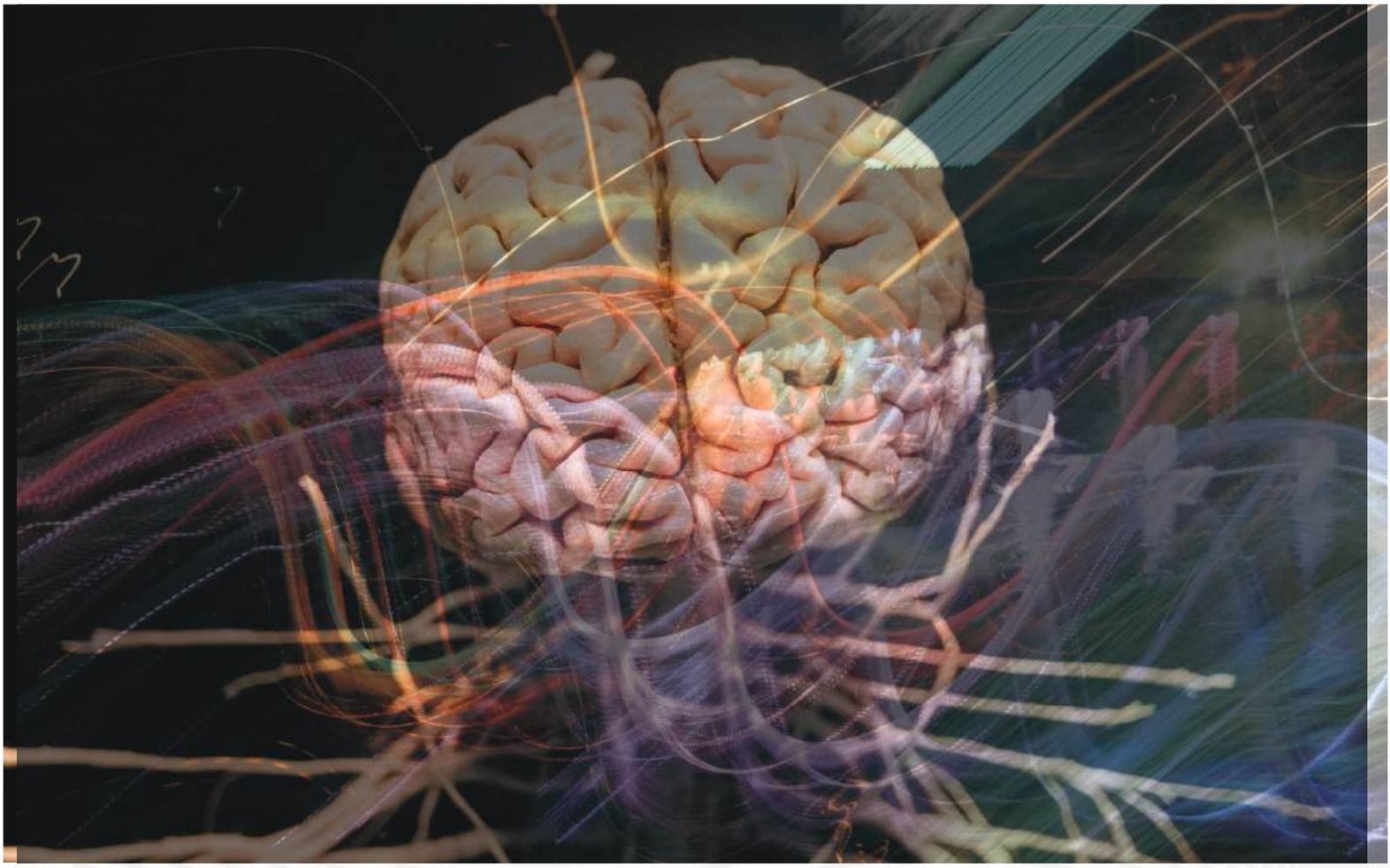
# CBR Currents

## Newsletter of the Centre for Brain Research, IISc

WAVE 6 MAY 2024



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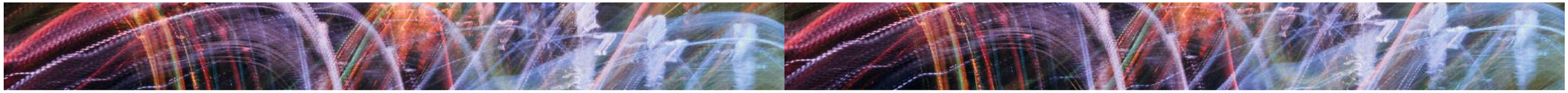


# Editorial

## A Continual Journey of Discovery and Collaboration

We are thrilled to present the sixth edition of CBR Currents, offering a glimpse into some of CBR's recent activities and accomplishments. At the heart (and brain!) of our endeavours lies a strong commitment to research and engagement aimed at alleviating the country's burden of dementia and other neurodegenerative diseases. In this mission enabled by support from the Pratiksha Trust and other visionary agencies, CBR embraces an interdisciplinary collaborative approach, forging partnerships with diverse yet aligned stakeholders.

This issue features a publication spotlight on an exciting finding (recently reported by Dr Adaikkan's group) that has advanced our understanding of feedback inhibition between major neuronal cell groups. This mechanism of communication intricately governs the overall patterns of neuronal activity in the hippocampus, thereby influencing spatial navigation and contextual memory.

