# The 45th Indian Biophysical Society Meeting

National Centre for Biological Sciences
Tata Institute of Fundamental Research

27th-29th March, 2023

Programme schedule can also be found at:
https://www.ncbs.res.in/events/indian-biophysical-society-meeting

# Contents

# About

## The Indian Biophysical Society

The Indian Biophysical Society (IBS), founded in 1965 and registered under the Act XXVI of 1961 at Kolkata with its office at Saha Institute of Nuclear Physics (SINP), has grown over the years. Presently, it is holding over 1000 Life-members from all parts of the country. The interdisciplinary nature of the society attracted scientists from not only Phyiscs, Chemistry and Biology, but also from other related areas too such as Biotechnology, Bioinformatics and Medicine.

The first IBS Executive Council (EC) comprised of Dr. D. M. Bose as its first President, N. N. Dasgupta and B. Mukherjee as Vice-Presidents, N. N. Saha as the Secretary, B. D. Nagchaudhuri as the Treasurer, and A. K. Saha, M. N. Rao and S. N. Chatterjee as Members of the Council.

IBS gives many awards to young and established scientists to promote biophysics in India. In addition to six poster awards and one young scientist award, IBS gives two travel awards to cover partial expenses for attending the IUPAB International Biophysics Congress held once every three years and the Asian Biophysics Association (ABA) meeting, which is held once in two years. These awards are: Prof. J. C. Bose award for senior scientists above 35 years of age and Prof. G. N. Ramachandran award for younger scientists below 35 years of age.

## The 45th IBS Meeting

The 45th Indian Biophysical Society Meeting will be held at the National Centre for Biological Sciences (TIFR), Bangalore, between March 27-29, 2023. The 2023 IBS meeting aims to highlight conceptual ideas and foundational aspects of biophysical phenomena across scales and will bring together a wide range of scientists.

The meeting will be comprised of multiple plenary and themed invited talks and poster sessions. Further, in addition to the established and prestigious G.N. Ramachandran Lecture, we will have the inaugural Simons Lecture at this meeting, hosted by the Simons Centre for the Study of Living Machines at the NCBS-TIFR. This lecture will highlight seminal contributions in the use of the quantitative sciences in investigating biological phenomena.

## Organizing committee

Shashi Thutupalli (NCBS, ICTS)
Madan Rao (NCBS)
Ranabir Das (NCBS)
Vinothkumar Kutti Ragunath (NCBS)

# Timetable

Please note that - TS: Tutorials, MS: Mini Symposia (Parallel Sessions), PS: Plenary Session **Microscopy and Cryo-EM** tutorial sessions will be held at Raspuri. **Mechanobiology** tutorial session will be held at Nucleus. **Quantitative Biology/Machine Learning** tutorial session will be held at Safeda.

## Day -1: Saturday, 25 March, 2023

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|---|---|---|---|
| 08:00–09:00 | **Registration** | | |
| 9:00–17:00 | TS | **Tutorial Session 1**<br>Vinothkumar Kutti Ragunath, Ruchi Anand, Ranabir Das | Microscopy, Cryo-EM |
| 9:00–17:00 | TS | **Tutorial Session 2**<br>Pramod Pullarkat, Bidisha Sinha, Venkatesan Iyer | Mechanobiology |
| 9:00–17:00 | TS | **Tutorial Session 3**<br>Vijay Krishnamurthy, Shaon Chakrabarti, Sundar Naganathan | Quantitative Biology/Machine Learning |
| 19:00 Onwards | **Dinner at main canteen (under the glass roof)** | | |

## Day 0: Sunday, 26 March, 2023

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|---|---|---|---|
| 08:00–09:00 | **Registration** | | |
| 9:00–17:00 | TS | **Tutorial Session 1**<br>Vinothkumar Kutti Ragunath, Ruchi Anand, Ranabir Das | Microscopy, Cryo-EM |
| 9:00–17:00 | TS | **Tutorial Session 2**<br>Pramod Pullarkat, Bidisha Sinha, Venkatesan Iyer | Mechanobiology |
| 9:00–17:00 | TS | **Tutorial Session 3**<br>Vijay Krishnamurthy, Shaon Chakrabarti, Sundar Naganathan | Quantitative Biology/Machine Learning |
| 19:00 Onwards | **Dinner at main canteen (under the glass roof)** | | |

*Note: Registration desk (in front of Dasheri auditorium) will be open on both these days.

# Day 1: Monday, 27 March, 2023

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|---|---|---|---|
| 8:00–9:15 | **Registration (in front of Dasheri auditorium)** | | |
| 9:15–9:30 | **Welcome remarks: Organisers of IBS 2023** | | |
| Plenary Session - 1.1 (Venue: **Dasheri**) | | **Assemblies and Evolution of Macromolecules**<br>Chair: Jayant Udgaonkar IISER, Pune | |
| 9:30–10:00 | PS | **Rama Ranganathan**<br>University of Chicago | The Evolutionary Design of Proteins |
| 10:00–10:30 | PS | **Satyajit Mayor**<br>NCBS Bangalore | Cells integrate mechanical and chemical inputs at the cell membrane by building active emulsions |
| 10:30–11:00 | PS | **Oskar Hallatschek**<br>UC Berkeley | Microfluidic Island Biogeography - Jam and Conquer |
| 11:00–11:30 | **Coffee** | | |
| Mini Symposium - 1.1 (Venue: **LH1, Haapus**) | | **Biomolecular Structure and Function - I**<br>Chair: Ruchi Anand, IIT Bombay | |
| 11:30–11:50 | MS | **Appu K Singh**<br>IIT Kanpur | Cryo-EM illuminates new biology of orphan receptors |
| 11:50–12:10 | MS | **Aravind Penmatsa**<br>IISc Bangalore | Insights into mechanisms of GABA uptake and transport inhibition by antiepileptic drugs |
| 12:10–12:30 | MS | **Aditi Borkar**<br>University of Nottingham | Structure probing of native RNA-protein complexes using Mass Spectrometry and Molecular Modelling |
| Mini Symposium - 1.2 (Venue: **Dasheri**) | | **Cell Membrane Biophysics**<br>Chair: PB Sunil Kumar, IIT Madras | |
| 11:30–11:50 | MS | **Thomas Pucadyil**<br>IISER Pune | Mechanistic analysis of membrane fission and discovery of novel fission proteins |
| 11:50–12:10 | MS | **Durba Sengupta**<br>NCL Pune | Specificity and Flexibility of Protein-Lipid Signatures |
| 12:10–12:30 | MS | **Sudipta Maiti**<br>TIFR, Mumbai | Extra-receptor signalling: how the lipid bilayer transduces neurotransmitter signals |
| 12:50–13:50 | **Lunch** | | |
| Mini Symposium - 1.3 (Venue: **Dasheri**) | | **Organization and Dynamics Across Scales**<br>Chair: Sudha Rajamani, IISER Pune | |
| 13:50–14:10 | MS | **Roop Malik**<br>IIT Bombay | A Force at the Edge : Lipids and Motors at Membrane Contact Site |

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| 14:10–14:30 | MS | **Pramod Pullarkat**<br>RRI, Bangalore | Tension buffering mechanisms in axons |
| 14:30–14:50 | MS | **Vishu Guttal**<br>IISc Bangalore | Physics-inspired data-driven models of collective motion |
| Mini Symposium - 1.4 (Venue: **LH1, Haapus**) | | **Biomolecular Structure and Function - II**<br>Chair: Neelanjana Sengupta, IISER Kolkata | |
| 13:50–14:10 | MS | **Shachi Gosavi**<br>NCBS, Bangalore | Understanding how conformational transitions can modulate the folding of proteins |
| 14:10–14:30 (online) | MS | **Raghavan Varadarajan**<br>IISc, Bangalore | Probing protein stability and gene function using saturation mutagenesis |
| 14:30–14:50 | MS | **Tanweer Hussain**<br>IISc, Bangalore | Yeast eukaryotic initiation factor 4B remodels the mRNA entry site on the small ribosomal subunit |
| 15:00–16:30 | **Poster Session / Executive Committee Meeting** | | |
| 16:30– 17:00 | **Tea break** | | |
| Vendor Talks (Venue: **Dasheri**) | | **Talks by sponsors showcasing products** | |
| 17:00–17:20 | PS | **P. Kumar**<br>ThermoFisher Scientific | |
| 17:20–17:40 | PS | **Saji Menon**<br>NanoTemper Technology | |
| 17:40–18:00 (online) | PS | **Aida Llauró Portell**<br>Lumicks | |
| 19:00 Onwards | **Dinner** | | |

