Abstracts

Title: DNA as Information
Speaker: Prof. Vijay Chandru, CMD, Strand Life Sciences.
Sanjay Biswas Memorial Lecture, 27th January: 9:00-10:00

Information Theory and Information Technology have had more or less coincident timelines with the story of DNA and Genomics over the last 65 – 75 years. Shannon's papers on information theory were published about half a decade before Crick-Watson. Shannon was always cautioning scientists on the indiscriminate use of information theory in their domains and yet was unwilling to dismiss the hypothesis that "the human being acts as an ideal decoder". The code being decoded is of course the DNA sequence. However, most biologists would dismiss this hypothesis as a metaphor that when taken too literally leads to a misleading picture of development as an expression of genetic information.

In this lecture, we will touch briefly on some of these philosophical controversies but focus more on the constructive or engineering aspects of this metaphor that has brought the most advanced ideas in computing to bear on the sequencing and annotation of the human genome. Today we are at the threshold of a new age of precision and personalised medicine that is affordable and accessible to increasingly larger segments of society.

Title: Cracking the code for visual objects
Speaker: Dr. S. P. Arun, Associate Professor, Centre for Neuroscience, IISc
27th January: 10:20-10:50

Vision is deceptively easy but in fact it is an extremely challenging computational problem. It is so challenging that we have made computers play chess but still cannot make them see. How does the brain do it? I will argue that the brain uses a sophisticated code for objects that makes recognition easy. This code operates according to systematic rules, incorporates knowledge about the world and enable simple decoding of relevant information. I will present recent findings from my lab elucidating object recognition at the behavioral and neural levels. For more information please visit: http://www.cns.iisc.ac.in/~sparun

Title: Computations underlying motor learning
Speaker: Puneet Singh, PhD student, BSSE, IISc
27th January: 10:50-11:10

Title: How reading changes letter representations: a double dissociation using orthographically distinct scripts in India
Speaker: Aakash Agrawal, PhD student, BSSE, IISc
27th January: 11:10-11:30

Reading is a recent cultural invention that exploits the intrinsic recognition capacities of our visual system. But does reading consist only of learning letter-sound mappings, or does it also fundamentally alter letter representations? This question has been difficult to address because (1) illiterates and literates everywhere differ along socioeconomic and cognitive dimensions that confound all comparisons and (2) in the Western world, nearly all languages use nearly the same Latin letters.

We addressed this question by exploiting the orthographic diversity of Indian languages. Specifically, we identified two distinct groups of students (both English-literate) but with one group fluent in reading the Telugu script but not the Malayalam script, and the other group fluent in reading Malayalam but not Telugu. To probe letter representations without reading, we used oddball visual search as a natural index of similarity between shapes.

In Experiment 1, both groups of readers searched for a Telugu letter among Telugu letters, or a Malayalam letter among Malayalam letters. The main result is a double dissociation: in both groups, searching among familiar letters was more efficient than searching among novel letters. However, letter representations were only subtly altered because search times were strongly correlated across literates and illiterates. In Experiment 2, we asked whether reading alters the relationship between familiar and novel letters. To this end, both groups of subjects performed searches with the target from one script and the distractors were from the other. The main result was again a double dissociation: in both groups, finding an unfamiliar letter was easier among familiar letters than vice-versa. In Experiment 3, to explore how letters combine in a word, we used two-letter strings with 5 possible letters at each position to form 25 two letter strings in each language. The main result was that non-native readers showed greater interactions between letters than native readers. Thus reading enables letters to

retain their identity inside a word. Taken together our results elucidate how reading changes shape representations to enable efficient letter and word recognition.

