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Electronic structure methods, developing molecular reaction dynamical methods

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Prof. González' current research focus is put at using highly accurate electronic structure methods, developing molecular reaction dynamical methods and interfacing both fields to achieve basic understanding of chemical processes and structure-function relationships as well as obtain quantitative predictions in molecules, biological systems and materials.

https://theochem.univie.ac.at/member/gonzalez

Microcanonical and finite-temperature ab initio molecular dynamics simulations on quantum computers

I. O. Sokolov[1], P. Barkoutsos[1], L. Moeller[1], P. Suchsland[1], G. Mazzola[1], I. Tavernelli[1]*

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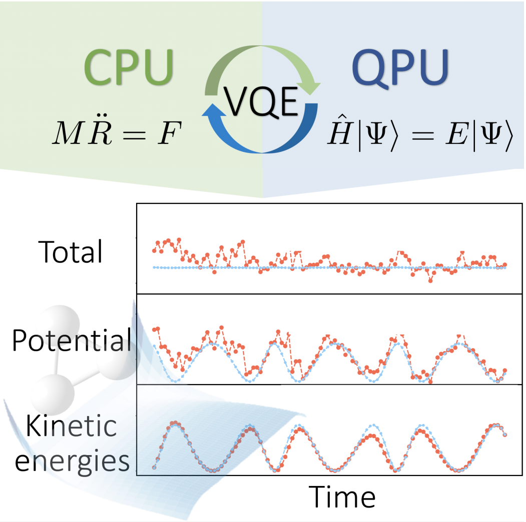
Ab initio molecular dynamics (AIMD) is a powerful tool to predict the properties of molecular and condensed matter systems. However, the quality of this procedure relies on the availability of rigorous electronic structure calculations. The development of quantum processors has shown great potential for the efficient evaluation of accurate ground and excited state energies of molecular systems, opening up new avenues for molecular dynamics simulations. In this talk, we address the use of variational quantum algorithms for the calculation of accurate atomic forces to be used in AIMD. In particular, we provide solutions for the alleviation of the statistical noise associated with the measurements of the expectation values of energies and forces, as well as schemes for the mitigation of the hardware noise sources (in particular, gate infidelities, qubit decoherence, and readout errors). Despite the relative large error in the calculation of the potential energy, our results show that the proposed algorithms can provide accurate MD trajectories in the microcanonical (constant energy) ensemble. Furthermore, exploiting the intrinsic noise associated to the quantum measurement process, we also propose a Langevin dynamics algorithm for the simulation of canonical, i.e., constant temperature, dynamics. Both algorithms (microcanonical and canonical) are applied to the simulation of simple molecular systems such as H_2 and H_3^+. Finally, we also provide results for the dynamics of H_2 obtained with IBM quantum computer ibmq_athens.



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Immersive Interactive Quantum Mechanics for Teaching and Learning Chemistry

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When learning chemistry, students are confronted with abstract chemical concepts that are often difficult to grasp. In fact, it is usually challenging to *intuitively* understand these concepts, because it is impossible to directly experience the molecular world with our human senses. Virtual (and augmented) reality technologies can offer a solution to this problem, in particular when based on a realistic quantum mechanical modeling, potentially in real time [1].

In this talk, we present an immersive learning setting based on an interactive exploration and manipulation of chemical systems, which are modeled in real-time with very fast quantum chemical methods. When manipulating a system, students get immediate visual and haptic (tactile) feedback; for this feedback to be perceived as fluent by humans, it needs to be delivered at a suitable frequency. This frequency can be as high as 1 kHz for haptic feedback. We review the algorithmic developments which were necessary to provide such a fluent feedback [2 - 6]. Finally, we showcase with a few prototypical examples how such a learning setting can offer students an intuitive understanding of core concepts of chemical reactions.

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AI guided synthesis of the GDB Chemical Space

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In previous work our group has exhaustively enumerated the chemical space of up to 11, 13, and 17 heavy atoms, the so-called generated databases (GDB). We have examined the synthetic feasibility of the GDB chemical space using computer aided synthesis planning. One of the approaches developed by the group in collaboration with AstraZeneca is AiZynthFinder, an open-source template based retrosynthetic planning tool. As the GDB project aims to tackle low molecular weight compounds in likeness to building blocks, we have augmented the underlying reaction datasets, built domain specific models such as for ring formations, and developed a rapid scoring methodology with uncertainty calibration to assess at scale which GDB molecules have potential to be synthesised in the wet lab.

Preliminary findings have shown that retrosynthetic routes can be found using AiZynthfinder for ca. 20 % of the compounds from a subset of GDB17 called GDBChEMBL displaying ChEMBL-like properties. We have expanded on these findings by using information about the predicted routes as training data for a machine learning based classifier capable of determining whether a synthetic route can be found for a given compound using AiZynthfinder or not, named the retrosynthetic accessibility score (RAscore). The RAscore has been trained on compounds from the ChEMBL database to make it generally applicable, and a more specific GDB based score has also been trained to demonstrate utility in domain-specific cases. RAscore presents a distinct advantage compared to running full retrosynthetic analysis on large sets of compounds, and computes at least 4500 times faster, enabling synthetic feasibility prediction to be conducted at scale, for instance in the virtual screening of databases of bioactive compounds.

In order to aid exploration of the GDB chemical space, the results are available to browse in a web-interface allowing for searching selected subsets, viewing synthetic routes, examining the building blocks used, and for which synthesis. We hope this will facilitate interest from our experimental counterparts and provide a tool for computational chemists to bridge the gap between simulation and the wet-lab.

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Neural networks meet non-covalent interactions: Chalcogen bonding in a solution

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Reliable description of competing non-covalent interaction represents a long-term goal of quantum chemistry. To overcome the shortcomings of static computations in implicit solvent, it is necessary to run molecular dynamics (MD) simulations of explicitly solvated system. However, *ab initio* MD is often prohibitively expensive for large scale simulations.

Herein we present a simulation protocol based on Neural Network Potentials (NNPs) [1] that reproduce the hybrid DFT energies and forces. While this approach has been increasingly used for studying solid state systems with low chemical complexity, its application for solvated molecular systems with many elements remains scarce. [2] In this work, we study the complex of 4,5,6,7-tetrafluorobenzo-2,1,3-telluradiazole and Cl^- solvated in tetrahydrofuran. This system contains two competing weak interactions, a chalcogen bond and anion-π, which are important in the supramolecular chemistry, organocatalysis and anion recognition.

We train two sets of NNPs: one using the periodic GFN0-xTB semiempirical Hamiltonian [3] as a cheap baseline potential, and second directly reproducing the DFT data. We observe a significant improvement of the free energy profile compared to the Amoeba polarizable force field. Moreover, we show that the baselined NNPs are more robust than the direct NNPs. Our approach demonstrates the importance of accurate DFT-based potentials and enhanced sampling techniques in the description of weakly bonded systems in solution.

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Osmotic transport at the aqueous graphene and hBN interfaces: scaling laws from a unified, first principles description.

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Novel liquid and charge transport behaviour can emerge in nanofluidics depending on the molecular-level interactions at aqueous interfaces, and provide new venues for water desalination and "blue'' energy conversion. Improving on our molecular-level picture of the interfacial structure of water and electrolyte solutions, provided by the so-called electric double layer (EDL), is key to further our understanding of osmotic transport in nanofluidics. Yet, a molecular-level picture of the EDL is to a large extent still lacking. Particularly, the role of the electronic structure has not been considered in the description of the diffuse layer. Here, we report enhanced sampling simulations based on ab initio molecular dynamics, aiming at unravelling the free energy of prototypical ions adsorbed at the aqueous graphene and hBN interfaces, and its consequences on nanofluidic osmotic transport. Specifically, we predicted the zeta potential, the diffusio-osmotic mobility and the diffusio-osmotic conductivity for a wide range of salt concentrations from the water and ion spatial distributions through an analytical framework based on Stokes equation and a modified Poisson-Boltzmann equation. Concentration-dependent scaling laws are observed, together with dramatic differences in osmotic transport between the two interfaces, including diffusio-osmotic flow and current reversal on hBN, but not on graphene. We could rationalize the results for the three osmotic responses with a simple model based on characteristic length scales for ion and water adsorption at the surface, which are found to be quite different on graphene and on hBN. Our work provides first principle insights into the structure and osmotic transport of aqueous electrolytes on two-dimensional materials and explores new pathways for efficient water desalination and osmotic energy conversion.

