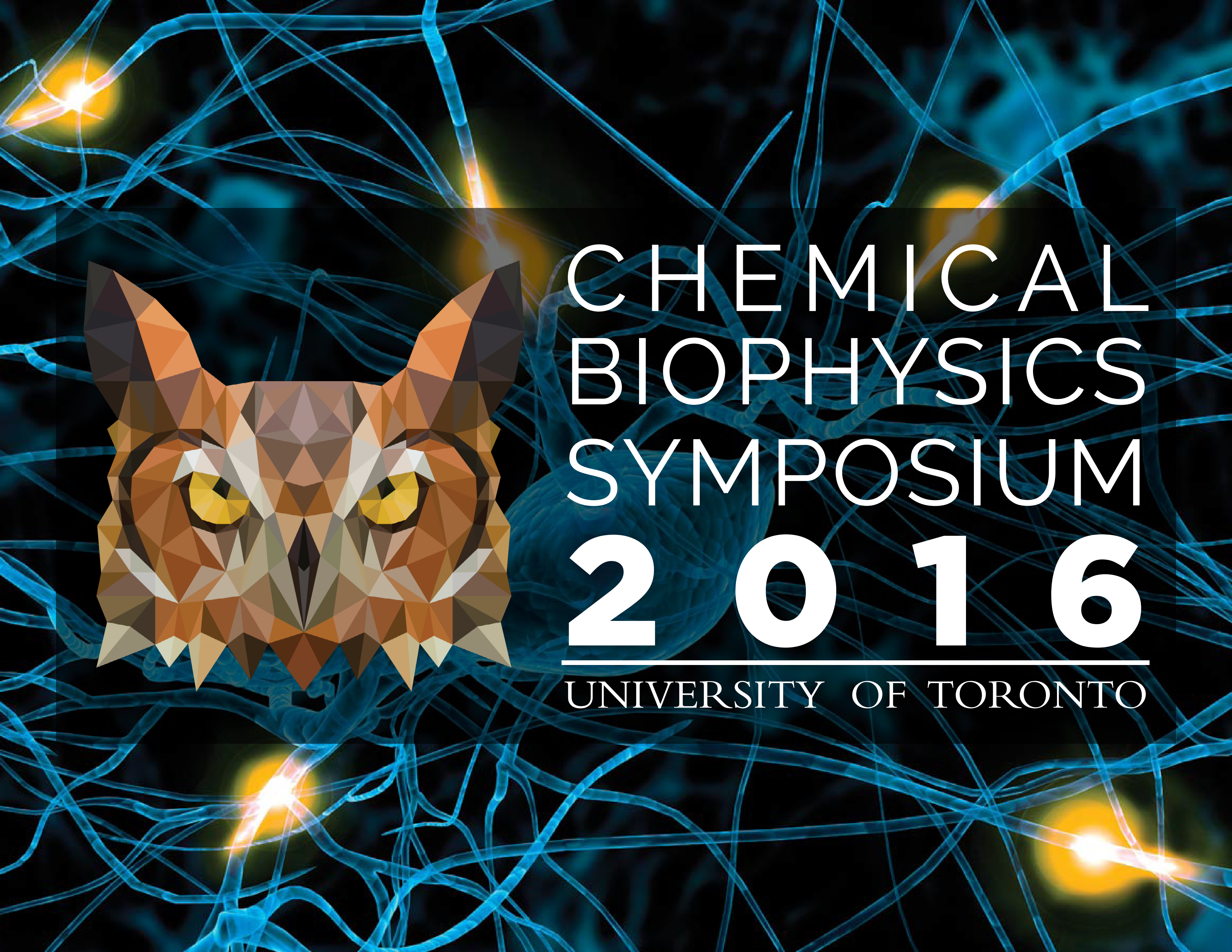
CHEMICAL
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Welcome to the 15th Annual CBP - Message from the Chair

It is my pleasure to welcome everyone to the 15th annual Chemical BioPhysics Symposium! For years CBP has served as an event that brings together researchers from across various disciplines including chemistry, biology, and physics. We are pleased to have researchers from various disciplines presenting their latest work, and we hope that you find CBP to be a unique opportunity to engage in fruitful discussions with colleagues from all around the world.

Year after year, the organizing committee is committed to improving the quality of the conference for our attendees. This year, we hope you take advantage of the Friday morning workshops that are offered, whether it is learning how to use Python or learning to apply your knowledge as an entrepreneur. Traditionally, a panel discussion is held on Friday. This year, we wanted to try something new so we invite you to join us for a light-hearted Q&A session with our invited panelists.

The CBP takes pride in providing an intimate atmosphere and fostering a close-knit scientific community. In addition to our invited speakers and contributed talks, we will also be hosting two lively poster sessions on Saturday. And of course, we have continued the tradition of hosting numerous social events and coffee breaks throughout the meeting so we encourage you take advantage of these opportunities to meet our keynote speakers, catch up with old friends, make new connections, and engage in stimulating discussions.

It is only until recently that I've come to realize how lucky our committee has been that the wise owl was consistently chosen as our symposium's mascot. It is after 15 years and a random Google search that we learned that when seen together, a group of owls is referred to as a *Parliament*. With this being said, I hope that our dedicated organizing members, aka *Parliament members,* have prepared what promises to be an exciting and memorable experience for everyone. We hope everyone has a HOOT and we look forward to seeing you again in 2017!

– Kris Kim –
Chair, CBP 2016

CBP 2016 Organizing Committee

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Friday, May 13th, Leslie L. Dan Pharmacy Building

Time	Event	Location
9:00 – 10:00 AM	**Registration**	**Main Lobby**
10:00 AM – 1:00 PM	**Workshop: Marcelo Ponce, SciNet** Introduction to Data Visualization using Python	**PB255**
	Workshop: Professor Cynthia Goh An Entrepreneurial Mindset: A Culture of Innovation and Bringing Science to Society!	**B150**
1:00 – 3:00 PM	**Registration**	
3:00 – 3:30 PM	Opening Remarks – Kris Kim	**B150**
Session I	**Chair**: Kris Kim Sponsored by FACETS by Canadian Science Publishing	
3:30 – 4:30 PM	**Sarah Heilshorn** (Stanford University) Protein –Engineered Materials for Regenerative Medicine	
4:30 – 4:50 PM	**Laleh Alisaraie** (Memorial University of Newfoundland) Computational Simulation of Antibiotic Resistance Enzyme APH(3')-IIIa in Complex with Deoxystreptamine-containing Aminoglycosides	
4:50 – 5:10 PM	**Kiril Fedorov** (University of Toronto) Prevention of Surface Fouling with a New Simple and Robust Coating on Medical Equipment	
5:10 – 5:30 PM	**Amani A. Hariri** (McGill University) Stepwise Growth of Surface-Grafted DNA Nanotubes Visualized at the Single Molecule Level	
5:30 – 6:15 PM	Panel Discussion: Q&A	
6:15 – 7:15 PM	**Dinner Buffet**	**Main Lobby**
Session II	**Chair:** Elnaz Alipour Sponsored by FACETS by Canadian Science Publishing	**B150**
7:15 – 7:35 PM	**Joshua Mogyoros** (University of Guelph) Flexibility of Bacterial Type IV Pili Determined Using Atomic Force Microscopy	
7:45 – 8:45 PM	**Alex Mogilner** (New York University) Design Principles of Mechanics and Transport in Self-Polarizing Actin-Myosin Network	

Saturday, May 14th, Leslie L. Dan Pharmacy Building

8:30 - 9:30 AM	**Continental Breakfast**		**Main Lobby**
Session III	**Chair:** Jennifer Tran		**B150**
9:30 – 10:30 AM	**Yan Yu** (Indiana University) Embracing Asymmetry: Designing Janus Interfaces to Image and Control Cellular Dynamics		
10:30 – 10:50 AM	**Danielle M. Charron** (University of Toronto) Biomimetic Dye Aggregation Enabling Nanostructure-Dependent Ratiometric Fluorescence		
10:50 – 11:10 AM	**Sissi de Beer** (University of Twente) Towards Unraveling and Eliminating Dissipation Mechanisms in Polymer Brush Friction		
11:10 – 11:30 AM	**Christina F. Calver** (McGill University) Exploiting Conjugated Polyelectrolyte Photophysics toward Monitoring Real-Time Lipid Membrane-Surface Interaction Dynamics at the Single-Particle Level		
11:30 AM – 12:30 PM	Poster Session I (Odd #)	Sponsored by FACETS by Canadian Science Publishing	**Main Lobby**
12:30 – 1:30 PM	**Lunch**		
Session IV	**Chair:** Amr Dodin	Sponsored by Nicoya Lifesciences	**B150**
1:30 – 2:30 PM	**Gabriela S. Schlau-Cohen** (Massachusetts Institute of Technology) Elucidation of the Photoprotective Mechanisms in Algal Light Harvesting		
2:30 – 2:50 PM	**Brendan Hussey** (University of Toronto Mississauga) Engineering a T7 RNA Polymerase for Programmable Transcription Initiation		
2:50 – 3:10 PM	**Sebastian Himbert** (McMaster University) Organization of Nucleotides in Different Environments: Implications for the Formation of First RNA under Prebiotic Conditions		
3:10 – 3:30 PM	**Vrathasha Vrathasha** (University of Delaware) Elucidating the Mechanism Behind CK2 Mediated Mesenchymal Stem Cell Differentiation Into Osteoblast and Adipocytes via BMPR1a Signaling		
3:30 – 4:30 PM	Poster Session II (Even #)	Sponsored by Avanti Polar Lipids	**Main Lobby**

Session V	**Chair**: Caroline Pao	**B150**
4:30 – 5:00 PM	**Hendrick W. De Haan** (University of Ontario Institute of Technology) Nonlinear Dynamics for the Translocation of the *fd* Virus through Nanopores: Euler Buckling at the Nanoscale	
5:00 – 6:00 PM	**Mark MacLachlan** (University of British Columbia) All Twisted Up: New Materials from Cellulose Nanocrystals	
6:00 – 6:30 PM	Break and travel to restaurant	
6:30 PM onwards	**Banquet Dinner:** Dim Sum King Seafood Restaurant 421 Dundas St. West, 2nd Floor Toronto, ON M5T 1G6	

Sunday, May 15th, Leslie L. Dan Pharmacy Building

9:00 – 10:00 AM	**Brunch**	**Main Lobby**
Session VI	**Chair**: Bryan Robertson	**B150**
10:00 – 10:30 AM	**Aleksandra Dabowska** (Lund University) Lipid Bilayers Direct Assembly of RNA Nano-Structures on Surfaces	
10:30 – 11:30 AM	**Herbert Levine** (Rice University) Cell Motility – From the Individual to the Collective	
11:30 – 11:45 AM	**Coffee break**	
Session VII	**Chair**: Duncan Smith-Halverson	
11:45 AM – 12:45 PM	**Donald Weaver** (University of Toronto) Designing New Chemical Entities to Inhibit Cytotoxic Protein Misfolding	
12:45 – 1:00 PM	**Closing Remarks**	

Abstracts

Oral Presentations

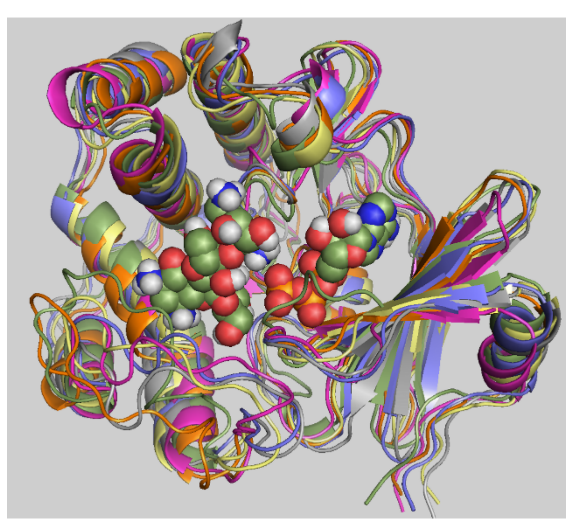
Protein-Engineered Materials for Regenerative Medicine **Session I, Fri 3:30 PM**

Sarah Heilshorn, *Stanford University*

Stem cell transplantation is a promising therapy for a myriad of debilitating diseases and injuries; however, current delivery protocols are inadequate. Transplantation by direct injection, which is clinically preferred for its minimal invasiveness, commonly results in less than 5% cell viability, greatly inhibiting clinical outcomes. We demonstrate that mechanical membrane disruption results in significant acute loss of viability at clinically relevant injection rates. As a strategy to protect cells from these damaging forces, we show that cell encapsulation within hydrogels can significantly improve transplanted cell viability. Building on these fundamental studies, we have designed a family of injectable, bioresorbable, customizable hydrogels using protein-engineering technology. By integrating protein science methodologies with simple polymer physics models, we manipulate the polypeptide chain interactions and demonstrate the direct ability to tune the material properties including hydrogel mechanics, cell-adhesion, and biodegradation. Through a series of *in vitro* studies, we demonstrate that material degradability is a critical requirement to maintain the "stemness" of neural progenitor cells in 3D hydrogels and that this effect is independent of mechanosensing through cytoskeletal contractility. Together, these data demonstrate that protein-engineered hydrogels may significantly improve transplanted stem cell retention and regenerative function.

Computational Simulation of Antibiotic Resistance Enzyme APH(3')-IIIa in Complex with Deoxystreptamine-Containing Aminoglycosides **Session I, Fri 4:30 PM**

Laleh Alisaraie, *Memorial University of Newfoundland*



Antibiotics are primarily provided to fight infectious diseases. Aminoglycoside antibiotics have been used to treat both gram positive and negative bacteria; however misuse of these drugs has resulted in high expression of antibiotic resistance enzymes, some of which alter the chemical structure of antibiotics, thus prevent them from binding to the 16S RNA site. This research has focused on the chemical alteration of aminoglycoside antibiotics by the 3',5"-phosphotransferase-IIIa. Aminoglycoside antibiotics with a 4, 5-disubstituted 2-deoxystreptamine ring are chemically modified at the 3' and 5" hydroxyl groups by the enzyme. In this project, computational calculations and simulations such as Molecular Dynamics were carried out for the structural analysis of the molecular complexes of the antibiotics with the enzyme, and the results will be discussed during the presentation.

Prevention of Surface Fouling with a New Simple and Robust Coating on Medical Equipment **Session I, Fri 4:50 PM**

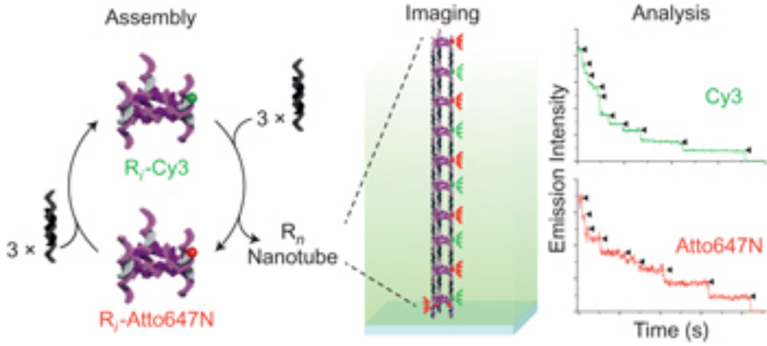
Kiril Fedorov, *University of Toronto*

Exposure of synthetic materials to body fluids may result in undesirable protein−material interactions that can potentially trigger deleterious biological processes such as thrombosis. The result is increased chances of heart attack, stroke or other cardiovascular complication after extravascular blood procedure. For our experiment we have chosen wide variety of materials including: poly (methyl methacrylate) (PMMA), poly (vinyl chloride) (PVC), several common plastics, metals and other types of materials used in the medical industry. All materials had undergone a coating procedure and were characterized with X-ray photoelectron spectroscopy, attenuated total internal reflection and contact angle goniometry. All characterization methods confirmed the coating to be stable and functional on all materials. Several of the coated materials (PVC, PC, steel 361) were tested directly for their compatibility with whole human blood. Antithrombogenicity was assessed after 2,5,10 and 60 min, 3 hours, 6 hours exposure to whole human blood dispensed at a shear rates of 1, 300, 900, 1000 and 1500 s^{-1}. Overall the coating had shown reduction at ~90% or more in adhesion and clot formation on all times and shear rates. Protein composition has also been analyzed with SDS –PAGE showing Vroman effect to be slowed significantly by the surface coating. Currently animal trials are ongoing. Overall the coating proved to be robust on wide variety of materials and has shown very high potential in blood compatibility.

Stepwise Growth of Surface-Grafted DNA Nanotubes Visualized at the Single Molecule Level **Session I, Fri 5:10 PM**

Amani A. Hariri, *McGill University*

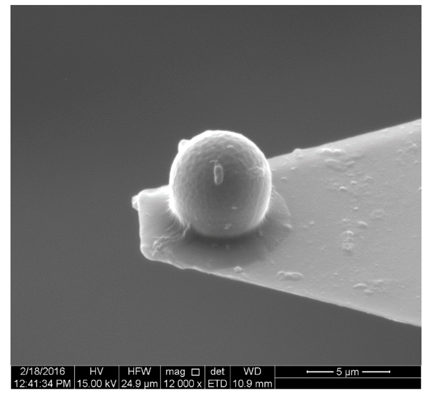
DNA nanotubes offer an exquisite high aspect ratio and rigidity, desirable attributes for the controlled assembly of hierarchically complex linear arrays. A major limitation towards the full realization of their potential is the ability to control positioning along their backbone and to minimize polydispersity in their manufacture. We report here a solid-phase synthesis [1-2] methodology of DNA nanotubes that circumvents these problems. Starting from a "foundation rung" specifically bound to the surface, we are able to serially incorporate in a cyclic scheme pre-fabricated DNA-rungs and linkers delivered and removed in a flow-through chamber in a controlled fashion. Each rung is orthogonally addressable. Prototype structures consisting of up to twenty repeat units, ca. 450 nm in contour length, were constructed. Single molecule fluorescence imaging further provides unique opportunities to inspect and validate the assembly process: Using fluorescently tagged rungs, single-molecule photobleaching studies proved the robustness and structural fidelity of the constructs and confirmed the incorporation of the rungs in quantitative yield (>95%) at each step of the cycle. Combined, the solid-phase synthesis strategy described and its visualization via single-molecule spectroscopy pave the way for the production of custom-made DNA nanotubes with distinct orthogonally addressable rungs laid out in a pre-determined manner along the nanotube backbone. The ability to analyze fidelity and incorporation at each stage of the assembly will in turn allow an in-depth analysis of the growth mechanism of the new structures [3].



[1] a. N.C. Seeman, Mol. Biotechnol. 37, 246-257, 2007, b. Zhang et al., J. Am. Chem. Soc. 116, 1661-1669, 1994
[2] F.A. Aldaye, Science 321, 1795-1799, 2008
[3] A.A. Hariri, Nat. Chem., 2015

Flexibility of Bacterial Type IV Pili Determined Using Atomic Force Microscopy **Session II, Fri 7:15 PM**

Joshua Mogyoros, *University of Guelph*



Type IV pili (T4P) are very thin protein filaments extended and retracted from the surface of certain Gram-negative bacteria. Pili play a major role in processes such as adhesion, twitching motility and biofilm formation. We used atomic force microscopy (AFM) to perform force spectroscopy measurements on T4P of *P. aeruginosa*. Bacteria were adhered to the end of an AFM cantilever that was brought into contact with a substrate, allowing the pili to adhere. Force-separation curves were collected by retracting the cantilever, corresponding to the stretching of the T4P that was well described by the worm-like chain (WLC) model. Distinct peaks were observed in the distributions of the best-fit values of the persistence length L_p on two different surfac es, providing strong evidence for close-packed bundling of very flexible T4P [1]. Surprisingly, the most prominent value of $L_p \sim 1$ nm is significantly less than the ~ 8 nm length of the PilA subunit. We have investigated this intriguing result by refining our protocol to combine AFM with fluorescence m icroscopy to isolate a single bacterium on a colloidal probe (as seen in the figure above), as well as critically examining the applicability of the WLC model.

[1] S. Lu et al., Biophys. J. 108, 2865, 2015

Design Principles of Mechanics and Transport in Self-Polarizing Actin-Myosin Network **Session II, Fri 7:45 PM**

Alex Mogilner*, New York University*

Cell motility is based on self-polarizing dynamic actomyosin network adhering dynamically to the surface. Two central questions about this motility are: what is the mechanics of spontaneous cell polarization, and how is actin transported from the rear to the front of the polarized moving cell. I will first present simulations of a 2D model of viscous contractile actin-myosin network with free boundary which, coupled with experimental data, suggests that a positive feedback between myosin aggregation and actin flow and a negative feedback between flow and stick-slip adhesion is the key to understanding self-polarization of fish epithelial keratocytes. Second, I will show that fluorescent microscopy and FRAP combined with mathematical modeling indicates that more than half of actin in the motile cell is not part of the rapidly turning over actin network but is a diffusing fraction of oligomers and monomers, most of which are not available for polymerization. Modeling suggests that such organization of the actin treadmill enables diffusion to recycle actin effectively and makes cell migration steadily, yet prepared for rapid focused acceleration. I will discuss implications of these findings for design principles of cellular self-organization.

