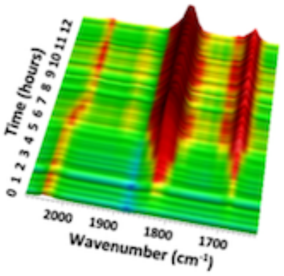

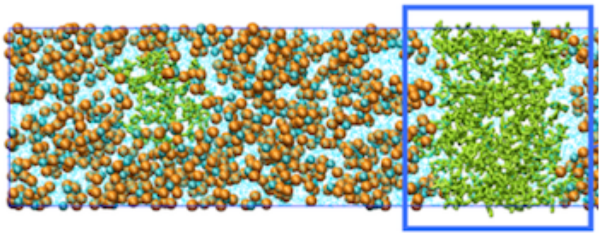

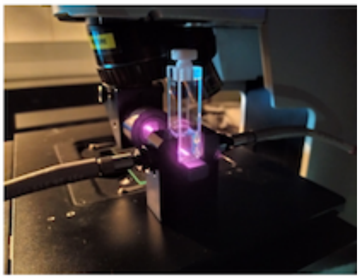

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9:00-9:15	Introduction
9:15-10:00	Daniel Borgis Laboratoire PASTEUR, ENS, PSL
10:00-10:20	Sophie Fourmentin UCEiV, Université Littoral Côte d’Opale
10:20:10:40	Lucas Martinez Uriarte LASIRE, Université de Lille
Break	
11:00-11:20	Lamia Nakhle UCEiV, Université Littoral Côte d’Opale
11:20-11:40	Damien Laage Laboratoire PASTEUR, ENS, PSL
11:40-12:00	Guillaume Stirnemann LBT, IBPC, Paris
Lunch break	
14:00-14:15	Pascal Granger (INC)
14:15-15:00	Sophie Le Caer NIMBE, CEA, Université Paris Saclay
15:00-15:20	Paul Clabaut Laboratoire de Chimie, ENS Lyon
15:20-15:40	Cecilia Herrero ILM, Université Lyon 1
Break	
16:00-16:20	Nawras Abidi Laboratoire de Chimie, ENS Lyon
16:20-16:40	Rika Tandiana ICP, Université Paris Saclay
16:40-17:00	Ozge Ozgurel PhLAM, Université de Lille

26 novembre 2020

9:15-10:00	**Rachel Schurhammer** Laboratoire MSM, Univ. de Strasbourg
10:00-10:20	**Kateryna Goloviznina** Laboratoire de Chimie, ENS Lyon
10:20:10:40	**Daniele Loco** LCT, Sorbonne Université
Break	
11:00-11:20	**Gautier Meyer** LEPMI, Université Grenoble Alpes
11:20-11:40	**Antonin Pardon** ILM, Université Lyon 1
11:40-12:00	**Alekos Segalina** LPCT, Université de Lorraine
Lunch break	
14:00-14:45	**Natalie Malikova** PHENIX, Sorbonne Université
14:45-15:05	**Thierry Azaïs** LCMCP, Sorbonne Université
15:05-15:25	**Paulo Peres De Sa Peixoto Jr** UMET, Université de Lille
Break	
15:45-16:05	**Wanlin Chen** LAMBE, Université d’Evry
16:05-16:25	**Guillaume Le Breton** ILM, Université Lyon 1
16:25-16:45	**Richard Asamoah Opoku** PhLAM, Université de Lille
16:45-17:00	Conclusion

Molecular density functional theory for predicting hydration free energies and solvation structures: General principles and latest update

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The principles of molecular density functional theory are briefly recalled and the capability of the theory to predict efficiently, albeit accurately, the hydration free-energies and microscopic solvent structure of molecular solutes is discussed for a variety of systems: spherical hydrophobic solutes, ions, water as a solute, and the Mobley's dataset including more than 600 drug-like molecules. The successes and the caveats of the approach are carefully pinpointed. The latest version of the theory includes so-called bridge functional contributions going beyond the lowest, second-order expansion in density, that is equivalent to the hypernetted chain (HNC) approximation in integral equations.[1-3] The overall functional is parameter-free in the sense that the only inputs are bulk water properties, independent of the solutes considered.[3] Compared to molecular simulations with the same force field and the same fixed solute geometries, the theory describes accurately the solvation free-energy and structure of both hydrophobic and hydrophilic solutes, although less so for anions and molecules containing strong H-bond acceptor sites. Overall, the methods yields a precision of order half a kT (0.3 kcal/mol) for the hydration free energies of the whole Mobley's dataset compared to Monte-Carlo simulations. Although not yet in its final version, the method appears now mature enough to be used in mixed electronic DFT/molecular DFT calculations that provides an intermediate, fully molecular description of the solvent lying between continuum PCM approaches and QM/MM simulations.[4]

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Supramolecular Eutectics as Solubilizers for Active Pharmaceutical Ingredients

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According to the Biopharmaceutical Classification System (BCS), up to 70% of the new chemical entities suffer from poor water solubility[1]. This represents a serious challenge to the successful development of new drugs in the pharmaceutical industry[2]. Many approaches have been taken to address the formulation challenges of poorly water-soluble drugs, including drug delivery systems such as liposomes, cyclodextrins, solid lipid nanoparticles, …[3]. In this context, deep eutectic solvents (DES), particularly those consisting of components from natural origin, have emerged as solvents of great promise for pharmaceutical applications because of their biodegradability, low toxicity and ability to dissolve chemically diverse compounds, including water-insoluble ones[4]. In this study we have investigated, along with classical DES, a new generation of DES called supramolecular deep eutectic solvents (SUPRADES)[5,6] based on cyclodextrins, cage molecules able to encapsulate various guests in their hydrophobic cavity and known for their use as functional pharmaceutical excipients to enhance drug solubility[3]. We were interested in comparing the solubilizing potential of these two classes and highlighting the benefit of combining the solubilization properties of a solvent and a drug carrier. Our results showed a significant increase in solubility for the different active pharmaceutical ingredients (APIs) studied, with factors ranging from 574 to 22440. For most of the studied APIs, the solubility was either equally enhanced in both DES, or more enhanced with the SUPRADES. So, we went beyond solubility assessment and investigated the formation of inclusion complexes in the SUPRADES. This hypothesis was validated by NMR studies.

Finally, the skin irritancy of the SUPRADES was evaluated on a 3D reconstructed human epidermis model according to the OECD TG 439 standard. Furthermore, the antibacterial and antifungal activities of the classical DES and the SUPRADES were determined on a Gram-positive bacterium (*Staphylococcus aureus*), a Gram-negative bacterium (*Escherichia coli*) and a yeast (*Candida albicans*). The SUPRADES were slightly more efficient than conventional DES, especially on the two bacteria.

