K S Vishalakshi • Mayur Subhash Punde • Anusha V • Kameshwar Rao • Kamalakara Rao • Priyanka S K • Venkata Madhusudhan • Bhuvaneshwari S

Hema R • Sampath C • Maithly Ramesh • Valmiki Sreenivasulu • Priya • Thanuja S • Indu Bala • Ravi Shankar • S Ashok Rao • Rekha V • Manikanta R • D Shrivastava • N Ram Prasad

R N Nagaraj • Vanitha M • G H Mohan • Nagaraju V • Babu P • Manjunath A • Lakshman Kumar N A • Muthana Shekhara • Gopi P

NATIONAL CENTRE FOR BIOLOGICAL SCIENCES

Manjunath S • Kumar R • Shashidhar V S • Amarnath • Nagaraju M C • Mahesh M V • Srikanth R • Himakar T • Anil Kumar N • Akash R • Dilip S • Padmavathi G V • Nikhil N • Aravind N

Kathik • Rohina • Manjunath S R • Poornachandra • Savitha • Anil Kumar M • H Krishnamurthy • H M Basavaraja • T Natarajan • Matturthi Ananda Prakash • Chandrashekara K S

Ponappa • Manjunath • Amarae Gowda • Balraju • Halesh Manjunath Reddy • Bhaskar Reddy • Paramanna • Ramesh • Lingaraju • Pradeep H S • Anand L • Somappa • Naveen

Ambili Dinesh • Pratap Y • Girish N S • Ashwini B • Parvathi Thangam • Srilatha V R • Kalyani B L • Theja Prakash • Suma • Sukanya • Vedavathi • Yashodha T N • Roopa

Ramya J • Susheealmma • Indira K • Yellamma • Parvathamma R • Lakshmi Raju • Manjula N • Suresh K A • Sidhartha S Swain • Vipin V • Mohandas D • Praveena R Gadagoli

Abhilash Reddy Anand Kumar N • Gangadhar Pujer • Harish N Kemparaju • Lawrence • Mallikarjun • Manikandan • Manjunath Hallikeri • Nagaraj M

Parameshwar • Prasad D Ramesh C • Shashikumar • Shivaprasad • Subramanya • Subrat Kumar Samal • Sukurusab • Suresh T D • Tajoddin • Venugopal • Swathi N • Priti Bhardwaj

Deepti Trivedi Vyas • Anand • Mounesh • Manjunath K R • Shivakumar • Venkatesh Srinidhi V • Hamsa S • Soumya M • Sowmya R • Amrita Mitra • Maruthi • Narashimaraju

Parvathamma • Chandra Shekhar G • Pradeep Kumar M • Jilesh Joseph • Srinivasa J • Kusha D H • Yuvarajan • Maha Rudra Nayak • A Anandaraj • Seetharam Naik • C Prashanth

Murthy • Rajesh K • Sujatha N • R Balasubramani • Umesh Gowda • Kumara M • Srinath H K • Chandra Sheel • Sukra Shekar M S • Bhaskar Poojari • Govindaraju K • Mahesh B

ANNUAL REPORT 2020–2021

Nataraj • Madeshappa D P • Rajanna • Prasanna Kumar • Sathish G • Devi Charan Niranjan Das • Lakshmaiah • Rajkumar Yellappa Desai

Naresha T N • Viswanathan • Mallappa K • K J Mahadeva • Nithyananda K • Siddaramu • Gajadhar Naik • Lokesh H D • Chamaraju • Veerendra • Hiralal Roy • Ajay Kumar

Nagabushan • Naresh P • Sundara • Shivaraj M • Anil • Ashok Kumar • Govardhan • Eshwar T • Manjegowda M N • Shekar M C • Abhishek • Prathap A S • Manjegowda R B

Ravindra Reddy • Raghavendra K P • Suresh K • Yanjarappa • M D Eazaz • Gurumurthy • Rangegowda • Arun • Sagar Nagavi • Manjunath • Ananda H B • Mallikarjuna D • Basavaraj

Hosamani • Mahesh J • Ravinaika Y • M N Muniraju (Late) • Gangadhar N • Yankamma • Prabha • Ramesh Basu • Pradeep O • Rangaswamaiah • Sushilamma • Bylappa • Kamalamma

Arogyaselvi • Kasthuri • Bhagyamma H • Mohan • Gowramma • Malathi Devi • Tippanna • Shashikala • S Ramesh Ranganatha C

Thank you

P Muniraju • Anthony Nirmala Kumari • Manjula • Muniswamy M • Kavitha • P Kuttimma • Sanjivaiah • Leelavathi • Gangadharappa • Nagaraj • Bhagyamma • Shanthala M

Chandrashekar • Nagesh D K • Premavathi • Rudramma • Radhika • Shivashankar • J Narayanaswamy • Srinatha • Manjunath • K Nagaraju • Ramesh R

To,
The people behind the scenes,
Thank you

NATIONAL CENTRE FOR BIOLOGICAL SCIENCES • ANNUAL REPORT 2020–2021

ncbs
National Centre for Biological Sciences
Tata Institute of Fundamental Research

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A Year of Recovery and Transitions

Satyajit Mayor
Director, NCBS

As this new century turns 21, we are hopeful of emerging from a really grave pandemic. Meanwhile, a number of important transitions have marked this year for NCBS.

Upinder Bhalla, our solitary Dean for eight years, decided to hang up his administrative gloves and return to the bench. As a parting gift, Upi (along with the NCBS steering group and members of the management board) worked to navigate a new executive structure at NCBS. We now have three Deans, one each for the faculty (Sanjay Sane), research and infrastructure (Raghu Padinjat), and academics (Raj Ladher), and a Head (Uma Ramakrishnan) of a new vertical covering outreach, communications, and research development. I would like to heartily welcome on board our new team, in place since July. I also welcome our new Head of Administration and Finance, Mr. Ravishankar, who joined us in April. Personally, I cannot thank Upi enough for his years of dedicated service to NCBS, and for painstakingly helping to put in place systems and processes that we all take for granted today. Having done this whilst still being an active scientist has been heroic and I salute him for his steadfastness and dedication. Thank you, Upi, from all of us at NCBS and the Bangalore Life Science Cluster!

We are sad to see Radhika Venkatesan depart. Radhika is moving to IISER Kolkata, leaving us much poorer in many departments, especially Chemical Ecology. I wish her all success in her future, and am very glad that she is able to move to newer pastures of her choice. We have had a number of new faculty join us over the past year. Swadhin Jana, Abhishek Bhattarcharya, Archisman Raju, and Tapomoy Bhattacharjee have all landed in the time of the pandemic, and will provide their accounts of setting up shop in this report.

I would like extend a warm welcome to M D Madhusudan, the first Obaid Siddiqi Chair in the History and Culture of Science at the Archives at NCBS, made possible due to generous CSR support from TNQ Technologies Pvt Ltd (TNQ). I am particularly grateful to Mariam Ram (Chairperson, TNQ) for her tremendous support of science and also for believing in keeping the vision of Obaid alive and vital in these trying times.

Smita Jain, who so successfully steered IndiaBioscience, one of NCBS's flagship programmes that serves the life science community nationally, has moved on to Cactus Communications. In her place, Shantala Haridas has taken over to helm this important effort. I thank Smita for making

IndiaBioscience the fabulous life science community resource that it has become today, and wish Shantala all success in the next phase of this programme.

This year has seen the retirement of the indomitable Shaju Varghese, the head of all things related to our well-being, food, shelter, and security. Shaju started at NCBS when the institute was barely one year old. He is replaced by three administrators. Prashant Murthy (NCBS) steps up to oversee canteen services, whilst Amit Kumar Sarkar (inStem), hospitality, and Anup Kumar (inStem), security, emphasise the importance of running a joint campus, especially in such times of transition. We wish Shaju all the best for his future and hope his energy and ideas of running our campus will not only continue to help those who follow him here but also serve as an example for other campuses who would do well with a force of nature called Shaju. After 30 years of service at DAE institutes, including 17 at NCBS, the effervescent Ashok Rao, our establishment officer, has moved on to become the Registrar of the Institute for Social and Economic Change in Bangalore, and we wish him all success.

We have sadly lost some of our colleagues over the year. Vinod Kumar from the Animal House succumbed to COVID-19, and fate snatched away two stalwarts, Natraj from our canteen and Muniraju from housekeeping. May their souls rest in peace. We deeply miss their presence on our campus.

While our scientific output and research has been extremely prolific this year, weathering the pandemic, a set of retractions of two research papers from NCBS faculty has been a sobering aspect of this year's academic activities. With the engagement of the TIFR Academic Ethics Committee, we have used these events to strengthen our research integrity process, putting in better practices for data integrity and also establishing an office of research integrity for the campus. I hope to report on its functioning next year. Extensive consultations with our academic community have also allowed Raj (Dean Academics) and myself to listen to the issues our community is facing, and we would like to assure our colleagues that we are taking heed of many of the issues raised and will strive to address them. As a start, we welcome the establishment of an Early Career Researcher Council for the campus and hail the founding members, led by an enthusiastic team of students and post-doctoral fellows, all invested in making the campus better.

In the past year, NCBS has also spearheaded many efforts that reflect our capacity to respond to the challenges of the moment. I briefly allude to two here, and others are mentioned in this report in the Flagship/ Highlights sections. Along with C-CAMP, funded via a Rockefeller Foundation-funded initiative called InDx, we have helped conduct around 1 million COVID-19 tests a day at a price 50 times lower than it was at the start of the pandemic. This platform, consisting of medium- and small- scale industries with academic institutes such as NCBS and inStem functioning as Centres of Excellence, will serve us well even for future grand challenges. We also serve as the Bangalore node of a multi-centric, retrospective, and prospective deep dive into clinical and environmental

COVID-19 genomic surveillance across multiple cities, again funded by the Rockefeller Foundation. These efforts reflect how NCBS has been able to rapidly operationalise programs which would have otherwise taken many years to set up, reflecting the societal value of long-term investments made in science, infrastructure, and the Life Sciences Cluster ecosystem we have established here.

I congratulate all our national and international award winners (listed on page 7) who make us all proud; Sumantra Chatterjee has been doubly recognised for his outstanding contributions towards understanding the severe mental health consequences of Fragile X.

The campus has led from the front in ensuring a safe working space. At the time of this writing, almost 85% of our campus is doubly vaccinated and by the end of the year, we will have achieved close to 100% vaccination. We have developed a saliva-based sampling protocol in-house that ensures that all our campus members are tested every week. These steps allow us to be fully functional during the pandemic. At the end of the day (or year) we must recognise that everything we do depends on having the right people with the right attitude at the right place and right time. The people who have worked behind the scenes ensure that we can all work to the best of our abilities at NCBS and at the wider campus. They are our unsung heroes, and this issue is dedicated to them.

NCBS Awards List 2020–2021

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

NATIONAL

Kushi Anand

(Post-doctoral Fellow with Varadharajan Sundaramurthy)
DBT-WT India Alliance – Early Career Fellowship
DBT-WT India Alliance • January 2021

Abhishek Bhattacharya

DBT-WT India Alliance – Intermediate Fellowship
DBT-WT India Alliance • January 2021

Soumyashree Das

DBT-WT India Alliance – Intermediate Fellowship
DBT-WT India Alliance • January 2021

Uma Ramakrishnan

Homi Bhabha Award in Science Education
Tata Institute of Fundamental Research
January 2021

Anjana Badrinarayanan

INSA Medal for Young Scientists
Indian National Science Academy • October 2021

INTERNATIONAL

Atul Joshi (PhD Alumnus)

John L Harper Early Career Researcher Award
British Ecological Society • April 2021

Sumantra Chatterji

Fellow of IUPS
International Union of Physiological Sciences
July 2021

FRAXA Global Champion Award
FRAXA Research Foundation • July 2021

Mahesh Sankaran

Infosys Prize in Biological Sciences
Infosys • December 2021

Academic Office

Raj Ladher

Dean of Academics

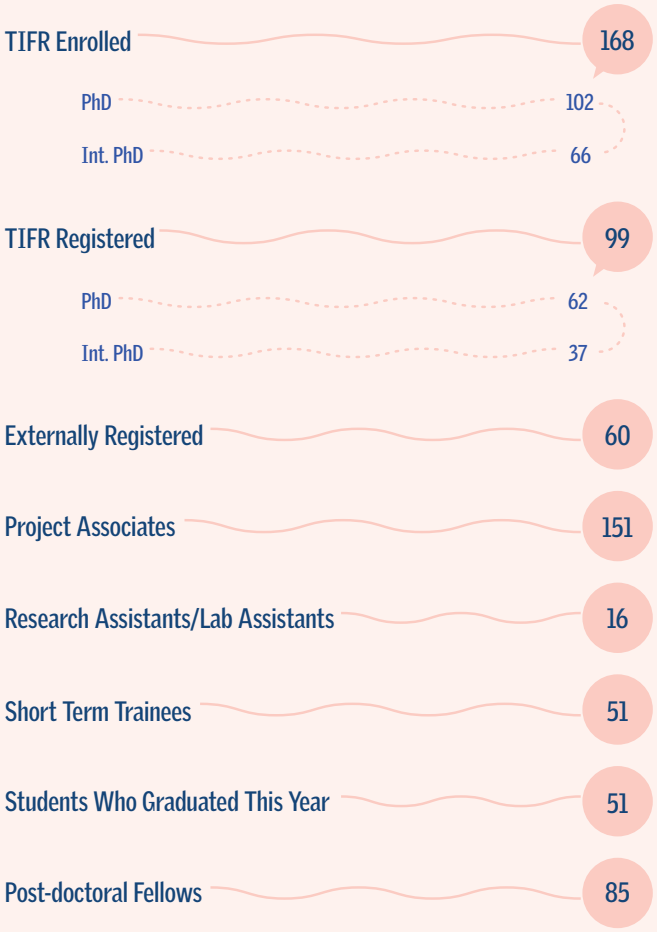
The NCBS Academic Programme is integral to our identity, and nothing is able to articulate our ambitions as clearly as the scientists we train.

It is daunting to be entrusted with something that really is at the heart of the institute. Following on from my predecessor's note in the last annual report, I would like to convey my deepest appreciation and gratitude to Mukund Thattai for handing over a smooth running Academic Programme. The structures and perspectives for growth that Mukund put in place have made that part of being the Head of (and now Dean of) Academics not so onerous. It is made that much easier by the Academic Office itself, with Mrs. Valsala Neyyan, Mrs. Anusha Balakrishna and of course, the ever-green Mrs. K. Vishalakshi. They have been there to welcome every new researcher. This year the office has grown a little with the addition of Mr. Vinod Kulkarni and Dr. Mayur Punde. This reflects not only the growth in the campus but also the complexities in navigating the ever-changing requirements of graduate programmes, granting agencies and reporting structures. The new management structure of NCBS meant that I was able to nominate two wonderful members of faculty to become Associate Deans of Academics: Deepa Agashe and Vatsala Thirumalai. They join myself, and Dasaradhi Palakodeti, inStem's Academic Coordinator, in steering the Academic Programme and implementing some of the changes that the coming years may bring. This year also saw the realisation of one of Mukund's efforts: the Campus Wellness Programme. Neha Panwar, our Campus Wellness Officer, is looking after the provision of mental and emotional health support for everyone on campus.

The challenges that 2020 threw up seemed like a practice run for 2021; the second wave was horrendous. We all know at least one person who sadly succumbed to COVID-19, and with multiple lock-downs, go-slows, severe pandemic measures, and heightened anxiety, academic life was brought to a stand-still and then went online. The normal vibrant interactions that marked campus life, the discussions over a cup of tea, chance meetings in the corridor, and brainstorming by the cryostat were replaced by pale imitations. However, from adversity came a sense of unity, a shared sense of purpose, that the only way that we will be able to function is not individually but collectively, that we all share the responsibility to keep ourselves and each other healthy.

With volunteers from every section of the institute providing insights into the nature of the disease, providing hands for the testing facility, bringing food to those isolating, interviewing and messaging contacts of someone who might be infected, and simply making sure that they were available if someone needed to talk, the sense of community has never been stronger.

It has been a long and exhausting year, and we do not know what course the pandemic will take. But it is worth highlighting the generosity of spirit and commitment of time that members of the campus community happily gave in caring for one another. In going that extra mile to make sure their colleagues were healthy, and remained healthy, they exemplified what this campus is, and it really is an honour to be able to work with these colleagues.



The number of students at NCBS for 2020–2021

Even in a public health crisis, science continues. 51 students graduated this year, either with a masters from the MSc Wildlife programme or with a doctorate from the PhD programme. We were able to welcome a new batch of students this year. 47 students joined (35 through the GS exam and 12 through competitive fellowships), bringing our total number of students to 228. Together with 167 project and research associates, 50 short-term trainees and of course, our 85 post-doctoral fellows, they constitute the enthusiastic, dynamic, and committed researchers that are the engines of discovery at NCBS. By leveraging the breadth and depth of research, it should be possible to provide each one with a unique set of skills and a multi-disciplinary perspective that will make our already great researchers, excellent.

NOTE BY DEAN, RESEARCH

Building Research Infrastructure for the Future

Raghu Padinjat
Dean of Research

From small beginnings in 1992 with a handful of faculty and students, NCBS has grown into an enterprise with 37 faculty and a strength of almost 1000.

Nimbleness in organisation and operations is both essential and possible for growth in the formative years of any institution. However, 29 years later, with a strength of 1000, maintaining administrative rigor along with the flexibility required to facilitate scientific discovery at the highest level is a challenging task. This is mentored by the Dean and over the last eight years, Upi Bhalla, as Dean of NCBS, carried out this balancing act with equanimity, in the face of many challenges. As I take over this mantle in my role as Dean of Research, I would like to place on record my appreciation for his efforts in administering NCBS with a view to creating the best possible infrastructure for science to flourish.

At the time of the last annual report, NCBS, along with the rest of the world, had been stunned by the emerging COVID-19 pandemic. During the first year of the pandemic, as the world struggled to understand and manage COVID-19 as a medical problem, we at NCBS grappled with keeping the institute operational while also participating in government efforts to support the application of science infrastructure and skills to the national COVID-19 response. Though we managed to do this effectively, the events that unfolded came at a significant cost in terms of research output and impact on the careers of scientists at every level-students, post-doctoral fellows, and faculty.

The second year of the pandemic has been marked by the devastating second wave in India but also lit up by the hope and expectation of a return to normalcy generated by the availability of COVID-19 vaccination. At NCBS, we put in place measures for managing COVID-19 as a medical problem, but with a keen eye for supporting safe return to regular work for our colleagues. The goal of this effort was to limit the damage to scientific output and support the recovery of academic careers for our students, post-doctoral fellows, and faculty. Many measures were undertaken with this goal in mind, but two stand out as highlights. First, my colleagues on campus put in a sustained and systematic effort to maximise COVID-19 vaccination coverage on campus to achieve protection from severe illness in the event of an infection. Second, in parallel, we developed and implemented a strategy for regular, weekly testing of all campus colleagues for asymptomatic SARS-CoV2 infection using saliva samples (detailed elsewhere in this annual report). This approach has instilled a collective sense of confidence that we can detect infections early and prevent the spread of COVID-19 on campus. These measures have allowed

the relaxation of COVID-19 restrictions on campus and the gradual return of normal research activities at NCBS. At the same time, our research facilities and scientific capabilities built up over the years allow us to continue participating in COVID-19 research activities. This would not be possible without the efforts of our dedicated administrative and technical services teams, who worked right through the last year of the pandemic, devising innovative solutions despite substantial difficulties created to their normal working practices due to COVID-19 management protocols.

At NCBS, we carry out fundamental research across a broad spectrum of the life sciences. Prior to the onset of the pandemic in early 2020, it was unimaginable that our research infrastructure and technical skills would contribute to the management of an infectious disease pandemic. At the same time, the research interests of our faculty have led them to participate and invest in research programs of national importance in India, such as the basic science underlying mental illness in humans (ADBS program, covered elsewhere in this report), the safeguarding of India's biodiversity (see proposed National Mission for Biodiversity and Human Well-Being in this report) and infectious disease biology (VISION). I am confident that the research infrastructure we develop as we pursue these programs will ultimately lead to the application of fundamental science to challenges relevant to the needs of society here in India. I look forward to working with my colleagues to developing and future-proofing the research infrastructure at NCBS for the years to come.

Communication and Engagement for the Future

Uma Ramakrishnan
Head, Outreach and Development

As a scientist, nothing gives me more joy than exploring the wonders of the natural world. But I wonder, how are humans affecting the natural world, and how this will change our future? And how does the work we do as scientists at NCBS help us face the future?

The last two years have brought our role as scientists in society into sharp focus. Suddenly, not just science but science communication became critical. Six months ago, I took on a new role at NCBS. I now help with outreach, communication, and development. I believe, now more than ever, that our connection to society as scientists is critically important. We must engage with the public, with institutions, and with philanthropists. Going forward, I think such engagements will define our future, even for small, basic science research institutions like NCBS.

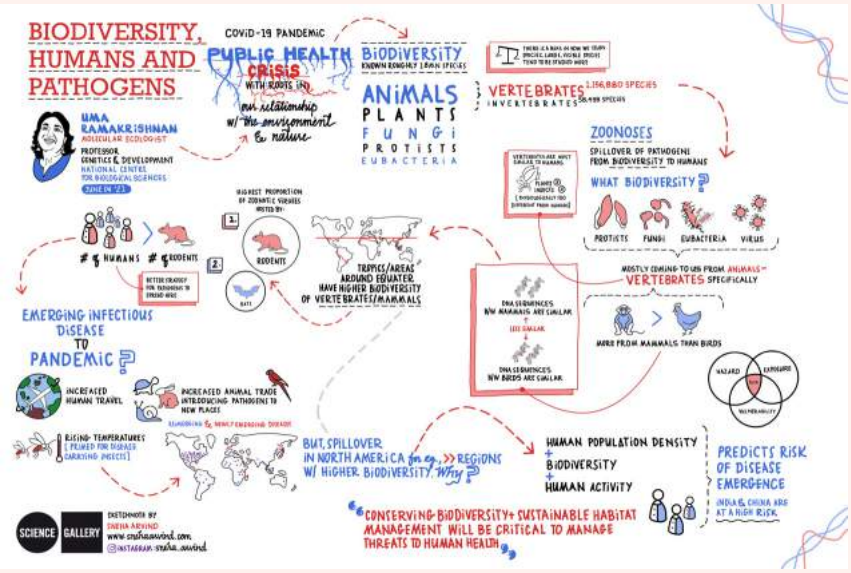
First, a bit of history about NCBS and science communication. Early on, former NCBS director K. VijayRaghavan encouraged the sharing of campus research through commissioned stories. Based at NCBS since 2005, Geoff Hyde, with help from the NCBS IT team, created a dedicated website for news stories from the campus and launched an NCBS YouTube channel. He also initiated a course in science communication for budding communicators. Working together with this group of young enthusiasts, Geoff created the news service for NCBS. By 2010, senior science journalist Anil Ananthaswamy became a frequent visitor to campus. He co-ordinated and taught the first science journalism course in 2011. This course was unique and transformative, and ran nine annual iterations.

When Geoff left NCBS in 2013, Savita Ayyar and Archana Shetty from the Research Development Office broadened the scope of the news service to include InStem, to put both institutions on Twitter, and create a process that allowed for planned news stories. Working ahead of time, Savita Ayyar, Archana Shetty, and Anusha Krishnan ensured that news stories on campus research were ready just as papers were released from embargo by journals, and shared these releases with dedicated social media channels. The team then created a news website, which showcased research news, campus news, the bigger picture, and a spotlight feature.

Since 2017, Mahinn Ali Khan, Head of BLiSc communications, has initiated several innovative and novel science communications activities on campus. She and her team spearheaded several public engagement events like Science Café, Open Day and a science exhibit on campus (with Museums and Field Stations) called Lab Culture. Mahinn Ali Khan took science engagement efforts like Science Café and Out of the Lab to

Falling Walls Engage in 2018, putting NCBS and BLiSc communications efforts on the international map. Together with Pavithra Ashok Kumar, Mahinn grew the social media footprint of our campus. With the rest of the team, Chandrakant Redican worked hard to initiate systematic science education and outreach from the campus. We are grateful to all these people for leading the way.

Meanwhile, as the breadth of research on the NCBS campus grew, so too did the institutional engagement and flagship programmes. As an outwards looking campus, NCBS anchored and collaboratively initiated programs like IndiaBioscience, Bengaluru Sustainability Forum, the Archives, and several others. Venkat Srinivasan and others in his team spearheaded the NCBS Archives, a space for institutional records, but also a curation centre for the contemporary history of biology in India. Our engagements with innovative and local communications venues like Science Gallery Bengaluru will continue. In my role as the Head, Outreach and Development, I hope to engage with outward-facing activities like science communication and outreach, institutional engagements and philanthropy, as well as core NCBS programmes like the Archives.



A scribe renders Uma Ramakrishnan's talk at the Contagion exhibit

So what do we look forward to? I sincerely hope that we will be able to effectively communicate the exciting and diverse science that is happening on our campus. I hope 2022 will allow in-person public engagement, and for us to re-initiate Open Day, Science Café, and campus exhibits. I hope we can re-initiate the science journalism workshops. With help from Sandeep Krishna, I hope NCBS will initiate deep and meaningful science outreach efforts. With help from Mukund Thattai, I hope that we will be able to bring in diverse, wide-reaching, high impact, and novel science communications channels. I hope that our interactions with national and international institutions will grow, because diverse perspectives will ensure that we do not become insular and small-minded. In summary, I hope that we will succeed in blurring the boundaries between us and the outside world, because only such engagement will that ensure we grow as scientists and people.

T105, daughter of Noor, looks through the grass at the Ranthambore Tiger Reserve. This was shot by Kaushal Patel, who is interested in the conservation of endandered species.

People Behind the Scenes

p. 16–27

Hospitality

Administration and Academics

Health and Safety

Technical Services

Campus Volunteers

People Behind the Scenes

The situation with the pandemic looked upbeat in January 2021. Cases were down, and we thought that maybe the worst was over. The campus was functioning more normally, and everyone was happy to be interacting in-person again. But before we knew it, we were hit by the second wave. The numbing tragedy unfolding around us in the country and city engulfed our campus. Yet research and COVID-19 associated activities continued. This was only possible because of the efforts of many people from various departments including hospitality, administration, academics, health and safety, technical services, and research facilities. In this section we pay tribute to them. We would not have made it through this year without them. Thank you!

Hospitality

Srinivasa

HOSPITALITY

Srinivasa joined the NCBS Hospitality team in 2011 as a guesthouse caretaker. He continued his excellent work during the COVID-19 pandemic and nationwide lockdown. Further, he contributed as a frontline staff member to provide food and beverages to those who were quarantined at the Parijata facility, donning PPE and sanitising the rooms, all long before he himself was vaccinated. He is a great person to work with and has multiple strengths. Thank you, Srinivasa!

Pradeep O

HOUSEKEEPING

Pradeep O has been working as a team member in housekeeping since 2011. He is hardworking and sincere, and is well-versed with modern cleaning equipment. This played an important role for campus operations during the pandemic. He was responsible for cleaning areas on campus (including various sectors and restrooms) that were closed off due to the presence of a case, and for getting these areas ready for regular use throughout the pandemic. We thank you, Pradeep!

CANTEEN

The campus canteens stayed open throughout the pandemic lockdowns to provide meals to those who were working on essential services. While every staff member was critical to these operations, Mahesh, in particular, contributed with passion and determination in these difficult conditions. He has been working in the canteen with sincerity and without taking leave, ensuring that the canteen services ran smoothly despite the COVID-19 pandemic. He also contributed tremendously to the COVID-19 vaccination camp efforts when vaccines were in short supply. He coordinated with the city municipality (BBMP) staff and helped to vaccinate most of the contract employees and staff on campus. He also volunteered after work hours and helped many people in the campus neighbourhood, including the Canara Bank Layout public health centre (PHC). We greatly appreciate your contributions, Mahesh!

Mahesh B

Sudhakar Mallick

SECURITY

This pandemic has profoundly affected life around the globe and in our campus. While the footfall on the campus went down since we were only operating essential services, the responsibilities of the security personnel increased manifold, requiring them to be more vigilant and alert and to adhere to the stringent COVID-19 protocols established for campus safety. Sudhakar Mallick has been a role model for the entire security team during this unprecedented situation. He has been continuously performing his responsibilities, especially at the main gates, arguably the place with maximum interactions with individuals on campus, even while most of his peers and colleagues were under the weather and unable to perform their duties. He put in extra hours with dedication and played a vital role in helping his colleagues. He trained his colleagues on how to observe COVID-19 protocols, while always remaining friendly. His spirit of responsibility demonstrated during the pandemic is noteworthy. Sudhakar Mallick, we thank you!

Administration and Academics

Manikanta R

ADMINISTRATION

Manikanta is a Project Assistant in the administration section at NCBS, with experience and training in accounts and administration. His roles include employee recruitment, joining and exit formalities, performance appraisals, personnel management, records management, pre-employment medical checks, HR metrics, and background verifications. Throughout his time here, we have seen Manikanta grasping concepts quickly, understanding policies and processes at NCBS, and handling all assigned tasks professionally and effectively.

During the pandemic, Manikanta's role was vital to the campus staying functional. He was always available on campus and sometimes single-handedly carried out all administrative tasks. His efforts during the vaccination drive ensured that all the staff and students on campus were vaccinated. He is perhaps known to everyone on campus, and known to be approachable, kind and helpful. We greatly appreciate all your efforts, Manikanta!

PURCHASE

The Purchase division is responsible for both routine and specialised procurements for the campus. Equipment and other materials for scientific research on the campus are dealt with by the team. The laboratories and facilities rely on the Procurement division's expertise in the bidding process for goods and services, negotiations, finalisation of contracts, and following due protocols and procedures for shipments. During the pandemic lockdowns, members of the division displayed great initiative in dealing with the unexpected challenges to the process of providing the research community with lab materials, cutting-edge equipment and services required. The team remains committed to ensuring that the best strategies are implemented for the smooth functioning of the procurement process with the existing constraints. This was extremely important, especially while sourcing all the materials mobilised for the campus COVID-19 sequencing and sample testing effort.

The Purchase Team

ACCOUNTS

Soumya M

When the pandemic struck and news of casualties around the world started pouring in, fear and panic gripped everyone. It forced us to think of staying safe indoors with our loved ones rather than taking the risk of going out, including to workplaces, where there was possible exposure to infection. However, the staff in the Finance and Accounts Section rose to the occasion and demonstrated exemplary dedication and incredible commitment. Their courage in handling the work, in the midst of pandemic-induced challenges and high pressure—due to constant changes at the workplace and at home—were exemplary. All the staff, at all levels, deserve our deepest gratitude, admiration and appreciation. Their perseverance and commitment during the pandemic allowed sustained efforts by scientists, faculty and other technical and administrative team members to keep essential services on the campus running without any interruptions.

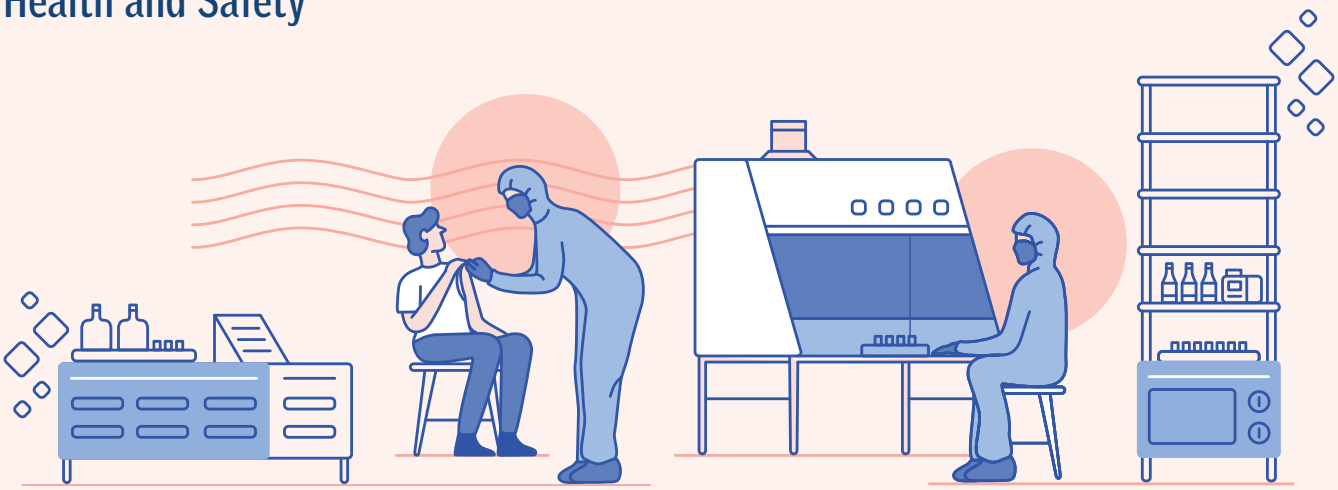
One staff member, Soumya M, stands out for her outstanding commitment. She worked tirelessly. Despite personal difficulties and while battling COVID-19 fears, she came to work almost everyday during the lockdowns, staying late hours when required, never missing deadlines and never complaining when additional work was entrusted to her. She worked on holidays and always obliged requests during odd hours when urgent payments had to be made electronically. She smiled while taking additional responsibilities on behalf of her colleagues when they could not come to office. She accomplished these assigned tasks with grace and positivity. We truly admire Soumya's dedication, her positive attitude towards work, her willingness to help her colleagues and her remarkable determination. Thank you, Soumya!

Anusha V

ACADEMIC OFFICE

At the Academic Office, we process academic recruitment, make sure PhD requirements are met, and that student coursework is completed. In addition, we compile reports for funders and government agencies. Throughout the pandemic, Anusha has been always dependable. She understands requirements well, and how to navigate them. She is the kind of employee who would be desired by any team. She has an incredible work ethic, a great attitude, and is always willing to help. She adjusts quickly to new team members and is unflappable, working well under pressure, and always with a pleasant smile and an upbeat manner. She goes all out to solve a problem, to be creative and to improve continuously. We are truly inspired by her personal commitment to making a difference to young researchers in these unprecedented and challenging times. Thank you, Anusha!

Health and Safety



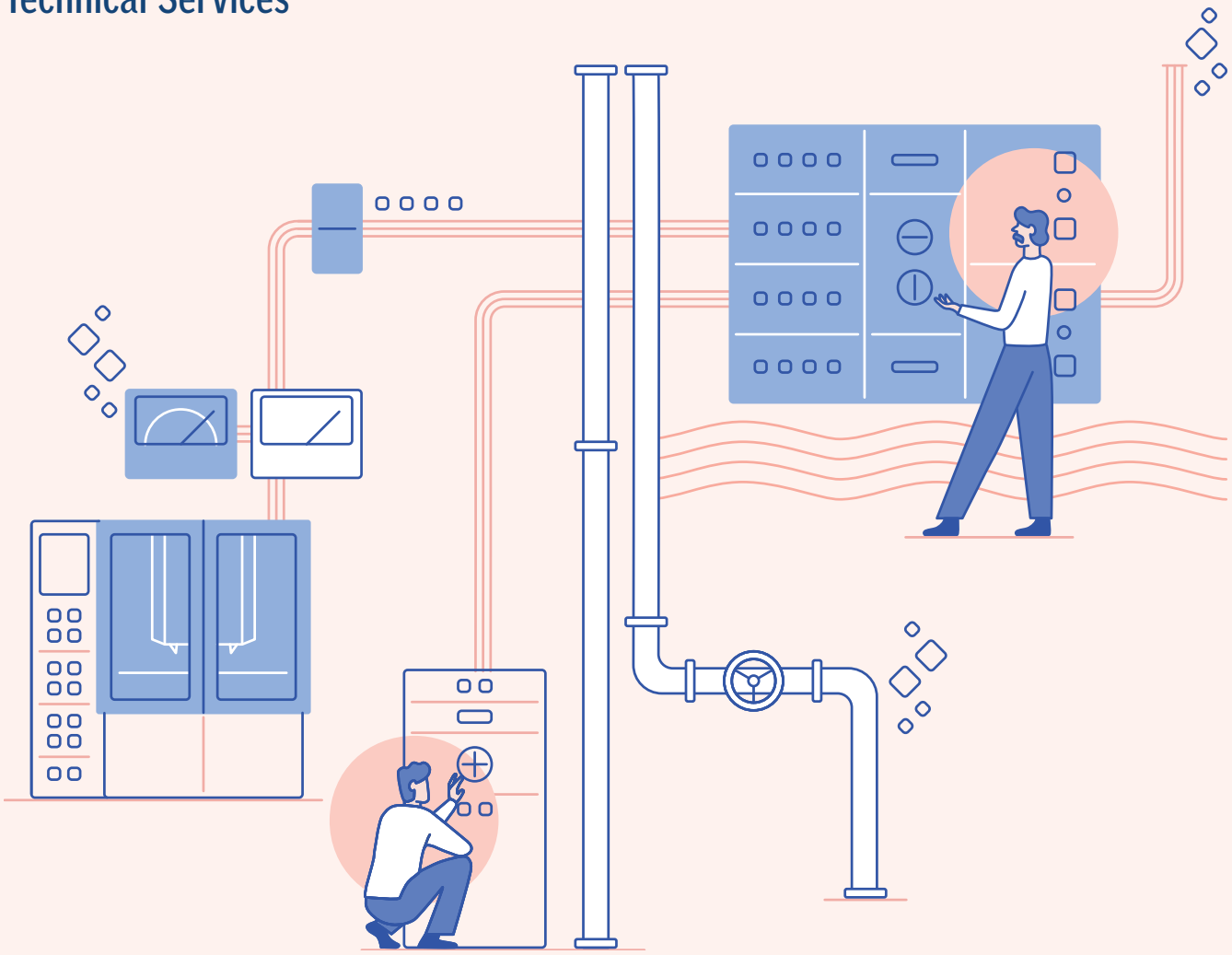
MEDICAL CENTRE

Over the last two years, the entire world has been engulfed by the COVID-19 pandemic. The medical team has been integral in providing comprehensive support to the campus, including helping patients with hospitalisation, home treatment, isolation, quarantine, and ensuring the well-being of everyone and smooth functioning of the campus. The medical centre also anchored vaccination for the campus community. Together, we continue to overcome this pandemic and are thankful for all the support from all campus colleagues.

In particular, we would like to acknowledge the work of Preethi A J, a staff nurse who has been taking care of all of us from the start of the pandemic. She has graced us with her knowledge as a nurse and her compassion as a person, and has remained a strong pillar right through the campus vaccination program. Vasanth, Thimmappa, and Mathialagan, our three ambulance drivers, provided unwavering support during these trying times, especially while handling patient transfers. We deeply appreciate their efforts to help the campus during these difficult times.

The Medical Centre Team

Technical Services



INSTRUMENTATION

Besides taking care of all equipment on campus, the Instrumentation team monitors all emergency equipment, and this had to be continued during the lockdowns. Avinash was entrusted with the responsibility of emergency response on behalf of the instrumentation support team, in order to ensure the smooth functioning of the common Instrumentation Facility and to monitor the emergency equipment.

Avinash Kumar

He was instrumental in setting up and installing the required equipment in the COVID-19 testing facility, configuring the setup for drug screening in the screening facility, and in designing and constructing the in-house fume hood for the liquid handling system. He was available at campus for support throughout the lockdown. Avinash was also a key member of the team that developed the test setup to ensure the efficiency of cloth masks.

He worked with Naveen Kumar to establish the instrumentation aspects of the COVID-19 testing facility, and coordinated the setting up of the vaccine immunology study with Dr. Mangai. Thank you to the entire instrumentation team, and to Avinash, in particular!

The Architecture Team

ARCHITECTURE

During the pandemic, the architecture team helped with campus measures to implement physical distancing and in track contacts in the event of a positive COVID-19 case. We divided all spaces into sectors, with barricades and QR codes at entry and exit points. This included signage in various spaces to educate the campus community. The team worked tirelessly to complete other commitments like handing over the Naidile hostel rooms, setting up lab facilities for new faculty, and other miscellaneous jobs like restoration and setting up of BSL-2 facilities, vertical expansion of laboratories, and creating office spaces at C-CAMP. All these activities had to be taken up with strict compliance to COVID-19 protocols. Sometimes our team would work from 8AM to 9PM, and often on holidays. Monitoring external vendors, obtaining permissions, gathering negative RT-PCR reports, and monitoring health parameters like temperature, was quite challenging for our team. Additionally, work often involved coordinating with other technical services and administrative teams to complete the job. The entire team has done an incredible job through the pandemic. Thank you to everyone who stepped up!

The IT Team

IT

The IT team provided support and ensured operation and maintenance of all lab servers, networks (both wired and wireless) and public display and surveillance systems for security. The team stepped up to address challenges due to lockdown restrictions. Since movement on the campus was restricted, end user issues were resolved using a remote tool/VNC/ RDP/command line/terminal, on-site visits or via telephone. Networks were upgraded in the hostel blocks so that students did not face connectivity issues during their work in the pandemic. Online remote tools were developed to meet user requirements. Procurement of consumables were also made available from a select list of vendors.

Most importantly, the team provided support to the COVID-19 testing facility by installing networking equipment along with computer peripherals. The IT team is still providing technical support for the ongoing saliva screening currently running on the campus. We are proud of everyone's work during these difficult times; thank you!

STORES

Rangappa's duties at the Stores unit on campus are to unload, transport and unpack material. His involvement was critical to running the Stores smoothly during the pandemic, especially when most of the staff were not able to reach the campus due to lockdowns or positive cases amongst their family or colleagues. He attended office almost every day, and even stayed in the office. He efficiently helped issue items from Stores, and helped with delivering necessary material to the COVID-19 testing lab. After the lockdown, he was instrumental in receiving material from vendors at the gate and in bringing them to the store. We thank you, Rangappa!

Rangappa S

CIVIL

The Civil team is responsible for maintenance of all infrastructure and buildings, aesthetics and landscaping of the campus. We are proud that our team members worked tirelessly through the peak of the COVID-19 pandemic, allowing for uninterrupted water supply, treatment of sewage, and landscaping, especially during the lockdowns.

The team also helped in setting up the COVID-19 testing facility on campus, fabricating and building in-house innovative products like sanitiser dispensers, hands-free door openers, and UV disinfection chambers. The team helped in keeping the campus clean at all times by installing automatic water dispensers and making drainage arrangements. We are delighted to work with a team that accomplished all this with accuracy and in a disciplined manner. Thank you to everyone for coming together in these efforts!

The Civil Team

ELECTRICAL

Needless to say, every staff member in the electrical team came together to help wth running essential services on campus. In particular, we would like to thank Parameshwar, a senior technician who was critical for the day-to-day operation of the electrical system during the pandemic. He never refused any work, even during the lockdown, and came to campus everyday. In fact, he worked all three shifts, almost 24/7, for a large part of the pandemic! We thank you, Parameshwar!

Parameshwar K S

LAB SUPPORT

K Thirumalaraju

Laboratory kitchen services ensure smooth operations of all research facilities on campus, and this was amplified during the COVID-19 lockdown restrictions, with an eye on keeping critical research services operational and attending to new research related to understanding COVID-19. In particular, K Thirumalaraju put in extra effort in running the laboratory kitchen activities smoothly by supervising the lab kitchen, including *Drosophila* media preparation, autoclaving, washing of glassware, and cell culture laboratory and cell line maintenance. Initial sector-based protocols required these services to be delivered sector-wise, and Thirumalaraju did this effectively by coordinating with students and others in lab support. He was critically involved in the upkeep of all the greenhouses during the pandemic, in coordination with other departments, and at times even attending breakdown calls during the night. He did all this without any hesitation, working beyond office hours to maintain important stocks for researchers. Most importantly, he inspired and encouraged his colleagues to work with him and complete tasks in a timely manner. We thank Thirumalaraju for everything he has done and continues to do for the campus.

Santosh Y Chavan

MECHANICAL WORKSHOP

During the pandemic, Santosh Y Chavan, a senior technician in the mechanical workshop, was often the only person in the workshop. He single-handedly ran the workshop, as his colleagues could not come for long periods of time due to travel restrictions or quarantine issues. He worked seamlessly, met all the requirements of the campus with commitment, patience, experience, and skill. He fabricated all the devices required by the campus to mitigate the spread of the pandemic, including the HEPA hood for the liquid handler, hand sanitiser boxes, and the saliva tube holder for the campus testing protocol. He is an asset to the campus. Thank you, Santosh!

HVAC

Chethan R

As is the case with every technical team, the HVAC team has dozens of people who came forward to help during the pandemic. For this report, we want to draw attention to the work of one individual, Chethan, who supervises HVAC systems on campus and takes a lot of responsibility and initiative to improve our operations. He has become the ‘go to guy’ for everything, from HVAC operations to electrical, electronics and mechanical troubleshooting. He is the only person who knows the BMS system thoroughly on the campus. During the pandemic, the campus HVAC still needed to run to keep essential services functional. Chethan and his team kept the HVAC plant and services up and running. He became the nodal person to arrange and maneuver personnel. He planned operations thoroughly and with foresight. He also attended to technical issues and complaints in the HVAC system anytime, day or night, during the pandemic. Thank you, Chethan!