Embracing Asymmetry: Designing Janus Interfaces to Image and Control Cellular Dynamics **Session III, Sat 9:30 AM**

Yan Yu, *Indiana University*

A cell is like a bustling city. Dynamics on various length and time scales, from receptor clustering and enzyme diffusion to vesicle trafficking, control how cells communicate and make decisions. In spite of the known significance of cellular dynamics, approaches to quantify these dynamics and to dissect their specific roles in cell functions are limited. In this talk, I will present my lab's research progress towards designing unique biointerfaces to enable the imaging and manipulation of live cells at high spatiotemporal resolution. Our research so far has capitalized on Janus particles, particles that have two "faces" like the Roman god Janus. I will show in the talk how the distinct chemistries on the surface of a single Janus particle allow us to manipulate immune cell functions, from phagocytosis to T cell stimulation, and to probe cellular dynamics in multi-dimensions beyond translation motion.

Biomimetic Dye Aggregation Enabling Nanostructure-Dependent Ratiometric Fluorescence **Session III, Sat 10:30 AM**

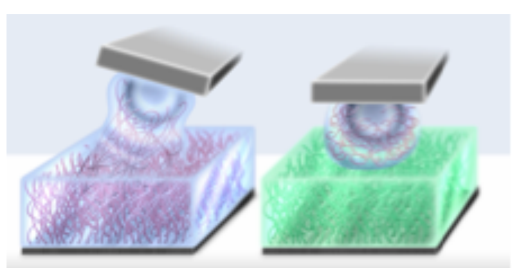
Danielle M. Charron, *University of Toronto*

Fluorescence is a versatile modality for reporting nanoparticle structural state due to the inherent sensitivity of fluorophores to dye interactions. This sensitivity enables manipulation of dye photophysical properties through controlled supramolecular assembly and disassembly. Dye interactions encoding unique fluorescence signals for intact and disrupted nanoparticles are particularly useful for monitoring nanomedicine stability and drug release by ratiometric fluorescence imaging. Current photophysical strategies including Förster resonance energy transfer employ two spectrally distinct dyes, which increases complexity for clinical translation. We have recently achieved nanostructuredependent ratiometric fluorescence by controlling the self-assembly of a naturally-derived bacteriochlorophyll dye within a compact lipoprotein nanocarrier. This nanosystem mimics the lipid and protein environment that promotes and modulates dye interactions within light harvesting complexes of photosynthetic bacteria. The aggregated dye fluoresces at 825 nm, while emission is shifted to 765 nm when the nanocarrier is disrupted. Bacteriochlorophyll aggregates exhibit excellent photostability, a stable fluorescence dynamic range, and are amenable to coloading with hydrophobic payloads for theranostic applications. Ratiometric fluorescence imaging distinguishes intact and disrupted bacteriochlorophyll aggregates with sufficient dynamic range in biological environments and using currently available instrumentation. Selfassembly is a flexible, dynamic, and responsive strategy for manipulating bacteriochlorophyll fluorescence that is applicable to many nanocarrier architectures such as liposomes and polymer micelles. Bacteriochlorophyll aggregation is a powerful new tool for drug delivery and theranostics due to its simplicity, robustness, and versatility.

Towards Unraveling and Eliminating Dissipation Mechanisms in Polymer Brush Friction **Session III, Sat 10:50 AM**

Sissi de Beer, *University of Twente*

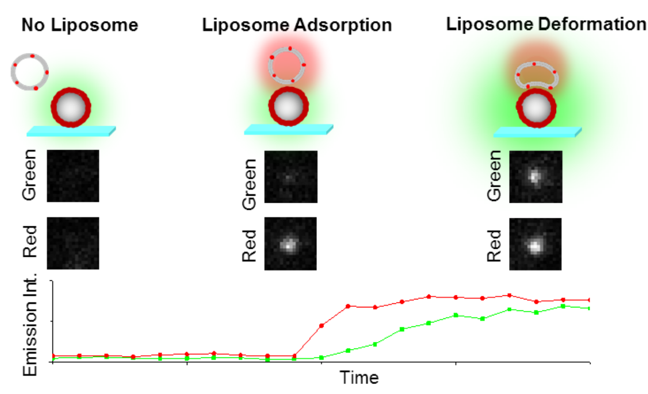
Polymer brushes are well known to lubricate high-pressure contacts, while they can keep a low-viscosity solvent in the contact, even at high normal loads. However, interdigitation of the polymers on the opposing surfaces can increase friction and result in wear due to scission and chain pull out.
I present a simple method to eliminate interdigitation. To do so, we setup an asymmetric contact of two immiscible polymer brush systems in both molecular dynamic simulations and atomic force microscopy experiments. For such immiscible polymer brush systems, we find that friction upon sliding is a few orders of magnitude lower than for symmetric miscible contacts and also wear of the coating is strongly reduced. Moreover, depending on the contact-geometry, direction of motion and brush characteristics, alternative dissipation channels dominate the friction forces. I will discuss the relative importance of the dissipation channels for realistic, rough surfaces and I will show how we can use this knowledge to control adhesion and friction in polymer brush contacts.



Exploiting Conjugated Polyelectrolyte Photophysics toward Monitoring Real-Time Lipid Membrane-Surface Interaction Dynamics at the Single-Particle Level **Session III, Sat 11:10 AM**

Christina F. Calver, *McGill University*

The interaction of conjugated polyelectrolytes (CPEs) with lipid membranes leads to dramatic changes in their photophysical properties [1,2]. The changes resulting from the insertion of CPEs within membranes include spectral shifts (aggregate to single-chain emission), emission enhancement, and poor exciton transport. In this presentation we show how these unique photophysical properties of CPEs can be exploited to observe membrane dynamics [3]. We report the real-time observation of the interaction between cationic liposomes and a charged scaffolding formed by the deposition of the conjugated polyanion onto 100 nm diameter SiO_2 nanoparticles (NPs). The interaction of the liposomes with the CPE promoted deaggregation of the polymer and led to large emission enhancements. Single-particle fluorescence studies exploited this phenomenon as a way to monitor the deformation of individual liposomes on surface-immobilized NPs. Cryo-TEM experiments complemented these results by yielding a structural view of the process. We foresee that the single-particle studies we report in this work may be readily extended to study membrane dynamics of other lipids including cellular membranes, where the ability to adjust topology in response to cues from charged biopolymer scaffoldings is essential to many cellular activities [4].



[1] P. Karam, A.T. Ngo, L. Rouiller, G. Cosa., Proc. Natl. Acad. Sci. U. S. A. 107, 17480-17485, 2010
[2] P. Karam, A.A. Hariri, C.F. Calver, X. Zhao, K.S. Schanze, G. Cosa, Langmuir 30, 10704-10711, 2014
[3] C.F. Calver, H.W. Liu, G. Cosa, Langmuir 31, 11842-11850, 2015
[4] H.T. McMahon, J.L. Gallop, Nature 438, 590-596, 2005

Elucidation of the Photoprotective Mechanisms in Algal Light Harvesting **Session IV, Sat 1:30 PM**

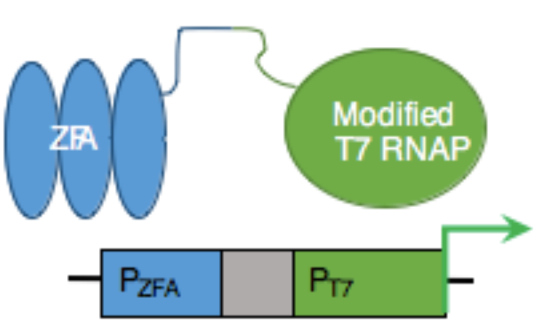
Gabriela S. Schlau-Cohen, *Massachusetts Institute of Technology*

In photosynthetic light harvesting, absorbed energy migrates through a protein network to reach a dedicated location for conversion to chemical energy. In green algae, this energy flow is efficient, directional, and regulated. The regulatory response involves complex and complicated multi-timescale processes that safely dissipate excess energy, thus protecting the system against deleterious photoproducts. We explore the mechanisms behind this photoprotective process in a light-harvesting complex implicated in dissipation, light-harvesting complex stress response (LHCSR). By characterizing the conformational states and dynamics of individual proteins, we identify the extent of energy dissipation in single LHCSR proteins and how the extent of dissipation changes in response to pH and carotenoid composition, two components known to play a role in photoprotection. From this information, we explore how individual complexes contribute to the balance between efficiency and adaptability in photosynthetic light harvesting.

Engineering a T7 RNA Polymerase for Programmable Transcription Initiation **Session IV, Sat 2:30 PM**

Brendan Hussey, *University of Toronto Mississauga*

Developing the next generation of medical, agricultural and sustainability biotechnology is limited by the complexity of natural biological systems; namely the dynamics and interactions between genetically encoded parts. Synthetic biology seeks to reduce the complexity by replacing natural biological components with simplified, synthetic control systems. Transcription is a major control step for biological systems and thus subject to a number of successful efforts for synthetic regulation, primarily in eukaryotes. These systems, however, rely primar ily on host components and thus are still largely entangled in the complex host processes. Additionally, prokaryotes, which represent a large fraction of hosts in industrial biotech, still lack the programmable activation systems of eukaryotes. Furthermore components are not readily transferable between the two, which is important for simplifying design. Thus, we first sought to design a programmable transcription activation s ystem in prokaryotes by combining the wealth of information on the strong phage T7 RNA Polymerase (RNAP) with the modular DNA binding proteins applied in eukaryotes. Importantly, T7 RNAP is a self-contained RNAP that interacts minimally with the host and is thus orthogonal. We reasoned that reducing T7 RNAPs natural affinity for DNA would allow for control of initiation through programmable DNA binding proteins. Second, due to the orthogonality of T7 RNAP, this system should be transferable to eukaryotes thus realizing a one-system solution for synthetic control. We show that indeed, T7 RNAP can be programmed to transcribe synthetic promoters via programmable DNA binding proteins and this interaction can be tuned with various molecular manipulations of promoter and protein. We also demonstrate the many limitations with currently characterized DNA binding proteins and how they translate into design constraints for this system.



Organization of Nucleotides in Different Environments: Implications for the Formation of First RNA under Prebiotic Conditions **Session IV, Sat 2:50 PM**

Sebastian Himbert, *McMaster University*

How nucleic acids first assembled and then incorporated into the earliest forms of cellular life 4 billion years ago remains a fundamental question of biology. It is postulated that prior to today's DNA, RNA, and protein-dominated world, RNA was used for genetic storage and as a catalyst for reactions, such as polymerization. RNA is a polymer chain of nucleotides linked to a ribose-phosphate backbone. Polymerization of nucleotides occurs in a condensation reaction in which phosphodiester bonds are formed. However, in the absence of enzymes and metabolism there has been no obvious way for RNA-like molecules to be produced and then encapsulated in cellular compartments, an essential first step in the origin of cellular life.

To support the hypothesis that environmental conditions in the neighbourhood of volcanic hydrothermal springs could act to organize monomeric nucleotides through various noncovalent interactions and chemical reactions in the prebiotic era, we investigated 5'-adenosine monophosphate (AMP) and 5'-uridine monophosphate (UMP) molecules captured in different matrices that have been proposed to promote polymerization, namely multi-lamellar phospholipid bilayers, nanoscopic films, ammonium chloride salt crystals and Montmorillonite clay [1]. Two nucleotides signals were observed in our X-ray diffraction experiments, one corresponding to a nearest neighbour distance of around 4.6 Å and a second, smaller distance of 3.45 Å. While the 3.45 Å distance agrees well with the distance between stacked base pairs in the RNA backbone, the 4.6 Å distance can be attributed to un-polymerized nucleotides that form a disordered, liquid-like structure. From the relative strength of the two contributions, the effectiveness of the different environment for producing RNA-like polymers was determined.

[1] S. Himbert, M. Chapman, D.W. Deamer, M.C. Rheinstadter, submitted to Scientific Report

Elucidating the Mechanism Behind CK2 Mediated Mesenchymal Stem Cell Differentiation Into Osteoblast and Adipocytes via BMPR1a Signaling **Session IV, Sat 3:10 PM**

Vrathasha Vrathasha, *University of Delaware*

Osteoporosis is a bone disease wherein bones become porous and are susceptible to breaking either due to lack of bone formation, increased bone resorption or both. Bone cells or osteoblasts originate from **mesenchymal stem cells (MSCs)** but MSCs also have the capacity to differentiate into adipocytes, fibroblasts, and chondrocytes and the mechanism regulating its differentiation into specific cell fate is still unknown. **BMP2** is a growth factor, which has been shown to be a promising potential treatment for osteoporosis. However, BMP2 has multiple effects on stem cell differentiation, driving MSCs into osteoblasts and adipocytes by a mechanism that is not fully understood. Therefore it is necessary to develop a new therapeutic treatment that can increase osteoblastogenesis.
One of the well understood BMP2 induced signaling occurs via BMPR-IA and BMPRII.**CK2** is an enzyme that has been shown to interact with BMPR-IA at three possible binding sites. Three peptides labeled CK2.1, CK2.2, and CK2.3 were synthesized mimicking these interaction sites. These peptides bind to CK2, preventing it from interacting with BMPR-IA at their respective sites and initiates specific downstream signaling that ultimately results in C2C12 cells(murine myoblasts) to take on a specific cell fate.

In order to determine the effects of the peptides CK2.1, CK2.2, and CK2.3 within the cell, a probe had to be developed. Therefore we conjugated the peptides to **Quantun Dots (QDs, CK2.1-QD, CK2.2-QD and CK2.3-QD).** QDs are semiconductor nanoparticles that are fluorescent under UV light and their various advantages make them desirable for live-cell imaging. FTIR spectroscopy was used to confirm the conjugation of QDs to the peptides, while confocal imaging showed its uptake and biological activity in C2C12 cells. This technique allows us to detect the peptides in inside the cell (Figure1).

Localization of CK2.3-Qdot inside C2C12 cells after day 1 of treatment

A) Control B) QD-CK2.3

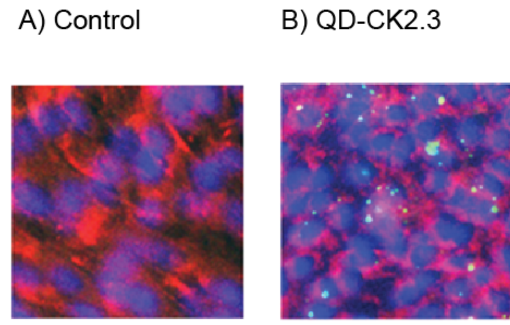


Figure 1: C2C12 cells were not treated (A) or treated with conjugated QDs (B). After day 1 of treatment, the cells are stained for CK2 alpha (red) and the corresponding conjugated QD (green). Image (B) depicts the uptake of CK2.3-QD into the cells.

Nonlinear Dynamics for the Translocation of the *fd* Virus through Nanopor es: Euler Buckling at the Nanoscale **Session V, Sat 4:30 PM**

Hendrick W. De Haan, *University of Ontario Institute of Technology*

The translocation of biopolymers such as DNA through nanopores has received a great deal of attention due to applications such as sequencing DNA or sorting polymers by size. In this presentation I will discuss results from a joint experimental-theoretical project examining the translocation of the filamentous *fd* virus through nanopores. The *fd* virus is relatively stiff with a persistence length on the order of its contour length. This is in contrast to typical translocation scenarios where the polymer is many Kuhn lengths in size. Experimental results for *fd* uncover complex nonlinear dynamics: the translocation speed increases superlinearly with the driving force, the mobility is force-dependent and transitions between scaling regimes with increasing virus length, and the variation in the translocation velocity increases dramatically with increasing driving force. All of these results can be explained by a simple physical picture in which the virus mechanically buckles as it is pushed through the pore and into the fluid on the opposite side of the membrane. This model is explored via Langevin dynamics simulations of the system. Consistent agreement between simulations and experiments verifies the underlying physics thus giving insight into heretofore unexplained experimental results. These findings demonstrate that for the translocation of semi-flexible polymers, the behaviour of the trans portion of the polymer – which is ignored in standard models – has a large impact on the translocation dynamics.

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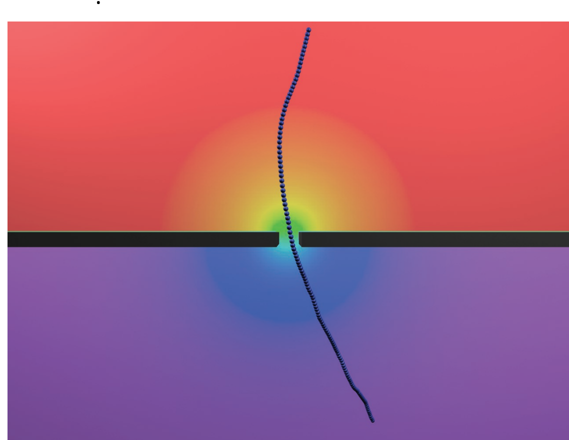

Figure 1: Snapshot from a simulation of the filamentous *fd* virus translocating through a nanopore. The heat map corresponds to the magnitude of the electric potential.

All Twisted Up: New Materials from Cellulose Nanocrystals **Session V, Sat 5:00 PM**

Mark MacLachlan, *University of British Columbia*

Nature is a remarkable source of inspiration for the self-assembly of complex structures. Bone and cellulose, for example, are two materials that have evolved in nature for the construction of extraordinary structures. Inspired by their diverse structures and properties, chemists are using these natural materials to construct new synthetic materials with fascinating properties.

Cellulose nanocrystals (CNCs) are obtained from biomass [1]. These crystals self-assemble into a helicoidal arrangement that mimics the organization of chitin in crab shells and chiral nematic (cholesteric) liquid crystals. This organization can be used as a template to construct composite films of CNCs and other materials, such as silica and polymers [2,3]. Thus, new responsive materials with photonic properties can be constructed [4].

In this talk, I will discuss our recent developments in this area as well as our efforts to understand the nanoscale organization in these materials.

[1] Y. Habibi, L. A. Lucia, O. J. Rojas, Chem. Rev. 110, 3479-3500, 2010
[2] K. E. Shopsowitz, H. Qi, W. Y. Hamad, M. J. MacLachlan, Nature 468, 422-425, 2010
[3] M. K. Khan, A. Bsoul, K. Walus, W. Y. Hamad, M. J. MacLachlan, Angew. Chem. Int. Ed. 54, 4304-4308, 2015
[4] M. Giese, L. K. Blusch, M. K. Khan, M. J. MacLachlan, Angew. Chem. Int. Ed. 54, 2888-2910, 2015.

Lipid Bilayers Direct Assembly of RNA Nano-Structures on Surfaces **Session VI, Sun 10:00 AM**

Aleksandra Dabowska, *Lund University*

The directed arrangement of nucleic acid nano-structures at interfaces is important for many applications, including therapeutics, diagnostic tools, and biomimetic systems. We used laterally mobile lipid bilayers to direct the self-assembly of RNA polyhedrons on surfaces. The adsorption of RNA building blocks onto fluid lipid bilayers composed of pure cationic or mixed cationic/zwitterionic lipid bilayers and their step-wise assembly into supramolecular structures were characterized using surface techniques, including quartz crystal microbalance with dissipation, ellipsometry, and microscopy. Here, the lipid bilayer acts as a scaffold on which the assembly of the 3D structure can be regulated by sequence specific interactions, surface charge and changes in the salt composition and concentration. In our approach, neither chemical modification of the surface nor of the RNA molecules is required to achieve controlled, nanoscale ordering over milliscale surface regions. This self-assembly strategy, where the organization and position of the RNA nanostructures can be controlled from the bottom-up, opens up new opportunities for the nanofabrication of functionalized surfaces.

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Cell Motility – From the Individual to the Collective **Session VI, Sun 10:30 AM**

Herbert Levine, *Rice University*

Cell motility is essential for many biological processes including wound healing, immune response, and cancer metastasis. For cells crawling on surfaces, motility involves a complex interplay between acto-myosin based force generation, adhesion to the substrate and chemical-based polarization to determine a direction. Here, we discuss our work aimed at developing integrative computational models of cell motility, ranging in complexity from simple geometrical models to complex phase-field approaches coupled to cytoskeletal mechanics. We also discuss efforts at using single cell models to understand the collective behavior of motile cells when they interact.

Designing New Chemical Entities to Inhibit Cytotoxic Protein Misfolding **Session VII, Sun 11:45 AM**

Donald Weaver, *University of Toronto*

Protein misfolding is a proteopathic process that is central to the pathogenesis of multiple diseases, both within the central nervous system (Alzheimer's dementia, frontotemporal dementia, Parkinson's disease, chronic traumatic encephalopathy) and external to the brain (type II diabetes). Of the multitude of protein misfolding disorders, Alzheimer's disease (AD) is amongst the most socioeconomically devastating. Currently 47 million people worldwide have AD and there are no disease modifying therapies available. Two strategies for designing possible therapeutics to AD will be presented. Both are based on extensive molecular modelling approaches using both density functional theory and empirical force field calculations. The first approach endeavours to design therapies which target the HHQK tetrapeptidic motif within beta-amyloid, interacting with this target using electrostatic interactions, particularly aromatic-cationic interactions. The second approach is based on homology modelling of proteins to produce a model receptor, termed CCM, against which 11.8 million compounds were screened in silico using a high throughput computational strategy. The strengths and weakness of both approaches will be discussed.