Unravelling the Impact of Halogen Bonds in Medicinal Chemistry with QM calculations

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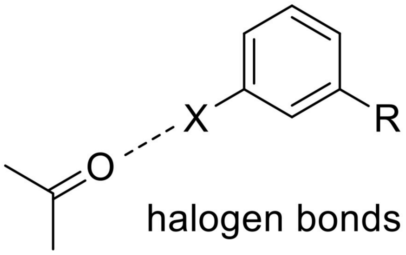
For the last decade medicinal chemists were challenged by increasingly difficult targets to discover new, potent drugs. These oftentimes deemed “undruggable” targets, nonetheless, share some features that make working on them worthwhile: i) they modulate disease relevant pathways in a way that could lead to new therapies, ii) it can be hard to achieve potent molecules, while keeping the required properties in check and iii) most importantly for a scientist, we are constantly expanding our knowledge to also apply unconventional methods in our day-to-day drug design process.



One of these more unconventional methods is to look for uncommon interactions in highly-resolved ligand–protein crystal structures, such as halogen bonds, and use quantum mechanical calculations to uncover different substitutions to increase the halogen bonding potential. Here we describe a specific ligand–protein halogen bond that (significantly) contributes to the ligand–protein interaction, and its incorporation into our ligand design.

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Pushing the limits of the Density Matrix Renormalization Group: from vibrational spectroscopy to quantum dynamics

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Simulation methods based on tensor factorizations, such as the density matrix renormalization group (DMRG) [1,2], are currently reshaping the limits of wave function-based quantum chemical algorithms. Tensor-based methods provide very compact parameterizations that can encode many-body wave functions by taming the high computational cost of Full Configuration Interaction and, therefore, enable large-scale exact quantum simulations. Chemical applications of DMRG have focused so far on time-independent electronic problems. In the present contribution, we show the potentiality of DMRG beyond this application field, by focusing on three simulation targets.

We first introduce the vibrational DMRG theory [3,4] to calculate the exact anharmonic vibrational energies of large molecular systems. Then, we apply DMRG to solve the time-dependent (TD) Schrödinger and show that the resulting algorithm, namely TD-DMRG [5,6], can accurately simulate ultrafast molecular processes occurring on multiple time-scales. Finally, we present an explicitly correlated DMRG variant, the transcorrelated DMRG (tc-DMRG) [7] that relies on the transcorrelated method [8] and enhances the accuracy of conventional DMRG for strongly-correlated molecules.

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How important are the residual nonadiabatic couplings for an accurate simulation of nonadiabatic quantum dynamics in a quasidiabatic representation?

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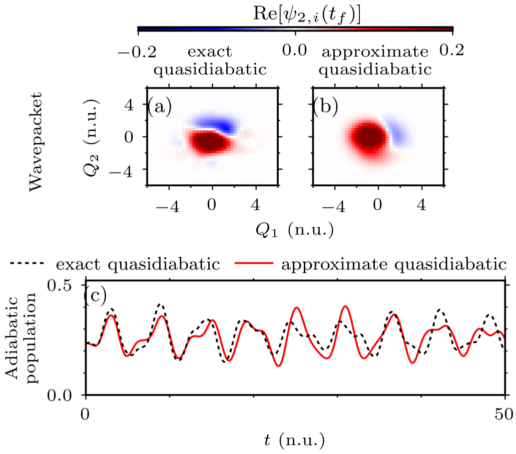
Diabatization of the molecular Hamiltonian is a standard approach to remove the singularities of nonadiabatic couplings at conical intersections of adiabatic potential energy surfaces. In general, it is impossible to eliminate the nonadiabatic couplings entirely—the resulting “quasidiabatic” states are still coupled by smaller but nonvanishing residual nonadiabatic couplings, which are typically neglected. Here, we propose a general method for assessing the validity of this potentially drastic approximation by comparing quantum dynamics simulated either with or without the residual couplings [1,2]. To make the numerical errors negligible to the errors due to neglecting the residual couplings, we use the highly accurate and general eighth-order composition of the implicit midpoint method [3,4]. The usefulness of the proposed method is demonstrated on nonadiabatic simulations in the cubic Jahn–Teller model of nitrogen trioxide and in the induced Renner–Teller model of hydrogen cyanide. We find that, depending on the system, initial state, and employed quasidiabatization scheme, neglecting the residual couplings can result in wrong dynamics. In contrast, simulations with the exact quasidiabatic Hamiltonian, which contains the residual couplings, always yield accurate results.



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Unravelling heavy-atom quantum tunnelling in spin transitions

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Intersystem crossing reactions involving the transition between electronic states of different spin are as essential as they are ubiquitous in nature. However, while within the last two decades multiple highly accurate spectroscopic methods have emerged that allow for time-resolved imaging of such reactions, their correct theoretical description still poses a major challenge. This fact often manifests itself in widely varying results for even the simplest molecular systems casting doubt on the validity of the underlying theory.

In a study of thiophosgene, a molecule that has drawn much attention from both experimentalists and theoreticians, we employed our recently extended golden-rule instanton theory[1] in conjunction with on-the-fly multiconfigurational electronic structure calculations in order to describe the occurring spin transition. It has been shown that heavy-atom quantum tunnelling speeds up the intersystem crossing by multiple orders of magnitude even at room temperature. The theory does not only provide results in excellent agreement with experiment, but, as opposed to methods based on wavefunction overlaps, also allows for direct and easily accessible insight into the reaction mechanism by locating the ''ideal tunnelling pathway'' or *instanton*. The trajectory on the product surface thereby travels at **negative** temperature or alternatively in negative imaginary time leading to an interpretation equivalent to that of particle-antiparticle annihilation. A substantial change in the reaction pathway of thiophosgene at low energies due to strong corner cutting reveals why previous one-dimensional tunnelling studies of the molecule were unable to capture the full picture of this reaction[2].

The generality and computational efficiency of the theory enables to describe nuclear tunnelling effects not only in spin transitions but also in electron-transfer reactions, light-matter interactions, electrochemistry and many other fields even for larger compounds relevant for example in organic synthesis as depicted in Figure 1.

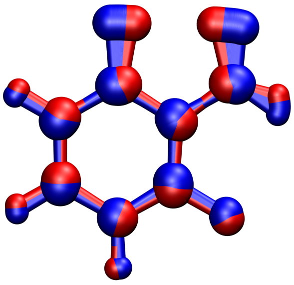

Figure 1: Instanton pathway for the cyclization of a triplet-phenylnitrene to a singlet-benzisoxazole at 50 K. The degree of delocalization indicates the amount of tunnelling the atoms undergo. The trajectories on the triplet and singlet surface are indicated in blue and red respectively.

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ΔSCF for Efficient Nonadiabatic Molecular Dynamics in Condensed Phase Systems

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Accurate calculation of excited electronic state properties in the condensed phase systems represents the main bottleneck for efficient application of semiclassical nonadiabatic molecular dynamics (NA-MD) methods for investigation of nonadiabatic processes in the condensed phase taking place after photoexcitation. A variational delta self-consistent field (ΔSCF) density functional theory (DFT) based method represents a potential approach to address the aforementioned constraints in addition to perturbative time-dependent density functional theory (TD-DFT). We applied a restricted Kohn-Sham formulation of ΔSCF with constrained and rounded occupation numbers for NA-MD and employed TD-DFT to aid in excited state SCF convergence and provide guess electronic state densities.[1] By utilizing the combined Gaussian and plane waves approach with periodic boundary conditions the method is easily applicable to full atomistic DFT simulations of condensed phase and it can be combined with subsystem density embedding to further expand its capabilities. This enables targeted modeling of specific excited states in the manifold of dense electronic transitions, as usually encountered in condensed phase systems, without compromising any accuracy in the description of the chromophore–environment interaction. We applied it to study the nonradiative deactivation mechanism of photoexcited diimide in water solution, and show the advantages and disadvantages of such a pragmatic new technique for efficient simulation of nonadiabatic processes in the condensed phase.[2] By expanding the excited electronic state density into a linear combination of singly excited ground state determinants, spin-orbit coupling terms can be easily evaluated and the NA-MD expanded with intersystem crossings between singlet and triplet states.

