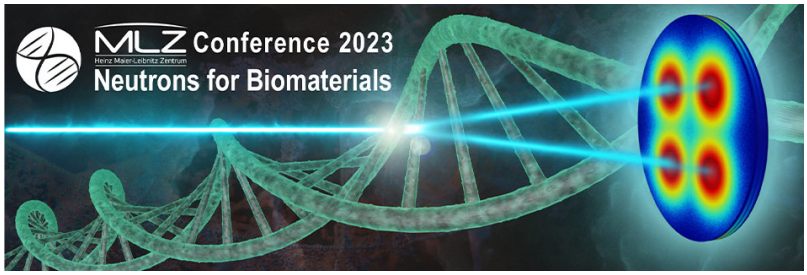

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Complementary approaches to obtaining thermodynamic parameters from protein ligand systems: challenges and opportunities and a case for neutrons

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Protein ligand interactions play an important role in biology and in order to influence this process in a targeted way increased understanding is necessary. The binding process is heavily influenced by its thermodynamic parameters. While the overall change in enthalpy can be easily measured using isothermal titration calorimetry (ITC) and the change in entropy and Gibbs free enthalpy then calculated this does not provide information about the individual components of these contributions. This presentation aims to discuss how the different components that are responsible for the total change in entropy can be isolated using different complementary techniques, as well as what the challenges faced for each method are and how they might be overcome or mitigated.
All discussions will be based on the system of streptavidin and biotin which will be used as a model system. Upon protein ligand binding, changes of conformational entropy occur in protein and hydration layer, as well as internal dynamics. In this study the binding of biotin to the tetramer streptavidin was investigated using quasi-elastic neutron scattering (QENS), as well as Thermal Diffusion Forced Rayleigh Scattering (TDFRS) and ITC. This specific interaction is enthalpy driven, with an opposing entropic component. An experimental investigation of the components of the entropy change, specifically the change in conformational entropy, indicates a change in conformational entropy strongly opposed to the binding. The adverse change in entropy therefore has to be compensated, with the strongest candidate being a supportive change in the entropy of the surrounding hydration layer. It is also of note that while the change in conformational entropy upon saturation with biotin is on the same order of magnitude as that of protein folding, no significant structural changes take place during the binding process.

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