IITB-Monash Research Academy

Indian Institute of Technology Bombay | MONASH University

An Indian-Australian research partnership

Project Title:	**Dynamics of Redox Proteins & Enzymes: theory and experiment**	
Project Number	**IMURA0888**	
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Research Clusters:

Research Themes:

Highlight which of the Academy's CLUSTERS this project will address? *(Please nominate JUST **one.** For more information, see www.iitbmonash.org)*		**Highlight which of the Academy's Theme(s) this project will address?** *(Feel free to nominate more than one. For more information, see www.iitbmonash.org)*	
1	*Material Science/Engineering (including Nano, Metallurgy)*	***1***	*Advanced computational engineering, simulation and manufacture*
2	*Energy, Green Chem, Chemistry, Catalysis, Reaction Eng*	2	*Infrastructure Engineering*
3	*Math, CFD, Modelling, Manufacturing*	3	*Clean Energy*
4	*CSE, IT, Optimisation, Data, Sensors, Systems, Signal Processing, Control*	4	*Water*
5	*Earth Sciences and Civil Engineering (Geo, Water, Climate)*	5	*Nanotechnology*
6	*Bio, Stem Cells, Bio Chem, Pharma, Food*	6	*Biotechnology and Stem Cell Research*
7	*Semi-Conductors, Optics, Photonics, Networks, Telecomm, Power Eng*	7	*Humanities and social sciences*
8	*HSS, Design, Management*	8	Design

The research problem

Define the problem

Redox proteins are essential for life, and redox enzymes provide natures catalysts. Yet, the underlying redox processes undertaken by these biomolecules are poorly understood. They are involved in metabolism and many other important physiological processes, and for many of these reactions electron transfer between their oxidation and reduction states are required.[1,2] Thus, the investigation of life sustaining processes we need to investigate the electron transitions in a pseudo-physiological enviroment. Enzymes catalyse a wide variety of essential chemical transformations with important applications in biotechnology, pharmaceutics and medicine.[3-5] The exploitation of the catalytic activity offers unprecedented possibilities for biotechnology applications, if the natural electron transfer chain could be replaced by a mediated or preferably a direct electron transfers from a solid state electrode to the protein.[6-9] Motivation to integrate redox proteins into an electrical circuit has both fundamental and applied value. Therefore, direct electrochemistry of enzymes has aroused great interest in biological and bio-electrochemical fields.[10,11] Although many electrochemical studies on enzymes have been undertaken, there remain many challenges in understanding basic conformational and redox data for enzymes.[12-14]

Historically, bio-electrochemistry proved challenging, as there were problems with protein denaturation at electrode surfaces and slow electron transfer.[15] Small molecule electron transfers reagents (mediators) were used to shuttle electrons between the electrode surface and proteins or enzymes in solution.[16] In such experiments, reactions are limited by the properties of the mediator and intrinsic protein/enzyme biochemistry cannot be measured directly. Therefore, it is significant to develop a new insight in the progress of the redox-active molecular centres of proteins with a new technology. Additionally, molecular simulations of enzymatic reactions at the atomistic level can provide fundamental mechanistic insight into enzyme electrochemistry. Further, molecular simulations can be combined with numerical modelling to develop kinetic models for electrochemical processes involving enzymes.

Student Summary

Despite our many advances, we remain ignorant of many fundamental biological processes. Even the simplest enzyme reactions, involving a small molecule transformation or passage of an electron via a metal centre to a product involves extensive complexity. This project will examine these basic processes, using bioelectrochemistry and other biophysical methods as well as molecular dynamics simulations to reveal these fundamental reactions in biology. We propose to apply this approach to investigate the role of reactive oxygen species (ROS) for aldehyde oxidase, which is a fundamentally important enzyme implicated in the aging process. The overarching goal will be to describe the key processes structurally and mechanistically, and identify the mechanism of operation of the enzyme in a physiological environment and when tethered to the electrode.

Project aims

Define the aims of the project

The aims of the project are:

1. Simulate structural and conformational transitions in enzymes using molecular

dynamics to understand the role of environment and surface confinement on redox processes;
2. Examine the mechanistic basis for redox enzymes using molecular dynamics and numerical models
3. Investigate the physical properties of enzymes using biophysical techniques like quartz-crystal microbalance with dissipation;
4. Use advanced theoretical and instrumental bio-electrochemical techniques to enable insights and understanding of redox-driven catalytic behaviour of enzymes in a biomimetic environment;
5. Investigate basic redox properties of selected enzymes to understand the mechanism required for their function in a pseudo-physiological environment;

Expected outcomes

Highlight the expected outcomes of the project including likelihood of patents

The following outcomes are expected,

1. Publications in high-impact journals
2. A PhD scholar with expertise in bioanalytical characterization tools, and multi-scale molecular simulations
3. Insight into the underlying basis of redox processes in enzymes, during catalysis
4. Build an understanding of mechanistic steps from simulations for understanding

How will the project address the Goals of the above Themes?

Describe how the project will address the goals of one or more of the 6 Themes listed above.

The project involves high-performance computing as it deals with large-scale molecular dynamics simulations requiring parallelized computer architecture and specialized numerical methods for handling large data sets. In addition, the project also involves the use of bioinformatics and statistical data analysis tools. Consequently, the project is relevant to the theme of Advanced Computational Engineering, Simulation and Manufacture.

The phenomenon which is the subject of this study occurs at nanometer length scales, and several biophysical characterization tools are routinely used in nanotechnology. Hence, this project is relevant to the Nanotechnology theme.

The fundamental molecular and electronic reactions that contribute to enzyme reactions will be gleaned, and hence expand our knowledge of biological chemistry and relevant to the theme of Biotechnology and Stem Cell Research.

Capabilities and Degrees Required

List the ideal set of capabilities that a student should have for this project. Be as specific or as general as you like. These capabilities will be input into the online application form and students who opt for this project will be required to show that they can demonstrate these capabilities.

The prerequisite skills needed in this project are a combination of mathematical modelling capabilities and knowledge of analytical/physical chemistry. Some experience with biology would be desirable but not essential.

Candidates with the following degrees are desirable,

1. B.Tech./M.Tech. in Chemical Engineering, Biochemical Engineering, Materials Engineering
2. M.Sc. in Chemistry (Physical Chemistry or Analytical Chemistry with Mathematics at the B.Sc. level)
3. M.Sc. in Physics (with interest in computations and biophysics)

Necessary Courses

List three tentative core courses relevant to the project that the student should complete during his/her coursework at IITB (the student will require to secure 8 point in these courses)

Potential Collaborators

Please visit the IITB website www.iitb.ac.in OR Monash Website www.monash.edu to highlight some potential collaborators that would be best suited for the area of research you are intending to float.

Select up to **(4)** keywords from the Academy's approved keyword list **(available at http://www.iitbmonash.org/becoming-a-research-supervisor/)** relating to this project to make it easier for the students to apply.

1. BioScience,Bio Medical Engineering
2. Computer Simulation
3. Bio Chemistry
4. Nanotechnology,nanoscience