Journal Club

Y. Zhang et. al., "Specific Ion Effects on the Water Solubility of Macromolecules: PNIPAM and the Hofmeister Series",

J. Am. Chem. Soc. 127, 14505 (2005)

10th Oct. 2015 Yoonnam Jeon

Abstract: Aqueous processes ranging from protein folding and enzyme turnover to colloidal ordering and macromolecular precipitation are sensitive to the nature and concentration of the ions present in solution. Herein, the effect of a series of sodium salts on the lower critical solution temperature (LCST) of poly(*N*-isopropylacrylamide), PNIPAM, was investigated with a temperature gradient microfluidic device under a dark-field microscope. While the <u>ability of a particular anion to lower the LCST generally followed the Hofmeister series, analysis of solvent isotope effects and of the changes in LCST with ion concentration and identity showed multiple mechanisms were at work. In solutions containing sufficient concentrations of strongly hydrated anions, the phase transition of PNIPAM was directly correlated with the hydration entropy of the anion. On the other hand, weakly hydrated anions were salted-out through surface tension effects and displayed improved hydration by direct ion binding.</u>



Introduction

> Ability of salts to precipitated certain proteins

- from an aqueous solution : follows Hofmeister series

 $\begin{array}{ll} CO_3{}^{2-} > SO_4{}^{2-} > S_2O_3{}^{2-} > H_2PO_4{}^- > F^- > CI^- > Br \sim NO_3{}^- > I^- > CIO_4{}^- > SCN^- \\ \leftarrow \text{kosmotropes (maker)} & (breaker) \text{ chaotropes} \rightarrow \end{array}$

PNIPAM poly(N-isopropylacrylamide)

- insoluble above its lower critical solution temperature (known for over 40 years)

> Salts effect on the LCST of PNIPAM

- previous reports : measurements are not of sufficient precision

- study with microfluidic apparatus [J. Am. Chem. Soc. 124, 4432 (2002)]







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Introduction

Polymer's interactions with various anions

- Determine : mechanism of aggregation and precipitation of PNIPAM

> Effects of Hofmeister anions on PNIPAM

: can be explained by 3 interactions

- Anions : can polarize an adjacent water molecule (H-O-H...amide)
- Anions : can interfere with hydrophobic hydration
- Anions ... polyamide





Results - Salt concentration dependent LCST



Results - 2 step transition of LCST



Salt concentration dependent 2 step transition





Results - Anion dependent 2-step transition





Modeling - Changes in the LCST with added salt

Salt concentration dependence

- Surface tension for hydrophobic/aqueous interface : linear
- Polarization of water in the first hydration shell : should depend linearly on

Propose : these effects can dominate the precipitation of PNIPAM

Direct ion binding to the polymer (saturation phenomenon)
: can be modeled with binding isotherm



Perturbation of PNIPAM's LCST can be modeled by

$$T = T_0 + c[M] + \frac{B_{m ax}K_A[M]}{1 + K_A[M]}$$
 Langmuir isotherm

Proportional to the hydration entropy (ΔS_{hydr}) of the anions

 T_0 : LCST of PNIPAM in the absence of salt c : constant has units of temperature/molarity [M] : molar concentration of salt B_{\max} : the increase in T_{trans} due to direct ion binding at saturation K_A : binding constant of the anion to the polymer



Fitted values of K_A , B_{max} , and c from LCST Measurements

					\square	c (°C/mol)	
anion	$\sigma^{\rm a}$ (mN L/m mol)	$\Delta S_{\text{hydr}}^{b}$ (J/K mol)	B _{max} (°C)	K _A (M ⁻¹)	initial	first step	second step
CO32-	2.6	-245	-	-	-25.1	-29.0	-9.7
SO42-	2.7	-200	-	-	-18.3	-23.1	-10.0
S2O32-	2.9	-180	-	-	-16.3	-20.3	-10.9
H ₂ PO ₄ -	2.3	-166	-	_	-11.5	-14.7	-8.3
F-	2.0	-137	-	_	-9.0		
C1	1.6	-75	-	-	-5.3		
Br ⁻	1.3	-59	0.7	2.7	-3.7		
NO3-	1.1	-76	0.6	2.9	-3.5		
I-	1.0	-36	1.1	4.3	-1.5		
C1O4-	1.4	-57	1.8	5.1	-6.4		
SCN-	0.5	-66	1.6	4.3	-1.4		

^a From ref. : *Arch. Biochem. Biophys.* **183**, 200 (1997) except for H₂PO₄⁻ ^b From ref. : Marcus, Y. *Ion Properties.* Marcel Dekker, 1997





Slope for the lower transition : correlated to the hydration entropy of the anions



Lower transition temp. : related to the dehydration of the amide group through a polarization effect



Idea

lower transition temp. for kosmotropes :

due to the perturbation of the solvation waters hydrogen-bonded to the amide rather than interaction with the hydrophobic portions of the molecules

Tested by solvent isotope studies



H-bond strength : ~5% stronger in $D_2O > in H_2O$

Chem. Rev. 55, 713 (1955), J. Chem. Phys. 41, 680 (1964)

 \rightarrow leads to an increase in the LCST on enthalpic grounds

J. Chem. Phys. B 103, 10400 (1999)

 $\Delta T_1 \sim 3\Delta T_2$: specific hydrogen bonds are being broken in the first step of the process

