55th Midwest Theoretical Chemistry Conference (MWTCC55)

Abstracts

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Oral Presentations

(In the order in which they appear on the conference schedule)

Strengthening the Ties between Wave Function Theory and Density Functional Theory

Paul Zimmerman
Department of Chemistry
University of Michigan

Two major domains of electronic structure—wave function theory and density functional theory—have complementary strengths and weaknesses. One is systematically improvable, the other not. One has rapidly rising costs with respect to system size while the other remains highly tractable. Although concepts such as the adiabatic connection and hybrid exchange have set up meaningful connections between WFT and DFT, bringing the two domains closer together would have immense value. This talk will introduce the Zimmerman group's efforts to transform near-exact wave functions into DFT-relevant quantities. In particular, I will show how close approximations to full configuration interaction can be translated into exchange-correlation potentials and energy densities. These two quantities—which are the core elements modeled by DFT functionals—are difficult to formulate and until now have been largely unavailable, especially for strongly correlated systems. The availability of FCI-derived, spatially resolved exchange-correlation may make it possible to generate new density functionals with higher accuracy as well as the ability to treat strong correlation.

Undirected Exploration and Screening of Binding Pockets with Flexible Topology

Fatemeh Fathi Niazi[1], Seungmin Yoon[2], Khadim Mbacke, and Alex Dickson[1,4]

[1]Department of Computational Mathematics, Science and Engineering, Michigan State University
[2]Department of Pharmacology & Toxicology, Michigan State University
[3]Department of Physics and Astronomy, Michigan State University
[4]Department of Biochemistry & Molecular Biology, Michigan State University

A common first step in drug design is virtual high throughput screening (VHTS), where a large number of potential drug molecules are computationally modeled in a protein binding pocket and filtered down to a smaller set of “hits” that can be further tested computationally or experimentally. Traditional strategies for VHTS do not account for ligand-induced conformational changes in proteins, as they typically rely on a single static structure to represent the protein. This neglects the role of binding entropy and the fact that different ligand molecules can induce slightly different conformations in the protein binding site that significantly affect the assessment of a given molecule’s fit. To address this challenge, we have developed a method called “Flexible Topology”, where a subset of atoms – typically representing a small molecule ligand – can continuously change their atomic identities, which are encoded by a set of attributes that parametrize the non-bonded interactions. These attributes are all implemented as dynamic variables that have masses and evolve in time using gradients of the energy function. In other words, the attributes feel forces from their surrounding environment and respond accordingly. In this way, by observing a set of flexible topology particles move and change in a ligand binding site, we can learn the preferences of a binding pocket. Here, we demonstrate how “undirected” flexible topology simulations can be used to explore ligand binding sites and reveal desirable properties of potential ligands. We use the beta-2 adrenergic receptor as an illustrative example and compare properties of flexible topology particle groups with a set of 29 B2AR ligand-bound crystal structures, covering 13 distinct ligands. We also show how the shape- and electrostatics-based virtual screening software “eon” from OpenEye can be used to find hits that come as close as possible to mimicking the orientation of our flexible topology atoms.

Theory-Driven Investigation into the Chemistry of Superheavy Elements and their Homologs

Alexander A. Rusakov[1]

[1] Oakland University

Knowing the chemistry of superheavy elements is key to their proper placement in the periodic table. Investigating such chemistry contends with the extreme scarcity of species primarily available in a one-atom-at-a-time regime and the high sophistication and cost of the experimental technique. While necessary, trusting the periodic trends in the elements' properties and the existence of lighter homologs lack reliability because of the dominance of extreme relativistic effects that upend the intuitively apparent tendencies. Uncovering the chemical homology of superheavy elements must be predicated on accurately modeling superheavy-element systems and their lighter homologs with relativistic quantum-chemical methods. In this presentation, I will focus on the following aspects of this work inspired by the recent cutting-edge experimental studies:

- Chemical homology of Cn/Hg, Nh/Tl, and Lv/Po. Our group's recent work points to At as the non-intuitive lighter homolog Nh. However, the potential homology with Tl remains underinvestigated, including gaps in Tl's behavior and speciation in thermochromatographic experiments. In light of the upcoming experiments on Hg, Tl, and Po, I will present preliminary theoretical findings on Hg, Tl, and Po speciation and adsorption energies in vacuum chromatography on quartz.
- Gas phase chemistry of small (super)heavy-element molecules and molecular ions. Based on the recent re-evaluation of the RaF properties, I will discuss the prospects of investigating the chemistry molecules containing the lightest (Ac) and heaviest (No, Lr) actinides and lighter superheavy elements studied with high-level relativistic wavefunction and DFT methods.

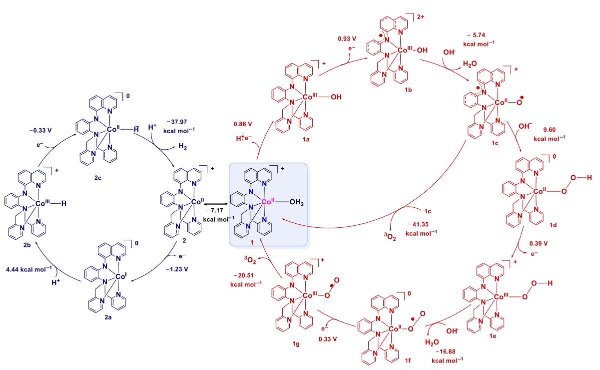
Mechanistic Studies and Theoretical Insights: From Water Splitting with Quinoline-Cobalt Complexes to the Surprising Thiol Selectivity in Furanosylations

Neha Rani, Boddu S. Ramakrishna, Carlos A. Lucecki, H. Bernhard Schlegel*, Cláudio N. Verani*and Hien M. Nguyen*
Department of Chemistry, Wayne State University, MI, USA

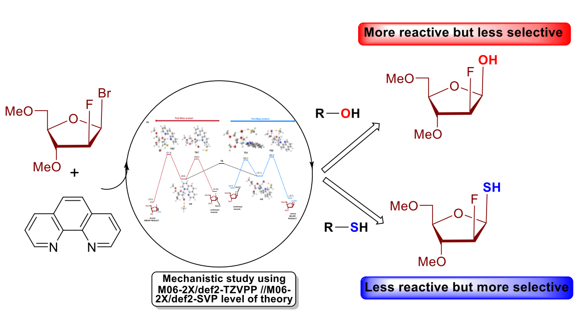
Water splitting by transition metal catalysts has emerged as a promising solution for the generation of green hydrogen fuel, aiming to replace the fossil fuel-based economy with a renewable, clean, and low-cost energy alternative. In this context, several novel, Earth-abundant cobalt-based catalysts have been developed experimentally and investigated by Density Functional Theory (DFT) studies. Hydrogen evolution proceeds via water dissociation and reduction steps involving high-spin Co^{II} and Co^{I} intermediates, with favorable hydride formation and H_2 release. Water oxidation involves proton- and electron-transfer events, leading to metal- and ligand-centered redox species and culminating in O_2 generation. These findings elucidate the interplay between metal- and ligand-centered redox processes, providing deeper insight into the catalytic promiscuity observed in cobalt-based water splitting systems.

On the second front, we investigated the unexpected lower reactivity but higher selectivity of thiols compared to alcohols in phenanthroline-catalyzed 1,2-cis O- and S-furanosylations. A combined computational and experimental investigation revealed that thiols, despite their higher nucleophilicity, exhibit lower reactivity but greater selectivity compared to alcohols in furanosyl reactions. Density Functional Theory (DFT) calculations revealed that stronger hydrogen bonding between alcohol-OH and bromide anions stabilizes transition states for O-furanoside formation, whereas thiols form weaker interactions, leading to higher reactivity for O-furanosides. Transition state analysis further indicates higher energy barriers for the formation of S-furanosides compared to O-furanosides, consistent with experimental results. Removing the bromide ion reduced selectivity differences between thiol and alcohol in furanosyl reactions. These findings emphasize the role of hydrogen bonding with bromide in controlling reactivity and selectivity, offering a deeper understanding of thiol and alcohol reactivity differences. Our study provides mechanistic insights and a robust synthetic approach for the selective formation of S-furanosides, expanding the toolkit for carbohydrate chemistry and peptide modification.

Quinoline-based Cobalt Catalysts



Phenanthroline-Mediated Furanosylations



Quantum Mechanical Perspectives on Transition Metal and Heavy Element Species

Bradley Welch[1], Jared Weidman[1], Benjamin Peyton[1], Nuno Almeida[1,2], Zachary Stewart[1], Jaxon George[1], Ebtisam Telb[1], and Angela K. Wilson[1]

[1] Michigan State University, Department of Chemistry, East Lansing, Michigan 48824
[2] California Environmental Protection Agency, Office of Environmental Health Hazard Assessment (OEHHA), Sacramento, California 95812

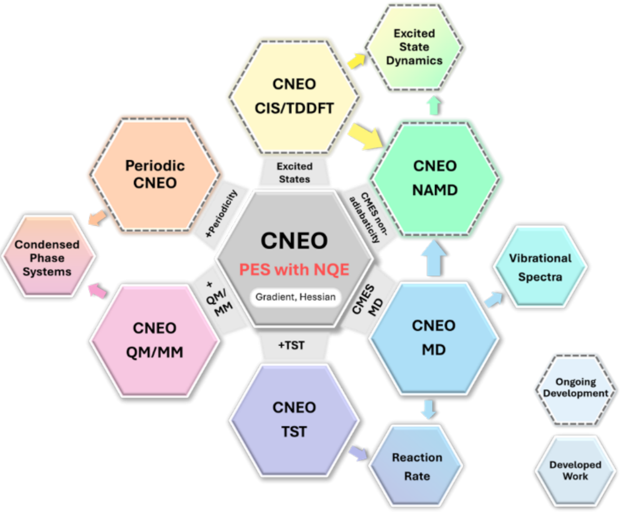
Transition metal and heavy element species are among the most complex molecular species, with many possible electronic configurations, partially filled higher-angular momentum states, often resulting in strong electron correlation effects and multi-reference wavefunction character. Strategies for addressing this complex chemistry, will be discussed, including our family of *ab initio* composite approaches, with examples of recent applications across the transition metal and heavy element spectrum. For the transition metals, our work in time-independent quantum mechanical methodologies will be discussed, as well as our real-time quantum electron dynamics developments.

Advancing the Modeling and Understanding of Hydrogen-Related Chemistry: The Constrained Nuclear-Electronic Orbital Framework for Nuclear Quantum Effects

Yang Yang
University of Wisconsin-Madison

Nuclear quantum effects (NQEs) are crucial for understanding many chemical and biological processes, particularly those involving hydrogen motion. However, accurately and efficiently incorporating NQEs into large-scale molecular simulations remains a significant challenge. To address this, we have developed the Constrained Nuclear-Electronic Orbital (CNEO) framework, which seamlessly integrates NQEs into quantum chemistry and molecular dynamics calculations that achieve both accuracy and computational efficiency.

The CNEO molecular dynamics (CNEO-MD) approach significantly outperforms conventional ab initio molecular dynamics (AIMD) in predicting vibrational spectra, especially for vibrational modes dominated by hydrogen motion. In addition, integrating the CNEO framework with transition state theory (CNEO-TST) enables more accurate predictions of hydrogen transfer reaction rates while maintaining computational costs comparable to conventional TST. Furthermore, CNEO calculations with periodic boundary conditions reveal that the preferred adsorption sites of hydrogen atoms on metal surfaces are modulated by NQEs. We have also developed CNEO excited-state methodologies, nonadiabatic dynamics frameworks, and hybrid quantum mechanics/molecular mechanics (QM/MM) approaches, all of which underscore the framework's capability to model complex chemical processes and biological systems with significant NQEs. These advancements establish the CNEO framework as a powerful and versatile tool for advancing the modeling and understanding of hydrogen-related chemistry and beyond.



Beyond Orthogonality: Nonadiabatic Chemistry through a Nonorthogonal Lens

Lee M. Thompson

University of Louisville, Department of Chemistry, 2320 S. Brook St., Louisville, KY 40292

Nonadiabatic processes underpin key phenomena in photochemistry, energy transfer, and catalysis. These processes are marked by strong interactions between electronic motion and a time-dependent external perturbation, such as light, electric fields, or nuclear motion, that induces coupling between the electronic eigenstates. Accurate computational modeling of such processes is essential but remains challenging due to significant orbital relaxation, multielectron excitations, and the need to capture multiple near-degenerate electronic states. To address these challenges, our group has focused on wavefunction theories that incorporate nonorthogonal determinant expansions to more effectively capture key components of the wavefunction. These methods exploit the flexibility of using configuration-specific orbitals, yielding compact, chemically intuitive representations of strongly correlated wavefunctions. In this work, I will describe how the nonorthogonal framework is being used for resolving challenges in modeling transition metal and lanthanide electronic structure, kinetics of energy transfer processes, and electron dynamics induced by low-kinetic energy photodetachment.

Recent Advancements in QM-EFP

George Elliott[1], Megan Schlinsog[1], and Mark S. Gordon[1]

[1]Iowa State University

The issue of scaling in *ab initio* techniques has been at the center of theoretical developments for some time. One key advancement in recent years was the development of hybrid quantum mechanics/molecular mechanics (QM/MM) techniques, where a region of chemical interest is defined using QM methods, whereas the chemical environment is modeled using classical, or semi-classical mechanics. A promising method for representing chemical environments is the Effective Fragment Potential (EFP) method.

The EFP method is an *ab initio*-based force field that has been shown to provide results that agree with second-order perturbation theory (MP2), and in some cases even with coupled cluster results (CCSD(T)). The interface of QM methods and EFP (QM-EFP), has been a recent focus in the further advancement of EFP. Recent progress in the development of QM-EFP energy and gradient code are presented in this talk. Specifically, recent work regarding the QM-EFP charge transfer energy, and the gradient of the exchange-repulsion energy.

Efficient Implementation of Multireference Algebraic Diagrammatic Construction Theory for Core-Excited States

Donna H. Odhiambo[1] and Alexander Yu. Sokolov[1]

[1]Department of Chemistry and Biochemistry, The Ohio State University, Columbus, Ohio 43210, USA

X-ray absorption spectroscopy (XAS) has emerged as a powerful tool for probing complex electronic structures with element specificity and temporal resolution, allowing novel investigations of transient photoinduced intermediates and the *d*-orbital manifolds of heavy-element complexes. Effective interpretation of these spectra requires theoretical modeling to establish structure-spectra correlations and identify spectroscopic fingerprints. Multireference algebraic diagrammatic construction (MR-ADC) theory provides an efficient and robust quantum chemistry approach capable of computing full excitation spectra and spectroscopic observables of strongly correlated systems. MR-ADC's multistate treatment is particularly advantageous for XAS, as it allows simultaneous computation of multiple excitations and provides consistent descriptions of states with different electronic character. This enables comprehensive modeling of core-to-valence transitions involving all orbitals. I will demonstrate the computational capabilities of our efficient spin-adapted implementation of core-valence separated MR-ADC for simulating XAS spectra through benchmark calculations of open-shell and multiconfigurational excited states, including the photodissociation of iron pentacarbonyl and the photoexcitation of pyrazine.

Mixed quantum–classical modeling of quantum materials

Alex Krotz,[1] Ken Miyazaki,[1] and Roel Tempelaar[1]

[1]Department of Chemistry, Northwestern University

Quantum materials are poised to unlock new technological opportunities, but it remains unclear how their behavior is governed by lattice vibrations (phonons). I will present our efforts at studying phonon-driven dynamics of quantum materials based on inexpensive mixed quantum–classical (MQC) methodologies. While such methods have traditionally been developed for molecules, we have recently reformulated them in momentum space tailored to solids. In addition, we have extended the applicability of MQC methods to topologically-nontrivial systems. As an exemplary application, I will present an investigation into spin–valley polarization dynamics of monolayer transition-metal dichalcogenides, where the microscopic detail afforded by our modeling framework allows us to identify exciton–phonon resonances as a key contributor to depolarization.

Single-Reference Theories for Calculating Electronic Spectra of Strongly-Correlated Systems

Sylvia J. Bintrim and Kevin Carter-Fenk

University of Pittsburgh, Pittsburgh, PA 15260, USA

Static (or strong) correlation is important for qualitatively correct modeling of photodynamics and is pronounced in atmospherically-relevant photolytic processes and the energy-relevant photochemistry of transition metal complexes. Unfortunately, many of the tools in the computational photochemist's toolbox that can adequately address the static-correlation problem are multireference methods that scale combinatorially with the number of correlated orbitals and are not black box, generally requiring the user to select an active space. Our group is searching for computational middle-ground approaches that adequately describe the qualitative features imposed on a system by static correlation while maintaining single-reference (polynomial) cost. We have recently introduced new Hermitian excited-state methods based on interfacing "addition-by-subtraction" coupled-cluster (CC) theory with the intermediate state representation (ISR). Addition-by-subtraction CC approaches remove problematic components of T_2 clusters to achieve better behavior for strongly-correlated systems, while the ISR approach is a Hermitian excited-state theory akin to the popular algebraic diagrammatic construction (ADC) method. However, unlike ADC, our CC-ISR(2) methods do not diverge when static correlation becomes important such as in the case of dinitrogen dissociation or homolytic bond cleavage more generally. The Hermitian construction of CC-ISR(2) also permits the correct description of avoided crossings and conical intersections where more common equation-of-motion approaches can fail. Our CC-ISR(2) approach retains excellent (0.2 eV) accuracy for vertical excitation energies and correctly predicts potential energy surface topography, which is crucial for photodynamic simulations. We are actively working on further improvements to the ground-state CC reference, and towards a formal unification of CC and ISR theories.

Bootstrapping the Electronic Structure of Quantum Materials

Anna O. Schouten, Simon Ewing, David A. Mazziotti

Department of Chemistry and The James Franck Institute, The University of Chicago, Chicago, IL

The last several decades have seen significant advances in the theoretical modeling of materials within the fields of solid-state physics and materials science, but many methods commonly applied to this problem struggle to capture strong electron correlation accurately. Recent widespread interest in quantum materials---where strong correlation plays a crucial role in the quantum effects governing their behavior---further highlights the need for theoretical methods capable of rigorously treating such correlation. Here, we present a periodic generalization of variational two-electron reduced density matrix (2-RDM) theory, a bootstrapping-type method that minimizes the ground-state energy as a functional of the 2-RDM without relying on the wavefunction. The 2-RDM is computed directly by semidefinite programming with *N*-representability conditions, ensuring accurate treatment of strongly correlated electronic systems. By exploiting translational symmetry, we significantly reduce computational scaling, enabling applications to realistic materials-scale systems. Additionally, we introduce an alternative to conventional energy band structures: natural-orbital occupation-number bands, which, being independent of mean-field assumptions, offer deeper insights into electron correlation effects. We demonstrate the effectiveness of this approach by applying the theory to hydrogen chains, molybdenum disulfide, and nickel oxide, showing that natural-orbital occupation bands correctly capture electronic character in regimes where density functional theory fails. This work represents a major step toward accurately describing the electronic structure of quantum materials using reduced density matrices rather than wavefunctions.

A large language model-type architecture for high-dimensional molecular potential energy surfaces

Xiao Zhu[1], Srinivasan S. Iyengar [2]

[1]Indiana University Bloomington
[2]Indiana University Bloomington

Computing high dimensional potential surfaces for molecular and materials systems is considered to be a great challenge in computational chemistry with potential impact in a range of areas including fundamental prediction of reaction rates. In this paper we design and discuss an algorithm that has similarities to large language models in generative AI and natural language processing. Specifically, we represent a molecular system as a graph which contains a set of nodes, edges, faces etc. Interactions between these sets, which represent molecular subsystems in our case, are used to construct the potential energy surface for a reasonably sized chemical system with 51 dimensions. Essentially a family of neural networks that pertain to the graph-based subsystems, get the job done for this 51 dimensional system. We then ask if this same family of lower-dimensional neural networks can be transformed to provide accurate predictions for a 186 dimensional potential surface. We find that our algorithm does provide reasonably accurate results for this larger dimensional problem with sub-kcal/mol accuracy for the higher dimensional potential surface problem.

Simulating absorption spectra using EOM-CCSD with a polarizable force field: Application to the GFP chromophore

Taylor Parsons[1],Andrew Snider[2], Arthur Pyuskulyan[2], Christine Isborn[2], and Marco Caricato[1]

[1]Department of Chemistry, University of Kansas, 1567 Irving Hill Road, Lawrence, Kansas 66045, United States
[2]Department of Chemistry and Biochemistry, University of California Merced, 5200 North Lake Rd, Merced, CA 95343 , United States

Accurately representing spectra for solvated systems is still problematic for simulations, particularly with polar solvents capable of forming hydrogen bonds. The spectral broadening induced by solvent-solute interactions can be difficult to replicate with simulations, even for fully QM methods such as TDDFT. One potential workaround is to utilize hybrid methods, where the solute of a system is treated with a higher level of theory, and the environment is treated with a lower level, cheaper method. An EOM-CCSD solute in a TDDFT environment has been shown to improve upon this broadening, but the unfavorable cost scaling of fully QM methods makes the study of many large systems difficult. One potential cost-saving method is to treat the solute with a QM level of theory, and treat the solvent with classical MM. Here, we present results for QM/MMPol (i.e., a polarizable force field) calculations applied to the anionic GFP chromophore solvated in both water and methanol, where the chromophore is treated with EOM-CCSD and the solvent is treated with MMPol. In MMPol, polarization is induced with a point dipole placed at each atomic center in the MM region, whose magnitude and direction are determined by the electric field from both QM and MM regions. We compare the QM/MM results with both gas-phase calculations and with the solvent treated as point charges. We show that, for both solvents under consideration, there is a consistent increase in broadness going from the gas-phase to point charges to MMPol. Additionally, we show that EOM- CCSD improves on broadness compared to TDDFT for each solvent representation.

Spin Relaxation and Chiral-optical properties of Solids from First-principles Density-Matrix Dynamics

Yuan Ping
University of Wisconsin-Madison

Ab-initio spin dynamics and transport simulations are critical for predicting new materials and realizing the potential of spintronics, spin-based quantum information science, and spin-selective photo-chemistry. In particular, simulations would be invaluable to predict key physical parameters including spin lifetime, spin diffusion and coherence length, magneto-optical spectra, and (spin)-photocurrent.

In this presentation we will introduce our recently developed real-time first-principles density-matrix dynamics (FPDMD) approach with electron-electron, electron-phonon, electron-impurity scatterings and self-consistent spin-orbit couplings[1-3]. The electron-electron interactions can be rigorously derived through nonequilibrium Green's function plus generalized Kadanoff-Baym ansatz [4]. We further extend this framework with Wigner functions for simulating spatial-temporal quantum dynamics and transport accounting for a range of quantum degrees of freedom (e.g., charge, spin, orbital, lattice).

We show our methods can accurately predict spin and carrier lifetime, spin diffusion length, and pump-probe Kerr-rotation signatures for disparate solids, with examples of Si, GaAs, 2D materials[5], and hybrid halide perovskites[6-7]. In particular, we show our recent study of how *g* factor fluctuations lead to spin dephasing in halide perovskites under external magnetic field, and the distinct electron-phonon contributions to spin and carrier relaxations and crucial dependence on crystal symmetry[7]. We next will introduce our recent progress of developing methodology for spin-optotronic signatures, such as circular dichroism [8,9] and circular photogalvanic effect [10] to chiral and broken-inversion-symmetry solids, and how they are correlated with continuous chirality measure for structural-property relations[10].

