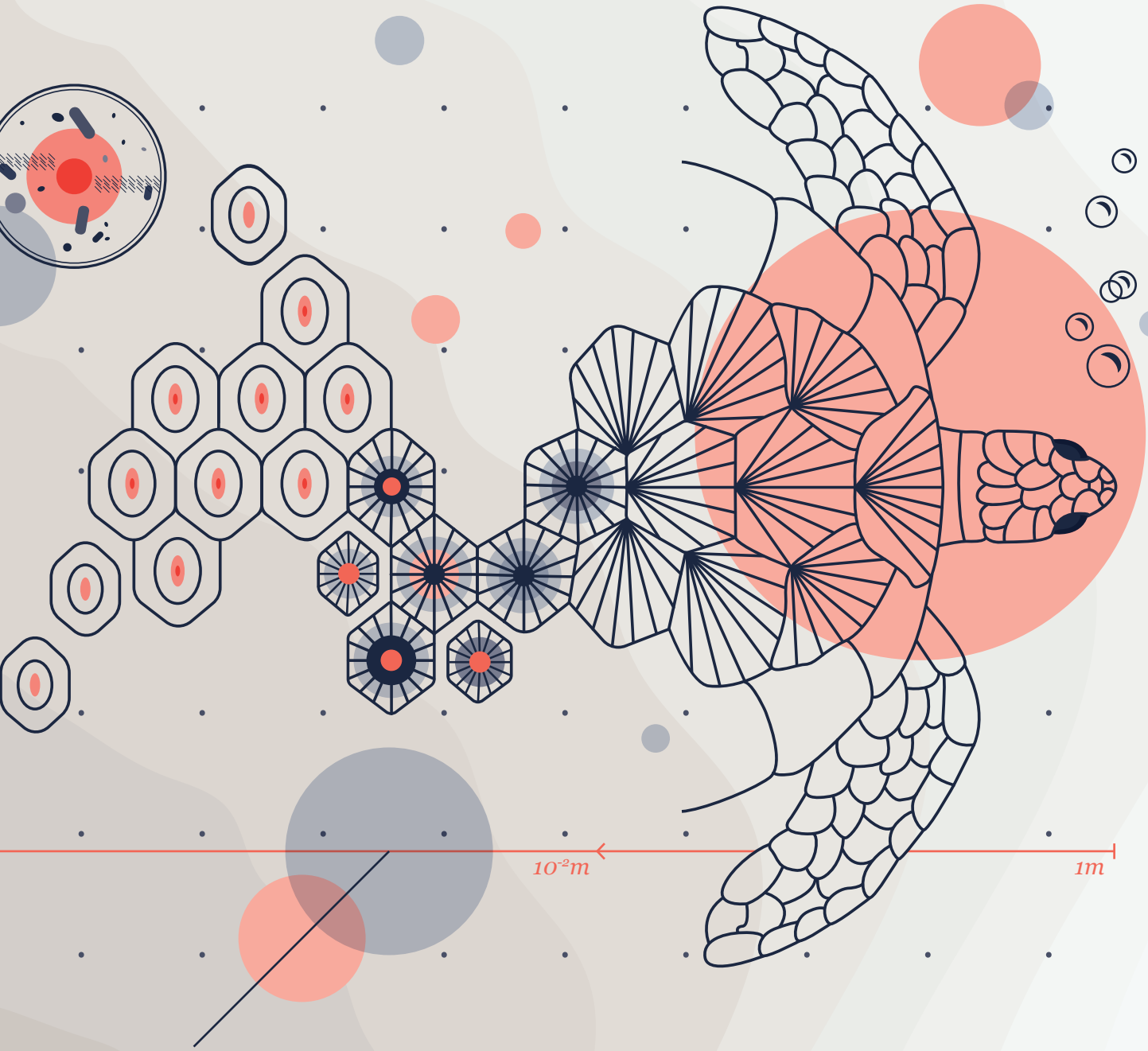
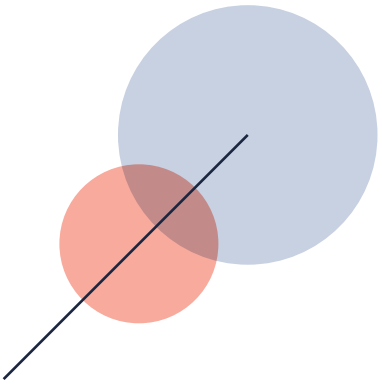
ncbs
National Centre for Biological Sciences
Tata Institute of Fundamental Research




# National Centre for Biological Sciences

ANNUAL REPORT 2017-18



# National Centre for Biological Sciences

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A cluster of gossamer-winged dragonflies from Dhara Mehrotra's exhibition "Through Clusters and Networks", as a part of the TIFR Artist-in-Residence programme
**PHOTO: DHARA MEHROTRA**

# CONTENTS

**SATYAJIT MAYOR**
Centre Director

## DIRECTOR'S NOTE

# Strategies for Future Proofing NCBS

As a Centre of Tata Institute of Fundamental Research, NCBS has navigated a year of uncertainty because of a variety of reasons. Dominant among these is a refrain questioning what autonomous institutes have achieved during their existence. This question reverberates throughout funding agencies that have supported fundamental research in the past. Rightfully, we who belong to these autonomous institutes of science must be answerable to those who repose their trust, faith, and money in us. For this we need to be relevant to the context that we work in, and also communicate our achievements.In the 25 plus years of NCBS's existence we have been trying to do more of the former, and it would be good to take stock of where we stand. I list a few of our highlights. What emerges is a host of efforts that make NCBS what it is today: a site for excellent basic research with a footprint that is enabling new paths of discovery and translation based on issues emanating from our own neighbourhood.

BEGINNING IN 2006, NCBS partnered the Centre for Wildlife Studies (CWS) and the Wildlife Conservation Society to initiate a Masters programme in Wildlife Biology and Conservation. This is one of India's most sought-after MSc programmes today. Our MSc in Wildlife Biology and Conservation has also brought new opportunities for us: it has literally brought our large and diverse ecosystem into our laboratories. This has emboldened some of our faculty to wholeheartedly engage in shaping a potentially transformative Mission programme on understanding India's Biodiversity and its role in human wellbeing. Uma Ramakrishnan is now a member of the Steering Committee for this Mission, along with Kamal Bawa (one of our Scientific Advi-

sors), and partner institution ATREE. In addition, NCBS faculty in partnership with the Wipro Foundation, the CSR entity of Wipro Ltd, has helped launch The Bangalore Sustainability Forum. The purpose of this forum is to create a coalition of resource people, research institutions, and action-oriented agencies to tackle one of the most pressing issues at our doorstep, the sustainability of the urban sprawl that is Bangalore.

Partnering the Department of Biotechnology, NCBS helped nucleate the Institute for Stem Cell and Regenerative Medicine (inStem) and set up the technology platform and incubator, Centre for Cell and Molecular Platforms (C-CAMP), almost 10 years ago. The intention was that as a combined space, we would be able to engage in more programmatic research with activities that could have translational potential. Instead of standing by and being asked to do things that we may not have the capacity to accomplish, several activities at NCBS–inStem–C-CAMP (which we now call The Bangalore Life Sciences Cluster or BLiSC) have been set up where important questions arising from our our own neighborhood have been taken on.

BLiSC is now funded by the DBT as a Cluster ecosystem, and is emerging as a role model for how a life sciences ecosystem may function. As a consequence of the engagement of NCBS-TIFR, inStem is also well on its way to standing on its own feet, as an equal partner in BLiSC. The establishment of the National Facilities for Mouse Genome Research and the inauguration of the National Cryo Electron Microscopy Facility by C N R Rao and Richard Henderson earlier this year, is a testimony of the cluster's multi-institutional character in enabling national facilities. The development of BLiSC, built around foundational multidimensional research and excellent core facilities, has also created a supportive ecosystem for biotech startups. This has enabled a few companies to reach a stage where they are in the process of going public. And we hope that in the long term this will pay back to the campus.

With the engagement of few of our faculty (Shona Chatterjee, Upi Bhalla, and Raghu Padinjat) with colleagues at the Centre for Brain Development and Repair at inStem and clinicians at NIMHANS, NCBS has helped create two valuable programmes on the study of mental disorders, the Centre for Neuro-Synaptopathies (CNS), and Accelerator programme for Discovery in Brain Disorders (ADBS). Here we look at a wide ranging set of questions ranging from understanding a monogenic disorder (CNS: Autism Spectrum Disorders) to the complex spectrum of neuropsychiatric disorders such as Bipolar Disorders and Schizophrenia (ADBS). The latter is firmly predicated on the long-term study of a cohort of patients at NIMHANS who carry this disease in familial fashion, to understand the basis of these complex mental disorders.

Public health initiatives are one more example of such translational efforts, and here, Sudhir Krishna's efforts at engaging in vaccine development against Dengue in a project generously supported by Mr. Narayana Murthy, is one exemplar. To realise this goal will require many deep partnerships with several agencies to increase the bandwidth of this initiative; NCBS could serve as one of the sites of research for this effort. Engaging in these local and national efforts with varied partners including other government institutes, NGOs, foundations, and citizen groups exemplifies organic growth, collaboration, and impact, and appears to be the NCBS way.

Another NCBS based organisation, built up over the past decade for bringing together a community of Life Science Researchers, is India-BioScience (IBS). NCBS has helped to nurture IBS during its formative years, and today IBS is supported by grants from the DBT and the Ministry of Human Resources. Led by its Executive Director, Smita Jain, IBS not only serves to disseminate best practices in research and hiring of young life science faculty all over the country, it also provides an awareness of alternative career opportunities for researchers outside the straight and narrow of academic research. We look forward to IBS providing a platform for Life Sciences researchers in the country, linking them up with the best opportunities for mobilising their most creative talents.

NCBS has also directly participated in nurturing leadership in the Life Sciences by exporting its best: we congratulate K. Vijayraghavan for becoming the Principal Scientific Advisor to the Prime Minister, Jayant Udgaonkar for becoming Director IISER, Pune, and Apurva Sarin, Director inStem, and wish them all the very best for their future endeavors.

But none of this would have happened without ensuring that the best possible science (Biology across Scales) is done by our faculty on our campus with the necessary resources to support these efforts. We have kept our focus on the science that we need to do to support such a multi-dimensional effort, and where the need or desire arises, individuals can realise larger goals in partnership with the most appropriate organisations. It has taken NCBS 25 years and counting, nurturing unique efforts such as Theory@NCBS in its course. Now joined by inStem, I strongly believe that we have a very fertile ecosystem where there are clear linkages between laboratory-based research, translational efforts, and questions that derive from our neighbourhood, underlining our relevance to our context.

Much of our efforts remain hidden without a commitment to effective

communication of our science and achievements outside our campus. To address this, here on behalf of BLiSC, I warmly welcome Mahinn Ali Khan, who has joined us to lead our Communications team. Several new initiatives with regards to the communication of our science by the use of different social media platforms have been enabled, and we look forwards to these efforts fructifying in the coming years and more robust communication of our relevance to context.

In terms of transitions, one more of our founding members, Gaiti Hasan, formally retired in November. We hope she will continue her association with NCBS in new avatars. As we gather age and wisdom, we must acknowledge more retirements; we celebrate, yeoman services of our Chief Architect, Poornima, without whom our campus would never have emerged as the excellent architectural space that it has come to represent, and N Shantakumari, the first administrative staff to be recruited to the NCBS campus, and someone who we have relied on for her dedication in several administrative departments at NCBS, from the academic office to human resources. These citizens of NCBS will be sorely missed.

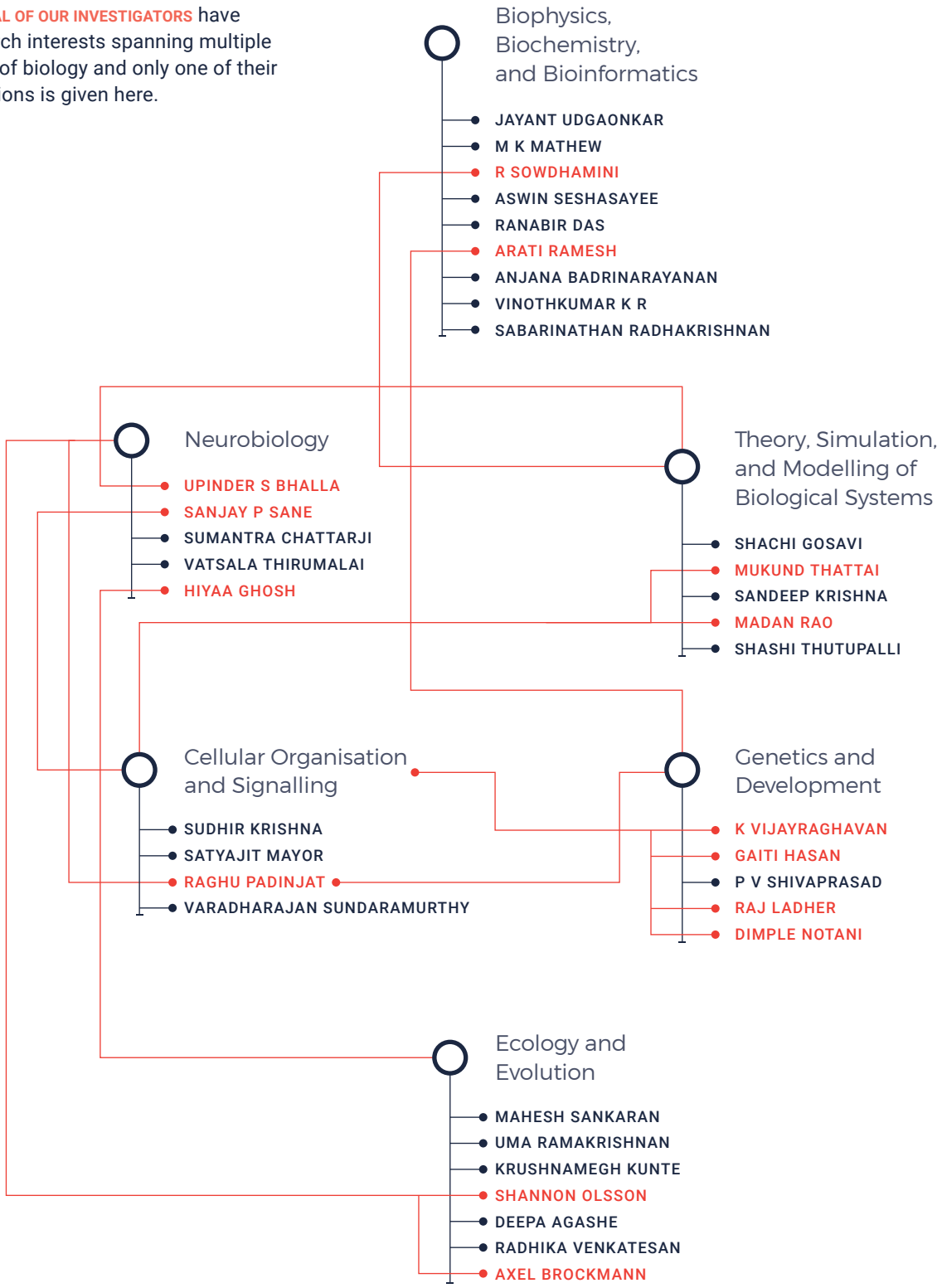
But we must look ahead and remain buoyant, and for this we must listen to what the voices are saying and read the writing on the wall. One shrill sound is about the resources we must bring in to sustain ourselves. We urgently need to diversify our funding streams, beyond the GoI. We need to create a robust funding strategy for accessing philanthropic donations, grants and endowments to accessing funds from Corporate Social Responsibility (CSR) funding.  Here we have made a small beginning, and on behalf of all of us at this campus, I would like to offer our sincere appreciation to Mr. T T Jagannathan, Chairman of TTK Prestige for his generous donation from their CSR funds, and the Infosys Foundation, both contributing towards our international outreach activities.

We also express our deepest gratitude to Sudha and Kris Gopalakrishnan and Dr. Kiran Mazumdar-Shaw, for their constant support and inspiration, enabling major research endeavours on the campus from their own philanthropic donations. We will grow this funding effort over the next year.

Some of the programmes outlined above have needed close interactions beyond the boundaries of individual laboratory-based research at NCBS. It has required an enabling ecosystem that BLiSC now provides. A crucial ingredient to create this ecosystem, has been the flexibility to take decisions locally. Despite considerable effort from the Steering Group and our Management Board at NCBS, this is something that still requires resolution with our parent institute, TIFR. Given all the positive outcomes, I hope by the time of the next report we will have a clearer picture of how this may be realised.

# MAP OF RESEARCH INTERESTS

**SEVERAL OF OUR INVESTIGATORS** have research interests spanning multiple areas of biology and only one of their affliations is given here.



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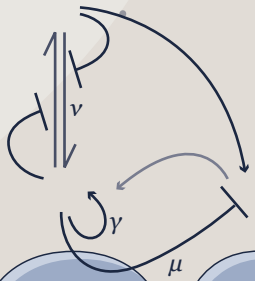


Computational Protein Folding and Functional Dynamics
SHACHI GOSAVI

The Origins of Complex Cells
MUKUND THATTAI

Dynamics of Biological Systems across Scales
SANDEEP KRISHNA

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

Collective Dynamics in Living Matter
SHASHI THUTUPALI

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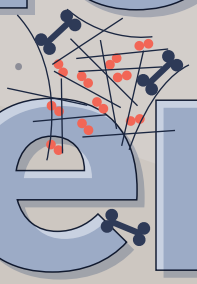

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1.1

**SHACHI GOSAVI**
*shachi@ncbs.res.in*

# Computational Protein Folding and Functional Dynamics

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 the folding rates of several proteins. The advantage of 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 the 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

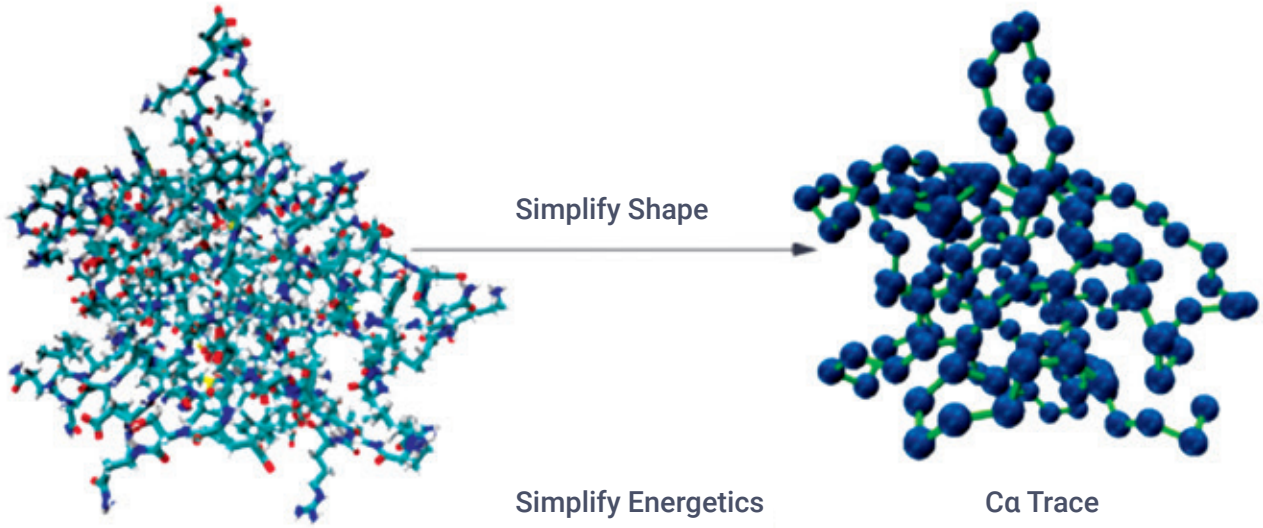
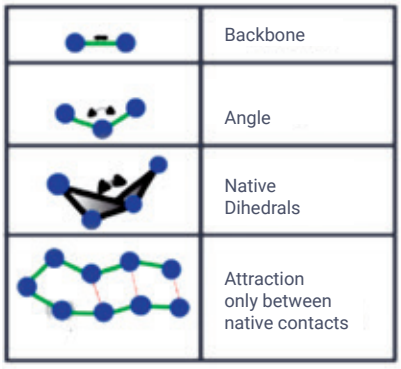



***Illustration of a coarse-grained structure-based model.*** *The protein shape is simplified by coarse-graining it to a Cα level. The energetic terms that contribute to the potential energy function are listed in the table. The parameters for these terms are all derived from the folded state of the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




Energetics Interactions

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.

**SELECT PUBLICATIONS**

Yadahalli, S. and Gosavi, S., 2017. Packing energetics determine the folding routes of the RNase-H proteins. ***Physical Chemistry Chemical Physics, 19***(13), pp. 9164-9173.

Mascarenhas, N.M. and Gosavi, S., 2017. Understanding protein domain-swapping using structure-based models of protein folding. ***Progress in Biophysics and Molecular Biology, 128***, pp. 113-120.

1.2

**MUKUND THATTAI**
*thattai@ncbs.res.in*

# The Origins of Complex Cells

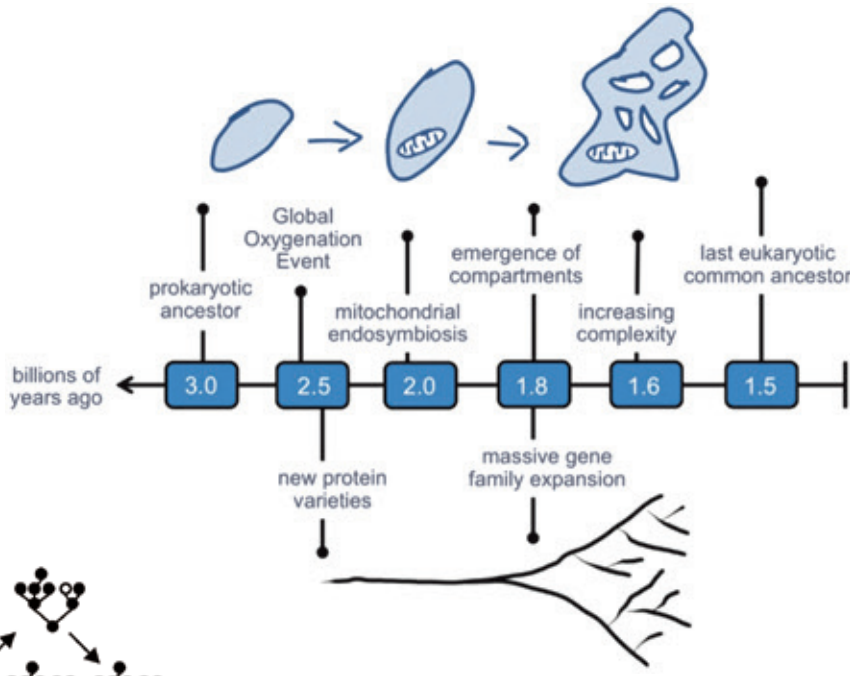
We use the eukaryotic membrane traffic system as a window to probe the emergence of complex cells two billion years ago. This effort combines population genetics, dynamical systems and graph theory, with genomics data and quantitative experiments.

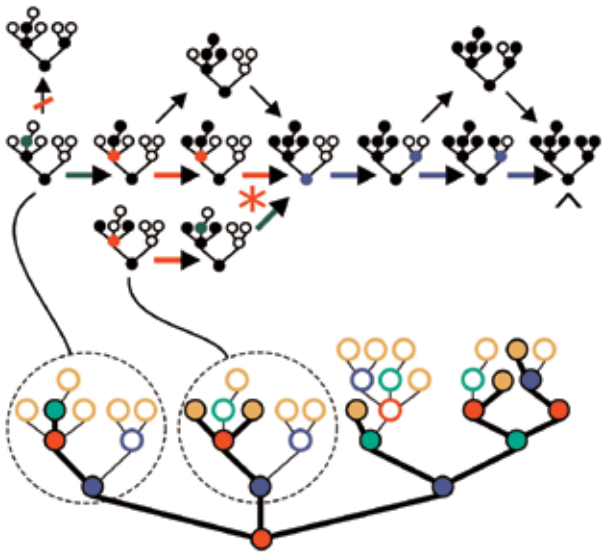
**WE ARE INTERESTED** in the ancient origins of the eukaryotic compartmentalised cell plan. Surprisingly little is known about this key phase of the evolution of life: eukaryotes began to diverge from bacteria during the global oxygenation event 2.5 billion years ago, but all living eukaryotes share a more recent common ancestor dating from about 1.5 billion years ago.

Data from modern eukaryotic genomes might allow us to reconstruct the intervening billion-year period during which quintessential eukaryotic features emerged: the nucleus, mitochondria, compartmentalised organelles, the cytoskeletal machinery, and vesicle traffic. In particular, we are pursuing two complementary research directions.

Forward in time: we analyse potential origin scenarios using biophysical and evolutionary simulations, to uncover general principles about the evolution of compartmentalised cells. Backward in time: we study the evolution of the molecular machinery underlying compartmentalisation using sequence data and phylogenetic techniques; we

***The acquisition of mitochondria was a watershed event, triggering massive gene family expansions and the emergence of the eukaryotic compartmentalised cell plan.*** *Our goal is to rigorously understand how changes at the genomic level drove changes at the cellular level.*



***The membrane traffic system of eukaryotes allows physical and chemical processes within the cell to be finely regulated.*** *For example, the successive compartments of the Golgi apparatus act as an assembly line for the construction of glycans, which are molecular trees made of sugar monomers. We have used the theory of algorithms to understand how the cell is able to build glycan trees with very few errors.*

especially concentrate on molecules that underwent eukaryote-specific gene family expansions, including Rabs, coat proteins, and SNAREs. The population-genetic mechanisms that generated the earliest compartmentalised cells continue to drive the diversification of eukaryotes. Our evolutionary perspective might therefore shed light both on ancient events as well as on modern lineage-specific and tissue-specific elaborations of traffic systems.

## SELECT PUBLICATIONS


Chib, S., Das, S., Venkatesan, S., Seshasayee, A.S.N. and Thattai, M., 2018. Using stochastic cell division and death to probe minimal units of cellular replication. ***New Journal of Physics, 20***(3), p. 035004.

Mani, S. and Thattai, M., 2016. Stacking the odds for Golgi cisternal maturation. ***Elife, 5***, p. e16231.

1.3

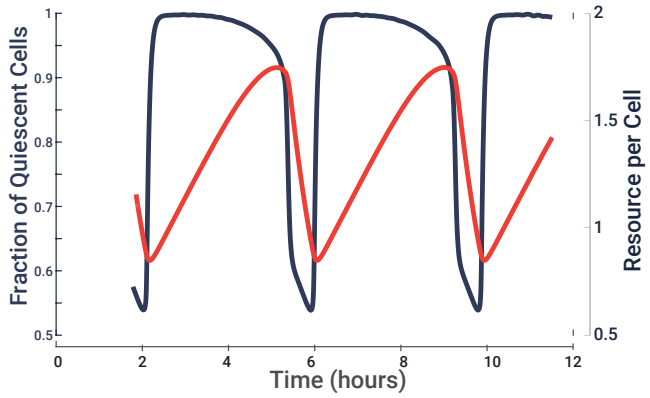
**SANDEEP KRISHNA**
*sandeep@ncbs.res.in*

# Dynamics of Biological Systems across Scales

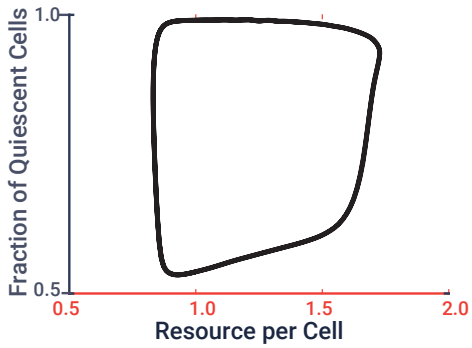
I'm interested in dynamical patterns in biological systems, ranging from molecules, to cells to populations.

**AT THE MOLECULAR LEVEL,** I'm interested in using a combination of experimental data and mathematical models to study the dynamics of different mechanisms of protein regulation and their role 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.

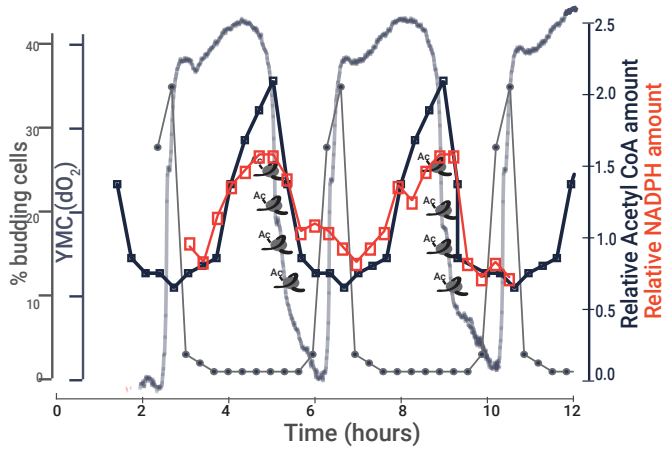
Model



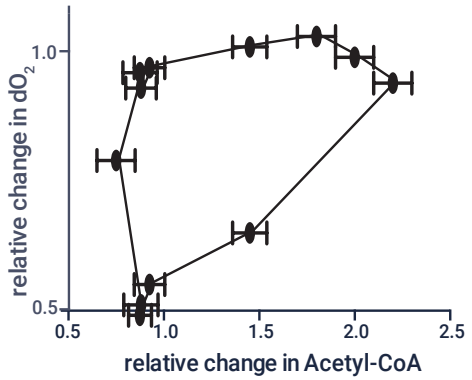

Model

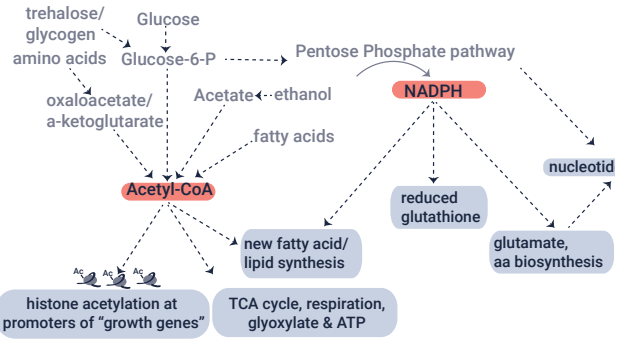



Experimental data




Experimental data




***Theory and experiments suggest that Acetyl-CoA is the metabolic trigger for the coordinated transition, from quiescence to proliferation, that underlies the yeast metabolic cycle***

## SELECT PUBLICATIONS


Suratekar, R., Panda, A., Raghu, P. and Krishna, S., 2018. Evidence of sinks and sources in the phospholipase C-activated PIP 2 cycle. ***FEBS Letters, 592***(6), pp. 962-972.

