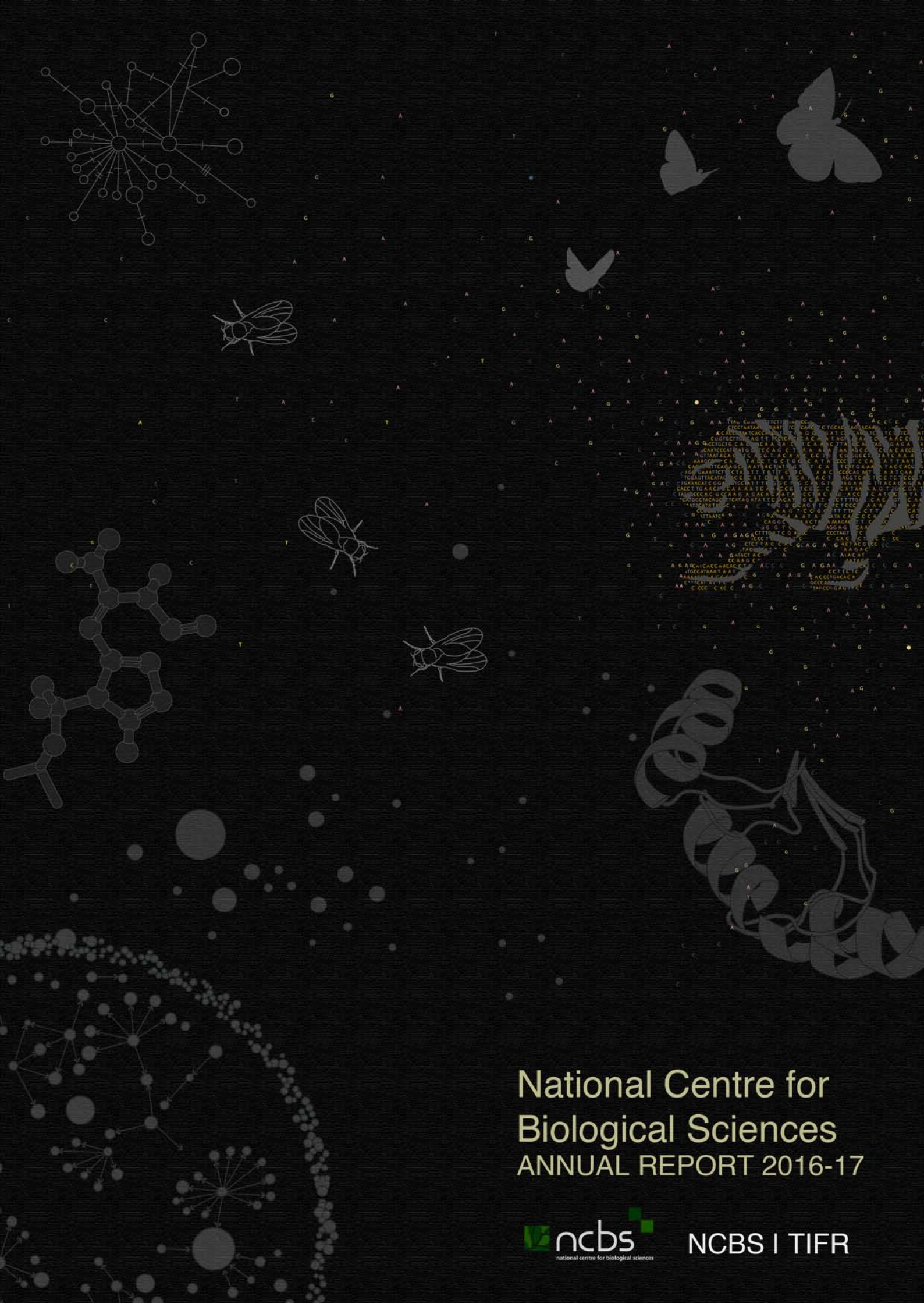

National Centre for Biological Sciences
ANNUAL REPORT 2016-17

ncbs
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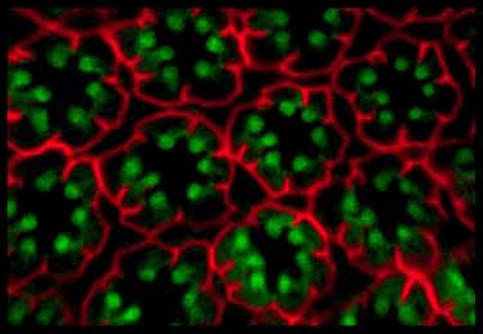
NCBS | TIFR



Research at NCBS spans a diverse set of questions in modern biology, from atomic to population level studies.

Images for the cover have been contributed by Gaiti Hasan, K VijayRaghavan, MK Mathew, Mukund Thattai, Radhika Venkatesan, Raghu Padinjat, R Sowdhamini, Shannon Olsson, Shashi Thutupalli, Sumantra Chattarji and Uma Ramakrishnan.

National Centre for Biological Sciences

NCBS | TIFR 2016- 2017

Photography by Jeswin Singh, Research Scholar, Sumantra Chattarji lab

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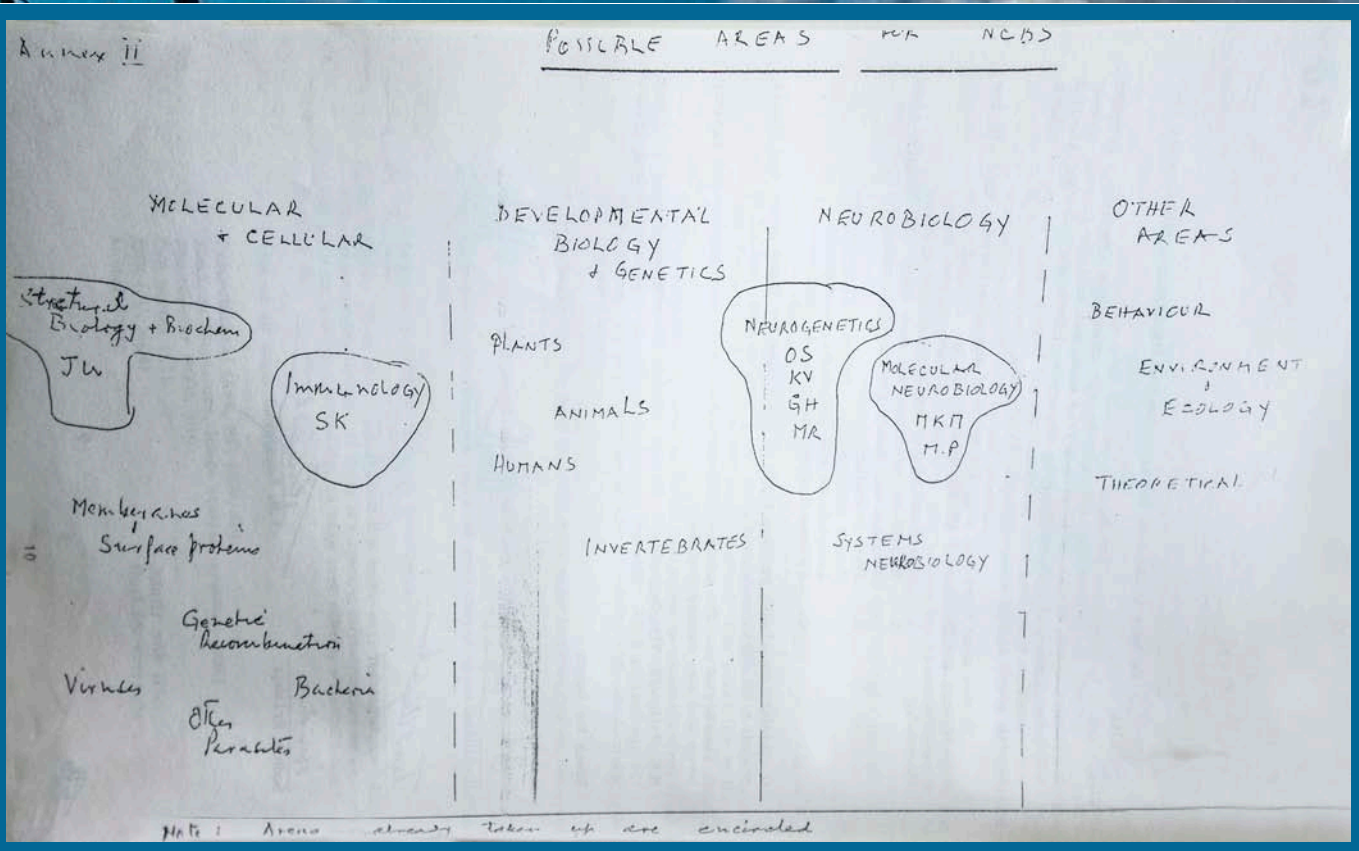


A 1993 sketch by Obaid Siddiqi, Founder, National Centre for Biological Sciences, of possible areas to grow at NCBS

NCBS at crossroads: 2017

The celebrations of our 25th year have come to an end, and as we reflect back at all that was showcased about our scientific efforts in various meetings and workshops, it is apparent that the vision of NCBS as articulated by Obaid Siddiqi (see his drawing -Biology across scales) is being realized in full measure. This is indeed a terrific achievement and we would be justified in saying that we have laid a strong foundation for a unique scientific institution. However, I strongly feel that we are at a fork in our journey ahead. A number of events over the past years necessitate a reevaluation of the functioning of NCBS for our sustained growth and relevance, and to help us chart a path for our future trajectory.

NCBS began as a separate Centre of TIFR in 1992, first in the Molecular Biology Unit at TIFR in Bombay, and then at the IISc Campus in Bangalore where our own laboratories were established. The movement outside Bombay was seen as a necessary step to grow in an independent manner and be relieved from the confines of Colaba where both space and a sense of possibility were at a premium. After a short period at IISc, we moved to our current campus at the University of Agricultural Sciences in 1999, where the seeds were sown for a unique opportunity in biological sciences.

Today NCBS is a premier institute for the basic biological sciences spanning a breadth of biology from molecules to ecosystems, with an excellent set of faculty peppering this spectrum. Serious theory in the Life Sciences in the form of the Simons Centre, and a nationally renowned Wild Life and Conservation Masters Course that has spawned many activities in Biological Sciences across the campus, and in the country, are just some examples of our success stories. Major outreach in different areas, especially natural history and ecology, have also come to fruition. Critical mass is also realized, today with NCBS collaborating vigorously with many excellent international and national agencies to create genuine possibilities for its scientists at many levels. As prescient as Obaid was, it is due to our interactions and engagement with each other at NCBS that we have grown rapidly to generate the breadth and critical mass necessary for us, without feeling that growth overshadows the culture of science at NCBS.

NCBS is today also seen as establishing new benchmarks for the functioning of research institutions in India, both academically and administratively. Several institutional structures such as Science and Research Administration, Core Facilities, and substantial new Laboratory Space as well as an Endowments Cell, have also been put into place. To this we warmly welcome Mr. Pawan Pawha, our new Head of Administration and Finance and look forward to his steering our administration in the right direction to help sustain and better these efforts.

To consider a future for NCBS, we must think more broadly. A close look at standalone biological research institutes the world over, outside University structures (and some within university structures), reveals a simple fact- many bastions of 'fundamental' research now engage their faculty in translational research to ensure their survival. Thus far, we have been able to escape this pressure, shielded behind the large folds of TIFR's skirts since funds for our research were a miniscule part of TIFR's kitty. But now we are very visible; we are now more than a quarter of TIFR's research budget, and expect this to grow if we want to sustain our science. So we are called upon to justify our science in terms of its 'translation or translational potential'. Whilst this is genuinely desirable, we must plan for this very seriously, rather than doing more of the same.

It is in this backdrop that we must make some choices: we have the possibility of teaming up with the ecosystem that we have helped to put together in Bangalore, in a more formal way where it is recognized that our fundamental science is a driver of a vibrant and thriving environment that also delivers on translation, alternatively, to go it alone we must build 'applicable' into our research, and in our hiring, and we need to discuss how this may be done.

This ecosystem for biological research that spans scale [from single molecules to ecosystems (NCBS)], thematics [from basic mechanisms underlying how cells chose their fate by a complex interplay of nature and nurture to the use of stem cells in translational research (inStem)], and technologies [development of core facilities and new technology necessary for Biology and innovation (CCAMP)], has emerged organically on this campus in the last ten years, thanks to the support of the Department of Biotechnology. Here we combine basic with translational research in a seamless fashion across different modes of doing science, PI-driven laboratories (NCBS), collaborative programs (inStem), and entrepreneurial ventures (CCAMP).

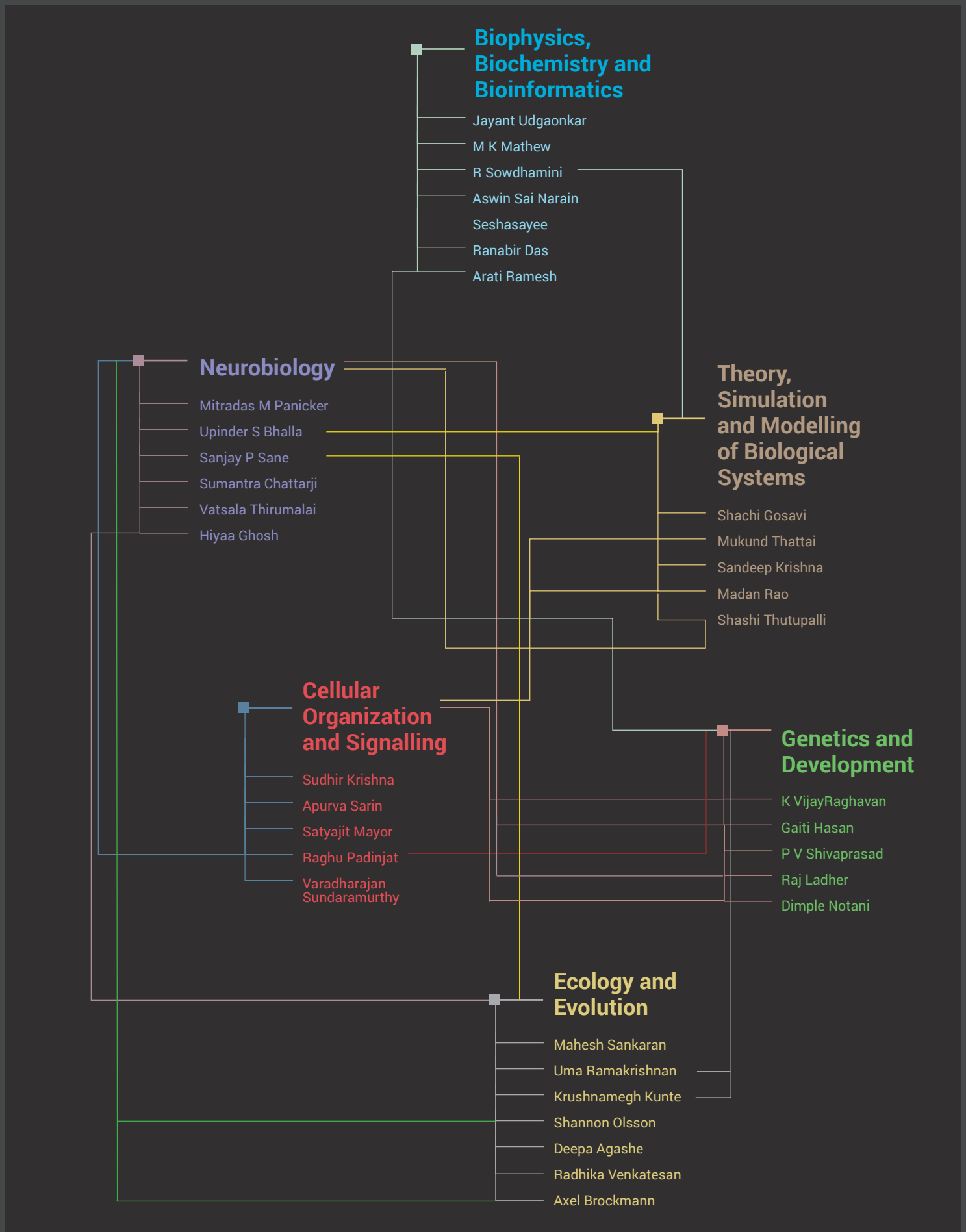
Several inter-institutional programmes are already emerging in the current ecosystem, a cross-campus structural biology initiative endowed with India's first Cryo-EM, a major national effort on a transformative chemical ecology programme that leverages the resources made available by CCAMP and UAS, to name a few. A major effort in looking at neuropsychiatric disorders is also ongoing, driven by scientists from NCBS, inStem and NIMHANS. A few of our NCBS colleagues have also used the inStem/CCAMP structure to diversify and expand the scope of their research.

All the above efforts are enabled by obvious synergies of the different institutional approaches to the biological sciences. These are positive developments but will require respectful cooperation between the entities on this campus to be sustained. An important ingredient of these initiatives is the ability to work together to leverage the benefits of scale without losing sight of the common purpose of doing excellent science. The distinct cultural values of each institution enable this environment, but their sustainability requires an enlightened mechanism to govern the interactions of this cluster of institutions so as to optimize both scientific and administrative synergies, without compromising individual institutional identities and directions. How this will be achieved must be a subject of major discussion in our faculty and with TIFR-DAE, where a functional flexibility of operation for NCBS is an essential requirement.

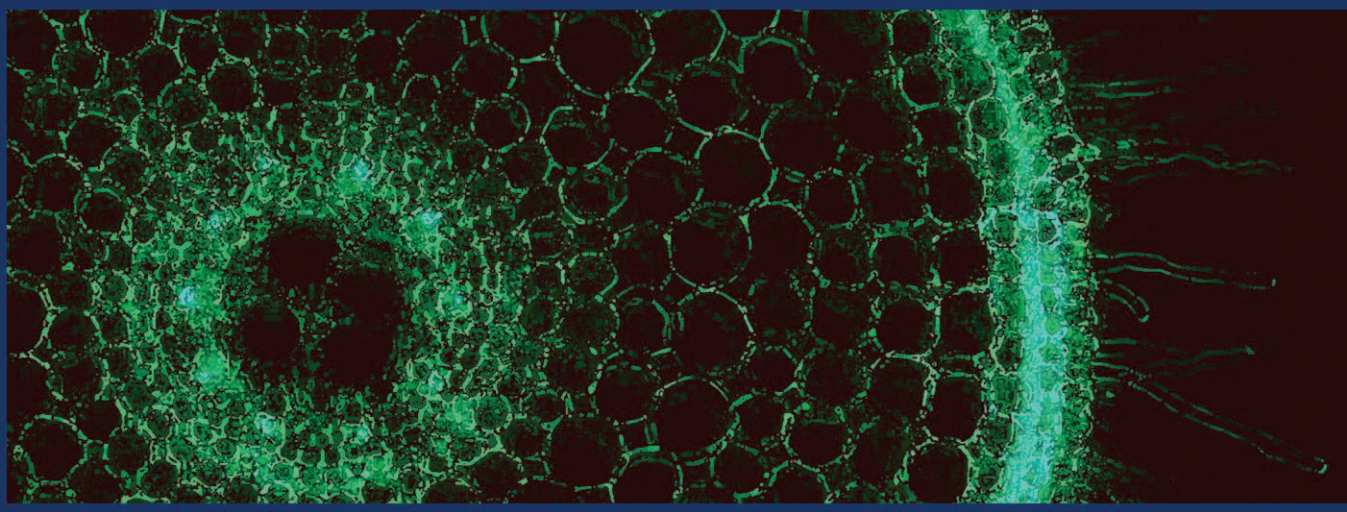
There is of course the alternative model about devolving into separate parts; NCBS, inStem and CCAMP may go their separate ways into three standalone institutions. This is easy to achieve, and does not need any thinking about a governance structure and elaborate collaboration arrangements. A natural outcome of this is the creation of fences between ourselves, and a coming together for an occasional collaborative project where we think the other may be a useful partner.

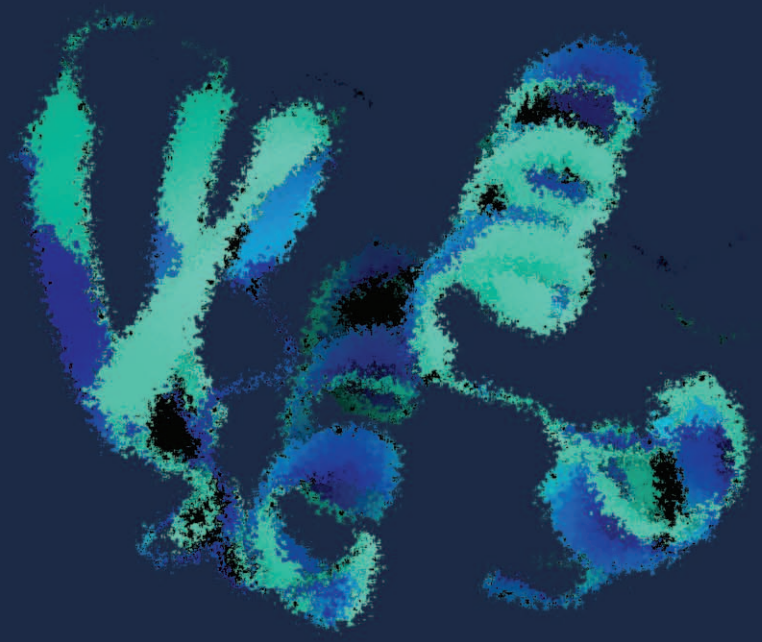
I strongly feel that in the long run for the kind of fundamental science we wish to do at NCBS, a vision of a shared campus is the path we should take, but we must choose the path we wish to follow collectively. This is the fork in our journey ahead. Individuals make up our culture, and open engaged interactivity and a shared concern for what is excellent science is sufficient ballast to withstand the fallouts of the path we may choose.

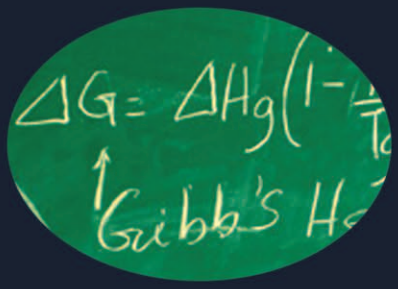
Satyajit Mayor
Centre Director

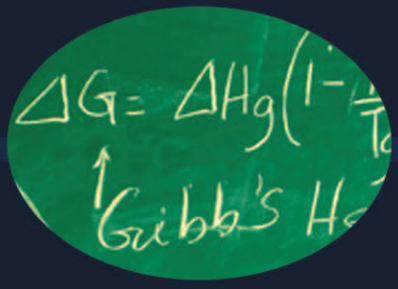


* Several of our investigators have research interests spanning multiple areas of biology and only one of their affiliations is given here.









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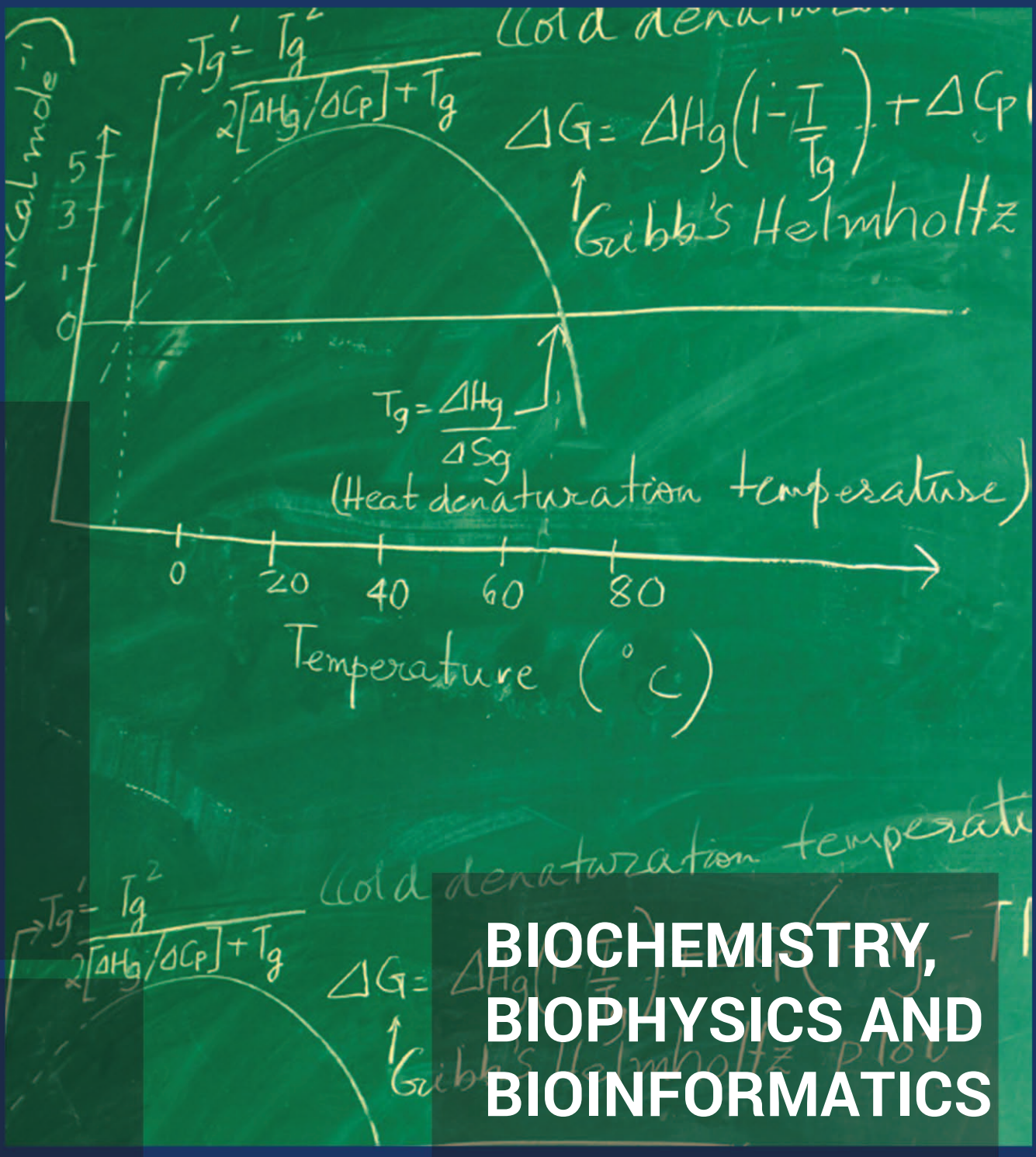


BIOCHEMISTRY, BIOPHYSICS AND BIOINFORMATICS

ASWIN S N SESHASAYEE 17 | RANABIR DAS 18 | ARATI RAMESH 19

HOW DO PROTEINS FOLD, UNFOLD AND MISFOLD?

