

5th BSSE Annual Research Symposium

Session 1: 24th January 09 30 -12 40 hrs. Keynote Lecture and Biomechanics

09 15 – 09 30 Inauguration

09 30 – 10 30 Sanjay Biswas Memorial Lecture by **Dr. Anurag Agrawal, IGIB**

10 30 – 11 00 Towards Bio-Cyber Physical Systems by **Prof. G.K Ananthasuresh and Prof. Sandhya Visweswariah, BSSE**

11 00 – 11 15 Break

11 15 – 11 55 AFM Force spectroscopy for mechanical characterisation of biological cell and soft sample by **Prof. Sitikantha Roy, IIT Delhi**

11 55 – 12 25 A non-dimensional mechanical model of the nucleus for predicting molecular mechanisms from nuclear morphology by **Dr. Sreenath Balakrishnan, BSSE**

12 25 – 12 45 Stress Fibre Growth and Remodelling Determines Cellular Morpho-elastic Response under Uniaxial Cyclic Stretch by **Aritra Chatterjee, BSSE**

12 45 – 13 45 Lunch

Session 2: 24th January 14 00 - 17 00 hrs. Neuroscience and Control Systems; Poster Session

13 45 - 14 25 Combined faculty talk by **Prof. Aditya Murthy & Prof. Ashitava Ghosal, BSSE**

14 25 – 14 45 Visual similarity account of reading jumbled words by **Aakash Agrawal, BSSE**

14 45 – 15 25 Computational neuroscience by **Prof. Rohit Manchanda, IIT Bombay**

15 25 – 15 45 Learning forward predictive model with neural networks by **Saurabh Kothari BSSE**

15 45 - 17 00 Poster session + High Tea

Day 2

Session3: 25th January 2019 09 30 - 12 40 hrs. Tissue engineering and drug delivery

09 30 - 10 10 Non-traditional approaches in drug delivery, diagnostics and biomaterials fabrication by **Dr. Shalini Gupta, IIT Delhi**

10 10 - 10 30 Disparate effects of PEG or albumin based surface modification on uptake of nano and micro particles by **Preeti Sharma, BSSE**

10 30 - 10 50 Investigation of pore forming intermediates of Listeriolysin O toxin coupled with its effect on lipid dynamics by **Ilanila I.P, BSSE**

10 50 - 11 20 Break

11 20 - 12 00 Magnetism in biomedicine: basics and applications by **Prof. Kannan M Krishnan, University of Washington**

12 00 - 12 40 Smart Nano textiles in Healthcare by **Prof. Deepthy Menon, Amrita University**

12 40 – 14 00 Lunch

Session4: 25th January 2019 14 00 -17 30 hrs. Industry and clinician talks, Poster session

14 00 - 14 30 Silk biomaterials for Rapid Wound Healing by **Vikas Tandon, Fibroheal**

14 30 - 15 00 Revolutionizing Respiratory Medicine with Biomedical Devices by **Dr. Uma Maheshwari, St. Johns Medical College Hospital**

15 00 - 16 00 Break + Poster session

16 00 - 17 30 Panel discussion on the transition from Biotechnology to Bioengineering in India and Closing remarks

Talk Abstracts

Sanjay Biswas Memorial Lecture by Dr. Anurag Agrawal, IGIB

Title Multi, Inter, and Trans: Brothers from Different Mothers

Abstract As a physician-scientist, I am often confronted by multi-, inter- and trans-disciplinary matters. While they superficially look similar, the genetics are very different. In my talk, we will explore how the coming together of disciplines accelerates scientific discovery, and why it is important that we recognise the inherent differences in the way this can happen. Using examples from my lab, I hope to illustrate the strengths and weaknesses of these brothers from different mothers; hopefully conveying that being prepared to cross boundaries, without preparation, is half the battle. Above everything else, I hope to share the joy of messy explorations of fields, where half of what you know is false and you don't know which half.

Prof. G K Ananthasuresh and Prof. Sandhya S Visweswariah

Title Towards Bio-Cyber Physical Systems

Abstract Biological cells sense, process information, and respond in their own right. Therefore, it is an interesting prospect to interface cells with engineered sensors and actuators using control and computation. As a small step towards that, the multidisciplinary CyberGut team in IISc is working to augment animal models for the gut-epithelium with engineered in-vitro models using gut-on-a-chip and active scaffold platforms. The other objectives of the CyberGut project are (a) to analyse the large data obtained using “cell sensors” to find hidden patterns and causative relationships using machine learning and to feed the inferences back to probe stochasticity in gut-biology; and (b) to perform genome level biological network analysis to identify regulatory proteins and then manipulate cellular responses, to pave the way for understanding and controlling gut-epithelium in a diarrheal disease condition. In this talk, ongoing work on engineering and biology aspects of the project will be discussed.

