Medicinal Chemistry **81**

Computational Chemistry **82**

Magnetization of metallic carbon nanotubes by paramagnetic centers

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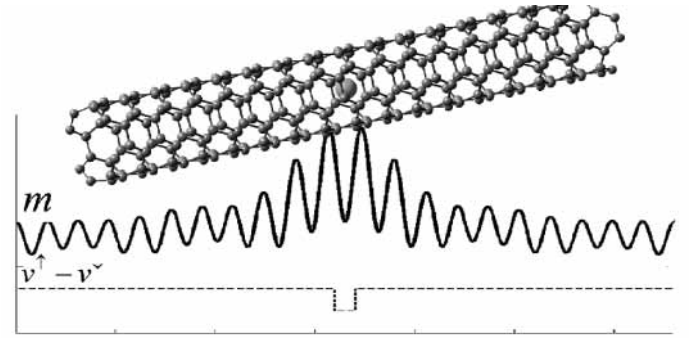
Gd-loaded carbon nanotubes recently have got interest as potential contrast agents for magnetic resonance imaging (MRI) [1]. A possible explanation of experimentally observed high relaxation enhancement is the spin-polarization of standing-wave-like electronic states of finite metallic nanotubes [2]. Perturbation theory calculations show that a paramagnetic center localized in a metallic nanotube causes a very inhomogeneous magnetization of the whole system. The effective spin-polarization potential was estimated from density functional theory calculations on model systems.



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Computational Chemistry **83**

Molecular Dynamics Approach to Characterize the Guanylate Cyclase PleD

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Cyclic di-guanosine-monophosphate (c-diGMP) plays an important role in modulating bacterial growth on surfaces [1]. Thus inhibition of the synthesis of c-diGMP is a potential target to combat biofilm-related infections. The recently solved crystal structure of the response regulator PleD from *C. crescentus* revealed an allosteric site at the stem-guanylate cyclase interface [2]. A first step towards medicinal application is a fundamental understanding of the mechanism of this feedback inhibition, especiallly since the GGDEF domain is abundant in the bacterial kingdom.

Molecular dynamics (MD) simulations are an ideal tool to gain information about the structure and the dynamics of the protein at a molecular level. Normal mode studies on several systems [3] have shown that the character of low frequency modes is correlated with significant conformational transitions which may be important for function. Complementary, correlated motions identify in detail residues which are essential to signal transduction either within the DGC domain or even from the distant D1 domain where the activation via phosphorylation occurs. Results on the native protein and on mutant R390A which is known to have a much lower affinity for c-diGMP binding will also be presented.

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Computational Chemistry **84**

Information extraction from the Evolving Factor Analysis

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The goal of our project (HES-SO n°11246) is to develop chemometric methods that enhance the development of chemical synthesis.

Semi-batch experiments are performed using a fully automated chemical reactor. Real-time analytical data, infrared (IR) spectra for instance, are synchronized with standard process variables [1]. In parallel to the on-line measurements, the reaction is followed by conventional chemical analysis such as gas chromatography (GC).

We have chosen an aldol condensation as a model reaction. IR spectra are preprocessed (wave number region selection, filtering) and processed by Evolving Factor Analysis (EFA) [2] to monitor the chemical reaction.

Influence of the pre-processing on EFA-results for real experimental data as well as for dynamically simulated data will be presented and compared.

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Computational Chemistry **85**

Impact of induced fit for ligand binding to proteins: Development of multidimensional QSAR technologies

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Quantitative structure-activity relationships (QSARs) are often employed to establish a correlation between structural features of potential drug candidates and their affinity towards a macromolecular target. In 3D-QSAR, the the involved molecules are represented by three-dimensional structures, allowing to quantify electrostatic forces, hydrogen bonds and hydrophobic interactions at the atomic level. Receptor models based on 3D-QSAR typically represent a binding-site surrogate with physico-chemical properties mapped onto its surface or a grid surrounding the ligand molecules, superimposed in 3D space (pharmacophore hypothesis). As such a single construct interacts with all ligands simultaneously, it does not allow for the simulation of induced fit (receptor-to-ligand adaptation) — a fundamental shortcoming of the technology. As this entity represents all but a receptor *surrogate*, the bioactive conformation, orientation and protonation state of the ligand molecules might be guessed at best. Multidimensional QSAR represents a subtle extension of 3D-QSAR attempting to overcome these limitations.
In this lecture, we present two novel concepts (*Quasar* [1] and *Raptor* [2]) and demonstrate their ability to predict binding affinities of large, chemically diverse sets of ligand molecules binding to G-protein coupled receptors, nuclear receptors and cytochrome P450 3A4. The results suggest that our approach may be used for the reliable prediction of binding affinities and adverse effects of drugs and chemicals prior to their synthesis.