## Day 2: Tuesday, 28 March, 2023

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|---|---|---|---|
| 8:00–9:15 | **Registration (in front of Dasheri auditorium)** | | |
| Plenary Session - 2.1 (Venue: **Dasheri**) | | **Chair: Madan Rao, NCBS Bangalore** | |
| 9:30–10:30 (online) | PS | **G.N. Ramachandran Lecture: David Baker** Institute of Protein Science | Protein Design using Deep Learning |
| 11:00–11:30 | **Coffee** | | |
| Mini Symposium - 2.1 (Venue: **Dasheri**) | | **Biomolecular Processing and Dynamics** Chair: Matthew MK, NCBS Bangalore | |
| 11:30–11:50 | MS | **Shovamayee Maharana** IISc Bangalore | RNA-RBP condensates sense cellular RNA and buffer immune response |
| 11:50–12:10 | MS | **Shivprasad Patil** IISER Pune | Dynamic Atomic Force Microscope for Viscoelasticity of Single Folded Domains of Proteins |
| 12:10–12:30 | MS | **Hagen Hofmann** Weizmann Institute | Allostery through DNA, drives phenotype switching |
| Mini Symposium - 2.2 (Venue: **LH1, Haapus**) | | **Biophysical processes in the Nucleus** Chair: Bidisha Sinha, IISER Kolkata | |
| 11:30–11:50 | MS | **Dimple Notani** NCBS, Bangalore | Understanding the enhancer code in regulation of transcription |
| 11:50–12:10 | MS | **Mahipal Ganji** IISc, Bangalore | Single-Molecule Analysis of DNA Base-Stacking Energetics Using Patterned DNA Nanostructures |
| 12:10–12:30 | MS | **Ranjith Padinhateeri** IIT Bombay | Predicting coarse-grained chromatin polymer properties from nucleosome-level contact data |
| 12:50–13:50 | **Lunch** | | |
| Plenary Session - 3.1 (Venue: **Dasheri**) | | **Simons Lecture** Chair: Mukund Thattai NCBS, Bangalore | |
| 13:50–14:50 | PS | **Manu Prakash** Stanford University | Recreational Biology: Topological Puzzles in cell biology |
| Mini Symposium - 2.3 (Venue: **Dasheri**) | | **Mechanics and Geometry** Chair: Arnab Gupta, IISER Kolkata | |
| 15:00–15:20 | MS | **Mandar Inamdar** IIT, Bombay | Active mechanics of epithelial monolayers |

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| 15:20–15:40 | MS | **Tamal Das**<br>TIFR-H, Hyderabad | Unravelling the mechanobiology of cell competition during cancer initiation |
| 15:40–16:00 | MS | **Prerna Sharma**<br>IISc, Bangalore | Enhanced mixing and inversion of vortex flow around confined microalgae |
| Mini Symposium - 2.4 (Venue: **LH1, Haapus**) | | **Systems Biology - I**<br>Chair: Gopalakrishnan Bulusu, IIIT, Hyderabad | |
| 15:00–15:20 | MS | **Rahul Siddharthan**<br>IMSc, Chennai | How transcriptions factors associate in 3D chromatin |
| 15:20–15:40 | MS | **Shaon Chakrabarti**<br>NCBS, Bangalore | Inferring principles of cell fate control from correlated cancer cell lineages |
| 15:40–16:00 | MS | **Shankar Mukherji**<br>WUSTL, St. Louis | Building the cell from unreliable parts: coordinating stochastic organelle biogenesis with cellular growth |
| 16:00–16:30 | **Tea Break** | | |
| 16:30–18:30 | **Poster Session** | | |
| 19:00 Onwards | **Banquet** | | |

## Day 3: Wednesday, 29 March, 2023

| | | | |
|---|---|---|---|
| 8:00–9:15 | **Registration (in front of Dasheri auditorium)** | | |
| Plenary Session - 2.2 (Venue: **Dasheri**) | | **Physical Principles in Development**<br>Chair: Maithreyi Narasimha, TIFR Mumbai | |
| 09:30–10:00 | PS | **GV Shivashankar**<br>ETH, Zurich | Mechano-Genomics of Cell-State Transitions |
| 10:00–10:30 | PS | **Dapeng Max Bi**<br>Northeastern University, Boston | Fluidity and rheological response in confluent epithelial tissues |
| 10:30–11:00 | PS | **Hiroshi Hamada**<br>Kobe University | Biophysical basis of left-right symmetry breaking in vertebrates |
| 11:00–11:30 | **Coffee** | | |
| Mini Symposium - 3.1 (Venue: **LH1, Haapus**) | | **Biomolecular Structure and Function - III**<br>Chair: Deepak Sinha, IACS Kolkata | |
| 11:30–11:50 | MS | **Tripta Bhatia**<br>IISER Mohali | Alpha-amylase and Lipid Membrane Interaction |
| 11:50–12:10 | MS | **Hema Chandra Kotamarthi**<br>IIT, Madras | Probing protein degradation by ATP-dependent proteases and proteasomes using single-molecule force spectroscopy |
| 12:10–12:30 | MS | **Markus Zweckstetter**<br>MPI, Göttingen | A tale of Tau: Associations and Phase Separation |
| Mini Symposium - 3.2 (Venue: **Dasheri**) | | **Modelling Across Scales**<br>Chair: R Swaminathan, IIT Guwahati | |
| 11:30–11:50 | MS | **Vijay Krishnamurthy**<br>ICTS Bangalore | Active Patterns in Cell Polarity and Cell Division |
| 15:10–15:30 | MS | **Kavita Jain**<br>JNCASR | Polygenic adaptation in large finite populations |
| 12:10–12:30 | MS | **Sandeep Krishna**<br>NCBS, Bangalore | Structural determinants of relaxation dynamics in a class of ligation-cleavage chemical reaction networks |
| 12:50–13:50 | **Lunch** | | |
| Mini Symposium - 3.3 (Venue: **Dasheri**) | | **Behaviour and Motion**<br>Chair: Vidyanand Nanjundiah, ICTS Bangalore | |
| 13:50–14:10 | MS | **Bibhu Ranjan Sarangi**<br>IIT-Palakkad | Active particles in soft confinement |

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| 14:10–14:30 (online) | MS | **Karen Alim** TU, Munich | Lesson from smart slime: How active flow networks process information for complex behaviour |
| 14:30–16:00 | **Poster Sessions** | | |
| 16:00–16:30 | **Tea Break** | | |
| Plenary Session - 3.2 (Venue: **Dasheri**) | | **Patterns in Biology** Chair: Shashi Thutupalli, NCBS Bangalore | |
| 16:30–17:00 (online) | PS | **Michel Milinkovitch** University of Geneva | The Unreasonable Effectiveness of Reaction-Diffusion in Vertebrate Skin Colour Patterning |
| 17:30–18:15 | **General Body Meeting** | | |
| 18:15–18:30 | **Closing Session: Poster Awards + Concluding Remarks** | | |
| 19:00 Onwards | **Dinner** | | |

# List of Abstracts – Talks

## Day 1: Monday, 27 March, 2023

### The evolutionary design of proteins

***Rama Ranganathan*** PS

Center for Physics of Evolving Systems; Biochemistry and Molecular Biology; Pritzker School for Molecular Engineering; BioCARS, Argonne National Laboratory, University of Chicago

Proteins can fold spontaneously into well-defined three-dimensional structures and can carry out complex biochemical reactions such as binding, catalysis, and long-range information transfer. The precision required for these properties is achieved while also preserving evolvability – the capacity to adapt in response to fluctuating selection pressures in the environment. What is the basic design of proteins that supports all of these properties? Going beyond direct physical analysis, statistical analysis of genome sequences have, in recent years, provided a powerful and general approach to this problem. Using different methodologies, this approach has revealed both direct structural contacts as well as collective functional modes within protein structures. In this talk, I will present approaches for probing the physical mechanisms implied by the evolution-based models and present ideas for how such mechanisms may be constrained by and originate from the dynamics of the evolutionary process. This work represents a step towards a theory for the physics of proteins that is consistent with evolution.

## Cells integrate mechanical and chemical inputs at the cell membrane by building active emulsions

***Satyajit Mayor*** PS

National Centre for Biological Science, TIFR, Bangalore, India

The surface of a eukaryotic cell interfaces with the external milieu constantly, decoding signals in the form of chemical and mechanical inputs. These cues are interpreted primarily by membrane receptors which are embedded in a plasma membrane templated by an active cortical actin meshwork. One such membrane receptor, the integrin receptor receive chemical inputs in the form of the extracellular matrix, and mechanical signals from the external mileu. These activate Rho A-dependent signalling cascades generating actomyosin stresses in the cell and activating mechanotransducers such as Vinculin. The activation of these two pathways result in the creation of a localized mesoscale liquid ordered (lo) domains consisting of nanoclusters of GPI-anchored proteins and lipids, resembling *active emulsions*. These membrane domains encode information about the nature of the substrate, regulating crucial aspects of integrin receptor function, including cell spreading, migration, and mechanical stiffness of the matrix. The active actin-membrane composite membrane therefore behaves as a mechano-responsive medium, serving to integrate chemical and physical cues presented at the cell surface.

