Phase Behaviour of Lysozyme Solutions

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Proteins are typically of nanometric size and anisotropic shape. Amino acid groups, and hydrophilic and hydrophobic subunits are the origin of charge patterns and distributions of hydrophobic patches on their surfaces, giving rise to complex protein interactions. In a first

attempt to apply colloid methods to protein solutions, the isotropic Derjaguin-Landau-Verwey-Overbeek pair potential was used to predict the phase behaviour. In other work [1,2], the effect of the anisotropic interactions was modeled by a simple square-well potential, disregarding the electrostatic interactions.

In our work, we use a patchy interaction model which includes the electrostatic repulsion and the anisotropic attraction. The latter is accounted for by an angularmodulated pair potential of Yukawa-type. Second-order thermodynamic perturbation theory base on a hard-sphere reference system is used to calculate the equilibrium phase diagram.





Our patchy model describes the gas-liquid phase coexistence curves overall quite well (see left figure). In particular, it captures the influence of added salt on the stability of the fluid phase. See here the calculated binodals in the figure on the right-hand side. The range of attraction predicted in our calculations is in good agreement with experimental results by Israe-lachvili and Pashley [Nature **300**, 341 (1982)]. This strongly suggests that the attractive interactions caused by hydrophobic patches on the protein surface dominate the phase behaviour in lysozyme solutions. The good agreement between the calculated and experimental binodal supports the assumption by Hoskins et al. [J. Chem. Soc., Faraday Trans. **92**, 4515 (1996)] that the asymmetric distribution of surface charges becomes non-influential for pH-values that are 2-3units separated from the isoelectric point. As a crucial test of our model, we have calculated the fluid-solid coexistence curve, using interaction parameters obtained from the experimental data at the gas-liquid critical point. We find reasonable good agreement between the experimental curve and our theoretical prediction.

[1] C. Gögelein, "*Phase Behaviour of proteins and colloid-polymer mixtures*", Ph.D. thesis, Heinrich-Heine-Universität Düsseldorf, November 2008.

[2] C. Gögelein, G. Nägele, R. Tuinier, T. Gibaud, A. Stradner, and P. Schurtenberger, "*A simple patchy colloidal model for the phase behaviour of lysozyme dispersions*", J. Chem. Phys. **129**, 085102 (2008).