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# Vibrational Density Matrix Renormalization Group

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Within the Born-Oppenheimer approximation, the computational characterization of molecular systems requires two steps. Electronic properties, such as potential energy surfaces, are obtained from the solution of the electronic Schrödinger equation. Those quantities then define the nuclear Schrödinger equation, whose solution determines the vibrational properties of the molecule. Several theories to solve the electronic Schrödinger equation have been extended to vibrational problems. Similarly to its electronic structure analog, vibrational self-consistent field (VSCF) fails to describe strongly-correlated systems, i.e. molecules characterized by large-amplitude modes, along which the potential energy surface displays several minima. An accurate description of such systems requires post-SCF approaches, such as vibrational configuration interaction (VCI). In VCI, vibrational states are computed from the exact diagonalization of the vibrational Hamiltonian in a given basis set. The range of applicability of VCI is, however, limited by its exponential scaling with the size of the target systems, a problem also known as the curse of dimensionality. A possible solution to this limitation is offered by the density matrix renormalization group (DMRG) algorithm [1]. However, the application of DMRG to vibrational problems has been hardly explored [2]. In the present contribution, we demonstrate how DMRG can be exploited to optimize vibrational wave functions expressed as matrix product states (MPSs) by encoding the vibrational Hamiltonian as a matrix product operator (MPO). The resulting algorithm will be referred to as vibrational DMRG (vDMRG). The major features of vDMRG will be presented by highlighting the most relevant differences with respect to its electronic analog. First, the extension of a general, MPS/MPO-based DMRG algorithm devised for electronic structure calculations to bosonic Hamiltonians, such as the ones encountered in vibrational simulations, will be presented [3]. A straightforward formulation of vDMRG optimizes the energy of the ground state, i.e. the zero-point vibrational energy. In vibrational calculations, by contrast to the electronic case, ground state energies are of little interest compared to excitation energies. To lift this limitation, in this contribution several energy-specific variants of vDMRG based on shift-and-invert techniques will be presented [4]. The coupling of the resulting algorithm with root-homing will also be discussed, to further increase the reliability of vDMRG in targeting excited states in regions with a high density of states.

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# Exploring Chemical Reaction Networks with KiNetX

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A tool for automated quantum mechanical exploration of molecular reactivity previously published by our group, Chemoton [1], generates complex chemical reaction networks and associated properties such as activation energies. The size of the networks quickly becomes intractable, in particular if the involved species cause multiple side reactions. Then, the relevant kinetics of a chemical species might be hidden under a myriad of reactive conformers. For a kinetic analysis, the chemical reaction network must be converted to a set of possibly stiff ordinary differential equations (ODE). Ideally, the resulting chemical kinetics analysis is then carried out under full error control. KiNetX [2] is a C++ software aimed at the analysis of complex chemical reaction networks and their efficient exploration. Our software has been developed to possess four features. It is able to convert the graph structure of the network into a set of ODE and to identify and prune kinetically irrelevant species. Moreover, it propagates the first-principle uncertainty in activation energies estimated by Chemoton [3] as uncertainty in concentration trajectories. Most importantly, it collects the knowledge acquired through this analysis and drives the chemical reaction network exploration of Chemoton, for instance, avoiding wasting resources exploring kinetically irrelevant portions of the graph or identifying critical paths where more refined calculation methods should be employed.

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# Reactive collision dynamics investigation of Methane-MgO$^+$

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Methane is the principle component of natural gas and acts as a greenhouse gas. The conversion of Methane into more valuable chemicals is not possible by ordinary redox or acid-base chemistry [1] . Hydrogen-atom Transfer (HAT) [1,2] was found to be important for Oxidative Coupling of Methane (OCM) [1] . OCM can therefore supply industry with value-added products, starting from cheaper and more abundant feedstock. The smallest possible species to be used in OCM is MgO to describe the following reaction:

$$[MgO]^+ + CH_4 \rightarrow [MgOH]^+ + CH_3^{\bullet}$$

Multi-Surface Adiabatic Reactive Molecular Dynamics (MS-ARMD[3]) simulations of the reaction of $[MgO]^+ + CH_4$ were performed on a fully-dimensional potential energy surface (PES). The PES, which describes HAT, was fitted to MP2 calculations. Reactive molecular dynamics simulations were performed using stratified sampling for $b$. Calculations were performed for $b = 0$ to $b_{max}$ ($\Delta b = 0.5$ Å). The thermal rate coefficient from trajectory calculations is determined using the formalism from Reference [4] and Reference [5] .

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# A QM/MM Study of the Dihydroxylation of Nitroaromatic Contaminants Catalyzed by Nitrobenzene Dioxygenase

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Oxygen activating enzymes play an important role in the biodegradation and detoxification of soil and water contamination by organic pollutants. [1] The conversion of persistent aromatic pollutants to their corresponding *cis*-dihydrodiols and catechols acts as the initial step in these processes and is carried out exclusively by *Rieske non-heme Fe dioxygenases*. We present a QM/MM study on the current interpretation of the mechanism of the dioxygenation of nitroaromatic compounds by *nitrobenzene dioxygenase* (NBDO), which has been established by previous experimental and DFT studies [2,3]. Reaction energies and barriers are compared to DFT results and the effect of the QM region's size is discussed.

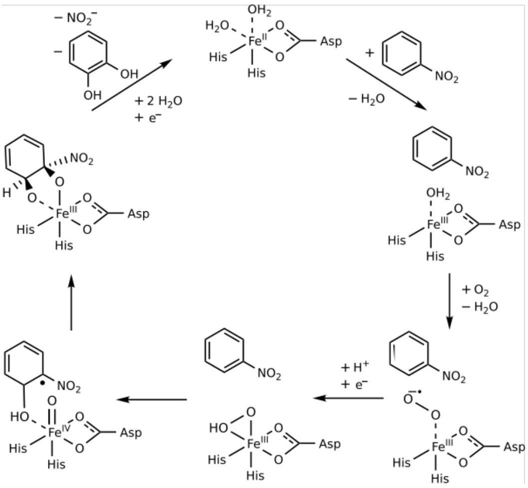

Figure 1: Current interpretation of the $O_2$ activation and dioxygenation of nitrobenzene based on previous experimental and theoretical studies [2, 3].

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# Ab Initio Instanton Calculations with GPR

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In statistics, Machine Learning Algorithms (MLA) are widely used nowadays to predict properties of unknown system from the knowledge of an ensemble oftraining points; Gaussian Regression Process (GPR) is a subclass of MLA specifically created for the prediction of continuous properties [1]. In chemistry, Ab Initio Instanton (ABI) methods are used to rigorously include multidimensional quantum tunneling in rate constant and to calculate tunneling splitting in degenerate, double well system [2]. The main drawback of ABI is the request of the global Potential Energy Surface (PES) or an ensemble of Quantum Chemistry (QC) calculations which pointwise expand the PES as Taylor series up to second order. The necessity of accurate PES forces the use of expensive QC models (CCSD(T)-F12 [3] or CASPT2 [4]), combined with the large number QC calculations, is the principal computational bottleneck for the application of ABI to medium-sized molecules.

Using GPR, we are able to find an expression for PES using only tens of QC calculations, instead of thousands of them; this reduction has been achieved with any lost in accuracy in the final results (<1%). As benchmark test, the tunneling splitting of $CH_4^+$ generated by the internal pseudorotation of three hydrogen atoms, has been investigated both theoretically by GPR-aided ABI calculations and experimentally by high resolution IR spectroscopy [5]. Also reaction rate constant between radical hydrogen and the series of the firsts alkanes (methane, ethane, propane) has also been studied [6] to show the accuracy of ABI results to fundamental research ares such combustion chemistry and astrochemistry.

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# $Al_xGa_{1-x}As$ crystals with direct band gaps larger than 2 eV from computational alchemy.

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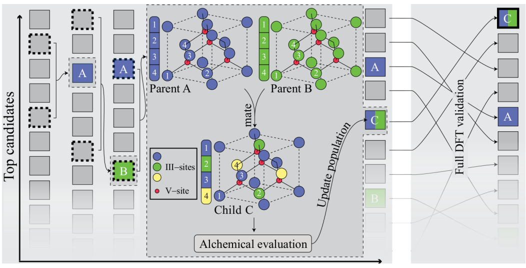
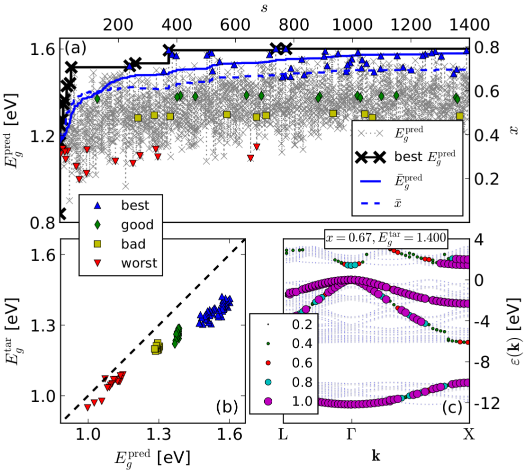
[1]Institute of Physical Chemistry and National Cente, [2]Institute of Physical Chemistry and National Center for Computational Design and Discovery of Novel Materials (MARVEL)

Alchemical perturbation in reciprocal space for periodic systems has never been explored. We design $Al_xGa_{1-x}As$ crystals with large direct band gap using computational alchemy within a genetic algorithm. Dozens of crystal polymorphs are identified for $x > 2/3$ with direct band gaps larger than 2 eV according to HSE approximated density functional theory. Based on a single generalized gradient approximated density functional theory band structure calculation of pure GaAs we observe convergence after visiting only 800 crystal candidates. The general applicability of alchemical gradients is demonstrated for band structure estimates in III-V and IV-IV crystals as well as for H 2 uptake in Sr and Ca-alanate crystals.





