doi:10.2533/chimia.2013.491 Chimia 67 (2013) 491–500

Computational Chemistry **CC01**

Modelisation of the Raman Optical Activity of solvated Λ−Rhodium-tris-ethylenediamine

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The vibrational optical activity of a chiral transition metal complex, namely Λ-Rhodium-tris-ethylenediamine is investigated within a Density Functional response Theory[1]. Making use of the availability of VCD and ROA experimental spectra, a methodological study allowed us to determine a practicable computational approach for an accurate analysis of the spectra of the solvated molecule.

Given the critical role played by the environment and by conformational effects [2, 3], the study involved a complete conformational analysis as well as the inclusion of the solvent effect via the use of a polarization continuum model [4] and the inclusion of explicit solvent molecules. With this study, we aim to demonstrate that reliable ROA spectra can be simulated with reasonable computational cost.

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Computational Chemistry **CC02**

Relation of exact Gaussian basis methods to the dephasing representation: twelve methods for computing time-resolved electronic spectra [1]

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We recently showed that the Dephasing Representation (DR) [2] provides an efficient tool for computing ultrafast time-resolved (TR) electronic spectra and that further acceleration is possible with cellularization [3]. Here we focus on increasing the accuracy of the DR by first implementing an exact Gaussian basis method (GBM), which benefits from the accuracy of quantum dynamics and efficiency of classical dynamics. The DR is then derived together with ten new method with intermediate accuracy and efficiency. These include the Gaussian DR, an exact generalization of the DR, in which trajectories are replaced by communicating frozen Gaussians evolving classically with an average Hamiltonian. The newly obtained methods are tested on time correlation functions and TR stimulated emission spectra in the harmonic potential, pyrazine, and quartic oscillator. Numerical results confirm that both the GBM and the Gaussian DR increase the accuracy of the DR. Surprisingly, in chaotic systems the Gaussian DR can outperform the presumably more accurate GBM, in which the two bases evolve separately. Finally, we discuss the relationship with other methods employing time-dependent Gaussians: Gaussian MCTDH [4], Multiple Spawning [5], and Coupled Coherent States [6].

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Computational Chemistry **CC03**

Exciton Coupling in Organic Electronic Assemblies: a Challenge for DFT Approximations

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'Single-stack' [1] of π-conjugated nanowires form one-dimensional organic nanofibrils. These constitute a promising and challenging approach to engineering future build-blocks for nanoelectronic circuits, and especially for photovoltaic devices.

These higly ordered assemblies generally exhibit complex UV-visible absorption bands arising from exciton coupling. The computational rationalization of these bands relies upon the consideration of at least two stacked chromophores.

Considering the size of the chromophores, TD-DFT remains the most suitable method to investigate excited-states. Unfortunately, the extent of exciton couplings amongst various chromophores was found to depend dramatically on the fraction of exact exchange in the long-range. Our study aims at elucidating the origin of the dependency and identifying the best performing approximation accross a range of representative $\pi - \pi$ stacked systems.

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Computational Chemistry **CC04**

Ligand Field Density Functional Theory Approach for Two-Open-Shell f and d electrons

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We present methodological advances tackling a rather complex problem of ligand field account of 4f and 5d two-open-shell model Hamiltonian, focused on the interpretation and prospection of an important optical effect, the so-called quantum-cutting processes. [1] In this respect, we use the frame of the original post-computational analysis algorithm named Ligand Field Density Functional Theory (LFDFT) [2][3] for the simulation of the $4f^n \rightarrow 4f^{n-1}5d^1$ transitions in rare earth compounds. Moreover the ligand field influence is also described by means of the Angular Overlap Model (AOM), taking the advent of convenient tractability in mapping the model on the computed data, and the intuitive insight offered by the AOM parameters.

As example, the non-empirical methodology is applied for the simulation of the optical properties of the (i) $4f^1$ and $4f^05d^1$ electron configurations and (ii) $4f^2$ and $4f^15d^1$ electron configurations [4] of the trivalent cerium and praseodymium ion doped in Cs_2NaYCl_6 and Cs_2KYF_6 with the elpasolite structure type, respectively, considering the following interaction: the two-electron effects, the ligand field influence and the spin-orbit coupling parameters.

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Computational Chemistry **CC05**

Solvent effects and nonadiabatic dynamics of $[Cu(dmp)_2]^+$

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Cu-diimine complexes are promising candidates for photoelectronic applications. Despite being extensively studied since the early '80s[1], a complete understanding of their photophysical and photochemical properties is still lacking. We will present a combined experimental and theoretical study of $[Cu(dmp)_2)]^+$ (dmp = 2,9-dimethyl-1,10-phenanthroline), aimed at elucidating the excited state mechanisms occurring within the femtosecond to nanosecond time domain. A static and time-resolved X-ray absorption study[2], interpreted using TDDFT adapted for core-hole excitations and molecular dynamics simulations do not confirm the previous assignment of lifetime shortening of the excited state in donor solvents (acetonitrile) to a metal centred exciplex. Instead, the phenomenon may be rationalised simply by the solvent dependent decrease of the ^{3}MLCT energy. In the femtosecond time domain, we employ the Multi Configurational Time Dependent Hartree (MCTDH) method [3] to perform wavepacket dynamic simulations to explore the nonadiabatic relaxation of $[Cu(dmp)_2)]^+$ following excitation into the S_3 state. Our results, in conjunction with previous experiments[4] allow us to rationalise the ultrafast dynamics of this complex. Importantly, the combination of experiment, quantum dynamics and molecular dynamics simulations makes it possible to describe the whole photo-relaxation mechanism of $[Cu(dmp)_2)]^+$.

