EUROPEAN SYNCHROTRON RADIATION FACILITY
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Experiment Report Form

	Experiment title: X-ray diffraction from fibrillar assemblies of amyloid-beta peptides from Alzheimer's disease	**Experiment number**: LS- 2229
Beamline: ID02	**Date of experiment**: from: 10 May 2013 to: 13 May 2031	**Date of report**: 26 Oct 2015
Shifts: 6	**Local contact(s)**: Peter Boesecke	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

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Report:

The amyloid-β (Aβ) peptide is the primary component of the extracellular senile plaques characteristic of Alzheimer's disease (AD). A mutation at residue number two (A2V), is associated with severe AD and results in enhanced fibril formation in vitro. By contrast, co-incubation of wild type Aβwith A2V analogue, or even with 6-mere peptide Aβ1-6(A2V), inhibits fibril formation. Interestingly unlike single component ones, mixed aggregates are labile structures, being readily destabilized upon dilution. Establishing the characteristics of the organization of amyloid is important for providing insights towards both pathology mechanisms and developing possible therapeutics for AD. The aim of the studie was to complement our ND data, clearly demonstrating structural differences between the wild type, the A2V and the mixed forms of Aβ (ILL Exp. 8-04-640), with high resolution small-angle (SAXS) and wideangle X-ray scattering (WAXS) data.

Lyophilized synthetic peptides, dissolved in distilled water at 10 mg/ml were slowly dehydrated in specially designed cells in the presence of a 7-T static magnetic field to induce alignment of the assemblies. Mixed systems were obtained by dissolving Aβ(1-28)A2V or Aβ(1-6)A2V in water at 5 mg/ml or 20 mg/ml, respectively, and adding the solution to the dry Aβ(1-28)WT. This protocol allowed to obtain oriented samples. Water (3µl) was locally added to the dry depositions just before measurement, allowing for scattered intensity. A second measurement was performed after a lagtime of 6 hours, to test for structure destabilization induced by hydration. SAXS data were collected with an incident X-ray wavelength λ = 1Å. For each measurement, 10 frames were taken with short exposure time (0.03 or 0.1 s, 1s deadtime) to avoid or test for radiation damage. For SAXS, an extended q range was selected (0.12 – 5.96 nm^-1) in the first stage, for a wider overlook. In the second stage, the q-range was restricted (0.019- 1.26 nm^-1) to allow for better definition in the region of interest. Collected images were processed and corrected with the ID02 software.

WAXS spectra were similar for all of the samples, showing a meridional peak at q= 13.3 nm^-1 , as expected, corresponding to the spacing between hydrogen-bonded β-strands within a β-sheet, as reported in Fig WAXS1

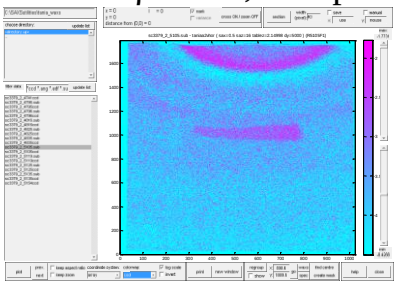
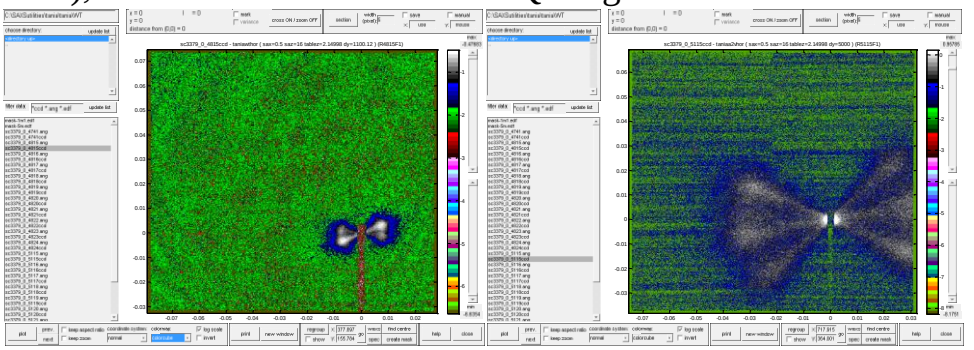
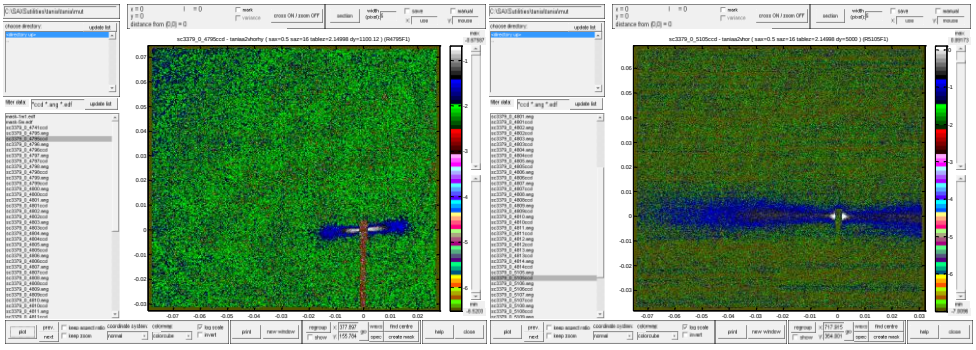