Campus Volunteers

During the lockdown, more than 70 students on campus organised themselves into volunteer groups for various tasks: making campus announcements to communicate briefings in person in English and Kannada, making sanitisers for the campus, helping stranded/quarantined individuals with essentials, assisting technical services teams with maintenance of campus property, organising a campus WhatsApp-based messaging group and email ticketing system for quick responses, running a dedicated campus phone line and a peer support group, and delivering medical assistance to the clinic's staff. By August 2020, the campus also started a contact tracing group. Student and staff volunteers stepped up to be primary communicators and interview contacts. A team of students, staff and faculty worked together to identify sectors/contacts using sector maps, point of contact lists, QR logs, handwritten registers, and card readers.

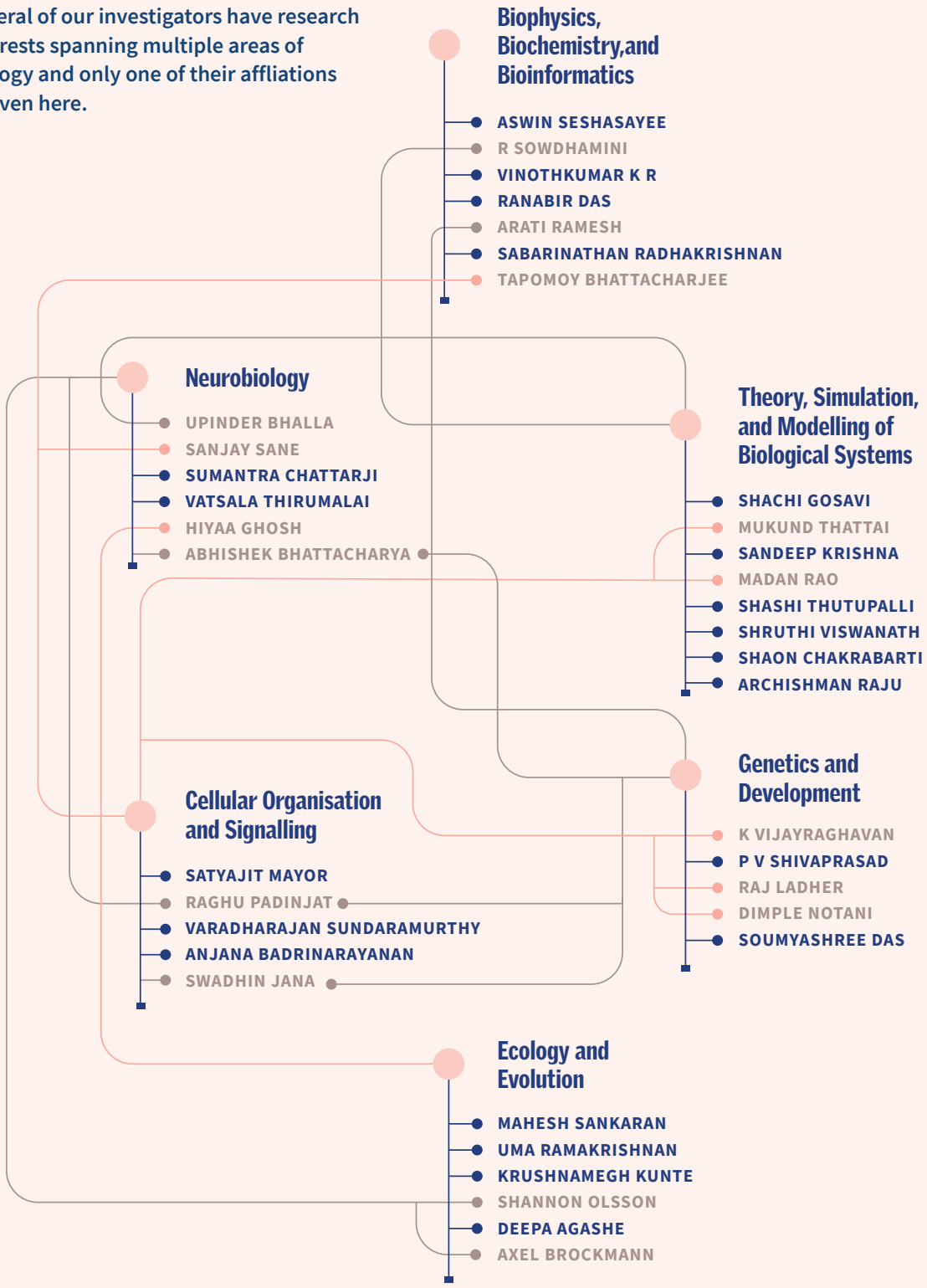
It has been humbling to see the students at work. While it was a collective effort, perhaps everyone would agree that Ravi Kumar Boyapati was one of the most active on-ground volunteers, starting from the first day of the lockdown in March 2020. He was everywhere, allaying fears of support staff, making sanitisers, spreading awareness about COVID-19 in English, Hindi and Kannada, and delivering essentials to COVID-19 positive individuals and quarantined folks. He was at it for over eight months on the trot, all in addition to his other work. The campus owes him and all the other volunteers a debt of gratitude.

River Terns

River Terns in flight at Madhai, Satpura Tiger Reserve. This was shot during a fieldcourse in the MSc Wildlife Biology and Conservation Programme by Abhijeet A V.

MAP OF RESEARCH INTERESTS

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



Starting a Career in the Pandemic

Starting a lab during the pandemic is challenging, but these varied accounts strike a common chord. Here is what four of our new faculty have to say.

ABHISHEK BHATTACHARYA

Starting a lab is one of the most exciting and romantic feelings in a scientist's career. However, starting the lab during the second wave of the COVID-19 pandemic, which also coincided with the financial year ending, taught me to be pragmatic. Not only was every aspect of the lab setup, which includes ordering new equipment and reagents, delayed, but constantly living with fear for the health and well-being of my family members became very stressful at times. But it's not over yet. These challenges definitely made me more resilient and certainly created stronger camaraderie amongst all of us who are facing them together.

ARCHISHMAN RAJU

Science is a social activity. As much as we have been brought up on the myth of the individual scientific, 'genius', it is clear today, more than ever, that most if not all of science is the vast concerted activity of a large number of individuals. Starting a career during a time you were meant to be isolated perhaps brought that out more than anything else could have. As a theorist, I was perhaps spared some of the logistical difficulties that my other colleagues faced. Nevertheless, being a new faculty is a lonely affair, different from graduate school where there is a certain camaraderie with your peers; or even from a post-doctoral fellow where the isolation is temporary. You are faced with new responsibilities and doubts about your capability to handle them. The only thing that can sustain you is interacting with others and being able to talk to them about their experiences. Furthermore, starting new scientific directions ultimately requires some connection to the problems that others around you are involved with. The pandemic, having created the isolation it did, made this interaction and connection almost impossible.

TAPOMOY BHATTACHARJEE

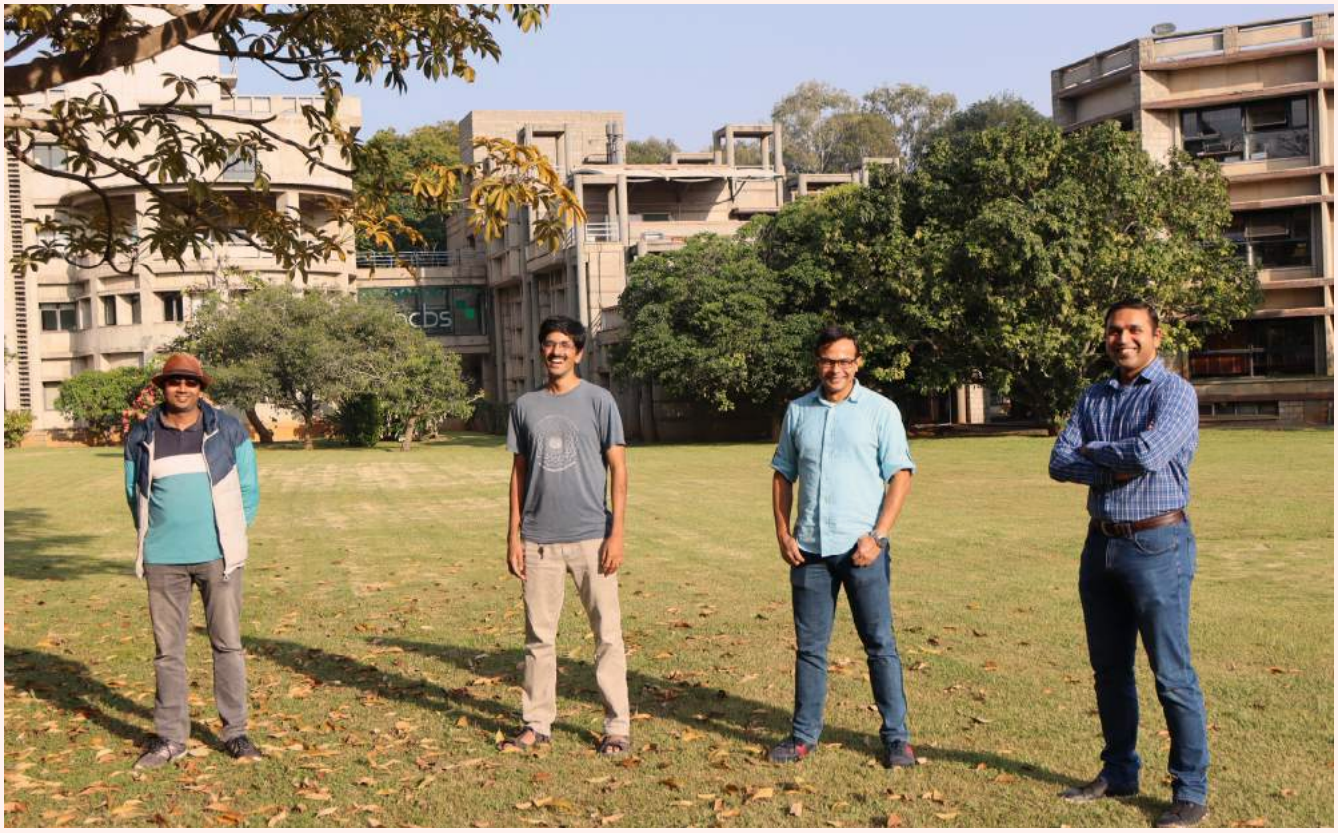
The pandemic has affected almost everything that is required for getting a new lab going. Starting from visiting nearby collaborators to getting new equipment, or finding extramural funding, everything has been impacted. But, the pandemic has created a bigger and more serious impact on the young scientist in making. With much empathy, every new lab needs to ensure that their new and upcoming member, who unfortunately have missed the opportunity to gain hands-on laboratory experience during

their undergrad/masters days due to the pandemic, get the proper care and attention to taste success.

SWADHIN JANA

My lab at NCBS-TIFR, India, opened its doors in the pre-monsoon of 2021. Life was difficult (and still is) as we have been physically cut off from our families and many of our friends for nearly two years. In particular, it was not easy to stay upbeat, having seen numerous close relatives struggle and even losing several of them. Unfortunately, our move to Bangalore coincided with the second wave of the pandemic in India, and it turned out that all of us were infected. Before I formally started my position, India entered the second round of lockdown. Staying home with a child was challenging, aside from beginning my role as the leader of the Organelle Biology Laboratory.

On the research front, COVID-19-related restrictions halted my grand plans of generating preliminary data for future projects. But I was working on a few manuscripts and their organisation and submission. I applied for and received an extension of my research grant in Portugal (IGC-FCT) and submitted a few grant proposals to support my new lab at NCBS. I expected things to be slow getting started during a pandemic, and they have been. My team of young researchers, who are entirely new to research, are giving their best to push the projects along. We've had our fair share of missing orders and bizarre delays on various fronts, but it feels like these delays could have been more significant without the finely tuned NCBS-TIFR system.



(left to right) Swadhin Jana, Archishman Raju, Abhishek Bhattacharya, and Tapomoy Bhattacharjee

This was shot at the Pachmari field station, during a fieldcourse in the MSc Wildlife Biology and Conservation Programme by Abhijeet A V

Red-Breasted Flycatcher

Theory, Simulation, and Modelling of Biological Systems

p. 34–47

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

The Whats, Hows, and Whys of the Eukaryotic Cell Plan
Mukund Thattai

Dynamics of Living Systems across Scales
Sandeep Krishna

Computational Protein Folding, Design, and Assembly
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Quantitative Cell Biology: Cellular Proliferation in Development and Disease
Shaon Chakrabarti

Origins and Organisation of Living Systems
Shashi Thutupalli

Integrative Structural Biology of Large Macromolecular Assemblies
Shruthi Viswanath

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

Madan Rao

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

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

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

Typically these active forces arise from:

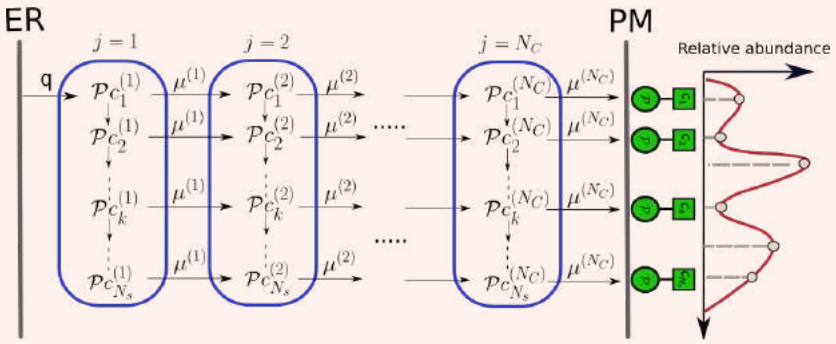
(a) the coupled dynamics of the cytoskeleton, motors, and cytoskeletal regulatory proteins, and

(b) the active dynamics of fission and fusion of organelles, and regulation of the flux of mass, stress, energy, and information.

Using the framework of active hydrodynamics, we study the mechanical response, pattern formation, symmetry breaking, hydrodynamic instabilities, and information flows in both in in vivo and in vitro reconstituted active systems.

Enzymatic reactions and transport networks in the secretory pathway

Schematic of an array of Golgi cisternae (blue) indexed by j=1, …, NC situated between the endoplasmic reticulum (ER) and plasma membrane (PM). Glycan-binding proteins Pc1(1) are injected from the ER to cisterna-1 at rate q. Superimposed is the transition network of chemical reactions (column) and intercisternal transfer (rows), the latter with rates μ. $Pc_k^{(j)}$ denotes the acceptor substrate in compartment j and the glycosyl donor c0 is chemostated in each cisterna. This results in a distribution (relative abundance) of glycans displayed at the PM (red curve) that is representative of the cell type. (Ref: Yadav, A., Vagne, Q., Sens, P., Iyengar, G. and Rao, M. 2020. Glycan processing in the Golgi--optimal information coding and constraints on cisternal number and enzyme specificity. bioRxiv.)

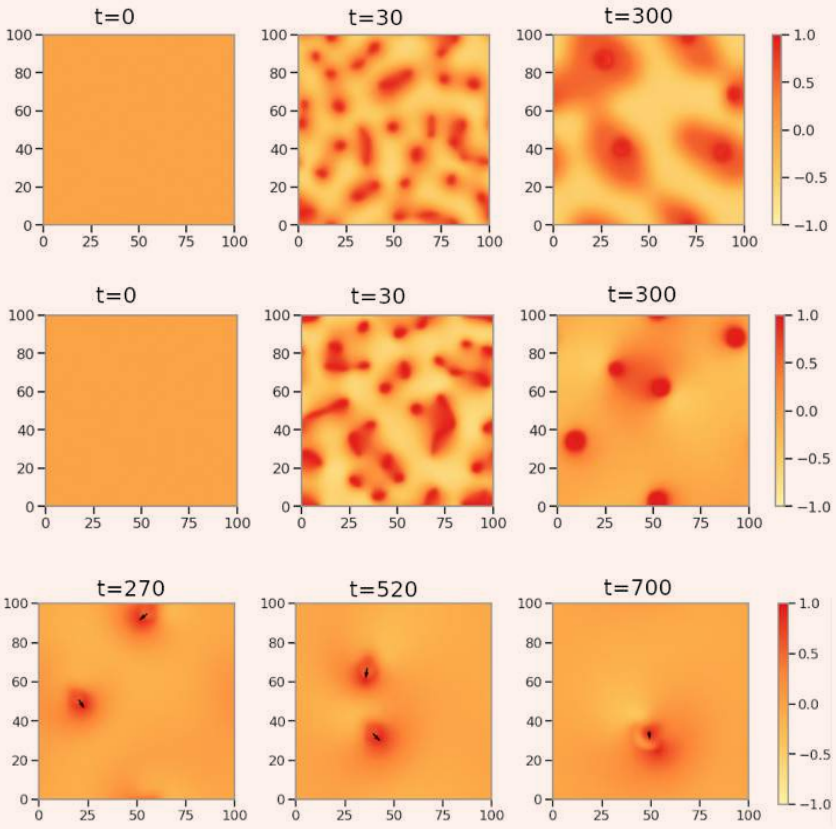


Active contractile stresses drive the emergence of active emulsions of segregated lipid domains at the cell membrane

(top) Coarsening dynamics of lo-domains driven by active contractile stresses at T>Tc. Spatial map of segregation parameter Φ (colour bar) shows coarsening of a symmetric mixture of lo and ld components, starting from a homogeneous state at t=0, leading to the formation of mesoscale domains of the lo-component at late times.

(middle) Spatial map of Φ shows coarsening into mesoscale domains of the lo-component at T<Tc .

(bottom) Phase segregated domains at T>Tc , showing non-reciprocal features in the dynamics of propulsion and growth. Nonreciprocity is apparent during the propulsive movements of domains of component A (arrows), which shows a phoretic reorientation of the direction of propulsion of one of the domains prior to coalescence. (Ref.: Bansal, A., Das, A. and Rao, M. 2021. Active segregation dynamics in the living cell. bioRxiv.)



PUBLICATIONS

Banerjee, J. P., Mandal, R., Banerjee, D. S., Thutupalli, S. and Rao, M. 2021. **Active ploughing through a compressible viscoelastic fluid: Unjamming and emergent nonreciprocity.** arXiv preprint arXiv:2109.10438.

Ramakrishnan, N., Gowrishankar, K., Kuttippurathu, L., Sunil Kumar, P. B. and Rao, M. 2021. **Active remodeling of chromatin and implications for in-vivo folding.** Accepted in Journal of Physical Chemistry.

The Whats, Hows, and Whys of the Eukaryotic Cell Plan

Mukund Thattai

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We use the membrane traffic system as a window to study the mechanistic and evolutionary origins of the eukaryotic cell plan. This effort combines phylogenetics, information theory, graph theory, dynamical systems and optimisation, along with genomic data and quantitative measurements.

As a physicist practising biology, I am interested in how cellular complexity emerges from microscopic disorder. My group is based within the Simons Centre for the Study of Living Machines at NCBS. We use biophysical, mathematical and computational principles to understand how cells work. We have been deeply involved in developing evolutionary cell biology as a rigorous field of study. We collaborate extensively: we work with computer scientists to develop mathematical formulations of cell-biological hypotheses, and with experimental cell biologists to test the predictions of our models.

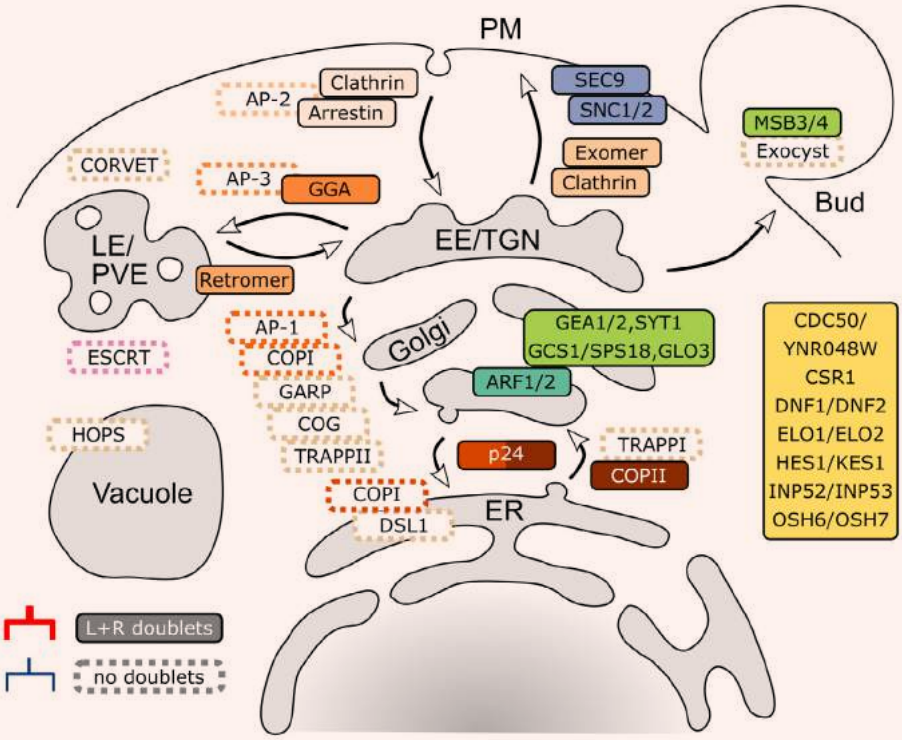
We ask

- What? We use genomic and phylogenetic methods to study the evolution of proteins involved in membrane traffic, to shed light on the natural history and diversity of this system across species and time.
- How? We use mathematical and computational methods to understand how the global structure of the membrane traffic system emerges from local molecular interactions.
- Why? We explore the selective advantage of having intracellular organelles and intra-organellar transport, with a particular focus on the structure and function of the Golgi apparatus.

Our most recent work focuses on detecting signatures of long-term selection acting on membrane traffic, and using optimisation principles to understand the activity of enzymes in the Golgi.

The budding yeast Saccharomyces cerevisiae is descended from a 100-million-year-old hybrid that originally had duplicate copies of each gene, one inherited from each parental species.

Over time, 90% of these doublets reverted to singletons. However, a disproportionate number of doublets persist in the membrane traffic apparatus, particularly in the secretory pathway. These patterns show how selection has sculpted the yeast membrane traffic system over evolutionary timescales.



PUBLICATIONS

Jaiman, A. and Thattai, M., 2020. **Golgi compartments enable controlled biomolecular assembly using promiscuous enzymes.** Elife, 9, e49573.

Bhattacharyya, A., Gupta, A., Kuppusamy, L., Mani, S., Shukla, A., Srivas, M. and Thattai, M., 2021. **A formal methods approach to predicting new features of the eukaryotic vesicle traffic system.** Acta Informatica, 58(1), 1–37.

Dynamics of Living Systems across Scales

Sandeep Krishna

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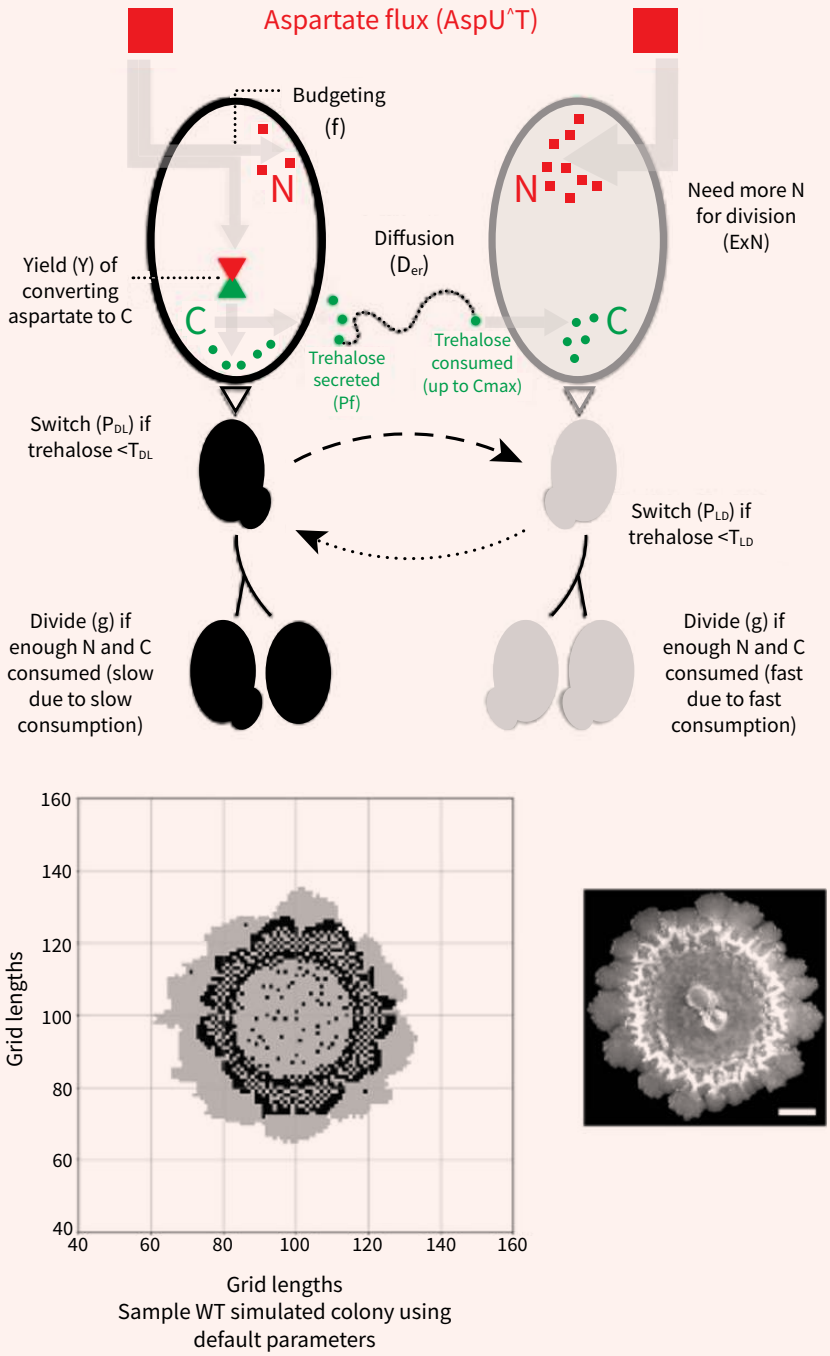
I study the complex, far-from-equilibrium dynamics of biological systems, ranging from molecules to cells to populations.

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

Carbon-nitrogen budgeting drives division of labour in a budding yeast colony.

The bottom panels compare the wild-type yeast colony (scale bar: 2mm) with a simulation from a mathematical model which includes the processes shown in the top panel (see Ref. 2 for more details).



PUBLICATIONS

Heltberg, M. L., Krishna, S., Kadanoff, L. P. and Jensen, M. H. 2021. **A tale of two rhythms: Locked clocks and chaos in biology.** Cell Systems, 12(4), 291–303.

Varahan, S., Sinha, V., Walvekar, A., Krishna, S. and Laxman, S. 2020. **Resource plasticity-driven carbon-nitrogen budgeting enables specialization and division of labor in a clonal community.** Elife, 9, e57609.

Computational Protein Folding, Design, and Assembly

Shachi Gosavi

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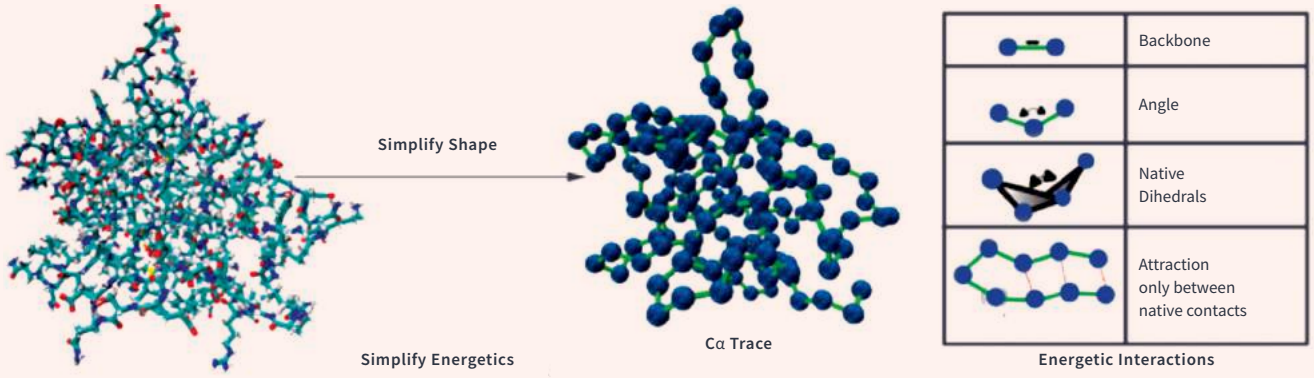
My group uses computational methods to understand the architecture of proteins. We are specifically interested in understanding how protein function and conformational dynamics affect the folding of proteins and how folding simulations can, by themselves, impart information on protein function.

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

Natural proteins have evolved to fold on a biologically reasonable timescale and to be as stable as is necessary to perform their function. However, selection directly acts only on the functional residues (where function could be binding, catalysis, cellular localisation, etc.). These functional residues cannot be mutated to make protein folding more efficient or protein stability any greater. Given the choice of only 20 amino acids at each position, it has become apparent that parts of the protein which function are likely to be the least foldable or stable. Functional regions thus perturb folding from the ‘ideal’ and we use SBMs to understand both, what ideal folding is, and how functional regions perturb it.

Cartoon of a coarse-grained structure based model

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



PUBLICATIONS

Jayanthi, L. P., Mascarenhas, N. M. and Gosavi, S. 2020. **Structure dictates the mechanism of ligand recognition in the histidine and maltose binding proteins.** Current Research in Structural Biology 2, 180–190.

Terse, V. L. and Gosavi, S. 2021. **The molecular mechanism of domain swapping of the c-terminal domain of the SARS-coronavirus main protease.** Biophysical journal 120(3), 504–516.

Quantitative Cell Biology: Cellular Proliferation in Development and Disease

Shaon Chakrabarti

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

Over the last year since I have joined NCBS and the Simons Centre, my lab has embarked upon a variety of research directions with cell proliferation forming the unifying element within these somewhat disparate cell-biology questions. Leveraging lineage correlations in cell populations to answer fundamental questions relating to control of cellular proliferation is another recurring theme in our research interests.

We are establishing a simple theoretical framework for understanding how population growth laws emerge in cancer cells during treatment with anti-cancer therapies, from fluctuations (non-genetic heterogeneity) at the single cell level. These fluctuations induce a variety of lineage correlation patterns which we are using as probes to understand how the circadian clock drives cell proliferation, and also to infer the phase of the circadian clock in single cells. Along with development of these theoretical frameworks, we have also been establishing single molecule FISH and live cell imaging protocols to quantify and utilise information hidden in the lineage correlations. Finally, we have been studying how epigenetic inheritance across cellular generations and the architecture of the epigenome can be shaped by simple physical laws such as diffusion.

Uncovering physical principles and control mechanisms of cellular proliferation.

(Center) Tracking cellular proliferation at the population level.

(a) MCMC inference results for single cell division times in the presence of cisplatin.

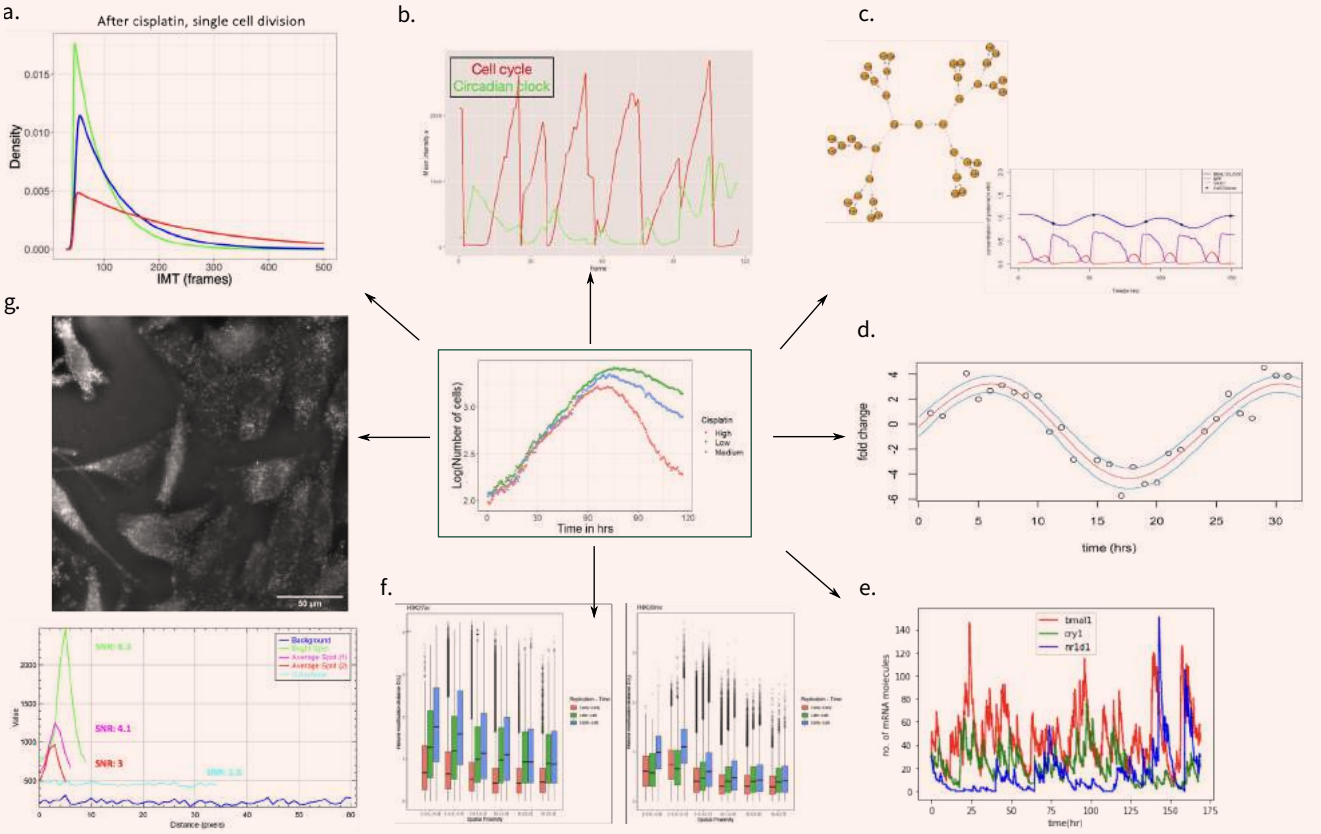
(b) Single cell intensity time-series of the circadian clock protein RevErba and the cell cycle. Data from Adrian Granada at Charité Universitätsmedizin Berlin.

(c) Lineage simulations that model both the circadian clock and cell cycle. (d.) Gaussian Process Regression to detect circadian oscillations from noisy time-series data with missing time points.

(e) Simulations of the circadian clock network incorporating bursty gene expression using the Telegraph Model.

(f) Patterns of epigenetic modifications arising from diffusion of histones.

(g) smFISH results on the Cbx5 gene, along with intensity quantification showing the signal-to-noise ratio (SNR) for some representative spots.



PUBLICATIONS

Poels, K. E., Schoenfeld, A. J., Makhnin, A., Tobi, Y., Wang, Y., Frisco-Cabanos, H., ... and Michor, F. 2021. **Identification of optimal dosing schedules of dacomitinib and osimertinib for a phase I/II trial in advanced EGFR-mutant non-small cell lung cancer.** Nature Communications, 12(1), 1–12.

Origins and Organisation of Living Systems

Shashi Thutupalli

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We are broadly interested in identifying the underlying principles of emergence and organisation (growth, maintenance, ecology and evolution) in living systems—towards this goal, we develop quantitative experiments combined with conceptual frameworks.

The key questions that drive us are distinct, unified by their probing of the multiple facets of the complex organisation of living systems through space and time:

(i) what design features (with a specific focus on spatio-temporal organisation) are required to create synthetic systems capable of displaying emergent computation, heritability, and evolvability?

(ii) what are the emergent dynamical patterns of interacting non-equilibrium active units/microbial species?

(iii) what are the energetic budgets of living systems and how do such energetic requirements scale with size and across evolutionary transitions (e.g. unicellular to multicellular)?

We broadly take two complementary approaches:

(i) Construct de novo, synthetic mimics of living matter: These studies serve as a kind of synthetic biology from a physical perspective and are likely to shed light on early evolution and the transitions therein. We study the ingredients required for self-assembly, replication, feedback, and evolvability by working with synthetic abiotic sub-components.

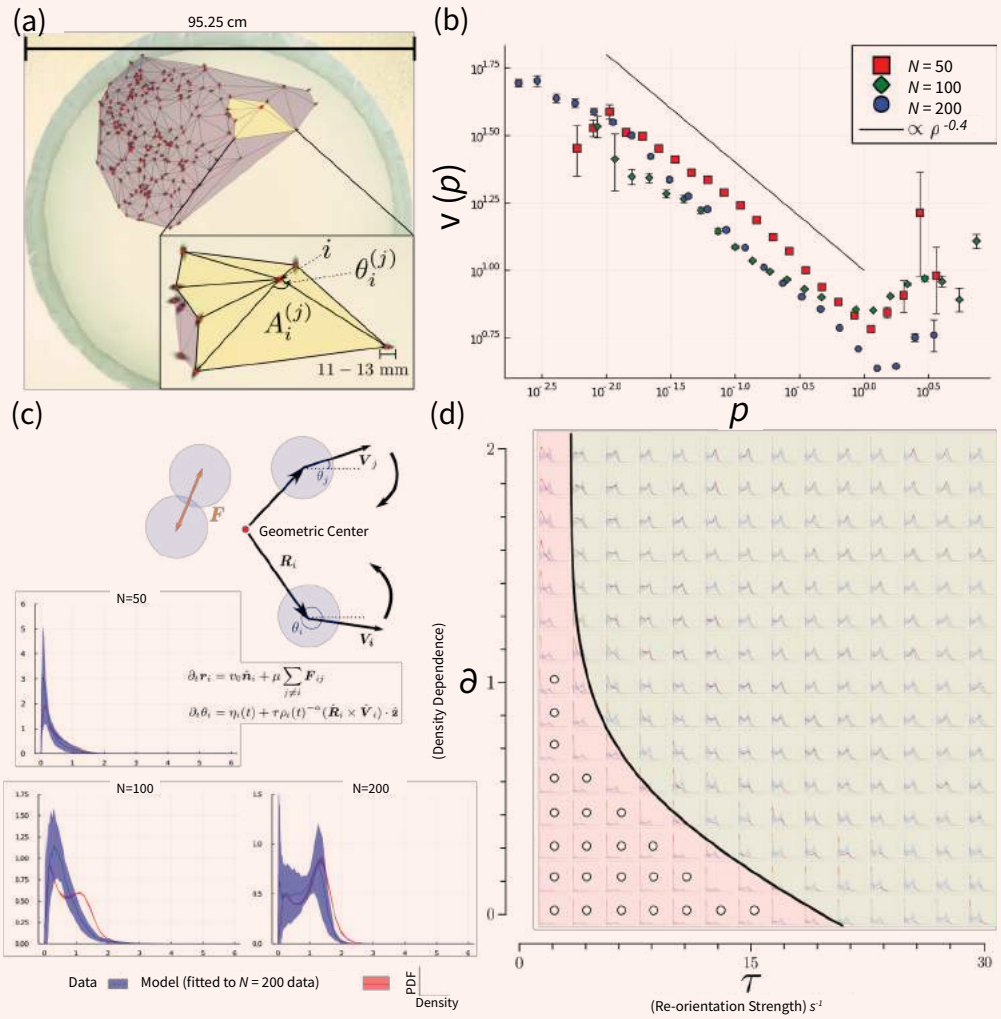
(ii) Probe the physical basis of organisation in cells and populations: This represents a kind of physical biology that will allow us to quantitatively identify the broadly universal features of cellular and population organisation. On the one hand, we investigate the emergent dynamical organisation of interacting species (e.g. bacteria and viruses) while on the other, we study energy budgeting and resource allocation at the level of single cells and how these budgets effect organismal size regulation and organisational transitions (e.g. unicellularity to multicellularity).

Motility Induced Phase Separation (MIPS) in whirligig beetle collective dynamics.

(a) Quantifying the collective motion of whirligig beetles.

(b) The speed of individual beetles depends on the local density in a power law fashion.

(c) A simple interacting active particle model of the whirligigs captures the collective dynamics, also shown in a phase diagram (d).



PUBLICATIONS

Devereux, H. L., Twomey, C. R., Turner, M. S., and Thutupalli, S. 2021. **Whirligig beetles as corralled active Brownian particles.** Journal of the Royal Society Interface, 18(177), 20210114.

Yang, X., Heinemann, M., Howard, J., Huber, G., Iyer-Biswas, S., Le Treut, G., ... and Foster, P. J. 2021. **Physical bioenergetics: Energy fluxes, budgets, and constraints in cells.** Proceedings of the National Academy of Sciences, 118(26).

Integrative Structural Biology of Large Macromolecular Assemblies

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shruthiv@ncbs.res.in

We seek to understand protein organisation in cells by characterising their structures in binary complexes, macromolecular assemblies, and nanoscale architectures. We use an integrative approach, combining data from biophysical, biochemical, genetic, and cell biology experiments, along with statistical inference and physical principles.

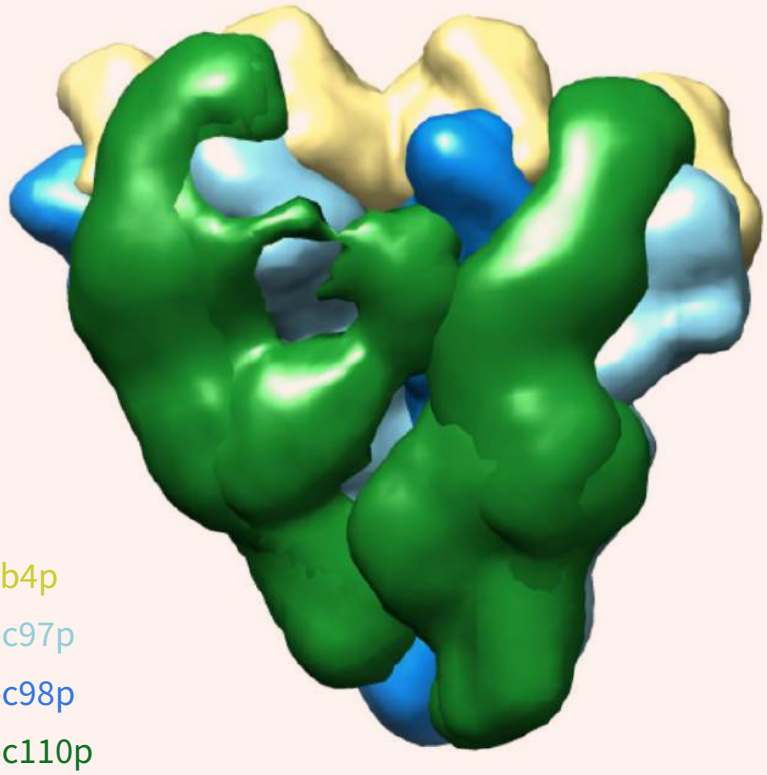
Large protein assemblies, such as the ribosome or proteasome, contain tens to hundreds of proteins, and act as molecular machines. The structures of these assemblies are key to understanding the mechanistic details of biological function. We seek to understand the organisation of these molecular machines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

Determining the structures of these assemblies using a single experimental method is challenging. Therefore, we use an integrative approach, combining data from biophysical, biochemical, genetics, and cell biology experiments, along with statistical inference, physical principles, and prior models. We are currently characterising assemblies in three broad areas: assemblies involved in regulating gene expression, including chromatin remodelers, assemblies at cell-cell junctions, and cellular machineries involved in cell division such as centriolar and centrosomal protein complexes.

Our other focus is on developing rigorous methods and software for the computational modelling of protein organisation at the above scales. Our current efforts are directed at improving sampling efficiency, annotating precision and optimising model representation for integrative modelling. Our methods are used by the worldwide PDB for validating integrative models.

Integrative structure of yeast Spc110p1-220 dimer bound to the γ-tubulin small complex suggests a mechanism for assembly and activation of the γ-tubulin ring complex that nucleates microtubules.

The figure shows the localisation density map for the ensemble of integrative models consisting of two adjacent γTuSCs, each bound to an Spc110p1-220 dimer. The map shows the positions of different parts of the complex in the ensemble of models from the top cluster (Brilot et al., 2021).