We then will show our recent progress on orbital relaxation and orbital transport in systems with and without inversion symmetry, which shows distinct mechanism from spin relaxation in semiconductors, which are critical for orbitronics applications. Finally, we will present recent work on first-principles prediction of spatial-temporal spin transport properties in graphene and chiral materials, where we show spin generation and dephasing in both coherent and incoherent transport, and discuss the distinction between chirality induced spin selectivity and Edelstein effects. Our results provide important insights for spin-optotronic properties and spin and orbital transport in chiral and non-centrosymmetric systems.

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Computational Discovery of New Materials for Singlet Fission in the Solid State

Noa Marom[1]

[1] Department of Materials Science & Engineering, Carnegie Mellon University, Pittsburgh, Pennsylvania 15213, USA

Intermolecular singlet fission (SF) is the conversion of a photogenerated singlet exciton into two triplet excitons residing on different molecules. SF has the potential to enhance the conversion efficiency of solar cells by harvesting two charge carriers from one high-energy photon, whose surplus energy would otherwise be lost to heat. The development of commercial SF-augmented modules is hindered by the limited selection of molecular crystals that exhibit intermolecular SF in the solid state. Computational exploration may accelerate the discovery of new SF materials. The GW approximation and Bethe–Salpeter equation (GW+BSE) within the framework of many-body perturbation theory is the current state-of-the-art method for calculating the excited-state properties of molecular crystals with periodic boundary conditions. However, its high computational cost is prohibitive for large-scale materials screening. Therefore, we develop materials discovery workflows that combine GW+BSE with low-cost physical or machine learned models. Using this approach, we have demonstrated three successful strategies for the discovery of new SF materials: (i) functionalization of known materials to tune their properties, (ii) finding potential polymorphs with improved crystal packing, and (iii) exploring new classes of materials. [J. Phys. Chem. C 128, 7841 (2024)]

Collective Optical Response and Local Molecular Dynamics in Disordered Light-Matter Systems

Hsing-Ta Chen, University of Notre Dame

Harnessing strong light-matter interactions holds immense promise for controlling molecular and material properties, including chemical reactions, energy transfer rates, and charge conductivity. The observation of Rabi splitting has been considered a spectroscopic hallmark for confirming strong light-matter coupling and polariton formation. However, this interpretation often overlooks the potential impact of significant disorder as induced by the electromagnetic environment. In this talk, we present theoretical work combining an effective model with electrodynamics simulations to develop a non-perturbative treatment of strong disorder. We find that strong disorder can induce a spectral splitting remarkably similar to Rabi splitting, but through a different mechanism involving the optical dark modes. This disorder-induced splitting is demonstrated for molecules near a plasmonic nanodisk of various shapes. This result fundamentally challenges the interpretation of spectral splitting as a signature of strong coupling, revealing that steady-state absorption spectra alone may not differentiate between polariton formation and strong disorder effects. We will further discuss potential approaches to distinguish whether a system exhibits strong coupling effects induced by polaritons or strong disorder effects dominated by the dark states.

Exploring the phase diagram of α-Sn using self-consistent GW

Gaurav Harsha[1], Selina Dirnbök[2], Lei Zhang[3], Vojtech Vlcék[4,5], Emanuel Gull[3], Dominika Zgid[1,3]

[1]Department of Chemistry, University of Michigan, Ann Arbor, MI 48109, USA
[2]Institute of Solid State Physics, TU Wien, 1040 Vienna, Austria
[3]Department of Physics, University of Michigan, Ann Arbor, MI 48109, USA
[4]Department of Chemistry and Biochemistry, University of California, Santa Barbara, CA 93106, USA
[5]Department of Materials, University of California, Santa Barbara, CA 93106, USA

We present a comprehensive investigation of semi-metallic and topological phases in α-Sn using ab initio relativistic self-consistent GW (scGW) theory, through the lens of numerical method development. Conventional density functional theory (DFT) predictions vary widely, from negative band-gap semimetals to zero-gap semiconductors, and fail to capture the strong dependence of topological properties on lattice distortions observed in experiments. By incorporating a high-level description of electron correlation through scGW, along with relativistic effects using exact two-component theory, we systematically study the electronic structure of α-Sn. Furthermore, using the newest numerical advances in handling analytical continuation, we present a novel analysis of the zeros of the ab-initio Green's function to characterize topological properties, with which we identify the emergence of a topologically insulating phase. We further determine a Dirac semimetal phase under anisotropic lattice strain by studying the band structure. Additionally, we find that the GW bands exhibit a visible temperature dependence, underpinning the high sensitivity of α-Sn's electronic structure—an effect not captured by ground-state theories. These findings provide critical insights into the interplay of correlation, relativistic effects, and structural deformations in the topological properties of a-Sn as well as into the development of numerical methods necessary to describe topological materials.

Multi-Reference Methods for Accurate Band Structure Calculations in Strongly Correlated Crystalline Periodic Systems

Bhavnesh Jangid, Daniel King, Matthew Hermes, Laura Gagliardi

Department of Chemistry, University of Chicago

The growing number of materials that lie between discrete molecules and extended solids such as metal-organic frameworks and organic semiconductors has created a pressing need for modeling strategies that can span both categories. Specifically, there is increasing demand for approaches that merge the real-space, molecular perspective used in computational chemistry with the reciprocal-space viewpoint of solid-state physicists. In this work, we present the Localized Active Space (LAS) method as a promising tool for modeling extended systems with localized and clustered electronic features. LAS expands upon the active space concept from multiconfigurational methods like Complete Active Space Self-Consistent Field (CASSCF) by constructing a product-form wave function across multiple molecular fragments. To adapt this to solids, we treat each unit cell as a fragment assigned to its own local quantum numbers, such as charge or excitation state. By introducing interactions between these LAS-based states referred to as LASSI, we build a robust framework for studying charge and energy transfer. This method also allows for the calculation of multiconfigurational band structures through ionization potential and electron affinities. We apply LASSI to systems including the one-dimensional hydrogen chain, polyacetylene, and strongly correlated materials like NiO, demonstrating its ability to connect quantum chemical and solid-state modeling.

Advancing large-scale excited-state materials simulations for quantum technologies

Victor Yu

Materials Science Division, Argonne National Laboratory

Understanding and predicting excited-state properties is critical for designing novel materials for quantum technologies. We have developed a powerful and versatile suite of first-principles excited-state simulation codes implementing time-dependent density functional theory, many-body perturbation theory, and quantum embedding theory. Our formulations circumvent the common computational bottleneck of summation over empty states and utilize low-rank approximations and localization techniques to achieve further acceleration. With excellent scalability to thousands of graphics processing units, our codes enable excited-state materials simulations at unprecedented scales, as showcased in the study of the interplay of extended and point defects in a large supercell containing 1727 atoms. The unique combination of multiple state-of-the-art excited-state simulation capabilities has led to the first comprehensive characterization of the impact of dislocations on the properties of nearby nitrogen-vacancy centers, opening new avenues for engineering spin qubits and demonstrating how advanced theoretical frameworks and high-performance computing can drive innovative scientific discoveries.

Characterization of electron transport in molecular devices and wires using active space methods

Andrew M. Sand[1]

[1]Department of Chemistry and Biochemistry, Butler University, Indianapolis, Indiana 46208 USA

Single molecule electronic devices have been the subject of many theoretical and experimental studies over the past many years due to their possible attractive use in the manufacture of smaller and tunable electronic components. From a theoretical direction, non-equilibrium Green's function approaches (NEGF) in combination with density functional theory (NEGF-DFT) has received considerable attention. However, in electronic structure calculations, DFT often struggles to adequately describe strong/multiconfigurational correlation effects. To more explicitly handle this type of correlation effect in the context of electron transport, an active space approach using multiconfiguration pair-density functional theory (MC-PDFT) with NEGF has been developed (NEGF-MCPDFT). This presentation will highlight some of the recent advances made in the NEGF-MCPDFT approach. When applied to the characterization of systems exhibiting considerable strong correlation, the MC-PDFT- and DFT-based approaches predict rather different transmission and conductance results, but in systems with low amounts of strong correlation, both approaches yield similar results. As with many active space approaches, additional care is required in the selection of an appropriate wave function reference, and some best practices (reference types, active space orbital selections, and active space sizes) will be highlighted in the context of the characterization of one-dimensional atomic wires.

Symmetry and Chemical Stability of 2D M_3X_8 (M = Nb, X= Cl, Br, I) and Other Ionic Kagome Materials.

Varsha Kumari[1], Julia Bauer[2, ¥] and Alexandru B Georgescu[3]

[1]*Department of Chemistry, Indiana University, Bloomington, Indiana 47405, United States.*

[2]*Department of Applied Physics, Yale University, New Haven, Connecticut 06520, United States.*

[3]*Department of Chemistry, Indiana University, Bloomington, Indiana 47405, United States.*

Correlated electron materials display a wide array of applications due to their interplay between charge, spin, orbital, and crystal structure leading to a wide variety of emergent states including magnetism and superconductivity. The 2D van der Waals transition metal Kagome halides M_3X_8, are a class of correlated materials showing potential multiferroic properties and spin liquid behavior which have recently been used in field-free Josephson diodes[1] for quantum computing applications. However, a limited number of these materials, only M = Nb and X = Cl, Br, I compounds are reported in the literature - as opposed to the wider variety of 2D dihalides and trihalides (MX_2 and MX_3). Using density functional theory, we show that these materials' chemical stability is driven by the symmetry of the trimer orbital formation across M_3 ions which stabilizes a breathing distortion. Using Crystal Orbital Hamiltonian Populations (COHP) and symmetry analysis we find that the materials that have been successfully synthesized have an optimal trimer orbital bonding/antibonding filling ratio. Our theoretical analysis easily extends to insulating Kagome oxides as well, including $Li_xScMo_3O_8$,[2] $Li_2InMo_3O_8$, and $LiZn_2Mo_3O_8$,[2] which all follow the same symmetry criterion. Finally, we use our analysis to propose new potential materials for potential synthesis.

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Unveiling phonon-assisted optical properties of MoS_2 bilayers

Gyanu P. Kafle[1] and Zhenfei Liu[1]

[1]Department of Chemistry, Wayne State University, Detroit, Michigan 48202, USA

Phonon-assisted photoluminescence (PL) is a fundamental mechanism in the optical response of layered materials, particularly in indirect bandgap systems such as bilayer MoS_2. Phonon-assisted processes involve momentum transfer via phonons, enabling otherwise forbidden radiative recombination of excitons. In this study, we first employ a first-principles *GW*-BSE approach (*G*: Green's function; *W*: screened Coulomb interaction; BSE: Bethe-Salpeter equation) to compute the quasiparticle electronic structure and optical properties of strained MoS_2 bilayers. Then, we compute the PL spectra of strained MoS_2 bilayers by explicitly investigating how the phonons affect the absorption spectra of supercells that are commensurate with the relevant phonons. The PL spectra are then obtained through the Roosbroeck-Shockley relationship. A rigorous analysis of phonon eigenmodes and their coupling with excitonic states reveals that transverse optical phonon modes are the dominant contributors to indirect emission. Furthermore, we observe a redshift in the PL peaks under strain, which we attribute to a decrease in the indirect bandgap. Our theoretical predictions are benchmarked against available experimental spectra, highlighting the critical role of phonons in tuning the optical properties of van der Waals layered materials. These findings offer valuable guidance for the design of advanced optoelectronic devices.

Coupled Cluster Accuracy at DFT Cost: Interpretable Graph-Network Based Machine Learning Models via Molecular Fragmentation

Krishnan Raghavachari

Indiana University, Bloomington, Indiana 47405, USA
e-mail: kraghava@iu.edu

The failure of available density functional (DFT) methods to compute accurate electronic structures and energies for complex systems is well documented. While newly developed dispersion corrected and long-range corrected density functionals offer improved results, the errors in thermochemical properties computed with DFT are often greater than 5 kcal/mol for many chemical processes. In this talk, we discuss a new fragmentation-based molecular representation framework designed for delta machine learning (Δ-ML) with the central goal of correcting the deficiencies of approximate methods such as DFT to achieve a high level of accuracy that is currently only achievable with sophisticated and computationally intensive methods such as coupled cluster theory.

Our framework is based on a judicious combination of ideas from fragmentation, error cancellation, and a state-of-the-art deep learning architecture. Broadly, we develop a general interpretable framework for molecular machine learning by incorporating the inherent advantages prebuilt into existing error cancellation methods such as the generalized Connectivity-Based Hierarchy. More specifically, we develop an attributed graph representation through a fragmentation-based encoding of local chemical environments. In addition, we incorporate electronic descriptors from DFT calculations in the Δ-ML model to achieve high accuracy for the calculation of electronic properties. Our QM/ML framework and its performance for theoretical thermochemistry, redox potentials, pK_a calculations, and NMR chemical shifts are analyzed and assessed in this presentation.

Guiding Deep-learning Model to Explore “Constraint” Protein Conformational Ensemble

Yanbin Wang[1], and Ming Chen[1]

[1] Department of Chemistry, Purdue University, West Lafayette, IN, 47907

Modeling protein conformations is essential for understanding their functions. However, obtaining atomically resolved conformational ensembles remains challenging, both experimentally and computationally. In recent years, deep learning methods have shown promise in predicting protein structures, but these models are typically trained on PDB structures and/or molecular dynamics simulations, which limits their applicability to proteins in homogeneous environments. In this work, we present an approach to guide existing models to sample constrained protein conformational ensembles, where constraints may arise from experimental measurements or interactions with external environments. By designing appropriate guided sampling algorithms, our method can generate constrained protein conformations without the need for additional training or fine-tuning. This approach significantly enhances the transferability of current deep learning models for protein structure prediction.

Impacts of Static Disorder on the Quantum Dynamics of Dissipative Two-Level Systems

Eleanor L Vandel[1] and Nancy Makri[1,2,3]

[1]Department of Chemistry, University of Illinois, Urbana, Illinois 61801, USA
[2]Department of Physics, University of Illinois, Urbana, Illinois 61801, USA
[3]Illinois Quantum Information Science and Technology Center, University of Illinois, Urbana, Illinois 61801, USA

Many dynamical processes occur in disordered media, such as large biomolecules. When the subsystem of interest is embedded in such a medium, the local environment can alter the system's electronic states, leading to an effect known as static disorder. In such situations the energies of the system's states must be sampled from a distribution, which is usually assumed to have a Gaussian form. Static disorder contributes to the measured Stokes shift and gives rise to inhomogeneous broadening of spectral line shapes. In spite of their significance, the effects of static disorder are rarely included in simulations of quantum dynamical processes because of the large computational cost associated with performing already demanding calculations for many realizations of the system Hamiltonian. As a result, much is unknown about the direct impact of static disorder on quantum dynamics. We use the numerically exact small matrix path integral (SMatPI) methodology[1] with the equivalence class path integral (EqC-PI) algorithm[2] to investigate the influence of static disorder on the time evolution of the reduced density matrix (RDM) for model two-level systems (TLS) in contact with Ohmic dissipative environments across various regimes. The dissipative TLS (also known as spin-boson) Hamiltonian[3] is ubiquitous; for example, it is often used to describe charge or exciton transfer in condensed phase environments. For a range of TLS asymmetries, we explore environments with high or low temperature, fast or slow baths, and weak or moderate system-bath coupling strengths. We find that static disorder alters the dynamics and equilibrium properties of the RDM in significant and often subtle ways, which can mimic effects associated with stronger or weaker dissipation. The impact of disorder is most pronounced at low temperatures, where it tends to suppress coherence and often induces upward shifts in the population of the higher-lying state, while the effects on off-diagonal RDM element and the eigenstate populations depend nonmonotonically on the asymmetry parameter. The population shift is weaker and reversed for some parameters at high temperatures. These results can help inform the consequences of static disorder on the many processes that can be mapped on TLS coupled to dissipative environments.

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Product Directed Exploration of Chemical Reaction Networks

Ericka Roy Miller[1], Andrew Marquardt[1], Thomas J. Burton[1], Brett M. Savoie[1]

[1]Department of Chemical and Biomolecular Engineering | University of Notre Dame

The search for mechanisms of complex chemical processes is a unifying quest across several application domains. In theory, these processes can be mapped onto chemical reaction networks (CRNs), where molecular species are connected by reaction pathways. In practice, the application of CRNs is limited by the explosion of potential reactions that arise during deep network exploration. However, in many cases both starting materials and final products are known. We posit that significant cost reductions can be attained by limiting CRN exploration to reaction pathways relevant to the formation of a given product. To this end, we reframe the CRN exploration problem from a single-ended (**R → ?**) search to a double-ended (**R → ? → P**) search. We then investigate the roles of chemical distance metrics and exploration rules on finding kinetically relevant reaction pathways of glucose decomposition and Li-ion electrolyte degradation.

Efficient Exploration of Protein-Ligand Alchemical Landscapes using Seeded Multisite Lambda Dynamics

Paige E. Bowling[1], Charles L. Brooks III[1]

[1]Department of Chemistry, University of Michigan

Alchemical free energy methods provide an efficient framework for estimating relative free energies in chemically complex systems, making them well-suited for drug and protein design applications. Recent advances have extended multisite λ dynamics (MSλD) to accommodate multiple simultaneous mutations of both protein and ligand sites. However, efficient sampling of diverse chemical substituents at each site remains challenging due to the exponential growth of nonphysical intermediate states. In this work, we apply MSλD to model mutations in HIV-1 Reverse Transcriptase (HIV-RT) at residues Y181 and Y188, along with eight substituents at each of three sites on an indole-derivatized inhibitor scaffold, yielding a combinatorial space of over 6,000 distinct protein–ligand combinations. We introduce a new seeding strategy for the biasing potentials used to flatten the alchemical landscape to improve exploration. These biases are initialized from independent free energy simulations of the protein and ligand in solvent, calculations that are already necessary to estimate the binding free energy. Our seeded approach significantly accelerates bias convergence, reducing the number of flattening steps from hundreds to tens of simulations. This enhanced efficiency enables simultaneous exploration of large combinatorial spaces of protein and ligand modifications, offering a promising strategy for rational drug design in resistance-prone systems such as HIV-RT. In this work, we will discuss the implementation of the bias-seeding strategy, its impact on convergence and sampling, and application to the design of HIV-RT non-nucleoside inhibitors.

Toward a Solution to the Static Correlation Error with a hybrid Density Functional 1-RDMFT Framework

Daniel Gibney, Jan-Niklas Boyn*

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455, United States

Kohn Sham Density Functional Theory (DFT) has established itself as the go-to method in computational chemistry and materials science due to its low computational costs and generally acceptable accuracy for most chemical problems. However, modern DFT continues to display significant limitations, including in the treatment of strongly correlated systems, where its single reference nature results in large errors. Recently a solution to this problem was proposed by combining traditional DFT exchange correlation (XC) functionals with a 1-Electron Reduced Density Matrix Functional Theory (1-RDMFT). Strong correlation effects are captured through a 1-RDM based functional while a DFT XC functional captures the remaining dynamical correlation. This framework yields large improvements over traditional DFT in the treatment of multi-reference problems, however, it currently relies on existing XC functionals, which were developed under the assumption that the 1-RDM remains idempotent and tend to be semi-empirical. Here, we benchmark a range of XC functionals for their ability to capture strong correlation and work towards developing a task-specific density functional for use within the hybrid 1-RDMFT framework. Additionally, we demonstrate the ability of this framework to elucidate electron entanglement in iron-sulfur metalloclusters.

On generalized eigenvalue problem in quantum algorithms for excited states

Prince Frederick Kwao, Srivathsan Poyyapakkam Sundar, Brajesh Gupt, Ayush Asthana

University of North Dakota

Abstract

Accurate modeling of molecular excited states is important in several areas of molecular sciences including studies that involve spectroscopy, photochemistry, photophysics among others. New quantum computing algorithms for the molecular ground and excited state problems may have a strong impact in advancing excited state quantum chemistry in the future. Among the algorithms proposed, the subspace algorithms, including Quantum Subspace Expansion (QSE) and Quantum Equation-Of-Motion (qEOM) and their derivatives show the most promise. However, most of these algorithms involve solving a generalized eigenvalue problem on a classical computer, which in presence of noise can be error prone. This study explores how the subspace-based excited state methods are impacted by sampling errors. We will present the difficulties that these methods may face in practical quantum computing scenarios. Then we will show that methods that have an eigenvalue equation as their working equation, such as Quantum Self-consistent Equation-of-Motion (q-sc-EOM), are more robust to shot noise compared with the ones that require solving a generalized eigenvalue equation as their working equation.

Memory kernels of the protein dynamics: developing non-Markovian models for large biomolecules

Siqin Cao[1], Bojun Liu[1], Yunrui Qiu[1], Ilona C. Unarta[1], Minyi Xue[1], and Xuhui Huang[1]

[1]Department of Chemistry, University of Wisconsin−Madison, Madison, Wisconsin 53706, United States

Conformational changes play important roles in many biomolecular systems. The Generalized Master Equation (GME) offers a powerful framework for investigating the functional changes of large biomolecules using Molecular Dynamics (MD) simulations at atomic resolution. In the GME models, protein conformations are modeled by a set of discrete conformational states, and the conformational dynamics are characterizing by the time-dependent transitions between them. We first developed the quasi Markov State Model (qMSM), a straightforward implementation of the GME that explicitly incorporates time-dependent memory kernels. qMSM has achieved success in capturing the slow dynamics of large protein systems such as Taq RNAP. However, the performance of qMSM is significantly hindered by numerical fluctuations resulting from MD samplings, which greatly restricts its applicability in studying the conformational dynamics of large biomolecules. To address the limitations of qMSM, we developed the Integrative Generalized Master Equation (IGME) to investigate protein conformational dynamics using an analytical solution of the GME. Unlike qMSM, IGME relies on time-integrated memory kernels rather than time-dependent kernel functions, which significant simplifies implementation and enhances numerical robustness. We demonstrated that IGME substantially outperforms previous methods in capturing the dynamics of large biomolecules, including Markov State Models (MSMs), Hidden Markov Models (HMMs), and qMSM. Meanwhile, we also noticed that collective variables (CVs) are critical for constructing effective state models for slow conformational dynamics. Therefore, we also developed the Memory Kernel Minimization-based Neural Networks (MEMnets) which can identify slow CVs optimized for generating state models. Based on our IGME theory, MEMnets incorporate non-Markovian dynamics by encoding them through memory kernels in continuous CV space. The architecture of MEMnets employs parallel encoder neural networks to project high-dimensional MD data into a low-dimensional latent space, where time-integrated memory kernels computed in the latent space is used as the objective function. Our results show that MEMnets significantly outperform State-free Reversible VAMPnets (SRVs) in identifying slow dynamics in large biomolecular systems. Notably, MEMnets produce converged and consistent models for large biomolecules, while SRVs often result in disconnected dynamics along the identified CVs, which holds promise to be widely used to study biomolecular conformational changes.

