Aqueous solutions: state of the art in ab initio molecular dynamics

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The simulation of liquids by ab initio molecular dynamics (AIMD) has been a subject of intense activity over the last two decades. The significant increase in computational resources as well as the development of new and efficient algorithms has elevated this method to the status of a standard quantum mechanical tool that is used by both experimentalists and theoreticians. As AIMD computes the electronic structure from first principles, it is free of ad hoc parametrizations and has thus been applied to a large variety of physical and chemical problems. In particular, AIMD has provided microscopic insight into the structural and dynamical properties of aqueous solutions which are often challenging to probe experimentally. In this review, after a brief theoretical description of the Born–Oppenheimer and Car–Parrinello molecular dynamics formalisms, we show how AIMD has enhanced our understanding of the properties of liquid water and its constituent ions: the proton and the hydroxide ion. Thereafter, a broad overview of the application of AIMD to other aqueous systems, such as solvated organic molecules and inorganic ions, is presented. We also briefly describe the latest theoretical developments made in AIMD, such as methods for enhanced sampling and the inclusion of nuclear quantum effects.

1. Introduction

Thales, recognized by Aristotle as the first philosopher in the Greek tradition, believed that water formed the
most fundamental building block of matter [1]. This sentiment was echoed later in the sixteenth century by the renaissance physician Paracelsus, who stated that ‘water was the matrix of the world and all its creatures’ [2; 3, p. 13]. While these ideas emerged at a time when nothing was known about the molecular structure of liquid water, the wisdom behind these thoughts is reflected in the extensive amount of effort that has been made in trying to understand the structural and dynamical properties of water and its ionic constituents in different environments using both theoretical and experimental approaches [4–11].

Before the early 1960s, the standard tools for quantifying the structural and dynamical properties of liquids were limited to experimental approaches. However, in their pioneering computer simulations, Stillinger and Rahman demonstrated that molecular dynamics (MD) could be used as a complementary method to probe the properties of liquids [12,13]. In MD, Newton’s equations of motion are solved numerically for a system of particles, yielding their phase space distribution (positions and momenta) as a function of time [14]. This gives access to the atomistic origin of both the thermodynamic and dynamical properties of the system. For example, MD simulations performed at different temperatures have elucidated the microscopic mechanism by which hydrogen bonds (HBs) form and break in water [13,15,16]. These simulations have also helped to provide a molecular basis for interpreting relaxation processes observed in vibrational spectroscopy experiments [11,17–19].

A critical part of performing MD simulations is to determine the forces on the particles which are used to propagate them in time [14]. The quality of these forces has an enormous impact on the accuracy of the physical quantities extracted from the simulations [15,20]. Most applications of MD typically involve the use of empirical potentials where the interactions between the particles are described by a set of analytical functions of structural parameters, such as distances, angles or dihedral angles (called force field). In most standard force fields, the parameters defining these functions remain fixed during the simulation, making them computationally efficient. This approach allows for the simulation of large system sizes and long simulation times, which are required for a realistic treatment of liquids, solid-state and biological systems [21–25].

Most standard force fields are faced with certain drawbacks. An important issue that comes up is the transferability of the interaction parameters to different chemical systems. In addition, most force fields do not explicitly account for the polarizability of the electrons [26,27]. These electronic effects can be quite critical, for example, in quantitatively describing the solvation phenomena of certain ions [24]. Most standard force fields cannot treat chemical processes involving bond breaking and formation. A prototypical example is proton transport in water, where covalent bonds continuously break and re-form [28]. In this case, a more general approach is required in which the electronic degrees of freedom are explicitly taken into account.

Among the proposed approaches to overcome these limitations, one of the most important developments in the field has been the combination of MD with first-principle calculations within the ab initio molecular dynamics (AIMD) framework [29–31]. The two standard approaches to AIMD are the Born–Oppenheimer molecular dynamics (BOMD) and Car–Parrinello molecular dynamics (CPMD) [29–32]. In these methods, the nuclei are numerically propagated in time in a similar manner as in the force-field approach. However, the forces on the nuclei at each MD step come from an electronic structure calculation. Hence, the response of the electrons to changes in the environment are intrinsically treated as the system evolves in time. Thus, polarization and charge-transfer effects are explicitly accounted for. AIMD has allowed for the study of numerous chemical systems ranging from liquids and solid-state materials to biomolecules. Besides providing a more accurate description of the structural and dynamical properties of these systems, AIMD has also been used to predict and interpret experimental observables directly linked to the electronic structure, such as infrared [33,34] and Raman spectra [35] or nuclear magnetic resonance (NMR) chemical shifts [36]. This has allowed for people in the physical, chemical, biological and engineering communities to probe the microscopic realm in much finer detail than ever imagined.

The focus of this review is to give the reader a broad perspective on the progress that has been made in the simulation of aqueous solutions. Owing to the vast amount of literature in this
area, our review focuses on the structure and dynamics of solutions and only briefly touches on spectroscopic and electronic properties. We begin §2 with a brief introduction to the basic concepts of the BOMD and CPMD methodologies. In §3, we discuss the progress that has been made in simulating liquid water and the transport properties of its constituent ions: the proton and the hydroxide ion. Section 4 briefly discusses the application of AIMD simulations to other species in bulk water as well as at interfaces. Section 5 touches upon recent theoretical developments that have been made to simulate aqueous systems with AIMD. Finally, we end with our conclusion in §6.

2. Ab initio molecular dynamics

As indicated earlier, AIMD solves the issues associated with the force-field approach by combining ‘on the fly’ a quantum mechanical description of the electrons with finite temperature MD. The accuracy of the methodology depends critically on the level of theory used to evaluate the ground state wave function \( \Psi_0(\{r\}, \{R\}) \) (where \( \{r\} \) and \( \{R\} \) represent the positions of the electrons and nuclei, respectively) of the many-body interacting system. This task is non-trivial and can be computationally very expensive. However, a number of approximations can be made to make this problem tractable while maintaining a high level of accuracy.

The most commonly used quantum mechanical approach that is used within this context is density functional theory (DFT). The determination of the energy and the wave function of any reasonably sized molecule is a formidable task. This is alleviated by the Born–Oppenheimer approximation, which asserts that, owing to the large difference in mass, the electrons move on a much faster time scale than the nuclei, which allows one to decouple their motion [37]. This implies that the electrons instantaneously and adiabatically follow the motion of the nuclei. Using this approximation, the many-body particle problem can be reformulated into a many-body electronic problem that Hohenberg & Kohn [38] then expressed in terms of the electronic density \( n(r) \), the nuclei being kept fixed. In this context, they demonstrated that the ground state of a non-degenerate system of interacting electrons is uniquely defined by the external potential, \( V_{\text{ext}} \), established by the nuclei. This was further reformulated by Kohn and Sham (KS), leading to the well-known KS DFT [39]. For more details on the theoretical aspects of DFT, the reader is referred to specific books on the subject and references therein [40–42].

Having determined \( n(r) \) and the corresponding KS energy \( E_{\text{KS}} \) for a given set of nuclear positions \( \{R\} \), the forces on these nuclei can be obtained. By using these forces in Newton’s equations of motion, one can then propagate the nuclei in a time-dependent manner. In practice, there exist two main methodologies to couple the electrons to the motion of the nuclei. These are the BOMD and CPMD methods. We now briefly review some of the key concepts behind these two approaches and refer the interested reader to other references for more details [29–31].