Abstracts

Poster Presentations

List of Posters

P01 **Modeling and Simulating Bacterial Twitchers Moving Across Surfaces**
Michael Greenberg and Hendrick W. de Haan

P02 **The Translocation Time through a Nanopore with an Internal Cavity is Minimal for Polymers of Intermediate Length**
Martin Magill, Ed Waller, Hendrick W. de Haan

P03 **An Efficient Finite-Difference Strategy for Sensitivity Analysis of Stochastic Models of Biochemical Systems**
Monjur Morshed, Brian P. Ingalls, Silvana Ilie

P04 **A Novel Model Reduction Approach for the Chemical Master Equation**
Midhun Kathanaruparambil Sukumaran, Marc R. Roussel, Brain P. Ingalls

P05 **What Makes a Biological System Robustly Homeostatic?**
Zhe F. Tang and David R. McMillen

P06 **Stacking of Red Blood Cells due to Depletion Effects**
Austin Nehring and Hendrick W. de Haan

P07 **Collective Dynamics of Diffusiophoretic Motors on a Filament**
Mu-Jie Huang and Raymond Kapral

P08 **Computer Simulation Study of Elastin-Like Peptide structure, Self-Assembly, and Mechanical Properties**
Quang Huynh and Régis Pomès

P09 **Modelling Listeria Invasion in the Face of Innate Immunity**
Hong Yi Shi Yang and Andrew D. Rutenberg

P10 **Nanoscale Spectroscopy and Simulations of Phospholipid Bilayers and Amyloid-beta Oligomers**
Elnaz Alipour, Alexander Stewart, Gilbert Walker

P11 **Inter-chain Entanglement Complexity in Compressed Polymer Mushrooms with Variable Chain Length and Excluded Volume Interaction**
G. A. Arteca and J. Harrison

P12 **Shear Induced Adsorption of Polymer Chains**
Venkat Bala

P13 **Simulated Titration and Diffenential Scanning Calorimetry of Chlorhexidine and DMPC**
Brad Van Oosten and Thad Harroun

P14 **The Lipid Bilayer Provides a Site for Cortisone Crystallization at High Cortisone Concentrations**
Adree Khondker, Richard J. Alsop, Jochen S. Hub, Maikel C. Rheinstädter

P15 **Computational Simulations and Experimental Studies on the Structure and Function of Lung Surfactant Protein B**
Mohammad Hassan Khatami, Ivan Saika-Voivod, Valerie Booth

P16 **New Players in Non-Homologous End-Joining Identified Using Computational PPI Modeling**
Daniel Burnside, Mohsen Hooshyar, Frank Dehne, Ashkan Golshani

P17 **Manganese Oxidation in Native Anoxygenic Photosynthetic Reaction Centers**
Chuck Protheroe and Làszlo Kàlmàn

P18 **Multichromic Supramolecular Dye Architectures for Advanced Light-Harvesting Applications**
Muhammad Yousaf and Bryan D. Kolvisto

P19 **Coherent Excitation of Molecules with Incoherent Light**
Amro Dodin, Timur Tscherbul, Paul Brumer

P20 **Structural Dynamics of Photocatalytic Water Oxidation**
Jordan S. Wentzell, Meng-Hua Sang, Robert Morris, R. J. Dwayne Miller

P21 **Two-Dimensional Electronic Spectra at Ambient Temperature Reveal Dominant Vibrational Coherence in Light Harvesting Complex (LHCII)**
Samansa Maneshi, Amy L. Stevens, Lu Chen, Valentyn L. Prokhorenko, Oliver P. Ernst, R. J. Dwayne Miller

P22 **Bioinspired Waveguide Array for Light Manipulation**
Kathyrn Benincasa, Hao Lin, Cecile Fradin, Kalaicheivi Saravanamuttu

P23
Serene Bayram

P24 **Solution-Phase Nano-scale Plasmon Coupling of Gold Nanoparticle Rings Scaffolded on Tobacco Mosaic Virus Capsid Protein**
Dan S. Petrescu, Omar K. Zahr, Julia Del Re, Serene Bayram, Amy Szuchmacher Blum

P25 **High Deformability and Particle Size Distribution of Monodisperse Phytoglycogen Nanoparticles Revealed By Atomic Force Microscopy Imaging**
Benjamin Baylis and John R. Dutcher

P26 **Spring! Break! Design of Elastic Protein Biomaterials**
Lisa D. Muiznieks and Fred W. Keeley

P27 **Waterproof Strong Chitosan Plastic**
Becky Winnick, Thanh-Dinh Nguyen, Mark J. MacLachlan

P28 **Characterization of Cellulose Nanostructure Using Super-Resolution Fluorescence Microscopy**
Mouhanad Babi and Jose Moran-Mirabal

P29 **Chemical Vapour Deposition for the Growth of Vertically Aligned Boron Nitride Nanotubes**
Cassandra Phillips, Adrienne Tamur, Gilbert Walker

P30 **Radioimmunoconjugates by Enzymatic Attachment of Metal-Chelating Polymers to Antibodies**
Penny J. Le, Shane Miersch, Yijie Lu, A.J. Boyle, S.S. Sidhu, R. M. Reilly, M. A. Winnik

P31 **Synthesis and Surface Modification of Lanthanide ($NaLnF_4$) Nanoparticles for High-Sensitivity Mass Cytometry Bioassays**
Lemuel Tong, Guangyao Zhao, Jothirmayanantham Pichaandi, Elsa Lu, Loyrn P. Arnett, Mitchell A. Winnik

P32 **Developing Blood-Brain Barrier Permeable Theranostic Nanomimetics with Applications in Alzheimer's Disease Therapy**
Maneesha Rajora, Juan Chen, Gang Zheng

P33 **Marangoni Effect-Driven Self-Healing Oleic Acid Self Assembled Monolayer**
Wei Chen and Eliot Fried

P34 **Gold Nanoparticles as Surface Enhanced Raman Scattering (SERS) Probes for Surface Protein Detection**
Samantha McWhirter, Caroline Pao, Gilbert Walker

P35 **Atomic Force Microscopy of Glycogen**
Kevin Yu, Mitchell Sullivan, Richard W. Loo, Berge Minassian, M. Cynthia Goh

P36 **Rod-like Cellulose Nanostructures for Delivery of Radionuclides to Tumours**
Rachel Keunen, Melinda Guo, Sohyoung Her, Shengmiao Zhang, Christine Allen, Mitchel A. Winnik

P37 **Aqueous-based Process of Fabricating Nanostructured Block Copolymer Films as Effective Marine Antifouling Coatings**
Kris S. Kim, Nikhil Gunari, Drew MacNeil, John Finlay, Maureen Callow, James Callow, Gilbert C. Walker

P38 **A New Group of Eubacterial Light-Driven Retinal-Binding Proton Pumps with an Unusual Cytoplasmic Proton Donor**
Andrew Harris and Leonid Brown

P39 **Investigation of Calmodulin - Nitric Oxide Synthase Interactions at Physiological Calcium Concentrations Reveals Stark Differences in Binding and Dynamics**
Michael Piazza, J. Guy Guillemette, Thorsten Dieckmann

P40 **The Molecular Basis of Ion Selectivity in the Voltage-Gated Sodium Channel**
Christopher Ing, Nilmadhab Chakrabarti, Ning Zheng, William A. Catterall, Régis Pomès

P41 **Mechanism of Amyloidogenesis of the Bacterial AAA+ Chaperone Regulatory ATPase Variant A**
Sze Wah Samuel Chan, Jason Yau, Christopher Ing, Kaiyin Liu, Patrick Farber, Amy Won, Vaibhav Bhandari, Nareg Kara-Yacoubian, Thiago Vargos Seraphim, Nilmadhab Chakrabarti, Lewis E. Kay, Christopher M. Yip, Régis Pomès, Simon Sharpe, Walid A. Houry

P42 **Mechanism of *Leishmania braziliensis* Hsp90 ATPase Activity Stimulation by Aha1 Cochaperone**
Thiago V. Seraphim, Yoshito Kakihara, Walid A. Houry, Júlio C. Borges

P43 **Characterization Of Novel Genes Involved In Ires Mediated Translation Initiation In *Saccharomyces cerevisiae***
Houman Moteshareie, Michael Silva, Ashkan Golshani

P44
Sasha Weiditch and Voula Kanelis

P45 **Probing Drug Binding to NBD1 of SUR2A, the Regulatory Subunit in Cardiac K_{ATP} Channels**
Miriam Park and Voula Kanelis

P46 **Understanding the Hydrophobic Effect using β-Cyclodextrin as a Model System**
Jayrd Sullivan and Mazdak Khajehpour

P47 **Probing the Conformational Dynamics of the Active Site of an OTU Deubiquitinase Enzyme**
Roy Hutchings and Mazdak Kajehpour

P48 **Towards Preparation of Protein Samples for Time-Resolved Structural Dynamics Studies**
Jessica Besaw and R. J. Dwayne Miller

P49 **Observing Conical Intersections through Ultrafast Electron Diffraction**
Kamil Krawczyk, Scott Murphy, R. J. Dwayne Miller

P50 **Congenital Hyperinsulinsm-causing Mutations Alter the Structure and MgATP Binding of SUR1 NBD1 in the Pancreatic K_{ATP} Channels**
Claudia Alvarez, Marijana Stagljar, Voula Kanelis

P51 **Design of a Photoactivatable 4E-BP for Optical Control of Protein Synthesis**
Huixin Lu, Mostafizur Mazumder, Andrew Wooley

P52 **Single-Molecule Dissection of the Conformations, Dynamics and Binding of the Disordered 4E-BP2 Protein**
Zhenfu Zhang, Alaji Bah, Julie D. Forman-Kay, Claudiu C. Gradinaru

P53 **Dimensions and Dynamics of Highly Cooperative Sic1-WD40 Binding: smFRET through a Polymer Physics Lens**
Gregory-Neal W. Gomes, Jianhui Song, Veronika Csizmok, Hue-Sun Chan, Julie Forman-Kay, Claudiu C. Gradinaru

P54 **Modelling Spatial Assemblies of Nucleoporins from Diverse Species**
Chad Gu and Anton Zilman

P55 **Live Fluorescence Microscopy as a Tool to Study Morphogen Dynamics during *Drosophila melanogaster* Embryonic Development**
Carmina Angeica Perez Romero, Tanguy Lucas, Teresa Ferraro, Nathalie Dostatni, Cecile Fradin

P56 **Force Generation by a Liquid Protein Droplet May Effect Membrane Curvature**
Kevin Stokely, Louis-Philippe Bergeron-Sandoval, Paul François, Stephen Michnick

P57 **Treatment of CK2.3 on Isolated Primary Cells Induces Bone Mineralization and Decreases Lipid Droplet Formation**
Hilary Weidner, Hemmanth Akkirju, Mark Eskander, Debbie Dibert, Anja Nohe

P58 **Inhibition of Differentiation of RAW264.7 Monocyte/Macrophage Cell Line to Osteoclasts by a Novel Peptide, CK2.3**
John Nguyen and Anja Nohe

P59
Jingjing Huang

P60 **tHairapy: Structural Abnormalities in the Hair of a Patient with a Novel Ribosomopathy**
Richard J. Alsop, Asfia Soomro, Maikel C. Rheinstädter

P621 **Fluorophore Photoprotection Mediated by Ni^{2+} for Extended Single-Molecule Imaging: Old Tricks for New Techniques**
Viktorija Glembockyte, Junan Lin, Richard Lincoln, Gonzalo Cosa

P62 **Structure-Activity Relationship Study of a Novel Chemosensor for Proximal Phosphorylation**
Aaron Cabral, Dzivana Kraskoushkaya, Patrick T. Gunning

P63 **Förster Resonance Energy Transfer as a Distance Probe for Gas-phase Ubiquitin**
Jocky C.K. Kung, Martin F. Czar, Benjamin Schuler, Rebecca A. Jockusch

P64 **Analysis of Biobased Products and Changes of Microstructure of 60Co-γ Irradiated Rapeseed Straw**
Chunyan Zhang, Xiaojun Su, Xingyao Xiong, Qiulong Hu, Xinghe Tan, Wensheng Qin

P65 **Overcoming The Challenge Of Intravenous Infusion Of Hydrogen Enriched Fluids: A Scavenger Solution For Reactive Oxygen Species In Hemorrhagic Shock**
Mohamed S. Hamam, Liqun Qui, Richard W. Loo, Jane B. Goh, Chung Ho Leung, Carlos Semprun, Joao de Rezende-Neto, M. Cynthia Goh

P66 **Spectroscopy of H20/TMAO at Hydrophobic Interfaces Large and Small**
Duncan Halverson, Chuan Leng, Gilbert C. Walker

P67 **Broadband Pump-Probe Spectroscopy Reveals Ultrafast Dielectric Response of Solvated Proteins and Molecules**
Chanelle C. Jumper, Tihana Mirkovic, Gregory D. Scholes

P68 **Impact of Low Power Microwave Irradiation on the Structure and Functions of Biological Systems at Constant Bulk Temperature**
Sina Mazinani

P01

Modeling and Simulating Bacterial Twitchers Moving across Surfaces

Michael Greenberg and Hendrick W. de Haan
Faculty of Science, University of Ontario Institute of Technology

Some bacterial species are capable of moving by using structures called Type IV Pili in order to pull themselves across semi-solid surfaces. When in large groups, these twitchers move in a collective manner that has not been accurately simulated and quantified. In this project, I have worked to develop a model of the collective motion of twitchers and to generate simulations of the swarming behaviour. A simple model will be presented in which the twitcher cells – which are represented by three bonded spheres – propagate via the application of a force within a certain range of orientation angles. The ease of motion is modelled by a jump probability that changes with position: it is easier for bacteria to move in regions where twitchers have already been and more difficult to expand into new territory. With this simple model, we find that collective motion arises naturally – particularly if some regions of the unexplored substrate are slightly easier to traverse than neighbouring regions. Since swarming twitcher cells are capable of carrying other species of bacteria along with them, detailed knowledge of the collective motion could be useful for developing methods to prevent the spread of infections.

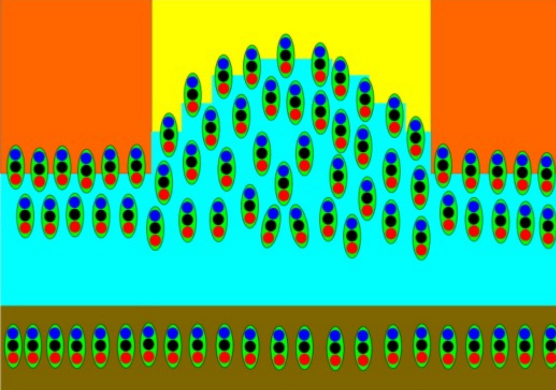

Figure 1: Schematic of the model for simulating bacterial twitchers moving across surfaces.

P02

The Translocation Time through a Nanopore with an Internal Cavity is Minimal for Polymers of Intermediate Length

Martin Magill, Ed Waller, Hendrick W. de Haan
Department of Modelling and Computational Science, University of Ontario Institute of Technology

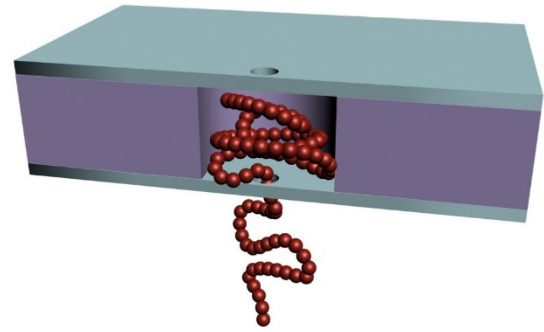

Figure 1: Illustration of the cavity-nanopore.

Nanopores are of great interest in the study of biological systems and the development of new scientific and industrial tools. Synthetic nanopores, constructed from silicon wafers or similar materials, show great potential for detecting, sorting, and manipulating polymers rapidly and efficienctly. Traditional nanopores are short cylindrical holes in a membrane, whose radii and lengths are comparable. The average translocation time of polymers electrically forced through such pores is a monotonic function of polymer length.

In the present work, we present a novel nanopore design, in which a hollow cavity is included between two traditional nanopores. Using numerical simulations of a model system, the average polymer translocation time through this new geometry is found to be a complicated function of length and driving force. For moderate driving forces, translocation time is minimal for some critical polymer length, with shorter chains slowed by entropic trapping, and longer chains slowed by virtue of their length. For larger driving forces, the effects of entropic trapping are suppressed as the chain is forced against the far side of the cavity. As such, translocation time is almost constant below the critical polymer length. Furthermore, the rich dynamics of this system can be explained by a simple free energy description. This model accurately predicts the relationship between the critical polymer length of the system and the strength of the driving force with no free parameters. These results suggest that the new pore geometry could be used as a highly selective filter for extracting polymers from solution, behaving as a band-pass filter for moderate driving forces and a low-pass filter for strong driving forces. Further, the filter threshold can be tuned dynamically using the relation predicted by the free energy model. Thus, this device opens up new applications for nanopores within nanofluidic devices.

P03

An Efficient Finite-Difference Strategy for Sensitivity Analysis of Stochastic Models of Biochemical Systems

Monjur Morshed*, Brian Ingalls*, Silvana Ilie**
**University of Waterloo.*
***Ryerson University*

Sensitivity analysis characterizes the dependence of a model's behaviour on system parameters. It is a critical tool in the formulation, characterization, and verification of models of biochemical reaction networks, for which confident estimates of parameter values are often lacking. We propose a novel method for sensitivity analysis of discrete stochastic models of biochemical reaction systems whose dynamics occur over a range of timescales. This method combines previously established finite-difference approximations and adaptive tau-leaping strategies to efficiently estimate the parametric sensitivities for stiff stochastic biochemical kinetics models, with negligible loss in accuracy compared with previously published approaches. We analyze several models of interest to illustrate the advantages of our method.

P04

A Novel Model Reduction approach for the Chemical Master Equation

Midhun Kathanaruparambil Sukumaran[#], Marc R Roussel[*], Brian P Ingalls[#]
[#]*Department of Applied Mathematics, University of Waterloo*
[*]*Alberta RNA Research and Training Institute, Department of Chemistry & Biochemistry, University of Lethbridge*

The dynamics of biochemical systems typically vary over multiple time scales, a phenomenon referred to as stiffness; this poses challenges to numerical analysis of system behaviour. By eliminating the fast modes, which correspond to fast time scales that are often not experimentally observed, a model reduction can be achieved. In our work, we use time-scale based reduction of the chemical master equation (CME), which gives the time evolution of the probability distribution in homogeneous biochemical systems. The slow and fast modes of the system correspond to small and large eigenvalues of the transition matrix of the CME. By a transformation generated from a set of left eigenvectors corresponding to slow eigenvalues, we remove the fast modes to arrive at a truncated model. The transformation was constructed so that the probability conservation is maintained in the truncated variable set. By this reduction, we attain a significantly reduced set of non-stiff differential equations. Moreover, the transformed truncation yields an exact representation of the initial condition of the original model, providing an optimal reduced representation of the original dynamics.

P05

What Makes a Biological System Robustly Homeostatic?

Zhe F. Tang and David R. McMillen
Dept of Chemical and Physical Sciences and Impact Centre
University of Toronto Mississauga

Homeostatic biological systems resist external disturbances, allowing cells and organisms to maintain a constant internal state despite perturbations from their surroundings. Many biological regulatory networks are known to act homeostatically, with examples including thermal adaptation, osmoregulation, and chemotaxis. Understanding the network topologies (sets of regulatory interactions) and biological parameter regimes that can yield homeostasis in a biological system is of interest both for the study of natural biological system, and in the context of designing new biological control schemes for use in synthetic biology. Here, we examine the mathematical properties of a function that maps a biological system's inputs to its outputs, we have formulated a novel criterion (the "cofactor condition") that compactly describes the conditions for homeostasis. We further analyze the problem of robust homeostasis, wherein the system is required to maintain homeostatic behavior when its parameter values are slightly altered. We use this condition to examine previously-reported examples of homeostasis, showing that it is a useful way to unify a number of seemingly-different analyses into a single framework. Based on the observation that all previous robustly homeostatic examples fall into one of three classes, we propose a "strong cofactor condition" and use it to provide an algorithm for designing new robustly homeostatic biological networks, giving both their topologies and constraints on their parameter values. Applying the design algorithm to a three-node biological network, we construct several robustly homeostatic genetic networks, uncovering network topologies not previously identified as candidates for exhibiting homeostasis.

P06

Stacking of Red Blood Cells due to Depletion Effects

Austin Nehring , Hendrick W. de Haan
Department of Material Science, University of Ontario Institute of Technology

The aggregation of red blood cells into coin-like stacks called rouleaux is associated with a number of underlying causes including infections and diseases such as cancer. Rouleaux formation occurs when the protein concentration in blood plasma is high. Hence, one possible cause for rouleaux formation is red blood cells clumping together due to depletion forces. In the case of several large objects suspended in a bath of small objects (the depletants), it is globally entropically favourable at high depletant concentration for the large objects to remain in contact since this gives more free space to the smaller objects. The depth of the resulting depletant potential is directly related to the density of the depletants. In this presentation I will present results from coarse-grained simulations investigating depletant induced rouleaux formation. Simulations are performed for different depletant and red blood cell densities. Rouleaux formation is observed to happen relatively suddenly at a critical depletant density. The rouleaux stacks are characterized in terms of the cluster size and the number of aligned red blood cells with the stack. Results indicate that the stacks form with a central, orderly aligned stack that has a maximum size after which additional red blood cells adhere to the sides of the stack yielding a more disordered morphology. The dependency of these results on the red blood density is also explored. Large scale systems that yield multiple rouleaux formation are investigated within the context of network formation via nucleation processes.

Figure 1: Illustration of red blood cells in rouleaux formation.

P07

Collective Dynamics of Diffusiophoretic Motors on a Filament

Mu-Jie Huang, Raymond Kapral
Chemical Physics Theory Group, Department of Chemistry, University of Toronto

A variety of uses have been proposed for synthetic chemically-powered nanomotors that exploit their autonomous directed motion. The collective dynamics of these and other active particles display features that differ from their equilibrium analogs. We investigate the collective dynamics of chemically-powered diffusiophoretic motors attached to a filament. Rotational Brownian motion is reduced substantially when a motor is attached to a filament and this improves motor performance. When many motors are attached to the filament structural and dynamical correlations that may extend over long distances arise. While some features of these correlations are due to packing on the filament, there are nonequilibrium effects that are due the local concentration gradients of reactive species produced by all motors. As the motor density on the filament increases beyond a critical value, the average motor velocity projected along motor internuclear axis switches from forward to backward directions. A knowledge of the collective dynamics of motors on filaments should prove useful when designing ensembles of synthetic motors to perform tasks such as cargo transport involving delivery of material to specific regions in complex media.