We also celebrate the completion of whole genome sequencing of over 10,000 individuals, marking a significant milestone for GenomeIndia, a nationwide multi-institutional consortium funded by DBT and spearheaded by CBR since 2020. This unprecedented achievement sets the stage for advanced genetic research that could potentially lead to improved public health interventions, drug development, and personalized medicine.

The months that went by brought opportunities to commemorate important dates like World Parkinson's Disease Day and International Women's Day. CBR also assembled an engaging and educational showcase for IISc Open Day, a much-awaited annual event instrumental in bridging the science-society gap by fostering awareness and enthusiasm for scientific inquiry. This edition provides snapshots of these events and more, underscoring the vibrant energy and dedication that characterise CBR's pursuits.

Under the archive on infrastructure, read about the state-of-the-art biomarker analysis facility housed by CBR. Additionally, the recurring section 'Diverse Discourses' features informative pieces by our students.

As we march ahead towards our ambitious goals, we look forward to the continued support of all key stakeholders and remain open to exploring innovative channels for synergy. We hope you enjoy flipping through the pages and would greatly appreciate your feedback.

Happy reading!



# Publication Spotlight

## Communication mechanisms among cell groups in the brain for spatial and contextual information processing

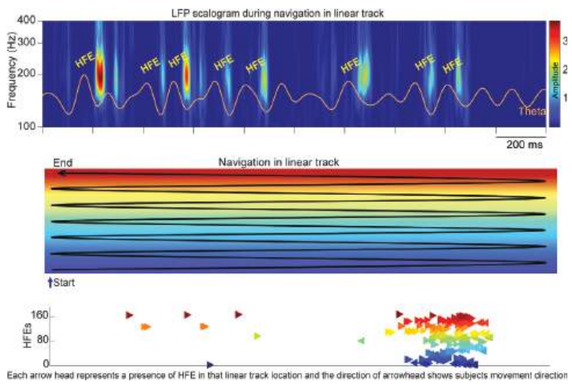
The hippocampus is a part of the brain area in the medial temporal lobe (MTL) and has been the subject of significant research since studies involving Patient H.M. in the 1950s. Patient H.M. had his MTL surgically removed to alleviate his epilepsy, but he developed anterograde amnesia (inability to form new memories) post-surgery. A series of studies with Patient H.M. underscored the crucial role of the hippocampus in memory and spatial navigation. Today, the intricate details of how cell groups in the hippocampus communicate to process learning, memory, and spatial navigation continue to be studied extensively at several institutions worldwide. A recent paper by Dr. Chinnakkaruppan Adaikkan's group at CBR sheds light on a specific type of communication known as feedback inhibition between major neuronal cell groups. This communication mechanism regulates the overall neuronal activity patterns in the hippocampus, regulating spatial navigation and contextual memory.

Communication between neurons happens at the synapses, where the sender neuron releases neurotransmitters, and the recipient neuron senses these neurotransmitters. Depending on whether the sender neuron releases activating or inhibiting neurotransmitters, the activity of recipient neurons is either activated or inhibited. These activating neurons are called excitatory neurons, and the inhibiting neurons are known as inhibitory interneurons. More than 70 percent of neurons in the brain are activating type, and the remaining 20 – 30 percent are interneurons. A complex cascade of events occurs at the synapse, including the fusion of the synaptic vesicles containing chemicals at the presynaptic membranes to release vesicles containing neurotransmitters.

Dr.Adaikkan and a postdoctoral researcher in his lab, Dr. Justin Joseph, in collaboration with Dr. McHugh's group at RIKEN, Japan, and Dr. Tsai's group at MIT, USA, genetically engineered mice and used adeno-associated viral vectors to selectively block the communication between activating neurons and the downstream inhibitory interneurons in a small region in the hippocampus known as CA1. Cleavage of vesicle-associated membrane protein, specifically in the hippocampal activating neurons in these mice, resulted in a complete loss of synaptic transmission between these cell groups. Using sophisticated techniques such as patch clamp recordings and cell-type specific optogenetics, the authors have demonstrated that this perturbation is so unique that these neurons can still generate action potentials and are physiologically active and normal- but their communication ability, specifically feedback inhibition, is reduced. Not surprisingly, the authors showed that contextual memory formation is impaired when feedback inhibition is selectively reduced in the hippocampus CA1 region.

Next, the authors addressed the central question of what the activity patterns in the hippocampus are during rest and spatial navigation when feedback inhibition is reduced. Addressing this question will facilitate our understanding

of neural processes underlying spatial navigation and memory. Activity patterns of neuronal cell groups in the hippocampus can be measured at multiple levels, including the sum of neuronal activities at the mesoscale level by hippocampal (i.e., intracranial) local field potential (LFP) recordings. Previous LFP recordings demonstrated the presence of several distinct activity patterns, broadly called theta, gamma, and ripple oscillations. In the hippocampus, theta oscillations (4-12 Hz; i.e., 4-12 cycles per second) are prominent during active exploration, gamma oscillations (30-100 Hz) are involved in binding together different aspects of sensory information and coordinating neuronal activity across brain regions, and ripples (100-200 Hz) are brief bursts of activity typically observed during rest or slow-wave sleep, and memory recall.




