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Computational Chemistry **CC 1**

Evaluation of the non(a)diabaticity of the quantum molecular dynamics using the dephasing representation of quantum fidelity [1]

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We propose two approximate methods for semiclassical calculation of the quantum fidelity in the non-Born-Oppenheimer dynamics. This quantity can be used to evaluate the dynamical importance of nonadiabatic or diabatic couplings between potential energy surfaces (PES) or of other terms in the Hamiltonian such as spin-orbit couplings. The acquired information can help reduce the complexity of a studied system without significantly affecting the accuracy of the quantum simulation. Another suitable application is the evaluation of accuracy of the approximate PES and couplings in comparison with high level PES without the need to run neither quantum nor classical dynamics on the expensive high level PES. Both methods can be considered a generalization of the dephasing representation (DR) [2-3] of quantum fidelity to several PES and their computational cost is the cost of dynamics of a classical phase space distribution. It can be implemented easily into any molecular dynamics program and also can utilize on-the-fly *ab initio* electronic structure information. We test the methods on three model problems introduced by Tully, on the photodissociation of NaI, and on-the-fly using CASSCF and MRCI methods.

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Computational Chemistry **CC 2**

Oxygen Dynamics and Energetics of Migration Pathways in Truncated Hemoglobin

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Truncated hemoglobin (trHbN) is a protein involved in NO dioxygenation [1,2] by converting nitric oxide to harmless nitrates ($Fe(II)O_2 + NO \rightarrow Fe^{+}(III) + NO_3^{-}$). The tunnel system of trHbN plays an important role in determining and controlling ligand entrance, migration, and rebinding.[2] Due to a greater affinity of Fe(II) for NO than for O_2, the first step of dioxygenation is expected to be the substitution of NO ligated to the heme group by free O_2 ($Fe(II)NO + O_2 \rightarrow Fe(II)O_2 + NO$). The three-point fluctuating charge model is used to reproduce accurately the dipole and quadrupole moments of O_2.[3] Molecular dynamics simulations of oxygen dynamics and migration in trHbN of *Mycobacterium tuberculosis* are studied with different approaches. Migration and exit pathways in multiple extended trajectories are analyzed in detail.[3] This provides structural properties about the ligand network which is found to be similar to NO network. A preliminary connectivity network for the ligand docking sites is built and the free energy profiles of migration are estimated by umbrella sampling. Differences between NO and O_2 network arise from the free energy profiles which are more complex for O_2. Energetic properties together with a statistical analysis like Markov network [4] suggest that trHbN network is designed for a dynamical storage of O_2.

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Computational Chemistry **CC 3**

TRAJECTORY-BASED SOLUTION OF THE NONADIABATIC QUANTUM DYNAMICS EQUATIONS : AN ON-THE-FLY APPROACH FOR MOLECULAR DYNAMICS SIMULATIONS

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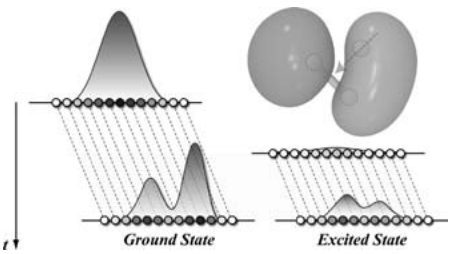
The non-relativistic quantum dynamics of nuclei and electrons is solved within the framework of quantum hydrodynamics using the adiabatic representation of the electronic states. An on-the-fly trajectory-based nonadiabatic molecular dynamics algorithm is derived, which is also able to capture nuclear quantum effects that are missing in the traditional trajectory surface hopping approach based on the independent trajectory approximation. The use of correlated trajectories produces quantum dynamics, which is in principle exact and computationally very efficient.
The method, called **NABDY** (**N**on**A**diabatic **B**ohmian **DY**namics), is first tested on a series of model potentials and then applied to study the molecular collision of H with H_2 using on-the-fly TDDFT potential energy surfaces and nonadiabatic coupling vectors [1].



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Computational Chemistry **CC 4**

Alignator – a computer program for induced-fit docking: Validation on the nuclear receptors

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A large majority of current techniques employed in the rational drug design rely on obtaining a 3D alignment of a set of compounds, which would mirror their relative arrangement within target-protein binding site. Correlating biological activity with the structural properties then helps with explaining the observed behavior (strong, weak or not- binding) and navigates research towards compounds having more favorable properties.

Computer-assisted molecular docking is the most popular technique for identifying binding poses. It is a remarkably complex procedure, because both ligand and protein may change their conformation upon binding. In order to decrease complexity and thus save computational time in screening, the protein is frequently treated as a rigid body. This might lead to satisfactory results for docking of congeneric series, but rather to a failure, if the docked ligand substantially differs from the template in terms of shape or volume. Keeping protein structure rigid simply does not allow for the proper accommodation of ligand in the binding site.

Alignator is a computer program for flexible docking of compounds based on the pharmacophore alignment. It generates ligand poses devoid of steric bumps and allows for the local induced-fit changes of the protein structure based on a combinatorial scan of the allowed side-chain conformations in the binding site. Key program features as well as validation results obtained at docking ligands to various nuclear receptors are presented.

Computational Chemistry **CC 5**

A quantum chemical data base approach for method development and data processing

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The computational power available to quantum chemists over the past decades has grown enormously, making increasingly complex systems feasible for accurate computation. Since the generation of the data (results) is no longer the bottleneck, the challenge now is to find strategies for structured storage, extraction (analysis) and interchange of data, thereby keeping the level of human intervention at a minimum.

Here we report on the implementation of a workflow scheme using TURBOMOLE [1] as program package, CML [2] as interchangeable output format as well as FoXlib [3] and eXist [4] to write and store the quantum chemical data. Extensions to CML will be presented, which now allow the use of the markup language as standard interchange and storage format for quantum chemistry codes in general. To illustrate the benefit of structured data processing, we present the results of an extensive study of the relative stability of the conformers of the ethene dimer using recently developed MP2-F12 methods [5].

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Computational Chemistry **CC 6**

Molecular docking using the Molecular Lipophilicity Potential as hydrophobic descriptor: impact on the GOLD docking performance

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GOLD is reliable docking software well known in the field of drug design [1]. At early steps of docking, it creates a list of *hydrophobic fitting points* inside the protein cavities that steers the positioning of ligand hydrophobic moieties. The generation of hydrophobic fitting points is based on the Lennard Jones potential between a carbon probe and each atom of the residues delimitating the binding site. To thoroughly describe hydrophobic regions in protein pockets and properly guide ligand hydrophobic moieties towards favorable areas, an in-house tool, the *MLP-filter*, was developed and applied. This new strategy retains only GOLD hydrophobic fitting points matching the rigorous definition of hydrophobicity given by the MLP, Molecular Lipophilicity Potential, a fragmental molecular interaction field that relies on experimentally determined n-octanol/water partition coefficients ($log\ P_{o/w}$) [2]. MLP computation inside binding sites of protein crystal structures from the Astex Diverse dataset and the PDB bind database revealed that a significant number of points, considered as hydrophobic by GOLD, were actually polar. To examine the impact of our new tool, re-docking experiments were performed with and without the use of *MLP-filter*. Reliable docking results were obtained by using our in-house tool that, moreover, increased the quality of docking results in cases of non polar cavities, outperforming the standard GOLD docking approach.

