

CENTRE FOR NEUROSCIENCE INDIAN INSTITUTE OF SCIENCE PROFILE



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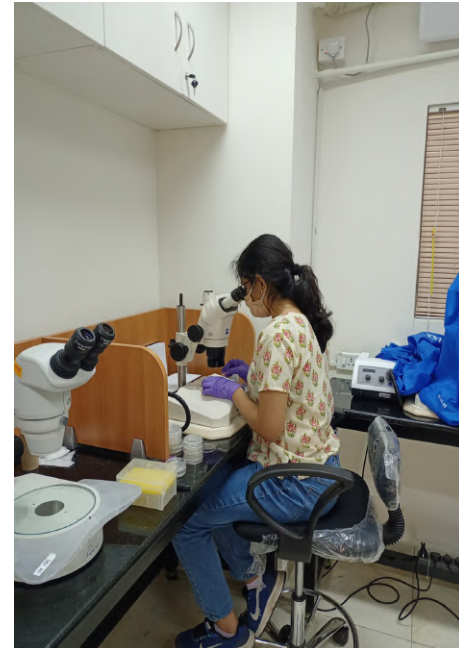
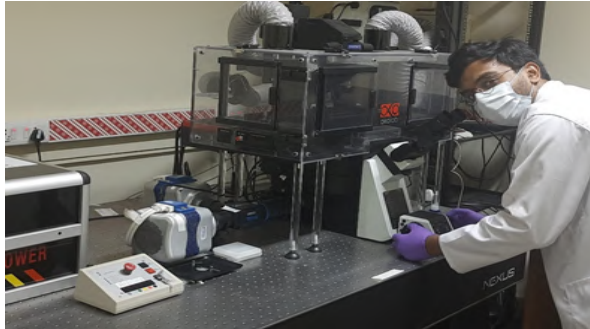
OVERVIEW

Understanding the brain is one of the great challenges in modern science. It is a prerequisite and a necessity if we are to diagnose, treat and cure brain disorders that now constitute a huge burden on modern society, including in developing countries.

The Centre for Neuroscience (CNS) was established in 2009 in the centenary year of IISc with the goal of pursuing research towards understanding the structure, function and development of the brain in health and disease. This requires studying the brain across different levels of organization using molecular, cellular, systems, behavioural and computational approaches. The diversity of these approaches is also reflected in the varied academic backgrounds of the faculty at CNS, many of whom have their undergraduate training in areas such as Engineering, Physics and Chemistry and Biology. We anticipate that such diversity is not only critical if we are to understand brain function but also provides a stimulating research environment for our students, who we anticipate, will imbibe the interdisciplinary ethos essential to neuroscience research.

In keeping with this vision, the primary faculty perform cutting edge investigator driven research at different scales using different approaches and model systems ranging from invertebrates such as *C. elegans*, to rodents, to non-human primates as well as human subjects and patients. In addition to investigator driven research, the faculty also leverage the expertise of researchers in other departments both within and beyond the institute to address highly complex problems and interdisciplinary questions in neuroscience that lie at the interface of clinical research, engineering and other areas of biology. In summary, the Centre is a relatively young initiative that is still in its growing years and has still many paths to traverse. One can certainly hope that with such a vibrant interdisciplinary and collaborative effort, research at the Centre for Neuroscience will contribute in a meaningful way to brain research in the years ahead.

Genetics Neural Networks
Behaviour Computational Modelling Neurons
Action Potentials Neural Development Synapse Neuroanatomy
Histology Receptors Neurotransmitters Attention Emotion
Vision Cell Biology Neurochemistry Imaging MRI Parkinsons Disease
Alzheimers Disease Electrophysiology Attention Decision-Making
Hippocampus Motor Control Neural Circuits Axonal Regeneration Multi
Photon Imaging Genetic Engineering Neuronal Stem Cells Optogenetics
Neuropharmacology Gene Regulation Signal Processing Decisions Astrocytes
Signal Transduction Neural Development Cortex
Signal Processing Psychophysics
Neurophysiology Microscopy
Neural Coding
Oscillations
Synapses



RESEARCH APPROACHES

Transgenic and knockout mice and genome editing

In-vivo imaging of neural networks

Live cell imaging

Single molecule tracking using super-resolution microscopy

Nanoscale Organization and Regulation of Post-Synaptic Density

Animal cognition & behavior

Primate neurophysiology (single unit recordings, arrays, microstimulation, behaviour)

Human cognitive neuroscience (behaviour, fMRI, EEG, TMS, tDCS)

EQUIPMENT

Multi-photon microscope-based in-vivo imaging system with sub-cellular resolution

Two-photon microscope for live-cell imaging

Live-cell super-resolution imaging with PALM and STORM microscopes

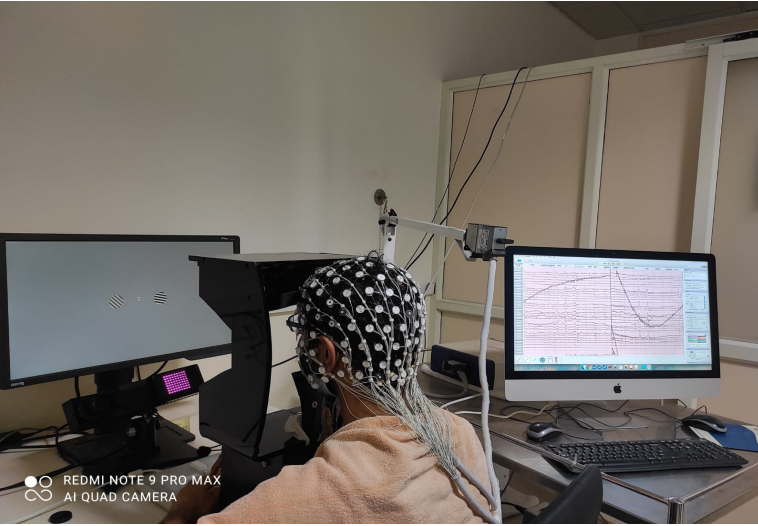
Inverted and upright Apotome and high-speed single-molecule imaging

Virus generation and purification facility

Small animal behavior monitoring and experimentation facility

Extracellular electrophysiology in awake behaving primates

fMRI compatible EEG and TMS



I PHD PROGRAM AT CNS

Students at CNS are exposed to cutting edge neuroscience research through the CNS faculty, whose interests span the gamut from molecular to systems and cognitive neuroscience. Research at CNS is highly interdisciplinary and reflects the diverse backgrounds of the faculty themselves. The department offers world class facilities and equipment together with a vibrant environment for research that consists of journal clubs and seminars. The department conducts national level and international level workshops regularly, where students get to interact with the best neuroscientists from India and abroad. As part of their PhD experience students are also given opportunities to travel to national and internal conferences to present their research.

The CNS PhD program is designed to provide a solid foundation of neuro-science to all students including those that do not have any prior background/experience in neuroscience. Incoming first year PhD students are not pre-assigned to an advisor but are instead asked to take the entire first semester to decide on the laboratory that they wish to join for their PhD. They are encouraged to talk to the faculty and students in each laboratory and also do a rotation in order to make an informed decision.

In addition, students take courses on molecular and systems neuro- science in the first semester and advanced readings and grant writing in the second semester, together with relevant courses offered by other departments.

This approach helps them to understand and provides them an opportunity to carry out neuroscience research in the area that interests them the most. The students make the final choice of their thesis advisor/laboratory by the end of the first semester. During the second semester students are expected to choose one of two advanced neuroscience courses either in systems and cognitive neuroscience or in molecular and cellular neuroscience, where they get exposed to the latest research in the field through reading and discussion of relevant research papers, learn to make presentations and generate original ideas under the guidance of the course supervisors.

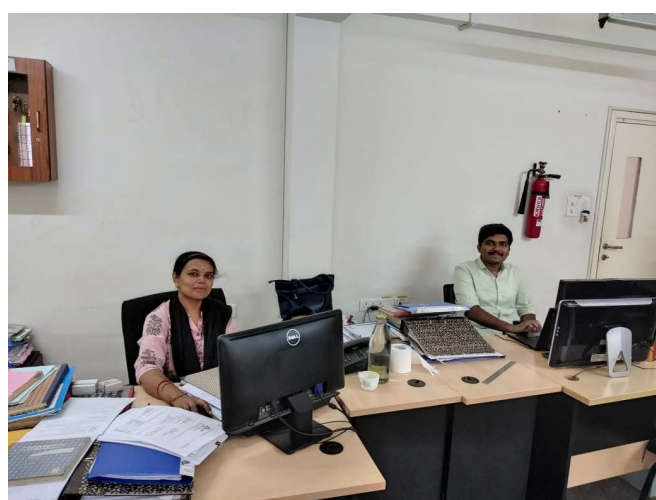
PhD students are required to take a total of 12 credits of coursework. Courses at IISc are rigorous and research oriented and emphasize understanding fundamentals rather than rote memory. At the end of their second year, PhD students are required to pass a comprehensive exam in which they are tested on their understanding of their course fundamentals as well as their research progress in the two years. They are also required to present their work on an annual basis in the form of a seminar.

PhD students are provided with a monthly stipend (as per institute norms) and with

accommodation in the student hostels at IISc. Campus life at IISc is extremely vibrant with a broad spectrum of cultural and sports activities.

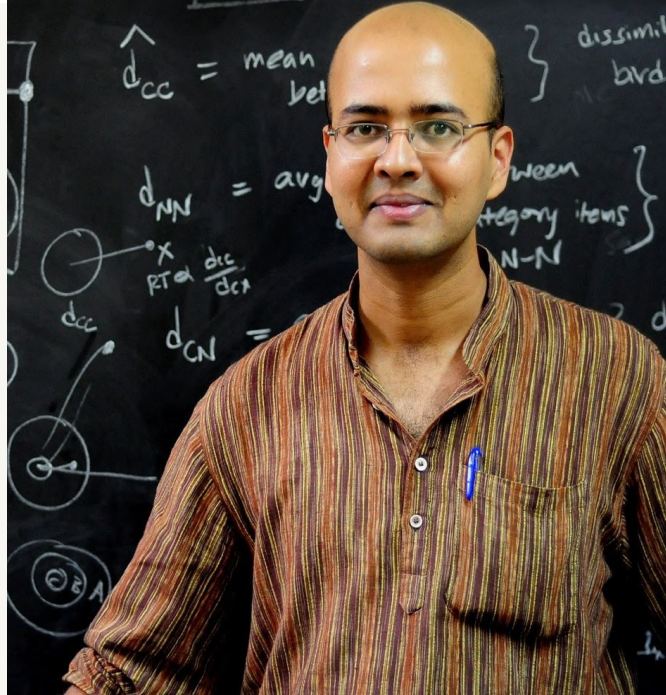
For more details about the admissions process for both PhD and integrated PhD programmes please see

