# The effect of Hofmeister anions on water network near protein surface

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## Abstract

We investigated the change of water network by resolved ions at interface to understand the ion effect near protein surface. The disruption of water network is observed near protein surface from our results through the decrease of H-bond number. Under ionic condition, H-bond decrease patterns are revealed differently along the Hofmeister anion series which is related with solubility of protein near protein surface while there are no specific ion effects over 5 Å region. This result has strong relation with ion distribution. Chaotropic anions showed higher preference near protein surface than kosmotropic anions. Additionally, we investigated the number distribution and orientation distribution of each configuration of water to confirm preferential orientation at organic phase/water interface. Our results showed that the water has mainly random distribution, but slightly there are preferential configuration for straddle structure at protein/water interface. For cation effect on water network, it also shows different disruption pattern of water network near protein surface.

## MD simulation & Criteria for distance from surface

Group 1. Pure liquid water

Group 2. 1 M ionic solution (NaCl, $NaBF_4$, NaSCN, $NaClO_4$)

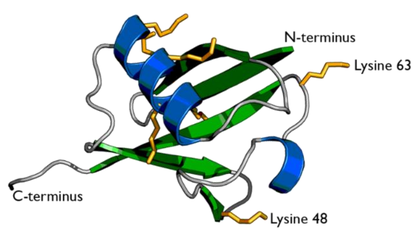
**Group 3. Ubiquitin in liquid water**

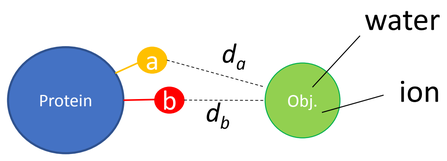
**Group 4. Ubiquitin in 1 M ionic solution (NaCl, $NaBF_4$, NaSCN, $NaClO_4$)**

TIP3P water model using SHAKE algorithm

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

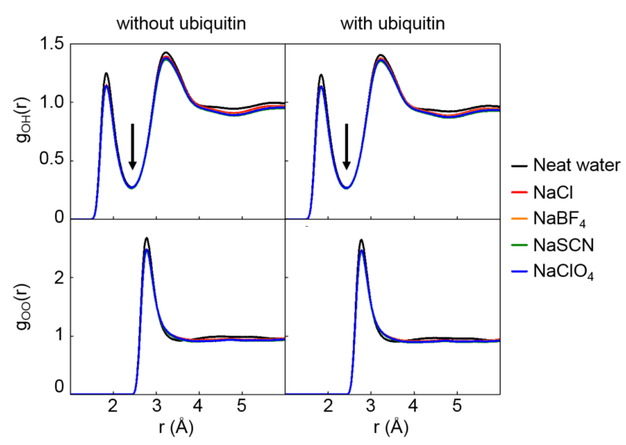
For ubiquitin system, to make higher accuracy, two times longer simulations were performed from individual start configuration



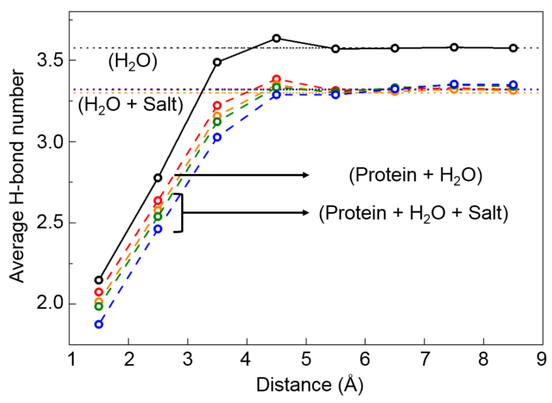

$d_a > d_b \rightarrow d_b$ : distance between protein and object

**$r_{1st}$=2.425 Å : H-bond criteria**



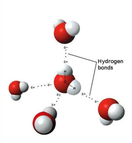

## Results

### ■ Hydrogen bond number of water




◆ **Bulk region (5 Å~) :**
There are no difference between ion types

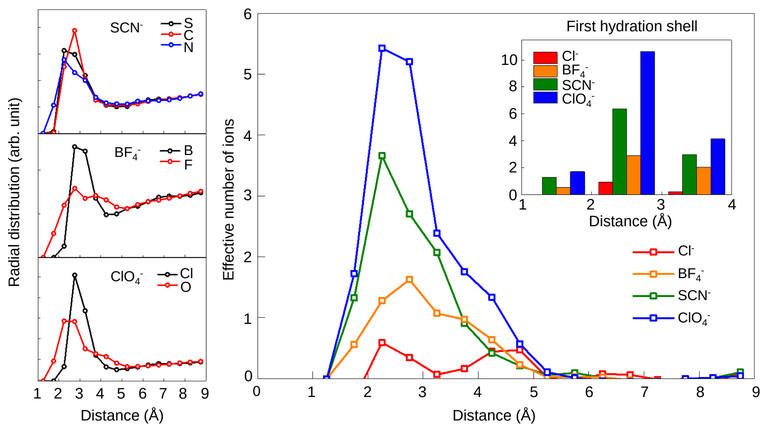
◆ **Near the protein surface :**
There are difference between ion types
→ **Short range effect of protein**