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The Challenge of Accurate Computation of Two-Photon Absorption Properties of Organic Chromophores in the Condensed Phase

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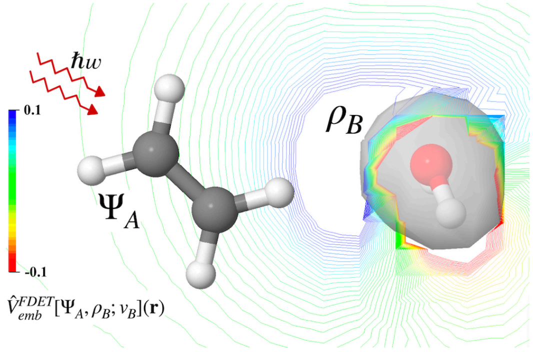
Two-photon absorption (TPA) spectroscopy offers a broad area for applications. It makes it possible to observe dark states, for which the dipole transitions are not permitted. The computation of TPA cross sections depends not only on one excited state but all the excited states according to the sum-over-states expression thus remaining a big challenge nowadays. Two strategies are applied to evaluate the effect of the environment on the TPA cross sections for two characteristic excited states of C_2H_4 upon complexation with H_2O. The supermolecular strategy provides the reference complexation-induced shifts and uses either the EOM-CCSD or ADC(2) method. The embedding strategy is based on frozen-density-embedding theory[1] (FDET) and uses only fundamental constants. The TPA cross sections from high-level supermolecular calculations are extremely basis-set-sensitive. Literature data and the present study indicate that accuracy of the absolute TPA cross sections below 100 atomic units and their shifts below 10 atomic units remains a challenge. The obtained FDET results show a similar basis-set behavior. For the largest basis set (d-aug-cc-pVQZ), TPA cross sections obtained from these two strategies are in excellent agreement. The complexation-induced shifts have the correct sign of the effect and a small (12−33%) relative error in magnitude[2]. The deviations of the FDET-derived shifts from the reference are of similar magnitude as the reliability threshold of the reference shifts.



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Instanton Theory Beyond Golden Rule: Three-state System

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Fermi's Golden Rule (FGR) is widely used for calculating rates of chemical processes ranging from photon absorption/emission, nuclear decay, nonadiabatic dynamics, scanning tunnelling microscopy, electron transfer, among others. In the context of nonadiabatic processes, we have recently shown that FGR can be applied within the semiclassical framework of instanton theory, with the major highlight being the inclusion of tunnelling while still using classical trajectories.

FGR has its limitations, one of them being that it cannot account for cases that involve a third state in the dynamics. Examples of such processes include long-range electron transfer in molecules and tunnelling via quantum dots and nanowires, both of which are seen as potential candidates for single-electron transistors. Additionally, spectroscopic processes like Raman spectroscopy also involve intermediate virtual states in their mechanisms.

We present an application of instanton theory using an extension of FGR for the case of a three-state system, where initial and final states are coupled via a third bridge state. Analogous to the two-state FGR case, this leads to a rate theory that gives us a simple, elegant and intuitive picture of what happens during long-range tunnelling.

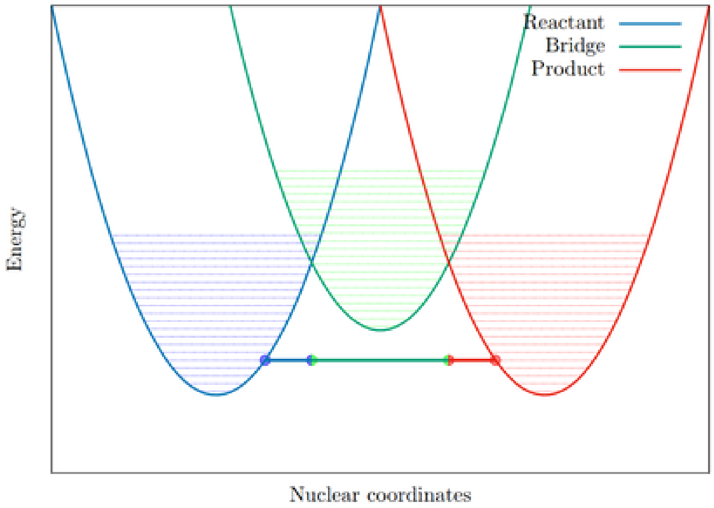

Figure 1: A simple model system where the reactant, bridge and product potentials are harmonic. The vibrational levels of each PES is given by dotted lines of the same colour. The instanton is given as a straight, solid horizontal line at ordinate equal to its energy. The dots on the instanton represent, from left to right, the turning point on the reactant PES, the hopping point between the reactant and bridge PES, the hopping point between the bridge and product PES and the turning point on the product PES.

Combining accuracy with linear-scaling efficiency: energies and nuclear gradients for a variational formulation of the Harris functional as correction to sub-system DFT

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We present an electronic structure method that combines the high accuracy of the Harris functional approach [1], which differs from the exact total energy only in second order deviations of the electron density, with the computational efficiency of block-sparse linear-scaling sub-system DFT [2]. The new method allows for simulations of the same accuracy as conventional Kohn-Sham calculations at near linear-scaling efficiency. The non-self-consistent nature of the Harris functional has been remedied by constructing a Lagrangian function which restores the variational condition by imposing stationarity with respect to the input density [3-5]. Nuclear gradients are then formulated as derivatives of the variational Lagrangian, allowing for ab-initio molecular dynamics simulations and the calculation of other properties. Embedded in the CP2K program package [6], our new implementation enables the treatment of periodic systems comprising molecular solvents, ionic liquids, and deep eutectic solvents.

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Diffusio-osmotic transport of hydrophobic solutes and slippage opacity of two-dimensional materials

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Surface-driven flows may contribute tremendously to the blue energy harvesting. In this work we establish a connection between the wetting properties of water in contact with different 2D materials and their heterostructures, and a diffusio-osmotic coefficient. By using a model [1] developed to describe hydrophobic hydration at the interface, we extract the potential of mean force (free energy of hydration) from 9 AIMD simulations: water on graphene, h-BN, MoS_2, and on their bilayer combinations with each other. We show, that the diffusio-osmotic coefficient of water transport on heterostructures is mainly dominated by the top layer in contact with water, and remains the same with adding a second layer of the same or different kind underneath.

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Optimal tunneling pathways for proton-coupled electron transfer reactions

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Nuclear quantum effects are essential for reliably predicting rates of hydrogen and proton transfer reactions. Semiclassical instanton theory locates the optimal tunneling pathway on the full, multidimensional potential energy surface (PES) and therefore constitutes a powerful tool for the prediction of accurate rate constants [1]. Recently, an instanton formulation of Marcus-Levich-Jortner theory has been introduced which extends the scope of the method to electron transfer reactions in the presence of a harmonic bath, subject to the golden-rule limit of small coupling between the PES involved in the transfer [2,3]. Importantly, golden-rule instanton theory is valid both in the normal as well as in the inverted Marcus regime.

Here, we report the application of golden-rule instanton theory to proton-coupled electron transfer (PCET) reactions. We predict rates, bath activation energies and optimal tunneling pathways for a variety of one- and two-PCET processes by optimising the instanton *on the fly*, employing accurate electronic structure methods for the underlying PES. Contrary to other approaches, our calculations can unravel the reaction mechanism on the full-dimensional PES without any need for further approximations. Changes in the optimal tunneling path as a function of temperature can easily be observed. Hence, next to predicting the reaction rate and activation energies, our *on-the-fly* instanton calculations also provide fundamental insight into the mechanistic aspects of PCET by explictly taking temperature-dependent tunneling effects into account.

