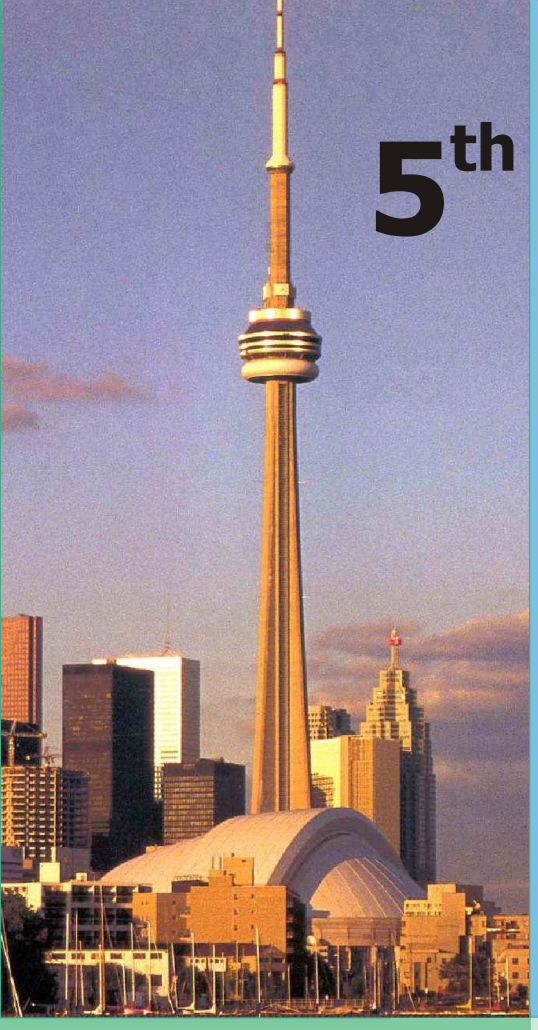

5th Canadian Computational Chemistry Conference

July 27 - 30, 2003

University of Toronto, Toronto, Ontario, Canada

Invited Speakers

Christopher Bayly (Merck Frosst, Canada)
Emily Carter (University of California, Los Angeles, USA)
Gordon Crippen (University of Michigan, USA)
Gabriele Cruciani (University of Perugia, Italy)
Julian Gale (Imperial College of Science, Technology and Medicine, UK)
Angel García (Los Alamos National Laboratory, USA)
Shekhar Garde (Rensselaer Polytechnic Institute, USA)
Phillip Geissler (University of California, Berkeley, USA)
Peter Grootenhuis (Deltagen Research Labs, USA)
Ajay Jain (University of California, San Francisco, USA)
Hannes Jónsson (Iceland)
Gilles Klopman (Case Western, USA)
Leslie Kuhn (Michigan State, USA)
Glenn Martyna (IBM, USA)
Ulf Norinder (AstraZeneca, Sweden)
Gilles Peslherbe (Concordia University, Canada)
Enrico Purísima (BRI Montréal, Canada)
David Reichman (Harvard, USA)
Pierre-Nicolas Roy (University of Alberta, Canada)
Michiel Sprik (Cambridge University, UK)
Peter Tieleman (University of Calgary, Canada)
Shaomeng Wang (University of Michigan, USA)
Tom Woolf (Johns Hopkins, USA)

Featured Sessions

Advances in Computational Biophysics: Soluble and Membrane Proteins
Computational Biophysics I: Protein Hydration, Dynamics, and Folding
Computational Biophysics II: Self-assembly, Membranes, and Transport
Reaction Pathways and Rough Energy Landscapes
Advances in Computational Methods
Drug Design I: Advances in Structure Based Design
Electronic Structure and Quantum Systems
Drug Design II: In-silico ADME/Tox in Drug Discovery

Organizing Committee

Jeremy Schofield, University of Toronto
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Final call for abstracts

The 5th Canadian Computational Chemistry Conference (CCCC5) is the continuation of a series of meetings held every three years intended to foster the excellence of computational chemistry in Canada. One of the principal goals of the conference is to highlight the impact of computational chemistry in academia, industry and society.

Abstract submission deadline: July 1, 2003

Registration fee: $130 (Students/Post Docs) $330 (all others)
Price includes Banquet and reception

Contact Info:

cccc5@chem.utoronto.ca

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Daily Program

Saturday, July 26, 2003	
5:00pm-8:00pm	**Registration** Main Lobby of the Department of Chemistry, 80 St. George Street
Sunday, July 27, 2003	
	Morning Session: 8:45am-12:35pm *Computational Biophysics: Protein Hydration, Dynamics, and Folding* Session Chair: Hue Sun Chan (University of Toronto, Biochemistry, Canada) **Rm 1160, Bahen Centre for Information Technology, 40 St. George Street**
8:45am-9:00am	Opening Comments: Régis Pomès (Hospital for Sick Children, Canada)
9:00am-9:45am	**Angel Garcia** (Los Alamos National Laboratory, USA) *Folding a Protein in the Computer – All Atom Stimulation of the Folding/Unfolding Thermodynamics of Protein A*
9:45am-10:30am	**Gordon M. Crippen** (University of Michigan, USA) *Progress in Predicting Human Metabolic Site of Metabolism 'In Silico'*
10:30am-10:45am	Coffee Break
10:45am-11:30am	**Wonpil Im** (The Scripps Research Institute, USA) *An Implicit Membrane Generalized Born Theory for the Study of Structure, Stability, and Interactions of Membrane Proteins*
11:30am-12:00pm	**Stuart Rothstein** (Brock University, Canada) *Efficient Generation of Low-Energy Folded States of Model Protein: Automated Histogram Filtering*
12:00pm-12:30pm	**Yaoqi Zhou** (University of Buffalo SUNY, USA) *Learning Folding and Domain Swapping from All-Atom Structures and Simple Parameters*
12:30pm-2:00pm	Lunch: Pay Your Own Way Dim Sum
2:00pm-4:00pm	**MDIT Workshop:** Régis Pomès and Lakshmi Kotra **Faculty of Pharmacy, 19 Russell Street**
	Afternoon Session: 4:00pm-6:15pm *Computational Biophysics: Self-Assembly, Membranes, and Transport* Session Chair: Régis Pomès (Hospital for Sick Children, Canada) **Rm 1160, Bahen Centre for Information Technology, 40 St. George Street**
4:00pm-4:45pm	**Shekhar Garde** (Rensselaer Polytechnic Institute, USA) *Proteins Under Stress: Molecular Simulation Studies of Pressure Effects on Proteins*
4:45pm-5:30pm	**Peter Tieleman** (University of Calgary, Canada) *Non-Equilibrium Simulations of Lipid Bilayers*
5:30pm-6:15pm	**Volkhard Helms** (Max Planck Institute of Biophysics, Germany) *Proton Transfer Reactions in Biological Systems Simulated with Q-HOP Molecular Dynamics*
6:30pm-8:00pm	Welcome Reception and BBQ Hart House Quadrangle

Monday, July 28, 2003	
	Morning Session: 9:00am-12:15pm *Reaction Pathways and Rough Energy Landscapes* Session Chair: Jeremy Schofield (University of Toronto, Chemistry, Canada) **Isabel Bader Theatre, 93 Charles Street**
9:00am-9:45am	**Hannes Jonsson** (University of Washington, USA)
9:45am-10:30am	**Phillip Geissler** (University of California, Berkeley, USA) *Statistical Mechanics of Reactive Trajectories: In and Out of Equilibrium*
10:30am-10:45am	Coffee Break
10:45am-11:30am	**David Reichman** (Harvard University, USA) *Models of Slow Dynamics in Glassy Media*
11:30am-12:15pm	**Tom Woolf** (Johns Hopkins University, USA) *Tools for Channels: Moving Towards Molecular Calculations of Gating and Permeation in Ion Channel Biophysics*
12:15pm-2:00pm	Lunch Hart House Quadrangle
2:00pm-4:00pm	**Poster Session I** **East Common Room of Hart House**
	Afternoon Session: 4:00pm-6:00pm *Advances in Computational Methods in Material Science* Session Chair: John Tse (National Research Council of Canada, Canada) **Isabel Bader Theatre, 93 Charles Street**
4:00pm-4:45pm	**Julian Gale** (Imperial College, United Kingdom) *The SIESTA Method and it's Application to Nanostructures*
4:45pm-5:30pm	**Michiel Sprik** (University of Cambridge, United Kingdom) *Electronic States in Aqueous Solution: Redox Reactions and Spectroscopy*
5:30pm-6:00pm	**M.A. (Tony) Whitehead** (McGill University, Canada) *Molecularly Self-Assembled Thin Films: Theory and Experiment*
Tuesday, July 29, 2003	
	Morning Session: 9:00am-12:30pm *Drug Design I: Advances in Structure-Based Design* Session Chair: Alan Cameron (ProMetic BioSciences Inc., Canada) **Isabel Bader Theatre, 93 Charles Street**
9:00am-9:40am	**Ajay Jain** (UCSF Cancer Research Institute, USA) *Molecular Surface Representation: Applications in Structure-Based Drug Design*
9:40am-10:20am	**Christopher Bayly** (Merck Frosst Center for Therapeutic Research, Canada) *Structure-Based Design of COX-2 Selectivity into Flurbiprofen*
10:20am-10:30am	Coffee Break
10:30am-11:10am	**Enrico Purisima** (National Research Council of Canada, Canada) *Issues in Parametrizing Emperical Binding Free Energy Functions*
11:10am-11:50am	**Maria Zavodszky** (Michigan State University, USA) *Modeling Protein Flexibility in Docking*
11:50am-12:30pm	**Shaomeng Wang** (University of Michigan, USA) *Structure-Based Discovery and Optimization of Novel, Potent and Selective*

