THEMOSIA-RCTF2024

ROUEN, 24-28 JUIN

Table des matières

24 juin 2024

Session 1A

(R)evolution(s) in Molecular Modeling: What Lies Ahead?

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Molecular modeling and simulations are currently undergoing a remarkable transformation, driven by groundbreaking advances in computing power, data sharing, artificial intelligence (AI), and advanced visualization and data analytics techniques. The advent of GPU computing and the arrival of exascale machines have dramatically expanded the realm of feasible simulations, shattering previously insurmountable barriers. In biological applications, tools such as AlphaFold have revolutionized this domain, enabling significant leaps forward. However, our discipline has yet to fully embrace and integrate such emerging technologies, presenting both challenges and opportunities for growth.

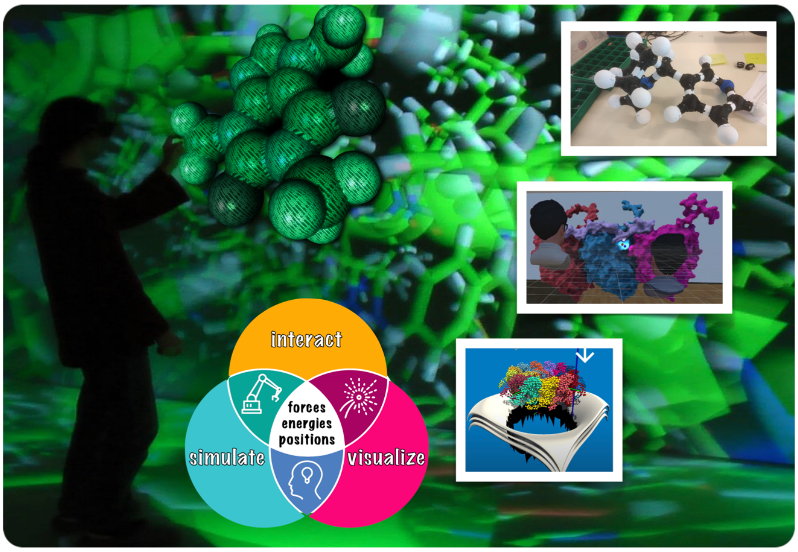

Figure 1. Emerging technologies for molecular modeling: advanced immersive visualization techniques for enhanced spatial perception of molecular structures; interactive simulations that enable real-time exploration and manipulation of molecular dynamics; collaborative virtual environments that facilitate seamless remote scientific collaboration; tangible smart molecular objects that combine 3D-printed physical models with digital data and interactive features.

This contribution will explore selected topics, including the transition to exascale simulations, the data-driven era in science, the ubiquitous integration of AI into our workflows, and the potential for adopting and leveraging new technologies within our field. Novel opportunities for global scientific collaboration, interactive simulations, virtual reality, visual analytics, and the incorporation of 3D-printed objects for molecular modeling and analysis tasks will be discussed.

Through this exploration, I aim to shed light on the transformative developments reshaping molecular modeling and simulation, offering insights into the exciting possibilities that lie ahead as we harness the power of cutting-edge technologies and collaborative efforts.

Keywords: exascale, artificial intelligence, virtual reality, interactive simulations, data.

Exploring the epigenetic regulation of DNA compaction with all-atom MD simulations

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Gene activity is tightly controlled by reversible chemical modifications called epigenetic marks, which are of various types and modulate gene accessibility without affecting the DNA sequence. Major advances come from investigations of such structural regulation at the first level of compaction of DNA, the so-called nucleosome, that is composed of ~146 base pairs of DNA wrapped around an octamer of histone proteins[1]. Indeed, post-translational modifications (PTMs) of histone proteins play are major epigenetic mechanisms. For example, lysine methylation usually promotes gene silencing while acetylation are marks of gene expression. Understanding the molecular mechanisms driving such epigenetic regulation is an active field of research, and many aspects remain to be described, such as how dedicated enzymes regulate the formation and removal of histone PTMs, and how these PTMs impact the nucleosome architecture through specific structural signatures.

Sirtuin 6 (SIRT6) is an NAD+-dependent histone H3 deacetylase that is prominently found associated with chromatin, attenuates transcriptionally active promoters and regulates DNA repair, metabolic homeostasis and lifespan. Unlike other sirtuins, it has low affinity to free histone tails but demonstrates strong binding to nucleosomes. It is poorly understood how SIRT6 docking on nucleosomes stimulates its histone deacetylation activity. Combining extended MD simulations to cryoelectron microscopy (cryoEM) approaches, we revealed the structure of the Sirtuin 6 (SIRT6) de-acetylase complexed to a nucleosome core particle[2]. We show that in this mode of interaction, the active site of SIRT6 is perfectly poised to catalyze deacetylation of the H3 histone tail and that the partial unwrapping of the DNA allows even lysines close to the H3 core to reach the enzyme, providing new insights into the potential dynamics of SIRT6 bound to a nucleosome, that help explain its substrate specificity.

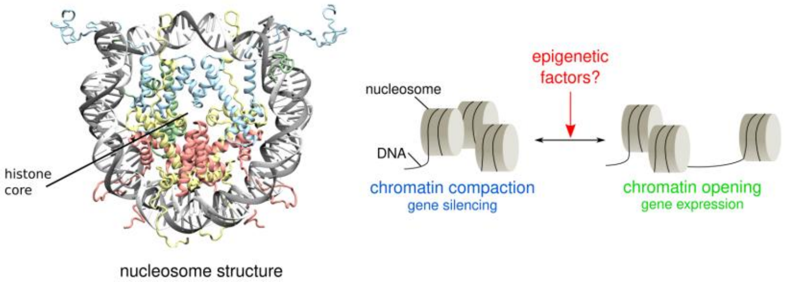

Figure 1. Left: Architecture of a nucleosome core particle (left), composed of ~147 base pairs wrapped around an octamer of histone proteins. Right: Epigenetic factors regulate DNA compaction and gene expression through fine tuned mechanisms that remain poorly defined.

<u>Keywords</u>: DNA compaction; epigenetics; histones post-translational modifications; MD simulations.

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Unravelling RNA chemical reactivity: Multiscale simulation and calculation of SHAPE probe/RNA interactions for better insight into experimental results

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RNA molecules are involved in most steps of genetic expression, including catalysis of central cellular functions. RNA functions crucially rely on both the specific 3D folding of the molecule, which in turn depends on the sequence and on how nucleobases pair through hydrogen bonds (secondary structure), and its conformation.[1] To overcome the lack of 3D structures, in the last decades, the number of chemical probing data has been largely increased and integrated into the prediction of 2D and 3D RNA structures with different levels of detail.[2] In particular, the SHAPE technology provides quantitative reactivity information for each nucleotide and has become the most popular among these techniques since it does not depend on the nature of the nucleotide, unlike other chemical probing techniques, and is amenable to high-throughput protocols. The probes are small-molecule electrophiles that acylate the 2'-hydroxyl group to form a 2'-O-adduct.[3-4] Although this approach is very popular and it is known that the SHAPE reaction is dependent on the local structural properties of each nucleotide, it has not yet been understood why different reactivities can be obtained for the same nucleotide depending on the probe used, and several questions associated with the relationship between structure, conformation, flexibility, and reactivity are still open. To overcome this, with the aim of using SHAPE data to predict bound and unbound RNA structures, we have first performed classical biased all-atom molecular dynamics simulations, using two different SHAPE probes, on a stable tetraloop of *Bacillus subtilis* yitJ S-box (SAM-I) riboswitch. SHAPE data for this system were experimentally obtained in our wet lab, allowing us to analyze the correlations between various geometric parameters and chemical reactivity. Moreover, to better understand our results and elucidate the SHAPE acylation reaction, we also performed QM/MM calculations on the same systems. Our investigations confirm that SHAPE reactivity is guided by the local flexibility of the different chemical moieties and the ribose, but also by the attack orientation of the SHAPE probe. Finally, we carried out QM calculations in the presence of a probe and a nucleotide, which reveal and give the first initial assessment of the potential reaction mechanism in the context of SHAPE reactivity. These results confirm the importance of the attack angle and emphasize the need for a more comprehensive understanding of the reaction mechanism underlying the SHAPE reaction.

KEYWORDS: RNA structures; Multiscale simulation; Reactivity; SHAPE technique

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Session 1B

Absorption in Al_{13} cluster using Real-Time TDDFT: transitions involving the continuum

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Unlike noble-metal nanoparticles (NPs) the localized surface plasmon resonance (LSPR) in Aluminum NPs occurs in the ultra-violet (UV) making them suitable for plasmonic application in the UV. This has stemmed research interest [1] in Al NPs and clusters despite their high sensitivity to oxidation and the difficulties in optical measurements high in the UV. From theoretical aspect optical properties of Al clusters is difficult to obtain as the LSPR is above the ionization energy implying transitions that involve contribution from states which are largely part of the continuum, in particular for the anion. To this end, quantum mechanical calculations of Al clusters from different groups differ radically as evidenced by optical absorption in and neutral [2, 3] charged [4, 5] Al_{13}.

In this work we present a systematic way to obtain absorption spectra for Al clusters within the framework of real-time time-dependent density-functional theory using the real-space code octopus [6]. This is done by systematic incorporation of contributions from “discretized" continuum states (which are not required to be explicitly calculated within RT-TDDFT,) to the propagation of occupied Kohn-Sham orbitals. The results are compared with linear-response TDDFT calculations where excited states are explicitly calculated. This comparison showed the advantages of grid based RT-TDDFT calculations which give correct spectra for all charge states, +1, neutral, and -1, of the Al_{13} cluster.

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Keywords: TDDFT, real-time, Metal clusters, DFT.

How does divalent ions content in the outer membrane of Gram-negative bacteria affect its properties?

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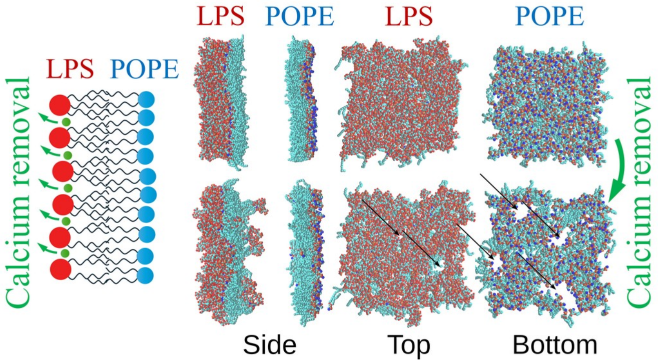

Figure 1. Illustration of the effect of a global stress on an asymmetric model of outer membrane of Gram-negative bacteria. The stress consists in the removal of all membrane-bound calcium ions and induces major membrane restructuring. For clarity, lipopolysaccharide (LPS) and phosphatidylethanolamine (POPE) components are presented separately in side and top views. Transient poration of the leaflets and positions of LPS flip-flooping are indicated by black arrows.

Over the past decades, polymyxins remain critical last-resort antibiotics against Gram-negative bacteria, despite their nephro- and neurotoxicity. However, the frequency of polymyxin-resistant bacterial strains is spiking, driving the need for alternative therapeutics eminently urgent.

One of the remarkable properties of polymyxins is their capacity to permeabilize the outer membrane of Gram-negative bacteria without utilizing protein channels. This membrane, characterized by its high rigidity due to the presence of lipopolysaccharides (LPS) in the outer leaflet, poses a formidable barrier to antibiotics. It is hypothesized that polymyxins disrupt this barrier by displacing divalent cations that bridge LPS molecules. Yet, the precise implications of this phenomenon on membrane structure and dynamics, as well as its significance in the mechanism of polymyxin action, remain a subject of debate.

We employed molecular dynamics simulations to model the effect of membrane-bound ions displacement. We investigated two non-resistant and two resistant models of the outer membrane of *Salmonella enterica*. We first focused on the effect of a large stress leading to the removal of all calcium ions, using atomistic simulations. We showed that this stress induces major membrane restructuring (Figure 1). Subsequently, we designed a collective variable (CV) that captures the local displacement of ions in a membrane. We applied enhanced sampling methods with this CV to estimate the impact of a local stress in the absence and presence of a polymyxin using both atomistic and coarse-grained simulations. Our findings offer an important insight in the consequences of membrane-bound divalent ions displacement, and help to seize its role in polymyxins mode of action.

Keywords: Gram-negative; bacteria; lipopolysaccharide; lipid; membrane; polymyxin; colistin; molecular dynamics

Molecular Modeling of NOX5 protein: Impact of the Initial Structure and Membrane composition

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Electron Transfer within proteins is an essential process for cellular activity. NADPH oxidases are transmembrane proteins whose main function in many organisms is the production of reactive oxygen species. In the NOX5 isoform, the reduction of dioxygen to superoxide ions occurs after several steps of electron transfer between redox cofactors (two hemes and a flavin) across the cell membrane. In a previous work of our group[1], the electron transfer between the hemes in the NOX5 protein was studied using molecular dynamics simulations based on the first experimental structure of a NOX protein.[2] Our aim is now to investigate the behavior of the NOX5 protein and the successive steps of electron transfer responsible for its activity using theoretical chemistry methods.

Recently, new experimental structures of NOX proteins[3][4] have been determined using cryo-electron microscopy showing rather large deviation from the previous model, which might have an impact on the electron transfer process. In this work we present molecular dynamics studies of the NOX5 protein, modeled with a classical force field representation in a biological environment (membrane, counter-ions, water). The construction of the models of the NOX5 protein will be described in detail, as well as the analysis of trajectories of several hundred nanoseconds in each redox state involved in the steps of transmembrane electron transfer. We will explore the role of the initial atomic positions (based on the two types of experimental data) and membrane composition.

The structural analysis of these trajectories will be described, as well as the first calculations of the electron transfer parameters in the framework of Marcus theory[5]. Our goal is the free energy ΔG of electron transfer. The comparison of the different simulations will provide information about the influence of the different simulation conditions on the structural and dynamic properties of the protein and on the electron transfer.

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Modeling the effects of photo-activated drugs in a biological membrane model by molecular dynamics simulations

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This study presents a comprehensive analysis of the interactions between photo-induced molecular switches and model lipid bilayers, alongside the molecular dynamics of the IgV domain of TIM-3 protein with lipid membranes, through advanced molecular modeling and simulation techniques. We explore the effects of a cyclocurcumin derivative, a potential agent for light-activated chemotherapy, on lipid bilayers mimicking cell membranes[1]. Utilizing classical molecular dynamics and enhanced sampling simulations via the coupling of ABF and Metadynamics (meta-eABF) to determining free energy profiles for the penetration of the switch in the membranes, we investigate the chromophore's interaction and penetration into membranes composed of 1,2-dipalmitoyl-sn-glycero-3-phosphatidylcholine (DPPC) and a complex mixture of DPPC, DOPC lipids and cholesterol. Our findings reveal concentration-dependent interactions with DPPC membranes and modulation of structural parameters through E/Z photoisomerization of cyclocurcumin derivative, offering insights into non-oxygen dependent therapies for hypoxic tumors[2]. In the more complex membrane, we showed that the cyclocurcumin derivative interacted differently, causing less profound damages and changes in the lipid bilayer[3]. However, for both membrane models we confirmed that the structural parameters of the bilayer are differently affected by two isomers, and hence can be modulated through photoswitching, offering interesting perspectives for future applications (Fig.1).

Furthermore, we characterize the interaction of the IgV domain of TIM-3 protein with a model lipid membrane, demonstrating stable yet dynamic complexes facilitated by phosphatidylserine-containing POPS lipids and Ca^{2+} ion. Enhanced sampling MD simulations highlight the thermodynamically favorable insertion of phosphatidylserine into the IgV binding pocket, suggesting mechanisms for modulating TIM-3 activity[4]. This study not only elucidates the molecular basis of lipid-protein interactions but also provides a foundation for future immunotherapy strategies targeting the TIM-3 pathway in cancer treatment.

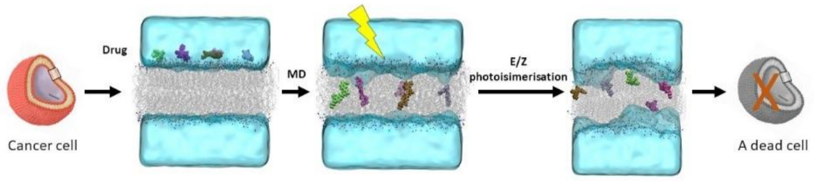

Figure 1. Schematic representation of the cell destruction process as a result of a cyclocurcumin derivative photoisomerization

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Keywords: cyclocurcumin, TIM-3, phosphatidylserine, molecular dynamics, photoisomerization, lipid membranes

Studies of ion channel activation and modulation via computer simulation

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Ion channels are ubiquitous membrane-embedded transport proteins crucial for life. The central function of ion channels lies on their ability to selectively transport ions given the appropriate stimuli *e.g.* voltage, mechanical force, temperature or pH, and provided their regulatory gates are open. Gating mechanisms can be further modulated by ligands, a fact consistent with the fine tuning of their activity to molecular cues and organism demands. In this talk, by selected examples from our work, I will provide an overview of the current knowledge we have about activation, permeation and selectivity of ion channels and I will describe some of the technical challenges we face to model ion channels using atomistic computer simulation.

KEYWORDS: biophysics; membrane proteins; classical molecular dynamics; enhanced sampling techniques; free energy

Sponsor SCM

Modeling materials with machine learning potentials, and how to fine-tune them with active learning

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Machine learning (ML) integrated into computational chemistry research has paved the way for transformative advancements, rapidly propelling our ability to predict new molecules, materials, and processes with the desired properties.

At the core of our efforts lies the Amsterdam Modeling Suite (AMS), a versatile framework facilitating exploration across multiple levels of theory from DFT to force fields, providing invaluable insights into potential energy surfaces (PESs) and mechanical and electronic properties. The AMS driver orchestrates advanced PES explorations and molecular dynamics (MD) with as well as Grand Canonical Monte Carlo (GCMC), harnessing energies and forces obtained from engines.

With this set up you can use electronic structure methods as well as (machine learned) force fields to calculate a wide range of properties and processes such as reaction rates, conformer populations, sorption isotherms, viscosity, stress tensors, thermodynamic stability, and chemical vapor deposition.

Use the AMS driver with on-the-fly machine-learned potentials like NEquIP[1] as well as preparametrized ML potentials such as ANI-1ccx[2], M3GNet[3], [3] and CHGNet[4] to efficiently calculate relevant molecules, materials, and processes for various applications such as batteries, catalysis, polymers, and carbon capture and storage. AMS's ParAMS module exemplifies a comprehensive framework for constructing training data from DFT engines and optimizing ReaxFF and DFTB parameters. Through the integration of active learning in ParAMS workflows, researchers can quickly create and refine machine learning potentials to tackle their diverse chemistry and materials optimization challenges.

As an example, we will demonstrate how the universal neural network potential M3GNet can predict critical properties of battery materials like intercalation energies and diffusion barriers, enabling faster materials screening to accelerate the innovation in the energy storage domain. While out of the box M3GNet predictions are reasonable, fine-tuning the M3GNet potentials gives access to DFT-level accuracy also for activated processes such as Li diffusion.

We would like to discuss with you how to collaboratively shape future developments where we envisage a dynamic landscape where AMS, bolstered by ML advancements, stands as a catalyst for transformative materials research, propelling innovation across multiple domains.

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Keywords: Materials modeling, machine learning, batteries.

25 juin 2024

Session 2A

Mechanistic investigations at the solid/water interface

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Reactions at the water/solid interface are central to develop more sustainable processes, from biomass upgrading to the use of unconventional activation as in photocatalysis and electrocatalysis. To gain atomistic insight on those reactions, modelling approaches were constantly improved in the past decade. Several approaches are available nowadays from continuum models to a full explicit description of the liquid water.[1] We will discuss the pros and cons of those methods using several examples.

Keywords: DFT ; ab initio molecular dynamics ; Solvent effect ; Catalysis

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Gold chemistry under ligand control. Computational chemistry and experiments : an ideal partnership to explore new reactivities and bonding situation.

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Long considered as a noble element, too inert and therefore useless in catalysis, the status of gold changed in the 1990s when interesting reactivities were discovered and applied in several reactions of industrial importance. During the past two decades, this homogeneous gold catalysis has grown spectacularly[1] and broadly applied. Besides the unique ability of gold complexes to activate $\pi_{C=C}$ bonds of unsaturated substrates towards nucleophilic addition, entirely new perspectives have been opened recently in gold Au(I)/Au(III) (photo)redox catalysis and careful ligand design played a crucial role to emulate unprecedented reactivity at gold.

In close collaboration with the team of D. Bourissou, we explore in depth the reactivity of new gold(I) and gold(III) complexes involving P-based chelate, hemilabile or ambiphilic ligands by combining experimental and computational studies. Thanks to rationale ligand design, pivotal transformations in many processes were made possible, intra or intermolecular oxidative addition of C-X bonds, challenging Csp^3-Csp^3 reductive elimination...[2] Recently, ligand-enabled oxidative fluorination of Au(I) with (P,N) ligand has also been investigated and light-induced Ar-F coupling at Au(III).[2]

These ligands opened up novel reactivities and new possibilities for catalysis. Recent and representative examples[3] are : i) the oxy-arylation of alkenes *via* Au(I)/Au(III) catalysis using (P,N) ligand; ii) the authentification of π-allyl Au(III)-complexes and the study of their reactivity toward β-diketo enolates. Special interest has also been devoted to the in-depth description of unusual bonding situation such as Au(I) carbene complexes and Au(III) π-allyl complexes.[4] In this oral presentation, the fruitful interplay between computational chemistry and experiments will be illustrated, with a focus on the contribution of DFT and computational tools for chemical bonding and reactivity studies.

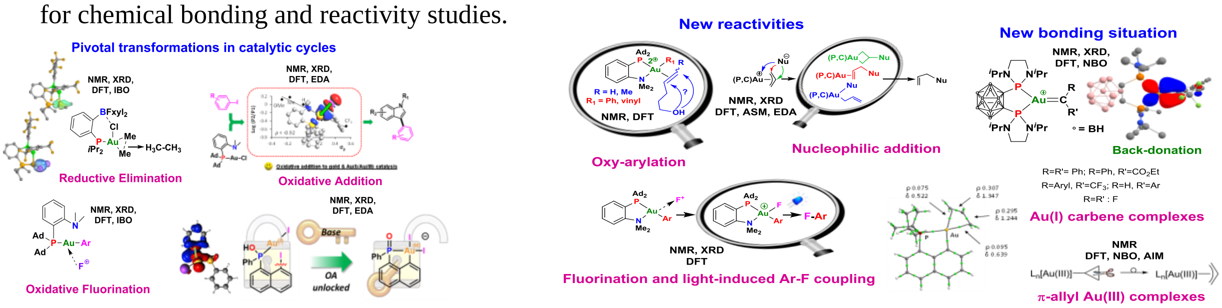

Figure 1. New reactivities and bonding situation at gold

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Keywords: Gold Catalysis - DFT calculations - Mechanisms - Electronic properties - Bonding situation

Effect of microhydration on DNA probe explored by Non-Adiabatic Dynamics

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The study of the native conformation of nucleic acids and its eventual perturbation induced by the coupling with the environment or external stimuli is fundamental to better assess the molecular mechanisms underlying their biological role.[1] Luminescent DNA probes [2] are tools of choice to evidence the presence of important structural modification of the nucleic acid structure. I will present a non-adiabatic dynamics study, performed with the surface hopping formalism,[3] on 2-thienyl-3-hydroxychromone, an environment-dependent luminescent organic DNA probe.[4] I will show that the solvent first-shell water molecules undergo a rather complex reorganization upon light excitation.[5] This also involves the triggering of a water-mediated proton transfer process which leads to the formation of the probe's tautomeric structure (Figure 1). The solvent-mediated transfer process globally diminishes the intersystem crossing efficiency, and hence the population of the triplet state manifold, as compared to the non-solvated systems. Our results also point out the non-innocent role of solvent networks in tuning complex photophysical processes, while opening competitive relaxation channels.

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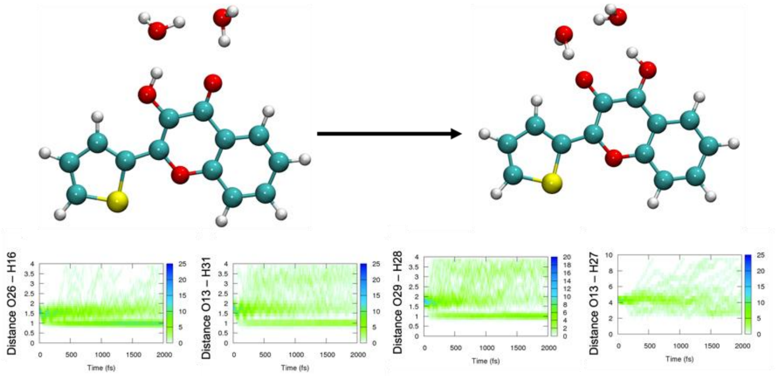

Figure 1. Tautomerization process

Keywords: Photochemistry, Non-Adiabatic dynamics, DNA probe.

Session 2B

Annotation and prediction of carbohydrate binding sites on protein surface

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Protein-carbohydrate (PC) interactions govern a wide variety of biological processes and play a crucial role in the development of different diseases. During the last decades, the release of an impressive amount of data on carbohydrate-binding proteins led to the emergence of first data driven methods for prediction of carbohydrate binding sites. Nevertheless, the performance of such models remains limited as compared to similar bioinformatics problems, and its correct evaluation is hindered by the lack of the reliable and non-redundant datasets. In the current study, we address this challenge and perform an exhaustive analysis of the diversity of PC interfaces and of its impact on prediction models accuracy.

We have gathered and annotated all the available information on PC interfaces found in the Protein Data Bank (PDB) in a user-friendly web-server, DIONYSUS: https://www.dsimb.inserm.fr/DIONYSUS/. Using a customized algorithm, we identified 46,984 PC complexes interacting with one of 3,500 carbohydrate-containing ligands of the PDB (increasing the number of these structures by orders of magnitude as compared to 900 ligand names available in the Chemical Component Dictionary). We performed an exhaustive study of PC interface diversity at different levels: by functional class of interaction, protein sequence identity and local geometrical similarity between the interfaces. Furthermore, we identified representative structures of different classes of PC interactions and used them to annotate PC complexes with missing functional information.

Finally, the developed database allows us to train several deep learning models based on protein language model encoding of the protein sequence combined to molecular graphs to encode protein structure. In-depth analysis of our model performance and its comparison to the previously published methods demonstrates significant improvements of carbohydrate binding site identification as well as highlights the remaining challenges in the field.

Keywords: protein-carbohydrate interactions; protein structure; binding site analysis; machine learning; structural bioinformatics.

Looking for Tetrazine-based red dyes: a theoretical insight

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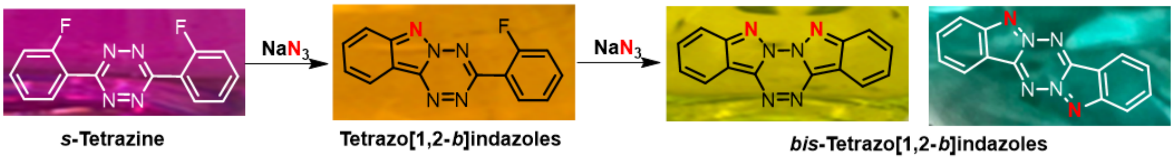
Among the large world of dye development, the ones emitting in the red or infrared wavelengths are of particular interest for their biological application. Moreover, small, rigid and planar molecules without (transition) metal are one of the many requirements for practical use in the OLED large-scale industry. In that respect, it has been shown that *N*-heterocycles-based molecules [1,2] are good candidates to match these requirements.



We have recently developed a way to synthesize a class of *N*-rich polyaromatics from ortho-fluorinated aryl-s-tetrazine [3,4], see the upper Figure. The UV absorption properties evolve strongly upon cyclization: s-Tetrazine is purple while the mono-cyclized tetrazo-[1,2-*b*]indazole is orange and the bis-cyclized tetrazo-[1,2-*b*]indazole is either yellow or dark-blue in its *cis* or *trans* forms, respectively.

In this presentation, I will present our theoretical efforts to rationalize the UV properties of this class of molecules and their derivatives. First, I will discuss the different steps needed to reproduce quantitatively the measured UV spectra by going beyond the vertical TDDFT calculation in order to understand the effects of the different substituents, for instance, amines, alcohol, and carbazole. Then, I will illustrate how the analyses of the electronic transitions, by detailing the charge transfer across the molecule[5] for instance, can drive the experimental design of more efficient molecules.

Keywords: Tetrazine, UV properties, TDDFT

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Modelling spectroscopic signatures of turns in short peptides

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Electronic Circular Dichroism (ECD) and Nuclear Magnetic Resonance (NMR) are experimental methods of paramount importance for the elucidation of polypeptide secondary structures. Among these structures, turns are essential patterns in bioactive peptides, but they are also much more difficult to characterize than helices or sheets due to the size of such motifs.

Starting with short peptides, in which turn conformations predominate, our goal is to predict the ECD and NMR signatures of turns[1]. Our work follows a previous theoretical study combining classical molecular dynamics and quantum chemistry calculations[2]. The latter are performed within a state-of-the-art hybrid QM/MM framework in which the environment effects are described using an advanced polarizable embedding scheme, and excited states are computed by Time Dependent-Density Functional Theory (TD-DFT)[3].

In this joint theoretical and experimental work, ECD and NMR spectra were first recorded on realistic peptides of biological interest, namely the Piv-Pro-D-Ser-NHMe and Ala-Phe-Ala (AFA) ones. From the computational side, ECD spectra and NMR indirect spin-spin coupling constant were simulated using the previously mentioned advanced theoretical methodology. The choice of the various parameters (force field, exchange-correlation functional, basis sets…) has been carefully assessed, as well as the convolution and fitting procedure following the spectra simulations. Our results showed that the designed protocol allows for a quantitative agreement between experimental and theoretical results, paving the way towards a better understanding of turn structures in solution.

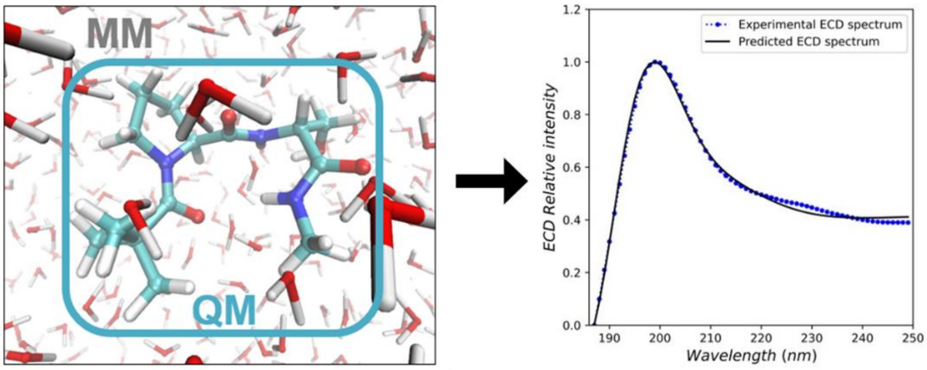

Figure 1. Solvated peptide (on the left) and its corresponding ECD spectra (on the right)

Keywords: turn conformation, electronic circular dichroism, nuclear magnetic resonance, time-dependent density functional theory, polarizable embedding, molecular dynamics.

Acknowledgements: LABEX SynOrg (ANR-11-LABX-0029), Region Normandie and CRIANN are thanked for funding and computational support.

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Revealing Solvent Effects on Chromophore Vibrational Spectra: Dynamic Insights from DFT/MM and Time-Series Analysis

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Understanding vibrational response of molecules in solution is crucial for various applications. However, accurately modeling these spectra requires accounting for environmental influences, emphasizing the importance of explicitly taking into account the environment with a hybrid DFT/MM approach.

By conducting a time-series analysis of dipole moment and polarizability tensor along a DFT/MM trajectory[1], we successfully model the vibrational Infrared (IR) and Raman spectra of organic chromophores derived from the triangulenium dyes family, specifically ADOTA$^+$ in aqueous solution[2]. Additionally, we extend our study to the Tata-Octyl molecule, comparing computational results to experimental spectra. Through comparative analyses with gas-phase and static-level spectra, we elucidate solvent-induced alterations in vibrational behavior, providing insights into solvent effects and anharmonicity.

Our work not only enhances our understanding of vibrational properties in solution but also highlights the potential of machine learning to accelerate DFT/MM simulations, offering a robust framework for future studies in this field.

Keywords: ab initio Molecular Dynamics; Hybrid Density Functionals; Time Series Analysis; Vibrational Spectra.