Decoding The Structural Dynamics of Fluorescent Dye-modified DNA Nanowires Using Classical Atomistic Simulations

Anton S. Perera, Reshma Mathew, Divita Mathur, Carlos E. Crespo-Hernández, and Shane M. Parker [1]

[1]Case Western Reserve University

Beyond DNA's well-known capability of storing genetic information, their use as smart building blocks for nanomaterials opens up a wide array of possibilities ranging from biosensing and light-harvesting to quantum information processing. Further development of such technologies relies highly on the fundamental understanding of the structural dynamics of such DNA-based nanomaterials, which can be achieved via physics-based simulations. Herein, we report simulating a system of double-stranded DNA (dsDNA) nanowires with Cyanine 3 (Cy3) and Cyaninie 5 (Cy5) dye modifications to study the energy transfer between the two dyes within this nanowire. The use of quantum mechanics to probe the dynamics of systems with large phase space, such as fully solvated dsDNA, is limited by current computing limitations. Nevertheless, the essential physics of inter-dye distance and dye orientation governing energy transfer can be captured by using classical mechanics. This also allows us to study multiple replicas/longer times to gather statistically significant data (ensemble sampling) on dsDNA nanowire conformations. Here, we performed 1 μs of molecular dynamics (MD) simulations of this system using the OL21 (DNA) and GAFF2-AMBERDYES (Cy3/Cy5) force fields, which led us to results that complement conclusions from our spectroscopic experiments. Through the analysis of the MD trajectories, we observe two distinct conformations with two inter-dye distances much shorter than the Förster distance (~5 nm), which agrees with high transfer efficiency, as the experiments suggest. We also observe that the angle between transition dipole moments of the two dyes tends to vary within a distinct range for the mentioned conformations. This study reveals the potential of physics-based simulations, even at a relatively simple classical mechanics theory level, in understanding the structural dynamics leading to energy transfer, thus paving the path to the further development of DNA nanomaterials.

Designing Fluorescent Protein-Based Anion Sensors for Live-Cell Imaging: A Computational Perspective

Vishaka Pathiranage[1], Cheng Chen[2], Whitney S. Y. Ong[3], Sheel C. Dodani[3], Chong Fang[2]*, and Alice R. Walker[1]*

[1]Department of Chemistry, Wayne State University, Detroit, MI, USA
[2]Department of Chemistry, Oregon State University, Corvallis, OR, USA
[3]Department of Chemistry and Biochemistry, University of Texas at Dallas, Dallas, TX, USA

Fluorescent proteins are widely used as biosensors to investigate the biochemistry of living cells and organisms. Among them, mNeonGreen (mNG) is one of the brightest green fluorescent proteins, recently engineered as a turn-on sensor for chloride ions, with a crystal structure resolved for chloride-bound mNG. Chloride, a highly abundant physiological anion, plays key roles as a counterion and secondary messenger, and its dysregulation is implicated in diseases such as hyperekplexia, cystic fibrosis, and epilepsy. To study chloride dynamics in cells, Dodani et al. developed the ChlorON series by mutating mNG, yielding ChlorON3 (mutated at K143 and R195), which showed the strongest fluorescence response to chloride. Notably, absorption and Raman spectra of ChlorON3 revealed significant differences from ChlorON1 upon chloride binding, suggesting underlying structural changes that enhance fluorescence. To explore these effects at the molecular level, we conducted classical molecular dynamics (MD) simulations and hybrid quantum mechanics/molecular mechanics (QM/MM) calculations on ChlorON variants, with and without bound chloride. Our analysis revealed that chloride induced structural variations, particularly in the hydrogen bonding network between the chromophore's N2 position and Arg88, contribute to the observed Raman spectral shifts. Moreover, restricted chromophore rotation around the ψ angle and altered H-bonding at the O2 and N2 positions influence absorption spectra, aligning well with experimental data. These findings underscore the role of conformational rigidity, rather than chromophore planarity, in driving enhanced fluorescence efficiency. Building on these insights, we proposed and tested new mutations that further modulate chromophore dynamics and ion sensing. Looking ahead, we aim to develop a machine learning model to predict mutations that enhance fluorescent protein performance for live-cell imaging applications.

Thursday Poster Presentations

(In the order of the poster number)

Relativistic Fully Self-Consistent GW for Molecules

Vibin Abraham[1], Gaurav Harsha[1], and Dominika Zgid[1,2]

[1]Department of Chemistry, University of Michigan, Ann Arbor, MI
[2]Department of Physics and Astronomy, University of Michigan, Ann Arbor, MI

We present a relativistic fully self-consistent GW (scGW) method using the exact two-component (X2C) Coulomb approximation for accurate ground and excited state calculations of heavy element molecules, without reliance on a mean-field reference. Our results show that scGW outperforms G0W0/PBE and removes starting-point dependence. Relativistic photoelectron spectra from scGW agree well with experiments, particularly for inner d-shell ionization potentials. The conserved total energy also enables accurate predictions of bond lengths and vibrational frequencies in heavy halogen dimers. This demonstrates scGW's applicability for precise ionization potentials, photoelectron spectra, and total energies in heavy element systems with reasonable computational cost.

UNREVELAING PHOTOPROTECTION MECHANIESMS IN THE FENNA-MATTHEWS-OLSON (FMO) LIGHT-HARVESTING COMPLEX

Osama Abuhammad[1], Lyudmila V. Slipchenko[1].

[1]*Department of Chemistry, Purdue University, West Lafayette, Indiana 47907, USA*

Contact: *oabuhamm@purdue.edu*

Photoprotection is a critical biochemical process that helps organisms to survive cellular damage caused by excessive sunlight. Under sunlight excitation bacteriochlorophyll molecules can undergo intersystem crossing to long living triplet state. In aerobic conditions, the triplet-state (bacterio)chlorophylls can transfer energy to molecular oxygen. This spin-allowed process generates highly reactive singlet oxygen that irreversibly reacts with nearby organic molecules, eventually leading to oxidative stress and damage to living cells.

Many photosynthetic proteins mitigate the damaging effect of excess solar radiation by incorporating carotenoid molecules whose low-lying triplet states become a sink for the excitation energy from which it safely dissipates into heat.

The Fenna-Matthews-Olson (FMO) pigment protein is essential in transferring excitation energy from the chlorosome antenna to the reaction center in green sulfur bacteria. Surprisingly, FMO complex doesn't contain any carotenoids, yet it's found to be exceptionally stable in aerobic conditions. Therefore, our goal is to understand the photoprotection mechanisms of this photosynthetic complex. Implications of this project are a rational design of bio-inspired light-harvesting antennas and the redesign of natural photosynthetic systems, opening new possibilities for regulating these systems in response to excess light.

We explore three possible mechanisms contributing to the photoprotection of FMO. One possibility is a physical barrier photoprotection mechanism that in which the protein backbone acts as a shield to prevent molecular oxygen from reaching BChl sites. To this end, we investigated the distribution of molecular oxygen in molecular dynamics trajectories and computed the binding free energy between O2 and BChls. Furthermore, we studied the energy transfer mechanism between the triplet BChl and O_2 utilizing quantum mechanical calculations, because the fast energy transfer depends on factors such as strong coupling and energy matching between donor and acceptor. Finally, we are investigating whether the photoprotection chemistry in FMO can be attributed to a redox-dependent excitation quenching mechanism and whether specific key amino acids play a role in this redox chemistry.

Computational studies of solvatochromic behavior of *para*-diacetyl phenylene diamine, a push-pull electron system

Anita Houston Adams[1], Alice R. Walker[1]

1. Department of Chemistry, Wayne State University, 5101 Cass Ave, Detroit, MI, 48202, USA

Fluorescence-based techniques are indispensable tools in both basic science and medical research, enabling the detection of molecules and the probing of chemical reactions in vitro and in vivo. Red fluorophores, particularly, are highly sought after for deep-tissue and whole-body imaging due to their ability to minimize background interference, as red light exhibits superior tissue penetration. The benzene-based para-diacetylphenylenediamine (*p*-DAPA) represents the smallest known red fluorophore, distinguished by its high fluorescence quantum yield and brightness. Despite its promising attributes, the influence of solvent on the photophysical properties of *p*-DAPA remains underexplored. Utilizing classical force field dynamics and ab initio Born-Oppenheimer molecular dynamics (BOMD) simulations in explicit solvent environments, we have systematically investigated the ground and excited state potential energy surfaces of *p*-DAPA. Our findings reveal that *p*-DAPA demonstrates significantly enhanced fluorescence in chloroform compared to water, attributed to the emergence of multiple nonradiative decay pathways in aqueous environments that are absent in chloroform. This study provides critical insights into the solvent-dependent photophysical behavior of *p*-DAPA, offering a foundation for optimizing its application in biological imaging and other advanced biomedical technologies.

First-principles investigation of the surface defects in CdS quantum dots

Moses Adeyemo, Gyanu Kafle, Zhenfei Liu

Department of Chemistry, Wayne State University, Detroit, MI 48202, USA

Abstract

The tunability of energy levels and optical properties in CdS quantum dots (QDs) renders them a distinctive choice for applications in electronics and optical devices. However, a major factor limiting their performance is the low photoluminescence, which is attributed to defect-induced in-gap states. Given the experimental difficulty in probing defects at an atomistic level, first-principles characterizations of the structure-property relationship of common defects can provide rational design rules. In this work, we utilize density functional theory and the many-body *GW*-BSE (*G*: Green's function; *W*: screened Coulomb interaction; BSE: Bethe-Salpeter equation) approach to investigate four types of surface defects: 2 Cd vacancies, 2 S vacancies, 2 Cd atoms replaced by 2 Pb atoms, and 1 S atom replaced by 1 Cl atom, in both wurtzite and zinc blende CdS QDs. In contrast to pristine QDs, our result reveals distinct in-gap states with significant localization of electron density around the defect sites, and we attribute these features to undercoordination and dangling bonds. Similarly, we observe changes in the optical properties compared to the pristine QDs. In summary, we systematically illustrate how structural imperfections modulate the electronic and optical properties in CdS QDs, providing insight into the defect-induced properties and surface passivation schemes.

Quasiparticle Electronic Structure of Interfaces Between TTF-TCNQ Monolayer and Metal Substrates

Amos Afugu[1] and Zhenfei Liu[1]

[1]Department of Chemistry, Wayne State University, Detroit, MI 48202, USA

The pair of tetrathiafulvalene (TTF) and tetracyanoquinodimethane (TCNQ) molecules has been known as organic metal and is important in studying the charge transfer in a donor-acceptor (D-A) pair. While their interaction in molecular crystals has been well studied, the behavior when the molecules are co-adsorbed on substrates can differ significantly from the crystalline phase. With a particular focus on Au(111) and Ag(111) substrates, we employ the first-principles *GW* (*G*: Green's function; *W*: screened Coulomb interaction) method in this work to investigate how different metallic substrates affect the electronic properties and charge transfer between TTF and TCNQ. In particular, we point out the necessity of re-computing the Fermi energy at the *GW* level, and quantitatively compare results from G_0W_0 and G_1W_0 in which quasiparticle orbitals are updated via diagonalization of the quasiparticle Hamiltonian, focusing on the change of electronic density and its impact on D-A interactions. Our calculations illustrate how the interfacial dielectric screening from metals with different work functions alters the charge transfer between TTF and TCNQ and between the substrate and the molecular adsorbates. Our work leads to novel insight into the interfacial charge transfer between a D-A pair and a substrate, providing a benchmark for subsequent experimental and computational studies.

Enabling Multireference Calculations on Multi-Metallic Systems with Graphic Processing Units

Valay Agarawal[1], Rishu Khurana[1,2], Cong Liu[2], Matthew R. Hermes[1], Christopher Knight[3], Laura Gagliardi[1]

[1] Department of Chemistry, University of Chicago

[2] Chemical Sciences and Engineering Division, Argonne National Laboratory

[3] Computational Science Division, Argonne National Laboratory

Modeling multimetallic systems efficiently enables faster prediction of desirable chemical properties and design of new materials. This work describes an initial implementation for performing multireference wave function method localized active space self-consistent field (LASSCF) calculations through the use of multiple graphics processing units (GPUs) to accelerate time-to-solution. Density fitting is leveraged to reduce memory requirements, and we demonstrate the ability to fully utilize multi-GPU compute nodes. Performance improvements of 5-10x in total application runtime were observed in LASSCF calculations for multimetallic catalyst systems up to 1200 AOs and an active space of (22e,40o) using up to four NVIDIA A100 GPUs. Written with performance portability in mind, comparable performance is also observed in early runs on the Aurora exascale system using Intel Max Series GPUs.

Computational Mechanochemistry

Alex Albaugh[1], Ali Seyedi[1]
[1]Wayne State University Department of Chemical Engineering & Materials Science

Mechanical forces can break chemical bonds, and chemical reactions can generate mechanical forces. Here we will share simulation and theoretical studies exploring both paradigms. We will present the rheological properties of mechanically interlocked polymers in flow. These polymers, characterized by topological links akin to chains, display unique flow behaviors, including lower stresses and increased tumbling compared to linear polymers. Our simulations reveal that fluid-induced mechanical forces can cause both chemical degradation through bond cleavage and physical degradation through slippage of interlocked components. Additionally, we will present our recently developed model for myosin, a biological molecular motor. This motor has two heads that walk hand over hand along an actin track. This motion generates mechanical forces from the hydrolysis of adenosine triphosphate (ATP). The model captures the full chemically driven cycle of myosin walking and opens the door to detailed thermodynamic study of its entropy production, efficiency, and mechanism. Taken together, our results showcase the interconnected roles of mechanical forces and chemical reactions in complex molecular systems.

Advancing Resonating Hartree-Fock Methods: Enhanced Convergence Algorithms for Predictive Photochemical Modeling

Qabas Alkhatib, Shane M. Parker

Case Western Reserve University

Understanding and predicting photochemical reactions and ultrafast photodynamic processes remains a significant challenge in computational chemistry, with broad implications for pharmaceutical development and materials science. To achieve substantial improvements in this field, we need to enhance electronic structure methods that can predict excited states accurately in complex molecular systems. The Resonating Hartree-Fock (ResHF) methodology is a promising method due to its ability to capture multi-reference character while maintaining computational efficiency compared to traditional methods. Building on our group's prior work, my research addresses a critical bottleneck in the current ResHF implementation: convergence challenges. While methods like CASSCF benefit from mature technologies for robust convergence and established guidelines regarding active space selection and state-averaging effects, ResHF still requires similar developments in its algorithms.

My project specifically addresses this gap by implementing quasi-Newton algorithms (such as BFGS) for ResHF calculations, targeting second-order energy convergence strategies that significantly improve both stability and computational efficiency when handling larger molecular structures. By addressing these challenges, my work contributes to a frontier area in electronic structure method development, to create truly predictive models for ultrafast light-driven processes in complex molecular architectures previously inaccessible to high-level theoretical treatment.

Keywords: Photochemical Reactions, Excited States, Non-adiabatic Coupling, Resonating Hartree-Fock, Convergence Algorithms, Quasi-Newton Methods.

Coupled cluster correlation energies for solids with a modified coulomb potential applied to the uniform electron gas

Sara Amano, William Z. Van Benschoten and James J. Shepherd
Department of Chemistry, Michigan State University, East Lansing, Michigan 48824, USA

We investigate a recently developed method for sampling the Coulombic potential in reciprocal space for periodic solids referred to as the mean potential[1]. The mean potential approach averages the Coulombic potential over the volume surrounding the grid points which are used to sample the Brillouin zone. We compare the new mean potential method to the typical probe-charge potential (Ewald) method[2] using a mean-field method, Hartree—Fock (HF), and correlated method, coupled cluster singles and doubles (CCSD). Calculations are done for the uniform electron gas (UEG) for a range of system sizes (N) and electronic densities characterized by the density parameter r_s.

We first investigate the Hartree—Fock (HF) convergence into the thermodynamic limit (TDL) $N \to \infty$. We find that the HF TDL energy from the mean potential and probe-charge potential do not agree. Additionally, we find that the mean potential HF energy for a given finite system size N is closer to the corresponding HF TDL estimate compared to the probe-charge potential. This observation suggests the mean potential may have smaller finite size effects. Following this, the CCSD method is used to account for the electronic correlation energy to improve the HF TDL estimate for the total energy. When accounting for the electronic correlation in the TDL estimates for the total energy, we find agreement between the mean potential and probe-charge potential.

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Theoretical Investigation of Mutation-Induced Changes in the Optical Response of the FMO Pigment-Protein Complex

Richmond Arhin[1], Sergei Savikhin[2], Lyudmila Slipchenko[1].

[1]Purdue University, Department of Chemistry, West Lafayette, Indiana 47906, USA
[2]Purdue University, Department of Physics and Astronomy, West Lafayette, Indiana 47906, USA

Pigment-protein complexes involved in light harvesting, such as the Fenna-Matthews-Olson (FMO) protein complex of green sulfur bacteria, are renowned for their near-perfect quantum efficiency in capturing sunlight and transferring excitation energy to the reaction center (RC). This remarkable occurrence in nature has been ascribed to evolutionary-optimized protein scaffolds that tune the intrinsic electronic properties of the individual pigments and couplings between them. However, the overlapping electronic absorptions of numerous pigments that make up the structure of photosynthetic complexes often lead to ambiguity in interpreting spectroscopic signatures, thus complicating our understanding of individual molecular interactions contributing to efficient energy transfer in these complexes.

Introducing point mutations, i.e., changes in protein amino acid sequence, is an established way of tracking the effects of the protein environment on the dynamics of the excitation energy transfer process. On par with experimental spectroscopic studies, computational molecular modeling is utilized to develop accurate correlations between structure and function in photosynthetic complexes. Our previous work demonstrated that quantum mechanics/effective fragment potentials (QM/EFP) models can accurately describe the absorption and circular dichroism spectra of the FMO complex and its mutants. In this study, we aim to create an efficient computational pipeline for predicting the effects of mutations on the optical spectroscopy of photosynthetic pigment complexes, using the FMO complex as a test case. The developed workflow will be utilized for the rational design of mutations with targeted effects on optical spectroscopy and energy transfer pathways in protein-pigment complexes.

Toward Rational Design of Electrochromic Polymer Systems

Shameera Badalge and Lyudmila V. Slipchenko

Department of Chemistry, Purdue University, West Lafayette, Indiana 47907,
USA.

Electrochromic polymers, which change color in response to an applied electric potential, have a wide range of uses, including smart windows and displays. The complex interactions between electrolytes and electrochromic polymers are critical to the functionality of electrochromic devices. The electrolyte used in electrochromic devices significantly impacts the color modulation of electrochromic polymers, as it tunes optical properties by providing local electric fields, facilitates ion transport, and maintains charge balance. Ion trapping in electrochromic polymers refers to the capture and retention of ions within the polymer matrix during electrochemical processes. This process is crucial for optimizing the performance of electrochromic devices, as it directly affects the material's color change dynamics and switching speed. Gaining a deeper insight into the mechanisms underlying ion transport and trapping is essential for the development of more efficient and responsive electrochromic materials.

To address the challenges associated with understanding the interaction between electrochromic polymers and electrolytes at the molecular level, we employ a combination of molecular dynamics simulations and polarizable QM/MM modeling using the effective fragment potential method. Molecular dynamics simulations are used to probe the distribution and diffusion of ions as a function of the oxidative state of the polymer. The UV-Vis spectra of the polymer in the oxidized and reduced states are computed with the polarizable QM/MM that explicitly takes into account interactions of the polymer with a heterogeneous environment. Our initial system of study is composed of the polymer containing carbazole (CBZ) and three thiophenes (T_3) in dichloromethane (DCM) solvent and Tetrabutylammonium hexafluorophosphate ($TBAPF_6$) electrolyte, for which detailed experimental information is available. Following the validation of our approach, we intend to extend this methodology to a broader range of synthesized electrochromic polymers and contribute to the rational design of electrochromic devices to enhance efficiency and operational lifespan.

Developing a Single Twist Angle Selection Method to Calculate the Binding Energy for 2D Materials

Ryan A. Baker[1], William Z. Van Benschoten[1], and James J. Shepherd[1]

[1]Michigan State University, Department of Chemistry, East Lansing, MI

Previous work developed the structure factor twist averaging (sfTA) approach for 3D bulk solids[1]. The sfTA approach uses the transition structure factor (TSF), which relates electronic correlation in solids to the coupled cluster singles and doubles (CCSD) cluster operator, to achieve twist-averaged (TA) CCSD-level accuracy at a reduced cost. The cost for the sfTA method is approximately a single CCSD calculation, whereas the traditional TA approach requires 100 (or more) CCSD calculations, incurring a proportional cost increase[1]. In this work we develop the sfTA method for treating 2D bulk solids. This allows us to calculate TA-level interlayer binding energies for real bilayer materials with various compositions at a reduced computational cost like the original sfTA method. This is accomplished by defining a binding TSF analogous to the original TSF, which relates the change in the electronic structure between a monolayer and a corresponding bilayer (two stacked monolayers). We compare the binding energies for the sfTA, binding sfTA, and TA methods in addition to a common single calculation approach referred to as Γ- point. We observe that our method generally has better agreement with TA for the calculated binding energy compared to Γ-point, which is consistent with the observations found in the original sfTA work. Additionally, we explore the binding energy landscape for binding sfTA as a function of the twist angle offset and observe that twist-angle-dependent patterns in the binding correlation energy are different from the lone mono- and bilayers.

This work was supported by the NSF under grant CHE-2526433. Computational resources were provided by the University of Iowa and Michigan State University.

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Mechanistic study of propene metathesis on heterogenous catalyst

Shreyaa Brahmachari[1] and Marco Caricato[1]

[1]Department of Chemistry, University of Kansas, 1567 Irving Hill Road, Lawrence, Kansas 66045, United States

The growing scarcity of propene, a critical feedstock in the petrochemical and polymer industries, has spurred interest in its production via olefin metathesis—a reaction mechanistically opposite to the Phillips-Triolefin Process. An important issue that hinders progress in this direction is the limited understanding of the reaction mechanism by the tungsten oxide on silica catalyst. This is due to the structural complexity of the amorphous support, which correlates with the activity of the sites. In this work, we employ density functional theory (DFT) calculations on cluster models of WO_2- doped amorphous silica to elucidate the complete mechanism of propene metathesis and provide structures and energetics of transition states and metallacyclobutane intermediates. We focus first on the activation stage, where the $W(=O)_2$ site reacts with 2-butene via a [2+2] cycloaddition to form a metallacyclobutane intermediate. This intermediate subsequently undergoes cyclo-reversion to generate a catalytically active tungsten-carbene species, which has energy higher than that of the starting materials. This is consistent with the experimental data that the active metal-carbene is transient and readily proceeds into the propagation stage. Furthermore, we investigate the energy barriers of the propagation cycle to form propene. The results show that the propagation cycle proceeds kinetically faster than the activation stage and follows the Herrison and Chauvin metathesis mechanism. We also want to design potentially better catalysts than the original WO_2 - silica catalyst by introducing activity promoters. Ongoing work is focused on elucidating the same reaction mechanism on this bimetallic catalyst and evaluate the role of the secondary metal in the enhancement of the catalytic activity.

Ab Initio Prediction of T_1 for a Spin-1 Molecular Qubit

Matthew Brauser, Philip Shushkov

Indiana University

The mechanisms of spin relaxation in spin-1 molecular qubits via vibrational modes remain incompletely understood. Ab initio methods for predicting spin relaxation times, including T_1, will provide insight into the phonon modes and processes most responsible for relaxation. Understanding these mechanisms will enable the rational design of qubits with improved coherence times. In this work, we demonstrate that by performing crystal lattice relaxation and calculating the derivatives of the *g*-, *D*-, and *f*-tensors, we can predict T_1 times for $Cr(o\text{-}tolyl)_4$ with reasonable accuracy compared to experimental values.

