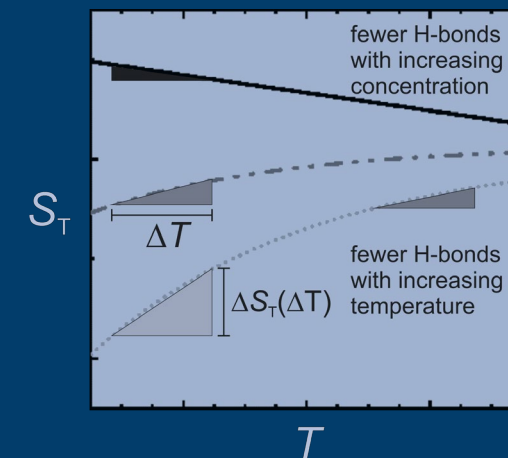
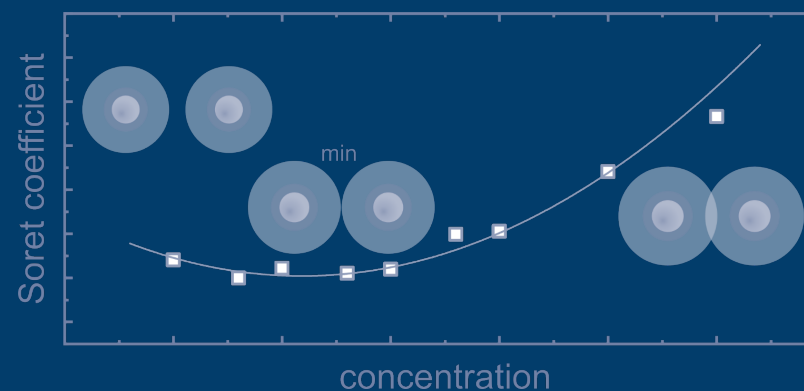


THERMODIFFUSION AS A PROBE OF HYDROPHILICITY IN ALKYL-SUBSTITUTED AMMONIUM SALTS

Institute of Biological Information (IBI)

