Computational Chemistry Days 2023

11. – 12.5.2023
University of Oulu

Contents

Session 1 – Thusday 11 May

13:10–13:35	Ilpo Vattulainen	What biomolecular simulations can offer? Understanding and controlling the function of membrane receptors associated to brain function at the level of a single molecule
13:35–13:55	Terttu Hukka	Molecular dynamics simulations of water in poly(L-lactic acid) matrix
13:55–14:10	Saara Lautala	Expanding the Paradigm of Structure-Based Drug Design: Molecular Dynamics Simulations Support the Development of New Pyridine Based Protein Kinase C-Targeted Agonists
14:10–14:30	Tatu Pantsar	What Defines the Length of Drug–Target Residence Time of a Small-Molecule Inhibitor: Insights from MD Simulations
14:30–14:50	Noora Aho	Constant pH molecular dynamics: investigating pH-dependent processes in biomolecules using computers
14:50–15:10	Vivek Sharma	Bending of inner membrane by a mitochondrial super-complex

What biomolecular simulations can offer? Understanding and controlling the function of membrane receptors associated to brain function at the level of a single molecule

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Although understanding the functioning of the brain is undeniably problematic, one could assume that it cannot be too difficult if the goal is to understand the functioning of individual cell membrane receptors that have a role in the functioning of the brain. The fact is that numerous drugs have been developed for the treatment of neurological diseases such as depression, and these drugs act or are assumed to act on individual receptors, and they also work. But even if the individual receptors could be identified, how can their operational environment, that is the nanoscale cell membrane region surrounding the receptor in living brain tissue, be determined without destroying the living target being studied. Further, if this were possible in living subjects, how can we be sure that the drug molecule developed for a neurological disease mainly affects exactly the receptor it is supposed to affect. Unfortunately, research in this field is very fascinating in the sense that even though there are plenty of active drug molecules known, there is not too much certainty about their mechanisms of action.

Computational science in the form of biomolecular simulations is quite useless without experimental support, but if experimental data are available to validate the simulation models and test the predictions they produce, computational science is undeniably a tool that generates insight that cannot be achieved with experimental research. In neurological processes, this condition is met – there is plenty of experimental data, and due to the complexity of the phenomena, the added value given by simulations is impressive.

As examples of this added value, we discuss the signaling mediated by neurotransmitters in synapses, and we highlight how simulations are able to reveal the mechanisms of action of neurotransmitters with their membrane receptors, such as receptors belonging to the GPCR family [1]. If the operating environment of these membrane receptors changes, as has been observed in several neurological diseases, the simulations further show how the function of the receptors is disturbed [2]. If the function of the receptors is to be restored, drug molecules can produce the desired response. With the help of simulations, however, it can be shown that drugs that have been developed and found to work, such as fluoxetine (Prozac) in the treatment of depression, do not necessarily interact with the receptor whose activity these drugs were supposed to regulate [3]. This fascinating result highlights the growing role of computational sciences in the development of new drugs.

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Molecular dynamics simulations of water in poly(*L*-lactic acid) matrix

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Poly(lactic acid) (PLA) is one of the most commonly studied [1] bio-based and biodegradable [2] polymer, which can be used in medical devices and also as a substitute for fossil-based thermoplastic polymers in certain applications. Water is known to help biodegradation, but it also simultaneously deteriorates mechanical properties of PLA. The details of the chemistry involved in the PLA–water interaction and the changes of the material properties are still not thoroughly clear in literature.

In this work, we use molecular dynamics (MD) simulations to investigate the poly(*L*-lactic acid) (PLLA)–water interactions at three different water concentrations. For PLLA, we use the model of Glova et al. [3]. Water is known to act in a manner of a plasticizer in various polymers lowering the glass transition temperature (T_g) [4]. We determine the effect of water on various PLLA properties, and in this study present the T_g–composition dependency. We compare our simulation results with the available predictive, theoretically and empirically derived mixing models, such as Fox and Gordon–Taylor, and also with experimental results reported in literature for related poly(*D,L*-lactic acid) (PDLLA)–water systems [5,6].

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Expanding the Paradigm of Structure-Based Drug Design: Molecular Dynamics Simulations Support the Development of New Pyridine Based Protein Kinase C-Targeted Agonists

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Mild activation of the enzyme protein kinase C (PKC) is of potential therapeutic value [1, 2]. The desired activation occurs when PKC C1 domain interacts with an intracellular membrane that incorporates the lipid second messenger 1,2-diacyl-*sn*-glycerol (1,2-DAG). Designing these therapeutics is however not without pitfalls, largely due to the complex binding environment of the lipid-water interface, as we have discovered previously [3]. We identified that the reason for failure of pyrimidine analogs designed to improve on the previous isophthalate derivatives were exactly the challenges caused by the lipid-water interface binding environment [3,4,5]. We observed that the propensity of harmful internal hydrogen bonding in the pyrimidine analogs is enhanced by the lipid environment, which then both obstructs binding and leads to unfavorable reorientation, and therefor prevents the correct accessing of the PKC C1 domain [3].

Interestingly, this crucial harmful interaction was only picked up by the more rigorous molecular dynamics simulations (MD), as structure-based docking predicted both isophthalate and pyrimidines both to bind well to the C1 domain [4,5]. Our investigation therefor highlighted the need for in silico simulations in the relevant environment already in the design phase. We have now by implementing lipid environment simulations in tandem with *in vitro* assays discovered a new promising generation of compounds, pyridines, which readily demonstrate the desired behavior of possible therapeutics; our most recent study yielded two new potential leads for therapeutic PKC modulation [6].

These results demonstrated the potential of simulations that include the membrane environment as a part of the PKC C1 domain modulator design process: both studies uncovered behaviors that can directly affect the activation of the target protein and were undetectable via traditional docking studies. Thus, this approach enhances the existing drug design workflow as an additional computational method to support the traditional CADD approach.

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What Defines the Length of Drug–Target Residence Time of a Small-Molecule Inhibitor: Insights from MD Simulations

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When a drug molecule binds to its target protein, it stays bound for some time before eventually unbinding the target. The actual time how long a drug molecule resides bound to its target varies among compounds. The lifetime of the drug-target complex may play a crucial role in drug efficacy, as a long target residence time can, in some cases, be important for drug efficacy. Understanding the underlying causes of drug-target residence time enables more rational drug design. However, little is known about the underlying causes of inhibitor residence time at the molecular level, which complicates drug optimization processes.

We employed long timescale all-atom molecular dynamics (MD) simulations to investigate two structurally similar p38α MAPK inhibitors with short and long residence times [1]. The selected inhibitors show comparable inhibitory activities in the biochemical assays with isolated enzymes, while in the cell-based MK2 translocation assay the inhibitor with longer residence time demonstrated better efficacy. In the contribution, I will discuss our key results and their implications for compound design when aiming for inhibitors with improved target residence time. In addition to the conducted classical MD simulations (~360 μs), we applied and combined Markov state modelling with metadynamics simulations and WaterMap simulations. We will highlight the importance of protein conformational stability and solvent exposure, buried surface area of the ligand and binding site resolvation energy for residence time. Finally, these observations on target protein behavior and the role of water molecules were confirmed with a structurally diverse small molecule kinase inhibitor that has an extremely short residence time.
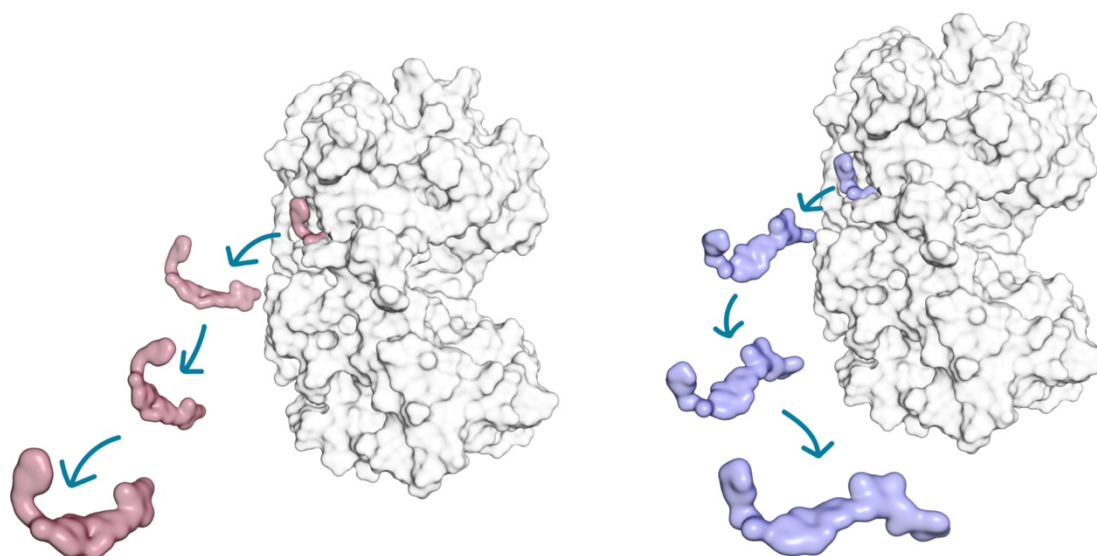
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Constant pH molecular dynamics:
investigating pH-dependent processes in biomolecules using computers

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pH is one of the key parameters affecting the function and dynamics of proteins and other biomolecules. Biological processes that depend crucially on the pH and involve protonation state changes occur for example in the energy production of cells, enzyme catalysis and membrane transport.

In addition to experimental methods, classical molecular dynamics (MD) simulations are widely used to study the dynamics of biomolecules at the atomic level. While in variables such as temperature and pressure are commonly fixed in MD to match an experimental setup, fixing pH has not been a standard option. Instead, the protonation states of titratable groups are initially chosen and fixed during the simulation, by selecting the statistically most probable protonations at the desired pH.

So-called *constant pH molecular dynamics* enables performing MD at a constant pH. It allows dynamic changes in protonation states during the MD simulations, by changing the charges of atoms on the fly depending on the pH set by the user and local electrostatic interactions. With constant pH MD protonation states are sampled along with atomic coordinates during the simulation, allowing the investigation of pH-dependent processes and for example running computational titration. We have fulfilled a long-term request from the simulation community and implemented an efficient and accurate constant pH MD routine into GROMACS, which is a popular open-source software for MD simulations of biomolecules. [1,2]

In my presentation, I will provide insights into the possibilities of studying pH-dependent biological systems using molecular dynamics. I will introduce our recently published constant pH MD implementation in GROMACS and discuss few interesting applications.