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Session 3A

AI-powered Protein Modelling and Design

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The field of computational protein design (CPD) is currently experiencing an unprecedented phase of development, significantly impacting biotechnology. Our advanced CPD technologies leverage a unique combination of automated reasoning and machine/deep learning algorithms, along with molecular modeling and simulation methods, to enable the rational design of tailored proteins. The original automated reasoning capacities provide accuracy and computational efficiency, while also offering the ability to integrate design requirements together with physics-based models and/or learning-based models from various sources of protein data (including, sequence, structure, biochemical/biophysical data). This comprehensive approach provides effective means to efficiently address design challenges and pursue complex design objectives, which can be indirectly learned through machine/deep learning. The synergy between these AI algorithms and molecular simulations empowers us to consider multiple molecular and conformational states crucial for protein function. In this presentation, I will focus on our latest advances in CPD, highlighting their capabilities, with an emphasis on their application in the field of enzyme, molecular assembly and protein binder engineering for biotechnologies and health.

KEYWORDS:. AI; protein design; molecular modelling; machine/deep learning; automated reasoning

Molecular mechanisms of phosphoester bond formation in abiotic conditions with reactive neural network potentials

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RNA, with its dual ability to store genetic information and catalyze chemical reactions, stands as a pivotal molecule in the quest to understand the origins of life: the earliest life forms might have relied solely on RNA[1]. However, the process of RNA polymerization, crucial for life's emergence, poses a formidable challenge in the absence of enzyme catalysts[2]. To shed light on potential mechanisms to expedite this reaction under abiotic conditions, a deeper comprehension of the uncatalyzed reaction mechanism is crucial. Experimental data remains sparse and inconclusive, while computational approaches face numerous hurdles. Factors such as significant entropic effects, involvement of solvent molecules, and the myriad of collective variables possibly involved in the reaction coordinates pose formidable challenges[3]. Neural network potentials offer a promising avenue, because they are in principle capable of addressing these obstacles by leading to reactive force fields with quantum accuracy[4]. However, their application to complex reactivity in condensed phases presents significant challenges.

We introduce a robust workflow to train such potentials, leveraging active learning of reactive structures through enhanced sampling methods, which is combined to the now well-established concurrential learning approach. Utilizing these models now enabling submicrosecond simulations, we employ enhanced sampling techniques, most notably transition path sampling, which enables to discern between various reaction pathways without presuming specific reaction coordinates. Consequently, we achieve unambiguous characterization of reaction kinetics, thermodynamics, and mechanistic intricacies[5]. Our findings favor a dissociative mechanism over an associative one, indicating the formation of a metaphosphate transition state with direct involvement of water solvent molecules. These insights not only rationalize previous ambiguous experimental results but also elucidate the temperature-dependence of the reaction rate, offering avenues for the design of more efficient abiotic catalysts and activating groups.

Keywords: Reactivity, Neural Networks, Enhanced Sampling, Free Energy Surface.

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Elucidating Novel Pathways for Prebiotic Glycine Synthesis: Merging Enhanced Sampling and Neural Network Atomic Potentials.

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Glycine has a central role in prebiotic chemistry inquiry as the simplest amino acid. While documented in meteorites[1], glycine's presence in the interstellar medium poses a persistent enigma. Nevertheless, the presence of alternative amino acids in meteoritic samples, inexplicable within the confines of the generally admitted Strecker mechanism[2], presents a compelling challenge [3].

We engage computational modeling, rooted in quantum mechanics, to navigate the complex chemical landscape of this synthesis. We employed *ab initio* Molecular Dynamics (AIMD) calculations with enhanced sampling techniques alongside neural network potentials, enhancing simulation scalability and affordability beyond conventional bounds[4].

This refined methodological framework[5], called MLMD, allows us to identify and explore of an uncharted 'oxy-glycolate path' for glycine synthesis. Building upon precedent investigations, our inquiry converges on two pivotal contributions: the unveiling of an unprecedented glycine synthesis route and the assertion of our new method as a potent instrument in probing chemical synthesis.

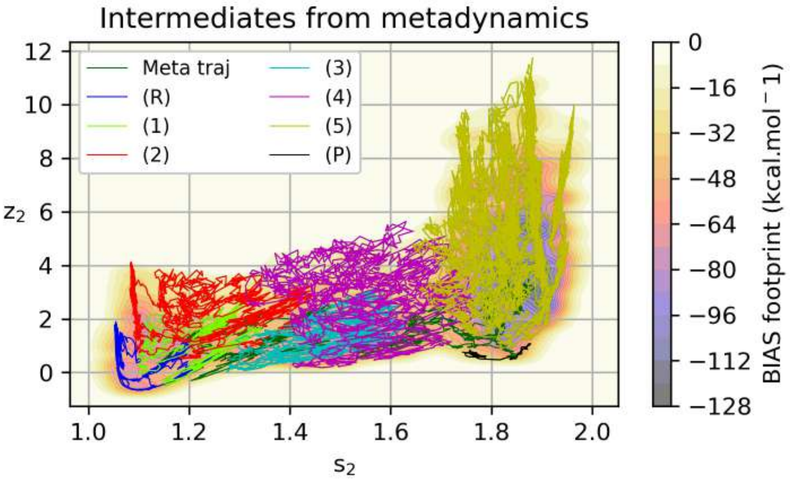

Figure 1. 2D graphics of the metadynamics trajectory that breaks toward glycine. The trajectory is colored with the initial set of intermediates out of the molecules observed during exploration of the chemical space.

Keywords: ab initio molecular dynamic; prebiotic chemistry; enhanced sampling; machine learning

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Recent Advances and Challenges in Machine Learning Representations of Molecules

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The intersection of machine learning, cheminformatics, and computational biology has grown significantly, particularly through a branch of machine learning dedicated to the representation of molecular graphs. This convergence is driving innovations, or is expected to drive innovations, in applications such as drug discovery, materials science, and chemical property prediction.

In this talk, we will discuss two main classes of approaches that have emerged at the forefront: Graph Neural Networks (GNNs) and Transformers. Rather than listing the numerous variants, we will focus on their core principles and the current challenges these approaches face. These challenges often involve incorporating physical rules into the representations, such as 3D geometry, symmetries, and long-range potentials.

Additionally, we will explore the paradigms used to learn these representations. Self-supervised learning has become a key framework for designing foundation models in natural language processing and computer vision. By examining the ingredients from these fields, we aim to understand the difficulties preventing the development of a foundation model for chemistry.

KEYWORDS: **machine learning; graph neural networks**.

Session 3B

Quantum Modelling and Electronic Structure Analysis in the Field of Materials Science

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Modelling based on various quantum chemistry codes is now part of the academic and industrial research landscape. The attraction of these simulation methods lies both in terms of the prediction of quantities that are sometimes difficult to extract at the experimental level for various materials whose interest is already well known, and in the possibility of exploring "unknown lands", upstream of synthesis work. In the more specific field of materials for energy or optics, it is now very well established that many key properties can be accessible by relying on this calculation tool, including in particular, structural and energetic characteristics related to the existence of point defects of more or less low content in the matrix, insertion/disinsertion phenomena, estimation of intercalation potentials in crystal systems or molecular redox potentials, activation energy of atomic jumps, etc. Even though a lot of information can be gathered directly by quantum chemistry calculation, already giving access to many possibilities of interpretation and also offering the possibility of opening the way to the transfer of this data in order to generate multi-scale models (*e.g.* in the field of matter transport phenomena that occur in batteries/fuel cells, etc.), the use of a more in-depth examination of the electronic structure can be very instructive. In many situations, this further step is of crucial help when searching for structure-property relationships.

This combination of approaches can be adopted in order to shed new light on Materials Science. Indeed, the route towards innovation and breakthrough can surely be accelerated thanks to the combination of quantum chemical modelling and methodologies belonging in particular to topological analysis of the electron density. In this area, the Quantum Theory of Atoms in Molecules ("QTAIM") method is of particular interest. Concerning materials for energy, while doping effects, oxygen/lithium or other metal (de-)insertion, effects of polymorphism, polyanion modulation, etc in inorganic matrices for M-ion batteries or Solid Oxide Fuel Cells traditionally constitutes one of the most prevalent playgrounds for computational studies, the more nascent field – in terms of development and applications – of batteries relying on organic electrode materials brings new perspectives and shifts the search in new directions. In this last context, the quest for most performant compounds is linked *e.g.* to new backbones identification, functionalization, isomerism, heteroatom substitution, redox centre change, etc. may benefits from the possibility to employ molecular modelling, prior to experiment, as a first estimation of their capabilities. By focusing on selective examples, the interest of quantum chemical modelling and topological analysis of the electronic structure applied to various compounds belonging either to organic or inorganic species will be illustrated in the purpose of driving the engineering search towards rationalization of phenomena and an educated guess of novel, innovating or optimized materials.

Keywords: Quantum Chemistry Calculations, Electronic Structure Analysis, Materials Characterization/Design, Structure-Property Relationships

Influence of the phytyl chain of chlorophyll *a* anionic on UV-vis spectra

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Plants contain chlorophyll-type molecules, which play a vital role in photosynthesis for several reasons. Photosynthesis, a well-known process, involves two distinct photosystems: Photosystem I (PSI) and Photosystem II (PSII). PSI acts as the catalyst in this reaction, utilizing light to transfer electrons from plastocyanin to ferredoxin. PSII serves as a catalyst and initiates the photosynthetic process. The negative charge is localized on a single chlorophyll molecule instead of two, as observed in the PSI dimer. To investigate electron transfer in PSII, it is imperative to understand the behavior of the chlorophyll *a* itself in gas phase.

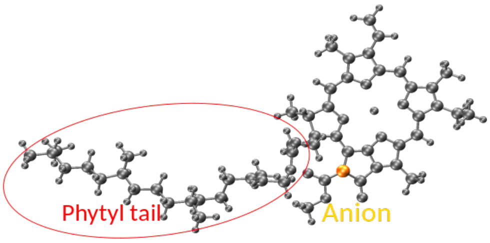

Figure 1: Chlorophyll *a* negative

This study aims to understand the effect of the phytyl chain on the UV-vis spectra of the chlorophyll *a* anionic in gas phase. Indeed, chlorophyll type molecule have a hydrocarbonated tail which is very flexible and moves a lot during dynamic, specially in gas phase. Based on a previous work, we used the molecule deprotonned on the macrocycle [1] presented on figure 1.
To answer this question, we built a step-by-step protocol. We carried out the Parallel Tempering molecular dynamic at the SCC DFTB method in deMonNano [2]. The exchange of configurations during parallel dynamics at various temperatures is a powerful tool for exploring the configuration space.
To understand how the phytyl chain moves, we deployed a clustering method called Hierarchical Density-Based Spatial Clustering of Applications with Noise (HDBSCAN) [3], [4]. This method belongs to the machine learning field and is applied on different kind of databases, it is used to group points of a database together called as cluster. In this idea, we built a database with representative measurements to characterize the phytyl chain in the space, using an angle and a distance between the macrocycle and the chain and a dihedral angle at the basis of the chain. We obtained different clusters representative of various configuration of the phytyl chain position in space.
To obtain UV-spectra specific for each configuration type, we have run TD-ADFT calculations with deMon2k [5]. We consider as reference chlorophyll $c2$ which is the chlorophyll a without the phytyl chain and with an alcohol instead. Throughout this project, we employed a combination of methods, machine learning tool and SCC DFTB parallel tempering. We applied these methods to investigate the observation and characterization of phytyl chain conformations and their impacts on absorption spectra.

Keywords: Parallel tempering, DFTB, TD-DFT, UV-vis.

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Session Poster 1

n°1

A Neural Network Potential Approach for the study of Phosphodiester Bond Reactivity

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The ability of RNA molecules to self-replicate by template-directed polymerization, together with the central role of RNA in contemporary biology for storing and transmitting genetic information, led to early proposals of RNA as a highly suitable candidate for the first self-replicating molecule. The activation of the mononucleotide phosphate groups would have been essential to facilitate polymerization in a prebiotic environment, while divalent ions were also found to be involved in this nonenzymatic polymerization process. In particular, magnesium ions, the dominant divalent cation in biological systems and the most available in the biosphere, are known to play a fundamental role in RNA stabilization and RNA catalysis [1].

The most common catalytic pathway involves a two-metal ion-dependent mechanism, proposed to be the general pathway of many nucleases, such as the Ribonuclease H enzyme [2]. Other nucleases, like the human APE1 enzyme, have been observed to exhibit catalytic activity in presence of a single metal ion [3]. As suggested by the RNA world hypothesis, contemporary catalytic polymerization mechanisms were probably preceded uncatalyzed polymerization facilitated by metal ions. Our aim is to understand the role of magnesium ions in the prebiotic formation of phosphodiester bonds.

The study of reactive mechanisms at quantum level is computationally very demanding. Machine learning-generated potential energy models offer efficiency comparable to classical force field models while maintaining ab initio accuracy and enabling submicrosecond simulations. However, their application to complex reactivity in condensed phases presents significant challenges. We employ an active learning workflow for the training of the potential energy models, while enhanced sampling techniques are used to generate reactive structures [4]. Consequently, we achieve unambiguous characterization of reaction kinetics, thermodynamics, and mechanistic intricacies. The phosphodiester reaction mechanism has been investigated and found to favor a dissociative mechanism involving the formation of a loose, metaphosphate-like state with the assistance of surrounding water molecules [5].

Supported by these insights, we investigate the role of magnesium ions in the phosphodiester bond formation mechanism, exploring their impact on the energetic barrier and on the pKa of the phosphate group. These factors could have significantly influenced the reaction rates in a prebiotic environment.

Keywords: prebiotic chemistry, reactivity, neural networks.

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n°2

Tunneling dynamics of H/Pd(111) and its effect on the quantum mechanical evaluation of the ISF

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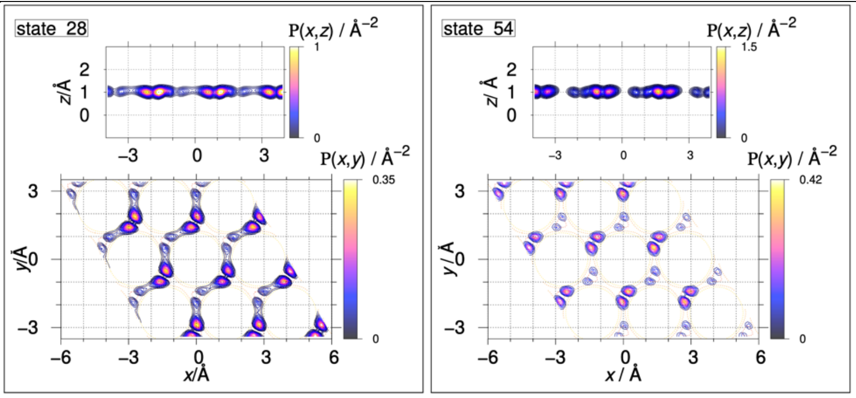
Understanding the properties and interactions of atoms and molecules on the surfaces of solids is crucial for many technological applications involving surface reactions such as the corrosion of metallic objects or heterogeneous catalysis. It is now well-established that many chemical processes are impacted by strong quantum effects involving the nuclei.

The topography of the multidimensional potential energy surface describing the interaction of atoms or molecules with the absorbing surfaces is rich of multiple adsorption wells and barriers that influence the diffusion of the adsorbates along the substrate. The resulting structure can be tackled either within the framework of a time-independent picture, i.e. by the calculation of the stationary states, or by studying the time evolution of the system starting from specific initial conditions. In this contribution, we adopt both approaches and relate the findings to observable quantities from HREELS [1] and ^{3}He-spin echo experiments [2], such as the intermediate scattering function (ISF).

The figure shows reduced probability densities (RPD) of two tunneling components related to the fcc and hcp equilibrium sites of H adsorbed on a 3x3 Pd(111) elementary cell.

Top: reduction over y. Bottom: reduction over z. RPD are superimposed on equipotentials ranging from 0 to 300 meV represented by dashed yellow lines (z = 90 pm).	

Keywords: quantum dynamics, surface science, quantum diffusion, spin-echo experiments, intermediate scattering function

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n°3

Asynchronous concerted mechanisms: coupling the reaction force constant and ELF / QTAIM analyses to locate primitive processes

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Many chemical reactions can involve either a stepwise or a concerted mechanism (synchronous or asynchronous). For some of them, it is possible to progressively switch from one type of mechanism to the other by modifying certain parameters of the reaction: nature of the solvent, nature of the substituents, intensity of a correctly oriented external electric field. This is the case, for example, with Diels-Alder and double proton transfer (DPT) reactions, which are the focus of this study.

For Diels-Alder reactions, we played on the nature of the diene and dienophile substituents to modify the reaction mechanism. For DPT reactions, we played on the strength of an external electric field oriented along the proton transfer direction,[1] in accordance with the reaction axis rule.[2]

To better understand the gradual transition from one type of mechanism to the other, we followed the evolution of the reaction force[3] (F) and reaction force constant[4] (κ) along the intrinsic reaction coordinate. We compared these evolutions with those of ELF or QTAIM descriptors adapted to describe the processes involved in these 2 types of reaction.

It appears that the minima of the reaction force constant (global quantity) correspond to particular points in the reaction profiles of the ELF / QTAIM descriptors (local quantities) (see Figure 1). This suggests that by coupling the 2 types of analysis, we can quantify the degree of asynchronicity of concerted mechanisms.

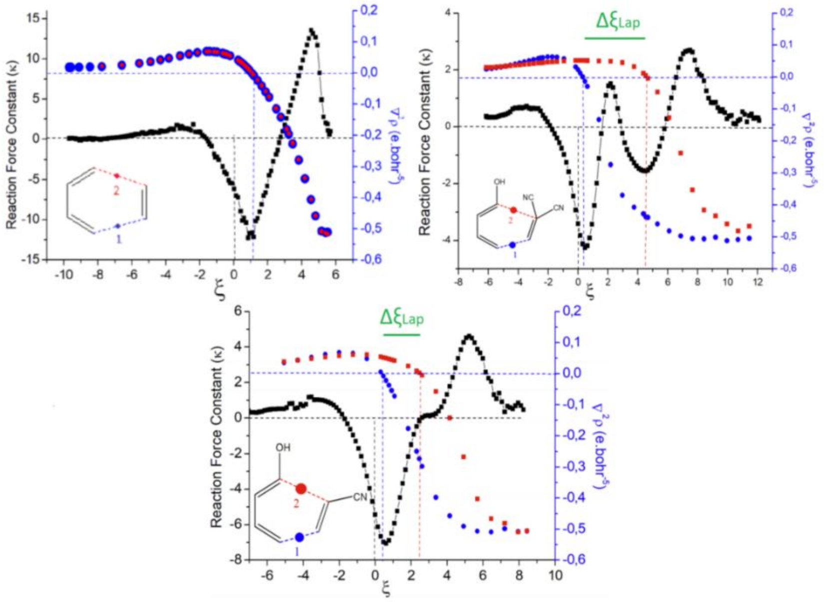

Figure 1. Superposition, for 3 Diels-Alder reactions, of the reaction force constant profile (black) and that of the Laplacian of electron density computed at the bond critical points of the two C-C bonds formed during the reaction (red and blue)

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Keywords: concerted mechanism, conceptual DFT, topological analysis, electric field, proton transfer

n°4

Calculating redox potential of flavoproteins with the AMOEBA force field

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Electron transfers are at the heart of many key biological processes such as photosynthesis and respiration. Such transfers rely on protein cofactors, either inorganic hemes or organic prosthetic groups like flavins, the redox properties of which are tailored to their proteic environment. Understanding redox properties of those cofactors is thus necessary to fully comprehend the chemical and biological processes involving electron transfers.

Redox potential of flavoproteins can be predicted with molecular simulations combining quantum chemistry calculations and molecular dynamics simulations using force fields to extensively sample the potential energy surface[1]. In the case of systems involving proteins, an accurate representation of electrostatic interactions is crucial hence the use of polarizable force fields, going beyond the monopolar approximation.

In this context, we aim at validating the use of the polarizable force field AMOEBA[2] for the prediction of the redox potential of flavoproteins. As there are no-preexisting set of parameters to describe flavins in the AMOEBA force field, a calibration step is carried out to generate such parameters for the different types of flavins (lumiflavin, flavin mononucleotide FMN, flavin adenine dinucleotide FAD) based on a process already used to calibrate a heme cofactor[3]. This method consists in performing QM calculations and calculations using the AMOEBA force field with Tinker[4] on different redox states of flavins to generate the parameters which then undergo a validation step. We will present here the first results obtained for the calibration procedure of the AMOEBA parameters for flavins and their validation.

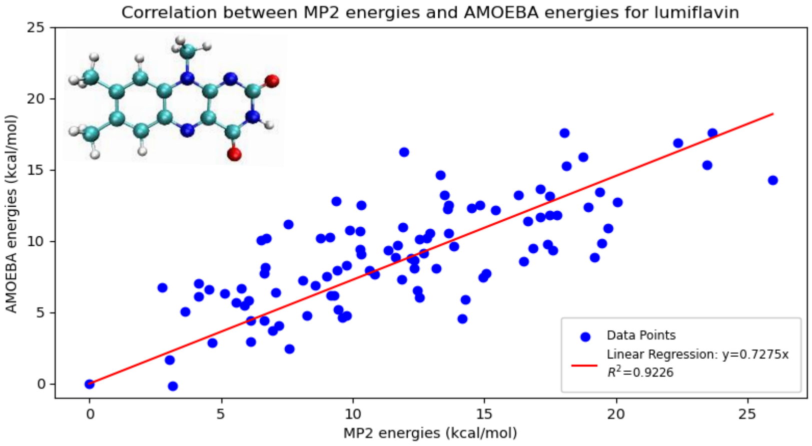

Figure 1. Comparison of MP2 energies and AMOEBA energies for the lumiflavin.

Keywords: polarizable forcefield, redox potential, molecular simulation, flavins, proteins

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n°5

Comparison of two machine learning interatomic potentials for bimetallic nanoparticles

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Heavy metal nanoparticles (NP) see a lot of developments and interests as radiosensitizers for radiotherapy. A new bimetallic Bi:Pt NP coated with PEG-based ligands was developed at ISMO, Paris Saclay using radiolysis. But what effects does the synthesis method have on the organization and surface of the NP?

Theoretical studies of bimetallic nanoparticles have been lagging those seen for noble metal nanoparticles such as gold and silver nanoparticles. This is due to the complexity of multicomponent systems which make proper characterization far more difficult than homogeneous systems.

Machine learning interatomic potentials (ML-IAPs) are quickly gaining importance in the field of theoretical chemistry and material sciences, as they offer cheaper alternatives to commonly used DFT calculations. In addition, they are positioned to bridge the lack of adequate force fields for molecular dynamics of complex systems.

Using our DFT reference data (PBE/LANL2DZ/HayWadt-ECP) for 59 atom bismuth-platinum nanoparticles, we will compare the results from a non linear fitting process, using the multi layer neural networks of DeepMD[1], and the linearly fitted parameters of the Chebyshev interaction model for efficient simulation (ChIMES)[2 ; 3].

We aim to provide a better picture on the suitability of the ML-IAPs available for bimetallic systems, weighing on the pros and cons of two design philosophies. In addition, we also intend to scale up our structural and vibrational results from the initial scope of DFT models to the experimental conditions of our systems counting tens or hundreds of thousands of atoms, far beyond the current capabilities of DFT methods.

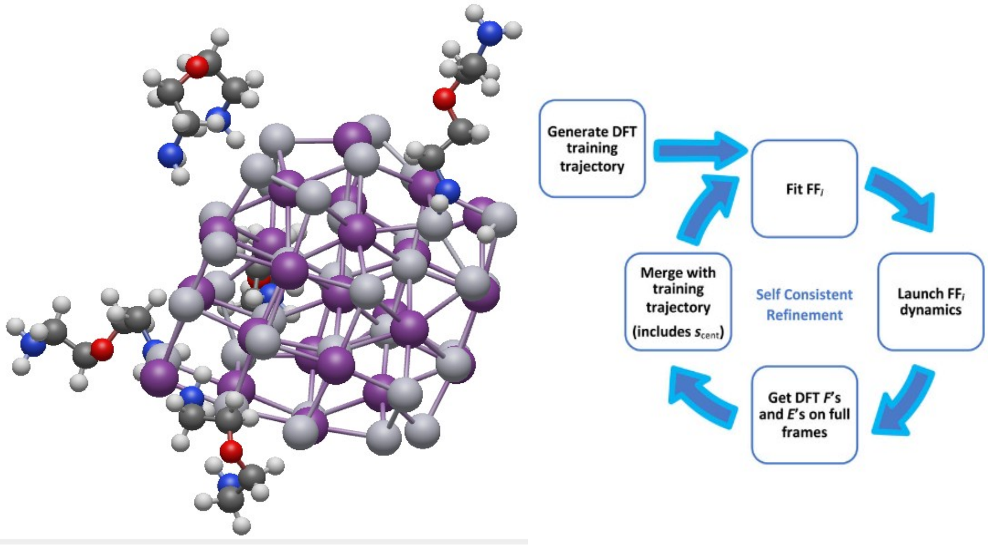

Figure: Model of the optimized bimetallic NP and scheme of the ChIMES refinement process

Keywords: Machine learned inter-atomic potentials (ML-IAPs); Heavy metal nanoparticles

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n°6

The Gradient Boosting Tree for the prediction of two-electron integrals

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A common bottleneck in most quantum chemistry (QC) techniques is the computation and handling of extremely numerous two-electron integrals. There is thus a continuous search for always faster methods to compute and store these integrals. In this work, we investigate the use of machine learning as a way to by-pass the direct computation of the two-electron integrals of a molecular system and facilitate their storage. We show that a gradient boosting tree Regressor (GBR) model can be trained to predict the values of two-electron integrals when only given a set of features describing each integral. This can be used to drastically reduce the memory cost of QC computations as only the parameters of the GBR are needed to be stored (instead of all the integral values). Those can then be used to compute the integrals on the fly. We also investigate the possibility of using GBR models to predict the two-electron integrals values of different basis sets or of different geometries of a molecule.

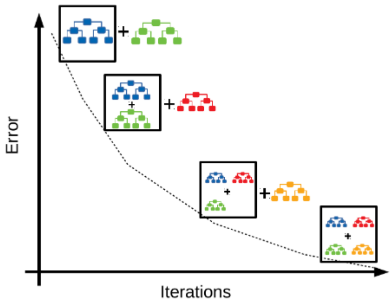

Figure 1. Gradient Boosting Tree illustration

Keywords: Machine Learning, Gradient boosting, Two-electron integrals, OVGF.

n°7

Computational investigation of vibronic effects on reverse intersystem crossing in CMA1 complexes

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Copper complexes featuring a carbene-metal-amide (CMA1) motif are characterized by linking carbene and amide ligands via a Cu(I) atom, forming a two-coordinate CMA motif. The photodynamics of CMA1 complexes predominantly rely on the properties of the carbene and amide ligands, with a minor contribution from the central coinage metal. Due to the well-separated frontier molecular orbitals, CMA1 complexes typically exhibit small energy gaps between their singlet and triplet states, facilitating access to the TADF channel.

Moreover, compared to purely organic TADF molecules, the inclusion of a coinage metal center in CMA complexes enhances spin-orbit coupling between singlet and triplet states, thus accelerating intersystem crossing and reverse intersystem crossing processes. Consequently, CMA1 complexes generally exhibit sub-microsecond-scale TADF lifetimes, which are significantly shorter than those of purely organic TADF materials.

A critical factor to consider in estimating rates for reverse intersystem crossing is the influence of molecular vibrations. Indeed, experimental evidence has shown that suppressing vibrational modes can greatly impact intersystem crossing processes, highlighting the necessity of accounting for vibronic effects in the phenomenon's description,

Therefore, we propose here a new investigation of CMA1 system based on the nuclear ensemble method[1] . We will show that accordingly to surface hopping dynamic[2], the reverse intersystem crossing process is strongly favored for a perpendicular orientation of the ligands. Indeed, this conformation alleviated a ^{3}MLCT$_{Cu \rightarrow MAC}$ state, channeling population from the triplet to the singlet manifold. These electronic transitions are concurrent with an elongation of the Cu-N and Cu-C bonds, alongside a reduction of the N-Cu-C bonding angle. From a coplanar geometry, the electronic population remains in the lowest-lying triplet state.

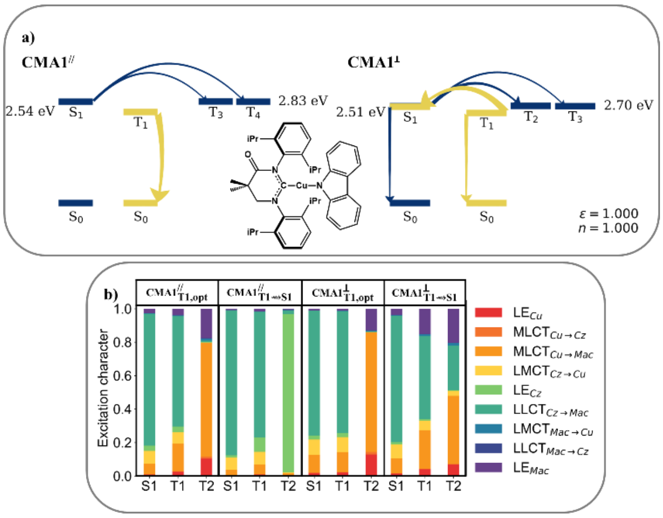

Figure 1a) Energy diagram of both configurations of CMA1. b) Electronic contribution associated to each transition

Keywords: TADF, Nuclear Ensemble Method, Photophysic properties

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n°8

Computational study of DNA three-way junctions

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DNA is a highly flexible biomolecule, which can adopt several types of structures besides the well-known double helix. When the DNA is under stress (for example during replication), and if the sequences allows it, DNA can form a three-way junction (TWJ) where three strands form a structure with a prismatic cavity (see Figure 1). This cavity can be filled with a ligand, which can block the replication if the ligand is well suited for the binding site. Thus, stabilizing TWJ can lead to cell deaths, and ligands for TWJ are putative anti-cancer drugs.

Several promizing ligands were identified by our experimentalist colleagues[1], but the optimization and rational design of new ligands is a long and tedious task, limited by the complexity of the organic synthesis[2]. We have thus decided to rely on computational chemistry to (1) reproduce experimental data, and then (2) propose new ligands. The main physico-chemical data to characterize the DNA/ligand interactions are folding temperatures: spectroscropic measurements at differents temperatures were performed and fitted to a sigmoid curve, which provides the temperature at which 50% of the structure is folded. We have thus designed a simulation protocole to compute folding temperature. After initial failure with brute force calculations, we have adopted a protocole based on hamiltonian replica exchange (REST2) which is a technique that is used for enhanced sampling. Promizing results were obtained, and a satisfactory correlation between computational and experimental temperatures were obtained. Thus, we have developed a protocol that can be used prior to synthesis to screen ligands.

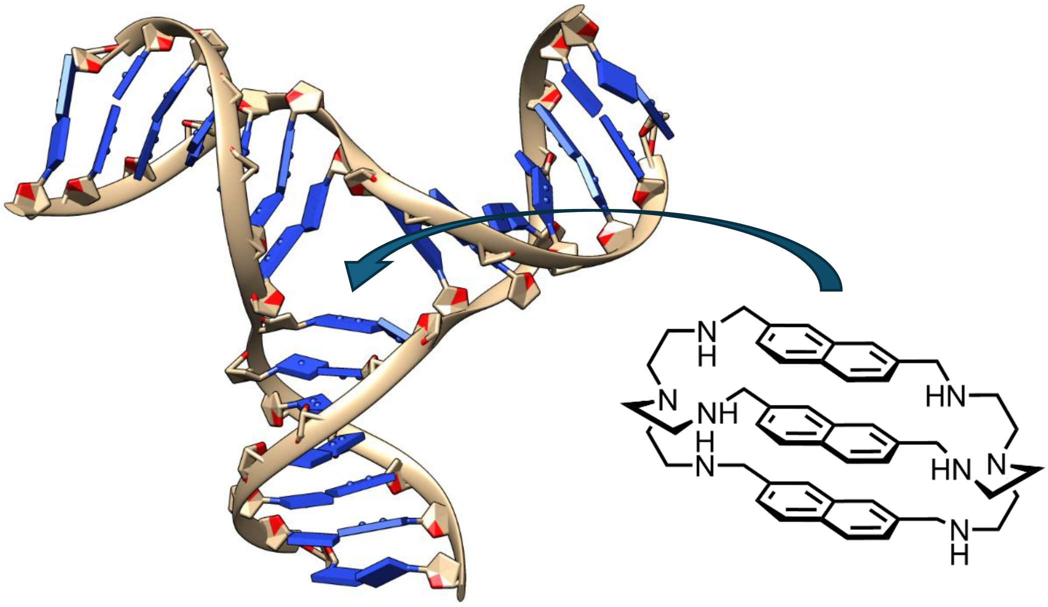

Figure 1. Model structure of DNA three-way junctions and example of a ligand.

