an alternate route for blood-flow which can preserve myocardial tissue. Collateral arteries have been associated with better survival in heart patients. Despite the high clinical significance, it is unclear how collateral arteries form. Recently, we showed that collateral arteries are built through Artery Reassembly—migration, proliferation, and coalescence of pre-existing coronary artery endothelial cells—which drives cardiac regeneration in mice. We showed that hypoxia-induced CXCL12 signalling activates Artery Reassembly. Interestingly, this process is age-dependent and is not observed in adult mice, unless administered with recombinant-CXCL12.

But why do adult endothelial cells fail to build collateral arteries (or regenerate hearts)? How do collateral arteries attain maturity? Is Artery Reassembly observed in other ischemia-prone critical organs, such as the brain? These are some of the questions we are currently pursuing. The outcome of these studies will help us gain insights into the poorly understood biology of collaterals and elucidate ways for their induction in the heart.

Artery Reassembly, a multi-step artery endothelial cell process, drives cardiac regeneration. *(A, B) Neonatal myocardial infarction develops hypoxic tissue (purple), (B) followed by induction of CXCL12 in the watershed, outward migration of artery ECs, (C) their proliferation and (D) coalescence into collateral arteries. Collateral formation by Artery Reassembly facilitates (E) neonatal heart regeneration.* *Modified from Das et al. Cell, 2019.*





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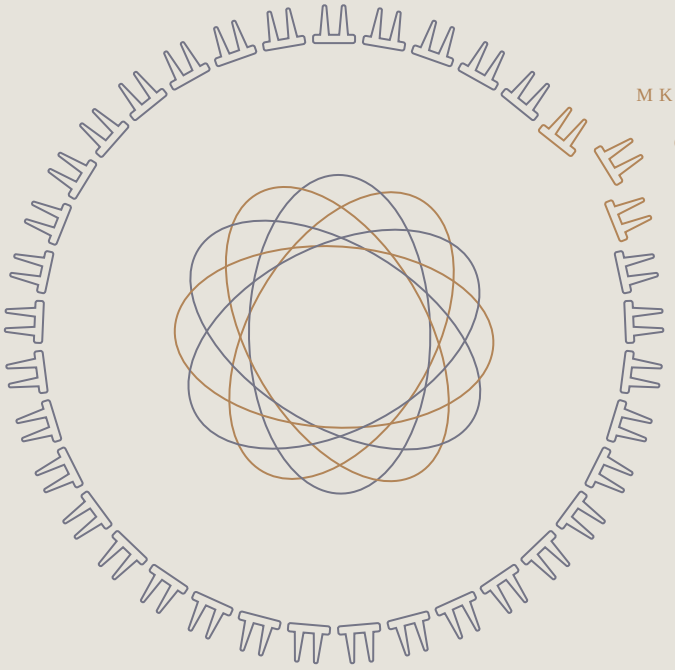


M K Mathew

Gaiti Hasan

Sudhir Krishna

Retirement Notes

M K Mathew Retires

Gaiti Hasan Retires

Sudhir Krishna Retires

M.K. Mathew Retires

This year, we see the end of an era as the last of the first guard retires. Professor M.K. Mathew, who has been an anchor at NCBS since the Mumbai days, and in many ways—from student selection and academic programmes, to the structure of the Annual Talks and the buildings themselves—his imprint marks the BLiSC campus.

I met Mathew in his pre-NCBS years at Caltech, where he was finishing up his work in the lab of Mark Tanouye. Mathew, Mani Ramaswamy, and I played basketball together and he had his uncanny accuracy even back then. Then Mathew vanished to this mysterious place called NCBS, and when, some years later, I was setting up to join NCBS myself, he was my primary email contact. I wrote to Jayant, Dean at the time, whose response was about two lines long, but Mathew helped sort me out as I worked through the initial visits and getting started.

It was Mathew who laid the foundations of the independent NCBS student programme. As the first Head of Academics, he carefully oversaw admissions and the entire academic structure. With so few students it would have been easier to just deal with each as they came, but instead he built scalable structures for admission, teaching, and each of the stages in a student's career. Many details have changed since, but the essence of Mathew's structure still guides the careers of all our students - scaled now to the hundreds.

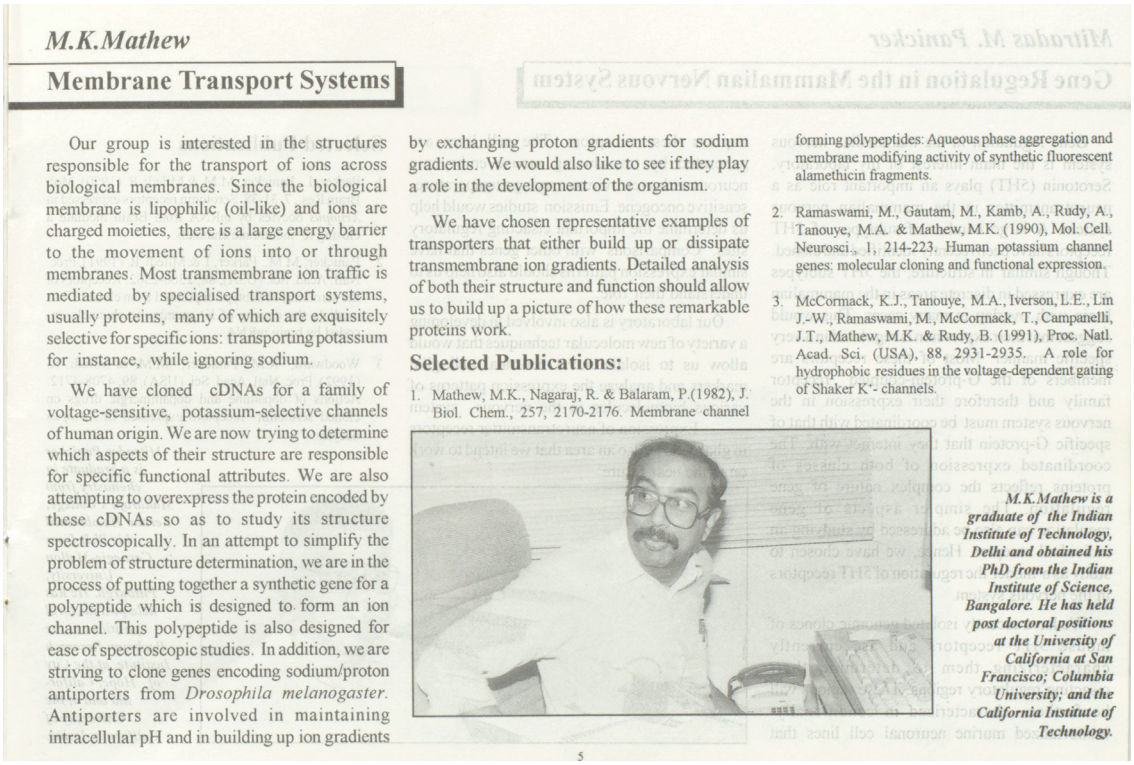
Also scaled beyond recognition is the centrepiece of our Annual Talks: the poster sessions. And his vigorous championing of it and its role in student interactions has ensured it retains all of its vibrance even today. Mathew set the standards for the best classroom manner, anchoring a course with Jayant that ran for 25 years. He also set the standards for mentorship, and was so popular that he served on as many as 25 thesis committees at any given time. He was awarded the TIFR Excellence in Teaching award in 2015 in recognition of his contributions.

A more tangible structural imprint came from his involvement in the original campus design. One could literally say he turned things around. He pointed out to the campus architect, Raj Rewal, that the then library (now Simons Centre) would have a much better outlook onto the lawn if it were rotated. So it was done, and the current coveted outlook onto the big lawn is his doing.

Structural Biology Meeting at IISc
(left to right) S. Mayor, J. Udgaonkar, M. M. Panicker, M.K. Mathew

Surely this institutional-scale, structural insight shared roots with his research into atomic-scale structures. Mathew developed a challenging and thoughtful research programme on the structure and function of ion channels. He set up the first, and still one of the only, functional bilayer membrane rigs in the country. Those were the exciting times before the first structures for the potassium channel. Mathew had a particular model—implemented in plastic, beads and wire for his incomparable lectures—for the gating of the channel by a twisting process. Today this is believed to be one of the major mechanisms by which channels open and close.

He was also our first plant scientist, and looked at salt tolerance mechanisms in rice. He had some of the most beautiful pictures of plant sodium fluxes using some of the early sodium-ion fluorescent reporters. In this capacity, as the NCBS representative plant person, he also was the anchor for our interactions with our campus host, GKVK. This may now seem routine, but there were phases of considerable excitement over many years, and Mathew's ever calm demeanor and his association with senior GKVK faculty helped steer us through these rapids.



M.K.Mathew

Membrane Transport Systems

Our group is interested in the structures responsible for the transport of ions across biological membranes. Since the biological membrane is lipophilic (oil-like) and ions are charged moieties, there is a large energy barrier to the movement of ions into or through membranes. Most transmembrane ion traffic is mediated by specialised transport systems, usually proteins, many of which are exquisitely selective for specific ions: transporting potassium for instance, while ignoring sodium.

We have cloned cDNAs for a family of voltage-sensitive, potassium-selective channels of human origin. We are now trying to determine which aspects of their structure are responsible for specific functional attributes. We are also attempting to overexpress the protein encoded by these cDNAs so as to study its structure spectroscopically. In an attempt to simplify the problem of structure determination, we are in the process of putting together a synthetic gene for a polypeptide which is designed to form an ion channel. This polypeptide is also designed for ease of spectroscopic studies. In addition, we are striving to clone genes encoding sodium/proton antiporters from *Drosophila melanogaster*. Antiporters are involved in maintaining intracellular pH and in building up ion gradients by exchanging proton gradients for sodium gradients. We would also like to see if they play a role in the development of the organism.

We have chosen representative examples of transporters that either build up or dissipate transmembrane ion gradients. Detailed analysis of both their structure and function should allow us to build up a picture of how these remarkable proteins work.

Selected Publications:

1. Mathew, M.K., Nagaraj, R. & Balaram, P.(1982), J. Biol. Chem., 257, 2170-2176. Membrane channel forming polypeptides: Aqueous phase aggregation and membrane modifying activity of synthetic fluorescent alamethicin fragments.
2. Ramaswami, M., Gautam, M., Kamb, A., Rudy, A., Tanouye, M.A. & Mathew, M.K. (1990), Mol. Cell. Neurosci., 1, 214-223. Human potassium channel genes: molecular cloning and functional expression.
3. McCormack, K.J., Tanouye, M.A., Iverson, L.E., Lin J.-W., Ramaswami, M., McCormack, T., Campanelli, J.T., Mathew, M.K. & Rudy, B. (1991), Proc. Natl. Acad. Sci. (USA), 88, 2931-2935. A role for hydrophobic residues in the voltage-dependent gating of Shaker K+- channels.

M.K.Mathew is a graduate of the Indian Institute of Technology, Delhi and obtained his PhD from the Indian Institute of Science, Bangalore. He has held post doctoral positions at the University of California at San Francisco; Columbia University; and the California Institute of Technology.

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Page on M. K. Mathew
This was sourced from a 1995 brochure about NCBS detailing the educational programmes and description of the various faculty at NCBS and their research. One of the first brochures focused solely on the work at NCBS, all of it carried when NCBS was based at the TIFR Building in IISc. Includes notes on the construction of the new campus. *Courtesy: Archives at NCBS*

Mathew has been, from the start, a patron of the athletic and choral arts on campus. He never lost his uncanny touch with the basketball, as we played in multiple courts on and off campus over the years. Once the swimming pool appeared he was in it year round, and we would complain to each other that the pool got longer every year. Long before the current cultural committee, Mathew and his lab and family were the anchors for the annual Christmas chorals, held in what is now the upper floor of Dolna.

Thus, in many ways, Mathew has shaped NCBS as we now know it. Many of the things we take for granted—almost inevitable because they work so well—were carefully crafted by him.

He continues his life-long service to institution-building through his association with IISER Thiruvananthapuram.

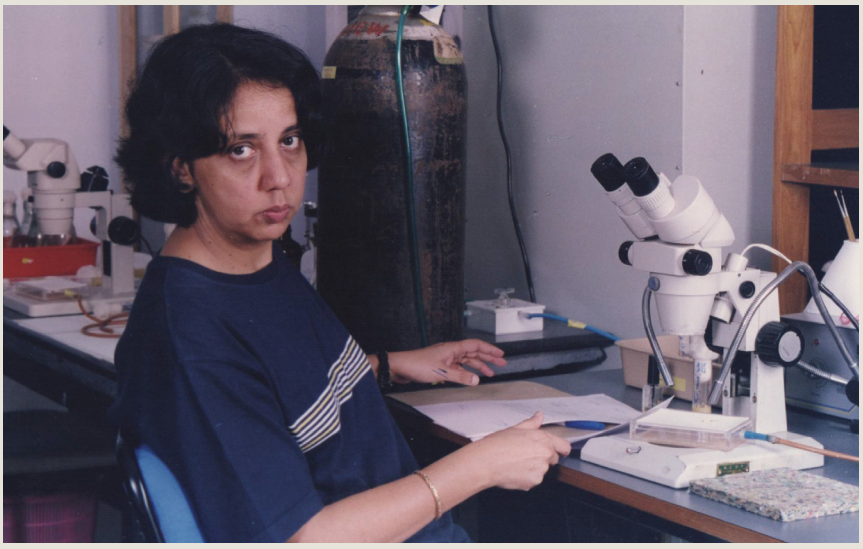
Gaiti Hasan Retires

Dr Gaiti Hasan, Senior Professor at the National Centre for Biological Sciences (NCBS), retires after a long and distinguished career. She joined the Tata Institute of Fundamental Research (TIFR), Mumbai in 1983 and except for a brief period of 2 years at Brandeis University, served continuously at TIFR for 35 years.

Gaiti's early education in the life sciences was at the University of Delhi and Jawaharlal Nehru University. Following this, she moved to England and obtained a PhD from the University of Cambridge. There, she worked under the supervision of Dr John Cordingley at the world-renowned Molteno Institute for Parasitology. Her PhD work was an influential study (Hasan, Turner & Cordingley, Cell 1983) leading to the description of novel mobile genetic elements in the parasite Trypanosoma brucei.

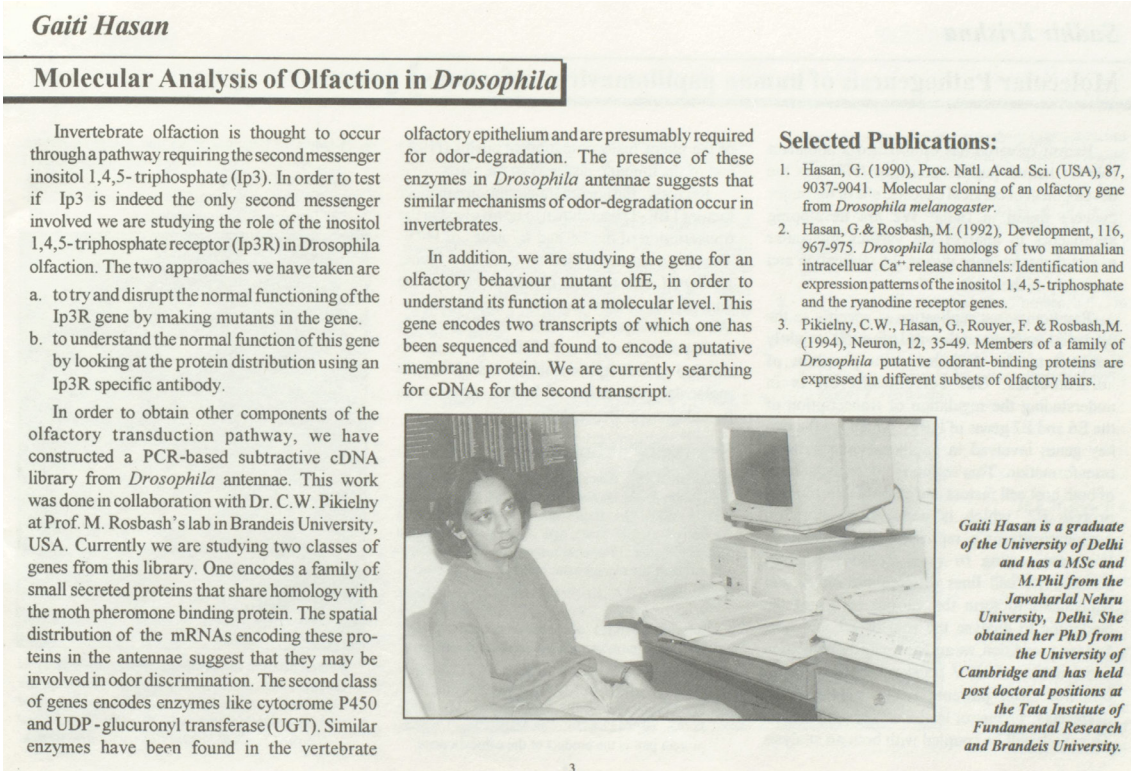
Gaiti began working at TIFR at the Molecular Biology Unit on the Bombay campus. Her foray into genetics and neuroscience was through an analysis of olfactory mutants in Drosophila, isolated around that period by Obaid Siddiqi and his student Veronica Rodrigues. With her skills in molecular biology, she used positional cloning to identify the molecular basis of the defect in the olfE mutant.

