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Distinguishing Weak and Strong Hydrogen Bonds in Liquid Water - A Potential of Mean Force Based Approach

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Abstract

Ability to form hydrogen bonds is one of the most important factors behind water’s many anomalous properties. However, there is still no consensus on the hydrogen bond structure of liquid water including the average number of hydrogen bonds in liquid water. We use molecular dynamics simulations of the polarizable iAMOEBA water model for investigating the hydrogen bond characteristics of liquid water over a wide range of temperatures and pressures. Geometric definitions of hydrogen bond often use a rectangular region on the plane of hydrogen bond distances and angles. In this work, we find that an elliptical region is more appropriate for the identification of hydrogen bonds, based on statistically favourable molecular configurations. The
two-dimensional Potential of Mean Force (PMF) landscape along the hydrogen bond
distance (O–H) and angle (O-H–O) is calculated for identifying the statistically favored
molecular configurations, which is then used for defining hydrogen bond formation as
well as the strength of a hydrogen bond. We further propose a new approach to
characterize the hydrogen bonds as strong ones when the PMF is smaller than -2 kT.
Using this definition, a consistent explanation for the different average numbers of
hydrogen bonds in water is obtained in agreement to literature. Simulations are also
performed with the rigid and non-polarizable TIP4P/2005 water model. Both water
models are qualitatively consistent in predicting the distribution of double-, single-, and
non-donor configurations, in line with experimental data, while the iAMOEBA water
model yields quantitatively closer results, including a 10-15% double-donor fraction at
90 °C and 1 atm. The method is also demonstrated to be applicable to the recent, and
more general three-dimensional PMF based definition of hydrogen bonds.

Introduction

Water’s structure and properties distinguish it from normal liquids and lay the foundation
for life on our planet. Because of its many anomalies, water has been significant in almost all
fields of human interest\(^1\) and rightfully so, water has been an important subject of scientific
research for a long time. In the pursuit of understanding the structure and properties of
water, molecular simulations have played an important role. From the very first evidence of
a Liquid-Liquid Critical Point (LLCP) in water by Stanley and co-workers in 1992,\(^2\) which
was later suggested through experiments as well,\(^3,4\) to very recent simulations that suggested
the location of the LLCP,\(^5,6\) molecular simulations have proved to be of high significance in
the study of water. Since the first model of water by Bernal and Flower,\(^7\) an array of water
models have been developed to represent water molecules in molecular simulations. Because
it is beyond the scope of the current work, interested readers are referred to excellent reviews
on the different classes of water models.\(^8-14\)
What makes water behave differently from most liquids, is its ability to form hydrogen bond networks. Hydrogen bonds are pivotal in many phenomena involving hydrophobic or hydrophilic interactions, like the folding of proteins and the assembly of micella.\textsuperscript{15} The existence of two characteristic structural environments in water, a low-density form and a high-density form, is also influenced by hydrogen bonds.\textsuperscript{16,17} Understanding hydrogen bonds is also crucial for describing phase behavior of water-containing systems with the advanced equations of state, which account for the association phenomena explicitly.\textsuperscript{18,19} In molecular simulations, hydrogen bond interactions are not defined a priori as a part of the underlying force-fields, but are often ‘assigned’ to water molecules, if they satisfy certain criteria in the simulation trajectory. The ‘assignment’ of hydrogen bonds is often based on geometric criteria, energetic criteria or a combination of both.\textsuperscript{15}

Experimental techniques like X-ray Adsorption Spectroscopy (XAS), X-ray Raman Spectroscopy (XRS) and X-ray Emission Spectroscopy (XES) have been used by different researchers to study the local structures in water.\textsuperscript{20–27} The average number of hydrogen bonds formed by a single water molecule has been estimated to range between 2 and 4 (at room temperature and pressure), based on various definitions of hydrogen bonds and the experimental technique involved.\textsuperscript{28} Two seminal articles by different research groups suggested two very different values for the average number of hydrogen bonds formed by a water molecule. Wernet et al. reported a value of 2.2\textsuperscript{24} and Smith et al. reported a value of 3.3.\textsuperscript{25} The interpretation of experimental results by Wernet et al. is in sharp contrast with the results from studies using molecular simulations, where most water molecules have tetrahedral co-ordination by forming 4 hydrogen bonds with its neighbors.\textsuperscript{24,27,29,30} From X-ray Diffraction experiments, they interpret that in the liquid state, water only forms two ‘ice-like’ or ‘strong’ hydrogen bonds with one strong donor and one strong acceptor, unlike the tetrahedral hydrogen-bonded state of ice \(I_h\). It is therefore important to understand what ‘ice-like’ or strong hydrogen bonds are, and if such hydrogen bonds can be identified based on physically relevant properties in simulations. A criterion for identifying hydrogen bond
that can also quantify the strength of hydrogen bonds is hence relevant.

