SUPPORTING INFORMATION

Generic pathways to stability in concentrated protein mixtures

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Saturation limit of pure lysozyme solutions

To estimate the saturation limit of lysozyme $L_{ZS}$ at the pH of 7.8 used in our experiments we exploit the data obtained by Retailleau et al, who determined $L_{ZS}$ as a function of pH and salt concentration for $3.3 \leq pH \leq 8.7$ and $0 \leq c_{NaCl} \leq 1.2$. An interpolation to pH = 7.8, yields: $L_{ZS} = 238.5 \text{ g l}^{-1}$ at $c_{NaCl} = 0 \text{ mM}$, $L_{ZS} = 66.8 \text{ g l}^{-1}$ at $c_{NaCl} = 100 \text{ mM}$, $L_{ZS} = 19.5 \text{ g l}^{-1}$ at $c_{NaCl} = 200 \text{ mM}$, $L_{ZS} = 11.7 \text{ g l}^{-1}$ at $c_{NaCl} = 300 \text{ mM}$, $L_{ZS} = 10.7 \text{ g l}^{-1}$ at $c_{NaCl} = 400 \text{ mM}$, and $L_{ZS} = 8.8 \text{ g l}^{-1}$ at $c_{NaCl} = 500 \text{ mM}$.

Saturation limit in pure lysozyme solutions and mixtures with $\alpha$-lactalbumin

We compare the saturation limit of lysozyme, as estimated from the data of Retailleau et al, to the concentration of lysozyme in the supernatant $c_{ZS}^{\alpha \rightarrow L_{ZS}}$ of our $\alpha$-lactalbumin / lysozyme systems with $c_{NaCl} = 100, 200, 300, 400$ and $500 \text{ mM}$ after an equilibration time of $\sim 2$ months in Fig. S1. To estimate $c_{ZS}^{\alpha \rightarrow L_{ZS}}$ we assume that the precipitates contain only lysozyme, the $\alpha$-lactalbumin remaining entirely in the supernatant, such that $c_{ZS}^{\alpha \rightarrow L_{ZS}} = c_{ZS}^{\alpha} - c_{\alpha}$, where we determine $c_{ZS}^{\alpha}$ in UV-Vis experiments (see Experimental section in the paper). For $c_{NaCl} = 400 \text{ mM}$ and $500 \text{ mM}$, we find a good agreement between $c_{ZS}^{\alpha \rightarrow L_{ZS}}$ and $S_{L_{ZS}}$ both in the mixtures ($0.1 \leq f_{L_{ZS}} \leq 0.9$) and in the pure lysozyme systems ($f_{L_{ZS}} = 1$, $c_{\alpha} = 0 \text{ g l}^{-1}$). This demonstrates that the presence of $\alpha$-lactalbumin hardly affects the saturation limit of lysozyme and that at these salt concentrations the crystallization process is complete after an equilibration time 2 months. By contrast, for $c_{NaCl} \leq 300 \text{ mM}$ $c_{ZS}^{\alpha \rightarrow L_{ZS}}$ significantly exceeds $S_{L_{ZS}}$ for both, the mixtures and the pure lysozyme systems. This indicates that the crystallization process is strongly delayed at these conditions, consistent with previous work reporting that the rate of lysozyme crystallization decreases with decreasing NaCl-concentration and supersaturation.

Notes and references