P08

Computer Simulation Study of Elastin-like Peptide Structure, Self-Assembly, and Mechanical Properties

Quang Huynh, Régis Pomès
Molecular Structure and Function, Hospital for Sick Children
Department of Biochemistry, University of Toronto

The protein elastin endows tissues such as skin, arterial walls, lung alveoli, and the uterus with the properties of extensibility and elasticity. The sequence of elastin comprises alternating hydrophobic and cross-linking domains. Elastin and elastin-like peptides self-aggregate via a liquid-liquid phase separation process. Although elastin has been the object of biophysical investigation for over eighty years, the structural basis for the self-assembly and the mechanical properties of elastin remains controversial. Elastin is structurally heterogeneous and must be described by an ensemble of structures, which has hampered detailed investigation by conventional methods of structural biology. Here we elucidate the structural ensemble of elastin by performing extensive molecular dynamics simulation on an elastin-like peptide modelled after the sequence of alternating hydrophobic and cross-linking domains of elastin. The results show that the cross-linking domains rich in alanine have a significant propensity for helical structures. In contrast, the hydrophobic domains rich in glycine and proline form only transient hydrogen-bonded turns. These secondary structure elements are local and do not involve extensive interactions between the individual domains. These results are important for settling the discrepancy between various models proposed for the structure and function of elastin and other self-assembled elastomeric proteins such as resilin and spider silks. In addition, these findings afford meaningful insight into the physical basis for the phase separation of disordered proteins.

P09

Modelling *Listeria* Invasion in the Face of Innate Immunity

Hong Yi Shi Yang, Andrew D. Rutenberg
Department of Physics and Atmospheric Science, Dalhousie University

Listeria monocytogenes is a food-borne pathogenic bacterium. Experimental studies of *L. monocytogenes* from an initial infection focus within a layer of uninfected cells shows that the number of infected cells grow linearly with time. This implies that the infection propagation speed is slowing with time. To understand this, we model the spread of *L. monocytogenes* in a two-dimensional layer of cells. We include a simplified propagating innate immune response that couples to the infection process. With no immune coupling, we obtain a quadratic Eden-like growth. Coupling the stochastic infections to an innate immune response, we obtain linear growth of the number of infected cells, qualitatively recovering the experimental result.

P10

Nanoscale Spectroscopy and Simulations of Phospholipid Bilayers and Amyloid-beta Oligomers

Elnaz Alipour, Alexander Stewart, Gilbert Walker
Department of Chemistry, University of Toronto

Here we present a multi-disciplinary comprehensive approach to understand the way amyloid-beta interacts with lipid bilayer membranes that mimics the phospholipid section of a neurite. In our first example, we describe how nanoparticles encapsulated by a phospholipid bilayer can serve as a host for determining a-beta oligomer cross-beta structure. We next describe how single mechanical pulling experiments can be used to measure the affinity or hydrophobic hydration energy or species in non-polar environments. We also describe how force microscopy can measure the line tension and spreading pressure of membrane bilayers upon adding species to the bilayer. In simulation work, we also consider the effect of membrane curvature and electric field on the way amyloid-beta interacts with lipid bilayer membranes that mimics the phospholipid section.

P11

Inter-chain Entanglement Complexity in Compressed Polymer Mushrooms with Variable Chain Length and Excluded Volume Interaction

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When confined within narrow slabs, the off-equilibrium geometrical entanglement in polymer brushes appears to depend more strongly on surface coverage than on the rate of compression, or the nature of the interaction between monomers [1,2]. Recently, we have shown that, in the absence of compression, reorganizations in grafting geometry can lead to “escape transitions” even in repulsive polymers [3]. These transitions correspond to a switch from configurations with high inter-chain entanglement to configurations where each individual chain is more self-entangled. These reorganizations appear to be triggered by the available space between chains and do not require more than excluded volume (hard-sphere) repulsions. In this work, we extend the analysis to the equilibrium inter-chain entanglement between two polymer mushrooms, each grafted to a different surface in a rectangular confining space. At low compression, the inter-chain entanglement increases with excluded volume as chains swell and interpenetrate; this effect, as expected, becomes more dominant for longer chains. In contrast, we find that there is a critical chain length at higher confinement where the inter-chain entanglement *decreases* with excluded volume. This behavior takes place without any major effect on the mean intra-chain shape, implying that it is the result of changes in relative orientation and self-avoidance of chains, and not associated with escape transitions. We have studied the conditions that lead to minimal entanglement by changing the grafting points, as well as considering pairs of chains that differ in length and excluded-volume interaction.

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[2] T. Carlsson, G.A. Arteca, J. Sundberg, C. Elvingson, PCCP 13 11757-65, 2011
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P12

Shear Induced Adsorption of Polymer Chains

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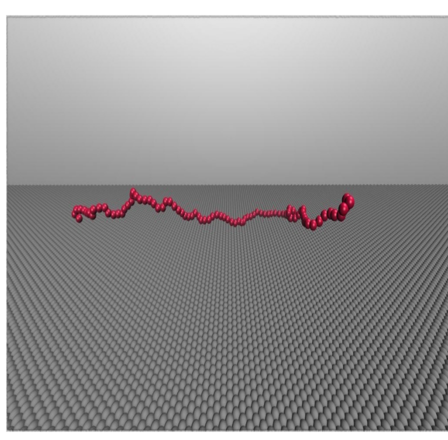

Adsorption of polymer chains onto surfaces in shear flows is quite an interesting and counterintuitive phenomena. The von Willebrand Factor (vWF), present in our blood that plays a vital role in thrombosis, exhibits shear induced adsorption. Proper understanding of such a phenomena can prove vital in the development of novel self-healing polymeric materials. In vitro experiments involving vWF have successfully observed its adsorption at high shear rates but the nature of hydrodynamic forces at play still remains elusive. Brownian dynamics (BD) studies with hydrodynamic interactions approximated by a Rotne-Prager-Blake tensor, find no adsorption unless a *catch-bond* type polymer-wall interaction is included.

We study this problem via molecular dynamics (MD) simulations using the open source tool LAMMPS. We adopt a coarse-grained bead-spring representation of the polymer coupled to an explicit solvent modeled by a thermal lattice-Boltzmann algorithm that accurately captures the full gamut of hydrodynamic interactions at all time scales.

In shear flows, polymer chains demonstrate stretch/recoil transitions causing severe loss of conformational entropy. Thus for the chain, under certain conditions remaining closer to the surface becomes energetically favorable. With a Lennard-Jones type polymer-wall interactions, we studied the effect of monomer mass and found that at certain shear rates, lighter and neutrally buoyant chains are more susceptible to remaining elongated and adsorbed on the surface for long durations. Heavier chains, as previously observed in the BD simulations were always found to escape into the bulk where they freely tumbled in the flow.

P13

Simulated Titration and Diffenential Scanning Calorimetry of Chlorhexidine and DMPC

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We have investigated the use of molecular dynamic simulations and the MARTINI force field to simulate isothermal titration calorimetry and differential scanning calorimetry techniques. The goal of these simulations was to observe how well they can reproduce the concentration effects of the addition of the small molecule chlorhexidine into a model DMPC membrane.
Chlorhexidine is a chemical antiseptic that acts specifically against the plasma membrane, causing leakage leading to cell death. It has therefore been shown to be effective against a wide range of bacteria in products such as: surgical hand washes, mouthwash, industrial sterilization and many other similar applications.
We were able to mimic an isothermal titration calorimetry experiment by repeatedly adding a 1% concentration of chlorhexidine into a DMPC membrane. With the increased chlorhexidine concentration, we observed a decreasing affinity between chlorhexidine and the membrane as well as a resulting increase in the reaction time before the system was equilibrated. We then performed a controlled cooling of the membrane with various chlorhexidine concentrations to mimic a differential scanning calorimetry experiment. A change in membrane structure accompanied by a spike in the specific heat was measured at specific temperature Tm signaling a phase transition. We then varied the concentration of chlorhexidine in order to observe trends in the change to Tm due to the addition of chlorhexidine.

P14

The Lipid Bilayer Provides a Site for Cortisone Crystallization at High Cortisone Concentrations

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Steroids are perhaps one of the most widely used groups of drugs in clinical anesthesiology today. The common mechanism of action of these steroids involves the binding to intracellular receptors, which causes the transduction of a biochemical cascade reducing the production of inflammatory prostaglandins. However, current understanding of this mechanism does not account for the conferring side effects, such as pain, known as “steroid flares”.
Cortisone is a commonly used steroid to treat many types of inflammation. The current mechanism of action disregards the plasma membrane as an inert interface irrelevant to the drug. In our experiments, we utilized X-ray diffraction of highly oriented, multi lamellar stacks of lipid membranes, and molecular dynamics (MD) simulations. We located the cortisone molecules within the bilayer, quantified its crystallization, and measured the respective insertion dynamics [1].
At low cortisone concentrations, the molecules were found to localize near the glycerol group of the lipid molecules, and decrease membrane width in a dose-dependent manner. The formation of cortisone crystallites was observed at higher concentrations, which conferred to a cubic lattice. While the cortisone molecules align parallel to the bilayers at low concentrations, they start to penetrate the hydrophobic core at higher concentrations. Trans-membrane crystallites start to nucleate when the membrane thickness has decreased such that cortisone molecules in the different leaflets can find partners from the opposite leaflet. The results manifests to potentiate a mechanism of action for “steroid flares” by forming crystallites in the bilayer, and offers greater understanding of the drug’s action.

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P15

Computational Simulations and Experimental Studies on the Structure and Function of Lung Surfactant Protein B

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Lung surfactant protein B (SP-B) is a 79 residue protein from the Saposin superfamily. Without SP-B we can not breathe. The main proposed mechanism of SP-B is to modify the phospholipid bilayer and monolayer structures at the air-water interface of alveoli. Because of the extreme hydrophobicity of SP-B, the experimental structure of SP-B has not yet been determined. Thus, we run 2-3 μs molecular dynamics (MD) simulations (employing OPLS-AA and PACE force fields), as well as 3 μs replica-exchange molecular dynamics (REMD) simulations (employing PACE force fields), of SP-B in a POPC bilayer. Our simulations produce low energy structures of SP-B in both parallel and tilted orientations with respect to the lipid bilayer, and suggest that salt bridges play a role in defining the overall structure. Interestingly, our results demonstrate the ability of SP-B to induce and stabilize defects in the lipid bilayer. Finally, as a step towards an experimental structure for SP-B, we predict the ^{15}N solid-state NMR spectra of the final structures of SP-B in the simulations. These are to be compared with the actual spectra of ^{15}N-labelled SP-B oriented samples being acquired as part of ongoing research in the lab.

P16

New Players in Non-Homologous End-Joining Identified Using Computational PPI Modeling

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Maintaining genomic integrity is essential to cell proliferation and the prevention of mutation-based diseases such as cancer. DNA double-breaks are the most detrimental form of DNA damage and can produce severe mutations and chromosomal rearrangements if ineffectively repaired. Non-homologous end-joining (NHEJ) is the primary pathway employed by mammals to remediate broken DNA strands and is therefore highly studied and believed to be largely understood. However, our recent work has identified several protein complexes that play important novel roles in successful NHEJ repair. By using computational tools that predict protein-protein interactions (PPIs) using co-occurring small motifs we have been able to implicate additional players in NHEJ repair. The identification of novel PPIs connected to NHEJ was used to predict function (guilt by association). Using *Saccharomyces cerevisiae* as a model, we have identified several complexes that interact with NHEJ machinery to facilitate accurate and efficient repair. The Pph3/Psy2 complex was shown to interact with Rad53 and Chk1 checkpoints to modulate cell cycle progression following DSBs. Spindle checkpoint factors Bub1/Bub2 were shown to accumulate at DSB repair foci and regulate NHEJ repair through phosphorylation of the DNA damage checkpoint Tel1. Lastly, a subunit of protein kinase A (Tpk1) was shown to greatly affect the efficiency of NHEJ via the phosphorylation of Nej1. Importantly, the findings originally demonstrated in yeast have translated to conserved pathways in human cell lines. Homologs of Bub1/2 and Tpk1 were shown to play similar roles in human and yeast NHEJ. Cumulatively, this work has significantly expanded our knowledge of the protein complexes that participate in the global cellular response to DSBs. Additionally, the discovery of novel functions in NHEJ for these complexes may have profound implications on understanding communication between cell cycle progression and DSB repair, cancer, predisposition to a multitude of genetic diseases, and future chemotherapeutic drug development.

Photosynthesis and Light-Harvesting

P17

Manganese Oxidation in Native Anoxygenic Photosynthetic Reaction Centers

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Approximately 3 billion years ago Nature designed a method to catalytically split water with sunlight, a process that humanity struggles to perform to this day. This manifested itself as the evolution from anoxygenic to oxygenic photosynthesis, a transition which had a profound impact on life and the Earth itself. Oxygenic photosynthesis uses water as an electron source, doubly oxidizing it via a manganese complex, and causing the water to split into the by-products of molecular oxygen and hydrogen ions. The evolution of this process involved the incorporation of manganese from the environment, into the electron transfer chain of anoxygenic photosynthetic organisms. Much can be learned about the pathway nature followed to solve this key energy conversion problem by studying the incorporation of manganese as a secondary electron donor to the anoxygenic bacterial reaction center (BRC), the protein responsible for photoelectric energy converison. The BRC is similar to the reaction centers which must have been present in ancient photosynthetic organisms. For the first time, we have direct evidence that native BRCs are able to utilize manganese as a potent secondary electron donor, an ability thought to only be possessed by oxygenic reaction centers. We accomplished this by coordinating manganese into a complex with a low potential, and a strong binding affinity to the BRC. This allows electron transfer to take place, while preserving the BRC's functionality. We have determined the binding sites of this complex in the BRC and the rates of electron transfer.

P18

Multichromic Supramolecular Dye Architectures for Advanced Light-Harvesting Applications

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Shape-persistent phenylacetylene macrocycles have been explored in a number of optoelectronic and light-harvesting applications, including two-photon absorption. Likewise, BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacenes) dyes have also been extensively used in material applications, owing to their tunable, intense absorption and sharp emission peaks exhibiting high quantum yields. Employing the BODIPY molecule orthogonal to the phenylacetylene-macrocycle results in energy transfer from macrocycle to the BODIPY core. The novel dye design could potentially be used in the dye-sensitized solar cells (DSSCs). The DSSC is a next-generation photovoltaic device that incorporates a dye molecule as a light-absorber. The dyes for the DSSC are generally comprised of a redox-active donor/chromophore (D) that is coupled through a conjugated linker (π) to an acceptor (A) capable of anchoring to TiO_2 (*i.e.* D-π-A motif). The BODIPY-macrocycle dye motif can be used as a π-spacer in the DSSC dye (as shown in Fig.) and could permit two-photon absorption resulting in panchromatic absorption.

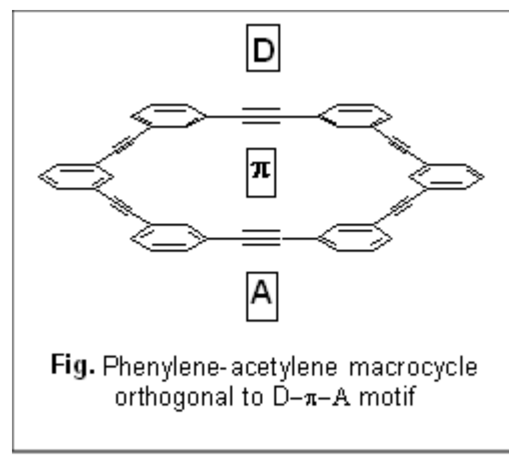

Fig. Phenylene-acetylene macrocycle orthogonal to D–π–A motif

P19

Coherent Excitation of Molecules with Incoherent Light

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Recent spectroscopic studies of the photosynthetic Fenna-Matthews-Olson (FMO) complex of green sulfur bacteria have revealed long-lasting oscillatory energy transfer [1] and suggested the potential role of quantum mechanical coherences in the remarkable efficiency of these complexes [2-4]. However, these studies were conducted with highly coherent femtosecond pulses of laser light which differ significantly from sunlight which is incoherent and incident on the system for much longer times. As a result, sunlight is known to excite very different states than coherent laser fields, producing steady-state incoherent mixtures of energy eigenstates that lack the definite phase relations that enable quantum interference [5, 6]. Notwithstanding this, a different form of coherence has been predicted in incoherently excited systems [7]. The nature and dynamics of these coherences will be explored and contrasted with those generated by coherent laser light [8, 9]. The robustness of these coherences in biologically relevant regimes of the light field is also discussed.

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P20

Structural Dynamics of Photocatalytic Water Oxidation

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Emission of carbon dioxide as a result of fossil fuel consumption has become an issue of growing concern in recent years. This has spurred intense research interest in alternative energy sources, including hydrogen. An ideal method of generating hydrogen in an environmentally friendly manner is artificial photosynthesis, whereby solar radiation is utilized to split water into its constituent elements of hydrogen and oxygen. Of particular interest is the water oxidation step, as this is the rate-limiting factor in artificial photosynthesis.

One of the most promising artificial water oxidation catalysts (WOCs) demonstrated to date is $[Ru(bda)(isoq)_2]$ (Figure 1). $[Ru(bda)(isoq)_2]$ has been synthesized from 2,2'-bipyridine-6,6'-dicarboxylic acid, methanol, and isoquinoline, according to literature methods. Crystallization of the complex has been accomplished via vapour diffusion of pentane and diethyl ether, generating needle crystals, which were characterized by NMR, x-ray crystallography, and SEM. Ultramicrotomy will be utilized for crystal sectioning, prior to Transmission Electron Microscopy (TEM) nanodiffraction analysis and LEED (Low Energy Electron Diffraction) experiments. In the first step of water oxidation, the $[Ru(bda)(isoq)_2]$ is expected to form a peroxo bridged intermediate, analogous to the intermediate reported for the 4-picoline analogue. Synthesis of this intermediate will enable water oxidation activity to be evaluated, with the formation of molecular oxygen induced by laser excitation. Following excitation, the resultant structural changes may be observed through femtosecond time resolved LEED.

Taking advantage of recent advances in atomically resolved structural dynamics, observation of structural changes accompanying photocatalytic water oxidation should now be possible. Such knowledge of reaction dynamics will open the door for future improvements in efficiency and cost effectiveness of artificial photosynthesis. These developments are of paramount importance to the rapidly evolving field of alternate energy, as artificial photosynthesis represents an ideal method of generating hydrogen for use as an energy source.

Figure 1: $[Ru(bda)(isoq)_2]$

P21

Two-Dimensional Electronic Spectra at Ambient Temperature Reveal Dominant Vibrational Coherence in Light Harvesting Complex (LHCII)

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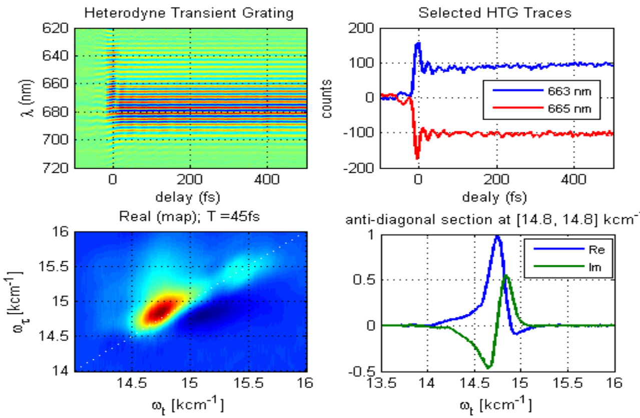

We present two-dimensional electronic spectra of LHCII trimers at ambient temperature, the most physiologically relevant temperature for higher plants. Our data mainly show intramolecular vibrational coherences that decay in sub-100fs time scale. This decay time is an order of magnitude shorter than the picosecond time scale observed in LHCII at the cryogenic temperature of 77K [1], where long-lasting oscillations were attributed to electronic coherences. Similar long-lived oscillations at 77K [2,3] and at room temperature [3] have been reported for the Reaction Center subunit of Photosystem II and attributed to excitonic coherences. In our experiment, the spectrum of broadband 18fs pulses overlaps well with the electronic states of Chla and Chlb (the Qy band) and the higher energy vibrational states. This wide bandwidth spectrum directly excites a coherent superposition of vibrational states. By measuring the Heterodyne Transient Grating signal as a function of the waiting time T, we directly observe vibrational coherences with oscillation periods of 20fs. We also extract the electronic coherence time from the anti-diagonal width of the 2D map at early delay times. The anti-diagonal width of the 2D map at the waiting time of 45fs, when the solvent response is completely absent, corresponds to a coherence time of 62fs. This result agrees well with the previous measurement in our group [4], where excitation bandwidth was restricted to electronic states and no direct coherent oscillations were observed. Here, we provide a detailed comparison of our two experiments, i.e., excitations with restricted and unrestricted bandwidths, and clarify the time scales of excitonic and vibrational coherences.