HONOURS AND AWARDS

2021 Associate Editor, Frontiers in Molecular Bioscience

PUBLICATIONS

Brilot, A. F., Lyon, A. S., Zelter, A., Viswanath, S., Maxwell, A., MacCoss, M. J., ... and Agard, D. A. 2021. **CM1-driven assembly and activation of Yeast γ-Tubulin Small Complex underlies microtubule nucleation.** Elife, 10, e65168.

Saltzberg, D. J., Viswanath, S., Echeverria, I., Chemmama, I. E., Webb, B. and Sali, A. 2021. **Using Integrative Modeling Platform to compute, validate, and archive a model of a protein complex structure.** Protein Science, 30(1), 250–261.

On a misty winter evening in Ranthambore Tiger Reserve when we were heading back to our base camp just before dusk, a tigress walked out of the bushes where a male was trying to court her.

This was shot by Abhinav Tyagi who is a PhD student studying landscape connectivity in central India.

Neurobiology

p. 50–59

Brain Homeostasis and Neuroinflammation
Hiyaa Ghosh

Physics, Neurobiology, and Ecophysiology of Insect Flight and Insect Architecture
Sanjay Sane

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

Brain Computation and Memory: From Molecules to Behaviour
Upinder Bhalla

Development, Modulation, and Function of Motor Systems
Vatsala Thirumalai

Brain Homeostasis and Neuroinflammation

Hiyaa Ghosh

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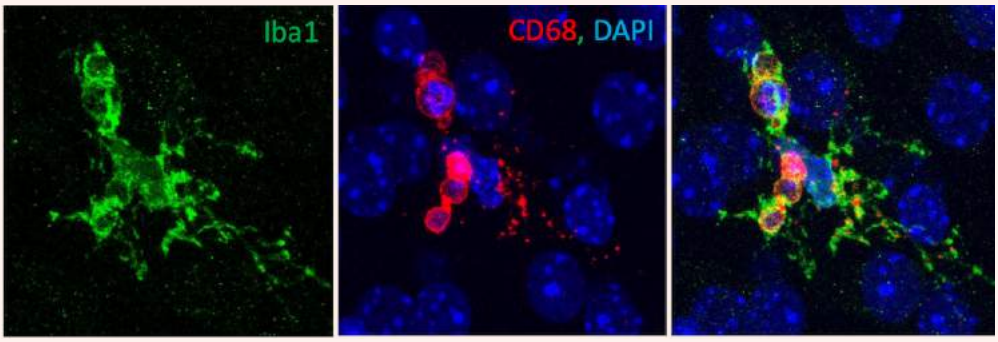
Research in my laboratory seeks to understand the genetic regulations that ensure homeostatic functioning of the adult brain.

The brain consists of neuronal and non-neuronal cells that function in an interdependent manner toward normal functioning of the nervous system. Research in my lab is focused on three cell-types of the adult brain: the neural stem cell, the neuron, and the microglia. We probe the genetic and molecular regulations that underlie their homeostatic functioning. The discovery of neural stem cells in the adult brain has ignited new hopes for regenerative medicine in the context of brain pathologies. However, we do not yet fully understand the whole spectrum of fate-potential and the regulators of adult neural stem cells (aNSC). Through our investigations into the fundamental principles of fate-regulation of the aNSC, we have revealed that the otherwise known to be 'CNS-friendly' adult neural stem cells have a latent inflammatory potential that needs to be proactively suppressed to promote normal adult neurogenesis. The newly revealed detrimental potential of the aNSC now needs to be investigated further in the physiological contexts of neuroinflammation. Another major interest of the lab lies in investigating the genetic regulation of mature neuronal maintenance. Neurons are one of the longest-living cell types in our body, with little capacity for regeneration or repair. We investigate mechanisms that govern the homeostatic functioning of mature neurons and seek to understand how neurons potentially adapt to dysfunctionalities or losses of individual neurons. In our recent study, we uncovered a novel gene-regulatory network that maintains the normal structure and function of neurons in the adult brain. We are currently investigating how these novel pathways maintain neuronal structure and examining physiological contexts for potential structure-function adaptation of adult neurons. Finally, as a third line of investigation, we study the regulation of microglial homeostasis and heterogeneity. Although known as the resident immune cells of the brain, microglia perform a myriad of non-immune functions. In order to fulfil the diverse requirements of its functions during homeostasis and immune activation, microglia adopt various manifestations. We seek to uncover the genetic programs that could govern a 'specialized' versus 'generic' functional manifestation of microglia in a context-dependent manner. Using single cell transcriptomics, we have recently identified a specialised subset of microglia that could be important for tissue homeostasis after injury response. Our overall goal is to decipher the fundamental principles of cellular homeostasis in the brain and correlate conditions of impaired or aberrant functionalities to deviations from the steady state at a cell-molecular level.

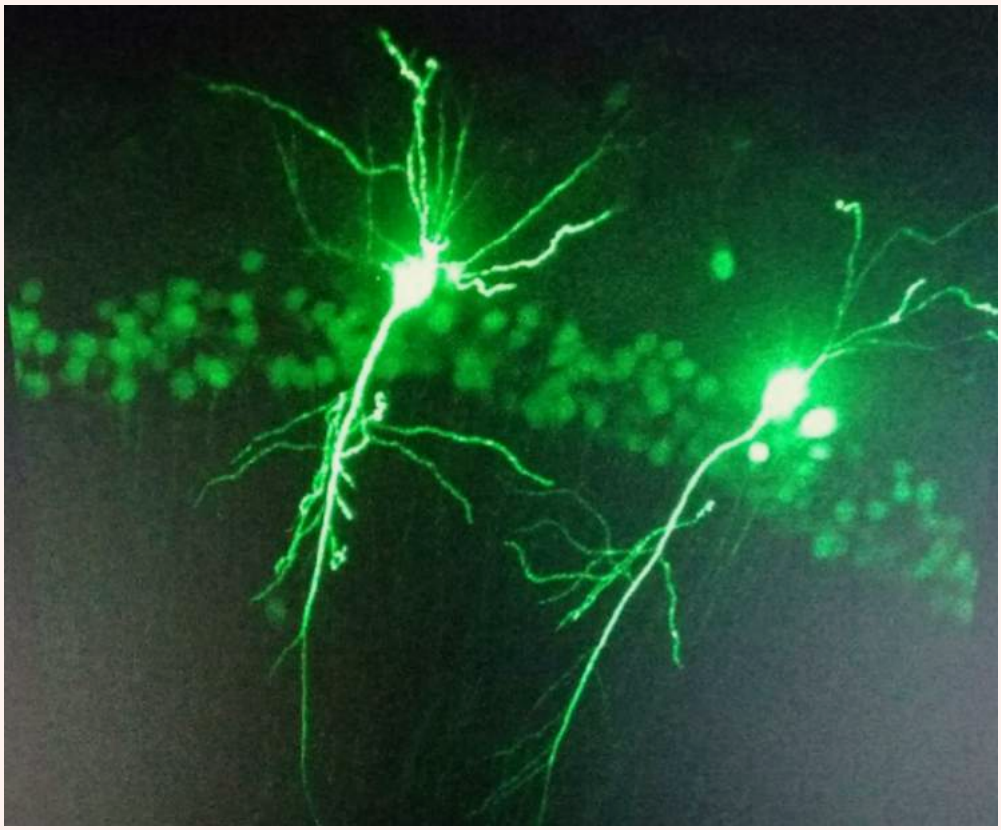
Phagocytic cups containing DNA in activated microglia.

Shown are phagocytic cups (red) with engulfed DNA (blue) in activated microglia (green) in mouse brain.



Projection neuron in mouse brain hippocampus.

Shown is the dendritic arborisation of a dye-filled pyramidal neuron from the CA1 region of the hippocampus.



PUBLICATIONS

Shariq, M., Sahasrabuddhe, V., Krishna, S., Radha, S., Nruthyathi, Bellampalli, R., ... and Ghosh, H. S. 2021. **Adult neural stem cells have latent inflammatory potential that is kept suppressed by Tcf4 to facilitate adult neurogenesis.** Science Advances, 7(21), eabf5606.

Sarkar, D., Shariq, M., Dwivedi, D., Krishnan, N., Naumann, R., Bhalla, U. S. and Ghosh, H. S. 2021. **Adult brain neurons require continual expression of the schizophrenia-risk gene Tcf4 for structural and functional integrity.** Translational Psychiatry, 11(1), 1–11.

NEUROBIOLOGY

Physics, Neurobiology, and Ecophysiology of Insect Flight and Insect Architecture

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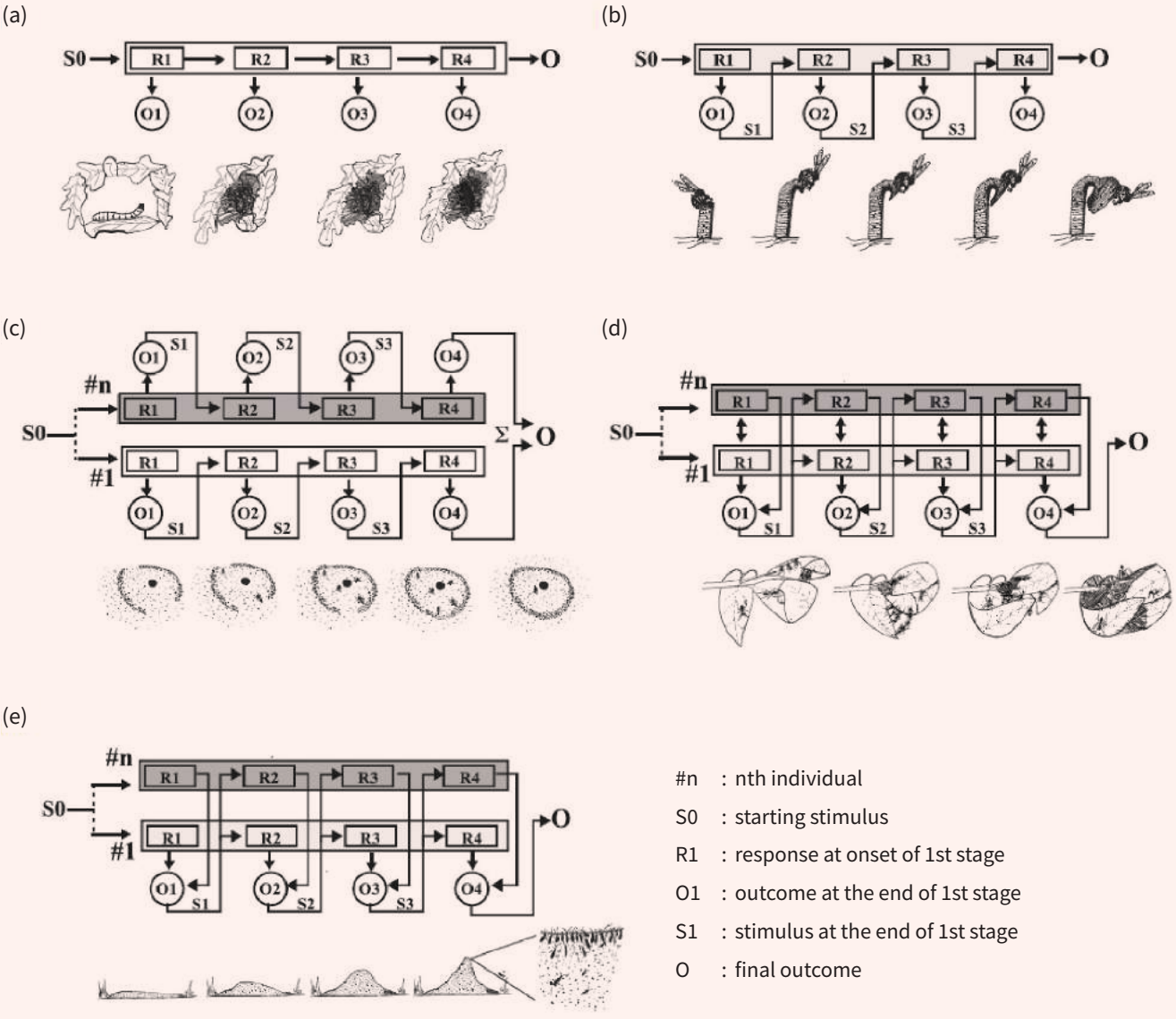
My laboratory studies the physical, neural, and ecological basis of insect flight and insect architecture. We study diverse flight-related behaviours including fast aerial manoeuvers, territorial chases, short-distance navigation tasks (such as foraging or odour-source localisation), long-distance migration,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

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

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

Five hypothetical processes underlying insect building, with specific examples (lower panel)

(a) Fixed-action patterned building of cocoon by silkworm (b) Markovian-building in *Paralastor* sp. (c) Collective building of ant-craters by *Dorymyrmex* sp. (d) Cooperative building of a nest in weaver ants, *Oecophylla* sp. (e) Coordinated building via insect-structure interaction in mound-building termites.



Current Opinion in Insect Science

HONOURS AND AWARDS

2020 Selected for the Japan Society for Promotion of Science Invitational Fellowship

2020 Selected as an Editor of the Journal of Experimental Biology

PUBLICATIONS

Sane, S. P., Ramaswamy, S. S. and Raja, S. V. 2020. **Insect architecture: Structural diversity and behavioral principles.** Current Opinion in Insect Science, 42, 39–46.

Deora, T., Sane, S. S. and Sane, S. P. 2021. **Wings and halteres act as coupled dual-oscillators in flies.** ELife, 10, e53824.

NEUROBIOLOGY

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

Sumantra Chattarji

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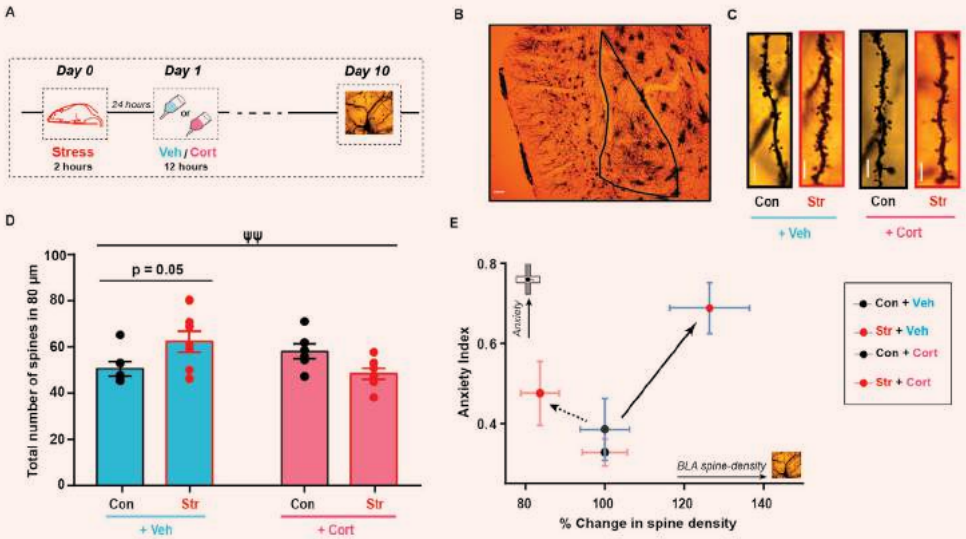
Debilitating emotional problems are a hallmark of stress-related psychiatric disorders. We use animal models to explore the neural basis of these phenomena in the brain's emotional hub, the amygdala, from molecular and synaptic mechanisms at one end, to their behavioural consequences at the other.

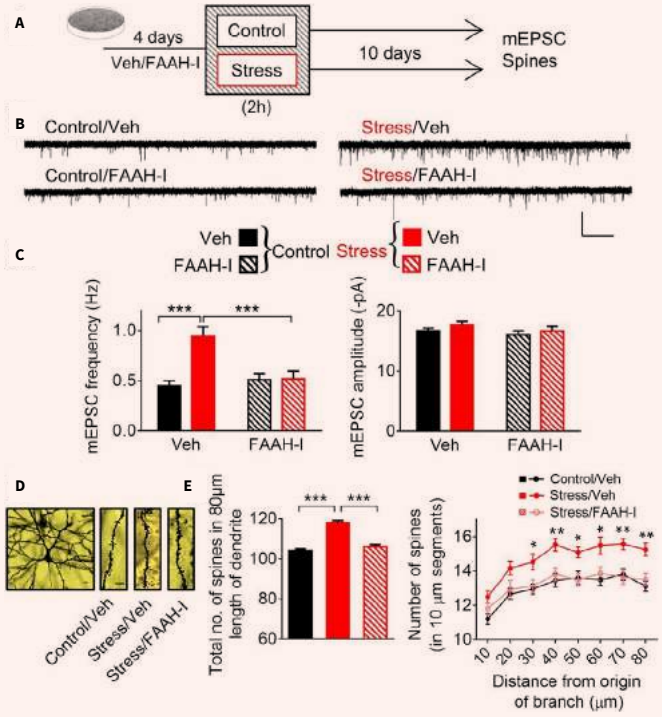
All memories are not created equal – some are more equal than others. For instance, emotionally salient experiences tend to be well-remembered, and the amygdala plays a central role in this process. But the rapid and robust encoding of emotional experiences, such as aversive memories, can become maladaptive;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

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

Experimental design. (A) Rats received either corticosterone or vehicle in their drinking water bottle for 12 h (noon to midnight), 1 day after stress. Spine-density in the basolateral amygdala (BLA) were quantified 10 days later. (B) Representative image showing a Golgi-stained coronal section of a rat BLA. Scale bar 200 µm. (C) Representative images of dendritic spines from the experimental groups. Scale bar 10 µm. (D) Post-stress corticosterone, but not vehicle, also prevented elevated spine-density in the BLA. (Control + Vehicle, N = 6 rats; Control + Corticosterone, N = 6 rats; Stress + Vehicle, N = 7 rats; Stress + Corticosterone, N = 7 rats). Ψ Ψ $p < 0.01$ in 'interaction' between factors stress and corticosterone, in two-way ANOVA. (E) Percentage change in BLA spine-density, normalised to respective controls, has been plotted along the x-axis and change in Anxiety Index of the same rats along the y-axis. While vehicle-treated stressed rats showed an increase in both spine-density and anxiety (diagonal solid arrow), these large changes in both cellular and behavioural measures were not seen with post-stress corticosterone treatment (diagonal dashed arrow). (Control + Vehicle, N = 6 rats, Stress + Vehicle, N = 7 rats, Control + Corticosterone, N = 6 rats, Stress + Corticosterone, N = 7 rats).



Stress-induced delayed increase in mEPSC frequency and spine density in BLA principal neurons is blocked by fatty acid amide hydrolase inhibitor (FAAH-I). (A) Experimental design depicting timeline of FAAH-I administration followed by stress, 10 d after which either mEPSC recordings were done or brains were processed for spine analysis. (B) Representative mEPSC traces. (Scale bar, 30 pA, 5 s.) (C) Vehicle (Veh)-treated stressed group has increase in mEPSC frequency 10 days after stress. This delayed increase is not observed in the FAAH-I–treated stressed group (control/vehicle: N = 16, stress/vehicle: N = 16, stress/FAAH-I: N = 16, control/FAAH-I: N = 16; stress: $F[1,60] = 11.79$, $P = 0.001$; drug: $F[1,60] = 6.04$, $P = 0.02$; interaction: $F[1,60] = 10.91$, $P = 0.002$, ***$P < 0.001$ (Left). Summary of average mEPSC amplitudes shows no difference between the 4 groups (Right). (D) Low-power photomicrograph of a Golgi stain-impregnated pyramidal neuron in the BLA (20×; Scale bar, 10 µm) (Left). Representative images of primary dendrites of BLA pyramidal neurons (40×; Scale bar, 10 µm) (Right). (E) Analysis of total number of spines on a primary branch of pyramidal neurons in the BLA shows an increase in spine density in the vehicle-treated stressed group (n = 25) compared to vehicle-treated controls (N = 29). FAAH-I treatment (N = 25) rescues stress-induced increase in spines in the BLA (one-way ANOVA, $F[2,76] = 58.17$, ***$P < 0.001$) (Left). Segmental analysis of dendritic spine density in each successive 10-µm segment along a primary branch in the pyramidal neurons in the BLA as a function of distance of that segment from the origin of the branch. Significant differences observed are indicated (for stress/vehicle vs. stress/FAAH-I) as follows: *$P < 0.05$, **$P < 0.01$ (repeated measures two-way ANOVA, Tukey's multiple comparisons test) (Right).



HONOURS AND AWARDS

2020 Elected associate member of European Molecular Biology Organisation (EMBO)

PUBLICATIONS

Yasmin, F., Colangeli, R., Morena, M., Filipski, S., van der Stelt, M., Pittman, Q. J., ... and Chattarji, S. 2020. **Stress-induced modulation of endocannabinoid signalling leads to delayed strengthening of synaptic connectivity in the amygdala.** Proceedings of the National Academy of Sciences, 117(1), 650–655.

Chakraborty, P., Datta, S., McEwen, B. S. and Chattarji, S. 2020. **Corticosterone after acute stress prevents the delayed effects on the amygdala.** Neuropsychopharmacology, 45(13), 2139–2146.

Brain Computation and Memory: From Molecules to Behaviour

Upinder Bhalla
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We study memory in health and disease across scales, from molecules to behaviour. We use optical recordings, optogenetics, and electrophysiology in vivo and in vitro, and develop multiscale computer models and techniques to understand how memories are formed and lost.

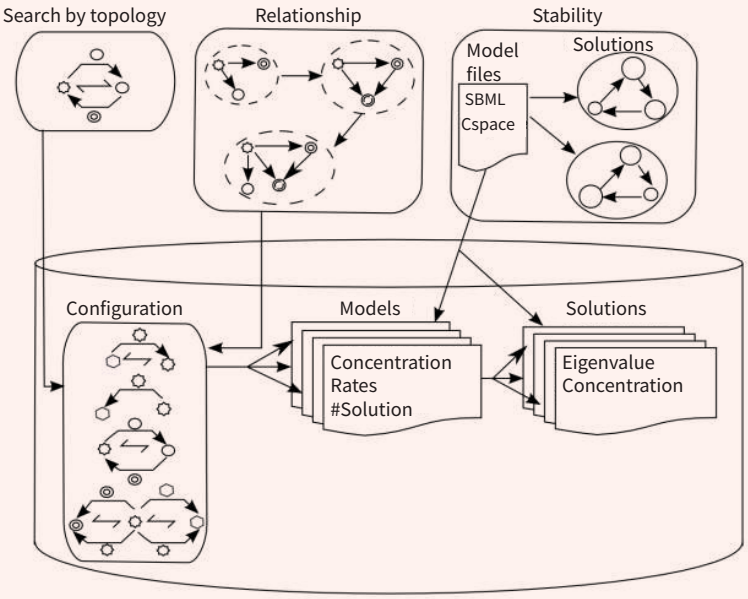
In vivo, we use two-photon imaging to monitor hippocampal activity from hundreds of neurons to watch how memory associations are formed and transformed through new stimuli and forgetting.

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

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

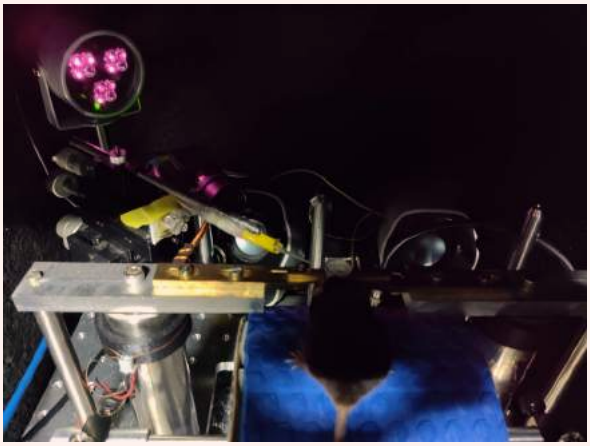
Capabilities of chemical SWITCHES database.

The database houses over 7 million models, of which 33,000 are bistable switches capable of memory storage. The database provides access to the reaction configurations and mathematical signatures of their stability.



Mouse training.

The mouse runs on the blue treadmill. It is exposed to a variety of stimuli, including speakers in the background, LED (to the left), and an air puff (tube supported by yellow tape). Its responses are monitored by a high-speed camera (purple reflection, above left speaker).



PUBLICATIONS

HarshaRani, G. V., Moza, S., Ramakrishnan, N. and Bhalla, U. S. 2021. **SWITCHES: Searchable web interface for topologies of CHEmical switches.** Bioinformatics, 37(16), 250–2505.

Bhatia, A., Moza, S. and Bhalla, U. S. 2021. **Patterned Optogenetic Stimulation Using a DMD Projector.** In Channelrhodopsin (173–188). Humana, New York, NY.

Development, Modulation, and Function of Motor Systems

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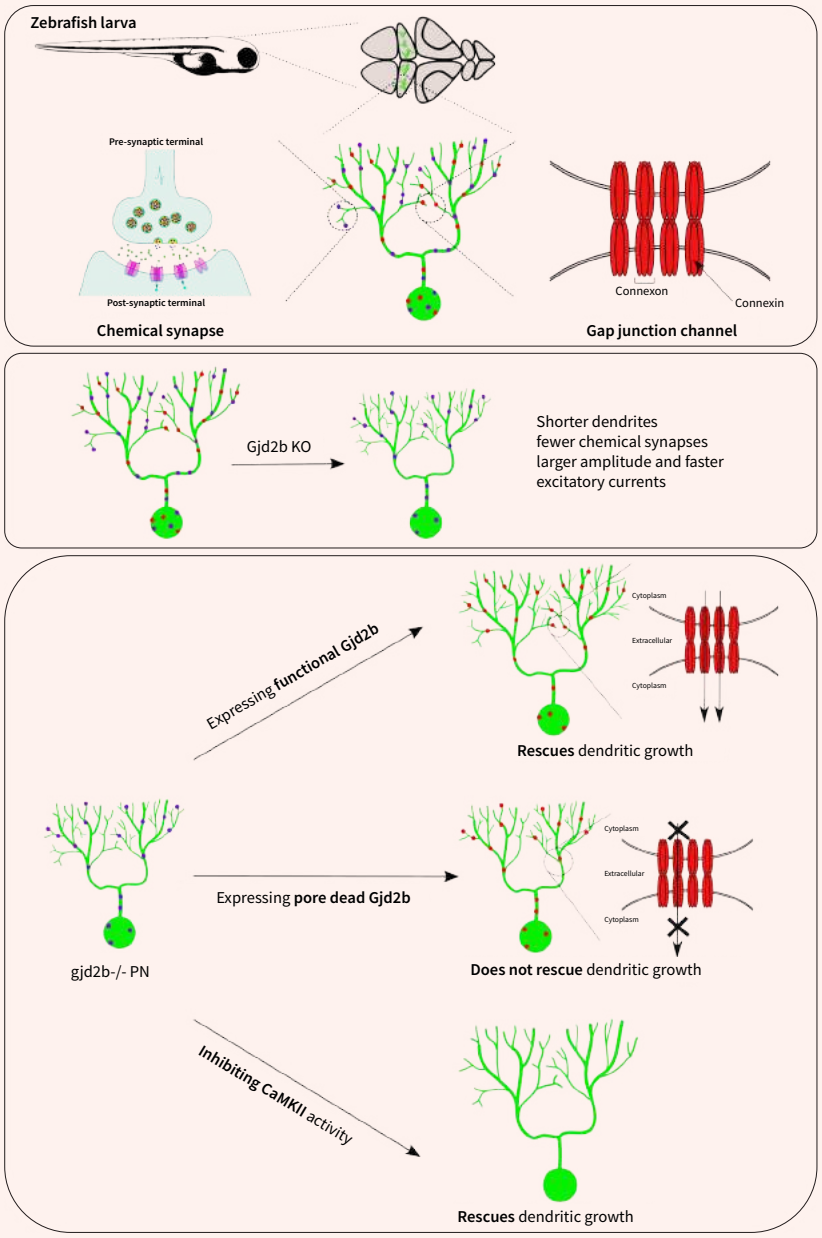
In vertebrates, locomotion is generated by multiple circuits in the brain and spinal cord acting in a coordinated fashion. We study how these circuits assemble and how they function at all stages of life.

Locomotion is essential for the survival of most animals, as it enables them to find food and reproductive partners as well as escape predators. My lab focuses on the function and development of brain circuits that control locomotion, using the small freshwater fish zebrafish as our model system. Our work aims to understand how sensory inputs are integrated by disparate circuits in the optic tectum, cerebellum, hindbrain, and spinal cord to generate appropriate locomotor behaviour. We also examine how locomotory circuits are assembled de novo, quite early in development when much of the nervous system is immature.

Recently, we established that gap junctions are crucial for cerebellar circuit assembly (Sitaraman et al. 2021). Our experiments showed that loss of a key neural gap junction protein via genetic mutation leads to Purkinje neurons that have smaller dendritic arbors and make fewer synaptic connections (Figure 1). Such deficits are certain to cause abnormal circuit computations.

In another study, we showed that *auts2a*, a gene homologous to human *AUTS2* and implicated in Autism spectrum disorders (ASDs), is important for setting neural excitability and maintaining robust and reliable escape behaviours. In zebrafish larvae mutant for *auts2a*, escape command neurons have lowered excitability and fail to fire, thereby affecting the reliability of escapes (Jha et al. 2021). This role of *auts2a* is likely to have parallels in other circuits and other organisms.

Graphical abstract representing experimental design and key results of Sitaraman et al. 2021.



HONOURS AND AWARDS

2018–23 Senior Fellow, Wellcome Trust DBT India Alliance

2020 Shanti Swarup Bhatnagar Award for Biological Sciences

2020–23 Program Committee, Society for Neuroscience

PUBLICATIONS

Sitaraman, S., Yadav, G., Agarwal, V., Jabeen, S., Verma, S., Jadhav, M. and Thirumalai, V. 2021. **Gjd2b-mediated gap junctions promote glutamatergic synapse formation and dendritic elaboration in Purkinje neurons.** Elife, 10, e68124.

Jha, U., Kondrychyn, I., Korzh, V. and Thirumalai, V. 2021. **High behavioural variability mediated by altered neuronal excitability in auts2 mutant zebrafish.** Eneuro, 8(5).

Barheaded geese in Madhai, Satpura Tiger Reserve. This was shot during a fieldcourse in the MSc Wildlife Biology and Conservation Programme by Abhijeet A V

Barheaded Geese

Ecology and Evolution

p. 62–73

The Honey Bee Lab

Axel Brockmann

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

In the last few years, we have established different behavioural paradigms and technical procedures to identify molecular and neural mechanisms involved in behavioural and cognitive capabilities of honey bees. For example, by time-training honey bees and using in-situ hybridisation, we demonstrated that the expression of the transcription factor Egr-1 in the small Kenyon cells of the mushroom bodies likely plays an important role in time-memory. Further, using mass spectrometry, we showed that the same neuromodulatory systems are used in individual search behaviour and social scouting, providing the first experimental evidence to show that social behaviours are based on the same neuronal mechanisms as the corresponding solitary behaviours.

In addition to our work on *Apis mellifera*, we have started ecological and behavioural studies on Asian honey bees, which are the most important pollinators in India. For example, we conducted studies on the geographic distributions of *Apis laboriosa* and bumble bees in the Himalayas. In addition, we published the first-ever comparative study on temporal and spatial foraging activities of the three major honey bee species in India. Together with colleagues from other universities and research institutes, we founded the Indian Pollinator Initiative to promote research and conservation of insect pollinators in India.

Foraging locations of two *A. cerana* (blue), two *A. florea* (red), and one *A. dorsata* (yellow) colonies around the NCBS campus, as inferred from waggle dances.

Large circles depict colony locations and dots indicate foraging locations (Young et al. 2021).

HONOURS AND AWARDS

2020 Associate Editor Frontiers in Insect Sciences - Section Insect Neurobiology

PUBLICATIONS

Chatterjee, A., Bais, D., Brockmann, A. and Ramesh, D. 2021. **Search behavior of individual foragers involves neurotransmitter systems characteristic for social scouting.** Frontiers in Insect Science, 1, 4.

Young, A. M., Kohl, P. L., Rutschmann, B., Steffan-Dewenter, I., Brockmann, A. and Dyer, F. C. 2021. **Temporal and spatial foraging patterns of three Asian honey bee species in Bangalore, India.** Apidologie, 52(2), 503–523.

Genetic and Ecological Factors Underlying Adaptive Evolution

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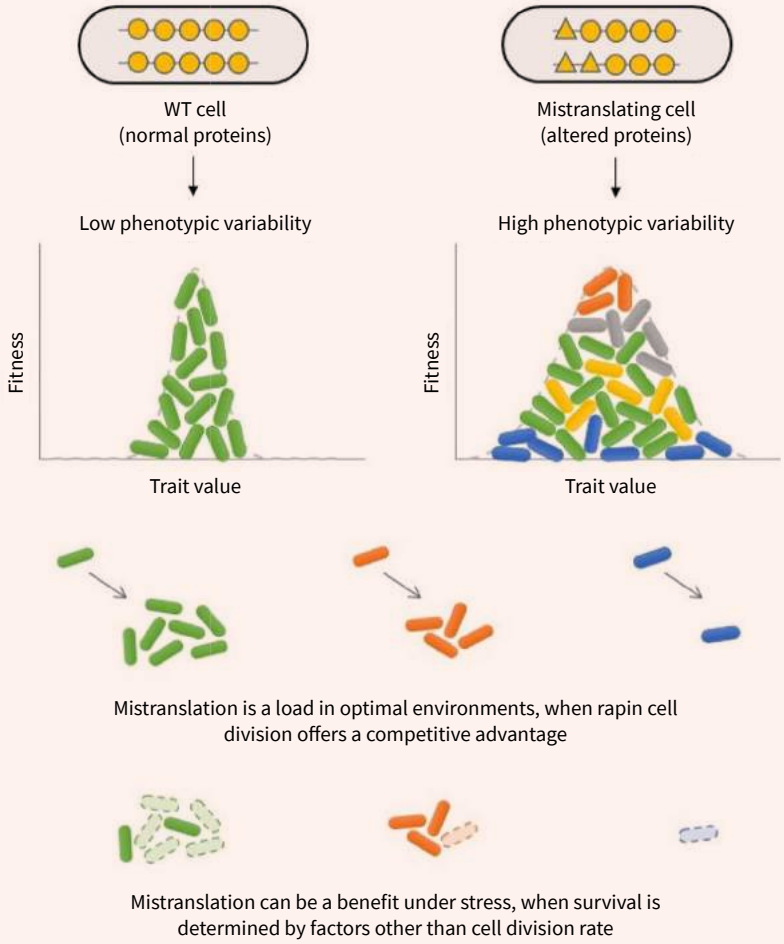
We aim to understand evolutionary processes, focusing on two themes: (a) The drivers and consequences of adaptation to new niches and (b) The evolutionary impacts of translational selection.

In the past year, we continued to analyse the impact of host-bacterial associations on the evolution and ecology of interacting partners. We focused on the red flour beetle, a generalist and widespread insect pest that both consumes and inhabits cereal flours. We found that specific bacterial taxa acquired from the flour are enriched in the beetle gut, and increase host fecundity and lifespan (Agarwal and Agashe, 2020). However, the bacteria are not essential for host survival or reproduction. Thus, changes in the microbiome. E.g. during invasion of a new type of flour, are detrimental but not lethal, setting up the potential for interesting ecological and evolutionary dynamics during microbiome colonization and assembly from environmental sources.

We also continued to analyse the impact of bacterial mistranslation, showing that increased mistranslation increases cell-to-cell as well as between-population variation in key growth parameters (Samhita et al. 2021). Thus, global mistranslation has the potential to alter the course of evolution by influencing the nature and degree of variation available for selection.

Summary of the proposed impact of mistranslation-induced variability on fitness (from Samhita et al. 2021)

Figure 8



HONOURS AND AWARDS

2021–2025 Elected Council Member of the European Society for Evolutionary Biology (ESEB)

PUBLICATIONS

Samhita, L., Raval, P. K., Stephenson, G., Thutupalli, S. and Agashe, D. 2021. **The impact of mistranslation on phenotypic variability and fitness.** Evolution, 75(5), 1201–1217.

Agarwal, A. and Agashe, D. 2020. **The red flour beetle Tribolium castaneum: A model for host-microbiome interactions.** PLoS One, 15(10), e0239051.

ECOLOGY AND EVOLUTION

Speciation, Adaptation, and Morphological Diversification in the Tropical Region

Krushnamegh Kunte

krushnamegh@ncbs.res.in

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

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

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

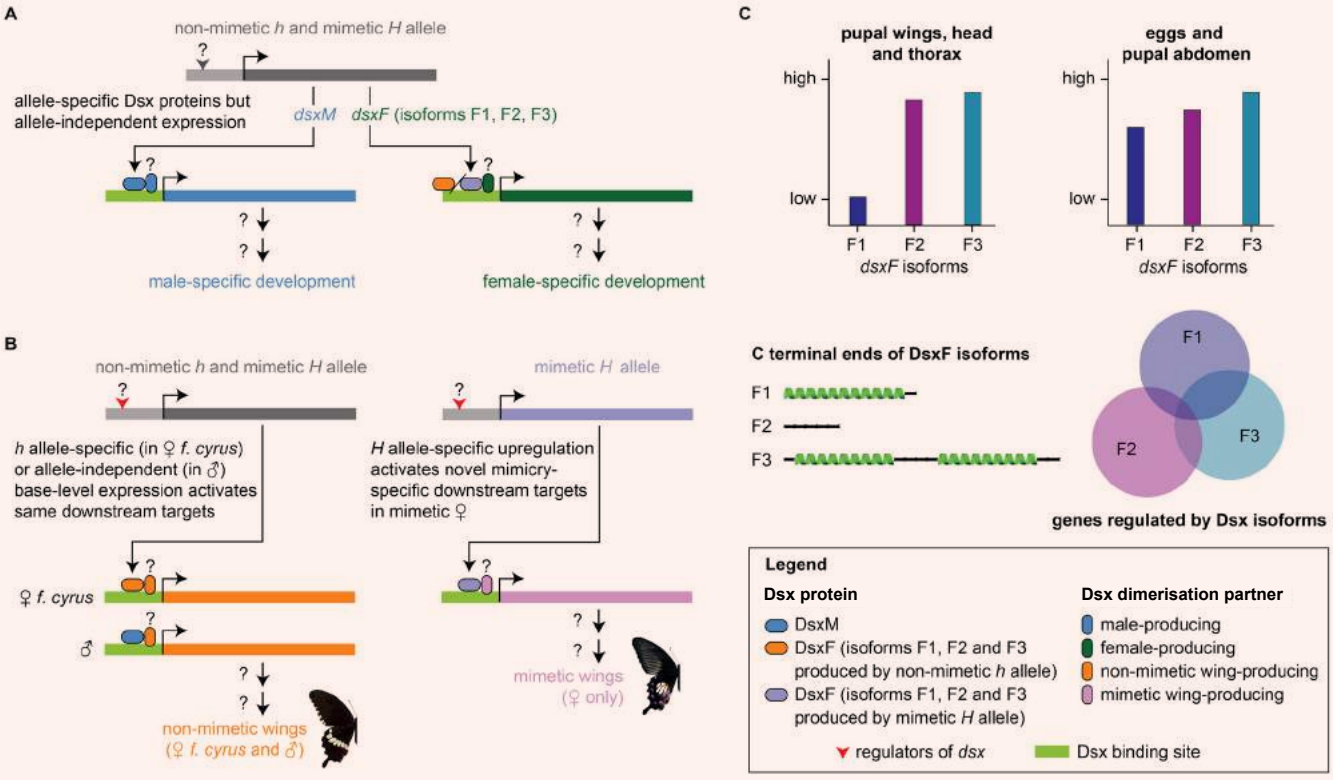
Our second study system is focussed on Indian butterflies. India's butterfly diversity is spread across four globally recognised biodiversity hotspots and offers virtually unlimited opportunities to study biogeography, community ecology, population biology, and conservation issues. Some Indian butterfly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

Proposed mechanism outlining the role of doublesex (*dsx*) in early-development sex differentiation and novel, late-development wing pattern polymorphism in *Papilio polytes*.

(a) Early embryonic sex differentiation and late developmental sex-specific reproductive traits (e.g. genitalia and eggs) are highly canalized and strictly sex-specific, irrespective of allelic polymorphism and alternatively spiced isoforms.

(b) Late developmental novel mimetic wing patterns are produced by a combination of allelic polymorphism, differential expression of alternatively spiced isoforms, and sex-limitation, with mimetic wing patterns expressed only in females that contain at least one copy of the mimetic H allele of *dsx*.

(c) A graphic representation of relative Dsx isoform activity in the regulation of polymorphic wings and other tissues. Dsx F1 is downregulated in relation to F2 and F3 during the production of secondary sexual traits, but expressed comparably during sex differentiation and basic reproductive traits. The C terminal ends of the three DsxF isoforms are different, and their downstream targets are probably different as well. The specific allelic variants, sex-specific and alternatively spliced Dsx proteins, and molecular identities of downstream targets of *dsx* that regulate mimetic wing patterns have recently been identified. This model has several unexplored aspects that need to be studied in the future, including upstream regulators of *dsx* in each context, precise downstream targets, and both allele- and isoform-specific and protein-interacting partners of *dsx*. Such genes, regulators and networks with as yet unknown molecular genetic identities and mechanisms are marked with '?'.



HONOURS AND AWARDS

2020–2021 Earthwatch Institute's Conservation of Species Fellowship.

PUBLICATIONS

Deshmukh, R., D. Lakhe and K. Kunte. 2020. **Tissue-specific developmental regulation and isoform usage underlie the role of doublesex in sex differentiation and mimicry in Papilio swallowtails.** Royal Society Open Science, 7(9):200792.

Hime, P. M., Lemmon, A. R., Lemmon, E. C. M., Prendini, E., Brown, J. M., Thomson, R. C., ... and Weisrock, D. W. 2021. **Phylogenomics reveals ancient gene tree discordance in the amphibian tree of life.** Systematic Biology, 70(1), 49–66.

Terrestrial Ecosystems and Community Ecology

Mahesh Sankaran

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

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

(a) how interactions and feedbacks between climate, biogeochemistry, fires, and herbivory influence the structure, composition, and stability of ecosystems and the cycling and sequestration of nutrients; and

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

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

Photo of our long-term monitoring plot in the Sigur Plateau

Credit: D. Kaikho

Quantifying plant water potential in the field

Credit: D. Kaikho

HONOURS AND AWARDS

2021 Elected Fellow of the Indian National Science Academy

2020 Elected Fellow of the Indian Academy of Science

PUBLICATIONS

Raghurama, M. and Sankaran, M. 2021. **Restoring tropical forest-grassland mosaics invaded by woody exotics.** Restoration Ecology, 29(8), e13491.

Kohli, M., Mijiddorj, T. N., Suryawanshi, K. R., Mishra, C., Boldgiv, B. and Sankaran, M. 2021. **Grazing and climate change have site-dependent interactive effects on vegetation in Asian montane rangelands.** Journal of Applied Ecology, 58(3), 539–549.

ECOLOGY AND EVOLUTION

Tracking the Objects of Insect Affections Across Species and Continents

Shannon Olsson

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

The NICE group listens to nature's chemical conversations across India's diverse ecosystems. This past year saw the culmination of two major projects.

First, as part of a project supported by the Coffee Board of India, we have assessed the ecology and ethology of the Coffee White Stem Borer beetle, which causes up to $40 million in damage to coffee each year. Our work identified features of hosts and non-host plants that can help develop new methods to ecologically control the pests and avoid the extensive use of insecticides while reducing the cost of plantation pest management.

Second, in collaboration with colleagues at University of Notre Dame and the Max Planck Institute for Chemical Ecology, we solved a 150-year-old mystery of how changes in chemical sensing between two populations can lead to speciation. Starting under an apple tree with one of Darwin's classmates, we found that tiny changes in the olfactory system of a fly can lead to changes in behaviour and potentially the beginning of a new species.

In addition to these projects, we continue our work on high-altitude pollination in the face of environmental change, innate object recognition by generalist pollinators, the impact of air pollution on wild systems, and the potential for remediation of microplastic pollution in our oceans through marine sponges.

A Coffee White Stem Borer beetle (*Xylotrechus quadripes*) inspecting a coffee stem, where the females lay eggs and the larvae feed on the wood, damaging or killing the plant in the process.

Photograph courtesy of Santosh Rajus.

An apple fly (*Rhagoletis pomonella*), one of the most well-known models for incipient ecological speciation.

Photograph courtesy of Shoot for Science: Deepak Kakara, Dinesh Yadav, Sukanya Olkar, and Parijat Sil.

HONOURS AND AWARDS

2021 Global Director, the echo network

2021 Founding Member of the Collaborative for Ecosystem-Based Adaptation for Resilient Incomes (EcoBARI)

2020 Counsellor, Asian-Pacific Society of Chemical Ecologists

2020 Member, Sigma Xi Research Honour Society

PUBLICATIONS

Rajus, S., Bhagavan, S., Kharva, H., Rao, S. and Olsson, S. B. 2021. **Behavioural ecology of the coffee white stem borer: Towards ecology-based pest management of India's coffee plantations.** Frontiers in Ecology and Evolution, 9, 17.