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Influence of the environment on the photo-dynamics of a photo-switchable fluorescent protein: solution vs micro-crystals

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Reversibly photo-switchable fluorescent proteins (RSFP) are increasingly applied in super-resolution fluorescence microscopies of biological cells. These proteins can be switched between a bright (*on*) and a dark (*off*) state, involving a *cis-trans* isomerization and a change of proton state of a chromophore within a β-barrel protein cage. Recent publications, have cast light on the photo-switching dynamics of an RSFP used commercially, *i.e.* the rsEGFP2[1,2]. The authors have combined time-resolved pump-probe absorption spectroscopy (TA) on proteins in solution with time-resolved crystallography (SFX) on microcrystalline proteins. The latter experiments revealed a twisted chromophore, halfway between the *trans* and *cis* isomers, formed transiently on the picosecond time-scale[1], followed by a protein rearrangement on the microsecond time scale[2]. TA showed that deprotonation occurs in milliseconds in the ground state[2]. Comparison of SFX and TA data implicitly assumes that photo-intermediates of the chromophore and their respective lifetimes are the same in crystal and solution phases. This assumption is reasonable, given that on average 50% of the crystal volume is occupied by solvent so that proteins maintain their functional flexibility. Nonetheless, we already showed that the deprotonation time constants were faster in the crystal state than in solution[2]. The origin of this difference remains elusive.

Here we discuss the difference of the *off*-to-*on* switching dynamics for a colloidal solution of microcrystals and of proteins in solution. We mainly focus on the *ns-ms* time range characteristic of some protein rearrangement and the deprotonation step. To study the influence of the environment on the protein dynamics different mutants and buffers including the crystallizing media $(NH_4)_2SO_4$ were considered. Our results show that the dynamics in presence of the crystallisation solvent are similar to the dynamics of the protein in micro-crystal phase. Furthermore, when the buffer is changed to different salts containing either NH_4^+ or SO_4^{2-} we can see that the dynamics are only affected when NH_4^+ cation is present, demonstrating the influence of this ion in the deprotonation dynamics of the protein. The comparison with different mutant leads to the conclusion that the complete chromophore solvation should be taken into account in the *Off* to *On* photodynamics.

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Solubilization Of *Eucaluptus Citriodora* Essential Oil In Formulations Based On Deep Eutectic Solvents And Cyclodextrins

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Keywords: cyclodextrin, deep eutectic solvents, essential oil, solubility

Abstract

Increasing the solubility of natural molecules constitutes a major topic in the pharmaceutical research field. A large number of studies report the use of organic solvents as a strategy to reach this goal. However, their toxicity disagrees with the human and the environment safety criteria. This led to the revelation of Deep Eutectic Solvents (DES) as novel green solvents, with great capacity to solubilize different bioactive molecules [1]. The use of cyclodextrins (CD) constitutes another approach, which exploits the ability of these cyclic oligosaccharides to encapsulate a variety of molecules in water, mainly by the mean of their hydrophobic cavity [2]. Herein, various choline chloride / urea / water / CD formulations were prepared and subjected to density and viscosity measurements before being investigated for their ability to reduce the volatility of the *Eucalyptus Citriodora* essential oil (EO) components, by the use of Headspace-GC. While a continuous increase of EO solubility was observed with increasing the wt% of DES in DES/water mixtures in the absence of CD, it was also shown that the use of CD requires the presence of water (30 wt%) in order to fully benefit from inclusion phenomena. Such results reinforce the interest of introducing water in DES in order to obtain solutions with both appropriate viscosity and solubilizing efficiency. Accordingly, this study demonstrated that the volatility of an EO could be significantly reduced by the use of CD/DES/water formulations, and that even more effective formulations can be obtained when using CD polymers.

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On the structure and dynamics of the hydrated excess proton

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The hydrated proton is ubiquitous in aqueous chemistry, including e.g. biochemistry and electrochemistry. The minimal structure of the aqueous excess proton $H_5O_2^+$ and the dynamical exchanges of the excess proton between neighboring water molecules have been actively studied, both experimentally and theoretically, but remain very difficult to characterize. Recently, considerable progress was made towards a molecular description of these ultrafast structural fluctuations owing to several major two-dimensional vibrational spectroscopy efforts [1,2]. Here, we present a simulation study of a hydrated excess proton in liquid acetonitrile and in liquid water. Our simulations combine a DFT-based description of the electronic structure with a ring-polymer molecular dynamics description of nuclear quantum effects. We discuss the structure and dynamics of the excess proton, the proton diffusion mechanism in water, and connect our simulation results with nonlinear vibrational spectra measured experimentally.

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Hydrophobic hydration crossover: the exception rather than the rule?

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Hydrophobic solutes and interfaces are ubiquitous in nature, and play a crucial role in a variety of processes, ranging from protein folding to emulsions. Based on thermodynamic considerations on cavity formation and on hard-sphere systems, the current consensus is that as a hydrophobic solute grow in size, a transition between two regimes occurs: for small solutes, hydration free-energy is dominated by its unfavorable configurational solvent entropy, scaling with the solute volume; for larger solutes, a transition toward a vapor-like interface would manifest itself in terms of a largely unfavorable solvation enthalpy. Recent Raman spectroscopy experiments have reported changes in hydration shell vibrational spectra that suggest that the crossover between these two regimes. could readily occur around small alcohol molecules at ambient pressure. Here, we combine molecular dynamics simulations and vibrational spectra calculations for a variety of systems, ranging from the alcohol molecular solutes used in these experiments to larger fullerenes of varying hydrophobicity. I will show that our results are in sharp contrast with this widely accepted picture. The existence of a thermodynamic crossover appears to be valid only for repulsive cavities, but is not seen for realistic solutes, including very hydrophobic ones. Even when it is present, this thermodynamic transition does not manifest itself in terms of sharp structural changes in the solute hydration shell ; instead, we evidence a progressive increase in the fraction of dangling OH groups, and a weakening of the rest of the hydrogen-bonds in the hydration shell. The results are in agreement with available thermodynamic data and experimental infrared spectroscopy results. Finally, we show that the absence of crossover from a structural perspective and the fact that it is not observed for solutes other than cavities strongly questions the interpretation of previous Raman spectroscopy measurements on alcohols of increasing size. We offer an alternative interpretation of these experiments that confirms our picture of a more progressive and subtle structural change.

Competition between electronic attachment and solvation revealed thanks to radiolysis

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A convenient way to generate charges (electrons and holes) in materials and to study their fate consists in using ionizing radiation.[1] Indeed, ionizing radiation penetrates in the depth of the material, generating charge carriers. During this presentation, we will focus on the behavior of electrons. Once generated, they can either solvate or attach to the molecule(s) of interest. We will illustrate this competition between both processes by two recent examples and show how this affects subsequent reactions.