	Ligands for the Dopamine 3 (D3) Receptor
12:30pm-2:00pm	Lunch Hart House Quadrangle
2:00pm-4:00pm	**Poster Session II** **East Common Room of Hart House**
	Afternoon Session: 4:00pm-6:30pm *Quantum Dynamics in Complex Systems I* Session Chair: Ray Kapral (University of Toronto, Chemistry, Canada) **Isabel Bader Theatre, 93 Charles Street**
4:00pm-4:45pm	**Emily Carter** (UCLA, USA) *Linking Quantum and Continuum Mechanics to Study Mechanical Response of Materials: Shocked, Stressed, and Embrittled Iron*
4:45pm-5:30pm	**Pierre-Nicholas Roy** (University of Alberta, Canada) *Rotational Solute Dynamics in Quantum Clusters*
5:30pm-6:00pm	**Alessandro Sergi** (University of Toronto, Canada) *Quantum-Classical Dynamics of Nonadiabatic Chemical Reactions*
6:00pm-6:30pm	**Yossi Elran** (University of Toronto, Canada) *Semiclassical IVR (Intial Value Representation) Treatment of the S-matrix*
6:30pm-6:45pm	Organizational Meeting for CCCC6
7:00pm-9:00pm	Banquet Great Hall of Hart House
Wednesday, July 30, 2003	
	Morning Session: 9:00am-12:15pm *Quantum Dynamics in Complex Systems II* Session Chair: Styliani Consta (University of Western Ontario, Canada) **Isabel Bader Theatre, 93 Charles Street**
9:00am-9:45am	**Glenn Martyna** (IBM, USA) *Manybody Polarization and Disperison Effects on Condensed Phase Systems*
9:45am-10:05am	**Victor Batista** (Yale University, USA) *Coherent Control of Cis/Trans Photoisomerization in Rhodopsin*
10:05am-10:35am	**Alexander Wang** (University of British Columbia, Canada) *Theoretical Studies of the Catalytic Mechanisms of the Periplasmic Nitrate Reductase*
10:35am-10:45am	Coffee Break
10:45am-11:30am	**Gilles Peslherbe** (Concordia University, Canada) *Ab Initio Excited-State Molecular Dynamics Simulations: Application to Cluster Photochemistry*
11:30am-12:15pm	**Zsolt Zsoldos** (SimBioSys Inc., Canada) *eHiTS: electronic High Throughout Screening*
12:15pm-2:00pm	Lunch Hart House Quadrangle
	Afternoon Session: 2:00pm-5:15pm *Drug Design II: In-Silico ADME/Tox in Drug Discovery* Session Chair: Sanjay Srivastava (AstraZeneca, Canada) **Isabel Bader Theatre, 93 Charles Street**

2:00pm-2:45pm 2:45pm-3:30pm	**Peter Grootenhuis** (Vertex Pharmaceuticals Inc., USA) *Enhancing Drug Discovery Through Computational ADME* **Gabriele Cruciani** (University of Perugia, Italy) *Process in Predicting Human Metabolic Site Metabolism 'In Silico'*
3:30pm-3:45pm	Coffee Break
3:45pm-4:30pm	**Gilles Klopman** (Case Western Reserve University, USA) *MCASE; A Computational Tool for the Rational Evaluation of the Hazard Potential of New Pharmaceuticals*
4:30pm-5:15pm	**Ulf Norinder** (AstraZeneca R&D Sodertalje, Sweden) *Rapid 'In Silico' Predictions of ADMET Properties Using Machine-Learning Techniques*

ABSTRACTS

57243

Coherent control of cis/trans photoisomerization in rhodopsin

Victor S. Batista, Samuel Flores
Yale University
225 Prospect Street

Coherent control of the photoisomerization of retinal in rhodopsin was simulated according to two different coherent-control schemes. First, a bichromatic coherent control scenario in the weak field limit was investigated. A coherent superposition of ground and excited vibrational wavepackets in the ground electronic state was photo-excited to the first excited electronic state using two different laser pulses of appropriate wavelengths to photo-excite both wave packet components to the same final energy state. The relative intensity and phase of the pulses were varied over their complete ranges and the resulting isomerization product yield was computed. Bichromatic coherent-control as demonstrated in spite of the rapid intrinsic decoherence phenomena induced by the vibronic activity, but only in the 3--5 % range over photoproduct yields. The second method involved a novel bichirped coherent control scenario in the strong field limit. Extensive coherent control was demonstrated providing results of broad experimental and theoretical interest. Simulations involved exact quantum dynamics calculations based on an empirical two-state two-mode model Hamiltonian that qualitatively reproduces all available spectroscopic information on rhodopsin. Work in progress on the development of a QM/MM model Hamiltonian for describing the cis/trans photoisomerization reaction in bacteriorhodopsin is also reported.

57244

A COMPUTATIONAL STUDY OF PENTA-CYCLO UNDECANE (PCU) CAGE LACTAM FORMATION.

Thishana Singh, Thishana Singh, Krishna Bisetty and Hendrik G. Kruger
Durban Institute of TechnologyDept.of Chemistry,Durban Institute of Technology,Box 1334,Durban,South Africa

The underlying philosophy of this work is based on the fact a molecular structure is all that is needed in the determination of reaction pathways of chemical reactions. This study involved an ab initio investigation of the mechanistic pathways for the conversion of the PCU dione 1 to a dihydroxy d-lactam 2. The mechanism proposed for this unique conversion was based on chemical intuition and it remained a challenge to use computational techniques to verify the kinetics and thermodynamics of the mechanism through finding the structures of intermediates, transition states and products. The study involved geometry optimization of the different PCU cage lactam species at the Hartree Fock (HF) level using the 3-21+G* basis set. The thermodynamic and kinetic results will be presented to verify and extend the mechanistic pathway for the formation of the PCU cage lactam.

57246

Learning folding & domain swapping from all-atom structures and simple parameters

Yaoqi Zhou, Apichart Linhananta, Hongyi Zhou, Chi Zhang
Department of Physiology & Biophysics, State University of New York124 Sherman Hall, Buffalo, NY 14214

Topology, commonly referred to the arrangement of the secondary structures of a protein, has been extensively studied for its role in protein folding. Recent work shows that topology alone can not account for all the variety of folding behavior found for the proteins within the same structural family. A question naturally arises: can the atomically-detailed native structure of a protein improve the prediction of folding mechanism? Here, we examined the effect of sidechain packing on the folding mechanisms of a beta-hairpin and a three-helix bundle protein. This is done by using a recently developed all-atom Go model and discontinuous molecular dynamics techniques. The results further lead to the development of a simple loop-contact-distance parameter that qualitatively captures the dual folding behavior of a loop. Moreover, it was showed that there is an intimate connection between folding and domain swapping, a possible cause of misfolding and aggregation.

57249

Theoretical Studies of the Catalytic Mechanisms of the Periplasmic Nitrate Reductase

Yan Alexander Wang*, Federico E. Zahariev, and Walter R. P. Scott
Department of Chemistry, University of British Columbia2036 Main Mall, Vancouver, BC, Canada

Based on the first crystal structure of dissimilatory nitrate reductase [J. M. Dias *et al*., Structure **7**, 65 (1999)], the reaction mechanism of an enzymatic reduction of nitrate to nitrite is studied by theoretical techniques. Interestingly, this enzyme requires two pterin cofactors for a Mo active site and a [4Fe-4S] cluster to function. To this date, the reaction cycle of this important enzyme has not been elucidated.The active site is simulated using a multi-layered approach. The Mo center and its close proximity are modeled with the B3LYP density functional, the pterin cofactors are modeled with the PM3 semi-empirical method, and the remaining part is treated with AMBER empirical forces. The interfaces between the layers are linked within the ONIOM scheme [S. Dapprich *et al*., Theochem **461-462**, 1 (1999)]. Fully solvated classical molecular dynamics simulations are performed on the complete system. We predict a sequence of conformational changes of the Mo site along the catalytic cycle. We then show that these conformational changes induce movement in the rest of the enzyme, pulling closer the distant [4Fe-4S] cluster (an electron donor). The proximity of the two metal centers at the end of the oxidation phase will trigger the reduction phase via electron transfer and finalize the entire catalytic cycle. In addition, we discuss the role of solvent, particularly the coordinated water molecules, and several alternative reaction paths.

57250

eHiTS: electronic High Throughput Screening

Zsolt Zsoldos, Aniko Simon, Irina Szabo, Zsolt Szabo, David Fung
SimBioSys Inc.135 Queen's Plate Dr, Unit 355, Toronto, ON M9W 6V1, Canada

eHiTS is an exhaustive flexible docking method which reaches the speed range of a few seconds per ligand, yet it provides higher accuracy than any other docking method published to date. Both the receptor cavity and the candidate ligands are described by a geometric shape and chemical feature graph based on distorted polyhedra. The graphs are mapped to each other with a fast systematic graph matching algorithm. This method typically generates millions of flexible ligand poses for a given receptor in a matter of seconds. The evaluation of such a vast set of poses demands a quick scoring function with reliable filtering abilities. eHiTS employs a radically new scoring approach based on local surface point contact evaluation. Properties of surface points are assigned with fine granularity, e.g. surface point properties of a polar atom in an aromatic ring would be very different along the edge of the ring from the faces of the ring. Hydrogen bonding is also expressed as localized and concentrated surface property along the specific proton or electron pair donation directions. Receptor surface points are also assigned pocket-depth information to express differences in dielectric constants on solvated surface points and deeply embedded cavity points. eHiTS was validated on a set of 390 PDB complex structures, and it is demonstrated that the program can identify the correct docking pose within 2A RMSD from the X-ray ligand for over 90% of the cases.

57251

Validation of the SPROUT de novo design program

Jacqueline M.S. Law, David Y.K. Fung, Zsolt Zsoldos, Aniko Simon, Zsolt Szabo, Imre Csizmadia
Department of Chemistry, University of TorontoDepartment of Chemistry, University of Toronto, Toronto, ON Canada, M5S 3H6

The validation of SPROUT version 4.11 was carried out on four receptor-ligand complexes: thrombin-NAPAP, calmodulin-AAA, Ras P-21-GDP and dihydrofolate reductase (DHFR)-methotrexate (MTX). These complexes were downloaded from the Brookhaven Protein Data Bank (PDB). For the thrombin-NAPAP complex, two structures very similar to NAPAP were generated. These two structures were similar in 3D structure to NAPAP but contained an extra hexane ring. For calmodulin-AAA and Ras P-21-GDP, the ligands generated were essentially identical to their original ligands. For DHFR, two ligands, one most similar in 2D structure and one most similar in 3D conformation were found. The successful regeneration of the ligands for each case proves the ability and applicability of SPROUT for designing strongly binding, successful drug candidates. When the program is executed with less restricted constraints, it generates a large number of novel structures that are structurally diverse,making it an ideal tool for de novo design.