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Computational Chemistry **CC06**

Evaluation of solvatochromic shift using the average electron density of solvent

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To determine the spectral shift, absorption band has to be calculated by summing up oscillator strength f_i and resonance frequencies ω_i over number of transitions i at corresponding position of nuclei R_j^B (j is total number of atoms in environment)in solvent. However for environment of flexible structure, averaging over a large number of orientations has to be applied. The computational cost of simulation of absorption band depends upon the number of configurations. The alternative approach has been proposed recently, where absorption bands are simulated by performing the orbital-free embedding calculations of the excitation energy at averaged solvent density $\langle\rho_B(\vec{r})\rangle$ [1,2]. We followed the same strategy in this work where instead of averaging f_i and ω_i over large number of configurations these quantities are evaluated for ensembled average electron density $\langle\rho_B(\vec{r})\rangle$ of environment. $\langle\rho_B(\vec{r})\rangle$ does not depend explicitly on geometry of solvent hence it can be used for evaluation of excitation energy. $\langle\rho_B(\vec{r})\rangle$ can be obtained from 3D reference interacting site model with the Kovalenko-Hirata closure approximation(3D-RISM-KH)[1,2] or by quantum molecular dynamic simulation.

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Computational Chemistry **CC07**

The Reactive Collision and Final State Analysis of NO and O Reaction

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The research involves the dynamical investigation of the NO+O $\rightarrow$ NO_2 elementary reaction, which is relevant to the Hypersonic Flight Regime of spacecrafts. For this purpose, first an analytical ground-state potential energy surface is constructed – based on high-level *ab initio* calculations and using polynomial based fitting ansatz – in order to carry out quasi-classical trajectory and quantum dynamic calculations.

At this stage of the research, we are calculating the ground-state potential energy surface for NO_2 molecule. As low-laying excited states give rise to a conical intersection near the dissociation region, a multi-reference methods using Dunning's standard correlation consistent polarized quadruple (cc-pVQZ) basis set are applied. Multi-reference configuration interaction (MRCI) calculations – with full valence complete active space (FV-CASSCF) wave function – are performed using program MOLPRO. The dynamic correlation is taken into account by the internally contracted MRCI method of Werner and Knowles and Davidson correction is used to estimate the effects of higher excitations (icMRCI+Q).

Preliminary results show difficulties, as at intermediate NO – O distances, the electronic structure calculations often converge to excited states, which cannot correlate adiabatically with the ground state of the dissociated NO + O system. In order to correct this, the symmetry and multiplicity of the wave functions will be fixed by defining it explicitly in the upcoming MOLPRO calculations.

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Computational Chemistry **CC08**

The Role of Water and Sodium Ions in μ-Opioid Receptor Activation

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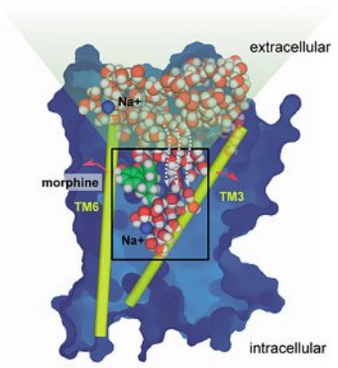
As GPCRs are implicated in many diseases, they are among the most important drug targets[1]. Although X-ray crystallography delivered high-resolution seven-transmembrane helix structures of a few GPCRs before and after activation [2], the details of the structural and dynamical transitions within the receptors still missed with static structures. In this context we here investigated the role of water and sodium ions during GPCR transmembrane signaling through 9.4μs full atom long time scaled molecular dynamics simulations.



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Computational Chemistry **CC09**

DFT studies of lignin vibrational structure

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Lignin is one of the three main biopolymers, together with cellulose and hemicellulose, which builds cell walls of plants. Lignin consists of aryl ethers, irregularly connected by a variety of linkages [1,2].

In the present work computational study of most dominant lignin linkages and their vibrational structure have been investigated using Density Functional Theory method. Full geometry optimization of lignin linkages has been done using StoBe code with cluster model and non-local functional (RPBE) approach. The calculations of the vibrational frequencies were performed with harmonic approximations as well as an anharmonicity fit in the Morse potential function, as implemented into StoBe code.

The theoretical vibration spectra of most dominant lignin linkages will be presented: β-O-4, α-O-4, 4-O-5, 5-5, β-β, β-1, β-5. The calculations include three different precursors based on cinamyl alcohol: coumaryl alcohol, coniferyl alcohol as well as sinapyl alcohol.

Presented theoretical investigations for variety of lignin linkages give the possibility of obtaining Vibrations Basis Set for experimental spectra interpretation.

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Computational Chemistry **CC10**

Spatial averaging : enhancement of the sampling of the configuration space for atomic clusters and biomolecules.

