Molecular reactions at aqueous interfaces

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Aqueous-interfacial and on-water molecular reactions across diverse chemistries

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Abstract

This review aims to critically analyze the current state of knowledge in the emerging field of chemical reactivity at aqueous interfaces. The area has evolved rapidly since the discovery of the so-called "on-water catalysis" effect, alluding to the fact that many chemical reactions experience a dramatic acceleration at the surface of water or different aqueous interfaces with hydrophobic media. The immense importance of this phenomenon is discussed first by reviewing some critical experimental studies in the fields of atmospheric and synthetic organic chemistry, as well as related research exploring the origins of life. The physicochemical aspects of the topic are analyzed afterwards. First, with a concise analysis of issues such as the structure, the dynamics, and the thermodynamics of adsorption/solvation processes at aqueous interfaces. Then, presenting the basic theories intended to explain interface catalysis, followed by the results of advanced ab initio molecular dynamics simulations. Though some topics addressed here have already been the focus of previous reviews, their interconnection across diverse disciplines has not been sufficiently highlighted in the literature. For this reason, this manuscript seeks to provide a common perspective by trying to identify the most fundamental issues still incompletely understood in this fast-moving domain.

Introduction

Chemistry at aqueous interfaces is a vast subject that encompasses processes from quite different domains. Specifically, we deal here with processes occurring at liquid water-vapor interfaces (or air-water interfaces) and the interfaces of liquid water with hydrophobic environments. **Figure 1** illustrates a few examples of systems that are covered by this review. Many chemical and photochemical reactions are dramatically accelerated when they occur at these interfaces, in comparison with gas-phase or bulk water, and this phenomenon is now designated as "on-water" catalysis.[1] The term chemistry "on-water" must be understood here in a broad sense, i. e. the chemistry that occurs at, or near aqueous interfaces in oil-water emulsions and other dispersed systems, aerosols, sprays, nano and micro water droplets, as well as extended air-water interfaces. It goes without saying that such a variety of systems may involve phenomena implying quite different mechanisms, which makes the implementation and interpretation of experimental measurements often a complex task. The potential implications of interfacial reactions are widespread because they are omnipresent in atmospheric, environmental, biological, prebiotic, or synthetic organic chemistry, to cite the most relevant domains. Interfaces of liquid water with either solids or biomolecules, as well as the surface of ice, share many similarities with the former but are not directly concerned by the subject of the present review.

The reasons underlying rate acceleration at aqueous interfaces remain unclear however. In contrast to bulk solvation, the theory of interfacial solvation is still in its early stages. The formation of hydrogen-bonds with dangling protons at the interface was first proposed to explain the catalytic role of the interface,[2] but many other causes can be invoked: confinement of reagents, partial solvation, preferential orientations, curvature in nanodroplets, water surface pH, etc. It is worth pointing out that physicochemical concepts from the bulk are not always applicable at interfaces, as the latter are disordered systems of nanometric thickness displaying sharp configurational fluctuations. Experimental studies based on macroscopic properties such as surface tension[3,4] have provided invaluable data on interfacial thermodynamics and structural properties. However, only with the progress of non-linear second-harmonic generation (SHG) and sum-frequency generation (SFG) spectroscopies,[5] and other interface-sensitive molecular techniques, the microscopic details of interfacial phenomena are being elucidated. In parallel, *ab initio* Molecular Dynamics (MD) simulations and related approaches have provided priceless information on these issues.[6-8]

Nevertheless, the literature remains scattered across various fields. In fact, despite the similarities between all these chemistries and the existence of some reviews on restricted aspects of the topic, a general discussion on the available experimental and theoretical studies, placing them in a shared perspective, is still lacking. In this review, we will provide such a perspective through a comprehensive and critical survey of the recent literature aiming to highlight the main challenges that need to be addressed in order to advance the state-of-the-art in the field.

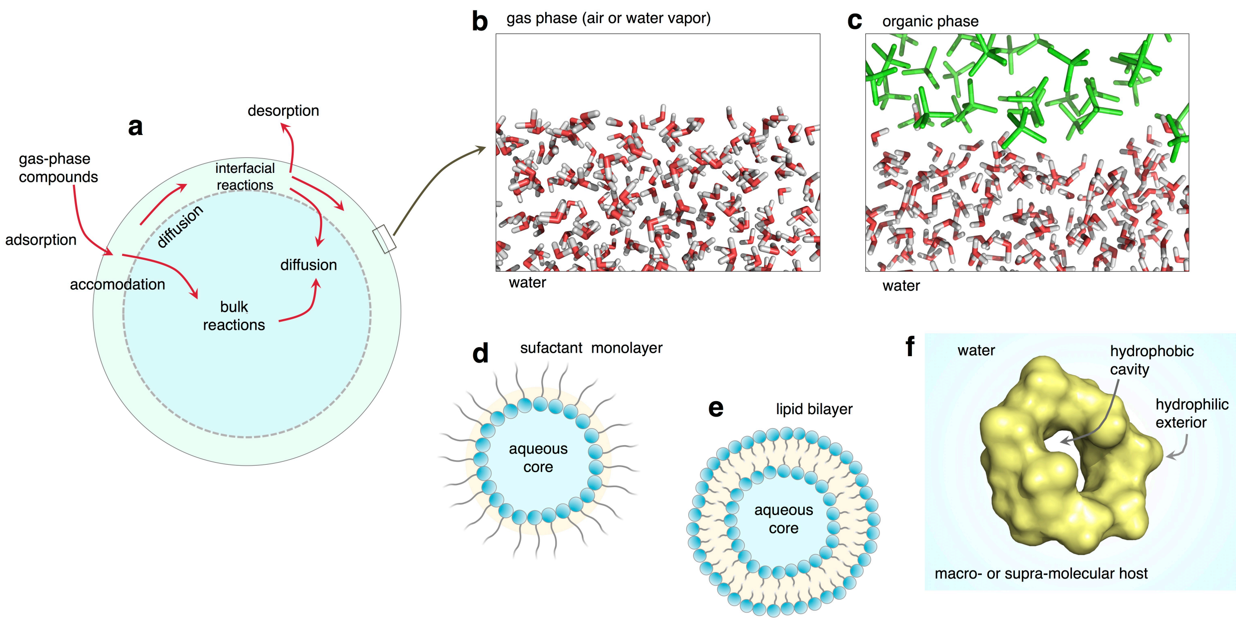

Figure 1. Aqueous interfaces contemplated in this review: a) the air-water interface at the surface of a water droplet with indications of the different processes that can take place, b) detail of the liquid water-vapor interface, c) interface of liquid water with a non-miscible organic solvent (CCl_4 here), d) inverted micelle in aqueous organic aerosols, e) vesicles, f) macro- or supra-molecular systems with a hydrophobic cavity that can host hydrophobic guest molecules.