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Computational Chemistry **86**

Intermolecular complexes from van der Waals to hydrogen bonds: benchmark calculations using subsystem formulation of density functional theory.

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Interaction energies in a large set of weak intermolecular complexes were derived using subsystem formulation of density functional theory [1]. The results were obtained using our new computer implementation of this formalism [2], allowing us to obtain the results close to the basis set limit. The investigated systems cover a wide range of interactions starting from the weakest ones comprising noble gas dimers to the hydrogen bonds. The calculated interaction energies, as well as the complete potential energy curves were compared with the reference data derived from high level ab initio calculations. The performance of two levels of approximation (gradient-free and gradient dependent) is discussed in detail. In view of practical applications of the formalism in studies of larger systems, the influence of the additional simplifications such as: using a smaller basis sets, non-variational, and partially variational [3] calculations, are discussed. In particular, it is shown that the variational calculations are indispensable for accurate description of hydrogen bonded complexes but can be avoided for a large class of complexes formed by rare gas atoms and non-polar molecules. In an attempt to rationalize the physical origin of very good numerical values of the interaction energies, the local behavior of key approximated quantities is analyzed.

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Computational Chemistry **87**

Ligand migration in complex environments.

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The notion of smooth and structured (rough) energy landscapes is an important concept in the discussion of dynamical processes in complex systems. Examples include the folding of proteins, the reaction of two end-groups in a polymer chain or the motion in bistable, metastable or periodic potentials.
We present results for the migration of CO between the primary binding site and the Xe4 pocket in myoglobin. For this system free energy surfaces were calculated using molecular dynamics simulations along one [1] and several reaction coordinates. The complex environment provided by the protein residues leads in general to rough free energy surfaces. A useful way to determine the reaction kinetics for such a system is to follow the temporal and spatial relaxation of an initial distribution $p(x,0)$ to the final (equilibrium) distribution. To this end the Smoluchowski equation (SE) is solved for the particular free energy function $V(x)$ or the multidimensional energy landscape. A numerically robust and computationally efficient algorithm to solve the SE for multidimensional systems involving rough interaction potential is employed [2]. The hierarchical nature of the algorithm (hierarchical discrete approximation or HDA) fully explores the fine- and coarse-grained structure of the potential and does not impose any restriction on its topology. The hierarchical grid allows to fully capture the roughness of the potential and achieve significant reduction of computational time compared to other discrete approximation methods. From the behavior of $p(x,t)$ the rebinding time for CO diffusing between different metastable states in myoglobin is calculated and compared with experiment.

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Computational Chemistry **88**

Reactive Molecular Dynamics Simulation of Proton Transfer in Proteins

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Proton transfer reactions are of fundamental importance in a wide range of chemical and biological processes. Theoretical investigations of these dynamical processes are therefore of great interest. The energetic barrier for proton and hydrogen transfer is often so high that transfer events happen only rarely. The long time scales involved complicate application of accurate dynamical studies using QM/MM molecular dynamics simulations.
Based on prototype systems such as the protonated water dimer, protonated ammonia dimer and protonated ammonia water hetero-dimer, multidimensional potential energy functions have been calculated. Using these, a force field representation has been developed to study the inter- and intra-molecular dynamics of the transfer events by molecular dynamics simulations. The flexible and adjustable implementation of the force field makes it transferable to a variety of systems with hydrogen bonding patterns and can reproduce the properties of the reaction potential of interest.
We present the application of the reactive force field to the dynamics of proton transfer in ferredoxin I. Proposed mechanisms [1] of the proton pathway from the protein side chain to a buried [3Fe-4S] cluster are investigated in terms of the dynamics and transfer rates. The role of functional water molecules [2] in the active side is discussed.

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Computational Chemistry **89**

Pre- and Post-processing Molecular Interaction Fields Tools in Receptor-based Drug Design Strategy towards Neurodegenerative Diseases.

