Available research topics for students seeking admission to SINP Ph.D. Programme in Biophysical Sciences from January 2018

Sl.	Principal Investigator, Division	Doctoral Research Area
1	Kaushik Sengupta, Biophysics & Structural Genomics	**Understanding and engineering muscle tissues on nanopatterned scaffolds:** Muscle tissues are formed from myoblasts which undergo a series of differentiation processes to reach myotube stage. These myotubes then fuse laterally to form myofibtils and ultimately builds up muscle fibre. Based on our knowledge of laminopathic mutations which cause muscular dystrophy we have shown that lamin A plays a vital role in muscle differentiation. Therefore mutation of lamin A leads to severe forms of muscular dystrophy of which one particular kind- cardiomyopathy is one of our principal interests. Our understanding of muscle differentiation process has led to the designing of various nanoscaffolds on which we would synthesize muscle tissue starting from embryonic stem cell. The nanoscaffolds which are being generated by lithography would mimic the extracellular matrix along with collagen and fibronectin to provide adequate chemical and mechanical force to drive the process of differentiation. The ultimate goal of the project is to synthesize implantable muscle tissue at the sites of trauma.
2	Soumen Manna Biophysics & Structural Genomics	**Any one of the following topics:** **1. Metabolic reprogramming in tumor microenvironment:** Apart from cancer cells, tumor microenvironment comprises of number of other cells including immune cells like macrophages, dendritic cells, cytoxic T-cell, NK cells, etc. Immune cells are generally expected to kill 'rogue' tumor cells. However, development of malignant tumor essentially reflects the failure of immune cells to do their job. It should be noted that the nutrient availability is often low in tumor microenvironment. Thus, it is intuitive that these cells would compete with each other for nutrients to survive and do their job. Thus, the ability of these cells to amass and effectively utilize nutrients could determine their viability and function. This study seeks to elucidate how malignant cells win this contest. Comparative analysis of metabolic reprogramming in different types of cells found in the tumor microenvironment will performed in isolation and in co-cultures. This study will combine mass spectrometry-based metabolomic analysis with cellular and molecular biology techniques. Outcome of these studies could fundamentally alter the existing understanding of tumor immunology. **2. Metabolism and Non-alcoholic fatty liver disease:** Non-alcoholic fatty liver disease (NAFLD) is a silent killer with increasing abundance in India and around the world. It is asymptomatic in early stages, increases

		risk for liver cancer, may eventually lead to total liver failure and death. Development of minimally-invasive method for early diagnosis and novel therapeutic strategies are highly warranted. Obesity is a risk factor for NAFLD. However, in India, incidence of NAFLD is observed even in people with normal or sub-normal BMI. It is known that the disease is initiated by fat deposition in liver and reactive oxygen species plays an important role in its progression. But the metabolic derangements that lead to fat accumulation in liver even without any significant intake of dietary fat is not well understood. The determining factors in progression of the disease are also unknown. This study aims to address these questions by integrating mass spectrometry-based metabolomics, proteomics and gene expression analysis using cell culture and animal models. Along with elucidation of the underlying mechanism, these might lead to identification of novel therapeutic strategies. Analysis of patient samples will also be carried out to identify signatures that can be used for diagnosis, prognosis and therapeutic intervention.
3.	Debashis Mukhopadhyay Biophysics & Structural Genomics	**Targeting RTK Signalling Pathways in Type II Diabetes Mellitus:** Complimentary to neurodegeneration we propose an integrated network approach using gene sequencing, proteomics, and other high-throughput experimental technologies to investigate the extent to which a neurodegenerative disease like AD and a metabolic disorder like T2DM are linked at the molecular level. Besides the possibility that T2DM may promote neurodegeneration independent of AD, we seek to understand whether AD can cause metabolic defects in a similar manner as T2DM, specifically through molecular pathways driven through Receptor Tyrosine Kinases (RTKs) that are perturbed in the event of deposition of brain β-amyloid or AICD (APP Intracellular Domain). Both of these protein fragments are found in AD brain and are believed to contribute to neurodegeneration. The mechanisms through which T2DM may perturb similar pathways will be looked into.
4.	Sampa Biswas Crystallography & Molecular Biology	**Any one of the following two topics:** 1. **Imparting hemoglobinase activity in cysteine proteases by structure guided rational design:** When hemoglobin is released from RBCs, it is extremely toxic. Nature, however, has provided a multitude of protective mechanisms that can detoxify free Hb. During hyper-hemolytic conditions, the scavenging system is saturated and free Hb readily distributes to tissues where it might be exposed to oxidative conditions leading to pathological conditions. It is therefore necessary to explore the scavenging system. Proteolytic degradation of cell free Hb molecules is a part of this mechanism. The proteases which can efficiently degrade Hb molecules are called hemoglobinases. In addition, hemoglobin degradation process also produces

