<table>
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<tr>
<th>Sr. No.</th>
<th>Name of Guide/ Co-guide</th>
<th>Title/s of research project</th>
<th>Special academic prerequisites</th>
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<tr>
<td>BT 1</td>
<td>Anirban Banerjee</td>
<td>Exploring role of autophagy in clonal evolution of Streptococcus pneumoniae</td>
<td>None</td>
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<td>BT 2</td>
<td>Anirban Banerjee</td>
<td>Evaluation of signaling mechanisms relating damage in the pathogen containing vacuole and bacterial killing</td>
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<tr>
<td>BT 3</td>
<td>Ambarish Kunwar</td>
<td>Computational study of interactions of various potential anti-cancer drugs with cancer drug-resistant tubulin isotypes</td>
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<tr>
<td>BT 4</td>
<td>Ambarish Kunwar</td>
<td>Computational Modelling of Changes in Cargo Transport by Molecular Motors with Temperature</td>
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<tr>
<td>BT 5</td>
<td>Ambarish Kunwar</td>
<td>Understanding isotype specific interaction of motor proteins with microtubules</td>
<td>None</td>
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<tr>
<td>BT 6</td>
<td>Ashutosh Kumar</td>
<td>Probing structure and recognition dynamics of proteins from SCF complex ubiquitin ligase</td>
<td>M.Sc. and M. Tech. in Biochemistry, Biotechnology, Chemistry and candidate should have Physics and Mathematics at undergraduate level.</td>
</tr>
<tr>
<td>BT 7</td>
<td>Debjani Paul</td>
<td>Growth and Competition in spatially extended bacterial colonies: Role of temperature</td>
<td>Physics (M. Sc.), Biophysics (M. Sc.), Chemical Engineering (B. Tech./M. Tech.), Biotechnology (B. Tech./M. Tech.) preferred. Other physical sciences and engineering disciplines may be considered.</td>
</tr>
<tr>
<td>BT 8</td>
<td>Debjani Paul</td>
<td>How does bacteria behave under microfluidic confinement?</td>
<td>Biotechnology (B. Tech./M. Tech.), Chemical Engineering (B. Tech./M. Tech.), Biophysics (M. Sc.), Physics (M. Sc.) preferred. Masters in any other biology or physical sciences discipline may also be considered.</td>
</tr>
<tr>
<td>BT 9</td>
<td>Debjani Paul</td>
<td>Measurement of physical properties of blood cells using microfluidics</td>
<td>Chemical Engineering (B. Tech./M. Tech.), Mechanical Engineering (B. Tech./M. Tech.), or Physics (M. Sc.) preferred. Masters in any other physical sciences/engineering discipline may also be considered.</td>
</tr>
<tr>
<td>BT 10</td>
<td>Kiran Kondabagil</td>
<td>Evolution and Mechanism of bacteriophage genome packaging systems</td>
<td>BTech/MSc in Biochemistry/microbiology/biotechnology or related areas</td>
</tr>
<tr>
<td>BT 11</td>
<td>Kiran Kondabagil</td>
<td>Comparative genomics of intracellular pathogens</td>
<td>BE/ME/BTech in any field; MSc/MTech/BTech in Bioinformatics/computational</td>
</tr>
<tr>
<td>BT 12</td>
<td>Samir K Maji</td>
<td>Development of amyloid based hydrogel for neuronal tissue engineering application</td>
<td>None</td>
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<tr>
<td>BT 13</td>
<td>Samir K Maji</td>
<td>Understanding familial forms of Parkinson’s diseases pathogenesis based on α-Synuclein familial mutations</td>
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<td>BT 14</td>
<td>Samir K Maji</td>
<td>Understanding aggregation and amyloid formation by human growth hormone (GH) and prolactin (PRL) associated with their secretory granules storage and release</td>
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<td>BT 15</td>
<td>Dulal Panda Co-guide - Anirban Banerjee</td>
<td>Understanding the cell division machinery of Streptococcus pneumoniae</td>
<td>None</td>
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<td>BT 16</td>
<td>Prasenjit Bhaumik</td>
<td>Understanding the structural basis of pore formation by pore forming toxins</td>
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<tr>
<td>BT 17</td>
<td>Prasenjit Bhaumik</td>
<td>Structure based development of potent antimalarial compounds targeting plasmapamins from P. falciparum</td>
<td>None</td>
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<tr>
<td>BT 18</td>
<td>S. Patankar Co-Guides- Pradip Rathod (Univ of Washington, Seattle and Manoj Duraisingh (Harvard School of Public Health, Boston)</td>
<td>Identification and characterization of candidate P. vivax proteins involved in invasion pathways</td>
<td>None</td>
</tr>
<tr>
<td>BT 19</td>
<td>S Sen</td>
<td>Computational modeling of cancer invasion and tumor heterogeneity</td>
<td>None</td>
</tr>
<tr>
<td>BT 20</td>
<td>Ranjith P.</td>
<td>Physics of chromatin organization in a cell nucleus</td>
<td>Should have degrees in M Sc Physics or B Tech or BE in engineering subjects like Computer Science, ECE, Mechanical, Aero etc.</td>
</tr>
<tr>
<td>BT 21</td>
<td>Rahul Purwar</td>
<td>Understanding the proteomics of cancer patients to improve CAR-T cell therapy</td>
<td>None</td>
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<tr>
<td>BT 22</td>
<td>Rahul Purwar</td>
<td>CAR-T cell therapy: targeting CD19 for B-ALL patients</td>
<td>None</td>
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<tr>
<td>BT 23</td>
<td>Rahul Purwar</td>
<td>Examining efficacy of humanized anti-CD19 CAR T cells</td>
<td>None</td>
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<tr>
<td>BT 24</td>
<td>P Phale</td>
<td>Studies on molecular mechanisms involved in the preferential utilization of aromatic compounds by Pseudomonas putida CSV86</td>
<td>None</td>
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<tr>
<td>BT 25</td>
<td>P Phale</td>
<td>Structure-Function studies on Carbaryl hydrolase</td>
<td>None</td>
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<tr>
<td>BT 26</td>
<td>Prakriti Tayalia</td>
<td>Scaffold-based cellular reprogramming</td>
<td>None</td>
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<tr>
<td>BT 27</td>
<td>P.J. Bhat Co-Guide: Supreet Saini. Dept. of Chemical Engineering</td>
<td>Identification of gene(s) required for speciation in yeast Saccharomyces cerevisiae</td>
<td>Student with Only B.Tech degree in any branch of science and engineering</td>
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### BME

