Self-Assembly of PEG/peptide Block Copolymers in the Solid State: A SAXS/WAXS Study

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The formation of amyloid due to misfolding of proteins and peptides is symptomatic of diseases including Alzheimers, bovine spongiform encephalopathy etc [1-6]. Amyloid results from fibrilisation as peptides adopt a cross-beta sheet structure, with beta strands perpendicular to the long fibril axis. We are presently investigating the self-assembly of fragments of Aβ(16-20), KLVFF and hydrophobically modified versions of this sequence, and additionally of PEGylated peptides. The ultimate aim is to derive peptide copolymers that bind to Aβ and disrupt fibrilisation. PEGylation is of interest because PEG is biocompatible and provides steric stabilisation improving blood circulation time.

We used SAXS/WAXS on beamline A-2 to investigate the antagonistic effects of PEG crystallization and peptide secondary structure formation in a series of PEG-peptide copolymers. Three copolymers were studied comprising PEG3000 and KLVFF, FFKLVFF or AAKLVFF. The peptide sequences are based on KLVFF, sequence Aβ(16-20) from the Aβ peptide and hydrophobically modified variants of this. The inclusion of additional hydrophobic units enhances the tendency for fibrilisation which is rather weak in the KLVFF homoplypeptide. Peptide FFKLVFF is insoluble in water but dissolves in methanol, in which it has a strong fibrilisation tendency [7]. Peptide AAKLVFF is water soluble and forms well-defined fibrils [8], whereas KLVFF is a weak fibrilliser in aqueous solution [7,9,10].

Fig.1 shows a comparison of room temperature SAXS profiles for the three copolymers. Only KLVFF-PEG shows a well-defined Bragg peak, there are low q shoulders for the other two.

![Figure 1: Comparison of SAXS data for three PEG/peptide Block Copolymers at 20°C](image-url)
Figure 2 illustrates the temperature-dependence for representative sample AAKLVFF-PEG

Figure 2: SAXS/WAXS data for AAKLVFF-PEG during a heat/cool experiment

The transition on heating/cooling above $T_m($PEG$)=55$ °C is obvious. There is a change in the SAXS data, possibly indicating microphase separation in the melt (broad shoulder around $q = 0.15$ Å$^{-1}$) and loss of WAXS peaks from crystalline PEG. The interplay between PEG crystallization and peptide secondary structure is fascinating, and this work is in preparation for publication.

References