7th Annual Georgia Tech Postdoctoral Research Symposium

Noon to 5 p.m. ET, Friday, March 18, 2022

Parker H. Petit Institute for Bioengineering and Bioscience (IBB)

Suddath Room (1128)

Abstract Book

Postdoctoral Services

Research Talk Session I: 12:00 – 12:55 p.m.

Lipidome Dynamics in an Ovarian Cancer Mouse Model
Olatomiwa O. Bifarin*, Samykuta Sah, David A. Gaul, Ruihong Chen, Murugesan Palaniappan, Facundo M. Fernández

Ovarian cancer (OC) is the fifth leading cause of cancer-related death in women, and particularly deadly is high-grade serous carcinoma (HGSC), the most frequent type of OC.

An HGSC Dicer-Pten Double-Knockout (DKO) mouse model was used to study the dynamics of lipidome changes in this OC subtype as the DKO mice mimic many features of the human disease. After two months of breeding, serum samples of DKO (n = 15) and DKO control (n = 15) mice were collected every two weeks for six months. Ultra-high performance liquid chromatography−mass spectrometry (UHPLC−MS) was used for serum lipidomic profiling. The dynamics of lipidomic changes were studied using univariate statistical methods, machine learning, and survival analysis.

Given the different death rate profile of control and DKO mice, each time point collection was converted to a percentage of the total lifetime of the individual mice, making the group comparison more robust. Percentage lifetimes were then binned into five different stages (0-30%, 30-45%, 45-60%, 60-75%, and 75-100% lifetime). Hierarchical clustering analysis revealed the clustering of longitudinal lipid abundance trajectories into four selected clusters, associated with distinct lipid phenotypes. Machine learning was used for DKO classification for the five different stages of OC progression, with the highest classification performance at 46-60% lifetime (Test set ROC AUC = 0.85). Altered lipid levels were observed for fatty acids (FA) and their derivatives, phospholipids, and sphingolipids. Early progression of OC is marked by increased levels of phosphatidylcholines and phosphatidylethanolamines. In contrast, later stages were marked by more diverse lipids alterations. The alterations provided evidence of perturbations in cell membrane stability, cellular proliferation, and survival, as our study provides the first in-depth, longitudinal lipidome dynamics study of ovarian cancer in the DKO mouse model.

Molecular Simulation of Adsorption and Diffusion in Nanoporous Rigid Amorphous Materials

Raghuram Thyagarajan* and David S. Sholl

The development of publicly available materials databases for materials including zeolites (IZA-SC), metal organic frameworks (CoRE-MOF), and inorganic materials (The Materials Project) has been a key enabler of high-throughput computational screening and data-driven discovery of materials for potential use in new technologies. We recently introduced a similar database for structures of porous rigid amorphous materials, an important class of materials for which no such resource was available. The database includes atomically detailed structures of disordered materials like amorphous carbons, kerogens, hyper-cross-linked polymers etc. generated using a wide range of simulation techniques by multiple research groups. We present extensive computational analyses for material characterization by calculating a series of scalar (e.g., accessible surface area) and vector (e.g., pore size distribution) descriptors. A variety of gas adsorption isotherms for both single component and binary mixtures are predicted for each structure. We also discuss the agreement between binary adsorption data and predictions from the Ideal Adsorbed Solution Theory.

In addition to adsorption isotherms, we have computed the diffusion coefficients of CH_4 and CO_2 in several of these structures. We present a diverse collection of molecular diffusivities in amorphous materials and examine their concentration dependence by comparing data from adsorption and diffusion simulations.

Characterization of Sulfur Aerosols in Fairbanks, AK During Extreme Winter Conditions

