

# 10th Annual CERMM Symposium

April 30th to May 2nd, 2010  
Montefiore Club, Montréal

## *Program and Book of Abstracts*



Office of the Vice-President,  
Research and Graduate Studies



# CERMM Director's Foreword

Envisioning the growing importance of computational and theoretical chemistry in modern research, the Concordia Faculty of Arts & Science supported and encouraged the establishment of the Centre for Research in Molecular Modeling (CERMM) in 2000. CERMM is now a multi-institutional research centre with 25 senior members from 10 institutions with diverse interests. These are exciting times for computational physicists, chemists and biochemists! The Canada Foundation for Innovation is funding *Compute Canada* along with provincial and industrial partners, a project that will allow Canada to remain at the forefront of computer-simulation-based research, and in particular, will provide Québec computational chemists with access to a state-of-the-art computing infrastructure which will be deployed in CERMM as part of the Réseau Québécois de Calcul Haute Performance.

The infrastructure available in CERMM has supported in the past the research of over 15 postdoctoral fellows, 50 graduate students and numerous undergraduate students in atmospheric, biological, inorganic, macromolecular, materials, medicinal, organic, physical, and polymer chemistry. The mission of CERMM is to promote excellence in research and graduate education in computational chemistry and biochemistry, to foster collaborations between researchers in different institutions, and to provide an interdisciplinary forum for experimentalists, modelers and theoreticians to combine their expertise to reach new frontiers in the molecular sciences. Accordingly, the CERMM symposium is the annual regional event where researchers and students with interests in computational physics, chemistry and biochemistry have the opportunity to showcase their work in the field.

This year, we are proud to hold our 10<sup>th</sup> anniversary Symposium, and hope to see many more. I would like to thank the Office of the Vice-President, Research and Graduate Studies for their support, Azuris Technologies for sponsoring part of the event, my CERMM colleagues and the CERMM students and postdocs for helping organize the symposium. As usual, they did a terrific job! I hope you will all enjoy a fruitful and stimulating symposium.



Gilles H. Peslherbe, CERMM Director

# Symposium Program

**Friday, April 30, 2010**

**17:00** Welcoming remarks

**Gilles Peslherbe**, Director, Centre for Research in Molecular Modeling

Discussion Leader: **Nicolas Moitessier** (McGill University)

**Benoît Roux** (University of Chicago)

*Computational study of the ligand-activated glutamate receptor*

**18:15** Reception

Sponsored by *Azuris Technologies*

**Saturday, May 1, 2010**

Discussion Leader: **David Wardlaw** (University of Western Ontario)

**9:30** **Robert Le Roy** (University of Waterloo)

*CO<sub>2</sub> in para-H<sub>2</sub>: From pair potentials to superfluid nanoclusters*

**10:10** **Chun Mak**, Qadir Timerghazin and Gilles Peslherbe (Concordia University)

*Ab initio molecular dynamics simulations of  $I^-(H_2O)_n$  ( $3 < n < 10$ ) excited-state relaxation dynamics: Cluster size effects on electron solvation*

**10:30** **Samir Mushrif** (Concordia University and McGill University), Alejandro Rey (McGill University) and Gilles Peslherbe (Concordia University)

*Investigating the adsorption and spillover of hydrogen on a carbon supported palladium cluster*

**10:50** Coffee Break

Discussion Leader: **Tucker Carrington Jr.** (Queen's University)

**11:20** **Christopher Corbeil** (National Research Council - Biotechnology Research Institute)

*Rapid prediction of solvation free energy*

**12:00 Jean-François Truchon** (Merck Frosst)

*Does electronic polarization give a net advantage in condensed-phase simulations? A QM/MM perspective*

**12:20 Soran Jahangiri** and Gilles Peslherbe (Concordia University)

*Theoretical investigation of molecular ion solvation in aqueous clusters*

**12:40** Wai Kong Yuen, Daniel Oblinsky and **Stuart Rothstein** (Brock University)

*Reptation quantum Monte Carlo: Application to ground-state properties of water*

**13:00** Lunch

Discussion Leader: **Guillaume Lamoureux** (Concordia University)

**14:15 Peter Tieleman** (University of Calgary)

*Watching lipids move: computer simulation of defects, flipflop, domains and fusion*

**14:55 Bilkiss Issack** and Gilles Peslherbe (Concordia University)

*Computational investigation of the effect of cholesterol on passive transport across lipid membranes*

**15:15** Patrick Maurer, Vibin Thomas and **Radu Iftimie** (Université de Montréal)

*A theoretical study of acid-base neutralization reactions: The computational model*

**15:35 Qadir Timerghazin** (University of Waterloo), Alex Brown (University of Alberta) and Pierre-Nicolas Roy (University of Waterloo)

*Pyramidalization effects in the ground-state cis-trans isomerization of the green fluorescent protein chromophore*

**15:55** Qadir Timerghazin (University of Waterloo) and **Ann English** (Concordia University)

*Insights into S-Nitrosothiol reactivity: Mechanism of acid-catalyzed hydrolysis*

**16:30** Poster Session

**18:00** Banquet

## Sunday, May 2<sup>nd</sup>, 2010

Discussion Leader: **Marcel Nooijen** (University of Waterloo)

**9:30** **Natalie Cann**, Shihao Wang and Rodica Pecheanu (Queen's University)  
*Chirality transfer in isotropic fluids, at interfaces, and in liquid crystals*

**10:10** Ana Nikolic (University of Toronto), Stéphanie Baud (Université Reims Champagne-Ardenne, France), Sarah Rauscher and **Régis Pomès** (Hospital for Sick Children and University of Toronto)  
*Catalysis of beta-sheet self-organization at water-hydrophobic interfaces*

**10:30** **Christopher Ing** (University of Waterloo), Konrad Hinsen (CNRS, France) and Pierre-Nicholas Roy (University of Waterloo)  
*Path Integral implementation in the molecular modeling toolkit*

**10:50** Coffee Break

Discussion Leader: **Pierre-Nicholas Roy** (University of Waterloo)

**11:20** **Gustavo Avila Blanco** and Tucker Carrington Jr. (Queen's University)  
*Non-product quadrature grids for solving the vibrational Schrödinger equation*

**11:40** **Xiao-Gang Wang** (Queen's University), Richard Dawes (Sandia National Laboratories), Tucker Carrington Jr. (Queen's University), and Ahren W. Jasper (Sandia National Laboratories)  
*Computing and understanding the rovibrational spectrum of nitrous oxide dimer: A tale of three isomers*

**12:00** **Lee Huntington** and Marcel Nooijen (University of Waterloo)  
*pCCSD: Parameterized coupled cluster theory with single and double excitations*

**12:20** **Randall Dumont** and Adam Lewis (McMaster University)  
*Quantum interference transistors - Simulation using Ernzerhof's Source-sink potential method*

