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Medicinal Chemistry **97**

Cationic Lipidoids for RNA Interference Therapy

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RNA interference therapy — the specific inhibition of endogenous protein expression — shows great promise for the treatment of hitherto untreatable diseases. As with all nucleotide-based therapy systems, a formulation must be found to effciently transport the DNA or small interfering RNA molecules into a cell in vivo. Recently, we have reported on a library of cationic polymers that act as DNA transfection vectors, protecting DNA from the degradation in the blood-stream and releasing the DNA-prodrug into the cytoplasm of target cells[1,2]. At this meeting we would like to present a new library of hundreds of di erent cationiclipidoid molecules. All weretested in vitro for their effciency to mediate DNA or siRNA transfection. We have identified structures that surpass state-of-the-art delivery systems and we have tested the most promising candidates in an extensive in vivo study. The communication will reveal powerful systemic protein knockdown in various disease models.

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Computational Chemistry **98**

The Emergence of Density Functional Theory in Computational Quantum Chemistry

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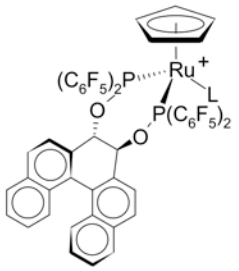
As a major method of computational quantum chemistry, Density Functional Theory (DFT) has made a remarkable breakthrough during the last 10-15 years. Today, DFT-based methodologies have become *de facto* standard techniques for routine modeling of organic, organometallic and inorganic systems, clusters, catalysts, new materials, surfaces, lead compounds in drug design, etc. In this presentation, some historical landmarks in the development of DFT will be outlined, emphasizing as well on its differencies with wavefunction-based methodologies. In addition, some recent DFT applications to large organic and organometallic systems, such as $[CpRu(PP)L]^+$ derivatives [1] will be discussed.



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Computational Chemistry **99**

Modeling Environmental Effects with Frozen Density Embedding

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An efficient implementation of the orbital free frozen-density embedding (FDE) scheme within density functional theory (DFT) [1] is presented. FDE is based on the partitioning of the electron density into an active embedded part and a frozen (environmental) part. It is demonstrated that FDE can, in combination with efficient approximations for the surrounding density [2], be used to model environmental effects on molecular properties, e.g., solvent effects on electronic spectra [3].
We also discuss the possibility to model the effect of more complex surroundings. In particular, the phenomenon of induced circular dichroism (ICD) is investigated, where the chiral compound is only described in terms of its frozen density. It is demonstrated that FDE can reproduce circular dichroism spectra of achiral compounds in complexes with chiral partner molecules very well [4].
The current implementation of FDE assumes excitations which are localized on the embedded system only. This offers some striking advantages in comparison to conventional TDDFT calculations for large systems. But there are also cases in which this approximation does not hold. This is discussed for the properties of a water molecule surrounded by water in a comparison of FDE with a classical polarizable force field [5]

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Computational Chemistry **100**

From Solvent Fluctuations to Quantitative Redox Properties of Quinones in Methanol and Acetonitrile

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We have employed a novel combination of density functional theory (DFT) and classical molecular dynamics simulations (MD) to provide quantitative values for key parameters of electron transfer reactions[1]. We have been able to rationalise the difference in redox potentials and reorganisation free energies of quinones due to chemical substitutions and to changes in their environments. Using two solvents with very similar dielectric properties, we are able to highlight the role of hydrogen bonding as a specific interaction that increases the reorganisation free energy.

Within our approach, redox properties are computed based on Marcus theory. An ensemble of configurations is generated using classical MD, but redox properties are obtained using the average and fluctuations of the vertical ionisation energy, which is computed using DFT[2]. This combines the strength of classical models, which lies in the accessibility of long time scales and thus in the statistical accuracy with which fluctuations can be evaluated, with the accuracy of the more elaborate quantum mechanical models. Indeed, DFT includes electronic relaxation and thus describes the solvent polarisation and changes in hydrogen bonding strength upon reduction. The new approach is both sufficiently general and efficient to allow e.g. for further exploration of redox properties of systems of biological interest in their native environment.

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Computational Chemistry **101**

Distributed Multipole Potentials for Molecular Dynamics Simulations

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Electrostatic force field potentials for Molecular Dynamics (MD) simulations are commonly represented by atomic point charges. It has been recognized for some time that this restricted model is not sufficiently flexible to describe important features of the molecular charge distribution. A more accurate representation of molecular electrostatic potentials can be derived directly from *ab initio* electron density distributions using the Distributed Multipole Analysis (DMA) [1]. The main difficulty for using atom-centered
multipoles in MD simulations is the anisotropy of these potentials, which requires the definition of local molecular reference axis systems. In particular, the intramolecular axis definition has to be consistent with the vibrational motions of the molecule.