As a visiting scientist in the laboratory of Michael Rosbash at Brandeis University, Gaiti cloned the gene encoding the inositol 1,4,5 trisphosphate (IP3 receptor) receptor from Drosophila. Parallel developments in the worlds



Gaiti Hasan at NCBS, 2001
Courtesy: Archives at NCBS

of inositol lipid signalling and olfaction suggested a role for this pathway in Drosophila olfaction, leading her to undertake this venture. While obtaining the cDNA for a gene might seem trivial in the modern era of genomics, at the time, cloning it yourself was an essential venture in itself, and the key to unlocking the function of any gene product in a cellular process. When she returned to the newly established NCBS at TIFR in 1992, Gaiti initiated a systematic and sustained analysis of mechanisms by which intracellular calcium signals could regulate physiology in the fly. Over the years she and her colleagues have mapped the mechanisms by which IP3 receptor mediated Ca2+ signalling regulates function in the nervous system. This has remained



Gaiti Hasan

Molecular Analysis of Olfaction in *Drosophila*

Invertebrate olfaction is thought to occur through a pathway requiring the second messenger inositol 1,4,5- triphosphate (Ip3). In order to test if Ip3 is indeed the only second messenger involved we are studying the role of the inositol 1,4,5- triphosphate receptor (Ip3R) in Drosophila olfaction. The two approaches we have taken are

a. to try and disrupt the normal functioning of the Ip3R gene by making mutants in the gene.
b. to understand the normal function of this gene by looking at the protein distribution using an Ip3R specific antibody.

In order to obtain other components of the olfactory transduction pathway, we have constructed a PCR-based subtractive cDNA library from *Drosophila* antennae. This work was done in collaboration with Dr. C.W. Pikielny at Prof. M. Rosbash's lab in Brandeis University, USA. Currently we are studying two classes of genes from this library. One encodes a family of small secreted proteins that share homology with the moth pheromone binding protein. The spatial distribution of the mRNAs encoding these proteins in the antennae suggest that they may be involved in odor discrimination. The second class of genes encodes enzymes like cytocrome P450 and UDP - glucuronyl transferase (UGT). Similar enzymes have been found in the vertebrate olfactory epithelium and are presumably required for odor-degradation. The presence of these enzymes in *Drosophila* antennae suggests that similar mechanisms of odor-degradation occur in invertebrates.

In addition, we are studying the gene for an olfactory behaviour mutant olfE, in order to understand its function at a molecular level. This gene encodes two transcripts of which one has been sequenced and found to encode a putative membrane protein. We are currently searching for cDNAs for the second transcript.

Selected Publications:

1. Hasan, G. (1990), Proc. Natl. Acad. Sci. (USA), 87, 9037-9041. Molecular cloning of an olfactory gene from *Drosophila melanogaster*.
2. Hasan, G.& Rosbash, M. (1992), Development, 116, 967-975. *Drosophila* homologs of two mammalian intracelluar Ca^{++} release channels: Identification and expression patterns of the inositol 1, 4, 5- triphosphate and the ryanodine receptor genes.
3. Pikielny, C.W., Hasan, G., Rouyer, F. & Rosbash,M. (1994), Neuron, 12, 35-49. Members of a family of *Drosophila* putative odorant-binding proteins are expressed in different subsets of olfactory hairs.

Gaiti Hasan is a graduate of the University of Delhi and has a MSc and M.Phil from the Jawaharlal Nehru University, Delhi. She obtained her PhD from the University of Cambridge and has held post doctoral positions at the Tata Institute of Fundamental Research and Brandeis University.

Page on Gaiti Hasan
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the focus of her lab with many new aspects of this problem, methods of analysis, and emerging model systems forming part of this scientific journey.

Gaiti was among the first group of faculty recruited to NCBS (along with Obaid Siddiqi, K. VijayRaghavan, Jayant Udgaonkar, M. K. Mathew, M. M. Panicker, and S. Krishna). Together, these colleagues worked tirelessly during the early years to build the centre and place it on a trajectory that has led to its present status as one of the premier life sciences research institutes in India. In particular, she served as Head of Academic activities between 2004 and 2009, guiding the development of the student and postdoc programme at NCBS. In addition, she also served on numerous committees at NCBS, TIFR, and more generally the science landscape in India.

In the course of her career, Gaiti mentored more than 20 PhD students. Many of us who were part of her lab recall that our environment was extraordinarily well-organised, equipped to the task at hand, and very focused on the goals of our research. A key feature of her mentoring style was for the student to pay a great deal of attention to what was to be achieved, how to get there, and to do so through high-quality scientific work. Waffling, from students, was not a sought-after quality in Gaiti's lab and students learnt to take responsibility for their work or were reminded to do so.

Over the years students from Gaiti's lab have gone on to establish themselves in many areas of science including running independent research groups in academia, the biotechnology industry, science communication, teaching, and other areas of the life sciences. Last but not least, Gaiti remains a role model of an individual who accomplished much in spite of the well-documented challenges faced by women in STEM both now and all those years ago, at the start of her academic career.

As she retires we celebrate her accomplishments and wish her all the best for the future.

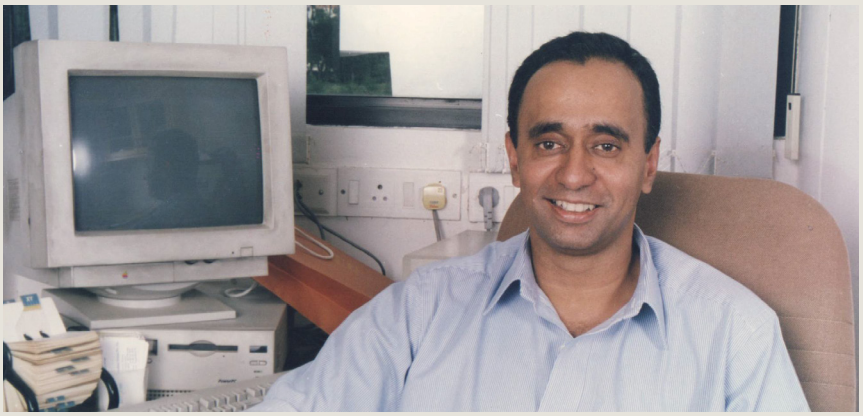
Sudhir Krishna Retires

Not everyone has a rich legacy of already being part of the TIFR family, strong Ayurvedic traditions, a background in clinical medicine, and Cambridge training all bundled into one. But Sudhir does. His uncle was the late Prof BV Sreekantan of TIFR and his grandfather, a famous Ayurvedic physician, Dr BV Pundit. Sudhir has an MBBS degree from St John's Hospital and a PhD from the University of Cambridge. Yet, he is downright simple and versatile. Sudhir can easily converse with people in his native Kannada or British English!

Sudhir joined NCBS in 1992 and has seen the institute literally grow with time. Those who have been on the campus long enough would have noticed Sudhir amble up to the canteen at 10 am for his favourite coffee and leave by 10.15 am. In fact, this habit was so disciplined that one can set their watch to it. Sudhir has always been interested in nurturing new facilities and ideas on the campus, and in mentoring new faculty.

Sudhir's research is interdisciplinary and includes fundamental science, vaccine design, and public health. His main research interests lie in human papillomavirus-driven cancers. Due to his lab efforts, the role of Notch signalling in such cancers have been revealed. He has also established excellent links with several medical colleges and cancer care centres in the country.

Sudhir, by nature, provides enormous independence to his lab colleagues to grow intellectually and drive their research. To give you an idea, Chitra Pattabiraman of his lab had followed her quests on infectious diseases of

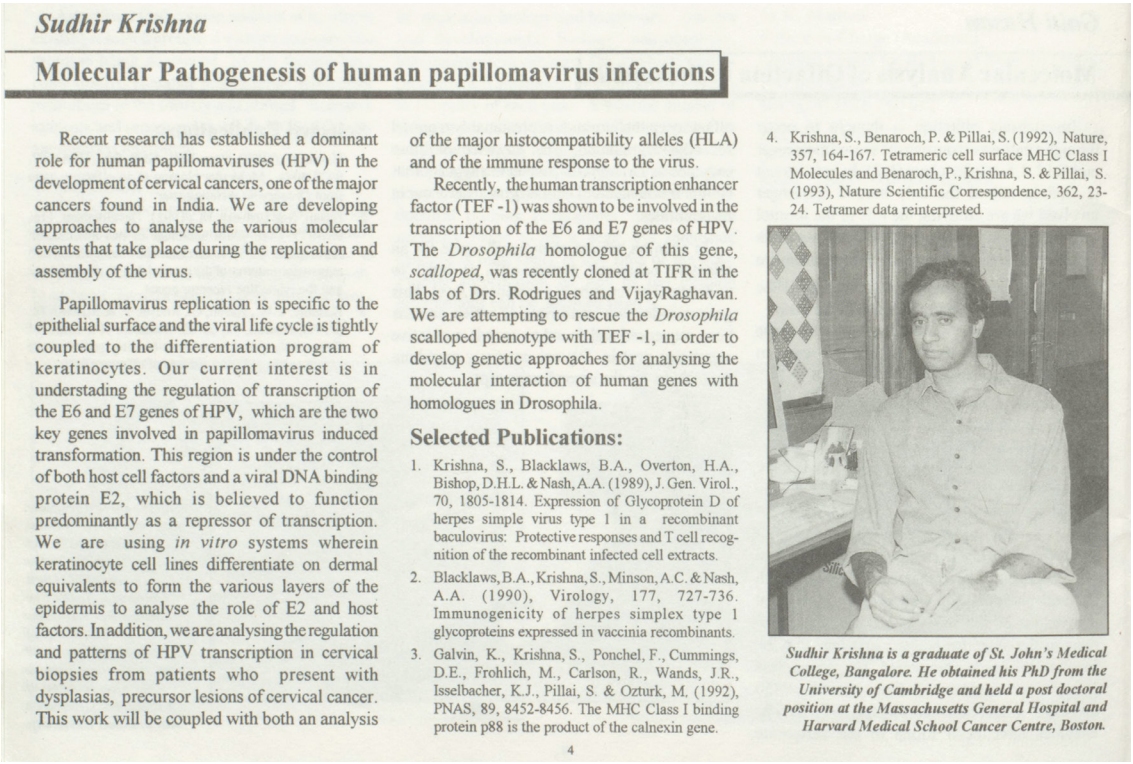


Sudhir Krishna at NCBS, 2001
Courtesy: Archives at NCBS

unknown origin. Sudhir provided her the intellectual freedom to pursue these questions and was also enthusiastic in offering her the required support. Indeed, including Mary Dias of St John's hospital, some of us ventured into this using the glue grant support from DBT fetched by Sudhir. Sudhir led exciting projects such as one on the dengue vaccine and other viral diseases by means of a grant funded by Dr Narayana Murthy (founder of Infosys). These efforts, where an exciting bunch of us work together, requires diverse expertise such as genomics, structural bioinformatics, public health, and so on.

For those who may regard Sudhir as a classic biologist, he proves us wrong with his attitude that embraces other fields of interest (such as public health, one health, vaccine design, and bioinformatics) and stays abreast with techniques such as genomics and personalised medicine. Indeed, as an offshoot of the Narayana Murthy support, he also engaged in a collaboration with a few African institutions with the purpose of capacity building, where some of us conducted workshops on bacterial sequencing and bioinformatics.

Sudhir's enthusiasm will take him far beyond his innings at NCBS. It looks like he has just scored a century. I am sure he will continue to surprise us to show how young he is in his thinking and practice of research!



Sudhir Krishna

Molecular Pathogenesis of human papillomavirus infections

Recent research has established a dominant role for human papillomaviruses (HPV) in the development of cervical cancers, one of the major cancers found in India. We are developing approaches to analyse the various molecular events that take place during the replication and assembly of the virus.

Papillomavirus replication is specific to the epithelial surface and the viral life cycle is tightly coupled to the differentiation program of keratinocytes. Our current interest is in understading the regulation of transcription of the E6 and E7 genes of HPV, which are the two key genes involved in papillomavirus induced transformation. This region is under the control of both host cell factors and a viral DNA binding protein E2, which is believed to function predominantly as a repressor of transcription. We are using *in vitro* systems wherein keratinocyte cell lines differentiate on dermal equivalents to form the various layers of the epidermis to analyse the role of E2 and host factors. In addition, we are analysing the regulation and patterns of HPV transcription in cervical biopsies from patients who present with dysplasias, precursor lesions of cervical cancer. This work will be coupled with both an analysis of the major histocompatibility alleles (HLA) and of the immune response to the virus.

Recently, the human transcription enhancer factor (TEF -1) was shown to be involved in the transcription of the E6 and E7 genes of HPV. The *Drosophila* homologue of this gene, *scalloped*, was recently cloned at TIFR in the labs of Drs. Rodrigues and VijayRaghavan. We are attempting to rescue the *Drosophila* scalloped phenotype with TEF -1, in order to develop genetic approaches for analysing the molecular interaction of human genes with homologues in Drosophila.

Selected Publications:

1. Krishna, S., Blacklaws, B.A., Overton, H.A., Bishop, D.H.L. & Nash, A.A. (1989), J. Gen. Virol., 70, 1805-1814. Expression of Glycoprotein D of herpes simple virus type 1 in a recombinant baculovirus: Protective responses and T cell recognition of the recombinant infected cell extracts.
2. Blacklaws, B.A., Krishna, S., Minson, A.C. & Nash, A.A. (1990), Virology, 177, 727-736. Immunogenicity of herpes simplex type 1 glycoproteins expressed in vaccinia recombinants.
3. Galvin, K., Krishna, S., Ponchel, F., Cummings, D.E., Frohlich, M., Carlson, R., Wands, J.R., Isselbacher, K.J., Pillai, S. & Ozturk, M. (1992), PNAS, 89, 8452-8456. The MHC Class I binding protein p88 is the product of the calnexin gene.
4. Krishna, S., Benaroch, P. & Pillai, S. (1992), Nature, 357, 164-167. Tetrameric cell surface MHC Class I Molecules and Benaroch, P., Krishna, S. & Pillai, S. (1993), Nature Scientific Correspondence, 362, 23-24. Tetramer data reinterpreted.

Sudhir Krishna is a graduate of St. John's Medical College, Bangalore. He obtained his PhD from the University of Cambridge and held a post doctoral position at the Massachusetts General Hospital and Harvard Medical School Cancer Centre, Boston.

