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Effect of freezing on amyloid peptide aggregation and self-diffusion in an aqueous solution

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Abstract

Pulsed-field gradient 1H NMR is employed to investigate the self-diffusion of amyloid Aβ-peptide in an aqueous buffer solution (pH 7.44) with a protein concentration of 50 μmol at 20°C. The self-diffusion coefficient of the peptide in a freshly prepared solution corresponds to its monomeric form. The storage of the solution at 24°C causes part of the peptide molecules to form amyloid aggregates as soon as over 48 h. However, the 1H NMR echo signal typical of aggregated molecules is not observed because of their dense packing in the aggregates and a large mass of the latter. A freezing-fusion of the solution after the aggregation does not cause changes in the self-diffusion coefficients of the peptide. After a peptide solution free of amyloid aggregates is subjected to a freezing-fusion cycle, part of the peptide molecules also remains in the monomeric form in the solution, while another part forms amyloid aggregates, with a portion of the aggregated peptide molecules retaining a high rotational mobility with virtually absolute absence of a translational mobility. The results obtained are interpreted in terms of the formation of "porous aggregates" of amyloid fibrils, with "pores" having sizes comparable with those of peptide molecules, though, being larger than water molecules. Peptide molecules, which do not form fibrils, are captured in the pores. Temperature regime is shown to be of importance for the aggregation of amyloid peptides. In particular, freezing, which is traditionally considered to be a method for the prevention from or temporary interruption of aggregation, may itself lead to the formation of amorphous amyloid aggregates, which remain preserved in solutions after their unfreezing. © 2008 MAIK Nauka.

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