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Keywords: MD simulations, enhanced sampling, replica exchange, folding temperature, DNA

n°9

Computational study of the pressure-sensitive mechanoluminescent response in polymorphs of an anthracene derivative

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Smart technological systems are nowadays omnipresent in our everyday lives. By responding to various external stimuli they contribute to more sustainability, energy efficiency and comfort. They range from smart windows that can switch between transparent and dark states triggered by heat or light,[1] piezoelectric floors where the pressure of a human's footstep or vehicle's movement is turned into electrical energy[2] to responsive prostethic skin that detects pressure, temperature and touch giving a more natural sense to the patient.[3] To add an additional layer of functionality and visual confirmation to smart technologies, mechanoluminescent (ML) materials that emit light in response to a mechanical constraint are of unique interest. In these systems, the application of pressure triggers a change in the supramolecular arrangement and may alter the structure of the molecular units which consequently impacts the emission wavelength and intensity.

In this work, we report a computational study of the ML properties of recently synthesized 9,10-bis((E)-2-(pyrid-2-yl)vinyl)anthracene (BP2VA) crystal polymorphs, which evidence drastic changes in their photoluminescence color upon exertion of external pressure.[4]

The crystal structure of the BP2VA molecule at zero and applied pressure, including cell parameters and molecular arrangement, is calculated using periodic density functional theory (DFT). The choice of computational method is validated beforehand by comparing with experimental results.[4] In a next step, the optical properties of dimers extracted from the optimized crystals are calculated using a hybrid QM/MM scheme, where the central dimer is treated at the time-dependent DFT level of theory.

The results, which compare well to experimental data, demonstrate that intermolecular exciton couplings play a leading role in the photophysical properties of these materials. Decomposition of the optically active excited states on a diabatic basis further allows to characterize the electronic transitions according to their local and charge transfer nature.

Keywords: Mechanoluminescence, Density Functional Theory, QM/MM Hybrid Schemes, Excited States.

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n°10 Dances with enzymes: Coarse-grained simulation of glycolytic enzyme assembly formation

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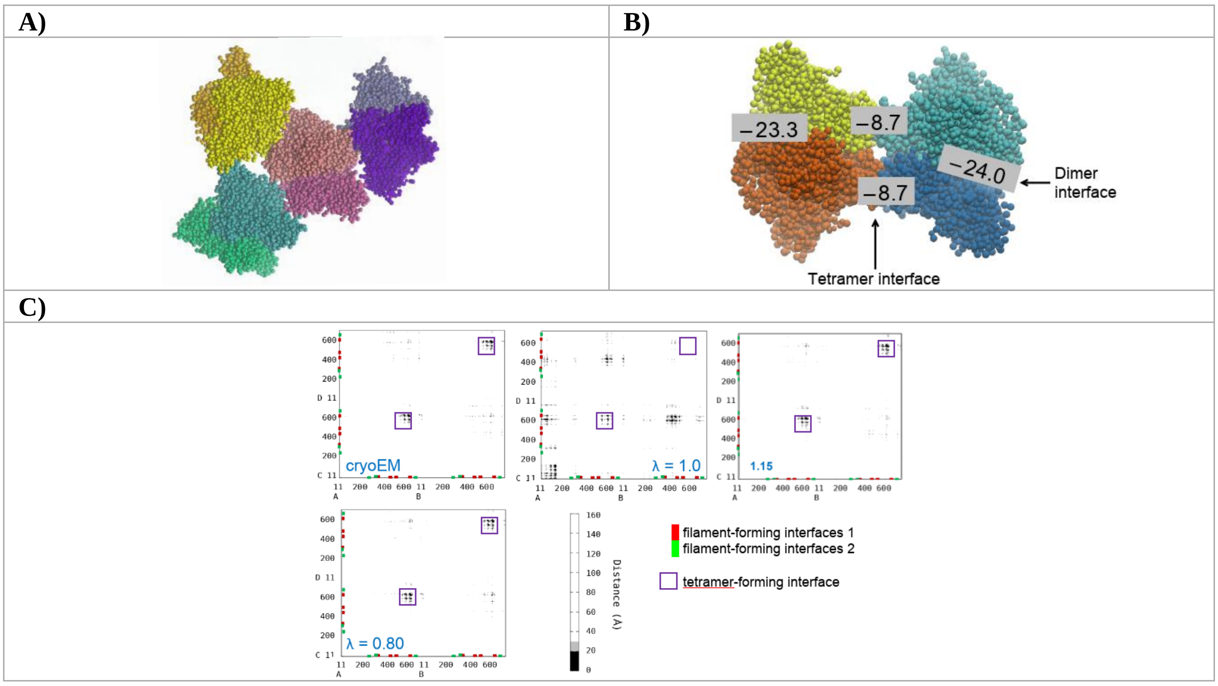
Various enzymes are able to interact with each other to form dynamic assemblies in cells. In particular, the human liver phosphofructokinase 1 (PFKL) has been identified as a prominent member of glycolytic enzyme assemblies and shown to form filaments[1,2]. However, the mechanism of the formation of these structures and their physiological roles remain poorly understood.

This work uses coarse-grained MD simulations to describe the assembly formation by PFKL. We investigate the stability of the PFKL tetramer and characterize the interactions between PFKL dimers using the Martini 3 force field and some rescaling factors[3,4]. Our results provide a starting point for a comprehensive description of the behavior of PFKL in glycolytic enzyme assemblies.

Figure 1. A) Tetramer and filament interfaces captured by Martini 3 are consistent with experimental data, but their relative stability is not accurate. B) Predicted binding affinities (kcal/mol) predicted by PRODIGY show a weak stability of PFKL tetramer interface which is not captured by Martini3, C) except when using a rescaling factor.



Keywords: glycolytic enzyme, enzyme assembly, coarse-grained simulation, force field rescaling

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n°11 Deciphering the fuzzy interaction between the Tau-R2 repeat and tubulin C-terminal tails with classical MD simulations

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Fuzzy complexes are a relatively new type of protein interaction involving one or more intrinsically disordered elements, which proved more and more biologically important in the past two decades[1]. Intrinsically disordered protein Tau is known to stabilize microtubules (MT), but little is known regarding its interaction with the intrinsically disordered C-terminal tails (CTTs) of tubulins[2]. We used all-atom molecular dynamics simulations to decipher the behavior of the R2 repeat domain of the Tau protein in complex with 3 tubulin monomers β-α-β. We built the C-terminal tails corresponding to isotypes βI-αI-βI and βIII-αI-βIII by homology. Our analysis confirmed the existence of a highly stable interface area involving Ser289, a serine notably phosphorylated in Alzheimer's disease[3], and revealed a modification of the dynamics of CTTs in presence of R2[4]. The latter result gives more weight to Lessard and Berger's idea that interactions between kinesins and MT could be indirectly mediated by the presence of Tau[5] [5]. We also propose a "wrapping mechanism" of the CTTs around R2 which might provide more insight regarding the stabilizing impact of CTTs in Tau/MT complexes. Finally additional simulations with explicit phosphorylations of R2-Ser285, R2-Ser289 and R2-Ser293 reveal interesting interaction patterns between the Tau peptide and tubulins involving sodium counterions.

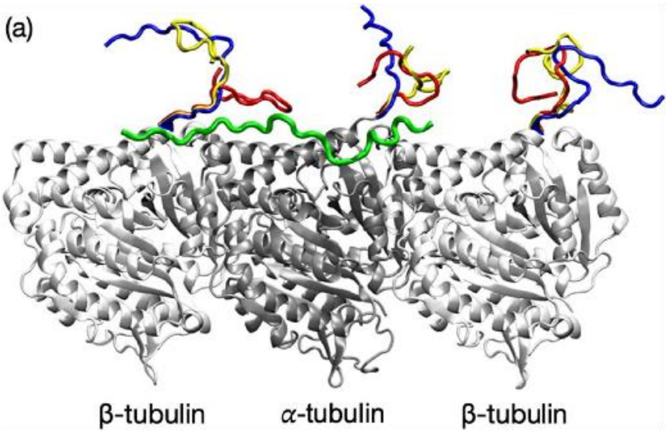

Figure 1. Starting structure of the tauR2/tubulin assembly for the βI-αI-βI isotype

Keywords: Molecular Dynamics, protein interactions, tubulin, tau, disordered proteins.

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n°12 Deciphering the Secrets of Madder Molecules through Computational Chemistry

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The captivating diversity and remarkable color properties of natural dyes molecules have long fascinated researchers. Madder is a plant known for being one of the main sources of natural red colorant. From its roots, more than 40 molecules from the anthraquinone family can be extracted with alizarin and purpurin being the most important ones.[1]

In our group, we used non-invasive spectroscopic techniques to measure some well-resolved UV-Vis, IR, or XAS spectra. Despite these complex methods, many data or chemical behavior cannot be obtained. In fact, several Madder dyes are not chemically stable when extracted from the roots and may not be found in the final objects. Furthermore, some of these dyes are more prone to photochemical degradation, resulting in color fading.[2]

To study these colored molecules, we have designed a reliable computational protocol which gives access to the most stable form and its related spectroscopic properties. We have first selected the most present colorant in madder, alizarin, as well as a more water-soluble analog, alizarin red S, and computed their spectroscopic properties, notably UV-Vis and NMR spectra. Our protocol enables us to characterize the impact of the solvent, *i.e.* water at different pH and its impact on the properties. We have also computed the color of the molecule according to the CIELAB framework and compared it to experimental measurements (see Figure 1).[3] Finally, this protocol has been applied to most of the colored molecules found in madder in order to create in the future an extensive open-data database.

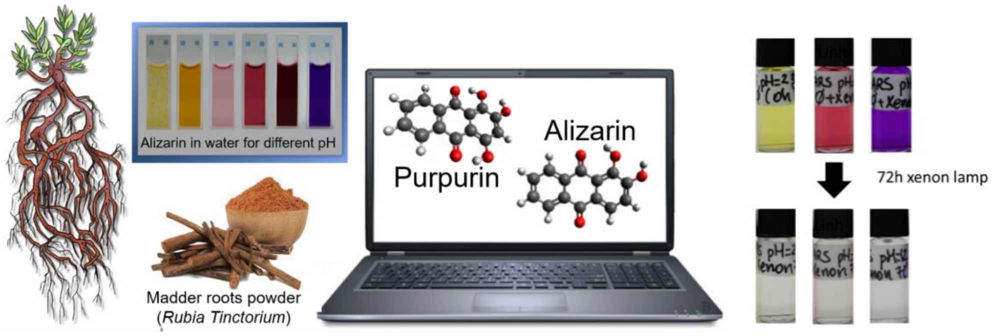

Figure 1. Representation of madder roots (left), alizarin and purpurin molecules (middle), and the color loss after light illumation (right).

Keywords: *Computational spectroscopy, cultural heritage, dye, DFT*

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n°13 Design, synthesis and properties of modular Chiral Phosphoric Acid Organocatalysts

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Recently, modular 9,10-diphenylanthracene receptors were developed via a reversible singlet oxygen cycloaddition[1]. This [4+2] reversible reaction allows the dearomatization of the anthracene moiety inducing a change from a planar geometry to a concave one for the endoperoxyde product.

This modular anthracene/$^1O_2$ system has not been explored in modular catalysis, where stimuli are limited to physical (light), electrochemical or chemical (ion, molecule) ones[2].

We aim to develop new modular organocatalysts, by modifying chiral phosphoric acids (CPA) based on *(R)*-BINOL which Brönsted acid activity have been well-explored and mechanisms were supported by extensive theoretical studies[3].

We designed customized modular catalysts, synthesised them and studied their propreties and catalytic activity in benchmark reactions and by molecular modelling.

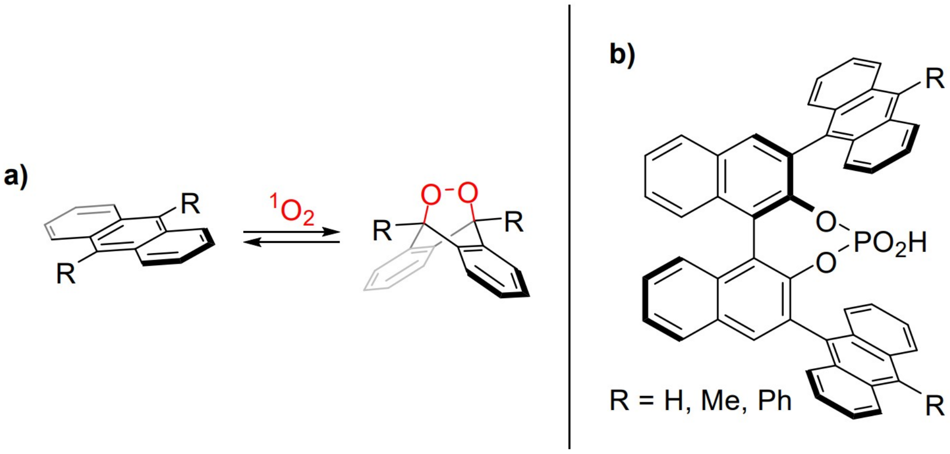

Figure 1. a) singlet oxygen modular system with 9,10-diphenylanthracene ; b) CPA for modular catalysis .

Keywords: Asymmetric organocatalysis, Modular catalalysis, Molecular modelling, DFT.

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n°14

DFT Calculations Reveal the Rules for the Design of Promising Single-Atom Alloy Catalysts

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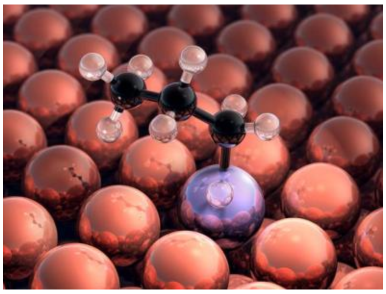
Single-Atom Alloys (SAA) are an emerging class of materials which have shown extraordinary development in recent years for applications in catalysis. They consist of coinage metal nanoparticles (Cu, Ag or Au) doped by substituting distant surface atoms by more active transition metal atoms. This doping strategy turns poorly reactive nanoparticles into catalysts with activities similar to pure transition metal nanoparticles and enhanced resistance to deactivating reactions (e.g. coking), thereby yielding longer lifespan. Despite these attractive properties, SAA catalysts escape the traditional trends used in heterogeneous catalysis (e.g. d-band center). Although this makes their design more complicated, it opens new opportunities in terms of attainable chemistries.

In order to better understand and predict the reactivity of SAAs, we considered two large screening studies aiming at identifying descriptors that capture the binding energy of catalytically relevant adsorbates at their surface. Using DFT calculations, we first identified the atomic charge of the dopant (arising from the electronegativity difference be dopant and the host) and the carbophilicity of the dopant as good descriptors for the binding of adsorbates on SAAs. It turned out that the binding energies of electron-rich adsorbates (H_2O, NH_3, OH) were well described using the atomic charge of the dopant (electrostatic interaction dominating). For dopant/adsorbate bonds that had a stronger covalent character, the binding energy of carbon was much better descriptor.[1] Our second screening studied aimed at gaining more insight into the binding mechanism of covalently bound species and providing an electronic understanding of the covalent bond. Considering 3d, 4d and 5d dopants in Cu, Ag and Au surfaces, we showed that binding energies were the strongest when the number of electrons brought by the dopant and the adsorbate abide by a rule of 10.[2] We showed that this corresponded to the saturation of the d-orbitals which provided increased stability to the metal/adsorbate bond. We showed that altogether these rules enabled the identification of the right dopant for a reaction of industrial interest, namely the reduction of nitrogen to ammonia.

All in all, these two studies provide unprecedented insights into the reactivity of single atom alloys and can serve as a guide for the design of new catalysts. It also contributed to the paradigm shift of the understandings of chemical bonds on metal surfaces.



C-H activation of propane on RhCu SAA (the Rh dopant is represented in blue)

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Keywords: DFT, catalysis, electron-count rule, descriptors

n°15 Dynamics of Protein–RNA Interfaces Using All-Atom Molecular Dynamics Simulations

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Facing the current challenges posed by human health diseases requires the understanding of cell machinery at a molecular level. The interplay between proteins and RNA is key for any physiological phenomenon, as well protein–RNA interactions[1]. For example, the formation of ribonucleoprotein particles (RNPs) including mRNAs is key for the post-transcriptional regulation of gene expression[2].As another example, many viruses manipulate the translation initiation complexes to ensure their replication, by recruiting the host ribosomes to translate their mRNA[3]. To understand these interactions, many experimental techniques have been developed, spanning a very wide range of spatial and temporal resolutions. In particular, the knowledge of tridimensional structures of protein–RNA complexes provides structural, mechanical, and dynamical pieces of information essential to understand their functions. However, obtaining high-resolution tridimensional structures through high-resolution techniques is still a challenging task as shown by the relatively small number of structures deposited in the Nucleic Acid Data Bank (NDB) [4]. The limited number of known complex structures is nevertheless constrained by the inherent flexibility of proteins and/or RNA and the size of the complexes. To overcome that, low resolution data have been used to model these structures. To get insights into the dynamics of protein–RNA complexes, we carried out all-atom molecular dynamics simulations in explicit solvent on nine different protein–RNA complexes with different functions and interface size by taking into account the bound and unbound forms. A detailed analysis was conducted on the RNA structure, including the change of ribose puckering upon binding for its potential interest to better understand biochemical reactivity data as SHAPE. Then, we focused on the characterization of the stability of their interfaces and interfacial water molecules. To determine the presence or the absence of interface substates, in each system, we analyzed in detail the time evolution of the contacts between interface residues and we performed a hierarchical clustering on our trajectories based on the interface residue–residue contacts. Moreover, we characterized the interactions at the interface and the interface geometries, as well as the evolution of the contacts between interface residues and water molecules and the pairs of residues involved in mediated interactions via water molecules. Finally, in the case of alternative interfaces obtained with our approach, we performed a dynamic network analysis to assess how the change of contacts at the interface could impact the communication in the complex and to gather novel biological insights.

Keywords: protein-RNA complexes; molecular dynamics simulations; interfaces; dynamics

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n°16

ELF$^{\&}$IGM: A Modern Take on Electron Localization Function Topological Analysis

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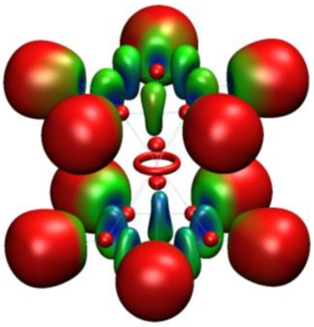
The Electron Localization Function [1] (ELF) has been successfully used to understand the concept of electron-pair localization in molecules and solids. The topological analysis of the ELF function enables the partitioning of the molecular space into ELF basins (core and valence basins, monosynaptic and polysynaptic) [2]. This is mainly based on the analysis of the gradient field of ELF, which is time-consuming and complex from an algorithmic perspective. Hence, there is a need for a rapid and easy identification of the nature of ELF basins. Our approach relies on the Independent Gradient Model (IGM) and its local descriptor δg. δg is a property of the Electron Density function that characterizes electron sharing between atoms when two or more electronic sources overlap. While zero values of δg correspond to monosynaptic basins, non-zero values correspond to polysynaptic basins. We implemented our approach within IGMPlot [3], open-source freeware that is used to identify and quantify a broad range of molecular interactions. The ELF basins are analyzed using the qg descriptor, a descriptor that we had designed to enhance the IGM-δg analysis. To illustrate and test our new analysis method, we selected about 100 typical systems. We calculated the ELF for each of these systems using IGMPlot. We compared our results with traditional ELF analysis methods using Topchem [4]. Our approach proved to be effective. It is worth mentioning that this new and very fast ELF$^{\&}$IGM analysis can be achieved with little preparation. It is therefore more suitable for pedagogical and practical use.

Figure 1. A 3D representation of the ELF isosurface of Ferrocene with IGMPlot



Keywords: Chemical bonds, Electron Localization Function (ELF), Quantum Chemical Topology (QCT), Electron Density (ED), IGMPlot.

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n°17

Enhancing QTAIM Implementation in ADF Software

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The Quantum Theory of Atoms in Molecules (QTAIM) [1] facilitates the analysis of electron density within molecular systems, offering insights into atomic interactions and structural features such as chemical bonds, rings, and cages.

Previously, the application of QTAIM within the Software for Chemistry & Materials (SCM) suite was limited. Our work specifically addresses this in the Amsterdam Density Functional (ADF) [2], where we have expanded the characterization of structural motifs, including atoms involved in rings and cages. Additionally, we have refined the decomposition of the dipole moment into its intra- and interatomic components [3]. Moreover, we developed a script using the Python Library for Automating Molecular Simulations (PLAMS) [4] to compute atomic polarizabilities.

Together, these developments not only enhance the functionality of the ADF software within the SCM suite but also broaden the scope of QTAIM applications, paving the way for research opportunities in chemistry and materials science.

Consequently, our implementation is poised to facilitate several applications such as UV-visible absorption and emission spectra, or electronic circular dichroism under realistic biological conditions, through the Polarizable Embedding (PE) approach [5]. Furthermore, our code can be extended, for example, to crystallography applications through integration with the BAND software (also part of the SCM suite).

Keywords: ADF, SCM, QTAIM, Polarizability

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n°18

Evaluation of non-covalent interactions with double-hybrid functionals

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Weak non-covalent intermolecular forces play a pivotal role in the behaviour of organic systems. However, the theoretical simulation of these interactions is difficult and requires models like density functional theory (DFT) combined with heavily parameterised empirical dispersion corrections.

In this work we illustrate how double hybrid functionals can provide an improved description of weak non-covalent interactions between small organic molecules, even without employing large basis sets and empirical corrections. The study focuses on systems extracted from the GMTKN30 database[1], specifically from the S66x8 subset, which contains high-level reference structures and energies for small organic molecular pairs at different intermolecular distances.

By comparing the results of single-point calculations employing Perdew–Burke–Ernzerhof Quadratic Integrated Double-Hybrid (PBE-QIDH)[2], hybrid functional (PBE0), and the simple generalized gradient approximation functional (PBE), we demonstrate the efficacy of our computational protocol.

The DFT approaches are combined with small basis sets such as def2-SVPD and DHSVP[3], as well as larger ones like def2-TZVPP. The further addition of an empirical dispersion correction D3(BJ)[4] for all functionals in combination with TZ and DHSVP basis sets completes the set of levels of theory across which we perform our comparative study.

Results, reveal that, for the PBEQIDH/DHSVP level of theory, dispersion energy does not necessarily improve the evaluation of weak interactions, thus reinforcing the idea that the combination between double hybrid functionals and small basis sets provides alone an accurate-enough description of these interactions at reduced cost.

Keywords: DFT, double-hybrid functional, non-covalent interactions.

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n°19

Exploring the mechanisms of damage of biomolecules under ionising irradiation with numeric simulations

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The study of the irradiation of living matter is a field of major clinical interest, whether it be for its deleterious physiological effects or for its use in radiotherapy. We work on the damage caused by ionising irradiations on two biosystems, one extracellular and one intracellular. The first is a triple helix of the polypeptide (Proline-Proline-Glycine)$_{10}$ designated as collagen mimetic peptide (CMP) **Fig. 1**, as it mimics the collagen protein, the main component of the extracellular matrix of animals. The second is the nuceosome **Fig. 2**, composed of an octamer of histone proteins around which a 147 bp long fragment of DNA is wrapped.

For these two systems, our approach aims at describing the whole phenomenon of the ionising irradiation in which we distinguish three phases. First the energy deposition, which takes place at a timescale inferior to 1 fs, corresponds to the impact of the ionising particle or photon on the electron cloud. We chose a QM/MM approach that allows to consider the entire molecular structure. The QM part is simulated under the Born- Oppenheimer approximation with RT-TD-DFT[1]. Then, the energy is dissipated into the vibrational modes of the bonds, which can lead to breaks. At this point, the B-O approximation is off, and we use an Ehrenfest method for the classical dynamics part of the QM/MM modeling. The corresponding timescale expands from 1 fs to 1 ps. Finally, we look at more macroscopic architectural modifications (ns to µs) with pure MM.

We started our simulations with CMP, as mass spectrometry experiments have been carried out to study the effects of ionising irradiation of CMP in the gas phase[2]. It provides us with a precise landscape of the disssociation and fragmentation at stake, which will allow us to test our simulation methodology, especially for the QM/MM-Ehrenfest part. We will see how our simulated products of ionising irradiation compare with the experimental data. If both match in a convincing manner, we will be able to focus on the molecular detail of the damage mechanisms. Thereby, we intend to use the CMP as proof of methodology to apply it to the nucleosome which is ten times larger than a CMP. Moreover, there is no available data about irradiations products of nucleosome, and no molecular entity of this size has ever been simulated using QM/MM-Ehrenfest.

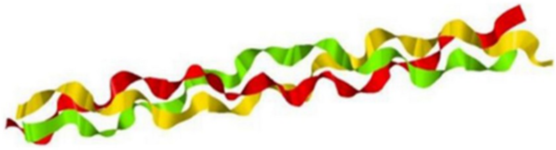

Figure 1. Collagen mimetic peptide[1]

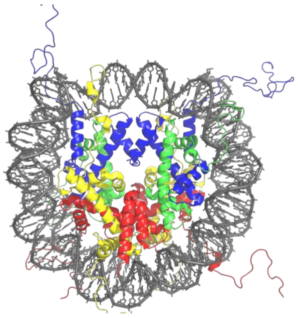

Figure 2. Nucleosome, © Richard Wheeler – Nuffield Department of Medicine, University of Oxford

Keywords: ionizing radiation, direct effects, biomolecules, QM/MM

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n°20

Exploring the substrate Specificity of Dihydroflavonol-4-Reductase.

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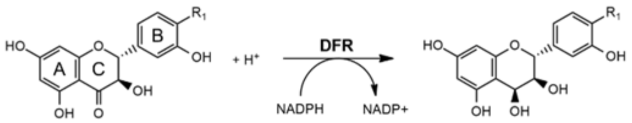
Dihydroflavonol 4-reductase (DFR) is a key enzyme in the biosynthesis of anthocyanins and catalyzes the reduction of dihydroflavonols to leucoanthocyanidins (see scheme 1). Some DFRs can convert dihydrokaempferol (DHK), dihydroquercetin (DHQ) and dihydromyricetin (DHM) irrespective of their B-ring hydroxylation pattern, whereas others show distinct substrate specificity. Differences apparently come from subtle mutations of the amino acid sequence. Despite an abundance of studies on DFR substrate specificity, there is still no systematic understanding of how the specificity is determined at the molecular level. This work addresses the DFR substrate specificity and structure-function relationship with respect to the B-ring hydroxylation pattern of the substrates.



Scheme 1. Reaction Mechanism catalyzed by Dihydroflavonol-4-Reductase Enzyme

In parallel of experimental DFR assays [1], Molecular Dynamics simulations are carried out on the substrate/enzyme complex in order to decipher the most important interactions that could improve or exclude an efficient enzymatic reaction, depending of the substrate. So far, the role of several catalytic amino acids involved in the reaction is well known[2], but the exact impact of amino-acids of the stabilizing pocket or of the second shell around the active site is not fully described (see Figure 1). Here, we will present our first investigations on their role using Molecular Dynamics protocols.

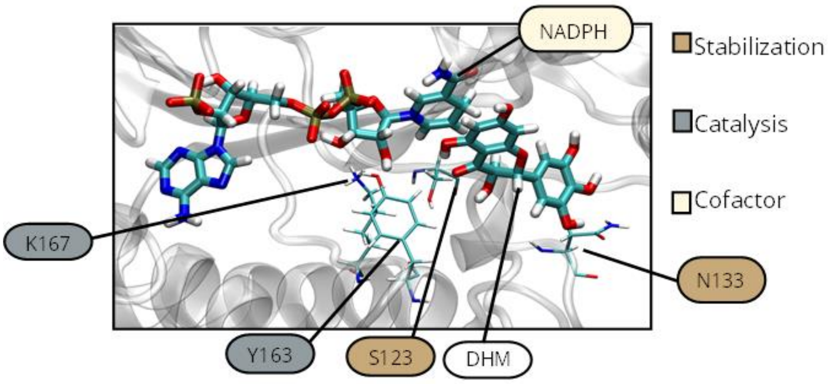


Figure 1. Dihydroflavonol-4-Reductase Active Site with Dihydromyricetin substrate

Keywords: Molecular Dynamics, Substrate Specificity, Dihydroflavonol-4-Reductase.

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n°21

From micro-solvation to solvation: Study of the interaction between pesticide, Ca^{2+} and water

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A large number of pesticides are authorised in the European Union and are used in agriculture. A better understanding of pesticides requires the study of their behaviour and fate in the environment (soil, water and air). This is a major challenge in order to limit their harmful impact on the environment. The global project in which my thesis subject is included follows a step-by-step approach to explore the interactions between a pesticide and the various components of a soil that can be modelled at the atomic scale. Thus, I am studying the micro-hydration[1] of two pesticides, fenhexamid (N-(2,3-dichloro-4-hydroxyphenyl)-1-methylcyclohexanecarboxamid) and metamitron (4-amino-3-methyl-6-phenyl-1,2,4-triazin-5-one), which are respectively a fungicide and an herbicide. Some results and the method used will be presented. First, in molecular dynamics with a DFTB potential, we extensively explore the potential energy surfaces of the Ca^{2+}-pesticide-$(H_2O)_i$ systems for i = 1-20. Along these trajectories, we select n structures that we optimise in DFTB. Among these minima, the m energy-lowest ones are re-optimised in B3LYP/6-311+G(2d,2p) to minimize basis set superposition error. The effects of dispersion are taken into account using the empirical corrections of S. Grimme (D3). In addition, the micro-hydration of the cation and the pesticide are studied through different characteristic energies[2] such as the relative energies of the different minima, the interaction, complexation and deformation energies, giving a better understanding of the micro-hydration of a pesticide interacting with a calcium. The first hydration spheres of the pesticide and the cation are also determined to rationalize the energetical.

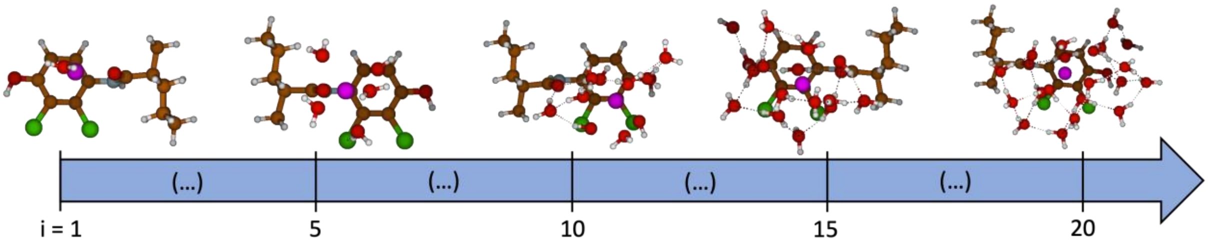

Figure 1. Optimized structure of the lowest-energy isomer for Ca^{2+}-fenhexamid-$(H_2O)_i$ for i= 1, 5, 10, 15 and 20.

Keywords: micro-solvation, pesticide, DFT, DFTB, Molecular Dynamics.