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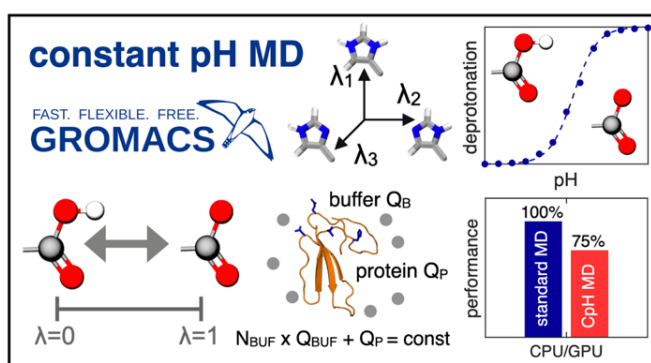
Bending of inner membrane by a mitochondrial supercomplex

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In many organisms, ATP is generated by utilizing the proton electrochemical gradient across the biological membrane. A complicated enzymatic machinery called the electron transport chain (ETC) is responsible for establishing the gradient across the membrane. Varying architectures and composition of ETC, called supercomplexes, have been observed in different organisms. The well-defined roles of supercomplexes are yet to be identified, but they likely serve to enhance energy efficiency. Here, data from coarse-grained simulations will be presented to show how *Tetrahymena thermophila* supercomplex, the structure of which has recently been resolved by cryo-EM, folds the membrane to a highly curved architecture that may have energetic consequences [1].
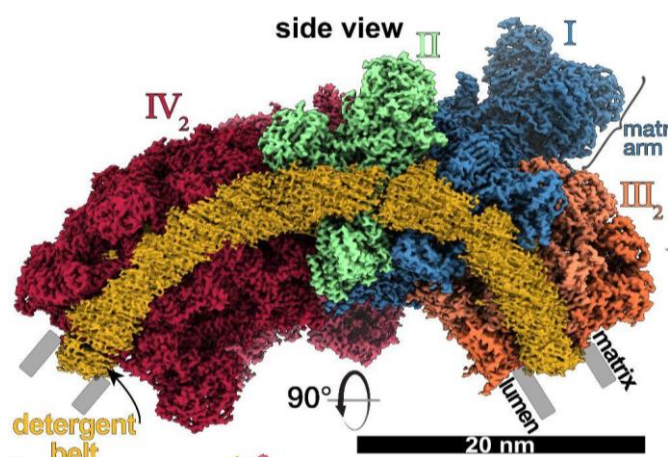
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Session 2 – Thusday 11 May

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15:40–16:00	Risto Laitinen	Chalcogen–Chalcogen Secondary Bonding Interactions
16:00–16:20	Laura Laverdure	Criteria for HER on Au_{25}-based nanoclusters
16:20–16:35	Ethan Berger	Raman spectra of 2D titanium carbide MXene from machine-learning force field molecular dynamics
16:35–16:50	Kati Asikainen	Hematite Clusters on Anatase TiO_2 Surface and Effect of Oxygen Vacancy: A First Principles Study
16:50–17:05	Hanan Ibrahim	Molecular size effect on the gas phase selective hydrogenation of substituted alkynes on PdAg (111) single atom alloy
17:05–17:25	Ygor Morais Jaques	Modeling of Self-Assembled Monolayers and their Wetting Properties for Surface Engineering
17:25–17:40	Kim Eklund	Elastic properties of binary d-metal oxides studied by hybrid density functional methods

Chalcogen-Chalcogen Secondary Bonding Interactions

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Secondary bonding interactions (SBI) [1] are intra- or intermolecular interactions that are longer than covalent single bonds, but shorter than the sum of van der Waals radii. They have also been called non-covalent bonding, soft-soft, closed-shell, semi-bonding, non-bonding, and weakly bonding interactions. In case of Group 17, 16, and 15 compounds, they are also known as halogen, chalcogen, and pnictogen bonds, respectively. The strength of SBIs involving p block elements increases upon going down the groups in the Periodic Table. The complete description of SBIs requires the consideration of orbital interactions ($n^2 \rightarrow \sigma^*$), as well as electrostatic and dispersion contributions [2].

Chalcogen-chalcogen SBIs have been explored by considering solid-state structures of all members in the series of $[Fe(C_5H_4E)_2E']$ (E, E' = S, Se, Te) using DFT calculations at PBE0/pob-TZVP level of theory involving periodic boundary conditions [3]. The intermolecular close contacts were considered by QTAIM and NBO analyses. The tellurium macrocycles $Te_n(CH_2)_{5n}$, $Te_n(CH_2)_{6n}$, and $Te_n(CH_2)_{7n}$ (n = 1-4) are also excellent models to study intermolecular Te···Te SBIs. The stacking of these molecules due to SBIs leads to infinitely long hollow tubes. Their bonding in the solid state has also been explored with DFT calculations involving periodic boundary conditions [4].

$Te_4(CH_2)_{20}$ 6.3 Å $Te_4(CH_2)_{24}$ 8.0 Å $Te_4(CH_2)_{28}$ 8.7 Å
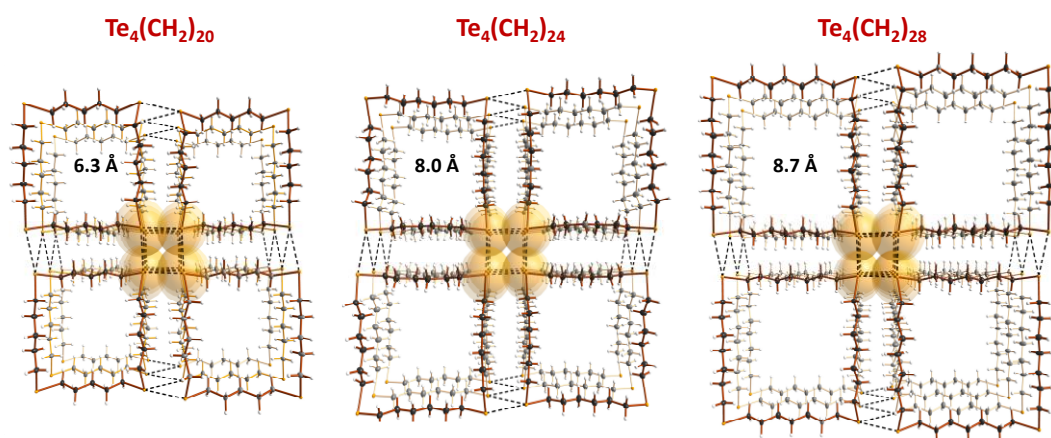
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Criteria for HER on Au$_{25}$-based nanoclusters

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The hydrogen evolution reaction (HER) is crucial in addressing climate change. Industrial scale hydrogen production, however, requires catalysts. Nanomaterials offer several advantages over conventional HER catalysts, notably the possibility of atomic precision in tailoring the intrinsic activity. Thiolate protected $MAu_{24}(SR)_{18}$ (M = Au, Cu, Pd) nanoclusters are of particular interest because the charge state and composition can be precisely tuned thereby altering the electrocatalytical activity towards HER. Here, we present a comprehensive computational study examining how the charge state and dopants affect the catalytic activity of $[MAu_{24}(SCH_3)_{18}]^q$ towards the Volmer step of the HER.

If a single adsorbed hydrogen atom is the key intermediate, then according to the Sabatier principle, its adsorption energy should be thermoneutral for an ideal HER catalyst. This reasoning is behind the scaling relations typically used to identify promising HER catalysts computationally. Our results show that adsorption energies alone are an insufficient criterion; experimentally relevant redox potentials, the corresponding catalyst's charge states, and the kinetic barriers should also be considered. With these parameters, we explain the relative activity of $MAu_{24}(SR)_{18}$ (M = Au, Cu, Pd) clusters reported by Kumar et al. [1] Our results validate a more thorough computational approach that includes redox potentials which determine charge to understand and screen electrocatalytically active nanoclusters.

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Raman spectra of 2D titanium carbide MXene from machine-learning force field molecular dynamics

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MXenes represent one of the largest classes of 2D materials with promising applications in many fields and their properties are tunable by altering the surface group composition. Raman spectroscopy is expected to yield rich information about the surface composition, but the interpretation of the recorded spectra has proven challenging. The interpretation is usually done via comparison to the simulated spectra, but there are large discrepancies between the experimental spectra and the earlier simulated spectra. In this talk, we present a computational approach to simulate the Raman spectra of complex materials which combines machine-learning force-field molecular dynamics and reconstruction of Raman tensors via projection to pristine system modes. This approach can account for the effects of finite temperature, mixed surfaces, and disorder. We apply our approach to simulate the Raman spectra of titanium carbide MXene and show that all these effects must be included in order to appropriately reproduce the experimental spectra, in particular the broad features. We discuss the origin of the peaks and how they evolve with the surface composition, which can then be used to interpret the experimental results.

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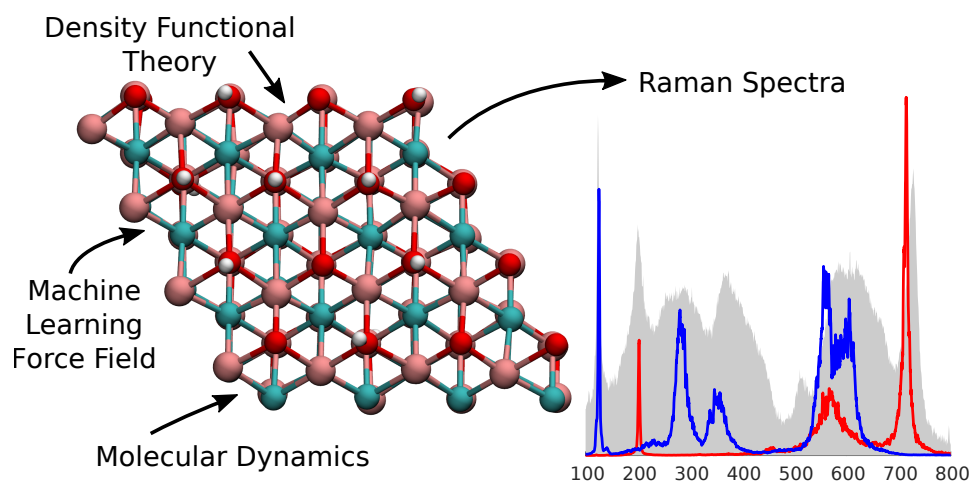
Hematite Clusters on Anatase TiO$_2$ Surface and Effect of Oxygen Vacancy: A First Principles Study

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The search of photocatalytic materials, used in several environmental applications, has become increasingly important during the recent years. The prototype material, TiO$_2$, has been intensively studied and a lot of attention has been paid to its 3.2 eV band gap, which is too large for visible light absorption, and quick recombination rate. Since TiO$_2$ is a cheap and abundant material, several methods have been developed to improve its properties. One way to proceed is to combine TiO$_2$ with other semiconductors with a smaller band gap. One such material is hematite, Fe$_2$O$_3$, which has a bulk band gap of 1.9–2.2 eV and earlier works have reported to improve photocatalytic properties of TiO$_2$ [1].

We have performed first principles calculations using the VASP code [2], in order to study the atomic, magnetic and electronic properties of (Fe$_2$O$_3$)$_n$ ($n = 1, 2$) clusters on the anatase TiO$_2$(101) surface [3]. The choice of a small cluster size was motivated by the earlier experimental study of Fe$_2$O$_3$ clusters on the TiO$_2$ surface [4]. We used the GGA+U approach in order to get more realistic band gaps for both hematite and TiO$_2$. We find that the adsorption of the clusters on the surface is energetically favorable, thus enabling the modification of the surface properties. Due to the adsorption, impurity states arise, narrowing the band gap. We observe a notable electron transfer from the cluster to the surface attributed to a formation of heterojunction in the heterostructure which may play a crucial role in the photocatalytic reactions. Low charge transfer at higher coverage can support the claim that increase in Fe$_2$O$_3$ concentration and cluster size can hinder the photoactivity of TiO$_2$ [4].

We also studied the possibility of altering the properties of the heterostructure by introducing an oxygen vacancy in the heterostructure of TiO$_2$ and (Fe$_2$O$_3$)$_1$. The vacancies are shown to further alter the electronic structure, and also locally affect the magnetic and charge transfer properties of the system. The results show that the oxygen vacancy can be widely used for tuning both the electronic and magnetic properties of the heterostructure of TiO$_2$ and Fe$_2$O$_3$.

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Molecular size effect on the gas phase selective hydrogenation of substituted alkynes on PdAg (111) single atom alloy

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Single-atom alloys (SAA), prepared by the dispersion of single active metals in less active host metals, are promising new catalysts with unique properties, such as improved activity and selectivity. The selective hydrogenation of alkynes into alkenes is an important process in the synthesis of many fine chemicals. The selective hydrogenation of acetylene (AC) into ethylene has been studied extensively on SAA catalysts, but less attention has been paid to the partial hydrogenation of phenylacetylene (PA) and the other higher substituted alkynes.