Page on Sudhir Krishna
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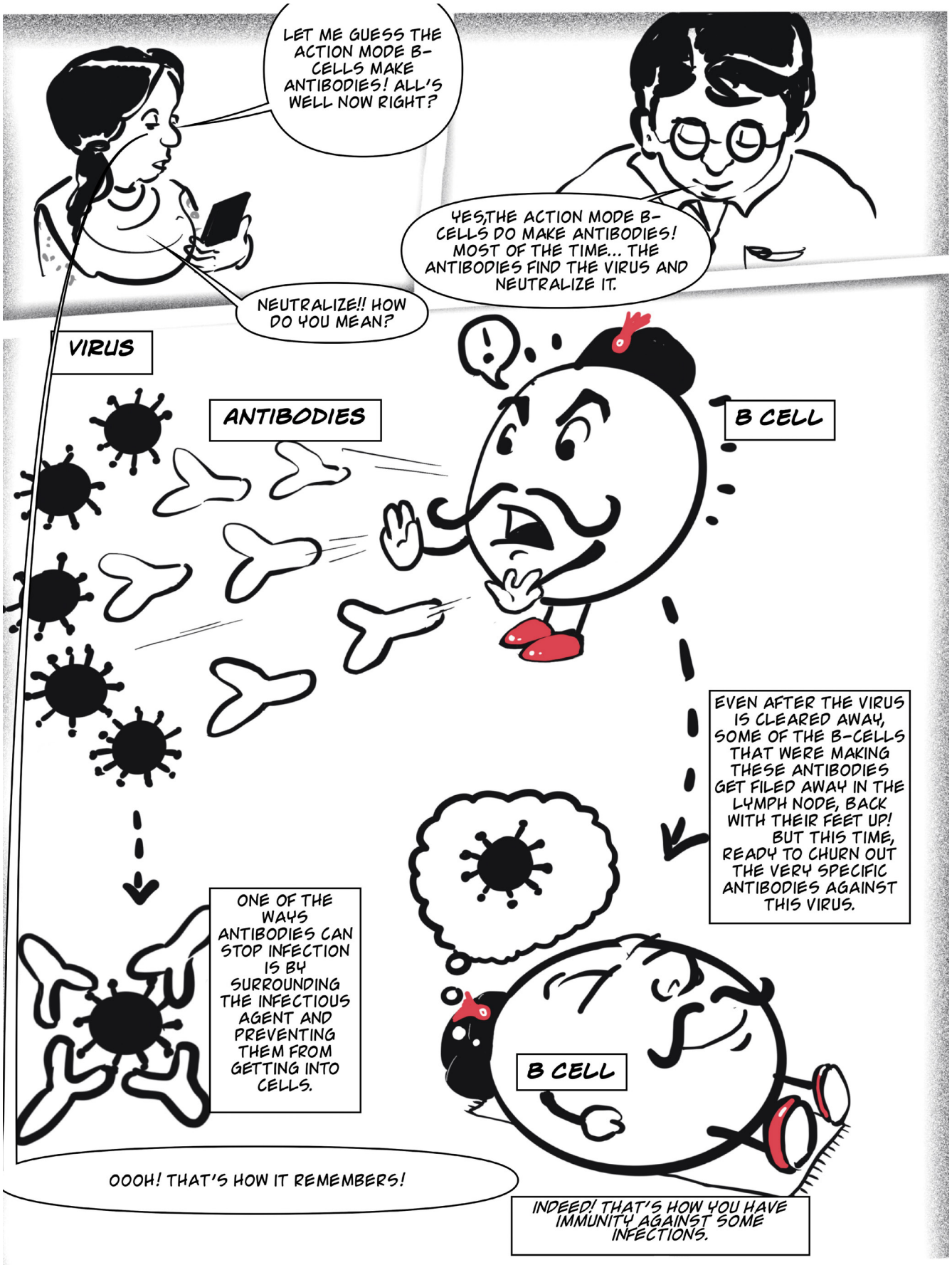
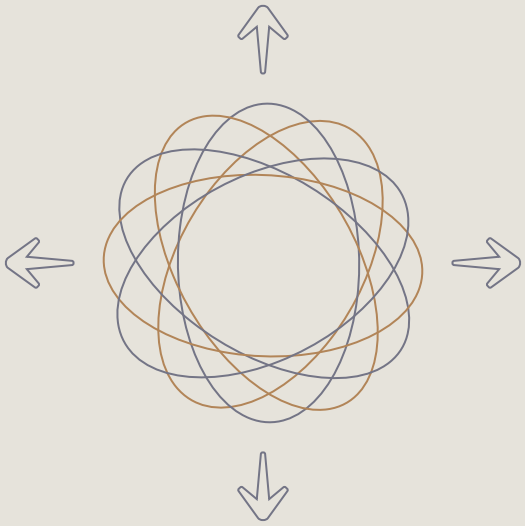


These pages are excerpts from a series created, designed, and written, by Arvind Ramanathan of DBT-inStem and Sonia Sen from TIGS-CI. They are illustrated by Arvind Ramanathan as a part of the Cluster's COVID-19 Response Initiative. The work was originally published on www.covid-gyan.in



Administration and Academics

Administration and Finance • Srinidhi V and K P Pandian
Masters Programme in Wildlife Biology and Conservation • Jayashree Ratnam
Research Facilities Report (2019-2020)

Administration and Finance

NCBS-TIFR was established as a Centre of TIFR in 1991, as approved by the Union Cabinet. In the three decades since its establishment, NCBS-TIFR has grown into an exceptional Centre of Excellence in the disciplines of biological sciences. Its faculty—past and present—has considerably influenced the advancing research frontiers in biological sciences, nationally and internationally. It has always been understood that for research and academic activities of the Centre to flourish and expand, the Administration and Finance Divisions need to be geared up to provide effective, efficient, and sustained support at all times.

In terms of the umbrella MoU dated July 22nd 2010—signed between Department of Atomic Energy (DAE) and Department of Biotechnology (DBT), Government of India—and the operational MoUs dated April 1st 2016—signed between NCBS-TIFR, the Institute for Stem Cell Science and Regenerative Medicine (DBT-inStem), and the Centre for Cellular and Molecular Platforms (C-CAMP), and on February 20th 2018 between NCBS-TIFR and DBT-inStem, the Centre operates within the larger ecosystem of the Bangalore Life Science Cluster (BLiSC).

As in previous years, the Administration and Finance Divisions worked towards continuous improvement in streamlining operation processes with a view to achieve optimum efficiency to meet the requirements of faculty, scientists, technical and administrative staff, and students on campus (including the hostels and residential quarters at Mandara). The focus was on key management principles of planning, organising, directing, regulating, and implementing with greater efficiency at each stage. These principles were modulated as per the requirements of the Centre operating within the

Details of human resources at NCBS-TIFR as of March 31st 2020 is below

PARTICULARS	SANCTIONED POSITIONS	FILLED POSITIONS	VACANCIES	DEPUTATION	PACHMARHI FIELD STATION
Academics	40	33	7	1	0
Scientific & Technical	69	28	41	0	1
Administrative	33	20	13	0	1
Auxiliary	5	4	1	0	7
Total	**147**	**85**	**62**	**1**	**9**

CATEGORY	NUMBER
Regular Staff	85
Pachmarhi Staff	9
Contract Staff	71
Outsourced	381
PhDs (Research Scholar)/ Int. PhDs (Junior Scholar)	150
JRF/SRF/ Project Assistants	101
Post-Doctoral Fellows	77
M.Sc. Wildlife	16
Graduate Trainees/ Interns	13
Total	**903**

Total footfall relating to NCBS is 903 as per details given above

BLiSC ecosystem. Efficient use of human and financial resources helped increase the productivity of individual employees towards achieving the operational objectives.

The member institutions of BLiSC complement each other's scientific and administrative activities. The Cluster comprises 1429 scientific and allied human resources and has emerged as a hub of top-class scientific capabilities and capacities in India. The BLiSC model is key to achieving scale and pooled infrastructure for high impact research and innovations. The administration and finance divisions of NCBS-TIFR have ably adapted themselves to work in the novel environment of shared services for optimal output and economy.

During the year 2019-20 the ratio of faculty to students was 1:11 which matches global standards of excellence. The expenditure of the centres on research and development has shown an increase from Rs. 693.42 crores in 2018-19 to Rs. 703.50 crores in 2019-20.

A highlight of 2019-20 was the study visit of the department-related Parliamentary Standing Committee on Science & Technology, Environment, Forests and Climate Change to the campus on December 29th 2019. The Committee had in-depth interaction with the senior management and faculty of the Centre and visited various scientific facilities on campus. The Committee was highly impressed by the high-quality research carried out at the Centre. The appreciation and directions provided by the chairperson and members of the Parliamentary Standing Committee have imparted a much-valued impetus to the research endeavours of the Centre.

The financial performance in 2019-20 can be termed satisfactory given the circumstances in which the functions were to be carried out. Fund constraints were one of the primary challenges that NCBS had to face in 2019-20, which did impact a few of the activities to a certain degree. Funds paucity didn't stop NCBS in pursuing its science-hunting; research was carried on with the same vigour and intensity in spite of some challenges, thanks to effective funds management and a Just-In-Time approach. Except for a few, most envisaged activities and procurements were met successfully. No incidence of default or non-compliance to statutory / non-statutory regulations were reported. Vendor obligations were generally met on time and no adverse reporting on any issues made it to the Audit Reports. NCBS fully migrated to online corporate banking and also stopped cash transactions: Government

The human resources and financial data for 2019–2020 at a glance

PARTICULARS	2018-19	2019-20
Research & Development	316.70	302.66
Extra Mural Grants	376.72	400.84
Salaries & Fellowships	246.68	296.94
Operational Expenditure	281.10	321.19
Construction	152.20	70.57
Total	**1373.20**	**1392.20**

of India implemented Bharatkosh for mandatory remittance of non-tax revenues to GoI on Bharatkosh portal electronically. This was implemented successfully.

Adminstrative Staff of NCBS

In addition, extra-mural funding supplemented research efforts to a greater extent. 70 new grants were added in the fiscal year 2019-20. These grants have helped support more than 200 researchers. The DBT, Science & Engineering Research Board (SERB), Department of Science & Technology (DST), Wellcome Trust-DBT India Alliance, Simons Foundation, The Human Frontier Science Programme (HFSP), Asian Office of Aerospace Research and Development (AOARD), Max Planck Institute (MPI), and the Ministry of Human Resource Development (MHRD) were among major funders under the extramural category. Shri N R Narayana Murthy, co-founder of Infosys, has been financially and morally supporting NCBS' Dengue Vaccine Development Programme through a generous contribution (Rs. Two Crore in 2019-20). Shri. S. Gopalakrishnan & Smt. Sudha Gopalakrishnan, Trustees of Pratiksha Trust, also contributed Rs. One Crore this year towards world-class research in neurobiology. Similarly, M/s TTK Prestige Limited also contributed Rs. 50 lakh this year towards the, "Shri T. T. Narasimhan Grant" that supports the, "Scientists Without Boundaries" programme.

I would like to take this opportunity to thank our faculty, students, partners, and the entire NCBS community for their continued support. I would also like to commend the administrative staff for their important contributions and continuing efforts in helping NCBS to function smoothly. I would also like to sincerely thank the DAE and TIFR for their endless cooperation and support, and for being the backbone of the Centre. I would also like to express my profound gratitude to all funding agencies and philanthropic donors for their kind patronage and continued support. I would also like to reassure you that we are focused and determined to meet the challenges whatever be the scale.

Srinidhi V.
Head, Finance

K. P. Pandian
Head, Administration

Masters Programme in Wildlife Biology and Conservation

The Masters Programme in Wildlife Biology and Conservation at NCBS is a unique model in higher education. It is a partnership between academic institutions and conservation NGOs, to deliver on our mission: to build capacity for the conservation of India's wildlife and natural ecosystems through a rigorous high-quality training programme.

Wild Gaur (Bos gaurus) in an agricultural field
Photo Credit: Kalyan Varma http://kalyanvarma.net/

Established in 2004, the Wildlife Biology and Conservation Programme admits 15 Indian students every two years, following a national entrance test and in-person interviews. Through three semesters of intensive coursework—followed by a field-based research project in the final semester—students are rigorously trained in the theory and practice of wildlife conservation science.

In 2016, the programme added an additional two places for international students from South, South-East, and Central Asia, to extend its mission of building capacity for conservation across the wider Asian region. Our first international students have come from Mongolia, Nepal, and Bangladesh. Now in its 17th year, the programme has produced 117 graduates who are today engaged in conservation research and on-the-ground action for conservation across India and further afield.

For the current cohort of students (2018-2020) in the programme, as for most field biologists across the world, 2020 has been a year like no other. At the time the early news of COVID-19 made the headlines and was declared

a global pandemic, our students were spread out in field sites across the country, many in remote and rural areas in Assam, Uttarakhand, Bengal, Tamil Nadu, the Andaman Islands, and the Lakshadweep Islands. Most students chose to stay put at their field sites as the national lockdown was announced, in the hope that they would be able to resume data collection after. In the challenging months that followed, as the lockdown extended from weeks to months, they hunkered down to wait it out in basic living conditions, far from the comforts of home, family and friends, and conscious that as outsiders in remote rural communities, they had to act very responsibly. We are very proud to say that our students met these challenges with great calm and resolution; while some volunteered to help with food and medicine deliveries to local elders in the community, others worked to raise funds for migrant relief and supplies to needy families, while yet others took to conservation action and outreach online.

Eventually, as restrictions lifted, some students were able to resume data collection, but for others, the optimal time for data collection had passed, as birds had stopped breeding, or dolphins had migrated down-river, or trees had stopped fruiting. If the challenge of staying in field conditions through this period was hard, the disappointment of not being able to collect the data and execute their projects as planned, was an even harder pill to swallow. Finally, when it was clear that no further work could be done, and inter-state travel resumed, students gradually began to return to campus, where they had to immediately quarantine for two weeks. Then began the task of writing up their research work, within the limits of the data collected, and complementing their work with secondary data and new and unplanned analyses. As of this writing, all students have submitted their dissertations and are awaiting their examiner reviews, while one student has even published a short note based on his field observations.

While jobs in conservation are hard to come by at any time, funding cutbacks have hit the conservation sector particularly hard in the wake of the pandemic. However, we are confident that these intrepid students—energised by their successful completion of this most challenging of field seasons and writing—will abide and find creative ways to engage with and contribute to conservation in the future.

Now more than at any other time, we are incredibly grateful to our network of dedicated faculty and resource people from institutions across the country; our student advisors and co-advisors, and our fantastic student alumni who

worked with and supported our students through this extended period. While we have always known that this support network makes our programme the unique space that it is, never was it clearer than in this unusual year. Our conservation village is alive and well, and we are very fortunate to be a part of this extended community.

As we enter another year, we look forward to expanding our programme to a consortium of multiple partners and diversifying our engagements in capacity building for conservation research, action, and engagement.

Jayashree Ratnam
Programme Director, Wildlife Biology and Conservation Programme

Lockdown art, by Kaushik Sarkar, Class of 2020, painted on pebbles from his field site in upper Assam, with study species of his class
Photo credit: Kaushik Sarkar

A working day in Ranthambore Tiger Reserve, from Sarang Mishrikotkar, Class of 2020
Photo credits: Sarang Mishrikotkar

Research Facilities Report (2019–2020)

Current scientific research depends extensively on the use of sophisticated and fast advancing technology platforms. Key to sophisticated equipment, is expertise and in-depth knowledge in operating and using the technology to develop newer scientific methods. Access to rapidly evolving genome engineering technologies and sophisticated biological manipulations at tissue and organismal level has driven scientific research to evolve more rapidly than envisioned a decade ago. Research laboratories with immediate access to cutting-edge technologies are able to address scientific questions at an accelerated pace. This is particularly imperative for complex experiments that require simultaneous use of several advanced technologies. This necessitates a pool of well-trained technicians with up-to-date knowledge in the use of these technology platforms. Centralised facilities such as ours offer training to both internal and external researchers, as well as offering technical and scientific advice.

Facilities Coordination Committee: Uma Ramakrishnan, Colin Jamora, Taslimarif Saiyed, Krishnamurthy H., Raghu Padinjat, and Upinder Singh Bhalla

The Animal Care and Resource Centre (ACRC) is a unique, state-of-the-art high barrier specific pathogen free (SPF) laboratory animal facility, providing services and resources to both institutional and external investigators. The Centre helps researchers accomplish animal research objectives while ensuring optimal welfare conditions and adherence to animal ethics regulations. Currently, the ACRC has over 300 strains of mice, over 12 lines of rats, 12 lines of zebrafish, and Xenopus laevis frogs. All mice and rat colonies are housed in individually ventilated caging (IVC) systems with a controlled environment in the animal rooms. The ACRC is currently used by 33 BLiSC labs and handles over 67 animal-based research projects per year. In the last year, the Centre trained 97 internal users and 21 external scientists in various aspects of lab animal management. There have been about 12 publications from the ACRC during the last year.

