Registration, refreshments, and poster set-up, 8:15—9:00

Opening remarks, 9:00—9:10

Talk 1, 9:10—9:28. Forced Topological Changes of a Protein Slipknot

Chengzhi He*, Hongbin Li
Department of Chemistry, University of British Columbia

The knotted polypeptide chain is one of the most surprising topological features found in certain proteins. Understanding how knotted proteins overcome the topological difficulty during the folding process has become a challenging problem. Theoretical studies suggest that slipknotted structure can serve as important intermediate in the transformation from unknotted structure to knotted structure. Here we use single-molecule force spectroscopy as well as steered molecular dynamics (SMD) simulations to investigate the mechanical unfolding of a slipknotted protein, AFV3-109. By applying force in different directions, we are able to untie the slipknot to a linear polypeptide chain as well as tighten it into a trefoil knot involving ~ 13 amino acid residues. Multiple pathways of untying and tightening are found by both single-molecule force spectroscopy experiments and SMD simulations, revealing that the kinetic partitioning mechanism governs the unfolding of the slipknotted protein. SMD simulations provide detailed molecular mechanisms of the protein unfolding and topological changes from slipknot to linear chain as well as from slipknot to trefoil knot.

Talk 2, 9:28—9:46. Simulated force spectroscopy of a badly-behaved protein, and the search for model-independent, universal misfolding mechanisms

Mona Habibi*, Joerg Rottler, Steven Plotkin
Department of Physics and Astronomy, University of British Columbia

We used single-molecule pulling molecular dynamic simulations to capture the detailed structural mechanism of the unfolding process for proteins linked to nerodegenerative diseases. In these simulations, a loop-truncated variant of superoxide dismuates (SOD1) was stretched from the N- and C-termini. Force-extension curves (FECs) of the protein were obtained for all-atom models, and the results compared to several coarse-grained (CG) models in common use, including AWSEM, AMH-G, and C-based G models. AWSEM is an associative memory Hamiltonian model with several physico-chemical based terms using a three-bead per amino-acid residue representation. AMH-G model is a more specific, non-additive structure based model using a three-bead representation, and C is the simplest available CG model in common use, wherein each residue is represented by only one bead. Only the results from the AWSEM model agree well with all-atom simulations.

Talk 3, 9:46—10:04. Magnetic Resonance Spectrocopy in Huntington's Disease.

Bretta Russell-Schulz*[1], Terri Petkau[2], Alex L. MacKay[3], Blair R. Leavitt[2]
1 Department of Radiology, University of British Columbia
2 Centre for Huntington Disease & Centre for Molecular Medicine & Therapeutics, University of British Columbia
3 Department of Physics and Astronomy, University of British Columbia

Huntington's Disease (HD) is a fatal neurodegenerative disease that causes cognitive, psychiatric and motor dysfunction. HD is an inherited disorder predicted through genetic testing. Clinical diagnosis is defined as manifestation of unequivocal motor abnormalities; however, many patients experience cognitive and psychiatric changes before diagnosis. Biomarkers for clinical trials are essential, not only in early HD but also in premainfest HD (pre-HD), subjects possessing genetic predisposition to HD but not yet clinically diagnosed. 1H-MRS can be used to determine concentrations of metabolites in the brain and examine metabolic changes in disease. Here we compare metabolite concentrations from controls, premanifest HD and early HD subjects over four years in the putamen (an early site of pathogenesis in HD). We found a measure of neuronal integrity (tNAA) and glial cells (mI) to be significantly different in early HD compared to controls at later visits, with pre-HD concentrations falling in between.

Talk 4, 10:04—10:22. How can memory retrieval inform planning? The case of distinctiveness-guided search

Jose J. F. Ribas Fernandes*, Clay B. Holroyd
Department of Psychology, University of Victoria

Planning, or the decision based on the simulation and evaluation of action consequences, is a core faculty of decision making. Knowledge about consequences of actions is dependent on episodic memory. Therefore, planning can be approached as a memory retrieval problem. By making this assumption, we import a classical mnemonic phenomenon, distinctiveness, and discuss how it can be applied to planning. Distinctiveness is defined as increased probability of retrieval for dissimilar items in a context, which would convert to preferential retrieval of distinctive states during simulation. In computational terms, distinctiveness thus becomes a criterion for searching a decision tree. We assume that dissimilarity would be informed by a combination of decision-relevant (reward) and irrelevant variables (perceptual properties). In addition, we assume that it could be flexibly modified to suit task demands. We instantiate the idea in a model of planning where states are proposed by distinctiveness-guided diffusion.

Coffee break, 10:22—10:45

Keynote Talk, 10:45—12:00. Grid Cells and the Dynamics of Entrohinal Cortex

Michael E. Hasselmo
Director, Center for Systems Neuroscience, Boston University

Episodic memory function is impaired by lesions of the entorhinal cortex, and entorhinal cortex shows the earliest loss of neurons in Alzheimers disease. My research focuses on understanding circuit mechanisms in the entorhinal cortex that might contribute to episodic memory. Extensive neurophysiological data demonstrates neural responses in entorhinal cortex and hippocampus that could contribute to coding of space and time for memory guided behavior. These responses include the coding of spatial dimensions of behavior by grid cells (Moser and Moser, 2008), place cells (OKeefe and Burgess, 2005), boundary cells and head direction cells, and coding of temporal dimensions by time cells (Kraus et al., 2013). I will present neurophysiological data indicating a role of cellular (Giocomo et al., 2007) and network oscillations (Brandon et al., 2011) in the generation of these spatial and temporal response properties. The intrinsic properties of entorhinal neurons including resonance and rebound spiking may contribute to the spiking properties of grid cells and head direction cells, including temporal coding relative to theta rhythm oscillations known as theta phase precession and theta cycle skipping (Brandon et al., 2013). I will also present a model of episodic memory as the encoding and retrieval of spatiotemporal trajectories (Hasselmo, 2009; 2012).

