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

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## 44 **Abstract**

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

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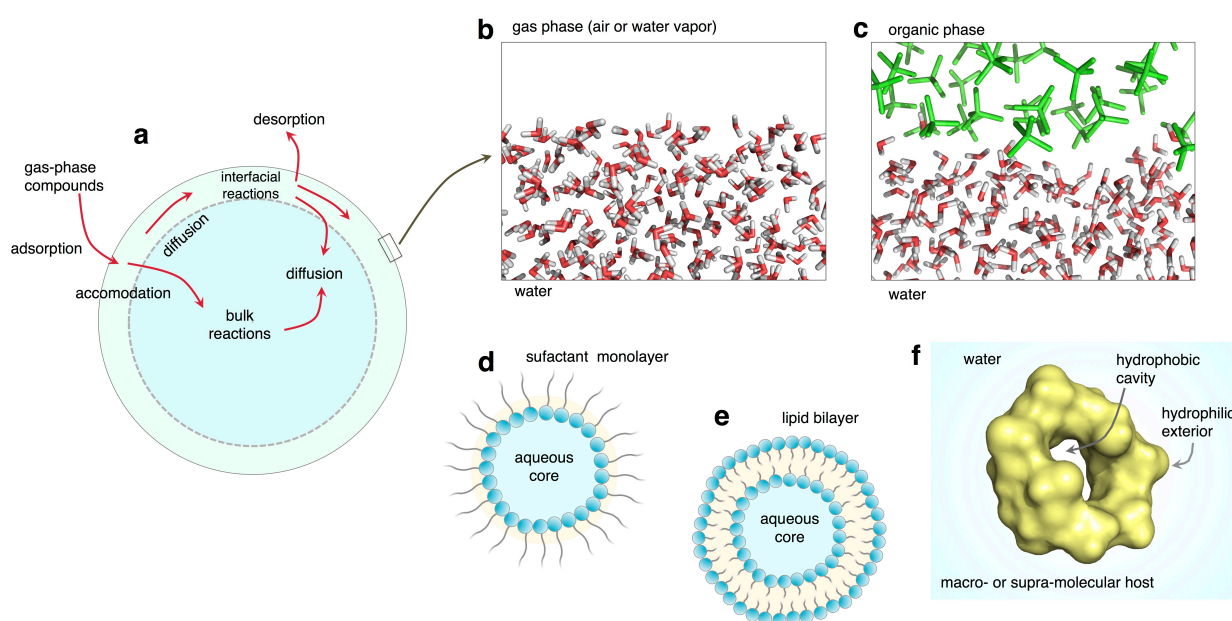
## 62 **Introduction**

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

79 The reasons underlying rate acceleration at aqueous interfaces remain unclear however. In  
80 contrast to bulk solvation, the theory of interfacial solvation is still in its early stages. The  
81 formation of hydrogen-bonds with dangling protons at the interface was first proposed to explain  
82 the catalytic role of the interface,<sup>2</sup> but many other causes can be invoked: confinement of  
83 reagents, partial solvation, preferential orientations, curvature in nanodroplets, water surface pH,  
84 etc. It is worth pointing out that physicochemical concepts from the bulk are not always  
85 applicable at interfaces, as the latter are disordered systems of nanometric thickness displaying  
86 sharp configurational fluctuations. Experimental studies based on macroscopic properties such as  
87 surface tension<sup>3,4</sup> have provided invaluable data on interfacial thermodynamics and structural

88 properties. However, only with the progress of non-linear second-harmonic generation (SHG)  
89 and sum-frequency generation (SFG) spectroscopies,<sup>5</sup> and other interface-sensitive molecular  
90 techniques, the microscopic details of interfacial phenomena are being elucidated. In parallel, *ab*  
91 *initio* Molecular Dynamics (MD) simulations and related approaches have provided priceless  
92 information on these issues.<sup>6-8</sup>

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



101  
102 **Figure 1.** Aqueous interfaces contemplated in this review: a) the air-water interface at the surface of a water droplet  
103 with indications of the different processes that can take place, b) detail of the liquid water-vapor interface, c)  
104 interface of liquid water with a non-miscible organic solvent (CCl<sub>4</sub> here), d) inverted micelle in aqueous organic  
105 aerosols, e) vesicles, f) macro- or supra-molecular systems with a hydrophobic cavity that can host hydrophobic  
106 guest molecules.

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## 112 **Chemical reactions at aqueous interfaces**

113 Many contributions in this field come from the atmospheric chemistry community because

114 reactions at the air-water interface of cloud water droplets and aqueous aerosols may proceed at

115 higher rates than gas-phase reactions, influencing the atmospheric budget of trace gases.<sup>9-12</sup>

116 Further interest comes from the field of synthetic green chemistry. The need to develop green

117 processes for the synthesis of organic compounds that decrease the negative environmental

118 impact of current industrial practices pleads for the use of non-organic solvents such as water.