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Monte Carlo (MC) methods are widely used in modern simulations, particularly because of their dimensional tolerance, that makes it possible to study systems of significant complexity. Nevertheless, problems in which "rare-event" issues arise are a particular challenge for such approaches.

Spatial averaging [1] is an efficient MC method which can be applied to those problems where important regions (e.g. minima) of the energy landscape may be difficult to sample with a standard method, such as Metropolis sampling. At the heart of the method is the realisation that from the equilibrium density a related, modified probability density can be constructed through a suitable transformation. This new density is more highly connected which increases the chances for transitions between neighbouring states which in turn speeds up the sampling. In order to transform the equilibrium density, Gaussian distributions with variable widths are used.

First successful investigations included the diffusion of small molecules in condensed phase environments [2] and localisation of lowest energy structures of Lennard-Jones clusters [3,4]. A more general implementation in CHARMM allowed us to study the conformation space of biomolecules [4].

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Computational Chemistry **CC11**

Application of the Chemical Hamiltonian to Zeroth-order Wavefunction and Energy for Intramolecular Symmetry-Adapted Perturbation Theory

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Intermolecular interactions play an ubiquitous role in chemistry and biology, with representative examples including protein-ligand interactions, supramolecular assembly, pre-reactive complexes, etc. The theoretical decomposition of intermolecular interactions into physically meaningful terms enhances our understanding of such processes. Among the various existing decomposition schemes, Symmetry-Adapted Perturbation Theory (SAPT)[1] may be considered as the most successful, as it naturally decomposes the interaction energy into physical and intuitive terms.

On the other hand, the analyses of intramolecular noncovalent interactions, which are responsible for phenomenon such as intramolecular charge transfer (e.g. transannular interactions), conformational and isomer energy differences as well as enzymatic activity are theoretically more challenging to assess, as no such physical energy decomposition scheme is available to date.

The present work attempts to fill the gap by obtaining a zeroth-order wavefunction and energy for an intramolecular variant of the SAPT formalism. The suggested theory optimizes orbitals with a proper scheme excluding interactions between the fragments of interest. Straightforward optimization schemes directly eliminating relevant overlap and Fock matrix integrals lead to undesirable convergence properties, hence a new scheme is proposed based on the Chemical Hamiltonian[2] approach originally used by Mayer.

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CC12

A novel adaptive mesh method for diagonalizing multidimensional quantum Hamiltonians

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We present a numerical method to obtain the eigenstates of an arbitrary multidimensional quantum Hamiltonian. The method works on the basis of i) a sampling procedure that optimizes the distribution of the grid points, and ii) the diagonalization of a real-valued sparse matrix which eigenvectors are the eigenstates evaluated at those selected grid points. Its potential applicability include any system described by the Schrödinger equation. We apply the method to find the first 50 eigen-energies and wave-functions of spinless quantum Lennard-Jones particles (up to 5) trapped in a 1D harmonic potential, a system which is under active debate due to its interesting dynamical properties [1,2]. We obtain the states of the bosonic and fermionic counterparts describing the *fermionization* of the former [2], and also describe the melting of the clusters at finite temperature.

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Computational Chemistry **CC13**

Optimal parameterization of force fields for thermal dynamics

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Simulating the dynamics of large number of atoms for ns timescales is only possible by using force fields. Standard force fields, such as the CHARMM force field [1] contain bonded and nonbonded energy terms. Their parameters can be classified as geometric ones (i.e. equilibrium bond length, vdW radius) and energetic ones (i.e. force constants, Lennard-Jones well depth).

However, geometric parameters don't determine the equilibrium structure as matching all the optimal geometric parameters cannot usually be fulfilled simultaneously. Furthermore, frequencies and the eigenvectors of normal mode vibrations also depend on the geometric parameters. Therefore, energetic and geometric parameters have to be tuned simultaneously to capture the reference geometry and vibrational data best. Due to the limited flexibility of force fields, a force field with its default parameter values is well applicable only within a limited range of temperatures. At higher temperatures the precise equilibrium geometry becomes less relevant, whereas the amplitudes of vibrations become more important, which would suggest another optimal parameter set.

Based on statistical thermodynamic considerations, we devised a novel method which simultaneously determines both geometric and energetic bonded parameters by capturing the vibrational distribution of atoms at a given temperature. Other tools usually disregard eigenvectors and temperature [2]. The algorithm is applicable to semi-rigid molecules, for which the normal mode picture is appropriate and requires only geometric and normal mode analysis data as reference. The method is also made applicable to X-ray diffraction data including isotropic and anisotropic B-factors.