Brandon MP, Bogaard AR, Libby CP, Connerney MA, Gupta K, Hasselmo ME (2011) Reduction of theta rhythm dissociates grid cell spatial periodicity from directional tuning. Science, 332: 595-599.
Brandon MP, Bogaard AR, Schultheiss NW, Hasselmo ME (2013) Segregation of cortical head direction cell assemblies on alternating theta cycles. Nature Neuroscience, 16(6): 739-748.
Giocomo LM, Zilli EA, Fransen E, Hasselmo ME. (2007) Temporal frequency of subthreshold oscillations scales with entorhinal grid cell field spacing. Science, 315:1719-22.
Hasselmo ME (2009) A model of episodic memory: Mental time travel along encoded trajectories using grid cells. Neurobiol Learn Mem. 92(4):559-73.
Hasselmo ME (2012) How We Remember: Brain Mechanisms of Episodic Memory. MIT Press: Cambridge, MA.
Kraus BJ, Robinson RJ, White JA, Eichenbaum H, Hasselmo ME (2013) Hippocampal Time Cells: Time versus path integration. Neuron, 78(6): 1090-1101.
Moser EI, Moser MB (2008) A metric for space. Hippocampus 18: 1142-1156.
OKeefe, J. and Burgess, N. (2005) Dual phase and rate coding in hippocampal place cells: theoretical significance and relationship to entorhinal grid cells. Hippocampus 15(7):853-66

Lunch, 12:00—12:40

Talk 5, 12:40–12:58. Exploration of locomotion in the ParA/ParB system

Lavisha Jindal*, Eldon Emberly
Department of Physics, Simon Fraser University

In many bacteria the ParA/ParB system is responsible for actively segregating DNA during replication. ParB precessively moves by hydrolyzing DNA bound ParA-ATP forming a depleted ParA region in its wake. Recent in-vitro experiments have shown that a ParB covered bead can traverse a ParA bound DNA substrate. It has been suggested that the formation of a gradient in ParA leads to diffusion-ratchet like motion of the ParB bead but its origin and potential consequences requires investigation. We have developed a deterministic model for the in-vitro ParA/ParB system and show that any amount of spatial noise in ParA can lead to the spontaneous formation of its gradient. The velocity of the bead is independent of this noise but depends on the scale over which ParA exerts a force on the bead and the scale over which ParB hydrolyzes ParA from the substrate. There is a particular ratio of these scales at which the velocity is a maximum. We also explore the effects of cooperative vs independent rebinding of ParA to the substrate. Our model shows how the driving force for ParB originates and highlights necessary conditions for directed motion in the in-vitro system that may provide insight into the in-vivo behaviour of the ParA/ParB system.

Talk 6, 12:58–1:16. Motor properties from persistence: a linear molecular walker in the absence of spatial and temporal asymmetry and its work output by external feedback

Martin J. Zuckermann*[1], Christopher N. Angstmann[2], Regina Schmitt[5], Gerhard A. Blab[3], Elizabeth H.C. Bromley[4], Nancy R. Forde[1], Heiner Linke[5] and Paul M.G. Curmi[6]
1 Department of Physics, Simon Fraser University
2 School of Mathematics and Statistics, University of New South Wales, Australia
3 Molecular Biophysics, Universiteit Utrecht, Netherlands
4 Department of Physics, University of Durham, United Kingdom
5 Solid State Physics and Nanometer Structure Consortium (nmC@LU), Lund University, Sweden
6 School of Physics, University of New South Wales, Australia

The direction of motion of linear molecular motors is usually defined by a spatial asymmetry of the motor or its track (or both). We present a model for a symmetric molecular walker that can directionally move along a symmetric track (leaving the track unmodified), powered by a temporally symmetric chemical cycle. Instead of using asymmetry, directionality is

achieved by persistence. At small load force the walker can take up to thousands of steps in the same direction until it stochastically reverses direction. We discuss a specific experimental implementation of a synthetic motor based on this design and find, using Langevin and Monte Carlo simulations, that a realistic walker can work against load force up to the order of pN with an efficiency of order 36%, comparable to that of kinesin. We also discuss how the walker can be turned into a fully persistent motor by using external feedback algorithms.

Talk 7, 1:16—1:34. Alignment of a magnetic filament in the presence of shear flow

D. Luesebrink*[1,2], J. Cerda[2], P. Sanchez[3], T. Sintes[2]
1 Physics, University of British Columbia
2 IFISC, University of the Balearic Islands
3 Physics, University of Vienna

Magnetic filaments are supramolecular magnetic polymers with technological applications ranging from magnetic memories, nanosensors, to magnetically-imprinted authentication. We present a numerical study of the behavior of a magnetic filament subjected to the simultaneous action of a fluid flow and an external magnetic field. The magnetic filament is represented by a coarse-grained bead-spring model where each bead carries a magnetic dipole. The hydrodynamic coupling of the filament with the flow is accounted for using Multi-Particle Collision dynamics. In the presence of flow and at zero external field the filament undergoes subsequent, aperiodic coiling-stretching transitions. These transitions are strongly inhibited by the external magnetic field, which is able to stabilize the filament, and induce a well-defined degree of alignment that depends on the balance between hydrodynamic and magnetic torques. Results of Poiseuille flow are investigated with respect to the persistence of initial conditions and compared to the case of uniform shear flow.

Talk 8, 1:34-1:52. Cell-ECM adhesion is required for force transmission during morphogenesis

Goodwin, K.*[1], Ellis S.[1], Lostchuck E.[1], Zulueta-Coarasa, T.[2], Feng, J.[3,4] Fernandez-Gonzalez, R.[2,5,6], Tanentzapf, G[1]
1 Department of Cellular and Physiological Sciences, University of British Columbia
2 Institute of Biomaterials and Biomedical Engineering, University of Toronto
3 Department of Mathematics, University of British Columbia
4 Department of Chemical and Biological Engineering, University of British Columbia
5 Department of Cell and Systems Biology, University of Toronto
6 Developmental and Stem Cell Biology Program, The Hospital for Sick Children, Toronto, Canada

Tissue morphogenesis requires force-generating mechanisms to drive the organization of cells into complex structures. These changes are achieved by coordinated action of the cytoskeleton and cell adhesion. Integrin-mediated cell-ECM adhesion is known to transduce traction forces in spreading and migrating cells. We therefore asked whether they perform a similar function in morphogenesis. In order to elucidate the mechanisms by which cell-ECM adhesion regulates tissue mechanics, we use Dorsal Closure (DC), an integrin-dependent process in Drosophila embryogenesis. We show that failure to regulate Cell-ECM adhesion results in abnormal tension in the amnioserosa, an extraembryonic epithelium required for DC. Mutations which modulate Cell-ECM adhesion result in defective DC and altered amnioserosa cell behavior. Quantitative image analysis and laser ablation experiments reveal a relationship between cell deformation and tension in the AS. We propose that Cell-ECM adhesion controls the transmission of forces across developing tissues to in order to promote specific morphogenetic outcomes.

