Mathias Casiulis  
*Spectral optimization for functional materials*

Designing materials with target bulk properties is a challenge, as emerging properties strongly depend not only on the nature of the composing elements, but also on their organization at all scales. To make matters worse, in many cases target properties are best understood via a Fourier-space representation of the relevant density field inside the material, which are even less intuitive to enforce.

I will present an algorithm that allows us to impose arbitrary features in the Fourier representation of field correlations in a material made of discrete particles. These properties may be imposed either in continuous or discrete Fourier space, and affect either a continuum set of particle positions/compositions or a discrete grid of material properties.

To illustrate the power of this method, I will describe how we made large systems with deep photonic bandgaps by imposing high-order rotational symmetries, thus creating a new class of functional materials called gyromorphs.

I will then present how this method could significantly improve upon current methods to find and characterize crystalline structures in simulations.

Michael Chen  
*Machine learning modeling of ab initio potential energy surfaces: enabling high-level PIMD simulations of candidate redox flow battery electrolytes*

Ab initio molecular dynamics (AIMD) simulations, where the forces and energies are generated at each time step by performing an electronic structure calculation, provide an appealing route to simulate reactive chemical dynamics. However, for disordered condensed-phase systems, a well-converged simulation typically requires many hundreds of atoms and oftentimes nanoseconds of trajectories. The computational expense of these simulations is further compounded if one wants to incorporate nuclear quantum effects via ab initio path integral molecular dynamics (PIMD) simulations. Machine-learned potentials (MLPs) have emerged as an extremely promising approach to model ab initio potential energy surfaces of condensed-phase systems while being orders of magnitude more efficient to evaluate.
In this talk, I will highlight our efforts in developing a reactive MLP to study a series of promising candidate redox flow battery electrolytes: mixtures of imidazole and levulinic acid. Our preliminary PIMD results for these electrolyte systems are providing insights into the microscopic origins of their experimentally observed composition-dependent conductivity trends. In particular, we show that the anomalously high proton diffusion rates in these systems arise from the prevalence of proton transfer reactions occurring along hydrogen bonded networks.

Muhammad R. Hasyim, Norah M. Hoffmann, Arkajit Mandal, and David R. Reichman
Excursions in Polaritonic Chemistry: Relaxation and Reaction Kinetics

Recent years have shown promise in how microcavities—optical devices capable of selectively trapping light at different frequencies—can modify reaction kinetics. By matching the photon frequency to a molecular transition, strong coupling leads to the formation of hybrid light-matter states known as polaritons, often coinciding with either the suppression or enhancement of these rates. This presentation presents two ongoing projects [1,2] that examine this emerging field of “polaritonic chemistry.” In the first work, we examine how the properties of supercooled liquids—the state of a liquid when cooled below freezing—can potentially be modified in optical cavities [1]. Here, we use a technique called cavity molecular dynamics (CavMD) [3], which provides a pure classical treatment of the problem to study how viscosity and other properties change inside the cavities. The second project explores further the quantum nature of the light-matter interactions, applying mixed quantum-classical (MQC) methods to study a toy model for polaritonic chemistry [2]. Initial findings suggest that by (1) removing Wigner sampling of classical degrees of freedom, (2) applying a multi-state version of the mapping approach to surface hopping (MASH) [4], and (3) treating the photon quantum mechanically, we obtain rates that are much closer to a fully quantum mechanical treatment of the problems.

[1] In collaboration with Prof. Norah Hoffmann at NYU
[2] In collaboration with Profs. Arkajit Mandal and David Reichman, at TAMU and Columbia, respectively.

Philipp Hoellmer, Tom Egg, Mathias Casiulis, and Stefano Martiniani
Efficiently Exploring Basins of Attractors to Sample Entropy

Legend has it that John von Neumann convinced Claude Shannon to name the average level of surprise (or uncertainty) of a random variable “entropy” because “nobody knows what entropy really is, so in a debate you will always have the advantage.” This talk leverages that advantage by presenting advancements in the basin-volume method for measuring the entropy of generic nonequilibrium processes. Here, the outcomes of the random variable are the stable structures in the system’s dynamics called basins of attraction. The intractable problem of counting such
basins is replaced by a tractable sampling problem. We will discuss challenges in that sampling approach and introduce a promising solution: a guided non-reversible Monte-Carlo algorithm that explores the basins of attraction efficiently. Additionally, we will preview exciting applications currently in progress that ultimately aim to answer the intriguing question: “How many materials exist?”