Krishna, S. and Laxman, S., 2018. A minimal "push–pull" bistability model explains oscillations between quiescent and proliferative cell states. ***Molecular Biology of the Cell, 29***(19), pp. 2243-2258.


## HONORS AND AWARDS

**Chaire Joliot for 2018-2019** from École Supérieure de Physique et De Chimie Industrielles de la Ville de Paris, France.

1.4

**MADAN RAO**
*madan@ncbs.res.in*

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

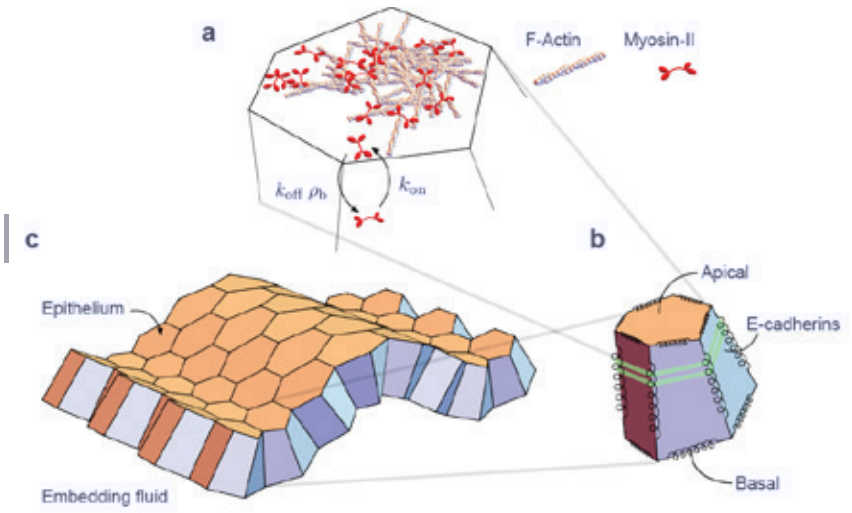
Our group studies the interplay between active mechanics, molecular organisation, geometry, and information processing in a variety of cellular contexts such as cell surface signalling and endocytosis, packing of chromatin within the nucleus, organelle biogenesis, and tissue morphogenesis.

**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.

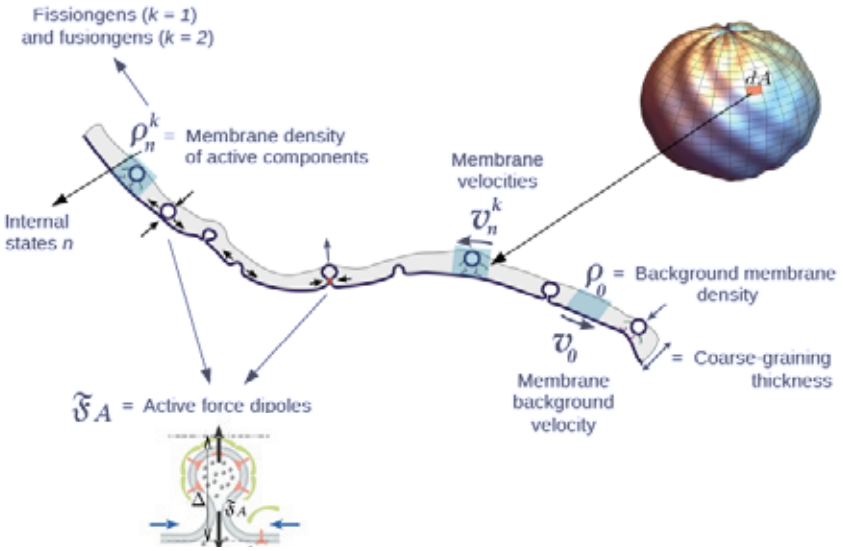
We explore new physical and chemical principles underlying biological organisation across scales, from functional biomolecules, to subcellular organelles, to the cellular and tissue scale. We are interested in the folding and packaging principles that govern the three dimensional functional organisation 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 fuelled by energy.

Typically these active forces arise from (i) the coupled dynamics of the cytoskeleton, motors, and cytoskeletal regulatory proteins, and (ii) 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.




***Schematic showing the elements of the covariant active hydrodynamics of epithelial tissue.***
*(a) The action of myosin-II motors on cortical actin at the apical cell surfaces leads to contractile stresses*
*(b) This leads to an (active) mechanical response of cells*
*(c) Cells enclose a fixed volume, and are tightly bound to each other by a localised belt of E-cadherin proteins on the lateral faces. The interplay between such cell-autonomous forces and the dissipation and displacement of the embedding fluid gives rise to tissue-scale deformations*




***Schematic showing the active stress dipoles generated as a consequence of fission and fusion of tiny cargo vesicles with the Golgi membrane.***
*The interplay between active stresses and elastic membrane stresses drive shape changes and hydrodynamic instabilities of the Golgi membrane.*

## SELECT PUBLICATIONS


Rupprecht, J.F., Vishen, A.S., Shivashankar, G.V., Rao, M. and Prost, J., 2018. Maximal fluctuations of confined actomyosin gels: dynamics of the cell nucleus. ***Physical Review Letters, 120***(9), p. 098001.

Nandi, S.K., Mandal, R., Bhuyan, P.J., Dasgupta, C., Rao, M. and Gov, N.S., 2018. A random first-order transition theory for an active glass. ***Proceedings of the National Academy of Sciences, 115***(30), pp. 7688-7693.


## HONORS AND AWARDS

**Sackler Fellowship for the Year 2018-2019**

1.5

**SHASHI THUTUPALLI**
*shashi@ncbs.res.in*

# Collective Dynamics in Living Matter

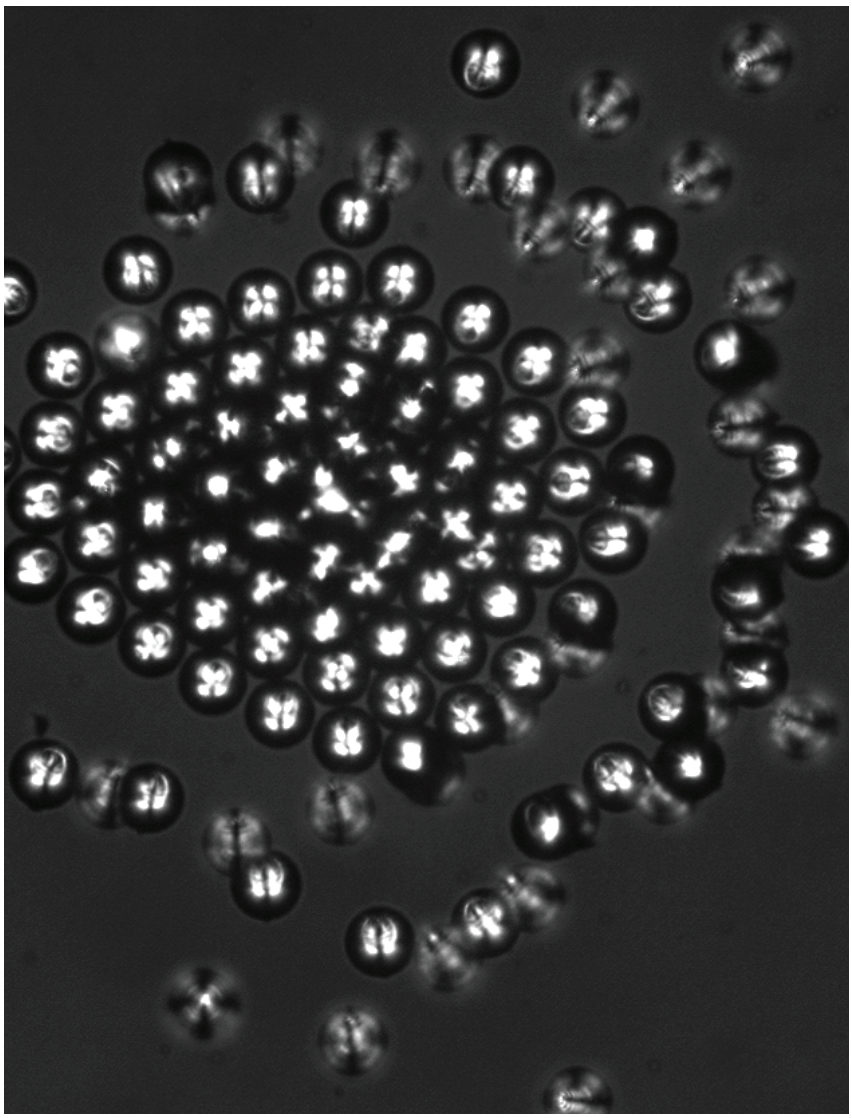
Our research programme aims for a broad understanding of the origins and organisation of living systems, with a particular focus on collective behavior. We are an interdisciplinary group combining experimental and theoretical techniques drawn from physics, engineering, and biology.

OUR GROUP USES experiment and theory to investigate the origins and self-organisation of living systems. Broadly, our research programme is comprised of two approaches:

I. Constructing *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. They are also likely to throw up new solutions that might be useful in engineering and biotechnology. We study the minimal ingredients for self-assembly, replication, feedback, and evolvability. Currently, our focus is on self-assembly in active systems, particularly towards understanding self-replication and origin-of-life scenarios.

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 have multiple research projects along these lines in which we inves-



***Pictured is a polarised optical micrograph of a spontaneously formed crystalline aggregate of swimming nematic liquid crystal emulsion droplets.*** *Each droplet is about 50 microns in diameter and is suspended in an aqueous solution containing surfactant. The spontaneous flow generated by these swimming droplets and other generalised active particles can lead to spontaneous crystallisation, collective motion, and phase-separation.*

tigate: a) the dynamics of cellular populations in response to fluctuating environments and extreme perturbations, b) the physical basis of cellular antigen processing, phage-bacteria interactions, c) chemical gradients and scaling in regenerating organisms, d) chemical reactions in crowded environments, and e) cellular phenomenological growth and death laws.

## SELECT PUBLICATIONS


Thutupalli, S., Geyer, D., Singh, R., Adhikari, R. and Stone, H.A., 2018. Flow-induced phase separation of active particles is controlled by boundary conditions. ***Proceedings of the National Academy of Sciences, 115***(21), pp. 5403-5408.

Liu, G., Patch, A., Bahar, F., Yllanes, D., Welch, R.D., Marchetti, M.C., Thutupalli, S. and Shaevitz, J.W., 2017. A motility-induced phase transition drives *Myxococcus xanthus* aggregation. ***arXiv preprint arXiv:1709.06012.***


## HONORS AND AWARDS

HFSP Young Investigator Grant

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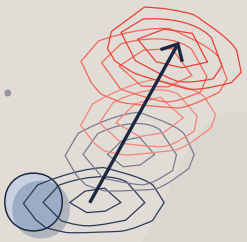

How do Proteins Fold, Unfold, and Misfold?
JAYANT UDGAONKAR

Mechano-Electric Feedback in the Heart
M K MATHEW

Computational Approaches to Protein Science
R SOWDHAMINI

Adaptation, the Bacterial Way!
ASWIN SESHASAYEE

Protein Quality Control and Host-Microbe Interactions
RANABIR DAS

Structure to Signalling: Insights into Bacterial Biology through RNA Structure
ARATI RAMESH

Regulation of DNA Damage Response and Repair
ANJANA BADRINARAYANAN

Membrane Protein Structure and Dynamics
VINOTHKUMAR K R

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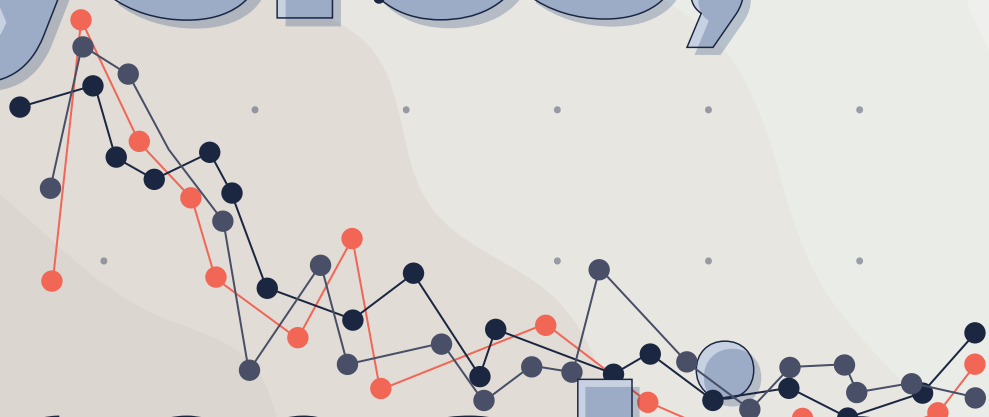
# d ormatics



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**JAYANT UDGAONKAR**
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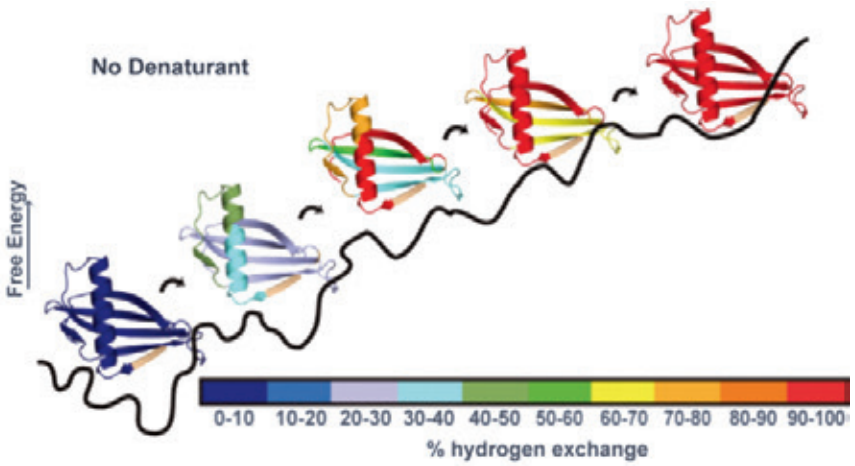
# How do Proteins Fold, Unfold, and Misfold?

The function of any protein is determined by its three-dimensional structure. We study how a polypeptide chain self-assembles into its correct conformation during folding, how the native structure of a protein disassembles during unfolding, and how a protein forms aggregates when folding or unfolding goes wrong.

IN ONE OF the most intriguing examples of biological wizardry, in every cell, every second, thousands of proteins self-pack into the unique shapes that hold the key to their function. In essence, a freshly-formed chain of amino acids bends, loops, twists, coils, and collapses on itself to produce the finished design. We know that these rearrangements are determined by chemical attractions between the amino acids. But in stark contrast to our knowledge of the digital precision by which DNA codes the sequence of amino acids, the chemical forces that direct folding act in an incompletely understood, nebulous way, much as the weather is ruled by physical processes. A predictive model for protein structure remains one of science's holiest grails, promising incredible benefits throughout the biomedical sciences.

In our lab, the quest is focused on observations of real instances of protein folding, unfolding, and misfolding—a complementary and ground-truthing approach to algorithm-based models. Using small proteins (e.g. PI3K SH3 domain, monellin), and techniques that monitor shape changes with nano- to-microsecond resolution, we are answering questions fundamental

*Gradual, diffuse changes in secondary structure during the uphill unfolding of monellin in native conditions.*




to solving the self-packing puzzle: Do proteins take shape gradually or in fits and starts? Is there only one folding sequence for each protein? How sensitive is folding to cellular conditions? What comes first—an "outline" of the shape or its details? We are also applying our expertise to protein unfolding and most recently to misfolding—an all-too-common problem that can cause proteins to aggregate into fibrillar masses, most tragically causing the neurodegeneration of Alzheimer's disease.

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Bhatia, S., Krishnamoorthy, G. and Udgaonkar, J.B., 2018. Site-specific time-resolved FRET reveals local variations in the unfolding mechanism in an apparently two-state protein unfolding transition. ***Physical Chemistry Chemical Physics, 20***(5), pp. 3216-3232.

2.2

**M K MATHEW**
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# Mechano-Electric Feedback in the Heart

Mechanical forces generated by pumping fluid in the heart feed back onto the electrical system. The mechanical stress is sensed by the integrin system and relayed to the hERG channel in the heart.

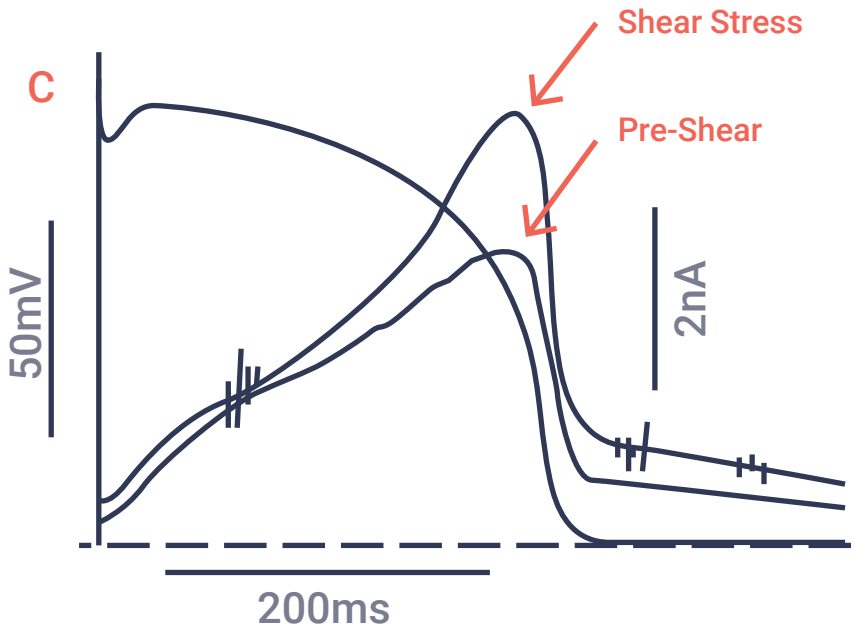
**THE BEATING OF** the heart is initiated by an elaborate and well-tuned electrical system that generates the cardiac action potential.

The firing of the action potential results in contractions of the musculature of the heart, and hence blood flow through the body.

The effect of mechanical forces at work during the heart beat on the electrical system of the heart have not (surprisingly) been investigated in detail so far. The fast component of the delayed rectifier potassium currents responsible for repolarisation of the cardiac action potential, Ikr, is encoded by the hERG channel. When HEK293T cells expressing hERG1a channels were exposed to laminar shear stress, there was a substantial increase in whole cell current. hERG1b, which lacks the PAS domain, and long QT mutants containing point mutations in the PAS domain were unaffected by shear suggesting possible involvement of the PAS domain in mechanosensation. Modulation of the whole cell current upon application of shear was found to be dependent on the integrin pathway.

Thus mechano-electric feedback modulates the hERG channel through the integrin pathway, thereby influencing the repolarisation current in the heart.

***Enhancement of hERG1a currents during rabbit action potential stimulus.*** *The stimulus is indicated by the left-most curve and uses the LEFT scale bar. The current traces are on the right and use the RIGHT scale bar. Shear increases total potassium conduction by hERG1a channels during an action potential stimulus (scale bar, 50 mV and 200 ms). Typical current traces before and during shear stress are shown. (Scale bar, 2 nA and 200 ms). The dashed line represents the zero current level (N=7).*

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Roy, S. and Mathew, M.K., 2018. Fluid flow modulates electrical activity in cardiac hERG potassium channels. ***Journal of Biological Chemistry, 293***, pp. 4289-4303.

2.3

**R SOWDHAMINI**
*mini@ncbs.res.in*

# Computational Approaches to Protein Science

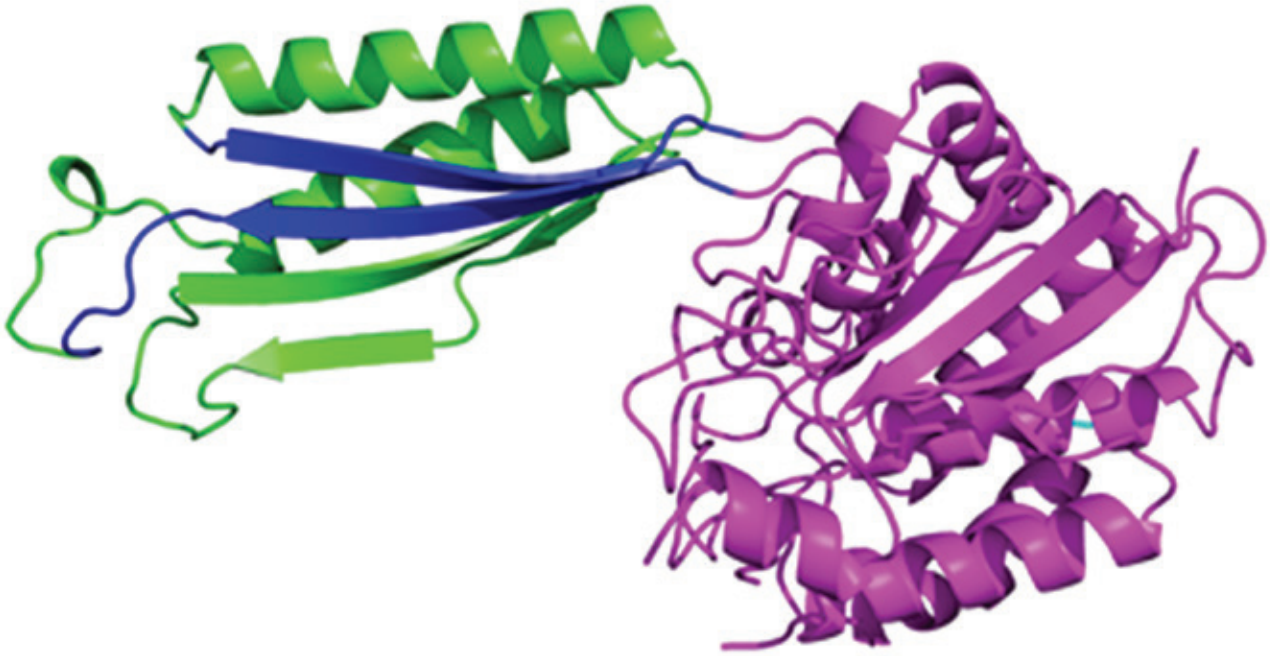
We employ computational algorithms to enable efficient function annotation of unknown gene products. Ongoing and future scientific endeavours are geared towards modelling protein/ligand interactions with applications in biomedical research and in plant genomics, aided by in-depth and collaborative projects.

**GENOME SEQUENCING** projects have enormous potential for benefiting human endeavors. However, just as acquiring a language's vocabulary does not enable one to speak it, databases that list the amino acid composition of proteins do not directly tell us much about these proteins' higher-level structure and function.

The most productive way to indirectly exploit these databases has been to start with the small number of proteins that are fully-characterised and to assume that other "similar" proteins will have a related structure and function. Proteins with very similar amino acid sequence are "no-brainers", but the real test, which our group largely focuses on, is to detect the "essential" similarity in proteins whose non-critical sections have experienced random rearrangements during evolution. In such cases, functionally similar proteins may have less than 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, others exploit characteristic features of specific protein types (e.g. the strong influence of disulphide bonds on the structures of extracellular proteins). These have been adapted into a number of widely-used publicly accessible web

resources (e.g. DIAL, iMOT, MODIP, FMALIGN). Applying these and other techniques, we have also carried out within- and cross-genome surveys of proteins from entire families and superfamilies. Finally, we have been able to use our improved understanding of the functionally-significant regions of proteins for the theoretical prediction of protein function.

***Domains in all antoate amidohydrolase from Escherichia Coli*** *(PDB ID 2IMO, Agarwal et al., 2007), shown as an example, to identify sequence homologues through computational searches. Due to the discontinuous regions (shown in blue colour), it often becomes hard to identify similar genes corresponding to individual domains (shown in green and pink).* Agarwal, R., Burley, S.K., Swaminathan, S. (2007) J. Mol.Biol. 368: 450-463.



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2.4

**ASWIN SESHASAYEE**
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# Adaptation, the Bacterial Way!

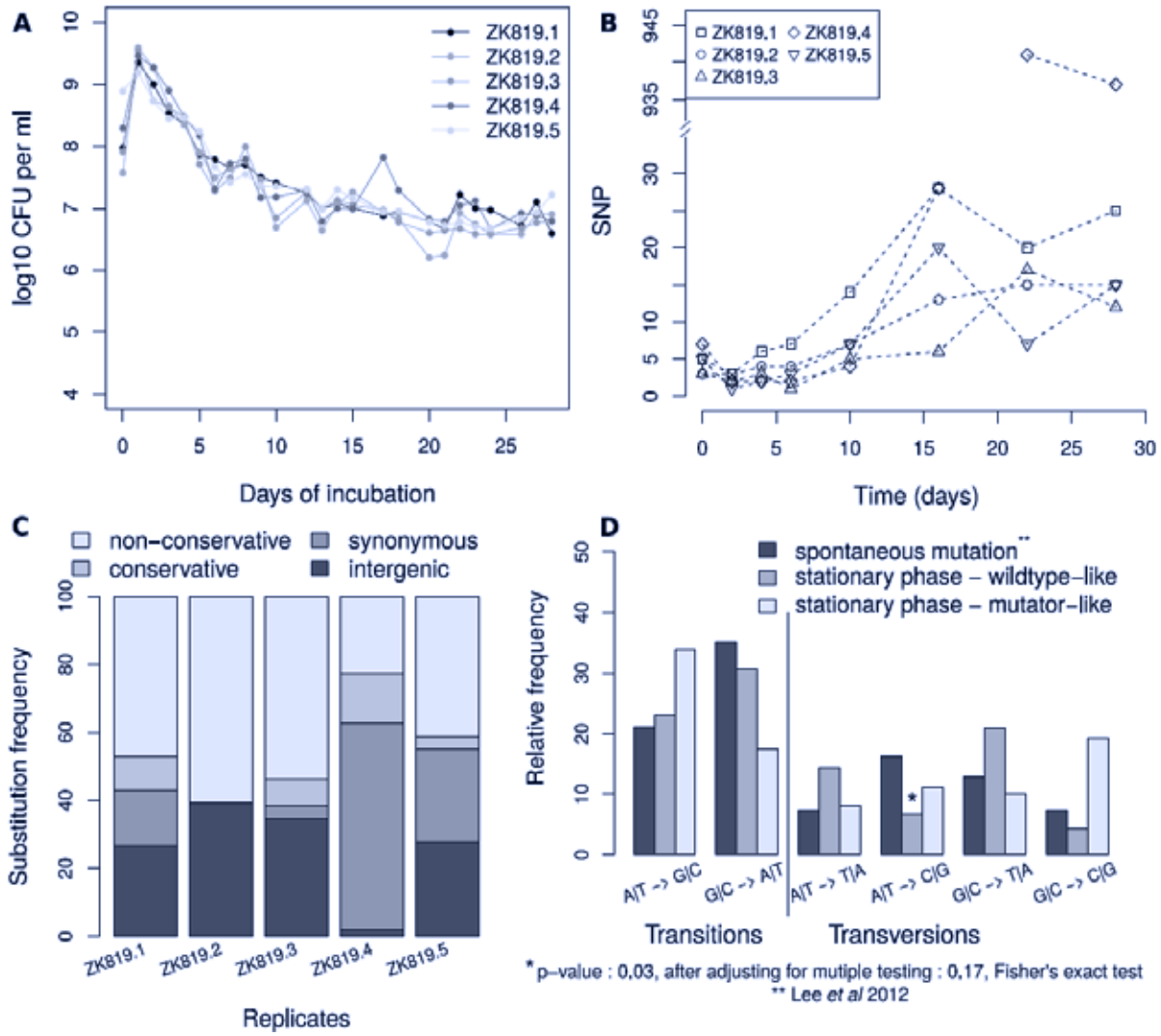
Bacterial adaptation to their environments is complex and multi-pronged. Not only do they use combinations of regulatory players to determine what molecules to produce when, they adapt often by changing their genetic makeup in small steps. We ask how these phenomena operate using genetics and number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

**THE MODEL BACTERIUM** *E. coli* can survive and divide independent of the origin of replication (oriC) under certain conditions, including those in which RNA-DNA hybrids, which can prime DNA replication, are stabilised (cSDR for constitutive stable DNA replication).

Are there discrete sites (oriK) from which such non-canonical replication initiation occur? Or are such sites distributed across the chromosome, consistent with the genome-wide prevalence of RNA-DNA hybrids in these strains? How does *E. coli*, whose genome organisation has evolved to maximise the outcomes of replication initiation from oriC adapt to cSDR?

Many bacteria undergo cycles of feast and famine. The bacterium *E. coli* metabolises nutrients to grow rapidly before facing a period of nutrient starvation. However, they continue to evolve, grow, and die during this phase of starvation, thus maintaining a dynamic population. What evolutionary strategies and regulatory adaptations do bacteria use during phases of prolonged starvation?

We use laboratory evolution experiments and next-generation genomics and bioinformatics to address this question.




***Spectrum of mutations accumulating in E. coli populations maintained in stationary phase.*** From Chib et al. Msphere 2017.

## SELECT PUBLICATIONS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2.5

**RANABIR DAS**
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# Protein Quality Control and Host-Microbe Interactions

The conjugation of ubiquitin and ubiquitin-like molecules to other cellular proteins regulates a broad range of eukaryotic cell functions. We focus on the role of this pathway in two important cellular processes: protein quality control and host-pathogen interactions.