The authors have performed a very sophisticated experiment in which they first reduced feedback inhibition in the CA1 hippocampal circuit, followed by recording neuronal activity and LFP from the hippocampus as the animals performed a navigation task. This allowed them to investigate the relationship between neural activity patterns and behavioral performance. The paper used various neural signal processing analyses and showed that hippocampal CA1 continues to drive theta and gamma oscillations during spatial navigation, even under reduced feedback inhibition. Notably, the speed with which subjects walk or run positively correlates with the power of gamma oscillations in the hippocampus, and this is not affected in the experimental subjects with reduced feedback inhibition. However, the action potential of the several neurons during theta was way higher in the experimental groups than in healthy subjects. Surprisingly, the authors showed that this higher neuronal activity during theta oscillations also generated a unique oscillatory activity pattern called high-frequency oscillatory events (HFEs). These HFEs appeared similar to ripples occurring during slow-wave sleep. Bayesian decoding of these HFEs revealed that they happened as clusters when the subjects were in one place and almost absent when the subjects moved to another place during spatial navigation. Commonly, this phenomenon is observed only in the action potential of cell groups in the hippocampus, which are known as place cells, and that place is called place field. Thus, HFEs mimic place cells.

In conclusion, the study revealed that the feedback inhibition communication between activating and inhibiting neurons in the hippocampus is crucial for local sparsity of neuronal action potential to represent a place. In its absence or reduction, the hippocampal CA1 becomes hyperexcitable, and spatial navigation and contextual memory are impaired.

Adaikkan C*, Joseph J, Foustoukos G, Wang J, Polygalov D, Boehringer R, Middleton SJ, Huang AJY, Tsai LH, McHugh TJ*. Silencing CA1 pyramidal cells output reveals the role of feedback inhibition in hippocampal oscillations. **Nature Communications.** 2024 Mar 11;15(1):2190. doi: 10.1038/s41467-024-46478-3. PMID: 38467602; PMCID: PMC10928166. * corresponding authors

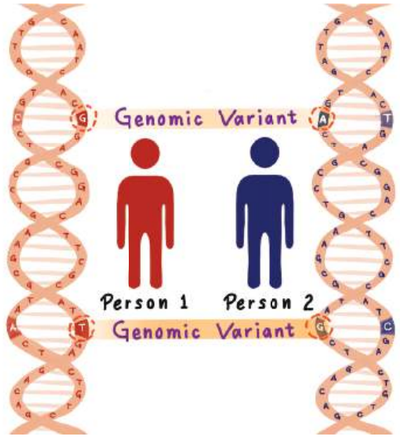
# GenomeIndia: A Jewel in CBR's Crown

**Bratati Kahali, Jothibasu V, Khader Valli Rupanagudi, Prathima Arvind, Shweta Ramdas, Yadati Narahari**

GenomeIndia, a visionary national project funded by the Department of Biotechnology,Government of India, was launched in January 2020 in consortium mode under the leadership of Prof. Vijayalakshmi Ravindranath, CBR's Founding Director. The project's ambitious goal is to sequence 10,000genomes from healthy Indian individuals spanning the length and breadth of the country. The primary aim of GenomeIndia is to construct a comprehensive catalogue of genetic variations for the Indian population that will better capture our unique diversity.

## Creating a Precious Resource for India's Public Health

While millions of genomes worldwide have been sequenced, the glaring gap lies in the severe under-representation of Indian populations in these global studies. Our population of 1.43 billion consists of more than 4600 ethnic groups, many of which are endogamous (that is, marriages within the

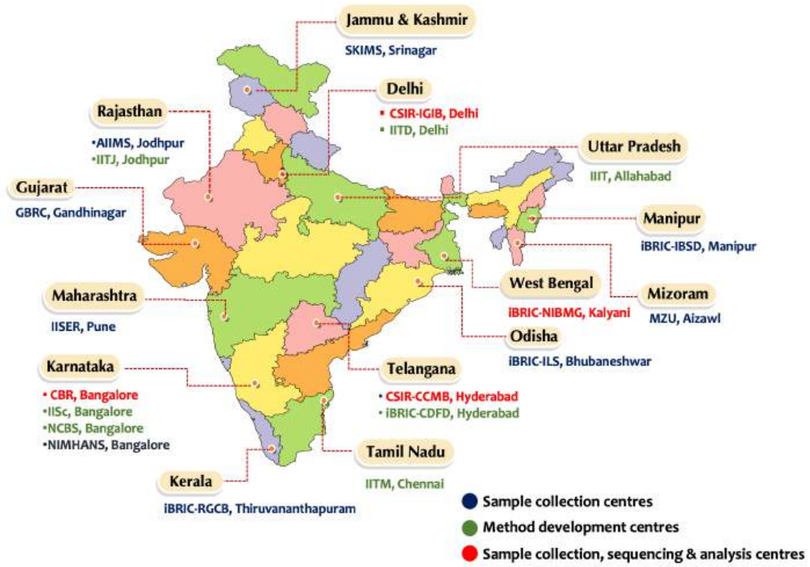



group). All these population groups have genetic variations unique to themselves, thus contributing to our unparalleled genetic diversity.