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Computational Chemistry **CC 7**

How to thermostat coupled heat and mass transport in MD simulations and other challenges from the world of foods

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The kinetics of phase transitions is an important part of material science in the food field. It is well known that phase transitions involve a coupled heat and mass transfer problem. In recent years several methods, both equilibrium and non-equilibrium, have been proposed to tackle this problem. A critical discussion of these methods will be given. As all proposed methods show an inherent system size dependency we have developed a new non-equilibrium method. With this we probe the kinetic growth limit via implementation of a modification of the stochastic rescaling thermostat, where the system is sliced into independent temperature coupling groups. We prove that this approach effectively removes latent heat locally, yielding a reliable estimate of the maximum crystallization/melting rate. This set-up is also used to investigate the effect of additives on the crystallization process as a function of their size and concentration.

Computational Chemistry **CC 8**

Multi-scale modelling of solvatochromic shifts based on frozen-density embedding theory

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The solvatochromic shift of lowest absorption band of coumarin 153 in solvents of various polarity are evaluated using the frozen-density embedding theory based methods [1]. Instead of averaging the shift over statistical ensemble, the average electron density of the solvent, $< \rho_B(\vec{r}) >$ is used to evaluate the average effect of the environment on the excitation energy of the chromophore. In the calculation, $< \rho_B(\vec{r}) >$ is used as frozen-density, which is evaluated using the statistical-mechanical approach [2]. The small deviations between calculated and experimental solvatochromic shifts confirm the approximant for the bi-functional of the non-electrostatic component of the orbital-free embedding potential is adequate for chromophores interacted with the environment by non-covalent bonds. The qualitative analyses of the origin of solvatochromic shifts are made using the graphical representation of the orbital-free embedding potential [3].

The second group of results concerning absorption spectra of fluorenone in Zeolite L will also be presented [4].

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Computational Chemistry **CC 9**

Electron transport across a corannulene-SWCNT junction

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In the present work we evaluate the quantum conductance from first principles in molecular nanojunctions based on corannulene-based molecules linked to two Single Walled Carbon Nanotubes (SWCNT's) electrodes. The interest in these particular molecules stems from recent experimental findings[1] showing the possibility of tuning their optoelectronic properties by modifying the structure at the nanoscale in a controllable way. In order to explore the effect of such tuning on the quantum conductance, we have chosen four representative substituted molecular systems to be inserted between the electrodes. To calculate the coherent transport properties of the nanojunctions, we follow the Landauer approach[2] that relates the quantum conductance of the conductor to the scattering properties of the system through the expression: $C(\varepsilon) = \frac{2e^2}{h} T(\varepsilon)$.

The transport characteristic are then obtained through a real space implementation of the Landauer formula in terms of maximally localized Wannier functions using the WANT code[2].

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Computational Chemistry **CC 10**

Computaional methods for finding the ideal nitrogen fixation catalyst

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Nature successfully fixes dinitrogen via the nitrogenase enzymes, but attempts to mimic nature, creating a synthetic nitrogen fixation cycle, have proven challenging. The industrial Haber-Bosch process involves both high pressures and temperatures [1], but two catalyst systems have recently been reported, by Schrock and then by Nishibayashi *et al*., which convert dinitrogen to ammonia at ambient temperature and pressure [2]. These catalysts are, however, destroyed under reaction conditions after a limited turnover.
Theory has provided fundamental insight into the Schrock catalyst [3], and we now report progress [4] in the search for new catalyst systems that can fix dinitrogen as well as Schrock catalyst, but that shows improved stability. The $[Si(o\text{-}C_6H_4\text{-}P^iPr_3)_3]^-$ (SiP_3) ligand system [5] is described with density functional theory. We detail the performance of [Fe(SiP_3)] and hypothetical [Mo(SiP_3)] catalysts in the key steps of the Schrock-cycle, comparing them to the Schrock catalyst itself. We also look in greater detail at the NH_3/N_2 ligand exchange process and perform a full analysis of the possible pathways to determine the barrier to this crucial step in the catalytic cycle.

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Computational Chemistry **CC 11**

Oxygen and Proton Reduction by Metallocenes in Non-Aqueous Media

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Recent electrochemical measurements at liquid-liquid interface [1] have shown that decamethylferrocene is capable of reducing aqueous protons leading to the evolution of hydrogen, regarded as an ideal candidate for energy supply in a sustainable manner. Moreover, decamethylferrocene can reduce molecular oxygen to hydrogen peroxide, which is highly desirable compound for fuel cell applications. How changing the metal affects these important reactions? Is the propensity towards proton and O_2 reduction significantly increased or diminished? Density functional theory computations have been performed to shed light on the reduction of aqueous protons to hydrogen under anaerobic conditions, and the reduction of oxygen to hydrogen peroxide under aerobic conditions by osmocene and ruthenocene [2]. Characterization of the active species is performed in order to elucidate the reaction mechanisms that govern the proton and oxygen reduction reactions. Rationalization of the experimentally observed trends [3] is established providing a step towards understanding the structure-reactivity relationship for the metallocene catalytic systems.

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Computational Chemistry **CC 12**

Multiregional Localized Molecular Orbitals

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Localized molecular orbitals play an important role in computational chemistry for two reasons. They provide a conceptual link between quantum mechanical wave function and so-called chemical intuition referring to bonds, core electrons and lone pairs. Apart from this conceptual contribution, LMOs proved to be very useful in reduced scaling computational methods.
In this paper we present a multi-fragmentary extension of regional localized molecular orbitals (RLMO) [1]. A sequence of unitary transformation enables to localize orbitals on a predefined set of molecular fragments. Only the one-particle density matrix and the overlap matrix are needed in the computational scheme. This approach to localization is expected to be very efficient in linear-scaling fragmentation methods.