IBI-4: Biomacromolecular Systems and Processes



28.10.2025 | BINNY RUDANI

SALT SOLUTIONS

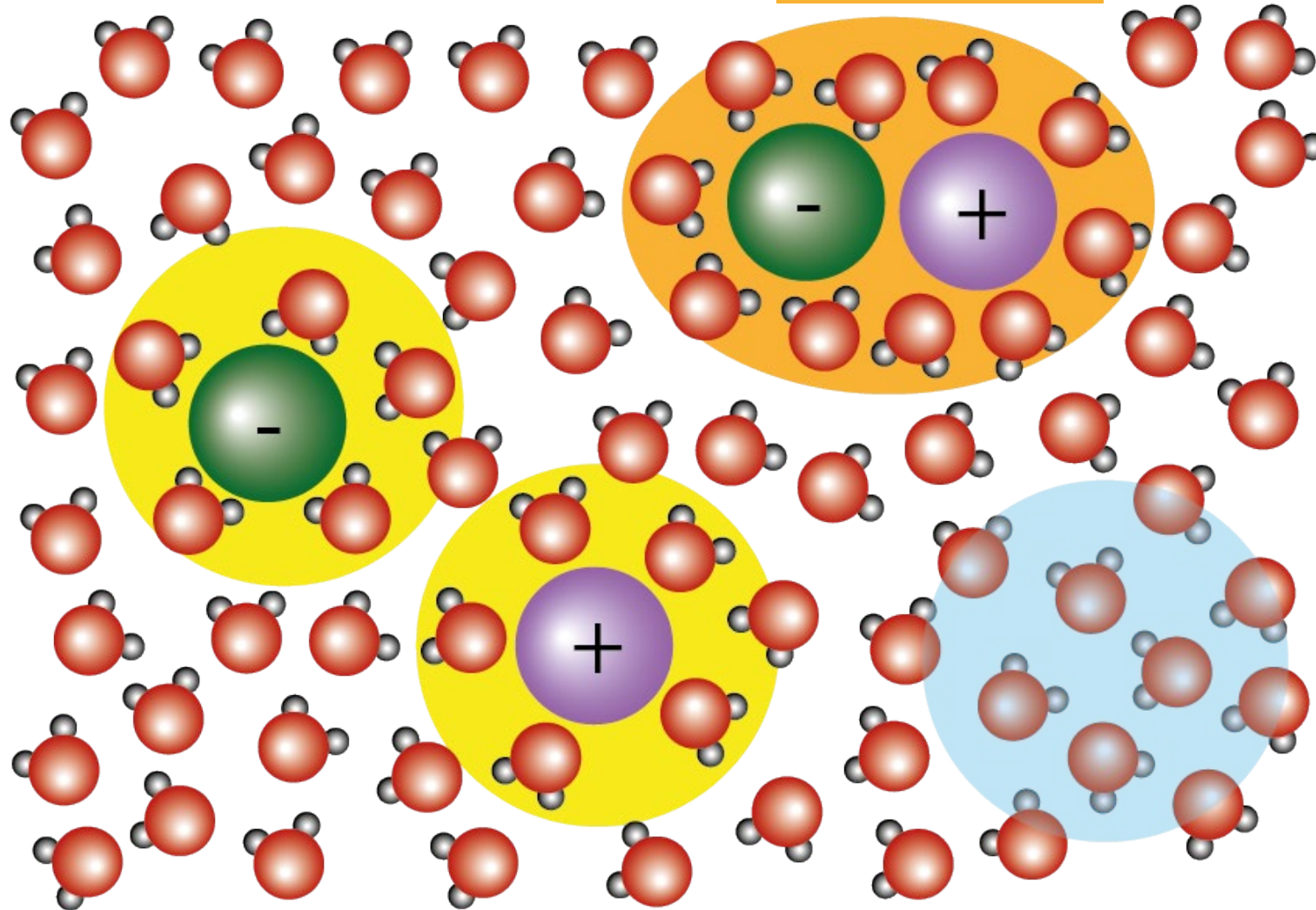
Complex view

aggregates

ion pairs

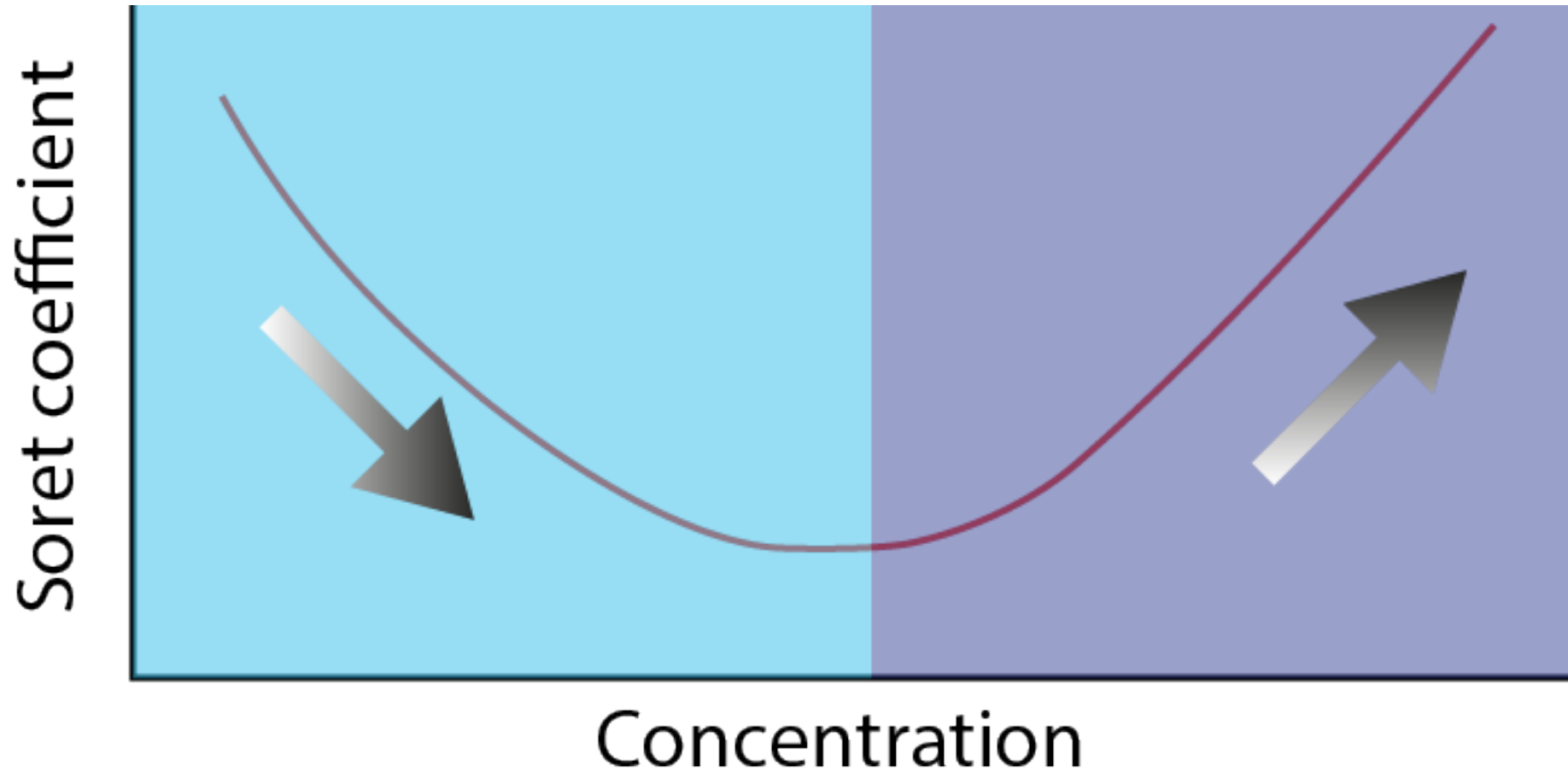
single ions

bulk water



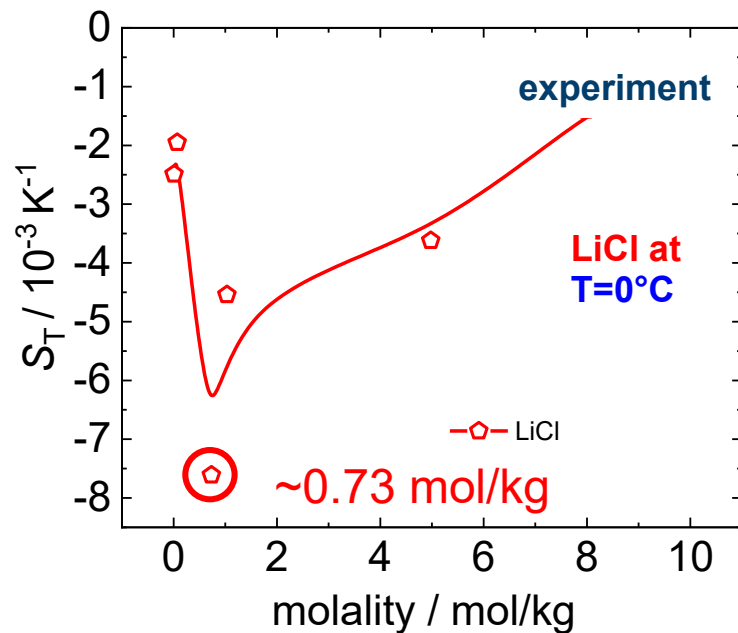
MINIMUM OF S_T WITH CONCENTRATION

Often observed in aqueous solutions of 1:1 electrolytes

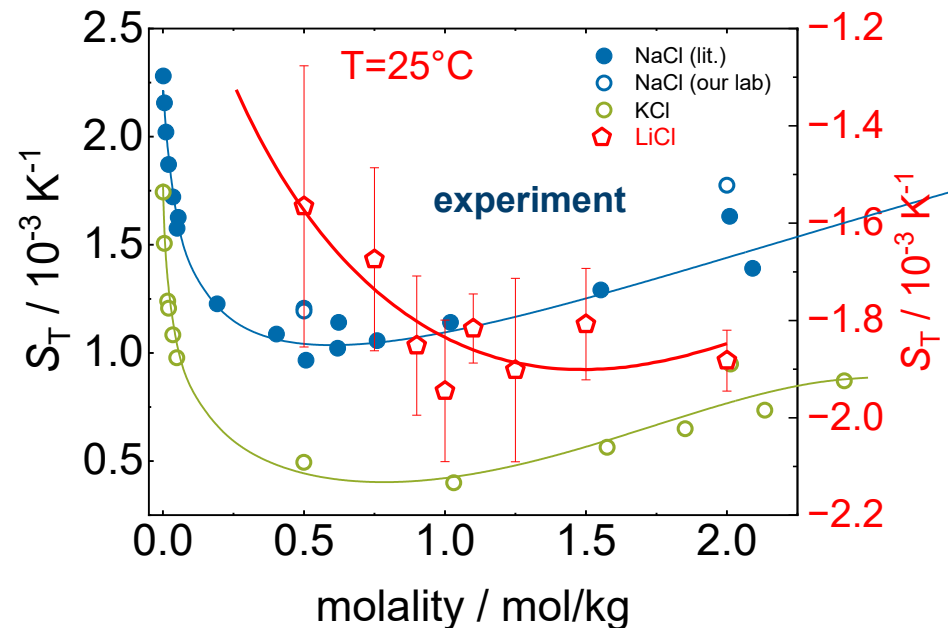


MINIMUM OF S_T WITH CONCENTRATION

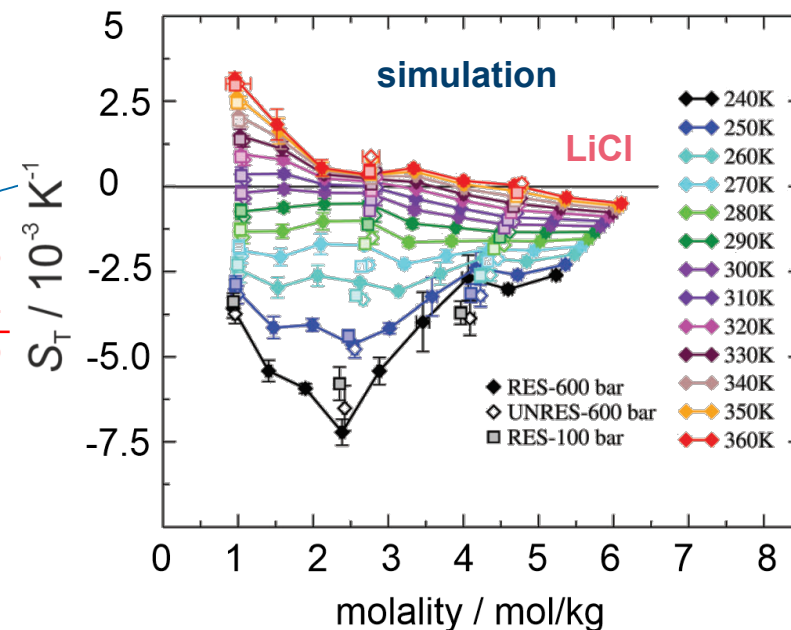
Often observed in aqueous solutions of 1:1 electrolytes



J. Colombani et al., JCP **110** (1999), 8622.



M. Jokinen et al., J. Membr. ScN. Lee, PCCP, **26** (2024) 7830i. **499** (2016) 234.



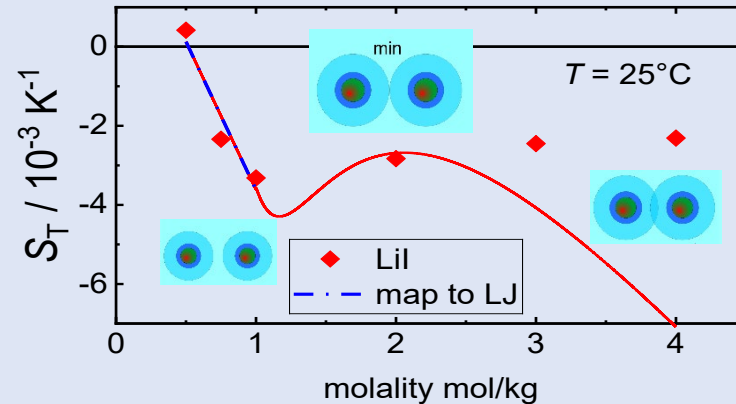
S. Di Lecce et al., PCCP **19** (2017), 9575.

Reason for the minimum of S_T at a specific concentration?

DESCRIBING THE MINIMUM OF S_T WITH CONCENTRATION

Both approaches use Lennard-Jones particle

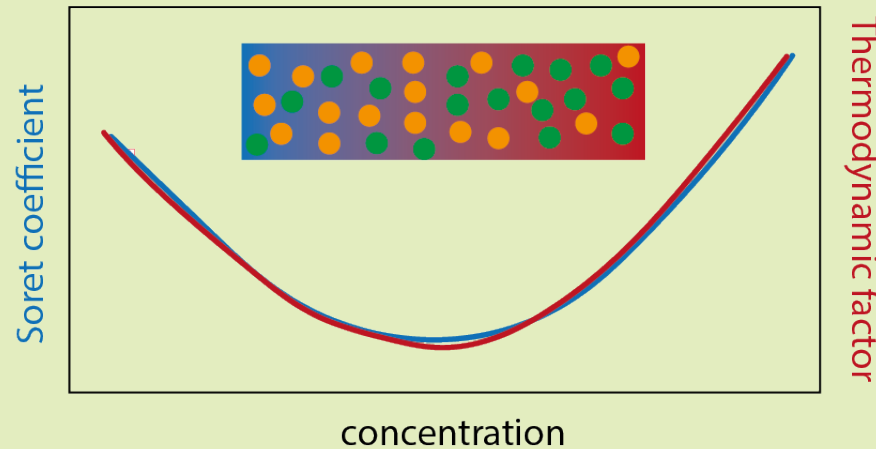
1.



- ion pairs assumed
- not a closed model
- localization of the minimum by the user

S. Mohanakumar et al., PCCP **24** (2022), 27380.

2.