57252

INTERACTIONS OF ISONIAZID AND ITS DERIVATIVES WITH MYCOBACTERIUM TUBERCULOSIS SUSCEPTIBLE ENZYME (S). A MOLECULAR MODELING AND DOCKING STUDIES.

Khawaja Sohail Qamar, Pazilah Ibrahim, Habibah Wahab
University Sains Malaysia2800 gentry town drive apt#35 antioch.ca 94509 USA.

In our studies we have attempted to explore the mechanism of action as well as resistance of isoniazid with the help of various Molecular modeling techniques. We have docked isoniazid, its derivatives and isonicotinic acyl-Nadh, into the wild-type and mutant-type, InhA; an enzyme involved in the biosynthesis of mycolic acids in Mycobacterium tuberculosis. All models of ligand and enzymes were generated with the help of AMBER program package which are then docked into the wild-type and mutant-type InhA active sites individually using computational automated docking package AUTODOCK 3.0, wherein a new hybrid Lamarkian genetic algorithm is implemented in complex with pseudo-Solis and Wets local search. In our first docking studies isoniazid and derivatives (un-activated) were found docked into the active site of both wild-type and mutant-type InhA in almost the same place and conformation where isonicotinic acyl-Nadh was present as predicted by earlier by earlier X-ray crystallographic studies. After careful analysis, INH11, INH12, INH13, INH14, INH8, INH10 and INH9 proves to be the most favourable anti-tubercular compounds in this order on ground of estimated free energies and other predicted energies. In case of derivatives (same as docked to wild-type InhA enzyme) docked to mutant-type InhA enzyme, INH11, INH6, and INH13 proved to be the most favourable compounds for mutant-type S94A strains.In our second docking studies, isonicotinic acyl-Nadh bounds with wild-type InhA in almost the same conformation as found by X-ray crystallography. The residue Phenylalanine 40 of the wild-type InhA was found to make specific interactions with the adenine rings of isonicotinic acyl-Nadh that might help to position the complex of activated form of isoniazid and Nadh but in case of mutant-type InhA, the adenine ring drifts away as a result of strong interactions of the mutant residue Alanine 94 with the phosphates in the middle of isonicotinic acyl-Nadh. The predictions of these interactions at the molecular level can be of primary importance in elucidating the resistance developed in the newly emerged mutant strains of Mycobacterium tuberculosis.

57256

Ab initio and DFT study of structural and thermochemical properties of $(NPF_2)_2$, $(NPX_2)_3$; X = H, F, Cl, Br, and $(NPF_2)_4$ phosphazenes

Hassan Sabzyan, Zahra Kalantar
Department of Chemistry,
University of Isfahan, Isfahan 81746-73441

Gas phase molecular structure and bonding, thermochemical stability and spectroscopic properties of $(NPF_2)_2$, $(NPX_2)_3$; X= H, F, Cl, Br, and $(NPF_2)_4$ cyclic phosphazenes have been studied employing quantum computational *ab initio* and DFT methods. Molecular geometries were optimized using RHF, B3LYP and B3PW91 levels of theory with 6-31G, 6-31G* and 6-31+G* basis sets. Thermochemical, vibrational and NMR shielding analysis have also been carried out on the optimized structures of these phosphazenes. This study showed that all of these compounds have planar structure and are thermodynamically stable in the gas phase. Furthermore, the identical values obtained for all P-N bond lengths in each $(NPF_2)_2$, $(NPX_2)_3$; X= H, F, Cl, Br, show that the π-bond system of the ring in this series of compounds has aromatic character. This is also approved by a population analysis carried out on the $(NPX_2)_3$ systems. It is also found that the P-N bond length in the six-member rings are shortened with increasing the electronegativity of the halogen substituents on the phosphorus atom, while the P-X bond length and X-P-X bond angle are decreased. In spite of the optimized planar structure, the π-bond system of the ring in $(NPF_2)_4$ does not show any aromatic character, and two distinct sets of P-N bonds exist in this phosphazene.

57258

Basis set effects on the intermolecular interaction of the F_2-F_2 system

Hassan Sabzyan, Mohammad-Reza Noorbala
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University of Isfahan, Isfahan 81746-73441, I. R. Iran

Intermolecular potential energy surface (IPS) for F_2-F_2 system has been examined using RHF, MP2 and DFT--B3LYP methods. A number of basis sets from the double-zeta and triple-zeta family were used in order to evaluate the basis set effects. These effects vary with the level of theory used. Counterpoise (CP) correction has been used to show the extent of the basis set superposition error (BSSE) on the potential energy curves obtained for F_2-F_2 system. CP corrections revealed that B3LYP and RHF levels of theory predict a totally repulsive interaction between the two monomers of F_2-F_2 system. The deepest BSSE-corrected potential well have been obtained at MP2 level of theory with 6-31G* basis set. At RHF and B3LYP levels of theory the least repulsive BSSE-corrected potential have been obtained with 6-31G* basis set. Effects of basis set on the characteristics of the calculated potential energy curves have also been analyzed based on the position of the potential minimum and its well-depth as well as its corresponding hard sphere collision diameter.

57259

Density Functional Theory Based Model Calculations for Accurate Bond Dissociation Enthalpies: A Single Approach for X-H, X-X, and X-Y (X, Y = C, N, O, S, Halogen) Bonds.

Erin R. Johnson, Owen J. Clarkin, Gino A. DiLabio
Steacie Institute for Molecular SciencesNational Research Council,
100 Sussex Drive, Ottawa, Canada, K1A 0R6

Molecule and radical enthalpies were computed using five model chemistries, which are differentiated by the method used for calculating geometries and scaled frequencies. For all the models, electronic energies were calculated using density functional theory (DFT) at the B3P86/6-311G(2d,2p) level of theory. The models were assessed for their ability to accurately predict the bond dissociation enthalpies (BDEs) of 33 X-H bonds and 28 X-X and X-Y bonds, where X,Y= C, N, O, S, and halogen. The mean absolute deviation (MAD) of the BDEs relative to experiment predicted using each of the five models is: AM1 = 2.1, PM3 = 1.7, HF/3-21G(d) = 1.7, B3P86/3-21G(d) = 1.4 and B3P86/6-31G(d) = 1.5 kcal/mol. The B3P86/6-311G(2d,2p)//B3P86/3-21G(d) and B3P86/6-311G(2d,2p)//B3P86/6-31G(d) models perform as well as G3(MP2) (MAD = 1.5) for the bonds in the test set and with a substantially lower computational cost. This is the first instance where a DFT based method has been shown to predict accurate BDEs for this diversity of bond types. The models also perform well for Si-H bonds and for Si-X (X=C, N, O) bonds in radicals but not for Si-X bonds in closed-shell molecules. Additional calculations indicate that the present models predict O-H BDEs relevant to antioxidants in slightly better agreement with experiment than previous models. The basis set dependence of the X-H BDEs is examined. The shortcomings of the present models are discussed, with particular emphasis on the failure of various DFT methods to adequately describe molecules with extensive delocalization.

57260

M.A. (Tony) Whitehead, Adam Dickie, Ashok Kakkar, Florence Quist
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801, Sherbrooke Street West, Montreal, Quebec, H3A 2K6

Geometric arguments produce the monolayer packing space and rapid optimisations give small,repeating symmetry unit cells that correctly represent an infinite monolayer surface.The recently developed Rigid-Rod Scanning Method, Periodic Geometry Optimisation Method and the Periodic Geometry Optimisation on Surfaces will be described and explained. Semi-empirical analysis of the monolayer symmetry units classify the infinite thin films as semiconducting materials, because of organised \pi-orbital overlap and the presence of acceptor band from the Sn headgroups of the surface anchored [Sn]-NEt_2 moieties with alkyne-terminated chromophores on Si(100)/SiO_2 substrates. Headgroup bonding governs the monolayer order and the calculations were able to design molecules which formed monolayers with the highest symmetries and most stable energies by increasing the chain length separations. Experimental illustrations of the accuracy of the theoretical predictions will be shown.

57261

Theoretical and Experimental Study of the Association of poly(styrene-maleic anhydride) chains: Formation of Nanotubes in Solution.

C. Malardier-Jugroot, T.G.M. van de Ven, M.A. Whitehead
Department of Chemistry, McGill University,
801 Sherbrooke Street W., H3A 2K6 Montreal, Canada.

Surface sizing is an important part of the paper making process. The sizing agent studied in this project is the poly(styrene-maleic anhydride) (SMA). Experimental studies have shown that SMA chains associate to form macro-coils at pH7; this association was proposed as a zipping process between the chains at the air/water interface and in water. No association has been observed at low or high pH.The first part of the theoretical study of SMA is the optimisation of the polymer in the gas phase at three pHs(3,7,12). A strong internal hydrogen bond has been found in the structure of SMA at pH7, which gives a linear structure to the polymer and allows a large number of polymers to associate by stacking interactions between the phenyl groups of SMA. The structure obtained at pH3 and 12 are helicoidal and do not allow association in the gas phase. Further theoretical investigations of SMA at pH7 in solution will give information about the stability of the association.This association has also been confirmed and identified by TEM techniques which gives reliable information about the association of different monolayers of SMA in solution.

57260

M.A. (Tony) Whitehead, Adam Dickie, Ashok Kakkar, Florence Quist
Chemistry Department, McGill University,
801 Sherbrooke Street West, Montreal, Quebec, H3A 2K6

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57264

Aggregation of the N-terminal SIV-gp32 peptide characterized with Molecular Dynamics simulations.