Title AFM Force spectroscopy for mechanical characterization of biological cell and soft sample.

Abstract Present research work is focused on the development of contact models and experimental methods for AFM force spectroscopy technique in soft material characterization, mainly polymer gels and live biological cells. We have addressed two of the most common issues in the analysis of nano-indentation data of soft materials. Firstly, the correction to bottom substrate effect arising during thin sample studies and second, the contact model for simultaneous evaluation of nonspecific adhesion property along with elasticity. The developed contact model has applications in the characterization of soft materials showing adhesive elastic nature. The effectiveness of improvements made in the contact models is experimentally validated by testing transversely isotropic polymer gels of different stiffness and live MCF-7 adenocarcinoma cancer cells. Further, the developed correction factor for finite thickness correction is incorporated into a dynamic contact model for micro-rheological study of live cells. The model is applied to study the micro-rheology of Human Mesenchymal stem cells and HCT-116 Colorectal cancer cells in the context of EMT (Epithelial to Mesenchymal transformation) in cancer progression. The main advantage of the proposed model is its closed-form expression, making it easy to use for AFM force spectroscopic data analysis. If time permits, we will discuss some other ongoing biomechanical problems ongoing in our lab.

Title A non-dimensional mechanical model of the nucleus for predicting molecular mechanisms from nuclear morphology

Abstract Morphology of the nucleus is an important regulator of gene-expression and therefore of cell function. Aberrations in nuclear morphology are an indicator of cellular dysfunction and have been used to diagnose various diseases such as cancer and laminopathies. From a biochemical perspective, changes in nuclear morphology are due to differences in the expression of proteins such as lamins and cytoskeleton. To obtain the molecular mechanism, these proteins are systematically probed by various experimental techniques. On the other hand, from a mechanical perspective, the shape of the nucleus is a result of the forces acting on the nuclear envelope and its mechanical properties. Hence, information regarding these mechanical factors is contained in the morphology of the nucleus. Here, we present a mechanical model to decompose the contributions of the forces and mechanical properties from the nuclear morphology and thereby indicate the molecular mechanism responsible for changes in the shape of the nucleus.

We assumed a simplified, axisymmetric model wherein two forces act on the nuclear envelope; (i) an inflating pressure and (ii) a compressive force from cortical actin akin to a flat plate pushing down on the nucleus. The governing equations of mechanical equilibrium revealed that the ensuing nuclear morphology depended only on two non-dimensional parameters; (i) the ratio between the inflating pressure and the elastic modulus of the nuclear envelope and (ii) the ratio between the compressive force and the inflating pressure. By simulating nuclear morphologies for a range of values of these non-dimensional parameters we predicted a relationship among nuclear shape parameters such as projected area, surface area and volume. Individual nuclei of Huh7 and HeLa cells were in close agreement (< 5% error) with this prediction. The aforementioned non-dimensional parameters corresponding to individual nuclei could be obtained by fitting our model to its nuclear shape parameters. By comparing these non-dimensional parameters between control and treated cells, we can discern the molecular mechanism responsible for changes in nuclear morphology.

In summary, we propose a novel method for obtaining the molecular mechanism responsible for changes in nuclear mechanics by merely analysing the nuclear morphology using a quantitative model. The procedure is as follows:

- a. Obtain the three-dimensional morphology of the nuclei of control and treated cells using confocal microscopy.
- b. Calculate the projected area, surface area and volume of each nuclei.
- c. Estimate the non-dimensional parameters from the nuclear shape parameters using our model.
- d. Analyse the differences in non-dimensional parameters between control and treated cells to obtain the molecular mechanism.

Title Stress Fibre Growth and Remodelling Determines Cellular Morpho-elastic Response under Uniaxial Cyclic Stretch

