

The (Super)Chaotropic Effect: A Computational Chemist's Perspective

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Hydrogen bonding and the hydrophobic effect underpin associative processes in water, while specific-ion effects are described by the Hofmeister concept of kosmotropic and chaotropic ions. The *chaotropic effect*, the pronounced affinity of large, especially superchaotropic anions for hydrophobic and neutral polar environments, represents a distinct assembly motif orthogonal to the hydrophobic effect. It governs molecular recognition and binding phenomena across biomolecular, soft-matter and solid-state systems [1].

Our findings highlight the power of computational chemistry, particularly density functional theory and molecular dynamics simulations in clarifying the (super)chaotropic effect. We introduced molecular descriptors that quantify chaotropicity [2] and distinguish the unique hydration patterns of kosmotropes, chaotropes, and hydrophobes. Computational studies of prominent superchaotropic anions, including boron clusters and polyoxometalates, demonstrate how these species interact with peptides, biological membranes and supramolecular assemblies [3]. The most significant application of these clusters is their function as innovative, broadband membrane carriers. They facilitate the transport of diverse hydrophilic molecules across biological membranes, without depending on conventional amphiphilic design principles [1].

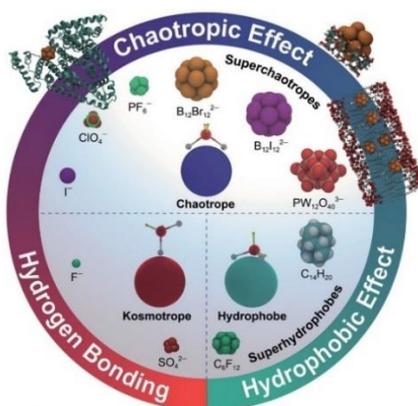


Figure 1. Illustration of the chaotropic effect as a molecular assembly motif in chemistry, shown as a principle distinct from the hydrophobic effect.

References:

- [1] (a) K. I. Assaf, W. M. Nau, *Angew. Chem. - Int. Ed.* **57** (2018) 13968–13981; (b) A. Barba-Bon, G. Salluce, I. Lostalé, K. I. Assaf, A. Hennig, J. Montenegro, W. M. Nau, *Nature* **603** (2022) 637–642.
- [2] G. Salluce, Y. Folgar-Cameán, A. Barba-Bon, I. Nikšić-Franjić, S. El Anwar, B. Grüner, I. Lostalé-Seijo, W. M. Nau, J. Montenegro, *Angew. Chem. - Int. Ed.* **63** (2024) e202404286.
- [3] A. Barba-Bon, A. El Haitami, C. Pasquier, I. Nikšić-Franjić, O. Diat, P. Bauduin, S. Cantin, W. M. Nau, *Angew. Chem. - Int. Ed.* **63** (2024) e202412834.