# Poster Presentations

1. *Novel bis-N-sulfinylhydrazines and their hydrogen-bonding patterns*  
**Irena Beylis** and Heidi Muchall (Concordia University)
2. *Experimental studies on the molecular structures of aromatic N-sulfinylhydrazine*  
**Stephen Boateng** and Heidi Muchall (Concordia University)
3. *Molecular polarizabilities in aqueous proton transfer reactions*  
**Andrei Buin** and Radu Iftimie (Université de Montréal)
4. *Quantum chemical calculations of gold cluster complexes with methanethiol*  
Julia Tofan-Lazar and **Ian Hamilton** (Wilfrid Laurier University)
5. *Conformational studies of some arabinofuranosides in solution and in complex with enzyme, Arabinanase Arb43A, using the long molecular dynamics and umbrella sampling simulations*  
**Shahidul Islam** (University of Waterloo), Mickey Richards (University of Alberta), Todd Lowary (University of Alberta) and Pierre-Nicholas Roy (University of Waterloo)
6. *A computational study of electronic structure and hydrolytic reactivity of various N-sulfinyl species*  
**Elena Ivanova** and Heidi Muchall (Concordia University)
7. *Combined theoretical and experimental investigation of bistable photochemical switches*  
Erwin Buncel (Queen's University), Robert Stairs (Trent University), Julian Dust (Memorial University), Zhiyuan Tian (Queen's University), Martin Wyer (Queen's University), **Thomas Kraft** (Queen's University) and Nick Mosey (Queen's University)
8. *Dynamics of glucose binding to glucokinase*  
**Monique Laberge** (Royal Military College, St-Jean)
9. *Can N<sub>2</sub>O bending really be neglectful in He-N<sub>2</sub>O Dynamics?*  
**Wang Lecheng**, Li Hui, Robert Le Roy and Dai Qianxie (University of Waterloo)
10. *Quantum monte carlo prediction of vibrational frequency shifts for CO<sup>-</sup>(pH<sub>2</sub>)<sub>n</sub> clusters*  
**Hui Li**, Robert Le Roy and Pierre-Nicholas Roy (University of Waterloo)
11. *The generation and reaction of nitrilimines*  
**Sima Mehrpajouh**, Gilles Peslherbe and Heidi Muchall (Concordia University)
12. *MM and high level ab initio QM studies on cation- $\pi$  interactions and their cooperativity with  $\pi$ - $\pi$  interactions*  
**Esam Orabi** and Guillaume Lamoureux (Concordia University)

- 13. *Technical note: Acquiring ab-initio points using a parallel Perl script***  
Hartmut Schmider (Queen's University), Chris MacPhee (Queen's University), **Yong Park** (Queen's University), Owen Clarkin (Queen's University and Steacie Institute for Molecular Science) and David Wardlaw (University of Western Ontario)
- 14. *Extension of the Source-Sink Potential (SSP) approach for multi-channel conductance calculations.***  
**Philippe Rocheleau** and Matthias Ernzerhof (Université de Montréal)
- 15. *Computational studies of NO diffusion in hemoglobin: Relevance in vasodilation***  
**Mariya Shadrina**, Denise Koch, Ann English and Gilles Peslherbe (Concordia University)
- 16. *Identifying and characterizing the acid dissociation intermediates in aqueous solution***  
**Vibin Thomas** and Radu Iftimie (Université de Montréal)
- 17. *Development of semi-empirical models for zinc metalloenzymes***  
**Shihao Wang** and Guillaume Lamoureux (Concordia University)
- 18. *Vibrational spectroscopy from first principles molecular dynamics simulations: Towards understanding of guanidinium-peptide interactions***  
**Xijun Wang** and Gilles Peslherbe (Concordia University)
- 19. *Exploratory computational studies towards the photo-induced degradation of lignin***  
**Lei Zhang**, Gilles Peslherbe and Heidi Muchall (Concordia University)
- 20. *Hartree-Fock and Kohn-Sham method for open systems***  
**Yongxi Zhou** and Matthias Ernzerhof (Université de Montréal)

# **ABSTRACTS**

## **Talks**



*Computational study of the ligand-activated glutamate receptor***Benoît Roux**

University of Chicago

Ligand-gated ion channels mediate information transfer at synapses. The binding of neurotransmitter molecules to the ligand-binding domains (LBDs) of these channels drives the opening of transmembrane pores, allowing the flow of select cations across the cell membrane. The ionotropic glutamate receptor ion channels (iGluRs) mediate excitatory responses at the vast majority of synapses in the brain and spinal cord. Our approach is to use equilibrium free energy computations based on detailed atomic models to elucidate the energetics that govern the allosteric mechanisms responsible for iGluR function. Ligand binding has been shown experimentally to proceed in two steps, in which rapid ligand docking is followed by slower domain closure. Understanding the energetics that govern these processes are critical to understanding the fundamental, microscopic basis for receptor activation. We compute the free energy of binding for ligands to iGluR using a novel methodology that rigorously accounts for the free energies of both docking and domain closure. The computations advance the understanding of the fundamental mechanisms by which dysfunction in iGluRs give rise to neurological disorders and will aid the design of novel iGluR ligands that can act as therapeutic agents.

*CO<sub>2</sub> in para-H<sub>2</sub>: From pair potentials to superfluid nanoclusters*

**Robert Le Roy**

University of Waterloo

Clusters of para-hydrogen have been predicted to exhibit superfluid behaviour, but to date, direct observation of this has been elusive. We believe that our comprehensive study of a system consisting of a CO<sub>2</sub> molecule solvated in para-H<sub>2</sub> clusters provides convincing evidence of this behaviour.

*Ab initio molecular dynamics simulations of  
 $I^-(H_2O)_n$  ( $3 < n < 10$ ) excited-state relaxation dynamics:  
Cluster size effects on electron solvation*

**Chun Mak, Qadir Timerghazin and Gilles Peslherbe**  
Concordia University

The photoexcitation of aqueous halides such as iodide results in the transfer of an electron from the anion to a solvent-supported orbital, leading to charge-transfer-to-solvent (CTTS) excited states that subsequently relax to produce solvated electrons, species implicated in numerous fundamental chemical and biological processes. Analogous CTTS excited states have been observed in iodide-water clusters,  $I^-(H_2O)_n$ , which have provided a valuable paradigm for investigating the microscopic processes involved in solvated electron formation. Recent time-resolved photoelectron spectroscopy measurements have revealed complex, cluster size-dependent relaxation dynamics in photoexcited  $I^-(H_2O)_n$  that result in the gradual stabilisation of the excited state. In this contribution, molecular dynamics simulations are performed to elucidate the role played by the iodine atom and individual solvent molecules in the experimentally observed stabilisation of the excess electron in excited  $I^-(H_2O)_n$  and understand observed changes in the excited-state dynamics as cluster size is varied. An accurate model chemistry specifically tailored to properly describe the ground, excited and ionised state potential energy surfaces of  $I^-(H_2O)_n$  is used in all simulations. Preliminary simulation results suggest that an intricate combination of solvent and iodine motion is required to stabilise the excited electron and highlight the great complexity of  $I^-(H_2O)_n$  CTTS relaxation dynamics.

*Investigating the adsorption and spillover of hydrogen on a carbon supported palladium cluster*

**Samir Mushrif**

Concordia University and McGill University

**Alejandro Rey**

McGill University

**Gilles Peshherbe**

Concordia University

The functionality of transition metal-doped carbon materials in catalytic and hydrogen storage applications is governed by the characteristics of their interaction with hydrogen. In this work the: (i) dissociative-chemisorption of diatomic hydrogen on a carbon-supported Pd cluster, (ii) the transport of atomic hydrogen on the cluster, towards the carbon support and (iii) the associative-desorption are modeled using the first-principles molecular dynamics and the longer time scale events are accelerated using the novel metadynamics technique. The energy surface along the reaction pathway is reconstructed. The findings reveal the crucial mechanistic details which can be leveraged to develop a better understanding of hydrogen spillover on functional carbon materials.

## *Rapid prediction of solvation free energy*

**Christopher Corbeil**

Biotechnology Research Institute, National Research Council Canada

Changes in solvation free energy during complex formation are a crucial element of binding free energies. With the ever increasing use of computational methods for prediction of binding affinities there is a need for rapid and accurate methods for the prediction of solvation free energies. The present study provides a comprehensive systematic analysis on the applicability of the linear interaction energy (LIE) approximation to the prediction of gas-to-water transfer (hydration) free energy. A highly correlative LIE model was achieved and tested on a diverse hydration dataset comprising 614 neutral and charged compounds with measured hydration free energies. We have analyzed the sensitivity of the LIE model to several parameters such as: continuum correction terms applied outside the explicit water shell, the impact of various charging methods, the applicability of single-conformer representation of the solute, and the inclusion of internal energy terms. A direct comparison of the LIE and free energy perturbation (FEP) approaches using the same force field and charging method shows that the LIE approximation is at least as accurate as the FEP approach at a fraction of computing time of at least one order of magnitude.