Abstract Mechanical forces are important determinants in development, from molecular assembly of the cell organelles to the constitution of an entire organ. The pioneering works of D'Arcy Thompson "On Growth and Form" was essential in establishing the importance of mechanics in biological systems. Adherent fibroblasts in tissues that undergo cyclic stretch, such as arteries and lung, are integral in determining the functional tissue response. Application of cyclic uniaxial stretch leads to reorientation of adherent cells on substrates from random to a well-defined and uniform angle perpendicular to the direction of stretch. The mechanistic reasons underlying active cytoskeletal remodelling, the individual and combined roles of the cytoskeletal proteins under dynamically stretched conditions, and their links to contractility however remain underexplored. In this study, we provide a novel growth and remodelling framework to study the effect of uniaxial cyclic stretch in fibroblast using both experimental and theoretical techniques. We show that uniaxial cyclic stretch induces lengthening and realignment in stress fibres which influences the cellular response. Realignment of stress fibres along a uniform perpendicular to the direction of applied stretch for prolonged duration also increases the effective elastic cell modulus. We also report significant increase in the overall actin fluorescent intensity and cortical actin thickness in fibroblasts as well as cell elongation along the reorientation direction under uniaxial cyclic stretch. Using cytoskeletal disruptor treatments, we further show that microtubules do not influence in cell stiffness or reorientation changes under cyclic stretch but are important in nuclear reorientation. Finally, based on our experimental observations we propose a biologically motivated theoretical model to incorporate the effects of amplitude and time duration of uniaxial cyclic stretch on a single cell. Finally, the model incorporates novel evolution equations for stress fibre growth and remodelling which, offers predictive capability in generating cellular morpho-metrics sensitive to a wide range of changes in experimental inputs.

Akash Agrawal, 5th Year Student, BSSE

Title Visual similarity account of reading jumbled words

Abstract Reading speed for jumbled words is not severely impeded if we preserve its end letters. This effect is popularly known as “Cambridge University Effect”. Various letter coding schemes fail to explain this effect. Here, we propose that the visual properties of our brain are sufficient to account for this effect. We begin by alleviating the problem of reading jumbled words into a visual search task. Next, we develop three models of varying complexity to understand how letters combine to form strings and tested them on two lexical tasks. 1) Scrambled word task. 2) Lexical decision task. Interestingly, the model can predict the time taken to solve scrambled words, and lexical decision time for non-words. It can also predict difficulty in reading jumbled WRODS and 7EX7 W17H NUM83R5. Thereby, we hope to have cracked the orthographic code.

Saurabh Kothari, 3rd Year Student, BSSE

Title Learning forward predictive model with neural networks

Abstract In our day to day life, we make variety of movements like reaching for a glass of water, handling a tool, holding a cup etc. To plan and control such movements, the brain is hypothesized to learn a forward predictive model that predicts how the body will react to the motor commands from the brain. In other words, the brain must learn to represent the nonlinear dynamics of body motion. To understand how the brain might do this, we are developing a biologically plausible neural network model to learn the forward predictive model for a virtual arm. The neural network model is implemented in Nengo simulator and the virtual arm is implemented in OpenSim.

Dr. Shalini Gupta, Department of Chemical Engineering, IIT Delhi

Title Non-traditional approaches in drug delivery, diagnostics and biomaterials fabrication

Abstract A major thrust in my group is to develop technologies for infectious disease management to curb the emerging threat of antimicrobial resistance, one of the biggest health challenges of our century. In this regard, I will demonstrate three research approaches taken by my group, each pertaining to the broad area of drug delivery, diagnostics and biomaterials fabrication. In the first, I will demonstrate a novel drug delivery platform to co-target cancer and intracellular bacterial infections in cancer. We all may not know that bacteria can behave as both cancer-causative and cancer-prevailing agents. Thus, targeting bacteria that otherwise escape antimicrobial action by host cell-localization is important to curb secondary infections that may lead to life-threatening conditions like sepsis. Another way to manage sepsis is through rapid and early bedside diagnosis. In the second example, I will showcase a simple and disposable point-of-care (POC) device called Septiflo™ that can not only identify but also stratify bacterial infections based on their Gram status under 10 min from a drop of human blood. While conventional diagnostic systems rely on amplifying minute quantities of DNA or measuring the late host response, our system works by detecting naturally amplified pathogen-associated molecular patterns that are unique footprints of infection. The preliminary clinical results look promising as they show better performance than existing methods for bacteremia diagnosis. Finally, I will illustrate how free-floating scaffolds of living cells can be simply and conveniently assembled using external AC electric fields. While the 1D and 2D cellular architectures serve as biomaterial constructs, the 0D bacterial microarrays are ideal for label-free bio sensing and single cell analysis.

