Program of the 29th CSTCC

CANADIAN ASSOCIATION OF THEORETICAL CHEMISTS | ASSOCIATION CANADIENNE DES CHIMISTES THÉORICIENS

UBC THE UNIVERSITY OF BRITISH COLUMBIA

Okanagan Campus

Kelowna, BC

June 27 - July 1, 2022

Canadian Journal of **Chemistry**

Canadian **Science** Publishing

I.   Schedule

CSTCC 2022 Program at a Glance

All events held in the Commons building (UBC Okanagan, Kelowna, British Columbia) unless noted otherwise

Monday, June 27
16:00 - 19:30 Registration
18:00 - 19:30 Opening mixer

Time	Tuesday, June 28	Wednesday, June 29	Thursday, June 30	Friday, July 1
	Introductory remarks (8:50 – 9:00) Organizers Chair: Robert Szilagyi	Chair: Paul Ayers	Chair: Dennis Salahub	Chair: Irina Paci
9:00 – 10:00	2019 CATC Honorary Lecture Dennis Salahub	Plenary Speaker Alan Aspuru-Guzik	Farnaz Heidar-Zadeh Paul Ayers	2022 CATC Honorary Lecture Gren Patey
10:00 – 10:30	BREAK	BREAK	BREAK	BREAK
	Chair: Michael Schurmann	Chair: Gabe Hanna	Chair: Erin Johnson	Chair: Heather Wiebe
10:30 – 11:00	Joshua Hollett	Erin Johnson	Thomas Baker	Robert Szilagyi
11:00 – 11:30	Jolene Reid	Tom Woo	Takeshi Yamazaki	James Gauld
11:30 – 12:00	Samira Siahrostami	Michael Schurmann	Alberto Otero de la Roza	Stacey Wetmore
12:00 – 13:00	LUNCH	LUNCH	LUNCH CATC Business Meeting*	Alex Brown
	Chair: Samira Siahrostami	Chair: Nelaine Mora-Diez		Closing remarks (12:30 – 12:31)
13:00 – 13:30	Leanne Chen	Rebecca Davis		
13:30 – 14:00	Albert Poater	Georg Schreckenbach		
14:00 – 14:30	Rachel Otero Crespo	Heather Wiebe		
14:30 – 15:00	BREAK	BREAK		
	Chair: Alberto Otero de la Roza	**Special Session** Chair: Gino DiLabio	TOUR,	
15:00 – 15:30	Sergei Manzhos	Rachelle Choueiri	(options provided)	
15:30 – 16:00	Richard Bowles	Lizandra Barrios Herrera	(dinner on your own)	
16:00 – 16:30		Adebayo Adeleke Eduardo Romero-Montalvo		
16:30 – 19:30	**Poster Session / refreshments provided**	**Banquet - busses leave at 5**	**Boat cruise leaves at 5:30**	

*Lunch will be provided

II. Abstracts

I. Oral Presentations

50 years of trying to understand natural and life sciences – learning from giants and from my students and postdocs

Dennis Salahub

Department of Chemistry, University of Calgary

I will try to capture some of the highlights of applied density functional theory from a personal perspective, in a fast-forward fashion at the beginning and then spending some time on recent projects and future work.

Two-electron density functional for electron correlation

Matthew Marcalinas and **Joshua Hollett**

University of Winnipeg

A correlation energy functional based on the introduction of the electron-electron coalescence cusp to the two-electron density is derived. The development of a functional based on the two-electron density, rather than the on-top density or the one-electron density, allows for an accurate assessment of the shape and width of the so-called "correlation hole" along with the errors associated with using alternatives to the two-electron density. Furthermore, such a functional completely avoids double-counting of electron correlation when applied to a two-electron density from a multireference wave function. The functional is evaluated on prototypical systems exhibiting different forms of correlation, including the helium atom, hydrogen clusters, and stretched bonds in a variety of molecules. The improvements over one-electron and on-top density functionals will be discussed along with details of the practical implementation and scaling with system size.

Theory and Mechanisms of Enantioselectivity for Catalytic Transformations

Jolene Reid

University of British Columbia

Computational explorations of enantioselective catalytic mechanisms are a common research endeavor often providing insight into the reaction not possible by experiment. Most investigations focus on new reaction and catalyst examples to reveal the noncovalent interactions at the core of enantioinduction with steric and aromatic interactions being the most common types. In contrast to the rapid developments in this area, revealing unique types of noncovalent interactions to be meaningful stereocontrolling elements in asymmetric catalysis is far less common. In this regard, we have recently characterized the iminium and thionium hydrogen bond as an important contact for determining the outcome of enantioselective catalytic reactions. This talk will describe our recent efforts in applying these new reaction models to understand asymmetric catalysis.

Using DFT to Guide Catalyst Discovery for Ammonia Synthesis

Samira Siahrostami

Department of Chemistry, University of Calgary

Ammonia is one of the most important industrial chemicals in the world, known not only as an essential raw material for fertilizer but also as an energy storage medium and carbon-free energy carrier. Currently, the industrial-scale NH3 synthesis relies on the century-old Haber-Bosch process, which requires harsh operating conditions including high temperature (400-500 °C) and high pressure (150-300 atm) using heterogeneous iron-based compounds as catalysts. Such process accounts for 1-2% of the world's energy supply and causes ca. 1% of total global energy-related CO2 emissions. As an attractive alternative to the Haber-Bosch process, the ambient electrocatalytic nitrogen reduction reaction (NRR), ideally powered by clean/renewable energies (e.g., solar or wind), has attracted great interest during the past few years. However, efficient NRR has proven to be very challenging to achieve up to now. In the past two years, the reduction of nitrate to ammonia has attracted much attention as an attractive process to reduce the negative environmental impact of nitrate by turning it into valuable ammonia. This method has proven to bypass the limitations of the NRR process and is highly competitive with the Haber-Bosch process. In this talk, I will discuss how we can use density functional theory calculations to understand the mechanism of the reaction and guide catalyst design for the reduction of nitrate to ammonia.

First-Principles Simulations of Ni-based Materials for Electrochemical Ammonia Oxidation

Leanne Chen

Electrochemical Technology Centre, University of Guelph

Coupling renewably generated electricity with waste chemicals to generate value-added products has potentially transformative benefits for society by curbing chemical emissions and mitigating climate change. One such waste chemical is excess ammonia from agricultural livestock production, which depletes nitrogen from the soil and has harmful health effects on human and aquatic life. Ammonia can be partially converted electrochemically to nitrate, and this mixture of ammonium nitrate can then be re-introduced into the nitrogen cycle as an upgraded form of fertilizer. In contrast to the reverse process nitrogen reduction, the mechanism of ammonia oxidation and in particular the formation of NOx species is comparatively less explored. In this talk, I will describe our recent efforts to map the reaction mechanism of electrochemical ammonia oxidation to dinitrogen, nitrite, and nitrate on oxidized Ni surfaces and discuss possible ways to direct selectivity toward oxygenated products using periodic density functional theory.

Predictive catalysis, calculations before experiments

Albert Poater, Sergio Posada-Pérez, Michele Tomasini, Anna Vidal, and Nicolas Joly

Institut de Química Computacional i Catàlisi and Departament de Química, Universitat de Girona, c/ Maria Aurèlia Capmany 69, 17003 Girona, Catalonia, Spain.

The ambition is to predict the most promising catalyst for CO_2, CH_4, and NxO conversion either on homogeneous or heterogeneous phase. The specific research objectives are to predict the fixation and functionalization of greenhouse gases applying predictive catalysis; and to explore new routes for H_2 production without a carbon footprint. In particular, the CO_2 cycloaddition to epoxides to give rise to cyclic carbonates has attracted much attention, trying to find out the catalysts and cocatalysts that enhance the performance of this reaction. In addition, other strategies will be tested to fixate and/or functionalize CO_2 by means of Frustrated Lewis Pairs, or N_2O by N-heterocyclic carbenes or both gases by diborylstannylene complexes. It is a two-way project. First, because it aims to be a meeting point from homogeneous catalysis to heterogeneous catalysis but also vice versa. Second, at the same time, it will also be multidisciplinary, as it will include experiments and then calculations, in this order, but here above all the order will be the reverse, making intensive use of predictive catalysis. This concept may seem distant and almost unattainable as machine learning is still due to the lack of data, but we must forget about this, we need to change the paradigm from now on and make calculations replace experimental scans, and that guide them to greater efficiency, while reducing the amount to save resources. But we must not forget that supercomputers consume energy, and this must be said in all honesty, so the green energy itself must sustain them in the near future.

Machine learning of potentials and functionals from sparse data and how to get insight with a black box method

Sergei Manzhos, and Manabu Ihara

School of Materials and Chemical Technology, Tokyo Institute of Technology

Machine learning (ML) has made its place in various subfields of computational and theoretical chemistry, most notably in construction of interatomic potentials, where ML is now routine, and most recently in construction of functionals for density functional theory (DFT), including exchange-correlation functionals and kinetic energy functionals, as well as in construction of pseudopotentials. In all these applications, ML is typically used for its ability to extract implicit knowledge in a black-box way with general approaches, as an alternative to using functions based on intuition or analytics. This is often done at the cost of a loss of physical insight. We will show that by structuring the function(al) representation by using staple methods like neural networks (NN) and Gaussian processes regressions (GPR) as building blocks of more involved methods based on high-dimensional model representation (HDMR), one can achieve enhanced fitting power as well as insight while fully preserving the general nature of the approach. On the examples of learning potential energy surfaces and kinetic energy densities for orbital-free DFT, we highlight how HDMR-NN and HDMR-GPR combinations allow working with extremely sparse data. We show that the GPR-HDMR combination also allows analyzing the roles of different sets of variables when fitting kinetic energy densities, generating elements of insight with a black box method. We show that this kind of combine approach is easy to use and to program, via GPR kernel design.

The nucleation one-step, two-step.

Richard Bowles

Department of Chemistry, University of Saskatchewan.

Nucleation is the activated process that controls the kinetics of first order phase transitions. Classical nucleation theory (CNT) describes the fluctuations responsible for nucleation as small clusters of the stable phase that need to overcome a single free energy barrier before they spontaneously grow. However, two-step nucleation, where the clusters appear to cross one barrier to sample states associated with an intermediate, metastable phase, before finally transforming to the stable state in a second step, have been observed in a growing number of systems, including nucleation in protein solutions [1] and in biomineralization [2].

This raises important questions concerning the nature of the 'intermediate' state clusters, their actual role in the nucleation mechanism, and how they may influence the nucleation rate. Using a simple lattice model, we show [3] that two-step nucleation can be understood in terms of a small system, first order phase transition that occurs within the fluctuation that is then superimposed on the nucleation of the bulk phases. The cluster size at which the fluctuation phase transition occurs is controlled by the thermodynamic state of the system. As a result, the nucleation mechanism evolves from a CNT-like, one-step process, to a two-step process as the system moves through the metastable phase diagram. We also find [4] that the nucleation free energy surface for the system is accurately described by a capillarity model originally developed by Iwamatsu [5]. Finally, a master equation approach is used to study how the microscopic kinetics of the fluctuation phase transition and cluster growth affect the transient and steady state nucleation rates on a simple model free energy surface [6].

[1] Yamazaki, T. et al. Two types of amorphous protein particles facilitate crystal nucleation. Proc. National Acad. Sci. 114, 2154–2159 (2017). [2] Gebauer, D., Völkel, A. & Cölfen, H. Stable Prenucleation Calcium Carbonate Clusters. Science 322, 1819–1822 (2008). [3] James, D. et al. Phase transitions in fluctuations and their role in two-step nucleation. J Chem Phys 150, 074501 (2019). [4] Eaton, D., Saika-Voivod, I., Bowles, R. K. & Poole, P. H. Free energy surface of two-step nucleation. J Chem Phys 154, 234507 (2021). [5] Iwamatsu, M. Free-energy landscape of nucleation with an intermediate metastable phase studied using capillarity approximation. J. Chem. Phys. 134, 164508 (2011). [6] Bowles, R. K. & Harrowell, P. The influence on crystal nucleation of an order-disorder transition among the subcritical clusters, arXiv preprint: 2109.12226 (2021).

Accelerated molecular and materials designd

Alan Aspuru-Guzik

University of Toronto and Vector Institute

In this talk, I will discuss the efforts by my research group and our network of collaborators towards the area of accelerated molecular design. In this area, the goal justifies the means: human intuition, theoretical chemistry models, classical and quantum simulation methods, artificial intelligence and chemical automation play a role. To design a molecule for a practical application, one has to incorporate elements from the fields mentioned above in a multidisciplinary manner. A focus on building-block approaches, synthesizability and the use of modern optimization methods has led my group to find interesting leads. I will use examples in the space of organic lasers, inverted singlet-triplet gap emitters, as well as reticular materials to motivate the approach.

Efficient Crystal-Structure Prediction using Dispersion-Corrected DFT

Erin Johnson

Department of Chemistry, Dalhousie University

While molecular materials are increasingly finding utility in energy applications, changes in molecular packing between different polymorphs can result in large variations in physical and chemical properties. Thus, one cannot optimize functionality at the single-molecule level; the crystal packing must be considered to optimize properties of a molecular material for targeted applications. Dispersion-corrected density-functional theory (DFT) has shown great promise in resolving the small energy differences between polymorphs required for successful first-principles crystal-structure prediction (CSP). However, the computational cost makes full plane-wave/pseudopotential DFT calculations impractical to apply to the vast number of candidate structures considered in a CSP search. Composite approaches, combining low-level geometry relaxation with high-level energy calculations, can greatly increase the efficiency of a CSP protocol. Additionally, numerical atom-centered orbitals (NAOs) provide significant time and memory savings over plane-wave basis sets and enable routine use of hybrid functionals. In this talk, progress towards CSP using DFT and the exchange-hole dipole moment (XDM) dispersion correction will be highlighted, as will recent work on crystal-property prediction through modeling polymorph and co-crystal dependent photoluminescence.

Finding Flies in the Ointment of Materials Databases using Simple Electron Counting

Tom K. Woo, Andrew White, Marco Gibaldi, Jake Burner, and Ohmin Kwon

Department of Chemistry and Biomolecular Sciences, University of Ottawa, Ottawa, ON

The recent advancements in data driven materials discovery have resulted in the creation of many large materials databases. In the field of metal organic framework (MOF) materials, the most popular database is the Computation-Ready Experimental (CoRE) MOF database which is composed of 14,000 experimentally characterized materials. CoRE promises to be contain structures that have been 'cleaned' and prepared for immediate use in atomistic simulations or similar. As a result, numerous studies have computationally screened the CoRE MOF database and used it for the development of machine learning models to identify high performing materials for various applications. Recently, we have discovered that 50% of the CoRE MOF structures contain serious problems, such as missing protons, missing counterions or incorrect framework charges. Further investigation found that these structural errors typically manifest themselves in metal oxidation states that are impossible, or not known, such as Li^{4+} or Zn^{1+}. As such we have developed an algorithm to automatically determine the metal oxidation states of materials from the atomic structure that we call MOSAEC (Metal Oxidation State And Electron Count). Given that MOFs are periodic and often contain large, delocalized charge-sharing domains, assigning the metal oxidation states is not a trivial task and has never previously been reported for periodic systems. In this presentation, we will describe how metal oxidation states can be used to identify problem structures in MOF databases and how they can be used to aid in the automation of preparing experimental X-ray crystal structures for computation. We also discus how problems in the CoRE database have permeated into numerous computationally generated MOF databases that are also commonly screened and used for data driven studies.