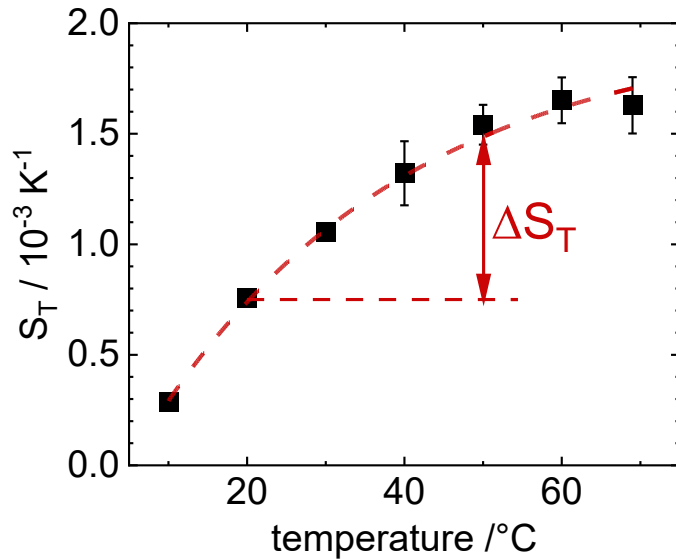
Approach not valid for electrolyte solutions

O.R. Gittus & F. Bresme PCCP **25** (2023), 1606.

TEMPERATURE DEPENDENCE

Typical temperature dependence of aqueous electrolyte solutions

ΔS_T is measure for
temperature sensitivity



$$\Delta S_T = S_T(T_{high}) - S_T(T_{low})$$

$$S_T(T) = S_T^\infty + A \exp\left(-\frac{T}{T_0}\right)$$

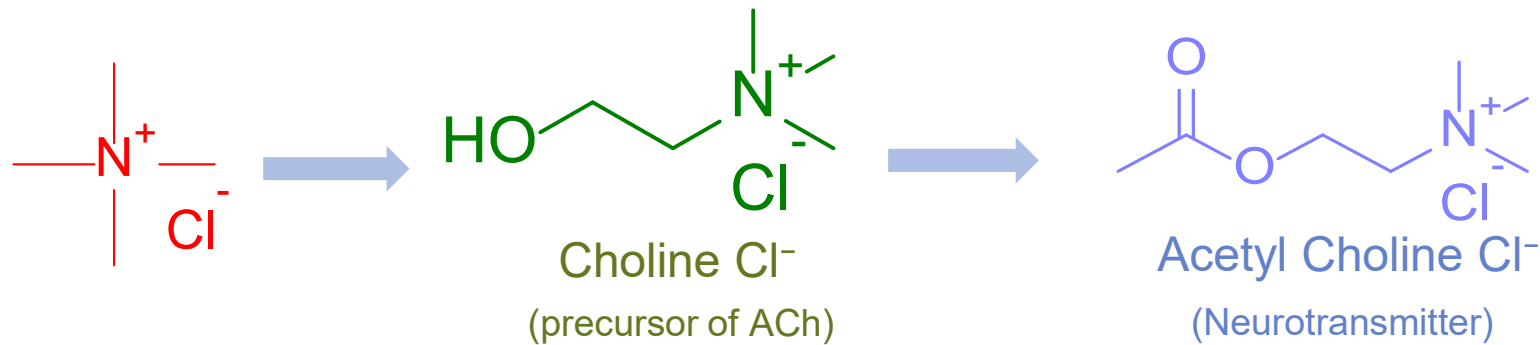
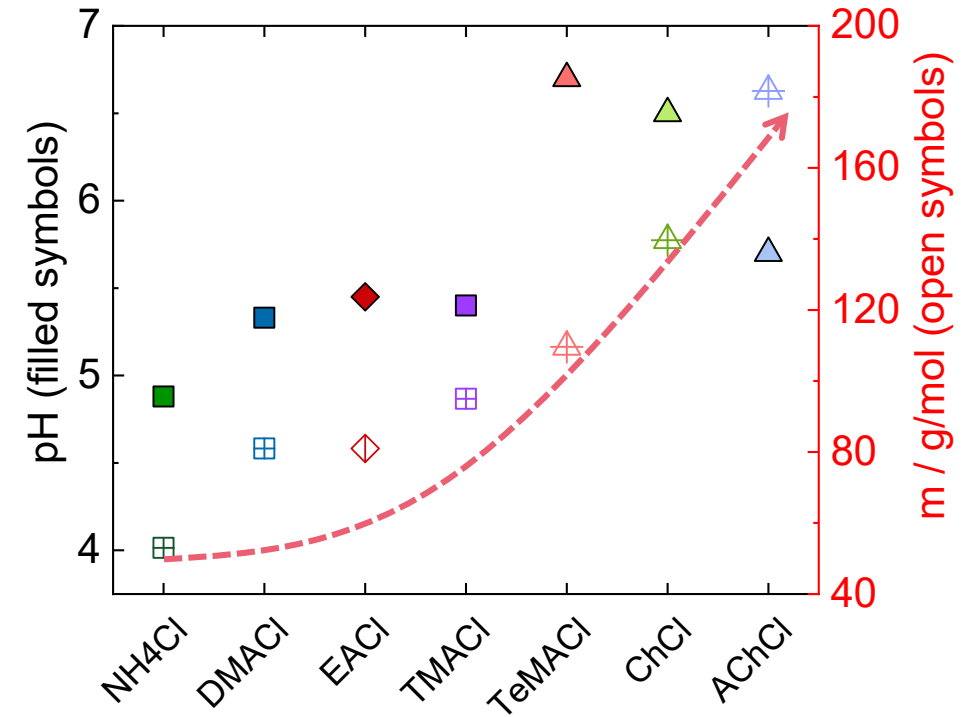
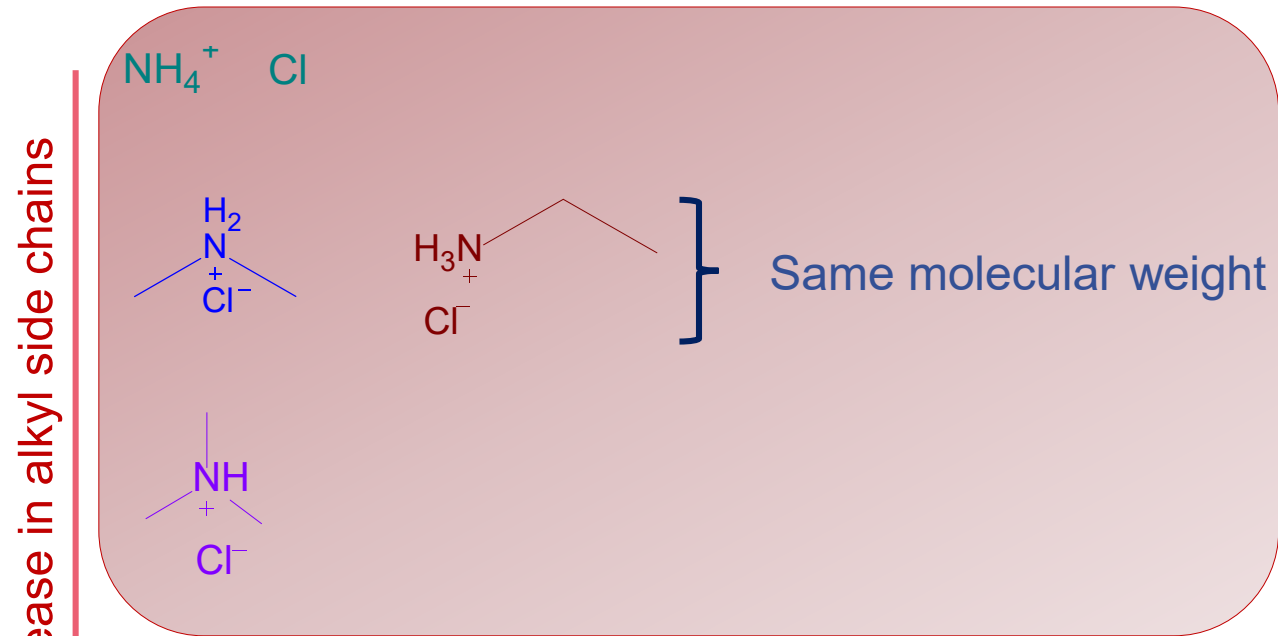
S. Iacopini, R. Rusconi, and R. Piazza, Eur. Phys. J. E, **19** (2006), 59–67

ΔS_T is measure for hydrophilicity,
which is typically described by $\log P$

D. Niether et al. PCCP, **20** (2018), 1012-1020

SYSTEMS

Overview of the studied ammonium salts





ONGOING STUDY ON AMMONIUM SALTS

Why ammonium salts?

Ammonium chloride (NH_4Cl) : alters synaptic transmission in neuronal networks and reduces synaptic vesicle release.

- Substituted ammonium salts with dimethyl (**DMACI**) or trimethyl (**TMACI**) or tetra (**TeMACI**) or ethyl (**EACI**) groups serves as a crucial intermediate in pharmaceutical synthesis to create drugs.

