

Beyond Hofmeister: Interactions Between Ions and Proteins in Water

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Recently, mechanisms underlying specific ion effects on protein solubility and stability, as expressed in the Hofmeister series of ions, have been firmly established at the molecular level. Further progress in understanding ion-specific effects in biological systems requires, however, to go beyond the simplifying concept of separate anionic and cationic Hofmeister series. What matters is not only the behaviour of individual ions at the protein surface but, to varying extents, also interactions between the salt ions themselves, both near the protein and in the bulk aqueous solution. Such effects become operational at relatively high salt concentrations and are distinct from non-specific electrostatic interactions, known for a long time to lead to salting-in at very low ionic strengths. As an example, concentrated guanidinium chloride acts as a strong denaturant of model peptides, whereas concentrated guanidinium sulfate does not. This difference arises from the passivation of the denaturing guanidinium cations by appreciable ion pairing with sulfate anions in the solution. Additionally, more specialized ion-binding sites with tailored functional groups and geometries, such as active sites of enzymes or membrane ion channels, are usually considered to be beyond the purview of generic Hofmeister effects. We show, however, that new insights may be gained by extending the realms of Hofmeister chemistry in this direction. Such extensions are possible since there is significant mechanistic overlap between the Hofmeister ion ordering and ion-specific interactions in these specialized ion-binding sites.

[1] Cremer, P. S.; Jungwirth, P.: Beyond Hofmeister. Nature Chemistry, 6 (2014) 261.