Day 1: 2nd January

Poster Number	Full Name	Affiliation	Title of Poster
1	Arun Shankar	Seth GS Medical College & KEM Hospital, University of Mumbai	Evaluation of Anti-Parkinson's activity of Herbominerals on Rotenone induced Parkinson's disease in Drosophila melanogaster
2	Anirudh C S	inStem Bangalore	Light sensing neurons in the flatworm brain mediate movement using an 'ancient' opsin photoreceptor
3	Surbhit Wagle	NCBS	FindSimWeb, an online tool for integrating neuronal data and signaling models
4	Aparna Thulasidharan	IISER Pune	VAP-P58S Aggregation as a Readout for Disease Progression in a Drosophila Model of Amyotrophic Lateral Sclerosis
5	Utkarsha Ghai	TIFR Mumbai	Studying the role of Serotonin during different developmental epochs using pharmacological & genetic tools
6	Amal Mathew	TIFR Mumbai	Identifying novel regulators and understanding the role of vesicular PI(4,5)P2 in synaptic vesicle precursor trafficking
7	MEHA PRAVIN JADHAV	NCBS	An in silico study of the ionic basis of bistability in Zebrafish Purkinje Neurons
8	Saismit Naik	IISER Pune	Investigating role of calcium propagation in Hippocampal neuron
9	Shivani Bodas	IISER Pune	Understanding the role of spectrin periodic cytoskeleton in mechanics of the developing axon
10	TULI PRAMANIK	TIFR Mumbai	Spatiotemporally variable recombination with respect to the floxed Ldb1 allele in the dorsal telencephalon of embryonic mice.
11	Sashaina Fanibunda	TIFR Mumbai	5-HT2A receptor stimulation: a SIRTain target to enhance mitochondrial function
12	Aaqifa Shaikh	Fergusson College	Effect of Ethanol on Drosophila and it's navigational abilities.
13	Ankit Sharma	JNCASR	ROLE OF PROTEIN HOMEOSTATIC PATHWAYS IN FLY MODEL OF HUNTINGTON'S DISEASE
14	Annapoorna P K	CCMB	Few histone lysine demethylases of KDM4/7 families mediate stress effects on hippocampal neurogenesis and behaviour in mice
15	Chinmayee L M	NCBS	Airflow information encoding by mechanosensory cephalic bristles in Oleander hawkmoth, Daphnis nerii
16	Rashi Monga	IISER Pune	To understand the development of Introductory Notes in the juvenile zebra finches
17	Aditi Bishnoi	IISc	Modulation of gamma frequency and amplitude by respiratory rhythms in the rat olfactory bulb
18	Shweta Vasaya	TIFR Mumbai	: Neuronal circuit for anxiolytic effects of a serotonergic hallucinogen
19	Nisha Ann Viswan	NCBS	AutSim: Modeling activity-driven synaptic cell biology in health and disease.
20	Abhishek Gupta	IIT Kanpur	Molfaction: The structured database of mosquito olfaction
21	PRATIK RAJEEV CHAUDHARI	TIFR Mumbai	Modulation of mitochondrial metabolism within limbic brain regions following early life stress in rodents
22	Swarn ('V. D. A.') Warshaneyan	Amity University	Molecular interaction studies between SLC6A9 and STX1A with screened neuroprotective phytochemicals for finding out their therapeutic significance against Obsessive-Compulsive Disorder (OCD)
23	C Siva Raju	University of Hyderabad	Simple and complex cells of the visual system of an insect
24	Kabir Vinay Dabholkar	IISER Pune	Modelling short-term plasticity in the Alzheimer's synapse
25	Smith Gupta	IIT Kanpur	Spike detection in whole-cell patch clamp recordings containing small-amplitude spikes
26	Bhanu Priya S	NCBS	Sequence Selectivity : Exploring a Sub-cellular Computation in the Network Context

Day 2: 3rd January

	Full Name	Affiliation	Title of Poster
27	Naga Nitin Sai Chandra Anisetty	IIT Bombay	How do striatal neurons facilitate approach/avoidance behavior?
28	Shefali Goyal	IIT Kanpur	Role of antennal lobe neurons in encoding synergistic response to lactic acid and carbon dioxide in Aedes aegypti
29	Upinder Singh Bhalla	NCBS	SANKET, FINDSIM, HOSS and MOOSE: A suite of projects for data and models of synaptic function.
30	Priyanka Ghosh	NBRC	Alpha oscillations are generated across common cortical networks for processing saliency in spatial and spatio-temporal visual attention tasks
31	Feba Chacko	IISER Pune	Role of energy states and CART in fear and extinction learning in rodents
32	Arun Neru	IISER Pune	Theta oscillations gate the transmission of reliable sequences in the medial entorhinal cortex
33	Vikrant Jaltare	College of Engineering, Pune	Role of ryanodine receptors in synaptic signaling at hippocampal dendritic spines
34	Jayapriya C S	IISER Pune	Role of formin 2 in the Zebrafish Neural Circuit Development
35	Aastha Singla	TIFR Mumbai	Modulation of mitochondrial metabolism within limbic brain regions following early life stress in rodents
36	Gaurang Mahajan	IISER Pune	Design principles shaping transmission at a hippocampal synapse
37	PRATIKSHA PAWAR	Dr. Dy Patil Biotechnology and Bioinformatics, Pune	Neuropsychiatry of Anorexia Nervosa
38	Joby Joseph	University of Hyderabad	Glimpses of the extrinsic neurons of the MB
39	Priyadharshini Srikant	IISER Pune	Alpha synuclein oligomers: central players in the olfactory impairment in Parkinson's disease?
40	Arjit Kant Gupta	IIT Kanpur	Understanding stereotyped behaviors using the insect olfactory system as a model
41	Praachi Tiwari	TIFR Mumbai	Chronic Gq Activation of Forebrain Excitatory Neurons in Postnatal Life Establishes Long Lasting Behavioral Changes
42	Vani Srinivasan	Delhi University	A 'viral' understanding of Parkinson's disease (PD)
43	Sneha Sagarkar	Pune University	BDNF regulation by DNA demethylation in hippocampus is involved in reward memory consolidation
44	Mahima Bose	TIFR Mumbai	Understanding mechanisms of neuron-glia cell-fate switch in the developing mouse forebrain
45	Karthikeyan R. Kannan	IIT Kanpur	Understanding the mode of action of mosquito repellents
46	MAHIMA PANDEY	Delhi University	Frontotemporal dementia: from molecular mechanisms to therapy
47	Koustav Halder	IISER Pune	Synaptic Vesicle Recycling Kinetics In Ca3 Presynapse.
48	Anal Kumar	NCBS	Analyzing the electrophysiological properties of CA1 pyramidal neurons of Fragile X syndrome mice using computational models
49	Saptarshi Soham Mohanta	IISER Pune	Deciphering the Dynamics of the Locust Olfactory System
50	Sarayu Ramakrishna	inStem Bangalore	APOE4 affects basal and NMDA mediated protein synthesis response in neurons by perturbing calcium homeostasis.
51	Aditi Agarwal	IISER Pune	Examining the role of the dorsomedial nucleus of the intercollicular complex (DM) in song production in zebra finches
52	Shreya Lakhera	IISER Pune	Asymmetry in any connections in EI-networks forms feedforward networks which generate activity sequences.
53	Rajdeep Bhowmik	IISER Pune	How good are humans in discriminating odors?

Poster Abstracts

Effect of Ethanol on Drosophila and it's navigational abilities.

Aaqifa Shaikh | Undergraduate Student | Fergusson College

Drosophila sp. or fruit flies are the most preferred model system for performing experiments as it's 75% genes are similar to humans. Ethanol (EtOH) or alcohol addiction accounts for a range of behavioral and mental problems.

Through are experiment we tried studying the effect of Ethanol on these flies. Different concentration of Ethanol were taken into consideration ranging from 10% to 45%. Ethanol was added to the medium according to varied concentrations and observations were done each day.

Molecular analysis couldn't be carried out as we are at UG level. A 2-D Maze was also made to study the navigational abilities of the flies.

Higher percent of EtOH seemed to be lethal and in the lower percent the flies were viable and some of them were abnormal with respect to the walking style and body dimensions.

Modulation of mitochondrial metabolism within limbic brain regions following early life stress in rodents

Aastha Singla | Integrated PhD student | TIFR Mumbai

Anxiety and depression are leading causes of disability that affect people across the lifespan. Early life stress like maternal separation in rodents results in life-long alterations in anxiety and depression-like behavior, as well as accelerated aging. The molecular, cellular, structural changes evoked by early stress that contribute to the lifetime risk for the development of psychopathology and remain to be clearly elucidated. Also, the underlying mechanisms that mediate the accelerated aging phenotype associated with a life-history of early life stress remain poorly understood.

Mitochondrial metabolism plays a central role in the regulation of brain function. However, very few studies have addressed the influence of early life stress on alterations in mitochondrial function and whether these contribute to the behavioural and cellular changes evoked by early stress. The preliminary evidence from our laboratory indicates a robust and lifelong reduction in the mitochondrial sirtuin, Sirt4, across the lifespan in rats subjected to early trauma. Moreover, the experiments suggest that the limbic brain region, prefrontal cortex, of maternal separated rats displays altered expression of mitochondrial biogenesis markers such as PGC1α, Sirt1, TFAM in postnatal and middle-aged animals. The influence of maternal separation in rats will be tested in various limbic circuits (prefrontal cortex, hippocampus, hypothalamus) at multiple time points across the lifespan. The primary thrust of our project is to understand the contribution of alterations in mitochondrial metabolism and function within limbic neurocircuits in mediating the persistent altered risk for psychopathology and accelerated aging that arise in rodent models following early stress.

Please note : I shall be a co-presenter with Dr. Pratik Rajeev Chaudhari on this poster.

Molfaction: The structured database of mosquito olfaction

Abhishek Gupta | Master's Student | IIT Kanpur

Olfaction is one of the most prominent senses in insects, which is essential for several behavioral functions including feeding and courtship. In insects, an odorant molecule is detected by the odorant receptor expressed in the olfactory receptor neurons (ORNs), located majorly on the antenna and maxillary palp. Each odor can generate spikes in multiple ORNs, and each ORN can identify a wide range of odor molecules. To understand the olfactory processing, one needs to identify the odors that a given OR responds to. Over the last two decades, researchers have employed several techniques such as single sensillum recording (SSR), electroantennography (EAG), empty-neuron system and other heterologous expression systems to deorphanize the ORs. Moreover, many studies have been conducted to check the overall behavioral responses in different mosquito species. We have compiled all the available odor responses in mosquitoes into a structured dataset. This dataset contains responses for >750 odors in >10 species of mosquitoes, collected from over 170 research articles. Besides aiding the literature review process, this dataset can facilitate an elaborate analysis of the essential features of an olfactory circuit. Here, we have reported some of these features that were hard to see in the individual research articles. In one such analysis, we show that landing assay (in mosquitoes) and T-maze (in Drosophila), used for measuring the behavioral response, in general, report lower preference index compared to other assays. We have also revisited some of the analyses previously done on the smaller datasets and tested them with the larger dataset. In conclusion, this comprehensive dataset can be used in designing experiments and analyzing the features of the olfactory circuit.