Title: Brain plasticity in hearing impaired population: Effects on conscious and unconscious visual processing
Speaker: Dr. Ramesh Kumar Mishra, Centre for Neural and Cognitive Sciences University of Hyderabad
27th January: 11:30-12:00

The loss of auditory input in hearing impaired individuals causes compensatory changes in visual processing in the Deaf brain. This neuroplasticity in Deaf and its consequences on visual processing has been a great topic of interest. Deaf individuals have been shown to be better at detecting and orienting to visual targets. This effect is particularly pronounced for objects located at visual periphery. I will discuss the attentional advantages we observed in the Deaf on an oculomotor cueing task. Deaf were found to be better at orienting attention to targets than normal-hearing individuals. But it is not known if such advantages observed for conscious stimuli also extend to the unconscious domain. Stimuli presented below the threshold of awareness are found to influence a subsequent conscious respnse, even when such a response is voluntary. Do the plasticity-induced changes in the Deaf influence such unconscious processing? We have observed that hearing impaired individuals show enhanced processing of unconscious stimuli compared to individuals with normal hearing. Whether this is because the Deaf are more perceptually aware of the unconscious stimuli is still an open question. These findings suggest that neuroplasticity in the Deaf leads to enhanced visual processing in both conscious and unconscious domains.

Title: Deciphering the control architecture of voluntary movements
Speaker: Varsha Vasudevan, PhD student, BSSE, IISc
27th January: 12:00-12:20

The motor system is corrupted by noise which can affect the system at various levels from the sensory stage to the execution of movements. This inherent noise in the system is reflected in the behaviour as the movement variability. Here, we use the pattern of variability to better understand the nature of control of biological movements.

In this work, the saccadic system has been used to study and understand variability in order to obtain better insight into the control of movements. Saccades are rapid eye

movements that increase the acuity of vision by bringing the target image near to the fovea in the eye. The inter-trial variability in the saccade trajectory is studied in conjunction with a stochastic saccade generation model for understanding the control of saccadic eye movements. The stochastic saccade generation model consists of a brainstem control circuitry of saccades with noise incorporated into the system at various levels. Three types of noise namely visual noise, premotor noise and oculomotor noise are hypothesised to be affecting the saccadic system. The model can simulate multiple trials of saccades and thus can be used to investigate the inter-trial variability of the saccades about its mean trajectory.

The dynamical evolution of variability of the saccade kinematics like angular displacement, velocity and acceleration were observed to be following a structured pattern during the movement. The model was able to predict this profile of variability across the population with high correlation. Thus the stochastic feedback model for saccade generation can be further used to understand how different sources of noise contribute to the movement profiles of saccades. The work suggests that understanding variability in movements is a powerful tool to investigate movement control. Thus studying how biological systems produce accurate movements in the presence of noise may help engineer artificial systems that are as effective as human systems in producing flexible and accurate movements.

Title: On the Limitations of Causality Measures in Neuroscience
Speaker: Aditi Kathpalia, PhD student, NIAS
27th January: 12:20-12:40

In neuroscience, to characterize the functional circuits underlying perception, cognition, behavior and consciousness, it is important to understand the causal relationships or effective connectivity between different parts of the brain. In order to make predictions, a stimulus is varied and its effect on neuronal activity is observed. If we can correctly predict the neuronal activity response based on stimuli, we have established a causal relationship between the two. However, a large part of brain's activity is internally generated and thus contributes to response variability despite constant stimuli. In such a case, to infer physical causality with a deliberate manipulation of the system is difficult. For this, many causality measures have been used including model-based approaches such as Granger Causality (GC) or Dynamic Causal Modelling and model-free approaches such as Transfer Entropy (TE) and Mutual Information. In this work we investigate the limitations of two most widely used methods – GC and TE. Their

performance as an appropriate connectivity metric for asynchronous measurements, effect of finite data size and noise is studied using simulated signals.