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It is nowadays of common sense that receptor-based virtual screening and molecular docking need meticulous post-processing analysis to be fully efficient [1]. With this aim in view, an assessment of binding mode predictions by a precise description of the physics of ligand/protein intermolecular interactions is proposed [2]. This technique called ScoreMxP is based on Molecular Interaction Fields (MIFs): the Molecular Lipophilicity Potential (MLP) and the Molecular Hydrogen-Bond Potentials (MHBPs). ScoreMxP appears to be highly complementary to consensus scoring strategies and could in a near future be integral part of it.
Another commonly accepted paradigm is that docking is less important than scoring in virtual screening campaigns [3]. Our drug design work towards biotargets known to be of crucial importance in human neurodegenerative pathologies such as Alzheimer and Parkinson's disease seems to be in disagreement with this opinion. Indeed, pre-processing refinement procedures in term of i) better description of hydrophobicity of the binding sites [4] and ii) keeping selected crystallographic water molecules inside the protein cavities not only yielded more accurate binding modes, but also greatly improved the prediction of inhibitor activity ranking.

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Computational Chemistry **90**

A 3D Solvatochromic Model of Blood-brain Barrier Permeation Based on Molecular Interaction Fields Descriptors

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Recently, a 3D solvatochromic model based on four molecular interactions fields, namely the Molecular Lipophilicity Potential (MLP), the acceptor and donor Molecular Hydrogen Bond Potential (MHBP) and the polarisability/dipolarisability GRID "DRY" field was developed to predict skin permeation [1].
This new 3D approach was applied to study BBB permeation of a series of compounds. The resulting model was validated with the transport coefficients kin measured on rat by *in situ* brain perfusion for an external set of compounds with high chemical diversity.
This 3D solvatochromic model points out the effect of intermolecular interactions on permeation (e.g. hydrophobicity) not only in term of the intensity of interaction but also in term of the radiance of fields. The spatial localizations of some molecular properties explain the improved predictive power of this 3D approach able to discriminate BBB permeation of external compounds. This work offers a novel tool useful in the early virtual screening of drug candidates.

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Computational Chemistry **91**

Atom centered potentials for London dispersion forces in density functional theory

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Density functional theory (DFT) has been very successful in understanding and predicting electronic structure properties of molecules. However, while some DFT exchange-correlation potentials show spurious binding for many van der Waals (vdW) complexes, it is generally not yet possible to correctly describe these nonlocal correlation effects within DFT using the local density approximation (LDA), the generalized gradient approximation (GGA) or the hybrid exchange-correlation functionals [1]. Recently, a scheme has been introduced to optimize atom centered nonlocal external potentials within the framework of DFT in order to systematically improve the description of molecular properties [2]. Here, a small library of dispersion corrected atom centered potentials (DCACPs) is obtained by the calibration of some typical vdW complexes such as $(N_2)_2$, $(CO_2)_2$, and benzene dimer. The DCACPs are then tested on (i) different configurations of $(N_2)_2$, $(CO_2)_2$ and $(H_2CO)_2$ (ii) on aromatic heterocycles stacking such as pyridine dimer, pyrimidine dimer and furan dimer, and (iii) on the potential energy surface of interaction for the parallel displaced benzene dimer [3]. While the additional computational cost is negligible for the DCACP-DFT calculations compared to conventional DFT calculations, the performance and transferability of the DCACPs are remarkably good [4] [5].

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Computational Chemistry **92**

Response properties of liquid water using Time Dependent Density Functional Theory

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Time dependent density functional theory (TDDFT) is used to compute the linear response of a sample made of 32 water molecules periodically replicated. We study the relaxation effects following two different perturbation schemes, namely a point charge disturbance and a sudden switch of an external electric field [1]. The approach, based on the real-time propagation of the Kohn-Sham equations, is used to compute the response and dielectric functions of liquid water. Results are compared with available experimental data [2,3].

