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# Effect of the polymer conformation on the structure of protein single-chain nanoparticles.

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Single chain nanoparticles (SCNPs) are unimolecular polymer chains folded or collapsed via intra-molecular cross-linking under high dilution, leading to sparse conformations and a topological polydispersity similar to that of intrinsically disordered proteins (IDPs). Currently, there is great interest in expanding this technology to biodegradable and biocompatible polymers, including proteins. Recently, we fabricated BSA-SCNPs via intramolecular cross-linking of denatured bovine serum albumin (BSA) using disuccinimidyl suberate (DSS) that mainly reacts with lysine moieties in a polypeptide. SANS measurements demonstrated that the denatured protein progressively shrinks along with a lowering of the scaling exponent by cross-linking, thus allowing for size control of the BSA-SCNPs.
To extend SCNPs to polypeptides, it is important to understand the role of the chain conformation of the precursor on the resulting SCNP morphology. For this, we have systematically varied the solvent conditions (pH, salt and denaturant concentrations) of BSA solutions as well as the cross-linker concentration and studied the resulting SCNPs by dynamic and static light scattering as well as small angle X-ray scattering. Our results indicate that the precursor conformation has an effect on the SCNP morphology as well as on the balance between intra- and inter-molecular binding. We will now probe the microstructure in an upcoming SANS beamtime.

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