The first one is imogolite nanotubes. Two types of inorganic aluminosilicate nanotubes are studied: one is hydrophilic on its external and internal surfaces (IMO-OH) while the second has a hydrophobic internal cavity due to Si-CH_3 bonds (IMO-CH_3), the external surface remaining hydrophilic. Picosecond pulse radiolysis experiments evidence that the electrons are efficiently driven outward. For samples with very few external water molecules (around 1% of the total mass), quasi-free electrons are formed. They can attach to a water molecule, generating the water radical anion, which ultimately leads to dihydrogen. When more external water molecules are present, solvated electrons, precursor of dihydrogen, are formed. The attachment of the quasi-free electron to water is a very efficient process and accounts for the high H_2 production at low relative humidities values. When the water content increases, the solvation of the electron is preferred. These latter species lead to H_2 production, but in a lower extent than quasi-free electrons.

The second one is fluoroethylene carbonate (FEC). We have investigated the degradation mechanisms induced by irradiation in FEC, a cyclic carbonate, which is an additive commonly used in lithium-ion batteries. Picosecond pulse radiolysis experiments performed in neat FEC evidence that the $FEC^{\bullet -}$ radical anion is directly formed by attachment of the quasi-free electron to FEC, the solvation of the electron being a minor channel. The same observation was also performed in propylene carbonate, a cyclic carbonate. This behavior is due to a high affinity of the solvent for the electron.[2] However, when FEC is a solute and not the solvent, the $FEC^{\bullet -}$ species is not observed. This latter species is no longer stabilized by the solvent, and linear radical anions are formed after ring cleavage. Reaction mechanisms are proposed to account for the formation of the various gases detected, which are mainly CO and CO_2.

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Investigating solvation at metal/water interfaces: the SolvHybrid tool fueled by the GAL forcefield

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Metal/water interfaces stand out by their ubiquitous presence and their computational complexity. A sufficient phase space sampling for water is indeed excessively costly to combine with an acceptable accuracy of computation of the water/metal interactions. Purely quantum simulations are ruled out in the general case because of their cost while classical simulations lack a suitable force-field to describe correctly these interactions. Herein, we propose a mixed quantum/classical strategy to evaluate the adsorption free energy of molecules on metallic surfaces in water, wrapped up in an easy-to-use computation package [1]. The software was used for benzene and phenol on Pt (111) surfaces and yield adsorption free energy within 10 kcal/mol of experimental values, compared to the more than 30 kcal/mol error committed by the widely used Polarizable Continuum Model [2]. This strategy opens the path to an easy evaluation of solvent effects at the interface at a moderate computation cost. We present also the original GAL17 forcefield [3] that was used to evaluate metal/water interactions in this program, along with the novel version GAL19 [4], that extends its applicability to (100) or (111) surface facets of any alloy composed of Cu, Ag, Au, Pd or Pt. GAL19 has demonstrated a very acceptable average accuracy of 1.0 kcal/mol prediction over more than 7000 configurations of single water molecules on the ten monometallic facets of the previously introduced metals. The reduced computational cost that it offers compared to DFT has allowed to equilibrate for more than 500ps several monometallic and alloy/water interfaces in a reasonable computer and human time, with an accuracy unmatched by precedent forcefields. Moreover, the unique possibility to tackle alloy/water interfaces computations in classical dynamics offers exciting new domains of applications. Overall, both this forcefield and the software will be valuable tools for any interfacial process investigation by offering a convenient tool for fast and accurate water reorganization. They could therefore be applied for heterogeneous catalyst development, electrochemistry, tribology problems, and generally any interfacial process study.

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Available in latest cp2k version, at https://github.com/cp2k/cp2k

Thermo-osmosis: the path to waste heat harvesting with nanofluidic systems.

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With a fast-growing energy production based mostly on fossil fuels, our society is in crucial need of new, sustainable energies. Nanofluidic systems could play a key role in the development of such new energies. In particular, we have explored the physical mechanisms at play in the thermo-osmotic transport (i.e. the flow generation from a temperature gradient). While the standard model stated that electrostatic enthalpy excess density of ions is the main contribution to thermo-osmotic transport [1][2], we explore the importance of talking into account the solvent and ionic solvation contributions [3]. It is indeed by including in the model the competition between these last two terms that a change of flow direction is predicted for a certain critical solvent concentration, expressed in terms of the Debye length, as has been already found in previous experimental work for thermo-phoresis [4] [5].