Talk 9, 1:52—2:10. Pheromone and Pheromone-binding Protein Partitioning in Varied Fluid Conditions

Mailyn Terrado*, Erika Plettner
Department of Chemistry, Simon Fraser University

Pheromone-binding proteins (PBPs) are small water-soluble proteins found in the sensory hairs (sensilla) of male gypsy moth antennae. These proteins are believed to transport the nonpolar pheromone, (+)-disparlure, across the aqueous lymph fluid in the sensillum to the odorant receptors of sensory neurons. Recently, fatty acids (FAs) were isolated and identified in the lymph fluid. These fatty acids were shown to enhance PBP-pheromone binding affinity. To investigate the effect of fatty acids in pheromone and PBP partitioning, an in vitro assay was designed to mimic the sensillar components. In this assay, a hydrophobic solid surface, fluid and vesicle suspension mimicked the cuticle, lymph, and neuronal membrane, respectively. Different fluid conditions were used to compare partition profiles of the pheromones and PBPs. The varied fluid conditions include: buffer only, PBP only, FA only, and FA + PBP treatments. Results showed that PBP alone could not retain most pheromones in the fluid phase and need the fatty acids to facilitate pheromone partitioning into this phase.

Coffee break, 2:10—2:30

Talk 10, 2:30-2:48. Numerical Investigation of the Effects of Microgravity on Stem Cell Modulation

Roza Vaez Ghaemi[1,2], Bahman Vahidi[1], Mohammad Hossein Sabour[3], Nooshin Haghighipour[4], Zakieh Alihemmati[1]
1 Division of Biomedical Engineering, Department of Life Science Engineering, University of Tehran, Iran
2 Department of Chemical and Biological Engineering, University of British Columbia

3 Department of Aerospace Engineering, University of Tehran, Iran
4 National cell bank of Iran, Pasteur Institute of Iran, Tehran, Iran

Several evidences are reported on the influence of the physical environment on the stem cells fate. It has been reported that cells in normal gravitational condition are spread with a spindle configuration, while in the simulated microgravity conditions, transform to a rounded non-spread shape. In this paper, the effects of microgravity on mechanical behavior of stem cells under flow-induced shear stresses were evaluated through a computational simulation. Using fluid structure interactions the influence of a well-defined flow passing over a single stem cell was simulated in two different gravitational conditions. The simulation was performed using arbitrary Lagrangian-Eulerian (ALE) formulation and adaptive mesh procedure using a 3D model of a stem cell discretized via finite element method.Focusing on fluid-structure interactions, we developed the first cell-scale model for investigation of the stem cell mechanical behavior. The results indicate the changes in mechanotransduction mechanisms as a result of microgravity which in turn affect the stem cell lineage commitment.

Talk 11, 2:48—3:06. Multiscale modeling of electrostatic interactions between double stranded DNA
Shahzad Ghanbarian*, Joerg Rottler
Department of Physics and Astronomy, University of British Columbia

We developed a coarse-grained (CG) model for double stranded DNA solvated by water molecules in the presence of divalent counterions. In order to include solvation effects arising from the discrete nature of the water molecules, short-ranged corrections were added to the pairwise interaction potentials such that the structure of counterions is consistent with results from corresponding explicit solvent simulations. The CG model succeeded in reproducing the like-charge attraction effect between DNA molecules in explicit solvent simulations at significantly reduced computational expense. This result proves that it is possible to capture complex multibody interactions between polyelectrolyte strands with two-body potentials. We also applied the CG model to study three DNA molecules in the presence of divalent counterions. The results show the emergence of attractive interactions for multiple DNA configurations. The CG models appear as a promising starting point for investigating the stability of DNA bundles in the presence of divalent counterions.

Talk 12, 3:06—3:24. Beyond Structure-Function Relation: A Biochemical Circuit with Kinetically Regulated Activation-Inhibition Switching
Jacob Price*, Hong Qian
Applied Mathematics, University of Washington

Living biochemical systems employ enzymes as regulatory agents. These enzymes, in equilibrium, have inherent affinities and functions determined by the molecular structures and atomic dynamics of both the enzyme and the substrates. These are all defined rigorously in terms of equilibrium thermodynamics, leading to the current emphasis on "structure-function relations" in biophysics: the function of a molecule is dependent only on its structure. I present here a simple system in which a signal molecule (or enzyme) can function as either an inhibitor or an activator of a product molecule in different environments, though the dynamics and rate constants of the reaction system are unchanged. This is caused by the fact that the system is not in equilibrium, but rather is in a non-equilibrium steady state. Since living biological systems are by definition far from equilibrium, this perspective sheds new light on the one-to-one correlation of form and function of enzymes.

Talk 13, 3:24—3:42. Modeling the mechanosensitivity of neutrophils passing through microfluidic channels
Tenghu Wu[1]*, James J. Feng[1,2]
1 Chemical and Biological Engineering, University of British Columbia
2 Department of Mathematics, University of British Columbia

Yap and Kamm (1,2) discovered that after passing through microfluidic channels, neutrophils may be activated by the mechanical deformation. They found that either small pore or fast flow rate could cause disassembly of the cytoskeletal network (CN) of the cell, which results in a sudden drop of the cell stiffness (fluidization). The CN disassembly is followed by activation of the neutrophil with formation of pseudopods. It is well known that the pseudopods protrusion is regulated by GTPase proteins. We propose a chemo-mechanical model for the fluidization and activation processes, based on the polarization of the Rac protein through wave-pinning. The 2D simulation deals with the mechanical interactions between the neutrophil and the surrounding fluid medium through the immersed boundary (IB) technique. The model captures the main features of the experimental observation.
1. B. Yap, and R. D. Kamm, Mechanical deformation of neutrophils into narrow channels induces pseudopod projection and changes in biomechanical properties, J. Appl. Physiol. 98:1930-1939 (2005).
2. B. Yap, and R. D. Kamm, Cytoskeletal remodeling and cellular activation during deformation of neutrophils into narrow channels, J. Appl. Physiol. 99:2323-2330 (2005).