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Computational Chemistry **CC14**

Ligand-Based Virtual Screening on Billions of Molecules

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Identifying new chemotypes is a major problem for many pharmaceutical industries.[1] *De novo* drug design may help to address the problem by *in silico* methods such as scaffold analysis, breeding of molecules by genetic algorithms and exhaustive enumeration of chemical space.[2] We applied already successful ligand-based on GDB-13.[3,4] Recently we published GDB-17 with more than 160 billion small organic molecules.[5]

Here we propose our solution to perform virtual screening on this large amount of molecules. Since we already know that we can identify bioactive molecules by Molecular Quantum Numbers (MQN),[6] we classified the entire database by them. Furthermore, we reordered the 42 MQN values and additionally added other features in order to have an optimized, faster and flexible virtual screening method. The resulting XMQN fingerprints were then divided into hash table improving remarkably the search speed by a factor of 5'000 in comparison to a linear search. Extracting the resulting structures depends almost entirely on the time of reading and writing the data on the hard drive. On 15 drug examples, we performed "scaffold hopping" defined by a ROCS score of 1.6 or higher and a Tanimoto Substructure fingerprint of 0.5 or lower.[7]

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Computational Chemistry **CC15**

Classical Molecular Dynamics Simulation of Porphyrin-Based Dye-Sensitized Solar Cells

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Inspired by their central role in photosynthesis, porphyrin-based dyes constitute an attractive biomimetic alternative to conventional Ru-based sensitizers. In a continuation of our characterization of the optical and electrochemical properties of porphyrin-based dye-sensitizers using implicit solvent density functional theory (DFT) and time-dependent (TD)DFT calculations, we developed a classical force field for a further investigation of the behavior of these dyes on a defect-free (101) surface of anatase. This force field approach was first applied to the dye YD2- O-C8 [1] and validated with respect to full ab initio and mixed quantum mechanical/molecular mechanical (QM/MM) reference simulations. Classical molecular dynamics simulations based on the newly developed force field are currently used for a systematic study of the aggregation behavior of the dyes on the TiO_2 surface as a function of coverage and binding mode.

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Computational Chemistry **CC16**

On-the-fly wave-packet propagation: Evaluation of vibrationally resolved electronic spectra of large systems

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It is often important to include vibronic couplings into spectra calculations in order to obtain satisfactory agreement with experimental results. It has been showed that on-the-fly semiclassical dynamics provides a powerful tool to evaluate vibrationally resolved absorption spectra [1]. The overall computational cost, however, restricts almost all of these methods to small systems. In case of larger molecules, the potential energy surfaces are usually approximated by harmonic potentials, which is often not a reliable description. On-the-fly wave packet propagation can fill this gap: Within the thawed-Gaussian approximation [2,3] (TGA) the nuclear wave packet is guided by a central trajectory, which feels the full anharmonicity of the potential, and the propagation of its width involves the local quadratic approximation. Due to its small computational costs, TGA can treat all vibrational degrees of freedom on an equal footing even in case of large systems. This is especially important for molecules where the global harmonic approximation for the potential energy surface is no more accurate and a study of each normal mode in terms of importance and harmonicity is tedious. Further more, this computational protocol is not limited to linear spectroscopy; nonlinear spectra such as time-resolved stimulated emission can be also evaluated. Comparison with experimental spectra, for example for dithiophene, shows that on-the-fly TGA is a well-suited method for vibrationally resolved spectra calculations.

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Computational Chemistry **CC17**

Real-time Quantum Chemistry

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Significant progress in the development of efficient and fast algorithms for quantum chemical calculations has been made in the past two decades. The main focus has always been the desire to be able to treat ever larger molecules or molecular assemblies—especially linear and sublinear scaling techniques are devoted to the accomplishment of this goal. However, as many chemical reactions are rather local, they usually involve only a limited number of atoms so that models of about 200 (or even less) atoms embedded in a suitable environment are sufficient to study their mechanisms. Thus, the question arises how fast one can obtain the quantum chemical results for reactions with a aforementioned constant size.

This problem is, however, not directly solved by the numerous linear-scaling techniques, which are available nowadays. In fact, ideas such as haptic quantum chemistry (HQC)[1,2] or interactive quantum chemistry[3, 4] require an immediate provision of quantum chemical information which demands the calculation of data in real time. We present a definition of real-time quantum chemistry, show its realm and discuss applications in the field of HQC [5]. For the latter, we show how a direct approach is possible by virtue of real-time quantum chemistry[5].

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Computational Chemistry **CC18**

Implementation of a massively parallel QC-DMRG code

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The Density Matrix Renormalization Group algorithm (DMRG) [1] employs a new wavefunction parametrization, tackling the problem of exponential scaling and thus allowing for calculations on larger systems than accessible for standard CAS-type methods. In recent years DMRG has become a true competitor of well-established quantum chemical methods (for applications in chemistry we may refer to our reviews in Refs. [2,3]). As the capabilities of DMRG calculations depend on the availability of an efficient implementation, we set out to provide a new and highly efficient program [4] based on the Maquis DMRG project (www.hp2c.ch/projects/maquis) for quantum chemical DMRG calculations. To facilitate the application of DMRG as a blackbox method, we have supplemented our program with an algorithm to automatically find an optimized orbital ordering. We will present first pilot calculations that demonstrate the accuracy and efficiency of this new DMRG program.

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Computational Chemistry **CC19**

Accessibility of the μ-Hydride Species in [FeFe] Hydrogenases

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[FeFe] hydrogenases, which catalyze proton reduction to form H_2, presumably feature a hydride species as key catalytic intermediate [1,2] for which two possible structures are discussed in the literature. One, in which a hydride is terminally bound to the 'distal' iron atom (terminal-H) and which is believed to be the key hydride species [3]. In the second possible intermediate, a hydride bridges the two Fe atoms of the $[2Fe]_H$ subsite (μ-H) and is thermodynamically more stable one than the first [4].