In this work, we study the hydrogenation pathways for phenylacetylene on PdAg SAA catalyst as well as on pure Pd and Ag surfaces, using the density functional theory. Our results show that the PdAg SAA improves the activity of the host metal Ag(111) by improving the binding of the reactants and by lowering the activation energies of the hydrogenation steps. However, our results show that the selectivity of the dilute SAA does not improve over pure host metal.

We address how the effectiveness of the SAA catalyst depends on the size of the adsorbate molecule by comparing three different alkynes: acetylene, phenylacetylene and diphenylacetylene. We observe that SAA improves on the binding of smaller molecules over larger ones relative to the host metal. This has implications for SAA catalyst design as the composition of the SAA catalyst depends on the size of reactant molecule.

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Modeling of Self-Assembled Monolayers and their Wetting Properties for Surface Engineering

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Plant surfaces commonly exhibit super-hydrophobicity, meaning that they efficiently repel water. The repelled water rolls off but also, e.g. drags dirt with it, thus keeping the surface clean. Replicating such behavior in the synthetic materials around us is of extreme importance for applications such as water harvesting [1], liquid manipulation [2], and directional oil-water separation [3]. This would allow making substantial progress in solving the global problems of clean water scarcity and the pollution of its sources. One way of achieving rapid water removal on synthetic materials surfaces is through topographically modifying the microstructure of surfaces and using highly repelling coatings, such as self-assembled monolayers (SAMs). SAMs provide high uniformity, high quality and are interesting prototyping coatings for tailoring surfaces and thin film design.

In the present work, we focused on control of the wetting behavior via design of octyltrichlorosilane (OTS) SAMs on a silica substrate. Our experimental characterization work showed that depending on the coverage of the SAMs, water contact angles change gradually from about 10° to 110° exhibiting a wide range of static and dynamic wetting behavior. Interestingly, the contact angle hysteresis and contact line friction are low both for the low-coverage hydrophilic OTS SAMs and the high-coverage hydrophobic SAMs. We mapped the molecular level structure and wetting characteristics of the OTS coatings via atomistic detail molecular dynamics simulations. The simulations results indicate that the low friction of both low-and high-coverage SAMs originates from the mobility of interfacial water molecules and can be connected with the SAM layer structure. The findings demonstrate a counterintuitive mechanism for slipperiness. The work enables further engineering of surface wetting characteristics via the SAM coatings and advancing our understanding of the relationship between surface roughness and wetting behavior. [4]

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Elastic properties of binary d-metal oxides studied by hybrid density functional methods

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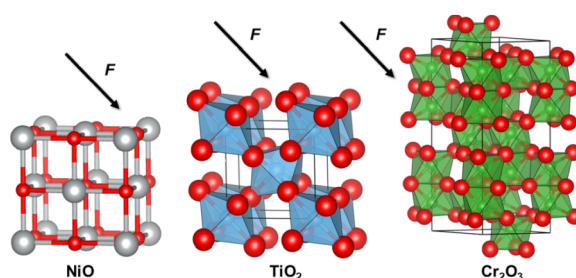
The detailed understanding of elastic properties and mechanical durability of ceramic materials is important for their utilization in advanced devices and as catalysts. For accurate representation of d-metal oxides and especially their magnetic ordering and geometries, hybrid density functional (DFT) methods are required [1]. We have carried out a systematic study of the elastic properties of binary d-metal oxides [2] with hybrid DFT at the DFT-PBE0 level of theory with TZVP basis set within the CRYSTAL code package [3].

The two implementations [4,5] within the CRYSTAL code result in both polycrystalline and single crystal bulk moduli, which are compared with experimental data. The bulk modulus date is then used to observe periodic trends in several structure types, namely rutile, corundum, and rocksalt. For both magnetic and non-magnetic d-metal oxides the used level of theory results in an accurate representation of elastic properties when compared with experimentally measured values.

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Session 3 – Friday 12 May

09:00–09:25	Theo Kurtén	Modelling peroxy radical recombination
09:25–09:45	Vishaka Kaim	Selective separation of scandium (III) from rare earth elements using novel quaternary ammonium based ionic liquids and its DFT study for the mechanism
09:45–10:05	Dage Sundholm	5th generation emitter molecules
10:05–10:25	Akseli Mansikkamäki	Main-Group Single-Molecule Magnets
10:25–10:40	Anand Chekkottu Parambil	Ligand-Metal interaction in Lanthanocene
10:40–11:00	Yavuz Dede	Theoretical study of activation of dioxygen by $[(H)Ni(OH)]^+$, non-innocence, electron transfer, and radicals

Modelling peroxy radical recombination

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The least volatile organic compounds participating in atmospheric new-particle formation are very likely accretion products from self- and cross-reactions of peroxy radicals: RO_2 + $R'O_2$. This class of reactions presents a remarkable challenge to computational chemistry methods, and has been identified as one of the unsolved problems in atmospheric chemistry [1]. The reaction path involves at least an initial pre-reactive complex ($RO_2…R'O_2$), a covalently bonded tetroxide intermediate (RO_4R'), and a subsequent product complex ($RO…O_2…R'O$). The tetroxide can only be formed on a singlet potential energy surface, while the O_2 co-product must be formed in its triplet ground state for the reaction to be thermodynamically feasible. The two alkoxy radicals (RO and R'O) in the product complex must therefore be coupled as a triplet, allowing the overall system to remain a singlet. The tetroxide decomposition thus involves no less than four unpaired electrons, making it impossible to describe with standard single-reference methods [2]. Even multireference methods struggle with the tetroxide decomposition step, with different methods and active spaces and sometimes leading to qualitatively different conclusions concerning, for example, the decomposition energetics, or the possible existence of a RO_3 intermediate.

In contrast, the tetroxide formation step can be treated using standard reaction kinetics approaches, and for systems with a non-negligible activation energy, master-equation calculations using high-level single-reference energies (albeit informed by our multireference reaction mechanisms) yield overall $RO_2 + R'O_2$ reaction rates in order-of-magnitude agreement with experiments [2]. For systems without activation barriers, similar accuracy for the overall rates can be reached through an even simpler semi-empirical approach, based on non-reactive molecular dynamics estimates of the pre-reactive complex lifetimes [3]. Branching ratios between different product channels are unfortunately more difficult to estimate, as they involve a competition between three or more very rapid (nanosecond-timescale) reactions of the weakly bonded $^3(RO…R'O)$ product complexes, including dissociation to free alkoxy radicals (radical channel), intermolecular H-shifts forming carbonyl + alcohol products (molecular channel), and intersystem crossings (ISCs) allowing accretion product formation (ROOR' channel) [4]. For chemically complex reactants, even more channels open up, for example alkoxy scission reactions, which upon subsequent ISC permit the formation of thermally stable ether and ester accretion products [5]. Especially the ISC rates are strongly dependent on the complex geometry, and machine-learning methods will likely be required to properly predict thermally-averaged ISCs for aerosol-relevant large $RO_2 + R'O_2$ systems.

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Selective separation of scandium (III) from rare earth elements using novel quaternary ammonium based ionic liquids and its DFT study for the mechanism

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The selective separation of scandium (III) from rare earth elements is an important topic in the field of hydrometallurgy due to the increasing demand for scandium in various industrial applications. Recently, quaternary ammonium-based ionic liquids (QAILs) have emerged as promising extractants for the selective separation of scandium (III) from rare earth elements. In this response, the experimental and DFT studies for the selective separation of scandium (III) from rare earth elements using novel QAILs has been discussed.

Experimental studies have been conducted to investigate the extraction behaviour of scandium (III) and rare earth elements using QAILs. It has been found that QAILs can selectively extract scandium (III) over rare earth elements from aqueous solutions at pH 3-5. The selectivity for scandium (III) extraction is attributed to the difference in the coordination chemistry of scandium (III) and rare earth elements. QAILs have a chelating effect on scandium (III) due to the presence of nitrogen atoms in the cationic moiety of QAILs. Moreover, the extraction of scandium (III) using QAILs is influenced by various parameters such as temperature, the concentration of extractant, and the acidity of the aqueous phase. Density functional theory (DFT) calculations have been carried out to elucidate the mechanism of scandium (III) extraction using QAILs. DFT calculations have shown that the complexation of scandium (III) with QAILs involves the formation of a chelate ring between the scandium ion and the nitrogen atoms of the QAILs. The energy of complex formation is found to be higher for scandium (III) than rare earth elements due to the smaller ionic radius of scandium (III) compared to rare earth elements. DFT calculations have also shown that the selectivity of QAILs for scandium (III) extraction is influenced by the steric hindrance of the QAILs.

In conclusion, experimental and DFT studies have shown that QAILs can selectively extract scandium (III) over rare earth elements from aqueous solutions. The selectivity of QAILs for scandium (III) extraction is attributed to the difference in the coordination chemistry of scandium (III) and rare earth elements. DFT calculations have provided insights into the mechanism of scandium (III) extraction using QAILs.

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5th generation emitter molecules

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Molecules with an unusual reverse order of the lowest excited singlet (S_1) and triplet (T_1) states are called 5th generation emitter molecules because delayed fluorescence with a very high quantum yield of luminescence is expected from them due to the inverted singlet-triplet gap. Heptazine (1,3,4,6,7,9,9b-heptaazaphenalene) derivatives belong to this class of molecules thanks to a combination of multiple resonance (MR) effects and a significant double excitation character. Excitation energies of the T_1 and S_1 states of heptazine derivatives calculated at the coupled-cluster and second-order multiconfiguration perturbation theory levels show that the singlet-triplet gap is indeed inverted as compared to the one expected from Hund's rule.[1]
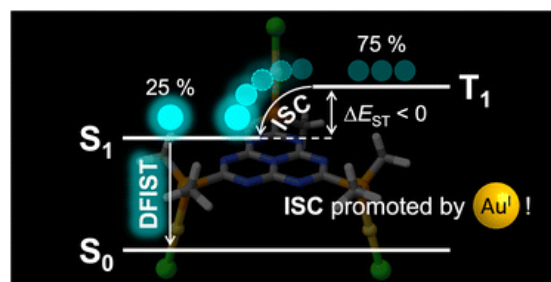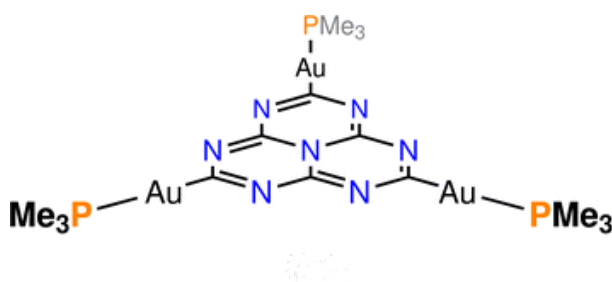
However, the rate constant of the intersystem crossing (ISC) is very small for symmetry reasons. The ISC rate can be increased by substituting heptazine with a heavy element. The substitution also breaks the symmetry leading to a faster ISC rate. We have designed gold(I) containing heptazine derivatives and studied computationally the effect of the gold(I) metalation and coordination on the optical properties of heptazine (see the figure). Ab initio calculations at the approximate second-order coupled cluster (CC2) and extended multiconfigurational quasi degenerate perturbation theory at the second order (XMC-QDPT2) levels show that the molecule has an inverted singlet-triplet gap due to the alternating spatial localization of the electron and hole of the exciton in the heptazine core. A non-vanishing one-electron spin-orbit coupling operator matrix element between T_1 and the S_1 state leads to a large ISC rate constant for the $S_1 \leftarrow T_1$ transition suggesting that the molecule represents this new family of complexes and may be the first reported organometallic 5th-generation emitter molecule.[2]

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Main-Group Single-Molecule Magnets

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Single-molecule magnets (SMMs) are molecules with a bistable magnetic ground state and that display slow relaxation of magnetization. [1] The two states of the ground doublet correspond to opposite orientations of the magnetic moment, and the slow relaxation implies that the system can be prepared in either one of these states for prolonged periods of time. This controllable magnetic ground state coupled with the small size of the molecules means that SMMs have possible applications in quantum information processing [1]. To date, the magnetic moment in all experimentally characterized SMMs originates from open d or f shells of d or f block metals. However, I recently showed at a theoretical level that it is possible to construct SMMs using the main-group element bismuth without any need for transition metals, lanthanides or actinides. Furthermore, due to the strong spin-orbit coupling of the heavy p-block element, on certain metrics it is possible that bismuth-based SMMs can have higher operational temperatures than even the best current SMMs based on dysprosium. Preliminary estimates of the stability of the bismuth-based SMM predict that it is experimentally accessible [3].