Closing remarks, 3:42—3:55
Even numbered posters present. Refreshments, 3:55—4:35
Odd numbered posters present. Refreshments, 4:35—5:15
Awards, 5:15
End, 5:30

Poster abstracts

1. Numerical Investigation of the Effects of Microgravity on Stem Cell Modulation

Roza Vaez Ghaemi[1,2]*, Bahman Vahidi[1], Mohammad Hossein Sabour[3], Nooshin Haghighipour[4], Zakieh Alihemmati[1]
1 Division of Biomedical Engineering, Department of Life Science Engineering, Faculty of New Sciences and Technologies, University of Tehran, Tehran, Iran. 2 Department of Chemical and Biological Engineering, Faculty of Biomedical Engineering, The University of British Columbia, Vancouver, BC, Canada. 3 Department of Aerospace Engineering, Faculty of New Sciences and Technologies, University of Tehran, Tehran, Iran. 4 National cell bank of Iran, Pasteur Institute of Iran, Tehran, Iran.
Several evidences are reported on the influence of the physical environment on the stem cells fate. It has been reported that cells in normal gravitational condition are spread with a spindle configuration, while in the simulated microgravity conditions, transform to a rounded non-spread shape. In this paper, the effects of microgravity on mechanical behavior of stem cells under flow-induced shear stresses were evaluated through a computational simulation. Using fluid structure interactions the influence of a well-defined flow passing over a single stem cell was simulated in two different gravitational conditions. The simulation was performed using arbitrary Lagrangian-Eulerian (ALE) formulation and adaptive mesh procedure using a 3D model of a stem cell discretized via finite element method. Focusing on fluid-structure interactions, we developed the first cell-scale model for investigation of the stem cell mechanical behavior. The results indicate the changes in mechanotransduction mechanisms as a result of microgravity which in turn affect the stem cell lineage commitment.

2. Gypsy Moth Pheromone Binding Protein-Ligand Interactions

Jurgen Sanes* and Erika Plettner
Department of Chemistry, Simon Fraser University.
Pheromone binding protein (PBP) is believed to be part of the transport of hydrophobic pheromone in sensory hairs of insects. The interactions of gypsy moth PBPs towards different pheromones and their selectivity for the recognition of the main sex attractant, (+)-disparlure, (7R,8S)-epoxy-2-methyloctadecane, are not completely understood. To address this problem, docking simulations of the protonated homology PBP models with the enantiomers of various ligands (disparlure, 5-oxadisparlure, 10-oxadisparlure, 5-thiadisparlure and 10-thiadisparlure) were performed together with a binding assay..
The result of molecular simulations revealed different amino acid residues in the binding sites of PBP, abrupt movement of specific amino acid residues at a certain pH, distinct amino acid-ligand interactions (sidechain donors/acceptors, H-arene bonding, backbone donors/ acceptors) and a difference between total energies of the best bound conformers of each protein-ligand complex. Overall, the results may correlate with the pKa values obtained from the binding assay, and explain the enantioselectivity of the gypsy moth PBPs.

3. 3D reaction-diffusion modelling of conifer embryo development

David Holloway*
Mathematics Department, British Columbia Institute of Technology.
Cotyledons are embryonic seed leaves. In monocots (e.g. grasses) and dicots (e.g. flowering plants), cotyledon number is rigidly controlled. In contrast, conifers have variable numbers of cotyledons, which form in whorled crown patterns. The spacing between cotyledons appears to be constant, such that larger embryos have more cotyledons. Morphogenesis of the cotyledon crown shape depends on chemical growth catalysts which locally drive surface growth. We have developed a reaction-diffusion model for the spatial patterning of these chemicals, coupled to surface growth, to explore the dynamic constraints shaping conifer embryos. Hormone-disruption experiments indicate a two-stage process, with a broad annular pattern localizing the finer-scale cotyledon pattern. With a two-stage model, we are characterizing the morphogenetic effects of different nonlinear kinetics in each stage, the coupling between stages, and the coupling of chemistry to growth. This guides new experiments to map spatial patterns in the embryos.

4. Investigating force-induced structural changes in single collagen molecules

Michael W.H. Kirkness[1]* and Nancy R. Forde[2]
1 Department of Molecular Biology and Biochemistry, Simon Fraser University. 2 Department of Physics, Simon Fraser University.
Collagen is a structural protein found in abundance throughout the body; one of the functions of collagen is to maintain tissue structure in the presence of external forces. However the effect of force on the collagens structure is not clear: (1,2) in the presence of an external force, collagen has been proposed to have one of two opposing structural changes: either overwinding, reducing its cleavage (1) or underwinding, increasing its cleavage (2). Using a high-throughput single-molecule stretching instrument, the centrifuge force microscope (CFM) (3), we are developing a technique to investigate

force-dependent structural changes of collagen under various loading conditions. Here, we report on our progress tethering, enzymatically cleaving and applying a tuneable external force to single molecules of collagen..
1. Camp, R., et al. (2011) JACS, 133, 4073-8.. 2. Adhikari, A., et al. (2012) JACS, 134, 13259-65.. 3. Halvorsen, K. and Wong, W. (2010) Biophys J., 98, L53L55..

