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Computational Chemistry **121**

Redox Potential and Metabolic Stability: Development of High Throughput Assays for Early Compound Profiling

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In recent decades pharmaceutical drug discovery and development has been challenged by identifying efficacious and safe drugs. Among others, extensive hepatic metabolism has been cited as one common problem partly associated with failures in early drug discovery and development. The CYP450 superfamily with its most important member CYP3A4 is responsible for most oxidative degradations [1, 2] so these molecules being rapidly and extensively metabolized are defined as compounds with low metabolic stability.

Standard early metabolic stability determinations are biological based mainly focusing on the degradation of drugs by microsomal or hepatic cell preparations. Usually these assays only deliver information on the rate of metabolism by the determination of the drug disappearance. A larger focus on structural aspects of drugs candidates could probably improve understanding of metabolic degradation processes and structure-effect relationships.

Therefore, the aim of our study was the development of a fast and easy profiling system, allowing improvement of the understanding of metabolic processes at the structural/compound level. This aim has been met by an electrochemically based approach which allows the identification of compounds/compound classes exhibiting a high probability of metabolic instability and phase-I metabolism processes.

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Computational Chemistry **122**

Adsorption of Isocyanic Acid and Water over the TiO_2 (101) and γ-Al_2O_3 (100) Surfaces: Theoretical Modelling of Catalyst Behaviour

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The adsorption of isocyanic acid (HNCO) and water was studied on the TiO_2 anatase (101) [1,2] and as well on the γ-Al_2O_3 (100) surface [3] using the ab-initio density functional theory (DFT) method with a cluster model. The objective of our research was to clarify the mechanism of the heterogeneous hydrolysis of HNCO. The $Ti_8O_{28}H_{24}$ cluster for the TiO_2 (101) surface and $Al_{11}O_{30}H_{27}$ cluster for the γ-Al_2O_3 (100) surface were used in further adsorption studies. The electronic structure of all clusters was calculated by DFT methods (StoBe code) using generalized gradient corrected functionals according to Perdew, Burke, and Ernzerhof (RPBE). Detailed analysis of the electronic structure in the clusters were carried out using Mulliken populations and Mayer bond order indices. The theoretical calculations show that isocyanic acid is adsorbed on both TiO_2 and Al_2O_3, involving surface O(x)-M(5) (x=2,3; M=Ti, Al) couples. Dissociative as well as molecular adsorption of HNCO and H_2O were found to be feasible, but their role in hydrolysis of isocyanic acid strongly depends on the availability of water in particular reaction steps. The dissociative adsorption of HNCO is energetically more favorable on both titania and alumina as well as competitive to water adsorption, supporting our initial assumption that the reaction mechanisms are very similar on both materials.

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Computational Chemistry **123**

Modelling the sorption dynamics of hydrogen storage materials using a reactive force field, ReaxFF

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In this work we are developing a reactive force field($ReaxFF_{NaAlH4}$)[1] to study the structural and dynamical details of hydrogen absorption/desorption processes in $NaAlH_4$ system. We have already sufficiently parameterized $ReaxFF_{NaH}$[2] to adequately describe H_2 desorption process in NaH. Parameterization of the reactive force field for NaH is done using density functional theory (DFT) data. Parameterizations of the energy expressions in $ReaxFF_{NaH}$ were done by fitting into the training set the *ab initio* derived equations of state (EoS) of pure Na and NaH condensed phases, reaction energies and bond dissociation profiles on small finite clusters. Phase transformations/crystal modifications in both Na and NaH systems during desorption process was accounted for by adding the high pressure phases of Na and NaH, in addition to the groundstate phases, to the quantum calculations.

The parameterized force field, $ReaxFF_{NaH}$, is used to study the dynamics governing hydrogen desorption in NaH. During the abstraction process of surface molecular hydrogen charge transfer is found to be well described by the parameterized force field. A molecular dynamics run is done, which shows that a clear signature of hydrogen desorption is the fall in potential energy surface during heating.