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Computational Chemistry **93**

Computation of Non-Adiabatic Coupling Using Time-Dependent DFT

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Many chemical reactions that occur after electronic excitation can pass through different reaction branches. A proper description of this type of reactions, for example the prediction of reaction rates, can only be achieved if non-adiabatic effects are taken into account. Time-dependent (TD) DFT [1] facilitates the calculation of electronic spectra and nuclear forces in electronically excited molecules. Several approaches have been undertaken to include non-adiabatic effects in *ab initio* molecular dynamics (AIMD) codes based on surface hopping (SH) [2], Ehrenfest dynamics [3] or Landau-Zener theory [4]. Here we present a TDDFT based method for the calculation of the non-adiabatic coupling (NAC) between electronic states. Similar to the SH approach of Tully [7], the NAC is used to calculate switching probabilities between different electronic states and incorporate Quantum Transitions in AIMD simulations. The method has been implemented in the plane wave code CPMD [8,9] and applied to intramolecular photoinduced electron transfer and cis-trans isomerisation in organic compounds.

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Computational Chemistry **94**

A study of the structural stability of the C-terminal domain of the mouse prion protein

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Despite the increasing amount of chemical knowledge on the C-terminal domain of the cellular isoform of the prion protein (PrP^c) and on its conversion into the scrapie isoform (PrP^{sc}), the atomistic details are still elusive [1]. Three different approaches have been used to investigate this intriguing problem and are here reviewed.
1. Among the factors compromising the structural stability of the PrP^c and initiating the refolding to the PrP^{sc} isoform, are the pH of the solution and the presence of salt [2]. In order to shed some light on the combined effect of both, we systematically simulated different protonation states (at pH2, pH4, pH7 as determined by Poisson-Boltzmann calculation) and ionic strength (0.0 M, 0.05 M, 0.1 M, 0.2 M in NaCl) using molecular dynamics (MD).
2. The propensity of the protein to misfold at pH4 was also investigate by means of the explicit solvent parallel tempering scheme [3] to enhance the sampling of the torsional conformational space at 300K.
3. Since the surface of the PrP^c is characterized by a markedly uneven distribution of positively and negatively charged residues [4], the effect of the electrostatic interaction due to a prion protein in proximity of another was probed. The protein-protein docking approach was used to produce some likely configurations that have been subsequently assessed by means of the MD.

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Computational Chemistry **95**

Theoretical Studies on the Electronic Properties and the Chemical Bonding of Transition Metal Complexes using DFT and Ligand Field Theory

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In this oral presentation, we give a brief outline of a recently proposed Ligand Field Density Functional Theory (LFDFT) model for single nuclear complexes and its extension to dimer transition metal complexes. Applications of the model to dinuclear complexes are illustrated for the interpretation of exchange coupling in the bis-μ-hydroxo-bridged dimer of Cu(II), to the magnetic exchange across the cyanide bridge in 3d-TM ion complexes. The same model has been applied to the description of the quadruple metal-metal bond in $Re_2Cl_8^{2-}$ .Our analysis of the chemical bonding are compared with results obtained using other approaches: i.e. the Extended Transition State model and the Electron Localization Function. It is shown that the DFT supported Ligand Field Theory provides consistent description of the ground and excited state properties of transition metal complexes. The advantages of this new approach in comparison to other method for the description of the ground and excited state electronic structure of TM complexes, such as ab-initio multireference CI and time-depending DFT methods will be discussed.

Computational Chemistry **96**

Asymmetric μ_2-1,1-azido bridged copper(II) complex: Experimental and DFT studies

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A new rare variety asymmetric μ_2-1,1-azido bridged copper (II) complex has been synthesized and characterized structurally and magnetically. X-ray study reveals that the Cu-N(azide)-Cu angles in this complex is 90.1^o. This is unusually low in comparison to that of the same angle in other end-on azido-bridged binuclear complexes reported so far. Though a strong ferromagnetic interaction between the metal centers is expected in the complex the coupling has actually been found to be antiferromagnetic ($J = -8.9\ cm^{-1}$), instead. To rationalize this paradoxical magnetic behavior, DFT calculation of this and other four complexes with very similar structure have been performed within broken symmetry (BS) framework and a magnetostructural correlation has been derived. The calculated magnetic coupling constants (J) are in excellent agreement [1], both in sign and in the magnitude of the exchange interaction, with the experimental data, and the spin density map is correctly reproduced.