FIG WAXS1

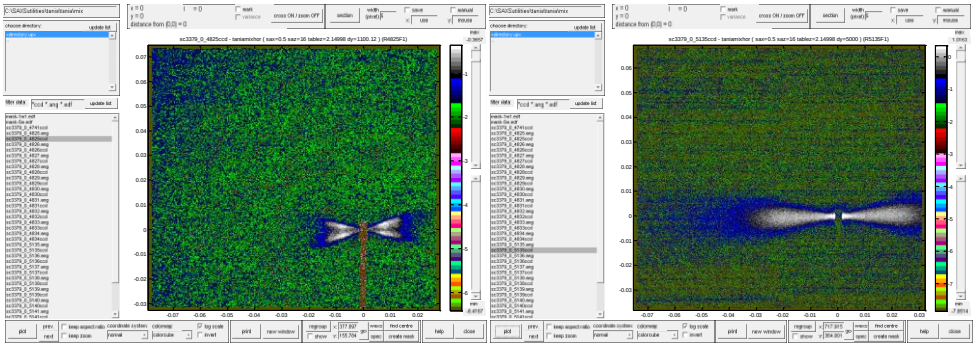
In the **SAXS region** samples displayed very different spectra, but, in all cases, no signal is present in the azymuthal direction in the SAXS region. Figures SAXS1 and SAXS2 report the two-dimensional images collected at different delays from hydration (immediately and 6h later), as described in MATMET. Q-ranges are stated in MATMED.



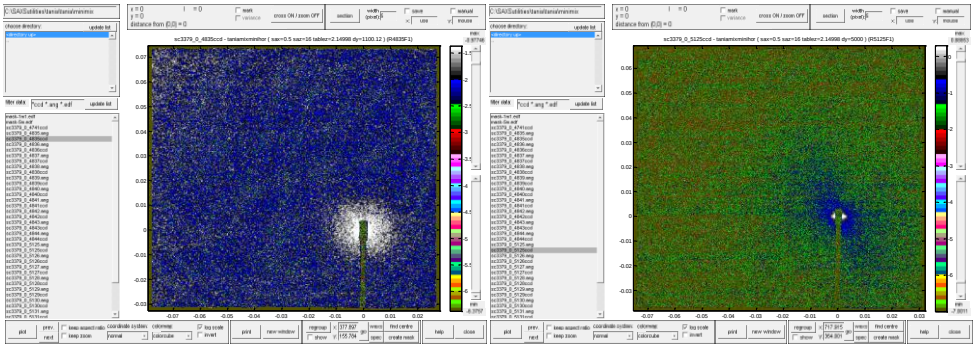
WT



A2V



WT+A2V



WT+ 1-6A2V

FIG SAXS1

FIG SAXS2