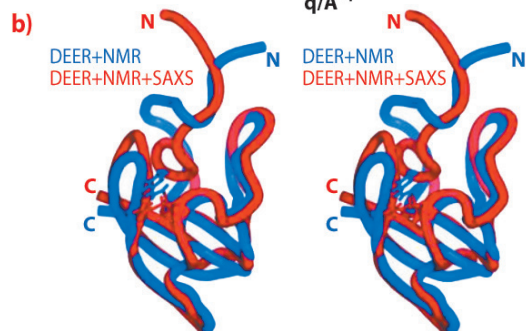


Fig. 67: Time-resolved pump-probe SAXS/WAXS of full length wild type PYP. Black: Experimental pump-on minus pump-off difference X-ray scattering data on PYP as a function of q . The X-ray probe pulse is applied 10 ms after the 460 nm pump pulse that probes the I_2' transient population. Blue: Theoretical difference scattering curve obtained using the DEER and NMR derived ensemble for the illuminated form minus the ground state. Red: Theoretical difference scattering curve obtained using the DEER, NMR and SAXS/WAXS derived ensemble for the illuminated form minus the ground state, after dynamical annealing calculations that included all experimental data simultaneously. The bottom panel shows a stereo image of the comparison of the average structures refined with DEER and NMR (blue) and combined DEER, SAXS/WAXS and NMR (red, PDB accession code: 2KX6) restraints simultaneously.



To the best of our knowledge, here we show the first application that uses simultaneous structure refinement from TR-SAXS/WAXS, DEER and NMR derived restraints. Furthermore, we have applied it to the problem of transient structural change of the PYP photoreceptor.

References

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Simple ultrasmall peptides self-assemble into fibrous structures found in Alzheimer's and other degenerative diseases

A large number of fatal degenerative diseases including Alzheimer's exhibit fibrous amyloid aggregates as a common pathological feature. Despite decades of investigations, how pathogenic amyloid structures develop out of naturally occurring proteins remains a mystery. Structural changes of the proteins by misfolding have been identified as one of the most likely causes of amyloid formation. We have rationally designed a novel class of ultrasmall aliphatic peptides of only 3 to 7 amino acids in length that can self-assemble to typical fibrous amyloid structures, see **Figure 68** [1].

Each of these tri- to heptapeptides contains a water-soluble 'polar head' and a water-insoluble 'tail' with decreasing hydrophobicity. This specific motif enables the molecules to self-assemble spontaneously in water to form hydrogels—stiff gels held together by stable fibrous aggregates. The honeycomb-like structures of the peptide scaffolds enable them to

entrap large amounts of water. We observed a complex stepwise mechanism of aggregation involving at least three different steps. The process of self-assembly to fibres and condensed amyloid aggregates is most likely driven by unexpected α -helical intermediates during the transition to cross- β fibres. Investigations using electron microscopy, spectroscopy and X-ray microdiffraction at the **ID13** beamline confirmed these conformational changes (**Figure 69**). Interestingly, the highly-

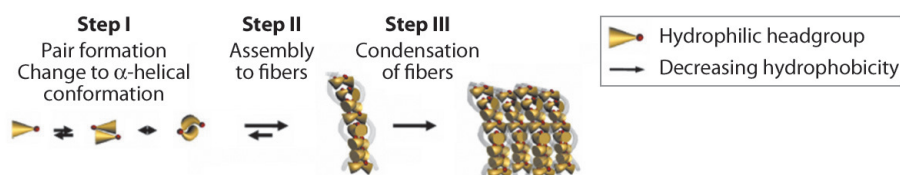


Fig. 68: Hypothetical self-assembly of peptide monomers into supramolecular networks of condensed fibres. Self-assembly is initiated by antiparallel pairing of two peptide monomers by changing to α -helical conformation. Subsequently, peptide pairs assemble to nanostructures and fibres and condense to fibrils resulting in hydrogel formation.

Principal publication and authors

- C.A.E. Hauser (a), R. Deng (a), A. Mishra (a), Y. Loo (a), U. Khoe (a), F. Zhuang (a), D.W. Cheong (b), A. Accardo (c,d), M.B. Sullivan (b), C. Riekel (c), J.Y. Ying (a) and U.A. Hauser (a), *Proc. Natl. Acad. Sci. USA* **108**, 1361-1366 (2011).
 (a) Institute of Bioengineering and Nanotechnology (Singapore)
 (b) Institute of High Performance Computing (Singapore)
 (c) ESRF
 (d) Center of BioNanotechnology and Engineering for Medicine (BIOMEMS), University Magna Graecia of Catanzaro (Italy)
 (e) Institute of Physics I, University of Cologne (Germany)