119 Experiments have shown that reactions in water microdroplets generated by electrospray

120 ionization undergo remarkable acceleration with respect to bulk-phase processes, and due to

121 large surface to volume ratio, the air-water interface is thought to play a key role.<sup>13-16</sup> Moreover,

122 dispersed systems such as polyelectrolyte solutions, micellar solutions, oil-in-water

123 microemulsions or vesicle dispersions, have been proposed to overcome water solubility

124 limitations and develop biomimetic reactors within which reactions can proceed.<sup>17,18</sup> Aqueous

125 interfaces have also been evoked as possible environments in which prebiotic processes could

126 have taken place and led to the origin of life. For instance, orientation, alignment and proximity

127 of functional groups is essential to the synthesis of peptides by the ribosome, and air-water

128 interfaces in inverted micelle atmospheric aerosols or in the surface of oceans and lakes could

129 have been a rudimentary prebiotic system mimicking this functioning.<sup>19,20</sup>

130 We have selected some illustrative experimental works, and organized them in four specific

131 (and to some extent, arbitrary) areas that are not disjointed, but rather overlap in many ways.

132

133 ***Atmospheric and environmental chemistry.*** The role of condensed matter in the Earth's

134 atmosphere is widespread. Aerosols scatter sunlight and serve as seeds for the formation of

135 clouds, which has significant consequences in climate regulation.<sup>21</sup> Condensed matter in its  
136 different forms also supplies a medium for chemical transformations. Well-known examples are  
137 the oxidation of SO<sub>2</sub> to sulfate in water droplets, which leads to acid-rain formation in the  
138 troposphere,<sup>22</sup> or the heterogeneous reactions that lead to ozone depletion in the stratosphere.<sup>23</sup>  
139 Indeed, despite a small volume fraction of atmospheric condensed matter (about 7% of the total  
140 volume of the troposphere contains clouds, and a moderately dense cloud contains about 5x10<sup>-7</sup>  
141 cm<sup>3</sup> of water per cm<sup>3</sup> of air),<sup>9</sup> its relevance is now recognized.<sup>9,24,25</sup> It influences the atmospheric  
142 budget of trace gases through the modification of the cycles of nitrogen, sulfur, and various  
143 atmospheric oxidants such as ozone.<sup>26,27</sup> In addition, some reaction pathways that are unfeasible  
144 in the gas-phase (e.g. ionic dissociations) may be quite favorable in the condensed phase,  
145 producing new species.<sup>28</sup> In line with the subject of this review, we put the focus on liquid water  
146 interfaces (water droplets, aqueous aerosols) even though the heterogeneous reactions at the  
147 surface of solid matter such as carbonaceous particles or mineral dust have comparable  
148 importance.

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

158 Adsorption of trace organic molecules on water film surfaces enhance their reaction with  
159 atmospheric oxidants.<sup>33</sup> Electrospray-mass-spectrometry studies<sup>34</sup> showed that when benzoate is  
160 allowed to react with OH radicals at the air-water interface, H-abstraction from the aromatic ring

161 is mainly observed. At the same time, this reaction is negligible both in the gas-phase and bulk  
162 water. The rationalization of this results goes in terms of the higher polarity of the transition state  
163 for the OH-radical addition compared to H-abstraction.<sup>34</sup> A similar experimental technique was  
164 used by Enami et al<sup>35</sup> to study the reactivity of isoprene at mildly acidic water surfaces showing  
165 that it can undergo cationic oligomerization. The authors suggested a superacidity behavior of  
166 the air-water interface with pH < 4 water, a result that has raised some debate (see below). Fatty  
167 acids, which are generally not sensitive to actinic radiation, produce aldehydes and other  
168 oxygenated species when a monolayer at the water surface is irradiated in the 280-330 nm  
169 region.<sup>12</sup> The process seems to involve UV-absorption to a triplet state followed by the homolytic  
170 OH dissociation or by reaction with an adjacent fatty acid molecule at the air-water interface.  
171 The conclusions of these experiments, however, have been challenged by subsequent studies by  
172 Shrestha et al<sup>36</sup> and Rapf et al,<sup>38</sup> who have emphasized the need of photoinitiators for reactions of  
173 this type to take place, as fatty acids are not themselves photoactive. Upon irradiation of  
174 nebulized pyruvic acid, zymonic acid has been observed among the products formed,<sup>39</sup> as  
175 opposed to other conditions, suggesting that it could be generated by reactions at the droplet  
176 surface. Other interesting interface-assisted photochemical processes can be found in the review  
177 by George et al.<sup>11</sup> Colussi and coworkers<sup>40-46</sup> have devoted considerable effort to the study of the  
178 ozonolysis reaction and the chemistry of the Criegee intermediate at the air-water interface,  
179 which are chemical processes with broad implications in the atmosphere, as they represent a  
180 major sink for unsaturated volatile organic compounds produced by plants, particularly isoprene  
181 and monoterpenes. The oxidation reaction of anthracene by ozone on aqueous surfaces was  
182 studied by Mmereki et al,<sup>47</sup> who showed that it may be of comparable importance to gas-phase  
183 oxidation by OH in the atmosphere. Chemistry at the surface of sea-salt aerosols and its  
184 atmospheric implications have been extensively studied by Finlayson-Pitts and coworkers, who  
185 have emphasized the role played by the air-water interface. For instance, the main sources of Cl<sub>2</sub>  
186 and Br<sub>2</sub> gases from sea-salt aerosols under dark conditions are the interfacial reactions of the



