The relation between the Hofmeister anions and water structure at protein surfaces

Euihyun Lee[a,b], Jun-Ho Choi[a,b], and Minhaeng Cho*[,a,b]

[a] *Center for Molecular Spectroscopy and Dynamics, Institute for Basic Science (IBS), Korea University, Seoul 02841, Republic of Korea*

[b] *Department of Chemistry, Korea University, Seoul 02841, Republic of Korea*

**E-mail: mcho@korea.ac.kr*

Abstract

Water has unique properties based on hydrogen bonding that is come from the specific atomic composition and molecular structure of water. These properties are crucial for the survival of life on the Earth. Thus, researched for water is highly important. Specially, we focused on these properties of water with protein and ions. To understand the relation between them, we carried out a molecular dynamics (MD) simulation. The result revealed that an effect of protein can affect ion distribution as well as water network only near the protein surface. And, the order of water network disruption followed the order of the Hofmeister anion series which is related with solubility of protein. Investigation for structural change of protein didn't show any significant change in our simulation. So, this result suggests that changes in the properties of the protein could originate from the disruption of the water H-bond network induced by ions with a higher affinity for the protein surface instead of direct protein residue-ion interactions. Additional investigation for orientational distribution of water molecules shows slight preference for interfacial water molecules, i.e. a straddle structure, within short ranges from the protein surface. Lastly, we found out that the cation effect on water network is also not negligible at the protein surface.

MD simulation details & Concept

Group 1. Pure liquid water
Group 2. 1 M ionic solution
Group 3. Ubiquitin(1UBQ) in liquid water
Group 4. Ubiquitin in 1 M ionic solution
Ion species : **NaCl, $NaBF_4$, NaSCN, $NaClO_4$**
TIP3P water model using SHAKE algorithm

Minimization → 2 ns **NPT equilibration**
→ 2 ns **NVT equilibration** → 10 ns **MD** * 6 times
at T = 298 K, p = 1 atm

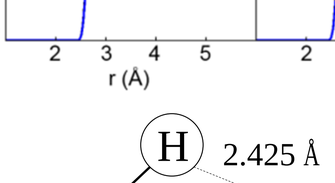
■ Hofmeister anion series

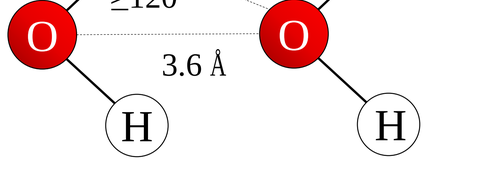
SO_4^{2-} > Cl^- > BF_4^- > ClO_4^- > SCN^-

Kosmotropic — Chaotropic

Kosmotropic	Chaotropic
High charge density	Low charge density
Order-maker	Order-breaker
(stabilize H-bonding network)	(disrupt H-bonding network)
Protein solubility ↓	Protein solubility ↑
Surface tension ↑	Surface tension ↓

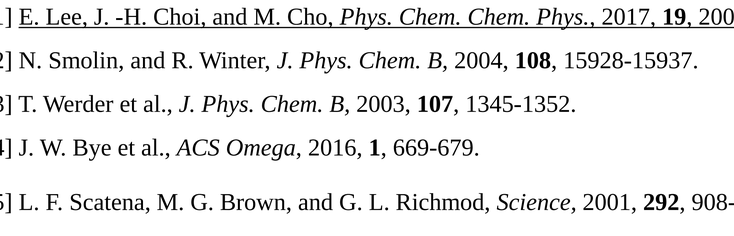
■ Distance criteria





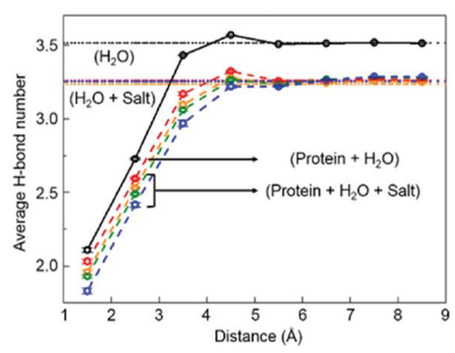
$d_a > d_b \rightarrow d_b$: distance between protein and object

