REGIONAL CENTRE FOR BIOTECHNOLOGY

Seminar series

Nanopore Biophysics: From Gene Sequencing to Gene Silencing

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Seminar Room

Abstract

Structure-Function relationship is ubiquitous in almost all of the nature's self-assembled systems. Specifically in biological systems, my main research interest is to study the dynamic heterogeneities in structural populations of proteins and DNA-protein complexes that regulate cellular function as well as stress response. Both, the DNA sequence, as well as its protein-driven & highly packaged form- the chromatin fiber, are examples of how nature regulates cellular functions by efficient organization and dynamic re-organization of biological structures. Misregulation of these structures at molecular scales lead to a variety of diseases, making it imperative to study the distributions and regulation of these biocomplexes. Since mid-90s, nanodevices, especially nanopore biosensing has shown astonishing resolution in single molecule detection and identification and have provided a unique framework to study heterogeneity between individual biocomplexes. This has lead to new and exciting applications in both biophysics and nano-biotechnology.

In this three-part talk, I will first present my work on design and development of a novel nanopore-based technology for ultra-fast and low-cost DNA sequencing. To achieve signal contrast required for single nucleotide differentiation, I engineered a unique combination of state-of-the-art solid-state nanopore technology with high speed fluorescence imaging at single molecule resolution. This has led to the emergence of the first synthetic nanopore based single-molecule DNA sequencing platform. In the second part of my talk, I will show first ever application of solid-state nanopores in screening structural states of nucleosomes and chromatin. By measuring voltage driven changes in ionic current as a single nucleosome translocates through a nanopore, I can detect subtle changes in nucleosomal sub-structural volume and charge state. This resolution of single molecule detection of DNA-bound local protein structure in label-free manner is unprecedented. Finally, I will talk about my future research work on studying epigenetic gene silencing by chromatin condensation using nanodevices. Molecular mechanisms that regulate condensation of chromatin structure, a key element in epigenetic gene control, is poorly understood. I will propose to develop a concerted biophysical, chemical and nanoscience based approach to study kinetics of architectural proteins-driven chromatin compaction by coupling nanopore biosensing to optical tweezers based force spectroscopy. The outcome of my proposed research will shed light on primary mechanism of chromatin folding and the role of chromatin architecture based gene-silencing in disease, DNA repair, aging and cancer.