In the present work I will discuss the concept of main-group SMMs and their design principles. The results are based on both high-level quantum-chemical multireference calculations and simple theoretical derivations. Considering both the availability of heavier main-group elements and the chemical feasibility of the possible structures, it is demonstrated that bismuth in the oxidation state 0 or tellurium in the oxidation state +1 are the most promising candidates for the experimental realization of main-group SMMs.

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Ligand-Metal interaction in Lanthanocene

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Organometallic compounds are those in which there is a metal-carbon bond present. In organometallic chemistry, Metallocene is a special class that has haptic covalent bonds between a metal ion and two arene/ring ligands surrounding it. In this set of compounds, the metal ion coordinates to the π-electron system of arene rather than individual atoms, forming haptic bonds. Lanthanocene is a metallocene with a lanthanide metal center and contrastingly these systems are often perceived to have electrostatic bonds. Recently, some of these systems were found to feature strong magnetic axiality useful to design, efficient single-molecule magnets [1].

Computational studies were conducted for bonding considerations of ligands: cyclopentadiene and cyclobutadiene with lutecium ion using Energy Decomposition Analysis [2] (EDA) and Natural Orbital Chemical Valence [3,4] (NOCV).

This study concluded that the interaction of lanthanide-carbon bonds was largely electrostatic in nature as expected by general norm, though it had a significant covalent contribution, and it doesn't greatly vary between different geometries studied. The covalency character was dependent on properties like substitution by bulkier ligands producing steric effects and the ring structure. An energy partitioning scheme with molecular orbital correlation diagrams was produced to provide insights into bonding characteristics qualitatively.
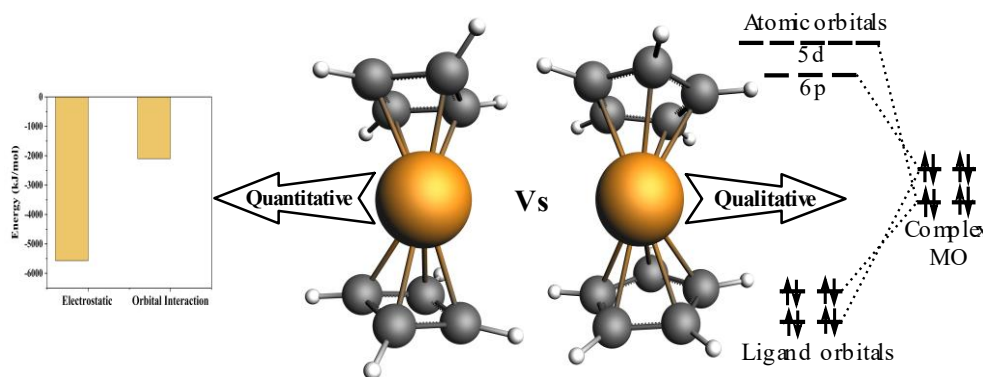
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THEORETICAL STUDY OF ACTIVATION OF DIOXYGEN BY [(H)Ni(OH)]$^+$, NON-INNOCENCE, ELECTRON TRANSFER, AND RADICALS

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[(H)Ni(OH)]$^+$ complex cation is able to activate dioxygen as well as methane in separate reactions.[1,2] This remarkable reactivity was shown to be due to the intramolecularly oxidized radicaloid hydroxyl ligand in the first excited quartet state. Here, activation of dioxygen by [(H)Ni(OH)]$^+$ was investigated using highly correlated Coupled Cluster and multi reference ab initio calculations as well as Density Functional Theory (DFT). Formation of hydroperoxo complex, a key intermediate for generation of all the observed products was corroborated. Orbitals and wave functions utilized to monitor the electron transfer events reveal that, after complexation of dioxygen with [(H)Ni(OH)]$^+$ an intramolecular electron transfer from the Ni-center to the hydroxyl takes place.[3] The productive spin surface is found to be the overall quartet generated directly by the addition of triplet dioxygen and quartet [(H)Ni(OH)]$^+$. The redox non-innocent character on the activator complex seems to help protect the reactive molecule in the hot state until the complex loosely binds to O$_2$ to initiate a dramatic reorganization in the electronic structure.
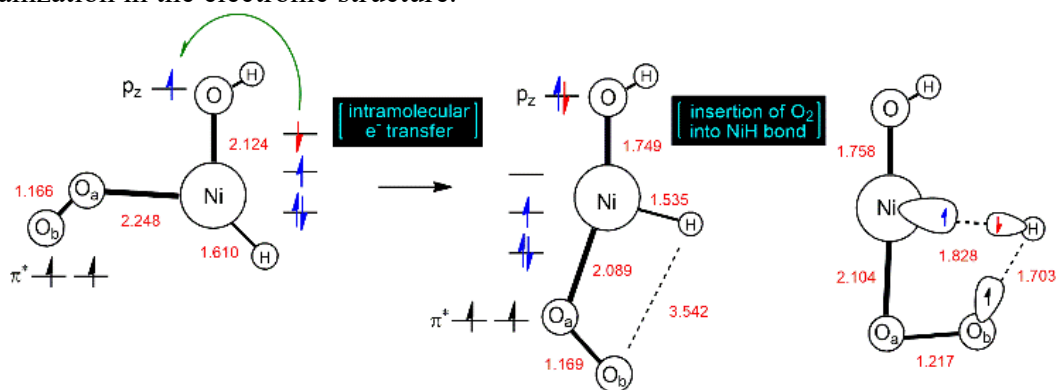
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Session 4 – Friday 12 May

12:00–12:20	Perttu Lantto	^{129}Xe NMR shift in molecular cavities
12:20–12:35	Gargi Sengupta	Acid dissociation in the aerosol-chemistry-cloud box model HAMBOX
12:35–12:50	Perttu Hilla	Multiscale modelling of Xe NMR biosensors
12:50–13:10	Stefan Taubert	Quantifying Aromaticity to Support Interpretation of Chemical Synthesis
13:10–13:30	Teemu Järvinen	Using Atomic Cluster Expansion in Molecular Dynamics
13:30–13:50	Susi Lehtola	Complete basis set limit studies of the numerical behavior of density functionals

^{129}Xe NMR shift in molecular cavities

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NMR spectroscopy of ^{129}Xe guest atom in molecular and materials cavities is increasingly used to obtain detailed, local information about the atomic and electronic structure of the host material. ^{129}Xe NMR spectral features are very sensitive to physical conditions-dependent dynamical processes and understanding them at the microscopic level requires theoretical first-principles modelling. In this presentation, I will show how modelling increases the amount of information obtained from simple ^{129}Xe NMR spectra as well as resolves and predicts new spectral features. Our approach combines state-of-the-art relativistic quantum-chemical (QC) calculations of the electronic structure and Xe NMR parameters with statistical Monte Carlo (MC) and molecular dynamics (MD) simulations of the whole host-guest system in solid or solvent environments. I will discuss few applications, in which we were able to predict unknown crystal structures of fluorophenol clathrates [1], give quantitative finite temperature estimates of Xe chemical shift inside the cavities of solid porous organic cage (POC) material [2], provide evidence of endohedral Xe in metal organic polyhedral (MOP) supramolecular complex [3] as well as its hidden diastereomers [4], predict and explain features of unexpected CEST signals in new shift regions for bridged resorcinarene cage (BRC) biosensor candidates [5], and confirm ^{129}Xe chemical shifts in a porous liquid of POC [6]. In these studies, the state-of-the-art modelling combined with modern experimental methods and analysis provides valuable, otherwise unattainable, information on, *e.g.*, the occupancies of the cavities, binding constants, thermodynamic parameters, exchange rates, as well as relaxation and diffusion parameters.

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Acid dissociation in the aerosol-chemistry-cloud box model HAMBOX

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Aerosols have a significant impact on the Earth's climate, human health, and the chemistry of the atmosphere. The acidity of aerosols is known to play a major role in determining their physicochemical properties and thus their impact on these areas [1]. Therefore, acidity of aerosol components is an important factor to consider when studying atmospheric aerosols.

Aerosol acidity is represented in climate models using observationally-based proxies, such as the pH of the bulk aerosol solution. However, these proxies do not always accurately represent the entire aerosol population, leading to large uncertainties in climate projections [2]. Additionally, the organic fraction, which often comprises significant amounts of components with acid functionality, is considered as un-dissociated and the H+ concentration in aerosols is assumed to have no contribution from the organic fraction [3]. Organic aerosols can make up 30–90% of the total aerosol mass, depending on the location and atmospheric conditions, and plays an important role in different atmospheric processes such as formation and growth of the new particles, and cloud droplet activation. Despite its abundance and importance, organic aerosol is still one of the least understood components of atmospheric aerosol [4]. The dissociation of the organic fraction could play a significant role in the measure of aerosol acidity and influence the aerosol microphyscial and chemical processes. Representing organic dissociation in climate models are therefore expected to improve the accuracy of the aerosol acidity representation and potentially lead to a better understanding of the role of organic aerosols in climate.

In this work, we have introduced organic dissociation in the ECHAM box model HAMBOX and assess its impact on sulfur chemistry and cloud microphysics via cloud droplet number concentrations (CDNC) and short-wave radiative effect (RE). We calculated CDNC for an air parcel, based on the predicted total aerosol population sulfate mass, and compared to predictions without accounting for organic dissociation. The resulting CDNC was then used to estimate the short-wave radiative effect from cloud formation using methods given by Bzdek et al. [5]. We found that the increased H^+ concentration from organic dissociation increases the kinetically driven oxidation of sulfur dioxide and the sulfate mass in the aerosol population is significantly increased, compared to simulations without accounting for organic dissociation. The increased sulfate concentrations in turn change the size distribution significantly and impact the estimation of CDNC and RE.

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Multiscale modelling of Xe NMR biosensors

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Signal intensity in nuclear magnetic resonance (NMR) spectroscopy is governed by the population difference between nuclear spin states. At room temperature the populations are almost equal, rendering NMR a method of low inherent sensitivity, requiring a high concentration of spins for a sufficient signal. Understanding chemical processes at the molecular level requires development of low-concentration NMR.

Advances in noble-gas hyperpolarisation [1] and indirect detection [2] have rendered it possible to use encapsulated ^{129}Xe as a probe for molecule-selective sensing in down to picomolar concentration. Xenon forms a non-covalently bound host-guest system with a cryptophane (Cr) cage, which is equipped with an affinity tag that selectively binds with an analyte. The binding event is reported by the chemically sensitive NMR signal of Xe. These systems are called Xe NMR biosensors (XBSs) [3].