We investigate the H_2-formation mechanism catalyzed by [FeFe] hydrogenases by means of density functional theory calculations with a large model of the active site, comprising the active center and important surrounding amino acids [5]. Two possible pathways to form the μ-H species are investigated in detail. μ-H formation via ligand rearrangement from the terminal-H species and μ-H formation via direct protonation of the Fe–Fe bond. We show that both pathways feature high barriers due to interactions with the protein residues surrounding the active site. In conclusion, the μ-H species seems to be kinetically inaccessible and H_2 formation at the active site of [FeFe] hydrogenases should proceed via the terminal-H intermediate.

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Computational Chemistry **CC20**

Structure–property relationships of Fe_4S_4 clusters unravelled by broken-symmetry density functional theory

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The chemistry of Fe-S cubane clusters can depend significantly on the anchoring constraints of a protein's backbone (see, e.g., its reactivity with respect to reactive oxygen species [1]). The sensitivity of Fe_4S_4 cluster properties (like potential energies, spin couplings, adiabatic detachment energies, inner-sphere reorganization energies and reactivities) on structural distortions was investigated for a model system of symmetrized $[Fe_4S_4(SH)_4]^{3-/2-/1-}$ clusters with fixed hydrogen atoms and compared with Fe_4S_4 clusters coordinated by ethyl thiolates with fixations according to the cysteines in crystal structures. These correlation diagrams can be very useful to systematize observations on related metalloenzymes in bioinorganic chemistry [2]. Potential energy surface plots [3] indicate that the cubane is flexible, because distortions of the anchoring atom distances by about ± 0.5 Å increase the potential energy by only about 3 kcal/mol. The minima of the potential energy surface of $[Fe_4S_4(SH)_4]^{2-/1-}$ are located at slightly smaller H-H distances compared to the $[Fe_4S_4(SH)_4]^{3-}$ cluster. Comparing the cubane geometries in the three differently charged states, the only significant difference is a shorter Fe-Fe distance of one Fe_2S_2 subcluster in $[Fe_4S_4(SH)_4]^{1-}$. Differences in the coupling scheme can change the reorganization energies by up to 10 kcal/mol.

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Computational Chemistry **CC21**

Elimination of the Translational Kinetic Energy Contamination in pre-Born–Oppenheimer Calculations

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We present a simple strategy for the elimination of the translational kinetic energy contamination of the total energy in pre-Born–Oppenheimer calculations [1] (for applications see e.g. Ref. [2]) carried out in laboratory-fixed Cartesian coordinates (LFCCs). The basis functions are constructed using explicitly correlated Gaussian functions (ECGs) and the global vector representation [3]. First, we observe that it is not possible to parametrise the ECGs so that the system is at rest in LFCCs and at the same time the basis functions are square-integrable with a non-vanishing norm. Then, by exploiting formal mathematical relationships between different forms of the ECGs we can identify and separate the translational contamination terms in the matrix representation of the kinetic energy operator in the LFCC formalism. We present numerical examples for the translational contamination and its elimination for the two lowest rotational energy levels of the singlet hydrogen molecule, corresponding to para- and ortho-H_2, respectively, treated as four-particle quantum systems.

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Computational Chemistry **CC22**

Finding the right Docking Parameters - A systematic Approach

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Modern medicinal chemistry programs require intense use of cheminformatics and computational chemistry for the design and discovery of novel drug molecules. Structure- and ligand-based design consist of computationally expensive tasks with a plethora of parameters that can be adjusted before running the calculations. The significance of docking results therefore depends to a large degree on the correct parameters chosen for the target in question. However, deciding which parameters are the right ones is not always an easy task.

We tackled this problem by enumerating large numbers of parameter combinations while docking against an MMP-13 target and comparing the results with biological data, both collected in-house and available from published results. We also analyzed the results thus gathered with respect to our expectations of what would be well suited parameters for the target in question.

We have shown before the benefits of functional programming in cheminformatics [1]. Now we demonstrate how the above computations could conveniently be set up using OpenEye's OEDocking [2] software together with a small library written in Scala [3] in purely functional style using an iteratee-based [4] approach to model data streams.

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Computational Chemistry **CC23**

Quantum chemical analysis of hydrogen bond strength in polymorphs of pyrimethamine

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The molecular structure and non-covalent interactions present in the polymorphs and pseudopolymorphs of pyrimethamine [1][2] were investigated using X-ray analysis. Each of these polymorphs have a different packing arrangement, but the basic building block is the $R^2_2(8)$ motif [3] formed by N-H...N hydrogen bonds. The packing differences of these polymorphs are due to contributions from N-H...O, N-H...Cl, other non-covalent interactions and molecular recognition process. We have computationally assessed the strength of the hydrogen bonded motifs present in these polymorphs by DFT based computations and analysed their electron densities using a recently introduced molecular descriptor (Single Exponential Decay Detector -SEDD) [4][5]. The advantages of using SEDD over Atoms in Molecules (AIM) and Electron Localization Function (ELF) will be presented.