Preeti Sharma, 3rd Year Student, BSSE

Title Disparate effects of PEG or albumin based surface modification on uptake of nano- and micro-particles

Abstract Surface modification of particulate systems is a commonly employed strategy to alter their interaction with proteins and cells. Past studies on nano-particles have shown that surface functionalization with polyethylene glycol (PEG) or proteins such as albumin increases circulation times by reducing their phagocytic uptake. However, studies on surface functionalized micro-particles have reported contradictory results. Here, we investigate the effects of surface functionalization using polystyrene particles with 4 different diameters ranging from 30 nm-2.6 μ m and coating them either with albumin or PEG. Our results show that with increasing particle size, surface functionalization has less to no effect on altering phagocytic uptake. The data also suggests that these differences are observed even with a dense arrangement of molecules on the surface (dense brush conformation for PEG conjugation), appear to be independent of the serum proteins adsorbing on particles surfaces and is independent of the endocytic uptake pathway. These results provide insight into the differences in the ability of surface modified nano- and micro-particles to avoid phagocytic uptake.

Title Investigation of pore forming intermediates of Listeriolysin O coupled with its effect on lipid dynamics

Abstract Listeriolysin O (LLO) comes under the class of cholesterol dependent cytolysin (CDC) pore-forming protein, that is secreted by a gram-positive bacterium *Listeria monocytogenes*. It causes listeriosis, a fatal disease to immune-compromised individuals as well as infants. LLO assists the bacteria, through a pH-dependent mechanism, to escape from the endocytic vesicle that is highly acidic in nature (pH 5.5). Pore formation has been studied and found to be initiated by the binding of LLO to cholesterol, followed by oligomerization of the monomers and insertion of transmembrane segments inside the bilayer to form a pore. Studies suggest that LLO transitions through an inactive intermediate state, called a pre-pore, in the pore formation process. Although LLO has been widely studied, there is very little information in the literature that connects the manner in which membrane lipid dynamics are modulated during pore formation. To address some these outstanding issues pertaining to LLO interaction and assembly on phospholipid membrane, we used fluorescence correlation spectroscopy (FCS) and FRET on artificial membrane systems.

Giant unilamellar vesicles (GUVs) composed of DOPC:DPPC:Chl::2:2:1, were used as model systems to study LLO interactions with membranes. LLO induced dye leakage of GUVs, revealed two distinct population of vesicles: leaked and unleaked. Interestingly, LLO was found to preferentially bind to the Ld region of GUVs on both leaked and unleaked vesicles. FRET was monitored between Alexa488-tagged-LLO and DiI-labelled-lipid. We observed significant FRET efficiency on leaked vesicles whereas it was rarely observed in unleaked vesicles supporting the connection between the pore states and leakage. Interestingly, lipid diffusivities as measured from FCS, also showed corresponding difference between leaked and unleaked vesicles. Leaked vesicles demonstrated enhanced lipid diffusivity in comparison to the unleaked vesicles. These results are attributed to the different structural changes that happen during the pore formation. They also shed light on the correlation between lipid dynamics and oligomeric intermediates, suggesting that lipid dynamics can potentially be used as a marker to distinguish between oligomeric states.

Prof. Kannan M Krishnan, University of Washington, Seattle.

Title Magnetism in biomedicine: basics and applications

Abstract Recent developments in synthesis and applications of magnetite nanoparticles, with negligible toxicity and favourable bio distribution, allows for reproducible control of their complex magnetic relaxation behaviour, even in “extreme” biological environments. This has enabled us to address two of the principal challenges in biomedical nanoscience and personalized medicine, i.e. detecting disease at the earliest possible time prior to its ability to cause damage (imaging and diagnostics) and delivering treatment at the right place, at the right time while minimizing exposure (targeted therapy with a triggered release). Central to this work is the size-dependent magnetic properties of nanoparticles and specifically tailoring their Néel and Brownian relaxation dynamics *in vivo* to any specific applied frequency. Further, such work requires coordinated efforts in synthesis of highly-monodisperse and phase-pure magnetite cores, biochemical surface functionalization, bio distribution and pharmacokinetic studies, advanced characterization, and modelling of magnetization response. Currently, our work is focused on Magnetic Particle Imaging (MPI), and to a lesser extent on diagnostic relaxometry and hyperthermia as a potential adjuvant therapy treatment of cancer.

Magnetic Particle Imaging (MPI) is an emerging, tracer-based, whole-body medical imaging technology with high image contrast (no tissue background) and nano-gram sensitivity to an optimized tracer consisting of an iron-oxide nanoparticle core and a bio functionalized shell. MPI is linearly quantitative with tracer concentration, and has zero tissue depth attenuation; it is also safe, uses no ionizing radiation and clinically approved tracers. MPI is the first biomedical imaging technique that truly depends on nanoscale materials properties; in particular, their response to alternating magnetic fields in a true biological environment needs to be optimized.