## THE UBIQUITIN PATHWAY

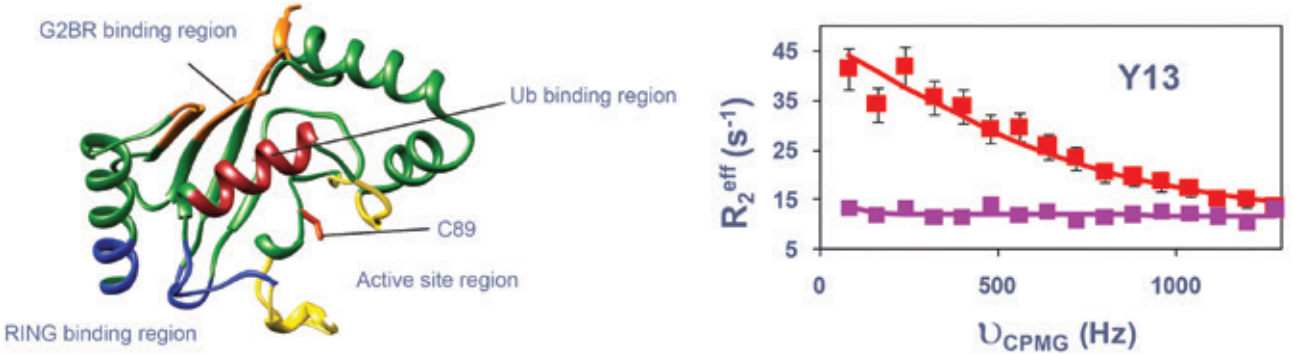
The conjugation of ubiquitin to other cellular proteins regulates a broad range of eukaryotic cell functions including protein degradation, cell cycle regulation, DNA repair, transcription, and endocytosis. We focus on the role of this pathway in two important cellular processes: protein quality control and host-pathogen interactions.

Protein quality control: Despite the aid of chaperones, a significant fraction of newly synthesised proteins ends up misfolded. Cells evolved protein quality control systems to ensure that these potentially toxic species are detected and eliminated. The best characterised of this mechanism is the ER-associated protein degradation (ERAD), which takes care of membrane and secretory proteins that are misfolded in the endoplasmic reticulum (ER). We are interested in investigating how proteins misfold, and how such misfolded proteins are identified, translocated, and ubiquitinated during ERAD.

Host-pathogen interactions: Viruses hijack the host machinery to their own advantage. During infection, several host defense mechanisms are destabilised by the virus using the ubiquitin-proteasome pathway. We study the interactions between viral factors and host proteins to understand this process.

Protein Design: We design proteins to create higher-order structures that may be used to deliver cargos. Our recent work involves designing stable domain swapped proteins.

We regularly use NMR spectroscopy to study structure and dynamics of proteins relevant to the projects. In addition, we employ various other biophysical, biochemical, and computational tools.




***Conformational dynamics in the Ubiquitin E2: Ube2g2 drives its activity.*** *Left panel: The interfaces with co-factors gp78 and Ubiquitin (Ub) are shown on Ube2g2. These regions have conformational dynamics as observed for a typical amino acid (Y13 right side), which indicates that Ube2g2 exists in multiple states. During the ubiquitination reaction, the catalytic 'active' states are selected by co-factors to proceed along the reaction coordinate.*

## SELECT PUBLICATIONS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Sengupta, I., Bhate, S.H., Das, R. and Udgaonkar, J.B., 2017. Salt-mediated oligomerization of the mouse prion protein monitored by real-time NMR. ***Journal of Molecular Biology, 429***(12), pp. 1852-1872.

2.6

**ARATI RAMESH**
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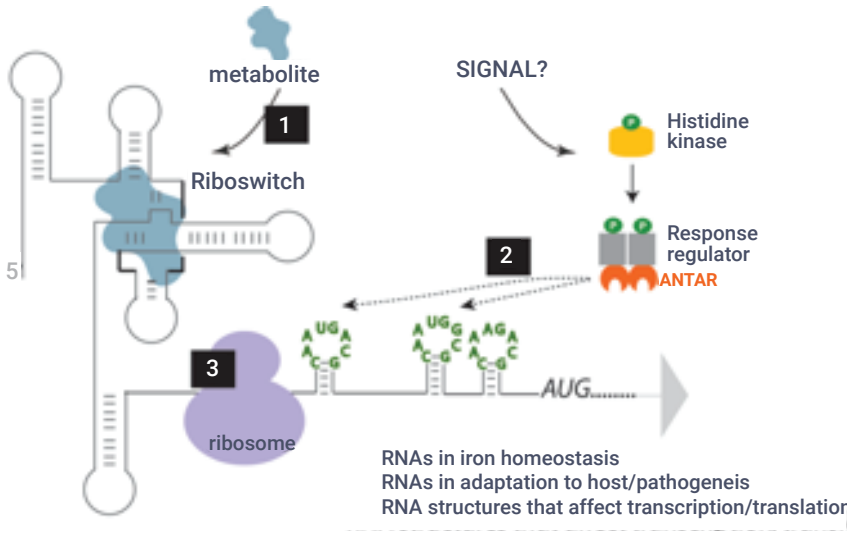
# Structure to Signalling: Insights into Bacterial Biology through RNA Structure

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

**MY LAB'S PROGRAM** addresses three broad areas, centred around RNA structure: 1) Identifying signalling pathways mediated by metaolite-binding riboswitches and protein-RNA complexes, 2) Design of RNA probes for cellular metabolites, and 3) understanding the role of RNA structure in fundamental RNA-driven processes like translation.

One of our efforts is towards identifying non-coding RNAs induced under infection-like conditions, in pathogenic bacteria. We have identified a class of RNAs in mycobacteria, that recruit the signalling ANTAR proteins. Phosphorylation of ANTAR (by a signal-responsive kinase) renders it capable of RNA recognition and control of operons in cis. ANTAR RNAs conserve structure rather than sequence, wherein the conserved structure marks ANTAR regulons for coordinated gene expression. ANTAR RNAs are linked to genes responsible for lipid breakdown across different mycobacteria, suggesting a conserved RNA-mediated response to conserved signals.

Another area of investigation is the role of RNAs in iron homeostasis. We have discovered two RNA families that are iron-responsive. These




***Areas of research in the lab:***

*1. Understanding mechanisms of metabolite sensing by Riboswitches*
*2. Identifying RNA-mediated signalling pathways via RNA-binding proteins*
*3. Understanding mechanisms of transitional and transcriptional control by RNA structures*

are distinct RNA families in terms of their sequence, structure, mode of iron sensing, and how they contribute to iron homeostasis. One family is restricted in its phylogenetic distribution and in the kinds of genesit is linked to, the other is widespread and appears to link iron homeostasis to sulfur metabolism. We are investigating the implications of these RNAs on iron-mediated redox reactions in the cell.

**HONORS AND AWARDS**

SERB-Early Career Research Award 2017

2.7

**ANJANA BADRINARAYANAN**
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# 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 maintenace of genome integrity.

**MY LAB IS** broadly interested in understanding the regulation of DNA damage response and repair in microbial systems *in vivo*. We employ a live-cell imaging-based approach in combination with genetic and molecular biology tools. While we primarily use bacterial systems to address these questions, our recent work has led us to look at asymmetric partitioning of damaged DNA in the context of bacteria as well as mitochondria.

**a. Damage response and cell cycle regulation: Regulation of recovery from DNA damage-induced stress in bacteria**
The aim of this project is to understand how bacterial cells subject to a pulse of DNA damage restore chromosome replication, segregation, and cell division.

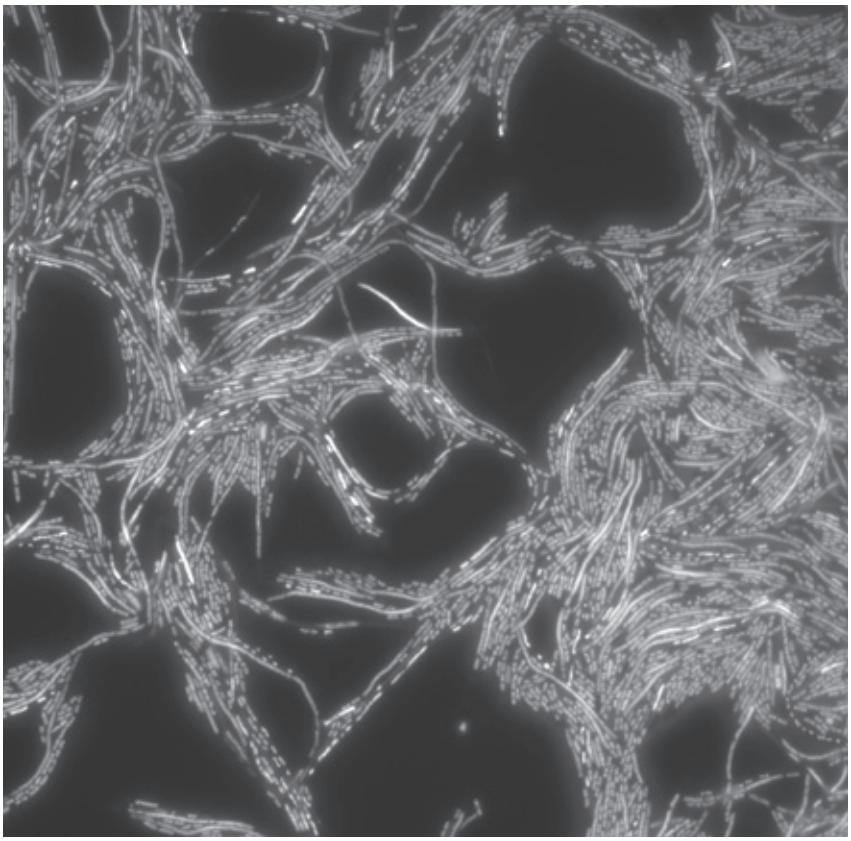
**b. Repair pathway choice: Replisome stability at DNA lesions and regulation of error-prone polymerase activity**
The aim of this project is to understand the mechanism of action and regulation of the translesional (TLS) repair pathway in *Caulobacter* and its impact on replisome stability and fork progression across DNA lesions.

**c. Repair pathway regulation: How are DNA double-strand break (DSB) ends organised during homology search?**

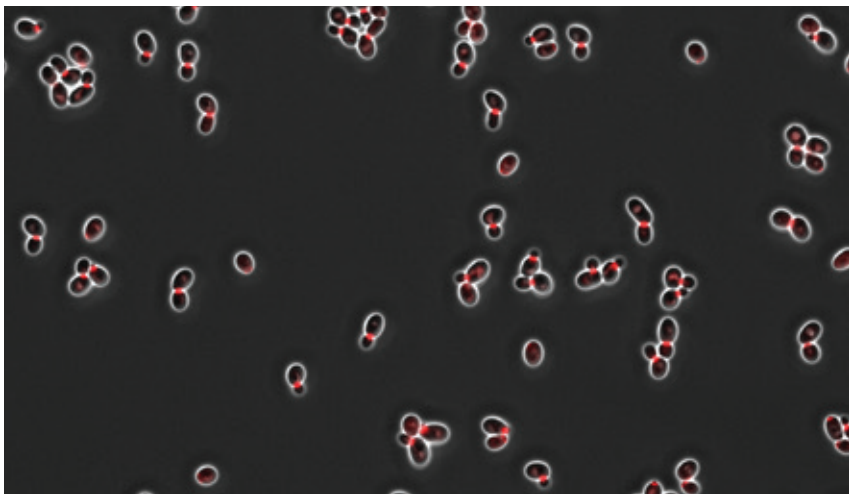
We aim to elucidate the organisation of processed DSB ends to understand how movement of the ends is coordinated for successful homology search and whether RecN plays a role in facilitating the same.

**d. Mitochondrial DNA repair mechanisms: How do cells regulate mitochondrial DNA damage response and repair?**

This is a relatively new area of research in the lab. We are interested in understanding how and when cells choose to repair mitochondrial DNA damage and how DNA copy number is maintained during this process.



***E. coli cells growing in the presence of DNA damaging agent.*** *Chromosome is marked in red using HU-mCherry*



***S. cerevisiae cells with mitochondria marked in red***

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## HONORS AND AWARDS

**Human Frontier of Sciences Career Development Award**

2.8

**VINOTHKUMAR K R**
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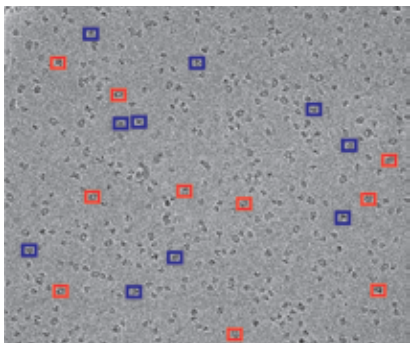
# Membrane Protein Structure and Dynamics

Membranes define a cell and proteins within the membrane mediate a wide range of functions including transport and signalling and are drug targets. Our aim is to elucidate the structure of membrane proteins, including enzymes and ion-channels, and understand how they function.

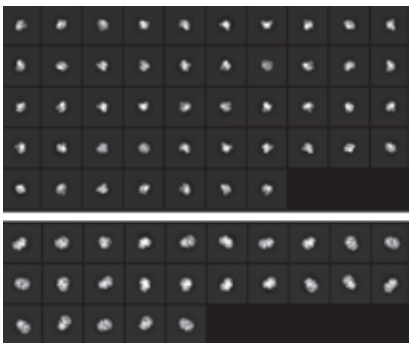
**MY RESEARCH INTEREST** over the years has focused on membrane protein structure and dynamics coupled with electron microscopy. Some of the challenges in membrane protein structural biology include low abundance, difficulty in over-expression of functional material, and stability in detergents. However, these problems can be bypassed by using single-particle cryoEM as this technique does not require the growth of protein crystals, and very little protein is required. Using the recent advances in single-particle cryoEM, cryotomography, and when necessary, X-ray crystallography, I would like to determine the structures and elucidate the function of a range of membrane proteins. My focus would be particularly centred on the rhomboid family of proteins and ion channels from the inner ear, including the whole mechano-transduction apparatus. Since the installation of the Titan Krios in the campus last year, we have managed to obtain many different macromolecular structures. The figure shows one such example—an enzyme involved in bioremediation.

One of the features of this enzyme identified via cryoEM is the dimer-tetramer equilibrium (Figures 1B & C). The high-resolution maps of the enzyme in both these states has allowed us to build a *de-novo* model of the enzyme (Figures 1D & E), identify an iron containing active site, as well as a substrate entry/exit pathway.

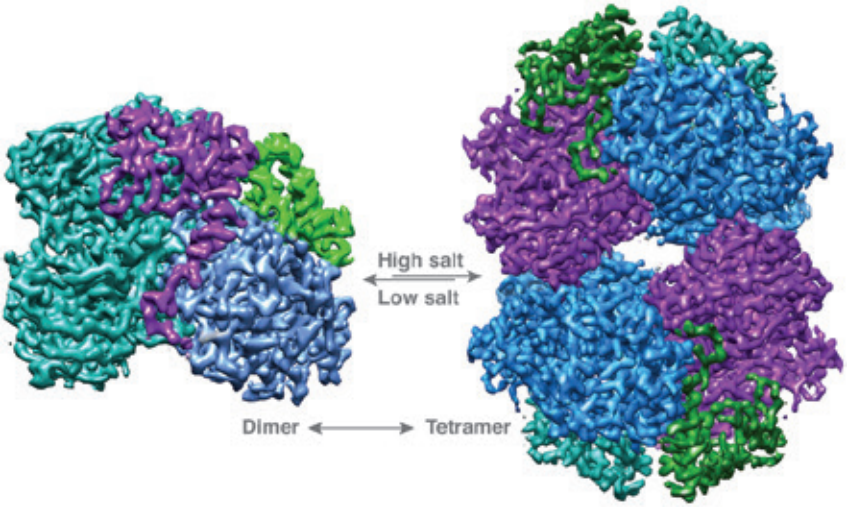


***(A) An electron micrograph of an enzyme, dimethyiformamidase showing two populations marked in red and blue boxes.*** *The enzyme comprises of two polypeptides measuring 85 and 15 kDa.*

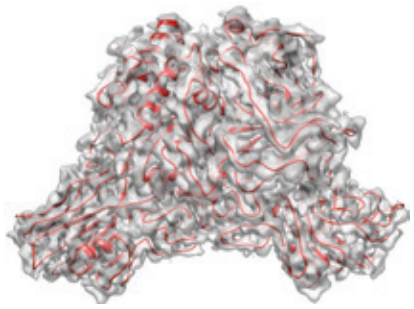
***(B) The 2D class-averages of the particles extracted from blue boxes (top panel) or red boxes (bottom panel) showing dimers (200 kDa) and tetramers (400 kDa).***



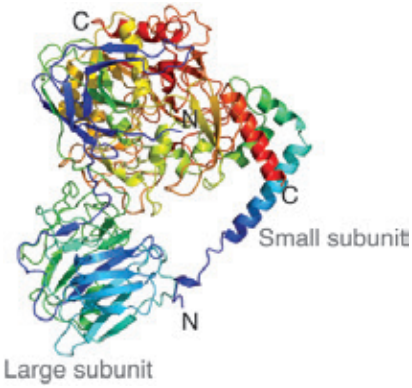
***(C) CryoEM maps of the dimer and tetramer. The nature of the oligomeric state is dependent on salt****. At higher salt concentrations, tetramers are more prevalent, whereas, under no-salt conditions, dimers are more prevalent.*




***(D) The polypeptide trace of the enzyme with the map in gray and the model in red.***



***(E) The fold of the monomer of the enzyme, which shows little resemblance to other structures in the PDB.*** *Both subunits are coloured in rainbow colours with the N-terminus in blue and the C-terminus in red.*

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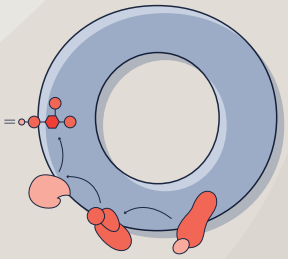
# Cellular Orga and Signa



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

Mechanisms of Membrane Organisation and Endocytosis
SATYAJIT MAYOR

Phosphoinsoitide Signalling in Cell Biology
RAGHU PADINJAT

Biology of Host-Pathogen Interactions during Intracellular Infections
VARADHARAJAN SUNDARAMURTHY

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**SUDHIR KRISHNA**
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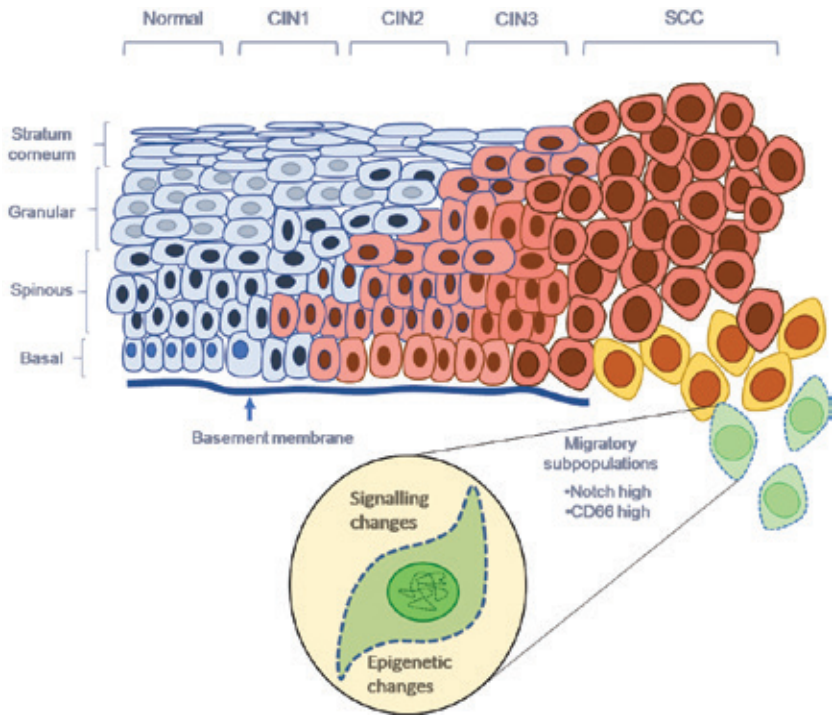
# Understanding Human Cervical Cancer Progression and Building a Biology-Medicine Interphase

Our group has two interests: i) understanding the nature of human cervical cancer progression with a particular focus on Notch signalling in a sub-set of CD66+ cells, and ii) enabling inter-campus biomedical efforts spanning diverse areas such as hematology, HLA platforms, Dengue vaccines, etc.

HUMAN CERVICAL cancers constitute a major burden of female malignancies in our country and are caused by papillomaviruses of the 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 (reviewed in Maliekal T. et. al., Oncogene 2008). Subsequently, we have identified a sub-set of CD66+ cells with distinctive promoting properties that is dependent on Notch signalling (Bajaj J. et al., Cancer Research 2011 and Pattabiraman C. et al., Cancer Research 2014). Ongoing work in the laboratory is also looking at how one can develop therapeutic strategies targeting CD66+ cells. The global genome analysis on human cervical cancer that we have been analysing reassuringly fits a major role for Notch signalling in human cervical cancer progression (in compilation) lending itself to the evolution of therapeutic targeting.

Since 2008, we have been working intensively with the St. John's




***Emergence of migratory populations in cervical cancers and the mechanisms that drive the phenotype***
Calvin Rodrigues et al., personal communication

Medical College campus and built extensive research laboratories, and explored joint teaching programmes with medical colleagues. We have now extended that programme to an international viral genomics effort focusing on Dengue genomics and vaccine development with an East African hub.

## SELECT PUBLICATIONS

Adurthi, S., Kumar, M.M., Vinodkumar, H.S., Mukherjee, G., Krishnamurthy, H., Acharya, K.K., Bafna, U.D., Uma, D.K., Abhishekh, B., Krishna, S., Parchure, A., Murali, A., and Jayshree, R. S. 2017. Oestrogen receptor-α binds the FOXP3 promoter and modulates regulatory T-cell function in human cervical cancer. ***Scientific Reports, 7***(1), p. 17289.

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3.2

**SATYAJIT MAYOR**
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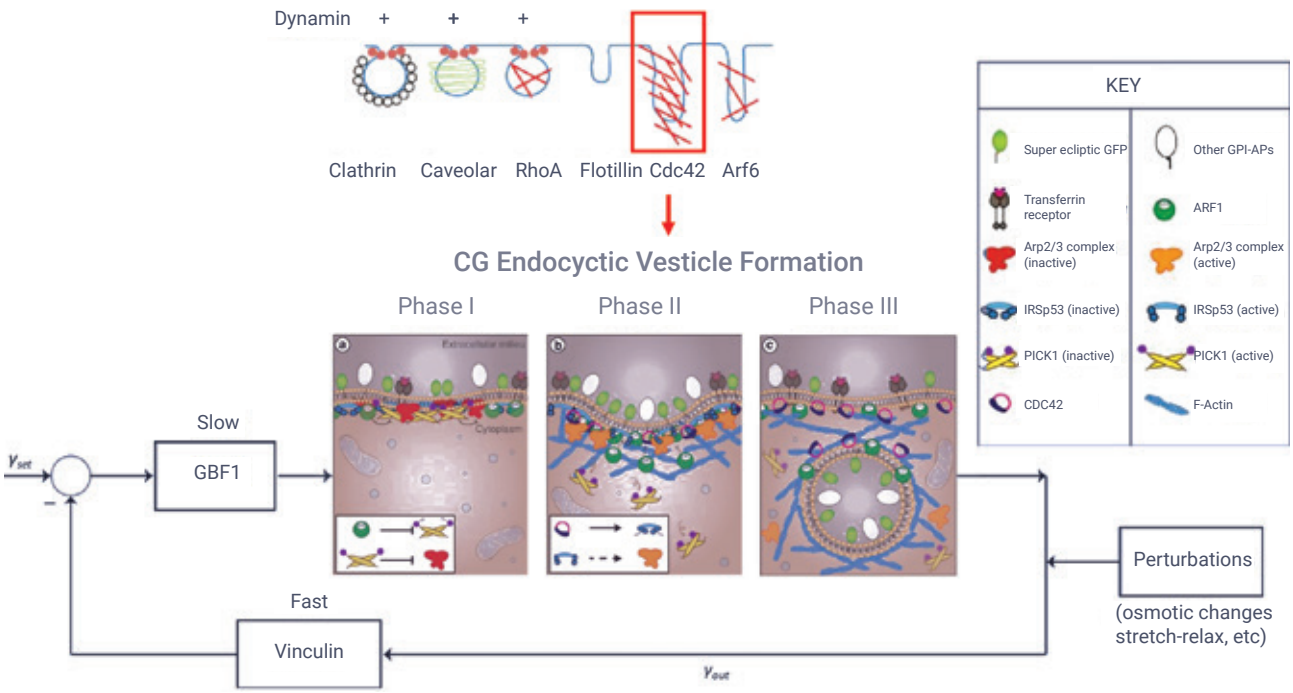
# Mechanisms of Membrane Organisation and Endocytosis

The principal focus of our laboratory is to uncover 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 a lipid bilayer made up of over 1000 different lipid and protein species. It does not merely separate the outside from the inside of a cell, but also mediates bilateral communication.

To understand how the eukaryotic cell responds and reacts to its environment, we study how cells can regulate the local organisation of its membrane constituents, while the membrane itself behaves like a two-dimensional fluid. Insights from a variety of studies, chiefly from our laboratory, show that the loca chemistry of the plasma membranes is finely tuned, and far from an equilibrium mixture.

We propose that the cell membrane behaves as an active actin-membrane composite, wherein underlying dynamic cortical actin filaments actively control the local composition of the plasma membrane. This results in the cell membranes' capacity to construct localised domains of distinct chemical composition. One of the numerous implications from such an understanding of membrane organisation is the ability of the cell to build signalling complexes and sort membrane constituents, in response to external stimuli. This is exemplified by the ability of the family of membrane receptors, the integrin receptors, to locally regulate the membrane in




response to the chemical (ligands) and physical (substrate stiffness) inputs they receive. We utilise observations in living cells at high spatial and temporal resolution, as well as *in-vitro* reconstitutions in artificial membranes to arrive at an understanding of the mechanisms and principles involved.

The cell membrane is also the site for the assembling endocytic machinery, in response to a number of extrinsic and intrinsic cues. To broaden our understanding of membrane homeostasis, we study a particular class of non-canonical endocytic pathways that functions in the absence of both clathrin and dynamin, and how this regulates the developmental programme in the context of a developing wing imaginal disc of *Drosophila*.

Recent work from our laboratory has revealed the spatial and temporal regulation patterns of a set of molecular machineries that are required for endocytic vesicle formation in these pathways (1).

Importantly, this pathway is responsible for the homeostatic control of cell membrane tension, utilising a mechano-chemical feedback mechanism involving a well characterised mechano-transducer called vinculin (2).

***Multiple endocytic pathways operate at the cell surface, and recent work in the laboratory has elucidated the molecular machinery for the functioning of a CDC42-regulated clathrin and dynamin-independent endocytic pathway.*** *This endocytic pathway functions to maintain membrane tension homeostasis via regulation by a mechano-transducer, vinculin.*

## SELECT PUBLICATIONS

Sathe, M., Muthukrishnan, G., Rae, J., Disanza, A., Thattai, M., Scita, G., Parton, R.G. and Mayor, S., 2018. Small GTPases and BAR domain proteins regulate branched actin polymerisation for clathrin and dynamin-independent endocytosis. ***Nature Communications, 9***(1), p. 1835.

Thottacherry, J.J., Kosmalska, A.J., Kumar, A., Vishen, A.S., Elosegui-Artola, A., Pradhan, S., Sharma, S., Singh, P.P., Guadamillas, M.C., Chaudhary, N., Vishwakarma, R., Trepat, X., Del Pozo, M.A., Parton, R.G., Rao, M., Pullarkat, P., Roca-Cusachs, P., and Mayor, S. 2018. Mechanochemical feedback control of dynamin independent endocytosis modulates membrane tension in adherent cells. ***Nature Communications, 9***(1), p. 4217.

3.3

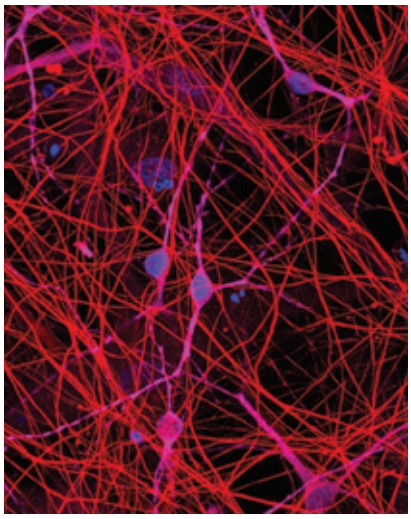
**RAGHU PADINJAT**
*praghu@ncbs.res.in*

# Phosphoinsoitide Signalling in Cell Biology

Chemical messengers based on the lipid phosphatidylinositol are part of an evolutionarily conserved mechanism of cell signalling. These molecules regulate key cell 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 this plays a key role in a number of physiological processes including early embryogenesis, lymphocyte development and function, as well as neuronal activity.