Examining the role of the dorsomedial nucleus of the intercollicular complex (DM) in song production in zebra finches

Aditi Agarwal | Undergraduate Student | IISER Pune

An adult male zebra finch produces a highly stereotyped song. The circuit imperative for the production of this stereotyped song involves HVC, a forebrain pre-motor nucleus, which provides motor commands to the areas downstream for the production of a song. Uva, one of the regions in midbrain, provides feedback to HVC and like HVC is also active during the song. Both HVC and Uva lesions result in the loss of acoustic and temporal features of the song. Uva receives input from various other nuclei. This then begs the question, what drives activity in Uva for the production of a stereotyped song?

One of the regions that project to Uva, DM, has been studied extensively in the context of call production. Electrical stimulation of DM with low current amplitudes elicits calls similar to bird's own learned calls. The role played by DM in the context of song production, however, remains elusive. Although, a few studies report that DM lesions have no effect on the song, these lesions were incomplete and hence through this study we aim to re-examine the role of DM in the context of song production.

We find that calls are elicited in the anesthetized state, similar to the previous literature. Preliminary DM lesion experiments suggest that partial DM lesions do not alter the song. Interestingly, lesions in an area close to DM abolishes the acoustic and temporal features of the song similar to that observed in HVC and Uva lesions. Histological evidence suggests that these

lesions were at the inferior-posterior border of ICo (Intercollicular complex) of which DM is a part. ICo is essential for courtship behaviours. Further experiments need to be carried out to examine the role of ICo in this context.

Modulation of gamma frequency and amplitude by respiratory rhythms in the rat olfactory bulb

Aditi Bishnoi | PhD Student | IISc

The local field potentials in the rat olfactory bulb (OB) are dominated by slow respiratory rhythms (RR, 1-10Hz) and gamma oscillations in the range 40-100Hz. The slow oscillations are tuned to the inhalation and exhalation respiration cycles in anesthetized and awake animals. Gamma oscillations reflect the reciprocal dendro-dendritic interactions between the projection neurons (Mitral/tufted cells) and inhibitory neurons (granule cells). The amplitude of gamma shows strong modulation with the phase of respiratory rhythms (RR), with the gamma burst starting shortly after inhalation and continuing till the end of exhalation. Gamma frequency also changes simultaneously within a single respiratory cycle, starting from ~100Hz at the late ascending phase of inhalation - and then reducing to ~ 40Hz at the end of exhalation. Previous studies suggest this wide band of gamma frequencies to be composed of two separate gamma oscillations; fast gamma (60-100) that occurs in the early phases of respiration and slow gamma (40-60) in the later phases, which correspond in timing with the high frequency burst responses of tufted cells and lower frequency bursts of mitral cells in the early and the late phases of respiration respectively. To better understand the temporal and spectral dynamics of gamma oscillations, we recorded LFPs from the OB of awake behaving rats engaged in foraging behaviour. We noticed that the changes in the gamma frequency within a respiratory cycle are more of a continuum; gradually increasing and then decreasing with the respiration phase, instead of previously reported discrete fast and slow gamma bands occurring in different phases of respiration. Interestingly, the frequency of the gamma oscillations rises and reaches maxima (~100Hz) earlier than the amplitude of gamma oscillation irrespective of the frequency of RR. Additionally, the latency with which the gamma frequency and amplitude reach their maxima from the start of the respiration cycle, gradually decreases as the sniffing becomes faster. This suggests a much more complex dynamics underlying the generation gamma oscillations in the OB.

Identifying novel regulators and understanding the role of vesicular PI(4,5)P2 in synaptic vesicle precursor trafficking

Amal Mathew | PhD Student | TIFR Mumbai

Synaptic vesicle precursors (pre-SVs) are formed in the cell body and exit the cell body by UNC-104/Kinesin-3. To understand the events that aid in unc-104 dependent exit of pre-SVs from cell body we decided to identify genetic modifiers of unc-104 that promote UNC-104-dependent transport. Enhancers of unc-104 likely disrupt events in pre-SV biogenesis and motor recruitment. Genetic modifier, tb205, was isolated from an enhancer screen performed on a mild cargo-binding defective allele of unc-104. tb205 has smaller PLM synapses and was mapped to the region between 0 and -1.74cM on Chromosome I. Whole genome sequence analysis identified 3 candidates between 0 and -1.74cM that had SNPs in tb205 and tb205;unc-104. Currently we are doing non-complementation assays to test whether tb205 is an allele of these candidates. We are also interested in classifying the enhancers based on their role in cargo biogenesis and motor recruitment. As UNC-104 binds to PI(4,5)P2 on vesicles and binding of UNC-104 is sensitive to the levels of PI(4,5)P2 we hypothesized that pre-SV trafficking in enhancers regulating cargo biogenesis are likely to be insensitive to levels of PI(4,5)P2 while enhancers acting on motor recruitment are likely to be sensitive to the levels PI(4,5)P2. We see that SVP trafficking in syd-2 mutants, which show defects in cargo biogenesis, is insensitive to the levels of PI(4,5)P2. We are currently testing the same for sam-4, an enhancer of unc-104 which likely aids in motor recruitment.

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Analyzing the electrophysiological properties of CA1 pyramidal neurons of Fragile X syndrome mice using computational models

Anal Kumar | PhD Student | NCBS

Fragile X Syndrome (FXS) is an intellectual disability disorder caused by mutations in fragile X mental retardation 1 (FMR1) gene resulting in low levels of functional FMR protein (FMRP). In neurons, FMRP regulates the expression levels of various ion channels, and proteins associated with synaptic plasticity. The decreased levels of FMRP in FXS thus leads to altered behavior of neurons such as hyper-excitability, hypo-excitability, elevated neurotransmitter release, and network discharge coordination in various parts of the brain.

A recent study from our lab has shown that elevated currents from small conductance calcium-activated potassium (SK) channels are partially responsible for the reduced spike numbers, elevated after-hyperpolarization (AHP), and increased variability in spiking observed in CA1 pyramidal neurons of FMR1 knock out (FMR1-KO) mice. In this project, we use computational approaches to study if changes in expression levels of other types of ion channels may also be causing these altered electrophysiological properties of fmr1-KO CA1 pyramidal neurons. Existing models of wild-type (WT) CA1 pyramidal neurons in the literature do not capture essential spike waveform characteristics such as AHP and after-depolarizations (ADP). Thus, we are currently building families of data-driven conductance-based models of FMR1-KO and WT CA1 pyramidal neurons using hand-tuning and multi-parametric multi-objective stochastic search. The maximal conductance of the various ion channels in these models will then be compared to find ion channels which may be responsible for the defects observed in FMR1-KO CA1 pyramidal neurons.

Light sensing neurons in the flatworm brain mediate movement using an 'ancient' opsin photoreceptor

Anirudh C S | PhD Student | inStem Bangalore

Light sensory systems are highly diverse in function and physiology and have evolved under varying selective pressures. The biology of visual systems across life forms has been a subject of extensive study. However light sensing can manifest in an extraocular manner as well. Multiple such light sensing networks can be present within the same organism and have been discovered in a wide range of phyla. Although some of the different functions that these extraocular light sensory systems perform have been identified, they still remain grossly understudied despite their abundance. In pursuit of better understanding such systems, we discovered in the planarian flatworm, an excellent model organism. Planarians possesses multiple light sensory systems each with distinct characteristics, varying functions and dynamic interactions. Their primary visual system consists of two simple cup shaped eyes capable of sensing visible light intensity gradients with high efficiencies. We had also shown previously that planarians possess a robust UV light avoidance response mediated by photoreceptors present all over their body. Finally, we have now discovered that the planarian brain houses a dispersed set of photoreceptor neurons that are also capable of mediating visible light avoidance. Surprisingly, these brain photoreceptors despite being few in number, are capable of sensing and avoiding visible light with efficiencies comparable to that of the planarian eyes. Furthermore, the opsin protein used to sense light in these neurons belongs to a unique opsin class called xenopsins which are found exclusively in the Lophotrochozoan super phylum. The signalling mechanisms of xenopsins and the nature of the neurons that they are present in are completely unexplored. This light sensory network presents a system with a unique evolutionary history that could yield important insights into opsin and photoreceptor neuron evolution.

ROLE OF PROTEIN HOMEOSTATIC PATHWAYS IN FLY MODEL OF HUNTINGTON'S DISEASE

Ankit Sharma | PhD Student | JNCASR

Neurodegenerative diseases affect millions of people world over and our understanding of the multi-system complexity underlying pathophysiology and treatment is not clear. We are interested in one such condition: Huntington's disease (HD), an autosomal dominant disorder caused due to an expanded polyQ stretch (>40) in the Huntingtin protein. Our focus is on the impact of expanded Huntingtin on neuronal health, in the context of how behaviour controlled by the neuronal circuit is affected. We have chosen a subset of the Drosophila circadian pacemaker circuit, which controls an assayable and robust behaviour namely rhythmic locomotor activity. Humans and animal models of HD exhibit compromised circadian rhythms and clock dysregulation accelerates the progression of neurodegeneration. In Drosophila we target a subset of circadian cells, the ventral lateral neurons (8-9 pairs), that are critical for the periodic patterns of activity/rest in absence of external time cues. We perturb the circadian neuronal circuit using expanded Huntingtin and probe the functional consequences both at cellular and behavioural level. We aimed to investigate the relative contributions of the proteostatic pathways namely the heat shock proteins and autophagy pathway towards dealing with pathogenic protein and their impact on HD pathophysiology. Even though, previous studies have shown that proteostatic pathways can be targeted to mitigate the bad effect of mutant proteins in various neurodegenerative conditions, but we still lack the detailed understanding of the molecular mechanisms behind these rescues. In this study specifically, we asked whether rescue is limited to immediate cellular functions or extends to functioning of the circuit as a whole in terms of behaviour. Through our studies, we aim to gain mechanistic insights into cellular pathways that are altered by the condition and propose efficient ways to counter disease progression. Beside this, Drosophila circadian model system can be a good system to investigate the effect of mutant Huntingtin protein on the circadian rhythms and detailed understanding of this can lead to different and more effective therapeutics approaches.