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Solvation Free Energies from Subsystem Density Functional Theory with Sampling

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Solvation effects on chemical processes in the condensed phase are critical for chemical reactivity. The scope of available strategies attempting to describe such effects reflect their importance; they comprise, e.g., implicit continuum solvation [1], molecular dynamic simulations [2], and explicit quantum mechanical description of solute-solvent interactions within a continuum model [3]. The former lacks description of directed interactions, whereas the latter two are either computationally costly or exposed to biased assumptions on the local solvent orientation.

Here, we present a new hybrid ansatz [4] using subsystem density functional theory [5] and a conductor-like polarizable continuum model [6] to quantify solute-solvent interactions. To determine the solvation energies, different sampling approaches are analyzed and compared. These include static sampling where configurations are obtained from incremental and systematical addition of solvent molecules to a solute-solvent complex [7] and dynamic sampling where configurations are taken as snapshots from a molecular dynamic simulation. Both are performed in an automatic and systematic fashion, eliminating any bias concerning the local solvation environment of the solute.

The sampling approaches allow for error estimation of the mean solvation energies of an ensemble of configurations which is usually not by default included in implicit solvation approaches. We evaluate the quality of our hybrid ansatz and the sampling approaches by comparing calculated activation barriers of reactions in different solvents to experimental results and implicit approaches.

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Rapid screening of nanopores in graphene for light hydrocarbons separation

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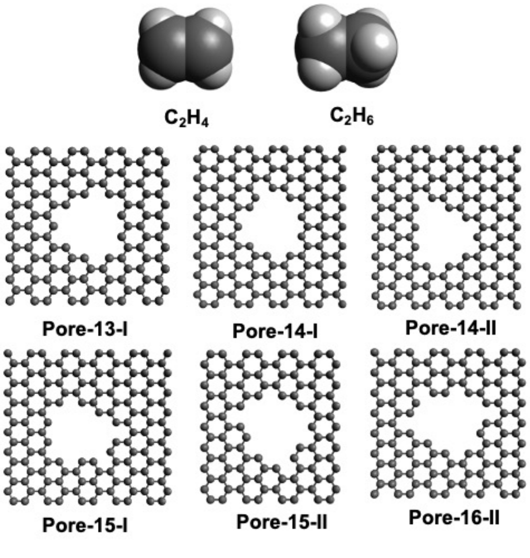
Ethylene (C_2H_4) is a critical to the chemical industry and is used in a wide range of sectors such as synthetic fibers, synthetic rubbers, synthetic plastics and agriculture, with annual production of 150 million tons. Ethylene is produced by steam cracking where ethane (C_2H_6) is also co-produced. Nevertheless, high purity ethylene (>99.5%) is required to be used for high grade polymerisation. However, separating C_2H_4 from C_2H_6 is inherently challenging given their similar size, chemical and physical properties. Currently, C_2H_4/ C_2H_6 separation is done using energy-intensive cryogenic distillation, representing 0.3% of the total world energy consumption.[1] Membranes have been considered as an attractive alternative to distillation; however, they are still not used for this separation due to their low performance. Due to its atomic thickness and mechanical strength, nanoporous single-layer graphene is regarded as the ideal membrane. If the right size of nanopores can be successfully etched in graphene, it will be possible to achieve this separation by the molecular-sieving mechanism with attractive selectivity. However, predicting the right pore-size distribution is challenging on the theoretical front. Given the large number of possibilities for nanopores in graphene, the screening of nanopores for this separation by molecular dynamic simulations is challenging.[2] Here, using a rapid screening method, we identified shape and size of nanopores to achieve C_2H_4/C_2H_6 separation.[3] We witnessed a range of 3 missing carbon atoms, highlighting the potential of nanoporous single-layer graphene for light hydrocarbon separation. Using this catalogue of selective nanopores, it is possible to plan experiments accordingly and thus, achieve light hydrocarbon separation at the lab scale.



Selective nanopores for C_2H_4/C_2H_6 separation screened using the 3D Visualization method. Top: Van der Waals representation of light hydrocarbons. Bottom: screened selective nanopores. Nanopores were named as follow: Pore-Y-X, where Y is the number of missing carbon atom and X is the probability rank of the nanopore isomer reported by Rajan et al.

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Unprecedented Water-Assisted Chemical Route Towards the Oxygen Evolution Reaction at the Hydrated (110) Ruthenium Oxide Surface: heterogeneous catalysis via DFT-MD & metadynamics simulations

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The biggest (or one of the biggest) issue that the world human population faces in this and the next century is the urgent need for clean and renewable technologies. Herein, spin-polarized Density Functional Theory Molecular Dynamics (DFT-MD) simulations, coupled with advanced enhanced sampling methods in the well-tempered metadynamics framework, are applied to gain a global understanding of RuO_2 aqueous interface in catalyzing the Oxygen Evolution Reaction (OER), and hence possibly help in the design of novel catalysts in the context of photochemical water oxidation. Notwithstanding RuO_2 is one of the most active catalyst toward OER, a plethora of fundamental details on its catalytic properties are still elusive, severely limiting its large-scale deployment.

An atomistic understanding of structural, electronic and mechanical properties bulk rutile RuO_2 and explicit solvent effects on (110)-RuO_2 facet are provided in the context of (photo)electrochemical conditions. We focus on the comprehension of the mechanistic interplay between surface wettability, interfacial water dynamics and surface chemical activity. Moreover, we provide a dependence of physical and chemical properties, such as surface electric field and work function, from different degrees of surface wettability of the (110)-RuO_2 facet.

Furthermore, the present study quantitatively assesses the kinetics, thermodynamics and the involved energies behind the OER at the (110)-RuO_2 catalyst surface revealing plausible pathways composing the reaction network of the O_2 evolution in both gas-phase and explicit solvent model. Albeit a unique efficient pathway has been identified in the gas-phase OER, a lowest-energy-requiring reaction route is possible when (110)-RuO_2 is in contact with liquid water. By estimating the free-energy surfaces associated to these processes, we reveal an unprecedented water-assisted OER mechanism which involves a crucial proton-transfer-step assisted by the local water environment making the OER a spontaneous process, i.e. no overpotential is required.

These findings pave the way toward the systematic usage of those techniques for the fine assessment of the activity of catalysts, fully including the entropic contributions due to finite-temperature and explicit-solvent effects. The proposed study will be embedded into the "Solar light to chemical energy conversion" priority research program at the University of Zurich, *LightChEC* consortium (*www.lightchec.uzh.ch*).

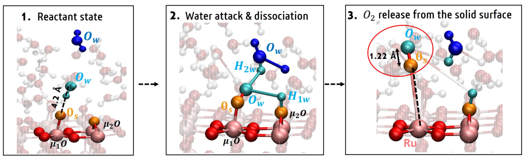

Fig. Water-assisted OER mechanism at the (110)-RuO_2 facet in explicit solvent model.

An implementation of Nuclear Velocity Perturbation Theory using a combined Gaussian and plane wave basis set

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Infrared spectroscopy in general and vibrational circular dichroism experiments in particular are invaluable tools for characterizing chiral systems. Using the Born-Oppenheimer (BO) approximation and density functional theory, the electric dipole moment derivatives (the atomic polar tensors or APTs) can be recovered by a perturbative treatment in which the solution of a set of coupled perturbed equations is required. In this way the dipole strengths of vibrational modes can be computed. The magnetic dipole moment derivatives (the atomic axial tensors or AATs) on the other hand are not accessible in this approach because the expectation value of the current density vanishes in the BO approximation.

A possible solution for this problem is the introduction of the complete adiabatic (CA) approximation. In this case the Hamiltonian operator includes the perturbation of nuclear velocities leading to the exact factorization of the nuclear and electronic wave functions. These CA wave functions can be combined with the velocity representations of the electric and magnetic dipole operators in order to compute APTs and AATs as well as the rotational strengths of vibrational modes. We implemented the nuclear velocity perturbation theory in the CP2K code package, which allows for efficient and accurate electronic structure calculations. The calculations combine an atom-centered Gaussian basis set with a basis of plane waves. Additionally, non-local pseudo potentials are used for the description of core electrons. We present our implementation and its application to chiral systems.

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Chemical Concepts in Automated Reaction Network Exploration

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Chemical concepts are a powerful tool for understanding chemical processes. Besides their descriptive and categorizing value, they could also be helpful for reactivity predictions, *i.e.*, to judge upon the feasibility of reactions based on information evaluated for the reactants only.