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Computational Chemistry **97**

The Myoglobin Cyanide complex - electronic structure, dynamics and IR spectra

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Ligand binding to Myoglobin is one of the best studied problems in molecular biology, with an exceptional wealth of experimental and theoretical information available [1]. However there are still issues which are not yet well understood in terms of ligand binding and dynamics. Here we investigate the binding of cyanide in the active site by computational means using both quantum chemistry and molecular dynamics in order to characterize this complex.
To understand the influence of the protein, the heme-cyanide interaction potential was calculated and fitted to an empirical form which was subsequently implemented into CHARMM. The influence of the protein was introduced both by performing MD simulations and by performing DFT calculations including the point charge electrical field of the protein environment. It was found that the two possible binding modes of the ligand differs considerably in electronic structure and that the protein clearly is biased to bind only one form. Other changes included an increased barrier to isomerization in the protein environment. A 3-center charge model [2] to describe the iron-ligand core of the complex is developed to include polarization as well as charge transfer effects. This model is then used to compute IR spectra, which relates experiment [3] to dynamical processes and structural information in the active site.

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Computational Chemistry **98**

Theoretical Design and Computational Analysis of Solvation Effects of Corannulene

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The molecular structure of corannulene ($C_{20}H_{10}$) has been investigated by quantum mechanical studies using a wide variety of basis set in order to study the correlation between the structure (bowl depth) and energy barrier. Previous work showed a correlation between the structure and the energy for a class of corannulene structures [1]. Theoretically, we have determined that the MP2/cc-pVDZ//B3LYP/cc-PVDZ methodology offers the best agreement with experiment, across a wide variety of functionalized corannulene.
A predictive theory is being developed for the modeling of the structures and dynamics of polynuclear aromatic hydrocarbon systems including the influence of solvation, based on some new experimental observations involving penta-arylcorannulene. In particular, investigations are made into the molecular nature of conformational gas and solution phase equilibria for corannulene-based structures affected by charge separation and influence of solvation. Modifications are being made to our general quantum chemical solvation algorithm, COSab [2], offering increased accuracy in assessments of solvent effects in electronic structure computations,

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Computational Chemistry **99**

Investigation of Protein-Ligand Interactions Using Combined Quantum-Mechanical/Classical and Mechanical/Electrostatics Pipeline Aided by Intelligent Grid-Infrastructure Deployment

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Many important and fundamental questions in biology and biochemistry can be better understood by investigations at the protein-ligand or drug-receptor level. A key goal in the proposed work is the development of new algorithms for the prediction of the binding phenomenon between proteins and ligands. While there are many possibilities for such a design, our choice is focused on a strategy that includes continuum models to account for the large-scale electrostatic interactions involved in the complex, combined with quantum mechanics for the more detailed analysis of the ligand and the direct protein-ligand interactions. We investigate the possibilities for embedding an adaptative Poisson-Boltzmann estimate of biological environment into the self-consistent field quantum mechanics for assessment of ligand-environment interactions.

The evolution of the theoretical method development is guided and refined based on the parallel investigation of a Pyridoxal 5'-phosphate(PLP)-dependent alanine racemase enzyme from *Geobacillus stearothermophillus* that gains considerable retro-aldol activity after a single active site mutation ($Tyr^{265}Ala$).

The theoretical method involves multiple tools and resources, including molecular modeling software, databases, and auxiliary tools. Therefore, an integrated pipeline using grid technology is currently under development, which will greatly facilitate the use of the sequence of tools, and will allow access to remote resources in real time. The grid infrastructure will be further enabled by scientific grid workflows involving high performance and/or high throughput computational tasks.