While LIE offers a quicker alternative to the longer FEP methods, LIE is still only a medium throughput screening approach. For virtual high throughput screening implicit solvation models are the only alternative, yet they lack the molecular detail of explicit models, such as the local ordering of water in the first hydration shell around a solute. This leads to effects that are captured by explicit solvation models and missed by continuum solvation models which replace the explicit waters with a continuous medium. We have therefore developed the First-Shell Hydration (FiSH) model as a first attempt to introduce first-shell effects within a continuum solvation framework. The FiSH model has been calibrated against linear interaction energy (LIE) data from molecular dynamics simulations. The FiSH model accurately reproduces contributing terms, absolute predictions relative to experimental hydration free energies, and functional class trends of LIE MD simulations. Overall, the implementation of the FiSH model achieves a very acceptable performance and transferability improving over previously developed solvation models, while being complemented by a sound physical foundation.

*Does electronic polarization give a net advantage in condensed phase simulations? A QM/MM perspective*

**Jean-François Truchon**

Merck Frosst Canada

The protein/ligand and water/solute electrostatic interactions are examined with a QM ligand-solute. The role of the electronic polarization vs static point charges is examined. Is there a net advantage of including electronic polarization? What role does the polarization self-energy play?

*Theoretical investigation of molecular ion solvation in aqueous clusters***Soran Jahangiri and Gilles Peslherbe**

Concordia University

The hydration structure and thermodynamics of selected biologically and atmospherically important molecular ions in medium-size water clusters have been investigated by molecular dynamics (MD) simulations and potential of mean force (PMF) calculations. The self-consistent charge density-functional tight-binding (SCC-DFTB) model was used to describe the atomic interactions, and the replica-exchange molecular dynamics (REMD) scheme was implemented in order to investigate the influence of conformational sampling and temperature effects on the ion hydration structure and thermodynamics. The PMFs obtained from conformational sampling with the computationally efficient SCC-DFTB were then refined with high level electronic structure theory calculations to produce first-principles PMFs. Based on the calculated PMFs, three solvation motifs were observed for the molecular ions under investigation: interior solvation is favored for Sulfate and Carbonate, Acetate and Thiocyanate exhibit surface solvation, while the solvation behavior of Nitrate and Nitrite depends on temperature and cluster size.

*Reptation quantum Monte Carlo:  
Application to ground-state properties of water*

Wai Kong Yuen, Daniel Oblinsky, and Stuart Rothstein  
Brock University

The reptation quantum Monte Carlo algorithm (RQMC) of Baroni and Moroni [*Phys. Rev. Lett.*, 82 (1999) 4745] is a recent and promising development. In this approach, one generates a large number of reptiles: sets of electron configurations arising from consecutive drift-diffusion moves. Within the fixed-node approximation, one extracts estimates of the exact energy from reptiles heads and tails (their first and last configurations of electrons, respectively), and estimates of expectation values for operators that do not commute with the Hamiltonian, from their middle configurations. An advantage over conceptually equivalent algorithms is that each estimate is free from population control bias. The time-step bias, however, may accumulate, adversely affecting one's ability to accurately estimate physical properties of atoms and molecules. For this purpose we investigate several alternative algorithms, each engineered to remedy this deficiency, while still simulating the target distribution for RQMC. The effectiveness of these approaches is demonstrated by an application to the ground-state of water.

*Watching lipids move: computer simulation of defects,  
flipflop, domains and fusion*

Peter Tieleman

University of Calgary

Computer simulation is a powerful method to study the properties of lipids in biological membranes. With increasing computer power and modern software sophisticated detailed models with thousands of lipids can be followed on time scales of hundreds of nanoseconds, while new coarse-grained methods can reach tens of microseconds on systems as large as vesicles. Biophysical and biochemical problems within reach include detailed free energy calculations on lipid-lipid interactions, membrane remodeling by proteins, pore formation due to electric fields or antimicrobial peptides, the details of monolayer compression, expansion, and breakdown, and direct simulation of protein-induced vesicle fusion. I will focus on two projects that illustrate the capabilities of computer simulations of lipids.

We investigated the thermodynamics of lipid-cholesterol interactions and calculated distributions and flip-flop rates for both lipids and cholesterol. Lipid flip-flop is slow on a physiological time scale. In contrast, cholesterol equilibrates rapidly between membrane leaflets with a strong dependence on lipid composition. Free energy calculations on cholesterol and the signaling lipid ceramide combined with large-scale equilibrium simulations are beginning to shed light on the thermodynamics of raft or nano-scale domain formation.

The coarse-grained MARTINI model is a useful approach to study large-scale phenomena such as monolayer behavior in models of lung surfactant. Lipid composition is a major determinant of the properties of lung surfactant, as are a number of surfactant proteins. Based on extensive simulations we show that a model of the surfactant protein SP-B induces spontaneous fusion between two vesicles in solution. SP-B also appears to be important for stabilizing vesicles attached to a monolayer when the monolayer is compressed beyond its limits and lipids are squeezed out of the interface.

[1] W.F.D. Bennet, J.L. MacCallum, M. Hinner, S.J. Marrink and D.P. Tieleman, *J. Am. Chem. Soc.*, 131 (2009) 12714.

[2] S.J. Marrink, A.H. de Vries and D.P. Tieleman, *Biochim. Biophys. Acta*, 1788 (2009) 149.

[3] S. Baoukina, L. Monticelli, J. Risselada, S.J. Marrink and D.P. Tieleman, *Proc. Natl. Acad. Sci.*, 105 (2008) 10803.

[4] S.J. Marrink, J. Risselada, S. Yefimov, D.P. Tieleman and A.H. de Vries, *J. Phys. Chem. B.*, 111 (2007) 7812.

*Computational investigation of the effect of cholesterol on passive transport across lipid membranes*

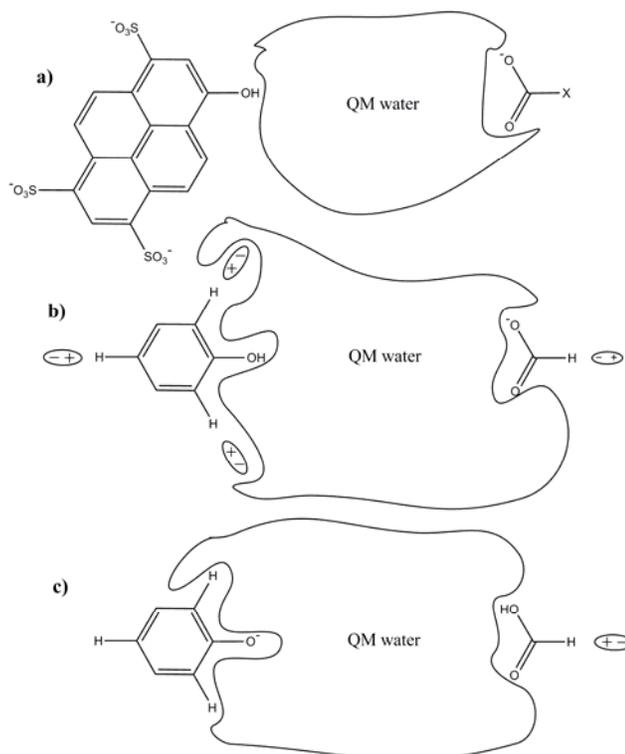
**Bilkiss Issack and Gilles Peslherbe**  
Concordia University

Essentially composed of lipid bilayers, proteins and carbohydrates, cell membranes are selectively permeable to small neutral molecules. Cholesterol is a natural component of animal cell membranes, present in varying concentrations depending on cellular functions, which modulates their physical properties, such as membrane fluidity and flexibility. It is also known to reduce the rate of passive transport across lipid membranes. The mechanism of action, however, is not clearly understood. In the present work, we investigate the effect of cholesterol on transport processes at the molecular level using computer simulations. In particular, molecular dynamics simulations are carried out for solutes inside model lipid membranes with different cholesterol contents to examine the influence of cholesterol on the partitioning and diffusion of solutes inside lipid bilayers. The results are analysed in terms of the hydrophilic and hydrophobic nature of solutes and the structural properties of cholesterol-containing membranes in order to identify the role of cholesterol in membrane transport.

