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Water, Properties of

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Water is well known for its unusual properties, which are the so-called “anomalies” of the pure liquid, as well as for its special behavior as solvent, such as the hydrophobic hydration effects. During the past few years, a wealth of new insights into the origin of these features has been obtained by various experimental approaches and from computer simulation studies. In this review, we discuss points of special interest in the current water research. These points comprise the unusual properties of supercooled water, including the occurrence of liquid–liquid phase transitions, the related structural changes, and the onset of the unusual temperature dependence of the dynamics of the water molecules. The problem of the hydrogen-bond network in the pure liquid, in aqueous mixtures and in solutions, can be approached by percolation theory. The properties of ionic and hydrophobic solvation are discussed in detail.

It is widely assumed that during the 4 billion years of evolution on our planet, life has adjusted to all properties of water and has taken advantage of any of the numerous unusual features of this liquid, which has been called “life’s matrix” (1–3). Water is made of the two most abundant cosmic elements besides the inert helium (4), and it has served as one of the initial compounds for the energetically induced reactions to form the first organic molecules. This reaction may have happened like in the Miller-Urey primordial earth atmosphere under the influence of electric discharge (5) or in the porous interior of icy comets under the influence of cosmic radiation (6). The abundance of water in our galaxy has been estimated as several ten-thousand earth oceans per sun, and it is distributed on planets, moons, comets, and dust grains mostly in the form of crystalline and amorphous ice. In the past few years, many new aspects of the microscopic structure, dynamic behavior, and role of water in biologically relevant molecular processes were obtained from computer simulation studies, which have been performed to understand various new experimental observations. Therefore, in this short review, we will strongly focus on the picture of water that developed from such computational studies. This review can by no means be complete but lists some points of special interest in the current water research. Because of the importance of water, numerous reviews and monographs on different aspects of water can be found (7–13).

Water appears in various condensed forms; 15 different crystalline ice structures are reported, as well as at least three amorphous (noncrystalline) ices and a similar number of metastable liquid water forms (14). This structural diversity has its origin in the elementary building blocks of water: the hydrogen bonds and the tetrahedral arrangement of H-bonded neighbors [which is often called the “Walrafen pentagon” (15)]. Both building blocks provide large structural flexibility. The strength as well as the directionality of the H-bonds is intermediate between van der Waals interactions and covalent bonds, which allows easy distortion of the perfect tetrahedral local arrangement and a versatile adjustment of the water structure to the changing thermodynamic conditions or the presence of solutes.

As we largely refer in this short review to simulation results, the following should be noted beforehand: The first molecular dynamics simulation studies of water by Rahman and Stillinger (16, 17) were received by the community of water researchers with great enthusiasm, as they demonstrated that the structural, dynamic, and thermodynamic properties of this complex liquid could be reproduced simultaneously to an astonishingly high degree by the use of a simple pair interaction potential, which was made up from Lennard-Jones and Coulombic contributions. This finding offered an unprecedented opportunity to study structural and dynamic details on the molecular level. To improve the reliability of the obtained simulation results

Advanced Article

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by a better quantitative agreement between simulation model and real water, many different interaction potentials were developed since then. Numerous comparative studies have been published. A recent compilation can be found in Reference 18; other examples, which focus on special properties, are given in the following sections. Despite these efforts, no current model is fully satisfactory, but the interpretation of simulation results in comparison with real water can be improved by taking into account the shift of the phase diagram between model liquid and real water.

Anomalies of Water and Polyamorphism

The exceptional rank of water is manifested by its unusual properties compared with most other liquids, the so-called "anomalies." These anomalies comprise thermodynamic as well as structural and dynamic properties, especially their pressure and temperature dependence. The key to understanding these properties lies in two competing influences on the local structure: the attempt to build low-density tetrahedral structures (with low energy) versus the tendency toward closer packing (with higher entropy) (19).