5. Mathematical Model of Neuronal Differentiation and Growth of Human Induced Pluripotent Stem Cells Seeded on Melt Electrospun Scaffolds

Meghan Hall[1]*, Nima Khadem Mohtaram[2]*, Stephanie Willerth[2], Roderick Edwards[1]
1 Mathematics and Statistics, University of Victoria. 2 Mechanical Engineering, University of Victoria.
We aim to derive a mathematical model of stem cell growth and neural differentiation on melt electrospun scaffolds. Based on experimental data, a compartmental ordinary differential equation model of neural stem, progenitor and terminally differentiated cells is developed to optimize experimental results. Using mathematical analysis and numerical simulations, the model can be used to determine the key factors controlling growth and differentiation of these cells when seeded on melt electrospun scaffolds. Once such key factors are identified, the dynamics of the model can be determined and the parameters modified to push the system into the desired state, corresponding to altering current experimental protocol in order to optimize growth and differentiation. Using melt electrospinning, we made poly (ϵ-caprolactone) microfibers with varied topographical properties to serve as biocompatible tissue-engineered scaffolds. We showed that a higher porosity scaffold could enhance cell viability and growth of seeded hiPSCs compared to a lower porosity scaffold.

6. Osmotic Inhibition of Alkaline Phosphatase

Oksana Yavroska, Chantal Carrier and John Chik*
Department of Chemistry, Mount Royal University.
Enzymes operate in an aqueous environment crowded with many other agents. In addition to specific interactions, these solutes may also indirectly modify enzyme behaviour through changes in water chemical potential as measured by the osmotic pressure. Using UV-visible spectrometry, we have measured the kinetics of para-nitrophenylphosphate (PNPP) hydrolysis catalyzed by bovine intestinal alkaline phosphatases in the presence of various solutes such as betaine, sucrose and various glycols. The effects of these osmolytes are analogous to classic, small-molecule competitive and uncompetitive inhibition. From this Michaelis-Menten kinetics perspective, it is suggested that osmotic inhibition is due to conformational changes resulting from dehydration of enzyme and/or enzyme/substrate complex.

7. Bioconjugation of Aurein Antimicrobial Peptides and Hyperbranched Polygycerol Systems

Prashant Kumar[1]*, Rajesh A. Shenoi[2], Benjamin. F. L. Lai[2], Michael Nguyen[1], Jayachandran N. Kizhakkedathu[2], Suzana K. Straus[1].
1 Department of Chemistry, UBC. 2 Department of Pathology, UBC.
Antibiotics have been used for decades to combat bacterial infection. However, there has been an increase in antibiotic resistance recently. Therefore, alternatives such as antimicrobial peptides which have little or no antimicrobial resistance are ideal candidates for therapy. However, two major problems faced when developing these peptides for therapeutics are cell toxicity and decreases in vivo activity. On the other hand, various polymers such as polyethylene glycols are are used for many different research purpose such as protein crystallization,, drug conjugation, and other medical application. Recently, there has been an increasing interest in poylglycerols (PGs) in biomedical applications due to their being highly biocompatible. These polymers have hydroxyl groups that are easily accessible for functionalization with various biomolecules such as RNA, DNA and proteins. We are currently synthesizing Aurein-Hyperbranched polyglycerol conjugates and characterizing using NMR. Recent data shows a decrease in toxicity of the conjugates when compared to peptide only.

8. Probing membrane fusion by daptomycin

Jin Zhang*, Suzana K. Straus
Department of Chemistry, UBC.
Daptomycin is a lipopeptide antibiotic that is composed of 13 amino acid residues. Since its first clinical use in 2003, daptomycin has played a major role in the treatment of infections caused by Gram-positive bacteria. Its activity requires calcium and target membranes content of lipids with acidic headgroup. Although lots of research has been done to study the mechanism, the antibacterial action of daptomycin is still under investigation. From a previous study, we know that daptomycin can induce membrane fusion in the presence of calcium ion. In order to study the factors that affect membrane fusion, calcium and various lipids with different concentrations were mixed with daptomycin. In addition, NBD-labeled daptomycin has been synthesized for future research using fluorescence methods.

9. Probing the interactions between U24 from HHV6A/7 and Proline rich binding domains

Yurou Sang[1]*, Walter R. P. Scott[1], A. Louise Creagh[2], Charles A. Haynes[2], Suzana K. Straus[1]
1 Department of Chemistry, UBC. 2 Michael Smith Laboratories, UBC.
U24 is a type II tail-anchored putative membrane protein unique to the Roseolovirus family, including HHV-6 and HHV-7. It contains an N-terminal proline-rich region and is believed to function by disrupting the signalling pathway in order to ensure the virus survival. Both species have been found linked to neurological disease, like MS and this unique membrane protein could be the reason. In order to elucidate the exact role of U24 in MS, we have investigated the interaction of U24s with other partners such as the SH3 domain from Fyn tyrosine kinase and WW domain proteins. GST pull-downs, ITC, NMR were used. The differences in binding observed for U24 from HHV-6A and -7 will shed light into the hypothesis that U24 may function by disrupting the signalling pathway involves proline-rich regions.

10. On a novel approach in erythropoiesis modeling

Frédéric Paquin-Lefebvre[1,2]*, Jacques Bélair[3]

1 Department of Mathematics, UBC. 2 Institute of Applied Mathematics, UBC. 3 Dpartement de Mathmatiques et de Statistique, Universit de Montral.

We consider erythropoiesis mathematical modeling, which is the process of erythrocytes production and its regulation by erythropoietin. We propose an erythropoiesis model extension which includes aging of mature cells. First, an age-structured model with moving boundary condition, whose dynamics are represented by advection equations, is considered. This model may then be transformed into a system of delay differential equations, where delays represent life and maturation times. Finally, a new model is introduced, which includes an exponential death rate depending on erythrocytes maturity level. A linear stability analysis allows to detect simple and double Hopf bifurcations emerging from variations of the gain in the feedback loop and from parameters associated to the survival function. Numerical simulations also suggest a loss of stability caused by interactions between two linear modes and the existence of a two dimensional torus in the phase space close to the stationary solution.

11. Scattering-based illumination for a feedback trap

Momčilo Gavrilov, Jan Koloczek, and John Bechhoefer

Department of Physics, Simon Fraser University.