Few histone lysine demethylases of KDM4/7 families mediate stress effects on hippocampal neurogenesis and behaviour in mice

Annapoorna P K | PhD Student | CCMB

It has been a long standing challenge to understand the molecular mechanisms that underlie the effects of chronic stress on brain and behaviour. Stress induced changes can precipitate the development of various neuropsychiatric disorders such as depression and anxiety. Epigenetic regulatory mechanisms which alter neural gene expression orchestrate some of these effects. Notable among these are histone modifications. Numerous studies have revealed changes in transcriptionally repressive histone methylation marks, H3K9me2/3 and H3K27me2/3 in reward and cognitive brain circuitries after exposure to psychological stress. These histone marks are targeted by some Jumonji-domain containing histone lysine demethylases (KDMs). However, their functions in mediating the effects of stress are elusive, particularly on hippocampal neurogenesis and associated affective and cognitive behaviour. Our data from chronic social defeat stress (CSDS) induced model of depression in mouse found perturbations in the levels of KDMs belonging to families 4 and 7 in the hippocampal neurogenic region, dentate gyrus (DG). Among the KDMs that showed changes at the transcript level is a novel demethylase, 4921501E09Rik. These KDMs possibly mediate stress effects on adult DG neurogenesis, as indicated by our data from ex vivo neural stem/ progenitor cell culture system. Of particular interest are members of KDM7 family as there are evidences of their involvement in neural development and differentiation. The novel demethylase, 4921501E09Rik functions differently than the other family members such as KDM7B (PHF8) in terms of its biochemical targets and changes in its levels in the DG after chronic stress. Based on our preliminary data, it appears that few demethylases of KDM4 and 7 families are involved in stress-induced hippocampal re-modelling by altering neurogenesis, causing depression and related affective and cognitive disorders.

VAP-P58S Aggregation as a Readout for Disease Progression in a Drosophila Model of Amyotrophic Lateral Sclerosis

Aparna Thulasidharan | PhD Student | IISER Pune

Amyotrophic Lateral Sclerosis (ALS) is a fatal, progressive neurodegenerative disorder, characterized by extensive loss of motor function. There are currently only two approved drugs for the treatment of the disease, with neither curing the disease. The Vesicle Associated Membrane Protein (VAMP) Associated Protein B (VAPB) locus was the 8th locus identified out of 32 known ALS loci (Abel et al,2012,). A missense mutation in the VAPB gene which results in the substitution of the 56th conserved Pro to Ser causes protein misfolding and aggregation (Nishimura et al., 2004). VAPB is known to interact with several other cellular components like microtubules, ER and several proteins (Lev et al., 2008). VAPB has also been found to interact genetically with TBPH and TBPH has been shown to modulate VAP aggregation (Deivasigamani et al.2014; Chaplot et al, 2019).

We aim to characterise and study the modulation of VAP(P58S) aggregation in a Drosophila model. We utilize a genomic promoter driven VAP(P58S) that rescues lethality of Drosophila VAP null mutants (Moustaqim-Barrette et al.,2014). Using age dependent imaging of drosophila adult brains, climbing assays and genetic knockdowns, we hope to understand roles played by VAP(P58S) aggregation and role of aggregation modulators in the progression of the disease.

Understanding stereotyped behaviors using the insect olfactory system as a model

Arjit Kant Gupta | PhD Student | IIT Kanpur

Animals rely on several genetically-hardwired or innate behaviors for their survival. For example, in insects, innate behaviors linked to foraging in search for food, searching for a mate, oviposition and avoiding harmful stimulus, are all crucial for survival and reproduction, and are therefore stereotyped across individuals. Olfactory cues play a central role in many of these behaviors. Genetic and environmental factors result in variability at every level in olfactory circuit: for example, olfactory receptor(OR) expression levels in olfactory receptor neurons (ORNs), number of ORNs, projection neurons (PNs) and their connectivities are different across individuals. At the next layer the connectivity from PNs to Kenyon cells(KCs) is random for every individual. Although one might expect the variability at all these levels to accumulate and result in highly inconsistent behaviors, flies must behave reliably in their environment. To what degree individual fly behavior is stereotyped is still not very clear. We use Drosophila melanogaster (Fruit fly) as a model system to measure stereotypy in olfactory behaviors and explore the role of various mechanisms (neuromodulation, feedback loops etc.) in controlling the degree of behavioral stereotypy. We have designed a high-throughput behavioral setup for measuring individual olfactory behavior in response to a panel of attractive and aversive odors to quantify behavioural stereotypy. We will perform two photon calcium imaging to measure response stereotypy at various levels in the olfactory circuit to test the role of various possible mechanisms in generating stereotyped olfactory behaviors. Since every sensory system deals with noise at various levels, understanding mechanisms of noise reduction in insect brain will help us understand sensory processing in various sensory modalities.

Evaluation of Anti-Parkinson's activity of Herbominerals on Rotenone induced Parkinson's disease in Drosophila melanogaster

Arun Shankar | PhD Student | Seth GS Medical College & KEM Hospital, University of Mumbai

The study was designed to validate the claims in Ayurveda regarding the efficacy of Ayurvedic drugs in neurodegenerative disorders. It was decided to conduct an efficacy study of two herbomineral drugs (Abhrak bhasma and Rajat bhasma) on Parkinson's disease induced chemically in Drosophila melanogaster (fly). Parkinson's disease has symptom descriptions in Ayurveda and modern medicine. The latter offers only the symptomatic therapy by replacing dopamine, the neurotransmitter involved, but does not slow down or reverse the loss of dopaminergic neurons.

Methods: Rotenone, in a final concentration of 125 µM, was induced for inducing Parkinson's disease in Drosophila melanogaster. Suitable concentration of herbomineral samples were selected on the basis of viability assays carried out in our lab. The group serving as negative control will not have the study drugs in the cornmeal medium and the flies from positive control will be fed with L-dopa dissolved in the medium in the concentration of 1 mM. The flies in the bottle will be maintained for a period of 7 days at 25OC. On the 8th day, they will be subjected to climbing assay. The brain tissue of Drosophila melanogaster will be dissected and be subjected to immunohistochemistry against Tyrosine hydroxylase.

Results: Climbing assays showed a significant reduction in the climbing/ motor ability between the contrel and disease control groups. There was a significant improvement in the climbing ability of flies fed with l-dopa and study drugs. Immunohistochemistry showed a significant reduction of dopaminergic neurons in the disease control group and a significant reduction in the loss of dopaminergic neurons.

Conclusion: The herbominerals were found to be effective in reducing the rotenone induced dopaminergic loss of neurons.

Theta oscillations gate the transmission of reliable sequences in the medial entorhinal cortex

Arun Neru | PhD Student | IISER Pune

Reliable sequential activity of neurons in the entorhinal cortex is necessary to encode spatially guided behavior and memory. In a realistic computational model of a medial entorhinal cortex (MEC) microcircuit, with stellate cells coupled via a network of inhibitory interneurons, we show how intrinsic and network mechanisms interact with theta oscillations to generate reliable outputs. Sensory inputs activate interneurons near their most excitable phase during each theta cycle. As the inputs change, different groups of interneurons are recruited and postsynaptic stellate cells are released from inhibition causing a sequence of rebound spikes. Since the rebound time scale of stellate cells matches theta oscillations, its spikes get relegated to the least excitable phase of theta ensuring that the network encodes only the external drive and ignores recurrent excitation by rebound spikes. In the absence of theta, rebound spikes compete with external inputs and disrupt the sequence that follows. Our simulations concur with experimental data that show, subduing theta oscillations disrupts the spatial periodicity of grid cell receptive fields. Further, the same mechanism where theta modulates the gain of incoming inputs may be used to select between competing sources of input and create transient functionally connected networks.

Sequence Selectivity : Exploring a Sub-cellular Computation in the Network Context

Bhanu Priya S | PhD Student | NCBS

Spatio-temporally ordered neural activity is a signature of salient sensory, motor, and cognitive events. Precise convergence of sequential inputs onto synaptic clusters on dendrites is implicated in sequence recognition, plasticity, and cellular state switching. How may such projections form, and what are the computational outcomes? We show that spatio-temporally ordered synaptic clusters of 3-6 inputs are likely even in random networks. We used rat hippocampal and cortical network statistics and modeled subcellular electrical and chemical sequence discrimination mechanisms. We mathematically and computationally demonstrate a tight interplay between subcellular sequence selectivity, morphology, network connectivity, and random background activity. Longer sequences are more informative, and elicit greater cellular selectivity, but noise and connection probabilities favor short sequences. Our results suggest that background activity, and the spatio-temporal scale of sequence discrimination are two crucial players which regulate a network's ability to recognize sequences.

Simple and complex cells of the visual system of an insect

C Siva Raju | PhD Student | University of Hyderabad

Optic lobe of insect is thought to include processing analogous to the retina, LGN and the Visual cortex (V1) in its various layers, lamina, medulla and the lobula. The anatomy and the cell types are well understood in certain insect systems like Drosophila and Calliphora. Also some types of neurons are well characterized in these systems.

We use in vivo electrophysiology and immunohistochemistry to functionally characterize neurons from the optic lobe of grasshopper Hierogliphus banian. We record from the neurons in the optic lobe while presenting a variety of stimuli including, grating, looming and white noise stimuli and inject dyes in the cells we record from to characterize their morphology. We use clustering of the responses and couple this with the confocal imaging to test if the cells are identifiable from a response vectors alone. Linear nonlinear models are fitted using the response to white noise to identify receptive field properties of the different spectral components. This model is used to predict the responses to the other set of stimuli and thus test if these can be characterized as simple or complex cells.

Airflow information encoding by mechanosensory cephalic bristles in Oleander hawkmoth, Daphnis nerii

Chinmayee L M | PhD Student | NCBS

Insect flight is a complex behavior that requires coordination of various reflexes in the body. For a stable fight, antennae have to be positioned to detect air speed and direction, the neck has to be positioned for gaze stabilization and wings have to move in a coordinated fashion. We have observed that moths undergo a warming phase, which lasts for 3-5 minutes, during which various sensors and muscles are prepared for flight. Interestingly, when certain mechanosensors on the head of the moths are stimulated, the warm-up phase is bypassed, triggering immediate coordination of body parts to initiate flight, within a second (Maitri, unpublished). We are studying the mechanism of this mode of flight initiation. I will be talking about the distribution of these mechanosensors on the head, the projection of the sensory neurons in the central nervous system and our approach to characterize them with electrophysiology.

Role of energy states and CART in fear and extinction learning in rodents

Feba Chacko | Undergraduate Student | IISER Pune

Cocaine-and-amphetamine-regulated-transcript (CART) is a neuropeptide that was discovered when its transcript was found to be expressed more in the rat brain when the animal was given cocaine or amphetamine. Further research showed the peptide to play a role in the freezing response, and also to be involved in appetite and homeostasis control (anorexic behaviour), reward and reinforcement, regulation of motor activity. Recently, it has also been shown to be crucial for the innate fear response pathway. Since the same neuropeptide is involved in fear response, learning, as well as homeostasis control, it would suggest that energy states of the animal could possibly affect how the animal responds to fearful stimuli and also how it recognises such stimuli upon further presentation. Verma et al. (2016) have indeed shown that the energy state regulates the memory formation and extinction of fear by other pathways using the fear conditioning paradigm. We were able to replicate this effect of starvation on memory and saw a similar trend in animals by briefly inhibiting CART activity, leading us to believe that CART is involved in some level in the learning of fear. We are currently studying the involvement of the peptide in extinction learning.