Kohn Sham decomposition of Excited States of Ag Nanowires

Jonathan T. Bvunzawabaya and Christine Aikens

Department of Chemistry, Kansas State University, Manhattan, KS 66506, USA

The Kohn-Sham (KS) decomposition of excited states in silver (Ag) nanoclusters and nanowires is achieved using components of normalized Casida eigenvectors derived from linear-response calculations. By leveraging the linear response of the real part of the KS density matrix and photoabsorption cross-sections from real-time time-dependent density functional theory (RT-TDDFT), this study reconstructs Casida-like eigenvectors and transition contributions. Previous work validated this approach for small benzene derivatives, demonstrating reliable agreement between RT-TDDFT and linear-response TDDFT (LR-TDDFT). Here, we rigorously test the method on Ag nanowires of varying sizes (Ag_4, Ag_6, and Ag_8). For this we carried out LR-TDDFT and RT-TDDFT calculations using the GPAW code at pvalence.dz/PBE level of theory. Results show that the approach consistently ranks prominent transitions across all nanowire sizes in agreement with the Casida method. Quantitative agreement (relative errors <0.10) is observed for dominant longitudinal and transverse transitions in smaller nanowires (Ag_4 and Ag_6). However, larger nanowires (Ag_8) exhibit significant discrepancies, with relative errors of ~0.25–0.35. This study demonstrates that RT-TDDFT-derived KS decompositions can qualitatively rank prominent transitions that contribute to excited states and optical response of Ag nanowires.

Constrained Nuclear-Electronic Orbital Density Functional Theory with Periodic Boundary Conditions: Nuclear Quantum Effects in Surface Hydrogen Dynamics

Zehua Chen[1], and Yang Yang[1]

[1]University of Wisconsin-Madison

We present an implementation of constrained nuclear-electronic orbital density functional theory (CNEO-DFT) with periodic boundary conditions, enabling quantum mechanical treatment of both electrons and select nuclei. Using the Gaussian-augmented plane wave framework in CP2K, we achieve computational cost comparable to conventional DFT. The position constraint on quantum nuclear densities establishes an energy surface that naturally incorporates nuclear quantum effects. The implementation includes analytic gradients for both classical nuclear coordinates and quantum nuclear expectation positions. For hydrogen on Pt(111), conventional DFT incorrectly predicts atop site as the most stable position, while both CNEO-DFT and DFT with perpendicular harmonic zero-point energy corrections identify the fcc hollow site as energetically favorable, highlighting the importance of nuclear quantum effects in determining correct adsorption geometries. Through calculations of differential H adsorption entropy on Pt(111), we find that at catalytically relevant temperatures, CNEO-DFT predicts entropy values that deviate from quantum results by only 0.2 J/mol/K, compared to classical deviations of 1.0 J/mol/K. At room temperature, CNEO-DFT captures half of the 5 J/mol/K deviation between classical and quantum results. This implementation enables efficient inclusion of nuclear quantum effects in periodic systems and is particularly valuable for studying hydrogen-containing materials.

Quasidegenerate Multireference Perturbation Theory for Accurate Simulations of Magnetic Properties

Nicholas Yiching Chiang[1], Alexander Yu. Sokolov[1]

[1] Department of Chemistry and Biochemistry, The Ohio State University, Columbus, Ohio 43210, United States

Theoretical studies of magnetic properties play a crucial role in advancing quantum technologies, including single-molecule magnets (SMMs) and quantum computing. Among these properties, the g-tensor offers valuable insights into the magnetic behavior of molecules, aiding in the design of promising materials for magnetic applications. In this work, we implement second-order quasidegenerate N-electron valence perturbation theory (QDNEVPT2) using the Breit–Pauli (BP) and exact two-component Douglas–Kroll–Hess (DKH) spin–orbit Hamiltonians for g-tensor calculations. We find that both BP and DKH Hamiltonians yield accurate results for molecules containing fourth- and fifth-period elements. However, only the DKH Hamiltonian provides reliable results for molecules containing sixth-period elements.

How Oligomers Govern the Cationic Polymerization of Phthalaldehyde

Elizabeth A. Doty[1], Anne J. McNeil[2], and Paul M. Zimmerman[3]

[1]University of Michigan
[2]University of Michigan
[3]University of Michigan

Phthalaldehyde is cationically polymerized into a macrocyclic polymer, cyclic poly(phthalaldehyde) (cPPA), via ring-expansion polymerization. We have uncovered experimental evidence for an oligomer of phthalaldehyde being produced during cationic polymerization. Herein we use kinetic models and density functional theory simulations to discern the mechanism for polymerization and the role of oligomer. The resulting model indicates that phthalaldehyde oligomer can reversibly backbite off from developing polymer chains. This work will provide new evidence that backbiting is crucial in producing oligomers in ring-expansion polymerizations, and that the reversibility of the backbiting process leads to the production of oligomer in tandem with polymer under polymerization conditions.

Evaluation of Diffuse Basis Sets for Simulations of Strong Field Ionization Using Time-Dependent Configuration Interaction with a Complex Absorbing Potential

Andrew Durden[1], H. Bernhard Schlegel[1]

[1]Wayne State University

Strong field ionization (SFI) can be modeled using Time-Dependent Configuration Interaction with a Complex Absorbing Potential (TDCI-CAP) on an atom-centered Gaussian basis set. Typical molecular basis sets are insufficient to describe the diffuse bound and continuum states that arise from the system's interaction with the strong field and absorbing potential. It is well known that diffuse Gaussians with even-tempered exponents (of the form 0.0001×2^n) are able to efficiently represent Rydberg and continuum states. In this work, we compare TDCI-CAP simulations of SFI across several molecules, with a range of absorbing bases that consist of aug-cc-pVTZ combined with various sets of even-tempered diffuse functions. To gain a rigorous understanding of the basis set effects for various exponents and angular momenta, we construct a hierarchy of absorbing basis sets by starting with a minimal set and adding one or two basis functions at a time. In single-centered cases we show that orbitals which lie close to the start of the absorbing potential contribute most to the ionization rate, but more diffuse exponents (0.0032, 0.0032, 0.0064, and 0.0064, for s, p, d, and f, respectively) are necessary to reproduce the shape of the angular dependence of SFI. We also show that in several cases (CO_2, SO_2), it is necessary for the tightest absorbing basis functions to meet the most diffuse molecular basis functions -- In other words, sensitive systems require there be no gaps in the series of even-tempered exponents from the valence into the Rydberg region. For systems with multiple heavy atoms, it is necessary to place the absorbing basis on all heavy atom centers. Such systems often exhibit extreme linear dependency issues, since very diffuse orbitals offset by a couple of angstroms have large overlap. To ameliorate linear dependency issues we introduce a scheme where diffuse orbitals with the same exponent on different atomic centers are contracted into a single "atomic orbital" basis function. In addition to mitigating linear dependencies, this scheme also decreases the cost of the calculation by reducing the number of molecular orbitals in the CI expansion. We compare TDCI-CAP simulations using this new contraction scheme with simulations that place the absorbing basis on all centers or at the centroid to demonstrate that the scheme is well-behaved in both small and elongated molecular systems.

Excited State Density: A Computational Investigation of the Δ-SCF Approach

Srijita Dutta[1] and Paul Zimmerman[1]
[1]Department of Chemistry, University of Michigan, Ann Arbor. MI, United States

Density Functional Theory and time dependent DFT (TDDFT) can simulate a wide range of interesting chemical and materials properties. The Delta Self-Consistent Field (Δ-SCF) method[1] sits somewhere between the two approaches, where excited states are treated in a simpler fashion than in TDDFT. Δ-SCF creates a non-Aufbau excited-state solution to the Kohn-Sham equations to model doubly excited state energies[2], core-electron spectroscopy and nonadiabatic molecular dynamics. While most studies of Δ-SCF have concentrated on excited-state energies, electron density also plays an integral role in influencing transition dipole moments, exciton localization and reactivity. In this work, we investigate the quality of excited-state electron densities obtained from Δ-SCF in comparison to a wave-function based method: Heat-Bath Configuration Interaction (HCI)[3]. An analysis of observed trends in relation to basis set size and exchange-correlation functional is presented.

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Quantum Nuclear Dynamics on a Distributed Set of Ion-Trap Quantum Computing Systems

Anurag Dwivedi[1], Phil Richerme[1], Srinivasan S. Iyengar[1]

[1]Indiana University Bloomington

Quantum nuclear dynamics plays a crucial role in understanding chemical reactions, biological processes, and material properties. However, accurately simulating their properties and spectra remains a significant computational challenge due to the exponentially growing complexity with system size, limiting our ability to precisely model realistic molecular system. Quantum computers, capable of naturally encoding and processing quantum states, hold great potential for overcoming these limitations.

In this work, we leverage IonQ Inc.'s 11-qubit trapped-ion quantum computer, Harmony, to study the quantum nuclear dynamics of a shared proton in a short, strong hydrogen-bonded system. We further demonstrate the first application of distributed quantum computing for chemical dynamics, employing a tensor network formalism to orchestrate computations across multiple quantum processors. For a range of initial quantum states, we experimentally drive the ion-trap system to emulate the evolution of the quantum nuclear wavepacket along a potential energy surface derived from electronic structure calculations. Following the preparation of the nuclear wavepacket, we extract observables such as the time-dependent spatial projections and characteristic vibrational frequencies, achieving good agreement with classical results. Vibrational eigenenergies obtained from quantum computations match those from classical simulations to within a fraction of a kilocalorie per mole, demonstrating chemical accuracy.

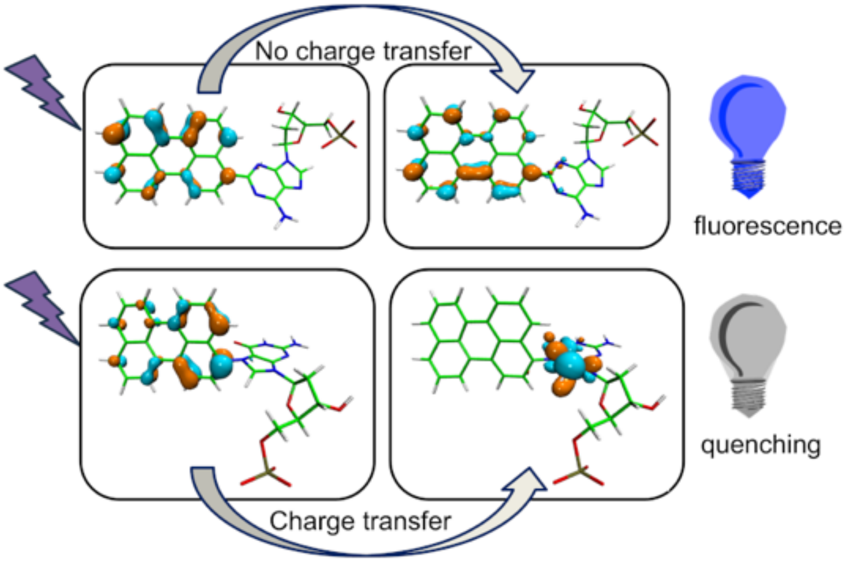
Controlling Fluorescence in DNA Probes: Structural Design of Perylene-Modified Nucleic Acids for Enhanced Imaging

Solomon Y. Effah, Mark A. Hix, Alice R. Walker

Department of Chemistry, Wayne State University, Detroit, Michigan 48202, United States

ABSTRACT

Real-time visualization of DNA replication is crucial for understanding cellular processes and developing targeted cancer therapeutics, yet designing effective fluorescent probes remains challenging. Our research combines state-of-the-art computational approaches to unravel the fundamental principles governing fluorescent DNA probe design. Using excited-state QM/MM dynamics with TDDFT (ωPBE functional) and classical molecular dynamics, we systematically investigated perylene-modified nucleotides across multiple attachment positions and nucleobases. We discovered that fluorescence properties are exquisitely sensitive to geometric factors - specifically, a critical 90° dihedral angle between perylene and nucleobase that triggers rapid fluorescence quenching through charge transfer pathways. This understanding enabled us to strategically control probe brightness through structural modifications. We demonstrate that phosphate groups stabilize excited states and reduce unwanted charge transfer, while ethynylene linkers maintain high fluorescence by restricting conformational flexibility. Remarkably, adenine-based probes exhibit superior stability compared to guanine derivatives, where attachment position dramatically influences photophysical properties. These insights provide clear design principles for developing next-generation fluorescent probes with optimized properties for biological imaging. Our computational framework not only advances fundamental photophysics but also accelerates the development of practical tools for studying DNA replication in cancer research and drug discovery. This work exemplifies how theoretical chemistry can drive innovations in biological imaging and disease research.



Optical Spectra Prediction of Water-Soluble Chlorophyll Proteins (WSCP)

Michael Eyeson[1], Andres Urbina[1] and Lyudmila Slipchenko [1]
[1]Department of Chemistry, Purdue University, 560 Oval Drive, West Lafayette, IN 47906.

A significant barrier to reprogramming the energy harvesting apparatus of photosynthetic plants and bacteria in order to increase their photosynthetic efficiency is the limited understanding of how protein structure depicts optical properties and energy transfer. Pigment-protein complexes (PPCs), the drivers of biological photosynthesis, absorb sunlight and transfer energy to reaction centers, facilitating chemical energy conversion and storage. Although the structures of chlorophyll-containing proteins are well characterized, accurately predicting their optical and electronic properties remains difficult due to the complexity of modeling large, electronically coupled pigments within a dynamically fluctuating protein environment. To this end, we apply computational techniques to predict the optical spectra of wild-type and site-mutated water-soluble chlorophyll protein (WSCP) variants. Our methodology combines molecular dynamics simulations, quantum mechanics/molecular mechanics (QM/MM) calculations, and Effective Fragment Potential (EFP) approaches. Our work aims to uncover how the surrounding protein environment influences chlorophyll's optical properties, providing new insights into energy transfer processes in PPCs and guiding strategies for improving bioenergy efficiency.

First Principles Simulations of Optical Rotation of Chiral Molecular Crystals

Emmanuel Forson[1], Taylor Parson[1], and Marco Caricato[1]

[1]University of Kansas

In this work, we present simulations of the optical rotation (OR) for five molecular crystals at density functional theory level with periodic boundary conditions (DFT-PBC). Calculations are compared with experimental measurements and show semi-quantitative agreement with experimental data for three of the crystals: tartatic acid, benzil, and pentaerythritol. For the other two crystals, aspartic acid and glutamic acid, the experimental data are two orders of magnitude larger than the calculated data. We provide some arguments that support the theoretical predictions and suggest that the experiments should be revisited. We also find that the position of H centers provided in experimental X-ray data is not sufficiently reliable for simulating OR, and better results are obtained when H atoms are allowed to relax while keeping heavier elements fixed at the experimental positions. Comparison with molecular cluster calculations with a better functional and a larger basis set indicate that the role of intermolecular interactions (reproduced with the PBC technique) are as or more important than the choice of model chemistry. Despite the current limitations in the level of theory that can be employed, these simulations provide a promising avenue to investigate the effect of intermolecular interactions on this sensitive electronic property of molecules and materials.

Abstract

Accelerating GW/BSE Calculations through Deep Generative Modeling of the Dielectric Eigenbasis

Joseph Frimpong[1], Jiawei Zhan[2], Victor Yu[1], Marco Govoni[3], Giulia Galli[1,2], Maria Chan[1]

[1] Argonne National Laboratory
[2] University of Chicago
[3] University of Modena and Reggio Emilia

Accurate prediction of excited-state electronic properties is pivotal for designing advanced optoelectronic and energy storage materials, but remains computationally prohibitive for large nanoscale systems due to the high cost of GW calculations. The Projective Dielectric Eigenpotential (PDEP) method, implemented in the WEST code, partially alleviates this bottleneck by circumventing explicit summation over virtual states. However, expensive iterative diagonalization is still required to obtain PDEPs. We present a novel machine learning-accelerated approach integrating deep generative models, specifically Variational Autoencoders (VAEs), with equivariant neural networks to predict PDEP eigenpotentials directly from atomic structures. Our method compresses high-dimensional PDEP data into a low-dimensional latent space and trains neural networks to map atomic configurations to this latent representation, enabling rapid reconstruction of the full eigenpotentials. Preliminary results on SiF_4 demonstrate the feasibility of this approach, with anticipated computational speedups of 10 times compared to conventional workflows. This acceleration will allow for accurate excited-state calculations, significantly advancing the exploration and design of next-generation nanoscale materials for semiconductor, photovoltaic, and quantum device applications.

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Simulations of Excited-State Dynamics of mStayGold

A.G Pramoda Sahan Kumari[1], and Alice Walker[1]

[1]Wayne State University

mStayGold is uniquely bright and photostable, with an excellent fluorescence quantum yield of 0.94. However, the relationship between protein and chromophore structure to these desirable features is not completely understood. We have applied SA-α-CASSCF to investigate the structure-function relationship of mStayGold on the first and second singlet excited states (S1 and S2) as compared to the ground state (S0). The excited state dynamics reveal significant dynamic conformational changes and possible state mixing. Interestingly, we find that the vertical S0□S1 transition has the dominant state contribution only 20% of the time, with significant contributions in the excited state dynamics appearing from S2□S1 and S2□S0 80% of the time. These findings suggest that the multireference character of the chromophore is enhanced in mStayGold, potentially explaining its unusual photostability.

LoA: An Extensible LLM-based Chemical Data Extraction Pipeline

M.F. Grougan[1], Mark A. Hix[1], Alice R. Walker[1]

[1]Wayne State University

Dataset creation is the backbone of all predictive machine learning technology. In the field of chemistry, large datasets of experimental data are scarce, especially for niche chemical properties and topics. In addition, creating these datasets is cumbersome and time-consuming. In this paper, we present an automatic tool for generation of such datasets via direct extraction by large-language models (LLM) from chemical literature. The tool utilizes two LLMs, one first to check if a research paper is relevant to the extraction task, and the other to perform the extraction when relevant. The tool is modular in that the specific LLM used is up to the user. The tool is also future proof because it can update itself via easy user incorporation of the newest available LLMs. To aid in the usage of the presented tool, we also tested and compared several LLMs for both roles. The process of gathering research papers is also automated for several popular chemical journals that offer open access. As such, we present a means by which enormous chemical datasets can be created with minimal effort and ∼80% accuracy for the purposes of training predictive machine learning models.

Automated SAPT/EFP workflow for accurate prediction of crystal lattice energies

Crystal structure prediction, the process of identifying the low-energy crystal structure of a molecule is one of the most challenging problems in computational chemistry to date. Assessing the stability of different crystallographic forms or polymorphs under given experimental conditions is crucial for the pharmaceutical industry, as it aids in maintaining strict property control. Therefore, the demand for computational techniques capable of predicting low-energy crystal structure(s) given only the molecular geometry and experimental conditions, is high.

Reliable prediction of crystal lattice energies of different polymorphs requires an accurate description of non-covalent interactions. Among those, short-range charge-penetration effects, long-range electrostatics, dispersion forces, and many-body effects are prone to computational inaccuracies depending on the chosen molecular modeling methodology. Sherrill and co-workers [J. Chem. Phys. **157**, 084503 (2022)] have previously studied the distance dependence of pairwise non-covalent interaction energies in the X23 dataset of molecular crystals using symmetry-adapted perturbation theory (SAPT). Despite the potentially high accuracy of many-body expansion methods, the computational cost remains prohibitively high for practical use in industry. We have utilized the effective fragment potential (EFP) method to compute the interaction energies in the X23 dataset and found that EFP accurately reproduces SAPT energies at medium and larger separation distances between interacting dimers. We have also inferred useful connections between convergence rates of EFP-SAPT discrepancies in crystal lattice energy components and chemical properties of the studied systems. Based on our results for the X23 dataset, we are designing a computationally efficient workflow incorporating the SAPT/EFP scheme for accurate calculation of lattice energies with the objective of applying it to drug molecules of interest to the pharmaceutical industry.

Automated Generation of Large-scale Biomolecular Datasets for Machine Learning

Mark A. Hix[1] and Alice R. Walker[1]

[1]Wayne State University, Detroit, MI, United States

Machine learning has arisen in recent years as a powerful tool for computational biochemists, enabling the identification of important characteristics in biomolecular systems, prediction of effects of modifications, and proposition of new molecules in pursuit of desired physical properties. However, a machine learning model can only be as good as the dataset upon which it was built. Therefore, it is critical to ongoing efforts to build consistent, high-quality, and large datasets. While an individual researcher may be able to produce high-quality simulations on a single system, and with care maintain consistency and uniformity when working on multiple systems, the scale necessary is intractable without automation. Here we present a set of tools in an automated workflow which can produce biomolecular simulation data at a scale which is presently limited only by available storage capacity, and is consistent and high quality. These tools are used to generate simulations of fluorescent proteins with varied chromophores along with calculated photophysical properties such as absorption and emission wavelengths.

In-silico Investigation of PFAS Influence on Nuclear Receptors

Deepak James[1], Narasimhan Loganathan[1], Jason Thieu[1], and Angela K. Wilson[1]

[1] Department of Chemistry, Michigan State University, East Lansing, 48824 MI

Per- and polyfluoroalkyl substances (PFAS) are a group of highly persistent, man-made chemicals used in numerous industrial and consumer applications for more than five decades. Among many PFAS compounds, the legacy PFAS molecules namely perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) are widely detected in the environment, breast milk, and blood. Because of the strong C-F bond, these compounds are non-biodegradable and their long half-life in humans could result in various toxicity effects in humans, including neurotoxicity, developmental toxicity, and hepatoxicity. At a molecular level, these toxicities are observed due to the activation of ligand induced nuclear receptors (NR) via PFAS. NR are a class of proteins that play a broad range of roles in cell differentiation/development, proliferation, metabolism, and the dysregulation of these receptors cause various conditions such as cancer, dyslipidemia, fertility issues and, hepatocarcinogenesis. Despite the valuable insights from experiments on the behavior of PFAS in NR, in-depth knowledge of the important residual interaction with PFAS is still poorly understood. The presentation will be focused on providing fundamental understanding of the influence of PFAS with NR protein classes using molecular docking and classical molecular dynamics simulations. The work will identify key residues responsible for the activation of NR and provide insights how PFAS can disrupt the xenobiotic metabolism.