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Computational Chemistry **CC 13**

LpxC: insights into substrate binding and selectivity

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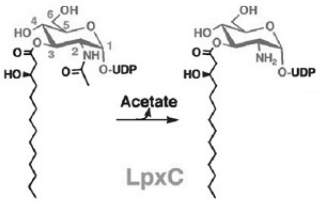
Lipid A constitutes the core of the complex lipopolysaccharide (LPS) molecules dominating the lipid composition of the external leaflet of Gram-negative bacteria outer membrane [1].
LpxC (UDP-(3-*O*-acyl)-GlcNAc deacetylase), a Zn^{2+}-dependent amidase, catalyzes the first committed step along lipid A biosynthetic pathway. Since its validation as an antibacterial drug target, several compounds have been reported to effectively inhibit LpxC activity and thus stop lipid A synthesis [2][3].
A model of the complex between LpxC and its natural substrate was reconstructed on the basis of the available X-ray and NMR structures. Molecular simulations were used to quantify species-specific and inhibitor-dependent LpxC conformational flexibility and to rationalize the enzyme's catalytic proficiency.



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Computational Chemistry **CC 14**

Theoretical study of NCO and COS hydrolysis over Al_2O_3 catalyst

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Hydrolyses are an important class of reactions in nature, which not only occur in liquid phase but also in heterogeneous gas phase reactions over solid catalysts. Two systems, in which catalytic hydrolyses are involved are the hydrolysis of isocyanic acid to ammonia in the selective catalytic reduction (SCR) of nitrogen oxides [1] and the hydrolysis of carbonyl sulphide, which results in the poisoning of methanation catalysts [2]. Both reactions can proceed over γ-Al_2O_3 as catalytic material. We tried to fully understand the mechanism of hydrolysis for both species by means of Density Functional Theory calculations (StoBe) with cluster model and non-local functional (RPBE) approach. For modelling the γ-Al_2O_3 catalyst an $Al_{15}O_{40}H_{35}$ cluster has been selected, which represents the (100) surface. Then the mechanism of the hydrolysis of isocyanic acid (HNCO) and carbonyl sulphide (COS) modeled on these clusters. Additionally, the theoretical studies have been compared with experimental data from DRIFTS and XAS investigations. In the most probable pathway, a water molecule attacks the –NCO and –COS groups, thereby forming carbamic acid and thiocarbonic acid, respectively, at the surface. In a further step those compounds are transformed to carbamate and thiocarbonic complexes, respectively. This leads finally to CO_2 desorption and NH_3 formation in case of isocyanic acid and to H_2S formation from carbonyl sulphide.

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Computational Chemistry **CC 15**

Ni_xPd_y nanoparticles stability at the γ-Al_2O_3 support: DFT studies

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Recently, surface modifications on a commercial Ni/Al_2O_3 catalyst during the production of methane from synthesis gas were investigated by *quasi in-situ* X-ray photoelectron spectroscopy (XPS) [1, 2]. In the present work we extended our DFT investigations to nickel-palladium nanoparticles, which has been also investigated also experimentally.

The Ni and Pd deposition and cluster growth phenomena on our home-made model catalyst samples (10 nm thick, polycrystalline γ-Al_2O_3 on Si(100)) were investigated experimentally by XPS and the molecular structure of the catalyst was investigated using Density Functional Theory calculations (StoBe) with cluster model and non-local functional (RPBE) approach. For the latter, $Al_{15}O_{40}H_{35}$ clusters have been selected representing the γ-Al_2O_3 (100) surface. Metal particles of different sizes were cut from a (100) surface and deposited on the $Al_{15}O_{40}H_{35}$ cluster in order to validate the deposition model determined by XPS.

Ni or Pd deposition on γ-Al_2O_3 follows a "modified" Stranski-Krastanov growth mode under the applied experimental conditions. The DFT results correspond well with the experimental data of the initial stage of metal deposition, where the formation of a partial metal monolayer is suggested.

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Computational Chemistry **CC 16**

Dephasing representation: defeating the efficiency of both quantum and classical simulations with semiclassics [1]

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Nowadays rigorous quantum mechanical (QM) calculations for many-particle systems remain out of reach, while classical (CL) simulations, although feasible, do not include QM effects at all. Semiclassical (SC) approximations take into account all QM effects through interferences of CL trajectories and, unlike full QM methods, are numerically affordable for complex systems even though challenging problems severely affects their numerical efficiency. We will describe an accurate SC approximation, called "dephasing representation" [2,3,4,5], which surprisingly is even *much faster* than the CL calculation.

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Computational Chemistry **CC 17**

Efficient use of accessibility in microRNA target prediction

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Considering accessibility of the 3'UTR is believed to increase the precision of microRNA target predictions. We show that, contrary to common belief, ranking by the hybridization energy or by the sum of the opening and hybridization energies, used in currently available algorithms, is not the most efficient way to rank predictions. Instead, we describe an algorithm which also considers only the accessible binding sites but which ranks predictions according to over-representation of the accessible seed matches [1]. When compared with experimentally validated and refuted targets in the fruit fly and human, our algorithm shows a remarkable improvement in precision while significantly reducing the computational cost in comparison with other free energy based methods. In the human genome, our algorithm has at least twice higher precision than other methods with their default parameters. In the fruit fly, we find five times more validated targets among the top five hundred predictions than other methods with their default parameters. The proposed method also allows combining the accessibility filter with a conservation filter using multiple sequence alignments [2]. Predictions in the human genome show that the combined filter increases precision more than either filter alone [3]. Moreover, it is shown that some conserved but non-functional sites can only be rejected by means of an accessibility cutoff.

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Computational Chemistry **CC 18**

Split-CAS and Direct-CI: A Combined Strategy to Enlarge the Orbital Space in Multiconfigurational Calculations

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Complete active space wave functions are constructed by variationally optimizing the expectation value of the energy with respect to the orbital and the Configuration Interaction parameters. The major limitation arises from the factorial scaling of the CI expansion with respect to the size of the active space. The associated system of secular equation is handled by simplified diagonalization techniques, e.g. Davidson algorithm. These technique rapidly reach their limit of applicability in terms of memory requirement. The aim of our research is to reduce the computational costs of big CASSCF calculations, by using the SplitCAS strategy [1]. Instead of reducing the size of the CI expansion, we retain the CAS ansatz, but separate it in two parts: a principal space (A) and an extended space (B), dim(A)<<dim(B). Only the principal space needs to be solved exactly (few thousands configurations), while the effect of the external space is treated perturbatively. The implementation of the perturbative correction requires considerable changes of the original Direct-CI algorithm. We will present here a new Direct-CI algorithm adapted to the SplitCAS approach.

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Computational Chemistry **CC 19**

Can Raman Optical Activity Discriminate Between Different Types of Protein β-Turns?