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Atomistic Molecular Dynamics (MD) simulations are used to investigate the aggregation of the N-terminal segment of the gp32 protein of the simian immunodeficiency virus (SIV). This hydrophobic peptide (named SIVwt) is believed to be involved in the fusion between the viral and cellular membranes, facilitating the penetration of the virus in the host cell. According to experiments, SIVwt forms colloidal aggregates in water and structured beta-sheet aggregates in DMSO. Thus, it constitutes an interesting model to study peptide aggregation. Simulations are able to mimic the helical twist of beta-sheet aggregates and the spontaneous self-organization of SIVwt into partially structured beta-sheet aggregates. A rationalization of the process is given in terms of kinetics and structural features. The ability of MD techniques to model the process of aggregation is also discussed in terms of reliability to reproduce peptide-peptide and peptide-solvent interactions.

57266

Fragmentation Mechanisms of Aqueous Clusters Charged with Ions

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Fragmentation processes of mesoscopic aqueous clusters with ions of similar sign are studied by coumputer simulation. In order to understand differences in the fragmentation that depend on the nature of the ion and the charge distribution the clusters contain positive (Ca^{+2}, K^{+},and Na^{+}) or negative (Cl^{-}) ions. Insight into the fragmentation mechanism is obtained by the theories of activated processes. Critical to this approach is the use of a new reaction coordinate that captures the shape fluctuations of the droplet that are responsible for the reaction. Reversible work profiles for the reaction are constructed along the reaction coordinate and dynamics are performed. The dynamics validates the use of the reaction coordinate and shows diffusive barrier crossing. It is found that for an even number of charges the clusters fragment unevenly, in contrast to analytical theories (Rayleigh Model) that predict even fission by considering only the energetic factors that determine the stability of charged droplets.

57274

Cluster size distributions of mixtures of methanol-ethanol in the vapor phase.

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Clusters of mixtures of ethanol and methanol formed above liquid samples are analyzed using experimental techniques and by computer simulations. 10.5 ev vacuum ultraviolet is a soft ionization techique that is used to fragment the hydroxylic groups and generate protonated clusters that are detected by TOF/MS. However in the experiment there are sources of supersaturation so the temperature, pressure conditions that the cluster distributions are observed are not well defined. The goal of the simulation is to determine the cluster size distributions, how they are modified by T,P conditions and the particular characteristics of the molecules that give rise to the special features of the distributions.

57275

Calculation of rate constants for E2 reactions in solution by No Barrier Theory.

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The E2 reaction is one of the simplest examples of a reaction which is concerted, despite the existence of stepwise alternatives, when the intermediates in both of the stepwise alternatives are unfavorable. We have examined a set of simple examples of this reaction by No Barrier Theory, and find that the rate constants can be calculated from the experimental equilibrium constants and distortion energies for each of the simple, one thing at a time, reaction dimensions needed to describe the overall reactions. ôNo Barrier Theoryö asserts that when only one thing happens in a chemical reaction there is no kinetic barrier, but only a quadratic potential function, and that the kinetic barriers associated with almost all chemical reactions result from the need for more than one simple thing to happen simultaneously in order for the reaction to occur. This theory permits calculation of the free energies of activation for chemical reactions given only the equilibrium constants in solution and the distortion energies corresponding to the hypothetical ôone thing at a timeö transformations.

57276

Equilibrium constants for carbocation formation in aqueous solution, by DFT calculations.

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Equilibrium constants for formation of solvated carbocations from the corresponding alcohols have been calculated for a series of cations, $ArCRR'^{+}$, and compared with experimental pK_R values (where these are available. Two explicit waters solvating the carbocation center are needed to give satisfactory agreement. For the most reactive "carbocations" this procedure leads to a transition state (identified by a single imaginary frequency) and not an intermediate. The level of calculation needed to match experiment was examined: calculations at the B3LYP/6-31G**, B3LYP/GTLarge, and G3MP2B3 levels; solvation by various continuum methods or cluster-continuum methods.

57278

Dynamical heterogeneity in a simulated glass-forming liquid studied via a four-point spatiotemporal density correlation function.

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We present a theoretical framework based on a fourth order spatiotemporal density correlation function, analogous to that used to investigate spin glasses, to describe dynamical heterogeneities in simulated glass-forming liquids. The four-point correlation function $g_4(r,t)$ and corresponding "structure factor" $S_4(q,t)$ measure the spatial correlations between the local liquid density at two points in space, each at two different times. We calculate both quantities in MD simulations of a binary Lennard-Jones mixture approaching the mode coupling temperature from above. Here, we examine the various contributions to $g_4(r,t)$, $S_4(q,t)$, and corresponding dynamical correlation length $\chi_r(t)$, as well as the corresponding order parameter Q(t) and generalized susceptibility $\chi_4(t)$ from temporarily mobile and immobile particles. We show that the dynamical correlation length $\chi_4(t)$, as well as the contribution to this length arising from localized particles, has a maximum as a function of time t, and the value of the maximum increases steadily in the temperature range approaching the mode coupling temperature from above.

57279

Interaction between amphotericin B derivatives and phospholipid bilayer û molecular dynamics studies

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Polyene macrolide antibiotic amphotericin B (AmB) is the golden standard in antifungal chemotherapy. Unfortunately, there are many drawbacks associated ith its low selectivity towards mammalian versus fungal cells. To improve AmB selectivity many new derivatives of AmB have been synthesized in our and other groups. Cell membrane is a molecular target for AmB. The antibiotic interacts with membrane lipids and in consequence forms trans-membrane ionic channels which are lethal for cells. However, detailed molecular mechanism of action of AmB is still not known. It is supposed that antibiotic-membrane interaction, as the first step to channel formation, may be important for AmB chemotherapeutic action. Therefore, molecular modeling studies of interactions between selected AmB derivatives and membrane surface were undertaken. These studies are the part of the broader interdisciplinary program on molecular basis of AmB and its derivatives action. The molecular dynamics simulations (1 ns each) of four AmB derivatives interacting with model membrane were performed. The model contained hydrated bilayer of phospholipids (100 molecules in each ayer) and single antibiotic molecule. The performed studies revealed differences in lateral diffusion pattern between AmB and its derivatives. It was also found that AmB derivatives interact in a different way than parent AmB molecule with the membrane surface. Detailed analysis of interaction between studied molecules and membrane will be presented.

57280

All-Atom Model of Protein Folding and Domain Swapping

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Though it is undisputed that protein function depends on detailed atomic structures, most theoreticians believe (for several valid reasons) that protein folding depends only on 'coarse-grained' native topology. This assumption is the foundation of 'coarse-grained' lattice models of proteins, which have been employed to illuminate universal characteristics of folding. We have constructed a 'high-resolution' all-atom simulation model that examines the possible roles of side-chain packing and detailed atomic contacts in folding. The model employs efficient piecewise-continuous hardcore and square-well interactions. The efficiency of the model allows the examination of folding behaviors at atomic-level resolution. Simulation studies using the model have revealed the crucial roles of atomic details in the folding mechanism (A. Linhananta and Y. Zhou, 2002, J. Chem. Phys. 117, 8983; Y. Zhou and A. Linhananta,2002, Proteins 47, 154) and cooperative behavior (Y. Zhou and A. Linhananta, 2002,J. Phys. Chem B 106, 1481) of proteins, as well as in domain-swapped protein aggregates (A. Linhananta, H. Zhou and Y. Zhou, 2002, Protein Science 11, 1695).

57281

Structural Optimization of Atomic Clusters by Tabu Search in Descriptor Space

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We present a new algorithm, Tabu Search in Descriptor Space (TSDS), for searching the global energy minimum structure of atomic clusters. In each cycle the algorithm generates many random cluster structures, transforms them by ``symmetrization of interatomic distances", and calculates structural descriptors. A model energy is calculated by interpolation in descriptor space. Clusters are then screened according to the model energy and only a small fraction (10% or less) are retained for energy evaluation. This cycle is repeated many times. In the final step, clusters are sorted by increasing energy and optimized by conjugate gradient. Tests on Lennard-Jones clusters show that a TSDS requires roughly ten to a hundred times fewer energy evaluations than a good genetic algorithm for discovering global minima. The TSDS looks like a promising method for optimization on energy surfaces calculated by first-principles. Results of optimization combining TSDS and Kohn-Sham DFT will be shown.

57282

Computer Modeling and Molecular Dynamics Simulation Studies of Multidrug Resistance Proteins

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By actively pumping drugs from the intracellular to the extracellular environment, some ABC transporters confer multidrug resistance to pathogens and human tumor cells. The recent publication of a number of three-dimensional, high resolution structures of ABC transporters has made it possible to employ computational methods to elucidate the functional mechanics of this versatile class of proteins. We present results of molecular dynamics simulation studies aimed at investigating the nature of structural changes that take place during the transport cycle. In particular, by identifying the least and most mobile segments as well as regions of collective correlated motion, we attempt to determine how conformational changes induced by ATP-binding and hydrolysis are relayed to the transmembrane segment where the substrate translocation event is executed.

57283

Using an adaptive kinetic Monte Carlo method to simulate the dynamics of surface diffusion and growth over long time scales

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An important challenge in theoretical chemistry is the time scale problem. Atomic motion can be simulated directly by integrating Newton's equations over a time scale of nanoseconds, but most interesting chemical reactions take place on a time scale of seconds. We have developed a methodology to bridge this time scale gap using harmonic transition state theory suitable for solid systems. Possible reactive events and their rates are found with a saddle point finding method called the dimer method. When enough events are found, a kinetic Monte Carlo algorithm is used to choose which event occurs so that the system's position can be advanced in time. This technique has two major advantages over traditional kinetic Monte Carlo -- atoms do not have to map onto lattice sites for classification and kinetic events can be arbitrarily complicated. The method is also easy to parallelize, and a distributed computing system, involving a hundred client machines, has allowed us to simulate the deposition of several thousand atoms on the timescales of metal surface growth experiments. We have studied the homoepitaxial growth of aluminum and copper using an EAM potential at 80K with experimentally relevant deposition rates of monolayers per minute using a multiple time scale approach. Atomic deposition events are simulated directly with classical dynamics for several picoseconds until the incident energy has dissipated, and the long time between deposition events is simulated with the adaptive kinetic Monte Carlo method. Our simulations indicate that the Al(100) surface grows much smoother then Cu(100) at temperature between 0 and 80K due in part to long range multi atom processes which enable aluminum atoms to easily descend from atop islands. The high rate of such processes is due to their low activation energy, which is supported by density functional theory calculations, and the trend that processes involving more atoms tend to have larger prefactors and be favored by entropy. The scheme is efficient enough to model the evolution of systems with ab-initio forces as well, for which I will show an example of the breakup of dopant clusters in silicon. Details about this project, and the distributed client can be found at http://eon.chem.washington.edu.