Feedback traps can create arbitrary virtual" potentials for trapping and exploring the dynamics of a single particle or molecule in solution. Feedback traps have been used to measure the physical and chemical properties of many types of biomolecules and to explore fundamental questions in non-equilibrium statistical mechanics. In a feedback trap, the particle position is measured periodically; after each measurement, one applies the force given by the gradient of virtual potential at the measured position. Here, we implement dark-field microscopy for observing a particle and improving position measurements. In our setup, we use wide-angle laser illumination of freely diffusing beads in water collecting scattered light in our detector while blocking the excitation laser beam. This new scattering-based technique gives several orders of magnitude higher count rates than commonly used fluorescence-illumination schemes. The higher count rates allow us to decrease the exposure time, increase trap bandwidth, and avoid complications related to photobleaching.

12. Measurement of the Temporal Coherence Length of Laser Diodes for Biomedical Applications

Daniel C. Louie[1]*, Lioudmila Tchvialeva[2], Tim K. Lee[2,3]

1 Electrical and Computer Engineering, University of British Columbia. 2 Dermatology and Skin Science, University of British Columbia. 3 Cancer Control Research Program, BC Cancer Agency.

Laser diodes are used extensively in biomedical applications. Knowing the temporal coherence function of a laser is crucial for techniques such as Optical Coherence Tomography and Speckle Contrast Imaging. However, laser diodes have a multi-peak emission spectrum, resulting in a coherence function that usually requires specialized equipment to measure. This project uses a rudimentary Michaelson Interferometer, modified to allow manual path length change and to use a single photodiode as a detector in order to avoid the typical requirements of long path lengths and 2D fringe pattern analysis. The results obtained from this method matched the results found by a specialized Fourier Spectrometer. A relationship between the laser diodes spectrum, its thermal properties, and their ultimate effect on the coherence length was discovered incidentally during this project. The method created for this project can be used to facilitate the use of laser diodes for future studies in biomedical optics.

13. Spatiotemporal periodicity of tooth turnover in leopard geckos from hatchling to juvenile stages

Theresa Grieco*, Joy Richman

Oral Health Sciences, University of British Columbia.

Many reptiles replace their teeth continuously, providing an opportunity to understand the regulation of tooth turnover. We present preliminary data from a longitudinal study of tooth replacement from hatching to juvenile stages of leopard geckos (Eublepharis macularius). Upper jaw wax impressions revealed dynamic patterns of tooth shedding and midline symmetry. Typically, a tooth is shed in one week and replaced by a functional tooth within the next week. When viewed as a spatial pattern across the tooth row over time, waves of tooth shedding pass through even and odd series from the back to the front of the jaw. The regularity of the observed patterns suggest emergent tooth turnover phenomena that may result from the order of tooth initiation between tooth families, local inhibitory influences within the jaw, and the rates of development within tooth families. Studies are currently underway to assess the influence of each of these factors.

14. Elucidating the mechanism by which mechanical force stabilizes Cell-ECM adhesion during development.

Pablo López-Ceballos[1]*, Katrin Hakonardottir[1], Alejandra Herrera-Reyes[2], Daniel Coombs[2] and Guy Tanentzapf[1].

1 Cellular and physiological sciences, UBC. 2 Department of Mathematics, UBC.

During development cells in multicellular organisms are arranged to form complex-three dimensional shapes. To achieve such complexity, cells form adhesive contacts with the extracellular matrix (ECM). During early embryonic development Cell-ECM adhesions are typically dynamic and transient but later on, as tissue architecture is consolidated, they become stable and long lasting. We are interested in the mechanisms that regulate this developmental transition. The principal mediators of Cell-ECM adhesion are the integrin family of adhesion receptors. Integrin-based adhesions undergo assembly and disassembly, or turnover and this regulates the duration and strength of Cell-ECM attachment. We are interested in how integrin-mediated adhesion turnover is controlled by mechanical force. We combine FRAP and mathematical modeling to elucidate the kinetics of adhesion complex turnover. Our analysis demonstrates a role for mechanical force in regulating turnover of Cell-ECM adhesions and in stabilizing cell adhesions over the course of development.

15. Consequences of Variability in Initiation Factors for DNA Replication
Mike Chomitz*, John Bechhoefer
Physics, Simon Fraser University.
In each cell cycle, the DNA of an entire genome must be copied, or replicated. Because the genome is large and replication is slow, the process starts at many locations (origins) along the genome. Each origin starts replicating (initiates) after S phase (the synthesis phase of the cell cycle) begins. Past work analyzing the replication profile of the model organism Saccharomyces cerevisiae (budding yeast) implies the existence of a mechanism set in place before replication starts. The mechanism, which has been ascribed to multiple initiators that are loaded at each origin, tightly defines initiation times for origins but loses effectiveness as time passes. This multiple initiator model (MIM) of replication control assumes, in its simplest form, that the number of initiators is constant at a given origin at each cell cycle. Recent experiments imply otherwise, and, in this poster, we investigate the consequences of this variability.

16. DNA replication: Inferring what happens and when
Laura Geisler[1]*, John Bechhoefer[2]
1 Physics, Technical university Dresden, visitor at Simon Fraser University. 2 Physics, Simon Fraser University.
The duplication of the cells genome by DNA replication is an important process for cellular life. During the synthesis phase (S phase) of the cell cycle, multiple particular sequences in the genome (replication origins) initiate DNA replication.Those initiations can be described as stochastic events.With multiple origins that initiate at different times, a key problem is to understand the spatiotemporal "program" of replication to understand the mechanisms determining where the origins are along the genome and when they initiate during S phase. Previous work introduced a machine-learning technique known as "Gaussian process regression" to infer initiation rates of replicated origins from experimental data.The technique works very well for small data sets, but is too slow for larger sets. In this poster, we present new mathematical methods that can scale to large data sets much more efficiently.These new methods will allow us to analyze experimental replication data atchromosome scales.