Design principles shaping transmission at a hippocampal synapse

Gaurang Mahajan | Post Doctoral Fellow | IISER Pune

Synapses across different brain regions display distinct form-function relationships. We investigated the interplay of fundamental design principles shaping the transmission properties of the excitatory CA3-CA1 pyramidal cell connection, a prototypic synapse for studying the mechanisms of learning in the mammalian hippocampus. This small synapse is characterized by probabilistic release of transmitter, which is markedly facilitated in response to naturally occurring trains of action potentials. Using a physiologically realistic computational model of the CA3 presynaptic terminal, we examined how unreliability and short-term dynamics of vesicular release work together to regulate the trade-off of information transfer versus energy use. We suggest that individual CA3-CA1 synapses are designed to operate near the maximum possible capacity of information transfer in an efficient manner. Experimental measurements reveal a wide range of vesicular release probabilities at hippocampal synapses, which may be a necessary consequence of long-term plasticity and homeostatic mechanisms that manifest as presynaptic modifications of release probability. We show that the timescales and magnitude of short-term plasticity render synaptic information transfer nearly independent of differences in release probability. Thus, individual synapses transmit optimally while maintaining a heterogeneous distribution of presynaptic strengths indicative of synaptically-encoded memory representations. Our results support the view that organizing principles that are evident on higher scales of neural organization percolate down to the design of an individual synapse.

Role of formin 2 in the Zebrafish Neural Circuit Development

Jayapriya C S | Master's Student | IISER Pune

Formin-2 belongs to the FMN family of formins, which are multi-domain proteins that are important during early development. Studies in chick embryo have shown that Fmn2 is required cell-autonomously by spinal neurons for midline guidance and pathfinding in vivo. The studies highlights that formin-2 plays a conserved role in neural development. Whole mount In situ hybridisation experiments in our lab have shown that formin-2 mRNA is enriched in the central nervous system and the retinal ganglion cell layers during the early developmental stage(1 day post fertilisation, dpf) in zebrafish. Fmn2 is downregulated in aged mice and de novo mutations in formin-2 can lead to intellectual and cognitive disabilities in humans. The retinotectal projection of zebrafish is a well-studied model system for the investigation of molecular mechanisms that underlie axon pathfinding and map formation. Larval zebrafish is a valuable model organism to study development of neural circuits. The retinotectal pathway in zebrafish provide an opportunity for studying the neural basis for visual behaviour in a living vertebrate. In my project, I look at the retinotectal pathway of the larval zebrafish at different stages of development starting from 3dpf. To decipher the role of formin-2 in this pathway, which is enormously important for the survival of the organism, we truncated the functional protein by injecting splice blocking morpholinos at single celled stage and check the structure of the axonal projection of RGC in the tectum in a transgenic line. I have seen a reduction in the volume innervated by the axonal projection of the RGC in the optic tectum in case of fmn-2 morphant zebrafish larvae. To further clarify that reduction in this volume is due to the truncation of formin-2, we are trying to normalise the volume to axonal projection of the RGC in optic tectum to the total volume of the optic tectum. We are also trying to see the calcium activity in the tectal neurons by providing a visual stimulus, to find if the reduction in the volume of axonal projection of RGC have any functional role to play.

Glimpses of the extrinsic neurons of the MB

Joby Joseph | Faculty | University of Hyderabad

A large class of the extrinsic neurons of the mushroom-body have now been characterized in a variety of species. In this poster I will discuss some results from our lab about the properties of some of the elements of this circuit in grasshopper and honeybee.

Modelling short-term plasticity in the Alzheimer's synapse

Kabir Vinay Dabholkar | Undergraduate Student | IISER Pune

Alzheimer's disease (AD) is a progressive neurodegenerative disease. One of the first brain areas to be impacted is the hippocampal formation, crucial for short-term learning and memory. Investigations on genetic models of AD and patients with familial forms of the disease suggest that loss in memory precede structural changes in the brain.

The calcium hypothesis of AD suggests that mutations linked to neuronal calcium mishandling may underlie the initial symptoms. Specifically, the AD related mutation to presenilin, a ubiquitous ER membrane protein, compromises the leak channel in the ER. In order to have a mechanistic understanding of this complex disease we constrain the problem to investigate changes in intracellular calcium signals within the synapses of hippocampus as the basis of modified plasticity leading to deficits in cognition. Our modeling investigation is carried out in a realistic geometry of a Schaffer collateral (CA3-CA1) synapse. We have developed a biophysical model of compromised ER leak as seen in AD synapses that leads to a calcium overload in the ER. We simulate the sequence of events leading to synaptic transmission and short-term plasticity in the presynaptic terminal of the CA3-CA1 synapse. We propose that augmented calcium signaling in AD synapses can cause rapid depletion of neurotransmitter. The contrasting dynamics of increase in release rate of vesicles from a small pool of available vesicles due to ER overload, and, the slow time scales of vesicle recycling, leads to compromised short-term plasticity.

Understanding the mode of action of mosquito repellents

Karthikeyan R. Kannan | PhD Student | IIT Kanpur

Mosquitoes spread many deadly diseases. Especially, Aedes aegypti causes diseases like Dengue, Chikungunya, Zika fever etc. Major proportion of the present day mosquito repellent products contains compounds like DEET, picaridin and IR3535. Among them DEET is considered as the gold standard because of its ability to drive off the mosquitoes effectively. But its effect lasts for only 3-4 hours from the time of application. There are some reports of DEET causing skin irritation as well. So, there is a need for a better repellent to address problems. Discovery of better repellents has been hindered by our limited understanding of the mechanisms by which DEET and other repellents affect the sense of smell in mosquitoes. In insects, olfactory information is conveyed through olfactory receptor neurons present on the antenna, which in turn synapse with the projection neurons (PNs) in the antennal lobe. These PNs, in a unique combination for every odor, convey the information to higher brain centers. A few hypotheses have been proposed for how DEET may act on the mosquito olfactory system: DEET may silence olfactory receptors tuned to human odors, it may activate a few olfactory receptors tuned to repulsion, or it may just interfere with the molecules of human odors and reduces the amount of odor reaching the mosquito. Limited data availability restricts us to test these hypotheses. We have designed a novel behavioural assay for mosquitoes, which allows accurate and unambiguous measurement of the behavioural effects of DEET. Further, we are developing genetically modified mosquitoes with calcium reporters to understand how DEET and other common repellents are coded in the higher brain centers. Our results will help in understanding how repellents function and may help in the search for more effective repellents in future.

A Three Pool Model For Vesicle Recycling In CA3 Synaptic Vesicles

Koustav Halder | Undergraduate Student | IISER Pune

Our knowledge of various types of synaptic plasticity as the basis of learning and memory has relied extensively on mechanistic understanding of signaling at hippocampal synapses. The CA3-CA1, a prototype synapse in the hippocampus shows intrinsic poor transmission of presynaptic signal that curiously gets tuned by changes in the presynaptic activity patterns. The probability of successful transmission and its activity dependent changes thereafter (presynaptic plasticity) is determined by several factors including the geometry of the synapse, the characteristics of the calcium signal and the molecular machinery for exocytosis. However the critical constraint for successful release is number of vesicles that are available for release (around 5-10). Additionally, the time taken for the vesicle pool resource to be replenished can be an order of magnitude longer compared to the ongoing electrical activity (~ 5 sec) . The available vesicles can therefore get quickly exhausted in response to typical bursting activity seen at this terminal. Apart from the low probability of release of vesicles at this synapse that limits depletion, vesicle recycling timescales are seen to be modified in an 'as-per-need basis'. This tuning influences both short-term plasticity (STP) and long-term plasticity (LTP) in the CA3-CA1 synapse. Despite knowledge of the molecular players, their structure and their role in synaptic vesicle recycling; an accurate, quantitative framework that describes the kinetics of vesicle recycling under different stimulus protocols is yet unknown.

Based on experimental insights derived from fluorescent tagging of vesicles across a broad range of stimuli, we have developed a model for vesicle recycling at the CA3 presynaptic boutons. The model consists of three distinct populations of vesicles, classified according to readiness for release. Through a combination of physiological data as well as analytic formulations, the model predicts the transfer rates of vesicles between the different populations, and by extension their rates of neurotransmitter refilling and release, as a function of the frequency of input stimulus to the CA3 pre-synapses. This release data is in accurate quantitative agreement with experimental release transients. Furthermore our model accounts for two different mechanisms for exocytosis, including full fusion and the more efficient form of exocytosis, the so called 'kiss and run' fusion (K&R) wherein the vesicle retains its membrane identity after neurotransmitter release, thereby accommodating faster recycling times. The model describes the shift in the incidence of these two distinct mechanisms governed by the frequency of their stimulus.

Given the fundamental role played by vesicle release dynamics in information processing in the hippocampus, the model developed here is valuable to predict synaptic plasticity profiles in response to diverse physiological activity and under pathological conditions when vesicle recycling kinetic pathways are modified.

Understanding mechanisms of neuron-glia cell-fate switch in the developing mouse forebrain

Mahima Bose | PhD Student | TIFR Mumbai

The cerebral cortex of the brain is a seat for cognition, memory, and language. The underlying developmental principles of it, are conserved from rodents to humans. The neocortex comprises of different cell types playing specific roles in its functioning. Two of the most abundant cell types, neurons and glia, come from a common pool of progenitors in the ventricular zone in a temporally regulated fashion. The initial developmental phase involves production of neurons which is followed by gliogenesis.

Interestingly, the ratio of neuron versus glia is essential for the proper functionality of the brain. Transcription factors-FOXG1 and LHX2, known to be crucial for various aspects of forebrain development are expressed throughout the embryonic period and postnatally. However, their genetic interactions in bringing about a properly developed brain is not completely elucidated. LHX2 has been shown to regulate the neuron-glia ratio in the hippocampus but not in the neocortex (Subramanian et. al. 2011).

We found the gene Foxg1 as a key determining factor to regulate neuron-glia ratio in the neocortex. Deletion of Foxg1 in conjunction with Lhx2 from the progenitors of the E15 cortical ventricular zone, by the method of in utero electroporation, causes premature astrogliogenesis. ChIP-seq analysis of the cortical cells at E15 showed a putative binding site of FOXG1 at the promoter-TSS of a key gliogenic gene-Nfia, which suggests a possible mechanism by which FOXG1 regulates the neuron-glia ratio. In the hippocampus, loss of Foxg1 and Lhx2, individually and in conjunction was seen to produce extra astrocytes. This gives us insights into differential gene regulatory mechanisms in the cortex and hippocampus with respect to regulation of neuron-glia ratio.