187 corresponding halide anion with OH and O<sub>3</sub>, respectively.<sup>48</sup> When concentrated NaCl aerosols  
188 are irradiated at 254 nm in the presence of O<sub>3</sub> to generate OH radicals, the observed amount of  
189 Cl<sub>2</sub> gas produced is in good agreement with estimates based on field measurements in the marine  
190 boundary layer.<sup>10</sup> At the surface of aqueous aerosols, halide ions (and also some cations)  
191 influence other interfacial reactions such as the production of NO<sub>2</sub> from photolysis of nitrate.<sup>49-51</sup>  
192 Some fundamental knowledge about the water effects on reactions at the air-water interface of  
193 water droplets and aqueous aerosols comes from the study of small water clusters and further  
194 details on this topic can be found in the review by Vaida.<sup>52</sup>

195  
196 ***Microdroplets as synthetic chemical reactors.*** Reactivity in microdroplets is emerging as an up-  
197 and-coming tool in synthetic organic chemistry. Acceleration of many organic reactions in  
198 aqueous media has been known for decades,<sup>53-56</sup> especially after the seminal work by Breslow  
199 and coworkers on the Diels-Alder reaction.<sup>57,58</sup> This is rather good news because one could  
200 consider water as the ideal green solvent. Studies by Sharpless and coworkers<sup>1</sup> pointed out that  
201 some reactions proceed optimally in pure water when insoluble reactants are stirred in the  
202 aqueous medium, and denoted such processes “reactions on-water”. Such processes occur in  
203 aqueous suspension and thus, hydrophobic effects might be claimed to provide the driving-force  
204 for rate acceleration. Yet, experimental results showed that observed rates are not the sole  
205 consequence of an effective concentration increase,<sup>1</sup> and since the pioneer work of Sharpless and  
206 coworkers,<sup>1</sup> “on-water” chemistry has been steadily expanding (see for instance the reviews by  
207 Butler and Coyne<sup>59</sup> and by Butler et al<sup>60</sup>).

208 In recent years, synthesis in small volume microreactors has been the subject of intense  
209 research.<sup>14</sup> This includes studies in microdroplets generated by a variety of electrospray and other  
210 spray mass-spectrometry methods,<sup>13,15,20,61-66</sup> levitated droplets,<sup>67</sup> thin films on surfaces<sup>68,69</sup> or  
211 microfluidic systems.<sup>70-73</sup> In many cases, the reaction rates are higher with respect to the  
212 reference bulk reaction (see a counterexample here<sup>74</sup>) but the effects responsible for such rate

213 accelerations are still unclear. Confinement of reagents and increased concentration (due to  
214 solvent evaporation) are probably important factors,<sup>14</sup> but the large surface to volume ratio  
215 characterizing these systems also points at specific interface effects.<sup>13-16</sup> Experimental data  
216 supporting this statement were reported by Cooks and coworkers<sup>75</sup> in the study of competitive  
217 substituent effects in Claisen–Schmidt reactions. Other experiments by Mellouli et al<sup>72</sup> using a  
218 biphasic microfluidic approach, which allows getting better control of the generated interfaces  
219 and water surface area, concluded that stabilizing hydrogen-bonds play a role in decreasing the  
220 activation energy, as previously suggested by Jung and Marcus<sup>2</sup> (see below). The observed rate  
221 increase is sometimes very large. For instance, the Pomeranz–Fritsch synthesis of isoquinoline in  
222 charged microdroplets generated by electrospray has been reported to be at least  $10^6$  times faster  
223 than in bulk.<sup>76</sup> Likewise, Enami et al<sup>77</sup> showed that Fenton ( $\text{Fe}^{2+} + \text{H}_2\text{O}_2$ ) and Fenton-like ( $\text{Fe}^{2+} +$   
224  $\text{O}_3$ ) reactions proceed  $10^3$ - $10^4$  faster at aqueous interfaces than in bulk aqueous media due to a  
225 modified geometry of the hydration shell of  $\text{Fe}^{2+}$ , which may have implications not only for  
226 advanced oxidation processes but also in atmospheric and biological chemistries. Other exciting  
227 results have been obtained by Lee et al,<sup>78</sup> who have observed spontaneous formation of hydrogen  
228 peroxide in sprayed water microdroplets. The authors have considered and analyzed several  
229 possible mechanisms and concluded that the process occurs at or near the interface, where the  
230 strong intrinsic electric field is enough to ionize hydroxyl anions, generating hydroxyl radicals  
231 that then recombine to form  $\text{H}_2\text{O}_2$ . Although the mechanism is not fully understood, the result is  
232 quite significant because  $\text{H}_2\text{O}_2$  has great importance in biomedical and industrial applications,  
233 and it is also a key compound in the atmosphere due to its oxidative capacity.<sup>79</sup> The results of  
234 Lee et al<sup>78</sup> have been supported by the work of Gao et al<sup>80</sup> showing that Dakin and Baeyer-  
235 Villiger oxidation reactions proceed in water microdroplets without the addition of any peroxides  
236 and acid or base catalysts, as usually required.<sup>80</sup>