<p>| BME 1 | Ambarish Kunwar | Comparative study of appliances used for orthodontic tooth movement using finite element modeling (FEM) | Prior experience of FEM preferred |
| BME 2 | Rohit Srivastava | Gold Based Nanostructures in Cancer Photothermal Therapy | Only INSPIRE/ FA category |
| BME 3 | S Sen | Tissue Adhesives for wound healing | None |
| BME 4 | Hari Varma | Developing a system for laser speckle based tomographic imaging of blood flow | (a) Master’s degree in physics/Biomedical/Photonics OR (b) Bachelor’s degree in Engineering with specialization: |</p>
<table>
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<th>Qualification</th>
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</table>
| BME 5   | Hari Varma   | Developing computational methods for laser speckle based tomographic imaging of blood flow.  
|         |              | Nature of work: computation/theory                                           | (a) Master’s degree in physics/Biomedical/Photonics/Mathematics. OR  
|         |              |                                                                               | (b) Bachelor’s degree in Engineering with specialization:  
|         |              |                                                                               | Electrical/Electronics/Instrumentation/Biomedical/Computer Science. |
| PS 1    | P Phale      | Genomic and Biochemical Characterization of Bacterial Isolates Degrading Atrazine and its Application in Herbicide Bioremediation | MSC + Net (UGC/CSIR- JRF) qualified  
|         |              | Only for Project work                                                        | |
| PS 2    | P Phale      | Bioremediation of Phthalate isomers: Studies on biochemical characterization of phthalate isomer dioxygenase and evaluation of biological parameters for effective bioremediation | MSC + Net (UGC/CSIR- JRF) qualified  
|         |              | Only for Project work                                                        | |

Prof. Rinti Banerjee  
Head
BT 1: Exploring role of autophagy in clonal evolution of Streptococcus pneumoniae
Many bacteria can infect and persist inside their hosts for long periods of time. Persisters are a subpopulation of bacterial cells that are often slow-growing or growth-arrested. The formation of persister cells establishes phenotypic heterogeneity within a bacterial population and has been hypothesized to be important for relapse of persistent bacterial infections. Our current work on pneumolysin (Ply), a cholesterol dependent cytolysin, produced by Streptococcus pneumoniae (SPN) revealed that Ply expression is stochastic in nature both in in vitro and in vivo. We hypothesize that low amount of Ply expression may lead to the persister SPN population that is responsible for persistent invasive pneumococcal disease. In this project we aim to understand the molecular basis for stochastic expression of Ply and foray into the role of autophagy in pathogen evolution.