## Microfluidic Island Biogeography - Jam and Conquer

***Oskar Hallatschek*** PS

UC Berkeley

Microbes often colonize spatially-constrained habitats, such as pores in the skin or crypts in the colon. The resulting micro-communities can be very stable and contribute to the long-term function of our microbiomes. Due to a lack of spatio-temporal observations, it is however unclear how these communities and their ecological functions arise. Using microfluidic devices to systematically vary ecological correlation lengths, we uncover sharp transitions between different colonization states with different evolutionary properties. Our results show that density-dependent passive diffusion can drive reproducing populations to a jamming threshold, which entails supreme resilience against invaders at the cost of a total loss of mixing and intra-species competition. These results elucidate how cell proliferation can drive unique non-equilibrium phase transitions (different from MIPS). The emerging sensitivity to scale, foreshadowed in the field of island biogeography, underscores the need to control for scale in microbial eco-evolutionary experiments.

## Cryo-EM illuminates new biology of orphan receptors

***Appu Kumar Singh*** MS

Department of Biological Sciences and Bioengineering, IIT Kanpur

Among the large family of G protein–coupled receptors (GPCRs) are many orphans, so called because their signaling reactions remain poorly understood. Among these is GPR158 which is highly expressed in the nervous system and implicated in processes from cognition to memory to mood. However, the structural organization and signaling mechanisms of GPR158 are largely unknown. We used single-particle cryo–electron microscopy (cryo-EM) to determine the structures of human GPR158 alone and bound to an RGS signaling complex. GPR158 has an unusual dimerization mode stabilized by a pair of phospholipids and the presence of an extracellular Cache domain, an unusual ligand-binding domain in GPCRs. The extensive set interaction at the dimeric interface locks GPR158 in a conformation that likely prevents G protein activation. RGS binds to the homodimer at a site that substantially overlaps the surface that binds G proteins, again preventing canonical G protein signaling. The binding of a ligand to the extracellular domain may regulate signaling through the RGS complex. I will talk about how our structural and functional study on orphan GPR158 provides insights into the unusual biology of orphan receptors and the formation of GPCR-RGS complexes, where instead of heterotrimeric G-proteins or arrestins, RGS is coupled to GPR158 to bring a paradigm shift in signaling pathways.

## Insights into mechanisms of GABA uptake and transport inhibition by antiepileptic drugs

***Aravind Penmatsa*** MS

Molecular Biophysics Unit, Indian Institute of Science, Bangalore

$\gamma$-aminobutyric acid (GABA) is a biochemical derivative of glutamate that serves as a major inhibitory neurotransmitter in the nervous system. GABA release activates postsynaptic GABAA and GABAB receptors and is transported back into neurons and glial cells through the activity of the GABA transporters (GATs). Altered GABA levels in the synapse tend to be one of the factors leading to seizures and epilepsies. GABA levels in the synapse can be restored by blocking GABA reuptake from neural synapses. My talk will focus on our recent work on the structural aspects of GABA uptake inhibition by antiepileptic drugs that target transport through both competitive and allosteric mechanisms. I will further highlight the mechanism of GABA recognition and its movement into cells using high-resolution cryoEM structure of GAT1

## Structure probing of native RNA-protein complexes using Mass Spectrometry and Molecular Modelling

***Aditi Borkar***

MS

Faculty of Medicine  Health Sciences, University of Nottingham

*Problem statement*: RNAs and their protein complexes (RNPs) are one of the most challenging systems to study as single molecules. They are laborious to synthesise; they constantly change shape, structure and binding partners in solution; and they are difficult to image via conventional structural biology techniques. Thus, our knowledge about RNP structure, dynamics and correlated function is limited, particularly in comparison to proteins. This has significantly hampered the development of therapeutic approaches that target RNPs for control of infectious and non-communicable diseases.

*Solution*: To address this bottleneck, we have been involved in challenge-driven method development for characterising structure and dynamics of native RNP complexes. One such method employed in our lab is 3D-OrbiSIMS. This is a first in class solid state Mass Spectrometry technique that combines high speed of Orbitrap analyser with high spatial resolution of secondary ion MS (SIMS) at pico-molar sensitivity. Using 3D-OrbiSIMS and novel data analysis pipelines for molecular modelling, we have demonstrated, for the first time, the utility of the technique for characterising structures of native biomolecular complexes. We have benchmarked the method for Cas9-guideRNA complex and have been using it to characterise key RNP complexes mediating host-pathogen interactions in HIV.

## Mechanistic analysis of membrane fission and discovery of novel fission proteins

***Thomas Pucadyil***

MS

IISER Pune

The lipid bilayer is highly resilient to rupture and explains why it was selected over the course of evolution to serve a barrier function. Yet fission, or the splitting of a membrane compartment, is a central theme in biology that manifests during cell division, organelle biogenesis and vesicular transport. Fission involves the local application of forces to bend and constrict a tubular membrane intermediate. Using a facile assay system of supported membrane nanotubes that can be tuned for size and lipid composition, we have analyzed fission mechanisms of candidate proteins and discovered novel proteins that catalyze fission. My talk will describe recent developments in our efforts at understanding the pathway to fission and expanding the repertoire of fission proteins.

## Specificity and Flexibility of Protein-Lipid Signatures

***Durba Sengupta, Shikha Prakash***

MS

CSIR-National Chemical Laboratory Pune

The molecular mechanisms underlying protein-lipid interactions are emerging and multi-scale simulations have been critical in identifying the specificity and energetics of these interactions. In this talk, we will highlight a few examples of charged lipid interactions with membrane bound proteins. In particular, we focus on the phopshoinisitol lipids (PIP lipids) and its interactions with the actin binding protein, cofilin. We show that coarse-grain simulations are able to reproduce cofilin-PIP2 interactions and that in a complex membrane, the maximal interactions with phosphoinositide (PIP) lipids, both PIP2 and PIP3 lipids. A good match was observed between the residues predicted to interact and previous experimental studies. The clustering of PIP lipids around the membrane bound protein leads to an overall lipid demixing and gives rise to persistent membrane curvature. Further, through a series of control simulations, we observe that both electrostatics and geometry are critical for specificity of lipid binding. Our current study is a step towards understanding the physico-chemical basis of protein-PIP lipid interactions.

## Extra-receptor signalling: how the lipid bilayer transduces neurotransmitter signals

***Sudipta Maiti***

MS

Tata Institute of Fundamental Research, Mumbai, India

Chemical signalling is essential to information processing in the brain. The key events of this process in the mammalian brain is the exocytotic release of signalling molecules by one cell and its binding to a receptor molecule on the recipient cell, which then transduces the chemical message. Here we ask: if we take the receptors away, can there still be signalling?

Using Optical spectroscopy, solid state NMR and AFM force spectroscopy, we show that the lipid bilayer responds to some signalling molecules, such as serotonin, and changes its order and mechanical properties. These changes can in principle modulate the processes which are membrane -mediated, such as exo- and endocytosis. It can also in principle affect the functioning of non-receptor molecules in the membrane. Using confocal and multiphoton microscopy, we also show that these effects occur in real cells. In fact nature appears to have optimized the emmbrane compositions of different organelles to tune them for neurotransmitter interactions. In summary, the lipid bilayer membrane can itself be a receptor for many signalling molecules. Potentially, our findings pave the way for a major new class of membrane-active but receptor-silent pharmacological agents which can affect biological function.

References: 1) Gupta et al., Unusual Robustness of Neurotransmitter Vesicle Membranes against Serotonin-Induced Perturbations, J. Phys. Chem. B, 2023, https://doi.org/10.1021/acs.jpcb.2c07464

2) Dey et al., Altered Membrane Mechanics Provides a Receptor-Independent Pathway for Serotonin Action, Chem. Eur. J., 2021, 27, 1–10

## A Force at the Edge : Lipids and Motors at Membrane Contact Site

***Roop Malik*** MS

IIT Bombay

How cellular organelles communicate between themselves is a subject of intense investigation. The extensively interconnected membrane of the endoplasmic reticulum (ER) may act as a common conduit for such communication because many different organelles can exchange lipids and proteins with the ER at ER-organelle membrane contact sites (MCS).

A fundamental physical constraint, however, appears to have been overlooked in the extensive literature related to MCS. Most organelles are too large to diffuse around freely inside the cell. How, then, can they find their cognate MCS at distant locations on the ER membrane? We therefore hypothesized that Motor proteins carrying an organelle could get switched from Transporter to Tether when the organelle reaches a specific MCS. Such a switch would allow organelles to sample the intracellular space with intermittent "pit-stops" at MCS, where they can exchange proteins/lipids with the ER for onward communication. I will discuss some experimental evidence to support this hypothesis.

## Tension buffering mechanisms in axons

***Pramod Pullarkat*** MS

Raman Research Institute, Bangalore

Axons are long tubular extensions of neuronal cells. These extensions are generated and maintained by a composite network of highly dynamic biopolymer filaments enclosed within a membranous tube. Owing to the dynamic, non-equilibrium nature of its structure, axons exhibit unique mechanical properties which are important for their development and function. This include non-linear viscoelastic responses, active contractility, stretch induced growth response, and tension buffering responses to protect axons against mechanical stress. We will discuss the origins of some of these responses and how the properties of the biopolymer matrix influence axonal stability.