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P22

Bioinspired Waveguide Array for Light Manipulation

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Natural compound eyes found in insects have many advantages such as fast movement detection, polarization sensitivity and a large field of view (FOV). The fabrication of artificial compound eyes with different features has become more popular for applications such as medical imaging, light collection and beam steering. We present a structure inspired by compound eyes found in nature, which consist of multiple polymer light channels, otherwise known as waveguides. The structure is made by launching an incandescent white light source into a photopolymer which results in the self-trapping of light and the permanent formation of waveguides due to irreversible polymerisation reactions. The waveguides were positioned radially and resulted in a large cumulative FOV of about 113°, which is >66% increase in FOV as compared to a control structure without waveguides. Potential applications for these structures include coatings for light collection energy materials (e.g. solar cells) and beam manipulation (e.g. output of LED's) which are further studied in this project.

Materials, Polymers and Nanomaterials

P23

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McGill University

Metallic nanostructures continue to fascinate scientists and draw efforts into their smart design owing to their ability to enhance light manipulation and confinement in small volumes. In particular, ring structures stimulated rapid growth in the field of plasmonics due to their great impact on sensing, lasing, and nonlinear optics technologies. Nanorings can also serve as optical antennas to achieve significant light enhancement within their cavities. In addition, appropriately shaping scatterers of light allows independent control of the effective permittivity and permeability which when made negative simultaneously, materials can exhibit a negative index of refraction. Amongst the numerous approaches to fabricate such metallic nanoring structures including colloidal lithography, chemical synthesis, nanoimprint lithography, and electron beam lithography, bottom-up self-assembly of metallic nanoparticles remains the most costeffective for their mass production. Herein, we use the TMVcp (Tobacco Mosaic Virus coat protein) command surface to grow and assemble silver nanoparticles. The versatility of TMV allows the formation of continous in addition to rings of discrete nanoparticles that are characterized by UV-vis and TEM. Darkfield imaging for individual structures reveals novel plasmonic modes. Discrete Dipole Approximation of AgNPs rings excited by plane wave incident fields shows plasmon broadening and red-shift in agreement with the experimental measurements. TEM clearly showed the formation of the rings composed of an average of 5-6 nanoparticles per ring as well as a central nanoparticle under appropriate pH conditions. Our silver rings are believed to be the smallest to date, and they can offer a testing material for existing theories.

P24

Solution-phase Nano-scale Plasmon Coupling of Gold Nanoparticle Rings Scaffolded on Tobacco Mosaic Virus Capsid Protein

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Nanophotonic metamaterials can be designed to manipulate electromagnetic waves with applications spanning nanophotonic circuitry, photovoltaics, tumor therapy, and signal detection enhancement in analytical techniques. Previous work has predicted that plasmonically coupled noble metal nanoparticles arranged in a ring would exhibit a strong magnetic dipolar response along with a negative index of refraction. Fabrication of nanomaterials with such precise geometries and arrangements, however, remains limited by the current resolution of top-down lithographic techniques. To achieve higher precision and reproducibility of nanostructure placement, bottom-up bio-molecular self-assembly techniques present an appealing alternative. By harnessing the diverse chemical functionality and self-assembling properties of biomacromolecular systems such as proteins, it becomes possible to chemically fabricate dynamic solution-phase nanophotonic metamaterials whose optical properties can be controlled *in vitro* by parameters such as ionic strength, pH, and temperature. Our studies explore the Tobacco Mosaic Virus (TMV) capsid protein, a structure displaying disk-like self-assembling capabilities, as a scaffold for generating rings of gold nanoparticles on the faces or edges of this supramolecular structure. A mutated TMV protein, S123C, which predominantly favored this disk phase, was found to bind nanoparticles non-covalently through charged surface residues on the face of the disk, as evidenced by TEM micrographs. Temperature and pH provided a way to physico-chemically tune the number of particles on the rings. Further mutation of this protein solvent-exposed the hitherto obstructed N-terminus, thereby affording a chemical handle on which to covalently bind nanoparticles. Bio-conjugation of a fluorophore allowed for spectroscopic quantification and confirmed increased tagging efficiency for this mutant along with selective conjugation of the N-terminus. Lipoic acid was immobilized at the N-terminus in this manner and covalently bound gold at the edge of the disk, thus providing a way to vary the ring diameter and robustness. UV/vis absorbance and dark-field scattering data confirm nano-scale plasmon coupling between particles.

P25

High Deformability and Particle Size Distribution of Monodisperse Phytoglycogen Nanoparticles Revealed By Atomic Force Microscopy Imaging

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We have used atomic force microscopy (AFM) imaging in water to determine the volume of hydrated monodisperse phytoglycogen nanoparticles adsorbed onto mica surfaces. By significantly reducing the interaction between the AFM tip and the “sticky” nanoparticles, we were able to obtain high quality images. We found that the adsorbed particles are highly deformed, forming pancake-like objects on the hydrophilic mica surface. By measuring the distribution of particle volumes, we calculated the average effective spherical radius of the hydrated particles, and compared this value with that measured in solution using small angle neutron scattering. These measurements illustrate the distinct advantages of AFM imaging over other imaging techniques, namely the ability to measure the height of objects in a liquid environment.

P26

Spring! Break! Design of Elastic Protein Biomaterials

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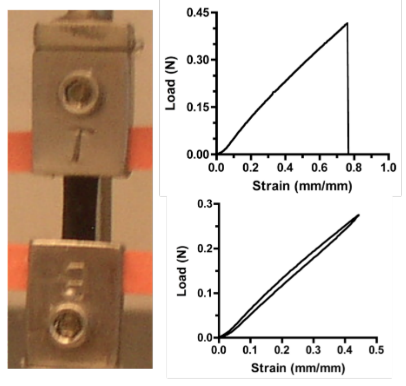

Elastin is an extracellular matrix protein of vertebrates that belongs to a class of proteins across biology whose main function is to confer elasticity to the material in which it is found. Although elastomeric proteins, including elastic fibres, spider silks and mussel byssal threads, have predominantly structural roles, polymer chains within cross-linked materials must remain substantially disordered for elastic function, as returning to a state of higher entropy after extension is a main driving force for elastic recoil. Conformational disorder is largely conferred by hydrophobic sequences that contain a high composition of structure-breaking proline and glycine residues. However, cross-linking domains differ substantially in structure between elastomeric proteins, and may be key to understanding the mechanical properties of natural biomaterials, which span orders of magnitude. A major emerging question is how structure, disorder and dynamics combine to modulate mechanical properties such as extensibility, tensile strength, and resilience. Here we describe three strategies for mechanically designing biomimetic elastic materials based on modifying the balance of structure and disorder of the protein monomer “building block”: (i) disrupting local structural motifs, (ii) adding extended secondary structure, and (iii) combining sequences from different species in an attempt to obtain composite material properties. These data inform structure (disorder)-function relationships of elastomeric proteins, and reveal great potential for fine-tuning material properties for diverse biomedical applications.

P27

Waterproof Strong Chitosan Plastic

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Conventional plastic products are made from petroleum, a non-renewable resource. The products are non-biodegradable and often contain compounds that are toxic to creatures on Earth, including humans. Even recyclable plastic can only be "downcycled," so it all eventually becomes persistent pollution. A newer bioplastic that is made from corn is biodegradable and renewable, but its production requires resource-intensive agriculture. Chitosan bioplastic, on the other hand, can be made from waste material - discarded crab and shrimp shells. Previous research has successfully produced strong chitosan bioplastic, but swelling and poor stability in water remain a challenge. Now, we have developed a facile new method to create chitosan bioplastic that remains strong even after soaking in boiling water. The additional antibacterial and wound-healing properties of chitosan make this material promising for application in food packaging and healthcare.

Figure 2. Transparent chitosan bioplastic on a paper UBC logo

P28

Characterization of Cellulose Nanostructure Using Super-Resolution Fluorescence Microscopy

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Cellulose – a major and critical component of plant cell walls – constitutes the largest component of Earth's biomass and is an attractive raw material to exploit in the production of biodegradable and renewable products, such as biocomposites, biofuels and other biomaterials. Manufacturing these products often entails the acidic or biochemical defragmentation of cellulose, a process that is limited by its crystalline and compact structure. In order to better understand these manufacturing processes and improve their efficiency, we require insight into the nanoscale structure of cellulose and the mechanism of its enzymatic hydrolysis. Herein, direct stochastic optical reconstruction microscopy (dSTORM) – a relatively new fluorescence imaging technique – is used to study the structure of fluorescein-labelled bacterial microcrystalline cellulose (BMCC) at the nanoscale. The ten-fold improvement in resolution offered by this technique unveiled regular repeating patterns of high and low fluorophore density regions on BMCC microfibrils that are hypothesized to represent disordered and crystalline regions of cellulose. Grafting cellulose using different dyes or labelling reactions produced similar patterns, evidencing that the dark regions are labeling chemistry-independent and are rather encoded within the native cellulose structure. The length of the dark regions were measured and their distribution was highly similar to previous measurements of cellulose nanocrystals using transmitted electron microscopy. The length of the microfibril dark regions were also determined to be dependent on the concentration of fluorescein during the grafting procedure, strongly suggesting that the observed labelling patterns are indeed due to intervening crystalline and disordered regions of cellulose microfibrils. Preliminary results from the dSTORM imaging of a fluorescently-labeled cellulase – CBHI-Cy5 – bound to labelled BMCC suggest this enzyme does not exhibit any preferential binding to either the crystalline or disordered regions of BMCC microfibrils.

P29

Chemical Vapour Deposition for the Growth of Vertically Aligned Boron Nitride Nanotubes

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Control of nanotube superstructure is highly desirable for the production novel devices. Boron nitride nanotubes (BNNTs) possess useful properties for a number of devices partly due to their high band gap (5.5 eV), thermal conductivity and intrinsic polarity. The rapid oxidization of materials and surface dewetting at 1200°C must be carefully controlled in order to facilitate the desired conformation.
We have attempted several different catalyst surfaces, growing temperatures and reaction times with the goal of synthesizing vertically aligned BNNTs. Titanium on silicon has shown many desirable characteristics for nanotube growth and thin films of less than 30 nm have been observed to show the greatest morphology control.

P30

Radioimmunoconjugates by Enzymatic Attachment of Metal-chelating Polymers to Antibodies

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Radioimmunoconjugates (RICs) consist of an antibody modified to carry radioisotopes, and are normally prepared by random modification of exposed amino acid side chains. Site-specific modification of an antibody that avoids altering its binding sites has improved targeting and increased tumour uptake. To study this effect in polymer-based RICs, we developed an enzyme reaction to modify antibodies with polymers at a single designated site. Enzyme reactive groups were introduced into both an antibody fragment and a metal-chelating polymer to enable a selective transamidation reaction catalyzed by microbial transglutaminase. Western blots of the reaction mixtures show that only antibodies with the enzyme reactive group reacted. These results suggest that the modification occurs only at the enzyme reactive group on the antibody. Our method allows us to study the effect of controlled antibody modification on tumour targeting, and will aid the development of RICs for cancer theranostics.

P31

Synthesis and Surface Modification of Lanthanide ($NaLnF_4$) Nanoparticles for High-Sensitivity Mass Cytometry Bioassays

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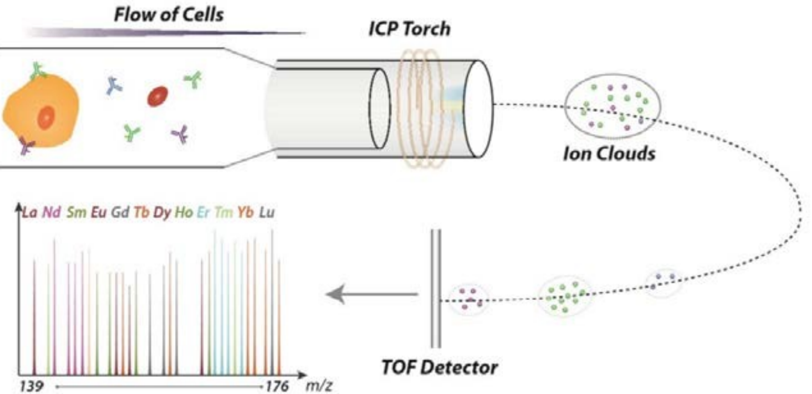

Single-cell analysis of cellular biomarkers reflects the state of a cell, and in cancer cells, can indicate the type of cancer and stage in its development. Expression of biomarkers can be assessed using labelled antibodies. In mass cytometry, many biomarkers can be analyzed simultaneously by tagging each type of antibody with a different metal isotope. This technique is able to achieve single mass unitresolution by exploiting time-of-flight inductively-coupled plasma mass spectrometry (see Figure). The signal is therefore proportional to the number of metal atoms per antibody. Currently, lanthanide (Ln) metals are the most used elemental tag, due to their stability and low cellular background. However, these common reagents contain only ~250 Ln atoms, and do not allow detection of low copy number biomarkers ($<10^3$ copies per cell). Therefore, we would like to use Ln nanoparticles (NPs) which contain $\sim10^4$ Ln atoms per particle. For use in mass cytometry the NPs are required to be uniform, colloidally stable in physiological media, and have functional groups for bioconjugation. We have synthesized a library of oleate capped $NaLnF_4$ NPs (Ln = Sm to Ho, and Y) using the co-precipitation method. These NPs can be synthesized with diameters ranging from 4 to 30 nm with a narrow size distribution (CV < 5%). Since the as-prepared NPs are hydrophobic, the NPs were transferred into aqueous buffer using two different surface modification strategies: 1) silica coating by reverse microemulsion and 2) lipid encapsulation by thin film hydration. Hydrophobic NPs coated with lipid micelles and hydrophilic NPs coated with liposomes demonstrated long term colloidal stability in saline buffers. Finally, functional groups were introduced for bioconjugation to secondary antibodies. Preliminary mass cytometry results with different cancer cell lines indicate that the NPs can specifically target cell-surface biomarkers.

P32

Developing Blood-Brain Barrier Permeable Theranostic Nanomimetics with Applications in Alzheimer's Disease Therapy

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Alzheimer's disease is a prevalent incurable neurological disorder that yields devastating implications, including memory loss and ultimately premature death, for the 500, 000 Canadian individuals it and its related dementias afflicts. Without the discovery of a curative intervention in the face of an aging Canadian population, it is expected that the number of Canadians affected by Azheimer's disease will double in less than 25 years. It is thus imperative that a suitable therapy is found which addresses the two major challenges in Alzheimer's disease drug discovery: 1) bypassing the blood-brain barrier (BBB), which prevents the passage of therapeutic agents from the blood stream into the brain, and 2) preventing and clearing the accumulation of toxic amyloid-β (Aβ) aggregates in the brain that are a source of the disease.

Here, the development of organic nanomimetics which overcome these challenges is presented. Two mutifunctional pyropheophorbide apolipoprotein E3 high density lipoprotein cholesterol (pyE-HDL) nanomimetics were formulated. The therapeutic advantages of these pyE-HDL particles stem from: 1) the inclusion of apolipoprotein E3 (apoE3) moieties which mediate transcytosis of nanoparticles across the BBB, 2) the ability of apoE3-HDL to chaperone the clearance of Aβ from the brain, 3) the ability to monitor nanoparticle delivery and BBB penetration in vitro and in vivo through the inherent optical properties of pyropheophorbide, and 4) the versatility of using an HDL-platform amenable to core drug loading for synergistic therapeutic action. Through the systematic variation of particle composition the size, stability and morphology of pyE-HDL particles were tuned to ultimately achieve stable 30 nm discoidal and cholesteryl oleate-loaded nanoparticles with activateable near-infrared fluorescence. These properties contribute to the applicability of the pyE-HDL platform as a theranostic BBB-traversing drug delivery vehicle, which going forward will be further verified by assessing BBB-permeability, Aβ affinity and disease-modifying efficacy in vivo.

P33

Marangoni Effect-Driven Self-Healing Oleic Acid Self Assembled Monolayer

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In this work, an acetone droplet is spread on an oleic acid self-assembled monolayer (SAM) resting at an air-water interface. This causes an elastic deformation and results in the formation of a hole. A surface tension difference is responsible for the size of the hole created and the results were corroborated by varying the acetone-water composition of the droplet. It was found that a higher acetone composition resulted in a larger hole size as a result of spreading caused by a greater surface tension difference. The elastic deformation of the SAM was studied by observing its stress-strain properties. In the acetone composition range of 33% and 100% within the droplet at a temperature range between 14°C and 36°C, no glassy region or plastic region was observed. The elastic deformation always follows with an elastic rebound due to acetone-water mixing, which results in the equilibration of the surface tension. The material properties of oleic acid SAM are characterized in a series of experiments based on the spreading of an acetone droplet at the air-liquid interface.

P34

Gold Nanoparticles as Surface Enhanced Raman Scattering (SERS) Probes for Surface Protein Detection

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Dept. of Chemistry, University of Toronto

Fluorescent markers conjugated to antibodies are the current gold standard for the detection of surface receptors of cells for diagnostic purposes, used in methods such as flow cytometry and fluorescence microscopy. However, their broad emission peaks causes problems where multiplexed detection is desired because spectral overlap limits the number of fluorophores that can be detected simultaneously. An alternative to this technology that is being investigated are surface-enhanced Raman scattering (SERS) markers. Raman dyes have narrow emission peaks, and we aim to use them to improve the limit of simultaneously detected probes. This project aims to create SERS probes that detect surface markers (CD20) that indicate the presence of abnormal B lymphocytes caused by chronic lymphocytic leukemia. The SERS probes are comprised of Raman-active dyes physisorbed to gold nanoparticles, which are encapsulated in a lipid bilayer and/or coated in polyethylene glycol (PEG) then conjugated to anti-CD20 antibodies. The methods of functionalization of these nanoparticles and their characterization will be described. Future applications for these nanoparticles, including dark-field imaging and flow cytometry, will also be discussed.

P35

Atomic Force Microscopy of Glycogen

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Lafora disease is one of five inherited forms of progressive myoclonic epilepsy, which can result in tonic-clonic seizures, occipital seizures, and decline in cognitive skills soon after onset. The disease is characterized by the presence of polyglucosans known as Lafora bodies in the cytoplasm of cells in the brain, liver, muscle and skin. These polyglucosans are abnormal glycogen molecules with very long glucose chains and poor branching. Atomic force microscopy (AFM) was used to probe the surface of these polyglucosans to determine their surface morphology. Samples were obtained from the purification of liver glycogen from laforin-deficient mice by knock-out of the EPM2A gene. AFM images confirmed a conformational change in Lafora-diseased glycogen when compared to wild type glycogen.

P36

Rod-like Cellulose Nanostructures for Delivery of Radionuclides to Tumours

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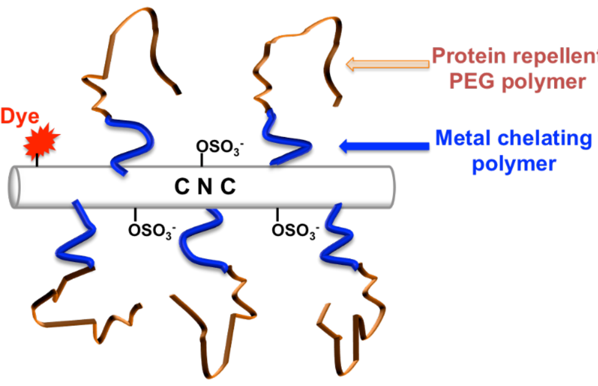
Rod-like nanoparticles have shown improved tumor penetration relative to their spherical counterparts. For this reason rod-like nanoparticles are desirable for drug-delivery applications. We investigate the modification of rod-like cellulose nanocrystals (CNCs) for the delivery of radionuclides to tumors. CNCs are both biocompatible and biodegradeable making them superior for drug-delivery. Through modification of these rod-shaped nanoparticles we can delivery radionuclides directly to tumors. We modify the CNCs using metal-chelating block copolymers with an exterior polyethylene glycol (PEG) block to minimize protein adsorption. PEG-PGlu(DPTA)$_{25}$-HyNic polymers were synthesized and coupled to CNCs using hydrazine nicotinamide (HyNic) coupling chemistry to form a bis-aryl hydrazone. The CNCs are readily modified and retain their structural properties after modification with fluorescent dyes and metal-chelating polymers. Preliminary evaluation in a human ovarian cancer cell line (HEYA8) demonstrated that these CNCs are non-toxic and their penetration properties can be readily assessed in multi-cellular tumor spheroids (MCTS) by optical imaging.



P37

Aqueous-based Process of Fabricating Nanostructured Block Copolymer Films as Effective Marine Antifouling Coatings

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Although effective, most known marine antifouling materials have been banned or regulated due to their toxicities. The search for environmentally friendly alternatives has sparked resurgence in the development of antifouling surfaces and alternative materials without heavy metals are desired. Nanostructured polymeric films have proven to be effective antifouling coatings due to their diverse chemical, physical, and mechanical properties. Unfortunately, standard fabrication techniques often require extensive annealing procedures that require volatile organic compounds (VOCs) and limit scalability. We report an aqueous based process of fabricating nanostructured poly(styrene-*block*-2 vinyl pyridine-*block*-ethylene oxide) (PS-*b*-P2VP-*b*-PEO) triblock copolymer films as effective antifouling coatings. A novel indirect dissolution technique was developed, allowing for the phase transfer of water insoluble PS-*b*-P2PV-*b*-PEO from a water immiscible organic phase to an aqueous environment, with the assistance of a diblock copolymer phase transfer agent. This process resulted in the self-assembly of PS-*b*-P2VP-*b*-PEO core-shell-corona type micelles in an aqueous solution while significantly reducing the release of VOCs. With surface probe microscopy techniques, adhesion forces, topographical images, and mechanical properties of nanostructured PS-*b*-P2VP-*b*-PEO films were collected. Adhesion forces were measured between BSA coated probes, with a radius of curvature of 10nm, applied at 50 pN of force against nanostructured PS-*b*-P2VP-*b*-PEO, PDMS, and uncoated Si/SiO_2 surfaces. Results showed that over 80% of adhesion forces measured between BSA-coated probes and PS-*b*-P2VP-*b*-PEO films were less than 20 pN, which was significantly lower than the average adhesion force of 217 ± 83 pN and 1.19 ± 0.42 nN measured against an uncoated Si/SiO_2 and PDMS coated surface, respectively. Furthermore, zoospore settlement analysis and field studies demonstrated the significant ability of nanostructured PS-*b*-P2PV-*b*-PEO films to resist protein adsorption.