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# 2D IR spectroscopy of Insulin: a combined experimental-computational study

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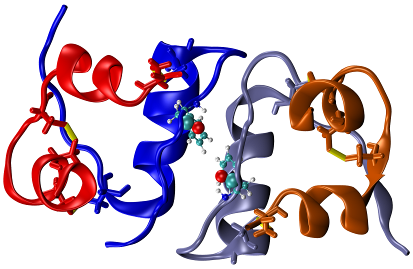
Manipulation and control of the dissociation of the Insulin dimer to two monomeric units (i.e. the functional form of the protein) is of great therapeutic importance. Recently, two-dimensional infrared spectroscopy (2D IR) – a technique that operates at the femtosecond-picosecond timescale – was used to investigate the dissociation dynamics of the Insulin dimer, systematically varying the temperature and concentration of the hormone [1]. Interpretation of such experimental spectra is often challenging and estimating the monomer/dimer composition is non-trivial. While at higher temperatures (e.g. 339K), essentially only monomers are present, it is difficult to isolate the dimeric form. Even at lower temperatures (e.g. 283K), only 50-80% of the composition is estimated to be the dimer. However, “pure-monomer” and “pure-dimer” spectra can be easily calculated computationally. In the most recent investigations, Tokmakoff et. al. use isotopically labeled insulin to explore the dimerization process. In parallel to this, we have explored the process using a complementary, computational approach, exploiting molecular dynamics (MD) and normal mode analysis. This builds on our previous investigations of the vibrational relaxation of N-methylacetamide, a small organic molecule that mimics peptide bonds in proteins [2].



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# How Do London Dispersion Interactions Impact the Photochemical Processes of Molecular Switches?

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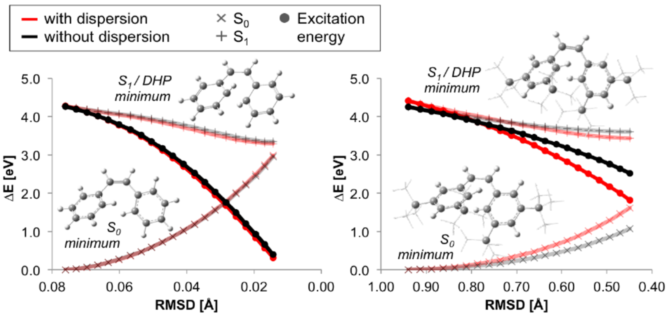
In the last two decades, linear-response time-dependent density functional theory (LR-TDDFT) has become one of the most widely used approaches for the computation of the excited-state properties of atoms and molecules[1]. Despite its success in describing the photochemistry and the photophysics of many molecular systems, its domain of applicability has been limited by several substantial drawbacks.

In particular, the most commonly underlined problems of LR-TDDFT comprise the correct description of Rydberg states, charge transfer excited states, doubly excited states and nearly degenerate states[2]. In addition to these shortcomings, the approximate functionals used in TDDFT are unable to fully describe London dispersion interactions. In this work, we aim at understanding the impact of van der Waals interactions on the properties of chemical systems beyond their electronic ground state. For this purpose, we performed excited state and molecular dynamics computations on the prototypical cis-stilbene molecule (**A**) and compared the results with its 3-3',5-5'-tetra-tert-butyl derivative(**B**). While the explicit treatment of London dispersion interactions results in negligible changes for the cis-stilbene, we show that these attractive forces have a substantial influence on the energetics and structural evolution of its substituted derivative. In the latter case, intramolecular dispersion interactions impact the outcome of the simulation qualitatively, leading to an increased preference for the photocyclization pathway. The methodological consequences of this work are not uniquely applicable to the illustrative stilbene case. In fact, this molecule is representative of a whole class of chemical situations, where dispersion dominates the interactions between the unexcited substituents of a photoexcited chromophore. This is, for instance, a common situation in organic photovoltaics where donor molecules are usually functionalized with long alkyl side chains to improve solubility and assembly[3].



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# Time scaling of Frozen-Density Embedding Theory for excited states calculations

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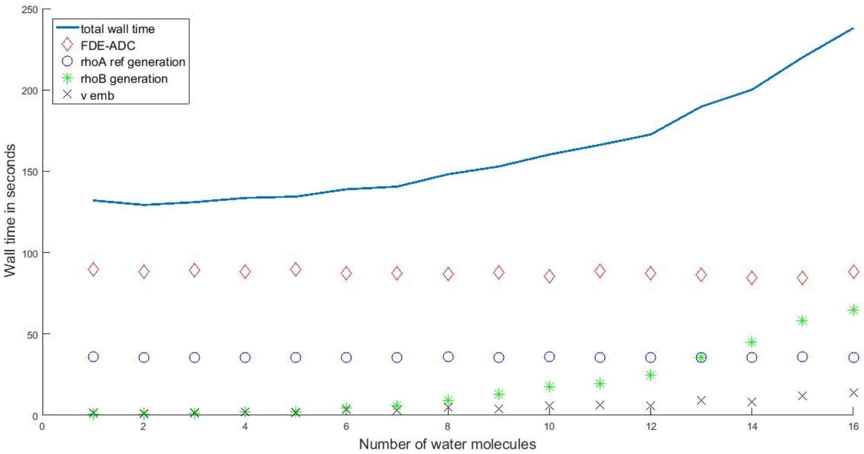
The scaling of Algebraic Diagrammatic Construction (ADC) [1] scheme for polarisation propagator and the combination of Frozen-Density Embedding Theory (FDET) [2,3] and ADC (FDET-ADC) [4] was analysed by comparison of the computing time in different calculations. The system considered in this analysis is an acrolein molecule embedded in several water molecules.

As the goal is to see how the computational cost of the methods develops, the number of water molecules in the model is successively increased.

This computational experiment will allow evaluating the range of application of these methods, as well as the time consuming step that could benefit the most of an optimization.



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# Calculating free-energy differences by conveyor belt thermodynamic integration.

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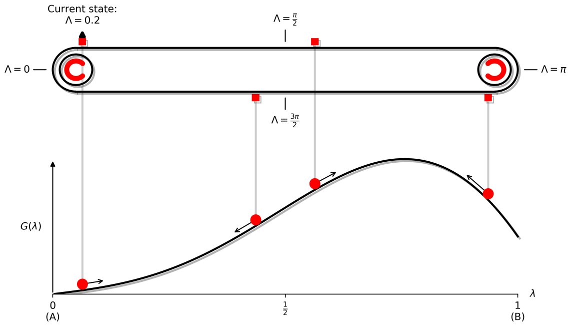
A new method is proposed to calculate alchemical free-energy differences based on molecular dynamics (MD) simulations, called the conveyor belt thermodynamic integration (CBTI) scheme. M replicas of the system are simulated at different values of the alchemical coupling parameter λ. As in λ-dynamics,[2] the λ-values associated with the individual systems can evolve in time along the simulation. However, they do so in a concerted fashion, determined by the evolution of a single dynamical variable Λ of period 2π controlling the advance of the entire conveyor belt (CB). As a result, the effective free-energy profile of the replica system along Λ is periodic of period 2π/M, and the magnitude of its variations over this period decays approximately with 1/M. When M is large, the variations becomes sufficiently small to enable a complete and nearly homogeneous coverage of the λ-range by the replica system. If desired, an additional memory-based biasing potential,[2] can be added to further homogenize the sampling, the preoptimization of which is computationally inexpensive.



The final free-energy profile along λ is calculated similarly to thermodynamic integration (TI),[3] by binning of the hamiltonian λ-derivative as a function of λ considering all systems jointly, followed by quadrature integration. The continuous and nearly homogeneous λ-sampling essentially eliminates quadrature errors and permits to bypass the preselection of a λ-points. Over plain TI the orthogonal sampling is enhanced, *i.e.* variable-λ paths to circumvent conformational barriers present at specific λ-values are available.