## Physics-inspired data-driven models of collective motion

***Vishu Guttal*** MS

IISc Bangalore

Self-propelled particle models of collective motion (e.g. Vicsek et al 1995 PRL) have inspired innumerable studies in both physics and biology of collective motion. However, this large body of theoretical and empirical studies have overlooked the intrinsic noise that arises in any finite collective. In this talk, I will present our recent work involving analytical theory, experiments, and data-derived discovery of stochastic differential equations. We show that intrinsic-noise can promote order in animal collectives. Further, we argue that data-driven discovery of models to be a promising avenue for both analysis of data as well as theory.

## Understanding how conformational transitions can modulate the folding of proteins

***Shachi Gosavi*** MS

NCBS Bangalore

In order to function, many proteins bind ligands and change shape. This conformational transition is what usually allows the protein to transmit a signal or perform catalysis or in some cases stop further activity. The energy landscapes of proteins which perform such conformational dynamics need to not only (1) enable protein folding to the correct ligand-binding capable initial structure but to also then (2) enable the change of shape to a specific final structure. Molecular dynamics simulations of dual structure-based models, models that encode both the initial and final structures of the protein, can be used to describe such conformational transitions. I will discuss the models, conformational transitions and folding of two structurally and functionally different proteins adenylate kinase (AKE) and cytolysin A (clyA). These model proteins help us understand how conformational transitions may modulate the folding landscapes of proteins.

## Probing protein stability and gene function using saturation mutagenesis

***Raghavan Varadarajan*** MS

Molecular Biophysics Unit, Indian Institute of Science, Bangalore

Protein stability is conventionally measured with individual purified proteins; this is both laborious and slow. We show that by using ligand binding as a readout for structural integrity, and coupling this to FACS and deep mutational scanning, it is possible to make high throughput stability estimates, and identify both stabilized and destabilized mutants. Isolation of stabilizing mutations is enhanced by introducing one or more destabilizing mutations at buried positions into a saturation mutagenesis library, and screening for suppressors. Suppressors located distal from the destabilizing mutation are typically able to suppress multiple destabilizing mutations and are thus global suppressors. Thermodynamic stabilisation is neither necessary nor sufficient for suppressor action. Instead, in diverse systems, we observe that individual global suppressors of buried -site mutants greatly enhance protein foldability, primarily through an increase in refolding rate parameters measured in vitro. In contrast, suppressors of exposed-site mutations, exert their effects through a decrease in unfolding rates. Synonymous mutations that do not change amino-acid identity are typically thought to be near neutral. Using the ccdAB operon as a test case, we show that many synonymous mutations can significantly perturb gene activity through a variety of mechanisms that includes changes in translation initiation, elongation, termination and folding. These diverse studies, highlight the myriad insights obtainable from saturation mutagenesis coupled to phenotypic readouts and deep sequencing.

## Yeast eukaryotic initiation factor 4B remodels the mRNA entry site on the small ribosomal subunit

***Tanweer Hussain*** MS

Department of Developmental Biology and Genetics, Indian Institute of Science, Bangalore

During the initial steps of protein synthesis, mRNA is recruited to the small ribosomal subunit and the start codon in the mRNA template is recognized. In prokaryotes, the base pairing of the Shine-Dalgarno sequence in mRNA with the anti-Shine-Dalgarno sequence present in the 16S rRNA helps in mRNA recruitment and places the start codon at the P-site. However, in the case of eukaryotes, there is a specialized group of factors called the eukaryotic initiation factor 4 (eIF4) factors that help in mRNA recruitment to the 40S. The eIF4 factors include the mRNA 5 cap recognizing factor eIF4E, the mRNA secondary structure resolving ATP-dependent RNA helicase factor eIF4A, and the scaffolding protein eIF4G. eIF4B, another eIF4 factor, was earlier thought to participate only as the eIF4A-helicase activity-stimulating protein. However, besides increasing the helicase activity of eIF4A, eIF4B plays an important role in mRNA recruitment. In yeast, eIF4B binds directly to the 40S head and helps in mRNA recruitment. Using cryo-electron microscopy, we show that yeast eIF4B binds to the 40S ribosomal subunit at the mRNA entry channel. In this talk, I will discuss the yeast eIF4B-bound ribosomal complex and how it provides insight into possible events during mRNA recruitment.

# Day 2: Tuesday, 28 March, 2023

## G.N. Ramachandran Lecture: Protein Design using Deep Learning

***David Baker*** PS

Institute of Protein Science

Proteins mediate the critical processes of life and beautifully solve the challenges faced during the evolution of modern organisms. Our goal is to design a new generation of proteins that address current-day problems not faced during evolution. In contrast to traditional protein engineering efforts, which have focused on modifying naturally occurring proteins, we design new proteins from scratch to optimally solve the problem at hand. We now use two approaches. First, guided by Anfinsen's principle that proteins fold to their global free energy minimum, we use the physically based Rosetta method to compute sequences for which the desired target structure has the lowest energy. Second, we use deep learning methods to design sequences predicted to fold to the desired structures. In both cases, following the computation of amino acid sequences predicted to fold into proteins with new structures and functions, we produce synthetic genes encoding these sequences, and characterize them experimentally. In this talk, I will describe recent advances in protein design using both approaches.

## RNA-RBP condensates sense cellular RNA and buffer immune response

***Shovamayee Maharana*** MS

Department of Microbiology and Cell Biology, Indian Institute of Science

Cells carry out many biochemical reactions simultaneously in the crowded milieu of cytoplasm to sustain life. Compartmentalization in form of large membrane-bound organelles and smaller, dynamic nucleic acid-protein condensates, helps in organizing these multicomponent biochemical reactions in cells. The condensate formation is driven by phase separation of low complexity domain-containing nuclear RBPs like FUS, EWSR1, TAF15, TDP43 and hnRNAP1 to form nuclear condensates like paraspeckle and splicing speckles. We had previously shown that cellular concentration of RNA can control condensate formation and the physical properties of the condensates, specifically high RNA/RBP concentration inhibited condensate formation, intermediate concentration favored liquid-like phase separation and the condensates formed at very low RNA/RBP ratio led to the formation of solid-like condensates or aggregates. I will present our recent work in Type I interferonopathy disease, Aicardi Goutières Syndrome (AGS) where the nucleic acid metabolism is implicated, showed that AGS with SAMHD1 mutations has altered RNA metabolism with an accumulation of ssRNA. The accumulation of RNA leads to global impairment of different cellular condensates and release of immunogenic self RNA which is stored in nuclear condensates- splicing speckles and cytoplasmic condensate- stress granules leading to inflammation. Taken together our work suggests that condensates can buffer immune response by sequestering self-immunogenic RNA. Phase separation of condensates is very susceptible to changes in cellular metabolism and microenvironment, hence we hypothesise that condensates can be the sensors for these changes and can lead to inflammation.

## Dynamic Atomic Force Microscope for Viscoelasticity of Single Folded Domains of Proteins

***Shivprasad Patil*** MS

IISER Pune

The advent of the atomic force microscope, along with optical tweezers, ushered in a new field of single molecule force spectroscopy, wherein the response of a single protein or a macromolecule to external mechanical perturbations is measured. Controlled forces ranging from pN to nN are applied to measure unfolding force distribution of a single protein domain. In a clamp type experiment, the folded protein is subjected to a constant force to measure the unfolding time distribution. Simultaneously, there were efforts to measure elastic and viscous response of a single domain by applying sinusoidal forces and measuring resulting deformations produced in a bid to quantify its viscoelasticity. The deformation's phase lag with respect to the applied force provides the elastic and viscous response of the protein, akin to oscillatory rheology. Despite numerous technical advances in AFM, an artefact-free measurement of a folded protein's viscoelasticity largely remains a challenge. In this talk, I review efforts to measure viscoelasticity of proteins using dynamic AFM, identifying pitfalls that make these measurements elusive. Finally, I discuss our new promising method, which reported viscoelasticity of a folded protein and reasons, that enabled such a measurement for the first time[1].

References: [1] Surya Pratap S. Deopa, Shatruhan Singh Rajput, Aadarsh Kumar, and Shivprasad Patil, *Direct and Simultaneous Measurement of the Stiffness and Internal Friction of a Single Folded Protein*, The Journal of Physical Chemistry Letters, 2022 13 (40), 9473-9479, DOI: 10.1021/acs.jpclett.2c02257

## Allostery through DNA drives phenotype switching

***Hagen Hofmann*** MS

Weizmann Institute

Allostery is a pervasive principle to regulate protein function. Here, we show that DNA also transmits allosteric signals over long distances to boost the binding cooperativity of transcription factors. Phenotype switching in Bacillus subtilis requires an all-or-none promoter binding of multiple ComK proteins. Here, we use single-molecule FRET to demonstrate that ComK-binding at one promoter site increases affinity at a distant site. Cryo-EM structures of the complex between ComK and its promoter demonstrate that this coupling is due to mechanical forces that alter DNA curvature. Modifications of the spacer between sites tune cooperativity and show how to control allostery, which paves new ways to design the dynamic properties of genetic circuits.