The density maximum at 4°C and the decrease of volume on melting of ice are well-known anomalies. More aspects of the extraordinary behavior of water have been brought into the focus of many researchers by the seminal articles of Angell on supercooled water (20, 21). In contrast to "ordinary" liquids, the isothermal compressibility and the heat capacity of water increase drastically during supercooling. This finding indicates strongly increasing volume and entropy fluctuations during cooling. A spectacular explanation for this behavior was delivered by a computer simulation study, which gave evidence for the existence of a (second) critical point of water buried in the deeply supercooled liquid region (19, 22) [see also the reviews by Stanley and Debenedetti (23, 24)]. This second critical point is considered the endpoint of an equilibrium line between two forms of (metastable) liquid water: a low- and a high-density liquid.

The two different liquids have their counterparts in the amorphous solid state: the experimentally well-studied high-density amorphous (HDA) and low-density amorphous (LDA) ice forms (25). However, it is still unknown exactly how the different amorphous ice forms and supercooled liquid water are connected or where the second critical point is located. A "no man's land" region largely prohibits direct experimental access to the low temperature liquid because of the inevitable onset of crystallization (24) in this region. Therefore, computer simulation studies, in which crystallization does not take place, have been used extensively to establish the existence of a liquid-liquid transition. The location of the corresponding second critical point strongly depends on the interaction potential that was used in these simulations (26–28). It may be shifted to negative pressures, which are correlated with the prediction of a van der Waals-like model developed by Poole et al. (19), in which such a shift occurs with decreasing hydrogen bond strength. In such

a scenario, the experimentally observed diverging fluctuations in supercooled water at ambient pressure do not develop by approach to the critical point; instead, these fluctuations develop by the approach to the spinodal line that emerges from the critical point at negative pressures. This finding could explain the early observation of Angell (20, 21), which suggested that all temperature-response functions and temperature coefficients diverge at the same temperature in ambient pressure supercooled water. The unavoidable crystallization occurs after passing the spinodal as it encounters a phase transition to the low-density liquid state, which has a local structure that is very similar to crystalline ice (29).

Some indirect experimental evidence exists for the liquid-liquid critical point hypothesis from the changing slope of the melting curves, which was observed for different ice polymorphs (30, 31). A more direct route to the deeply supercooled region, by confining water in nanopores to avoid crystallization, has been used more recently by experimentalists. These researchers applied neutron-scattering, dielectric, and NMR-relaxation measurements (32–35). These studies focus on the dynamic properties and will be discussed later. They indicate a continuous transition from the high to the low-density liquid at ambient pressure. The absence of a discontinuity in this case could be explained by a shift of the second critical point to positive pressures in the confinement. This finding correlated with simulations, which yield such a shift when water is confined in a hydrophilic nanopore (36).

Although the presented scenarios are still under discussion, the existence of a first-order like transition between metastable high- and low-density supercooled water with a second critical point at negative pressures in bulk water and positive pressures in confinement is strongly suggested (29). Alternatively, singularity-free scenarios are discussed to explain the properties of supercooled water (24, 29).

As indicated above, the study of amorphous solid water in bulk and in confinement is an important source of information for the understanding of the liquid. In fact, water was the first liquid to show "polyamorphism": the mentioned existence of high density and low-density amorphs. Amorphous solid water can be produced experimentally along very different routes by vapor deposition, by pressurizing crystalline ice, or by fast temperature quench of tiny droplets. Also, different subsequent annealing procedures have been used. Recently, also a very high-density form (VHDA) of amorphous ice was observed and shown to be distinct from HDA (37). Neutron scattering data revealed that the transformation between HDA and VHDA is related to an increasing population of "interstitial" water molecules (38). Simulation studies indicate that VHDA (not HDA) should be considered as the amorphous solid counterpart to the high-density liquid water phase at ambient conditions (39, 40). The question whether the HDA to VHDA transition is also first-order like (as LDA to HDA) is not yet resolved (41, 42). The important influence of the preparation method has been revealed by several studies. In Koza et al.'s (43) neutron-scattering experiments, HDA and VHDA seem to be heterogeneous at the length scale of nanometers, and different forms of HDA were obtained depending on the exact preparation process (43). The role of multiple metastability and

hysteresis has to be studied in more detail. By annealing of HDA at normal pressure, Tulk et al. (44) found evidence for the existence of several amorphous ice states. The possible existence of multiple liquid-liquid phase transitions in liquid water was first suggested by Brovchenko and co-workers (27, 45) from extensive Gibbs-Ensemble Monte Carlo simulations of various water models.

