BiophysTO Lunchtime Talks

Hue Sun Chan

Departments of Biochemistry & Molecular Genetics,
University of Toronto

How Does an Enzyme Unknot DNA? Statistical Mechanics of Disentangling by Topoisomerases

Closed DNA circles can be knotted or linked (catenated). Such entanglements can be extremely detrimental biologically. Enzymes known as type-II topoisomerases (topoIIs) resolve topological entanglements by passing one double-stranded DNA segment through another. Thus topoIIs are critical for cellular replication and genome stability. TopoIIs can reduce knot population by as much as 90 times and catenane population by ~ 16 times. These experimental observations raise a fundamental question: How does a relatively small enzyme discern the global topology of a much larger DNA and disentangle it so effectively? Using coarse-grained lattice and wormlike models of DNA, we elucidated the mathematical/physical principle of topoII function by demonstrating that it is achievable by recognizing and acting at DNA juxtapositions with specific local geometries. We verified in particular that selective segment passage at hook-like juxtapositions can reduce knot and catenane populations as dramatically as seen in experiments. TopoIIs also regulate DNA supercoiling. One of their effects on DNA supercoils is narrowing the distribution of linking number. The present analysis highlights a general connection between local geometry and global topology in polymer configurations. Our theory predicts a general scaling relation among a topoII's unknotting, decatenating, and supercoil narrowing capabilities. The predicted scaling relation is essentially identical to that observed experimentally for several topoIIs from a variety of organisms, indicating that the different disentangling powers of the topoIIs likely arise from variations in the hooked geometries they select. Ramifications of our findings will be discussed in the context of recent experimental advances in assessing various proposed topoII mechanisms.

Host: Dr. Walid A. Houry

(Refreshments and pizza will be provided)

Thursday, February 25, 2016 – 12:00 pm, noon
Davenport Room, Chemistry Building
(and via streaming to Davis Building 4001 UTM)