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n°22

From triplet to singlet: exploring fluorescence enhancements in organic materials

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Energy transfer has been in the center of a manifold of optics, photonics and optoelectronic applications. Usually, triplet excitons contribute negatively to a device's efficiency, especially in organic light-emitting diodes (OLED). Experimental studies have been able to demonstrate simultaneous singlet-singlet (SS) and triplet-singlet (TTS) FRET from a single donor material (NPB) [1]. To explore this further, we used Density Functional Theory (DFT) to analyze the geometry and normal modes of NPB and the acceptor (DCJTB) molecules. By employing the nuclear ensemble method, we obtained the absorption and emission spectra for both materials. Additionally, we calculated the intersystem crossing (ISC) rates and phosphorescence spectra of NPB regarding the triplet excited state. In previous experimental studies, it has been observed that changes in the acceptor concentration can lead to alterations in the system's polarizability [2] . This effect influences fluorescence spectra due to their dependence on the dielectric constant, subsequently impacting how intersystem crossing, emission, and transfer rates are calculated. To gain further insights into these dynamics, we developed a Kinetic Monte Carlo (KMC) algorithm based on electronic structure parameters from differently polarized systems. Using this approach, we investigated energy transferring, internal conversion, and non-radiative contributions as the acceptor concentration increased. The first mentioned experimental work attributed the intense decay in exciton lifetime to non-radiative processes. Our results indicate that TTS does occur, which is in agreement with experimental results. The authors claim that the observed lifetime decay is mostly attributed to non-radiative decay in the donor. Nonetheless, the same decay was well reproduced without taking any form of non-radiative process into consideration. In conclusion, our study sheds light on the simultaneous SS and TTS transfers and provides valuable insights into energy transfer mechanisms. These findings contribute to the advancement of optics, photonics, and optoelectronics, particularly concerning organic light-emitting diodes.[1]

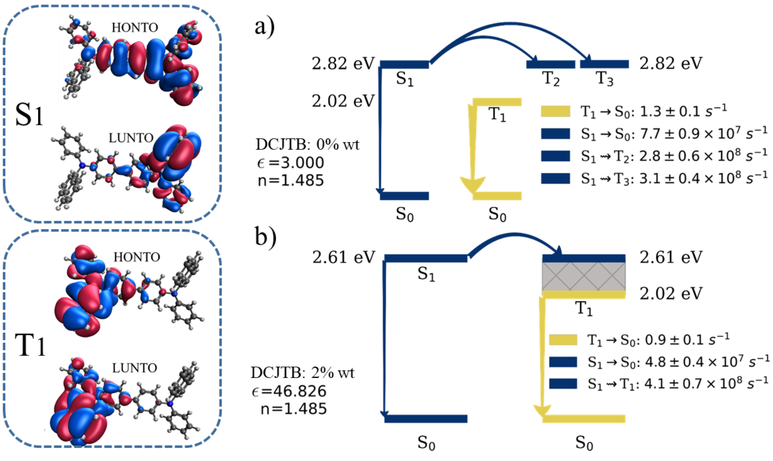

Figure 1: NTOS for the S_1 and T_1 states along with energy level diagrams of NPB with (a) 0\% DCJTB concentration and (b) 2% concentration. Curved and straight arrows represent ISC and emission, respectively.

Keywords: triplet to singlet, afterglow, delayed fluorescence, excitons

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n°23

Heat capacity of nitric acid by molecular dynamics

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Corrosion due to nitric acid in concentrated mediums is an active domain of investigations in nowadays-nuclear fuel reprocessing plants[1]. However, the complexity of the medium, due to the presence of strong electrolytes and thus heavy deviations from ideal behavior, hinders the determination of species activities required to predict speciation of the system[2]. Empirical models exist in the literature[3], but require the use of, sometimes many, adjustable parameters. Theoretically, species activity can be derived knowing the free enthalpy of the system, thus we aim to compute nitric acid-water mixtures free enthalpy. First, we investigate reproducing by molecular dynamics the heat capacity of pure nitric acid, and then of the binary mixture.

Keywords: molecular dynamics, nitric acid, free enthalpy, thermodynamics

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n°24 High-Pressure Response of the Coupled Dynamics of Lipids and Membrane Proteins

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Cell membranes consist of a complex assembly of lipids and proteins that are essential to normal cellular function through their role as physical barrier, chemical filter or signal converter. The understanding of the interplay between the lipid properties, the collective physical properties of the membrane and the protein conformational landscape is key in order to explain the membrane protein function. Experimentally, high hydrostatic pressure can be used as a tool to modulate the lipids dynamics as well as a way to smoothly modulate the protein dynamics without denaturation. By combining high resolution liquid-state NMR and molecular dynamics (MD) simulation, we are characterizing the coupled dynamics of lipids and proteins in response to high pressures at the molecular level. We first demonstrate that state-of-the-art lipid forcefields enable to quantitatively reproduce the membrane phase transition at increasing pressure. As observed experimentally, the presence of a membrane protein such as OmpX shifts the phase transition to higher pressures. The MD simulations are then instrumental in providing a molecular picture of the protein's effect on the membrane lipids, in particular by providing a spatial resolution (that is, how lipids in contact with the protein are affected differently from those that are further away) that is not accessible in the experiments. In turn, we also characterize the lipid effect on the protein, and show that protein side-chains facing toward the membrane are very sensitive to the lipid phase transition, whereas groups pointing toward the protein core are much less affected, as suggested by the experimental results.

Keywords: Biological membranes, Hydrostatic Pressure, Membrane proteins, Lipids, Molecular dynamic simulations.

n°25

In silico Identification of Potential TRPM7 Inhibitors for the Treatment of Pancreatic Ductal Adenocarcinoma

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Pancreatic cancer is projected to become the second leading cause of cancer-related mortality by 2030.[1] Approximately 90% of pancreatic cancers are pancreatic ductal adenocarcinomas (PDAC), which affect the exocrine part of the pancreas. The mortality rate associated with PDAC is very high because it is often diagnosed at an advanced stage. The only treatment that can improve the 5-year survival rate of patients to 20% is surgery, but this option is available for less than 15% of patients.[2] Therefore, PDAC is a significant public health issue, making it crucial to better understand its development.

Our collaborators' research has highlighted the overexpression of the cation channel TRPM7 (Transient Receptor Potential Cation Channel Subfamily M Member 7) in PDAC, which is associated with poor survival.[3] TRPM7 is a non-selective cation channel essential for the intestinal absorption of divalent cations[4] and for maintaining cellular magnesium (Mg^{2+}) homeostasis.[5] The TRPM7 protein contains a functional kinase domain at the C-terminal, which belongs to the class of α-kinases.[6] Our collaborators have observed that TRPM7 regulates the migration and invasion of pancreatic cancer cells.[7]

Figure 1. Blind docking of the reference compound TG100-115.

Currently, there are no specific blockers for the kinase function of TRPM7. Therefore, we have implemented a 'docking' screening of the CERMN chemical library. From this screening, we selected about ten compounds that were evaluated in vitro. The tests revealed two candidate molecules capable of inhibiting the kinase domain of TRPM7.

Keywords: Screening, Docking, TPRM7 channel, Pancreatic cancer.

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n°26 Intelligent modeling and classification of NMR spectroscopic data

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This poster presents the research project of my Cifre thesis at Evear extraction in partnership with University of Lyon 1, on the modeling and intelligent classification of NMR spectroscopic data, utilizing a 400MHz NMR spectrometer and AI models trained on 4 Nvidia L4 GPUs. The main goal is to develop a metric for comparing two NMR spectra, enabling rapid and precise detection of similarities. This approach facilitates the identification of components in complex samples which would associate each peak in the NMR spectrum with a specific molecule.Particular attention is given to the classification of plants from their NMR spectra, aiming to specifically identify the studied plant among a defined set. This methodology relies on detecting the unique characteristics present in each spectrum, allowing for accurate recognition of the molecules comprising the sample. Early results on a machine learning workflow based on a random forest algorithm will be presented.This project promises to significantly improve the speed and accuracy of chemical compound identification, offering potential applications in various scientific and industrial fields. It represents a notable advancement in the use of NMR spectroscopy, opening new perspectives for the exploration of spectroscopic data in research and beyond.

Keywords: NMR, AI, Metabolomics

n°27 Investigation of gold and silver clusters using reactive force fields and machine learning potential

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Gold and silver nanoparticles (NPs) have attracted significant attention in various scientific fields due to their remarkable optical, electrical, thermal, and biological properties. Capping these nanoparticles with alkylthiolates gives protective capabilities, allowing for the precise tuning of their characteristics and the formation of Self-Assembled Monolayers (SAMs) with specific architectures, as defined by Wood's notation. For silver NPs, experimental investigations have revealed the formation of a √(7×7) R19.1° assembly, occasionally accompanied by the creation of an Ag_2S shell through sulfidation, resulting in substantial system restructuring. For gold NPs, two distinct assemblies: √(3×3) R30° and c(4×2) have been found, with the latter characterized by the unique phenomenon of staple formation.

This theoretical study employs molecular dynamics simulations to assess the consistency of the current force field parametrization for these complex systems. Given the impracticality of employing quantum calculations due to their computational costs, we utilize a reactive force field, specifically ReaxFF, which gives a balance between computational cost and accuracy. Furthermore, our chosen parametrization is expected to provide precise descriptions of adsorption sites compared to Density Functional Theory (DFT). Our research initially focuses on silver surfaces and NPs up to 10 nm in size, comparing the stability of different assemblies within SAMs. Additionally, we investigate various properties to validate their agreement with prior experimental findings and to uncover any potential surface restructuring phenomena.

In the case of gold NPs, as the existing force field parametrization proves inadequate for these systems, we introduce an innovative approach using machine learning potential. We present our model and demonstrate its effectiveness in describing gold NPs.

This comprehensive theoretical study advances our understanding of the behavior of gold and silver nanoparticles capped with alkylthiolates, providing insights into their stability, reactivity, and surface restructuring phenomena. Our findings contribute valuable insights that bridge the gap between theoretical predictions and experimental observations, furthering our ability to control and harness the potential of these nanoparticles in various applications.

Keywords: nanomaterials, molecular dynamics, machine Learning

n°28 Multiscale Simulations to Unveil the Role of Divalent Cations in Ribozyme Catalysis

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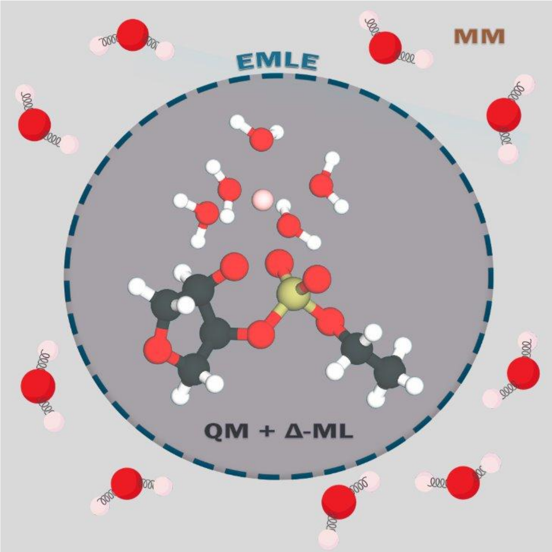
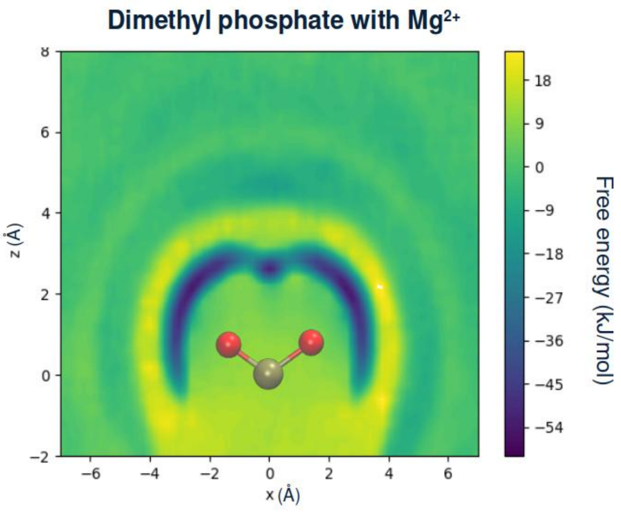
Experiments have shown that the Hammerhead ribozyme catalytic activity vary greatly depending on the nature of the ion in solution: it is 10000 times faster with magnesium ions than sodium ions and 500 times faster than with calcium ions.[1] We aim to provide a molecular explanation for this phenomenon combining advanced conformational exploration with a dynamic exploration of the multiple reaction pathways with the QM/MM-MD Adaptive String Method (ASM).[2] However, we are limited to using semi-empirical functionals for the QM description of such large systems, which affects the accuracy of our simulations. To address this issue and improve accuracy while retaining sampling quality, we propose a QM+ΔML/MM approach, incorporating Machine Learning corrections to achieve DFT-level accuracy without increasing computational cost. We plan to use a newly developed physics-based electrostatic embedding scheme (EMLE) that allows us to apply a ML model trained solely on the QM subsystem *in vacuo*, thus reducing the cost of training the model and allowing for more flexibility of the model.[3] Here we are showing the preliminary result we got so far on a model system focused on the phosphodiester bond only and starting from a deprotonated state to simplify the implementation of the protocol.

Another challenge in such systems is to ensure proper sampling of the different ion binding modes, that are separated by high kinetic barriers.[4] We thus investigate different enhanced sampling strategies to alleviate this issue.





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<u>Keywords</u>: RNA, ions, reactivity, ML, enhanced sampling

n°29 Structural Analysis of the *Drosophila Melanogaster*'s GSTome

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Glutathione transferase (GST) is a superfamily of ubiquitous enzymes, multigenic in numerous organisms which generally presents an homodimeric structures. For instance, GSTs are involved in numerous functions as chemical detoxification as well as chemoperception in mammals and insects[1]. GSTs catalyze the conjugation of their cofactor, the reduced glutathione (GSH) to xenobiotic electrophilic centers. To achieve this catalytic function, GSTs are made of a ligand-binding site and a GSH binding site per subunit. The GSH-binding site (G-site) is very specific and the hydrophobic substrate binding site (H-site) allows the binding of diverse substrates. In addition, the G-site presents a high conservation among GSTs. The chemical diversification in plant during the evolution was probably an important evolutive driver leading to the GSTs diversification, especially in insects. This encourages the study of insect GSTs to understand how spontaneous mutations/insertions/additions in the sequences modify the stability, selectivity, and the catalytic efficiency of this superfamily of enzymes. The Universal Protein Database (UniProt) registers 36 GST sequences in the fly, *Drosophila melanogaster*'s (*D. mel*), which are distributed in 7 classes and composing its GSTome. GST subunit structures are characterized by a $\beta\alpha\beta\alpha\beta\beta\alpha$ thioredoxin-like fold in its N-terminal part (Domain I) and an α-helical domain in its C-terminal part (Domain II). Domain I is quite conserved among GSTs and contains specific residues critical for GSH binding and catalytic activity whereas Domain II is quite variable both in sequence and structure, and this diversity determines the ample and distinct hydrophobic substrate specificities observed for the different enzymes. Finally, the interface of dimerization between the two subunits also plays a crucial role in the stability and catalytic activity of GSTs.

The goal of the present work is to study the complete GSTome of *D. mel* from its 36 sequences and structures to determine how changes in the amino-acid sequence modifies the structural characteristics of GSTs, particularly in the binding sites and in the interface of dimerization. First, we predicted 3-D atomic structures of each GST using the AlphaFold program developed by DeepMind[2] and compared them with existing X-ray crystallography experimental structures (7 over 36 of them have been resolved). We also characterized their global and local fold using secondary structures predictions and free-energy landscape analysis of internal coordinates such as backbone and side-chain dihedral angles. Second, we used Multiple Sequence Alignment (MSA) technique coupled with AlphaFold predicted 3-D structures to characterize the relationship between sequence and structural fingerprints of GST enzymes,. Finally, we applied Normal Mode Analysis using the Anisotropic Network Model[3] to compute the thermal B-factors of all GSTs of *D. mel*. Particularly, we extracted the flexibility profiles of GST enzymes and identify key residues that are systematically involved in the ligand binding/dimerization processes and thus playing a crucial role in the catalytic function. This methodology will be extended to guide the *in silico* design of synthetic GST enzymes with new/optimal catalytic properties for detoxification applications.

Keywords: Glutathione transferase, *Drosophila melanogaster*, AlphaFold, Multiple Sequence Alignment, Normal Mode Analysis

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26 juin 2024

Session 4A

Quantum chemistry with Clifford and Green

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In this talk I will present the latest results of two ongoing projects.

First, I will discuss an original approach to study periodic Coulomb systems. The main idea is to isolate a supercell, containing several unit cells, from the periodic structure and modify its topology to that of a Clifford Torus. While an ordinary torus is curved, a Clifford torus is flat. Therefore the supercell can be represented on it without deformation. Like an ordinary torus, a Clifford torus has no boundaries which makes the extrapolation of the results to the thermodynamic limit smooth. I will show how we have successfully applied our strategy to the calculation of Madelung constants and Wigner crystals [1] [2] [3]

Second, I will discuss an approach based on many-body Green's functions that uses a multi-channel Dyson equation that couples different many-body Green's functions. I will mainly focus on the multi-channel Dyson equation that couples the one-body Green's function to the three-body Green's function to model photoemission spectral functions. Unlike the standard (single-channel) Dyson equation the multi-channel Dyson equation puts quasi-particle and satellite excitations on an equal footing. I will show how this can lead to an improved description of spectral functions [4].

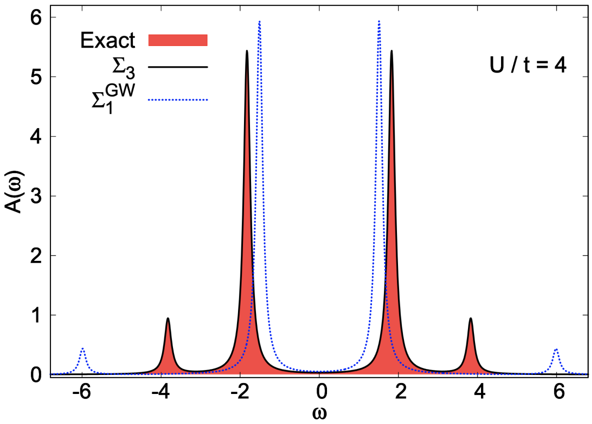

Figure 1. Spectral function of the Hubbard dimer with 2 electrons. Exact result (red filled); the multichannel Dyson equation (black solid line); GW (blue dotted line).

Keywords: periodic systems, Clifford torus, Green function.

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Ground and excited state properties of heavy element systems from relativistic (embedded) coupled cluster calculations

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Accurate electronic structure calculations have become an indispensable tool to understand the molecular properties of heavy and superheavy elements. Such approaches help make sense of the underlying complex physical processes probed by experiments, or in the case such experiments are unfeasible due to the heavy elements' radiotoxicity. In this presentation I will outline our contributions to developments of coupled cluster approaches based on four-component Hamiltonians for ground[1] and excited/ionized states[2], as well as response properties[3], and discuss their application to investigating species such as actinides[4]. Furthermore, I will show how these can be combined with more approximate approaches through embedding theories, to enable the investigation of species in complex environments such as in solution[5] or at interfaces[6].

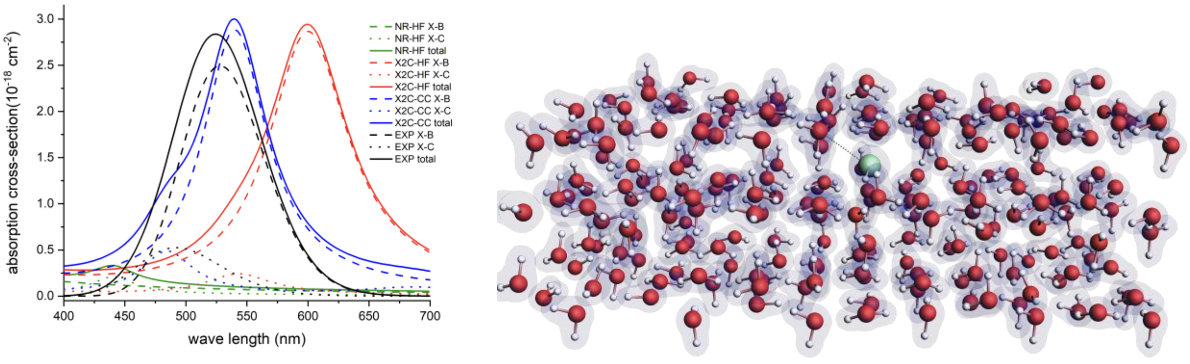

Figure 1. Left: one-photon absorption spectrum of the I_2 molecule obtained from with non-relativistic (NR) and relativistic (X2C) Hartree-Fock and coupled cluster damped response theory calculations[3]. Right: Structural model employed in CVS-EOMIP-in-DFT calculations to determine the 2p core electron binding energies of chloride and HCl on amorphous ice[6.]

Keywords: relativistic coupled cluster, response theory, core spectra, embedding

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Molecular dynamics study of the photonastic phenomenon: photochemical reaction in a polymer environment

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Photonastic materials perform light-induced movements, transforming light energy into mechanical energy, akin to the motions observed in plants and flowers. This study focuses on bio-inspired polymeric photoactuators with applications in microfluidics, biomedics, soft robotics, and motors. A polymer thin film containing photoactive molecules, particularly photochromes, can exhibit significant shape changes upon light excitation. By employing computational chemistry and particularly molecular dynamics (MD) simulations, we investigate the molecular processes governing the macroscopic behavior of these systems, which in our case consists of a derivative of azobenzene (AZ) embedded in a polybutadiene (PB) matrix.[1] Two types of chemical bonds between AZ and PB are tested, pure van der Waals interactions and a covalent bond. Our aim is to propose a strategy to investigate the coupling between the photochemical reaction and the intramolecular relaxation of the polymer. In a previous study, we assumed that these processes occurred at different time scales, the photo-induced reaction being considered instantaneous compared to the polymer relaxation.[2] However, subsequent results indicate that the characteristic time for the intramolecular relaxation of the polymer is roughly the same as the photo-induced reaction time (~ 100 fs to 1 ps). To improve the description of the system, we consider both phenomena simultaneously in the following way. A purely classical molecular mechanics model of AZ photoswitches in both their ground and first excited states (S_0 and S_1) is calculated. The photoreaction is modelled by switching between these two potential energy surfaces (PES). During MD simulations, we mimic electronic excitations and decay by switching between the S_0 and S_1 force fields along the photoreaction coordinate, while allowing the polymer chains to rearrange concomitantly. The local pressure tensor maps of the whole system are analyzed as a function of time after the switch to the S_1 PES. This molecular-scale exploration contributes to a comprehensive understanding of photonastic phenomena and the mechanical response of polymer-photochrome systems.

Keywords: photonastic materials, molecular dynamics, photochemical reaction, intramolecular relaxation.

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Session 4B

Improving the efficiency of embedded cluster approach with the aid of the Fast Multipole algorithm

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Over time, electrostatic embedded cluster approaches (cf. Figure1) have proven very efficient for studying semi-conductors and insulators. The strategy is to put most of the computational effort on the area of interest, the cluster, using accurate but demanding quantum mechanical (QM) methods to describe it. The cluster is then electrosatically embedded into point charges (PCs) to take into account the effect of the environment, in an approximate fashion. A thin isolating shell of effective-core potentials (ECPs) surrounds the QM cluster to prevent over-polarization in the QM region. In particular, this approach has been used in theoretical spectroscopy studies of oxide surfaces under catalytic oxidation conditions, in combination with accurate QM methods, to properly model the antiferromagnetic properties.

In order to go beyond and reach real-surface electro-catalysis with accurate atomistic structure description under *operando* conditions, it is necessary to increase the cluster size. today, it appears that the necessary number of point charges to reach convergence, depending on the property of interest, can go up to $N_{PC} = 10^4$ if not 10^6 for QM clusters made of 200-300 atoms. However, for more than 10^5 point charges, the evaluation of the point-charge electrostatic energy becomes one of the most demanding step of the whole SCF calculation (scaling in $O(N_{PC} \times N_{BF}^2)$, with N_{BF} the number of basis functions). Among existing solutions, the well established Fast Multipole Method (FMM) algorithm[1] provides a way to reduce the scaling to $O(N_{PC} + N_{BF}^2)$.

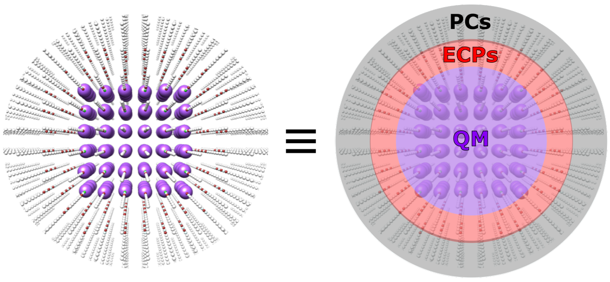

Figure 1: ECM scheme.

The aim of this work is to implement the FMM algorithm to make these QM/MM calculations faster which should allow us to investigate surface environment effects on active catalytic sites. This implementation is done in ORCA[2].

We first implemented the algorithm for interactions between point charges only (PCs/PCs). The calculation of the total Coulomb energy is then accelerated by more than ten times compared with a calculation without algorithm, with an accuracy in the order of micro Hartree. This first step enabled us to validate the implementation and to better measure the impact of the various model parameters on calculation time and accuracy.

Adapting the algorithm to QM/PCs calculations require the evaluation of multipole expansion of an electronic distribution. These integrals are currently evaluated using the McMurchie Davidson scheme for each pair of orbitals in the quantum system. The evaluation of the distant interactions with the point charges using the FMM method, then alllows a drastic acceleration of the evaluation of the one-electron integrals during the formation of the Fock matrix, which leads to a decrease in the total calculation time of the sytem. With the evaluation of the multipole moments becoming the limiting element in the evalution of the one-electron integrals, another way of calculating them is currently being investigated.

Keywords: ECM, Coulomb interactions, FMM, ORCA.

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Diving into the continuum with resonances

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In quantum chemistry, the Hamiltonian spectrum contains continuum states in addition to the usual bound states. Among those continuum states can be found the so-called “resonances”, which are metastable states resembling bound states.[1] However, due to their metastability, resonances have a finite lifetime which makes them differ from the regular bound states and lead to interesting properties. For this reason, resonances are studied in various fields involving electron-molecule collisions, from biochemistry (DNA damage induced by ionizing radiation or the development of radiosensitizers against cancer) to interstellar chemistry (extraterrestrial synthesis of prebiotic molecules).[2,3]

The unbound nature of resonance states creates various theoretical challenges because of the necessity of accounting for the coupling of the bound part of the wave function with the continuum. Several methods have been specifically developed to describe accurately such states and notably their lifetimes. However, at the current stage, one of the state-of-the-art methodologies to describe resonances of medium-sized molecules remains the complex absorbing potential (CAP) technique (which consists in the addition of a complex one-electron potential to the usual Hamiltonian) combined with coupled-cluster with singles and doubles (CCSD).[4] Unfortunately, the resulting errors for resonances are one to two orders of magnitude larger than obtained with state-of-the-art methods for bound states. This aspect underlines the necessity of improving the description of the electronic structure of resonances. Answering this call, we propose to combine the CAP technique with selected configuration interaction (SCI). This choice is motivated by the ability of SCI to provide highly-accurate excitation energies for bound states, allowing to faithfully benchmark more approximate methods.[5] In this contribution, we will give a concise overview of resonance states, the CAP methodology, and the SCI method, before investigating the performances of CAP-SCI and CAP-CCSD on various ubiquitous resonance states.

Keywords: Electronic Structure Theory, Excited States, Resonances, Complex Absorbing Potential, Selected Configuration Interaction.

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One Dimensional Model for Relativistic Quantum Chemistry

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It is important to take into account the effects of special relativity in the quantum description of chemical systems with heavy elements. The relativistic effects account for gold's color, mercury's liquid state at room temperature and are responsible for the efficiency of lead-acid batteries in cars [1]. Relativistic electronic-structure computational methods have been developed in the no-pair approximation, and are now routinely applied on molecular systems. Hence, the next challenge is to go beyond the no-pair approximation by including the quantum-electrodynamics (QED) effects of virtual electron-positron pairs. Such description is needed to recover some properties, even in very simple systems, *e.g.* the Lamb shift in the Hydrogen atom.

In this work we are interested in an one-dimensional model of relativistic hydrogen-like atom using delta-potential interactions. It is motivated by the non-relativistic version of this model which leads to the same ground-state energy and radial wave function as the three-dimensional one. We are using an effective QED Hamiltonian which includes the effect of the vacuum polarization, and the creation of electron-positron pairs, but does not include the photons degree of freedom [2,3,4]. In this model we are able to make accurate QED calculations [5] which can be used to develop a more rigorous mathematical background on which the development of a one-dimensional relativistic-DFT (RDFT) can be properly investigated. This development could be a next step towards understanding QED effects and being able to do *ab initio* calculations based on a QED background.

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Keywords: relativistic quantum chemistry, QED, Lamb shift, 1D model, hydrogen-like atom

Coupling Molecular Density Functional Theory with Wave-Function methods to study excited states in aqueous solution

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Most of the chemical properties of a molecule are governed by its electronic structure. This is why electronic structure calculations play a central role in theoretical and computational chemistry. However, most chemical processes occur in solution rather than in a vacuum. Furthermore, the solvent significantly impacts chemical reactions or solute properties. Yet, precise quantum chemistry calculations are often conducted in vacuum, neglecting the solvent's role, or using a continuum solvent model that overlooks its molecular nature. A more direct approach to accounting for solvent effects while retaining a molecular description is to explicitly include solvent molecules in quantum (QM) calculations[1]. However, this substantially increases computational costs, scaling polynomially with the number of electrons.

When the solvent does not react with the solute, a common strategy involves treating solvent molecules with molecular mechanics (MM) using a classical force field. This method reduces computational costs for the bulk of the system while maintaining a QM description of the crucial part: the solute. This approach is known as QM/MM. Molecular Dynamics (MD) is often chosen as the MM method for such studies, but it is the most expensive MM method. Another QM-MM strategy involves liquid state theories (LST), particularly Classical Density Functional Theory (cDFT). In brief, cDFT computes the grand-potential and equilibrium liquid density by minimizing a functional of the solvent density. Like its electronic counterpart, cDFT is theoretically sound, but practical utilization requires approximations in selecting the functional describing particle interactions, in this case, solvent molecules.

In the present work, we propose coupling quantum calculations with the hybrid continuum/molecular description of the solvent provided by molecular density functional theory (MDFT). Two crucial features of our method include computing both electronic and molecular densities self-consistently and considering electrostatic interactions as point charges. We validate this new framework by computing excited state properties of two molecules, water, and formaldehyde, in both vacuum and aqueous solvent. Then, we compare our method with state-of-the-art approaches using a coupled cluster (CC) level of theory for the QM part and a molecular[2] or continuum[3] description of the solvent. Our results demonstrate that even in the simple case of the water molecule, our approach yields results closer to the molecular description of the solvent than pure continuum approaches. Additionally, we investigate the impact of the level of theory used to describe the QM part in the MDFT calculation. To rationalize predicted excitation energies, we also compute the dipole moment of both ground and excited states in vacuum and solution.

Keywords: Solvation, QM/MM, Wave-Function Methods, DFT, Excited States.

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Session 5A

From electron delocalization to predicting superconductivity

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A room temperature superconductor is probably the most desired system in solid state phys-ics. So far, the greatest advances, cuprates, pnictides and number of others were obtained in a serendipitous way. As there is no clear theory for these superconductors, it is difficult to pre-dict where progress will be made. In contrast the Bardeen-Cooper-Schrieffer (BCS) theory gives a clear guide for achieving high Tc, and hydrogen seems to be a main clue. Within this approach, the recently reported superconductivity at 190 K in compressed H2S [1] has been arguably the biggest discovery in the field since the superconducting cuprates nearly 30 years ago.

However, a microscopic understanding of why this particular material features such a strong coupling is still missing. We have recently shown that the underlying chemical structure and bonding need to be characterized for a good comprehension of the chemical composition-superconductivity relation.

We have resorted to superconducting DFT within Tight Binding models showing that the normal state DFT can be used to characterize the bonding in superconductors. Based on these results, we have defined two global quantities derived from the Electron Localization Func-tion [2] which characterize i) the molecularity and ii) the metallicity of hydrogen compounds [4].

We have constructed a database of binary and ternary hydrogen-based compounds with available critical temperatures and shown that these two indexes allow to characterize i) the type of crystal and ii) its superconducting nature (critical temperature), respectively. Thanks to machine learning algorithms (decision trees), a very good correlation has been obtained for predicting superconducting critical temperature in all these compounds. This goes be-yond our initial proposition [3] which was only applicable to binary compounds.

These developments are now available at a public code, Tcestime [5]; which allows to pre-dict in a simple and fast manner the critical temperature from a DFT calculation. A server to make this calculation online will also soon be available. We hope that these developments will open the possibility for a real high-throughput screening of new potential low pressure high critical temperature superconductors and, at the same time, sets clear paths for chemically engineering better superconductors.

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Keywords: Superconductivity, ELF, electron delocalization.

Theoretical study of PhenoxyAmidine, Bis(salicylamidine) Ligands and their Zinc and Aluminum complexes

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Salen aluminum complexes are considered as benchmark catalysts for the stereocontrolled polymerization of rac-lactide.[1] Bis(salicylamidine) (FAlen) ligands are salen analogs in which the imine moiety is replaced by an amidine. Compared to phenoxy-imine (FI), amidine ligands are less sensitive to reducing or nucleophilic reagents. Also, the presence of the π-donor NR_2 group enhances the ability of the amidine moiety to stabilize electron-deficient metal ions such as Ti, Al or Zn.

