Water: The Forgotten Chemical, Edited by Denis Le Bihan and Hidenao Fukuyama. PanStanford Publishing, Singapore (2011), 399 pages.

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The latest volume on water comes from the PanStanford Publishers, edited by Denis Le Bihan and Hidenao Fukuyama, conceived upon the assertion that “water deserves to be seen as the prime ‘biological molecule’, and its importance should not be taken for granted”. It comes across as a collection of musings and informed essays on various aspects of water mostly connected with its important status as the biological solvent. The levels of different chapters in this volume, many of which are written by preeminent experts in the field of aqueous solutions in general, varies a lot, spanning in fact the whole area accessible on the one side to undergrads and on the other to seasoned researchers. I am not sure who it is that forgot water, but I assume that the title refers to the role of water as a de facto biological molecule. As noted by one of the editors themselves, the book should not be considered for continuous reading. It is rather a collection of essays in six chapters dealing with the structure of the water molecule, water as a solvent, water at interfaces, water and cell membranes, water and cell structure/physiology, and finally water, health, and life.

Because of the way this volume was conceived, the accessibility of various chapters varies a lot. So does their quality, and several of the chapters are real gems and are a delight to read. Among these, I would certainly include those written by Martin Chaplin (The Water Molecule, Liquid Water, Hydrogen Bonds, and Water Networks), Marie-Claire Bellissent-Funel (Protein Dynamics and Hydration Water), Yingxi Zhu (How Water Meets a Hydrophobic Interface), Bernard Cabane (Hydrophobic Molecules in Water), Mounir Tarek (Water and Membranes: Insights from Molecular Dynamics Simulations) and Hyok Yoo et al. (Characteristics of Water Adjacent to Hydrophilic Interfaces) to name a few. Some of these chapters are indeed presented as a type of essay and they could serve as a very a propos introduction to the subject of water in biological systems. I need to stress that I appreciate the selection the editors made for the authors of the chapters. We can read not only the mainstream consensus on the properties of water in the biological milieu but also some less well

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established, but nevertheless very interesting experimental results and interpretations by, e.g., Pollack and his coworkers. Time will tell what, if anything, we can make of charge separation and liquid crystalline ordering of water adjacent to orienting surfaces.

For the first chapter of Part 1 (The Structure of the Water Molecule), the editors most appropriately approached Martin Chaplin, who has not only been writing about the importance of water in cell biology but has also set up a very informative and easily accessible on-line resource on water structure and science (<http://www.lsbu.ac.uk/water/>). In his contribution to this volume, Chaplin deals with the structural features of the water molecule, its dynamics, and the (hydrogen bond) interaction between several water molecules that leads to clustering of water molecules in the liquid phase and to various anomalous properties of the molecule and its aggregates as they relate to biology. The chapter is indeed written in an essay manner and lacks references, but the avid reader can certainly delve deeper by just following the leads given in Chaplin's on-line resources.

Part 2 (Water as Solvent) is introduced by the account of protein dynamics by Marie-Claire Bellissent-Funel. She has been active in the water field for many years and has contributed significantly to our knowledge of the interaction between water and other biological (macro)molecules that are accessible via scattering and relaxation techniques. She introduces the properties of water in contact with hydrophobic as well as hydrophilic surfaces and continues to give a more detailed account of water-protein interactions. She adds additional weight to the recently proposed slaving dynamics of protein moieties to the peripheral hydrated water dynamics as introduced by Frauenfelder and coworkers. Quite different methods of investigation thus lead to similar conclusions that the strong coupling between the internal protein dynamics and the vicinal water dynamics is essential for proper functioning of proteins. The subject of water influencing the properties of the dissolved proteins is then picked up by Mikio Kataoka and Hiroshi Nakagawa in their chapter on the Effects of Hydration on Protein Dynamics.

Extensive neutron scattering experiments strongly indicate that the hydration water stiffens the harmonic properties of proteins. In this way, it also suppresses the harmonic motion around the equilibrium configuration. This hydration rigidification of proteins might be interesting for the action of some of the antifreeze proteins. The next chapter in this part of the book, by Norio Yoshida and coworkers, heads in the direction of a theoretical statistical mechanical investigation of the molecular recognition processes involving vicinal water molecules of functional proteins. The recognition mechanism is tied to a detailed statistical mechanical analysis of the configurational statistics of water molecules around active moieties of various proteins. This chapter is a bit difficult to follow for somebody without a sufficiently detailed background in statistical mechanics and in particular the reference interaction site model. Part 2 of the book concludes with a superb contribution by Bernard Cabane on Hydrophobic Molecules in Water written in the illuminating French tradition of physical chemistry. This chapter in particular is a delight to read and the description of the molecular mechanisms involving tannins and their interaction with water in aqueous solutions is very informative even for a reader who works nowhere close to the subject matter.