(a) Born–Oppenheimer molecular dynamics

The essence of the BOMD approach is that, at every MD step, an electronic structure calculation is performed. In this context, the propagation of the nuclei and determination of the electronic ground state are completely independent. BOMD can thus be incorporated into any MD numerical integrator by feeding it with forces coming from an ab initio calculation. In DFT, one begins by minimizing the KS energy of a system of interacting electrons that is described by the Hamiltonian \( \mathcal{H}_e \)

\[
\min_{\Psi_0} \langle \Psi_0 | \mathcal{H}_e | \Psi_0 \rangle = \min_{\{\phi_i\}} E_{\text{KS}}[\{\phi_i\}],
\]

with respect to a set of orthonormal mono-electronic wave functions \( \{\phi_i\} \) which are referred to as the KS orbitals. For a closed-shell system, the electronic density is expressed as \( n(r) = \sum_{i}^{\text{occ}} 2|\phi_i(r)|^2 \), so that \( E_{\text{KS}} \) is written as a functional of the \( \phi_i \)'s. Including the nuclei–nuclei
interaction term, the KS functional looks like

\[ E_{KS}(\{\phi_i\}) = T_s(\{\phi_i\}) + \int dr V_{ext}(r)n(r) + \frac{1}{2} \int dr V_H(r)n(r) + E_{ions}(R) + E_{xc}[n], \]  

(2.2)

in which the first and second terms represent the kinetic energy of the non-interacting electronic reference system and the external potential energy because of the electron–nuclei interaction, respectively. The third and the second last terms are the classical electrostatic energy of the electron density and the nuclei–nuclei interaction energy, respectively. Finally, the last term is the contribution from the exchange–correlation interaction. Although the existence of a universal exchange–correlation functional can be postulated from the work of KS, its analytical form is unknown and an approximate expression has to be used. Choosing the appropriate form for the exchange–correlation term is a non-trivial task and the quality of the simulations can significantly be affected by this choice. The reader is referred to the literature for more detailed reviews on this topic [40,41].

\( E_{KS} \) depends only on \( \{R\} \) and is equivalent in MD to the potential energy that comes from the force field. Consequently, the Lagrangian for the BOMD approach can be formulated as a function of solely \( \{R\} \) and \( \{\dot{R}\} \)

\[ L_{BO}(\{R\}, \{\dot{R}\}) = \frac{1}{2} \sum_{I=1}^{N} M_I \dot{R}_I^2 - \min_{\{\phi_i\}} E_{KS}(\{\phi_i\}, \{R\}). \]  

(2.3)

Using the Euler–Lagrange equation, the corresponding equation of motion is then given by

\[ M_I \ddot{R}_I = -\nabla_I \left[ \min_{\{\phi_i\}} E_{KS}(\{\phi_i\}, \{R\}) \right]. \]  

(2.4)

The right-hand side of equation (2.4) describes the force acting on the nucleus \( I \). Its evaluation is performed using the Hellman–Feynman theorem that allows for a convenient evaluation of the derivative of the total energy with respect to \( R_I \) [43]. When the \textit{ab initio} forces are coupled with a standard numerical MD integrator, one obtains a BOMD trajectory.

The BOMD approach is found in most of the popular AIMD codes, such as CP2K (http://cp2k.berlios.de), CPMD (http://www.cpmd.org/, Copyright © IBM Corp. 1990–2008, Copyright © MPI für Festkörperforschung Stuttgart 1997–2001), Quantum ESPRESSO [44], VASP [45] and CASTEP [46].

(b) The Car–Parrinello approach

In BOMD, the computational bottleneck involves converging the electronic wave function at every MD step. In 1985, the revolutionary approach by Car and Parrinello provided a way to get around this problem in an elegant and accurate manner which is now referred to as CPMD [32].

In contrast to BOMD, where the propagation of the electronic and nuclear degrees of freedom are explicitly decoupled, the idea of CPMD is to artificially introduce a classical coupling between them. In practice, this is achieved by associating a fictitious mass, \( \mu \), with the electronic degrees of freedom. Within the context of MD, this implies a fictitious dynamics of the \( \phi_i \)'s which automatically evolve with the motion of the nuclei to adopt an electronic structure close to the electronic ground state energy, \( \min_{\{\phi_i\}} E_{KS}(\{\phi_i\}, \{R\}) \). This is mathematically expressed within the Car–Parrinello extended Lagrangian

\[ L_{CP}(\{R\}, \{\dot{R}\}, \{\phi_i\}, \{\dot{\phi}_i\}) = \frac{1}{2} \sum_{I} M_I \dot{R}_I^2 + \mu \sum_{I} (\dot{\phi}_I \dot{\phi}_I) - E_{KS}(\{\phi_i\}, \{R\}) + \sum_{\text{occ},\text{occ}} \sum_{i,j} \Lambda_{ij}(\langle \phi_i | \phi_j \rangle - \delta_{ij}), \]  

(2.5)
where the $\Lambda_{ij}$s are the Lagrange multipliers that dynamically guarantee the orthonormality of the $\phi_i$’s. The second term on the right-hand side of equation (2.5) describes the fictitious classical dynamics of the $\phi_i$’s. By applying the Euler–Lagrange equation to both the nuclear and electronic degrees of freedom, we obtain the following Car–Parrinello equations of motion:

$$\mu \ddot{\phi_i} = -\frac{\delta E_{KS}}{\delta \langle \phi_i \rangle} + \sum_j \Lambda_{ij} \langle \phi_j | \phi_i \rangle$$  \hspace{1cm} (2.6)

and

$$M_i \ddot{R}_i = -\nabla_i [E_{KS}((\phi_i), (R))] = -\frac{\delta E_{KS}}{\delta R_i} + \sum_{ij} \Lambda_{ij} \frac{\delta}{\delta R_i} \langle \phi_i | \phi_j \rangle.$$  \hspace{1cm} (2.7)

Car & Parrinello [32] showed that if $\mu$ is chosen sufficiently small, then the nuclei and electrons are adiabatically decoupled and do not exchange significant heat. Under these conditions, the electrons are said to be ‘cold’ and the electronic wave function remains close to the Born–Oppenheimer surface as the nuclei are propagated in time. Several studies have shown that, by a careful selection of the fictitious mass of the electrons, the CPMD approach is able to reproduce structural and dynamical properties obtained from BOMD simulations. While the CPMD approach circumvents the need to converge the wave function at every MD step, integrating the equations of motion associated with the electronic orbitals requires the use of much smaller time steps than in BOMD. To take advantage of the strengths of both methodologies, newer approaches involving the coupling of nuclear and electron dynamics have further been proposed [47].

In the preceding discussion of the BOMD and CPMD methodologies, the nuclei are treated classically. In many applications involving the simulation of light elements, such as hydrogen atoms, quantum effects of the nuclei can also play a very important role. The gold-standard method for the inclusion of quantum effects in MD simulations is the path integral (PI) formulation of quantum statistical mechanics [48–50]. Within this framework, the quantum partition function of a particle is isomorphic to a classical partition function of $P$ classical particles that interact through a nearest-neighbour harmonic interaction. The BOMD and CPMD formalisms mentioned above have been extended to allow for the simulation of quantum nuclei with AIMD. The interested reader is referred to a review by Tuckerman ([30] and references therein) for mathematical details on the PI formalism and also recent methodological developments which allow for more efficient simulation of quantum effects [51,52].