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Computational Chemistry **124**

New non-empirical approximation to the Orbital-Free Effective Embedding Potential

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The Orbital-Free Effective Embedding Potential $v_{eff}^{KSCED}[\rho_A,\rho_B]$ is used in the large multiscale simulations of molecular complexes in the condensed matter (see for instance [1]). One of the crucial components of the $v_{eff}^{KSCED}[\rho_A,\rho_B]$ in one electron equations for embedded orbitals (see eq. 20-21 in [2]) is the term $v_t[\rho_{A,}\rho_B]$ arising from the non-additivity of the kinetic energy. In present work, the new approximation for $v_t[\rho_{A,}\rho_B]$ obeying the exact limit in the vicinity of the nuclei of the environment is proposed[3]. To validate the adequacy of the new potential, the test set comprising charged, polar and non-polar molecules has been chosen. The new approximation significantly improves the results in the case where the charged species are involved in the interaction. For the neutral complexes the improvement is less significant. The influence of the new approximation to $v_t[\rho_{A,}\rho_B]$ on the excitation energies of the embedded organic chromophores and the f-orbital levels of the lanthanides is also discussed.

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Computational Chemistry **125**

Modern Semiempirical Molecular Orbital Methods for Condensed Phase Systems.

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Semiempirical (SE) molecular orbital methods have a long history that goes back to the 1930s when the first germs of the SE approximations appeared in treating π electrons within the context of Hückel theory. The development of new SE methods, their improvement and application to larger and more complex systems has continued throughout the years [1,2] with important achievements from the computational community at the University of Zurich [3]. Although the application of first–principles methods to system of several hundreds of atoms can be considered an established practice nowadays, there is still a need for SE Hamiltonians for the treatment of problems beyond the capabilities of *ab initio* or density functional theory methods. The availability of recent accurate parameterizations [2] and the high computational efficiency (on average 3 orders of magnitude faster than corresponding DFT calculations) make the Semiempirical framework the perfect tool to explore and characterize chemical processes. One of the main limitations for the application of SE methods to condensed phase systems is the lack of a correct treatment of the long–range coulomb interactions. In this talk will be presented an effective "Semiempirical consistent" extension to periodic systems, achieved exploiting a multipolar Ewald summation scheme [4]. The possibility of treating correctly condensed phase systems allows the use of Semiempirical methods in multiple time-step (SE/DFT) integrations schemes: preliminary results will be shown.

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Computational Chemistry **126**

Reaching the Highest Covalent Bond Multiplicity: a Theoretical and Experimental Evidence of Newly Identified Di-Uranium Compounds

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The number of electron pairs that occupies the region between two atoms determines the multiplicity of a chemical bond. Until the early sixties, the triple bond of N_2 was assumed to be the largest multiple bond. Afterwards, experimental evidence has shown the formation of quadrupole bonds in transition metal compounds[1]. More recently, highly accurate theoretical works have helped to assess in a more systematic way the concept of multiple bond throughout the whole periodic table[2]. A further challenge was introduced when studying the chemistry of actinides that have the f shell available to form bonds. The theoretical existence of the quintuple bond of the U_2 molecule was predicted[3], but no experimental evidence had confirmed its existence.

In this new work, we attempt to apply the principle of quantum mechanics at very high level of accuracy using CASSCF/CASPT2 method to predict newly multiple bonded actinide species that can be isolated experimentally by means of laser ablated spectroscopy. In particular, the IR spectrum based on the reaction between Uranium and molecular Fluorine has been interpreted and gives enough evidence of the formation of novel dimers like U_2F_2, U_2F_4 and U_2F_6 [4].

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Computational Chemistry **127**

Toward efficient wavefunction based linear scaling energy minimization

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We will present an efficient direct energy functional minimization algorithm for electronic structure theory [1]. The technique provides a computationally very efficient tool that requires only few matrix multiplications per self-consistent-field iteration. We propose to exploit the invariance property of the total energy, through unitary transform, to generate "on the fly" sparse wavefunction. To achieve this goal, we propose the use of a sparseness function based on the l1-norm [2]. Sparsity of the wavefunction will be discussed for some large systems.