Hydrogen Bond Network

In the perfect crystalline structure of "ordinary" (hexagonal) ice, each water molecule is H-bonded to four tetrahedrally arranged neighbors. From the comparison of the enthalpies of sublimation, melting, and evaporation, it can be concluded that about 80% of all H-bonds survive the melting process. Despite the wide range of possible definitions of intact versus broken H-bonds (46), it is therefore generally accepted that the water molecules in the liquid form at any instant a random, quasi-infinite, space-filling network (8, 47, 48). This network is subject to constant restructuring ["transient gel" (49)], the lifetime of the individual bonds are in the subpicosecond range (46, 50, 51). Computer simulations revealed that this network could be described quantitatively by combinatoric calculations and percolation theory (52).¹

The physical mechanisms, which are connected with this primarily topological phenomenon of the existence of a percolating H-bonded network, are still not analyzed in depth. Nonetheless, several observations have been compiled recently that show a correlation between the existence of a spanning network and properties of physical and biological relevance (53-56). These observations concern the occurrence of phase separation in mixtures as well as the conformational transition and function of biomolecules. Computer simulations revealed that the phase separation in a water/tetrahydrofuran mixture is preceded by the formation of mesoscopic structures, but "spare" H-bonded clusters in the organic rich phase, which grow to be space filling at phase separation with a fractal dimension $d_f = 2.5$, as expected for a percolation cluster in an infinite three dimensional system (55, 57). Such percolating networks have also been detected by neutron-scattering experiments in completely miscible aqueous solutions (58).

The space-filling network, which is identified in pure water at ambient conditions, even exists in supercritical water; the corresponding line of percolation transitions is an extension of the boiling line (55). The close relation between demixing phase transition and percolation transition of physical clusters has also been used in simulations to localize the liquid-liquid transition region in supercooled water. The lowest density amorphous water phase (solid or liquid) has been characterized by the presence of a percolating network

of well-ordered (ice-like tetrahedral), four-coordinated water molecules, whereas in high-density amorphous water phases, a percolating network of tetrahedrally bonded molecules is missing (54).

The formation of spanning H-bonded water networks on the surface of biomolecules has been connected with the widely accepted view that a certain amount of hydration water is necessary for the dynamics and function of proteins. Its percolative nature had been suggested first by Careri et al. (59) on the basis of proton conductivity measurements on lysozyme; this hypothesis was later supported by extensive computer simulations on the hydration of proteins like lysozyme and SNase, elastine like peptides, and DNA fragments (53). The extremely interesting question of protein hydration is a huge field by its own but beyond the scope of this article.

Dynamics of Water Molecules

The molecular motion in water has been studied for decades with all available modern spectroscopic and scattering methods, including neutron scattering, nuclear magnetic and dielectric relaxation, infrared spectroscopy, and light scattering. Each applied method probes different aspects of the motional behavior on different length and time scales. As NMR furnishes diffusion coefficients and integrals over reorientational correlation functions, quasielastic neutron scattering reveals information on the short-time translational and rotational motion. The results that were obtained for a wide range of temperature and pressure conditions have been interpreted in the frame of translational and rotational diffusion models. The temperature dependence of characteristic parameters like reorientation and residence times has been discussed in detail (12, 60-62).

That water is so fluent is an apparent contradiction to the fact that the space-filling network of hydrogen bonds is made up of bonds that have an interaction energy strength well above the thermal energy $k_B T$. This puzzle was resolved by showing the importance of network defects: The presence of an excess (fifth) neighbor in the first neighbor shell of water molecules allows the intermediate formation of bifurcated H-bonds, which provides a low-energy barrier path for reorientation and coupled translational motion (63-65). Consequently, a decrease of the local water density (which makes the presence of an excess neighbor less probable) decreases the mobility of water molecules. For example, this effect has been observed by NMR experiments in the hydration shell of convex hydrophobic particles, in which the molecular mobility is decreased (66). However, it does not decrease to such an extent that one could speak of "icebergs," as this is still done occasionally (see the section entitled "Hydrophobic hydration and interaction"). In cold water, the increasing expansion of water reduces the mobility of the water molecules in addition to the pure thermal activation, which leads to a strong non-Arrhenius temperature dependence of reorientation times, diffusivity, and viscosity (20) (see below).