Computational Chemistry **100**

DNA-BINDING OF RUTHENIUM-ARENE ANTICANCER DRUGS

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The discovery of cisplatin as an anticancer drug led to considerable interest in metallopharmaceuticals. Problems remain associated with their use, including general toxicity, drug resistance and low selectivity. Recently, organometallic ruthenium(II)-arene complexes showed their potential to overcome this drawback. Rational drug design requires a detailed understanding of structure-property relationships at an atomistic level.
We performed classical MD and mixed QM/MM Car-Parrinello MD simulations[1] to rationalize the binding mode of two series of anticancer ruthenium arene-complexes to DNA. The bifunctional[2] $[Ru(\eta^6\text{-arene})X_2(PTA)]$ (**1**) and the monofunctional[3] $[Ru(\eta^6\text{-p-cymene})Xen]^+$ (**2**) series of compounds were both bound in different ways to the sequence d(CCTCTG*G*TCTCC)/d(GGAGACCAGAGG), where G* are guanosine bases that bind to the ruthenium compounds through their N7 atom. As reference, the same sequence was also simulated without any drug and in its canonical, unperturbed B-DNA form.
The local and global structural modifications of DNA upon complexation were analysed in detail. The differences of the DNA-interaction-properties between the two series of compounds as well as with respect to the canonical B-DNA are discussed and linked to experimental observations. In particular, an atomistic description of a Watson-Crick base-pair break upon binding of **2** to dsDNA is proposed. The selectivity of **2** for guanine was shown by MD docking studies. Fundamental differences between binding of **1** and **2** to single stranded DNA (ssDNA) and dsDNA are rationalized.[4]

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Computational Chemistry **101**

Large amplitude motion on the SecA protein: A molecular dynamics study of the *Bacillus Subtilis* SecA motor protein

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The ATPase protein SecA is the "motor" that drives the bacterial protein secretion system. By successive ATP binding cycles the SecA protein is able to transform chemical into mechanical energy and translocate proteins across the periplasmatic membrane. Starting from a recently determined crystal structure from *Bacillus Subtilis* [1] (PDB 1TF2), molecular dynamics simulations performed in our laboratories show a large conformational change when ADP is replaced by ATP in the binding pocket indicating a possible mechanism for the functioning of the motor. We are also able to reconcile structural differences between ADP bound crystal structures subject to monomeric and dimeric crystalization conditions [1,2].
Normal mode analysis and domain motion (Dyndom) [3] studies are presented in detail in order to characterize the large conformational changes of the protein. Results from these studies together with electrostatic analysis for the ADP/ATP binding site are used to suggest a possible mechanism for the functioning of the SecA motor.

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Computational Chemistry **102**

Computational Studies of $C_6H_{11}^+$ and $C_4H_7^+$ Species in Solution Using the Explicit Solvent Model

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Computational studies *in vacuo* on potential energy surfaces relating to substituted $C_6H_{10}^+$ and $C_4H_7^+$ cationic species revealed the presence of several conformers where the cationic moiety adopts the form of a protonated cyclopropane and of bicyclobutonium, respectively. These species are stabilized by the high degree of charge delocalization and in addition incorporate the pentavalent carbon.

To determine whether these carbocations are also stabilized in solution, we investigate in the present contribution the behavior of these species in the presence of explicit solvent molecules in order to study the media effects. In the cation-water supermolecules thus generated, the solvent molecules are hydrogen-bonded to the central cationic moiety of the cluster, thus mimicking the first solvation shell. This methodology was further improved by combining the fully optimized cation-water cluster geometry with the reaction field model (PCM method) where a continuous dielectric field was used to simulate the bulk of the solvent. Several density functional methods were used for these investigations and their results will be compared with the post-Hartree Fock computations. The structure, properties and relative stabilities of reaction intermediates that revealed extended charge delocalisations and sometimes-unusual bonding properties will also be discussed.

Computational Chemistry **103**

Integration of MLP and MHBPs molecular interaction fields into VolSurf environment for the prediction of solubility

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VolSurf[1] is a widely used computational tool that explores the physicochemical property space of a molecule starting from 3D interaction energy grid maps. The basic concept of VolSurf is to compress the information present in 3D grid maps into few quantitative 2D numerical descriptors. VolSurf is basically integrated with GRID[1] Molecular Interaction Fields (MIFs). Molecular Hydrogen-Bonding Potentials (MHBPs[2]) is a tool that explores three-dimensional H-bonding properties while Molecular Lipophilicity potential (MLP[3]) offers a three-dimensional representation of lipophilicity. These molecular interaction fields were successfully related with pharmacokinetic properties of drugs candidates[4]. This work is devoted to extend the integration of the MxPs (MLP and MHBPs) fields into VolSurf environment and to determine their ability to predict water solubility using Quantitative Structure-Activity Relationships (QSAR) models.

