Hydrogen-bond dynamics and proton transfer in nanoconfinement

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CHAPTER 1

Introduction

1.1 Hydrogen bonds

Attractive molecular forces can be considered as “glue” keeping all ordinary matter together. They prevent the objects in our macroscopic world, including ourselves, from falling apart into individual molecules. Of the several types of molecular interactions that can be distinguished perhaps the most interesting one is the hydrogen bond. The hydrogen bond has been discovered about a century ago. [1, 2] It is an attractive interaction between a hydrogen-bond donor X—H, where X is an electronegative atom, and a hydrogen-bond acceptor Y which is another electronegative atom or moiety. This can be depicted in the following way: X—H$\cdots$Y, where $\cdots$ denotes the hydrogen bond. [3] The attractive force arises from Van der Waals forces but also has a covalent contribution. [4] The latter makes the hydrogen bond much more directional than conventional Van der Waals forces. [5, 6] Also, it makes hydrogen bonds strongly chemically selective. For example the binding energy of N—H$\cdots$N in guanine-cytosine base pair is much stronger than between the adenine-thymine pair. [7] Since the discovery of the hydrogen bond this seemingly simple interaction has proved to be tremendously important for the understanding of the physical and chemical properties of many molecular systems. The hydrogen bond strength is typically only a few $\mathrm{k_B}T$ but can in some cases also be much larger.[8] The binding energy depends on temperature, pressure and the chemical structure of the donor and acceptor.

The hydrogen bonds play a very important role in the functioning of life at the molecular level. They are involved in the stabilization and functioning of the major components that the living cell is comprised of, ranging from DNA (Figure 1.1a), proteins, membranes, cellulose and, very importantly, water. Why hydrogen bonds are so important in life at a molecular level remains a matter of discussion. However, it is clear that the properties of hydrogen bonds such as the selective binding, directionality and low binding energy meet the requirements for sustaining the highly dynamic but at the same time structured environment of the living cell.

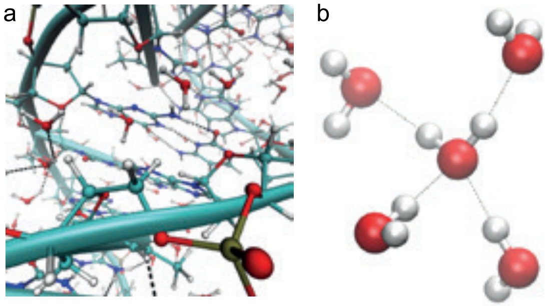

Figure 1.1: a) DNA base-pairs are coupled by hydrogen bonds. The atomic coordinates used to generated the image were obtained from the RCSB PDB database. [9] b) A water molecule bound to four neighboring water molecules.

1.2 Water

Water is a prime example of a compound of which the physical properties are largely determined by its ability to form hydrogen bonds. It is by far the most abundant liquid on earth and one of the most abundant molecules in the universe (together with CO and H_2). [10] 70% of the earth's surface is covered by water and all living organisms consist of on average around 70% of water. [11, 12] Water is perhaps the most studied compound. In the living cell, water does not merely operate as a spectator molecule but it is actively involved in the folding of proteins, cell signaling and binding site recognition. [13] Water, especially in its liquid form, exhibits many unusual properties that are very different from other liquids. Well known examples that we experience in our daily lives include that ice floats on liquid water (which means that the density of the solid state is lower than the liquid state) and that water is not a gas but a liquid at room temperature, which is surprising considering its low molecular weight. Over 70 of these anomalous physical properties have been counted. [14] Many of the remarkable properties of water can be directly related to the ability of water to from a three-dimensional network of hydrogen bonds. As demonstrated in Figure 1.1b the number of hydrogen bonds that a single water molecule can potentially form is four; it can accept and donate two hydrogen bonds. In ice all the binding sites are occupied so that it forms a highly symmetrical tetrahedral network. In liquid water not all the binding sites are occupied: it is slightly under-coordinated. Most studies show that on average 3.5 binding sites are occupied. [15–18] This means that liquid water has local tetrahedral character but that there is also some disorder. The hydrogen bond network is highly dynamic due to the low binding energy of the hydrogen bonds (around $5{\cdot}k_\mathrm{B}T$ [16]): hydrogen bonds are continuously being stretched, broken and formed on a picosecond time scale by thermal fluctuations. [19] Furthermore, hydrogen bonding of water affects the electronic distribution of the lone pairs. As a consequence the binding energy of the hydrogen bond depends on how many hydrogen bonds (donating or accepting) the water molecules already possess. This gives water collective properties, i.e. breaking one hydrogen bond affects the binding properties of all the neighboring water molecules. The fast dynamics, the cooperativity and the combination of local ordering and disorder make it extremely challenging to accurately assess the intermolecular structure and dynamics. Directly studying the hydrogen bond network would require a combination of Ångstrom spatial resolution and femtosecond temporal resolution. Unfortunately, at the moment there are no experimental techniques available that meet both these requirements.