<https://admissions.iisc.ac.in>





FACULTY PROFILES



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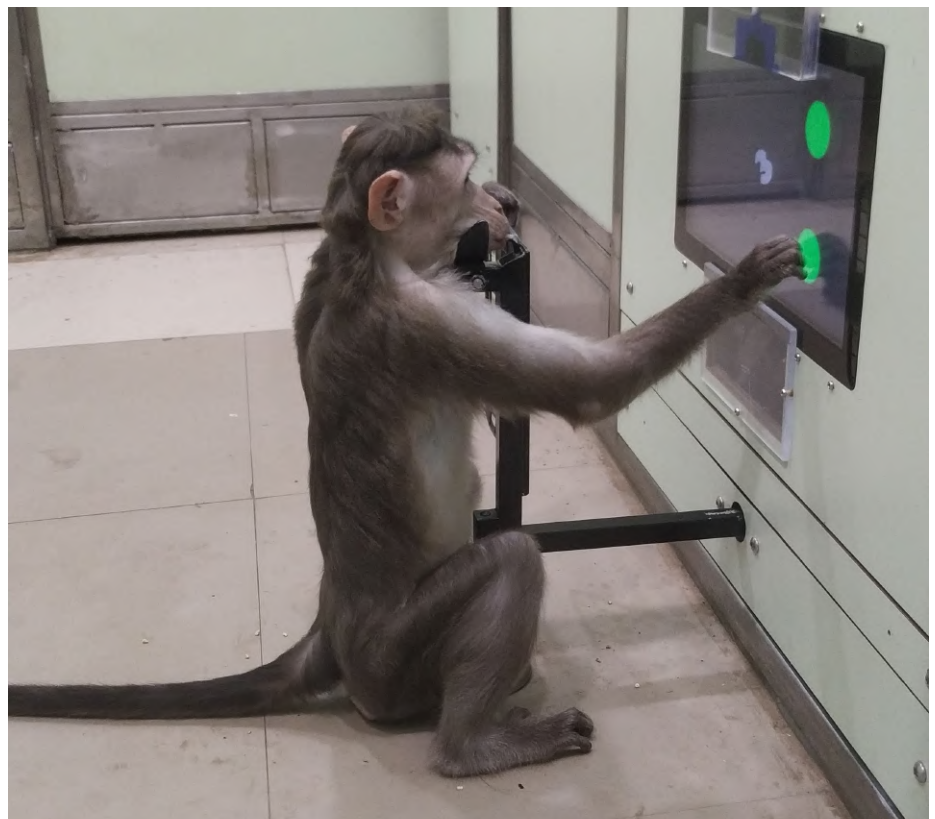
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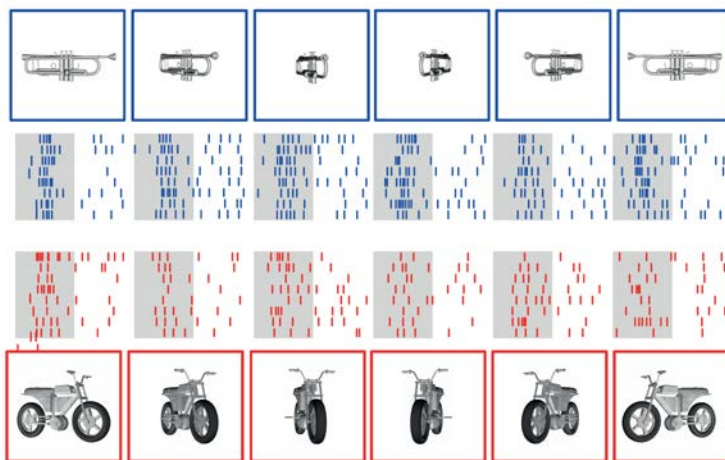
Selected Publications:

1. Jacob G, Katti H, Cherian T, Das J, Zhivago KA & **Arun SP** (2021) A naturalistic environment to study visual cognition in unrestrained monkeys, **eLife** 10: e63816
2. Jacob G, Pramod RT, Katti H & **Arun SP** (2021) Qualitative similarities and differences in visual object representations between brains and deep networks. **Nature Communications**, 12: 1872.
3. Agrawal A, Hari KVS & **Arun SP** (2020) A compositional neural code in high-level visual cortex can explain jumbled word reading. **eLife**, 9:e54846.
4. Agrawal A, Hari KVS & **Arun SP** (2019) Reading Increases the Compositionality of Visual Word Representations, **Psychological Science**, 30:1707-23.
5. Ratan Murty NA & **Arun SP** (2018) Multiplicative mixing of object identity and image attributes in single inferior temporal neurons. **PNAS**, 115:E3276-85

I received my B.Tech from the Indian Institute of Technology (Bombay), and MS and PhD from Johns Hopkins University, all in Electrical Engineering. I completed my postdoctoral research at Carnegie Mellon University and then joined IISc. I am fascinated by how the brain transforms sensory information into perception.



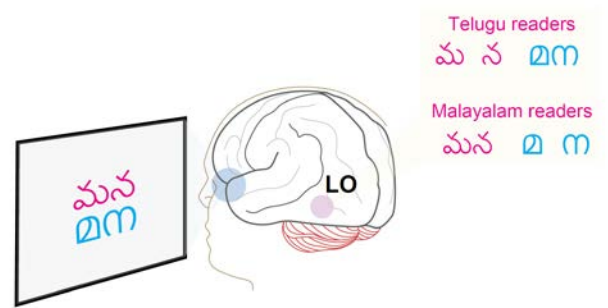
OBJECT RECOGNITION



Dynamics of 3D view invariance in a single IT neuron.

Responses of a single IT neuron are shown to a trumpet and a motorbike at multiple views. Each row represents a trial, and ticks represent the times of action potentials produced by the neuron. IT neurons show a gradual development of viewpoint invariance over response.

From Ratan Murty & Arun (2015)



Reading expertise reduces adjacent letter interactions, making words more discriminable. A Telugu reader looking at Telugu (magenta) and Malayalam (cyan) letter strings perceives Telugu letters as further apart, allowing for easier parsing. Likewise a Malayalam reader perceives Malayalam letters to be further apart. These changes in visual processing matched best with an object-selective region (LO) in the brain.

From Agrawal, Hari & Arun, 2019

We recognize objects easily every day, but object recognition is in fact a very difficult problem. Even leading computer algorithms do not match human performance today. Object recognition is not easy for the brain either: a series of cortical areas, taking up ~40% of the brain, is dedicated to vision. But we know very little about the rules by which the brain transforms what we see into what we perceive. What is the nature of this representation? What are the underlying rules?

Approach

Our approach to this problem is best understood through an analogy to colour. We see millions of colours but it is well known that colour perception is three-dimensional. Any colour we perceive can be represented using three numbers. Can we do likewise for the millions of shapes we see? Do shapes also reside in a low-dimensional space?

To gain insight into these questions, we perform behavioural and imaging experiments in humans and record the electrical activity of

neurons from monkey visual cortex.

In the human experiments, we probe the underlying perceptual representation using behavioural tasks such as visual search or categorization and investigate the underlying representation using fMRI and TMS. In the monkey experiments, we probe the representation at the level of single neurons in the inferotemporal cortex, an area critical for object recognition. We work with these diverse types of data to build, test and validate computational models of object recognition.

For more information

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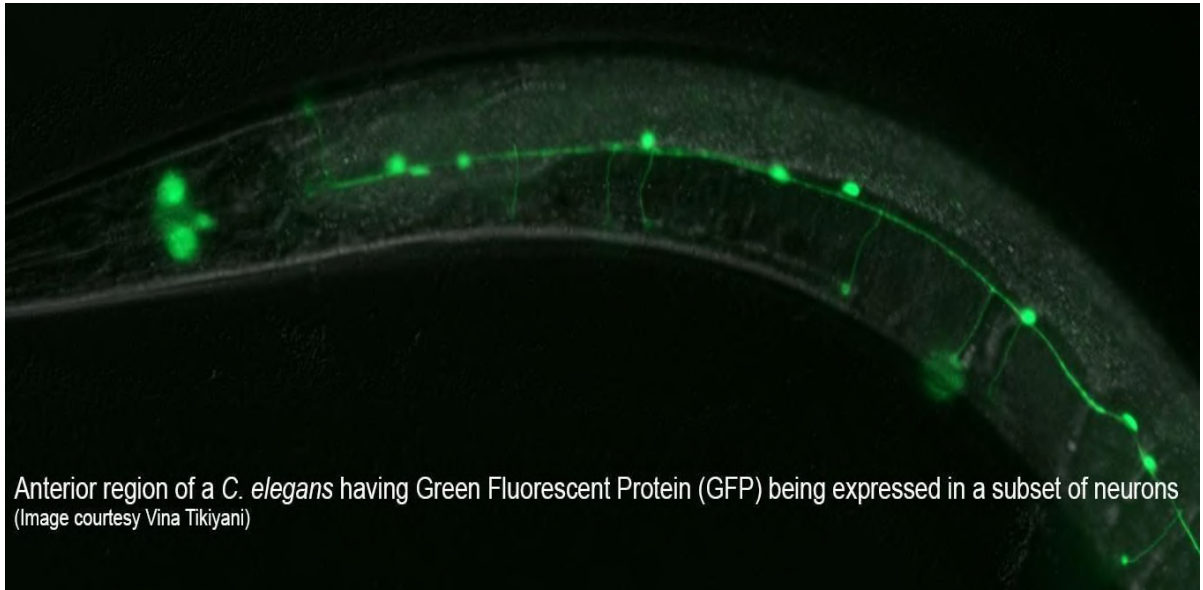
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Selected Publications:

1. Pandey P, Singh A, Kaur H, Ghosh-Roy A and **Babu K** (2021). Increased dopaminergic neurotransmission results in ethanol dependent sedative behaviors in *Caenorhabditis elegans*. **PLoS Genetics**, 17(2):e1009346.
2. Dahiya Y, Rose S, Thapliyal S, Bhardwaj S, Prasad M and **Babu K** (2019); Differential regulation of innate and learned behavior by CREB1/CRH-1 in *Caenorhabditis elegans*. **The Journal of Neuroscience**, 39(40): 7934-46.
3. Tikiyani V, Li L, Sharma P, Liu H, Hu Z and **Babu K** (2018) Wnt is regulated by the tetraspan protein HIC-1 through its interaction with Neurabin/NAB-1. **Cell Reports**, 25(7): 1856-71
4. Sharma P, Li L, Liu H, Tikiyani V, Hu Z and **Babu K** (2018) The Claudinlike protein, HPO-30, is required to maintain LACHRs at the *Caenorhabditis elegans* neuromuscular junction. **Journal of Neuroscience**, 38(32): 7072-87.
5. Bhardwaj A, Thapliyal S, Dahiya Y and **Babu K** (2018) FLP-18 functions through the G-protein coupled receptors NPR-1 and NPR-4 to modulate reversal length in *Caenorhabditis elegans*. **Journal of Neuroscience**, 38(20):4641-54.