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# Local resolution of the identity approach for time dependent density functional perturbation theory

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Time dependent density functional perturbation theory (TDDFPT) has proven as powerful standard approach for the treatment of excited states and response properties paving the way for the theoretical description of various types of spectroscopy. To enable large-scale calculations and broad applicability, we present a local resolution of the identity (LRI) approach for TDDFPT as implemented in the Gaussian and plane waves (GPW) framework of the CP2K program package [1,2]. Within LRI, the atomic pair densities are approximated by an expansion of one-center fit functions avoiding the computationally demanding description of the total density on real-space grids. LRI has already been successfully applied to ground-state density functional theory (DFT), showing that the linear scaling of the GPW-DFT method can be retained while the prefactor for the grid operations is reduced, accelerating calculations by up to a factor of 10 [3]. Pursuing the work on ground-state DFT, we outline the implementation strategy of the LRI approach for the time-dependent regime and show first results.

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# Towards efficient, accurate, scalable, and transferable quantum machine learning with AM-ons: The “DNA” of chemistry

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Exploration of chemical space will improve our comprehension of chemistry, and help design new materials. Unfortunately, the number of theoretically possible stable chemicals exceeds the number of atoms in our solar system. Reliable and general virtual exploration campaigns remain prohibitive due to computational complexities of quantum chemistry methods, such as density functional theory and post Hartree-Fock methods. Over the last few years, quantum machine learning (QML) models have been introduced to accelerate predictions throughout chemical space. However, the efficiency, accuracy, scalability, and transferability (EAST) required to freely navigate chemical space has not yet been reached. Here we show how to use an active local training approach to generate QML models with EAST. Our algorithm systematically fragments any query compound into constituting quasi-atoms, dubbed Atoms-in-Molecules (AM-ons), combining machine learning (efficiency), with AMon convergence in terms of size (accuracy), locality (scalable), and number (transferable). Many *ab initio* fragmentation strategies already address scalability, but trade accuracy and transferability for speed, or continue to suffer from steep scaling pre-factors. While transferable by design, popular cheminformatics models, e.g. based on extended connectivity fingerprint descriptors, demonstrably fail when applied to quantum properties. Unprecedented low prediction errors of the AMon based QML model, on par with experimental uncertainty, numerically demonstrate EAST for NMR shifts, electronic energies, atomic charges and forces, core-electron excitations, and polarizability. Systems studied include the oligo-peptide chignolin (1UAO, beta-hairpin model), large biomolecules, Watson-Crick DNA base pairs, bulk silicon, eleven thousand organic molecules, common polymers, water clusters, and doped *h*BN sheets. Conceptually, AMons encode the “DNA” of chemistry, effectively extending Mendeleev’s table to also account for chemical environments. Their use amounts to a dramatic dimensionality reduction, thereby representing an important stepping stone towards a deeper understanding of chemical space.

# Analysis of the formation, structure and dynamics of a calcium phosphate aggregate using molecular dynamics simulations

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Amorphous calcium phosphate is one of the most common phases observed in humans, and investigations of the tailbone of zebrafish suggest that it is the initial precipitate prior to crystallization into hydroxyapatite.[1] Nevertheless, its structure is still under debate. In a recent account, Habraken et al showed that this phase initially forms as a calcium deficient structure composed of $[Ca_2(HPO_4)_3]^{2-}$ units.[2] However, the speciation was calculated in the presence of TRIS, which carries a positive charge and could thus favor a higher phosphate content. In contrast, recent simulations of supersaturated calcium phosphate solutions propose the formation of Posner's cluster, $Ca_9(PO_4)_6$, during the initial stages of calcium phosphate mineralization.[3] The free energy of interaction between the ions, however, was not calculated and the simulations were short.

Here, a force field shown to capture the free energy of interaction between calcium and phosphate ions, their individual solvation energies as well as the structure of bulk mineral phases, has been used to investigate their aggregation in supersaturated solutions.[4] The results show the formation of a large aggregate in equilibrium with smaller clusters and ions in solution. During the simulation, the larger aggregate goes through a very slow relaxation (> 100ns) observed by monitoring the Ca-P coordination number, which over time increases towards larger values. Through a time dependent structural and dynamical analysis, we explore the evolution of the properties of this hydrated aggregate and comment on how these could be tuned by organic molecules present within living systems.

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# First-Principles Simulations of Aqueous CO/Pt(111) Interface

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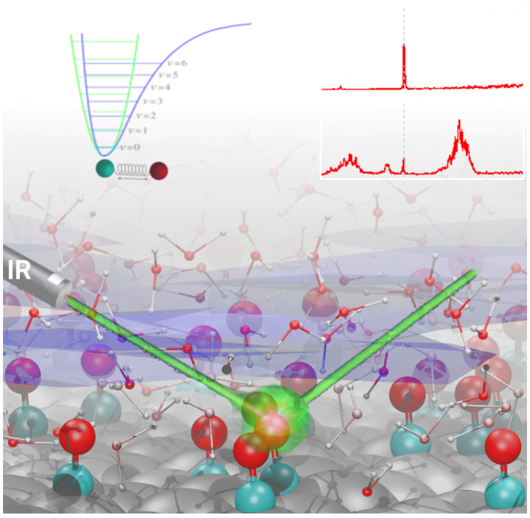
We discuss the structural, electronic and vibrational properties of an adsorbed CO monolayer in the presence of liquid water at room temperature, as obtained by ab-initio molecular dynamics simulations. The water molecules at closest distance from the substrate form a bi-layer, where they are co-adsorbed at empty surface sites and with relatively rigid orientation, at difference with the bulk liquid above. The presence of water affects the CO stretching mode. Co-adsorbed water strengthens the backbonding to CO, which leads to the red shift of about 40 cm−1. The synergy between the first bi-layer and the bulk liquid induce the further polarization of the CO bond, which changes the transition dipole and results in the CO intensity enhancement. It is also verified that no hydrogen bond is effectively present between CO and bulk water. These findings provide new insight into the physics of the surface/adsorbate/solvent interface, thus clarifying the experimental observation, to be exploited for the design of improved catalysts.



# Revealing the Structure-Property Relationship of Organic Hole Transport Materials in Perovskite Solar Cell

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Recently, organometallic halide perovskite solar cells (PSCs) have been considered as promising candidates for photovoltaic applications [1]. In high performance PSCs, hole transport layers are incorporated into the device to enhance power conversion efficiency and stability [2]. Materials based on small organic molecules make desirable hole transport materials (HTMs) for PSC applications because they possess well-defined structures, form smooth interface with the perovskite layer, are capable of low-temperature solution processing, and are easily modified to fulfill the property requirements through rational molecular design [3]. It is well known that the most promising HTMs should fulfill several requirements: they should (1) possess a suitable ionization potential (IP) to enlarge the open-circuit voltage (Voc), (2) transport charges efficiently from the perovskite/HTM interface to the electrode, (3) avoid absorption within the range of the solar spectrum and (4) be hydrophobic to protect the underlying perovskite layer by slowing the invasion of moisture [4]. In contrast to these well-known design principles, a comprehensive understanding of the structure-property relationship remains lacking, which hampers the discovery pace of new HTMs. As a result, investigating the non-trivial structure-property relation with the aid of computer simulations is beneficial. Here, we demonstrate that high-performance HTMs can be achieved through a sophisticated balance involving molecular modifications to the substitution moieties, substitution sites, heteroatoms, alkyl chain length and the number of substituted side arms. The general trends that can be drawn from each modification along with rationalization from a molecular viewpoint create a powerful set of tools for rational designs of futur HTMs.

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# Revealing chemical patterns by combining sketch-map with the density overlap region indicator

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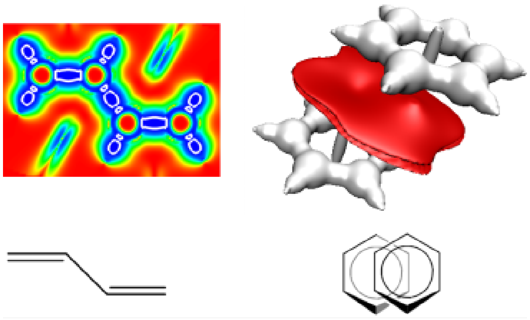
The Density Overlap Region Indicator[1] (DORI) is a density-based scalar field, which reveals covalent bonding patterns and non-covalent interactions simultaneously. The present work[2] goes beyond the traditional static quantum chemistry use of scalar fields and illustrates the suitability of DORI for analyzing geometrical and electronic signatures in highly fluxional systems. Examples include a dithiocyclophane, which possesses multiple local minima featuring a different extend of π-stacking interactions; DORI is then employed to capture fingerprints of CH-π and π-π interactions throughout the temperature-dependent rotational processes of a molecular rotor. Finally, it serves to examine the fluctuating π-conjugation pathway of a photochromic torsional switch (PTS). Molecular dynamic trajectories are obtained using the REMD@DFTB framework,[3] which combines density functional tight binding in DFTB+ and replica exchange molecular dynamic as implemented in the dynamic driver i-PI.[4] Attention will be placed on post-processing the large amount of generated data and on reducing their dimensionality combining DORI with the sketch-map dimensionality reduction algorithm.[5]



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# How does halogenation change binding affinity of ligands in a protein cavity?

