Submittee: Mark Zajac
Date Submitted: 2013-03-12 13:36
Title: Frontiers in Biophysics 2013
Event Type: Conference-Workshop

Location:
Earth Science Building (ESB), on campus, at the University of British Columbia.

Dates:
Marhch 2nd, 2013

Topic:
Application of quantitative methods to biology.

Methodology:
Events included a total of ten talks by participants, grouped into three sessions. There was also a rapid-fire session of poster previews, with a one-minute, single-slide presentation from each participant, with follow-up questions during the poster session itself.

Objectives Achieved:
Participants met to exchange ideas and information.

Scientific Highlights:
The keynote address for 2013 was "What can computational modeling tell us about cell motility?" by Professor Charles Wolgemuth, from the University of Arizona.

Organizers:
Gou, Jia, Department of Mathematics, UBC // Knutsdottir, Hildur, Department of Mathematics, UBC // Liao, Laura, Department of Mathematics, UBC // Mata, May Anne, Department of Mathematics, UBC // Herrera Reyes, Alejandra Herrera Reyes // Zajac, Mark, Department of Mathematics, UBC //

Speakers:
"Imaging prion fibrils by atomic force microscopy to determine their bending rigidities and elastic moduli" by Guillaume Lamour, Department of Biochemistry, University of British Columbia.
ABSTRACT: Prion diseases such as Creutzfeldt-Jakob or mad cow diseases originate from the misfolding and aggregation of prion proteins, with invariably lethal outcome. In this study we generate mammalian prion fibrils with reproducible morphological properties and investigate their

mechanical properties by atomic force microscopy. Fibril shapes are analyzed statistically using worm-like chain models that describe the bending of semi-flexible polymers under thermal fluctuations. This way we quantify the persistence lengths of several different types of prion fibrils (wild-type and mutants). Using fibrils heights we derive, for each fibril type, an estimated elastic modulus, which we check directly using recent AFM technology that monitors frequency changes in the second normal mode of the AFM cantilever. We find that both methods complement each other well and overall provide a system that could be used to correlate prion fibrils stability to their potential biological effects in cell lines or animal models. /// "Using deuterium nuclear magnetic resonance spectroscopy to study the effects of fluorescent probes on lipid membranes" by Sherry Leung, Department of Physics, Simon Fraser University. ABSTRACT: The lipid raft hypothesis postulates that nano-scale lateral compositional heterogeneity in cell membranes plays functional roles. Fluorescence techniques are routinely used to study membranes and fluorescent probes are widely available, but only recently have systematic studies on probe behaviour emerged. It was found that probe behaviour can be altered by membrane composition, for example. Using 2H NMR, we showed that trace amounts of the carbocyanine probe DiIC12 are enough to alter phase coexistence behaviour of membranes, while the equipartitioning probes, Laurdan and another carbocyanine probe DiOC18, had little effect. Complicating the picture is the fact that non-equipartitioning probe, naphthopyrene, also did not affect membrane phase coexistence. Most biological molecules are only present in the cell in small amounts. In addition to shedding light on why micron-scale phase separation is observed in model membranes, but not in living cells, our work can elucidate the mechanism by which minor cellular components function. /// "Studying biomechanics at the single-molecule level with optical tweezers" by Naghmeh Rezaei, Department of Physics, Simon Fraser University. ABSTRACT: Optical tweezers are a technique that use focused laser light to trap microscopic objects, which has provided unique insight into mechanical processes involved in protein and DNA kinetics, mechanics, structure, etc. We use optical tweezers to study the mechanical properties of short proteins that play a vital role in providing structural support for the body. Elastin and collagen are two important structural proteins: we study their mechanical response to an applied force, and try to understand how it relates to molecular structure and might impact their biological function. Our goal is to reveal how changes in chemical composition affect mechanical properties, to relate this to macroscopic defects that lead to disease, and to inform the design of new biomaterials. /// "Modeling spatial interactions between breast cancer cells and macrophages" by Hildur Knutsdottir, Department of Mathematics, University of British Columbia. ABSTRACT: Experiments have shown that breast cancer cells invade into surrounding tissues and organs alongside macrophages. The two cell types communicate via a short ranged chemical signaling loop. We use reaction-diffusion partial differential equations to study the spatial interactions of these cells both analytically and numerically. We ask under what conditions aggregation of the two cell types is expected to occur. A linear stability analysis reveals that changes in chemical secretion, chemical degradation, chemotaxis coefficients and steady state concentrations in the model could eliminate the spontaneous aggregation of cells. Comparing the continuum results with simulations of a discrete cell-based model, we find good qualitative agreement. /// "Computational Models for Epigenetic Mechanisms - Overview" by Karthika Raghavan, IRMACS Center, Simon Fraser University. ABSTRACT: Definition and characterization of the role of Epigenetic mechanisms have gained immense momentum since the completion of the Human Genome Project. The human epigenetic layer, made of DNA methylation and multiple histone modifications, (the 2 key elements), is known to regulate the cellular events. Aberrations in DNA methylation supported by an abnormal landscape of histone modifications have been associated with Cancer initiation and development. The presentation here describes the framework of a theoretical micromodel (EpiGMP) that investigates the effect of histone modifications and gene expression for defined levels of DNA methylation. This micromodel has been applied to (i) test networks of genes involved in colon cancer and now currently (ii) being applied to an agent-based model to explore the chromatin remodelling inside the human genome. Ultimately, the goal is to provide coherence about these low level molecular changes that determine physical traits for normal and disease conditions in an organism. /// "Measurement of Drug Accumulation in Single Acute