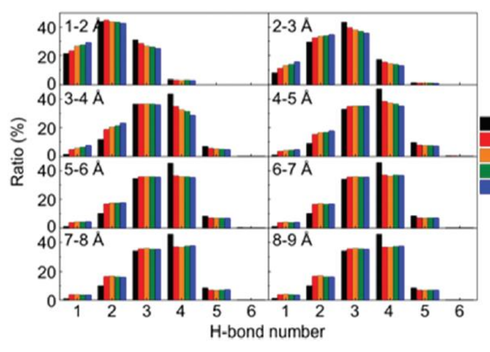
■ H-bonding criteria

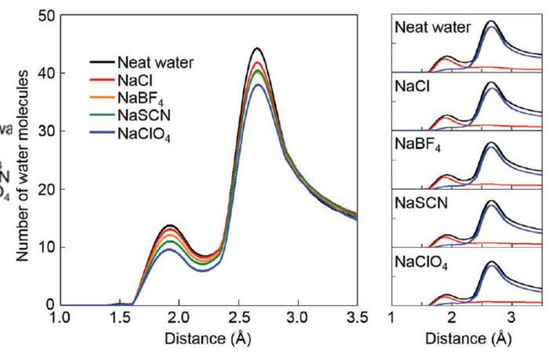


Results

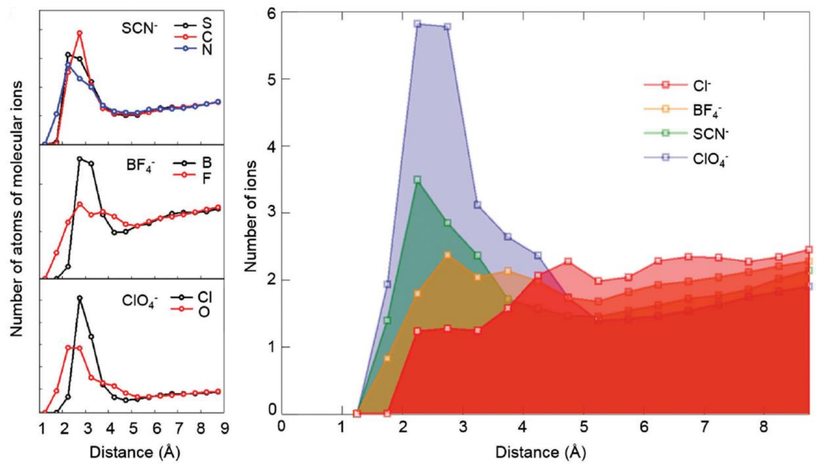
■ Breaking of water network structure





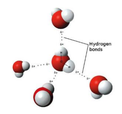


■ Ion distribution from the protein surface



The order of breaking
(H-bond number of water and Number of water)
→ ClO_4^- > SCN^- > BF_4^- > Cl^-

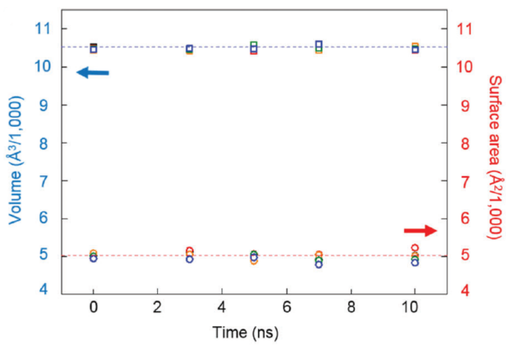
The order of number of ion
→ ClO_4^- > SCN^- > BF_4^- > Cl^-