Many studies have been reported in the literature to quantify the strength of hydrogen bonds in water, both experimentally\textsuperscript{31–34} and computationally.\textsuperscript{15,35–37} The Potential of Mean Force (PMF) landscape along hydrogen bond geometries is one property utilized, although not extensively, in the literature\textsuperscript{15,38} to study hydrogen bonds. Kumar and co-workers computed the PMF landscape of SPCE water in molecular dynamics (MD) simulations and used them to define hydrogen bonds in water.\textsuperscript{38} Using PMF, Sapir and Harries computed the free energy change of hydrogen bond formation and the entropic and enthalpic contributions to free energy of hydrogen bond formation in MD simulations.\textsuperscript{15} In a very recent article, Dočkal et al.\textsuperscript{39} used the spatial distribution function (SDF) of atoms around each other to calculate the three-dimensional PMF, and subsequently identify continuous bond regions in space. These continuous bond regions correspond to the configuration of water molecules which are hydrogen bonded.\textsuperscript{40} They also extended the definition to identify intermolecular bonds in heterogeneous systems or systems in confinement.\textsuperscript{41} This method, even though more computationally expensive, has advantages in bringing down the arbitrariness in defining hydrogen bonds in computer simulations. It is also capable of quantifying some characteristic properties that are of relevance like the volume of the bonding region.

In the present work, we identify favourable molecular configurations from molecular simulations, projected on to the Oxygen–Hydrogen (O–H) distance - Oxygen-Hydrogen–Oxygen (O-H–O) angle plane, by calculating the two-dimensional PMF. The PMF landscape along these hydrogen bond geometries is then used to define hydrogen bonds, and quantify their strengths, thereby reducing the arbitrariness involved in defining hydrogen bonds. We also utilize the PMF landscape to identify strong, ‘ice-like’ hydrogen bonds. We compare the results of double-, single-, and non-donor fractions in liquid water to those reported in the literature and find that the nature of the distribution is well captured in simulations when a PMF based definition for strong hydrogen bond is used. Finally, we demonstrate the PMF based distinction of strong and weak hydrogen bonds can also be extended to the more
general three-dimensional PMF based definition of hydrogen bond proposed by Dočkal et al. 40

Methods

Molecular simulations

Molecular simulations were performed using the polarizable iAMOEBA water model, 42 which reproduces the vapor, liquid, and solid-state properties of water like density, dielectric constant, self-diffusion coefficient and vapor-liquid equilibrium curve with good accuracy in simulations. 43 A brief discussion on the summary of evidence of iAMOEBA’s ability to capture liquid, vapour, and solid phase properties of water has been included in the Supporting Information, of which Table S1, Fig. S1, the associated discussion, and the cited references thereof will help the readers appreciate the applicability of the model in the study. A system of 256 water molecules was used for the study and the initial dimension of the simulation box was based on the density of the system at the given thermodynamic state. Periodic boundary conditions were applied in all directions for avoiding surface effects in the simulation. Pressure and temperature were kept constant using Berendsen barostat (coupling time 1 ps) and thermostat (coupling time 0.1 ps) respectively. 44 Time integration was performed using the Velocity-Verlet algorithm, 45 with a time step of 1 fs. The length of the simulation trajectories ranged from 10 nanoseconds for higher temperatures to 27 nanoseconds for super-cooled conditions. Simulations using the iAMOEBA water model were performed using Tinker 8. 46

For comparison, simulations were also performed with the TIP4P/2005 water model, 47 a rigid and non-polarizable model capable of reproducing liquid phase properties of water like density, self-diffusion coefficient, surface tension, etc. 43,48 The number of molecules, the dimension of the simulation box, periodic boundary conditions, and lengths of simulations were maintained as described above for simulations with the iAMOEBA water model. Leapfrog
algorithm\textsuperscript{49} was used to generate molecular trajectories with a time step of 1 fs. The temperature and pressure in the system was maintained using Nose-Hoover thermostat\textsuperscript{50–52} (coupling time 1 ps) and Parrinello Rahman barostat\textsuperscript{53,54} (coupling time 2 ps). Simulations using TIP4P/2005 model were performed with Gromacs 2020.\textsuperscript{55}

In all simulations, the trajectory during the first nanosecond was not used for the subsequent analysis. About 850 nanoseconds of molecular simulation trajectory were analyzed for the study, in total. Results mentioned in this work are based on the simulations performed using the polarizable iAMOEBA water model unless specifically mentioned otherwise. The visualization of the molecular structure was done using Visual Molecular Dynamics 1.9.2.\textsuperscript{56}

**PMF calculation**

The two-dimensional PMF along the O–H distance ($r$) and the O-H–O angle ($\alpha$) is calculated from the pairwise correlation function $g(r, \alpha)$, following the method adopted by Kumar et al.\textsuperscript{38} We compute the two-dimensional pairwise correlation function $g(r,\alpha)$, which is the ratio of the number of hydrogen atoms at a distance between $r$ and $r+\delta r$ from oxygen atoms, which forms an O-H–O angle between $\alpha$ and $\alpha+\delta\alpha$, to the same quantity if the molecules were non-interacting. The denominator in the above definition can be calculated as $\rho \times 2\pi r^2 \sin(\alpha) \delta\alpha \delta r \times 2$. The multiplying factor of 2 is to take into account two hydrogen atoms for every water molecule in the system. The PMF is then calculated using equation 1.

\begin{equation}
W(r, \alpha) = -kT \ln (g(r, \alpha))
\end{equation}

where $k$ is the Boltzmann constant, and $T$ is the temperature. The region on the $r$-$\alpha$ plane where PMF is less than zero corresponds to a physically favorable arrangement of molecules. This region can be defined by an elliptical geometry, with an upper limit for $r$. We use this region of favorable configurations to demarcate between hydrogen bond and non-hydrogen
bond geometries in water and define two molecules to be hydrogen-bonded if their mutual orientations fall in this elliptical region.