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On the basis of density-functional calculations, vibrational Raman optical activity (ROA) signatures are established which can be used to identify β-turns, an important secondary structure element in proteins. Several reliable signatures were identified [1] and related to other signatures proposed in the literature.
In addition, the possibility of predicting the extended amide III frequencies of oligopeptides such as β-turns using a simple model is investigated. The extended amide III region in vibrational spectra is particularly sensitive to changes in secondary structure. To investigate this sensitivity, we have performed density-functional calculations on the model system *N*-acetyl-L-alanine-*N*-methylamide, which have been analyzed using the concept of localized modes [2]. We study the dependence of the local-mode frequencies and coupling constants on the torsional angles ϕ and ψ. This enables us to set up a local-mode model for a better understanding of the structural sensitivity of the extended amide III region [3].
All vibrational spectra have been calculated with the program SNF [4] employing a modified version of TURBOMOLE which allows for computationally demanding ROA calculations on large model systems [5].

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Computational Chemistry **CC 20**

Thermodynamics of the monomerization of a Re(V) dithiolato dimer with imidazole-based ligands: A theoretical investigation

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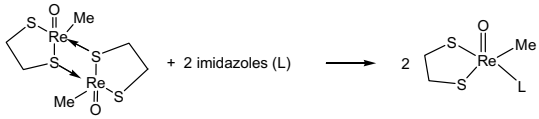
The thermodynamics of the monomerization of a Re(V) dithiolato dimer, {MeReO(edt)}$_2$ (edt = 1,2-ethanedithiolate) with imidazole-based ligands (imidazole, 1-methylimidazole, 1-ethylimidazole, indazole, benzimidazle and pyrazole) were investigated by DFT calculations in gas phase, benzene and acetone solution.



The effective core potential of Hay and Wadt with a double-ξ valence basis set (LANL2DZ) was chosen to describe Re. The 6-311G* basis set was used for other atoms. Geometries of complexes were fully optimized and to evaluate and ensure the optimized structures of the molecules, frequency calculations were carried out using analytical second derivatives. From thermochemistry results, the values of $\Delta H < 0$ and $\Delta S < 0$ for monomerization reactions were obtained which means the reactions are enthalpy-driven. The overall monomerization processes are thermodynamically more favorable for acetone and benzene solvent as compared with gas phase, and with increasing the basicity of ligands the free energy of the reactions is decreased.

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Computational Chemistry **CC 21**

Accelerating calculations of ultrafast time-resolved electronic spectra with various high order split-operator algorithms

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Calculations of ultrafast time-resolved electronic spectra require performing the quantum dynamics, i.e., solving the time-dependent Schrodinger equation. We explore how these demanding calculations can be accelerated by increasing the time step required for convergence of exact quantum simulations without sacrificing the accuracy [1]. For this purpose, we compared various split-operator methods [2] of the 1st to 4th order. Besides the usual 4th order algorithm with real coefficients we also considered an algorithm with complex coefficients and an algorithm using the gradient of the potential. Our results show that while the last two methods require fewer Fast Fourier Transforms at each step, the complex method diverges for dense spatial grids and the gradient method's order decreases to the 2nd order for sparse grids [1].

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Computational Chemistry **CC 22**

Semiclassical calculation of ultrafast time-resolved electronic spectra

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We investigate [1] the applicability of selected semiclassical methods based on the initial value representation [2] in combination with symplectic integrators for the computation of ultrafast time-resolved electronic spectra. Particular interest is devoted to the theoretical properties as well as numerical behaviour of *Frozen Gaussians Approximation* (FGA) and the *Heller-Hermann-Kluk-Kay* (HHKK) propagator, which have been shown to be applicable even in high dimensional systems [3] as opposed to standard quantum methods. Several applications in the field of spectroscopy [4] have been also reported. On particular examples, it is found that even the rather simple FGA can give reasonable prediction of the electronic spectra. It turns also out that the HHKK approach is numerically slightly hindered in the presence of chaotic behaviour; therefore we discuss possible improvements to this method such as trajectory filtering, modified sampling of the initial conditions and time averaging techniques [5]. Finally, comparisons are made with the cellularized versions of the FGA and HHKK algorithms, with possible generalizations [6] taken into account.

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Computational Chemistry **CC 23**

Four-Electron Reduction of O_2 by Tetrathiafulvalene

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The catalytic four electron reduction of O_2 into water is a mandatory step to the development of efficient fuel cells.[1] The most widely used catalysts are based on platinum, but the search for alternative biomimetic solutions circumventing the use of precious metal has been very active. Preliminary experiments suggest that the excellent electron donor properties of Tetrathiafulvalene (TTF) along with its ability to form assembled π-π-stacked structures could lead to the four-electron reduction reaction from oxygen to water in acidic medium.[2]

The present DFT study investigates the four-electron reduction reaction pathway of oxygen by TTF and identifies a set of assembled TTF structures that exhibit a variety of intermolecular interactions by π-π stacking, weak hydrogen bonding, and sulfur-sulfur interactions. To account for the weak dispersive forces caracteristic of these systems, standard functionals are combined with a density-dependent dispersion correction developed in our laboratory.[3] Geometries were optimized with the M06-2X functional designed and fitted to reproduce weak interactions.

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Computational Chemistry **CC 24**

Efficiency of Stochastic and Genetic Algorithms for Characterizing Molecules with Unique Bonding Patterns

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The computational quest for molecular candidates challenging conventional chemical bonding paradigms (e.g. molecular wheels, multicenter bonding) has attracted a great deal of attention over the last two decades. The viability of such systems is necessarily assessed through the characterization on the potential energy surface (PES) of the lowest energy form of the given chemical composition. Whereas dozens of search algorithms have been developed for this purpose, only a few are general and simple enough to become standard everyday procedures. The simple random search [1] and Genetic Algorithms (GA) [2] are among these: but how do these approaches compare on typical isomeric searches? We compared the performance of the two approaches for the exploration of the PES of prototype planar carbon-containing systems CB_6^{2-} [3] and C_2Al_4 [4]. We also discuss the potential advantages of using a low-cost semi-empircal method (e.g. PM6) in the pre-optimization step instead of B3LYP/3-21G.

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Computational Chemistry **CC 25**

Tree Monte Carlo

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The development of high performance computers makes more and more computing power available. To use this potential, novel algorithms have to be adopted that display increasing potential for parallelization. In the case of molecular simulations, the scalability of Molecular Dynamics (MD) is ultimately limited, and the step by step integration essentially serializes the procedure. Here, we present a Tree Monte Carlo (TMC) algorithm which allows for calculating many molecular configurations simultaneously. Using a speculative approach, various pathways, accounting for both rejectance and acceptance of proposed moves, can be computed in parallel. Key to this approach is the fact that generating configurations for the Monte Carlo algorithm is cheap and can be performed without computing forces [1]. The TMC procedure respects at least the sufficient balance condition [2], and in fact the sequence of used Monte Carlo moves is independent of the number of simultaneously computed tasks. The parallel efficiency of the TMC algorithm depends on the acceptance probabilities of the moves as well as the number of used computing units. The most important aspect in Monte Carlo algorithm is an efficient configurational change, which should be as huge as possible, but sufficiently small. For computational expensive models, like DFT, approximated potentials can be used to generate the configurational change.
Further efficiency gains will come through dynamic process termination and acceptance estimation. Finally, the algorithm is well suited to be implemented in a Fault Tolerant context, which might become essential on future architectures.

