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Structure of Neat Protein Single-Chain Nanoparticles from Partially Denatured BSA by SANS

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Protein nanoparticles can outperform polymer nanoparticles due to their versatility, biodegradability and low immunogenicity. We have exploited our previous experience in the preparation and characterization of synthetic unimolecular single-chain nanoparticles (SCNPs) to synthesize polypeptide SCNPs based on proteins. The conformational changes due to chain folding or collapse, i.e, an increase in compactness that goes along with size reduction, are best probed with small angle scattering and in particular small-angle neutron scattering (SANS), due to high contrast and no radiation damage.
Here SCNPs were synthesized with partially denatured BSA with succinimide type linkers containing three and six methylene spacer groups. The degree of internal cross-linking was followed simply and efficiently via 1H-NMR spectroscopy. Moreover, the associated structural changes —as probed by SANS—reveal that the denatured protein has a random-coil-like conformation, which progressively shrinks with the cross-linker addition. The longer cross-linker exhibits slightly more efficiency in chain compaction, with similar reactivity at a given cross-linker concentration but a somewhat stronger size reduction. This simple and effective method is applicable to a wide range of compact proteins, which denature in urea and have appropriate reactive amino acids, leading to the synthesis of biodegradable polypeptide SCNPs for a range of applications.

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