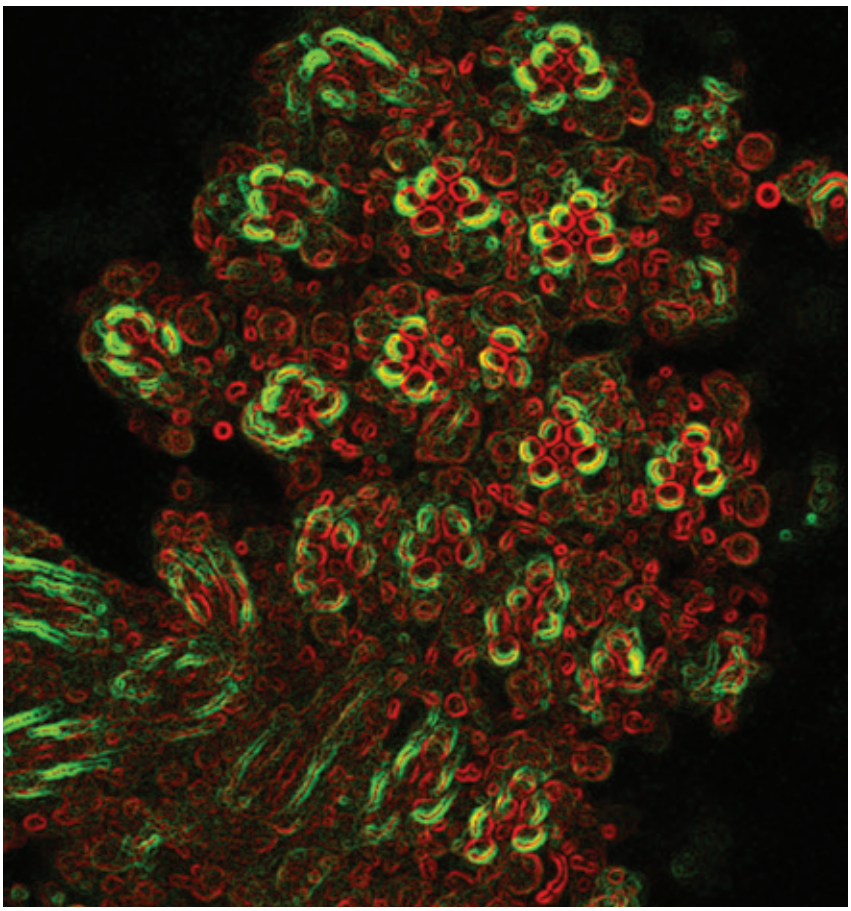
The overall goal of our work is to understand how the architecture of this signalling cascade is designed to optimally deliver physiological outputs. The work is multidisciplinary and done using a combination of *Drosophila* and human disease models. Over the last year we have uncovered the function 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



***Neurons and neural network:*** *Day 60 neurons differentiated from neural stem cells costained with the neuronal markers neurofilament (red) and MAP2 (magenta), and counterstained with DAPI (blue)*

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.



***Visualising membrane contact sites in Drosophila photoreceptors:*** *Confocal image showing close apposition of plasma membrane (Phalloidin) and sub-microvillar cisternae (RDGB).*

**SELECT PUBLICATIONS**


Yadav, S., Thakur, R., Georgiev, P., Deivasigamani, S., Krishnan, H., Ratnaparkhi, G. and Raghu, P., 2018. RDGBα localization and function at membrane contact sites is regulated by FFAT–VAP interactions. ***Journal of Cell Science, 131***(1), p. jcs207985.

Viswanath, B., Rao, N.P., Narayanaswamy, J.C., Sivakumar, P.T., Kandasamy, A., Kesavan, M., Mehta, U.M., Venkatasubramanian, G., John, J.P., Mukherjee, O., Purushottam, M., Kannan, R., Mehta, B., Kandavel, T., Binukumar, B., Saini, J., Jayarajan, D., Shyamsundar, A., Moirangthem, S., Kumar, K.G.V., Thirthalli, J., Chandra, P.S., Gangadhar, B.N., Murthy, P., Panicker, M.M., Bhalla, U.S., Chattarji, S., Benegal, V., Varghese, M., Reddy, J.Y.C., Raghu, P., Rao, M., and Jain, S. 2018. Discovery biology of neuropsychiatric syndromes (DBNS): a center for integrating clinical medicine and basic science. *BMC Psychiatry, 18*(1), p. 106.

3.4

**VARADHARAJAN SUNDARAMURTHY**
*varadha@ncbs.res.in*

# The Biology of Host-Pathogen Interactions during Intracellular Infections

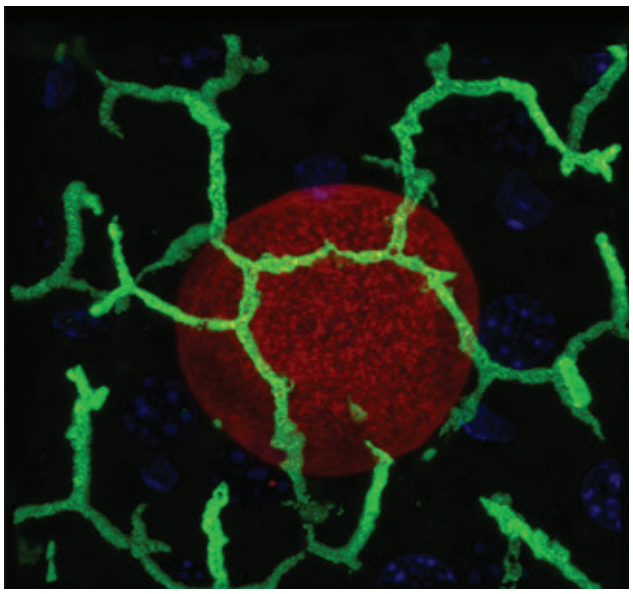
The broad goal of our lab is to understand the interactions of intracellular pathogens with host cells, with particular interest in the modulation of host trafficking pathways. We combine cell biological methods, high content imaging, and computational approaches, along with conventional cell and molecular 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, *M. tuberculosis* that causes tuberculosis and the liver stage of *Plasmodium* spp, that causes malaria.

The 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 of the two pathogens with the host systems at molecular, cellular, and tissue levels.

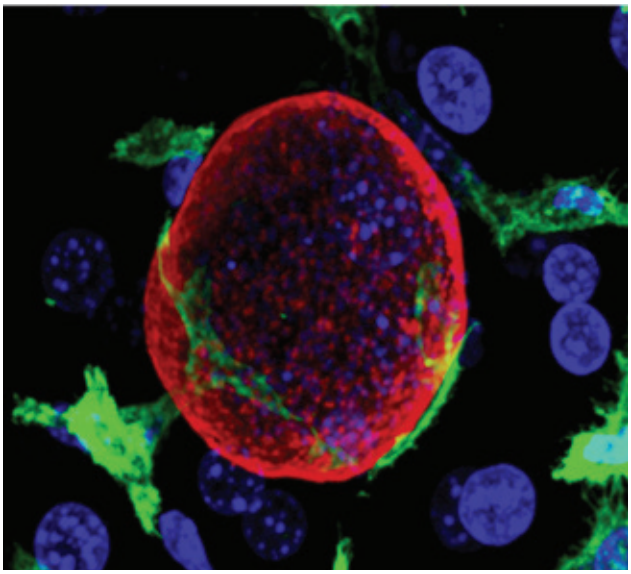
Recent results show that both pathogens cause global alterations in the organisation and dynamics of the host cell enodcytic network. These alterations include sub-cellular redistribution of specific endosomal pools and an increase in the number and content of distinct endosomal populations, specifically in the infected cells. 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.

Alternatively, modifying the endolysosomal pathways in differ-



*Malarial parasite (red) surrounded by the host bile canalicular network*

*Host macrophages (green) surround the giant Plasmodium containing vacuole (red) during liver stage development*



ent ways results in elevated levels of pathogens in the cells. The results show extensive re-wiring of host endocytosis machinery during intracellular pathogenesis and suggest that this pathway plays a crucial role in maintaining the homeostasis of an infected cell. These results provide further support for host-directed therapeutics against infectious diseases.

**SELECT PUBLICATIONS**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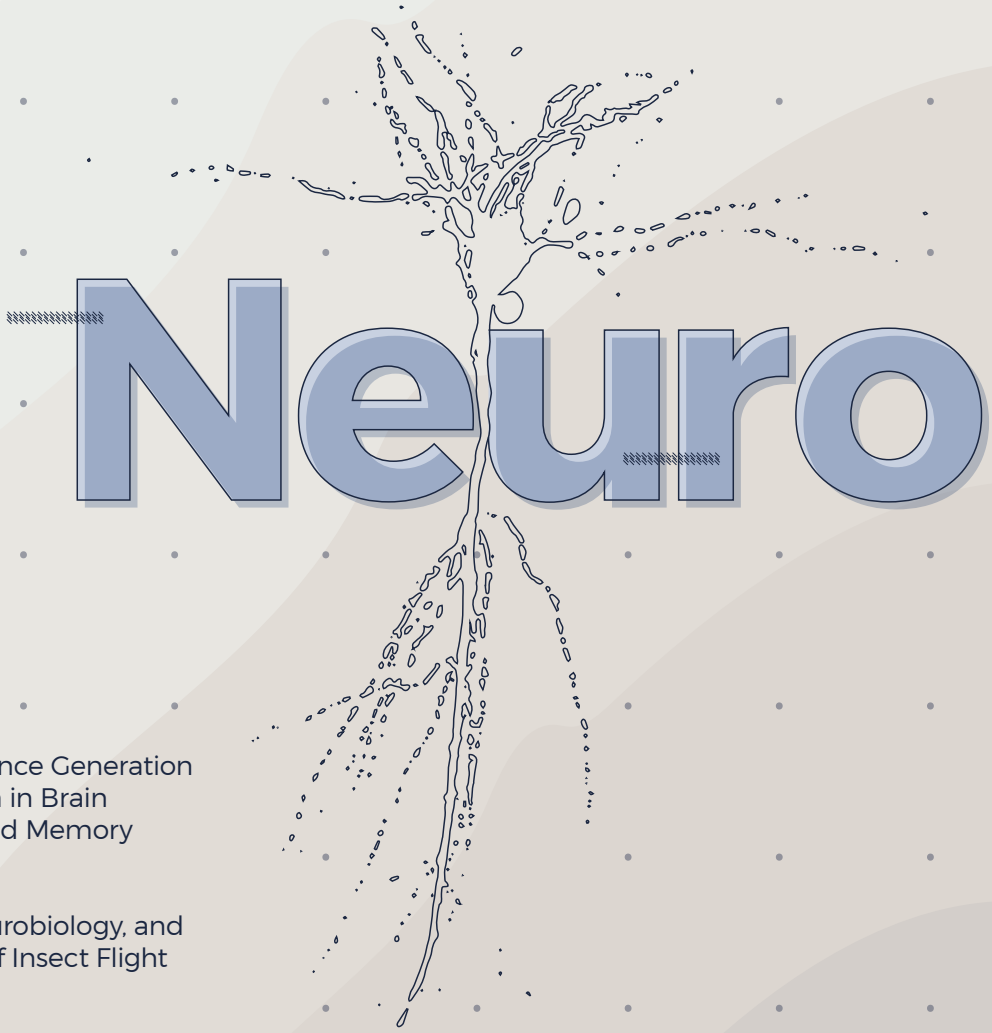
Sundaramurthy, V., Korf, H., Singla, A., Scherr, N., Nguyen, L., Ferrari, G., Landmann, R., Huygen, K. and Pieters, J., 2017. Survival of *Mycobacterium tuberculosis* and *Mycobacterium bovis* BCG in lysosomes *in vivo*. ***Microbes and Infection, 19***(11), pp. 515-526.

# Neuro



# biology

4

4.1

**UPINDER S BHALLA**
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# Neuronal Sequence Generation and Recognition in Brain Computation and Memory

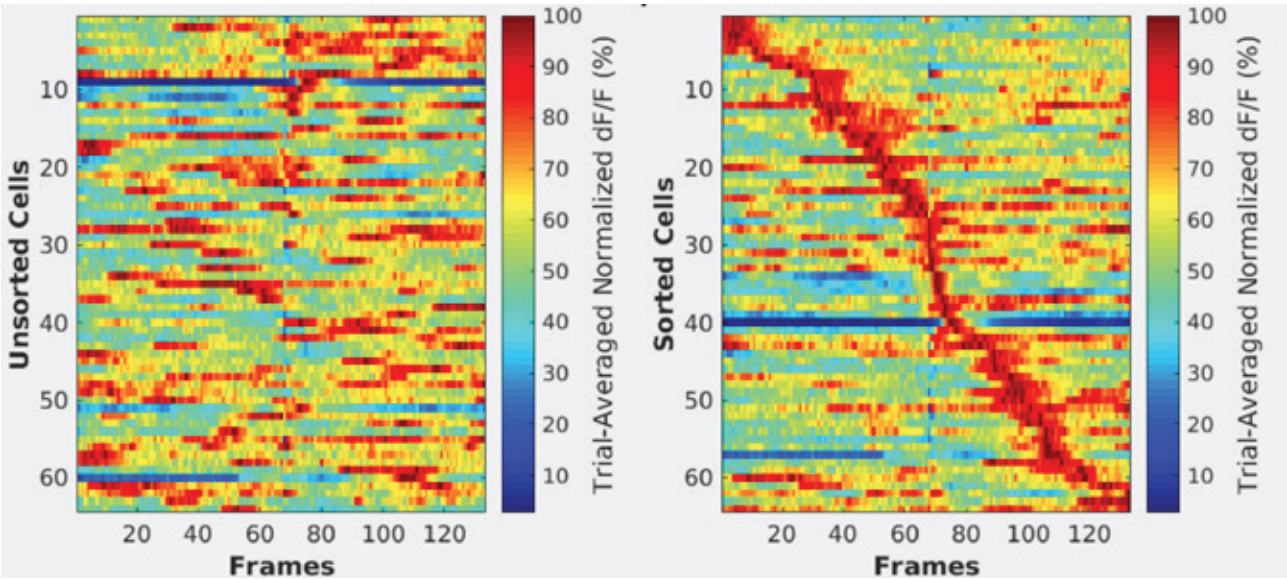
Speech, music, motion, and thought all involve sequential activity of ensembles of neurons. We use optical and electrical recordings *in vivo*, and *in vitro*, and multiscale computer models to understand sequence recognition and memory as fundamental computations in the brain.

*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.

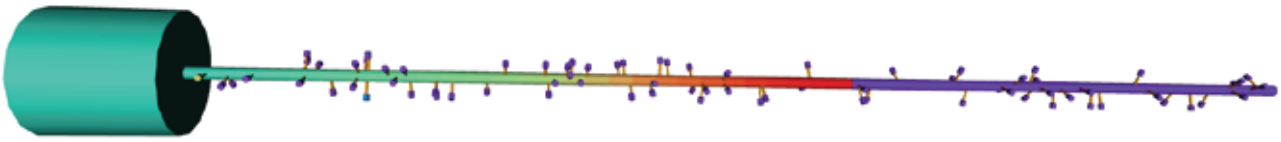
*In vitro*, we use optogenetics to deliver precise patterned stimuli to the hippocampal network. We perform single-cell patch recordings to study complex summation and the encoding of neuronal computation through amplitude and timing. We also use optogenetic patterned inputs to analyse how sequences can be discriminated by single cells.

We have developed a multiscale simulator, MOOSE, to model brain functions across scales. It is part of a framework for closely linking models to experiments (FINDSIM) that we use to develop a comprehensive model of cellular signalling in health and disease. We use our own and collaborator data to compare cellular responses between healthy and fragile-X mouse neurons. We also use MOOSE to model subcellular computations underlying sequence discrimination and memory.

We combine all these modelling and experimental threads into network models of brain sequence computation.




***Brain activity sequence formation during learning.*** *Many cells are monitored using 2-photon imaging, and when they are ordered by activity peak we see emergence of peaks of activity that span the entire duration of the trial (~10 seconds). Note that the associative learning happens in a short window around frame 70.*



***Ball-and-stick model of a neuron decorated with synaptic spines that support biochemical computations leading to sequence selectivity.***

## SELECT PUBLICATIONS

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Viswan, N.A., HarshaRani, G.V., Stefan, M.I. and Bhalla, U.S., 2018. FindSim: A framework for integrating neuronal data and signaling models. ***Frontiers in Neuroinformatics, 12.***

## HONORS AND AWARDS

**Infosys Prize for the Life Sciences 2018**

4.2

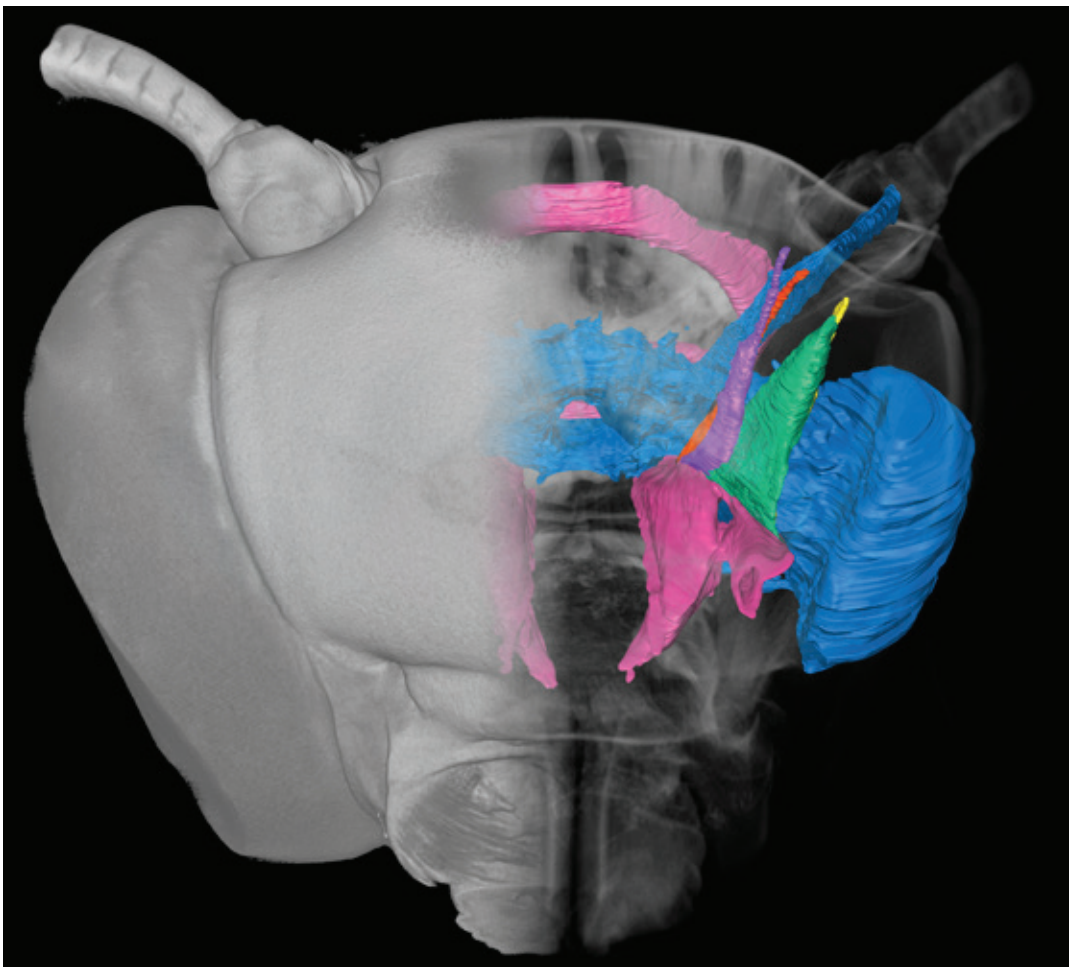
**SANJAY P SANE**
*sane@ncbs.res.in*

# 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 manoeuvres, 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. The spectacular evolutionary success of insects owes to the fact that they 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 manoeuvrability. 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 thermosensory organs and communicated to the central nervous system, which generates appropriate motor responses in the form of movement of head, legs, and wings. 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.



***A frontal view of the head of a hawk-moth and its internal structures which include the brain (blue), antennal muscles (purple, orange, yellow, and green), and the tentorium (pink).*** *We have extensively explored the structure and function of antennal sensory inputs and their influence on antennomotor outputs, and on flight.*

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

## SELECT PUBLICATIONS


Sant, H.H. and Sane, S.P., 2018. The mechanosensory-motor apparatus of antennae in the oleander hawk moth (*Daphnis nerii*, Lepidoptera). ***Journal of Comparative Neurology, 526***(14), pp. 2215-2230.

Saxena, N., Natesan, D. and Sane, S.P., 2018. Odor source localization in complex visual environments by fruit flies. ***Journal of Experimental Biology, 221***(2), p. jeb172023.


## HONORS AND AWARDS

**Fellow of the Indian Academy of Sciences (2018)**

4.3

**SUMANTRA CHATTARJI**
*shona@ncbs.res.in*

# 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 behavioral 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 behavioral, morphometric, molecular, and electrophysiological techniques to analyse stress-induced modulation of neuronal structure and function in the amygdala.

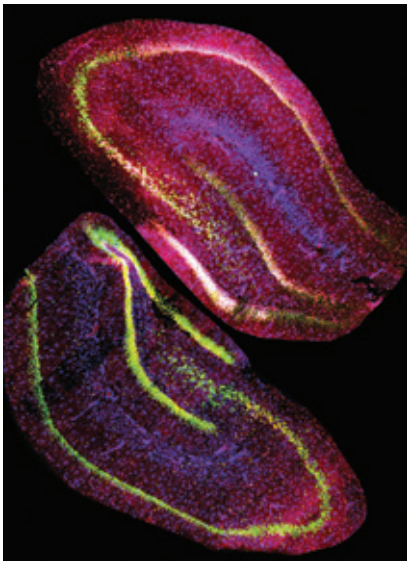
We have identified unique features of stress-induced plasticity in the amygdala, which are strikingly different from those seen in the hippocampus, and could have long-term consequences for behavioral symptoms seen in affective disorders.

In earlier studies, stress-induced plasticity in different brain regions was viewed as a stand-alone effect manifested as a property intrinsic to individual structures. Further, function was inferred from analysis


***The effects of chronic stress on extinction recall depend on whether the fear memory was formed before or after stress*** (Rahman et al., eLife, 2018). *(a) In control animals, fear conditioning enhances freezing, which is subsequently reduced by extinction. This is accompanied by, first an increase and then a reduction, in theta activity in both the basolateral amygdala (BLA) and dorsal medial prefrontal cortex (dmPFC). Also, stronger dmPFC-BLA theta synchrony and dmPFC-to-BLA directional influence is seen during fear and extinction recall. Thus, the direction of changes in freezing are mirrored by in vivo electrophysiological changes in both the BLA and mPFC (indicated by *), although 10 days after conditioning, fear expression no longer depends on BLA activity.*

*(b) When fear memories were formed before exposure to chronic stress, recall of fear extinction was not affected. Although theta activity in the BLA exhibited a persistent increase, its bidirectional regulation was normal in the mPFC. Stress also disrupted mPFC-BLA theta-frequency synchrony and directional coupling. However, fear memories formed 10 days before no longer depend on BLA activity. Consequently, the expression of fear after extinction reflects normal regulation of theta activity in the mPFC (*), not theta hyperactivity in the BLA.*

***The nature of the translational response to stress in neurons remains largely unexplored.*** *Even less is known about how glia are affected. Using a click-chemistry-based method to label the de novo proteome in live brain slices, we found that a brief stressor causes an immediate upregulation of protein synthesis in both amygdalar and hippocampal neurons and astrocytes. However, these two areas eventually exhibit opposite temporal profiles of protein expression well after the end of stress (Madan & Gupta et al., Hippocampus, 2018). This image shows enhanced neuronal and astrocytic protein synthesis in hippocampal slices from stressed (top) and unstressed (bottom) rats.*



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.

## SELECT PUBLICATIONS

Rahman, M.M., Shukla, A. and Chattarji, S., 2018. Extinction recall of fear memories formed before stress is not affected despite higher theta activity in the amygdala. ***eLife, 7***, p. e35450.

Rahman, M.M., Kedia, S., Fernandes, G. and Chattarji, S., 2017. Activation of the same mGluR5 receptors in the amygdala causes divergent effects on specific versus indiscriminate fear. ***eLife, 6***, p. e25665.

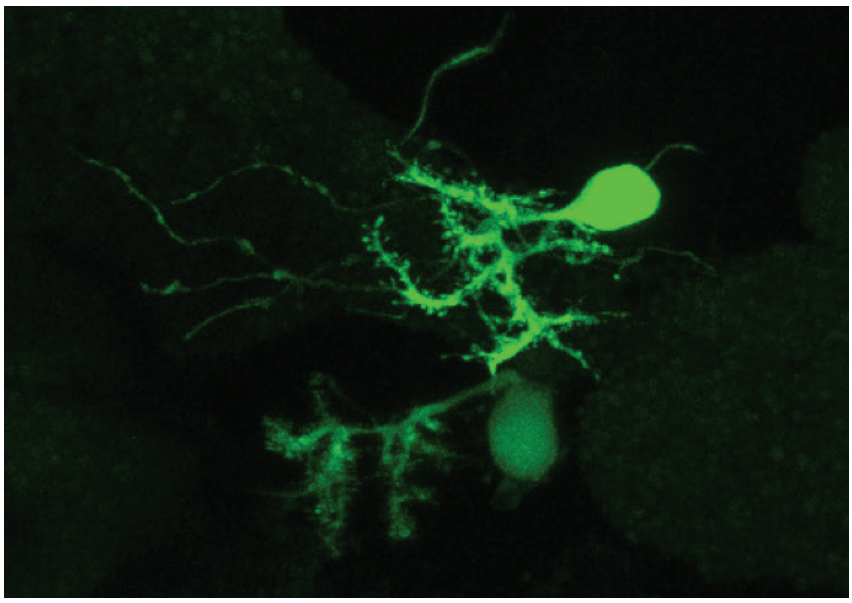
4.4

**VATSALA THIRUMALAI**
*vatsala@ncbs.res.in*

# Development, Modulation, and Function of Motor Systems

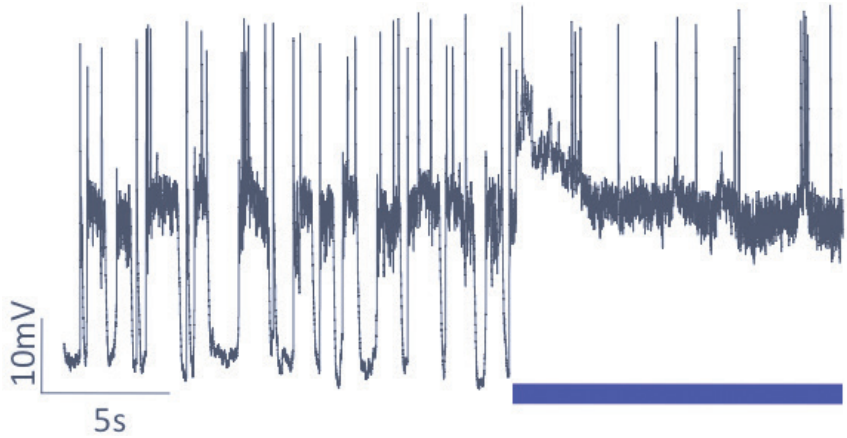
In vertebrates, locomotion is generated by multiple circuits in the brain and spinal cord acting in a co-ordinated fashion. We study how these circuits assemble and how they function at all stages of life.

**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 fresh water 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. 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 synaptic information transfer and neuromodulation of this circuit.



***Purkinje neurons in larval zebrafish.*** *The Ca8 enhancer is used to target fluorescent calcium-sensitive and optogenetic proteins to single or groups of Purkinje neurons.*

***Whole-cell patch clamp recording from a Purkinje neuron expressing Channelrhodopsin-2.*** *Blue light stimulation (indicated by the blue bar) depolarises the neuron and switches it to the up state.*




## SELECT PUBLICATIONS

Kondrychyn, I., Robra, L. and Thirumalai, V., 2017. Transcriptional complexity and distinct expression patterns of auts2 paralogs in *Danio rerio*. ***G3: Genes, Genomes, Genetics***, pp. g3-117.

Jabeen, S. and Thirumalai, V., 2018. The interplay between electrical and chemical synaptogenesis. ***Journal of Neurophysiology, 120***(4), pp. 1914-1922.

## HONORS AND AWARDS

**Wellcome Trust DBT India Alliance Senior Fellowship,** awarded in November 2017

**Board of Reviewing Editors, eLife** (since November 2017)

4.5

**HIYAA GHOSH**
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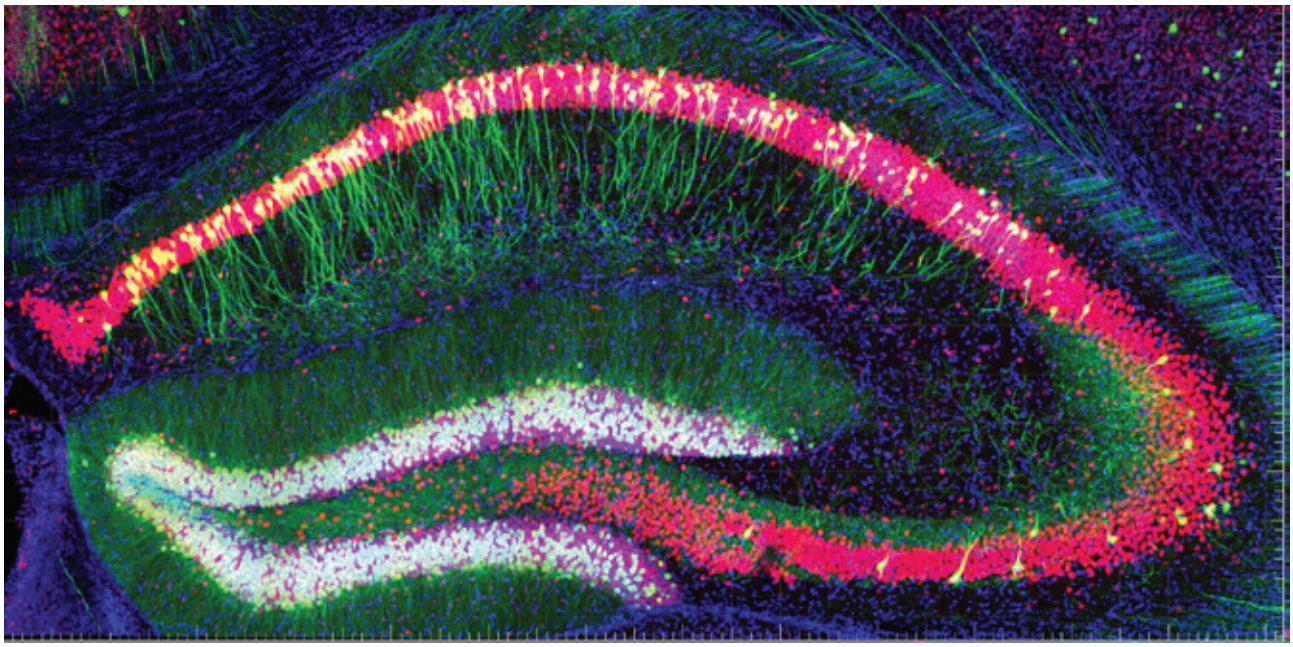
# Molecular Regulations of Cellular Functions in the Brain

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

**WHAT UNDERLIES** the longevity of neurons, which happen to be one of the most elaborate and long-living cell type of our body, yet have little capacity for regeneration or repair?