Building on these properties, our group has synthesized different FA and FAlen ligands together with coordination complexes with aluminum and zinc metals.[2] Many structures could be resolved by X-Ray diffraction: they revealed a wide range of different coordination modes and geometries of the ligands around the metals. In particular, the FAlen ligand can adapt its denticity (from κ^2 to κ^4) to the electron density of the metal.[3]

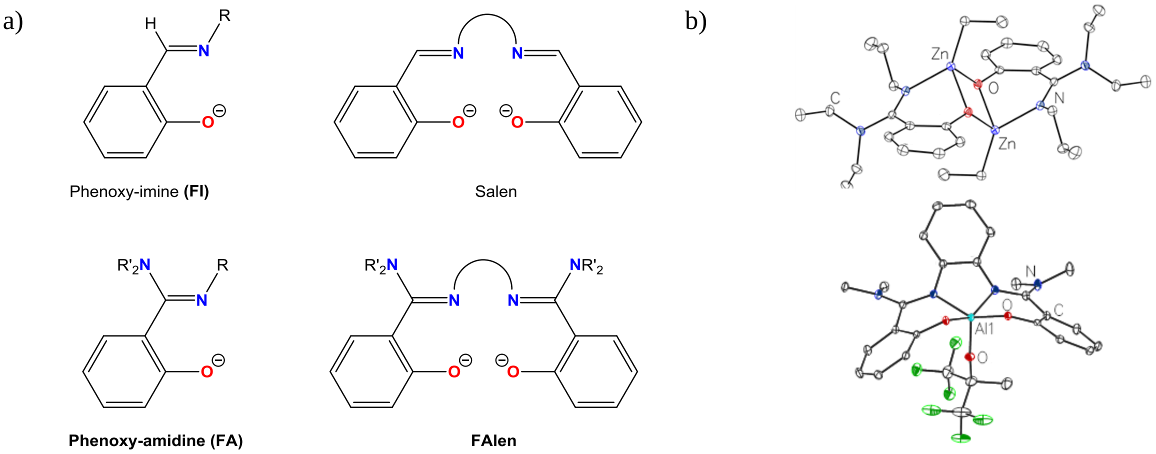

Figure 1. a) Molecular structures of the phenoxy-amidine and FAlen ligands. b) X-Ray structures of two complexes. Color codes: C in white, N in blue, O in red, Zn in blue, Al in turquoise, F in green.

In this communication, I will present our theoretical studies of these ligands and their complexes to illustrate the link between their electronic structure and their flexibility. In particular, we will discuss the impact of the cis/trans isomers of the amidine moiety on its coordinating ability.

Last, their unique coordination properties will be used in the controlled ring-opening polymerization (ROP) of rac-lactide.

Keywords: Amidine – NBO – Organometallic chemistry - ROP

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Ti Finishing (off) the Klopman–Salem modeltle

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Using information pertaining to excited states to predict or rationalize the reactivity of a molecule is deeply rooted in the Perturbation Theory of Quantum Mechanics. Indeed, the perturbation theory starts by projecting the perturbed wave function upon the excited states wave function of the unperturbed system. The pioneers that used this approach to describe the reactivity of the ground state were Pearson[1] and Bader[2] . They even proposed a set of rules based symmetry to unveil which excited states are triggered and among them, which drive the reaction. We have tried for several years to follow their footsteps by looking at the electron density polarization through transition densities [3,4].

$$\Delta\rho(\vec{r}) \approx 2\sum_{k\neq 0}\frac{\Delta_0^k\rho(\vec{r})}{E_0^{(0)}-E_k^{(0)}}\int \Delta_0^k\rho(\vec{r}\,')P(\vec{r}\,')d\vec{r}\,'$$

This approach has resulted in a proposal to define two new concepts; namely the polarization entropy and the polarization temperature [5].It is believed that both polarization entropy and temperature open a new avenue to define temperature dependent DFT descriptors. More recently, we have also looked at the information provided by the diagonal element of the linear response function[13] again through the transition densities. The aim of this talk is to present these new concepts and several supporting examples.

$$\chi(\vec{r},\vec{r}) = \left(\frac{\partial^2 E}{\delta v(\vec{r})\delta v(\vec{r})}\right)_N = \left(\frac{\delta\rho(\vec{r})}{\delta v(\vec{r})\delta v(\vec{r})}\right)_N = 2\sum\frac{\rho_0^k(\vec{r})\,\rho_0^k(\vec{r})}{\left(E_0^{(0)}-E_k^{(0)}\right)} = 2\sum\frac{\left(\rho_0^k(\vec{r})\right)^2}{\left(E_0^{(0)}-E_k^{(0)}\right)}$$

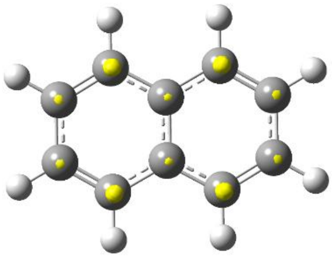

Figure 1. Map of the diagonal element of the linear response function for naphthalene

Keywords: Conceptual DFT, Klopman-Salem Model, Polarisation density, Temperature, Entropy

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Distribution of hydrolysis energies by molecular simulation and machine learning

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To address the issues of the long-term containment of high-activity nuclear waste, several solutions have been studied, among which vitrification, which has been adopted by many countries. The glass containers are projected to be stored in deep clay wells: this raises the question of how the long-term exposure to underground water will alter the glass by hydrolysis, as it will need to withstand both autoirradiation and external degradation from the environment for geological timescales. Hence, this induces research into special formulations to obtain desirable properties in order to efficiently contain the radionuclides, but also into accurately modelling the interplay of the different mechanisms of glass alteration.

Experiments have shown that the alteration is a complex and multistep process. The rate of corrosion is influenced by many factors (temperature, pH, water composition…) but are mainly driven by glass structure and composition[1]. However, realistic long-term experiments and simulations are not tractable: we then endeavor to predict the distribution of the hydrolysis energies instead.

Using simplified models of nuclear glasses, we calculate dissociation and reformation barriers (see Figure 1) using molecular simulations[2], with both classical and ab initio molecular dynamics (MD) coupled with rare event sampling techniques such as the Blue Moon ensemble method[3] or the potential of mean force (PMF) method. These calculations are also used to evidence descriptors which can account for the variations of energetic barriers. Machine learning[4] (ML) methods allow us to show the best correlations between descriptors and the barriers. The end goal of this project is to develop a ML model that can quickly and accurately predict hydrolysis energies using a given starting configuration. Further down the line, this model could be integrated into Monte-Carlo simulations of glass alteration.

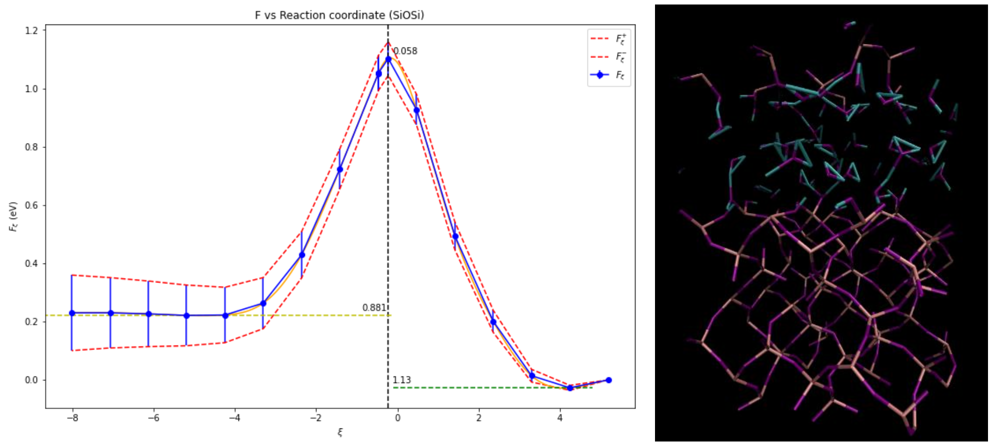

Figure 1. Left: Hydrolysis free energy profile obtained with the Blue Moon ensemble method on a silicate cluster. Right: Water-silicate glass interface.

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Keywords: glass alteration, molecular dynamics, machine learning.

Session 5B

Exploring Chemical Reactivity based on Conceptual DFT and Quantum Chemical Topology coupling

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This contribution presents a mechanistic methodology designed to identify the favourable reaction pathway between reactants at low computational cost. The methodology draws on the conceptual Density Functional Theory [1] and the quantum chemical topology approach. [2] Two different descriptors will be presented. The first relies on the difference between the local interacting chemical potentials [3] of the reactants in agreement with the Sanderson's equalization principle. [4] The second approach uses the so-called dual descriptor condensed over the ELF topological domains. [5] Illustrative examples will be provided for non-covalent donor-acceptor systems as well as for some reactive systems. Finally, the strengths and limitations of the presented approaches in predicting chemical reactivity will be outlined.

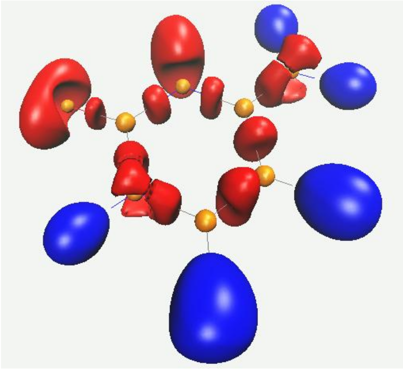

Figure 1. Condensed dual descriptor in ELF domains for the guanine. Color code: blue: electrophilic, red nucleophilic, orange : aphilic.

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Keywords: Conceptual DFT. Chemical Potential. ELF. Dual Descriptor.

Stable Astatine-211 labeling assisted by charge-shift bonding

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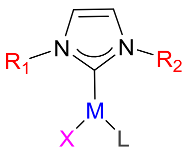
A growing attention is seen in one of the isotopes of astatine, ^{211}At which has a half-life of 7.2h and emits high-energy α particle (5.9-7.4 MeV) upon decay with a short path length (80-100 µm). Application of ^{211}At for cytotoxicity for nearby malignant cells in targeted α therapy of cancers is of particular interest.[1] Yet, the main challenge against its successful use, is the production of an in vivo stable ^{211}At-labelled motif that would avoid its indiscriminate release in non-targeted tissues. This is especially owing to the limited known chemistry of this rarest radioelement. Following earlier attempts to attach astatide (At$^-$) to a soft transition metal center, we have studied ^{211}At-labeled Rh(I), Ir(I) and Au(I) complexes of *N*-heterocyclic carbene (NHC, Fig. 1).[2]

As astatine is a heavy element (Z = 85), it is important to account for relativistic effects, notably spin-dependent ones in its theoretical investigation. Therefore, DFT calculations in a two-component (2c) formalism were performed. The bond dissociation energy (BDE) of the complexes in gas phase showed the bond strength in the order Rh-At < Ir-At < Au-At. This trend was confirmed in the aqueous phase where the heterolytic dissociation of the Au-At bond is more difficult by about 95 and 80 kJ/mol than those of Rh-At and Ir-At, respectively. Also, from the Gibbs free energy of halogen exchange reactions, the Au(I) complex showed superiority in terms of selectivity for astatide against competitive chloride (notable concentrations encountered *in vivo*), and agrees with experiment which demonstrated its good stability in human blood serum at 37°C. A deeper understanding necessitates the study of the nature of the metal-At bonds through computational means, which is otherwise difficult if not impossible experimentally. AuX (X= F - I) diatomic species were found to exhibit charge-shift bonds (CSBs), a type of bond that exists along with the classical electron-pair bond families, namely the covalent and the ionic bonds.[3] Studying the diatomic AuAt bond may therefore, shed light on the investigated NHC-metal complexes. The QTAIM and ELF topological analysis were performed on the 2c spinors obtained from PBE0/dhf-TZVP-2c calculations, allowing us in particular to reveal the spin-orbit coupling (SOC) effects on the characteristics of the bonds.[4]

The QTAIM study of AuAt notably shows typical features of ionic bonding but without significantly charged atoms. SOC is even able to reverse the sign of the partial charges. While a significant sharing of electron-pair between Au and At is evidenced, no ELF bonding basin is found. Do these findings also characterize the metal-halogen bond in the NHC complexes and can we rationalize the trends on BDEs and Au selectivity between astatide and chloride?



M: Rh(I), Ir(I), Au(I)
L: cyclooctadiene*
X: Cl, I, At
R_1,R_2: 2,6-di*i*sopropylphenyl

Figure 1. Studied NHC-metal complexes; *no L when M = Au(I).

Keywords: astatine, relativistic DFT, spin-orbit coupling, charge-shift bonding, quantum chemical topology.

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Anharmonic vibration-translation-rotation of diatomic molecule encapsulated in hydrated clathrate cages

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Hydrate clathrates are crystalline compounds composed of water molecules that form cages in which small molecules are encapsulated, depending on the thermodynamic conditions of formation [1]. Two systems are studied: (i) Carbon monoxide hydrate, which can be considered an important component of the carbon cycle in the solar system, since CO gas is one of the predominant forms of carbon [1]. (ii) The H_2 clathrate hydrate, which is of great interest because of to its potential as a hydrogen storage material [2].

The aim of this work is to solve the time-independant Schrödinger equation, to calculate the anharmonic Vibration-Translation-Rotation (VTR) levels of diatomic molecules trapped in the clathrate hydrates. We will then calculate the vibrational shift of the diatomic molecules resulting from its encapsulation in the water cage.

In our calculations, we use a quantum dynamics code, ElVibRot [3], and two recent potentials [2,4]. (fitted with a neural network and derived from ab initio calculations at CCSD(T)-F12a) to evaluate the interactions between the trapped molecule (CO or H_2) and H_2O molecules. We will present our results of quantum calculations of the anharmonic levels of the VTR motions of H_2 and CO trapped in H_2O cages. We will then deduce the order of magnitude of the vibrational shift of them that has been measured experimentally [5] and also the influence of the 3-boby contributions on the VTR levels.

KEYWORDS: Diatomic**;** clathrate; vibration; translation; rotation; anharmonic.

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Perylene Diimide Dyes: Modeling the Molecular Motion of Supra-molecular Aggregates in solution

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The optoelectronic properties of perylene diimide (PDI) dyes, coupled with their relatively low production costs, have attracted considerable interest in recent years for various applications, ranging from solar cell devices and electronic displays to cancer treatment[1,2]. The PDI molecules have the capacity to spontaneously self-assemble into ordered one-dimensional nanostructures in solution, resulting in aggregates of modulable size and shape[3,4]. This self-assembly process is influenced by a delicate balance of non-covalent interactions, including hydrophilic, hydrophobic, and π-stacking. In particular, the nature of the core substituents, either in bay or imide position (see Figure1a), influence the structural and physicochemical properties of the self-assembled nanostructures[2]. In turn, the differences induced in the supramolecular arrangments by the modulated inter-molecular interactions have a strong impact on the optical properties and the photophysical response. This makes computational investigations of such multi-level systems much more challenging than those designed for single molecules. The relationship between the aggregate's structures and their photophysical responses may lead to establish design guidelines in developing innovative materials and technology.

In this framework, the present work aims to delve into the fundamental principles governing the self-assembly of PDI molecules in solution, providing insights into the model of the motion of these $\pi-$stacked aggregates and their interaction with the surrounding environment. Extensive Molecular Dynamics simulations were conducted for systems comprising two to twelve layers of PDIs in solution, employing a highly accurate QMD-FF[3], previously derived from specific QM data, and developed to represent both PDI's flexibility and its intermolecular interaction patterns. A post-processing protocol was implemented to examine the structural properties and dynamics of $\pi-$stacked systems in solution. The PDIs' motion along the MD trajectories was characterised by designing geometrical supramolecular descriptors. In addition, the rotation of the pendant chains resulted in the interconversion of the two possible isomers (syn/anti), at a monomeric level. The anti/syn transition of every PDI unit within the various aggregates underwent a comprehensive analysis. Moreover, the interaction energies between solute-solute/solute-solvent were studied in detail. The latter was widely investigated by computing pair correlation functions and three-dimensional density distributions. This approach could be employed as a general protocol to conduct in-depth structural analyses of different supramolecular systems that share similar properties with PDI's dyes.

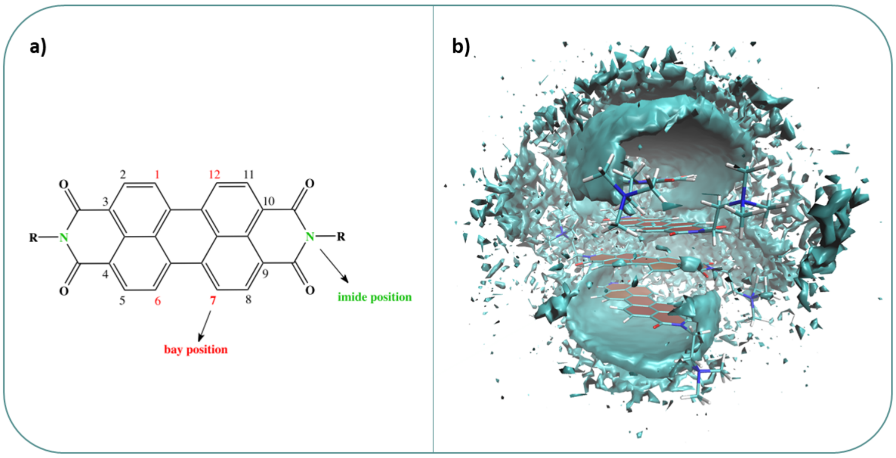

Figure 1: a) PDI molecular structure, highlighted in red and green the key substitution positions. b) showing the tetramer aggregate in the solution.

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Prix Gaston Berthier

Modelling of Photochemical Reactions through Non-adiabatic Dynamics Simulations

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Photochemical reactions, triggered after absorption of a photon, hold great potential for a wide range of applications, opening up otherwise impossible reactive pathways, expanding chemical space, and offering routes for green synthesis. The control of molecular structure using light in light-controlled molecular switches, known as photochromes, can be used for novel applications, such as smart materials, or light-controlled drug delivery.[1] Understanding the mechanisms underlying photochemical reactions can enable the intelligent selection and design of molecules for such applications. Studying these reactions theoretically requires a specialized toolbox of methods, especially since the majority of photochemical reactions are what we call "non-adiabatic", meaning they involve radiationless transitions between electronic states. The most powerful methods in the theoretical toolbox to deal with such reactions are non-adiabatic dynamics (NAD). These methods allow for a time-dependent modelling of the mechanisms underlying photochemical reactions, while accounting for the breakdown of the Born-Oppenheimer approximation which leads to non-adiabatic processes.

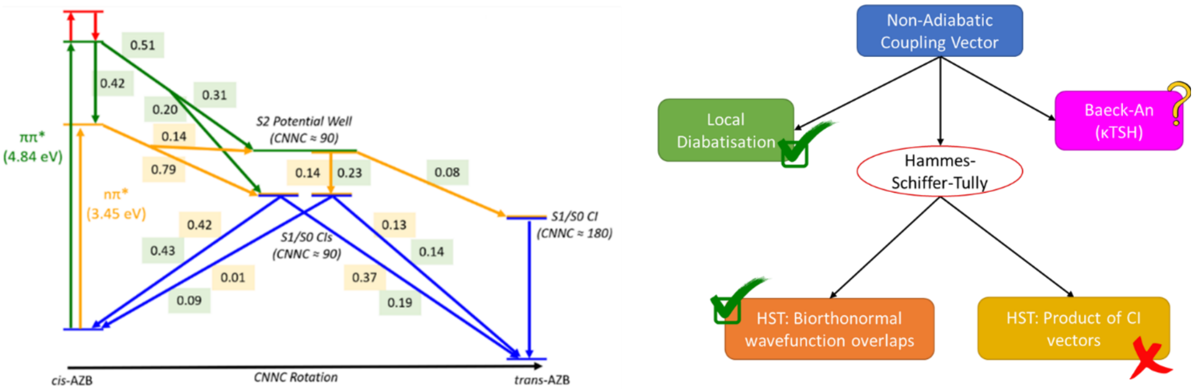

Figure 1. *Left*: Relaxation pathways of *cis*-azobenzene ; *Right:* Different approximate approaches to TSH.

In this presentation, I will first demonstrate the potential of NAD methods as powerful tools to complement experiment and to understand and predict properties and mechanisms of photochemical reactions. To this end, I will discuss primarily the modelling of the azobenzene photochrome, where theoretical modelling[2] using NAD allows for an explanation of the lower quantum yield experimentally measured after excitation to the second (ππ*) compared to the first (nπ*) excited state.[3] After demonstrating the potential of NAD simulations, I will discuss some different approaches to the popular Trajectory Surface Hopping (TSH) method. By presenting the impact approximations can have on the final results for a set of photochemical reactions, I will demonstrate the importance of rigorous testing for such simulations, as well as the potential for cheaper NAD simulations.[4]

<u>Keywords</u>: photochemistry, excited states, non-adiabatic dynamics.

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Session Poster 2

n°1

Anomalous propagators and the particle-particle channel of correlation

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The successful one-body Hedin equations[1] and two-body particle-hole Bethe-Salpeter equation [2] are based on the linear response to an ordinary time-dependent external potential.[3] In this work, it will be shown that one could alternatively consider the linear response to a pairing potential, *i.e.* a non-number-conserving one-body potential. This perturbation requires the introduction of anomalous propagators to be described and leads to a new closed set of equations for the one-body propagator which is analog to Hedin's equations. The lowest self-energy approximation of this set, *i.e.* the analog of the famous GW approximation, is the particle-particle T-matrix approximation.[4] This approximation is already known in the literature, but the present work sets a functional derivative framework which allows for systematic approximation beyond the T-matrix. Finally, considering anomalous propagators and pairing potentials also naturally leads to a two-body particle-particle Bethe-Salpeter equation. While this equation can also be formulated without anomalous propagators, the new expression of the kernel derived in this work makes it much more practical. The similarities with the particle-hole Bethe-Salpeter equation will also be discussed.

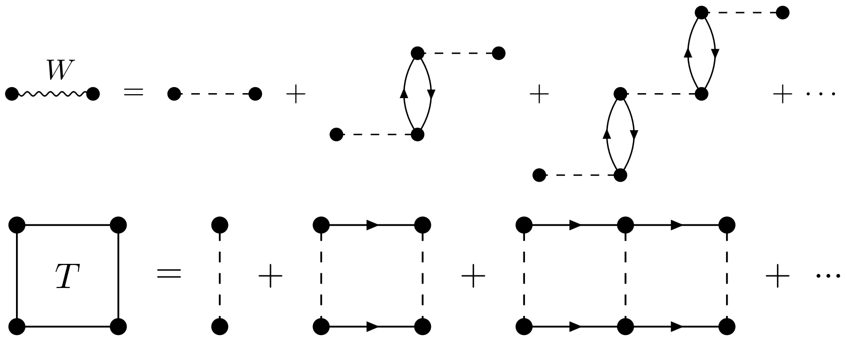

Figure 1: The screened interaction W (wiggly line) is computed as a resummation of bubble diagrams. The dashed lines correspond to the Coulomb interaction. The effective interaction T correspond to a resummation of ladder diagrams. The exchange counterpart of each diagram represented in T should be included as well but has not been represented here.

Keywords: Many-body perturbation theory, Green's functions, anomalous propagators, pairing potential

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n°2

How to design a prebiotic self-replicating system: A Simulation-Guided Conformational Space Study of the Hairpin Ribozyme

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A key question for the RNA world hypothesis[1] is the emergence of autocatalytic networks in abiotic conditions without protein-based enzymes. **Ribozymes** (RNA enzymes) are likely components. However, large ribozymes, which are known to form self-replicating networks[2], cannot have self-assembled from the short RNA fragments available in abiotic conditions. On the other hand, typical short ribozymes tend to favor the cleavage reaction over the required ligation for the formation of larger molecules. In this study, we propose to **investigate the link between size, sequence, and catalytic properties** by studying a model system, the hairpin ribozyme. Indeed, this ribozyme can be found in various sizes, all sharing a common catalytic core, and experimental studies have shown accelerated ligation for the longest version when compared to the minimal structure[3].

Here, we aim to provide a molecular understanding of the tertiary structure effect on the ligation/cleavage equilibrium using all-atom molecular dynamics with enhanced sampling[4], and to clarify the reaction thermodynamics and mechanism. Before shedding light on the behavior of the hairpin ribozyme, we demonstrate the crucial importance of using specific enhanced sampling techniques to provide a **reliable conformational landscape of self-reactive species -**like ribozymes-, for which pre-catalytic structures are not experimentally available[5].

When comparing hairpin ribozymes of different sizes but with identical active site, and consistently with the experiments, our simulations indicate an increased **accessibility of reactive conformations** as the ribozyme gets larger. We identify differences in the S-turn structural motif between each system which we relate to the rearrangement of the catalytic site, suggesting the importance of **long-range effects.**

By capturing the free energy landscape of different versions of the hairpin ribozyme, this study lays the groundwork for 1) elucidating the cleavage/ligation mechanism and 2) investigating at a quantum level whether the hairpin accelerated reactivity can be attributed to the **stabilization of mechanistic intermediate species**.

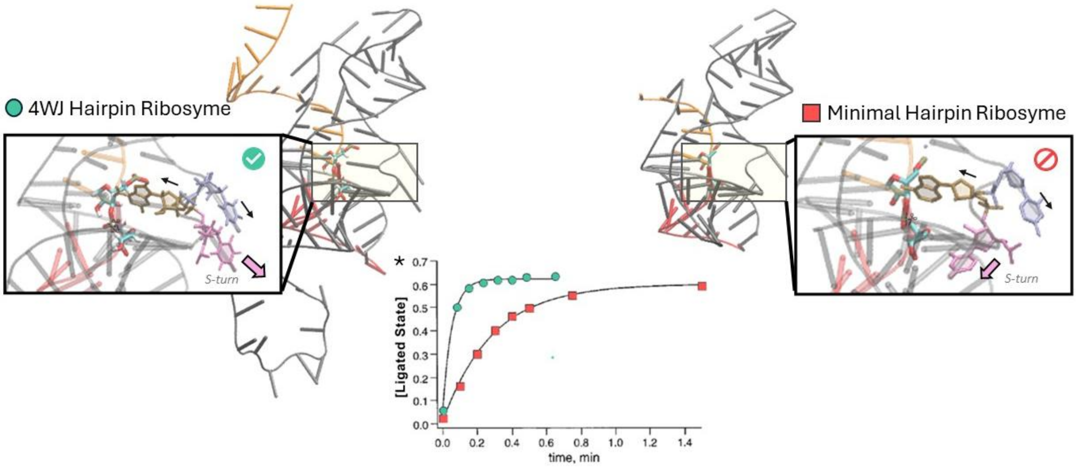

Figure 1. The Difference in Ligation Reactivity between the Hairpin Ribozyme Sequences is Related to the Arrangement of their S-turn Structural Motifs. *(* adapter from[3]).*

Keywords: Ribozymes, Enhanced Sampling Molecular Dynamics, Tertiary Structure Effects, Reactivity,

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n°3

Interaction Between *Yersinia pestis* Ail Outer Membrane Protein and the C-Terminal Domain of Human Vitronectin

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Understanding the role and function of transmembrane proteins in bacteria is of paramount importance in microbiology and immunology research. Particularly, the investigation of transmembrane proteins in pathogenic bacteria is essential for elucidating mechanisms of virulence and immune evasion. Among the human diseases caused by bacteria, plague had a profound impacr throughout history, reshaping societies and leaving an indelible mark on the human experience. Despite advances in medicine and hygiene, the bacterium responsible for the plague remains a persistent and dangerous threat, underscoring the continuing importance of vigilance and research in the figth against this infectious disease.

Yersinia pestis, the causative agent of plague, evades the human immune system by using plasma vitronectin proteins to protect itself from lysis. This shielding effect is facilitated by the interaction between vitronectin and the bacterial transmembrane protein Ail, which protrudes from the outer membrane of the bacteria. Extensive all-atom long-scale molecular dynamics simulations conducted on Ail within a realistic bacterial membrane model, demonstrated the formation of a stable complex[1] which is driven by interactions involving the disordered regions of these two proteins.

Furthermore, the identification of the key amino acids responsible for mediating this complexation has shed light on specific mechanisms by which Y. pestis evades the immune system. These findings not only offer insights into bacterial evasion tactics but also have the potential to inform the development of novel antibacterial strategies.

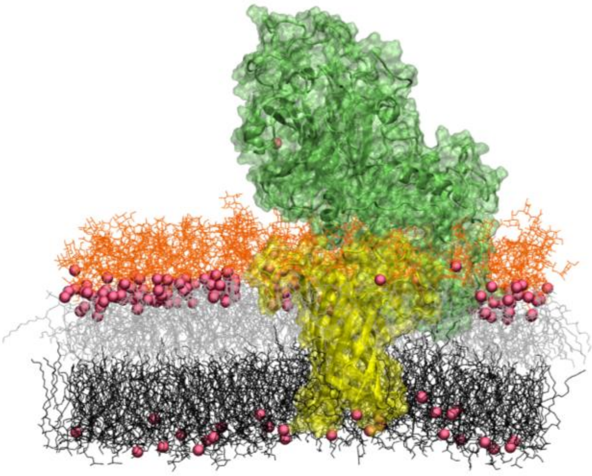

Figure 1. Representative snapshot of the Ail/Vitronectin complex embedded in the *Y. pestis* outer membrane environment. The bacterial protein is represented in yellow, while the human plasma protein is shown in cyan. Lipids and sugars are represented in lines and Ca^{2+} ions are shown in van der Waals

Keywords: molecular dynamics, protein-protein interaction, bacteria

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n°4

Mechanism of latent allostery in *E. Coli* dihydrofolate reductase (DHFR)

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Allostery regulates the activity of a protein by changes at a site away from the active site. This regulation typically occurs through ligand binding, but the effect of a distal mutation on the activity of a protein can be seen as latent allostery. Since 1964, several models have been proposed to describe allostery. Some involve global conformational changes, such as the Monod-Wyman-Changeux (MWC) model[1], while others rely on changes in the vibrational modes of the protein, such as the dynamic allostery model proposed by Cooper and Dryden[2]. However, there is still no consensus and the theoretical explanation of allostery remains elusive. In this study, we focus on *E. coli* DHFR, in which distal mutations at site G121 have been shown to affect hydride transfer between the cofactor NADPH and the ligand H3F[3]. Using replica-exchange molecular dynamics simulations, we show that the effect of G121V on hydride transfer can be explained by a conformational equilibrium shift due to steric interactions, from conformations in which the NADPH and H3F cycles are parallel to conformations in which they are perpendicular. Using Oanca et al.'s implementation of EVB for Gromacs[4], we show that parallel conformations are much more reactive than perpendicular ones, and that the main effect of the Met20 loop on reactivity is to stabilize the parallel conformation, rather than to provide a specific electrostatic environment as previously thought[5]. The equilibrium shift is consistent with a MWC-type model of allostery. Using out-of-equilibrium MD simulations, we then propose a mechanism for the transition pathway from the parallel conformation of WT to the perpendicular conformation of G121V, where the typical time is hundreds of ns, ruling out the hypothesis of dynamic allostery. This mechanism could be considered as a mechanism for latent allostery in *Ec*DHFR.

<u>KEYWORDS:</u> Allostery ; Monod-Wyman-Changeux ; DHFR ; Protein

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n°5

Title Modeling of clusters of silver and hydrocarbon at the SCC-DFTB level: a challenge

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The main aim of our research is to understand the formation and richness of stardust components and the role of metals in their growth. Particularly in carbon-rich dust, and especially in Polycyclic aromatic Hydrocarbons (PAHs), for which current formation models, which ignore the role of metals, are inadequate. More specifically, our work consists of carrying out theoretical studies on model systems made up of aggregates of silver and hydrocarbons, for which experimental results have already been obtained. Indeed, the formation of silver nanoparticles and a wide variety of molecules, in particular PAHs ($C_{14}H_{10}$ and $C_{16}H_{10}$) has been demonstrated experimentally during studies aimed at forming dust analogues by laser and plasma vaporization[1]. We would therefore like to study the structures, stability and formation of large aggregates. The use of the SCC-DFTB (Self-Consistent Charge Density Functional based Tight Binding) approach appeared to us as a method of choice for describing the electronic structure. The effectiveness of this method is based on the parameterization of atomic pairs. Parameters already exist ($DFTB^{hyb}$) but we were not satisfied with them because they were created and optimized for other systems than the ones we are interested in. We therefore propose a new set of parameters where the repulsion between pairs of atoms is obtained from MRCI data ($DFTB^{\gamma}$)[2]. In order to validate this new set of parameters we determine the geometrical structures and energy data for the model systems Ag_nC and Ag_nH, with $DFTB^{\gamma}$ and $DFTB^{hyb}$ and compare them to well-known DFT results[34]. Similar studies are carried out for more complex systems with different nature of chemical bonds, such as $Ag_nC_mH_p$ (m=1-3, n=2, p=0-2) and Ag_n-$C_{10}H_8$ aggregates, which have covalent bonds and weak metal-ligand bonds respectively. In most cases $DFTB^{\gamma}$ gives results closer to the DFT results than $DFTB^{hyb}$. Thanks to this study we are currently applying the $DFTB^{\gamma}$ Hamiltonian to the determination of the most stable structures of $Ag_nC_{2n}H_{0/n}$ complexes that would form in experimental reactors. These structures are determined by a global exploration method (Parallel Tempering Monte Carlo) performed with the deMonNano code[5]. We will present our initial results in this presentation.