The DMA formalism has been implemented into the CHARMM force field. Using water as a test system, small water clusters, bulk water and cavity waters in cytochrome P450 are investigated. Furthermore, the generalization of DMA to pharmaceutically relevant molecules is presented.

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Computational Chemistry **102**

Classical Dynamics on Multiple Potential Energy Surfaces

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Current standard force fields are in general not flexible enough to describe processes involving changes in electronic structure, such as the change in spin state that often occurs upon ligand binding at metal centers or in electron transfer reactions inside proteins. We present a general implementation of a method (reactive molecular dynamics (RMD))[1] that can treat such processes that can be well described by a diabatic surface crossing, but can also be seen as a general way to describe a reactive process such as irreversible ligand binding in terms of surface crossings. As a prototype problem we apply RMD to cytochrome P450, both in the resting state and with an inhibitor present in the active site. Results concerning inhibitor binding to other proteins are presented as well

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Computational Chemistry **103**

Density Functional Studies of Naphthalenediimide Acceptors and Dialkoxynaphthalene Donors as Building Blocks in Supramolecular Architecture

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The creation of synthetic ion channels and pores from building blocks that are not known to occur in nature is a topic of increasing scientific concern. Previous work showed that naphthalenediimides (NDI) substituted on *p*-octiphenyl rigid-rods, self-assemble into ion channels that open in response to molecular recognition of dialkoxynaphthalene (DAN) intercalators [1]. Highly cooperative and selective ligand gating by DAN proceeds *via* conformational changes of closed supramolecular structure, which untwist to give open and weakly anion selective ion channel.

In this contribution the electronic structures, energies, and equilibrium geometries of NDI and DAN were studied by density functional methods. Impact of different substitution patterns on their electronic structures was also investigated. Computations on model systems such as NDI-NDI and NDI-DAN-NDI complexes were undertaken in order to asses their capability to form the π stacks in supramolecular assemblies. Several hybrid functional methods have been used together with moderate and large basis sets. Molecular Dynamics simulations of synthetic ion channels, which incorporate the π stacks of NDIs will also be discussed.

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Computational Chemistry **104**

The Isomers of the Dimer $(ClO)_2$ Revisited.

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The analysis of the first *in situ* measurements[1,2] of ClO radical dimerization points to the lack of full understanding of its role in the ozone depletion. The molecular structures of Cl_2O_2 isomers, and transition states, vibrational frequencies, vertical excitation energies, and the relative energies of $2ClO \rightarrow Cl_2O_2 \rightarrow ClOO+Cl \rightarrow OClO+Cl$ reactions are reported employing up to the CCSD(T)/ aug-cc-pVQZ level of theory. Our best estimate for the dissociation energy hc D_0 of ClOOCl relative to 2ClO is ~ hc 6800 cm^{-1}, considerably larger than the most recent experimental estimates[3,4] of ~ hc 5700 cm^{-1}. The chlorine chlorite ClOClO is found to be weakly bound, by ~ hc 3400 cm^{-1}. The chloryl chlorite $ClClO_2$ is observed to be stabilized with respect to the chlorine peroxide ClOOCl , and is predicted to lie ~ 500 cm^{-1} lower than ClOOCl. $ClClO_2$ is found not to be significant for ClO self-reaction due to a high barrier for association. Further, the isomerizations appear unlikely under stratospheric conditions as the transition states are found to lie even higher above the reactants than previously reported[5] by DFT methods. We also discuss the relation to recent work on parity violation and stereomutation tunneling in this molecule[6].

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Computational Chemistry **105**

REMD simulations of Prion Protein Misfolding: Towards the Scrapie Isoform

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Protein misfolding, associated with an increase of β-sheet content and nonomer aggregation, are hallmarks of a number of neurodegenerative lisorders. Prion protein (PrP) misfolding plays a key role in several ransmissible spongiform encephalopathies, among which Creutzfeld-Jakob nd bovine spongiform encephalopathies [1]. Currently, many compu- ational efforts are devoted to elucidating structural properties of the lisease-transmitting scrapie isoform (PrP^{Sc}), of which no experimental tructure is available. In the present study, full atom, explicit solvent rion misfolding simulations were conducted at high temperature, start- ng from the NMR structure of the benign cellular isoform (PrP^{C}) of the rion protein. In order to characterize the specificities of prion misfold- ng and to validate the molecular dynamics protocols, similar simulations were performed with the doppel protein, a prion analog possessing a very imilar fold but low sequence homology (26%) that is not involved in amy- oid fibril diseases [2]. Replica exchange molecular dynamics [3] protocols were adapted in order to explore the multitude of prion misfolding path- ways and to assess the energetic barriers underlying the conversion of PrP^{C} into PrP^{Sc}. The rarely sampled β-sheet rich conformations could e segregated into high energy (putative transition state) and low energy tructural models of different folds. Monitoring the secondary structure ontent during the simulations enabled to evaluate the β conformation ropensity along the sequence for the prion and for the doppel control eference.