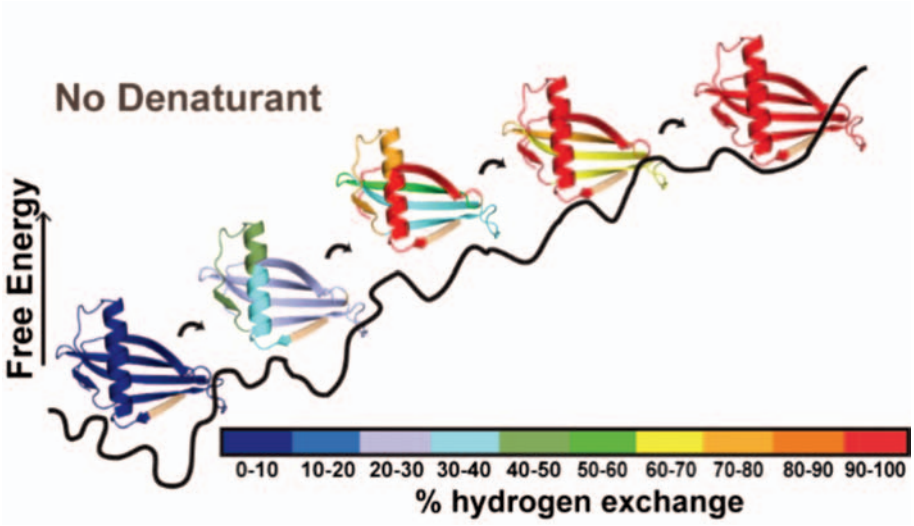
Jayant B Udgaonkar

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 dissembles during unfolding, and how a protein forms aggregates when folding or unfolding goes wrong.

Publications

Moulick, R. & Udgaonkar, J.B. (2017). Identification and structural characterization of the precursor conformation of the prion protein which initiates misfolding and oligomerization. J. Mol. Biol. 429, 886-899

Aghera, N. and Udgaonkar, J. B. (2017) Step-wise assembly of β-sheet structure during the folding of a SH3 domain revealed by a pulsed hydrogen exchange-mass spectrometry study. Biochemistry 56, 3754–3769



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

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 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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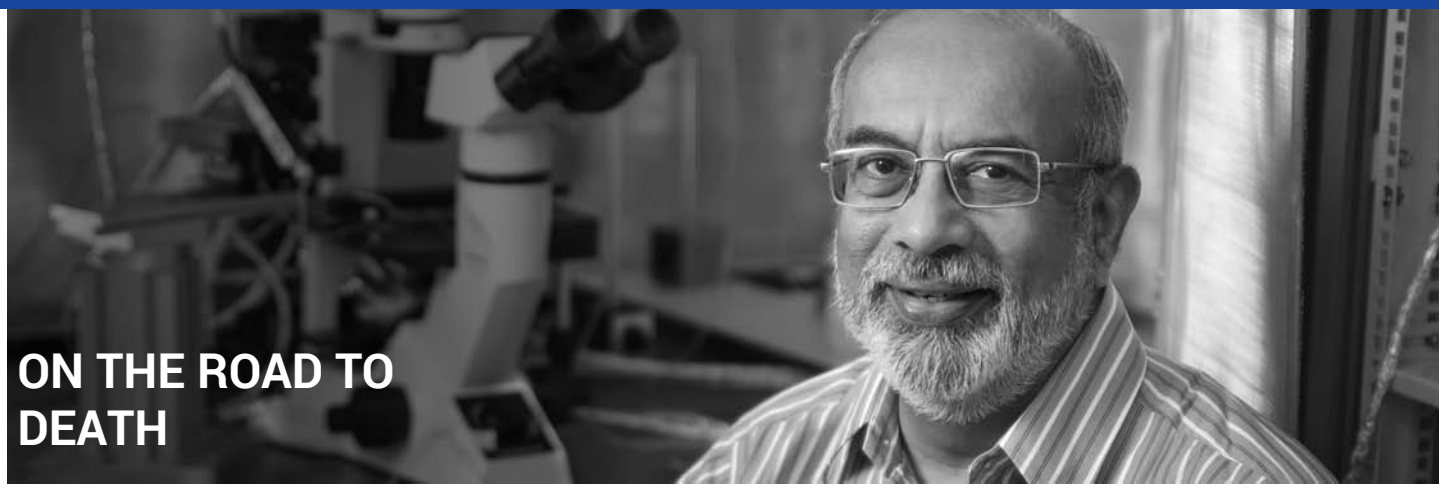
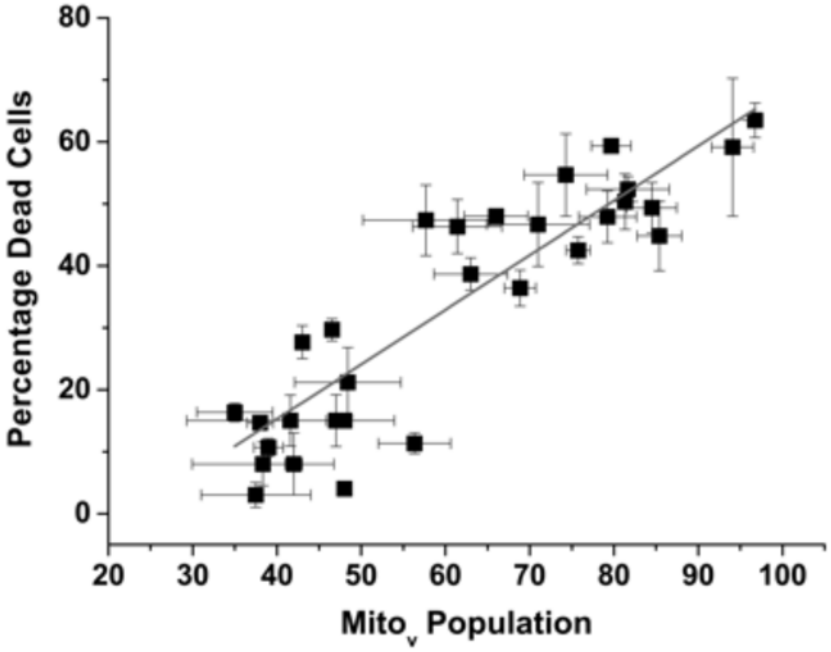


ON THE ROAD TO DEATH

M K Mathew

Cell death pathways initiated by the mitochondrion can be abrogated by the activity of anti-apoptotic proteins such as Bcl2 and Hexokinase. One mechanism for this is the retention of the Voltage Dependent Anion Channel in the cytosol, essentially reducing its levels in the mitochondrion.



Correlation between the percentage of cells in which heterologously expressed VDAC is localised to mitochondria (Mito$_v$) and cell death. The best fit line has an R value of 0.81

The mitochondrion serves as an integrator of signals reporting on the health of a cell and, if the situation arises, initiates a death cascade. The latter process involves the Voltage Dependent Anion Channel (VDAC), a protein resident in the outer membrane of mitochondria. Heterologous expression of VDAC can induce cell death, which can be mitigated by concomitant overexpression of Hexokinase. We report that upon overexpression, fluorescently tagged VDAC is distributed between the cytosol and mitochondria. However, cell death ensues only when the protein, which is synthesized on cytoplasmic ribosomes, migrates to the mitochondrion.

Further, coexpression of rat Hexokinase II (rHxKII) can delay the translocation of human VDAC1 (hVDAC1) protein to mitochondria and thereby inhibit VDAC-induced cell death. Variation in the level of HxK protein as seen endogenously in different cell lines, or as experimentally manipulated by silencing and overexpression, can lead to differential VDAC translocation kinetics and related cell death. Intriguingly, in otherwise unperturbed cells in culture, there is a small but significant amount of soluble VDAC in the cytosol present in a complex with HxK. This complex could well determine how a cell is poised with respect to incoming thanatopic signals, thereby tilting the survival/death balance in pharmacologically interesting situations, such as neurodegeneration and cancer.

Publications

Dubey, A.K., Godbole, A. & Mathew, M.K. (2016) Regulation of VDAC trafficking modulates cell death. Cell Death Discov. 2, 16085; doi:10.1038/cddiscovery.2016.85

Lall, S. & Mathew, M.K. (2017) Dynamics of Membrane Proteins in Membrane Organization and Dynamics. Springer Series in Biophysics in press

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COMPUTATIONAL APPROACHES TO PROTEIN SCIENCE

R Sowdhamini

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

Publications

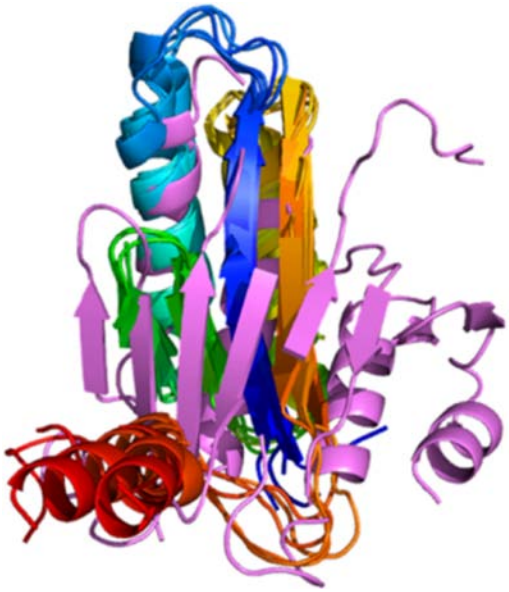
Karpe, S.D., Jain, R., Brockmann, A. and Sowdhamini, R (2016). Identification of complete repertoire of Apis florea odorant receptors reveals complex orthologous relationships with Apis mellifera. Genome Biology and Evolution, pii evw202.

Gandhimathi, A., Pritha G., Sridhar H., Oommen. K. Mathew and Sowdhamini, R (2016). PASS2 database for the structure-based sequence alignment of distantly related SCOP domain superfamilies: update to Version 5 and added features. Nucleic Acids Research, 44(D1):D410-4. doi: 10.1093/nar/gkv1205.

Honors and Awards

JC Bose fellowship (2016-2021)

Visiting Professorship in the University of Nantes, June-July 2017



Sequence alignment of divergent protein domains, which belong to a superfamily, is facilitated by the comparison of structural properties – such as secondary structure, solvent accessibility and hydrogen bonding patterns.

Sequence alignments serve as evolutionary models and, where relevant, can be helpful to recognise highly deviant members – the outliers. Shown are the structures of domains of the thiamine-HMP binding proteins that belong to the highly popular ferredoxin fold, in the superimposed form. An "outlier" member is shown in pink colour (Gandhimathi et al., 2013, 2016).

Reference:

Gandhimathi A., Anu Nair, Hariharaputran S. and Sowdhamini R. (2013) Rebelling for a reason: Protein structural "outliers". PLoS ONE 8(9):e74416.

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 structure 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 the members of various entire protein 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.

ADAPTATION THE BACTERIAL WAY!

Aswin Sai Narain Seshasayee

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.

Bacteria, besides being agents of a variety of infectious diseases, are the most predominant form of free-living life known on Earth. Some bacteria live in stable environments, such as in a symbiotic relationship with a host; others can live across multiple habitats each presenting its own set of nutrients and adversaries. This leads to two key points which are of interest to us:

(a) Any given bacterium should code for only those genes that would allow it to make optimal use of the conditions prevailing in its set of habitats.

(b) Regulation is critical especially to organisms that traverse multiple types of habitats to ensure that only those genes required at any given time point are expressed.

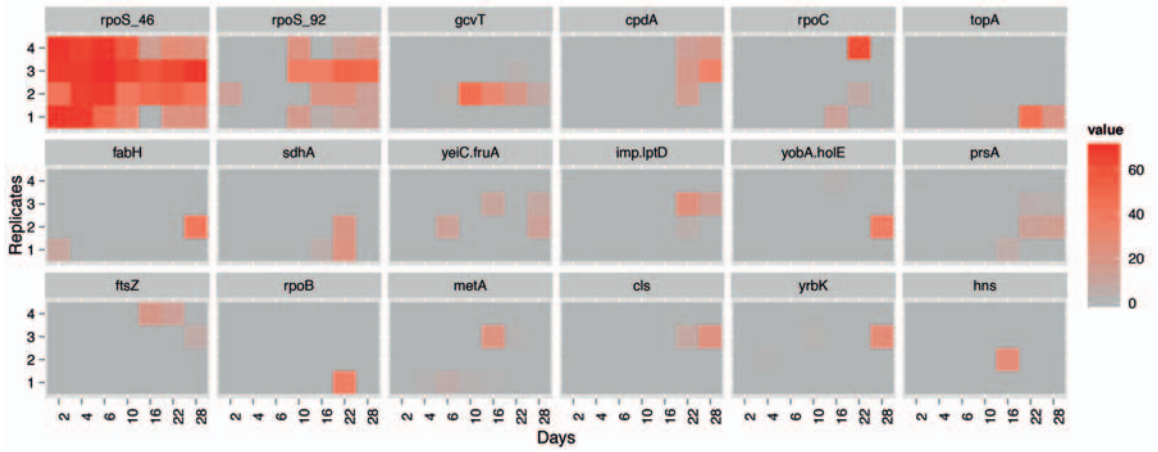
The primary focus of our research is to investigate bacterial regulatory systems from the stand-point of both their occurrence in diverse bacterial genomes and their role in achieving global and function-specific gene expression control in model bacteria such as *Escherichia coli*.

We tackle our research questions using genome-scale techniques. We observe evolution in real-time in the laboratory and use techniques that interrogate the bacterial genetic material, and its functional readouts, in full to understand the mechanisms by which bacteria adapt to their circumstances, including those that involve the management of starvation and resistance to stress and perturbations that disrupt its genetic architecture.

Publications

Chib, S., Ali, F., Seshasayee, A.S.N. (2017) Genomewide Mutational Diversity in Escherichia coli Population Evolving in Prolonged Stationary Phase. mSphere. 2(3).

Khedkar, S., Seshasayee, A.S.N. (2016) Comparative Genomics of Interreplichore Translocations in Bacteria: A Measure of Chromosome Topology? G3 (Bethesda). 6(6):1597-606.



The appearance (intensity of red colour represents the prevalence of the mutation) and disappearance of mutations in bacterial populations evolving under deep stationary phase.

POST-TRANSLATIONAL MODIFICATIONS IN HOST-PATHOGEN INTERACTIONS

Ranabir Das

Viral factors hijack the host machineries to their own advantage. During infection, several host defense mechanisms are destabilized by using the ubiquitin-proteasome pathway. This group studies the interactions between viral factors and host proteins to understand this process.

Publications

Sengupta, I., Bhate, S., Das, R., Udgaonkar J.B.*, (2017), Salt-binding induced oligomerization of the mouse proin protein monitored by real time NMR, J. Mol. Biol., 429(12): 1852-1872. *Corresponding authors.*

Chakrabarti, K.S., Li, J., Das, R., Byrd, R.A.*, (2017), Conformational dynamics and allostery in E2:E3 interactions driving ubiquitination: Ube2g2 and gp78, Structure, 25(5):794-805. *Corresponding authors.*

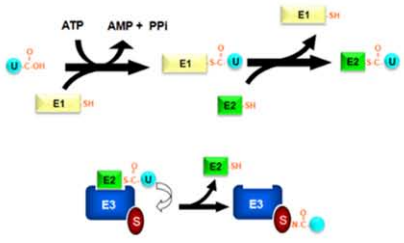
The Ubiquitin Pathway

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.

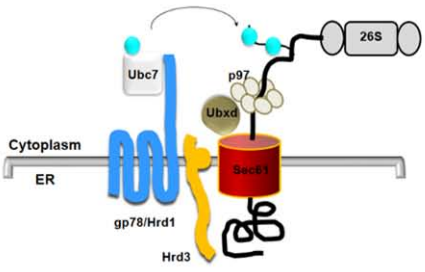
Protein Quality Control: Despite the aid of chaperones, a significant fraction of newly synthesized proteins ends up being misfolded. Cells have evolved protein quality control systems to ensure that these potentially toxic species are detected and eliminated. The best characterized of this mechanism 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 to investigate how proteins misfold? How are misfolded proteins 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 destabilized by the virus using the ubiquitin-proteasome pathway. We study the interactions between viral factors and host proteins to understand this process.

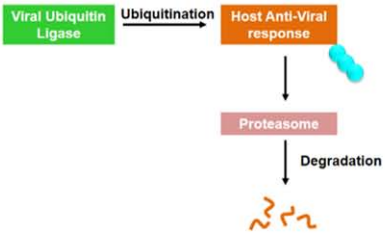
We regularly use NMR spectroscopy to study structure and dynamics of proteins relevant to the projects. In addition, we employ various other biophysical, biochemical and computational tools.



Ubiquitination – A Multi-step reaction



ER Associated Degradation



Viral hijack of the host Ubiqutin pathway

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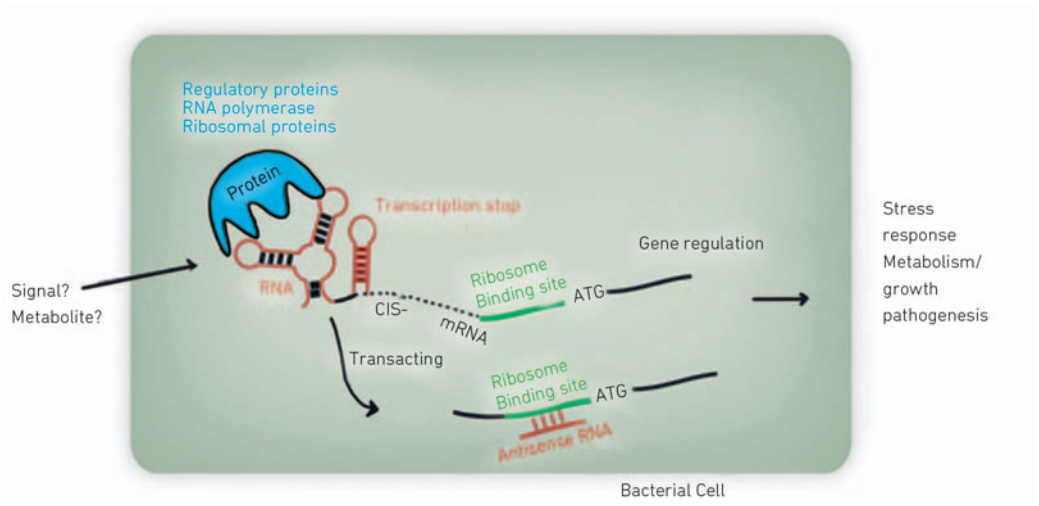
STRUCTURAL STUDIES OF RIBOSWITCHES AND RNA-BINDING PROTEINS IN BACTERIA

Arati Ramesh

We are currently focused on understanding structural and functional mechanisms by which non-coding RNAs bind intracellular metabolites to control the expression of downstream genes. We are particularly interested in understanding their roles in bacterial pathogenesis with an emphasis on mycobacterial species.



Bacterial gene regulation by ligand sensing RNAs and RNA-protein complexes.

Publications

DebRoy, S., Gebbie, M., Ramesh, A., Goodson, J.R., Cruz, M.R., Van Hoof A, Winkler, W.C and Garsin D.A. (2014). A riboswitch-containing sRNA controls gene expression by sequestration of a response regulator. Science. 345(6199), 937-40.Comment by Chen J. and Gottesman S. in Science

Ramesh, A. and Winkler, W.C. (2014) Metabolite-binding ribozymes. BBA Gene Regulatory Mechanisms. 1839(10):989-994.

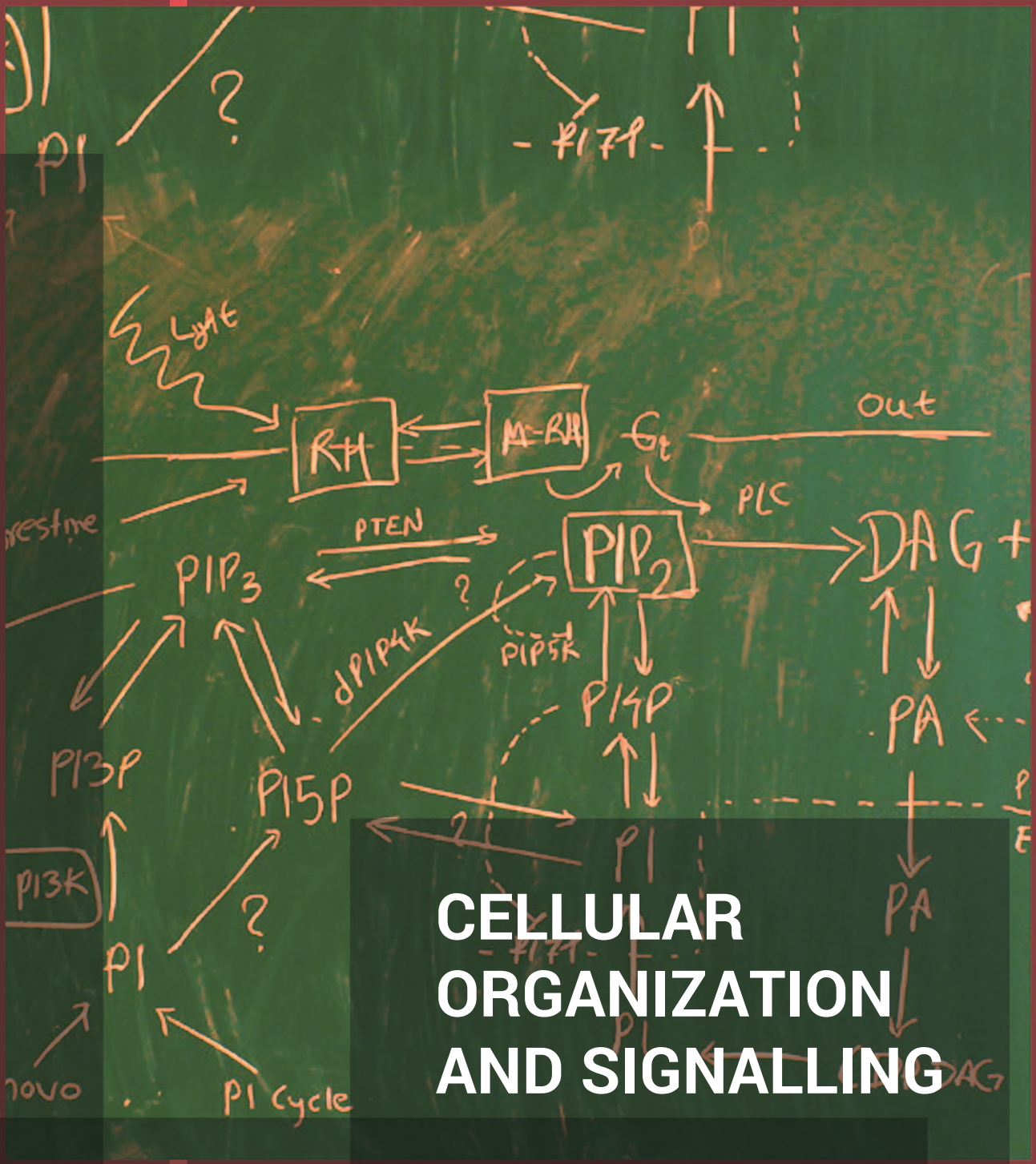
Ramesh A. (2015) Second messenger-sensing riboswitches in bacteria. Semin. Cell Dev. Biol. 47-48, 3-8.

All organisms sense and respond to their environment. This response requires the precise regulation of genes. It is becoming increasingly evident that a major mode of gene-regulation is through non-coding RNAs. Bacteria being particularly adept at cellular economy use RNAs to control a number of processes such as growth, metabolism, adaptations and responses to changing environments, etc. My lab is interested in understanding how bacteria use RNAs to sense and respond to environmental cues. Using a combination of approaches that include X-ray crystallography, RNA-protein biochemistry, biophysical, bioinformatics and *in vivo* methods, we study regulatory RNAs and RNA-protein complexes in bacteria.

We are particularly interested in a class of non-coding RNAs called riboswitches, which directly bind cellular metabolites to control the expression of downstream genes. These sensory RNAs fold into complex three-dimensional architectures that are fine-tuned to recognize their cognate ligand. Our goal is to understand how RNAs create the structural diversity needed to bind diverse metabolites, what kind of metabolites are recognized by naturally occurring RNAs, and how this ultimately leads to genetic control.

Regulatory RNAs often function not in isolation, but as intricately woven protein-RNA networks. This collaboration between regulatory RNAs and their protein partners is of fundamental importance to bacterial biology. My lab seeks to identify protein-RNA networks that control genes involved in bacterial pathogenesis with an emphasis on mycobacterial species.

SUDHIR KRISHNA 22 | APURVA SARIN 23 | SATYAJIT MAYOR 24



CELLULAR ORGANIZATION AND SIGNALLING

RAGHU PADINJAT 25 | VARADHARAJAN SUNDARAMURTHY 26

UNDERSTANDING HUMAN CERVICAL CANCER PROGRESSION AND BUILDING A BIOLOGY-MEDICINE INTERPHASE

Sudhir Krishna

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

Publications

Ammothumkandy, A., Maliekal T. T., Bose, M. V., Sunder Singh, S. S., Rajkumar, T., Thejaswini, B., Giri, G. V. and Krishna, S (2016). CD66 and CD49f expressing cells are associated with distinct neoplastic phenotypes and progression in human cervical cancer. European Journal of Cancer, 60, 166-178.

Arya, D., Sasikala, P. S., Ross, C., Dasaradhi, P., Shang, L. & Krishna, S (2017). MiR-182 regulates percentage of myeloid and erythroid cells in chronic myeloid leukemia. Cell death and disease: 8, e2547;

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 and is dependent on Notch signalling (Bajaj J. et al., Cancer Research 2011 and Pattabiraman C. et al., Cancer Research 2014). Currently, following the work of Aswathy Ammothumkandy and collaborators from Kidwai Memorial Hospital showing that CD66+ cells are associated with metastasis progression and have distinct roles in migration, Calvin Rodrigues and Leanna Rose Joy are exploring the role of epigenetic regulators in cervical cancer progression and analyzing antibodies that target CD66+ proteins.

Since 2008, we have been working intensively with the St. John’s medical college campus and built extensive research laboratories, explored joint teaching programs with medical colleagues, developed gene editing and NGS platforms that will enable better HLA typing (Gowda, M. et al., 2016) and supported Chitra Pattabiraman and colleagues in developing a viral genomics program.

Top left: Dr.Cecil Ross, Dr.Karuna Ramesh, Deepak Arya, Shankar Rao. Top right: Lynn Pais, Sweta Srivastava, Srinag, Katte Rao. Bottom (from left to right): H Krishnamurthy, NCBS; Deepak Arya, Gene editing, CML; Maria Bukelo, Pathologist, Clinical research fellow; Neha Vyas, Faculty, SJRI

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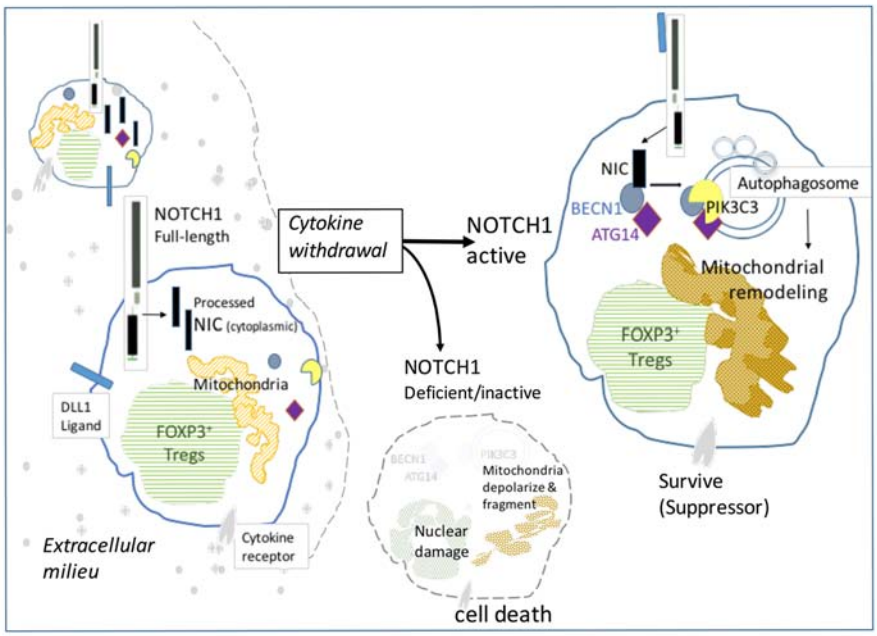
SIGNALLING STRATEGIES REGULATING CELL SURVIVAL

Apurva Sarin

Metabolic reprogramming in mature T-cells in the mammalian immune system, is intertwined with decisions of differentiation and homeostasis. Metabolic plasticity is necessitated by the changing niches that T-cell subsets function in. Our research explores how nutrients govern transitions critical for T-cell function.