**Elliptical cut-off for identifying hydrogen bonds**

![Figure 1: Fitting an ellipse to iso-PMF contour line. The actual iso-PMF contour line is fitted with an ellipse, with an upper cut-off limit for the O–H distance. For illustration, the fit of an ellipse to the iso-PMF contour corresponding to PMF = 0 kT (extracted from the PMF landscape of iAMOEBA water at 290 K) is shown in the figure. The region of the contour to the left of the maximum value of O–H–O angle (Angle_{max}) is used to do the elliptical fit. The distance cut-off (distance_{cut}) is the O–H distance when the O-H–O angle tends to zero. Molecules which have mutual orientations lying in the blue shaded region are identified to be hydrogen bonded.](image)

In this work, we identify hydrogen bonds based on the PMF landscape as described here. The regions of PMF ≤ 0 kT and PMF ≤ -2 kT which are of interest to the current study are observed to be well captured by an ellipse. The contour lines corresponding to a particular value of interest (for example PMF=0 kT or -2 kT) are extracted using OriginPro 2019 (OriginLab Corporation, Northampton, MA, USA). These curves are divided into two parts, the elliptically curved part (marked A in Fig. 1) and a near vertical portion (marked B in Fig. 1). Part A of the curve describes the contour line until the O-H—O angle (\(\alpha\)) reaches its maximum value (Angle_{max}). Only Part A of the curve is used to calculate the parameters of the ellipse that would fit the contour (curve fitting is done by minimizing the least square
error). The fitted ellipse, along with an upper limit for the O—H distance \( \text{distance}_{\text{cut}} \), is subsequently used to describe the entire contour. The value of \( \text{distance}_{\text{cut}} \) is taken to be the O—H distance \( (r) \) when the O-H—O angle tends to zero. The following equations describe the region enveloped by the elliptical fit (blue shaded region in Fig. 1).

\[
\frac{(r - r_c)^2}{r_r^2} + \frac{(\alpha - \alpha_c)^2}{\alpha_r^2} \leq 1
\]  

(2)

\[ r \leq \text{distance}_{\text{cut}} \]  

(3)

where \( r_c, \alpha_c, r_r, \) and \( \alpha_r \) are the parameters that describe the ellipse and \( \text{distance}_{\text{cut}} \) is the upper limit for the O—H distance. We identify two molecules to be hydrogen bonded if both equations 2 and 3 are satisfied. The parameters calculated for iAMOEBA and TIP4P/2005 water models at different temperatures and pressures are available openly.\(^{57}\)

**Estimation of hydrogen bonds from SDF**

We also demonstrate that the PMF based definition of ‘strong’ hydrogen bonds is extendable to the general definition of hydrogen bond developed by Dočkal and coworkers.\(^{40}\) SDF is the relative probability of the occurrence of a *monitored particle* as a function of its position in a local reference frame centered on a *reference particle*.\(^{39,40}\) For the study of water, where the molecule is non spherical, we consider a whole water molecule as a reference particle, and the basis vectors of the local reference frame is given by equations 4, 5 and 6.

\[
\vec{e}_1 = \frac{\vec{OH}_1 + \vec{OH}_2}{\| \vec{OH}_1 + \vec{OH}_2 \|}
\]  

(4)

\[
\vec{e}_2 = \frac{\vec{OH}_1 - \vec{OH}_2}{\| \vec{OH}_1 - \vec{OH}_2 \|}
\]  

(5)
\[ \vec{e}_3 = \vec{e}_1 \times \vec{e}_2 \]  

(6)

where O represents the position of the oxygen atom of the reference particle, H\(_1\) and H\(_2\) are the reference positions of the two hydrogen atoms of the reference particle. SDF(x,y,z), which is the ratio of the number of monitored particles at the position (x,y,z), in the local reference frame defined by base vectors \(\vec{e}_1\), \(\vec{e}_2\) and \(\vec{e}_3\), was then computed as described by Dočkal et al.\(^{40}\) The three-dimensional PMF, W(x,y,z), can be calculated directly from the SDF profile by equation 7.

\[
W(x, y, z) = -kT \ln (SDF(x, y, z))
\]  

(7)

Either hydrogen atoms or oxygen atoms of the neighboring molecules may be chosen as the monitored particle. SDF profiles can therefore be calculated for the occurrence of an oxygen atom near the reference water molecule (the water-oxygen SDF profile), and for the occurrence of a hydrogen atom near the reference water molecule (the water-hydrogen SDF profile). Two profiles, cut-through the x-y plane for representation, are shown in Fig. 2a and 2b, respectively. The water-oxygen SDF profile has two regions of high values (near two hydrogen atoms of the reference molecule), marked as regions 1 and 2 in Fig. 2a. These constitute the continuous bond regions, i.e, when an oxygen atom of the neighboring water molecule lies in one of these regions, we consider the two molecules to be hydrogen bonded. Alternatively, the water-hydrogen SDF profile shows three distinct high-SDF (or equivalently, low PMF) regions, as shown in Fig. 2b (marked 3, 4 and 5). Occurrence of high SDF regions 3 and 5 is because of the hydrogen atoms that are connected to the oxygen atoms appearing in regions 1 and 2 in the water-oxygen SDF profile. Therefore, only the high SDF region close to the oxygen atom of the reference molecule is to be considered (region 4 in Fig. 2b) to define the continuous bond region using the water-hydrogen SDF profile.