## Understanding the enhancer code in regulation of transcription

***Dimple Notani***

MS

NCBS, Bangalore

Expression of genes is controlled by DNA sequences that are distal from the promoters known as enhancers. They regulate target genes by establishing looping with the promoter. There are thousands of enhancers in mammalians genomes and they act in a cell-type specific manner. Although discovered over forty years ago, how enhancers regulate their promoters remains poorly understood. Further, the enhancers that drive cyclic signaling response, are reversibly dynamic as opposed to developmental enhancers, adding another layer of complexity to this conundrum.

Using genomic techniques that quantify the alterations in TF binding, nascent transcription, three-dimensional architecture during the course of estrogen signaling, our work has revealed that chromatin state under basal signaling is the key to signaling response. Certain regions in the genome are bound by estrogen receptor (ER) even before the exposure to ligand. These regions act as a seed to give rise to ER bound enhancer clusters and ER condensates to drive the signaling response. Further, these and other enhancer clusters do not function as sum-of-all but they rely on complex hierarchies that cannot be predicted in silico. I will discuss how enhancers and condensates regulate the genome organization and how promiscuous transcription and mutations in these enhancers leads to diseases and cancer.

## Single-Molecule Analysis of DNA Base-Stacking Energetics Using Patterned DNA Nanostructures

***Mahipal Ganji***

MS

IISc, Bangalore

DNA double helix structure is stabilized by the base-pairing and the base-stacking interactions. Base-stacking interactions originating from hydrophobic interactions between the nucleobases predominantly contribute to the duplex stability. A comprehensive understanding of dinucleotide base-stacking energetics is lacking owing to the unavailability of sensitive techniques that can measure these weak interactions. Earlier studies attempting to address this question only managed to estimate the base-stacking interactions in either bulk sample or in a bundle of DNA helices, however, disentangling base-stacking interactions on individual DNA strand was enigmatic. By combining multiplexed DNA-PAINT imaging with designer DNA nanostructures, we experimentally measure the free energy of dinucleotide base-stacking at the single-molecule level. Multiplexed imaging enabled us to extract binding kinetics of an imager strand with and without additional dinucleotide stacking interactions in a single imaging experiment, abolishing any effects of experimental variations. The DNA-PAINT data showed that a single additional dinucleotide base-stacking results in as much as 250-fold stabilization for the DNA duplex nanostructure. We found that the dinucleotide base-stacking energies vary from -1.18 ± 0.17 kcal/mol to -3.57 ± 0.08 kcal/mol for C|T and A|C base-stackings, respectively. We demonstrate the application of base-stacking energetics in designing DNA-PAINT probes for multiplexed super-resolution imaging. Our results will aid in designing functional DNA nanostructures, DNA and RNA aptamers, and facilitate better predictions of the local DNA structure.

## Predicting coarse-grained chromatin polymer properties from nucleosome-level contact data

***Ranjith Padinhateeri*** MS

Department of Biosciences and Bioengineering, Indian Institute of Technology Bombay, Mumbai

Making coarse-grained chromatin models is essential to interpret experimental data and to simulate and predict chromatin organization/dynamics. It is common to model chromatin as a bead spring chain, with each bead representing lengths 1kb, 10kb, or 100kb of the genome. However, we do not know the physical dimensions (radius) of these beads and the properties (stretching elasticity, bending elasticity, etc.) of the chain. To bridge this gap, we simulated a large ensemble of chromatin configurations at near-nucleosome (200bp) resolution, consistent with recently published Micro-C data. We then systematically coarsegrained the configurations and predicted quantities essential for chromatin polymer representation. We predict the size (physical dimension) of chromatin beads for a range of scales from 1kb to 100s of kb and compute various polymer properties such as stretching elasticity, bending fluctuations, and intrinsic angle among polymer beads. Unlike the prevalent notion, we show that coarse-grained chromatin polymer beads should be considered as soft particles that can overlap, and we propose an overlap parameter. We show that accounting for such overlap is necessary to predict 3D distances from simulations accurately. Our results also show how chromatin polymer properties vary along the genome depending on the local chromatin state

## Simons Lecture: Recreational Biology - Topological Puzzles in cell biology

***Manu Prakash*** PS

Stanford University, Woods Institute for the Environment

Recreational mathematics involves mathematical puzzles and games, often appealing to children and untrained adults, inspiring their further study of the subject. Can a similar analogy be drawn in biology? Without making any claims of usefulness, we will explore a wide range of topological puzzles in cellular physiology: Can single cells be toroidal in nature? Can cytoskeletal geometry encode complex behavior in free living protists? Do cells get stuck in topological traps? Finally, we will reflect on role of curiosity as an engine for discovery in life sciences.

## Active mechanics of epithelial monolayers

***Mandar Inamdar*** MS

Indian Institute of Technology, Bombay

Epithelial tissue is formed of a monolayer of polygon-like cells that are connected to each other via cell-cell junctions. These monolayers exhibit some of the most fascinating mechanical behavior that is observed in active matter. In epithelial tissues, interaction between cellular biochemistry, signalling, and cytoskeletal machinery leads to the generation of active forcing. This cell-level mechanochemistry can produce long-range spatio-temporal patterns of cellular strains and junctional remodeling within the tissue. In many cases, just a few key ingredients of cell-level dynamics are sufficient in dictating the broad nature of kinematic and stress patterns in epithelial tissues. In this context, I will present some of our work on modeling collective cell migration and morphogenesis in epithelial monolayers.

## Unravelling the mechanobiology of cell competition during cancer initiation

***Tamal Das*** MS

Tata Institute of Fundamental Research, Hyderabad

Cell competition is a collective process of sensing and eliminating ‘unfit’ cells by the normal cells, towards maintaining tissue fitness, form, and function. In our body, it underlies a fundamental anti-tumour activity called the epithelial defence against cancer (EDAC). EDAC involves non-cell autonomous removal of the transformed cells. Those cells, if allowed to persist, would otherwise initiate cancer. In spite of its physiological significance, the mechanisms underlying EDAC remain largely elusive. In our group, we are trying to unravel how cellular forces and tissue mechanics regulate EDAC. To this end, we first found that the mechanical stiffness of the extracellular matrix is a critical parameter in EDAC and matrix stiffening attenuates the defence against activated HRAS-transformed cells. Next, we discovered that before the transformed cells extruded out, they experienced compressive stress. Interestingly, we found that it is not the proliferative differential but a mechanical differential that generates this compressive stress and drives the competition between normal and transformed cells. Finally, we are elucidating the role of nuclear mechanics in this process. Taken together, our discoveries have disrupted the conventional landscape of cancer research by enforcing a mechanobiological view of cancer initiation.

## Enhanced mixing and inversion of vortex flow around confined microalgae

***Prerna Sharma*** MS

IISc, Bangalore

Extreme confinement of microorganisms between rigid boundaries often arises in their habitat, yet measurements of swimming mechanics in this regime are absent. We show that strongly confining the microalga Chlamydomonas between two parallel plates not only inhibits its motility through contact friction with the walls but also leads, for purely mechanical reasons, to inversion of the surrounding vortex flows. Our experimental data naturally leads to a simplified theoretical description of flow fields based on a quasi-2D Brinkman approximation to the Stokes equation rather than the usual method of images. We find that the vortex flow inversion provides advantage of enhanced fluid mixing despite higher friction. Overall, our results offer a comprehensive framework for analyzing the collective flows of strongly confined swimmers.

## How transcriptions factors associate in 3D chromatin

***Rahul Siddharthan*** MS

The Institute of Mathematical Sciences, Chennai

Transcription factors (TFs) regulate genes combinatorially. The logic of their cooperative or competitive action has been studied in detail across model organisms but mainly in the context of linear, contiguous genomic sequence such as promoters. However, sequentially distant regions of DNA are brought into spatial proximity by the 3D conformation of the genome, enabling distal gene regulation by enhancers. The study of such 3D TF-TF interaction is nascent. Here we examine in detail, across multiple cell lines, such cooperation or competition among TFs both in sequential and spatial proximity (using chromatin conformation capture assays) on one hand, and based on both in vivo binding as well as TF binding motifs on the other. We ascertain significantly co-occurring ("attractive") or avoiding ("repulsive") TF pairs using robust randomized models that retain the essential characteristics of the experimental data. TFs organize into two groups, with intra-group attraction and inter-group repulsion. This is true for both sequential and spatial proximity, for both in vivo binding and motifs. The two TF groups differ significantly in their genomic and network properties, as well in their function—while one group regulates housekeeping function, the other potentially regulates lineage-specific functions. Our results suggest a complex pattern of spatial cooperativity of TFs that has evolved along with the genome to support housekeeping and lineage-specific functions.

## Inferring principles of cell fate control from correlated cancer cell lineages

***Shaon Chakrabarti*** MS

NCBS, Bangalore

Rapid technological advances are now allowing measurements of various biological parameters at the single cell level. While such univariate distributions provide interesting insights into cell-to-cell variability and heterogeneity in cell states, much less explored and understood are the implications of correlations amongst single cells. Particularly in cellular populations that are growing and dividing, there is increasing realization that lineage correlations can provide key biological insights that cannot be gleaned simply from single-cell distributions alone.