3. Water and its constituent ions: the excess proton and the hydroxide ion

Owing to the importance of polarization and charge transfer effects, an accurate description of the structure and dynamics of polar protic and aprotic solvents requires an *ab initio* treatment. Consequently, a number of AIMD studies have provided illuminating insight into the microscopic features of the properties of these solvents, which are often very challenging to probe experimentally. This is particularly true for polar protic liquids where the HBs play a critical role in tuning macroscopic properties, such as the viscosity, dielectric constant and heat capacity. In this regard, liquid water has been an important system for many theoretical studies owing to its complex and anomalous behaviour under different thermodynamic conditions [53,54]. In this section, we briefly highlight some of the progress that has been made in the simulation of bulk water and refer the interested reader to the literature for more details on this topic. Thereafter, we provide a more comprehensive analysis of the transport properties of the proton and hydroxide ion in liquid water.

(a) Bulk water

The nature of the HB has been a subject of intense investigation in the literature [55–57]. Owing to its quantum nature, the strength of the HB is delicately tuned by the coupling of several
effects of the underlying electronic structure. These effects include the electrostatic interactions, polarization and charge transfer effects. Numerous studies in the last two decades have shed light on the electronic, structural and dynamical properties of liquid water. One of the most important case studies for the application of the CPMD method was the simulation of liquid water [58]. Laasonen and co-workers showed that the radial distribution functions ($g(r)$) of ab initio liquid water were in modest agreement with the $g(r)$ obtained from X-ray diffraction experiments (figure 1) [59]. The $g(r)$ obtained from AIMD showed that ab initio water was quite overstructured, suggesting that the water molecules form stronger HBs than in reality. Galli and co-workers [64] later also showed that structural properties in liquid water can be quite sensitive to the choice of the fictitious mass of the electrons. Future studies also shed light on the electronic and dielectric properties of liquid water. In particular, instantaneous polarization effects captured by maximally localized Wannier functions showed that the dipole moment of AIMD exhibited much larger variation than a fixed dipole typically used in empirical potentials [65–67].

The discrepancies evidenced by this pioneering simulation laid the foundation for many of the theoretical issues that have been revisited in numerous publications [31,64,65,68–83]. There continues to be an ongoing lively debate on the molecular origins of these discrepancies. On the one hand, Sprik et al. [68] demonstrated in the case of three GGA exchange–correlation functionals that the $g(r)$ of water is quite sensitive to its parametrization. Among the issues attributed to the GGA approximation, the lack of exact exchange contribution [69,70,76] and

Figure 1. (a) O–O and (b) O–H $g(r)$ of liquid water. The solid lines represent the results obtained from a CPMD simulation performed at room temperature [58]. The dashed lines represent experimental results [59]. The production AIMD simulation was performed on 32 classical heavy water molecules for 1.5 ps. The exchange–correlation interaction was described using the Becke–Perdew generalized gradient corrected functional [60,61] and the core valence interaction was described by ultrasoft pseudo-potentials [62,63]. (Reprinted with permission from [58]. Copyright © 1993, American Institute of Physics.)
dispersion interactions [77,79–81] has proved to be critical in tuning the properties of ab initio water. On the other hand, the low mass of the hydrogen atoms dictates that nuclear quantum effects (NQEs) are likely to play a significant role, particularly for the O–H \( g(r) \). Using empirical force fields [84–86] and later AIMD [82,83], several studies have confirmed that NQEs result in a significantly enhanced delocalization of the covalent O–H bonds, which in turn reduces the tendency for water to be overstructured.

Although the dust has not entirely settled on the origins of the observed discrepancies, recent work by Car and co-workers seems to suggest that it is the coupling of all these factors in concert that tunes the enthalpic and entropic contributions to the free energy landscape of water, and hence the \( g(r) \) (R. Car 2012, personal communication). To confirm this assertion, more experimental and theoretical works are needed to probe the properties of water beyond examining such structurally averaged properties as the \( g(r) \), which tend to wash out a lot of its underlying complexity.

(b) Proton and hydroxide ion in water

One of the most fundamental aspects associated with liquid water is the spontaneous auto-ionization of a water molecule leading to the proton and the hydroxide ion. It is the dynamic equilibrium between water and these ions that determines the pH of water. Their presence induces a perturbation to the structural and dynamical properties of the surrounding HB network. Furthermore, these species play a role in many physically relevant processes in the biochemical and atmospheric sciences. We now focus on the progress that has been made in characterizing the structural and dynamical properties of the proton and the hydroxide ion in liquid water. These examples demonstrate how AIMD simulations have provided unique and rich insight into the physico-chemical mechanisms of proton and hydroxide transfer that are often inaccessible with current experimental approaches.

(i) The excess proton

The structure and motion of the proton in water has been a subject of intense investigation in the fields of chemistry, physics and biology. Over 200 years ago, von Grotthuss attempted to understand the electrolysis of metals dissolved in water. In some cases, instead of reducing the dissolved metal, he observed the decomposition of water. By considering water as a mixture of oxygen and hydrogen species, Grotthuss hypothesized that these elements could be charged by the applied electric field. He imagined that these charge carriers formed ‘wires’ at the anode and cathode along which they continuously move in a domino-like effect [5,28,87]. These ideas laid the foundation for what is now referred to as the Grotthuss mechanism (figure 2). This process, described as structural diffusion, was later invoked to rationalize why the ionic mobility of the proton is much larger than that expected from hydrodynamic theory [88]. The early twentieth century later found many of the great scientific icons like Hückel, Hund, Wannier and Debye working on understanding the properties of water’s constituent ions [89]. It is the collective contribution of the aforementioned studies that has led to the advancement of our understanding of the structural and dynamical properties of the proton in liquid water. However, one of the important missing ingredients was an accurate atomistic description of both the structure of the proton and its transport phenomena.

Soon after the success of the CPMD method in simulating liquid water [58], it became clear that this methodology could help to probe the molecular properties of the proton. The first CPMD simulations of the excess proton in water by Tuckerman et al. [90,91] were performed classically in a box of 32 water molecules. Given the computational resources at the time, this was quite an achievement. At the time of these simulations in the early 1990s, there was an ongoing discussion on the solvated state of the proton in liquid water. Two limiting states were proposed, the Eigen and the Zundel cations [92,93]. The former consists of the proton localized on one water molecule forming a hydronium ion \( \text{H}_3\text{O}^+ \) that is strongly solvated by three water molecules forming the
Figure 2. The Grotthuss mechanism for proton transfer (PT) along a water wire is illustrated. Initially, the proton is localized on a water molecule in the top left corner (indicated by an asterisk (*)). In the Grotthuss mechanism, a sequence of jumps (black arrows) of different protons results in the transfer of the excess charge along the wire.

Figure 3. (a) The Eigen cation where the proton is localized on one water molecule and (b) the Zundel cation where the proton is shared between two water molecules.

Eigen cation $\text{H}_9\text{O}_4^+$, while in the latter the proton is delocalized between two water molecules forming an entity that resembles an $\text{H}_5\text{O}_2^+$ species. These two ions are illustrated in figure 3. The pioneering simulations by Tuckerman et al. showed that both the Eigen and Zundel cations are present in water. These studies examined the structural properties of water around the oxygen in which the proton is localized, separately for the $\text{H}_9\text{O}_4^+$ and the $\text{H}_5\text{O}_2^+$ cations, and found remarkable signatures in the $g(r)$’s of the individual species (figure 4). The CPMD simulations suggested that the dominant state in liquid water was the Eigen cation and that the Zundel species was an intermediate that formed as the proton transferred from one water molecule to the next.

