IITB-Monash Research Academy

Indian Institute of Technology Bombay | MONASH University

An Indian-Australian research partnership

Project Title:	**Chromatin as a polyelectrolyte: DNA-bending and 3D organization**
Project Number	**IMURA0790**

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Research Academy Themes:

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. Advanced computational engineering, simulation and manufacture
2. Infrastructure Engineering
3. Clean Energy
4. Water
5. Nanotechnology
6. Biotechnology and Stem Cell Research

The research problem

Assembling chromatin, in vitro, is a difficult challenge in the field of biotechnology. Chromatin is nothing but the packaged form of DNA---a long string polymer that carries our genetic information. Challenges in chromatin assembly arise primarily due to the fact that it is a complex polyelectrolyte system of charged DNA polymer and many other proteins. The 3D organization of the chromatin is decided by myriads of proteins that bind onto the DNA and bend and twist the DNA in space. One way of overcoming this problem, and understanding the science behind chromatin assembly is to do in vitro experiments with DNA in the presence of molecules that mimic the action of the proteins. Certain dendrimers (polymers with complex branched architecture) exhibit protein-like DNA-binding behaviour that can compact DNA. Understanding these artificially folded DNA structures and the science behind their assembly process will help us in understanding chromatin assembly in vitro. The aim of this project is to examine how the 3D organization of DNA is regulated by interactions of DNA-bending and twisting factors. DNA is negatively charged and bending factors are often positively charged. The organization of the DNA is not only decided by DNA elasticity and the curving of DNA due to these factors but also by their electrostatic interactions. How elasticity combined with the polyelectrolyte nature of the systems affects the organization of folded DNA structures is an interesting and yet to be solved question that is of vital importance to biology and to biotechnology.

Project aims

The aim of this project is to develop computational algorithms based on polymer models, that enable the study of the 3D organization and dynamics of folded DNA, taking into account DNA polymer bending elasticity, twist elasticity and the presence of electrostatic interactions between DNA and DNA-bending and twisting factors. The project supervisors combine expertise in experiments (Banaszak Holl), and theoretical analysis and computer simulations (Padinhateeri and Jagadeeshan). The group of Banaszak Holl has pioneered the experimental assembly of various DNA-bending factors onto DNA and the creation of chromosome-like folded DNA structures. The groups of Padinhateeri and Jagadeeshan have developed theories and carried out simulations of polymers and polyelectrolyte systems that are models for biological macromolecules. Though the project will be primarily computational in nature, the simulations will be motivated and guided by the experiments carried out in Professor Banaszak Holl's group. Experimental data will be used to refine and tune computational models in order to obtain convergence between theory and experiment, and lead to the development of models with predictive capability.

Expected outcomes

The outcomes of the project will include:

(i) The development of a validated software tool that can directly compute 3D organization of the DNA given certain DNA-bending factors

(ii) Understanding the role of electrostatic interactions and bend/twist elasticity in the higher order assembly of DNA.

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

The project addresses an important question in the theme area of biology/biotechnology. Understanding the organization of folded DNA and the electrostatic interactions of DNA with DNA-binding factors will greatly help in understanding chromatin organization and in reconstituting chromatin in biotechnology experiments.

Capabilities and Degrees Required

The following capabilities are essential:

1. Excellent training in mathematics and numerical methods (biology knowledge is not mandatory)
2. Proven experience with computer programming in high level languages
3. Ability to write and communicate fluently
4. Strong background in Engineering/Physics (Either M Sc in Physics or B Tech/BE in Mechanical/Chemical/Electrical Engg)
5. While the topic has a biological context, students without a background in physics or engineering will not be considered

Please provide a few key words relating to this project to make it easier for the students to apply.

Polymer dynamics, Brownian dynamics simulations, DNA packaging