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Computational Chemistry **CC 26**

Ab Initio-based Electron Transfer Through π-Stacked Nucleobases

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A first-principles methodology has been implemented into the *ab inito* computational suite GAMESS for calculating the electronic coupling between donor and acceptor states of small biomolecular systems involved in electron transfer reactions. This method calculates the nonadiabatic electron transfer reaction rate from the electronic coupling, which is based on the calculation of the effective Hamiltonian from a Green's function operator.[1,2] The efficacy of this method and implementation are demonstrated on small model hydrocarbon and peptide donor-acceptor systems. This methodology is then applied to the study of electron transfer properties through various π-stacked nucleic acid structures to investigate the relationship between nucleobase sequence, structural orientation, and predicted charge transfer reactivity with high accuracy quantum mechanical methods.

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Computational Chemistry **CC 27**

Protein Structure Prediction Using Genetic Algorithms

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Protein structure predictions, which aim to elucidate the complete conformation of a protein from sequence information, remain to be a complex multivariate problem in addition to being computationally intensive. Here we present a 2-level genetic algorithm (GA) to effectively partition the search into backbone and side chain conformational searches. Additionally, this allows the utilization of structural statistical information for both domains in an additive or selective fashion in stages.

The first level GA optimizes the Phi and Psi angle of the protein backbone. Each conformation (chromosome) of the backbone has an associated (sub)optimal side chain conformation that is searched using the 2nd level GA. The search proceeds to find a near optimal solution to the prediction problem and is then fine tuned using a molecular dynamics study.

Computational Chemistry **CC 28**

Automatic Generation and Refinement of Potential Energy Surfaces using IMLS Fits of different order

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The study of molecular reactivity requires a detailed knowledge of the potential energy surface (PES) of the molecular system [1]. We present a new method for the automatic generation of new surfaces and the refinement of existing PES employing IMLS (Interpolating Moving Least Squares [2]) fits of different order [3].
The method is based on finding the minimum of the negative squared difference between two surfaces generated by IMLS fits of different order as described by Dawes et al. [4]. The least defined point, which should be added next to improve the fit, is expected to give the global minimum on this difference surface. In contrast to the work of Dawes et al. [4], here, the search for the global minimum is performed applying a simulated annealing procedure, which is very efficient and therefore leads to a fast convergence of the refinement process. The efficiency of this new algorithm is demonstrated at different model cases. Potential applications in the area of molecular reacitivity studies, especially in the framework of haptic quantum chemistry [5], are discussed as well.

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Computational Chemistry **CC 29**

CASCI-Type Wave Function Expansion for Very Large Active Spaces

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In quantum chemistry, electronic wave functions are usually represented as configuration-interaction (CI) expansions. However, the dimension of this many-particle basis grows binomially with the number of orbitals and electrons present in the molecules under study.
We present an efficient procedure to construct CI-type electronic wave functions of molecular systems that require very large active spaces for a qualitatively correct description of their electronic structure [1]. Our procedure is based on the density-matrix renormalization group (DMRG) algorithm [2] that provides the necessary information in terms of the eigenstates of the reduced density matrices. DMRG can handle much larger active spaces without truncating the complete N-particle Hilbert space which allows one to obtain qualitatively correct wave functions and energies even for very difficult electronic structures [3].
Compared to the purely numerical DMRG optimization scheme, an analytic wave function in terms of a CI expansion provides deeper insights into the electronic structure of the corresponding molecules under study and allows a better understanding of the convergence behavior of the DMRG algorithm. Because of the binomial scaling of the Hilbert space with the size of the active space, a sophisticated Monte Carlo sampling routine has been implemented that constructs an accurate representation of the electronic wave function.

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Computational Chemistry **CC 30**

Embedding vs supermolecular strategies in evaluating the hydrogen-bonding-induced shifts of excitation energies

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Shifts in the $\pi \rightarrow \pi^*$ excitation energy of cis-7-hydroxyquinoline, induced by hydrogen bonding with small molecules, obtained with the frozen-density embedding theory (FDET)[1], are compared with the results of the high-level equation-of-motion coupled-cluster (EOMCC) calculations with singles, doubles, and completely renormalized triples [2], corrected to restore the property of size intensivity, which provide the reference *ab initio* data, the supermolecular time-dependent density functional theory (TDDFT) calculations, and the available experimental data. Unlike in the supermolecular EOMCC and TDDFT cases, where each complexation-induced spectral shift is evaluated by performing two separate calculations, one for the complex and another one for the isolated chromophore, the FDET shifts are evaluated as the differences of the excitation energies determined for the same many-electron system, representing the chromophore fragment with two different effective potentials. It is demonstrated that the spectral shifts resulting from the FDET calculations employing nonrelaxed environment densities are in excellent agreement with the reference *ab initio* data, whereas the supermolecular TDDFT results are in disagreement with the reference [3,4].

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Computational Chemistry **CC 31**

Low Temperature Gas Phase Structures and IR Spectra of Amino Acids and Polypeptides Predicted by DFT Methods

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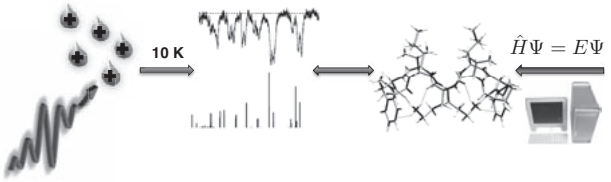

DFT methods are important tools for predictions of electronic structure and energetics of biologically and pharmaceutically relevant molecules providing an interpretation of spectroscopic experiments at the atomistic level.
In our initial benchmarking studies on bare and microsolvated protonated tryptophan we have assessed the performance of various popular DFT methods to predict the lowest energy structure associated with the high-resolution experimental IR spectrum at low temperature. For the low-energy structures, the harmonic vibrational frequencies were calculated and compared with high resolution experimental IR spectra on the cold ions. With the adequate methodology in place we have solved the 3D structure of a decacpeptide, gramicidin S, isolated in gas phase, by matching our calculated vibrational frequencies to the experimental cold ion IR spectrum at 10 K [1]. To our knowledge gramicidin S is the largest molecule for which the accurate low temperature gas phase structure has ever been determined. At the same time it is of great pharmaceutical relevancy due to its antibiotic activity. The structure presented here may serve as a starting point for the rational design of gramicidin S analogs.