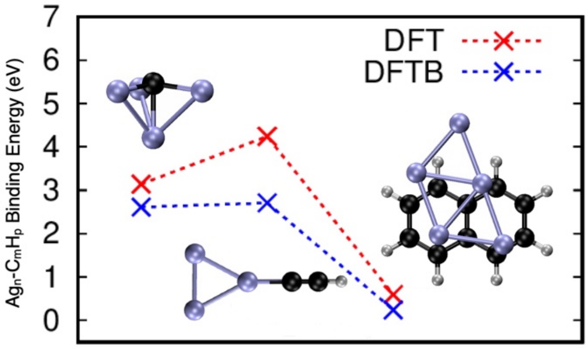

Figure 1: Binding energy of Ag_nC, $Ag_nC_mH_p$ and Ag_n-$C_{10}H_8$ clusters obtained from DFT with B3LYP-D3BJ functionals (red) DFTB with DFTBγ Hamiltonian (blue).

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n°6

Modification of water dynamics under vibrational strong coupling from molecular dynamics simulations

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In the present contribution, we studied how liquid water properties are modified when the system is coupled with a (virtual) Fabry-Perot cavity. At this end, we have employed the Cavity-Molecular Dynamics formalism[1] and a fully atomistic representation of liquid water, which are able to mimic key features of light-matter hybridization under vibrational strong coupling (VSC). The cavity frequency (ω_c) was set to different frequencies corresponding to different modes in the IR spectrum of liquid water : low frequencies (librational modes), medium frequencies (bending mode) and high frequencies (O-H stretching modes).
From simulations, we had access to both equilibrium and dynamical properties. Statistical properties (like water structure or hydrogen bond exchange barriers) should not change throughout the entire frequency range. On the other hand, dynamical properties, and notably the diffusion coefficient and the hydrogen bond jump rate constant[2], could be affected by the coupling with the cavity, showing different behaviors (and intensities) depending on the resonant conditions. An effect on the diffusion coefficient is obtained when the cavity is in resonance with the O-H stretching or with the librational motions, while the effect on the hydrogen bond dynamics occurs only when it is resonant with the librational motions.
In conclusion, we have observed that by using a simple molecular dynamics approach, it is possible to observe an effect of vibrational strong coupling, in particular if the cavity frequency is resonant with pertinent matter modes, in the present case the librational modes of liquid water. More developed models could then be used to understand the effect of VSC on different kinetic properties directly on condensed matter simulations.

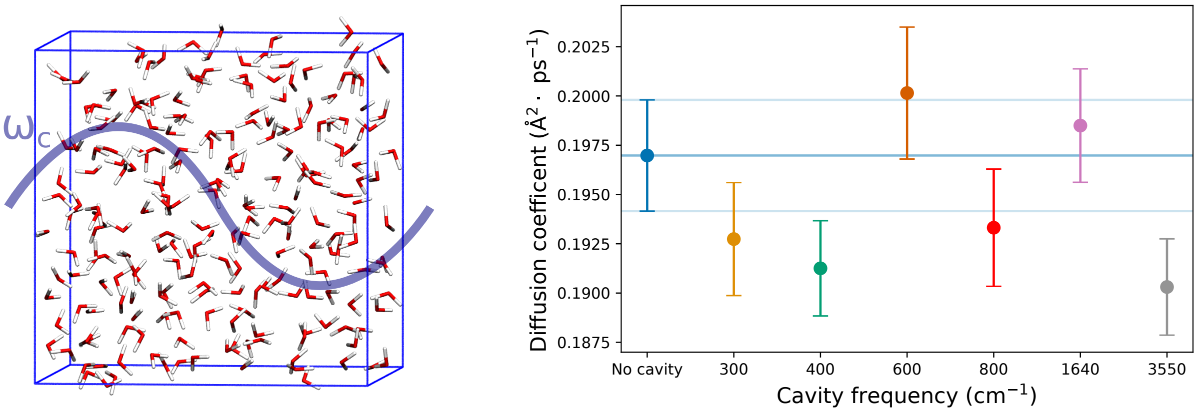

Figure 1: Box of liquid water in a virtual cavity represented by its frequency (ω_c) and the diffusion coefficient calculated without and within this cavity for various values of ω_c.

Keywords: Molecular dynamics, vibrational strong coupling, water properties

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n°7

Molecular simulations to investigate the molecular mechanism of B. subtilis rRNA maturation

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In *Bacillus subtilis*, the final maturation of the 5S RNA is performed by RNase M5, a 190 residue enzyme mostly found in Firmicutes, which cleaves the double stranded rRNA precursor on both sides of a double stranded stem. This reaction requires a ribosomal protein cofactor (UL18), that allows the rRNA to adopt the proper conformation for recognition and cleavage. Previous studies have suggested that the cleavage occurs in two steps, starting with the removal of the 3′ extension before cleavage of the 5′ strand [1]. In a recent work performed by C. Tisné's team [2], details of the interaction between M5 and the 50S ribosome particle were obtained combining the cryo-EM structure of the complex and X-ray structures of the two domains of M5. The aim of our study is first to assess the stability of the complex (active site and interface) and then to investigate its catalytic mechanism. The observation of two Mg^{2+} ions in a recent a crystal structure of the protein suggests a **two ion-mechanism**, comparable to that of RNAse H [3]. Capturing the interaction between divalent cations and nucleic acids is a challenge for simulations, due to electronic polarization and possible charge transfer effects. We have thus tested different force fields to **model this complex active site**, and shown that our scaled charge ECC approach is very promising [4]. Structural characterization and the study of RNA-protein interface dynamics were carried out using 4 replicas of 500 ns in standard simulation as well as **advanced sampling methods** [5]. We characterized the fluctuations of this relatively small interface, and showed that they give rise to distinct active site geometries, prone to react along different reaction pathways. From the main identified conformations, the mechanistic study was set up using a mixed QM/MM-MD description called "**adaptive string method**" [6], which dynamically samples possible reaction paths.

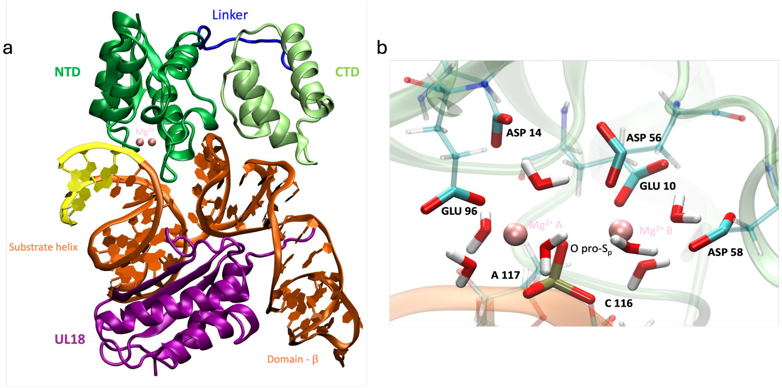

Figure 1: **a)** Simulated complex between M5, a rRNA fragment, and the protein uL18 cofactor **b)** Structure of M5 active site after repositioning of the scissile phosphate in between the two magnesium ions

Keywords: Ions-RNA/Protein interactions, enhanced sampling method, enzyme mechanism, QM/MM-MD.

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n°8

Multi-scale modeling of the dissolution/growth dynamics of metallic copper clusters during synthesis or catalysis processes

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Copper nanoparticles (Cu NPs) are well known and widely used for their catalytic and plasmonic properties. In both cases, the control of size and shape is essential for a good control of the physicochemical properties. Understanding the processes involved in the synthesis of these NPs is attractive as it could open the way to rational control. However, this is a complex task because many synthetic processes take place at high temperatures, which allow many competitive reactions to take place. In this context, the recent results published by Vrancken et al.[1] are interesting because they described a synthetic process that takes place close to room temperature. It is based on the thermal decomposition of an alkyl copper reagent leading to a Cu precursor, which then evolves towards the formation of Cu NPs after stabilization with thiolates. Whereas the stabilization step is extensively reported, the formation of Cu$^{(0)}$ precursors is unusual in the context of Cu NPs synthesis. The decomposition reaction itself has been known for a long time, having been first described in 1970 by Whitesides et al.[2] It is proposed to take place in a two-step mechanism. A first copper alkyl (**1_L-1_L**) reacts by ß-hydride elimination to form an alkene and a Cu-hydride intermediate (**2_L**) (Figure 1). A second copper alkyl then reacts with the intermediate copper hydride by reductive elimination to give an alkane and Cu$^{(0)}$ (**3_L-3_L**) (Figure 1).

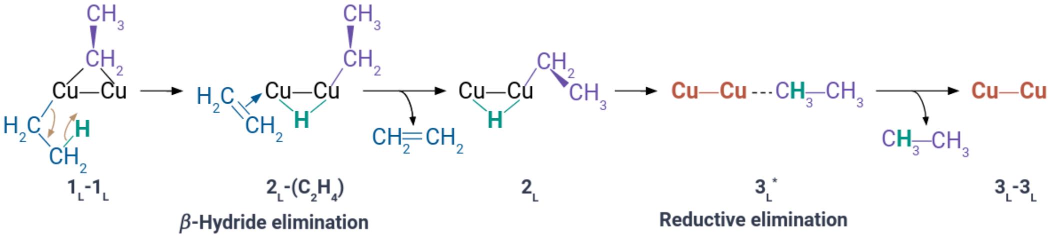

Figure 1 – Thermal decompostion mecanism made of a reaction of ß-hydride elimination (left) and reaction of reductive elimination (right) where the green H is a hydride, red copper atoms are metallic copper atoms and L is a Lewis base, represented in this study by trimethylphosphine (PMe_3) or tetrahydrofuran (THF) (not represented here).

This mechanism highlights the formation and reactivity of the intermediate copper hydride (**2_L**), a chemical species of high added value for its many applications, particularly in the field of energy conversion. It is indeed proposed as a reaction intermediate in CO_2 conversion and methanol upgrading. Kinetic studies by Kochi et al.[3] have shown that the reaction is accelerated by the introduction of metallic seeds in the reaction medium, among which Cu$^{(0)}$ seeds, demonstrating an autocatalytic behavior. In particular, they propose the formation of multinuclear mixed valence Cu$^{(I)}$-Cu$^{(0)}$ intermediates during the course of the reaction, which can act as catalytically active species. In addition, the reaction can occur with or without phosphine additives in the reaction medium, the role of which is not clearly understood.

In this presentation, we will examine the effects of adding metallic copper to the reaction medium, as well as the effects of ligands on the relative stability of the species involved.

Keywords: Copper catalysts, density functional calculations, reaction path, copper hydride

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n°9

Multi-scale molecular dynamics study of the “still” enigmatic protein TSPO

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Translocator protein (TSPO), a mitochondrial membrane protein, has been extensively studied and its functional role is still debated and continues to be enigmatic. While its primarily role could be the cholesterol transport in the mitochondria outer membrane, it is also supposed to be involved in other biological processes, such as steroids biosynthesis or porphyrin transport. In this respect, the protein is now considered as an interesting therapeutic target for Alzheimer’s disease, since the cholesterol is a neurosteroids precursor. From a structural perspective, several structures have been already solved. Moreover, the protein is highly dynamic in nature and has been proved to exist in several oligomeric states. Two proteins from bacteria (R. sphaeroides and B. cereus) have been solved by means of X-ray crystallography. The mouse structure, the only solved mammalian form, has been resolved by NMR methodology. However, this last structure was a matter of discussion due to the detergents used. In global, structural information on its implications, mechanism and dynamics along the cholesterol translocation remain scarce and elusive.

In order to gain more insights into this protein, we employed a multi-scale approach based on molecular dynamics (MD) simulations. First, we addressed the oligomerization question by conducting several coarse-grained MD simulations. We considered two different initial configurations: one with pair of TSPO monomers distantly placed in a model of bilayer composed of DMPC/cholesterol mixture (same conditions as in the NMR experiment) and the other with preformed dimer models with different interfaces. Among the entire set of simulations, we observed that not all the dimers were stable, indicating some specificity in dimerization. Furthermore, we identified stable TSPO dimers with high propensity specific interfaces, some of which were consistent with experimental observations. The existence of asymmetric interfaces suggests the potential formation of higher-order oligomers. Refinement of the stable interfaces through all-atoms resolution MD simulations revealed that the dimers formed were highly stable. Importantly, we obtained a detailed view of the molecular mechanism of cholesterol translocation, which involves specific interactions with the protein.

Secondly, because TSPO is known to accommodate a large set of ligands, we explored the molecular mechanism of ligand binding and the impact of ligand binding onto the dynamics of the protein using MD simulations at atomistic resolution. We considered the experimental NMR structure but also, a homology model (HM) of the mouse TSPO, based on the x-ray solved structure of the bacterial TSPOs, in order to assess the impact of the structure quality on the results. Despite having a very similar 3D fold, the calculations revealed that subtle 3D differences affect the protein dynamics: the NMR structure is much more flexible compared to the HM one. Surprisingly, the NMR structure remains dynamic in the presence of the ligand, which is not the case for the HM one. It is so rigid that the ligand becomes unstable and almost leaves the cavity. This sheds light on the versatile dynamics of the protein itself and raises questions about the 3D structure in its proper environment.

Keywords: molecular dynamics, protein-protein interactions, flexibility, protein-ligand complex

n°10

Novel Approach for Predicting Vertical Electron Attachment Energies in Bulk-Solvated Molecules

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When low-energy electrons interact with molecules, they can give rise to transient anion states, commonly known as resonances. These states are formed through vertical electron attachment processes and have the potential to induce various forms of DNA lesions, including base damage, single- and double-strand breaks, crosslinks, and clustered lesions that are challenging to repair. So far, most experimental and theoretical studies have investigated the formation of resonances of (bio)molecules in gas phase or in microsolvated environments.

Since cellular environments are mainly composed of water molecules, it is crucial to understand how bulk water affects the resonances of (bio)molecules. Given the existing gap of studies on resonances of bulk-solvated molecules, we propose a novel theoretical-computational approach [1] to address this void, in the framework of DFT and TDDFT, which were recently shown to be able to describe the attachment of an extra electron whether it is located in a valence state [2] or in a long-range state [3], and a QM/MM scheme taking into account solvation effects. Our approach combines the Multi-Basis-Set (TD-)DFT [2] and self-consistent sequential quantum mechanics/molecular mechanics polarizable electrostatic embedding (scPEE-S-QM/MM) [4] methods.

We apply this combined methodology to predict the vertical electron attachment energies of 1-methyl-5-nitroimidazole (1M5NI), a well-known radiosensitizer model, in bulk water. We analyze the rapid mutual polarization between the resonances (both shape and core-excited) of 1M5NI and the surrounding bulk water environment. Overall, while the polarization of the environment is clearly sensitive to the solute charge, causing a significant impact on the vertical electron affinity and consequently on the attachment electron energies, it does not have a significant impact on the excitation energies of the anion.

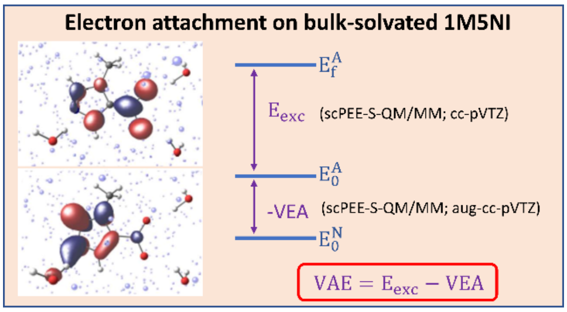

Figure 1. Depiction of the vertical electron attachment energy (VAE) computed with the combination of the Multi-Basis-Set (MBS) and scPEE-S-QM/MM methods.[1]

Keywords: Resonance, Electron Attachment, TDDFT, QM/MM, solvation

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n°11

On the Electrical analogy of the Condensed Linear Response function from CDFT

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Within this poster presentation, the diagonalized element from the Condensed Linear Response function stemming from conceptual density functional theory (CDFT)[1] will be discussed. Mainly, using the definition of the Condensed Linear Response function [2] ($\chi(r, r')$), on the relationship between the variation in electron density and the variation in external potential leads us to propose an analogy with a capacitor. This analogy will be presented on several molecules (such as H_2, HCN, HCCH, ...) where the results appears promising. And leads us to a better understanding of the linear response function and, therefore, chemical reactivity [3] .

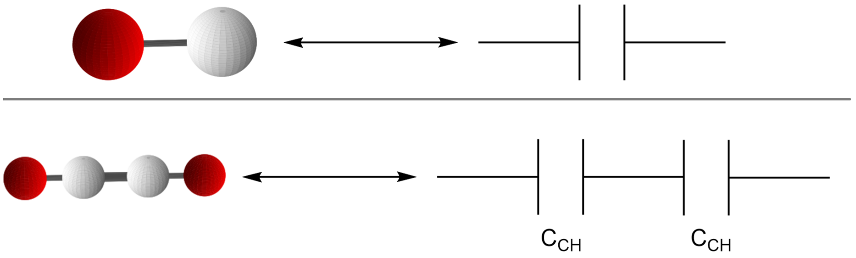

Figure 1: On top, the schematic representation of the first eigenvector of the Linear Response function for H_2. This eigenvector is analogous to a single capacitor. On the lower part, the schematic representation of the second eigenvector of the Linear Response function for acetylene (HCCH). This eigenvector is analogous to two capacitor in series.

Keywords: Conceptual DFT; Condensed Linear Response function; Capacitance

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n°12

On the mapping of a vibrational Hamiltonian model on a quantum computer.

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As a relatively new topic, simulation of the vibrational structure problem with qubit-based quantum computers raises several questions [1,2]. Unlike the fermionic particules in electronic structure, bosons do not follow the Pauli exclusion principle. For the simulation of fermions one can map directly the occupation of a spin orbital or the parity on the state of a qubit. Mapping a bosonic system, wich is a more than two-level system, on a qubit basis is not straightforward and encodings that overcomes this issue have been developed [3,4]. Here we present some of these encodings with their advantages and drawbacks. To do so, we focus on a one mode tunnelling system, with a double-well potential using an harmonic oscillator basis set. We highlight the importance of ordering operators in the second quantized formulation of the Hamiltonian, due to the truncation of the supposed infinite basis. Our study point out that significant errors occur, in the eigenvalues computation, if the second quantized Hamiltonian is not properly ordered.

Figure 1. Illustration of the aim of the study i.e. to map a model Hamiltonian with a one mode double-well potential on a quantum computer.

Keywords: Quantum Computing, Vibrational eigenproblem, Unary Encoding, Binary Encoding

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n°13

On the Mechanism of Hydrogen Spillover on Metal-Doped Carbon Materials

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Hydrogen spillover (H-spillover) is the surface migration of activated hydrogen atoms from a metal particle, on which they are generated, to a support. This phenomenon has been widely studied for its implication in hydrogen storage and catalytic reactions involving hydrogen. Its existence on carbonaceous materials is well established, but questions remain regarding its mechanism and the involvement of the different groups located at the surface. In this presentation, we will show how, by combining both experimental and theoretical data, we have been able to study the mechanisms of H-spillover on oxidized carbon nanotubes (Figure 1). We'll be looking at the role that the different surface groups such as carboxylic acids or hydroxyl groups can play in the H-spillover reaction on carbon materials. Finally, the role of water, present in small quantities on the surface of oxidized carbon nanotubes, will also be analyzed.

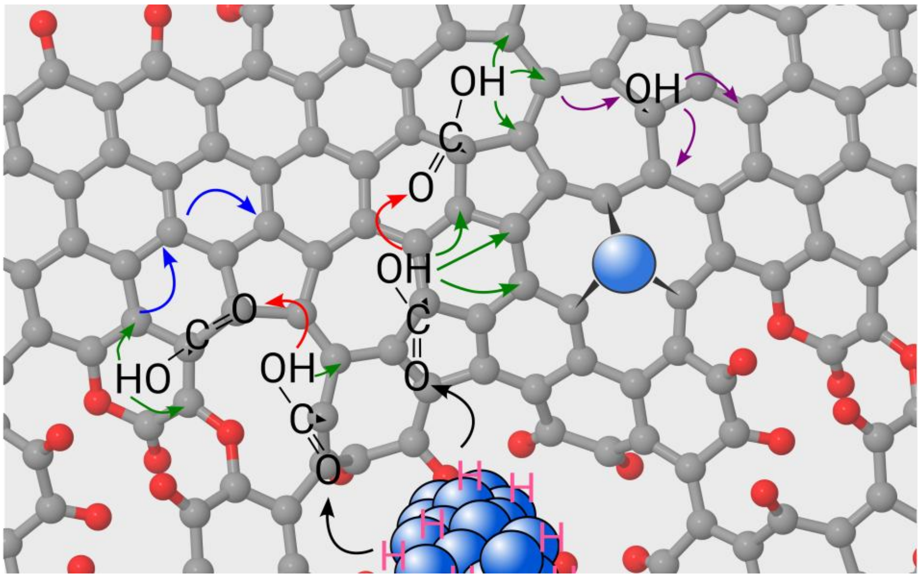

Figure 1. Schematic representation of the possible steps involved in the H-spillover on the oxidized carbon support.

KEYWORDS: Hydrogen spillover, carbon materials, DFT calculations, oxygen functional groups, surface chemistry

n°14

Quantum dynamics around PPEs' conical intersections for both spectroscopic and real-time studies

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In this presentation, we discuss the use of nonadiabatic quantum dynamics for the study of different poly(phenylene) ethynylenes (PPEs, fig. 1 left), building-blocks of light-harvesting dendrimers.

PPEs exhibit strongly nonadiabatically coupled electronic excited states. In this context, the Born-Oppenheimer approximation breaks down, which requires molecular dynamics to explicitely take into account the coupling between the electronic excited states. We propose linear and quadratic vibronic coupling diabatic model Hamiltonians for reproducing the PESs of the simplest PPEs. We use these diabatic potentials and inter-state couplings to run quantum dynamics calculations using the Multi-Configuration Time-Dependent Hartree (MCTDH) formalism for explicit wavepacket propagation.

The first building block of interest is the symmetrically *meta*-substituted phenylene (m22, fig. 1 left). The absorption spectra of m22 and its localized 2-ring fragment (p2, fig. 1 left) are similar.[1,2] However, their emission spectra are different, with m22 exhibiting an unusual Stokes shift of about 2000 cm^{-1}. In a recent work[3], we identified this red-shifted spectrum as a contribution resulting from the strong inter-state coupling between the first two electronic excited states (fig. 1 right), mostly due to acetylenic vibrations.

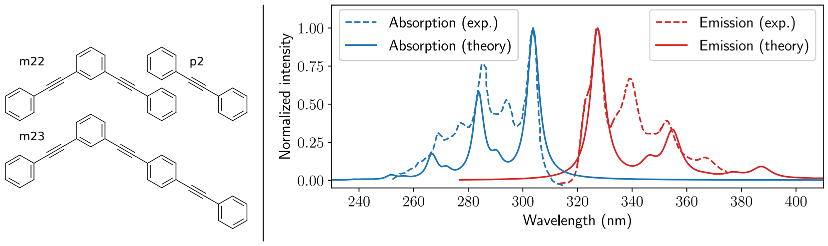

Figure 1. Left: poly(phenylene)ethynylenes studied in this work. Right: Absorption and emission spectra of m22 (normalized intensity), experimental measurement[1] and theoretical simulation[3]

The second building block of interest is an asymmetrically *meta*-substituted PPE (m23, fig. 1 left) for which excitation-energy transfer (EET) occurs thanks to different branch lengths hence a significant energy gradient. Using analogous Hamiltonian models and wavepacket propagation, we are able to reproduce the expected ultrafast (< 25 fs) EET from an excitation on the shortest branch toward the second branch.[4] We further characterize the EET phenomenon *via* electronic-vibrational relations, vibrational energy analysis and evaluation of the electronic coherence.

Keywords: quantum dynamics, nonadiabatic coupling, vibronic coupling, uv-visible spectroscopy, excitation-energy transfer

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n°15

Simulating Attochemistry: Which Dynamics Methods to Use?

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Since the advent of the first attosecond pulse in 2001,[1] its application on polyatomic molecules has given birth to the field of attochemistry. The large energy bandwidth of such laser source will coherently populate multiple electronic states i.e. a coherent electronic superposition. A particular challenge of this field is the accurate theoretical simulation of the molecular coupled electron-nuclear dynamics induced by an electronic wavepacket. Using an example system with two cationic electronic states of fluorobenzene where a conical intersection is located in the vicinity of the Franck-Condon point (FC), we assess the accuracy of mixed quantum-classical methods such as Tully surface hopping and classical Ehrenfest for attochemical simulations. For the reference quantum wavepacket dynamics, we use Direct Dynamics variational Multiconfigurational Gaussian (DD-vMCG) method[2]. Upon coherent ionization to the two lowest cationic states, mixed quantum-classical methods with independent trajectories predict inaccurate trends for the nuclear dynamics and heavily underestimate the contribution of the derivative coupling to the average nuclear motion compared to the full quantum dynamics.[3]

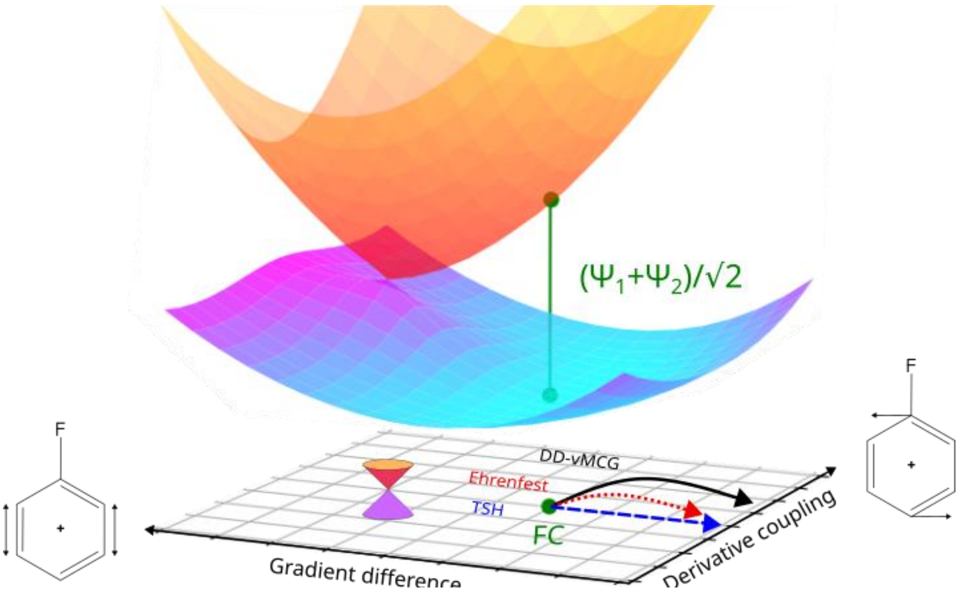

Figure 1. Scheme showing the average nuclear dynamics in the branching space, gradient difference and derivative coupling coordindate, induced by an initial electronic coherent superposition at the neutral Franck-Condon point using the Tully surface hopping, classical Ehrenfest and DD-vMCG methods

Keywords: attochemistry, nonadiabatic dynamics, computational chemistry

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n°16

S$_N$Ar analysis on thiophene derivative with conceptual DFT

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Thiophenes are heterocycles of industrial interest which have attracted considerable attention due to the wide scope of applications. For instance, substituted thiophenes are currently used to synthetize materials with photophysical properties and electrochemical systems but also more and more for therapeutical applications (Figure 1).[1,2]

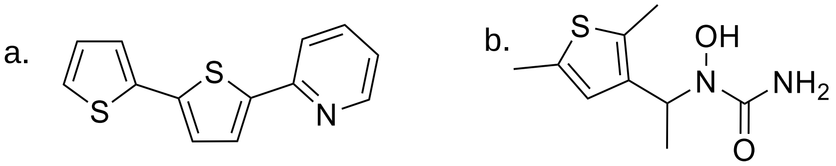

Figure 1. Structure of thiophenes derivatives for polymers (a) and anti-inflammatory (b) applications.

We studied the formation of amino substituted thiophenes through aromatic nucleophilic substitution. S$_N$Ar on thiophenes have been thoroughly studied experimentally.[3,4] In particular, Boubaker *et al.* measured the electrophilicities of many thiophenes derivatives in the Mayr electrophilicity scale.[5] However, quantum analysis are rarely provided.

In this work, we used quantum approaches to study the influences of 7 substituents on the S$_N$Ar mechanism (Figure 2).

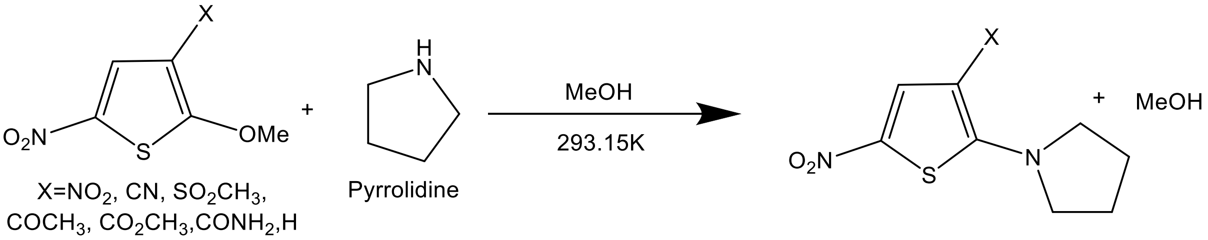

Figure 2. Reaction equation of the substituent substitution on thiophenes

We then used conceptual DFT and Topological approaches to rationalize the evolution of the computed activation energies with quantum descriptors, such as Parr electrophilicity or the LUMO energy We will show that the reactivity of the thiophene derivatives nicely correlates with global descriptors but that explaining the relative reactivity of the thiophenes sites is not as easy.

Keywords: Thiophene, mechanism, conceptual DFT, quantum descriptor.

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n°17

Structural study and diffusion of lithium in materials for $Li_yMn_{1.5}Ni_{0.5}O_4$ (LMNO) battery cathodes

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Li-ion battery technology is essential for many applications and currently represents the most mature technology for zero-carbon urban transport. The spinel-type compound $Li_yMn_{1.5}Ni_{0.5}O_4$, has an excellent capacity available quickly[1], and a high operating potential 4.7 V thanks to the use of redox couples (Ni^{2+}/Ni^{3+}) and (Ni^{3+}/Ni^{4+}) during the insertion/disinsertion of Li^+. Composed of non-critical transition metal elements, these materials were identified as good candidates for high-power applications [1]. Contrary to the description commonly proposed in the literature [2], recent measurements of neutron diffraction coupled to a DFT study show the existence of a single polymorph with variable plane defect densities as a function of nickel content and synthesis temperature [3].

The objective of this study is to elucidate precisely the structural, electronic, magnetic and electrochemical properties of $Li_yMn_{1.5}Ni_{0.5}O_4$ (y = 0, 0.5 or 1) spinel cathode materials (LMNO) as well as to assess the energy barriers that Li^+ ions must overcome during their diffusion. This data is essential for designing new, efficient Li-ion batteries. To this end, we use the density functional theory with GGA functionals (PBE, …), functionals corrected by the Hubbard-DFT+U model and hybrid functionals (HSE06, …) to study the properties of these transition metal oxides. The projected electronic state densities (PDOS) and the structural parameters (cell parameters, bond lengths) are systematically analyzed and compared to the literature.

We will show that if the functional GGA PBE correctly reproduces the geometrical characteristics and the stability of the half-lithiated material (y=0.5), it does not reproduce the lithium intercalation voltages of these materials. The addition of the Hubbard correction (DFT+U) allows to obtain an average operating voltage in agreement with the experiment but leads to worse structural characteristics and semi-lithiated compound (y=0.5) would be unstable, which is inconsistent with the experimental results [1–3]. The use of a hybrid HSE06 functional gives a better description of structural and electronic properties, but with significant computational costs.

Finally, the migration of Li^+ ion in the spinel structure of these materials occurs from a tetrahedral site (Td) to another Td site via an empty octahedral site (Oh). Two different channels are identified based on the distribution of Ni^{x+} and Mn^{4+} ions surrounding this empty Oh site. Energy barriers of Li diffusion obtained using the elastic band method (cNEB) [4] is found to be compatible with experimental results and literature [5].