## *A theoretical study of acid-base neutralization reactions: The computational model*

Patrick Maurer, Vibin Thomas and Radu Iftimie  
Université de Montréal

Ultrafast, time-resolved investigations of acid-base neutralization reactions have recently been performed using photoacids containing 8-hydroxypyrene-1,3,6-trisulfonic acid trisodium salt (HPTS) and various Brønsted bases. Two conflicting neutralization mechanisms have been formulated by Mohammed *et al.*, *Science*, 310 (2005) 83 and Siwick *et al.*, *J. Am. Chem. Soc.* 129 (2007) 13412 for the same acid-base system. Herein we formulate an *ab initio* molecular dynamics based computational model which is able to investigate the validity of the proposed mechanisms in the general context of ground-state acid-base neutralization reactions. The present approach employs 2,4,6 tricyanophenol (exp. pKa 1) as a model for excited-state HPTS\* (pKa 1.4) and carboxylate ions for the accepting base, in conjunction with our recently-proposed dipole-field/QM treatment [Maurer *et al.*, *J. Chem. Phys.*, 132 (2010) 074112] of the proton donor and acceptor molecules, which allows us to tune the free energy of the neutralization reaction to any desired value. We demonstrate that the dipole-field/QM model reproduces correctly key properties of the tricyanophenol acid molecule including gas-phase proton dissociation energies and dipole moments, and condensed-phase hydration structure and pKa values.



*Pyramidalization effects in the ground-state cis-trans isomerization  
of the green fluorescent protein chromophore*

**Qadir Timerghazin**

University of Waterloo

**Alex Brown**

University of Alberta

**Pierre-Nicholas Roy**

University of Waterloo

Green fluorescent protein and its analogues have found widespread use in biology and biochemistry as fluorescent markers. One of the interesting properties demonstrated by some fluorescent proteins is a reversible cis-trans photoisomerization of the chromophore. In many cases, the ‘dark’ trans-form of the chromophore formed as a result of photoisomerization can undergo a spontaneous thermal re-isomerisation back into the fluorescent cis-form. The mechanism of this ground-state cis-trans isomerization is expected to depend both on the intrinsic properties of the chromophore, as well as the on the protein environment. In this contribution, we will discuss hitherto ignored effects of pyramidalization at the carbon atoms involved in the rotation along the C=C bond in the free green fluorescent chromophore molecule based on *ab initio* calculations and molecular dynamics simulations.

*Insights into S-Nitrosothiol Reactivity:  
Mechanism of Acid-Catalyzed Hydrolysis*

**Qadir Timerghazin**  
University of Waterloo

**Ann English**  
Concordia University

S-Nitrosothiols (RSNOs), compounds containing the nitroso (SNO) functional group, play an important role in the storage and transport of nitric oxide NO in biological systems. It has been proposed in the literature that the reaction of nucleophiles, such as thiols or water, at the nitroso sulfur may lead to nitroxyl (HNO), another biologically active species. In this contribution, we present a computational study of acid-catalyzed hydrolysis of RSNOs in order to assess the relative reactivity of the nitroso nitrogen and sulfur atoms towards nucleophiles. Consideration of the resonance representation of RSNO electronic structure elucidates how RSNO reactivity can be controlled by Lewis-acid catalysts both in vitro and in vivo. The computational results will be discussed in conjunction with our recent experimental results.

*Chirality transfer in isotropic fluids, at interfaces, and in liquid crystals***Natalie Cann, Shihao Wang and Rodica Pecheanu**

Queen's University

A solvent molecule located near chiral solutes or surfaces can acquire some transient chirality. The nature of the solvent, the characteristics of the solute or the surface, the relative orientations, and other factors impact the induced chirality. The assessment of solvent chirality will be briefly discussed, followed by an examination of the magnitude, spatial extent, and regional chirality transfer in isotropic fluids, at several chiral surfaces relevant to chiral chromatography, and in liquid crystalline fluids.

*Catalysis of beta-sheet self-organization at water-hydrophobic interfaces***Ana Nikolic**

University of Toronto

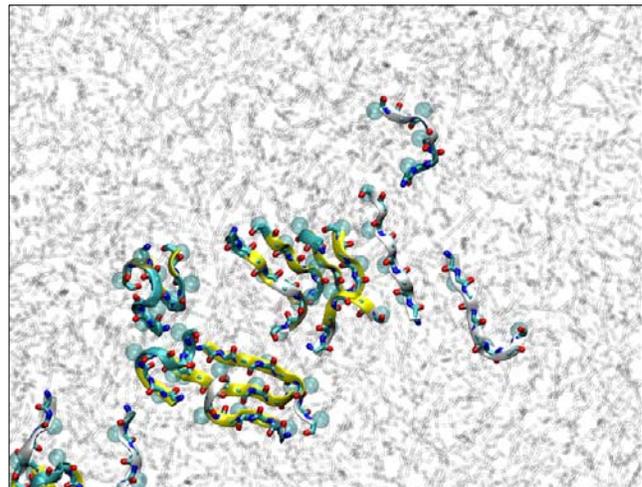
**Stéphanie Baud**

Université Reims Champagne-Ardenne, France

**Sarah Rauscher and Régis Pomès**

Hospital for Sick Children and University of Toronto

The capacity to form beta-sheet structure and to self-organize into amyloid aggregates is a property shared by many proteins. Severe neurodegenerative pathologies such as Alzheimer's disease are thought to involve the interaction of amyloidogenic protein oligomers with the neuronal membrane. To understand the experimentally-observed catalysis of amyloid formation by lipid membranes and other water-hydrophobic interfaces, we examine the physical and structural basis of peptide adsorption and aggregation in a model membrane using molecular dynamics simulations at the atomistic level of detail. Blocked amphipathic octapeptides with simple, repetitive sequences, (Gly-Ala)<sub>4</sub> and (Gly-Val)<sub>4</sub>, are used as models of beta-sheet-forming polypeptide chains found in the core of amyloid fibrils. Placed in aqueous solution in the presence of an n-octane phase mimicking the nonpolar core of lipid membranes, the peptides spontaneously partition at the octane-water interface. The adsorption of nonpolar sidechains displaces the peptides' conformational equilibrium from a heterogeneous ensemble characterized by a high degree of structural disorder towards a more ordered ensemble favoring beta-hairpins and elongated beta-strands. At the interface, peptides spontaneously aggregate and rapidly evolve beta-sheet structure on a 10-to-100-ns time scale, while aqueous aggregates remain amorphous. Catalysis of beta-sheet formation at the water-nonpolar interface results from the combination of the hydrophobic effect and of reduced conformational entropy of the polypeptide chain. While the former drives interfacial partition and displaces the conformational equilibrium of monomeric peptides, the planar interface further facilitates beta-sheet organization by increasing peptide concentration and reducing the dimensionality of self-assembly from three to two. These findings carry general implications for the formation of beta-sheets on the surface of globular proteins and for amyloid self-organization at hydrophobic interfaces.