Implications of the existence of a liquid-liquid phase separation for the dynamic behavior of water have been discussed by Angell et al. (67, 68), who postulated a crossover from

¹ A "percolating" network forms an uninterrupted path between opposite boundaries of a system. The word "spanning" is used when the system has no boundary, like the surface of a single sphere. In this case, the degree of connectivity, at which a "spanning" network appears, is detected by the distribution of finite clusters in analogy to a percolation transition.

a so-called fragile to a strong glass-forming liquid behavior because of a transition into the region of the low-density liquid at deep supercooling. Possible mechanisms were discussed that dominate the molecular mobility in the different temperature ranges (69), which lead to different temperature dependences: At high temperatures, as mentioned above, the switching through bifurcated H-bonds is most effective and is connected with a low activation energy. At lower temperatures beyond the density maximum, a strong non-Arrhenius behavior with increasing apparent activation energy is produced by the development of a more perfect local order, which enforces an approach to structural arrest of the water molecules in the cages of their neighbors (70). This arrest is then overcome at even lower temperatures by jump diffusion (71, 72); in other models by the collective relaxation of the cage of neighbors (73). Finally, in the locally well-ordered, low-density liquid, when approaching the glass transition, the formation of Frenkel-type defect pairs may enable a diffusion behavior that parallels the "strong glass former" Arrhenius line of the Angell plot (69).

The expected crossover could not be studied experimentally in pure water because of the onset of crystallization at strong supercooling. Recently, the possibility to supercool water to a much larger extent than bulk water, when it is confined to small pores, has been exploited (34). From dielectric spectroscopy and quasielastic neutron-scattering experiments on water confined in the nanopores of clays and silica glass, a transition (crossover) from a strongly activated non-Arrhenius motional behavior to a low activation energy Arrhenius line at even lower temperatures has been observed (32, 33). This observation correlates with the expected fragile-to-strong transition when crossing from "normal" to low-density water. Using such experiments in an extended pressure range, the position of the second critical point could be estimated for the confined water. This fragile-to-strong dynamic crossover was also observed for the hydration water of biomolecules (proteins and DNA) (74, 75). Most interestingly, this crossover occurs at the same temperature as the so called "protein glass transition," which suggests that this transition in the dynamics of the protein is the result of the approach to the above-mentioned extension of the liquid-liquid equilibrium line of the solvent (the so-called Widom line of the second critical point of water). It has to be mentioned here that some controversy still surrounds the origin of this abrupt change in the temperature dependence of the mobility of the water molecules: This behavior has also been attributed to the limitation of the spatial extension of fluctuations in confinements (76).

Hydrophobic Hydration and Interaction

The "hydrophobic effect" is manifested thermodynamically by the low solubility (large positive solvation free energy) that nonpolar molecules or aggregates experience in water (for more extensive reviews, see References 77–79). The hydrophobic effect is of great relevance for a variety of phenomena, which include protein folding as well as the structural organization of amphiphilic aggregates. The latter are forming micelles of various topology, as well as lyotropic mesophases and lipid membranes.

Surprisingly, the low solubility of small-sized particles does not stem from a weak interaction of particles with their surrounding water environment (77). For example, the heat of solvation of methane in water at ambient temperature is of similar magnitude as the heat of vaporization of pure liquid methane (80). The positive solvation free energy of small apolar particles at low temperatures is the consequence of negative solvation entropy, which overcompensates for the negative solvation enthalpy. It is widely believed that this "entropy penalty" is caused by the orientation order introduced to the hydration-shell water molecules as they try to maintain an intact hydrogen bond network (77). Parallel to the entropy decrease observed for low temperatures, theoretical and experimental studies also indicate a slowing down of the translational and reorientational dynamics of water in the hydration shell of an apolar moiety (66, 81–83). Another thermodynamic signature of hydrophobic hydration is the large positive solvation heat capacity. The heat capacity increase is attributed to the temperature-induced mutual interactions among the solvent molecules in the hydration shell (84). It is considered to be caused by the progressing disintegration of the hydrogen bond network around the solute with increasing temperature (77, 84). Because the solvation of small apolar moieties is accompanied by an entropy decrease of the solvent, the formation of contact pairs of apolar particles is a way to reduce this "entropy penalty." The tendency to form apolar contact pairs in solution is termed "hydrophobic interaction" and essentially controlled by the solvent. Because the association of small apolar particles is entropically favorable, a temperature increase leads to more stable apolar contacts. "Hydrophobic interaction" is a classic example of an "entropic force."

