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Evolution of the structure and dynamics of bovine serum albumin induced by thermal denaturation

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Studying thermal protein denaturing provides valuable information on structural and dynamic aspects related to protein function. Here, we use small-angle and quasielastic neutron scattering (SANS and QENS) to shed light on the denaturing of bovine serum albumin (BSA) in the presence and absence of NaCl.

SANS reveals the temperature-dependent formation of a crosslinked BSA network. The sensitivity to NaCl-mediated protein charge screening is furthermore shown to decrease with increasing BSA concentration. A comparison of the dynamical signal from ratios of inelastic and elastic fixed-window scans (FWS) with the dynamical confinement obtained from the apparent mean-squared displacement [1] suggests that the signatures of denaturation observed on nanosecond time scales are dominated by temperature-induced changes of the dynamics. Changes of the local confinement, on the other hand, only contribute weakly. After denaturation, the dynamics is slowed down in the presence of NaCl, while the stability and dynamics of the native solution do not appear to be affected by salt.

Our approach offers a framework for a comprehensive, multi-method characterisation of thermal protein denaturing [2].

[1] Hennig *et al.*, Soft Matter **(8)**, 2012, 1628-1633.

[2] Matsarskaia *et al.*, PCCP, 2020, Accepted Manuscript. DOI: 10.1039/D0CP01857K

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