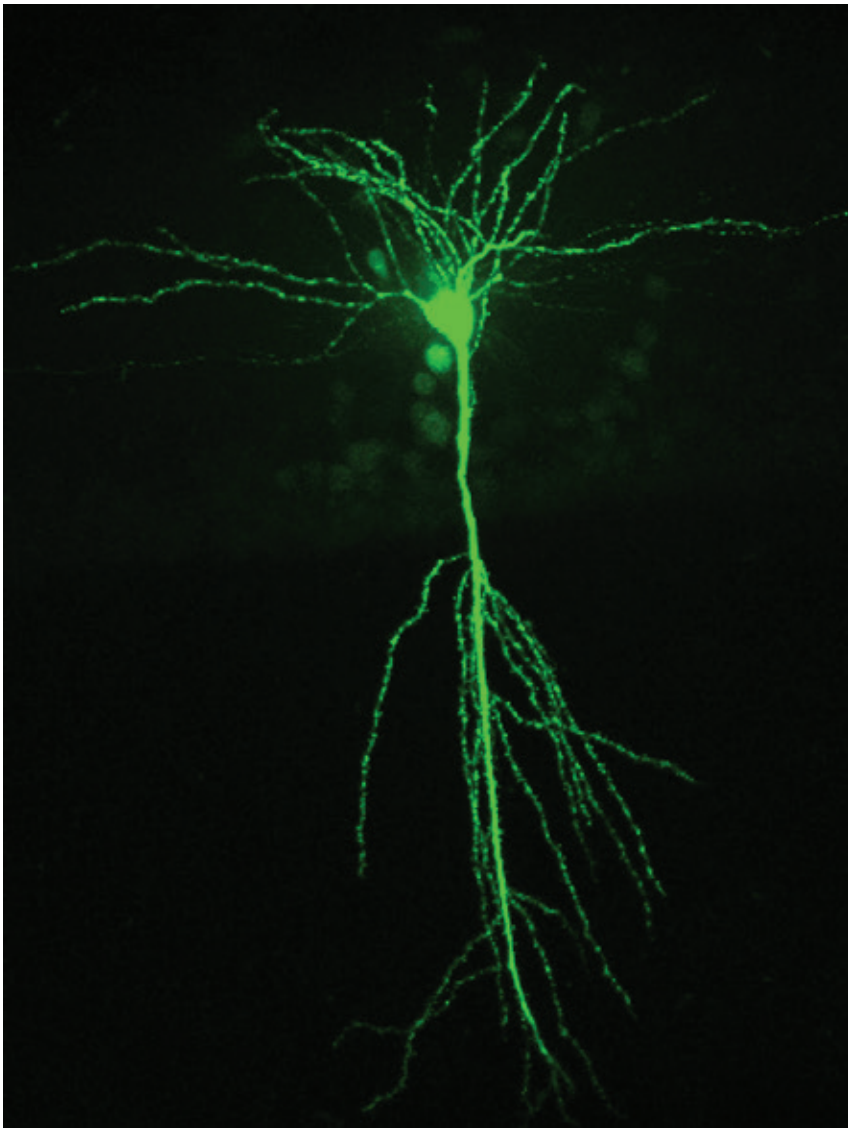
While majorly post-mitotic, the adult brain does retain capacity for new neuron generation; a process termed as “adult neurogenesis”. What determines the fate and potential plasticity of the adult neural stem cells during adult neurogenesis? These are questions related to the molecular regulation of cell-intrinsic processes that, on the one hand, influence the individual cellular outcome, but on the other hand, also potentially instruct intercellular interactions. Studies in my lab are directed towards understanding the genetic programme that underlie cell intrinsic processes and inter-cellular interactions governing adult brain functioning.

Using the mouse as our model organism, we employ transgenic models for specific spatial and temporal deletion of genes, fate-mapping, high-resolution microscopy, high throughput sequencing, morphometric, biochemical, and behavioural studies to investigate molecular regulations in the old and new neurons, and microglia in the adult brain. The overall goal is to gain insights into the homeostatic processes in the healthy brain, in order to be able to better correlate conditions of impaired functionalities to specific cellular processes.

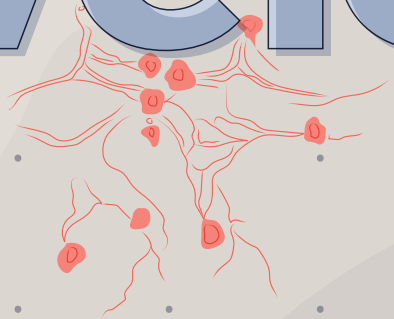


***The adult mouse brain hippocampus:*** *Sparsely labelled neurons from a GFP-reporter mouse*

***Pyramidal neuron from the adult mouse brain hippocampus, individually dye-filled for morphometric tracing***



# Gen a Develo



Development of Neural Circuits and Muscles and the Emergence of Behaviour
K VIJAYRAGHAVAN

Calcium Signalling Regulates Gene Expression Changes during Neural Circuit Maturation
GAITI HASAN

Epigenetics and Small Silencing RNAs
P V SHIVAPRASAD

Development and Morpho-genesis of the Inner Ear
RAJ LADHER

Chromatin Dynamics in Gene Regulation
DIMPLE NOTANI

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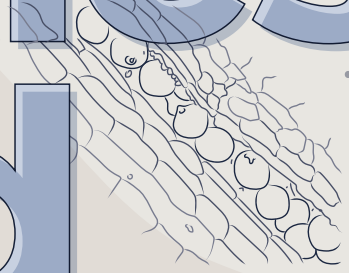

5

5.1

**K VIJAYRAGHAVAN**
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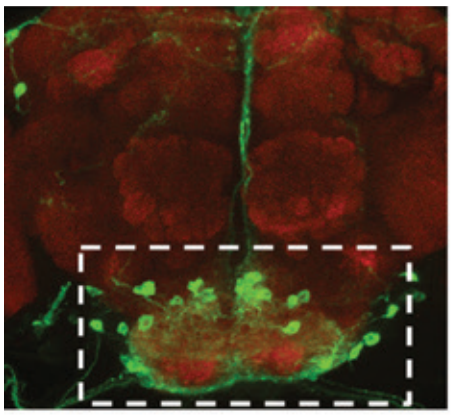
# Development of Neural Circuits and Muscles and the Emergence of Behaviour

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*.

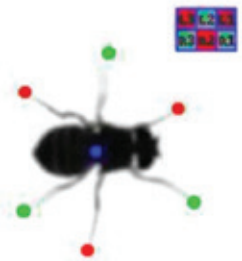
**WE ASK HOW** the nervous system processes information and affects bodily movements. The nervous system and musculature are two modalities intertwined in this process. We have uncovered cellular and molecular effectors crucial to development and function in both modalities. We employ the technical facilities in *Drosophila* to address these questions definitively.

We recently identified a single pair of neurons that prevent the extension of the proboscis in response to bitter taste. In collaboration with Mani Ramaswami's group, we dissected the role of Atxin-2 domains that influence ribonucleoprotein granule assembly; that they are required for long term memory. We are also trying to investigate the role of ribonucleoprotein granule clearance through proteostatic pathways in memory formation.

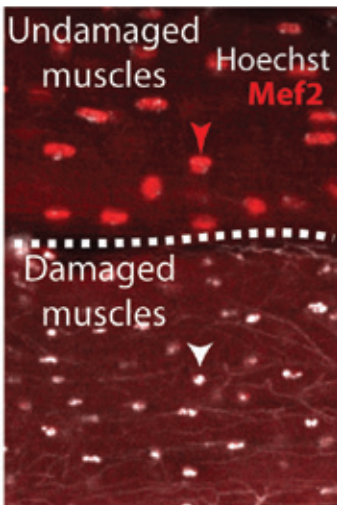
The lab has developed methods to accurately measure *Drosophila* movement, which is downstream of neural processing. Through them, we have uncovered the role of GABAergic neurons in coordinating leg movement. Further refinements to these methods can discern subtle changes in locomotion of *Drosophila* neurodegenerative disease models.



Neurons controlling proboscis extension



Accurately measuring *Drosophila* walking




Fundamental questions about musculature are being addressed. We have uncovered that internal muscle architecture is governed by cues from motor neurons. We are asking how thousands of nuclei in each muscle cell coordinate muscle homeostasis. In addition, we are investigating muscle repair through a resident stem cell population and what neural and mechanical cues affect their function.

Taken together, significant strides are being made in building an integrated picture of neural and muscle function.

## SELECT PUBLICATIONS

Bohra, A.A., Kallman, B.R., Reichert, H. and VijayRaghavan, K., 2018. Identification of a single pair of interneurons for bitter taste processing in the *Drosophila* brain. ***Current Biology, 28***(6), pp. 847-858.

Gowda, S.B., Paranjpe, P.D., Reddy, O.V., Thiagarajan, D., Palliyil, S., Reichert, H. and VijayRaghavan, K., 2018. GABAergic inhibition of leg motoneurons is required for normal walking behavior in freely moving *Drosophila*. ***Proceedings of the National Academy of Sciences, 115***(9), pp. E2115-E2124.

5.2

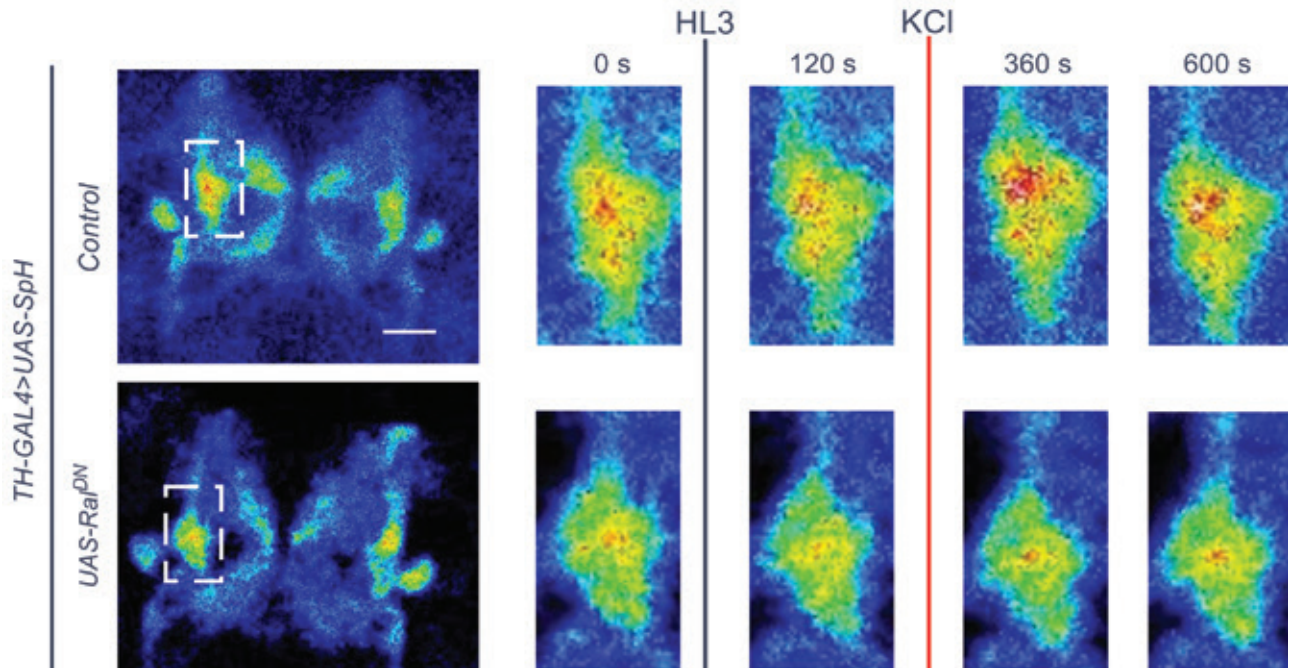
**GAITI HASAN**
*gaiti@ncbs.res.in*

# Calcium Signalling Regulates Gene Expression Changes During Neural Circuit Maturation

In *Drosophila*, intracellular $Ca^{2+}$ signalling by the inositol 1, 4, 5-trisphosphate receptor and store-operated calcium entry (SOCE) regulates the formation and function of motor circuits that control flight. Through a global screen for SOCE-regulated changes in gene expression, we have discovered that synaptic function in the maturing flight circuit requires the small GTPase Ral.

**CELLULAR EVENTS** are often mediated by spikes of cytoplasmic calcium, which either enter the cell from the external milieu, or are released from internal stores.

My group studies intracellular $Ca^{2+}$ release in response to the second messenger Inositol 1, 4, 5-triphosphate and its role in neuronal physiology. In *Drosophila*, intracellular $Ca^{2+}$ signalling by the inositol1, 4, 5-trisphosphate receptor (InsP3R) followed by dSTIM/dOrai-mediated store-operated calcium entry (SOCE) regulate the formation and function of the flight neural circuit. In the past year, we have investigated downstream mechanisms that are altered upon reduced intracellular calcium signalling. We show that intracellular calcium signalling regulates gene expression in flight circuit neurons at the time of synapse formation and maturation. One of the SOCE-regulated genes, Ral, is required for synaptic release during neural circuit formation. These findings are significant in suggesting possible means of therapeutic intervention for human diseases such as Spino-cerebellar ataxias and Parkinson's syndrome, where the InsP3R and SOCE are thought to play a causative role.




***Loss of synaptic vesicle release is observed in dopaminergic neurons (TH-GAL4) of the Drosophila brain upon expression of Ral$^{DN}$, a dominant-negative mutant form of Ral.*** *Synaptic release was measured by change in fluorescence (more red) of Synapto-Phluorin (SpH) by delivering a de-polarising stimulus of KCl after 120s. Panels on the left are images of the Drosophila central brain and panels on the right are high-magnification images from boxed regions in the left image.*

## SELECT PUBLICATIONS

Richhariya, S., Jayakumar, S., Abruzzi, K., Rosbash, M. and Hasan, G., 2017. A pupal transcriptomic screen identifies Ral as a target of store-operated calcium entry in *Drosophila* neurons. ***Scientific Reports, 7***, p. 42586.

Richhariya, S., Jayakumar, S., Sukumar, S.K. and Hasan, G., 2018. dSTIM and Ral/Exocyst mediated synaptic release from pupal dopaminergic neurons sustains *Drosophila* flight. ***eNeuro***, pp. ENEURO-0455.

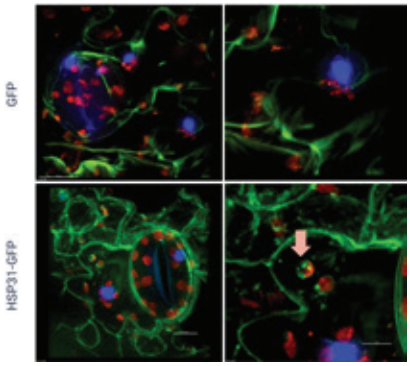
5.3

**P V SHIVAPRASAD**
*shivaprasad@ncbs.res.in*

# Epigenetics and Small Silencing RNAs

A number of epigenetic regulatory layers are superimposed on the genome. In plants, small RNA regulators play a major role in the establishment and maintenance of epigenetic marks. We are interested in understanding the mechanisms of small RNA biogenesis, their functions, and their role in epigenetics.

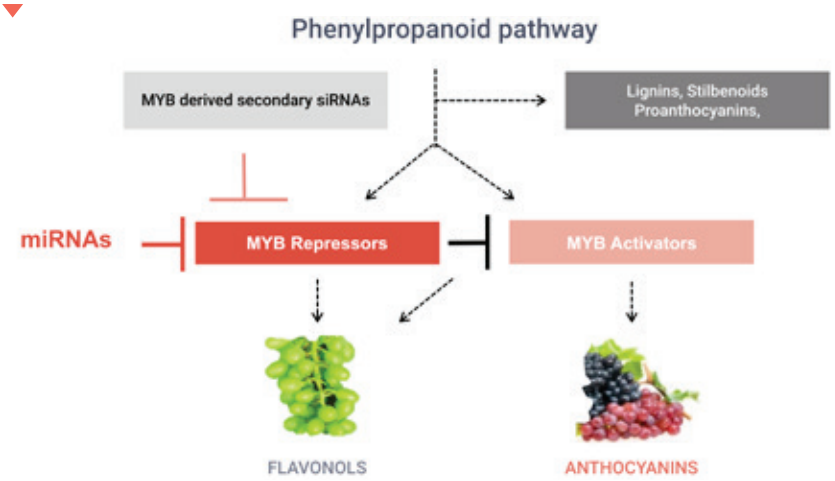
**PLANT SMALL (S)RNAs** are processed from stem-loop structures containing precursor RNAs, or from completely complementary dsRNA substrates by Dicer-like (DCL) proteins. sRNAs of Micro(mi)RNA class are produced from structured precursors by DCL1 with the help of dsRNA binding partners. It is not known what determines biogenesis and abundance of sRNAs and miRNAs, beyond a ubiquitous requirement for a stem-loop or a dsRNA structure. We have previously shown that miRNA-miRNA* loop length determines the abundance of miRNAs (Jagtap and Shivaprasad, 2014). In addition, we have observed unusually high GC content and specific sequence signatures among plant miRNAs. A specific GC signature is maintained across plant miRNAs by having position specificity for G or C. We show that RNA binding domain 1 of HYL1, a dsRNA partner of DCL1, is responsible for the observed GC signature among miRNAs. In support of this observation, hyl1 mutants lack precise processing abilities and accumulate miRNAs at much lower levels (Anushree et al., under revision). Using rice as a model system, we have also identified how dsRNAs are generated from genomic repeats by a novel clade of plant-specific polymerases. Using grapes, *Arabidopsis*, tobacco, and rice as model systems, we have identified

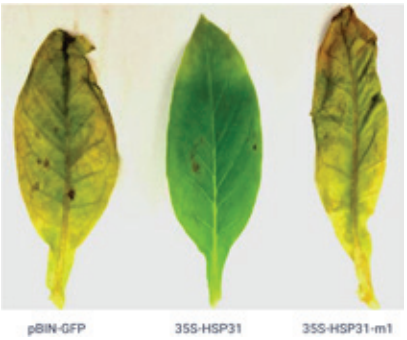



***Mitochondrial targeting of HSP31, a PARK7 homolog, is required to prevent cell death.*** *Upon treatment with 5mM $H_2O_2$, HSP31 relocalises to mitochondria to initiate cytoprotection through its methylglyoxalase activity (from Prasad et al., 2017). Arrow indicates localisation of HSP31 in mitochondria.*

***Engineering grapes for production of specific anthocyanins and flavonols***

***Regulation of phenylpropanaoid pathway by plant miRNAs. miRNAs regulate MYB transcription factors to control anthocyanin and flavonol biosynthesis.***




***Transgenic plants expressing HSP31 are resistant to fungal infection.*** (Prasad et al., 2017)

that plant miRNAs also regulate plant secondary metabolic processes that produce important metabolites such as anthocyanins, lignins, and flavonols.


***VvMYB114 is a repressor of anthocyanins and promoter of flavonol biosynthesis.***

## SELECT PUBLICATIONS

Melvin, P., Bankapalli, K., D'Silva, P. and Shivaprasad, P.V., 2017. Methylglyoxal detoxification by a DJ-1 family protein provides dual abiotic and biotic stress tolerance in transgenic plants. ***Plant Molecular Biology, 94***(4-5), pp. 381-397.

Das, S., Hegde, A. and Shivaprasad, P.V., 2018. Molecular characterization of a new begomovirus infecting *Synedrella nodiflora* in South India. ***Archives of Virology***, pp. 1-4.

## HONORS AND AWARDS

**Special Issue Editor,** Front Plant Sci. 2018

5.4

**RAJ LADHER**
*rajladher@ncbs.res.in*

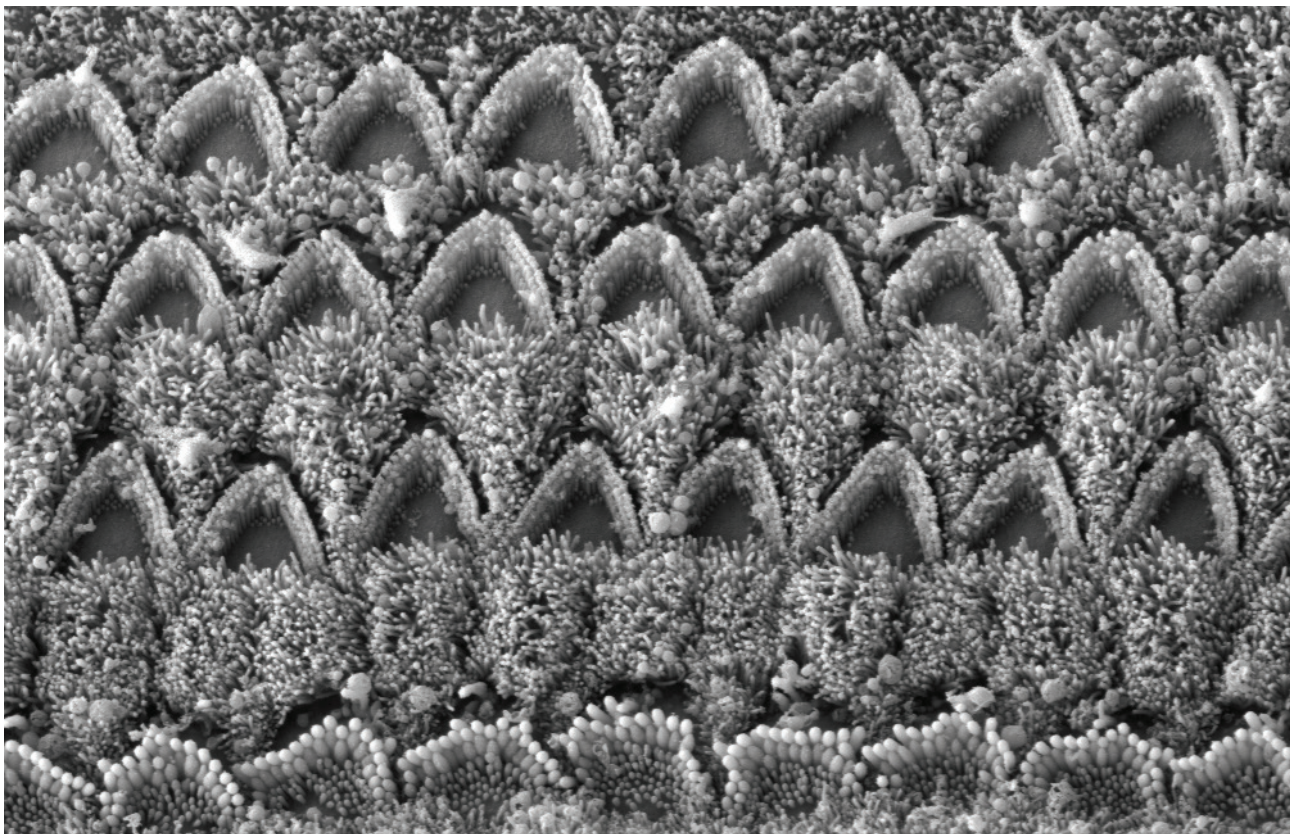
# Development and Morphogenesis of the Inner Ear

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 sub-cellular changes that drive morphological adaption 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 and 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



***Scanning Electron Micrograph of the mouse Organ of Corti before the onset of hearing.*** *Shown are the mechanosensory hair cells, with the modified apical architecture, known as stereocilila.*

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.

**SELECT 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. ***Proceedings of the National Academy of Sciences, 115***(33), pp. 8388-8393.

Ladher, R.K., 2017, May. Changing shape and shaping change: Inducing the inner ear. In ***Seminars in Cell & Developmental Biology*** (Vol. 65, pp. 39-46). Academic Press.

5.5

**DIMPLE NOTANI**
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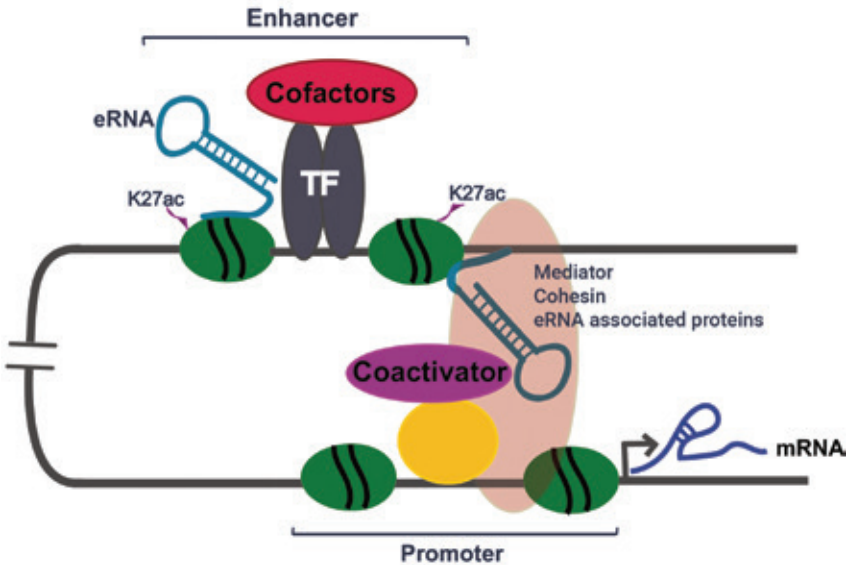
# Chromatin Dynamics in Gene Regulation

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 that regulate the target gene transcription by delivering important protein cargos to the promoter. While the biological importance of enhancers has been long appreciated, a mechanistic understanding of how enhancers regulate the genes dynamically during the short burst of signalling remain unsolved. Using oestrogen signalling that peaks at 1h and declines at 3h after ligand stimulation, we show that unliganded ERα 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. The clustered enhancers overlap with the ERα puncta in nuclei that




*The schematic depicts the functional anatomy of an enhancer-promoter unit: Functional enhancers, recruit lineage and tissue-type specific transcription machinery, triggering eRNA transcription leading to target gene activation via looping.*

are induced in a ligand-dependent manner. CRISPR-based deletion of persistent sites disrupts the formation of clustered enhancers as well as the corresponding ERα puncta, resulting in the loss of E2-dependnet induction of gene expression. Finally, ERα clustered enhancers are highly enriched in Mediator1 binding, suggesting their existence as ERα condensates. Our work thus establishes the role of persistent unliganded ERα binding in priming enhancer clusters and transient robust gene regulation in a ligand-dependent fashion.

## SELECT PUBLICATIONS

Jayani, R.S., Singh, A. and Notani, D., 2017. Isolation of nuclear RNA-associated protein complexes. In ***Promoter Associated RNA*** (pp. 187-193). Humana Press, New York, NY.

Li, W., Notani, D. and Rosenfeld, M.G., 2016. Enhancers as non-coding RNA transcription units: recent insights and future perspectives. ***Nature Reviews Genetics, 17***(4), p. 207.

## HONORS AND AWARDS

Invited as an **editorial member for the newly launched journal "Life Science Alliance"** jointly launched by EMBO and the Rockefeller and Cold spring harbor press.

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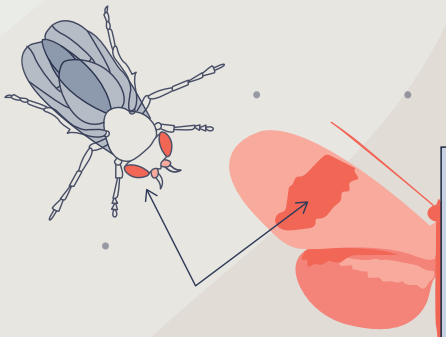


Terrestrial Ecosystems and Community Ecology
MAHESH SANKARAN

Deconstructing Indian Biodiversity: Evolutionary Origins and Future Prospects
UMA RAMAKRISHNAN

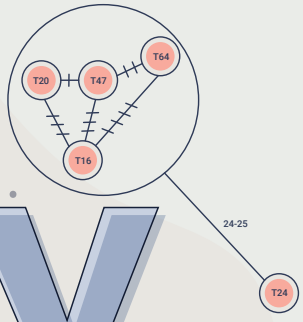
Tracking the Objects of Insect Affections Across Species and Continents
SHANNON OLSSON

Speciation, Adaptation, and Morphological Diversification in the Tropical Region
KRUSHNAMEGH KUNTE

Genetic and Ecological Factors Underlying Adaptive Evolution
DEEPA AGASHE

Chemical Ecology of Plant-Insect-Microbe Interactions
RADHIKA VENKATESAN

Molecular Mechanisms of Animal Behaviour
AXEL BROCKMANN

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6

6.1

**MAHESH SANKARAN**
*mahesh@ncbs.res.in*

# 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, 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.

(b) How projected changes in climate, such as increasing variability of rainfall, increased frequency of droughts, increasing aridity in the tropics, nitrogen and phosphorus deposition, and rising $CO_2$ will impact ecosystem function, stability, and services.

Most of our research is carried out in savanna ecosystems in Africa and India. We are now extending this work to encompass a wider range of ecosystem types, including rainforests and grasslands.

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 sub-continent, with the goal of bringing a comprehensive understanding of biome-scale vegetation and nutrient dynamics in the sub-continent.

## SELECT PUBLICATIONS


Dohn, J., Augustine, D.J., Hanan, N.P., Ratnam, J. and Sankaran, M., 2017. Spatial vegetation patterns and neighborhood competition among woody plants in an East African savanna. ***Ecology, 98***(2), pp. 478-488.

Tiruvaimozhi, Y.V., Varma, V. and Sankaran, M., 2018. Nitrogen fixation ability explains leaf chemistry and arbuscular mycorrhizal responses to fertilization. ***Plant Ecology, 219***(4), pp. 391-401.


## HONORS AND AWARDS

**SERB Distinguished Investigator Award**

**Coordinating Lead Author for the Land Degradation and Restoration Assessment of the Intergovernmental Science Policy Platform on Biodiversity and Ecosystem Services (IPBES)**

6.2

**UMA RAMAKRISHNAN**
*uramakri@ncbs.res.in*

# Deconstructing Indian Biodiversity: Evolutionary Origins and Future Prospects

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. Do we know what this diversity is? How has this diversity come to be? How are we impacting this diversity? My research attempts to address these questions. We conduct fieldwork to sample behavioural, ecological, and genomic data from these wild populations. We analyse these data in population genetic and phylogenetic contexts to better understand the evolution, population ecology, and conservation of populations.