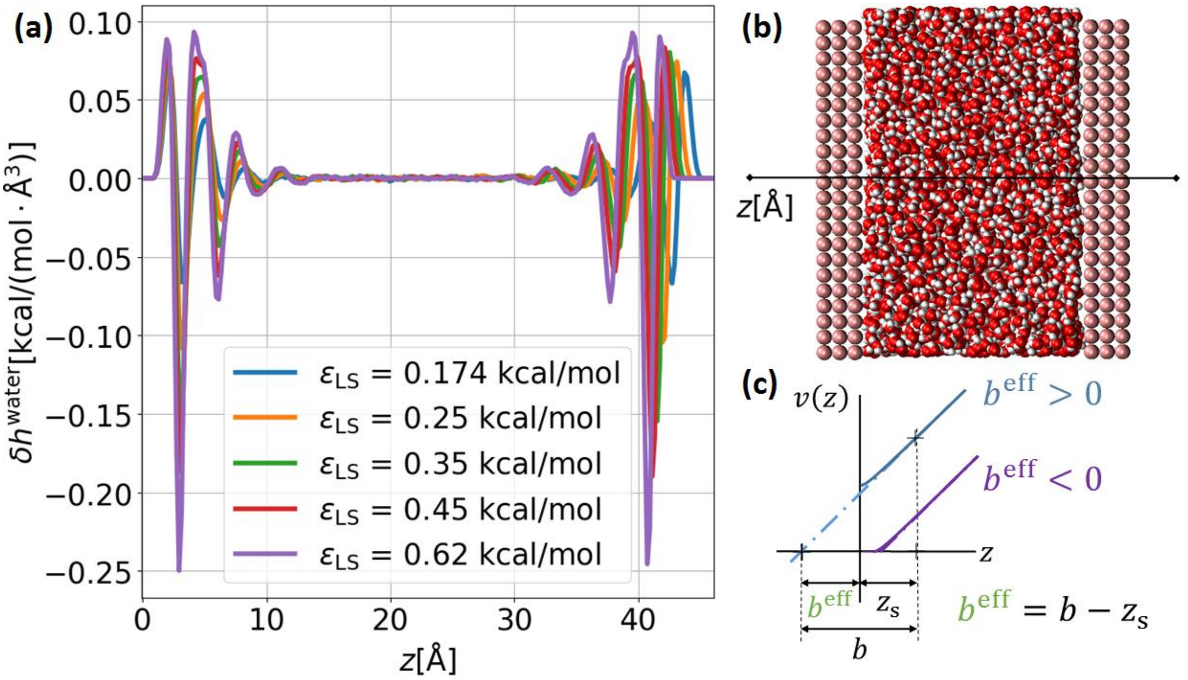

Figure 1. (a) Water enthalpy excess profile for different liquid-solid interaction energies (εLS) that correspond to different contact angles varying from 140° to 40°. **(b)** Simulated system consisting in pure water enclosed between two parallel planar Lennard-Jones walls, employed for the computation of water enthalpy excess profiles. **(c)** Schematic of the thermo-osmotic velocity profile close to the wall. We developed our model taking into account the presence of wall slip *b.* We proposed an effective description of the system in terms of b_{eff} where z_s is the shear plane position. For the non-slip situation z_s accounts for the effect of a stagnant liquid layer close to the wall.

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Revisiting the active sites on MoS_2 in aqueous solution via grand-canonical DFT: The role of water dissociation

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MoS_2 is a promising low-cost catalyst for the hydrogen evolution reaction (HER). However, the nature of the active sites remains a subject of debate [1]. By taking the electrochemical potential explicitly into account using grand canonical density functional theory (DFT) in combination with the linearized Poisson-Boltzmann equation [2], we herein revisit the active sites of 2H-MoS_2. In addition to the well-known catalytically active edge sites, also specific point-defects on the otherwise inert basal plane provide highly active sites for HER [3]. Given that HER takes place in water, we also assess the reactivity of these active sites with respect to H_2O. The thermodynamics of proton reduction as a function of the electrochemical potential reveals that four edge sites and three basal plane defects feature thermodynamic overpotentials below 0.2 V [4]. In contrast to current proposals, many of these active sites involve adsorbed OH. The results demonstrate that even though H_2O and OH block "active" sites, HER can also occur on these "blocked" sites, reducing protons on surface OH/H_2O entities (see Figure 1). As a consequence, our results, revise the active sites, highlighting the so far overlooked need to take the liquid component (H_2O) of the functional interface into account when considering the stability and activity of the various active sites.

KEYWORDS: MoS_2, hydrogen evolution reaction, grand-canonical DFT, water interface, active sites

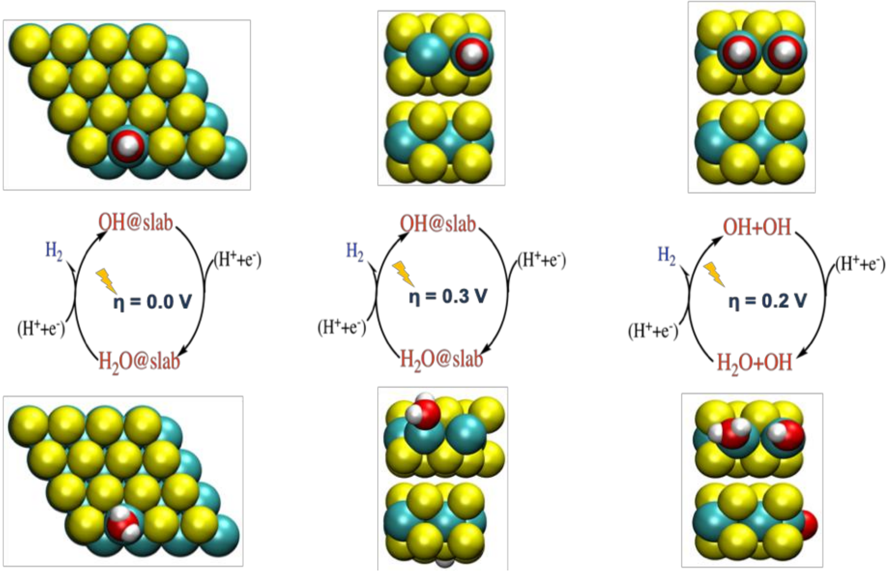

Figure 1: Catalytic cycles for production of H_2 from adsorbed H_2O and OH at different sites of 2H-MoS_2

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Probing the structural properties of the water solvation shell around gold nanoparticles: a computational study

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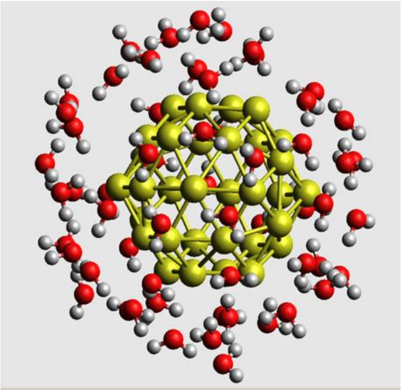
Gold Nanoparticles (GNP) have been demonstrated to be a highly versatile material for applications in diverse fields, among which as adjuvants in radiotherapy for cancer treatment.[1] This has motivated research activities into the underlying mechanisms that result upon the irradiation of GNP. Sicard-Roselli et al. proposed that in addition to the other physical mechanisms (Auger's electrons or Compton scattering), that the structure of water layers near the interface of GNP plays a significant role in facilitating production of hydroxyl radicals under irradiation.[2,3] Experimental observations have provided compelling evidences for the modified water structure on the surface of GNP[4]. In this work, a systematic computational approach was performed to investigate the water structure in the first solvation shell. Initially, the physical and structural properties of water molecules in the presence of GNP of increasing sizes were analyzed using classical molecular dynamics. The orientation of water molecules was measured in order to quantify the distribution of the dangling water configurations, which is a characteristic of the interfacial water molecules. The results demonstrate that the water molecules in the first solvation shell rearrange to accommodate the presence of GNP. Furthermore, for the largest size GNP, the water molecules rearrange to form a 2D hydrogen bond network.

Subsequently, the DFTB method was used to investigate the electronic interactions and the vibrational density of states. The interaction between water molecule and GNP involves charge transfer, due to the overlap of the frontier orbitals. As such, the water structure at the interface is assumed to result from an interplay between charge transfer and the formation of hydrogen bonds. Meanwhile, the analysis of vibrational density of states, particularly O-H stretching modes, demonstrates a decrease in the strength of the hydrogen bond networks as the size of GNP increased. Our theoretical study provides evidence for the structural changes in water solvation shell due to the presence of GNP, consistent with experimental observations.