Developments in DFT/MRCI for Excited Electronic States

Michael Schuurman[1,2] and Simon Neville[1]

[1] *National Research Council Canada*

[2] *Department of Chemistry and Biomolecular Sciences*

The combined density functional theory and multireference configuration interaction (DFT/MRCI) method fills a unique niche in the landscape of excited-state electronic structure theory. In particular, DFT/MRCI possesses the folliowing desirable characteristics: (i) the possibility of "black box" impelementation; (ii) accurate vertical excitation energies; (iii) low computational cost, rendering it applicable to large molecules, and; (iv) an ability to describe a large range of electronic states, including those of multiference, Rydberg, and double-excited, and charge transfer character. Here a number recent developments using this formalism will be described, including a 'pruning' algorithm to remove a priori the deadwood configurations from the CI wave function as well as a perturative approximation the replaces explicit diagonalization of the full DFT/MRCI Hamiltonian with a small, effective Hamiltonian. Both these developments significantly expand:q the range molecules amenable to description using this formalsim.

Evaluating the Roles of Reactive Intermediates in Amino Catalysis

### Rebecca Davis

University of Manitoba

Aminocatalysis has attracted attention as a catalytic method in large part due to the high stereoselectivity that can be achieved. This is typically attributed to the difference in activation energy of the diastereomeric transition states in the addition step. However, little attention has been paid to the roles and the relative stabilities of intermediates that lie downstream of the addition step. Recent mechanistic work and reports of unexplained selectivity patterns suggest that downstream intermediates may play a significant role in determining stereoselectivity. Herein, we present our DFT studies on the reaction pathway of γ-amination mediated by dienamine activation and comparing it with the enamine mediated α-amination. This work provides insight into the impact of the downstream intermediates in directing the stereochemical outcome of these enentioselective reactions.

Quantum-chemical modelling of 2D materials

Georg Schreckenbach

Department of Chemistry, University of Manitoba, Winnipeg, MB, R3T 2N2, Canada

Research into two-dimensional (2D) materials (analogues of graphene) spans physics, chemistry, and materials science. Accordingly, quantum-mechanical modelling of 2D materials can use approaches and questions that come from physics as well as from chemistry. In this presentation, I will present some examples from our recent work in this area, including: (i) transition metal dichalogenide heterostructures, (ii) interactions of 2D materials with actinides, (iii) interface between 2D material and conducting polymers. I will focus on the kinds of questions that can be addressed, the choices one have to be made in terms of methodology and models, the challenges that arise in this process, and the unique contributions that computational chemistry can make in this area.
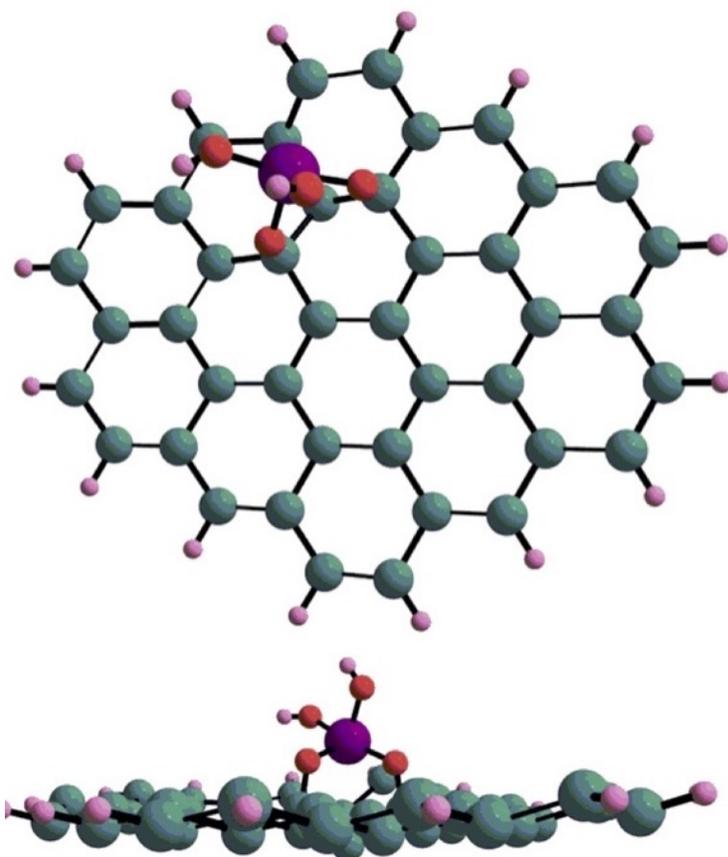
Computational studies of pressure effects on complex systems

Heather Wiebe

Department of Chemistry, Vancouver Island University

High pressure environments are prevalent in our universe, ranging from the relatively modest pressure of the deep ocean to the extreme high pressure of planetary cores. Unlike temperature, which accelerates all elementary reactions regardless of their mechanism, increases in pressure will favour only those reactions that yield a decrease in the volume of the system, according to the fundamental thermodynamic relationship: $\Delta V = \left(\frac{\partial \Delta G}{\partial p}\right)_T$. Application of pressure can therefore induce some very interesting and unexpected chemical and physical transformations. Pressures on the order of 1 kbar will result in the unfolding of most proteins, due to the loss of internal cavities and hydration of previously buried amino acid residues in the unfolded state.[1] Extreme high pressures can result in surprising changes in the electronic properties of materials, such as the transformation of sodium to a transparent insulating material at 2 Mbar[2] and the recent discovery of solid metallic hydrogen at 4.25 Mbar.[3]

Unfortunately, extreme high pressure conditions are difficult and expensive to generate in a laboratory setting. Molecular dynamics simulations provide an attractive alternative for studying processes at high pressure. In this talk, I will review our recent work on the kinetic isotope effect in metallic hydrogen using path integral molecular dynamics, and our investigation into the physico-chemical mechanism of pressure resistance in proteins from deep-sea organisms using alchemical free energy calculations and Archimedean displacement volumes.

[1] J. Roche et al, Proc. Natl. Acad. Sci. USA, 109, 6945-6950 (2012) [2] Y. Ma et al, Nature, 458, 182-185 (2009) [3] P. Loubeyre et al, Nature, 577, 631-645 (2020)

Electrochemical ammonia oxidation on β-NiOOH surfaces from first principles

Rachelle M. Choueiri and Leanne D. Chen

Electrochemical Technology Centre, University of Guelph

The electrochemical ammonia oxidation reaction (AOR) is a promising method for the treatment and upcycling of excess ammonia in wastewater effluent as well as a key step in facilitating the ammonia economy—a proposal to use ammonia as a primary fuel in a closed-loop fashion at ambient temperatures and pressures. Ammonia use as a fuel in direct ammonia fuel cells (DAFCs) is supported by an existing ammonia transport infrastructure used for fertilizer distribution, a high volumetric and mass energy density (which surpasses liquid H2 and is comparable to crude oil), and potentially high selectivity to forming benign nitrogen gas and water as an exhaust. Ammonia is also an excellent hydrogen carrier due to its ease of liquefaction and relatively low flammability compared to H2. Electrolysis of ammonia via AOR can selectively produce only hydrogen and nitrogen gas as products at ambient or close-to-ambient conditions. β-Ni(OH)2/NiOOH are attractive AOR electrocatalyst materials due to their lower costs and higher resistance to poisoning relative to well-studied Pt-based AOR catalysts. Currently, the β-Ni(OH)2/NiOOH system suffers from high overpotentials which are on the order of 1 V greater than the theoretical potential for nitrogen gas production. Experimentally, transition metal dopants have been shown to lower the AOR overpotential and influence the reaction selectivity for both transition metal and β-Ni(OH)2/NiOOH systems, improving catalyst performance. To address a lack of computational study of AOR on these surfaces and to provide a basis for future work investigating the observed effects of metal dopants on AOR catalyst activity, we employed density functional theory (DFT) calculations to generate free energy diagrams for various potential pathways toward dinitrogen, nitrite, and nitrate production on the pristine β-NiOOH surface. Our discussion begins with a systematic comparison of the various β-NiOOH structures proposed in the literature (both theoretical and experimental) and our rationale for selecting the bulk structure that forms the base of our calculations. Phase diagrams of the surface vacancies likely to exist at experimental conditions will also be presented. Finally, we examine the Gibbs free energy of potential AOR intermediates adsorbed on the (0001) facet of β-Ni(OH)2 and β-NiOOH. We compare the calculated thermodynamic pathways for AOR towards dinitrogen, nitrite, and nitrate production for all surfaces studied using the thermodynamic limiting potentials computed at experiment-relevant pH values with the computational hydrogen electrode (CHE). Our mechanistic work includes a comparison of all N-N coupling possibilities en route to forming nitrogen gas in order to find the lowest energy NHx-NHy coupling path. The computational methodology established and calculated potential-determining steps for various vacancy-containing surfaces will provide a base for future computational screening studies involving metal-doped β-NiOOH and rational catalyst design.

Active-Learning Strategy to Search for the Global Minima of Ni-Ceria Nanoparticles: The case of $Ce_{4-x}Ni_xO_{8-x}$ (x =1, 2 ,3)

Lizandra Barrios Herrera[1], Maicon P. Lourenço[2], Jiří Hostaš[1], Patrizia Calaminici[3], Andreas M. Köster[3], Alain Tchagang[4], and Dennis R. Salahub[1]

[1] *Department of Chemistry, CMS Centre for Molecular Simulation, IQST Institute for Quantum Science and Technology, Quantum Alberta, University of Calgary, 2500 University Drive NW,Calgary, AB, T2N 1N4, Canada.* [2] *Departamento de Química e Física, Centro de Ciências Exatas, Naturais e da Saúde (CCENS), Universidade Federal do Espírito Santo, 29500-000, Alegre, Espírito Santo, Brazil.* [3] *Departamento de Química, CINVESTAV, Av. Instituto Politécnico Nacional 2508, AP 14-740, México D.F. 07000 México.* [4] *Digital Technologies Research Centre, National Research Council of Canada, 1200 Montréal Road, Ottawa, ON, K1A 0R6 Canada.*

Ni-CeO2 nanoparticles (NPs) are promising nanocatalysts for water splitting and water gas shift reactions due to the ability of ceria to temporarily donate oxygen to the catalytic reactions and accept oxygen after the reaction is completed. Therefore, elucidating how different properties of the Ni-Ceria NPs, such as size, composition, and electronic structure, relate to the activity and selectivity of the catalytic reaction is of crucial importance for the development of novel catalysts.

In this work we use machine learning (ML) regression and its uncertainty – an active-learning (AL) strategy – for the global optimization of Ce(y-x)NixO(2y-x) (x=1, 2, 3; y=4) nanoparticles guided by density functional theory (DFT) calculations. The method allows the learned structure-energy relationship to improve iteratively when more data are obtained from DFT calculations of promising structures indicated by the AL.

The progress of the on-the-fly AL method from different independent AL runs are reported. The electronic structure and magnetic properties of the "putative" GM found by AL are analyzed by plots of the density of states, the spin density, the electron localization function and by population analysis, such as Mulliken, and Bader analysis. Additionally, further investigation of the NPs by mass scaled parallel-tempering Born Oppenheimer molecular dynamic (PT-BOMD) resulted in the same GM structures found by AL, demonstrating the robustness of our AL search to learn from small datasets and assist in the global optimization of complex electronic structure systems, such as Ni-Ceria NPs.

A deep Aurum reservoir: Stable compounds of two bulk-immiscible metals under pressure

Adebayo A. Adeleke[1,2,4], Stanimir A. Bonev[2], Christine J. Wu, Ericmoore E. Jossou[3], Yansun Yao[1], and Erin R. Johnson[4]

[1] *Department of Physics and Engineering Physics, University of Saskatchewan, Saskatoon, Saskatchewan S7N 5E2, Canada* [2] *Quantum Simulation Group, Materials Science Division, Lawrence Livermore National Laboratory, Livermore, California 94550, USA* [3] *Nuclear Science & Technology Department, Brookhaven National Laboratory, Upton, New York 11973, USA* [4] *Department of Chemistry, Dalhousie University, Halifax, Nova Scotia B3H 4R2, Canada*

The Earth's crust is known to be depleted of gold, among other slightly heavy noble metals transported by magma from the Earth's mantle to the crust. The bulk silicate Earth (BSE) model also suggests significant depletion of Au in the silicate mantle itself, which cannot be explained by the amount of Au in the mantle's magma. This implies that Au could remain in the lower mantle and form stable compounds, especially with iron, which is the predominate element within the core. While Fe does not form binary compounds or a bulk alloy with Au under ambient conditions, it may do so at the elevated pressures found in the Earth's interior. Here, using density-functional methods, we investigated the possibility of identifying stable, binary Fe-Au compounds at pressures up to 210 GPa. We found three such Fe-Au compounds, which are stabilized by pressure and notable electron transfer, including an orthorhombic AuFe4 phase that is ferromagnetic in nature with Au possessing a significant magnetic moment. Our result demonstrated that under sufficient compression, Au can react with Fe and indeed, the Earth's core could be holding more Au than we thought.

The "On Water" Effect in Organic Reactions

Eduardo Romero-Montalvo and Gino DiLabio

Department of Chemistry, The University of British Columbia, 3247 University Way, Kelowna, British Columbia, Canada, V1V 1V7

Aqueous organic chemistry (AOC) has received considerable attention in the past few decades because it represents a cheap and accessible green alternative to traditional organic solvent chemistry. Though AOC was originally developed for reagents that are soluble in water, the field has expanded to include reactions where reactants are not necessarily miscible with water. In this context, the "on water" effect occurs when an organic reaction is accelerated in the presence of a water-organic interface compared to the same reaction in an organic solvent or solventless conditions. Although some mechanisms have been proposed to explain this effect, there is still no agreement on the molecular origin of this phenomenon. Understanding the chemistry involved in heterogeneous aqueous-organic media has important implications in biochemistry, prebiotic and atmospheric chemistry. This talk will explore some of the experimental and computational efforts toward understanding the "on water" effect.

Additive Variational Hirshfeld (AVH) Atoms-in-Molecules

Farnaz Heidar-Zadeh

Queen's University

It is common to use electron density to partition a system into atomic regions. The necessity for such a partitioning scheme is rooted in the unquestionable role of atoms in chemistry. Nevertheless, atomic properties are not well-defined concepts within the domain of quantum mechanics, as they are not physical observables. One of the most popular families of atoms-in-molecules models is the Hirshfeld partitioning schemes. [1-2] The various flavors of the Hirshfeld scheme mainly differ in choosing the reference proatomic density that is being used to define the fuzzy atomic densities. To resolve the ambiguity in choosing the reference proatomic density, we first justify the pervasiveness of Hirshfeld atoms-in-molecules partitioning. [3-5] Specifically, we prove that the family of f-divergence measures is necessary and sufficient for deriving Hirshfeld partitioning, and realize that among all possible f-divergences, only the extended Kullback-Leibler information measure is a suitable choice. This motivates our new partitioning method, called the Additive Variational Hirshfeld (AVH) partitioning which defines the proatomic density as a convex linear combination of the spherically-averaged charged atomic electron densities. The AVH method is implemented in the ChemTools software package [6], and its robustness is confirmed by testing it on chemically diverse datasets. Considering its unique mathematical properties and our favorable numerical results, we believe that AVH has the potential to supplant other partitioning methods.

1. Bonded-atom fragments for describing molecular charge densities. Theor. Chim. Act. 1977, 44,129-138. 2. Information Theory, Atoms in Molecules, and Molecular Similarity. Proc. Natl. Acad. Sci. 2000, 97, 8879-8882. 3. Information-theoretic approaches to atoms-in-molecules: Hirshfeld family of partitioning schemes. J. Phys. Chem. A. 2018, 122, 4219-4245. 4. How pervasive is the Hirshfeld partitioning? J. Chem. Phys. 2015, 142, 044107. 5. Minimal basis iterative stockholder: atoms in molecules for force-field development. J. Chem. Theory Comput. 2016, 12, 3894-3912. 6. https://chemtools.org/

The QC-Devs Software Ecosystem

Paul Ayers and Farnaz Heidar-Zadeh

Department of Chemistry & Chemical Biology, McMaster University

QC-Devs (qcdevs.org) is an international software community devoted to developing sustainable software for quantum chemistry, physics, and the computational sciences. Our goal is to make programming accessible to researchers, to catalyze scientific collaboration, and to promote precepts of sustainable software development. Towards this end, we are actively developing free, open-source, and cross-platform libraries for scientific computing, focusing on theoretical and computational chemistry. We're adapting some of the same principles to develop free and open-source educational materials (qchem.qc-edu.org).