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Computational Chemistry **106**

Electron Transfer Properties of Azurin from Pseudomonas Aeruginosa by Hybrid QM/MM Molecular Dynamics Simulations

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The reduction potential and the reorganization energy of Azurin from Pseudomonas Aeruginosa [1] has been investigated by Grand Canonical hybrid Car-Parrinello/molecular mechanics simulations [2,3]. Our simulations point out that an accurate description of the environment surrounding the metal binding site and of the finite-temperature fluctuations of the protein structure are fundamental for a correct quantitative description of the electronic properties of this system. Our results, in excellent agreement with experiments [4], reveal that the small reorganization energy, which is crucial for efficient electron transfer rates, is mainly due to solvent reorganization at the protein surface. Our calculations open the way to theoretical investigations on key issues in photoactive metalloproteins, like biological redox reactions and biological electron transfer.

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Computational Chemistry **107**

Intramolecular Electron Transfer in Bis(methylene) Adamantyl Radical Cation: A Finite Temperature Study using SIC Corrected DFT

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Self-interaction corrected (SIC) DFT has been used to investigate the first principle molecular dynamics of intramolecular hole transfer (HT) in Bis(methylene) Adamanthyl Radical Cation (BMA). This approach allows the investigation of the topology of the free energy surface that governs the HT process at room temperature (300 K). The thermal activation of all degrees of freedom provides an important additional information about the mechanisms involved in the HT process, which goes beyond the zero temperature vibration analysis on the potential energy surface. The efficient sampling of the region of intersection between the ground state and the first excited state is obtained with the addition of a restrained potential which forces the system near the seam of intersection. Our study confirms and extends the previous obtained CASSCF results and shows that there is no predominant degeneracy-lifting mode even at room temperature. On the contrary, the regime of HT in BMA is strictly nonadiabatic as in the low temperature energy driven regime (adiabatic trapping hypothesis). In addition, we performed a thermodynamic integration along selected reaction coordinates to estimate the activation free energy barrier, which, together with the magnitude of the nonadiabatic coupling matrix element, is essential for the computation of the HT rate at room temperature.

Computational Chemistry **108**

Full-Featured Simulation of Reconstructive Phase Transitions

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Reconstructive phase transitions are of fundamental importance. The simplicity of the structural types involved contrasts with the theoretical and experimental difficulty in assessing their mechanisms. Combining advanced molecular dynamics simulations and modeling approaches [1-6] we elucidate mechanisms at the atomic level of detail, without overdriving of simulation parameters or imposing artificial constraints on the system. This allows an unbiased identification of the mechanisms of phase transitions in ionic and semi-conducting materials at experimental conditions [1-4,7]. Apart from isolated nucleation events, also multiple, coexisting nuclei are accessible. This opened the study of the morphogenesis of interface and grain boundary formation from coalescing domains of different orientations. The latter act as preferred nucleation centers, and cause an asymmetry between forward and backward transition [8]. The role of chemical composition in driving domain formation and interface propagation can be investigated [9]. New perspectives for simulations of phase transitions in periodic and finite systems at an unprecedented level of detail are being developed.

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Computational Chemistry **109**

Probing combined proton and electron transfer along a hydrogen-bonded ammonia wire using time dependent density functional theory

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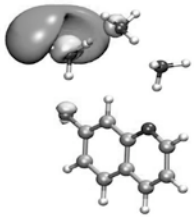
The mechanisms and dynamics of proton and hydrogen atom transfer are of great importance in biosystems, and in general, acid-base chemistry. Recently, the entrance channel, reaction threshold, and mechanism of an excited-state hydrogen atom transfer reaction along a unidirectionally hydrogen-bonded ammonia 'wire' have been characterized both experimentally and with *ab initio* single point calculations [1].

Time dependent density functional theory (TDDFT) combined with molecular dynamics (MD) offers a possibility to investigate the above mentioned reaction at finite temperature. Furthermore, this provides an opportunity to sample the multi-dimensional configurational space of this specific process.