237 It is worth reminding that reactions in microdroplets and electrospray-mass spectrometry  
238 techniques are not only interesting from the point of view of analysis and synthesis, as

239 mentioned above, but also to study a wide variety of problems in atmospheric,<sup>35,43,45</sup> biomedical<sup>81-</sup>  
240 <sup>83</sup> or other domains in which aqueous interfaces play a central role. Moreover, possible scale-up  
241 of microdroplet chemical synthesis by heated ultrasonic nebulization opens interesting industrial  
242 perspectives.<sup>84</sup> Finally, it must be noted here that experiments with electrospray techniques and  
243 their interpretation as purely interfacial reactions have raised certain controversy in the literature  
244 because of the possible influence of ions<sup>85</sup> and gas phase chemistry.<sup>86</sup> Two illustrative examples  
245 of the controversy will be commented on below.

246  
247 ***Prebiotic chemistry.*** The role played by aqueous interfaces on the chemical mechanisms that led  
248 to the origin of life on Earth has received considerable interest in recent years. It is explained by  
249 the fact that compartmentalization, as well as the emergence of genetic materials, is considered  
250 to be a key prerequisite in the long journey towards protocells capable of growth, division and  
251 Darwinian evolution.<sup>87</sup> Colloidal systems, resulting from self-organization of amphiphilic  
252 molecules in aqueous environments, provide such suitable compartments in which complex  
253 chemical reactions could have taken place in the prebiotic era. In particular, vesicles formed in  
254 bulk waters (lakes, rivers) have attracted considerable attention because the amphiphilic bilayer  
255 that separates the aqueous interior from the exterior media in these structures bears a  
256 resemblance to cell membranes.<sup>17,18,88-90</sup> In such confined volumes, molecular crowding increases  
257 the probability of reactive encounters between chemical species, and at the same time, limits the  
258 diffusion of products. Hence, the synthesis of complex biomolecules required for the  
259 development of primitive living organisms is strongly favored compared to similar reactions in  
260 bulk.<sup>73</sup> Though molecular crowding is not the only important feature controlling the chemical  
261 reactivity inside the vesicle, and several works have emphasized the importance of the interface  
262 in terms of molecular alignment, electric charge, pH, etc. For instance, experiments have shown  
263 that the polycondensation of aminoacids and peptides is assisted by the lipidic bilayer, not only

264 as a favorable environment for the reaction to take place,<sup>91,92</sup> but also as an active acid-base  
265 catalyst.<sup>93</sup>

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

281 Experiments in microdroplets have been reported as well. Lee et al<sup>100</sup> have observed  
282 spontaneous reduction of several organic molecules without assistance of reducing agents,  
283 catalysts of external charges, which could represent an essential reduction route in prebiotic  
284 conditions. The mechanism is unclear but might involve the oxidation of  $\text{OH}^-$  at the droplet  
285 surface, likewise in the spontaneous formation of  $\text{H}_2\text{O}_2$  described above.<sup>78</sup> Nam et al<sup>101</sup> have  
286 studied aqueous microdroplets containing a mixture of sugars and phosphoric acid, and observed  
287 that phosphorylation proceeds spontaneously in such conditions. The effect has been ascribed to  
288 a cancellation of the entropic barrier when the process occurs at the surface of the microdroplet,  
289 whereas such barrier prevents the uncatalyzed reaction to proceed in bulk solution. Nam et al

290 have also reported the synthesis of uridine<sup>101</sup> and other ribonucleosides<sup>20</sup> in an aqueous  
291 microdroplet containing D-ribose, phosphoric acid, and a nucleobase. As an example of the  
292 controversy surrounding some results obtained with electrospray techniques, Jacobs et al<sup>86</sup> have  
293 reported different conclusions for the reaction between sugars and phosphoric acid. The authors  
294 have used an experimental setup in which droplet generation is separated from ionization, so that  
295 they have been able to analyze different possible sources of rate acceleration. They have  
296 concluded that part of the products could originate from gas-phase chemistry, which in some  
297 cases may complicate the interpretation of rate acceleration in droplets generated by  
298 electrosprays or its variants.

299 The preceding results exemplify the role aerosols and microdroplets could have played for the  
300 generation of chemical complexity in prebiotic chemistry,<sup>19</sup> which could have also involved  
301 sunlight-driven processes.<sup>102</sup>

302  
303 ***Reactions at organized molecular interfaces.*** Quite a diverse variety of processes can be placed  
304 in this category that includes systems possessing an organized amphiphilic interface with ability  
305 for molecular recognition, possibly including a binding site, and compartments that can host  
306 chemical reactions. Of course, some systems described above belong to this category, such as the  
307 vesicles hosting prebiotic chemical reactions or the atmospheric organic aerosols structured as  
308 inverted-micelles. Chemical reactions in biological membranes could be included in this class of  
309 interfacial processes too.<sup>103</sup> Nevertheless, the focus here is on synthetic reactions in water that  
310 mimic the functioning of enzymatic catalysis in biology, which have particular interest in the  
311 field of Green Chemistry. The term “artificial enzymes” was coined by Breslow,<sup>104,105</sup> who  
312 introduced the use of functionalized macromolecules, mainly cyclodextrins, as water-soluble  
313 catalysts that can host a non-polar reactant guest in a hydrophobic cavity. The design of enzyme  
314 mimics or “chemzymes” is a field of intense research,<sup>106-109</sup> which has turned into the more  
315 general one of “molecular reaction vessels”. Antibody catalysts or “abzymes”,<sup>110</sup> functionalized

316 nanomaterials or “nanozymes”,<sup>111,112</sup> dendrimers,<sup>113,114</sup> micellar<sup>115</sup> and other disperse interface-rich  
317 structures (polyelectrolyte solutions, microemulsions, vesicles, ..),<sup>18</sup> as well as enzymes confined  
318 in small-volume environments<sup>17</sup> have been considered in detail previously. Therefore they will  
319 not be further described here.