A Notch1-Autophagy signalling axis controls cell survival and function in murine T-regulatory cells.
(Reproduced with permission from Sarin & Marcel, Autophagy, Volume 13, pg 446-447, 2017.)

Publications

Marcel, N. and Sarin, A. (2016) Notch1 regulated autophagy controls survival and suppressor activity of activated murine T-regulatory cells. eLife, 5:e14023

Marcel, N., Perumalsamy, L.R., Shukla, S.K., Sarin, A. (2017). The lysine deacetylase Sirtuin 1 modulates the localization and function of the Notch1 receptor in regulatory T cells. Sci Signal. 10(473). pii: eaah4679. doi: 10.1126/scisignal.aah 4679.

Remodeling and repair require recruitment of new cells by cell division and specialization, as also retrenchment, by deletion of redundant cells. In many tissues in adult animals, this is an ongoing process, critical for homeostasis. While an over-simplification, it is almost as though minute-to-minute, cells weigh up a multitude of internal and external signals, some which favor existence, others deletion. In each instance, the outcome depends on a variety of potential signals, as also differing signal-sensitivities of cells.

We work on T-cells to understand signal integration controlling such outcomes. T-cells work in highly variable micro-environments and metabolic reprogramming in response to nutritional cues is an important determinant of cell function. We largely rely on the recapitulation of many of these events in the culture dish and in mouse models, in order to explore molecular controls operating within cells as well as interactions between cells. Our research is revealing how inputs from receptors of the Notch family of proteins integrate metabolic programmes underlying cell fate decisions in T-cells and consequently, maintenance of lineage stability in activating environments.

Identifying molecular underpinnings defining these interactions as also a more general description of Notch activity in other contexts, are ongoing efforts.

MECHANISMS OF MEMBRANE ORGANIZATION AND ENDOCYTOSIS

Satyajit Mayor

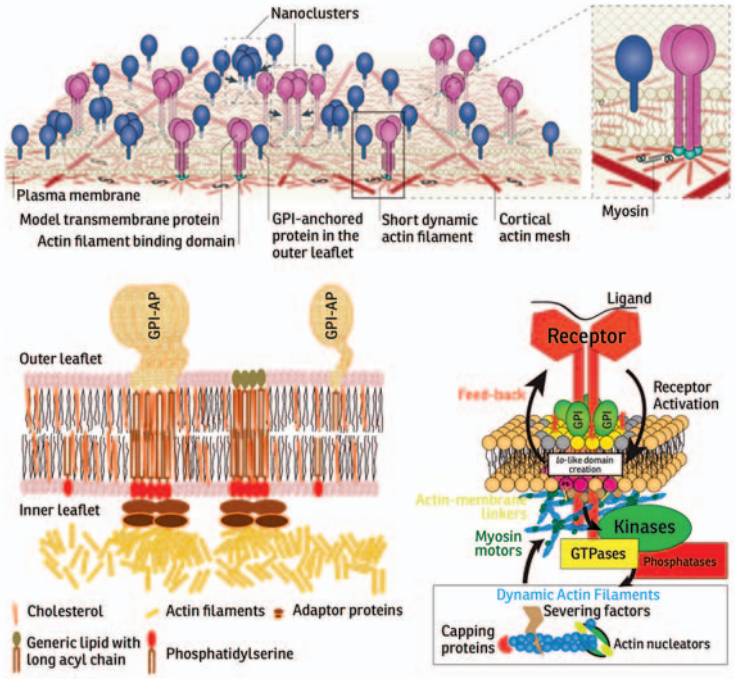
The principal focus of our laboratory is to uncover physico-chemical rules that govern local organization of the cell membrane and connect this to cellular and organismal physiology. Specifically, we ask how does the cell build functional signalling complexes at the plasma membrane? What are the requirements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

Publications

Taylor, M.J., Husain, K., Gartner, Z.J., Mayor, S., Vale, R.D. (2017) A DNA-Based T Cell Receptor Reveals a Role for Receptor Clustering in Ligand Discrimination. Cell. 169(1):108-119

Hemalatha, A., Prabhakara, C., Mayor, S. Endocytosis of Wingless via a dynamin-independent pathway is necessary for signalling in Drosophila wing discs. Proc Natl Acad Sci U S A. 113:45; E6993–E7002

Sezgin, E., Levental, I., Mayor, S., Eggeling, C. (2017). The mystery of membrane organization: composition, regulation and roles of lipid rafts. Nat Rev Mol Cell Biol. doi: 10.1038/nrm.2017.16



Nanoclusters are built by contractile actin platforms, resembling asters, and transbilayer coupling and mechanisms for nanocluster formation of outerleaflet lipid-anchored proteins.

The primary focus of our laboratory is to understand physico-chemical principles behind the organization of the plasma membrane in a living cell and how this informs cell and organismal physiology. Specifically we wish to understand how a eukaryotic cell constructs signalling complexes at the plasma membrane and regulates endocytic processes. The local and global control of membrane composition is also an emerging question in the laboratory.

The plasma membrane does not merely separate the outside from the inside of a cell but mediates bilateral communication. To understand how eukaryotic cells respond and react to their environment, we study how a cell can regulate the local organization of its membrane constituents, while the membrane itself behaves like a fluid matrix. New insights from a variety of studies, including that from our laboratory, show that the local chemistry of these 2D plasma membranes is finely tuned and far from an equilibrium mixture. We are providing a new framework wherein the cell membrane behaves as an active composite, with the underlying dynamic cortical actin filaments controlling the local composition of membranes. There are numerous offshoots from such an understanding of membrane organization. Among them, we now seek to explain how cells can construct signalling complexes and sort membrane constituents, in response to their environment. The cell membrane also is 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 also study endocytic mechanism, in particular a class of non-canonical endocytic pathway that functions in the absence of both clathrin and dynamin, and how this regulates the developmental program in the context of a developing wing imaginal disc of *Drosophila*.

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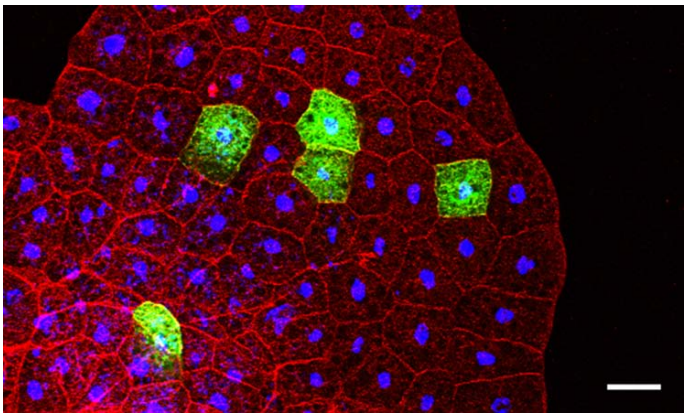
PHOSPHOINOSITIDE SIGNALLING IN CELL BIOLOGY

Raghu Padinjat

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 cellular signalling mediated by these molecules.



Cell signalling *in vivo* using *Drosophila*: The *Drosophila* larval fat-body stained for actin (red) and the nuclei (blue, DAPI). The cells in green express GFP because of a heat-inducible genetic construct that causes somatic gene recombination. Scale: 50 µm

Publications

Kamalesh, K., Trivedi, D., Toscano, S., Sharma, S., Kolay, S., Raghu, P. (2017) Phosphatidylinositol 5-phosphate 4-kinase regulates early endosomal dynamics during clathrin-mediated endocytosis. J Cell Sci. 130(13):2119-2133.

Thakur, R., Panda, A., Coessens, E., Raj, N., Yadav, S., Balakrishnan, S., Zhang, Q., Georgiev, P., Basak, B., Pasricha, R., Wakelam, M.J., Ktistakis, N.T., Raghu, P. (2016) Phospholipase D activity couples plasma membrane endocytosis with retromer dependent recycling. Elife.16;5.

Architecture of phosphoinositide signalling systems

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 sub-cellular 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, polarized 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.

We mainly use *Drosophila* as our model system; the goal is to discover key principles of signal transduction that are likely to be conserved during evolution but are experimentally more tractable in *Drosophila*. It is hoped that in the medium term, our analysis in *Drosophila* will inform studies of equivalent signalling pathways in mammalian models with more immediate biomedical relevance. 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.

BIOLOGY OF HOST-PATHOGEN INTERACTIONS DURING INTRACELLULAR INFECTIONS

Varadharajan Sundaramurthy

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 to address these questions.

Publications

Sundaramurthy, V., Korf, H., Singla, A., Scherr, N., Nguyen, L., Ferrari, G., Landmann, R., Huygen, K., Pieters, J. (2017). Microbes Infect. Survival of Mycobacterium tuberculosis and Mycobacterium bovis BCG in lysosomes in vivo. pii: S1286-4579(17)30097-7. doi: 10.1016/j.micinf.2017.06.008. PMID:28689009 (*corresponding author).*

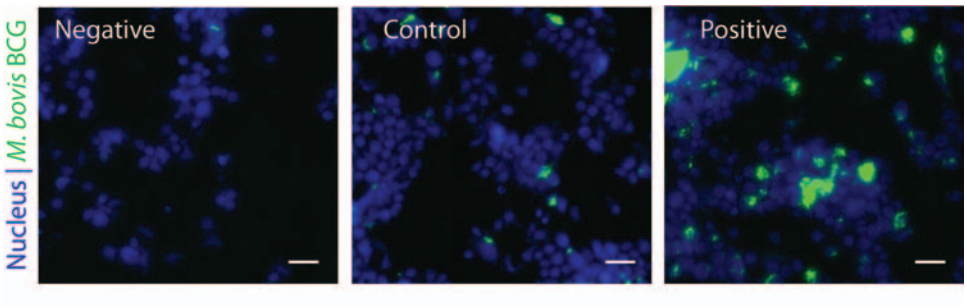
Caicedo JC, Cooper S, Heigwer F, Warchal S, Qiu P, Molnar C, Vasilevich AS, Barry JD, Bansal HS, Kraus O, Wawer M, Paavolainen L, Herrmann MD, Rohban M, Hung J, Hennig H, Concannon J, Smith I, Clemons PA, Singh S, Rees P, Horvath P, Linington RG, Carpenter AE. (2017). Data analysis strategies for image-based cell profiling. Nat Methods. 14(9):849-863.

Honors and Awards

Invited to give a talk in Cold Spring Asia meeting on Bacterial Infection and Host Defense, Suzhou, China, April 2017

Intracellular pathogens are often considered as master cell biologists. They understand the host cells perfectly and manipulate them in subtle and non-subtle ways to ensure a successful infection. A successful infection is a complicated and fascinating process that entails the entry of the pathogen, establishment and maintenance of an intracellular niche, acquisition of nutrient and development cues, replication and finally exit from the host cell. This whole sequence of events of course occurs within the contours of the host cell, utilizing the host cellular machinery and often in the face of direct counter attacking measures from the hosts.

Pathogens and host cells have co-evolved for a long time and hence the host-pathogen interface offers fascinating glimpses into the forces that have shaped the contours of pathogenesis. The broad goal of my lab is to understand the contours of these interactions at multiple levels by studying the modulation of critical host pathways by pathogens and exploiting the potential of this knowledge for drug discovery. In particular, I am interested in understanding the modulation of host trafficking pathways by two very different pathogens, namely *Mycobacterium* and *Plasmodium*, the causative agents of the deadly diseases tuberculosis (TB) and malaria, respectively. Towards this, I aim to apply a combination of chemical genetics, quantitative image analysis and high content screening tools together with conventional cell and molecular biological approaches.



Fundamental host cell processes such as trafficking are altered to generate and sustain the fine balance often associated with the intracellular survival of pathogens such as *M. tuberculosis*. In our lab, we are trying to gain a comprehensive and quantitative understanding of this 'equilibrium', and identify perturbations that tilt this balance in either ways.

The figure above shows human macrophages infected with *M. bovis* BCG in its equilibrium state (central panel, "control"),and treatment with perturbations that either kill the intracellular bacteria (left panel, "negative") or result in enhanced bacterial survival (right panel, "positive"), without affecting the viability of the host cells. Such perturbations will give mechanistic insights into the factors governing the equilibrium between intracellular mycobacterial infections and host cells. Scale bar = 100 μm.

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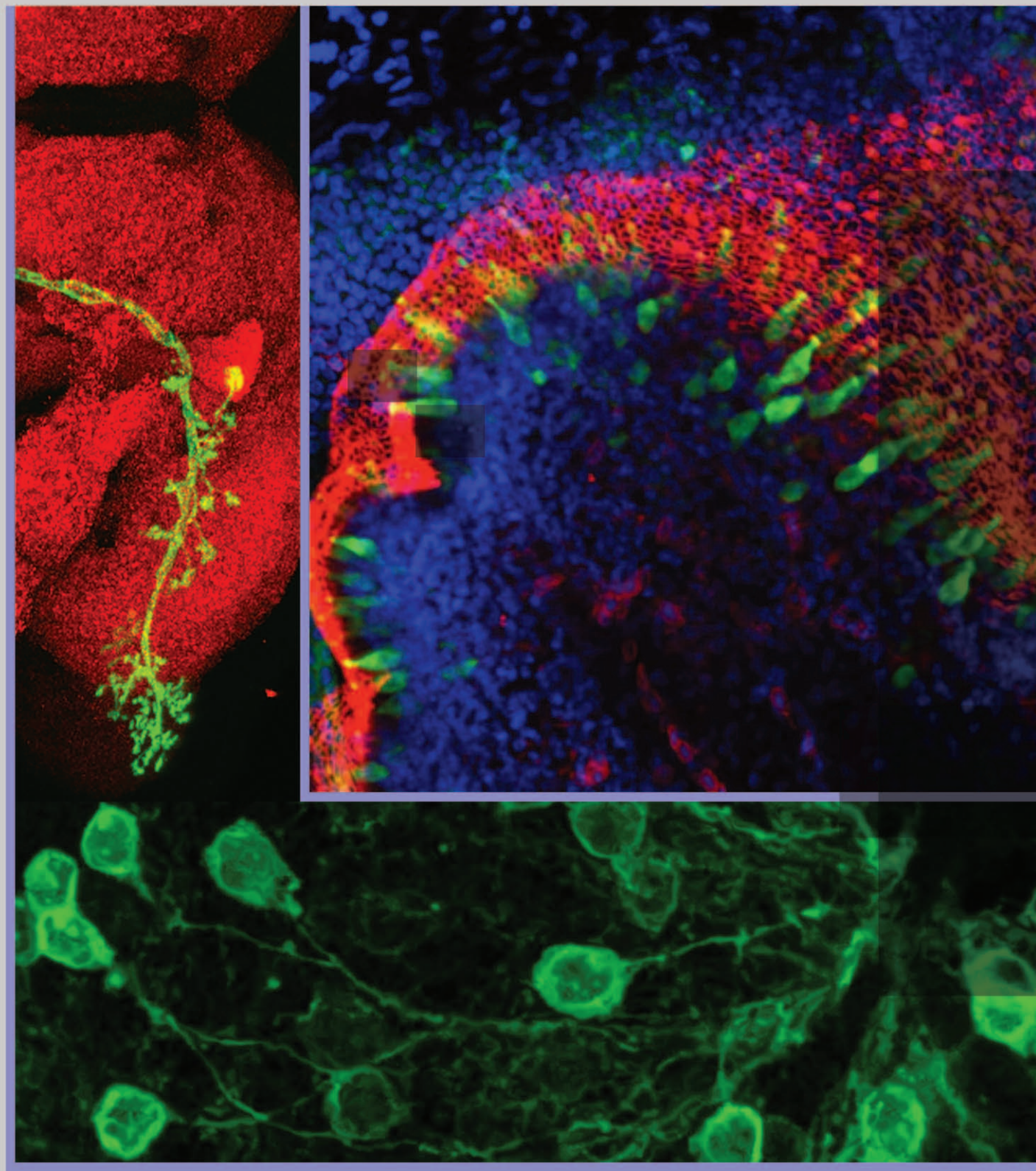
Photography by Pritha Ghosh, Research Scholar, R Sowdhamini lab



M M PANICKER 30 | UPINDER S BHALLA 31 | SANJAY P SANE 32

NEUROBIOLOGY

SUMANTRA CHATTARJI 33 | VATSALA THIRUMALAI 34 | HIYAA GHOSH 35

ROLES OF SEROTONIN IN NEURAL AND NON-NEURAL SYSTEMS

Mitradas M Panicker

The role of serotonin in the nervous system and in pluripotent stem cells is being explored using *in vitro* cellular models and transgenic mice. Cellular models from individual-specific pluripotent stem cells are being used to study Alzheimer's disease.

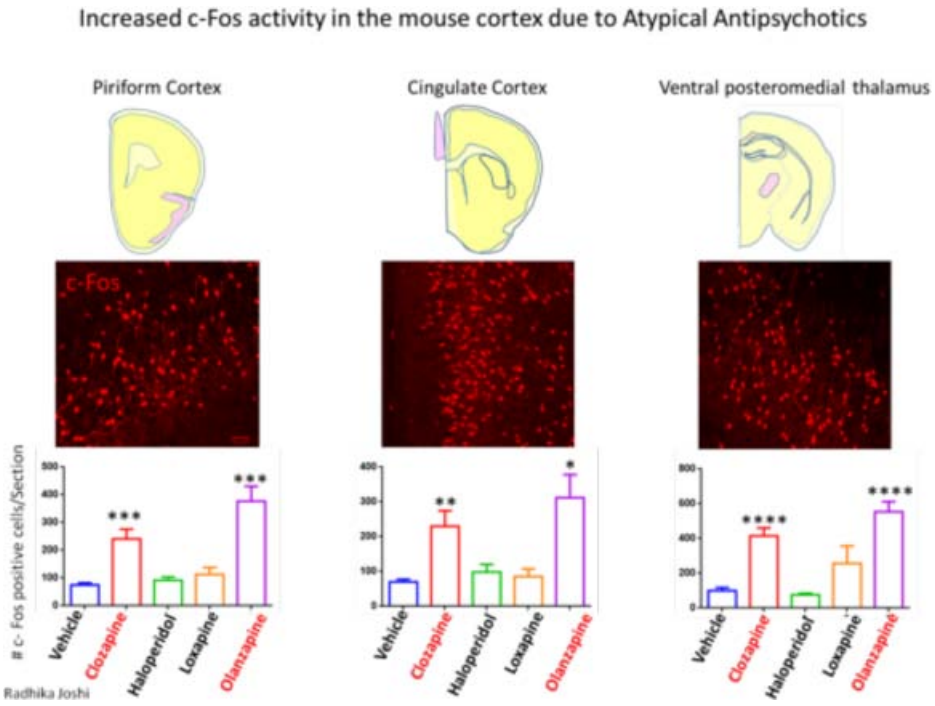
Publications

Joshi, R.S., Quadros, R., Drumm, M., Ain, R., Panicker, M.M. (2017) Sedative effect of Clozapine is a function of 5-HT$_{2A}$ and environmental novelty. Eur Neuropsychopharmacol. 27(1):70-81

Muthusamy, T., Mukherjee, O., Menon, R., Prakash, Bangalore M, Panicker, M.M. (2016) A Method to Identify and Isolate Pluripotent Human Stem Cells and Mouse Epiblast Stem Cells Using Lipid Body-Associated Retinyl Ester Fluorescence. Stem Cell Reports. 7(2):306.

Serotonin (5-HT), a major neurotransmitter has a major role in human behaviour and physiology. We have spent the last few years trying to understand the role of the serotonin 5-HT$_{2A}$ receptor subtype and its interaction with its endogenous agonist i.e. 5-HT, partial agonists i.e. dopamine and clinically used drugs such as antipsychotics.

We generated a transgenic mouse that lacks the 5-HT$_{2A}$. Behavioural analysis of these mice, with and without antipsychotics have provided unique insights to the role played by antipsychotics in modulating behaviour. We find that sedation, caused by the atypical antipsychotic – Clozapine is affected by the environment at low doses but not at higher doses. Clozapine seems to exert its effects both in a 5-HT$_{2A}$ dependent and independent manner. Using the c-fos TRAP system devised by Luo and colleagues, we have also identified neurons in different regions of the brain that get activated by antipsychotics using a fluorescent reporter. We have established human induced pluripotent stem cells from control and patient samples with Late Onset Alzheimer's disease (LOAD) and generated isogenic lines from these with different APOE alleles. We have also identified retinyl esters as a novel endogenous fluorescent marker for 'primed' pluripotent stem cells.



Immediate early gene c-Fos expressing cells marked by tdTomato expressing neurons in the mouse cortex on acute administration of antipsychotics.

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SINGLE NEURON SEQUENCE RECOGNITION AS A BUILDING BLOCK FOR BRAIN COMPUTATION AND MEMORY

Upinder Singh Bhalla

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 and are modified when mice learn new tasks.

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 analyze how sequences can be discriminated by single cells.

We have developed a multiscale simulator, MOOSE, to model brain functions across scales. We use our own and collaborator data to compare cellular responses between healthy and fragile-X mouse neurons. These results provide input to a comprehensive model of molecular signalling from transcription control to the synapse.

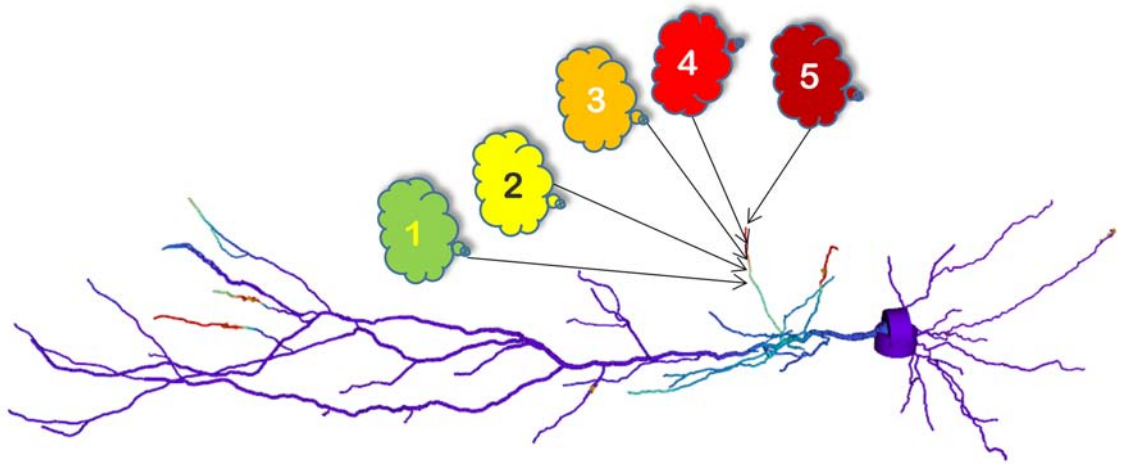
We have shown that sequence discrimination emerges from reaction-diffusion signalling in small dendritic zones. We are examining how such computations may generalize to different time-scales and yield plasticity effects such as formation of new synapses. We are also devising models to study how information may be robustly maintained for extended periods in the synapse.

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

Publications

Bhalla, U.S. (2017). Synaptic input sequence discrimination on behavioral time-scales mediated by reaction-diffusion chemistry in dendrites. eLife 6. pii: e25827. doi: 10.7554/eLife.25827.

Nair, A.G., Bhalla, U.S., Kotaleski, H. (2016). Role of DARPP-32 and ARPP-21 in the Emergence of Temporal Constraints on Striatal Calcium and Dopamine Integration. J. PLoS Comput Biol. 12(9):e1005080. doi: 10.1371/journal.pcbi.1005080.



Model neuron with schematic of converging sequential input onto a dendrite. Colored clouds indicate ensembles of input neurons. Red indicates regions of dendrite with high activity due to local reaction-diffusion signalling response to ordered input.

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THE PHYSICS, NEUROBIOLOGY AND ECOPHYSIOLOGY OF INSECT FLIGHT

Sanjay P Sane

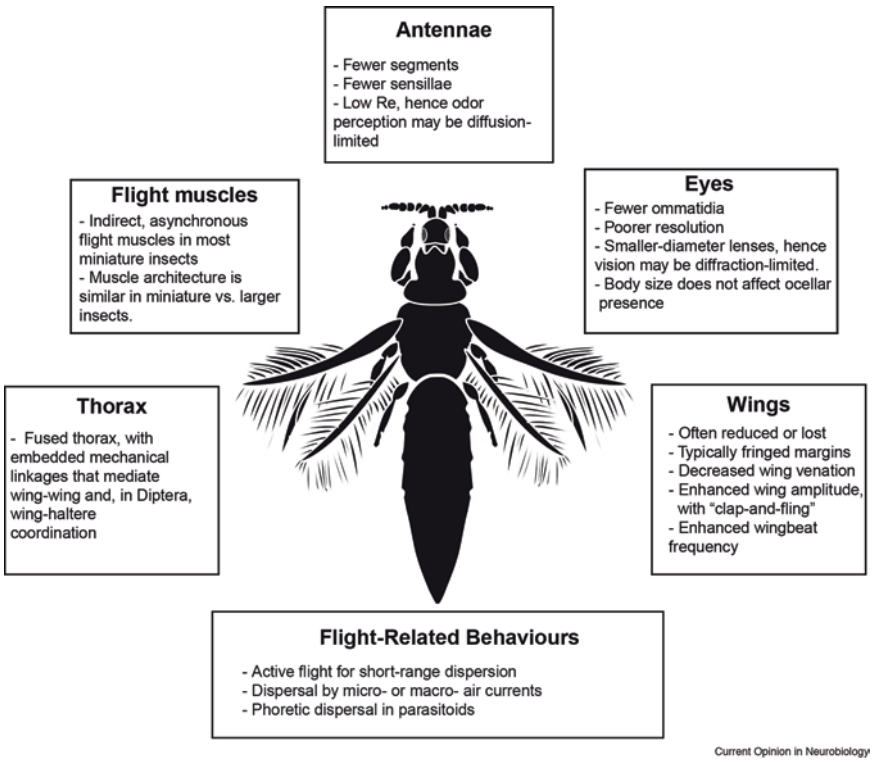
My laboratory explores the mechanisms of insect flight. We study the biomechanical, neurobiological, physiological and ecological underpinnings of various flight-related behaviours. These include fast aerial manoeuvres, territorial chases, short-distance navigation tasks such as foraging or odour-source localization, and long-distance navigation tasks such as migration.