Frontotemporal dementia: from molecular mechanisms to therapy

Mahima Pandey | Undergraduate Student | Delhi University

Frontotemporal dementia (FTD) is a heterogeneous clinical syndrome characterized by frontotemporal lobar degeneration (FTLD). Neuropathologically, FTLD is characterized by abnormal protein deposits and almost all cases can now be classified into three major molecular subgroups based on specific accumulating proteins with the most common being FTLD-tau and FTLD-TDP (accounting for ~40% and 50%, respectively) and FTLD-FET (accounting for ~5–10%). In this special issue, the molecular and genetic basics as well as clinical approaches and therapeutics are reviewed in a poster.

Neurodegenerative disorders are a major social and economical challenge in our aging society, and we need to be prepared to see millions of demented patients in the near future. While research on Alzheimer's disease (AD), the most common form of dementia, has made rather dramatic progress during the last three decades, specifically for our understanding of its molecular mechanisms and genetics, and lead to novel therapeutic attempts, research on frontotemporal dementia (FTD) has lagged a bit behind.

It was back in 1892, when Arnold Pick described the first patient with frontotemporal lobar degeneration (FTLD) of the brain with the clinical presentation of presenile dementia and aphasia (Pick 1892), a heterogeneous clinical syndrome now known as FTD (Woollacott and Rohrer 2016). FTD accounts for about 5–15% of dementia cases and is the second most common cause of presenile dementias. Ten years ago, the underlying cause was known in only a minority of cases that were associated with abnormalities of the microtuble-associated tau protein or gene (MAPT). Therefore, molecular and cellular FTD research was often more or less a 'side-product' of AD research given the commonality of tau pathology.

However, within the last decade, FTD research has stepped out of the shadows with numerous groundbreaking discoveries, such as the identification of several novel FTD disease genes and proteins allowing almost all FTD cases to be subgrouped into three major molecular categories based on specific accumulating proteins with the most common being FTLD-tau and FTLD-TDP (accounting for ~40% and 50%, respectively) and FTLD-FET (accounting for ~ 5–10%). Within the FTLD-TDP subgroup, the subset of cases caused by C9orf72 mutations show dipeptide repeat protein (DPR) deposition in addition to TDP-43 pathology. Genetic forms of FTLD-tau are associated with mutations in the MAPT gene; familial forms of FTLD-TDP are most often

associated with defects in the genes GRN or C9orf72, while mutations in VCP and TARDBP are only very rarely found in FTLD-TDP; all neuropathologically confirmed FTLD-FET cases have thus far not been associated with a known gene defect, however, mutations in the FUS gene are on occasion described in patients with clinical features of FTD.

As people nowadays are more focused about neurodegenerative diseases such as Alzheimer's, Parkinson's etc the disorders like FTD are not highlighted. In order to highlight FTD and aware people about it I would like to present a poster on the topic frontotemporal demenitia: from molecular mechanism to therapy.

An in silico study of the ionic basis of bistability in Zebrafish Purkinje Neurons

Meha Pravin Jadhav | PhD Student | NCBS

Purkinje neurons play an important role in cerebellar functioning. Electrophysiological studies have shown that these neurons display bistability both in rodents (Williams et al., 2002; Lowenstein et al., 2005) and in zebrafish (Sengupta and Thirumalai, 2015). The neurons can stably exist in two different state (up and down) characterised by different resting membrane potentials and modes of firing. The ionic mechanisms of bistability in mammals have been studied to some extent but those in zebrafish are unexplored. Although previous studies provide some clue, we do not know the entire repertoire of ionic channels expressed in larval zebrafish. In this case, an in silico model allows us to explore the various ionic conductances that give rise to bistability in a simpler setting. This will allow us to answer two important questions: First, is bistability a somatic phenomenon or is it shaped by the synaptic inputs that the neurons receive. Second, which ion channels contribute to bistability and how do they interact with each other. Using the NEURON simulator (Version 7.7, Hines et al., 2009), we have built a multi-compartmental model of the Purkinje neuron. The ionic channels were adapted from a mammalian Purkinje neuron models (Akemann and Knopfel,2006 and Masoli et al., 2015), with kinetics modified for zebrafish physiological temperatures.

How do striatal neurons facilitate approach/avoidance behavior?

Naga Nitin Sai Chandra Anisetty | PhD Student | IIT Bombay

Based on how rewarding or aversive an experience is, mammals choose to repeat or avoid that particular experience. This is the tenet that guides action selection in mammals. There are two key pathways in the ventral basal ganglia of mammals that regulate the selection of actions. The direct pathway projections send a disinhibitory response to the thalamus whereas the indirect pathway projections send an inhibitory response to the thalamus.

The main input center in these pathways is the striatum and the neurons present in them are called Medium Spiny Neurons (MSN). These neurons are divided into dMSN-iMSN pairs (dMSN: direct pathway MSN expressing D1 dopamine receptor; iMSN: indirect pathway MSN expressing D2 dopamine receptor). The glutamatergic excitatory inputs received by each neuron in this pair are similar but the strength of the synaptic connections vary after every consecutive experience of reward/aversion. When dMSN becomes relatively more excitable then the direct pathway takes over. Opposingly, indirect pathway takes over when iMSN becomes relatively more excitable. The direction of strengthening of these neurons is determined mainly by the neuromodulator dopamine.

We have computationally modeled these neuron pairs and our findings help explain how dopamine differentially modulates the excitability of dMSN and iMSN. Thus, inherent biophysical differences between the two neurons determine their differential responses for the same glutamatergic inputs, an idea that needs to be further elucidated.

AutSim: Modeling activity-driven synaptic cell biology in health and disease.

Nisha Ann Viswan | PhD Student | NCBS

Autism is a set of complex neurodevelopmental disorders caused by mutations and errors in biochemical signaling networks. In addition to behavioural symptoms, there are known discrepancies in electrical activity and synaptic connections. We used detailed biochemical pathway modeling to study synaptic events in neurons from control and autism spectrum disorder (such as Fragile X syndrome) animal models. In order to ease the challenging task of parameter optimization and validation of the models, we have developed a pipeline called FindSim (Framework for Integrating Neuronal Data and SIgnaling Models). The pipeline integrates a curated database of experimental conditions and readouts with detailed models to drive simulations that precisely map to the experiments. FindSim can incorporate multiple kinds of experiments, including pharmacological time-series, dose-response, bar-chart, reaction parameters, as well as electrophysiological experiments such as LTP/LTD. Each such simulated experiment receives a score based on how closely the model outcome matches the experimental data. We utilized the scores from the entire dataset of experiments in a series of parameter sweeps and automated parameter optimization searches, in a hierarchical manner, to improve the fidelity of the model. The refined model will be used to make pharmacological predictions about drug interventions, side-effects, combinatorial treatments, and also to address genetic compensatory effects in control and diseased state(s). We also will use the model to explore the mGluR theory of autism, and how exaggerated protein synthesis leads to hyperexcitability.

Chronic Gq Activation of Forebrain Excitatory Neurons in Postnatal Life Establishes Long Lasting Behavioral Changes

Praachi Tiwari | PhD Student | TIFR Mumbai

The early postnatal life marks a critical period when neural circuits are plastic and amenable to change depending on environmental cues, and a history of early life stress is known to be associated with psychological vulnerability. Previous work from our and other labs have shown that in environmental models of early life stress, the animals show persistent increased anxiety in adulthood. We hypothesized that increasing activation of cortical excitatory neurons by activating Gq mediated signaling during the postnatal critical window is sufficient to bring about long-lasting increase in anxiety and depressive-like behavior in adulthood. A perturbation for postnatal day 2 to postnatal day 14 showed that animals displayed an increase in anxiety and despair-like behaviour, and exhibited impaired sensory-motor gating. Similar perturbation in adolescence or adulthood, however did not result in any significant change in anxiety and depressive-like behavior. Taken together, these results indicate that chronic activation of Gq-signalling in cortical excitatory neurons in first two weeks of postnatal life, but not in any other window of life is sufficient to evoke long-lasting changes in emotional behavior.

Modulation of mitochondrial metabolism within limbic brain regions following early life stress in rodents

Pratik Rajeev Chaudhuri | Post Doctoral Fellow | TIFR Mumbai

Pratik R. Chaudhari, Aastha Singla, Sashaina Fanibunda, Ullas Kolthur-Seetharam, Vidita A. Vaidya

Anxiety and depression are leading causes of disability that affect people across the lifespan. Early life stress like maternal separation in rodents results in life-long alterations in anxiety and depression-like behavior, as well as accelerated aging. The molecular, cellular, structural changes evoked by early stress that contribute to the lifetime risk for the development of psychopathology and remain to be clearly elucidated. Also, the underlying mechanisms that mediate the accelerated aging phenotype associated with a life-history of early life stress remain poorly understood.

Mitochondrial metabolism plays a central role in the regulation of brain function. However, very few studies have addressed the influence of early life stress on alterations in mitochondrial function and whether these contribute to the behavioural and cellular changes evoked by early stress. The preliminary evidence from our laboratory indicates a robust and lifelong reduction in the mitochondrial sirtuin, Sirt4, across the lifespan in rats subjected to early trauma. Moreover, the experiments suggest that the limbic brain region, prefrontal cortex, of maternal separated rats displays altered expression of mitochondrial biogenesis markers such as PGC1α, Sirt1, TFAM in postnatal and middle-aged animals. The influence of maternal separation in rats will be tested in various limbic circuits (prefrontal cortex, hippocampus, hypothalamus) at multiple time points across the lifespan. The primary thrust of our project is to understand the contribution of alterations in mitochondrial metabolism and function within limbic neurocircuits in mediating the persistent altered risk for psychopathology and accelerated aging that arise in rodent models following early stress.

Neuropsychiatry of Anorexia Nervosa

Pratiksha Pawar | Master's Student | Dr. Dy Patil Biotechnology And Bioinformatics, Pune

Pratiksha Pawar and Neelima Dubey

Highest mortality due to a psychiatric disorder is caused by Anorexia Nervosa[1]. Anorexia is characterized by a distorted body image and the core psychological feature of this illness is the overvaluation of shape and weight. People with eating disorders have the physical capacity to tolerate extreme self-imposed starvation and report an inability to distinguish emotions from bodily sensations in-general.

Candidate gene studies in eating disorders have mostly focused on genes encoding proteins that implicate the regulation of feeding and body weight, as well as genes involved in neurotransmitter pathways regulating eating behavior[2]. Genome-wide association study conducted by Watson et al showed results identifying eight significant loci that implicate metabo-psychiatric origins for anorexia nervosa[3]. Cross-disorder GWAS for Anorexia and Obsessive-compulsive disorder, shows strong positive genetic correlations with other psychiatric phenotypes like bipolar disorder, neuroticism as well as negative genetic correlations with metabolic phenotypes[4]. This paper discusses evidence that shifts focus solely from external influences, such as social, cultural and family environmental factors, to include internal influences that integrate genetic and neurobiological contributions to the illness. Understanding the underlying factors will help create better strategies to develop novel treatment options.