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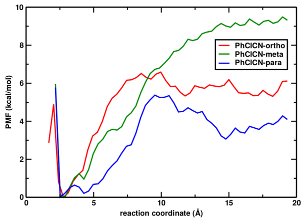
The purpose of this work is to investigate the effect of halogenation on the binding affinity of ligands and also to consider the effect of substitution pattern (ortho, meta, para) on dynamics and binding of the ligands in a protein. Actually, halogens are widely known to contribute to ligand-protein interactions, thereby received great attention in drug design. A survey of launched drugs showed that 25% are organohalogens of which organochlorines dominate, composing 57% of halogenated drugs [1]. In this work we have studied binding affinity of chlorobenzonitrile (PhClCN) in the nonpolar cavity of T4 lysozyme. All the calculations have been done by CHARMM molecular dynamics simulations package. The CN group in the ligand is a spectroscopic probe (local reporter of the electrostatic environment) for studying the binding, electric field and dynamics of the ligand in the cavity. Theoretical investigations have confirmed that the electrostatic environment in the protein cavity shifts the peak frequency in the linear absorption spectrum of CN group [2]. The shift approximately correlates with the relative binding free energy, which it means the stronger the binding the larger, the red shift. In this work three different ortho, meta and para isomers of chlorobenzonitrile have been chosen to study the frequency shifts of CN group in different ligands and correlate the changes to the binding modes of the ligands. After 10 ns of production run, it was realized that 4-chlorobenzonitrile leaves the cavity after 5ns of simulation. On the contrary, 2-chlorobenzonitrile (both isomers), and 3-chlorobenzonitrile stay in the protein pocket. The binding free energies of PhClCN ligands in lysozyme have been calculated using umbrella-sampling method (see figure(1)).



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# Tungsten oxide clusters in solution stabilized by boron nitride nanomesh

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Early transition-metal oxide clusters $(MO_3)_3$(where M = Mo or W) are well known to be very efficient catalysts; however, on most solid substrates, they are stable only at very low temperatures[1]or at low coverages[2]. In a previous work,[3]it was shown using a tungsten STM tip in aqueous solution, that individual monodisperse cyclic tris(tungsten(VI) trioxide) clusters $(WO_3)_3$spontaneously form as linear oligomers.In this combined experimental and computational work, we show that the boron nitride nanomesh is a robust template for molecular self-assembly in solution. We demonstrate through high-resolution STM and XPS, that the (WO

In this combined experimental and computational work, we show that the boron nitride nanomesh is a robust template for molecular self-assembly in solution. We demonstrate through high-resolution STM and XPS, that the $(WO_3)_3$clusters are stably formed on the boron nitride nanomesh, at room temperature. The clusters are arranged in a peculiar triangular-shaped configuration placed in the pores of the nanomesh, with different number of forming $(WO_3)_3$units. DFT simulations using the CP2K code are employed to confirm the triangular-shape forming units, which are indeed the $(WO_3)_3$clusters. A high-resolution STM averaged image of a single cluster is compared to a simulated-STM image, showing a good agreement between the two (Fig.1). We

We therefore confirm that the boron nitride nanomesh is a robust template to trap and stabilize $(WO_3)_3$ clusters, at room temperature and under electrochemical conditions, allowing the investigation of reactive catalytic reactions.

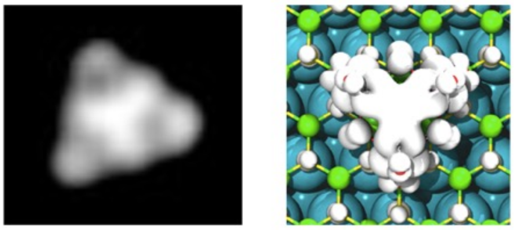

Fig. 1: Averaged EC-STM image of a triangular $(WO_3)_3$cluster adsorbed on h-BN/Rh(111) nanomesh (left) at a STM sample bias of +0.6 eV. (right) Simulated STM of a $(WO_3)_3$ cluster on h-BN/Rh(111) nanomesh at a bias of +1 eV. Rh atoms are cyan, B atoms are green and N atoms are yellow.

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# NMR Meets Machine Learning: Orders of Magnitude Faster Chemical Shifts Predictions in Solids

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A revolution in solid state NMR occurred with the introduction of Gauge Including Projector Augmented Waves (GIPAW): a density functional theory (DFT) based method to calculate chemical shifts in the solid state.[1,2] In particular, thanks to the combination of chemical shift calculations and experimental measurements, solid state NMR proved to be a powerful method for structure elucidation of amorphous materials and microcrystalline solids.[3,4] However, the high computational cost associated with the DFT chemical shift calculations represents a severe limitation in the approach, preventing both efficient high throughput screening of potential crystalline structures and the application to larger and more complex crystals.

In the past few years, machine learning (ML) methods have shown to be a powerful tool to bridge the gap between the need for high accuracy calculations and limited computational power in many areas of chemical and physical science. Here we propose a machine learning framework to predict chemical shifts in solids, based on Gaussian Process Regression using local SOAP fingerprints.[5,6]

To train this model we used DFT chemical shifts of a set of 2000 molecular crystals, chosen to be as diverse as possible. We then demonstrate the prediction performance on a set of 500 crystal structures randomly chosen and not already present in the training set. We obtain $R^2$ coefficients between the chemical shifts calculated with DFT and with ML of 0.97 for $^1$H, 0.99 for $^{13}$C, 0.99 for $^{15}$N, and 0.99 for $^{17}$O, corresponding to RMSEs of 0.49 ppm for $^1$H, 4.3 ppm for $^{13}$C, 13.3 ppm for $^{15}$N, and 17.7 ppm for $^{17}$O (to be compared with the DFT accuracy: RMSEs of 0.43 ppm for $^1$H, 2.2 ppm for $^{13}$C, 5.4 ppm for $^{15}$N, and 7.2 ppm for $^{17}$O). We show that the model can be used in an NMR crystallography protocol in combination with CSP to correctly determine the structure of cocaine and 4-[4-(2-adamantylcarbamoyl)-5-tert-butylpyrazol-1-yl]benzoic acid. We also show that it is possible to calculate the NMR spectrum of very large molecular crystals (>1000 atoms) within a few CPU minutes, in contrast with the CPU years required by DFT. The program used to calculate shifts using this protocol is called ShiftML, available as an online server at http://shiftml.epfl.ch.

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# Wavefunction Frozen Density Embedding: an analysis of the errors in excitation energies.

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The unfavourable scaling of quantum mechanic methods renders any explicit treatment of the environment unfeasible. Multi-scale methods -i.e. based on interfacing treatment at different levels of theory for different parts of the system- were hence developed in order to go beyond simple gas phase calculations. Among them, Frozen Density Embedding Theory (FDET)[1,2] describes the effect of a frozen electron density of the environment, $\rho_B(\mathbf{r})$ on the wavefunction of the system of interest ($\Psi_A$). FDET exhibits large flexibility: any choice of methods for the subsystems A and B is possible, including for instance the generation of $\rho_B(\mathbf{r})$ as a superposition of densities. Additionally, the multi-level approach of this formalism can be further extended by combination with other environment models (e.g. PCM, MM).

Contrary to conventional FDET, which requires macrocycles to calculate the embedding potential self consistently, linearised FDET[3] relies on a single calculation of the embedding potential, considerably speeding up the procedure with no significant loss in accuracy. Furthermore, while conventional FDET leads to a different embedding potential for each state, linearised FDET leads to a state-independent embedding potential resulting in orthogonal states.

In our research, we aim at assessing the scope and limitations of such protocol by investigating the relation between the theoretical approximations of the model and chemical properties. Factors such as the overlap of $\rho_A(\mathbf{r})$ and $\rho_B(\mathbf{r})$ and the delocalisation of the excitation have been analysed on a dataset of 52 supermolecular clusters. The distance dependence of the error and of said factors has been investigated in order to discern different error components. Furthermore, the relation between the error on the one hand, and the dipole moment and polarisability of the two subsystems on the other, has been investigated in order to better understand the influence of induction on the performance of the method.

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# A study of the Diels-Alder reaction between 2,3-dibromo-1,3-butadiene and maleic anhydride

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The Diels-Alder reaction, in which a diene reacts with a dienophile forming a cyclic product, is one of the most used reactions in the synthesis of organic rings. There has been many studies about whether or not this is a concerted process and, if so, whether it happens in a synchronous or an asynchronous manner [1, 2]. The (a)synchronicity is usually defined from the (a)symmetry of the transition state structure but recent simulations show that both, synchronous and asynchronous additions are present even for symmetric transition states [3,4].