Understanding XBSs at the molecular level is pivotal in their continued development. Computational modelling is required to achieve such microscopic information on, e.g., the chemical exchange of free and host-bound Xe and H_2O, NMR chemical shift (CS) of Xe, and nuclear spin dynamics of the entire XBS. By using molecular dynamics simulations and quantum-chemical calculations we have been able to, e.g., demonstrate the important role of explicit H_2O molecules in the exchange of Xe [4], and show that the average CS of Xe depends linearly on its coordination number through the action of so-called paramagnetic channels during collisions with other atoms.

In addition, we have observed the formation of water channels (hydrogen-bonded networks) through the cavity of water-soluble Crs. The dynamics of H_2O molecules in such channels is stabilised by lone-pair oxygens on the structure of the host, having important consequences on the energetics of XBSs. By computationally analysing the NMR relaxation rates of ^{1}H spins in stabilised H_2O molecules we propose NMR measurements to confirm the existence of water channels.

The talk will cover the computational methodologies and workflows required for multiscale modelling of XBSs and shed light on the microscopic details of Cr-confined Xe and H_2O, crucial for the development of XBSs as a method of low-concentration NMR.

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Quantifying Aromaticity to Support Interpretation of Chemical Synthesis

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Aromaticity can be assessed based on the magnetic criterion: a molecule being able to sustain a diatropic magnetically induced ring current is considered aromatic. We can model the ring-current paths and ring-current strengths (susceptibilities) using the GIMIC method (Gauge-Including Magnetically Induced Current) [1]. Aromatic stabilization or antiaromatic destabilization can lead to certain synthetic routes being preferred. In this contribution, I will discuss two cases [2,3], where we have been able to provide evidence for such stabilization and destabilization due to aromaticity and antiaromaticity, respectively, and thus help experimentalists to explain the stability and reactivity of certain synthesized molecules.

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Using Atomic Cluster Expansion in Molecular Dynamics

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In recent times there has been significant progress in the development of Machine Learned Interatomic Potentials (MLIPs). The *Atomic Cluster Expansion* (ACE) [1,2,3,4] is a particular flavour of these new MLIPs which has been shown to give an excellent cost/accuracy balance for a range of systems. We give a brief introduction to ACE, show how ACE models can be trained on *ab initio* datasets and then employed in molecular dynamics simulations with near *ab initio* accuracy. We also discuss a few cases where ACE has been successfully used and where we expect ACE to work well. Finally, we mention ongoing developement of ACE methodology in electronic structure and what can be expected in the future.

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Complete basis set limit studies of the numerical behavior of density functionals

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Thanks to the improvements in algorithms and approximations accrued during several decades of development, as well as the amazing advances made in computer engineering, density functional theory (DFT) has become widely used across various disciplines to understand the structure and behavior of materials starting from first principles. Motivated by this success, many new density functional approximations (DFAs) are published every year; our Libxc library [1] containing over 600 DFAs at the moment. Despite this seemingly large number of available functionals, only few new DFAs get used by others than their original developers, and even fewer actually become widely used in the literature. Although the assumption is that new functionals are better than old ones, this is often not the case, as has been shown in the rich literature full of benchmarks on various functionals' accuracy on various properties of various systems, see ref. 2 for a recent many-faceted review, for example.

However, the numerical behavior of density functionals has been investigated to a much smaller extent. In this contribution, I will discuss our recent works related to the study into the well-behavedness of density functionals. In our definition [3], a well-behaved density functional should yield total energies that converge smoothly to the complete basis set (CBS) limit by (i) affording smooth convergence to the quadrature grid limit at fixed density, (ii) a smooth convergence of the self-consistent field (SCF) procedure within a fixed basis set, as well as (iii) rapid convergence to the CBS limit in calculations with increasingly large basis sets. However, we have shown that many recent density functionals break this criterion. Already at fixed electron density, many functionals such as r^2SCAN are ill-behaved in the evaluation of the total energy of atoms [3]. Fully numerical calculations [4-7] allow studying the effect of relaxing the density in self-consistent calculations, which demonstrate that most Minnesota functionals are ill-behaved already for the hydrogen atom [7], producing large oscillations in the Laplacian of the density $\nabla^2 n$. The Li and Na atoms are also challenging for Minnesota functionals, as well as the recent B97M-V and ωB97M-V functionals of Mardirossian and Head-Gordon [8].

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Poster Session – Thursday 11 May

1	Mohammad Bagheri	A large database of Raman spectra created with optimized computational workflow
2	Christopher Daub	Molecular dynamics simulations of peroxy radical interactions
3	Toni Eskelinen	Luminescence Properties of Zn(II) and Pb(II) complexes with Phenanthro-diimine Ligands
4	Galib Hasan	Computational Studies of Reaction Routes for 3(RO···OR') Intermediates Formed in Peroxy Radical Self- and Cross-Reactions
5	Eetu Hyypiö	Spin polarization transfer simulations of lactate ester molecules
6	Noora Hyttinen	Predicting liquid-liquid phase separation in ternary organic–organic–water mix- tures using COSMO-RS
7	Tiia Jacklin	Computational chemical shift of xenon in carbon nanotubes
8	Josef Kehrein	POxload: Predicting the Drug Loading of Polymer Micelles by QSPR Modeling
9	Ville Kuorikoski	Computational Studies on the Blood-Brain Barrier Transporters SMVT, CAT1 and MCT1
10	Atif Mahmood	Induced current densities in porphyrin nanostructures
11	Jiří Mareš	A new chance for an old, Amber-like force- field
12	Pau Mayorga Delgado	Self assembly of mixed surfactants in water
13	Megha Mohan	^{13}C NMR of Paramagnetic Layered Double Hydroxides (LDH)
14	Mario Mäkinen	Modelling the growth of zincone ALD/MLD hybrid thin films: a DFT study
15	Luukas Nikkanen	Deep learning in infrared spectroscopy
16	Ari Pyykkönen	Massive spin contamination in Fe(V)bis(imido): A first-principles pNMR study
17	Markus Rauhalahti	Exploring the conformational states of experimental and predicted respiratory complex I structures
18	Assa Sasikala Devi	Tuning the properties of Janus van der Waals hetero structures by varying interface terminations: A first principles investigation
19	Petr Štěpánek	Unexpected ^{13}C-NMR shifts in carbon nanomaterials
20	Phuoc Thao Nguyen Le	Tailoring Carbene-Metal-Amides for Thermally Activated Delayed Fluorescence: A Systematic Computational Study on the Effect of Cyclic (Alkyl)(amino)carbene
21	Ruifeng Wang	Construction of a rapid screening strategy for potential anti-adipogenic polyphenols based on lipid rafts
22	Oleksii Zdorevskyi	QM/MM MD Simulations of Horizontal Proton Transfer Pathways in the Antiporter-like Subunits of Mitochondrial Respiratory Complex I
23	Hugo Åström	Gaussian basis set truncation errors in weak to intermediate magnetic fields

A large database of Raman spectra created with optimized computational workflow

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Raman spectroscopy is a widely used material analysis technique based on the vibrational properties of materials. Raman spectra provide information about the vibrational modes, atomic structure, and chemical composition of materials but spectrographic analysis relies on comparison to known spectra. Hence, experimental databases of spectra have been collected but limited to well-known materials or the materials may contain significant amount of impurities of unknown identity, for instance.

The spectra can also be simulated using atomistic first-principles methods to complement experimental databases. However, current methods for the simulations of Raman spectra are computationally demanding. Thus, the existing databases of computational Raman spectra contain only a fairly small number of entries.

We present an optimized workflow to calculate the Raman spectra which can reduce the computational cost [1] and takes full advantage of the phonon properties found in existing material databases [2]. The workflow was benchmarked and validated by comparison to experiments and previous computational methods for select technologically relevant material systems. Using the workflow, we performed high-throughput calculations for a large set of solid materials (5099) belonging to many different material classes and collected the results in a database that can be browsed online on the CRD website. [3]

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Molecular dynamics simulations of peroxy radical interactions

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Biimolecular interactions between peroxy radicals (RO_2) are key reactions in atmopheric chemistry. So far, most of our research on this topic in the Atmospheric Computational Chemistry group has focused on improving our calculations of the energetics of these reactions and on understanding the stationary states of the reactions (reactants, products, and transition states)[1-3]. The focus of my work has been on doing molecular dynamics (MD) simulations of these systems, in order to better understand the different possible reaction paths and to go beyond the transition state theory (TST) approach to calculating reaction rates of interest to atmospheric scientists.

In my talk, I will present some results from two different MD approaches. First, I will show what we have learned from simple empirical force-field based methods[4,5]. Although these cannot simulate the bimolecular reaction itself, they are surprisingly accurate for predicting the lifetime of complexes of two peroxy radicals. By simulating thousands of collisions between peroxy radicals, and computing the histogram of association lifetimes, we have demonsrated a strong correlation between this lifetime and the experimental rate coefficient for those reactions which are barrierless. This allowed us to make some predictions of experimental reaction rates for large α-pinene-derived peroxy radicals relevant in models of atmospheric aerosol formation. I will also present some new results on the extension of the collision simulations to also include peroxy radical-water complexes.

The second part of my talk will focus on metadynamics simulations using the CASSCF electronic structure method to study the dissociation of two systems involved in peroxy radical chemistry, namely $CH_3O_2CH_3$ and $CH_3O_4CH_3$. Modelling the free energy of $CH_3O_2CH_3$ dissociation into 2 CH_3O radicals is straightforward, and gives results agreeing well with the results of energetic calculations and TST. On the other hand, the variety of possible disocciation pathways from the tetroxide intermediate $CH_3O_4CH_3$ renders it difficult to design active spaces of orbitals which can describe all of them. I will discuss our progress in meeting these challenges.

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Luminescence Properties of Zn(II) and Pb(II) complexes with Phenanthro-diimine Ligands

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Phenanthrene-based pyridyl-imidazole (**L1**) and its anthracene (**L2**) and phosphonium (**L1P$^+$**) derivatives were used as N,N-chelating ligands to construct complexes [Zn(**L1**)Cl$_2$], [Zn(**L2**)Cl$_2$], [Zn(**L1P$^+$**)Br$_2$]$^+$ and [Pb$_3$Br$_8$(**L1P$^+$**)$_2$] and the photophysical properties of the title complexes were investigated both experimentally and computationally.[1,2] All complexes were luminescent in the solid state with the Zn(II) complexes showing fluorescence from either a ^{1}CT or $^1\pi$-π* state. However, due to high spin-orbit coupling associated with lead, phosphorescence emission with $^3\pi$-π* parentage was observed for the Pb(II) complex. Electronic structure calculations at the (Time Dependent-) Density Functional Theory level were used to shed light on the nature of the excited states responsible for the emission.

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Computational Studies of Reaction Routes for ^{3}(RO···OR') Intermediates Formed in Peroxy Radical Self- and Cross-Reactions

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Atmospheric aerosol (liquid or solid particles suspended in air) have major health effect since they are the main diverse of air-pollution-related mortality. They also affect the climate by forming cloud condensation nuclei [1]. Gas phase dimer (accretion product) formation is regarded as a significant reaction in the atmosphere because it can lead to the formation of very-low volatility highly oxygenated organic molecules (HOMs), which later form aerosol particles [2]. On the other hand, organic peroxy radical (RO_2) are the key intermediates in the chemistry of the atmosphere. One of the main sink reactions of RO_2 is the recombination reaction RO_2 + R'O [3]. This reaction goes through an intermediate complex (RO…$^3O_2$…OR'). The $^3O_2$ is very weakly bound, and evaporates from the system, giving a ^{3}(RO…R'O) dimer cluster. This dimer has three major reaction channels: 1) R_H=O + R'OH 2) ROOR', and 3) RO_2+ R'O_2.