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Computational Chemistry **128**

Selective Calculation of High-Intensity Vibrations in Molecular Resonance Raman Spectra

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We present an intensity-driven approach for the selective calculation of vibrational modes in molecular resonance Raman spectra [1]. The method exploits the ideas of the mode-tracking algorithm [2] for the calculation of pre-selected molecular vibrations and of Heller's gradient approximation [3] for the estimation of resonance Raman intensities. The gradient approximation allows to construct a basis vector for the subspace iteration carried out in the mode-tracking claculation which corresponds to an artificial collective motion of the molecule that contains the entire intensity in the resonance Raman spectrum. Subsequently, the algorithm generates new basis vectors from which normal mode guesses are constructed. It is then possible to provide estimates for (i) the accuracy of the approximations obtained for the normal modes, and (ii) the intensity of these modes in the final resonance Raman spectrum. This approach opens up the way to resonance Raman calculations for protein models.

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Computational Chemistry **129**

First-Principles Investigation of the Schrock Mechanism of Dinitrogen Reduction

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The reduction of dinitrogen to ammonia is a very important reaction both for living organisms and the chemical industry. In nature, reduction is performed at ambient conditions employing nitrogenases as efficient catalysts. In industry, reduction is normally performed using the Haber–Bosch process at elevated pressure and temperature. For decades, a more elegant way of reducing dinitrogen has been much sought-after. Recently, Schrock et al. synthesized several well defined mononuclear molybdenum complexes that are capable of catalytically reducing dinitrogen to ammonia. It turned out that efficient catalysis can only be achieved with very bulky ligands like $HIPTN_3N$ [1].

We report on our detailed investigations of the catalytic cycle employing density functional methods [2–4]. We explicitly take into account the full $HIPTN_3N$ ligand without approximating it by model systems. It is demonstrated that the nature of the substituents does have a profound influence on the reaction energies. A mechanistic study of the NH_3/N_2 exchange has been carried out [5].

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Computational Chemistry **131**

Ligand Migration In Carbonmonoxy Neuroglobin

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Neuroglobin (Ngb), a recently discovered heme-protein [1] of the globin family, shows an interesting feature earlier found in several plant hemoglobin and cytoglobin. In the absence of an exogeneous ligand at the sixth coordinating position of the heme iron, the distal His64 can bind in a competitive fashion with gaseous ligands, like CO, NO and O_2 to the heme iron. In this work we analyze CO migration pathways in deoxy NgbCO using Molecular Dynamics (MD) simulations. From forty 1 ns unbiased MD trajectories on deoxy NgbCO, eight different stable docking sites can be differentiated. Some of these cavities are reminiscent of those found for CO migration in myoglobin (Xe1, Xe2, Xe4). Comparisons of wt Ngb with F28L and F28W NgbCO mutants revealed a facilitated CO transfer to the Xe4 docking site depending on the size of the residue in position 28. This effect was also reported for L29 myoglobin mutants [2]. Furthermore, Ngb possess a large distal side cavity which is divided into five docking sites. Opening and closure of two tertiary rebinding pockets in this region depends on the orientation of the Pro52 sidechain.

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Computational Chemistry **130**

TD-DFT Study on “Proton vs Hydrogen” Transfer in Hydrogen-Bonded Ammonia Wire

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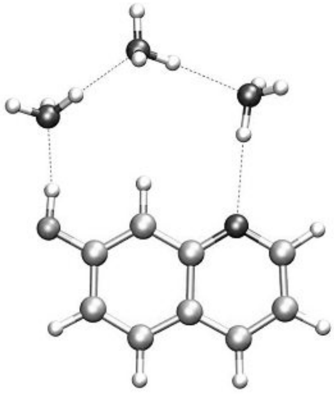
7-HydroxyQuinoline (7HQ) is a bifunctional hydrogen-bonding molecule which acts as a H-bond donor at the OH group and as an acceptor at the N atom. Electronic excitation strongly modifies the acid-base properties of this molecule at both positions rendering the hydroxyl group more acidic and the N atom more basic. It is well established that the 1:3 bridged complex between a single 7HQ and 3 ammonia molecules ($7HQ\text{-}(NH_3)_3$) gives rise to enol→keto tautomerization process, of the heteroaromatic chromophore compound, upon photoexcitation.[1]



Our present efforts are aimed to understand the electronic character of the excited state involved in the tautomerization performing non-adiabatic excited state dynamics.