## INDIAN BIODIVERSITY: TRACKING ITS HISTORY, CONSERVING ITS FUTURE

Just as a good dictionary reveals as much about culture as language, the genome of a species not only defines an organism, but also reflects its evolutionary journey and maybe, predicts the future fitness of individuals of the species. Once cryptic, these biological lexicons are yielding to new, cutting-edge methods of genomic analysis, providing incredible information about a species' history, and potentially its future destiny. In my group we embrace both outlooks, one goal being to understand the evolutionary history of Indian biodiversity, and the other, to better conservation efforts for threatened mammals of the Indian subcontinent.

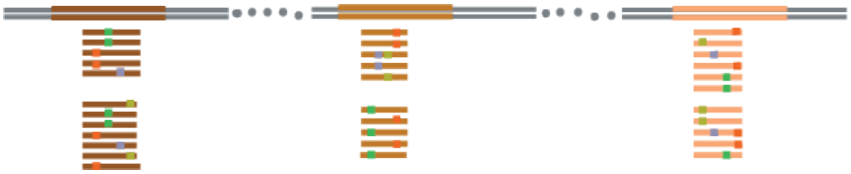
More fundamentally, we apply molecular methods in combination with computational techniques that we have developed for the analysis of modern and archival DNA. We aim to detail the genetic variation between wild populations of tigers, for example, and to determine when and why it came to be.

Are the differences due to meaningful adaptations or are they just an accumulation of demographics and migration-driven idiosyncrasies? In India, increase in human popu-

*We are collecting hair from identified individuals from Ranthambore and using these biological samples to investigate maternity and paternity relationships in this wild population*

lations have of course devastated many of our fellow mammals.

Ongoing conservation efforts must be informed by genetic analysis to establish if threatened populations have sufficient heterogeneity for unaided survival, and if not, the appropriate remedial measures. In conjunction with on-the-ground teams around the country, we are already supporting conservation projects for tigers, leopards, and vultures, a list that we know can only lengthen.



| | locus1 | locus2 | locus3 |
|---|---|---|---|
| TIG 1 | A/T | A/G | C/T |
| TIG 2 | A/G | T/G | A/T |

## SELECT PUBLICATIONS


Thatte, P., Joshi, A., Vaidyanathan, S., Landguth, E. and Ramakrishnan, U., 2018. Maintaining tiger connectivity and minimizing extinction into the next century: Insights from landscape genetics and spatially-explicit simulations. ***Biological Conservation, 218***, pp. 181-191.

Natesh, M., Atla, G., Nigam, P., Jhala, Y.V., Zachariah, A., Borthakur, U. and Ramakrishnan, U., 2017. Conservation priorities for endangered Indian tigers through a genomic lens. ***Scientific Reports, 7***(1), p. 9614.


## HONORS AND AWARDS

**Wellcome Trust DBT India Alliance Senior Investigator Award (2017)**

**Executive Committee and International Core Faculty, Program in Conservation Genomics, Stanford University (2018)**

6.3

**SHANNON OLSSON**
*shannon@ncbs.res.in*

# Tracking the Objects of Insect Affections Across Species and Continents

The Naturalist-Inspired Chemical Ecology group studies how animals, and especially insects, identify objects in nature. They 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.

RESEARCH IN the "NICE" Group traverses Himalayan meadows, ecologically sustainable agriculture in Coorg, and pollution in Bangalore —anywhere insects are important, which is nearly everywhere on Earth. This past year saw the culmination of three collaborative projects.

First, in collaboration with Karin Nordström at U. Uppsala and Flinders University, we studied how cosmopolitan pollinators can identify objects across climates, which have important implications for our understanding of pollination as a global ecological service (Nordström et al., 2017).

Second, in collaboration with Prof. Jeff Feder at U. Notre Dame, we have identified specific changes in the neural circuitry of olfaction that are driving speciation in the well-known *Rhagoletis pomonella* fruit fly system (Tait et al.,in review). Such neurological changes provide the first direct link between the brain and the evolution of new species.

Finally, in collaboration with Uma Ramakrishnan at NCBS, we have established a pipeline for large scale field sampling of volatiles that has allowed us to assess odour profiles of blackbuck mating territories in Rajasthan (Nair et al., 2018). We also participated in other publications and several scientific and outreach events, including multiple popular articles and TEDx.


***Our recent journal cover by Nair et al. in collaboration with Uma Ramakrishnan showing a blackbuck (Antilope cervicapra) lek at Tal Chappar Wildlife Sanctuary, Rajasthan, India***
Photo credit: Rupsy Khurana

***Calcium imaging of the fly Rhagoletis pomonella to examine odour processing in the brain leading to speciation.***
Photo credit: National Geographic's Shoot for Science – Deepak Kakara , Dinesh Yadav, Sukanya Olkar, Parijat Si.

## SELECT PUBLICATIONS

Nair, J.V., Shanmugam, P.V., Karpe, S.D., Ramakrishnan, U. and Olsson, S., 2018. An optimized protocol for large-scale *in situ* sampling and analysis of volatile organic compounds. ***Ecology and Evolution, 8***, pp. 5924-5936

Nordström, K., Dahlbom, J., Pragadheesh, V.S., Ghosh, S., Olsson, A., Dyakova, O., Suresh, S.K. and Olsson, S.B., 2017. *In situ* modeling of multimodal floral cues attracting wild pollinators across environments. ***Proceedings of the National Academy of Sciences, 114***(50), pp. 13218-13223.

## HONORS AND AWARDS

**Microsoft Foundation, PI, 0.9 M INR 2017-2018**

**Tata Trusts Foundation, PI, 4.9 M INR 2017-2020**

6.4

**KRUSHNAMEGH KUNTE**
*krushnamegh@ncbs.res.in*

# 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 the Indian region. We specifically 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.

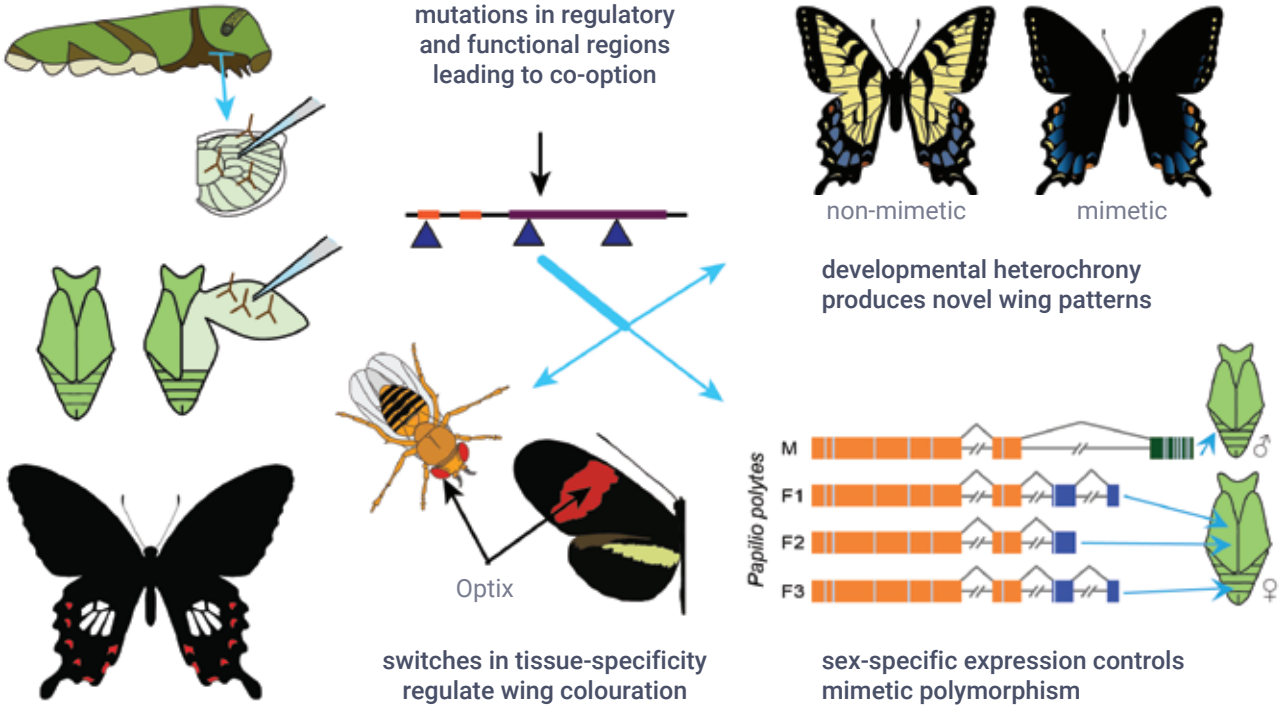
Our first study system is Batesian mimicry, which is a phenomenon whereby unprotected prey species (called "mimics") gain protection from predators by mimicking toxic or otherwise protected species (called "models"). Predators learn to avoid models based on prior experience, and subsequently avoid eating mimics due to misidentification.

Hundreds of mimetic insects, and especially butterflies, are known from tropical forests. There is tremendous variation in Batesian mimicry—mimicry can be sexually monomorphic, and polymorphic or

sex-limited within and across species. Our research aims to understand selective pressures that favour such variation in mimetic colour patterns, and uncover its genetic basis.

Our second study system is Indian butterflies. India's butterfly diversity is spread across four globally recognised biodiversity hotspots, and it 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 problems. We study all these phenomena as part of our various ongoing projects.

***Mimicry in Butterflies – the muse, the palette, and the artist.***
*A caterpiller prepares for its legendary transformation from a pupa into a colourful butterfly. Through this metamorphosis, a bag of developmental genetic tricks lays down bright colour patterns that help the butterfly attract its mates and warn or fool its predators.*




## SELECT PUBLICATIONS


Deshmukh, R., Baral, S., Gandhimathi, A., Kuwalekar, M. and Kunte, K., 2018. Mimicry in butterflies: co-option and a bag of magnificent developmental genetic tricks. ***Wiley Interdisciplinary Reviews: Developmental Biology, 7***(1), p. e291.

Joshi, J., Prakash, A. and Kunte, K., 2017. Evolutionary assembly of communities in butterfly mimicry rings. ***The American Naturalist, 189***(4), pp. E58-E76.


## HONORS AND AWARDS

Our paper on evolutionary assembly of butterfly mimicry rings, published in The American Naturalist, won the **American Society of Naturalists' 2018 Presidential Award**, "honoring an outstanding article published in The American Naturalist in the previous year".

6.5

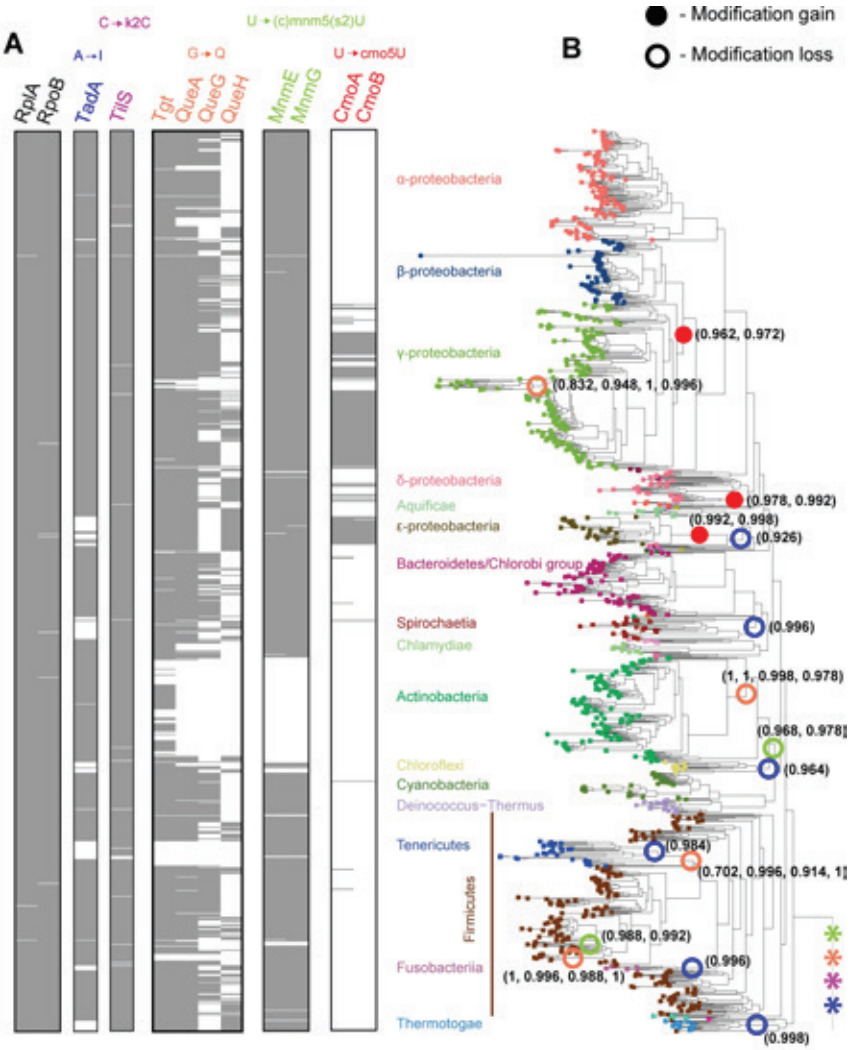
**DEEPA AGASHE**
*dagashe@ncbs.res.in*

# Genetic and Ecological Factors Underlying Adaptive Evolution

Our lab combines diverse approaches to understand the evolutionary and ecological processes underlying adaptive evolution. We often use experimental evolution of insects and bacterial systems to determine the dynamics of adaptation under new genetic and ecological selective pressures.

**A CENTRAL GOAL** of modern biological research is to understand the ecological drivers and genetic basis of evolutionary change in organisms, which is important to address a number of fundamental questions in biology. Organisms frequently face new, changing, or otherwise challenging environments, which are thought to drive a large proportion of evolutionary adaptations. However, different populations and species often respond differentially to the same environmental change, potentially altering their evolutionary trajectories. For instance, some organisms flourish in new environments, whereas others go extinct. What factors determine individual and population-level responses, and what are the processes and molecular mechanisms that mediate adaptation to new habitats?

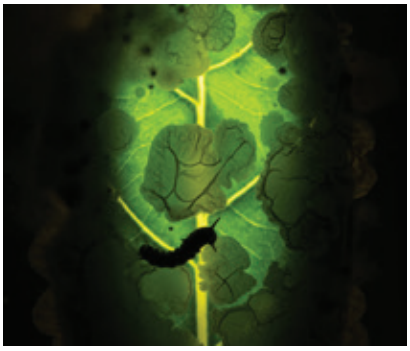
We address evolutionary processes and constraints acting at three different levels: (1) genetic and genomic features that can limit cellular growth, (2) phenotypic and genetic tradeoffs that may constrain adaptation, and (3) inter-species associations that may either limit or facilitate population growth and establishment.




***The evolutionary history of bacterial tRNA modifications.***

*(A) Columns indicate the presence (gray) or absence (white) of various tRNA modifying enzymes as noted above each column, with two essential housekeeping proteins (RpoB- RNA polymerase beta subunit and RplA- 50S Ribosomal protein L1) as positive controls for homology detection.*

*(B) A phylogenetic tree showing the evolutionary relationships between 1093 bacterial species. Filled and open circles respectively mark the infer-red major gains and losses of tRNA modifications. Circles are coloured by the modification, as indicated in panel A. Values in parent-heses indicate the posterior probability of each gain or loss event. Asterisks at the root of the tree indi-cate the presence of the respective modification.*



***A larva of Danaus chrysippus (Plain Tiger butterfly) crawls on the leaf of its host plant Calotropis gigantia sprawling with bacteria and fungi.*** *The leaf was incubated with nutrient-rich media to unravel the magnificent microbial diversity in the larval diet.* © Kruttika Phalnikar and Shoot for Science.

## SELECT PUBLICATIONS


Diwan, G.D. and Agashe, D., 2018. Wobbling forth and drifting back: The evolutionary history and impact of bacterial tRNA modifications. ***Molecular Biology and Evolution, 35***(8), pp. 2046-2059

Phalnikar, K., Kunte, K. and Agashe, D., 2018. Dietary and developmental shifts in butterfly-associated bacterial communities. ***Royal Society Open Science, 5***(5), p. 171559.

6.6

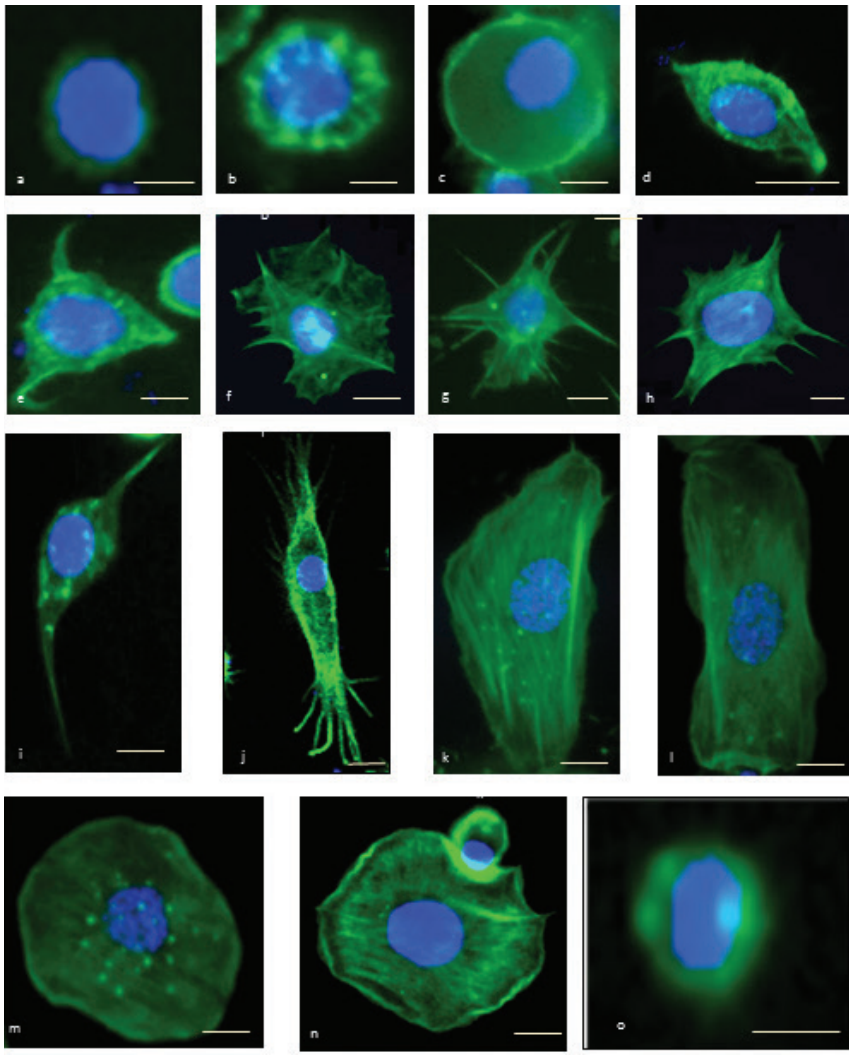
**RADHIKA VENKATESAN**
*radhika@ncbs.res.in*

# Chemical Ecology of Plant-Insect-Microbe Interactions

Chemical ecology is the study of chemically mediated interactions in nature. We study such interactions spanning from biochemistry to ecosystems addressing plant defence responses and their regulation by phytohormones, insect detoxification mechanisms, and evolutionary origins of plant defence responses.

**CHEMICAL ECOLOGY** is the study of chemically mediated interactions among organisms. We study such interactions between plants and insects. Plants possess many defences against herbivory that can be direct or indirect. Indirect defence includes Herbivore-Induced Plant Volatiles (HIPVs) that act as signals for attracting predators and parasitoid wasps. Since plant metabolites are key mediators of such complex interactions in nature, we study their role in regulating insect adaptation and parasitoid attraction. Insects lack adaptive immunity but harbor effective innate immune systems. On the other hand, parasitoid wasps have strategies such as injection of viruses and venom that can overcome insect immune responses. We study tri-trophic interactions between plants, insect herbivores, and parasitoids, asking how parasitic wasps choose their hosts. Can insect herbivores resist parasitisation? Since survival of parasitoid progeny strictly depends on the host, we examine the role of plant secondary metabolites in parasitoid choice.

We have found that parasitoid choice is altered by the presence



***Hemocyte profile of Spodoptera litura larva.*** *(a) prohemocyte, (b) oenocytoid, (c) granulocyte, (d) plasmatocyte, (e) podocytes, (f) vermiform cells, and (g) spread plasmatocytes with filapodia (granular and agranular).*

of certain plant metabolites. Further studies will reveal the exact nature of these compounds and their role in parasitoid survival. We also study the role of HIPVs in regulating insect physiology and behavior. 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.

## SELECT PUBLICATIONS


Agarwal, K., Haldar, S., Boland, W. and Venkatesan, R., 2018. Chemical ecology of bracken ferns. In ***Ferns: Ecology, Importance to Humans and Threats*** (pp. 58-96). Nova Science Publishers.

Khan, I., Prakash, A., Issar, S., Umarani, M., Sasidharan, R., Jagadeesh, N., Lama, P., Venkatesan, R. and Agashe, D. (2018) Female chemical warfare drives fitness effects of group sex ratio. ***The American Naturalist, 191***(3), pp. 306-317.

6.7

**AXEL BROCKMANN**
*axel@ncbs.res.in*

# Molecular Mechanisms of Animal Behaviour

Honey bees allow us to combine observations of individual behaviour under natural conditions and molecular analyses of the brains of these individuals. Combining both experimental strategies, we aim to identify molecular pathways and neural circuits underlying higher behavioural capabilities, like time-memory and communication of navigational information.

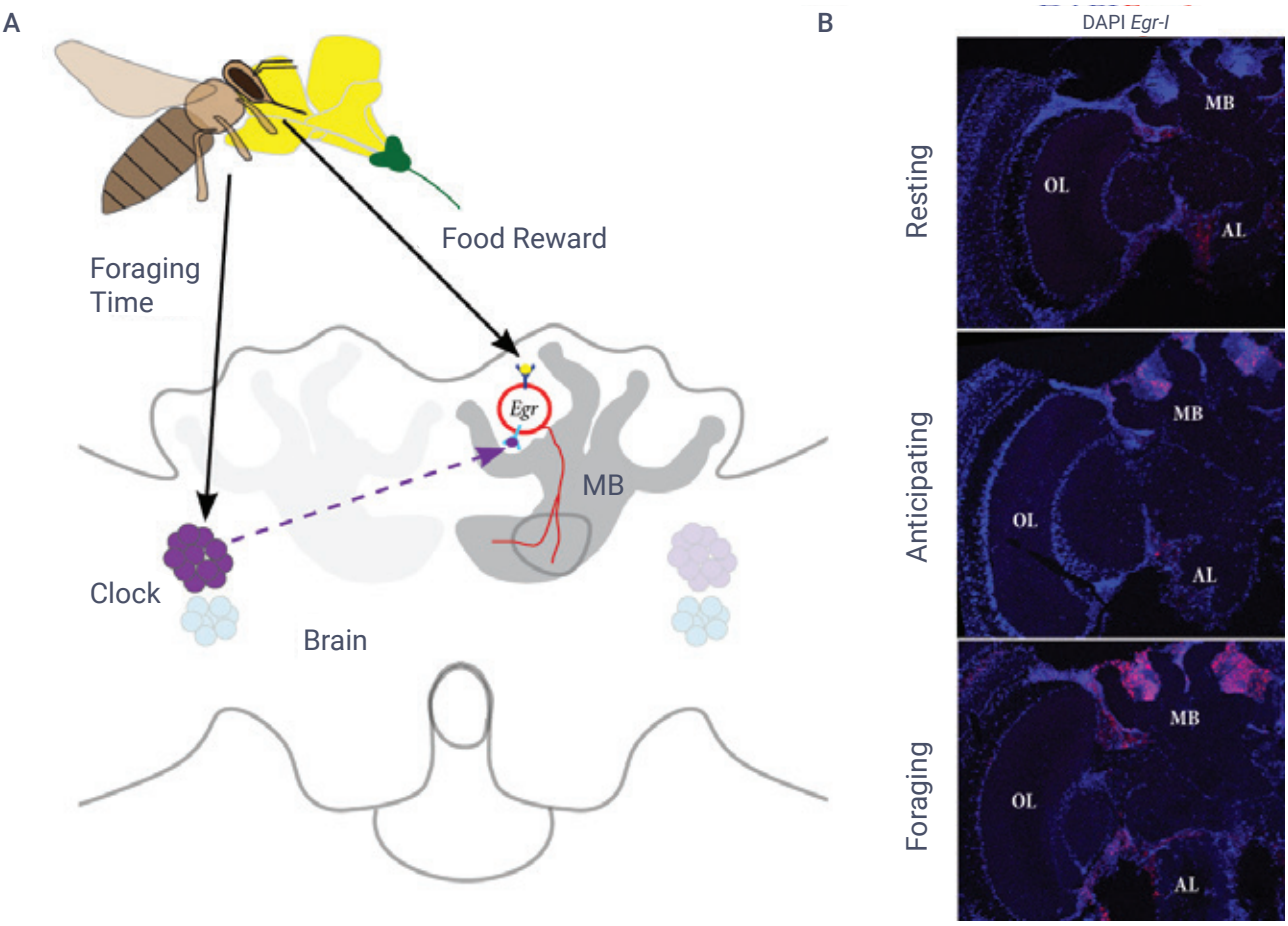
OUR LONG-TERM Research in the honey bee lab focuses on two major research areas:

a. Molecular processes involved in complex behaviours, and
b. Diversity and evolution of behaviour among honey bees.

In the last year, we made major progress in the following two research projects:

**I. MOLECULAR MECHANISMS INVOLVED IN DAILY FORAGING**
We showed that active foraging induced an upregulation of the immediate early gene, Egr-1, as well as select downstream genes involved in learning and memory. More importantly, time-training over several days resulted in an upregulation of Egr-1 in anticipation of foraging behaviour. We are convinced that these findings are a first step in identifying molecular processes involved in time-space memory in insects.

**II. UPDATING OF DANCE INFORMATION IN INDIVIDUAL HONEY BEE FORAGERS**
Analysis of dance behaviour of individual foragers before and after shifting feeder distance showed that most foragers need several visits to the new location to gener-




***Egr-1 expression in resting, anticipating, and foraging honey bee***
*(A) Hypothetical model of the interaction of reward perception and the circadian clock involved in generating time-memories. Foraging behaviour activates reward-dependent upregulation of Egr-1 in the mushroom bodies. In parallel, repeated foraging at the same time of day leads to anticipatory activation of Egr-1 expression. We hypothesise, that this effect is regulated by the circadian clock. (B) In situ hybridisation showing Egr-1 expression in resting, anticipating, and foraging honey bees.*

ate a new information dance. Most of the foragers showed a gradual update of dance information suggesting that generating dance information involves two different memories; a short term "working memory" and a long term memory. Our behavioural paradigm opens the possibility to investigate the molecular processes involved in honey bee dance behaviour.

## SELECT PUBLICATIONS

Shah, A., Brockmann, A. and Jain, R., 2018. Egr-1: a candidate transcription factor involved in molecular processes underlying time-memory. ***Frontiers in Psychology, 9***, p. 865.

Singh, A.S., Shah, A. and Brockmann, A., 2018. Honey bee foraging induces upregulation of early growth response protein 1, hormone receptor 38 and candidate downstream genes of the ecdysteroid signalling pathway. ***Insect Molecular Biology, 27***(1), pp. 90-98.

# New Faculty

SABARINATHAN RADHAKRISHNAN

of Biophysics, Biochemistry, and Bioinformatics

7

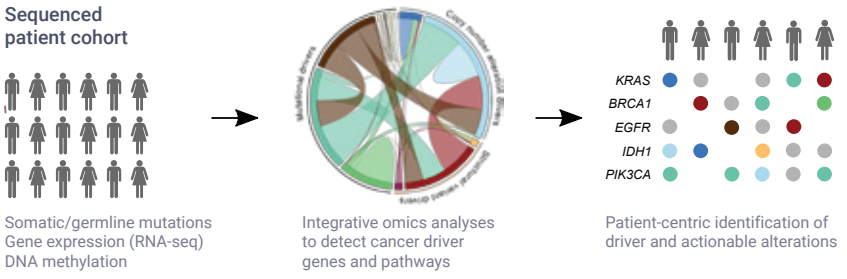
**SABARINATHAN RADHAKRISHNAN**
*sabari@ncbs.res.in*

# 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.

**DNA IN THE CELLS** of our bodies contains all the information required to ensure correct cell function. However, the accumulation of DNA alterations or mutations, can cause the cells to grow and divide uncontrollably, leading to tumour formation and metastasis. In order to prevent and treat the disease, it is of paramount importance to fully understand the genetic and molecular basis of the disease, such as which gene(s) are affected by the mutations and how they alter cellular functions.

We address these questions through the analysis of large-scale cancer genomics datasets (whole genome/exome and transcriptome) generated by the national and international cancer genome projects, and with a particular focus on Indian populations by sequencing and analysing tumours from cancer patients. We develop computational methods to integrate different levels of genomic information to identify the genes and pathways that are altered due to mutations and are likely drivers of cancer in individual patients.




***The schematic diagram represents the multi-omics approach to identifying cancer driver mutations in individual patients***

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Administration and Finance
PAWAN KUMAR PAHWA

Research Development Office
VINEETHA RAGHAVAN

Research Facilities:
Report 2017–2018

Bangalore Life Sciences Cluster:
Communications Office

# emics nd tration

8

8.1

**PAWAN KUMAR PAHWA**
Head, Administration & Finance

# Administration and Finance

The administrative department of NCBS-TIFR has always worked towards continuous improvement in streamlining the administrative process and to achieve the desired results. During 2017-18, we focused on the key management principles of planning, organising, directing, and regulating for greater efficiency. These principles were modulated as per the requirements of NCBS with regards to strategic planning, restructuring of processes, team building, and delegation of responsibilities. With the introduction of human resource management tools, the Centre has been able to increase the productivity of individual employees towards achieving the desired optimum levels.