In our study, we have performed a systematic conformation search on the ^{3}(RO…R'O) dimer cluster on the triplet potential energy surface using a state-of-the-art quantum chemical approach [4,5,6,7]. Then we tried to calculate the reaction rate of three channels: evaporation or dissociation to RO + R'O, a hydrogen shift reaction forming R_H=O + R'OH, and a "spin-flip" (intersystem crossing) leading to the formation of ROOR' "dimer" accretion products. We have found that all these channels are indeed competitive (with typical rates of at least greater than 10^6 s^{-1}, and many have rates exceeding 10^{10} s^{-1}) in the atmosphere. Our recent studies [7] suggest that alcohol + carbonyl and ROOR' accretion formation channels are competitive for small and medium sized RO_2. However, for complex R or R' the binding energy effect may render the H-shift channel uncompetitive over ISC. The overall results suggests that the computationally proposed novel RO_2 + RO_2 reaction mechanism is qualitatively compatible with experimental results on accretion product formation and may thus play a key role in the formation of organic aerosols.

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Spin polarization transfer simulations of lactate ester molecules

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The signal produced by Nuclear Magnetic Resonance (NMR) is inherently weak, and thus it is of interest to amplify it. The SABRE-Relay method has been developed at the University of York [1], set on amplifying the signal in the ^{1}H and ^{13}C NMR spectra of different target molecules. The aim of our computational research is to model the situation in the experiments and answer how the signal becomes enhanced. The interesting molecules used in the experiments, and therefore in the computational study, are lactate esters, of which methyl lactate can be seen below. We carry out spin dynamics simulations using DFT-computed spin-spin coupling networks for the spin systems formed by methyl, ethyl and butyl lactate and investigate the transmission of spin density from the initially fully polarized OH proton to the other ^{1}H- and ^{13}C-nuclei in the systems. We investigate the effects of the coherent dynamics on the polarization transfer.
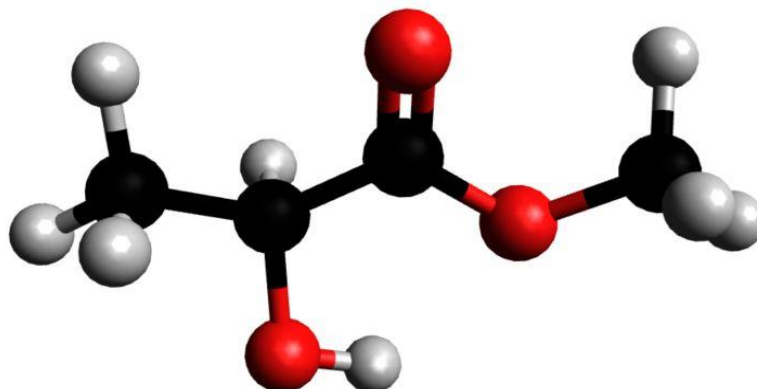
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        The Journal of Physical Chemistry Letters 2022 13 (29), 6859-6866
        DOI: 10.1021/acs.jpclett.2c01442

Predicting liquid-liquid phase separation in ternary organic–organic–water mixtures using COSMO-RS

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Liquid-liquid phase separation (LLPS) affects the water uptake of aerosol particles in the atmosphere. Mahrt et al. studied LLPS in particles containing proxies or primary and secondary organic aerosol (POA and SOA, respectively) under various relative humidity (RH) conditions [1]. They observed LLPS in more mixtures at relatively high RH (45% or 90%) than in dry conditions (RH<5%). This indicates that the increasing water content leads to phase separation in ternary SOA–POA–water mixtures. Here, LLPS was predicted in ternary mixtures containing water and two organic compounds using conductor-like screening model for real solvents (COSMO-RS) [2]. A computational method, such as COSMO-RS, allows for the estimation of new information on mixing states and mixtures that cannot be accessed experimentally.

COSMO-RS predicts LLPS in all of the studied ternary mixtures containing water and POA and SOA, due to the limited solubility of the hydrophobic POA proxies in water. However, the RH needed to reach high enough water content in the mixtures depends on the two organics. For example, water activity is close to 1 (corresponding to 100% RH) at phase separation in *cis*-pinonic acid–diethyl sebacate–water mixture [2]. This agrees with the experimental observations, where no LLPS was observed below 90% RH [1]. On the other hand, two phases were observed in particles comprising dioctyl phthalate and *cis*-pinonic acid [1]. Based on COSMO-RS predictions, LLPS occurs under lower RH than in the mixture containing diethyl sebacate, around 40% RH.

In addition to computing the entire phase diagram, the possibility of LLPS can be assessed with activity coefficients of each constituent in the infinite dilution in the other two constituents. For example, the activity coefficient of *cis*-pinonic acid in water, diethyl sebacate and dioctyl phthalate is relatively high, signalling LLPS in the binary mixtures. Because of the very low solubility of organics in water (in case of LLPS), water activity is close to 1 at phase separation. The RH required for LLPS is therefore close to 100 %, unless other phase separations form from the interaction between the two organic compounds.

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Computational chemical shift of xenon in carbon nanotubes

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After carbon nanotubes (CNTs) were found they have, because of their unique electric and mechanical properties, been extensively studied using a wide range of different methods, one of which is nuclear magnetic resonance (NMR). Though fast relaxation of nuclear spins makes the ^{13}C NMR measurements difficult, both experimental and computational studies of CNTs have been done.

An alternative approach is to measure a probe ^{129}Xe atom that has flexible, large electron cloud sensitive to its surroundings and temperature. Experimental Xe NMR for CNTs have been carried out but no computational studies exist. In this study [1], we compute, for the first time, the trends of the chemical shift of xenon at several sites in close vicinity of different types of CNTs. The obtained results are useful in interpreting both former and current experimental data.

We report ^{129}Xe shift inside and outside of multiple single-wall CNTs. We study tubes with different chiralities, both chiral (n,m) and achiral $(n,0)$ nanotubes, some of which belong to the semiconducting $(R = (n - m) \bmod 3 = 1, 2)$ and quasi-metallic $(R = 0)$ families. The dependence of the chemical shift on the diameter of the CNT is also investigated. Periodic infinite-length as well as finite Clar-cluster models are used. Additionally, a double-wall CNT and a few nanotube bundles consisting of identical CNTs, are studied. In bundles, four xenon sites are considered: inside (I) and outside (O) surfaces, in the groove (G) of two tubes, and in the interstitial (IC) channel between three tubes.

Our results indicate that the Xe shift is not sensitive to the chirality of the CNT but there is a slight shift difference between semiconducting and quasi-metallic families. Tube diameter dependence is clear only for narrow CNTs. We also show that the Xe shift inside the CNT is close to zero or even negative with respect to the low-density Xe gas reference. The shift inside the CNT is slightly larger for quasi-metallic than for semiconducting family in the same diameter range.

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POxload: Predicting the Drug Loading of Polymer Micelles by QSPR Modeling

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Amphiphilic ABA-triblock copolymers, comprised of poly(2-oxazoline) and poly(2-oxazine), can solubilize poorly water-soluble drugs; they form micelles with exceptionally high drug loading [1]. However, loading capacity (LC) and loading efficiency (LE) are highly dependent on the chemical structures of both the loaded drug and the monomers which contain readily-tunable sidechains [2]. Recently, a cheminformatics-driven QSPR modeling approach showed promising results for predicting such parameters [3].

In this work, experimental results from several recent publications [2-7] were combined with in-house data to create an extended database of nearly 3000 formulations, varying in polymer and drug structure, drug concentration and the time point for measuring solubilization. 2D polymer-drug mixture descriptors were calculated and used for building different QSPR prediction models, focusing on varying levels of LC and LE. The models were then used to screen larger drug libraries (FDA, DrugBank). We envision validating our models with additional experiments and providing a web tool for scientists to assess the usage of these polymers as delivery systems for novel drug candidates.
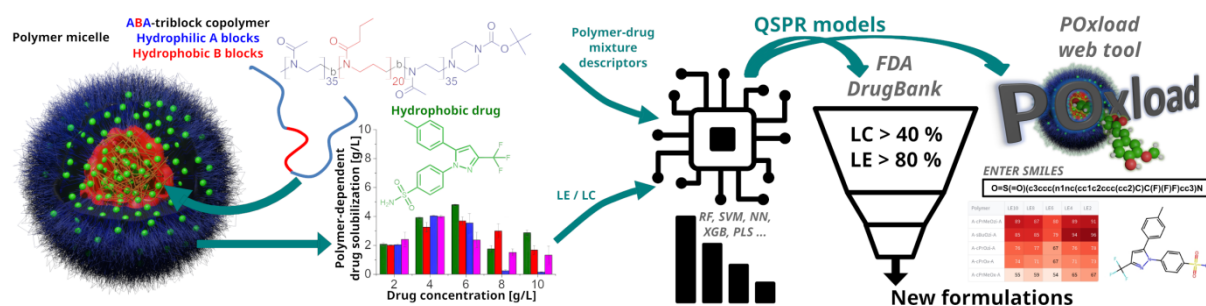
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Computational Studies on the Blood-Brain Barrier Transporters SMVT, CAT1 and MCT1

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The challenge of targeting drugs to the central nervous system lies in the blood-brain barrier, which prevents most drugs from reaching the brain. In order to treat neurological diseases, drugs need to reach the target tissue in the central nervous system. To achieve this, the blood-brain barrier contains transporter proteins, such as the sodium-dependent multivitamin transporter, monocarboxylate transporter 1, and cationic amino acid transporter 1, that can be taken advantage of. The project aims to investigate the utility of these three transporters in enhancing brain drug delivery using 3D *in silico* models for each transporter. Molecule libraries will be screened to support prodrug design, and structural analysis can help in improving the binding selectivity of the found molecules. Molecular dynamics simulations will be conducted to study the behavior of the proteins and their transport mechanisms. These computational methods can aid the research in simulating the system in ways that are not possible experimentally. So far, the simulations have revealed a novel conformational state which requires further investigation. Observed conformation changes and states can give a better understanding about the internal interactions and dynamics of the protein and thus shed light on its mechanism of action. This is crucial information when designing prodrugs on novel targets which can open new pathways for drugs to reach the brains.
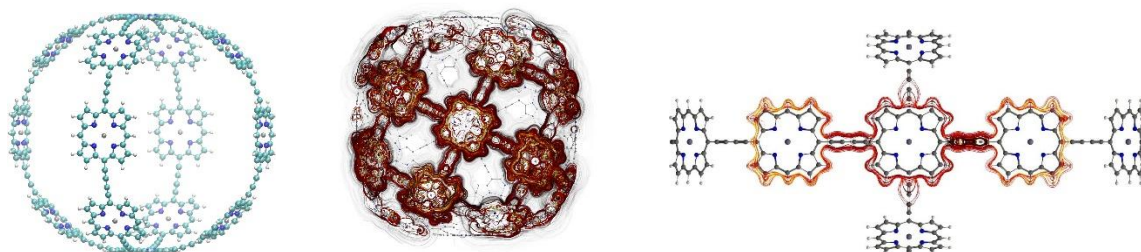
Induced current densities in porphyrin nanostructures

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Magnetically induced current densities (MICD) of Zn-porphyrinoid nanostructures have been studied at the density functional theory (DFT) level using the B3LYP functional. The studied Zn-porphyrinoid naostructures consist of balls (two crossing porphyrinoid belts), tubes, rings and clam-shell like molecule. The Zn-porphyrin units are connected to each other via butadiyne linkers as in rings and a recently synthesized porphyrinoid cross-belt structure.[1-3] The studied nanotubes are constructed by connecting the neighbors via ethyne bridges at their meso carbon atoms.[4,5] A clam-like molecule has porphyrin units connected on one side via butadiyne linkers and on the other side they are fused. The MICDs are calculated using the gauge-including magnetically induced currents (GIMIC) method.[6,7] Current-density pathways and their strengths were determined by numerically integrating the MICD passing through selected planes that cut chemical bonds or molecular rings. The current-density calculations of the nanoballs and rings show that they are globally non-aromatic but locally the individual porphyrin rings are aromatic but are 20% weaker than in a single Zn porphyrin, whereas oxidation leads to globally aromatic cations sustaining ring currents that are somewhat stronger than observed for a Zn porphyrin. Calculations of the current densities show that there is a paratropic ring current around the nanotubes. Fusing porphyrinoids as in the fully fused cross-belts and clam-shell molecules results in complicated current-density pathways that differ from the ones usually appearing in porphyrinoids. The neutral fused cross-belts molecule is antiaromatic, whereas its dication is non-aromatic.