P38

A New Group of Eubacterial Light-driven Retinal-Binding Proton Pumps with an Unusual Cytoplasmic Proton Donor

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Microbial rhodopsins are a versatile family of photoactive retinal-binding membrane proteins, which are widespread geographically and taxonomically. One of the main functions of microbial rhodopsins is outward-directed light-driven proton transport across the plasma membrane, which can provide sources of energy alternative to respiration and chlorophyll photosynthesis. Proton-pumping rhodopsins are found in *Archaea* (*Halobacteria*), multiple groups of *Bacteria*, numerous fungi, and some microscopic algae. This work describes a new group of efficient proteobacterial retinal-binding light-driven proton pumps which lack the carboxylic proton donor on helix C (most often replaced by Gly) but possess a unique His residue on helix B. The typical representative of the group (from *Pseudomonas putida*) was characterized spectroscopically and through site-directed mutagenesis, which suggested that the unique histidine at position 37 likely forms a proton-donating complex involving water molecules compensating for the loss of the carboxylic proton donor.

This work has been published in BBA – Bioenergetics: Harris, A. *et al.* A new group of eubacterial light-driven retinal-binding proton pumps with an unusual cytoplasmic proton donor. *Biochim. Biophys. Acta.* 1847, 1518–29 (2015).

P39

Investigation of Calmodulin – Nitric Oxide Synthase Interactions at Physiological Calcium Concentrations Reveals Stark Differences in Binding and Dynamics

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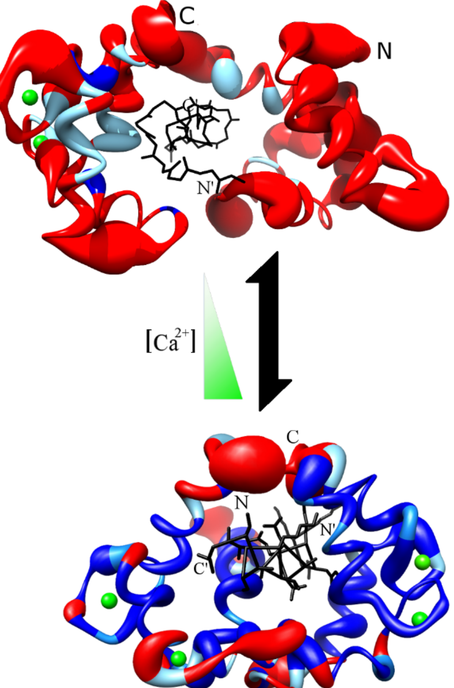
Department of Chemistry, University of Waterloo



Intracellular Ca^{2+} is an important regulator of many cellular functions. Calmodulin (CaM) is a small acidic protein that serves as a Ca^{2+} sensor and control element for many enzymes. Nitric oxide synthase (NOS) is one of the proteins that is activated by CaM and plays a major role in a number of key physiological and pathological processes. CaM has previously been shown to act like a switch that causes a conformational change in NOS. This allows for the electron transfer between the reductase and oxygenase domains through a process that is thought to be highly dynamic. We have used NMR spectroscopy to determine the solution structure of the complex of the endothelial NOS peptide with CaM at the lowest Ca^{2+} concentration (225 nM) required for CaM to bind to eNOS. The complex has a Ca^{2+}-replete C-lobe bound to the eNOS peptide and a loosely associated Ca^{2+} free N-lobe. The binding and dynamics of this complex were further analyzed using surface plasmon resonance (SPR), H/D exchange and ^{15}N relaxation NMR spectroscopy. SPR was used to determine the kinetic binding constants (on and off rates and affinity constant) of CaM and eNOS peptide interactions at 225 nM Ca^{2+} and saturated Ca^{2+}. Our data highlights remarkable differences in the binding and dynamic properties of CaM-eNOS at high millimolar Ca^{2+} concentrations when compared to nanomolar physiological Ca^{2+} concentrations. These results illustrate that studies of CaM-NOS interactions performed at saturated Ca^{2+} concentrations do not provide a complete picture of this interaction because the differences in intramolecular dynamics only become visible at physiological Ca^{2+}.

P40

The Molecular Basis of Ion Selectivity in the Voltage-Gated Sodium Channel

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[2]*Biochemistry, University of Toronto*
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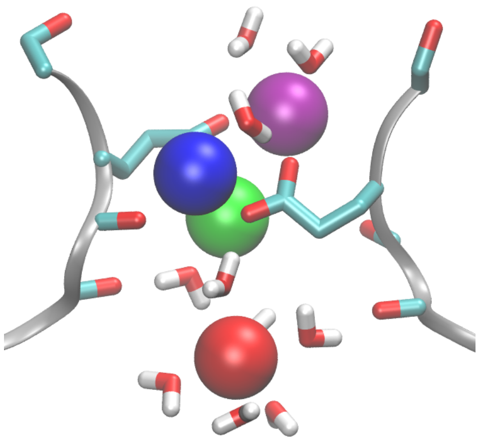

Ion channels are a class of transmembrane proteins that facilitate critical physiological processes such nerve impulses, muscle contraction, and cell signaling in both eukaryotic and prokaryotic organisms. The relationship between structure and function of voltage-gated sodium channels provides a foundation for understanding the molecular basis for disease-causing mutations as well as drug and toxin binding identified within this class of proteins. Molecular dynamics simulations have been critical to the study of ion permeation and selectivity in voltage-gated sodium channels, and have led to the identification of preferred ion binding sites, ion binding modes, as well as a consensus mechanism by which ion conduction occurs. However, the molecular basis of sodium selectivity over other ions like potassium and calcium remains poorly understood. Here we present results of more than 175 million CPU hours of all-atom simulations of a voltage-gated sodium channel, totaling nearly 1.0 millisecond of aggregated biological time. In this work, we performed a systematic comparison of simulations performed with Na^+, K^+, and a mixture of both Na^+ and K^+ in the closed-state model of bacterial sodium channel NavAb. The molecular basis of selectivity was examined using experiments with the wildtype sequence, selectivity-altering mutations, channel-fluctuation altering mutations, multiple sidechain protonation states, application of hyperpolarizing and depolarizing voltages, and varying applications of artificial protein restraints. This work reveals the intimate coupling of channel fluctuations to ion conduction as well as selectivity, and provides a new framework for understanding selective ion transport in all channels.

P41

Mechanism of Amyloidogenesis of the Bacterial AAA+ Chaperone Regulatory ATPase Variant A

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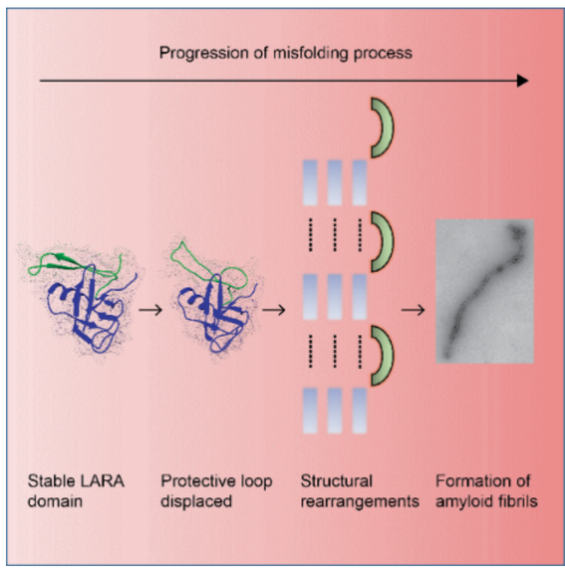
Amyloids are stable structures that have a cross-β fibrillar architecture stacked perpendicular to the fibril axis. Amyloids are present in all kingdoms of life from prokaryotes to higher eukaryotes. Some amyloids have physiological functions while others are associated with human diseases. However, the precise mechanisms of amyloid formation remain to be elucidated. Surprisingly, we discovered that a bacterial *Escherichia coli* chaperone-like ATPase, Regulatory ATPase Variant A (RavA), and specifically the LARA domain within RavA, readily forms amyloids under acidic conditions at elevated temperatures. RavA has been implicated in modulating the proper assembly of membrane respiratory complexes and was also found to interact with the acid stress enzyme, the inducible lysine decarboxylase, to form a cage structure. The LARA domain consists of an N-terminal loop region followed by a folded core, which forms a β-sandwich-like fold. Using a combination of biochemical and biophysical approaches, such as nuclear magnetic resonance spectroscopy, we determined that the folded core was amyloidogenic and that the N-terminal loop region has a protective role to reduce protein aggregation. In molecular dynamics simulations at neutral pH, we observed a specific salt bridge interaction that stabilized the interaction of the N-terminal loop with the folded core. This interaction was disrupted at low pH, hence, explaining the low pH requirement for the amyloid formation process. Deletion of the N-terminal loop region lowered the barrier for amyloid formation and additional mutational analysis specifically localized this destabilization effect to several important arginine residues on the N-terminal loop region. Overall, this study reports on a novel amyloid forming protein and highlights a protein structure that has a protective role to prevent amyloid formation (highlighted in figure below). These findings shed light on important questions in bacterial pathogenesis as well as provide key information on the biophysical mechanisms of protein misfolding.



P42

Mechanism of *Leishmania braziliensis* Hsp90 ATPase Activity Stimulation by Aha1 Cochaperone

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Hsp90 is a central molecular chaperone involved in proteostasis, cell signaling, genome maintenance, transcription and translation. This molecular chaperone is a homodimer formed by three domains (N, M and C-domains) and undergoes several conformational changes during its functional cycle. Hsp90 has low ATPase activity and its function is driven by cochaperones, such as Aha1. Aha1 is formed by two domains (N and C-terminal) and accelerates Hsp90 ATP hydrolysis through the stabilization of Hsp90 in a closed state. In spite of its importance for Hsp90 function, Aha1 proteins from protozoa are poorly studied and in this work we aimed to characterize the interaction mechanism between *Leishmania braziliensis* Aha1 (LbAha1) and Hsp90 (LbHsp90). Structural techniques including circular dichroism and SAXS revealed that LbAha1 is an elongated protein formed by two independent domains connected via a flexible linker. We found by isothermal titration calorimetry that LbAha1 interacts with LbHsp90 through a network of electrostatic and hydrogen bond interactions. Moreover, LbAha1 directs LbHsp90 towards a closed conformational state and stimulates LbHsp90 ATPase activity through a positive cooperative mechanism. Analyzing interactions between several LbHsp90 and LbAha1 constructs, we found that LbAha1 N-terminal domain and Hsp90 M-domain form the core of LbAha1-LbHsp90 complex. LbAha1 is only able to activate LbHsp90 when its N- and C-terminal domains are physically connected. In addition, we observed that LbAha1 constructs lacking the linker region or with a mutated linker interact but do not direct LbHsp90 to a closed ATPase competent state. These findings reveal that the linker between LbAha1 N- and C-terminal domains is not merely flexible, being essential and a novel region for LbAha1-mediated LbHsp90 activation. To address the importance of these findings *in vivo*, we constructed a yeast *aha1*Δ strain for complementation assays. Full length LbAha1 complements yeast *aha1*Δ and experiments with several LbAha1 constructs are in progress.

P43

Characterization Of Novel Genes Involved In Ires Mediated Translation Initiation In *Saccharomyces Cerevisiae*

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During translation, mRNA is read by translation machinery to produce a polypeptide chain that folds into a protein. In eukaryotes, the primary method of regulation for the initiation of this pathway is done through the 5'-cap-dependant mechanism. However, another type of machinery is employed by these higher organisms whereby translation can be initiated, without 5'-capcomplexes, by direct binding of the ribosome to specific regions of mRNA in the 5′-UTR, called Internal Ribosome Entry Sites (IRES). IRESs are secondary structures that are formed on mRNA molecules through complementarity. Having received considerable attention in the last two decades as a result of their association to pathological as well as physiologically adverse conditions, much research has been attributed to furthering our knowledge of this process through functional genomics and the identification of novel genes involved in this pathway. Here we conducted follow-up studies in an attempt to investigate the role of MS1, MS2, and MS3 in IRES mediated initiation of translation in Saccharomyces cerevisiae. Originally five genes candidates were selected for further investigation; three of which showed promising results based on our functional assays. These candidates were subjected to drug sensitivity tests, followed by quantitative RT-PCR and Western blot analysis to measure their gene expression at both transcriptional and translational levels, respectively. Our results from these experiments established that these genes are likely to be involved in IRES-mediated translation. The mechanism of cellular IRES is not completely understood and thus characterization of novel genes is important in expanding the current comprehension on this process.

P44

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The last gene in the genome of the bacteriophage HK97 encodes an HNH endonuclease, named gp74. Biochemical and phage-based studies have demonstrated a role for gp74 in HK97phage morphogenesis, which was initially predicted based on the conservation of the genome organization of HK97 and other phages. Similar findings have been demonstrated in the phage φSLT. In the genome of HK97, the gene for gp74 is adjacent to the genes encoding the terminase enzymes (TerS and TerL) which collectively bind ATP, lineate phage DNA for head packaging, and catalyze the reaction for head and tail connection. Experimental evidence demonstrates reduced DNA digestion upon mutation of metal binding residues within the HNH motif of gp74, postulating a requirement for metal binding at the HNH site to aid in regulation ofterminase activity. The goal of this work, is to understand the molecular basis by which gp74 activates the terminase-mediated digestion of phage DNA. Using nuclear magnetic resonance we have gained information of the location of specific metal binding residues within gp74 and the affinity of gp74 for different divalent metal ions. Our NMR resonance assignments of gp74 indicate that gp74 posses a fold that is similar, but not identical to the distantly-related protein Gmet_0936. NMR data on gp74 provides the only structural characterization of HNH endonucleases related to gp74 to date. Considering the conserved genomic organization amongst many phages featuring adjacent HNH and terminase genes and the few demonstrated HNH-mediated terminase activities in other phages, we predict that control of terminase function by HNH proteins is a wide-spread regulatory mechanism. Thus, this work promises to elucidate basic regulatory mechanisms necessary for overall phage morphogenesis.

P45

Probing Drug Binding to NBD1 of SUR2A, the Regulatory Subunit in Cardiac K_{ATP} Channels
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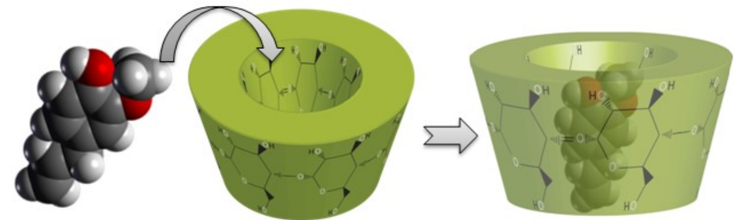
Department of Chemical & Physical Sciences, University of Toronto Mississauga

ATP- sensitive K+ (KATP) channels are key players in biological processes, including regulation of action potential in the heart. KATP channels are formed from two different types of proteins: 4 copies of a pore-forming Kir6.x protein and 4 regulatory sulphonylurea receptors (SURs) that surround the pore. SUR proteins are members of the ATP binding cassette (ABC) superfamily of proteins and contain two membrane spanning domains and two nucleotide binding domains (NBD1 and NBD2). MgATP binding and hydrolysis at the SUR NBDs results in opening of the Kir6.x channel gate. The NBDs of the cardiac SUR proteins (SUR2A) are also binding sites for the KATP channel opener (KCO) drug pinacidil and for molecular chaperones. The mechanisms by which KCOs increase KATP channel gating are largely unknown, but previous work in our lab indicates that they increase the affinity of the NBDs for nucleotide. Additional studies are necessary to (a) determine which NBD residues are involved in drug binding and (b) whether novel KCOs and pharmacological chaperones can correct disease-causing mutations. To this end, we are studying drug binding to SUR2A NBD1 using NMR spectroscopy. Changes in the 2D 15N- 1H correlation spectra of NBD1 indicates that the KCO pinacidil and chaperone drugs interacts with residues in the C terminal helix of the domain, which is confirmed through mutagenesis of candidate drug binding residues. Further, we perform fluorescence nucleotide binding studies with and without drugs to probe perturbations of ATP binding upon drug binding. The NMR data will be used to construct structural models of the NBD1-drug complex. The molecular- level understanding of NBD/drug interactions offered by our studies are critical in developing more potent and selective drugs for cardiovascular diseases

P46



Understanding the Hydrophobic Effect using β-Cyclodextrin as a Model System
Jaryd Sullivan, Mazdak Khajehpour
Department of Chemistry, University of Manitoba

Cyclodextrins (CD) are cyclic oligosaccharides consisting of 6, 7, or 8 α-1,4-linked Dglucose units with a truncated cone structure. Three polymers of CD exist: hexamer (αCD), heptamer (β-CD), and octamer (γ-CD). It has previously been demonstrated that cyclodextrins are useful models for exploring guest-host chemistry as they have hydrophobic centers while retaining moderate to high solubilities in aqueous mediums. Guest-host chemistry examines weak, non-covalent intermolecular interactions such as electrostatic, van der Waals, hydrogen bonds, and hydrophobic interactions to address scientific questions. We hypothesize that as salt concentration increases, the hydrophobicity of the cavity is increased thereby facilitating faster binding of the probe 2,6 Anilinonaphthalene-6-Sulfonic Acid (2,6 ANS). From steady-state fluorescence experiments, sodium chloride appears to increase fluorescence which can be related to an increase in 2,6 ANS binding to the cavity of βCD. With temperature-jump fluorescence spectroscopy data we were able to determine that sodium chloride is involved in the final step of the mechanism—drawing water out of the sugar cavity. We believe the increase in ligand binding is due to a decrease in the activity of water. Our results indicate that 31 ± 6 water molecules are disrupted for every molecule of 2,6 ANS that binds to the cavity of βCD. Therefore, water molecules surrounding cyclodextrin and located inside the cavity are drawn towards the area of lower activity. This supports the idea that NaCl is lowering the activity of water. Once the hydrophobic lining of the cavity is exposed, 2,6 ANS can establish energetically favorable, hydrophobic interactions rather than maintain contact with the surrounding waters—lowering the energy of the system. In summary, sodium chloride effectuates ligand binding by decreasing the activity of water thereby enhancing hydrophobic interactions.

P47

Probing the Conformational Dynamics of the Active Site of an OTU Deubiquitinase Enzyme

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Department of Chemistry, University of Manitoba

Enzymes are fundamental to cell function. Despite this, exactly how enzymes work remains unknown. Enzymes exist as 3D folded structures determined by their amino acid sequence. These structures are necessary for function. Solving these structures using methods such as X-ray crystallography provides great insight into protein function at the molecular level. However, these methods only provide structural detail about a single stable conformation. In reality, enzymes change their 3D conformation frequently during the course of a reaction, thus the structure of a single conformation will provide incomplete information. To completely understand how enzymes function, we must understand their dynamics – their changes in conformation over time. To study enzyme dynamics, we have used the catalytic domain of Otu1, a deubiquitinase from yeast. Deubiquitinases are enzymes that catalyze the breakdown of ubiquitin, and play an important role in regulating cell functions including immune response and signal transduction [1]. Our goal is to completely understand the conformational changes that occur during the Otu1 reaction cycle. First we must examine the dynamics of the free enzyme. The crystal structure of Otu1 contains a loop of amino acids that covers the active site where catalysis takes place [2]. We hypothesize this loop must open up to allow the active site to access substrate. In our model, Otu1 exists in equilibrium between an open-loop conformation and a closed-loop conformation. We have employed a series of ligand-binding experiments using stopped-flow fluorescence spectroscopy to examine the dynamics of the free enzyme, and have determined the loop opening rate to be about 100 s^{-1}.

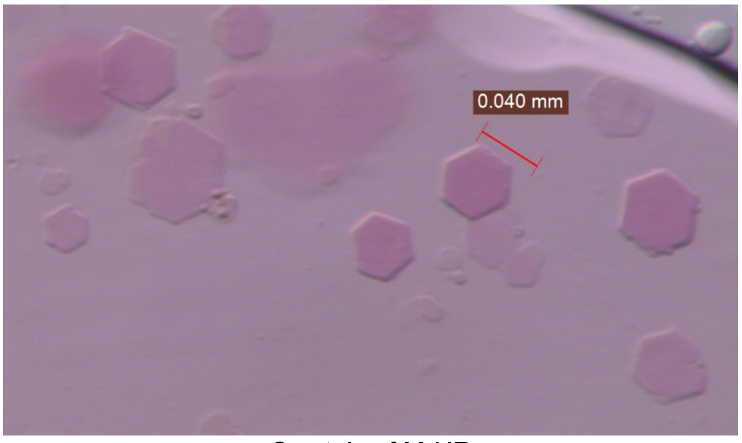
[1]: Komander et al. Nat Rev Mol Cell Biol 10, 550-63, 2009
[2]: Messick et al. J Biol Chem, 283, 11038-49, 2008

P48

Towards Preparation of Protein Samples for Time-Resolved Structural Dynamics Studies

Jessica Besaw, R.J. Dwayne Miller
Department of Chemistry, University of Toronto

One of the holy grails of science is to observe atomic motions on the relevant timescales of structural transitions, which has recently been made possible through the development of *femtosecond* electron diffraction and x-ray diffraction techniques [1]. This Ph.D. work attempts to extend these time-resolved structural dynamics techniques to biological systems in order to resolve the structure-function relationship by which chemistry is transduced into biological functions. In the first phase of this research, standard molecular biology techniques are employed to make crystalline protein samples for later use in time-resolved studies. This poster will present the results to date for optimizing crystallization of two protein systems: (1) catalase and (2) Mastigocladosis repens halorhodopsin (MrHR).