Myeloid Leukemia (AML) Patient Cell Using the Microfluidic DEP chip and the Clinical Implications" by Avid Khamenehfar, Department of Chemistry, Simon Fraser University. ABSTRACT: The reversal effect of MDR inhibitors on single cell drug accumulations has been measured in order to improve drug sensitivity on the cancer cell. The measurement is achieved using a new microfluidic chip designed to combine dielectrophoresis with the same-single-cell analysis (SASCA). A MDR cell has low initial drug accumulation and an obvious reversal effect in terms of substantial fold increase in drug accumulation. We have applied the method to measure acute myeloid leukemia (AML) patient cells. We have found 78% correlation between our SASCA measurement results and patient clinical outcomes, and we envision such a method may provide useful information for clinical monitoring of patients undergoing chemotherapy in the future. /// "Gene-Gene Interactions Controlling Reliable Formation of Fly Segments" by David Holloway, Department of Mathematics, BC Institute of Technology. ABSTRACT: In early fruit fly embryos, expression of the gap genes determines the future pattern of body segments. Building on experimental data and previous models, we show how the mutual interactions of two gap genes, hunchback (hb) and KrÃ¼ppel (Kr; both activated by the spatially-graded maternal protein, Bicoid) create a stripe of hb expression responsible for the mid-body parasegment 4. hb-Kr interactions are modelled at the cis-regulatory level, with low binding site occupancy activating and high occupancy inhibitory. Using stochastic modelling, we predict that Kr stabilizes the precise location of the hb expression boundary. This has recently been corroborated experimentally. /// "Occlusion of micro-capillaries by malaria-infected red blood cells" by Tenghu Wu, Chemical and Biological Engineering, University of British Columbia. ABSTRACT: Malaria-infected red blood cells (iRBCs) can easily occlude micro-capillaries because of their anomalous stiffness and stickiness compared with health red cells. Previous work suggested three factors in the loss of deformability of iRBCs: (i) the stiffening of the membrane, (ii) the reduction of the cellâ€™s surface/volume (S/V) ratio, and (iii) the presence of solid parasites inside the cell. These factors have been examined in experiments and simulations of the stretching of iRBCs by optical tweezers. In this work, we investigate the influence of the three factors on the blockage of micro-channels by using the smoothed particle hydrodynamic method. Three micro-fluidic channels with different constricting pore sizes (Thickness Ã— Wide = 4.8 Ã— 4.8, 4.0 and 3.2 microns) are employed. Our results indicate the solid parasites as the main agent for micro-capillary occlusion. The decrease of cellâ€™s excess surface area causes blockage of the medium channel. Besides, the elevated membrane stiffness significantly increases the transit time of the iRBCs in the small channel. /// "A Vector-Host Model for Coinfection by Barley Yellow Dwarf Virus" by Margaret-Rose Leung, Department of Physics, Simon Fraser University. ABSTRACT: The lipid raft hypothesis postulates that nano-scale lateral compositional heterogeneity in cell membranes plays functional roles. Fluorescence techniques are routinely used to study membranes and fluorescent probes are widely available, but only recently have systematic studies on probe behaviour emerged. It was found that probe behaviour can be altered by membrane composition, for example. Using 2H NMR, we showed that trace amounts of the carbocyanine probe DiIC12 are enough to alter phase coexistence behaviour of membranes, while the equipartitioning probes, Laurdan and another carbocyanine probe DiOC18, had little effect. Complicating the picture is the fact that non-equipartitioning probe, naphthopyrene, also did not affect membrane phase coexistence. Most biological molecules are only present in the cell in small amounts. In addition to shedding light on why micron-scale phase separation is observed in model membranes, but not in living cells, our work can elucidate the mechanism by which minor cellular components function. /// "Modelling cotyledon growth in conifer tree embryos" by Ignacio Rozada, Department of Mathematics, BCIT. ABSTRACT: Recent developments in experimental biology have provided insight in the early development of conifer tree embryos. We will discuss the features and early results of using a Turing-type model to describe cotyledon growth in conifer tree embryos (which can have up to 15, as opposed to the standard one or two on all other plants). A one-way coupled system of two Brusselator models is used, in connection to two biological processes that have been observed to occur in cotyledon development.

Links:
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