**1 to 4 Å**

**Ubiq (black)**
>
**NaCl (red)**
>
**$NaBF_4$ (orange)**
>
**NaSCN (green)**
>
**$NaClO_4$ (blue)**

### ■ The number distribution of ions

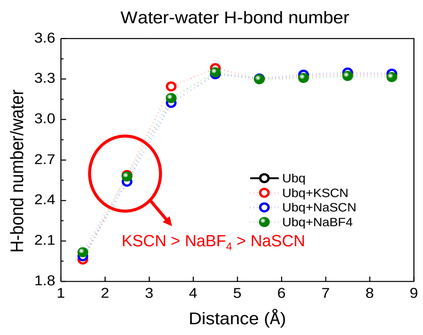



**Near protein surface : $ClO_4^-$ > $SCN^-$ > $BF_4^-$ > $Cl^-$**

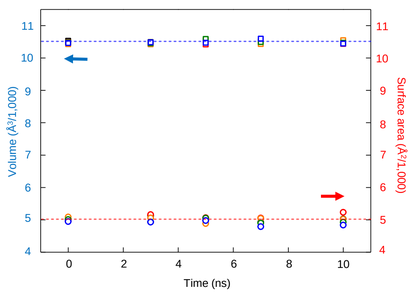
**Short range effect of Protein**

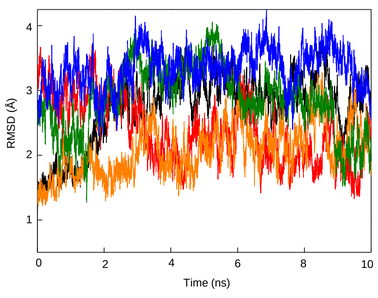
### ■ The cation effect near protein surface

$Na^+$ : 2.3 ~ 2.4 Å (high ND)
$K^+$ : 2.8 ~ 3.0 Å (low ND)
Preference : $Na^+ > K^+$




### ■ Surface area, Volume, and RMSD of ubiquitin

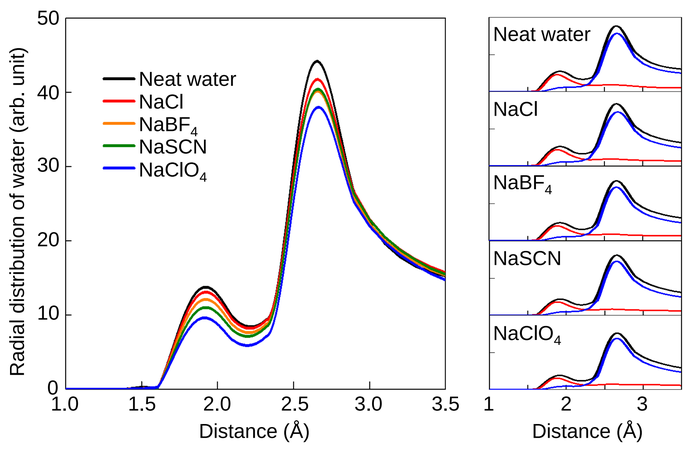


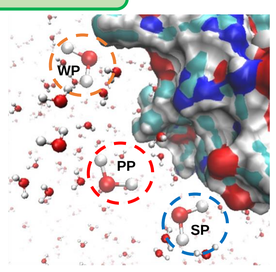



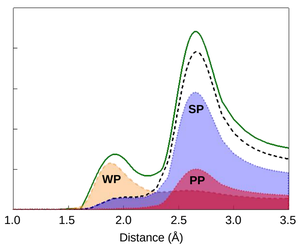

◆ These results didn't show significant change for structural information.

◆ There are other reasons that make change of protein properties.

### ■ The number distribution(ND) of water

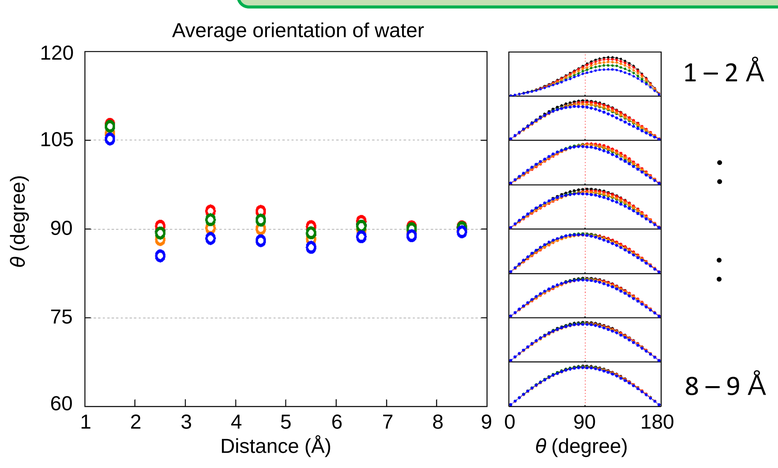



**The number of water within 3.6 Å** ▶ **Ubiq > NaCl > $NaBF_4$ > NaSCN > $NaClO_4$**

### ■ The orientation distribution(OD) of water




◆ Water molecules mainly have random distribution even near protein surface.

◆ But there is slightly preference for the straddle structure between organic phase and liquid water phase. (in connection with ND)

## Reference

[1] N. Smolin, and R. Winter, J. Phys. Chem. B 2004, 108, 15928-15937.

[2] T. Werder et al., J. Phys. Chem. B 2003, 107, 1345-1352.

[3] J. W. Bye et al., ACS Omega 2016, 1, 669-679.

[4] L. F. Scatena, M. G. Brown, and G. L. Richmod, Science 2001, 292, 908-912.

## Conclusion

- Difference of water network by ions is occurred only near protein surface along the Hofmeister series.
- The interaction between protein and ion is not main reason of the change of protein properties.
- H-bond number of water is strongly related with the ion number distribution.
- The water configuration from ND and OD of water revealed their orientation is mainly random, but they slightly have preferential orientation for straddle structure.
- The difference of H-bond number of water for KSCN, NaSCN show the cation effect for protein surface.