The goal of this presentation is to familiarize the audience with the current QC-Devs software landscape and philosophy. We'll discuss the (sometimes painful) lessons we've learned along the way, and describe how we've arrived at our current (yet constantly evolving) software development principles and protocols. In addition, we'll discuss the future development of QC-Devs and encourage others to join the team.

Lanczos recursion on a quantum computer for the Green's function and wavefunctions

Thomas E. Baker

Department of Physics, University of York, Heslington, York YO10 5DD, United Kingdom

By taking advantage of the superposition of quantum states, the hope is that algorithms not available to a classical computer can be run efficiently on a quantum computer. By doing so, larger and more exact solutions for quantum chemistry models may be possible. The question of which algorithm to use is the subject of recent research; however, it has already been shown that many classical algorithms will not be efficient on the quantum computer.

One method that I propose to use is a direct application of Lanczos' method [1]. The quantum computer is a natural vehicle to surpass the limits of this method on classical computers and has several advantages in terms of other quantum algorithms. Solving the problem in this way also gives access to the continued fraction representation of the Green's function. I will also discuss extensions using excitations [2] and how the same techniques can be applied to obtain exact density functional theory with a minimum of measurements of the wavefunction [3].

[1] T.E. Baker, "Lanczos recursion on a quantum computer for the Green's function and ground state" *Phys. Rev. A* **103**, 032404 (2021) [arXiv: 2008.05593] [2] T.E. Baker, "Block Lanczos method for excited states on a quantum computer" (2021) [arxiv: 2109.14114] [3] T.E. Baker and D. Poulin, "Density functionals and Kohn-Sham potentials with minimal wavefunction preparations on a quantum computer" *Phys. Rev. Research* **2**, 043238 (2020) [arXiv: 2008.05592]

Good Chemistry with QEMIST Cloud

Takeshi Yamazaki

Good Chemistry Company

In recent decades, the growth in computational power has allowed us to improve computational chemistry methods for higher scalability and greater accuracy. Computational chemistry has contributed to the discovery of molecules and materials by providing insight into chemical processes that are sometimes not measurable by experiments. In addition, recent advancements in quantum computing have allowed us to envision an even brighter future for computational chemistry in life and materials sciences down the road.

The quantum simulation division, within quantum computing software company, 1QBit, based in Vancouver, British Columbia, has recently branched out and formed a new independent venture, named Good Chemistry. Good Chemistry's primary focus is on the development of a computational chemistry platform to further accelerate material design and discovery processes.

In this presentation, we would like to talk about our team's R&D effort in the area of quantum chemistry, including the development of our computational chemistry platform, QEMIST Cloud [1]. QEMIST Cloud is a cloud-native platform that works with any cloud computing platform, such as Amazon Web Services and Azure. Through a simple python-based API, QEMIST Cloud enables users to run quantum chemistry calculations on both conventional computers and quantum computers. The platform has several features including incremental Full CI (iFCI) [2] for scalable and highly-accurate correlation energy calculations. In addition, we would also like to touch on method development and experimental demonstration of quantum chemistry calculations on quantum hardware to minimize quantum resources while maintaining accuracy [3,4].

[1] https://goodchemistry.com/qemist-cloud/

[2] J. Chem. Phys., 146, 104102 (2017); J. Chem. Phys., 146, 224104 (2017).

[3] J. Chem. Phys., 155, 034110 (2021).

[4] Communications Physics, 4, 245 (2021).

Improved methods for the development of basis-set incompleteness potentials

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[2] *Univesrity of British Columbia*

The main hurdle in the calculation of the kinetics and thermochemistry of chemical reactions in supramolecular systems is the correct description of the molecular orbitals of the super-molecule. The errors introduced by an insufficiently populated basis set - called basis-set incompleteness errors - are quite substantial and, in the case of non-covalent intearctions, they can exceed 100% of the total binding energy. A few years ago, we introduced basis-set incompleteness potentials (BSIPs) as a way to mitigate basis-set incompleteness in density-functional theory (DFT) calculations. BSIPs are similar to effective core potentials but they do not replace any electrons. Instead, they introduce an energy correction that approximately accounts for the shortcomings of the basis set, allowing running an almost-complete-basis-set calculation at the cost of a calculation using a small or minimal basis set. In this talk, we report on the progress regarding the development of BSIPs. Specifically, a new fitting procedure based on a massive regularized linear least-squares technique is employed and we demonnstrate the excellent performance of the reulting BSIPs with a few practical examples.

How Water Freezes: Molecular Simulations of Heterogeneous Ice Nucleation

Gren Patey, Abhishek Soni, Yi Ren, and Lian Pharoah

University of British Columbia

Pure liquid water can be supercooled to temperatures approaching - 40$^{\mathrm{o}}$C. Indeed, it has been estimated that if all water in the Earth's hydrosphere (10^{18} metric tonnes) were cooled to - 20$^{\mathrm{o}}$C, the time required to observe one homogeneous ice nucleation event would exceed the age of the universe. Hence, most ice nucleation on the Earth's surface or in the atmosphere must occur by heterogeneous nucleation involving a foreign substrate. Currently there is much interest in heterogeneous ice nucleation, particularly because ice nucleation in the atmosphere leads to ice cloud formation, and consequential effects on climate. Laboratory experiments can identify substances which serve as good ice nuclei (often inorganic compounds such as AgI, mineral dust such as clays, and assorted organic matter) but, due to the short time and small length scales involved in ice nucleation, experiments provide very little information about the microscopic mechanisms of ice nucleation. Molecular dynamics simulations of model systems can fill this knowledge gap, and identify the molecular or atomistic features necessary for a substrate to effectively nucleate ice. Our systematic investigations of "good" and "bad" ice nuclei reveal how the lattice structure and detailed atomistic morphology of a surface combine to determine its ice nucleating ability.

Structure and Function of [4Fe-4S]-Peptide Maquettes from Computational Modelling and Experiments

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Experimental and theoretical investigations of iron-sulphur (Fe-S) systems are essential in understanding, optimizing, and designing processes for considering Fe-S minerals as natural resources, synthesizing Fe-S nanoparticles as catalytic systems, and understanding the function of Fe-S metalloenzymes. Our work focuses on the family of [Fe-S] clusters coordinated with a short peptide (9- to 16-mers), also known as 'maquettes' of [Fe-S] metalloproteins. We work on specific peptide sequences that contain only three Cys residues (CxxxCxxC) in order to create site-differentiation among the Fe-sites of a [4Fe-4S] cluster that is one of the key requirements for chemical reactivity beyond redox chemistry. Given that the cluster assembly mechanism and the peptide coordination are not known, we devised a computational modelling workflow to monitor favourable peptide conformation for cluster binding as a function of amino acid sequence (AMBER, NVT MD simulations:
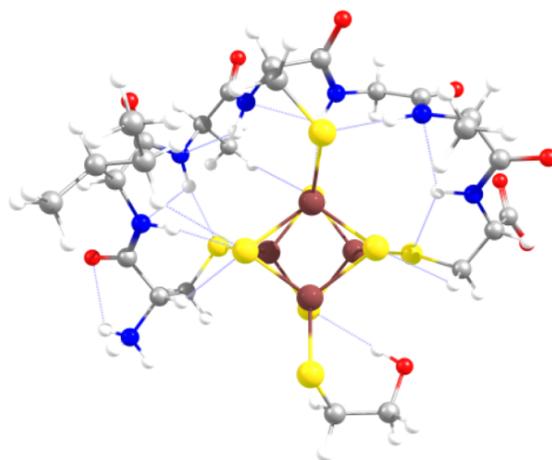
$[Fe_4S_4(bME)(ClACGAC)]^{2-}$

). The selection of peptide sequences was carried out using bioinformatics methods. The results of computational modelling were followed up with reconstitution experiments, where we find that the yield of [4Fe-4S]-maquettes correlates with the frequency of the peptide forming favourable cluster binding nest and the predicted cluster binding energies. Both the experiments and the computational simulations support the ligand-exchange mechanism between a pre-assembled cluster and the peptide ligand.

Computational Studies On The Biologically Important Sulfilimine (S=N) Crosslink Bond in Collagen IV

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Despite the prevalence of nitrogen and sulfur in biological systems, and in the proteinogenic amino acids, S-N bonds are not widely found in biological systems. Indeed, currently, only approximately 100 S-N containing biomolecules are known. Many of these are metabolites, but it is now known that this bond is also exploited in proteins. For instance, protein tyrosine phosphatase 1B reversibly forms a cyclic sulfenylamide to protect its active site cysteinyl from oxidative damage. More recently, however, Type IV Collagen has been found to contain a sulfilimine (S=N) bond crosslink between a methionine (Met93) and a lysine (Lys211) or hydroxylated lysine (Hyl211). Presently, this is the only known such occurrence of this bond in nature. Collagen IV is the most abundant molecular species of the basement membrane and is a critical component of the lamina densa [1], a sub-layer of the basement membrane [2]. In particular, it forms a network that provides a scaffold for other components of the basement membrane [3]. It has been suggested that collagen IV has critical roles in wound healing[4] and embryogenesis [5], while its Improper functioning is associated with several diseases [6,7]. Notably, the sulfilimine crosslink in Collagen IV has been implicated as having played a critical role in evolution. Unfortunately, despite its ubiquitous occurrence and biological importance, much remains unclear or unknown about Collagen IV's sulfilimine bond, including its formation, the impact of involving Lys211 or Hyl211, and its very nature. Indeed, synthetic sulfilimine bonds have been discussed as potential superbases, yet in biological systems it is generally indicated as being neutral. We have applied a multi-scale computational approach to systematically examine the mechanisms by which a sulfilimine crosslink could be formed, and the nature of the resulting bond. In addition, we have examined the impact of the bond forming between Met93 and Lys211 versus Met93 and Hyl211. We will be presenting some of the results we have obtained.

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Enzymatic Processing of Nucleic Acids: From DNA Repair to Gene Regulation

Stacey Wetmore

University of Lethbridge

Many enzymes control the chemistry and biology of modified nucleic acids in cells. For example, DNA modifications arising as damage must be repaired or bypassed for cell survival. Alternatively, enzymes introduce or remove DNA modifications as part of epigenetic regulation or generate modification cascades to impart diverse RNA structures and functions. These biomolecular machines can also be harnessed in medicine and nanotechnology. For example, understanding the function of natural enzymes can inspire the engineering of new proteins to facilitate the production of novel nucleic acid-based biomaterials, while understanding how DNA damage evades repair or bypass can assist developing cancer treatments with greater efficacy. However, critical information about molecular reactions (transition structures, barrier heights) is difficult to obtain from experiments at least in part because key species along reaction pathways are short lived. Indeed, most currently available mechanistic information for enzymes that process nucleic acids has been conjectured from crystal structures or mutagenesis experiments. Therefore, computational chemistry has a unique role to play in characterizing the molecular details of enzyme catalyzed reactions that form and break bonds at modification sites, between nucleobases and sugars (glycosidic bonds), and within phosphodiester backbones, which form the basis of modified nucleic acid chemistry.

With this goal in mind, research in the Wetmore group uses a multipronged computational approach to understand important cellular reactions. Specifically, molecular dynamics (MD) simulations are used to provide information about nucleic acid structure and how repair enzymes bind to a range of modified nucleic acid substrates. Subsequently, combined quantum mechanics–molecular mechanics (QM/MM) methods are used to uncover the details of the catalytic mechanisms. This talk will provide a survey of some of the recent topics of interest in the Wetmore lab related to the enzymatic processing of nucleic acids. The information uncovered is vital for the future design of highly selective and potent small molecule inhibitors for disease management and the design of new enzymes that can process modified nucleic acids as biotechnological tools.

Fitting Potential Energy Surfaces in Sum-of-Product Form: Application to Vibrational Spectroscopy

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The multi-configuration time-dependent Hartree (MCTDH) approach is a powerful tool for studying quantum dynamics, as well as for determining the vibrational states (energies and wavefunctions) of molecules/molecular complexes. However, the efficient use of MCTDH requires the potential energy surface (PES) and kinetic energy operator (KEO) to be represented in sum-of-product (SOP) form. In this talk, I will introduce MCTDH, the reasons for the need for SOP form, and approaches our group has used to fit SOP PESs based upon ab initio data [1-5]. A brief introduction will be given to one approach we have applied for generating SOP PESs using a single layer neural network with exponential activation functions (so-called expNN). We have successfully applied this methodology to developing accurate SOP PESs for HFCO and HONO [1-4]. More recently, we have developed a semi-automatic adaptive sampling and fitting procedure for generating SOP PESs based on a high-dimensional model representation is presented [5]. The adaptive sampling procedure and subsequent fitting relies on energies only and can be used for re-fitting existing analytic potential energy surfaces in SOP form or for direct fits from ab initio computations. The method is tested by fitting ground electronic state potential energy surfaces for small to medium sized semi-rigid molecules, i.e., HFCO, HONO, and HCOOH, based upon ab initio computations at the CCSD(T)-F12/cc-pVTZ-F12 or MP2/aug-cc-pVTZ levels of theory. Vibrational eigenstates are computed using block improved relaxation in the Heidelberg MCTDH package and compared to available experimental and theoretical data. The new potential energy surfaces are compared to the best ones currently available for these molecules (including those from expNN) in terms of accuracy, including of resulting vibrational states, required numbers of sampling points, and number of fitting parameters. The present adaptive procedure leads to compact expansions and scales well with the number of dimensions for simple potentials such as single or double wells. [1] E. Pradhan and A. Brown, J. Chem. Phys. 144, 174305 (2016). [2] E. Pradhan and A. Brown, J. Mol. Spectrosc. 330, 158-164 (2016). [3] E. Pradhan and A. Brown, Mol. Phys. 118, 12 (2020). [4] E. Pradhan and A. Brown, Phys.Chem.Chem.Phys., 19, 22272 (2017). [5] A. Aerts, M.R. Schäfer, and A. Brown, J. Chem. Phys. 156, 164106 (2022).

II.   Poster Presentations

Effects of Dispersion Corrections on the Theoretical Description of Bulk Metals

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Addition of a dispersion correction to standard Kohn-Sham density-functional theory (DFT) is essential for accurate description of non-covalent intermolecular interactions. Several dispersion-corrected density functionals (DC-DFs) have been shown to exhibit remarkable transferability to hard solids at equilibrium conditions. Despite the considerable body of computational development and studies on DC-DFs, their transferability and performance has not been systematically examined for metallic systems at equilibrium or under isotropic compression. In this study, we extensively examine the ability of selected DC-DFs to describe the equations of state (EOS) for selected elemental metals and intermetallic compounds up to several gigapascals of pressure. EOS-derived properties, such as the equilibrium volume (V0), the bulk modulus (B0), and its pressure derivative (B0'), were then evaluated with and without thermal effects and the results compared with experimental reference data. The results of this study establish the optimum dispersion corrections for accurate description of compressed metals.

Modeling Dielectric and Optical Response Properties in Molecular Nanoparticle Doped Metal Oxides

Archita Adluri, Irina Paci, and Brett Henderson

University of Victoria

Understanding dielectric and optical responses of metal-oxides and silicates is increasingly important in multifunctional materials for electronic and optical applications, especially as these materials miniaturize and reach the quantum scale.