1. Mortality Rates in Patients With Anorexia Nervosa and Other Eating Disorders - A Meta-analysis of 36 Studies Jon Arcelus, LMS, MSc, FRCPsych, PhD; Alex J. Mitchell, MRCPsych; Jackie Wales, BA; et al.

2. Kaye W. Neurobiology of anorexia and bulimia nervosa. Physiol Behav. 2007 [PMC free article] [PubMed] [Google Scholar].

3. Watson, H.J., Yilmaz, Z., Thornton, L.M. et al. Genome-wide association study identifies eight risk loci and implicates metabo-psychiatric origins for anorexia nervosa. Nat Genet 51, 1207–1214 (2019).

4. Examination of the Shared Genetic Basis of Anorexia Nervosa and Obsessive-Compulsive

Disorder Zeynep Yilmaz,1,2,a Matthew Halvorsen.

Alpha synuclein oligomers: central players in the olfactory impairment in Parkinson's disease?

Priyadharshini Srikant | Project Assistant | IISER Pune

Parkinson's disease (PD) is the second most prevalent neurodegenerative disease, characterized by the degeneration of dopaminergic neurons in the midbrain regions due to the aggregation of alpha synuclein protein. Olfactory impairment is one of the prodromal symptoms of PD present in 70-90% of the patients. In this study, we investigated the extent of olfactory dysfunctions caused by different aggregated forms of alpha synuclein. We generated the oligomeric and fbrillar forms of human wild-type alpha synuclein in vitro and injected in the olfactory pathway of C57 BL6/J wild type mice. We administered the aggregated forms through intranasal delivery as well as stereotaxic injections in specific layers of olfactory bulb (OB). These different groups mice - monomers, oligomers and fibrils injected, were then trained on olfactory disrimination tasks using simple and complex stimuli. Our results show more severe olfactory deficits with the oligomers injected mice compared to fibrils and monomers injected animals. To understand the cellular basis of olfactory dysfunctions, we incubated the olfactory bulb primary neuronal cultures with different aggregated forms of the protein. The oligomers caused faster neurite collapse compared to fibrillar and monomeric forms justifying the extent of olfactory dysfunctions we observed in the injected mice. Currently, we are trying to understand the mechanisms by studying the mitochondrial dynamics in primary OB neurons incubated with different aggregated forms of alpha synuclein.

Alpha oscillations are generated across common cortical networks for processing saliency in spatial and spatio-temporal visual attention tasks

Priyanka Ghosh | PhD Student | NBRC

The ability to detect and orient attention toward salient, significant changes around us is critical to human survival. While we need focussed attention for any goal-directed behavior, the temporal component of attention becomes very important in conditions that demand rapid shift of attention. Do the underlying neural signatures involved in this attentional shift remain same with varying task conditions?

In our study, we investigated the effect of saliency on two different task conditions in the visual domain: one, where both the task and salient stimulus were static/stationary and second, where both were dynamic/moving. With a visual search task designed for the static condition and a moving dots task for the dynamic condition, EEG and behavioral data were collected from 22 right-handed healthy volunteers (21-29 years, 11 females).

We observed that along with a slower reaction time in trials with saliency, the spectral power in the alpha frequency band (averaged across all 64 sensors) was also significantly higher as compared to the trials without saliency for both the static and dynamic tasks. The increase in alpha power was very similar in both the task conditions. It is noteworthy that though the deployment of attention for a static task is very different from that of a dynamic task, their spectral patterns behave similarly upon the occurrence of saliency, elucidating a more general role of alpha oscillations in processing saliency which is invariant to task conditions. Also, the many common underlying sources of alpha activity like the right insula, the lateral pre-frontal cortex, left and right anterior temporo-parietal junction (regions of the Ventral Attention Network) and the right visual association areas obtained through source reconstruction using eLORETA across the two task conditions, suggest the role of common cortical areas that aid the process of reorientation to process a salient stimulus. Though some recent fMRI studies have re-evaluated the role of rTPJ, this is the first EEG study to show a causal influence between its sub-regions (posterior rTPJ in particular is activated only if the salient distractor is behaviorally relevant, which is present only in the dynamic task) through a time-varying Granger causality approach.

How good are humans in discriminating odors?

Rajdeep Bhowmik | PhD | IISER Pune

While you are in a fruit shop, can you distinguish tangerine from the orange using only sense of smell?What about an apple from an orange?These examples involve complex (orange vs. tangerine) and relatively simple odor discriminations (apple vs. orange) in the background of mixed fruity odors. We attempted to study olfactory discriminations in healthy human subjects using different stimuli of varying complexity. The popular methods, for example sniffin' sticks tests, introduce high variability because of the lack of precision with the stimulus properties. Here,we present a method where we have devised a fully automated system which requires very little intervention from the experimenter and delivers highly precise and temporally controlled odor pulses.In response to a set of stimuli, subjects are required to report "same" or "different" by pressing on different response buttons. The indicisive subjects have the option to receive the same pair of stimuli by pressing on a "repeat" button. We have tested the olfactory discrimination skills of subjects coming from various places in India using monomolecular odorants or binary mixtures of monomolecular odorants belonging to different chemical classes. Our results show that the discrimination accuracy shown by human subjects decreases with increasing complexity. We also show dependency of reaction times on the complexity of the odor pairs tested. This method, thus, provides a reliable and efficient way to address different questions related to discriminable odor space for healthy subjects. As reported in the case of many neurodegenerative diseases like Parkinson's and Alzhimer's, the sense of smell is among the first sensory systems to get affected. We plan to extend our studies to develop a prognostic strategy that can be used for early detection and extent of olfactory deficits in patients with neurodegenerative diseases.

To understand the development of Introductory Notes in the juvenile zebra finches

Rashi Monga | Project Asistant | IISER Pune

Adult male zebra finches are song birds that produce stereotyped vocalizations. Their song serves as a model system to broadly understand neural mechanisms underlying production of complex learned motor sequences. Adult finch song consists of variable short duration repetitive vocalizations called Introductory Notes (INs) followed by a stereotyped motif (sequence of vocalizations). The song goes through various stages of development- Sub-song stage (30-45 days post hatch), Plastic song stage (45-60 days post hatch), and crystallized song stage (post 90 days). Juvenile finches learn the song from their father during the early stage. Sub-song has no acoustic and temporal structure observed in the adult finches. The plastic song stage marks the presence of highly variable, yet identifiable structures. Post 90 days, the song gets crystallized and the bird repeats a stereotyped motif. The stereotyped motif is preceded by variable number of short duration syllables called Introductory Notes (INs). Since adult finch song begins with INs, we are interested in assessing whether syllables similar to INs are also present in the early developmental stages of song.

We use syllable duration distribution of the first few syllables to identify them in the sub-song. We observe that the first few syllables are more stereotyped in the syllable duration than other syllables. This analysis suggests that syllables similar to INs are present in the sub-song stage. We further need to characterize the distribution of INs in the plastic song stage and how their development correlates with the development of the song. This analysis can further help us elucidate whether same circuits initiate the song in both the young and adult birds and can allow us to trace potential brain regions responsible for production of INs.

Long-range signal propagation in pyramidal neuron dendrites mediated by store calcium regulation

Saismit Naik | Undergraduate Student | IISER Pune

Regenerative calcium release from intracellular (ER) stores may provide a basis for functionally important long-range signalling in dendrites of hippocampal CA1 pyramidal neurons. However, the conditions under which such signals can be initiated and stably propagated are not well-understood. We aim to systematically explore the biophysical and geometric parameters behind initiation and propagation of calcium waves by developing a spatially-extended computational model of calcium dynamics in an ER-containing dendrite. We hope to gain an improved mechanistic understanding of an under-studied mode of neuronal calcium signaling that can overcome the limitations imposed by the purely diffusive spread of intracellular signals; with possible implications for information transmission, processing and storage in pyramidal neurons.

Deciphering the Dynamics of the Locust Olfactory System

Saptarshi Soham Mohanta | Undergraduate Student | IISER Pune

The antennal lobe, the insect equivalent of the olfactory bulb in mammals, is a dense network of excitatory projection neurons and inhibitory interneurons. This network generates elaborate spatiotemporal patterns of activity in response to an odor. Computational models of the antennal lobe have typically assumed that the input to the inhibitory interneurons is a narrowly tuned. That is, each interneuron responds reliably to a small subset of odor inputs and not to others. However, several experiments have shown that this is not the case. Interneurons arborize extensively across the antennal lobe and receive input from nearly 70% of all odor receptor neurons in the antennae. Therefore, odor input to different LNs is not as distinguishable as one would expect if the neurons are narrowly tuned. The goal of this project is to understand the effect of broad odor tuning on the repertoire of spatiotemporal patterns the network can generate and its role in odor discrimination. To this end, we first constructed a detailed network model of the insect antennal lobe and stimulated it with odor inputs that were based on experimental recordings of a population of olfactory receptor neurons. We then used the responses of projection neurons to drive an array of Kenyon cells in the mushroom body. In addition to projection neuron input, Kenyon cells also received feedback inhibition from a single GABAergic neuron that ensured a sparse response. Our model was able to replicate some critical features observed in the antennal lobe and mushroom body activity in in-vivo experiments. The population of PN showed a distinct oscillatory LFP. We were able to tune the parameters of the model to generate an onset and a sustained offset response to odor stimulation. As seen in experiments, the model PNs and LNs exhibited patterning over multiple time scales. We could tune the inhibitory output of the giant GABAergic neuron (GGN) such that the responses of Kenyon cells were sparse.

APOE4 affects basal and NMDA mediated protein synthesis response in neurons by perturbing calcium homeostasis.

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The APOE4 isoform of Apolipoprotein E (APOE) is one of the most well-established risk factors for Alzheimer's disease (1,4). Though APOE4 is shown to cause synaptic defects such as reduced dendritic spine density, dendritic length (2,3,4), poor spatial learning and memory (3,4), the molecular mechanisms behind APOE4 mediated defects are not well understood. We studied the effect of APOE4 on synaptic translation and our results show that APOE4 affects basal protein synthesis in rat primary cortical neurons. More importantly, we also show that NMDA mediated protein synthesis response is lost in APOE4 treated neurons. We show that the protein synthesis dysregulation is linked to the perturbation of calcium homeostasis caused by APOE4. Our preliminary experiments further indicate that the source of APOE4 mediated calcium influx could be through voltage-gated calcium channels (VGCCs). Hence, we hypothesize that the APOE4 mediated synaptic defects are caused due to APOE4 mediated perturbation of calcium homeostasis resulting in the inhibition of both basal and cue mediated synaptic translation. We are currently trying to elucidate the link between APOE4 and VGCCs.