1.3 Confinement and surface effects

In the past decade the effect of confinement on water has gained considerable interest. [20–31] The main motivation for studying water in confinement is that most of the water in the living cell is found in nanometer volumes. [13] In small water volumes the hydrogen bond network is spatially limited. Because many physical properties rely on the ability of water to form an extended hydrogen bond network, it can be expected that the physical properties of water are influenced by confinement. This raises a number of important questions: does water in these nanoscopic water volumes behave the same as in the bulk or is there an effect of confinement? What is the extent of such a confinement effect? To what extent is this effect determined by the chemical nature of the confining interface (hydrophilic, hydrophobic, charged/neutral, non-hydrogen bonding, hydrogen bond accepting/donating)? What is the influence of the confinement geometry?

Reverse micelles are an excellent model system for studying water in nanoconfinement. Reverse micelles are isolated surfactant-coated water droplets of well-defined size dispersed in an apolar solvent. Studying these systems allows for great flexibility. The size can be easily tuned by changing the water surfactant ratio: $w_0 = [\mathrm{H_2O}]/[\mathrm{Surfactant}]$, and by tuning the parameters such as temperature and the type of apolar solvent, the geometry of the water volume can be tuned to a spherical or tubular shape. Furthermore, by choosing between different surfactants with either cationic, anionic or nonionic head groups the chemical nature of the confining surfaces can be changed.

Information on the dynamics of the hydrogen bond network can be obtained from the reorientation dynamics of water molecules. Mid-infrared pump-probe spectroscopy can be used to study the reorientational dynamics of water molecules ranging from less than a picosecond to several picoseconds (the time window in which the dynamics can be measured is limited by the vibrational relaxation time of the probed vibration, typically the OD or OH-stretch). Such studies have shown a strong slowing down of the dynamics upon confinement. The reorientational dynamics of water in ionic surfactants can be well described with a core shell model, where the core behaves as normal (bulk) water, and the shell exhibits strongly reduced dynamics [21, 23] In this case the confinement effect does not extend beyond the first solvation layer. Ions are also known to have an effect on the reorientation dynamics. The counter-ion concentration in ionic reverse micelles scales inversely with the size. For small reverse micelles, for example with $w_0 = 5$, the counter ionic concentration is as high as 11 molal and significantly slows down the dynamics. [32, 33] In nonionic reverse micelles the interior is not perturbed by charges and there slowdown is only a result of confinement.

Nonionic reverse micelles are less extensively studied and the core/shell model has not yet been tested. [27, 34] In chapter 3 the core/shell model of water in nonionic (Igepal) reverse micelles is carefully investigated by studying both the water dynamics with time-resolved infrared spectroscopy and the reverse micelle structure with small-angle x-ray scattering.

The reorientational dynamics of molecules can also be assessed using dielectric relaxation spectroscopy (DRS). This method is not as specific as infrared spectroscopy as it measures the reorientation of all dipolar species present in a sample. An advantage, however, is that also slow dynamics can be resolved as the timescale of the technique has no lower limit in the measured frequency range. Another difference is that DRS is more sensitive to the collective reorientation of water molecules. A combined interpretation of the reorientation dynamics obtained with DRS and infrared pump-probe spectroscopy has led to a deeper understanding of the hydrogen bond dynamics in many systems. [35–37] Apart from a slowdown, confinement effects can also be observed by a change in the magnitude of the dielectric response. [38, 39]

Studies on water dynamics in reverse micelles have mainly been focused on a size-dependence in a spherical geometry. [21, 22, 28, 31, 34, 40–43] However, nanoconfined water in the living cell can take many different shapes. In chapter 4 the dielectric response of water is investigated in nonionic reverse micelles of tubular and spherical shapes. The results from the dielectric relaxation measurements are compared with infrared pump-probe measurements.