However, it is not clear to what extent such predictive power exists [1]. Automated reaction network exploration algorithms [2, 3] may help to produce the data for the extensive statistical analyses that are necessary to answer this question [1].

We have put forward the idea to guide the exploration of reaction networks based on first-principles heuristics [4, 5]. If a prediction protocol based on chemical concepts, evaluated from the electronic structure of reactants, proves to have a certain degree of reliability – even if it is only to rule out clearly unreactive reaction coordinates – it would be a promising tool to be applied in this context [1].

Hence, there is a mutual relationship between reactivity predictions based on chemical concepts and automated reaction network exploration, on which we will further elaborate in this presentation.

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Fast prediction of correlation energies for Møller–Plesset perturbation theory: atomic contribution model and machine learning

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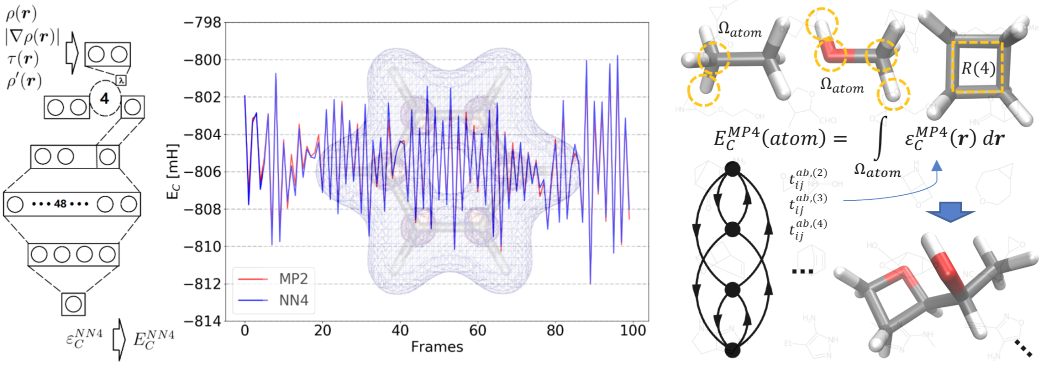
Various post-Hartree–Fock methods have been adopted to calculate correlation energies of chemical systems, but time complexity usually prevents their usage in large scale. We propose a density functional approximation, based on an artificial neural network consisting of recursive layers, on a newly introduced descriptor "orbital energy weighted electron density", which can be readily employed to produce results comparable to 2nd order Møller–Plesset perturbation (MP2) ones. Various systems have been tested and the transferability across basis sets, structures, and nuclear configurations has been evaluated. Moreover, a concise and fast model for the fast estimation of dynamic correlation energy is introduced. Dynamic correlation energy calculated by up to 4th order Møller–Plesset perturbation (MP4) theory can be predicted with 0.16 % error using only 1.3 % of the dataset as reference/training data.



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Tailoring absorption and fluorescence spectra for nanoporous materials

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State-of-the-art computational approaches to describe photophysical and photochemical processes in extended materials most often rely on linear response time-dependent density functional theory, representing a well-established tool which is feasible and robust to enable broad applications[1]. However, when aiming for high-throughput screening on the large scale, the computation of excited-state properties becomes tedious as it is in comparison to ground-state properties theoretically more challenging, requiring an accurate description of exact exchange, as well as computationally more demanding, exhibiting a less favorable scaling and thus higher computational cost. Aiming for a pragmatic and efficient pre-screening tool for the large-scale characterization of porous materials, we propose a combined hybrid functional and semi-empirical tight binding scheme exploiting the concepts of the auxiliary density matrix method (ADMM)[2] and the simplified Tamm-Dancoff approximation (sTDA)[3]. Among the existing techniques to improve the unfavorable basis-set dependence of exact Hartree-Fock exchange, ADMM has proven to be a reliable approach to achieve significant speedups without significant accuracy loss, being based on the idea of constructing an auxiliary density matrix for the evaluation of the exact exchange term and correcting the thereby introduced error by a density functional contribution. The setup for the reference ground-state treatment is complemented by employing the sTDA tight binding ansatz for the excited state: sTDA relies only on global, atom-specific parameters requiring no pair-wise or bond-specific parameterizations while being at the same time computationally cheap and physically reasonable. It employs semi-empirical electron-repulsion operators but keeps or even improves the description of the long-range electrostatic interactions. The implementation of the combined hybrid-ADMM and sTDA approach in CP2K[4] is benchmarked for a series of covalent organic frameworks and results regarding the description of absorption as well as fluorescence spectra are presented assessing the performance for excited-state gradients, adiabatic excitation energies and corresponding spectra.

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Predicting Enzymatic Reactions with a Molecular Transformer

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The implementation of biocatalytic steps in synthetic processes remains challenging because it is very difficult to predict whether a particular substrate might actually be converted by an enzyme to the desired product. Computer-assisted synthetic planning (CASP) comprises a range of artificial intelligence approaches to predict reaction products from reactants or reagents, or vice-versa, and to plan retrosynthesis[1]. Here we asked the question of whether CASP might be exploited to predict the outcome of enzymatic reactions for organic synthesis.

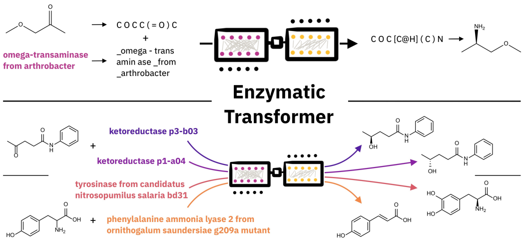

Figure 1. General concept of the Enzymatic Transformer training.

We set out to use multi-task transfer learning combining the 1 million USPTO reaction dataset as a source of general chemistry knowledge with 32.000 enzymatic reactions collected from the scientific literature as a source of specialized knowledge (Figure 1). Such transfer learning strategy was recently shown to enable the Molecular Transformer[2] to predict complex regio- and stereo-selective reactions at the example of carbohydrates[3]. One of the novelties of this work is that we combined SMILES language for the substrates with human language for the enzyme descriptions[4]. Hence, Enzymatic transformer not only learns to interpret the SMILES language but also natural language, as used by human experts to describe enzymes and their mutations. We obtained 62% accuracy when using multi-task transfer learning based on the full description of the enzymes. However, model performance was limited by database size and was lower with enzymes for which only few examples were available. Furthermore, analysis of successes and failures showed that model performance is also limited by the occurrence of database entry errors. Model performance can probably be increased by using larger and higher quality training dataset. However, our approach should be generally useful to develop models capable of assisting chemists in implementing biotransformations for chemical synthesis.

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Evaluating Quantum Mechanical Tunnelling Splittings with Instanton Theory

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Instanton theory is a semiclassical approximation to the path-integral formulation of quantum mechanics. This theory allows for a description of quantum tunnelling in terms of dominant tunnelling pathways. Application of the aforementioned theory allows us to obtain a computationally efficient method of computing reaction rates and tunnelling splittings in molecular systems.[1,2] Additionally, in combination with machine-learning approaches[3,4] and a divide-and-conquer algorithm for evaluating fluctuations along the instanton pathway[7], the approach becomes less computationally demanding and is numerically stable even at very low temperatures. We have previously developed a semiclassical instanton formulation to compute tunnelling splittings wherein the local minima in the two wells have the same energy, but the widths differ slightly.[5] Recently, by making use of the projected flux correlation function, we have been able to extend our method such that we are able to evaluate tunnelling splittings not only for systems wherein the two wells have differing widths, but also for a 'true' asymmetric system wherein the energies of the wells themselves also differ slightly.[6] In addition to this, we are further developing the current theory such that we can also evaluate tunnelling splittings of vibrationally-excited states. We shall demonstrate this by benchmarking our method using a set of one- and two-dimensional models, for which our results compare favourably with numerically-exact quantum mechanics. Additionally, we also demonstrate the results of our method for some multidimensional systems (e.g. Malonaldehyde and its various isotopically-substituted versions).