In this talk, I will demonstrate how lineage correlations in cell-fate after drug treatment allow inference of underlying cell-fate control mechanisms in cancer cells. Utilizing an experimental setup where both single cell kinetics as well as population dynamics are recorded for the same cells, I will show how the ubiquitous exponential growth model (and generalizations such as age-structured models), fail to predict population growth rates of drug-treated cancer cells from single cell measurements. In essence, the widely used birth and death rates play very little role in establishing the population dynamics of drug treated cells. I will argue that the key to resolving this paradox lies in accounting for cell-fate correlations, which indicate that fate decisions occur well before addition of the drug, suggesting a Darwinian rather than Lamarckian origin of cell fate. Finally, I will argue how our results are consistent with recent experiments where a lack of reduction in barcode diversity was interpreted as indicative of drug-induced cell fate decisions.

## Building the cell from unreliable parts: coordinating stochastic organelle biogenesis with cellular growth

***Shankar Mukherji*** MS

WUSTL, USA

Perhaps the defining feature of the eukaryotic cell is its organization into membrane-bound compartments known as organelles. While the processes underlying the biogenesis of individual organelles are often well-known, the precision with which individual cells exert quantitative control over individual organelle properties, such as number and size, and coordinate these properties at systems-scale across the cell's many different types of organelles remain frontier problems in cell biology and biophysics. Using a combination of theory and quantitative fluorescence imaging, I will describe our recent efforts to show that cells exhibit substantial limits to the precision with which they can control organelle numbers and sizes, but despite this appear to collectively organize systems-level organelle biogenesis into specific "modes" that balance the need for cell growth to be both robust yet responsive to the environment.

# Day 3: Wednesday, 29 March, 2023

## Mechano-Genomics of Cell-State Transitions

***G.V.Shivashankar*** PS

ETH Zurich  Paul Scherrer Institute, Switzerland

Extracellular mechano-chemical signals regulate gene expression programs and cell-state transitions, although the underlying mechanisms are still unclear. In this talk, I will first highlight the tight coupling between cell geometry/mechanics, 3D chromosome organization, and gene expression. I will then discuss how sustained mechanical signals, through cell-geometric confinement, can induce cell-state transitions and provide avenues to rejuvenate aging cells. Furthermore, I will show that spatio-temporal alterations in chromatin organization, identified using fluorescence imaging combined with machine learning, can serve as robust biomarkers for cell-state transitions in tissue microenvironments. Collectively, our results may have important applications in regenerative medicine and early disease diagnostics

## Fluidity and rheological response in confluent epithelial tissues

***Dapeng Max Bi*** PS

Department of Physics Northeastern University

Biological processes, from morphogenesis to tumor invasion, spontaneously generate shear stresses inside living tissue. The mechanisms that govern the transmission of mechanical forces in epithelia and the collective response of the tissue to bulk shear deformations remain, however, poorly understood. Using a minimal cell-based computational model, we investigate the constitutive relation of confluent tissues under simple shear deformation. We show that an initially undeformed fluidlike tissue acquires finite rigidity above a critical applied strain. This is akin to the shear-driven rigidity observed in other soft matter systems. Interestingly, shear-driven rigidity can be understood by a critical scaling analysis in the vicinity of the second order critical point that governs the liquid-solid transition of the undeformed system. We further show that a solid like tissue responds linearly only to small strains and but then switches to a nonlinear response at larger stains, with substantial stiffening. Finally, we propose a mean-field formulation for cells under shear that offers a simple physical explanation of shear-driven rigidity and nonlinear response in a tissue.

## Biophysical basis of left-right symmetry breaking in vertebrates

***Hiroshi Hamada*** PS

RIKEN Center for Biosystems Dynamics Research

Our body looks left-right (L-R) symmetric from outside, but visceral organs are L-R asymmetric in terms of their shape, position and size. L-R asymmetry of the body is established early during development. In many of vertebrates including mammals, breaking of L-R symmetry takes place at the region of the embryo called the left-right organizer (the node in the mouse embryo) and involves uni-directional fluid flow generated by motile cilia at the left-right organizer. The fluid flow is sensed by another type of cilia, immotile cilia located at the periphery of the node. When immotile cilia sense the flow, Ca2+enters the cell, and stimulates degradation of the target mRNA (Dand5 mRNA) via Bicc1 and Ccr4 complex. The RNA-binding protein Bicc1 recognizes the specific sequence of the 3'-untranslated region of Dand5 mRNA, recruit Ccr4 and induces degradation of the mRNA. This flow-stimulated Dand5 mRNA degradation occurs only on the left side, generating the first molecular asymmetry in the embryo. It remains to be seen how the Bicc1-Ccr4 complex is activated by Ca2+. A long-standing question in the field has been what precisely immotile cilia at the node sense: do they sense a chemical molecule transported by the flow, mechanical force generated by the flow or something else? We have addressed this issue by employing biophysical methods such as optical tweezers, and have obtained the results suggesting that mechanical stimuli to immotile cilia induces Ca2+ transients and Dand5 mRNA degradation via immotile cilia. Asymmetric bending of immotile cilia on the both sides in response to the flow and anisotrophic localization of channel protein Pkd2 in immotile cilia explain why the leftward flow activates immotile cilia on the left side but not those on the right side.

## Alpha-amylase and Lipid Membrane Interaction

***Tripta Bhatia*** MS

IISER Mohali

We prepared giant unilamellar vesicles (GUVs) of cell size to study their interactions with peptides, proteins. Amylase is an important amylolytic enzyme that participates in the hydrolysis of starch, the most common carbohydrate in nature. We experimentally investigate the interaction of alpha-amylase with the lipid membrane and show that, below a threshold concentration of enzyme, the rigidity of the membrane is enhanced. The mechanical properties of GUVs are experimentally quantified by vesicle fluctuation analysis (VFA). The VFA technique can be used to extract information about the physics of the membrane contour fluctuations of giant vesicles visible under optical microscopy. Our data estimate a quantitative coupling between membrane asymmetry and flexibility.

## Probing protein degradation by ATP-dependent proteases and proteasomes using single-molecule force spectroscopy

***Hema Chandra Kotamarthi*** MS

Department of Chemistry Indian Institute of Technology, Madras

Protein degradation is an essential cellular process that maintains protein homeostasis and is carried out by ATP-dependent proteasomes and proteases. These act as mechano-enzymes, unfolding and translocating substrate proteins mechanically that are to be degraded in an energy-dependent manner during cycles of ATP hydrolysis. Optical tweezers-based singlemolecule assays, in addition to providing information on motor properties such as translocation velocities and stepping kinetics, also revealed previously hidden mechanisms during unfolding and translocation. Double-ring protease ClpAP with ATPase rings D1 and D2 has been probed using these assays to understand the functioning and coordination of individual rings. Our single-molecule experiments have dissected the effect of the non-hydrolyzing D1 module on the unfolding and translocation of substrates by ClpAP. Although in the wild-type enzyme, the D1 module hydrolyses only 10 percent of total ATP turned over by ClpAP, abolishing this hydrolysis reduced the unfolding rate of a model substrate 10-fold and the average translocation velocity by 60 percent. These single-molecule results suggest that defects in ATPhydrolysis in the D1 ring cause loss of coordination between the two rings resulting in the misfiring of the D2 motor domain and provide new insight into the functional importance of the ClpA D1 ATPase module and the role of coordination between each ClpA AAA+ ring. Our current research involves probing the influence of the substrates and ligands on unfolding, oligomerization and ATPase rates of hexameric ATPase, Mpa of Mycobacterium Tuberculosis proteasomal complex.

## A tale of Tau: Associations and Phase Separation

***Markus Zweckstetter*** MS

MPI, Göttingen

Cells contain multiple compartments dedicated to the regulation and control of biochemical reactions. Cellular compartments that are not surrounded by membranes can rapidly form and dissolve in response to changes in the cellular environment. The physicochemical processes that underlie the formation of non-membrane-bound compartments in vivo are connected to liquid-liquid phase separation of proteins and nucleic acids in vitro. Recent evidence suggests that the protein tau, which plays an important role in Alzheimer's disease and other neurodegenerative disorders, phase separates in solution, forms tau phases with microtubules, and associates with phase-separated RNA-binding protein granules in cells. In my presentation I will review the experimental evidence that supports the ability of tau to phase separate and form biomolecular condensates. I will further discuss my lab's efforts to target tau phase separation and the spreading of tau aggregates in the brain using small molecules.

## Active Patterns in Cell Polarity and Cell Division

***Vijay Krishnamurthy*** MS

ICTS Bangalore

Mechanical forces in cells and tissues arise primarily from the nonequilibrium ATP-consuming activity of the cytoskeleton. At larger scales of description, hydrodynamic flows resulting from these active stresses lead to the emergence of spatiotemporal patterns. We will first show that such hydrodynamical flows trigger the establishment of anteroposterior polarity in C. elegans zygotes –a guided self-organization pattern. Next, we will demonstrate that these active stresses drive the geometrodynamics of cell and tissue shapes. In particular, we will discuss our ongoing work to model ingression asymmetries during cytokinesis within this framework.