Recent advances in molecular-beam experiments allow now conformational separation of isomers by electrostatic deflection of a molecular beam based on their different dipole moments [5]. Hence, the separation of the *s*-cis and *s*-trans conformers of a diene is possible as long as they meet the experimental requirements for this technique.

We aim to experimentally and computationally explore the detailed mechanism of the Diels-Alder reaction between conformationally selected 2,3-dibromo-1,3-butadiene and supersonically cooled maleic anhydride. We have recently studied the potential energy surface of this reaction (finding that it goes through a symmetric transition state) and the kinetics of the possible dissociation and isomerization of the product with RRKM calculations [6]. We are now using multi-surface adiabatic reactive molecular dynamics (MS-ARMD) [7] to understand which initial conditions will lead to a reactive event. The trajectories try to simulate a crossed molecular beam experiment and thus start with the two molecules approaching each other. They then collide and may form a van der Waals complex that can live for several picoseconds, dissociate or lead to the Diels-Alder product.

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# Atomistic Simulations: Vibrational Probes for Structural Studies

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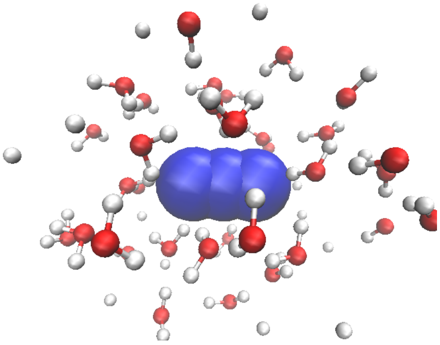
Spectroscopic experiments have become highly sensitive to the solvent dynamics around suitable probes. To interpret such data, accurate representations of inter- and intra molecular interactions are essential for quantitative and predictive atomistic simulations. In this work, we investigate the structural dynamics and infrared spectroscopy of -N3 in Azidoalanine (AHA) and CF in 4-Fluorophenol in the gas phase and water [1, 2]. Azide-derivative amino acids are quite useful spectroscopic probes for studying structural changes in protein in solution and halogenated groups are relevant in pharmaceutical applications and also potentially useful spectroscopic probes for infrared spectroscopy. All the dynamics around the mentioned compounds are characterized by Molecular Dynamics simulation with CHARMM. Reproducing kernel Hilbert space[3] (RKHS) interpolation technique is used to represent the global potential energy surface (PES) and DVR3D[4] program to calculate vibrational frequencies for bound states.



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# Reactivity of Carbon Allotrope Prism $C_{20}$

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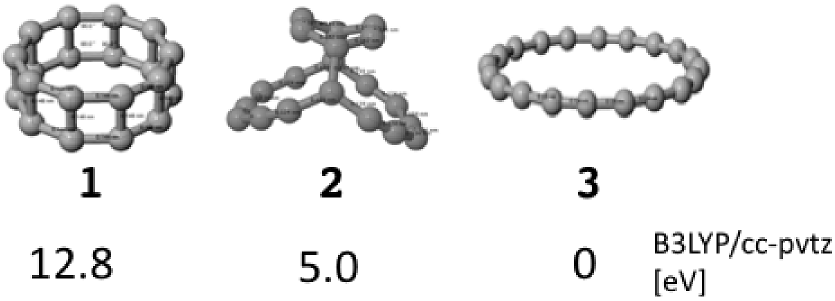
The existence of a carbon allotrope family in a prism form, prism $C_{2n}$, was computationally predicted in 2015. [1] The prism $C_{20}$ (**1**) is composed of two layered $C_{10}$ monocyclic rings [2], which are connected to each other with 10 vertical bonds. The structures and energy were determined at several levels of DFT calculations. The lowest energy barrier from $C_{20}$ was associated to a bond breaking reaction at the two adjacent vertical bonds, which was calculated with the SHS-ADDF method [3] within the GRRM software program package. In this study, we have investigated the reactivity of $C_{20}$ with ab initio MD simulations by using the CP2K code. Metadynamics simulations have been conducted with two types of collective variables (colvars): coordination colvars and combined colvars of the distance of all of the vertical bonds. Both of the simulations have resulted in a tricyclic $C_{20}$ (**2**) via a vertical bond break. The structure **2** has not been found in the previous study of QM-based exploration of $C_{20}$ isomers and reactions [4]. The energy of **2** relative to monocyclic $C_{20}$ (**3**) was 5.0 eV, whereas that of **1** was 12.8 eV at the B3LYP/cc-pvtz level.



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# Machine Learning Models for Homogeneous Catalysis

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Molecular volcano plots have shown the ability to predict catalyst performance based on a simple descriptor (*i.e.,* binding energies).[1-2] As such, these tools have clear implications for the high-throughput screening of catalysts. The current bottleneck, however, lies in the time required to determine the descriptor variables that require the use of relatively slow DFT computations. Clearly, it would be beneficial to increase the rate at which both the molecular geometries and the associated descriptors could be accessed while still maintaining reasonable accuracy. The application of quantum machine learning (ML) models represents an attractive route that provides virtually instantaneous access to the descriptor for any species. Today, fundamental electronic properties are accurately predicted (lower than hybrid DFT error) using ML models with reduced computational costs.[3-4] Here, we exploit ML models to accelerate the screening of descriptors for a prototypical Suzuki C-C cross-coupling reaction (*i.e.,* to predict the binding energies of transition-metal complexes). We show that SLATM representation[5] based ML models systematically outperform all alternative models (MAE = 2.8 kcal/mol). Of the 18,062 compounds predicted, 727 candidates were identified as having a promising thermodynamic profile for the catalytic cycle. This subset was then further refined by species having an estimated price lower than $10 per mmol (49 catalysts in total). Interestingly, low-cost earth-abundant metal complexes (Cu and Ni) appear in the favorable binding energy range. Our results demonstrate that ML techniques can be applied to the computational discovery of promising catalysts for C-C cross-coupling reactions.

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# Concerted steps on $CeO_2$ enable vinyl chloride production through ethylene oxychlorination

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In the context of polyvinyl chloride (PVC) production, $CeO_2$ was found to enable the manufacture of ethylene dichloride (EDC) and vinyl chloride (VCM) *via* ethylene oxychlorination in a single step, in contrast to the conventional process that requires two unit operations.[1,2] Since the oxychlorination mechanism on this oxide remained poorly understood, the complex reaction network was investigated by Density Functional Theory, steady-state catalytic tests, and temporal analysis of products. This initially revealed that the most likely VCM production mechanism features the conventional (*i.e.* two-step) formation of EDC by addition of two chlorine atoms to ethylene on a chlorinated $CeO_2$ surface and a subsequent concerted extraction of HCl to form VCM (Figure 1), characteristic of $CeO_2$.[2] Side pathways, leading to minor products, such as 1,2-dichloroethene, were found possible starting from EDC or VCM. CO is generated from combustion of chlorinated species, while $CO_2$ is formed by CO oxidation or directly from ethylene. To couple the calculated activation energies of all main and side pathways to the observed activity and selectivity trends, a microkinetic model is being developed. *Operando* determination of the chlorine coverage by prompt gamma activation analysis in a broad range of conditions will be included to support the *ab-initio* theoretical approach by linking it to the calculated chlorine coverage derived from the microkinetic model. In summary, our work highlights the complex chemistry of chlorinated compounds on the $CeO_2$ surface, indicating that concerted steps are possible and represent the key selectivity driver of this material.

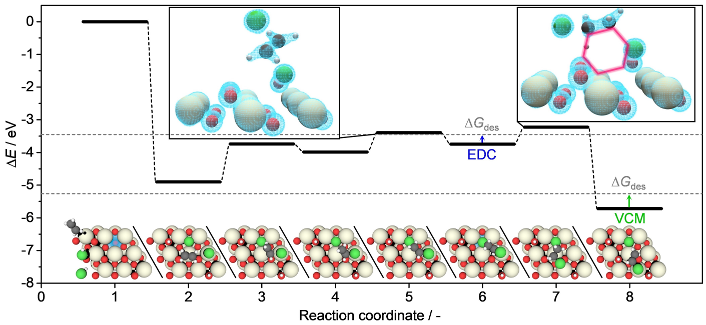

**Figure 1** Reaction profile of VCM formation from ethylene over $CeO_2$. The insets depict an individual (left) and a concerted (right) transition state. The blue overlay represents the charge density, plotted at an isosurface level of 0.2309 $|e^-|Å^{-3}$.