Advanced Insights into Non-Adiabatic Dynamics and Ring-Opening Mechanisms of Oxazole and Isoxazole

Paul Javed[1], Briony Downes-ward[3], Arthur G. Suits[3], Daniel Rolles[2], Christine M. Aikens[1]

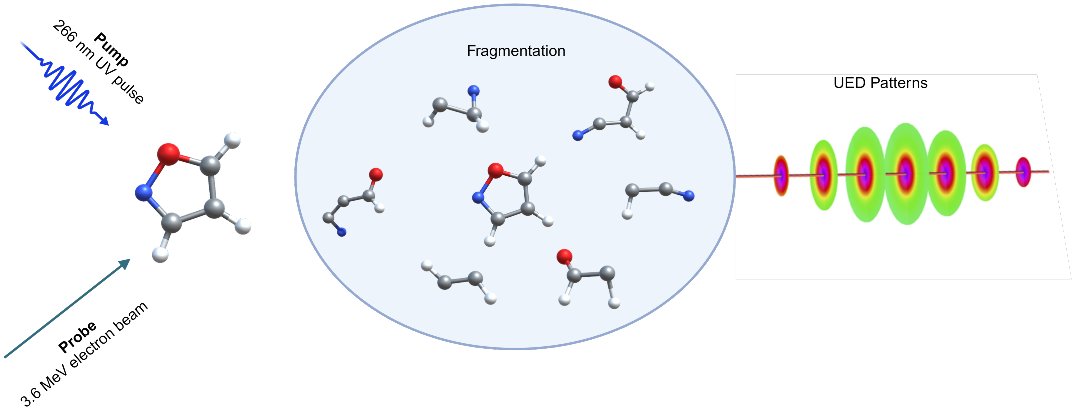
[1] Department of Chemistry, Kansas State University, Manhattan, KS 66506, USA

[2] Department of Physics, Kansas State University, Manhattan, KS 66506, USA

[3] Department of Chemistry, University of Missouri, Columbia, MO 65211, USA

This study aims to investigate the photoinduced ring-opening dynamics in oxazole and isoxazole using ab initio non-adiabatic molecular dynamics simulations. Employing the State-Averaged CASSCF (12,10)/aug-cc-pVDZ level of theory, we explored the excited-state dynamics using the trajectory surface hopping and explored the ring-opening mechanisms of these heterocyclic compounds. Initial conditions were generated using Wigner sampling, and trajectories were propagated for up to 1,000 fs. Our results reveal distinct photochemical behaviors for oxazole and isoxazole: in isoxazole, we observed O–N bond breaking within an average time of 41.46 fs, predominantly through the $S_2 \rightarrow S_1 \rightarrow S_0$ relaxation pathway, while in oxazole significant C–O bond elongation with substantial geometric changes and ring puckering were noted, particularly at S_1/S_0 crossing points. Conical Intersections were characterized to quantifying trajectory bifurcation into distinct photoproduct channels; detailed time evolution of geometric features (azirine, bicyclic ring, and nitrile ylide) and fragments was also done. We tracked bond lengths, ring-puckering angles, to reveal metastable conformers. Moreover, direct UED comparison via simulated diffraction patterns from time-resolved snapshots was performed to validate predicted ring-opening timescales and geometric distortions against experimental ultrafast electron diffraction data. The comprehensive insights into population dynamics, quantum amplitudes, branching ratios, and photoproduct channels—enhanced by machine-learning classifiers to automate photoproduct identification and predict branching ratios based on early-time geometric descriptors—not only deepen our understanding of five-membered heterocycle photochemistry but also have significant implications for the rational design of photoactive materials and photochemical synthesis strategies.

Graphical Abstract:



Bound charge layering near ions in water: Moving beyond Born theory

Kasun Gamage[1] Min-Sang[1] Sherwin Singer[1]

The Ohio State University, United States.[1]

gamage.7@osu.edu[1]

Abstract - This work analyzes the response of aqueous solvent to a dissolved spherical ion in terms of the bound charge, the net charge of the solvent near the solute. This provides an alternative to the standard Born continuum theory which assumes that the ion lies in a spherical cavity within a dielectric continuum and places the bound charge in an infinitely thin layer on the cavity surface. For a spherical ion, the cavity radius should be close to the distance of closest approach of solvent to the ion. However, when regarded as an adjustable parameter required to align theoretical and experimental solvation free energies, the required cavity radius is unexpectedly small and resides within the ion's excluded volume. This challenges the physical basis of Born's theory and highlights the need for a solvation model that produce "the right answer for right reason". We prove that the total bound charge surrounding an ion is equal to the bound charge of a dielectric continuum, thus providing a useful constraint on solvation models. Unlike continuum theory the true bound charge has a well-organized structure of strongly oscillating layers of counter- and co-charge, that is, layers of opposite and the same charge, which is essential for explaining the strong solvation response of aqueous solvent. Moving beyond the spherical ion, we report preliminary steps to develop simple analytical models based on molecular reality that can replace the continuum theory for the solvation response of polyatomic solutes.

Keywords: Ion Solvation, Born Theory, Dielectric response, Electrostatics

Misfolding with entanglements explains decades-old stretched protein folding kinetics

Yang Jiang[1], Yingzi Xia[2], Ian Sitarik[1], Piyoosh Sharma[2], Hyebin Song[3, 4], Stephen D. Fried[2, 5] *, Edward P. O'Brien[1, 3, 6] *

1. Department of Chemistry, Pennsylvania State University, University Park, PA 16802, USA
2. Department of Chemistry, Johns Hopkins University, Baltimore, MD 21218, USA
3. Bioinformatics and Genomics Graduate Program, The Huck Institutes of the Life Sciences, Pennsylvania State University, University Park, PA 16802, USA
4. Department of Statistics, Pennsylvania State University, University Park, PA 16802, USA
5. Thomas C. Jenkins Department of Biophysics, Johns Hopkins University, Baltimore, MD 21218, USA
6. Institute for Computational and Data Sciences, Pennsylvania State University, University Park, PA 16802, USA

The thermodynamic and kinetic origins of stretched-exponential protein folding kinetics has been understood for decades. What remains unknown is the structural origins of this class of kinetics, specifically, the nature of the non-native ensembles of structures and how they give rise to the large free energy barriers that partition the energy landscape into parallel, non-interconverting folding pathways. Here, we address this unresolved question using a combination of simulations and limited proteolysis (LiP) and cross-linking (XL) mass spectrometry (MS), applied to the protein phosphoglycerate kinase (PGK) from *S. cerevisiae* and *E. coli*. We first show that the simulation model recapitulates the experimental observation that this protein exhibits stretched-exponential kinetics. We then demonstrate that the folding pathways that give rise to this class of kinetics are misfolded states involving a change of entanglement status: either forming a non-native, non-covalent lasso entanglement, or failing-to-form a native entanglement, which is also kinetic trap that the protein must backout of by losing some of its native structure. Using MS, we show that for *E. coli* PGK some of these misfolded states are long lived kinetic traps, persisting two hours after folding conditions have been re-established through a denaturant-dilution jump. Cross-referencing our simulation structures to the LiP-MS and XL-MS data, we propose misfolded structural ensembles that are consistent with these data. The resulting ensembles are heterogeneous, with gains and losses of entanglements in different regions along PGK's primary structure. The free energy barriers separating these alternative misfolded states arise from already folded portions of the primary structure that must unfolded out of these misfolded states. This heterogeneity of misfolded states and barrier heights leads to a hierarchy of timescales described by a power-law distribution called a stretched exponential function. Thus, these results suggest that this class of protein misfolding can explain the origin of stretched-exponential folding kinetics.

Simulations of mGrape: Mechanistic Understanding of Red-to-Green Emission Shifts in Chloride Sensing

Widana Kaushalya, Alice R. Walker

Wayne State University

Fluorescent proteins are vital tools in biological imaging, with red fluorescent proteins (RFPs) being particularly advantageous for deep-tissue imaging due to their greater penetration depth and reduced phototoxicity. However, there are few available RFP chloride sensors. Our collaborators introduced key amino acid mutations to the RFP mGrape that provide chloride sensitivity, but also induce a fluorescence emission shift from red to green. To gain a deeper understanding of its photophysical properties and fluorescence behavior, particularly the color tuning from red to green, we apply classical force field molecular dynamics and excited-state QM/MM Born-Oppenheimer dynamics simulations to characterize its excited-state behavior. Our computational study reveals that water-mediated hydrogen bonds and π-π stacking interactions are critical for the red fluorescence observed in wild-type mGrape. In the mutated system, the absence of these interactions results in the loss of red emission and the enhancement of green fluorescence, effectively converting the mutant into a green chloride-sensitive sensor without directly modifying the chemical structure of the chromophore. These findings not only advance the rational design of optimized fluorescent chloride sensors but also offer broader insights into designing new red fluorescent proteins.

Bridging Wavefunctions and Density Functionals: Unlocking Accurate Data for Functional Development

Vaibhav Khanna[1], Bikash Kanungo[2], Jeffrey Hatch[1], Joshua Kammeraad[1] and Paul M. Zimmerman[1]

[1]Department of Chemistry, University of Michigan, Ann Arbor, MI, United States
[2]Department of Mechanical Engineering, University of Michigan, Ann Arbor, MI, United States

Density Functional Theory (DFT) is one of the most widely used electronic structure methods in chemistry, physics, and materials science, striking a balance between accuracy and computational efficiency. However, its accuracy is fundamentally limited by the choice of the exchange-correlation (XC) functional, which remains an approximation in all practical applications. A key shortcoming of existing functionals is their failure to reproduce critical features of the exact XC potential, such as the asymptotic -1/r decay and the step at integer electron transitions—features essential for correctly describing ionization energies, band gaps, and dissociation limits. In this work, we take a data-driven approach to improving DFT by generating XC potentials from full configuration interaction (FCI) calculations. Using a large Slater basis, we systematically recover key features of the exact XC potential across atomic systems and analyze their behavior. Additionally, we compute exchange-correlation energy densities via an aufbau path integral, ensuring consistency with total XC energy values from FCI. These highly accurate DFT quantities establish a benchmark for diagnosing errors in existing functionals and guiding the development of new approximations that incorporate wavefunction-level accuracy while retaining DFT's efficiency.

Sequence-Based Determinants of Peptide Residence Time on a Class-B GPCR

Ceren Kilinc[1], Katie M. Babin[2], Augen A. Pioszak[2], Alex Dickson[1,3*]

[1]Department of Biochemistry and Molecular Biology, Michigan State University, Lansing, Michigan

[2]Department of Biochemistry and Physiology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma

[3]Department of Computational Mathematics, Science and Engineering, Michigan State University, Lansing, Michigan

The calcitonin receptor-like receptor (CLR), a class B G protein-coupled receptor (GPCR), is involved in diverse physiological processes including inflammatory responses, vascular regulation, and pain modulation. CLR forms functional complexes with three different Receptor Activity-Modifying Proteins (RAMP1-3) and the activities of CLR:RAMP complexes are regulated by the selective binding of hormones and neuropeptides, among which the calcitonin gene-related peptide (CGRP) plays a central role in pain signaling and migraine pathophysiology. In recent years, several small molecule and antibody therapeutics targeting CGRP signaling mechanisms have received FDA approval for migraine. Recently, Dr. Pioszak's laboratory has developed a "sustained signaling" variant of the CGRP peptide (called "ssCGRP") with four mutations in its extracellular domain (ECD)-binding fragment. ssCGRP shows long-duration cyclic AMP signaling on the CGRP receptor (CLR:RAMP1) and different segments of the peptide have shown potential to act as both potent agonists and antagonists. This is driven solely by improved binding affinity to the ECD of the CGRP receptor complex. However, the underlying dynamics that govern this slow unbinding rate remain poorly understood, yet are of the utmost importance for the design of new, more effective therapeutics not only for migraine but also for broader indications. Here, we use the weighted ensemble–based method Resampling of Ensembles by Variation Optimization (REVO) to generate unbinding trajectories of CGRP and ssCGRP bound to the CLR:RAMP1 ECD. We then constructed Markov State Models (MSMs) to investigate the unbinding pathways and residence times of both peptides. Experimental biolayer interferometry measurements in our study showed that ssCGRP exhibits a significantly slower off-rate and longer residence time than wild-type CGRP, and our computational approach provides a molecular-level explanation for this difference. Our simulations reveal distinct unbinding pathways, with ssCGRP occupying more stable intermediate states and encountering higher kinetic barriers to dissociation. These findings demonstrate the power of enhanced

sampling approaches in elucidating unbinding pathways, defining the determinants of residence time, and offering valuable insights for peptide-based therapeutic design.

Kinetics Oriented Drug Design with MSλD+US

Thanh T. Lai[1] and Charles L. Brooks III[1,2]

[1]University of Michigan at Ann Arbor, Biophysics Program

[2]University of Michigan at Ann Arbor, Chemistry Department

Drug-target residence time can be a strong indicator of drug efficacy for certain protein targets and is governed by the free energy landscape the drug traverses during its unbinding process. However, rationally optimizing residence time is difficult as it requires an understanding of the ligand unbinding pathway and the interactions in the protein-ligand transition state. In this study, we develop a computational workflow to investigate ligand unbinding processes by combining random acceleration molecular dynamics (RAMD) and multisite λ dynamics + umbrella sampling (MSλD+US). In contrast to conventional umbrella sampling, MSλD+US facilitates the exploration of both configurational and chemical space, which is afforded coupling ligands of interest to a dynamical λ parameter. This workflow characterizes unbinding potentials of mean force, and the resulting free energy barriers are used to discriminate between ligands with residence times that differ by orders of magnitude. We test this workflow on an inhibitor dataset targeting the Human N-HSP90 protein, which contains small molecules with residence times spanning several orders of magnitude.

Practical Effective Fragment Potential: making polarizable QM/MM more accessible

Jack Lawrence[1], Lyudmila Slipchenko[1]

Purdue university[1]

The Effective Fragment Potential (EFP) method is an ab initio-based polarizable force field that offers a computationally efficient approach to modeling non-covalent interactions in heterogeneous molecular systems. EFP-based quantum mechanics/molecular mechanics (QM/EFP) models have been demonstrated to provide quantitative agreement with experimental observables in redox-active and photosynthetic proteins. Despite recent successes, preparing EFP or QM/EFP calculations for a new system is tedious and time-consuming even for an experienced user. This work provides a step-by-step guide to setting up QM/EFP excited state calculations for bacteriochlorophyll pigments in the Fenna-Matthews-Olson (FMO) protein, as well as instructions for extending the developed workflow for an arbitrary biological system. The tutorial addresses the logic and implementation of the main steps in preparing the QM/EFP job, including defining the QM region, system fragmentation, and EFP parameter generation. The workflow utilizes Python and Bash scripts as well as GROMACS, GAMESS, and Q-Chem software packages. This work aims to make the polarizable EFP method more accessible to researchers interested in modeling photochemistry in complex environments.

Evaluation of Gradients in the GW Method with the Resolution of Identity

Jianhao Li[1], Pavel Pokhilko[1], Chia-Nan Yeh[2], Miguel Morales[2], Dominika Zgid[1]

[1]University of Michigan, Ann Arbor, USA
[2]Flatiron Institute, New York, USA

Green’s function methods have become powerful tools in materials science and computational chemistry due to their reasonable accuracy and affordable computational cost. These methods are most commonly used for predicting ionization potential (IP) and electron affinity (EA) in molecules, fundamental band gap in solids and thermodynamic properties. However, the evaluation of gradients—essential for geometry optimization, vibrational analysis, and response properties such as magnetic dipole moments—has not yet been addressed in the existing Green’s function codes.

In Green's function theories, the grand potential can be expressed solely in terms of the finite-temperature one-particle Green’s function and self-energy. We demonstrate that gradients of the grand potential can be evaluated using the method of Lagrange multipliers. Additionally, to reduce the computational cost, the resolution of identity (RI) can be utilized to approximate two-electron integrals. In this case, the computational cost of the gradient evaluation scales as $O(N^4)$, where N is the number of orbitals in a molecule. Asymptotically, this computational scaling is the same as the parent scGW method, making the approach affordable for geometry optimization as well as evaluation of other response properties.

Out-of-distribution detection: exploring transition states in the hyperspherical latent space

Bojun Liu[1], Jordan G. Boysen[1], Ilona C. Unarta[1], Xuefeng Du[1], Yixuan Li[1], and Xuhui Huang[1]

[1]Department of Chemistry, University of Wisconsin−Madison, Madison, Wisconsin 53706, United States

Identifying transitional states is crucial for understanding protein conformational changes that underlie numerous biological processes. Markov state models (MSMs), built from Molecular Dynamics (MD) simulations, capture these dynamics through transitions among metastable conformational states, and have demonstrated success in studying protein conformational changes. However, MSMs face challenges in identifying transition states, as they partition MD conformations into discrete metastable states (or free energy minima), lacking description of transition states located at the free energy barriers. Here, we introduce Transition State identification via Dispersion and vAriational principle Regularized neural networks (TS-DAR), a deep learning framework inspired by out-of-distribution (OOD) detection in trustworthy artificial intelligence (AI). TS-DAR offers an end-to-end pipeline that can simultaneously detect all transition states between multiple free minima from MD simulations using the regularized hyperspherical embeddings in latent space. The key insight of TS-DAR lies in treating transition state structures as OOD data, recognizing that they are sparsely populated and exhibit a distributional shift from metastable states. We demonstrate the power of TS-DAR by applying it to a 2D potential, alanine dipeptide, and the translocation of a DNA motor protein on DNA, where it outperforms previous methods in identifying transition states.

Geometric Learning for Biological Kinetics

Zige Liu, University of Wisconsin-Madison

Geometric learning, a subfield of deep learning focused on non-Euclidean data, offers powerful tools for studying biological processes, including protein conformational change and molecule self-assembly. We introduce the application of invariant and equivariant graph neural networks (GNNs) to model the kinetics of these complex systems. By representing molecules as graphs, GNNs learn intricate relationships between conformations and elucidate their kinetic behaviors. Invariant GNNs capture crucial structural information, distinguishing each conformation according to its connectivity and preserving rotational invariance for symmetric systems. Equivariant GNNs admit positional information, enabling the modeling of vector quantities like forces and velocities, and preserving the underlying physical symmetries. Both frameworks can be integrated with VAMP or TSDar score to identify key transition states and dominant kinetic pathways. This geometric approach provides a robust framework for understanding and predicting biological kinetics, with potential applications in s drug discovery and molecular design.

BF-CMD: Centroid Molecular Dynamics Using Bead-Fourier Path-Integrals

Nathan London[1] and Mohammad R. Momeni[1]

[1]Division of Energy, Matter and Systems, School of Science and Engineering, University of Missouri—Kansas City

Nuclear quantum effects (NQEs) play a critical role in a number of chemical phenomena, including reaction rates and vibrational spectra, and therefore, their accurate incorporation in dynamical simulations is essential for creating a truly predictive theory. Propagating complex condensed phase and interfacial systems with thousands of degrees of freedom (DOFs) fully quantum mechanically with quantum nuclei is beyond current computational capabilities. Methods to efficiently and accurately incorporate NQEs into classical MD simulations are thus a key area of developmental focus. One particular branch of research is utilizing Feynman's path-integral (PI) formulation of quantum statistical mechanics. Methods based upon PI formulation, such as PIMD, centroid MD (CMD), and ring polymer MD (RPMD), extend classical MD simulations to include some NQEs like zero-point energy and quantum tunneling through introducing multiple "replicas" of the system connected with harmonic springs. The additional copies of the system retain a similar computational cost scaling to classical simulations, making PI methods attractive for large-scale simulations. An alternate PI formulation, bead-Fourier (BF) PIs, introduces fluctuations along the imaginary time path between replicas (known as "beads") through a Fourier series. The addition of the Fourier components reduces the number of beads to converge equilibrium properties, which can reduce problems associated with extended ring polymers, including the lack of ergodicity during sampling, as well as the flattening of effective potentials in CMD methods. Here we introduce the BF-CMD method, where we utilize BF-PIs to generate the CMD effective potential. We showcase the method by calculating position autocorrelation functions of model systems. Our results show that with the inclusion of just a single Fourier component, we can achieve the same accuracy as conventional discretized CMD with a significant reduction in the number of beads needed.

Self-Consistent Field Stability Analysis for Chemical Bonding Analysis, Geometry Optimization and Transition State Calculations

Leticia Madureira[1*], Tomasz Kowalewski[1]
*leticiam@andrew.cmu.edu

[1]Carnegie Mellon University, Pittsburgh, PA, USA, 1513-3819.

This research addresses key challenges in computational chemistry related to the accurate modeling of chemical bond formation and breaking, with a particular focus on the critical issue of electronic correlation. The study proposes the use of stability analysis for Kohn-Sham (KS) wavefunctions to identify true local minima and saddle points in Potential Energy Curves (PECs) of diatomic molecules and extends its capability to enable geometry optimizations of small molecules using Self-Consistent Field stability analysis (referred as Stable, after the keyword used by Gaussian, where it was implemented for the first time). By combining stability analysis with Density Functional Theory (DFT), this work evaluates a computationally affordable alternative to multireference methods, such as the Complete Active Space Self-Consistent Field (CASSCF), Multireference Configuration Interaction (MRCI), and N-Electron Valence State Pertubation Theory (NEVPT2), making it suitable for larger molecular systems where accurate static and dynamic correlation is crucial.

This methodology is particularly relevant to studies in catalysis, including Atom Transfer Radical Polymerization (ATRP), where the equilibrium between dormant species and actively propagating chains is highly sensitive to the stability and reactivity of the Cu(II)-X} bond (X = Br, Cl, F). This bond is characterized by significant Pauli repulsion between the 3d and np orbitals, posing challenges for traditional DFT methods to model such interactions accurately. By first validating the stability analysis approach in simpler diatomic systems, it becomes feasible to address the electronic correlation problem in more complex transition metal complexes.

Additionally, this study seeks to leverage stability analysis to enhance the detection of symmetry breaking in DFT calculations, which is essential for accurate transition state modeling. DFT methods often struggle with transition state calculations due to Self-Interaction Errors (SIEs), which can artificially favor delocalized states and underestimate reaction barriers, especially near stretched bonds or transition states where spin and spatial symmetry breaking are common. Without properly detecting these instabilities, DFT calculations may fail to represent the true nature of the potential energy surface, leading to inaccurate energy barriers and poor predictions of reaction dynamics. By implementing a framework for DFT+Stable, this research aims to overcome these limitations, ensuring more reliable identification of transition states and providing greater accuracy in modeling bond dissociation and chemical reactions.

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Fragmentation-Based ML Method for Accurate Prediction of NMR Chemical Shifts for Large Biomolecules

Surya Sekhar Manna, Sruthy K. Chandy,[1] and Krishnan Raghavachari*

Department of Chemistry, Indiana University, Bloomington, Indiana 47405
e-mail: ssmanna@iu.edu

Accurate calculations of NMR chemical shifts for large biomolecules (e.g., peptides, nucleic acids) using quantum mechanical (QM) methods remains a significant challenge. The primary obstacle lies in the steep scaling of accurate quantum mechanical calculations with system size. To overcome this limitation, our group has developed a systematic fragmentation-based approach known as the Molecules-in-Molecules (MIM) that is applicable for large biomolecular systems. Over the past decade, several variations of MIM have been successfully applied to compute various chemical properties such as vibrational spectra (IR, Raman, VCD, ROA), protein–ligand interaction energies, and NMR chemical shifts.[1-3] Our goal in this study is to leverage the simplicity and accuracy of our DFT-based MIM-NMR model to develop and train a machine learning model (MIM-ML) with minimal loss of accuracy to make faster predictions that are applicable to larger systems.

We have employed a novel machine learning (ML) framework to predict both ^{1}H and ^{13}C NMR chemical shifts for large proteins and nucleic acids. For each system, the lowest-energy conformer is identified through low-level DFT calculations to ensure a reliable structure for MIM implementation. The single layer MIM1 fragmentation-based DFT protocol with microsolvation model (including a small number of explicit water molecules + SMD implicit solvation) has been used to calculate the NMR chemical shifts, and the DFT calculations then provide the training data set for our ML models. Importantly, we have included structural and electronic descriptors derived from the cost-effective GFN2-xTB semiempirical method in our ML model. Our trained ML model has been applied to predict chemical shifts for unknown protein and nucleic acid systems and benchmarked against experimental data. Our formalism will be presented in this work along with available results for large proteins and nucleic acids.