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Computational Chemistry **CC 32**

Applications of the Molecular Lipophilicity Potential in AutoDock

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The molecular lipophilicity potential (MLP) [1] is a fragment-based molecular interaction field that has found broad applications in computational chemistry and ligand-based drug design. It is nowadays routinely used for 3D-QSAR. Further enhancements showed that the MLP can also successfully be applied in target-based methods. A simple MLP-approved adjustment of the definition of protein cavity hydrophobic areas allowed an overall gain of GOLD docking accuracy [2].

The open source docking tool AutoDock [3] uses pre-calculated grid maps that contain energy information about various types of possible interaction potentials. An embedment of a new lipophilicity term into the generation process of these maps might help improve the overall docking performance, especially on hydrophobic targets. Recent simulations influencing apolar (carbon) as well as polar (H-bond donor and acceptor) grid maps in respect to the MLP showed promising perspectives. Furthermore, additional information given by the molecular hydrogen-bonding potentials (MHBPs) [4], is also under study to gain a more accurate description of polar binding sites.

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Computational Chemistry **CC 33**

Mössbauer spectroscopy for heavy elements

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Mössbauer (MB) spectroscopy is a sensitive spectroscopic technique, that probes tiny changes in the energy levels of Mössbauer active nuclei. The electron density at the nucleus (contact density) is strongly related to the calculation of the isomer shift in MB spectroscopy. For heavy nuclei, the contact density is affected by relativistic effects, i.e., its calculation in a non-relativistic framework employing the point charge approximation for the atomic nucleus leads to substantial errors. A more elaborate description of the contact density is obtained in a fully relativistic framework, where the nucleus is described by a finite nuclear charge distribution and the contact density thus takes finite values. In our benchmark study [1], we investigate the contact density for the series HgF_n ($n = 1, 2, 4$) with respect to the neutral atom in the framework of scalar-relativistic one-component, two- and four-component relativistic theory. Various density functionals were tested and compared to highly accurate finite-field four-component CCSD(T) calculations. It is found that DFT is not able to recover the non-monotonous decrease in the contact density, that can be attributed to changes in the population and the polarization of the $6s_{1/2}$-orbital of mercury.

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Computational Chemistry **CC 34**

A Generalized-Gradient Approximation Exchange Hole Model for Dispersion Coefficients

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Density functional approximations fail to provide a consistent description of weak molecular interactions arising from small electron density overlaps. A simple remedy to correct for the missing interactions is to add *a posteriori* an attractive energy term summed over all atom pairs in the system. For general applicability, the dispersion coefficients used in such corrections should depend on the electron density, with no increase in the computational cost. We present a simple method for computing accurate density-dependent dispersion coefficients. The model, called XDM(sC-BR), relies on a generalized gradient-type approximation to Becke and Johnson's exchange hole dipole moment formalism.[1] Our most cost-effective variant gives a mean absolute error in the C_6 coefficients for 90 complexes below 10%.[2] These dispersion coefficients are combined with our density dependent damping function.[3] The inclusion of the missing long-range van der Waals interactions in density functionals using the derived coefficients leads to highly accurate typical noncovalent interaction energies. The dominant classical Hirshfeld partitioning BLYP-dDXDM(sC-BR) gives, for instance, a mean absolute deviation of only 0.14 kcal mol^{-1} for the S22 training set.
We discuss general improvements obtained for standard density functionals such as PBE, BLYP and B3LYP and present results for a broad variety of benchmark sets featuring both, intra- and intermolecular weak interactions.

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Computational Chemistry **CC 35**

Modeling of Anion-π Interactions of Substituted Naphthalenediimides : Structure and Function

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Contrary to the popular and widespread cation-π interactions, applications of the anion-π counterpart are quite rare. The question whether anion-π interactions could be used in supramolecular context to create significant function such as transmembrane transport, sensing or organocatalysis is attractive but also challenging.[1]

In this contribution is described DFT modeling for series of anion-π complexes. Noteworthy binding energies between naphthalenediimides (NDIs) and several types of anions were also computed. The experimentally observed anion transport selectivity was in addition confirmed by theory. Anion-π interactions were systematically modulated during the modeling by NDI core substitutions as well as by structural variations of N-aromatic moieties.[2] The computational simulations together with tandem mass spectroscopy demonstrated that anion-π interactions account for function.[3] The molecular modeling was also used to design appropriate substrates benefiting from enhanced halogen bond bindings.

The anion-π interactions have the potential to catalyze organic reactions *via* the stabilization of anionic transition states. This concept was probed by DFT simulations of organocatalysis for hydrogenation transfer, which will also be discussed in this contribution.

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Computational Chemistry **CC 36**

Ligand Binding Study of Carbonic Anhydrase 2

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Carbonic anhydrases (CAs) are ubiquitous metalloenzymes that catalyze the reversible hydration of carbon dioxide with remarkable efficiency. CAs have been the focus of many biophysical studies of protein-ligand interactions. Today, at least 25 clinically used drugs are known to display pronounced CA inhibitory properties [1]. To design a protein with particular properties, understanding the influence of residues is crucial. In this work we report on a computational strategy that allows predicting strong inhibitors and potentially beneficial mutations of the protein. The active site of most CAs contains a Zn(His)3 which is essential for catalysis. The carbonic anhydrase protein is ideal for the design of potent and selective inhibitors.
We report a Molecular Mechanics Generalized Born Solvent Approximation (MMGBSA [2]) study comparing the binding free energy for 18 sulfonamides. Using this method, not only the total binding free energy, but also the influence of a particular residue can be examined. Thus the effect of mutations on key residues on the binding can be determined. To validate the simulations, we compare the results with published biophysical data as well as with a simulation using QM/MM simulations with the Self-consistent charge Density-Functional Tight-Binding (SCCDFTB [3]) method. Results show a high (up to R = 0.90) correlation between the predicted values and biophysical data.

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Computational Chemistry **CC 37**

QUANTIFICATION OF INTRAMOLECULAR CHARGE TRANSFER EFFECTS BY BLOCK LOCALIZED WAVE FUNCTION

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The extent of electronic delocalization (i.e. intramolecular charge transfer) can be quantified by comparing the energy of absolutely localized states to that of the canonical (ground state) state. Unfortunately, the construction of diabatic states issued from Valence Bond (VB) theory is computationally very expensive due to the non-orthogonality of the orbitals. Alternatively, the Block Localized Wave function approach, developed by Mo and al. [1] incorporates the physical intuition of VB at the computational cost of Hartree-Fock or Kohn-Sham density functional theory. The electrons are divided into several blocks, each expanded on a restricted number of atomic orbitals. The doubly occupied orbitals are orthogonal within one block (like canonical MOs), but non-orthogonal between different blocks and localized in terms of their basis function expansion (like VB group orbitals). The restriction imposed on the MO expansion thus enables the selective suppression of orbital interactions. The orbital expansion coefficients of the diabatic state are obtained by a self-consistent optimization. A number of algorithms can be used to optimize these BLW orbitals. We previously implemented in Dalton an algorithm proposed by Gianinetti et al. [2] to analyze the extent of charge transfer in cyclic systems [3,4]. In order to extend the scope of applications to a broader variety of molecules, we here present the implementation and applications of a more general algorithm [5].