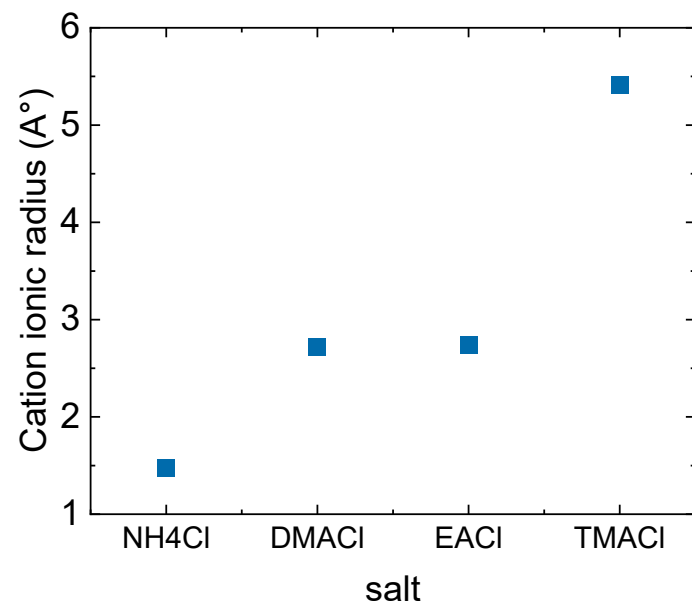
Biological relevant quaternary salts:

- **Acetylcholine chloride (ACh)**: neurotransmitter in PNS, directly involved in nerve signal transmission, muscle contraction, and memory formation.
- **Choline (Ch)**: precursor to acetylcholine. Biological functions including membrane integrity, cell signaling, and methyl group metabolism. Synthesis of phosphatidylcholine and sphingomyelin, which are critical components of cell membranes.

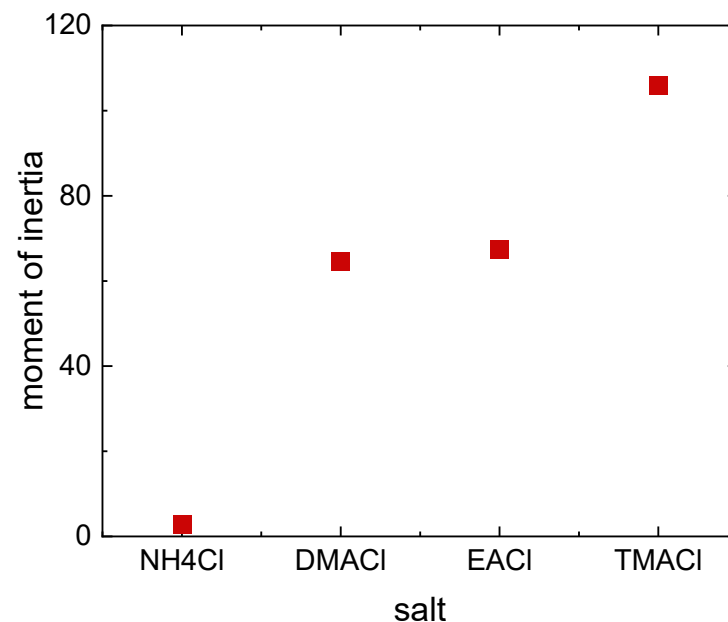
Understanding these salts through thermophoretic studies can provide valuable insights into hydration.

R. M. Lazarenko et al. *Sci Rep* **7** (2017), 5061, P. I. Naggy et al. *PCCP* **14** (2012), 849-847, S. Bindra et al. *RSC Adv.* **14**(2024), 27657-27696, S. Monti et al. *PCCP* **13** (2011), 6270-6279, P.E. Mason et al. *PCCP* **26** (2024), 3208, J. Morita et al. *Sci Rep* **6** (2016), 20995

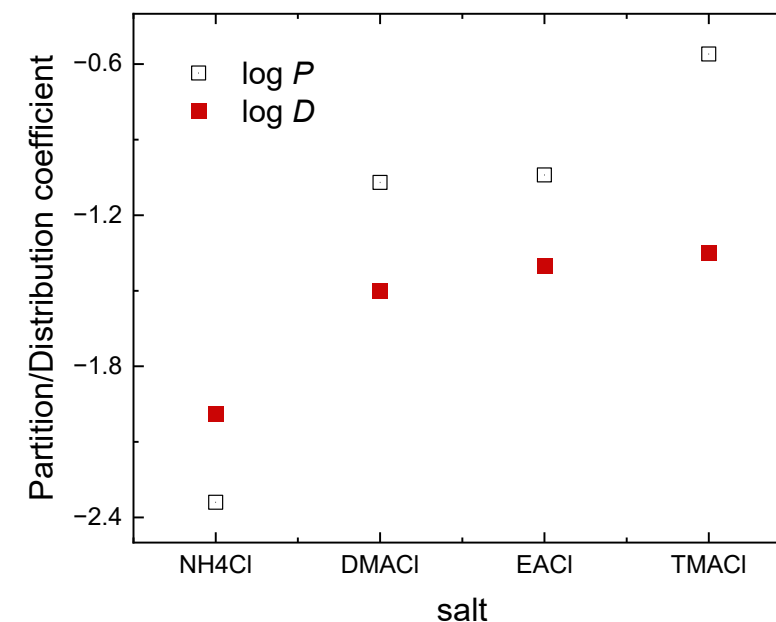
PROPERTIES OF THE STUDIED SALTS:



Literature values



Calculation using *Chem3D*



Calculation using *Marvin 16.5.2.0, ChemAxon*

Wang et al. *ACS Omega* **7** (2022), 33732-33748

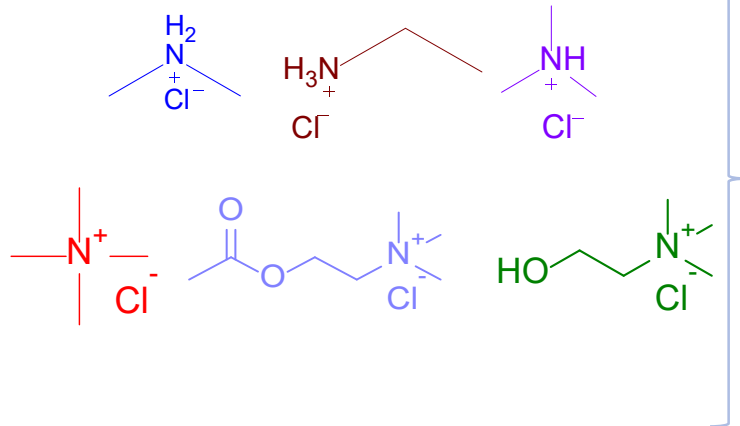
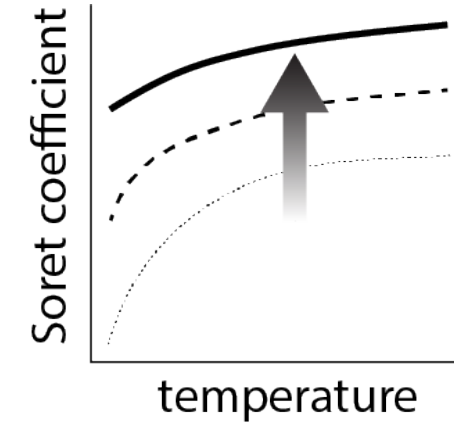
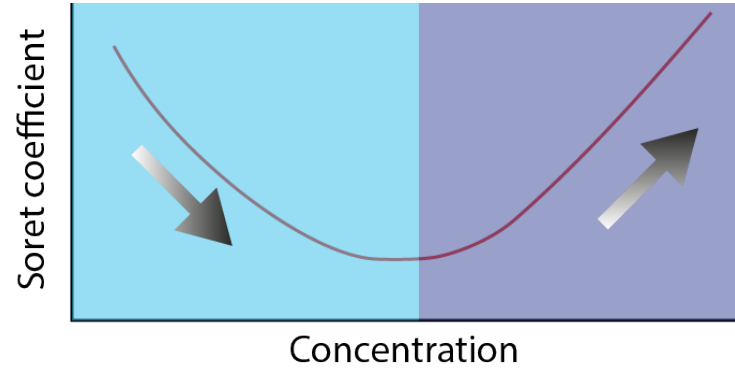
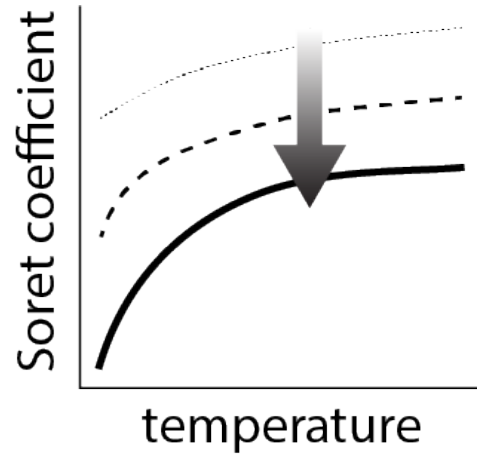
Zhao et al. *Sol. RRL*, **6** (2022), 2100923

R. H. Boyd et al. *J. Chem. Phys.* **51** (1969), 1470-1474

H. I. Kim et al. Dissertation (Ph.D.), California Institute of Technology (2008).

RESULTS

We performed temperature and concentration dependent measurements (1m-4m; 15-45°C)