Either the water-oxygen SDF, water-hydrogen SDF, or a combination of both may be
Figure 2: Illustration of SDF profiles of iAMOEBA water at 298K and 1 atm, cut through the x-y plane. The high SDF regions demonstrate the existence of continuous bond regions, which may be used for defining hydrogen bonds. (a) The water-oxygen SDF profile has two regions (marked 1 and 2 in the figure) of high SDF, which constitute the continuous bond region. (b) The water-hydrogen SDF profile has three regions of high SDF values (marked 3, 4 and 5 in the figure). However, the continuous bond region is only constituted by region 4. High SDF values of regions 3 and 5 are because of the hydrogen atoms that are part of neighbouring molecules whose oxygen atoms appear in regions 1 and 2 of the water-oxygen SDF profile.
used for defining a hydrogen bond.\textsuperscript{40} For the current work, we use the water-oxygen SDF profile, and define a molecule (reference molecule) to be hydrogen bonded to its neighbor (monitored molecule) if the oxygen atom of the monitored molecule lies in the continuous bond region close to either of the hydrogen atom of the reference molecule. We define the continuous bond region as the largest possible continuous region that contains the minimum of PMF (or maximum of SDF), with PMF values less than a specified value.

\textbf{Results and Discussion}

Geometric criteria often characterize two molecules to be hydrogen-bonded if the characteristic distance and angle lie within a specified rectangular region on the distance-angle plane. While O–O\textsuperscript{30,58,59} and O–H\textsuperscript{60–62} are the two most widely used characteristic distances for identifying hydrogen bonds, the widely used characteristic angles are O–H–O\textsuperscript{63,64} and O–O–H angles.\textsuperscript{65–67} Even though O–O distance is a widely used characteristic distance to characterize hydrogen bonds in simulations, we believe that this brings with it an arbitrariness associated with not considering the position of the hydrogen atom involved in hydrogen bond formation. We therefore use the O–H distance and O–H–O angle as the characteristic length and characteristic angle for identifying hydrogen bonds, to ensure that the position of hydrogen atom is used in the characterization of hydrogen bonds formation. When the O–H distance (r) and O–H–O angle (\(\alpha\)) are used for defining a hydrogen bond, the hydrogen bonding region is a rectangle on the r–\(\alpha\) plane that is enclosed by upper limits on r and \(\alpha\) (\(r_c\) and \(\alpha_c\) respectively). If the mutual positioning of two molecules are such that r and \(\alpha\) values lie within this rectangle, they are considered to be hydrogen-bonded. The reproduction of average number of hydrogen bonds per water molecule is often used as a justification for selecting these cut-off criteria (the boundaries of the rectangular region: \(r_c\) and \(\alpha_c\)) while characterizing hydrogen bonds in simulations.\textsuperscript{29,30,36} Our results suggest that this, although necessary, is not a sufficient justification of choosing the cut-off values for
Geometric criteria (Table S2 in the Supporting Information suggests that different rectangular criteria can yield similar numbers for the average number of hydrogen bonds formed by water molecules). Even when the average number of hydrogen bonds is the same for different combinations of the cut-off values, they may assign hydrogen bonds between different sets of water molecules, resulting in the same average number of hydrogen bonds. An example from our simulations is shown in Fig. 3a and 3b for a case where two different cut-off criteria result in the same number of hydrogen bonds for a given water molecule, but the molecules to which it is hydrogen-bonded differ. As much as this may appear trivial that the molecules to which a water molecule differ with the cut-off, it lays down the necessity for a consistent way in which hydrogen bonds can be defined in simulations.

Figure 3: Representation of a molecule (oxygen atom represented as a green sphere) forming four hydrogen bonds with its neighbors (oxygen atom represented as red spheres). Hydrogen bonds were determined using two combinations of cut-off values: (a) $r_c=3.5$ Å and $\alpha_c=35^\circ$, (b) $r_c=2.75$ Å and $\alpha_c=40^\circ$. Both the cut-off conditions result in the water molecule forming 4 hydrogen bonds, but to a different set of neighboring water molecules. The molecule that is circled is identified as a hydrogen-bonded molecule when the corresponding cut-off criterion of the image are used, but not when the other cut-off criterion are used.
Figure 4: Hydrogen bond configurations identified in relation to the region of PMF less than zero on the distance-angle (r-\(\alpha\)) surface (shaded blue region) using (a) the Kuo-Mundy hydrogen bond criterion\(^1\) and (b) the elliptical cut-off criterion described in this work. It is observed that the Kuo-Mundy cut-off criterion does not sample the entire region that is favorable according to statistical thermodynamics, and also samples configurations outside the favorable region.

