

# Understanding Microscale Thermophoresis: Contributions by simple building blocks of proteins

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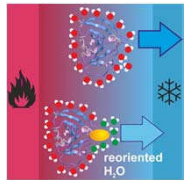
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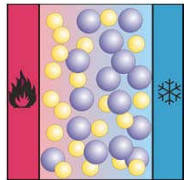
## Introduction [1]

Microscale Thermophoresis (MST) gained a lot of interest as analytical approach to monitor protein-ligand binding reactions. Since this method needs less sample compared to calorimetric methods it is therefore very useful for pharmaceutical applications.



Recent experiments for various amides and sugars showed a clear correlation of the temperature dependence of the Soret coefficient with the hydrophilicity, quantitatively described by the logarithm of the 1-octanol/water partition coefficient  $P$ . To check the empirical correlation between the temperature sensitivity of Soret coefficient as function of  $\log P$  we performed additional measurements of various alcohols.

## Thermophoresis



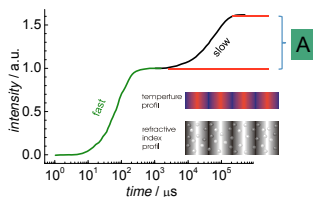
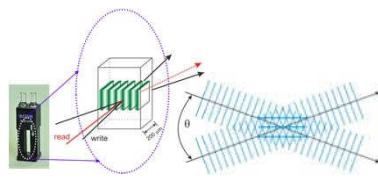
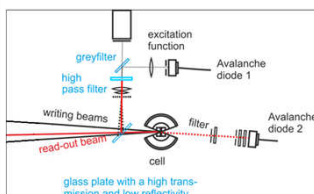
Flux  $\vec{j}$  along a temperature gradient  $\vec{\nabla}T$ :  
(1) Thermal diffusion  $D_T$  along a temperature gradient  $\vec{\nabla}T$   
(2) Fickian diffusion  $D$  along the induced concentration gradient  $\vec{\nabla}c$

$$\vec{j} = -D\vec{\nabla}c - c(1-c)D_T\vec{\nabla}T$$

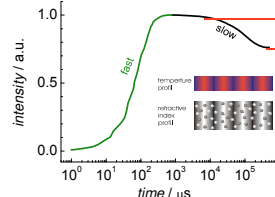
Steady state ( $\vec{j}=0$ ) defines the Soret coefficient  $S_T$ :

$$S_T \equiv \frac{D_T}{D} = -\frac{1}{c(1-c)} \frac{\Delta c}{\Delta T}$$

## IR-TDFRS Setup [2]

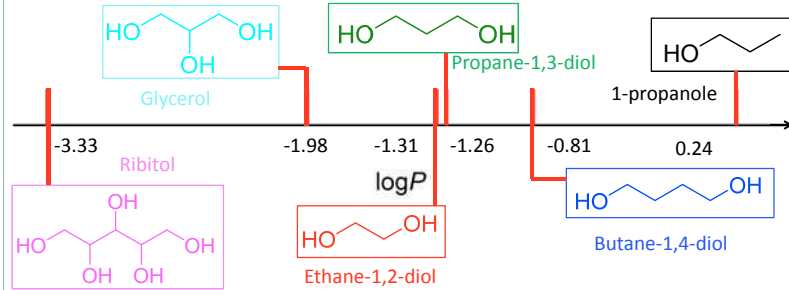


$$\zeta_{\text{het}} = \frac{(1 - e^{-t/\tau_{\text{th}}}) - A(1 - e^{-t/\tau})}{\text{temperature}}$$

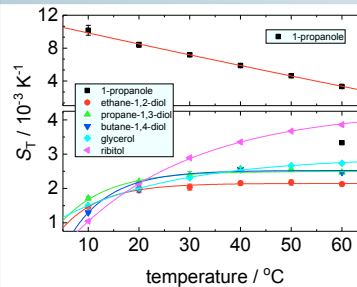


$$A = \frac{(\partial n / \partial c)_{p,T} D_T}{(\partial n / \partial T)_{p,c} D} c(1-c)$$