Title: Divisive gain control in the hippocampal CA3-CA1 network mediated by tight excitation inhibition balance
Speaker: Sahil Moza, NCBS
27th January: 12:40-13:00

Neurons encode and communicate by integrating and thresholding incoming electrical signals. Understanding this signal summation process is vital for understanding the computations neurons and neuronal networks perform. We pose these questions in the hippocampal network, as it is well characterised at single cell and network level. Hippocampus consists of a network of CA3 neurons, which gives mainly excitatory and feedforward inhibitory connections to a network of CA1 neurons. It has been shown that CA1 neurons integrate subthreshold inputs linearly (Cash, J. Neuro, 1998). However, due to the nature of the stimulation methods, these studies have either non-physiological input, or have only looked at pairwise input summation (Poirazi, Neuron, 2003). We wanted to ask how multiple realistic excitatory and inhibitory inputs from CA3 sum at CA1. We found that feedforward inhibition from CA3 normalizes the excitatory input, such that the summation gain at CA1 is inversely proportional to the number of inputs. In absence of fast inhibition, there is reduced change in gain, and summation approaches linearity. Moreover, we observe that inhibition is directly proportional to excitation for all network subunits in CA3-CA1, suggesting tight Excitation-Inhibition balance (Vogels, Nat. Neuro, 2009) in the network. This process can be consequential in filtering and expanding the dynamic range of the cell.

Title: Is immunology like astronomy?
Speaker: Prof. Grant Lythe, Professor, University of Leeds
27th January: 14:00-14:30

There are approximately 400000000000 T cells in your body, about the same as the number of stars in our galaxy. We cannot manually count, let alone examine the interior machinery of, many cells or stars in situ. Those cells and stars that we can see, we only see at one instant of their long lifetimes. Instead, we have to rely on extrapolation from small samples and on indirect measurements, deducing what we can about processes in the interior from observations of their surface, imaging and data analysis, and

computational models. T cells are produced in the thymus and circulate through a human body, using T-cell receptors to probe the surfaces of antigen-presenting cells they come into contact with. How many different types of T cells do we have? The number of T cells of one type is an integer that increases or decreases by one cell at a time, when a cell divides or a cell dies. Immune responses rely on encounters between T cells and dendritic cells in lymph nodes. Stochastic models of immune system dynamics, describing millions of cells that interact with each other and with their environment, are more realistic than deterministic ones. Fortunately, stochastic models are also practical because analytical and numerical methods, and open-source software, are available.

Title: Conformational selection by an α-Pore forming toxin upon cholesterol binding drives membrane rupture

Speaker: Pradeep Sathyanarayana, PhD student, BSSE, IISc

27th January: 14:30-14:50

Title: How similar are your networks?

Speaker: Vasundhara Gadiyaram, PhD student, IMI, IISc

27th January: 14:50-15:10

In recent times, successful interpretations of large and complex systems such as brain, communications, social, biological and financial systems are becoming possible by investigating networks constructed from local connections. Analysis of such networks frequently requires a comparison between similar networks to find closeness between each other. Spectral approaches are powerful in capturing minute differences between networks, but most of them are based upon clusterings obtained from Fiedler vector or selected dominant modes. This reduction may lead to loss of information, especially if the networks are quite similar to each other. Also, the methods based on eigen values alone cannot distinguish between iso-spectral and isomorphic networks.To fill this gap in network comparison methods, a similarity scoring method for network comparison has been developed, which considers the spectra and the complete set of eigen vectors of the networks and quantifies both local edge difference and global clustering changes in the networks. The development of the score and its applicability are discussed along with a few examples from protein structure networks and financial stock markets.

Title: Insights into the transcriptional regulation of human macrophage polarization using a systems approach

Speaker: Sathya Baarathi. SR, IISc. Mathematics Initiative Program (IMI)

27th January: 15:10-15:30

Macrophages are highly dynamic immune cells which play an essential role in immune regulation and tissue homeostasis. They show diverse functional phenotypes in response to environmental cues, with each phenotype having well defined transcriptional and metabolic features. Gene expression profiling has been extensively used to study the activation states of macrophages. To identify the most robust and highly reproducible macrophage activation types, we have performed a consensus clustering on publicly available transcriptome data of differential macrophage gene expression profiles upon exposure to different immunostimulants. This resulted in 6 different macrophage activation subtypes with well defined class and stimulant specific transcriptional signatures. Network analysis of stimulant specific Gene Regulatory Networks (GRN) revealed "differentially regulated" paths and epicenters mediating these class specific changes. Further, comparison of the maximally perturbed paths across different stimulants revealed the existence of a highly plastic core regulatory components which efficiently regulates the target gene expression profile, depending upon the stimulant. Through this analysis, a minimal set of Transcription Factors (TFs) which can efficiently classify multiple macrophage polarization states was also identified, and the relevance of these TFs in disease classification based on macrophage transcriptome profiles has been studied.