Computational Chemistry **132**

DFT study of the binding of the N3 dye and its deprotonated forms to anatase(101)

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The N3-anatase interface is of great importance in current dye sensitized solar cells (DSSC), since devices based on TiO_2 nanoparticles and $Ru(dcbpy)_2(NCS)_2$ dyes exhibit one of the best performance. A problem still under debate for this system is the binding geometry of these dyes to the anatase surface[1,2].

We employed density functional theory methods to identify the most favourable binding modes. To describe the system approriatly, DFT+U had to be used to correct for self interaction errors. In the first step a large number of initial geometries were optimized. For the resulting structures, the IR-spectrum was calculated[3] and compared to experimental data. In this way we were able to identify two different binding modes, which are in good agreement with experiment and favourable from an energetical point of view.

Our results indicate that both structures are present in DSSC, depending on the pH and the protonation of the dye.

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Computational Chemistry **133**

Targeting the Imatinib-resistant T315I mutant of Abl: Design, synthesis and experimental validation of potent inhibitors

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Chronic myelogenous leukemia (CML), characterized by unregulated proliferation of myeloid cells in the bone marrow, accounts for 15 to 20 % of all adult leukemia cases in the Western population. The molecular cause for the disease is a characteristic translocation between chromosome 9 and 22 which results in the so called Philadelphia chromosome (Ph) and in the formation of the chimeric BCR-ABL gene. In CML the protein product of this hybrid gene is a constitutively active protein kinase. BCR-ABL kinase drives the pathogenesis of CML through the phosphorylation and activation of a broad range of downstream substrates playing a critical role in cellular signal transduction and transformation. ABL tyrosine kinase therefore represents an interesting therapeutic target and many potent inhibitors have been developed and brought to the clinic in recent years, including Imatinib, Nilotinib and Dasatinib.

However, the T315I mutant form of BCR-ABL, which is frequently found in CML patients, mediates complete resistance to Imatinib and many of the next generation Abl kinase inhibitors like Dasatinib and Nilotinib. Therefore, there is an eminent need for the development of drugs which are active against the T315I mutant of ABL.

Here we present the design and testing of compounds with a novel scaffold, compared to known BCR-ABL inhibitors, which are able to inhibit the T315I mutant of ABL in the nM range and in some cases even potently inhibit ABL wt.

Computational Chemistry **134**

Benchmarking and extension of algorithms for exhaustive computational search of local minima

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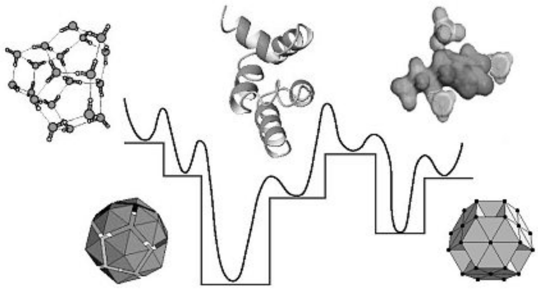
Exploring the Potential Energy Surface (PES) essentially involves exhaustive finding of stationary points. The identification of the global minimum, which has received most of the attention so far, motivated the development of methods or specific algorithms such as basin-hopping, simulated annealing, Car-Parrinello based approaches, genetic algorithms and even stochastic approaches [1,2]. For the exhaustive identification of low-lying local minima, however, chemical intuition is still heavily relied upon, and this can be a problem when the chemistry of a given system is not well known. In the present work, we propose to automate, benchmark and extend one stochastic and one deterministic algorithm to various model reactions and systems including the dehydration of amino-triborane and endohedral clusters.