Crystals of MrHR

[1] R. J. D. Miller, *Science* 343, 1108-1116, 2014

P49

Observing Conical Intersections through Ultrafast Electron Diffraction

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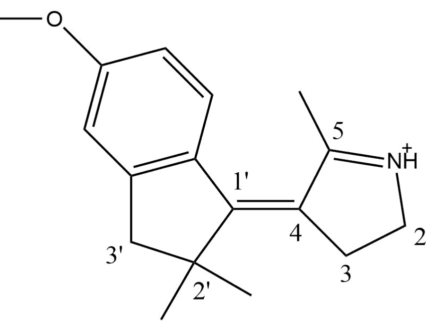

Figure 1: The photoswitch, ZAP.

Fundamental processes in nature, including vision, water splitting, and carbon dioxide reduction are made possible by an extraordinary degree of evolutionary optimization that exploits the presence of a conical intersection. Conical intersections occur when the potential energy surfaces of the ground and excited states of a molecule cross at a single point, leading to new electronic dynamics and increased transition efficiencies. Rhodopsin, the visual pigment of superior animals, has a conical intersection. This leads to a highly optimized and ultrafast structural change in the retinol portion of the protein upon photoexcitaton – the primary step in the process of vision. The focus of this research is on an indanylidene pyrroline photoswitch, nicknamed ZAP (Figure 1) [1]. This compound is designed based on the photophysics of retinol, mimicking the cis-trans isomizeration of its 1'-4 carbon-carbon double bond. ZAP possesses a conical intersection, meaning that non-adiabatic quantum mechanical considerations reduce the number of relevant atomic motions to a set of key modes. Thus, the atomic motions pertaining to rhodopsin's function in vision will be experimentally probed by means of ultrafast electron diffraction (UED). This is possible due to the fact that UED combines the temporal resolution of ultrafast optical spectroscopy with the structural determination of diffraction techniques, meaning that ultrafast motions may be seen experimentally. Single crystals of the compound have been grown and analyzed by X-ray crystallography (Figure 2). Currently, pump-probe spectroscopy is being performed on thin crystals to determine the ideal excitation and time scale of the isomerization prior to performing electron diffraction experiments. The data will construct a 'molecular movie' of ZAP in motion, further elucidating the structure-function relationship of rhodopsin.

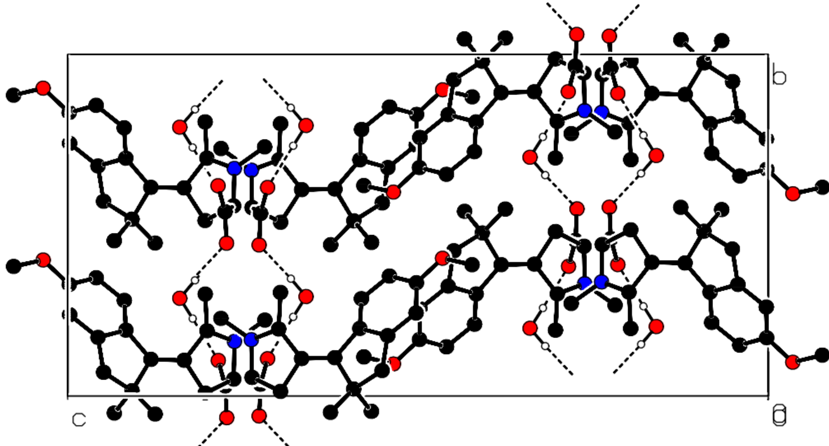

Figure 2: A unit cell lattice of single crystalline ZAP, displayed along the b-axis direction.

[1] J. Briand, O. Bräm, J. Réhault, J. Léonard, A. Cannizzo, M. Chergui, V. Zanirato, M. Olivucci, J. Helbing, S. Haacke, *Physical Chemistry Chemical Physics*, 3178-3187, 20

P50

Congenital Hyperinsulinsm-causing Mutations alter the Structure and MgATP Binding of SUR1 NBD1 in the Pancreatic K_{ATP} Channels

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ATP-sensitive potassium (KATP) channels are key players in insulin secretion from the pancreas. KATP channels are regulated by the sulfonylurea receptor 1 (SUR1) protein. Sulfonylurea receptors (SUR) are multi-domain proteins that are part of the ATP binding cassette (ABC) superfamily of transporters. Like other ABC proteins, SUR proteins contain two membranespanning domains (MSDs) and two nucleotide binding domains (NBD1 and NBD2). Coupling helices link the cytosolic ends of helices in the MSDs and bind the NBDs. However, unlike other ABC proteins, SUR proteins lack transport function. Instead, MgATP binding and hydrolysis at the SUR NBDs cause conformational changes that lead to the opening of the KATP channel pore. Proper functioning of the KATP channels is vital for insulin secretion from the pancreatic ß cells. Misregulation of KATP channel trafficking and gating as a result of SUR mutations results in disorders of insulin secretion. The research presented here investigates the structural and functional consequences of the congenital hyperinsulinism-causing mutations (C717Δ, G716V, R824G, R837Δ and K890T) localized in NBD1 domain of the human pancreatic-specific SUR1 protein. Our nuclear magnetic resonance (NMR) and fluorescence data show that the hyperinsulinism mutation K890T in NBD1 causes overall changes in the protein conformation that likely disrupt interactions with other domains of the SUR protein, such as the coupling helices and NBD2. Moreover, functional characterization shows that the mutation K890T decreases the affinity of the domain for MgATP. Size-exclusion chromatography data show that the other hyperinsulinism mutations studied here (C717Δ, G716V, R824G, R837Δ) produce mostly aggregated protein, likely as a result of misfolding of NBD1 or compromised MgATP binding. Misfolding of NBD1 may be the underlying cause of reduced KATP channel trafficking seen with these mutations and subsequent decreased KATP channel gating. Our data provide molecular and functional details describing how mutations in SUR NBD1 cause hyperinsulinism.

P51

Design of a Photoactivatable 4E-BP for Optical Control of Protein Synthesis

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Synapse formation and function in neurons requires the precise spatiotemporal control of protein synthesis (translation). The dysregulation of translation and of eIF4E, a key regulator of translation initiation, in neurons has been implicated in mental disorders such as autism. Unfortunately, the gene knock-ins and knock-outs used to study these disorders offer only crude spatiotemporal control of protein expression (timescales of days/weeks). Optogenetic tools, in contrast, can be controlled in minutes with a spatial scale as small as a single synapse. Here, we present a new optogenetic tool for the control of translation in neurons. To assess function in vivo, we developed an assay using a strain of *Saccharomyces cerevisiae* which requires human eIF4E for growth. From a panel of 19 structure-based designs, we identified one promising construct: a fusion of a circularly permuted LOV2 domain from *Avena sativa* (cLOV) and 4E-BP2, an inhibitor of eIF4E and translation initiation. In blue light, yeast expressing the cLOV-4EBP2 inhibitor grew significantly slower compared to the dark. When the primary binding site of 4E-BP2 was mutated to non-binding, inhibition was lost and growth was restored back to wild-type. In vitro studies showed that blue light caused cLOV-4EBP2 to bind to eIF4E while dark state cLOV-4EBP2 was inhibited from binding eIF4E. This process was found to be reversible and repeatable. To improve the light-dark difference of activity, we screened a random library of additional mutants based on the successful structure-based design in the *S. cerevisiae* strain. One promising construct that showed very strong inhibition under low levels of blue light was identified and studies are currently underway to validate function.

P52

Single-Molecule Dissection of the Conformations, Dynamics and Binding of the Disordered 4E-BP2 Protein

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Intrinsically disordered proteins (IDPs) play critical roles in regulatory protein interactions. Cap-dependent translation initiation is regulated by the interaction of eukaryotic initiation factor 4E (eIF4E) with disordered eIF4E binding proteins (4E-BPs) in a phosphorylation dependent manner. Single molecule fluorescence resonance energy transfer (smFRET), fluorescence correlation spectroscopy (FCS), time-resolved fluorescence anisotropy (TRFA) were used to detect and assess the structural changes and sequence-specific local chain motions of 4E-BP2 upon phosphorylation and upon binding to eIF4E.

Multiparameter smFRET analysis reveals changes in the conformational ensemble responding to phosphorylation, denaturation, salt and pH. Nanosecond scale dynamics in 4E-BP2 were observed by site-specific FCS, and were tentatively assigned to formation of transient chain contact formation. Our data suggests that multi-site phosphorylation of the protein slows down the proximal chain motions and also modulates the kinetics of distal regions. Segmental rotational correlation times and wobbling cone angles extracted for different sites along the chain provide a rigidity map of this IDP and can be used to evaluate its binding mode to eIF4E.

P53

Dimensions and Dynamics of Highly Cooperative Sic1-WD40 Binding: smFRET through a Polymer Physics Lens

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A large number of proteins, termed intrinsically disordered proteins (IDPs), fail to fold into well-defined three-dimensional structures. Many of these IDPs are associated with diseases, such as cancer or neurodegenerative disorders. In contrast to well-folded proteins, the polymer properties of IDPs are often crucial aspects of their functions. Correspondingly, to develop a better understanding of how disorder gives rise to function, I use a polymer-physics-based approach to analyze data from ensemble and single-molecule fluorescence spectroscopy experiments. In particular, I study Sic1 - a cyclin-dependent kinase inhibitor which must be phosphorylated on at least six sites (termed Cdc4 phosphodegrons, CPDs) in order to allow its recognition by the WD40 binding domain of Cdc4. Because WD40 appears to have only a single CPD binding site, the highly-cooperative switch-like dependence on the number of phosphorylated sites of Sic1 cannot be accounted for by traditional thermodynamic models of cooperativity. The binding of an IDP to a single receptor with a single binding site requires more experimental attention to determine its physicochemical/mechanistic basis. I address this by developing a toolkit which combines single molecule and ensemble fluorescence experimentation with polymer physics theory and simulations.

P54

Modelling Spatial Assemblies of Nucleoporins from Diverse Species

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TP-cargo complex	Schematic representation	MW(kDa)	Results
NTF2		33	TP-cargo penetrate into Nup aggregates
Imp β - IBB		103	TP-cargo penetrate into Nup aggregates
Imp β - IBB-GFP		131	No penetration
Imp β - IBB-MBP-GFP		172	No penetration
(Imp β - ZsGreen) × 4		520	Recovery of penetration

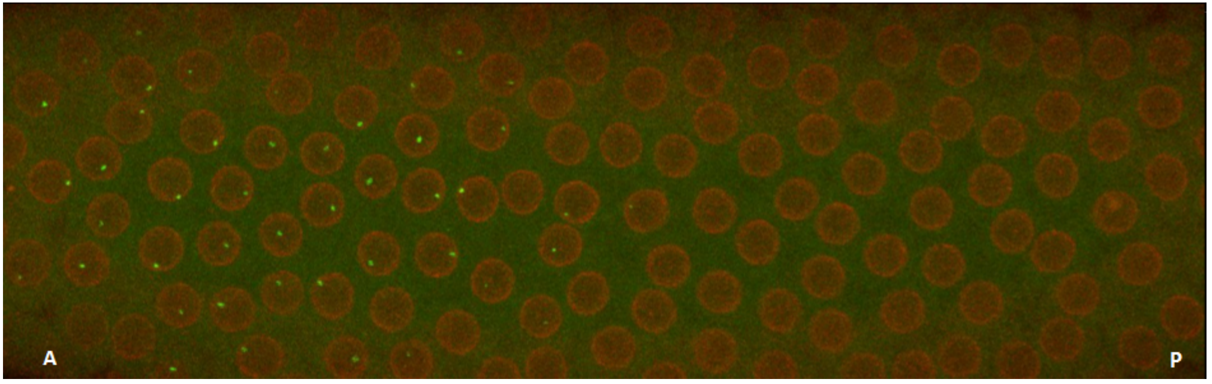
Intrinsically-disordered nucleoporins found inside the nuclear pore complex (NPC) are responsible for selective transport through the nuclear membrane. Nucleoporins carry repetitive Phenylalanine-Glycine (FG) motifs, which allow them to interact with each other, as well as binding to transport protein-cargo complexes via hydrophobic interaction. In-vitro experiment (Schmidt and Görlich, eLIFE 2015) demonstrated that soluble nucleoporins spontaneously form dense phase aggregates. Selective penetration of transport proteins-cargo complexes into the dense phase were observed. These observations may suggest that the formation of a gel-like phase composed of nucleoporins as a mechanism for NPC selectivity.

We employ a simple biophysical model based on polymer theory to describe the observed phase separation behaviour in the nup98 family of nucleoporins, derived from different eukaryotic species. We are able to capture the essential features of nup98 aggregation behaviour by a minimal set of coarse-grained parameters, corresponding to the average inter-FG repeat and transport protein-FG repeat attraction strength, as well as the transport protein versus FG domain size ratio. Our model predicts the spontaneous formation of dense aggregates composed of a mixture of nuceloporins and transport protein-cargo complexes. In agreement with experiment, when the size of the cargo complex is varied, our model predicts that while an increase in the size of the cargo complex significantly decreases its penetration into the dense phase, the recovery of significant penetration for a large cargo into the aggregate can be achieved by increasing the effective transport protein-FG domain interaction strength. Our model demonstrates a successful application of simple polymer physics to model the spatial assembly of a mixture containing a component of flexible, intrinsically-disordered protein.

P55

Live Fluorescence Microscopy as a Tool to Study Morphogen Dynamics during *Drosophila melanogaster* Embryonic Development

Carmina Angelica Perez Romero*, Tanguy Lucas~, Teresa Ferraro~, Nathalie Dostatni~, Cecile Fradin*
*McMaster University
~Institute Curie



In embryos, cell differentiation occurs via the formation of spatial gradients of molecules called morphogens, which control the expression of a number of target genes determining cell identity. A common model to study morphogens is the Bicoid gradient, which determines anterio-posterior (AP) patterning in fruit fly. We are interested in understanding how a noisy morphogen input can give a precise output of its target, and accomplish robustness during embryonic development. Here, we apply novel methods to label the nascent mRNA of target gene, to detect the fluctuations in signal caused by the periodic creation of new mRNA at transcription sites) in order to measure the rate of transcription of the Bicoid target gene, hunchback, in each nucleus along the AP axis (see Figure).

Systematic measurements will allow us to determine which factors influence this transcription rate (e.g. morphogen diffusion rate, morphogen/target concentration, and polymerase activity at the target promoter), especially in the border region where there is a switch between expression and no expression. Given the rapidity of establishment of a precise transcriptional response, our hypothesis is that this response at the border relies on a memorization process, allowing nuclei to recall Bicoid concentration from one cycle to the next, by keeping track of the Hunchback promoter transcriptional status across mitosis. Future experiments aiming to challenge this hypothesis, using novel methods in live embryonic imaging are discussed.

P56

Force Generation by a Liquid Protein Droplet May Effect Membrane Curvature

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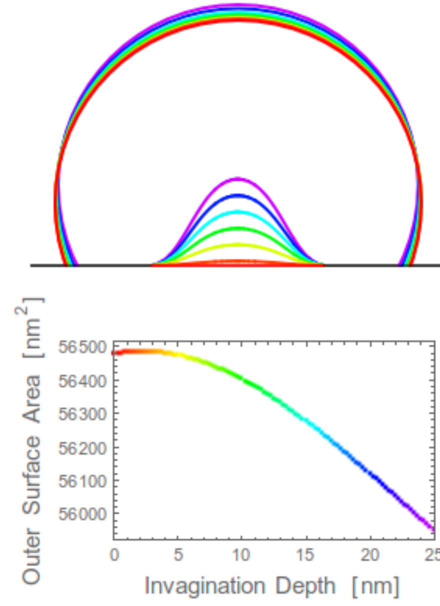
***Physics Department, McGill University*



Clathrin-mediated endocytosis is an important process by which external cargo is carried into the cell, without which cells could not function. Many of the proteins involved have been identified. However, the way these proteins interact with each other or the cell membrane to generate force is unclear, and the biomechanics by which deformation of the cell membrane is effected are not understood.

We propose a physical solution to this problem. Here, a fluid droplet of proteins condenses out of the cytosol and wets onto the cell membrane at endocytic sites. This is in agreement with both the rapid fluorescence recovery of proteins, and the exclusion of large ribosomes, at such sites. The surface tension between droplet and cytoplasm will drive the droplet to assume a spherical shape. If the contact between droplet and membrane remains constant, due to the wetting interaction, conformational changes to the droplet can effect curvature of the membrane. We investigate the conditions under which this may occur, and derive an approximate value for the droplet surface tension necessary to overcome the energetic barriers to membrane invagination in *S. cerevisiae*.

P57

Treatment of CK2.3 on Isolated Primary Cells Induces Bone Mineralization and Decreases Lipid Droplet Formation

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Osteoporosis is a bone disease that is characterized by low bone density. This leads to deterioration of the bones, which ultimately increases the chances for more bone fractures or breaks. This can add up to be very expensive (both emotionally and fiscally), and the costs will only steadily rise as the population of elderly increases. On a cellular level the histology of a normal bone is a balance between bone forming (osteoblasts) and bone remodeling cells (osteoclasts). Osteoporosis is characterized by having more osteoclast activity, than osteoblast activity. Our lab has investigated how BMP2 is able to signal osteoclastogenesis in osteoporotic patients. BMP2 binds to its dimerized receptors and signals for CK2 to be released from BMP2RIa, which leads to osteoclastogenesis. Our lab has designed a novel peptide known as CK2.3 that binds to CK2 thus inhibiting it from binding to a specific portion of the receptor BMP2RIa. My project is to further investigate how treatment of CK2.3 will affect primary isolated cells extracted from osteoporotic patients. Previous research in our lab had shown that treatment of CK2.3 increases the mineralization and reduces lipid droplet formation.

P58

Inhibition of Differentiation of RAW264.7 Monocyte/Macrophage Cell Line to Osteoclasts by a Novel Peptide, CK2.3

John Nguyen, Anja Nohe
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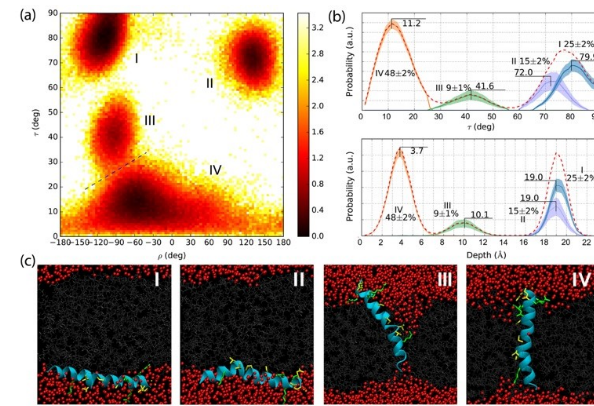
Equaling activity between bone resorption by osteoclasts and bone formation by osteoblasts is important in normal bone remodeling process. When this balance is offset, it can lead to various bone diseases such as osteoporosis which is characterized by over activity of osteoclast. Studies have shown bone morphogenetic protein 2 (BMP2) has a directly effect on osteoclasts by increasing expression of genes involve in enhancing differentiation and fusion of mononuclear pre-osteoclasts to mature multinucleated osteoclasts. Our lab previously identified casein kinase 2 (CK2) as a binding protein on BMP2 receptor type Ia (BMPRIa) and a regulator of BMP2 signaling pathway. We also identified three potential binding sites for CK2 on BMPRIa and designed three peptides to block its interaction on BMPRIa at these three sites.
The focus of this project is on peptide CK2.3 which blocks the interaction of CK2 at amino acids 475-479 on BMPRIa. Our previous data showed that CK2.3 increased bone mineralization and decreased osteoclast activity in mice. This project is aiming to elucidate the effect of CK2.3 on the differentiation of osteoclasts from its monocyte/macrophage precursor cells. The result reveals that CK2.3 inhibits the differentiation of osteoclast from RAW264.7 monocyte/macrophage cells at 100nM. However, as higher concentrations, 500nM and 1000nM, the inhibition effect of CK2.3 decreases or diminishes by an unknown mechanism.

P59

Jingjing Huang
Department of Biochemistry, University of Toronto



Transmembrane (TM) proteins constitute more than 53% of current drug targets. Structure and function of TM proteins can be modulated by the lipid membrane environment. It is thus of great interest to investigate interactions between TM protein and lipid bilayer (LB). One way to quantify such interactions is to probe orientations of peptides/protein in membrane. However, the intimate relationship between TM proteins and LB limits the use of many standard experimental techniques to determine their structures and functions in vivo such as magnetic resonance spectroscopy, circular dichroism, infrared spectroscopy, etc. because most of the current experimental approaches are impossible to conduct in the native environment and are restricted in providing a detailed description of unperturbed native conformations or functions. Despite providing investigations of molecular details, current standard simulation, for example, all-atom (AT) molecular dynamics simulation is still limited due to shorter timescale it provides compared with many fundamental molecular and physiological events of interest. Coarse-grained strategies have been proposed to push timescale limitations but its reduced chemical resolution and fundamentally affected thermodynamic properties hinder their applications. Therefore, a new protocol, Rapid Orientation of Membrane Protein (ROMP) has been developed to predict orientations of peptides in LB. In this specific case, melittin has been used as model peptide. Massive ensemble-based simulations have been conducted to systematically and statistically investigate orientation of melittin in LB, from which four conformations, surface-bound-1, surface-bound-2, transmembrane and pseudo-transmembrane have been demonstrated statistically and simultaneously for the first time. Distribution and time evolutions of distribution for these four conformations have been analyzed, which indicates surface-bound-1 and transmembrane are the most preferred states while pseudo-transmembrane state is least populated. Our study also confirmed that ROMP can be applied to predict peptide orientation in membrane.