Here, we will first show that TDDFT gives a qualitatively correct description of the potential energy surface in agreement with the CASSCF single point calculations. After having validated the TDDFT result, we have carried out molecular dynamics simulations in the $\pi\pi^*/\pi\sigma^*$ excited state manifold. The initial configuration for the simulations were taken from an equilibration run performed at 300 K. A reaction profile of the joint proton and electron transfer process will be presented.



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Computational Chemistry **110**

Sink or Swim? Weighing Interations in a Hydrophobic Environement.

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Many significant drug-receptor interactions involve small-molecules interacting with a protein embedded in a hydrophobic lipid bi-layer. Here, protein-membrane and membrane mediated protein-protein interactions found in a non-uniform system such as a membrane bilayer are investigated by applying the GAMESS-COSab quantum mechanical implementation of a dielectric continuum solvation model. Special focus is placed on evaluating the energetic contributions arising from non-electrostatic interactions of the membrane with an embedded protein as well as calculated thermodynamic quantities. These factors are analyzed both qualitatively and quantitatively in order to assess the importance of these factors in contributing to drug-receptor specificity as well as calculated properties such as binding strength. These results will inform future developments to the GAMESS-COSab algorithm that will be better suited for studying molecular systems of this kind. An overview "flow-chart" formulation of how these theoretical improvements might be implemented directly into the GAMESS-COSab SCF procedure will also be presented.

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Computational Chemistry **111**

An *ab initio* study of binding energies of hydrogen bonded dimers of formamide

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Among the high-level correlated *ab initio* approaches, the CCSD(T) (coupled-cluster with singles, doubles and noniterative triple excitations) method has proven to give excellent results for structures and binding energies of molecules and dimers. However, the steep dependence of the CCSD(T) method on the number of basis functions ($\sim N^7$) precludes the use of large basis sets for all but the smallest systems. It has been noted that the ΔCCSD(T) correction term, given by the difference of the MP2 and CCSD(T) stabilization energies, $\Delta CCSD(T)=\Delta E_{MP2}-\Delta E_{CCSD(T)}$, becomes nearly constant for basis sets of quite moderate size. This suggests that the CCSD(T) interaction energy at the basis set limit, $D^{\infty}_{e,CCSD(T)}$ can be estimated sufficiently accurately from the MP2 interaction energy at the complete basis set (CBS) limit $D^{\infty}_{e,MP2}$ and the ΔCCSD(T) calculated with a smaller basis set.

Here, we calculated the MP2 binding energies of five hydrogen bonded dimers of formamide using aug-cc-pVXZ basis sets up to quintuple zeta (X= 2,3,4,5). The binding energies are extrapolated to the complete basis set (CBS) and vary over the range between -14.9 and -5.6 kcal/mol. ΔCCSD(T) terms are evaluated using the 6-31G(d,p), 6-31G*(0.25), 6-31+G(d,p), aug-cc-pVDZ and the aug-cc-pVTZ basis sets. The 6-31+G(d,p) basis set already gives reliable ΔCCSD(T) correction terms. The correction energies are between -0.10 and -0.42 kcal/mol. For the strongest dimer this correction is 0.7% of the MP2 CBS limit binding energy, for the weakest it is 8.1%. This latter result implies that weak hydrogen bonding interactions tend to be severly underestimated by MP2 calculation. B3LYP, PBE and PW91 density functionals are benchmarked against those energies, of which the PW91 functional performs best.

Computational Chemistry **112**

DNA-Binding of Ruthenium-Arene Anticancer Drugs

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Organometallic ruthenium(II)arene complexes have emerged as promising novel anticancer compounds. However, little is known about their molecular mechanism of action.

Using Car-Parrinello molecular dynamics (CP-MD), we calculated the free energy profile for the hydrolysis reaction of [(arene)Ru(II)(en)(Cl)] (**1**) in explicit quantum water. Gas phase CPMD simulations and potential energy calculations at the DFT and MP2 level of theory rationalize the exclusive chemoselectivity of **1** towards guanine. Three different reaction pathways and the corresponding transition states have been identified.

Subsequently, we performed classical MD and mixed QM/MM CPMD simulations to characterize the binding mode of two series of ruthenium(II) arene-complexes to dsDNA. The monofunctional **1** and the bifunctional [(arene)Ru(PTA)$(L)_2$] (**2**) series of compounds were both bound to a 12-mer.[1] The free energy profile for the reaction of **1** with dsDNA has been obtained. A tailor made force field for compound **1** was derived from our QM/MM trajectories using a new force matching approach.