Figure 1: The magnetically induced current density in the nanoball and in a cross-belt porphyrinoid structure.

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A new chance for an old, Amber-like forcefield

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The Amber-like forcefield has been greatly succesfull in molecular dynamics (MD) simulations of biomolecules and other systems as well. As a great advantage, there are several excellent software packages to choose from. There are also tools to get parameters for molecules that are not present in the forcefield, in applications like *in silico* drug screening. This gives a rather effortless ingredients for a large-scale molecular simulations. For example, the Antechamber suite of Amber package assigns general atom force field (GAFF) types for Lennard-Jones (LJ) parameters and bonding interactions, whereas the partial charges are obtained by semi-empirical calculation.

Here we are interested in a mixture of simple surfactants, decanoate and hexanol in water solution, in a combined NMR/MD study. Using the GAFF/Antechamber, we have 9 LJ parameters (two parameters per one LJ interaction) inherited from the GAFF atom types and 52 partial charges. The partial charges are the only specific parameters for the newly parameterized molecule. The accuracy of the simulation depends on these charges. Moreover, there is usually freedom to choose from several water models, where *e.g.* OPC model has very different partial charges compared to SPC or TIP4P models. Study of surfactants is one of many cases where the intermolecular interactions largely determine the results. That is where using "blindly" assigned partial charges fitted to an electron density of the molecule, obtained as a quick approximation in Antechamber seems to be an insufficient investment. Here blindly refers to the fact, that other molecules (in particulain water) have been possibly parameterized by different methods and there is no connection to intermolecular energies or forces. The three set of forces: solvent-solvent, solvent-solute and solute-solute, can be out of balance resulting in incorrect aggregation behaviour.

We have therefore reassigned the atom types of our molecules, and obtained 17 common, (atom-type specific) LJ-parameters, and 53 atom-type-pair specific, between atoms of surfactants and solvent (water and sodium ions). On the other hand, we have currently only 17 partial charges, belonging always to a distinct atom type, as in the case of LJ-parameters. Therefore the total number of parameters (pair for each LJ) is 157 as compared to 71 from Antechamber, which are fitted agains gradients of accurate QC calculations (ωB97X-D4; def2-QZVPP). The separate LJ-pair interactions constitute independent parameters for solvent-solute forces, along with solute-solute interactions, whereas the solvent-solvent parameters are left untouched, keeping the well-known properties of the chosen water model as it is. LJ-interactions present only part of the interactions, in our approach, the electrostatic interactions are still interdependent and the LJ potential may not be able to correct for it sufficiently. Nevertheless, the flexibility of our parameterization is much larger compared to the GAFF-Antechamber parameters, and more importantly the parameters are obtained using forces from high-level QC calculation. Analysis of the parameters together with results of preliminary simulations will be presented.

Self assembly of mixed surfactants in water

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Atmospheric aerosols have an important role on the water-droplet growth and thus, cloud formation [1]. Some of their constituents are surfactants having typically long carbon chains with a hydrophilic head and a hydrophobic tail. Understanding the dynamics and the geometrical distribution of surfactants in water are of utmost importance to build climate models.

Some of the most important surfactants present in the atmosphere are the sodium decanoate, hexanol, sodium dodecyl sulfate (SDS) and sodium hexanoate. In NMR experiments it is observed that once sodium decanoate and hexanol are mixted in water, they have the same diffusion coefficient, D. On the other hand, in a mixture of SDS and sodium hexanoate, different D are observed for each one of the surfactants. This indicates that the decanoate and hexanol cluster together while SDS and hexanoate do not. The goal of this project is to support or provide alternative arguments for the conclusions reached from experiments by computational means.

Representations of the two experimental mixtures were computed by means of classical atomistic molecular dynamics (MD) simulations. Trajectories of 5 microseconds were obtained for two oppositely distributed starting configurations: all the surfactants clustered together on one hand and spread apart on the other. Systems consisting on 200/50 (decanoate/hexanol), 100/100 and 100/2000 (SDS/hexanoate) were studied. The simulations were performed with the GROMACS [2] software with the AMBER force field [3].

The MD simulations were not in disagreement with the experiments for both mixed systems. Thus, these results will be beneficial while providing more accurate models to study the climate, since the distribution of these polar molecules within the droplet and on its surface helps us to gain insights on the cloud albedo [4], which has a decisive effect on cooling or warming the atmosphere.

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^{13}C NMR of Paramagnetic Layered Double Hydroxides (LDH)

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LDHs are ionic solids with a characteristic layered structure consisting of positively charged metal cation layers and intercalated anion layers, which maintain the charge neutrality [1]. Mg_2Al-LDH materials with carbonate (CO_3^{2-}) anion layer have been synthesized in which a definite amount of divalent Mg is replaced with paramagnetic Ni^{2+} to get a series of samples with increasing Ni concentration of 18%, 34%, 68% and 84% [2]. ^{13}C solid-state NMR of these materials has been recorded. It has been found that the ^{13}C NMR shielding tensor has three distinct eigenvalues, i.e, it possesses both anisotropy and rhombicity (asymmetry). This is the same for the natural Mg_2Al-LDH, but both the anisotropy and asymmetry are strongly dependent on the concentration of the paramagnetic Ni ion doping. We use computational approaches to explain these experimental observations.

The contributions to the total ^{13}C shielding tensor of the intercalating CO_3^{2-} can be divided into an orbital contribution (analogous to shielding in closed-shell substances) within the CO_3^{2-} ion and both short and long-range paramagnetic contribution of the metal-oxygen layers. The long-range paramagnetic contribution arises due to the dipolar part of the hyperfine coupling, which is modelled as a lattice sum over the randomly distributed Ni-ions in the II-valued sites furnished with electron-spin susceptibility giving rise to a localized point dipole at each Ni centre [3]. This effect constitutes an important contribution to both the anisotropy and asymmetry, whereas the isotropic shift only changes a little as observed experimentally. It is observed that the close-range contributions - especially the contact terms are crucially important in attaining a qualitative agreement with the experimental data for both the isotropic ^{13}C shift and its eigen values. This is the due to the negative spin density delocalising from the cation layers to the cation sites in the interlayer space.

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Modelling the growth of zincone ALD/MLD hybrid thin films: a DFT study

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Thin films can be fabricated using atomic and molecular layer deposition (ALD and MLD). By combining these two methods, one can fabricate hybrid thin films. Possible future applications of these hybrid thin films include photoelectric devices, sensors, solar cells, protective coatings, flexible electronics, and thermoelectric energy harvesting. The fabrication process of hybrid thin films is not fully known from the perspective of the chemical reaction mechanisms. Chemical reactions used to fabricate these hybrid materials are adsorption reactions, which can be studied using density functional theory (DFT) -modelling, and thus we can reveal chemistry happening in the reactor during the thin film fabrication process.

DFT was used to study adsorption reactions responsible for the growth of hybrid thin films. Hybrid thin films under investigation consisted of diethyl zinc and an organic phenol, which was either 4-aminophenol or hydroquinone, depending on the thin film. These thin films were studied using both gas-phase reactions, and surface models. The surface models consisted of ethyl-saturated zinc oxide and the adsorbing organic precursor.

Modelling of the reaction pathways was conducted using the GPAW program. DFT was used with Perdew–Burke–Ernzerhof (PBE) exchange and correlation functional. Van der Waals correction TS09 was used due to weak interactions caused by the ethyl ligands. Relaxed surface scans were used to find energetically favorable structure for the physisorption reaction of 4-aminophenol on the zinc oxide surface. All of the reaction barriers were calculated using nudged elastic band -method with climbing image. Bader analysis was used to study the effect of ethyl ligands of the surface on the adsorption reactions.

The precursor adsorbed to the surface through exothermic physisorption, and after that more strongly using either ligand-exchange or dissociation reaction. 4-aminophenol reacts more stronger with its hydroxyl group. Key step of the total reaction is the removal of the ethyl group as ethane. We have identified some ethyl removal processes and they depend on the coverage of ethyl.

Deep learning in infrared spectroscopy

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We have used DeepMD [1], which is a deep learning program based on the TensorFlow–framework, to perform molecular dynamics simulations lasting up to a nanosecond with near MP2–precision. The dipole moment was predicted along the trajectory of the simulation using a neural network. The infrared spectra is obtained as the Fourier transform of the autocorrelation function of the time derivative of the dipole moment [2].
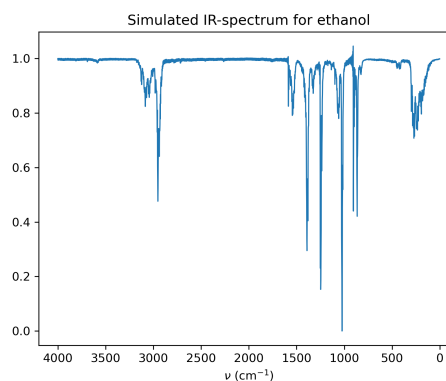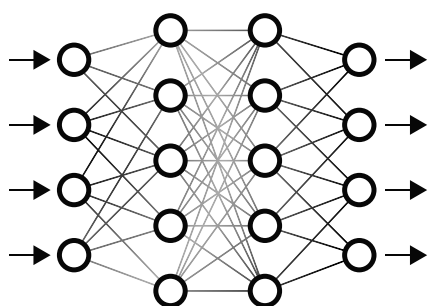
Molecular structures were obtained by running `xtb`–metadynamics simulations [3]. This allowed the deep learning model to see more extreme geometries on the potential energy surface. The MP2 calculations of forces and dipole moment were performed for randomly chosen structures along the trajectory using Turbomole [4]. The molecular dynamics simulations were run with LAMMPS [5]. The deep learning model was taught using GPU accelerated learning provided by CSC's Puhti HPC. A spectrum for ethanol has been successfully simulated (see figure). We are working our way up to simulate bigger molecules to see how the method scales with the size of the molecule.

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Massive spin contamination in Fe(V)bis(imido): A first-principles pNMR study

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The NMR spectrum of the paramagnetic transition metal complex Fe(V) bis(imido) has been recently recorded by Martinez *et al.* [1] The current paradigm for theoretical calculation of NMR chemical shifts for paramagnetic systems is based on the modern form of the Kurland-McGarvey theory, which parametrizes the nuclear shielding in terms of EPR parameters: the g-tensor, the zero-field splitting (ZFS) and hyperfine couplings (HFCs). Within the previously developed quantum chemical "standard method", the g-tensor and the ZFS are computed at the complete active space SCF (CASSCF) and n-electron valence state perturbation theory (NEVPT2) level, while density functional theory (DFT) with a hybrid exchange-correlation functional is employed for the HFCs. This methodology typically yields qualitatively or semi-quantitatively correct results. In the present study of the computational NMR shifts of the Fe(V) bis(imido) complex, standard hybrid functionals fail to produce even the correct order of magnitude according to experiment for the chemical shifts of a part of the molecule. The cause is revealed to be an extreme case of the spin contamination problem associated with hybrid DFT employing unrestricted formalism, in which different electronic spin states are artificially mixed in. In order to alleviate the spin contamination issue and improve agreement with experiment, so-called local hybrid functionals are employed in this work in the computation of the HFCs. In the standard, global hybrid functionals, the amount of exact Hartree-Fock exchange energy is constant throughout the molecule, whereas in local hybrids, the admixture is position-dependent. Even though agreement with experiment is still not satisfactory, the local hybrid results show significant reductions in spin contamination and notable improvement in chemical shifts compared to global hybrid functionals. The *ab initio* DLPNO-CCSD method is also tested, with results partly worse than, and partly better than the best of the local hybrids.