Title: Evolutionary advantages of cross-talk between two-component signalling systems of *Mycobacterium tuberculosis*

Speaker: Dr. Narendra M. Dixit, Associate Professor, Chemical Engg., IISc

27th January: 15:50-16:20

Two-component signalling systems (TCSs) are the primary instruments with which bacteria sense and respond to environmental changes. Each TCS comprises a sensory histidine kinase (HK) and a response regulator (RR) protein. The HK is autophosphorylated in response to an environmental cue, following which it activates its cognate RR for downstream gene expression. Each bacterium carries many distinct

TCSs, each typically for a different cue. TCSs are also thought to be highly specific: HKs typically activate their cognate RRs alone. Thus, the more complex the environment in which a bacterium lives, the more the TCSs it must contain. Surprisingly, Mycobacterium tuberculosis (Mtb), a pathogen that survives in harsh host environments, has far fewer TCSs than soil bacteria. Further, in striking contrast to the prevalent paradigm of specificity, recent experiments have shown extensive cross-talk between the TCSs of Mtb. In this talk, I will present an evolutionary paradigm that explains the peculiarities of Mtb. Limited cross-talk can be an advantage if an organism has to respond to a pre-determined program of cues. It can be used to prime the organism for upcoming cues and initiate adaptive responses early on. In addition, the organism can afford to limit the number of TCSs its genome must encode. Our recent modelling work suggests, using multiple lines of investigation, that Mtb has evolved to capitalize on these advantages of cross-talk. Preventing cross-talk between the TCSs of Mtb may thus present a novel target of intervention.

Title: Kinetic analysis of two component signalling systems (TCSs) in *Mycobacterium tuberculosis*

Speaker: Gaurav Sankhe, PhD student, BSSE, IISc

27th January: 16:20-16:40

The ability to sense and adapt to the host responses is one of the key attributes that *Mycobacterium tuberculosis* possesses that allows it to successfully establish tuberculosis. TCSs are central to bacterial adaptation and present promising drug targets. A TCS typically consists of two proteins: a sensory protein -sensor kinase (SK) and an effector protein - response regulator (RR). The mechanisms and rates of most of the reactions involving bacterial TCS proteins are undetermined because of technical challenges arising due to the unstable chemistries of the phosphorylated SK and RR proteins. In the present study various kinetic parameters of TCS reactions, namely, SK autophosphorylation and SK to RR phosphotransfer rates and their binding affinities were determined. After demonstrating the equivalence of conventional PAGE (Polyacrylamide Gel Electrophoresis)/autoradiography based assays with an optimized HTA (High Throughput Assay) platform, the HTA platform has been used to measure the kinetics of autophosphorylation rapidly. The absolute values of SK autophosphorylation rates were estimated by fitting a mathematical model describing the reaction events to the data. Thus, the HTA along with the mathematical model provides a facile tool to obtain the kinetic parameters faster and reliably than the conventional PAGE/autoradiography. Furthermore, the binding affinities of a few SK-

RR interactions were evaluated using MST (microscale thermophoresis). The autophosphorylation rates and the binding affinities of SK-RR interactions yield the set of feasible interactions governing the network of TCSs in *Mycobacterium tuberculosis*.

Title: Identification of Nucleoside tri-phosphate binding space (NTPome) in *Mycobacterium tuberculosis* by a systematic sub-structural analysis.