Kayane Dingilian*, Michael Battaglia, James Campbell, Jingqiu Mao, Rodney Weber

Sulfur aerosols play an important role in public health and meteorology. As one of the primary components of PM 2.5 (particulate matter at size 2.5 μm and below), they are highly toxic, and within clouds, they impact rainfall and the properties of the Earth's atmosphere. Under the unique conditions of Fairbanks, AK in the winter, sulfur chemistry is not well-understood. In extreme cold and low light, traditional aerosol formation pathways are very slow – yet Fairbanks remains one of the most severely polluted cities in the world due in part to its strong temperature inversion patterns that trap unclean air at the surface. We recently identified hydroxymethane sulfonate (HMS) as an important constituent of sulfur-based aerosols in highly polluted events and isolated the species in ion chromatography analysis. A product of the reaction of formaldehyde and the ions sulfite and bisulfite, HMS is especially remarkable because its detection implies the presence of supercooled aqueous chemistry in normally freezing conditions. As part of an ongoing international effort led by the University of Alaska at Fairbanks, we employed both online instruments - mist chamber, particle-into-liquid-sampler (PILS) - as well as offline filter analyses of PM 2.5 to investigate the formation of HMS, sulfate, and other sulfur-based aerosols. We also gathered data on common pollutants such as chloride, nitrite, and nitrate, and we are studying their correlation to HMS and sulfate. Thus far, during January and February of 2022, we detected levels of HMS and sulfate as high as approximately 5 and 30 $\mu g/m^3$ in PILS measurements. Characterizing the relative abundance of HMS and other sulfur-containing aerosols in PM 2.5 as well as their chemistry in relation to one another will not only improve the accuracy of atmospheric models but also advance the understanding of atmospheric chemistry and air quality under extreme conditions.

Lightning Talk Session I: 1:00 – 1:30 p.m.

Antarctic Krill (*Euphausia superba*) Kinematics in Relation to Chemical, Physical and Photic Stimuli: From Video Analysis to an Individual-based-model

Nicole Hellessey*, Marc Weissburg, David Fields, and Nicholas Record

Antarctic krill (*Euphausia superba*) are at the centre of the Antarctic ecosystem. Little is known about what stimuli cause individual krill swimming behaviours to change, what causes aggregation into schools and swarms, or what cues the movement and structure of aggregations. In this study we are constructing an individual-based-model (IBM) that scales up from individual to aggregate behaviour. Using a horizontal flume, we examined krill swimming kinematics and behaviour in relation to chemical, physical and photic stimuli. Our video analysis has the ability to clarify: search/foraging or avoidance behaviour in relation to chemical stimuli, the grouping and alignment of krill in a current and their ability to exit/enter a current (physical stimuli), energy efficient swimming (positive stimuli in high flow), maintenance of a heading under low photic conditions, as well as how search behaviours differ in low photic conditions. Krill swimming in high flow showed few strong directional changes (low frequency of large turn angles) that would indicate active searching, which may be a response to the energetic demands of not reducing drag when flow is high. In contrast, krill turned more frequently in low flow conditions, regardless of chlorophyll level, suggesting that the energetic demands of not aligning to current direction may constrain foraging. Roughly 1/3rd of krill tracks in low flow conditions had bimodal swim velocities and more skewed swim velocities, suggesting more behavioural flexibility when krill do not have to confront strong flows. Heading was more consistently aligned with the flow in low photic conditions which reduced their ability to “search” even when chemical stimuli were added to the low photic conditions. Krill swimming velocities decreased significantly in low photic as well as in negative chemical stimuli conditions. Information and analysis gathered from this study will be used to construct an individual-based-model (IBM) for Antarctic krill.

PSP: A toolkit for efficient generation of 3D atomic-level polymer models

Harikrishna Sahu*, Huan Tran, Kuan-Hsuan Shen, Joseph H. Montoya and Rampi Ramprasad

Typically, 3D atomic models are required for physics-based simulations of materials. Within the specific area of polymer science, an automatic engine for generating such polymer models is needed. We have developed a python toolkit named Polymer Structure Predictor (PSP) for suggesting a hierarchy of polymer models, ranging from oligomer/infinite polymer chains to sophisticated amorphous models [1], which can be used downstream in physics-based simulations. The only input of PSP is the simplified molecular-input line-entry system (SMILES) strings of the repeat unit of the polymer. The performance of PSP was tested by comparing the generated models with the known experimental data of several polymers. The output files can be directly used with several computational software, such as VASP, ORCA, LAMMPS, and GAMESS, allowing automation for computing properties. PSP has already been used in the polymer version of computational autonomy for materials discovery (CAMD) [2], establishing extensive databases for polymer bandgap and charge injection barriers that power the Polymer Genome platform (www.polymergenome.org).