In this talk, I will introduce the underlying physics of MPI, the alternative approaches to image reconstruction, and describe recent results in the development of our highly optimized and functionalized nanoparticle tracers for MPI. I will then present state-of-the-art imaging results of preclinical *in vivo* MPI experiments of cardiovascular (blood-pool) imaging, stroke, GI bleeding, and cancer using rodent models. I will also discuss a related diagnostic method using magnetic relaxation and illustrate its use for detecting specific protease cancer markers in solution. Overall, I will demonstrate a multidisciplinary approach that is essential to move biomedical nano-magnetics into the next phase of innovative translational research and commercialization, emphasizing the development of quantitative *in vivo* imaging, and image guided therapy including validation of delivery and therapy response.

Prof. Deepthy Menon, Amrita University

Title Smart Nanotextiles in Healthcare

Abstract The development of smart nanotextiles has the potential to revolutionize various realms encompassing healthcare, sports, military applications and fashion. This is achievable either through the integration of novel nanomaterials, fibers, coatings, etc. onto conventional textiles, or by the use of nanofabrication techniques that provide the textile with nanoscale dimensions. Nanoscale engineering of this kind would bestow new functionalities to the textiles including self-cleaning, sensing, drug delivery, tissue regeneration, etc. Our group has recently developed smart nanotextiles having nanofibrous geometry from biodegradable polymers by utilizing a variant of the conventional electrospinning process. Tunability in mechanical properties, drug release, etc. was readily achieved from these biodegradable nanotextiles fabricated from nano yarns, which are bundles of thousands of nanofibers themselves. This talk will address the current research in the field of smart nanotextiles, from fiber manipulation and development, to two diverse end uses in medicine, viz., drug eluting implants and vascular grafts.

Dr. Uma Maheshwari, St. John's Medical College Hospital

Title Revolutionizing the Practice of Respiratory Medicine with Biomedical devices

Abstract The physician's foray into the world of biomedical design dates to the early 19th century, when Rene Theophile Hyacinthe Laennec, invented the stethoscope. The invention of this device was a necessity, as it was used as an interface between the ear and the patient's chest to enable a 'modest' method of listening to heart and lung sounds! We have moved on from then to the present day to digital stethoscopes, life support machines, lab-on-a-chip, robotic surgeries, telemedicine and clinical decision support systems.

This talk will focus on discussing how medical devices have seamlessly integrated into clinical practice and aid in the diagnosis and treatment of respiratory diseases. Some of the desirable features of existing devices from an end user's perspective will also be highlighted.

Poster Abstracts

Jayashree V, 3rd Year Student, BSSE

Title Chitosan based dual drug delivery system for wound healing of chronic Diabetic Foot Ulcers

Abstract Diabetic Foot Ulcers(DFU)is a common complication in patients with type I diabetes. They are chronic wounds that either heal much more slowly or fail to heal. Poor healing may be a consequence of increased infiltration of phagocytic cells such as neutrophils and macrophages at the wound site, which is thought to result in chronic local inflammation. Currently, there are no good strategies to promote healing in these wounds but are managed clinically through wound debridement, pressure off loading, topical application of antibiotics and frequent dressing of wounds, to prevent them from worsening. Even with appropriate wound management, in many individuals gangrene formation occurs, ultimately leading to limb amputation.

Our hypothesis is that healing of diabetic ulcers may be promoted by reducing the local inflammation and providing the necessary factors for tissue regrowth. To test this hypothesis, we are developing a sequential drug delivery system to deliver an immunosuppressant for suppressing the inflammation followed by growth factors(GF) to assist the proliferation of endothelial cells and fibroblasts.

Specifically, a chitosan-based scaffold system loaded with immunosuppressant rapamycin and growth factors have been developed. Rapamycin dispersed homogenously throughout the scaffold whereas growth factors are first encapsulated into chitosan microspheres which is further entrapped inside the same scaffold allowing a dual release from the same scaffold. Preliminary data of dual release of rapamycin and a model protein for GF, BSA-FITC suggests a two-day fast release of 80% of encapsulated rapamycin as desired. About 50% of the protein was found to be released in 24 hours wherein, a delay of 24-36 hours was anticipated before start of protein release. Alternate strategies are being attempted to delay the release of protein after which the efficacy of the in-vitro release system will be tested in-vivo for healing of surgically induced dermal wounds in high fat diet induced obese model of rat +/- and diabetic mice model.