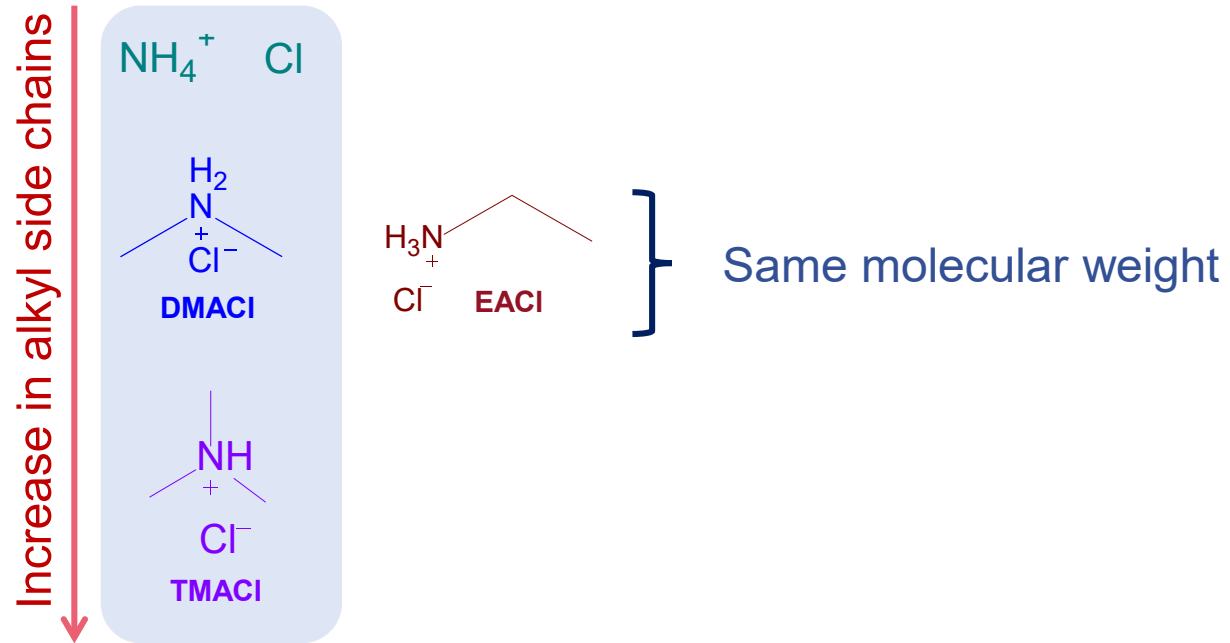
No minimum in the investigated range

Minimum at high temperatures around 1.5 m

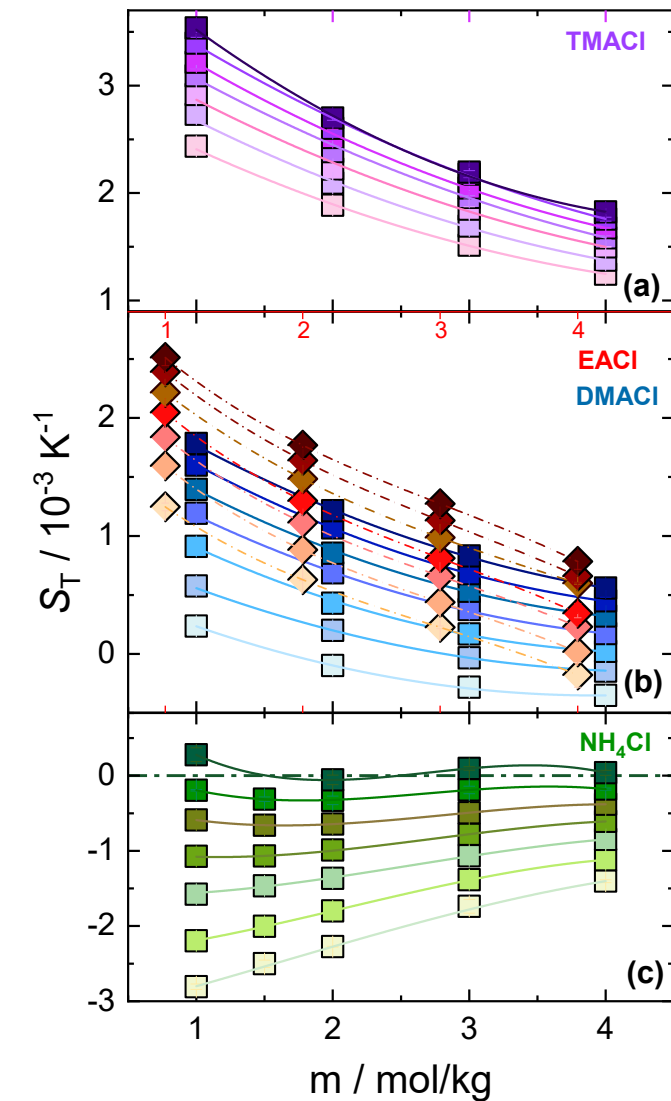


ALKYL-SUBSTITUTED AMMONIUM SALTS

Without quaternary salts



CONCENTRATION DEPENDENCE OF S_T



- S_T decreases with added salt concentration
- Majorly thermophobic behaviour

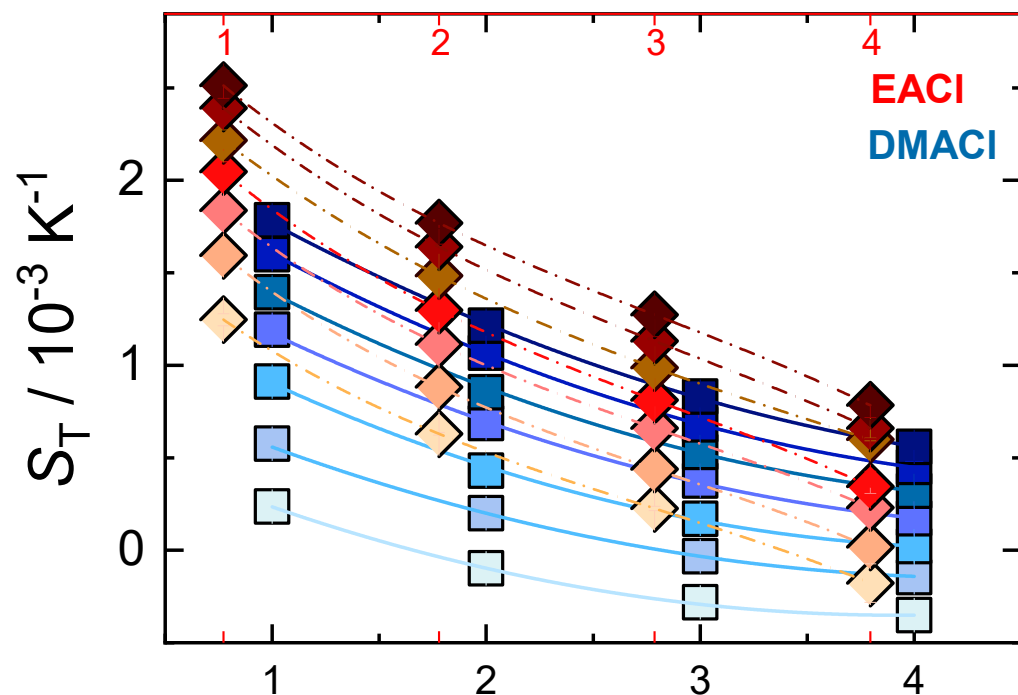
- S_T : EACI > DMACI

- Non-monotonous and negative S_T
- Thermophilic behaviour
- $T \geq 35^\circ\text{C} \rightarrow$ minimum ~ 1.5 m

S_T increases with increase in alkyl substitution:
 $\text{NH}_4\text{Cl} < \text{DMACI} < \text{EACI} < \text{TMACI}$

CONCENTRATION DEPENDENCE OF S_T

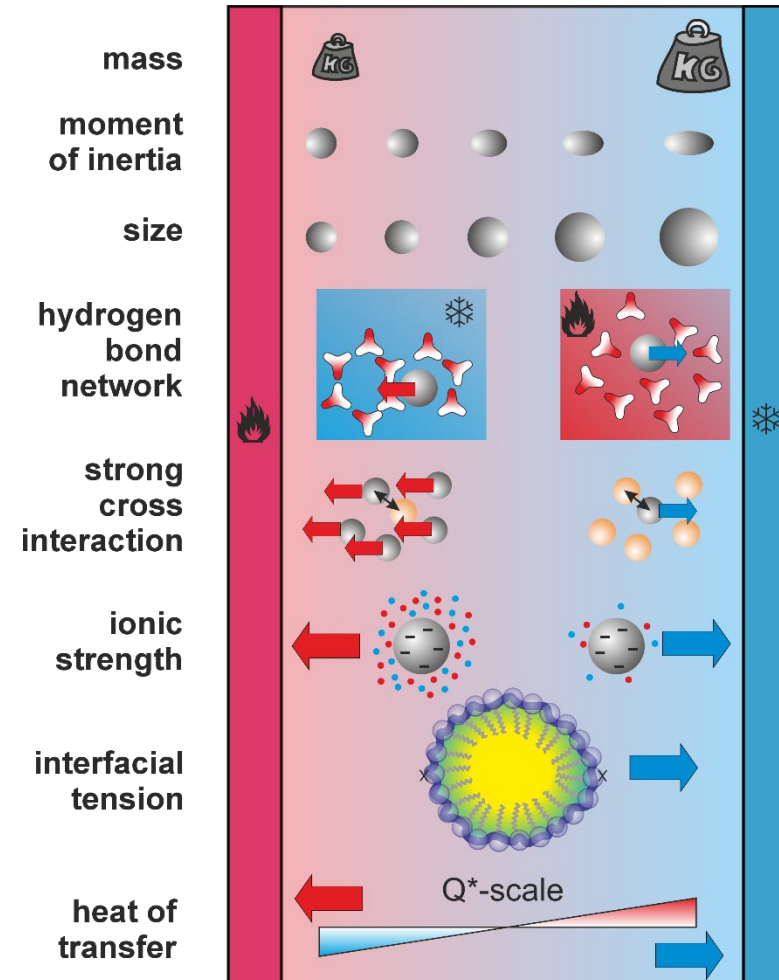
Moment of inertia : EACI and DMACI



Moment of inertia (I):
EACI (480) > DMACI (340)
EA (67.5) > DMA (64.5)