I graduated with a PhD in developmental biology from the Institute of Molecular and Cell Biology (IMCB-A*STAR) that was part of The National University of Singapore. My PhD work was conducted in with Professor Bill Chia laboratory in Singapore and King's College, London. I then joined the laboratory of Professor Josh Kaplan as a postdoctoral fellow at the Department of Molecular Biology, Massachusetts General Hospital, Boston, USA. Upon completion of my postdoctoral training, I started my own laboratory as an Assistant Professor at Indian Institute of Science Education and Research (IISER), Mohali, India. In May 2019, I moved to the Centre for Neuroscience.

MOLECULES AND MECHANISMS UNDERLYING SYNAPTIC FUNCTION



Anterior region of a *C. elegans* having Green Fluorescent Protein (GFP) being expressed in a subset of neurons
(Image courtesy Vina Tikiyani)

Unlike our brain that has billions of neurons and trillions of synapses, the free-living nematode *Caenorhabditis elegans* has 302 neurons and around 7000 synapses. Our laboratory is interested in understanding two fundamental questions in synaptic biology:

1. How do a class of tetra span protein called claudins function in neurons and synapses? To address this question we are looking at aspects of neuronal and synaptic development and function in claudin mutants and are looking at the expression pattern of claudins at the synapse. Our recent work has implicated two *C. elegans* claudins in maintaining normal levels of postsynaptic receptors at the neuromuscular junction.
2. We are also interested in understanding molecules and mechanisms underlying normal locomotory behavior in *C. elegans*. More specifically we want to find out how small peptides (neuropeptides) that are sent out by one neuron affect the same and/or neighboring neurons and how this action by neuropeptides and their receptors affects locomotion.

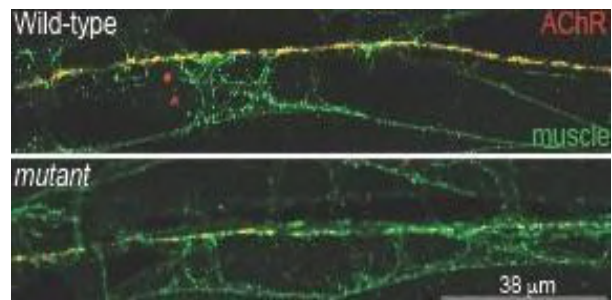


Image : Mutants in a claudin show a reduction in acetylcholine receptor levels (red) at the neuromuscular junction. The body-wall muscles are marked in green. Image from Sharma P., Lei L., et al; 2018 and image courtesy Pallavi Sharma.

Our laboratory uses genetics, imaging techniques including neuronal imaging, FRAP, optogenetic experiments, electrophysiological recordings and cell and molecular biology techniques including CRISPR-Cas9 and RNAi to better understand the molecular mechanisms underlying neuronal and synaptic function.



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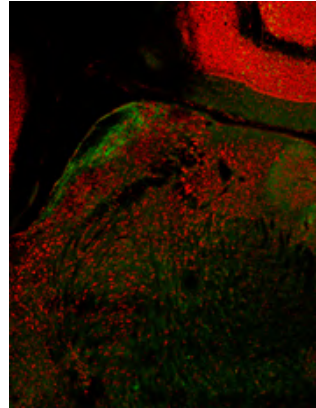
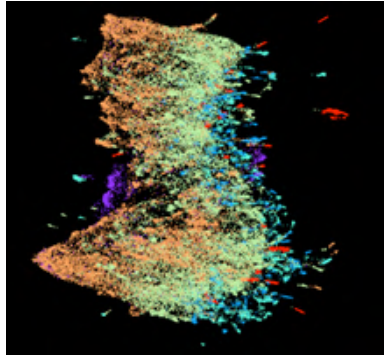
Selected Publications:

1. **Barik A**, Sathyamurthy A, Thompson J, Seltzer M, Levine A, and Chesler A, A spinoparabrachial circuit defined by Tacr1 expression drives pain. 2021. **eLife**, 10:e61135.
2. **Barik, A.**, & Chesler, A. T. (2020). Parallel Parabrachial Pathways Provide Pieces of the Pain Puzzle. **Neuron**, 106(6), 873-875.
3. **Barik, A.**, Thompson, J. H., Seltzer, M., Ghitani, N., & Chesler, A. T. (2018). A brainstem-spinal circuit controlling nociceptive behavior. **Neuron**, 100(6), 1491-1503.
4. **Barik, A.**, & Krashes, M. J. (2018). Remembering a Bad Taste. **Neuron**, 100(4), 765-767.
5. Ghitani, N., **Barik, A.**, Szczot, M., Thompson, J. H., Li, C., Le Pichon, C. E., ... & Chesler, A. T. (2017). Specialized mechanosensory nociceptors mediating rapid responses to hair pull. **Neuron**, 95(4), 944-954.
6. **Barik, A.**, Li, L., Sathyamurthy, A., Xiong, W. C., & Mei, L. (2016). Schwann cells in neuromuscular junction formation and maintenance. **Journal of Neuroscience**, 36(38), 9770-9781.

I did my B.Tech in Biotechnology at SRM University, Chennai, and my PhD in Neuroscience with Dr Lin Mei at the Medical College of Georgia, Augusta. During my PhD, I worked on the cellular and molecular mechanisms of neuromuscular junction development and maintenance. Next, I wanted to explore another facet of the peripheral nervous system - somatosensation - specifically, what are the neural circuits underlying the sensation and perception of somatosensory information from the periphery. To pursue my interests in somatosensation, I moved to the National Institutes of Health to work in the laboratory of Dr Alexander Chesler. In my postdoctoral work, I identified a specific population of neurons in the parabrachial nucleus as being essential for generating affective responses to pain. In 2020 I joined the Center for Neuroscience as a principal investigator and plan to study the molecules, cells, & circuits that drive responses to pain and itch.



NEUROBIOLOGY OF PAIN AND ITCH



How does our brain direct defensive responses to noxious stimuli? Stepping barefoot on a pin could be excruciatingly painful and would evoke both a rapid physical reaction and an emotional response. We may rub our feet where it hurts, scream in pain, and move away from the spot to avoid re-stepping on the pin so as to avoid experiencing the pain a second time. We would also remember the spot on the floor where the pin was and avoid the area until we know there are no more pins lying around. In essence, all of our physical and mental faculties could be momentarily taken over by a relatively inconsequential event and produce long-lasting behavioural changes. In our laboratory, we seek to understand how specific groups of neurons in the brain are able to drive specific aspects of such defensive behaviours.

How do these neurons receive the pain information? What are their molecular characteristics? What is their anatomical architecture? How do these neurons communicate with the rest of the nervous system? We intend to answer these questions by leveraging molecular and optogenetic tools to manipulate behaviour, map circuits, and record neural activity in mice.

How are the maladaptive mechanisms underlying chronic pain and itch? Pain and itch are fundamentally protective in nature. However, these useful protective mechanisms can become a burden when they become chronic or outlast the stimulus. When and where these otherwise beneficial mechanisms become pathological remain poorly understood. In our laboratory, we study how these conditions might be linked to alterations in specific brain areas in terms of their connectivity, molecular composition, and activity.



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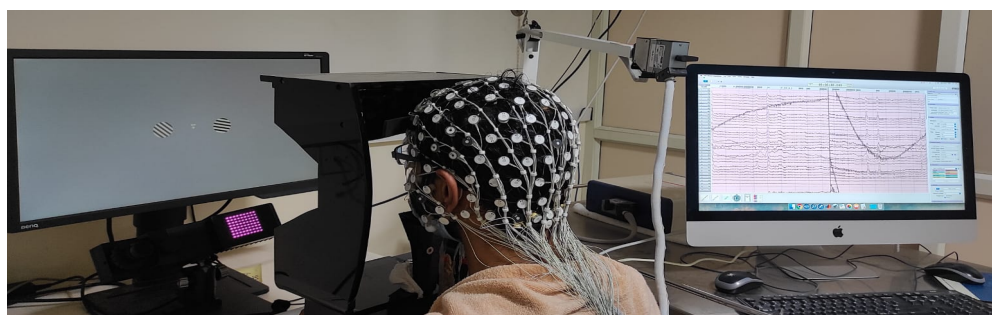
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Selected Publications:

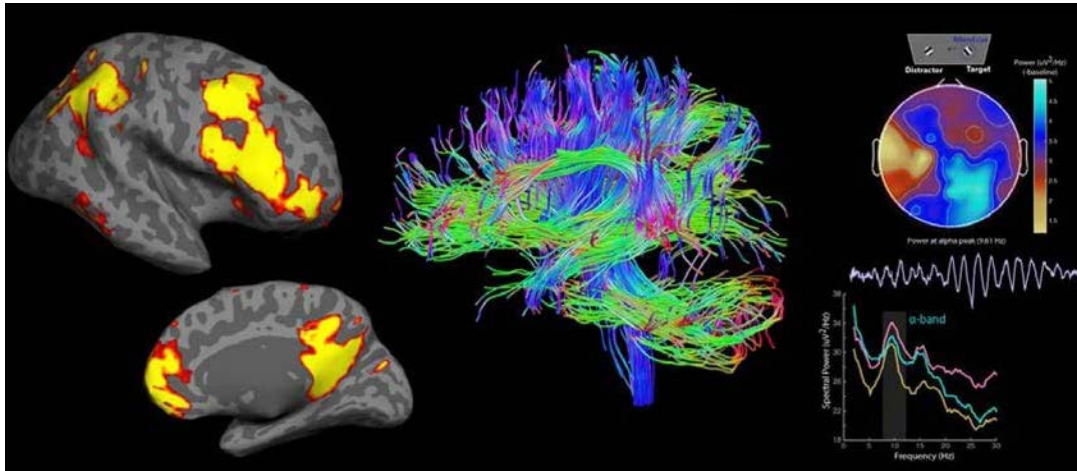
1. Sreenivasan, V., Kumar, S., Pestilli, F., Talukdar, P., and **Sridharan, D** (2022). GPU-accelerated connectome discovery at scale. **Nature Computational Science** 2, 298–306.
2. Chauhan, K., U, M, B., Shenoy, P., Gupta, M., and **Sridharan, D** (2022). Robust outlier detection by de-biasing VAE likelihoods. **IEEE/ CVF Conference on Computer Vision and Pattern Recognition (CVPR)**, New Orleans, LA, USA, pp. 9871-9880.
3. Chinchani, A, M., Paliwal, S., Ganesh, S., Chandrasekhar, V., Yu, B, M., and **Sridharan, D.** (2022) Tracking momentary fluctuations in human attention with a cognitive brain-machine interface. **Commun Biol.** 2022 Dec 8;5(1):1346.
4. Sawant, Y., Kundu, J, N., Radhakrishnan, V, B., and **Sridharan, D.** (2022) A Midbrain Inspired Recurrent Neural Network Model for Robust Change Detection. **J Neurosci.** 2022 Nov 2;42(44):8262-8283.
5. Sreenivasan, V., and **Sridharan, D.** (2019) Subcortical connectivity correlates selectively with attention's effects on spatial choice bias. **Proceedings of the National Academy of Sciences** 116 (39) 19711-19716 .