*Path integral implementation in the molecular modeling toolkit*

**Christopher Ing**

University of Waterloo

**Konrad Hinsen**

CNRS, France

**Pierre-Nicholas Roy**

University of Waterloo

By extending the Molecular Modelling Toolkit (MMTK) software package to support a path integral representation of an atom, we can obtain structural and dynamical properties, for any classical molecular dynamics simulation, including quantum effects. To test our implementation, short simulations were performed using a stochastic Langevin thermostat for He-CO<sub>2</sub> clusters of 0.5K. Equilibrium properties of our system were in agreement with high-accuracy PIMC results published by Li *et al.*

*Non-product quadrature grids for solving  
the vibrational Schrödinger equation*

Gustavo Avila Blanco and Tucker Carrington Jr.  
Queen's University

Up to today, the calculation of vibrational energy levels of molecules with more than five atoms was mainly achieved with three different alternatives: 1) Perturbation theory [Papousek and Aliev "Molecular Vibrational-rotational Spectra" (Studies in Physical and Theoretical Chemistry) **1982**; Elsevier Science Ltd], 2) Variational or DVR (discrete variable representation) calculations with an appropriate contraction of the multidimensional basis set using product quadrature grids ["Vibrational energy levels of CH<sub>5</sub><sup>+</sup>" X.-G. Wang and T. Carrington Jr. *J. Chem. Phys.* 129 (**2008**) 234102] 3) Variational configuration interaction methods where an approximation to the potential in N-mode terms is required ["Extensions and tests of "multimode": a code to obtain accurate vibration/rotation energies of many-mode molecules " S. Carter, J.M. Bowman and N.C.Handy; *Theor. Chem. Accts.*, 100 (**1998**) 191]. Here we propose a different alternative where pruned product basis sets and non-product quadrature grids are used. Using a pruned basis set mitigates the "Curse of Dimensionality". When used in conjunction with a non-product quadrature grid it is possible to compute potential matrix elements or potential matrix-vector products efficiently. This makes it possible to use iterative methods like the Lanczos algorithm, which obviate the need to store the Hamiltonian matrix, to compute spectra. If an efficient pruning condition is available, this Lanczos-based approach can deal with vibrational problems where the computational effort is too large in other methods, either because (in the second alternative) the product grid is too huge or (in the third alternative) because a) the potential cannot be represented by lower N-mode terms and/or b) the Hamiltonian matrix cannot be stored. Examples for 6 atom molecules as CH<sub>3</sub>CN and C<sub>2</sub>H<sub>4</sub> will be presented to explain the new method.

*Computing and understanding the rovibrational spectrum  
of nitrous oxide dimer: A tale of three isomers*

**Xiao-Gang Wang**

Queen's University

**Richard Dawes**

Sandia National Laboratories

**Tucker Carrington Jr.**

Queen's University

**Ahren W. Jasper**

Sandia National Laboratories

Nitrous oxide dimer is an intriguing molecule composed of two linear monomers weakly bound to each other. Experimentally, spectra of two isomers have been observed. The most stable isomer has a well-known slipped-antiparallel, non-polar geometry. In 2007, Moazzen-Ahmadi, McKellar, and co-workers observed a second isomer which has a slipped-parallel polar geometry. In this talk we present the first detailed theoretical study of the dynamics of  $(\text{NNO})_2$  and a new, highly accurate, 4D (rigid monomer) potential surface. The new surface accurately describes the polar and non-polar isomers and also T-shaped isomers. An interpolating moving least squares (IMLS) fitting method was used to construct a surface from about 2000 points obtained with the explicitly correlated CCSD(T)-F12b method together with Peterson VTZ-F12 basis sets. The rovibrational spectrum is computed using discrete variable representation and spherical harmonic basis functions for vibrational coordinates, Wigner functions for rotational coordinates, and a Lanczos algorithm. The calculated rovibrational levels agree well with experimental results of the non-polar and polar isomers. We find that the polar isomer can tunnel between two equivalent wells, tunnelling splittings are computed, and the tunneling pathway is identified. Lastly, states belonging to a third isomer (T-shaped with N atom pointing inwards) are found which might be observable experimentally.

*pCCSD: Parameterized coupled cluster theory with single and double excitations***Lee Huntington and Marcel Nooijen**

University of Waterloo

The primary characteristics of traditional single-reference coupled-cluster (CC) theory are size-extensivity, size-consistency, invariance under orbital rotations of the occupied and virtual space, and exactness for 2 electrons in the case of CCSD, 3 electrons for CCSDT, and so forth. It is interesting to ask whether or not CC theory is the only theory which exhibits these desirable properties, and moreover if it is not, whether the traditional CC approach is perhaps the most accurate choice.

In this work, we propose a continuous class of methodologies that are related to CC and are inspired by the coupled-electron-pair approximations (CEPA). It is shown that one can systematically improve on CCSD and obtain geometries, harmonic vibrational frequencies, and total energies from a parameterized version of CC theory (picking a particular member from a continuous family of approaches) that often approaches the accuracy of CCSD(T). Also, the parameterized methodology is surprisingly accurate for single-bond-breaking phenomena. The method has been implemented in ACES2, and more recently a localized pair natural orbital (LPNO) version of the methodology has been implemented in the ORCA program developed in Prof. Frank Neese's group at the University of Bonn. This latter approach allows applications to intermediate-sized (50-100 atoms) molecular systems.

*Quantum interference transistors - simulation using Ernzerhof's source-sink potential method*

**Randall Dumont and Adam Lewis**  
McMaster University

Conduction through a sufficiently small single molecule is "ballistic" - i.e. described in terms of energy eigenstates delocalized across the molecule. Transmission of electrons through the molecule results from transmission resonances that can be tailored into a broad transmission band. Introducing arms onto a single chain molecular conductor causes reflection resonances which block transmission. These can be tailored into a broad reflection band within the transmission band. Turning such resonances on or off affords switching of the current - transistor behavior. Having smooth and broad transmission and reflection bands gives the device a fast response time - in accord with the time energy uncertainty principle. These characteristics of molecular conduction are illustrated through simulations of molecular conduction using the source-sink potential method of Ernzerhof.

# **ABSTRACTS**

## **Posters**



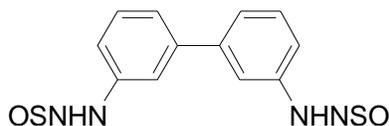
*Novel bis-N-sulfinylhydrazines and their hydrogen-bonding patterns*

**Irena Beylis and Heidi Muchall**

Concordia University

Aromatic N-sulfinylhydrazines (Ar-NH-N=S=O) can form hydrogen-bonded dimers, and dimer formation is governed by substitution on the aromatic ring. While dimerization is hindered through ortho-substituents, even methyl substitution in meta- or para-position influences the electronic structure and leads to weaker dimers than for the unsubstituted Ph-NH-N=S=O. A second NH-N=S=O group within a molecule allows for the formation of supramolecular assemblies. While computationally it is shown that chains, sheets, rings or helices can be formed, it is not possible to predict which of these would be formed for a certain bis-sulfinylhydrazine.

Here we present the different strategies towards the synthesis of bis-sulfinylhydrazines (O=S=N-NH-R-NH-N=S=O) with varying backbones R, the synthesis of **1** and (hopefully) its structure. The overall goal is to provide fundamental insight into the requirements (geometric and electronic) for a certain type of self-assembled arrangement.



**1**

*Experimental Studies on the Molecular Structures  
of aromatic N-sulfinylhydrazine*

**Stephen Boateng and Heidi Muchall**  
Concordia University

N-Phenyl-N'-sulfinylhydrazines (Ph-NH-NSO) can form hydrogen-bonded dimers. Our recent experimental IR studies have shown that dimerization of PhNHNSOs is only possible with a substituent in either meta- or para-position on the aromatic ring. Furthermore, the effect of the position and nature of the substituent on the three H-bond forming bonds N-H, ortho C-H and S=O have been investigated computationally, and it was revealed that electron withdrawing substituents have a greater effect on the frequencies and geometries than electron donating substituents.

This current study is to shed more light on the dimerization behavior of PhNHNSOs through quantitative NMR dilution experiments. Through the choice of substituents with vastly different Hammett constants, such as NO<sub>2</sub> and OCH<sub>3</sub>, in meta- and para-position, we expect to show the participation of the ortho C-H bond in the H-bonding network.

Encouragingly, for the unsubstituted PhNHNSO, the <sup>1</sup>H NMR dilution results in CDCl<sub>3</sub> from the limit of detectability to the limit of solubility show concentration dependent shifts in  $\delta$  for the (N)H nucleus and the (ortho C)H nucleus.