## System



## Results



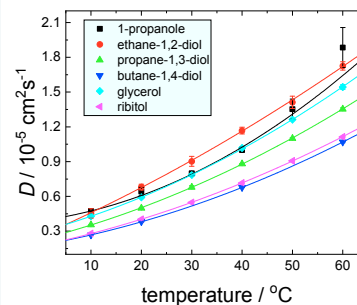
$S_T(T)$  of 1-propanol can be described with the empirical equation:

$$S_T(T) = S_T^\infty + S_T^0 \exp\left(\frac{-T}{T_0}\right)$$

$S_T(T)$  of the other polyhydric alcohols follows an empirical equation suggested by Piazza<sup>[3]</sup>

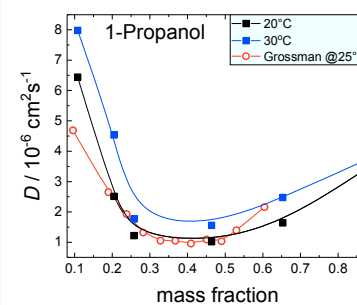
$$S_T(T) = S_T^\infty \left[1 - \exp\left(\frac{T^* - T}{T_0}\right)\right]$$

With increasing mass and number of hydroxy groups  $\Delta S_T(T)$  increases.



With increasing temperature diffusion increases, which is expected because the viscosity of solution decreases.

Diffusion coefficient decreases with increasing chain length and number of hydroxy groups.

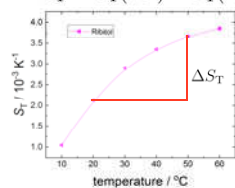


Around a mass fraction of 0.35 the diffusion coefficient shows a minimum. Only at very low concentrations single molecules diffusion is observed.

Grossmann and Ebert<sup>[4]</sup> explained the diffusion minimum by the formation of clusters with eight 1-propanol molecules and 40 water molecules in the hydration layer of the cluster.

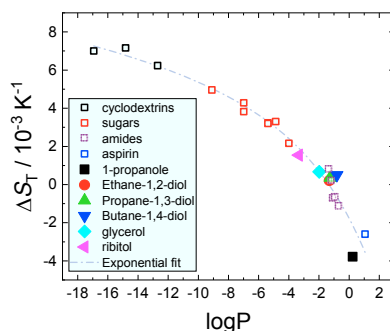
## Conclusion

$$\Delta S_T = S_T(50^\circ) - S_T(20^\circ)$$



Hydrophilic compound:  $\log P < 0$

$$\log P = \log\left(\frac{[\text{solute}]_{\text{octanol}}}{[\text{solute}]_{\text{water}}}\right)$$



- Hydrophilic alcohols with negative  $\log P$  follow the empirical correlation.
- Measurements of 1-propanol with a positive  $\log P$  are difficult due to formation of aggregates.

## References

- [1] D. Niether, H. Kriegs, J. K. G. Dhont, and S. Wiegand. Peptide model systems: Correlation between thermophilicity and hydrophilicity. *J. Chem. Phys.* **2018**, 149, 044506
- [2] S. Wiegand, H. Ning, and H. Kriegs. Thermal Diffusion Forced Rayleigh Scattering Setup Optimized for Aqueous Mixtures. *J. Phys. Chem. B* **2007**, 111, 14169-14174
- [3] S. S. Iacopin and R. Piazza. Thermophoresis in protein solutions. *Europhys. Lett.*, **63**, **2003**, 247-253
- [4] G. H. Grossmann and K. H. Ebert. Formation of clusters in 1-propanol-water-mixtures. *Berichte Der Bunsen-Gesellschaft-Physical Chemistry Chemical Physics*, **85**, **1981**, 1026-1029.