Publications

*Deora, T., Gundiah, N and Sane, S.P. * (2017) Mechanics of the thorax in flies Journal of Experimental Biology 220 (8), 1382-1395*

Sane, S. P. (2016) Neurobiology and biomechanics of flight in miniature insects. Current Opinions in Neurobiology, 41, 158–166*

*Khurana, T.R., Sane, S.P. * (2016) Airflow and optic flow mediates antennal positioning in flying honeybees eLife 5, e14449*



How miniaturization affects flight-related structures in insects.

By any measure, insects are the most successful organisms to ever inhabit Earth. Arguably, their evolutionary success owes to the fact that they were the first animals to evolve flight and have maintained their mastery over the aerial habitat. Across various scales of size and neural complexity, insects are capable of flying with exquisite speed, control and manoeuvrability. Their wings flap rapidly - often at frequencies of hundreds of wing 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 a variety of sensors including visual, olfactory, mechanosensory, hygro and thermosensory *etc.* and communicated to the central nervous system, which then generates appropriate motor responses in the form of movement of head, legs, wings *etc.* Thus, 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.*), it is essential to conduct a multi-disciplinary study of the entire chain of events from sensory input to motor output to flight force generation.

My laboratory combines the input from physics, engineering, biomechanics, neurobiology, muscle mechanics and behavioural biology to address diverse flight-related phenomena. To study these questions, we use diverse techniques such as high-speed videography, behavioural measurements, neuroanatomy and neurophysiology.

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DIVERGENT PATTERNS OF STRESS-INDUCED PLASTICITY ACROSS THE BRAIN: CELLS, CIRCUITS AND MEMORIES

Sumantra Chattarji

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

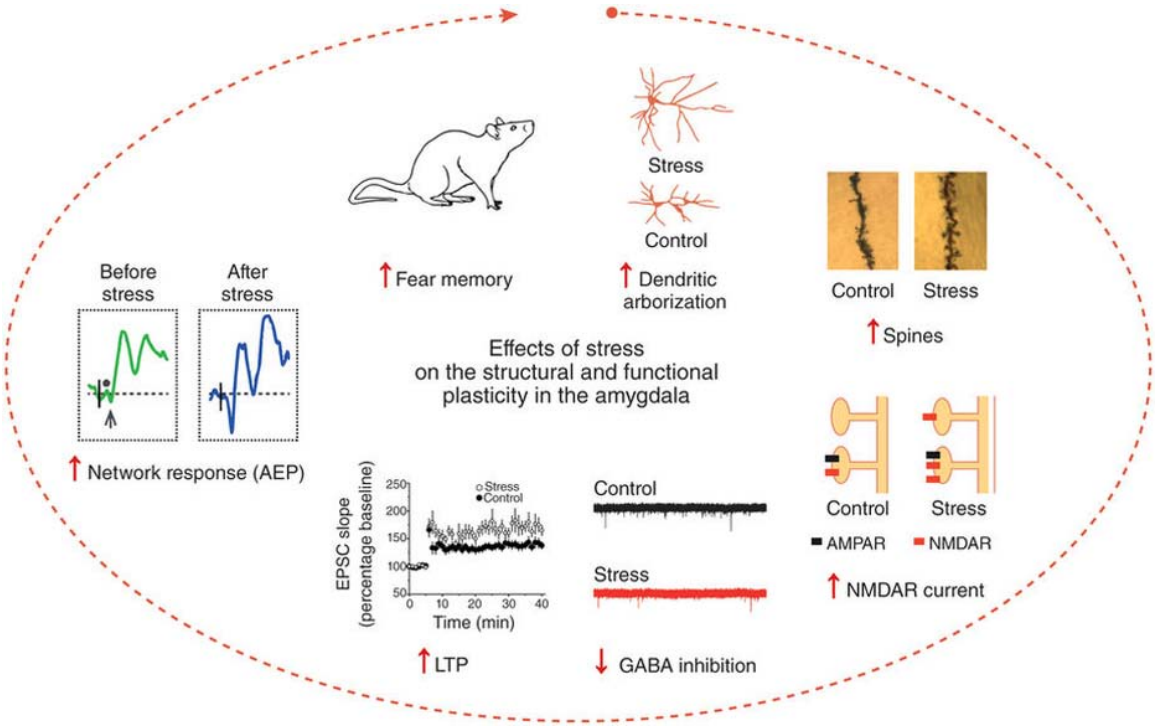
Memories come in many different flavors, some more potent than others. Emotionally significant experiences tend to be well remembered, and the amygdala has a pivotal role in this process. But the rapid and efficient encoding of emotional memories can become maladaptive — severe stress often turns them into a source of chronic anxiety. What are the cellular mechanisms underlying these powerful emotional symptoms? To answer this question, we have been using a range of behavioural, morphometric, *in vitro* and *in vivo* electrophysiological tools to identify neural correlates of stress-induced modulation of amygdala structure and function — from cellular and synaptic mechanisms to their behavioural consequences in rodents. Our findings point to unique features of stress-induced plasticity in the amygdala, which are in striking contrast to those seen in the hippocampus and cortex (1), and could have long-term consequences for pathological fear and anxiety exhibited in people with affective disorders.

In addition to behavioural experience, the genes we inherit can also cause cognitive and emotional dysfunction. Strikingly, individuals afflicted with certain types of autism spectrum disorder often exhibit impaired cognitive function alongside high anxiety and mood lability. Hence, we are extending our analyses to genetically engineered mice to identify cellular and molecular targets that can be used to correct symptoms of Fragile X Syndrome, the leading genetic cause of autism.

Publications

Rahman, M. M., Kedia, S., Fernandes, G., Chattarji, S. (2017) Activation of the same mGluR5 receptors in the amygdala causes divergent effects on specific versus indiscriminate fear. eLife DOI: 10.7554/eLife.2566

Chattarji, S., Tomar, A., Suvrathan, A., Ghosh, S., and Rahman, M. M. (2015) Neighborhood matters: divergent patterns of stress-induced plasticity across the brain. Nature Neuroscience 18, 1364–1375. doi:10.1038/nn.4115.



Stress enhances fear by forming new synapses with greater capacity for LTP in the lateral amygdala.

DEVELOPMENT, MODULATION AND FUNCTION OF MOTOR SYSTEMS

Vatsala Thirumalai

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.

Publications

Kondrychyn, I., Robra, L., Thirumalai, V. (2017) Transcriptional Complexity and Distinct Expression Patterns of auts2 Paralogs in Danio rerio. G3 (Bethesda). 7(8):2577-2593

Robra, L., Thirumalai, V. (2016) The Intracellular Signalling Molecule Darpp-32 Is a Marker for Principal Neurons in the Cerebellum and Cerebellum-Like Circuits of Zebrafish. Front Neuroanat. 10:81

Honours and Awards

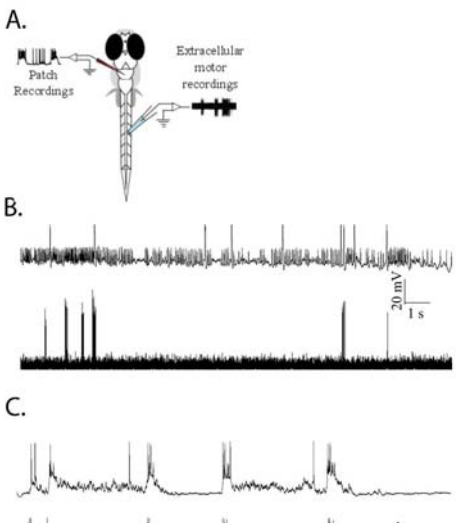
Early Career Reviewer and Guest Editor, eLife

Editorial Board, Journal of Neurophysiology.

Reviewing Editor, Frontiers in Neural Circuits.

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.



Dual mode representation of motor episodes in Purkinje neurons. A: Schematic of preparation. Whole cell current clamp recordings from Purkinje neurons and suction electrode recordings of motor neuron spikes were acquired simultaneously. B: When a Purkinje neuron is in the tonic firing mode (top trace), sodium spikes are not correlated with motor episode bursts (bottom trace). C: When the same cell is switched to the bursting mode, sodium spikes are highly correlated with motor episodes. Calcium spikes in the tonic mode (large amplitude events in top trace) are correlated weakly with motor episodes.

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MOLECULAR REGULATIONS OF CELLULAR FUNCTIONS IN THE ADULT BRAIN

Hiyaa Ghosh

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

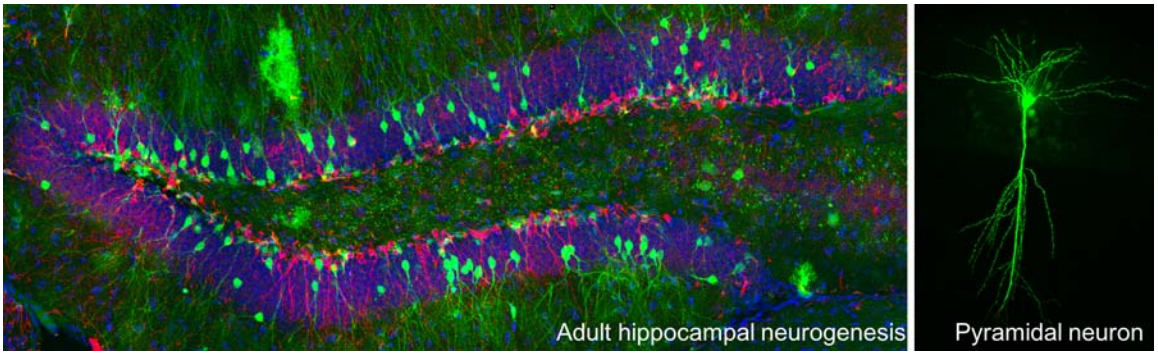
What underlies the longevity of neurons, which happen to be one of the most elaborate and long-living cell type of our body, yet have little capacity for regeneration or repair? While majorly post-mitotic, the adult brain does retain capacity for new neuron generation; a process termed as adult neurogenesis. 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, potentially instruct intercellular interactions. Studies in my lab are directed towards understanding the genetic program that underlie cell intrinsic processes and intercellular interactions governing adult brain functioning.

Using mouse as our model organism, we employ transgenic models for specific spatial and temporal deletion of gene, 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.

Publications

Bunin, A., Sisirak, V., Ghosh, H.S., Grajkowska, L.T., Hou, Z.E., Miron, M., Yang, C., Ceribelli, M., Uetani, N., Chaperot, L., Plumas, J., Hendriks, W., Tremblay, M.L., Häcker, H., Staudt, L.M., Green, P.H., Bhagat, G., Reizis, B. (2015) Protein Tyrosine Phosphatase PTPRS Is an Inhibitory Receptor on Human and Murine Plasmacytoid Dendritic Cells. Immunity. 43(2):277-88

Ghosh, H.S., Ceribelli, M., Matos, I., Lazarovici, A., Bussemaker, H.J., Lasorella A, Hiebert, S.W., Liu, K., Staudt, L.M., Reizis B. (2014). ETO family protein Mtg16 regulates the balance of dendritic cell subsets by repressing Id2. J Exp Med. 211(8):1623-35.



Left: *Dentate Gyrus* showing indelibly marked neural progenitors and their progeny in green, and immature neurons in red, in the hippocampal neurogenic region. Right: A pyramidal neuron of the CA1 region of hippocampus, individually dye filled in a brain slice for tracing morphology.

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K VIJAYRAGHAVAN 38 | GAITI HASAN 39 | P V SHIVAPRASAD 40

GENETICS AND DEVELOPMENT

RAJ LADHER 41 | DIMPLE NOTANI 42

DEVELOPMENT OF NEURAL CIRCUITS AND MUSCLES AND THE EMERGENCE OF BEHAVIOUR

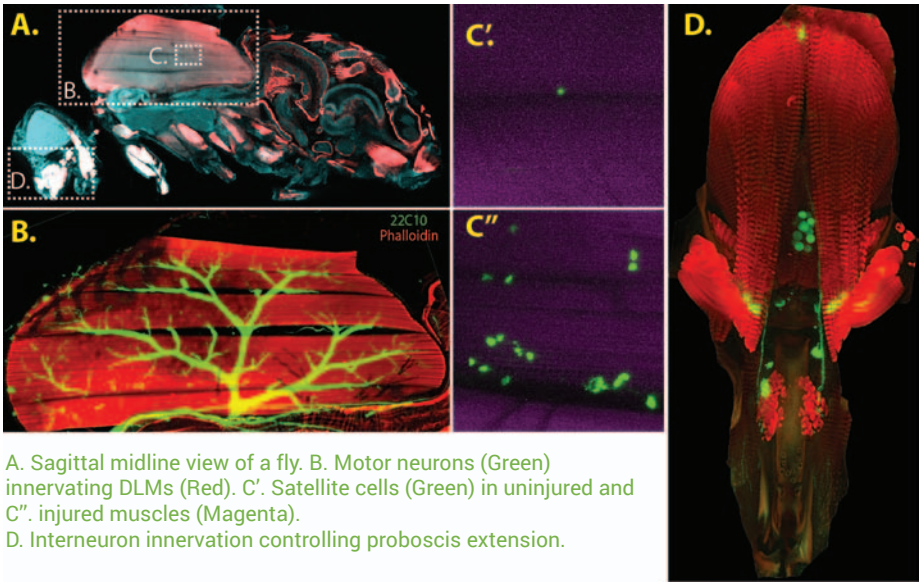
K VijayRaghavan

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*.

Publications

Gunage, R.D., Dhanyasi, N., Reichert, H., VijayRaghavan, K. (2017) Drosophila adult muscle development and regeneration. Semin Cell Dev Biol. 72:56-66

Chaturvedi, D., Reichert, H., Gunage, R.D., VijayRaghavan, K. (2017) Identification and functional characterization of muscle satellite cells in Drosophila. eLife. 6. pii: e30107.



A. Sagittal midline view of a fly. B. Motor neurons (Green) innervating DLMs (Red). C′. Satellite cells (Green) in uninjured and C″. injured muscles (Magenta).
D. Interneuron innervation controlling proboscis extension.

Complex structures and functions in animals emerge from sequential recruitment of conceptually simple mechanisms: first, to achieve the overall design during development; then to maintain the details as adults. Fruitflies, or more technically *Drosophila*, have for a century been a reliable model for human design, and in our lab, we use fruitflies to study several aspects of development, behaviour and repair.

In muscles, we study the fundamental mechanism of myogenesis and repair, which is remarkably similar in vertebrates and invertebrates. We recently discovered satellite cells populations in insects muscles that are similar to stem cells known to be essential for muscle repair in vertebrates.

Finally, via work on circuits that underlie gustatory and olfactory behaviour, performed significantly in collaboration with Mani Ramaswami, we seek to reveal global principles of neural circuit homeostasis and plasticity. Our work draws on the tools and concepts of molecular biology, genetics, microscopy and developmental and behavioural biology - whatever is needed to produce a truly holistic understanding of animal sensory and motor systems. In addition, through inStem, our group attempts to use our genetic technologies and biological insight for translational medicine.

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MOTOR CIRCUIT DEVELOPMENT AND FUNCTION

Gaiti Hasan

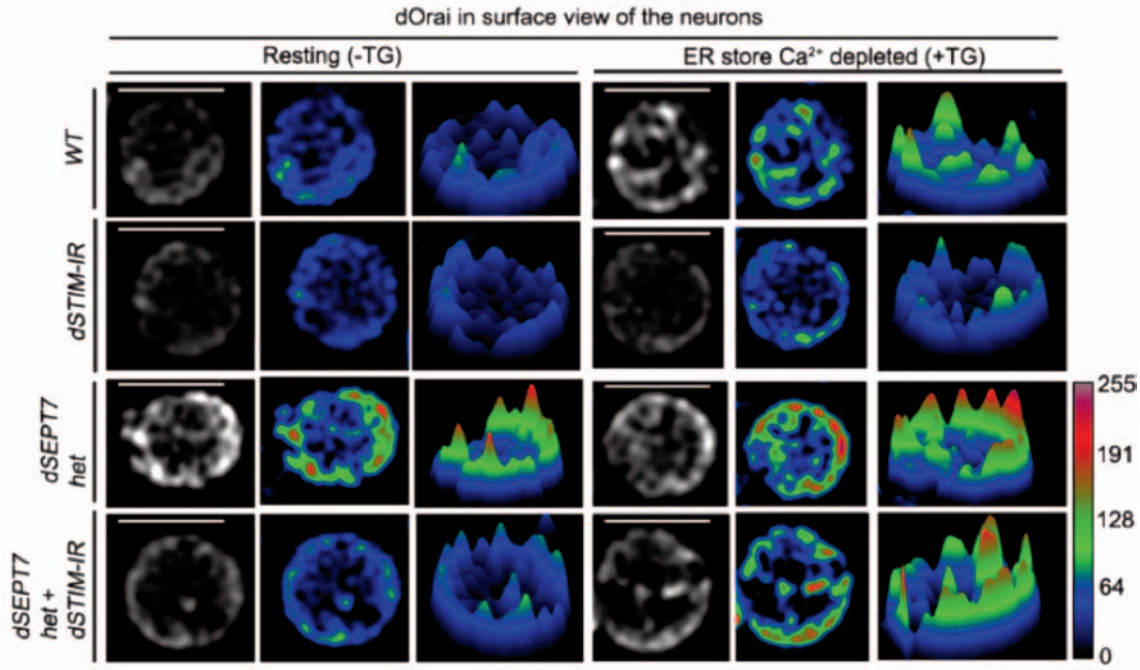
In *Drosophila*, intracellular Ca^{2+} signalling by the inositol 1,4,5-trisphosphate receptor and the store-operated channel (dOrai) regulates the formation and function of motor circuits that control flight. Recently we have identified Septin 7, a cytoskeletal protein, as a negative regulator of the Orai channel in neurons. These findings suggest that agonists of store operated calcium entry might serve as a therapeutic intervention for certain neurodegenerative disorders.

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 the mechanism of 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 inositol 1,4,5-trisphosphate receptor ($InsP_3R$) and the store-operated channel (dOrai) regulate the formation and function of neural circuits. In the past year we have identified new regulators and regulatory mechanisms of intracellular calcium signalling. These findings are significant in suggesting agonists of Store Operated Calcium Entry (SOCE) as a possible means of therapeutic intervention for human diseases where the $InsP_3R$ is thought to play a causative role. Thus, we have developed the *Drosophila* mutants for the $InsP_3R$ as a model for understanding molecular mechanisms of neurodegeneration where intracellular calcium signalling is causal. The findings from these studies have opened up new areas of therapeutic interventions in Spino-cerebellar Ataxias and Parkinson's syndrome – a neurodegenerative disorder that specifically affects dopaminergic neurons.

Publications

Jayakumar, S., Richhariya, S., Reddy, O.V., Texada, M.J., and Hasan, G (2016). Drosophila larval to pupal switch under nutrient stress requires IP_3R/Ca^{2+} signalling in glutamatergic interneurons. eLIFE 2016; DOI:http://dx.doi.org/10.7554/eLife.17495

Deb, B.K., Pathak, T., and Hasan, G. (2016) Store-independent modulation of Ca^{2+} entry through Orai by Septin 7. Nat. Comm. doi:10.1038/ncomms11751



The store-operated calcium channel dOrai is located on the cell surface. In resting wild-type neurons (WT) it appears diffuse but upon store-depletion it can form clusters that can be visualized by immuno-staining with an antibody against dOrai (top row). In neurons with reduced levels of the store-calcium sensor dSTIM, dOrai clustering is reduced (second row), but the opposite is seen in neurons with reduced levels of dSEPT7 (third row). In fact, dSEPT7 can restore dOrai clustering (and function) in neurons with reduced dSTIM (last row).

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EPIGENETICS AND SMALL SILENCING RNAs

P V Shivaprasad

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 mechanism of small RNA biogenesis, their functions and their role in establishment of epigenetics.

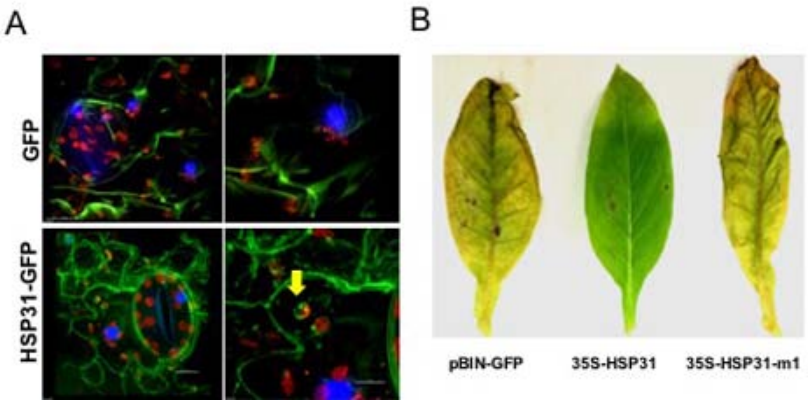
Publications

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

Das, S., Singh, R., Shivaprasad, P.V. (2017). Artificial induction and maintenance of epigenetic variations in plants. Plant Gene Silencing: Phenomena and Applications. CABI publishers, UK.

Awards and honours

M.H. Marigowda memorial lecture during Marigowda Centenary Celebrations, Lalbagh, June 2017.



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

B. Transgenic plants expressing HSP31 are resistant to fungal infection.

Small RNAs are a group of key molecules resulting from RNA silencing pathways. They regulate transcription and translation of their target RNAs. Small RNAs are also important factors in initiating and maintaining heritable changes in gene expression without changes in DNA sequence ('epigenetics'). Small RNAs and epigenome modifications impact every aspect of eukaryotic development and disease. Our laboratory is interested in understanding the pathways and mechanisms that generate small RNAs and epigenome modifications in plants. During the past few years, we have uncovered two striking features of plant small RNA biogenesis. We found length of loops in micro(mi)RNA precursors is critical for miRNA biogenesis. miRNA biogenesis machinery prefers shorter loops. Additionally, using purified Dicer-like complexes from wheatgerm we show that DCL3 can cleave structured RNAs unlike previously predicted.

Our group has characterized functions of few novel small RNAs. For example, we have recently identified and characterized a cluster of miRNAs that regulate anthocyanin accumulation in grapes. A differentially expressing miRNA likely involved in domestication-associated phenotypes has been identified from rice. We use various biochemical, genetic, bioinformatic and whole-genome approaches in a wide variety of model plants to understand biogenesis and functions of small RNAs.

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DEVELOPMENT AND MORPHOGENESIS OF INNER EAR

Raj Ladher

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

The mouse inner ear – the inner ear has been filled with white paint and visualized in situ, within the head.

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

Publications

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

Mak, S-S., Alev, C., Nagai, H., Wrabel, A., Matsuoka, Y., Honda, A., Sheng, G., Ladher, R.K. (2015) Characterization of the finch embryo supports evolutionary conservation of the naive stage of development in amniotes. eLife. doi:10.7554/eLife.07178

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CHROMATIN DYNAMICS IN GENE REGULATION

Dimple Notani

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

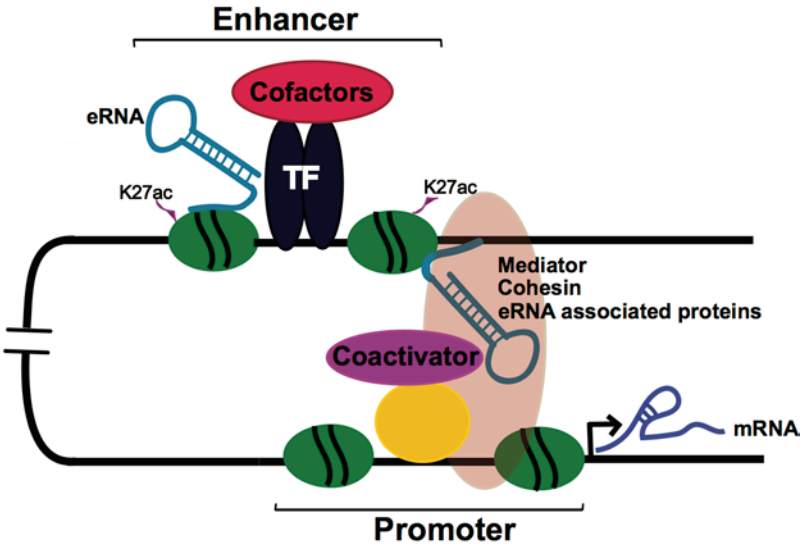
Publications

Jayani, R.S., Singh, A., Notani, D (2017). Isolation of Nuclear RNA-Associated Protein Complexes. Methods Mol Biol. 1543:187-193. doi: 10.1007/978-1-4939-6716-29.

Li, W., Notani, D., Rosenfeld, M.G. (2017) Enhancers as non-coding RNA transcription units: recent insights and future perspectives. Nat Rev Genet. doi: 10.1038/nrg.2016.4

Eukaryotic gene expression is tightly controlled in a spatio-temporal manner by virtue of dynamic genome organization. Accumulating 3D genomic maps suggest that whole genome is comprised of large topological domains and these domains are further divided into sub-domains that involve the extensive DNA loops among the regulatory elements such as enhancer, promoter and boundaries. Thus, these subdomains are of varying transcriptional status and exhibit differential histone modifications. TADs exert important constraints on chromosomal architecture; yet, by unknown mechanisms, they allow spatial and temporal changes in gene expression.

We are interested in understanding the role enhancers and associated non-coding RNAs(eRNAs) play in establishing/perturbing the transcriptional state of a given loci/chromosome by modulating the TADs or chromatin-territories that may involve its physical repositioning in 3D-space of nucleus. We use locus specific and genome-wide tools to uncover such dynamic behaviour of otherwise stable chromatin territories. Further, we are working towards identifying the protein complexes that eRNAs recruit to activate or repress the target coding genes.



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.

