Time-resolved SANS study of structure formation in a solution of the globular protein Lysozyme

Christensen, Christian Kolle; Lindner, Peter; Tanaka, Shinpei; Klösgen, Beate

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**Introduction**

Protein crystallization has been studied widely for many years, and still remains a bottleneck in solving the structure of proteins. As a part of a study on protein crystallization under confinement, the stability of solutions of the globular protein lysozyme was studied by small angle neutron scattering (SANS). The solutions were probed by time-resolved SANS experiments and the recorded data report on the development of a structure.

**Method**

**Instrument**

The samples were studied by SANS at D11 at the ILL. The instrument is shown schematically in Fig. 1.

**Sample composition**

Lysozyme aqueous solutions of 1, 2, 4, and 8% (wt/wt) with 2 or 4% NaCl were measured for up to 7.5h after preparation, in 1.5h intervals. These initial compositions cover a range of stable and supersaturated conditions as illustrated in Fig. 2.

**Results**

- **Lysozyme form and size**
  
  SANS data from a pure dilute (3.4 wt%) protein solution were used to confirm the prolate ellipsoidal shape of the lysozyme, with $R_p$=11 Å and $R_a$=18 Å. The best fit (Fig. 4) was obtained using the ellipsoidal form factor and a structure factor calculated for charged, spheroidal particles in a dielectric medium, using the Hayter model.

- **Bragg peaks**

  In one case, 4% (wt/wt) lysozyme solution with 4% (wt/wt) NaCl, two peaks (at $q$=0.21 Å⁻¹ and $q$=0.28 Å⁻¹) forming over time were observed. Simultaneously, at low $q$ ($q$<0.02 Å⁻¹) the signal decreased. The peaks correspond to real space distances of 30Å and 22Å, respectively. The peaks resemble Bragg peaks, suggesting that tiny crystals were formed.

**Conclusion**

The size and shape of lysozyme was confirmed by SANS on a dilute lysozyme solution. The effective structure factor shows a nearest neighbor peak. In one sample two sharp peaks as well as a decrease in low q scattering were observed. These Bragg-like peaks probably originate from growing small crystallites, at the expense of monomers in solution. The observation was made only in the sample 4% protein/4%NaCl. Possibly the crystal formation was coincidentally captured in the beam for this particular sample, as different from the others, especially the 8% protein/4%NaCl sample.

**References**


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