The local and global structural modifications of DNA upon complexation were analysed in detail 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. Fundamental differences between binding of **1** or **2** to single stranded DNA (ssDNA) and dsDNA are rationalized.[2,3]

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Computational Chemistry **113**

Theoretical investigations on strained silicon semiconductors.

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Nowadays, silicon is one of the most popular semiconductor materials. Due to its availability and properties, it is widely used as a basis of various electronic devices, computers or transistors. However growing demands for computational performance brings new challenges for material science and engineering to develop and apply a novel solutions that would, at least temporary, satisfy the needs. One of such solutions, is a long known concept of minimization of electronic devices, which among its obvious advantages, has a limitation given by properties of given material. In case of silicon this barrier can be partially overcome by inducing strain in this compound, commonly on $Si_{(1-x)}Ge_x$ alloy.
In such strained silicon, electrons flow up to 70% faster, which results in increase of performance of electronic devices build in this technology for about 30-40%.
In present work we have studied effects of strain on band-structure of silicon and distribution of forces in Si - $Si_{(1-x)}Ge_x$ structures by applying pseudopotential plane-wave density functional theory.[1] For accurate estimations of bandgap energies we have used GW-approximation,[2] which is proven to give very reliable results. Our long-stand aim is construction of theoretical model of Metal-Oxide Semiconductor Field-Effect Transistor (MOSFET) with strained silicon channel, which will allow us to get insight into distribution of pressure in such devices.

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Computational Chemistry **114**

Dynamics and Free Energy Profiles of Proton Transfer Pathways in Ferredoxin I

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Proton transfer reactions are of fundamental importance in a wide range of chemical and biological processes. The energetic barrier for proton and hydrogen transfer is often so high that transfer is a rare process. The long time scales involved complicate application of accurate dynamical studies using QM/MM molecular dynamics simulations. Based on prototype systems multidimensional potential energy functions have been calculated. The flexible and adjustable implementation of the force field makes it transferable to a variety of systems where proton/hydrogen transfer is involved.
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 particular the role of functional water molecules [2] in the active side is explored by molecular dynamics simulations. Using a combination of the reactive force field with transition path and umbrella sampling methods provides the free energy profiles of possible reaction pathways of the proton transfer step.

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Computational Chemistry **115**

***Ab initio* water using dispersion corrected atom centered potentials within density functional theory**

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Even though water has been the most studied liquid by molecular simulations, its microscopic nature remains elusive. Water displays intricate behaviours as a result of the delicate interplay between different types of interactions such as H-bonding and many-body polarisation.

Density functional theory (DFT) employing generalised gradient approximation (GGA) has been the *ab initio* method of choice in solid-state and liquid studies due to its computational efficiency. For DFT-GGA water, the first peak in the oxygen-oxygen radial distribution function is over-structured compared to diffraction data and the diffusion constant is too low [1]. In addition, *ab initio* Monte Carlo results indicate that DFT-BLYP water may be less dense than the true liquid [2].

Due to the importance of non-bonded interactions in water, the effect of dispersion corrected atom centered potentials (DCACPs) [3] on the description of DFT-BLYP water is of great interest. Here we report the structural and dynamic properties of liquid water from our Car-Parrinello molecular dynamics studies using the DCACP-augmented BLYP functional. Properties such as radial distribution functions, mean square displacements, molecular dipole moments, and hydrogen bond statistics will be presented.

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Computational Chemistry **116**

Competition Between Proton and H-Atom Transfer in Green Fluorescent Proteins

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The Green fluorescent proteins (GFPs) have been found in numerous bioluminescent organisms, like the jellyfish Aequorea victoria[1]. They can be used as fluorescent marker in cell biology and therefore, many studies are devoted to understand their complex photochemistry. The chromophore responsible for the green fluorescence is involved in a hydrogen bonded wire composed of a water molecule, a serine, and a glutamate residue.
It exhibits two absorption maxima at ~395 nm and 475 nm which correspond to the neutral and anionic forms of the chromophore, respectively; The second absorption band is the experimental proof of the deprotonation of the chromophore, induced by expected proton transfer along the wire. Nevertheless, recently, Vendrel *et. al.*[2] have shown that rather H-atom transfer occurs between the chromophore and the water molecule in the C_s symmetry, analog to the "photoacid" 7-hydroxyquinoline involved in a H bonded wire of three ammonia molecules[3]. Based on the knowledge of the latter system, questions are arising: Does the GFP chromophore exhibit the same behavior as 7-hydroxyquinonline, i. e. $\pi\pi^*$-$\pi\sigma^*$ crossing, which can be predicted with a computational "low cost" method? Is there any competition between Proton and H-atom transfer and does the environnement of the water molecule play a role in this competition? First results using CIS calculations are shown for the first step of the reaction path as well as SAC-CI calculations to compare with experimental electronic excitations.