*Molecular polarizabilities in aqueous proton transfer reactions*

**Andrei Buin and Radu Iftimie**

Université de Montréal

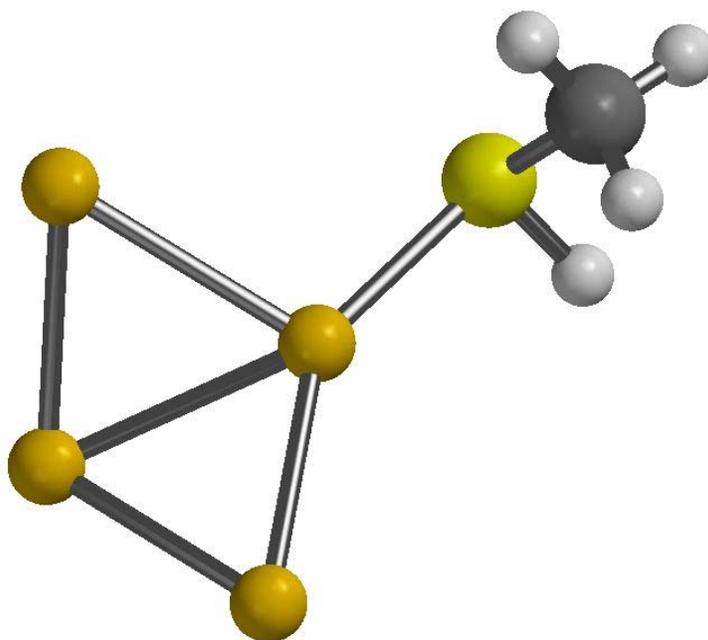
Dipole polarizabilities of individual ions and molecules are computed from first principles in three condensed-phase systems: pure water, pure hydrofluoric acid, and an equimolar mixture of water and hydrofluoric acid in which HF is mostly ionized. We find that the polarizability of fluorine and oxygen centers varies linearly with the value of the bond order, which measures the local degree of advancement of the ionization reaction. This observation explains the validity of the Lorentz-Lorenz formula for mixtures of acids and water and could have important practical consequences concerning the construction of empirical polarizable reactive force fields. The present results also suggest that the average isotropic polarizability of a chemical entity changes substantially only when that entity is involved in charge-transfer processes.

## Poster 4

### *Quantum chemical calculations of gold cluster complexes with methanethiol*

**Julia Tofan-Lazar and Ian Hamilton**  
Wilfrid Laurier University

Reactions of gold clusters and methanethiol have been studied experimentally by Ko-ichi Sugawara (AIST, Japan). The reaction rate was found to be strongly dependent on the size of the gold cluster. Our quantum chemical calculations support this experimental observation.



## Poster 5

*Conformational studies of some arabinofuranosides in solution  
and in complex with enzyme, Arabinanase Arb43A,  
using the long molecular dynamics and umbrella sampling simulations*

**Shahidul Islam**

University of Waterloo

**Mickey Richards**

University of Alberta

**Todd Lowary**

University of Alberta

**Pierre-Nicholas Roy**

University of Waterloo

Furanosyl moities are highly flexible and have been suggested to play an important role in the survival and pathogenicity of different disease causing organisms in the human body. A deeper understanding of the conformational preference of furanosyl molecules is therefore an important area of research. In this study, a conformational study on a series of mono and oligo arabinofuranosides was carried out with long molecular dynamics (MD) and umbrella sampling simulations using the AMBER force field and the GLYCAM carbohydrate parameter set. The rotamer population distribution about the exocyclic C-C bonds and the puckering distributions of the rings obtained from umbrella sampling simulations were found in excellent agreement with those obtained from long MD simulations. We therefore propose using the umbrella sampling simulations for larger oligomers where long MD simulations become impracticable. As a case study, we used both umbrella and long MD simulation on  $\alpha(1\rightarrow5)$ -linked L-arabinofuranose hexasaccharide in complex with an enzyme Arabinanases (Arb43A) and found that umbrella sampling simulation indeed gives reliable results. A direct comparison to experimental vicinal proton-proton coupling constants ( $3J_{H,H}$ ) and available Karplus relationships reveals that for  $\alpha$ -arabinofuranosyl systems, Manor's equations [Manor *et al.*, *Biochim. Biophys. Acta*, 340 (1974) 472.] yield the best  $3J_{H,H}$ , while the generalized Karplus relationship provides the best  $3J_{H,H}$  for methyl  $\beta$ -D-arabinofuranoside. Similarly, the best trend in rotamer population distribution for  $\alpha$ -arabinofuranosyl systems was obtained from Manor's equations, while the generalized Karplus relationship provides rotamer population distribution very similar to simulations for  $\beta$ -D-arabinofuranoside. We also confirm the appropriateness of a Langevin thermostat in simulations of this type of molecules.

*A computational study of electronic structure  
and hydrolytic reactivity of various N-sulfinyl species*

**Elena Ivanova and Heidi Muchall**  
Concordia University

Since their discovery more than a century ago [1], N-sulfinyl species (R–N=S=O) have found a wide application in synthetic organic chemistry for heterocyclic addition reactions [2]. Despite that long history certain features of N-sulfinyl compounds were not fully understood or questionable. For example, it is known that the substituent has a dramatic effect on RNSOs reactivity with water, varying from explosive (CINSO) [3] to a mild reactivity exhibited by N-sulfinyl amides (RCONSO) and hydrazides (RCONHNSO), to a complete inertness for N-sulfinyl hydrazines (RNHNSO) [4].

In the present work, we report the results of the comparative computational study of the hydrolysis of various classes of N-sulfinyl species (amines, hydrazines, hydrazides and amides with R=H, Me and Ph). We use the approach that has proven to be sufficiently descriptive and not computationally expensive: B3LYP 6-31+G(2d,2p) model chemistry for the “two water molecule” model [5]. The electronic structures of N-sulfinyl hydrazides and amides are reported for the first time. The effect of the substituent on the NSO moiety is discussed through an analysis of the electron density and orbital interactions within the frames of the Quantum Theory of Atoms in Molecules (QTAIM) [6], Natural Bond Orbital (NBO) and Natural Resonance (NRT) Theories [7].

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## Poster 7

### *Combined theoretical and experimental investigation of bistable photochemical switches*

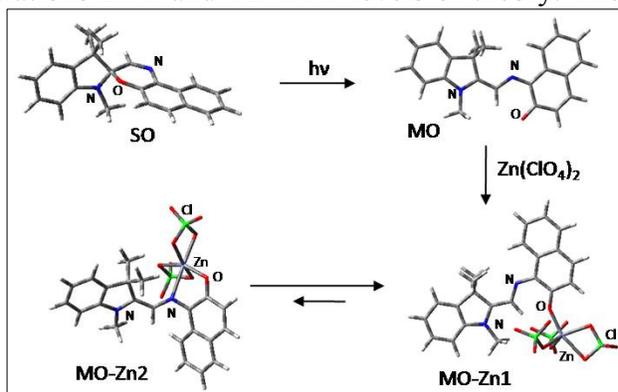
**Erwin Buncel**  
Queen's University

**Robert Stairs**  
Trent University

**Julian Dust**  
Memorial University

**Zhiyuan Tian , Martin Wyer, Thomas Kraft and Nick Mosey**  
Queen's University

Photoswitchable molecules are of interest in the development of imaging, recording and memory devices. A key requirement of effective photoswitches is bistability – the ability to persist in either of two distinct forms. In this presentation, the results of experimental and theoretical investigations of a photoswitchable spironaphthoxazine (SO) will be discussed. SO undergoes a reversible ring opening/closure upon irradiation between a spirocyclic (closed form) and an acyclic merocyanine (MO isomer, open form). The thermal equilibrium between these two forms is significantly shifted toward the spirocyclic form, even at  $-30.0^{\circ}\text{C}$ . The addition of zinc perchlorate decreases the thermal reversion of by a factor of 15, significantly improving bistability. Furthermore, the introduction of zinc results in a new absorption band that is readily distinguishable from those arising from SO and MO individually. The effects of adding zinc to the SO-MO system were explored through calculations DFT and TD-DFT levels of theory. The calculations attribute the improved bistability of the system to complex formation between MO and zinc perchlorate (see Scheme). The relative energetics of possible complexes (MO-Zn1 and MO-Zn2) are explored and a clear description of the interaction between MO and zinc perchlorate will be presented. The calculations also shed light on the origin of new bands in the absorption of spectra of the Mo-Zn complexes. These details will also be discussed.