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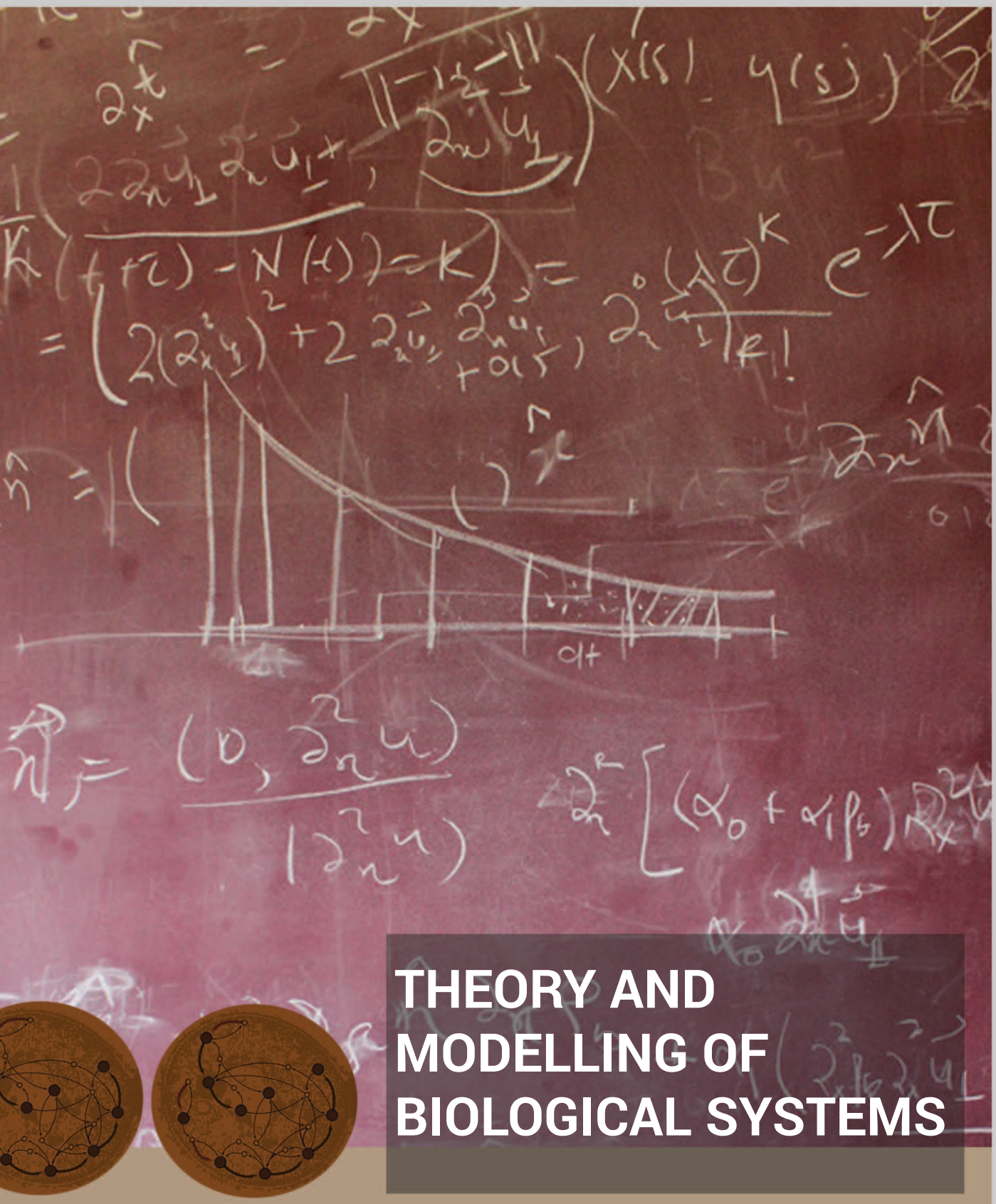
Photography by Ravi Kumar Boyapati, Research scholar, Axel Brockmann lab

SHACHI GOSAVI 46 | MUKUND THATTAI 47 | SANDEEP KRISHNA 48



THEORY AND MODELLING OF BIOLOGICAL SYSTEMS

MADAN RAO 49 | SHASHI THUTUPALLI 50

COMPUTATIONAL PROTEIN FOLDING AND FUNCTIONAL DYNAMICS

Shachi Gosavi

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 inform on protein function.

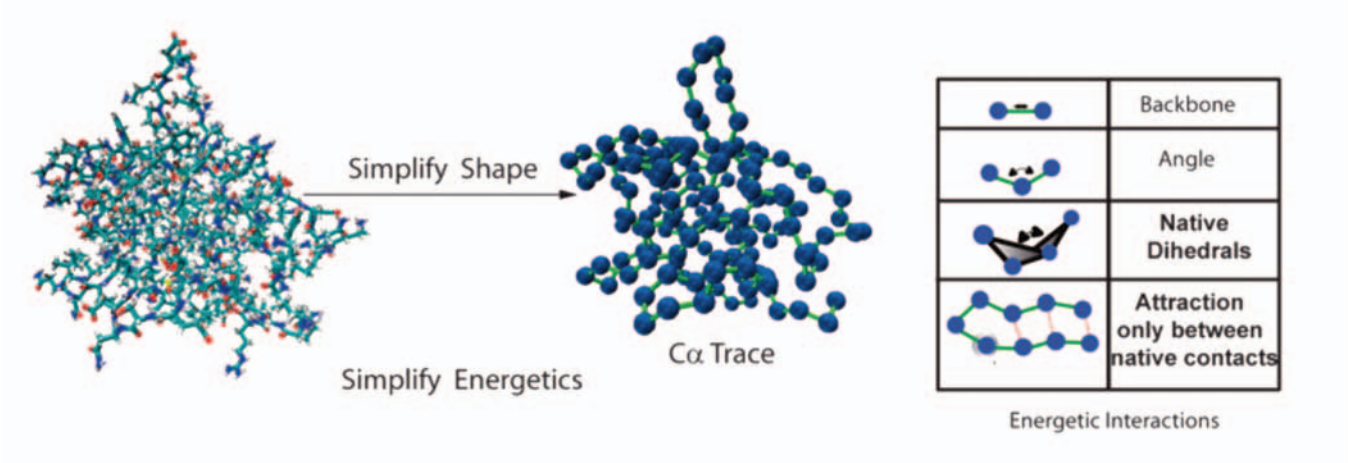
Publications

Yadahalli, S., and Gosavi, S. (2017). Packing energetics determine the folding routes of the RNase-H proteins. Phys. Chem. Chem. Phys.19(13), 9164-9173.

Mascarenhas, N. M. and Gosavi S. (2017). "Understanding protein domain-swapping using structure-based models of protein folding." Prog. Biophys. Mol. Biol. 128, 113-120.

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 function could be binding, catalysis, cellular localization, etc.). These, functional residues cannot be mutated to make protein folding more efficient or protein stability greater. Given the choice of only twenty amino acids at each position, it has become apparent that parts of the protein which function are likely to be the least foldable or stable. Functional regions thus perturb folding from the "ideal" and we use SBMs to understand both what ideal folding is and how functional regions perturb it.



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

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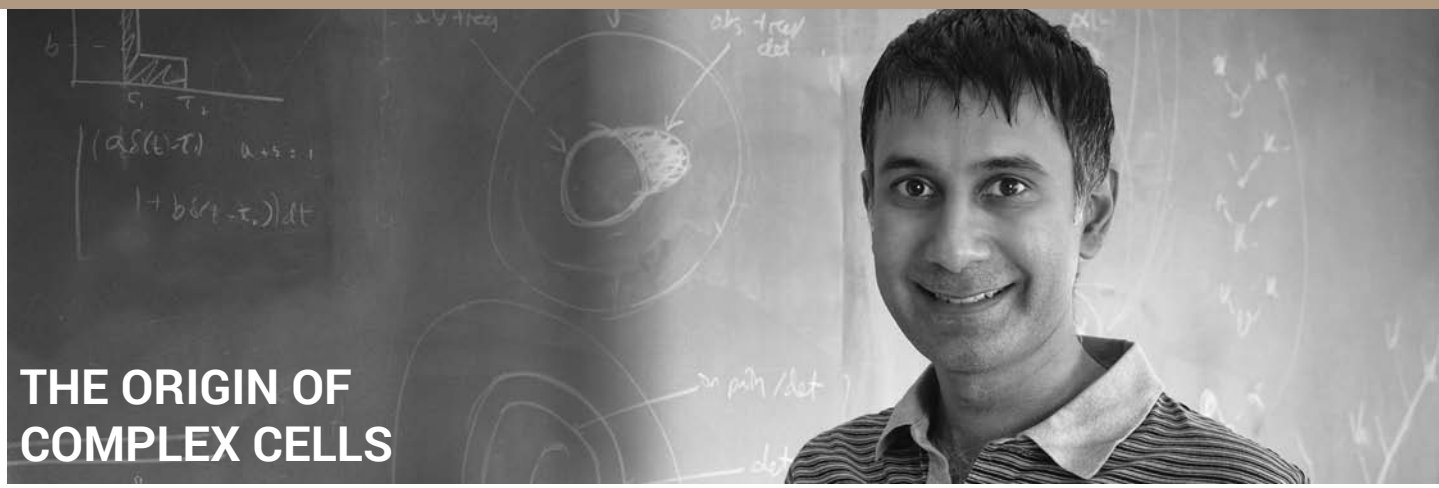
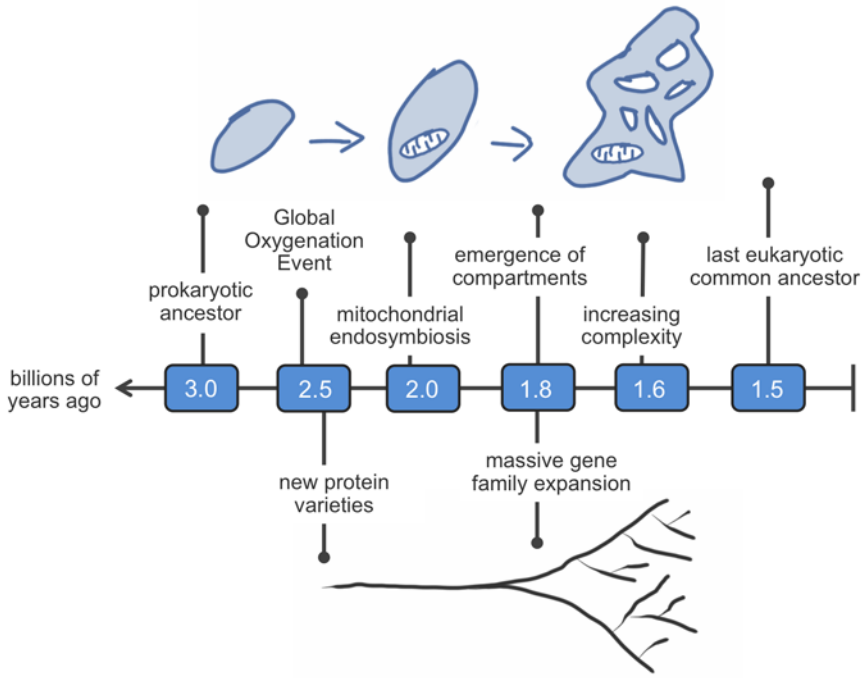


THE ORIGIN OF COMPLEX CELLS

Mukund Thattai

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.



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

We are interested in the ancient origins of the eukaryotic compartmentalized 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, compartmentalized organelles, the cytoskeletal machinery, and vesicle traffic. In particular, we are pursuing two complementary research directions. Forward in time: we analyze potential origin scenarios using biophysical and evolutionary simulations, to uncover general principles about the evolution of compartmentalized cells. Backward in time: we study the evolution of the molecular machinery underlying compartmentalization using sequence data and phylogenetic techniques; we 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 compartmentalized 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.

Publications

Mani, S. and Thattai, M. (2016). Stacking the odds for Golgi cisternal maturation. eLife, 5, p.e16231.

Purkanti, R. and Thattai, M. (2015). Ancient dynamin segments capture early stages of host–mitochondrial integration. Proceedings of the National Academy of Sciences, 112(9), pp.2800-2805.

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DYNAMICS OF BIOLOGICAL SYSTEMS ACROSS SCALES

Sandeep Krishna

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

Publications

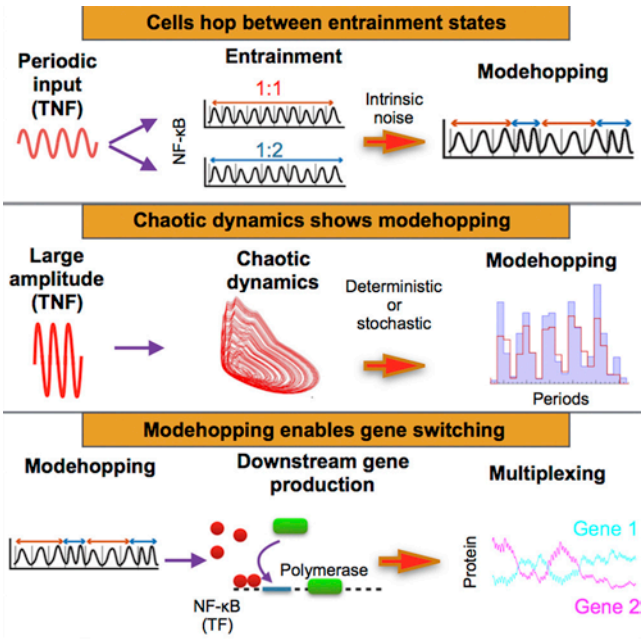
Sinha, V., Goyal, A., Svenningsen, S. L., Semsey, S. & Krishna, S. (2017) In silico evolution of lysis-lysogeny strategies reproduces observed lysogeny propensities in temperate bacteriophages, Front. Microbiol. 6, 1386.

Heltberg, M., Krishna, S. & Jensen, M. H. (2017) Time correlations in mode hopping of coupled oscillators, J. Stat. Phys. 167, 792.

Heltberg, M., Kellogg, R. A., Krishna, S., Tay, S. & Jensen, M. H. (2016) Noise induces hopping between nf-kb entrainment modes, Cell Sys. 3, 532.

At the molecular level, I am interested in using a combination of experiments 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 bacterial ecosystems and phage-bacteria communities to understand issues related to long-term coexistence and coevolution of multiple species.



Experimental and theoretical evidence for mode-hopping in the periodically driven NF-κB signalling pathway (*Heltberg et al., 2017*). Such mode-hopping allows more complex regulatory control of downstream genes, thus allowing the NF-κB system to differentially express hundreds of target genes in response to multiple input triggers.

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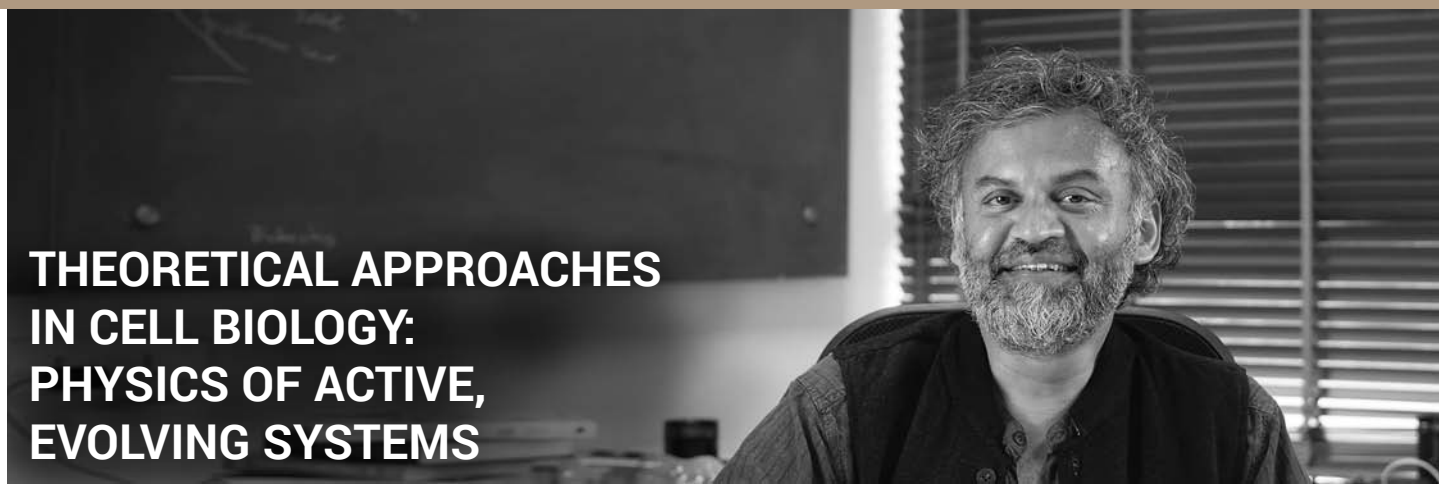
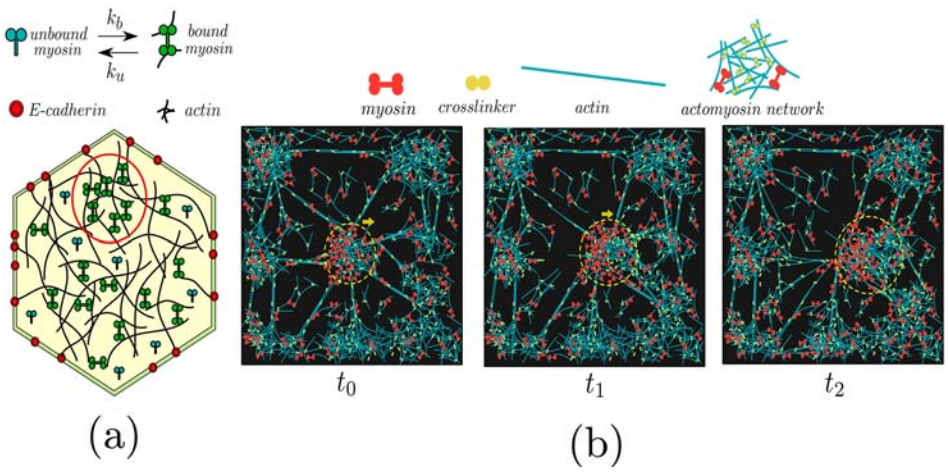


THEORETICAL APPROACHES IN CELL BIOLOGY: PHYSICS OF ACTIVE, EVOLVING SYSTEMS

Madan Rao

Our group studies the interplay between active mechanics, molecular organization, 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.



(a) Schematic showing the elements of the active elastomer description of the medial actomyosin mesh in the apical region of a cell belonging to the tissue. The actin filaments are attached to the cell junctions via E-cadherin (red dots). Myosin minifilaments bind (unbind) with rates k_b (k_u) and when bound, apply contractile stresses on the actin filament meshwork - the red circle demarcates a region of higher mesh compression. Both actin filaments and myosin minifilaments undergo turnover.
(b) Schematic showing the results of the nonaffine deformation of the active elastomer with turnover. The snapshots at times $t_0 < t_1 < t_2$ show intranetwork flow of an actomyosin-dense region (enclosed within the yellow circle) resulting from active stress induced unbinding and rapid turnover of the actin in a transient actomyosin network.

Publications

Husain, K. and Rao, M. (2017). Emergent Structures in an Active Polar Fluid : dynamics of shape, scattering and merger, Phys. Rev. Lett. 118, 078104 .

Banerjee, D., Munjal, A., Lecuit, T. and Rao, M. (2017). Actomyosin pulsation and flows in an active elastomer with turnover and network remodeling, Nat. Comm. 8, 1121.

Awards and honours

Distinguished Alumnus Award 2016 of IIT Bombay.

Labex CelTisPhysBiol Chair 2016, Institute Curie, Paris.

Elected as Fellow of the Indian National Science Academy, 2016.

Awarded the Sackler Fellowship for the year 2018-2019

We are interested in how living systems, composed of physical entities such as molecules, molecular aggregates and driven far-from equilibrium, have self-organized (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 organization 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 organization 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, organization 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.

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COLLECTIVE DYNAMICS IN LIVING MATTER

Shashi Thutupalli

Our research program aims to provide an understanding of collective outcomes (mechanical and evolutionary) in living systems using quantitative approaches rooted in the framework of disordered, non-equilibrium matter. At the heart of our approach are experimental probes of theory driven ideas.

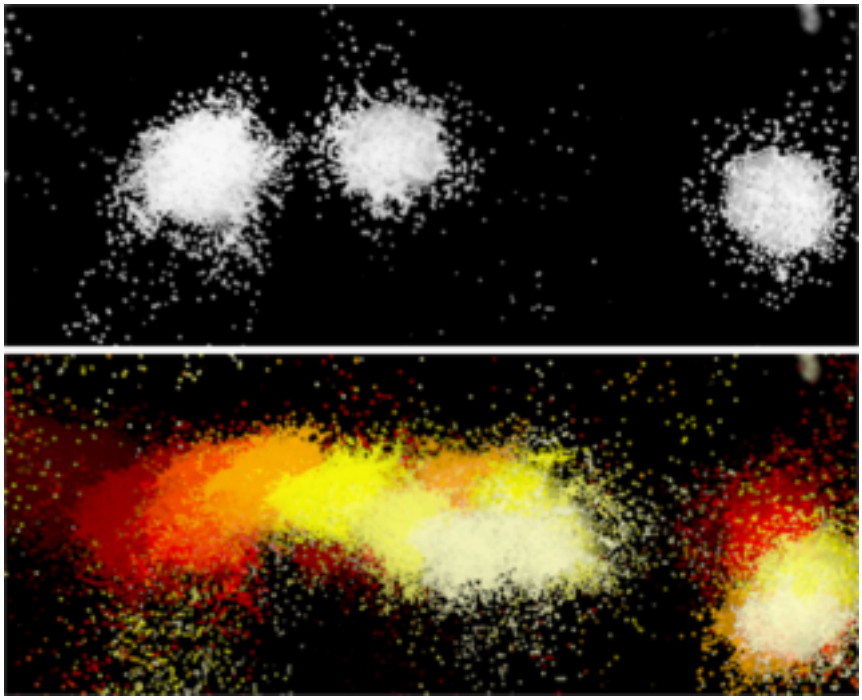
Publications

Liu, G., Patch, A., Bahar, F., Yllanes, D., Roy, D., Welch, M., Marchetti, C., Thutupalli, S. and Shaevitz, J. W. (2017). A motility-induced phase transition drives Myxococcusxanthus aggregation",arXiv:1709.06012.

Thutupalli, S., Uppaluri, S., Constable, G. W. A., Levind, S. A., Stonea, H. A.,Tarnitad, C. A., and Brangwynne, C. P. (2017) Farming and public goods production in C. elegans populations. Proc. Natl. Acad. Sci.114, 9, 2289-2294.

Awards and honours

Head of Max Planck Partner Group, MPI for Dynamics and Self-Organization, Gottingen, Germany



Collective dynamics in active matter. Top: A snapshot of cluster formation in a large population of self-propelled particles (each white dot is an active emulsion droplet which is 50 microns in diameter). Bottom: Dynamics of the collision and merging of the active clusters with time encoded in color.

Cell populations, biological tissues, highly coordinated animal groups and interacting populations are a form of complex material or dynamical system with emergent coherent properties that arise from mechanical, biochemical and socially mediated interactions between individuals. Unlike in purely physical processes, the individual in a biological ensemble is capable of transmitting, integrating and processing information, tuning dynamically adaptive responses and evolving.

Such a perspective naturally suggests two complementary approaches: (i) to distill unifying physical principles that govern biological systems by probing them as a unique state of matter or as a unique class of dynamical systems and (ii) to construct *de novo*, simple physical mimics of biological systems to study the minimal ingredients for computation, feedback, decision-making and evolvability.

These studies of complexity in living systems 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.

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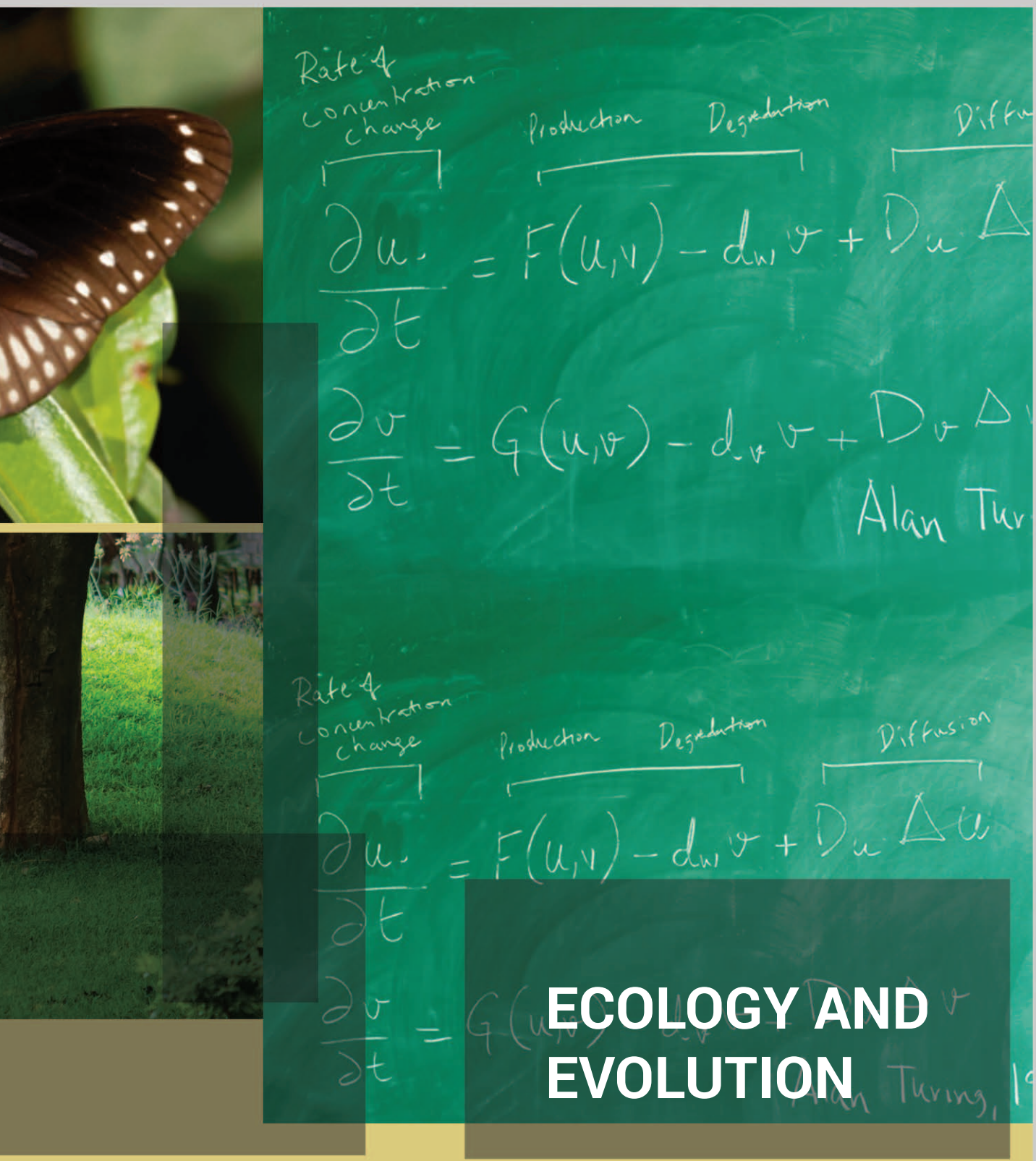
KRUSHNAMEGH KUNTE 56



ECOLOGY AND EVOLUTION

SHANNON OLSSON 57 | DEEPA AGASHE 58

RADHIKA VENKATESAN 59 | AXEL BROCKMANN 60

TERRESTRIAL ECOSYSTEMS AND COMMUNITY ECOLOGY

Mahesh Sankaran

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.

Publications

Dohn, J., Augustine, D. J., Ratnam, J., Hanan, N. P and Sankaran, M. (2017). Spatial vegetation patterns and neighborhood competition among woody plants in an East African savanna. Ecology 98: 478–488, DOI: 10.1002/ecy.1659.

Osuri, A.M., Ratnam, J., Varma, V., Alvarez-Loayza, P., HurtadoAstaiza, J., Bradford, M., Fletcher, C., Breuer-Ndoundou, H.M., Jansen, P.A., Kenfack, D., Marshall, A.R., Ramesh, B.R., Rovero, F. and Sankaran, M. (2016). Contrasting effects of defaunation on aboveground carbon storage across the global tropics Nature Communications, DOI: 10.1038/ncomms11351

Honors and awards

Coordinating Lead Author for the Land Degradation and Restoration Assessment of the Intergovernmental Platform on Biodiversity and Ecosystem Services (IPBES); chapter on 'Direct and indirect drivers of land degradation'

Review editor for upcoming IPCC AR6 Special Report on "Climate change, Land use and Food security"

Current research in the lab is grouped around the following broad themes that examine:

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.

