Charge-Driven Assembly of Proteins

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The handling and manipulation of proteins poses several interesting challenges. Remarkably, protein crystallization, despite being the dominating tool in structural biology, is still more art than science. Other forms of protein assembly are equally important, but follow a different pathway, which may lead to, e.g., gelation. In order to shed light on the underlying mechanisms of aggregation, the use of charges and the tailoring of the electrostatic interactions of proteins turn out to be extremely versatile. Multivalent counterions have been found to induce a rich phase behavior of protein solutions, including a reentrant condensation and a metastable closed-loop liquid-liquid phase separation (LLPS) [1]. The LLPS can be used to optimize conditions for protein crystallization, with the interface between the phases of different density playing a key role [2,3]. Different crystallization processes can be identified throughout the phase diagram, leading to different crystal morphologies [1,4]. Interestingly, high-resolution crystal structures show that trivalent ions act as ion-bridges between two proteins in the crystal [4]. Crystallization close to the first transition seems to follow the classical one-step nucleation process directly from a omogeneous solution. Under other conditions around the LLPS, crystallization rather follows a two-step nucleation process with an intermediate precursor state. Protein clusters seem to play an important role for the nucleation [5], although possibly different from what is naively expected. Evidence for the formation of protein clusters upon addition of multivalent ions is provided by both small angle scattering and dynamic light scattering [5,6,7]. Finally, we will discuss opportunities of following the different types of aggregation phenomena and their associated kinetics in situ by real time scattering experiments 7].

[1] F. Zhang et al., Soft Matter 8 (2012) 1313-1316
F. Zhang et al., Phys. Rev. Lett 101 (2008) 148101
[2] P.R. ten Wolde, D. Frenkel, Science 277 (1997) 1975-1978
[3] P.G. Vekilov, Cryst. Growth Des. 4 (2004) 671-685
[4] F. Zhang et al., J. Appl. Cryst. 44 (2011) 755-762
[5] F. Zhang et al., Faraday Disc. 159 (2012) 313-325
[6] D. Soraruf et al., Soft Matter 10 (2014) 894
[7] A. Sauter et al., in preparation