ACRC Crew: Mohan G. H., Aurelie Jory-Lily, Latha Chukki, Shwetha Reddy, Yogesh C., Sreenivasulu T., Vinodkumar D., Manjunath A. M., Rupa Kumari, Lalitha, Arpana H., and Shruthi M.

Faculty Advisory Committee: Colin Jamora, Raj Ladher, Hiyaa Ghosh, Arjun Guha, Vatsala Thirumalai, Tina Mukherjee, and Raghu Padinjat

The Animal Care and Resource Centre

The Biosafety Facility at the NCBS comprises dedicated BSL-2 and BSL-3 laboratories. The BSL-2 laboratory facilities are equipped with class-2 biosafety cabinets and essential equipment to perform in vitro experiments on known risk group-2 (RG-2) infectious agents and transfection studies. Additionally—based on risk assessments and approvals from regulatory committees—the NCBS BSL-2 facility also permits the study of clinical specimens.

Between 2019 and 2020, users have accessed the BSL-2 facility for transfection studies alone (mostly lentiviral/retroviral), and from May 2020 onwards, we have seen ongoing COVID-19 related experiments.

The BSL-3 laboratory suites have two independent workspaces (LAB-1 and LAB-2). LAB-1 is dedicated to experiments involving Mycobacterium tuberculosis while LAB-2 is used for studies on risk group-3 viral agents. During August 2020, the BSL-3 LAB-2 was commissioned for in vitro studies on COVID-19 (SARS-CoV-2).

Biosafety Facility Crew: Jagadish Sampath and Ranjith P. P.

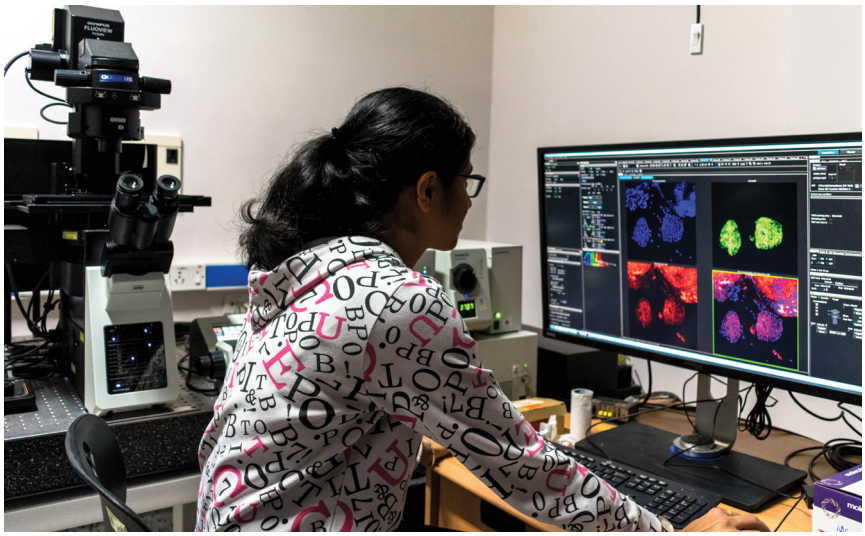
Faculty Advisory Committee: Shivaprasad P. V., Varadharajan Sundaramurthy, Colin Jamora, and Sunil Laxman

The Biosafety Facility

The Central Imaging and Flow Cytometry Facility (CIFF) is equipped with 19 high-end microscopes and 11 flow cytometers. The CIFF is an operator-free facility which caters to the needs of both internal and external researchers. The facility clocked in 18,664 hours of use between 2019 and 2020 alone. Perennial training programmes in imaging and flow cytometry are conducted at the CIFF and are open to basic and clinical researchers. The facility has trained 171 internal and 51 external researchers between 2019 and 2020, who have published 51 papers in peer-reviewed journals.

CIFF crew: Feroz M. H. Musthafa, Divya A., Raksha K., Kulkarni R., Ankitha K. B., Anil Kumar H. V., and Krishnamurthy H.

Faculty Advisory Committee: Anjana Badrinarayanan, Raj Ladher, Sanjay Sane, Vinoth Kumar KR, Srikala Raghavan, Arjun Guha, and Shashi Thutupalli



The Central Imaging and Flow Cytometry Facility

The Electron Microscopy (EM) Facility is equipped with a high-resolution Transmission Electron Microscope (Tecnai T12 G2 spirit), a high-resolution Field Emission Scanning Electron Microscope (Merlin Compact VP) fitted with cryo-stage, and a Micro-Computed Tomography (micro-CT) machine.

The biological sample preparation lab is equipped with ultra-microtome, critical-point dryer, sputter coaters, chemical hoods, a plunge freezer, and dissection microscopes. As this is an operator-free facility, the EM facility teaches internal users to operate various equipment themselves and also caters to the needs of external users. Since April 2019, the EM facility and the facility personnel have been acknowledged in 15 publications or preprints.

EM Facility Crew: Santosh Kumar, Sunil Prabhakar, and Anjana M. U.

Faculty Advisory Committee: AAnjana Badrinarayanan, Raj Ladher, Sanjay Sane, Vinothkumar K. R., Srikala Raghavan, Arjun Guha, Varadharajan Sundaramurthy, and Shashi Thutupalli

The Fly Facility

The Fly Facility (FF) generates approximately 150-200 transgenic flies, and 20-30 CRISPR-based mutants annually. In recent years, the Fly Facility has provided services in molecular DNA cloning using various molecular techniques, making it the only facility worldwide that provides a complete CRISPR service from designing and cloning molecular constructs, injections, and screening to the generation of desired genomic manipulations in Drosophila melanogaster. The facility maintains ~8,000 different fly strains for internal users and also supports researchers in technology development in the area of Drosophila genome engineering. In the last year, the Fly Facility catered to 14 internal users on a monthly basis and 50 external users. In addition, it trained three users in different methods in fly genetics, and was acknowledged for its contributions in 15 publications.

FF Crew: Deepti Trivedi, Yashwantha, Srividhya A., Hemavathy C., Anitha V. A., Nataraj N., Kishore V., Shwetha H., Jithin R., Doyel Dasgupta, and Homica Arya

Faculty Advisory Committee: Raghu Padinjat and Tina Mukherjee

The Genomics Facility

The Genomics Facility includes both a Sanger sequencing and Next Generation Genomics Facility (NGGF). The Sanger sequencing facility is equipped with a ultra-modern 48 capillary Sanger sequencing machine, and provides plasmid, PCR product sequencing, and genotyping services to internal and external researchers in short turnaround times.

The NGGF is equipped with one sophisticated, high-throughput, next generation sequencing platform (Hiseq2500), and two bench-top next generation sequencing platforms (Miseq and Ion Proton). The NGGF caters to the next generation sequencing needs of internal and external researchers, while providing user training and support in NGS library preparation using various protocols (DNA, mRNA, small RNA, ChIP, metagenomics, etc.) and sequencing. The NGGF trained 23 researchers between 2019 and 2020, and has been acknowledged in 33 published papers.

Genomics Facility Crew: Awadhesh Pandit and Vijay Soni

Faculty Advisory Committee: Aswin Seshasayee, Deepa Agashe, Dimple Notani, and Dasaradhi Palakodeti

The Green House Facility has seven greenhouses that allow researchers to maintain pure/transgenic strains of plants and insects, and to study plant-animal interactions. The greenhouses are equipped with adjustable and fully automated climatic control systems to control light, temperature, and humidity levels using special lights, shading screens, evaporative pads, fan cooling systems, heaters, humidifiers, and dehumidifiers.

Green House Facility Crew: Ranjith P. P., Thirumala K., Narasimha Raju, and Parvatamma

Faculty Advisory Committee: Shivaprasad P. V., Mahesh Sankaran, Krushnamegh Kunte, Uma Ramakrishnan, and Sanjay Sane

The Green House Facility

The High Performance Computing Facility caters to the ever-increasing demands for high-performance computing from our scientific community. The facility at NCBS is a symbiosis of computing, network, graphics, and visualisation. The facility is a functionally distributed, super-computing environment, with shared memory systems, up-to-date computing systems, and open source software packages – all of which are interconnected via Infiniband network. The facility is equipped with three high-performance computer clusters and hosts 300 TFlops of computing power in total with 8 GB memory per core.

The facility also includes one storage system with a parallel file system, providing a bandwidth of 20GB/s, as well as one storage system with 100,000 IOPS and an overall usable capacity of 1.8 PB.

IT Crew: Baruah P. K., Rajshekar K. S., Rajesh R., Chakrapani, Alok B., Divya K., Subramani R. P., Vishnu K., Mohammed T., Divyashree M., and Shashank G.

Faculty Advisory Committee: Vinothkumar K. R., Sabarinathan Radhakrishnan, and Upinder Singh Bhalla

The Mouse Genome Engineering Facility (MGEF) provides services and training to generate genetically modified mouse models using the latest gene editing and transgenic technologies. Other operational domains include the generation of specific pathogen-free mice through strain re-derivation and embryo transfer techniques.

Additionally, the MGEF team has expertise in mouse sperm and embryo cryopreservation, cryo-recovery, and in vitro fertilisation. It also continues to provide services to backup, archive, and resurrect frozen mouse sperm or embryos from internal and external Indian and international collaborators. This portfolio of services allows the MGEF to regularly add and share new mouse stocks consolidated in a national mouse repository. The MGEF organises several hands-on workshops throughout the year allowing scientists from all over India to acquire skills in the latest mouse genome engineering, embryo microinjection, stock cryopreservation, and assisted reproductive technologies to enhance mouse colony management possibilities. Over the last year the MGEF generated 11 new mouse models, including a series of new humanised-ACE2 mouse models to enhance COVID-19 based research and therapeutics in India. The MGEF has also provided training to 30 Indian students and scientists and carried out over 135 mouse stock cryo-archiving or rederivation projects for scientists nationwide in 2019 and 2020.

MGEF Crew: Aurelie Jory-Lily, Shilpa B. A., Jasper Chrysolite Paul, Saumya Mary Mathew, and Latha Chukki

Faculty Advisory Committee: Colin Jamora, Raj Ladher, Hiyaa S Ghosh, Arjun Guha, Vatsala Thirumalai, Tina Mukherjee, and Raghu Padinjat

The Mouse Genome Engineering Facility

The Mass Spectrometry (MS) resources on campus aim to provide researchers with modern techniques and equipment to characterise biomolecules such as metabolites, proteins with post-translational modifications, glycans, and lipids. The facility is equipped with advanced technology and is actively involved in developing new analytical methods required to facilitate on and off-campus research. In addition to providing MS-based structural characterisation services, the MS facility also provides online and on-site 3–5

day training programmes on the use of different LC-MS/MS technologies such as lipidomics, proteomics, metabolomics, and glycomics.

In the period 2019–2020, 81 internal and external researchers were trained before the pandemic situation came to light, and the facility's contribution was acknowledged in 18 publications.

MS Crew: Chhaya Patole, Padma Ramakrishnan, Sabyasachi Haider, Alifia Jaffer, Raviswamy M, Srinivas Rao, Radhika Reddy, Nithin S, and Tanmayi

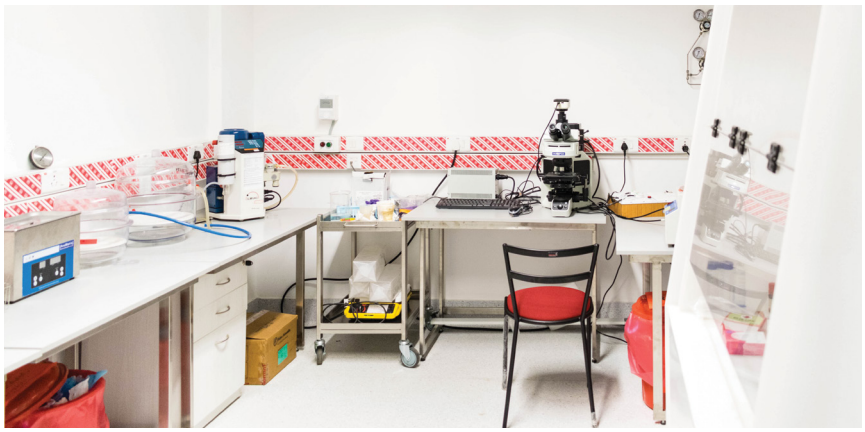
Faculty Advisory Committee: Arvind Ramanathan, Sunil Laxman, and Raghu Padinjat

The Mass Spectrometry

The Microfluidics and Microfabrication Facility (MMF) is equipped for Su8 photolithography and PDMS fabrication technologies, along with a cutting edge Class 10000 cleanroom and sub-micron resolution mask aligner. It provides micro-fabricated device delivery and equipment access for the needs of internal and external researchers. The customised training programmes in the facility are open to academic and industrial researchers and companies. The MMF is being enhanced with further design and plastic microfluidic device fabrication capabilities, and trained 52 researchers and innovators between 2019–2020.

MMF Crew: Subhash K.M., SriCharan Lakkaraju, and Feroz M.H. Musthafa

Faculty Advisory Committee: Anjana Badrinarayanan, Raj Ladher, Sanjay Sane, Vinothkumar K. R., Srikala Raghavan, Arjun Guha, and Shashi Thutupalli



The Microfluidics and Microfabrication Facility

The Nuclear Magnetic Resonance Facility (NMR) is equipped with two machines (800 MHz and 600 MHz) with cryo- probes. The facility aids in studies that focus on the de novo structure determination of macromolecules such as proteins and nucleic acids, and their dynamics in the picosecond to millisecond time scales. NMR spectroscopy is a versatile technique for calculating chemical shift perturbations (CSPs) during protein-protein, protein-ligand, and protein-nucleic acid titrations. In structural biology, real time NMR is extensively used to understand the folding pathways of proteins. The facility provides round-the-clock service for both internal and external users, and periodically conducts training programmes for new users, as well as hands-on training sessions for regular users. During the last year (2019-2020), the NMR facility trained 8 researchers and has been acknowledged in 10 published papers.

NMR Crew: Purushotham Reddy P.

Faculty Advisory Committee: Ranabir Das, Arati Ramesh, Minhaj Sirajuddin, and Vinothkumar K. R.

The Nuclear Magnetic Resonance Facility

The Museum Collection Room

The Museum and Field Stations Facility (MFS) organised various outreach events for school children at the Pachmarhi field station this year such as Vulture Awareness, Wildlife Week, and Moth Day. In partnership with the BLiSC Communications office, the MFS worked with labs at NCBS and DBT-inStem to organise the Lab Culture exhibitions that drew more than 2500 students from schools and colleges in and around Bangalore. A taxidermy workshop was organised and trained five researchers in the collection, preservation, and long-term care of mammal specimens.

The collections have moved to a new location at the DBT-inStem building; a substantially larger space with contemporary facilities. The new space is being set up to expand our existing research collections. The facility has been central in the identification of several new species of reptiles and invertebrates with 18 publications of species descriptions.

MFS staff: Vivek Ramachandran, Tarun Karmakar, Savita Chib, and Aswathanarayana G.

Faculty Advisory Committee: Uma Ramakrishnan, Sanjay Sane, Mahesh Sankaran, Krushnamegh Kunte, and Shivaprasad P. V.

The Radioactivity Facility has been classified as a Type-2 radioactive laboratory. The facility is equipped to handle 32P 55Fe, 125I, 3H, and 14C isotopes, and operates strictly within the guidelines set by the AERB. New users undergo a rigorous training programme under the supervision of the campus radiation safety officer. In addition to the use of radionuclides, the training programme also includes modules on the safe disposal of radionuclides as per safety regulations. Additionally, the facility also has a cobalt-based gamma irradiator used to irradiate animal cells.

