

Viewpoint

Biological Water or Rather Water in Biology?

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There has been a lot of discussion about biological water recently. Books¹⁻² and reviews³⁻⁵ were written in the past years and a special issue of the Journal of Chemical Physics was dedicated to the topic in 2014.⁶ Interestingly, papers on biological water are mostly confined to chemistry and physics journals, being remarkably rare in biological or biochemical literature. So, what is actually the biological water, we physical chemists are so concerned about? Definitions vary from “soft” to “hard” ones. A soft definition describes biological water as any water around a biomolecule (i.e., protein, DNA or RNA, or a piece of a cellular membrane) that has properties distinct from those of the aqueous bulk.⁷⁻¹⁰ More hard definitions operate with mutual tailoring of thermodynamic and dynamic properties of the biomolecule and surrounding waters,¹¹⁻¹⁵ and even with covering the protein by a shell of functional water molecules which can “slave” its motions⁵ and propagate to considerable distance.¹⁶ Finally, the recent hardest interpretations invoke in their extreme form, which can hardly be considered as strictly scientific any more, the notion of cellular water as a distinct species which itself is able to carry the biological functionalities.¹⁷⁻²⁰

There is little doubt that a layer of non-bulk water exists around a biomolecule.⁷ The relevant question is how thick such a layer is and to what extent its properties differ from those of the aqueous bulk. Let us first get a semi-quantitative estimate of the thickness, focusing on electrostatic interactions which dominate in water. The range of these interactions is governed by the Debye screening length,²¹ which amounts to less than 1 nm for the physiological ionic strength of about 150 mM. The physiological solution thus has a remarkable ability to screen out electrostatic interactions, which could hardly propagate beyond some 1-3 water molecules from the surface of the biomolecule. Still, several solvent layers can represent a non-negligible fraction of available water in the crowded cellular environment.⁴ Moreover, individual biomolecular functional groups can come close enough to each other such that topological characteristics of the protein or DNA surface can in principle combine with properties of interfacial water molecules in-between these groups.²²⁻²³

For the above reasons, the relevant question is not only how many water molecules are influenced by the biomolecule, but also how much. Leaving aside the small number of water molecules trapped in protein concave pockets of varying depth,²⁴⁻²⁶ the remaining ~90 % of interfacial water molecules are only modestly slowed down by the presence of the biomolecule.^{10, 27} Indeed, previous reports of a more dramatic, orders of magnitude slow-down^{5, 28} can be attributed largely to motions of the protein itself rather than to water.²⁷ It is thus safe to conclude that the protein surface influences rather weakly the surrounding water molecules. Various spectroscopic methods, as well as molecular dynamics simulations, report detectable changes in the immediate water shell next to the protein compared to bulk water behavior.^{5, 7, 10-13, 15} Changes in next solvent layers grow progressively weaker and eventually, at around 1 nm

from the protein surface and beyond, become accessible largely to techniques with a sufficiently large “yardstick”, such as the terahertz or dielectric spectroscopies.^{13, 16, 29-30}

Two messages follow from our analysis. The first one, addressed to biologists and biochemists, who tend to focus their attention primarily to the biomolecules, is that water does matter. Moreover, since the interfacial water layer covering the biomolecule has distinct properties from the aqueous bulk it is often not satisfactory to describe the aqueous solvent merely as a structureless continuum with a dielectric constant of bulk water. Such an approach can capture the longer-range dielectric effects of the solvent on the biomolecule,³¹ nevertheless, in many cases local interactions between functional groups at the solute surface with adjacent water molecules are important and require atomistic description.³² The good news is that in most cases one or two layers of explicit “granular” waters around the solute surrounded by a dielectric continuum represent a satisfactory description of the solvent effects.³³⁻³⁴