These simulations also provided detailed insight into the microscopic aspects of the mechanisms by which the proton migrates in water. After 200 years, these studies confirmed the qualitative picture imagined by Grotthuss, but now for the first time a molecular window
Figure 4. (a) O*–O and (b) O*–H radial distribution functions for the Eigen and Zundel cations and pure water. In the Eigen cation, the O* atom corresponds to a single hydronium oxygen, whereas in the Zundel cation O* corresponds to the two oxygen atoms sharing the proton. The distribution functions for the H$_5$O$_2$$^+$ are represented by solid lines, for the H$_9$O$_4$$^+$ by dotted lines and for water by dashed lines. The 0–0 $g(r)$ of the Zundel cation is more compressed than that of the Eigen cation owing to the presence of a more delocalized proton between the shorter O–O bonds (see corresponding O–H $g(r)$). (Reprinted with permission from Tuckerman et al. [91]. Copyright © 1995, American Institute of Physics.)

into the microscopic events involving proton transfer (PT) was unveiled. These details still remain extremely challenging to probe experimentally. One of the interesting features that was observed in the simulations was that one out of the three water molecules solvating the central hydronium was particularly compressed at approximately 2.5 Å. This short and hence strong HB was coined as the ‘special bond’ or ‘special pair’ which facilitated the frequent excursions of the proton between the limiting H$_9$O$_4$$^+$ and H$_5$O$_2$$^+$ states [90,91,94]. This process involved the interconversion between strong and weaker HBs resulting in a broad distribution of intermediate states also known as the Zundel continuum [93,95].

Perhaps one of the most exciting features of the calculations was the discovery of the rate-determining step of PT, which involves the reorganization of the surrounding solvent around both the proton donor and acceptor. Numerous studies using both AIMD [96,97] and empirical valence bond approaches [8,94,98,99] later provided a more quantitative description of this process. The overall picture of the mechanism is illustrated in figure 5. In its stable Eigen cation state, the oxygen of the hydronium accepts a weak HB and is thus relatively hydrophobic compared with the oxygen in neutral water (figure 5a). The PT process begins with frequent back-and-forth
excursions between the donor and acceptor. These are known as rattling events which do not lead to successful PT. Figure 5a,b illustrates the process by which the water molecule that accepts the proton loses an HB donated to it. Recall that this event makes this water molecule more likely to accept the proton. In addition to this, figure 5c,d further shows that the water that loses the proton accepts a new HB, thereby destabilizing its ability to host the proton. It is the combination of these two events that leads to the successful transfer of the proton. The combination of all these collective processes is commonly referred to as the ‘pre-solvation’ criterion for PT in water [94,97].

Since the time of Wigner, it has been well appreciated that NQEs could have a significant impact on the statistical mechanical properties of particles, as protons [100]. Owing to the intrinsic quantum behaviour of the proton, an important aspect of the AIMD simulations has been the study of the role of NQEs on its properties. Marx et al. pioneered the first CPMD simulations in which NQEs were included using the PI formalism [101] in a box consisting of 32 water molecules. Each quantum particle was treated with an equivalent eight beads, making it a computationally challenging calculation. While the inclusion of NQEs did not qualitatively change the overall features of PT, the quantum simulations displayed some interesting features. To highlight these aspects of the process, the authors introduced the PT coordinate ($\delta$), which was defined as the difference in Euclidean distance between the transferring proton and the two oxygen atoms of

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure5.png}
\caption{Main steps leading to a successful PT. (a) Stable Eigen cation state of the proton and its surrounding environment. The opaque water molecule donates a weak HB to the hydronium. (b) The water molecule that accepts the proton loses an HB that is being donated to it. (c) The current hydronium accepts a new HB which destabilizes its ability to host the proton. (d) Successful PT. The asterisks (*) denote the water molecule that hosts the proton. (Adapted from fig. 4 in Berkelbach et al. [97].)}
\end{figure}
Figure 6. Averaged distribution function $P(\delta, R_{oo})$ of the proton displacement $\delta$ relative to the $O_aH_2O_b$ bond midpoint (asymmetric stretch coordinate) and the corresponding oxygen–oxygen separation $R_{oo}$ between the two neighbouring oxygen atoms $O_a$ and $O_b$ from quantum (a) and classical (b) simulations at 300 K. In (a), the averaged local coordination number of $O_b$, $n(\delta, R_{oo})$, is superimposed on $P(\delta, R_{oo})$ using a color code: $n$ decreases from yellow (approx. 4) to red to green to blue (approx. 3.5). The reader is referred to the original reference for a more detailed description of the reaction coordinates shown in this figure [101]. (Reprinted with permission from Nature Publishing Group. Image courtesy of Mark Tuckerman.)

the water molecules sharing this proton. When this coordinate is plotted against the distance between the oxygen atoms sharing the proton ($R_{oo}$), one obtains a ‘banana’ shape distribution which shows that the PT is coupled to the compression of the oxygen atoms (see figure 6a, b, which shows the projection of the distribution along the $\delta$ and $R_{oo}$ coordinates) [101]. The classical simulations indicated that the barrier for PT is approximately 0.5 kcal mol$^{-1}$, while NQEs made the process essentially barrierless. Thus, NQEs have the effect of increasing the delocalization of the proton shared between the two water molecules and subsequently increase the likelihood of observing species that have more Zundel-like character. Tuckerman et al. also showed that NQEs soften the barrier associated with the pre-solvation process, which is coupled to the PT process as described earlier. Many of these features have now been reinforced in recent AIMD studies of PT in solid-state systems [102–105].

(ii) The hydroxide ion

While there now exists a consensus on the structural and dynamical properties of the proton in water, arriving at the same for the hydroxide ion has been significantly more challenging [96,106,107]. Historically, the work on $OH^-$ began with the assumption that its transport mechanisms could be inferred from inverse symmetry arguments based on what was known for the proton [88]. For an enlightening discussion of more historical details, the reader is referred to a review by Marx and co-workers [107]. This led to the notion of the ‘mirror image’ concept, whereby it was suggested that the transport mechanisms of the ions were similar by assuming that their solvation topologies were the same. Thus, instead of the excess proton hopping along the wire shown in figure 2, a proton ‘hole’ (the $OH^-$) is moved by successive hydrogen shifts. This mechanism, however, does not explain the difference in conductivity between the ions that has been measured experimentally [89]. This suggests that the mirror image mechanism does not capture the complete physics. AIMD simulations of $OH^-$ in water have thus played an important role in disentangling the underlying differences in transport mechanisms of the ions. We now highlight some of the key aspects that have been learnt from AIMD simulations on the structural and transport properties of $OH^-$ in water.
Figure 7. (a) The ground state structure of solvated OH\(^-\) (H\(_9\)O\(_5\)\(^-\)) predicted by Tuckerman et al. The opaque water molecule is only weakly bonded to the OH\(^-\) ion. (b) The intermediate formed as part of the pre-solvation process during the transfer of the OH\(^-\) ion (H\(_7\)O\(_4\)\(^-\)). (c) The Zundel anion (H\(_3\)O\(_2\)\(^-\)).

Similar to the excess proton, the pioneering studies by Tuckerman et al. [90,91] on OH\(^-\) using the Becke–Lee–Yang–Parr (BLYP) functional initially focused on treating the nuclei classically in a small box of 31 water molecules. In these simulations, OH\(^-\) accepts four strong HBs in close to a square planar arrangement forming the H\(_9\)O\(_5\)\(^-\) species (figure 7a), where the OH\(^-\) anion is also capable of donating a weaker HB. Thus, the surrounding solvent is significantly perturbed compared with a tetrahedrally coordinated water molecule. These structural features of OH\(^-\) appear to be different from microsolvation, thermochemical and spectroscopic experiments of small hydrated OH\(^-\) clusters, which suggested a smaller first coordination sphere [108,109]. As the OH\(^-\) ion induces a large structural perturbation to its surrounding solvent environment, it appears as though much larger hydrated clusters will be required to capture the environment that the defect experiences in liquid water [107].