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Computational Chemistry **CC 38**

Molecular Dynamics Simulation of Nitric Oxide in Myoglobin

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Myoglobin (Mb) is a single-chain globular protein containing a heme group and is found in muscle tissue of vertebrates in general. While Mb has been known as a dioxygen storage protein, Mb has also the capability to catalyze reactions involving small molecules by concentrating and orienting diatomic molecules such as NO, CO, and O_2. [1] From previous studies, it has been discovered that there are multiple cavities inside Mb and that small ligand molecules can migrate between various cavities. [1-2]
Molecular dynamics (MD) simulations of proteins can provide detailed information that cannot be obtained directly from the experiments, and are considered as an indispensable complement to the experimental methods. In this work, we carried out the classical MD simulations of myoglobin with a nitric oxide (NO) molecule inside it and investigated the properties and dynamics of the system in detail. While the electrostatic interactions are commonly described by point charges on atoms in the classical MD simulations, the accuracy of the model can be improved by including higher multipole moments (MTPs) in addition to point charges. Due to the unpaired HOMO electron of NO, the molecule does not have the cylindrical symmetry around the molecular axis, which necessitates more sophisticated treatment for MTPs on NO. We used modified CHARMM code with MTPs on the NO molecule up to quadrupole moment in order to treat the NO molecule more accurately in the classical MD simulations of NO-containing myoglobin.

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Computational Chemistry **CC 39**

Investigation of *h*-BN/Rh(111) Nanomesh Interaction with Water and Phthalocyanine

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The hexagonal boron nitride nanomesh is a corrugated structure with a periodicity of 3.22 nm, which is formed self-assembly by decomposition of borazine on a clean Rh(111) surface at high temperature[1]. Small water clusters[2], nano-ice crystals[3] and other organic molecules have been observed trapped in the pore of the nanomesh, which makes the nanomesh an interesting template for self-assembly of ordered and distant molecule arrays.

Our DFT model of the nanomesh reproduces the structural corrugation and modulation of the electrostatic potential. Moreover, the STM topography and projected DOS are also consistent with the experimental ones. Hence, we employ this model to better understand structural and electronic properties of molecular systems adsorbed on the nanomesh, thus contributing substantially to the interpretation of the experiment. In particular, we could assign the most probable structure of the nano-ice crystal observed by experimental STM, by comparing different water lattices and the related distribution of dipole moments. We also address open questions about optimal adsorption site, orientation, and mobility of organic molecules, like phthalocyanine, deposited on the nanomesh.

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Computational Chemistry **CC 40**

Molecular Dynamics of MbNO – differences in heme response to binding and release of NO.

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Myoglobin (Mb) is the one of the most intensively studied heme protein over the last two decades. Due to its biological function related to storing and releasing oxygen in muscle tissue, as well as to its relatively small size it has been chosen as a representative system to study binding of oxygen and other diatomic molecules to the heme, and studying associated protein response. Although binding of diatomic ligands is one of the most fundamental processes occurring in living systems, its nature is still not well understood. The progress in ultrafast spectroscopic techniques brought a new insights about structural changes on the sub-picosecond scale. Experimental findings alone, however, are not able to explain the complex and heterogenous dynamics. Therefore molecular dynamics (MD) simulations are the method of choice

Our present investigation is focused on MbNO. In the light of recent experimental findings[1] we investigate at atomistic level the process of nitric oxide binding to the heme in myoglobin, with aim of understanding causes and differences in the time scales of instantaneous heme planar-to-domed transition, and longer reverse process related to NO dissociation and rebinding, respectively.

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Computational Chemistry **CC 41**

Non-empirical crystal structure determination of the complex PEG-$AgNO_3$ using Rietveld refinement and Monte Carlo simulation.

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The determination of the crystal structure from X-ray powder diffraction pattern is a major scientific challenge. A first attempt to solve a powder diffraction was estabilished since 1967. [1] The methodology [2] evolved since the Rietveld refinement is coupled with a Monte Carlo method in order to determinate the molecular structure.
In the present work, the molecular structure of PEG-$AgNO_3$ (PEG stands for Polyethylene glycol) is determined from powder X-ray diffraction using Monte Carlo method. The approach is to find out an adequate crystal structure starting model rather than extracting the structural information from the diffraction pattern. Then, a Riedveld refinement is developed by fitting the calculated theoretical diffraction pattern to the measured experimental one.
The principal problem of this approach is to obtain a sufficiently good starting structure model. Two concepts were investigated: (a) Replace the silver by potassium atoms, the crystal structure of which has been previously determined [3], and (b) observe the behavior of the complex while the ligand is modified by increasing the amount of ethoxy group within the PEG cluster, the crystal structures of which have been available.
The results corresponding to each concept are particularly similar and constitute a first model for the crystal structure of the PEG-$AgNO_3$ complex.

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Computational Chemistry **CC 42**

On binding and reactivity of potent covalent inhibitors of fatty acide amide hydrolase

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Covalent inhibitors have gained renewed interest in the drug discovery community because of recent effective drugs that function through a covalent mechanism. In this study, we investigated the mode of action of covalent inhibitors of the membrane-bound fatty acid amide hydrolase (FAAH) enzyme, which is a promising target for drug discovery in the field of pain and inflammation [1],[2]. Based on crystallographic data, we built a realistic model system of FAAH bound to the membrane to perform classical molecular dynamics (MD) and quantum mechanics/molecular mechanics (QM/MM) simulations [3]. We investigated both binding and reactivity of some representative FAAH inhibitors, which have been used to generate clinical candidates. These lead compounds were also compared with the main FAAH endogenous substrate, i.e. anandamide.
Overall, our goal is to improve the understanding of the mode of action of covalent FAAH inhibitors. This could help in the rational design of new and better compounds.