## Polygenic adaptation dynamics in a large, finite population

***Kavita Jain*** MS

JNCASR Bangalore

Although many phenotypic traits are determined by a large number of genetic variants, how a polygenic trait adapts in response to a change in the environment is not completely understood. I will describe our recent results on the adaptation dynamics of a large but finite population evolving under stabilizing selection. It is known that in an infinitely large population, selective sweeps at a major locus are prevented and adaptation proceeds exclusively via subtle changes in the allele frequency; in contrast, we find that the chance of sweeps is substantially enhanced in a finite population and therefore polygenic adaptation can occur via small to moderate changes in the allele frequencies at many loci as well as large shifts in the allele frequencies at a few loci.

## Structural determinants of relaxation dynamics in a class of ligation-cleavage chemical reaction networks

***Sandeep Krishna*** MS

NCBS Bangalore

Understanding the relationship between the structure of chemical reaction networks and their reaction dynamics is crucial for understanding the functioning of living organisms. While some network-structural features are known to relate to the steady-state characteristics of chemical reaction networks, mathematical frameworks describing the links between out-of-steady-state dynamics and network structure are still underdeveloped. Here, we examine the relaxation dynamics, after large perturbations, of a class of minimal chemical reaction networks consisting of the ligation and cleavage reactions of simple polymers. These networks satisfy mass-conservation and other key properties of general chemical reaction networks. We find three types of relaxation dynamics: exponential, power-law, and plateau. We show that three features computed from a submatrix of the network's stoichiometric matrix are sufficient to predict the type of the dynamics, namely, (i) the rank, determining the existence of a steady-state; (ii) the left null-space, being related to conserved quantities in the dynamics; and (iii) the stoichiometric cone, dictating the range of achievable chemical concentrations. We further show that these three quantities also predict the type of relaxation dynamics of combinations of our minimal networks, larger networks with many redundant pathways, and a real example of a metabolic network.

## Active particles in soft confinement

***Bibhu Ranjan Sarangi*** MS

IIT Palakkad

The motion of a passive Brownian particle is a manifestation of equilibrium thermal fluctuations. On the other hand, active particles which are self-propelled are capable of taking energy from the environment and converting it into directed motion. The active particles moving in an homogeneous environment without physical confinements have been investigated both theoretically and experimentally. However the effect of confinement on active particle dynamics is an emerging area of research due to its relevance to biological systems. We have investigated the effect of soft boundaries on the Brownian dynamics of active particles. In this talk we will discuss some of our recent results obtained from confined natural active particles.

## Lesson from smart slime: How active flow networks process information for complex behaviour

***Karen Alim*** MS

TU Munich

Propagating, storing and processing information is key to take smart decisions – for organisms as well as for autonomous devices. In search for the minimal units that allow for complex behaviour the slime mould Physarum polycephalum stands out by solving complex optimization problems despite its simple make-up. Physarum's body is an interlaced network of fluid-filled tubes lacking any nervous system, in fact being a single gigantic cell. Yet, Physarum finds the shortest path through a maze. We unravel that Physarum's complex behaviour emerges from the physics of active flows shuffling through its tubular networks. Flows transport information, information that is stored in the architecture of the network. Thus, tubular adaptation drives processing of information into complex behaviour. Taking inspiration from the mechanisms in Physarum we outline how to embed complex behaviour in active microfluidic devices and how to program human vasculature.

## The Unreasonable Effectiveness of Reaction-Diffusion in Vertebrate Skin Colour Patterning

***Michel Milinkovitch*** PS

Laboratory of Artificial Natural Evolution (LANE), Dept. of Genetics Evolution, University of Geneva, Geneva, Switzerland SIB Swiss Institute of Bioinformatics, Geneva, Switzerland

First, I will show that scale-by-scale ontogenic colour change dynamics has evolved independently in multiple species of lizards. Second, I will show that deterministic reaction-diffusion (RD) can quantitatively predict, not only the bulk statistical properties of adult patterns, but also, more surprisingly, a large proportion of the scale-by-scale patterns of individual animals. Third, I will discuss how we identify and quantify the sources of the residual error of individual scale-by-scale patterns. Finally, I will show that RD models predict, in ocellated lizards, unsuspected subtle colour sub-clustering that correlates with the colours of the scales' neighbours. Hyperspectral imaging and histological analyses indicate that colour sub-clustering is present in real lizards, confirming the numerical model non-trivial prediction.

# Posters Presenters

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|---|---|
| Sarita Puri | University of Milano, Italy |
| Krishnakanth Baratam | IISc, Bangalore |
| Yogavel Manickam | ICGEB, Delhi |
| Bharti Yadav | IISc, Bangalore |
| Rajeswari Appadurai | IISc, Bangalore |
| Subrata Dasgupta | IIT Bombay |
| Sayantan Dutta | Stanford University |
| Soham Chakraborty | Ashoka University |
| Swati Kumari | NII, Delhi |
| Premananda Basak | Bose Institute, Kolkata |
| Avishek Kar | CSIR- IMMT Odisha |
| Amit Naglekar | CSIR-NCL, Pune |
| Santosh Kumar Raut | IISc, Bangalore |
| Brataraj Ghosh | IISER Kolkata |
| Pankaj Gautam | IIT Ropar |
| Hrushikesh Malshikare | CSIR-NCL, Pune |
| Satya Chaithanya Duggisetty | IISc, Bangalore |
| Jumpei Yamagishi | University of Tokyo |
| Sangram Kadam | IIT, Bombay |
| Nitin Kumar | IIT, Delhi |
| Archit Gupta | IISER Mohali |
| Mukundan S | IISER, Pune |
| Sk Habibullah | IISc, Bangalore |
| Kunal Rai | IIT Hyderabad |
| Subhamoy Jana | IACS, Kolkata |
| Jigmi Basumatary | IISc, Bangalore |
| Shuvadip Dutta | IIT, Bombay |
| Vinoth Manivannan | IIT, Bombay |
| Suraj Singh | IIT Palakkad |
| Tanmoy Ghosh | IISER, Kolkata |
| Sanket Patil | IIT Bombay |
| Aditya Singh Rajput | ICTS-TIFR, Bangalore |
| Jashaswi Basu | IISER Pune |
| Sidhanta Swayam Prakash Das | IISc, Bangalore |
| Subham Kumar Tripathy | IIT Bombay |
| Binayak Banerjee | IISER, Kolkata |
| Ziaul Hasan | Jamia Millia Islamia, Delhi |
| Deepak KV | Manipal Academy of Higher Education |
| Swarnendu Roy | IISER Kolkata |
| Deepak Mehta | RRI, Bangalore |
| Akash Kumar Jha | IIT Bombay |

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|---|---|
| Sumanta Kar | IISER Kolkata |
| Ayesha Zeba | Bangalore University |
| Suman Hait | University of Calcutta |
| Souradeep Das | IISER, Pune |
| Abhinav Banerjee | IISc, Bangalore |
| Sasthi Paul | IISER, Mohali |
| Mitradip Das | TIFR, Mumbai |
| Mujahid Hossain | University of Hyderabad |
| Mohammad Arsalan Ashraf | RRI, Bangalore |
| Jijith M | IIT, Madras |
| Soham Mukhopadhyay | University of Calcutta |
| Sudip Pal | TIFR, Mumbai |
| Vigneshwaran Kannan | IMSc, Chennai |
| Himaja Deverakonda | BITS Pilani, Hyderabad |
| Debarati Paul | Bose Institute, Kolkata |
| Bidisha Das | CSIR-IICB, Kolkata |
| Kajal Sundaray | CSIR-IMMT, Odisha |
| Jigyasa Watwani | ICTS- TIFR, Bangalore |
| Shweta Kumari | IIIT, Hyderabad |
| Tithi Mandal | IISER, Kolkata |
| Karthika S Nair | CSIR-NIIST, Kerala |
| Debadrita Basu | Bose Institute, Kolkata |
| Kusum Lata | IISER, Mohali |
| Atreyi Chakraborty | IISER, Pune |
| Swayamshree Senapati | IIT, Bhubaneswar |
| Lydia Mathew | IIT, Bombay |
| Vishakha Goswami | IIT Delhi |
| Meghadeepa Sarkar | IISER, Pune |
| Rituparna Saha | IIT, Kharagpur |
| Gauri Patki | IISER, Pune |
| Srestha Roy | IIT, Madras |
| Uma Swaminathan | IISER, Pune |
| Barsa K.J. Godsora | IIT, Bombay |
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| Anjana Peethambaran Menon | IIT Bombay |
| Debashree Behera | IISc, Bangalore |
| Shabih Fatema | IIT, Delhi |
| Himanshi | IIT Guwahati |
| Silky Bedi | INST, Mohali |
| Nayanika Sengupta | IISc, Bangalore |
| Monika Phougat | JNU, Delhi |
| Sagarika Dash | IIT Kharagpur |
| Pehu Kohli | IISc, Bangalore |
| Nuzelu V | IIT Guwahati |
| Sweta Pradhan | NIT Rourkella |