Previously we modeled the polarization of molecular-scale silver inclusions in a magnesium oxide matrix on permittivity (dielectric constant κ), using the Modern Theory of Polarization and Car-Parinello Molecular Dynamics (CPMD) in the QuantumEspressso code. The introduction of metal cluster dopants and molecular-scale inclusions (¡30 atoms) in a dielectric matrix provided an opportunity for tunable field-response properties a challenge to accurately model computationally due to electron correlation effects when considering the full electronic and ionic polarization. The quantum properties of these metallic nanoparticles depend strongly on their size and shape, a characteristic that can be exploited in changing the response properties of a material, whereas the small nanoparticle size can help limit the issues of conduction and current leakage.

Here we expand our model to various metal oxides (MgO, TiO2, SiO2 etc..) doped with transition metal molecular nanoparticles (mNP's) inclusions as well as effects of structural changes and oxygen vacancies in the interfacial region. The quantum properties of these metallic nanoparticles depend strongly on their size and shape, a characteristic that can be exploited in changing the response properties of a material. We established several trends as well as identified issues with modeling including quantum of polarization effects and interfacial structural defects.

Comparison of Trajectory Outcomes for H_2 + H_2 using two Potential Energy Surfaces

Abid Afzal and M.E. Mandy

Chemistry Program University of Northern British Columbia

Molecular hydrogen is the dominant molecular species present in the interstellar medium and has an important role in the cooling of shocks that are associated with star formation. The two mechanisms of cooling are collisional dissociation and collisional excitation followed by quadrupole emission. Modelling the role of dissociation in this cooling needs detailed information on the state specific dissociation rate coefficients. The goal of this research is to compare the trajectory outcomes on the Hinde PES with those on the BMKP2 PES to assess whether it is required to do extensive and more expensive calculations on the Hinde PES to determine state specific rate coefficients for dissociation of H_2 + H_2 to supersede those previously determined with the BMKP2 surface.

A molecular simulation study of KDP solution structure: A journey into the unknown

Aradhana Anil and Peter Kusalik

University of Calgary

Potassium dihydrogen phosphate (KH2PO4, abbreviated as KDP) is the blueprint for a set of hydrogen-bonded ferroelectrics. Irrespective of KDP's comparatively simple structure, it has attracted the interest of many theoretical and experimental researchers because of its fascinating properties associated with this hydrogen bond system that features a significant isotope effect. Its unique piezoelectric, ferroelectric, and electro-optic properties are of great importance. Due to their piezoelectric effect, KDP crystals have wide applications in conventional and nuclear weapon fuse, accelerometers, sonar generators antisubmarine detectors, and underwater acoustic transducers. In addition, KDP crystals have also been widely used as a photoelectric material in laser communication. Thus, KDP crystals are an important material across a range of applications in both consumer and high technology fields.

Recent experimental studies have shown some interesting nucleation and crystal growth behavior in supersaturated KDP solutions. Growth of microfibers indicating quasi-one-dimensional growth has been observed and it is shown that one of these microstructures formed has the same molecular structure and symmetry identical to the type lV monoclinic crystal structure that was previously found to exist only under high pressure. In addition, the microstructures formed which are centrosymmetric can produce efficient second-harmonic generation. Although the underlying molecular mechanism responsible for the quasi-one-dimensional growth has not yet been discovered, changes in solution structure have been reported, and pre nucleation clusters and multistep nucleation pathways have been proposed. The ability to grow such microstructures opens the potential application of KDP in micro photonics. Experimental studies to date indicate that a thorough study of the solution microstructure of KDP is essential to understand the underlying mechanism of nucleation and crystal growth from an aqueous solution. It is noteworthy that there are no previous molecular simulation studies reporting the observation of KDP crystal growth or nucleation. Our objective is to reveal how solution structure may impact crystallization behavior while uncovering the fundamental features of the ordering process underlying crystal formation from KDP solution. In this presentation, we will examine several different force-field models for aqueous KDP solutions and will report results for their solution structure. Through comparison with experimental results, we will identify the most suitable model. The models will also be tested for their ability to reproduce the experimental crystal structure. Analysis of ion clusters that appear in supersaturated solutions will also be reported.

Theoretical modeling of atomic layer deposition self-catalyzing precursors for SiO2 thin films

Julien Appleby-Millette Irina Paci, Sofia Donnecke, and Chao-Ming (Elvis) Ting

University of Victoria

Atomic layer deposition (ALD) plays a key role in the formation of high control thin films. A two-step self-limiting process is used for producing high purity SiO2 films. Without a catalyst SiO2 deposition is very slow. Known catalysts for SiO2 deposition are NR3-type compounds which lower the deposition temperature and increase film quality. Binding the catalyst to the precursor helps control the surface orientation and enhances the reaction rates. This work focuses on characterizing deposition using (NMe2)x-Si-(OMe)4-x type catalytic precursors. Surface coordinated geometries are complex for SiO2 due to the large number of DoF which can obscure true minima. Ab initio molecular dynamics (AIMD) and direct dynamics (DD) were used to probe the surface geometries at temperatures of interest for minimization. The gas phase geometries were treated with nudged elastic band (NEB) methods to search the transition state space.

Transport phenomenon in Protic Ionic Liquids: Insights from MD studies

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Protic ionic liquids (PIL) have been interesting in terms of their applications due to moderate - high electrical conductivity and workable viscosity at optimal temperatures. We have previously studied pyridine-acetic acid system (the simplest protic ionic liquid) using ab-initio molecular dynamics (AIMD), where we couldn't reproduce computationally the intriguing conductivity maximum vs mixing ratio known for this system, but were able to explain the maximum by developing a kite-model using the liquid structure observed in the simulations. Currently, we are using molecular mechanics (MM) to simulate the traditional pyridine-acetic acid system, reproduce its conductivity maximum computationally, and further substantiate our kite model proposed earlier. To address a possible effect of delta-pKa on the position of the maximum, we are simulating pyridine-trifluoro acetic acid system for comparison. The recent progresses we made regarding this will be discussed.

Active-Learning Strategy to Search for the Global Minima of Ni-Ceria Nanoparticles: The case of $Ce_{4-x}Ni_xO_{8-x}$ (x =1, 2 ,3)

Lizandra Barrios Herrera[1], Maicon P. Lourenço[2], Jiří Hostaš[1], Patrizia Calaminici[3], Andreas M. Köster[3], Alain Tchagang[4], and Dennis R. Salahub[1]

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Ni-CeO2 nanoparticles (NPs) are promising nanocatalysts for water splitting and water gas shift reactions due to the ability of ceria to temporarily donate oxygen to the catalytic reactions and accept oxygen after the reaction is completed. Therefore, elucidating how different properties of the Ni-Ceria NPs, such as size, composition, and electronic structure, relate to the activity and selectivity of the catalytic reaction is of crucial importance for the development of novel catalysts.

In this work we use machine learning (ML) regression and its uncertainty – an active-learning (AL) strategy – for the global optimization of Ce(y-x)NixO(2y-x) (x=1, 2, 3; y=4) nanoparticles guided by density functional theory (DFT) calculations. The method allows the learned structure-energy relationship to improve iteratively when more data are obtained from DFT calculations of promising structures indicated by the AL.

The progress of the on-the-fly AL method from different independent AL runs are reported. The electronic structure and magnetic properties of the "putative" GM found by AL are analyzed by plots of the density of states, the spin density, the electron localization function and by population analysis, such as Mulliken, and Bader analysis. Additionally, further investigation of the NPs by mass scaled parallel-tempering Born Oppenheimer molecular dynamic (PT-BOMD) resulted in the same GM structures found by AL, demonstrating the robustness of our AL search to learn from small datasets and assist in the global optimization of complex electronic structure systems, such as Ni-Ceria NPs.

Investigating the Antioxidant Activity of Cannabidiol

Zhehan Jia, Paul Bouthillier, Max Walton-Raaby, Tyler Floen, and Guillermo Garcia-Diez

Thompson Rivers University

Cannabinoids have been of recent research interest due to their antioxidant properties, particularly their potential to prevent oxidative stress, which is linked to various diseases and health conditions. This study explores the primary, secondary, and tertiary antioxidant activity of cannabidiol (CBD), the second most abundant cannabinoid in cannabis sativa. The M06-2X or the M06 functional is used combined with the SMD solvation method and the 6-31++G(d,p) basis set. Water and pentyl ethanoate are the solvents considered at physiological pH to simulate hydrophilic and hydrophobic environments.

The primary activity study focuses on the quenching of methoxy and peroxyl radicals by CBD via hydrogen-atom transfer (HAT) reaction, considering all the possible reaction sites of CBD in both water and pentyl ethanoate. Radical-adduct formation and single-electron transfer (SET) reactions are also considered. The rate constants of the exergonic reactions are calculated.

The secondary activity study explores the aqueous CBD complex formation with Cu^{2+} and Fe^{3+} and their subsequent reduction by reaction with the superoxide radical anion or ascorbate. Various coordination numbers and high- and low-spin options are explored. If the SET rate constant for the reduction of these complexes is significantly smaller than that of the reduction of the free metal ions in solution, the subsequent formation of hydroxy radicals during the Fenton reaction of the Haber-Weiss cycle could be inhibited, significantly reducing their damaging effects.

The tertiary activity study focuses on the CBD repair of a damaged leucine as a lateral chain in a protein environment, simulated by N-formyl leucinamide, by HAT reaction. Only the hydroxy hydrogens of CBD, and the repair of the β and δ sites of leucine are considered, as the repair of these sites have produced the highest rate constants in previous studies by our group.

ARC-MOF: A Diverse Database of Over 280,000 MOFs with DFT-Derived Partial Atomic Charges and Descriptors for Machine Learning

Jake Burner, Ohmin Kwon, Marco Gibaldi, Scott Simrod, and Tom K. Woo

University of Ottawa

Metal-organic frameworks (MOFs) are a class of crystalline materials composed of metal nodes or clusters connected via semi-rigid organic linkers. Owing to their high surface area, porosity, and tunability, MOFs have received attention for various applications. One such application is gas separation and storage. Computational methods have been used to expedite design and discovery of MOFs. For example, atomistic grand canonical Monte Carlo (GCMC) simulations have been shown to provide relatively accurate estimates of the gas adsorption properties of MOFs if the structure is known. Notably, these simulations require partial atomic charges for the framework and guest atoms. Ideally, these charges are derived from a DFT calculation. However, such calculations can be computationally expensive for large-scale screening, so empirical partial charge assignment methods are often employed.

In addition to brute-force GCMC screening, machine learning (ML) and other data-driven methods have been used to screen large databases and successfully develop new experimentally synthesized and validated MOFs for CO2 capture. To enable data-driven materials discovery for any application, the first (and perhaps most crucial) step is the curation of a database. This work introduces the ab initio REPEAT charge MOF (ARC-MOF) database. This is a diverse database of over 280 000 experimentally characterized and hypothetical MOFs spanning all publicly available MOF databases. ARC-MOF contains MOFs with DFT-derived partial atomic charges for GCMC screening, as well as pre-computed descriptors for out-of-the-box machine learning applications. An in-depth analysis of the diversity of ARC-MOF with respect to the currently mapped design space of MOFs was performed – a critical, yet commonly overlooked aspect in past publications of MOF databases. Using this analysis, balanced subsets from ARC-MOF for various machine learning purposes have been identified. Other chemical and geometric diversity analyses are presented, with an analysis on the effect of charge assignment method on GCMC simulated gas uptakes in MOFs.

Chirality in helical packings of confined hard spheres

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Hard spheres confined to narrow, quasi-one-dimensional channels have been shown, in experiment [1] and simulation studies [2,3], to spontaneously form structures not observed in the bulk, such as single, double and triple helices, depending on the diameter of the channel. These helices are inherently chiral, despite being formed from non-chiral substituents, and the chirality of the perfect structures can be easily described in terms of their right hand (P) and left hand (M) twist directions. However, the presence of defect pairs in the helix that locally reverse the twist direction [4] complicate the identification of chiral structures. This work explores the use of geometric chirality measures for the identification of chirality and shows that the concentration and distribution of the defects has a significant effect.

Right-handed Helix   Left-handed Helix   Helix with defects
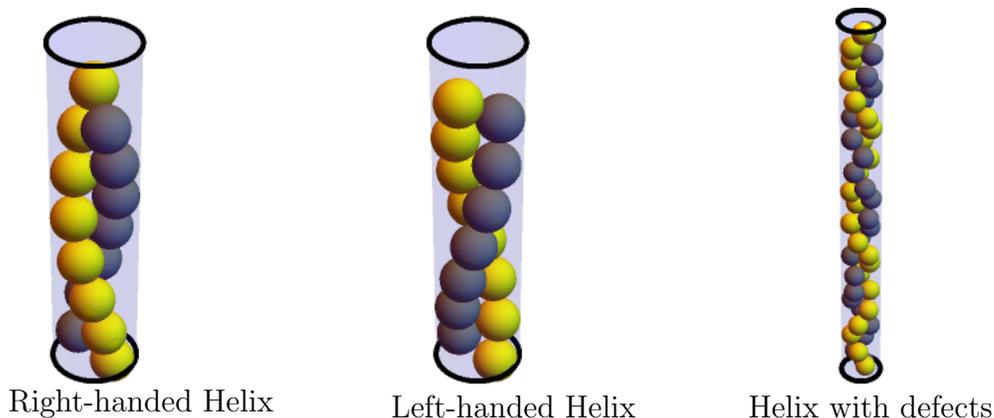
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Can We Discover (and Define) Directional Molecular Interactions Directly from Molecular Dynamics Data?

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Directional intermolecular interactions play a key role in many physical and biological processes. In particular, hydrogen bonds play a central role in protein-ligand binding [1] and in maintaining the stable secondary structure of proteins. But what is a hydrogen bond? Can we discover the presence of hydrogen bond, and define the characteristic features of hydrogen-bonding interactions, directly from data? To elucidate hydrogen bonding, we analyze liquid-phase molecular dynamics trajectories to discern highly probable directed intermolecular interactions. Our approach clusters high-dimensional data using kernel density estimation and gaussian processes, then dimensionality reduction to find a geometric parameterization for hydrogen bonding. The proposed approach is validated by revealing the FH...F bond in hydrogen fluoride and the OH...O bonds in water and methanol. Equilibrium geometries of dimers in the studied systems are found to be consistent with results available in the literature. The average lifetime of the OH...O type hydrogen bond and its temperature dependence are determined, and found to be consistent with results from inelastic neutron scattering experiments. [1] R. Ferreira de Freitas and M. Schapira, "A systematic analysis of atomic protein–ligand interactions in the PDB," Med. Chem. Commun., vol. 8, no. 10, pp. 1970–1981, 2017, doi: 10.1039/c7md00381a.

Poisoning density functional theory with benchmark sets of difficult systems

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Large benchmark sets like GMTKN55 [1] let us analyse the performance of density functional theory over a diverse range of systems and bonding types. However, routine calculation of over 1500 relative energies and 2500 single point energies is (a) a costly and (b) can potentially obscure large errors through averaging, giving a false sense of security. Previous work developed the 'Diet' benchmark sets consisting of 30, 100, and 150 relative energies, which is capable of reproducing the key results of the full GMTKN55 database, addressing point (a). [2] This work introduces the 'Poison' benchmark sets, consisting of 30 relative energies and representing some of the most difficult-to-model systems in the GMTKN55 database, addressing point (b). [3] Discussion will focus on the results of these poison benchmark sets, which show that general GMTKN55 rankings are not necessarily consistent with poisoned rankings. These suggest that common benchmarking strategies may need to be revisited when modelling difficult chemical systems.

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The pan-Canadian Computational Chemistry Course (PC4) Program: A collaborative approach to training graduate students in applied computational chemistry

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Canada has a strong and close-knit theoretical and computational chemistry community in its university system. The community is small - on average, one faculty member per department per university - in comparison to other sub-disciplines in chemistry, and this makes it difficult for individual chemistry departments to offer robust computational training programs at the graduate level. The PC4 project is a collaborative approach to address this important gap in computational chemistry training at the graduate level. The project gathers faculty from institutions across Canada with the aim of developing and delivering graduate-level applied computational chemistry courses. In addition to creating a standard, high-quality, and sustainable training program in the field, students are expected to benefit from an experience that goes beyond the single instructor/single institution model and exposure to a wide the latest research. We expect the PC4 model to be extendable to students outside of Canada, thereby addressing the UN Sustainability Goals 4 and 10, Quality Education and Reduced Inequalities. This presentation will outline our approach to the PC4 project and some of the challenges we encountered.