I completed my Bachelors and Masters (Dual) Engineering degrees from the Indian Institute of Technology (IIT) Madras. As a Stanford Graduate Fellow, I studied the dynamics of attention-related brain networks using functional neuroimaging (fMRI). I completed my Ph.D. investigating the role of the midbrain in selective attention, with a combination of in-vivo and in-vitro electrophysiology and neuromorphic modeling. As a Dean's Postdoctoral Fellow at the Stanford University School of Medicine, I develop neural and behavioral assays for teasing apart component processes of attention.

As an Associate Professor, former DBT Wellcome Trust India Alliance Fellow and (now) DST SwarnaJayanti Fellow, I lead the Cognition, Computation and Behavior Lab at the Centre for Neuroscience (CNS) at IISc. Our Lab studies the neural basis of attention and decision-making behaviors with both experimental (fMRI, EEG, TMS, tACS) and computational modeling approaches. As an Associate Faculty of the Department of Computer Science and Automation (CSA), I collaborate with Google Research to develop deep learning models for reliable, automated disease diagnosis with medical images.



NEURAL COMPUTATIONS UNDERLYING COGNITION



Goals:

- Investigating neural computations underlying attention with neuroimaging (functional/diffusion MRI).
- Identifying the causal role of brain regions in attention with transcranial neurostimulation (TMS/tACS).
- Linking brain and behaviour with computational and deep learning models.

How does our brain enable us to pay attention selectively to certain important objects in the world, and to ignore other, irrelevant ones? What happens in the brain when we make important decisions? Our research focuses on understanding the neural basis of cognitive phenomena such as perception, selective attention and decision-making. We seek to identify key mechanisms by which specific brain regions and neural oscillations contribute to these phenomena in humans. In order to accomplish this goal, we pursue a highly inter disciplinary approach.

First, we measure and analyze brain activity as subjects perform attention-demanding tasks involving complex decisions. For this, we employ state-of-the-art techniques such as functional magnetic resonance imaging (fMRI), electrophysiology (EEG) and machine-learning. Second, we quantify and visualize structural and functional connectivity in the brain using emerging techniques such as diffusion MRI and Granger causality. These techniques can also help us identify abnormalities in connectivity patterns in patients with cognitive disorders.

Third, we investigate how specific brain regions contribute to attention and decision-making using non-invasive neuro-stimulation techniques, such as transcranial electrical and magnetic stimulation,(tES/ tMS). Finally, we seek to simultaneously perturb and record neural activity in the brain with combinations of brain stimulation and recording technologies such as interleaved fMRI-tMS and simultaneous EEG-tES.

A second, emerging area of research in the lab involves applying artificial intelligence (AI) algorithms, including deep learning, for understanding brain mechanisms of attention, in healthy individuals, and its decline, in neurodegenerative disorders.

A strategic combination of these techniques, along with quantitative analysis of behavior, has the potential to significantly advance our understanding of how cognitive phenomena emerge in the human brain and how they shape behavior.



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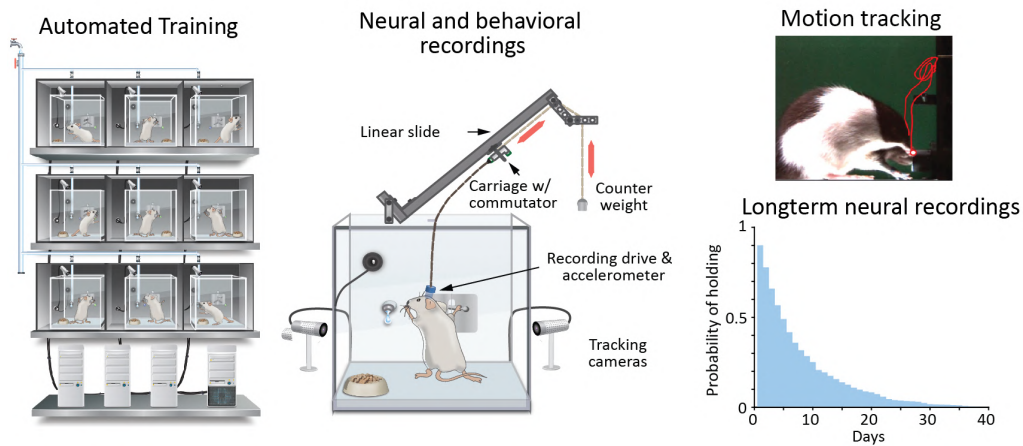
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Selected Publications:

1. **Dhawale A.K.**, Wolff S.B.E., Ko R., Ölveczky B.P. (2021). The basal ganglia control the detailed kinematics of learned motor skills. **Nature Neuroscience**, 24, 1256–1269.
2. **Dhawale, A. K.**, Miyamoto, Y. R., Smith, M. A., & Ölveczky, B. P. (2019). Adaptive regulation of motor variability. **Current Biology**, 29(21), 3551-3562.
3. **Dhawale, A. K.**, Poddar, R., Wolff, S. B., Normand, V. A., Kopelowitz, E., & Ölveczky, B. P. (2017). Automated long-term recording and analysis of neural activity in behaving animals. **Elife**, 6, e27702.
4. Modi, M. N., **Dhawale, A. K.**, & Bhalla, U. S. (2014). CA1 cell activity sequences emerge after reorganization of network correlation structure during associative learning. **Elife**, 3, e01982.
5. **Dhawale A.K.**, Hagiwara A, Bhalla US, Murthy VN, Albeanu DF (2010) Non-redundant odor coding by sister mitral cells revealed by light addressable glomeruli in the mouse. **Nature Neuroscience** 13(11): 1404-1412.

I received my undergraduate training in Life Sciences and Biochemistry at St. Xavier's College in Mumbai. My doctoral research was on sensory coding in the olfactory bulb and hippocampus, supervised by Dr. Upinder Bhalla at the National Centre for Biological Sciences in Bangalore. During my PhD, I also collaborated closely with Dr. Dinu Albeanu at Cold Spring Harbor Laboratory in New York to develop optogenetic approaches to study olfactory circuits. During my postdoctoral training with Dr. Bence Ölveczky at Harvard University, supported by Life Sciences Research Foundation and Charles A. King Trust fellowships, I developed new experimental platforms to study how the brain learns and executes skilled movements.

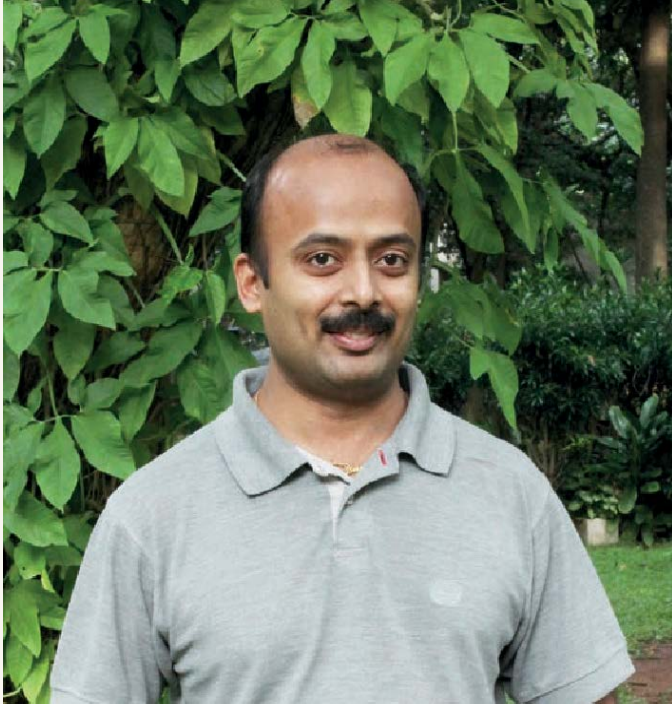
NEURAL BASIS OF SKILL LEARNING



Performing an ace tennis serve or checkmating an opponent in chess can seem like daunting tasks for a novice. Yet we take it for granted that, given enough practice and time, we can all become expert practitioners of such skills. The brain's ability to solve complex learning challenges is an incredible feat whose speed and efficiency is unmatched by machine intelligence. However, little is known about this ability and the neural circuits that underlie it.

This is because most laboratory studies of learning typically focus on simple tasks that can be solved within a few sessions. In contrast acquiring a new skill is a noisy, trial-and-error driven process that typically spans weeks and months. Thus, to understand the neural basis of skill learning, we need new approaches to monitor changes in behaviour and neural activity over these long timescales.

We employ an interdisciplinary strategy to investigate the neural basis of skill learning in rodents. (1) Using a fully-automated behavioural training system we acquire large datasets as animals learn to solve complex motor and foraging tasks. (2) We infer trial-by-trial learning strategies by performing detailed analysis of these massive datasets in concert with computational modelling utilizing reinforcement learning theory. (3) Using targeted perturbations of neural circuits in combination with a new experimental platform to automatically record the spiking activity of large ensembles of neurons continuously (24/7) over weeks and months in behaving animals, we investigate how the learning algorithms we have identified through behavioural analysis are implemented in the brain.



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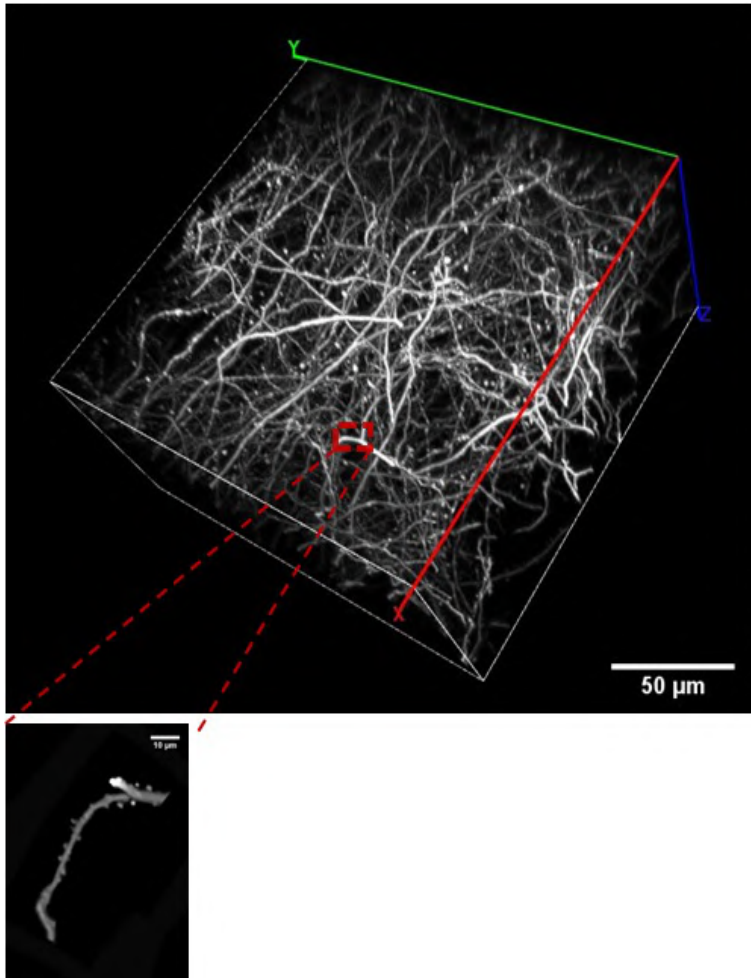
Selected Publications:

1. Suraj Kumar, Aditya Singh, Vijay R Singh, Jude B George, and **J Balaji**. "Saturation Dynamics Measures Absolute Cross Section and Generates Contrast within a Neuron", **Biophysical Journal** (111) 1328-1336 (2016).
2. A Singh, S Kumar, VP Singh, A Das, and **J Balaji** (2017) Flavor Dependent Retention of Remote Food Preference Memory. **Frontiers in Behavioral Neuroscience**, 11(7).
3. . Meenakshi, P., and **Balaji, J.** Neural Circuits of Memory Consolidation and Generalisation. **J Indian Inst Sci** 97, 487–495 (2017).
4. Meenakshi P, Suraj K Singh and **Balaji J**, "In vivo Imaging of Immediate Early Gene expression dynamics segregates neuronal ensemble of memories of dual events", **Mol Brain** 14, 102 (2021)..
5. Shridhar, S., Singh, V. P., Bhatt, R., Kundu, S., and **Balaji, J.** "A new paradigm for investigating temporal order memory shows higher order associations are present in recent but not in remote retrieval." **Experimental Brain Research**, (2022), 240(2), 611–629.
6. Meenakshi, P. K., Mehrotra, D., Nruthyathi, N., Almeida-Filho, D., Lee, Y., Silva, A., and **Balaji, J.** "Novel measures of Morris water maze performance that use vector field maps to assess accuracy, uncertainty, and intention of navigational searches." **Hippocampus** (2022).

I did my undergraduate training at Jamal Mohammad College of Bharathisadan University, Trichy, where I obtained both my Bachelors and Masters Degrees. After my undergraduate training, I joined Prof. Sudipta Maiti at the Tata Institute of Fundamental Research for doctoral research where I developed several optical tools to follow the release dynamics and sequestration of serotonin using its native fluorescence in live neurons. For my post-doctoral training, I worked with Prof. Timothy Ryan at Weil Cornell Medical College of Cornell University, New York and later with Prof. Alcino Silva at the David Griffin School of Medicine, UCLA.



NEUROBIOLOGY OF LEARNING AND MEMORY



Section of mice brain (200 x 200 x 150 μm) that is imaged in vivo is reconstructed in 3D to show the neuronal architecture. The scale bar is 50 μm. Location of the imaging area (RSc) in the mice brain is shown as an illustration. The area shown within red square is enlarged to show the spines located on the dendrites.

Research in our lab is focused on understanding how memories of past events influence the acquisition of new memory and experiences. Using mice as a model system, we follow the neuronal correlates of memory. We follow changes accompanying acquisition, formation, and retrieval of memory through in-vivo two-photon imaging. Longitudinal imaging of the same mice over the entire process of memory consolidation provides us a unique ability to watch, follow and study these processes as they happen. We combine this ability with small animal behaviour and molecular genetics to investigate:

- i) How the internal representation of remote events (events that happened a long time ago) that are similar in nature but distinct in content are encoded.
- ii) When such events are encoded in two (NMDAR dependent and NMDAR independent) molecularly independent pathways, how do their corresponding internal representations change at cellular and synaptic scale?
- iii) How multiple memories interact with each other and influence future behaviour.
- iv) What happens to temporal information in such representations of old memories.



ADITYA MURTHY

Professor

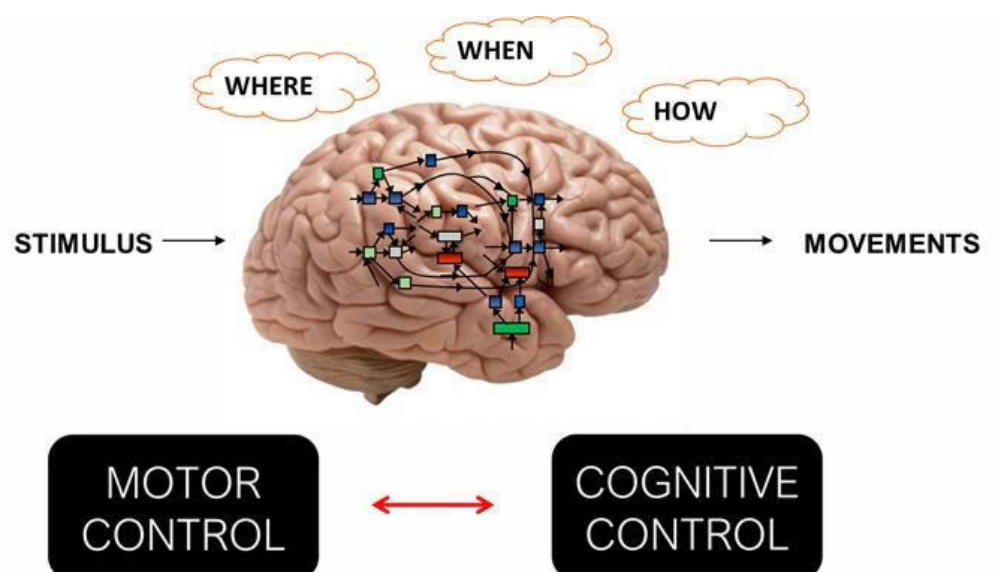
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Selected Publications:

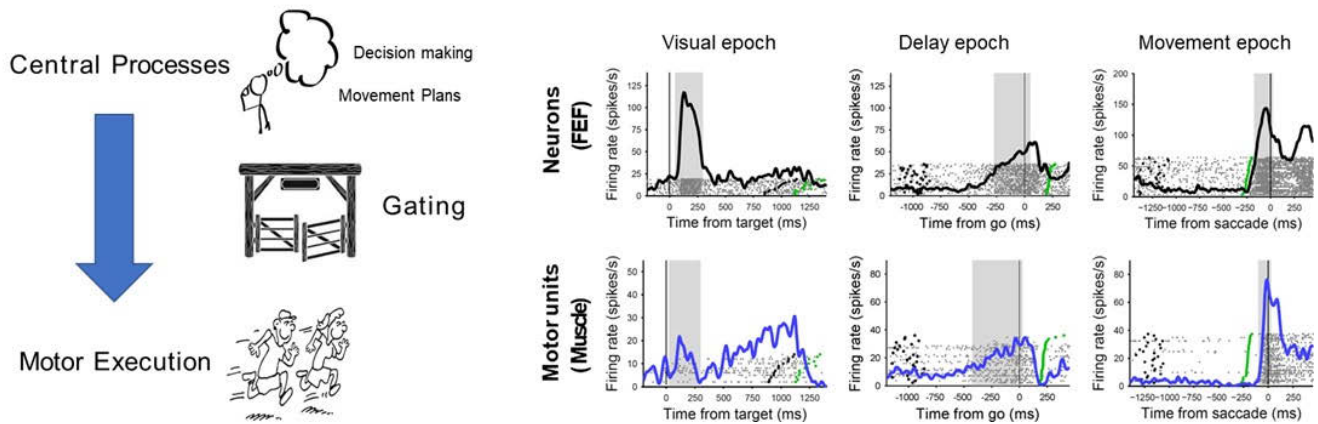
1. Satya Rungta, **Aditya Murthy**. Context-specific early recruitment of small motor units in the shoulder muscle reflects a reach movement plan. **J. of Neurophysiology**. 29(5):1094-1113 (2023).
2. Debaleena Basu, Naveen Sendhilnathan, **Aditya Murthy**. Neck muscle activity reflects neural patterns of sequential saccade planning in head-restrained primates. **J. of Neurophysiology**. 128: 927–933, (2022).
3. Rungta S, Basu D, Sendhilnathan N, **Aditya Murthy**. Preparatory activity links the frontal eye field response with small amplitude motor unit recruitment of neck muscles during gaze planning. **J Neurophysiology**. 126(2):451-463. (2021)
4. Puneet Singh, Ketan Jhunjhunwala, Albert Stezin, Abhishek Lenka, Pramod Kumar Pal, Ashitava Ghosal, **Aditya Murthy**. Basal ganglia contributions during the learning of a visuomotor rotation: Effect of dopamine, deep brain stimulation and reinforcement. **Eur J Neurosci**. 50(8):3349-3364. (2019)

My undergraduate training was at St. Xavier's College, Mumbai and Bombay University, where I obtained my Bachelors and Masters degrees, respectively. I received my Doctorate under the guidance of Dr. Allen Humphrey in the Department of Neurobiology at the University of Pittsburgh. During my Doctoral research I studied the neural mechanisms involved in the processing of motion in the visual system. I did my postdoctoral research with Dr. Jeffrey Schall at Vanderbilt University where I studied the primate visuomotor system with the goal of correlating neural activity with behaviour.



MOVEMENT CONTROL

Central processes and motor execution



All goal directed behaviour whether it involves playing an instrument or singing a song involves the precise coordination and control of many muscles together. For this to occur, the brain must decide, plan, execute and get feedback on the movement. The lab seeks to understand the computations that enable goal directed behaviour with an emphasis to understand the basis of flexibility and control that is the hallmark of intelligent action. Our research interests span the fields of visual perception, decision-making, and the generation of motor behavior and involve the application of cognitive/psychophysical, neuropsychological, and electrophysiological techniques.

Currently, the lab uses a combination of high-density surface EMG recordings during voluntary movements to probe and test the relationship between the patterns of motor unit recruitment and movement initiation and control using behavioral and neurostimulation approaches in normal human subjects and those with motor disorders such as Parkinson's Disease. Besides giving insight into how information processed in motor areas is read out by muscles during voluntary movements, we wish to delineate the neural basis of flexible sensorimotor gating. We hope that such a line of research could be used to develop novel treatments for motor disorders and develop assistive non-invasive brain-machine interfaces.



