UNIVERSITY OF ALBERTA
FACULTY OF MEDICINE & DENTISTRY

BME SEMINAR

Department of Biomedical Engineering

Date: 2017 Jun 29, Thursday
Time: 10:00 AM – 11:00 AM
Venue: 1-075 Research Transition Facility

A Combined Computational & Experimental Investigation of Polynucleotide Binding Polymers for Therapeutic Applications

Deniz Meneksedag-Erol

MSc, PhD Candidate
Departments of Biomedical Engineering, and Chemical & Materials Engineering
University of Alberta

Abstract:

Polynucleotide binding polymers have a wide range of therapeutic applications including delivery systems for therapeutic polynucleotides, and antithrombotic drugs for extracellular nucleic acid-mediated thrombogenic events. This dissertation explores polynucleotide binding polymers in these two avenues, with combined computational and experimental approaches. Particular emphasis was placed on computational studies to probe structural features of polymers and polymer-polynucleotide complexes at the all-atom level. The first line of studies in this dissertation explored polymers employed in the delivery short interfering RNA (siRNA), a synthetic polynucleotide capable of silencing the overly-expressed genes in malignant cells. Particularly, polymer design and dynamics of polymer-siRNA complex formation, structural features of polymer-siRNA complexes for enhanced functional performance, and the effect of anionic substances of the physiological milieu on polymer-siRNA complex integrity were investigated.

The results demonstrated that there exists a hydrophobic-hydrophilic balance in designing siRNA delivery systems, determining the functional performance of the resulting complexes. Polymer-siRNA complexes were found to accommodate the presence of other polynucleotides in their periphery without losing their integrity; however, they experienced a vast variety of conformational states in the presence of heparin, a sulfated glycosaminoglycan found on cell membrane and extracellular milieu. Our efforts to investigate the polynucleotide binding polymers designed to arrest the prothrombotic activity of DNA revealed the importance of polymer structural design; self-interacting polymers exhibited poor DNA binding, which could be detrimental for their functional antithrombotic performance. This dissertation demonstrated the proof-of-concept for employing computational approaches in conjunction with experimental studies where applicable, in efforts to develop “better” polymer therapeutics for different applications.

All Are Welcome