BT 2: Evaluation of signaling mechanisms relating damage in the pathogen containing vacuole and bacterial killing.
Following endocytosis in eukaryotic cells, pathogenic bacteria due to expression of pore forming toxins or various secretion systems puncture holes in the endosomal membranes. This leads to myriad of events, ranging from recruitment of autophagy adaptors targeting endosomes towards autophagic degradation, maintenance of vacuole to propel bacterial multiplication inside endosomes, cytosolic escape and cell to cell spread of the pathogen etc. However, these different outcomes depend not only on the extent of damage on the endosomal membrane but also on initiation of specific signaling cascades. In this project, we aim to explore the different host-cell signaling mechanisms resulting in recruitment of these various machineries, such as autophagic machinery, ubiquitination machinery etc. and connect it to the extent of damage in the endosomes caused by differential expression of a bacterial pore forming toxin.

BT 3: Computational study of interactions of various potential anti-cancer drugs with cancer drug-resistant tubulin isotypes
Microtubules are essential for cell division and are important target for various anti-cancer drugs. Microtubules are polymers of tubulin monomers whose sizes are few nanometers. Disruption of microtubule dynamics induced by anticancer drugs leads to cell growth arrest and hence leading to cell death. There are many drugs which display toxicity towards multidrug resistant cells and destroys non-dividing cells. A complete understanding of interaction of such drugs with tubulin is essential to develop better analogues in future for effective cancer treatment.
The goal of proposed research is to develop a molecular level understanding of interactions of these drugs with tubulin using Molecular Docking and Molecular Dynamics (MD) Simulation while working very closely with experimentalists.

Reference:

BT 4: Computational Modelling of Changes in Cargo Transport by Molecular Motors with Temperature
ATP driven linear molecular motors are responsible for transporting the cargos as well as producing forces to maintain cellular structures and functions. The molecular motors often function as a team. Recent single molecule experiments have revealed that activities of these
motors changes with temperature. However, how changes in the activity of individual motors can affect the team work is not very well understood. The goal of this project is to understand how transport and force generation by a team of motor proteins changes due to change in temperature by developing computational models.

Reference:

**BT 5: Understanding isotype specific interaction of motor proteins with microtubules**
Collective transport and force generation by a team of motor proteins is important for many vital cellular processes including cell division. It is know that microtubules are essential for cell division and therefore they are important targets for many anti-cancer drugs. Overexpression of different tubulin isotypes are associated with drug resistance which arises from inability of various drugs to bind to tubulin. Cancer cells have abnormal mitotic behaviour. Recent experimental observations suggest that functional properties of motor proteins also change in such cancer cells where overexpression of different tubulin isotypes are observed. However, a molecular level understanding of how the interaction of different motor proteins involved in mitosis changes in presence of different isotypes is still lacking. A molecular level understanding of these interaction would help to design new therapeutic approaches targeting both motor proteins and microtubules, novel formulations to enhance the efficacy of existing anti-cancer drugs and expand their therapeutic spectrum. A combinations of computational approaches combining Molecular Modelling, Molecular docking and Molecular dynamics (MD) simulations will be used in this project to understand motor-microtubule interaction.

Reference:

**BT 6: Probing structure and recognition dynamics of proteins from SCF complex ubiquitin ligase**
Ubiquitin-dependent proteolysis machinery regulates protein abundance and in turn serves as a central regulatory function in many biological processes. The SCF (Skp1-Cullin-F-box protein) complex ubiquitinates a broad range of proteins involved in cell cycle progression, signal transduction and transcription. In SCF complex, Skp1 is an adaptor protein, which directly interacts with F-box proteins and cullin-1. This complete assembly is responsible for targeting proteins for the ubiquitin-mediated degradation. Different SCF complexes vary in their F-box proteins, which are specific for the ubiquitination of their substrate proteins. Therefore, understating of structural basis of recognition of F-box and functionality of different proteins is crucial for delineating their role in the cell cycle regulation. In this project, we will explicate structure, dynamics and protein-protein interactions of skp1, F-Box proteins using various biophysical and biochemical approaches. Such information will be crucial for designing specific drug for a particular type of cancer.