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Current address:

[1] Kenneth S. Pitzer Theory Center and Department of Chemistry, University of California, Berkeley, CA, 94720 USA

In silico Investigation of the Impact of PFAS on Fresh Water Organisms

Rana I. Massoud, Semiha K. Bali, Angela K. Wilson

Michigan State University, Department of Chemistry, East Lansing, MI 48864, U.S.A

Per- and polyfluoroalkyl substances (PFAS) are a family of synthetic, heavily fluorinated compounds that are known for desirable properties such as water and oil repellency and stability at extreme temperatures. These properties have made PFAS very useful in products ranging from carpeting to food packaging. However, a number of PFAS have been linked to detrimental impacts upon the environment and health. A major source of PFAS accumulation in the environment is aqueous firefighting foams (AFFF), which contain a variety of PFAS, including PFOA, PFOS, and PFHxS. PFAS contamination from industrial and airport (civilian and military) sites in areas such as the Great Lakes, have resulted in bioaccumulation in organisms in the environmental ecostructure.[1]

It has been shown that PFAS are proteophilic in nature, with affinities to a number of types of proteins, including nuclear receptors (NRs).[2,3] NRs are a family of transcription factors that, when activated, regulate numerous physiological processes such as gene expression, metabolism, and reproduction.[3] In this computational research, the impact of PFAS on rainbow trout and Daphnia magna has been investigated, by using molecular dynamics (MD) simulations and binding free energy calculations to understand how PFAS bind to NRs involved in growth and reproduction pathways.

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Actinide Monoxide Thermochemistry using Heavy Element Correlation Consistent Composite Approach (f-ccCA)

Lara McMonigal, Bradley Welch, and Angela K. Wilson

Department of Chemistry, Michigan State University, East Lansing, Michigan

The thermochemistry of actinide molecules can be difficult to achieve given the hazards and practical challenges such as significant radioactivity. Given these challenges, experimental thermochemical quantities for actinide molecules often have large experimental uncertainties. Actinides are also difficult to address using computational chemistry approaches, given the size of the systems, the need to account for relativistic effects, and many low-lying states. To achieve thermochemical predictions of the actinides, while considering extensive computational cost, the correlation consistent Composite Approach for heavy (f-block) species (f-ccCA) is an ab initio composite method designed to accurately predict thermochemical quantities of actinide molecules, at reduced cost compared to other methodologies required to achieve similar accuracy. Examples of the utility of the methodology are provided for the prediction of thermochemical energies.

Ionization Energies via Normalization-corrected Density Functional Theory

Wenlan Miao[1], Kiril Datchev[2], and Adam Wasserman[1,3]

[1] Department of Physics, Purdue University, West Lafayette, IN 47906
[2]Department of Mathematics, Purdue University, West Lafayette, IN 47906
[3]Department of Chemistry, Purdue University, West Lafayette, IN 47906

Standard density-functional calculations require that the ground-state electronic density of a system integrate exactly to the total number of electrons in that system. However, we have recently shown* that the accuracy of the energies may be improved through a normalization correction scheme (NC-DFT) in which the correct number of electrons N is replaced by a fictitious one, N+ΔN. In this poster I will show various examples in 1D, 2D, and 3D cavities where Weyl asymptotics are used to derive ΔN for the Thomas-Fermi approximation, and highlight the corresponding corrections to the ionization energies. The energy errors are reduced from the order of 1% to 0.01% for N = 1000. Furthermore, using appropriate ΔN into the Local Density Approximation (LDA) reduces the exchange energy error of noble-gas atoms by a factor of up to 40.

*A. Clay, K. Datchev, W. Miao, A. Wasserman, K. J. Daas, K. Burke, Approximate normalizations for approximate density functionals. 2025. arXiv: 2504.03845[physcis.chem-ph]. URL: https://arxiv.org/abs/2504.03845v1

Friday Poster Presentations

(In the order of the poster number)

Quantum Electrodynamics of Molecular Internal Rotation

Rejwan Ali[1], Email <alimd.rejwan@stonybrook.edu>

[1]Stonybrook University

From dihedral energy term in molecular mechanics or force field in classical molecular simulation or experimental microwave spectroscopy, internal rotation has been a subject of interest. The topic will continue to play important role as current state-of-art ab initio approach although are showing some promising results but still limited under theoretical framework to understand rotation-induced experimental or theoretical results in several independent scientific areas but with same physics conditions. Since conformation induced reactions are very common in biomolecules and enzyme reactions; this area indeed need some fresh theoretical approach to apply the best possible tools to understand basic mechanism of chemical bonding. Our recent results are showing current ab initio packages are almost like historical Bohr model in this context of internal rotation, with some facts revealed but more to come; the results are strongly indicative of spectroscopy experiments for internal rotation in weak dimers. In this work we will present our recent progress with QFT approach to address internal rotation of molecules at very fundamental level as in following schematic. Also we will discuss putative design of experiment to verify the hypothesis.

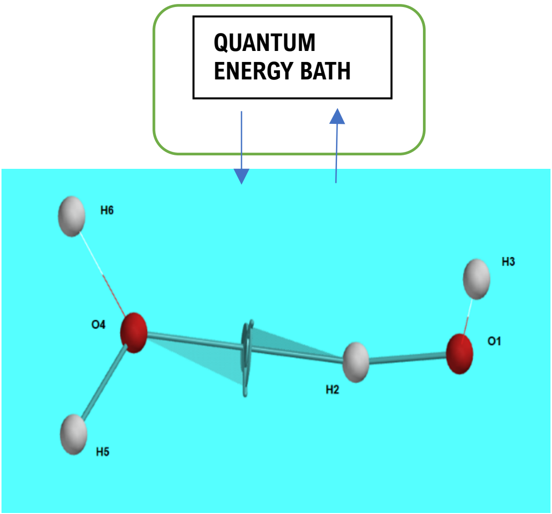

Fig.1: Internal torsion can be actuated by several mechanisms like external field in vacuum or molecular medium.

Energy Absorbed by non-radiative process can be treated with additional exchange term in Hamiltonian.

$$H = H_R + H_I + H_{IR} + H_{EX}$$

Where, H_R = Rigid Rotational Energy
H_I = Internal Rotational Energy
H_{IR} = Interaction Energy Term for Rigid and Internal Rotations
H_{EX} = Coupled Energy Exchange Term

Rare Event Kinetics in Biology: Integrating Weighted Ensemble Molecular Dynamics and Markov Models

Samik Bose[1], Ceren Kilinc[2], and Alex Dickson[1,2]

[1]Department of Computational Mathematics Science and Engineering, Michigan State University, East Lansing, MI - 48824, USA.
[2]Department of Biochemistry and Molecular Biology, Michigan State University, East Lansing, MI - 48824, USA.

Biophysical processes such as drug (un)binding to a target protein or protein (mis)folding into toxic aggregates often occur on timescales ranging from seconds to hours – far beyond the reach of standard all-atom molecular dynamics (MD) simulations. Although MD is widely considered as one of the most informative computational tools for capturing biomolecular motion *in silico*, its practical limitations are significant. For example, simulating a system of 100,000 atoms typically yields ~100 nanoseconds of data per day on a high-performance GPU cluster. At that rate, capturing a full drug (un)binding event could require on the order of 10^8 days, rendering direct simulation infeasible. Such slow processes are referred to as *rare events* due to their infrequent sampling in conventional MD. To address this, the weighted ensemble (WE) algorithm has emerged as a powerful rare event sampling method for accessing long-timescale biomolecular phenomena [1,2]. As an unbiased approach, WE is particularly suited for calculating kinetic properties such as transition rates, a key metric closely tied to drug efficacy [3]. However, rate estimates derived directly from WE simulations often suffer from poor statistical convergence, as only the reactive trajectories contribute to the calculations. On the other hand, history-augmented Markov state models (MSMs) offer a complementary strategy. These models describe the evolution of a system as a sequence of transitions between discrete states over a defined lag time (τ). MSMs are effective for capturing the kinetics of complex systems and, importantly, include both reactive and non-reactive trajectories, offering broader statistical sampling [4]. Combining WE with MSMs, therefore, holds great promise for improving the accuracy and robustness of kinetic predictions. However, the combined approach presents critical methodological challenges, especially when using an MSM lag time that exceeds the interval between two WE resampling steps. In this presentation, I will demonstrate a comprehensive WE-MSM method that can tackle this challenge [5]. The method, when applied to a complex biomolecular system of inhibitor unbinding from soluble epoxide hydrolase (sEH), significantly outperform existing standalone WE or MSM based methods at kinetic predictions.

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The multi-occupancy effect, a roadblock in wavefunction methods, from 3d-metals to lanthanides

Matheus M. F. Moraes[1], Lee M. Thompson[1]

[1]University of Louisville

The double d-shell effect is a well known problem for wavefunction based modeling of first-row transition metal containing systems. The standard definition of this effect is mainly practical, in short, it is the necessity to consider a second active d-shell in multireference calculations.[1] Such a purely practical definition prevents the development of alternative and more efficient ways to account for this effect. On the other hand, the multi-occupancy definition proposed by Moraes and Aoto attempts to explain the root cause of the double-d-shell effect.[2] Based on this alternative point of view, we developed an approach that relies on a balanced set of orbitals, the Partially Fixed Reference Space (PFRS) protocols,[2] which maintains accuracy but is less costly. In this work we show that the multi-occupancy effect can be observed and must be considered in other chemical systems, focusing in particular lanthanide-containing systems. Additionally, we will explore how the coupling of the PFRS protocols with non-orthogonal approaches[3] has the potential to both improve accuracy and reduce computational cost.

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Exploration of strong field ionization process at above the barrier regime using TDCI-CAP

Deep Mukherjee[1], Andrew S. Durden[1], H. Bernhard Schlegel[1]

1. Department of Chemistry, Wayne State University

Time dependent configuration interaction with complex absorbing potential [1, 2] has been successful in understanding the strong field ionization processes in atoms and molecules in the tunneling regime. When the applied electric field is further increased beyond the effective nuclear electric field, ionization rate is enhanced further. This process is called above the barrier ionization process [3].

Our study shows that the ionization rate for the above the barrier ionization process is sensitive to the placement, width, and the height of the absorbing potential. As the absorbing potential placed further from the ionized system, the pattern of the time dependent ionization rate shows a damped oscillatory behavior for simple atoms, (e.g. Argon) and molecules (e.g. water, ethylene etc.). We have further observed the TDCI simulation of Hydrogen atom showing similar behavior confirming the single electronic nature of these processes.

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Modeling vibronic effects in photosynthetic complexes

Isaac Ofori[1], Andres Urbina[2] and Lyudmila Slipchenko [3]
[123]Department of Chemistry, Purdue University, 560 Oval Drive, West Lafayette, IN 47907.
[1]iofori@purdue.edu

Long-lived quantum coherences observed in photosystems are hypothesized to be the source of the high quantum efficiency in photosynthesis. Vibronic interactions in pigment-protein complexes have been proposed to facilitate this phenomenon, with the low-frequency region (<250 cm^{-1}) of the vibrational spectral densities (phonon band) being the critical region for the excitation energy transfer.

The goal of this project is to investigate the role of vibronic interactions in photosynthetic energy transfer using molecular modeling. To accomplish this, we aim to model optical spectra, explicitly taking into account both vibronic and environmental effects.

The Fenna-Matthews-Olson (FMO) complex of a green sulfur bacteria, which is responsible for tunneling excitation energy from the chlorosome to the reaction center, is used as a model system. In our previous work, we demonstrated that a proper sampling of protein thermal fluctuations, combined with polarizable quantum mechanics/molecular mechanics (QM/MM) excited state calculations, provides an excitonic Hamiltonian in excellent agreement with experimental optical spectroscopic measurements.

In this project, we build upon this development and compute spectral densities of the individual bacteriochlorophyll (BCL) pigments in FMO using the excitation energies from a series of time-correlated QM/MM dynamics trajectories. The individual spectral densities are used to build a vibronic Hamiltonian, from which optical fluorescence and absorption spectra of FMO can be evaluated and compared to the experimental findings. This work will provide insight into the role of vibrations in excitonic energy transfer and may illuminate approaches for designing cost-effective models that efficiently predict vibronic effects in coupled systems.

Implementation of the Core-Valence Separation Scheme in Extended CIS: Applications to Core-Level Spectroscopy

Avik Kumar Ojha[1], John M. Herbert[1]
[1]The Ohio State University

The extended configuration interaction singles (XCIS) method extends single-excitation theories to open shell molecules by redefining excitation levels to include spin-adapted double substitutions traversing singly occupied orbitals. This size-consistent, variational approach improves the description of low-lying excited states in these open-shell systems with the same computational scaling as configuration interaction singles (CIS). The key advantage of XCIS is its improved accuracy in describing a greater number of low-lying excited states in these systems compared to the restricted open-shell CIS (ROCIS) method. We have recently implemented core-valence separation (CVS) approximation in order to study the x-ray absorption spectroscopy (XAS) mainly K-edge and L-edge, by keeping the necessary excitations that involve core orbitals. By restricting the excitation space, CVS reduces computational cost and memory usage while avoiding spin contamination. We have studied different systems to investigate how the doubly substitutions affect the excited states and the shape of K-edge and pre-edge for the open shell systems. This work also investigates XCIS's ability to predict spectra for various protonated and two-center, three electron hemibonded systems.

From accurate wavefunctions to DFT

Wavefunction methods are theoretically well understood, and we know exactly how to improve their accuracy, but their computational cost is high, restricting their practical use to small systems. Density functional theory is computationally inexpensive but not always chemically accurate. Worse still, unlike in wavefunction theory, increasing the computational cost does not reliably improve its accuracy. I will discuss how to calculate highly accurate densities using selected CI and perturbation theory. Then I will briefly explain how to use these densities to create exchange-correlation potentials for training machine-learned density functionals.

Accelerated Scaffold-Guided Free Energy Profiling of Aquaporin Channel Inhibitors via Umbrella Sampling and Multisite Lambda Dynamics

Blessing Oloyede[1], Dr. Arghya Chakravorty[2], Dr. Charles Brooks III[3]

University of Michigan

Membrane-bound targets like *Plasmodium falciparum* aquaporin (PfAQP) present major challenges for in-silico ligand screening due to their size, flexibility, and the computational cost of sampling for each analog. We introduce a two-stage framework that combines umbrella sampling with Multisite Lambda Dynamics (MSλD) to efficiently generate relative potential of mean force (PMF) profiles for analog series based on a shared core scaffold. First, umbrella sampling is used to define a reference PMF for ligand translocation through the PfAQP channel. MSλD is then employed to derive analog-specific PMFs relative to this pathway, enabling rapid comparison of energetic profiles across ligand variants—without rerunning full umbrella sampling for each. This strategy significantly reduces computational overhead while preserving high-resolution insight into channel energetics and ligand behavior. This foundational stage will inform subsequent screening: low-energy wells identified in the PMF will be mined for pharmacophoric features, guiding rapid docking and virtual screening. Top-scoring hits will be fed back into MSλD for refinement and optimization. This approach lays the groundwork for an efficient, scaffold-anchored design cycle that scales to complex, dynamic membrane targets like aquaporins.

Imaginary-Time Small Matrix Path Integral

Rapti Pal and Nancy Makri

Department of Chemistry, University of Illinois at Urbana-Champaign

Simulating the dynamics and equilibrium properties of molecular systems embedded in an environment is crucial to understanding many chemical phenomena. Real-time path integral methods, such as the quasiadiabatic propagator path integral[1] (QuAPI) and the more recently developed small matrix path integral[2] (SMatPI) allow the fully quantum mechanical simulation of system-harmonic bath dynamics at finite temperatures without encountering the exponential scaling of the time-dependent Schrödinger equation. The iterative QuAPI algorithm has also been adapted to the calculation of time correlation functions and thermal equilibrium properties.[3]

We have developed a small matrix decomposition of the Boltzmann operator, which leads to a SMatPI algorithm in imaginary time. The algorithm eliminates the tensor storage requirements of QuAPI, allowing the efficient quadrature-based calculation of thermal properties in multistate systems. By avoiding Monte Carlo sampling, the imaginary-time SMatPI algorithm performs well even in situations where the multidimensional integrand exhibits a sign problem. We demonstrate the performance of the algorithm by calculating the equilibrium excited state occupation, the internal energy and the purity of symmetric and asymmetric two-level systems and of model cyclic trimer and pentamer Hamiltonians that are plagued by a sign problem, for various parameters. Our results establish imaginary-time SMatPI as a powerful technique for computing equilibrium properties of system-bath Hamiltonians that is well-suited to systems exhibiting spin or electronic frustration that is often associated with sign problems.[4]

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Lifetime of Strongly Correlated States on Near-Term Quantum Computers

Lillian I. Payne Torres[1], Anna O. Schouten[1], and David A. Mazziotti[1]

[1]The University of Chicago

Here we study the lifetime of strongly correlated stationary states on quantum computers. We find that these states develop a nontrivial time dependence due to the presence of noise on current devices. After an exciton-condensate state is prepared, its behavior is observed with respect to unitary operations that should preserve the stationarity of the state. Instead of stationarity, however, we observe nontrivial time dependence in which the large eigenvalue of the particle–hole reduced density matrix—the exciton population of the condensate—decays toward unity, reflecting the loss of entanglement and off-diagonal long-range order. The result offers insight into the challenge of simulating strongly correlated systems on near-term quantum devices and highlights the importance of developing novel strategies for error mitigation that can preserve many-body correlations.

Analytic Gradient for Resonating Hartree–Fock: Towards Nonadiabatic Molecular Dynamics

Praseetha Prakash and Dr. Shane M Parker

Case Western Reserve University, Cleveland, Ohio

There is a pressing need for new excited-state electronic structure methods that balance accuracy and efficiency, an essential requirement for integration into nonadiabatic molecular dynamics (NAMD) simulations across complex reaction landscapes[1]. Previous work in our group led to the development of a numerically stable version of the Resonating Hartree–Fock (ResHF) method, yielding energies that closely match those from state-averaged complete active space self-consistent field (SA-CASSCF) calculations. Notably, ResHF also reproduces the charge-transfer behavior of lithium fluoride, comparable to state-specific CASSCF (SS-CASSCF)[2]. Building on these, my current work focuses on deriving forces (i.e., energy gradients) for the ResHF using a Lagrangian formalism incorporating Lagrange multipliers to ensure variational consistency. This is essential for performing geometry optimization and real-time NAMD applications. These developments aim to establish ResHF as a viable and accessible tool for exploring photochemical dynamics.

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High-accuracy exchange-correlation potentials from Kohn-Sham inversion in a Slater basis

Bishnu Prasad Rakshit[1], Vaibhav Khanna[1], Paul Zimmerman[1]

[1] Department of Chemistry, University of Michigan, Ann Arbor, MI, USA

Density functional theory (DFT) is a widely used and intuitive ab-initio method to simulate molecules and materials with many electrons. Under the Kohn Sham formalism the electrons experience an effective potential which consists of classical contributions and a quantum exchange correlation potential (v_{xc}). The exact form of v_{xc} is unknown and is in practice modeled using approximate density functionals. In contrast, wavefunction-based methods (WFT) are better at capturing electron correlation, with full configuration interaction describing all correlation within a basis. Moreover, in most electron structure problems Gaussian Type Orbitals (GTO) are used, even though Slater type orbitals (STO) have the correct electron density characteristics near the nucleus and at longer distances. In this work, the DFT v_{xc} is constructed by inverting near-FCI quality electron densities in an STOs basis. The reconstructed v_{xc}s show the correct key features near the nucleus and asymptotic decay at longer distances even with a finite basis. This WFT derived v_{xc} data will prove useful to guide the development of improved functionals.

Anomalous Ionic Current in Charged Boron-Nitride Nanotubes

Pavel Rehak[1] and Petr Král[1,2]

[1] Department of Chemistry, University of Illinois at Chicago

[2] Departments of Physics, Chemical Engineering, and Pharmaceutical Sciences, University of Illinois at Chicago

Current is induced by either a concentration gradient of ions or external electric field, causing osmo-diffusion of Li^+, Na^+, and K^+, flowing in basic aqueous solution (pH = 11) through negatively charged Boron-Nitride Nanotubes (BNNT). In bulk solution K^+ has the highest current and Li^+ has the lowest current. In these charged BNNT the reverse trend is true, with Li^+ ions having the largest current, and K^+ ions having the lowest current. We perform molecular dynamics (MD) simulations to elucidate flow of these ions in the BNNTs. We calculate 3-D radial (diffusive by random motions) and 1-D axial (drift induced by electric field) velocities of these ions in the tubes. We also use ab initio and DFT calculations to model reactions of these cations with OH groups in charged BNNT. Then we model our MD simulations to reflect the effects of these chemical reactions. We saw that K^+ retains its fastest diffusive 3-D velocity but has the slowest drift 1-D axial velocity, whereas Li^+ has the next fastest diffusive 3-D radial velocity, but the fastest drift 1-D axial velocity [1].

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Canonical Force Fields for Interatomic Interactions

Luis A. Rivera-Rivera[1] and Jay R. Walton[2]

[1]Department of Physical Sciences, Ferris State University, Big Rapids, MI 49307, USA

[2]Department of Mathematics, Texas A&M University, College Station, TX 77843-3368, USA

Abstract

Canonical approaches are applied to generate potentials and forces for interatomic interactions from *ab initio* data. The methodology has the advantage of generating highly accurate potentials and forces with a minimum number of *ab initio* points and without the need to fit or interpolate the *ab initio* data. Pair potentials and forces generated by canonical approaches are highly accurate and suitable for molecular dynamics simulations under extreme conditions of high temperature and pressure.

Distance and Orientation Dependence of Triplet-Triplet Energy Transfer Couplings Based on Nonorthogonal Multireference Wave functions

Saptarshi Saha[1], Megan J. Mackintosh[1], Lee M. Thompson[1], and Pawel M. Kozlowski[1]

[1]University of Louisville, Louisville, Kentucky 40292, USA

Triplet-triplet energy transfer (TEnT) has significant contributions in different photochemical, photobiological, and energy science processes. The best-known form of TEnT is the Dexter energy transfer (DET). DET is well described by the four-state model which includes initial and final states (D*A and DA*) as well as charge transfer (CT) states (D^+A^- and D^-A^+). Two model systems, namely naphthalene dimer and the 2,2′-bifluorene molecule were utilized to investigate the role of distance and orientation of the molecular fragments on the energy transfer process. For naphthalene dimer, in D_{2h} symmetry, x, y and z distances (in Å) between the naphthalene monomers were varied and the electronic coupling elements (ECEs) plotted corresponding to them. Maxima in the ECE curves were seen corresponding to regions of greatest π and π* orbital overlap, whereas minima were observed along π orbital nodes. For 2,2′-bifluorene, the variation of ECEs was studied with respect to the torsional angle between the two fluorene rings connected through the C2-C2¢ bond. Spin density plots and biorthogonal orbitals were used to verify that the correct diabatic electronic structure of the TEnT states were determined. As a future direction, we will extend our investigations to determine the importance of TEnT pathways in various photosensitized catalytic reactions and other applications.