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

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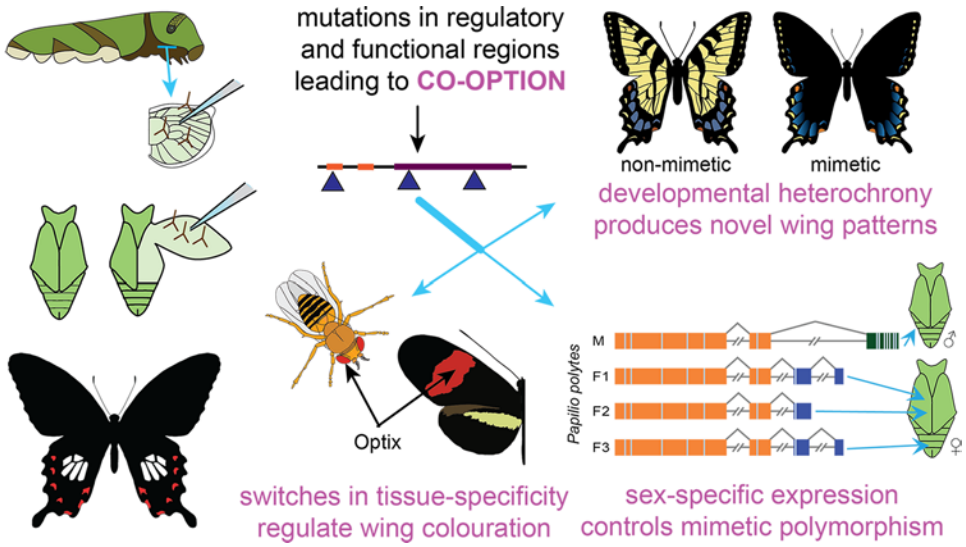
SPECIATION, ADAPTATION AND MORPHOLOGICAL DIVERSIFICATION IN THE TROPICAL REGION

Krushnamegh Kunte

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



Publications

Deshmukh, R., Baral, S., Gandhimathi A., Kuwalekar M., and Kunte, K. (2017). Mimicry in butterflies: co-option, and a bag of magnificent developmental genetic tricks. WIREs Developmental Biology. doi: 10.1002/wdev.291.

Arnold, M. L. and Kunte, K. (2017). Adaptive genetic exchange: a tangled history of admixture and evolutionary innovation. Trends in Ecology and Evolution, 32:601–611. Recommended by Faculty of 1000.

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

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 organization 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, polymorphic or sex-limited within and across species. Our research aims to understand selective pressures that favor such variation in mimetic color patterns, and uncover its genetic basis. Read more about this work on our lab website.

Our second study system is Indian butterflies. India’s butterfly diversity is spread across four globally recognized 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.

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DECONSTRUCTING INDIAN BIODIVERSITY: EVOLUTIONARY ORIGINS AND FUTURE PROSPECTS

Uma Ramakrishnan

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.

Publications

Natesh, M., Atla, G., Nigam, P., Jhala, Y.V., Zachariah, A., Reddy, A.P., Borthakur, U., Ramakrishnan, U. (2017). Conservation priorities for endangered Indian tigers through a genomic lens. Sci Rep. 7(1):9614.

Agarwal, I and Ramakrishnan, U (2017) A phylogeny of open-habitat lizards (Squamata: Lacertidae: Ophisops) supports the antiquity of Indian grassy biomes. Journal of Biogeography, DOI: 10.1111/jbi.12999

Awards and honours

2017: Welcome Trust DBT India Alliance Senior Investigator Award

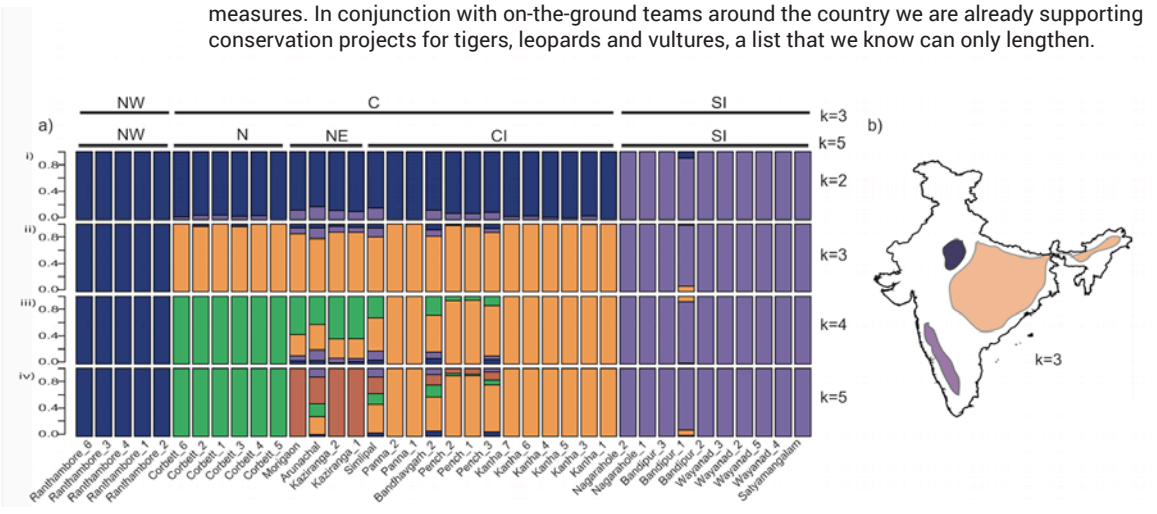
2016: Parker Gentry Conservation award; Fulbright Fellow

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 or 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 of 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 populations 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.



Genetic clusters as inferred from (a) Admixture, at different values of K (2–5). Each vertical bar indicates a single individual, with the Y axis depicting the proportion derived from each cluster. The optimal suggested value of number of clusters was K?=?3; (b) depicts the geographical extant of the three clusters inferred at K?=?3; (c) Principal components analysis depicting the first and second principal components and (d) A phylogenetic network constructed in SplitsTree4. (*Natesh et al., Sci Rep. 2017 Aug 29;7(1):9614*).

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TRACKING THE OBJECTS OF INSECTS' AFFECTIONS ACROSS SPECIES AND CONTINENTS

Shannon Olsson

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 cues and make decisions.

The NICE group is interested not only in the what and how of insect object identification, but how insects have evolved to identify objects in a range of environments, and how they can evolve to detect new objects, such as invasive species. In our second full year of existence, our research has lead to three major breakthroughs.

First, in collaboration with Karin Nordström at U. Uppsala and Adelaide, we have investigated what factors hoverflies use to categorize suitable flowers in three different climate regions, including hemiarboreal Uppsala, Sweden, alpine Sikkim and tropical Bangalore. Our results provide unique insights on how cosmopolitan pollinators can identify objects across climates, which have important implications for our understanding of pollination as a global ecological service.

Second, in collaboration with Prof. Jeff Feder at U. Notre Dame, we have identified a small set of neural cells on the antenna of recently diverged fruit-infesting races that respond to key odours from apple or hawthorn fruit (Tait et al., 2016). Our work is significant in its implication that even for such complex behaviours as host choice, tiny changes in the nervous system can have dramatic effects on a species, even on an evolutionary timescale.

Finally, our group has successfully developed a virtual reality arena capable of high precision delivery of both complex visual and odor stimuli. Our system is world-unique in its ability to accurately measure flight behaviour of insects in response to precisely controlled multimodal stimuli on a millisecond timescale.

Publications

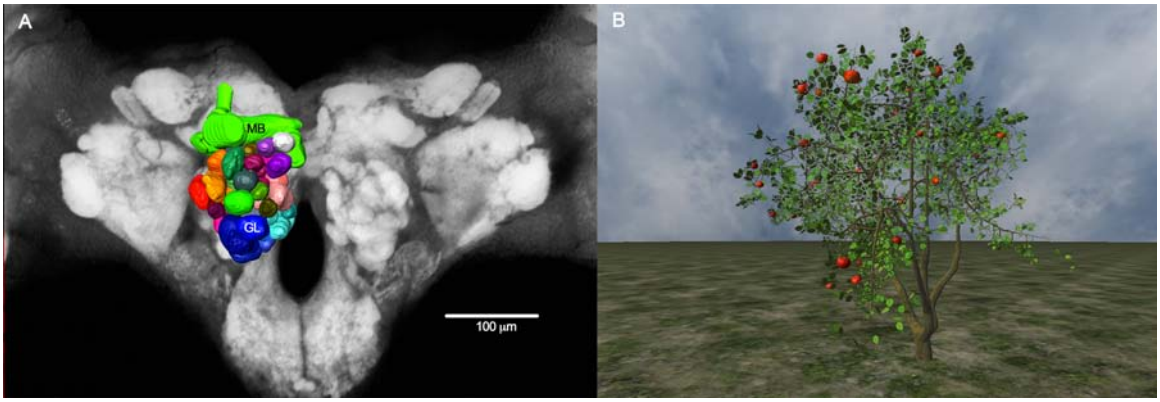
Olsson, S.B. and the Bengaluru Consortium (18 authors; 2017) New frontiers for chemical ecology: Reconfirming a commitment to the Gothenburg resolution. J Chemical Ecology, 43(1): 2-3.

Tait, C., Batra, S., Ramaswamy, S.S., Feder, J.L., Olsson, S.B. (2017) Sensory specificity and speciation: a potential neuronal pathway for host fruit odour discrimination in Rhagoletis pomonella. Proc. Roy. Soc. B, 283 20162101; DOI: 10.1098/rspb.2016.2101.

Honors and Awards

INK Fellow

India -United Nations Pinning for Research Excellence by Gandhian Scholars



A. 3D antennal lobe (AL) and mushroom body (MB) reconstruction of an adult apple fly brain overlaid onto Z-projection micrograph. Specific AL glomeruli (GL) are indicated with color.

B. The apple tree as rendered in our virtual reality arena.

GENETIC AND ECOLOGICAL FACTORS UNDERLYING ADAPTIVE EVOLUTION

Deepa Agashe

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.

Publications

Agashe, D (2017). The road not taken: Could stress-specific mutations lead to different evolutionary paths? PLoS Biology 15(6):e2002862

Khan, I., Prakash, A.*, Agashe, D. (2017). Experimental evolution of insect immune memory vs. pathogen resistance. Proceedings of the Royal Society of London B, 284(1869). (*Equal contribution)*

Awards and honours

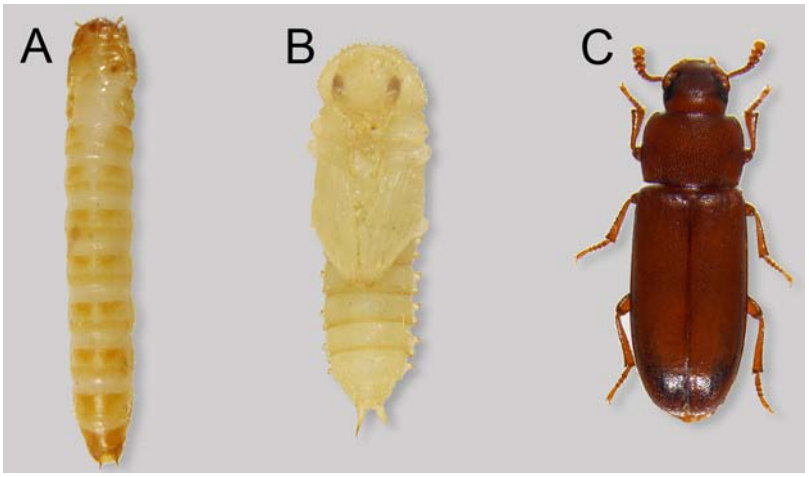
Associateship, Indian Academy of Sciences (2017-2020)

Wellcome Trust-DBT India Alliance Intermediate Fellowship (2018-2023)

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. For instance, how many mutations are responsible for rapid adaptation to novel environments? What are the mechanisms responsible for major behavioural and phenotypic changes in animals, and can we predict how species will adapt to global climate change? Our major goal is to understand the evolutionary and ecological processes underlying adaptive evolution. We address two broad questions:

1. What evolutionary and ecological factors govern the evolution of bacterial genomes, and how often do the observed patterns reflect adaptive (vs. stochastic) evolution?

2. What evolutionary and ecological factors govern insect adaptation to new environments?



Life stages of the red flour beetle *Tribolium castaneum*, our main insect model system in the laboratory. A. Larva; B. Pupa; C. Adult

CHEMICAL ECOLOGY OF PLANT-INSECT-MICROBE INTERACTIONS

Radhika Venkatesan

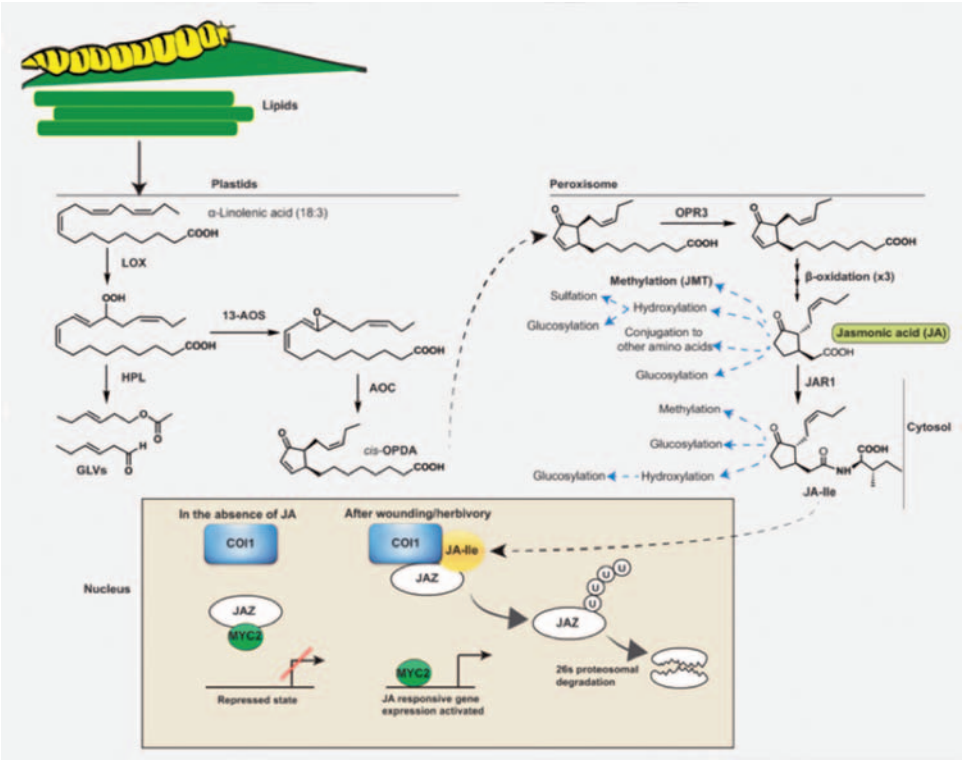
Chemical ecology is the study of chemically mediated interactions in nature. We study such interactions spanning from biochemistry to ecosystems addressing plant defence responses and their regulation by phytohormones, insect detoxification mechanisms and evolutionary origins of plant defence responses.

Chemical ecology is the study of chemically-mediated interactions among organisms. We study such interactions between plants, insects and microbes. Plants, the energy support system for life on this planet, are sessile and cannot run away from their enemies. They have evolved sophisticated means to tackle the various challenges they might encounter. The co-evolution between plants and insects is a major reason for the biodiversity seen around us. We study plant defense responses against insects and their regulation by phytohormones. Insects, on the other hand, have adapted to their dietary challenges and often exhibit remarkable tolerance to poisons in their host plants. Some insects also have the ability to sequester the toxins from their host for their own defense. We study the insect adaptation mechanisms with the aim to understand the co-evolutionary arms-race between plants and insects. We also examine the role of insect gut microbes in insect adaptation to host plants.

Publications

Radhika, V., Ueda, N., Tsuboi, Y., Kojima, M., Kikuchi, J., Kudo, T., Sakakibara, H. (2015). Methylated Cytokinins from the Phytopathogen Rhodococcus fascians Mimic Plant Hormone Activity. Plant Physiol. 169(2):1118-26

Radhika, V., Kost, C., Bonaventure, G., David, A., Boland, W. (2012) Volatile emission in bracken fern is induced by jasmonates but not by Spodoptera littoralis or Strongylogaster multifasciata herbivory. PLoS One. 7(11):e48050.



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MECHANISMS OF ANIMAL BEHAVIOUR

Axel Brockmann

We are interested in the organization and mechanisms of animal behaviour. How do animals do what they do and what are the underlying neural and molecular mechanisms? Our primary experimental paradigm is daily foraging activity, which involves all the higher behavioural capabilities demonstrated for honeybees.

Publications

Murata, S., Brockmann, A., Tanimura, T. (2017). Pharyngeal stimulation with sugar triggers local searching behavior in Drosophila. J Exp Biol. pii: jeb.161646.

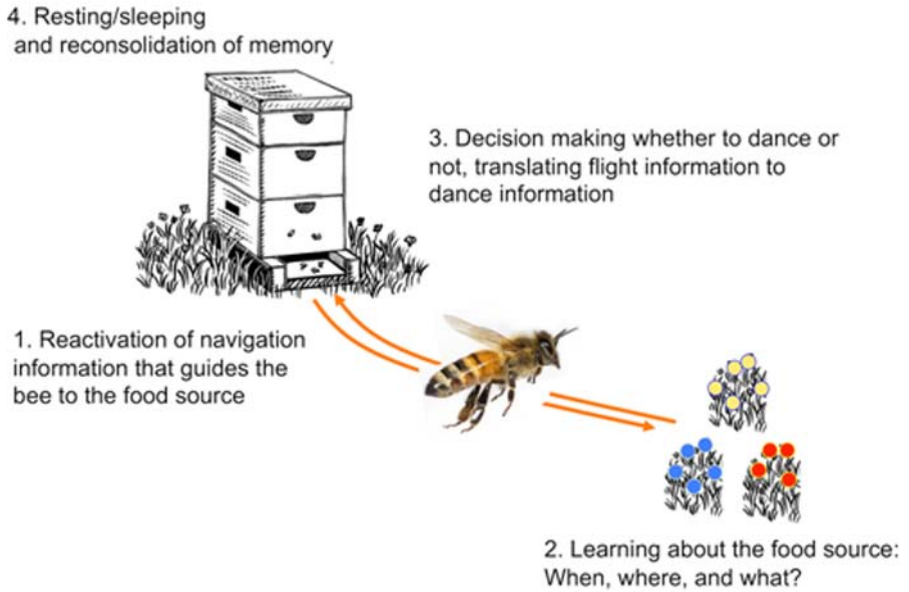
Karpe, S.D., Jain, R., Brockmann, A., Sowdhamini, R. (2016). Identification of Complete Repertoire of Apis florea Odorant Receptors Reveals Complex Orthologous Relationships with Apis mellifera. Genome Biol Evol. 8(9):2879-2895.

I am interested in the mechanisms of animal behaviour. Honeybees provide the opportunity to study mechanisms of behaviour at the level of the individual and the level of the social organization. Moreover, honeybees are one of the few animal model systems to study the interaction between individual behaviour and social organization. We are able to manipulate the social structure and analyze its effects on the individual's behaviour, brain physiology, and brain gene regulation.

So far, most behavioural and neurobiological research on honeybees focused on the European-African species *Apis mellifera*, unfortunately neglecting the variability in social organization and individual behaviour among honeybee species. Honeybee species particularly vary in colony organization, worker activity and longevity, pheromone communication and dance language communication. A special focus of my lab will be research on Asian honeybee species native to India: *Apis florea* (the red dwarf honeybee), *Apis dorsata* (the giant honeybee), and *Apis cerana* (one of the Asian cavity nesting honeybees). The genomes of all three species are currently sequenced which will open the possibility to analyze the molecular underpinnings of behavioural differences and the evolution of these behaviours.

In addition to studies on honeybee behaviour, I plan to expand my research on *Drosophila*. Currently, we are developing lab assays that can be performed with honeybees and flies. The neurogenetic tools available for *Drosophila* allow identifying neural circuitries involved in specific behaviours, and the hope is that *Drosophila* can help to identify neural circuits involved in honeybee behaviour.

In search of the molecular underpinnings of foraging related cognitive processes



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Photography by Debshankar Banerjee, Research Scholar, Madan Rao lab

LECA

NEW INVESTIGATORS

REGULATION OF BACTERIAL DNA DAMAGE REPAIR

Anjana Badrinarayanan

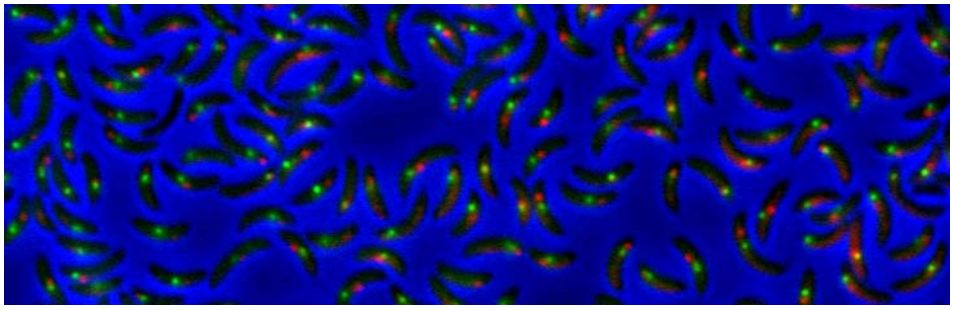
Cells constantly face the threat of DNA damage. Incorrectly repaired or unrepaired damage can lead to mutations, loss of genetic information or even cell death. We study how DNA damage repair is regulated in bacteria to ensure the maintenace of genome integrity.

Maintenance of life requires the preservation of genomic integrity. Double-strand breaks (DSBs) are a particularly lethal form of DNA damage and incorrectly repaired or unrepaired DSBs can lead to mutations, loss of genetic information and even cell death. Cells in all domains of life are capable of faithful DSB repair via homologous recombination, which requires an unbroken, homologous copy of DNA as template for repair. Apart from recombination, eukaryotes and some bacteria also use an alternative end-joining pathway, which does not require a second copy of duplex DNA for repair. Although error-prone, this pathway avoids the lethality of a DSB, making it important. While extensive biochemical experiments have been useful in understanding the key events underlying DSB repair *in vitro*, how repair is facilitated *in vivo* remains poorly understood. Recent advances in molecular and cellular biology techniques have now opened the doors to studying mechanisms of repair and the regulation of this process in living cells. This is particularly important, as repair has to be coordinated with other cellular processes such as DNA replication and cell division as well as carried out under the constraint of chromosome structure. The goal of my research group is to understand how DNA repair pathways are regulated to ensure the maintenance of genomic integrity.

We use a combination of genome-scale assays as well as quantitative live cell imaging techniques, along with genetic and cell biological read-outs to investigate repair in two bacterial model systems: *Caulobacter crescentus* and *Pseudomonas aeruginosa*.

The current focus of the group is to study the mechanisms of double-strand break (DSB) repair in living cells. Specific research projects are to address the following:

1. How is DSB repair via homologous recombination regulated *in vivo*?
2. What is the molecular mechanism of end-joining repair in bacteria?
3. How is the process of pathway choice between error-prone and high fidelity repair modulated?



Caulobacter cells with fluorescently labelled chromosomal loci in red and green.

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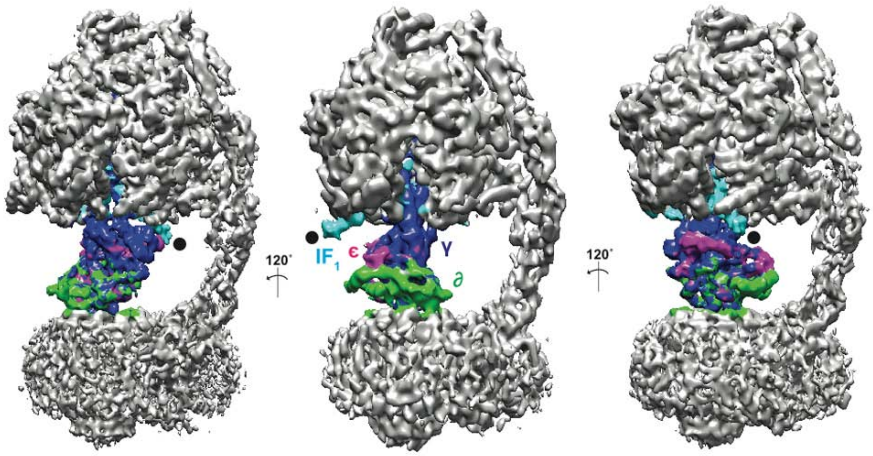
MEMBRANE PROTEIN STRUCTURE AND DYNAMICS

Vinothkumar Kutti Ragunath

Membranes define a cell and proteins within the membrane mediate 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 cryomicroscopy. Some of the problems traditionally associated with membrane protein structures including the amount of protein and ability to grow crystals can be overcome with single particle cryoEM. Using cryoEM and when necessary X-ray crystallography, I would like to determine the structure and elucidate the function of a range of membrane proteins including enzymes, channels and transporters in particular rhomboid family of proteins and ion channels from sperm. In the near future, I would like to expand into imaging some of these proteins in their native cellular environment by electron tomography.

Although, cryoEM has become very popular, it is clear from theoretical calculations that there is still room for technical improvement in particular specimen preparation and detectors. The figure below illustrates how superior quality maps of highly dynamic ATP synthase can be obtained with less particles with improved detectors. Thus, another research interest of mine is to obtain better quality EM images thereby realising the full potential of cryoEM.



Class 1
 # 19949, 4.4 Å

Class 2
 # 7150, 6 Å

Class 3
 # 10545, 4.8 Å

As the molecules in solution are rapidly frozen, different functional states of macromolecules that might exist can be trapped and computationally classified to obtain many different structures, and thus the dynamics of macromolecules can be studied by cryoEM. The mitochondrial F_1F_0-ATP synthase from *Pichia angusta* in three different states is shown as an example here. ATP synthases are dynamic enzymes that use the proton gradient to synthesise ATP and can exist in multiple different states. Using a protein inhibitor found in mitochondria, the enzyme has been trapped in different states and computationally these states can be separated from a mixture of population. The central stalk that consists of three proteins is coloured in different colours (blue, magenta and green) and the inhibitor protein in cyan. The three states are related roughly by 120° rotation. This example is also used to emphasise how better resolution maps with lesser particles can be obtained with better detectors.

Photography by Ravi Kumar Boyapati, Research scholar, Axel Brockmann lab

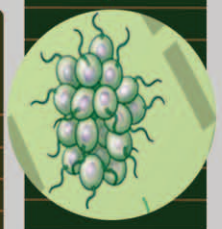
Meetings and

January

Futures in Biology
11th to 14th Jan, 2017

NCBS Annual talks

February

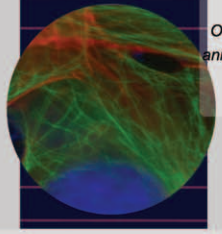


Emergence and Evolution of Biological Complexity
4th to 6th Feb, 2017

A discussion on the physical principles underlying the emergence of complexity in biological systems.

March

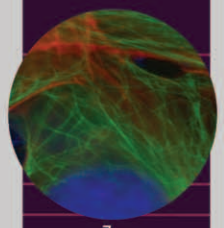
April



Experimental and Theoretical Approaches to Cell Mechanics
23rd April to 6th May 2017

Hands on lecture course to understand the mechanisms operating within the cells.