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# Understanding Artificial Water Splitting - In Silico Study and Design of Water Oxidation Catalysts

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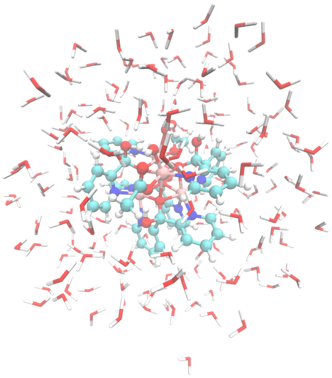
Nowadays, artificial water splitting is a promising solution to the imminent energy crisis caused by the expected depletion of fossil fuels towards the end of the century. The term water splitting refers to the conversion of water into molecular oxygen and hydrogen. The energy required to enable this process is often provided directly or indirectly by the sun.

Chemically, water splitting is divided into two half reactions, water oxidation and water reduction. Both processes consist of multiple chemical reactions and require the presence of a catalyst. The goal of our work is to understand the fundamental principles of those catalysts. In particular we are interested in the reaction mechanism and environmental effects. To this end, we investigate water oxidation catalysts such as the cobalt-based cubane $\{Co_4O_4\}$ or mononuclear  by means of forefront ab initio molecular dynamics approaches. Our models include explicit solvation which allows to investigate crucial solvent-solute interactions during catalysis. Those studies provide a rationalization of experimental observations and lay the basis for design criteria leading to potential novel catalysts with higher catalytic potency.



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# Error-Controlled Exploration of Chemical Reaction Networks with Gaussian Processes

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For a theoretical understanding of the reactivity of complex chemical systems, relative energies of stationary points on potential hypersurfaces need to be calculated to high accuracy.[1,2] Due to the large number of intermediates present in all but the simplest chemical processes, approximate quantum chemical methods are required that allow for fast evaluations of the relative energies, at the expense of accuracy. Despite the plethora of benchmark studies, the accuracy of a quantum chemical method is often difficult to assess.[3,4] In addition, a significant improvement of a method's accuracy (e.g., through reparameterization) is rarely possible.

We present a novel approach that allows for the systematic, problem-oriented, and rolling improvement of quantum chemical results through the application of Gaussian processes.[5] Due to its Bayesian nature, reliable error estimates are provided for each prediction. A reference method of high accuracy can be employed, if the error associated with a particular calculation is above a given threshold. The new data point is then added to a growing dataset to improve the model, and as a result, all subsequent predictions. Previous predictions are validated by the updated model to ensure that uncertainties remain within the given confidence bound. We demonstrate our approach at the example of a complex chemical reaction network.

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# Molassembler: Molecular graph interpretation, modification and conformer generation with stereopermutational treatment of multidentate and haptic ligands

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In the automated exploration of chemical reaction networks, algorithms are needed to distinguish compounds and generate conformational ensembles. In our chemical reaction network exploration[1], the backing library RDKit[2] limits the types of modelable compounds to organic compounds. We present a novel modeling approach to molecular configuration with which the treatment of inorganic structural elements becomes tractable within familiar molecular library interface patterns. Notably, the library enables the interpretation of stereocenter configurations from Cartesian coordinates into an abstract index of permutation in bonding situations involving multidentate and even haptic ligands for an extensible set of central symmetries up to square antiprismatic. Stereocenters are recognized via a IUPAC sequence rules[3] compliant substituent ranking algorithm and offer symbolic permutation computation considering linking and relative statistical occurrence weights. Molecular graphs can retain stereoconfiguration information on edits causing ranking changes and ligand additions or removals, providing continuity in editing. Conformer generation is based on four spatial coordinates Distance Geometry[4] algorithms and includes the transfer of triangle inequality smoothing to a graph shortest-paths calculation[5].

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# Water slip and osmotic transport on two-dimensional materials from ab initio molecular dynamics

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A vast amount of clean energy (so called blue−energy) can be generated by the mixing of salt and fresh water. Experiments of osmotic transport through nanotube membranes and two-dimensional nanopores have reported on extremely high conversion efficiencies, and have hinted at the role of the electronic structure of materials on osmotic and liquid transport at the nanoscale. However, there has been little to no attempt to understand the role of electronic structure of materials on osmotic transport and flow at liquid/solid interfaces so far. Here, I will present results on the slip of water on two dimensional materials computed from ab initio molecular dynamics simulations, and I will discuss the role of the underlying potential energy surface obtained from first principles on the prediction of slip at different interfaces and how this can affect nanoscale osmotic transport.

# The Effects of S-Nitrosylation on the Conformational Dynamics of Myoglobin

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S-Nitrosylation is a type of post-translational modification that occurs in a variety of proteins by the covalent attachment of nitrogen monoxide group (NO) to the thiol side chain of cysteine or to transition metal centers. Further, it is known that S-nitrosylation directly impacts the regulation of numerous signal transduction pathways in cellular systems. [1] However, the effects of the modification on the conformational dynamics of protein structures yet to be fully understood.

Herein, the main objective of the study is to understand the effects of S-Nitrosylation of Cys-10 to the conformational behavior of myoglobin protein. Two different complexes based on the wild-type myoglobin (PDB entry 2NRM) [2] and S-Nitrosylated Myoglobin have been prepared, and both systems are solvated in water with a buffer region of 15 Å with the final dimensions of 74Å x 74Å x 74Å. Important bonds (S-N, N=O) and torsion angle (C-S-N=O) were parametrized by the means of density functional theory at B3LYP/6-31G** level. Molecular dynamics simulations have been carried out using CHARMM36 force field [4] as defined in with CHARMM [3] software package. RMSD values between X-Ray structures and simulations were calculated to be around 1.3Å, which indicates a good conformational agreement. In addition, radial distribution functions and corresponding coordination numbers of the simulated S-NO have been investigated to understand water dynamics around NO group as well. As a future work, distributed charge model [5] going to be applied to simulations to have a better understanding of the effects of multipoles to S-NO probe.

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# Fast and accurate energy predictions with alchemical perturbation

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Traversing chemical space is one of the key challenges in modern computational chemistry. Exhaustive sampling however is prohibitively expensive for any large number of possible molecules. This is due to the level of theory required and the sheer number of possible molecules. We present a method to obtain fast yet reliable estimates of similar molecules obtained by alchemical perturbation. In this method, we treat the difference in pseudopotential between two iso-valence-electronic molecules as perturbation to the electron density. Using first order perturbations around one density obtained by DFT, we then can efficiently estimate energies of neighbouring molecules in chemical space.

A simple rescaling of the resulting total electronic energies is sufficient to obtain a median absolute error of 1kcal/mol vs DFT for a large variety of halogenated small organic molecules for same geometries. For relaxed geometries, we obtain a median absolute error of 0.5 kcal/mol vs DFT from multiple alchemical predictions. This is within the inherent error of the DFT reference data, but can be obtained at a fraction of the cost, since none of the predicted energies require a new self-consistent electron density.

These energy predictions allow for gradient search in chemical space where one SCF calculation on one molecule is used to predict the energies of similar molecules, the most promising of which then is selected for the next optimisation step. This local approach complements machine learning approaches that can quickly identify potentially interesting molecular topologies.

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# Statistical Analysis of Semiclassical Dispersion Corrections

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Semiclassical dispersion corrections developed by Grimme and coworkers have become indispensable in applications of density functional theory. We present an in-depth assessment of the fit parameters present in semiclassical (D3-type) dispersion corrections by means of a statistically rigorous analysis. We find that the choice of the cost function generally has a small effect on the empirical parameters of D3-type dispersion corrections. However, the weighting scheme in the cost function can significantly affect the reliability of predictions. In order to obtain unbiased (data-independent) uncertainty estimates for both the empirical fit parameters and the corresponding predictions, we carried out a nonparametric bootstrap analysis. The mean prediction uncertainty obtained by bootstrapping is not much larger than previously reported error measures. On the basis of a jackknife analysis, we find that the original reference set is slightly skewed, but our results also suggest that this hardly affects the prediction of dispersion energies. A rigorous analysis of error accumulation arising from different parameterizations reveals that error cancellation does not necessarily occur, leading to a monotonically increasing deviation in the dispersion energy with increasing molecule size. We discuss this issue in detail at the prominent example of the C 60 “buckycatcher”. We find deviations between individual parameterizations of several tens of kcal/mol in some cases. Hence, in combination with any calculation of dispersion energies, we recommend to always determine the associated uncertainties for which we will provide a software tool [1].

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# Can we predict how pharmaceuticals will crystallize?

