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Protein crowding in solution, frozen and freeze-dried states: small-angle neutron and X-ray scattering study of lysozyme/sorbitol/water systems SUSAN KRUEGER, NIST, SHEILA KHODADADI, Delft Univ. of Tech., NICHOLAS CLARK, NIST and Amgen, ARNOLD MCAULEY, Amgen, VIVIANA CRISTIGLIO, ILL, NARAYANAN THEYENCHERI, ESRF, JOSEPH CURTIS, NIST, EVGENYI SHALAEV, Allergan — For effective preservation, proteins are often stored as frozen solutions or in glassy states using a freeze-drying process. However, aggregation is often observed after freeze-thaw or reconstitution of freeze-dried powder and the stability of the protein is no longer assured. In this study, small-angle neutron and X-ray scattering (SANS and SAXS) have been used to investigate changes in protein-protein interaction distances of a model protein/cryoprotectant system of lysozyme/sorbitol/water, under representative pharmaceutical processing conditions. The results demonstrate the utility of SAXS and SANS methods to monitor protein crowding at different stages of freezing and drying. The SANS measurements of solution samples showed at least one protein interaction peak corresponding to an interaction distance of $\sim$ 90 Å. In the frozen state, two protein interaction peaks were observed by SANS with corresponding interaction distances at 40 Å as well as 90 Å. On the other hand, both SAXS and SANS data for freeze-dried samples showed three peaks, suggesting interaction distances ranging from $\sim$ 15 Å to 170 Å. Possible interpretations of these interaction peaks will be discussed, as well as the role of sorbitol as a cryoprotectant during the freezing and drying process.

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