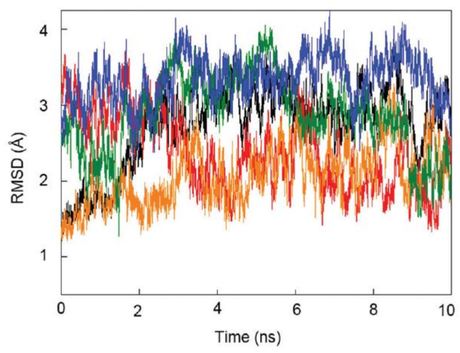


◆ This order follows Hofmeister series

◆ Short range effect of protein → water, ion

■ Change of volume, surface area, and RMSD of protein

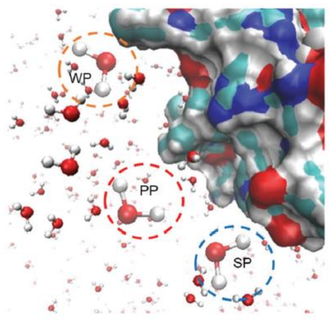


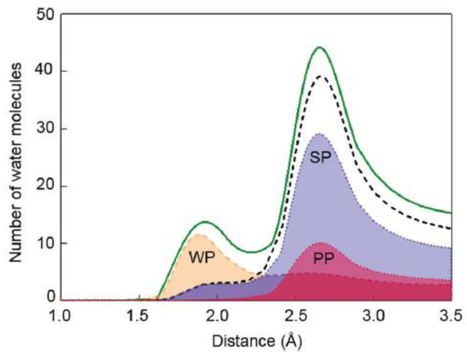


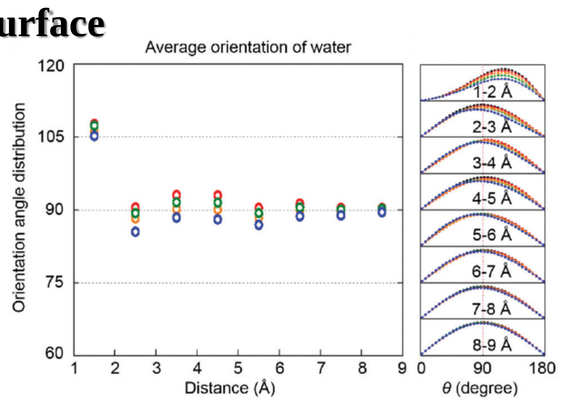
For 10 ns, there are no significant change. Thus, reason of protein solubility change is not denaturation from direct interaction of ions with residues on the protein surface.

◆ These results suggest that the reason of protein properties change is come from perturbation of the water network near the protein surface.

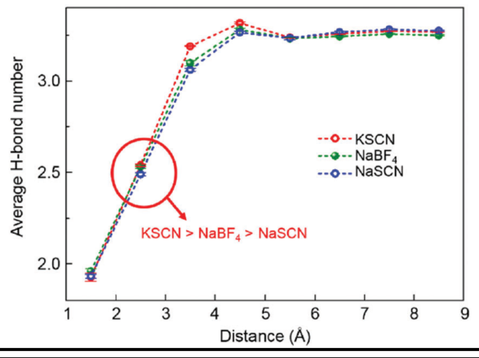
■ Orientation of water molecules near the protein surface







■ Cation effect for water networks within the hydration shell



Na^+ : 2.3 ~ 2.4 Å (high density)
K^+ : 2.8 ~ 3.0 Å (low density)
Positional preference : $Na^+ > K^+$

◆ The cation effect is often disregarded or treated as weaker than the anion effect. But, this effect is not negligible.

Reference

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Conclusion

- The perturbations due to ions at the protein surface only act as very short range effect within the first hydration shell of the ubiquitin
- The specific ion effects could originate from ions within the first hydration shell, which affect protein solubility by modulating the water structure rather than directly interacting with protein surface residue
- Chaotropic anions have a strong affinity for the protein surface due to their hydrophobicity
- The straddle configuration is predominant, which is a characteristic feature of interfacial water