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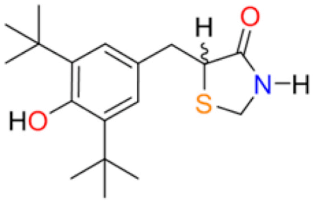
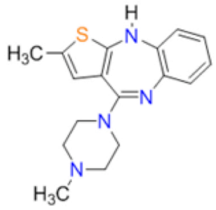
Crystal Structure Prediction (CSP) methods were developed on the assumption that an organic molecule would crystallize in its most stable crystal structure. Even implementing this approach is a challenge to computational chemistry methods,[1] as shown by the Cambridge Crystallographic Data Centre’s blind tests.[2] Polymorphism adds additional challenges, as this is usually a kinetic phenomenon with metastable polymorphs being unable to transform to the more stable structure in the solid state. CSP is being developed as an aid to polymorph screening [3] through calculating the crystal energy landscape, the set of crystal structures that are thermodynamically plausible as polymorphs. However, the crystal energy landscape usually includes more crystal structures than known polymorphs, raising the question as to why more polymorphs are not found.[4] This can be due to the approximations in the calculations, particularly the use of lattice energies rather than free energies but also the lack of consideration of kinetics. Sometimes the prediction of a putative polymorph can allow the design of a specific experiment to find it, for example by using an isomorphous crystal of another molecule as a template.[5] More commonly, the crystal energy landscape can rationalize observations of complex crystallization behavior, such as the occurrence of disorder [6]. Whilst the crystallization behavior of some molecules is easily predicted, many pharmaceuticals and chiral compounds really challenge our understanding of crystallization and ability to model thermodynamics[7].





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# Many-Pair Expansion: A Systematically Improvable Scheme for Correcting DFT Errors

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Many-pair expansion (MPE) [1,2] is a systematically improvable hierarchy of density functional approximations to the total energy of a many-body system. The key idea is the decomposition of the total electron density into a sum of localized two-electron v-representable subsystem densities. The recently introduced Self-Attractive Hartree (SAH) [3] decomposition is a practical method to partition electron density into such fragments, which are obtained through a regularized maximization of self-repulsion. The resulting set of eigenvalue equations resembles Kohn-Sham equations for electrons experiencing self-attractive Hartree potential and external potential common for all fragments. For such obtained subsystems, a series of non-interacting and interacting potential inversions is performed to systematically improve any density functional approximation used as a starting point. Already low orders of MPE can account for strong correlations and dispersion interactions, which is shown for Hubbard and PPP hamiltonians. An implementation for ab initio hamiltonians will be also presented together with initial results for several small molecules.

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# On the implementation, benchmark and application of Frozen Density Embedding Theory

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The majority of chemical processes occur in the condensed phase which may change molecular properties drastically. Thus, including environmental effects into quantum chemical calculations is necessary for an adequate description of these systems. In practice, however, the high computational demand of accurate quantum chemistry methods prevents an explicit treatment of the environment, particularly for systems of biological interest. Multi-level methods reduce the computational cost by treating environment and target molecule(s) at different levels of theory. Among such methods, Frozen Density Embedding Theory (FDET)[1,2] provides a formal framework in which the whole system is described by means of two independent variables: the embedded wavefunction and the density associated with the environment. The FDET approach can conveniently be combined with perturbative methods, e.g. the Algebraic Diagrammatic Construction (ADC) scheme for the polarization propagator[3]. The current implementation of FDE-ADC[4,5] uses the linearized FDET formalism[6], which in comparison to conventional FDET, is significantly less expensive computationally and more importantly leads to self-consistency between the energy and embedding potential while simultaneously preserving the orthogonality of the embedded wavefunctions for each electronic state.
52 molecular model systems were studied using FDE-ADC(2) and compared to their ADC(2) reference of the full system. The molecular test systems exhibit molecule-environment interactions of varying strength ranging from dispersion interaction to multiple hydrogen bonds. The resulting differences in excitation energies between reference and embedding method were analyzed in view of the magnitude of the shift and other descriptors relevant in the context of FDET. Furthermore an application to electronically excited states of a biological system (human cellular binding protein II) is presented.

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# Achieving a Favorable Trade-off between Accuracy and Computational Efficiency for Quantum Chemical Methods

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Choosing a quantum chemical method prior to a calculation usually means to compromise between accuracy and speed. In practice, single-determinantal approaches such as Kohn–Sham density functional theory (DFT) are usually chosen for feasibility reasons. On the example of our WCCR10 set of ten measured gas-phase ligand dissociation energies of large transition-metal complexes [1], we studied the trade-off between accuracy and computational efficiency for quantum chemical methods.

Several of the reactions in the WCCR10 set even represent hard problems for state-of-the-art correlated quantum chemical methods such as explicitly correlated single-reference coupled-cluster and multi-reference perturbation theory approaches [2].

It turns out that dispersion-corrected DFT approaches achieve a satisfactory agreement with coupled-cluster approaches for the WCCR10 set [2]. We can, however, obtain the ligand dissociation energies for the WCCR10 set three orders of magnitude faster when applying semiempirical molecular orbital (SEMO) models. Unfortunately, the results obtained with popular SEMO models deviate severely from the results obtained with correlated methods or with DFT. Consequently, we analyzed [3] the formalism of contemporary SEMO models to determine how we could capitalize on the computational efficiency without sacrificing the accuracy of the results. In our analysis, we put a special emphasis on the neglect of diatomic differential overlap (NDDO) approximation. Based on our findings, we proposed a way to construct a NDDO-SEMO model which is seamlessly related to more accurate quantum chemical methods [3]. For this NDDO-SEMO model, we can systematically assess the trade-off between accuracy and computational efficiency.

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# Density Functional Embedding Theory: a Gaussian and Plane-waves Implementation for Periodic Systems

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Density functional embedding theory (DFET) is a powerful multiscale approach to electronic-structure of complex systems. DFET assumes separation of the system into subsystems, which interact via the unique embedding potential [1]. One of the subsystems is then treated at the higher level of theory, whereas the environment and the interaction between them are described with density functional theory (DFT) [1], thus, combining high accuracy with computational efficiency in a rigorous quantum mechanical fashion.

Here the implementation of DFET within the Gaussian and Plane-waves (GPW) method [2] in the CP2K program [3] is presented. GPW provides a natural bridge between the local Gaussian basis description of the subsystems and the delocalized embedding potential and allows for an efficient implementation for the extended systems using the versatile CP2K toolkit. The implementation can utilize MP2, RPA and hybrid DFT as a high-level methods for the embedded region within CP2K and allows for linking to external software. Computational performance is discussed and applications of DFET to liquid and solid systems are presented.

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# Artificial Intelligence and Chemistry: What can we learn?

T. Laino[1,2], T. Gaudin[1], P. Schwaller[1]

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In this talk, I will present few Artificial Intelligence (AI) strategies applied to the field of predicting organic chemistry reactions [1] and to optimize the composition and process for the production of metal alloys with tailored mechanical properties, relevant to metallurgical industries. First, I will present the usage of a translation problem by introducing a template-free sequence-to-sequence model, trained end-to-end and fully data-driven to predict the outcome of organic chemistry reactions. In this context, we propose a tokenization, which is arbitrarily extensible with reaction information. Using an attention-based model borrowed from human language translation, we improve the state-of-the-art solutions in reaction prediction on the top-1 accuracy by achieving 80.3% without relying on auxiliary knowledge, such as reaction templates or explicit atomic features.

In the context of metal-alloy design and optimization we will present the use of variational autoencoders (VAE) to transform discrete data into a continuous representation. Subsequently, optimization algorithms search for an alloy's optimal properties in the previously obtained continuous representation. Both frameworks will be presented and discussed.

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# Torsional potentials of oxalyl halides and their thiocarbonyl derivatives: Challenges for contemporary density functional approximations.

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Accurate predictions of torsional potential energy profiles are crucial to correctly sample conformational degrees of freedom. Comparing currently popular density functionals to CCSD(T) we have investigated many small organic closed-shell molecules with conjugated hetero double bonds, i.e. oxalyl halides and their thiocarbonyl derivatives. Typically, density functional approximations (DFA) are assumed to provide reasonable energy estimates for such systems and properties. For molecules containing heavy halogens, however, nearly all DFAs fail to reproduce barrier heights accurately, and some even introduce spurious minima. Dispersion corrections show no improvement, and analysis of the results suggest that the self-interaction error is at the heart of the problem. Calibrated torsion-corrected atom-centered potentials can rectify some of the shortcomings of PBE, and also improve on σ-hole based intermolecular binding in oxalyl bromide dimer and crystal.

## Neural Network based Potential Energy Surfaces for Molecular Dynamics Simulations

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[1]Departement Chemie, Universität Basel

Despite the ever-increasing computer power, accurate ab initio calculations for large systems (thousands to millions of atoms) remain infeasible. Instead, approximate empirical energy functions are used. Most current approaches are either transferable between different chemical systems, but not particularly accurate, or they are fine-tuned to a specific application. In this work, a data-driven method to construct a potential energy surface based on neural networks is presented. Since the total energy is decomposed into local atomic contributions, the evaluation is easily parallelizable and scales linearly with system size.

The method is accurate across chemical and configurational space. The possibility to use small molecules as reference data to predict larger structures is also explored. Because of this, high-level ab initio methods, which are computationally too expensive for large molecules, become feasible for generating the necessary reference data used to train the neural network.