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Computational Chemistry **117**

Continuous Symmetry Measure and Molecule symmetrization

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Continuous Symmetry Measure (CSM)[1,2] aim to define near symmetry and correlations with symmetry dependent molecular properties. In this contribution it is introduced a definition of CSM which makes use of the point group theory projection operator. The application of this definition to the electronic density is straightforward. A symmetric electronic density with respect the group *G* of order is defined as

$$\tilde{\rho}(\mathbf{r}) = \frac{1}{n_G} \sum_{\mu}^{n_G} S_\mu \rho(\mathbf{r})$$

where S_μ identify one of the n_G symmetry operations of the group *G*. The CSM is then obtained via a minimization of a distance function. In a simple case it is an Euclidean distance

$$D = \int |\tilde{\rho}(\mathbf{r}) - \rho(\mathbf{r})|^2 d\mathbf{r}$$

This definition can be extended[4]. It is possible to introduce, within this formalism, a CSM using geometrical points or a wave function which reduces to the previously proposed measures respectively by D.Avnir[1] and S.Grimme[3].
In the particular case of geometrical points this procedure can be used for graphical tools: It will allow a user to ask for a symmetrization of an input structure with respect a given point group. The current implementation (limited to few groups) will still require a chemical knowledge but should determine a much faster graphical interface user interaction.

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Computational Chemistry **118**

An ab initio Investigation of the DNA Photolyase Repair Activity

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The most common type of DNA damage caused by UV radiation is the [2 + 2] cycloaddition of two adjacent pyrimidine bases which yields cyclobutane pyrimidine dimers (CPDs) [1]. DNA photolyases use light energy to repair the CPD lesions by transfering an electron to the cyclobutane ring. The resulting radical anion then splits into two pyrimidines and transfers back the excess electron to the enzyme. The purpose of our work is to shed light on the atomistic details of the reaction mechanism, first in vacuo and then in its natural environment, i.e. within DNA. We address this issue by using a hybrid Car-Parrinello quantum mechanical/molecular mechanical (QM/MM) approach, in which the splitting of the cyclobutane ring is described at the density functional (BLYP) level of theory while the complex DNA environment and solvent are treated with a classical force field.

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Computational Chemistry **119**

Electronic structure of Di-cyano Di-iminophosphorane Ethylene and DFT study

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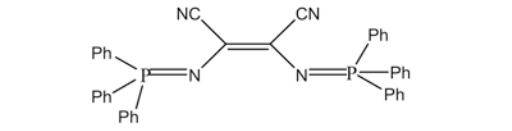
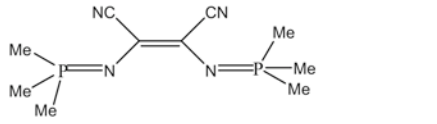
The synthesis of two Di-cyano Di-iminophosphorane Ethylene **A** and **B** is reported as well as the crystalline structure of **A**.



A



B

The cyclic voltammograms of these compounds are characterized by two oxidation waves at $E_{1/2}(1)$= 0.4545 (**A**) and 0.809 (**B**) V/SCE, $E_{1/2}(2)$= 0.314 (**A**) and 0.53 (**B**) V/SCE. Electrochemical and chemical (ferrocénium hexafluoro phosphate) oxidations of **A** and **B** lead to EPR spectra exhibiting hyperfine interaction with four ^{14}N and two ^{31}P nuclei. These coupling agree with those predicted by DFT calculation for the corresponding radical monocation. As shown by the SOMO, the unpaired electron is delocalized on the full Π system. The stability of the cation is dependant upon the substituant on the phosphorus.

Computational Chemistry **120**

Properties of hydration water at the ice-binding face of antifreeze proteins

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The crystal structures of antifreeze proteins from the beetle *Tenebrio molitor*[1] and the caterpillar from *Choristoneura fumiferana*[2] both contain structural water molecules in the region of the ice-binding surface. These water molecules have been suggested to play a role in the protein-ice recognition process by increasing the size and specificity of the ice-binding site[2]. Although the two protein structures have many features in common, the structural waters are found in different locations.

Using both Molecular Mechanical (MM) and Quantum Mechanical/Molecular Mechanical (QM/MM) methods, we have calculated the binding energies of hydration water in the crystallographically observed positions in order to determine whether the observed differences are due to energetic or crystal packing effects.

We have also investigated the dynamical properties of the hydration waters at a range of temperatures using Molecular Dynamics (MD) simulations. Finally, the effect of the choice of water model on the results has been assessed.

