Die unterschätzte Rolle des Wassers bei biologischen Prozessen – der THz Tanz des Wassers

Prof. Dr. Martina Havenith

Physikalische Chemie II, Ruhr-Universität Bochum

"Why is water the unique fluid in which life occurs? What is the role of water in the myriad of processes – from catalysis to molecular recognition- that make up metabolism in the cell ?" has been named as one of the top future challenges in chemistry.

Terahertz (THz) spectroscopy is a new tool to probe subtle changes in the hydration dynamics. THz spectroscopy gives a direct access to the collective, (sub-)psec hydrogen bond dynamics, the fingerprint of the water dynamics. [1,2]

Molecular understanding of biological recognition processes is surely a major prerequisite for future drug design. Protein-ligand binding is favorable when the change in free energy $\Delta G=\Delta H-T\Delta S$ is negative. *Up to now, calorimetric measurements are all based on heat transfer and are thus inherently* ***slow*** (with relaxation times of typically 1 - 100s, depending on the system and method applied) *and restricted to* ***equilibrium conditions***, so only either the bound or the unbound state – or stationary mixtures of both (determined by the equilibrium constant K) are characterized in terms of ΔG and ΔH. We propose that the THz spectrum of hydration water around solutes can be correlated with changes in entropy $\Delta S(t)$. In a proof of principle experiment on solvated alcohols we could show that this proposed correlation indeed holds [4]. THz calorimetry maps the solvent reorganization and will allow to record calorimetric properties far beyond equilibrium conditions.

Traditional bulk calorimetry yields enthalpy and entropy values as *ensemble averages* that *include* the contributions of the solute and solvent, as well as coupled solute-solvent interactions. Our scientific vision is to introduce ultrafast "THz-Calorimetry" , i.e. to correlate the THz spectrum with entropy changes of the solvent under *non-equilibrium* conditions with envisioned time resolutions of nano seconds. I will present linear and non-linear THz experiments to probe the change in hydrogen network dynamics in real time with ns or even fs time resolution [3]. Applications included enzymatic reactions, protein folding or charge transfer in electrochemical cells.

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[3] H. Wirtz, S. Schäfer, C. M. Hoberg, K.M. Reid, D. Leitner, M. Havenith,. Biochemistry **2018**, 57 (26), 3650–3657

[4] F. Böhm, G. Schwaab, M. Havenith, Angew. Chem. Int. Ed. **2017**, *56,* 9981–9985