Radioactivity Facility Crew: Ranjith P. P. and Ashwin Nair

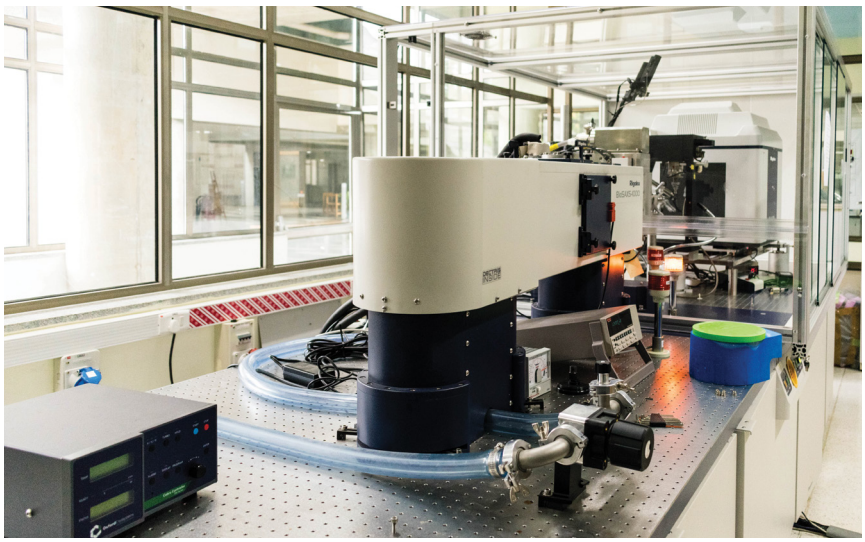
Faculty Advisory Committee: Shivaprasad P.V., Arati Ramesh, Sunil Laxman, and Colin Jamora

The Radioactivity Facility

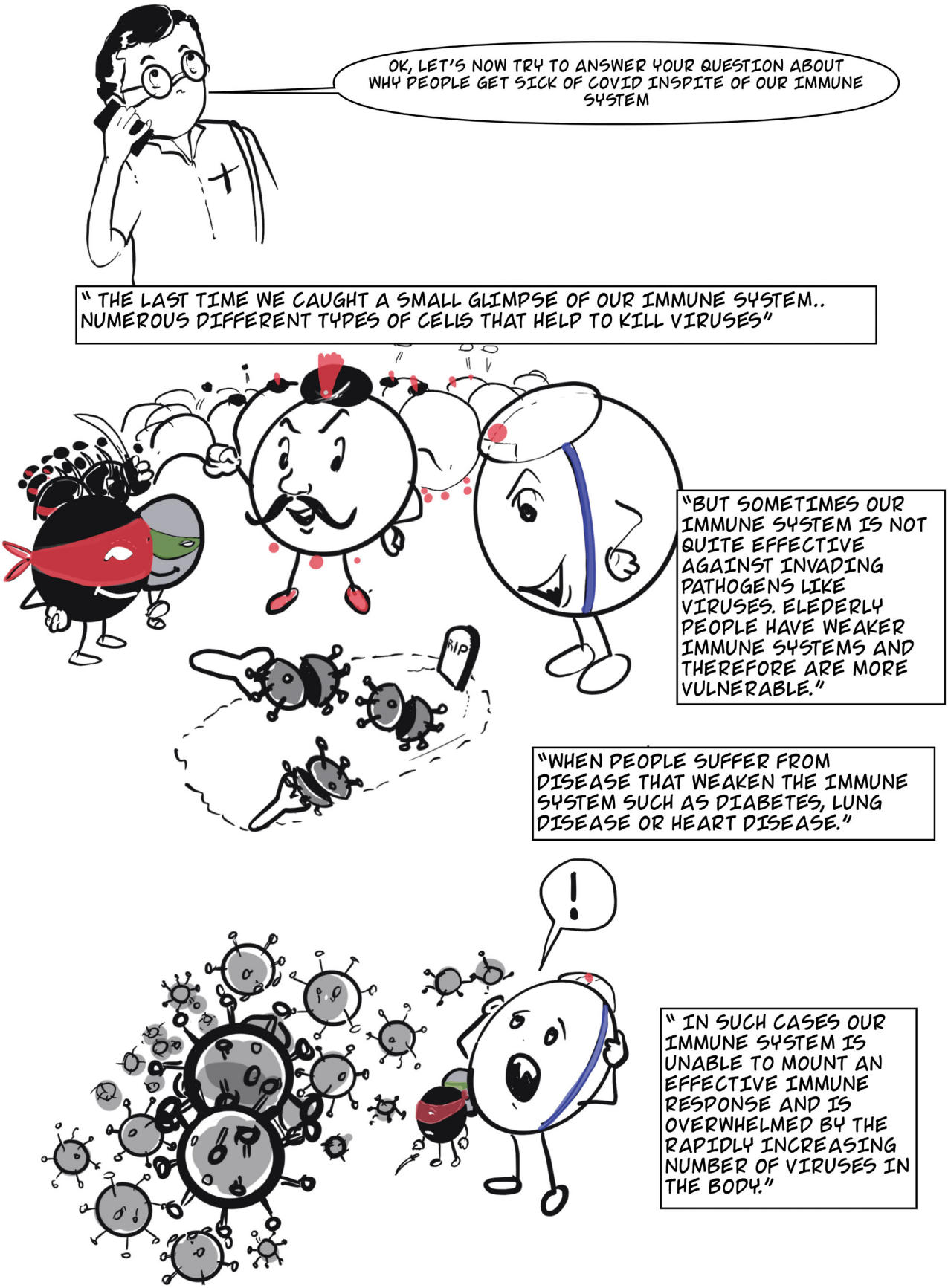
The X-Ray Facility's aim is to provide the necessary infrastructure and expert support for on-campus users, as well as those from outside academia, and industry, who wish to undertake structural studies of biological macromolecules in a crystalline state or in solution. The facility offers high-end instruments and training for setting up crystallisation, screening, data collection, processing, and three-dimensional structure determination of biological macromolecules. The facility is equipped with an automated nano dispenser robot, UV microscope, FR-X X-ray diffractometer, and BioSAXS-1000, in addition to up-to-date versions of computing software for data analysis and automated structure solution from the data collected. The facility has trained 22 internal and external users, and some of them published 6 papers in peer reviewed journals in 2019-2020.

X-Ray Crew: Nishant Kumar Varshney

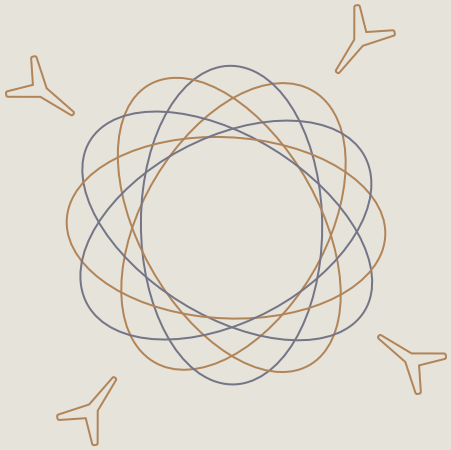
Faculty Advisory Committee: Ranabir Das, Arati Ramesh, Minhaj Sirajuddin, and Vinothkumar K. R.



The X-Ray Facility



These pages are excerpts from a series created, designed, and written, by Arvind Ramanathan of DBT-inStem and Sonia Sen from TIGS-CI. They are illustrated by Arvind Ramanathan as a part of the Cluster's COVID-19 Response Initiative. The work was originally published on www.covid-gyan.in



Bangalore Life Science Cluster

Research Development Office • Vineetha Raghavan
Activities of the Communications Office of the BLiSC • Mahinn Ali Khan

Research Development Office

Research at the Bangalore Life Science Cluster (BLiSC) which includes NCBS, DBT-inStem and C-CAMP, spans a diverse range of questions and approaches in the broad area of life sciences. The Research Development Office (RDO) was created to facilitate research and training at the Cluster, via research funding and research collaborations.

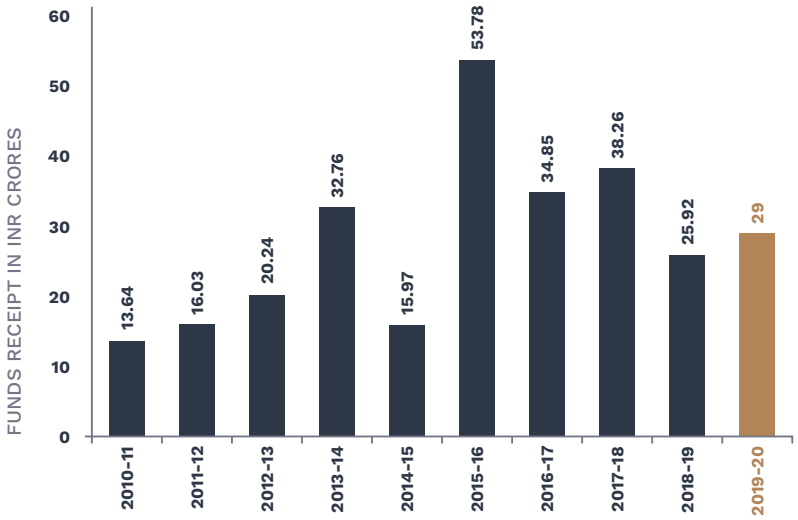
In 2020, the RDO completed a decade of operations at BLiSC, supporting the diverse needs of the campus in fundraising, grants management, and contract negotiation for research funding from national and international funding agencies, corporate sources, and charitable organisations.

Generous funding from the Government has been invaluable in establishing large institutional programs on campus such as the Programme on Chemical Biology and Therapeutics (CBT), BLiSC for Multiscale Basic and Applied Research in the Biological Sciences (B-LIFE), the Programme on Chemical Ecology, the Centre for Neurodevelopmental Synaptopathies (CNS), the National Mouse Research Resource (NaMoR), and the Macromolecular Crystallography and Scattering Facility. The RDO manages all these large programmes.

The campus has also invested considerable efforts into developing a mixed funding portfolio including charitable funding to complement funding from Government and international grants on campus. The Accelerator programme for Discovery in Brain disorders using Stem cells (ADBS) at NCBS and DBT-inStem (in collaboration with NIMHANS), which is jointly supported by the Department of Biotechnology (DBT), Government of India and the Pratiksha Trust, is a successful example of such mixed portfolio funding. Generous funding from Mr. Narayana Murthy and the Simons Foundation continue to support the Dengue Vaccine Development programme and the Simons Centre for Living Machines respectively.

A recent donation to NCBS from Mr Srikanta Gopalakrishnan and Mrs Radhika Gopalakrishnan has enabled the institution of the, "Siddharth Gopalakrishnan Memorial Endowment Fund," to honour and perpetuate the memory of its alumnus, Dr Siddharth Gopalakrishnan. This endowment aims to encourage outstanding students at the BLiSC via poster awards and fellowships to support attendance at courses and workshops. The first Siddharth Gopalakrishnan Poster award was awarded by the donors during the last NCBS annual talks in January 2020.

Generous Funding from the TTK Prestige Group continues to support our vision of, "Science Beyond Boundaries" at NCBS and DBT-inStem. This has significantly boosted our Campus Fellows Programme, enabled us to support International researchers at BLiSC, and also institute the, "TT Narasimhan Travel Awards," at NCBS and DBT-inStem, which assists students and postdoctoral fellows to attend international conferences and workshops. The generosity of our philanthropic partners such the Infosys foundation, Dr. Kiran Mazumdar-Shaw, and the Wildlife Conservation Trust continues to support the BLiSC Endowment Fund which was initiated in 2016 for research, training, innovation, and outreach.



Extramural funds at NCBS (in Crores INR)

As the pandemic continued to spread across the country this year, private and public sector companies stepped up their Corporate Social Responsibility (CSR) efforts to fight COVID-19 pandemic. Our campus received generous donations from the Azim Premji Philanthropic Initiatives, the Punjab National Bank Housing Finance Limited, Standard Chartered Global Business Services, Nuclear Power Corporation of India Limited, and IQVIA, to augment institutional testing infrastructure and facilities to respond to the global health crisis, as well as to develop innovative methods to test the SARS-CoV-2 virus.

The RDO has also supported the establishment of national and international collaborations via grants and agreements, and facilitated interactions with potential collaborators. These efforts have now received a boost via a

Research Management Fellowship awarded to Dr. Vineetha Raghavan by the India Research Management Initiative (IRMI) of the DBT-Wellcome Trust India Alliance. Through this fellowship, the RDO aims to develop and augment the global engagement efforts of the BLiSC campus.

A notable new addition to our international partnerships is the institutional collaboration with King's College, London to promote collaborative initiatives in scientific research, training, and education.

Work at the RDO is made possible by a dynamic and professional team which is committed to offering several key services to the campus at the boundaries of science, management, resource development, planning, and outreach.

We look forward to a rewarding journey ahead for the RDO, supporting campus research funding, the Endowment Fund, and research collaborations.

Vineetha Raghavan
on behalf of the RDO teams: Grants and Research collaboration (GRC) and Resource Development and Planning (RDP) Unit

The Resource Development and Planning Unit
Vijai Dharmamony, Development Officer

The Research Development Office team
From left to right: Malini Pillai, Vineetha Raghavan, M C Aruna, and Roshan Kumar

SciComm 2020 – Engagement in the New Normal

During a time of crisis, science communication plays an indispensable role—acting as a conduit between scientists and the press and public, an engagement partner to researchers, and a mouthpiece for the campus—the glue that holds us together at a time of separation, distancing, and remote working.

In March 2020, the news of burgeoning COVID-19 cases in India necessitated a reevaluation of the functioning of the BLiSC campus. All in-person outreach efforts came to a grinding halt. Along with the rest of the world, we shifted our working lives online. Almost overnight, we had to recalibrate our resources and renegotiate our abilities to cater to an audience that was home-bound, isolated, and struggling with the uncertainty of the time. It has been a lesson in adaptation to see how we could connect with people, pique curiosity, and then, sustain engagement with our scientific content.

CovidGyan

The Communications Office represented NCBS and DBT-inStem in the pan-institutional and multilingual effort called CovidGyan – a website created to disseminate science-based information in response to the pandemic. Mobilised in a matter of days, covid-gyan.in focused on helping the public understand, avoid, and navigate through COVID-19, with an emphasis on reliable information and scientific developments.

From ideation to implementation, the Communications Office was involved in every step of the process. We designed and organised popular live events such as the ***WebGyan*** *and* ***Sundowner Sessions****, in addition to other roles:*

- *Collaborating with DBT-inStem's Arvind Ramanathan to launch his popular science comic*
- *Organising and hosting nine WebGyan sessions (COVID-19 science talks)*
- *Creating and hosting 10 Sundowner Sessions (community interactions)*
- *Designing and running a short story and poster competition*

Engagement & Outreach

Adaptability was integral to continue running our popular outreach initiatives such as the BLiSC Science Cafe. In spite of limitations, we went on to build new initiatives and collaborated with scientists who delivered talks to a wide audience base. One step toward this greater outreach is the connection we established with the ***People's Archive of Rural India (PARI)****, to facilitate outreach in sectors where we lack access and experience.*

(top) ***WebGyan offers expert insights into topics pertaining to the pandemic and has covered a gamut of concepts***

(right) ***OutsideIn is a popular lecture series dedicated to making Ecology accessible to school students***

It has been delightful to see more outreach efforts spearheaded by faculty and we have eagerly supported them. These include the ***Indian Pollinator Initiative*** *organised by Axel Brockmann (in collaboration with other leading researchers in the field), the* ***Public Health Lecture Series*** *with Sudhir Krishna, and Aswin Sai Narain Seshasayee's* ***Weekend Chat with Researchers****.*

In terms of new initiatives, we launched two themed series of highly interactive, popular science talks under our ***Science and the City*** *banner:*

- ***The OutsideIn Ecology Series*** *initiated by R. Sowdhamini has a regular, dedicated audience for discussions ranging from microbes to ecosystems. 24 sessions have taken place between June and December 2020, with a full calendar for the new season beginning in January of 2021.*

- ***The Human Body InsideOUT Series*** *tackles different topics within human anatomy, and is hosted by the Head of Academics – NCBS, Raj Ladher, with five talks so far.*

In addition, NCBS is one of the ***Life Science Across the Globe (LSAG)****'s sister institutes spread across five continents, and our role in promoting the talks has been a successful one.*

Digital Communication

The Communications Office is responsible for building awareness about campus research through our social media engagement, press relations, and wide-reaching digital campaigns. We ensure that key research papers by all the labs receive due attention and that the public is afforded an opportunity to interact with our faculty through our various programmes.

Our digital reach has been built through sustained efforts over the years, and grown significantly in the past year with an up-to-date mailing list and a strong institutional social media presence. We support the initiatives of the ***Bengaluru Sustainability Forum, Science Gallery Bengaluru, the Biodiversity Collaborative/ National Mission on Biodiversity and Human Well-Being, the echo network, Museum and Field Stations Facility, and the Archives at NCBS*** *with their press relations, outreach, webinars, and public engagement.*

This year we adopted new tools and technologies to help minimise the disruption of remote working. We quickly familiarised ourselves with software platforms to assist in our online migration. Today, the Comms Office also delivers training programmes to help other campus personnel and students run their own programmes independently.