57284

Distributed Computing -- or How to get 10000 CPUs without paying a cent.

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The number of users connected to the internet is growing faster than ever before. High speed connections are becoming more and more common, and will soon be the norm in many countries across the world as the modem goes the way of the dinosaurs. This, combined with the fact that the average computing power of a home machine is now comparable to that of supercomputers just a few decades ago, means that there are massive amounts of computing resources becoming available, all linked through one common medium û the internet. With the recent influx of data from genome sequencing projects, microarrays and other large scale high throughput experiments and simulations, supercomputing power of this magnitude can come in very handy. The Distributed Folding Project, a grid computing approach to the protein folding problem, is one of several such projects designed to make use of these computational resources. Through it we have also discovered a whole distributed computing subculture. Many considerations must be made in order for a project to appeal to users and get them to donate computer time. This includes details of implementation, keeping proper statistics and results, and posting privacy policies prominently, as well as providing stable software which runs invisibly in the background without slowing down other activities. To date we have sampled 100 billion protein structures over a period of 18 months, and have close to 10000 CPUs participating from over 100 countries across the world.

57286

Generalized Correlation of Tertiary Structure of Protein With NMR Chemical Shifts: A Fast and Easy Computational Approach

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The main goal in the present study is to develop a novel generalized semi-empirical parameterization approach that can be effectively applied to predict protein NMR chemical shifts with reasonable accuracy. By making some approximations, a set of generalized parameterization equations, which is based upon overall tertiary structure of protein, is obtained for calculating the protein NMR chemical shifts. The calculations based upon these new equations can follow routine semi-empirical LCAO-SCF molecular orbital calculations. Such calculations should be feasible for large biomolecules. To examine and improve the theoretical model, these new equations have been employed to carry out practical computations on C-13 NMR chemical shifts for four protein molecules. Overall parameterization results show a promising accuracy not only for backbone C (CA) chemical shifts of individual residue of proteins, but also for C (CB), C and even for CD, CE and CG chemical shifts that are located in the side-chain.

57287

Generalized Correlation of Tertiary Structure of Protein With NMR Chemical Shifts: A Fast and Easy Computational Approach

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57288

Electronic Excitation Spectra of Azabenzenes: Pyridine, Pyrimidine, Pyridazine, and Pyrazine Studied by the Symmetry Adapted Cluster Configuration Interaction (SAC-CI) Method

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The ground state and the valence and Rydberg singlet and triplet excited states of azabenzenes (pyridine, pyrimidine, pyridazine, and pyrazine) were examined with the use of the symmetry-adapted cluster (SAC) and SAC configuration interaction (SAC-CI) method. Detailed characterizations and the structures of the bands in the vacuum ultraviolet (VUV) and electron energy loss (EEL) spectra were theoretically clarified by calculating the excitation energy, oscillator strength, and second moment for each excited state. The present SAC/SAC-CI theoretical spectra, including both the singlet and triplet excited states, have well reproduced the electronic excitation spectra of azabenzenes, providing a firm assignment of all low-lying n*-->π*, π-->π*, π-->σ*, and n--> σ * valence excited states observed in the vacuum ultraviolet spectrum and electron energy-loss spectrum. The accuracy and the assignment of the present results are compared with those of previous theoretical studies by CASPT2, EOM-CC, and STEOM-CC methods.

57290

Synthesis and analysis of two novel classes of bis-benzimidazoles synthetic binder of tRNA Phe: 2,2'-bis(4-hydroxyphenyl)-6,6'-bis-benzimidazole and 2,2`-bis (3,5-dihydroxyphenyl)- 6,6`-bis- benzimidazole

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Ligands binding to DNA have been extensively studied for many years now, but in recent years there has been an increase in the recognition of RNA as a potential drug target. This is because of the serious diseases caused by RNA viruses such as HIV 1,2, the important biological roles of RNA, and the absence of RNA repair enzymes. All living cells have a range of DNA repair enzymes in order to correct damage, which results from external factors such as radiation and external chemical agents. These can cause damage or remove parts of some nucleotides, causing defects in function of these nucleotides. In the case of DNA there are several cellular repair mechanisms, as direct reversal of damage and excision repair of altered residues, which will correct or repair such damage. These repair mechanisms can reduce the effectiveness of some drugs. The absence of such mechanisms for RNA makes RNA itself a good target for designing new drugs3. Benzimidazole families bind strongly and reversibly to E.Coli tRNAPhe 4,5. The present study describes the synthesis and analysis of symmetrical benzimidazole ligands (2,2'-bis (4-hydroxyphenyl)-6,6'- bis benzimidazole 1, 2,2'-bis (3,5-dihydroxyphenyl)-6,6'-bisbenzimidazole 2) targeted to bind to tRNA, based on lead structures already identified in the laboratory. Their physical and chemical properties were studied by a variety of techniques and their binding characteristics for RNA and DNA were analyzed.

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57291

How a small change in structure can produce a large difference in antineoplastic activity: a theoretical comparison between Dolastatins 11 and 12

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Molecular Mechanics (MM) and Dynamics (MD) calculations in vacuo and in water have been performed for the natural cyclodepsipeptides Dolastatins 11 and 12 isolated from the sea hare Dolabella Auricularia. The analysis of the MD trajectories for the two systems can give useful insight on the backbone structural features, side-chain and peptide-water interactions as well as on the inter- and intra-molecular hydrogen bonds. A comparison between the selected and analysed lowest energy isomers shows the different conformational behaviour of the compounds. Finally, with the aim to ascertain a structure-activity relationship for the two peptides, the interactions of both Dolastatins with water, generic hydrophobic environment, magnesium and calcium ions have been investigated by means of the GRID program. This work has been done in the framework of MEMOBIOMAR-MIUR project.

57293

An Empirical Energy Function for Mixed Metal Clusters Based on Morse Potentials and Electronegativity Equalization

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The Scaled Morse Potential (SMP) is an empirical function that allows very easy and reasonably accurate calculation of energies for metal clusters of elements in group I, IB, and a few others. But, in general, the SMP is unreliable for alloy clusters because it is based on a purely covalent picture of bonding. To correct this deficiency, we added to the SMP an ionic term that is modeled after the electronegativity equalization principle and the charge equilibration (Qeq) method of Rappe and Goddard [J. Phys. Chem. 1991, 95, 3358]. Addition of this ionic term greatly improves agreement with experiment for heteroatomic diatomic molecules.In this poster, we present details of our implementation of the Qeq method and some preliminary results for small alloy metal clusters.

57295

The “ring-flip” mechanism of serine proteases: a density functional theory analysis

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With the name 'serine proteases' we define a class of proteolytic enzymes which catalytic activity is linked to the presence of a particular serine residue located in the active site. Being present in all living orgaisms, this class of enzymes is extremely numerous and the variety of their biological functions is considerably wide-ranging. Moreover, these features made them also the most studied class of enzymes, both experimentally and theoretically. Notwithstanding, a significant amount of details in relation to their catalytic mechanism still remains unknown. In this work we explore the possibility of a recently proposed variant of the generally accepted catalytic mechanism of serine proteases, which involves the rotation of the histidine's imidazolium ring [Ash E.L., Sudmaier J.L., Day R.M., Vincent M., Torchilin E.V., Coffman Haddad K., Bradshaw E.M., sanford D.G. and bachovchin W., Proc. Natl. Acad. Sci. U.S.A., **97**, 10371 (2000)]. The energy cost of this 'ring-flip' mechanism is evaluated within Density-Functional Theory (DFT) on a model of the active site of serine protease. Furthermore, as a validation of the theoretical model, we show the correlation between the experimental and the calculated Nuclear Magnetic Resonance (NMR) ^{15}N shieldings.

57296

A NOVEL ATOMISTIC FORCE FIELD MODEL OF TRYPTOPHAN WITH OFF-PLANE CHARGES FOR BIOMOLECUALR SIMULATION

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Atomistic level computer simulation is one of the most powerful techniques for studying biochemical systems and predicting their behaviors. In this work, we present a novel force-field model of Trp which improves the accuracy of atomistic simulations, such as Molecular Dynamics (MD) and Monte Carlo, of biochemical systems involving aromatic amino acids. The existing standard force-field models (GROMOS and OPLS) of Trp and other aromatic amino acids were shown to overestimate their hydrophobicity by over 50%. We believe this discrepancy is due to the planar structure of the atomic sites, which oversimplifies the thickness of the pi-electron distribution perpendicular to the plane. The new model improves the standard Trp models by introducing charge sites outside the aromatic ring plane. MD simulations of the solutions of the Trp, Phe and Tyr solutions in water and in cyclohexane using the new model were performed and the free energy of solvation was calculated via the thermodynamic integration method. The new model improved the solvation energy calculation significantly and was shown to perform well in both polar and apolar solvents. The off-plane charge model was also applied to the calculation of the cation-pi binding energy between benzene and sodium ion and improved the binding energy both in vacuo and in water. The new model is of special interest to computer simulation of protein structure, interaction and folding process in membranes, where aromatic amino acids, Trp in particular, play a critical role.