Tait, C., Kharva, H., Schubert, M., Kritsch, D., Sombke, A., Rybak, J., ... and Olsson, S. B. 2021. **A reversal in sensory processing accompanies ongoing ecological divergence and speciation in Rhagoletis pomonella.** Proceedings of the Royal Society B, 288(1947), 20210192.

ECOLOGY AND EVOLUTION

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

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

Indian biodiversity: tracking its history, conserving its future.

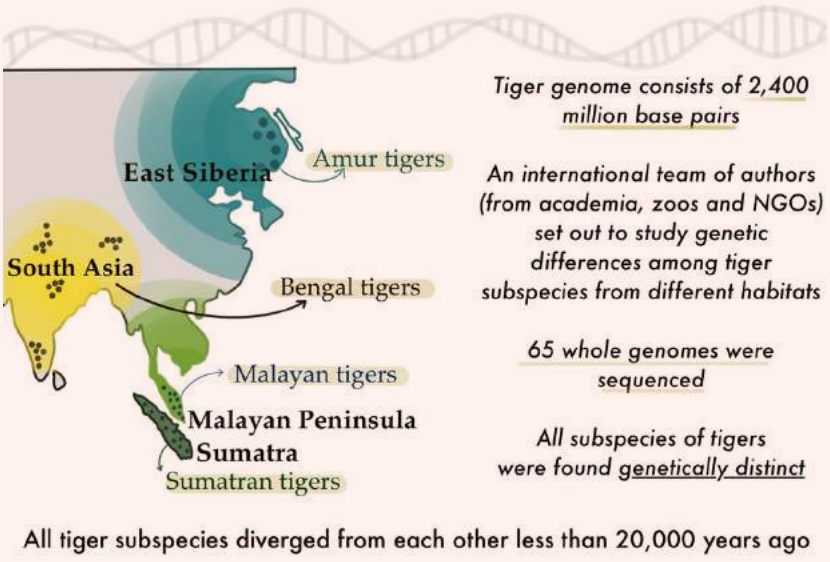
An individual's genome defines it, reflects its evolutionary journey, and can be used to predict its future survival. Today, we are able to completely read the genome of an individual, thanks to novel, cutting-edge genomic sequencing methods. Genomes from several individuals provide information about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

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

A captive pseudomelanistic tiger at Nandankanan Biological Park, Bhubaneswar, India.

Photo captured by Dr. Rajesh Kumar Mohapatra, Biologist, Nandanakana Biological Park (rajesh.wildlife@gmail.com).

An illustration on the main results of Armstrong et al., 2021, by Pallavi Raj Sharma.



HONOURS AND AWARDS

2020 Homi Bhabha Award for Science Education, TIFR

PUBLICATIONS

Sagar, V., Kaelin, C. B., Natesh, M., Reddy, P. A., Mohapatra, R. K., Chhattani, H., ... and Ramakrishnan, U. 2021. **High frequency of an otherwise rare phenotype in a small and isolated tiger population.** Proceedings of the National Academy of Sciences, 118(39).

Armstrong, E. E., Khan, A., Taylor, R. W., Gouy, A., Greenbaum, G., Thiéry, A., ... and Ramakrishnan, U. 2021. **Recent evolutionary history of tigers highlights contrasting roles of genetic drift and selection.** Molecular Biology and Evolution, 38(6), 2366–2379.

This is one of the most threatened hornbill species in India, the Rufous-necked Hornbill. It was shot by Siddharth Srinivasan who is an MSc wildlife student with a keen interested in birds.

Rufous-Necked Hornbill

Biochemistry, Biophysics, and Bioinformatics

p. 76–87

Structure to Signalling: Insights into Bacterial Biology Through RNA Structure

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We are fascinated by all aspects of RNA structure. Using biochemical/ structural approaches, we investigate how RNAs create the chemical complexity required to sense diverse cellular metabolites and proteins, how natural signal-sensing RNAs function, and how these molecules can be exploited to develop RNA-based biosensors.

The continued resurgence of COVID-19 with multiple variants underlines the need for diagnostics that are easily adaptable to the changing virus. Using the concept of toehold RNA-based switches, we have developed RNA biosensors for ultrasensitive detection of SARS-CoV-2 and its prominent variants (Figure 1). In our assay, isothermal amplification of a fragment of SARS-CoV-2 RNA coupled with the activation of our biosensors leads to a conformational switch in the sensor. This leads to the translation of a reporter-protein e.g. LacZ or Nano-lantern, which is easily detected using colour/luminescence. This assay reaches a sensitivity down to attomolar SARS-CoV-2 RNA, which is detected with bright colour that is easily visualised by eye or quantified using a spectrophotometer. This makes our assay deployable all the way from a well equipped laboratory to a low-resource setting anywhere in the world. This PHAsed NASBA-Translation Optical Method (PHANTOM) using our engineered RNA biosensors reports on viral RNA in human patient samples, and compares well with RT-qPCR tests. This work presents a powerful and universally accessible strategy for detecting COVID-19 and its prominent variants.

Moonlighting enzymes link metabolism and RNA-mediated signalling. A prominent example is the TCA-cycle enzyme aconitase, which moonlights via RNA-binding under iron-limitation. By recognizing IRE (Iron Responsive Element) RNAs, found in ferretin/ferroportin/transferrin receptor mRNAs, this system controls iron homeostasis. Few IREs are reported in bacteria even though highly conserved aconitase enzymes are ubiquitous. We set out to identify IREs across bacteria, using covariance-based bioinformatics to search for IRE-like structures in bacterial genomes. Taking a small number of IRE sequences from eukaryotes with the reported bacterial IREs, we determined common structural constraints. By weighting these differences in the covariance search, we have begun to successfully identify IRE RNAs across bacteria (Figure 2). In *Pseudomonas aeruginosa*, an opportunistic pathogen, iron is essential for virulence. Here, we have identified IRE RNAs in the bacterioferretin (bfr) and aconitase mRNA transcripts. We show that the bfr IRE RNA recruits the AcnA enzyme in

the absence of iron. Chemical probing of the RNA and several mutants allowed us to identify a core stem-loop structure that appears to be essential for IRE-aconitase interaction; we also identify features of this stem-loop that are unique to pseudomonas IREs. We find sequence level differences in the AcnA enzymes that make the *pseudomonas* protein unique compared to other bacterial AcnA enzymes. We exploit these protein and RNA differences to understand the basis of IRE-aconitase interactions in pseudomonas.

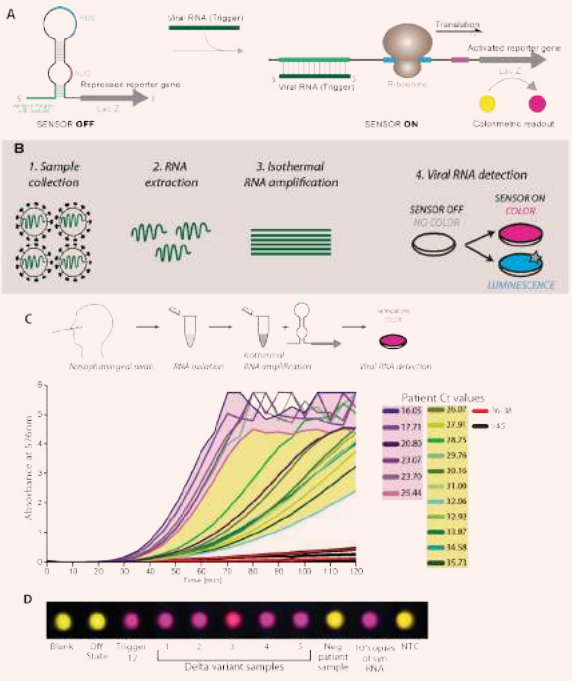

Figure 1
A-B) Toehold RNA based biosensors are designed to specifically sense SARS-Cov-2 RNA. Coupled RNA amplificationand biosensor detection results in attomolar sensitivity.

C-D) Sensors report on COVID-19 (and the prominent Delta variant) in patient nasopharyngeal samples, with easily detectable colour.

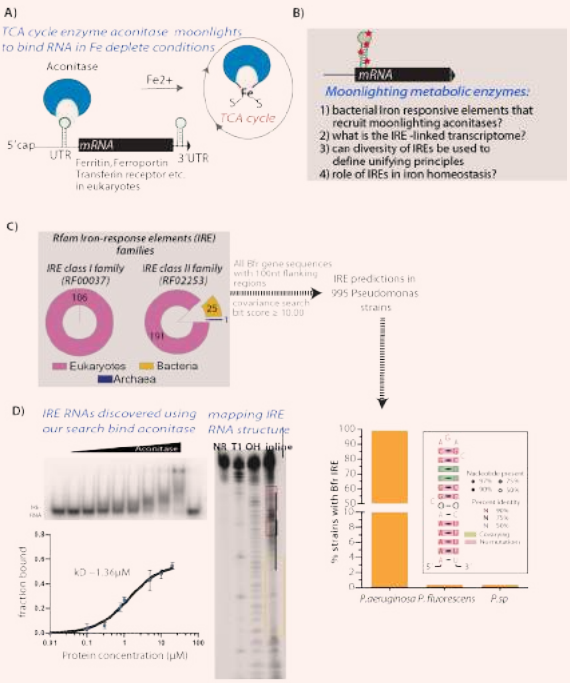

Figure 2
A) Metabolic enzymes that moonlight as RNA-binding proteins:

B) Questions we aim to address in bacteria.

C) Covariance search for IRE RNAs leads to indentification of IREs in *Pseudomonas*.

D) Characterisation of IREs from *Pseudomonas* shows Aconitase A-based control.

PUBLICATIONS

Chakravarthy, A., Anirudh, K. N., George, G., Ranganathan, S., Shettigar, N., Suchitta, U., ... and Ramesh, A. 2021. **Ultrasensitive RNA biosensors for SARS-CoV-2 detection in a simple color and luminescence assay.** Life Science Alliance, 4(12), e202101213.

Mehta, D. and Ramesh, A. 2021. **Diversity and prevalence of ANTAR RNAs across actinobacteria.** BMC Microbiology, 21(1), 1–15.

Adaptation, the Bacterial Way!

Aswin Seshasayee

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

Bacteria adapt to their circumstances by altering their gene expression states or, over longer time-scales, by effecting selection over genotype changes. Changes in the genome occur via various often detrimental processes and bacteria encode mechanisms to address these. One of these is non-homologous end-joining repair (NHEJ), which is a potentially error-prone alternative to the more common homologous recombination. We have used comparative genomics approaches to identify NHEJ components across thousands of sequenced bacterial genomes. NHEJ is sporadically distributed across different classes of bacteria. The last common bacterial ancester is devoid of NHEJ. NHEJ components are acquired multiple times in bacterial evolution, with subsequent losses observed in several cases. Clear evidence of horizontal acquisition of NHEJ is obtained from the presence of these components on plasmids in a limited set of bacteria. Though we could find little evidence for recent horizontal acquisition of chromosomally-encoded NHEJ components, a broader analysis of archaea suggests early horizontal transfers across bacteria and archaea Finally, the presence of NHEJ correlates with genome properties that might limit the availability of a second copy of the chromosome for homologous recombination, the predominant mode of DNA repair in bacteria, to be effective.

In addition to our work on bacterial genomes, we have deployed our expertise in analysing these genomes towards setting up a pipeline for identifying and analysing sequence variants in SARS-CoV-2 genomes.

Figure 1: The sporadic distribution of NHEJ components across the bacterial phylogenetic tree.

From Sharda et al. 2020.

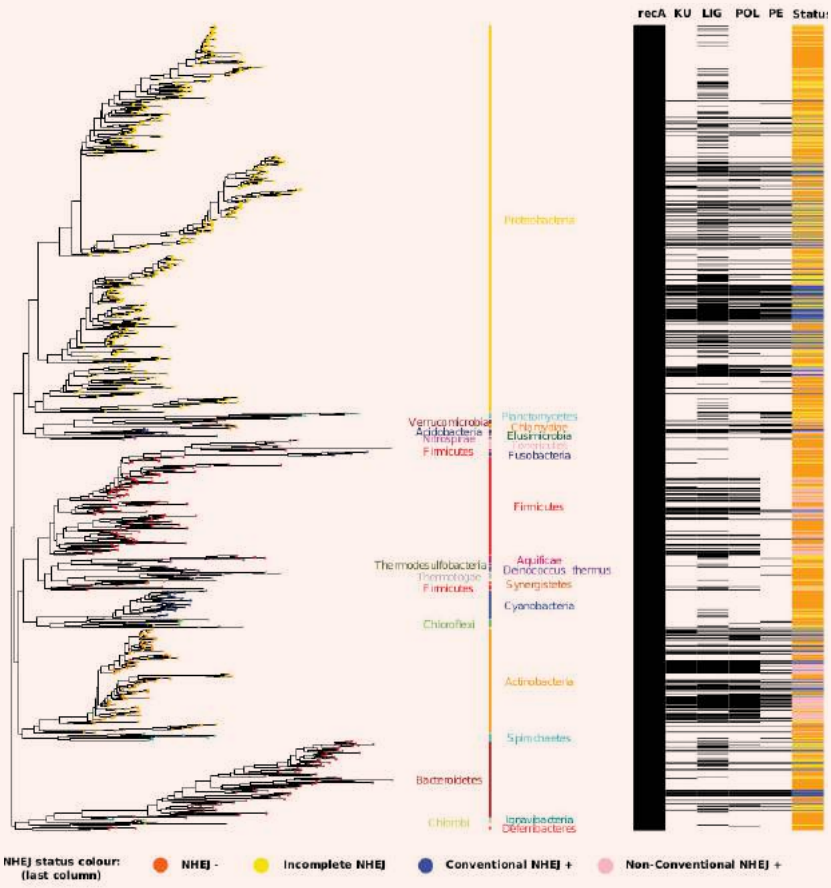
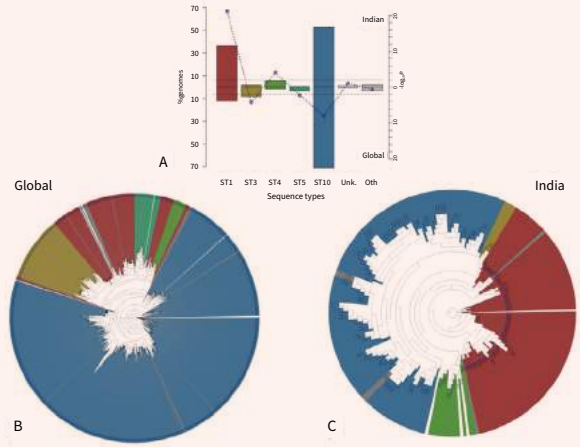


Figure 2: The distribution of SARS-CoV-2 sequence types globally and in India early in the first wave (upto May 2020).



PUBLICATIONS

Sharda, M., Badrinarayanan, A. and Seshasayee, A. S. N. 2020. **Evolutionary and comparative analysis of bacterial nonhomologous end joining repair.** Genome biology and evolution, 12(12), 2450–2466.

Ali, F., Sharda, M. and Seshasayee, A. S. N. (2020). **SARS-CoV-2 sequence typing, evolution and signatures of selection using CoVa, a Python-based command-line utility.** bioRxiv.

Computational Approaches to Protein Science

R. Sowdhamini

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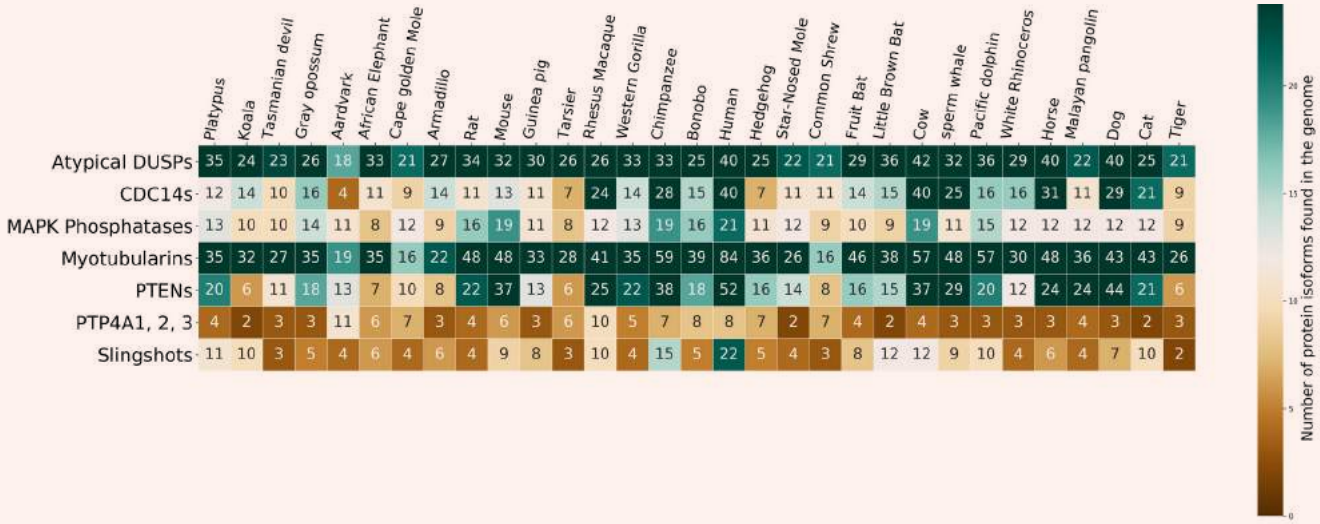
We employ computational algorithms to enable efficient annotation of functions to unknown gene products. Our ongoing and future projects are geared towards modelling protein/ligand interactions with applications in biomedical research and plant genomics, aided by in-depth, collaborative scientific ventures.

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

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

Number of genes with sequence signatures of dual specificity phosphatases in different mammalian genomes (Bhattacharyya and Sowdhamini, 2021), marked within boxes and columns, respectively.



PUBLICATIONS

Bhattacharyya, T. and Sowdhamini, R. 2021. **Genome-wide survey of tyrosine phosphatases in thirty mammalian genomes.** Cellular Signalling, 84, 110009.

Karpe, S. D., Tiwari, V. and Ramanathan, S. 2021. **InsectOR—Webserver for sensitive identification of insect olfactory receptor genes from non-model genomes.** PLoS One, 16(1), e0245324.

Protein Modifications in Host-Pathogen Interactions

Ranabir Das

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

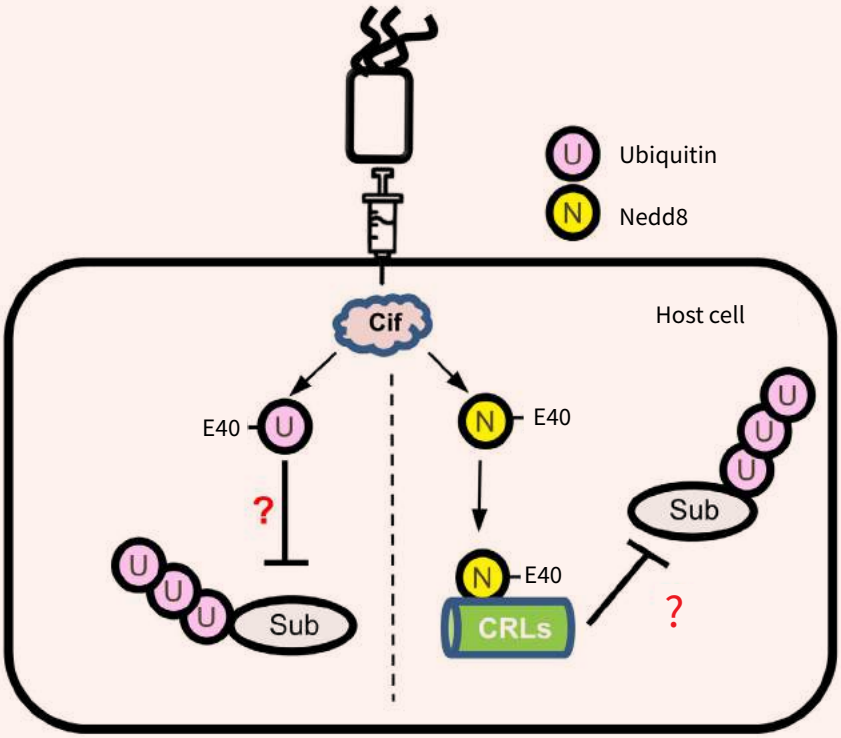
Our group studies the role of post-translational modifications (PTMs) in host-pathogen interactions. Recent results from our lab provided the first structural insights into a collective action of ubiquitination, SUMOylation, and phosphorylation that enhances the activity of the herpes simplex virus protein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

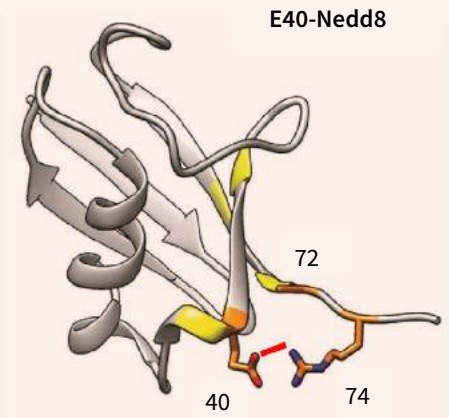
Crosstalk between PTMs is also invaluable for the life-cycle of the human cytomegalovirus, another member of the herpes virus family (Tripathi et al. 2019, Tripathi et al. 2021). A few insect viruses encode a ubiquitin variant—the central player in ubiquitin signalling—to create unique ubiquitin polymers that the host cannot regulate (Negi et al. 2020). Methods have been developed in the lab to measure the kinetics of protein post-translational modifications in real-time with high efficiency (Habibullah et al. 2020, Tripathi et al. 2020).

In a separate study, the lab has uncovered an intriguing mechanism, where deamidation of the host ubiquitin-like protein Nedd8 modulates the dynamics of the Cullin RING ligases to regulate host cycle progression and deplete the host NFkB immune response (Mohanty et al. 2021). We have begun to scratch the surface of the repertoire of PTM crosstalk in host-pathogen interactions. It is of great interest to explore how they modulate the pathogen's life cycle and the host immune response.

Bacterial inactivation of the host ubiquitin and Nedd8 signalling.

Schematic illustration showing the mechanism of ubiquitin/Nedd8 signalling inactivation by bacterial cycle inhibitory factors (Cifs). The Cifs deamidate a particular glutamate residue (Q40) and convert it to glutamic acid (E40) in both ubiquitin and Nedd8. Subsequently, the process of substrate ubiquitination is inhibited. Nedd8 conjugation activates Cullin-RING ligases (CRLs) to ubiquitinate and degrade cell-cycle repressors. However, the deamidation of Nedd8 inactivates CRLs. Recently, we have shown that deamidation creates a new intramolecular salt-bridge in Nedd8, which interferes with its functional interactions and inhibits its activity (Mohanty et al. 2021.)





PUBLICATIONS

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

Mohanty, P., Chatterjee, K. S. and Das, R. 2021. **NEDD8 deamidation inhibits Cullin RING ligase dynamics.** Frontiers in Immunology, 12, 3289.

Deciphering Genetic and Molecular Alterations in Cancers

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

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

We address these questions through the analysis of large-scale cancer genomics datasets (whole genomes, exomes, and transcriptomes) by using computational approaches and functional analyses. We also develop computational methods to integrate different levels of genomic information to identify cancer driver genes and pathways altered in individual patients. In a recent study, with Dr. Murali Bashyam at CDFD, we have analysed the whole-exome sequencing of early-onset sporadic rectal cancers in the Indian population and identified *ARID2* as a novel tumor suppressor (Figure 1).

We are also interested in studying how certain driver genes influence chromatin structure and gene regulation in cancer cells. Recently, we have found that mutant p53 (together with other transcription factors) can affect the local chromatin structure, which results in gain or loss of chromatin accessibility in regulatory regions and subsequent gene expression changes in a tumor-type specific manner (Figure 2).

Figure 1: Frequently mutated cancer genes identified in early-onset sporadic rectal cancers in India.

The heatmap represents the type of protein-affecting mutations observed in each gene (row) and patient sample (column). Genes predicted as putative cancer drivers are highlighted in red.

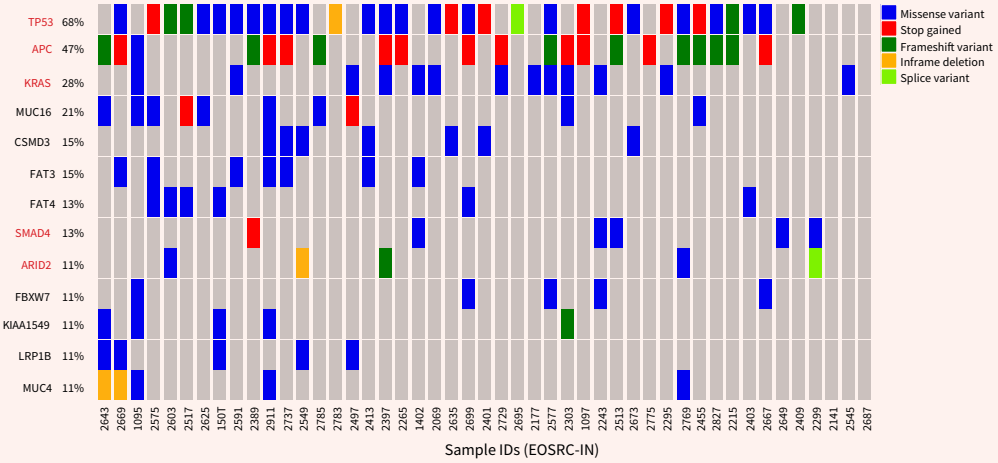
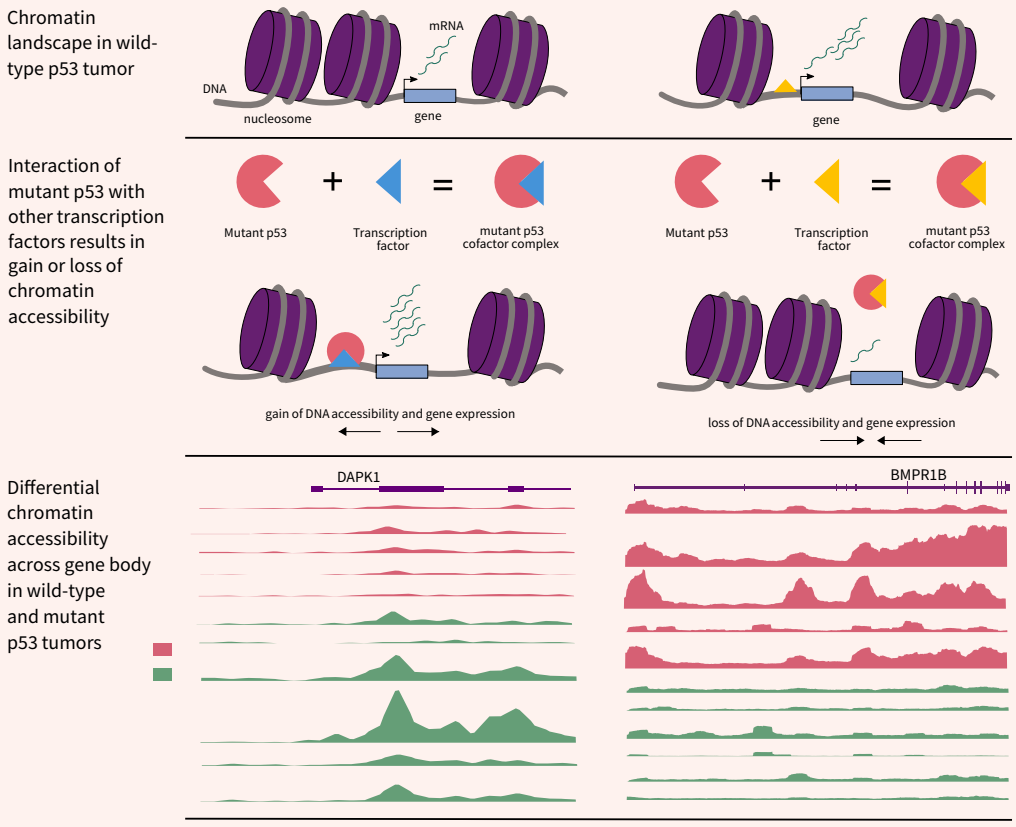


Figure 2: Differential chromatin accessibility in mutant p53 tumors as compared to wild-type p53 tumors in breast-infiltrating ductal adenocarcinoma.



HONOURS AND AWARDS

2021–25 DBT/Wellcome-Trust IA Intermediate Fellowship

PUBLICATIONS

Dhaka, B. and Sabarinathan, R. 2021. **Differential chromatin accessibility landscape of gain-of-function mutant p53 tumours.** BMC Cancer, 21(1), 1–15.

Bala, P., Singh, A. K., Kavadipula, P., Kotapalli, V., Sabarinathan, R. and Bashyam, M. D. 2021. **Exome sequencing identifies ARID2 as a novel tumor suppressor in early-onset sporadic rectal cancer.** Oncogene, 40(4), 863–874.

Structures of Macromolecules and Dynamics

VinothKumar KR

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Our research is driven by the curiosity of how macromolecules function in the cell. We are interested in a wide range of biological problems, from proteins in the membrane that carry out proteolysis and flipping to those that regulate translation and interesting microbial enzymes.

Our broad interest lies in tackling challenging and interesting biological problems, particularly at the membrane interface. Some of the systems we study are intramembrane proteases, the mechanism of peptide resistance in bacteria, membrane junctions, and microbial enzymes with biotechnological potential. We use a number of biochemical and biophysical tools with cryoEM as the major technique. The projects described below highlight some of the work that is being carried out by our group.

High-resolution structures of macromolecules by cryoEM can now routinely be obtained in short period and these are important for deciphering mechanisms and for drug discovery. The structure of an enzyme that is part of the glycine cleavage system is used as an example to illustrate the speed of structure determination with cryoEM and how it can be used to pursue interesting mechanistic questions (Figure 1).

The ability to obtain good grids for cryoEM is still a bottleneck and we have been using human erythrocyte catalase as a test specimen to understand the behaviour of proteins during freezing, as this can result in preferred orientations and exposure to air (Figure 2). We are interested in finding small molecules to mitigate the preferred orientation issue and to prevent protein denaturation at the air-water interface.

Figure 1: CryoEM of an aminotransferase.

(A) Two views of the cryoEM map of a hexameric bacterial aminotransferase, with each monomer coloured individually.

(B) The high resolution of the maps (~2.3 Å) allows modelling of the water molecules (red spheres), with the protein is shown in surface representation.

(C) One monomer of the enzyme is shown in cartoon representation with water molecules in red spheres and bound ligand in stick representation (yellow). In panels B and C, the location of the ligand is marked with a black circle.

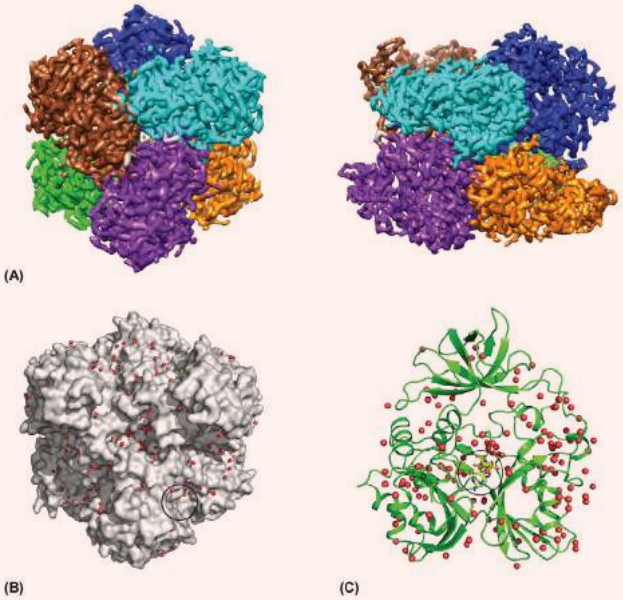
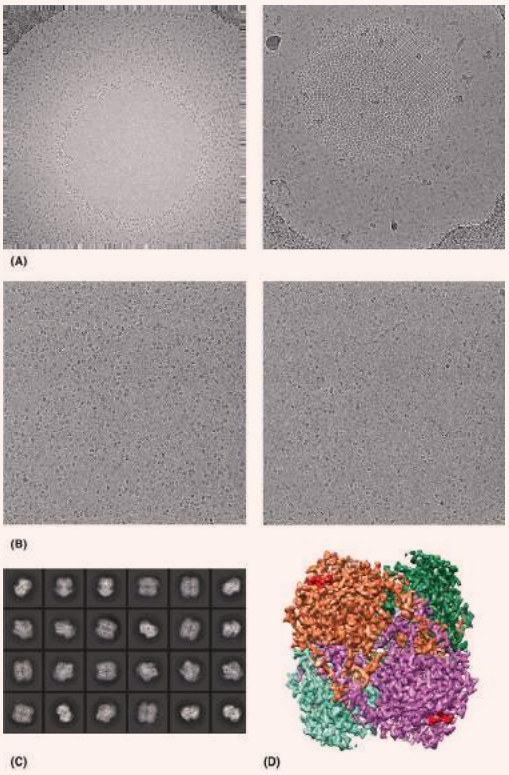


Figure 2: CryoEM of human erythrocyte catalase.

(A) Two micrographs show the behaviour of human erythrocyte catalase during freezing. The molecules tend to adapt preferred orientations.

(B) Use of small molecules as additives can help in overcoming the preferred orientation of molecules and subsequent 2D class averages (panel C) reveal different views and high-resolution features.

(D) Such images can be then used to obtain a high-resolution 3D map of catalase. Each monomer is coloured individually and the NADP molecule is coloured in red.



PUBLICATIONS

Vinothkumar, K. R., Arya, C. K., Ramanathan, G. and Subramanian, R. 2021. **Comparison of CryoEM and X-ray structures of dimethylformamidase.** Progress in Biophysics and Molecular Biology, 160, 66–78.

Nasrallah, C., Cannone, G., Briot, J., Rottier, K., Berizzi, A. E., Huang, C. Y., ... and Lebon, G. 2021. **Agonists and allosteric modulators promote signaling from different metabotropic glutamate receptor 5 conformations.** Cell Reports, 36(9), 109648.

This was shot at Madhai, Satpura Tiger Reserve, during a fieldcourse in the MSc Wildlife Biology and Conservation Programme by Abhijeet A V

Rhesus Macaque

Genetics and Development

p. 90–99

Chromatin Dynamics in Gene Regulation
Dimple Notani

Development and Morphogenesis of the Inner Ear
Raj Ladher

Epigenetics and Small Silencing RNAs
Shivaprasad P V

Investigating the Role of Endothelial Cells in Cardiovascular Regeneration
Soumyashree Das

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

Chromatin Dynamics in Gene Regulation

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

During basal signalling, the transcription factors are present in the nucleus binds in unliganded form (pre-seeds) with enhancers that are initially silent but become active upon ligand (hormone) exposure and thus, shape the signalling response. These enhancers recruit mega-protein assemblies in response to ligands. At the mesoscale, these assemblies are phase-separated enhancer condensates (Saravanan et al. 2020). These findings have enormous scope in understanding the dynamic signalling response and hold promise for therapeutic interventions in disease pathologies that rely on signalling.

Our recent work on the 9p21 locus, which is the most reproducible GWAS (genome-wide association studies) hotspot, has shown for the first time that functional enhancers form equal-weight networks. These findings explain why mutations in certain enhancers are more causal (Farooq et al. 2021). Similarly, using rare genetic variations associated with prostate cancer susceptibility in men of African ancestry, we have shown how rare variants can convert a weak enhancer into a hormone-responsive enhancer that enhances susceptibility to prostate cancer (Walavalkar et al. 2020a, Walavalkar et al. 2020b). Our work demonstrates how enhancers assist in genome organisation into mega base size bins known as topologically associating domains (TADs) (Islam et al. bioRxiv. 2021).

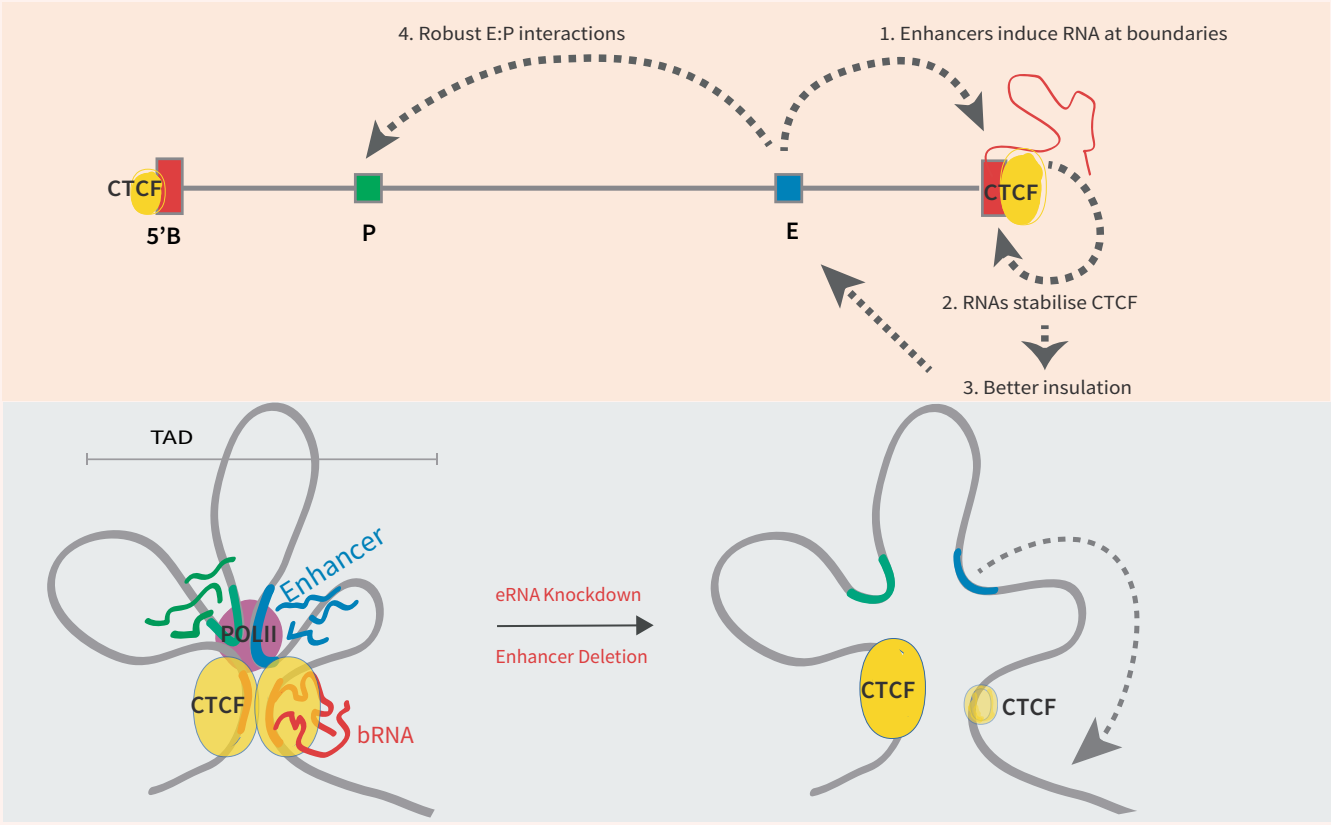
This model depicts that

1. Active enhancer physically interacts with the boundary and activates boundary RNA (bRNA) transcription at the boundary.

2. The bRNA in return stabilises the CTCF at these boundaries,

3. The insulation of these TADs is strengthened.

4. This favors intra-TAD enhancer: promoter interactions to facilitate robust gene transcription. TbRNA/enhancer deletion reduces the bRNA levels, which triggers the loss of CTCF and insulation of TADs. Enhancer:promoter interactions weaken in these scenarios, which causes concomitant loss of gene transcription (Islam et al. 2021).



HONOURS AND AWARDS

2020–24 EMBO Global Investigator

2016–21 Wellcome-IA intermediate Fellowship

PUBLICATIONS

Walavalkar, K., Saravanan, B., Singh, A. K., Jayani, R. S., Nair, A., Farooq, U., ... and Notani, D. 2020. **A rare variant of African ancestry activates 8q24 lncRNA hub by modulating cancer associated enhancer.** Nature Communications, 11(1), 1–14.

Saravanan, B., Soota, D., Islam, Z., Majumdar, S., Mann, R., Meel, S., ... and Notani, D. 2020. **Ligand dependent gene regulation by transient ERα clustered enhancers.** PLoS Genetics, 16(1), e1008516.

Development and Morphogenesis of the Inner Ear

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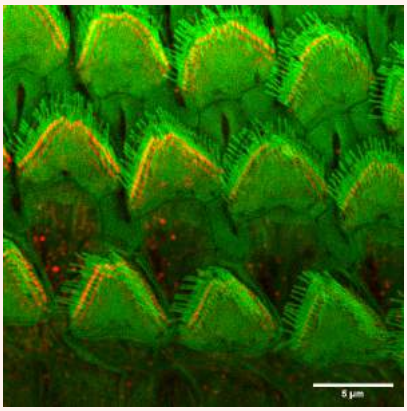
We want to understand the blueprint for making an inner ear, with particular emphasis on how cells integrate extrinsic instructions, the genes that they control, and the cellular and subcellular changes that drive morphological adaptation to mechanosensory function.

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

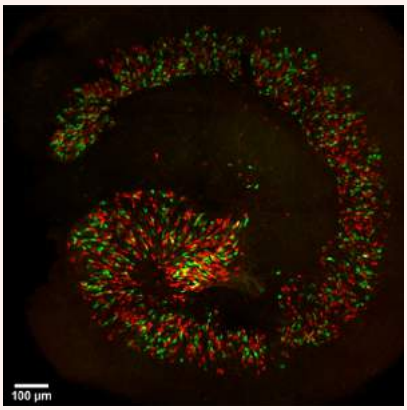
The formation of these cells is also a consequence of instructions. How do inner ear cells receive these instructions and then decode and implement them? What are the physical and molecular responses of cells to these dynamic genetic and epigenetic cues? How can variation be introduced into the development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

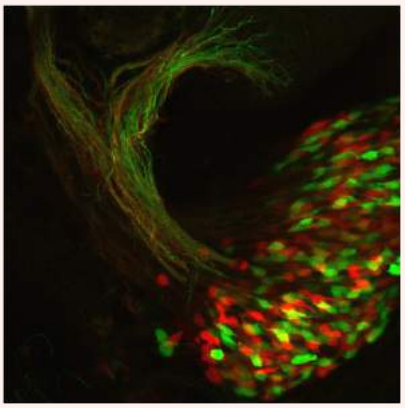
The mechanosensory stereocilia of mouse inner ear hair cells, stained for actin (in green) showing the localisation of the actin bundling protein TrioBP.



Tracing cell lineages in the inner ear.

Stochastic expression of genetically encoded green and red fluorescent protein in the organ of corti (left) and the auditory neurons (right), components of the auditory sensory epithelium in mammals.





PUBLICATIONS

Honda, A., Kita, T., Seshadri, S. V., Misaki, K., Ahmed, Z., Ladbury, J. E., ... and Ladher, R. K. 2018. **FGFR1-mediated protocadherin-15 loading mediates cargo specificity during intraflagellar transport in inner ear hair-cell kinocilia.** Proceedings of the National Academy of Sciences, 115(33), 8388–8393.

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

Epigenetics and Small Silencing RNAs

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

sRNAs are a group of key molecules resulting from RNA silencing pathways. They regulate transcription and translation of their target RNAs by associating with argonaute (AGO) protein effectors. sRNAs are also important factors that initiate and maintain heritable changes in gene expression without changes in DNA sequence (epigenetics). sRNAs and epigenome modifications impact every aspect of eukaryotic development and disease. Our laboratory is interested in understanding the pathways and mechanisms that generate sRNAs and epigenome modifications in plants. We use various biochemical, genetic, bioinformatic, and whole-genome approaches in a wide variety of model plants. During the reporting period, we have uncovered the functions of two new players in plant silencing.

Host encoded RNA-dependent RNA polymerases are special enzymes found in plants, worms, and fungi. They generate double-stranded (ds) RNA triggers for RNA silencing across eukaryotes. Among the three clades, α- and β-clade members are key components of RNA silencing and mediators of stress responses across eukaryotes. However, γ-clade members are unusual in that they are represented in phylogenetically distant plants and fungi, and their functions are completely unknown. Using genetic, bioinformatic, and biochemical methods, we find that γ-clade RNA-dependent RNA polymerases (RDRs) (OsRDR3 and OsRDR4) from rice are involved in development as well as in the regulation of expression of specific coding and non-coding RNAs (Fig. 1; Jha et al. 2021).