Defining hydrogen bond based on PMF

The PMF landscape along O–H distance (r) and O-H–O angle (\(\alpha\)) exhibits a global minimum at small distances (r \(\sim\) 1.75 Å) and near-linear orientations (\(\alpha\) \(\sim\) 0 degrees),\(^15\) similar to the results reported by Kumar et al.\(^38\) using the SPCE water model. This non-positive free energy basin on the PMF landscape (W \(\leq\) 0 kT) is because of the statistically favored orientations of molecules in this region, and hence, this region provides us with a physically based definition for hydrogen bond in molecular simulations. It is noticed that this global minimum PMF distance (\(\sim\) 1.75 Å) is very close to the location of the first peak of the O-H radial distribution function observed, both in our simulations and in the literature (\(\sim\) 1.8 Å).\(^42\) An interesting observation is that all molecular configurations with very low O–H distances do not lie on the statistically preferred region on the r-\(\alpha\) plane (Fig. 4). The closer the oxygen (Acceptor) and hydrogen (Donor) atoms are, the smaller is the range of \(\alpha\) which corresponds to a negative PMF. The rectangular regions used for the definition of hydrogen bond usually over-look this behavior. For example, the rectangular cut-off criteria devel-
oped by Kuo and Mundy, is based on reasonably capturing the experimentally determined distance distribution of hydrogen bonds at 300 K. While it captures the experimental hydrogen bond distance (r) distribution, the Kuo-Mundy hydrogen bond definition also samples configurations that are outside the favorable molecular configurations determined by PMF (Fig. 4a). The region of hydrogen bonds as laid out by the PMF based definition can be well described by an ellipse, with an upper cut-off for the hydrogen bond length (Fig. 1 and Fig. 4b). The statistical physics based definition described above yields an average of 3.45 hydrogen bonds per water molecules at 298K, close to the number (3.3) from experiments reported by Smith et al.

Effect of temperature and pressure

Conventional geometry based definitions of hydrogen bonds used in molecular simulations are independent of the temperature and pressure of the system. However, experimental studies suggest that the range of permissible geometries of hydrogen bonds becomes narrower with reduction in the temperature of the system. The PMF landscapes along r and \( \alpha \) with different temperatures and pressures shown in Fig. 5a and 5b respectively, are in line with experimental results (Fig. S2 and S3 in the Supporting Information present the PMF landscapes for temperatures from 230 to 370 K and pressures from 1 to 1000 atm). The area of the statistically favorable region on the r-\( \alpha \) plane was found to decrease with temperature implying that at lower temperatures, a smaller range of geometric combinations is favorable for the formation of hydrogen bonds (Fig. 6a). However, the depth of the PMF well decreases nearly linearly with temperature (Fig. 6c). This means that the free energy change associated with changing the orientation of two molecules from a fully hydrogen bonded state to a bulk configuration increases when the temperature is lowered. This behavior is suggestive of stronger hydrogen bonds at lower temperatures. We note that the unit of energy used here is not absolute but temperature-dependent, and gives the value of PMF in relation to the magnitude of thermal fluctuations at the temperature of the system. The depth of
the PMF well is shown to decrease with temperature, with reference to the magnitude of thermal fluctuations of the system. In terms of absolute values (e.g. in J/mol), the depth of the PMF well is smaller at lower temperatures, which indicates lower ‘absolute’ strength of hydrogen bonds at lower temperatures. When a hydrogen bond is broken, however, the free energy barrier to be crossed while doing so is provided by thermal fluctuations in the system, and therefore it is more meaningful to measure the strength of hydrogen bonds in relation to the magnitude of thermal fluctuations in the system. Interestingly, a change in pressure of the system does not show an impact on the geometric configurations or the depth of PMF well (Fig. 6b and Fig. 6d). The weak impact of pressure on the PMF landscapes is possibly due to the low values of isothermal compressibility of water at the conditions studied. Both iAMOEBA and TIP4P/2005 models under-predict the compressibility of water, leading to an even lower effect of pressure on the system. The behavior of PMF landscape has been observed to be consistent for the non-polarizable TIP4P/2005 water model as well. However, the TIP4P/2005 model has a deeper and narrower PMF landscape (as suggested by the area and the depth of the negative PMF region), suggestive of stronger hydrogen bonds with smaller geometric distortions permissible, in comparison to the polarizable iAMOEBA water model.

**Strength of hydrogen bonds**

The free energy change when bringing the mutual orientation of two molecules from a state $1 \ (r_1, \ \alpha_1)$ to a reference state $(r_{ref}, \ \alpha_{ref})$ can be calculated from the difference between the PMF values at the respective states $W(r_{ref}, \ \alpha_{ref}) - W(r_1, \ \alpha_1)$. Consequently, the free energy change while bringing the mutual orientation of two molecules from a non-interacting state $(W(r_{ref}, \ \alpha_{ref})=0)$ to a given state is the value of PMF at the given state (Fig. S4 in the Supporting Information gives an illustration). The more negative the PMF value of a given configuration, the more stable is the molecular arrangement. We used the PMF values corresponding to the mutual orientations of the hydrogen-bonded molecules to quantify the
Figure 5: Variation of the PMF landscape of the iAMOEBA water model with temperature and pressure. The PMF landscape along distance ($r$) and angle ($\alpha$) at (a) various temperatures at 1 atm and (b) various pressures at 298 K. Temperature is observed to have a pronounced impact on the PMF landscape, whereas pressure does not show a significant impact.