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Computational Chemistry **135**

A Computational Study of Tetrathiafulvalene (TTF) Fused with a Strong Acceptor

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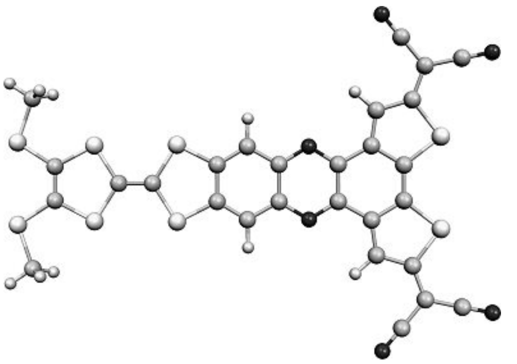
Charge transfer transitions can be studied in donor-acceptor (D-A) systems. Tetrathiafulvalene (TTF) is a good donor unit in such D-A systems [1] which are of prime interest on account of their potential applications in molecular electronic devices.

Herein, we will present a computational study of TTF fused with a new strong acceptor [2]. The aim is to understand the electronic structure of the ground- as well as low lying electronic excited-states.



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Computational Chemistry **136**

Square Peg. Round Hole. Lessons from Robotics on the Application of Neural Networks to Receptor Surface Representations.

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When the 3D structure of a receptor is unknown, the molecular similarity between a series of known interacting ligands is often used to characterize structural features responsible for biological activity. “Similarity” is based on the detectable changes induced in the receptor by the ligand. Since the ligand-induced perturbations on the molecular surface of the receptor often vary in a non-linear fashion between ligands, typical linear regression methods are inadequate to accurately describe the relationship.[1] Ligands also can activate variant signal transduction pathways to different degrees, making it necessary to redefine conventional notions of activity, agonism and antagonsm in these models.[2] As a further complication, “activity” in many cases, is due to the combined effect of several receptors being simultaneously activated by one receptor. Such complications often require one to include more than one endpoint in the structure-activity relationship model.[3]

Our present work focuses on the development of 5 varieties of supervised and unsupervised Neural Networks commonly used in robotics for

(1) A “Fuzzy” logic classification of activity/efficacy of ligand-receptor interactions across a family of receptors (rather than a single receptor)
(2) Modeling of quantum mechanical structural and property descriptors based on this classification scheme in a reduced descriptor space.
(3) Mapping of this descriptor space back to 3D space for comparison with experimental data.

The methodology provides an improved framework for the representation and validation of receptor surface models against biological data.

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Computational Chemistry **137**

Nickel deposition on γ-Al_2O_3: modelling of metal particles behaviour at the support

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Recently, surface modifications of 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]. The conclusion was that the stability of Ni clusters with different cluster sizes on the γ-Al_2O_3 support can be influenced by the type of deposition, which was the topic of our further experimental and theoretical studies about surface modifications.

On home-made model catalysts, Ni metal deposition by thermal evaporation in UHV and consecutive XPS characterisation were carried out. In parallel, the molecular structure of model Ni/γ-Al_2O_3 catalyst used during methanation of synthesis gas was investigated using DFT method with cluster model and non-local functional (RPBE). Ni clusters with different size were cut from the (100) Ni surface and deposited at the $Al_{15}O_{40}H_{35}$ cluster in order to validate deposition model determined by XPS analysis.

Our experimental studies suggest that a kind of Stranski-Krastanov growth model can explain Ni deposition on γ-Al_2O_3, namely firstly, a partial Ni monolayer is deposited and, secondly, on top of this "layer" three dimensional islands of Ni metal are growing. Theoretical DFT calculations show that nickel atoms adsorb on Al_2O_3 (100) with deposition energy -0.9 eV/Ni atom. The preferred adsorption sites are hole positions between surface oxygen centres. This corresponds quite well to the partial monolayer growth found by XPS analysis. Ni prefers to be localized at AlO_4 tetrahedrons between rows of AlO_5. This finding corresponds quite accurately with a coverage "0.5 ML" of nickel found experimentally as maximum of the first deposition stage.

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Computational Chemistry **138**

Core Electron Spectroscopy of Oligopeptides in Aqueous Solution

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Recently, an approach for calculating X-ray absorption spectra based on the transition potential method combined with the Gaussian and augmented-plane wave method (GAPW) has been introduced [1]. For this type of spectroscopy, the promotion of a core electron to an unoccupied orbital and the resulting relaxation of the electronic structure has to be appropriately modeled. The GAPW formalism allows for efficient DFT all-electron calculations of extended systems, making this framework appealing for condensed phase X-ray spectroscopy.