Monocots such as rice have additional members of AGO, such as AGO17, functions of which are unknown. AGO17 is highly expressed in reproductive tissues. We find that overexpression of the rice AGO17 results in robust growth and increased yield, whereas its silencing results in reduced panicle length, less fertility, and poor growth. sRNA transcriptome analysis revealed the mis-regulation of several micro (mi) RNAs and other categories of sRNAs in silenced and overexpression lines, in agreement with its likely competition with other AGO1 clade members. Targets of differentially expressed miRNAs include previously unreported target RNAs coding for proteins involved in development, phase transition, and transport (Fig. 2; Pachamuthu et al. 2021).

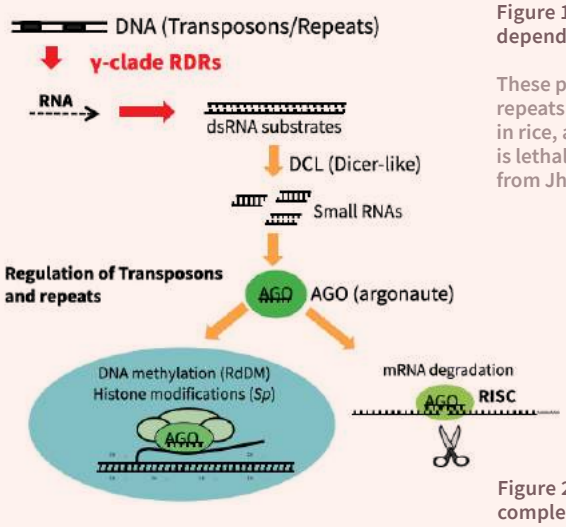
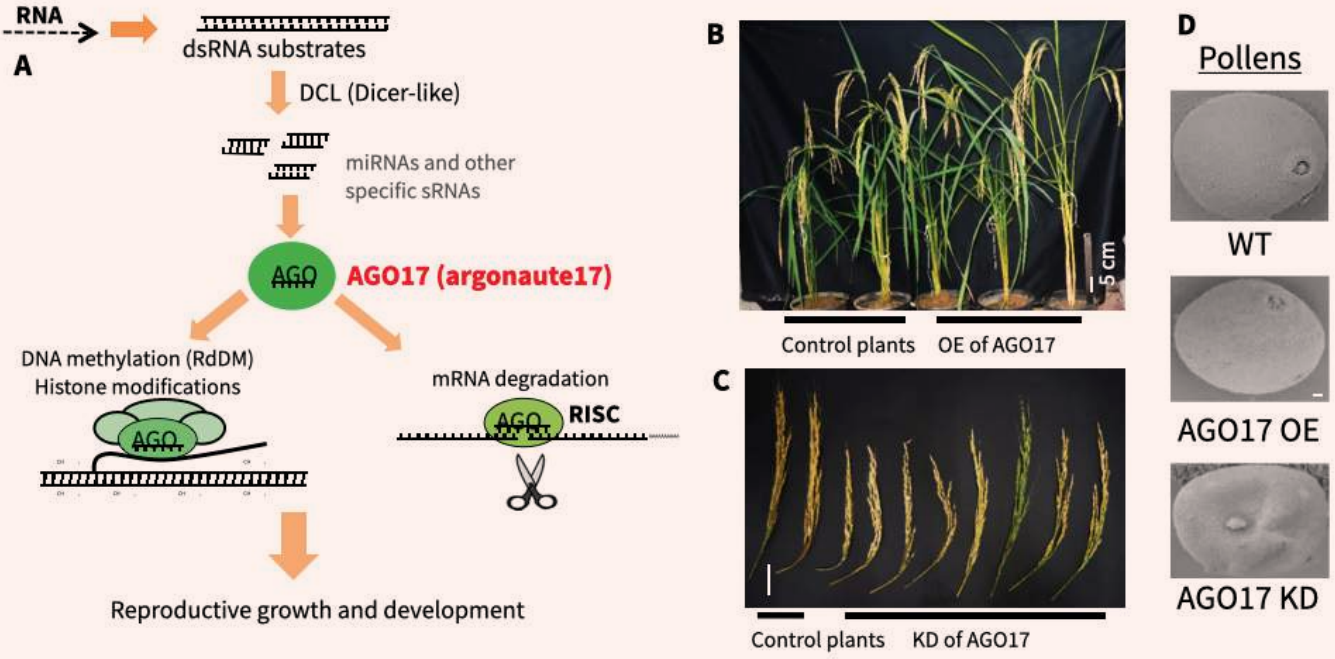


Figure 1 (left): RNA dependent RNA polymerases of γ-clade have both DNA- and RNA-dependent RNA polymerase activities (red arrows).

These polymerases generate dsRNA triggers from transposons and specific classes of repeats in rice genome. We find that they regulate silencing of repeats and transposons in rice, and possibly in other plants. They are crucial for plants, since their knockdown is lethal, while their overexpression improves growth, development, and yield (adapted from Jha et al., 2021).

Figure 2 (below): Argonaute (AGO) proteins are the effectors that form ribonucleoprotein complexes with small (s)RNAs to mediate targeting of complementary nucleic acids.

We show that rice AGO17, the function of which was previously unknown, is involved in the silencing of specific mRNA targets in rice reproductive tissues (A). Knockdown (KD) of AGO17 lead to poor growth, while its overexpression (OE) leads to enhanced growth (B, C). AGO17 is required for normal development of pollens (SEM image, D) (adapted from Pachamuthu et al. 2021).



PUBLICATIONS

Jha, V., Narjala, A., Basu, D., TN, S., Pachamuthu, K., Chenna, S., ... and Shivaprasad, P. V. 2021. **Essential role of γ-clade RNA-dependent RNA polymerases in rice development and yield-related traits is linked to their atypical polymerase activities regulating specific genomic regions.** New Phytologist, 232(4), 1674–1691.

Pachamuthu, K., Swetha, C., Basu, D., Das, S., Singh, I., Sundar, V. H., ... and Shivaprasad, P. V. 2021. **Rice-specific Argonaute 17 controls reproductive growth and yield-associated phenotypes.** Plant Molecular Biology, 105(1), 99–114.

Investigating the Role of Endothelial Cells in Cardiovascular Regeneration

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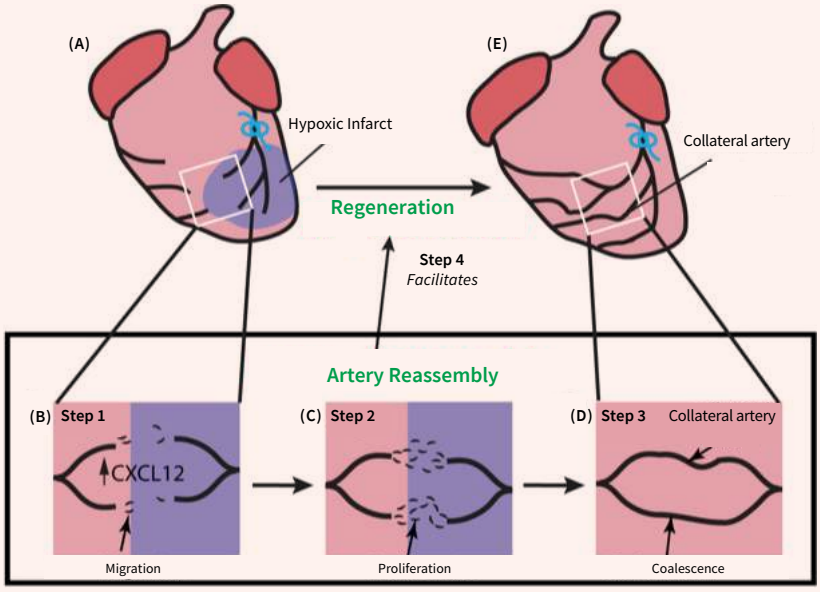
We investigate the cellular and molecular mechanisms utilised by endothelial cells (ECs) during coronary vascular remodelling, in development and disease. We use genetic mouse models, whole organ imaging, and cardiac functional assays to understand how ECs contribute to cardiac regeneration.

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

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

Artery Reassembly, a multi-step artery endothelial cell process, drives cardiac regeneration (Modified from Das et al. 2019).

(A, B) Neonatal myocardial infarction develops hypoxic tissue (purple), followed by (B) induction of CXCL12 in the watershed, outward migration of artery ECs, (C) their proliferation and (D) coalescence into collateral arteries. Collateral formation by artery reassembly facilitates (E) neonatal heart regeneration.



PUBLICATIONS

Red-Horse, K. and Das, S. 2021. **New research is shining light on how collateral arteries form in the heart: A future therapeutic direction?** Current Cardiology Reports, 23(4), 1–5.

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

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

We endeavour to assemble a layered view of the principles of development culminating in behaviour. Muscles, the nervous system, and their interplay at cellular and molecular resolution remain our focus, using *Drosophila*.

In *Drosophila* indirect flight muscles, the coordinated assembly of the contractile apparatus of myofibrils starts in the pupae. In collaboration with Benny Shilo and Eyal Schejter's groups at the Weizmann Institute of Science, Israel, our observations highlight a role for microtubules in the establishment of myofibril and sarcomere spatial patterns and size (1).

Ataxin2 (Atx2) mediates ribonucleoprotein granules assembly and disassembly, which when misregulated correlates with muscle and neuro degeneration. In collaboration with Mani Ramaswami's group at Trinity College Dublin, we have found its targets and stabilizing function is possibly mediated by the 3' UTR and domains that have opposite roles in RNP formation (2). We have uncovered the *Drosophila* neural circuitry underlying habituation to sweet taste. Inhibitory inputs to the motor neurons mediate responses that are weak for novel stimuli but potentiated for familiar stimuli.

In collaboration with Maneesha Inamdar's group at JNCASR, we have uncovered challenge-specific functions and heterogeneity in immune cell progenitor pools of *Drosophila* larvae.

Figure 1
A. The detailed spatial organisation of filaments can be seen as magnified views of the boxed regions panel G. Cross-sectioned microtubules are seen below. (orange-shaded hollow circles, myosin (green arrowheads) and actin filaments (pink arrows). (1)

B. *Drosophila* S2 cells expressing Atx2 protein with a C-terminal SNAP tag. Atx2DLsm form large cytoplasmic granules:

(i) that are much larger than WT Atx2 granules (ii). Atx2 with an additional Lsm domain in place of the middle intrinsically disordered region (mIDR) to create 2XLsm forms smaller granules compared to WT Atx2 in S2 cells (iii). deletion of cIDR domain blocks Atx2 granule formation (iv). (2)

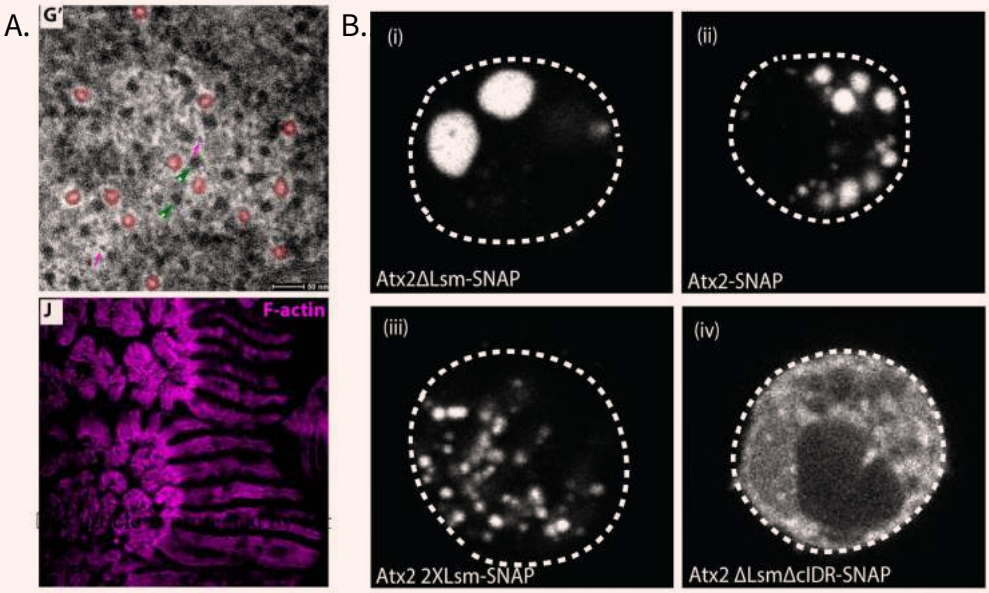
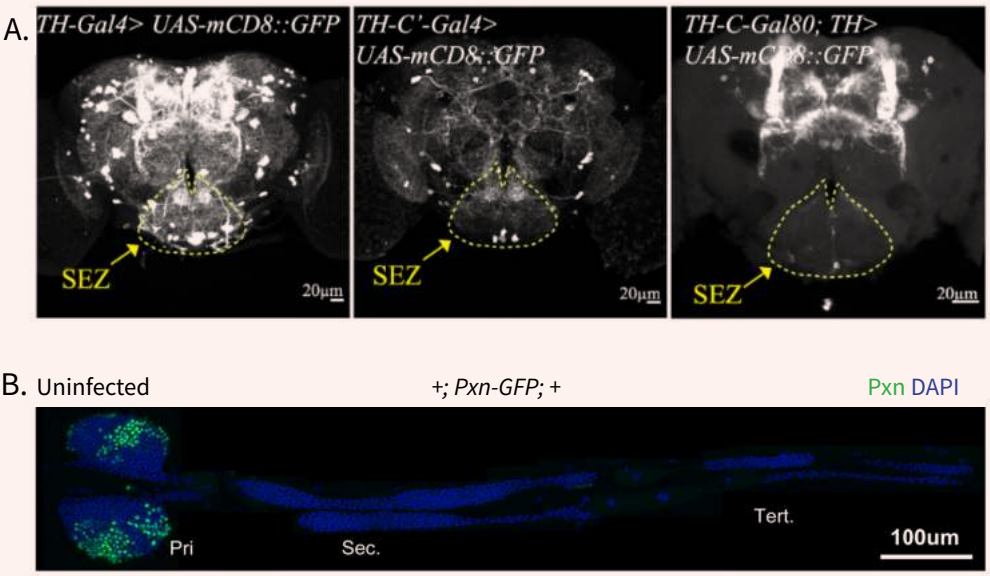


Figure 2
A. Combining TH-C-Gal80 with TH 657Gal4 blocks expression in TH-C' subset of neurons only, as observed by GFP expression658 (SEZ represents subesophageal zone). (3)

B. Toll/NF-kB or Notch or JAK-STAT signalling reporter activity (green) in the lymph gland lobes. (4)



PUBLICATIONS

Dhanyasi, N., VijayRaghavan, K., Shilo, B. Z. and Schejter, E. D. 2021. **Microtubules provide guidance cues for myofibril and sarcomere assembly and growth.** Developmental Dynamics, 250(1), 60–73.

Singh, A., Hulsmeier, J., Kandi, A. R., Pothapragada, S. S., Hillebrand, J., Petrauskas, A., ... and Bakthavachalu, B. 2021. **Antagonistic roles for Ataxin-2 structured and disordered domains in RNP condensation.** Elife, 10, e60326.

This shot was taken at the Mandara Hostel (NCBS), Bangalore by Abhijeet A V

Apis *dorsata*

Cellular Organisation and Signalling

p. 102–109

Microbial DNA Damage Response and Repair
Anjana Badrinarayanan

Phosphoinositide Signalling in Cell Biology
Raghu Padinjat

Mechanisms of Membrane Organisation and Endocytosis
Satyajit Mayor

Biology of Host-Pathogen Interactions during Intracellular Infections
Varadharajan Sundaramurthy

Microbial DNA Damage Response and Repair

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

Central to life is the propagation of genetic material. Thus, cells must ensure faithful duplication and segregation of DNA across generations. The importance of this process is highlighted by the presence of checkpoints to regulate cell cycle progression and cell division, coupled to the surveillance of genome maintenance. Checkpoints for genome integrity maintenance are universally conserved across domains of life, as are the mechanisms for repair and error correction. Although repair is essential for genome maintenance, some pathways are also sources of mutagenesis. Thus, cells must regulate repair pathway choice (to ensure that the appropriate pathway is employed during repair) and control the activity of error-free and error-prone repair systems (to ensure balance between genome integrity maintenance and rates of stress-induced mutagenesis). This becomes particularly relevant in microbial systems that live in constantly fluctuating environments, where modulation of these pathways can have a significant impact on cellular adaptation and survival under stress.

Successful DNA repair requires three steps to occur accurately:

(a) regulation of cell cycle to ensure that cells do not divide before repair has been completed;

(b) repair pathway choice to ensure that the right pathway is employed to repair damaged DNA;

(c) modulation of activity of error-free and error-prone repair systems to maintain genome integrity while also increasing chances of survival under stress.

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

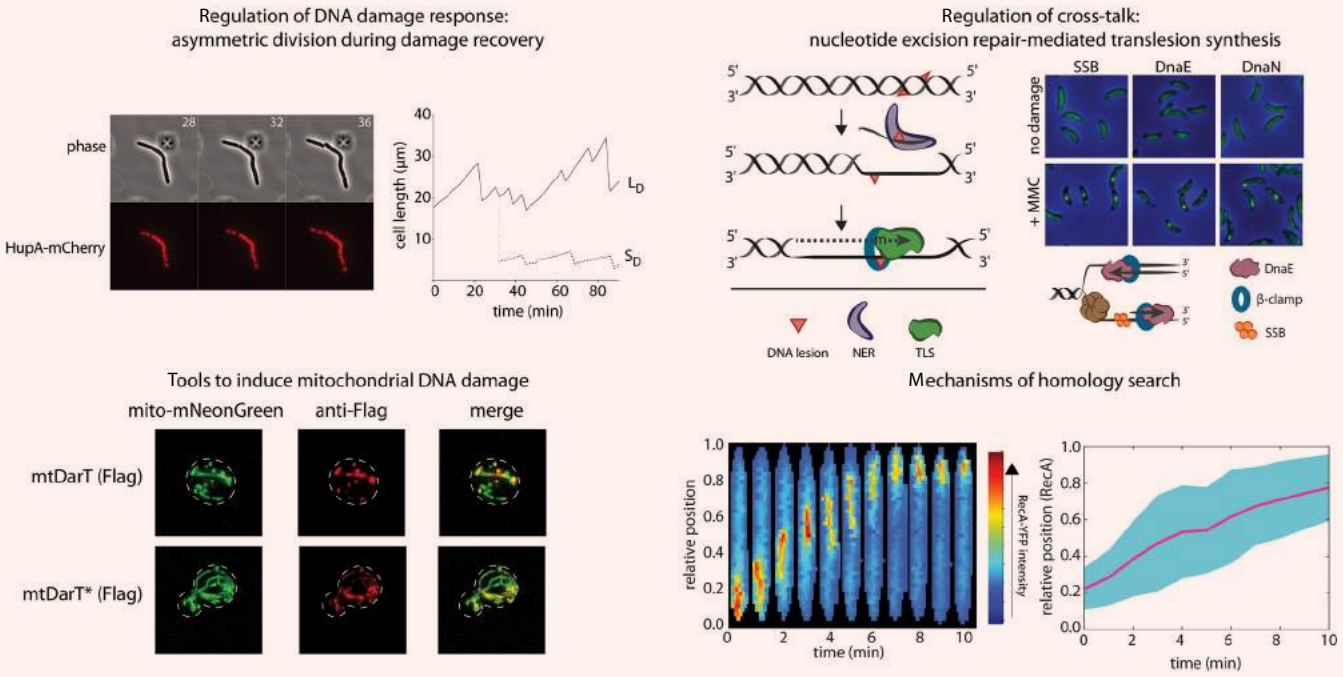
Some questions we are currently working on are:

Damage response and cell cycle regulation

- Understanding the bacterial adaptive response
- How is mitochondrial DNA damage sensed and DNA repair regulated?

Repair pathway choice and regulation

- Regulation of error-prone translesion synthesis and its crosstalkwith other repair pathways in bacteria
- Mechanism of homology search: role of the SMC protein, RecN



Representative schematics and figures from some ongoing projects in the lab.

HONOURS AND AWARDS

2021 DBT-Wellcome India Alliance Intermediate Fellowship

PUBLICATIONS

Chimthanawala, A., Parmar, J., Kumar, S., Iyer, K. S., Rao, M. and Badrinarayanan, A. 2021. **SMC protein RecN drives translocation and remodelling of RecA filament for homology search.** bioRxiv.

Joseph, A. M., Daw, S., Sadhir, I. and Badrinarayanan, A. 2021. **Coordination between nucleotide excision repair and specialized polymerase DnaE2 action enables DNA damage survival in non-replicating bacteria.** Elife, 10, e67552.

Phosphoinositide Signalling in Cell Biology

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

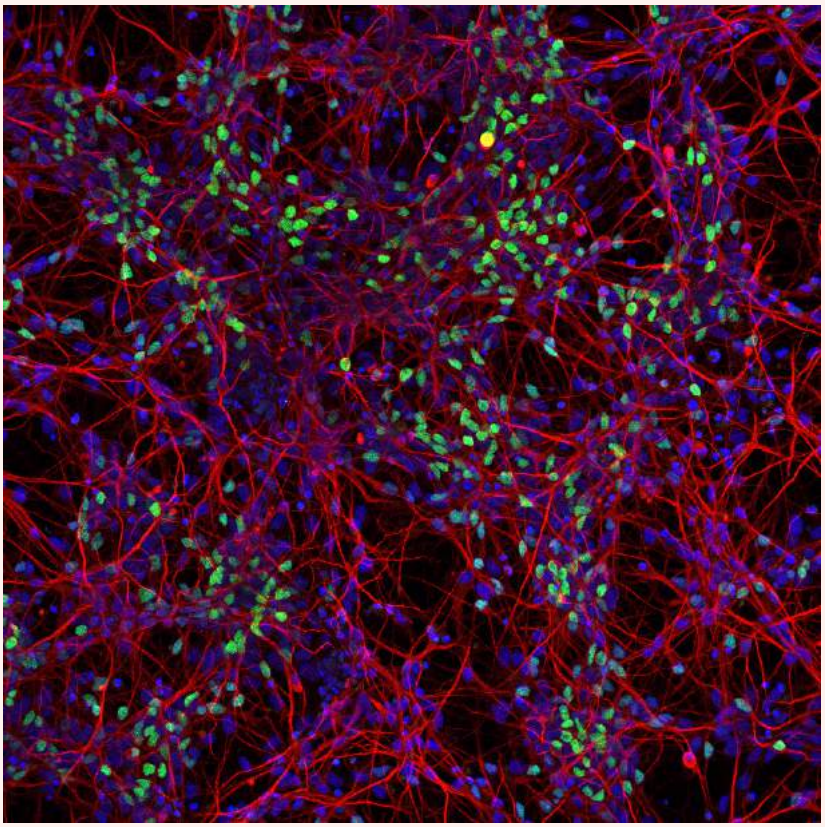
Our long-term scientific interest is to understand cellular communication mediated by lipid molecules generated by the metabolism of phosphatidylinositol. Phosphoinositide signals provide molecular control for key subcellular processes such as membrane remodelling, cytoskeletal function, transcription,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

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

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

Cultures of human stem cell-derived neural cells at 30 days in vitro.

Neurons are marked by the mature neuronal marker MAP2 (red) and deep layer specific marker CTIP2 (green).



PUBLICATIONS

Trivedi, D., Vinitha, C. M., Bisht, K., Janardan, V., Pandit, A., Basak, B., ... and Raghu, P. 2020. **A genome engineering resource to uncover principles of cellular organization and tissue architecture by lipid signaling.** Elife, 9, e55793.

Nath, V. R., Mishra, S., Basak, B., Trivedi, D. and Raghu, P. 2020. **Extended synaptotagmin regulates membrane contact site structure and lipid transfer function in vivo.** EMBO Reports, 21(9), e50264.

Mechanisms of Membrane Organisation and Endocytosis

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

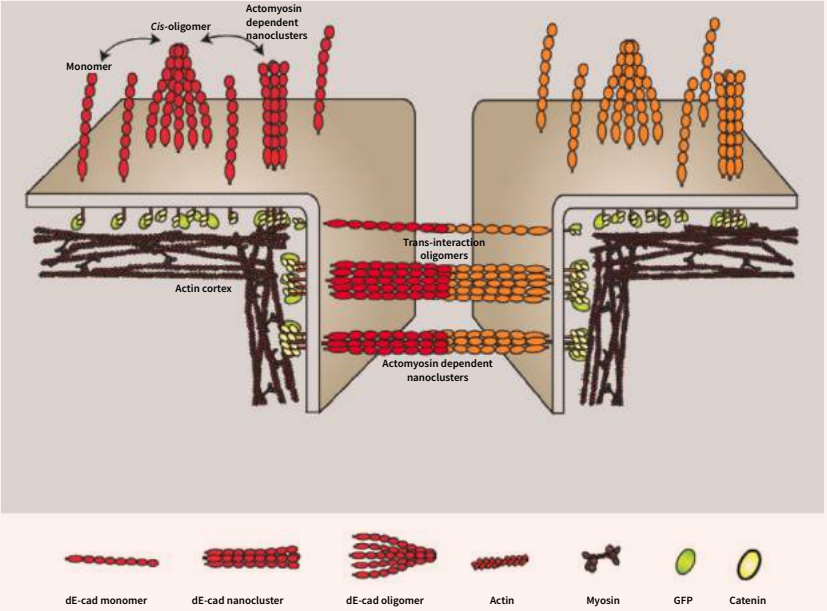
The plasma membrane is the hub of signalling processes mediating bilateral information transfer and endocytic activities. We continue to study how local membrane heterogeneities arise and how endocytic trafficking is regulated in a membrane that resembles a macromolecular assembly teeming with activity and local heterogeneities. Our studies provide a compelling picture of the cell membrane as an active composite of the lipid bilayer with a dynamic cortical actin layer beneath, wherein, dynamic actin filaments help in controlling the local composition of the membrane, and endocytic processes help regulate global composition and tension in the membrane.

Specifically, we have investigated the organisation and dynamics of a transmembrane cell adhesion protein E-cadherin, using various biophysical techniques such as Forster's Resonance Energy Transfer (homo-FRET) and Fluorescence Correlation Spectroscopy (FCS) adapted to a microscope. We found that E-cadherin expressed in a tractable model system such as *Drosophila* hemocytes forms cortical actin-dependent nanoclusters at both the nanoscale (~10 nm) and the mesoscale (100-300nm). These arise from an interplay between protein-protein aggregation, diffusion, and active clustering behaviour of the protein (Chandran et al. 2021). Such an active organisation provides a tunable mechanism governing the strength of cell-cell adhesions. This is likely mirrored in the embryonic epithelia, where dynamic dE-cadherin based adherens junctions are continuously being remodelled during development.

Exploiting our deep understanding of endocytic pathways and processes, my laboratory colleagues teamed up with the laboratories of Varadha Sundaramurthy, Arjun Guha, Praveen Vemula, and Ram Vishwakarma from IIIM, Jammu, to identify FDA-approved drugs that could modify cellular entry of SARS-CoV-2 by inhibiting endosomal acidification process (Prabhakara et al. 2021). These drugs are now in advanced stages of clinical trial.

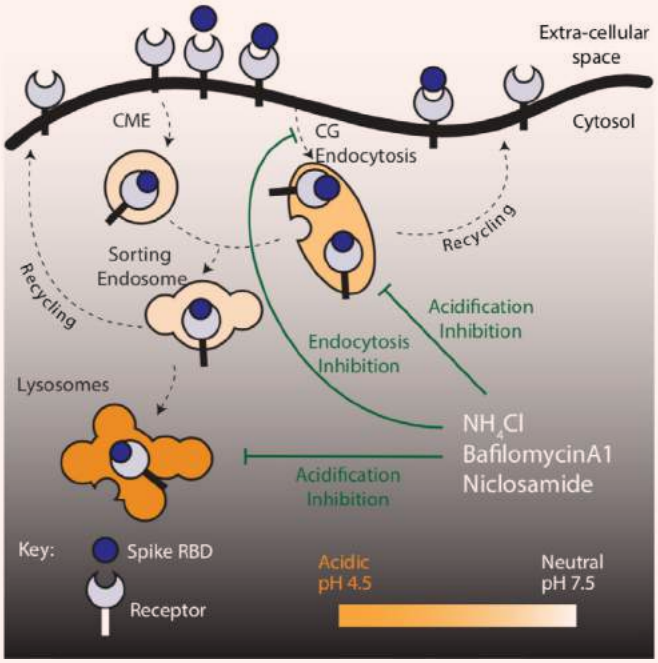
The schematic shows that *Drosophila* E-cadherin forms two kinds of nanoscale assemblies: loosely packed oligomers and dense nanoclusters.

Extracellular *cis* interactions produce oligomers, and cytoplasmic interactions with actomyosin remodel the oligomers into nanoclusters, which are necessary for regulating strong, stable cell adhesions.



The receptor binding domain of the spike glycoprotein of the SARS-CoV-2 virus interacts with receptors at cell surface and is internalised via the CLIC/GEEC(CG) pathway.

Acidification inhibitors neutralise the pH of endosomes and block entry via the CG pathway. Niclosamide, a protonophore and an FDA-approved drug, also increases the pH of endosomes and blocks uptake via the CG pathway. Spike pseudovirus infection assays confirm that acidification inhibitors, including Niclosamide, prevent viral transduction.



PUBLICATIONS

Chandran, R., Kale, G., Philippe, J. M., Lecuit, T. and Mayor, S. 2021. **Distinct actin-dependent nanoscale assemblies underlie the dynamic and hierarchical organization of E-cadherin.** Current Biology, 31(8), 1726–1736.

Prabhakara, C., Godbole, R., Sil, P., Jahnavi, S., Gulzar, S. E. J., van Zanten, T. S., ... and Mayor, S. 2021. **Strategies to target SARS-CoV-2 entry and infection using dual mechanisms of inhibition by acidification inhibitors.** PLoS Pathogens, 17(7), e1009706.

Biology of Host-Pathogen Interactions During Intracellular Infections

Varadharajan Sundaramurthy

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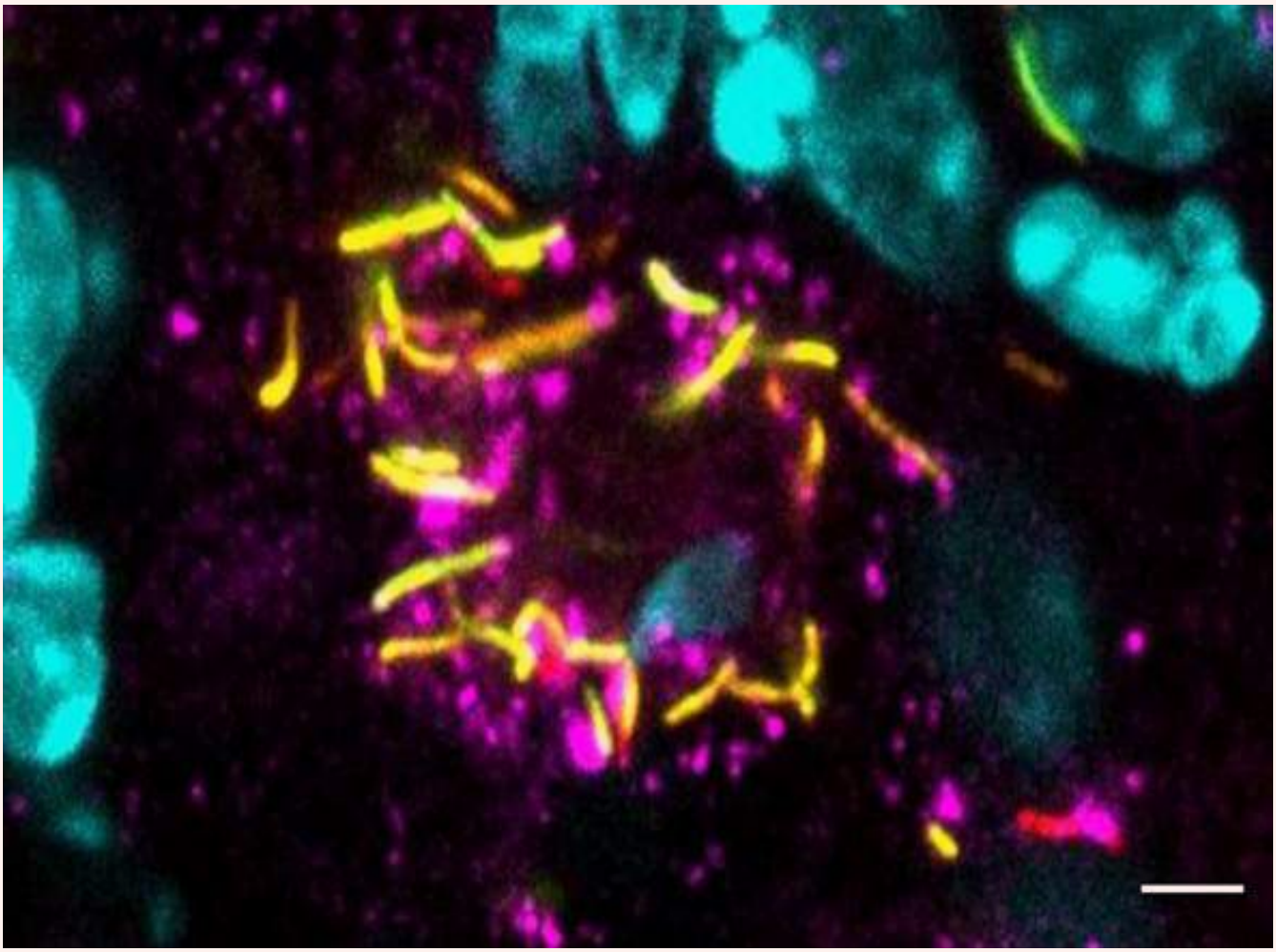
The broad goal of our lab is to understand the interactions between intracellular pathogens and host cells, with a particular interest in the modulation of host cellular pathways. We exploit this knowledge for host-directed therapeutics against infectious diseases.

My lab works on host-pathogen interactions, specifically on how fundamental host cellular processes such as trafficking (endocytosis, autophagy, and lysosomes) are modulated by intracellular infections. We combine cell biological methods, high content imaging, and computational approaches with conventional cell and molecular biology tools. We address distinct aspects of these interactions at the molecular, cellular, and tissue scales across a broad range of intracellular pathogens including virus (SARS-CoV-2), bacteria (*M. tuberculosis*), and parasites (*Plasmodium* spp, liver stage). Simultaneously, we aim to exploit this knowledge for drug discovery to identify small molecules that can be used as adjuncts in host directed therapeutics.

Our recent results show a requirement of a functional endo-lysosomal pathway for the uptake and survival of many intracellular pathogens, while these pathways are concomitantly and actively modulated and altered by the pathogens. These alterations include subcellular redistribution of specific endosomal pools and an increase in the numbers and contents of distinct endosomal populations specifically in the infected cells. In case of *M. tuberculosis* infections, the endosomal system influences the infectivity of the pathogen, and lysosomes distinctly modulate their intracellular survival. Abrogation of these alterations by chemical modulation results in killing of the pathogen in further enhancing their survival. Thus, the host-pathogen interface represents a finely nuanced space where two dynamic systems reciprocally influence each other. Current work in the lab is centred on addressing specific examples of these interferences, and in exploiting this knowledge to identify small molecules that can be potential host-directed therapeutic agents.

Section from M. tuberculosis (green) infected mouse lung immunostained for the autophagosome marker LC3 (magenta). Nuclei are stained with DAPI (cyan).

Scale bar is 5 µm



PUBLICATIONS

Prabhakara, C., Godbole, R., Sil, P., Jahnavi, S., Gulzar, S. E. J., van Zanten, T. S., ... and Mayor, S. 2021. **Strategies to target SARS-CoV-2 entry and infection using dual mechanisms of inhibition by acidification inhibitors.** PLoS Pathogens, 17(7), e1009706.

Subhash, N. and Sundaramurthy, V. 2021. **Advances in host-based screening for compounds with intracellular anti-mycobacterial activity.** Cellular Microbiology, e13337.

Sloth Bear

A sloth bear cools off in a pool during the hot summers. This was shot by Aditi Prasad, who is a PhD student and works on tigers at the Ranthambore Tiger Reserve.

New Faculty

p. 112–119

Mechanisms of Electrical Synapse Formation, Regulation, and Function
Abhishek Bhattacharya

Emergence and Control in Development and Evolution
Archishman Raju

Organelle Biology: Implications in Physiology and Diseases
Swadhin Jana

Active Living Material in Complex Environments
Tapomoy Bhattacharjee

Mechanisms of Electrical Synapse Formation, Regulation, and Function

Abhishek Bhattacharya

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We are investigating the fundamental principles regulating formation, diversification and functioning of electrical synapses, which is a conserved, critical, yet much understudied feature of the nervous system to ultimately better understand how the nervous system works.

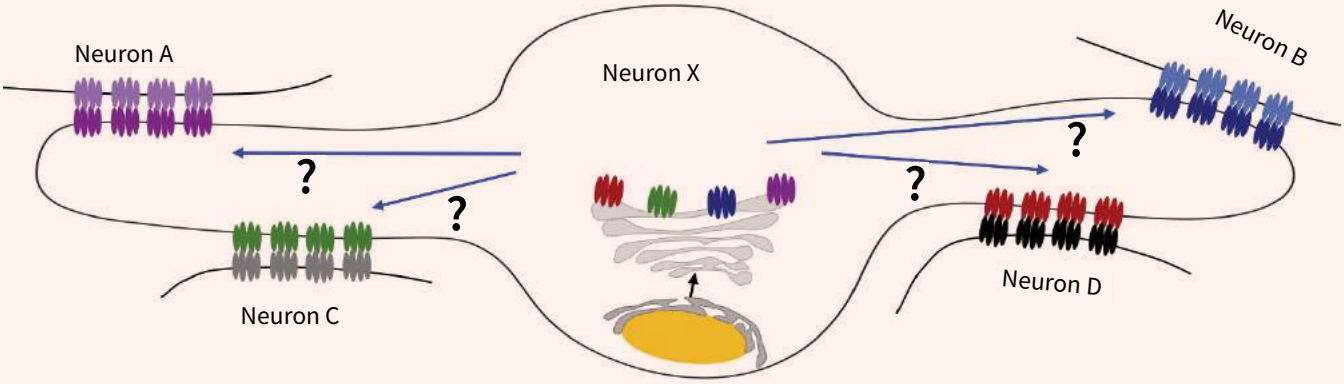
Cellular communication in a nervous system is primarily governed by chemical and electrical synapses. While the complex biology of chemical synapses has been widely studied, electrical synapses have remained understudied, despite playing conserved and critical roles in the establishment and functioning of the neural circuit. Our overall research goal is to understand the fundamental molecular principles regulating the assembly and functioning of the electrical synapse connectome, areas that are still very poorly understood.

I found that members of the innexin gene family, which encodes the components of multimeric electrical synapses channels, are expressed in a complex, neuron-type-specific combinatorial pattern in the *C. elegans* nervous system. Moreover, individual neurons often simultaneously express multiple electrical-synapse-channel-components and utilise them to form molecularly distinct synapses with specific partner neurons.

By utilising the specific strengths of *C. elegans* as a model organism, we intend to understand the underlying molecular determinants that enables individual neurons in a connectome to form molecularly, and thereby functionally distinct, electrical synapses with different synaptic partners; how plastic changes in the electrical synapse network are achieved in response to intrinsic and extrinsic cues and how electrical synapses on glial cells then regulate nervous system development and function.

An individual neuron 'Neuron X' may utilise different electrical-synapse-channel-components to form molecularly distinct synapses with specific partner neurons A, B, C, and D.

What are the underlying molecular mechanisms required to achieve such component-specific or synapse-specific diversity?



Emergence and Control in Development and Evolution

Archishman Raju

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I am interested in the theoretical modelling of cell fate specification during development, both to make more parsimonious representations of data as well as to clarify broader concepts.

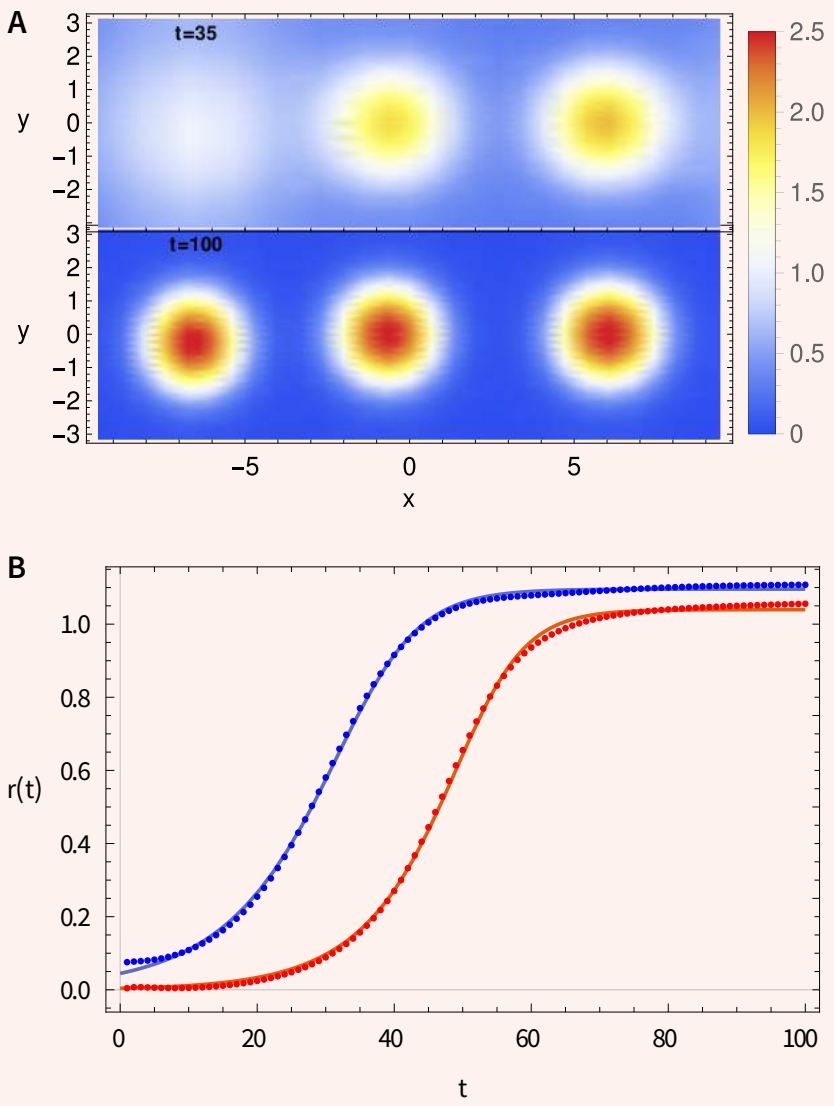
The modelling of cell fate specification in biology is often done using gene regulatory models, which try to model the detailed interactions of known genetic components. I have been working on an alternative proposal which mathematically formalises the geometry of the 'Waddington landscape'. This organises several different models in developmental biology under a common framework, showing the potential universality of such descriptions. It is also useful to fit experimental data on cell fates and brings out the common geometry of different biological processes.

Waddington's landscape had consequences not simply for development but also for evolution. He argued that the landscape would allow for 'genetic assimilation' and faster evolution, which he partially tried to demonstrate with his experiments in *Drosophila*. I am currently working on whether this idea can be formalised and differentiated from traditional population genetics models.

The relevant behaviour of Turing patterns is geometrically in a low dimensional space.

(A) A simulation of a model of Turing pattern formation in two dimensions, which shows the emergence of three spots that are asymmetrical in space and time.

(B) Our theory predicts that all of the complexity of the two-dimensional behaviour in space can be collapsed onto one differential equation independent of space, which has a universal form. The solid curves show the theoretical curve and the points are obtained from numerical simulations.



PUBLICATIONS

Rand, D. A., Raju, A., Saez, M., Corson, F. and Siggia, E. D. 2021. **Geometry of Gene Regulatory Dynamics.** Proceedings of the National Academy of Sciences, 118(38), e2109729118.

Organelle Biology: Implications in Physiology and Diseases

Swadhin Chandra Jana

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We, the Organelle Biology Laboratory (OBL), investigate the mechanisms for building, diversifying, evolving and maintaining organelles, primarily cytoskeleton, centrosome, cilia (we fondly call them 3Cs), in the developmental, physiological, and pathological conditions in organisms through a multifaceted approach.

Essential eukaryotic structures, the cytoskeleton, centrosome, cilium, mitochondria, and lysosome, are implicated in numerous human diseases, including degenerative diseases, cancer, and ciliopathies (they affect one in every three individuals). Affected individuals have a reduced quality of life, and their treatment places a significant financial burden on healthcare systems and patients' families. Despite these organelles importance to human health, our knowledge of their roles in pathologies is limited.

The OBL primarily focuses on the cytoskeleton, centrosome, and cilium. Numerous signalling processes vital for organism development and homeostasis are regulated by centrosomes that organise the cytoskeleton of cycling cells and by cilia that act as cellular antenna, with various functions. We, for example, ask:

1) What controls the organisation of several critical building blocks of 3Cs?