| | |
|---|---|
| Paulomi Sanyal | IISc, Bangalore |
| Shivani Karalia | NII, Delhi |
| Sindhu M | IISc, Bangalore |
| Anusha Chandrashekarmath | JNCASR, Bangalore |
| Neha Paddillaya | IISc, Bangalore |
| Simerpreet Kaur | INST, Mohali |
| Nibedita Ray Chaudhuri | Bose Institute, Kolkata |
| Nikita Saibo | IIT Kharagpur |
| Smrithi Krishnan R | RGCB, Thiruvanathapuram |
| Pooja Joshi | RRI, Bangalore |
| Rashima Prem | NII, Delhi |
| Rupasree Brahma | SINP, Kolkata |
| Sarika Hinge | Savitribai Phule Pune University |
| Geetika Chouhan | TIFR, Mumbai |
| Lipika Baidya | IISc, Bangalore |
| Simran Arora | TIFR, Mumbai |
| Susmita Sarkar | TIFR, Hyderabad |
| Tinku Dhankar | UM-DAE CBS, Mumbai |
| Shreedha Prabhu | TIFR, Mumbai |
| Kirthi Joshi | University of Hyderabad |
| Debanjana Das | TIFR, Mumbai |
| Surabhi Lata | University of Hyderabad |
| Lubhanshi Garg | TIFR, Mumbai |
| Anantha Sri Sailapathi | University of Madras |
| Swadha Gupta | Central University of Gujarat |
| Debjani Bagchi | MSU, Baroda |
| Nandita Bajpai | MSU, Baroda |
| Santosh Devi | JNU, Delhi |
| Vignesh Ganesan | IIT Bombay |
| Aditya Shrivastava | TIFR Bombay |
| Debsankar Saha Roy | TIFR Bombay |
| Sharon Jose | IISER Kolkata |
| Arpan Dey | TIFR Bombay |
| Shabnam | JNU, Delhi |
| A.Kirithiga | AMET, Kanathur |
| Sini Porathoor | IIT, Bombay |
| Shashank Shekhar | IIT, Hyderabad |
| Sankarshan Talluri | NCBS, Bangalore |
| Sangeetha Balasubramaniam | IISc, Bangalore |
| Debayan Purkait | SINP, Kolkata |

# Useful Information

**Talks** will be held at two lecture halls: **Haapus(LH-1)** and at **Dasheri** at NCBS, Bangalore. All plenary sessions are at **Dasheri**.

**Registration** will be open on all days in front of Dasheri auditorium. Preferably register during 8:00-9:00 or 13:00-14:00 to avoid delay.

**Breakfast** on all days will be served in the main canteen (first floor). **Lunch and Dinner** during the tutorial/workshop (25th, 26th March) will be in the main canteen (first floor, under glass roof). **Lunch and Dinner** for the meeting from 27th-29th March will be served in inStem Canteen, first floor.

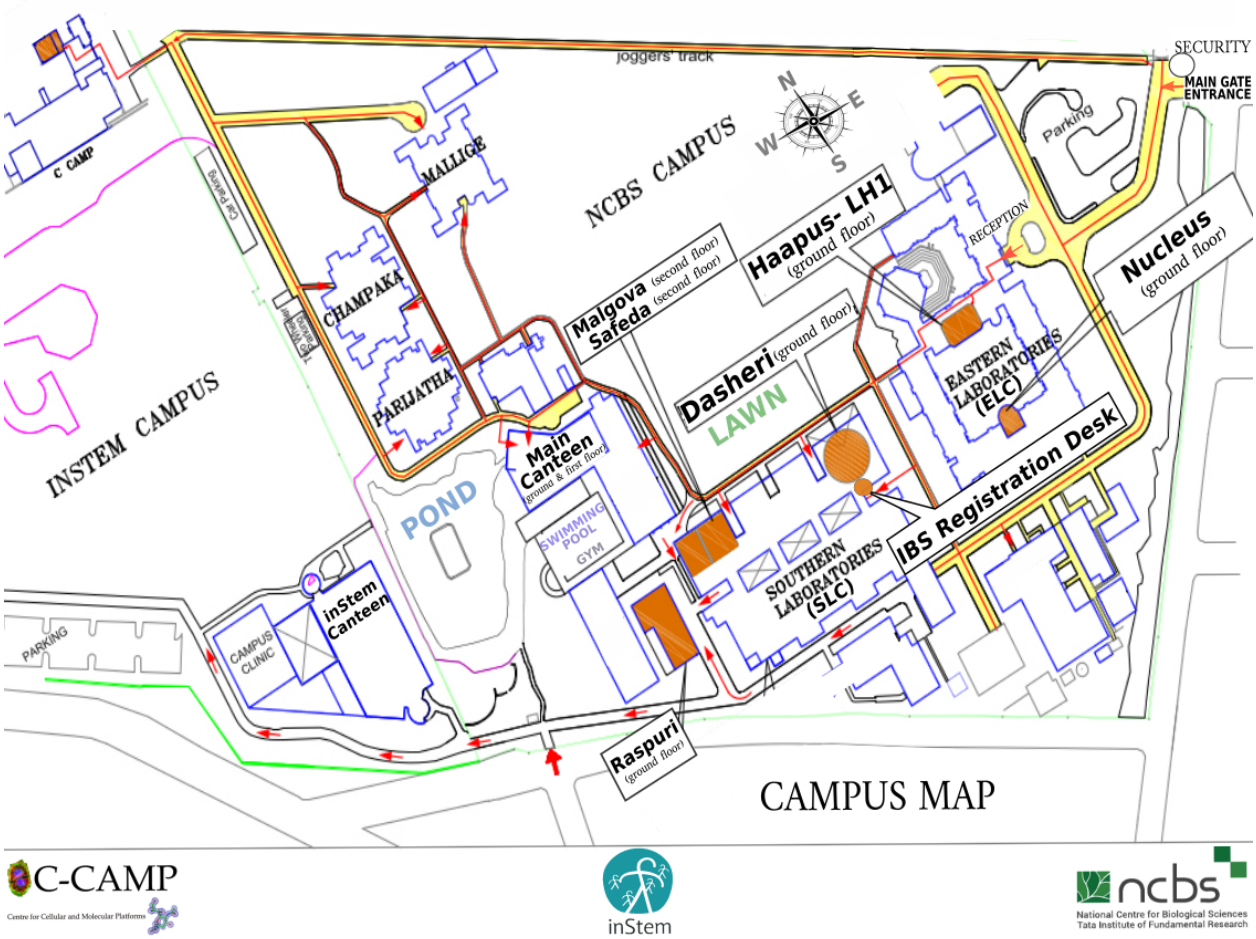
The **poster session** will be held in the **Colonnade** of the Southern Lab Complex (SLC).

**Wi-Fi** details:
1) Connect to 'NCBS Hotspot'.
Open any web page on your browser, it will display a login form. Upon submitting the form you will receive an activation email and 10min time to access it. Open that email and click on the link within to get 24hr internet access.
2) Use your Eduroam login if you have one

**Useful Numbers**: Please don't hesitate to reach us in case you need help or information.

**NCBS Reception**
91 80 23666001 / 02
91 80 23666018 / 19
91 80 67176001 / 02
91 80 67176018 / 19
**Emergency Numbers in Bangalore**
Ambulance 108; Police 100
**Student Volunteers**
Abhishek: +91 9986860048
Partha: +91 8137856911
Nishant: +91 9810010292
Saptarshi: +91 9731932843
Shailesh: +91 8217288268
Swati: +91 9618414487
**Organiser contact details**
Madan Rao: +91 9886538926
Vinothkumar K.R: +91 9148088867
Ranabir Das : +91 9740561300

# Finding your way around the Campus




**Important Venues**

1) Main gate: where the buses and cabs enter and leave the campus; pickup point for Uber/Ola cabs.
2) Reception: where you can get all the information. You can also book NCBS cabs from here.
3) IBS Registration desk: where you register for the conference.
4) Dasheri auditorium: where plenary sessions and some mini symposiums will take place.
5) Haapus (LH1) auditorium : where some mini symposiums will take place.
6) Colonnade: location of poster session.
7) Main Canteen: breakfast will be served in the first floor. Lunch and dinner for tutorial/workshop under glass roof area, first floor.
8) Instem Canteen: Lunch and Dinner for meeting (27th-29th March) will be served in the first floor.
9) Raspuri, Nuclues, Safeda : Venues for tutorial sessions.
10) Parijatha, Champaka, Mallige, Naidile: Accomododation for participants.

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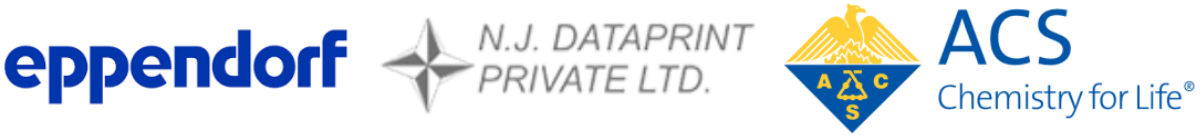
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