Hoang, H. and Galliero, G. *Eur. Phys. J. E* **45** (2022), 42

Gittus, O.R., and Bresme, F. *J. Chem. Phys.* **159** (2023), 114503

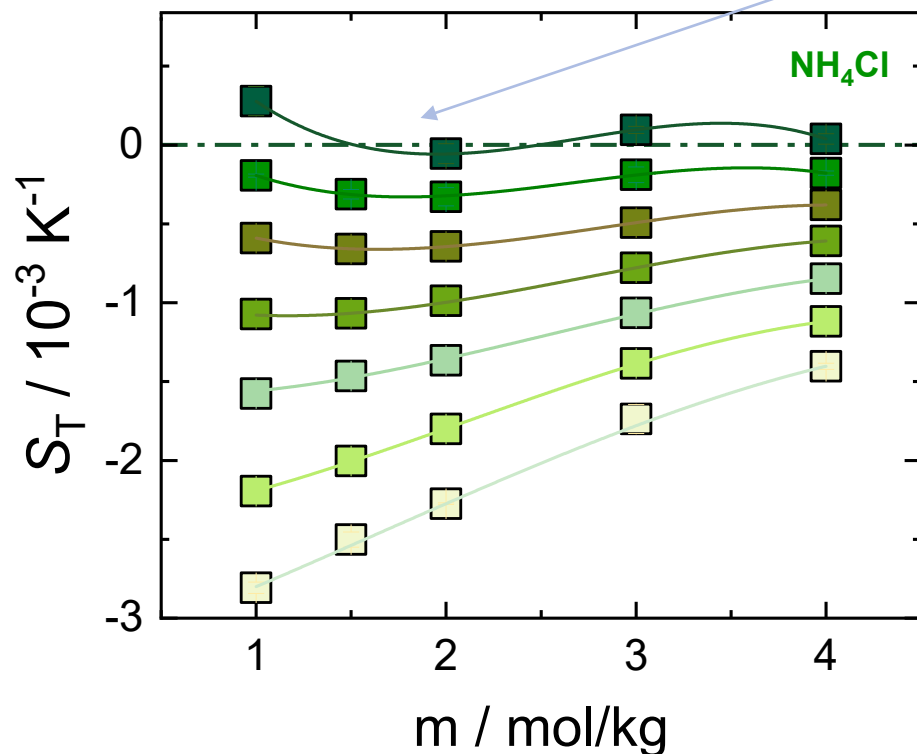


CONCENTRATION DEPENDENCE OF S_T

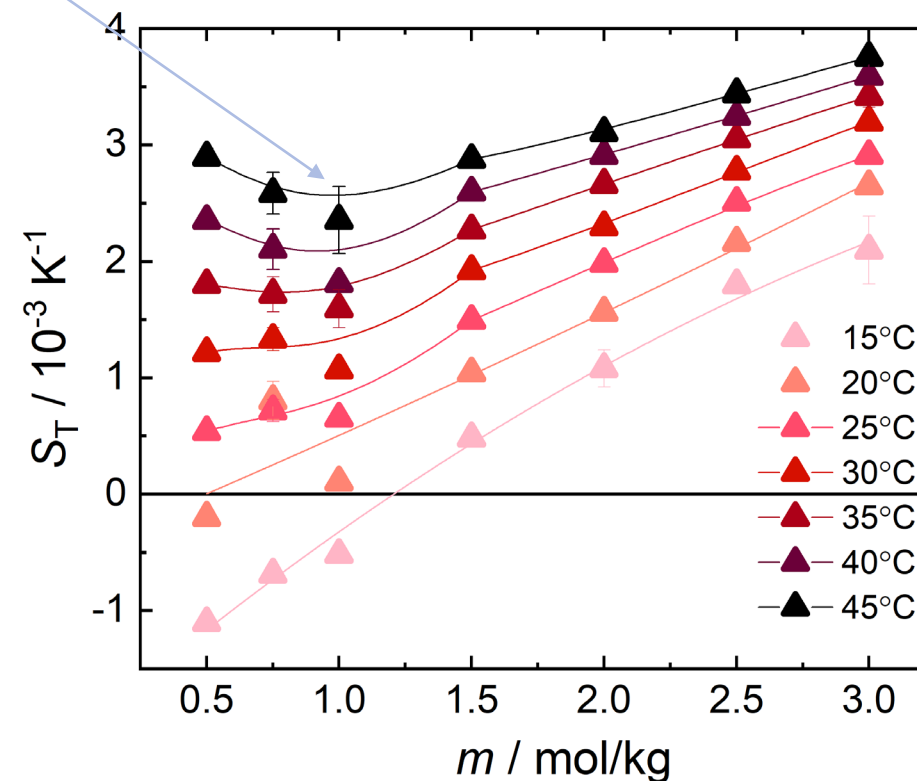
Minimum in S_T



NH_4Cl



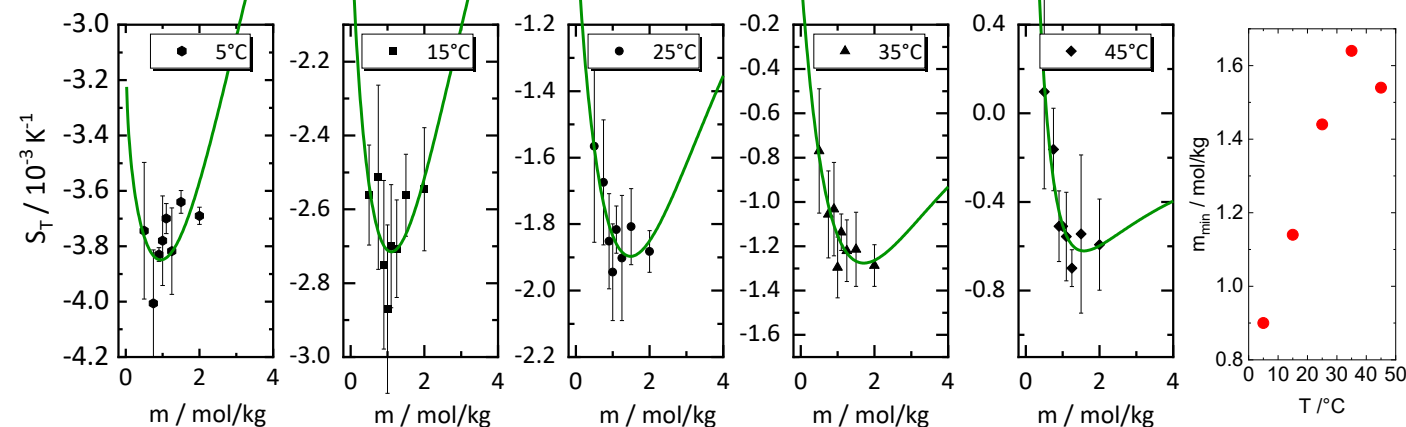
CsI



- Similar behavior with concentration!
- Weaker H-bond between salt and water
- $R_{\text{hs}} = 0.5\text{nm} (\text{NH}_4\text{Cl}) < 0.6\text{nm} (\text{CsI})$

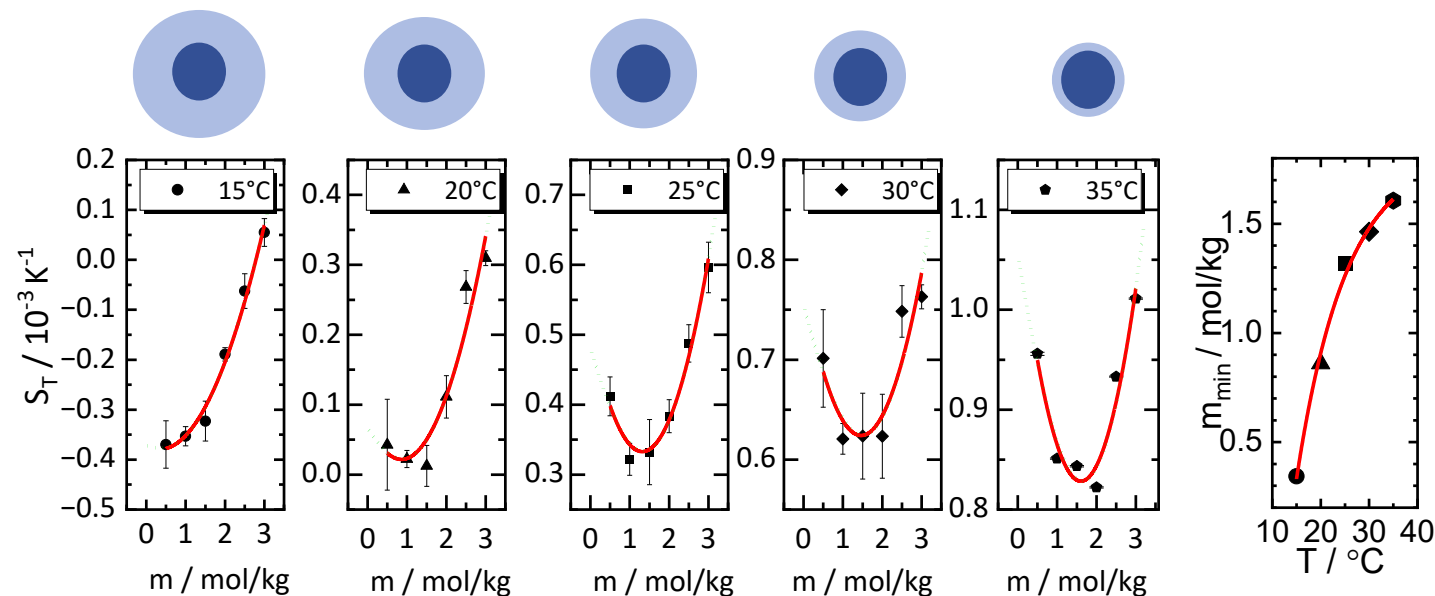
DOES THE MINIMUM MOVE WITH TEMPERATURE?