PSP is expected to benefit a wide number of academic and industrial research activities, realizing automation in polymer discovery. In the context of the emerging polymer informatics ecosystem, this toolkit will substantially reduce efforts to develop extensive databases of computed polymer properties. Besides, simpler visual models of polymeric materials would likely aid in polymer synthesis research, benefiting experimental polymer scientists.

References:

[1] H. Sahu, K.-H. Shen, J. H. Montoya, H. Tran, R. Ramprasad, Polymer Structure Predictor (PSP): A Python Toolkit for Predicting Atomic-Level Structural Models for a Range of Polymer Geometries, submitted.

[2] J. H. Montoya, K. T. Winther, R. A. Flores, T. Bligaard, J. S. Hummelshøj, M. Aykol, Autonomous intelligent agents for accelerated materials discovery, Chem. Sci., 2020, 11, 8517-8532.

Native Protein Structures and Stabilities at Nanomolar and Picoliter Quantities using Triboelectric Nanogenerator Ion Mobility-Mass Spectrometry

Daniel D. Vallejo*, Julie Arslanoglu, Caroline Tokarski, Facundo M. Fernández

Native mass spectrometry (MS) has found widespread success in measuring native-like protein structures in the gas-phase and, when combined with ion mobility (IM), capable of measuring their collision cross sections (CCS) and stabilities. These methods are well validated, but often rely on samples that are abundantly available through repeated recombinant expression. For ultra-precious and irreplaceable samples from paintings, protein content can be far below the micromolar and microliter levels required for robust protein experiments. Triboelectric nanogenerators (TENG) and IM-MS are capable of measuring protein size and stability rapidly from ultra-small sample quantities. Here, TENG-IM-MS is used to characterize standard proteins and proteins relevant to paintings, showing native protein structures can be obtained even at nanomolar and picoliter quantities.

We measured CCS values of three standard proteins using either TENG or a DC power supply for the nanoelectrospray ionization (nESI) process. We found Bovine Serum Albumin (BSA), Cytochrome C (CytC), and Alcohol Dehydrogenase (ADH) generated native-like structures under both conditions. For BSA, ConA, and ADH under DC conditions CCS measurements were 4499±50, 5980±29, and 7533±35 Å2 and under TENG conditions were 4523±55, 5957±26, and 7526±28 Å2, respectively. These measurements are within 0.25% of each other and all within 1.5% of the protein CCS database. At low concentrations, 500nm and 100nm, for ovalbumin (OVA) we measured the RMSD of the CCS to be 3.4% and 5.9% vs. the 10µM control samples, respectively. The pulsed nature of TENG required less sample than the average nESI experiment with each pulse using approximately 20pL of sample. For low concentrations approximately ~24 pulses or 480pL were required for adequate signal intensity, but for highly concentrated samples as little as two pulses were needed requiring only 40pL of sample. Our presentation will detail our most recent data and analysis for proteins at nanomolar and picoliter quantities.

Efficient Computation of Conformal Prediction Set

Eugene Ndiaye*

If you predict a label y of a new object with pred_y, how confident are you that y= pred_y? Conformal prediction methods provide an elegant framework for answering such a question by establishing a 95% confidence region for an unobserved response of a feature vector based on previous observations of responses and features, without assumptions about the data distribution. Although attractive, the computation of such a confidence set turns out to be infeasible in general, and is still considered an open problem. I advocate a simplification of the problem and propose to be satisfied with approximating these confidence sets to a prescribed precision. To do this, I will introduce hopefully weak assumptions about the prediction problems, in order to obtain feasible calculations and convincingly demonstrate how our approaches can effectively quantify prediction uncertainty for several machine learning algorithms.

Are marine-terminating glaciers retreating due to climate change or natural variability?
John Erich Christian*, Alexander Robel, Ginny Catania

Glaciers in mountain and polar regions have retreated dramatically over the last century. However, while ice loss is expected in a warming climate, formally attributing the observed changes to human forcing is a statistical challenge that must account for how glaciers dynamically respond to natural climate variability versus human-driven trends. Such analyses have indeed shown that the retreat of mountain glaciers is a clear signal of human-driven warming, far exceeding the fluctuations that could be expected due to variability alone.