320

### 321 **Solvation at the water surface**

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

330

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

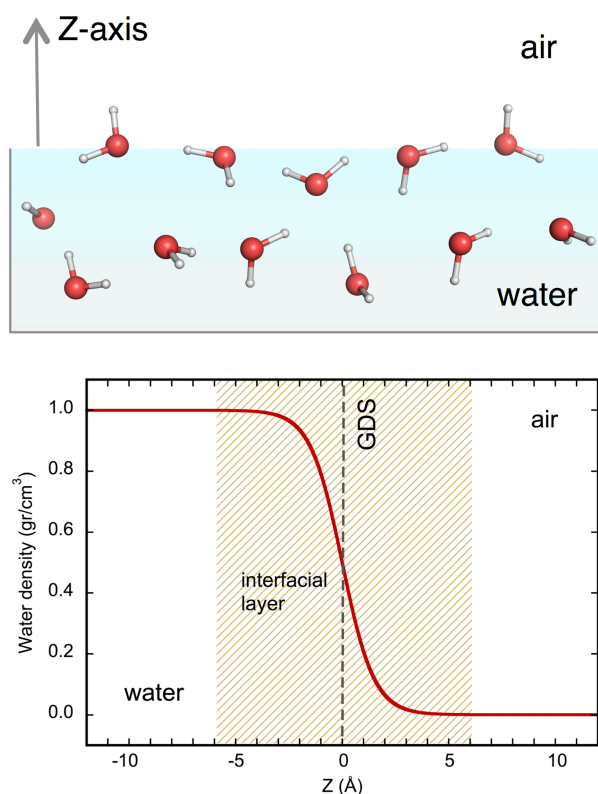
342  $\rho(z) = \frac{\rho_o}{2} (1 + \tanh(\frac{z-z_G}{\delta}))$  (1)

343 where  $\rho_o$  is the bulk density,  $Z_G$  is the position of the Gibbs-dividing-surface ( $Z$  at which

344  $\rho(z) = \frac{\rho_o}{2}$ ). Values of  $\delta$  can change significantly with the theoretical model<sup>124-127</sup> but common

345 values are 10-15 Å at 300K.

346



347

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

352

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

359 Particularly relevant to chemical reactivity is the acid/base character of the water surface, i.e.  
360 its ability to donate or accept protons, an issue that remains incompletely elucidated and has  
361 raised intense controversies in the literature. This issue is connected, on the other hand, to the  
362 properties of water in nanoconfined environments such as inversed micelles, a topic that we will  
363 not develop here but which has attracted a lot of attention, while it remains incompletely  
364 understood (see for instance the works by Levinger and coworkers<sup>137,138</sup>). Interestingly,  
365 experiments and calculations reveal unforeseen acid/base behavior of aqueous interfaces. For  
366 instance, HCl is fully dissociated at the interface but HNO<sub>3</sub> is essentially in its molecular  
367 form,<sup>139-141</sup> unless ions are present,<sup>142</sup> and HCOOH dissociates faster at the interface than in the  
368 bulk.<sup>143</sup> Vibrational spectroscopic studies of the ionization state of the L-phenylalanine  
369 aminoacid indicated a decrease of the pK<sub>a</sub> of its polar groups at the air-water interface.<sup>144</sup>  
370 Depending on experiments and calculations (see for instance<sup>145-157</sup>), apparent opposite  
371 conclusions have been deduced for the interface affinity of hydronium and hydroxide ions and  
372 their spatial distribution, though most recent SFG experiments on D<sub>2</sub>O-air interface indicate that  
373 the hydrated proton is much more surface-active than the hydroxide anions.<sup>158</sup> Discordant results  
374 are probably explained by inherent difficulties in interpreting experiments, and by the limited  
375 accuracy of numerical simulations, besides the fact that results from different methods may  
376 correspond to different probing depths. Electrospray mass spectrometry experiments by Colussi  
377 and coworkers<sup>35,148,149,159</sup> led them to conclude that (in their own words):<sup>160</sup> “(1) water is more  
378 extensively self-ionized at the surface than in the bulk, and (2) interfacial H<sub>3</sub>O<sup>+</sup> is a stronger acid  
379 (a “superacid”) and interfacial OH a stronger base than their bulk counterparts likely due to  
380 limited hydration”. According to these authors, the acidic or basic behavior of the surface of  
381 water would rather be interpreted in terms of the availability of proton or hydroxide ions at a  
382 given pH, with pH~3 being neutral (instead of 7 as in bulk).<sup>148,149,161</sup> An enhanced autolysis of  
383 water at hydrophobic interfaces due to the strong local electric-field gradient was already  
384 reported by Beattie<sup>162</sup> (with an isoelectric point around pH 4) trying to explain the contrasting