Michael Kilgour

*Multi-Type Point Cloud Autoencoder: A Complete Equivariant Embedding for Molecule Conformation and Pose*

The point cloud is a flexible representation for a wide variety of data types, and is a particularly natural fit for the 3D conformations of molecules. Extant molecule embedding/representation schemes typically focus on internal degrees of freedom, ignoring the global 3D orientation. For tasks that depend on knowledge of both molecular conformation and 3D orientation, such as the generation of molecular dimers, clusters, or condensed phases, we require a representation which is provably complete in the types and positions of atomic nuclei and roto-inversion equivariant with respect to the input point cloud. We develop, train, and evaluate a new type of autoencoder, molecular O(3) encoding net (Mo3ENet), for multi-type point clouds, for which we propose a new reconstruction loss, capitalizing on a Gaussian mixture representation of the input and output point clouds. Mo3ENet is end-to-end equivariant, meaning the learned representation can be manipulated on O(3), a practical bonus for downstream learning tasks. An appropriately trained Mo3ENet latent space comprises a universal embedding for scalar and vector molecule property prediction tasks, as well as other downstream tasks incorporating the 3D molecular pose.

Jinggang Lan

*Dynamics of the charge transfer to solvent process in aqueous iodide*

In this talk, I will discuss the intricate interplay between the dynamics of the electron and the solvent polarization occurring in the charge-transfer-to-solvent process in aqueous iodide. Through the combined use of ab initio molecular dynamics and machine learning methods, we investigate the structure, dynamics and free energy as the excited electron evolves through the charge-transfer-to-solvent process, which we characterize as a sequence of states denoted charge-transfer-to-solvent, contact-pair, solvent-separated, and hydrated electron states, depending on the distance between the iodine and the excited electron. Our assignment of the charge-transfer-to-solvent states is supported by the good agreement between calculated and measured vertical binding energies. Our results reveal the charge transfer process in terms of the underlying atomic processes and mechanisms.
Joseph Lawrence

Semiclassical instanton theory for reaction rates at all temperatures

Instanton theory is a rigorous semiclassical theory that describes the rate of tunneling through a barrier. The standard theory is only applicable at low temperatures below the “crossover temperature” where tunneling dominates. The theory therefore fails to capture the transition between the high-temperature regime and the low-temperature regime. Here I will discuss how an alternative derivation of instanton theory results in a theory that is valid at all temperatures. The resulting theory is a rigorous asymptotic approximation to the exact path-integral expression for the rate constant in the limit that \( \hbar \rightarrow 0 \). For a series of model systems and parameter regimes it is shown to give excellent agreement with the exact quantum rate.

Federica Maschietto

Decoding Allosteric Function Through Structural and Environmental Parameters

Allosteric control is a powerful method for regulating enzymes, promising significant biomedical advancements and drug design potential. However, limited molecular-level understanding of allosteric mechanisms hinders the discovery of new drug targets. One key element of allosterism is the set of thermodynamic changes – influenced by enthalpic and entropic factors – caused by protein structure modifications and other external factors. Here, we discuss an approach based on protein network analysis from molecular dynamics, supported by experimental assays, to investigate the molecular basis of enzymatic activity and its regulation. By inducing targeted conformational changes in key protein regions essential for catalytic function and intersubunit coordination, we examine the resilience of communication pathways between catalytic motifs and propose new ways to regulate catalytic activity. Using Imidazole Glycerol Phosphate Synthase (IGPS) as a case study, we show that structural modifications and environmental factors can both activate IGPS for catalysis similarly to its natural activator and propose methods to regulate catalytic activity, such as converting IGPS from V-type to K-type allostery. These results provide new perspectives on allostery modulation and offer innovative approaches to controlling enzyme functions.