Title Heterogeneity in arabinose operon gene expression in bacteria

Abstract The ability to conditionally control the expression of specific genes using external inducers is useful to study the effect of gene products on cell physiology. Inducible plasmid systems are designed for a variety of applications, ranging from gene over expression for protein purification to low basal level expression for studying toxic gene products. Hence, a highly controlled system is desirable.

The arabinose inducible pBAD series of bacterial vectors offer such a tuneable and tightly regulated system for gene expression. At the population level, expression from this promoter is graded, with medium levels of expression at intermediate levels of arabinose. However, studies have shown that the arabinose expression vectors have an all-or-none response at the single cell level. Initially attributed to the heterogeneity in the expression of the transporter AraE, this phenomenon persists in non-arabinose metabolizing cells even with a constitutively expressed transporter.

High gene expression noise, which is a measure of cellular heterogeneity, is particularly pronounced in promoters under low inducer levels. In addition to intrinsically present stochasticity, this noise might further be amplified by the architecture of the gene network motifs. Previously, we reported a bimodal distribution of fast degrading version of (fd)GFP expression cloned under the PBAD promoter at intermediate inducer levels [3]. Interestingly, bulk level mRNA quantification showed similar transcript levels between GFP-positive and GFP-negative cells, possibly indicating post transcriptional regulation of gene expression in the cells.

Combined with fdGFP expression monitoring, that captures protein dynamics more efficiently than its long lived wild-type counterpart, we employed a single molecule RNA quantification technique, smRNA-FISH, to determine whether the observed protein heterogeneity indeed stems from transcriptional heterogeneity at the single cell level. In this technique, GFP mRNA are labelled with multiple Cy5 tagged probes. Fluorescence microscopy and subsequent processing of the micrographs is done to determine the RNA count per cell. Simultaneous single cell GFP imaging is also done to capture protein level heterogeneity. Such co-analysis of transcription and translation can provide insights into the origin of heterogeneous gene expression.

Ameya Dravid, 2nd Year Student, BSSE

Title Resolvin nano-carriers for treatment of osteoarthritis

Abstract Osteoarthritis (OA) is the most common form of arthritis. This disease is characterized by degradation of cartilage and subchondral bone, loss of function of the affected joint and subsequent pain. Initiation of cartilage damage can be due a variety of factors like obesity, age and joint trauma. This damage releases damage associated molecular patterns (DAMPs) in the synovial fluid which are recognized by cells in the joint like synovial macrophages. These cells subsequently release pro-inflammatory cytokines like IL-1 β , TNF- α and IL-6 in the surrounding synovial fluid, which then causes more damage to the proximal cells and cartilage. This initiates a vicious cycle of damage in the affected joint.

Traditionally prescribed therapies, like corticosteroids, have resulted in suboptimal outcomes due to low retention in body and poor targeting to the joints. Lipid mediators derived from omega-3 fatty acids (such as Resolvin D1) have been shown to effectively resolve inflammation and pain and promote tissue healing in range of inflammatory conditions such as periodontal diseases and airway inflammation. These are powerful drugs that act at a cellular level and actively signal the resolution of inflammation. We plan to study the effect of Resolvin D1 (RvD1) on surgically induced OA knee joint. We expect that RvD1-loaded Nano carriers will increase the retention of RvD1 inside knee joint and ameliorate the inflammation-induced damage.

Alakesh Singh, 2nd Year Student, BSSE

Title Measuring Neutrophil residence time at implant sites In vivo using mice models

Abstract Immune response against biomaterial implants is a major challenge for biomedical industry. Innate immune cells respond to the implant, by creating an inflammatory microenvironment, which eventually leads to implant fibrosis. Among the many different cells that take part in this immune action, recently neutrophils have been shown to play an important role in establishing the inflammation. However, many questions regarding the role of neutrophils remains unanswered. One of the primary questions is the length of neutrophil survival at implant sites. We are interested to know for how long neutrophils are recruited at the implant site. To answer this question, we plan to model neutrophil kinetics in tissues mathematically with the help of rate equations and validate the equation rate parameters with the help of experimental data. Our final objective is to uncover the kinetics and residence time of neutrophils in tissues for better understanding of the crosstalk that happens at the immuno-synthetic interface.

