The Physics of Protein Self-Assembly:
Colloidal Interaction Models of Protein Phase Behavior

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Protein self-assembly processes are of interest in medicine, pharmaceutical industry and food engineering. They are, e.g., relevant in the context of drug formulation and diseases, such as cataract formation and diabetes, as well as food gels, like yoghurt and cheese. Self-association processes of proteins can lead to condensed phases which might be ordered, such as crystals, or amorphous, such as fibers or gels. Some phases, such as amyloid fibrils, are directly related to diseases. Despite their different morphologies, the formation of all these self-assembled structures is driven by similar thermodynamic and kinetic factors governed by the same underlying set of protein interactions.

In this talk, I will present some of our recent contributions examining the phase behavior and interactions of protein solutions in the presence of sodium chloride as well as cosolvents, such as glycerol and guanidine salt [1-3]. We experimentally determined the metastable gas-liquid binodals, the crystallization boundary, and the second virial coefficient of lysozyme solutions, using optical microscopy and light scattering, respectively.

The experimental phase diagrams are qualitatively compared to those of coarse-grained colloidal models, namely square-well and patchy interactions [1]. For a number of different solution conditions, we find that if the temperature axis of gas-liquid binodals is scaled by the second virial coefficient as an effective temperature, the binodals collapse onto a master curve and closely follow those of short-ranged square-well fluids. This finding suggests that the extended law of corresponding states (ELCS), as proposed by Noro and Frenkel for simple fluids, also holds for the complex interactions governing protein phase behavior [2]. This is an interesting finding which, in addition, can be exploited to devise a new approach to estimate the second virial coefficient based simple lab experiments, namely cloud-point temperature measurements [3].

[1]   F. Platten et al., *J. Chem. Phys.* **142**, 174905 (2015).
[2]   J. Hansen et al., *Phys. Chem. Chem. Phys.* **18**, 10270-10280 (2016).
[3]   F. Platten et al., *J. Phys. Chem. Lett.* **7**, 4008-4014 (2016).