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Computational Chemistry **104**

Quantum Chemistry evaluation of pi character on Metals - ligands bonding in transition metal Complexes with $[MCl3Y]^{-1}$ (M= Pt, Pd, Ni and y = pyridine, carbene)

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Density functional studies have been carried out for bond decompositions analysis of the [MCl3Y]-1 (M: Pt; Pd, Ni and Y: pyridine, carbene) complex based on the local density approximation including nonlocal corrections for correlation and exchange self-consistently. Influence of steric effect has been investigated, both in plane structure (all atoms are in the same plane) and out of plane structure (two chlorines are perpendicular to the plane of the Y ligands) of $[MCl3Y]^{-1}$. The electron donation from pyridine or carbene ligands make the metal more electron rich (sigma donation), and in order to compensate this increasing electron density, a filled metal d-orbital may interact with the empty pi* orbital on the Y ligand(pi back donation). The computed results show that the contribution of the pi back-donation to the orbital energy term is slightly the same with Pd and Pt metals for both carbene and pyridine ligand while this contribution increases with Ni. Pyridine has been found to be good acceptor than carbene and the steric interaction is little dominated by Pauli repulsion that implies a strong destabilizing of orbital molecular orbital of the complex.
It's also shown that the repulsive interactions between occupied nd metal orbital and occupied σ_{NC} orbital were found weak in the M-Y bond for pyridine compared to carbene. Influence of the variation of bond length, the basis sets and the relativity effect of the M-Y (and thus the orbital energy) to be done.

Keywords: Bonding analysis, Donor-acceptor bonds; Energy partitioning; Transition metal complexes; ELF; Density; Mulliken Population Analysis

Computational Chemistry **105**

Spin-Densities and Magnetic Exchange in Transition Metal Dimers

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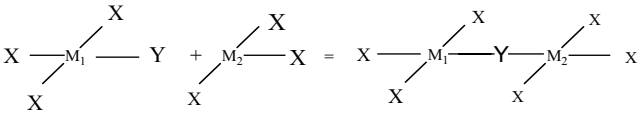
A new conceptual model of calculating magnetic exchange integrals based on spin-densities of the magnetic building blocks of a transition metal dimer complex is presented. It a first step the spin density on the bridging ligand Y resulting from charge transfer and spin polarization due to the open shell M_1 in a M_1X_nY moiety is calculated. In a second step, the coupling of the same ligand Y with a single electron open shell configuration (radical) with the metal on a neighboring M_2X_mY moiety is calculated. Finally, the spin-density from the first step is utilized to properly reduce the exchange integral of the X_mM_2-Y metal-ligand radical coupling bringing it in line with the spin-density distribution in the dimer complex. An application of this recipe to the calculation of the exchange coupling between square planar CuX_4^{2-} entities, sharing a common corner or edge ($Cu_2X_7^{3-}$ or $Cu_2X_6^{2-}$, respectively, X=F^-,Cl^-) is given. Results are discussed in comparison with the broken symmetry method [1] and a recently proposed DFT-based ligand field computational scheme. [2] The new approach allows to deduce and analyze in a rough but theoretically justified way exchange coupling integrals within a small fraction of computational times compared to usual ab-initio or DFT approaches.



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Computational Chemistry **106**

The Cycloaddition of Acridizinium cation with Ethylene and Allene: A Theoretical Study

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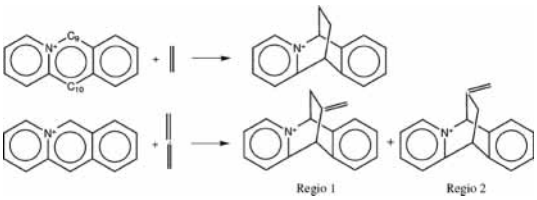
Acridizinium (ACR) cation undergoes cationic Diels-Alder cycloaddition with allene and ethylene. Positive charge on ACR is expected to strongly influence the mechanism of the reaction. Bradsher and coworkers have performed the reaction between ACR and ethylene[1] and proposed concerted mechanism for this reaction because the intermediate carbonium ion could not be detected during the reaction[2].



The cycloaddition of ACR with ethylene and allene have now been modeled at DFT level. Computed Frontier Orbital Energy analysis predict that these reaction are expectedly inverse electron demand type and follows concerted mechanism with extremely asynchronous transition structures. Both frontier orbital control and electrostatic interaction favors high reactivity of C9 over C10 in ACR. The effect of *peri* strain in ethylene reaction and the regio selectivity in allene reaction are examined. Computed bond orders show bond making and breaking in the reaction path in greater detail.

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