Chemical reactions at aqueous interfaces

Many contributions in this field come from the atmospheric chemistry community because reactions at the air-water interface of cloud water droplets and aqueous aerosols may proceed at higher rates than gas-phase reactions, influencing the atmospheric budget of trace gases.[9-12] Further interest comes from the field of synthetic green chemistry. The need to develop green processes for the synthesis of organic compounds that decrease the negative environmental impact of current industrial practices pleads for the use of non-organic solvents such as water. Experiments have shown that reactions in water microdroplets generated by electrospray ionization undergo remarkable acceleration with respect to bulk-phase processes, and due to large surface to volume ratio, the air-water interface is thought to play a key role.[13-16] Moreover, dispersed systems such as polyelectrolyte solutions, micellar solutions, oil-in-water microemulsions or vesicle dispersions, have been proposed to overcome water solubility limitations and develop biomimetic reactors within which reactions can proceed.[17,18] Aqueous interfaces have also been evoked as possible environments in which prebiotic processes could have taken place and led to the origin of life. For instance, orientation, alignment and proximity of functional groups is essential to the synthesis of peptides by the ribosome, and air-water interfaces in inverted micelle atmospheric aerosols or in the surface of oceans and lakes could have been a rudimentary prebiotic system mimicking this functioning.[19,20]

We have selected some illustrative experimental works, and organized them in four specific (and to some extent, arbitrary) areas that are not disjointed, but rather overlap in many ways.

Atmospheric and environmental chemistry. The role of condensed matter in the Earth's atmosphere is widespread. Aerosols scatter sunlight and serve as seeds for the formation of clouds, which has significant consequences in climate regulation.[21] Condensed matter in its different forms also supplies a medium for chemical transformations. Well-known examples are the oxidation of SO_2 to sulfate in water droplets, which leads to acid-rain formation in the troposphere,[22] or the heterogeneous reactions that lead to ozone depletion in the stratosphere.[23] Indeed, despite a small volume fraction of atmospheric condensed matter (about 7% of the total volume of the troposphere contains clouds, and a moderately dense cloud contains about 5×10^{-7} cm^3 of water per cm^3 of air),[9] its relevance is now recognized.[9,24,25] It influences the atmospheric budget of trace gases through the modification of the cycles of nitrogen, sulfur, and various atmospheric oxidants such as ozone.[26,27] In addition, some reaction pathways that are unfeasible in the gas-phase (e.g. ionic dissociations) may be quite favorable in the condensed phase, producing new species.[28] In line with the subject of this review, we put the focus on liquid water interfaces (water droplets, aqueous aerosols) even though the heterogeneous reactions at the surface of solid matter such as carbonaceous particles or mineral dust have comparable importance.

When atmospheric trace gases interact with a water droplet, several phenomena can take place (**Figure 1**) including uptake, diffusion and reaction at the surface, desorption, mass-accommodation, diffusion and reaction in the bulk.[29] Bulk reactions are relatively well-understood[30] but not those occurring at the air-water interface. Several studies have confirmed that the efficiency of interfacial processes in the atmosphere may be quite significant, compared to bulk processes.[7,11,31-33] This is due in part to the high surface to volume ratio characterizing atmospheric droplets and aerosols. However, there is evidence of specific effects that accelerate chemical and photochemical reactions at aqueous interfaces; some particular examples using different experimental platforms are outlined below.

Adsorption of trace organic molecules on water film surfaces enhance their reaction with atmospheric oxidants.[33] Electrospray-mass-spectrometry studies[34] showed that when benzoate is allowed to react with OH radicals at the air-water interface, H-abstraction from the aromatic ring is mainly observed. At the same time, this reaction is negligible both in the gas-phase and bulk water. The rationalization of this results goes in terms of the higher polarity of the transition state for the OH-radical addition compared to H-abstraction.[34] A similar experimental technique was used by Enami et al[35] to study the reactivity of isoprene at mildly acidic water surfaces showing that it can undergo cationic oligomerization. The authors suggested a superacidity behavior of the air-water interface with pH < 4 water, a result that has raised some debate (see below). Fatty acids, which are generally not sensitive to actinic radiation, produce aldehydes and other oxygenated species when a monolayer at the water surface is irradiated in the 280-330 nm region.[12] The process seems to involve UV-absorption to a triplet state followed by the homolytic OH dissociation or by reaction with an adjacent fatty acid molecule at the air-water interface. The conclusions of these experiments, however, have been challenged by subsequent studies by Shrestha et al[36] and Rapf et al,[38] who have emphasized the need of photoinitiators for reactions of this type to take place, as fatty acids are not themselves photoactive. Upon irradiation of nebulized pyruvic acid, zymonic acid has been observed among the products formed,[39] as opposed to other conditions, suggesting that it could be generated by reactions at the droplet surface. Other interesting interface-assisted photochemical processes can be found in the review by George et al.[11] Colussi and coworkers[40-46] have devoted considerable effort to the study of the ozonolysis reaction and the chemistry of the Criegee intermediate at the air-water interface, which are chemical processes with broad implications in the atmosphere, as they represent a major sink for unsaturated volatile organic compounds produced by plants, particularly isoprene and monoterpenes. The oxidation reaction of anthracene by ozone on aqueous surfaces was studied by Mmereki et al,[47] who showed that it may be of comparable importance to gas-phase oxidation by OH in the atmosphere. Chemistry at the surface of sea-salt aerosols and its atmospheric implications have been extensively studied by Finlayson-Pitts and coworkers, who have emphasized the role played by the air-water interface. For instance, the main sources of Cl_2 and Br_2 gases from sea-salt aerosols under dark conditions are the interfacial reactions of the corresponding halide anion with OH and O_3, respectively.[48] When concentrated NaCl aerosols are irradiated at 254 nm in the presence of O_3 to generate OH radicals, the observed amount of Cl_2 gas produced is in good agreement with estimates based on field measurements in the marine boundary layer.[10] At the surface of aqueous aerosols, halide ions (and also some cations) influence other interfacial reactions such as the production of NO_2 from photolysis of nitrate.[49-51] Some fundamental knowledge about the water effects on reactions at the air-water interface of water droplets and aqueous aerosols comes from the study of small water clusters and further details on this topic can be found in the review by Vaida.[52]