17. Interaction between U24 from Human Herpesvirus Type-6A or Type-7 and Proline-rich Binding Domains
Yurou Sang[1], Walter R. P. Scott[1], A. Louise Creagh[2], Charles A. Haynes[2], and Suzana K. Straus[1]
1 Chemistry, University of British Columbia. 2 Michael Smith Laboratories, University of British Columbia.
U24 is a type II tail anchored putative membrane protein unique to the Roseolovirus family, including HHV-6 and HHV-7. It contains an N-terminal proline-rich region and is believed to function by disrupting the signalling pathway in order to ensure the virus' survival. HHV-6A is a neurovirulent virus as it is often found in multiple sclerosis (MS) patients. On the other hand, HHV-7 does not have a direct link to MS but might be implied indirectly. Both type of U24 have been found to affect the endocytic recycling of transferrin receptors in T-cells and it is possible that this function leads to improper response of immune system in MS patients..
In order to elucidate the exact role of U24 in MS, we have investigated the interaction of this protein with other partners such as the Fyn-SH3 domain and WW domains using pulldowns, ITC, NMR and MD simulations.

18. Using optical tweezers to assess the role of inter-protein interactions in collagen self-assembly
Tuba Altindal*, Marjan Shayegan, Evan Kiefl and Nancy R. Forde
Department of Physics, Simon Fraser University.
Collagen is a structural protein that self-assembles into fibrillar structures in the extracellular matrix. Collagen self-assembly into fibrils relies on specific interactions between these proteins. Here, we describe our studies using optical-tweezers-based passive microrheology to investigate how the removal of telopeptides - short non-helical regions flanking the triple helical domain of collagen - influences interactions between collagen molecules. We find that telopeptides contribute substantial elasticity to collagen solutions at timescales from 10 msec to 1 sec and telopeptide-intact collagen solutions deviate from the single-mode relaxation Maxwellian behavior at low frequencies with increasing concentration, suggesting the presence of transient telopeptide-collagen interactions.

19. On the possibility of predicting extinction using time series population data
Takashi Nakamura*
Mathematics, British Columbia Institute of Technology.
In this presentation we will discuss the possibility of predicting catastrophic change, that could lead to extinction, in the time series data of a population following a stochastic Lotka-Volterra type dynamics. The Lotka-Volterra systems exhibit bifurcation phenomena when a parameter is smoothly changed. In the deterministic case, a stable fixed point becomes unstable and bifurcation occurs. The result is a collapse of one of the populations. The centre manifold theory states that in a many-dimensional dynamical system the dynamics is restricted to a lower dimensional manifold near a bifurcation point. We apply the singular spectrum analysis (SSA) to the time series of one of the populations obeying the generalised Lotka-Volterra equation with a random driving force (birth rates). We show that a simple index, computed from the eigenvalues obtained from SSA, indicates the reduction of dimensionality near the bifurcation point.

20. Exploring the binding properties of U24 protein from Human Herpes Virus type 6A and WW domains
Rui Zhang*, Yurou Sang, Suzana K. Straus
Chemistry, UBC.
The binding properties of the protein U24 from Human Herpes Virus type 6A (HHV-6A) were investigated. U24 from HHV-6A is recognized as a tail anchored membrane protein with a proline rich region at its N-terminus. As known

proline-rich ligand scaffolds, WW domains are crucial binding domains in different cellular signaling pathways. Therefore, studying the interaction associated between WW domains and U24 could shed light into the role of U24 during HHV-6A infections.

21. Alignment of a magnetic filament in the presence of shear flow

D. Luesebrink[1,2], J. Cerda[2], P. Sanchez[3], T. Sintes[2]
1 Physics, University of British Columbia. 2 IFISC, University of the Balearic Islands. 3 Physics, University of Vienna.
Magnetic filaments are supramolecular magnetic polymers with technological applications ranging from magnetic memories, nanosensors, to magnetically-imprinted authentication. We present a numerical study of the behavior of a magnetic filament subjected to the simultaneous action of a fluid flow and an external magnetic field. The magnetic filament is represented by a coarse-grained bead-spring model where each bead carries a magnetic dipole. The hydrodynamic coupling of the filament with the flow is accounted for using Multi-Particle Collision dynamics. In the presence of flow and at zero external field the filament undergoes subsequent, aperiodic coiling-stretching transitions. These transitions are strongly inhibited by the external magnetic field, which is able to stabilize the filament, and induce a well-defined degree of alignment that depends on the balance between hydrodynamic and magnetic torques. Results of Poiseuille flow are investigated with respect to the persistence of initial conditions and compared to the case of uniform shear flow.

22. Computational Modeling of Functional Amyloids and Peptide Aggregation

Roy Nassar* and Jörg Gsponer
Center for High-Throughput Biology, UBC.
Amyloid fibrils have been associated with various incurable diseases such as Alzheimers, Parkinsons, Huntingtons, ALS and type II diabetes. These fibrils are highly ordered structures of protein aggregates stabilized in a so called cross-beta configuration by intermolecular interactions. Therefore, understanding the underlying structure, formation and toxicity of amyloid fibrils has attracted many efforts owing to the potential implications in medicine (drug design) as well as in biotechnology. Interestingly, recent studies have led to the discovery of naturally occurring aggregates that are non-pathological, but are incorporated into cellular processes to serve diverse biological functions (peptide hormones storage, structural templates, regulatory switches and prions). This work consists of computational approaches aiming at investigating physical and chemical properties of these two types of aggregates. Are there features that distinguish between them? We are also interested in the molecular mechanisms of amyloid formation and hence employ molecular dynamics simulations to investigate these early oligomeric states that might display different kinetic tendencies in functional and toxic aggregates.

23. Elucidating Interactions within Iron Uptake Regulatory Proteins using X-ray Adsorption Spectroscopy

Mustoe, Chantal[1]*; Meghan Verstraete[2]; Murphy, Michael[2]; Kennepohl, Pierre[1]
1 Chemistry, University of British Columbia. 2 Microbiology, University of British Columbia.
Despite the fact that 20% of the human population carries Staphylococcus aureus as part of their normal skin flora, this bacterium is a leading cause of bacterial infections worldwide and is the single leading cause of hospital-acquired infections. Key to the bacteriums establishment of human infection is the acquisition of iron from the host environment. In S. aureus, the protein SbnI, which itself is regulated by heme, plays an important regulatory role in the acquisition of iron. S K-edge and Fe K-edge XAS experiments have been used to probe the interactions between a cysteine residue in the C-terminus of SbnI (C244) and the coordinating heme. Elucidating these interactions could provide key insights into S. aureus use of host iron thus providing new strategies for drug development.