Xiaolin Pan

Fast and Accurate Prediction of Tautomer Ratios in Aqueous Solutions via Siamese Network

Tautomerization plays a critical role in numerous chemical and biological processes, impacting factors such as molecular stability, reactivity, biological activity, and ADME-Tox properties. Many drug-like molecules exist in multiple tautomeric states in aqueous solutions and complicating drug discovery. Predicting these tautomeric ratios and identifying the predominant species rapidly and accurately is crucial for computational drug discovery. In this study, we introduce sPhysNet-Taut, a deep learning model fine-tuned with experimental data leveraging the Siamese network, built upon a pre-trained model. This model predicts tautomer ratios in aqueous solutions using MMFF94-optimized geometries directly. On an experimental test set,
sPhysNet-Taut surpasses all other methods, achieving state-of-the-art performance with an RMSE of 1.9 kcal/mol on the 100-tautomer set and an RMSE of 1.0 kcal/mol on the SAMPL2 challenge, and providing the best ranking power for tautomer pairs. This work not only provides a useful deep learning model for predicting tautomer ratios, but also provides a protocol for modeling pairwise data. To facilitate user-friendliness, we developed a readily accessible tool to predict stable tautomeric states in aqueous solutions, enumerating all possible tautomeric states and ranking them using the sPhysNet-Taut model.

**Stephanie Portillo-Ledesma**, Minna Hang, Zilong Li, and Tamar Schlick
*Exploring chromatin and gene architecture with a nucleosome-resolution mesoscale model*

In eukaryotes, DNA is wrapped around cores of 8 histone proteins (2 copies of H2A, H2B, H3, and H4) to form the nucleosome. Chains of nucleosomes further fold and organize into the chromatin fiber. Such 3D organization of the genome is crucial for packing the long DNA into a micrometer cell nucleus and regulating gene expression. Understanding genome organization and its epigenetic regulation is essential to decipher its role in cell processes and disease development and progression. In this talk, I will present our chromatin mesoscale model and its application to study the HTT gene involved in Huntington’s disease and the regulation of chromatin architecture during rod photoreceptor maturation.

**Irén Simkó**
*Water trimer: Intermolecular vibrational states and tunneling splittings from rigorous 12D quantum calculations*

Water trimer is undoubtedly the most important hydrogen-bonded molecular trimer. It is the smallest water cluster in which nonadditive three-body interactions are present, essential for accurately describing bulk water and ice. Hydrogen-bond rearrangement dynamics of water trimer gives rise to a complex far infrared spectrum, which is challenging to understand and simulate. In this project, we determined the intermolecular vibrational states of water trimer from rigorous 12D (rigid monomer) quantum calculations. We solved the vibrational Schrödinger equation using the variational technique, employing a product-contracted basis formed by 9D intermolecular bending [1] and 3D intermolecular stretching eigenstates. The computed 12D spectrum and tunneling splittings agree well with the available experimental results, showing the high quality of the potential energy surface. Furthermore, we analyzed the coupling between the intermolecular bending and stretching modes and studied the role of the three-body interaction.

Hydrogen bonds play a crucial role in determining the structural and dynamical properties of water, aqueous solutions, and biomolecules like DNA and proteins. Despite extensive research using advanced experimental and theoretical methods, the high dimensionality and complexity of bulk systems make it challenging to quantitatively characterize hydrogen bonds, their cooperativity, and rearrangement dynamics.

Noncovalently bound molecular trimers are key in understanding these interactions, as they are the smallest clusters where essential nonadditive many-body interactions arise. These trimers serve as ideal candidates for testing the accuracy of computed three-body interactions by comparing high-level bound-state calculations on potential energy surfaces (PESs) with spectroscopic data.

While methods for full-dimensional quantum calculations of rovibrational states of molecular dimers exist\(^1\), no comparable methodology for hydrogen-bonded molecular trimers was available until recently. Over the past two years, we developed a computational methodology for rigorous full-dimensional (12D) quantum calculations of fully coupled intramolecular and intermolecular vibrational states of hydrogen-bonded trimers of flexible diatomic molecules\(^2\). This method was first applied to the HF trimer\(^3\), followed by the HCl trimer\(^4\), using ab initio many-body PESs. These advancements provide a new level of accuracy in studying the complex interactions within hydrogen-bonded trimers.

In this talk, I will introduce a new full-dimensional potential energy surface (PES) for the HF trimer, referred to as PES-2024, which leverages advances in ab initio electronic structure theory. To evaluate the quality of the new 12D PES-2024, rigorous 12D quantum calculations of the fully coupled intra- and intermolecular vibrational states of the HF trimer are performed and compared with experimental data and an older ab initio many-body PES of Quack and Suhm (QSS PES). Our findings indicate that the new PES-2024 provides a more accurate description of the intra- and intermolecular vibrations of the HF trimer than the QSS PES.