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5-HT2A receptor stimulation: a SIRTain target to enhance mitochondrial function

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Neuronal mitochondria are crucial organelles that regulate bioenergetics, and also modulate survival and function under stress. In addition, mitochondria subserve specialized functions of synaptic transmission, Ca2+ homeostasis, neuronal excitability and modulate structural and functional plasticity in neurons. Mitochondria are thus at the epicenter of supporting distinctive neuronal functions in the brain across lifespan. However the cues that influence mitochondrial biogenesis and function in neurons remain poorly elucidated. We have previously demonstrated a novel role for the neurotransmitter serotonin (5-HT) in the modulation of mitochondrial biogenesis and function, via the 5-HT2A receptor-SIRT1-PGC-1α axis, which facilitates stress adaptation in forebrain cortical neurons (Fanibunda et al., 2019).

We have further extended these studies to characterize early events following 5-HT2A receptor stimulation, which are a precursor to enhance mitochondrial biogenesis. Chronic 5-HT2A receptor stimulation with the agonist DOI, increased cortical mtDNA and ATP levels in a SIRT1-dependent manner. Seahorse analysis performed on isolated mitochondria derived from cortices of vehicle- and DOI-treated rats revealed enhanced state-2 (via complex-I/II) and state-3 (complex II-dependent) respiration and ATP production rate following DOI administration, demonstrating an increase in OxPhos efficiency.

Further experiments are underway to tease apart the initial signaling events downstream of 5-HT2A receptor stimulation, which lead to the recruitment of Sirt1. Acute pharmacological elevation of endogenous serotonin levels, by combined treatment with tranylcypromine and L-tryptophan, resulted in a significant increase in Sirt1 transcript levels in the prefrontal cortex, which was abrogated in 5-HT2A receptor loss of function mice. 5-HT2A receptor stimulation of cortical neurons in vitro, in the presence of 5-HT2A receptor antagonist MDL100,907 or specific inhibitors for pPLC/pERK/PI3-kinase/PKA/PKC pathways, are underway to delineate downstream signaling events. Further, experiments to determine pCREB recruitment at the Sirt1 promoter and SIRT1 activity assays, following DOI stimulation are in progress. These

studies will establish whether Sirt1 is a bonafide transcriptional target of 5-HT2A receptor activation. 5-HT2A receptors are highly expressed in limbic neurocircuitry, with strong implications in the regulation of anxiety and depressive-like behavior. Our present work will identify drug targets downstream of the 5-HT2A receptor to ameliorate mitochondrial dysfunction, which has implications in ageing, neuropsychiatric and neurodegenerative diseases.

Role of antennal lobe neurons in encoding synergistic response to lactic acid and carbon dioxide in Aedes aegypti

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Aedes aegyti is a vector for a number of hazardous diseases like dengue, chikungunya and Zika virus. According to WHO, each year 390 million people are affected by dengue fever alone. Aedes use a variety of cues to orient themselves toward a suitable host which includes heat, moisture, visual stimuli, carbon dioxide, and odors released from humans like lactic acid, acetone, octen-3-ol, and several others. Carbon dioxide is known to be very important for long-range attraction while other host odors play an important role in short-range orientation of the mosquito towards the host. Various researchers have studied the behavior and sensory neuron responses of mosquitoes to understand the mechanism behind their attraction towards an odor stimulus to find better strategies to control the mosquitoes. Researchers found that when lactic acid and carbon dioxide are given together, attraction to the mixture is higher than the sum of attraction to the individual odors. This synergistic behavior is difficult to explain at the level of sensory organs because lactic acid is detected on the antennae and carbon dioxide is detected on the palps. There is no interaction observed at the receptor level between these organs. However, sensory neurons from both antenna and palp synapse with projection neurons and local neurons in the antennal lobe. Projection neurons also receive excitatory and inhibitory inputs through lateral connections formed by the local neurons. Since the information for both lactic acid and CO2 can be encoded in the same PNs, we hypothesize that the synergistic behavior seen for the mixture of these two odors might be generated at the level of the antennal lobe in the brain. We are trying to understand the synergistic response to lactic acid, carbon dioxide and their mixtures in the antennal lobe using whole-cell patch recording from the antennal lobe neurons in Aedes aegypti.

Understanding the role of spectrin periodic cytoskeleton in mechanics of the developing axon

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Neuronal development includes processes like neurite outgrowth, elongation, maturation, path finding, and synapse formation. All of these processes are shaped by mechanical forces which could be environmental, like surface stiffness or an intrinsic property, like the rest tension. In neurites, mechanical tension has shown to influence neurite growth(Bray, 1984; Dennerll et al.,1989), synaptic vesicle clustering(Siechen et al., 2009) and axonal transport (Ahmed & Saif, 2014).However, not much is known about the biophysics of neural development and its relationship with cytoskeletal arrangement and dynamics.

The present study examines the spectrin periodic cytoskeleton in the purview of mechanics. Stimulated emission depletion (STED) microscopy of β-II spectrin stained chick DRG neurons across developmental time, shows the presence of spectrin lattice with a periodicity of ~190 nm as observed in other neuronal types (Xu et al; 2013, J. He et al.2016). In DIV-2, the spectrin lattice was discontinuous and observed in patches along the axonal shaft unlike in DIV-5, where it was more or less continuously arranged and prevalent. Axonal ablations which would give a measure for the rest tension were carried out for DIV-1 and 5 neurons. Snapping distance (a measure of tension) of axons increased over development, suggesting an increase in tension which correlates with an increase in prevalence of spectrin lattice. The gap-length (retraction) reduces with depletion of spectrin at DIV5 compared to DIV1. In this context, axonal ablation not only serves as a measure of mechanical tension but could also serve as a model for regeneration/degeneration studies.

Asymmetry in any connections in EI-networks forms feedforward networks which generate activity sequences.

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Sequential neuronal activity is associated with tasks like spatial navigation and encoding memory and time. Several computational models exist that use supervised or unsupervised learning to explain the emergence of sequential activity of neurons. Recently, Spreizer et al have proposed that correlated spatial asymmetry on the connectivity of neurons can generate neuronal activity sequences without the need for supervised or unsupervised learning. Here we investigate how correlated spatial asymmetry in different types of connections (i.e. excitatory (E) to inhibitory (I), I to E, E to E and I to I) affect the sequences. First, we show that the correlated spatial asymmetry in any of the four types of connections is sufficient to generate neuronal activity sequences. We found that when correlated spatial asymmetry is present in inhibitory connections, sequences are slower. We also show that feedforward networks formed by the correlated spatial asymmetry predict the activity sequences and are the causal mechanism of sequence generation. Finally, we examine noise correlations in background activity to compare the structure of biological and model networks.

Neuronal circuit for anxiolytic effects of a serotonergic hallucinogen

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Hallucinogens like DMT, LSD and psilocybin have been shown to have positive effects on alleviating mood disorders. Although serotonergic psychedelics are being widely studied to understand the possible mechanism of hallucinations, the mechanistic underpinnings of their anxiolytic effects still remains unknown. Using 2,5-Dimethoxy-4-iodoamphetamine (DOI), a hallucinogen that acts on the Serotonin 2a receptor, we saw that the anxiolytic effects of this drug are dose dependent. It is not yet understood how an acute systemic administration of DOI can change the neuronal activation profile across the brain to exhibit a dose dependent effect on mood state. Using c-Fos immunohostochemistry, we plan to understand how the activation of regions involved in anxiety-like behaviors is modulated under the effect of hallucinogens and target these areas to further elucidate the neurocircuit that regulates anxiolysis via hallucinogenic compounds.

Spike detection in whole-cell patch clamp recordings containing small-amplitude spikes

Smith Gupta | PhD Student | IIT Kanpur

During an action potential, membrane voltage of a typical neuron increases by nearly 100 millivolts from its resting value, and rapidly falls back to it within a few milliseconds. In insects, projection neurons relay the olfactory information from the antennal lobe to the mushroom body in a variety of temporal spiking patterns. Whole-cell patch clamp recordings from the cell body can be used to detect these signals, and some of these recordings can have spikes with amplitudes as small as 2 mV in Drosophila or mosquitoes. Moreover, the spikes are often riding on relatively large depolarizations, which makes it challenging to distinguish them from noise or sharp EPSPs present in the signal. For spike detection in such neuronal recordings, we propose a deterministic algorithm that classifies a peak as an action potential via parameterizing on its shape and the context of its occurrence. Peaks are first selected according to their sharpness, and subsequent filtering is done based on the rise from the resting potential. The algorithm facilitates accurate spike detection that can be used for better interpretation and analysis of patch clamp data from neuronal recordings in invertebrates.

BDNF regulation by DNA demethylation in hippocampus is involved in reward memory consolidation

Sneha Sagarkar | Faculty | Pune University

Sneha Sagarkar, Priyanka Chavan, Kiran Landage, Madhura Sapre, Amul Sakharkar

Reward is a fundamental cognitive function of the brain which increases the likelihood of growth and reproduction. The reward circuit comprises a crucial neural conduit between context of the reward and events that precede them. This association process is critical for memory-guided decision-making, which is reported to go awry in mental illnesses such as binge eating disorders, drug addiction and schizophrenia. Learning induces persistent, long-lasting transcriptional changes that contribute to storage of memories. Moreover, transcription is regulated via epigenetic mechanisms. Epigenetic changes of memory-related genes such as BDNF play a crucial role in formation, maintenance and retrieval of memories. DNA methylation status of BDNF is associated with fear memory formations. Therefore, the current study focuses on studying the role of DNA methylation in regulating reward memory formation.

METHODS: The adult male rats were conditioned to seek sweet food pellets in one of the arms of Y maze for 15 min/day over one week. The conditioned place preference of the trained animals was examined, and animals were immediately scarified after the test session of 15 min. The expression of BDNF transcripts along with DNA demethylation factors in the hippocampus were measured post conditioning. The levels of cytosine methylation and the hydroxymethylation at the BDNF promoters were also examined.

RESULTS: Animals spent significantly more time in the arm conditioned to sweet food compared to no food arm. Expression of GADD45α and Tet1 increased significantly in the hippocampus of conditioned animals. Likewise, the conditioning to sweet food also up regulated the peptide and mRNA levels of transcript I, IV and IX. Concurrently, the hydroxymethylation at the BDNF promoter IV and IX was also increased.

CONCLUSIONS: These results suggest that DNA demethyation plays an important role in reward memory consolidation via regulation of BDNF expression in hippocampus.

FindSimWeb, an online tool for integrating neuronal data and signaling models

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Modeling neuronal signaling is a complex and multiscale problem. It involves simulating the intricate network of biochemical signaling, protein synthesis, and electrical components in a neuron. A generic model that is rigorously refined and validated using experimental data is of high scientific value and much desirable. Framework for Integrating Neuronal Data and Signaling Models (FindSim) is a structured specification that allows anchoring experimental data with signaling models. FindSim enables encoding the experimental conditions in a signaling model. Running an experiment with FindSim results in a score and a comparative graph plot to measure the performance of the model with the data reported in the literature. This kind of curated data is used to optimize the model parameters. An optimized model can further be used to test out disease-related hypotheses and design drug molecules. Here we report, a website we have developed to use FindSim in a user-friendly and interactive manner. The website has an interactive widget to visualize the model layout. Currently, we are developing a pipeline to enable running model optimization using this web-tool. Since model optimization is a computation-intensive job and requires running several experiments in parallel, the pipeline would send the optimization tasks to Neuroscience Gateway (NSG) High-Performance Clusters.