These calculations also provided useful insight into the electronic properties of H\(_3\)O\(^+\) and OH\(^-\). For both these ions, Tuckerman et al. [91] were able to compare their electronic density of states (DOS) with that of pure water. If the ions induced a large perturbation in the local electronic structure, this would be manifested in the DOS. These studies showed that while the DOS of the excess proton was very similar to that of pure water, OH\(^-\) introduces new features into the DOS which were attributed to the presence of H\(_9\)O\(_5\)\(^-\) and a species with a smaller hydration shell (H\(_7\)O\(_4\)\(^-\)) (see figure 7a,b for structures). It is exciting to note that recent electron spectroscopy experiments have been able to probe the local electronic structure of OH\(^-\) in water and confirm its hyper-coordinated solvation structure [110].

Tuckerman and co-workers also laid the foundation for the mechanism by which the hydroxide ion propagates through water. This process bears some similarities to the motion of the excess proton in that it also involves a pre-solvation process. The studies showed that fluctuations in the surrounding solvent could lead one of the HBs in the H\(_9\)O\(_5\)\(^-\) species to break. This leaves the OH\(^-\) accepting three HBs in a tetrahedral arrangement forming the H\(_7\)O\(_4\)\(^-\) anion (figure 7b). In this configuration, a transient Zundel anion (H\(_3\)O\(_2\)\(^-\), figure 7c) is formed which causes a migration of the anionic defect and subsequently reforms the stable and relatively immobile H\(_9\)O\(_5\)\(^-\) species. In contrast to the proton, the motion of OH\(^-\) is coupled to geometrical factors involving its angular orientation relative to the surrounding water molecules [111]. Tuckerman et al. showed that the PT event appeared to be most favourable when the angle \(\theta\) between the OH\(^-\) axis and one of the three HBs was close to the H–O–H angle of a water molecule [111]. This is illustrated in the probability distribution function plotted in figure 8b, which shows a strong tendency to constrict along \(\theta\) as PT occurs. These molecular details that were probed by the AIMD simulations still remain experimentally inaccessible.

The role of NQEs was also examined for the OH\(^-\) ion. Similar to the excess proton, NQEs significantly lower the PT barrier approximately from 1.28 to 0.34 kcal mol\(^{-1}\). However, the distribution along the PT coordinate \(\delta\) still retains its double-well character, which demonstrates that the Zundel anion H\(_3\)O\(_2\)\(^-\) of the ‘mirror-hole’ mechanism is an unstable intermediate state.
Figure 8. The normalized two-dimensional probability distribution function, \( P(\delta, \theta) \), of the proton displacement coordinate, \( \delta \), and the angle, \( \theta \), between the OH\(^-\) covalent bond axis and the O–O vector of the most active HB for the classical (a) and quantum (b) simulations at 300 K. The reader is referred to the original reference for a more detailed description of the reaction coordinates shown in this figure [111]. (Reprinted with permission from Nature Publishing Group.)

This is in contrast to the excess proton in which NQEs completely wash out the barrier for PT along \( \delta \). As indicated earlier, the classical simulations (figure 8b) suggest that PT events appear to be most likely when the transiently formed hydrated OH\(^-\) (H\(_2\)O\(_3\)) has a tetrahedral geometry. The inclusion of NQEs significantly softens the angular coordinate \( \theta \), which implies that PT resulting in the OH\(^-\) transfer can occur quite easily even if the overall geometry is distorted and non-tetrahedral [111].

In contrast to H\(_3\)O\(^+\), AIMD simulations of OH\(^-\) seem to show surprising sensitivity to the choice of the exchange–correlation functional [96,106,107]. The disconcerting factor at this point is that different functionals change both the structural and dynamical properties of OH\(^-\) in a rather drastic manner. One of the main discrepancies comes from the difference in solvation structure predicted by the Perdew–Wang 1991 (PW91)/Perdew–Burke–Ernzerhof (PBE) and BLYP/Hamprecht–Cohen–Tozer–Handy (HCTH) functionals. The former yields an OH\(^-\) that accepts three HBs and is subsequently more labile, giving a diffusion constant that is much larger than that predicted from experiments [112]. On the other hand, both BLYP and HCTH yield a similar solvation structure where OH\(^-\) accepts four HBs. However, these two functionals yield a different diffusion constant for OH\(^-\). Based on the current empirical evidence, Marx and co-workers [96,106,107] have advocated that the BLYP functional appears to give the best description of OH\(^-\). It is likely that different functionals delicately tune the balance of both polarization and charge transfer effects and subsequently change both the structural and dynamical properties of the defect and its solvent environment. However, establishing the electronic origin of these discrepancies remains unresolved.

(iii) The contact ion pair: H\(_3\)O\(^+\) – OH\(^-\)

The studies of the properties of H\(_3\)O\(^+\) and OH\(^-\) in bulk water have opened up other exciting applications. One of the most important in this regard is the study of the dynamic equilibrium between water and its constituent ions. It is this dynamic equilibrium that determines the pH of water under different conditions. Most of the acid–base neutralization studies have been interpreted within the framework of the model proposed by Eigen and de Maeyer in the 1960s [89]. This model attributes the rate-limiting step of recombination to the approach of the solvated species by a Grotthuss-like structural diffusion mechanism until a contact distance of about 6 Å where the contact ion pair is formed (figure 9) [113]. The subsequent recombination is then a downhill process. This is a good, effective model, but it does not provide a molecular picture of the underlying mechanism. Thus, the dynamic equilibrium between water and its constituent ions has been investigated with AIMD through both the process leading to the ionization of a water molecule and its time-reversed process, the recombination of the ions.
Figure 9. Contact ion pair formed by a water wire linking the hydronium and hydroxide ions in liquid water when they reach the contact distance at 6 Å. The labels 1–4 refer to the coordinates used to track the compressions of the wire. Labels 1–3 refer to the individual O–O bond lengths while 4 refers to the length of the entire wire given by the sum of all three O–O bond lengths 1–3.

Besides being a topic of fundamental interest in physical chemistry, studying these processes in liquid water has also faced methodological challenges. In particular, as the ionization of water is a rare event, standard AIMD simulations would not be able to simulate this process. Instead, one must employ enhanced sampling algorithms (see §5a). These methods allow one to explore the underlying free energy surface more efficiently. In 2002, Chandler and co-workers [114] used a combination of transition path sampling (TPS) and CPMD simulations to examine the ionization of liquid water in a box of 32 water molecules using the BLYP functional [4]. For the first time, a molecular movie of how the contact ion pair can be generated was revealed from the simulations. These studies suggested that the ionization of water is driven by rare electric field fluctuations that transiently stabilize or destabilize the O–H bond. The TPS trajectories also suggested that the breakage of a HB wire bridging the ions (figure 9) was necessary to stabilize the ions separated by the solvent. If we invoke microscopic reversibility, the studies by Chandler and co-workers impose important mechanistic details on the time-reversed process of the recombination of hydronium and hydroxide ions. In particular, these studies suggest that, as long as a wire bridges the ions, shuttling of the protons along it is guaranteed and neutralization occurs.