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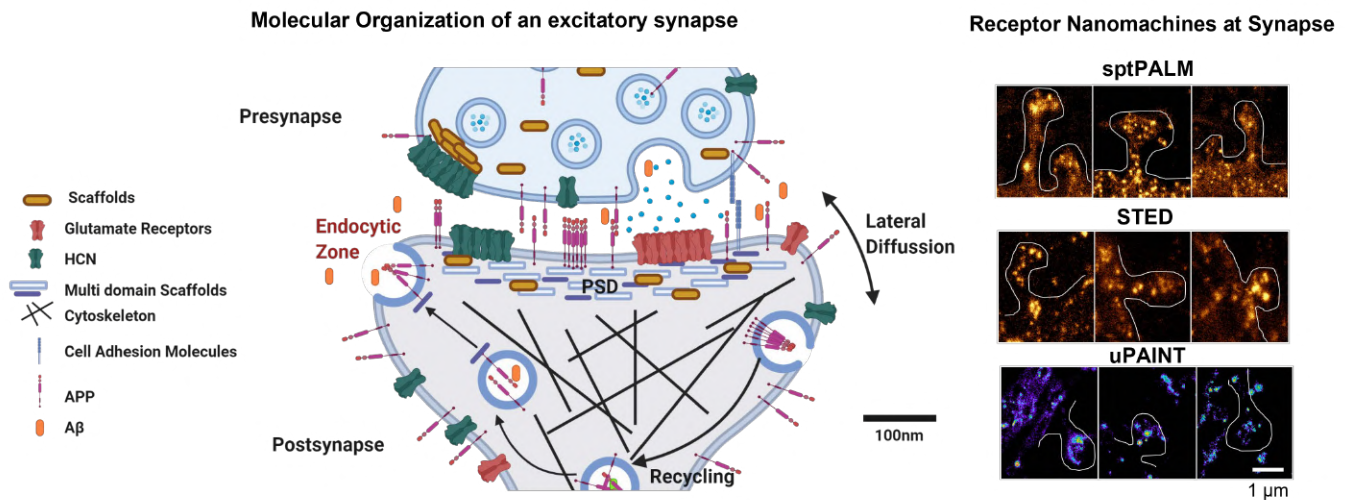
Selected Publications:

1. Mangalwedhekar, M., Singh, N., Thakur, C.S., Seelamantula, C.S., Jose, M., **Nair, D.**, Achieving nanoscale precision using Neuromorphic localization microscopy, (2023) **Nature Nanotechnology** ,18, 380–389.
2. Rajeev, P., Singh, N., Kechkar, A., Butler, C., Ramanan, N., Sibarita, J.B., Jose, M., **Nair, D.**, (2022) Nanoscale Regulation of Ca²⁺ Dependent Phase Transitions and Real-time Dynamics of SAP97/ hDLG. **Nature Communications** 13 (1), 1-18.
3. Kedia, S., Ramakrishna, P., Netrakanti, P.R., Singh, N., Sisodia, S.S., Jose, M., Sathish Kumar, Mahadevan, A., Ramanan, N., Nadkarni, S., and **Nair, D.** (2021). Alteration in synaptic nanoscale organization dictates amyloidogenic processing in Alzheimer's disease, **iScience**, 24(3) 101924.
4. Kedia, S., Ramakrishna, P., Netrakanti, P.R., Jose, M., Sibarita, J.-B., Nadkarni, S., and **Nair, D.** (2020). Real-time Nanoscale Organization of Amyloid Precursor Protein. **Nanoscale** 12 (15), 8200-8215.
5. Koltun, B., Ironi, S., Gershoni-Emek, N., Barrera, I., Hleihil, M., Nanguneri, S., Sasmal, R., Agasti, S.S., **Nair, D.**, and Rosenblum, K. (2020). Measuring mRNA translation in neuronal processes and somata by tRNA-FRET. **Nucleic Acids Research** 48, e32-e32.

I completed my Masters in Physics at IIT Madras, Chennai before moving to Leibniz Institute for Neurobiology (LIN) in Magdeburg, Germany for my PhD. After my PhD, I moved to Bordeaux, France to pursue my post-doctoral research with Dr. Daniel Choquet. There I used state-of-the-art single molecule microscope techniques to study the localization and movement of synaptic molecules at the nanoscale.



NANOBIOLOGY OF SYNAPSES IN HEALTH AND DISEASE



In the central nervous system, synapses form the basic functional units of connectivity between two neurons. The formation, remodeling and elimination of synapses refine the microcircuitry in the brain. The synapse is a complex molecular machine, which changes its structure and composition during neuronal development and plasticity. It contains hundreds of proteins choreographed into a micron sized machine overseeing the fidelity of brain function. The components of the synapses play a major role in synaptic transmission and synaptic plasticity, which are thought to underlie learning and memory. Interestingly most of the diseases has a direct impact on the number, position, and movement of molecules in and out of synapse contributing towards synaptic loss or dysfunction thus affecting the normal behavior of the brain. Though many of the neurological and neurodegenerative disorders are thought to begin as 'synaptopathies' or synaptic dysfunction, the minute deficits in the molecular organization that contributes to the onset of such diseases still remain vague.

It has been an enigma how information is processed at a single synapse by realtime control

of function and position of several molecules. This is partly because of the inaccessibility to garner information to resolve structures less than a few 100nm. The development of superresolution imaging methods that break the diffraction limit allows monitoring the real-time (milli-seconds) synaptic organization at the nanoscale (10-50nm). The observations from our group as well as others over last decade provide conclusive evidences that synapse is organized into assembly of several nanomachines, that modulates and control the efficiency of synaptic transmission. The work in our lab attempts to dissect the fundamental role of this dynamic nanoscale organization of synaptic molecules to understand how synapse process and relay information. To achieve this, we follow an interdisciplinary research paradigm at the interface of high-end microscopy, molecular biology, single cell gene editing, optogenetics and cellular neuroscience. All this information is expected to contribute towards a better understanding of how synapses function at the molecular scale and provide fundamental insights into signal processing at single synapses in health and disease.



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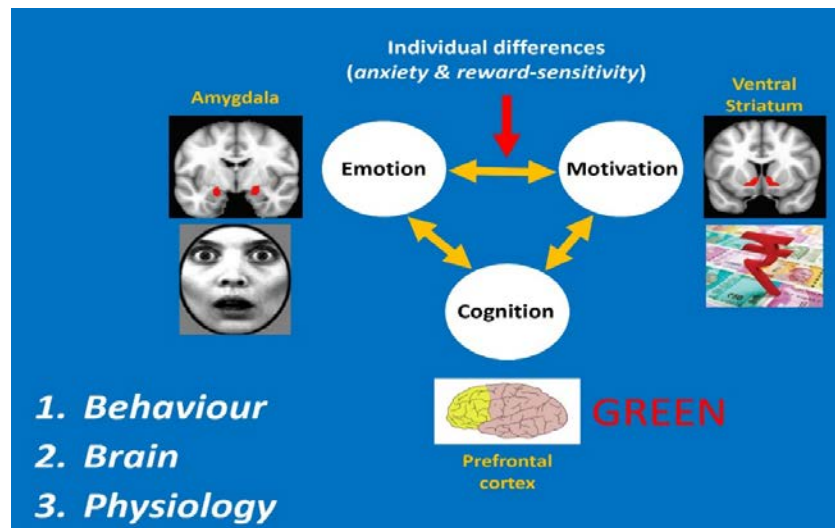
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Selected Publications:

1. Chakravarthula LC, and **Padmala S** (2022), Arousal-driven interactions between reward motivation and categorization of emotional facial expressions. **Frontiers in Psychology**, 13, 985652.
2. Limbachia C, Morrow K, Khibovska A, Meyer C, **Padmala S**, and Pessoa L (2021), Controllability over stressor decreases responses in key threat-related brain areas. **Communications Biology**, 4(1), 1-11
3. Meyer CT*, **Padmala S*** and Pessoa L (2019), Dynamic threat processing. **Journal of Cognitive Neuroscience**, 31(4), 522-542.
4. **Padmala S**, Sirbu M and Pessoa L (2017), Potential reward reduces the adverse impact of negative distractor stimuli. **Social Cognitive and Affective Neuroscience**, 12(9), 1402-1413
5. Lim SL, **Padmala S** and Pessoa L (2009), Segregating the significant from the mundane on a moment-to-moment basis via direct and indirect amygdala projections. **PNAS** (USA), 106(39), 16841-16846.

I received a Bachelor's degree in Biomedical Engineering from Osmania University, Hyderabad followed by a Master's degree in Biomedical Engineering from the University of Memphis, USA. Then, I worked for more than a decade in Dr. Luiz Pessoa's laboratory of Cognition and Emotion investigating brain mechanisms of emotional processing and interactions between emotion, motivation, and cognition in healthy adult humans using behavioural and functional MRI (fMRI) techniques. As a National Science Foundation (NSF) Graduate Research Fellow, I investigated interactions between appetitive and aversive processing during perception and attention and received my PhD from the interdisciplinary Neuroscience and Cognitive Science (NACS) program at University of Maryland, USA. After my PhD, I continued working at the University of Maryland as an Assistant Research Scientist and joined Centre for Neuroscience as an Assistant Professor in March 2019.

INTERACTIONS BETWEEN EMOTION, MOTIVATION, AND COGNITION



Throughout our lives, emotional and motivational factors influence our thoughts and actions. Hence, we need to understand how emotion, motivation, and cognition interact in the human brain.

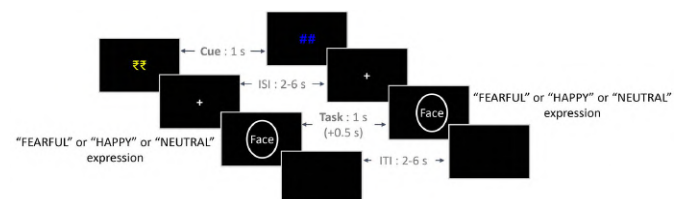
Knowledge of brain mechanisms underlying these interactions is not only relevant to our healthy lives but also has potential clinical relevance. In mental disorders such as addiction, anxiety, and depression, cognitive impairments due to compromised emotional and/or motivational processing are extensively reported. Therefore, a deeper understanding of brain mechanisms underlying interactions between emotion, motivation and cognition will help us better understand the anomalies in neurobiological mechanisms associated with these disorders and potentially improve treatment strategies. Despite this, our understanding of how these factors interact in the brain is rudimentary. This is because the majority of the past work focused on investigating emotional, motivational and cognitive processing in an independent fashion.

Our work attempts to fill some of these critical gaps in our knowledge base by investigating interactions between emotion, motivation, and cognition in the healthy adult human brain. We primarily employ behavioral and functional MRI (fMRI) methods combined with psycho-physiological

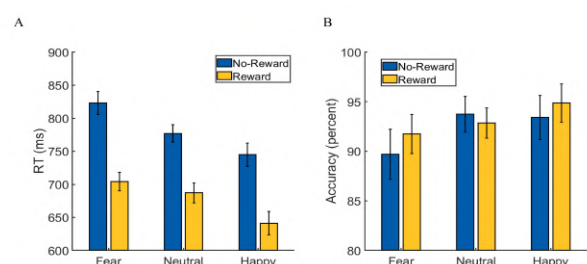
measurements (e.g., skin conductance responses) in our research.

Additionally, we focus on understanding how individual differences in self-reported anxiety and reward-sensitivity influence these interactions.

Our most recent work is focused on investigating interactions between reward motivation and categorization of emotional facial expressions.



During reward and no-reward conditions signaled by an advanced cue, participants were asked to categorize the emotional expression of a facial stimulus. Reward prospect facilitated the categorization of happy and fearful expressions relative to the neutral ones (Chakravarthula L & Padmala S, 2022).