Benchmarking computational approaches for predicting performance of high spin metal systems during oxygen reduction

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University of Victoria

The design of platinum-group-metal free catalysts for the oxygen reduction (ORR) is an active area of research in the renewable energy industry. Using quantum chemistry calculations to model the ORR of new non-precious metal catalysts has the potential to expedite their design, however there are still significant challenges when simulating these systems. Accurate capturing the energetics for the reaction of oxygen with transition metals - containing, particularly square-planar Metal-N-C (MNC) catalysts, is challenging. Primarily, this is due to the high multiplicities of such systems, as well as large electron correlation energies during bond formation and breaking. We benchmark the four-electron pathway across a number of small molecule and periodic MNC-catalysts using varying levels of theory. We explore tradeoffs between system size and the computational method used. The value of ab-initio molecular dynamics in predicting reactivity and whether experimental performance can be predicted by simulation in meaningful ways will also be discussed.

Modelling the Repair of Protein Radicals by Phenolic Antioxidants

Tyler Floen, **Max Walton-Raaby**, and Nelaine Mora-Diez

Thompson Rivers University

Oxidative stress is a biological process that has been linked to many diseases; hence, understanding its prevention and repair is essential in medicine. This study focuses on the repair of damaged leucine as a lateral chain in a protein environment simulated by N-formyl leucinamide by a group of 13 phenolic antioxidants with a single reaction site. Hydrogen atom transfer (HAT) and single electron transfer (SET) were the repair reactions studied thermodynamically and kinetically at the M06-2X(SMD)/6-31++G(d,p) level of theory in pentyl ethanoate and water at physiological pH. These solvents simulate the lipidic and aqueous media that a damaged protein may be exposed to.

The SET repair reactions were very endergonic and had small rate constants, which indicates their lack of biological relevance. This result is also influenced by the high aqueous pKa values of these antioxidants. All HAT reactions were very exergonic and, in general, it was found that the more exergonic the reaction the larger its rate constant, as stated by the Bell-Evans-Polanyi principle. However, for several repair reactions this principle was violated, which shows the need for computational kinetics studies to properly assess the tertiary antioxidant activity of a species.

The rate constants for the HAT repair reactions were found to be $\delta > \beta > \gamma$. From these results, the antioxidant activity of 7 polyphenolic compounds was also investigated by considering the fastest repair reaction found (the δ HAT repair in pentyl ethanoate). Some of the HAT reactions studied had rate constants in the diffusion limit which indicates their biological relevance.

Calculating the Aqueous pKa of Phenols: Predictions for Antioxidants and Cannabinoids

Max Walton-Raaby, Tyler Floen, Guillermo Garcia-Diez, and Nelaine Mora-Diez

Thompson Rivers University

Aqueous pKa values are essential for understanding the behaviour of chemical species, such as those used as drugs, in buffer systems, or to study enzyme performance and antioxidant activity. Phenolic compounds play important roles in these applications; however, there are limited experimental aqueous pKa values reported. In this study, three calculation schemes, five functionals (M06-2X, B3LYP, BHandHLYP, PBE0, TPSSTPSS), and two solvent models (SMD and IEFPCM) are used to predict pKa values using a set of 15 phenols to evaluate the accuracy of these predictions. Nitrophenols were not predicted well in any scheme, hence mean absolute errors (MAE) were calculated including and excluding these molecules. The best performance (with a MAE of 0.46 pKa units excluding nitrophenols) was achieved at the M06-2X(SMD)/6-311++G(d,p) level of theory using the acid-base equilibrium: HA + Ref- $\rightleftharpoons$ A- + HRef, where HRef is the reference acid used (phenol). Two other functionals, B3LYP(SMD) and BHandHLYP (SMD), were quite similar in performance with MAE of 0.57 and 0.55 pKa units, respectively (excluding nitrophenols). Aqueous pKa predictions were performed for a set of 13 phenolic antioxidants, and 10 pharmaceutically interesting phenolic cannabinoids. These 23 molecules are the subject of kinetic studies by our group for which their aqueous pKa values are needed.

Complexes of Copper and Iron with Aminoguanidine, Pyridoxamine, Ascorbic Acid, and a Model Amadori Compound: Exploring Secondary Antioxidant Activity

Guillermo García-Díez[1], Roger Monreal-Corona[1], Rafael Ramis[2], Nelaine Mora-Diez[1]

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Glycation is a natural process in which sugars in the bloodstream attach to various nucleophilic molecules which are present in the body. Amadori compounds are formed in this reaction, which may then further react and become advanced glycation end-products (AGEs). These can have deleterious effects on health. This process can be halted by scavenging carbonyl and radical species, and chelating metal ions, such as Cu(II) and Fe(III). Several molecules have been tested as potential glycation inhibitors, such as pyridoxamine (PM) and aminoguanidine (AG). It is expected that these molecules will hinder the formation of AGEs if they coordinate to copper and iron more strongly than Amadori compounds. In a set of investigations, we decided to explore the stability of the complexes PM and AG form with the aforementioned metal ions, as well as complexes with ascorbic acid (ASC) and a model Amadori compound (AMD). In all cases we employed the M05(SMD)/6-311+G(d,p) level of theory. Acid-base properties and physiological pH were always considered. We found that PM forms the most stable compounds with both metal ions, followed by AMD, and then AG and ASC. This agrees with experimental research, as only PM can prevent the formation of AGEs. Moreover, the Fe(III) complexes proved to be much more stable than the Cu(II) complexes when PM was the ligand, but the contrary was true when considering AG.

Furthermore, we also explored the secondary antioxidant activity of both AG and PM, considering the most stable complexes with Cu(II) and Fe(III). A compound is said to present this activity if it can coordinate to Cu(II) or Fe(III) and slow down the rate constant of the first step of the Haber-Weiss cycle. In this reaction, any of these two metal ions reacts with either the superoxide radical anion or the ascorbate anion. We found that the most stable complexes of AG with Cu(II) and Fe(III) can slow down the first step of the Haber-Weiss cycle when the reductant is ascorbate. In the case of the superoxide anion, AG did reduce the rate constant when considering Cu(II), albeit to a much lesser degree. However, this is not the case with Fe(III). On the other hand, PM did present strong antioxidant activity, even when the reducing agent was the superoxide radical anion. Once again, this is in agreement with experimental data, as both AG and PM can prevent the oxidation of ascorbic acid in the presence of Cu(II) and Fe(III). Thus, at physiological conditions, PM will preferentially form complexes with Fe(III), and AG with Cu(II). When PM is present at sufficiently high concentrations, the most stable complexes will be formed, and this molecule will show its secondary antioxidant activity. This collection of work sets the way for future studies with potentially new drugs to inhibit glycation. [1-3]

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Predicting the aqueous pKa of benzimidazoles and opioids

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The acid-base properties of a molecule determine many of its physicochemical and biological characteristics, such as solubility and rate of absorption. The extent to which a molecule will be protonated or deprotonated can be determined by means of its pKa. Thus, this value is of paramount importance when considering the pharmacology of a given compound. We decided to revisit a series of studies which Brown et al. [1,2] did on the acid-base properties of benzimidazoles. They made use of several approaches to correctly predict the pKa values of these molecules, backing up the results with experimental data. First, they employed different acid-base equilibria, but for much better results a quantitative structure-properties relationship (QSPR) equation was derived, where a set of descriptors is related to known properties of the compounds that are being explored. They came up with an equation which properly predicted the aqueous pKa values of simple benzimidazoles. Given that since the publication of these results new experimental values for the pKa of benzimidazoles have appeared in the literature, we have decided to test once again the equation, and improve it in case it failed.

Following the previous procedure, we also decided to study the possibility of predicting the aqueous pKa of opioids. Recently, Alexander et al. [3] published their work on fluorinated derivatives of morphine. It has been shown that reducing the pKa of opioids could diminish their side effects, as these would selectively target inflamed tissues, which have a lower pH (6-6.5). Placing fluorine atoms close to the basic nitrogen would lower its pKa value. We thought that it would be of interest to devise a method to properly predict the pKa of opioids, so that new fluorinated analogues could be screened before being synthesized. Various pKa predicting approaches are tested using experimental values found in the literature to be able to predict new fluorinated opioids able to better target inflamed tissues.

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Do you know where your protons are? Identifying structural errors in experimental structures towards the development of chemically realistic building blocks for HT screening of MOFs.

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Interest has grown immensely for the application of metal organic frameworks (MOFs) in numerous gas adsorption and separation processes, such as CO2 capture. High throughput computational screening of MOFs for these processes is now commonplace. For this purpose, several databases of experimentally characterised MOFs have been developed that contain tens of thousands of structures that have been 'cleaned' for computational screening. The potential material pool has expanded even further towards the range of millions of structures with the introduction of hypothetical MOF (hMOF) databases. Nearly all hMOF structures are generated using combinations of structural building units (SBUs) extracted from experimental MOFs, which have been found to contain high rates of structural errors (i.e. excluded protons, disordered atoms, improperly labelled framework charges, etc.). Undetected errors pose a considerable threat to the accuracy of results obtained by previous— and future— MOF screenings as they completely alter the system being studied during periodic DFT calculations (i.e. different number of electrons, nuclei, etc.). This work introduces a manual investigation effort aiming to identify common errors present in hMOF structures and study how these errors influence electrostatic potential fitted charges and GCMC-simulated gas adsorption properties. A novel repair protocol was developed to generate a library of over 1500 'HEALED' SBUs that are ideal for the generation of chemical accurate hypothetical materials. This library represents one of the largest collections of SBUs in the field to date, and it represents an important step towards improving the reliability of HT hMOF materials screenings.

Thermodynamics and inherent structure landscapes of confined k-next nearest neighbour lattice fluids.

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The way particles pack together into jammed, mechanically stable structures, known as inherent structures, has implications for the thermodynamic, structural and dynamic properties of fluids, glasses and athermal granular systems. However, analytical results for packing problems in bulk, continuous systems are challenging and few exact results are known. Confining the system to narrow quasi-one-dimensional channels simplifies the packing problem and opens up the possibility of obtaining analytical results. It also introduces a new length scale that leads to the stabilization of packing environments not observed in bulk systems. This work develops a confined k-next nearest neighbour lattice model, the lattice version of hard spheres in the continuum, where the transfer matrix method is used to develop exact results for the thermodynamic properties of the fluid, as well as the inherent structures. The nature of the packings in confinement and the density distribution of inherent structures is examined as a function of the confining channel diameter.

Proof-of-concept for a loss-free excitonic quantum battery

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In a world where the role of quantum technologies is rapidly increasing, the need for nanoscale energy storage devices is crucial. One of the promising candidates is the so-called quantum battery (QB) – a quantum system capable of storing and discharging energy. Over the past several years, there has been a great deal of theoretical work on developing practical architectures for QBs. One of the main obstacles in developing a robust QB is the leakage of stored energy from the QB to its environment. To overcome this obstacle, our group recently proposed an architecture consisting of a network of identical atoms with exchange symmetries, which supports the existence of symmetry-protected dark states – states in which the QB is decoupled from its environment [1]. It was shown that when excitation energy is stored in these states, the QB is loss-free (see Figure 1). On the other hand, when the symmetry is broken by attaching another thermal bath, for example, the QB begins to discharge its stored excitation energy (see Figure 1). These results offer a promising strategy for constructing QBs capable of operating efficiently in thermal environments.
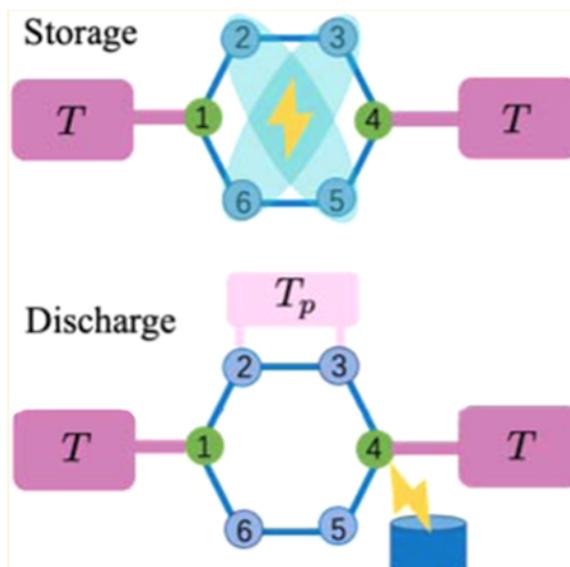

Figure 1: Para-benzene-like network model of an excitonic QB in the storage phase (top) and discharge phase (bottom). T and T_p denote the temperatures of the thermal baths and symmetry-breaking bath, respectively.

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The Dynamics of SERS Substrates and the Formation of Hotspots and Picocavities

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Single molecule surface enhanced Raman spectroscopy (SM-SERS) sees spikes in the intensity of the signal which has been attributed to hotspots and picocavities where intense localized electromagnetic fields can be found. Recently, it has been shown that substrate reconstruction is linked to the formation of hotspot and picocavities indicating that the SERS substrates are not as static as previously perceived. In this paper we use DFTB+ to simulate picocavities in order to explore the factors that affect the substrate dynamics. The simulations were run using two hemispheres made of gold that were either 8, 9, or 10 Å in radius that were placed at varying distances from 3.0-10 Å with either 2, 4, or 6 thiols placed between the two hemispheres. Each system was run at 300 or 500 K. Through over a 100 different simulations temperature and adsorbate density were the biggest contributing factors to substrate reorganization. The two factors worked concurrently to create nanostructures on the surface of the gold SERS substrate that was simulated. Higher temperatures caused the substrate to reorganize at a faster rate but also increased the extent to which the substrate would reorganize. Adsorbate molecules would pull up certain atoms to create adatoms, with an increased density of adsorbate molecules adatoms and nanostructures would form more frequently. Distance between the two gold surfaces affected solely the ability of adatoms from one surface to be transferred to the other surface. During the simulations it was also observed there was a drive to reach a stable equilibrium structure which could be mitigated with increased temperature and adsorbate density due to creating a shallower potential energy surface (PES) on the substrates. These simulations demonstrate the dynamic nature of SERS substrate and the advantage of using simulations in order to study these anomalies.

Dielectric Metal/Metal Oxide Nanocomposites: Modeling Response Properties at Multiple Scales

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High-$\kappa\mp$ dielectrics are important materials for dynamic memory devices, CMOS gate dielectrics, and energy storage in high energy density capacitors. Adding polarizable inclusions to these materials can enhance and increase tunability of their static dielectric constant by the adjustment of the composition, size, and loading of inclusions. Continuum methods such as dielectric mixing formulas and finite element analysis offer some predictive power for matrix-inclusion composites, but cannot be directly applied to composites with small inclusions, for which quantum and interfacial effects dominate. Here, we develop an adjustable finite element approach to calculate the permittivities of composites consisting of a metal-oxide matrix with nanometer-scale silver inclusions. The approach involves defining an appropriate continuum inclusion and interfacial layer based on the electronic structure of the material and solving the Laplace equation with appropriate boundary conditions. We demonstrate that the model can capture many of the relevant polarization effects in a metal/metal oxide nanocomposite, including those that contain arbitrarily-small inclusions, at a fraction of the computational cost of performing the full quantum mechanics.

Two-electron density functional for electron correlation

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A correlation energy functional based on the introduction of the electron-electron coalescence cusp to the two-electron density is derived. The development of a functional based on the two-electron density, rather than the on-top density or the one-electron density, allows for an accurate assessment of the shape and width of the so-called "correlation hole" along with the errors associated with using alternatives to the two-electron density. Furthermore, such a functional completely avoids double-counting of electron correlation when applied to a two-electron density from a multireference wave function. The functional is evaluated on prototypical systems exhibiting different forms of correlation, including the helium atom, hydrogen clusters, and stretched bonds in a variety of molecules. The improvements over one-electron and on-top density functionals will be discussed along with details of the practical implementation and scaling with system size.