Contrasting the behavior close to small apolar solutes, water behaves differently at an extended (planar) interface. Here, the thermodynamic features are mostly governed by water's interfacial tension, which is essentially enthalpic in nature (weakening with increasing temperature). Consequently, at some length-scale a "crossover" has to occur (85, 86) from an entropy to an enthalpy dominated solvation behavior. Recent studies indicate that this transition appears at a length-scale significantly below 1 nm (87, 88).

The thermodynamic signatures of small apolar particle hydration can be modeled by simple two-state models (89–92) that solely focus on water's hydrogen bonding as supposedly dominating effect. Stronger hydrogen bonds close to an apolar particle are counterbalanced by fewer possible hydrogen bonds. Silverstein et al. (92) consistently related experimental data that described water's hydrogen bond equilibrium with hydrophobic solvation calorimetric data. Their calculations suggest that at lower temperatures, the hydrogen bonds are more intact than in the bulk, whereas at high temperatures, hydrogen bonds are more broken. The model moderately readopts older theories by Franks and Evans in their so called "iceberg" model (93), in which the hydrophobic particles were thought to be stabilizing structured ice-like entities in water. However, because the entropy change experienced by a water molecule in a hydrophobic hydration shell is about five times smaller than a crystal-like environment (77), the "iceberg" model too strongly exaggerates

the degree of ordering that is present in a hydrophobic hydration shell (77). Simple two-state models seem to fail in reliably predicting absolute solvation free energies (77) because altering hydrogen bonding does not provide sufficient information to determine the entropic "free volume contribution" (94, 95).

A conceptually complementary approach to describe hydrophobic effects has been introduced by Pratt and colleagues (78, 96). Their information theory (IT) model is based on an application of Widom's potential distribution theorem (97) combined with the perception that the solvation free energy of a small hard sphere, which is essentially governed by the probability to find an empty sphere, can be expressed as a limit of the distribution of water molecules in a cavity of the size of the hydrophobic particles. Because the distribution functions are essentially determined by density fluctuations of water at the molecular scale, the IT model relates the hydration and interaction of hydrophobic particles with the temperature dependence of waters thermodynamic response functions, such as expansivity and compressibility.

An instructive, simplified computer model for water is the "Mercedes-Benz" (MB) model of Silverstein et al. (98). It has been shown to capture qualitatively the anomalous thermodynamic behavior of water as well as the thermodynamic features of the hydrophobic effect. The MB-model notably captures the effect of increasing particle size. A hydrophobic particle of about twice the size of a water molecule is found to increase the free energy by a different mechanism, namely by increasingly breaking the hydrogen bonds. Similar to the thermodynamic behavior observed for planar interfaces, the mechanism increases the enthalpy but has only little effect on the entropy and heat capacity. The simulations indicate that at a large, extended inert surface, water is geometrically unable to form its maximal number of hydrogen bonds to other water molecules. Thus, enthalpically costly "dangling" hydrogen bonds form pointing toward the interface (99, 100).

Realistic three-dimensional computer models for water were proposed already more than 30 years ago (16). However, even relatively simple effective water model potentials based on point charges and Lennard-Jones interactions are still very expensive computationally. Significant progress with respect to the models ability to describe water's thermodynamic, structural, and dynamic features accurately has been achieved recently (101–103). However, early studies have shown that water models essentially capture the effects of hydrophobic hydration and interaction on a near quantitative level (81, 82, 104). Recent simulations suggest that the exact size of the solvation entropy of hydrophobic particles is related to the ability of the water models to account for water's thermodynamic anomalous behavior (105–108). Because the "hydrophobic interaction" is inherently a multibody interaction (105), it has been suggested to compute pair- and higher-order contributions from realistic computer simulations. However, currently it is inconclusive whether three-body effects are cooperative or anticooperative (109).