Project outcomes: Project will provide exact insight into binding surface of Skp1 to F-box protein, which is an important druggable surface for anti-cancer drugs.
BT 7: Growth and Competition in spatially extended bacterial colonies: Role of temperature

Bacterial colonies form spectacular patterns as they spread on the surface of a petridish. The exact morphology of the pattern depends on a variety of physical and biological aspects such as the softness of the agar medium, nutrient concentration, motility of the bacteria, temperature, pressure, etc. Although several studies have investigated the role of temperature on growth of well-mixed cultures of bacteria, how temperature modifies the growth and competition in spatially extended bacterial colonies is largely unexplored. The aim of the present project is to investigate, using the experimental set-up and protocol already developed in our lab, the role of temperature on spreading and competition in bacterial colonies.

BT 8: How does bacteria behave under microfluidic confinement?

Description: While the behavior of microorganisms in large-scale liquid cultures is studied extensively, it is not at all obvious how they respond and adapt to three-dimensional confinement. It turns out that they can sense and respond to confinement in rather unexpected ways. For example, a collective behavior like quorum sensing has been exhibited by a single bacterium confined within a microfluidic droplet. [1] E. coli normally executes a random walk motion in bulk liquids; but has been found to systematically swim on the right-hand side inside a micron-sized channel. [2] The goal of this interdisciplinary project is to understand how the motility, growth and gene expression of microorganisms differ within very small constrictions comparable to their behavior in large volumes. We will use both microfluidics and microbiology techniques to address this question.


BT 9: Measurement of physical properties of blood cells using microfluidics

Description: The aim of the project is to study the physical (mechanical) properties of blood cells using microfluidics. Properties like cell size, shape and deformability can be useful in diagnosis of many diseases (e.g. cancer, infections, etc.) The conventional approaches to measure mechanical properties of cells require expensive pieces of equipment, and are time intensive. This poses challenges for examining large populations of cells to either obtain statistically valid conclusions or in identification of rare sub-populations. We propose to use simple microfluidic chip designs to measure the elastic constants of cells (more specifically, blood cells). Other than elastic constants, physical properties like cell velocity, shape change, the path followed by single cells, viscosity of the cell suspension, etc. can also give some useful information about the health of cells. Once the physical properties of single cells are characterized, we can develop various applications, such as, sorting mixtures of cells into sub-populations, platelet counting, whole blood cell counting, etc.

BT 10: Evolution and Mechanism of bacteriophage genome packaging systems

Genome translocation is a complex process requiring spatial and temporal coordination of several proteins. In large double stranded DNA phages, it is carried out by extremely powerful molecular motors that utilize the energy of ATP hydrolysis to power the translocation of DNA into preformed empty capsids. These motor proteins process DNA at very high speeds of up to
2000 bp/sec (~ 600 nm/sec) completing the packaging process in a few minutes. That they do so at very high fidelity is a testament to their robustness in assembling the virus particle. This project involves two aspects; (1) understand the evolution of terminase-type packaging systems in bacteriophages by bioinformatics and (2) biochemical and biophysical studies on the components of the genome translocation machinery of bacteriophage N4.

**BT 11: Comparative genomics of intracellular pathogens**

Eukaryotes are prone to infection by a variety of intracellular pathogens that include a large number of viruses, certain bacteria and certain protozoa. Some of the major human diseases such as tuberculosis, leprosy, listeriosis, malaria, flu, toxoplasmosis, smallpox, etc., are caused by obligate intracellular parasites that reproduce inside the host cells. Clues to the evolutionary success of these diverse group of intracellular parasites lie in their genome. Availability of whole genome sequences of a large number of these pathogens provides an opportunity to understand the underlying common evolutionary themes. This computational project involves unraveling of these common themes by comparative genomic approaches.

Candidate is expected to be proficient in C++, Python, Matlab, R program etc. Biology background is not a must, but the candidate should be willing to learn biology and take basic biology courses during the first two semesters.

**BT 12: Development of amyloid based hydrogel for neuronal tissue engineering application**

Recently, we showed hydrogel based on special type of protein/peptide self-assembly called “amyloid” are suitable for stem cell differentiation to neuron like lineages. In this project, we want to develop non-toxic amyloid based hydrogel for functional neuron development in test tube as well as in animal model such as Parkinson’s disease animal model.

Project will involve designing peptides, purifying protein, biophysical, cell biological techniques, extensive use of stem cells.