THE GROWTH IN infrastructure and facilities on our campus has posed new challenges due to an increase in the complexity of multiple tasks that need to be handled by individuals and operational units across the institution. The challenge therefore, is to devise appropriate strategies to harness the available resources and deploy them optimally. The growth also demanded constant overview of the cost centres at regular intervals.

The Human Resource Module put in place during 2017-18 helped NCBS-TIFR identify and specify the job requirements and essential skill sets required for specific tasks. This has resulted in greater efficiency and productivity across our department. The concept of job rotation was introduced within the organisation to promote versatility of staff members for the greater benefit of the Centre. Some work processes such as the employee database portal, reimbursement of expenses, HR, and other work manuals have also been made available online.

NCBS-TIFR has always taken great pains to protect nature and natural resources. Awareness was generated within the campus community regarding sustainable usage of natural resources, and to make the campus eco-friendly by reducing usage of plastic items and paper.

**During the year 2017-18 the ratio of faculty to students was 1:8 which matches global standards of excellence. The institute's expenditure on research and development has shown a healthy increase of 15% (from Rs.446.52 in 2016-17 to Rs.515.1 million in 2017-18).**

On account of several serious and support-worthy research

*Administration Department at NCBS*

| Particulars | 2016-17 (INR in millions) | 2017-18 (INR in millions) |
|---|---|---|
| Research and Development | 446.52 | 515.1 |
| Extra Mural Grants | 325.14 | 363.58 |
| Salaries and Fellowships | 182.9 | 231 |
| Operational Expenditure | 254.6 | 269.5 |
| Construction | 127.1 | 265.1 |
| **Total** | **1336.26** | **1644.28** |

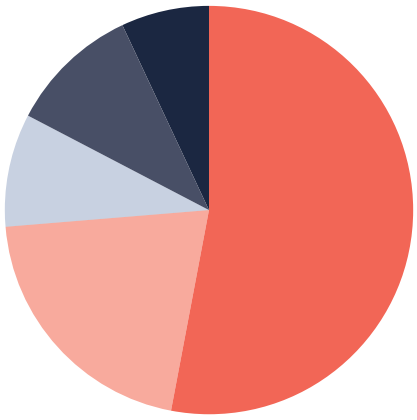
proposals submitted by various Principal Investigators of the institute, there has been an appreciable growth in obtaining extramural grants from various funding agencies as well as philanthropic sources. Fifty one new projects/fellowships were added over the last 12 months.

The Department of Biotechnology (DBT), Science & Engineering Research Board (SERB), the Department of Science & Technology (DST), Wellcome Trust-DBT India Alliance, Simons Foundation, MMV Medicines for Malaria Venture, Max Planck Institute, and the Ministry of Human Resource Development (MHRD) were the chief sources of extramural funding.

*Financial Progress Chart*

Dr. Kiran Mazumdar-Shaw of M/s Biocon donated Rs. 3 Crores towards the establishment of the Bangalore Life Sciences Cluster Endowment Fund. Shri N R Narayana Murthy of M/s Infosys, has donated a sum of Rs. 1 Crore to the Dengue Vaccine Development Programme.

*Manpower during year 2017-18*




*NCBS in Numbers**

| | |
|---|---|
| Post Doctoral Appointments | 122 |
| PhD Students | 157 |
| Masters Students | 16 |
| Junior and Senior Research Fellows | 138 |
| Administration and Auxiliary (including trainees) | 61 |
| Scientific and Technical Staff (including trainees) | 47 |
| Number of Faculty (including visiting scientists) | 40 |

*As of December 2018

A sum of Rs. 50 Lakhs was contributed by M/s TTK Prestige Limited to the Shri T T Narasimhan Grant for supporting the project entitled, *Scientists Beyond Boundaries*.

On the whole, 2017-18 was a vibrant year of dynamic resurgence and fulfillment. The administration and finance divisions set up processes and procedures to provide unstinted support for the academic and research interest of the institute. The support thus provided has enabled NCBS to fulfill the objectives of its mandated activities.

8.2

**VINEETHA RAGHAVAN**
*vineethar@ncbs.res.in*

# Research Development Office

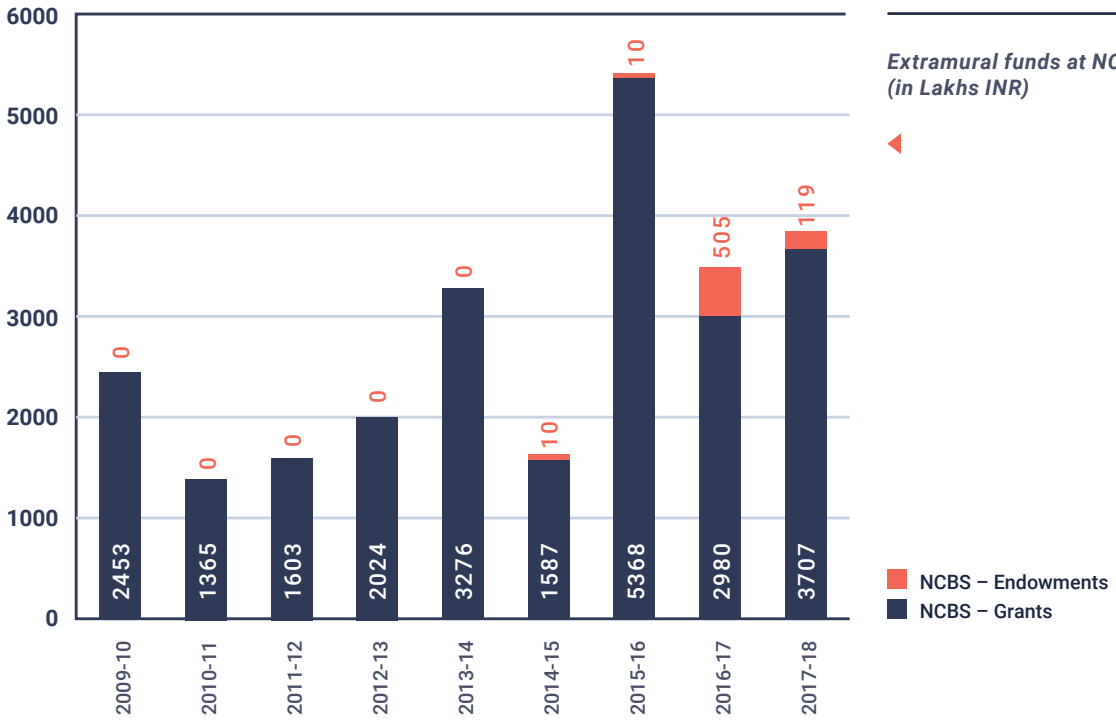
Research at the Bangalore Life Science Cluster, which includes NCBS, inStem, and CCAMP, spans a diverse range of questions and approaches in the broad area of life sciences. The Research Development Office (RDO) was created to facilitate research and training at the Cluster, by helping researchers apply for, and manage research funding.

OVER THE COURSE of the last eight years, the RDO has supported the diverse needs of the campus in fundraising, grants management, and contract negotiation for obtaining research funding from funding agencies, corporate sources, and charitable organisations.

Generous funding from the Government of India has been invaluable in establishing large institutional programmes on campus such as the Centre for Chemical Biology and Therapeutics (CCBT), Bangalore Life Sciences Cluster for Multiscale Basic and Applied Research in the Biological Sciences (B-LIFE), the Chemical Ecology Programme, the National Mouse Research Resource (NaMoR) and the Macromolecular Crystallo-graphy and Scattering Facility. The RDO manages all these large programmes.

The campus has also invested considerable effort into developing a mixed funding portfolio including charitable funding to complement funding from the Goland international grants. Some successful examples of programmes benefitting from such mixed funding include the Centre for Brain Development and Repair (CBDR) at inStem, which is supported by the Shanta Wadhwani Foundation and the Department of Biotechnology (DBT). More recently, the Pratiksha Trust and DBT have supported a major programme on “Accelerating the application of Stem cell technology in Human Disease” (ASHD) at NCBS and inStem, with institutional collaborations with NIMHANS.

In 2017, the TTK Prestige Group awarded a generous grant for supporting our vision of *Scientists Beyond Boundaries*, which has given a significant boost to our Campus Fellows Programme and enabled support to international researchers at BLiSc. In addition, this grant also enables students and postdoctoral fellows to attend international conferences and workshops through the T T Narasimhan Travel Awards which complements the InfoSys Travel Awards.




*Extramural funds at NCBS (in Lakhs INR)*

Other notable philanthropic donations this year were from Mr. Narayana Murthy for supporting the Dengue Vaccine Development Programme and the Simons Foundation for renewed support towards the Simons Centre for Living Machines. Through the generosity of our philanthropic partners, we initiated an Endowment Fund in 2016 for research, training, innovation, and outreach. NCBS has received corpus donations from the Wildlife Conservation Trust, the Infosys Foundation, and Dr. Kiran Mazumdar-Shaw.

Work at the RDO is made possible by a dynamic and professional team who are committed to offering several key services to the campus at the boundaries of science, management, and outreach. We look forward to a reward-ing journey further ahead for the RDO, supporting campus research funding and the Endowment Fund.

*The team at the Research Development Office*

8.3

# Research Facilities
## REPORT 2017–2018

Modern scientific research is critically dependent on the use of sophisticated and rapidly advancing technology platforms often operating on a high throughput scale. Therefore, the success of biological research depends on access to such technology platforms. These technology platforms evolve rapidly—driven by the development of new experimental methods as well as instrumentation that allows such methods to be implemented at a practical level. In addition, given the complex nature of the instrumentation required for such technology platforms, it is essential to have human resource capital that is well trained in state-of-the-art knowledge of the use of such technology platforms, and the ability to train institute scientists in the use of these facilities. The research facilities at NCBS are designed to meet these requirements.

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

### COMMON RESEARCH FACILITIES AT NCBS

The Animal Care and Resource Centre (ACRC) is a unique state-of-the-art barrier-protected Specific Pathogen Free (SPF) laboratory animal facility which provides services and resources for investigators to accomplish animal research objectives while ensuring optimal welfare conditions and animal ethics regulations. Currently, ACRC has >200 strains of mice, >12 lines of rats, and 12 lines of Zebrafish and *Xenopus laevis*. All mice and rat colonies are housed in Individually Ventilated Caging (IVC) systems with a controlled environment in the animal rooms.

ACRC Crew: **Mohan G H, Aurelie Jory-Lily, Sangeetha B, Latha Chukki, Sreenivasulu T, Vinodkumar D, Manjunath A M, Rupa Kumari, and Shruthi M**

Faculty Advisory Committee: **Raj Ladher, Hiyaa Ghosh, Colin Jamora, Arjun Guha, and Ramkumar Sambasivan.**

The Biosafety Facility in NCBS provides class 2 biological safety cabinets which allow the propagation of viruses as well as human tissue samples. The facility is equipped with equipment and consumables required for this work.

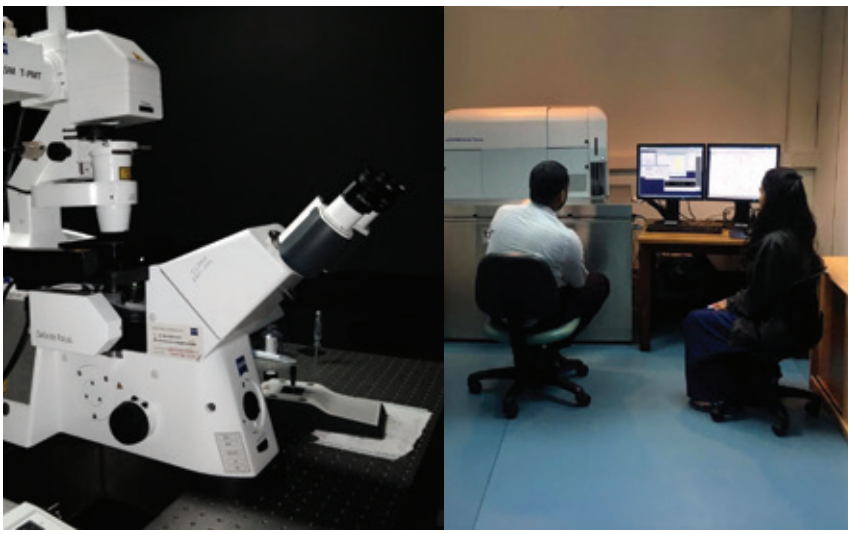
Biosafety Facility Crew: **Jagadish Sampath, and Ranjith P P**

Faculty Advisory Committee: **P V Shivaprasad, Varadharajan Sudaramurthy, Colin Jamora, and Sunil Laxman**

The Central Imaging and Flow Cytometry Facility (CIFF) is equipped with 22 state-of-the-art high-end microscopes and 10 flow cytometers. CIFF is an operator-free facility which caters to the needs of internal and external researchers. The perennial training programmes in imaging and flow cytometry conducted at CIFF are open to basic and clinical researchers.

CIFF Facility Crew: **H Krishnamurthy, Feroz M H Musthafa, A Divya, Amit Cherian, N Ranjana, Minni Kappen, Reena C, R Kulkarni, and H V Anil Kumar**

Faculty Advisory Committee: **Vatsala Thirumalai, Raj Ladher, and Srikala Raghavan**



***The Imaging Station (left) and the flow cytometer (right) at the Central Imaging and Cytometry Facility (CIFF)***

The Computing Facility is equipped with three high performance clusters and a centralised data storage system. The computing clusters deliver a computing power of 280 TFlops in total. Data storage of upto 750 TB caters to the storage needs of on-campus researchers. Users are given basic instructions and equipped to install and run required applications.

IT Crew: **P K Baruah, Rajshekar K S, Rajesh R, Chakrapani, Rifat N, Deanish M A, Arindam D, Alok B, Divya K, Subramani R P, and Kishore R**

Faculty Advisory Committee: **Sandeep Krishna, Madan Rao, and R Sowdhamini**


***The Fly Facility generates genetically engineered fruit flies and houses more than 10,000 distinct Drosophila melanogaster stocks in a controlled environment.***

The Fly Facility caters to the needs of *Drosophila* biologists within and outside of NCBS. It maintains approximately 16,000 different fly strains, and also generates transgenic flies. The fly facility also supports researchers in technology development in the area of *Drosophila* genome engineering and also trains researchers in transgenic *Drosophila* husbandry.

FF Crew: **Deepti Trivedi, Gajendra, Basavaraj, Yashwantha, Srividhya A, Hemavathy C, Anitha V A, Vinitha C M, Nataraj N, Kishore V, Shwetha H Manna Ghalia, and Janani S V**

Faculty Advisory Committee: **Gaiti Hasan and Tina Mukherjee**

The Green House Facility is equipped with a fully automated climatic control system to control light, temperature, and humidity using special lights, shading screens, evaporative pad and fan cooling system, heaters, humidifiers, and dehumidifiers for work on plants or plant–animal interactions.

Crew: **Ranjith P P, K Thirumala Raju, and Ashok Kumar**

Faculty Advisory Committee: **P V Shivaprasad and Mahesh Sankaran**

The Electron Microscopy Facility is equipped with two electron microscopes, including a high-resolution TEM (Tecnai T12 G2 spirit), a high-resolution FESEM (Merlin Compact VP), Cryo-SEM, and a biological sample preparation lab. The EM facility also trains on-site researchers. This is an operator-free facility used by both internal and external researchers

EM Facility Crew: **Deepti Negi and Saloni Sharma**

Faculty Advisory Committee: **Sanjay Sane and Srikala Raghavan**

The Genomics Facility includes both Sanger sequencing and a Next Generation Genomics Facility (NGGF). The facility is equipped with two state-of-the-art Sanger sequencing machines. The DNA sequencing facility provides plasmid, PCR product sequencing, and genotyping services to internal and external researchers in very short turnaround times (1–2 days). The NGGF is equipped with one state-of-the-art high throughput next generation sequencing platform and two bench-top next generation sequencing platforms. The NGGF caters to the next generation sequencing needs of internal and external researchers. The NGGF also provides user training and support in NGS library preparation using various protocols (DNA, mRNA, small RNA, ChIP, metagenomics etc.) and sequencing.

Genomics Crew: **Awadhesh Pandit and Tejali Naik**

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

The High Throughput Screening and High Content Imaging Facility (HTS/HCI) is equipped with five integrated liquid handlers which can perform multiple activities in parallel in 96, 384, and 1536 formats. The HTS has two high-end cell imagers which can read fluorescence in confocal mode. The facility also houses a BSL2 cell culture lab. The screening facility is an expert-assisted facility which caters to both internal and external, academic and industrial users. The screening facility also offers training programmes on HTS

HTS Crew: **Chandan Mitra**

Faculty Advisory Committee: **Varadharajan Sundaramurthy and Ramkumar Sambasivan**

The Museum and Field Stations Facility is presently equipped with four field stations and a state-of-the-art research collections and museum gallery space. The facility streamlines our field research and teaching operations, provides space for taxonomic research and long-term archival of important biodiversity-related materials, and facilitates broad societal engagement through its museum space and outreach activities.

MFFS Crew: **Vivek Ramachandran, G Aswathanarayana, Anup Prakash, Chengappa, Raghvendra, and Shashank Ongole**

***Mass Spectrometry Facility***

Faculty Advisory Committee: **Uma Ramakrishnan, Sanjay Sane, and Krushnamegh Kunte**

The Microfluidics and Microfabrication Facility is equipped for Su8 photolithography and PDMS fabrication technologies. It is being equipped with a state-of-the-art Class 10000 cleanroom and sub-micron resolution mask aligner. It provides a holistic experiment design to micro-fabricated device delivery and equipment access for the needs of internal and external researchers. The customised 1 to 4 week training programmes in the facility are open to basic and clinical researchers.

MMF Crew: **Feroz M H Musthafa**

Faculty Advisory Committee: **Uma Ramakrishnan, Sanjay Sane, and Krushnamegh Kunte**

The Mass Spectrometry (MS) resources on campus aim to provide researchers with state-of-the-art techniques and equipment to characterise biomolecules. A number of modern instruments for the separa-

***Nilgiri Field station at Emerald, near Ooty.*** *A view from the field station with Emerald dam and tea estates.*

***A seed trap at Sirsi, North Karnataka***

tion, identification, and quantitation of all major biomolecules by mass spectrometry-based approaches are available. In addition to providing MS-based structural characterisation services, the MS facility also provides training on the use of different LC-MS/MS technologies, as well as in developing new analytical methods required to facilitate on and off campus research.

Crew: **Dhananjay Shinde, Chhaya Patole and Raviswamy M**

Faculty Advisory Committee:
**Radhika Venkatesan, Sunil Laxman, and Axel Brockmann**

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 generation of specific pathogen-free mice through strain re-derivation and embryo transfer techniques. It also provides services for embryo and sperm cryopreservation, and the maintenance of a Laboratory Mouse Archive and Repository, as well as *in vitro* fertilisation procedures for resurrecting frozen mouse sperm or embryos.

Crew: **Aurelie Jory-Lily, Shilpa B A, Reena V, Debajeet Das, Jasper Chrysolite Paul, Saumya Mary Mathew, and Latha Chukki**

Faculty Advisory Committee:
**Raj Ladher, Hiyaa Ghosh, Colin Jamora, Arjun Guha, and Ramkumar Sambasivan**

The Nuclear Magnetic Resonance (NMR) Facility is equipped with two machines (800 MHz and 600 MHz) with cryo probes (in cryoprobes, the signal:noise ratio is ~4–5 times higher than room temperature probes). The facility aids structural biology studies that focus on *de novo* determination of protein and nucleic acid structures, as well as their dynamics. In structural biology, real time NMR is extensively used to understand folding pathways of proteins. Real time NMR also aids in obtaining the Michaelis-Menten constant ($K_M$) for enzyme substrate reactions. The facility also offers services for structure determination of syntactic organic and naturally derived compounds isolated from plants and insects.The facility provides round-the-clock service for both, internal and external users, and periodically conducts training programmes for new users, and also offers hands-on training sessions for regular users.

NMR Crew: **P Purushotham Reddy**

Faculty Advisory Committee:
**Ranabir Das, Jayant Udgaonkar, S Ramaswamy, Minhaj Sirajuddin, and Arati Ramesh**

The Radioactive Facility has been classified as a Type 1 radioactive laboratory. The Rad Lab is equipped to handle $^{3}H$, $^{32}P$,$^{14}C$, $^{55}Fe$, and $^{45}Ca$. The facility offers a rigorous training programme for new users under the supervision of the Campus Radiation Safety Officer. In addition to the use of radionuclides, the training programme includes modules on the safe disposal of radionuclides in line with regulations.

Radioactive Facility Crew: **Ranjith P P and Ashwin Nair**

Faculty Advisory Committee:
**P V Shivaprasad, Ranabir Das, Jayant Udgaonkar, S Ramaswamy, Minhaj Sirajuddin, and Arati Ramesh**

8.4

# Bangalore Life Sciences Cluster

## COMMUNICATIONS OFFICE

The BLiSc Communications Office aims to bring about greater awareness of and interaction with the Cluster via a robust science engagement model that comprises communication, outreach, and promotion of the research at NCBS, inStem, and C-CAMP—thereby reinforcing its reputation for innovation and scientific excellence.

We support NCBS by providing communications counsel and services to augment its presence through various channels and engagement initiatives. The Communications Office maintains an updated, online repository of publications, popular science articles, and news reports of NCBS research. In addition, we have created (written and designed) articles, while nurturing publicity and growing reach via our social media channels.

### OUTREACH AND SCIENCE ENGAGEMENT

This past year, the Communications Office has been involved in several existing outreach initiatives, as well as launching a few maiden platforms for science engagement.

June saw the advent of several science engagement events, primarily, our sci-outreach programme – Science and the City. The programme currently features two outreach initiatives: Science Café and Out of the Lab.

Our monthly Science Cafés are informal, relaxed exchanges of scientific knowledge, research, and ideas. The events bring scientists to the public to speak at different social venues in the city.

To our delight, our Science and the City programme was nominated for Falling Walls Engage 2018—The International Conference on Future Breakthroughs in Science and Society, and we were invited to Berlin to present our initiatives.

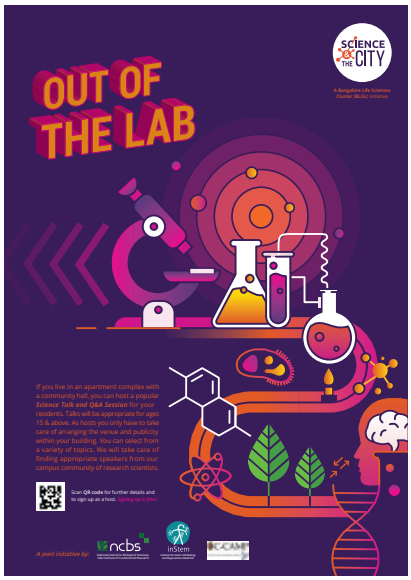
This past year we partnered with Mandram (a platform that promotes Tamil language and literature) for The Jigyasa Project—an avenue to deliver science talks in Kannada and Tamil. The second installment of The Jigyasa Project—with additional talks in Hindi—took place in December, and was well received by the public and media alike, with enthusiastic endorsements from the science community and beyond.

The BLiSc has facilitated visits to the campus from several school and colleges. Here, students are introduced to different laboratories and facilities within the Cluster, view live demos, and interact with

scientists. We have hosted over 200 students from different schools, colleges, and institutes from across the country.

*Participants rally around the BLiSc Science Café poster after an enjoyable talk on neuroscience by Dr. Vatsala Thirumalai, organised by the Communications Office.*

*Posters for a Science Café and an Out of the Lab initiatives, under the Science and City outreach programme of the Bangalore Life Sciences Cluster*


*Participants gather around Dr. Shashi Thutupalli's experiment during his BLiSc Science Café talk at Studio C9, organised by the Communications Office.*

We co-hosted science communication conferences and symposiums including the popular Science Comm '18 in association with Swissnex India—a day-long event that featured speakers from Switzerland and India talking about their unique endeavours in the field of science communication.

This year, we also hosted science communications workshops on our campus by several prolific scicomm personalities such as Dr. Meenakshi Prabhune (University of Göttingen), Sir Prof. David Speigelhalter (University of Cambrige), Prof. Douglas Sipp (RIKEN), Dr. Adria LeBoeuf (Weizmann Institute of Science), and Dr. Samuel Lagier (TEDxLausanne).

The Communications Office has also supported NCBS in its student science programmes likeSPEEC-Up 2018, and the Student Conference on Conservation Science (SCCS). We also helped with the publicity of on-campus events like the Biology of Butterflies Conference, the EMBO Size and Shape Conference, the annual Open Science Day—which saw over 1000 attendees— and the popular Moth Day.

We worked on the launch of the National Cryo-EM facility earlier this year, hosted Nobel laureates (Prof. Richard Henderson, Prof. Tomas Lindahl, and Prof. Venki Ramakrishnan), and exhibited the work of TIFR Artist-in-Residence, Dhara Mehrotra, on campus.

*Dr. Adria LeBoeuf and Dr. Samuel Lagier regaling the audience with how to use improv theatre tricks to do better science communication, at the Swissnex ScienceComm'18 event at NCBS*

*School children engaged in some lepidoptera-inspired science art at the NCBS Moth Day, 2018*

*Volunteers running through the last-minute details and sharing a few laughs a few days before the EMBO Size and Shape workshop*

*Sitana attenboroughii*, a new species of fan-throated lizard described from coastal Kerala. The new species was named after the renowned and celebrated naturalist Sir David Attenborough by a team including researchers from NCBS.
**PHOTO: KALESH SADASIVAN**

## NCBS MEETINGS AND WORKSHOPS 2018

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.

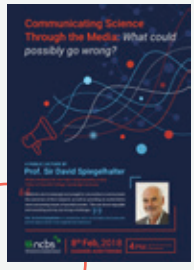
# January


JANUARY 24, 2018
TO JANUARY 25, 2018

National CryoEM Facility Inauguration Meeting

India's most technologically advanced CryoEM unit established on campus

# February




JANUARY 24, 2018
TO JANUARY 25, 2018

Communicating Science Through the Media: What Could Possibly Go Wrong? – A talk by Sir David Spiegelhalter

Focused on communicating the outcomes of scientific research and its social implications, with an AMA on Twitter

# March


MARCH 02, 2018

RNA Aggregation and Neurodegenerative Disease

The Importance of Science Communication – Ron Vale

Two compelling talks on incurable diseases and the digital challenges for science in the 21st Century

# April


APRIL 17, 2018

Beyond the Lab & Outreach in Science – a workshop by Meenakshi Prabhune

A hands-on workshop about careers beyond science and scientist engagement

# June


BLiSc's Science & the City initiative is launched

JUNE 17, 2018

Out of the Lab: Talk by Dr. Megha

JUNE 24, 2018

BLiSc Science Cafe: Talk by Dr. Deepa Agashe

# July


JULY 16, 2018 TO JULY 28, 2018

8th Annual Science Journalism Workshop

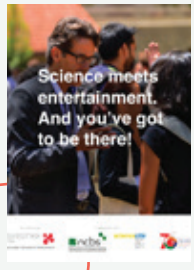
The definitive workshop for science journalists across the country to hone their science writing skills

# September

SEPTEMBER 04, 2018
TO SEPTEMBER 08, 2018

## EMBO Workshop: Size and Shape

An international workshop focused on multi-level organisations in biology

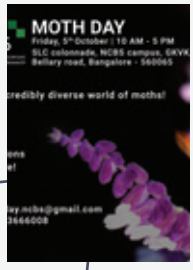



SEPTEMBER 27, 2018

## Swissnex ScienceComm '18

A two-day workshop on science and entertainment in partnership with the Swiss Consulate, Bangalore

# October

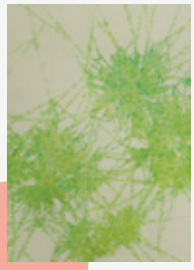



OCTOBER 05, 2018

## Annual Moth Day

A day long showcase of NCBS' lepidoptera and entomology research

# November



NOVEMBER 15, 2018
TO FEBRUARY 28, 2019

## Through Clusters & Networks – an exhibition by Dhara Mehrota as part of TIFR's Artist-in-Residence programme

An artistic rendition of biological concepts inspired by BLiSc's researchers

# November


NOVEMBER 16, 2018

## Annual Science Open Day

A science communication initiative showcasing BLiSc's research to school children

# December


15 DECEMBER 2018

## The Jigyasa Project II – Science in Regional languages (Kannada, Tamil, and Hindi)

A platform for science talks in regional languages for hard-to-reach audiences

9.1

# Science and the City

## SCIENCE CAFE

In June 2018, the Bangalore Life Sciences Cluster (BLiSc) proudly launched its science outreach programme: Science and the City. Science and the City kickstarted with two initiatives to take our scientists out of the laboratories into public, interactive spaces: Science Café and Out of the Lab.

Our monthly Science Cafés are informal, relaxed exchanges of scientific knowledge, research, and ideas. The events bring scientists to the public to speak at different social venues in the city—so far, we've covered key areas like Indiranagar, Koramangala, Whitefield, HSR Layout, Richmond Town, and Lal Bagh among others. NCBS scientists who have participated so far include Deepa Agashe, Mukund Thattai, Shannon Olsson, Vatsala Thirumalai, Shashi Thutupalli, and Uma Ramakrishnan. We were also invited to host a Science Café in Mumbai, Shillong, and Guwahati!

***Science Café:*** *Dr Deepa Agashe regales the audience with incredible facts about the billions of bacteria around us at the first Science Café talk, organised by the Communications Office*


***Science Café:*** *Dr Mukund Thattai sketches his concept of life on a flip chart at a Science Café event in Indiranagar, organised by the Communications Office*

***Out of the Lab:*** *Megha, a post-doc at NCBS, delivers a talk on nutrition in Drosophila at an apartment complex in Koramangala, Bangalore*

## OUT OF THE LAB

Out of the Lab is a unique platform where citizens invite our post-doc fellows to deliver popular talks and host Q&A sessions in their residential complexes, apartment blocks, and neighbourhood community centres. There have been five iterations of the Out of the Lab venture, and we hope to target more neighbourhoods in the upcoming months.