We further spread our efforts towards previously outsourced collateral, designing artworks and editing videos in-house. Nurturing our social media base, we ensured the Cluster's science, capacities, and COVID-19 response efforts garnered the attention they deserved.

We scripted, shot, and edited videos for the Brain Research Awareness week, the Research Development Office, #unite2fightcorona campaign, and National Science Day. We also adopted video as a medium to communicate

The Science Cafe shifted to an online forum in May, following the last memorable session at a community space in the city

research papers and created videos for Jayashree Ratnam, and for R. Sowdhamini's Shankpushpi paper.

School and College Outreach

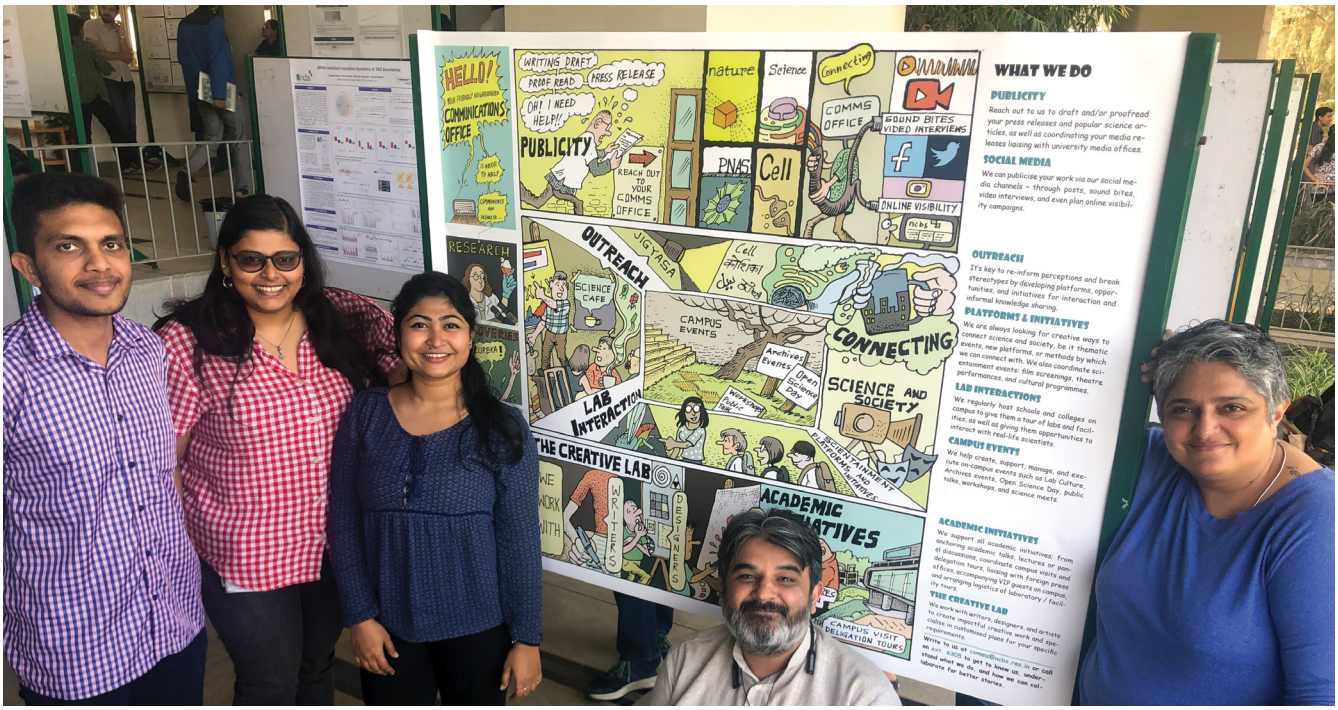
In the short months pre-lockdown, we managed to facilitate visits for 100 students. In normal circumstances we host over 1000+ a year, on average. One of our sustained objectives has been to take science communication beyond the confines of the English language. Two efforts this year have seen our attempts realised:

- ***Fly Varga:** We partnered with the campus' Fly Facility to host an outreach programme at a local school in Bangalore. The medium of interaction was Kannada, which is one of our chief objectives, i.e. to take outreach beyond the English medium*

- ***Rural School Outreach Programme:** We facilitated conversations between NCBS scientists and students from remote colleges that ordinarily would not have access to the high-end science performed at NCBS. We conducted two talks by Deepa Agashe and Sanjay Sane for students of the Prof. RMC College, Akurdi (Maharashtra) with the scientists speaking in Marathi. This received an overwhelming response and we are planning more talks in the future with other faculty, and in different regional languages.*

In the annus infortunatus that was 2020, we saw SciComm emerge as a powerful tool for the dissemination of public health messages, management of outreach initiatives, and to facilitate the shift from a 3D world of

Fly Varga, an outreach session in Kannada conducted by the Fly Facility team with students at a government school



The Communications team at our poster for the Circle of Life–NCBS Annual Talks 2020

engagement to one that was virtual. I like to think we have taken it on the chin and emerged not much worse for wear. And if anything, fortified by the challenges we encountered.

The year comes to a close, and we continue to stay agile and responsive. The team is abuzz with questions of not only what, but how innovative we can be in communicating our science and building a community that asks important questions, shares knowledge, and grows as one.

Each year, NCBS hosts a range of meetings and workshops aimed at providing our faculty and students with national and international exposure to cutting-edge research and developments, as well as connecting our campus with schools, colleges, and the wider public. This year, the majority took place online.

JANUARY

26-29 JANUARY 2020

EMBO Symposium on Calcium Signalling: Molecular mechanisms to role in health and diseases

Organised by Prof Gaiti Hasan with EMBO and India Alliance to highlight the latest scientific and technical advances in Ca2+ signalling

FEBRUARY

3-5 FEBRUARY 2020

Meeting on Conflict and Cooperation in Cellular Populations (CCCP 2020)

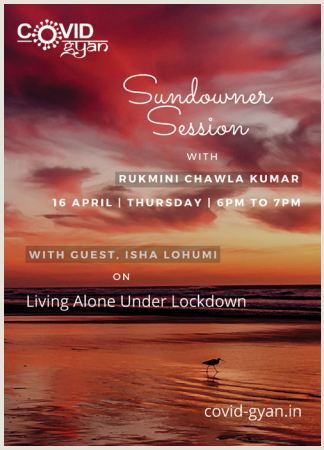
Discussion of three broad areas of research relating to cellular communities

MARCH

2 FEBRUARY-22 MARCH 2020

Undergraduate Lecture Series in Advanced Biology 2020

The 7th series of lectures, organised by the Post-Doctoral Fellows Association, for college students from the city



APRIL

16 APRIL 2020

Launch of CovidGyan's Sundowner Sessions

A first-in-its-series science engagement platform organised under the CovidGyan initiative aimed at building a community network

MAY

7 MAY 2020

CovidGyan's WebGyan by Prof Rob Phillips: Where is Euler now that we need him?

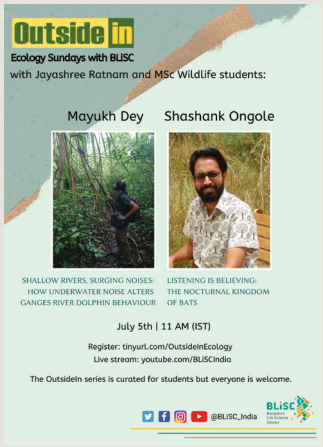
A public lecture on a by-the-numbers overview of viruses and viral mechanics of the SARS-CoV-2

JUNE

13 JUNE 2020

COVID Combat Zone Insights

A discussion on COVID-19 clinical management at the front lines; part of the Dengue Project's Public Health Lecture Series



JULY

5 JULY 2020

OutsideIn with MSc Wildlife: Jayashree Ratnam, Mayukh Dey, and Shasank Ongole

Talks on river dolphins and bats in the Western Ghats

AUGUST

12 AUGUST 2020

Life Science Across the Globe with NCBS

The LSAG visits India! Talks by Prof Uma Ramakrishnan and Dr Jayashree Ratnam

SEPTEMBER

4 SEPTEMBER-
30 OCTOBER 2020

Perspectives for Research on Pollination

The first edition of the Indian Pollinator Initiative webinar series with nine talks by experts

14-18 SEPTEMBER 2020

International Humboldt Day

A symposium of talks by leading biogeographers from across the globe

OCTOBER

3 OCTOBER 2020

Reading for Change with David Quammen and Anil Ananthaswamy

A conversation on Spillover and UN Sustainable Development Goal 3-Good Health and Well-Being

16 OCTOBER 2020

The Human Body InsideOUT

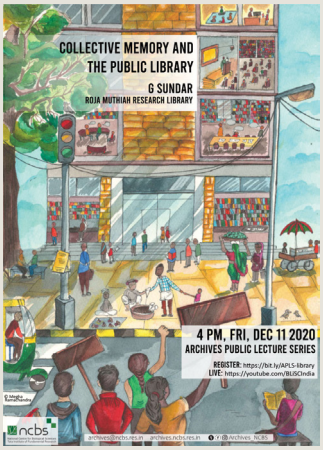
Public Lecture by Dr Arvind Ramanathan on Skeletal Muscle, part of a series on anatomy

NOVEMBER

12 NOVEMBER 2020

WebGyan: Ask Me Anything about Tapestry Pooling for COVID-19 Testing

A session with the PIs involved in the project



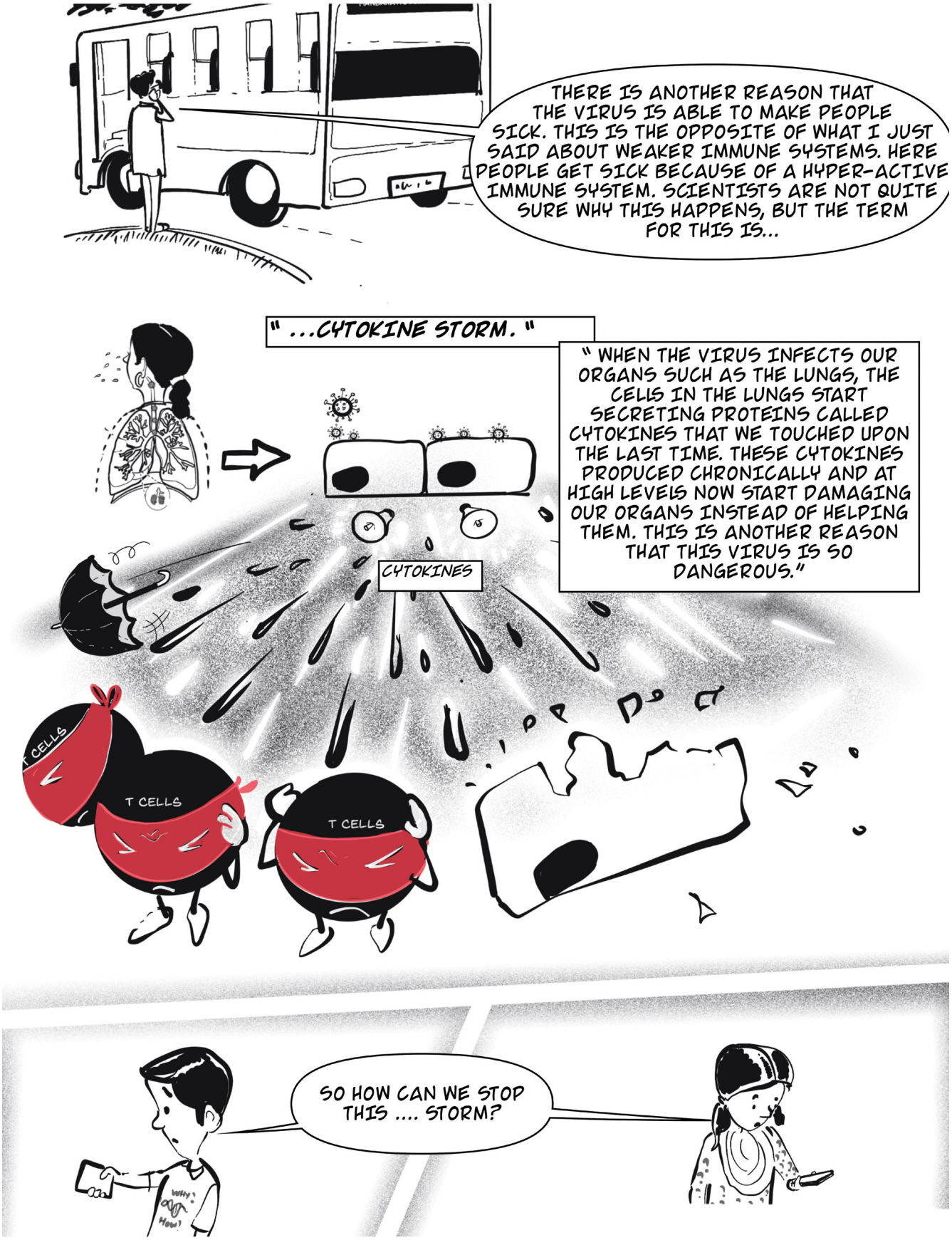
DECEMBER

9 DECEMBER 2020

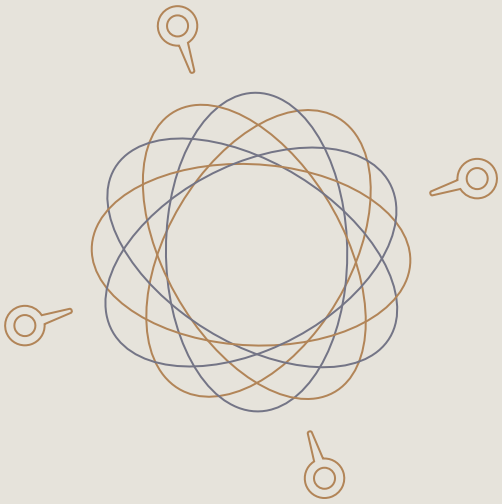
Archives at NCBS: Obaid Siddiqi Chair in the History and Culture of Science

Through funding from TNQ Technologies, the Archives formalised the creation of a chair in the History and Culture of Science

Read more: Archives at NCBS Section



These pages are excerpts from a series created, designed, and written, by Arvind Ramanathan of DBT-inStem and Sonia Sen from TIGS-CI. They are illustrated by Arvind Ramanathan as a part of the Cluster's COVID-19 Response Initiative. The work was originally published on www.covid-gyan.in



NCBS COVID-19 Response

NCBS Pandemic Response Effort • Uma Ramakrishnan, Varadha Sundaramurthy, and Raghu Padinjat

NCBS Pandemic Response Effort

Over the last year, the world has been in the grips of a pandemic, something relatively unique in our lifetimes. The pandemic has challenged all of us, as individuals, societies, institutions, and nations.

At NCBS we sought to face these challenges with a combination of service, science, and safety. We are proud to highlight the NCBS institutional response to the COVID-19 pandemic, where we attempted to serve the needs of the nation and develop research that may benefit humanity. We also attempted to keep our campus a safe space through these difficult times. We highlight below the various components of the campus response.

Service: Setting Up a Laboratory to Test for COVID-19

In early April, it became clear that adequate testing would prove to be critical in managing the pandemic in India. At the request of the Government of India, NCBS—in partnership with DBT-inStem—rapidly set up and operationalised a COVID-19 testing laboratory on campus.

In a very short span of time, existing infrastructure was re-purposed to set up a state-of-the-art testing centre, with dedicated areas for the various modules of sample reception, aliquoting, RNA extraction, RT-PCR, and reporting. Robust SOPs were set up for each of these modules.

We launched the lab on April 13th 2020, with all the necessary permissions in place. The testing centre started with a very enthusiastic set of volunteers from the student and postdoc community, with significant support from staff, and oversight from faculty. The testing centre worked around the clock until October 2020, following which it has been operational six days a week. To date, this laboratory has processed 80,000+ samples from across the state of Karnataka, working in partnership with the state government apparatus and local health officials.

