



Investigating Protein Stabilization/Denaturation in the Presence of Ions and Osmolytes

by Prof. Paul Cremer

Department of Chemistry,
Texas A&M University

Abstract:

The presence of salts and osmolytes in aqueous solution has a profound effect on processes ranging from enzyme turnover rates and protein folding to colloidal assembly and macromolecular precipitation. The basic properties of these solutes were first demonstrated at the end of the nineteenth century. For example, urea is known to be a powerful protein denaturant, while ammonium sulfate is used as a common precipitant in protein crystallization studies. Unfortunately, a molecular level understanding of how these species operate is still lacking in the twenty-first century. To help remedy this problem, we have employed a combination of microfluidic and spectroscopic techniques to investigate the role that salts and osmolytes play in both hydrophobic collapse and protein aggregation. This work indicates that Hofmeister ions, especially anions, affect phase transitions in solutions of biomacromolecules through direct interactions with the polymer molecules and their first hydration shells. Moreover, indirect effects on macromolecular behavior through changes in bulk water structure are minimal. By contrast, common denaturants such as urea appear to influence the folding and unfolding of proteins via indirect effects that probably do involve changes in water structure.

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Room PH 3344

Contact:

Prof. Roland Netz, netz@ph.tum.de, phone: 089 289-12394