Understanding Bulk Nickelates Superconductivity: Impact of Pressure, Strain and Electron Correlation

Bipasa Samanta and Alexandru Bogdan Georgescu

Department of Chemistry, Indiana University, Bloomington, Indiana 47405, United States

The discovery of superconductivity in bulk nickelates under moderate pressure in 2023(1), which share structural similarities with cuprates but exhibit a transition temperature (Tc) around that of liquid nitrogen (80 K), has reignited interest in exploring superconductivity across the nickelate family. Although the application of stress and strain has been linked to the onset of superconductivity in these materials, the precise atomistic mechanism driving superconductivity at certain stress levels remains unresolved. Since the d^9 electronic configuration, crucial in cuprates, is absent in nickelates, previous theoretical frameworks are inadequate for explaining this phenomenon in nickelates. Thus, to investigate why a Ni-O-Ni straight bond develop a superconductivity in $La_3Ni_2O_7$, we performed a first-principles study to explore the interplay between electronic and crystal structure transitions in these multi-layered materials under various stress. Our study provides an in-depth analysis of the effects of pressure and strain on the structural, electronic, and magnetic properties of this class of materials. Using standard DFT parameters, our first-principles calculations accurately capture the transition pressure of approximately 15 GPa for the orthorhombic (or monoclinic) to tetragonal phase transition, which is in agreement with experimental results reported to date. Further, $La_3Ni_2O_7$ is also recognized as a strongly correlated material, where electron-electron interactions play a crucial role in shaping its electronic behaviour. We explored the influence of electronic correlations on the transition pressure and structure by varying the applied Hubbard parameter (U_{eff}). Our results indicate a competition between U_{eff} and pressure in controlling the magnetic moment. A lower U_{eff} promotes the dimerization and structural transition required for superconductivity, while a higher U_{eff} leads to electron localization and high spin states, preventing the necessary electron delocalization needed for Ni-O-Ni dimer formation.

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Weighted ensemble enhanced sampling for the elucidation of drug binding pathways

Daniel Santos[1], Yao Fu[1], Sean McCarty[1], and Terra Sztain[1]

[1]University of Michigan

Understanding how small-molecule inhibitors dynamically bind to their protein targets remains a major challenge in computational drug discovery. Traditional molecular dynamics simulations often fail to capture the full binding process due to the rare and long-timescale nature of these events. Here, we apply weighted ensemble (WE) enhanced sampling, implemented through the WESTPA framework, to simulate the binding pathway of Nirmatrelvir, an FDA-approved SARS-CoV-2 main protease (Mpro) inhibitor. Our system models the wild-type Mpro and captures full, atomistic binding trajectories spanning from initial diffusion to encounter complex, pre binding, to productive binding. These simulations reveal intermediate states, including encounter complexes and metastable, nonproductive binding poses, that are not evident in the static crystallographic structure. Dimensionality reduction (PCA) and clustering analyses highlight correlated motions and key residue interactions that contribute to early binding events. Notably, we identify several residues involved in initial contact formation that are absent from the resolved inhibitor-bound structure, suggesting potential targets for future mutational or drug-resistance studies. These preliminary results demonstrate the power of WE simulations in mapping realistic binding pathways and provide a foundation for subsequent studies comparing wild-type and mutant Mpro variants. This work also highlights methodological challenges in WE setup and convergence, offering insights for future applications in dynamics-based drug design.

Correcting DFT with Δ-ML: Interpretable GNN Model with CBH-1 Fragments for Total Atomization Energy

Deep Jyoti Sapkota, Jinay Devendra Panchal, Alec J. Sanchez, Surya Sekhar Manna and Krishnan Raghavachari*
Department of Chemistry, Indiana University, Bloomington, Indiana 47405
e-mail: dsapkota@iu.edu

The accurate prediction of thermodynamic properties (total atomization energy, heat of formation, etc.) using quantum chemical methods is challenging due to an accuracy-cost tradeoff. Additionally, the inherent errors associated with different density functionals add to the complexity of this problem. In this work, we introduce a Delta-Machine Learning (Δ-ML) model for the prediction of total atomization energies (TAEs) using a Graph Neural Network (GNN) formalism. The GNN model is used to learn and predict the systematic errors associated with computationally efficient DFT methods (B3LYP) relative to highly accurate composite methods (G4MP2) using the effective contributions of nodes (heavy atoms) and edges (heavy-atom bonds) of molecules. We used the GDB-9 dataset with up to 9 heavy atoms and total of ~130k molecules for our Δ-ML study. Additionally, a bond-centric CBH-1 (Connectivity Based Hierarchy with rung 1) treatment has been implemented to extract fragmentation-based GNN features. The fragments are embedded with a structure-based vector representation (Mol2vec) to produce rich input features for edges to train our GNN model. Our results suggest that fragmentation-based framework can correct the systematic errors associated with B3LYP for the prediction of TAEs to well within chemical accuracy (~1 kcal/mol compared to G4MP2). Furthermore, we developed an interpretable Δ-ML model to understand the individual edge-contributions toward the prediction of TAE. Overall, this study yields insights on the edge-wise (bond energy) Δ-ML contributions for the prediction of TAEs with the accuracy of G4MP2 level.

Generalized Molecular Property Imputation Using a Flexible Transformer Architecture

Andrew B. Schofield[1], Tianfan Jin[2], Ericka Roy Miller[1], and Brett M. Savoie[1]

[1]University of Notre Dame
[2]Purdue University

Chemical data is fundamentally sparse, as molecular structures can serve as database keys for countless properties. Ideally, it would be possible to convert between databases with different properties for each molecule, or to fill in missing properties based on those that are available, or to fuse databases with partially overlapping properties. However, classical data imputation strategies based on primitive interpolation or structural regressors fail at these tasks. Even in predicting a single property, there is typically additional known property information that is neglected or an incomplete structure that makes traditional methods unwise or inapplicable. Here, we present a more general paradigm of chemical property imputation that uses all available information in imputation, fusion, and conversion tasks. A robust transformer model architecture was developed for these generalized imputation tasks. The resulting models, trained in multiple trials using a dataset of approximately 16M organic molecules and 23 properties, accurately and flexibly impute missing data, a capability that other modern methods lack. Finally, we proffer an imputation protocol utilizing the same architecture to accurately predict missing values within sparse datasets trained solely from internal data. The suitability of this protocol for general imputation is demonstrated by two case studies in which sparse data is imputed with an average R2 values of 0.79 and 0.85. These advances should herald more versatile modeling approaches and enhance our collective understanding of molecule-property relationships.

Molecular-level insights on the influence of clay interfaces interactions with ADONA

Christina E. Schumm, Narasimhan Loganathan, James Hager, and Angela K. Wilson

Department of Chemistry, Michigan State University, East Lansing, Michigan, 48823.

Due to the toxic nature inherent to legacy per- and polyfluoroalkyl substances (PFAS), there is a growing need for less toxic alternatives. Dodecafluoro-3H-4,8-dioxanonanoate (ADONA) is an important replacement utilized extensively in fluoropolymer production; however, it is now known for its significant toxicity. Over the last decade, elevated levels of ADONA have been shown in surface soils and sediments surrounding manufacturing plants which poses a possible threat to nearby drinking water sources. Soils and sediments have a prominent role in PFAS mobility, and understanding how major soil components influence this process for ADONA will be critical for future remediation. Utilizing classical molecular dynamics (MD) simulations, this study elucidates important mechanistic insight about how three prominent clay minerals effect the fate and transport of ADONA.

Unraveling Abnormal Collective Effects: Non-Monotonic Number Dependence in Cavity Electron Transfer

Shravan Kumar Sharma[1], Prof. Hsing-Ta Chen[1]

University of Notre Dame

Abstract:

Strong light-matter coupling within an optical cavity leverages the collective interactions of molecules and confined electromagnetic fields, giving rise to the possibilities of modifying chemical reactivity and molecular properties. While collective optical responses, such as enhanced Rabi splitting, are often observed, the overall effect of the cavity on molecular systems remains ambiguous for many molecules. Our work investigates the non-adiabatic electron transfer process in electron donor-acceptor pairs influenced by collective excitation and local molecular dynamics. Using the timescale difference between reorganization and thermal fluctuations, we derive analytical formulas for the electron transfer rate constant and the polariton relaxation rate. These formulas apply to any number of molecules (N) and account for the collective effect as induced by cavity photon coupling. Our findings reveal a non-monotonic dependence of the rate constant on N, which can be understood by the interplay between electron transfer and polariton relaxation. As a result, the cavity-induced quantum yield increases linearly with N for small N (as predicted by a simple Dicke model) but shows a turnover and suppression for large N. We also interrelate the thermal bath frequency and the number of molecules, suggesting the optimal number for maximizing enhancement. The analysis provides an analytical insight for understanding the collective excitation of light and electron transfer, helping to predict the optimal conditions for effective cavity-controlled chemical reactivity.

A Photochemical Crossroads: The (Z)/(E) Equilibrium Determines Emission or Cyclization of 2'-Hydroxychalcone

Peyton D. Simpson[1], Matheus M. F. de Moraes[2], Megan J. Mackintosh[3], Lee M. Thompson[4], and Pawel M. Kozlowski[5]
[1]University of Louisville, Louisville, KY
[2]University of Louisville, Louisville, KY
[3]University of Louisville, Louisville, KY
[4]University of Louisville, Louisville, KY
[5]University of Louisville, Louisville, KY

The molecule 2'-hydroxychalcone (2HC) exhibits unique photo processes, including excited-state proton transfer and photoisomerization. While many of the major components of the photochemistry of 2HC have been reported previously, there remains a lack of consensus concerning the importance of the proton transfer step and its contribution to the isomerization. Herein, we employed second-order n-electron valence state perturbation theory (NEVPT2) to investigate the potential energy surfaces of 2HC's low-lying singlet and triplet excited states with several key reaction coordinates, focusing on the mechanism for photoisomerization and emission. Our results exhibited excellent agreement with previous experimental studies and are qualitatively consistent with previous theoretical works but provide a more accurate modelling of the excited states. Additionally, we investigated the importance of the equilibrium between the (*Z*)-keto and (*E*)-keto isomers in the ground state which was not considered in previous works. The excitation of the (*Z*)-keto and (*E*)-keto leads to distinct photochemical reactions where the photochemistry of the former involves fluorescence and phosphorescence while the latter involves a photocyclization via a conical intersection. This improves the current understanding of the photochemistry of 2HC that can be extended to spectral tuning to enhance or inhibit fluorescence and cyclization of 2HC and its derivatives.

Mudslide: An open-source framework for Non Adiabatic Dynamics

Mrigank Singh and Shane. M. Parker

Case Western Reserve University, Cleveland, OH

Here, we introduce *Mudslide* an open-source Python framework developed entirely by our research group to perform nonadiabatic molecular dynamics simulations using model Hamiltonians or potentials derived from ab initio calculations. It currently supports several established dynamics methods including Fewest Switches Surface Hopping (FSSH), cumulative FSSH (c-FSSH) and Ehrenfest dynamics. In addition, it contains a broad set of 1D and 2D scattering models as well as interfaces to Turbomole, OpenMM, and more.

Mudslide is designed for clarity, modularity, and ease of extension: a primary goal of Mudslide is to allow users to provide their models or interfaces by writing their own model class in python.

In comparison to existing packages, Mudslide emphasizes transparency. While other programs may offer broader molecular capabilities or advanced sampling techniques, Mudslide offers a lightweight, highly adaptable platform for algorithm development.

Although still work in progress, our long-term goal is to establish Mudslide as a central hub for flexible, open-source dynamics simulations which will foster collaboration and innovation in nonadiabatic dynamics. The code is available at github.com/smparker/mudslide under the open-source MIT license.

Wigner Crystallization in a 1D Lattice Model

Gabriel J. Smith[1], and James J. Shepherd[1]

[1] Department of Chemistry, Michigan State University, East Lansing, MI 48824, USA

In this poster, we will present our work on the one-dimensional Wigner crystal realized in a lattice model system. This important crystallization in solids is investigated using full configuration interaction (FCI) and full configuration interaction quantum Monte Carlo (FCIQMC). This model is of fully spin-polarized electrons interacting through screened Coulomb potential on a 1D lattice ring. This poster will present a unique aspect of this model system, where the total Hilbert space can be partitioned into two disjoint spaces that can be used to help predict the point where the Wigner crystal becomes the more favorable phase.

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Orbital Rotation Hessian and Stability of Nonorthogonal Multiconfigurational SCF Wavefunctions

Zihui Song[1] and L. M. Thompson[1]

[1]University of Louisville

Second-order approaches for optimization of non-orthogonal multi-configuration self-consistent field (NOMCSCF) wavefunctions provide improved algorithmic robustness to more reliably and efficiently determine variationally minima in wavefunction parameter space. In this presentation, I describe our work deriving, implementing and applying second-order NOMCSCF optimization methods, including the coupling of orbital rotation parameters and configuration interaction coefficients. I will outline our findings regarding the stability of NOMCSCF wavefunctions with regard to orbital rotation parameters optimized under different spin symmetry constraints. The presentation will highlight how NOMCSCF wavefunctions are connected by eigenvectors of the orbital-rotation Hessian matrix and reveal correlation within the wavefunction, generalizing the analysis of single determinant wavefunctions to different-orbitals for different configurations approaches.

Small Matrix Path Integral Studies of Energy Transfer with Distance-Dependent Coupling

Alyssa M. Spencer[1], Nancy Makri[2]

[1]University of Illinois Urbana-Champaign, Department of Chemical and Biomolecular Engineering
[2]University of Illinois Urbana-Champaign, Department of Chemistry

The small matrix decomposition of the path integral (SMatPI) offers an efficient, fully quantum mechanical method for simulating excitation energy transfer (EET) in molecular aggregates at finite temperatures, where each monomer consists of two (ground and excited) electronic states coupled to any number of intramolecular normal mode vibrations. By circumventing the large storage requirements of iterative tensor-based algorithms, the SMatPI algorithm is applicable to multistate processes characterized by long memory. The present work extends the method by allowing the electronic coupling parameters to depend on the distance between the monomers. The intermolecular distance is allowed to oscillate over time, introducing a time-dependent term in the system Hamiltonian that alters the time evolution of the electronic populations. The EET dynamics of a model dimer is investigated under a variety of parameters at both the microstate and ensemble level.

Improving Slater Orbital Integration Accuracy through Prolate Spheroidal Coordinates

Alexander Stark[1], Nathan Meier[1], Jeffrey Hatch[1], Duy-Khoi Dang[1], Joshua Kammeraad[1], Paul Zimmerman[1]

[1]University of Michigan

Abstract

The core of electronic structure calculations is the integration of forces exerted on and by electrons and nuclei in a system. Some of these interactions have forms which manifest in such a way that makes integration challenging depending on the choice of basis (specifically Slater Type Orbitals (STOs)). This difficulty lies in the fact that Slater functions on multiple centers do not have a known analytically integrable form. Many methods have been developed to ease the numerical integration, an example being Becke Partitioning (BP)[1] where space is partitioned between atomic regions. Becke and others have noted the benefits to using a prolate spheroidal (PS) coordinate system to integrate over diatomics.[2] The use of PS coordinates was, however, not generally applicable to larger systems where some Hamiltonian elements require 3 centers integrations, such as Coulomb integrals within the Resolution of the Identity approximation. A third center is added in the PS coordinate grid in this work, where we will note the challenges and steps taken to handle a third center. Performance analysis is conducted through Full Configuration Interaction(FCI) calculations on small polyatomic molecules. The presented method's ability to utilize high angular momentum functions allows for convergence to be achieved in larger basis sets, in contrast to BP[3].

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Reactions of S-PEEK with H and OH Radicals in Fuel Cells:
Thermodynamics and Transition States

Jonathan E. Stevens[1]*, Mercedes A. Bales*[1]

Sulfonated polyether (ether) ketone (sPEEK) membranes are potential candidates for proton-transfer membranes in hydrogen fuel cells, but they degrade due to reactions with hydroxy radicals. This study uses M062X hybrid density functional calculations to explore the reactivity of sPEEK with OH radicals and H radicals in a water environment. In fuel cells, OH, H, and OOH radicals are present, with OH radicals believed to particularly contribute to the degradation of sPEEK. In this investigation, reactions of sPEEK with OH and H radicals were analyzed. One type of reaction studied was the abstraction of hydrogen atoms from sPEEK by OH radicals. The thermodynamics and in one instance, barrier to these reactions are computed. The thermodynamics of other reactions involving the reaction of OH and H with the SO_3H group present in sPEEK membranes were also studied.

1.University of Detroit Mercy, Department of Chemistry and Biochemistry

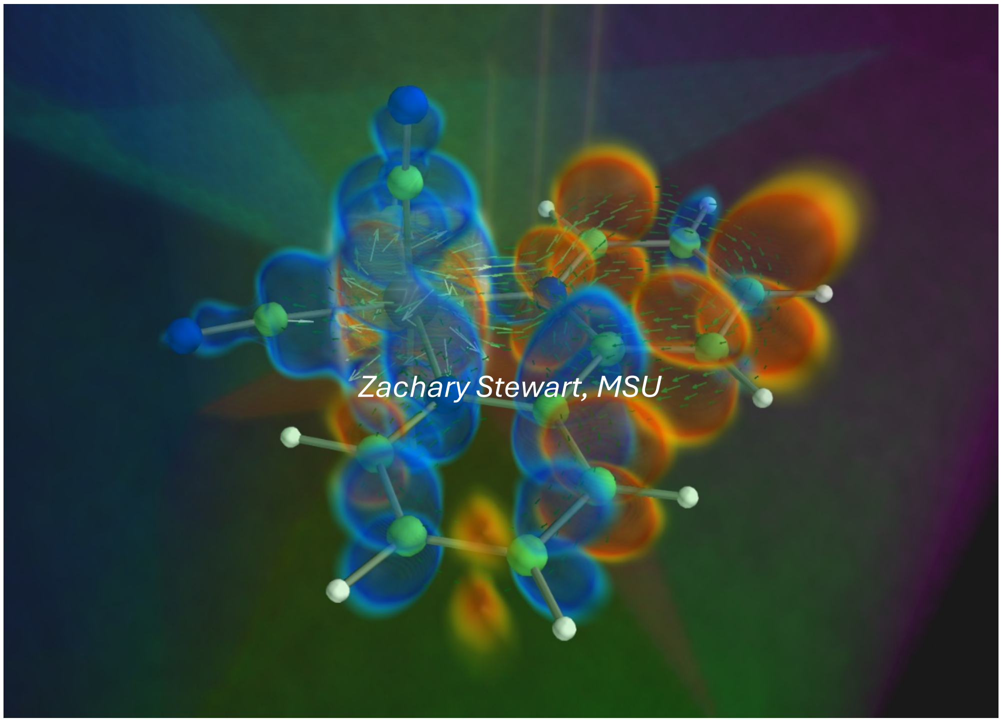
Laser-Driven Relativistic Electron Property Dynamics in Metal Complexes

Zachary Stewart, Angela K. Wilson

Michigan State University, Department of Chemistry, East Lansing, Michigan

Advances in ultrafast spectroscopy have increased the viability of simulating and predicting electron dynamics in molecular systems, such as electronic density and spin behaviors through the use of specifically controlled external perturbations such as laser pulses. The use and development of time-dependent methodologies for modeling the dynamics of electronic systems computationally is an active field and has potential use for the development of molecular systems that utilize relativistic spin properties.

One approach to simulating the electron dynamics of molecular systems is by using time-dependent spin-orbit configuration interaction (TD-SOCI), a wavefunction based active space method which propagates a relativistic configuration interaction wavefunction with external perturbations. The underlying theory of TD-SOCI will be covered, and progress on the use of TD-SOCI for the analysis and modeling of the interaction of laser pulses with transition metal complexes will be highlighted. Induced metal-to-ligand charge transfers, spin-flips, and spin separations can be demonstrated and visualized by one-body operators applied to the TD-SOCI wavefunction properties electronic density, spin density, and electronic current density.



Decoding Fluorescence Retention in DsRed: Insights from Molecular Dynamics and Machine Learning

Janya Subasinghe[1], Sebastien Hebert[1], Alice R. Walker[1]

[1]Department of Chemistry, Wayne State University, 5101 Cass Ave, Detroit, MI, 48202

Fluorescent proteins (FPs) have revolutionized biological imaging, enabling visualization of cellular structures and dynamic processes with high specificity. Among these, DsRed was the first red fluorescent protein discovered from *Dicosoma* coral. It stands out for its longer wavelengths, reduced background autofluorescence, enhanced photostability, and potential for deep-tissue imaging. However, its tetrameric form is cytotoxic and prone to aggregation in living cells, necessitating monomerization. Unfortunately, mutations intended to monomerize DsRed often remove fluorescence, limiting its practical applications. The physical mechanisms underlying this loss remain poorly understood, hindering precise spectral modifications. This study bridges the photophysical understanding of wild-type (WT) DsRed with previously attempted mutations to establish principles for monomerization that retain or improve fluorescence brightness. Classical molecular dynamics (MD) simulations were performed to analyze ground-state dynamics, revealing distinct behaviors among subunits in tetrameric and monomeric forms. Subunits A and C, and B and D exhibited similar dynamics in the tetramer, while monomerized subunit A behaved significantly differently, consistent with the observed loss of fluorescence. Clustering analysis and hydrogen bonding patterns supported these findings. To further probe excited-state dynamics, QM/MM simulations demonstrated analogous behavior between Chains A and D, as well as Chains B and C in the tetramer in the excited state. These results underscore the structural and dynamic interdependence among subunits that contribute to fluorescence retention in the tetrameric state. Building on these insights, our long-term goal is to leverage machine learning to analyze 3D structures of wild-type and mutant DsRed proteins. By identifying key residues critical for fluorescence, this approach aims to guide the design of fluorescent proteins with enhanced brightness and stability. Such advancements could extend beyond DsRed, paving the way for the development of superior fluorescent proteins for a wide range of imaging applications.

Physical mechanisms of a non-canonical green fluorescent protein protein indicator for Anion

Mfon V. Sunday[1]†, Ke Ji[2]†, Derik A. Adams[2]†, Weicheng Peng[2,3], Sheel C. Dodani[2]*, Alice R. Walker[1]*
[1] Department of Chemistry, Wayne State University, Detroit, MI 48202
[2] Department of Chemistry and Biochemistry, The University of Texas at Dallas, Richardson, TX 75080
[3] Department of Biological Sciences, The University of Texas at Dallas, Richardson, TX 75080

Fluorescent proteins (FPs) demonstrate a range of essential optical properties that make them exceptional for sensing applications. These properties include photoswitchability, which enables super-resolution imaging, as well as adjustable optical reactivity. Their capacity to selectively detect various chemicals and analytes is vital for their numerous roles in scientific research. As a result, a variety of FP-based sensors have been developed through both natural discovery and laboratory-driven evolution. However, the use of these protein-based sensors for anion detection in aqueous environments remains underexplored. This study introduces a new anion indicator called Clytia gregaria (CgreGFP). We performed constant pH molecular dynamics simulations (CpHMD) alongside experimental investigations on four different anions using the CgreGFP framework. Our simulations uncovered a potential binding region for these anions, emphasizing key amino acid residues that offer valuable insights. These discoveries may inform future mutations intended to enhance the specificity and selectivity of this protein for sensing applications.