Large marine-terminating glaciers emanating from the Greenland ice sheet have also retreated recently, but several factors unique to these glaciers have precluded attribution to human causes. These glaciers have thresholds in their dynamic state, such that if sufficiently perturbed, they may undergo sustained retreat even without further climate forcing. The retreats observed in the last few decades are correlated with modes of natural ocean variability, creating uncertainty as to whether the retreats were triggered by natural variability or human-driven climate trends.

We developed a new framework for assessing these unique threshold dynamics in the context of random climate variability and human driven trends. We use a numerical model to simulate a hypothetical glacier representative of those in Greenland. We run thousands of simulations of the glacier, each with a unique realization of random climate variability, and assess how often sustained retreats are triggered. By comparing groups of these simulations both with and without human-driven climate trends, we can quantify how much human forcing has increased the likelihood of sustained retreat. This framework offers a way to quantify the human role in marine-terminating glacier retreats, and could help fill a major gap in the overall attribution of modern ice loss to human-driven climate change.

Research Talk Session II: 1:40 – 2:40 p.m.

Study of the interfacial shear strength of carbon nanotube yarn with matrix resins after chemical treatment
Keenan J. Mintz*, Jefferson Bourdeau, Bodiuzzaman Jony, Kishor Gupta, Satish Kumar

Carbon composites are important materials that have been increasingly used in recent years for flight applications due to their high specific strengths. An important characteristic of these composites is the interfacial shear strength (IFSS) between the carbon material and the matrix resin, as insufficient load transfer across the resin-carbon material surface will limit the strength of the overall composite. In this presentation, the improvement of the IFSS between carbon nanotube (CNT) yarn and an epoxy resin will be explored. Previous work has shown that treatment of CNTs with hydrogen peroxide in basic solutions can assist in removing amorphous carbon while preserving the structure of the CNTs. Based on this work, CNT yarn was treated with a hydrogen peroxide/ammonium hydroxide (15 wt% for each component) solution at different temperatures and times. For these treated yarns, IFSS was measured using a single fiber pullout test in epoxy resin (EPON-862). Treatment at 80 °C for 5 h produced an increase in IFSS of 47% compared to pristine yarn. Treatment at lower temperatures showed limited efficacy, while reduced treatment time (30 min) at 80 °C still showed an increase in IFSS (36% compared to pristine yarn). These results show that this is a promising approach for improving the strength of CNT yarn composites.

Effects of acute stress on rigid learning, flexible learning and value-based decision-making in spatial navigation
Qiliang He*, Elizabeth Beveridge, Vanesa Vargas, Ashley Salen, and Thackery Brown

We often learn and make decisions in stressful situations. How acute stress affects learning and decision-making has been studied for decades, but few studies have investigated whether stress affects rigid (i.e., repeating learned behaviors) and flexible learning (i.e., learning the structure of the task) differently, and even fewer studies have investigated how stress affects flexible learning when it is contingent on the outcome of rigid learning. Furthermore, few studies have investigated how stress affects the way memory was utilized from such learning experience to inform value-based decision-making. In the current study, participants first learned to find locations of various objects in a virtual environment from a fixed starting location (rigid learning), and then learned to find the same objects from unpredictable starting locations (flexible learning) in the same environment. Participants then decided whether to reach goal objects from the fixed or unpredictable starting locations, with different penalties associated with each option. We find that stress impairs rigid learning only in females, but does not impair flexible learning. When examining how earlier learning influence subsequent decision-making using a computational model, we find that stress reduces memory integration in both genders, making participants focus more on recent episodic memory and less likely to integrate information from other related sources in decision-making. Collectively, our results show how acute stress impacts different memory systems and the communication between episodic memory and decision-making.

Unravelling Water-Ion Dynamics in Reverse Osmosis Membranes with Nuclear Magnetic Resonance Spectroscopy

Mahsa Abbaszadeh*, Marta C. Hatzell

The exact nature of ion and water transport in polymeric membranes is often ambiguous and depends on the complex interplay between polymer structure and dynamics that facilitate transport. We have investigated the dynamics-transport of water and sodium ions in complex ionic mixtures of a polyamide polymer using solid-state NMR spectroscopy. Water and sodium ion diffusion measurements are made using pulsed-field gradient NMR diffusometry. The energy barriers for water and ion transport within the active layer of RO membrane are assessed using magic angle spinning (MAS) and static NMR spectral line shape analysis. Through monitoring 13C, 23Na, and 1H NMR nuclei, quantitative insights into diffusion of water (1H), sodium mobile ion (Na+), and polymer membrane dynamics (13C) are extrapolated. Furthermore, spin-lattice (T1) relaxation time of sodium and water ions are investigated to obtain quantitative insight into how sodium and water ions rotational movements occur in the absence and presence of other competing seawater cations such as potassium.