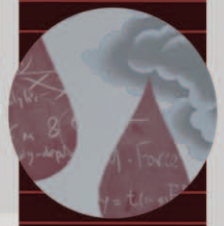
May



JAX-India Seminar
30th May, 2017

On mouse colony management, animal health, optimizing breeding schemes and more.

June



Physics of Life 2017
18th to 25th June 2017

5th NCBS-Simons Annual Monsoon School.

Only a few workshops and meetings are listed here. For a complete list and calendar of events, please visit www.ncbs.res.in/events or scan the QR code:

Workshops

DST-SERB School in Chemical Ecology
3rd to 16th July 2017

A workshop dealing with various aspects of chemical ecology.

Computational Approaches to Memory and Plasticity
19th Jul to 3rd Aug, 2017

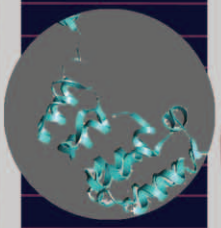
A summer school on the theory and simulation of learning, memory and plasticity in the brain.

7th Annual Science Journalism Workshop
6th to 19th Aug, 2017

A workshop to impart the basic skills necessary for communicating science to the lay person via the written word.

Bangalore Microscopy Course
17th to 24th Sep, 2017

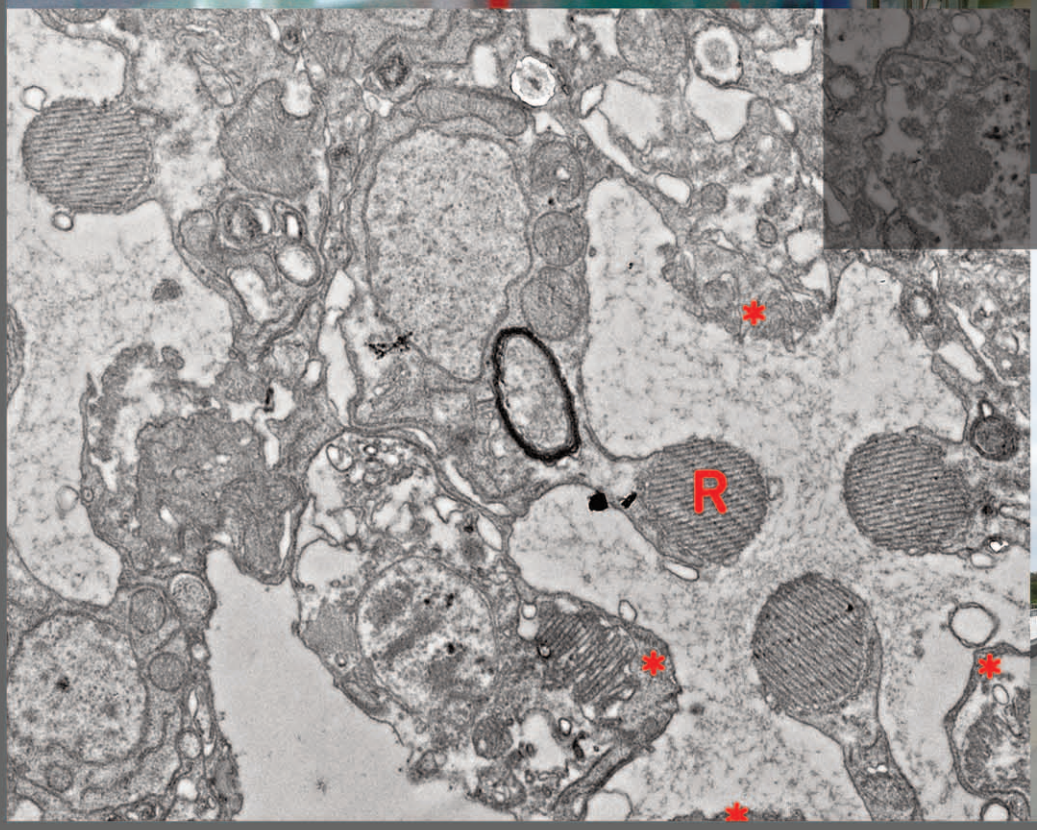
This course provides didactic and hands-on training in state-of-the-art optical microscopy techniques.

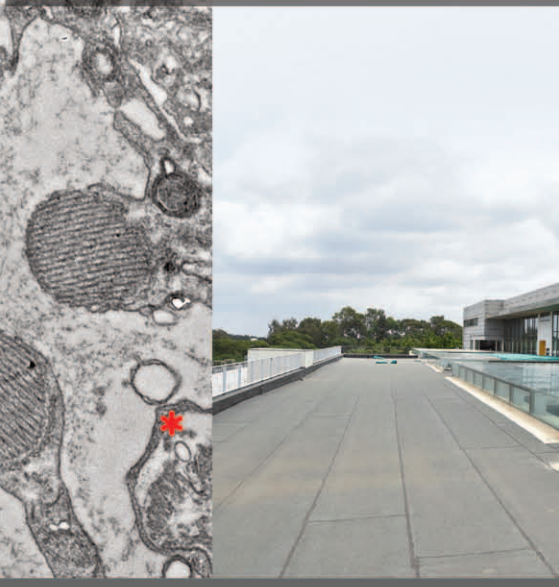


Structure Across Scale
7th to 8th Oct, 2017

Plant insect interactions across gradients
16th to 17th Nov 2017

An Indo-German workshop





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ACADEMICS AND ADMINISTRATION

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Academic Programmes at NCBS : Making Connections

This has been a year of growth and change for our campus, characterized by new connections within India and internationally. We have kicked off multiple post-doctoral fellowship schemes with partner institutions around the world, including the University of Cambridge in the UK, the Max Planck Institute in Germany, Institut Curie in France, and RIKEN in Japan. Our internship programmes for undergraduates are thriving, as we host students from the IITs, IISERs, BITS Pilani, MSU Baroda, and Manipal University. Our continuing engagement with the Tibetan diaspora allows Tibetan students from schools across India to work at labs on campus. Our flagship Chemical Ecology programme attracts students from Northeast India, from six partner institutions including IBSD Sikkim and Rajiv Gandhi University Arunachal Pradesh, to train in laboratories on our campus. The JGEEBILS Examination consortium continues to expand and now includes 17 institutions across India, serving as a central hub for students applying to biology PhD programmes across the country. We were very excited to welcome our alumni from around the world on the occasion of NCBS's 25th year celebrations. Finally, closer to home: we are very excited to welcome our largest incoming group of PhD students.

Connections are also at the heart of student training and mentorship. Our goal is to train the next generation of researchers in the life sciences. This is a field that is rapidly growing and changing. It is impossible to squeeze every known aspect of biology into a standard curriculum, nor would this be desirable since it would be out of date within the year. Instead, we train our students to become perpetual learners, to reach out into areas beyond their comfort zone, and to make connections between disparate facts and phenomena and thereby derive biological insight. Our PhD and Integrated PhD students plunge into science from the day they arrive on campus: they are taught about research ethics and methodology, they rotate in multiple laboratories before choosing which one to join. They are exposed to the latest data and trained to critically evaluate scientific evidence, through a packed calendar of campus seminars and interdisciplinary journal clubs. They are taught to communicate their science in the Annual Work Seminars and the Sympotein seminar series. They are exposed to state-of-the-art techniques in hands-on workshops such as the Bangalore Microscopy Course. Students in the Masters Program in Wildlife Biology and Conservation have an intensive curriculum that combines on-campus coursework along with work at field sites across India, from the Sikkim Himalayas and the Western Ghats to the Andaman Islands. Through fieldwork these students learn the art of research even as they generate new knowledge to promote the cause of conservation. The end product of this training, mentorship and research is far beyond a thesis: it is a well-rounded researcher, ready to take the next step in an independent research career.

Mukund Thattai,
Head, Academic Activities

Administration and Finance

Administration plays a vital role in overall functioning of the Campus. It is very important for efficient functioning of the Centre. The role of administrator involves a great deal of multitasking. We have to work with teams, oversee the operations within the centre, manage groups, coordinate with management and engage in planning according to the needs of the centre. It is a link between various departments and ensures the smooth flow of information from one part to the other. An effective and accommodative administration is a must for any organization, especially for research centres such as NCBS so as to ensure professional and smooth conduct of research activities. The role of administration in a research institution such as NCBS is helping Faculty carry out research and representation of institute's interests in the ever-growing complexity, changing economic conditions and needs of the society. Administration at NCBS is involved in coordinating dissemination and implementation of policies, procedures and guidelines and facilitating inter and intra department co-ordination within NCBS, Tata Institute of Fundamental Research (TIFR) and Department of Atomic Energy (DAE). Similarly, Finance at NCBS acts as a primary point of contact for faculty / researchers requiring financial / administrative assistance right from the proposal stage to post award management of research funding and ensures compliance with all applicable regulations and policies.

The profound growth in terms of infrastructure and facilities in the recent years at our campus has posed new challenges to administration and finance in handling multifunctional tasks within stipulated time period with limited resources. Various constituent attempts have been made to make challenges look smaller with better administrative procedures and process to achieve desirable healthy result.

In January 2017, NCBS reached one of the most important milestones - the Silver Jubilee of its establishment. The institute is ever-striving to break its own established norms of excellence so as to enhance its excellent reputation in research, teaching and mentoring worldwide and become a centre of excellence in biology.

During the last few years, NCBS has grown in size and stature. The 'Financial Progress' table on the adjoining page shows our growth, both physical and financial, during the year 2016-17 as compared to the previous year 2015-16. It is observed that expenditure on Research & Development has shown a healthy increase of 27% (from Rs. 350.92 million to Rs. 446.52 million) while there has been a constant expenditure pattern observed in extramural spending.

Salaries and fellowships has seen increase of 29% during the corresponding period mainly due to implementation of Seventh Central Pay Commission w.e.f. 01.01.2016. There is a substantial reduction in operational expenditure i.e., 20% as compared to the figures of 2015-16.

There is a constant growth in obtaining Extramural grants from various funding agencies and also philanthropic fundraising. Thirteen new grants were added over the last 12 months. Besides, three endowment donations were received during this period totalling to Rs. 5.10 crore including the one from M/s Infosys Foundation (Rs. 5.00 crore) towards corpus funding for travel fellowships.

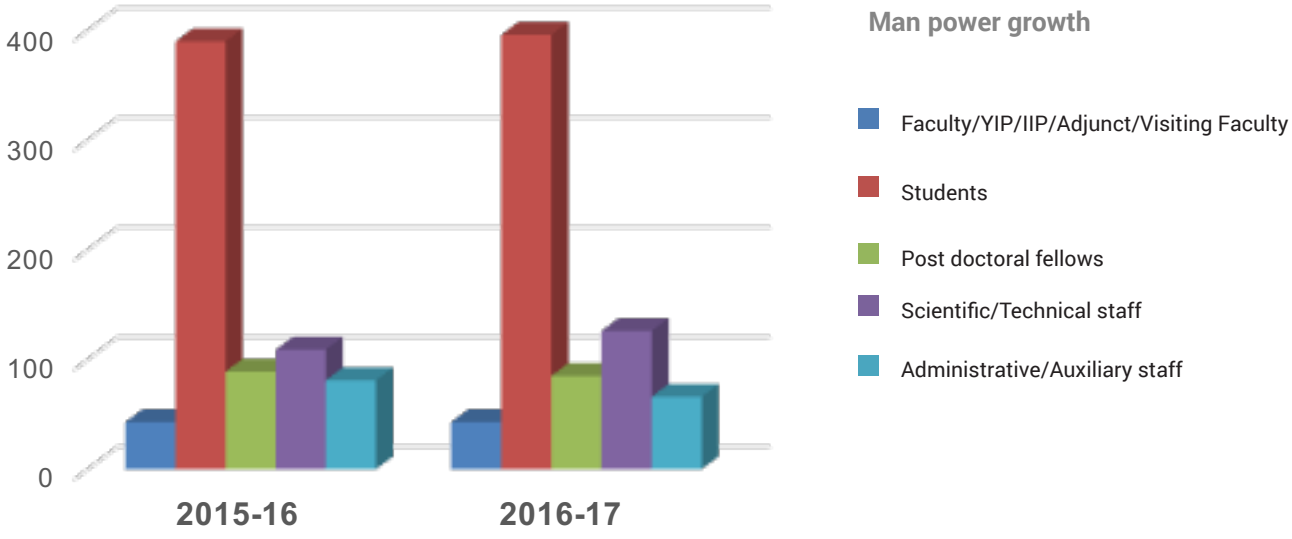
Other significant activities carried out in the recent time includes successful implementation of TIIS (TIFR's Integrated Information Systems), an in-house developed integrated ERP software solution for TIFR and initiation of uploading of GFR-19A for extramural funds on Public Financial Management System (PFMS), a web-based online software application developed and implemented by the Office of Controller General of Accounts.

I would like to sincerely thank all my colleagues for their continued support and also contribution from Tata Institute of Fundamental Research and Department of Atomic Energy for being the backbone of NCBS. I would also like to express my profound gratitude to all the funding agencies and philanthropic donors for their kind patronage and continued support.

Pawan Kumar Pahwa
Head, Administration & Finance

Financial Progress

EXPENDITURE (Rupees in Millions)			
Sl. No	**Particulars**	**2015-16**	**2016-17**
1	Research & Development	350.92	446.52
2	Extra Mural Grants	331.16	325.14
3	Salaries & Fellowships	141.33	182.90
4	Operational Expenditure	317.44	254.60
5	Construction	63.67	12.71
	Total	**1204.52**	**1221.87**



Man power growth

- Faculty/YIP/IIP/Adjunct/Visiting Faculty
- Students
- Post doctoral fellows
- Scientific/Technical staff
- Administrative/Auxiliary staff

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, via research funding. The office continues to offer a concerted mechanism for managing these activities across the three member institutes of the Bangalore Life Science Cluster.

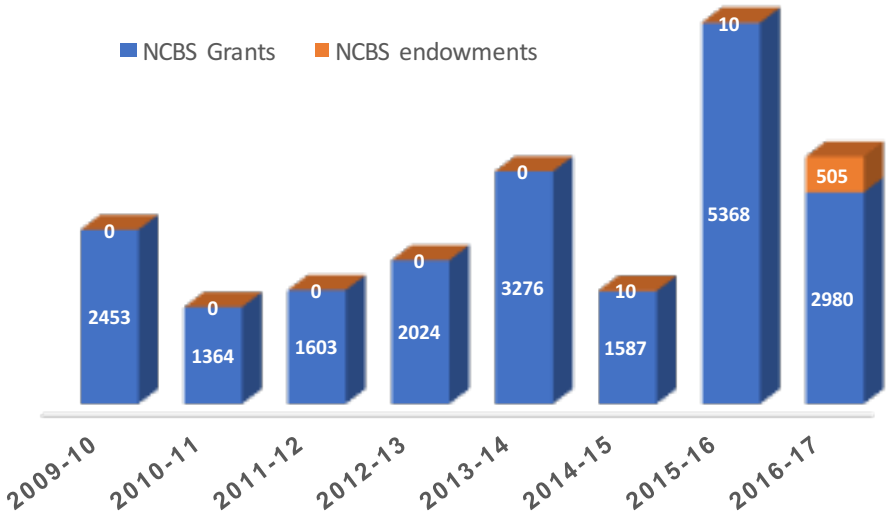
Over the course of the last seven years, the Sponsored Research team within the RDO has continued supporting the diverse needs of the campus in fundraising, grants management and contract negotiation for research funding from funding agencies, corporate sources and charitable organizations. More recently, the Developmental Activities team at the RDO has started working across with campus colleagues and external individuals and organizations to identify fundraising priorities, facilitate campus funding from philanthropic sources, manage donor engagement events, communications matters and build sustainable relationships with donors.

2016 marked the 25th year of the creation of NCBS and this was an appropriate time to create an Endowment Fund for research, training, innovation and outreach. Sustained effort from an extended team of campus colleagues and the generosity of our philanthropic partners resulted in the initiation of the Endowment Fund. NCBS received corpus donations from the Wildlife Conservation Trust, the Infosys Foundation and Dr Kiran Mazumdar Shaw. Generous support from the Infosys Foundation has enabled the creation of travel awards for students to travel, attending international conferences and workshops and broadening their horizons in collaborator laboratories worldwide.

The Cluster campus was the venue for a learning session titled "IPI Thematic Session on Philanthropy for Science, Research and Innovation" for philanthropists, including representatives from the Tata Trust, coordinated by the India Philanthropic Initiative. Noted philanthropists Mr Kris Gopalakrishnan and Dr Kiran Mazumdar Shaw steered the session, which had representation from several Indian research organizations including ICTS-TIFR and TeamIndus, together with philanthropists and Foundation staff.

Developing the portfolio of philanthropic and other support to the campus has required sustained work from the team on all fronts, including our outreach activities. Work at the RDO is made possible by a well-knit group of dynamic and professional individuals, entrepreneurial in spirit and firmly committed to offering several key services to the campus at the boundaries of science, management and outreach. With a vibrant team, emerging opportunities on the campus and new connections on the outside, we look forward to a rewarding journey further ahead for the RDO, supporting campus research funding and the Endowment Fund.

Savita Ayyar
Head, RDO



Major Extramural funds and Endowment donations received at NCBS (in lakh INR)


AS LAB

Research Facilities

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 with state-of-the-art knowledge in the use of such technology platforms and able to train institute scientists in the use of such facilities. The research facilities at NCBS are designed to meet these requirements.

Facilities Coordination Committee: *R Padinjat, A S N Seshasayee, S Krishna and U S Bhalla*

Common research facilities at NCBS

Animal Care and Resource Center (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 plus strains of mice, more than 12 lines of rats, 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 GH, Aurelie Jory, Sangeetha B, Latha Chukki, Kamlesh KV, Sreenivasulu T, Vinodkumar D, Manjunath AM, Rupa Kumari, Akshay Bhatt and Shruthi M.*
Faculty Advisory Committee: *R Ladher, H Ghosh, C Jamora and R Sambasivan*

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: *Ranjith PP and Bhoomika S*
Faculty Advisory Committee: *P Shivaprasad, V Sundaramurthy, C Jamora and S Laxman*

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 need of the internal and external researchers. The perennial training programs in imaging and flow cytometry conducted at CIFF is open to basic and clinical researchers.

CIFF crew: *H Krishnamurthy, Manoj Mathew, Navya Jain, A Divya, Amit Cherian, N. Ranjana and HV Anil Kumar*
Faculty Advisory Committee: *V Thirumalai, R Ladher, and S Raghavan*

Computing Facility is equipped with 3 high performance clusters and 1 centralized data storage system. The computing clusters deliver a computing power of 280 TFlops in total. A data storage of 750 TB, caters to the storage needs of on-campus researchers. Users are given basic instructions following which they are equipped to install and run the applications.

IT Crew: *PK Baruah, Rajshekar KS, Rajesh R, Chakrapani, Rifat N, Deanish MA, Arindam D, Alok B, Divya K, Subramani RP and Kishore R,*
Faculty Advisory Committee: *Sandeep Krishna, Madan Rao and R Sowdhamini*

Electron Microscopy (EM) Facility is equipped with two electron microscopes including high-resolution TEM (Tecnai T12 G2 spirit) and high-resolution FESEM (Merlin Compact VP), Cryo-SEM as well as 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: *Nagendra Pratap Singh, Deepti Negi and Saloni Sharma*
Faculty Advisory Committee: *S Sane and S Raghavan*

Fly Facility is a one of its kind facility that caters to the needs of *Drosophila* biologists within and outside of NCBS. It maintains approximately 16000 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 transgenesis and *Drosophila* husbandry.

FF crew: *Deepti Trivedi, Gajendra, Basavaraj, Yashwantha, Srividhya A, Hemavathy C, Anitha VA, Vinitha CM, Nataraj N, Kishore V, Shwetha H, Manna Ghalia and Janani SV*
Faculty Advisory Committee: *G Hasan and T Mukherjee*

Genomics Facility includes both Sanger sequencing and a Next Generation Genomics Facility (NGGF).The facility is equipped with 2 state-of- the-art Sanger sequencing machines. DNA sequencing facility provides plasmid, PCR product sequencing and genotyping services to the internal and external researchers in very short turnaround time (1-2 days). NGGF is equipped with one state-of- the-art high throughput next generation sequencing platform and two benchtop next generation sequencing platforms. NGGF caters the next generation sequencing needs of the internal and external researchers. NGGF 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: *A Seshasayee, D Agashe, D Notani and D Palakodeti*

Greenhouse Facility is equipped with 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 to work on plants or plant-animal interactions.

Crew: *Ranjith PP, K Thirumala Raju and Ashok Kumar*
Faculty Advisory Committee: *P V Shivaprasad and M Sankaran*

High Throughput Screening and High Content Imaging Facility (HTS/HCI) is equipped with 5 integrated liquid handlers which can perform multiple activities in parallel in 96, 384 and 1536 format. HTS has two high-end cell imagers which can read fluorescence in confocal mode. The facility also houses a BSL2 cell culture lab. Screening facility is an expert-assisted facility which caters to both internal and external academic and industrial users. Screening facility offers training program on HTS.

HTS Crew: *Shahab Uddin MS and Chandan Mitra*
Faculty Advisory Committee: *V Sundaramurthy and R Sambasivan*

Museum and Field Stations Facility is presently equipped with four field stations and research collections. The goal of this facility is to streamline our field operations, provide space for long-term archival of important biodiversity-related materials, and provide opportunities for public outreach to efficiently and effectively connect to the larger society and the stakeholders.

MFFS crew: *Varad Giri, Tarun Karmakar, Chengappa and Raghvendra*
Faculty Advisory Committee: *K Kunte, U Ramakrishnan and S Sane*

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 customized 1 to 4 week training programs in the facility is open to basic and clinical researchers.

MMF crew: *Feroz M H Musthafa*
Faculty Advisory Committee: *S Thutupalli, S Chattarji and P Vemula*

Mass Spectrometry (MS) resources on campus aim to provide researchers with state-of- the-art techniques and equipment to characterize biomolecules. A number of modern instruments for the separation, identification and quantitation of all major biomolecules by mass spectrometry based approaches are available. In addition to providing MS based structural characterization services, the MS facility provides training on the use of different LC-MS/MS technologies as well as develop new analytical methods required to facilitate on- and off-campus research.

Facility Crew: *Dhananjay Shinde and Raviswamy M*
Faculty Advisory Committee: *R Venkatesan, S Laxman and A Brockmann*

Mouse Genome Engineering Facility (MGEF) provides services and training to generate genetically modified mouse models using the latest gene editing and transgenesis 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, maintenance of the new Indian Laboratory Mouse Repository and *in vitro* fertilization procedures for resurrecting frozen sperm or embryos.

MGEF Crew: *Aurelie Jory, Jaya Purushotham, Shilpa B A, Reena V and Latha Chukki*
Faculty Advisory Committee: *R Ladher, H Ghosh, C Jamora and R Sambasivan*

Nuclear Magnetic Resonance (NMR) Facility is equipped with 2 machines for structural biology studies. The facility provides service for both internal and external users and periodically conducts training programs for new users.

NMR Crew: *P Purushotham Reddy*
Faculty Advisory Committee: *R Das, J Udgaonkar, S Ramaswamy, M Sirajuddin and A Ramesh*

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 program for new users under the supervision of the Campus Radiation Safety Officer. In addition to the use of radionuclides, the training program includes modules on the safe disposal of radionuclides in line with regulations.

Radioactive Facility Crew: *Ranjith PP and Ashwin Nair*
Faculty Advisory Committee: *P V Shivaprasad, C Jamora, A Ramesh and S Laxman*

Photography by Sahil Lall, Research Scholar, MK Mathew Lab

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Twenty-fifth anniversary celebrations

NCBS commemorated its Silver Jubilee in 2016 with a number of conferences, workshops, outreach initiatives and other events continuing throughout the year. The celebrations culminated in our customary Annual Talks, 11-14th Jan 2017.

The Science and Society programme at NCBS seeks to promote a public understanding of science framed with larger historical, sociological and philosophical perspectives, and to understand and engage with themes and perspectives of intellectual foundations, human dimensions and impacts of scientific and technological development, particularly in biology. To realize these goals, a number of outreach and educational events were performed. Celebration of the 25th year of NCBS began with an exhibition on history of NCBS and a panel discussion to remember the person, scientist and institution builder, Prof. Obaid Siddiqi. The panel discussion was led by Ramachandra Guha and included Prabhat Patnaik, Dunu Roy, Imrana Qadeer and VijayRaghavan. Together with this commemorative event, the NCBS Alumni association hosted its second alumni meeting to connect our sizeable number of associates spread all over the world. The meeting encompassed talks by distinguished Alumni, brainstorming sessions on alumni activities and special lectures by eminent personalities within India.

Second, over eight public lectures were held over the past year covering topics from the History of Science to the applications of neuroscience in the science/society interface. As part of our thematic lecture series/ book projects, we hosted three sessions titled Future of Nature, a programme curated by ecological historian Mahesh Rangarajan together with Jayashree Ratnam and Ajith Kumar from our Wildlife and Conservation Science Program. The series provided a view from a historian, social and ecological perspective of what we have done to our immediate neighborhood and our planet. Guest faculty Prof. Dhruv Raina from Jawaharlal Nehru University and Prof. Gordon McOuat from Kings College, Halifax, Canada also taught an introductory seminar course exploring the philosophical underpinnings of science and social science; the science and society relationship, the HPS approach (Situating Science), and transcultural perspectives of science and the non-west. The course was attended by participants from four different institutions across Bangalore.

On 22 October we celebrated Foundation Day, commemorating the date when formal orders by the Department of Atomic Energy were issued to convey approval and sanction of the Govt of India for setting up NCBS. The programme on this day included a public lecture by P. Balaram on “Reflections on the Birth of NCBS and the Evolution of the Biological Sciences in India Over the Past Four Decades”, cultural and social programmes organized by staff members and their family, and a Rudraveena concert by Bahauddin Dagar.

NCBS Foundation Day included cultural programmes by staff and students, a public lecture by Prof P Balaram and a Rudraveena concert by Bahauddin Dagar.

Finally, what began with an exploratory exhibition in September 2016, was expanded in October 2016 as the Archives Project. These exhibitions explored the history of NCBS beginning with its roots in TIFR, Mumbai and included interesting installations displaying 25 years of science and thematic areas of research explored at NCBS, progress achieved in these and related areas, creation of new programmes and project, etc.

Several efforts were made this past year to expose students and the public to the science and the excitement at NCBS.

Jagriti Theatre in collaboration with NCBS as part of a Wellcome Trust UK funded project ran a theatre-science project on Antibiotic resistance and produced a play 'The Vaidya's Oath'.

From January 13, 2017 to March 31, 2017, the Seeds of Culture and exhibition, curated by Scholar in Residence, Annamma Spudich, focused on the pivotal role that Indian botanical-medical knowledge systems had in shaping the history, geography, and the study of natural sciences and medicine in the pre-modern world. This exhibition highlighted books, journals, scrolls, etc. that are invaluable resources of the many vanished regional medicines and therapies of India, not found in Indian classical medical texts.

November 12 was celebrated as Science Day. Students from several schools across Karnataka had the opportunity to visit NCBS and partake in a number of exhibits, experiments, and hands-on demonstrations of the wide variety of research performed at NCBS. This event incorporated a wide number of faculty, students, and staff on campus to share the exciting research currently being performed.

Top: Displays of NCBS archives exhibition. Bottom left: NCBS Science Day, and bottom right: a theatre-science project on Antibiotic resistance.