		some important bioactive peptides which act as peptide hormones, neurotransmitters, neuropeptides etc. The aim of this project is to understand the hemoglobin specificity of a hemoglobinase at a molecular level. Subsequent attempts will be made to impart hemoglobinase activity on a human protease, cathepsin-L, by structure-based protein engineering approach. The engineered enzymes will have potential for pharmaceutical applications in patho-physiological conditions related to hyper-hemolysis and to produce specific biologically active peptides from globin chains of Hb. Malarial hemoglobinases will be used as a template for this study. 2. **In silico design and generation an efficient thermostable collagenase by structure based protein engineering:** Collagen constitutes approximately 25-33% of the total protein in mammals and is the main components of the extracellular matrix (ECM). Collagens are composed of three α chains of primarily repeating Gly-Pro-X triplets, and three chains then intertwine, staggered by one residue and coiled, to form a right-handed super-helix. Triple-helical structure provides collagens with exceptional mechanical strength and broad resistance to the proteolytic degradation. The proteolytic processing of collagen (collagenolysis) is critical in ECM remodelling. Hydrolysis of interstitial intact triple-helical collagens occurs by a limited number of proteases called collagenase. Collagenases have significant implications in health, diseases and in industry. In this project we like to impart collagenolytic activity by designing substrate specificity of a protease, taking structural signatures from naturally occurring collagenolytic proteases. We shall further try to combine thermostability and collagenolytic property in a single variant so that we would obtain a thermostable collagenase suitable for industrial applications.
5.	Montu K Hazra Chemical Sciences	**1. Infrared Spectroscopy, Photochemistry and Dynamics of Several Important Molecules and Their H-bonded Complexes Related to Atmospheric Chemistry:** This project is devoted to improve our understanding the atmospheric chemistry at molecular level. In our atmosphere, the energy comes from the Sun mainly in the form of visible light and when this light reaches our Earth through atmosphere, Earth-surface becomes warm and radiate infrared radiation back into space in the form of heat. Therefore, infrared spectroscopy including both the fundamental and overtone transitions of the atmospheric constituents and their complexes in the laboratory, which are interconnected with atmospheric measurements, is highly important. **2. Spectroscopy and Photo-Physics of Molecular Complexes Mimicking Nucleic Acid-Base Pairs:** This project is devoted to learn precisely about their intrinsic hydrogen-bonding/stacking/van der Waals