Microdroplets as synthetic chemical reactors. Reactivity in microdroplets is emerging as an up-and-coming tool in synthetic organic chemistry. Acceleration of many organic reactions in aqueous media has been known for decades,[53-56] especially after the seminal work by Breslow and coworkers on the Diels-Alder reaction.[57,58] This is rather good news because one could consider water as the ideal green solvent. Studies by Sharpless and coworkers[1] pointed out that some reactions proceed optimally in pure water when insoluble reactants are stirred in the aqueous medium, and denoted such processes "reactions on-water". Such processes occur in aqueous suspension and thus, hydrophobic effects might be claimed to provide the driving-force for rate acceleration. Yet, experimental results showed that observed rates are not the sole consequence of an effective concentration increase,[1] and since the pioneer work of Sharpless and coworkers,[1] "on-water" chemistry has been steadily expanding (see for instance the reviews by Butler and Coyne[59] and by Butler et al[60]).

In recent years, synthesis in small volume microreactors has been the subject of intense research.[14] This includes studies in microdroplets generated by a variety of electrospray and other spray mass-spectrometry methods,[13,15,20,61-66] levitated droplets,[67] thin films on surfaces[68,69] or microfluidic systems.[70-73] In many cases, the reaction rates are higher with respect to the reference bulk reaction (see a counterexample here[74]) but the effects responsible for such rate accelerations are still unclear. Confinement of reagents and increased concentration (due to solvent evaporation) are probably important factors,[14] but the large surface to volume ratio characterizing these systems also points at specific interface effects.[13-16] Experimental data supporting this statement were reported by Cooks and coworkers[75] in the study of competitive substituent effects in Claisen–Schmidt reactions. Other experiments by Mellouli et al[72] using a biphasic microfluidic approach, which allows getting better control of the generated interfaces and water surface area, concluded that stabilizing hydrogen-bonds play a role in decreasing the activation energy, as previously suggested by Jung and Marcus[2] (see below). The observed rate increase is sometimes very large. For instance, the Pomeranz–Fritsch synthesis of isoquinoline in charged microdroplets generated by electrospray has been reported to be at least 10^6 times faster than in bulk.[76] Likewise, Enami et al[77] showed that Fenton (Fe^{2+} + H_2O_2) and Fenton-like (Fe^{2+} + O_3) reactions proceed 10^3-10^4 faster at aqueous interfaces than in bulk aqueous media due to a modified geometry of the hydration shell of Fe^{2+}, which may have implications not only for advanced oxidation processes but also in atmospheric and biological chemistries. Other exciting results have been obtained by Lee et al,[78] who have observed spontaneous formation of hydrogen peroxide in sprayed water microdroplets. The authors have considered and analyzed several possible mechanisms and concluded that the process occurs at or near the interface, where the strong intrinsic electric field is enough to ionize hydroxyl anions, generating hydroxyl radicals that then recombine to form H_2O_2. Although the mechanism is not fully understood, the result is quite significant because H_2O_2 has great importance in biomedical and industrial applications, and it is also a key compound in the atmosphere due to its oxidative capacity.[79] The results of Lee et al[78] have been supported by the work of Gao et al[80] showing that Dakin and Baeyer-Villiger oxidation reactions proceed in water microdroplets without the addition of any peroxides and acid or base catalysts, as usually required.[80]

It is worth reminding that reactions in microdroplets and electrospray-mass spectrometry techniques are not only interesting from the point of view of analysis and synthesis, as mentioned above, but also to study a wide variety of problems in atmospheric,[35,43,45] biomedical[81-83] or other domains in which aqueous interfaces play a central role. Moreover, possible scale-up of microdroplet chemical synthesis by heated ultrasonic nebulization opens interesting industrial perspectives.[84] Finally, it must be noted here that experiments with electrospray techniques and their interpretation as purely interfacial reactions have raised certain controversy in the literature because of the possible influence of ions[85] and gas phase chemistry.[86] Two illustrative examples of the controversy will be commented on below.

Prebiotic chemistry. The role played by aqueous interfaces on the chemical mechanisms that led to the origin of life on Earth has received considerable interest in recent years. It is explained by the fact that compartmentalization, as well as the emergence of genetic materials, is considered to be a key prerequisite in the long journey towards protocells capable of growth, division and Darwinian evolution.[87] Colloidal systems, resulting from self-organization of amphiphilic molecules in aqueous environments, provide such suitable compartments in which complex chemical reactions could have taken place in the prebiotic era. In particular, vesicles formed in bulk waters (lakes, rivers) have attracted considerable attention because the amphiphilic bilayer that separates the aqueous interior from the exterior media in these structures bears a resemblance to cell membranes.[17,18,88-90] In such confined volumes, molecular crowding increases the probability of reactive encounters between chemical species, and at the same time, limits the diffusion of products. Hence, the synthesis of complex biomolecules required for the development of primitive living organisms is strongly favored compared to similar reactions in bulk.[73] Though molecular crowding is not the only important feature controlling the chemical reactivity inside the vesicle, and several works have emphasized the importance of the interface in terms of molecular alignment, electric charge, pH, etc. For instance, experiments have shown that the polycondensation of aminoacids and peptides is assisted by the lipidic bilayer, not only as a favorable environment for the reaction to take place,[91,92] but also as an active acid-base catalyst.[93]