We focus on excitation spectra of oligopeptides in aqueous solution. The calculations were performed along classical MD trajectories and compared with reported experimental spectra [2]. The analysis of conformation dependent signal patterns of absorption leads to the interpretation of the transitions in therms of secondary structure modifications and dynamical reorientation of hydrogen bonds between donor–acceptor partners: this latter involving both intra– and intramolecular interactions, in particular with the surrounding waters. This technique opens new perspectives towards the characterization of the nature of the H–bonds, possibly clarifying how the number and the strength of the local coordination sphere affects the spectra.

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Computational Chemistry **139**

Large Scale Ab Initio Molecular Dynamics Based On Hybrid Density Functionals

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Kohn-Sham density functional theory (DFT) has become a highly efficient tool for studying the electronic structure of molecules. The usage of models based on the generalized gradient approximation (GGA) for exchange and correlation effects allows to describe and predict chemical processes fairly accurately. Despite the success of GGA-models, it becomes more and more clear, that some of the failures in standard DFT can only be addressed by hybrid functionals, i.e. approximations containing exact Hartree-Fock exchange (HFX). However, for large systems the calculation of HFX in hybrid DFT is computationally much more demanding due to poor scaling with system size and basis set quality. Therefore, ab initio molecular dynamics (MD) of large molecules and systems in condensed phase with hybrid density functionals have so far found little application.

In this work, we present our approach to overcome this drawback. We implemented a broad variety of techniques and algorithms [1] into CP2K [2], a freely available quantum chemistry package. We have thus obtained an efficient and robust tool for the study of systems containing a few hundred atoms based on hybrid DFT. We demonstrate the applicability of our method with extensive simulations of liquid water and the investigation of some systems for which GGAs fail to give a qualitatively correct description.

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[2] The CP2K developers group, http://cp2k.berlios.de/

Computational Chemistry **140**

Approximation of NMR Chemical Shifts in Large Molecules

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Computation of NMR parameters is a powerful tool to complement or help in the assignement of experimental spectra[1]. The aim of this work is to introduce and validate a suitable approximation offering reasonable accuracy to evaluate chemical shifts of NMR active nuclei in large molecules. While accurate chemical shifts can be computed for small isolated sys¬tems, the presence of neighbouring molecules or groups in larger molecules can drastically influence to the long range contribution to the chemical shift anisotropy[2]:

$$\delta_{\text{total}} = \delta_{\text{short range}} + \overbrace{\delta_{\text{electrostatic}} + \delta_{\text{remote current}} + \delta_{\text{solvent}}}^{\text{long range}}$$

Molecular motion also influences the measured chemical shift. Taking all these contributions into consideration inevitably leads to an increased cost of the computation. Distinct approximations offering reasonable accuracy for evaluating electrostatic and motional effects on the chemical shift of benchmark systems are presented and compared.

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Computational Chemistry **141**

π–Delocalization in Linearly Conjugated Oligomer Chains: A Donor-Acceptor-Interaction Based Scheme of Analysis

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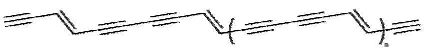
We present a scheme for the evaluation of electron delocalization in linearly conjugated compounds which is based on the Natural Bond Orbital (NBO) theory. The scheme is illustrated by means of an investigation of the evolution of electron delocalization as a function of the chain length in polyacetylene (PA), polydiacetylene (PDA) and polytriacetylene (PTA) oligomers, which differ by the number of ethynyl-spacers incorporated in the chain.

PA

PDA



PTA

The scheme tracks the development of the orbital interaction energies of adjacent unsubstituted bonds within linearly conjugated systems. These values are shown to reach saturation after a characteristic oligomer size. The profile of interaction energies allows drawing conclustions on the effective conjugation length of the oligomer chain investigated.