**BT 13: Understanding familial forms of Parkinson’s diseases pathogenesis based on α-Synuclein familial mutations.**

α-Syn aggregation into oligomers and amyloid fibrils are associated with Parkinson’s disease (PD) pathogenesis. Although 90% of the PD diseases are sporadic (unknown causes and/or environmental factors), rest 10% of the PD cases are caused due to faulty genes-associated with aggressive form of familial PD. In this project, we will study how different familial mutants of α-Syn effect its aggregation and toxicity both in vitro and in neuron cells. We will develop structure-toxicity relationship of various α-Syn aggregates formed by wild type and mutant proteins, which will help to understand the pathogenesis of PD.

**BT 14: Understanding aggregation and amyloid formation by human growth hormone (GH) and prolactin (PRL) associated with their secretory granules storage and release**

Aggregation and amyloid formation by protein/peptides are mainly associated with human diseases. However recent studies showed that amyloids could perform native functions of the host organism. For example, it has been shown that protein/peptide hormone in pituitary stored as amyloid-like structure and subsequently release the functional hormone when needed. Therefore a tight regulation is required for amyloid formation so that they can be reversible and will not cause any toxicity in cells. However how this type of reversible aggregation occurs in cells by protein/peptides is largely unknown. Using two important human protein hormones (Prolactin and growth hormone), we would like to address how they aggregate in test tube and in
cells. Further how they release the functional hormone upon signaling also will be studied. Biophysics, structural biology, cell biology techniques will be heavily used for this study.

**BT 15: Understanding the cell division machinery of Streptococcus pneumonia**

Streptococcus pneumoniae is an important human pathogen, which causes a variety of diseases including middle ear infections, sinusitis, pneumonia and meningitis. The bacterial cell division machinery can be an important target for developing novel antibacterial agents. Therefore, understanding the cell division machinery of Streptococcus pneumoniae is an important research topic.

**BT 16: Understanding the structural basis of pore formation by pore forming toxins**

Pore forming toxins (PFTs) are well known for their roles in pathogenic attack as well as evading the host defence mechanisms. Many disease-causing microorganisms secrete these pore forming toxins that drill holes into human cell membrane to develop pathogenesis. The PFTs belonging to the membrane attack complex/perforin (MACPF) and cholesterol-dependent cytolysin (CDCs) form giant pores to induce severe damage. So far, cell lysis by pore formation is believed to be one of the major processes by which pathogens invade human cells. Hence, delineating the detailed mechanism of how MACPFs/CDCs assemble on membranes and what signal triggers the structural collapse leading to the pore formation would guide into the development of new compounds that can target these proteins to prevent pathogenic infections.

This project will involve structural studies on CDCs from pathogenic bacteria and MACPFs from parasites. The recombinant toxins will be cloned, expressed and purified. The functional characterization of the pure proteins will be performed by biochemical and biophysical studies. Crystal structures of the toxins will be determined. The dynamics of pore formation by these toxins will be monitored using Cryo-electron microscopy (Cryo-EM) and atomic force microscopy (AFM). Molecular dynamics (MD) simulations will be used to understand the conformational flexibility of these toxins. Mutagenesis and fluorescence studies will be performed to assign the roles of amino acids in pore formation. Structure based compound screening will be done for identifying inhibitors to prevent pore formation process by these toxins. The results of this project would provide the molecular insights into the mechanism of pore formation.

**BT 17: Structure based development of potent antimalarial compounds targeting plasmepsins from P. falciparum**

Malaria is endemic in over 100 countries and is responsible for infecting 300-500 million people annually and the death of 1-3 million people, mostly pregnant women and children. The causative agents responsible for human malaria are five Plasmodium species (P. vivax, P. ovale, P. malariae, P. knowlesi and the most lethal P. falciparum). Due to the complexity and rate of parasite mutation coupled with regional variations, and emergence of P. falciparum strains which are resistant to inexpensive antimalarial agents such as chloroquine and sulfadoxine/pyrimethamine, there is constant pressure to find new and lasting chemotherapeutic drug therapies. The Plasmodium aspartic proteases, known as plasmepsins (PMs), have been identified as promising targets for the development of novel antimalarial drugs.