385 observed electro-osmotic properties of microfluidic channels. On the theoretical side, water self-  
386 ionization has been found to be more favorable in water clusters of 20<sup>163</sup> or 21<sup>164</sup> water  
387 molecules, compared to bulk solution. This unexpected result is probably a consequence of the  
388 topology of the hydrogen-bond network, and could serve as a clue for elucidating the acid/base  
389 properties of water in extended aqueous interfaces. A complete survey and a comparative  
390 analysis of experimental and theoretical data before 2016 can be found in the review of Agmon  
391 et al<sup>165</sup> and in the paper by Saykally.<sup>166</sup> As an example of the ongoing discussion, one can refer to  
392 the experiments on isoprene oligomerization in aqueous electrosprays and mildly acidic water by  
393 Enami et al<sup>165</sup> that we have mentioned above. Gallo et al<sup>165</sup> have carried out another study of this  
394 system by comparing the reactivity in electrosprays and isoprene–water emulsions with adjusted  
395 pH, in an attempt to differentiate between pure interfacial effects and effects due to the  
396 conditions characterizing the electrosprays experiments (charge separation, concentration of  
397 reactants). According to these authors, the absence of chemical reactions in emulsions suggests  
398 that the high-voltages in the electrosprays play a key role, leading to charge-separation that  
399 facilitates the formation of partially hydrated, highly-reactive hydronium ions, that then catalyze  
400 the process. The author's conclusion was supported by theoretical calculations comparing the  
401 reactivity of (H<sub>3</sub>O<sup>+</sup>)(H<sub>2</sub>O)<sub>n</sub> clusters of different size. Further works by Colussi and Enami<sup>161</sup> and  
402 Gallo et al<sup>167</sup> have discussed the effects that the partial solubility (milimolar level) of isoprene in  
403 water might have on the fate of reactions in the case of isoprene-water emulsions. It is worth  
404 mentioning in this respect the work by Butler et al,<sup>60</sup> who used the *endo/exo* preference in  
405 Huisgen cycloadditions to classify reactions (in-water vs on-water) as a function of the  
406 hydrophobicity of one of the reactants, i.e. its water solubility: on-water reactions do not display  
407 increased *endo*-effects relative to organic solvents, in contrast to in-water reactions. To sum up,  
408 the case of isoprene oligomerization emphasizes the difficulties to derive definite conclusions  
409 about interface effects on reactivity and the presence of on-water catalysis. The combined use of

410 multiple analytical platforms and of elaborated numerical simulations will be most useful to test  
411 different hypotheses and get more insights in this field.

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

415

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

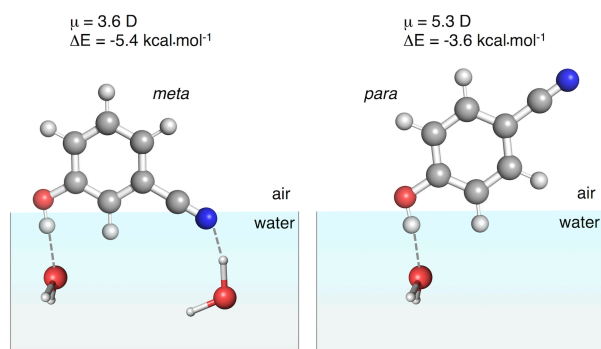
425 However, with regard to the solvation power of aqueous interfaces, the use of the concept of  
426 “solvent polarity” entails some difficulties. In fact, experimental attempts to characterize the  
427 polarity of aqueous interfaces using second-harmonic spectroscopy have led to conflicting  
428 results. On one hand, Eisenthal and coworkers<sup>172</sup> tried to derive an interface polarity scale  
429 ( $E_T(30)$ ) for a betaine dye at several water interfaces. They deduced a simple relationship  
430 according to which the polarity of a liquid interface is the arithmetic average of the polarity of  
431 the two bulk phases, pointing at a dominant effect of long-range solute-solvent interactions. For  
432 the air-water interface, the polarity would be close to that of a low polar solvent. On the other  
433 hand, further measurements with coumarin derivatives<sup>173</sup> and other dyes<sup>174,175</sup> have demonstrated  
434 the limitations of the “arithmetic average” rule, claiming that the polarity of aqueous interfaces is  
435 not a well-defined concept. The apparent “polarity” of the interface strongly depends on solute’s

436 structure since subtle modifications of the later (stereochemistry, hydrophobic groups) can  
437 produce significant changes on the former. This is because the solute's position and orientation  
438 relative to the interfacial boundary rely on its structure, and so does the water response.