Distinct population groups differ in their genetic makeup and exhibit different risk factors for diseases. Consequently, findings from human genetics research from other populations of the world cannot be extrapolated to Indians. It is crucial to undertake studies that rigorously account for our own variations for better clinical practice. Moreover, sequencing our population is a first step towards bringing genetics to the world of personalized medicine. A national resource like GenomeIndia is a tremendous boon to clinicians in helping to find genetic diagnoses for patients with complex and rare disorders.

This effort has the potential to revolutionise healthcare, empowering clinicians and basicresearchers, and leading to transformative precision interventions. The impact of GenomeIndia,therefore, extends far beyond the lab, promising a healthier nation in the future.

## The GenomeIndia Consortium




GenomeIndia comprises dedicated scientists and researchers from 20 partner institutions,with some of the institutions playing multiple roles. CBR is playing a pivotal role as the national coordinator for this project.
Prof. Y. Narahari, former Director of CBR, is one of the joint national coordinators of this project, the other being Prof. Thangaraj from CCMB, Hyderabad. The centres are listed below.

### Sample Collection, Sequencing, and Analysis Centres

Centre for Brain Research (CBR), IISc Campus, Bengaluru
CSIR-Centre for Cellular and Molecular Biology (CSIR-CCMB), Hyderabad
CSIR Institute of Genomics & Integrative Biology (CSIR-IGIB), New Delhi
iBRIC-National Institute of Biomedical Genomics (iBRIC-NIBMG), Kalyani

### Sample Collection Centres

All India Institute of Medical Sciences (AIIMSJ), Jodhpur
Gujarat Biotechnology Research Centre (GBRC), Gandhinagar
iBRIC-Institute of Bioresources & Sustainable Development (iBRIC-IBSD), Manipur
Indian Institute of Science Education and Research (IISERP), Pune
iBRIC-Institute of Life Sciences (iBRIC-ILSB), Bhubaneswar
Mizoram University (MZU), Aizawl
National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru
iBRIC-Rajiv Gandhi Centre for Biotechnology (iBRIC-RGCB), Thiruvananthapuram
Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar

### Method Development Centres

iBRIC-Centre for DNA Diagnostics and Fingerprinting (iBRIC-CDFD), Hyderabad
Indian Institute of Information Technology (IIITA), Allahabad
Indian Institute of Science (IISc), Bengaluru
Indian Institute of Technology Delhi (IITD), New Delhi
Indian Institute of Technology Jodhpur (IITJ), Jodhpur
Indian Institute of Technology Madras (IITM), Chennai
National Centre for Biological Sciences (NCBS), Bengaluru

### Biobanking and Data Archival Centres

Biobank at the Centre for Brain Research (CBR)
Data Archival at Indian Biological Data Centre (IBDC)

## Expected Outcomes and Impact of GenomeIndia

- Develop a reference set of genetic variations for the Indian population by carrying outwhole genome sequencing of 10,000 samples from 99 ethnic groups.
- Create a biobank of 20,000 blood samples for future genome analyses.
- Make available genomic data for public access (digital public goods) for academic/research purposes through IBDC.
- Design genome-wide and disease-specific genetic chips for low-cost diagnostics andresearch activities.
- First big step towards developing genome-based precision medicine in India.
- Inspire India's young minds to explore the exciting area of genomics research and innovation for the betterment of the health of the Indian population.

## DBT Event to Celebrate the Success of the GenomeIndia Project (February 27, 2024)

An event was organized in New Delhi by the Department of Biotechnology to celebrate the achievement of completing the whole genome sequencing of 10,000 individuals. Dr. Suchita Ninawe, Advisor, DBT, and Dr.

Richi Mahajan, Scientist D, DBT were the principal organizers of this event. The distinguished invitees to the meeting included Dr. Jitendra Singh, the Hon'ble Minister of Science and Technology, and Dr.Rajesh Gokhale, Secretary, DBT.

During the event, Dr. Suchita Ninawe first introduced the origins of the GenomeIndia initiative. "Led by the Centre for Brain Research located in the Indian Institute of Science campus, the consortium of dedicated scientists across the 20 national institutes of GenomeIndia has embarked on the task of whole-genome sequencing of 10,074 representative individuals across 99 communities, covering all major ethnic populations of the country. The revelations from ongoing analyses promise not only a deeper understanding of our collective genetic heritage but also lay the groundwork for targeted clinical interventions and the future of personalized healthcare", she said.

Prof. Thangaraj brought out the need for the GenomeIndia project and Prof. Narahari presented the significance of thedeliverables of the GenomeIndia Project: Biobank of 20,000 samples for future investigations; Whole genome sequencing of 10,000 samples; Digital public goods archived at the Indian Biological data Centre (IBDC); flagship paper for the global audience on the genetic diversity of India based on the studies; design of genetic chips for faster diagnosis; scientific findings from multiple working groups investigating different research questions; and finally inspiring young researchers and students to take up the exciting area of genomics research.

Prof. Rajesh Gokhale, Secretary, DBT, commended the Coordinators and scientists who greatly contributed to this coveted project and said "The data is being archived at the Indian Biological Data Centre (IBDC) set up by the Department of Biotechnology, Government of India at the Regional Centre for Biotechnology (RCB), Faridabad. This digital public goods will democratize data and become a valuable national resource, fostering large-scale human genetic studies and empowering nationwide research efforts by the Indian and even the global research community. The database of harmonized genetic variants will empower worldwide variant interpretation efforts and is likely to be the foundational resource for next-generation basic and clinical research in India. As the scientific community eagerly awaits the forthcoming insights, GenomeIndia stands as a step forward of India's commitment to deep science by advancing genetic research in public health interventions, drug development, and tailored treatment to the individuals of our nation."