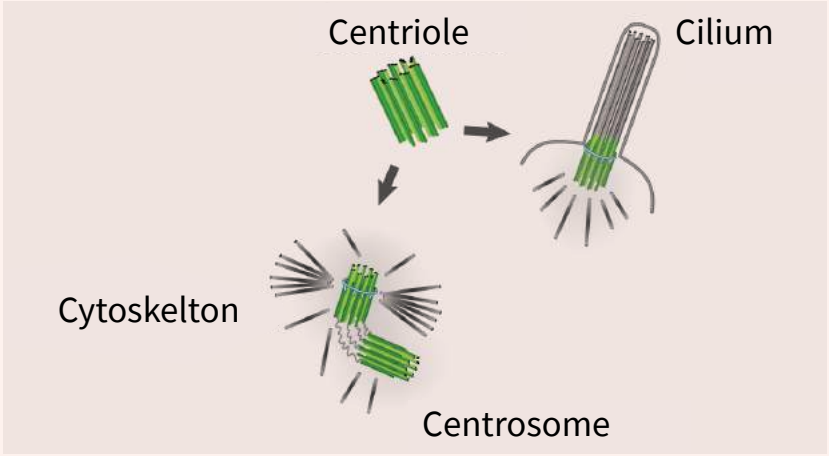
2) How are different portions of these structures assembled?

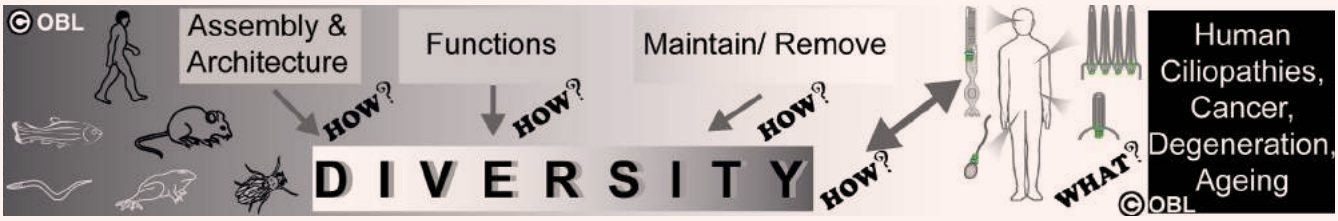
3) How are these vital structures maintained and why do they go awry in pathological conditions? We apply a combination of approaches/techniques/tools (biophysics, biochemistry and bioinformatics, genetics, transcriptomics, proteomics, advanced imaging, electrophysiology, and animal behaviour). We also apply our acquired knowledge in chemical biology, biomedicine, and biotechnology.

Figure 1 (top): Scheme shows the dual life of centriole in centrosome and cilium.

Centrosomes are evolutionarily conserved centrioles surrounded by pericentriolar material (PCM) and act as major cytoskeleton organising centres. During 'centrosome-to-cilium' conversion (C2Cc), some centrioles acquire critical structures to become the base of the cilia.

Figure 2 (below): The scheme displays a few questions the OBL address.





HONOURS AND AWARDS

2018–22 Principal Investigator, FCT Research Grant, FCG-IGC, Portugal

PUBLICATIONS

Jana, S. C., Dutta, P., Jain, A., Singh, A., Adusumilli, L., Girotra, M., ... and Ray, K. 2021. **Kinesin-2 transports Orco into the olfactory cilium of Drosophila melanogaster at specific developmental stages.** PLoS Genetics, 17(8), e1009752.

Jana, S. C. 2021. **Centrosome structure and biogenesis: Variations on a theme?.** In Seminars in Cell & Developmental Biology (Vol. 110, 123–138). Academic Press.

NEW FACULTY

Active Living Material in Complex Environments

Tapomoy Bhattacharjee

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We aim to discover new physical and biological principles emerging from the interactions between mammalian cells, bacteria, and their microenvironments. We use bioprinting techniques to create designer multicellular systems and probe them at three-dimensional biological interfaces.

We aim to explore the basic principles that control how mammalian cells and bacteria behave in a complex 3D microenvironment. We design and fabricate biomimetic 3D media to mimic the natural habitats of mammalian cells and bacteria. We fine-tune the material properties of the media to explore how cells respond to changes in their microenvironments. Leveraging the self-healing properties of our 3D media, we have developed a custom-built 3D-printing process. We can design complex 3D structures of any types of mammalian cells and bacteria. Combining this bioprinting platform with confocal microscopy, we aim to explore a spectrum of interesting areas that include understanding the dynamics of biomimetic gels, exploring bacterial growth and response to antibiotics in 3D, designing long-term cultures of 3D-printed tissues, studying the interaction between microbes and mammalian tissues in 3D, and investigating mechanically assisted maturation of tissues. Our lab is a diverse group of people working at the interface of engineering, physics, biology, and materials science.

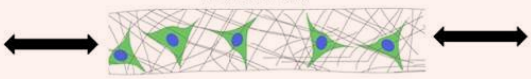
Our lab will aim to design 3D structures out of mammalian cells and bacteria and probe them at various physical and chemical conditions.

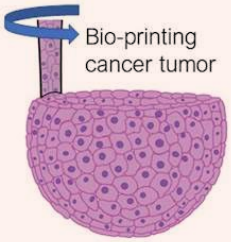
Designer communities at 3D bio-interfaces

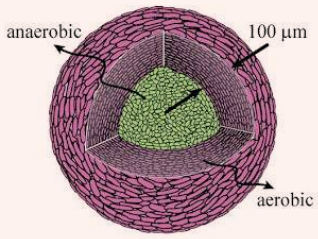
Design multicellular communities
controlled size, shape and spatial composition

Bacterial colony at competing gradient

Microtissue

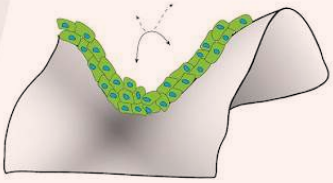




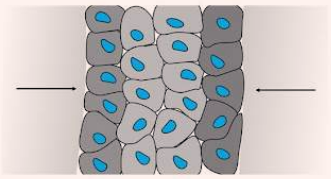


Probe at complex biological interfaces
- Competing chemical gradients
- Curved, deformable interfaces
- Oscillatory mechanical stimuli
- Ecological emulsions

deformable interfaces



transport in tissue



Explore scientific questions
- Transport at 3D bio-interfaces
- Self assembly, maturation and failure
- Evolution and adaptation

HONOURS AND AWARDS

2021 Member of the Community Engagement Committee, Division of Biological Physics, American Physical Society

PUBLICATIONS

Bhattacharjee, T. and Datta, S. S. 2019. **Bacterial hopping and trapping in porous media.** Nature Communications, 10(1), 1–9.

Bhattacharjee, T., Zehnder, S. M., Rowe, K. G., Jain, S., Nixon, R. M., Sawyer, W. G. and Angelini, T. E. 2015. **Writing in the granular gel medium.** Science Advances, 1(8), e1500655.

Indian Scops Owls

Indian Scops Owls in a roost at Madhai, Satpura Tiger Reserve. This was shot during a fieldcourse in the MSc Wildlife Biology and Conservation Programme by Abhijeet A V.

Administration and Academics

p. 122–145

Administration, Procurement, and Finance

G Ravi Shankar
Head, Administration and Finance

NCBS-TIFR was established as a Centre of TIFR in 1991, as approved by the Union Cabinet. In the three decades since its establishment, NCBS-TIFR has grown into an exceptional Centre of Excellence in the disciplines of biological sciences. Its faculty, past and present, have considerably influenced the advancing research frontiers in biological sciences, nationally and internationally. It has always been understood that for the research and academic activities of the Centre to flourish and expand, the Administration (includes Purchase and Hospitality divisions) and Finance Divisions need to be continuously geared up to provide effective, efficient, and sustained support at all times. That has been all the more true in the face of the devastating pandemic that has disrupted lives, livelihoods, and the economy across the globe.

We came across new challenges due to the pandemic, which called for a sustained focus on the safety and health of all members of the BLiSC campus while also ensuring that the duties of the various divisions continued.

Despite the financial crisis, limitations in manpower, and limited visiting hours, the Centre was able to cater to the needs of the students, faculty, and staff deployed at NCBS. All the departments in Administration and Finance continue to work towards streamlining the administrative processes and achieving the desired results. We are happy to note the staff have been able to meet the new challenges posed by the pandemic and resulting safety procedures. An increase in the complexity of tasks that hinged on various individuals and operational units across the institution have been met by the dedication of our teams.

The procurement division played a major role in mobilising materials for COVID-19 swab and saliva testing, and sequencing in a timely and efficient manner. There was continuous support with the procurement of specialised equipment for all the scientific research, with expertise in the finalisation of contracts and agreements. The staff showed a great deal of initiative in dealing with the unexpected and an abiding commitment towards providing effective services to the campus researchers for all projects.

When the management decided to start the campus COVID-19 vaccination drive, it was a new challenge for us. Facilitating the vaccine drive for the campus community required coordination with the Bruhat Bengaluru Mahanagara Palike (BBMP) and other health departments in the city. A particular challenge was the transport of adequate vaccine doses to the

Campus Medical Centre during the initial phases of the vaccination drive. Nonetheless, by September 2021, 83% of campus personnel were fully vaccinated and some of their family members as well.

Another important effort to ensure the safety of campus members was the commute to and from work. Through the provision of cab, shuttle, and buggy services during the pandemic-related lockdowns, we were able to reduce the risks faced by the researchers and other staff while commuting.

Additionally, by introducing work from home (WFH) options within NCBS, the staff were able to continue working in versatile modes, to the benefit of the Centre. The Human Resource Module put in place during 2020–2021 helped the NCBS staff work with flexibility, and this has resulted in greater efficiency and productivity across the staff.

The details of manpower as on 31st March, 2021 is as follows:

Particulars	Sanctioned Positions	Filled Positions	Vacancies	Deputation	Pachmarhi Field Station
Academics	40	34	6	2	0
Scientific & Technical	69	34	35	0	1
Administrative	33	23	10	0	1
Auxiliary	5	5	0	0	6
Total	147	96	51	2	8

Contract Staff

Temporary contract staff	76
Manpower deployed through various oursourced agencies	381

Even in the midst of such a tumultuous time, the financial performance for the financial year 2020–2021 was satisfactory. The funding constraint remained one of the key challenges, further aggravated this year in the wake of economic disruption due to the pandemic. Initiatives undertaken by NCBS to support COVID-19-related research projects, the establishment of a testing facility, and the development of novel strategies and protocols for testing, etc. put additional strains on finances. But thanks to the undaunting support of the Department of Atomic Energy, TIFR, and several philanthropic corporate contributions, NCBS was able to successfully achieve most of the envisaged objectives and activities for the year, and meet its societal obligations in these challenging circumstances.

NCBS continues to comply with stipulated statutory and non-statutory regulations of the regulatory framework, and there was no adverse reporting on any of the issues included in the Audit Reports for the financial year.

During the year, 50 new grants were added to the ever-growing list of extramural support. The Department of Biotechnology, Science and Engineering Research Board, Department of Science and Technology, Department of Health Research (GoI), Wellcome Trust-DBT India Alliance, Wipro Foundation, Simons Foundation, The Human Frontier Science Program, University of Edinburgh, Action on Hearing Loss, UK, and The Open University, London were the major contributors in the extramural category. Shri N R Narayana Murthy, the co-founder of Infosys, has been financially and morally supporting the Dengue Vaccine Development Programme through his generous contributions. Shri. Gopalakrishnan and Smt. Sudha Gopalakrishnan, Trustees of Pratiksha Trust, continued their generous support this year in helping the cause of world-class research in neurobiology. Also, our special thanks to M/s TNQ Technologies Pvt. Ltd. for helping us realise our long-cherished dream of setting up the Obaid Siddiqi Chair (in the History and Culture of Science) at the Archives at NCBS, through extensive financial support.

We take this opportunity to express our deepest gratitude and appreciation to all our supporters (financial, moral, and intellectual) for their continued support and generosity, and for the faith and confidence they place in NCBS.

Further, we would like to highlight the vital and timely support of Indian corporations, including the Nuclear Power Corporation of India Ltd.,

The Administration and Finance Team

Azim Premji Philanthropic Initiatives Pvt. Ltd., Standard Chartered Global Business Services Pvt. Ltd., and IQVIA RDS (India) Pvt. Ltd., for their extraordinary support and generous contributions to COVID-19 research and testing activities. This support is what made it possible for NCBS, right at the beginning of the crisis, to participate in the COVID-19 response and testing effort from our campus. Our ability to deploy funds from these contributions made it possible to benefit more than 1 lakh people, meeting testing requests from the Karnataka state as well as the BBMP. The tests were provided free of cost, which was greatly appreciated by the Government of Karnataka. A great deal of credit goes to these corporations, and we are extremely grateful for their contributions.

Expenditure (Rupees in Millions)

Particulars	2018–19	2019–20	2020–21
Research & Development	316.70	302.66	183.40
Extra Mural Grants	376.72	400.84	374.62
Salaries & Fellowships	246.68	296.94	268.43
Operational Expenditure	281.10	321.19	261.86
Construction	152.20	70.57	0.19
Total	1373.20	1392.20	1088.50

Last but not the least, our deepest thanks to the real heroes behind all these achievements—our employees. We would like to express our deepest appreciation for our employees. All staff—outsourced, contractual, and permanent—deserve our deepest gratitude, admiration, and appreciation for the perseverance and commitment shown by them during the pandemic in supplementing the efforts of our students, faculty, and other technical and administrative teams and keeping the essential services of campus running without any interruption to research activities.

I would specially acknowledge the contributions of Shri K P Pandian (Head, Administration), Shri K V Ramanathan (Head, Purchase) Shri S Ashok Rao (Head, Establishment), Shri Srinidhi V (Head, Finance), and Shri Shaju Varghese (Head, Services).

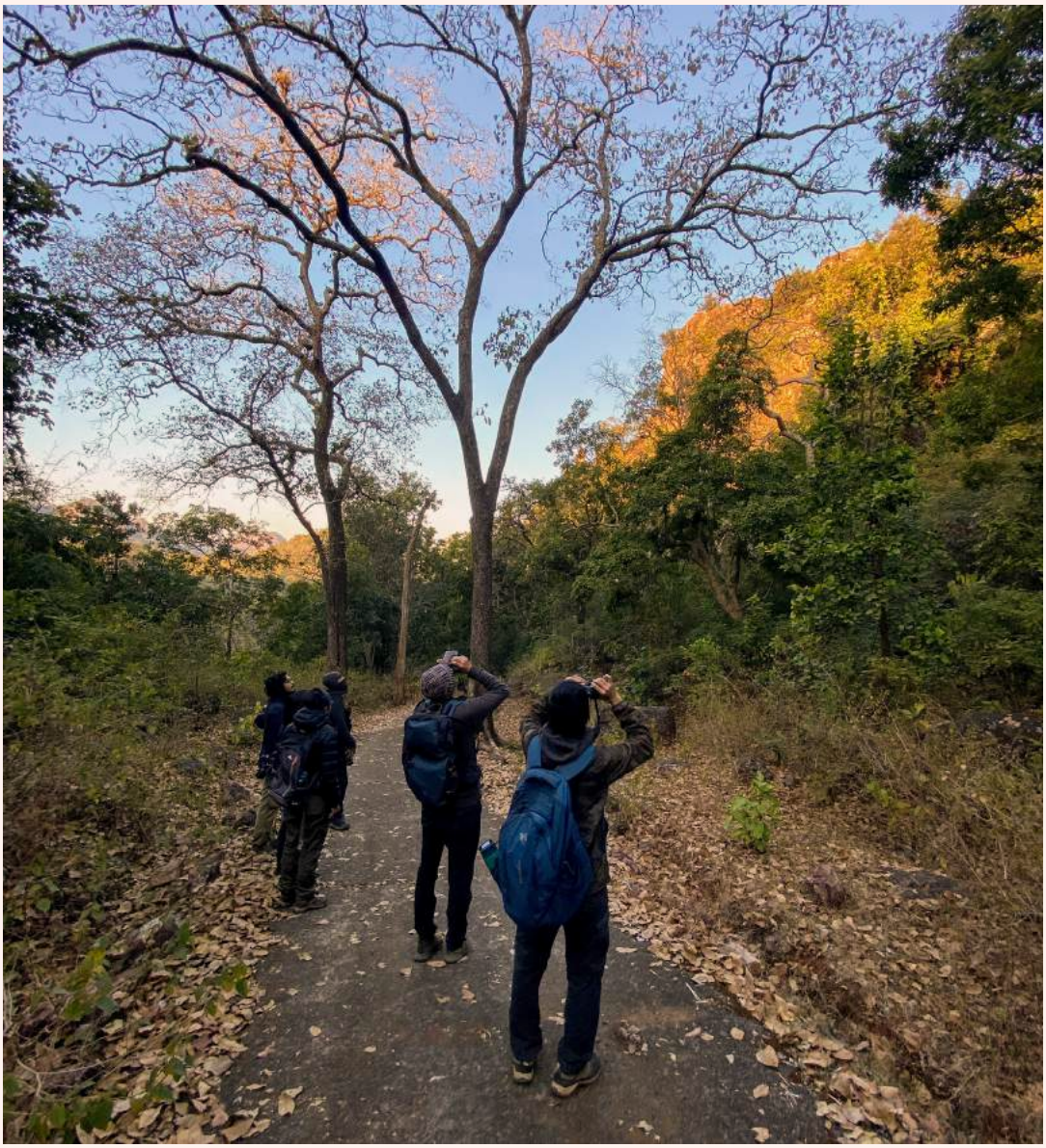
I would also like to take this opportunity to thank our faculty, students, partners, and the entire NCBS community for their continued support during the year 2020–2021.

Master's Programme in Wildlife Biology and Conservation

The Master's Programme in Wildlife Biology and Conservation is a distinctive Academia-NGO partnership for capacity building in higher education. This unique coalition of conservation NGOs and academic institutions aims 'to build capacity for conservation of India's wildlife and natural ecosystems through a rigorous high-quality training programme'.

Since its inception in 2004, the programme has worked for excellence in training through intensive coursework and field research projects. Spread across four semesters, the program involves intensive coursework covering fundamental disciplines such as Ecology, Statistics, GIS, and Remote Sensing and interdisciplinary courses such as Conservation Ecology and Practice, Ecological History, and Conservation Law and Policy, to name a few. Students travel to various field sites across India to understand the ecology and unique conservation challenges. In the final semester, students conceive, plan, and execute a field-based research project, which contribute to knowledge gaps in the ecology of various species and natural habitats, and in some cases, also contribute directly to conservation outcomes. With an intake of 15 students from India in the first 6 cohorts, and an additional 2 students from South, South-East, and Central Asia since 2014, we have trained 117 graduates as of 2020, who

Looking for mudskippers during the marine ecology course at Salim Ali Sanctuary, Goa.



Bird watching in the Satupura Tiger Reserve, Madhya Pradesh, Goa.

through their research and conservation action safeguard our natural heritage.

The ongoing global pandemic has resulted in a tumultuous year for the cohort of 2020–22. The initial wave meant that the course had to be moved to an online mode with the first semester being taught wholly in this medium. Given the hands-on nature of this program, this was difficult and required both faculty and students to adapt and scale their expectations. Despite this, most courses were successfully delivered with minimal disruption. As inter-state travel resumed, the students finally arrived on campus in January 2021.

The prevalent restrictions on campus necessitated a move to the NCBS field station at Pachmarhi. Both faculty and students spent four weeks cloistered in splendid isolation at this remote location with a resumption of in-person classes.

The second wave resulted in some of our field trips being either cancelled or postponed and teaching moved online once again. With wider vaccine availability and dropping case numbers, we have now resumed our third semester on campus with a combination of online and in-person classes. We had wonderfully productive field trips to the Western ghats and a marine ecology field visit to the Western coast.

Our dedicated faculty and resource people from across the conservation sphere have supported the programme and students through these trying times. As with previous years, this unique support system has bolstered the programme, ensuring the students were buffered from the prevailing situation. We are, as always, very grateful to this network of individuals and institutions for their support and commitment.

These are exciting times for the program, with a conservation consortium taking shape, as we expand our partnerships and widen the scope of our activities. The Nature Conservation Foundation (NCF), has come on as a full-time partner on the program and talks with other institutions are ongoing. The Habitats Trust (THT) now funds three fellowships that cover the costs of three students in the program. We also had a change in guard with our long time director Dr. Ajith Kumar's retirement and Dr. Jayashree Ratnam, formally assuming the position. We are expanding the programme and building a core faculty team to helm the programme in the new decade.

Population estimation course at Pachmarhi

The Archives at NCBS

The Archives at NCBS is a public centre for the history of contemporary biology in India. Over 50,000 processed objects across 18 collections are in various forms, ranging from paper-based manuscripts to negatives to photographs, books, fine art, audio recordings, scientific equipment, letters, and field and lab notes. The 2000-square-feet physical centre in the Eastern Lab Complex (ELC) basement at NCBS includes space for research, processing, exhibitions, recording, and a leading-edge storage facility with monitors for temperature, light, humidity, air quality, water, fire, pests, and noise. The Archives has one underlying philosophy of enabling diverse stories and three broad aspirations: education through archival material, building a consortium of archives with a discovery layer for the public to find, describe, and share archival material and stories, and reimagining the archives as a space to strengthen the commons.

THE FIRST OBAID SIDDIQI CHAIR IN THE HISTORY AND CULTURE OF SCIENCE

In 2020, the Archives at NCBS formalised the creation of a chair in the History and Culture of Science, through generous support from TNQ Technologies. After reviewing a large number of high calibre applications, MD Madhusudan was the Review Committee's unanimous choice as the first recipient of the Obaid Siddiqi Chair. M D Madhusudan is working on two projects along with his collaborators. The first project, with Hari Sridhar and Preeti Venkatram, is the Making of Indian Conservation, an archive of oral history interviews and other material that chronicles the engagements of diverse constituents with conservation across India's living lands and waters over the last 50 years, and produces a scholarly treatise in this unexplored area. The second, with Pradeep Koulgi, is the India Open Land Cover Project, an open geospatial archive of natural and anthropogenic land cover types over time (for India) based on public earth-observation data and open code.

COLLABORATIONS

The Archives at NCBS continues to lead the development of Milli, a network of individuals and communities interested in the nurturing of archives. The digital platform for Milli will allow the public to find, describe, and share archival material and stories. Milli facilitates discussions in the community around issues of diversity, archival standards, conservation, physical and digital access, pedagogy, privacy, and the development of inclusive description standards. The annual week-long free Milli Sessions have seen over 1500 registrants over two

years, over 400 active participants from all across the country, and 40+ partnering institutions (in 2020 and 2021).

The Archives at NCBS collaborated with Mary-Rose Abraham, Nikhil Nagaraj, and Gayathri Vaidyanathan on the podcast series, Scrolls and Leaves, an immersive-sound podcast exploring the margins of history, science, and cultures. Season 1: Trade Winds, which launched in September 2021, narrates how movement and migration across the Indian Ocean changed us. It was produced with support from the Mellon Sawyer Seminar at Yale University, IndiaBioscience, DBT/Wellcome Trust India Alliance, and NCBS.

In 2020, the Archives worked with Divij Joshi to start a project on archives and the law. This led to a guidebook prototype in 2021. The Archives at NCBS intends to extend it into a larger initiative, 'Archives, Ethics and the Law in India: A Guidebook and Training Programme for Archivists in India'.

NEW ACCESSIONS AND MAINTENANCE

In 2021, the Archives completed processing the papers of T S G Sastry, M M Panicker, and K Ullas Karanth, with the efforts of Gaayatri Chandrasekharan, Umm-E-Salama Udaipurwala, and Sanjna Yechareddy. The papers cover histories in the fields of neurobiology, ecology, and cosmic ray physics. The Archives also received the papers of B V Sreekantan, the former director of TIFR. It received a generous donation from the Trustees of the M S Swaminathan Research Foundation (MSSRF) of the papers of M S Swaminathan. Yechareddy, with help from Ravi Kumar Boyapati, led the processing of new accessions in this collection, in addition to new oral history interviews as part of her project on women in science.

Abhishek Banerjee, a consultant conservator, completed the condition analysis of new collections, conservation of various paper manuscripts, and drafted plans for a new conservation lab at NCBS. Boyapati and Neha Panwar continued revisions for the soon-to-be-public preventative checklist and crisis management protocol. In addition, the Archives started a project in 2021 to digitise its new collections. This, along with an upgrade of the digital cataloguing platform by early 2022, will significantly increase the volume of publicly accessible collections.

CAMPUS COVID-19 COLLECTION

The new COVID-19 collection aims to document the campus' response to the pandemic. This is an opportunity to contextualise the current events for the historical record. It is also an experiment in archival methods, and an effort to see the challenges in archiving around a contemporary crisis. This work was started in 2020 by Ananya, but paused in the wake of the second national wave of the pandemic in India in early 2021. It is now being led by Udaipurwala and will draw on physical and digital material, as well as short oral history interviews.

The new logo for the Archives at NCBS

LOGO

The Archives at NCBS got a new logo. Designed by Anoopa John, with initial input from Aditi Mishra, the origins of the logo are in the 'a' (for archives), the treble clef in music (the idea of stories), and the ampersand (for inclusivity and the in-between nature of the archive). It is a way to think about the stories that emerge from archival material, and the archives as a connector between different kinds of spaces. The symbol form is a nod to various South Asian scripts. The loops in the logo double as a way to think about cell division, and as a basis for life. The brown tones acknowledge colours at the archives, both of the space and the historical material.

INVITED TALKS

The Archives at NCBS was invited to present at the annual conference of the International Council on Archives Section on University and Research Institutions (ICA SUV), the 26th International Congress on the History of Science and Technology (ICHST), and the Third Workshop on Scientific Archives (Contemporary Archives of Science and Technology, ICA SUV). In India, it gave online lectures at the Homi Bhabha Centre for Science Education, Advance Information Network (ADINET) of Libraries in Gujarat, and Azim Premji University.

ARCHIVES GALLERY

The Archives received 24 proposals for its call for the third exhibition, Boundaries. The winning proposal, 'Bodies at Sea', by Kamini Rao (Studio Slip) and Devika Sundar, was unanimously chosen by the Review Committee. 'Bodies at Sea' traverses the boundaries between the visible and unknown, examining the hidden complexity of our interior bodies alongside oceanic bodies of the deep sea. The exhibition will be installed in early 2022.

REVIEW

The Archives at NCBS serves on the review committees of the Indian Institute of Technology Madras (IITM) Archives, the Indian Statistical

Institute Archives and the MSSRF. It is also now represented in the Encoded Archival Descriptions – Technical Sub-committee (Society of American Archivists) and an institutional member of the International Council on Archives.

OUTREACH

The Archives Public Lecture Series is a monthly public fixture to initiate dialogue and debate on an array of diverse topics and histories of ideas. Most talks in 2021 were held online and covered diverse topics including the launch of the Obaid Siddiqi Chair, internet infrastructure, and histories of design, grief, virtue, and the kolam, and reflections on governance, polio eradication, and the Brahmaputra. In late 2021, the series moved back to being held in person, collaborating on the 44th edition in December 2021, with Azim Premji University, IIIT Bangalore, and St Joseph's College.

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

Visitors to the 'Herbs, Maps and Medicine' exhibition at the Archives at NCBS Gallery, which was on display between March 2020 - December 2021.

Research Facilities Report (2020–2021)

From the whole organism to atomic and molecular levels, understanding biological processes depends on the use of sophisticated and fast advancing technology platforms. To make the best use of this equipment, an in-depth knowledge of operating and using the technology is paramount for developing newer scientific methods. Over the past decade, access to rapidly evolving genome engineering technologies, sophisticated biological manipulations at the tissue and organism levels as well as ultra-precise measurement techniques have driven the advancements in our understanding of fundamental biology. Research laboratories with immediate access to state-of-art technologies can address complex scientific problems at a rapid pace. This is particularly imperative for sophisticated experiments requiring the simultaneous use of different advanced technologies. Centralised facilities at NCBS provide cutting edge technology along with the state-of-the-art expertise required to make optimal use of such technology platforms. These facilities also train internal and external researchers, aiding in generating a pool of well-trained scientists in India and worldwide. The contribution of the research facilities has been acknowledged in over 150 publications during 2020–21.

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

ANIMAL CARE AND RESOURCE CENTRE

The Animal Care and Resource Centre (ACRC) is a state-of-the-art high barrier Specific Pathogen Free (SPF) health status laboratory animal facility that provides services and resources for both institutional as well as external investigators to accomplish animal research objectives while ensuring high standards of animal welfare and full compliance with exacting animal ethics regulations. Currently, the ACRC has over 360 strains of mice, over 22 lines of rats, and over 40 lines of zebrafish. All the mice and rat foundation colonies are housed in Individually Ventilated Caging (IVC) systems, with a controlled environment in the animal rooms. The ACRC is currently used by 33 BLiSC labs and handles over 66 animal-based research projects per year. Over the last year, the ACRC has trained 260 internal animal users and 6 external scientists in various aspects of lab animal management. There were 12 publications from the ACRC over the last year.

ACRC Crew: **Mohan G H, Aurelie Jory-Lily, Latha Chukki, Yogesh C, Sreenivasulu T, Manjunath A M, Rupa Kumari, Lalitha, Sathish S, Sharath D P, Poornima K, Rakesh P, Unnikrishnan M, Mathan Raj G, and Abhirup Dutta.**

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

The Animal Care and Resource Centre

BIOSAFETY FACILITY

The Biosafety Facility at NCBS comprises dedicated BSL-2, and BSL-3 laboratories. The BSL-2 laboratory facilities are equipped with class-2 biosafety cabinets and essential equipment to perform in vitro experiments on known risk group-2 (RG-2) agents and cell-based transfection studies. Additionally, based on risk assessments and approvals from regulatory committees, the BSL-2 facility permits the study of clinical specimens. BSL-3 laboratory suites have two independent workspaces: LAB-1 and LAB-2. LAB-1 is dedicated to experiments involving *Mycobacterium tuberculosis* while LAB-2 is used for studies on risk group-3 viral agents. During 2020–2021, the BSL-3 facility LAB-2 partition was commissioned for in vitro studies on SARS-CoV-2. Overall, 12 users were trained for BSL-3 facility and 10 users trained for BSL-2 facility. The annual validation protocol for biosafety cabinets and ventilation system of the BSL-3 facility for the year 2020 was completed during January'2021.

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

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

CENTRAL IMAGING AND FLOW CYTOMETRY FACILITY

The Central Imaging and Flow Cytometry Facility (CIFF) is equipped with 19 high-end microscopes and 11 flow cytometers. CIFF is an operator-free facility that caters to the needs of both internal and external researchers. The facility was used for 12974 hours in 2020–2021 The perennial training

programmes in imaging and flow cytometry conducted at CIFF are open to basic and clinical researchers. The facility has trained 107 internal and 17 external students/researchers on microscopy/flow cytometry in 2020–2021 and resulted in 35 papers in peer-reviewed journals.

CIFF Crew: **Feroz M H Musthafa, Raksha K, Rukmini Kulkarni, Ankitha K B, Anil Kumar H V, and Krishnamurthy H**

Faculty Advisory Committee: **Anjana Badrinarayanan, Raj Ladher, Sanjay Sane, Vinoth Kumar K R, Arjun Guha, and Shashi Thutupalli**

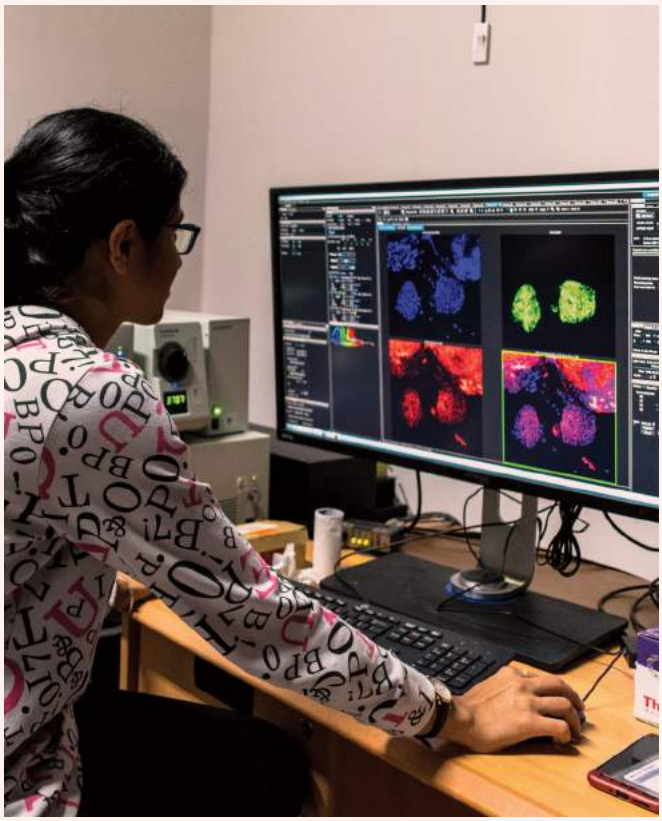
ELECTRON MICROSCOPY

The Electron Microscopy (EM) Facility is equipped with a high-resolution Transmission Electron Microscope (TEM Tecnai T12 G2 spirit), a high-resolution Field Emission Scanning Electron Microscope (Merlin Compact VP) fitted with cryo-stage, and a Micro-Computed Tomography (micro-CT) machine. The lab is equipped with an ultra-microtome, plunge freezer, carbon coater, plasma cleaner, chemical hood, and knife maker to process biological samples at room temperature and in cryo conditions for TEM. A critical point dryer, sputter coater, dissection microscopes, and various stains are also available in the facility for sample preparation. The EM facility trains internal users to use various equipment themselves and also caters to the needs of external users. This is an operator-free facility. Since April 2020, the EM facility and the facility personnel have been acknowledged in 10 publications.

EM Facility Crew: **Priti Bhardwaj, Sunil Prabhakar, and Anjana M U**

Faculty Advisory Committee: **Raghu Padinjat, Raj Ladher, and Vinoth Kumar K R**

The Biosafety Facility



The Central Imaging and Flow Cytometry Facility

FLY FACILITY

The Fly Facility generates approximately 150–200 transgenic flies, and 20–30 CRISPR-based mutants annually. In recent years, the fly facility has provided services in molecular DNA cloning using various molecular techniques, making it the only facility worldwide that provides a complete CRISPR service from designing and cloning molecular constructs, injecting, and screening to generating desired genomic manipulations in *Drosophila melanogaster.* The facility maintains ~8,000 different fly strains for internal users. It also supports researchers in technology development in the area of *Drosophila* genome engineering. In the last year, the fly facility catered to 14 internal users monthly and 50 external users. In addition, it trained two users in different methods in fly genetics, and was acknowledged for its contributions in 17 publications and preprints.

FF Crew: **Deepti Trivedi, Yashwantha K, Srividhya A, Hemavathy C, Anitha V A, Nataraj N, Kishore V, Jithin R, Bilal Akhtar, and Sravya Mothe.**

Faculty Advisory Committee: **Raghu Padinjat and Tina Mukherjee**

The Fly Facility

GENOMICS FACILITY

The Genomics Facility includes both Sanger sequencing and the Next Generation Genomics Facility (NGGF). The Sanger Sequencing facility is equipped with a 48-capillary Sanger sequencing machine and provides plasmid and PCR product sequencing, and genotyping services to internal and external researchers in very short turnaround times. The NGGF is equipped with at high-throughput next generation sequencing (NGS) platform (Hiseq2500), two bench-top NGS platforms (Miseq and Ion Proton), and one Single Cell Genomics platform (10x Genomics). The NGGF caters to the next generation sequencing needs of internal and external researchers, and provides user training and support in NGS library preparation using various protocols (DNA, mRNA, small RNA, ChIP, metagenomics, etc.) and sequencing. The NGGF trained 13 researchers in 2020–2021, and has been acknowledged in 37 published papers.

The Genomics Facility

Genomics Facility Crew: **Lakshminarayanan C P, Kumar Virbhadra, and Awadhesh Pandit**

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

GREENHOUSE FACILITY

The Greenhouse Facility has 7 greenhouses that allow researchers to maintain pure/transgenic strains of plants and insects and study plant-animal interactions. The greenhouses are equipped with adjustable and fully automated climatic control systems to control light, temperature, and humidity levels using special lights, shading screens, evaporative pads, fan cooling systems, heaters, humidifiers, and dehumidifiers.

Greenhouse Facility Crew: **Ranjith P P, K Thirumalaraju , Narasimha Raju, and Parvatamma**

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

The Greenhouse Facility

HIGH PERFORMANCE COMPUTING FACILITY

The High Performance Computing Facility caters to the ever-increasing demands for high performance computing from our scientific community. The facility at NCBS is a symbiosis of computing, network, graphics, and visualisation. The facility is a functionally distributed supercomputing environment and shared memory systems with state-of-the-art computing systems and open source software packages all of which are inter-connected via an Infiniband network. The facility maintains a high-speed network backbone to the campus LAN. The facility is equipped with three high-performance computer clusters and hosts 300 TFlops of compute power in total, with 8 GB of memory per core. The facility also includes one storage system with a parallel file system, providing a bandwidth of 20GB/s, as well as one storage system with 1 Lakh IOPS with an overall usable capacity of 1.8 PB.

IT Crew: **P K Baruah, Rajshekar K S, Rajesh R, Chakrapani, Alok B, Divya K, Subramani R P, Vishnu K, Raghavendra B, Rakesh S, and Dinakar M**

Faculty Advisory Committee: **Vinoth Kumar K R, Sabarinathan Radhakrishnan, and Upinder Singh Bhalla**

MASS SPECTROMETRY FACILITY

The Mass Spectrometry (MS) Facility of the BLiSC provides researchers with high-spec technologies to characterise biological and chemical entities such as metabolites, glycans, lipids, proteins, biosimilars, antibodies, and synthetic lab molecules. The facility is actively involved in developing new analytical methods required to facilitate on- and off-campus research. In addition to providing MS-based structural characterisation services, the facility also provides post-translation identification and quantitation of the above-mentioned biomolecules using labelled and label-free workflows. The MS facility also provides online and on-site 3–5-day training programmes on the use of different LC-MS/MS technologies such as lipidomics, proteomics, metabolomics, and glycomics. In 2020–2021, 8 researchers were trained, and the contribution of the facility was acknowledged in several publications.

The Mass Spectrometry

MS Crew: **Alifia Jaffer, Sohail Khan, Jyothi Prabha, Theja P P, Padma Ramakrishnan, Nirpendra Singh, and Chhaya Patole**

Faculty Advisory Committee: **Arvind Ramanathan, Ranbir Das, Krishnamurthy H, and Raghu Padinjat**

MOUSE GENOME ENGINEERING FACILITY

The Mouse Genome Engineering Facility (MGEF) provides services and training to generate, maintain, and cryo-archive genetically modified mouse models using the latest gene editing and assisted reproductive technologies. Other operational domains include the generation of specific pathogen-free mice through strain re-derivation and embryo transfer techniques. Additionally, the MGEF team has expertise in mouse sperm and embryo cryopreservation, as well as in cryo-recovery and in vitro fertilisation, and continues to provide services to backup, archive, and resurrect frozen mouse sperm or embryos from internal and external Indian and international collaborators. This portfolio of services allows the MGEF to regularly add and share new mouse stocks consolidated in a national mouse repository. The MGEF organises several hands-on and online workshops throughout the year, allowing scientists from all over India to acquire skills and to enhance mouse colony management possibilities in India. Over the last 6 years, the MGEF has generated 25 new mouse knock-out, knock-in and transgenic mouse models, including a series of new humanised-ACE2 mice that are being used in the COVID-19 vaccine and therapeutics studies. In 2021, the MGEF has provided live online demo training to 45 Indian students and scientists and carried out over 100 mouse stock cryo-archiving or rederivation projects for scientists nationwide.

MGEF Crew: **Aurelie Jory-Lily, Mahesh Sahare, Shilpa B A, Arpana H, Vaishak Nair P, Suba Soundarya S A, and Latha Chukki**

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

The Microfluidics and Microfabrication Facility

MICROFLUIDICS AND MICROFABRICATION FACILITY

The Microfluidics and Microfabrication Facility is equipped for Su8 photolithography and PDMS fabrication technologies, along with a state-of-the-art Class 10000 cleanroom and sub-micron resolution mask aligner. It provides micro-fabricated device delivery and equipment access for the needs of internal and external researchers. The customised training programmes in the facility are open to both academic and industrial researchers and companies. The facility provides design and experimental planning support as well as testing capabilities. It is being enhanced with further plastic microfluidic device fabrication capabilities. The facility has trained 117 researchers, students, and innovators during 2020–2021 through online and offline modalities.

MMF Crew: **Subhash K M and Feroz M H Musthafa**

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

The Museum Collection Room

The Nuclear Magnetic Resonance Facility

MUSEUM AND FIELD STATIONS FACILITY

The Museum and Field Stations Facility organised various outreach events for school children at the Pachmarhi field station this year, such as Vulture Awareness, Wildlife Week, Moth Day, etc. The facility worked with labs at NCBS to organise the Lab Culture exhibitions that drew more than 2500 students from schools and colleges. The collections have been moved to a new location at the inStem building. This is a substantially larger space with state-of-art facilities. The new space is being setup up to expand our existing research collections. A taxidermy workshop was organised and trained five researchers in the collection, preservation, and long-term care of mammal specimens. The facility has been central to the identification of several new species of reptiles and invertebrates, with 18 publications of species descriptions.

MFS crew: **Vivek Ramachandran, Tarun Karmakar, Savita Chib, and Aswathanarayana G**

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

THE NUCLEAR MAGNETIC RESONANCE FACILITY

The Nuclear Magnetic Resonance (NMR) Facility is equipped with two machines (800 MHz and 600 MHz) with cryo-probes. The facility aids in studies that focus on the de novo structure determination of macromolecules such as proteins and nucleic acids, and their dynamics in the picosecond to millisecond time scales. NMR spectroscopy is a versatile technique for calculating chemical shift perturbations (CSPs) during protein-protein, protein-ligand, and protein-nucleic acid titrations. In structural biology, real-time NMR is extensively used to understand the folding pathways of proteins as well as enzyme kinetics. The facility provides 24-hour service on all 7 days of the week for both internal and external users, and periodically conducts training programs for new users,

as well as hands-on training sessions for regular users. During 2020–2021, the NMR facility trained 6 researchers and has been acknowledged in 13 published papers.

NMR Crew: **Purushotham Reddy P**

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

RADIOACTIVITY FACILITY

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

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

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

The Radioactivity Facility

STEM CELL FACILITY

The Stem Cell Facility (SCF) provides services and training for research using human pluripotent stem cells (hiPSC/hESC). We provide a BSL-2 shared space stem cell facility that is used to culture, edit, and image stem cells. Our services include, derivation of iPSCs, detailed characterisation and expansion of iPSCs, genome engineering of stem cell lines using CRISPR/Cas9 technology, and lineage-specific differentiation of iPSCs. We have high end infrastructure such as vertical and horizontal biosafety cabinets, microscopes for fluorescent and live imaging, sorters, tri-gas

incubators, cell counters, and nucleofectors. We have separate rooms for the quality control of stem cell lines (quarantine room) and for regular stem cell cultures (clean room). In the past year, the SCF has trained 14 users in approved methods of stem cells culturing practices that meet international standards.

SCF Crew: **Deepti Abbey, Niharika Patlolla, and Anagha Mohan**

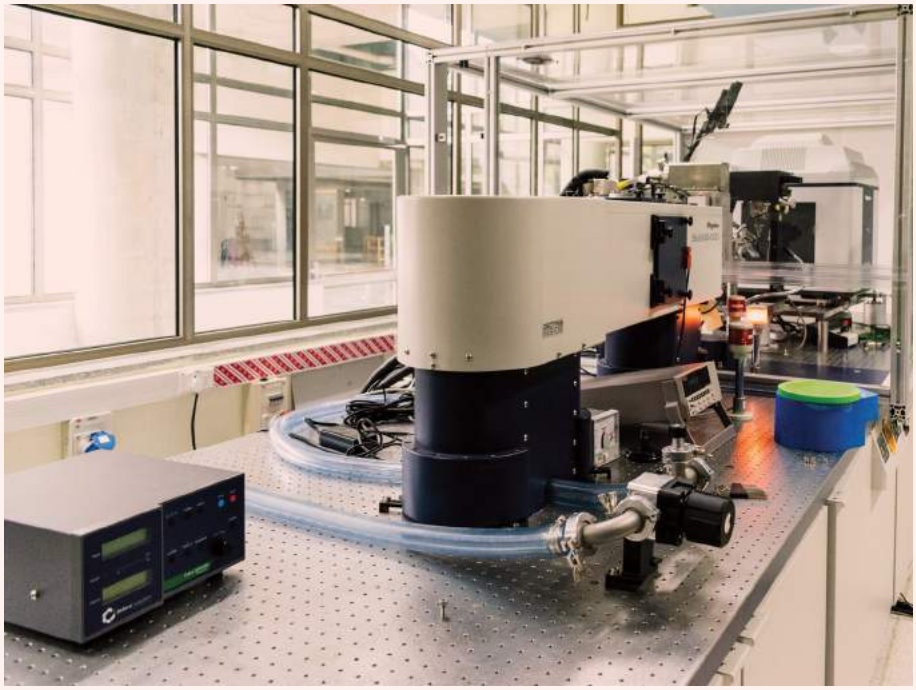
Faculty Advisory Committee: **Colin Jamora and Raghu Padinjat**

X-RAY FACILITY

The X-Ray Facility aims to provide the necessary infrastructure and expert support for internal and external academic and industry users in structural studies of biological macromolecules in a crystalline state or in solution. The facility offers high-end instruments and training for setting up crystallisation, screening, data collection, processing, and three-dimensional structure determination of biological macromolecules. The facility is equipped with an automated nano dispenser robot, UV microscope, FR-X X-ray diffractometer, BioSAXS-1000, and up-to-date versions of computing software for data analysis and automated structure solution from the data collected.