Other possible prebiotic chemical reactors are the inverted micelles structures of atmospheric organic aerosols.[94-96] In these systems, the organic content may be quite high (up to 50%), and there is direct evidence that palmitic and other fatty acids form the organic film on the exterior of marine aerosols.[97,98] Interestingly, it has been shown that the size of bacteria and viruses can be predicted from atmospheric aerosols by combining atmospheric aerodynamics and gravity equations.[95,96] Here too, the role of the interface has been emphasized and supported by different studies. Using infrared reflection absorption spectroscopy (IRRAS) and Langmuir trough methods, Griffith and Vaida[99] have observed peptide-bond formation in the Leucine ethyl ester condensation process in presence of Cu^{2+} ions at the air-water interface. Such condensation reactions are thermodynamically and kinetically unfavorable in aqueous environments, but at the air–water interface, there's evidence suggesting the spontaneous peptide bond formation. The interaction of Cu^{2+} ions with the amine group of the Leucine ester might play a role by inducing an orientational change. Note that the probe depth of the IRRAS technique can be as large as 1–2 μm, i. e. much larger than other interface sensitive techniques such as SFG, for instance, but this probe depth was considered suitable for the reactive region of interest.[99]

Experiments in microdroplets have been reported as well. Lee et al[100] have observed spontaneous reduction of several organic molecules without assistance of reducing agents, catalysts of external charges, which could represent an essential reduction route in prebiotic conditions. The mechanism is unclear but might involve the oxidation of OH^- at the droplet surface, likewise in the spontaneous formation of H_2O_2 described above.[78] Nam et al[101] have studied aqueous microdroplets containing a mixture of sugars and phosphoric acid, and observed that phosphorylation proceeds spontaneously in such conditions. The effect has been ascribed to a cancellation of the entropic barrier when the process occurs at the surface of the microdroplet, whereas such barrier prevents the uncatalyzed reaction to proceed in bulk solution. Nam et al have also reported the synthesis of uridine[101] and other ribonucleosides[20] in an aqueous microdroplet containing D-ribose, phosphoric acid, and a nucleobase. As an example of the controversy surrounding some results obtained with electrospray techniques, Jacobs et al[86] have reported different conclusions for the reaction between sugars and phosphoric acid. The authors have used an experimental setup in which droplet generation is separated from ionization, so that they have been able to analyze different possible sources of rate acceleration. They have concluded that part of the products could originate from gas-phase chemistry, which in some cases may complicate the interpretation of rate acceleration in droplets generated by electrosprays or its variants.

The preceding results exemplify the role aerosols and microdroplets could have played for the generation of chemical complexity in prebiotic chemistry,[19] which could have also involved sunlight-driven processes.[102]

Reactions at organized molecular interfaces. Quite a diverse variety of processes can be placed in this category that includes systems possessing an organized amphiphilic interface with ability for molecular recognition, possibly including a binding site, and compartments that can host chemical reactions. Of course, some systems described above belong to this category, such as the vesicles hosting prebiotic chemical reactions or the atmospheric organic aerosols structured as inverted-micelles. Chemical reactions in biological membranes could be included in this class of interfacial processes too.[103] Nevertheless, the focus here is on synthetic reactions in water that mimic the functioning of enzymatic catalysis in biology, which have particular interest in the field of Green Chemistry. The term “artificial enzymes” was coined by Breslow,[104,105] who introduced the use of functionalized macromolecules, mainly cyclodextrins, as water-soluble catalysts that can host a non-polar reactant guest in a hydrophobic cavity. The design of enzyme mimics or “chemzymes” is a field of intense research,[106-109] which has turned into the more general one of “molecular reaction vessels”. Antibody catalysts or “abzymes”,[110] functionalized nanomaterials or “nanozymes”,[111,112] dendrimers,[113,114] micellar[115] and other disperse interface-rich structures (polyelectrolyte solutions, microemulsions, vesicles, ..),[18] as well as enzymes confined in small-volume environments[17] have been considered in detail previously. Therefore they will not be further described here.

Solvation at the water surface

The hydrogen-bond network formed by water molecules in the liquid state, and its cooperative character, confer this environment its unique properties. At the surface of water, the network is inevitably disrupted and the physical and chemical properties of molecules lying there (hydrogen-bonds, dipole moment, acidity, etc) differ from those in the bulk. To address how these changes affect chemical reactivity is a complex issue that requires a close examination of the structure and properties of the water surface. This section reviews some theoretical and experimental aspects on structural (hydrogen-bonding), chemical (acid/base) and solvation (dynamics, thermodynamics) properties of the liquid water-vapor interface.

Chemical properties of the water surface. The structure of the water surface has been a subject of intense debate for many years.[116] Most of the current knowledge comes from SFG vibrational spectroscopy and from calculations. Du et al[117] reported the first SFG spectrum of the liquid water-vapor interface and the authors concluded that about 20% of water molecules display a dangling bond, the free OH bond that is projected into the vapor phase. This result predicted by pioneer MD simulations[118,119] was subsequently confirmed and rationalized by classical SFG and ab initio simulations.[120-122] Further theoretical studies support a 2D H-bond network of interfacial waters (the water “skin”) with oscillating OH bonds around a plane parallel to the instantaneous surface.[123] A schematic view of the water surface is displayed in **Figure 2**, which also shows a typical density profile from classical MD simulations. The thickness δ of the air-water interface is usually deduced from the density profile $\rho(z)$ by fitting a function:

$$\rho(z) = \frac{\rho_o}{2}\left(1 + \tanh\left(\frac{Z - Z_G}{\delta}\right)\right) \quad (1)$$

where ρ_o is the bulk density, Z_G is the position of the Gibbs-dividing-surface (Z at which $\rho(z) = \frac{\rho_o}{2}$). Values of δ can change significantly with the theoretical model[124-127] but common values are 10-15 Å at 300K.