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Computational Chemistry **CC24**

Simulation of the Absorption Spectra of N-cyclohexyl-2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-amine Solvated in Dimethyl Sulfoxide

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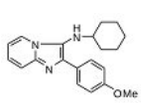
N-cyclohexyl-2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-amine (Flugi-6, see the figure below) is one of a family of Flugi molecules synthesized with combinatorial chemistry [1], where Flugi is an acronym for florescent molecules synthesized by Ugi type reactions. The absorption spectra of Flugi-6 in dimethyl sulfoxide are simulated by taking into account the inhomogeneous broadening explicitly. To this end, a statistical ensemble taken from molecular dynamics simulation is used and instantanous spectra are calculated using a method based on Frozen-Density Embedding Theory [2,3,4]



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Computational Chemistry **CC25**

Force Field Development for Modeling Quarterthiophene Nanofibrills

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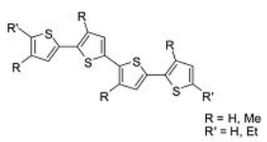
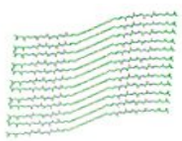
New oligothiophene-oligopeptide hybridized nanofibrills are of great interest for their potential use in photo-voltaic devices and organic transistors [1] [2]. However, in previous reported work, the modeling of conformational properties of extensively-conjugated systems entails a unique challenge for classical force fields, such as General Amber Force Field [3].



1



2

The new developed parameters were validated in the thiophene derivatives of type **1**, which offers improved accuracy compared to original AMBER ff99SB parameters. Our current efforts focus on the applying the new parameters set in modeling self-assembled quaterthiophene nanofibrills **2**.

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Computational Chemistry **CC26**

MQN-Mapplet: Interactive Access to Millions of Molecules on your Desktop

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The chemical space describes an ensemble of all organic molecules to be considered when searching for new drugs and can be broadly divided into the known and unknown chemical spaces. Chemical space as such contains infinite number of possibilities for molecules [1] and one of the challenge always remain is the visualization and navigation in this "chemical space", in way to get quick and broad view of its content. To address this problem we have used the concept of multidimensional property spaces in which the dimensions are assigned to selected numerical descriptors of molecular structure [2]. This multidimensional property spaces then can be visualized by projecting it in lower dimensions (2D or 3D) with the help of principal component analysis (PCA). Based on this concept here we introduce the development of the MQN-mapplet which is a Java application giving interactive access to the structure of small molecules in large databases via color-coded maps of their chemical space. These maps are projections from a 42-dimensional property space defined by 42 integer value descriptors called molecular quantum numbers (MQN) [3]. In contrast to other databases browsing site, one can start the exploration of chemical space with MQN-Mapplet without using any query molecule. The application is freely available for download at www.gdb.unibe.ch

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Computational Chemistry **CC27**

ωB97X-dDsC: A density functional approximation designed to describe π-radical dimer cations

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Two of the most important shortcomings of standard density functional approximations are (1) the lack of long-range correlation and (2) the self-interaction error. The former dramatically affects the description of non-covalently bonded complexes, whereas the later results in poor description of charge transfer excitations and binding energies of e.g., radical dimer cations. These two shortcomings worsen the electronic structure characterization of pi-dimer radical cations, which are highly relevant with regards to their role played in the field of organic electronics. *A-posteriori* dispersion corrections can generally provide the missing stabilizing energy in dispersion complexes. On the other hand, long-range corrected exchange (LC) functionals are capable of correcting the asymptotic decay of the exchange potential, and minimizing the overstabilization of fractionally charged fragments. Unfortunately, achieving the subtle balance between long-range exchange and dispersion correction is highly challenging.[1] With the objective of improving the description of pi-radical dimer cations, we follow the spirit of Chai and Head-Gordon[2], and propose a functional, which combines the global hybrid functional B97 jointly optimized into an LC functional augmented by our density-depdendent dispersion correction[3]. We expect the new approximation ωB97X-dDsC to provide accurate results on the challenging test-set Orel26rad[1] featuring mixed valence dimers as realistic models of organic electronics precursors.

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Computational Chemistry **CC28**

Implementation of exact and approximate methods for quantum molecular dynamics induced by the interaction with the electromagnetic field

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We have implemented a general split-operator algorithm of arbitrary order in accuracy for exact nonadiabatic quantum dynamics of a molecule interacting with a time-dependent electromagnetic field. Then, we have developped several approximations in this formalism: the Condon approximation, time-dependent perturbation theory, the rotating wave approximation, the separation of time scales, and the ultrashort and extreme ultrashort pulse length approximations. Furthermore, every possible combination of these generators has been tested. We present the theoretical treatments together with the numerical implementation for the exact solution and their approximations. Finally, numerical simulations on the well known four-dimensional vibronic coupling model of pyrazine are reported.

Computational Chemistry **CC29**

Perfomance of Dispersion-Corrected Atom-Centered Potentials: Non-equilibrium gas phase geometries and condensed matter systems.