Computational investigations into one- and two-photon absorption properties of Super-Folder Green Fluorescent Protein containing an amino-substituted non-canonical chromophore

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In both one- and two-photon bioimaging, fluorescent proteins are now commonly used. While many have been designed/engineered to have different photophysical properties, such as absorption/emission wavelength, brightness, or decreased phototoxicity/photobleaching, research continues on new variants. One promising track of research is to investigate beyond the 20 canonical amino acids to incorporate non-canonical amino acids into fluorescent proteins.[1,2] One example is the work accomplished by Zhang and Ai[3] where they demonstrate the capability of an amino-substituted tyrosine residue to perform a green-to-red conversion of the absorption spectra of various green fluorescent proteins. In the present work, strategies to red-shift superfolder Green Fluorescent Protein (sfGFP) are presented. To accomplish this task, time-dependent density functional theory is used to benchmark the photophysical properties of both the neutral and anionic forms of the canonical and non-canonical chromophores in isolation. We then apply Quantum Mechanical/Molecular Mechanical (QM/MM) approaches to determine the photophysical properties of sfGFP. Analogous QM/MM computations on the amino-tyrosine substituted chromophore in sfGFP are performed to examine the differences between the neutral and anionic chromophore, Z and E isomers, the barrier to isomerization, as well as the role of nearby residues and waters on the photophysical properties. (1) Salem, M. A.; Twelves, I.; Brown, A. Prediction of Two-Photon Absorption Enhancement in Red Fluorescent Protein Chromophores Made from Non-Canonical Amino Acids. Phys. Chem. Chem. Phys. 2016, 18 (35), 24408–24416. https://doi.org/10.1039/c6cp03865d. (2) Rossano-Tapia, M.; Olsen, J. M. H.; Brown, A. Two-Photon Absorption Cross-Sections in Fluorescent Proteins Containing Non-Canonical Chromophores Using Polarizable QM/MM. Front. Mol. Biosci. 2020, 7 (June). https://doi.org/10.3389/fmolb.2020.00111. (3) Zhang, S.; Ai, H. Wang. A General Strategy to Red-Shift Green Fluorescent Protein-Based Biosensors. Nat. Chem. Biol. 2020, 16 (12), 1434–1439. https://doi.org/10.1038/s41589-020-0641-7.

The Intermolecular Interactions of Pyrene and its Oxides in Gas Phase and in Toluene Solution

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In this work, the Conformer-Rotamer Ensemble Sampling Tool, (CREST) with the underlying semi-empirical GFN2-xtb method was used for automated geometry explo- ration of the homodimers of pyrene, pyrene-4,5-dione, and pyrene-4,5,9,10-tetraone, along with the heterodimer of pyrene and pyrene-4,5,9,10-tetraone. Geometries and energies of the dimers were further refined at the ωB97X-D4/def2-TZVP level of theory, both in gas phase, and in toluene solution. Computations in solutions were handled using the CPCM (Conductor-like Polarizible Continuum Model) and SMD (Solvation Model based on Density) models. Two previously unidentified pyrene-homodimer con- formations are identified, and the effects of oxidation on the geometries and energies of dimerization are explored; in general, oxidation leads to stronger intermolecular interac- tions, and decreased solubility in toluene. For selected dimers, DLPNO-CCSD(T)/cc- pVTZ/SMD(Toluene) energies are determined at the DFT geometries, and illustrate the accuracy of the ωB97X-D4 approach, with an MAD of 1.47 kJ/mol.

Process level optimization of materials for CO2 capture using multi-scale and machine learning accelerated simulations

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CO2 capture technologies are being explored to reduce greenhouse gas emissions. Solid adsorbent-based processes using porous materials are emerging as an alternative to current energy intensive solvent-based processes. The challenge is to find the right material that can minimize the energy and cost of CO2 capture. Here, metal organic framework (MOF) materials have attracted the most attention due to their chemical diversity and tunability. Researchers have computationally screened hundreds of thousands of MOFs and put forward promising candidates based solely on their equilibrium adsorption properties without knowing how these properties relate to the performance of the adsorbent at the process scale. In order to determine this, one must perform detailed, macroscopic process simulations on a specific gas separation process. In this work, multi-scale modeling that combines atomistic simulations and detailed process simulations was used to optimize materials for CO2 capture in a four-stage pressure swing adsorption system. Machine learning models were developed to accelerate both the atomistic simulations and the process modelling to achieve a practical scheme to optimize the composition and structure of a MOF that minimizes the energetic cost of CO2 capture (or other performance indicators). A previous screening of experimentally characterized MOFs that took over a year to complete identified a MOF with an energy of CO2 capture as low as 217 kWh/MT CO2. Using our new accelerated workflow, hundreds of MOFs have been identified with energies of less than 200 kWh/MT CO2 within a few days.

Robust Machine Learning Models for DFT Quality Atomic Partial Charge Predictions in MOFs

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As an important class of porous materials, MOFs have gained increasingly more interest due to their tunability and to their exceptional gas adsorption properties for gas storage and separation applications. Numerous high-throughput virtual screening (HTVS) studies have been performed that rely on atomistic Monte Carlo simulations to predict each material's gas adsorption properties. The quality of these predictions relies on the partial atomic charge parameters used for the MOF framework atoms. For this purpose, DFT derived electrostatic potential fitted charges are best, but these require a full periodic DFT calculation of the MOF, which comes at a heavy computational cost. To overcome this bottleneck, we have developed rapid machine learning models to predict partial atomic charges in MOFs. Importantly the models were trained on a large and diverse database of approximately 300K MOFs for which periodic DFT calculations have been performed providing charges on tens of millions of atoms. Different descriptors and the combinations of them as the input for the machine learning models were explored. These descriptors describe the atomic environments for each atom within the MOF, including atomic-property-weighted radial distribution functions, atom-centered symmetry functions, chemical-bonding-based average properties, accessible area of the atom, etc. Several machine learning methods have been explored, including graph neural networks, multilayer perceptron neutral networks, and decision-tree based models. The models can produce charges with a MAD of 0.05 e- compared to the DFT charges for most elements and can do so for a whole MOF in mere seconds.

Conservative potentials for a lattice-mapped, coarse-grain scheme with fuzzy switching functions

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Coarse-grained (CG) models reduce the number of degrees of freedom in a system, allowing the dynamics of large systems to be studied for longer times. Many CG models have been developed since the way of generating a CG system highly depends on the question one is interested in. It is common to treat one or multiple molecules as one CG bead by their center of mass. However, this way fails to study non-bonded particles since the motion of free particles disperses them and disintegrates the cluster. The conservative potentials, arising from CG mapping schemes[1] for non-bonded atomistic particles, are studied. These schemes map atomistic particles to fluid element-like cells whose centers lie on a regular, cubic lattice. Equilibrium atomistic molecular dynamics trajectories for a liquid and gaseous Lennard-Jones fluid are converted to CG ones, from which CG probability distribution functions are calculated. We extend the past work[2] by applying fuzzy switching functions at the boundary regions of subcells. Atomistic particles are shared by multiple subcells and produce a continuous change to CG mass elements when they cross the boundary of subcells. A full mass matrix is required to describe the behaviour of the CG potential. As the boundary gets fuzzier, we observe a transition from discrete to continuous distributions for diagonal mass elements. This transition produces a quantitative measure to when continuum theories like fluctuating hydrodynamics are appropriate to describe the system. Non-zero correlations among all CG variables are calculated, and found to depend strongly on the degree of fuzziness. In particular, those for the diagonal mass elements decrease in magnitude and there exists a specific value of the fuzziness for which the correlations are zero. Other correlations are strong only when the fuzziness is quite large, so there is a tradeoff between the complexity of the interactions in the system and the degree of fuzziness between the subcells. However, if the number of particles in a subcell is large enough, and the fuzziness is moderate, the CG potential is found to be well-approximated by a generalized, quadratic function. For a homogeneous system, a few unique parameters are needed to reconstruct the CG potential. These potential parameters can also be evaluated from theory using atomistic particle distribution functions. [1] Lynn, H.; Thachuk, M. Equations of motion for position-dependent coarse-grain mappings obtained with Mori-Zwanzig theory. J. Chem. Phys. 2019, 150, 024108. [2] Luo, S.; Thachuk, M. Conservative Potentials for a Lattice-Mapped Coarse-Grained Scheme. J. Phys. Chem. A 2021, 125, 6486-6497.

Volumetric effect of amino acid substitution in pressure-adapted deep-sea proteins revealed through molecular dynamics simulations

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The effect of pressure on chemical equilibria is determined by the reaction volume ΔV defined as the difference in partial molar volume between the product V_P and reactant V_R states and determined experimentally as the pressure derivative of the Gibbs energy of reaction. $\Delta V = V_P - V_R = \frac{\partial \Delta G}{\partial p}$ Equilibria with negative ΔV will favour the product state upon application of pressure, whereas equilibria with positive ΔV will favour the reactant state. Protein denaturation is a process with a negative ΔV, which means that increased pressure typically results in dissociation of protein subunits, local conformational changes or even large-scale unfolding. Despite this, there are many marine organisms that thrive in the high pressure environment of the deep sea, thanks to evolutionary adaptations that stabilize their proteins against the denaturing effect of pressure. One example is the enzyme lactate dehydrogenase (LDH), which has been observed to have 21 amino acid substitutions in the deep sea fish Coryphaenoides armatus, compared with the shallow-water fish Gadus morhua.[1] However, the mechanics of how these substitutions contribute to high-pressure stability in C. armatus are unknown. One of the possible mechanisms an increase in the ΔV of denaturation, disfavouring the denatured state at high pressure. Insight into the volumetric properties of these amino acid substitutions may be beneficial for the development of enzymes that can catalyze reactions under high-pressure. We used the molecular dynamics-based Archimedean Displacement technique[2] to investigate the effect of amino acid substitution on the denaturation ΔV of LDH. The volume of the protein is taken to be the difference in volume between a simulated system of solvent containing the protein and a simulated system containing the same quantity of solvent without the protein. Since LDH is a tetramer, denaturation can occur through two mechanisms: dissociation of the monomer subunits or complete unfolding of the protein. Here, we present results for the $\Delta \Delta V$ of each denaturation mechanism in pure water, as well as in the presence of the stabilizing agent trimethylamine-N-oxide.

[1] A. A. Brindley et al, PLoS ONE, 3, e2042(2008) [2] H. Wiebe et al. J. Phys. Chem. C 116, 2240–2245 (2012)

Volumetric effect of amino acid substitution in pressure-adapted deep-sea proteins revealed through molecular dynamics simulations

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The effect of pressure on chemical equilibria is determined by the reaction volume ΔV defined as the difference in partial molar volume between the product VP and reactant VR states and determined experimentally as the pressure derivative of the Gibbs energy of reaction. $\Delta V = VP - VR = \partial \Delta G \partial p$ Equilibria with negative ΔV will favour the product state upon application of pressure, whereas equilibria with positive ΔV will favour the reactant state. Protein denaturation is a process with a negative ΔV, which means that increased pressure typically results in dissociation of protein subunits, local conformational changes or even large-scale unfolding. Despite this, there are many marine organisms that thrive in the high pressure environment of the deep sea, thanks to evolutionary adaptations that stabilize their proteins against the denaturing effect of pressure. One example is the enzyme lactate dehydrogenase (LDH), which has been observed to have 21 amino acid substitutions in the deep sea fish Coryphaenoides armatus, compared with the shallow-water fish Gadus morhua.[1] However, the mechanics of how these substitutions contribute to high-pressure stability in C. armatus are unknown. One of the possible mechanisms an increase in the ΔV of denaturation, disfavouring the denatured state at high pressure. Insight into the volumetric properties of these amino acid substitutions may be beneficial for the development of enzymes that can catalyze reactions under high-pressure. We used the molecular dynamics-based Archimedean Displacement technique[2] to investigate the effect of amino acid substitution on the denaturation ΔV of LDH. The volume of the protein is taken to be the difference in volume between a simulated system of solvent containing the protein and a simulated system containing the same quantity of solvent without the protein. Since LDH is a tetramer, denaturation can occur through two mechanisms: dissociation of the monomer subunits or complete unfolding of the protein. Here, we present results for the $\Delta\Delta V$ of each denaturation mechanism in pure water, as well as in the presence of the stabilizing agent trimethylamine-N-oxide.

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Quasiresonant energy transfer in $H_2(v,0)$ + $H_2(v',0)$

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Energy transfer in molecular hydrogen plays an important role in the cooling of shock fronts in star-forming regions of the interstellar medium. Because shocked gas is far from equilibrium, state-specific information is required. To date, full dimensional quantum calculations are feasible only for collisions involving only low (v,j) states lying below 1 eV of internal energy. Yet cross sections are needed for energy transfer involving states with higher internal energy. These are not currently accessible through quantum calculations and must be obtained by other methods such as quasiclassical trajectories.

Quasiresonant energy transfer occurs when internal energy is preserved in a collision with redistribution among internal degrees of freedom. In this study, quasiclassical trajectories were carried out on two potential energy surfaces for the $H_2 + H_2$ system to examine how well collisional outcomes conform to the energy gap law. Transitions of the type $H_2(v,0)$ + $H_2(v',0) \rightarrow H_2(v+1,0)$ + $H_2(v'-1,0)$ or $H_2(v-1,0)$ + $H_2(v'+1,0)$ are examined as a function of collisional energy Deviations from the exponential gap law are expected due to the anharmonicity of H_2 and the accessibility of the rotational degrees of freedom. This is explored as a function of collisional energy and initial vibrational states. Insights gained may be used to estimate cross sections for transitions of interest.

The two six-dimensional potential energy surfaces used are the Hinde and the BMKP2 surface. The former is believed to be more accurate with respect to weak interactions., while the latter is a global surface which does not break down for large vibrational excitation. Results from calculations on both potentials will be compared.

Modeling the Vanadium Dioxide Metal-Insulator Transition Using Local Minima of the DFT+U Formalism

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The DFT+U method is frequently employed to improve the first-principles description of strongly correlated materials. However, it is prone to deliver metastable electronic minima as in some cases different self-consistent electronic structure solutions are obtained depending on the initial occupation choice in the strongly correlated orbital space. While these local minima of the DFT+U method are often considered as computational artifacts, their physical meaning and relationship to true excited states remains unclear. We investigated the possibility of theoretically modeling transformations in the solid state which require thermal or optical excitations of electrons by taking into account the metastable states of the computationally undemanding DFT+U formalism on the example of the VO2 metal-insulator transition. Vanadium dioxide is well-suited as model system due to its distinct change in V d orbital occupations during its metal-insulator transition which can be used to manipulate the resulting electronic structure. We find the total DFT+U energy of VO2 to have a pronounced multi-minima character with strongly varying electronic structure characteristics and relative phase stabilities between the occurring local minima which can be sampled by choosing different initial V d orbital occupations. These local minima lie on different electronic potential energy surfaces and ionic relaxation results in different structures which can be assigned to VO2 high- and low-temperature phases, as well as other metastable phases, matching experimental literature. The identified metastable electronic states can hence be used to model the collapse of the VO2 band gap at elevated temperatures, upon photoexcitation, or during other phase transformations between semiconducting VO2 phases. Our results suggest that local DFT+U minima can indeed carry physical meaning while they remain underreported in theoretical literature on transition metal oxides like VO2. Tuning the U parameter to obtain multiple minima with the DFT+U approach can also potentially allow to model excitations in other suitable solid-state systems at much lower computational cost compared to e.g. time-dependent DFT, while providing decent agreement with experiment.