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Selected Publications:

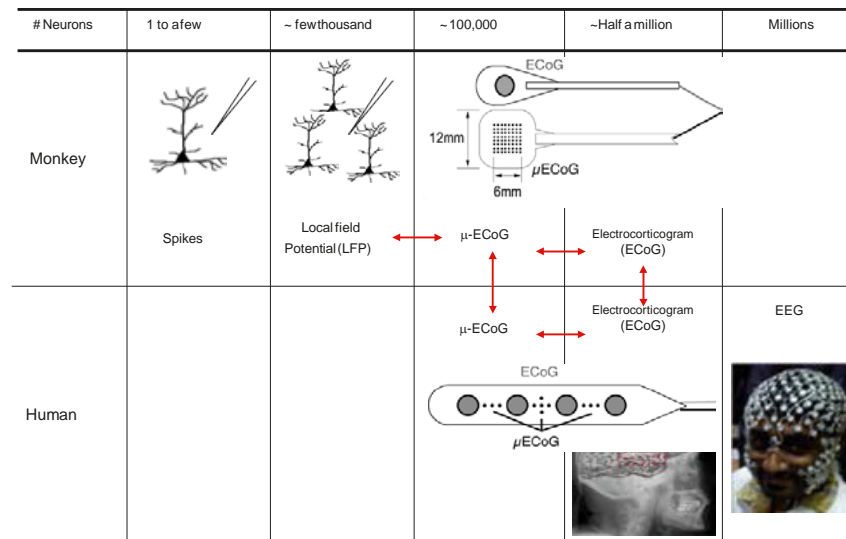
1. Murty DVPS, Manikandan K, Kumar WS, Ramesh RG, Purokayastha S, Nagendra B, Abhishek ML, Balakrishnan A, Javali M, Rao NP and **Ray St** (2021). Stimulus-induced Gamma rhythms are weaker in human elderly with Mild Cognitive Impairment and Alzheimer's Disease. *eLife*. 10:e61666 DOI: 10.7554/eLife.61666.
2. Prakash SS, Das A, Kanth ST, Mayo JP, **Ray St** (2021) Decoding of attentional state using high-frequency local field potential is as accurate as using spikes. *Cerebral Cortex*. Vol 31(9): 4314-4328.
3. Murty DVPS, Manikandan K, Kumar WS, Ramesh RG, Purokayastha S, Javali M, Rao NP, **Ray St** (2020) Gamma oscillations weaken with age in healthy elderly in human EEG. *Neuroimage*. Vol 215, Article 116826.
4. Dubay A and **Ray St**, (2019), Cortical electrocorticogram (ECoG) is a local signal. *Journal of Neuroscience*. 39(22):4299-4311.
5. Shirhatti, V., & Ray, S. (2018). Long-wavelength (reddish) hues induce unusually large gamma oscillations in the primate primary visual cortex. *Proceedings of the National Academy of Sciences*, 115(17), 4489-4494.)

I received a B. Tech in Electrical Engineering from IIT Kanpur and a PhD in Biomedical Engineering from the Johns Hopkins School of Medicine. For the doctoral degree, I worked with Drs (Late) Kenneth Johnson, (Late) Steven Hsiao, Ernst Niebur and Nathan Crone and studied the neural mechanisms of high-gamma activity in both human and non-human primates. My post-doctoral training was with Dr. John Maunsell in the Department of Neurobiology at Harvard Medical School, where I studied the neural mechanisms of gamma oscillations in non-human primates



NEURAL MECHANISMS OF SELECTIVE ATTENTION

STUDY OF ATTENTION AT MULTIPLE SCALES OF RECORDING



Our senses convey rich and detailed information about the external world, but we can selectively attend to some details while ignoring others. This capacity for selective attention is critical for survival and essential for complex tasks. Problems with controlling and directing attention, such as attention deficit hyperactivity disorder (ADHD), can impair the ability of individuals to function normally. Attentional mechanisms have been studied at several different recording scales – from single neurons in monkeys to diffuse population measures such as electro or magneto encephalography (EEG/MEG) in humans. However, the relationship between signals recorded from such different scales is poorly understood.

The long-term goal of this research is to elucidate the mechanisms of attention by linking the neural recordings obtained from these vastly different scales. In particular, we focus on particular oscillations in the brain, such as the alpha (~10 Hz) or gamma rhythms (30-80 Hz), which are

modulated by the attentional load, and can readily be recorded from both micro and macroelectrodes. Several types of recording scales are investigated.

In humans, we record using EEG electrodes and also collaborate with neurosurgeons who work with epileptic patients and record from electrodes placed directly on the brain (called electrocorticogram or ECoG). In non-human primates (NHPs) trained to perform an attention task, we record from microelectrodes as well as ECoG and EEG electrodes. Apart from studying attention, this approach allows us to understand the neural basis of EEG, which has direct applications in the diagnosis of brain disorders and in brain machine interfaces. We also develop signal-processing tools to study brain signals, which are highly non-stationary and often require special analysis techniques.



MINI JOSE DEEPAK

Ramalingaswami and IYBA Faculty Fellow

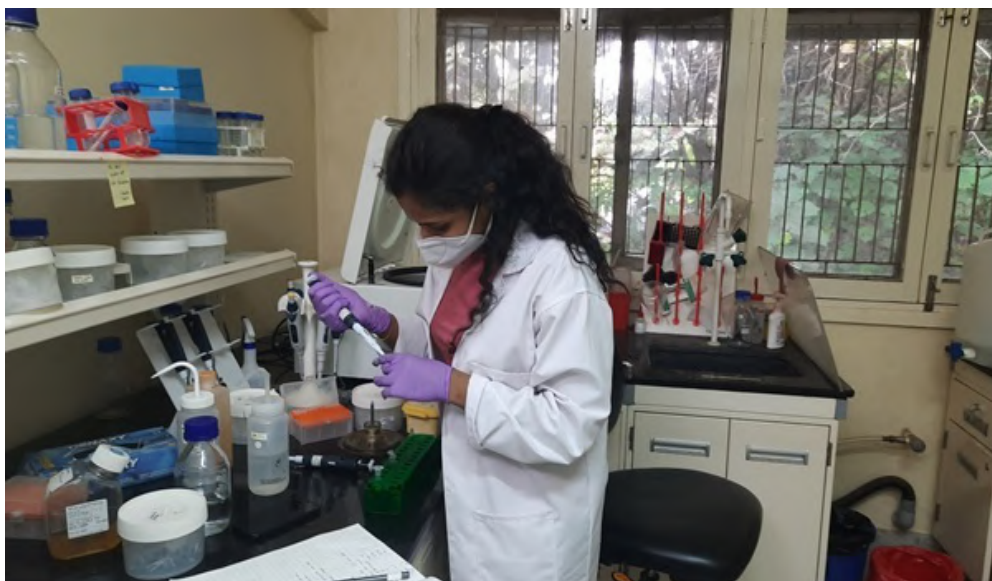
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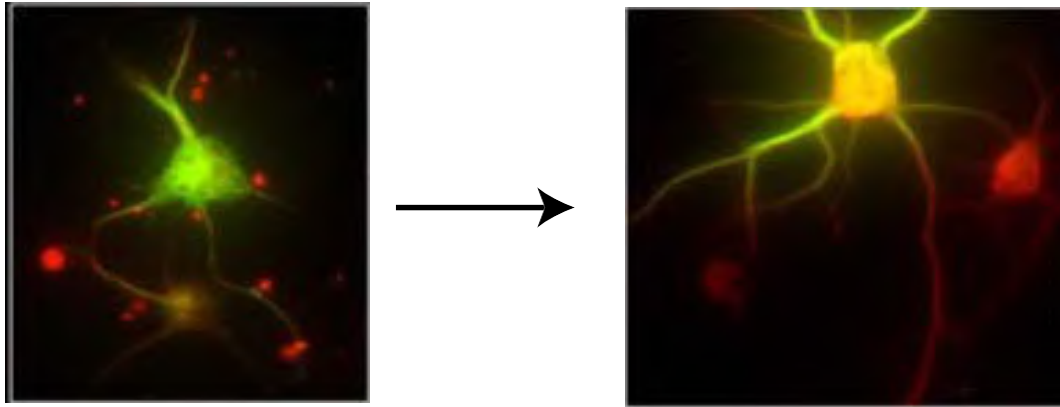
Selected Publications:

1. Mangalwedhekar R., Singh N., Thakur C.S., Seelamantula C.S., **Jose M.**, Nair D. (2023). Achieving nanoscale precision using Neuromorphic localization microscopy, **Nature Nanotechnology**, 18(4), 380-389.
2. Rajeev P., Kechkar A., Butler C., Ramanan N., Sibarita J.B., **Jose M.**, Nair D. (2022). Nanoscale Regulation of Ca²⁺ dependent phase transitions and real time dynamics of SAP97/hDLG, **Nature Communication**, 13(1), 4236.
3. **Jose M.***, Sivanand A., Channakeshava C (2021). Cholesterol is a critical determinant for hippocampal neuronal polarity. **Frontiers in Molecular Neuroscience**, 14(746211).
4. Kedia S., Mandal K., Netrakanti P.R., **Jose M.**, Sisodia S.S., Nair D. (2021). Nanoscale organization of Nicastrin, the Substrate Receptor of the γ -Secretase Complex, as Independent Molecular Domains. **Molecular Brain**, 14(1), 158.
5. Tanwar, M., Kateriya, S., Nair, D., & **Jose, M***. (2021). Optogenetic modulation of real-time nanoscale dynamics of HCN channels using photoactivated adenylyl cyclases. **RSC Chemical Biology**, 2(3), 863-875.

I obtained a Masters in Physics from Indian Institute of Technology Chennai. My PhD training was with Prof. Eckart Gundelfinger (Dept. of Neurochemistry & Molecular Biology) and Dr. Werner Zuschratter (Special Lab for Electron and Laserscanning Microscopy) at Leibniz institute of Neurobiology, Magdeburg, Germany. I did my postdoctoral training in the Nano-photonics group of Prof. Brahim Lounis and Dr. Laurent Cognet at the University of Bordeaux, France, and later in the Dynamics of Cell growth and Cell Division group of Dr. Derek McCusker at the European Institute Chemistry and Biology, University of Bordeaux, France. I joined CNS as a Ramalingaswami fellow in September 2015, where I study molecular mechanisms underlying neuronal polarity establishment.



NEURONAL POLARITY AND DEVELOPMENT



How do neurons differentiate?

Differentiating mouse hippocampal neurons (Left-24 hrs and Right-4 days in vitro), colabelled with a combination of antibodies against beta tubulin III (red) and Map2 (green). The neurons exhibit a symmetric to asymmetric growth along development.

My group focuses on addressing a fundamental, yet important question in neuroscience: How is polarity established during neuronal development or how do the neurons differentiate? Differentiation of neuronal processes into subtypes namely, axons and dendrites, remain to be a highly intriguing but critical mechanism for survival during neuronal development. It plays a key role in establishing specialized neuronal processes to form cell-cell contacts or synapses, crucial for signal processing in the brain.

Lipid metabolism has been shown to hold the key to major fundamental processes including neuronal differentiation. In my lab, we try to unravel the molecular mechanisms underlying neuronal polarity using a multidisciplinary approach combining molecular biology, genetic engineering, pharmacology, Optogenetics and multiple advanced microscopy paradigms including FRET, FLIM and single molecule based superresolution microscopy. A combination of state-of-the-art interdisciplinary paradigms is adopted to understand the collective spatiotemporal events resulting in complex neuronal structure and function using rodent hippocampal neurons as a model system.