## Poster 8

### *Dynamics of glucose binding to glucokinase*

**Monique Laberge**

Royal Military College, St-Jean

Glucokinase is a liver and pancreas enzyme with low affinity for glucose for which it displays a sigmoidal binding curve. However, unlike other allosteric enzymes that feature active sites on several subunits activated and inactivated in a concerted manner, glucokinase is monomeric. Hence, the molecular basis its allosteric behavior is not well understood. Herein we show that the dynamics of the enzyme in its substrate-free and substrate-bound conformations can be described using normal mode analysis. The analysis reveals that substrate binding to the active site induces a global conformational change in enzyme conformation that can account for the allosteric properties of this monomeric enzyme, thus providing new insight into the collective motions that allow glucokinase to function as a glucose sensor. Funding from NSERC grant 9988-06 and FQRNT 2010-PR-133873 is acknowledged.

*Quantum monte carlo prediction of  
vibrational frequency shifts for CO(pH<sub>2</sub>)<sub>n</sub> clusters*

**Hui Li, Robert LeRoy and Pierre-Nicholas Roy**

University of Waterloo

Para-H<sub>2</sub> molecules, which, like 4 He atoms, are spin zero bosons, they might also show superfluid behavior at low temperature. Recent spectroscopic studies of molecules embedded in helium droplets suggests that a new route for investigating superfluidity of para-hydrogen (p-H<sub>2</sub>) is to consider p-H<sub>2</sub> clusters doped with a single chromophore molecule (such as CO, CO<sub>2</sub>, N<sub>2</sub>O, or OCS). High resolution infrared spectra of CO in (H<sub>2</sub>)<sub>N</sub> cluster have been studied by the McKellar and coworkers, who observed R(0) rotational transition have been assigned up to N=9 for b-type series and N=14 for the a-type series with the help of reptation of Monte Carlo simulations.

Recently, Raston and coworkers indirectly determined band origin shifts for C-O stretching in small clusters with N up 7. Such studies stimulated current theoretical predictions of vibrational frequency shifts for larger clusters, and performing critically comparison between experimental and theoretical shifts in smaller clusters.

Vibrational band origins simulations need a potential energy surface which included the vibrational coordinates. Recently, we determined a five a five-dimensional analytical 'Morse/Long-Range' potential energy surface for CO-H<sub>2</sub>, which explicitly depends on the C-O stretch vibrational motion, and also incorporates the correct angle-dependent inverse-power long-range behaviour. We have used this new potential in path-integral Monte Carlo simulations to predict both the rotational dynamics and the shift of the C-O band origin for CO doped in p-H<sub>2</sub> clusters in order to provide definitive theoretical evidence whether superfluidity exists for p-H<sub>2</sub> cluster doped with CO, and if so, what cluster size it begins.

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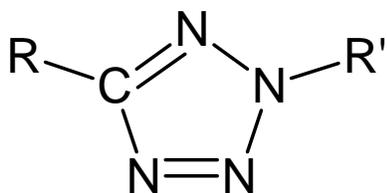
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*The generation and reaction of nitrilimines*

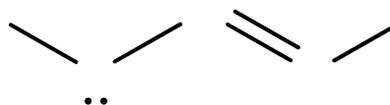
**Sima Mehrpajouh, Gilles Peslherbe and Heidi Muchall**

Concordia University

Tetrazoles **1** decompose thermally to give nitrilimines (**2**, R-CNN-R'), whose electronic structure varies widely with the substituents R and R'. In particular, for R, R' = H, the carbenic contribution to the resonance structure is small; while for NH<sub>2</sub>-substitution Natural Resonance Theory predicts 70% carbene character. This has large implications for the reactivities of substituted nitrilimines. The goal of this work is to identify nitrilimines with large carbenic contributions to their resonance structure, so that can undergo [1+2] cycloaddition reactions with unsaturated systems, in contrast to the common [3+2] cycloadditions of nitrilimines with only a small carbenic character. The former nitrilimines will later be generated experimentally. Twelve tetrazoles **1** known in the literature have been analyzed with respect to changes in geometry and orbital interactions, which are correlated to the activation energies for their decomposition. A Natural Bond Orbital analysis of the twelve nitrilimines indicates that six of them possess an electron lone pair on the carbon atom, which suggests a potentially high carbenic character.



**1**



**2**

*MM and high level ab initio QM studies on cation- $\pi$  interactions  
and their cooperativity with  $\pi$ - $\pi$  interactions*

**Esam Orabi and Guillaume Lamoureux**  
Concordia University

Cation- $\pi$  interactions are non-covalent interactions known to play important roles in protein-ligand interactions, molecular recognition, permeation of ions in some channels, and stabilization of protein structures.  $\pi$ - $\pi$  interactions have been found to stabilize the structures of DNA, RNA, and proteins and are also utilized in binding of drugs. *Ab initio* quantum mechanical calculations of  $\text{Li}^+$ ,  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{NH}_4^+$  in complex with benzene, benzene dimers, and benzene trimers have been performed at the MP2/6-311++G\*\* level of theory. The results show that cooperativity exists between cation- $\pi$  and  $\pi$ - $\pi$  interactions; the presence of one strengthens the other, as evidenced from the calculated synergetic energy term. Potential energy surfaces for the interactions between the four cations and benzene have been generated at the same theory level. Polarizable empirical force field models for cation- $\pi$  interactions have been parameterized using the *ab initio* energy surfaces. The obtained models have been found able to generate the *ab initio* surfaces and predicting the cooperativity between the two non-covalent interactions.

## Poster 12

### *Technical Note: Acquiring ab-initio points using a parallel Perl script*

**Hartmut Schmider, Chris MacPhee, Yong Park**  
Queen's University

**Owen Clarkin**  
Queen's University and Steacie Institute for Molecular Science

**David Wardlaw**  
University of Western Ontario

In this note, we present a systematic way of performing a large number of *ab-initio* calculations on a parallel platform using a set of scripts programmed in Perl. We show a few application examples based on the exploration of potential-energy surfaces. However, the method is applicable for project that requires thousands of ab-initio computations, or for that matter any other type of parametric study.

*Extension of the Source-Sink Potential (SSP) approach for multi-channel conductance calculations.*

**Philippe Rocheleau and Matthias Ernzerhof**

University of Montreal

In molecular electronics, molecules are connected to macroscopic contacts and the current passing through is studied as a function of the applied voltage. We focus on modeling the transmission of electrons through such a molecular electronic device (MED). Based on a simple Hückel Hamiltonian to describe the pi electrons in conjugated systems, the SSP method [1,2,3] employs complex potentials to replace the wavefunction of the infinite contacts in a rigorous way. The initial SSP approach [4] was limited to two one-dimensional contacts, here we extend the approach to multiple channels, i.e., to two-dimensional contacts including transverse modes. We describe the development of the method and illustrate it with applications.

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[4] P. Rocheleau and M. Ernzerhof, *J. Chem. Phys.*, 130 (2009) 184704.

*Computational studies of NO diffusion in hemoglobin: Relevance in vasodilation*

**Mariya Shadrina, Denise M. Koch,  
Ann M. English and Gilles H. Peslherbe**  
Concordia University

Hemoglobin (Hb) is the most abundant component of red blood cells (RBCs). This protein transports Fe(II)heme-bound oxygen ( $O_2$ ) from the lungs to the tissues, and the cooperative binding of  $O_2$  is accompanied by a transition from a low-affinity, unligated T-state to a high-affinity, ligated R-state of the protein. Regulation of blood flow in the microcirculation is controlled by physiological oxygen ( $O_2$ ) gradients in the vessels, which undergo vasodilation and vasoconstriction [1]. Endothelium-derived NO is a principal activator of vasodilation and binds to the unligated Fe(II) heme of Hb. On aeration, Hb changes conformation from T- to R-state and some of the Fe(II)-bound NO undergoes transfer to Cys $\beta$ 93, forming S-nitrosohemoglobin (SNO-Hb), which is proposed to be vasoactive [2]. The reported crystal structure of SNO-Hb [3] suggests that S-nitrosation occurs exclusively on the surface Cys $\beta$ 93 residues but the mechanism of NO transfer from the heme to the thiols is unknown. Diffusion of NO molecules through intramolecular hydrophobic channels connecting the heme and Cys $\beta$ 93 was investigated computationally. Diffusion pathways in the different conformational states of the Hb tetramer were thoroughly examined by molecular dynamics simulations. No direct pathway between the heme and Cys $\beta$ 93 was found. In T-state Hb, NO was observed to quickly escape from the  $\beta$ -subunit to the central cavity between the subunits whereas other conformations of Hb retain NO within the  $\beta$ -subunit. Similar long spiral channels with different NO escape times and exits were found for NO at the heme of the  $\alpha$ -subunits of Hb. The relevance of intramolecular NO diffusion in Hb and its role in vasodilation are discussed in light of the computational results.