Tracing the physico-chemical mechanism of pressure resistance in deep-sea proteins using alchemical free energy calculations

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Biological systems are very sensitive to the pressure of their environment. For example, high hydrostatic pressure can lead to the denaturation of proteins, which is incompatible with life. Despite this, deep-sea organisms thrive in a high pressure environment due to evolutionary adaptations that allow them to resist the denaturing effects of pressure. One example of such an adaptation is amino acid substitutions in their proteins, which have been observed in many species of deep-sea organisms.[1,2] However, the molecular mechanism by which these amino acid substitutions grant pressure-resistance is currently unknown. One explanation is that these substitutions result in an overall stabilization of the folded state over the pressure-denatured state, resulting in an increased ΔG of unfolding and a less favourable process.

In this work, the pressure-resisting effect of amino acid substitutions was studied on the enzyme lactate dehydrogenase from two related species: the Atlantic cod Gadus morhua, and a deep-sea fish, Coryphaenoides armatus. Twenty-one amino acid substitutions have been found in Coryphaenoides armatus lactate dehydrogenase compared with the Gadus morhua protein,[1] and these substitutions consist of a mixture of exposed, buried, nonpolar and polar residues. Alchemical free energy calculations were performed in order to calculate the effect each substitution had on the thermodynamics of unfolding. Here we present our findings, which indicate that thermodynamic stabilization of pressure-resistant proteins at high pressure occurs as a result of changes in interaction with the solvent water.

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A DFT study of the nitrous oxide functionalization for the preparation of triazolopyridine and triazoloquinoline scaffolds

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The functionalization of nitrous oxide for the synthesis of triazolopyridines and triazoloquinolines, which are useful building blocks for heterocycle synthesis, was reported by Severin et al. in 2021.[1] The reaction was performed in two steps: the first consisting of the lithiation of 2-alkylpyridine and 2-alkylquinoline derivatives, and the second one involving nitrous oxide for its functionalization to triazolopyridine and triazoloquinoline scaffolds. In the present study, the whole reaction mechanism of the functionalization of nitrous oxide for the synthesis of triazolopyridine and triazoloquinoline scaffolds has been unveiled by means of DFT calculations. The rate determining step of such transformation is found to be the hydrogen transfer from the former carbanion to the oxygen of the nitrous oxide species to yield the intermediate diazo species, being this able to cyclize to the final desired scaffold. Theoretical calculations also show the direct correlation between the product yield for the studied transformation and the energy barrier of the rate determining step. Moreover, the mechanism for the reaction of trans-1,2-di(pyridyl)ethylene with alkyllithium reagents and the formation of ester-functionalized triazolopyridines were also unveiled showing a similar profile. We also predict the feasibility of the preparation of 2 and 3-nitrogen containing scaffolds by means of the reported methodology, as well as sulfur and oxygen-containing diazo species.

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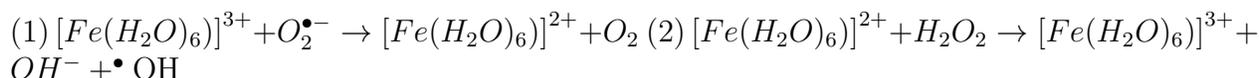
Theoretical Study of Iron Complexes with Lipoic and Dihydrolipoic Acids: Exploring Secondary Antioxidant Activity

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Following the theoretical study of the secondary antioxidant activity of the deprotonated forms of lipoic (LA) and dihydrolipoic (DHLA) acids through their formation of complexes with Cu(II),[1] the present work focuses on the complexes that these species can form with Fe(III).[2] To this effect, the thermodynamic stability of twenty-nine Fe(III) complexes with various deprotonated forms of LA and DHLA, with coordination numbers 4, 5 and 6, is studied at the M06(SMD)/6-31++G(d,p) level of theory in water under physiological pH conditions at 298.15 K. The twenty-four exergonic complexes are used to evaluate the secondary antioxidant activity of DHLA and LA relative to the Fe(III)/Fe(II) reduction by $O_2^{\bullet-}$ and ascorbate, the first step of the Haber-Weiss cycle (see eq (1)). The second step of this cycle (called the Fenton reaction, see eq (2)), leads to the formation of biochemically harmful $^\bullet$OH radicals. A compound is found to have secondary antioxidant activity if its complex with Fe(III) (or with Cu(II)) is able to significantly slow down the first step of the Haber-Weiss cycle.

(1) $[Fe(H_2O)_6)]^{3+} + O_2^{\bullet-} \rightarrow [Fe(H_2O)_6)]^{2+} + O_2$ (2) $[Fe(H_2O)_6)]^{2+} + H_2O_2 \rightarrow [Fe(H_2O)_6)]^{3+} + OH^- + ^\bullet OH$

Rate constants for the single-electron transfer (SET) reactions are calculated. The thermodynamic stability of the Fe(III) complexes does not fully correlate with the rate constant of their SET reactions, but more exergonic complexes usually exhibit smaller SET rate constants. Some Cu(II) complexes and their reduction to Cu(I) are also studied at the same level of theory for comparison. The Fe(III) complexes appear to be more stable than their Cu(II) counterparts. Relative to the Fe(III)/Fe(II) reduction with ascorbate, DHLA can fully inhibit the formation of $^\bullet$OH radicals, but not by reaction with $O_2^{\bullet-}$. Relative to the Cu(II)/Cu(I) reduction with ascorbate, the effects of DHLA are moderate/high, and with $O_2^{\bullet-}$ they are minor. LA has minor to negligible inhibition effects in all the cases considered.

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Different Methods to achieve Origin-Independence in Decomposition of Nonlinear Optical Properties

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The decomposition of (non)linear optical properties (NLOPs, e.g., polarizability, hyperpolarizabilities...) is not straightforward because it runs into the issue of origin-dependence: all obtained atomic contributions will depend on your choice of origin. This means the obtained values will change if the arbitrary origin of coordinates is moved, and also the contribution of a given functional group is modulated based on its distance from the origin, rather than just its nature and environment.

These NLOPs are derivatives of the energy. In our work, we decompose the energy into atomic contributions (to then obtain the atomic NLOP contributions), and we show that, without any assumptions or approximations, one can consider only the origin-independent energy terms, and the obtained value, which is fully origin-independent, will be related to the total property by a specific exact factor that depends exclusively on the property, as can easily be shown through a simple mathematical demonstration. This makes it possible to perform a decomposition completely avoiding the terms that introduce origin-dependence (i.e., the dipole moment operator).

In our current studies, we consider the possibility of achieving full origin-independence through other means. Here we do a systematic study and a comparison of the different methods, across a broad number of systems and molecular sets.

A computational study of chemical shifts in MX_2 and MX_4 (M=Ge,Sn,Pb; X=Cl,Br,I) group 14 metal halides: Inverse versus normal halide dependency

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Perovskites and perovskite-like materials with the general formule ABX_3 or A_2BX_6, where A is an inorganic (e.g. Cs^+) or organic (e.g. methylammonium=$CH_3NH_3^+$) cation, B a dication (e.g. Pb^{2+},Ge^{2+} or Sn^{2+}) and X a halide (Cl^-, Br^-, I^-) or mixture of halides, have received a great deal of attention due to their applicability in photovoltaic and optoelectronic devices. Due to their potential use, these materials have been characterized using a variety of different experimental and computational methods. Solid-state NMR has been shown to be an ideal experimental tool providing information about the local structure and even dynamic effects of halide nuclei. Experiments show that, depending on the perovskite, the chemical shift of the B centre can exhibit either a normal (NHD) or inverse halide dependency (IHD). Computational studies, using density functional theory (DFT), of chemical shifts on molecular models of perovskites, i.e., BX_6^{4-} octahedra, or perovskite-like materials, i.e., BX_6^{2-} octahedra, show good agreement with experimental measurements and even more, are able to capture the NHD and IHD behaviour, e.g., [1-4] Motivated by these findings, the chemical shifts in a series of metal halides in group 14, i.e., MX_n for M(II, IV)=Ge, Pb, Sn and X=Cl, Br, I, have been investigated computationally. Two key (computational) aspects are considered for these systems containing heavy elements: relativistic effects (with scalar ZORA) and spin-orbit coupling (SOC). Based on DFT results (PBE0/TZ2P), a natural bond order (NBO) partition of the chemical shielding tensor into its diamagnetic, paramagnetic, and SOC components is performed. The partitioning shows the key role SOC plays in reproducing the observed NHD and IHD trend for M(II, IV) nuclei. For completeness, the electric field gradients (EFG) of all quadrupolar nuclei (^{35}Cl, ^{73}Ge, ^{79}Br, ^{119}Sn, ^{127}I, ^{207}Pb) are computed to permit comparison with future experimental measurements.

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Graph Convolution Neural Network for Projected Density of States predictions

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Machine learning models recently demonstrated prominent results in predicting materials properties and accelerating materials discovery [1]. However, they still fail in predicting complex material properties (particularly bandgaps) or maintaining accuracy in the low-data regime.

Graph Convolution Neural Networks (GCNNs) became the de facto standard for encoding crystal structures of arbitrary size. They showed high accuracy in predicting additive properties of the materials, e.g. total energy, which can be represented as a sum of energies of single atoms. However, we find that they fail to predict atomic interactions that result in delocalized properties, such as molecular orbitals and the resulting electronic bandstructure, even in the simplest 2-level system case.

Here, we developed a material representation that retains the locality of atomic contributions to the final molecular orbitals and band structure. Our GCNN trained on band structure data from the Materials Project database [2] with elements from s, p, d, and f blocks is capable of making accurate predictions of projected densities of states even when training on a dataset with less than 5000 materials.

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Influence of the Excitation Wavelength on the Computation of First Order Hyperpolarizabilities using Optimally Gap Tuned Range Separated Hybrid Functionals

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Application of computational techniques to nonlinear optical spectroscopy provides significant insights in the prediction and explanation of the experimental behaviour of various systems. The determination of the second harmonic generation (SHG) hyperpolarizabilities of chromophores with varying degrees of charge transfer by computational means is an important test of the capability of these approaches. In this study, we computationally investigate the hyperpolarizabilities of the three nitroaniline isomers, para-nitroaniline (pNA), ortho-nitroaniline (oNA), meta-nitroaniline (mNA) by density functional theory (B3LYP, LC-BLYP, ωB97, and ωB97XD) with reference to gas phase CCSD/aug-cc-pVDZ results and experimental measurements conducted in the presence of solvent.(1) In particular, the emphasis is on understanding the trend in measured hyperpolarizabilities (pNA¿oNA¿mNA) as well as the effect of excitation wavelength. For the range separated functionals (LC-BLYP, ωB97, and ωB97XD) optimal gap tuning of the range separation parameter is performed such that Koopman's theorem is satisfied. (2) The resultant hyperpolarizabilities from the tuned functionals are compared to the untuned functionals. The effect of the excitation wavelength is apparent on the computed hyperpolarizabilities of the isomers, as the hyperpolarizability trend is broken at the static limit and for excitation wavelengths near the electronic resonances (250 nm). The need for optimal gap tuning of range separated hybrid functionals becomes more apparent at the highest wavelength (1907 nm) and the static limit for reproduction of the experimental trend and CCSD/aug-cc-pVDZ results respectively. Additionally, the excitation wavelength is also found to influence optimal gap tuning of range separated functionals where at 1907 nm and the static limit, the behaviour is pathological while at 1064 nm it reverts to the typical behaviour associated with optimal gap tuning.(3)

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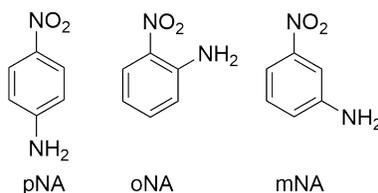
Molecular Simulations of Bulk Aqueous Nanobubbles

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Nanobubbles are nanoscale gas-filled systems in water with a diameter lesser than 1000 nm. Due to their smaller size and their long-term stability (up to months), there are various applications available in numerous fields. Medicine, agriculture, water remediation, washing, and mining are some of them. However, there is a lack of information on the stability of the nanobubbles. In this project, the pressure inside different sized nanobubbles was measured to find the Laplace pressure involvement within them. Two different methods were used to calculate the radius of the bubbles based on the density changes over the systems. Further, the effect of cut-off length on pressure was optimized and identified a relatively large cut-off length is required for these simulations. For all simulations, Gromacs software and a standard (atomistic) water model was used. The results for the pressure values will explore whether they are consistent with the Laplace pressure for the measured radius of the bubbles; if this is not the case, this suggests there may be other factors acting on the surface of the bubble, which may be important in helping to stabilize the nanobubbles in water

Mechanistic insights into the proton conductivities of phosphonate hydrogen-bonded organic frameworks: An ab-initio molecular dynamics study

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Hydrogen fuel cells are a clean alternative to traditional lithium-based power sources because their waste products are only water and heat. The development of solid-state proton exchange membranes (PEMs), a key component of hydrogen fuel cells, is an active area of research, due to their higher heat and pressure resistance over their liquid counterparts. Hydrogen-bonded organic frameworks (HOFs) – solid, microporous, organic materials that are held together by hydrogen bonds – have shown high proton conductivities, but they are typically less stable under ambient conditions. Recently, two HOFs, namely GTUB5 [1] and UPC-5a [2], were developed that are chemically stable and thermally stable up to 250°C and 125°C, respectively. These systems contain porphyrin-phosphonate linkers, with the main chemical difference being that UPC-5a contains a nickel atom in its porphyrin core while GTUB5 does not. Under high relative humidity (r.h.), the activation energies of GTUB5 and UPC-5a are 0.14 eV (at 90% r.h) and 0.20 eV (at 95% r.h.), respectively, suggesting that both GTUB5 and UPC-5a conduct protons via a Grotthus mechanism. However, the proton conductivity of UPC-5a is 4 orders of magnitude higher than that of GTUB5 (viz., $3.42 Sm^{-1}$ vs. $4.20x10^{-4}Sm^{-1}$). Although the structures possess similarities, it is expected that fundamental differences at the atomic level lead to this large difference in proton conductivities.

To gain insight into the proton conduction mechanisms of both HOFs, Born-Oppenheimer molecular dynamics (BOMD) simulations are performed. Systems with 8 and 10 water molecules (corresponding to high relative humidities) in the pores are considered, each at three different temperatures. For each system, the diffusion coefficient of the excess proton in each pore (1 pore in GTUB5 vs. 3 pores in UPC-5a) is calculated and substituted into the Nernst-Einstein equation to estimate the proton conductivity (σ). Using the proton conductivities at the three different temperatures for a given relative humidity, we estimate the activation energy of the proton transfer from the slope of the linear Arrhenius plot of $log(\sigma[S * cm^{-1}])$ vs. $1000/T[K^{-1}]$. The results for the two HOFs are compared and contrasted to build a picture of the proton conduction mechanisms and, in turn, elucidate the structural/dynamical factors that contribute to the large difference in proton conductivities.

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XDM dispersion with local orbitals: Implementation in the FHIaims package

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Post-self-consistent dispersion corrections are among the most popular approaches to incorporate London dispersion into density-functional theory (DFT). Many such corrections have been proposed in the literature, including Grimme's Dn family, the Tkatchenko-Scheffler (TS) model, and the many-body dispersion (MBD) method. The exchange-hole dipole moment (XDM) model is an accurate and non-empirical way of incorporating dispersion that uses a damped asymptotic dispersion energy expression, but calculates the dispersion coefficients to any order from the converged electron density and kinetic-energy density. XDM has been show to be an excellent choice for modelling intermolecular interactions between gas-phase organic molecules, in molecular crystals, layered materials, and more. In this work, we present our recent implementation of XDM in the Fritz Haber Institute ab initio molecular simulations (FHI-aims) electronic structure package, with which we can carry out XDM-corrected DFT calculations using local orbitals. This is an important development because it allows the inexpensive application of XDM-corrected hybrid functionals to periodic solids. The performance of the new implementation was assessed for a battery of tests, including the S22×5 and S66×8 molecular benchmarks, the X23 set of molecular-crystal lattice energies, and a collection of layered materials. Hybrid functionals based on B86bPBE, in combination with XDM, perform excellently for both the gas-phase and solid-state benchmark tests. In particular, the 50% global hybrid B86bPBE50-XDM achieves a mean absolute error (MAE) for the X23 set of 0.65 kcal/mol, which is the lowest MAE yet reported for any DFT-based method to our knowledge. At the same time, the asymptotic linear scaling of the underlying method makes the new XDM-corrected hybrid functionals an excellent choice for modeling molecular systems, materials, and their interfaces.