Molecular interaction studies between SLC6A9 and STX1A with screened neuroprotective phytochemicals for finding out their therapeutic significance against Obsessive-Compulsive Disorder (OCD)

Swarn ('V. D. A.') Warshaneyan | Undergraduate Student | Amity University

Swarn ('V. D. A.') Warshaneyan, Shantanu Durgvanshi, Prachi Srivastava

Obsessive-Compulsive Disorder (OCD) is a disease of the mind, marked by recurring intrusive thoughts ("compulsions") and urges to do certain things repeatedly ("obsessions"), with a lack of control on them and their intensity affecting the patient's everyday life. It is observed to be associated with several other psychiatric problems, such as depressive/anxiety/tic/bipolar disorder & Attention-Deficit Hyperactivity Disorder (ADHD), with the cause being unknown and possessing genetic components. It is also known for an increased suicide risk in patients. Many different approaches are being tried to develop an effective treatment method for OCD but still this area of research is somewhat neglected. In the current course of work, there is an attempt to signify the computational approaches with reference to target identification, molecular docking and intense in silico analysis. In this study, two proteins among the identified five targets (SLC1A1, SLC6A3, SLC6A4, SLC6A9 and STX1A), which have been identified in the development and progression of OCD symptoms, were selected. i. e., SLC6A9 and STX1A. Targets functionality can be assessed from the 3D structure of proteins and hence, their 3D models were generated through Modeller v9.22 and verified using SAVES v5.0 (also submitted to PMDB). Modelled structures were utilized for molecular docking studies by using PatchDock and FireDock. Interaction studies were done with selected phytochemicals, which were chosen by text mining relevant publications. Primary selection was done through Molinspiration and Lipinski's Rule of Five and secondary selection using PreADMET for their viability as drug candidates. Final screening was based on docking score. In the current study, the best results are of Aphidicolin, Forskolin and Salvinorin A for SLC6A9, while Retinal, Forskolin and Geranylgeranyl Pyrophosphate for STX1A. Considering both results suggests that Forskolin can be a good potential therapeutic agent for OCD.

Spatiotemporally variable recombination with respect to the floxed Ldb1 allele in the dorsal telencephalon of embryonic mice.

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Ldb1 is a protein cofactor that participates in several multiprotein complexes and has diverse functions in the developing brain. Since Ldb1 null mutants do not survive past embryonic day (E) 10.5 (Mukhopadhyay et al., 2003), we employed a conditional knockout strategy using multiple Cre lines to examine the role of Ldb1 in the development of the dorsal telencephalon.

Kinare and Pal, 2019 showed that the Ldb1 protein encoding locus is spatio-temporally resistant to Cre recombinase-mediated genetic knock-out strategies. Their results can be summarised as follows: early acting transgenic Cre lines that is, Foxg1Cre can faithfully recombine the ldb1 locus, however, Emx1Cre10.5 showed a medio-lateral gradient of recombination in its domain of activity. Surprisingly, the group also found that NestinCre which acts from E11.5 was able to bring about complete deletion in the diencephalon and ventral telencephalon but not in the dorsal telencephalon.

Additionally, given the fact that all the transgenic Cre lines that Kinare and Pal, 2019 used were activated in the progenitors, it would be interesting to check if this locus is spatiotemporally resistant to recombination in postmitotic cells as well. In order to do this, we are using NexCre which is activated specifically in postmitotic cells.

Our results highlight the importance of examining recombination efficiency when interpreting dorsal telencephalon-specific phenotypes using standard Cre lines.

SANKET, FINDSIM, HOSS and MOOSE: A suite of projects for data and models of synaptic function.

Upinder Singh Bhalla | Faculty | NCBS

G.V. Harsha Rani, Nisha Visvan, Surbhit Wagle, Upinder S. Bhalla and the SANKET consortium

The synapse is a staggeringly complex computational and structural system, and it carries out these functions through tightly coupled chemical, electrical and structural events. The SANKET consortium seeks to develop approaches to tackle this complexity, with implications for synaptic functions in brain computation and also in neurological disease. The researchers draw upon multiple simulation tools, but with a core approach that involves developing accurate models with a close match and validation from in-house experiments as well as published data. These tools and datasets are all open-sourced. Typical projects include signalling in autism, mechanisms of synaptic plasticity, and the interplay between neurons and astrocytes. The typical workflow in each project is

1. Identify signaling and neurophysiological mechanisms core to the system of interest,

2. Develop a multiscale model (typically combining biochemical signalling, trafficking, protein synthesis, and neurophysiology) to represent the system.

3. Perform experiments, and mine the literature, to assemble a dataset of structured experiment definitions.

4. Constrain and optimise the model using this dataset and the HOSS tools.

5. Analyse the model(s) for better understanding the system, and to motivate further experimental exploration.

6. Develop models of disease, such as mutated signalling pathways, so as to predict leads for diagnosis and treatment.

Overall, the SANKET consortium is an open, data-driven, and principled effort to reproducibly develop a better understanding of complex neuronal processes and to embody this understanding in models.

Acronyms:

SANKET: The Signalling and Neurophysiology Knowledge-resource for Experiments and Theory. [Sanket means signal in Sanskrit]

MOOSE: Multiscale Object-Oriented Simulation Environment:

https://moose.ncbs.res.in

FINDSIM: Framework for Integrating Neuronal Data and SIgnaling Models

    http://findsim.ncbs.res.in, http://findsimweb.ncbs.res.in

HOSS: Hierarchical Optimization for Systems Simulations

DOQCS: Database of Quantitative Cellular Signaling

    https://doqcs.ncbs.res.in

Studying the role of Serotonin during different developmental epochs using pharmacological & genetic tools

Utkarsha Ghai | PhD Student | TIFR Mumbai

Serotonin (5-HT) has been shown to be a critical neurotransmitter that modulates mood. In terms of the pathways that it affects its known to regulate cyclic AMP (cAMP) levels, CREB mediated transcription and many biochemical pathways that are known to affect plasticity and most recently to mitochondrial metabolism and bioenergetics, Fanibunda S. et al. 2019.

The most widely used antidepressant Fluoxetine (Prozac) which is a Selective Serotonin Reuptake Inhibitor(SSRI) acts by increasing the levels of serotonin at the synapse by blocking the uptake by the serotonin transporter has been shown to mediate age dependent effects. The time window in which Fluoxetine is administered often profoundly determines the behavioral outcome with evidence indicating that elevation of serotonin in postnatal, juvenile and adult life can have diverse behavioral outcomes. The underlying molecular mechanisms that result in such different behavioral outcomes are unknown. We would explore the downstream mechanisms that serotonin either increased using pharmacological agents or by genetic manipulation can modulate in these different time windows.

Our results show that indeed fluoxetine leads to different changes in the bioenergetics of certain brain regions which are known to be involved in mediating these behaviours majorly the hippocampus and the medial prefrontal cortex. Administration of fluoxetine during the postnatal period leads to an increase in anxiety and despair-like behaviour while showing a decrease in ATP, and proteins involved in mitochondrial biogenesis and function such as Sirt1, TFAM and VDAC. Contrasting to these results administration of fluoxetine during the juvenile period leads to a decrease in anxiety and despair-like behaviour accompanying an increase in ATP and proteins such Sirt1 and VDAC.

Since, Hollis F. et al. (2015) showed that bioenergetics can be one of the pathways that impacts these behaviours it would be interesting to check if these contrasting results during different developmental epochs observed due to an increase in the serotonin levels are causal or correlative with respect to the anxiety and despair- like behaviours observed.

A 'viral' understanding of Parkinson's disease (PD)

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Parkinson's disease is the second most common neurodegenerative disease prevalent in human society after Alzheimer's. It is characterized by breakdown of dopaminergic neurons specific to the Substantia Nigra Pars Compacta (SNPc) region of the mid-brain. It involves other subsequent conditions such as accumulation of alpha-synuclein clusters in the region-specific neurons, mitochondrial dysfunction and others. Physiological conditions comprise of motor dysfunction- Posture instability, a stable resting tremor in the extremities of the body, nuchal (neck) and facial rigidity, muscle rigidity and slurred speech. Treatments for Parkinson's include:

• 	Replacement of neurotransmitter dopamine- administration of L-DOPA and other drugs that mimic dopamine

• 	Deep Brain Stimulation treatment for reducing the effect of motor dysfunction.

Certain viruses like Influenza cause post-infection encephalitis (brain damage) and subsequent physiological conditions very similar to those observed in PD. This phenomenon is known as Viral Parkinsonism. This syndrome is characteristic of a number of viral infections and though many can even be treated/reversed by L-DOPA treatment; they do not show characteristic features of PD like alpha-synuclein aggregation and are considered pheno-copies of the disease. Parallel research shows cross-reactivity between viral antibodies and alpha-synuclein clusters.

Thus one can hypothesize Parkinson's to be an autoimmune disorder, where mis-folded alpha-synuclein becomes a trigger for neuro-degeneration. Alpha-synuclein clusters demarcate Parkinson's from other phenocopies, yet most of the treatment provided to PD patients target the physiological conditions common to both PD and Viral Parkinsonism, i.e. L-DOPA treatment.

While Viral Parkinsonism holds the answer to a number of questions regarding the physical manifestation of PD, the cross-reactivity between viral antibodies and alpha-synuclein clusters can be a start point to understand the biochemical and immunological similarities between the two. Thus presented is a theoretical triangular niche of Parkinson's disease, Viral Parkinsonism, and viral infection for a deeper understanding of PD and its possible cure.

Role of ryanodine receptors in synaptic transmission and mediating metaplasticity at hippocampal dendritic spines

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Calcium release from intracellular stores of endoplasmic reticulum (ER) can potentially modulate synaptic transmission and plasticity in the hippocampus. Contribution of IP3 receptors on the ER to postsynaptic signaling has been established previously, however, the precise role of ryanodine receptors (RyR), the second important pathway of calcium release from the ER remains unclear. We use a physiologically realistic computational model of the CA1 dendritic spine that includes the predominant activity of type 3 RyRs (RyR3), which are predominantly expressed in hippocampus, to investigate the functional implication of these receptors. Our analysis highlights an important role for local depletion and refilling of the ER in shaping its contribution via RyR-gated calcium release. We have systematically characterized the role of RyRs in modulating activity-dependent synaptic plasticity. This study, together with previous work on IP3 receptors, contributes to a broader understanding of store-mediated metaplasticity at individual CA1 synapses.