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Computational Chemistry **121**

The description of water in biomolecular simulations

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It is now well-known that water molecules at protein surfaces exhibit different behaviour to bulk water[1]. However, Molecular Dynamics (MD) simulations of solvated proteins routinely use water models originally designed for bulk water simulations. This is mainly due to the fact that forcefields for biomolecular simulations have been parameterised for use with a specific water model in order to obtain a balance between water-water and protein-water interactions. The Charmm22 forcefield[2], for example, was designed for use with a modified TIP3P model[3].

In order to assess whether the Charmm22 forcefield can be safely used with other water models (such as TIP4P or TIP5P[3,4]) and whether any of these water models are indeed capable of accurately describing the energetics and dynamics of hydration water, we have investigated the effect of the choice of water model on the solvation structure around small model compounds such as N-methyl-acetamide as well as on the dynamics of small proteins.

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Computational Chemistry **122**

Theoretical Ab-initio Study of Triaziridines

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The primary goal of this work is to study with high level computational methods the chemical system N_3H_3, with particularly emphasis on the triaziridine class of molecules, to better understand the synthetic challenges to these species. Triaziridines are cyclic compounds with two stereoisomers (cis and trans). They have 6 π electrons, a number that fits the famous Hückel law of aromaticity (4n + 2), but their geometry, as shown by Gimarc and Trinajstić [1] should not be planar because both bonding and anti-bonding Molecular Orbital (MO) in the π system are filled.
Triaziridines are label structures that are very difficult to synthesize. The first experimental evidence of Triaziridines (1977) was the complex Triaziridine-Ag-zeolite [2], and subsequently, (1980-1982) only a few organic substituted triaziridines have been prepared [3 a,b]. An additional motivation for such pursuits is the potential use of triaziridines as high energy materials [4].

We present a full ab-initio study of structure, mechanism, and relevant properties for a complete set of N_3H_3 isomers and their substituted analogues in order to answer some of these questions of stability and reactivity.

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Computational Chemistry **123**

Theoritical study of Corannulene: Solvent Effects, Reactions at Solid/Liquid Interfaces and Crystal Packing

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The molecular structure of corannulene (c20H10) has been investigated by quantum mechanical studies in order to study the structure of the molecule, its dynamic behavior and its properties [1].
Investigations are made into the conformational gas and solution phase equilibria for corannulene based structure. An effect computational solvation method has been developed in our group (COSab), which enable a more accurate assessment of molecular properties from first principles in a solvent environment [2].
The possibility to use this method for modelling reactions at solid/liquid interfaces has been examined. And new possibilities in theoretical modeling of structures in their crystalline environment has also been explored.

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Computational Chemistry **124**

Wavelet Investigation of $La_{0.5}Ca_{0.5}CoO_{3-\delta}$ X-Ray Absorption Data

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Fourier-transformation (FT) of X-ray absorption fine structure spectra (EXAFS) has been widely used to obtain structural information from X-ray absorption data. However, using FT it is not possible to separate the scattering contributions of nearest neighbor atoms with similar distances.
Due to recent success in wavelet analysis of extended X-ray absorption fine structure data (EXAFS) we analyzed the EXAFS data of $La_{0.5}Ca_{0.5}CoO_{3-\delta}$. We used Morlet wavelets to see if it is possible to distinguish between the Co-La and Co-Ca scattering paths. Applied to EXAFS spectroscopy, the wavelet transform is decomposing the EXAFS signal in the wave vector (k) and in the radial dimensions. With FT analysis of an EXAFS signal we obtain only information about the distances of the back scattering atoms, while WT shows additionally at which energies the back scattering takes place. The obtained result shows that some scattering paths can be separated in $La_{0.5}Ca_{0.5}CoO_{3-\delta}$, but the Co-La scattering path is too much overlapping with the Co-Ca scattering path to be separated unambiguously.

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Computational Chemistry **125**

Molecular Dynamics Simulations of $CaCl_2$ Aqueous Solutions

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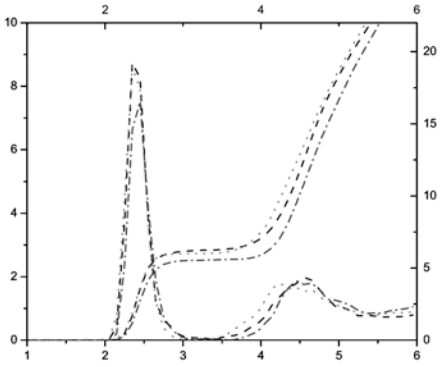
Car-Parrinello Molecular Dynamics simulations have been used to investigate structural and energetic properties of $CaCl_2$ aqueous solutions. Results of 1 M $CaCl_2$ solutions are consistent with a previous study of a single Ca ion in a periodic box of 54 water molecules [1] and show no effect of the chlorine at low concentrations.