Strength of hydrogen bonds. The idea of ‘strong’ hydrogen bonds has been discussed in the literature, and experimental studies using XAS and XRS by Wernet et al.\textsuperscript{24} implied that a majority of liquid water molecules formed only 2 ‘strong’ hydrogen bonds, in contrast with the general notion that most water molecules form 4 hydrogen bonds in water.\textsuperscript{25,28,38} Wernet and co-workers based their calculations on the similarity of the X-Ray spectrum of bulk liquid and that of ice-surface (where each molecule forms only two hydrogen bonds). Their study concluded that on average, a water molecule forms 2.2 ‘strong’ hydrogen bonds at 25 °C and 1 atm. For studying strong hydrogen bonds, we looked at the configurations of hydrogen bonds in ice I$_h$ crystal using the polarizable iAMOEBA water model. The hydrogen bond configurations along $r$-$\alpha$ surface in ice I$_h$ at 230 K is shown in Fig. 7a. We observe that about 92% of the hydrogen bonds formed lie in the region of $W \leq -2 \kT$, at 230 K. Out of an average $\sim 3.97$ hydrogen bonds formed by a water molecule in ice I$_h$ crystal, $\sim 3.67$ hydrogen bonds lie in the region of $W \leq -2 \kT$ at this temperature.

The average number of hydrogen bonds formed by a molecule, against the corresponding
Figure 6: Effect of temperature and pressure on the hydrogen bond geometries of iAMOEBA and TIP4P/2005 water models. The area of the statistically favorable region ($W(r, \alpha) \leq 0$ kT) (a) increases with increase in temperature and (b) keeps almost unchanged when pressure changes. The depth of $W(r, \alpha)$ well (c) decreases with increase in temperature and (d) does not change noticeably with pressure.

PMF $W(r, \alpha)$ was studied, to analyze the strengths of hydrogen bonds formed when a molecule is involved in exactly two, three, four, five or six hydrogen bonds. Liquid water on average, forms 2.41 hydrogen bonds in the region of $W \leq -2$ kT (Summarized in Table 1) at 298 K and 1 atm. This is close to the estimate of the number of strong hydrogen bonds in liquid water reported by Wernet et al.\textsuperscript{24} In agreement with this observation and the previously discussed analysis of hydrogen bonds in ice I$_h$, we categorize a hydrogen bond as strong if it lies in the region of $W \leq -2$ kT (the free energy change associated with completely breaking the configuration is at least twice the magnitude of thermal fluctuations.
Figure 7: (a) The distance-angle (r-$$\alpha$$) configurations of hydrogen bonds in ice I$_h$ crystal simulations at 230 K, using the iAMOEBA water model. The green region represents the elliptical region that defines the hydrogen bond, corresponding to $$W(r,\alpha) \leq 0\ kT$$. The blue region shows the area on the r-$$\alpha$$ plane where $$W(r,\alpha) \leq -2\ kT$$ that defines the strong hydrogen bond. (b) Distribution of the Double-Donor (DD), Single-Donor (SD), and Non-Donor (ND) configurations at 298 K and 1 atm in simulations, compared with the experimental results reported by Wernet et al.$^{24}$

The average number of hydrogen bonds formed by a water molecule as a function of temperature is shown in Fig. 8a. The average number of hydrogen bonds nearly linearly decreases with temperature for both the iAMOEBA and TIP4P/2005 water models. Pressure...
Table 1: Identification of the number of strong and weak hydrogen bonds based on the PMF of hydrogen bond configurations at 298 K and 1 atm. On average, water molecules are observed to form 3.45 hydrogen bonds, out of which 2.41 are strong hydrogen bonds. This definition of a ‘strong’ hydrogen bond (configurations with $W(r,\alpha) < -2\ kT$) yields an average number of hydrogen bonds formed close to the results of Wernet et al.\textsuperscript{24}

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Strong H-bonds</th>
<th>Weak H-bonds</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All molecules</td>
<td>2.41 ± 0.91</td>
<td>1.04 ± 0.68</td>
<td>3.45</td>
</tr>
<tr>
<td>Molecules forming 6 H-bonds</td>
<td>2.93 ± 1.0</td>
<td>3.07 ± 1.01</td>
<td>6</td>
</tr>
<tr>
<td>Molecules forming 5 H-bonds</td>
<td>3.08 ± 0.98</td>
<td>1.92 ± 0.85</td>
<td>5</td>
</tr>
<tr>
<td>Molecules forming 4 H-bonds</td>
<td>2.85 ± 0.94</td>
<td>1.15 ± 0.70</td>
<td>3</td>
</tr>
<tr>
<td>Molecules forming 3 H-bonds</td>
<td>2.08 ± 0.80</td>
<td>0.92 ± 0.62</td>
<td>3</td>
</tr>
<tr>
<td>Molecules forming 2 H-bonds</td>
<td>1.37 ± 0.66</td>
<td>0.63 ± 0.51</td>
<td>2</td>
</tr>
</tbody>
</table>

Figure 8: (a) Variation of the average number of hydrogen bonds (all hydrogen bonds and strong hydrogen bonds) formed by the iAMOEBA and TIP4P/2005 water models with temperature at 1 atm. (b) The distribution of the number of hydrogen bonds formed by water molecules in simulations at 298 K and 1 atm. By our definition of a ‘strong’ hydrogen bond, the minority of water molecules form 4 hydrogen bonds. It was observed to not have a significant impact on the average number of hydrogen bonds formed in water (Detailed results are given in Table S6 and Table S7 in the Supporting Information). It is interesting to note that the difference between the water models in terms of the average number of hydrogen bonds formed by a water molecule is more pronounced when looking at strong hydrogen bonds. We also observe that by using our PMF based definition of strong hydrogen bonds ($W \leq -2\ kT$), not many water molecules form the tetrahedral hydrogen-bonded network, that is 4 hydrogen bonds, whereas most water molecules form 4
hydrogen bonds when the $W \leq 0 \text{kT}$ definition is used (Fig. 8b).