Constrained Iterative Hirshfeld Charges: A Variational Approach

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One of the most useful pieces of information extracted from quantum mechanical calculations is the atomic properties like charges and multipole moments. These are commonly used in force field development, conceptual density functional theory, and dispersion interaction energy calculations, just to name a few. Because atomic properties do not correspond to a quantum mechanical observable, there is an inherent ambiguity in calculating them. However, their effectiveness and practical utility have driven the development of various methods for decomposing a molecule into atomic components. One of the most established family of partitioning schemes, inspired by Hirshfeld [1], uses reference proatom densities to compute the share of an atom in the molecular density. Characterizing the mathematical, chemical, and computational features of these schemes is an active topic of research [2,3,4].

Iterative Hirshfeld is one of the most commonly used variants of Hirshfeld scheme[5], which self-consistently updates each proatom so that they have the same number of electrons as the corresponding atom. We recently developed a variational procedure for the iterative Hirshfeld method. This not only provides an elegant mathematical framework for iterative Hirshfeld, but also provides a straightforward approach for adding constraints when computing atomic densities. This has many applications, for example in force-field parameterization, one often wants to constrain a portion of an amino acid residue to have a specific charge. In this presentation, the constrained iterative Hirshfeld is introduced and compared to the information-theoretic approaches, like constrained scaled Hirshfeld and constrained additive variational Hirshfeld. In addition, we present our assessment of the chemical and computational quality of these methods for different representative systems.

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Molecular Dynamics Study of the Diffusion of a Hydrophobic Drug in a Disordered Block Copolymer Micelle

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Previously, all-atom molecular dynamics (MD) simulations of a single hydrophobic drug molecule in a series of poly (ethylene oxide-b-caprolactone) (PEO-b-PCL) pseudo-micelles were performed to gain insight into the drug-polymer interactions and drug diffusion. Although some insights into the hydrogen-bonding interactions could be obtained from these simulations, it was not possible to capture the full effect of the interactions on the drug diffusion dynamics. All-atom MD simulations of drug diffusion from stable drug-loaded micelles are prohibitively costly due to the very long timescales associated with drug release from such systems. To reduce the computational cost, in this study, we performed an all-atom MD simulation starting from a disordered structure of a full Cucurbitacin B (CuB)-loaded PEO-b-PCL block copolymer micelle in water. We found that the ensuing drug diffusion out of the micelle is mediated first by the formation of water-PCL bonds and breaking of water-PEO bonds, and then by the formation of water-CuB bonds. The CuB and water dynamics yielded nonlinear sub-diffusive mean-squared displacements, owing to the molecular crowding in the micelle and hydrogen bonding interactions between the water/CuB molecules and polymer chains. Finally, we found that the hydrogen bonding and diffusion dynamics in the pseudo-micelle are not representative of those in the full micelle. The computational approach used in this study is expected to yield molecular-level information that can aid in understanding in-vitro drug release data from nano-sized polymer micelles.

The "On Water" Effect in Organic Reactions

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Aqueous organic chemistry (AOC) has received considerable attention in the past few decades because it represents a cheap and accessible green alternative to traditional organic solvent chemistry. Though AOC was originally developed for reagents that are soluble in water, the field has expanded to include reactions where reactants are not necessarily miscible with water. In this context, the "on water" effect occurs when an organic reaction is accelerated in the presence of a water-organic interface compared to the same reaction in an organic solvent or solventless conditions. Although some mechanisms have been proposed to explain this effect, there is still no agreement on the molecular origin of this phenomenon. Understanding the chemistry involved in heterogeneous aqueous-organic media has important implications in biochemistry, prebiotic and atmospheric chemistry. This talk will explore some of the experimental and computational efforts toward understanding the "on water" effect.

The pan-Canadian Computational Chemistry Course (PC4) Program: A collaborative approach to training graduate students in applied computational chemistry

Alireza Sadeghifar[1], **Gino DiLabio**[2], Erin Johnson[1], Georg Schreckenbach[1], and Tom Woo[1]

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Canada has a strong and close-knit theoretical and computational chemistry community in its university system. The community is small - on average, one faculty member per department per university - in comparison to other sub-disciplines in chemistry, and this makes it difficult for individual chemistry departments to offer robust computational training programs at the graduate level. The PC4 project is a collaborative approach to address this important gap in computational chemistry training at the graduate level. The project gathers faculty from institutions across Canada with the aim of developing and delivering graduate-level applied computational chemistry courses. In addition to creating a standard, high-quality, and sustainable training program in the field, students are expected to benefit from an experience that goes beyond the single instructor/single institution model and exposure to a wide the latest research. We expect the PC4 model to be extendable to students outside of Canada, thereby addressing the UN Sustainability Goals 4 and 10, Quality Education and Reduced Inequalities. This presentation will outline our approach to the PC4 project and some of the challenges we encountered.

Bayesian Optimization for Efficient Parameterization of LiX Forcefields for Molecular Dynamics

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In many ways, the accurate molecular dynamics simulation of lithium halides is a deceptively difficult problem. At first glance, the binary lithium salts appear to be about as simple a chemical system as one can conjure up. However, recent theoretical investigations of the landscape of lithium halide crystal structures paint a more complex picture. Due to the relative ion sizes of lithium vs its counter-anion, these salts have multiple low-energy crystal structures that compete to complicate their structural chemistry. A recent investigation by our group revealed that the relative energies of these crystal structures are highly dependent on the details of the attractive and repulsive interactions between ions, particularly the strength of London dispersion. Therefore, modeling the interaction potentials of lithium halides proves to be a particularly difficult problem compared with other binary salts. Many of the classical forcefields currently available for lithium halides get the lowest-energy crystal structure wrong, particularly for LiBr and LiI. Furthermore, even those forcefields that get the correct low-energy structure right tend to yield incorrect relative energies for the competing low-lying metastable structures. Furthermore, the melting points for most available lithium halide forcefields are far from experiment, indicating a recurring issue with the high-temperature thermodynamic behaviour of the solid phase, liquid phase, or both.

In the work presented here, we use multiple experimental structural, energetic, and thermochemical data points combined with a set of theoretical high-accuracy lithium halide metastable crystal energies and geometries as targets for a computationally efficient Bayesian Optimization scheme to optimize pairwise classical forcefield parameters for lithium halide molecular dynamics simulations. We validate the resulting forcefields in finite temperature molecular dynamics simulations to test their energetics and most stable crystal structure at high temperature. We also calculate model melting points and liquid properties, comparing our results with the available experimental data.

The figure below is an outline for the procedure used in this work.
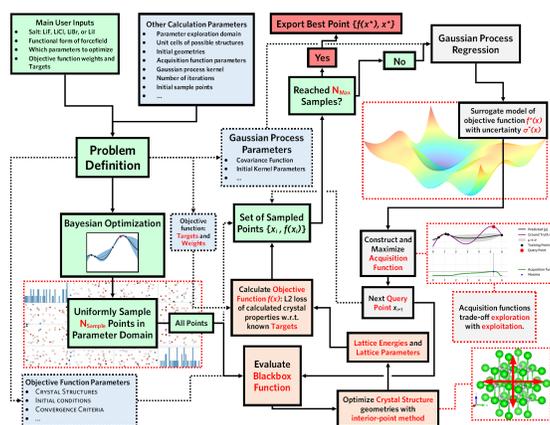
Multi-scale modelling of metal-organic frameworks

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University of Calgary

Metal-Organic Frameworks (MOFs) have a broad range of applications (e.g., gas storage and catalysis). While a great number of MOF compounds are reported in the literature, there have been few studies probing the self-assembly process. The problem is suitable for computational studies, but they fall short due to the limited timescales of all-atom simulations. To allow simulations to reach much longer timescales, we are optimizing effective potentials that would accelerate the simulations by up to three orders of magnitude. Given a reference all-atom simulation, the uniqueness of the optimized solution can be guaranteed in theory. However, transferring these potentials to slightly different systems remains a difficult problem in practice. We employ a bottom-up approach, where the potentials are optimized for systems in increasing order of complexity, beginning with single-component systems. Once validated, the effective potentials will be used to run large scale coarse-grained simulations that enable us to identify the local structural units appearing as part of the self-assembly process. ![a small MOF nucleus](2x2-nosolvent.png)

Representing Surface Properties of Molecules As an Alignment-Free Spectrum for Cheminformatics

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The use of a spectrum is ubiquitous across chemistry as it is used to correlate chemical structure to an interpretable signal. On the other hand, molecular surfaces are a common representation of a molecule as certain chemical concepts are thought to occur on the boundaries of a molecule. Motivated by signal processing and computational geometry, we represent a function on the molecular surface as a spectrum that encodes information about the geometry of the surface and its properties. This poster shares our ideas and results for developing alignment-free and property-specific molecular similarity measures for predicting molecular properties in cheminformatics.

Computational Study of the PINOylation Mechanism at Benzylic C-H Bonds

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In nature, benzylic C(sp3)-H bonds are easily oxidized to alcohol and aldehyde groups. These molecules have a wide range of application, for example as pharmaceutical compounds. The challenge in developing synthetic methods to gain access to benzylic alcohols and aldehydes is that, under most conditions, they are directly further oxidized to carboxylic acid groups. Stahl's group developed a new approach (to be described in a forthcoming publication): The radical of phthalimido-N-oxyl (PINO) is used as hydrogen atom transfer reagent, abstracting a hydrogen atom from the benzylic position. Another PINO radical then traps the generated benzylic radical in a mechanism here referenced as PINOylation. This PINOylated compound can easily be further transformed into the desired alcohols and aldehydes via photochemical reaction. The PINOylated compounds and their specific mechanism of synthesis are of interest because they display significant scope. In one of two observed products, the PINO molecule is bonded to the substrate via a C-O bond. The other product, unexpectedly, has the O atom incorporated into the ring of PINO via expansion, and bonds to the substrate via a C-N bond. For almost all studied substrates, both products are observed, and their ratios are not influenced by varied reaction conditions. Of all variables, the different substituents on the substrates have the largest influence on the ratio and formation of products. This computational DFT study of the PINOylation reaction mechanism seeks to elucidate how substituents affect product ratios.

Calculating the Aqueous pKa of Phenols: Predictions for Antioxidants and Cannabinoids

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Aqueous pKa values are essential for understanding the behaviour of chemical species, such as those used as drugs, in buffer systems, or to study enzyme performance and antioxidant activity. Phenolic compounds play important roles in these applications; however, there are limited experimental aqueous pKa values reported. In this study, three calculation schemes, five functionals (M06-2X, B3LYP, BHandHLYP, PBE0, TPSSTPSS), and two solvent models (SMD and IEFPCM) are used to predict pKa values using a set of 15 phenols to evaluate the accuracy of these predictions. Nitrophenols were not predicted well in any scheme, hence mean absolute errors (MAE) were calculated including and excluding these molecules. The best performance (with a MAE of 0.46 pKa units excluding nitrophenols) was achieved at the M06-2X(SMD)/6-311++G(d,p) level of theory using the acid-base equilibrium: HA + Ref- $\rightleftharpoons$ A- + HRef, where HRef is the reference acid used (phenol). Two other functionals, B3LYP(SMD) and BHandHLYP (SMD), were quite similar in performance with MAE of 0.57 and 0.55 pKa units, respectively (excluding nitrophenols). Aqueous pKa predictions were performed for a set of 13 phenolic antioxidants, and 10 pharmaceutically interesting phenolic cannabinoids. These 23 molecules are the subject of kinetic studies by our group for which their aqueous pKa values are needed.

Hydrate nucleation in water nanodroplet: size dependence

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Clathrate hydrates are ice-like structures in which hydrogen-bonded cages formed by water encapsulate guest molecules (e.g., methane). Understanding of clathrate nucleation in water nanodroplets is not only of great scientific interest, it also has significant implications for industrial processes (e.g., the hydrate blockage inside the oil/gas pipeline, CO_2 sequestration and natural occurrence of clathrates in sedimental environments). Yet, despite recent efforts devoted into the understanding the molecular level mechanisms, these have remained elusive. To examine the impact of the size of water nanodroplets on the microscopic mechanisms of nucleation of gas hydrates, extensive MD simulations have been performed with systems where a water nanodroplet is surrounded by a non-aqueous liquid comprising one of the pure guest species (H_2S, C_3H_8, CH_4, CO_2, C_2H_6) or their mixtures. For all the systems studied, the nucleation events have been observed under the current simulation time scales (500ns) with only pure H_2S guest species systems or with nuclei dominated by the H_2S species in mixed-guest systems. With pure H_2S guest systems, the impact of the size of water nanodroplets on the hydrate nucleation behavior has been studied over a range of temperatures. The dissociation temperature dependence of the crystallite size for H_2S sI is well described by the Gibbs-Thomson equation and provides a reasonable estimate for the interfacial tension. Our results show that a decrease in size or increase in temperature not only causes an increase in the induction time for the nucleation but also results in a tendency of the nuclei appear at the center of the nanodroplet. Additionally, according to analyses of the hydrate structures, we find that the hydrate nuclei initiated with incomplete cages subsequently grow to essentially fill the water nanodroplet and are eventually dominated by complete cages. These amorphous hydrate nuclei exhibit motifs of both sI and sII structures. This work provides new insights into the kinetic behavior of hydrate nucleation practically within water nanodroplets

Automated Assignment of Metal Oxidation States in MOFs and its Application in Identifying Structural Errors

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Metal oxidation state and electron counts are two electron bookkeeping formalisms that are widely used by inorganic and organometallic chemists to assess the feasibility of proposed structures as well as to map and understand catalytic cycles. Despite not corresponding to any "real" physical atomic property, these bookkeeping formalisms have fantastic predictive ability in terms of the stability and reactive chemistry of metal complexes. In the simple case of a molecular compound with a single metal center the oxidation state assignment is straightforward. However, with periodic MOFs, there are often large, delocalized charge-sharing networks involving several distinct metal centers that can even give an experienced chemist some pause when manually assigning oxidation states. In this work we describe an automated algorithm for assigning metal oxidation states and electron counts in MOFs that we call MOSAEC (Metal Oxidation State And Electron Count). MOSAEC will assign whatever oxidation state (correct or incorrect) implied by the input structure. We have found that impossible or improbable metal oxidation states are a very strong indicator of structural problems found in experimentally derived MOF structures. This allows for the detection and screening of structural errors that are difficult or impossible to detect via existing means. Applying this screening technique to two popular experimentally derived MOF databases that are often used for computational screening, shows an alarmingly high error incidence of over 50%.

Combined experimental and computational study of the chemical reactivity and optical properties of carbon nitride and its analogues

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Carbon nitride (CNx) has emerged as a highly promising photocatalytic polymer and has been under intense study over the last few years. The interest stems from its properties as an active metal-free photocatalyst and its simple and facile synthesis from inexpensive nitrogen-rich organic precursors. As an organic polymer, CNx can be transformed and shaped in different ways to suit its intended applications, therefore it is necessary to extensively study its structural and electronic properties. In this work, we intend to investigate the electronic structure of CNx and its analogues including precursors and intermediates from a combined experimental and computational approach considering its chemical reactivity and optical properties. Specifically, melamine is adopted as the precursor for the formation of CNx and its intermediates, melam, and melem (see figure).

Melamine   Heptazine   Carbon nitride
(tri-s-triazine)   (melon)