# Real time TDDFT for absorption and Raman spectroscopy

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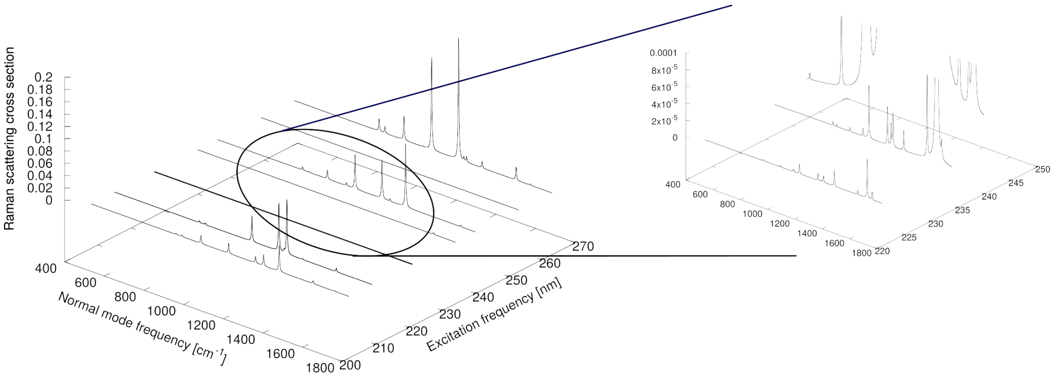
[1]University of Zurich

Time-dependent density functional theory (TDDFT) is nowadays an essential tool to study excited states and spectroscopic properties. Complementary to the standard approaches in the energy/frequency domain approaches using linear response TDDFT, a direct numerical integration of the time dependent Schrödinger equation is also viable and gives rise to a family of real time propagation (RTP) methods. Spectra can be obtained via a Fourier transform of certain properties which naturally resolves the whole frequency range in solely one simulation. Distinct advantages of RTP methods are the applicability to complex systems due to its favorable scaling and the fact that interactions with external fields are treated non-perturbatively, making non-linear spectroscopy feasible for larger systems [1].

We have used real time TDDFT to calculate absorption and Raman spectra. Non resonance and resonance Raman spectra (RRS) are obtained in just one simulation run, which allows to 'tune' the excitation frequency as in an actual experiment. The results are compared to standard approaches such as linear response TDDFT and, in case of RRS, with the excited state gradient approximation of Heller et al. [2].



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# Poly(triazine imide): Promising two-dimensional nanoporous nanosheet for molecular sieving.

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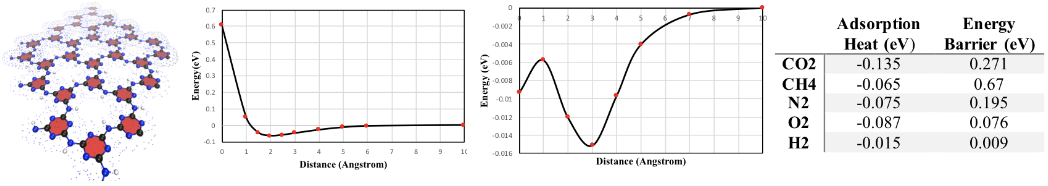
[1]Institute of Chemical Sciences & Engineering (ISIC), [2]Institute of Materials Science & Engineering

style="text-align: justify;">Two-dimensional (2d) nanoporous materials are an emerging material platform for highly energy-efficient, size-selective molecular separations.[1]As a new member of the 2d nanoporous materials, poly(triazine imide) or PTI has attracted extensive attention because of its promising properties for energy storage, conversion, sensor, and energy efficient 2d membrane usages.[2] PTI is a 2d network composed of imide-bridged triazine units.[3]The way the triazine units are linked produces pores with an interesting size for several challenging separations.(Fig. 1)



|  | Adsorption Heat (eV) | Energy Barrier (eV) |
|---|---|---|
| **CO2** | -0.135 | 0.271 |
| **CH4** | -0.065 | 0.67 |
| **N2** | -0.075 | 0.195 |
| **O2** | -0.087 | 0.076 |
| **H2** | -0.015 | 0.009 |

(a) (b) (c) (d)

Figure 1. a. PTI sheet Potential energy profile for b. CH4 and c. H2 at different distances from PTI membrane. d. Adsorption Heat and energy barrier of light gases (H2, CO2, O2, N2, and CH4)

In this work, density functional theory (DFT) calculations were performed to investigate the capability of PTI membranes for the separation of light gases ($H_2$, $CO_2$, $O_2$, $N_2$ and $CH_4$) by molecular sieving. Different van der Waals corrections were studied and benchmarked against more advanced technique. Based on the free-energy barriers and heats of adsorptions, the molecular selectivities were calculated. It was observed that the PTI can efficiently separate $H_2$ from $CO_2$, $N_2$ and $CH_4$. Interestingly, it could yield one of the best separation performance for the $O_2/N_2$ separation. Such a PTI sheet could have ubiquitous impacts on tremendous energy and technological applications.

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[2] Kessler et al., *Nat. Rev. Mater.***2017**, *2*, 17030.
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# Conceptual Framework of Molecular Electronics

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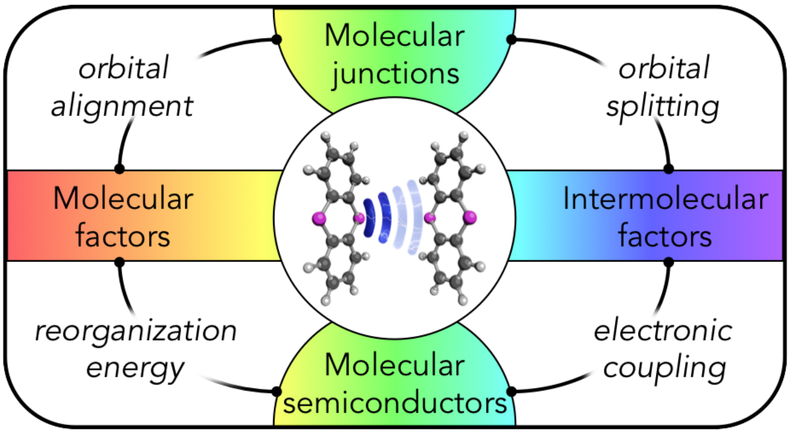
Non-covalent interactions are important across a range of organic electronic materials, from molecular semiconductors (e.g., the crystalline organic semiconductors) to molecular junctions (such as dimer bridges in scanning tunnelling microscope experiments). These intermolecular interactions depend on the nature of molecular cores and define not only the stability of their non-covalent assembly, but also its charge transport properties.[1]



In the present contribution, we draw a parallel between the transport in the nanogap between metallic electrodes and charge carrier mobility in the bulk of an organic semiconductor.[2] We show that, within the model approximations, the same systems are consistently among the best and the worst performers, with similar principles guiding their performance in the two types of materials. More generally, we establish a conceptual framework for various non-covalent molecular electronic architectures that connects intrinsic properties of molecular cores with the properties of their non-covalent assemblies (see Figure). These results demonstrate the unifying footprint of the fundamental electronic structure of molecular cores on the diverse charge transport properties and offer the design strategies for more conductive organic electronic devices.

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# Unravelling the chemical nature of anaerobic methane oxidation: a two-electron redox process facilitated by water

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Conversion of methane to methanol is an industrially very important process, as it provides a sustainable route from an abundant and clean component of natural gas to one of the main precursors for chemicals synthesis. An efficient stepwise conversion process catalyzed by copper-exchanged zeolites has been suggested, [1] and the configuration of active sites has been carefully characterized. [2]

We have recently proposed a conceptually new direct "anaerobic" conversion route of methane into methanol over the copper-exchanged mordenite zeolite, using water as the source of oxygen [2]. In this process, the two-electron redox reaction with water leads to the formation of molecular hydrogen, which itself is a valuable species. The detailed mechanism of hydrogen release and the regeneration of the catalyst, however, requires further investigation. We have shown that water molecules play a crucial role in this process, acting both as a stabilizing agent for removing the methanol, and a necessary source of oxygen to recover the catalyst by oxidizing the copper species. However, in order to identify the actual reaction pathway, all possible intermediates and the connecting reaction barriers need to be systematically sampled, a task which calls for molecular dynamics simulations.

We found that the hydrogen atoms of the water molecules are highly mobile, and their transfer is often facilitated by the copper atoms of the active center. Up to four transition states can be identified, all of which include hydrogen transfer. As there is never a direct abstraction of protons into the gas phase, the calculated transition state barriers are moderate, and should be consistent with the experimental necessity for higher temperature and higher water pressure.

Here we critically evaluate the results of the mechanistic study, discuss the role of water and copper hydrate intermediates for facilitating the energetically favourable release of hydrogen, and propose a detailed mechanism of such an "anaerobic" oxidation process.

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