X-Ray Crew: **Nishant Kumar Varshney**

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



The X-Ray Facility

Retirement Note: Shaju Varghese

Shaju Varghese, Administrative Officer at NCBS-TIFR retired after 37 years of service in the TIFR system. He initially began working at the hospitality services at the TIFR Colaba campus in May 1984. When NCBS was founded, following interactions with Prof. Obaid Siddiqi, the founding director of NCBS, he moved to Bangalore to manage hospitality services at this new centre of TIFR. Under his stewardship, the hospitality services at NCBS grew over the years, from supporting the needs of about 30 people in 1993 to about 1500 people at the time of his retirement in 2020.

A key requirement for a productive and stimulating research environment is a high-quality working space. This must include dining facilities, accommodation, and gardens, in addition to laboratories and other work spaces. Not only do these need to be built to a high standard, they must be well-maintained and aesthetically pleasing. Doing this over a long period of time is challenging and Shaju accomplished this at NCBS over the 28 years that he served the institute. During his time at NCBS, Shaju grew and managed several areas including dining services, hostels, guest houses, security services, and housekeeping. The NCBS campus and its facilities are the envy of visitors from all over the world; this is in no small measure due to the high standards with which Shaju trained and managed his workforce.

Since early 2020, NCBS, like everyone else, has been affected by the COVID-19 pandemic. In addition to regular research work at the campus being severely disrupted, NCBS was called on by the Government of India to set up and run services to manage the pandemic for the nation, including the establishment and operation of a COVID-19 testing facility. This meant that the campus needed to be kept operational and that the staff coming in to work had to be supported by the hospitality services. Despite several challenges arising from lockdowns and other factors in the city, hospitality services were uninterrupted and helped support campus operations. In addition, as part of the campus COVID-19 management system, hospitality services set up and serviced a quarantine facility for campus colleagues and also facilitated sanitisation of campus spaces when positive cases were found. Shaju's experience and leadership were critical in delivering this at a high standard. As he retires after a long innings at NCBS-TIFR, we wish him all the best and acknowledge his many contributions to the institute.

(page 144) Mr. Shaju Varghese effortlessly supervised, grew and maintained dining services, hostels, guest house, security services and housekeeping on the NCBS campus for 28 years.

In this photograph, he is seen at his best, supervising the set up of a public dinner in the NCBS lawns.

This was shot at Madhai, Satpura Tiger Reserve, during a fieldcourse in the MSc Wildlife Biology and Conservation Programme by Abhijeet A V

Ruddy Shelduck

Flagship Programmes

p. 148–164

Discovery Biology of Severe Mental Illness

Bangalore Sustainability Forum

IndiaBioscience

Science Gallery Bengaluru

Simons Centre

Discovery Biology of Severe Mental Illness

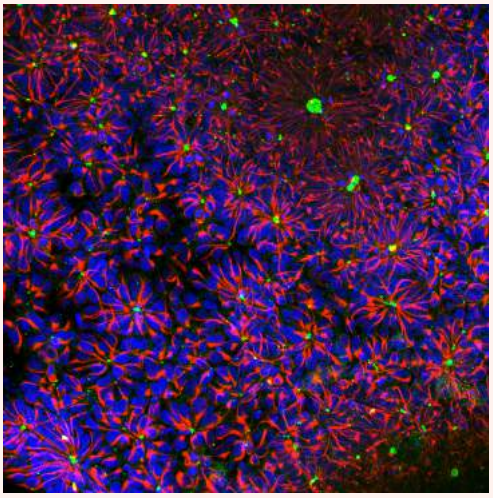
Severe mental illness is a major source of disability in young adults, with about 2–3% of the population at risk of developing these disorders both in India and across the world. These disorders are recognised as major non-communicable diseases (NCD) and significant contributors to morbidity, as articulated by the World Health Organisation's New Delhi call for action on combating NCDs in India. Given this huge disease burden, the development of novel ways to diagnose and treat mental illness will have important positive social and economic benefits. To achieve this goal, there is a pressing need to understand the mechanistic basis of these disorders; such discovery could form the basis for the development of novel diagnostic and therapeutic approaches.

The Accelerator programme for Discovery in Brain disorders using Stem cells (ADBS) is a venture to understand the genetic and cellular basis of severe mental illness by harnessing the power of modern human genetics and stem cell technology. This programme uses modern stem cell technology to create cellular models of the brain derived from human subjects with a strong history of severe mental illness. The overall goal is to uncover the genetic, cellular, and molecular basis of mental illness and relate these to clinical findings. ADBS is a collaborative initiative of three institutions from Bengaluru, India: The National Centre for Biological Sciences (NCBS), the Institute for Stem Cell Science and Regenerative Medicine (inStem), and the National Institute for Mental Health and Neurosciences (NIMHANS). ADBS has been supported during 2016–2021 by the Department of Biotechnology, Government of India, and the Pratiksha Trust.

The ADBS programme studies five major forms of severe mental illness (SMI): schizophrenia, bipolar disorder, obsessive compulsive disorder, substance dependence, and dementia. All of these disorders are known to have an inherited basis. However, despite their high heritability, to date few genetic correlates that can account for this high heritability have been identified. In order to study these disorders, in collaboration with the Department of Psychiatry, NIMHANS, the ADBS programme has assembled a prospective cohort of families with a strong family history of SMI from the endogamous populations of India. The ADBS programme is pursuing three distinct but interactive lines of analysis on these families: (i) The families have been clinically studied in depth to understand changes in structure and function at multiple levels of brain organisation; they will now be followed over a period of 20 years at 3-year intervals to define the temporal development of disease through regular and detailed clinical phenotyping. (ii) We have established about 100 induced pluripotent stem

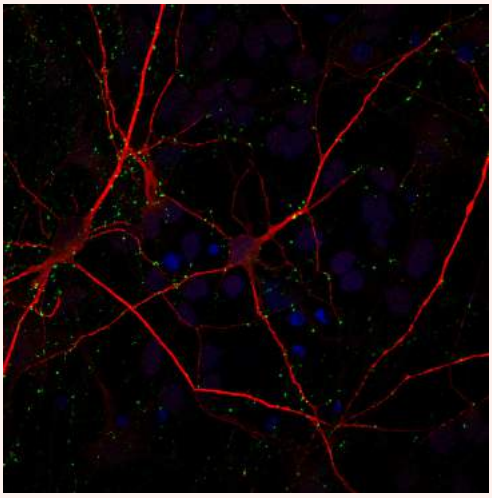
cell lines from affected individuals from these families and unaffected controls. These lines are being used to generate cellular models and mechanistic aspects of cellular neurobiology that lead to disease. (iii) Next Generation Sequencing and family-based bioinformatics analysis is being used to uncover the genetic basis of SMI. (iv) Genome editing technologies for the analysis of genetic variants using stem cell derived models of brain cells have been developed.

The multiple types of data generated by the ADBS programme are being assembled into an integrated database to facilitate the application of sophisticated methods of data analysis to uncover new disease biology. The stem cell lines and other biomaterials have been assembled into a biorepository that will allow the sharing and use of this resource to drive discovery biology in the area of SMI. The ADBS programme has instituted mechanisms to facilitate the sharing of data and resources generated through its activities.



Human neural stem cells derived from hiPSC differentiation.

Typical neural rosette structures are seen. Apical ZO-1 adherens junction marker (green) and Nestin, the neural stem cell marker (red) are shown.



Cortical neurons differentiated from human neural stem cells from a 30-day in vitro culture.

Neuronal markers synapsin (green) and MAP2 (red) are shown.

PUBLICATIONS

Pallikonda, H. A., Singh, P., Thakur, R., Kumari, A., Krishnan, H., Philip, R. G., ... and Raghu, P. 2021. **Genomic sequencing of Lowe syndrome trios reveal a mechanism for the heterogeneity of neurodevelopmental phenotypes.** bioRxiv.

Akhtar, B., Bhatia, P., Acharya, S., Sharma, S., Sharma, Y., Aswathy, B. S., ... and Padinjat, R. 2021. **A human stem cell resource to decipher the biochemical and cellular basis of neurodevelopmental defects in Lowe Syndrome.** bioRxiv.

Sharma, Y., Saha, S., Joseph, A., Krishnan, H., and Raghu, P. 2020. **In vitro human stem cell derived cultures to monitor calcium signaling in neuronal development and function.** Wellcome Open Research, 5, 16.

Viswanath, B., Rao, N. P., Narayanaswamy, J. C., Sivakumar, P. T., Kandasamy, A., Kesavan, M., ... and Jain, S. 2018. **Discovery biology of neuropsychiatric syndromes (DBNS): a center for integrating clinical medicine and basic science.** BMC Psychiatry, 18(1), 1–13.

Bangalore Sustainability Forum

The Bengaluru Sustainability Forum (BSF) is an inter-institutional collaborative initiative to address the long-term sustainability of urban and peri-urban landscapes with a focus on Bengaluru. It was founded in January 2018 with the intention of tackling sustainability questions in the local context through conversation and programmes involving the city's expertise, including the public, academics, professionals, activists, and governance bodies; it aimed to serve as the starting point for such initiatives across Indian cities. The participating institutions at BSF are the National Centre for Biological Sciences, the Ashoka Trust for Research in Ecology and the Environment, Azim Premji University, Biome Environmental Trust, Science Gallery Bengaluru, and Wipro Ltd.

BSF's main objective is to encourage working together across a broad range of stakeholders to establish long-term collaboration and dialogue, and to reduce the distance between research on sustainability and the public. We do this primarily by creating opportunities for interdisciplinary conversations and funding local, innovative, cross-disciplinary, collaborative projects on urban sustainability through our Small Grants Programme.

The Small Grants Programme has thus far been awarded for 29 projects over 4 cohorts in the areas of Urban Biodiversity, Urban Climate Change, Urban Water, and Urban Waste Management.

Bengaluru Sustainability Forum events

Mural at Cubbon Park Metro Station, BSF Small Grants Project 'Namma Ooru Namma Neeru'
Image credit: Yash Bhandari, Art In Transit

Connecting students to local biodiversity, BSF Small Grants Project 'Suttha Muttha'
Image credit: Gousia from FTLC

BSF Small Grants Project 'A Field Guide in Kannada on Common Avenue Trees'
Image Credit: S. Karthikeyan

To facilitate discussions and exchange of knowledge BSF, has organised:

- Retreats on specific aspects of urban sustainability like urban biodiversity, urban waters, and urban climate change, where curated groups of participants could exchange thoughts and ideas with each other across the boundaries of expertise and domains of work.
- An exhibition on renewable energy in collaboration with the German Consulate and the Indo-German Energy Forum at NCBS.
- A weekend of public interaction on the topic of urban waters as part of Science Gallery Bengaluru's exhibition 'Submerge' at the Bangalore International Centre in January 2020.

When in person programming became difficult, we moved online with:

- Climate Conversations: discussions on climate change in the urban context exploring what cities need to do to be climate ready, how preserving ecology (or a failure in doing so) affects climate change and risks of future pandemics, and the idea of climate justice. These were organised in collaboration with the Bangalore International Centre with the support of Jenny Pinto and Raj Shailesh.

- The Reading For Change series, hosted in partnership with the Science Gallery Bengaluru and Champaca Book Store, where books became a gateway to understanding the UN Sustainable Development Goals in the context of our daily lives.

- A hybrid online and offline game on air quality called 'The Search' that looked at the connections between our actions and air pollution. The Search was developed with Science Gallery Bengaluru and was available as part of the Church Street First initiative of the Department of Urban Land Transport.

- An online workshop on food and sustainability with Edible Issues and Science Gallery Bengaluru for their exhibition 'Phytopia'.

- Webinars and events with the Small Grants Project Grantees exploring their learnings and experiences from the projects.

Poster for Reporter's Workshop at Bengaluru Biodiversity Charche, part of the BSF Small Grants Project 'The Why & How of Bengaluru's Biodiversity'

Image from an interdisciplinary project for a sustainable and just future

As part of our effort to explore newer ways of engaging with the people, we are producing a podcast, 'Ooru', in which we mull over Bengaluru city and it's future, looking at what is being done or needs to be done to plan for the city's sustainability.

With the belief that the definition of what constitutes a sustainable city needs to be expanded to include aspects like public health, BSF also supported a pilot study on wastewater screening in Bangalore Water Supply and Sewerage Board (BWSSB)-managed sewage treatment plants for the presence of SARS-CoV-2 RNA. This became a first step towards building a better understanding of the possibility of disease surveillance in the city. In addition to detecting the SARS-CoV-2 RNA in wastewater, this study set up the framework and requisite collaborations to successfully implement wastewater epidemiology for public health purposes. We hope that active engagement with BWSSB will help build the capabilities of both institutions—BWSSB and NCBS—to strengthen knowledge sharing in the city.

BSF remains committed to it's vision of enabling multidisciplinary interactions and building synergies for working towards urban sustainability, with the belief that all the human and non-human residents of the city deserve a life of dignity with access to pure air, clean water, and healthy and safe surroundings.

Email: bsf@ncbs.res.in
Twitter | Instagram | Facebook: @sustainBLR

IndiaBioscience

The seeds for what would eventually become IndiaBioscience (IBS) were sowed around a dinner table conversation in 2007. Since its inception in 2009, IBS has been housed at, supported, and nurtured by NCBS.

IBS has set out to fill a unique niche in the ecosystem of the life sciences in India, by being a catalyst to promote changes that affect the culture and practice of the field, through engagement with academia, government, and industry at various levels. Thus our motto, 'Engaging communities, enabling change'.

Over the course of the pandemic (as many in this community) we had to reinvent many of our activities to fit with the current times. We also used this opportunity to explore new avenues for engaging with our community. Below is a snapshot of our recent activities.

GROWING A COMMUNITY

The Young Investigators' Meetings (YIMs) have been our flagship event (pre-dating IBS itself). We organised the YIM and Post-Doctoral Fellow (PDF) Satellite Meeting in a virtual format in March and May of 2021 respectively. We strived to maintain the hallmarks of the YIMs: a unique platform for creating communities that discuss and cultivate Indian science careers as well as science. It brings together science

Once in a lifetime opportunity; the IBS team and the IUBS organising team gearing up for a fascinating tak by Jane Goodall

Nostalgia; some present and past IBS member on an post lunch photo session on the NCBS campus

administrators, prospective applicants, researchers, grant advisors, and established scientists to interact, network, and foster collaborations while showcasing Indian science to the global community at large. Aurnab Ghosh, Bushra Ateeq, and Sharmista Banerjee joined us as mentors for YIM 2021. Twenty institutions participated in the PDF Satellite Meeting, including NCBS and inStem.

On the IBS website, we have an interactive map of life science researchers in India. This interactive Young Investigator (YI) database includes information on geographic locations and research disciplines and was created to be a platform that help YIs grow their networks and develop new collaborations. We invite YIs in the BLiSc community to join this database.

FACILITATING THE COMMUNITY

A key focus of IBS is to provide avenues for the life science community to enhance their skill sets.

Our Crafting Your Career (CYC) programme, which falls under this objective, aims to raise awareness among life science students and post-doctoral researchers about the different science careers in India, to help them identify their true calling, and develop skills to navigate their career paths with confidence. Six online webinars were conducted. We also conducted a survey to assess the impact of the CYC workshops and received an overwhelming response. We will continue to grow this program.

In our shared commitment to promoting life sciences, we joined hands with EMBO to organise online seminars to impart, update, and practice soft skills. These small group trainings include individualised assessments. In January 2021, we organised a Workshop on Oral Communication in Science for 21 selected PhD students/postdoctoral fellows.

Going digital; the IBS team and Organising Committee for the first virtual YIM: YIM 2021

To help researchers navigate the national and international funding scenario, IBS has carried out initiatives such as the International Grants Awareness Program (iGAP) (agencies covered: EMBO, HFSP, MSCA, DAAD) and put together a booklet, Means to a Beginning - Funding Opportunities for PhD Students and Post-docs in India.

SHINING A LIGHT ON THE COMMUNITY AND ITS NEEDS

The IBS website, with a monthly viewership of over 1 lakh, is a one-stop online portal for communicating scientific advancements and disseminating resource materials and opportunities in the life sciences in India. Through it, we bring visibility to Indian research and researchers by publishing a large number of articles, news pieces, and resources including e-books, booklets, and posters relevant to the Indian life science community.

The discussion around the topic of mental health in academia has been growing in recent times. In September 2021, we published a compendium of mental health related articles titled ‘Drishti – Mind Matters in Academia’ in an effort to put a spotlight on these issues and destigmatise the conversation around mental health.

BUILDING A NETWORK OF UNDERGRADUATE EDUCATORS

IBS strives to provide a platform for undergraduate biology educators of India to network, share their ideas and challenges, and build their pedagogical skills. This year, we published several articles written by educators, including articles on resolving misconceptions in biology in a classroom, on using games as pedagogical tools in higher education, and more. We have launched a series of webinars for educators this year. We had a panel discussion in June on the importance of networking, featuring L S Shashidhara, Shakila Shamsu, and Mayuri Rege; we had a webinar in October on digital education in the ‘new normal’, where Charu Dogra described the ways in which digital tools could be utilised in the classroom for inquiry-based learning. A total of nearly 200 educators attended these webinars. We hosted a webinar on November 18 on the implementation of the National Education Policy 2020.

EXPLORING NEW MEANS FOR OUTREACH

We extensively relied upon digital means of outreach to share and disseminate in-house generated and curated content via webinars, podcasts, and the website. This year we launched a new podcast series, 'In Conversation with a Mentor' featuring L S Shashidhara, Deepanwita Chattopadhyay, Sanjay Mishra, and B B Nath. We were the publicity partners and technical hosts for the IUBS Centenary Lecture Series featuring- Rattan Lal, Sean B Caroll, and Jane Goodall.

As a digital means to engage with the life science community, we have explored ways to grow and increase the engagement on our social media accounts and mailing groups. Every Tuesday, we highlight select jobs, grants, and events via a #SJT thread on Twitter. This year we initiated #FundaySunday to highlight exciting examples of science communication. We also send out periodic newsletters to a community of over 15000.

Taking meaningful networking to a digital platform at the PDF Satellite Meeting 2021

In an effort to promote the practice of outreach, especially amongst talented young scientists, we launched the IndiaBioscience Outreach Grants (IOG) last year. This year , the IOG was awarded to six teams including one with members from the BLiSC community, the Science Stage: Communicating Science Through Theatre, led by Sonia Sen.

PARTNERSHIPS

While primarily supported by the Department of Biotechnology, GOI, IBS also received support from an IRMI RM Grant (DBT/ Wellcome Trust India Alliance) and Ministry of Education under the Pandit Madan Mohan Malviya National Mission for Teachers and Teaching (PMMMNMTT). We have also continued existing partnerships and forged new ones with Azim Premji University, Cactus Communications, TNQ Technologies, IUBS, EMBO, etc.

The IBS team comprises Manjula Harikrishna, Shantala Hari Dass, Shwetha C, Suchibrata Borah, Vijeta Raghuram, and Zill-e-Anam. We invite you to engage with us, visit our website, write for us, contribute to our projects such as #FundaySunday and iGAP, participate in our webinars/ workshops/podcasts, or drop by to chat about what we could do together!

Stay Healthy | Stay Curious | Stay Engaged

Our in-house workshop for Crafting Your Career (CYC) in science

Science Gallery Bengaluru

The Science Gallery Bengaluru (SGB) is a not-for-profit public institution for research-based engagement targeted at young adults. We work at the interface between the natural and human sciences, and engineering and the arts through a Public Lab Complex, ever-changing exhibitions, and mentorship programmes.

SGB was established with founding support from the Government of Karnataka and three academic partners: Indian Institute of Science, NCBS, and Srishti Institute of Art, Design, and Technology. It is a member of the Global Science Gallery Network with sister galleries in Atlanta, Berlin, Detroit, Dublin, London, Melbourne, Rotterdam, and Venice.

NCBS is our Collaborating Academic Partner. We receive strategic, infrastructure, and programme support from our Academic Partners on a continuous basis. We also get access to the allied network of students and researchers, who are active participants of our programmes.

The Science Gallery Bengaluru team with the mediators and musician Rahul Ram after his performance 'Songs of the River' at SUBMERGE

Gauri Gharpure, PhD scholar at NCBS and a Science Gallery Bengaluru Mediator, in conversation with visitors at ELEMENTS

Our mission is to 'bring science back into culture' through:

- Empowering Young Adults with our Mentorship Initiative that encourages non-evaluative, self-motivated, hands-on learning. We provide exposure to research practices and nurture future research pioneers and active citizens.

- Open Research at our Public Lab Complex that encourages open-ended experiments through collaborations for young adults and experts. We provide access to research tools and outcomes outside institutional walls to catalyse antidisciplinary thinking and intergenerational co-inquiry.

- Shaping Culture with our Public Engagement and Community Initiatives that contribute to building a society with critical appreciation for the rigour of science and an ability to ask good questions, and participate in better informed public debates.

SGB's building complex is under construction and opens to visitors in 2022.

Our motto 'Science Culture Experiment' redefines public engagement in science to move beyond participation towards active experimentation.

SCIENCE GALLERY BENGALURU PROGRAMMES

SGB began its public engagement activities in 2019. Since then, we have organised four exhibitions:

- **ELEMENTS (5 October – 11 October 2019)**, a week-long pop-up exhibition that marked the 150th anniversary of Mendeleev's periodic table

- **SUBMERGE (15 December 2019 – 30 January 2020)**, our first 45-day exhibition-season, which also supported the Government of Karnataka's Year of Water initiative

- **PHYTOPIA (21 August – 30 August 2020)**, our 10-day long, first fully online pop-up exhibition, which also supported the UN General Assembly's International Year of Plant Health 2020 initiative

- **CONTAGION (30 April – 31 December 2021)**, which explored the transmission of diseases, emotions, and behaviours. CONTAGION Phase One ran for 45 days as our first fully digital exhibition-season, leading to Phase Two that concludes on 31 December 2021.

As we began to establish ourselves as a cultural space in the city, we participated in the Indian Institute of Science's Open Day 2020. We further showcased PHYTOPIA at the India Science Festival 2021. We also began our programming on the global stage by showcasing events from SUBMERGE at the Science Gallery Garden in the Ars Electronica 2020

The Science Gallery Bengaluru team with Jahnavi Phalkey, our Founding Director, at the NCBS campus

Shashi Thutupalli engaging with young adults in a tutorial after his public lecture "Without water: between life and death" at SUBMERGE

festival. In January 2021, we extended our reach by co-organising the International Youth Symposium with all the nodes of the Science Gallery Network.

As a part of our long-term commitment to the Anthropocene, we co-hosted 'Energiewende', an exhibition about Germany's renewable energy practices, at NCBS in partnership with the Bengaluru Sustainability Forum, the Consulate General of the Federal Republic of Germany, and the Indo-German Energy Forum. We also participated in the Anthropocene Curriculum, a research and public engagement programme with the Haus der Kulturen der Welt (HKW), Berlin.

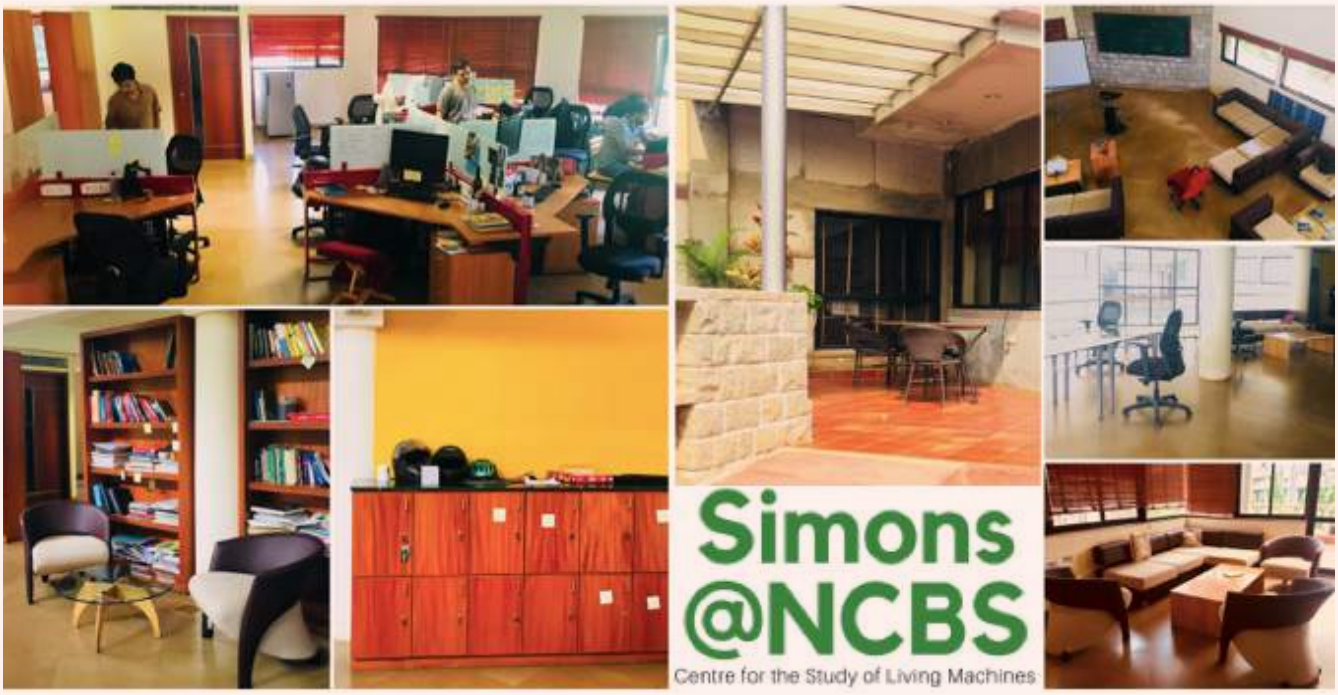
We continued to work with the Bengaluru Sustainability Forum and Champaca Bookstore to organise the Reading for Change programme, which encourages people to think about the UN Sustainable Development Goals as facets of their daily lives. This programme has moved online since the start of the pandemic.

To support frontline efforts during the first wave of the pandemic, we conducted training modules for youth volunteers in partnership with the Azim Premji Foundation. We also developed online learning modules on the pandemic in collaboration with Agastya International Foundation, which reached over 100,000 young students across India. For the general public, we ran a social media campaign, 'Co-Vids' with short videos where experts across the world shared their top three questions on the pandemic.

Simons Centre

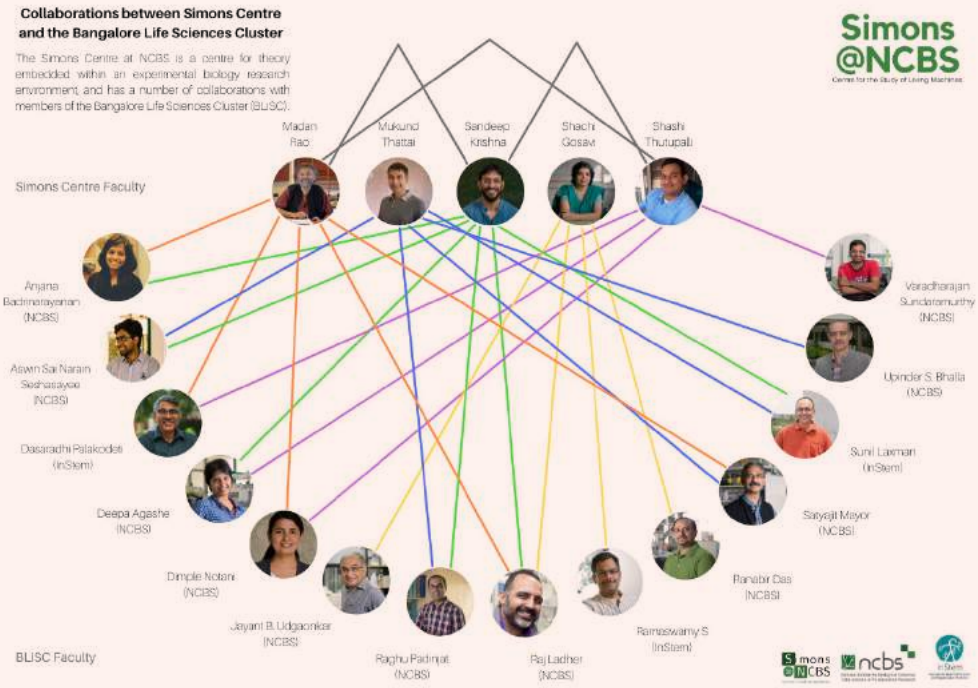
The Simons Centre for the Study of Living Machines is a dedicated space for the study of molecules, cells, and organisms as living machines: products of natural selection which consume energy to achieve specific goals.

Our research relies on interdisciplinary approaches that blend theory and experiment in order to solve fundamental biological problems spanning a range of lengths and timescales: from protein function, computational cell biology, and evolution to the physics of active systems.



The Simons Centre at NCBS was established in 2013 through a 5-year $1 million grant from the Simons Foundation, which was renewed for another 5 years in 2018. It brought together five NCBS faculty and their research groups with an aim to foster an environment of active collaborations between theory and experiment in biology.

At present, the Centre comprises the following faculty members and their groups: Archishman Raju, Madan Rao, Mukund Thattai, Sandeep Krishna, Shachi Gosavi, Shaon Chakrabarti, and Shashi Thutupalli. The current Advisory Committee of the Simons Centre at NCBS includes



Frank Julicher (MPI for the Physics of Complex Systems, Dresden) and Rob Phillips (California Institute of Technology, USA).

Keeping true to the vision of 'Biology without Boundaries', the Centre has grown into a fully-functional 'centre for theory, embedded within an experimental biology research environment', and serves as an international hub for researchers from physics, mathematics, computer sciences, and engineering backgrounds to engage with biological problems.

The work culture and ethos of the Centre also specifically prioritises frequent and deep interactions, random collisions of ideas, and sustained collaborative efforts involving the use of theoretical approaches. This has allowed us to nucleate entirely new avenues of research and led to a number of successful collaborations within topics like:

- evolution of cellular compartments
- cooperation and conflict within yeast populations
- novel methods for designing protein assemblies
- active regulation of membrane organisation and function
- distributed control of lipid signalling pathways
- bacterial defenses to phage infections
- mechanics of tissue morphogenesis
- fundamental limits of cellular replication

Over the years, the Centre's work has been concentrated on three collaborative research themes, Cellular Compartments; Organismal Communities; and Programmable Landscapes, which build on our members' overlapping interests as well as the local strengths of our experimental research environment.

With the backing of the Simons Foundation, the Centre has also organised several thematic meetings and workshops to enable a rich cross-fertilisation of ideas across disciplines, such as the 'Emergence and Evolution of Biological Complexity' meeting in February 2017, the 'Interface of Biology and Theoretical Computer Science' meeting in December 2016, and the 'Conflict and Cooperation in Cellular Populations' meeting in October 2016.

In addition, the Centre frequently organises retreats in which Simons Centre students, post-doctoral fellows and faculty interact in an informal setting. We also have a vibrant visitor's program that has been a continuous source of new information and new interactions.

To spread the culture of interdisciplinary life sciences research we have also been organising the 'Simons-NCBS Annual Monsoon School - Physics of Life' for undergraduates with backgrounds in the physical sciences and engineering. This school has managed to attract some of the best undergraduate talents in the country and has already begun paying direct dividends in the form of attracting Monsoon School alumni to eventually join NCBS as promising graduate students.

Shot at Hesarghatta Lake, Bengaluru
by Krushnamegh Kunte, who is
an associate professor interested in
biodiversity and evolutionary biology

Apharitis *lilacinus*

Erythropalum scandens

These are tropical climbers with colourful fruits. They are native to India and South China. This was shot by Ansil B R at Kadumane.

Bangalore Life Science Cluster

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Research Development Office

COVID-19 Pandemic and Indigenisation of Diagnostics

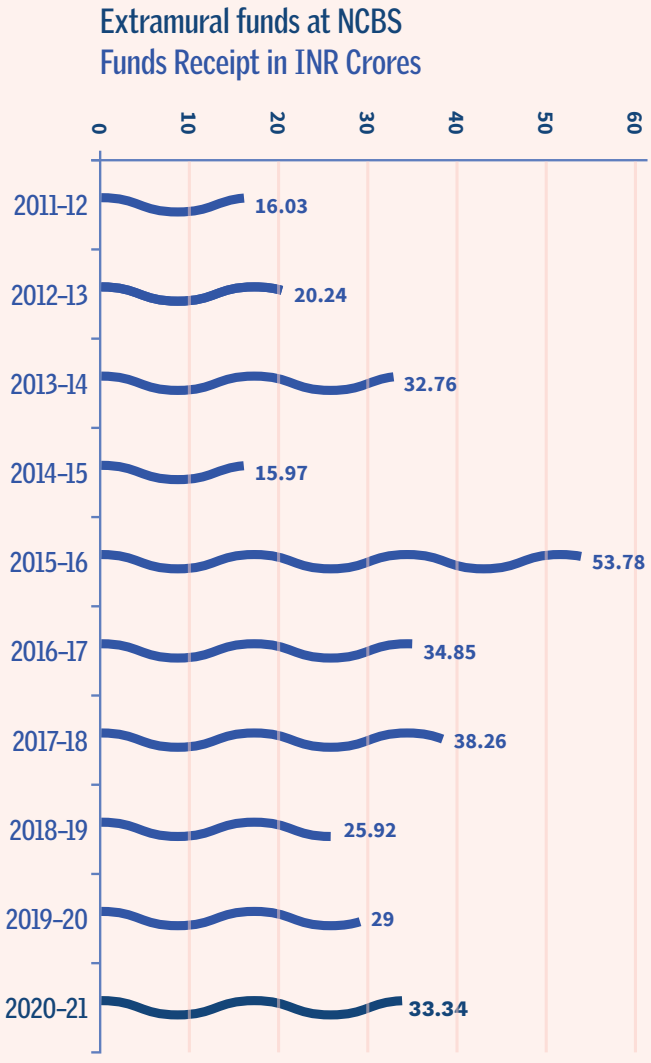
Innovating and Building Digital Outreach and Engagement

Research Development Office

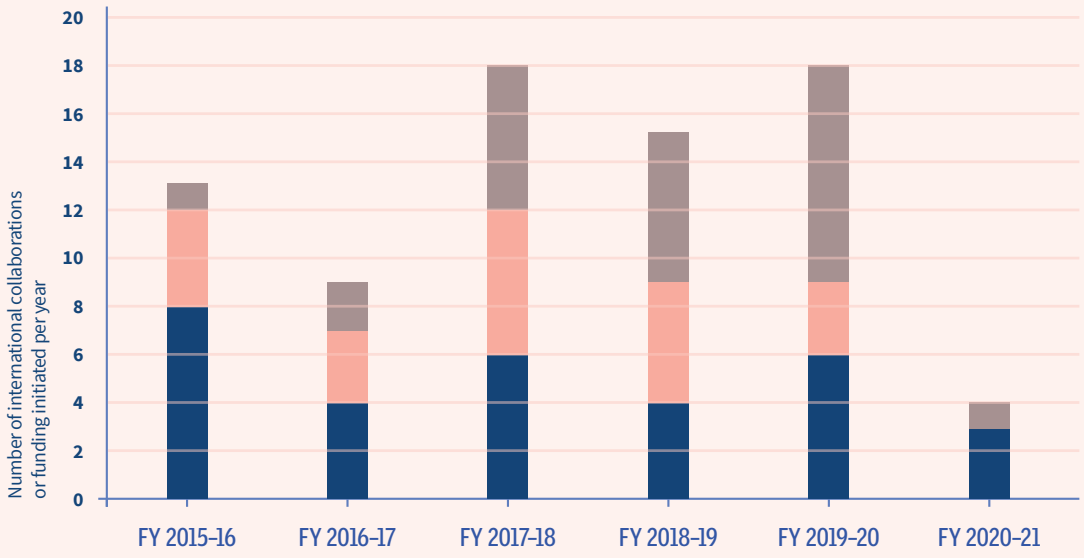
Vineetha Raghavan

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

Since 2020, the entire world has been in the grip of the COVID-19 pandemic. In response to this pandemic, government organisations, private and public sector companies in India have stepped up to support resources for testing facilities, research, and innovation to aid the management of the COVID-19 pandemic.



International Collaboration/ Funding Facilitated at BLiSC by RDO
Fund Recipts at NCBS (in INR Crores)



With support from the Department of Biotechnology, Government of India, a COVID-19 biorepository has been established on the BLiSC campus. NCBS is a partnering member of the Indian SARS-CoV-2 Genomics Consortium (INSACOG), jointly initiated by the Union Ministry of Health and Department of Biotechnology (DBT) with the Council for Scientific and Industrial Research (CSIR) and Indian Council of Medical Research (ICMR), to monitor the genomic variations in SARS-CoV-2. Recently, under the Mission COVID Suraksha scheme of BIRAC, the campus has received funding for supporting preclinical studies for COVID-19 research, diagnostics, and drug development.

Our campus has continued to receive generous donations from Azim Premji Philanthropic Initiatives, Standard Chartered Global Business Services, and IQVIA as part of Corporate Social Responsibility (CSR), to augment institutional testing infrastructure and facilities to respond to the ongoing pandemic as well as to develop new and innovative methods for COVID-19 testing. Unilever (including Hindustan Unilever Limited and Unilever Industries Private Limited) has funded a study to understand immune responses to SARS-CoV-2 and its accumulating variants in vaccinated people. This consortium, of which NCBS is the lead, consists of partners from Bangalore (NCBS, inStem, St John's Research Institute, Bangalore Baptist Hospital), Vellore (CMC, Vellore), and Pune (Pune Knowledge Cluster).

NCBS is also a partner in a consortium of collaborating clinical and research institutions to track SARS-CoV-2 variants through genomics, bioinformatics, and global data sharing. This is a part of philanthropic financial support from the Rockefeller Foundation to CSIR-CCMB for enhanced clinical and environmental surveillance by viral genome sequencing to better track SARS-CoV-2 today and monitor future threats tomorrow.

In addition to the funding for COVID-19 research, in the financial year

2020–21, the Habitat Trusts provided partial support to the Masters in Wildlife Programme at NCBS by instituting 'The Habitat Trusts Scholarship' for students in this programme.

Generous support from TNQ Technologies, a global leader in scientific, technical, and medical publishing has enabled the Archives at NCBS to formalise a Chair in the History and Culture of Science, the first of its kind in India. They also provide strong support and stability for the activities for the Archives. TNQ Technologies has contributed CSR funds to NCBS to support the activities of IndiaBiocience. CSR funding from Cactus Communications also supports the science communication and outreach efforts of IndiaBioscience, a programme initiated by NCBS for science outreach to fill the gap in the life science sector in India.

The RDO continues to support the establishment of national and international collaborations via grants, agreements, and the facilitation of interactions with potential collaborators. A few institutional international collaborations facilitated on campus include but are not limited to the University of Edinburgh, UK; Center for iPS Cell Research and Application (CiRA), Kyoto University; Duke-NUS, Singapore; University of Cambridge, UK; MPI-CBG, Germany; Institut Curie, France; and iTHEMS, RIKEN, Japan; Open University, UK. A notable new addition to our international partnerships is the institutional collaboration with King's College, London to promote collaborative initiatives in scientific research, training, and education. This collaboration was initiated this year with the award of three seed grants for supporting research in the field of neurosciences.

The RDO achieved a significant milestone in 2020 of completing a decade of operations at the BLiSC campus. This milestone was highlighted in an invited article by the RDO titled 'Celebrating a Decade of Success-Research management at a research institute in India' in the Mar/Apr, 2021 issue of the National Council of University Research Administrators (NCURA) Magazine, in their issue dedicated to 'Celebrating success'.

Work at the RDO is made possible by a dynamic and professional team who are committed to offering several key services to the campus at the boundaries of science, management, resource development, planning, and outreach. We look forward to a rewarding journey further ahead for the RDO, supporting campus research funding and research collaborations.

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

COVID-19 Pandemic and Indigenisation of Diagnostics

In March 2020, as the world was beginning to battle COVID-19, India grappled with its preparedness to manage the pandemic. There was 80% dependence on global markets for diagnostic kits, their components, and reagents. It was imperative that the country's molecular diagnostics community step up to manufacture affordable, accessible, and high-quality indigenous diagnostic kits. In the early days of the pandemic, the cost of each RT-PCR test was about INR 5000. This was not affordable and hence not accessible to a majority of the population in a scenario where controlling the pandemic was highly dependent on a test-track-isolate approach.

As the virus continued to mutate and spread across the country, more than 30 million cases were reported in India alone till June 2021. In this context, building a support system for indigenous diagnostic manufacturers became a vital step towards developing self-reliance in a range of diagnostic kits. This would facilitate the identification and testing of new variants, assuring safety in workplaces.

The CCAMP-InDx programme was conceptualised as a response to this need to support Indian diagnostic manufacturers and drive indigenous manufacturing. The programme was flagged off to establish a strong supply chain network of Indian micro, small and medium enterprises (MSMEs) and work alongside them to ensure that international standards of quality were met and capacities scaled up. The goal was to reach a stage where these manufacturers would be able to produce, supply, and execute 1 million indigenous diagnostic kits per day.

This programme is funded by The Rockefeller Foundation and executed by the C-CAMP, Bangalore, India. It constitutes a governance teams that offer strategic directions, a programme management unit, a functional team with operational responsibilities, and the Centres of Excellence (CoEs) for scientific and technical support.

With the onset of the pandemic in India, the first phase was dominated by multiple challenges that made India fall short of the demand for COVID-19 testing across the country. The four dimensions of the key challenges were the primary focus areas for the programme: cost of the tests, access for all, quality of the tests, and availability through supply chain management.

C-CAMP is helping fill these gaps through

1. Indigenisation
2. Optimisation
3. Commercialisation
4. Scale-up

In building the country's self-reliance in molecular diagnostics, CCAMP-InDx is at the forefront of uniting local manufacturers, service providers, regulators, government agencies, and, most importantly, research institutions to leverage knowledge and expertise in building quality and capacity for molecular diagnostics.

CCAMP-InDx is a pioneering programme in indigenising deep-tech manufacturing in the country by removing supply chain impediments and bypassing the issues of lack of marketplace and service providers. It has set up cross-disciplinary collaborations across the value chain in the country, with the final aim of helping Indian companies make global impacts in the yet out-of-reach arena of deep-tech.