Water at interfaces is the subject matter of Part 3. The subject is beautifully introduced by Yingxi Zhu in her account of the hydrophobic interface in water. There are many unknowns and quite a few surprises in this venerable experimental field. I was amused to read that 20 years after Adrian Parsegian and myself published a paper on an electrostatic-surface stability interpretation of the hydrophobic force in which we stated that the range of these anomalously long-range hydrophobic forces "seems[s] to increase monotonically with the

year in which the measurement is made” the situation is not much improved. The anomalous range of interactions between macroscopic hydrophobic surfaces is still discussed vigorously and seems to be attributed more to bubble bridges, capillary waves, and water ejection from between the interacting hydrophobic surfaces than to long-range electrostatic interactions, which was the interpretation that we put forward two decades ago. The next chapter comes from the lab of Gerald H. Pollack who has gained some notoriety for espousing the view of the extremely long range ordering effect of macromolecular surfaces on water. The controversy here goes all the way back to the brilliant work of Gilbert N. Ling. Pollack and coworkers claim that water behaves almost like a liquid crystal and creates macroscopically large regions of order close to biological interfaces with a colloid exclusion zone that furthermore leads to a charge separation in such a perfectly ordered system. The experiments seem to be relatively straightforward but I am not sure whether the explanation provided makes sense. This remains to be seen, and should be followed with an open mind.

Part 4 is dedicated to Water and Cell Membranes. Mounir Tarek takes the lead with his contribution on the molecular dynamics of membranes. In particular, he deals with the problem of electroporation, i.e., stability of a membrane towards high external electrostatic fields. He analyses the sequence of reorganizations in the membrane due to water protrusions into the hydrophobic core of the lipid bilayer that eventually lead to pore formation. Only simulations can at this point give a detailed molecular picture of pore formation. Giuseppe Zaccai, co-author of a recent opus magnum on methods of molecular biophysics, and his coworkers then take the lead in explaining the wealth of information that neutron scattering can yield on the question of water in membranes and cells. They pick up again the theme of vicinal structured and slower water but this time within the more sensible framework of locally ordered structures. Maybe a few molecules thick, these structures are in accord also with other experiments on hydration interactions between biological macromolecules.

The problem of water migration across a membrane is then detailed in the contribution of Yoshinori Fujiyoshi and his coworkers. The question of how water moves through water-permeable channels is addressed via the electron crystallography method that has been used to advantage in the case of aquaporins. The conclusion of the studies described in this chapter is that the water molecules seem to pass through the channel in a single-file arrangement following a clearly defined route. In some sense, one could describe this single-file transport as a transient proton wire threading through the water-permeable channel. The final chapter in this part of the book is written by John H. Crowe and deals with Water, Membranes and Life without Water. It brings together the self-assembly of lipid bilayers and the ordering of alkyl chains within the hydrophobic core. Dehydration exposes membranes to severe hydration stress that can be quantified in terms of hydration interactions between lipid bilayers in a multilayer system. Various sugars, in particular trehalose, seem to confer stability on dehydrated membranes and proteins, stabilizing their structure even in the absence of water. The way they accomplish this task is not completely clear, but it is plausible that they either concentrate water at the interfaces, thus preserving their solvation, or simply replace the hydrogen bonds usually offered by the vicinal waters by their own hydrogen bonds.

Water and Cellular Structure defines Part 5 of this volume. Frank Meyer introduces the role of interfacial water for cell architecture and function on the level of the cells as well as on the level of enzyme complexes. Sachiko Tsukita and her coworkers then discuss in detail the role of water for forming tight junctions of epithelial cell sheets, whereas Makoto Kinoshita introduces the role of the septic cytoskeleton for the functional organization of the

plasma membrane. The final chapter by Pierre Magistretti and coworkers deals with water movement associated with neuronal activity as revealed by holographic microscopy. There seem to be two types of water movement connected with neuronal activity: slow and fast movements, associated with water diffusion processes in the brain, the direct connection still fairly out of reach.

The last part of the book is dedicated to Water, Health and Life. The two chapters written by the two editors of the book, Denis Le Bihan and Hidenao Fukuyama, both deal with water and the brain. They introduce and analyze the role of water, cell membranes, and diffusion of water in brain functional imaging. Diffusing water molecules in tissues encounter various constraints due to the structure and organization of cells in tissues. Thus engendered anisotropies in diffusion can be quantified by the formalism of the diffusion tensor introduced by Peter J. Basser of NIH. The diffusion tensor-based MRI is in fact used to map the wiring diagram of the entire living human brain, defining its connectome. Explaining the diffusion properties of tissues is an extremely demanding task that has to deal with the topology and connectedness of tissues as well as the properties of vicinal water at the cellular surfaces that drastically modifies its dynamics. The changes in water properties that accompany various physiological and pathological states of tissues and cells have been clearly demonstrated but are still relatively poorly understood. Even less is known about the overall circulation of water in the body in general and in the brain in particular, though clearly this kind of circulation is essential for various functions of the body and the brain. Very appropriately, the last chapter of the book, written by Gilles Boeuf, introduces water as the key molecule of life. The role of water in ancient life is examined in detail and the ionic and osmotic properties of aqueous solutions as they transpire in various life processes is described. The ancient ocean and its ionic composition obviously made a very important impact on the composition of life fluids ever since the transplantation of life from the oceanic cradle to its land modification. This chapter ties into all the other aspects of the connectedness of water and life that have been invoked already in the previous chapters.

In summing up, I think the editors did a favor to the scientific, and in particular the water research community, by bringing together a varied collection of authors with strong and fascinating views on the various aspects of the relationship between this eccentric chemical (as Felix Franks put it) and life. I believe that this book will be able to satisfy the curiosity of undergrads as well present an illuminating read for more seasoned researchers, making sure that water's deep and essential connectedness with life remains unforgotten as we delve ever more deeply into the secrets of life.