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A novel quantum-classical approach to electronic nonlinear spectroscopy

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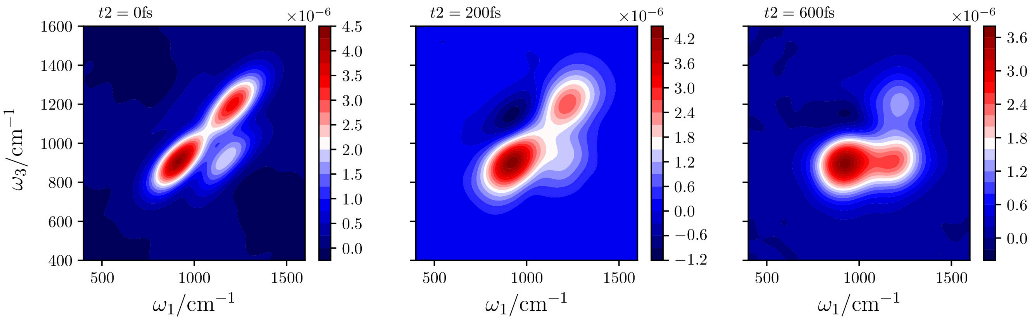
Nonlinear spectroscopy offers a powerful tool for investigating microscopic quantum dynamics. However such quantities are often challenging to obtain theoretically for complex condensed phase systems, due to the large number of degrees of freedom.

For nonadiabatic systems, computationally cheap semiclassical approximations for the full electron-nuclear dynamics can be derived with the use of mapping variables [1,2]. Within these approaches the electronic subsystem is mapped exactly onto a fictitious system, which has a well-defined classical limit. The dynamics associated with the mapped system is then described by an ensemble of classical trajectories. In particular, we have recently developed a new classical-trajectory mapping-based technique, called spin-PLDM [3], which is able to obtain the relatively short time quantum dynamics extremely accurately, does not suffer from over-damped coherences and can be applied to calculate both single and multi-time correlation functions. These characteristics make it ideally suited for obtaining optical response functions.

In this poster, we will show how spin-PLDM can be applied to accurately and efficiently compute the various optical response functions that contribute to the nonlinear electronic spectra of nonadiabatic condensed phase systems, such as a Frenkel biexciton model and the Fenna-Matthews-Olsen complex. Because each optical response function is calculated independently within our approach, contributions from different dynamical pathways can be separated from the full signal, giving further insight beyond what can be achieved directly from experiment.



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Tailored Coupled Cluster Theory in Varying Correlation Regimes

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[1]Laboratory of Physical Chemistry, ETH Zurich, [2]Universität Wien, Institut für theoretische Chemie

We present a comprehensive study[1] of the tailored coupled cluster (TCC) approach[2,3], based on hydrogen model systems. The TCC method allows the treatment of strongly correlated systems by replacing amplitudes in the single reference coupled cluster wave function with amplitudes from a previous active space calculation. The inclusion of fixed amplitudes from a multi-configurational calculation causes the TCC wave function to be symmetry broken and no longer size consistent. In our work we investigate these issues by employing the electronic energy, as well as the overlap with the full configuration interaction as diagnostics based on different reference wave functions. We find that utilizing the determinant with the highest weight in the active space provides the best choice as reference by reducing the error originated by the symmetry breaking. Since the quality of the amplitudes from the active space depends on its size, we apply active spaces of different size. We observe that TCC yields the best results by including all orbitals with a large single-orbital entropy in the active space. Additionally, the size-consistency error of TCC can be decreased by increasing the number of orbitals in the active space.

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Real-Time Haptic Chemistry: Dive Hands-First into the Molecular World

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The concept of real-time quantum chemistry (RTQC) was introduced for the first time by Haag and Reiher in 2012 [1]. This opened the floor to novel ways in which we as chemists, but also as learners can interact with molecular systems. Before then, interactive chemistry was usually done based on force fields. The quantum aspect of the molecular world couldn’t be grasped. With the introduction of concepts such as the mediator potential, we can now feel forces based on semi-empirical calculations even for large systems and without any time delay [2]. The idea is simple: In the background, an electronic structure calculation is performed continuously with a new one starting every time one is finished. From the results, a potential well is created based on their energy, gradients and atomic second derivatives. Until the next electronic structure calculation based on new positions is finished, the mediator potential delivers feedback to the user in real time. This does not have to be only visual feedback, but can also be force feedback. While manipulating a structure by dragging an atom across the screen, the user can feel the force operating on the atom. This application has been demonstrated to be useful for research in computational chemistry [3,4].

In the presented project, this concept of RTQC is used in the development of learning tasks that should help students understand concepts such as potential energy surfaces, activation barriers, or reaction mechanisms. It has been hypothesized that one reason why chemistry is a hard field to study is the multiple levels of understanding involved [5]. Any observation in the laboratory can be explained by considering the reactions occurring, the molecules present, the conditions of the environment. Those aspects can be represented using element symbols, equations, and formulas. For chemists, this is one single chunk of information. We make the translation between these levels automatically. However, novices have to do the connections between the macroscopic, the molecular, and the symbolic level actively. Especially at the beginning, it is hard to not confuse the different levels and to not overgeneralize. Students show misconceptions which stay quite robust until later in their academic career, until they are practicing chemists or teachers, which could be avoided by facilitating learning at this early stage [6].

Why is this important for chemistry research? Students having misconception will become chemists having misconceptions. Chemistry education might not be chemistry research in itself, but its research on the future of chemistry research which makes investment in it of major importance. In this contribution, we share the preliminary results of this project, which consist on one hand of the (mis)conceptions held by ETH students and on the other hand of the development of this learning environment.

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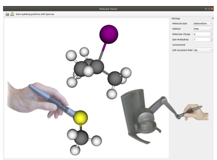

Using GAFF topologies and RE-EDS to calculate relative hydration free energies in GROMOS

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Free-energy differences between pairs of end states can be estimated based on molecular dynamics (MD) simulations using standard methods such as thermodynamic integration (TI). Replica-exchange enveloping distribution sampling (RE-EDS), on the other hand, allows the sampling of multiple states in a single simulation [1,2]. In this work, relative hydration free energies are calculated for a series of benzene derivatives using the RE-EDS approach in GROMOS. GAFF topologies are converted to a GROMOS-compatible format with the novel amber2gromos program. The results obtained with RE-EDS are compared to the experimental and simulated values from the FreeSolv database [3]. In addition, the estimated free-energy differences in water and in vacuum are compared to TI simulations carried out with GROMACS. The results show that the hydration free energies calculated with RE-EDS for multiple ligands are in good agreement with both the experimental data and pairwise TI values. This work serves as a validation that GAFF topologies can be used with the GROMOS simulation package and the RE-EDS approach.

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Quantum-DFT Embedding Algorithm for Electronic Structure Calculations

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In the near future, material discovery and drug design will be aided by quantum computer assisted simulations. These have the potential to target chemical systems intractable for the most powerful classical computers. However, the resources offered by near term quantum computers are still limited. Thus, it is necessary to investigate hybrid quantum-classical computational schemes, like the embedding algorithm we recently proposed [1]. In this work, we rapidly scaled up quantum-assisted simulations of molecular systems by means of embedding the quantum electronic structure calculation into a classically computed environment at the DFT level of theory. This allowed us to obtain significant energy corrections for a number of simple molecules, ranging from water to oxirane, in their strongly correlated limit (in the dissociation limit).

Applications of this embedding method will have significant impact, as it paves the road towards quantum-assisted studies of more complex molecular systems in the near future. In this talk, I will present an extension of our work [1], where we interface the open source framework for quantum computing, Qiskit [2], with the highly parallelized classical code CP2K [3]. The seamless integration of these two codes has enabled us to investigate significantly larger systems without being limited to comparatively small basis sets or lower quality exchange--correlation functionals.

