# Experimental report

01/09/2022

**Proposal:** 9-13-916 **Council:** 4/2020

**Title:** The dynamics of elastin-like peptides upon hydrophobic collapse

**Research area:** Soft condensed matter

**This proposal is a new proposal**


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**Samples:** elastin-like peptides in D2O buffer

| Instrument | Requested days | Allocated days | From | To |
|---|---|---|---|---|
| D22 | 1 | 1 | 14/06/2021 | 15/06/2021 |
| IN16B | 2 | 0 | | |
| IN5 | 2 | 0 | | |


## Abstract:

Elastin-like peptides (ELPs) are artificial polypeptides mimicking the hydrophobic repeat units of the insoluble protein elastin which provides elasticity to several biological tissues. One of the main features of ELPs is a hydrophobic collapse upon crossing a lower critical solution temperature (LCST), which makes them an intriguing tool for advanced biomaterials, protein purification and drug delivery. In addition, it is widely accepted that this hydrophobic collapse is key for the elastic properties of elastin. However, a comprehensive structural and dynamic characterization of the collapse process and the final, collapsed state is still missing. Using fully hydrogenated and partially deuterated ELP molecules, we aim for a comprehensive understanding of the hydrophobic collapse in ELPs by combining structural, dynamical and thermodynamic signatures using SANS (D22) and QENS (IN16B, IN5) and complementary techniques. Crucially, the partial deuteration will allow for elucidation of the dynamic contributions of the peptide backbone and side chains. Our study will provide valuable insights into the molecular nature of the hydrophobic collapse of ELPs and its role in biomedicine.

**Experimental report - 9-13-916 (D22, 14/06/2021-15/06/2021)**

**Towards a microscopic picture of coacervation in elastin-like polypeptides**

**Scientific background.** Elastin is a key protein of the extracellular matrix, and provides elastic properties to biological tissues – such as lung, arteries, skin, ligaments and cartilage – with extraordinary long-term stability and resilience. Besides this fundamental role for life, elastin and the related elastin-like peptides (ELPs) have been intensively and successfully used for biomaterials and biomedical applications such as drug delivery and protein purification in the last decade. ELPs are artificially designed biomolecules mimicking the hydrophobic repeat units in elastin. These repeat units undergo a hydrophobic collapse upon crossing a lower critical solution temperature (LCST), which causes both compaction of individual chains, and association of chains into coacervates (Fig.1). Although key to the elasticity of elastin and the stimulus response of ELPs, a comprehensive mechanistic characterization of the static and dynamicaspects of the collapse is missing. This is due to the difficulties in disentangling dynamical and structural aspects of assemblies, individual molecules and chain motions. The hydrophobic collapse and the related phase transition has been studied in detail for a range of ELP sequences. However, the dynamical state in the collapsed hydrophobic domains is still highly debated, the alternatives being a fluid-like structure 6 versus a specific stacking of beta-turn motifs. In addition to their imminent physiological and biomedical relevance, ELPs also represent models for intrinsically disordered proteins (IDPs) whose coacervation has a profound impact on cellular processes and organization. A mechanistic description of the driving forces behind coacervation in these systems open new opportunities for fundamental understanding and applications.

**Experimental results.** Temperature-dependent SANS data on the ELP GVG(VPGVG)$_{42}$ were taken on D22 using a sample-detector distance of 17.6 m. A selected data set is shown in Fig. 1.

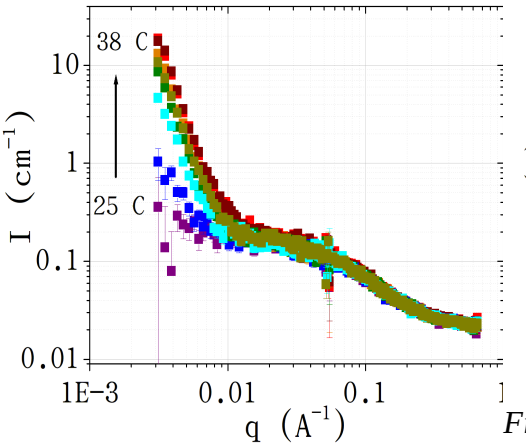


*Figure 1: SANS data on long ELP (se GVG(VPGVG)42).*

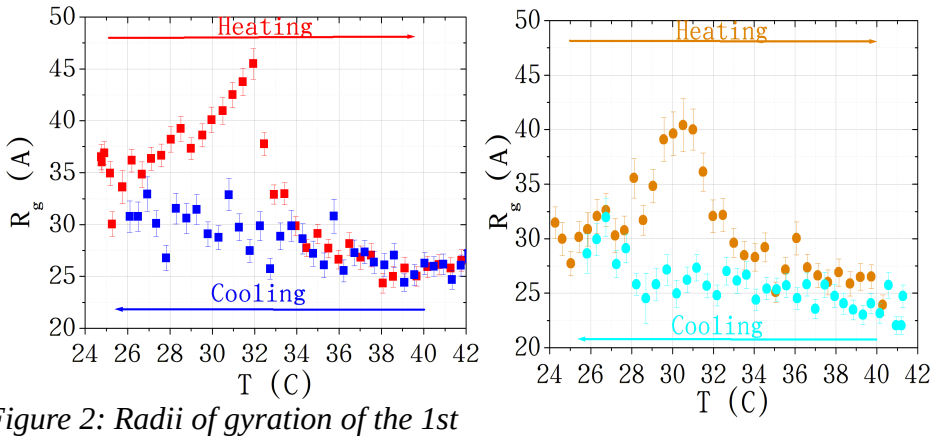


*Figure 2: Radii of gyration of the 1st (centre) and 2nd (right) heat-cool cycle.*

The pronounced increase in scattered intensity at low q (left panel of Fig. 1) as a function of temperatures indicates a potential self-assembly of the peptides into larger assemblies. This assembly was reversible upon cooling the sample back down, even though hysteresis effects were observed (centre and right panels). We note that a detailed, quantitative analysis of these data is still ongoing.

**Conclusions.** In combination with QENS data on the samples shown above (experiment 9-13-954 on IN5), we obtain detailed insights into the structural and dynamic properties of this long ELP upon its temperature-driven hydrophobic collapse. Detailed data analysis is in progress and a corresponding publication is in preparation.