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MD Investigation of the organic/inorganic ions selectivity at the air-liquid interface

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Aerosol particles are known to have a direct impact on the climate by directly absorbing and scattering solar radiation and indirectly by acting as cloud condensation nuclei. The main contribution to aerosol emission comes from the ocean through the production of sea spray aerosols (SSA), that mainly consist of organic and inorganic species, formed in different sizes and shapes, depending on their mixing ratios.

Experimentally Cochran et al (2016) showed how surface activity impacts the selective transfer of species from solution to the aerosol phase. Our study aims at verifying their observations by means of molecular level simulations. We chose a series of mono- and dicarboxylates (containing 4, 6 or 8 carbon atoms) with their possible counterions (K^+, Na^+, Ca^{++}, Mg^{++}). Firstly, equilibrium energies of carboxylate-inorganic ion complexes in gaseous phase were obtained by quantum chemical calculations (DFT & post-HF) to compare them with force-field results. Then, we employed classical molecular dynamics approach to model these ions solvated in a water slab. Polarizable force-field water model are applied to quantify the effect of polarization.

These calculations will allow to derive some trends on the enrichment of ions at the liquid−air interface compared to their eventual partitioning in the bulk phase. This work will overall contribute to a better understanding of the aerosol reactivity.

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Force field optimization and structural studies for deep eutectic solvents.

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Deep eutectic solvents (DES), mixtures of pure compounds, typically Lewis or Brønsted acid or basis, for which the eutectic point temperature is below that of an ideal liquid mixture, have become a promising alternative to ionic liquids (ILs) in the development of sustainable solvents. DES have been reported to possess many of the physico-chemical properties of ILs, such as a low vapor pressure, relatively wide liquid range, and non-flammability, without necessarily having their drawbacks. The most notable difference with ILs is certainly the fact that they are much easier to prepare leading to significant lower production costs compared to the former. Furthermore, a lot of the numerous constituents currently used to prepare DES are bio-sourced and biodegradable which is generally not the case for ILs.[1] Molecular dynamics (MD) simulations are a valuable tool to get structural and dynamical properties of liquids. Their use in the field of ILs, has for instance led to the prediction of a nanostructural organization in these liquids, and thus to the understanding of their unique dual-solvation property.

This presentation will focus on recent MD simulations studies on deep eutectic solvents. The first part is devolved to force field development of DES in order to reproduce static, structural as well as dynamical properties of the latter. In particular we present an alternative method to obtain Force Field parameters to those commonly used in the literature which rely on the scaling of atomic charges. We show that the sole refinement of Lennard-Jones parameters of atoms involved in the H-bond network enables for an accurate description of static, dynamical and structural properties of typical choline chloride based DES.[2] In the second part, we present the latest results of MD simulations on the menthol-thymol mixtures[3]-were we focus on the H-bonding structure and dynamics as a function of the system composition in order to get further insights of the typicality of these interactions in deep eutectics solvents.

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Polarisable force field for protic ionic liquids and deep eutectic solvents

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The relevance of molecular dynamics simulations of ionic liquids stands on the quality of the underlying interaction model, or force field, which comprises intra- and intermolecular potential energy terms that determine conformations, energetics, ordering and dynamics of molecular and ionic systems. Traditional fixed-charge force fields reproduce well the structural and thermodynamic properties, but the predicted dynamics is too slow when compared to experiment. One of the remedies is to introduce explicit polarization into existing fixed-charge force fields, for example through Drude induced dipoles [1] placed on the atomic sites. The existing effective van der Waals interaction parameters, typically a Lennard-Jones potential, should be rescaled in order to avoid double counting of the polarization (induction) effects, which are now represented explicitly [2]. Following this approach, the existing fixed-charge CL&P [3] force field was transformed into a polarisable version, CL&Pol, validated on different classes of aprotic ionic liquid [4].

Extension of the CL&Pol to protic ionic liquids and deep eutectic solvents requires correct description of strong hydrogen bonds and also of interactions with small, densely-charged ions, not available in the force field until now. An additional charge-dipole damping function was introduced in order to prevent a so called “polarization catastrophe” caused by excessive attraction between a small, densely-charged atom (like hydrogen) and a Drude dipole, as illustrated in Figure 1. A Tang-Toennies damping function [5] was implemented in LAMMPS and parametrized that allows to obtain stable MD trajectories. [6]

The CL&Pol force field was validated with a protic ionic liquid (ethylammonium nitrate) and a DES (choline-chloride–ethylene glycol). It reproduces equilibrium and dynamic properties, liquid and solid structure at consistent levels, much improved from fixed-charge models.

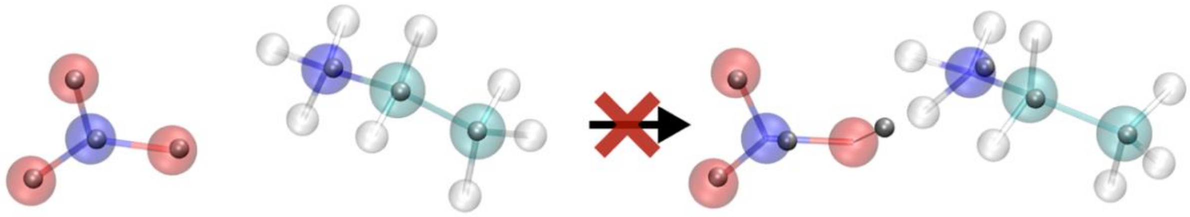

Figure 1: Schematic representation of the “polarization catastrophe” (right) in ethylammonium nitrate and its preventing with charge-dipole damping (left).

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Polarizable Dynamics applied to a Diels–Alder reaction in hyperbaric conditions

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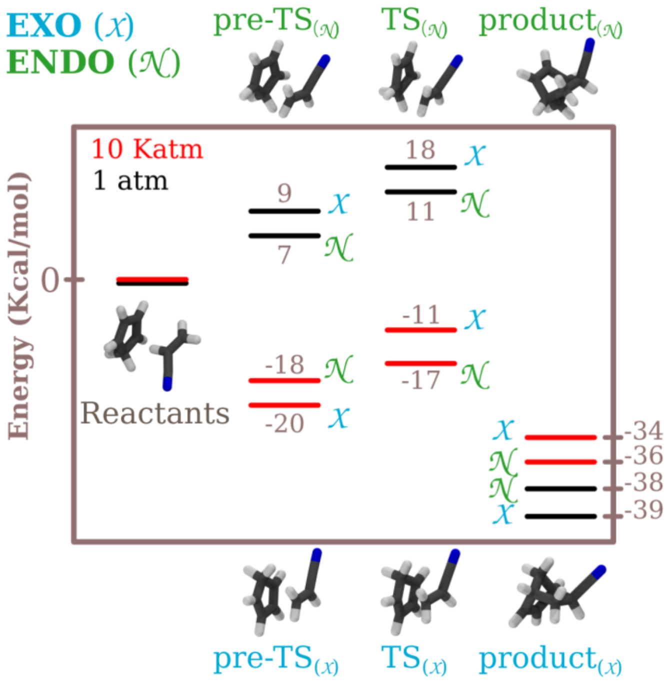
Quite often Chemistry takes place in solution, and the solvation medium may strongly affect, various and in variegate manners, chemical processes and reactions.