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

449 Finally, in **Figure 4**, we illustrate the differences between the bulk-water and air-water  
450 interface reaction-field potentials, i. e. the electrostatic potentials created by the polarized water  
451 medium, in the case of methanol obtained by MD simulations.<sup>178</sup> Methanol is an important  
452 atmospheric compound and its air-water interface affinity and structure have been thoroughly  
453 described by SFG spectroscopy measurements and theoretical simulations.<sup>5,178</sup> As shown in  
454 Figure 4, , there are topological differences between the two potentials that do not correspond to  
455 those that would be expected for two media differing simply by their "polarity" gradation. The  
456 potentials around the OH groups are indeed quite similar, while a large difference appears  
457 around the CH<sub>3</sub>-group, which is of course the consequence of a preferred orientation of methanol  
458 at the interface. Roughly, the CH<sub>3</sub>-group points towards the air layer (and is basically not  
459 solvated), and the OH-group points towards the water layer (and has an almost complete  
460 hydration shell), although the details of the solvation dynamics discussed below draw a slightly  
461 more complicated picture.

462

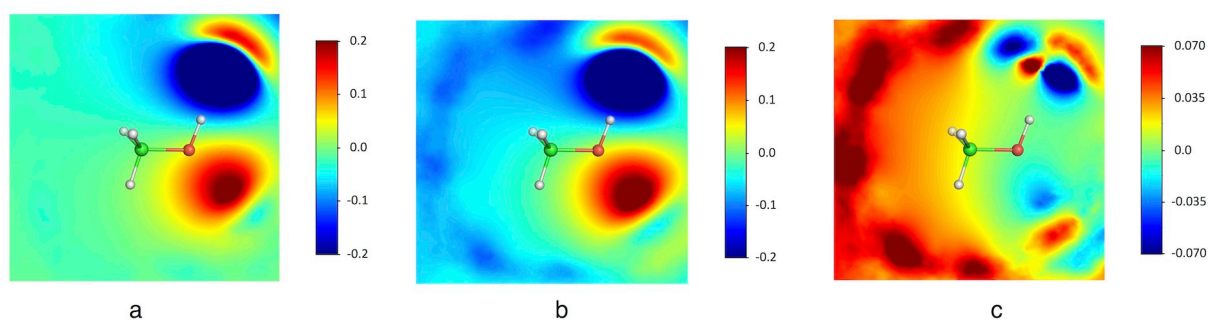


463

464 **Figure 3.** Schematic view of the *meta*- and *para*-isomers of cyanophenol adsorbed at the air-water interface  
 465 showing the expected hydrogen-bonds with water molecules. The plotted values for the gas-phase dipole moment  
 466 ( $\mu$ ) and for the electrostatic interaction energy with the interface ( $\Delta E$ ) have been obtained using quantum chemistry  
 467 calculations and a simple dielectric model of the air-water interface.<sup>171</sup> The values reveal that despite a lower dipole  
 468 moment of the *meta*-isomer with respect to the *para*-isomer, its electrostatic interaction energy is higher (in absolute  
 469 value) owing to the possible simultaneous contact of both polar groups with the water surface.

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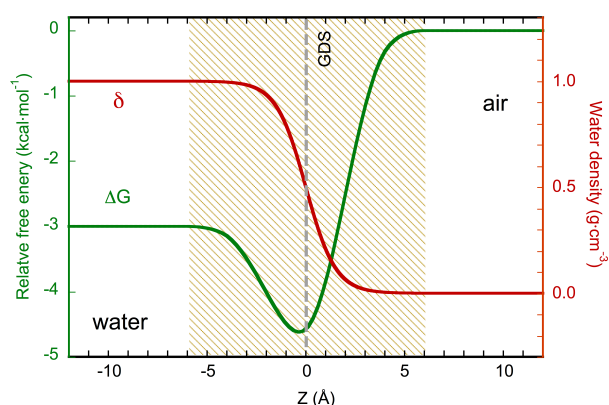
473 **Figure 4.** Calculated electrostatic potential (atomic units) created by the solvent water molecules surrounding  
 474 methanol. The graphs correspond to time averages of the potential obtained from QM/MM Molecular Dynamics  
 475 simulations.<sup>178</sup> The surfaces are displayed in an arbitrary methanol-fixed coordinate system but in the simulation  
 476 there are no constraints imposed to the methanol or water molecules, which are flexible to vibrate, rotate and  
 477 translate. Graph (a) corresponds to the calculation at the air-water interface: the left green part reveals that at the  
 478 interface, the average potential around the methyl group is close to zero, as corresponds to the fact that this group is  
 479 most of the time pointing towards the air layer. Graph (b) corresponds to the calculation in bulk water: as shown, the  
 480 potential in the right part (around the OH group) is very similar to the potential obtained at the interface, but the  
 481 potential around the methyl group (left part, blue-green surface) is significantly different. In the bulk, water  
 482 molecules around the methyl group undergo orientational polarization, and may form weak hydrogen-bonds with the  
 483 methyl H atoms. Graph (c) displays the difference between the two potentials (interface – bulk): it confirms that the  
 484 most relevant disparity holds for the region around the CH<sub>3</sub> hydrophobic group.