Dr. Jitendra Singh, the Hon'ble Minister of Science and Technology, formally announced the success of GenomeIndiaand described the project as one of the pioneer initiatives of the Government of India funded through the Department of Biotechnology, Ministry of Science and Technology. He had the following to say: "Recognizing the exceptional genetic landscape of the Indian population, this initiative set for itself the ambitious goal to identify and catalogue the genetic variations of diverse Indian populations by sequencing the whole genomes of 10,000 healthy individuals representing all major ethnic groups across the country. I am happy to announce the completion of whole genome sequencing of 10,074 individuals from 99 communities, representing all major linguistic and social groups of the Indian population. By unraveling the genetic intricacies of the Indian population, the project lays the foundation of Genomic Hub as an opportunity for India to enter the emerging field of personalized medicine. A "Reference Genome for Indian Population" created under the project will lead to a better understanding of the nature of diseases and specific interventions essential for various ethnic groups. The GenomeIndia project will place India on the world map of genome research and will collectively facilitate future large-scale human genetic studies for researchers across the globe. GenomeIndia led by a consortium of 20 national institutes exemplifies the significance of collaborative, nation-wide, mission-oriented scientific partnerships driven by visionary funding by the Department of Biotechnology, Government of India. I congratulate all the contributors for this successful endeavour."

The following explainer on the GenomeIndia initiative was launched: https://drive.google.com/file/d/1p4W7vsnGcBRePuCb4qjW29jeOyHTQgZu/view?usp=sharing

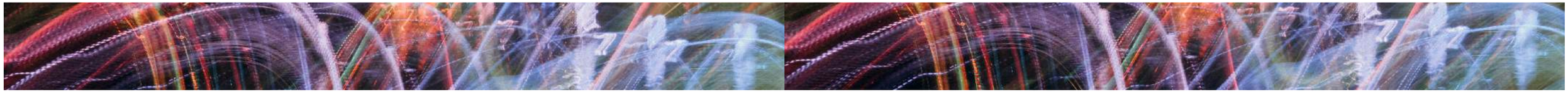
The following booklet was also released: https://online.flippingbook.com/view/609518129/18/

Here is the link to the video recording of the event: https://www.youtube.com/watch?v=EEPld3bW6zQ

## In Closing

GenomeIndia exemplifies the significance of collaborative, nation-wide, mission-oriented scientific partnerships driven by visionary funding by the Department of Biotechnology, Government of India. By unraveling the genetic intricacies of the Indian population, the project lays the foundation for advancements in public health interventions, drug development, and personalized medicine.As the scientific community anticipates the forthcoming insights, GenomeIndia stands as a beacon of India's commitment to deep science by advancing genetic research for the benefit of every citizen of our nation.

CBR, as the coordinator of the consortium, is pleased to have played a key role in the planning and execution of this project. CBR continues to drive the scientific agenda of this nationwide project to ensure the completion of all major deliverables by July 15, 2024, the date of its formal closure.



# Diverse Discourses

In thissegment of CBR Currents, we aim to feature the vibrant voices resonating within CBR's community of doctoral candidates, postdoctoral fellows, and other budding researchers. Stay tuned as we unveil their captivating explainers, innovative ideas, and insightful perspectives spanning an array of exhilarating research domains.

## Brainy Basis for Being Brainy: The Big Bang Theory of Brains

**Mr Rajath D**

One might argue that we humans are the brainiest beings this planet has ever seen. But why? What sets humans apart from the plethora of creatures inhabiting this planet and makes us the most intelligent? Does the brain size and weight have something to do with this? What made early humans diverge from apes about 2 million years ago? Let us embark on a thrilling ride to figure out the basis of human intelligence. Let us begin with the macro perspective and then deep-dive into the micro realm.

Image by freepik

### Efficient neuronal scaling

To begin with, we might think that human distinctness stems from us having more neurons. But wait, elephants and some species of dolphins and whales have way more neurons than we do, but they are not as brainy as we are. So, more neurons don't equate to higher intelligence.
There is one chart where we stand as the undisputed toppers - the number of neurons in the cerebral cortex. We have 16 billion cortical neurons. Orangutans and gorillas have about 9 billion and chimps, around 6 billion. Elephants, which have about 250 billion total neurons in the brain, only have around 5.6 billion cortical neurons. So, cortical neurons are a big deal in making us extraordinary. This proves the efficiency of neuronal scaling in humans.

### Efficient brain-body ratio

Our brain accounts for only 2 percent of our total body weight but uses 20 percent of the total energy generated by the body. Hence, along with having a mega brain, it is also important to have a small body so that energy requirement of the brain is feasible. This is where animals like elephants fail.

### Ape-human discriminator – the theories

Well, going by that logic, human dimensions are more comparable to those of apes than to those of elephants; this would imply that apes should also be as smart as we are. But they apparently aren't! Then, how did early humans diverge from apes and why did human brain size quadruple 2.5 million years ago? Let us now look into two interesting theories on this.