We have recently revisited this fascinating problem, focusing on the time-reversed recombination process [6]. Our simulations show that the existence of the HB wire is necessary but not a sufficient condition for neutralizing the ions. In addition, we find that, although a wire always links the ions, the contact ion pair can exist in a quasi-stable state. Instead, the recombination process requires a sizeable collective compression of the wire, which leads to a concerted motion of protons. This is different from the modern view of the Grotthuss mechanism of proton and hydroxide transfer, which has been shown theoretically to be a stepwise process (see above). These results have important implications for the mechanisms of the auto-ionization of water. First, the simulations suggest that hypercoordinated water molecules (those that accept three HBs from nearby donors) are likely to serve as nucleation sites for water ionization. It is interesting to note that Dellago and co-workers have recently shown using an empirical water model (SPC/E) that the strength of the electric field along the O–H bond is more enhanced for water molecules that accept three HBs. Besides the hypercoordination, to eject the proton to contact distance, a collective compression of at least four water molecules is necessary. These calculations provide a more nuanced picture to the phenomenological model proposed over 60 years ago by Eigen and de Maeyer [89]. An important lesson from both the old [4] and newer studies [6] is that phenomena associated with liquid water can be in much longer range than expected. With the current computational advancements, studying much larger system sizes will be possible and may bring other interesting surprises for both experimentalists and theorists in this field.
4. *Ab initio* molecular dynamics simulation of chemical species in liquids

The success of the application of AIMD to the study of water and its constituent ions has further motivated other important applications on liquids, such as inorganic ions and organic molecules in aqueous solution or near interfaces. Historically, studying these systems has been limited to only experimental techniques. Among them, neutron and X-ray scattering experiments, extended X-ray absorption fine structure (EXAFS) and X-ray absorption near-edge structure (XANES) give access to radial distribution functions and thus to information about the average structure of the liquid. On the other hand, NMR and infrared (IR) spectroscopies provide information both on the chemical environment of the individual species as well as on the dynamical properties of the liquid. AIMD has allowed for many of these experimental observables to be determined from first-principles calculations. In this context, BOMD and CPMD have been used as fundamental tools to complement, understand and even motivate experimental measurements. Seeing the growing importance of these studies, we provide in the following a broad overview of some of the recent applications of AIMD simulations to aqueous systems that were not discussed in the previous section.

(a) Ions and inorganic species in aqueous solution

One of the obvious extensions to the study of pure liquid water and its ionic constituents has been AIMD of other solvated ions. Among the vast amount of published work, the simulation of mono-atomic alkaline [115–118], earth alkaline [119–127] and halide [128–133] ions in water has formed an important part of these studies. CPMD simulations have provided molecular details into the structure and dynamics of water in the hydration shells of these ions which have helped to complement various experiments. For example, Kropman & Bakker [134] performed mid-infrared nonlinear spectroscopy experiments to study the dynamical properties of the hydration shell of various halides. They found that water molecules in the first hydration shell of the halides are characterized by an average residence time that is about 20–50 times slower than that of bulk water. They attributed this observation to the strong mutual interaction of the water molecules around the anions. AIMD simulations have been conducted and have also evidenced long residence times in the first solvation shell of Br$^-$ [132,133]. In addition, the calculations were also able to characterize the asymmetric structure of the solvation shell as well as the variation in the residence times of different water molecules. As highlighted by Raugei & Klein [132,133] the *ab initio* description of Br$^-$ allows for a realistic treatment of both polarization and charge transfer effects which are crucial to reproduce the long residence times. Another interesting example that particularly stands out has been the combination of CPMD simulations with experimental studies to determine the coordination number of Ca$^{2+}$ in solution. Both X-ray diffraction and EXAFS experiments suggested that the coordination number of Ca$^{2+}$ varied between six and eight. By contrast, neutron diffraction studies proposed a wider range between six and 10. Using CPMD simulations, Lightstone *et al.* [123] and Ikeda *et al.* [124] have demonstrated that the first solvation shell of Ca$^{2+}$ is structurally heterogeneous with energetic degeneracy in the coordination number which could possibly account for the various experimental observations. In addition, as these techniques spherically average the radial coordinates, it is challenging to probe the three-dimensional structure of the hydration shell. In this regard, the AIMD studies have also shown that the first hydration shells of both Ca$^{2+}$ and Mg$^{2+}$ are structurally anisotropic. Mixed systems consisting of ion pairs with varying concentrations have also been studied [128,130,131,133,135,136]. In the case of NaOH and KOH [137], a clear influence of the counterion on the hydration structure of the hydroxide ion has been demonstrated.

The application of AIMD simulations has also been extended to other elements of the periodic table. For example, by combining neutron diffraction experiments and AIMD simulations, Pasquarello *et al.* [138] have demonstrated the fivefold coordination nature of the Cu$^{2+}$ ion in water. These results challenged the commonly held view of the classical sixfold coordination structure generally assumed for such metallic elements. A similar study was performed some
years later by Swaddle et al. [139] for the trivalent aluminium ion. By combining high-pressure $^{17}$O NMR experiments and CPMD simulations, they showed that in the intermediate pH range, $4.3 < \text{pH} < 7$, the low pH stable structure $\text{Al(H}_2\text{O)}_6^{3+}$ undergoes deprotonation, causing the loss of one water molecule which leads to a five-coordinated $\text{Al(H}_2\text{O)}_4\text{OH}_2^{+}$ species (see figure 10 for a molecular picture of these two species). Although these findings contradict the classical view that $\text{AlOH(aq)}^{2+}$ conserves an octahedral structure in this pH range, they are however supported by $^{27}$Al NMR experiments [140–142]. The hydration properties of other metal ions, in particular $3d$ and $4d$ transition metal ions [143–152], have also been the subject of numerous computational studies which have shed light on their redox properties and chemical reactivity. A representative example of this kind of work is the study, by Blumberger et al. [144], of the redox reaction between copper and silver, $\text{Ag}^{2+} + \text{Cu}^+ \rightarrow \text{Ag}^+ + \text{Cu}^{2+}$. To do so, they performed independent studies for both half-redox reactions, $\text{Ag}^{2+} + e^- \rightarrow \text{Ag}^+$ and $\text{Cu}^+ \rightarrow e^- + \text{Cu}^{2+}$, using a grand-canonical extension of AIMD [153]. Despite the complexity of this reaction, they were able to reproduce its experimental redox free enthalpy ($-1.8$ eV compared with $-1.7$ eV from their calculation). More interestingly, by examining the $g(r)$ from the simulations, Blumberger and co-workers were able to map out how the energetics of the full redox reaction are correlated with the reorganization of the hydration shell of the ions (figure 11). The authors further interpreted the differences in redox chemistry of Cu and Ag from the drastically different solvation properties of $\text{Cu}^+$ compared with $\text{Cu}^{2+}$ as opposed to rather similar ones between $\text{Ag}^+$ and $\text{Ag}^{2+}$.