Recent evidence from our lab is one of the first which signifies the stark effect of a transient alteration in membrane resulting in altered membrane viscosity and Brownian diffusion, thereby resulting in long term deficits in neurite outgrowth and polarity establishment (Jose et al, Front. Mol. Neur. 2021). Our study also emphasizes the importance of addressing this condition at an early developmental phase, when the deficits can be rescued by precise control of the membrane lipid balance. Thus, this study identified membrane cholesterol as a critical factor for axo-dendritic specification and a key molecule for determining neuronal architecture.

Combining optogenetics with super resolution microscopy, we showed how photoactivation controls the stochastic organization and lateral random movement of single molecules of HCN channels, crucial in regulating the membrane potential, in live cells by altering the intracellular cAMP levels (Tanwar et al, RSC Chem. Bio., 2021). This study shows one of the first paradigms combining these state-of-the-art techniques to alter the biochemical maps of ion channels in live cells. Our current studies focus on understanding the correlation of these pathways and their implication in multiple developmental and neurodegenerative disorders.



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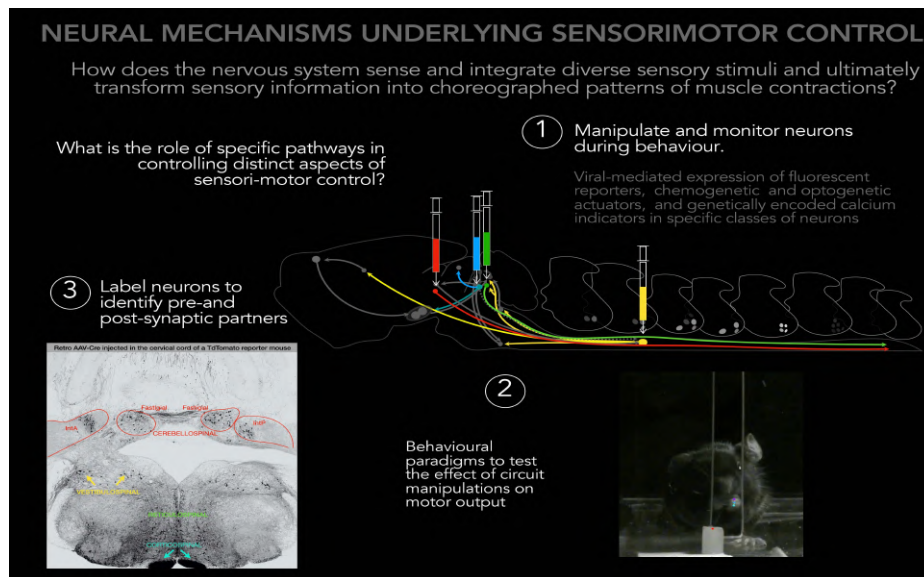
Selected Publications:

1. Chaterji S, Barik A, **Sathyamurthy A**. Intraspinal injection of adeno-associated viruses into the adult mouse spinal cord. **Star Protocols**, Sept 2021.
2. **Sathyamurthy A**, Barik A, Dobrott CI, Matson KJE, Stoica S, Pursley R, Chesler A, Levine AJ, (2020), Direct Cerebellospinal Pathways Regulate Motor Performance and Motor Learning, **Cell Reports**, 31(6), 107595.
3. Dobrott C, **Sathyamurthy A**, Levine AJ, (2019), Decoding cell type diversity within the spinal cord, **Current Opinion in Physiology**, 8, 6.
4. **Sathyamurthy A***, Johnson KR*, Matson KJE, Dobrott CI, Li L, Ryba AR, Bergmann TB, Kelly MC, Kelley MW, Levine AJ, (2018), Massively Parallel Single Nucleus Transcriptional Profiling Defines Spinal Cord Neurons and Their Activity during Behavior, **Cell Rep**, 22(8), 2216-2225.
5. Barik A, Li L, **Sathyamurthy A**, Xiong WC, Mei L, (2016), Schwann Cells in Neuromuscular Junction Formation and Maintenance, **Journal of Neuroscience**, 36(38), 9770-81.

I received my B.Tech in Biotechnology from SRM University, India (2008), and Ph.D in Neuroscience (2014) from the Medical College of Georgia, USA. During my Ph.D work in Dr Lin Mei's lab, I focused on the cellular and molecular mechanisms underlying cerebellar development. I then joined Dr Ariel Levine's laboratory at the National Institutes of Health, USA, where I focused on understanding the molecular basis for functional heterogeneity in the spinal cord and how spinal neurons are integrated into CNS-wide circuits for motor control. This work led to the identification of a previously-unappreciated, circumscribed population of neurons in the cerebellum - cerebellospinal neurons - which provides direct inputs to the spinal cord and contribute to distinct aspects of motor control.

I joined the Center for Neuroscience, Indian Institute of Science, as a Ramalingaswami Faculty Fellow in October 2020, and my lab is interested in understanding how the integrative action of the brain and the spinal cord enables movement and how dysfunction of the underlying neural circuitry leads to sensori-motor disorders.

NEURAL MECHANISMS UNDERLYING SENSORIMOTOR CONTROL



Our sensory systems are our windows to the world around us, and we constantly rely on what we sense and perceive to select and execute actions that help us survive and thrive.

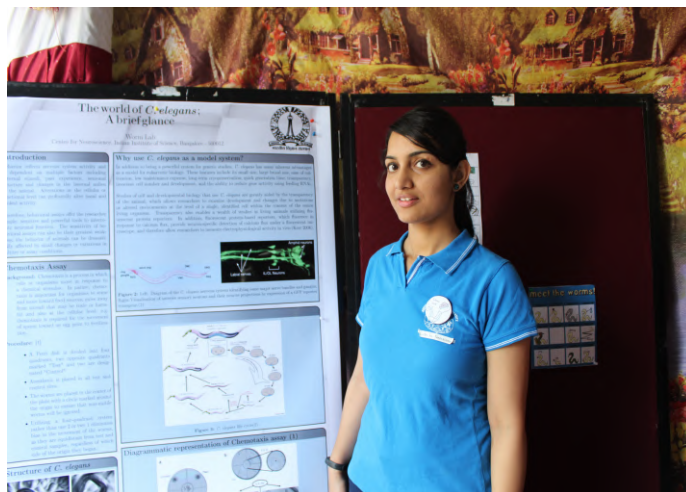
For example, let's examine the simple process of crossing a busy road. In order to reach the goal of safely crossing to the other side before the road becomes busy again or to select a direction that would help us avoid bumping into vehicles, we engage the senses of vision and audition to assess oncoming traffic, the sense of proprioception to know where the different parts of our body are located with respect to the traffic and each other, and the sense of touch and pain to know if we have encountered an obstacle in the path – maybe a loose tyre. And lest someone steps on a piece of glass, they would have to suppress this pain response in the presence of oncoming traffic, and modify their gait so as to safely reach the other side.

Importantly, information from these complementary sensory streams need to be integrated in a timely manner and acted upon to bring about adaptive behaviours. How does the brain accomplish this remarkable feat with such ease? Which specific brain regions are involved in this process?

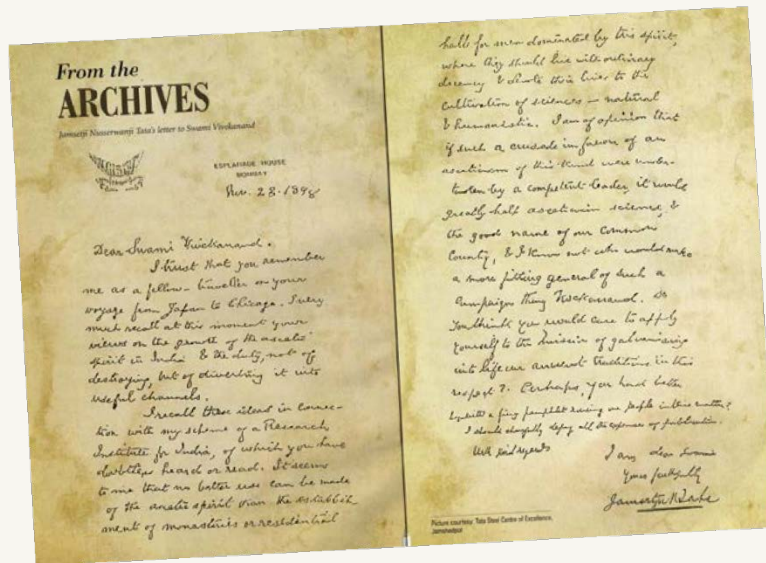
To address this, we use genetic techniques in mice to manipulate and monitor neural circuits nucleated in the cerebellum and the spinal cord with the goal of unravelling (a) the neural mechanisms underlying the sensation, perception, and integration of diverse somatosensory stimuli such as proprioception, touch, pain, b) where and how sensorimotor circuits interface with those that regulate our internal states such as a stress or fear, and c) how activity in these circuits enable precise execution of relevant behaviours.

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| OPEN DAYS @ CNS



PAGES FROM HISTORY



HISTORIC LETTER OF J.N. TATA TO SWAMI VIVEKANANDA ON 23 NOVEMBER 1898

Dear Swami Vivekananda,

I trust, you remember me as a fellow traveler on your voyage from Japan to Chicago. I very much recall at this moment your view on the growth of the ascetic spirit in India and the duty, not of destroying, but of diverting it into useful channels. I recall these ideas in connection with my scheme of Research Institute of Science for India, of which you have doubtless heard or read. It seems to me that no better use can be made of the ascetic spirit than the establishment of monasteries or residential halls for men dominated by this spirit, where they should live with ordinary decency and devote their lives to the cultivation of science, natural and humanistic. I am of the opinion that, if such a crusade in favor of an asceticism of this kind were undertaken by a competent leader, it would greatly help asceticism, science, and the good name of our common country; and I know not who would make a more fitting general of such a campaign than Vivekananda. Do you think you would care to apply yourself to the mission of galvanizing into life our ancient traditions in this respect? Perhaps, you had better begin with a fiery pamphlet rousing our people in this matter. I should cheerfully defray all the expenses of publication.

With kind regards,
I am dear Swami
Yours faithfully,
Jamsetji Tata



Jamsetji Nusserwanji Tata
(1839 - 1904)

H.H. Sri Krishnaraja Wodeyar IV
(1884 -1940)

The Indian Institute of Science (IISc) was founded in 1909 as a result of the joint efforts of Jamsetji Nusserwanji Tata, the Government of India, and the Maharaja of Mysore. In 1886, Jamsetji Tata conceived of a university of science that will work for the benefit of India, and in 1898 created an endowment for establishing such an institution. The Government of India then took up the effort, and, in consultation with scientists in England and in India, decided to locate the Institute in Bangalore, where the Maharaja of Mysore, Shri Krishnaraja Wodeyar IV, donated 372 acres of land. The Institute was formally vested in 1909, the foundation stone was laid in 1911, and the first batch of students started their studies in the same year.

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