### 1. The cooking theory

To address the above questions, an anthropologist named Richard Wrangham, a student of Jane Goodall, came up with the "cooking theory". He observed that the diet of present-day apes consists of tuberous items and raw meat, which are not enough to supply the required amount of energy to the body, let alone a big, power-hungry brain. He hypothesized that learning how to cook would have helped human brains swell in size, because it partially digests food prior to consumption. As a result, the body need not invest a lot of energy into digesting the food, opening up avenues for brain development. This theory is supported by colon reduction, which occurred around the same time as the brain size explosion, indicating better digestion.
But hold on, there is a catch! The brains of early humans got big around 2.5 million years ago. The earliest known evidence of controlled fire by humans dates back to 1.5 million years ago, which is a million years later than the brain size boost. Hence, the cooking theory doesn't seem very likely.

### 2. The fermentation theory

A recent study (published in November 2023) proposes that the consumption of fermented, instead of cooked food, might have helped. Like cooking, fermentation also extracts a lot of calorific value from raw food. Researchers think that the discovery of fermented food might have been a happy accident from caching food in pits inside caves. The fact that fermented foods are present in all communities and cultures around the world, both old and new, supports this theory.

### The molecular lens

Understanding the molecular basis of the phenomenon is crucial to get the holistic picture. So, let us now look through the molecular lens to understand the phenomenon better.

### 1. More Glucose Transporters (GLUT) meet the energy demands

Proteins are the most important components of any life. Their production is commanded by DNA which is the genetic material or the genome.
Gregory Wray and colleagues at Duke University hypothesized that higher energy consumption of the brain should be reflected in the levels of glucose transporters (GLUT) in the brain. To test this, they analysed mRNA from brains and muscles of humans and chimps. They discovered that the brain-specific GLUT gene is 3 times more active in humans than in chimps, whereas the muscle-centric GLUT gene is 1.6 times more active in chimps than in humans. This suggests that humans have somehow evolved ways to redirect more energy to brain than muscles, whereas apes seem to prioritise the opposite. This finding demystifies, to a certain extent, the higher energy consumption of the human brain.

### 2. Potential role of a DNA segment in revving up the process

Human Accelerated Regions (HARs) are specific regions in the human genome which are drastically different from the same regions in the genomes of close evolutionary relatives of humans. These can potentially explain the human-ape divergence.

Gregory Wray and Debra Silver at Duke University hypothesized that HARs might play crucial roles in brain development. They isolated HAR5 from humans and chimps and put them into separate groups of growing mice embryos. They monitored brain development in these mice. They

observed that the mice which got the dose of human HAR5 had 12 percent bigger brains compared to mice that had received the dose of chimp HAR5. They observed that the human HAR5 was more active and caused rapid proliferation of neurons. Human HAR5 has more mutations than the chimp HAR5, indicating evolutionary pressure.

## Wrapping it up

The macro and micro aspects discussed here attempt to explain the phenomenon of human brain expansion. But we are just scratching the surface. Researchers believe that the brain size expansion was not merely due to a couple of mutations but rather the result of many more in various other genes crucial for brain development, which are yet to be uncovered.

*Mr Rajath D is a PhD student in the group of Dr Sivaprakasam Ramamoorthy. His thesis focuses on molecular studies of Tau isoforms in the context of neurodegenerative diseases.*

# Clean Air and Oxygen are Good for the Brain. Polluted Air and Reactive Oxygen Species, not so much.

**Dr Sumedha Mitra**

Image by freepik

Did you know that pure air and healthy lungs can help us stay sharp? Pollutants in air, apart from hurting our lungs, can hurt our brains too.

Reactive Oxygen Species or ROS are generated as natural byproducts of processes like breathing and metabolism in the body. As the name suggests, these are molecules that contain oxygen and are highly reactive, meaning they have a higher tendency to react with other molecules in their environment. As we age, the ability of our bodies to maintain the delicate balance between antioxidants and ROS is lost. In this case, however, oxygen isn't the good guy. ROS contains oxygen in its free radical form, which is starkly different from the molecular form in which we inhale it. Accumulation of ROS within cells can damage the smaller organelles within the cell and spark the cell's inflammatory processes as a defence response.

Studies have shown a high correlation between increased concentration of pollutants in air and poor cognitive performance. How exactly and to what extent these pollutants enter and affect the brain, is a question that researchers are still trying to answer. Numerous studies have shown people with poorly functioning lungs to perform poorly in cognitive tests. How do these pollutants affect the brain? Do they first enter the bloodstream from the lungs and then pass into the brain? There is some evidence supporting this line of reasoning. Air pollutants happen to exist across a wide range of sizes, and the really tiny ones can actually cross the blood-brain barrier (a usually well-guarded gate protecting our brain) and enter it. What about the other pollutants with larger sizes? Some researchers have hypothesised that these pesky pollutants can't enter the brain but can indirectly hurt it. Firstly, the larger pollutants, much like the Greek Trojan Horse, can carry several chemicals in one particle. These chemicals may include metals like manganese which are known to be neurotoxic. These pollutants entering the blood flow via the lungs can induce the formation of ROS and cytokines in blood.