Keywords: Lithium diffusion, Spinel cathode materials, LMNO, Operating Voltage, DFT

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n°18

Structure of Flexible Chiral Molecules and Unconventional Solvents by Vibrational Circular Dichroism Spectroscopy

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Vibrational circular dichroism (VCD) unveils molecular conformational nuances by discerning absorption differences in right- and left-circularly polarized light within the infrared range. This subtle technique elucidates molecular interactions, especially those that are sensitive to hydrogen bonding, thereby offering particular insight into the structure of unconventional solvents. Interpreting VCD signals necessitates meticulous comparison with theoretical models. However, incorporating environmental effects posed challenges, now mitigated by advancements in computational modeling. Notably, simulating VCD spectra in highly structured liquids like Ionic Liquids (ILs) presented formidable hurdles due to pervasive long-range interactions. We have recently proposed a new methodology based on classical molecular dynamics simulations associated with the AMOEBA polarizable force field to calculate VCD spectra of flexible molecules [1]. A first study of a chiral and flexible molecule, namely phenylcyclohexanediol in a solvent of dimethyl sulfoxide (DMSO) was made successfully, leading to the calculation of infrared and VCD spectra. This work has now been extended to ILs, particularly spirocyclic pyrrolidinium with BF_4^-. Modeling both the infrared and VCD spectra for these systems reveals useful insights into their properties and the complex interactions with their environment.

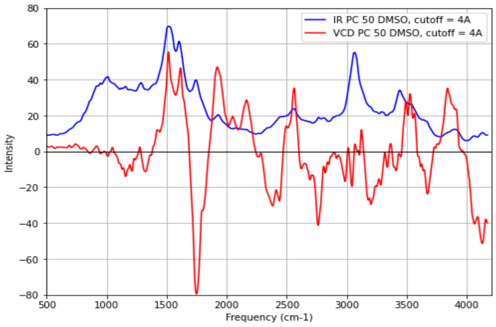

Figure 1. Infrared and VCD spectra of phenylcyclohexanediol in a box of solvent (DMSO)

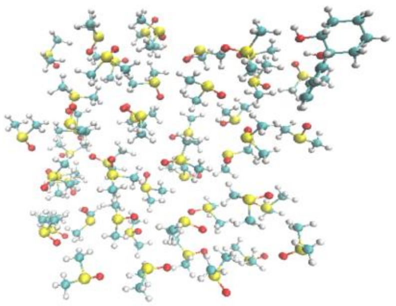

Figure 2. Phenylcyclohexanediol in a box of DMSO

Keywords: Vibrational circular dichroism (VCD); AMOEBA; polarization.

n°19

Theoretical and experimental study of the micro-hydration of an ion-molecule reaction involving the formation of a peptide-type bond

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Previous studies have shown that the presence of explicit water molecules can lower the energy barrier to the formation of a C-N peptide bond between acetic acid and methylamine[1].

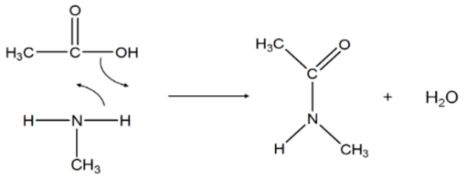

Figure 1: Reaction to form methylacetamide from acetic acid and methylamine.

A dual theoretical/experimental approach was therefore taken to understand the role of non-covalent interactions on reactivity by studying the ion-molecule reactivity between hydrated protonated acetic acid aggregates and methylamine.

The experimental study used a molecular jet coupled to mass spectrometry (CERISES "Collision Et Réactions d'Ions Sélectionnés par Electrons de Seuil") to mass-select hydrated acetic acid aggregates for reaction with methylamine[2,3].

The theoretical study was carried out using density functional theory, coupled with interpretative tools from theoretical chemistry such as quantum theory of atoms in the molecule and molecular electrostatic potential, to understand the role of non-covalent interactions on reactivity.

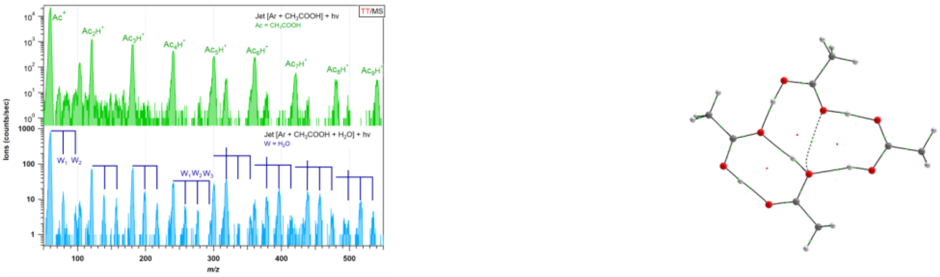

Figure 2: Mass spectra of acetic acid aggregates. QTAIM image of an acetic acid aggregate.

Keywords: Mass spectrometry, Micro-hydration, DFT, QTAIM, MESP, non-covalent interaction.

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n°20

Theoretical investigation of Janus MoSSe/Ga2SSe heterostructures for photocatalytic applications

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The two-dimensional Janus van der Waals heterojunctions, as novel asymmetric materials, have become highly promising photocatalysts due to their superior electronic structure and optical properties. In particular, the electronic properties of the type-2 band arrangement enable them to effectively separate photogenerated electrons and holes as Z-type photocatalysts,[1] and to transport the charge carriers along different pathways,[2] maintaining strong reduction and oxidation abilities, similar to green observations of plant photosynthesis.[3-5]

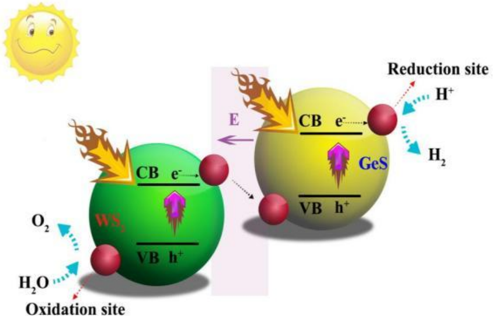

Figure 1. Principles of reactions of the direct Z-scheme system.[6]

In this work, we have systematically investigated the electronic structure and photocatalytic performance of MoSSe/Ga2SSe heterojunctions using density functional theory (DFT). Considering the interlayer van der Waals interaction, two exchange-correlation functionals (PBE and HSE06) have been used. By screening different interlayer distances and stacking patterns, multiple stable configurations have been ultimately obtained. Based on these stable configurations, the HSE06 functional appears to be superior to the PBE one with a more accurate bandgap. Subsequently, we have calculated with the HSE06 functional a series of properties, including band structures, density of states, electrostatic potentials, charge density differences, optical absorption coefficients. After analysis, these heterojunctions exhibit strong absorption performance in the visible and ultraviolet light ranges.

<u>Keywords</u>: heterojunctions; MoSSe/Ga2SSe; DFT.

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n°21

Theoretical study of the catalyzed formation and properties of fluorinated cyclopropanes

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As the smallest cycloalkane, the cyclopropane ring is wide spread in both natural and synthetic bioactive molecules.[1] Indeed, its introduction into molecules of biological interest can enhance its biological properties by increasing their bioavailability and metabolic stability due to its high structural rigidity.[2] The fluorine atom displays singular properties thanks to its high electronegativity and its small size. By combining the features of the fluorine atom and cyclopropanes, fluorinated cyclopropyl motifs are of very high interest for the discovery of new bioactive molecules.[3]

This work focuses on understanding the mechanisms of catalytic enantioselective cyclopropanation reaction using density functional theory (DFT, M06-L exchange-correlation functional) with an implicit solvation model (SMD). We were interested in reactions presented in the figure 1[4]. The main aim is the design of new enantioselective synthetic pathways of cyclopropane.

Two main steps were identified:

(1) The generation of the catalytic active Rh-carbene through N_2 elimination.
(2) The formation of the fluorinated cyclopropane.

This molecular modeling helps identifying the structural and electronic features that are responsible for the observed yields and selectivities.

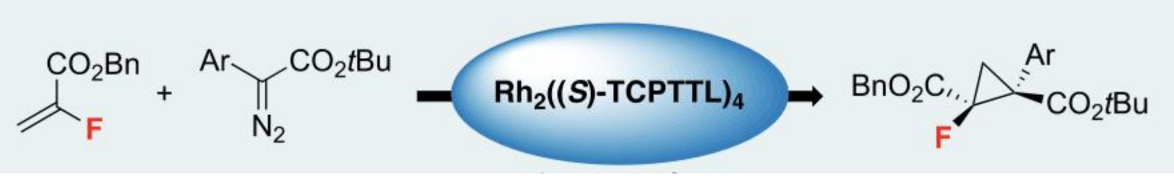

Figure 1. Catalytic Enantioselective cyclopropanation of α-Fluoroacrylates.[4]

Keywords: DFT calculations, fluorinated olefin, diazo, rhodium, cyclopropanes.

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n°22

Theoretical study to understand the physicochemical processes of gas analyte interactions with functionalized materials

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New wearable gas sensors based on functionalized 2D materials, notably on carbon nanotube, graphene, or MoS_2, have been developed to detect sub-ppm-level NO_2, NO, CO, or CO_2 pollutants, in a highly selective manner, in urban environments. This theoretical study targets to give an overview of the adsorption processes and electronic properties of the resulting gas sensor at the molecular scale.

First, functionalized material surfaces by physisorption macromolecules, such as metal porphyrins or metal phthalocyanines, are modelled with a procedure based on the density functional theory (DFT) with inclusion of long-distance van der Waals interactions [1, 2, 3]. The effect of the adsorption of these functionalizing molecules on the electronic structure of the material surface is studied. Then, we focus on the interaction of gas molecules (NO_2, NO, CO …) with the nanomaterials before and after functionalization. This modeling study is based on the use of standard codes (GAUSSIAN for macrocyclic and gas molecules [4], and CRYSTAL [5] for surfaces of functionalized materials with adsorbed gas) and compared to experimental results.

Such modelling approach brings insights to better understand the processes occurring at the gas/functionalized material layer interface, particularly concerning the charge transfers between the different elements of the sensor, (gas + functionalizing molecules + material), and the type of doping of the material after functionalization and after adsorption of gases.

This work is carried out as part of the ANR SENS-CO project.

KEYWORDS: Functionalization, 2D materials, gas surface interaction, DFT.

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n°23

Ab initio molecular dynamics simulations of alumina oxide/water interfaces

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The surfaces and interfaces of metal oxides play an important role in many natural and technological processes such as mineral dissolution, adsorption/desorption reactions, pollutant transport in groundwater, corrosion, and heterogeneous catalysis. In all these processes the structure of the water at the interface with the oxide is a key factor. This is what we investigate with DFT-MD simulations (DFT-based Molecular Dynamics).
We will review our works on a-alumina oxide Al2O3/liquid water interfaces, where we unravel the intertwined structural arrangement of surface and liquid water at the interface. Chemical reactivity is highly dependent on surface structure and speciation at the interface with the solvent, therefore the pre-requisite knowledge of the following points: type of surface, surface sites protonation state (O, OH, OH2), water molecules organization due to the presence of the solid, water and surface site orientations and hydrogen bonding networks. Of particular interest is the comprehension of the H-Bond network formed between the surface aluminols and interfacial water molecules, in terms of which surface chemical types are involved in the network, and in terms of strength of H-Bonds. Also of importance is the relationship between interfacial structures and vibrational signatures. These signatures are calculated from the DFT- MD trajectories (SFG, Sum Frequency Generation) and are compared to experiments.

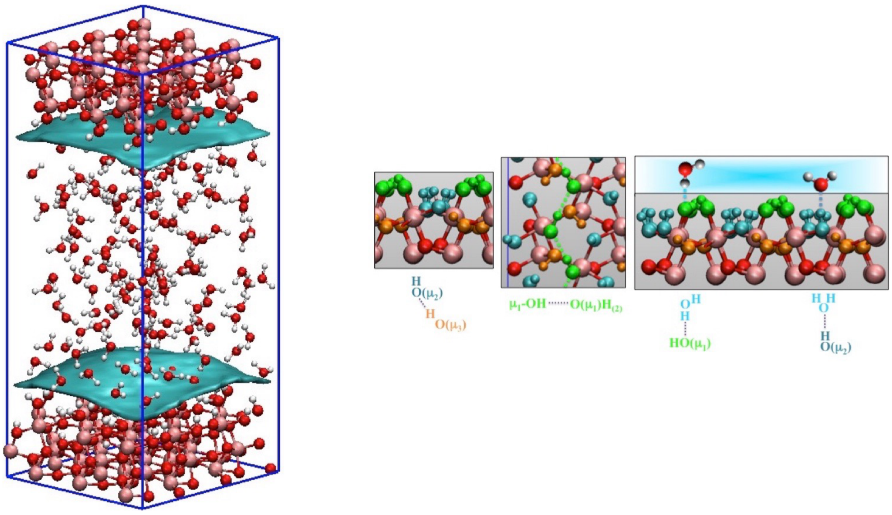

Figure 1. Simulation box (left) and schematic representation of the hydrogen bonding at the interface (right).

KEYWORDS: oxide/water interfaces, ab initio DFT-MD, SFG.

n°24

Ultrafast Hydrogen Migration in a Photoionized Glycine by a Mixed Quantum-Classical Dynamics

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We have theoretically investigated the ultrafast intramolecular hydrogen migration in the glycine molecule ionized by XUV attosecond pulse train of duration 1.5 fs as experimentally observed by Castrovilli et al.[1]. Since the interaction of the pulse with the molecular system leads to ionization, standard quantum chemistry methods used to describe excited bound states break down and methods which accurately describe electronic continuum states are in order. We have used the correlated single channel approach as implemented in the Tiresia code[2] to calculate the dipole matrix elements, the cross-sections of a singly ionized glycine and the ionization probabilities are evaluated for a specific attosecond pulse train of duration 1.5 fs used in the previous experiment[1]. The coupled electron-nuclear dynamics is described by the Trajectory Surface Hopping (TSH) [3] method. We do observe a hydrogen migration as shown in the snapshots of the TSH dynamics displayed in figure 1. The migrations mostly occur when the active state reaches the cationic ground state. Further calculations are currently performed using the Heidelberg Multi-Configurational Time-Dependent Hartree (MCTDH)[4] package on a linear vibronic coupling model in order to study coherence effects which lack in the TSH method.

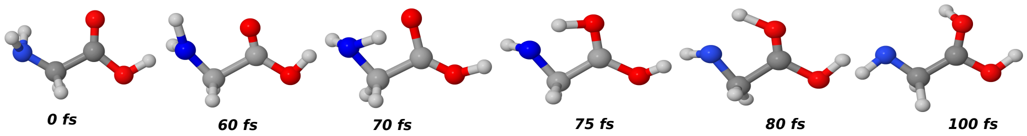

Figure 1: Snapshots of the geometries during the dynamics showing the hydrogen migration .

Keywords: Photo-ionization probability, hydrogen migration, trajectory surface hopping, glycine.

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n°25

Unveiling the reactive conformation of PEP Carboxylase with molecular dynamics

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The next time you drink a mojito on the terrace, you'll think of PEPC. Sugar cane and a number of other plants such as maize, sorghum and rye are plants with a photosynthesis mechanism called C4[1]. In these plants, CO2 fixation during the Calvin-Benson cycle is preceded by a CO2 capture step by the enzyme PEP Carboxylase (PEPC); this enzyme catalyses the reaction between bicarbonate (i.e. hydrated CO2) and the substrate PEP (phosphoenolpyruvate). C4 plants have a lower water requirement than other plants, which could prove to be crucial in the context of global warming and water shortages[2]. Our ultimate aim is to understand the growth of these plants by studying the reactivity of the enzyme responsible for carbon capture.

The active site of PEPC is located close to a mobile loop that isolates the active site from the solvent[1]. The opening/closing of this loop therefore plays a crucial role in the reactivity of the enzyme. The open structure of this loop was solved only in 2018 and no closed structure is currently known. In this project, we aimed at answering the question: « is it possible to predict a closed conformation that can be used to understand the catalytic activity of the enzyme? ». To do so, we developed a methodology based on:

1. the analysis of the potential energy of the psi and phi angles during short simulations out of equilibrium;
2. simulations with a modified force field based on results from the previous analysis, followed by enhanced sampling simulations;
3. clustering by a new methods and estimation of the most stable conformation by forcing the reopening of the loop.

This methodology was tested on enzymes for which the open and the closed conformations was known, and we observed a very good agreement between the experimental closed structure and the predicted one. Encouraged by these results, we tested the method on the PEPC to obtain as closed conformation

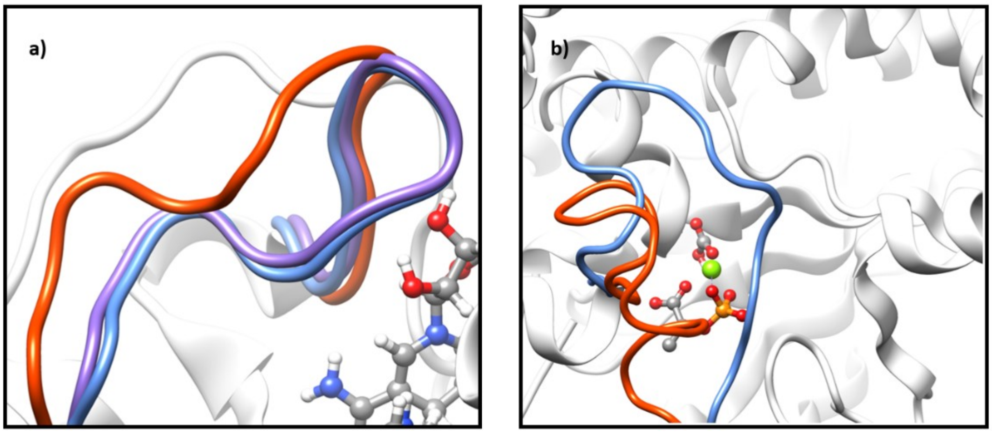

Figure 1. **a)** Superposition of the crystallographic structure of DHFR in orange (open) and Closed (purple) and the predicted (blue). **b)** Superposition of the crystallographic structure of PEPC in orange (open) and the predicited (blue).

Keywords: Molecular dynamic , PEPC ,Methodological developement

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n°26

UV-Vis spectra of organic dyes: unraveling the sources of band broadening

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Molecular materials have been under the spotlight for several decades due to their capacities of being used for photovoltaic and optoelectronic applications, accompanied by their lightweight and ease of chemical tuning from their organic nature.

While extensive experimental studies have been conducted on the photophysical properties of such systems, theoretical investigations often do not provide a complete depiction of the complexity of the mechanisms involved, and thus further studies are needed. Time-Dependent Density Functional Theory (TD-DFT) has been for the last few years routinely used to obtain by calculation the vertical absorption energies, while the reproduction of the UV-Vis spectra band shape received less attention. Aiming at calculated the UV-Vis bands in condensed phase, it is necessary to consider the different sources of broadening, i.e static disorder, vibronic coupling, temperature effect and/or exciton coupling.

This contribution will discuss the theoretical methodologies needed to simulate the different sources of broadening, in particular for the UV-Vis absorption bands of aromatic molecules in their crystalline phase. Using a QM/MM electrostatic embedding scheme as a first approach, static disorder can be simulated to reproduced experimentally seen broadening of UV-Vis spectra.[1] Vibronic contributions, which mainly contribute to the fine structure and dynamic disorder to the UV-Vis spectra can be obtained for molecular structures from first principles calculations, using a Fermi Golden Rule based formalism, leading to an estimation of the vibronic and temperature effects.[2] Discussions of the state of the art of calculations and limits will be discussed. Then, preliminary results of our studies on organic molecules and organic molecular crystals will be presented.

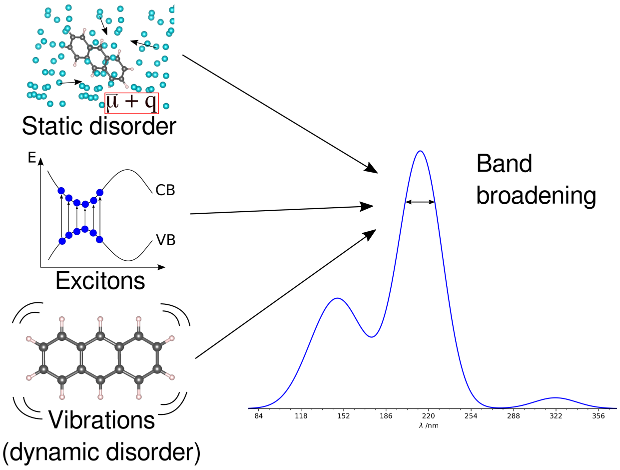

Figure 1: Sources of broadening in a molecular material.

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Keywords: Vibronic coupling, QMMM, molecular crystals

n°27

Velocity adjustment in surface hopping

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Surface hopping simulates nonadiabatic dynamics by evolving a swarm of independent trajectories involving multiple electronic states. Trajectories are propagated on a single surface, and hops between them are based on a stochastic algorithm. This surface change occurs at small but finite potential energy gaps when the potential energy instantaneously changes. Therefore, to ensure total energy conservation during the dynamics, the nuclear kinetic energy must be changed to compensate for the potential energy variation. The proper way to change the kinetic energy is by rescaling the nuclear velocities in the direction of the nonadiabatic coupling vector. However, in many cases, those vectors are not available. Thus, what are the alternatives to rescale velocities? A common choice is the momentum direction, but this can induce an abnormal amount of back hoppings, leading to unphysical dynamics. In this work,[1] we compared different ways of rescaling the velocity after a hooping occurs, taking fulvene and a protonated Schiff base (PSB4) as examples, assessing their population decays and reaction yields. The different sets of dynamics have the velocity adjusted in either nonadiabatic coupling (**h**), gradient difference (**g**), or momentum directions (**p**-fullKE). For the latter, in addition to the conventional algorithm, we explored the performance of a reduced kinetic energy reservoir approach recently proposed[2] (**p**-redKE). Our results show that the dynamics of fulvene (Figure 1) is susceptible to the velocity adjustment chosen, but *cis*-PSB4 is not. We correlate this result to the topographies near the conical intersections. When nonadiabatic coupling vectors are unavailable, the **g** direction is the best adjustment option. If this is also not available, a semiempirical vector direction (**h**-FOMO-CI) or the **p**-redKE direction become an excellent option to prevent an artificial excess of back hoppings. We conclude that the precise velocity adjustment direction is less crucial for describing the nonadiabatic dynamics than the kinetic energy reservoir's size.

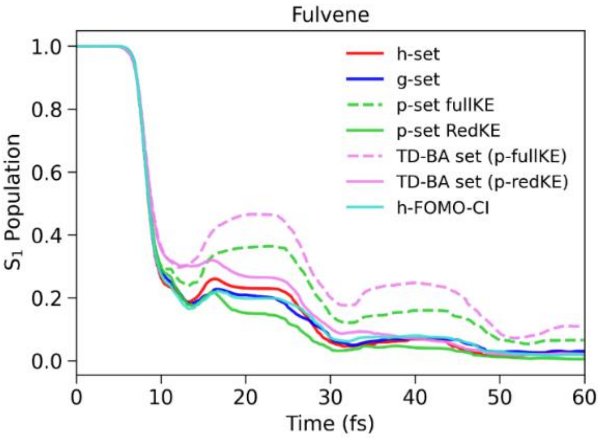

Figure 1. Excited state population evolution of fulvene computed with different velocity adjustments.

Keywords: Excited state dynamics, surface hopping, conical intersections.

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27 juin 2024

Session 6A

Making Sense of Electrical Noise by Simulating Electrolyte Solutions

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Seemingly unrelated experiments such as electrolyte transport through nanotubes, nano-scale electrochemistry, NMR relaxometry and Surface Force Balance measurements, all probe electrical fluctuations: of the electric current, the charge and polarization, the field gradient (for quadrupolar nuclei) and the coupled mass/charge densities [1],[2]. Using molecular and mesoscopic simulations, it is possible to predict the fluctuations of these observables from the dynamics of ions and solvent molecules, thereby enabling experimentalists to decipher the microscopic properties encoded in the measured electrical noise. This presentation will illustrate this idea, focusing on quadrupolar NMR relaxation as a probe of subpicosecond collective dynamics in aqueous electrolyte solutions[3],[4] and on the link between the electrode charge fluctuations in nanocapacitors and the dynamics of the interfacial electrolyte.

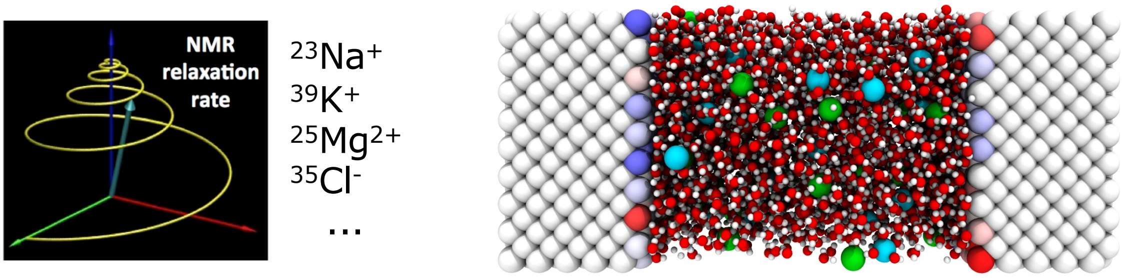

Figure 1. Left: the NMR relaxation rate of quadrupolar ions (with spin I>1/2) reflects the collective dynamics of their environment via the fluctuations of the electric field gradient. Right: the electrode charge fluctuations in a nanocapacitor, related to the frequency-dependent impedance, reflect the dynamics of the confined liquid.

Keywords: Electrical fluctuations, NMR relaxation, nanocapacitors, dynamics, electrolytes.

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Fast calculation of solvation structure and thermodynamics in supercritical CO_2

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Growing concern about the environmental impact of industrial activities is driving the chemists to develop more ecological processes. A major goal is to design new range of solvents, “greener” but as efficient as the widely used organic solvents. Supercritical CO_2 ($scCO_2$) is an interesting alternative.[1] It is non-toxic to humans and the environment, non-flammable and can be easily fine-tuned to precisely control the solvation power. The $scCO_2$ is used in several industrial processes: extraction of natural products, impregnation of polymer matrices, water purification or synthesis of nanoparticle A wider use of such ecological solvent would however require an accurate for predicting the solvation properties.

Different approaches exist to estimate the solvation properties in supercritical fluids. Industrial chemists rely on accurate parametric models, but many parameters must be fitted for each solute and each new solvent.[2] Molecular simulations (MD or DFT) are more flexible than the parametric models and can accurately calculate the solvation free energy and the other solvation properties: structure, enthalpy, molar volume. But despite enormous progress, MD is still too expensive to be considered as a predictive tool for large scale investigations (many solutes, different solvents and solvent mixtures and different thermodynamical conditions).[2]

We will present a powerful alternative strategy based on classical density functional theory (cDFT), a liquid-state theory. Such approaches provide the same solvation properties as MD, but at a cost that is 1000 times cheaper from a computational point of view.[3] In our work, we built the excess free energy functional and compared the structure and the solvation free energy of a CO_2 in $scCO_2$ obtained with cDFT and MD. Our results are excellent and for a much lower cost (see Table 1 and Ref.[4]). In this talk, we will detail the method, the implementation and the perspective for the development of a new accurate, flexible, and ultrafast prediction tool for solvation properties in $scCO_2$.

Table 1 : Free energy of solvation ($kJ.mol^{-1}$) of a CO_2 molecule in $scCO_2$ at $T = 1.05\ T_c$ and for different reduced densities. For our model, $T_c = 305$ K and $\rho_c = 454$ kg.m-3

	0.4 ρ_c	**0.7 ρ_c**	**0.8 ρ_c**	**Numerical cost**
MD	-0.689	-1.09	-1.21	20 000 h.CPU
cDFT	-0.689	-1.08	-1.19	1 min.CPU

<u>Keywords</u>: supercritical CO_2, liquid-state theories, solvation properties, classical DFT

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SIMULATING FLUORESCENCE: AN INVESTIGATION OF TRIAZAPENTALENES DECAY PATHWAYS

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Fluorescent compounds have diverse applications in many technological fields such as bio-imaging, chemical sensors, and light-emitting devices (OLEDs).[1] In any fluorescence applications, achieving precise control of the emission wavelength as well as of its intensity is key to success. Fluorescence occurs usually on the nanosecond timescale and thus obtaining an experimental overview of the exact mechanisms involved remains challenging.

In this presentation, I will present an in-depth theoretical study of the emissive properties of a series of 1,3,6-triazapentalene (TAP) molecules. While the bare TAP core is experimentally reported to be non-fluorescent ($\Phi_f = 0$), many TAP derivatives are good emitters. Indeed, TAPs present a broad range of fluorescence quantum yields (Φ_f ranging from 0.1 up to 0.8).[2] To investigate the phenomena at work behind this behavior, various theoretical approaches are combined. First, we simulated high-resolution UV-Vis spectra using vibronic calculations.[3] Then, the fluorescent quantum yields are simulated, and to this end the kinetics rates of both radiative processes (k_r) and internal conversion (k_{IC}) are estimated.[4] While this scheme is sufficient to accurately simulate most of the experimental trends, some compounds still stand out and present unexpectedly low quantum yields. Interestingly, in the bare TAP core, a conical intersection between the ground state (GS) and first excited state (ES) is easily reached during ES relaxation, hence explaining the quenching of the fluorescence. To assess the relative importance of such non-radiative pathways in other compounds, the presence of Minimal Energy Crossing Points (MECP) between the GS and ES is investigated. Finally, the kinetics of such processes (k_{MECP}) are evaluated and included in our quantum yield simulations, providing an accurate depiction of the fluorescence intensity in this molecular series, on par with experimental observations.

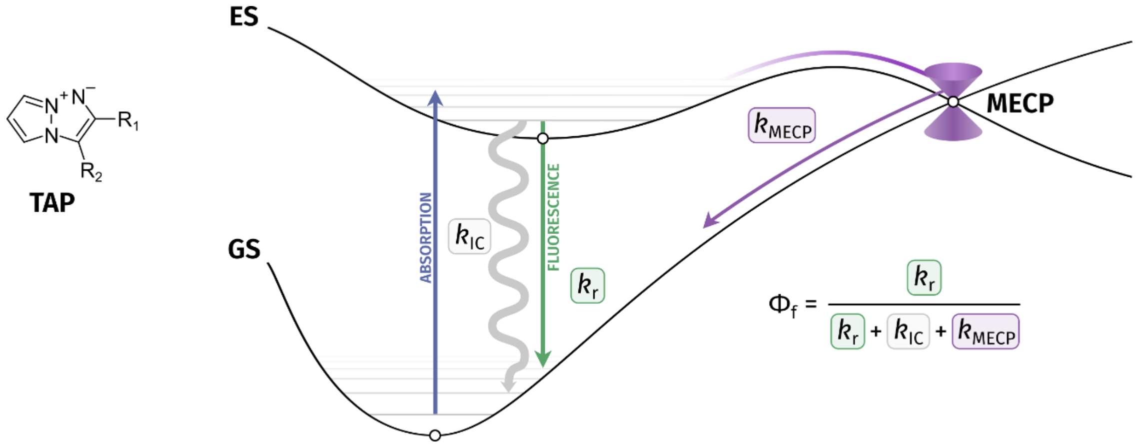

Figure 1. Jablonsky diagram featuring the different radiative (k_r) and non-radiative (k_{IC}, k_{MECP}) processes included in our fluorescence quantum yield (Φ_f) simulations.

Keywords: Fluorescence, TD-DFT, Quantum yield, Vibronic, Conical intersection

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Session 6B

Modelling Aqueous Electrolyte with Molecular Density Functional Theory

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Molecular Density Functional Theory (MDFT) is a flavor of classical DFT designed to study the solvation of chemically complexed solutes in a molecular solvent. The solvent is described by a density field. Due to the presence of the solute molecule, represented by an external potential acting on the solvent, this density is perturbed and become inhomogeneous. The DFT ansatz guarantee the existence of a functional of the solvent density that reaches its minimum for the equilibrium solvent density and that is equal to the solvation free energy at this minimum[1]. This theory has proved to be competitive with respect to state-of-the-art simulation techniques for the description of the solvation of a wide range of solutes into molecular solvent such as water and acetonitrile [2]. It is actually possible to generalize the theory to describe a mixture of liquid, each being described by its own density field. In this talk, I will show how this development can be used to describe the solvation of an electrolytic solution. I will start by the simplest model of electrolytic solution that is the primitive model where cation and anion are described by identical sphere of opposite unity charges while the solvent is modelled by a dielectric medium of homogeneous permittivity. A more evolved approach where the solvent is explicitly represented by a third density field will be presented afterwards.