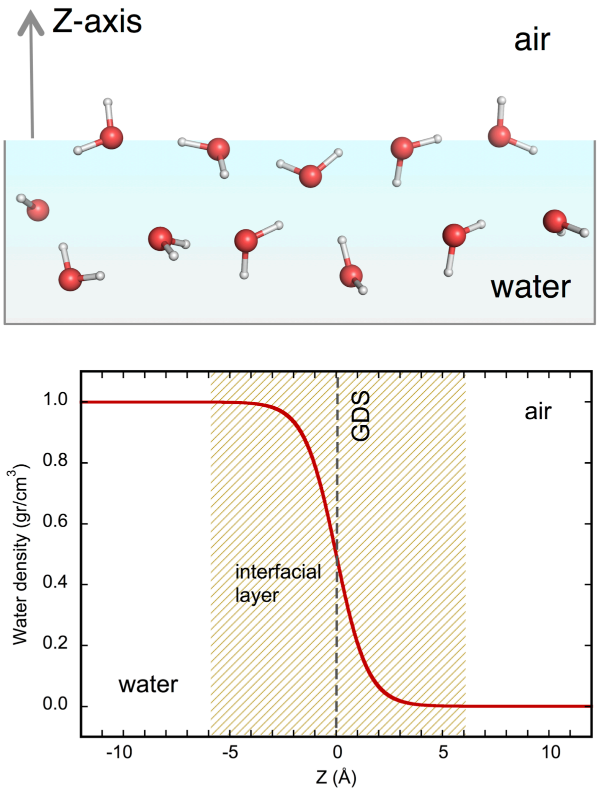

Figure 2. Schematic structure of the water surface showing free OH groups pointing towards the air layer, and typical density profile of water at the air-water interface from MD simulations. The vertical dashed-line indicates the Gibbs-dividing-surface (GDS) where the density is half of the bulk density. The width of the interface layer depends on simulation models but is typically in the range 10-15 Å.

The dynamics of water reorientation has been a broadly studied subject, both in bulk water (see for instance Laage and Hynes[128]) and at interfaces.[127,129-136] Simulations[130] and experiments using femtosecond pump/probe vibrational sum-frequency spectroscopy[129] have shown that reorientation of free OH groups in the liquid-vapor interface takes place on a subpicosecond time scale, i. e. several times faster than in bulk. In contrast, simulations by Verde et al[127] have shown that reorientation of bonded OH groups happens at a rate similar to that of bulk water.

Particularly relevant to chemical reactivity is the acid/base character of the water surface, i.e. its ability to donate or accept protons, an issue that remains incompletely elucidated and has raised intense controversies in the literature. This issue is connected, on the other hand, to the properties of water in nanoconfined environments such as inversed micelles, a topic that we will not develop here but which has attracted a lot of attention, while it remains incompletely understood (see for instance the works by Levinger and coworkers[137,138]). Interestingly, experiments and calculations reveal unforeseen acid/base behavior of aqueous interfaces. For instance, HCl is fully dissociated at the interface but HNO_3 is essentially in its molecular form,[139-141] unless ions are present,[142] and HCOOH dissociates faster at the interface than in the bulk.[143] Vibrational spectroscopic studies of the ionization state of the L-phenylalanine aminoacid indicated a decrease of the pK_a of its polar groups at the ait-water interface.[144] Depending on experiments and calculations (see for instance[145-157]), apparent opposite conclusions have been deduced for the interface affinity of hydronium and hydroxide ions and their spatial distribution, though most recent SFG experiments on D_2O-air interface indicate that the hydrated proton is much more surface-active than the hydroxide anions.[158] Discordant results are probably explained by inherent difficulties in interpreting experiments, and by the limited accuracy of numerical simulations, besides the fact that results from different methods may correspond to different probing depths. Electrospray mass spectrometry experiments by Colussi and coworkers[35,148,149,159] led them to conclude that (in their own words):[160] *"(1) water is more extensively self-ionized at the surface than in the bulk, and (2) interfacial* H_3O^+ *is a stronger acid (a "superacid") and interfacial OH a stronger base than their bulk counterparts likely due to limited hydration"*. According to these authors, the acidic or basic behavior of the surface of water would rather be interpreted in terms of the availability of proton or hydroxide ions at a given pH, with pH~3 being neutral (instead of 7 as in bulk).[148,149,161] An enhanced autolysis of water at hydrophobic interfaces due to the strong local electric-field gradient was already reported by Beattie[162] (with an isoelectric point around pH 4) trying to explain the contrasting observed electro-osmotic properties of microfluidic channels. On the theoretical side, water self-ionization has been found to be more favorable in water clusters of 20[163] or 21[164] water molecules, compared to bulk solution. This unexpected result is probably a consequence of the topology of the hydrogen-bond network, and could serve as a clue for elucidating the acid/base properties of water in extended aqueous interfaces. A complete survey and a comparative analysis of experimental and theoretical data before 2016 can be found in the review of Agmon et al[165] and in the paper by Saykally.[166] As an example of the ongoing discussion, one can refer to the experiments on isoprene oligomerization in aqueous electrosprays and mildly acidic water by Enami et al[35] that we have mentioned above. Gallo et al[85] have carried out another study of this system by comparing the reactivity in electrosprays and isoprene–water emulsions with adjusted pH, in an attempt to differentiate between pure interfacial effects and effects due to the conditions characterizing the electrosprays experiments (charge separation, concentration of reactants). According to these authors, the absence of chemical reactions in emulsions suggests that the high-voltages in the electrosprays play a key role, leading to charge-separation that facilitates the formation of partially hydrated, highly-reactive hydronium ions, that then catalyze the process. The author's conclusion was supported by theoretical calculations comparing the reactivity of $(H_3O^+)(H_2O)_n$ clusters of different size. Further works by Colussi and Enami[161] and Gallo et al[167] have discussed the effects that the partial solubility (milimolar level) of isoprene in water might have on the fate of reactions in the case of isoprene-water emulsions. It is worth mentioning in this respect the work by Butler et al,[60] who used the *endo*/*exo* preference in Huisgen cycloadditions to classify reactions (in-water vs on-water) as a function of the hydrophobicity of one of the reactants, i.e. its water solubility: on-water reactions do not display increased *endo*-effects relative to organic solvents, in contrast to in-water reactions. To sum up, the case of isoprene oligomerization emphasizes the difficulties to derive definite conclusions about interface effects on reactivity and the presence of on-water catalysis. The combined use of multiple analytical platforms and of elaborated numerical simulations will be most useful to test different hypotheses and get more insights in this field.