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Prediction of Moessbauer Parameters in a Douglas-Kroll-Hess Framework

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Moessbauer spectra supplement other spectroscopic techniques and support the structure determination of molecular and electronic structures. Theoretical predictions of the isomer shift and quadrupole splitting based on *ab initio* calculations of the electron density at the nucleus and the electric field gradient, respectively, are helpful in the interpretation of such spectral data. A reliable prediction of accurate electron densities as well as electric field gradients at nuclei requires relativistic effects to be taken into consideration. The scalar-relativistic variant of the Douglas-Kroll-Hess (DKH) [1,2] unitary transformation technique provides a suitable framework to treat relativistic effects and has been extended to the analytical calculation of molecular properties avoiding the so-called picture change error [3], which results form calculating the desired property from non-DKH-transformed (i.e. non-relativistic) property integrals. In a recent study on the nuclear quadrupole moment of ^{119}Sn and the quadrupole splitting in a variety of tin compounds we demonstrated the reliability and stability of our picture-change-corrected DKH approach [4]. An extension of this approach to the calculation of the isomer shift in iron compounds is in progress in our laboratories.

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Computational Chemistry **143**

A Subsystem TDDFT-Response Formalism for Studying Natural Light-Harvesting Complexes

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Natural light-harvesting complexes accomplish the first two essential steps in photosynthesis: (i) absorption of solar light and (ii) transfer of the excitation energy to the photosynthetic reaction center. The details of the excitation energy transfer (EET) processes depend crucially on the excited states of the pigment molecules present in the light-harvesting complexes, which are influenced by interactions with surrounding proteins as well as by aggregation phenomena related to excited-state interactions.

A subsystem formulation of time-dependent density-functional theory (TDDFT) [1] is presented that is capable of describing both types of effects. It is shown that this approach is well suited to investigate general spectroscopic properties of a particular chromophore for which the environmental response is important. In particular, characteristic features of excitonically coupled chromophores in absorption and circular dichroism spectra are accessible. Moreover, accurate and efficient approximations to this formalism can be found, so that it can be applied to problems connected to photosynthesis. This is demonstrated in a study on protein-pigment interactions and EET couplings in the light-harvesting complex LH2 of purple bacteria [2].

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Computational Chemistry **144**

Theoretical Study of Spherophanes: Geometrical and Electronic Structures

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A set of novel supramolecular cage-structures, spherophanes, has been studied at the density functional B3LYP level. Full geometrical structures optimizations have been made with 6-31G and 6-31G(d) basis sets followed by frequency calculations and their electronic energies have been evaluated at B3LYP/6-31++G(d,p). Three different symmetries have been adapted during the optimizations: C_1, C_i, and O_h. The results show almost the same geometrical parameters and energies for all three symmetries. It has been found that the benzene rings are more distorted in the case of spherophane1 which can be due to the long distance interactions between the hydrogen atoms. In addition, the bonds between the benzene rings are very long to prevent π-electrons delocalization between them. These spherophanes show portal openings of 2.596 Å in Spher1, 4.000 Å in Meth2, 3.659 Å in Oxa3, and 4.412 Å in Thia4. It has also been observed, in regard of eventual host-guest interaction studies, that the nearest atoms to the center of the cavities are the carbons bonded to the X groups. Set apart the HOMO of Thia4, the results at B3LYP/6-31++G(d,p) show that the spherophanes' HOMO and LUMO orbitals are almost similar to those of a free benzene molecule. They belong to the irreducible representations E_u and E_g of the O_h point group, respectively. However, the Thia4's HOMO is a symmetric linear combination of two 3p sulphur atomic orbitals that has a_{2g} symmetry. These supramolecules have a relatively large HOMO-LUMO gap of 2.89eV(Spher1), 5.26eV(Meth2), 5.73eV(Oxa3), and 4.82eV(Thia4). The standard molar enthalpies of formation at 298.15K have been evaluated, the obtained values for B3LYP/6-31G(d) are, in kcalmol^{-1}, 595.24, 193.92, -107.51, and 404.80 for Spher1, Meth2, Oxa3, and Thia4, respectively. The reported IR and ^{13}C NMR spectra of these spherophanes were calculated are very simple due to their highly considered symmetry, O_h.

