NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

School of Biological Sciences
College of Science

Seminar Announcement

Compaction of DNA, Nucleosomes & Chromatin

Date: 25 May 2018

Time: 4 p.m.

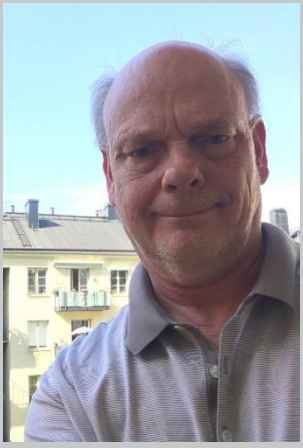
Venue: Classroom 1, SBS

I will present two recent ongoing projects related to compaction of DNA in the genome:

i) Structure and Dynamics of Telomeric Nucleosomes and Chromatin

Eukaryotic genomic DNA is condensed into chromatin, a higher-order nucleoprotein complex with 146bp of DNA wrapping around the histone octamer (HO) forming the nucleosome core particle (NCP). A string of nucleosomes bound by the linker histone H1 and connected by linker DNA fold into the so-called called “30nm” chromatin fibre, which compacts into metaphase chromosomes.

Human telomeres constitute the protective structure at the end of the chromosomes with repetitive TTAGGG sequences that are about 10kbp. Almost nothing is known about telomeric chromatin structure and dynamics at the detailed molecular level and the consequences of its unique repetitive DNA sequence. In collaboration with the Daniela Rhodes group, we have characterised the telomeric 145 bp DNA NCP with biophysical methods and determined its structure at 2.2 Å resolution with X-ray crystallography. We have designed and prepared in vitro reconstituted telomeric chromatin fibres and performed initial characterisation of its structural and dynamic properties using EM and single molecule magnetic tweezer experiments.



Speaker:

Prof. Lars Nordenskiöld
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ii) Hierarchical Multi-Scale Modelling of DNA and Chromatin

Bio-computational approaches have recently developed tremendously, enabling all-atom MD simulations of large biopolymers to be rigorously performed. However, the modelling in atomistic detail of chromatin fibres at mesoscale, is still not computationally feasible. Simplification of this problem, requires implementation of multiscale coarse-grained (CG) models based on rigorous effective potentials. We have developed an approach for systematic hierarchical multiscale CG modeling of chromatin based on the so-called inverse Monte Carlo method. As a test case we set out to simulate the DNA toroid formation induced by the presence of multivalent cations, from first principles without underlying assumptions. Simulations at two levels of CG models of DNA, enabled modeling of DNA condensation at mesoscale level. Remarkably, the simulation of a single DNA molecule (10 kbp) results in the formation of a single toroid with distinct hexagonal packing as predicted by Cryo-EM characterization of kb sized DNA in the presence of $CoHex^{3+}$ or $spermidine^{3+}$.

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