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Van-der-Waals interactions play a crucial role in biological and pharmaceutically relevant systems. Unfortunately, standard density functional theory (DFT) calculations within generalized gradient approximations (GGA) fail to account for these weak interactions. In recent works, dispersion-corrected atom-centered potentials (DCACPs) have been developed to account for long-range dispersion forces between molecules within a DFT/GGA framework. DCACP are based on the idea of representing a non-local dispersion interaction potential as a sum of atom-centered semilocal potentials.

$$v_{\rm xc}^{\rm extended} = \; v_{\rm xc} + \textstyle\sum_{\rm I} v_{\rm I}^{\rm DCACP}(\mathbf{r},\mathbf{r'}) \qquad (1)$$

$$v_I^{\rm DCACP}(\mathbf{r},\mathbf{r'}) \;\; = \textstyle\sum_{\ell=0}^{\ell_{\max}} \sum_{m=-\ell}^{+\ell} Y_{\ell m}^I(\hat{\mathbf{r}}) p_\ell^I(r) \sigma_1 p_\ell^I(r') Y_{\ell m}^{I*}(\hat{\mathbf{r}}') \qquad (2)$$

where $r = r - R_I$ is the distance from the electron to the position of nucleus I, and $p_\ell^I(r)$ is the normalized projector, embraced by spherical harmonics. Such a choice of sets of functions has several advantages. First, separating variables reduces the computational cost of the non-local dispersion term from N^6 to N^3. Second, the exponential decay of projectors allows to introduce a cutoff on the radial grid, making calculations cheaper. Thirdly, as DCACP use only unoccupied channels in the Goedecker-Teter-Hutter (GTH) pseudopotentials, there is no necessity to modify the code, when planewave calculations are performed. Within this approach dispersion interactions can now be accurately described by DFT at the cost of roughly a standard GGA functional.

Here, we demonstrate that by adding more terms to the expansion (2) one can retrieve the correct R^{-6} asymptotics of the tail of the interaction curve. Additionally, we present results on the physisorption of organic molecules on gold surface and show that DCACP parameters can be determined as a functionals of electronic density.

Computational Chemistry **CC30**

Role of sampling in evaluating classical time autocorrelation functions

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We analyze how the choice of the sampling weight affects efficiency of the Monte Carlo evaluation of classical time autocorrelation functions. Assuming uncorrelated sampling or sampling with constant correlation length, we propose a sampling weight for which the number of trajectories needed for convergence is independent of the correlated quantity, dimensionality, dynamics, and phase-space density [1]. In contrast, it is shown that the computational cost of the "standard" algorithm sampling from the phase-space density may scale exponentially with the number of degrees of freedom. Yet, for the stationary Gaussian distribution of harmonic systems and for the autocorrelation function of a linear function of phase-space coordinates, the computational cost of this standard algorithm is also independent of dimensionality.

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Computational Chemistry **CC31**

DFT Study of Anion Transporters that Use Anion-π and Halogen Bond Interactions

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Compared to other non-covalent interactions, applications of the anion-π interactions and halogen bonds in organic and bioorganic chemistry remain still limited. The question whether these two interactions could be used to create interesting function such as transmembrane transport or sensing is quite attractive but also challenging.[1]

Modeling by DFT methods was undertaken in order to evaluate the ability of organic molecules such as naphthalenediimide (NDI) to transport anions through the membrane. Different electronic properties and namely the binding energies were evaluated by several density functionals. Anion-π interactions were also systematically modulated during the modeling via NDI core substitutions as well as by structural variations of N-aromatic moieties. The computational simulations demonstrated that anion-π interactions together with other weak non-covalent interactions account for function.[2]

DFT methods were also used to evaluate properties of organic molecules that can for the transmembrane transport put in work both interactions: anion-π as well as the halogen bond. The modeling of halogen bonded transporters was further extended to fluorinated alkanes, which can efficiently transport anions through the membrane exclusively by means of halogen bond interactions.[3]

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Computational Chemistry **CC32**

Modeling of an RNA hairpin that modulates the alternative splicing of SMN2: a gene involved in Spinal Muscular Atrophy

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Spinal Muscular Atrophy (SMA) is caused by mutations in the SMN1 gene, which disrupt the synthesis of SMN protein. SMN2, a gene 99% identical to SMN1 but with a different splicing pattern, can also produce SMN protein, although at lower levels. Manipulating the splicing of SMN2 to boost SMN production can compensate for the lack of SMN1. A number of cis and trans acting factors are known to regulate SMN2 splicing. However, the importance of RNA secondary structure in the processing of SMN2 transcripts has been poorly investigated. In this work, we study the role of a 19-nt RNA hairpin in the regulation of SMN2 alternative splicing. To do this, we have generated a battery of nucleotide substitutions in the sequence of such RNA hairpin; which negatively affect its formation, as confirmed by the base stacking sensor 2-amino purine (2AP) and circular dichroism. These changes can originate in some cases SMN2 splicing patterns similar to SMN1, and they proportionally improve the assembly of members of the splicing machinery to SMN2. To decipher the nature of the conformational changes induced by these nucleotide substitutions, and to identify which particular conformations can favor SMN2 splicing, we are currently modeling the folding of this RNA hairpin by in silico molecular dynamics (MD), both in its wild type and substituted forms. We believe that this comparative analysis will help understand the influence of RNA structure on the negative regulatory role played by this hairpin in SMN2 splicing.