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Time-reversible and norm-preserving implicit split-operator algorithms for the nonlinear time-dependent Schrödinger equation

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We want to solve general nonlinear time-dependent Schrödinger equations using an efficient method that preserves the geometric properties of the exact flow. Usually, these are solved using explicit algorithms. However, these algorithms are geometric only with simple nonlinear Schrödinger equations and are not valid in the general case. For example, the explicit TVT split-operator algorithm can be used for solving general nonlinear Schrödinger equations but it loses its second-order accuracy and time-reversibility. In a previous paper,[1] we solved this issue by using the implicit midpoint method, which preserves the geometric properties of the exact flow and shows second-order accuracy. Because it is symmetric and time-reversible, it can be composed to obtain higher-order geometric integrators,[2-3] which are more efficient, by several orders of magnitude, than any of the explicit methods.[1] This algorithm has the advantage of being applicable to both separable and nonseparable Hamiltonians.

Here, we will demonstrate and numerically verify for the nonlinear problem of local control theory [1] that, by abandoning the explicit nature of split-operator algorithms, we obtain implicit geometric split-operator algorithms that are more efficient than their explicit versions. We will also show that, for separable Hamiltonians, these implicit split-operator algorithms are more efficient than the implicit midpoint method.

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Simulation of quantum entanglement with classical trajectories

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A long-standing challenge in mixed quantum-classical trajectory simulations is the treatment of entanglement between the classical and the quantal degrees of freedom. We have developed a novel approach [1] which describes the emergence of entangled states entirely in terms of uncoupled and deterministic Ehrenfest-like trajectories. For a two-level quantum system in a classical environment, this is derived by mapping the quantum system onto a path-integral representation of a spin-1/2. We demonstrate that the method correctly accounts for coherence and decoherence and thus reproduces the splitting of a wavepacket in a nonadiabatic scattering problem. In contrast to many alternative methods, the path-integral approach can properly treat system with multiple crossings. This discovery opens up a new class of simulations as an alternative to stochastic surface-hopping or coupled-trajectory approaches.

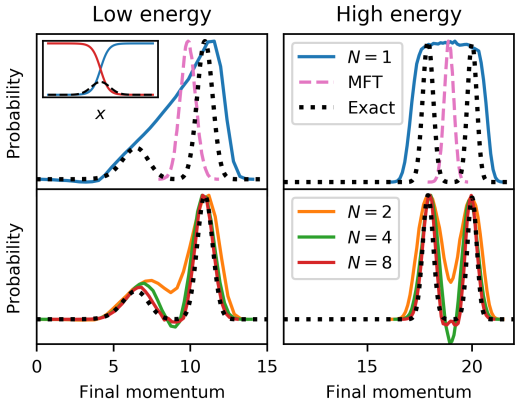

Figure: Probability distribution of the nuclear momentum after an avoided crossing. The inset shows the diabatic potentials (solid lines) and coupling (dashed line). A wavepacket enters from the left on the lower surface with a narrow distribution of kinetic energies at roughly 1.5 (left panels) or five (right panels) times the asymptotic energy difference. Mean-field theory (dashed line) gives a single peak around the average momentum, while linearized spin mapping (*N=1*) gives a broadened peak that envelopes the exact wavepacket distribution (dotted line). For higher numbers of spin, *N*, the spin path-integral method correctly reproduces the wavepacket branching.

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Low-data regime yield predictions with uncertainty estimation using deep learning approaches

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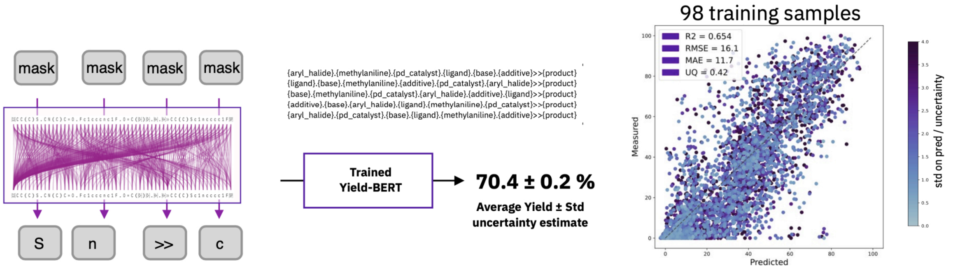
Artificial intelligence is driving one of the most important revolutions in organic chemistry. Multiple platforms, including tools for reaction prediction and synthesis planning based on machine learning, have successfully become part of the organic chemists' daily laboratory work, assisting in domain-specific synthetic problems. Unlike reaction prediction and retrosynthetic models, the prediction of reaction yields has received less attention in spite of the enormous potential of accurately predicting reaction conversion rates. Reaction yields models, describing the percentage of the reactants converted to the desired products, could help chemists navigate reaction space, optimize reactions, and accelerate the design of more effective routes. Here, we investigate high-throughput experimentation data sets [1, 2] and show how data augmentation on chemical reactions can improve yield predictions' accuracy, even when only small training sets are available. Previous work used molecular fingerprints [3], physics-based [1] or categorical descriptors [4] of the precursors. In our work, we fine-tune natural language processing-inspired reaction transformer models on different augmented data sets to predict yields solely using a text-based representation of chemical reactions [5, 6]. When the augmented training sets contain 2.5% or more of the data, our models outperform previous models, including those using physics-based descriptors as inputs. Moreover, we demonstrate the use of test-time augmentation to generate uncertainty estimates, which correlate with the prediction errors.



Pretrained
reaction *BERT*

Fine-tuned
on *augmented*
reaction SMILES

- Models perform well even in *low-data* regime
- *Test-time* augmentation to *estimate uncertainty*

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A computational study of kinetic trapping of noble gases in metal organic frameworks

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Kinetic trapping of gases in porous materials can be achieved if release of the guest molecules, which were loaded at high pressure and temperature, is hindered at normal conditions due to high activation barriers. In this work, we investigated the activation barriers of Xe and Kr gases in MFU-4-X (X=Cl,Br) metal organic frameworks [1] using Nudged Elastic Band (NEB), Molecular Dynamics (MD) and Metadynamics (MtD) studies based on the semi-empirical tight binding approach GFN1-xTB as implemented in CP2K [2,3]. The parameterisation of GFN1-xTB is based on a minimal basis set and the method therefore fails to capture the anisotropic electron density of halogen bonds. As a remedy, we introduced a Buckingham-type correction potential by fitting the dissociation curves of halomethane and noble gas pairs. We performed NEB, MD and MtD simulations assessing the halogen-corrected GFN1-xTB ansatz on 4 model systems, comparing 2 MFU-4 frameworks each loaded with 2 different noble gases and obtaining activation energies that are in agreement with experimental results.

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Accessing the Conformational Space of Cyclosporin A in Chloroform Using RDCs as Tensorial Constraints

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Accurate description of the conformational ensemble in solution is crucial for a proper understanding of molecular properties like passive membrane permeability or biomolecular recognition. NMR data are a primary source of information providing insight into conformational space. But even for moderately sized molecules, an exhaustive determination of molecular mobility is seldom possible based on experimental data alone. Instead, computational approaches like molecular dynamics simulations are employed that incorporate experimental data as constraints.

Besides commonly used NOE-derived distances and J-coupling constants, also anisotropic NMR properties like residual dipolar couplings (RDCs) are used for this purpose. In case of a rigid molecule, translation of RDCs into structural constraints requires fitting of a single global alignment tensor. But in flexible systems, different conformers may align differently and translation of RDCs into structural constraints requires a very large body of experimental data to reliably fit multiple tensors. A recently developed tensor-free approach by Luy and coworkers based on time-averaged molecular dynamics with orientational constraints (MDOC) opens new possibilities [1]. The rotational averaging of each individual tensorial RDC restraint in combination with NOE-distances and J-couplings provides an alternative way to generate conformational ensembles for flexible molecules based on NMR data including RDCs.

This new approach is evaluated for the immunosuppressive cyclosporin A, a cyclic undecameric peptide. In order to explore the accessible conformational space with the MDOC approach, RDCs were recorded in a compressed gel in $CDCl_3$. RDCs could be obtained for every C-H and N-H bond in the molecule. This data was then used in an MDOC simulation together with NOE-derived distances and J-coupling values from the literature [2,3].