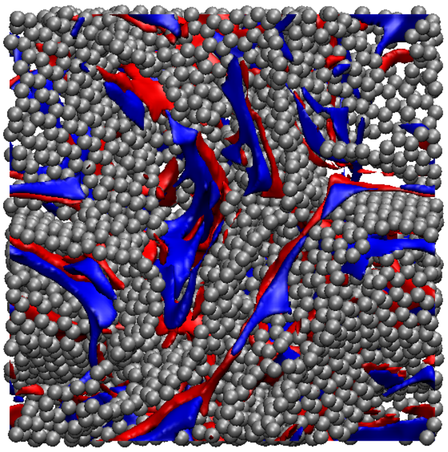

Figure 1. Density of sodium (red) and chloride (blue) into a carbide-derived carbon predicted with MDFT.

Keywords: classical DFT, electrolyte, statistical physics

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Ab initio study of doped NiOOH surfaces for electro-oxidation of organic molecules

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Chemicals are mainly synthetized from fossil fuel-derived precursors. One big challenge of our century is to replace these precursors with more renewable ones, for example with biomass-derived precursors. 5-hydroxymethylfurfural (HMF) can be extracted from cellulose or hemi-cellulose and can be electro-oxidized into 2,5-furandicarboxylic acid (FDCA). FDCA can replace terephthalic acid for the synthesis of polyethylene terephthalate (PET). Nickel oxyhydroxide (NiOOH) surfaces are well-known as efficient anode materials for water electro-oxidation during the oxygen evolution reaction (OER) and are also promising for HMF to FDCA electro-oxidation. The efficiency of this electrode is experimentally shown to be enhanced with metal-doping for OER and electro-oxidation of HMF. In the present work, we perform a Density Functional Theory (DFT) investigation of the impact of metal-doping on the electrochemical reactivity of NiOOH surfaces. Based on experimental studies and the literature of metal-doping for OER, we chose to dope NiOOH with 6 different metals: Co, Cu, Fe, Ga, Mn and Sc. Periodic Density Functional Theory (using VASP, and the PBE-dDsC functional) computations of the relative stability of the relevant bulk of nickel hydroxide ($Ni(OH)_2$) and NiOOH were performed with a doping density from 0% to 25%. The relative stabilities of NiOOH and doped-NiOOH surfaces were calculated at the same level of theory. The effect of the electrochemical potential was modeled by grand-canonical DFT (GC-DFT) in conjunction with the linearized Poisson-Boltzmann equation.

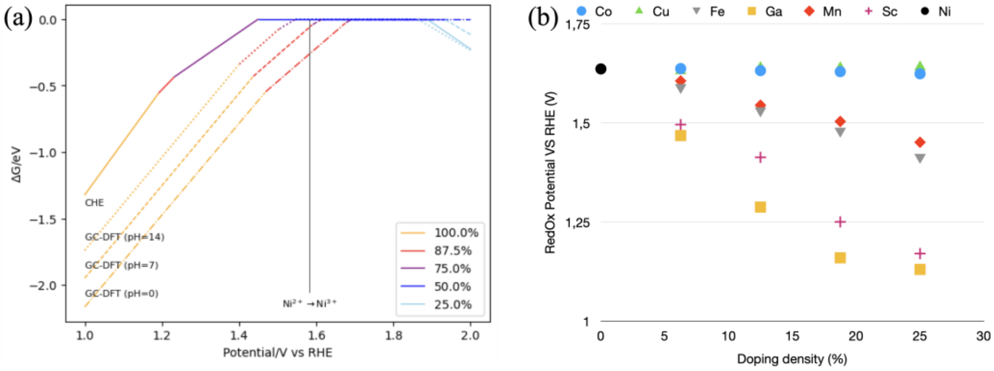

Figure 1. (a) Relative stability of hydrated NiOOH surfaces with CHE and GC-DFT methods; (b) Red/Ox potential of $NiOOH/Ni(OH)_2$ bulks with a doping density from 0% to 25% in Co, Cu, Fe, Ga, Mn and Sc.

Figure 1a shows the most stable hydrogen coverage of pure NiOOH surface as a function of the electrochemical potential at computational hydrogen electrode (CHE) and GC-DFT levels. Taking the electrochemical potential explicitly into account via GC-DFT has a significant impact on the results and shows that at the studied potential (HMF electro-oxidation at ~1.5 V) the hydrogen coverage is between 50 and 87.5% and depends on pH. The evolution of the Red/Ox potential of $NiOOH/Ni(OH)_2$ with an changing doping density is shown in Figure 1b. Three behaviors are observed out: Co, Cu have no impact, Fe, Mn linearly decrease the potential with an increase of doping, while Ga and Sc strongly destabilized bulk structure of doped-$Ni(OH)_2$. The impact of the doping on the surface state (H-coverage) and the electro-oxidation of HMF will be presented to illustrate the effect of tuning the electrocatalyst on its activity.

Keywords: DFT, electrochemistry, surface, doping

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Simulation of Electrolyte Molecule Degradation on Electrode Surfaces: A Comparison of Methods - Molecular Dynamics and Genetic Algorithm

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All-solid-state batteries (ASSBs) with a polymer electrolyte have emerged as a promising solution to address the growing demand for efficient energy storage systems and reduce overall energy consumption[1]. These batteries utilize a solid-state electrolyte composed of a polymer material, offering numerous advantages over traditional liquid electrolytes[2]. However, the utilization of a lithium metal anode gives rise to several additional challenges[3]. Namely, the intricate relationship between electrolyte degradation mechanisms and the growth of the electrode-electrolyte interface. This investigation aims to describe such a mechanism and predict the possibility of avoiding it in order to extend battery's lifespan.

In the present work, ab initio molecular dynamics (AIMD) simulations and Genetic Algorithm (GA) using density functional theory (DFT)[4] are employed to investigate the degradation of a polymer electrolyte on distinct lithium metal anode surfaces. To this purpose, we realized different systems with isolated molecules of the electrolyte on Li-metal: one molecule of FEC (solvent) and one molecule of LiFSI (lithium salt) (figure 1). Then, we investigated the decomposition of these molecules, with and without the protective layers consisting of inorganic materials (Li_2O, LiF) and carbon-based 2D materials (Graphyne, Graphdiyne). The current study is devoted to comparing two methods in terms of computation time and the quality of results.

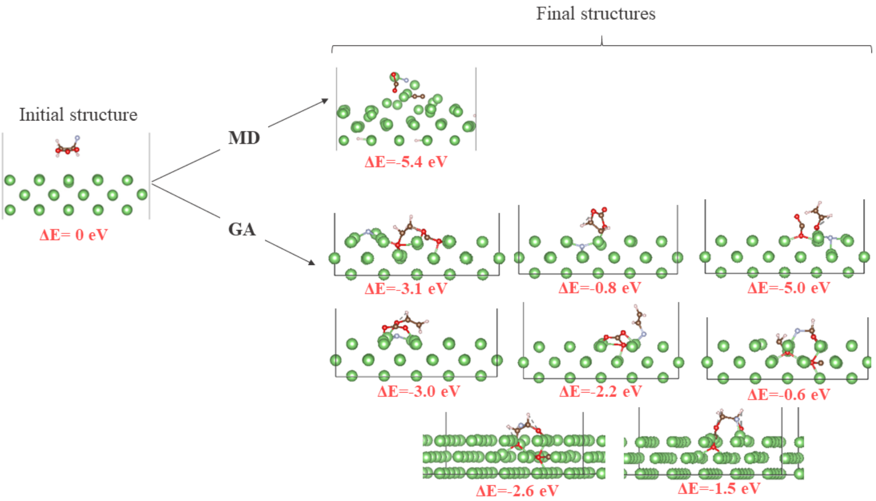

Figure 1. Decomposition products for FEC on Li surface using two methods: MD (Molecular Dynamic) and GA (Genetic Algorithm)

Keywords: Density functional theory; Li-metal battery; Electrodes protection; Solid electrolyte interphase.

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Enhancing Thermoelectric Efficiency of Organometallic Molecular Junctions by Quantum Interference

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Due to their size where quantum effects dominate the carriers transport, Molecular Junctions (MJ) offers a rich field for both experimental and basic science exploration. Since the proposal of Aviram and Ratner for constructing molecular rectifiers[1], the number of investigations in MJ is growing, as long as the fine-tuning capability of chemical structure and electronic configuration enables the design of different applications such as conducting wire[2]. Among their possible functions, MJ can present interesting thermal and thermoelectric properties, that could be used to fabricate energy nano-converters and nano-coolers[3]. The presence of metals in molecular systems can promote the frontier orbitals closer to the Fermi level and induce quantum interference, leading to highly conductive molecular wires with increased thermoelectric properties[4]. Quantum interference (QI) effects influence the transmission probability of charge carriers across molecular junctions, Fano resonance and anti-resonance being the manifestations of this phenomenon. In this work, by molecular design, we explore QI for electronic transport in linear response regime to increase significantly the Seebeck coefficient. QuantumATK[5] simulations were performed to tackle this question using non-equilibrium Green functions associated with density function theory (DFT) calculations (GGA rev-PBE/DZP and SZP for Au). The electronic and transport properties of different organometallic systems will be presented, which includes charged and spin polarized molecular junctions. A comparison with experimental results will also be provided.

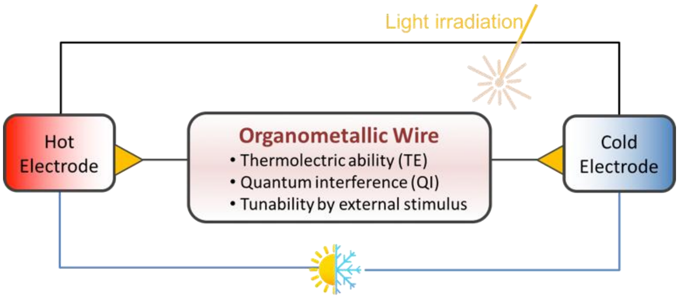

Figure 1. Thermoelectric ability can be improved by Quantum Interference and external stimulus.

<u>Keywords</u>: charge transport, energy conversion, thermoelectricity, molecular junctions, Fano resonance.

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28 juin 2024

Session 7A

Twists and Turns in Nanocarbon Materials Modelling

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The anisotropy of low dimensional carbon nanoobjects such as graphene opens up possibilities for structural distortion modes and behavior not available to three-dimensional crystals. This talk explores the structure of edge dislocations in layered materials, using a combination of DFT and related tools with experimental support. Different dislocation orientation results in families of radically different structure types which exploit the available out-of-plane dimension [1,2]. Folding creates distinct Raman spectroscopic signatures [3] and can lead to local band gap variation in layered materials such as boron nitride [4].

The resulting low-symmetry folded, rolled, distorted and rippled sheets are interesting, not only in themselves, but also for the void spaces they create. There are a number of ways carbon can be used to confine other materials, either modifying bulk behavior or inducing unique low-dimensional change in the materials they are hosting [5]. Examples include the formation of new 1D material phases of intercalants such as phosphorus [6]. Via a combination of theory and experiment, we show that encapsulation within intermediate diameter cavities (1.5-2.5 nm) results in red phosphorus-like chain formation, and from this are able to build up a low-dimensional phase diagram for phosphorus constrained in carbon cavities.

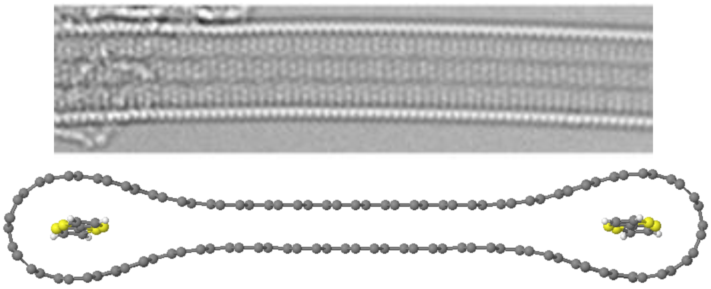

Figure 1. (top) Experimental image of phosphorus filled single walled carbon nanotube (bottom) collapsed carbon nanotube with filling of the edge cavities.

Keywords: Carbon, DFT, Defects, dislocations, structure.

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Advances and Challenges in Modeling Water Clusters and Liquid Water

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Understanding the properties of water, in its various phases and at different interfaces, is a key subject in numerous chemical, physical, and biological processes.[1] This is evidenced through the numerous experimental and theoretical studies on water that have been published over the past decades. In the latter cases, despite its simple molecular structure, accurately modelling water remains a significant challenge due to its complex hydrogen-bonding network and the nuclear quantum effects that influence its behaviour.[2]

In this presentation, I will discuss recent advancements in the theoretical modelling of water clusters and liquid water conducted at the LCPQ (Laboratory of Quantum Chemistry and Quantum Physics). Emphasis will be placed on the methodologies employed, including self-consistent-charge density-functional based tight-binding (SCC-DFTB) formalism [3], molecular dynamics and path-integral molecular dynamics approaches,[4] and enhanced sampling methods. I will highlight the benefits and limitations of these approaches, particularly focusing on the issues of sampling of potential energy surfaces and inclusion of nuclear quantum effects (NQEs). Additionally, I will present recent studies from our group at LCPQ, showcasing our efforts in enhancing the accuracy of water models. Finally, I will explore the potential of Machine Learning (ML) tools to improve the modelling of water.

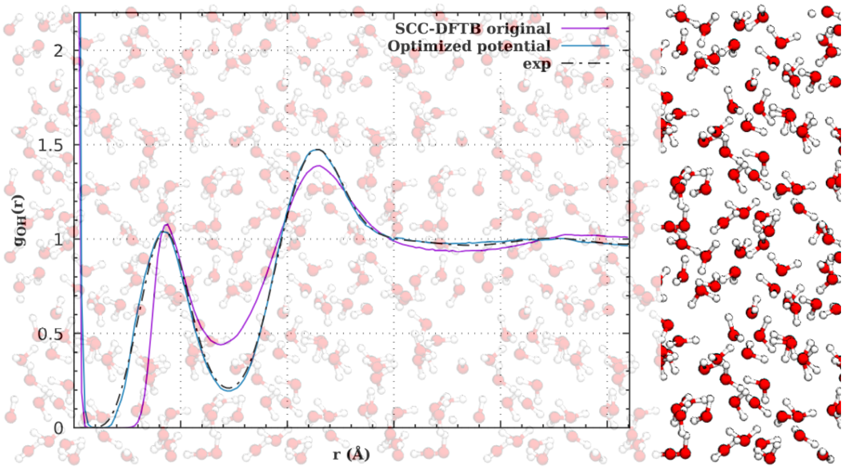

Figure 1: O-H pair radial distribution function of liquid water obtained from the original and optimized SCC-DFTB potentials as compared to the experimental curve.

Keywords: Aqueous Systems, Molecular Dynamics, Enhanced Sampling, Machine Learning.

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Molecular dynamics of post-lithium battery electrolytes : priorities and challenges

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In the current search for alternatives to Li-ion batteries to satisfy rising global demand for energy storage, liquid electrolytes remain at the center of research and development efforts. Their composition varies greatly,[1] [2] as some alkaline and alkaline-earth ion electrodes are incompatible with the carbonate-based solvents traditionally used for Li-ion batteries. Furthermore, even viable systems show deviations from the conduction behavior of Li-ion systems, which resists straightforward experimental explanation.[3] To this end, classical Molecular Dynamics (MD) is an invaluable tool to bridge the gap between experimental observations and atomistic scale phenomena to investigate what causes a system to function or fail. We present our work through two model systems: a glyme-based Ca-ion battery electrolyte and a carbonate-based Na-ion battery electrolyte. First, we discuss the cost-benefit of taking into account physical effects such as polarisability and nuclear quantum effects (i.e. the zero-point energy) based on the physical properties of these electrolytes (e.g. dielectric constant, infrared spectra). In the latter part, we analyze the simulations performed with the previously discussed parameters, using the unconventional tools of graph theory to draw connections between the changing ion transport properties and the modified solvation spheres of cations. Lastly, we project how this kind of analysis may be advantageous to study the enigma that is the build-up of the solid-electrolyte interface, as well as what effects would remain relevant in the case of an applied potential.

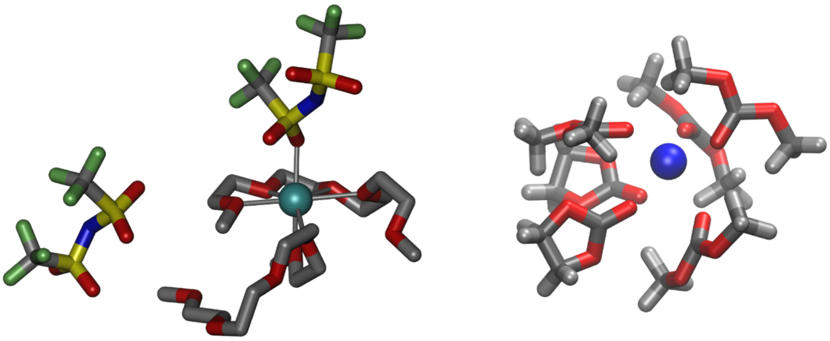

Figure 1: Solvation sphere examples in two different electrolyte systems

Keywords: classical molecular dynamics ; battery electrolytes ; post-lithium batteries ; graph theory.

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Session 7B

Fingerprint of Dipole Moment Orientation of Water Molecules in Cu^{2+} Aqueous Solution Probed by X-ray Photoelectron Spectroscopy

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The electronic structure and geometrical organization of aqueous Cu^{2+} have been investigated using X-ray photoelectron spectroscopy at the Cu L-edge combined with state-of-the-art ab initio molecular dynamics and a quantum molecular approach designed to simulate the Cu 2p X-ray photoelectron spectrum. The calculations offer a comprehensive insight into the origin of the main peak and satellite features. It is illustrated how the energy drop of the Cu 3d levels (≈ 7 eV) following the creation of the Cu 2p core hole switches the nature of the highest singly occupied molecular orbitals from the dominant metal to the dominant molecular orbital nature of water. It is particularly revealed how repositioning the Cu 3d levels induces the formation of new Bonding (B) and Antibonding (AB) orbitals, from which shake-up mechanisms toward the relaxed H-SOMO operate. As highlighted in this study, the appearance of the shoulder near the main peak corresponds to the characteristic signature of shake-up intra-ligand ($1a_1$ →H-SOMO ($1b_1$)) excitations in water, providing insights into the average dipole moment distribution (≈36° degrees) of the first-shell water molecules surrounding the metal ion and its direct impact on the broadening of the satellite. It is also revealed that the main satellite at 8 eV from the main peak corresponds to (metal/$1b_2$ →H-SOMO ($1b_1$) of water) excitations due to a Bonding/Antibonding (B/AB) interaction of Cu 3d levels with the deepest valence O2p/H1s 1b2 orbitals of water. This finding underscores the sensitivity of XPS to the electronic structure and orientation of the nearest water molecules around the central ion[1].

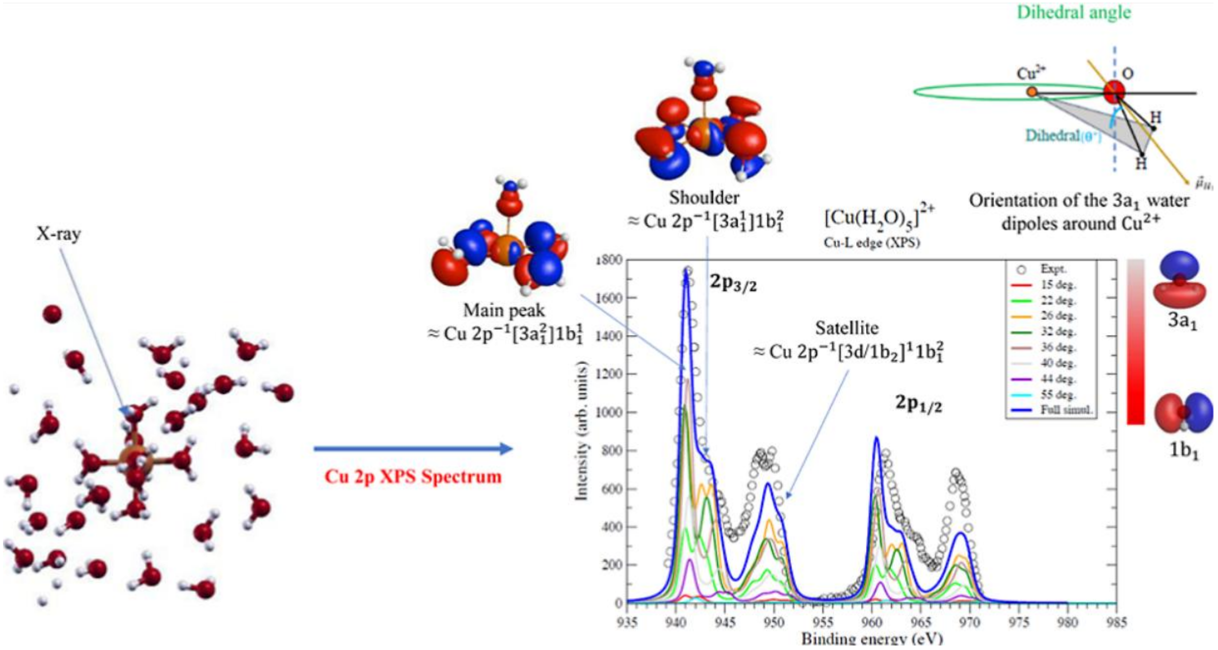

Figure 1. The illustration of the developed . In the left, the cluster is displayed. In the right panel, spectra are computed for different values of the dihedral angle.

<u>Keywords</u>: Ab initio, Molecular Dynamics, X-ray photoelectron spectroscopy

1 Mosaferi, M. et al. Fingerprint of Dipole Moment Orientation of Water Molecules in Cu2+ Aqueous Solution Probed by X-ray Photoelectron Spectroscopy. Journal of the American Chemical Society.

Collision-induced dynamics of PAH-water clusters

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Polycyclic Aromatic Hydrocarbons (PAHs) are a family of molecules that have several research interests, especially in environmental science and astrochemistry. In the dense and cold regions of the interstellar medium (ISM), it is believed that PAHs could condense on the icy surface of interstellar nanograins and interact with other molecules like water[1]. Understanding PAH-water interactions motivated both experimental and theoretical studies, to which our group has contributed significantly[2,3]. With theoretical models, exhaustive studies can be conducted to cover the diversity of the PAH family in the ISM: different charge states, (de)protonation states, PAHs with side groups, PAH clusters, etc.

We present here a study on collisions involving protonated pyrene, where pyrene (Py) is a PAH ($C_{16}H_{10}$), and water clusters: (Py-H)$(H_2O)_n$. The collisions were simulated by on-the-fly Born-Oppenheimer Molecular Dynamics (BOMD), along with the Self-Consistent Charge Density Functional based Tight-Binding (SCC-DFTB) potential to compute the electronic energy[4]. This potential, which can be seen as an approximation of the Density Functional Theory (DFT) method, allows inexpensive calculations that still maintain a quantum description of the electrons. Thousands of simulations (of around 20 ps) can be run in a reasonable amount of computational time.

Low-energy (50 meV) collisions of astrophysical interest between protonated pyrene and water molecules ($n = 1-4$) were simulated. High-energy (7.5 eV) collision-induced dissociations by argon atoms were simulated as well ($n = 1-5$), to complement experimental results[5].
Properties such as sticking efficiency, influence of the protonation site, structures of the adducts, and branching ratios were derived from these calculations. Due to its symmetry, pyrene presents three non-equivalent protonation sites. Successive collisions at low energy with water molecules reveal different types of PAH-water interactions according to the protonation site (proton transfer, pyrene oxidation, etc.). As for the structural properties, they were compared to "classic" Monte Carlo simulations. On the other hand, collisions at high energy with an argon atom provide data that were gathered up as mass spectra. The question of the charge (de)localisation will also be addressed.

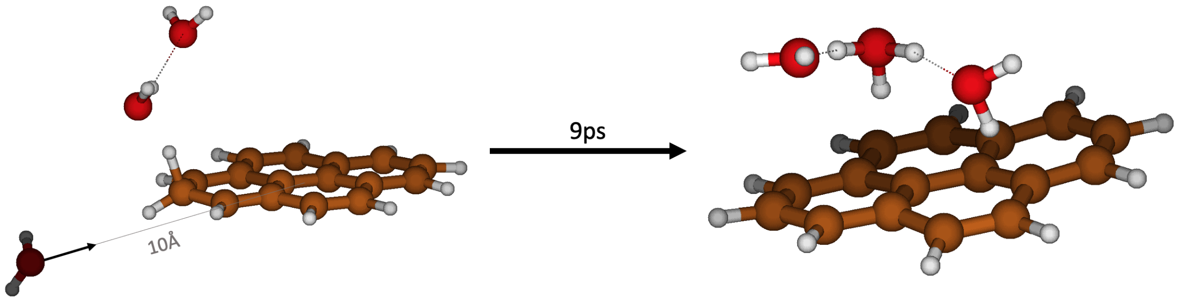

Figure 1: Illustration of a collision at 50 meV, between a water molecule and (Py-H)$(H_2O)_2$

Keywords: PAH, water, DFTB, molecular dynamics, collision

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Predicted high energy density MN_8 with polynitrogen monolayers based on fused 18-rings acting as cryptand

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The application of polynitrogen as a high-energy density material (HEDM) is hampered because of the high reactivity of most predicted allotropic phases of nitrogen. However, mixing nitrogen with other elements M can help to overcome this kinetic instability. By modulating pressure, MN_x products can be stabilized and then quenched to obtain "polymerized nitrogen" and nitrogen-rich compounds. Our theoretical exploration of different M-N binary phase diagrams under pressure[1,2] has resulted in the emergence of appealing N-based molecular motifs like chains or layers. For instance, we predicted the isolation of a layered unsaturated 18-crown-like N_8 material.[3] We explored the possibility of predicting the emergence of novel and viable nitrogen-rich MN_8 compounds by mixing an electropositive metal with the unsaturated moieties.[4] Our investigation involved a wide range of solid-state compounds MN_8 under pressure, with M supporting different oxidation numbers such as Na^+, Ag^+, Ca^{2+}, Pb^{2+}, Y^{3+}, and Hf^{4+}. By assessing dynamical (phonons), thermodynamic (enthalpies), and kinetic (AIMD) stabilities, we predicted over 14 viable compounds with different crystalline phases. To locate the different phases of the 2D 18-crown-6 MN_8, we used the evolutionary algorithm “USPEX”[5] combined with DFT calculations at various levels of theory (PBE, PBE-D3(BJ), r^2SCAN+rVV10, or HSE06) depending on the evaluated property (structure, energy, phonons, AIMD, DOS, COBI, energy gap, bands, etc.). The results of our exploration indicate that the extended crown-like N_8 net is a stable and common topological motif, which is stabilized by cations through ionic interactions. We also investigated the stoichiometric modulation of the metal intercalant M into the interlayer spaces of M_x@2D-N_8 ($x = 0.5 - 1$). These metal 18-crown-6 ring-based polynitrogen compounds, as expected due to their high nitrogen content (eight nitrogen atoms per metal), could potentially serve as new high-energy density materials the detonation velocity ranges from 10.1 to 17.9 km.s−1 , which is higher than the experimentally determined range of explosive (CH2)4(NNO2)4 HMX (VoD ~9.1 kms−1). Additionally, a prospective study was conducted to examine the stabilizing capability of 18-crown-6 2D-N_8 towards molecular cations such as H_3O^+ and NH_4^+.

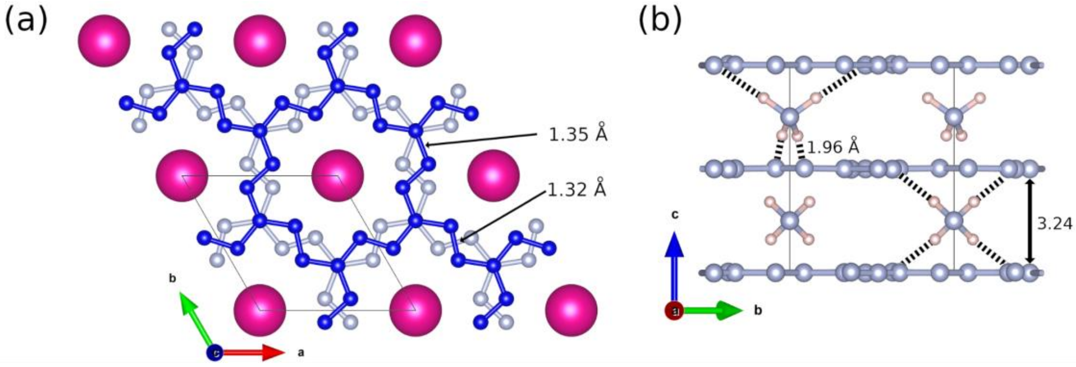

Figure 1. Crystal structures of (a) *P6/m* Rb@2D-N_8 and (b) *Ccc*2 (NH_4^+)@2D-N_8.

Keywords: HEDM; periodic-DFT; Evolutionary Algorithm; Material Design

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Morphology of Ru nanoparticles at titania-water-interface – A computational study

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Introduction

Biomass conversion is one of the key ways forward in solving the problem of dwindling resources. This requires the ability to transform highly oxidized molecules into value added molecules, often requires hydrogenation. One commonly used catalyst for the hydrogenation of biomass molecules is Ru supported over TiO_2. The difficulty in studying the catalyst is that it is used in water, making its surface state hard to determine.

Prior research into the surface state of the Ru-water interface[1] has shown that in the presence of water and under realistic reaction conditions (500K), adsorbed water molecules fully dissociate. This paves the way for investigating more realistic systems, in particular subnanometric (~10 atoms) Ru nanoparticles adsorbed on titania.

Materials and Methods

Global optimization was performed by using the PGOPT[2] program to generate numerous and varied nanoparticle morphologies (Ru_{10} supported on TiO_2 anatase 101) with different combinations of water molecules and varying degrees of splitting of these water molecules. Several thousand structures were thus generated and optimized using the CP2K software (PBE functional), allowing for the free energy of the system to be studied according to different structural parameters. A typical structure obtained through this method is shown in Fig. 1.

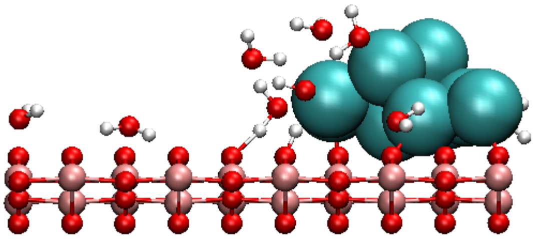

Figure 1. Ru_{10} supported on TiO_2 (anatase 101)

Results and Discussion

The stability of nanoparticles can be analyzed according to the number of water molecules adsorbed, the potential splitting of these water molecules into H + OH or 2H + O, and a variety of morphological parameters.

Fig. 2 shows the free energy of the most stable configuration obtained for different numbers of water molecules adsorbed on the nanoparticle and differing degrees of water dissociation.

z	0	1	2	3	4	5	6	7	8
0	0,00	-1,78	-3,44	-4,12	-7,03	-6,14	-7,46	-9,38	-10,47
1		-1,92	-3,44	-4,74	-4,81	-6,34	-7,29	-9,40	-9,97
2		-1,56	-3,30	-4,00	-5,21	-6,35	-7,90	-9,46	-10,24
3			-1,86	-4,50	-6,64	-6,36	-9,69	-7,44	-10,69
4			-0,41	-3,79	-4,74	-9,40	-8,49	-10,55	-9,89
5				-2,52	-5,73	-9,10	-9,10	-8,81	-8,25
6				-1,65	-4,02	-6,81	-8,40	-8,82	-7,49
7					-2,25	-4,97	-7,15	-9,62	-10,46
8					-0,80				

Figure 2. Free energy (eV, at 500K and water saturation pressure) of the most stable configuration obtained according to the number of water molecules adsorbed on the nanoparticle (horizontal axis) and the number of broken bonds on the water molecules (vertical axis), i.e. the degree of water dissociation.

This establishes the presence of OH adsorbed on the nanoparticles, a key species used to explain reaction mechanisms on Ru nanoparticles but for which there has been no direct of evidence of its presence up until this point.

Significance

This computational study into the surface state of Ru nanoparticles at the titania-water interface allows for a better understanding the *in situ* behavior of a common biomass conversion catalyst, the surface state of which, was, until now, poorly characterized. In particular this work shows evidence for the presence of key OH species adsorbed on Ru nanoparticles.

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<u>Keywords</u>: grand canonical sampling, nanoparticle

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