An analysis of computer simulations of water at different pressures by Hummer et al. (110) suggested that hydrophobic contact pairs become increasingly destabilized with increasing pressure. The proposed scenario could explain the

pressure denaturation of proteins as a swelling in terms of water molecules that enter the hydrophobic core by creating water-separated hydrophobic contacts. Additional support for the validity of Hummer's IT-model analysis has been achieved by pressure-dependent computer simulation studies of isolated pairs of hydrophobic particles, as well as rather concentrated solutions of hydrophobic particles (111, 112). Recently, the pressure-induced swelling of a polymer composed of apolar particles at low temperatures can be observed (113).

Ion Hydration

As already suggested by Max Born in 1920 (114), the large negative solvation free energies of ions in aqueous solution can be explained by mostly purely electrostatic effects, which assume water to be represented by a dielectric continuum (115). Small changes of the ion diameter are found to affect the solvation free energies strongly. The measured solvation free energies roughly scale with the third power of the ion diameter, as proposed by the Born theory (115). However, a structuring effect on the first hydration shell water is obvious and has been experimentally determined by X-ray and neutron scattering techniques (116–119). In case of an anion, the first shell water molecules form a hydrogen bond type configuration in which the OH-bond points toward the anion (118), although on average it does not point exactly to the center of the ion (117). For the case of cations, the water molecules are found to be pointing with their oxygen toward the ion. The water dipole axis, however, seems to exhibit an average tilt of about 30 degrees with respect to the ion-water-oxygen connecting vector (117, 119). Recent first principles simulations of aqueous salt solutions suggest that this might be an artifact caused by averaging a rather broad tilt angle distribution (120). In those simulations, the dipole vector that points directly toward the ion is the most likely configuration of a broad distribution. Earlier classic MD simulations had revealed a more tilted "lone-pair"-type of ion-water bonding (121), which was possibly a consequence of the tetrahedral charge distribution of the employed water model (17) and is perhaps an artifact.

Ionic Influence on Hydration Water and Bulk Water

Salts are known to influence several properties of aqueous solutions in a systematic way (122, 123). The effect of different anions and cations seems to be ordered in a sequence; this theory was already proposed by Hofmeister in 1888 (124) from a series of experiments on the salts ability to precipitate "hen-egg white protein." Numerous other properties of aqueous salt solutions are also found to be systematically salt dependent, such as the surface tension or the surface potential (122). However, the exact reason for the observed specific cation and anion sequences is still not fully understood (125). Model calculations (126), as well as nuclear magnetic relaxation experiments (127), propose a delicate balance between ion adsorption and exclusion

at the solute interface. This balance is tuned by the solvent (water) structure modification according to the ion hydration (128, 129) and hence is possibly subject to molecular details.

In principle, two different mechanisms have been proposed on how the ions influence protein stability. Firstly, it has been suggested that a modification of water's structure is the origin of the Hofmeister sequence (130). It has been hypothesized that some ions "kosmotropes" enhance the structure that surrounds the ions, which leads to a strengthening of the hydrophobic effect and thereby stabilizes the proteins (131). However, the ions that break the structure that surrounds the ions ("chaotropes") have been considered to weaken the hydrophobic effect and hence destabilizes the native state of proteins. It has been suggested that the competition between ionic charge and ionic size determines whether an ion is a chaotrope or a kosmotrope (126, 132–135). A completely alternative explanation for the Hofmeister series has been suggested by Timasheff and colleagues (123, 136). They consider the differences in salt-protein binding as the main effect for destabilizing proteins. Their analysis of thermodynamic data provided evidence suggesting the salts that denature proteins tend to be bound to proteins, whereas the salts that stabilize proteins tend to be excluded from the protein surface. Using volumetric data of Timasheff et al. (123, 136) on the effect of numerous salts on bovine serum albumin, recently Shimizu et al. (137) could show by using a Kirkwood-Buff theory framework that the water-mediated protein-salt interaction is an important driving force for the protein denaturation. A recent simulation study on a highly idealized model system by Zangi et al. (138) came to a similar conclusion. They could show that the ion-adsorption mechanism is largely controlling the association behavior of two hydrophobic plates (138). Depending on the chosen combination of ions, salting-in, as well as salting-out scenarios could be obtained.