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How to Accelerate Double-Hybrid Calculations to Determine Cohesive Energies in Metal Organic Framework

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Double-Hybrid functionals allow an accurate description of intermolecular interactions but an inquire Hartree-Fock calculations for the determination of ground-state densities and response densities. Due to the large prefactor of Hartree-Fock calculations, it is still dominating computational costs and hardly uses accelerators. We will discuss the Auxiliary Density Matrix Method (ADMM) and the recent Resolution-of-the-Identity approach (RI-HF) in CP2K to further reduce computational costs and better exploit GPUs of modern Hybrid computers while maintaining the superb performance of the underlying Double-Hybrid functional.

Autonomous Reaction Network Exploration in Homogeneous and Heterogeneous Catalysis

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Autonomous computations that rely on automated reaction network elucidation algorithms may pave the way to make computational catalysis on a par with experimental research in the field.

Several advantages of this approach are key to catalysis:
(i) automation allows one to consider orders of magnitude more structures than would be accessible by manual inspection, eventually with full resolution of structural varieties and conformations as well as with respect to the types and number of potentially important elementary reaction steps (including decomposition reactions that determine turnover number),
(ii) fast electronic structure methods with uncertainty quantification warrant high efficiency and reliability in order to not only deliver results quickly, but also to allow for predictive work, and
(iii) a high degree of automation reduces processing errors because little human interference is required.

In this work, we first review the state of the art in this research area, then discuss important conceptual issues that eventually determine feasibility and reliability, and finally demonstrate an implementation of these concepts applied to a catalytic system.

Nonadiabatic Quantum Transition State TheoryInstanton Rates beyond Golden Rule

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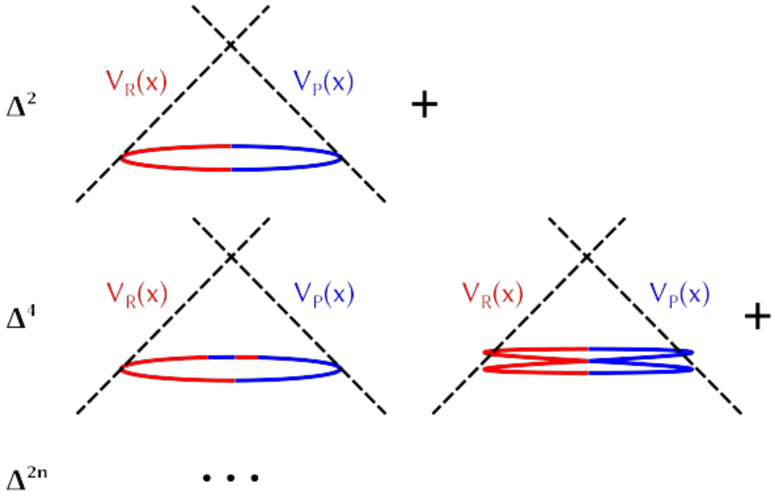
[1]Departement Chemie und Angewandte Biowissenschaften

Fermi’s golden rule formula [1] gives the reaction rate for a transformation between two diabatic states for small diabatic coupling Δ. While the exact formula is only computationally tractable for simple model potentials, there exist several approximations that can be readily applied to realistic chemical processes. Among them is golden-rule (GR) instanton rate theory [2-3], which accounts for nuclear zero point energy and quantum tunnelling by repurposing the tools of purely classical mechanics, making it a practical method for studying polyatomic systems. Even so, GR instantons only describe the leading-order contribution to the exact nonadiabatic rate in the limit Δ → 0, and subsequent terms are by no means always negligible. We present the instanton formulation of the next-order contribution and discuss how this new theory gives a rigorous estimate of the error introduced by the golden rule and paves the way for a nonadiabatic instanton rate theory correct to all orders of Δ.



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Chemoton 2.0: Automated Exploration of Reaction Networks

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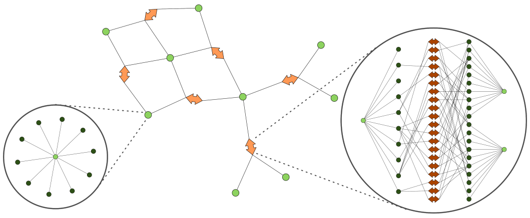
In recent years, much algorithm development was devoted to the computer-based automated exploration of reaction networks.[1]
In parts, this can be attributed to the potential role in the automation and acceleration of Design-Make-Test-Analyze (DMTA) cycles for new materials and chemical processes.
All of these reaction network based methods aim at establishing a sufficiently complete reaction network in order to allow for reliable predictions, detailed understanding, and eventually, the design of chemical processes. A complete reaction network consists of all thermodynamically and kinetically relevant intermediates and all reaction paths that connect them. Already due to conformational diversity, the reaction network generated for relatively simple chemical processes can be vast if they are to be complete. This poses a set of challenges for methodology and software, which we have analyzed and discussed recently.[2]

Here, we will present the current developments of our mechanism exploration automaton, called Chemoton[3], in its latest version 2.0.[4]



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Inferring missing molecules in incomplete chemical equations

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[1]IBM Research Europe

Deep-learning models applied to chemical reactions have received much attention in recent years: from the design of algorithms for forward reaction prediction and retrosynthetic analysis that help chemists plan the design and execution of chemical syntheses, to the generation of reaction fingerprints and prediction of reaction classes [1], yields [2], activation energies [3], or sequences of experimental steps [4].

Several of the latter predictive models require all the reagents to be specified, including solvents and catalysts. Unfortunately, both algorithms and chemists do not provide any guarantee of generating complete chemical reaction equations. It is therefore desirable to infer the missing molecules to provide higher quality data and to comply with a larger class of machine learning models. In fact, an algorithm fulfilling this task can also be used for data curation of reactions extracted from electronic notebooks or from the literature.

Interestingly, the task of inferring missing compounds in a reaction equation is a generalization of forward and single-step retrosynthetic prediction models. As a consequence, a properly tuned algorithm completing partial reaction equations also a forward or retrosynthetic prediction model.

We present a deep-learning model based on the transformer architecture that infers the molecules in partial reaction SMILES strings [5]. This model does not contain any chemical knowledge except the one learned from the data during training. We illustrate its application for data curation, as well as its use for forward and retrosynthesis prediction.

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To tunnel or not to tunnel - in the aqueous ferrous-ferric system

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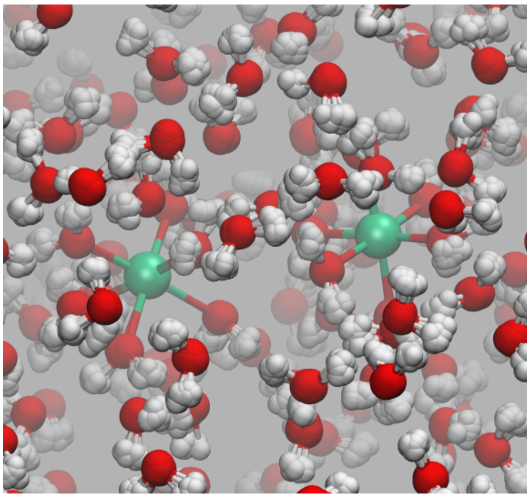
There has been a long-standing controversy on the role of nuclear tunnelling in the electron transfer of the aqueous ferrous-ferric system and accordingly the necessity of often computationally costly quantum rate calculations. We want to introduce our newly developed Golden-Rule Quantum Transition State Theory (GRQTST), which is an efficient, path-integral method. [1] A path-integral method such as GRQTST requires only a number of classical MD simulations which are linked to each other via the path-integral formalism. The computational cost is therefore comparable to that of classical MD simulations, while however capturing nuclear quantum effects (NQEs).

We show successful application of our new quantum rate theory to this challenging, atomistic problem and we can predict the tunnelling enhancement in this electron transfer process to be on the order of magnitude of 10. [2]



The tunnelling enhancement factor predicted by GRQTST is 6 times smaller than that of Wolynes theory. [3] Whilst we cannot make a conclusive argument on which if any of these theories predicts the rate correctly, we have shown in previous work that Wolynes theory and GRQTST agree well for the spin-boson model. [1] The discrepancy of these two theories for this system therefore calls into question the common approach of mapping the aqueous-ferrous-ferric system to the spin-boson model to obtain a rate prediction. In fact, we argue that the aqueous ferrous-ferric electron transfer cannot generally be captured by mapping to a spin-boson model in the quantum limit.

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