Minimum concentration varies with temperature



Lithium Chloride

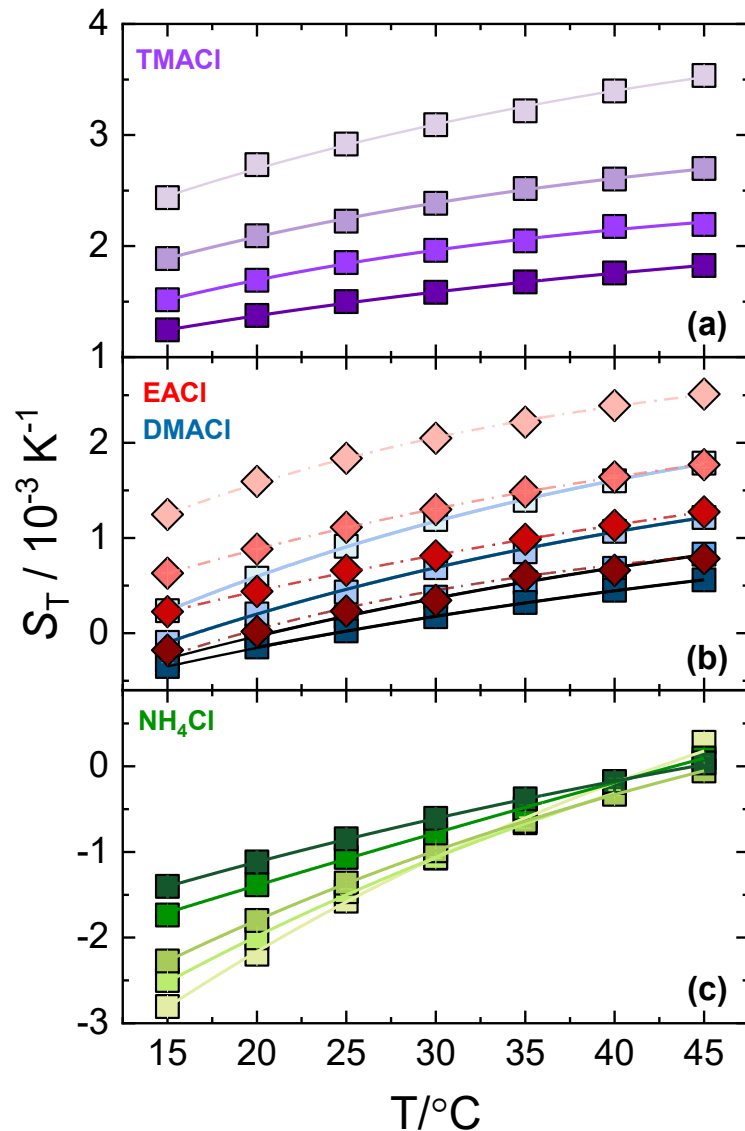
Lee et al. PCCP 26 (2024) 7830–7836.



Guanidinium Chloride

Rudani et al., J. Chem. Phys. **160** (2024) 214502

TEMPERATURE DEPENDENCE OF S_T



S_T increases with increase in temperature

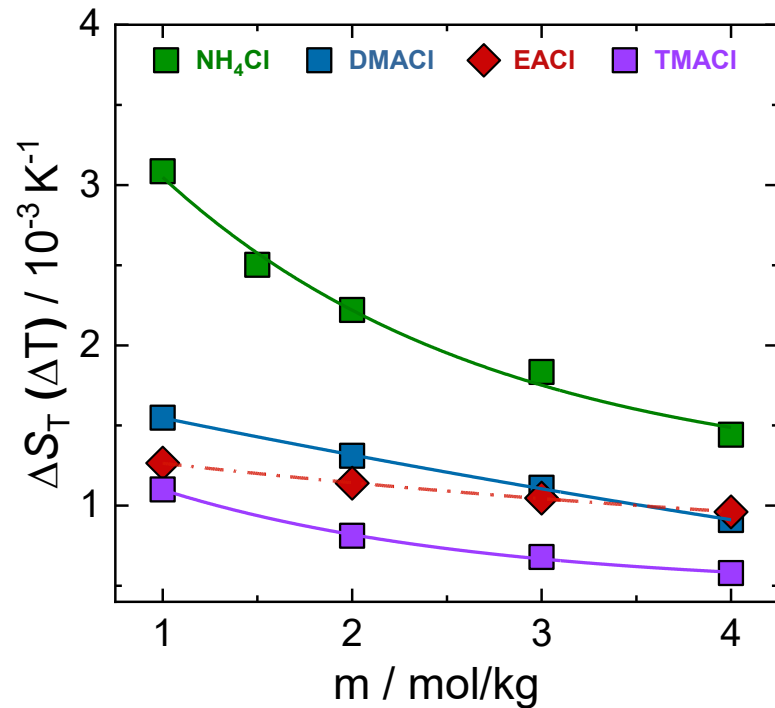
$$S_T(T) = S_T^\infty + A \exp\left(-\frac{T}{T_0}\right)$$

S. Iacopini, R. Rusconi, and R. Piazza, Eur. Phys. J. E, **19** (2006), 59–67

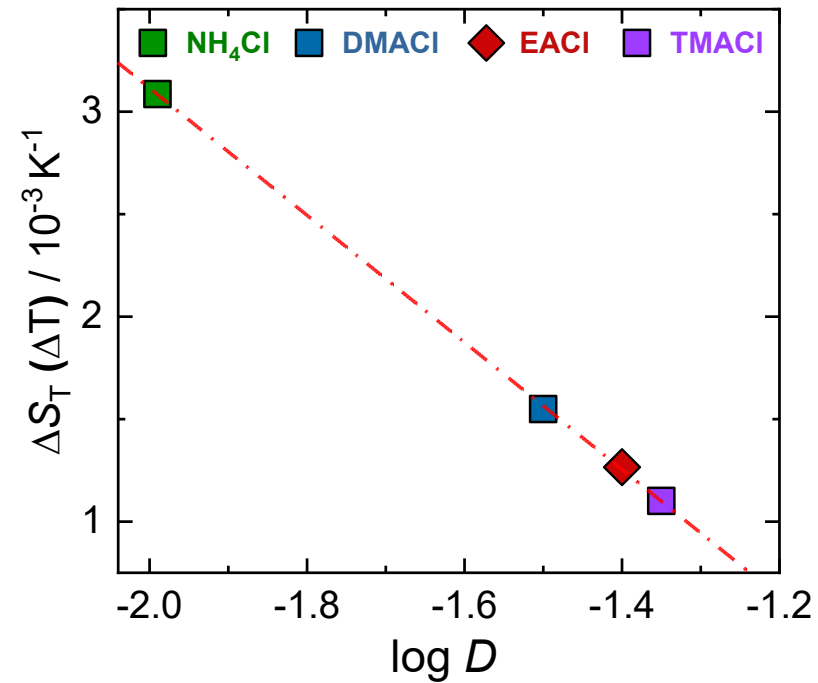
$$\Delta S_T = S_T(45^\circ\text{C}) - S_T(15^\circ\text{C})$$

TEMPERATURE SENSITIVITY OF S_T

Correlation with log P



$\Delta S_T(\Delta T)$ decreases with increase in concentration

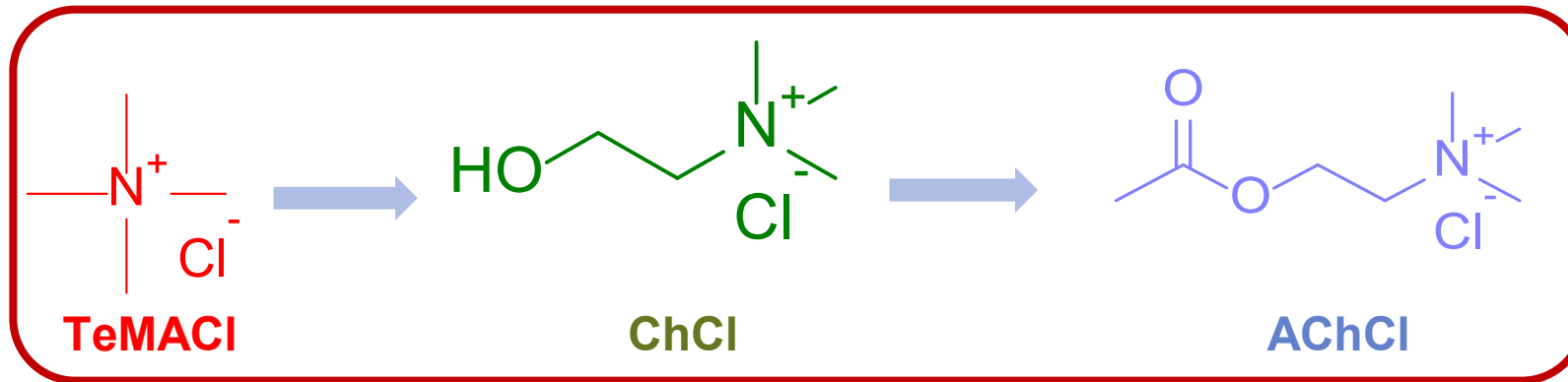


Temperature sensitivity ($\Delta S_T(\Delta T)$) decreases with increase in alkyl substitution or decrease in hydrophilicity