2 M $CaCl_2$ water solutions have been studied in terms of radial distrubution functions and coordination numbers (figure). Contact and solvent separated Ca-Cl ion pairs formation have been observed, as in XRD experiments.

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Computational Chemistry **126**

Towards Rational Design of Ruthenium CO_2-Hydrogenation Catalysts: Elucidation of Reaction Pathways

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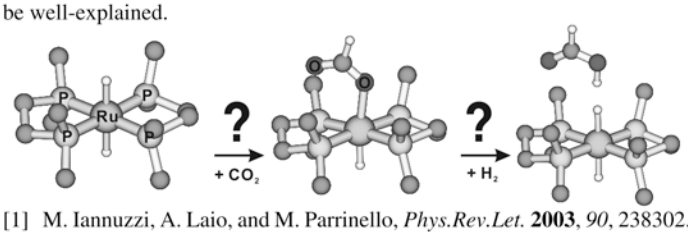
Complete reaction pathways relevant in homogeneous CO_2 hydrogenation by a Ru dihydride catalyst ($Ru(dmpe)_2H_2$, dmpe = $Me_2PCH_2CH_2PMe_2$) are investigated by *ab initio* metadynamics [1]. We are able to reproduce the main steps of the processes, identify the reaction intermediates, and evaluate the corresponding free energy profiles. Our simulations indicate that the CO_2 insertion for the formation of formate complex proceeds via a concerted-insertion mechanism. It is a rapid and direct process, throughout a relatively small activation barrier, which is in agreement with what observed experimentally. The H_2 insertion to the formate-Ru complex and the formation of formic acid, instead, occurs via an intermediate Ru(η²-H_2) complex, where the molecular hydrogen interacts with the Ru center. This step has been identified as the rate-limiting step of the reaction. Hence, we propose a simple measure of the catalytic activity based on the analysis of the electronic structure of the corresponding transition-state. Taking this measure, the relation between different ligands and the experimental catalytic activities can be well-explained.



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Computational Chemistry **127**

First principles molecular dynamics study of radiation damage of graphite and carbon nanostructures

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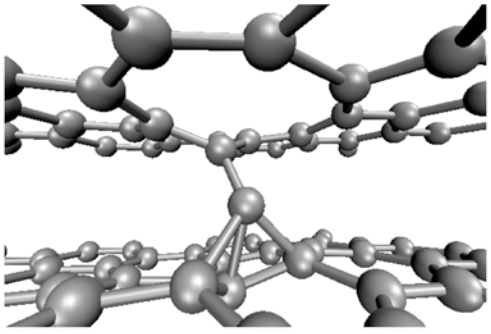
Understanding the mechanisms of radiation-induced defect formation in carbon materials is crucial in nuclear technology [1] and for the manufacturing of nanostructures with desired properties [2]. Using first principles molecular dynamics we performed a systematic study of the non-equilibrium processes of radiation damage in graphite on the picosecond timescale. Our study reveals a rich variety of defect structures (Frenkel pairs, in-plane topological defects) with formation energies of 5-15 eV. In addition, the study clarifies the mechanisms underlying their creation and predicts unexpected preferences towards certain structures.



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Minisymposium Inorganic and Coordination Chemistry **128**

Applications of Tris(mercaptoimidazolyl)hydroborato Ligands for Modeling Sulfur Rich Active Sites and For the Synthesis of Metallaboratranes

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The *tris*(2-mercapto-1-R-imidazolyl)hydroborato ligand, [Tm^R], is a versatile tripodal ligand that provides an [S_3] coordination mode that has diverse applications which range from modeling the active sites of zinc enzymes to the synthesis of olefin polymerization catalysts. In the vast majority of cases, the [Tm^R] ligand coordinates in a tridentate manner *via* the three sulfur atoms (Figure a), but more complex coordination modes have also been observed. For example, one of [Tm^{Ph}] ligands of the lead complex $[Tm^{Ph}]_2Pb$ coordinates with an "inverted" ^{4}–configuration (Figure b). An important recent development in the application of [Tm^R] ligands, as observed by several research groups, is concerned with the discovery that the B–H entity is reactive and may be cleaved by a metal center to generate "metallaboratranes" (Figure c) which feature a M→B dative bond. The bonding and reactivity of these novel compounds will be described.