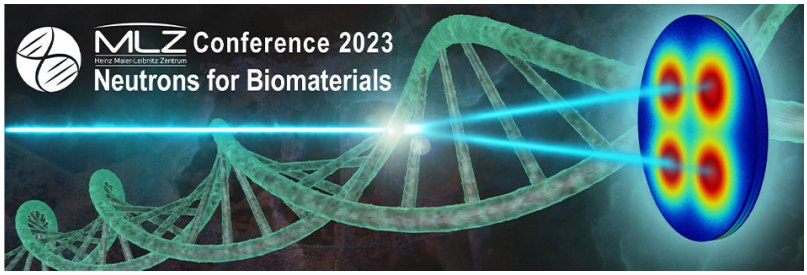

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Effect of the chain conformation on the structure of protein single-chain nanoparticles.

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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. For this purpose, we fabricated BSA-SCNPs via intramolecular cross-linking of denatured bovine serum albumin (BSA) using disuccinimide ester linkers that mainly react 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 (length and concentration) and studied the resulting SCNPs by dynamic and static light scattering as well as small angle neutron scattering. Our results indicate that the precursor conformation has an effect on the SCNP morphology. In particular, we found that more extended precursor conformations are able to collapse more as the intramolecular cross-links are increased. In addition, a longer cross-linker is more effective in chain compaction due to its ability to form larger intramolecular loops.

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