To our delight, our Science and the City programme was nominated for Falling Walls Engage November 2018—The International Conference on Future Breakthroughs in Science and Society, and we were invited to Berlin to present our initiatives.

9.2

# Public Outreach

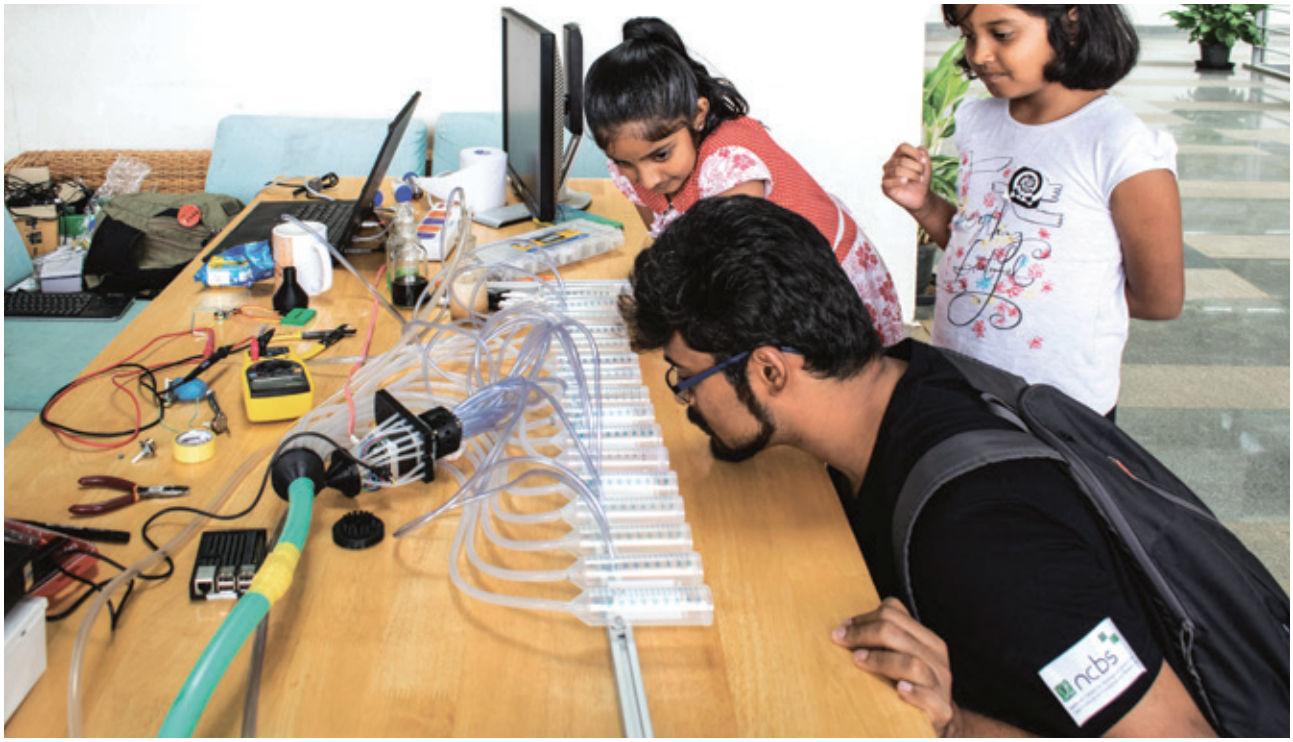
### MOTH DAY

*A mounted collection of moths on display at the NCBS Moth Day showcases the wide range of species and wing patterns*

The annual Moth day is a student-driven outreach event which seeks to focus on the importance of biodiversity and its role in our lives. Here, moths are the synecdoche for insects in general. It focuses on how moths (and insects) function in their day-to-day life—how they see the world, perceive sounds, sense odours, sense balance during flight, and so on. It also highlights some of the unique features that have made the Lepidoptera (moths, butterflies, and skippers) such highly successful organisms from an evolutionary standpoint. For instance, because of their overwhelmingly nocturnal lifestyles, most moths require special adaptations for sight, and to fly or evade bat sonars. This, in turn, influences their specific habitats, and those of the flowers they pollinate.

The principal purpose of Moth Day is to inspire love and curiosity for insects in public, and to communicate to them the importance of insects beyond the standard description of them as *pests*. Thus, we highlight their role in the food chain, and in pollinating plants, and effectively holding entire ecosystems together. Another major purpose that outreach events such a Moth Day serve is to train future scientists to communicate to the lay public the substance and importance of science, and to do so in language that is accessible and interesting.

We invite several neighboring schools and colleges to attend the event, including vernacular schools. This has helped build ties with them, which we hope can be developed further in the coming years. In addition to school students, a large number of interested citizens have attended Moth Day. In 2018, the total attendance for Moth Day exceeded 700. Many of the interactions have



*Children learn to hone their olfactory senses on a range of scents from coffee to chocolate, to better appreciate the sensory mechanisms in moths*

*An enthusiastic bunch of kids draw butterflies and moths at the NCBS Moth Day*

continued and have led to research internships. Another important feature that has been highlighted in recent Moth Day events is the role of insects, and moths in particular, as indicators of habitat health. In times when we are witnessing a massive and alarming drop in insect biodiversity, this takes on an urgency as never before.

## OPEN SCIENCE DAY

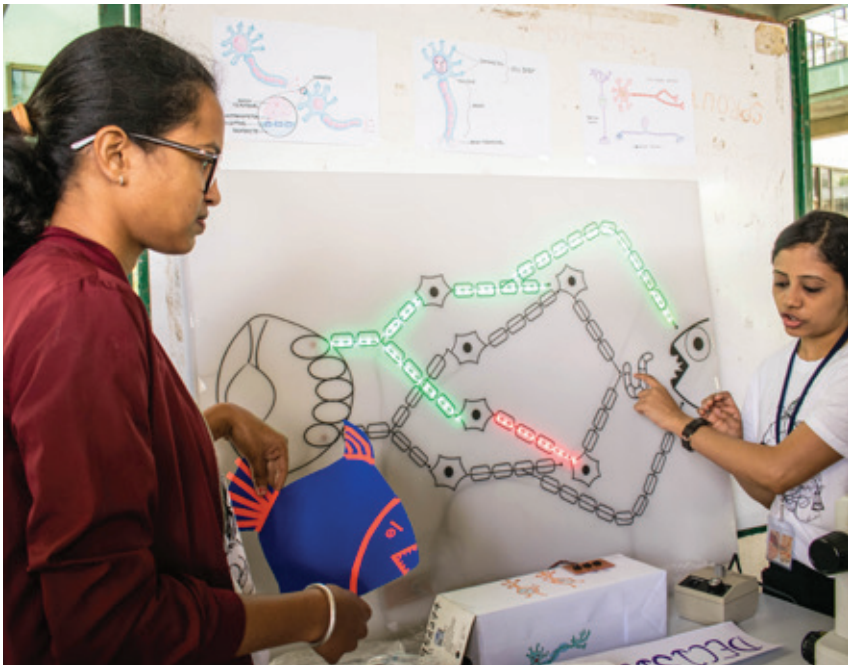
On November 16th, 2018, the Bangalore Life Sciences Cluster, hosted the Open Science Day 2018. From 9 AM to 5 PM our campus opened its doors to school students aged 12 and upwards, (as well as curious adults) for an exciting day of science demonstrations, experiments, exhibits, games, and interactions with scientists.

The day-long event had an estimated footfall of over 1000+ people, of which 600 students came from prior notified schools. Around 12 schools attended, some of which were from remote places like Hassan, Mandya, and Gauribidanur. In addition, there was also a two-hour slot allocated for Kannada-speaking schools and each laboratory had a person or two present to deliver their science in Kannada.

During the event, many laboratories from NCBS showcased the latest research being undertaken by their groups. Laboratory representatives made arrangements to explain the science to high school students, college students, and visitors without a science background. Captivating visual posters, interactive demonstrations, and games helped visitors understand the research and facilitated their participation in the discussions with NCBS scientists.

The exhibits showcased multiple themes of scientific research ranging from animals and ecosystems to cells and molecules. It proved to be a fun-filled day of learning and interaction for students and scientists alike.

*A real human brain on display at the Bangalore Life Sciences Cluster's Science Day*



*A demonstration of how neurons work in zebrafish at the Bangalore Life Sciences Cluster's Science Day*

9.3

# Science Communication

### SWISSNEX SCIENCECOMM '18 – SCIENTAINMENT

BLiSc co-hosted the popular ScienceComm '18 in association with Swissnex India. It was a day-long event that featured speakers from Switzerland and India talking about their unique endeavours in the field of science communication, with a focus on scientainment.

### JIGYASA PROJECT – 2 EDITIONS

This past year, a partnership with Mandram (a platform that promotes Tamil language and literature) resulted in The Jigyasa Project—an avenue to deliver science talks in regional languages. Our first iteration in June, included science talks in Kannada and Tamil from themes like neuroscience and the language of science, to free software and intellectual property. The second iteration in December featured Kannada, Tamil, and Hindi talks on the theme of, *Traditional Knowledge meets Modern Science*. Both events were well-received by the public and media alike, with enthusiastic endorsements from the science community and beyond.

### TALKS & WORKSHOPS

Prof. Sir David Spiegelhalter
Dr. Meenakshi Prabhune
Prof. Ronald Vale
Prof Douglas Sipp (RIKEN, Japan)
Dr. Adria Leboeuf and Dr. Samuel Lagier
Dr. Kollegala Sharma

BLiSc hosted several science communications workshops on campus by noteworthy personalities such as Dr. Meenakshi Prabhune (University of Göttingen, Germany), Prof. Sir David Speigelhalter (University of Cambrige, UK), Prof. Ronald Vale (University of California, USA), Prof. Douglas Sipp (RIKEN, Japan), Dr. Adria LeBoeuf (Weizmann Institute of Science, Israel) and Dr. Samuel Lagier (TEDxLausanne, Switzerland), and Dr Kollegala Sharma (Central Food Technological Research Institute, Mysore, India).

9.4

# TIFR Artist-in-Residence Exhibition

In a one-of-its-kind initiative, the Bangalore Life Sciences Cluster (BLiSc) hosted the 'Through Clusters and Networks' exhibition as a culmination of the Artist-in-Residence Outreach Programme, NCBS-TIFR Bangalore 2018. As a hub of excellence in biological research, we realise that research problems can be approached from different perpectives, and varied sources of inspiration. To encourage collaboration at every level, the Artist-in-Residence programme is an endeavor to translate science into art.

THE EXHIBITION SHOWCASES the work of visual artist, Dhara Mehrotra. She draws inspiration from diverse aspects of landscape and its ecology—such as pollen, dandelions, grass, moss, and flower petals—with an emphasis on clusters and space to evoke a sense of fluidity and boundlessness.

During the residency, Dhara collaborated with various laboratories and

*A mixed audience eagerly listens to Dhara Mehrotra, the artist, provide an overview of the research at the Bangalore Life Sciences Cluster that inspired her artwork*

scientists—namely Deepa Agashe, Shannon Olsson, Sunil Laxman, Dasaradhi Palakodeti, Shashi Thutupalli, Aswin Seshasayee, Anjana Badrinarayanan, and Radhika Venkatesan—to explore and observe the idea of self-organisation in science and nature. Her project, *Through Clusters and Networks*, is the product of her interaction with the scientists on campus, and offers a closer look at how fungi and plants communicate with each other via a "Wood Wide Web". The project is an attempt to complement the artistic intuition with the logic and rigors of scientific method. It delves into the form and structural topology of fungal networks (mycelia), that spread several miles underground, connecting the roots of trees, plants, and all vegetation, cycling life energy through them.

The exhibition is on at the Science Gallery, in the new inStem building till February 15th, 2019.

Explore more of Dhara's work at http://www.dharamehrotra.com/

*An artistic rendition of the Wood Wide Web represents the subterranean mycelia networks by which flora communicate at the Through Clusters and Networks exhibition*

*A cluster of gossamer-winged dragonflies commands attention at Dhara Mehrotra's exhibition Through Clusters and Networks, at the Science Gallery, housed in the new inStem building*

9.5

# Inauguration of National CryoEM Facility

On 25th January 2018, the national cryo-electron Microscopy (cryoEM) Facility was officially inaugurated by Prof. C N R Rao and Dr. Richard Henderson (Nobel Prize winner for Chemistry in 2017) at the Bangalore Life Sciences Cluster (BLiSc).

***Prof. C N R Rao officially inaugurates the national cryoEM facility at the Bangalore Life Sciences Cluster campus***

THE OCCASION was marked by a symposium with invited speakers including Dr Richard Henderson (Laboratory of Molecular Biology, Cambridge, UK), Prof. Werner Kuehlbrandt, Prof. Wolfgang Baumesiter and Prof. Stefan Raunser (Max-Planck Institute for Biophysics, Frankfurt, Germany), and Prof. Richard Kuhn (Purdue University-Indiana, USA). Over thirty structural biologists, and a good number of students and post-docs attended the symposium.

Furthermore, a unique grant was offered by the BLiSc and Thermo Fisher Scientific to develop cryomicroscopy capacities for five new users with no prior experience in structural biology.

So far, the National cryoEM facility has been a great success due to its easy accessibility and ability to produce good quality data. Since molecular structure determination via cryoEM has risen sharply in the last few years, this national facility will play a major role in helping Indian scientists carry out cutting-edge research. Future goals include expanding the facility to integrate cell and structural biology, and building a correlative microscopy setup to allow researchers to study *in-situ* macromolecules and cellular processes.

*Dr S Ramaswamy of inStem reveals the inner workings of the cryoEM machine after the official inauguration*


*Dr. Vinothkumar K R, Prof. C N R Rao, Dr. Richard Henderson, and Prof. Satyajit Mayor line up in front of the new cryoEM unit installed at the Bangalore Life Sciences Cluster campus*

9.6

# The Biology of Butterflies: Creating a Flutter at NCBS

In the Victorian era, a love of butterflies was considered by some to be a sign of lunacy. The study of butterflies has come a long way since then. Hundreds of scientific groups all over the world are currently engaged in cutting-edge research in evolutionary biology, behaviour, ecology, systematics, biogeography, genetics, developmental biology, biodiversity conservation, and physics, with butterflies and moths as their focal study organisms.

THE INTERNATIONAL CONFERENCES on the Biology of Butterflies (ICBB) offers scientists working on butterflies an excellent professional forum in which they can share their latest discoveries and academic news. Initiated in 1981 in London, the ICBBs have taken place every four years or so since 1994. The 8th ICBB was hosted on 11th to 14th June 2018 at NCBS, and was organised by Dr. Krushnamegh Kunte (NCBS) and Dr. Ullasa Kodandaramaiah (IISER Thiruvananthapuram). It was the first time an ICBB was held in a biodiverse developing country, giving a nod to the increasing value of research on tropical butterflies and the growing participation of tropical biologists. The conference talks were organised in themed symposia that covered contemporary topics of considerable scientific value as well as societal relevance, such as: (a) impact of weather trends and climate change on butterfly populations, (b) diversification and speciation in the tropics, (c) pattern formation and wing development, and (d) global citizen science monitoring of butterflies for science, education, and conservation. The speakers presented a broad swath of science involving methods in field ecology, molecular genetics, genomics, and evolutionary developmental biology, reflecting the breadth of emerging butterfly model systems.

In conjunction with the ICBB, the campus hosted a butterfly-themed philately and art exhibition for the general public. The Indian postal service produced and released a special postal cover to commemorate the first Asian ICBB.

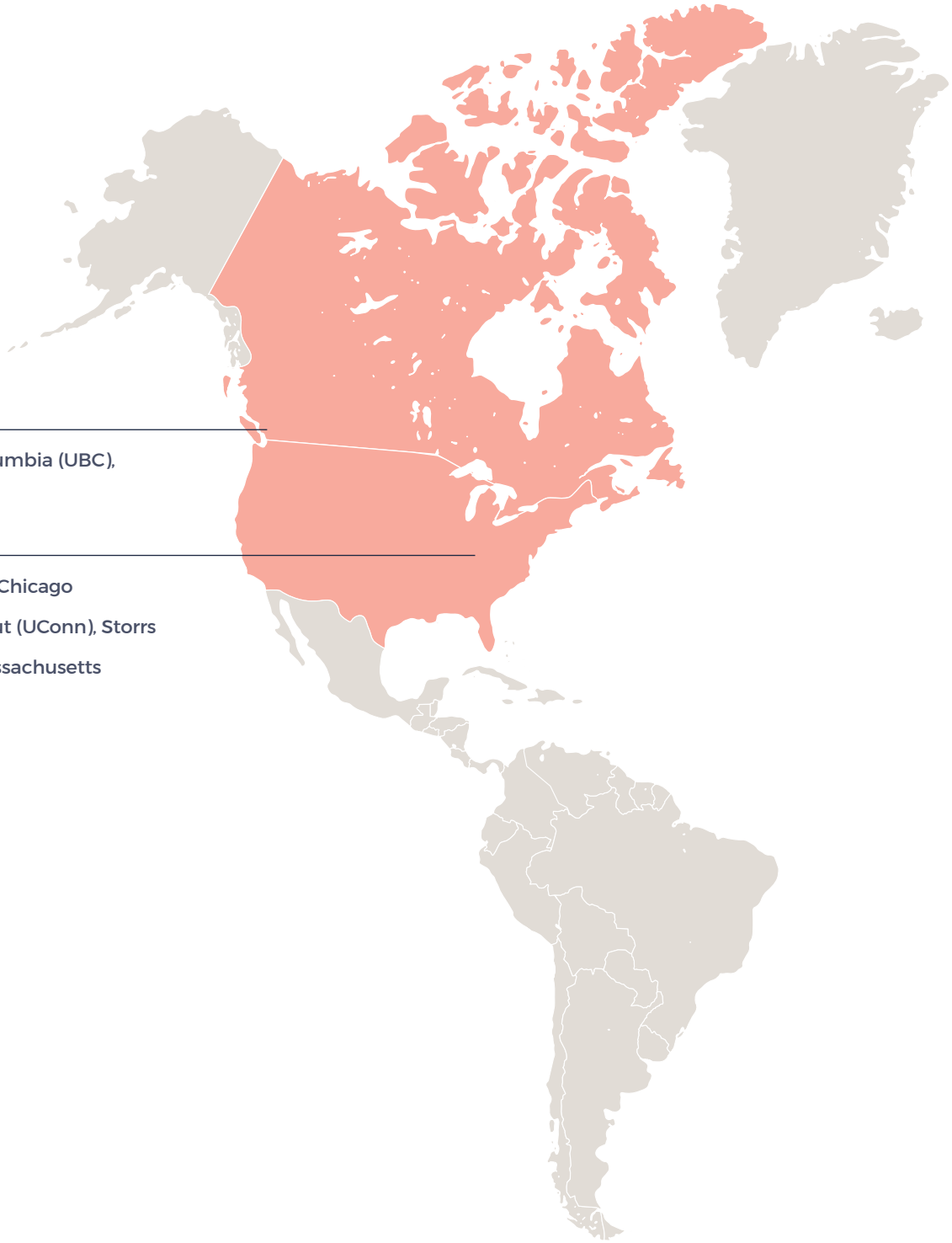
At the 2014 Finland conference, the 2018 India bid had received overwhelming support from attendees, with the promise of inspiring a new, strong generation of tropical butterfly biologists. This conference will hopefully cast a long shadow on the growth of young butterfly biologists in tropical countries who might some day lead scientific research on butterflies and other insects around them. NCBS strives to serve as a centre of excellence and a strong support group for this rising research community. Read more at **http://www.biologyofbutterflies.org/**

***The 130 conference participants represented over 15 countries from six continents, and a large contingent of PhD students and post-docs.*** *Image courtesy: ICBB 2018*

***Some of the plenary speakers and organisers of ICBB 2018 (L to R): Fred Nijhout, Larry Gilbert, Krushnamegh Kunte, Naomi Pierce, and Antónia Monteiro.*** *Image courtesy: ICBB 2018*

***A post-conference training workshop at Honey Valley, Coorg, introduced students to major research themes and associated methods that are especially relevant in tropical forests and in the Oriental context.*** *Several faculty members from the ICBB taught at the workshop. Image courtesy: Larry Gilbert.*

# NCBS INTERNATIONAL COLLABORATIONS



CANADA

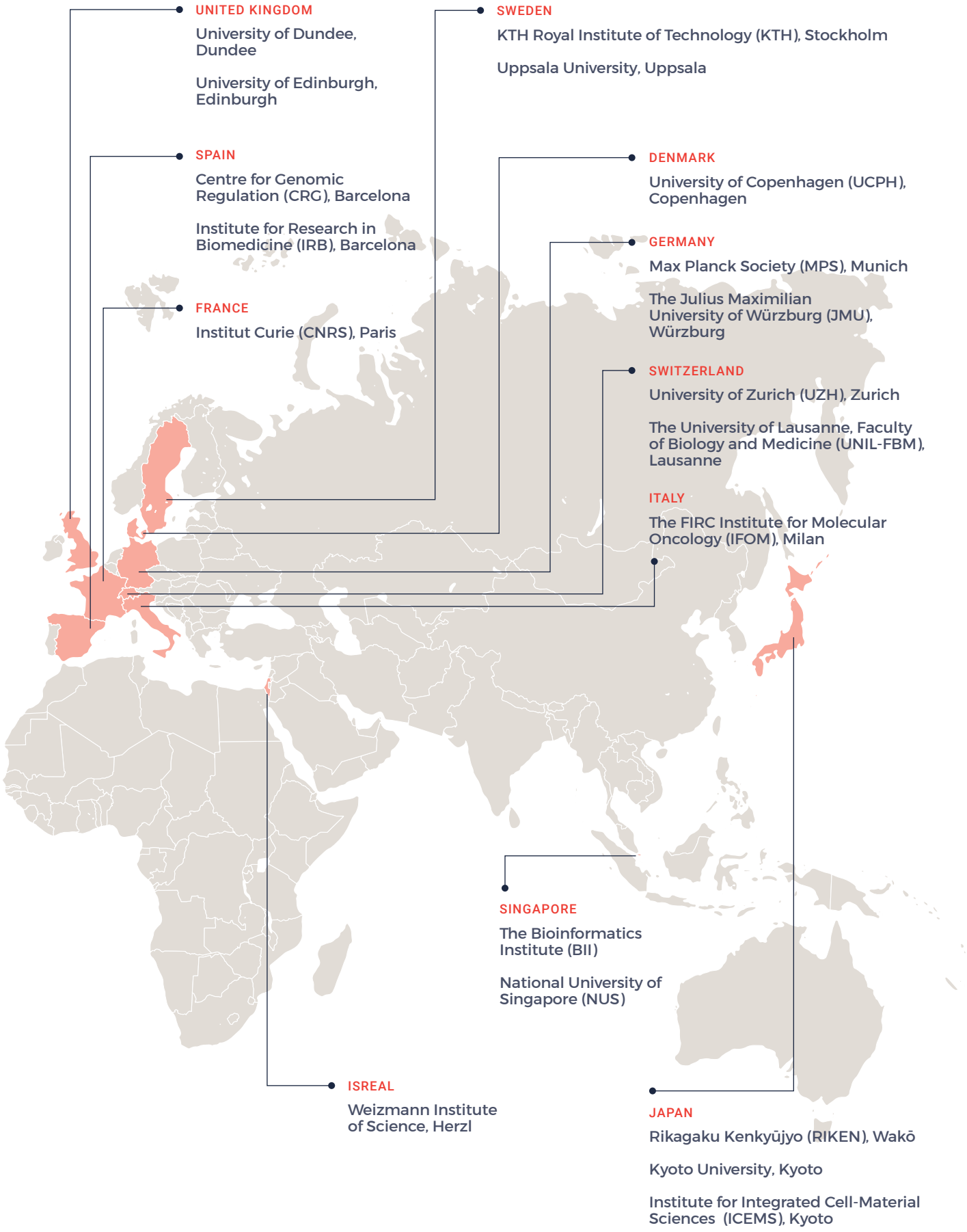
University of British Columbia (UBC), Vancouver

USA

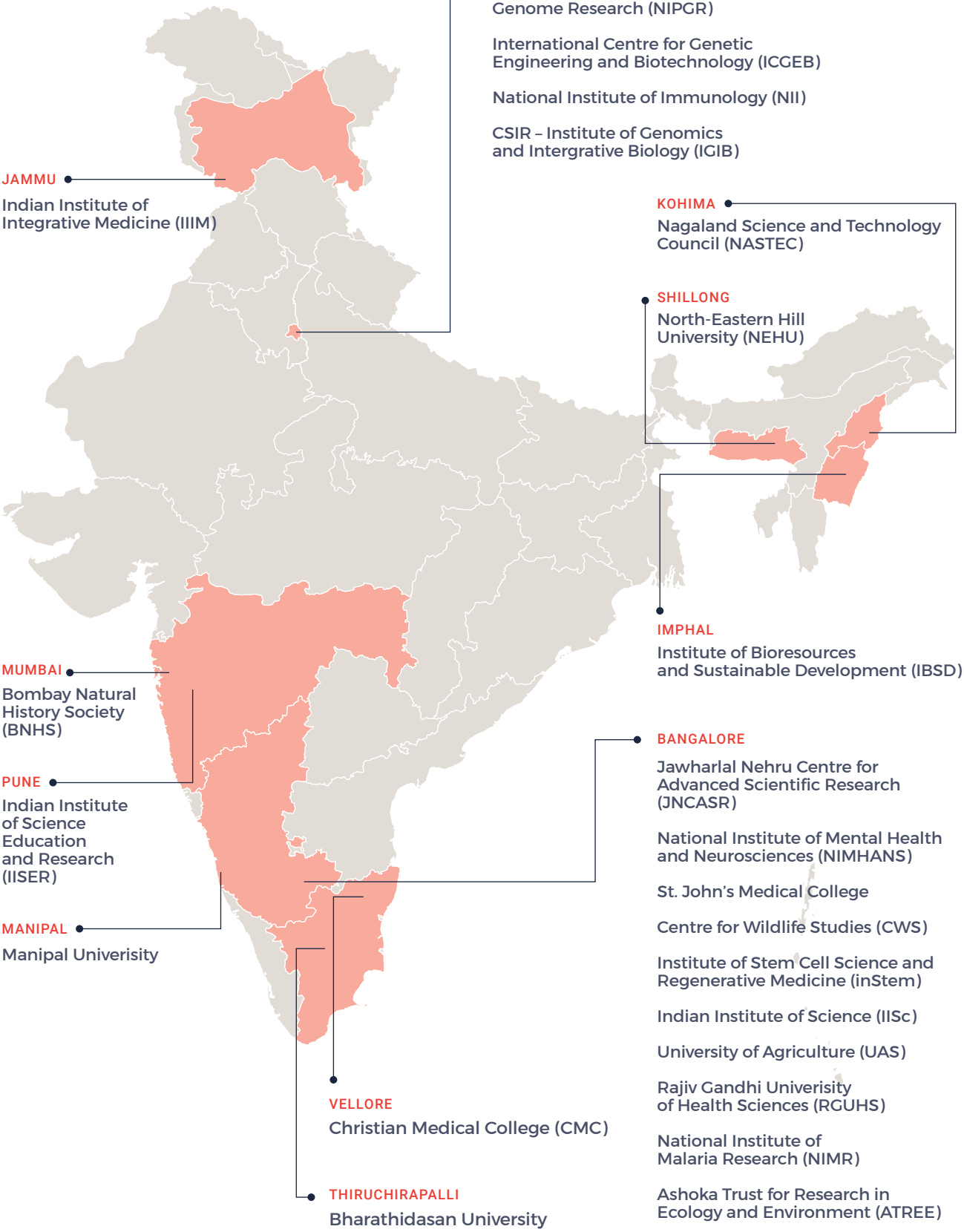
Loyola University (LUC), Chicago

University of Connecticut (UConn), Storrs

Brandeis University, Massachusetts


UNITED KINGDOM
University of Dundee, Dundee
University of Edinburgh, Edinburgh
SWEDEN
KTH Royal Institute of Technology (KTH), Stockholm
Uppsala University, Uppsala
SPAIN
Centre for Genomic Regulation (CRG), Barcelona
Institute for Research in Biomedicine (IRB), Barcelona
DENMARK
University of Copenhagen (UCPH), Copenhagen
GERMANY
Max Planck Society (MPS), Munich
The Julius Maximilian University of Würzburg (JMU), Würzburg
FRANCE
Institut Curie (CNRS), Paris
SWITZERLAND
University of Zurich (UZH), Zurich
The University of Lausanne, Faculty of Biology and Medicine (UNIL-FBM), Lausanne
ITALY
The FIRC Institute for Molecular Oncology (IFOM), Milan
SINGAPORE
The Bioinformatics Institute (BII)
National University of Singapore (NUS)
ISREAL
Weizmann Institute of Science, Herzl
JAPAN
Rikagaku Kenkyūjyo (RIKEN), Wakō
Kyoto University, Kyoto
Institute for Integrated Cell-Material Sciences (ICEMS), Kyoto

# NCBS NATIONAL COLLABORATIONS



**NEW DELHI**

National Institute of Plant Genome Research (NIPGR)

International Centre for Genetic Engineering and Biotechnology (ICGEB)

National Institute of Immunology (NII)

CSIR – Institute of Genomics and Intergrative Biology (IGIB)

**JAMMU**

Indian Institute of Integrative Medicine (IIIM)

**KOHIMA**

Nagaland Science and Technology Council (NASTEC)

**SHILLONG**

North-Eastern Hill University (NEHU)

**IMPHAL**

Institute of Bioresources and Sustainable Development (IBSD)

**MUMBAI**

Bombay Natural History Society (BNHS)

**PUNE**

Indian Institute of Science Education and Research (IISER)

**MANIPAL**

Manipal Univerisity

**BANGALORE**

Jawharlal Nehru Centre for Advanced Scientific Research (JNCASR)

National Institute of Mental Health and Neurosciences (NIMHANS)

St. John's Medical College

Centre for Wildlife Studies (CWS)

Institute of Stem Cell Science and Regenerative Medicine (inStem)

Indian Institute of Science (IISc)

University of Agriculture (UAS)

Rajiv Gandhi Univerisity of Health Sciences (RGUHS)

National Institute of Malaria Research (NIMR)

Ashoka Trust for Research in Ecology and Environment (ATREE)

**VELLORE**

Christian Medical College (CMC)

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