Innovating and Building Digital Outreach and Engagement

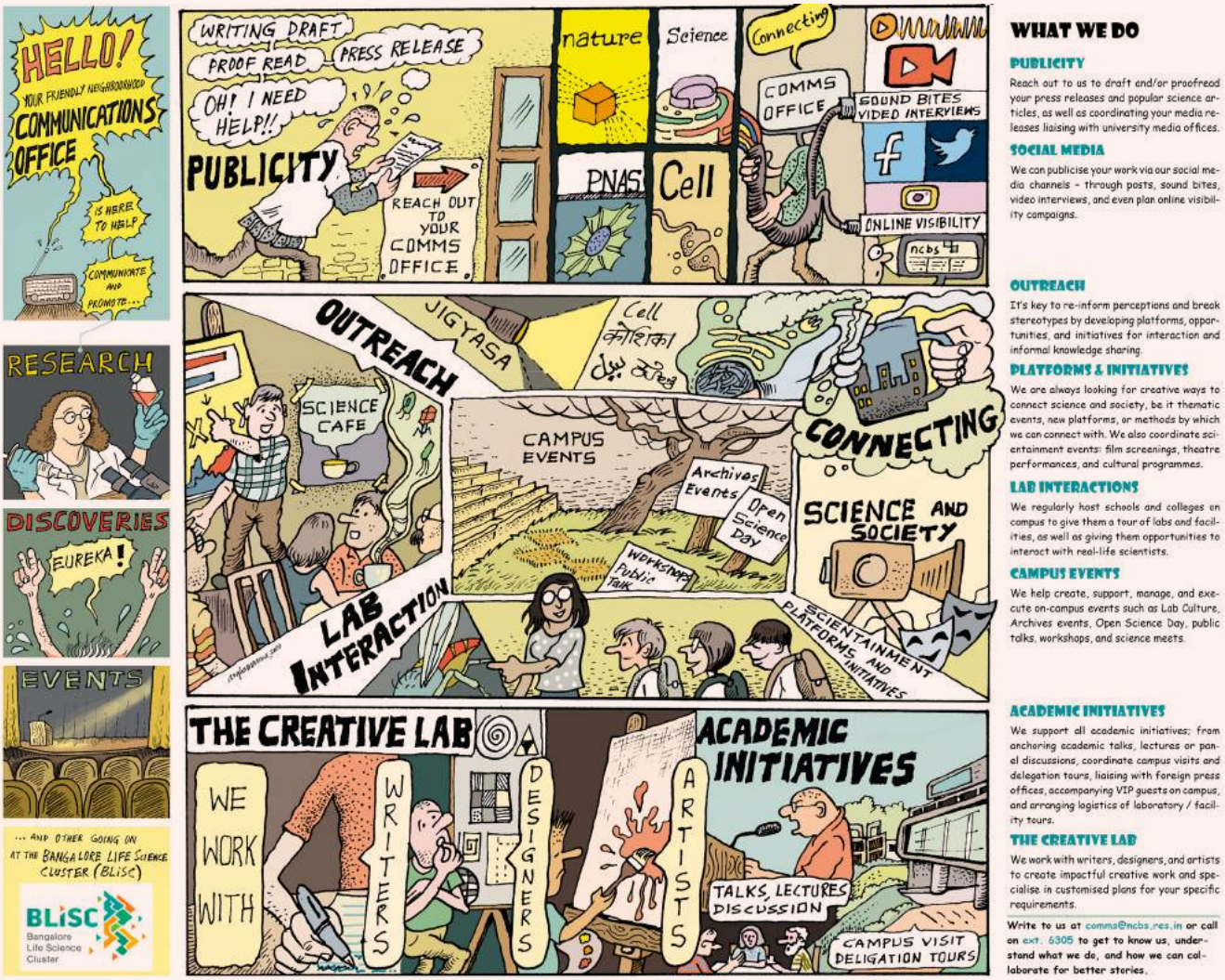
Pavithra Ashok Kumar

The Communications Office at the Bangalore Life Science Cluster (BLiSC) serves as a conduit for scientists from our campus and people outside to connect in meaningful ways. While public engagement seems most meaningful in person, with the continuing pandemic, digital engagement was necessary. This challenged us to be more inventive in our activities to spark curiosity, to engage, and to inform.

As the science engagement and communication partners of campus scientists, we are responsible for building awareness about and interest in campus research through our social media, press relations, and wide-reaching digital campaigns. Prior to the pandemic, we were also able to facilitate campus visits for students of schools and colleges from Bengaluru and all over the country to experience laboratory settings and have in-depth interactions with researchers. Since 2020, we sought new means and mechanisms to help bridge this gap between live interactions and knowledge-sharing by the laboratories.

OutsideIn is a set of Ecology talks by experts in diverse fields, curated for young audiences

Lab in Focus was a digital deep dive into the lives and science of researchers, one lab at a time.



What we do at BLiSC
Activities of Communications Office at BLiSC

An exciting venture we launched to bring science into the homes of our virtual audiences. Lab in Focus was a digital deep dive into the lives and science of researchers, one lab at a time. We had the opportunity to showcase the Biodiversity Lab led by Krushnamegh Kunte, and the Adaptation Lab led by Deepa Agashe in March and April 2021, before the second wave of the pandemic shook the nation, and the campus.

Since March 2020, NCBS has been a strong partner in the covid-gyan.in initiative, a pan-institutional, multi-lingual effort to combat misinformation about the virus and associated pandemic, with an emphasis on reliable information and scientific developments. In the second wave of the pandemic, led by Uma Ramakrishnan, our team revived CovidGyan. We organised a set of informative WebGyan sessions with experts, touching upon indigenous diagnostics, pandemic complexity, and vaccine hesitancy. We also organised a community interaction-based Sundowner Session on grief in the workplace, a topic that resonated with many in our audience.

While we collectively mourned and experienced a more trying year than we could have imagined, the research done on campus manifested in a slew of fascinating publications. We ensured that research papers by all the labs continued to receive due attention through tailored

communications, and were also keen to support the Cluster's COVID-19 response efforts. We worked to ensure these garnered the attention they deserved. We shared the excitement of these discoveries, the nuances of scientific theories, and stages of the scientific process of research via articles, social media posts, and audio visual formats.

Moumita Mazumdar and Raghul M R continued creating the bulk of our creatives in-house, including event posters and videos for NCBS, DBT-inStem, and C-CAMP, with inputs from the organisers and team. These have been especially important for our online presence and reach. Our digital reach has been built through sustained efforts over the years, and grown significantly in the past two years, with a large mailing list and strong institutional social media presence. Our mailing lists continued to receive timely updates on interesting events from the Cluster and affiliates.

In addition to our research community, we also supported the initiatives of the Bengaluru Sustainability Forum, Science Gallery Bengaluru, the Biodiversity Collaborative/National Mission on Biodiversity and Human Well-Being, the echo network, Museum and Field Stations Facility, and the Archives at NCBS with press relations, webinars, and public engagement.

HIGHLIGHTS OF OUR DIGITAL SCIENCE ENGAGEMENT

We digitally celebrated National Science Day, with a sci-art competition and the BLiSCQuiz hosted by Berty Ashley, which were well-received. Our team also created and launched two videos highlighting our exceptional Mouse Genome Engineering Facility and Next Generation Genomics Facility with the facility heads—in line with the theme of the day—on the future of science, technology, and innovation.

(right) We digitally celebrated National Science Day, with a sci-art competition, the BLiSCQuiz hosted by Berty Ashley, and by launching videos highlighting our exceptional Mouse Genome Engineering Facility and Next-Generation Genomics Facility.

(below) On 22 July 2021, Prof. Gagandeep Kang, Prof. Sandhya Koushika, and Sangeeta Iswaran discussed vaccine hesitancy in India in a WebGyan session

The OutsideIn Ecology series, started in 2020, remained a popular series in 2021. Initiated by R. Sowdhamini and organised by the Communications Office, the themes of discussion ranged from the tiniest of microbes to the scale of ecosystems. 31 sessions were organised between June 2020 and April 2021, and have reached nearly 3000 people, either live or through recordings. Another themed series that proved popular, the Human Body InsideOUT, explored various facets of our anatomy over the course of five talks in 2020. These series were possible as audiences and scientists alike were largely home-bound and keen to discuss and learn from each other's perspectives.

We also participated in international digital engagement. NCBS is one of eight sister institutes spread across five continents that partner in Life Science Across the Globe (LSAG), and is the anchor for India. Our role in promoting the talks has been a successful one, both with the weekly sessions and monthly seminars of 2021.

KNOWLEDGE-SHARING AND SKILL-BUILDING FOR SCIENCE COMMUNICATION, ENGAGEMENT, AND OUTREACH

Early in 2021, we launched the BLiSC Comms Bulletin. We published six editions highlighting the science communication and engagement activities of campus communications personnel. Designed by Siddharth Kankaria, with inputs from Amrita Tripathy, Chandrakant Redican, Debarshini Chakraborty, Mahinn Ali Khan, and myself, we were able to recap past activities and invite interest in upcoming events. We hope that this bulletin attracted additional campus members to communications and building related skills. We also pivoted from hosting webinars to training others in the community to hosting their programmes independently.

We continued to support and expand the set of laboratories exploring Twitter and Youtube for their initiatives, allowing them to grow the digital presence of the Cluster alongside institutional handles. One of these efforts was the Bugbears Lab's Weekend Chat with Researchers on Youtube, which has had two seasons thus far! Several campus scientists deliver talks online regularly and through these activities, reach out to school students and young citizens. We see tremendous scope for information shared directly by students and faculty. This seems like an inclusive and exciting avenue for science communication in the future as the campus grows in research themes, with new laboratories, and more flagship programmes.

To help create a community of science communicators who can assist each other learn and grow, the BLiSC Media Club was born in September 2021. We hope the club will serve as fertile ground for the spread of communication skills and help bolster the science engagement and outreach efforts of the campus. By equipping more researchers to share the science they are working on or are curious about themselves, the spread of accurate and intriguing information can continue to meet increasing interest from our audiences, whether they are digital or offline. We look to a hybrid model of interactions in the future.

Although opportunities for outreach with school children have been limited, a fruitful partnership with CARE India holds promise for interactions with children from underserved communities in rural and semi-urban areas. A series of initial interactions for girl students with faculty and student scientists at NCBS and inStem were organised in February and March 2021.

The outreach efforts from the Cluster, led by Sandeep Krishna, with the Parikrma Humanity Foundation's unique set of schools are taking shape for a long-term programme of interactions. These will also enable the campus to build new ties to the local communities that surround the physical space we occupy.

We hope there will be many in-person events in 2022, to communicate the exciting science that continuously unfolds on the campus. As many of our team move to new roles, including Chandrakant, Mahinn, and myself, we are glad to see the campus blossom with more science communication, engagement, and outreach efforts.

The Communications team at their poster for the Circle of Life-NCBS Annual Talks 2020

Basking Green Bee-eater in Heseghatta Lake in the outskirts of Bangalore. This was shot by Ansil B R who, is a PhD student.

Green Bee-Eater

Highlights of the Year

p. 180–190

Meetings and Workshops Calendar 2021

Sequencing Genomes through the Pandemic

Securing India's Environmental Future
for the Well-Being of Her Citizens

Saliva Screening to Safeguard the Campus from COVID-19

The VISION Platform: Vaccine Immunology Studies –
Indian Outbreak-Response Network

Meetings and Workshops Calendar 2021

January

6–9 January 2021

Zooming through Biology, a four-day lively discussion on biology

February

28 February 2021

As part of National Science Day celebrations, BLiSC arranged a Sci-Art Competition and the BLiSCQuiz.

March

9 March 2021

A Brief History of the Next Pandemic, a special interdisciplinary panel on pandemics with Dr. Chinmay Tumbe, Dr. Gauri Divan, Mr. Nadir Godrej, and Prof. Vijay Chandru

April

3–4 April 2021

4th National Post Doctoral Symposium: Mission to help scholars transition to diverse career paths/STI sectors

May

5 May 2021

Life Science Across the Globe was relaunched as a series of monthly seminars with eight sister institutes

June

17 June 2021

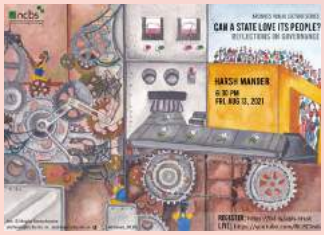
Dr. Taslimarif Saiyed and Prof. S Ramaswamy discussed **'Made in India diagnostics in the context of COVID-19'** in a WebGyan session

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

July

7 July 2021

NCBS hosted Life Science Across the Globe for a seminar on the **'Origins of Humans and Culture'**



August

13 August 2021

A talk by Harsh Mander on **'Can a State Love its People? Reflections on governance'**

September

18 September 2021

Humboldt Day celebration event with five speakers from around the globe and a panel discussion

October

22 October 2021

Archives Public Lecture Series: In Digital Exile - Narrating Urban Histories with Rachel Lee, Mareike Hetschold, and Laura Karp Lugo

November

17 November 2021

London Global Cancer Week: Updating the Economics of the War on Cancer with Dr. Dimple Notani, Dr. Pawan Mehrotra, Dr. Ravi Kannan, and Prof. Smita Srinivas

December

17 December 2021

Archives Public Lecture Series: Understanding Inequality with Reetika Khera

Sequencing Genomes through the Pandemic

SARS-CoV-2 and COVID-19 have occupied our thoughts and dominated our lives over the last two years. We initiated COVID-19 testing on campus in April 2020, and sequenced a hundred genomes from the positive cases in 2020. In early 2021, we began to understand that certain genomic strains of the virus were more transmissible. Realising the need for genomic surveillance to rapidly detect variants of concern, the Union Ministry of Health and Department of Biotechnology (DBT), with the Council for Scientific and Industrial Research (CSIR) and Indian Council of Medical Research (ICMR) initiated the Indian SARS-CoV-2 Genomics Consortium (INSACOG). A consortium of 28 National Laboratories, INSACOG monitors the genomic variations in SARS-CoV-2. The inStem and NCBS were early participants in INSACOG, and have sequenced over 5000 genomes since January 2021.

INSAGOG data have already yielded several insights. We know, for example, that various SARS-CoV-2 lineages or strains are common and that their frequencies have changed over time. Today, most positive cases are dominated by variants of the Delta lineage. But how did this happen? How exactly did the virus change? Do these changes matter from a clinical and epidemiological perspective? Answering these questions is not scientific curiosity, but critical in preparing for upcoming waves. It also requires a very targeted sampling strategy, for which we have identified hotspots of infection. Recently, with support from the Rockefeller Foundation, NCBS, in partnership with institutions in Hyderabad, Delhi, and Pune, has launched a retrospective and prospective sequencing campaign, hoping to gain a detailed understanding of how the virus is changing dynamically over time, and how and why this matters to disease outcomes. The prospective surveillance also includes a wastewater testing and environmental surveillance strategy.

The NCBS-inStem sequencing facility has been crucial in these sentinel surveillance efforts. Awadhesh Pandit, the Genomics Facility Manager says, ‘The Whole Genome Sequencing of community-based COVID-19 samples provides an unbiased way to detect new coronavirus strains. The campus Next Generation Genomics Facility (NGGF) has been involved in the sequencing of COVID-19 samples for the last one and a half years. It has been a great learning experience that will help us prepare better for, and quickly contain any future outbreaks’.

The current sequencing efforts will continue with an aim to track the emergence of new variants. inStem-NCBS has a Biosafety Level 3 (BSL-3) Facility for viral cultures and currently is gearing up to set up an Animal BSL-3 Facility. These facilities, in combination with the sequencing effort, will enable the campus to better understand the virulence and the infectivity of the new variants.

Dr. Awadhesh Pandit with the Illumina Hiseq2500 at the Next Generation Genomics Facility, BLiSC

Securing India's Environmental Future for the Well-Being of Her Citizens

Covering about 2% of the global land expanse, India harbours nearly 8% of the world's biodiversity. Recognised as one of the 17 'megadiverse' countries, India hosts 4 of the 36 global biodiversity 'hotspots', and is one of the eight centres of global food-crop diversity. Natural services just from India's diverse forests amount to at least INR 128 trillion/year. Local ecosystem services sustain livelihoods of a large proportion of the rural population, currently estimated to be 650 million people.

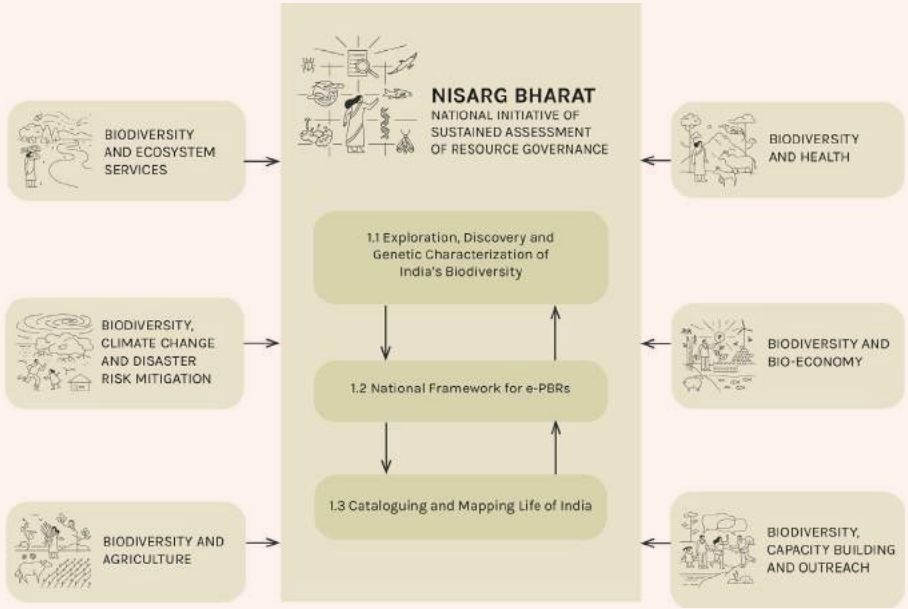
Yet as millions of Indians look to the future, we realise that there are significant environmental challenges. How will we tackle these? In an ambitious bid to take this challenge head on, the Biodiversity Collaborative has proposed a National Mission on Biodiversity and Human Well-Being. This proposed mission aims to mainstream biodiversity, so that all considerations of the future will involve biodiversity and all Indians will understand how and why it matters.

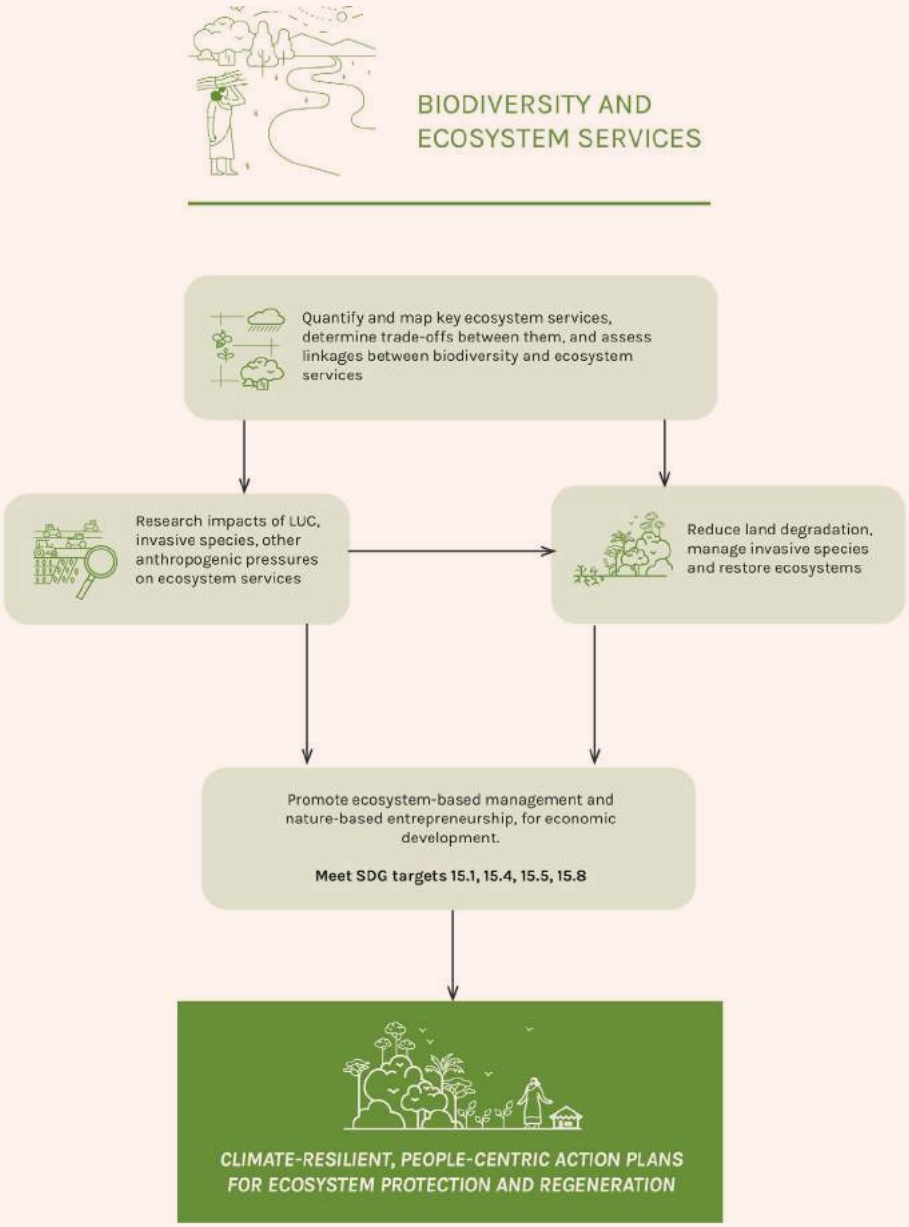
Uma Ramakrishnan, Mahesh Sankaran, and Shannon Olsson from NCBS participated in putting together the detailed project report for this effort. Uma Ramakrishnan and Mahesh Sankaran contributed to the Biodiversity and Ecosystem Services vertical (see next page) and over the last two years, have been working with several others to put together guidelines and policy documents for ecological restoration, invasive species management, and landscape scale conservation and its prioritisation. These activities are a critical component of the mission.

Together with Suhel Quader (NCF), Shannon Olsson has helped develop the outward-facing aspects of the mission, including capacity building, citizen science, and communication. In preparation for these aspects, they compiled a series of databases, surveys, working groups, workshops, and related documentation to offer insights on current standing and the needs for harnessing the capacities of a wide range of stakeholders to positively contribute towards biodiversity science and human well-being. Among many other highlights (see below), the team organised India's first two National Conferences on Citizen Science for Biodiversity in 2020 and 2021, attended together by over 1000 participants from all walks of life across India.

The Ministry of Environment, Forest, and Climate Change, Government of India, is expected to launch this unique National Mission on Biodiversity and Human Well-Being soon. Until then, we will continue to work together and encourage our understanding of India's vast biodiversity and its importance for our lives and livelihoods.

From Bawa et al. 2021, the envisioned vertical and planned framework for the proposed mission.

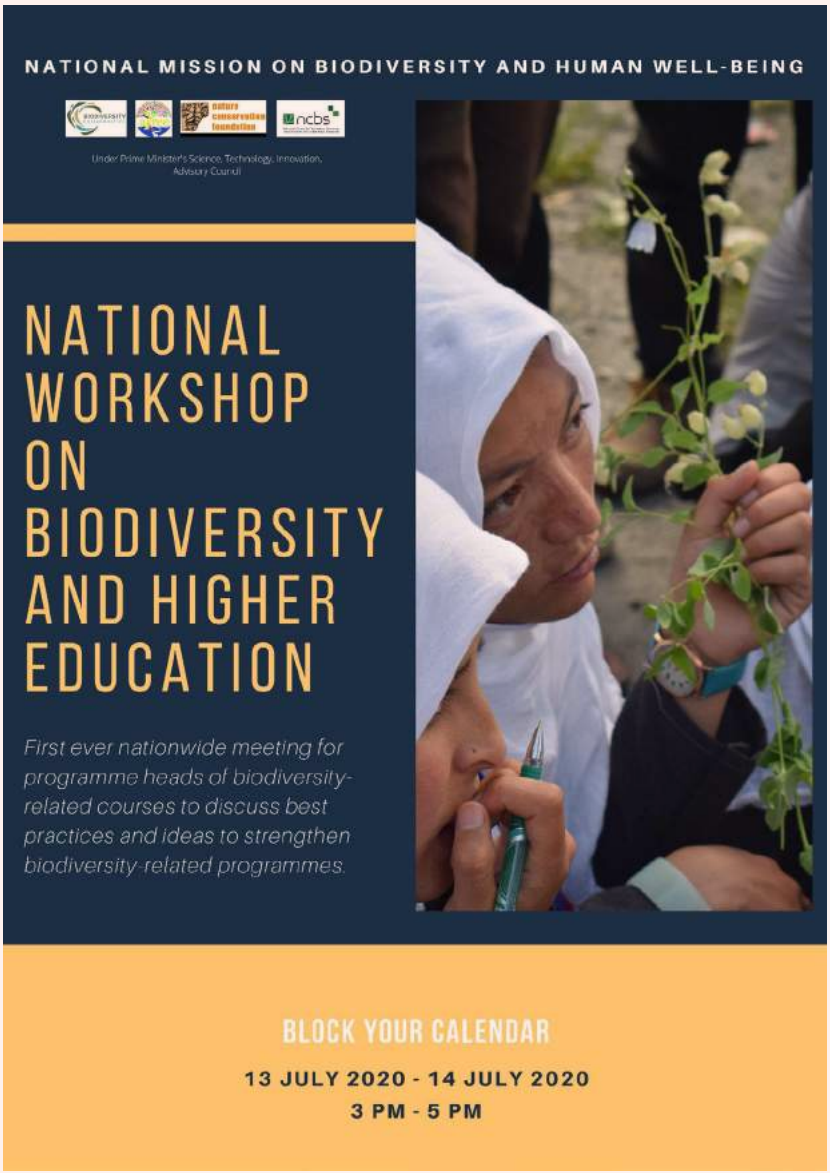


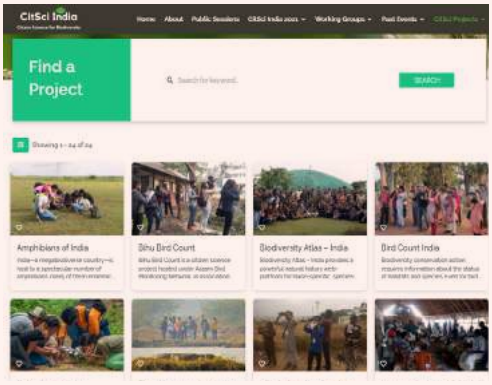


(right) National Workshop for Capacity Building with Policy Brief

(bottom left) CitSciIndia 2021 National Conference

(bottom right) National Citizen Science Repository.





PUBLICATIONS

Bawa, K. S., Sengupta, A., Chavan, V., Chellam, R., Ganesan, R., Krishnaswamy, J., ... and Vanak, A. T. 2021. **Securing biodiversity, securing our future: A national mission on biodiversity and human well-being for India.** Biological Conservation, 253, 108867.

Saliva Screening to Safeguard the Campus from COVID-19

Over the last two years, all of us have had our nose and throat scratched as part of the COVID-19 test. Following this, we have waited with bated breath, sometimes for several days to find out whether we are positive. These tests require skilled personnel to collect samples and are invasive. The timely execution of the tests requires reagents for extracting viral genetic material (RNA) and performing RT-PCR, and there are often supply chain issues with timely acquisition of reagents for these processes.

What if we had a quick, self-sampling based approach that could be used to screen people for COVID-19? Such an approach would be very valuable specifically in places like our campus, where many people work together and where we want to avoid clusters of infections. Through the pandemic, scientists across the world have attempted to address this question, and one relatively good solution they proposed was the use of saliva as a sample source for SARS-CoV-2 screening.

In late 2020, a team of researchers on the NCBS campus worked in collaboration with clinicians Dr. Carol and Dr. Sindhulina from Bangalore Baptist Hospital to validate how accurate saliva is compared to the gold standard nasopharyngeal swabs as a source of sample for COVID-19 testing. Their results suggested relatively high concordance, and that storage of the saliva following collection (instead of immediate testing) results in poorer concordance.

In early 2021, in cognizance of these results, mathematical modelers at NCBS investigated trade-offs between the enhanced screening capabilities offered by saliva (because it is non-invasive and self-collection is possible) and its efficacy. These simulation models revealed that despite slightly lower efficacy, if used widely, saliva screening on campus could pick up positives, and most importantly, incipient clusters of infection.

Finally, a third team of scientists and staff from NCBS and inStem set up the logistics for the collection of saliva samples, testing them by RT-PCR, and speedy reporting of results. They developed very effective standard operating procedures that included digital tracking of self-collected saliva samples, efficient workflows for testing, and rapid, SMS-based reporting of results to campus members. Several innovative technical solutions were devised to make the process affordable for use on scale. The saliva-based screening on campus has been operational since May 2021. All campus staff attending work are tested once a week and to date, over 2000 samples have been tested as part of this programme.

We are incredibly proud of our efforts here. We took a scientific question and turned it into a practical application for campus safety. Of course, our efforts were critically dependent on the services provided by the testing team and the technical services group. The testing team at BLiSc includes several dedicated microbiologists and a lab head. This team has been functional for over a year now, after the initial volunteer-driven testing effort early in the pandemic. We take this opportunity to thank the testing team, and especially its present lead, Harsha P K and her predecessor B. Santosha. We also thank many members of the BLiSc Technical and Research Services Team led by P C Gautam for coming up with several innovative solutions to implement saliva testing for COVID-19 screening. Their work and continued dedication has been critical for supporting safeworking on the BLiSc campus! The development of the campus saliva testing program was supported by InDx.

The testing team at InStem and Harsha P K, seen in the centre in the second row, leads a small but dedicated group that runs the COVID-19 Testing Laboratory and COVID-19 Biorepository on campus.

Since its inception in April 2020, the testing laboratory has tested over 2 lakh samples from throughout Karnataka. They are now an important part of analysing saliva samples from BLiSC members who are tested on a weekly basis, as an overall campus surveillance program to quickly identify and contain potential infections. In addition, Harsha takes the lead in curating the inStem/NCBS COVID-19 Biorepository that currently has 7000+ samples, which scientists from both academia and industry have utilised to test new anti-SARS-CoV-2 therapies and develop/optimise diagnostic kits made in India.

The VISION Platform: Vaccine Immunology Studies – Indian Outbreak-Response Network

Vaccination has emerged as a very effective tool in our armoury to mitigate the medical and socio-economic devastation caused by the pandemic. Two of the most widely used COVID-19 vaccines in India, Covishield™ and Covaxin™, have been administered to almost 81% of our population. All COVID-19 vaccines, including Covishield™ and Covaxin™ have been developed on remarkably rapid timescales and approved for emergency use in the population. As a result, in contrast to what we are normally used to in the field of vaccine development, many questions remain unanswered about how long immune responses will last, whether this immunity will protect against new and emerging variants, and if any other factors such as nutritional status will determine the effectiveness of the vaccines. Answering these questions requires the application of basic immunology in the setting of human clinical studies.

To address some of these questions, NCBS has nucleated a group of Clinical Research Centres and Research Institutes to carry out a study on various aspects of the COVID-19 vaccine response in humans. This is a multi-institutional and multi-city study; participating clinical centres include Bangalore Baptist Hospital and St. John's Medical College Hospital from Bangalore, Christian Medical College, Vellore, and the King Edward Memorial Hospital and Research Centre along with Symbiosis Hospital and Research Centre from Pune. Along with NCBS, several private and public research institutes in Bangalore (Institute for Stem Cell Science and Regenerative Medicine, a DBT Institute, and St. John's Research Institute) and Pune [Indian Institute for Science Education and Research, Pune (IISER-Pune), CSIR-National Chemical Laboratory (CSIR-NCL)] are part of this study. This group has been named the VISION platform: Vaccine Immunology Studies – Indian Outbreak-response Network. The VISION platform is coordinated by Dr. Mangai Ashokan, is mentored by a steering group chaired by Prof. Gagandeep Kang, and includes Profs. Vineeta Bal, Annapurna Vyakarnam, Satyajit Mayor, Raghu Padinjat, and L S Shashidhara.

Through its clinical partners, the VISION group is enrolling 800 healthy participants aged 18–45 years (400 in each city) to study the immunogenicity of COVID-19 vaccines. This clinical cohort will include both vaccine-naïve seronegative and seropositive participants. VISION will follow their immune response over 12 months, after vaccination with either Covishield™ and Covaxin™, vaccines administered in their respective approved vaccination schedules. The outcomes of this study

should lead to a better understanding of the immune response to current COVID-19 vaccination strategies and help develop more effective vaccination strategies.

The VISION platform is enabled by the Office of the Principal Scientific Advisor to the Government of India to stimulate collaborations between industry and academia. From the industry sector, Hindustan Unilever Ltd. (HUL) and Unilever Industries Pvt. Ltd. (UIPL) R&D have provided generous CSR funding for this study. NCBS wishes to thank Dr. Vibhav R Sanzgiri, Executive Director R&D, HUL and UIPL, and Sanjiv Mehta, Chairman and Managing Director, HUL, for their unstinting support.

In addition to the immediate study on COVID-19 vaccinology, we expect that VISION will evolve into a sustainable platform that brings together clinical and basic science using 'multi-omics' analyses to understand the human immune response to emerging pathogens and vaccines. An enduring collaborative clinical and research platform will be essential to manage future waves of COVID-19 as well as other pandemics.

Turning (a) VISION into reality.

Seen here are the team coordinating the VISION activities across all the sites and performing the scientific component for the NCBS-Baptist cohort.

Collaborations

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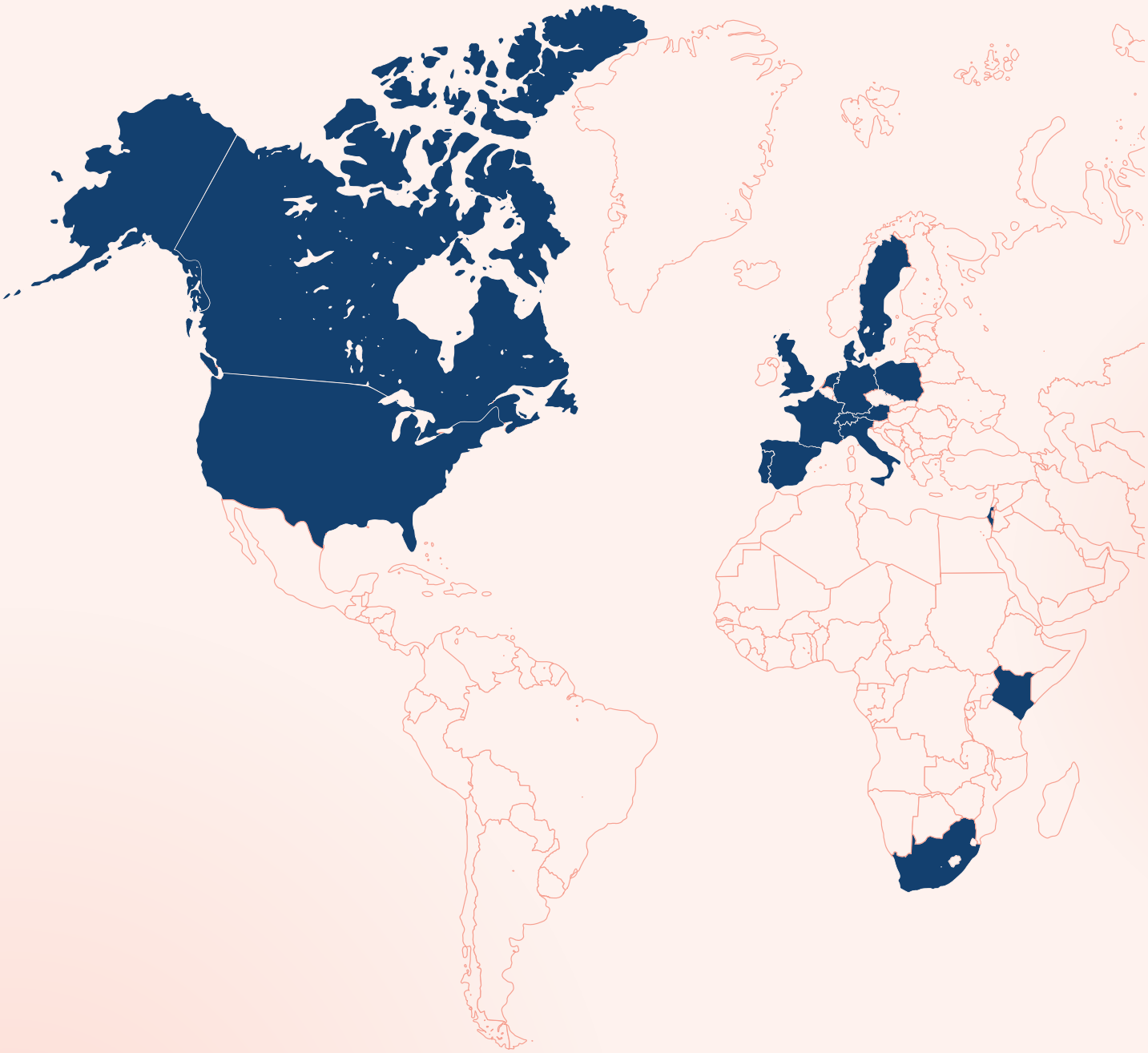
NCBS International Collaborations

NCBS National Collaborations

NCBS INTERNATIONAL COLLABORATIONS



List of all the international institutions:

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

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

UNITED KINGDOM
- Natural History Museum, London
- University of Cambridge
- Univerisity of Edinburgh
- University of Warwick
- John Innes Centre
- Durham University
- University of Leeds
- University College, London
- Nottingham Trent University
- King's College, London
- The Open University

NCBS INTERNATIONAL COLLABORATIONS

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

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

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

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

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

AUSTRIA
- University of Vienna

NETHERLANDS
- University of Groningen

POLAND
- Nencki Institute of Experimental Biology, Warsaw

SWITZERLAND
- University of Geneva

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

PORTUGAL
- Instituto de Medicina Molecular (IMM), Lisbon

ISRAEL
- Technion University

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

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

MALAYSIA
- International Medical Univerisity, Malaysia

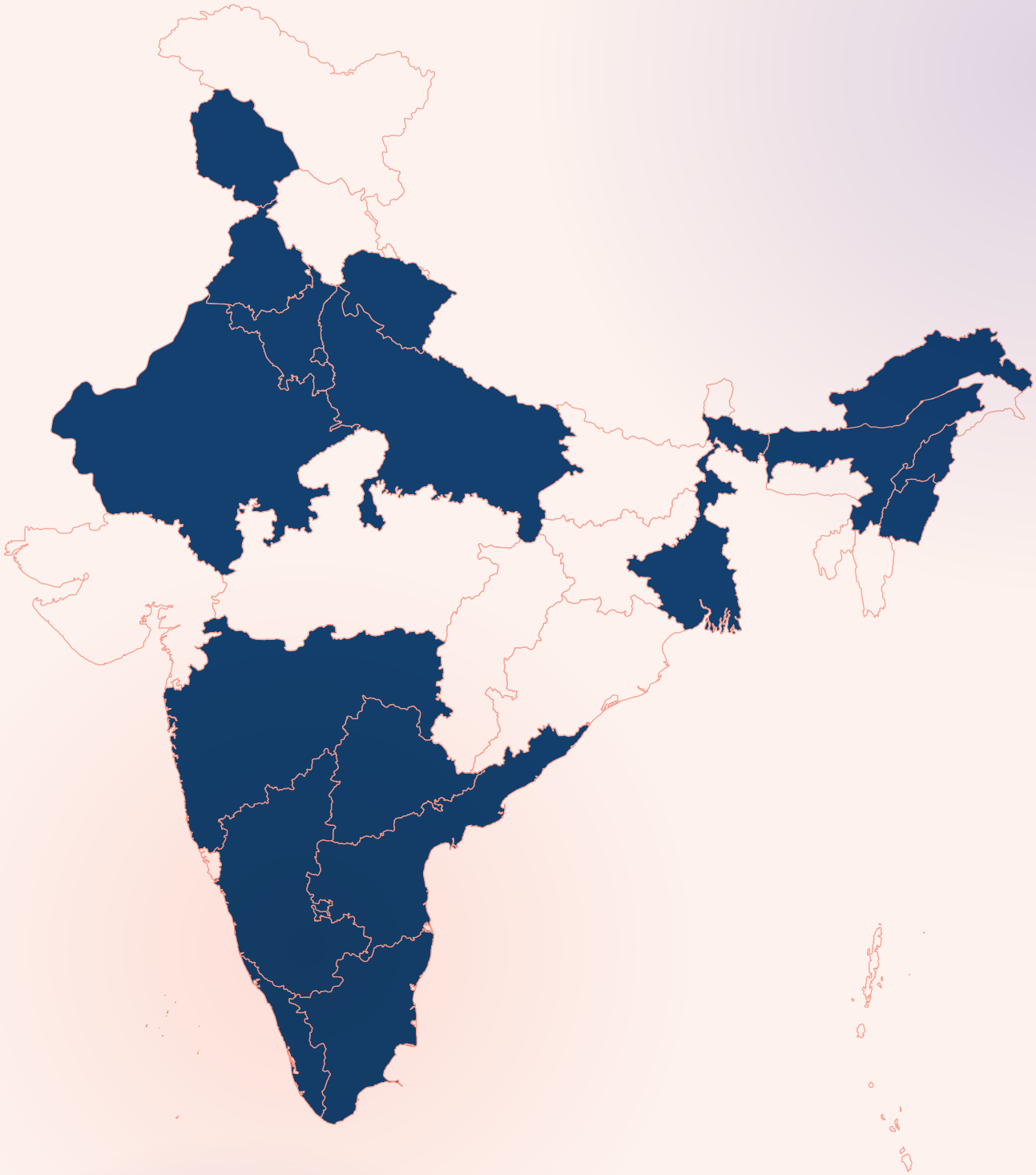
SOUTH AFRICA
- South African National Parks

KENYA
- University of Nairobi

NEW ZEALAND
- University of Otago, Dunedin

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

NCBS NATIONAL COLLABORATIONS



NCBS NATIONAL COLLABORATIONS

List of all the national institutions:

KARNATAKA (BANGALORE)
- Indian Institute of Science
- Institute of Bioinformatics and Applied Biotechnology (IBAB)
- Raman Research Institute
- Ashoka Trust For Research in Ecology and the Environment
- Foundation for Ecological Research, Advocacy and Learning
- Jawaharlal Nehru Centre for Advanced Scientific Research
- Gandhi Krishi Vignana Kendra (GKVK)
- International Centre for Theoretical Sciences
- National Institute of Mental Health and Neuro-Sciences
- Kidwai Memorial Institute of Oncology
- Nature Conservation Foundation
- Cytecare Hosptials Pvt. Ltd
- Punjab National Bank
- St. John's Medical College Hospital
- Bangalore Baptist Hospital
- National Conservation Foundation (FIG Tree Learning Centre)
- Rajiv Gandhi University of Health Sciences
- Society For The Promotion of Area Resource Centers
- IQVIA RDS (India)
- Azim Premji Philanthropic Initiatives
- Wipro Foundation
- Foundation for Neglected Disease Research(FNDR) Tata Institute for Genetics and Society(TIGS)
- Long Term Ecological Observatories for Climate Change Grassland
- Apollo Hospital (Dr. Ravindra M Mehta)
- Bangalore Water Supply and Sewerage Board (BWSSB)
- CBCI Society for Medical Education

KARNATAKA (MYSORE)
- Nature Conservation Foundation

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

MAHARASHTRA (MUMBAI)
- Tata Institute of Fundamental Research
- Indian Institute of Technology
- Bhabha Atomic Research Center (BARC)
- Bombay Natural History Society
- Tata Memorial Hospital
- Thackeray Wildlife Foundation
- Tata Memorial Centre
- Unilever Industries Private Limited

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

ARUNACHAL PRADESH
- Rajiv Gandhi University

KERALA
- Indian Insitute of Science Education and Research, Thiruvananthapuram
- Malabar Cancer Centre, Thalassery
- VPS Lakeshore Hospital, Kochi

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

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

RAJASTHAN
- Indian Institute of Technology
- Central University of Rajasthan
- All India Institute of Medical Sciences
- Government of Rajastan

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

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

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

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

TAMIL NADU (REST OF TN)
- Bharathidasan University, Tiruchirapalli
- Christian Medical College, Vellore

UTTAR PRADESH
- National Botanical Research Institute, Lucknow

PUNJAB
- Indian Institute of Science Education and Research, Mohali

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

MANIPUR
- Institute of Bioresources and Sustainable Development

NAGALAND
- Nagaland Science Council

ASSAM
- Indian Institute of Technology, Guwahati

The People Behind The Scenes
Design Note

Last year, the annual report was a reminder of how resilient the campus was through the pandemic year. This year was no different. However, in order for it to continue functioning in that manner, it needed the assistance of several people who toiled tirelessly to keep the campus running. In an effort to recognise their effort, this year's theme is the People Behind the Scenes. The theme aims to recognise the work done by different teams and individuals and their contribution towards keeping the campus safe and functioning smoothly during the pandemic.

This theme is a way for the campus to show its gratitude. Hence, we decided to treat the report as a Thank You Note to all the people who helped along the way. Typically, we would have created a visual articulating this idea. Instead, we have decided that everyone needs to know the actual people behind the scenes. Hence, we have their names on the cover as a part of this note. We selected the wavy pattern as a subtle nod to the ripples that they make through their work. On the cover are the names of 483 persons, covering staff from various departments – Academic Office, Accounts, Administration, Architecture, Civil Maintenance, Dean's Office, Dispatch, Dolna Creche, Electrical, Front Office, Grants, Guest House, Hospitality, Housekeeping, HVAC, Instrumentation, IT, Lab Support, Landscape and Horticulture, Library, Mechanical Workshop, Meetings Office, Purchase, QA and QC, Security Services, Stores, Support Staff at the COVID-19 Facility, Support Staff at the Medical Facility, Research Facilities, Water Supply, and Communications.

Inside the report, we have a section called the People Behind the Scenes, where each department has nominated one person or a team that made an outstanding contribution to their work. Here, we have incorporated illustrations made by the very talented Leeza John. The illustrations highlight the work done by each department on campus – Hospitality, Administration and Academics, Health and Safety, Technical Services, and Campus Volunteers.

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