Aspartic proteases participate in a wide variety of cellular processes in the eukaryotic organisms. The genome of the human malaria parasite P. falciparum is known to encode ten PMs (PM I, II and IV-X and histo-aspartic protease (HAP)), four of which (PM I, PM II, PM IV and HAP) share 50-79% amino acid sequence identity, reside within the food vacuole, and are directly involved in degradation of human hemoglobin.
Whereas the precise role of PMs VI-X has not been elucidated, interesting new data have been published regarding the function of PM V. That enzyme, which has very low sequence identity with other PMs, has been shown to be localized in the endoplasmic reticulum (ER) and plays a role in intra-erythrocytic biology. During the intra-erythrocytic growth, malaria parasites export hundreds of proteins to remodel their host cell. The proteins which need to be exported are synthesized in the ER and cleaved at a conserved PEXEL (Plasmodium export element) motif, which allows translocation into the host cell via an ATP-driven translocon, called the PETEX (Plasmodium translocon of exported proteins) complex. The current findings showing that PM V recognizes the PEXEL motif, cleaves at the correct site, and is essential for parasite viability, makes it a novel and important target to develop antimalarial drugs.

The objective of the proposed research project is to perform structural and functional studies on PMs to obtain cross-reactive inhibitors that could be used for therapeutic control of malaria. Molecular biological approaches will be taken to clone PMs VI-X. Expression of these recombinant proteins will be done in E.coli. Biochemical and biophysical characterizations of the pure proteins will be performed. Crystallization and structure solution of PMs as complexed with inhibitors will be performed. The high affinity inhibitors will be tested on P. falciparum culture to investigate their antimalarial activities. The results from this study would help us to design better inhibitors which can be developed to potent antimalarial drugs.

**BT 18: Identification and characterization of candidate P. vivax proteins involved in invasion pathways**

Malaria, caused by P. falciparum and P. vivax parasites, is a leading cause of morbidity and mortality globally. In a unique collaboration, researchers at the International Center for Excellence in Malaria Research (funded by the US National Institutes of Health), Goa Medical College, and IIT Bombay have identified novel parasite proteins recognized by the human immune system. The next question is to assess whether some of these proteins are involved in parasite invasion pathways and can be blocked for possible therapeutic applications. The project involves bioinformatics to shortlist relevant parasite proteins, expression of these proteins using conventional techniques and new technologies developed at PradipRathod’s lab at the University of Washington, Seattle, and high throughput screening of the reactive proteins in different types of malaria patient samples. Finally, invasion assays will be done in genetically modified human reticulocyte stem cells. These will be in collaboration with ManojDuraisingh’s lab at the Harvard School of Public Health and allow mechanistic studies of the role of the new proteins in invasion. The PhD student will work primarily at IIT Bombay with trips to Goa Medical College and be co supervised by Swati Patankar (IIT Bombay), PradipRathod (Univ of Washington, Seattle) and ManojDuraisingh (Harvard School of Public Health, Boston).

**BT 19: Computational modeling of cancer invasion and tumor heterogeneity**

Abstract: Tumors consist of multiple cell sub-populations including cancer stem cells (CSCs), transiently amplifying cells (TACs) and terminally differentiated cells (TDCs), with the CSC fraction dictating the aggressiveness of the tumor and drug sensitivity. In epithelial cancers, tumor growth is influenced greatly by properties of the extracellular matrix (ECM), with cancer progression associated with an increase in ECM density, stiffness. However, the extent to which increased ECM confinement induced by increase in ECM density influences tumor growth and post treatment relapse dynamics remains incompletely understood. The aim of this project is to develop computational models for studying the influence of physical properties of tumor microenvironment on tumor heterogeneity, and the implications of this heterogeneity on cancer invasion.
**BT 20: Physics of chromatin organization in a cell nucleus.**

Abstract: Nucleus of a cell is a puzzling self-organized system that is capable of “making decisions” based on signal that it receives. In this work we will examine this problem using ideas from physics and other branches of engineering.

**BT 21: Understanding the proteomics of cancer patients to improve CAR-T cell therapy**

CAR-T cell have shown remarkable success in the clinic for the treatment of CD19+B cell malignancies such as B-ALL. However, efficacy (anti-tumor potential) of these cells critically depend on their survival and longevity in the patient. So far there exist limited knowledge on why in certain patients CAR T cells don’t live longer and don’t show effective anti-tumor immunity. In this project student will examine the global gene expression profile and global proteome profile of the patients to identify the biomarkers which are important for the effective CAR-T cell therapy.

**BT 22: CAR-T cell therapy: targeting CD19 for B-ALL patients**

CAR-T cell therapy has demonstrated remarkable success in long-term remission of relapsed or refractory B-ALL. However, this technology has not yet been designed and developed in India. Considering socioeconomic conditions of patients in our country, CAR-T-cell therapy developed by scientists in western countries will be unaffordable to majority of them. To harness this technology and bringing it to the clinic in India at affordable-cost, there is a clear need of developing indigenous CAR-T cell technology platform. Recently, we developed the CAR-T cell platform and testing their efficacy. With this translational project, we will generate CAR-T cells from T-cells of relapse or refractory B-ALL patients and test their efficacy in killing autologous malignant-B cells in ex-vivo settings.