25th Year Annual Talks (11th-14th January 2017)

NCBS celebrated its 25th anniversary with a year of scientific meetings, activities spanning science and society, and outreach events. The Annual Talks were the culmination of this effort. We marked the occasion with special lectures by many of the scientific members of our Management Board, lectures by our Scientific Advisors, and by several special invitees.

We had a particularly stellar group of visitors, who were also serving as part of our 5-year reviews of faculty. Nobel Laureate, Prof. Randy Scheckman also visited the campus during the talks and gave a Special lecture on *Sorting of small RNAs into extracellular vesicles secreted by human cells*.

In a departure from previous Annual Talks, we had a special session devoted to Science and Society where NCBS hosted a series of talks by innovative thinkers from sciences, arts, businesses and academic spheres. This was kicked off by an introduction to an exhibit on *Traditional Indian Medicine through Western Eyes- "Seeds of Culture"*, curated by Annamma Spudich, scholar in residence, NCBS. Prof. VijayRaghavan, NCBS faculty member and Secretary of the Department of Biotechnology, gave an overview of trends in institution building in India. Prof. Indira Chowdhury, Founder-Director of the Centre for Public History at the Srishti Institute of Art, Design and Technology, Bengaluru gave her perspective on Institutional History in India through her talk "*The predicaments of institutional legacy: The archives of TIFR and what they tell us about molecular biology."* This was followed by a stirring account of Public health, research policy, and practice in India- *"Can neuroscience address India's public health needs: from myths to reality"* by Prof. Vikram Patel (member of a policy group that's developing India's first national mental health policy; co-founder of an NGO, Sangath and Co-director of the Centre for Global Mental Health at the London School of Hygiene & Tropical Medicine).

We also heard about *Research and the Endless Frontier* from Kris Gopalakrishnan (Co-founder of Infosys and Co-founder of Axilor Ventures-a venture capital platform for young entrepreneurs) with a perspective on research and the linkages with industry. This session highlighted the broad span of the engagement of NCBS with globally important matters of public health, science policy, and institution building. Finally, Prof. Janaki Nair, writer and Professor, Jawaharlal Nehru University, Delhi concluded the session with a short talk on *Biology through the lens of the human sciences* and a panel discussion on the *Role of Social Science in the Future of Biology*. The endeavor facilitated discussions on thought provoking ideas to broaden our perspectives and expand our ongoing interactions with the society.

Upinder S Bhalla
Dean, NCBS

Selected pictures from the Annual Talks

NCBS Alumni meet (December 12th, 2016)

Looking back at the growth of NCBS, among our most visible and far-reaching effort has been the training a new generation of life scientists. Reconnecting with our alumni, now spread across continents, was a major highlight of our NCBS@25 celebrations. Some have made their mark in academia, others have moved to careers in education, policy, science journalism, conservation, or even as entrepreneurs and inventors.

On December 12th, 2016 we hosted our second NCBS Alumni Meeting as part of our NCBS@25 celebrations. We were very excited to welcome alumni from across the world, who had made an effort to attend this very special occasion. At this event Upinder Bhalla, the Dean of NCBS, spoke to alumni about how the campus has grown over the years, with the addition of new research streams, new experimental facilities, and field stations across India. Mr. Rakesh Godhwani of IIM Bangalore spoke about the power of Alumni Associations. We held a panel discussion on a path to a self-sustaining alumni group, one that would serve as a permanent resource for all its members. The alumni had the chance to visit the laboratories and campus facilities, with the Buggy tour being a very popular highlight.

At the Alumni Meeting, we were proud to confer our first Distinguished Alumnus Award on Dr. Sudipto Roy, who spent the years 1993-1998 pursuing his PhD at NCBS. His PhD work, under the mentorship of K. VijayRaghavan, focused on muscle and neural development in Drosophila. He is currently a Senior Principal Investigator at the Institute of Molecular and Cell Biology in Singapore. Through his research, Dr. Roy has made key contributions to our understanding of vertebrate development, especially on muscle patterning and more recently on cilia and ciliopathies.

Dr. Roy looked back fondly at his memories of NCBS in its earliest days, recalling: “If there was one thing that I were to remember most vividly about my time at the NCBS, it has to be the exhilarating experience of being part of an open lab concept, where students and postdocs from different groups and working with diverse aspects of biology, worked in a common lab and shared common reagents! Unlike many ambitious projects in India, which start off with great pomp and circumstance only to fizzle out rapidly, the NCBS has stood the test of time. In the past 25 years, the NCBS has established itself as a premier research institute in Asia, whose mandate (thankfully) remains investigation into the fundamental questions encompassing all aspects of biology, ranging from molecules to organisms, all the way to evolution and ecosystems“ exactly as Obaid had envisioned all those years ago.

As a way to maintain links with our alumni, we have created the NCBS Alumni Card which gives a lifetime of access to our campus and its facilities. We have instituted an up-to-date database of over 200 alumni, and started along the path to constitute a formal NCBS Alumni Association. Our goal is to have active chapters of the Association across the world, especially where there are large clusters of alumni such as in the US, UK, Germany, or Singapore. Members of the Association will have a voice in the future direction of NCBS as we begin our next 25 years of existence.

Mukund Thattai
Head, Academic Activities

Dr Sudipto Roy gets distinguished alumnus award during the NCBS Alumni meet

The NCBS Museum and Field station Facility

NCBS has established a unique Museum and Field Stations Facility to spearhead research and outreach in biodiversity and conservation.

Since the early 2000s, NCBS has significantly expanded into the areas of ecology, evolution and conservation biology. As the next phase of this growth in research, training and outreach activities, NCBS established the Museum and Field Stations Facility in 2016. The goal of this facility is to streamline our field operations, to provide space for long-term archival of important biodiversity-related materials, and to provide opportunities for public outreach through which we will connect to both stakeholders and society at large.

The facility maintains an air-conditioned, climate-controlled Research Collections unit that is unique in Asia. It holds biodiversity-related and other materials important for phylogenetic, population genetic, and other evolutionary, taxonomic, ecological and conservation research. This includes geo-referenced data and a DNA library for specimens. We envision this facility to serve a broad range of scientists who can utilize a long-term reference for biodiversity-related work in India.

The NCBS Science Museum also provides opportunities for students and the general public to interact with scientists and learn about latest discoveries in biological sciences. The museum provides a major interface for NCBS to interact with society that also supports our research and gains from our findings.

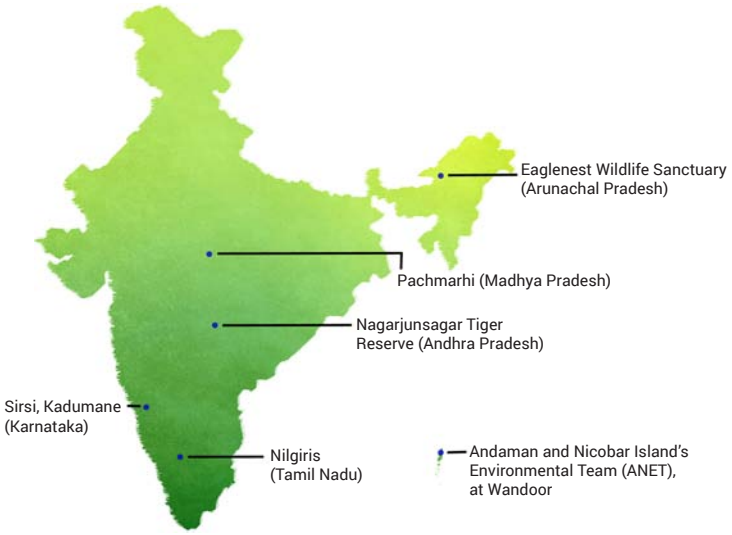
The NCBS-Pachmarhi Field Station

NCBS currently has six field stations all over India. A new wildlife field station was set up this past year on the former site of the High-Energy Gamma Ray Observatory (HEGRO) at Pachmarhi, in the state of Madhya Pradesh.

This field station aims to serve researchers who study diverse aspects of the flora and fauna of Central India. Pachmarhi is located at the heart of the Satpura National Park, and in close proximity to Kanha Tiger Reserve, Pench National Park, Tadoba Tiger Reserve, Melghat Tiger Reserve, etc. The paucity of data on Central Indian flora and fauna coupled with the richness of the fossil record and abundance of Neolithic cave paintings provide unique opportunities for natural history research in this region. The field station is housed in an approximately 7 acre area within a recently refurbished British-era bungalow, with other amenties including 8 dorm rooms, 4 flats, electricity, internet, offices, labs and workshops, transport vehicles, and a full complement of personnel.

In addition to research, the NCBS-Pachmarhi Field Station will also serve to popularize wildlife sciences among students from local schools and colleges who can use this infrastructure to conduct small or large research projects under direct supervision of the top scientists in the country. For example, the field station will host several short courses throughout the year conducted by top international scientists. We hope that this new station will lead to a greater awareness of the importance of forest ecology and conservation among scientists, students, and the public at large.

The Pachmarhi field station



Various NCBS-field stations all over India.

Chemical Ecology Network Program

This year marked the launch of the “Twinning Network Program on Chemical Ecology” initiative in India.

This multi-institutional program is a new collaborative and interdisciplinary programme in Chemical Ecology between institutions in the North Eastern Region (NER) and partners in Bangalore - NCBS, IISc and UAS. The DBT-funded initiative is aimed at building new scientific capacity in India to provide unique training and career development opportunities for aspiring and established scientists particularly from the Northeast. The program encompasses 24 research projects with 15 Junior Research Fellows, 9 Postdoctoral Scholars, and 22 Principal Investigators from five Northeast and three Bangalore Institutes.

This program has also initiated several capacity development activities steered by NCBS. First, a five months coursework with over 250 hours of teaching and 12 instructors, was organised for the Junior Research Fellows. This was designed to develop a general understanding of chemoecological rationale and thinking. The Fellows were also provided training on the use of tools and techniques in Chemical Ecology in the Indian Institute of Integrative Medicine, Jammu and Agilent Technologies, Bangalore.

In addition to research and capacity building, the initiative has also stimulated several outreach activities. For the second consecutive year, the program was exhibited in the DST Science Express Climate Action Special (SECAS) II. The train covered 19,000 km and was exhibited at 68 stations across India with over 24.7 lakh visitors, Additionally, a series of online/blended lectures on Chemical Ecology in 8 Northeast states is now underway including participants from up to 15 institutes across the Northeast region and an estimated 600-700 students. We are hopeful that this multi-institutional and multi-disciplinary programme linking Bangalore and Northeast institutes will lead to new scientific developments that increase our understanding of chemo-ecological interactions in the incredibly biodiverse NE region.

The Archives at NCBS

On May 18, 2016, Satyajit Mayor, the Centre Director of the National Centre for Biological Sciences (NCBS), formally announced the initiation of an Archive in a memo to the Centre's faculty, students and staff. This announcement was made on the occasion of the institution's 25th anniversary.

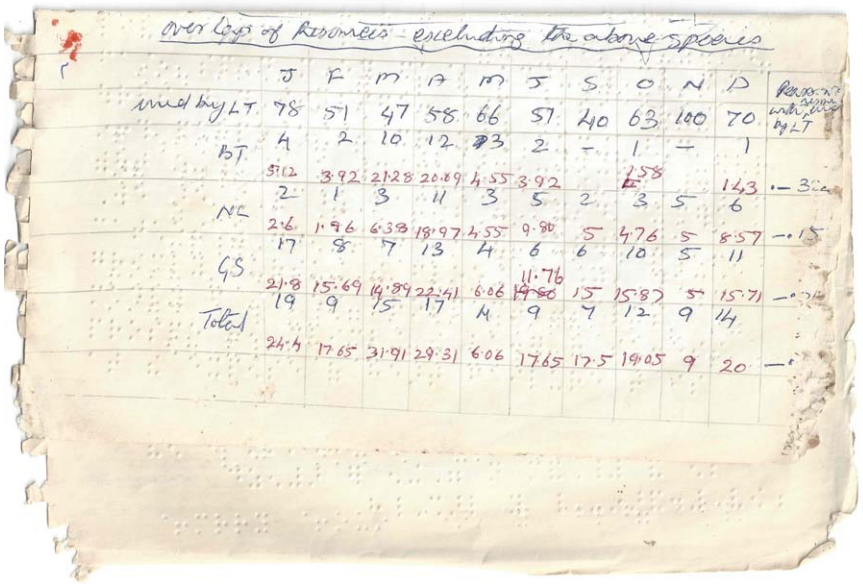
The Archives at NCBS is a repository that is dedicated to holding institutional records that capture its organizational and scientific history. Such records shall be made available for legal, administrative and historical purposes. Through the records preserved in its collections, the Archives will assist in connecting the dots on scientific and organizational trajectories. It is also a collecting Archive: through an active accessioning programme, it hopes to shed light on decisions regarding the course of biological research not just in the institute but also in the country. The Archives is governed by an Archives Review Committee and released its Policy on February 1, 2017. The physical and digital archive (http://archives.ncbs.res.in) will be open for research and public use by July 2018.

On October 22, 2016, the Archives released its first physical exhibit on the occasion of the 25th anniversary of NCBS. The physical exhibit brings forth the history of biology in the TIFR/NCBS complex, focusing on the spaces, facilities, people, and research areas from across the Centre's past and present. In addition, the Archives released a digital exhibit titled "Thirteen ways" (http://archives.ncbs.res.in/exhibit/13ways). The exhibit is a pilot project that tries to bring to light multiple interpretations of NCBS, weaved by the voices of over 70 storytellers, 600 photographs, official records, letters, and the occasional lab note.

In addition to the setting up of a repository, the Archives is also undertaking three other conceptual projects over the coming two years. The first – by summer 2018 – is to release an open source storytelling template as an additional layer to the Archives digital portal. This is a space where researchers, students and the public can form diverse stories from archival material. This will then branch out by 2019 to other archives to develop an interconnected archival digital repository.

The second project is on developing standards across archival material. To this end, the Archives at NCBS has been invited to join in the second pilot phase of the Social Networks and Archival Context Cooperative (SNAC-C), which operates out of the University of Virginia in the United States. The SNAC Cooperative (http://socialarchive.iath.virginia.edu/about.html), which includes the Smithsonian Institution, Harvard University and the U.S. National Archives and Records Administration, is an effort to connect archival material across the world and help discover, locate, and use distributed historical records. The Archives at NCBS will be the first such member institution from Asia.

The third conceptual project is on embedding material from science archives and research in archival repositories in a pedagogical framework. In July 2018, soon after it is open to the public, the Archives will draft a plan to work on pilot projects with students in schools and colleges, engaging them to draw meaning from archival material in their own research and offer interpretations of the same.



Ajith Kumar's field notes from 1982-83, written on Braille paper (sourced from a church in the United States, since resources were limited, and the paper turned out to be good non-blotting paper, useful out in the field). The notes are for studies on how four species of tree living mammals co-exist and compete for same resources in the Anamalai Hills, Tamil Nadu.

Image credit: Archives at NCBS. Courtesy of Ajith Kumar.

Professor Mitradas M Panicker retires

Professor Mitradas M Panicker's name suggests associations across the breadth of the country. Professor Panicker is a Mumbaikar, having spent his early years in what was then Bombay. On joining NCBS in the early 90's, he was referred to as Mitra or Das, besides the more common Panic.

These associations with the coasts notwithstanding, his working life has been spent in the landlocked city of BungleUru. Clearly a difficult person to place in a cubby hole, he has a BSc and an MSc (sort of) in Chemistry, a PhD working on bacterial genetics, and then a career chasing neurotransmitter receptors. Initially the fast acting variety of ionotropic glutamate receptors, and then the slower metabotropic serotonin receptors. And thus to serotonin itself, which now appears to be involved in everything from determining the state of stem cells, to sleep (perchance to dream), and everything in between.

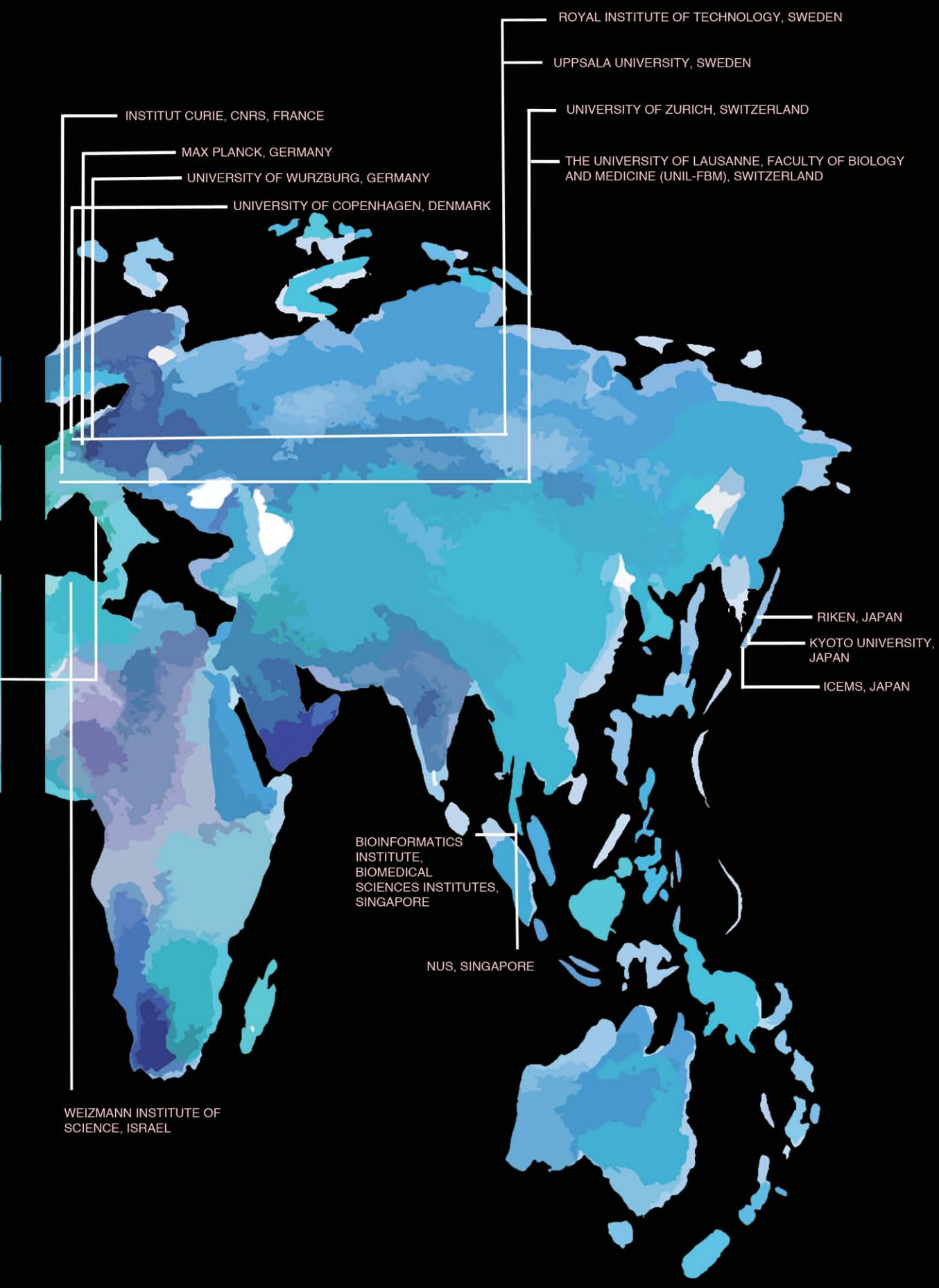
Panicker was one of the first few scientists to join NCBS and arrived with a million ideas on just about everything, especially techniques. He very soon became the go-to guy for any molecular biology issues, set up the first oligonucleotide synthesiser in NCBS and then the first DNA sequencer as well, and ran both for a while. He soon became the resident shrink and spent the evenings counselling students on matters ranging from the stomach to the heart and probably everything else. Very much the Friend, Philosopher and Guide for the early batches of NCBS students. So much so that he was generally acknowledged to the be the *de facto* Director of NCBS from sun down to sun up.

Professor Panicker's exploration of everything new has done much to demonstrate to the world at large that the most advanced technologies could be successfully implemented here. This contributed to establishing a reputation of NCBS being at the forefront of research in modern biology. Well before stem cell research became a bandwagon, he collaborated with an IVF clinic in Bombay to develop four human embryonic stem cell lines. This was in 2001, and was internationally recognised - in fact, these were among a very limited number of lines generated anywhere in the world to be approved by the US government for stem cell research. As one of India's leading stem cell-ologists, he co-wrote and submitted, in 2006, the grant proposal that resulted in inStem. Still on the stem cell theme, he worked with clinicians and scientists from NIMHANS on establishing iPSC lines from Alzheimer's patients. This work then lead to the establishment of a major centre based in NIMHANS and NCBS for creating a registry of iPSC lines derived from patients suffering from various neurodegenerative diseases and their families. It is typical of the person that his contributions are not trumpeted and, in all probability, are not even suspected by most on campus.

His 2004 patent application for a novel assay to screen for antipsychotic drugs was among the first by an NCBS researcher. The US patent was awarded in 2009. The patent made waves and a company stationed equipment in his lab and funded research to develop the assay further. His human stem cell work was also attractive to industry with Cardion entering into a collaborative research agreement in 2001, the first such agreement in NCBS. Having been bitten by the bug, he has continued patenting and has two applications in the works at present. He is also threatening to set up a slew of companies (well, at least one) to take these projects forward. Professor Panicker is a recently married retiree (Mrs. Panicker is a former student of NCBS, and will soon be his new boss). He plans to go back to the bench (in California), and run companies (in India), while bouncing babies on his knee. Not an easy proposition, but we would not bet against the dashing Professor Panicker pulling it off.

M.K. Mathew
J. B. Udgaonkar

NCBS INTERNATIONAL COLLABORATIONS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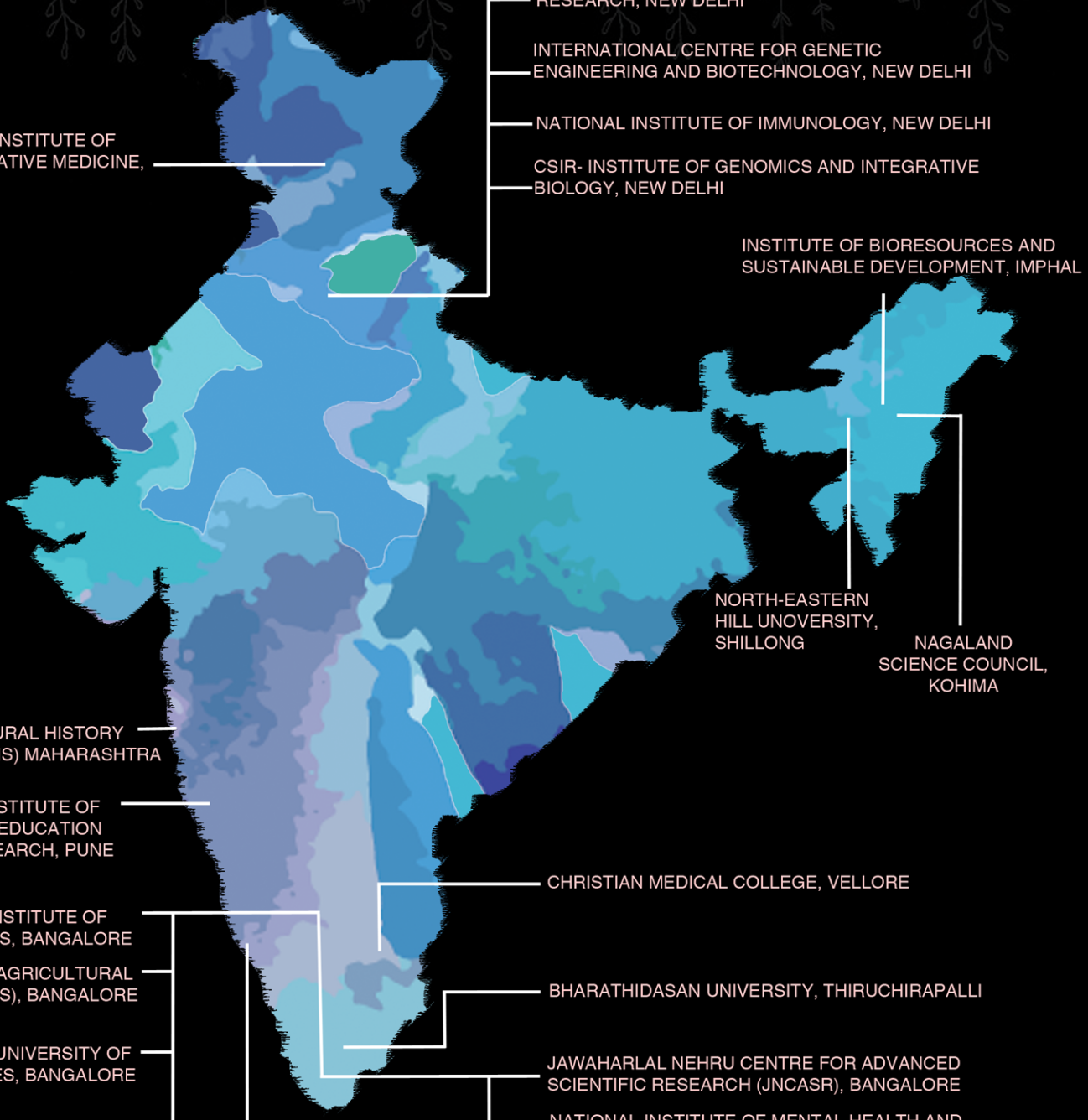

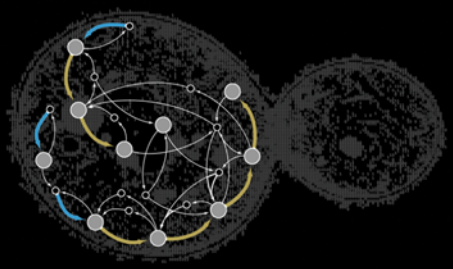

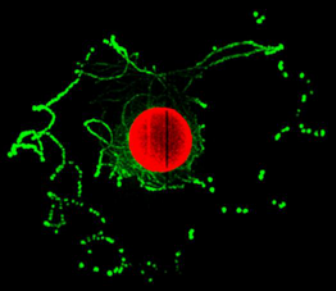

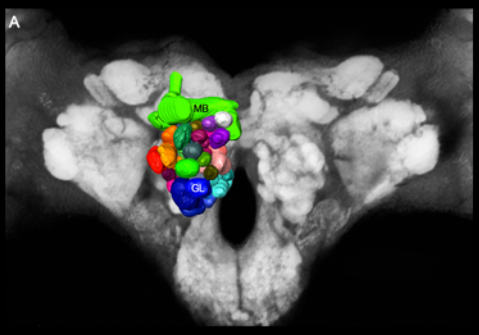

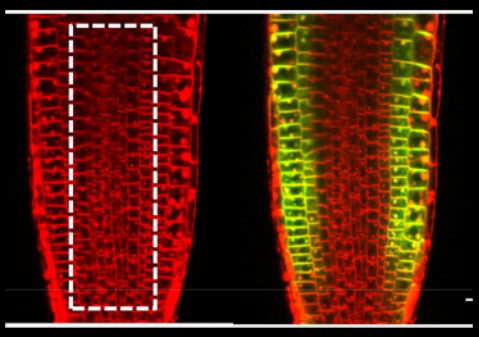

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