Computational Chemistry **CC33**

Extending automatic peak-picking

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Peak peaking is pivotal for the automatic analysis of NMR spectra. Usually, peak-picking reduces to discriminating peaks from a noise threshold and is performed individually for each spectra. This task that is readily performed by an expert, can still be challenging for an algorithm and is certainly a bottleneck for automatic analysis, such as assignment or structure elucidation. Here we would like to extend the definition of peak-picking by appending a validation step that allows to weight or rank each peak according to their compatibility with all the available information, either from different spectra (redundancy) or from the knowledge of the experiment type (expertise) as proposed earlier for symmetrization purposes[1]. This approach guarantees that a peak is still the result of a significant observation: each peak detected at a certain position and with a certain signal to noise ratio (S/N) is further given a weight or confidence factor, determined by the *a priori* probability or expectation to detect a signal at that particular position based on information collected from other peaks within the same spectrum or within another one. For example an artefact in a proton spectrum, for which no corresponding peak is found neither in COSY nor in HSQC spectra will be poorly ranked despite its significant S/N ratio.
Implemented in a semi-automatic fashion, this allows to easily highlight "problematic" signals and ask for user intervention to resolve the issue. For fully automatic processes, this approach allows to only select peaks that can be trusted to a certain level of confidence.

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Computational Chemistry **CC34**

Accelerating Quantum Instanton Calculations of Kinetic Isotope Effects

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With the help of Feynman path integral formalism and Quantum Instanton approximation it is possible to compute rate constants of reactions for which quantum effects can not be neglected [1], while the procedure of thermodynamic integration with respect to mass allows to compute KIE's with efficient Monte Carlo (MC) integration procedures [2]. Going beyond standard methods, however, leads to significant increase in computational cost, mainly because MC integration has to be done over a configuration space of increased dimensionality. We accelerate these calculations using the following approaches. The first uses higher order Boltzmann operator splittings, allowing faster convergence to the quantum result [3]. The second uses advanced MC estimators decreasing the statistical error and hence the MC simulation length needed for a given precision [4, 5]. Here we combine these two procedures and test the new method on the model H+HH $\rightarrow$ HH+H rearrangement, its muonium and muonic helium analogues (studied by experimental and exact quantum methods at [6]) and the reaction C_2H_6+H $\rightarrow$ C_2H_5+H_2.

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Computational Chemistry **CC35**

Distinguishing Reaction Mechanism Pathways: Beyond Energy Profiles

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Electronic structure computations are often employed as a tool to deduce the mechanisms of reactions observed in the laboratory. Typically, the geometries and energies of various minima and transition states (TS) on a potential energy surface are identified, which yields the most favorable pathway, generally based upon the heights of relevant TS barriers. The situation, however, becomes unclear when different pathways cannot be differntiated solely based on a reaction's energy profile. Here, we use an unexpected Rh catalyzed C-H functionalization process to illustrate that interpreting reaction mechanisms using energy profiles determined by electronic structure computations is not always possible. Instead, a quantitative picture of intermediate and product evolution can be obtained using rate constants computed from Transition State Theory and numerically solving the kinetic differential equations in order to distinguish competing pathways.

Computational Chemistry **CC36**

A comparative study of DFT molecular and periodic calculations on small Iron complexes

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Complexes with a small number of Iron centres were studied through classical DFT molecular calculations and compared with analogous periodic DFT calculations and, where possible, with experimental data. The geometrical parameters, the values of some properties and the duration of the calculations were all taken into account in this study. The usefulness of the approximations used in doing these calculations was also taken into consideration. The LF-DFT method [1] is also explored for these systems as a cheap, but quite accurate, preliminary approach.

[1] M. Atanasov, C. A. Daul, C. Rauzy, A DFT Based Ligand Field Theory, *Structure and Bonding,* **2004**, *106*, 97-125.

Computational Chemistry **CC37**

Classical Molecular Dynamics on Rhodopsin

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Rhodopsin is a G-Protein Coupled Receptor (GPCR) that is present in the human eye. This receptor is part of the class A GPCRs and forms a template for hundreds of receptors that are included in class A. Hence, if the process of rhodopsin activation can be understood, it could provide new insight into the mechanism of activation of also other GPCRs besides rhodopsin. The receptor rhodopsin is built from: seven trans membrane domains, three intracellular loops, three extracellular loops, a C terminus, an N terminal domain and a retinal molecule that is covalently bound to the receptor in the active site. The retinal molecule has to be isomerised from a cis configuration to a trans configuration in order to induce a cascade of conformational and configurational changes, which will lead to the activated state of the receptor. In 2010, Neri *et al.* [1] published the process that was observed after single cis/trans isomerisation of one retinal moiety in a rhodopsin dimer. It was concluded that an indirect opening of the G protein interaction site occurred in the classical molecular dynamics simulations. However, when the human eye is exposed to light, it is also possible that instead of one retinal molecule, both retinal molecules are isomerised in a rhodopsin dimer. It is not known if the activation process that takes place during single retinal isomerisation also occurs when the rhodopsin dimer is doubly isomerised. In this project we focus on the rhodopsin dimer in order to compare both singly and doubly isomerised systems through classical molecular dynamics and to investigate the similarities and differences between the two processes.

[1] Neri, M. *et al. Biochem.* **2010**, *49*, 4827-4832.