Finally, one should note that ab initio MD simulations of the water liquid-vapor interface have highlighted the augmented reactivity with respect to excess protons and electrons by an analysis of the HOMO and LUMO energies at interfacial layers.[122]

The "polarity" of the water surface. Solvent polarity has been a widely used concept in Chemistry to rationalize solvation phenomena.[28] Following the « like dissolves like » principle, polar solvents are likely to dissolve polar compounds and favor their most polar conformations. Non-polar solvents, on their side, are likely to dissolve non-polar compounds. Though a precise definition of "solvent polarity" is not straightforward, the use of empirical parameters derived from linear Gibbs energy relationships has been very popular in Organic Chemistry.[28] In Computational Chemistry, polarizable continuum models based (essentially) on the static dielectric constant of the solvent have been very successful to study processes in bulk solution,[168] and more recently at interfaces as well.[169-171]

However, with regard to the solvation power of aqueous interfaces, the use of the concept of "solvent polarity" entails some difficulties. In fact, experimental attempts to characterize the polarity of aqueous interfaces using second-harmonic spectroscopy have led to conflicting results. On one hand, Eisenthal and coworkers[172] tried to derive an interface polarity scale ($E_T(30)$) for a betaine dye at several water interfaces. They deduced a simple relationship according to which the polarity of a liquid interface is the arithmetic average of the polarity of the two bulk phases, pointing at a dominant effect of long-range solute-solvent interactions. For the air-water interface, the polarity would be close to that of a low polar solvent. On the other hand, further measurements with coumarin derivatives[173] and other dyes[174,175] have demonstrated the limitations of the "arithmetic average" rule, claiming that the polarity of aqueous interfaces is not a well-defined concept. The apparent "polarity" of the interface strongly depends on solute's structure since subtle modifications of the later (stereochemistry, hydrophobic groups) can produce significant changes on the former. This is because the solute's position and orientation relative to the interfacial boundary rely on its structure, and so does the water response.

Theoretical studies can clarify the issues in the definition of interface polarity. Classical and first-principles MD simulations of glyoxal (O=CH-HC=O) have shown that water interfaces selectively stabilize the polar *cis*-conformer (the two polar C=O bonds pointing in the same direction) over the apolar *trans*-conformer (C=O bonds pointing in opposite directions).[176,177] This result can be explained by the fact that both, stereochemistry and polarity favor the interaction of the *cis*-isomer with the interface. Stereochemistry and polarity, however, do not always go in the same direction, as in the case of *meta*- and *para*-cyanophenol isomers. Ab initio calculations using a dielectric model[171] show that despite its lower polarity, the *meta*-isomer has a higher interface affinity because, in this case, but not in the case of the *para*-isomer, the -CN and -OH groups can simultaneously interact with the aqueous layer (**Figure 3**).

Finally, in **Figure 4**, we illustrate the differences between the bulk-water and air-water interface reaction-field potentials, i. e. the electrostatic potentials created by the polarized water medium, in the case of methanol obtained by MD simulations.[178] Methanol is an important atmospheric compound and its air-water interface affinity and structure have been thoroughly described by SFG spectroscopy measurements and theoretical simulations.[5,178] As shown in Figure 4, , there are topological differences between the two potentials that do not correspond to those that would be expected for two media differing simply by their "polarity" gradation. The potentials around the OH groups are indeed quite similar, while a large difference appears around the CH_3-group, which is of course the consequence of a preferred orientation of methanol at the interface. Roughly, the CH_3-group points towards the air layer (and is basically not solvated), and the OH-group points towards the water layer (and has an almost complete hydration shell), although the details of the solvation dynamics discussed below draw a slightly more complicated picture.

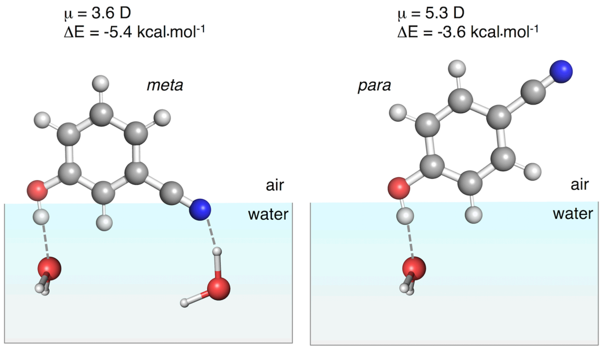

Figure 3. Schematic view of the *meta*- and *para*-isomers of cyanophenol adsorbed at the air-water interface showing the expected hydrogen-bonds with water molecules. The plotted values for the gas-phase dipole moment (μ) and for the electrostatic interaction energy with the interface (ΔE) have been obtained using quantum chemistry calculations and a simple dielectric model of the air-water interface.[171] The values reveal that despite a lower dipole moment of the *meta*-isomer with respect to the *para*-isomer, its electrostatic interaction energy is higher (in absolute value) owing to the possible simultaneous contact of both polar groups with the water surface.