Currently, no consensus can be reached whether the presence of ions have an effect on the water structure at distances beyond the first hydration shell. Lebermann and Soper (129) used neutron diffraction to compare the effects of applied pressure and high salt concentrations on the hydrogen-bonded network of water. They found that the ions induce a change in structure equivalent to the application of high pressures, and that the size of the effect is ion-specific (129). Similar effects have been reported by Botti et al. (139, 140) who studied the solvation shell of H^+ and OH^- ions in water. Mancinelli et al. (141) could show that a structural perturbation caused by monovalent ions (in aqueous solutions of NaCl and KCl) exists outside the first hydration shell of the ions. Their study emphasized longer ranged ion-induced perturbation and shrinks of the second and third coordination shells of water molecules, whereas the first neighbor shell is largely unchanged. The O-O pair correlation function of water was modified by the ions in a manner closely analogous to what happens in pure water under pressure. In contrast, recent molecular dynamics simulations of water in aqueous $CaCl_2$ solutions indicate unequivocally that the changes of the water structure caused by the presence of ions in solution cannot be emulated as a pressure effect because of the local nature of such structure perturbation (142). A recent extensive MD simulation study by Holzmann et al. (143) indicates that the ion-induced structuring of water beyond the second hydration

shell of NaCl is caused by increasing pressure; it is also found to be strongly temperature dependent. The "structuring effect" is particularly observed in the supercooled salt solution, which apparently tends to stabilize water's high-density liquid form.

Conclusion

Liquid water provides a unique wealth of unusual liquid/solvent properties, many of which have been exploited by nature during the evolutionary process. As we have tried to show, many of water's unusual properties, or "anomalies," stem from water's tendency to form a roughly four-coordinated hydrogen bond network. Computer simulations indicate that many effects can be explained in great detail by simulations based on molecular models. A pattern reveals that in water, hydrogen bond-based local-order (entropy) and interaction energies have the beneficial tendency to compensate each other, which is important for many solvation processes and for water structuring and phase behavior. The small size of the water molecule and its effective hydrogen-bond formation make it a particularly helpful agent in the process of protein folding; it is deemed essential to enable protein motions.

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See Also

Hydration Forces

Watson–Crick Base Pairs: Character and Recognition

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The unique Watson–Crick arrangement of hydrogen-bonded bases in DNA accommodates two different, complementary purine–pyrimidine pairs, A·T = T·A and G·C = C·G, in a common spatial setting. Nature takes advantage of these isomorphous structures, which store genetic information in terms of the proton donor and acceptor atoms that hold the bases in place. As outlined here, the Watson–Crick base pairs carry other chemical signals that are used to recognize and to process specific sequences of bases. The relative stabilities of G·C versus A·T pairs reflect their different electronic structures. The distributions of electronic charge on the exposed major-groove and minor-groove edges of the base pairs present unique motifs for direct sequence recognition, and the deformations of the paired bases from ideal, planar configurations provide subtle, indirect recognition elements. The biologic significance of the latter signals is not fully understood but is becoming clearer as more and more high-resolution structures of DNA and RNA are determined.

The simple, yet elegant structure of double-helical DNA—two sugar-phosphate strands wrapped along antiparallel right-handed pathways around a central core of stacked and hydrogen-bonded base pairs—provides the molecular basis to interpret the storage, duplication, and rearrangement of genetic information. The same type of base pairing persists in double-stranded RNA, DNA–RNA hybrid duplexes, and synthetic multi-stranded polymers, such as PNA (1), which allow the chemical message to be duplicated, transcribed, blocked, and so on. The information reported below draws on the three-dimensional spatial arrangements of Watson–Crick base pairs and bound ligands in the

many DNA and RNA structures now stored in the Nucleic Acid Database (NDB) (2).

Complementarity

Classic Watson–Crick base pairs are formed by unique hydrogen-bonding interactions between the nitrogenous bases of DNA and RNA. The purine adenine associates specifically with the pyrimidine thymine in DNA (or the related unmethylated analog, uracil, in RNA), and the purine guanine interacts

Advanced Article

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