Cytokines are signalling molecules that cells use to warn each other about invasions by bad agents and get into high alert or inflammatory mode. This isn't always good because this results in the DNA (the molecule coding for proteins making up an organism) within these cells to become stressed and thereby stop coding or incorrectly code the proteins building the blood-brain barrier. As a result of this, the barrier becomes leaky, allowing the bad guys (ROS and cytokines) to enter the brain and cause damage.

At CBR, we are investigating the extent to which air pollution is causing damage to the cognitive abilities of aging populations in Karnataka. Is this damage by air pollutants on cognitive performance direct? Or is cognition getting affected due to poor lung function? These are some questions we are currently seeking to answer.

*Dr Sumedha Mitra is a PhD student in the group of Dr Jonas S Sundarakumar. She investigates the role of ambient air pollution on cognitive health in an aging cohort.*

# Events @ CBR

CBR hosted/participated in numerous exciting events over the past few months. This section presents highlights of some of the most no table activities since the last Wave of *CBR Currents*.

## CBR's showcase at the IISc Open Day

IISc Open Day is an annual flagship event that offers an immersive experience into the world of cutting-edge research and innovation being pursued in the Indian Institute of Science campus. Visitors engage with groundbreaking projects, interact with leading scientists, and explore the institute's state-of-the-art facilities, inspiring a passion for science and discovery.Over 5500 members of the public, spanning various age groups, visited CBR on IISc Open Day (24 February 2024). Co-ordinated by Dr Smitha Karunakaran, CBR's showcase featured poster presentations highlighting its ongoing research projects, and a captivating display detailing the intricacies of the human brain. Additionally, there were neuroscience quiz contests, engaging demonstrations (including real-time brain activity detection using a headband EEG setup and cardiac autonomic function testing), and educational fun activities for children and the elderly.



## Announcement of the success of GenomeIndia

On 27 February 2024, Dr. Jitendra Singh, Honourable Minister of State for the Ministry of Science and Technology, Government of India, graciously announced the completion of whole genome sequencing of over 10,000 individuals from across India,marking a significant milestone in the GenomeIndia initiative funded by DBT and spearheaded by CBR. Dr. Singh hailed this accomplishment as a watershed moment for India, as it will lead to genetics-based remedies, besides giving a substantial boost to the public healthcare system in the country. For further details, please refer to the section titled 'GenomeIndia: A Jewel in CBR's Crown' above.

## Women's Day

In honour of International Women's Day, on 7 March 2024, CBR orchestrated a thought-provoking open forum led by faculty members, postdoctoral researchers, and students. Delving into the profound challenges encountered by women researchers, the event passionately explored strategies to dismantle gender disparities within academia and its allied domains. This empowering exchange of opinions and ideas also underscored CBR's unwavering commitment to inclusivity and diversity in the pursuit of scientific excellence.

## Roundtable Discussion with the Bavarian University Presidents

Director Prof. Hari was among the esteemed panelists invited to participate in a roundtable discussion with Bavarian University Presidents, jointly hosted by the Bengaluru Science and Technology Cluster and the Bavarian-Indian Centre for Business and University Cooperation on 28 March 2024. Distinguished representatives from leading Bavarian universities, alongside eminent figures from various Indian academic institutions, industry,

and incubators, convened for this significant gathering. The discussion centered around identifying strategic domains for fostering academic and research collaboration between India and Bavaria. There was palpable enthusiasm for research on the aging brain and associated disorders.

## Bangalore Neuroscience Meeting

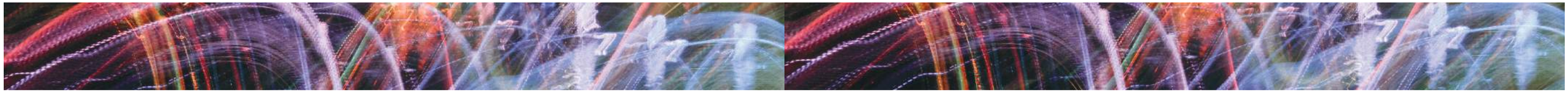
CBR participated in the inaugural Bangalore Neuroscience Meeting organised by the Center for Brain and Mind (CBM), National Centre for Biological Sciences, Bangalore, on 4 April 2024. This gathering aimed to bring together neuroscientists in Bangalore, fostering an atmosphere of knowledge exchange, collaborative research, and the overall enrichment of the local neuroscience research ecosystem. Prof. Hari delivered an overview of CBR's mission, underscoring the importance for translational research in the realm of brain aging. Faculty member Prof. Thomas Gregor Issac shared preliminary findings from CBR's flagship studies, igniting curiosity and discussion among attendees. Among the esteemed dignitaries, Dr. Kris Gopalakrishnan made a notable contribution to a panel discussion, shedding light on the challenges and opportunities confronting the Bangalore neuroscience community. Emphasising the pivotal role of data sharing among neuroscientists, Dr. Gopalakrishnan championed the acceleration of discoveries and the translation of these breakthroughs into tangible solutions for individuals grappling with neurological disorders.