57297

Assessment of a Computational Scheme for the Study of Group I and II Metal Cation-Ligand Clusters

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The thermochemistry and geometries of Group I and II metal cation complexes with water, ammonia, formaldehyde, and formamide are essential to understand the solvation and desolvation processes occurring in biological systems. However, experimental data are only available for the interaction of Group I metal cations with water and methanol. The thermochemistry and geometries of metal cations with the other mentioned ligands are less well characterised. Theoretical methods afford an alternate method to understanding these systems. This study was designed to generate an optimal B3LYP-based computational scheme for the calculation of metal cation-ligand clusters. The B3LYP method with various Pople-basis sets were calibrated against the G2 method, which is found to correspond well with experimental data and CCSD(T) calculations, where available. The geometries converge only t he 6-311+G(3df,3pd) level. Basis set superposition errors (BSSE) are found to vary from ~0.2 to ~5 kcal mol^{-1}, and are significant for all basis sets smaller than 6-311+G(3df,3pd). Geometry convergence and BSSE disappearance occur only at the 6-311+G(3df,3pd) level, and hence this is the ideal method to employ.

57298

Efficient generation of low-energy folded states of a model protein: automated histogram filtering

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We investigate a highly frustrated off-lattice model, consisting of a chain of 69 beads which are either hydrophobic, hydrophilic, or neutral in nature, and which folds into a six-stranded β-barrel structure. Applying distance geometry software to small sets of energy-optimized simulated annealing structures we obtain novel, low-energy structures up to 40 times faster than by doing additional simulated annealing runs. Over 200 000 locally-optimized structures are generated in total, of which nearly 33 000 are unique. We introduce computer-automated histogram filtering, a technology for clustering high-dimensional data. We "filtered" this large set of unique structures, identifying the various regions of the potential energy surface (or energy basins) from which they had been drawn. Selecting the basins containing the lowest energy structures we construct regional partition functions which enable us to make an estimate of the glass transition temperature.

57299

QUANTUM MONTE CARLO STUDY OF THE STATIC ELECTRICAL PROPERTIES OF H

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Our objective is to develop Monte Carlo (MC) algorithm to estimate the exact polarizabilities and high-order hyperpolarizabilities for isolated atoms and molecules: $< \Phi_0 | P_{op} | \Phi_0 >$. Although an existing pure diffusion MC algorithm provides expectation values over the exact electron distribution, it has a serious bias. A new algorithm using Caffarel's stochastic reconfiguration MC method has a minimum bias, but the expectation values are taken over the so-called 'mixed distribution': $< \Phi_0 | P_{op} | \Psi >$, where Ψ is an inputted, approximate wave function. In this paper we connect these two methods to get the exact expectation values with minimum bias. We illustrate our algorithm by computing electronical properties for H atom, and comparing our results with highly-accurate literature values.

57301

Semiclassical Dynamics with Constraints

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The semiclassical initial value representation (SCIVR) is a promising method for the incorporation of quantum effects in a classical molecular dynamics (MD) simulation of complex molecular systems. A general approach, based on the SC IVR theory, has been developed for the study of rigid molecular systems in Cartesian coordinates. The main advantage of the method is that it obviates the need to define a new coordinate system. It also allows the computation of energy levels from the Fourier transform of the auto-correlation function. The approach has been successfully applied to a simple system involving the dynamics of the water bender [B.B. Harland and P.-N. Roy, J. Chem. Phys. **118**, 4791 (2003)]. The phenol-water system is used to illustrate further developments of the technique. In addition, the approach is also being implemented in the context of the Molecular Modeling Toolkit (MMTK) [K. Hinsen, J. Comp. Chem.**21**, 79 (2000)], a software for the MD simulation of classical systems. The extension enables a general treatment of semiclassical quantum dynamics within MMTK.

57302

Modelling Atomic Cluster Energies with Scaled Morse Potentials

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We model the energy of simple metals (Li, Na, K, Cs, Cu, Ag, Au) by a pairwise sum of empirical Morse functions. The three parameters of the Morse functions are made to depend on atomic coordinations and take values intermediate between those of the diatomic molecule and those of the bulk solid. This 'Scaled Morse Potential' (SMP) gives generally good agreement to experiment and first-principles theory for surface energies, surface relaxation, and the trends in cohesive energies and interatomic distances in clusters as function of size. But the SMP can not account for energy variations caused by spin subshell closings, and by orbital degeneracy (or Jahn-Teller distortions) associated with the shape of the cluster. In particular, the SMP incorrectly predicts that the global minima structures of all metal clusters maximize coordination, ie, they are like the global minima of a Lennard-Jones potential. We corrected the SMP by adding a trivial 'spin subshell term', and a not-so-trivial 'shape term' inspired from ellipsoidal jellium results. We will give details of our SMP and methods of calculations. We will show cluster energies and structures for global minima obtained by SMP with and without corrections, and compare them to first-principles calculations and experiments where possible.

57303

A Theoretical Analysis of the Conformational Behaviour of Substituted Methylenecyclohexanes.

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The use of the PBE0 hybrid density functional theory method in conjunction with the COSMO solvation model allowed us to reproduce, both qualitatively and quantitatively, the experimentally observed conformational compositions of 2-substituted and 2,7-disubstituted methylenecyclohexanes. An analysis of the composition makeup revealed several different interactions that are influencing the overall equilibrium. It was found that the endo (general) anomeric effect plays a significant role in the equilibrium, and that the ôunsaturation effectö possibly comprises two effects.

57304

Aggregation behavior of a membrane peptide

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Membrane proteins play an important role in cell biology, carrying out many essential cell functions, yet our knowledge of the sequence-structure-function relationship is much less profound for membrane proteins than for soluble proteins. This study focuses on the simple peptide MS1, a hydrophobic version of the leucine-zipper GCN4-P1 peptide by changing the exterior side chains of the water soluble peptide to apolar side chains. The hydrophobicity of the interface is interrupted at a central position, at which an Asn residue forms a hydrogen bond with an Asn from the second helix of the dimer. MS1 has be shown to exists in a monomer-dimer-timer equilibrium in micelles, mediated by the Asn side chain. Our simulations of MS1 peptides in the membrane mimicking octane environment show to reproduce the association behavior of MS1. The peptides associate into very stable dimers and even trimers. The polar Asn residue inside the membrane bilayer turns out to be critical for the dimerization, in agreement with experiments. Dimer structures are only stable if hydrogen bonds between Asn side chains are formed, while other dimers are transient structures.

57305

Quantum-Classical Dynamics of Nonadiabatic Chemical Reactions

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A reactive flux correlation function formalism for the calculation of rate constants for mixed quantum-classical systems undergoing nonadiabatic dynamics is presented. The linear response formalism accounts for the stationarity of the equilibrium density under quantum-classical dynamics and expresses the rate constant in terms of an ensemble of surface-hopping trajectories. Calculations are carried out on a model two-level system coupled to a nonlinear oscillator which is in turn coupled to a harmonic heat bath. Relevant microscopic species variables for this system include two stable states, corresponding to the ground state adiabatic surface, as well as another species corresponding to the excited state surface. The time-dependent rate constants for the model are evaluated in the adiabatic limit, where the dynamics is confined to the ground Born-Oppenheimer surface, and these results are compared with calculations that account for nonadiabatic transitions among the system states.

57311

Monte Carlo Simulations of Model Antibody Binding Sites: Assembled versus Isolated Loops

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The antigen binding site of all antibodies is comprised of six flexible peptide loops on the surface of a rigid β-barrel framework. These six peptide loops are called 'hypervariable' in that they are variable in both composition and length. That the hypervariable region is inherently flexible is confirmed experimentally, for example, by poor resolution in many X-ray crystal structures. A complete description of the distribution of loop conformations is desirable in order to correlate flexibility of the hypervariable loop region with antibody specificity and selectivity. We present results of Monte Carlo simulations on individual model hypervariable loops and show how the results can illustrate relative flexibilities of loops having different length and/or primary sequence. In addition, we have performed simulations on a three loop assembly. Analysis of the conformations explored by the assembled loops show that each of these loops assumes a subset of conformations explored by the loop in isolation. Therefore, in our model, interloop interactions do not induce the loops to assume totally novel conformations. The impact of these computational results on the 'induced fit' *versus* 'pre-exisiting equilibrium' explanation for experimentally observed conformational differences in the antibody binding site between isolated antibody and antigen-antibody complex, is discussed.

57314

Automated Histogram Filtering for Energy and Geometry Optimization of Wavefunctions

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To optimize parameters in wavefunctions for use in quantum Monte Carlo simulations, we wrote FORTRAN codes to automate a previously manually performed histogram filtering procedure, implementing some methodological improvements which promise its application to a much larger number of parameters and reproducibility in the analysis. To evaluate the effectiveness of the automated algorithm, we studied two separate test cases: two wavefunctions of different complexity, both describing the hydrogen molecule, and both consisting of a basis set of Slater-type orbitals and a Schmidt-Moskowitz Jastrow electron correlation factor. In each case, the data consisted of a modest number of nominally optimal sets of the respective wavefunction's variational parameters generated by means of variational Monte Carlo simulations in conjunction with conjugant gradient energy minimizations. We succeeded at reproducing the optimal variational energy found by the manual technique, and improved upon the previous optimal geometry for the molecule, thus demonstrating the effectiveness of our approach. Furthermore, our approach is seen to be robust to changes in the algorithmic variables employed in our codes such as the number of histogram bins.

57317

Proton transfer in mixed quantum-classical systems

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Proton transfer is of great general importance to many processes in chemistry and biology. Studies of proton transfer in condensed phases require that one consider the dynamics of quantum systems with a large number of degrees of freedom. However, it is not computationally feasible to perform full quantum mechanical simulations of such systems. Therefore, one is led to consider the dynamics of a quantum subsystem coupled to a classical bath. An approach to studying such a composite system is quantum-classical molecular dynamics (QCMD). The main idea is to treat a few crucial degrees of freedom (e.g. a proton) quantum mechanically and the rest of the system (e.g. a solvent) classically. A simple model for a proton transfer reaction (AH-B <--> A^-- H^+ B) in a linear hydrogen-bonded complex (AH-B) dissolved in a polar liquid solvent will be investigated using QCMD.

57318

A comparison of virtual screening methods.