		interactions and dynamics via hydrogen-bonding interfaces. In this research project, various convenient species/systems will be designed and generated in the gas phase by either supersonic jet or laser desorption environments to get good testing grounds in resolving many of the complexities found in larger complex molecular network. **3. Study of New reactions or Mechanisms of Potential Atmospheric Importance for the Earth, Mars and Outer Space:** In this project, both the energetics and kinetics of the new reactions or mechanisms will be explored as accurate as possible to find the potential impact of the reactions over existing or currently accepted reactions or mechanisms. Quantum Chemical Calculations, Statistical Thermodynamics, Conventional Transition State Theory (CTST), Canonical/Micro−canonical Variational Transition [CVT, μVT(E), E,J−μVT] State Theories, Hard-Sphere Collision Theory (HSCT) and Variable-Reaction-Coordinate-Variational Transition Sate Theory (VRC-VTST) will be used thoroughly to explore the potential impact of the reactions in the atmosphere.
6.	Susanta Lahiri Chemical Sciences	**Any two of the following topics:** 1. **Exploring the natural archive of Sundarban and North-East India:** For the first time we have explored Sundarban to draw the base-line data of its natural radioactivity content. One of my Ph.D. students is working in this area in collaboration with the Department of Environmental Science, University of Calcutta. However, there is enormous scope in this area still pending. The Ph. D student would be responsible for mapping paleo-climatic pictures of these areas by measuring ^{10}Be, ^{14}C and other cosmogenic radionuclides. (S)he has to develop separation techniques of minuscule amount of these radionuclides from very complex matrix for quantitative measurement of these radionuclides. The major part of the work will be carried out by Accelerator Mass Spectrometry at IUAC Delhi. Apart from these, the candidate has to measure other primordial and anthropogenic radionuclides in continuation of the current work. 2. **Simulation of converter target related chemistry:** The multi mega watt converter targets converts protons to neutrons for fundamental physics research. One of my Ph.D. students is currently involved in converter target related chemistry experiments. This is the first systematic attempt to unfold the chemistry of converter targets. Again this field has also enormous scope to investigate further. The new Ph. D student will be responsible to device thermo-chromatographic apparatus for easy release of the minute amount of the radionuclides (in order of pico-gram) from tons of converter target. The student will develop other chemistry

		also. This is a broader line project between physics and chemistry. 3. **Development of new materials for exploring the properties of superheavy element:** There are not many reports on the chemistry of superheavy elements if compared with the main Periodic Table. The difficulty in production (~1 atom/per day) and their very short half-lives (~ few seconds to minute) for lower superheavy elements (104-108) is mainly responsible for fewer attempts to discover their chemical properties. Till date only very few ion exchangers (liquid/solid) have been used. Candidate will be responsible to develop new ion exchanger or other materials, which fits to the properties of superheavy elements. 4. **Light and heavy ion activation for production and separation of clinically important radionuclides:** We are successfully involved more than a decade in this field. More than half a dozen of my students did Ph. D in this area. A well explored but till lots to do in this area. Candidate will be responsible to develop new green separation techniques for accelerator produced radionuclides from their target matrix applicable to administer to human directly.
7.	Dulal Senapati Chemical Sciences	**Nanosurface Induced Excited State Dynamics in Expense of Low Electric and Magnetic Field:** The role of highly anisotropic magneto-plasmonic nanostructure or nanostructure assemblies and their associated surface for many fold electric and magnetic-field induced surface enhanced intersystem crossing (SEISC) is a new venture in molecular dynamics. With preliminary success, we are in a process to develop the field to control the molecular excitation for manipulating the excited state. Depending on the strength of the magnetic field or electric field we will be able to achieve superlative excited state spin modulation through surface enhanced electron spin-orbit (L•S) or nuclear spin-electron spin (I•S) coupling. By optimizing the size, shape and composition of nanosurface; distance between the nanosurface and the molecular system; electronic nature of the molecular system; electron distribution on the surface and the polarity of the solvent we can easily control the extent of resultant spin conversion to generate a specific excited state exclusively. A plausible explanation with respect to the spin flipping, spin rephrasing and magnetic-field induced hyperfine splitting to control the spin dynamics has been put forward to explain the resultant spin modulation or spin anisotropy (S/T).