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Theoretical Investigation of the Adsorption of Organic Molecules on Pt Surfaces

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The theoretical study of the adsorption of organic molecules on platinum and on other transition metal surfaces is of fundamental importance for the investigation of reaction mechanisms in heterogeneous catalysis [1-3]. Density Functional Theory is the standard tool for such studies, since the systems are typically too large for analysis with post-Hartree-Fock calculations. We have investigated several methods for the description of a metal surface using (i) periodic slabs and (ii) clusters for the modeling of the metal, and (i) Gaussian-Plane-Wave, (ii) Plane Waves, or (iii) localized basis sets for the expansion of the wave function [4-6]. Physico- chemical properties of the metal as well as the adsorption properties of organics are compared using the different methods. Applications to the study of chiral surface modification of platinum catalysts complements the theoretical investigation [7].

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Computational Chemistry **147**

Designing PET Tracers for HSV1-TK-based Gene Therapy Using Molecular Ddynamics

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Therapeutically efficient nucleoside analogues against Herpes Simplex Virus 1 are selectively activated via its Thymidine Kinase (HSV1-TK). Further metabolized to triphosphates, they inhibit viral replication by blocking the viral DNA-polymerase. Being trapped inside the cell due to their negative charges, they are suitable for Positron Emission Tomography (PET) to monitor HSV1-TK activity *in situ*. Here, we apply molecular dynamics to the design of PET tracers for HSV1-TK-based gene therapy. With this method, we assess the stability of HSV1-TK regions allowing binding of experimentally determined high affinity substrates and spot more flexible regions where substitutions could be beneficial. To this end, 3 different high resolution crystal structures of HSV1-TK in complex with their respective substrates have been used. We present the protocol setup as well as the method validation combining AMBER 9.0 [1] and NAMD 2.6 [2], including a 50 ps minimization-equilibration and a 5 ns trajectory simulation. To evaluate docking poses of substrate analogues previously generated with Gold 3.1.1 [3], the above-mentioned protocol has been applied and the results have been compared to the reference simulations. Subsequently, first substitutions possibly improving the binding affinity are pointed out.

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Computational Chemistry **146**

Zero field splitting of a $[FeCl_4]^{3-}$ subsystem in $SrCl_2$:Fe^+

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As M. Moreno et al [1] found experimentally, in $SrCl_2$:Fe^+ an isolated Fe^+ impurity undergoes a big off-centre motion from the center of a $FeCl_8^{7-}$ cube to a position close to the center of a $< 100 >$ face. Despite huge distortion the associated well depth is found to be only 0.28eV. From previous calculations one knows, very small excitations from ground state are possible, where zero field splitting (ZFS) plays an important role.
In an EPR experiment, only $|\frac{3}{2}, -\frac{1}{2} > \rightarrow |\frac{3}{2}, \frac{1}{2} >$ trainsition were well detected [1].

This observation can be explained from the result of our fine structure calculation that shows a ZFS of the ground state $^4A_2$ by more than $200\,cm^{-1}$, which is higher than microwave photon energy, and thus, is not observed [1].
The therefore needed ZFS and its D-value (ZFS-tensor) have been calculated in this study for a $FeCl_4^{3-}$ subsystem. This has been done using a non-empirical Ligandfield approach, for which parameter were calculated using ligand field density functional theory (LFDFT)[2].

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Computational Chemistry **148**

A LFDFT Study of the EPR Parameters and Magnetic Susceptibility of Cobaltocene

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In transition metal chemistry low-lying excited states are common. Explicit treatment of the correlation is necessary in order to understand and predict the properties of coordination complexes. This is achieved within the non-empirical ligand field (LF) approach [1] – CI within the active space of Kohn-Sham (KS) orbitals with open d-shells. With the frozen KS orbitals obtained in the avarage of configuration DFT calculation, the energies of all single determinants in the corresponding active space is calculated and used to deduce LF and Racah parameters. Spin orbit coupling constant ζ is evaluated as described in [1c]. These parameters are introduced in a LF program to calculate the multiplet energies as well as the EPR parameters [1].

We apply our DFT based Ligand Field model to analyze the magnetic properties of the cobaltocene, Jahn-Teller instable metallocene. Calculation of g- and A- tensors [1d], and magnetic susceptibility of this complex is presented, compared to the experimental findings [2], and analyzed in terms of the parameters that determine the ground state potential energy surface of this molecule.

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