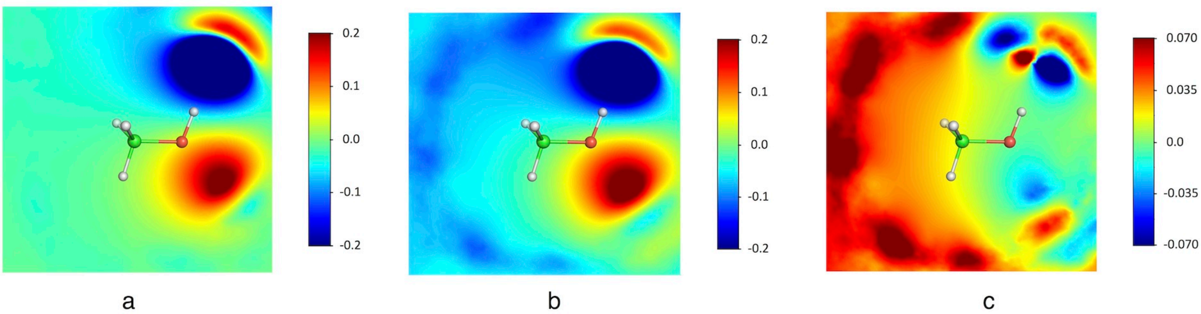

Figure 4. Calculated electrostatic potential (atomic units) created by the solvent water molecules surrounding methanol. The graphs correspond to time averages of the potential obtained from QM/MM Molecular Dynamics simulations.[178] The surfaces are displayed in an arbitrary methanol-fixed coordinate system but in the simulation there are no constraints imposed to the methanol or water molecules, which are flexible to vibrate, rotate and translate. Graph (a) corresponds to the calculation at the air-water interface: the left green part reveals that at the interface, the average potential around the methyl group is close to zero, as corresponds to the fact that this group is most of the time pointing towards the air layer. Graph (b) corresponds to the calculation in bulk water: as shown, the potential in the right part (around the OH group) is very similar to the potential obtained at the interface, but the potential around the methyl group (left part, blue-green surface) is significantly different. In the bulk, water molecules around the methyl group undergo orientational polarization, and may form weak hydrogen-bonds with the methyl H atoms. Graph (c) displays the difference between the two potentials (interface – bulk): it confirms that the most relevant disparity holds for the region around the CH_3 hydrophobic group.

Thermodynamics and dynamics of solvation. The energetics of solvation at aqueous interfaces is a vast subject with extensive literature and a multitude of facets. The specific topics dealt with here are those that could be considered most relevant for understanding chemical reactivity of organic compounds at air-water interfaces. In the field of atmospheric chemistry, several reviews have already been published describing the uptake and accommodation processes, the energetics of interface adsorption, and the experimental techniques.[4,29,33] MD simulations have allowed, on the other hand, to obtain the potential of mean force for the adsorption and accommodation processes of many chemical species. One of the most remarkable findings of these studies (see for instance[32,33,124,125,179-186]) has been the significant interface affinity, not only of hydrophobic or amphiphilic organic molecules, which is an expected result, but of small polar systems and even ions as well. An archetypal free energy profile for moving a neutral water-soluble compound from the gas-phase to bulk water across the air-water interface is shown in **Figure 5** (the solvation of ions is considered in deeper detail below). The free energy decreases from air to bulk with a minimum at the interfacial layer. These profiles are useful to obtain Henry's constants and surface excess properties.[182] Theoretical analysis[181] of the solvation of organic molecules in water droplets has revealed that the surface preference is principally due to enthalpic effects. Namely, the total water–water interaction energy is more negative when the solute is at the surface of the droplet because, when it is in the bulk, some water-water hydrogen-bonds are disrupted. Entropic effects further enhance the surface preference when the system bears large apolar groups (e.g. 4-5 carbon atoms or longer hydrophobic chains).

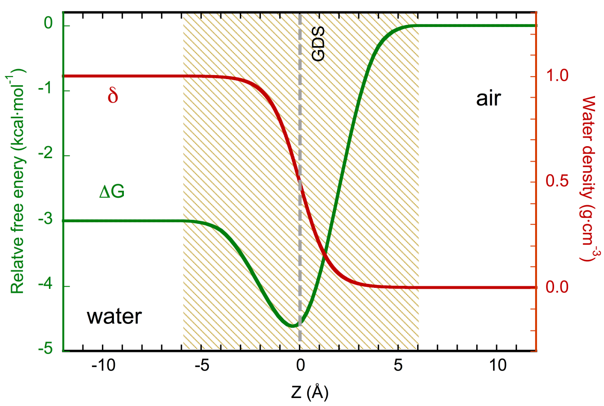

Figure 5. Schematic plot for the relative free-energy profile (ΔG, green) for a neutral (water soluble) solute crossing the air-liquid water interface. The density profile of water (δ, red) is also shown. The free energy decreases from the air layer (right part of the figure) to the interface, where it displays a minimum (hatched area) close to the Gibbs-dividing-surface (GDS, Z=0 here), then increases from the interface to the bulk. Note that the width of the interface layer (hatched area) is about 1nm. Depending on the solute's structure and on its hydrophilicity/hydrophobicity character, the free-energy profile can display substantial differences, e.g. a free-energy maximum can occur between the interfacial layer and the bulk water, and the sign of the relative air-bulk water free-energy can be reversed.

The molecular dynamics of solutes adsorbed at the air-water interface displays two fundamental differences with respect to the bulk. First, axial oscillations of the solute's position across the average interface plane may be quite large and this implies concomitant fluctuations of the instantaneous hydration shell. This is illustrated in **Figure 6** for methanol at the air-water interface.[178] Second, due to the asymmetry of the interface and the existence of preferred orientations of the solute, the interface orientational dynamics differs in general from the bulk. Reorientational relaxation at the interface can be characterized by time- and polarization-resolved pump-probe SFG spectroscopy[187] or by MD simulations. Calculation of the rotational autocorrelation functions of the methane derivatives MeCl, MeCN, and MeOH, which are important organic compounds in the troposphere, shows that the reorientation decay times increase with their hydrogen-bonding capability, i. e. with the strength of their interface anchoring.[178]