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Exploring the conformational states of experimental and predicted respiratory complex I structures

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Recent advances in experimental methods, particularly in high-resolution cryo-EM, and Alphafold2's breakhtrough in structure prediction, have led to a revolution in structural biology [1]. The advances are particularly evident in the study of large biomolecular complexes.

Respiratory complex I (CI) is the first enzyme in the respiratory chain responsible for energy production in mitochondria and bacteria [2]. It is a large protein complex consisting of ca. 45 individual subunits, which efficiently catalyze proton translocation across the membrane in strong coupling to the reduction of ubiquinone. Even though the proton pumping mechanism of CI remains to be understood, the advent of high-resolution Cryo-EM structures and molecular simulations have brought understanding of several catalytic states that may form during enzyme turnover [3].

In this study, we conducted a comprehensive analysis of all published experimental CI structures alongside their Alphafold2 predictions, examining their conformational landscape and the structural features associated with the catalytically relevant states. To enable this analysis, we developed automated and general pipelines for processing the heterogeneous structural data.

Our findings contribute to a deeper understanding of the structural determinants associated with CI's various states, offering valuable insights into the enzyme's function and mechanism. The automated data processing methods have a potential for broad applicability within the structural biology community, enabling researchers to harness the power of experimental and predicted structural data in tandem.

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Tuning the properties of Janus van der Waals hetero structures by varying interface terminations: A first principles investigation

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The ever-growing energy needs demand technological development related to photo catalysis. Conventional photo-catalytic materials suffer from low quantum efficiency, charge-recombination, and chemical back-reactions. Janus van der Waals hetero structures, are 2D materials where a metal atomic layer M is sandwiched between layers X and Y of two different chalcogen, halogen, or pnictogen atoms owing to finite out-of-plane dipole moments, and possess enhanced photocatalytic properties due to their intrinsic Rashba effect, strongly bound excitons, and strong interaction with light [1]. In this study, two dimensional (2D) GaAs/MoSSe Janus interfaces were investigated using first principles calculations. The effect of different atomic terminations on the interface stability, electronic properties and charge transfer at the interfaces were analyzed and found that conducting properties are altered with respect to different terminations. Metallic states are formed at the stable MoSSe/GaAs interface due to the presence of 2D occupied antibonding states in MoSSe and the band alignment at the interface. We demonstrate that the non-symmetric structure of MoSSe Janus material plays a key role in controlling the electronic properties of the stable Janus interface, which will be crucial deciding factor for practical applications [2].

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Unexpected ^{13}C-NMR shifts in carbon nanomaterials

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Graphynes (GYs) are a class of two-dimensional carbon materials. Due to their unique structure, they have been proposed for a variety of applications, such as separation of gases, cleaning of water, or as new electrode materials for large-capacity batteries.

GYs can be formally derived from graphene by inserting linear C-C links into its structure. Depending on the number of such inserted links and their positions, a large variety of structures can be created with a broad range of pore sizes and electronic, chemical and mechanical properties. Since the application of GYs is determined by their structure, it is important to have tools for its reliable investigation.

In this contribution we discuss the nuclear magnetic resonance (NMR) as such tool. NMR is a non-destructive method and provides highly localized, nucleus-specific information. We investigated its suitability for graphynes by theoretical calculations of 13C-NMR chemical shifts for a set of graphyne systems (α-graph(di)yne, β-graphyne, γ-graph(di)yne, rhombic gryphyne, and 6,6,12-graphyne) [1]. The calculations revealed that NMR is indeed capable of separating different GY structures. Interestingly, it also showed that the GYs provide unexpected NMR chemical shifts that are often in contradiction to the usual range of shifts appearing in typical organic molecules with similar carbon hybridization. Further analysis showed that even the bond lengths in these systems are different from typical bond lengths in analogous organic molecules.

The results show that although NMR is a powerful technique to distinguish the GY structures, the unique nature of these systems might require quantum-chemical computations to correctly interpret the spectra and assign the chemical shift signals.

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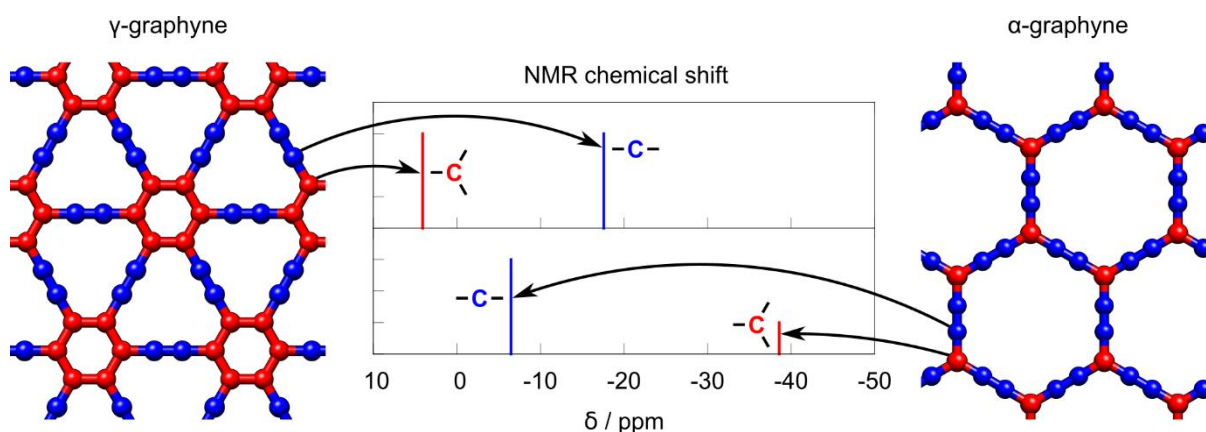
Tailoring Carbene-Metal-Amides for Thermally Activated Delayed Fluorescence: A Systematic Computational Study on the Effect of Cyclic (Alkyl)(amino)carbene

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Carbene-Metal-Amides (CMAs), a novel class of thermally activated delayed fluorescence (TADF) emitters, have been shown to exhibit extraordinary photoluminescence properties, and are on their way in making OLED devices. Thanks to a small excited singlet-triplet gap with nearly zero exchange energy (ΔE_{ST}), the conversion from triplet to singlet state (T1/S1) occurs rapidly, resulting in a photoluminescence quantum efficiency of up to 100%.[1]

Cyclic (alkyl)(amino)carbenes (CAACs) form a central constituent of the CMAs.[2] Here we report a systematic computational study on the effects of the CAACs on the photoluminescence properties of the CMAs, aiming at design and optimization of new TADF emitters based on carbene-gold-carbazolate complexes. DFT and TD-DFT calculations at MN15[3]/def2-TZVP[4,5] level have been carried out for over 60 complexes, with focus on experimental synthesis prospects. Both S0-S1 and S0-T1 excitations are characterized as charge transfer from HOMO to LUMO, such that the HOMO and LUMO are mainly localized on the amide and Au-carbene moieties, respectively. We demonstrate that for this series of compounds ΔE_{ST} is strongly correlated with the overlap of the participating orbitals, S0-S1 oscillator strength, and vertical S0-S1 and S0-T1 excitation energies. Hence, compromises are required in fabricating potential TADF emitters with low ΔE_{ST} and high photoluminescence quantum yield (PLQY). Systematic structural modifications reveal strategies for controlling ΔE_{ST}, which decreases especially by substituting the CAACs by aromatic rings containing electron withdrawing groups. Ground and excited state geometry optimizations indicate that carbene and amide adopt nearly coplanar orientation in the S0 and T1 states, but prefer rotation to perpendicular orientation in the S1 geometry.

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Construction of a rapid screening strategy for potential anti-adipogenic polyphenols based on lipid rafts

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Obesity poses a serious threat to human health on a global scale [1, 2]. Identifying compounds with anti-adipogenic activity through rapid screening could potentially offer solutions to address this public health issue. Polyphenols are abundant micronutrients that are present in the human diet and are involved in a wide range of biological activities; thus, it is regarded as potential anti-adipogenic compounds [3, 4]. Due to the large number of polyphenols, it is a challenge to rapidly evaluate whether candidate polyphenols have anti-adipogenic activity. Previous study showed that the lipid rafts, enriched with sphingolipids and cholesterol, are considered a potential target of polyphenols for the regulation of cellular processes and diseases [5]. Here, a strategy was developed to rapidly screen for active polyphenols targeting lipid rafts using molecular dynamic simulation, and then this strategy was validated by 3T3-L1 preadipocyte assay [6]. This screening strategy consists of six steps, which are 1) activity measurement, 2) parameter calculation, 3) model construction, 4) activity classification, 5) activity prediction of candidates, and 6) experiment validation of candidates. Therefore, this rapid screening strategy we proposed in the present study is high throughput, inexpensive, regents free and effort saving.

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QM/MM MD Simulations of Horizontal Proton Transfer Pathways in the Antiporter-like Subunits of Mitochondrial Respiratory Complex I

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The molecular mechanism of respiratory complex I (NADH:ubiquinone oxidoreductase) has remained one of the biggest mysteries in bioenergetics. Being the largest enzyme in the respiratory chain, it couples the electron transfer process to proton pumping across the inner mitochondrial membrane, spatially separated by ~200 Å from one another. This phenomenon raises an enigmatic question: how does the energy released from the redox reaction can be transmitted for such long distances? In our work, we advocate the hypothesis that it can be accomplished by the translocation of protons along the central hydrophilic axis of the enzyme - a highly hydrated region revealed by the structural data [1-4]. We utilise state-of-the-art quantum mechanical/molecular mechanical (QM/MM) simulations to study the dynamics of horizontal proton pathways in the high-resolution structure of respiratory complex I from *Yarrowia lipolytica* [4]. We apply QM/MM free energy umbrella sampling simulations to various proton routes bridging highly-conserved protein residues of the ND2 subunit of the enzyme. Our results show low free energy barriers and favourable thermodynamics for the proton pathway laterally spanning the entire ND2 subunit. For the first time, we emphasize the critical role of tyrosine residues in coordinating the transmission, and show reasonable energetics for the proton transfer in interfacial regions of the ND2 subunit with the adjacent ND4L and ND4 subunits. Our results elucidate the long-range energy translocation processes in the membrane part of the enzyme, casting doubts on the canonically admitted proton pumping models in respiratory complex I.

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Gaussian basis set truncation errors in weak to intermediate magnetic fields

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Atoms and molecules in magnetic fields have been studied computationally to a large extent, mainly employing Gaussian basis sets. However, large basis set truncation errors are a problem in these types of calculations. We perform fully numerical electronic structure calculations on atoms with $Z \leq 18$ in the presence of an external magnetic field. We obtain basis set truncation errors by comparing these results to a variety of Gaussian basis sets. This way we identify the problematic areas of the GTOs, which can serve as a base for improving the basis sets for electronic structure calculations in magnetic fields.