Anil Vishnu G K, 2nd Year Student, BSSE

Title Development of MEMS sensors for cancer tissue characterization

Abstract Cancer has grown to be a universal health problem. Non-Communicable Diseases (NCD) which had a global share of 70% of the total deaths in 2015 have become a major health burden. Within cancer, breast cancer has now grown to be the most common cause of female malignancy in both the developing and developed world accounting for the major cause of death of women globally. Conventional diagnosis involves taking a biopsy of suspicious region with lump, which will then be processed, sectioned (grossing) and stained. A pathologist then determines the nature of the sample by observing the morphology of the tissue. Often Immunohistochemical staining may be required to establish a diagnosis. While the conventional histopathological methods remain the gold standard, there are improvements that we could bring about with the help of technology. Some of these limitations that could be improved with technology are the difficulty in identifying the progression from premalignancy to early malignancy, false negatives necessitating a second biopsy, low sensitivity from frozen samples etc. We propose an alternate diagnostic modality by measuring the electrical, thermal and mechanical properties of cancer tissues and in future use them to help stage the biopsy sample better with an idea towards better prognosis. In this work, we propose a microengineered biosensor that can measure the electrical and thermal properties of tissue from multiple points on the tissue and use it to study how these properties change as cancer progresses.

Harsh Chajjer, 2nd Year Student, BSSE

Title Theoretical expedition into Flaviverse

Abstract Hepatitis C virus (HCV) infection is a global health problem. It is reported that about 2 million of the world population is affected annually and most of those infected develop chronic liver disorder. HCV belongs to the family of positive sense single stranded RNA (+ssRNA) viruses, Flaviviridae. Due to the nature of genome, the same substrate, +ssRNA, is required for translation, replication and virus assembly. In addition, virus induces re-organization of host membranes, to form vesicular structures where viral genome replicates. We propose a cellular model that includes these viral processes, to describe infection due to +ssRNA viruses.

A system of coupled ordinary differential equations was used to model the time evolution of various viral molecular species in the cell. Key assumption used in the model: viral genome and polymerase interact to form replication complex, but the number is limited by the host membrane that can be re-organized. This allowed us to build a more concise, mean- field model (compared to existing ones) which quantitatively captures the experimental reports. However, being a deterministic mean field model, it fails to capture infection heterogeneity arising due to low copy number of viral products (~1 to 100) inside the cell during the start of the infection. We observe that random fluctuations in this stochastic regime can significantly alter the viral output.

Using a stochastic model framework and parameters from mean field model, we aim to quantify infection properties like viral infectivity, number and diversity of viral progenies. Such analyses can provide novel insights about (i) viral fitness function(s) and evolutionary trade-offs imposed on the virus, and (ii) how virus evolves effective strategies to sustain infections.

Pallabi Mitra, 2nd Year Student, BSSE

Title Investigation of relation between PARP proteins and cardiac hypertrophy

Abstract The poly(ADP-ribose) polymerase (PARP) family of 17 proteins are important enzymes that catalyse the post-translational modifications in proteins. Their activity is dependent on oxidized nicotinamide adenine dinucleotide (NAD⁺), abnormal changes in which can affect cellular metabolism and in turn lead to heart failure. Hence it may be hypothesised that a relationship may exist between PARP family of proteins and cardiac hypertrophy. A similar relation between SIRTUINS, another family of proteins that catalyse post-translational modifications of proteins, and cardiac hypertrophy is already very well established. This work involves screening of various PARP proteins to check for any relation to hypertrophy.

Pallavi Raj Sharma, 2nd Year student, BSSE

Title Dry powder micro- and nano- carriers for treatment of TB lung infections

Abstract WHO has declared *Mycobacterium tuberculosis*, the causative organism of tuberculosis (TB) as one of the high priority pathogens owing to the high global morbidity and mortality of the disease. India has the highest TB burden worldwide along with the highest incidence of drug-resistant strains. The current treatment regime has several shortcomings – long treatment time, patient non-compliance and development of resistant strains. Hence, there is an urgent need for novel TB therapeutics. One potential therapy is the application of bacteriophages, which are viruses that infect and lyse bacteria specifically. Phages have been used as therapy for decades and have advantages over antibiotics. The challenge lies in successfully delivering them to the site of infection. This project aims to deliver dry powder formulations of phages to the TB-infected lungs and explore their therapeutic potential. Inhalation route will allow targeted delivery to the organ of interest but requires particles to be in micron range to get deposited in the deep lung. To address this, polymeric micro and nano-carriers will be used for optimum deposition and other particle engineering approaches will be made to enhance targeting to the TB-infected macrophages.

Title Cellular senescence in 3D

Abstract Cellular senescence is essentially described as a process in which cells cease dividing and undergo distinctive phenotypic alterations. To study the biological mechanisms of aging, it is essential to mimic the conditions in human body-which is the 3D environment. Herein, we wish to create a 3D model for studying cellular senescence in a more *in-vivo* like conditions. For the abovementioned work, porous scaffolds made with biocompatible polymers are being fabricated. The study involves assessing the survivability and sensitivity of senescent cells, to observe the changes in extent of DNA damage between 2D and 3D, to check the effects of various senolytic drugs on the model.