Room temperature spectra and spin lattice relaxation times indicated the presence of both mobile and rigidly held ionic species in the polyamide at different levels of relative humidity. The concentration and temperature dependance of relaxation times and chemical shifts have been investigated. NMR relaxation measurements detect how the water rotation is modified by sodium and potassium cations in polyamide membrane.

Results show that at low relative humidity and in the presence of competing ions, there are sodium ion resonances for crystalline sodium ions and rigidly held sodium ions on the surface. With increasing relative humidity and decreasing competing ions, the resonance suggests solution-like dynamic rotational movements of sodium ions in polyamide. The results confirm the change in activation energy barrier for sodium and hydrogen ion permeation in polyamide upon presence of potassium ions.

Spatially Resolved Lipidomic Profiling of Ovarian Cancer Using Ultrahigh Resolution Mass Spectrometry Imaging

Xin Ma*, Andro Botros, Sylvia R. Yun, Eun Young Park, Olga Kim, Ruihong Chen, Murugesan Palaniappan, Jaeyeon Kim, Facundo M. Fernández

Ovarian cancer (OC) is one of the deadliest cancers among women as no effective screening tools are available at its early stage. Furthermore, the detailed mechanism of OC progression and metastasis remains unclear. We conducted spatially resolved lipidomic profiling of ovarian cancer tissues collected from a double-knockout (DKO) and a triple-mutant (TKO) mouse models. To investigate lipid distributions and alterations in these models, we performed imaging experiments on tissue sections in an ultra-high-resolution FTICR mass spectrometer and compared the profiles between DKO and TKO tissues using PCA. Comparisons against control animals were also conducted to identify altered pathways and better understand OC progression. This is the first comprehensive spatially resolved lipidomic profiling of OC by ultra-high-resolution MS using tissues from different animal models.

Images were collected at a spatial resolution of 50 µm. For TKO sections, ~180 lipids were putatively annotated, with phosphotidylethanolamine (PE) and phosphatidylcholine (PC) being the major lipid classes identified. Among the sections collected from different TKO mice, no obvious trends or clear clusters were observed based on PCA. Unlike PE and PC that are distributed more evenly in the entire tissues, ether phosphatidic acids (PA-O) and ether phosphatidylinositols (PI-O) were accumulated in specific tumor sub-regions of TKO tissues.

DKO tissues showed high similarity among them, and most lipids in the tumor regions of the DKO tissues exhibited high heterogeneity, except for fatty acids. PA-O and PI-O accumulated in sub-regions where the tumor has not fully developed. PE and PC were localized in regions that had developed obvious tumors. This finding suggests that the OC progression in DKO tissues may associate with the consumption of PA and PI and production of PE and PC. Sections collected from different DKO mice showed slightly larger differences than TKO mice. It suggested OC development in DKO tissues may originate from different sub-regions of the reproductive system than in TKO animals.

Development of a stochastic ice sheet model

Vincent Verjans*, Alex Robel, Helene Seroussi

The Greenland and Antarctic ice sheets hold 99% of the freshwater ice on Earth. Their evolution under a changing climate will be key to future levels of sea-level rise. Ice sheet models represent the dynamics of ice sheets, given some prescribed boundary conditions such as atmospheric and oceanic conditions. Studies show that ice sheet model predictions are strongly sensitive to the climatic forcing prescribed. Most ice sheet model simulations use only a single representation per climatic scenario, assumed to represent climatic conditions for a given level of global warming. However, this approach neglects irreducible uncertainty associated with internal climatic variability and thus cannot capture the range of possible future climatic conditions under which ice sheets may evolve. Current model studies of the Greenland and Antarctic ice sheets do not account for such internal variability, essentially due to the computational difficulty of running different simulations from a variety of forcings generated from external climate models. Furthermore, some ice sheet processes exhibit a high degree of non-linearity and complexity or depend on mechanisms acting at spatial scale much finer that the current spatial scale of ice sheet models. This implies that they cannot be fully captured by current ice sheet models in a deterministic way.