8.	Padmaja Mishra Chemical Sciences	**Exploration of the activity of DNA repair inhibitors: Future targets to improve cancer therapy:** A better understanding of the Double strand DNA repair (DDR) will not only enrich our knowledge of cancer development but also help to identify druggable targets of cancer intervention within the DDR network. This wills also provide a proper mechanism to assist the future discovery of novel, potent and specific drug candidates for the improvement of existing cancer therapy. This project will mainly focus on drugs that will inhibit the proteins and enzymes that enhance and assist the DNA repairing process, thus leading to programmable cell death.
9.	Gautam Garai Computational Sciences Diviaion	**Study of pathogenic gene prediction in plants and/or animals:** Sometimes it is difficult to detect pathogenic genes for some destructive pathogens by time-consuming and expensive molecular biological experiments in lab. In such cases computational methods provide an alternative way to solve this problem. The purpose of the study is to develop some novel tools to identify pathogenic genes in plants and its effect in animals and vice versa.

The following projects may be available subject to the vacancy on January 1, 2018

Sl.	Principal Investigator, Division	Doctoral Research Area
1.	Oishee Chakrabarti Biophysics & Structural Genomics	**Any two of the following topics:** **Re-organisation of intracellular organelles in glioblastomas:** So far there are ample examples in the literature to support that intra- and extra-cellular signalling pathways are perturbed during the genesis of cancer. Similarly, perturbations in the cell cycle check points are also known causes of cancer. However, there is dearth of evidence to suggest that structural changes at the intracellular level expedite the inception of oncogenesis. This project will aim to characterize and delineate how intracellular organellar structures (ER, mitochondria and lysosomes) change in glioma-derived cells. Mitochondrial fission and ER-mitochondria fusion events will be studied in the cell lines and then in the mouse tumours generated. **Characterization of ER stress by meta-network analysis of unfolded protein response (UPR):** Endoplasmic reticulum (ER) is one of the most important organelles found in the cells of eukaryotes. Protein folding and trafficking are two very important functions performed exclusively by the rough endoplasmic reticulum (RER) in cells. In secretory cells, the proteins produced by ER estimates up to ~30% of the total proteome. Proteins which fail to achieve properly folded conformation for their optimal activity are removed by the ER through a process called ER associated degradation (ERAD). Unregulated accumulation of unfolded or misfolded proteins at the ER leads to ER stress. Previous studies indicated that expression of only small number of miRNA was induced under ER stress while the majorities were either unaffected or down-regulated. Hence, to understand the regulatory mechanism of UPR directed by miRNAs, it is important to look at the whole repertoire of UPR miRNA and mRNAs during a particular condition. **The role of histone methyltransferases in non-histone protein methylation:** Histone methyltransferases are involved in gene regulation by modifying histone tails and therefore fine tune gene expression. However there are several instances where histone methyltransferases have been found to methylate non histone proteins. It is suggested that modification of autophagic cargo proteins by arginine methylation may provide a regulatory mechanism for modulating autophagic degradation efficiency during selective autophagy. It will be interesting to determine how these methylation changes affect selective autophagy (such as mitophagy and lipophagy) in mammalian systems and general autophagy in a neurodegenerative disease (Amyotropic lateral sceloris) and liver diseases in the future.

2.	Chandrima Das Biophysics & Structural Genomics	**Characterization of the nonhistone targets of newly discovered E3 ubiquitin ligase UBR7 and its implications in cancer:** We have recently identified that E3 ubiquitin ligase UBR7 can monoubiquitinate core histone. Interestingly, we have identified few of the nonhistone interacting partners of UBR7. We would be characterizing them as new substrates of UBR7. These proteins have important role in cell cycle progression and have direct implication in cancer. Understanding the role of UBR7-mediated ubiquitination of these proteins can identify a novel mechanism of tumor suppression. **Epigenetic regulation of chromatin by the PHD Finger transcription factor promoting neuronal differentiation programs: insights on their anti-cancer mechanism:** Chromatin readers/effectors are involved in recruiting chromatin-modifying/remodelling complexes to regulate gene expression programs in a spatio-temporal manner and hence they are emerging as important regulators of oncogenesis. Two such chromatin readers with which we are extensively working are ZMYND8 and Sp110. We would be investigating their role in promoting neuronal differentiation programs. Further, we would also study their role in promoting transdifferentiation programs in cells, whereby they might emerge as novel candidates for differentiation therapy in future.