Several factors were critical to the success of this effort. The volunteers, staff, and faculty collaboratively implemented this diagnostic facility, allowing the campus to contribute positively to the pandemic. The initial work was supported by philanthropic grants, and moving forward, this effort is being stabilised through the appointment of full-time dedicated personnel.

Service: CovidGyan

In April 2020, several scientific institutions across the country—including TIFR, IISc, and NCBS—came together to set up a multilingual website

dedicated to disseminating scientifically accurate information about COVID-19. Launched on the 3rd of April 2020 (https://covid-gyan.in/press_release), the CovidGyan website includes videos, infographics, articles, research conversations and analyses, myth busters, and various other types of content. As far as possible, content is translated into various languages for maximum visibility and readership. Most recently, CovidGyan has begun to engage with the student community by hosting a poster and science fiction story writing competition.

Science: COVID-19 Research Projects

At the request and with the support of the Department of Biotechnology (DBT), Government of India, NCBS and DBT-inStem are in the process of setting up a COVID-19 biorepository to enable research into this topic. In addition, a number of faculty have harnessed their technical expertise to participate in different COVID-19 research projects. Examples of these efforts include:

i. *In silico drug discovery and structural validation for COVID-19*
ii. *Participation in SARS-CoV-2 genome sequencing efforts in partnership with other national institutes*
iii. *A high-throughput cell biology screen to identify FDA-approved compounds that inhibit viral entry and replication in appropriate human cell lines*
iv. *Computational approaches to facilitate faster and more effective testing for COVID-19 using a pooled testing strategy*
v. *Development of an indigenous highly sensitive SARS-CoV-2 detection test that uses room temperature amplification and some unique structural properties of the SARS-CoV-2 RNA*
vi. *Development of humanised mouse models for SARS-CoV-2 infection. Development of organoid models for SARS-CoV-2 infection.*
vii. *Isolation and propagation of SARS-CoV-2 from Indian COVID-19 patients and establishment of SARS-CoV-2 infection assays in multiple cell lines for drug discovery research*

These efforts have been possible due the available research infrastructure and human resource capabilities that NCBS has built up over the years.

NCBS COVID-19 Response 2020

Starting in early March 2020, the NCBS response to the COVID-19 situation was managed with the assistance of a core coordination group—consisting of senior scientists and administrators—meeting regularly to review the situation, respond to ongoing changes in the situation of a national emergency, and provide advice on the management of the centre. The overall principle has been to keep the centre operational whilst bearing in mind the health and safety of its members, and respond positively to meet the national

Student volunteer Ansil B. R. and NCBS faculty Dr. Varadharajan Sundaramurthy in PPE at the BLiSC COVID Testing Centre. *Photo credits: Dr. Uma Ramakrishnan, NCBS*

needs during the pandemic. Much of this was done in collaboration with the other partner institutions of the Bangalore Life Science Cluster, namely DBT-inStem and C-CAMP.

Safety: Campus Management and Safety

A number of policy decisions were taken early on to prevent the arrival of COVID-19 on campus. The overall principle of these decisions was to keep the campus safe but operational to the extent possible. The measures employed included:

- *health screening prior to campus access*
- *partitioning the campus into sectors to reduce mixing*
- *reduced density of staff via a shift system*
- *enhanced sanitisation of physical space*
- *robust mechanisms to monitor personnel movement between sectors*
- *sustained programmes to educate staff on the SOPs and ensure compliance*
- *dedicated quarantine facility*
- *weekly sentinel testing of campus colleagues in collaboration with government authorities in Bangalore*

Communication mechanisms were put in place to disseminate information on ongoing events and campus operating guidelines to all campus colleagues. These measures allowed the campus to retain operational capability even

during the initial severe lockdown 1.0 and continue to contribute scientifically to the ongoing COVID-19 response.

Service & Safety: Volunteering Efforts on Campus

During the lockdown, more than 70 students on campus were organised into volunteer groups to tackle various tasks:

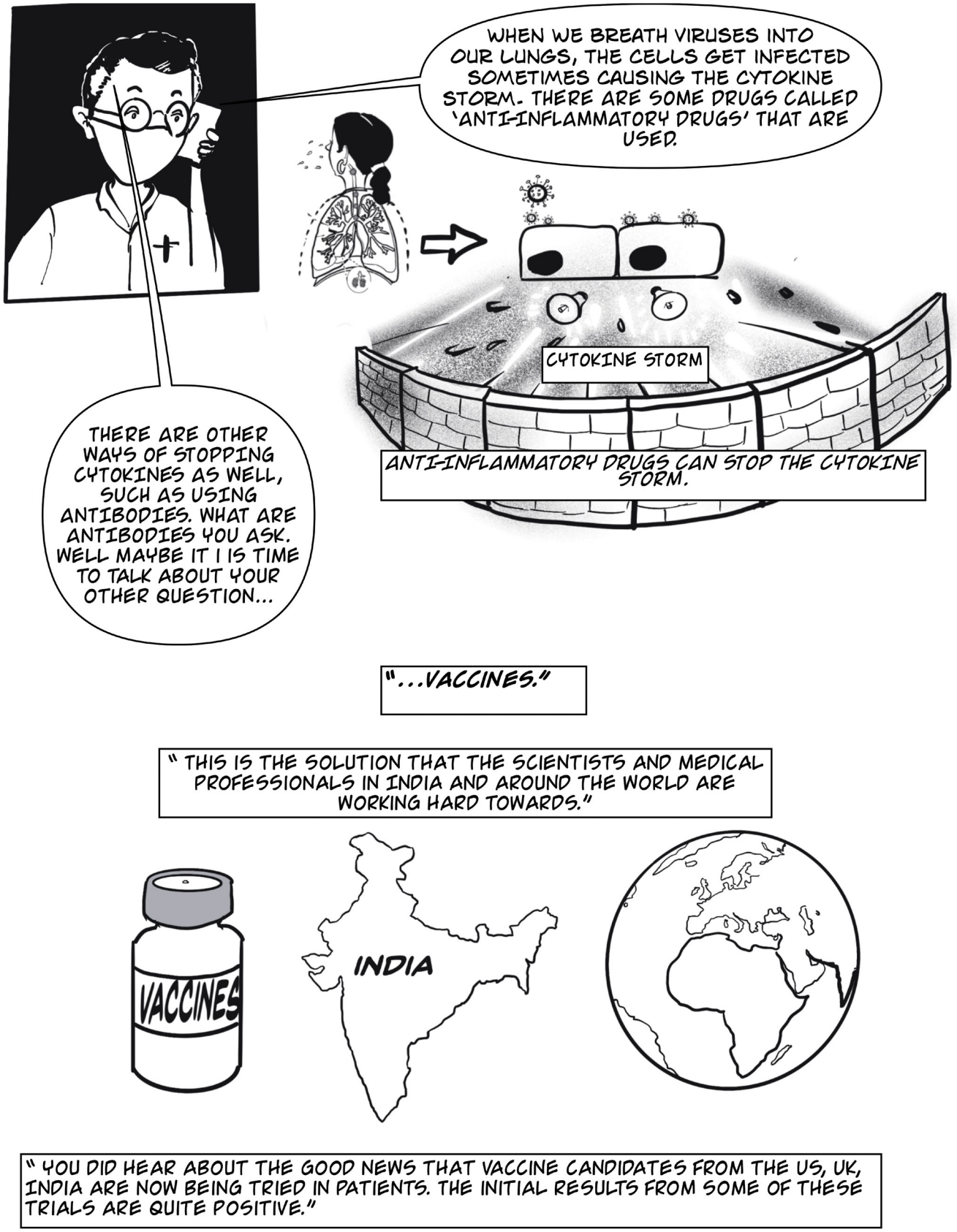
- *making campus announcements to communicate COVID-19 precautions and briefings in person in English and Kannada*
- *making sanitisers for the campus*
- *helping stranded/quarantined individuals with essentials*
- *assisting technical services teams with maintenance of campus property*
- *managing a campus WhatsApp-based messaging group and email ticketing system for quick responses*
- *running a dedicated campus helpline and a peer support group*
- *medical assistance to the clinic's staff*

With increasing operations on campus, students, faculty, and staff also came together to start a contact tracing group. Teams worked together to identify sectors/contacts using sector maps, point-of-contact lists, QR logs, handwritten registers, and card readers. They then communicated with and interviewed the primary and secondary contacts.

As we end 2020, we realise that this year has tested our strength and resilience as a campus like never before. We did not fall short. On the contrary, our background as scientists and a scientific campus has allowed us to make significant contributions in a very practical and time-sensitive manner in these difficult times.

How will this year affect our future? We have participated in several national and international efforts precipitated by COVID-19, and the bridges we have built will continue to enrich us. We have interfaced with health officials in the state, and integrated a little better into our local milieu. As a community, we came together across the boundaries of laboratories and institutions, and such cohesion will strengthen our ability to retain the open and collaborative campus culture. In our future, science continues to be the key lens through which we visualise the world and life, and we are happy to be well acquainted with the journey already.

Read more about the campus COVID-19 response here: https://www.ncbs.res.in/content/blisc-ncbs-instem-c-camp-responses-covid-19



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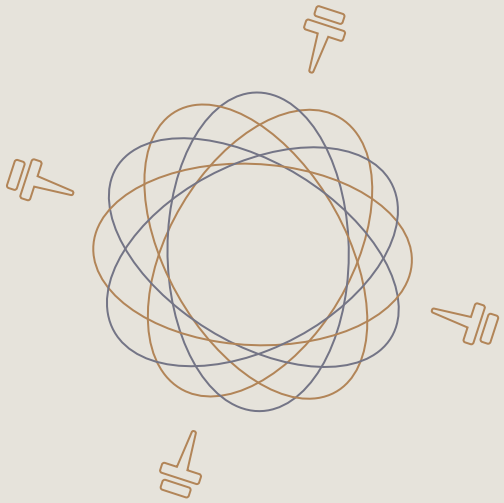


Archives at NCBS

Archives at NCBS: Annual Report 2019-2020 • Venkat Srinivasan

Archives at NCBS: Annual Report 2019-2020

The Archives at NCBS (http://archives.ncbs.res.in/) is a collecting space for institutional records as well as the history of contemporary biology in India. The currently accessible collections include five manuscript collections, seven institutional collections, three artefact collections, two bibliographic collections, and an oral history collection. The holdings are in various forms, ranging from manuscripts to negatives to photographs, books, fine art, audio recordings, scientific equipment, letters, and field and lab notes. The physical archive is located in a 2000-square-feet space in the Eastern Lab Complex (ELC) basement at NCBS. It includes space for research, processing, exhibitions, recording, and a leading-edge storage facility with monitors for temperature, light, humidity, air quality, water, fire, pests, and noise.

The Archives continues to function with one underlying philosophy—of enabling diverse stories—and three broad aspirations: education through archival material, building a consortium of archives with a discovery layer for the public to find, describe and share archival material and stories, and reimagining the archives as strengthening commons and public spaces.

COVID-19 Archive

In the wake of the COVID-19 global pandemic and the resultant challenges faced, the Archives at NCBS has launched a community archiving project to document the collective and lived histories of people associated with the institution. The collection (being conceptualised by Ananya, an assistant archivist) is likely to comprise mostly oral history interviews with the campus community, in addition to material donated by them, such as the volunteer and documentation work carried out by campus members like Ravi Kumar Boyapati.

Chair in the History and Culture of Science

The Archives at NCBS has formalised the creation of a chair in the History and Culture of Science. This was made possible through generous support from TNQ Technologies, a global leader in scientific, technical, and medical publishing (STM publishing). With this focus on a cross-disciplinary approach, the Archives at NCBS will develop as a foundational "lab", building teaching and research capacity of academics in the sciences and humanities. The recognition of this need by TNQ Technologies has established strong roots for a public research centre that augments a nuanced understanding of the field. The support—spread over three years—will go toward funding a new

chair and related projects, and sustenance of this Archive through staffing and other core operations.

Collaborations

The Archives at NCBS collaborated with the Centre for Public History, Srishti Institute of Art Design and Technology, Bangalore, in hosting the first Winter School in Public History 2020: Public Lives of Objects. This included six faculty members from Europe and India, and over 20 students from across India.

The Archives has helped set up the Milli Consortium, a network of archives and a digital platform anchored around three interlinked spaces for discovery, interpretation, and narration from archival material. Milli hosted a seven-day online seminar on the occasion of International Archives Week (IAW) between June 8-14, 2020. The talks, featuring more than 40 speakers from four countries, were attended by over 600 participants (https://www.milli.link/iaw2020/).

The Archives at NCBS is collaborating with Mary-Rose Abraham, Nikhil Nagaraj, and Gayathri Vaidyanathan on a podcast series, "Scrolls and Leaves" (http://scrollsandleaves.com/). An immersive-sound podcast exploring the margins of history, science, and cultures, it presents little-known stories from around the world to help contextualise the present. It is being produced in collaboration with the Archives at NCBS, and with support from IndiaBioscience, DBT/Wellcome Trust India Alliance, and NCBS.

Collaborations with subject-matter experts have strengthened the Archives' interdisciplinary initiatives. These include research connecting copyright law, archives and data privacy (led by Divij Joshi), and a groundbreaking project on the making of Indian conservation over the last 50 years (led by Hari Sridhar and his collaborator, MD Madhusudan).

New Accessions and Maintenance

This year, the Archives has accessioned and processed three collections related to the research of T. S. G. Sastry, M. M. Panicker, and K. Ullas Karanth. The papers cover histories in the field of biochemistry, neuroscience and stem cells, environmental conservation, zoology, and cosmic ray physics (kept on loan). Highlights from the Archives' work on preservation this year include Abhishek Banerjee's novel conservation work on two prominent oil paintings from the 1950s by S. H. Raza and H. A. Gade, and Neha Panwar's development of a unique crisis management protocol that could serve as a template for other archives.

Invited Talks

The Archives at NCBS was invited to present a talk as part of the online seminar series hosted by Janelia Research Campus on, "Archives as

crucible, archives as commons: Re-thinking an archive for the sciences". This was a part of the larger, "Life Science Across the Globe" programme of which NCBS is a member along with other sister institutions.

The Archives was invited to present talks on the same topic at various institutions around the country, such as the Centre for Studies in Social Sciences (CSSS) Kolkata, Indian Institute for Science Education and Research (IISER) Pune, and Serendipity Arts Festival Virtual 2020.

Art, Science, and the Archive

The Archives is currently exhibiting its second exhibition, "Herbs, Maps & Medicine: An interpretive exhibition of commerce and spice". It looks at the histories of medicine and the spice trade. The physical space is constructed as an interactive marketplace of knowledge and includes original objects and reproductions from over a dozen repositories around the world.

The Archives at NCBS has had two artists in residence over the course of the year. Neeraj Sebastian's work has captured the spaces and people around campus—observational paintings inspired by realism. Megha Jairaj has engaged with the themes of note taking and repetition that one sees so often in archival collections.

Review

An external review committee visited the Archives between November 2019 and January 2020, and assessed its current work and future plans. The committee was headed by Mariella Soprano (Senior Archivist for Collection Management at the Caltech Archives, USA). Among the many recommendations, the committee recognised the potential in the Archives to become a nodal centre for a South Asia based collection development and directed ways to attain the same.

The Archives at NCBS is also now on the review committees of the upcoming archives at the Indian Institute of Technology Madras (IITM) and the M.S. Swaminathan Research Foundation (MSSRF).