Speaker: Raghu Bhagavat, PhD student, IMI, IISc

27th January: 16:40-17:00

Nucleoside tri-phosphate (NTP) ligands mediate a large number of cellular processes. While ATP acts as energy currency molecule, GTP has functional roles in signal transduction processes and as co-factors of enzymes. Here, we seek to identify the NTP binding proteome (NTPome) in *M. tuberculosis (M. tb)*, a deadly pathogen. The first level of input comes from an earlier study where we had modeled the *M. tb* proteome at a structural level, from which a set of 13858 small-molecule binding pockets was available to us. From a recent work in the laboratory, we had identified 27 different structural motifs that recognize NTP ligands, and serve as NTP binding signatures. Using this as the second line of input, we scanned the 13858 *M. tb* pockets using in-house sub-structure matching and alignment tools. We find that 1761 proteins or 43% of the proteome can bind NTP ligands. This not only provides functional clues for 315 hypothetical proteins, but also provides the precise list of binding site residues in each case with a possible binding pose of the ligand. Further, using a high throughput experimental method of dye-ligand affinity chromatography, we validate 45 proteins to be binding NTP ligands, of which 4 are hypothetical proteins. Thus, identification of the NTPome is not only helpful for functional annotation of proteins, but also in providing clues for useful drug targets.

Title: Oscillatory synchrony and sensory representations: insights from insect olfactory system.

Speaker: Dr. Nitin Gupta, Assistant Professor, IITK

28th January: 09:00-09:30

Oscillatory synchrony among neurons occurs in many species and brain areas, and has been proposed to help neural circuits process information. One hypothesis states that oscillatory input creates cyclic integration windows: specific times in each oscillatory

cycle when postsynaptic neurons become especially responsive to inputs. With paired local field potential (LFP) and intracellular recordings and controlled stimulus manipulations we directly test this idea in the locust olfactory system. We find that inputs arriving in Kenyon cells (KCs) sum most effectively in a preferred window of the oscillation cycle. With a computational model, we show that the non-uniform structure of noise in the membrane potential helps mediate this process. Further experiments performed in vivo demonstrate that integration windows can form in the absence of inhibition and at a broad range of oscillation frequencies. Our results reveal how a fundamental coincidence-detection mechanism in a neural circuit functions to decode temporally organized spiking.

Title - Study of neural regulation of innate immune responses in C. elegans against Gram-positive and Gram-negative bacteria
Speaker: Anjali Gupta, PhD student, BSSE, IISc
28th January: 09:30-09:50

The survival of an organism depends on its ability to sense potential threats and develop defense mechanisms to fight against infections. The mechanism of regulation of immunity by direct sensing of environmental cues by the nervous system is not known. Using a simple host-pathogen system, Caenorhabditis elegans-Enterococcus faecalis/ Pseudomonas aeruginosa, we want to understand how sensory perception of environmental cues by the nervous system regulates the susceptibility to an infection using genetics and modeling approaches. Genetically, to understand if the amphid sensory organ of C. elegans plays a role in sensing of E. faecalis or P. aeruginosa, we have created amphid neurons ablation lines and testing them for survival on these bacteria. Preliminary results show that different neurons respond differentially to different pathogens. We, then, want to use modeling to study neural network inferencing so as to relate network stimulus (involved in innate immune responses) to neuronal response.

Title: Distance constrained synaptic plasticity model and control of C. elegans neuronal networks
Speaker: Rahul Badhwar, PhD student, IITJ
28th January: 09:50-10:10

Brain research has been driven by inquiry for principles of brain structure organization and its control mechanisms [1]. Brain is a complex system comprising of large number

neurons that interact with each other giving rise to its functions. Hence, going beyond reductionist approaches, holistic study of structure and function of brain as a networked system is expected to yield insights into its architecture, evolution and control [2], [3]. With this view, we asked questions addressing brain structure organization and its control. Neuronal wiring diagram of C. elegans, the only complete connectome available till date, presents an incredible opportunity to learn basic governing principles that drive structure and function of its neuronal architecture. Rooted in the notion of network controllability and driver nodes, we probed the nature of control in CeNN [4]. We identified 'driver neurons' in this network and studied their 'phenoframe' and 'genoframe' that encode for phenotypic and genotypic features, respectively. The driver neurons are primarily motor neurons located in the ventral nerve cord and contribute to biological reproduction of the animal. Beyond identification and characterization of driver neurons of CeNN, we created network models of CeNN to scrutinize role of features that confer controllability, small world nature and prevalence of feedforward motifs [5]. Using empirically observed distance constraint in the neuronal network as a guiding principle, we created a 'distance constrained synaptic plasticity model' that simultaneously explained all of these features. These studies highlight the importance of systems-level models of brain networks and provide insights into their structure, function and control.

