

# The stressed solvent: THz calorimetry probing the solvent in action

Martina Havenith

*Department of Physical Chemistry II, Ruhr-University Bochum, 44780 Bochum, Germany*

*martina.havenith@rub.de*

Key concepts of characterizing solvent thermodynamics are firmly established in the sense of global properties of homogeneous bulk systems under thermodynamic equilibrium conditions. However, it is intriguing to see how local solvation phenomena in nano-heterogeneous environments determine the reactivity and selectivity in solution, receptors, and enzymes, and even the function of electrocatalysts. While macroscopic solvation can be tracked by traditional calorimetry approaches, local solvation and processes in non-equilibrium cannot. Terahertz (THz) spectroscopy probes the intermolecular interaction between water molecules provides an opportunity to determine the contribution of the solvent to the total free energy of a reaction. Systematic spectroscopic studies revealed that the THz spectrum fingerprints any changes with respect to hydrogen bond strength, tetrahedrality, dynamics, which are all of major importance to rationalize and predict the outcome of a reaction. While the individual changes might be small, the large amount of solvent involved makes this contribution a major driving force for fundamental reactions.

We present here a spectroscopic approach, which gives direct access to the two main contributions at : Using THz spectroscopy to probe the frequency range of the intermolecular stretch ( $150\text{-}200\text{ cm}^{-1}$ ) and the hindered rotations ( $450\text{-}600\text{ cm}^{-1}$ ), the local contributions due to cavity formation and hydrophilic interactions can be traced back [1]. This allows to deduce separately the hydrophobic (i.e. cavity formation) and hydrophilic (enthalpic) contributions to thermodynamics, as shown for hydrated alcohols as a case study. THz calorimetry have also uncovered when local mutation serves as a game changer for protein dynamics [2]. These measurements allow conductivity measurements in micelles, and probe hydration within supramolecular nanocages, or even in the vicinity of an electrified interface. Local “solvation hotspots”, such as the so-called liquid liquid phase separation membraneless compartments in a cell are suspected to trigger neurotoxic protein aggregation. There are indications that the phase separation is entropy driven, with the solvent playing a decisive role.

In the future, time resolved THz probe experiments will allow to dissect hydration contributions in inhomogeneous mixtures and under non-equilibrium conditions. Typically, especially for biological reactions, there is a subtle balance between a favourable enthalpy and an unfavourable entropic term, which almost cancel, thus allowing to fine tune reactions based on THz screening.

## References

1. S. Pezzotti, F. Sebastiani, E.P. van Dam, S. Ramos, V. Conti Nibali, G. Schwaab, M. Havenith, *Angew. Chem. Int. Ed.*, e202203893 (2022)
2. E. Adams, S. Pezzotti, J. Ahlers, M. Rüttermann, M. Levin, A. Goldenzweig, Y. Peleg, S. Fleischmann, I. Sagi, M. Havenith, *JACS Au* 1, 1076–1085 (2021)