Outreach

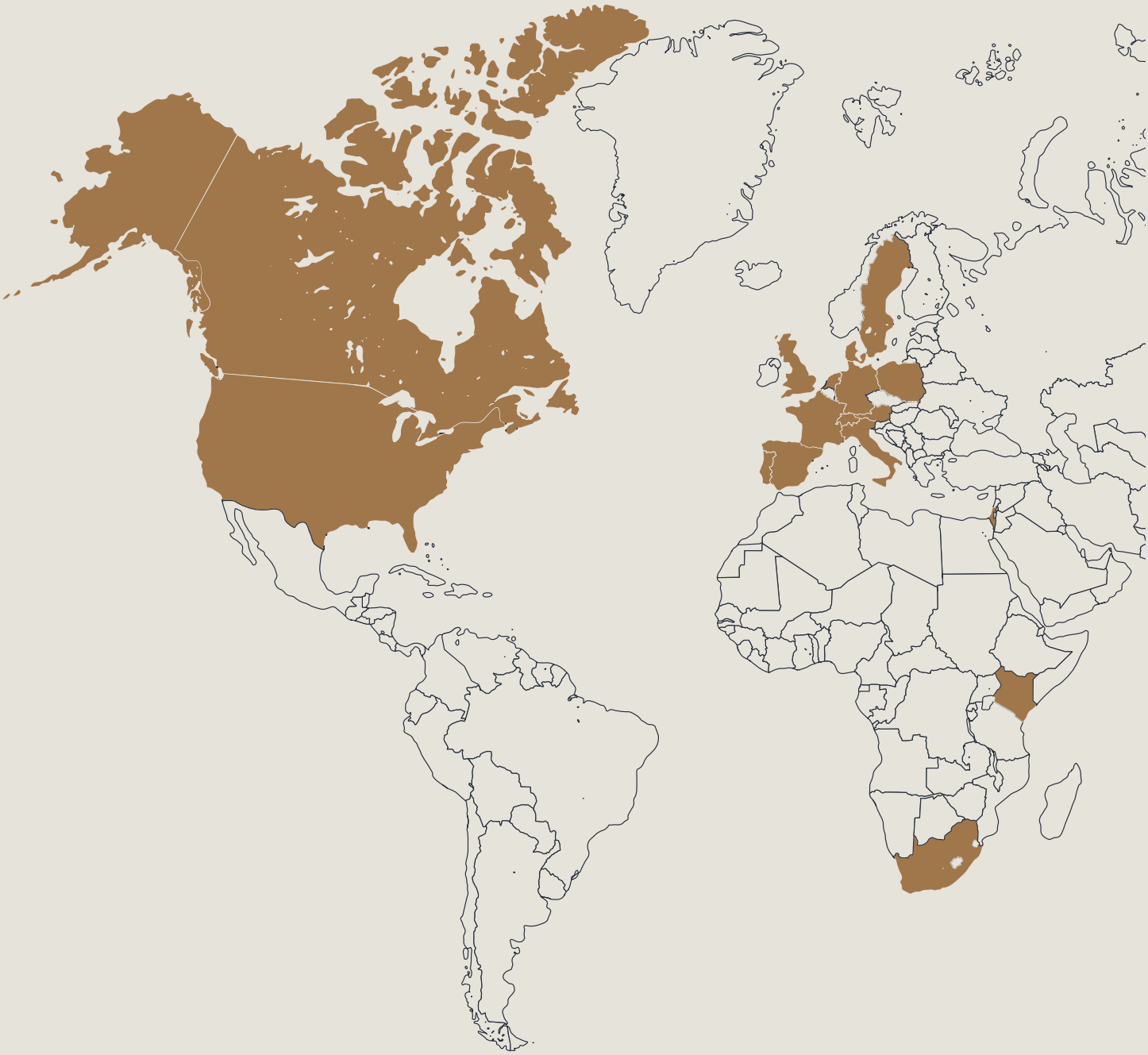
The Archives Public Lecture Series has been our monthly forum for talks framed around explorations in and around archives. This series, in its 32nd edition as of December 2020, brings people from various backgrounds to initiate dialogue and debate on an array of diverse topics. Talks this year were held online and offline and covered diverse topics including the history of the Indian Constitution, Partition and the strains of migration, queer histories, and collective memory through libraries as public spaces.

(left to right) ***Michael Hausser, Scott Edwards, and Venki Ramakrishnan browse through material at the Archives at NCBS during a visit as part of the Annual Talks on January 17, 2020***

Context Series

In an attempt to bring different kinds of public spaces for meaningful unstructured conversations, the Archives at NCBS started a Context series. In January 2020, noted lawyers, Malavika Prasad and Gautam Bhatia, gave a seminar on, "Introduction to Indian Constitution and Law-Making" at Rangasthala, a public venue in central Bangalore. This was brought together by the Archives at NCBS along with the Centre for IT and Public Policy, IIIT Bangalore and Champaca bookstore.

The Archives maintains an active social media presence on various channels:
https://twitter.com/archives_ncbs
https://www.instagram.com/archives_ncbs/
https://www.facebook.com/archives.at.NCBS/



List of all the international institutions:

UNITED STATES OF AMERICA

- *University of Minnesota*
- *Albert Einstein College of Medicine, New York*
- *University of Connecticut*
- *Florida State University*
- *City University of New York*
- *University of Florida at Gainesville*
- *University of Georgia*
- *National Cancer Institute, NIH*
- *University of Massachusetts, Amherst*
- *New York University (NYU)*
- *University of California, San Francisco*
- *Purdue University*
- *University of California, San Diego*
- *Boise State University*
- *Michigan State University*
- *Colorado State University*
- *University of Southern California*
- *Brandeis University*
- *UT Southwestern Medical Center*
- *Stanford University*
- *Agricultural Research Service*
- *New Mexico State University*
- *Penn State University*
- *State University of New York*
- *University of California, Berkeley*
- *University of Notre Dame*
- *Cardiff University*
- *University of Chicago*
- *George Mason University*
- *Cold Spring Harbor Laboratories*

CANADA

- *University of Waterloo*
- *McGill University*
- *University of Guelph*
- *Université Laval*
- *University of Nova Scotia*

UNITED KINGDOM

- *Natural History Museum, London*
- *University of Cambridge*
- *Univerisity of Edinburgh*
- *University of Warwick*
- *John Innes Centre*
- *Durham University*
- *University of Leeds*
- *University College, London*
- *Nottingham Trent University*

FRANCE
- *University of Bourgogne*
- *ESPCI Paris*
- *University of Reunion*
- *University of Nantes*
- *Inserm, Paris*
- *CNRS, Montpellier*
- *Pierre and Marie Curie University (UPMC)*
- *University of Burgundy, Dijon*
- *Institut Curie, Paris*
- *Institute Sophia Agrobiotech*

GERMANY
- *Zoological Research Museum Alexander Koenig*
- *Max Planck Institute for Dynamics and Self-Organisation*
- *Max Planck Institute of Molecular Cell Biology and Genetics*
- *Max Planck Institute for Mathematics in the Sciences*
- *University of Würzburg*
- *Martin-Luther-University Halle-Wittenberg*
- *Max Planck Institute for Chemical Ecology*

SPAIN
- *Universitat Autònoma de Barcelona*
- *Institute for Bioengineering of Catalonia(IBEC)*
- *The Institute of Photonic Sciences (ICFO)*

DENMARK
- *Technical University of Denmark (DTU)*
- *Niels Bohr Institute*

ITALY
- *IFOM the FIRC Institute of Molecular Oncology, Milan*
- *IBP, Naples*

AUSTRIA
- *University of Vienna*

NETHERLANDS
- *University of Groningen*

POLAND
- *Nencki Institute of Experimental Biology, Warsaw*

SWITZERLAND
- *University of Geneva*

SWEDEN
- *Lund University*
- *Stockholm University*
- *KTH Royal Institute of Technology*

PORTUGAL
- *Instituto de Medicina Molecular(IMM), Lisbon*

ISRAEL
- *Technion University*

JAPAN
- *National Institute of Advanced Industrial Science and Technology (AIST)*
- *Nagoya University*
- *Kyoto University*
- *Riken Research Institute, Japan*
- *Shinshu University*

SINGAPORE
- *Singapore Immunology Network, SIgN A*STAR*
- *Bioinformatics Institute, A*STAR*
- *Temasek Life Sciences Laboratory*
- *Nanyang Technical University*
- *National University Singapore*
- *Duke-NUS Medical School*

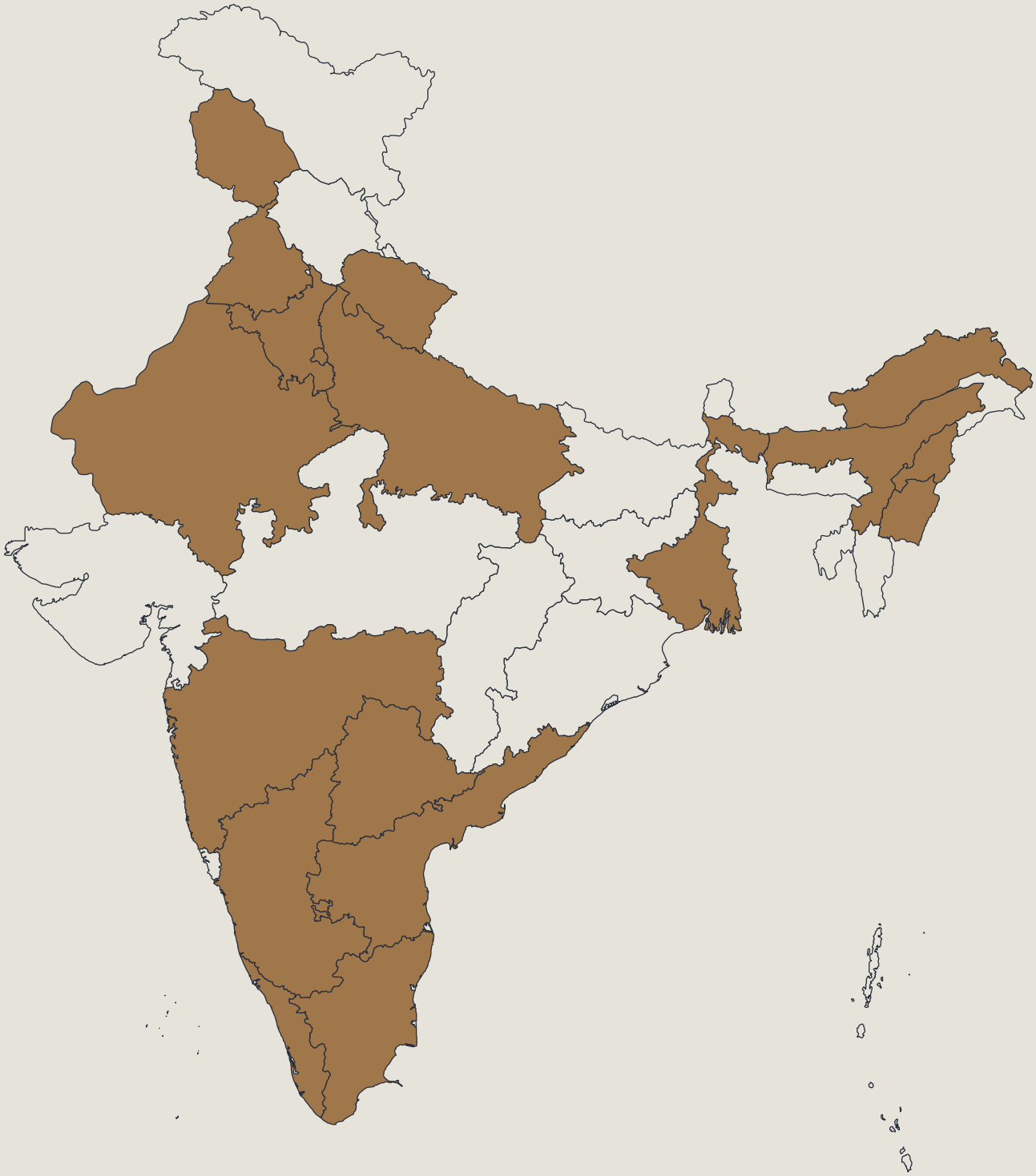
MALAYSIA
- *International Medical Univerisity, Malaysia*

SOUTH AFRICA
- *South African National Parks*

KENYA
- *University of Nairobi*

NEW ZEALAND
- *University of Otago, Dunedin*

AUSTRALIA
- *The University of Queensland*
- *Centenary Institute*
- *University of Adelaide*



List of all the national institutions:

KARNATAKA (BANGALORE)
- *Indian Institute of Science*
- *Institute of Bioinformatics and Applied Biotechnology (IBAB)*
- *Raman Research Institute*
- *Ashoka Trust For Research in Ecology and the Environment*
- *Foundation for Ecological Research, Advocacy and Learning*
- *Jawaharlal Nehru Centre for Advanced Scientific Research*
- *Gandhi Krishi Vignana Kendra (GKVK)*
- *International Centre for Theoretical Sciences*
- *National Institute of Mental Health and Neuro-Sciences*
- *Kidwai Memorial Institute of Oncology*
- *Nature Conservation Foundation*

TELANGANA (HYDERABAD)
- *University of Hyderabad*
- *Center for Cellular and Molecular Biology(CCMB)*
- *Tata Institute of Fundamental Research*
- *Centre for DNA Fingerprinting and Diagnostics (CDFD)*
- *International Institute of Information Technology (IIIT)*

MAHARASHTRA (MUMBAI)
- *Tata Institute of Fundamental Research*
- *Indian Institute of Technology*
- *Bhabha Atomic Research Center (BARC)*
- *Bombay Natural History Society*
- *Tata Memorial Hospital*

MAHARASHTRA (PUNE)
- *Indian Institute of Science Education and Research*
- *Agarkar Research Institute*
- *Savitribai Phule Pune University*

ARUNACHAL PRADESH
- *Rajiv Gandhi University*

MANIPUR
- *Institute of Bioresources and Sustainable Development*

NAGALAND
- *Nagaland Science Council*

ASSAM
- *Indian Institute of Technology, Guwahati*

KERALA
- *Indian Insitute of Science Education and Research, Thiruvananthapuram*

DELHI
- *Institute of Genomics and Integrative Biology*
- *All India Institute of Medical Sciences*
- *National Institute of Immunology*
- *National Institute for Plant Genome Research*
- *University of Delhi*
- *International Centre for Genetic Engineering and Biotechnology (ICGEB)*

WEST BENGAL
- *Indian Institute of Science Education and Research, Kolkata*

RAJASTHAN (JODHPUR)
- *Indian Institute of Technology*
- *Central University of Rajasthan*
- *All India Institute of Medical Sciences*

JAMMU AND KASHMIR
- *Indian Institute Of Integrative Medicine, Jammu*
- *University of Kashmir, Srinagar*

HARYANA
- *Ashoka University, Sonipat*
- *Regional Centre for Biotechnology, Pali*

UTTARAKHAND
- *Indian Institute of Technology, Roorkee*
- *Wildlife Institute of India, Dehradun*

TAMIL NADU (CHENNAI)
- *Chennai Mathematical Institute*
- *MS Swaminathan Research Foundation*
- *Indian Institute of Technology Madras*
- *Adayar Cancer Institute*

TAMIL NADU (TIRUCHIRAPPALLI)
- *Bharathidasan University*

UTTAR PRADESH
- *National Botanical Research Institute, Lucknow*

PUNJAB
- *Indian Institute of Science Education and Research, Mohali*

ANDHRA PRADESH
- *Indian Institute of Science Education and Research, Tirupati*

Making a Difference: Design Note

The design concept for this year's annual report emphasises two things – the TIFR Council's review of NCBS, and NCBS' response to COVID-19.

The biggest takeaway from the TIFR Council's review was that NCBS is a young research institution that has had an immense impact in the field of fundamental research in a short span of time. In metaphorical terms, it is like a dandelion head with many florets carrying seeds. While appearing small, their influence is far reaching.

In addition to this, the campus responded to the pandemic through various initiatives, including assisting the State of Karnataka and the country through research, testing, science communication, and volunteering efforts, as well as measures to counter its effects inside the campus. The visual of the dandelion further illustrates this resilience.

The abstract dandelion on the cover is made of eight unique parts. At its core is a simple dynamic spirograph that is reflective of the energy and commitment of NCBS. Around the core are the crucial activities and entities associated with NCBS – the Administration and Academics department, the Archives at NCBS, the Bangalore Life Science Cluster, collaborations with other institutions, and NCBS' response to COVID-19 - each with their own icons. These icons are also used inside the report to highlight their corresponding sections.

The next ring is made of 37 Pis for all the 37 Principal Investigators, three of whom are retiring this year, seen breaking away from this ring.

Finally, there are three rings of binary numbers representative of the huge data collection that is integral to the work done by the institution. The spray of numbers suggests the dispersal of this information. When translated, these binary numbers read as "National Centre for Biological Sciences Annual Report 2019-2020".

This work would have been impossible if it were not for the support of the Communications Department. I have to make a special mention of Dr. Satyajit Mayor, Director, NCBS and Dr. Raj Ladher, Head of Academics, NCBS, whose inputs were invaluable for developing this work.

Anoopa John
Designer

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Tata Institute of Fundamental Research

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