References [1] E. R. Kandel, J. H. Schwartz, and T. M. Jessel, Principles of neural science, 4th ed. McGrawHill, 2000. [2] O. Sporns, Networks of the brain. MIT Press, 2011. [3] Y.-Y. Liu, J.-J. Slotine, and A.-L. Barabási, "Controllability of complex networks.," Nature, vol. 473, no. 7346, pp. 167–73, May 2011. [4] R. Badhwar and G. Bagler, "Control of neuronal network in Caenorhabditis elegans," PLoS One, vol. 10, no. 9, p. e0139204, 2015. [5] R. Badhwar and G. Bagler, "A distance constrained synaptic plasticity model of C. elegans neuronal network," arXiv1603.03867 (In Press Phys. A), 2017.

Title: To hold on to or to let go: Decoding the Bladder using Biophysical Computation

Speaker: Nilapratim Sengupta, Research Scholar, IITB

28th January: 10:10-10:30

Our current focus of studies at the Computational Neurophysiology Lab, Department of Biosciences and Bioengineering, IIT Bombay is towards investigating the cellular level biophysical mechanisms in the bladder that give rise to different facets of bladder

function such as bladder contractility, sensory transduction and control of bladder function via known neural pathways. Deviations from bladder physiology result in a range of disorders, including urinary incontinence. Urinary incontinence or loss of bladder control is a pathophysiological condition that has its basis in the altered cellular physiology of the components that comprise the bladder wall resulting in symptoms which include bladder overactivity as well as increased neural input to the central nervous system via the afferent pathways. The underlying causes of urinary incontinence are varied and severely impact the quality of life both physiologically as well as psychologically. The aim of our research is to study bladder biophysics in order to delineate bladder function at cellular and tissue level by developing biophysically detailed computational models that mimic key aspects of bladder activity. The larger aim of our work is to then use our knowledge towards unravelling possible mechanisms that underlie bladder pathology.

Title: Stores, Waves and Glue

Speaker: Rishikesh Narayanan, Molecular Biophysics Unit, Indian Institute of Science, Bangalore.

28th January: 10:50-11:20

Calcium stores in the endoplasmic reticulum (ER) plays crucial roles in various aspects of neuronal physiology and pathophysiology. Release of calcium from these stores through inositol trisphosphate (InsP3) and ryanodine receptors expressed on the ER membrane have been shown to play critical roles in mediating short- and long-term neuronal plasticity and in sustaining actively propagated waves of calcium within or across cells. The first part of this talk will focus on a computational study that identified a novel form of intraneuronal interaction between ion channels on the dendritic plasma membrane and InsP3 receptors on the ER membrane (Ashhad and Narayanan, 2013). In this study, quantitative analyses involving experimentally constrained computational models revealed a bell-shaped dependence of calcium released through InsP3 receptors (during the propagation of a calcium wave) on the density of a specific potassium channel. The theme of the talk will shift to interactions across cell-types for the second part, with a focus on neuron-glia communications. Glial cells, as could be inferred from their etymology involving glue, were long considered as passive accessories in the nervous system to provide support and protection for neurons. This rather limited view

has been challenged by several lines of experimental evidence that have uncovered the active participation of glial cells in brain physiology, plasticity and pathology. An important breakthrough was the discovery of gliotransmission, the ability of glia to release transmitter molecules that could bind onto neuronal receptors to regulate neurophysiology. Gliotransmission is partly mediated by calcium released through InsP3Rs residing on glial ER stores, resulting in calcium waves that can propagate across the glial syncytium through gap junctions. A combination of electrophysiological and computational techniques was recently employed to demonstrate a novel form of interaction between glial cells and active neuronal dendrites (Ashhad and Narayanan, 2016). Specifically, this study demonstrated that gliotransmission, acting through differentially localized slow neuronal receptors, results in strikingly large voltage deflections in neuronal dendrites, with the strength and spread of these deflections critically regulated by dendritic ion channels. Together, these two studies delineate novel regulatory roles for ER calcium stores and InsP3 receptors in neuronal physiology, plasticity and pathophysiology.