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A comparison of results obtained with several commercially available virtual screening methods will be presented. Our tests involved multiple protein targets, each with several known ligands. For each of the protein targets at least one relevant protein-ligand complex structure was available. Our simulated screening deck, which was used in all the virtual screening tests, comprised 1000 molecules from a cleansed version of the MDDR and the additional known ligands. We attempted to run experiments with each method that were as similar as possible. Detailed analysis of the results, including consensus analysis of results obtained with different programs, will be presented.

57319

The investigation of various intrapeptidic interactions including cation-π, hydroxyl-π, π-π stacking, salt bridges, disulfide linkages and sulfhydryl interactions

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The folding and stabilization of proteins are critical aspects to the definition of their biological functions. While hydrophobic forces play a large role in this process, a growing interest in the various intrapeptidic interactions is revealing significant influences made by these other weak forces. This study investigates numerous possible interactions between the ligands of the 20 essential amino acids contained within our bodies' proteins. Such interactions include the various possible salt bridges, cation-π interactions, hydroxyl-π interactions, π-π-stacking, disulfide linkages, and sulfhydryl interactions. Interactions are studied in both gas and liquid phases under the molecular mechanics (CFF and CHARMM) and DFT levels of theory. Not only will this study be useful in characterizing and comparing how each of these methods treat these individual interactions, but from this we hope also to elucidate various trends in intrapeptidic binding and stabilization forces.

57321

Reversible Folding of a Natural Peptide in Aqueous Solution by Molecular Dynamics Simulations in Explicit Solvent

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Understanding protein folding is one of the mostchallenging problems in molecular biology. The RN24 analogue of the so-called C-peptide consists of the amino-terminal 13 residues of ribonuclease A, and it was found to assume a helical conformation in water. Here we present a molecular dynamics (MD) simulation study of this natural peptide in explicit water. Four MD simulations were carried out, for a total simulation time of 2.7 μs, starting from both an extended and an ideal α-helical conformation. Both the cutoff and the PME methods were used for the calculation of the electrostatic interactions, in order to investigate the influence of the electrostatic scheme. In all four simulations we observed several folding and unfolding events, as well as misfolding events leading to β-hairpin conformations. Although the helical conformation does not appear to be predominant, our results are in very good agreement with published NMR data. To our knowledge, this is the first reversible MD simulation of a natural non-repetitive peptide in explicit water.

57322

OZONOLYSIS OF ALKENES: THEORETICAL STUDIES OF OH, HO$_2$ AND EPOXIDE PRODUCED FROM DECOMPOSITION OF PRIMARY OZONIDE

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Ozonolysis of alkenes is initiated by the cycloaddition of ozone to the double bond to form a primary ozonide (POZ). Decomposition of the vibrationally excited POZ is a major source of various organic pollutants. The dominant mechanistic pathway is generally believed to be a concerted cleavage of the C=C and the O--O bonds to form a Criegee intermediate (CI) and an aldehyde followed by unimolecular decompostion of the vibrationally excited CI. We report {\it ab initio} calculations of the ethene and propene POZ using DFT-BH&HLYP, CCSD(T) and QCISD(T) methods. Our results suggest the favoured pathway to be the non-concerted cleavage of the POZ to a diradical oxy-peroxy intermediate forming CI and aldehyde. Competitive channels towards formation of OH, HO_2 and epoxides are also studied.

57324

A Comparative Molecular Field Analysis on a {\it Rhodococcus erythropolis} Enzyme of Biocatalytic Importance: Elucidation of the Regions of Steric and Electrostatic Significance within the Enzyme's Active Site

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Biological catalysts are often employed as effective tools to synthesize chiral compounds from achiral starting materials. A strain of the bacterium *Rhodococcus erythropolis* (IGTS8 BKO-53) has been shown by Holland et al. to oxidize a wide range of simple sulphides to enantiomerically pure sulphoxides in good yields. Although this organism has been widely studied, there is not yet a clear picture of the 3-dimensional shape of the enzyme that catalyzes this sulphoxidation reaction. We have employed a form of 3-dimensional quantitative structure activity relationship (3-D QSAR) in order to elucidate the important interactions within the enzyme's active site. This method, called a comparative molecular field analysis (CoMFA), examines the interactions (steric and electrostatic) between a series of compounds and a probe atom in a cubic space around the compounds, and relates this data to experimentally determined activity data for these compounds. Using this method we can create a picture of the areas of steric and electrostatic significance of the enzyme's active site.

57325

Nonadiabatic trajectory studies of photodissociation dynamics in $NaI(H2O)_n$ clusters

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We present a theoretical study of the photodissociation dynamics of $NaI(H2O)_n$ [n=1-4] clusters. The NaI system has been a prototype system for the study of photodissociation dynamics involving curve crossing of covalent and ionic states. A semiempirical valence-bond approach is employed to describe the electronic structure of NaI, while classical potentials are used for the water-water and ion-water interactions. The cluster photodissociation dynamics, including possible nonadiabatic transitions between the NaI excited and ground electronic states, are simulated with the ômolecular dynamics with quantum transitionsö method. We show that the excited state population decays faster with increasing cluster size, because of the dynamical stabilization of the outer, ionic branch of the excited state potential by solvent molecules. As observed previously for NaI(H2O), the reversed polarity of NaI in the Franck-Condon region of the excited state causes the evaporation of 95% to 100% of the water molecules before NaI reaches the curve crossing region, i.e. within 200 fs of excitation. We discuss possible probe schemes in order to monitor the cluster photodissociation in time and make a connection with experiment.

57326

Competition between Ion-Dipole and Hydrogen-Bonded Interactions in Halide Acetonitrile Complexes

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A comprehensive computational study of the structure and stability of halide-acetonitrile clusters with ab initio molecular orbital theory and density-functional theory will be presented, along with an analysis of the bonding interactions within the framework of the quantum theory of Atoms-In-Molecules. Changes in the geometry and vibrational spectra of the acetonitrile molecule complexed with halide anions, and the competition between ion-dipole and hydrogen bonded interactions in halide-acetonitrile clusters will be discussed.

57327

A molecular dynamics study of calmodulin: evidence of interdomain coupling and structural collapse on the nanosecond timescale

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Recent experimental results indicate a coupling between the N- and C-terminal domains of the calcium regulatory protein calmodulin (CaM), as well as a collapse of the extended structure under certain conditions. Here we present a 20 nanosecond (ns) molecular dynamics simulation of Ca^{2+}-CaM in which both phenomena are observed. Within the first 5 ns of the simulation, the extended crystal structure collapses to a compact state with dimensions similar to complexes of CaM with target peptides. This collapse is driven in part by interactions between basic residues in the central linker region and the N-terminal helix. These interactions correlate with the closing of the calcium-binding EF-hands in the N-terminal lobe, suggesting a mechanism by which interdomain coupling reduces the calcium affinity of these domains. Other factors contributing to the structural collapse, such as the loss of specific mainchain and sidechain hydrogen bonds, are also in agreement with experimental results. While interactions between the terminal lobes in the compact state are mediated by the peptide-binding regions of CaM, the high accessibility of crucial Met residues indicates that the collapsed structure may be biologically active.

57329

In silico high-throughput screening and computer-aided structure-based design for discovering novel inhibitors that target RNA

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The vast majority of drug targets are proteins, most often enzymes. DNA and ribonucleic acids, on the other hand, have much less frequently been used as drug targets to date. The recent work on the ribosome demonstrates nonetheless that ribonucleoproteins provide excellent targets for developing new antibacterials and potentially antivirals.We have been testing available computational tools for use with RNA, which forms well-defined 3D structures with clefts and binding pockets reminiscent of protein and precedes proteins in the translation pathway; inhibition of the function of a single RNA molecule would result in inhibition of the function of multiple proteins. Thus, small molecules binding RNA specifically would combine the advantages of antisense and RNAi strategies with the established medicinal chemistry of small molecule therapeutics. 3D structures of RNA-small molecule complexes determined by X-ray crystallography and NMR were used to evaluate the performance of the programs Dock and AutoDock in the RNA environment. We evaluated docking accuracy, (how well the native structure can be reproduced computationally), scoring accuracy (how closely the experimentally determined Ki can be evaluated), and reproducibility (over multiple independent runs). Our results show that native structures could be reproduced within 2.5A in over 50% of the cases. Furthermore, AutoDock can well estimate the binding constant. For more than half of the test complexes, the native ligand scored among the top 15% within a test database containing known drugs. In summary, we have validated structure-based design tools directed at RNA targets; we are now in the process of conducting large scale computational screening of two different RNA targets derived from essential regulatory signals in pathogenic viruses with the diversity subset of the NCI database. We aim to find promising and chemically new lead structures directed at these viral RNAs.

57331

The Hydrolysis of N-Sulfinyl Compounds: A Computational Study

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N-sulfinyl (N=S=O) compounds are widely used regents in synthetic organic chemistry. Depending on structure, these compounds exhibit different reactivity towards water: some of them hydrolyze very easily while some are steam distillable. In this work, quantum chemical calculations are used to study the intermediates and thermochemistry of the hydrolysis of selected N-sulfinyl compounds. The effects of catalysts and solvent are investigated and the nature of the inter- and intra-molecular bonding in the intermediates and transition structures is studied with the Atoms-In-Molecules (AIM) and Natural Bonding Orbitals (NBO) methods.

57332

Energy landscapes at the divide between crystallization and glass forming behaviors

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We studied the glass forming behavior in binary mixtures of NaCl and CsCl, using constant pressure MD simulations. Starting from pure NaCl, which crystallizes readily even at quench rates typical for MD simulations, we increase the CsCl content allowing us to capture the transition between crystallization and glass formation in quenched specimens. The resulting glasses have relatively low fictive temperatures. Structural and energetic analyses are applied to both the thermalized systems and the inherent structures corresponding to the system relaxed to the local potential energy minimum. Models of the energy landscape and their relation to glass forming tendency in this system are proposed and compared with previous studies using constant volume simulations.