**BT 23: Examining efficacy of humanized anti-CD19 CAR T cells**

CAR-T cell therapy has demonstrated remarkable success in long-term remission of relapsed or refractory B-ALL. Multiple targets have been investigated for the treatment of B cell malignancies and only CD19 moved to the clinic. However, there are reports of cancer relapse after CD19+CAR-T cell therapy and these relapse tumor cells were CD19 negative. Hence we need to develop CAR-T cell therapy beyond CD19. With this project we will design, develop and test the efficacy of anti-CD37+CAR-T cells in CD37+malignancies.

**BT 24: Studies on molecular mechanisms involved in the preferential utilization of aromatic compounds by Pseudomonas putida CSV86**

Pseudomonas putida CSV86 preferentially utilizes aromatics and organic acids over glucose. The strain showed diauxic growth profile with utilization of aromatics/organic acids in the first while glucose in the second log phase. Studies on the glucose transport system showed the involvement of 43 kDa periplasmic glucose binding protein (GBP) and 40 kDa outer membrane carbohydrate selective channel (OprB). Analysis of genome sequences of various Pseudomonas species revealed that putative sequences coding for different sub-units of glucose/sugar ABC (ATP binding cassette) transporter are present in close proximity to genes coding for GBP and OprB. Metabolic studies and whole-cell glucose uptake analysis of CSV86 also showed that the glucose transport across the cell surface is mediated by the high affinity, intracellular phosphorylative pathway, not by the direct oxidative pathway. In addition, involvement of GBP and OprB in glucose transport led us to hypothesize that the glucose transport in strain CSV86 is mediated through a high affinity, periplasmic GBP dependent glucose ABC transporter. This transporter is
proposed to be a hetero-tetramer (α2bg). All these components of the glucose transport system were found to be glucose inducible and repressed by aromatics and organic acids. Besides glucose metabolism, strain showed induction of aromatic degrading enzymes even in the presence of organic acids or glucose, which may also assist strain to utilize aromatics over glucose. This also suggests the probable modifications/modulations in the regulatory features in the metabolism. The novel property of the strain can be exploited in the metabolic engineering of strain for diverse aromatic compounds.

This project aims to study the regulation of the metabolic as well as transport genes by different regulator molecules in order to understand the molecular mechanisms of aromatics and organic acid mediated repression of the glucose metabolism.

References:

BT25: Structure-Function studies on Carbaryl hydrolase

Carbaryl (1-naphthyl N-methylcarbamate), a carbamate pesticide, has been used widely in the agriculture. Carbamate pesticides (such as carbaryl, carbofuran, fenobucarb, methomyl, oxamyl, etc.) are competitive inhibitors of acetylcholinesterases. The carbaryl degradation pathway is initiated by a key enzyme carbaryl hydrolase which hydrolyses carbaryl to yield 1-naphthol and methylamine as the products. Pseudomonas sp. strain C5pp degrades carbaryl via utilizing it as a sole source of carbon and energy. The draft genome of strain C5pp revealed the presence of a new carbaryl hydrolase encoding gene, mcbA. The sequence and functional analysis suggest that carbaryl hydrolase belongs to a new family of esterase. In strain C5pp enzyme is found to be present in the periplasm. The unique feature is that, it has transmembrane domain (TMD) and signal peptide sequence at the N terminal. Carbaryl hydrolase has been expressed, purified and characterized.

The proposed project will involve the site-directed mutagenesis to identify the key amino acid residues involved in the catalysis as well as the substrate specificity of the enzyme. The recombinant and mutant proteins will be crystallized to determine the 3-D structure which will help in determining the molecular mechanism involved in the catalysis and substrate recognition. This study will help to developing variants that possess wide substrate specificity for related pesticides with better efficiency. Further detail mutation studies/analysis will help to elucidate the role and significance of TMD region and understand the compartmentalization of carbaryl degradation pathway in this strain.