Since a while, the effect of high pressure regimes (HPRs) has also been recognized as a mean to affect the kinetics of certain organic reactions. Under an HPR, reactions unfeasible in conventional conditions are activated, often increasing chemo-, regio- and stereo-selectivity.[1]



In this context, we investigated the pressure effects on a prototypical Diels–Alder reaction in the condensed phase, by means of different modeling tools.

Since the HPR can modify the solute-solvent interactions, we have adopted a physically grounded description of the solvent through the AMOEBA polarizable force field,[2] coupled with a quantum chemistry method to treat the solute reacting species, in a variational polarizable QM/AMOEBA scheme.[3]

To sample adequately the large number of solute–solvent configurations, we resorted to a sequential approach: first performing fully classical polarizable molecular dynamics at low (1 atm) and high (10 katm) pressure for both the endo and exo diastereomers, and then including the quantum treatment of the solute performing short QM/AMOEBA dynamics.

The multiscale modeling approach reveals how the reaction profile at high pressure remarkably differs from that at 1 atm, showing a submerged transition state (TS) and a pre-TS structure lower in energy (see included picture). The different solvation between the endo and the exo pre-TS is revealed as the driving force toward a greatly increased preference of the reaction for the endo product at high pressure.[4]

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Structural study of ionic liquid aggregates in an aqueous biphasic system using small-angle neutron scattering.

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Phase separation in an aqueous biphasic system is the result of subtle balance between entropy and enthalpy of the system, both varying with temperature. It is highly dependent on the systems, and not clearly understood yet. In order to get more insight into the driving mechanisms of the phase separation, microscopic structural investigations are invaluable information. Small-angle neutron scattering (SANS) techniques are suited for the study of both micro and mesoscopic organisations and have been used to highlight the formation of spherical micelles of ionic liquid (IL) in aqueous solutions[1]. By contrast, very little studies have been done on that subject for aqueous biphasic solutions (ABS) where acid is added to the IL and the water, apart from evidence of similar aggregation behaviors in the IL-rich upper phase[2].
SANS measurements were performed at the ISIS and the ILL neutron sources on ABS samples to study IL micelles form and structure, using $P_{44414}Cl$ ionic liquid along deuterated nitric, hydrochloric and sulfuric acids. The micelles have been found to be cylindrical with a radius around 15 Å similar to the radius of the spherical micelles formed in acid free solutions and a variable length ranging from 50 Å to 1500 Å depending on the acid type, the acid concentration and the solution temperature.
The change in the self-aggregation behavior of the ionic liquid as a function of the latter parameters is discussed and correlated to the phase separation phenomenon.

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Studying the local structure of imidazolium ionic liquids using Hyper Raleigh Scattering

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Ionic liquids (ILs) are liquids that are entirely composed of ions. These liquids represent a new class of solvents that have attracted a lot of interest over the last 15 years due to being a potential sustainable alternative to volatile organic solvents, as well as having unique and adjustable properties that can be selected with an appropriate choice of their ionic components. ILs have a promising range of applications in domains as varied as synthesis, electrochemistry, ion extraction, nanotechnology and so on. As they are made up exclusively of cations and anions, ILs are expected to have interesting local structures and interactions at the nanoscale within their volume. Such information is crucial to understanding the intrinsic properties of these liquids.

Among the many different spectroscopic techniques, Hyper Raleigh Scattering (HRS) is recognized as a powerful technique to probe the local organization in liquids. The HRS technique is based on the principle of the conversion of two photons from a fundamental pulsed laser into a double energy photon. A highly sensitive detection permits the collection of this nonlinear intensity scattered by molecules within the volume, see Figure 1. As this process is forbidden in centrosymmetric media, it will intrinsically highlight the local organization of the bulk liquids, from short range (molecular symmetry) [1,2] to long range (intermolecular correlation) [3]. In this work the selected hydrophobic room temperature ILs are composed of the standard asymmetric imidazolium derivatives cations [$C_n$mim] (such as n = 2, 4, 6, 8, and 10) together with the unique bis(trifluoromethylsulfonyl)imide anion [NTf_2]$^-$, see Figure 1 for the structure of the [C_6mim] [NTf_2] IL. Polarization resolved measurements on the HRS intensity have been performed on these ILs, giving us more clues on the organization of their molecules. We will particularly discuss our results on the correlation of structure at longer ranges.

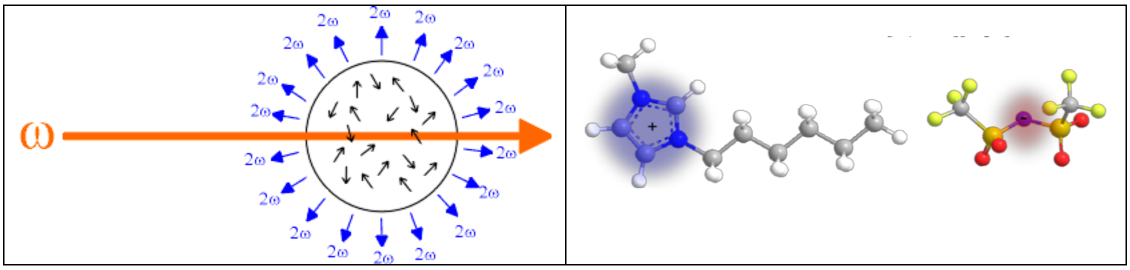

Figure 1: (Left) Principle of Hyper Raleigh Scattering. The black arrows represent the dipoles of molecules which, by their local asymmetry, convert two photons of energy ω into one photon of energy 2ω. (Right) Illustration of the anion and cation of the C6 ionic liquid.