Owing to the increase in computational power, the development of highly scalable algorithms and the improvement of theoretical approaches over the last 20 years, the AIMD methodology has further been applied to more chemically complex ions and inorganic species in water. In particular, these studies include a large variety of metallic oxides and complexes where the properties of the system strongly depend on both the pH and the concentration of the metallic species [154–166]. For example, in the case of molybdenum, these studies have unravelled the influence of pH on species such as $\text{MoO}_2(\text{OH})_2$ [161]. The corresponding structural modifications have proved to be fundamental for the subsequent chemical condensation leading to polyoxometalates. In addition, in a number of these works, AIMD simulations have been

**Figure 10.** Snapshot of the initial $\text{Al(H}_2\text{O)}_6^{3+}$ geometry (a) and the five-coordinate $\text{AlOH}^{2+}$ ion (b) that forms in the CPMD simulations. The surface identifies the inner-coordination spheres, and dashed orange lines show the tree-like array of HBs that stabilizes the structure. The $\text{AlOH}^{2+}$ ion was initially formed by removing an $\text{H}^+$ from an $\text{Al(H}_2\text{O)}_3^{3+}$ equilibrated with $58 \text{H}_2\text{O}$ molecules (for clarity, most are not shown) in a cubic cell (12.4 Å). It converted within 0.8 ps to a five-coordinate structure that persisted for the length of the simulation (10 ps). (Image courtesy of Thomas W. Swaddle, Eric Bylaska and William H. Casey. Reprinted with permission from [139]. Copyright © 2005 Science.)
combined with an *ab initio* evaluation of the NMR parameters of the studied solutes to allow for a direct comparison with experimental measurements. For example, in the case of iron cyanide complexes, a large geometry dependence of the $^{57}\text{Fe}$ chemical shift has been proposed from AIMD [158,159]. In this context, Bühl and co-workers [158,159] proposed unusual temperature dependencies or isotope effects for the $^{57}\text{Fe}$ chemical shift of these complexes. Although not directly verified experimentally, measurements on ferrocene seem to support their hypothesis [167].

(b) Organic and organo-metallic chemistry

Since its early developments, quantum chemistry has found a wealth of applications in organic and organo-metallic chemistry. The continuous increase in the complexity of experimentally synthesized molecules as well as their industrial applications have motivated a large amount of static *ab initio* calculations. In these studies, the solvent, when taken into account, is typically treated in a continuum manner. In a number of cases, these approximations can lead to inaccurate results. As a consequence, the coupling of AIMD with an explicit treatment of the solvent is a crucial step in providing a better understanding of various aspects of organic and organo-metallic chemistry.

Needless to say, the physical properties of organic and organo-metallic molecules, for example vibrational properties, crucially depend on their interaction with the surrounding water molecules. Consequently, there have been a number of applications of AIMD devoted to the structural characterization of molecules in water. Perhaps a more interesting application is in using AIMD to study chemical reactions in water. For example, this has been performed for the prototypical chemical reactions E1/E2 eliminations between a substituted pyridinium ion and the
hydroxide ion [168], and for the $S_N2$ substitution of $\text{CH}_3\text{Cl}$ by $\text{Cl}^-$ [169]. In §5a, we provide a more general discussion on theoretical approaches specifically developed to deal with more complex chemical reactions.

When dealing with reactions involving complex electron transfers, such as redox reactions, AIMD can also provide important insight into the underlying mechanisms. Such studies have been conducted by Baerends and co-workers [170–172], who studied several aspects of fenton-like reactions involving the ironoxido $\text{FeO}^{2+}$ intermediate. Among their various results, they demonstrated that the aqueous solvent decreases the energy barrier of the oxidation of methanol to formaldehyde by $48 \text{kJ mol}^{-1}$ compared with the gas phase [172]. The authors obtained similar results for the oxidation of methane to methanol [171]. They were able to rationalize these observations by showing that the solvent significantly perturbs the electronic structure of the $\text{FeO}^{2+}$ intermediate.

An important quantity in acid–base chemistry is the $pK_a$ of the acid–base groups. Although this quantity is not available directly from unbiased AIMD simulations, it is possible to evaluate $pK_a$’s by performing constrained simulations in combination with thermodynamic integration. In particular, Sulpizi & Sprik [173] proposed a statistical mechanical theory in the spirit of Widom-like particle insertion, to calculate thermodynamic free energies using the distributions of the vertical energy gap associated with the insertion or deletion of a proton. Using this approach, the authors have been able to calculate the $pK_a$ of various compounds, such as HCl, HCOOH and $\text{H}_2\text{S}$. Other similar approaches have been applied to evaluate the $pK_a$ of more complex species, such as $\text{P(OH)}_5$ [174], histidine [175], benzoquinone [176], pentaoxyporphoranes [177] and HPO chelators [178].

(c) Ions at interfaces

While the focus of this review has been on the progress of AIMD simulations in providing theoretical insight into the structural and dynamical properties of ions in liquid water, the great majority of applications that are of biological or engineering interest involve aqueous systems near different interfaces [24,179–183]. It is beyond the scope of this review to cover all these interesting and important topics and we only highlight a couple of examples.

The air–water interface has attracted quite a bit of attention from both the experimental and theoretical communities [184–186]. Besides being a topic of fundamental interest as one of the most generic hydrophobic interfaces, chemical phenomena occurring at this interface are critical for understanding the atmospheric chemistry of oceanic surfaces and sea water aerosols. Owing to its inherent asymmetry, the air–water interface is characterized by water molecules with many dangling bonds. AIMD simulations of pure liquid water at the air–water interface have illuminated the changes in the hydrogen bonding properties of water near the interface and the subsequent effects on the surface potential of water [187–190]. Besides characterizing the thickness of the interface, these simulations have also been able to quantify the relative propensity of the water molecules acting as donors or acceptors of HBs. These studies have helped to complement and interpret numerous experiments probing both structural and dynamical properties of the surface of water [191,192].

Another closely related topic is the anomalous tendency for specific ions to bind to the surface of water. In this regard, there is currently an ongoing lively debate on the pH of the surface of water. The current state of the literature indicates that there are two contradictory views on this subject. Most theoretical studies indicate that the hydronium ion has a higher binding affinity for the air–water interface than the hydroxide ion, leading to the notion that the surface of water must be acidic [185]. The results of these theoretical studies have been corroborated by observations made from nonlinear surface-specific spectroscopic techniques of acids and bases [193]. The conclusion that the surface of water is acidic contradicts electrophoretic experiments which show that air bubbles in water migrate towards the positive electrode [194]. This has been interpreted as an enhancement of hydroxide ions near the bubble, which gives it a characteristic negative charge [186]. However, AIMD simulations indicate that the hydroxide
ion is only weakly bound at the air–water interface [189]. More recently, enhanced charge transfer between water molecules at the oil–water interface has been proposed to play a significant role in causing the negative charge observed at the interface [188]. The issue still remains unresolved.

Besides the aforementioned studies at the air–water interface, there is an entire field of interesting applications involving the simulation of water and ions near inorganic solid-state surfaces, such as crystalline [195–200] and amorphous silica [201], bio-glasses [202], rutile [203–208], geothite [209] and alumina [210]. These studies have provided detailed information on the structural and dynamical properties of water subjected to different structural and electrical perturbations. For example, AIMD simulations of ions and water near amorphous silica have shown that the surface is characterized by hydrophilic and hydrophobic patches, which in turn modulates the local water density at the surface [201]. One of the tantalizing aspects of these types of simulations is that one is also able to explore the chemical reactivity of water at interfaces. For example, in the late 1990s Andreoni and co-workers [210] used CPMD simulations to show that water could dissociate on the surface of alumina even in the absence of defects. More recently, Scipioni et al. [211] have shown that different metals can change the mechanism of PT along water wires at metallic surfaces.