24. Modeling Posterior Lateral Line Primordium in Zebrafish

Dhananjay Bhaskar*, Cole Zmurchok*, Hildur Knutsdottir, Leah Edelstein-Keshet
Mathematics, UBC.
The lateral line system in Zebrafish consists of sensory organs that detect water flow over the surface of the animal. Formation of the posterior lateral line (PLL) takes place early in development when a cohort of roughly 125 cells migrates along the length of the fish periodically depositing neuromasts, which contain a mechanosensory hair cell at their centre. Directional migration of the PLL primordium is characterized by the presence of chemokine Sdf1a along the migration path and it's role in establishing polarized Wnt and FGF signalling systems. We will describe mathematical and computational models that we are using to study coordinated directional cell migration and the role of chemokine signalling in neuromast formation.

25. Enzyme Kinetic Studies and Molecular Docking Simulations in the Oxidative Transformation of 3-Chloroindole by Cytochrome P450cam Mutants

Shaima Kammoonah*, Erika Plettner
Chemistry, Simon Fraser University.
Cytochrome P450cam, a monooxygenase isolated from Pseudomonas putida, catalyzes the hydroxylation of (1R)-(+)-camphor. We have constructed a mutant library of this enzyme through sequence saturation mutagenesis to increase its substrate scope. My focus is on the oxidative dehalogenation of 3-chloroindole by P450cam mutants. The proposed mechanism for the hydroxylation of 3-chloroindole suggests that two consecutive oxidations by P450cam generate isatin, while one oxidation gives an epoxide intermediate. Enzyme kinetic studies and molecular docking simulations are performed to understand the effect of specific mutations on the activity of the enzyme, affinity of the substrate, and the positioning of

amino acid residues in the active site. These studies will enable us to focus on enhancing the steps that yield the products or intermediates of interest. Substrate turnover is monitored via UV-VIS spectroscopy and gas chromatography-mass spectrometry.

26. Rationally Designed Dynamic Protein Hydrogels with Reversibly Tunable Mechanical Properties

Na Kong*, Qing Peng, Hongbin Li
Chemistry, University of British Columbia.

Here we report the engineering of a stimuli-responsive protein hydrogel with dynamic mechanical properties based on mutually exclusive proteins. Using a well-established photochemical crosslinking strategy, we crosslinked the aqueous solution of this redox-responsive protein into solid hydrogels. We found that oxidation and reduction of the disulfide bond occurring at molecular level leads to significant changes of the physical and mechanical properties of the hydrogel on the macroscopic scale. When the disulfide bond is reduced, the hydrogel swells to a higher degree and is mechanically more compliant. When the disulfide bond is oxidized, the hydrogel becomes stiffer and shows a 3-fold increase in its Youngs modulus. The mechanical and physical properties of the hydrogel can be cycled between the two distinct states reversibly in response to the redox potential. This novel protein hydrogel with dynamic mechanical and physical properties may find applications in the field of material sciences and tissue engineering.

27. Natural scene movie responses and cortical states in anesthetized cat V1

Martin A Spacek*, Nicholas V Swindale
Ophthalmology, University of British Columbia.

We recorded spikes from dozens of neurons simultaneously across layers of isoflurane-anesthetized cat primary visual cortex (V1), using high-density silicon microelectrodes. Responses to repeated natural scene movie clips had remarkably sparse, precise, reliable events. Neurons had distinct temporal patterns of response events, some precise to within 20 ms. Cortical state was quantified from the frequency distribution of deep-layer local field potential, switching spontaneously between synchronized (1/f) and desynchronized (broadband). Contrary to reports in anesthetized rodents, responses were more precise and reliable during the synchronized than desynchronized state. This is surprising, because the desynchronized state under anesthesia is thought to correspond to attending periods in awake animals, and responses are known to be enhanced during attention. Our results therefore question the analogy between cortical states in anesthetized and awake animals. One possible, testable, explanation for this result is that cats have stimulus feature maps in V1, but rats do not.

28. Measuring whole white matter damage in the dorsal spinal cord: a comparison of histology and MRI

Rhys Chappell[1]*, Evan Chen[2]
1 General Science, University of British Columbia. 2 Biomedical physics, University of British Columbia.

Magnetic resonance imaging (MRI) provides detailed images without the use of ionizing radiation, and may be used to assess damage to the central nervous system in patients with spinal cord injuries (SCI). More than 86 000 Canadians currently live with a SCI, and the costs associated with this total over $3.6 billion annually..
In this study SCI was modeled with a dorsal column incision that severs white matter (WM) axons. The subsequent axonal degeneration was observed through MRI and histology at three and eight weeks post injury..
Histology analysis shows increased macrophage presence in WM post injury, as well as increased axon content staining. MRI data indicates that these changes correlate to decreased MRI values for WM cranial and caudal to the injury at three weeks..
With further study these correlations between MRI and histology data may be used to assess MRI images of human SCI patients with WM damage.

29. AFM study of the potential controlled incorporation of liposomes into an octadeanol covered Au(111) electrode.

Amanda Musgrove and Dan Bizzotto*
AMPEL & Department of Chemistry, University of British Columbia.

The incorporation of DOPC liposomes (100 nm diameter) into a octadecanol coated Au(111) electrode surface was studied using both in-situ fluorescence microscopy and AFM imaging in an electrochemical environment. The potential drop across the adsorbed octadecanol layer was a critical variable which could allow or prevent the incorporation of the liposomes onto the Au surface. At potentials where the layer was stable and well formed, the liposomes were not observed to become associated with the surface. When the potential was made more negative, the potential dependent formation of defects allowed the liposomes to become incorporated and when removing the potential the liposome - octadecanol hybrid layer was stable. This approach can be used to create adsorbed lipid layers with the possible incorporation of membrane proteins onto the solid surface.