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Vibronic spectra of a perylene diimide dye in solution through a mixed quantum-classical scheme

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In the last two decades several time-independent and time-dependent (TD) methods have been proposed to compute fully quantum spectra, although, for large systems they basically rely on harmonic approximation for the potential energy surfaces and therefore they are suited for rigid systems rather than for flexible ones.[1,2] On these grounds, a number of mixed quantum classical (MQC) approaches, where quantum and classical refers to the way the nuclear motion is treated, have been proposed. In this context, the Adiabatic Molecular Dynamics generalized Vertical Hessian (Ad-MD|gVH) approach was very recently introduced and is aimed to simulate the electronic spectra of flexible dyes in condensed phase, yet preserving their vibronic features.[3] The Ad-MD|gVH approach relies on the separation of nuclear degrees of freedom in stiff (quantum) and soft (classical) modes assuming that the former modes are much faster than the latter (adiabatic hypothesis). In this framework, the spectrum is obtained as a conformational average (over the soft modes) of vibronic spectra (for the stiff modes) that are obtained through the Generalized Vertical Hessian (gVH) vibronic approach. Specifically, the average is performed over snapshots extracted from molecular dynamics (MD) runs.[3]

In our work, to test the accuracy in the simulation of the optical absorption spectra by the Ad-MD|gVH approach, we have considered an extensively investigated perylene diimide (PDI) dye (Figure 1), whose absorption spectrum shows a strong vibronic progression.[4,5]

First, the differences in the sampled soft modes and their consequences on the prediction of the absorption spectra are evaluated by comparing the results obtained by means of a specifically parameterized quantum-mechanically derived force field (QMD-FF) and of a general-purpose transferable FF (GAFF) with those of a reference ab initio MD (AIMD) in the gas phase, in both a purely classical scheme (ensemble average) and in the Ad-MD|gVH framework.

Next, classical ensemble average and Ad-MD|gVH predictions are also obtained for the PDI dynamics in acetonitrile solution. As far as the solvent effects are concerned, we considered different embedding schemes of increasing complexity, and we have shown that to reproduce the solvent shift expected from experiments, one must explicitly takes into account the mutual solute-solvent polarization.

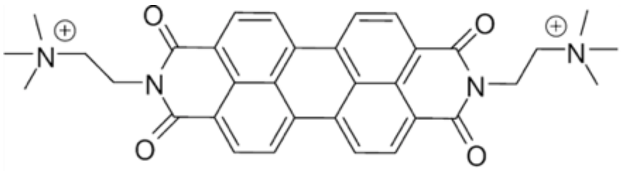

Figure 1. Chemical structure of the N,N′-bis(2-(trimethylammonium)-ethylene)-perylene-3,4,9,10-tetracarboxylic acid bis-imide PDImolecule

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Ions govern interfacial water dynamics in concentrated protein solutions

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Proteins function in crowded aqueous environments (cells, blood plasma etc.) interacting with a diverse range of compounds, most notably with dissolved ions. These interactions are very important for their proper biological functioning. In the present study we combine NMR relaxation experiments and theory to probe water dynamics in concentrated aqueous solutions of hen egg-white lysozyme (LZM) and bovine serum albumin (BSA). The experiments reveal that presence of salts (NaCl or NaI) in these solutions leads to an opposite ion-specific response for the two proteins: an addition of salt to LZM solutions increases water relaxation times with respect to the salt-free case, while for BSA solutions a decrease is observed. Further, the magnitude of the change depends on the position of the ion in the Hofmeister series. We have already reported on such trends at a single Larmour frequency [1]. Here we extend the NMR dispersion data to several Larmour frequencies and we develop a multi-scale model, which reproduces the experimental data over a large frequency range, 10kHz to 110MHz. The core of the model lies in the modification of the protein surface roughness and thus access to surface water sites via specific ion-binding. [2]

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How tracking confined water with solid state NMR?

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Confined water molecules are ubiquitous in various natural (proteins, cells, biominerals) and synthetic systems (mesoporous materials). We will show in this contribution how solid state NMR (ssNMR) spectroscopy is a well-adapted tool to characterize confined water at the molecular level and reveal key features such as interfacial interactions and dynamical behavior. Various examples will be highlighted including drug delivery systems, liposomes, and bone tissue.

Tracking protein-protein assembly using water protons NMR chemical shifts

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Abstract

Proteins interaction (attractive or repulsive) is one of the most important topics in biophysics. The protein-protein interaction is one of the main factors governing the rheology of fluids rich in proteins. Protein-protein interactions are also responsible for the formation of a wide range of large molecular buildings displaying crucial biological functions. It has been widely reported that in most protein-protein interactions there are an important H-bond network formed by water molecules between the neighbor protein molecules. It has also been reported that the structure of these surface layers of water molecules is sensitive to proximity of the neighbor's molecules. Thus, quantitatively monitoring the evolution of the structure of water surface layers can be a quite interesting probe to study protein-protein interaction. Protons chemical shifts, as measured by NMR are probably the most sensitive method to measure hydrogen bond strength and, thus, water structure. However, this specific information is hard to obtain since the very abundant signal of bulk water often masks the one(s) of water layers at the protein surface. In the present work, we have NMR pulse field gradient technique to monitor specifically the strength of water molecules at the surface of proteins and their evolution in repulsive and attractive conditions. Pulse field gradient technique is able to eliminate signal of bulk fast moving (translation diffusion) water molecules allowing one to measure the signal of the protein-associated water molecules. We have quantified the difference in water bond strength in different conditions of temperature, concentration of proteins and in the present of water bond disrupting molecules as polysaccharides and monosaccharide. These data indicate that the measurement of water chemical shifts can give quantitative information about the structural adjustment of the protein surface upon protein-protein interaction.

DFT-MD simulation on water/SAM-silica interfaces of various hydrophobicity

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Our group has been focusing on studying how the interfacial boundary conditions modulate the interfacial HB-Network of water molecules and any surface in regard.

The influence of the hydrophobicity/hydrophilicity at the atomic level on the interfacial water structure has been previously unraveled by our research on silica/water interfaces by DFT-based Molecular Dynamics simulations.[1-4] In particular, we have found that the interfacial water molecules above a hydrophobic surface prefer to form water-water H-Bonds parallel to the surface, which leads to a two dimensional water network (2DN)[5] structure also called Horizontal order, whereas above a hydrophilic surface vertical ordered structures based on surface-water HBonds are favored, called Vertical order.

Inspired by these results, we now generalize the horizontal/vertical water order structures on a microscopic platform made of self-assembled monolayer chains (SAMs) anchored on a silica substrate, identical to the platforms used in several experiments for unraveling hydrophobic/hydrophilic interfacial structures.

We will present our structural results on water/OTS-silica (hydrophobic) and water/PEG-silica (hydrophilic) by DFT-MD simulations. These systems are very large in size and several 100' ps DFT-MD trajectories could be obtained through a European PRACE-2019/20 project. SFG (Sum Frequency Generation) vibrational spectra are extracted from the simulations and directly compared to Prof Petersen's SFG experiments in Bochum-Germany. The assignments of these spectra are done through the microscopic structures unraveled from the trajectories (from both the SAMs and water points of view).