P60

tHairapy: Structural Abnormalities in the Hair of a Patient with a Novel Ribosomopathy

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A clinical challenge exists when catching and treating diseases arising from *de novo* mutations, as there is not necessarily a defined diagnostic protocol. Recently, we were approached by a family in the Netherlands, whose son was diagnosed with a mutation on RPS23 which influences his ribosomes (a ribosomopathy). His symptoms include autism, elastic skin, and thin/brittle hair [1]. This diagnosis had taken two years and required many tests, and the family is interested in learning how this process could be made quicker in the future. We undertook a biophysical characterization of the patient's hair, to understand whether the patient's hair can be used as a tool to diagnose his specific disease.
Hair samples from the patient and his family (mother, father, and 3 siblings, all without the RPS23 mutation) were acquired and tested using optical microscopy, tensile tests, and X-ray diffraction. From optical microscopy, we observe that the patient's hairs are intact, although 20% thinner than his family's. While the Young's modulus of his hair was within normal limits, X-ray diffraction revealed that the molecular structures of both lipid and keratin in his hair are unchanged [2,3]. However, diffraction revealed a reduced lipid content (relative to keratin), likely directly related to his disease [4]. The results indicate that X-ray diffraction tests of hair could be a diagnostic tool for this ribosomopathy.

[1] Ricki Lewis, JAMA, 2015
[2] F-C. Yang, Y. Zhang, M.C. Rheinstadter PeerJ, e619, 2014
[3] Y. Zhang, R.J. Alsop, A. Soomro, F-C. Yang, M.C. Rheinstadter. PeerJ, e1296. 2015
[4] R.J. Alsop, A. Soomro, Y. Zhang, M. Pieterse, A. Fatona, K. Dej, M.C. Rheinstadter. PLoS ONE 11, e0149619, 2016

P61

Fluorophore Photoprotection Mediated by Ni^{2+} for Extended Single-Molecule Imaging: Old Tricks for New Techniques

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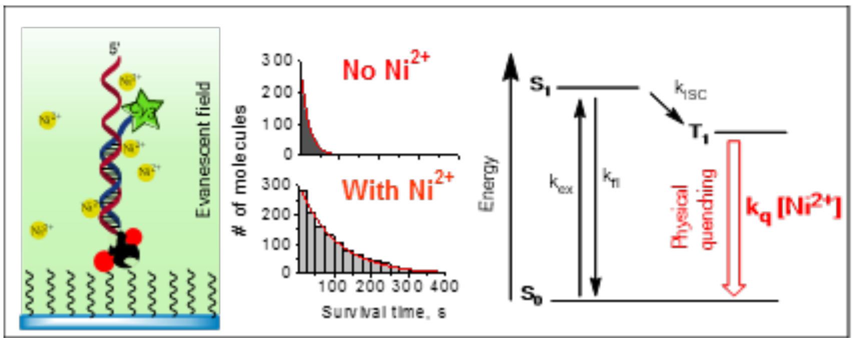

Understanding the photophysical properties of fluorophores and mitigating unwanted photophysical processes such as blinking and irreversible photobleaching is of great interest for improving single-molecule fluorescence imaging.[1] The photostability of reporter fluorophores dictates the amount of photons, and in turn, the amount information that may be acquired from a molecule of interest before photobleaching occurs. In this talk we will discuss a novel approach to photostabilize a number of dyes used for single-molecule imaging. The approach relies on using Ni^{2+} as a solution additive to quench triplet excited states of the dyes, thereby eliminating one of the key intermediates in the photobleaching pathway. Through a combination of single-molecule studies and ensemble mechanistic studies, we first demonstrated that Ni^{2+} can be used as a triplet quencher for single-molecule fluorescence imaging providing a much desired physical quenching route (chemically inert) to increase the photostability of Cy3.[2] We then explored the scope of this approach showing that it can be extended to wide range of single-molecule dyes and demonstrated that, differently from other common used triplet state quenchers, Ni^{2+} can be used to photostabilize both green- and red-emissive dyes, which is much desired for multicolor imaging applications.

[1] V. Marx, Nat Meth 12, 187, 2015
[2] V. Glembockyte, R. Lincoln, R., G. Cosa, J Am Chem Soc 2015

P62

Structure-Activity Relationship Study of a Novel Chemosensor for Proximal Phosphorylation

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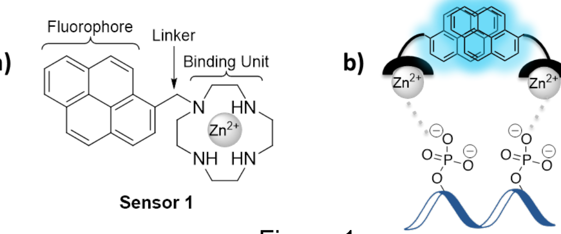

Figure 1.

Phosphorylation is a universal post-translational protein modification found in both healthy and diseased states. While it is widely recognized that the presence or absence of phosphates on a protein affects its activity, the effect of the spatial arrangement of phosphates in motifs is less understood. To this end, the Gunning group has previously developed a novel fluorescent chemosensor 1 (Figure 1a) that selectively detects proteins containing proximal phosphorylation sites in aqueous solutions, gels and membranes. Sensing is achieved through a turn-on fluorescent excimer mechanism, where two sensor units bind to two or more proximal phosphates via a chelated-Zn^{2+} centre. As a result, their pyrene reporter units stack, leading to excimer formation which is accompanied by a distinct red-shifted emission with respect to the monomer (Figure 1b). This sensor technology presents great promise for the development of *in vitro* diagnostic tools for disease screening and research in the phosphoproteome. The aim of this study was to understand how each of the sensor's components affect sensitivity and selectivity of this system. A structure-activity relationship study was thereby performed to explore the three components of the sensor: the Zn^{2+}-chelate binding group, the reporter fluorophore and the linker. This was done by synthesizing a small library of sensors which varied one or two of the three units with respect to the original sensor 1. The sensors were evaluated against model peptides and common proteins of various phosphorylation states through fluorescence intensity titrations in aqueous solution. The results of this study will be presented.

P63

Förster Resonance Energy Transfer as a Distance Probe for Gas-phase Ubiquitin

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Mass spectrometry has been employed to study biological molecules such as proteins since the invention of soft ionization techniques. However, the effects of desolvation, a necessary step in mass spectrometry analysis, on the structure of proteins are not well understood. A range of methods, including ion mobility spectrometry and hydrogen/deuterium exchange, have been used to elucidate these effects. While these methods lend useful insight, detailed and localised information about gaseous protein structure is still lacking. Our laboratory is developing technology which combines mass spectrometry with fluorescence spectroscopy in order to improve the understanding of how biomolecular structure changes upon desolvation. We have recently shown that Förster Resonance Energy Transfer (FRET) can be used to probe gas-phase protein structure as a function of its charge states [1].
To further develop FRET as a probe for gas-phase biomolecule structure, here a multi-site FRET study of the protein ubiquitin is conducted. Several ubiquitin variants were fluorescently labelled with Alexa Fluor 488 (the FRET donor) and Alexa Fluor 594 (the acceptor) and their conformation, and conformational changes, were probed within a quadrupole ion trap (QIT) mass spectrometer that is modified for optical spectroscopic experiments. Initial analysis of the steady state fluorescence emission measurements suggests that ubiquitin ions with 5+ and 6+ charge states have more compact conformations whilst 7+ ions have a more extended structure. Steady state measurements of the 7+ ions indicate that there are two distinctive conformations within this charge state. Ultimately, by combining our FRET measurements with computational modeling and other gas-phase experiments, we hope to elucidate the effects of desolvation on the stability structure of ubiquitin and other proteins.

[1] M.F. Czar, F. Zosel, I. König, D. Nettels, B. Wunderlich, B. Schuler, A. Zarrine-Afsar, and R.A. Jockusch, *Analytical Chemistry* 87, 15, 2015

P64

Analysis of Biobased Products and Changes of Microstructure of ^{60}Co-γ Irradiated Rapeseed Straw

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[a] College of Food Science and Technology, Hunan Agricultural University
[b] Hunan Provincial Key Laboratory of Crop Germplasm Innovation and Utilization, Hunan Agricultural University
[c] Hunan Collaborative Innovation for Utilization of Botanical Functional Ingredients, Hunan Agricultural University
[d] The Institute of Vegetables and Flowers, Chinese Academy of Agricultural Sciences
*[e] Department of Biology, Lakehead University *Corresponding authors.*

In this study, rapeseed straw was pretreated with ^{60}Co-γ irradiation and digested with cellulase to improve sugar production. Our analysis of pretreated straw composition demonstrated remarkable increases in both total reducing sugar release and degradation of cellulose, hemicellulose and lignin. At a dose of 1200 kGy irradiation, 39.3 times more reducing sugars were released, comparing to the untreated control straw (35.34 *vs* 0.90 mg/g). Except the increase of reducing sugar content, more types of sugar compounds were detected. Enzymatic digestion of the irradiated straw resulted in 79.21% and 75.59% degradation of cellulose and hemicellulose, respectively. After treatments with different doses, the total reducing sugars increased by 4.6 to 392.50 mg/g from 86.18 mg/g in the control. Analyses with X-ray diffraction, infrared spectroscopy, and scanning electron microscopy showed that the microstructure of the irradiated straw was significantly changed. By adopting GC-MS using ethyl acetate fractions of water extracts from untreated and pretreated straws, 32, 17, and 5 different kinds of fatty acids, aromatics and furans were detected, respectively. Twenty-two types of fatty acids were detected in the non-irradiated straw sample, with a content of 19.99%. No significant changes of types and contents of fatty acids were observed, in doses from 400 to 1000 kGy for treatment. Once the irradiation dose was increased to 1200 kGy, the types of fatty acids were reduced from 22 to 14, and the content was significantly decreased, from 19.99% to 6.23%. In untreated straw, only 5 types of aromatic compounds were detected in very small amounts, and as low as 0.75%. But with the irradiation treatment, both the types and contents of aromatic compounds were increased. The furan compounds were only detected when the irradiation dose reached 1000 kGy or higher, and the type of which were different in straws treated with different irradiation doses.

P65

Overcoming The Challenge Of Intravenous Infusion Of Hydrogen Enriched Fluids: A Scavenger Solution For Reactive Oxygen Species In Hemorrhagic Shock

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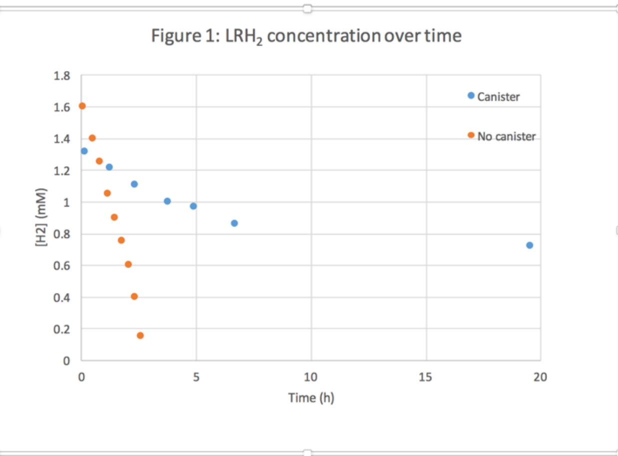
[1]*Department of Chemistry, University of Toronto*
[2]*Li Ka Shing Knowledge Institute, St. Michael's Hospital, University of Toronto*

Reactive oxygen species (ROS) play an important role in the development of tissue and organ dysfunction in inflammatory states. Hydrogen dissolved resuscitation fluids has recently emerged as a free radical scavenger in several experimental conditions that lead to ROS production. However, hydrogen (H_2) does not readily dissolve in aqueous fluids, hindering intravenous delivery of adequate intravascular levels during infusion.
We devised a novel technique to dissolve hydrogen gas in Lactated Ringer's (LR) solution utilizing simple chemical and physical principles in a custom-built canister. The canister stores and delivers the LR/H_2 solution intravenously and has been successfully implemented in a hemorrhagic shock animal model.
Supersaturated levels (> 0.8 mM) of hydrogen enriched LR (LRH_2) were produced and delivered intravenously in animal models. No gas embolism was detected and an adequate response to resuscitation was shown in all animals. Moreover, hydrogen levels in LR solution remained supersaturated for up to 7 hours, allowing for prolonged resuscitations periods in animals (Figure 1).
This is a novel technique to deliver hydrogen concentrations intravenously in a clinically relevant and stable solution. Hydrogen levels remain stable over the course of the infusion and is a promising method to be used in future investigations into hydrogen's action as a ROS scavenger.



P66

Spectroscopy of H20/TMAO at Hydrophobic Interfaces Large and Small

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Department of Chemistry, University of Toronto

Recent work from our group raises the possibility that an aqueous solution of trimethylamine N-oxide (TMAO) will behave differently at a large hydrophobic interface (on the order of several molecules) than at smaller one (such as an isolated hydrophobe). In the present work, sum frequency generation spectroscopy (SFG) is used to investigate the behaviour at a large interface, and Raman spectra are analyzed using self-modelling curve resolution (SMCR) to investigate the smaller interface. We find that the addition of TMAO forces the population of water molecules towards a more ice-like structure. The shift occurs in the bulk, but the shift is much more evident near both hydrophobic interfaces than in it is in the bulk. We also provide evidence that the concentration of TMAO at the larger interface is greater than that at the smaller interface, which supports results from earlier work.

P67

Broadband Pump-Probe Spectroscopy Reveals Ultrafast Dielectric Response of Solvated Proteins and Molecules

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[2]*Department of Chemistry, Princeton University*

The Stokes Shift measures the difference between the maxima of absorption and fluorescence spectra and is affected by the dielectric properties of the solvent. This dynamic response to charge redistribution upon light absorption of solute molecules occurs over a wide range of timescales, from femtoseconds to nanoseconds. The Stokes shift can be captured in various timescales by time dependent fluorescence spectroscopy (ps-ns), fluorescence upconversion (80 fs time resolution), transient birefringence (20 fs resolution) and photon echo peak shift spectroscopy (50-100 fs). The advancement of methodologies that can resolve femtosecond time dynamics have revealed that a large proportion of the solvation response can be assigned to an ultrafast inertial response. In this work we demonstrate the use broadband pump-probe spectroscopy to capture the femtosecond solvation dynamics of phycobiliproteins and oxazine dye in different solvents. Broadband impulsive excitation generates vibrational wavepackets that oscillate on the excited state potential energy surface, phase shifting at the global minimum of the surface as a function of probe wavelength over time. This node allows us to follow the free energy changes of the excited state potential energy surface, which maps out the solvation time correlation function. This method resolves an isotope effect on the inertial solvation response (Figure 1) as well as captures how protein-buried chromophores are sensitive to the solvent dynamics outside of the of the protein environment.

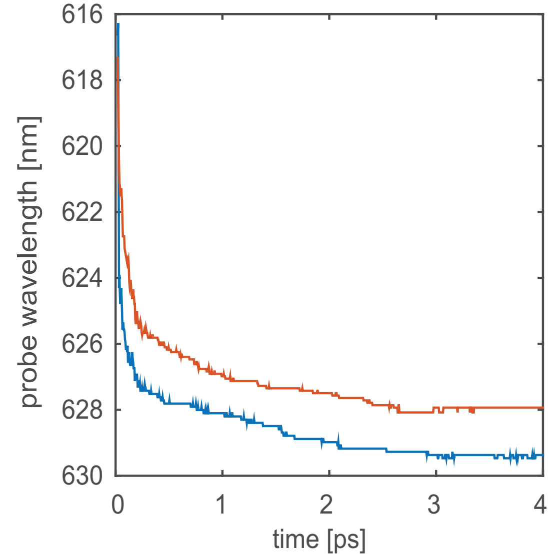


Figure 1: Minimum of excited state potential energy surface of oxazine 170 in methanol (blue) and deteurated methanol (red)

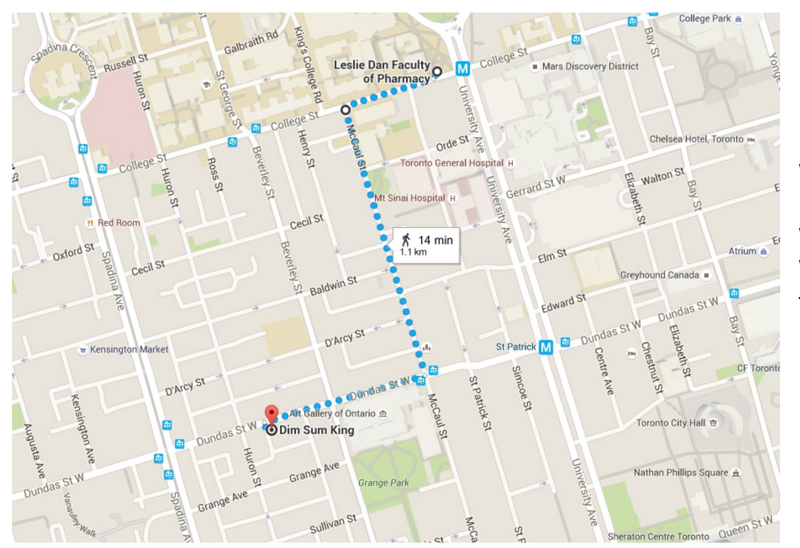
P68

Impact of Low Power Microwave Irradiation on the Structure and Functions of Biological Systems at Constant Bulk Temperature

Sina Mazinani
Department of Biotechnology, Brock University

Impact of microwave irradiation on biomolecules and biological systems has been a controversial issue over the past decades. Majority of the reported studies have faced heavy criticism and were considered unreliable due to the fact that the temperature of the studied systems, in most cases, was not controlled properly, leaving the room for the observed impact to be attributed to heating alone. Our lab however, has developed a robust system that allows the researcher to keep the bulk temperature of the studied sample relatively constant (±2 °C) under microwave irradiation by means of simultaneous cooling.
The impact of low power (≤10 W) microwave irradiation on enzymatic activity of trypsin, alkaline phosphatase and α-amylase was investigated at constant bulk temperature. While hydrolysis of casein by trypsin was significantly accelerated under microwave irradiation, as compared to control at same temperature without microwave irradiation, no significant change was observed in the activity of microwave irradiated alkaline phosphatase and α-amylase towards the hydrolysis of 4-nitrophenyl phosphate and starch, respectively. Furthermore, *Escherichia coli DE3* in Lysogeny broth (LB) media showed significantly slower growth while under low power (≤10 W) microwave irradiation as compared to control without irradiation at the same temperature (37 °C). Viability test results (the difference in the number of colony forming units between two conditions) were consistent with the observed pattern.

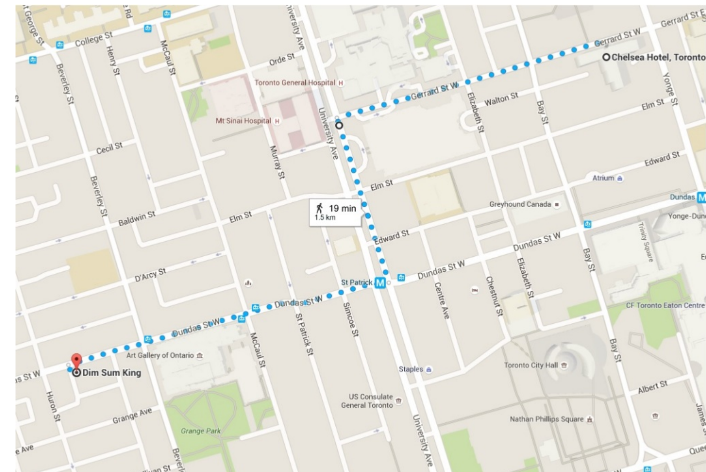
Banquet Dinner: Directions to Dim Sum King

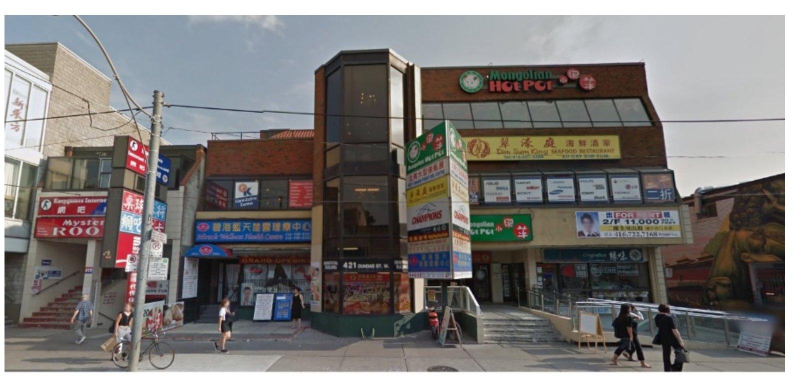


From Leslie L. Dan Pharmacy Building:
Walk west on College St. until McCaul St.

Walk south on McCaul St. until Dundas St. W
Walk west on Dundas St. W until you reach Dim Sum King on the south side of the street

From the Chelsea Hotel:
Walk west on Gerrard St. W until University Ave
Walk south on University Ave until Dundas St. W
Walk west on Dundas St. W until you reach Dim Sum King on the south side of the street





Outside view of Dim Sum King:

Meet us on the second floor of the building!

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