References: 1. Ashhad, S and Narayanan, R. (2013) Quantitative interactions between the A-type K+ current and inositol trisphosphate receptors regulate intraneuronal Ca2+ waves and synaptic plasticity, The Journal of Physiology (London), 591 (7): 1645–1669.

2. Ashhad, S and Narayanan, R. (2016) Active dendrites regulate the impact of gliotransmission on rat hippocampal pyramidal neurons, Proceedings of the National Academy of Sciences (USA), 113(23): E3280–E3289.

Title: Understanding cerebellum granular layer network computations through mathematical reconstructions of evoked Local Field Potentials

Speaker: Harilal Parasuram, PhD student, School of Biotechnology, Amrita University, Kerala, India.

28th January: 11:20-11:50

Understanding population activities of underlying neurons reveal emergent behavior as patterns of information flow in neural circuits. Population of neurons generate extracellular currents due to electrical activity, an electrode usually reads the activity as

a Local Field Potential (LFP) signal. Progress in studying the origin and nature of such signal is crucial for understanding neuronal mechanisms and activity. The somatosensory activity in the cerebellar granular layer corresponds to sensory and tactile input has been observed by recording LFP from the Crus-IIa regions of cerebellum in brain slices and in anesthetized animals. This work focuses on understanding cerebellar circuit function through mathematical modeling of LFP. Cerebellar granular layer LFP was reconstructed from a detailed biophysical model of Wistar rat cerebellum granular layer network. The LFP mechanism during in vitro condition was reconstructed in network model and used to generate the in vivo TC wave forms observed in the experiments. The work also included the development of LFPsim, a NEURON-based GUI tool for computing population LFP activity and single neuron extracellular potentials.

Title: Computational Model of a Pathogenic Bacteria: Many Questions, Some Answers
Speaker: Dr. Santanu Datta, Bugworks India
28th January: 12:30-13:00

Almost all bacteria are networked by over 4000 interconnected genes. Predicting its life-behaviorand its dependence on its environment and nutrient stimuli is one of the central problems of microbiology. Classically this has been done by experiments where single changes in media constituents resulted in change in growth characteristics. With the advent of genetic engineering, we were able to delete or modify a gene and observe its behavior. However these experiments are time consuming and often vary within the species as its gene network have minor differences which sometimes lead to major outcomes. With over 70% of the genes in most pathogenic bacteria annotated, the time is ripe to stitch the network in a computer model and stress test the stimulus and response characteristics. We have built a computer model of the bacteria E.coli which can be pathogenic, commensal or non- pathogenic depending on the presence or absence of a few genes.Various questions about the function of the genes such it essentiality, vulnerability, possibility of being an antibiotic target, its effect on growth rate, its role in the formation of a biofilm have been queried in this model. We will discuss the basics of model building and various questions and answers and how the predictions of the model have been verified experimentally.

Title: Gut microbiome and human health
Speaker: Sharmila S. Mande, Ph.D, Chief Scientist and Head,Bio-sciences R&D Division, TCS Innovation Labs, Tata Consultancy Services Ltd.
28th January: 14:00-14:30

Our body harbours ten times more microbes than our own cells. This microbial community (called microbiome) is therefore expected to have huge influence on our health and well being. Metagenomics, an emerging field, is rapidly becoming the method of choice for studying microbiomes present in various parts of the body. Recent studies have indicated the role of gut microbiomes in several diseases/disorders and have also suggested their role in nutrient absorption, immuno-modulation motor-response, and other key physiological processes. Gut microbial communities have also been shown to act as reservoirs of antibiotic resistance. In order to obtain biologically meaningful insights from the enormous volume of microbiome data generated from sequencing platforms, it is necessary to have appropriate analytics approaches. Efficient computational methodologies are needed for management as well as analyses of the data. Some of the exciting outcomes from analytics in a few selected gut microbiome studies will be highlighted during my talk.

