Understanding Microscale Thermophoresis: Contributions by simple building blocks of proteins

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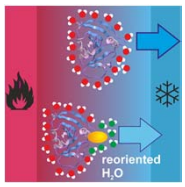
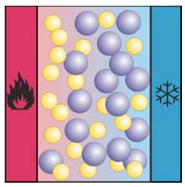
Introduction [1]

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



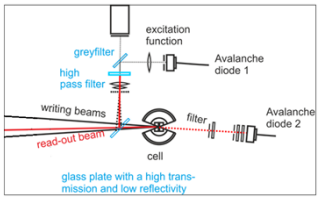
Flux $\vec{j}$ along a temperature gradient $\vec{\nabla}T$:
(1) Thermal diffusion D_T along a temperature gradient $\vec{\nabla}T$
(2) Fickian diffusion D along the induced concentration gradient $\vec{\nabla}c$

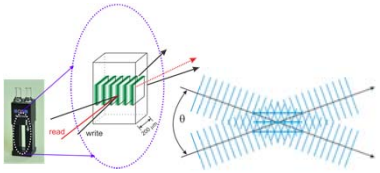
$$\vec{j} = -D\vec{\nabla}c - c(1-c)D_T\vec{\nabla}T$$

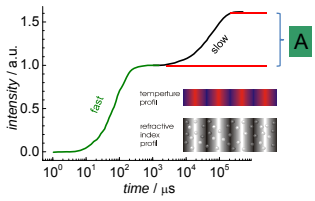
Steady state ($\vec{j}$=0) defines the Soret coefficient S_T:

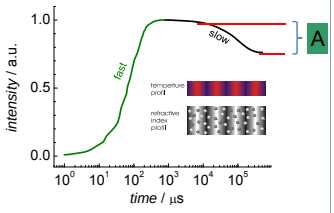
$$S_T \equiv \frac{D_T}{D} = -\frac{1}{c(1-c)}\frac{\Delta c}{\Delta T}$$

IR-TDFRS Setup [2]





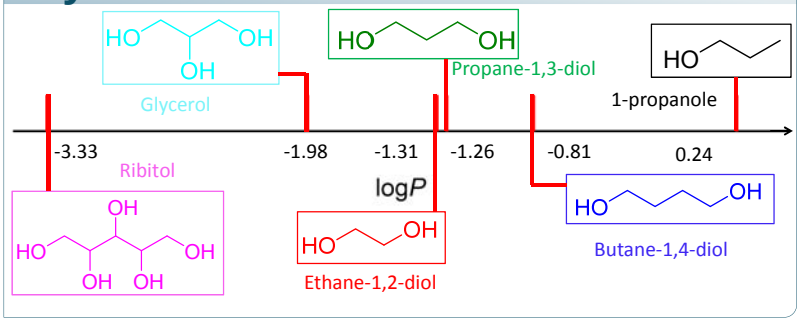




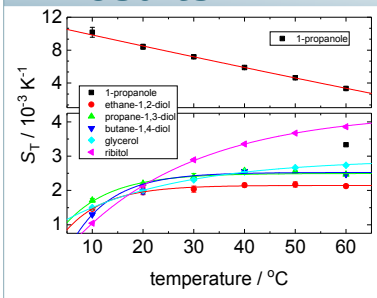
$$\varsigma_{het} = \frac{\left(1-e^{-t/\tau_{th}}\right)}{\text{temperature}} - A\left(1-e^{-t/\tau}\right)$$

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

System



Results



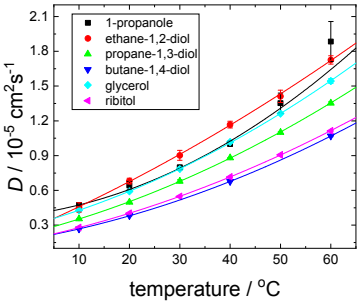
S_T(T) of 1-propanol can be described with the empirical equation:

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

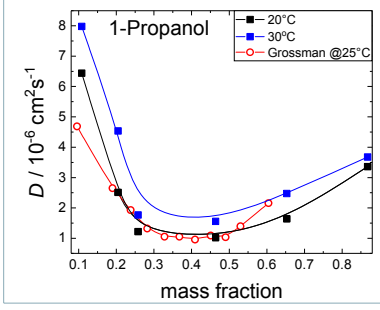
S_T(T) of the other polyhydric alcohols follows an empirical equation suggested by Piazza[3]

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

With increasing mass and number of hydroxy groups ΔS_T(T) increases.



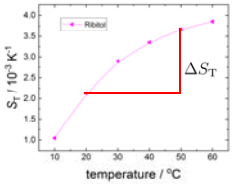
With increasing temperature diffusion increases, which is expected because the viscosity of solution decreases.
Diffusion coefficient decreases with increasing chain length and number of hydroxy groups.

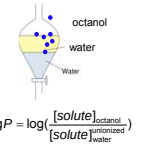


Around a mass fraction of 0.35 the diffusion coefficient shows a minimum. Only at very low concentrations single molecules diffusion is observed.
Grossmann and Ebert[4] explained the diffusion minimum by the formation of clusters with eight 1-propanol molecules and 40 water molecules in the hydration layer of the cluster.

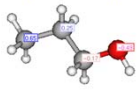
Conclusion

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

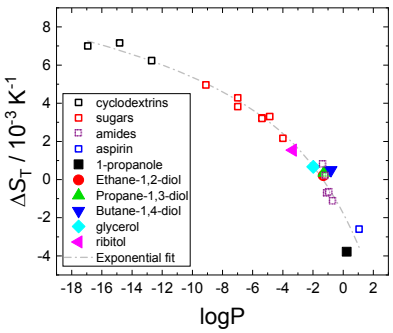




Hydrophilic compound: log*P* < 0



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



- 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

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[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.