1.4 Proton transfer

The proton transfer reaction is a fundamental process in chemistry and biology. In the beginning of the 20th century, conductivity measurements on aqueous electrolytic solutions revealed that proton diffusion is very different from the diffusion of other ions. It was shown that the mobility of protons in water is exceptionally high compared to other ions (see Figure 1.2a). The conductivity of the other ions (i.e. salts) could be well explained through hydrodynamic diffusion [45, 46] but accounting for the anomalously high mobility of protons required a new diffusion mechanism. Inspired by an early 19th century manuscript by Theodor Grotthuss,

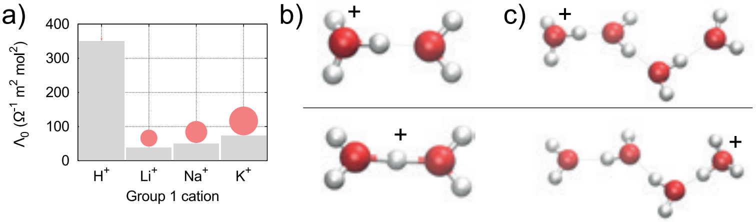

Figure 1.2: a) The molar conductivity of the first four group 1 ions. The red spheres indicate the relative size of the alkali ions. The proton radius is around 100,000 times smaller than Li^+. For the alkali ions the mobility reduces with the ionic radius. A smaller ionic radius results in more water hydration and therefore a larger hydrodynamic radius which means slower diffusion. Based on that trend the proton mobility is anomalously large. [44] b) Zundel-Eigen exchange resulting in a net movement of the protonic charge. The proton moiety relocates to a different position by relaying the covalent bond and the hydrogen bonds. Oxygen atoms are indicated by red dots and hydrogen atoms by white dots. c) Long-range proton transfer of a water wire involving multiple water molecules.

it was proposed that the high mobility of protons originates from a fast exchange of acidic protons for hydrogen atoms from neighboring water molecules. [45–47] The exact mechanism that allows for the proton exchange is still under debate and, to date, proton transfer in water or other hydrogen bonded systems remains an active subject of study. [48–53]

When protons are dissolved in water they immediately react (with water) forming a continuum of different molecular complexes. [48, 53] The presence of a continuum of structures is demonstrated in the mid-infrared activity of aqueous protons showing a continuous absorption between 400 and 4000 cm^{-1}. [54, 55] [1] The protonated water complexes can be subdivided in limiting H_3O^+ Eigen-type cations (also known as Hydronium) and $H_5O_2^+$ Zundel-type cations depicted in Figure 1.2b. [56] In a simplified picture (Figure 1.2b), proton transfer in water can be achieved by the sequential exchange between Eigen and Zundel structures, the so-called Grotthuss hopping. [50, 57] Grotthuss hopping results in a large net movement of the protonic charge with only minimal displacement of the atomic coordinates. Simulations have indicated that Grotthuss hoping can take place over multiple water molecules at once (Figure 1.2c). [48, 49]

Photoacids are a convenient system for studying proton transfer reactions. [51, 52, 58–61] Upon photo-excitation, the pH of a photoacid can drop, by several orders of magnitude, due to charge transfer from the acidic proton to the aromatic part of the molecule. [62, 63] Therefore photo-excitation can result in the release of a proton. The use of (ultra) short laser pulses to excite these molecules enables the study of proton dynamics with femtosecond time-resolution.

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[1] Note that IR spectra of well-defined complexes give rise well-defined peaks in the IR absorption spectra.

In chapter 5 a molecular machine is studied that uses photo acidity to perform a targeted task, acting as a molecular proton crane. Upon photo-excitation the molecule transports a proton from one site of the molecule to another site via a brownian rotatable side group. The structural evolution that is associated with the proton transfer is followed using UV-pump IR-probe spectroscopy.

In chapter 6 a photo-base is studied that reversibly exchanges a proton or deuteron for a lithium cation upon photo-excitation. This exchange mechanism is facilitated by the photo-basic properties of the molecule. The structural changes that are involved with the exchange are followed using UV-pump IR-probe spectroscopy.

Proton diffusion often takes place in nanoconfined water volumes. For example, in the living cell, in the intermembrane space in mitochondria [64–66] and in the thylakoid lumen in chloroplasts [67], where protons are stored for the energy supply of the living cell. Nanoconfined proton transfer also takes place in industrial applications such as the Nafion proton exchange membrane in the hydrogen fuel cell. [68, 69] Because the diffusion of protons requires the concerted motion of many water molecules, proton diffusion could be very strongly affected by nanoconfinement. Up to date such a confinement effect has however not yet been experimentally investigated. In chapter 7 dielectric relaxation spectroscopy is employed to measure the conductivity of protons in HCl doped spherical and tubular reverse micelles of different size in the GHz frequency range. The conductivity at high frequency reveals the field-induced displacement of ions inside the reverse micelles which can be related to the microscopic diffusion constant.

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