Images credit: @NCBS_Bangalore

## Parkinson's Disease Awareness Program

To commemorate World Parkinson's Disease (PD) Day,CBR was pleased to host (on 6 April 2024) a PD awareness program organised by Parkinson's Disease & Movement Disorders Clinic and supported by PD Avengers (a global alliance to end Parkinson's) and the Keep Moving Foundation. Attended by approximately 150 participants, including researchers, healthcare providers, PD patients, and caregivers, the program featured expert lectures, firsthand experience-sharing sessions, and valuable networking opportunities. Faculty member Prof. Ravi Muddashetty served as one of the scientific co-organisers of this impactful event. CBR researchers Dr. Latha Diwakar, Dr. Albert Stezin, and Dr. Shweta Ramdas delved into crucial topics such as animal models, biomarkers, and genetics within the framework of PD, enriching the discourse and advancing understanding in this critical field.



## Session on IP generation and patenting

For the benefit of its students and research staff, CBR conducted a special educational session on IP generation and patenting in life sciences on 17 April 2024. Facilitated by the Intellectual Property and Technology Licensing (IPTeL) Office of IISc, this session offered insights into various forms of IP, the fundamental requirements of patents, the patenting process, and key considerations for building an IP portfolio


## Distinguished Visitors to CBR

CBR has had the opportunity to host many distinguished visitors and invitees over the past few months. Most of them are potential collaborators and had extensive interactions with the CBR faculty and staff; technical lectures were delivered by some of the guests.

**The list includes:**

- Prof. Nambi Seshadri, University of California San Diego
- Dr. John Jumper, Google DeepMind (facilitated by TNQ Technologies)
- Padma Vibhushan Dr. Vasudev K Aatre, former Head of the Defence Research and Development Organisation (DRDO)
- International delegates from the Ministry of External Affairs' Indian Technical and Economic Cooperation (MEA-ITEC) program on 'Science, Technology, and Innovation Policy'(STIP)
- Prof. Jack Feldman, University of California Los Angeles
- Ms. Nirmala Govindan Pullur, Philanthropist
- Prof. Margaret C McDonald, University of Pittsburgh
- Prof. CB Sanjeevi, Karolinska Institute
- Teams from Siemens, GE Healthcare, and Athera Ventures
- Team of collaborators from the Asian Bipolar Genetics Network (ABIGNET) - Prof. Steven E Hyman (Chair, CBR International Advisory Board), Prof. Peter Zandi, Prof. Hailiang Huang
- Dr. Radha S Murthy, Dementia India Alliance
- Dr. Raja Suresh, Arizona State University Research Enterprise (ASURE)
- Dr. Rudra Pratap, Plaksha University
- Prof. Vikram M Gadre, Indian Institute of Technology Bombay
- Dr. Harish Mysore, IEEE India Operations
- Prof. Ingrid Hotz, Linköping University
- Prof. Anurag Kumar, former IISc Director, and Prof. Pamela Kumar, Foundation for Science, Innovation and Development(FSID)

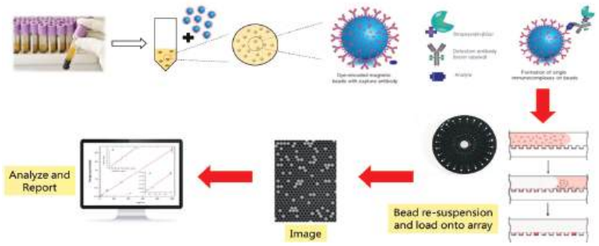
# Infrastructure @ CBR

The generous core funding provided by the Pratiksha Trust, coupled with the unwavering support from esteemed organizations such as the Tata Trusts, DBT, DST, SKAN Research Trust, DBT/ Wellcome Trust India Alliance, and Fidelity Foundation, has been instrumental in establishing CBR's cutting-edge infrastructure dedicated to pioneering research on the aging brain and aging-related brain disorders. Through this recurring section of *CBR Currents*, we aim to inform our readers about the state-of-the-art facilities housed within the Centre.

## Biomarker Analysis Facility

Early diagnosis and treatment are undergoing a revolution driven by disease detection at the molecular level. A challenge facing the field is the presence of protein biomarkers for early diagnosis in very low abundance. Conventional immunoassay technology has a lower limit of detection in the upper femtomolar range (10-$^{16}$ M), while digital immunoassay technology has improved detection sensitivity three logs, reaching the attomolar range (10–$^{18}$ M).


The single molecular array (Simoa) HD-X analyzer, developed by Quanterix, USA, is one of the world's most sensitive diagnostic, fully automated immunoassay platforms with multiplexing and custom assay capabilities. Utilizing Simoa bead-based technology, it isolates individual paramagnetic beads in arrays of femtolitre-sized wells and detects single-enzyme labeled protein molecules on these beads. This technology boasts 1000 times greater sensitivity than traditional ELISA, along with high efficiency and reproducibility. The Simoa technology at the heart of the platform enables the detection and quantification of biomarkers previously difficult or impossible to measure, paving the way for new applications in life science research, in-vitro diagnostics, companion diagnostics, blood screening, and more. Therefore, the HD-X analyzer represents the future of advanced research and diagnostics.




Assay Workflow: Immunoassay isolation

The Simoa HD-X enables best-in-class assay performance for quantification of protein biomarkers in small volumes of serum, plasma, or cerebrospinal fluid. It facilitates both single- and multi-plex assays across various areas of medical research and diagnostics, including neurology, oncology, cardiology, inflammation, and infectious diseases.

The CBR fraternity at the aging brain research showcase hosted on
**IISc Open Day, 24 Feb 2024**

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