The second and arguably more important message is addressed to our community of physical chemists. An attempt to formulate it in a somewhat lighter tone is presented in Figure 1. While water including its interfacial layer,¹⁵ as well as ions and osmolytes,³⁵ plays a key role in establishing the homeostasis, it is primarily the biomolecule itself which carries the biological function. It is a fact that individual water molecules and ions in binding pockets of enzymes can play an important role.³⁶ However, there is little direct evidence that collective motions of the hydration layer are decisive for protein function, potentially save for extreme conditions of strong dehydration or cooling^{11, 14-15, 37-38} (although even there the degree of water involvement in biological functionality is a matter of debate³⁹⁻⁴⁰). As physical chemists who naturally tend to understand water better than biomolecules we may sometimes have a tendency to overemphasize the role of the former at the expense of the latter. For this almost psychological reason and, more

importantly, due to the scientific reasoning outlined above I would argue that *the term biological water should be dropped*. It is perfectly justifiable to talk about water in biology and discuss the role of interfacial water around biomolecules with its distinct properties. However, using the term biological water with all its connotations toward a hypothetical state of cellular “vicinal water” carrying biological function⁴¹⁻⁴² might be bringing us dangerously close to the long overcome concept of “vis vitalis”.⁴³⁻⁴⁵

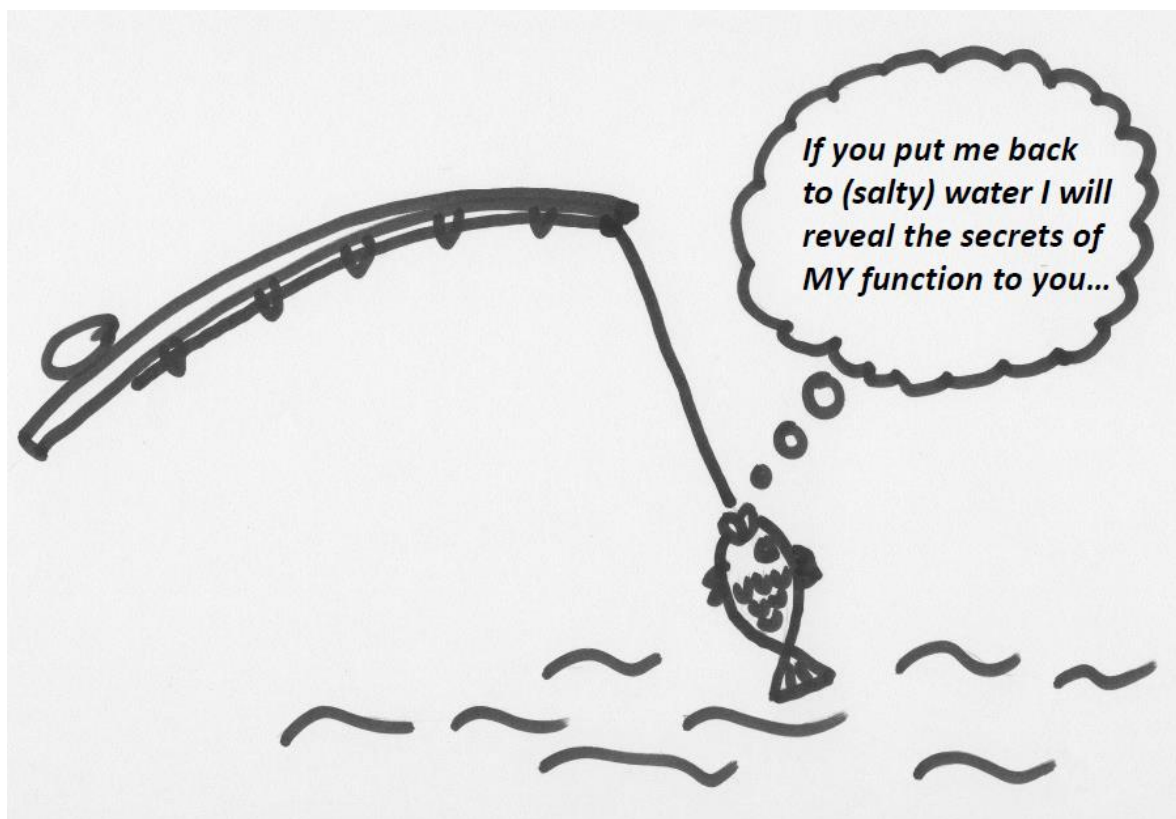


Figure 1: A cartoon representing the key message of the Viewpoint: Water (with salt ions and osmolytes) is essential for proper functioning of biological molecules, but the functionality dominantly belongs to the biomolecule itself (represented as a fish in my amateurish drawing).

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