485

486 **Thermodynamics and dynamics of solvation.** The energetics of solvation at aqueous interfaces  
 487 is a vast subject with extensive literature and a multitude of facets. The specific topics dealt with  
 488 here are those that could be considered most relevant for understanding chemical reactivity of  
 489 organic compounds at air-water interfaces. In the field of atmospheric chemistry, several reviews  
 490 have already been published describing the uptake and accommodation processes, the energetics

491 of interface adsorption, and the experimental techniques.<sup>4,29,33</sup> MD simulations have allowed, on  
492 the other hand, to obtain the potential of mean force for the adsorption and accommodation  
493 processes of many chemical species. One of the most remarkable findings of these studies (see  
494 for instance<sup>32,33,124,125,179-186</sup>) has been the significant interface affinity, not only of hydrophobic or  
495 amphiphilic organic molecules, which is an expected result, but of small polar systems and even  
496 ions as well. An archetypal free energy profile for moving a neutral water-soluble compound  
497 from the gas-phase to bulk water across the air-water interface is shown in **Figure 5** (the  
498 solvation of ions is considered in deeper detail below). The free energy decreases from air to  
499 bulk with a minimum at the interfacial layer. These profiles are useful to obtain Henry's  
500 constants and surface excess properties.<sup>182</sup> Theoretical analysis<sup>181</sup> of the solvation of organic  
501 molecules in water droplets has revealed that the surface preference is principally due to  
502 enthalpic effects. Namely, the total water–water interaction energy is more negative when the  
503 solute is at the surface of the droplet because, when it is in the bulk, some water-water hydrogen-  
504 bonds are disrupted. Entropic effects further enhance the surface preference when the system  
505 bears large apolar groups (e.g. 4-5 carbon atoms or longer hydrophobic chains).

506



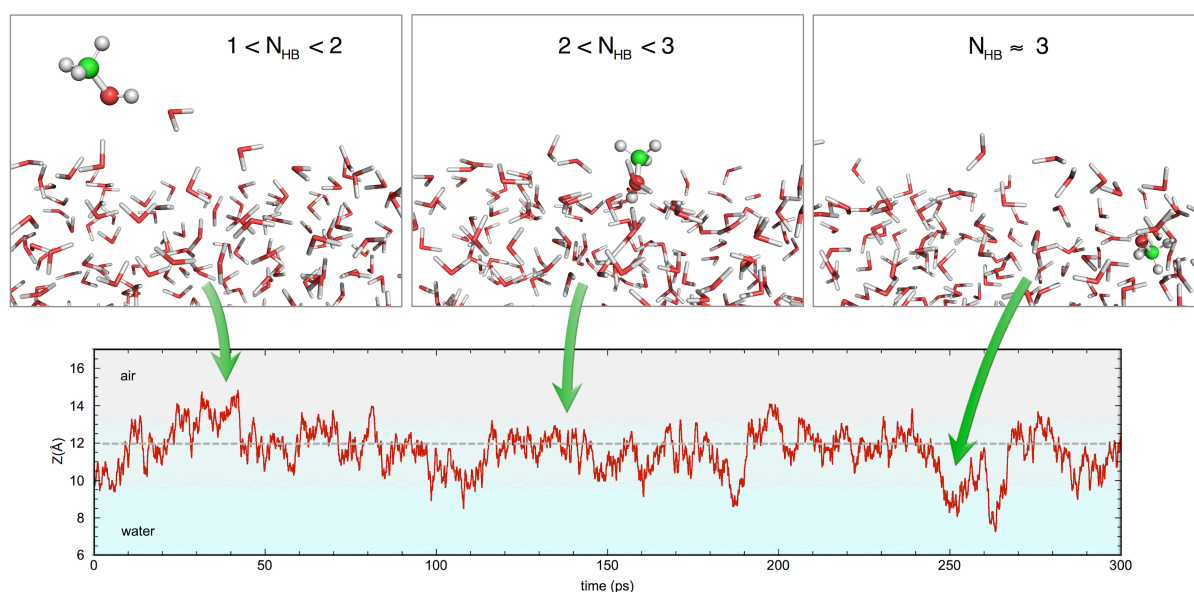
507

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

515

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

528



529

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

535

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

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

559 The interface affinity of ions has been explained (at least qualitatively) by a favorable balance  
560 between electrostatic and cavitation energies.<sup>199,204,205</sup> The later represents the energy cost  
561 required to disrupt water-water interactions in the medium in order to create a hole where the ion



562 is placed. The cavitation energy drops when the ion moves from bulk to the interface, and for  
563 bulky soft ions it can overcompensate the loss of favorable ion-water electrostatic interactions. In  
564 such a case, the ion stabilizes at the interface. The role of anion polarizability has been  
565 emphasized<sup>179,195</sup> and though correlation with interface affinity is not always apparent,<sup>206</sup> this term  
566 must be taken into account for a quantitative description of the adsorption energetics, as recently  
567 reported for aqueous solutions of  $\text{ClO}_4^-$  using SFG spectroscopy.<sup>205</sup> Under the effect of the local  
568 electric field (the permanent field due to the asymmetry of the interface and the ion-induced  
569 reaction-field), the electronic cloud of large polarizable anions is distorted and the induced  
570 dipole moment contributes to enhancing the solvation of the ion at the interface.<sup>192</sup> Solvation  
571 dispersion-forces may also influence interfacial adsorption,<sup>199,204</sup> specially at oil-water  
572 interfaces.<sup>188</sup>

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