57333

The KvAP Voltage-Gated Potassium Channel: a molecular dynamics study

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The recent X-ray structure of a voltage gated potassium channel (KvAP) has given a unique and exciting first glance of the structural basis of voltage gating. The crystal structure, however, raises a number of important questions and reconciliation of the structure with some of the existing data is difficult. To investigate the possibility that the crystal structure is somewhat distorted due to the conditions during crystallization, including the presence of antibodies and significant truncation, we have carried out molecular dynamic (MD) studies in both a lipid membrane and membrane-like environments. We also employ a novel technique to build a model taking into account both the lower resolution structure of the whole protein, and the higher resolution structure of the isolated paddle. Areas of high mobility and regions that may act as a hinge are predicted, as well as specific structural changes leading to different model structures. These models will enhance our ability to better define the mechanism of voltage gating and channel conductance while elucidating some of the questions surrounding the crystal structure.

57334

Probing Protein-ligand Association with Free Energy Simulations in Four Dimensions

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Novel computational techniques for the calculation of excess chemical potentials in full-atomic systems of biological scale are explored. Simulations are carried out via molecular dynamics, incorporating an imaginary fourth spatial dimension as a computationally efficient means of turning on or turning off interactions. The generality, effectiveness, and reliability of the method are demonstrated for the calculation of the hydration free energy of polar and non-polar molecular solutes, as well as ionic species. The absolute binding free energy of various protein-ligand systems differing in the size, hydration state, and accessibility of the binding pocket, is analyzed. Finally, the extension of the four-dimensional method to applications in the identification of binding sites and to the calculation of relative free energy changes through molecular replacement is discussed.

57343

Effect of Adatom-to-Adatom Separation on the Reactivity of 1,4-Dihalobenzenes in Reactions on Si(111)7x7 Surfaces

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A computational investigation was undertaken to determine the energetics and mechanisms of bond dissociation of prototypical aromatic dihalides, such as 1,4-dibromobenzene and 4,4'-dibromobiphenyl, on simple models of the Si(111) 7x7 reconstructed surface. The dissociation of the halogen-carbon bonds in these compounds is shown to be assisted by the formation of the silicon-halogen bond, the overall reaction being exothermic. It is shown that there exist a 'favorable' Si-Si separation which depends on the Br-Br separation in the substrate molecule. For a 1,4-dibromobenzene molecule positioned between two silyl groups, the lowest energy barrier for the symmetric Br-C bond dissociation is for a Si-Si separation of 10.2┼. In the case of 4,4'-dibromobiphenyl this distance is 13.8┼. The preferred separation favoring the dissociative reactions of aromatic dihalides is consistent with accumulated recent experimental evidence from our group. It is also shown that the sequential bond breaking results in two barriers, each of which is lower than the barrier for the simultaneous bond breaking. Thus, it appears that the surface-assisted Br-C bond dissociation in these molecules occurs sequentially favoring particular adatom-adatom separations which are ~3 - 4 ┼ larger than the Br-Br internuclear separation in the substrate molecule.

57347

Molecular Quantum Similarity Modelling of COX-2 Inhibitors

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Molecular Quantum Similarity [1,2] stands as a procedure to quantitatively state a measure of resemblance between two molecular structures based on their respective electronic distributions. When this methodology is applied to all pairs of a given molecular set, the resulting Molecular Quantum Similarity Measures (MQSM) can be used as molecular descriptors for QSAR modelling [2]. The methodology is presented from the basic theoretical background, which includes generation and usage of fitted electronic densities [3] and molecular superposition [4], prior to the calculation of the measure. As an application example, a set of Cyclooxygenase type II (COX-2) inhibitors is tested for correlation between enzyme inhibition capacity and MQSM-based descriptors, yielding to satisfactory models.

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57356

Reaction of Chlorinated Benzenes with Si(100)2x1: a Theoretical Study

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Theoretical (HF+DFT) investigations of the adsorption of chlorobenzene (ClPh), 1,2- and 1,4-dichlorobenzene (1,2-diClPh and 1,4-diClPh) on a silicon (100) surface are reported for the first time, and are compared with one another and with benzene. Binding energies for various structures with the molecules attached on-top and in-between the surface dimer-rows are correlated with the STM experimental data. Novel structures with the molecules linking two dimer rows, stabilised by detachment of Cl (or H) atoms forming Cl-Si (or H-Si) bonds, are described. For 1,4 and 1,2 binding, these linking structures are predicted to attach the phenyl ring parallel or perpendicular to the Si surface, respectively, while preserving its aromaticity. The potential-energy barriers between several different structures are evaluated, and compared with available experimental evidence. For 1,4-diClPh it is shown that the potential energy barrier for the second Cl transfer is significantly lower than for the first one in contrast to the gas-phase, and comparable to the barrier for lifting the Bz-ring into a vertical position and forming a singly-bonded 'displaced' structure. The predicted barrier-heights are consistent with the experimentally-observed relative occurrence of the on-top, linking, and displaced structures.

57357

An efficient Monte Carlo method for calculating ab initio transition state theory reaction rates in solution.

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We present an efficient Monte Carlo method for the rapid sampling of important solvent and solute configurations in condensed-phase reactions. The method has been designed for mixed quantum mechanics/molecular mechanics calculations in which the ab initio equations for the reactive solute are solved in the presence of the molecular mechanics solvent charges. The novelty of the method consists of using a guiding potential method in combination with simulation tempering to obtain a rapid exploration of the relevant solvent+solute state space. The algorithm allows thorough exploration of the state space in the context of an ab initio calculation even when the dielectric relaxation time of the solvent is long. It is demonstrated that calculations of rates of chemical transformations taking place in solvents of medium polarity can be performed with an increase in the cpu time of only a factor of four with respect to gas-phase calculations for similar statistical resolutions.

57358

Modelling the Charge Distribution of Gas-Phase Protein Complex Dissociation

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The dissociation of gas-phase protein complexes, produced by electrospray ionization techniques in mass spectrometry, has been studied using electrostatic models. In experiments, it is found that charged protein complexes dissociate with asymmetrical charge distributions, that is charges are not equally divided among the daughter ions after breakup. Our goal is to understand the reason for this asymmetry using charged ellipsoids as models. Charge sites are placed on ellipsoids of various sizes and orientations, and charges are then distributed among these sites. Charge configurations that produce the lowest electrostatic energy are the found. Results will be presented showing the effect of size and orientation on the charge asymmetry. These will also be contrasted with previously reported results for spherically-charged drop models. The ellipsoids used here more closely model actual protein complexes by using charge sites to represent basic residues, and by incorporating a broad variety of shapes. The model does assume though that proton transfer occurs on a timescale that is fast compared with the rate of dissociation of the protein complex.

57360

Structure of Human α-Tocopherol Transfer Protein As Predicted by Comparative Protein Modelling Patrizio G. Cassolato, Heather L. Gordon, Jeffrey K. Atkinson

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A comparative model of human α-tocopherol transfer protein (TTP) was constructed, that resembles 3D structure of the native protein. RRR-α-tocopherol was subsequently docked into this model, using a combination of Metropolis-Monte Carlo and Molecular Dynamics, to investigate the mode by which it binds to TTP. The final results of this investigation will be compared to those results obtained by x-ray crystallography, to ascertain the accuracy associated with this comparative model. Vitamin E consists of eight different ôvitamersö and is an important nutrient and antioxidant required for maintaining human heath. Hepatic differentiation of \alpha-tocopherol from other vitamers results in the RRR-α-tocopherol isomer being favoured for incorporation into nascent very low density lipoproteins before distribution to cellular membranes. The differentiation of α-tocopherol is associated with the TTP, but the tertiary structure of TTP is as yet unknown. This structure will be key in defining the mechanism by which discrimination of α-tocopherol by TTP occurs.

57362

Theory of the Two Step Enantiomeric Purification of 1,3 Dimethylallene.

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A two step optical control scenario is applied to the purification of a racemic mixture of 1,3 dimethylallene. In the first step, three linear perpendicular laser pulses are applied in a cyclic adiabatic passage scheme that is capable of distinguishing between L and D enantiomers. In the second step, a sequence of pulses are used to convert one enantiomer to its mirror imaged form. This scenario, which only negligibly populates the first excited electronic state, proves ideal for systems which may suffer losses from dissociation and internal conversion upon electronic excitation.

57365

Semiclassical IVR (Initial Value Representation) Treatment of the S-matrix

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Semiclassical techniques have, in recent years, become very popular for calculations of quantum phenomena. These methods can, in principle, be applied to treat molecular dynamics and perform calculations of various quantities such as the (scattering) S-matrix, a key ingredient for the description of a large number of dynamical phenomena, including reactive scattering. Unfortunately, among semiclassical calculations of reactive scattering, only the recent propagator-based treatment of Garashchuk, Tannor and Light has achieved qualitatively accuracy, but has done so only at the expense of a large number of classical trajectories and with the use of an expression that is dependent on initial and final interfragment distances. The original semiclassical IVR treatment of the S-matrix was developed almost three decades ago by W. H. Miller and R. A. Marcus, (MM). This method is potentially capable of yielding scattering amplitudes using orders of magnitudes fewer trajectories than required by the more recent techniques based on semiclassical IVR expressions for the time-dependent propagator. Unfortunately, application of the MM IVR is hampered by a number of problems, including the uncertain definition of the phases appearing in the IVR integrand, the inaccuracy of the results in many cases, and the inapplicability of this technique for the treatment of reactive tunneling. On the other hand, the IVR propagator based expressions, while relatively accurate, require a large number of trajectories and also are dependent on arbitrary parameters. In our work, we address these problems by deriving a new uniform IVR formula for the S-matrix from integral expressions for time-independent wave-functions. In addition to resolving ambiguities in the original MM expressions, our treatment requires a relatively small number of trajectories for convergence, compared to propagator-based methods and is independent of arbitrary parameters. A computational algorithm exploits the mathematical and physical properties of the S-matrix in order to obtain the best possible results. We apply our method to two test cases.In both cases good agreement with quantum calculations is obtained and the number of trajectories for computations at a limited number of energies is far smaller than required by existing semiclassical propagator-based methods. For the case of reactive scattering,a new computational stategy is introduced for performing integrations over chaotic chattering regions that takes into account the fractal nature of the integrand.