(d) Beyond liquid water

This review has focused on the simulation of aqueous solutions, both pure water and water used as a solvent. However, the application of AIMD not only is restricted to aqueous systems but also provides a general methodology that can be used to study different types of liquids. In particular, there have been a number of AIMD simulations of organic and ionic liquids because of their particular relevance in synthesis chemistry and industrial applications. Therefore, the atomic structures of solvents such as methanol have been studied using CPMD and BOMD simulations [212,213]. These studies have been extended further to characterize the structure and the reactivity of ions and molecules in these solvents [214–220]. For example, Handgraaf & Meijer [217] have provided the first evidence of a solvent-mediated mechanism for the ruthenium-catalysed transfer hydrogenation of formaldehyde. The authors demonstrated the need for an explicit treatment of the organic solvent within an ab initio framework to accurately describe this chemical process.

Other less common liquids have also been the subject of AIMD simulations. This is the case for liquid ammonia that is used industrially for the dissolution of alkali metals and other salts. The structural and dynamical properties that have been extracted from AIMD simulations are in the modest agreement with experimental measurements, which has evidenced the role of NQEs and the sensitivity to the choice of the exchange–correlation functional [221–223]. Similar studies have also been performed on liquid HF [224,225] and HCl [226] and more recently on liquid phosphoric acid H₃PO₄ [227]. H₃PO₄ has remarkable properties that have been characterized experimentally. It presents a very high proton conductivity (0.15 S cm⁻¹ above its melting temperature) comparable to that of protons in water, whereas the conductivity of phosphorus atoms is about 4.5 times lower. Based on CPMD simulations, Vilčiauskas et al. [227] proposed a structural diffusion mechanism to explain this anomalously high conductivity. In contrast to bulk water, where consecutive PTs require solvent reorganization at each jump of the proton (see above), the presence of extended, strong and highly polarized hydrogen bonded chains allows for fast correlated PTs over several molecules before solvent reorganization occurs.

5. Theoretical progress in ab initio molecular dynamics

The development of AIMD and its large impact on the scientific community have been inextricably associated with the increase in computational power and the development of efficient algorithms. Despite the continuous progress in this area, the applications of AIMD are still
restricted to relatively short simulation lengths and system sizes. In this context, we now provide a brief description of some of the latest developments made in our group to overcome this issue.

(a) Enhanced-sampling approaches for simulating activated processes

Typical time scales accessible in AIMD are of the order of several tens of picoseconds for systems consisting of 100–300 atoms. This allows for a good convergence of various equilibrium properties but is generally far too short to study activated processes characterized by barriers that are several orders of magnitude larger than $k_B T$. Prototypical cases are chemical reactions or isomerization of molecules in solution that do not spontaneously occur on the time scale of AIMD. Consequently, the free energy surface of the chemical system is not properly sampled in the AIMD simulation.

Numerous enhanced sampling methods have been proposed to overcome the sampling problem that plagues all MD simulations. Among them, umbrella sampling [228], transition path sampling [114] and metadynamics [229–231] have proved to be very successful in providing insight into the mechanisms of numerous chemical reactions. In the last decade, our group has invested significant effort in the development of metadynamics (MetaD). Hence, in the following, we focus our discussion on its applications. MetaD has been applied to the study

Figure 12. Example of metadynamics simulation in a one-dimensional model potential. The time $t$ is measured by counting the number of Gaussians deposited. (a) Time evolution of the collective variable during the simulation. (b) Schematic of the progressive filling of the underlying potential (thick line) by means of the Gaussians deposited along the trajectory. The sum of the underlying potential and of the metadynamics bias is shown at different times (thin lines). (Image courtesy of A. Barducci. Reprinted with permission from [233]. Copyright © 2011 John Wiley & Sons, Ltd.)
of biomolecular compounds, phase transitions in material science, solid–liquid interfaces and chemical reactions [232,233]. For chemical reactions, the combination of AIMD with MetaD is often required to describe bond-breaking and bond-forming processes.

In MetaD, the sampling of the free energy surface is accelerated by introducing an additional bias potential to the Lagrangian of the AIMD (see equations (2.3) and (2.5)). This potential, \( V_G \), induces a force acting on some user-defined degrees of freedom, called collective variables (CVs), to discourage the system from revisiting the already sampled parts of the free energy surface. In the most commonly used continuous direct MetaD approach, the bias potential acting at time \( t \) on the state described by the set of nuclear coordinates \( R \), \( V_G(R, t) \), is written as a time-dependent sum of Gaussian functions

\[
V_G(R, t) = \int_0^t dt' \omega \exp \left( - \sum_{i=1}^d \frac{(S_i(R) - S_i(R(t')))^2}{2\sigma_i^2} \right),
\]

where \( \sigma_i \) is the width of the Gaussian associated with the \( i \)th CV, \( d \) is the number of CVs and \( S_i(R) \) is the value of the \( i \)th CV. \( \omega \) is an energy rate defined by \( \omega = W/\tau_G \), where \( W \) and \( \tau_G \) are the Gaussian height and the deposition stride, respectively. By defining a small number of CVs (usually two or three) that efficiently discriminate between the various states of the studied transition pathways, the application of \( V_G \) allows the system to escape local minima of the free energy surface as shown in figure 12. This allows one then to obtain an estimate of the free energy surface in the CV space from \( V_G(R, t) \) [231,234].

MetaD in combination with AIMD is perfectly suited to the study of chemical reactions in water [235]. As such, it is internally implemented in CPMD (http://www.cpmd.org/, Copyright © IBM Corp. 1990–2008, Copyright © MPI für Festkörperforschung Stuttgart 1997–2001) and CP2k (http://cp2k.berlios.de) and can be easily interfaced to other AIMD codes through the PLUMED external plugin [236]. AIMD-MetaD has been applied to the study of the dissociation of acetic acid [237], the condensation of tungstate ions [238,239] and the hydrolysis of formamide [240,241], ethyl formate [242] and cisplatin [243] in water.

6. Conclusion

Our goal here was to give the reader a glimpse of the virtual world that is possible with AIMD. In this contribution, we have reviewed the progress that AIMD has made in the last 30 years in enriching our understanding of aqueous solutions. We paid particular attention to both the structural and dynamical properties of water and its constituent ions, the hydronium and hydroxide, which still remain challenging systems to characterize both theoretically and experimentally. Making the connection between theoretical observables obtained from AIMD and experiments will continue to pose a challenging problem for people in this field, particularly when looking at water in different environments. In this regard, Galli and co-workers [244] have recently performed an interesting analysis probing the structure of salt water under confinement using X-ray absorption spectroscopy. We expect that more studies similar to these will provide illuminating insights into the properties of water. In addition, we also gave a brief survey of the application of AIMD to other ions, organic molecules in water as well as aqueous systems at interfaces. Many of these calculations have helped to interpret, complement and even motivate new experiments. Finally, we touched upon the challenges facing AIMD and highlighted some of the progress that has been made in our group in mitigating the sampling problem. We hope that the discussions in this contribution and literature review herein will serve as a good starting point for the non-specialist reader. Although there has been significant progress in this field, many challenges still remain. In the next few decades, more effort will need to be placed on developing newer methods that will allow for first-principles simulations of large aqueous systems for long simulation periods. It will indeed be an enormous feat when we can simulate hydrated proteins and DNA molecules with AIMD.
Funding statement. Financial support from the European Union (grant no. ERC-2009-AdG-247075) is gratefully acknowledged.

References


166. Wrackmeyer B, Tok OL, Herberhold M. 2001 57Fe NMR of ferrocenes by 1h 57Fe inept techniques. *Organometallics* 20, 5774–5776. (doi:10.1021/om010756m)