References:
Trivedi VD, Jangir PK, Sharma R, Phale PS. (2016) Scientific Reports 6, 38430; doi: 10.1038/srep38430
BT 26: Scaffold-based cellular reprogramming

T-cell immunotherapy is an evolving and emerging form of cancer therapy that has recently yielded significant positive advances. Here, patient’s own immune cells are collected and modified with a T-cell receptor (TCR) or a chimeric antigen receptor (CAR) against the tumor antigen and reinfused into the patient’s body to treat cancer. However, issues related to infusion of cells such as cell death require multiple high doses of cells to be infused leading to other complications and side effects. By incorporating a scaffold-based gene delivery approach, the T cells can be modified with the requisite receptors in situ without requiring ex vivo manipulation. The main objective of this project is to recruit and reprogramme T cells in vivo using a scaffold based growth factor and gene delivery mechanism. A lentiviral gene delivery approach for in vivo cellular programming will be used to improve persistence, engraftment and effector functions of T cells, while also avoiding issues related to ex vivo cell manipulation. Three-dimensional scaffolds and hydrogels may also be used as immunological microenvironments for delivery of ex vivo programmed immune cells. This approach can be extended to recruitment and reprogramming of other progenitor and stem cells in applications such as tissue engineering and regeneration.

BT 27: Identification of gene(s) required for speciation in yeast Saccharomyces cerevisiae

Abstract: How do species originate is a fundamental problem in biology. This project involves setting up in vitro evolution experiments to isolate yeast strains under sympatric conditions that lose the ability to mate as a function of generations of growth. Once such strains are isolated, the genetic basis of the above phenomena would be elucidated using classical molecular genetic approach. This approach would also involve mathematical modeling to obtain deeper insights in to the process of speciation.

BME – BIOMEDICAL ENGINEERING

BME 1: Comparative study of appliances used for orthodontic tooth movement using finite element modeling (FEM)

Malocclusion is one of the very common medical problems in dentistry. Many types and different levels of malocclusion have been identified and over the time many devices have been developed to correct these abnormalities. These devices are called orthodontic appliances and since most of these have been developed empirically, it requires ample amount of expertise and experience to apply them for the treatment. Despite the advancement of these appliances and wide available variety, there are instances when the desired correction could not be achieved and there is always a certain amount of uncertainty involved in the treatment of malocclusion. The finite element method can provide a quantitative as well as visual description of malocclusion and its correction at different levels of treatment. Traditionally, orthodontic tooth corrections were done without such information and it involved a higher degree of unpredictability and risk. The computational modeling of stomatognathic structures using FEM can significantly improve the malocclusion treatment. The goal of this project is to do a comparative study of appliances used for orthodontic tooth movement using finite element modeling for development of better appliances in future.

Reference:
BME 2: Gold Based Nanostructures in Cancer Photothermal Therapy

For the localized treatment of a tumor in a more controlled fashion, several stimuli-responsive nanocarriers and minimally or non-invasive techniques like photothermal therapy (PTT) have emerged. NIR light-triggered thermoresponsive theranostic nanoshell consisting of both Liposome and Poly lactic-co-glycolic acid) as core and biocompatible gold as shell (Au Liposome/PLGA NS) have been synthesized and well characterized by various techniques. Surface plasmon resonant gold shell over different NPs core is assembled by ascorbic acid-driven in situ reduction. Core to shell diameter ratio is controlled to tune the peak in NIR region. This project will look at finding new gold based nano structures as photo thermal agents and looking at a comparison of such structures with the reported ones in literature in terms of photo thermal efficiency in in vitro and an in vivo model.

BME 3: Tissue Adhesives for wound healing

Aim of the project is to develop photocurable hydrogels as tissue adhesives that also exhibit antimicrobial activity and contain growth factors to stimulate wound healing. These gels would potentially minimize medical complications due to blood loss, initiate wound healing process and maintain minimal or no infection throughout the recovery.

BME 4: Developing a system for laser speckle based tomographic imaging of blood flow (Nature of work: Experiment)

To develop laser based speckle contrast imaging system to measure blood flow. The system development involves design of optical laser scanning, phantom making and detection using cameras. The detected data is post processed using “inversion algorithms” to get three-dimensional reconstruction of blood flow.

BME 5: Developing computational methods for laser speckle based tomographic imaging of blood flow. (Nature of work: computation/theory)

To develop computational algorithm based on finite element method or Monte Carlo algorithms needed for laser based speckle contrast imaging system. The algorithm will be validated against the experimental data.

PS category - Only for Project work

PS 1 Genomic and Biochemical Characterization of Bacterial Isolates Degrading Atrazine and its Application in Herbicide Bioremediation

PS 2 Bioremediation of Phthalate isomers: Studies on biochemical characterization of phthalate isomer dioxygenase and evaluation of biological parameters for effective bioremediation