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Computational Chemistry **CC 43**

Calculation of $[GdDOTA \cdot (H_2O)]^-$ Zero Field Splitting with LFDFT using an embedding potential

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Paramagnetic Gd(III) induces a strong NMR-relaxation enhancement of neighboring water protons [1]. For better understanding the spin relaxation of Gd(III) ions in solution, the zero field splitting (ZFS) plays an important role determinating the former. [2]. With the peculiar stereochemical properties for the macrocyclic ligand DOTA (1,4,7,10-tetraaza-1,4,7,10-tetrakis (carboxymethyl) cyclododecane) [3], $[GdDOTA \cdot (H_2O)]^-$ is even one of the most relevant contrast agents for MRI [3].
'The Magnetic and spectroscopic properties of the lanthanide ions depend on the f electron structure, which is generally understood in the framework of a model where the f orbitals are considered shielded from the chemical environment.' [1] The description of the multiplet structure and energies of states in this given basis of f spinors are obtained with the ligand field density functional theory (LF-DFT) [4]. This method has already been adapted to a smaller Gd(III) system, $Gd(H_2O)_8]^{3+}$ [1], in the present work we apply it for the calculation of the ZFS of $[GdDOTA \cdot (H_2O)]^-$, using an embedding potential to describe the ligand influence in the DFT calculations.

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Computational Chemistry **CC 44**

CO transfer between Fe of heme and Cu_B in cytochrome c oxidase

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Cytochrome c oxidase (CcO) is a protein involved in catalysis of the terminal step in cellular respiration in mitochondria or bacteria, which is a transfer of four electrons from cytochrome c to dioxygen [1].In fact, the cytochrome heme a_3 and Cu_B form a binuclear center that is the site of oxygen reduction. In contrast to O_2, CO forms a stable complex with enzyme. Due to a greater affinity of CO for Cu_B than for Fe(II) of heme a_3, CO binds to Cu_B when Fe-CO bond is broken. There are several mechanisms for the transfer of CO from Fe(II) to Cu_B: elongation of Fe-CO followed by rotation, by forming intermediate Cu_B-OC state or by forming free CO. To figure out the mechanism, potential energy surfaces (PES) have been build based on DFT calculations, B3LYP functional and LANL2DZ (for Cu and Fe) and 6-31g basis sets have been used. The effective potential has been build based on the PES. Both three-point fluctuating charge model [3], that reproduces accurately the dipole and quadrupole moments, and standard point charge model of CO have been used. A three-point fluctuating charge model for CO is thus developed and implemented by the group in CHARMM. MD simulations of CO are studied with different models. Dynamics of CO bound and unbound to Fe of heme is analyzed in detail.

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Computational Chemistry **CC 45**

Mechanistic Insights for the Retroviral Integrase-DNA assembly

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Retroviral integrase (RI) binds viral DNA strands and fuses them into the chromosomal DNA of the host cell. It has been therefore a preferential target for HIV-1 drug development. RI integration and inhibition mechanisms were however largely unknown, till the recent resolution of the integrase-viral DNA complex structure from the prototype foamy virus (PFV) [1]. This structure finally unveils the general structural architecture promoting viral integration, and will pave the way for a rational development of improved HIV RI inhibitors [2][3].

In this study, we investigate the reaction mechanism leading to the formation of the RI-DNA complex using quantum mechanics/molecular mechanics (QM/MM) simulations. The structural and kinetic characterization of this initial step of DNA integration will provide useful insights for the development and optimization of new potent inhibitors.

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Computational Chemistry **CC 46**

Oxygen Coordination to the Active Site of Hmd in Relation to [FeFe] Hydrogenase

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Hydrogenases are enzymes which catalyze the reversible oxidation and formation of molecular hydrogen. The technical application of [FeFe] hydrogenase, the class of enzymes that shows the highest catalytic H_2 formation activity, is limited by its high O_2-sensitivity. One postulated mechanism for the dioxygen induced inhibition is triggered by O_2 coordination to the active site [1]. In sharp contrast the H_2 oxidizing mono-iron hydrogenase (Hmd) is not irreversibly inhibited by O_2.
Here we present a study on energetic differences in oxygen coordination to cluster models of the active sites of Hmd and [FeFe] hydrogenase as obtained from DFT calculations. Whereas O_2 coordination is clearly exothermic for [FeFe] hydrogenase, it is endothermic for Hmd [2]. By application of a recently proposed unifying concept to structurally and electronically relate both active sites [3] we obtain an inversion in O_2 affinity by mutual first-shell ligand exchange. In this context a CN^- to CO ligand exchange reveals the largest impact on coordination energy [2]. Furthermore the effect of this exchange on the stability of intermediates and reaction barriers of the postulated regular catalytic cycles (i.e. hydrogen formation/oxidation) is investigated. The results may indicate why both enzymes are in need for different mechanistic pathways and why they exhibit different reactivity.

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Computational Chemistry **CC 47**

Study of Thorium salts in water by Molecular Dynamics.

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The hydration of actinides is a topic that attracts the attention of many chemists, as this process is of relevance to environmental problems. Th(IV) is the "first" actionoid cation and it can form highly coordinated aquacations. Early XAS experiments suggested a coordination number of 10 ± 1 in HClO4. Recently, comparing crystal and liquid structures of Th(IV) indicated that in presence of Br- a homoplectic tenfold coordinated aqua-ion was proposed.

We present the results of a simulation study of Th(IV) in water by employing different force fields. (1) NEMO type potentials was developed for systems composed of Th(IV), Br^-/Cl^- and water as recently done for Ln3+[1]; (2) a simpler polarisable force field based on ionic radii has been also developed to investigate the dynamical behavior of this system, in a fashion similar to the one employed to study Ln3+ hydration [2]. By combining these methods we obtain results in good agreement with available EXAFS data [3], and we propose an approach that can be transferable to other related systems for which little experimental data are available.

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Computational Chemistry **CC 48**

How Can Reaction Barriers Dictate Ground State Properties?

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Our laboratory has recently introduced a quantum chemical approach enabling the direct probing and tuning of electron delocalization effects on molecular response properties.[1] The proposed methodology first constructs a specific resonance (i.e. Lewis) structure, in which conjugative interactions are "disabled" by using the simplest variant of valence bond theory that is the block-localized wavefunction method.[2] The approach defines the intermediate electron-localized state self-consistently at the density functional theory level. Computations of the molecular response properties are performed on the standard (delocalized) structures and those with "non-interacting" (localized) double bonds. Illustrative applications served to clarify abnormal chemical shifts of π-conjugated systems and solve long-standing organic chemistry problems.[1]
We now demonstrate that the ground state properties (e.g. $^1J_{cc}$-coupling constant) of a series of substituted semibullvalenes fully correlate with the activation barrier of their respective Cope rearrangement. In other words, our analysis is supportive of a fascinating picture that is the fingerprint of the transition state in the ground state, which enables the direct estimation of kinetic parameters from the ground state properties. This electronic phenomenon, that is impossible to demonstrate experimentally[3], has been first hypothesized and demonstrated for other pericyclic reactions (e.g. Diels-Alder).[1b]

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