

Water is one of the most ubiquitous and essential solvents in biological and chemical molecular systems and thus water profoundly affects the molecular functions. Despite its significance, the molecular-level understanding of how water modulates these functions remains unanswered due to the inherent experimental challenges in probing hydration structures. In this study, I developed a novel methodology that combines state-of-the-art laser spectroscopy with mass spectrometry to investigate hydration structures in micro-hydrated molecular systems. This approach revealed critical insights into the indispensable role of water in molecular functions.

1) Cooperative hydration effect on ion recognition

Ion recognition is vital in biological systems because the membrane potential in cells is regulated by molecules that selectively bind a specific ion. Valinomycin (VM), a naturally occurring ion-selective molecule, selectively encapsulates K^+ over Na^+ with $\sim 10^4$ times higher affinity. However, the recognition mechanism remained unresolved due to inconsistency between experiment and theory. I have found by gas-phase IR spectroscopy that VM-alkali metal complexes have a similar structural motif regardless of the size of the bound ion [*Phys. Chem. Chem. Phys.* **25**, 4481 (2023)]. This clearly shows that the K^+ selectivity cannot be explained solely by size matching of the cavity size and ionic size. In contrast, the IR spectra of mono-hydrated $M^+VM(H_2O)_1$ exhibit a significant difference between high-affinity (K^+) and low-affinity (Na^+) ions. Whereas K^+VM retains its structure upon single water hydration, $Na^+VM(H_2O)_1$ undergoes conformational distortion due to the direct interaction between Na^+ and water. The low selectivity of Na^+ is ascribed to hydration-induced structural distortion [*J. Phys. Chem. Lett.* **14**, 5567 (2023)]. Further studies confirmed that this hydration effect is crucial not only for VM but also for other famous ion-selective molecules, such as crown ethers [*J. Am. Chem. Soc. in press*]. These findings redefine ion recognition by highlighting the role of hydration.

2) Hydration-induced proton transfer

Although proton transfer is one of the most fundamental chemical reactions, the underlying mechanism remains debated between the two models. One is the Grotthuss mechanism, in which the proton is shuttled to the nearest water molecule along a H-bonded water network. The other is the vehicle mechanism, where the proton diffuses as a hydronium ion (H_3O^+). I have developed a new method to determine which type of proton transfer occurs in micro-hydrated systems using the cutting-edge ion trap technique and laser spectroscopy [*Phys. Chem. Chem. Phys.* **24**, 5774 (2022)]. Based on this technological innovation, I found that vehicle-type proton transfer happens in smaller hydrated clusters and the proton transfer mechanism is switched from vehicle to Grotthuss with increasing the number of water molecules [*Chem. Sci.* **15**, 2725 (2024)]. These results provide a robust framework for understanding proton transfer in molecular systems in synergy with theoretical calculations [*J. Am. Chem. Soc.* **146**, 3023 (2024)].

In summary, I have revealed novel physicochemical phenomena in hydration-triggered molecular functions and chemical reactions using cutting-edge gas-phase spectroscopy. These findings establish a new interdisciplinary field focused on solvation-function relationships ranging from chemical biology to materials science.