We will in particular show how the SFG theoretical spectra match the experiments, and how the high dynamicity of the PEG chains at the interface with the water due to the PEG-Oxygens being in pursuit of the water molecules at the interface is the essential key to the understanding of the SFG spectra. Horizontal and vertical orders of the water interface respectively in contact with OTS and PEG chains will be revealed and shown in perspective to the SFG signatures. This will allow us to validate a new and innovative microscopic descriptor of hydrophobicity and hydrophilicity at the molecular level.

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Second Harmonic Generation at liquid interface: a multi-scale numerical approach

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In many fields of chemistry and physics, it is essential to understand the structure and dynamics of interfaces, such as gas-liquid, solid-liquid or liquid-liquid interfaces. The inherent asymmetry of the forces present at these interfaces influences their properties and determines in large part their chemical composition, molecular structure, dielectric and transport properties. In this context, surface analytical tools directly monitoring molecular organization and molecular adsorption at interfaces are highly desirable.

Second order non-linear optical methods, Sum Frequency Generation (SFG) or Second Harmonic Generation (SHG) for instance, are methods of choice to probe interfaces: they are non-intrusive, intrinsically surface specific and the signal collected can contain structural and dynamical information on fluid interfaces. However, it is not always straightforward to interpret the outcomes of these experiments. Indeed, if several aqueous solution/air interfaces are now well characterized by the SHG technique, the link between the macroscopic non-linear susceptibility tensor χ and the microscopic hyperpolarizability β is still debated. We have therefore developed a multi-scale numerical approach to gain insight into the link between the molecular structure of the liquid interface and the surface-Second Harmonic Generation signals.

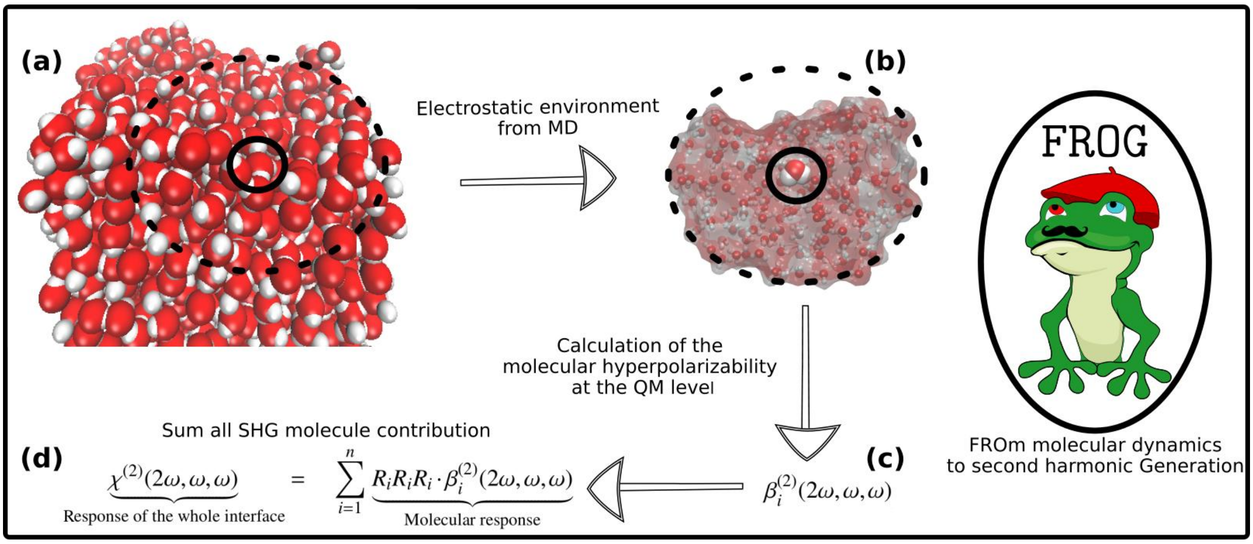

Figure 1: Scheme of the home-made software FROG calculating molecular hyperpolarizabilities β(2ω,ω,ω) within an electrostatic embedding framework at the QM level using DALTON [1]. The surface SHG susceptibilities χ(2ω,ω,ω), is obtained by summing up the contributions of all the molecules in the laboratory frame.

Our numerical method (named FROG: FROm molecular dynamics to second harmonic Generation) starts from a microscopic structure provided by a classical Molecular Dynamic (MD) run, Figure 1 (a). For each molecule at the interface, we use the Density Functional Theory within a Polarizable Embedding (PE) framework [2] to solve the electronic states, Figure 1 (b). Then, the quadratic response scheme is used to extract molecular hyperpolarizabilities $\beta(2\omega,\omega,\omega)$, Figure 1 (c). This procedure has already provided trustful results for water in the bulk phase [3]. Finally, the experimental observable of the interface, $\chi(2\omega,\omega,\omega)$, is approximated by the sum of all the individual local molecular contributions [4], Figure 1 (d).

In this presentation, I shall briefly present the numerical procedure, and discuss our recent results on the water liquid-vapor interface. These results show that some very common approximations used to analyze the SHG results are not valid at the water liquid-vapor interface. In particular, within our approach, the Kleinman symmetry is respected at the molecular level, in all the layers forming the interface, from the bulk towards the vapor. This result raises questions, and the modeling of the SHG signal of the aqueous interface remains a challenge.

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Theoretical core spectroscopy of molecules interacting with ice surfaces

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Ice plays an essential role as a catalyst for reactions between atmospheric trace gases. The uptake of trace gases to ice has been proposed to have a major impact on geo-chemical cycles, human health and ozone depletion in the stratosphere [1]. X-ray photoelectron spectroscopy (XPS) [2], serves as a powerful technique to characterize the elemental composition of such interacting species due to its surface sensitivity. Given the existence of complex physico-chemical processes such as adsorption, desorption and migration within ice matrix, it is important to establish a theoretical framework to determine the structural and electronic properties of these molecules or species under different conditions such as temperature and concentration. The focus of this work to construct an embedding methodology employing Density Functional (DFT) and Wave Function Theories (WFT) to model and interpret photoelectron spectra of adsorbed halogenated species on ice surfaces at the core level with the highest accuracy possible.

We make use of an embedding approach utilizing full quantum mechanics to divide the system into subunits that will be treated at different levels of theory [3]. The goal is to determine core electron binding energies and the associated chemical shifts for adsorbed halogenated species such as molecular HCl and the dissociated form, Cl^-, either at the surface or embedded in the liquid-like layer [4]. The core energy shifts are compared to the data derived from the XPS spectra [4].

We show that the use of a fully quantum mechanical embedding method, to treat solute-solvent systems is computationally efficient, yet accurate enough to determine the electronic properties of the solute system (halide ion) as well as the long-range effects of the solvent environment (ice).

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