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*Identifying and characterizing the acid dissociation intermediates  
in aqueous solution*

**Vibin Thomas and Radu Iftimie**  
Université de Montréal

Despite the ubiquity of aqueous acids in chemical and biological systems, a molecular level description of acid ionization and dissociation remains elusive. The common representation in the introductory chemistry texts that the acid (AH) dissociate to give hydronium ion ( $\text{H}_3\text{O}^+$ ) and  $\text{A}^-$  is too simplistic which masks all the intermediate structures. Here, we show how we successfully identified and characterized the various stages of acid dissociation intermediates including proton shared species and contact ion pairs using car-parinello molecular dynamics with on the fly maximally localized wannier orbitals and the infrared spectral decomposition technique on trifluoroacetic acid-water system and hydrogen fluoride-water system. The important conclusions obtained from these investigations are: a) Proton shared forms exists in aqueous solution of hydrogen fluoride b) Proton shared species can be distinguished from un-ionized species by the presence of an intense structureless continuous absorption below  $1700\text{ cm}^{-1}$ . Contact ion pairs are found in the aqueous solution of trifluoro acetic acid. Their formation is indicated by the disappearance of C=O stretching vibration at  $1700\text{ cm}^{-1}$  and by the appearance of the symmetric and antisymmetric stretching vibration band at  $1400$  and  $1600\text{ cm}^{-1}$ . We also made an important observation on how the hydration shell participates in the discrete stages of acid dissociation.

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*Can N<sub>2</sub>O bending really be neglectful in He-N<sub>2</sub>O dynamics?*

**Wang Lecheng, Li Hui, Robert Le Roy and Dai Qianxie**

University of Waterloo

The shift of the vibrational band origin of a chromophore molecule probe solved in a nano droplet provides powerful insights regarding the nature of microscopic solvation. A new high-level 4D potential energy surface has been calculated for He-N<sub>2</sub>O, which takes account of both the dymmetric (Q1) and asymmetric (Q3) motion of the N<sub>2</sub>O monomer, and two vibrationally averaged 2D surfaces were then obtained by averaging over the N<sub>2</sub>O motion in the (v1, v2, v3)=(0, 0, 0) and (0, 0, 1) vibrational levels. A PIMC simulation average over the difference between those surface then gives predicted vibrational frequency shifts for N<sub>2</sub>O-(He)<sub>n</sub> clusters. While this methodology gave excellent agreement with experimental observations for CO<sub>2</sub>-(He)<sub>n</sub> clusters, it fails here. We speculate that the problem is due to the neglect of N<sub>2</sub>O bending, and propose an inexpensive method of incorporating the effective N<sub>2</sub>O bending in the cluster dynamics.

*Development of semi-empirical models for zinc metalloenzymes*

**Shihao Wang and Guillaume Lamoureux**  
Concordia University

Semi-empirical models based on the neglect of diatomic differential overlap (AM1, RM1, PM3) have been widely used in mechanistic studies of organic reactions. However, those models were generally parameterized from small organic molecules, and are not accurate enough for zinc-catalyzed reactions in enzymes. A new methodology is developed to parameterize the models for hydrolysis reactions in zinc metalloenzymes. The training set is prepared by high level *ab initio* data, which includes fragments of the enzyme active sites. A scoring function is defined by the most relevant properties, such as bond lengths, angles, proton affinities, reaction energies and barriers. The parameterization process contains random searching in the parameter space and minimization of the scoring function. This process is repeated for each element until the parameters are converged. The final parameter set performs very well in the testing set.

*Vibrational spectroscopy from  
first-principles molecular dynamics simulations:  
Towards understanding guanidinium-peptide interactions*

Xijun Wang and Gilles Peslherbe  
Concordia University

The guanidinium ion plays an important role in biochemistry, and in particular, it is known to affect the stability of proteins [1]. Experimental infrared spectral studies have provided some evidence of molecular interactions between guanidinium and proteins or small peptides when they are mixed together in aqueous solutions [2]. However, the nature of these interactions remains unclear. Computational studies are thus necessary to help gain insight into the exact nature of the molecular interactions and explain the observed experimental spectral signatures. As a first step, we investigate the hydration structure of the guanidinium ion and the effects of hydration on its vibrational spectra. To that effect, Car-Parrinello molecular dynamics simulations are performed of the guanidinium ion, both in the gas phase and the aqueous phase, and vibrational spectra are calculated as the Fourier transform of the system dipole-dipole auto-correlation function. The choice of simulation cutoff and functional is discussed, as well as the spectral band assignment.

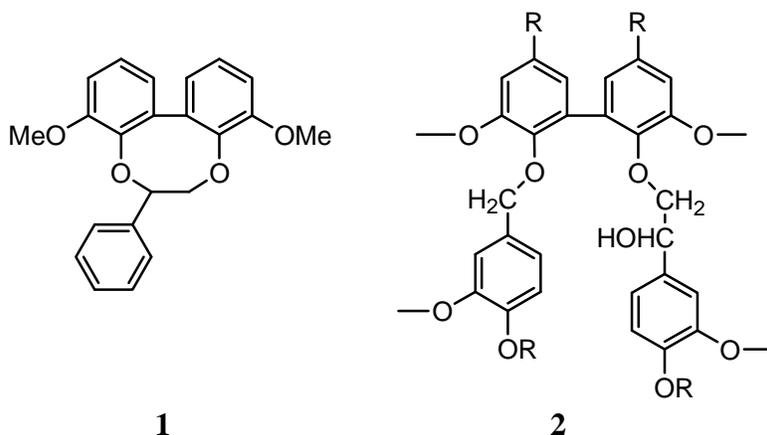
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*Exploratory computational studies towards  
the photo-induced degradation of lignin*

**Lei Zhang, Gilles Peslherbe and Heidi Muchall**  
Concordia University

Lignin is a three-dimensional phenolic polymer and is amongst the most abundant biopolymers on earth. The photo-induced degradation of lignin is an important and complicated process, through which phenoxy radicals are produced via different pathways and may be further oxidized into quinones causing photo-yellowing. While the contribution of different pathways is still under debate, their roles in the photo-induced yellowing of lignin-rich, high-yield, mechanical pulps are also ambiguous. In this work, as a first step towards these studies, we evaluated the photo-induced fragmentation of dibenzodioxin (1) and its biphenyl derivative (2), which are highly photo-sensitive structural elements involved in chemical pulping and bleaching, using a computational approach validated for acetone photolysis.



*Hartree-Fock and Kohn-Sham method for open systems*

**Yongxi Zhou and Matthias Ernzerhof**

Université de Montréal

The source-sink potential (SSP) method [1,2] provides a simple description of electron transport through molecules. Starting from the tight-binding approach, the infinite contacts are replaced by complex potentials. Extending SSP, we describe how to introduce complex potentials into the Hartree-Fock and the Kohn-Sham method. Doing so enables us to model open systems with a current passing through, while accounting for exchange and correlation effects. The implementation of these methods and initial results will be discussed.

[1] F. Goyer, M. Ernzerhof and M. Zhuang, *J. Chem. Phys.*, 126 (2007) 144104.

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