The low density liquid form of water is characterised by maximising hydrogen bonds and by forming local tetrahedral environments in water.\textsuperscript{16} We find that the fraction of water molecules forming 4 strong hydrogen bonds in water (Fig. 8b), is very close to the estimate of the low density liquid fraction $\sim 0.15$ calculated by Russo and Tanaka at 298 K and 1 atm from simulations of the ST2 water model.\textsuperscript{17} It is very appealing to employ this approach in the future to characterize the two structural forms of water.

![Distribution of Double-Donor (DD), Single-Donor (SD), and Non-Donor (ND) fractions in liquid water at different temperatures and 1 atm. Double-donor fractions are found to decrease with temperature. Considering all hydrogen bonds ($W \leq 0 \text{kT}$) leads to classifying more than 50% water molecules to be double donors at all temperatures. Whereas the definition of strong hydrogen bonds ($W \leq -2 \text{kT}$) leads to the majority of molecules to be single or non donors at 370K.](image)

Figure 9: Distribution of Double-Donor (DD), Single-Donor (SD), and Non-Donor (ND) fractions in liquid water at different temperatures and 1 atm. Double-donor fractions are found to decrease with temperature. Considering all hydrogen bonds ($W \leq 0 \text{kT}$) leads to classifying more than 50% water molecules to be double donors at all temperatures. Whereas the definition of strong hydrogen bonds ($W \leq -2 \text{kT}$) leads to the majority of molecules to be single or non donors at 370K.
It is also of interest to note that the iAMOEBA water model captures the distribution of double-, single-, and non-donor fractions (at 298 K and 1 atm) in water (for strong hydrogen bonds) more accurately, even though both models qualitatively reproduce the inherent nature of the distribution as reported by experiments (Fig. 7b). The change of the distribution of double-, single-, and non-donor configurations in liquid water against temperature and pressure was also investigated as part of this study. As shown in Fig. 9, with the definition of a strong hydrogen bond, the fraction of double donors is reduced from 55% to about 14% when the temperature changes from 230 K to 370 K, for the iAMOEBA water model. A closely resembling trend is observed for the case of the TP4P/2005 water model as well. The reduction in the double-donor fraction with temperature consequently leads to an increase in single- and non-donor configurations in water (Detailed numbers can be found in Tables S8-S11 in the Supporting Information). The less restrictive definition of hydrogen bond (W \leq 0 \text{kT}) also suggests a decline in the double-donor fractions in water, but it predicts that more than 50% water molecules are double donors even at temperatures as high as 370 K. The experimental studies by Wernet et al.\textsuperscript{24} reports a double-donor fraction of \(\sim\) 10% at 90°C and 1 atm. The definition of strong hydrogen bonds as described in this work is able to estimate the double-donor fraction of 13.9% at 360 K (87°C).

**Distinguishing strong hydrogen bonds from SDF**

We also demonstrate that the method of distinguishing strong and weak hydrogen bonds based on the two-dimensional PMF can be extended to the general approach developed by Dočkal et al.\textsuperscript{40} based on the SDF. Using the three-dimensional PMF landscape (calculated by equation 7), we define a given molecule (reference molecule) to be hydrogen bonded to its neighbor (monitored molecule) if the oxygen atom of the monitored particle lies in the three-dimensional continuous bond region near either of the hydrogen atoms of the reference molecule (regions marked 1 and 2 in Fig. 2a). We define the continuous bond region as the largest continuous region containing the local maximum of SDF, with a condition that value
of PMF in the region is less than or equal to 0 kT. For defining a strong hydrogen bond, we redefine the continuous bond region as a subset of the original continuous bond region, where PMF is less than or equal to -2 kT. The volume of the continuous bond region is calculated to be 7.01 Å³, and a region of volume 2.05 Å³ is estimated as the continuous bond region for the formation of strong hydrogen bonds. The minimum of PMF is observed to be around -3.63 kT at ∼ 1.83 Å from the reference molecule, which are close to the corresponding values from the two-dimensional PMF based approach. We also investigated the effect of temperature and pressure on the continuous hydrogen bond region (See Fig. S5a and S5b respectively in the Supporting Information). Very similar temperature and pressure trends were obtained, when compared to the two-dimensional PMF landscape. We observe that the minimum value of PMF in the continuous bond region increases with temperature, indicative of stronger and more stable hydrogen bonds at lower temperatures.

