Adsorption of Amyloid beta (1-40) peptide to the air/water interface and to lipid monolayers

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The major component of Amyloid plaque found in the brain of patients with Alzheimer disease is a 39 to 43-amino acid residues β-amyloid peptide (Aβ) derived from transmembrane amyloid precursor protein (APP). Normally this peptide exists in monomeric or dimeric form in cerebrospinal fluid. During aging the peptide aggregates into β-sheet containing fibrils. Since Aβ is composed of a transmembrane and an extracellular part of APP, interactions with phospholipid membranes could play an important role for Aβ folding and toxicity [1, 2].

Phospholipid monolayers can be used as model membranes to study the influence of the lipid structure on the secondary peptide structure as well as the influence of the peptide on the lipid organisation. Since Aβ is an amphiphilic peptide it has pronounced surface activity. Adsorption to the air/water interface leads to a decrease of the surface tension and reaches equilibrium at a surface pressure of approximately 18 mN/m. In the presence of DPPC and DMPE monolayers at zero pressure (96 Å²/molecule), Aβ shows similar behavior. It penetrates into the lipid monolayer and the same equilibrium surface pressure is reached. After pretreatment with HFIP, Aβ has mostly random coil conformation in aqueous solutions as revealed by CD (circular dichroism) spectra. In contrast, IRRAS (infrared reflection absorption spectroscopy) shows that adsorbed Aβ forms β-sheet oriented parallel at the pure air-water interface and at DPPC and DMPE monolayers at low surface pressure. The phase behavior of the zwitterionic phospholipid monolayers is not changed due to peptide adsorption and penetration, i.e. the phase transition from liquid-expanded to condensed is observed at the same surface pressure as for pure lipids. Thus at low surface pressure Aβ adsorbs to and penetrates into the lipid monolayers and compresses the lipid molecules inducing the phase transition in the phospholipid monolayers. Further compression leads to a squeezing out of the peptide from the lipid monolayer. If the lipid monolayers were compressed to 30 mN/m before addition of Aβ, no peptide adsorption was observed.

Figure 1: Contour plots of the corrected X-ray intensities as a function of the in-plane component $Q_{xy}$ and the out-of-plane component $Q_z$ of the scattering vector of DPPC on water (left) and on an aqueous Aβ solution (0.37 µM) (right) at 20 °C and 20 mN/m.
GIXD (grazing-incidence X-ray diffraction) experiments were performed at BW1, HASYLAB, DESY, to understand which structural changes in the lipid monolayers can be induced by the peptide adsorption. Aβ was adsorbed to the pure air/water interface and to zwitterionic DPPC, DPPE and DMPE monolayers at low and high surface pressures. The phospholipid structures remain unchanged at all surface pressures (Figure 1). At low surface pressure a slight broadening of the lipid Bragg peaks was observed indicating a decrease of positional order due to peptide penetration and dilution of lipid molecules in the monolayer.

The adsorbed peptide (only at low surface pressure and at the air/water interface) shows two Bragg peaks at $Q_{xy} = 1.33 \text{ Å}^{-1}$ ($\Delta Q_{xy} = 0.065 \text{ Å}^{-1}$) and $Q_{xy} = 0.16 \text{ Å}^{-1}$, ($\Delta Q_{xy} = 0.031 \text{ Å}^{-1}$) (Figure 2). The first weak (therefore not seen in Fig. 1) peak corresponds to a distance of 4.7 Å, which is characteristic for $\beta$-sheet. These data are in agreement with our IRRAS experiments at the air-water interface. The second peak reveals a repeating distance of 39 Å. Both peaks disappear after squeezing out of the peptide at high surface pressure and appear again after expansion of the monolayer and re-penetration of Aβ.

![Contour plot of the corrected X-ray intensities as a function of the in-plane component $Q_{xy}$ and the out-of-plane component $Q_z$ of the scattering vector of Aβ on water in the small angle region (left) and integrated X-ray intensity of the diffraction peak at 1.33 Å$^{-1}$ vs. $Q_{xy}$.](image)

References