Title: Mechanics of Non-woven Fibrous Matrices and Their Interactions With Cells
Speaker: Dr. Sovan Lal Das, Associate Professor, IIT Kharagpur
28th January: 14:30-15:00

Our work aims to understand the relation between the structure and mechanics of the non-woven fibrous matrices using only two structural parameters- lengths and orientations of the fibers. We have utilized probability density functions to incorporate the structural variations among fibrous matrices in the formulated constitutive model. We have studied the response of fibrous matrices at macroscopic scale, where matrices were applied with uniaxial elongations or shear (as in mechanical testing), and at microscopic scale, where the response of matrix against localized forces was studied. At the macroscopic scale, the model reveals the non-linear elastic and viscoelastic nature of fibrous matrices with static and dynamic loadings, respectively. The structure dependent model predictions at the macroscopic scale match with the experimental observations for small as well as large strains. It is also shown that the measurements

performed at the macroscopic scale are not directly applicable to the cells present on the matrix as the mechanical properties sensed by the cells are also dependent on the matrix structure.

Cellular forces, applied by the cytoskeleton and conveyed via the focal adhesions, help cells in assessing the microscopic mechanical properties of the underlying substrates. Our study demonstrates that for moderately aligned fibrous matrices, the anisotropic elasticity arising due to fiber structure might lead to cell elongation and polarization of stress-fibers. The influence of the boundary conditions applied on fibrous matrices was visible in terms of high and low microscopic stiffness near fixed and free boundaries, respectively. This suggests that fibrous matrix samples with desirable stiffness gradients can be obtained by appropriate modulation of boundary conditions.

Title: Investigating the changes in biomechanics of hepatocytes upon Hepatitis C Virus infection

Speaker: Sreenath Balakrishnan, PhD student, BSSE, IISc

28th January: 15:00-15:20

Diagnosing diseases using mechanical rather than chemical changes of tissue or cells can be faster, cheaper and will require fewer biological samples. In the past couple of decades, the importance of mechanics in biology and its correlation with diseases like cancer, malaria etc. has been established. In this work, we aim to investigate the changes in the mechanics of cells upon virus infection and we use Hepatitis C Virus and its infection in liver cells as a model system. We have characterised the changes in mechanics of the nucleus of liver cells upon HCV infection. In particular, we have studied the changes in morphology and stiffness of the nuclei. Using modelling, we propose a mechanism for these changes in morphology and stiffness. Further we look for evidence for the underlying mechanism by using biochemical assays.

Title: A Computational Model of Large-scale Nuclear Architecture

Speaker: Ankit Agrawal, PhD Student, The Institute of Mathematical Sciences, Chennai

28th January: 15:20-15:40

A recent model for nuclear architecture stresses the importance of active (energy consuming) processes in determining the large-scale organization of chromatin. For example, a territorial organization of chromosomes in interphase according to chromosome territories is a basic feature of large-scale nuclear architecture. Such architecture is also known to be non-random since gene rich regions often tend to be more centrally located than gene-poor regions, while there is also some evidence for radial positioning of chromosomes by size. The earlier model considered variations of activity arising from gene density, but that model was incapable of incorporating cell type specificity of chromosome organization. The more refined model presented here considers gene expression as a proxy for activity. Using this model, we recover the spatial separation of euchromatin and heterochromatin seen in vivo as well as show that theoretical predictions compare well to experimental results for the distribution functions of gene density and chromosome centre of mass obtained through chromosome painting. We also show that active chromosomes are rougher and less spherical, that the active and inactive X chromosomes are differentially positioned and that the contact probability for each chromosome follows a power law with a range of exponent values comparable to those seen in experiments.