We develop the first ice sheet model that includes stochastic capabilities. We use random fluctuations to capture the nature of possible forcings and mechanisms for ice sheet models. Stochasticity accounts for both internal climate variability and uncertainty in poorly constrained mechanisms. This modeling framework will allow to simulate the range of past and future scenarios of ice sheet change. Ultimately, we want to quantify the impacts of natural climatic fluctuations and small scale randomness on ice sheet evolution.

Lightning Talk Session II: 2:45 – 3:10 p.m.

New models generalizing permutations
Orli Herscovici*

Permutations are one of a basic combinatorial objects finding its immediate applications in Probability, Biomathematics, Physics, and other areas. Enumeration of permutations based on different properties of permutations leads to new discoveries, for example, in theory of Orthogonal Polynomials and Number Theory.

We can observe new fascinating properties of familiar objects when q-analogues appear. A generalization known as q-analogue brings with it not only some parameter q, but also a change of rules. Even the four familiar operations like (+, −, ×, :) may be changed in order to adjust some q-analogue. For each polynomial or mathematical object like, for example, a differential operator, more than one q-analogue can be constructed. Therefore, one can ask what is the meaning of that specific q-analogue, how does it enrich the knowledge about the original mathematical object, is it connected to other objects, and if yes, then how?

In 1950s, Carlitz proposed a very theoretical q-analogue of the exponential function, that found its applications in Statistical Mechanics in 1980s. He studied different q-analogues of polynomials. In 1970s his study provided a recurrence relation, which, at first sight, had no combinatorial base at all.

Finally, 40 years later, a new generalized model of permutations gave a very natural explanation for a phenomenon hiding behind the equation. In this talk we consider further properties of those generalized permutations.

Vapor Phase Infiltration for Advanced Chemical Separations: Process Design for Hybrid Organic-Inorganic Membranes

Emily McGuinness*, Fengyi Zhang, Yi Ren, Yifan Liu, Benjamin Jean, Ryan Lively, Rampi Ramprasad, Mark Losego

Vapor phase infiltration (VPI) creates hybrid organic-inorganic materials by infusing the bulk of polymers with vapor phase metalorganic precursors and co-reacting them with water vapor to form metal oxides. Due to the vapor phase nature of this process, polymeric materials with a wide variety of form factors (from fabrics to thin films) can be transformed into these organic-inorganic hybrids. These materials exhibit unique properties that differ from the starting polymer. Examples include enhanced mechanical toughness and elongation at break, photoluminescence, and electrical conductivity. In this work, we explore the use of VPI to create hybrid membranes with increased solvent stability facilitating chemical separations inaccessible to the starting polymer. For example, PIM-1, a prototypical polymer of intrinsic microporosity, is currently a strong candidate for energy saving separation processes. One of PIM-1's advantages is its solution processibility that allows it to take on a variety of membrane forms (from thin film composites, to hollow fibers, and even to 3D printed materials). However, this solution processibility has the disadvantage in that PIM-1 cannot operate in separation processes that contain good solvents or plasticizers for the polymer (such as tetrahydrofuran and ethanol respectively). To overcome this obstacle, VPI has been used to infuse bulk PIM-1 (with a variety of form factors) with aluminum oxyhydroxide. The resulting hybrid material has shown repeatable performance as a membrane in solvents ranging from toluene to ethanol to even tetrahydrofuran with high rejection of large molecular weight molecules and a sharp molecular weight cutoff. In addition to the application and use of these membranes, a discussion on the fundamental processes inherent to VPI that make such properties possible will be conducted.

Interaction Energy Contribution of H-bonded Synthetic Hachimoji DNA Nucleobase Pairs

Rameshwar L. Kumawat* and C. David Sherrill

Synthetic Hachimoji DNA nucleobase pairs are investigated with the DFT and SAPT variant of intermolecular perturbation theory, yielding a rigorous decomposition of the interaction energy into electrostatic, dispersion, induction, and exchange contributions. Total interaction energies extrapolated to the complete basis set limit are compared with corresponding MP2 and CBS and estimated CCSD theory results. Further, a comparison of the interaction energy contribution of H-bonded natural DNA and synthetic DNA is done.