$\Delta S_T(\Delta T) : \text{NH}_4\text{Cl} > \text{DMACI} > \text{EACI} > \text{TMACI}$

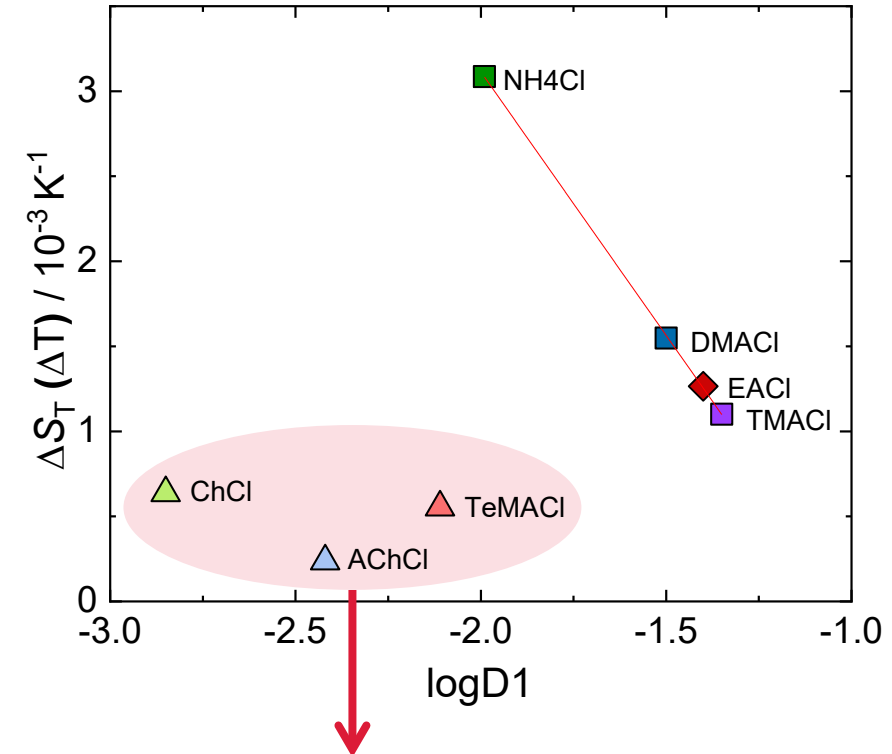
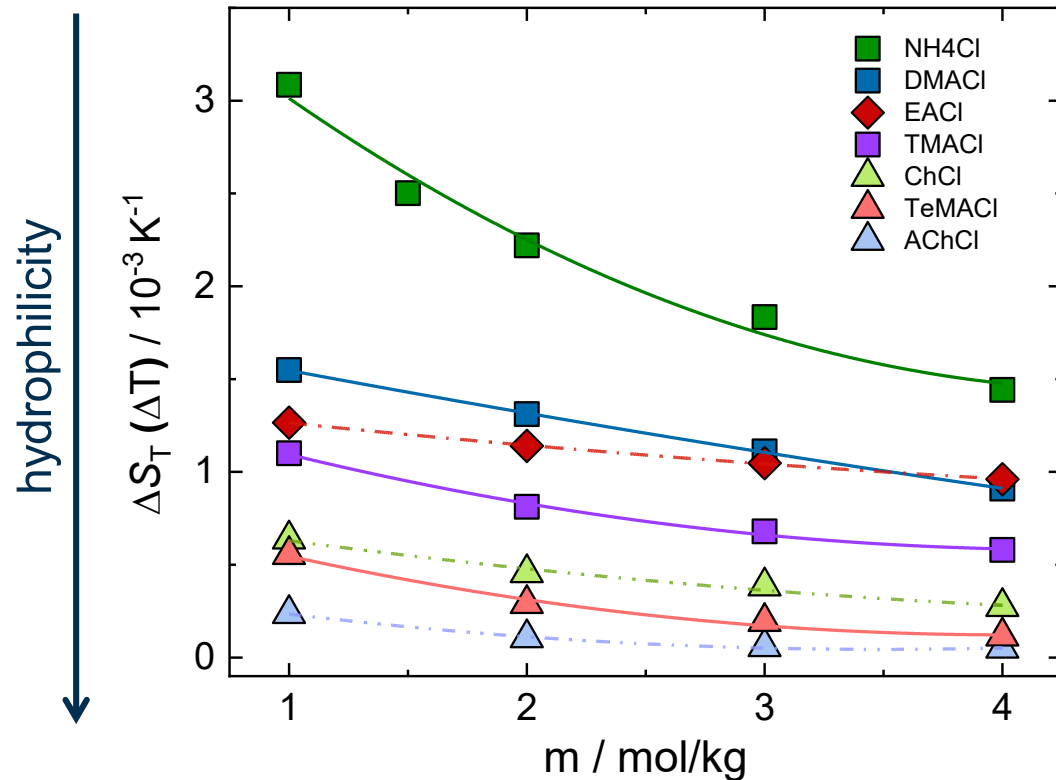
QUATERNARY AMMONIUM SALTS

With complex organic groups



TEMPERATURE SENSITIVITY OF S_T

Correlation with log P



Salts with large organic groups: Difficult to calculate log D

Expected hydrophilicity trend : **ChCl** > **TeMACI** > **AChCl**

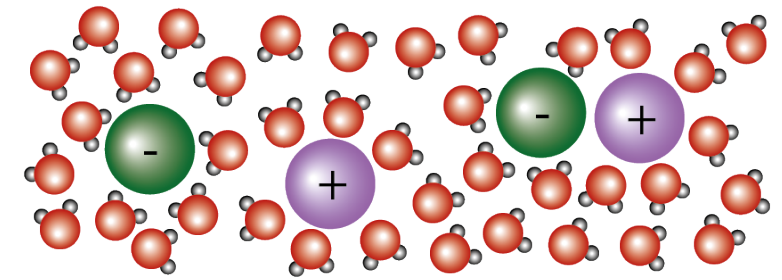
Support from simulations!!!

D. Niether et al. PCCP, **20** (2018), 1012-1020



TAKE HOME MESSAGE

Thermodiffuion of aqueous salt solutions is complex



- Only ammonium chloride shows thermophilic behavior and its S_T value increases with concentration. Other all primary, secondary and tertiary ammonium salts shows opposite trend to ammonium salts.
- Thermophoretic behavior of salts show major influence by alkyl substitution on the cation.
- $\Delta S_T(\Delta T)$ / hydrophilicity at a particular concentration decreases with increase in alkyl substitution: **NH₄Cl** > **DMACl** > **EACl** > **TMACl**
- For the complex quaternary salts with organic group, $\Delta S_T(\Delta T)$: **ChCl** > **TeMACl** > **AChCl**

FINISHED AND FUTURE PROJECTS

✓ Guanidinium salts:

[Rudani, B. A., Jakubowski, A., Kriegs, H., Wiegand, S. Deciphering the guanidinium cation: Insights into thermal diffusion. J. Chem. Phys. 2024,160,214502.]

✓ Minimum in S_T in different salt solutions:

[Rudani, B. A., Briels, W.J., Wiegand, S. Analyzing the concentration-dependent Soret coefficient minimum in salt solutions: an overview. PCCP., 2025,27, 4746-4755.]

✓ Influence of α -Helical Content on the Thermodiffusion of Apomyoglobin

[Rudani, B. A., Docter, S., Schott-Verdugo, S., Buitenhuis, J., Stadler, A.M., Gohlke, H., Wiegand, S. Influence of α -Helical Content on the Thermodiffusion of Apomyoglobin. Langmuir, 2025.]

➤ Thermodiffusion as a Probe of Hydrophilicity in Alkyl-Substituted Ammonium Salts

Manuscript under preparation for The European Physical Journal E (EPJE) in a topical issue of the IMT 16 conference

➤ Thermodiffusion of aqueous Quaternary Ammonia salts

Interpreting the results and writing a manuscript (collaboration Holger Gohlke, IBG 4)

➤ Chelating agents: Calcium-sodium EDTA (ITC+TDPRS measurements)

Experimental work ongoing

- Protein ligand binding

Myoglobin binds with ligand e.g. protoporphrin IX, sodium tetradecylsulfate

ACKNOWLEDGEMENT



Wim Briels



Simone
Wiegand



Peter Lang
(head IBI-4)



... more theory in progress

Thanks for your attention