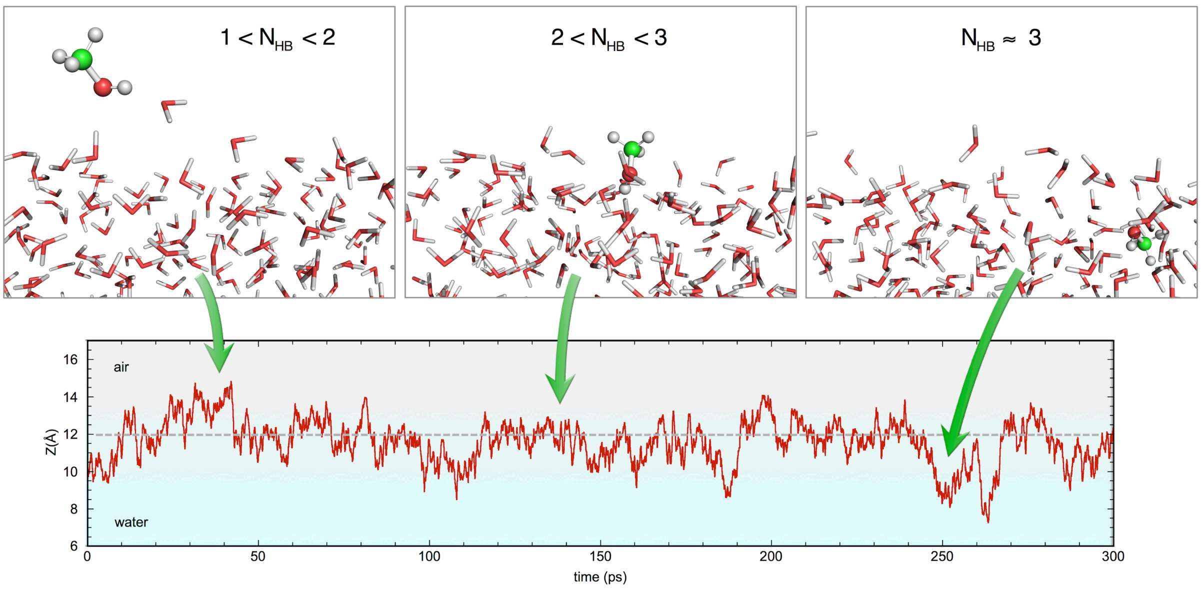

Figure 6. QM/MM MD simulation of methanol at the air-water interface.[178] The lower panel shows the fluctuations of the solute's axial position (Z-axis) with respect to the average interface plane (Z=12Å). The snapshots in the upper panel illustrate different situations in which the methanol molecule, depending on its relative position with respect to the interface (air or water layers) is more or less hydrated; the average number of methanol-water hydrogen-bonds (N_{HB}) in different cases is indicated.

Interface affinity of ions. Ions in the outermost interface layers are more easily available to catalyze chemical reactions (e.g. on sea salt-aerosols) and it is therefore crucial to set-up a scale of interface affinity values. Beyond that, interface affinities are valuable to establish kosmotropic/chaotropic scales, predict the surface tension of electrolyte solutions or explain the Hofmeister series.[188,189] In the classical view of electrolytes that considers the interface as an abrupt discontinuity between two dielectric continuum media,[190] the air-water interface is devoid of ions. In such models, the point-charge q in a dielectric with dielectric constant ϵ_1 (water) interacts with its image charge $q' = q(\epsilon_1 - \epsilon_2)/(\epsilon_1 + \epsilon_2)$ in the dielectric with constant ϵ_2 (air), and therefore is repelled from the interface ($\epsilon_2 < \epsilon_1$). The divergence found in this model for ions approaching the interface can be untangled for finite radii ions.[191] Although a full understanding of the topic is still lacking, many endeavors have been made to get beyond the classical view. The macroscopic view from surface tension and electrostatic potential measurements has been supplemented by data from interface-sensitive spectroscopic techniques such as SFG, by elaborated dielectric continuum theories and MD simulations, providing new insights.[179,188,189,192-200]

Hard non-polarizable ions (such as F^- or the alkali cations), and multiply charged ions (such as sulfate) behave classically and are repelled from the interface, but large polarizable anions (such as I^- or Br^- and to a lower extent Cl^-), display a propensity for the air-water interface. The case of hydronium discussed above is an exception, and its interface affinity results from specific hydrogen-bonding properties. Though it goes beyond the limits of the present review, the stability of the solvated electron at aqueous interfaces has also been studied[201-203] because of potential implications in numerous chemical processes (radiation chemistry, electron-transfer, redox and electrochemical reactions, etc).

The interface affinity of ions has been explained (at least qualitatively) by a favorable balance between electrostatic and cavitation energies.[199,204,205] The later represents the energy cost required to disrupt water-water interactions in the medium in order to create a hole where the ion is placed. The cavitation energy drops when the ion moves from bulk to the interface, and for bulky soft ions it can overcompensate the loss of favorable ion-water electrostatic interactions. In such a case, the ion stabilizes at the interface. The role of anion polarizability has been emphasized[179,195] and though correlation with interface affinity is not always apparent,[206] this term must be taken into account for a quantitative description of the adsorption energetics, as recently reported for aqueous solutions of ClO_4^- using SFG spectroscopy.[205] Under the effect of the local electric field (the permanent field due to the asymmetry of the interface and the ion-induced reaction-field), the electronic cloud of large polarizable anions is distorted and the induced dipole moment contributes to enhancing the solvation of the ion at the interface.[192] Solvation dispersion-forces may also influence interfacial adsorption,[199,204] specially at oil-water interfaces.[188]

Cations are dragged to the interface from the bulk through the electrostatic interactions with the anions and cumulate in nearby inner layers,[192] although their distribution is quite sensitive to the type of counterions present.[189] Anions and cations interact differently with water, and according to Levin and dos Santos,[188] alkali cations are repelled from the interface because they are strongly hydrated, while anions may behave either as kosmotropes or chaotropes. The distribution of anions and cations near the air-water interface is also influenced by the electrostatic potential originated by the orientation of water molecules at the interface, although the role of this surface potential still remains unclear.[207] Indeed, classical calculations using point-charge force-fields predict the air layer to be more electropositive than water (in congruence with the image of dangling protons pointing towards the air layer), while explicit treatment of the electronic cloud in ab initio simulations predicts the opposite trend.[179,188,208] Thus, the anionic adsorption predicted with polarizable force-fields is probably overestimated.[188] The adsorption energy of ions has been decomposed in entalphic and entropic terms in some cases,[179] and the simulations by Caleman et al[209] and Otten et al[198] concluded that adsorption of