Rui Wang
Computational Topology-Driven Machine Learning Models for Protein-Protein Binding Free Energy and RNA-like Structure Predictions

Topological Data Analysis (TDA) applies topology principles to extract meaningful insights from complex and high-dimensional datasets. It has witnessed success in various topics in biosciences. However, Persistent Homology (PH), the widely used tool in TDA for years, lacks the capability to capture 1) non-topological information (e.g., shape evolution of biomolecules) and 2) directed relationships (e.g., gene regulation networks). Therefore, we introduced two mathematical approaches called Persistent Spectral Graphs and Persistent Path Laplacians to address these two limitations. The integration of these computational topology-based methods with machine learning techniques could help with both protein-level and RNA-level research and address public health issues. For example, we built a PSG-based AI model (TopLapNet) to predict the binding free energy changes caused by mutations in the interaction between the virus's Spike protein and the human ACE2 receptor/therapeutic antibodies. This approach greatly helped forecast upcoming prevailing SARS-CoV-2 viral variants and their mutational impact on vaccine/antibody treatment. Furthermore, the powerful PSG tool can also extend to RNA-level analysis. We employed PSG-based representations to describe over 110 million possible dual graphs with no more than nine vertices. Utilizing clustering methods, we separated these dual graph topologies into two distinct clusters: RNA-like and non-RNA-like. Notably, in the RNA-like cluster, 97.3% of existing RNA motifs find a matched 2D graph topology, marking the best results to date.

Yuanqing Wang
Non-convolutional Graph Neural Networks

Rethink convolution-based graph neural networks (GNN)---they characteristically suffer from limited expressiveness, over-smoothing, and over-squashing, and require specialized sparse kernels for efficient computation.

Here, we design a simple graph learning module entirely free of convolution operators, coined \textit{random walk with unifying memory} (RUM) neural network, where an RNN merges the topological and semantic graph features along the random walks terminating at each node. Relating the rich literature on RNN behavior and graph topology, we theoretically show and experimentally verify that RUM attenuates the aforementioned symptoms and is more expressive than the Weisfeiler-Lehman (WL) isomorphism test.

On a variety of node- and graph-level classification and regression tasks, RUM not only achieves competitive performance, but is also robust, memory-efficient, scalable, and faster than the simplest convolutional GNNs.
Dopamine redox reactions are crucial in brain science because dopamine is key to how the brain works and communicates. Understanding these reactions helps in creating better treatments and diagnostic tools for brain disorders. In collaboration with the experimental group, where they have found that increasing the Phosphate buffered saline (PBS) solvent concentration can lead to the decreasing of FSCV sensitivity, we aim to investigate how changes in Debye length induced by varying solvent concentrations affect the rate of redox reactions. In our work, we built a multilayer solvation model to theoretically investigate how solvent plays a role in the dopamine redox reaction rate. In the solvation model, the first layer is adjacent to the nanographene electrode, with a thickness equal to the Debye length for the specific PBS concentration. The second layer represents the bulk solution region. The two layers are characterized by distinct dielectric constants to effectively model the heterogeneous environments near the electrode. Density Functional Theory (DFT) and transition state theory have been applied to model the redox reaction mechanism and compare the energy barriers at various solvent concentrations. This approach aims to enhance our understanding of how dopamine sensitivity is influenced by the PBS solvent from a thermodynamic perspective.

Rhiannon Zarotiadis
Ab-initio Quantum Electrodynamics - Lighting the way to Photonic Qubits

In the field of quantum optics, intricate quantum effects such as bound states, spontaneous emission, or superradiance can be observed under extreme conditions, e.g., ultracold temperatures. Theoretically, these processes can be captured by simple model systems. Recently, a large effort has been made to find similar effects under experimentally less severe conditions, since these quantum phenomena may play a key role in quantum control and quantum information theory. In order to go beyond commercially inaccessible, extreme experimental setups, novel experimental and theoretical approaches are required. Ab-initio quantum electrodynamics in a cavity is such a theoretical approach. It is inspired by quantum optics but goes beyond existing approaches by combining a quantum optics framework with polaritonic chemistry and materials science. To this end, we study the existence of such quantum phenomena for light-matter interactions in molecules using scalable methods such as mean-field Ehrenfest dynamics.