Fragmentation-Based ML for Accurate Prediction of Electron Affinities and Ionization Potentials

Debashis Swain, Surya Sekhar Manna, Sarah Maier, and Krishnan Raghavachari*

Department of Chemistry, Indiana University, Bloomington, Indiana 47405

E-mail:debswain@iu.edu

Quantification of the electron affinity (EA) and ionization potential (IP) for molecules is of fundamental importance to their electronic structures and chemical reactivities. While highly accurate wave function theories like CCSD(T) can replicate experimental values, widely used Density Functional Theory (DFT) frequently struggles to achieve chemical accuracy (<1 kcal/mol) for predicting EAs and IPs. Previously, our group demonstrated that integrating chemical intuition through fragmentation-based error cancellation strategies enables DFT to achieve chemical accuracy for vertical IPs.[1]

In this study, we have used a judicious combination of ideas from fragmentation, error cancellation, and delta machine learning (ΔML) models to correct DFT calculated adiabatic EAs and IPs of neutral molecules with respect to their G4MP2 benchmark data. We systematically evaluated several ML algorithms, including Extreme Gradient Boosting Regression (XGBR), Gradient Boosting Regression (GBR), Random Forest Regression (RFR), Support Vector Machines (SVM), and Graph Neural Networks (GNN) to capture the intricate relationships between the accuracy of DFT calculations and chemical structure. We demonstrate that incorporating electronic features from DFT (ΔML+) can significantly improve overall model performance. Finally, we trained our models to perform reverse adiabatic EA predictions (treated as adiabatic IPs for stable anions), achieving chemical accuracy.

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EPISOL: a fast implicit solvent solver for chemical and biological systems based on 3DRISM theory.

Peter Swanson[1], Siqin Cao[1], Xuhui Huang[1,2]

[1]University of Wisconsin-Madison, Department of Chemistry, Theoretical Chemistry Institute

[2]University of Wisconsin-Madison Data Science Institute

Three-dimensional reference Interaction Site Model (3DRISM) calculations are a method for determining solvent density, distribution, and various thermodynamic properties including solvation-free energy. In contrast to extracting these properties from an explicit-solvent simulation which may take hours or days to perform, with 3DRISM, this time can be cut down to a single calculation spanning seconds to minutes. Herein we introduce our 3DRISM software, EPISOL. Compared to existing software, EPISOL shows increased performance, memory usage, and convergence rate alongside an easy-to-use GUI. Our software also includes our recent advances in integral-solvation theory, including hydrophobicity-induced density, and ion-dipole corrections. We provide example calculations spanning biological and material systems containing hundreds of thousands of atoms and compare our results to existing databases.

Ehrenfest Dynamics on Potential Energy Surfaces Obtained from Nonorthogonal Wavefunction Theories

Hoang Tran, Matheus M.F. Moraes, and Lee M. Thompson

University of Louiville

Molecular switches, such as azobenzene, have attracted considerable attention due to their remarkable properties and diverse applications. Previous studies have demonstrated that external electric fields can influence their isomerization,(1) prompting interest in achieving full control over this process. Given the inherently nonadiabatic nature of isomerization, computational approaches beyond the Born-Oppenheimer approximation are necessary,(2) with careful consideration of computational cost. The implemented methodology is designed to accurately capture both nuclear and electronic dynamics by providing a high-resolution solution to the time-dependent Schrödinger equation, enabling the study of attosecond-scale evolution in many-electron systems.

We present an integration of resource-efficient Ehrenfest dynamics (ED) with the recently developed time-dependent nonorthogonal multi-configuration self-consistent field (TD-NOMCSCF) method to study the laser-induced isomerization of azobenzene and its derivatives. Our ED implementation supports both on-the-fly and fitted dynamics, accommodating cases where analytical gradients are not yet available for nonorthogonal wavefunction theories. Meanwhile, TD-NOMCSCF enables compact and efficient wavefunction propagation by evolving both orbitals and CI coefficients. This project aims to provide critical insights into ultrafast laser-driven molecular switching and contribute broadly to the field of laser-induced chemical transformations. Moreover, nonorthogonal wavefunction methods are poised to drive major advances in cost-effective electronic structure calculations.

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From Wavefunctions to Machine-Learned Functionals: A Symbolic Regression and GNN Approach for Non-Local Density Dependence

Soumi Tribedi[1,2], Zehua Wang[3], Ambuj Tewari[3] and Paul M. Zimmerman[1]

[1]Department of Chemistry, University of Michigan, Ann Arbor, Michigan
[2]Michigan Institute for Data & AI in Society, University of Michigan, Ann Arbor, Michigan
[3]Department of Statistics, University of Michigan, Ann Arbor, Michigan

Density Functional Theory (DFT) has been the cornerstone for computational studies of reaction mechanisms and the properties of molecules and materials. Its success stems from the Hohenberg–Kohn (HK) theorem, which asserts that the electronic ground state is fully determined by the electron density.[1] While exact in principle, practical applications of DFT depend critically on approximations of the exchange–correlation (XC) functional. Within the Kohn–Sham (KS) framework,[2] errors in the functional derivative can lead to significant inaccuracies in orbitals and densities, contributing to challenges such as self-interaction errors, delocalization errors, and failures in strongly correlated systems. We propose a strategy to compute exchange–correlation potentials directly from accurate wavefunction calculations within a Slater orbital basis, providing improved electron densities near nuclei and in asymptotic regions.[3] Building on this, we develop a non-local deep learning framework to train a new density functional that accurately predicts both the XC energy and its potential. Our approach employs atom-centered density descriptors, created by projecting real-space electron densities onto carefully designed basis functions. These basis functions are constructed via symbolic regression to optimally represent the behaviour of exchange–correlation potentials at nuclear positions as well as in the far field. Coupled with a message-passing graph neural network architecture, we train a machine-learned DFT functional capable of capturing the non-local dependence of exchange–correlation terms on the electron density.

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Atoms to Molecules in Challenging Dimers

Alvin Uppgard, Yuming Shi, Adam Wasserman

Abstract

Density Functional Theory (DFT) has proven itself as the practical workhorse for quantum mechanical calculations in many fields. Nevertheless, there are still several types of systems where current, state-of-the-art, XC functionals lead to incorrect results or have great difficulty converging. This is particularly the case for systems with strong multireference character or significant charge transfer, where the single Slater determinants of the noninteracting Kohn-Sham systems struggle to provide an adequate description. We use Partition-DFT (P-DFT) on a number of such challenging systems to recreate the reference density from atomic fragment densities using a unique partition potential and ensemble treatment within the fragments. How the partition potential and the ensemble weights deform the density is explored with reference to the Chemical Deformation Density and the oriented promolecular densities. Our results show that the ensemble weights capture the nearly isoenergetic orientational effects that precede binding, which depend on the choice of isolated reference density. Consequently, our partition potential isolates the remaining density deformation due to chemical bonding. This gives intuitive insight into the density deformations of chemical bonding without any arbitrary choice for the reference densities of isolated atoms.

Assessing the Transferability of EFP Parameters for Protein-Ligand Interaction Energy Calculations

Andres S. Urbina, Lyudmila V. Slipchenko

Department of Chemistry, Purdue University, West Lafayette, IN 47907

Elucidating the interactions between proteins and ligands is essential for structure-based drug design (SBDD). Rapid and accurate computation of protein-ligand interaction energies is important for generating diverse, high-quality data sets suitable for training machine learning (ML) models. Here, we present the FEFP strategy, which leverages the transferability of precomputed effective fragment potential (EFP) parameters using the flexible EFP approach, applied when both geometric and energetic criteria are satisfied. We evaluate the performance of precalculated EFP parameters derived from the inactive CDK2 receptor on new structures of inactive CDK2, active CDK2 and ERK2. Our results show that the FEFP strategy accurately reproduces standard EFP pair interaction energies between ligands and residues. In addition, protein-ligand interaction energies obtained with FEFP closely match those calculated with standard EFP and strongly correlate with experimental binding affinities. This approach enables efficient computation of protein-ligand interaction energies for large-scale applications in SBDD and ML.

A new class of protein misfolding revealed by all-atom simulations and supported by experiments

Quyen V. Vu[1,2], Ian Sitarik[2], Yang Jiang[2], Yingzi Xia[3], Piyoosh Sharma[3], Divya Yadav[3], Hyebin Song[4, 5], Mai Suan Li[1, 6], Stephen D. Fried[3,7], Edward P. O'Brien[2,4,8]

[1]Institute of Physics, Polish Academy of Sciences; Al. Lotnikow 32/46, 02-668 Warsaw, Poland.
[2]Department of Chemistry, Penn State University; University Park, Pennsylvania, United States.
[3]Department of Chemistry, Johns Hopkins University, Baltimore, MD 21218, United States.
[4]Bioinformatics and Genomics Graduate Program, The Huck Institutes of the Life Sciences, Penn State University; University Park, Pennsylvania, United States.
[5]Department of Statistics, Pennsylvania State University, University Park, PA, United States.
[6]Institute for Computational Sciences and Technology; Quang Trung Software City, Tan Chanh Hiep Ward, District 12, Ho Chi Minh City, Vietnam.
[7]T. C. Jenkins Department of Biophysics, Johns Hopkins University, Baltimore, MD 21218, United States.
[8]Institute for Computational and Data Sciences, Penn State University; University Park, Pennsylvania, United States.

Several mechanisms intrinsic to a protein's primary structure are known to cause monomeric protein misfolding. Coarse-grained simulations, in which multiple atoms are represented by a single interaction site, have predicted that a novel mechanism of misfolding exists involving off-pathway, non-covalent lasso entanglements, which are distinct from protein knots and slip knots. These misfolded states can act as long-lived kinetic traps and, intriguingly, may structurally resemble the native state. Here, we examine whether such misfolded states occur in long-timescale, physics-based all-atom simulations of protein folding, focusing on ubiquitin and λ-repressor. Our findings confirm the formation of these entangled misfolded states in this higher-resolution model, some of which share structural similarities with the native state. However, due to the small size of ubiquitin and λ-repressor, these misfolded states are short-lived. In contrast, coarse-grained simulations of a larger, typical size protein, IspE, reveal several long-lived misfolded clusters with non-native entanglements. The structures composing these misfolded clusters are consistent with the proteolysis profile from limited proteolysis mass spectrometry and the crosslinking profile from crosslinking mass spectrometry. Using an Arrhenius extrapolation from all-atom simulations we estimate these IspE misfolded clusters can persist for extended periods, potentially months, while remaining soluble. Our results suggest that metastable subpopulations of misfolded, self-entangled states with altered structure can persist for long timescales in both all-atom simulations and experiments.

Modeling Materials Under Extreme Conditions: Stochastic DFT and Machine-Learned Potentials

Jake Vu and Ming Chen

Department of Chemistry, Purdue University, West Lafayette, IN 47907

Materials exposed to extreme conditions, such as high temperatures or deep-Earth pressures, present challenges for conventional modeling approaches. We address two distinct problems that arise in this regime. First, we consider warm dense matter, where elevated electron temperatures render traditional electronic structure methods inefficient and often inapplicable. To overcome this, we employ stochastic Density Functional Theory (sDFT) with noise reduction techniques to enable linear-scaling simulations of metals at finite temperatures. Second, we examine deep-Earth materials where anharmonic lattice dynamics are critical. Classical force fields such as CLAYFF fail to capture these effects, limiting their predictive power. Here, we highlight the use of machine-learned interatomic potentials trained on ab initio data as an alternative that can reproduce anharmonic behavior. Together, these two approaches demonstrates how we can overcome the limitations of standard techniques and enable modeling of complex materials across under varying extreme environments.

Comparing Fully Self-Consistency GW (scGW) and Fully Self-Consistency Vertex-Corrected GW (scGWΓ) with Tensor Hypercontraction

Munkhorgil Wang[1], Ming Wen[1], Pavel Pokhilko[1], Chia-Nan Yeh[2], Miguel A. Morales[2], Dominika Zgid[1,3]
[1]Department of Chemistry, University of Michigan, Ann Arbor, Michigan 48109
[2]Center for Computational Quantum Physics, Flatiron Institute, New York, New York 10010
[3]Department of Physics, University of Michigan, Ann Arbor, Michigan 48109

An approximation in the GW method is the omission of vertex term, Γ, which accounts for higher-order interactions captured by polarizability and self-energy. Previous studies of GWΓ have been limited to G_0W_0 or quasi-particle self-consistent schemes, which remain reference-dependent and can inherit errors from the starting point. In this work, we eliminate that dependency by performing fully self-consistent vertex-corrected GW calculations enabled by tensor hypercontraction (THC) to remove any bias from the initial guess and isolate the true effect of vertex on quasiparticle energies.

To make these fully self-consistent vertex-corrected GW calculations tractable, we employ THC to decompose the four-index electron repulsion integrals (ERIs) into two-index objects. This decomposition dramatically lowers both memory requirements and computational cost enabling advanced GW schemes to be applied to larger systems.

We implement and compare a hierarchy of approximations: the second-order exchange (SOX) term and several screened variants (static-SOSEX, static-2SOSEX, static-G3W2, dynamic-SOSEX, dynamic-2SOSEX), considering both fully frequency-dependent and static screening. First ionization potentials are then computed for 29 small molecules [1] and the GW100 test set [2], providing clear benchmarks for the role, and limits, of vertex corrections in predictive GWΓ calculations.

By including the vertex exclusively in self-energy, while preserving the original polarizability, we eliminate the confounding influence of modified screening and examine how adding of vertex shifts both absolute energies and relative trends. Our study covers a broad range of molecular systems and reveals that, instead of improving the agreement with experimental data, the inclusion of vertex corrections induces a nearly uniform shift in the predicted ionization potentials. This suggests that their primary effect is a global energy offset rather than an enhancement in relative accuracy as observed in our earlier work [3, 4].

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Scalable and Physically Constrained Framework for Fitting DFTB Repulsive Potentials to Large, Diverse Datasets

Anson Wang[1], David Yaron[1]

[1]Carnegie Mellon University

Density Functional Tight Binding (DFTB) theory is an efficient computational method that approximates the electronic Hamiltonian with precomputed integrals from Density Functional Theory (DFT). However, an empirically parameterized repulsive potential is required to account for the systematic error of this approximation. We present a flexible, automated framework using convex physical constraints allowing for the fitting to large volumes of data, previously not possible without nonphysical artifacts appearing in the potentials. Training on CCSD(T)*/CBS data, we achieve a 53% reduction in mean absolute error versus MIO potentials, while maintaining physically smooth transferable potentials. This framework provides a scalable path to systematically refining DFTB models and offers insights into developing physically meaningful machine learning potentials.

DiffPIE: Guiding Deep Generative Models to Explore Protein Conformations under External Interactions

Yanbin Wang[1], and Ming Chen[1]

[1] Purdue University

Proteins play crucial roles in life processes such as catalysis, signal transduction, immune response, and molecular transport. Many of these functions are mediated by external interactions between a protein and other chemical species, including proteins, nucleic acids, and organic molecules. Furthermore, in therapeutic applications, protein functions can be influenced by interactions with unnatural chemical species, such as molecular organic linkers, inorganic materials, and polymers.

Predicting protein conformational ensembles under the influence of external interactions remains a significant challenge both experimentally and computationally. While deep generative models have been developed to predict protein structural ensembles, their application to systems involving external interactions remains largely unexplored.

In this work, we present a method that integrates a deep generative model with physics-based interaction modeling to predict protein conformations under external constraints. Without requiring any retraining or fine-tuning of the generative model, our approach can efficiently and accurately predict protein conformations covalently constrained by organic linkers, as well as protein conformations adsorbed on gold surfaces.

Quantum Electrodynamics Time-Dependent Configuration Interaction Theory

Jared D. Weidman and Angela K. Wilson

Department of Chemistry, Michigan State University, East Lansing, MI

The field of polaritonic chemistry has gained attention in recent years due to the possibilities of modifying chemical reactivity by strongly coupling molecules to optical cavity modes. Alongside experimental advances in cavity-modified photochemistry, new theoretical methods have emerged for explaining and predicting polaritonic phenomena. In particular, the quantum electrodynamics time-dependent configuration interaction (QED-TDCI) method has been developed to model laser-induced electron dynamics of molecules inside of cavities. The QED-TDCI method propagates a mixed electron-photon wavefunction in real time in the presence of an external electric field. The coupling of the molecule to the cavity is included using the Pauli-Fierz Hamiltonian, which is formed in the direct product basis of electronic CI states and photon number states. The QED-TDCI method reveals how strong light-molecule coupling can alter ultrafast charge migration and dipole-switching dynamics, suggesting new routes for controlling molecular processes with cavity quantum electrodynamics.

Self-consistent *GW* simulated band structure of endotaxial layered Sb_2Te_3/Sb_2 material

Ming Wen[1], Tung Tat Nguyen[1], Shane Smolenski[2], Yimo Hou[3], Yi-Shin Shen[2], Na Hyun Jo[2], Rachel Goldman[3], Emanuel Gull[2], and Dominika Zgid[1,2]

[1]Department of Chemistry, [2]Department of Physics, [3]Department of Material Science and Engineering, University of Michigan, Ann Arbor, MI.

A series of misfit Sb_2Te_3/Sb_2 layered materials were synthesized and characterized. We used angle-resolved photoemission spectroscopy (ARPES) to investigate the electronic structure and novel quantum states. Self-consistent *GW* (sc*GW*) calculation results were also conducted to compare with experimental observations. The revealed saddle point feature depends on the Sb_2Te_3/Sb_2 composition. Another accidental band crossing (ABC) near the Fermi level also evolves inside the first Brillouin Zone, which suggests possible unique surficial topological states.

Exploring Mechanochemistry under Hydrostatic Pressure

Taveechai Wititsuwannakul and Paul M. Zimmerman

Department of Chemistry, University of Michigan, Ann Arbor, Michigan 48109, USA

Mechanical forces induce qualitative changes in mechanisms, rates, and equilibria of chemical reactions, opening new avenues for chemical applications which complement conventional chemistry. These force-induced reactions imply that mechanical forces such as compressive forces can distort potential energy surfaces (PESs), leading to the perturbation and shifting of transition states or the disappearance of intermediates. As a result, knowledge of the initial reaction landscape is insufficient to represent force-induced pathways, which may change qualitatively. To model and gain a deeper understanding of how compressive forces alter reaction mechanisms at the atomistic level, we have developed an integrated approach combining the growing string method (GSM)[1-3] with the *eXtended* hydrostatic compression force field (X-HCFF)[4] to automatically locate reaction paths under hydrostatic pressure. This tool has been tested on the intramolecular proton transfer from **1** to **2** (Figure 1), a transformation which does not proceed under thermal conditions but is triggered by a hydrostatic pressure of 9 GPa. This presentation will outline the workflow of our approach and demonstrate how it provides mechanistic insights into this transformation, highlighting its potential as a promising tool for exploring mechanochemistry.

Key words: mechanochemistry, compressive force, GSM, X-HCFF, and hydrostatic pressure

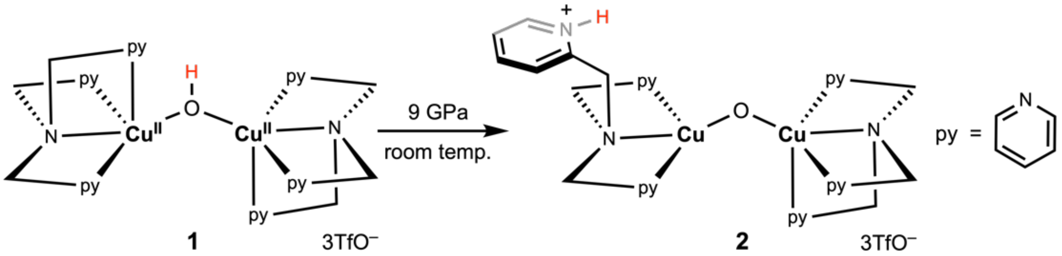

Figure 1. Transformation of **1** to **2** induced by mechanical force under hydrostatic pressure.

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Fully-connected Neural Network for T_s in DFT: Exact Conditions and Non-local Information

Ulises Zarate[1], Yuming Shi[1], and Adam Wasserman[1]

[1]Purdue University

Orbital-free density functional theory (OF-DFT) is an appealing approach to obtain the ground state density and energy of electronic systems. However, its usefulness is constrained by the unknown non-interacting kinetic energy functional, $T_s[n]$. While approximations for this functional exist, these are limited to narrow families of systems. Recently, Machine Learning techniques have been used to model $T_s[n]$ attempting to capture non-local effects. The resulting functionals exhibit energies within chemical accuracy but their applicability is limited to the training set. They are also too demanding in terms of data and computational resources. To maintain accuracy and target linear scaling, we propose the alternative approach to train a Fully-connected Neural Network (FNN) using semi-local information and enforcing two exact physical conditions. After training such network for 2-electron systems, we obtained agreement with the exact energies. Further training the FNN with information from homonuclear diatomic molecules and the kinetic energy densities of their constituent atoms, we obtained energies comparable to those from the best semi-local analytical functionals (APBEK and rAPBEK) for a wide range of organic molecules.he abstract starts here.

Constrained Nuclear-Electronic Orbital Molecular Dynamics (CNEO-MD): Incorporating Nuclear Quantum Effects into Classical Dynamics for Vibrational Motions and Proton/Hydride Transfer

Yuzhe Zhang, Yang Yang

University of Wisconsin-Madison

We present a novel approach, constrained nuclear-electronic orbital molecular dynamics (CNEO-MD), for efficiently incorporating nuclear quantum effects (NQEs) into classical molecular dynamics. With minimal additional computational cost compared to conventional *ab initio* molecular dynamics (AIMD), CNEO-MD significantly enhances the accuracy of simulating systems where hydrogen dynamics are crucial. Our method accurately predicts vibrational spectra, particularly for proton-transfer systems such as hydrogen-bonded clusters, where conventional AIMD often fails. Additionally, CNEO-MD provides more realistic reaction free energy profiles. For instance, in the double proton transfer of a formic acid dimer, CNEO-MD correctly captures the reduction in the free energy barrier due to proton quantum delocalization, unlike AIMD, which overestimates this barrier. These results demonstrate that CNEO-MD is a promising tool for describing NQEs with high accuracy and efficiency, offering substantial improvements with negligible computational overhead.

Orbital-Level Insights into Photophysical Properties of Molecular Crystalline Materials

Ali Abou Taka[1,2], Mohana Shivanna[1], Savini Bandaranayake[1], Joseph E. Reynolds III[1], Neil C. Cole-Filipiak[1], Mohana Shivanna[1], Mark Allendorf[1], Krupa Ramasesha[1], Vitalie Stavila[1], and Laura M. McCaslin[1]

[1] Sandia National Laboratories, Livermore, CA, USA
[2]University of California, Merced

Organic donor–acceptor (D–A) co-crystals have emerged as promising candidates for next-generation optoelectronic applications due to their tunable and distinctive photophysical properties. However, the immense chemical space of potential D–A pairings present a significant challenge for understanding how molecular structure governs excited-state dynamics. Time-resolved techniques such as ultrafast UV pump, UV–vis probe transient absorption spectroscopy (TAS) are widely employed to investigate these dynamics, yet interpretation is often complicated by spectral congestion and overlapping signals. To overcome these limitations, we combine TAS measurements of both D–A dimers and co-crystals with non-adiabatic mixed quantum–classical dynamics simulations. This combined experimental–computational strategy allows us to disentangle competing relaxation pathways—such as internal conversion and intersystem crossing—and assign transient spectral features with greater confidence. Through detailed orbital analysis, we identify systems with significant S_1 charge transfer character and establish connections between excited-state dynamics and molecular electronic structure. Our results demonstrate a design framework that integrates spectroscopy, electronic structure, and dynamics, offering guidance for the development of co-crystals with tailored optoelectronic properties.