Table 2: Hydrogen bond statistics of iAMOEBA water at 298 K and 1 atm estimated from the modified general definition by Dočkal et al.\textsuperscript{40}

<table>
<thead>
<tr>
<th></th>
<th>All H-bonds (W ≤ 0 kT)</th>
<th>Strong H-bonds (W ≤ -2 kT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume of bond region (Å³)</td>
<td>7.01</td>
<td>2.05</td>
</tr>
<tr>
<td>Number of H-bonds</td>
<td>3.23 ± 0.89</td>
<td>1.99 ± 1.03</td>
</tr>
<tr>
<td>Double donor fraction</td>
<td>0.65 ± 0.03</td>
<td>0.25 ± 0.03</td>
</tr>
<tr>
<td>Single-donor fraction</td>
<td>0.31 ± 0.03</td>
<td>0.50 ± 0.03</td>
</tr>
<tr>
<td>Non-donor fraction</td>
<td>0.04 ± 0.01</td>
<td>0.25 ± 0.03</td>
</tr>
</tbody>
</table>

The hydrogen bond statistics of iAMOEBA water (at 298 K, 1 atm) obtained from the three-dimensional PMF based definition are shown in Table 2. The results are similar to those obtained from the two-dimensional PMF based definition. The analysis estimates that out of 3.23 hydrogen bonds which are formed by a water molecule on an average at 298 K and 1 atm, 1.99 are strong. We also observe that a W ≤ 0 kT condition results in majority of the molecules (∼ 65%) to belong to the double-donor configuration. On the other hand, while considering strong hydrogen bonds, we find that the majority of water molecules (∼ 50%) belongs to single donor configuration. These results agree closely with the estimates from
The temperature trends of number of hydrogen bonds and the fraction of double-, single- and non-donor configurations were also investigated, and they are observed to be in line with the results from the two-dimensional PMF landscape (See Fig. S6a and S6b in Supporting Information for detailed results).

Conclusions

The definition of hydrogen bond in simulations based on a sharp cut-off is bound to bring some level of arbitrariness because, in reality, the change from a hydrogen-bonded state to a non-hydrogen bond is not a sharp phenomenon. An investigation of statistically favorable molecular orientations in liquid water could help in making the geometric definition for hydrogen bonds in simulations more meaningful and physics based. The Potential of Mean Force (PMF) landscape calculated from simulations is observed to exhibit a low energy basin at low O–H distances and small angles, providing us with a statistical physics based definition for hydrogen bonds in water. We also report the variation of the PMF landscape with temperature and pressure of the system. The PMF well is observed to grow deeper and the area of the favorable region is observed to become smaller with a reduction in temperature. We infer that a narrower range of orientations forms a hydrogen bond at lower temperatures, and the hydrogen bonds are more stable at lower temperatures.

A PMF based definition, unlike the conventionally used geometric criteria for hydrogen bonds, can also categorize hydrogen bonds based on their strength. We observe that out of the 3.45 hydrogen bonds formed by a water molecule, only 2.41 are ‘strong’ hydrogen bonds. These results are able to provide a bridge between the two contradicting numbers reported in the literature by Wernet et al. and Smith et al. The definition of a strong hydrogen bond based on PMF, is also able to capture the qualitative distribution of double-, single-, and non-donor fractions in water as reported by Wernet et al. Both water models studied yield
similar results, while the fractions predicted by the polarizable iAMOEBA water model was found to be closer to the experimental results. We also demonstrate that the PMF based distinction of strong and weak hydrogen bonds can be extended to the three-dimensional PMF based method laid out by Dočkal et al. Even though it is computationally more expensive, the three-dimensional PMF based approach has advantages. It does not require the projection of configurational information on a choice of two-dimensional planes. Instead, it uses the full information of the mutual positioning of atoms in three-dimensional space. The method also can compute quantities of relevance like the volume of bond regions per molecule. We find that restricting the definition of bond region based on PMF is capable of yielding the statistics of ‘strong’ hydrogen bonds estimated from the two-dimensional PMF based method and the experimental results by Wernet et al.

Hydrogen bonds form the basis of water’s many anomalous properties. The two states model of water, which provides an intuitive understanding of water’s properties in the ambient and super-cooled regimes, depend heavily on the hydrogen bonded structure of water. The low density structural form is characterized by formation of hydrogen bonds with the nearest neighbors, and it would be appealing to utilize the concept of strong hydrogen bonds as proposed in this work in the characterization of low density structural form in water. For instance the fraction of water molecules forming 4 strong hydrogen bonds in water, as per our definition, is very close to the estimate of 0.15 by Russo and Tanaka at 298 K and 1 atm. The procedure laid out also has the possibility to be extended to heterogeneous systems to characterize hydrogen bonds in a systematic way in simulations. Since a PMF based definition inherently takes into account the underlying inter-molecular interactions in simulations, it lays down a consistent way to define hydrogen bonds in simulations for different models of water, at different conditions of temperatures and pressures, for homogeneous and heterogeneous systems.
Supporting Information Available

A brief discussion on the iAMOEBA water model; Illustrations on variations of PMF with temperature and pressure; The reference state shown in a complete PMF landscape; Average number of hydrogen bonds from rectangular criteria; Effect of temperature and pressure on the three-dimensional continuous bond region; Data for Fig. 7 to Fig. 9 and Table 1. This information is available free of charge via the Internet at http://pubs.acs.org/.

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Graphical TOC Entry