Priyanka Jayal, Department of Biochemistry, IISc

Title Towards the establishment of ectopic human liver tissue in immunocompromised mice as a model for Hepatitis C virus studies

Abstract Infection with Hepatitis C virus (HCV) is associated with the inflammation of the liver leading to cirrhosis and hepato-carcinoma. Presently there is small animal model deficit. Thus, through the approach of hepatic tissue engineering, establishment of human ectopic liver tissue in immunocompromised mice as a model for HCV infection was planned. For the development of a 3D HCV model system, a copolymer cryogel of PEG-gelatin and alginate (PAG) was synthesized and 3D hepatic culture was established. Significant increment in cell number, human serum albumin secretion and urea biosynthesis along with prolonged viability was observed for 3D culture over monolayer culture. Hepatic cell lines undergo dedifferentiation, but when grown in 3D format significant upregulation in the transcript levels of Phase I and Phase II enzymes and hepato-specific transcription factors was observed. Scanning electron microscopy and immunofluorescence studies showed formation of hepato-spheres and the expression of HSA, EpCAM and HCV (co) receptors namely CD81 and claudin-1. Binding and uptake of HCV-like particle established the permissiveness of 3D cultures to HCV. Quantitation of negative strand of RNA genome of the virus through qRT-PCR from the JFH1 (HCV strain, 2a genotype) infected 3D cultured hepatocytes, along with detection of HCV envelope proteins established it as an infection and propagation model for HCV. Detection of HSA in serum samples of mice and immunohistochemistry of excised implants asserted *in vivo* proliferation of implanted hepatocytes and integration with host vasculature. Thus, we established a 3D hepatic culture, as a model for studying HCV and screening anti-HCV drug candidates.

Balasubramani, Jawaharlal Nehru University (JNU), New Delhi

Title Drug repurposing approach to target DNA gyrase from *Mycobacterium tuberculosis*

Abstract Owing to the rise in drug resistance in tuberculosis combined with the global spread of its causative pathogen, *Mycobacterium tuberculosis* (Mtb), innovative antimycobacterial agents are urgently needed. To address this problem, we have employed drug repurposing approach to discover novel FDA-approved drugs to inhibit Mtb growth. Here, we have used essential Mtb enzyme, DNA gyrase, a promising and potential target for novel anti-tuberculosis therapeutics. High-throughput screening of compounds (using FDA-compounds library) was done against the active site of Mtb DNA gyrase, the region of ATP binding (N-terminal domain) pocket on gyrase B subunit. Here, we identified total of four compounds (Drug97, Drug45, Drug77 and Drug38) tightly binds to ATPase binding pocket of N-terminal domain of gyrase B (MtbGyrB47). We investigated both inhibition of Mtb DNA gyrase and the inhibitory activity against in vitro growth of Mtb and *M. smegmatis* (Msm) by FDA-drugs. Among which, Drug97, an anthracycline antibiotic (used as an anticancer drug), was found to be a potent inhibitor of Mtb DNA gyrase. Low- μ M inhibition of Mtb DNA gyrase was correlated with their low- μ M minimum inhibitory concentrations for all screened FDA-drugs. Drug97 exhibited IC₅₀ value of $0.6 \pm 0.14 \mu$ M against MtbGyrB47, kD values of $0.06 \pm 0.21 \mu$ M and MIC₉₀ values of 0.12μ g/ml. Our results strongly suggest that the screened compounds (anthracyclines) target mycobacterial DNA gyrase, inhibits gyrase catalytic cycle and retard Mtb growth. Hence, anthracyclines inhibitors of Gyrase B exhibit many of the characteristics required for their consideration as a potential front-line antimycobacterial therapeutic.

Manisha Behera, IISc (UG student), C/o- Kaushik Chatterjee:

Abstract Developing biodegradable polymeric scaffolds with surface modifications has gained significant interest towards biomedical applications. We employed the use of cerium coated PCL-gelatin nanofibers to culture primary cardiomyocytes to study the scavenging of cardiac ROS by cerium. Such a system will provide a platform to culture cardiomyocytes free of oxidative stress. These cells can then be used for implantation in damaged heart and provide better regeneration capability as compared to cells propagated on surfaces without cerium nanoparticles.

Prof. K L Baishnab, NIT Silchar

Abstract A Low power Neural amplifier for Brain Machine interface to input signals in the range of 100 micro volt to 400 micro volt