Changes in the Dynamics of Protein during Amyloid Fibril Formation Detected by Neutron Scattering

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Amyloid fibrils are filamentous protein aggregates that are found as deposits in patients of a range of human diseases including Alzheimer's disease, Parkinson's disease, and senile systemic amyloidosis. These abnormal protein aggregates and/or intermediate structures towards the mature fibrils are related to pathogenesis of these diseases. Elucidation of the mechanism of amyloid fibril formation is therefore important for elucidation of the mechanism of pathogenesis. Since partial unfolding of a normal protein is likely to trigger the formation of the fibrils, characterization of "dynamics" of the protein should be important.

We investigated the dynamics of hen egg-white lysozyme (HEWL), which forms amyloid fibrils in high concentration of ethanol, as a model system of amyloid fibril formation. We employed neutron scattering that can directly measure the dynamics of proteins at picosecond time and ångstrom length scales. The elastic incoherent neutron scattering measurements showed the different dynamics of HEWL in the monomer and the amyloid fibril states [1]. Here, to characterize further the dynamics during the amyloid fibril formation, we carried out the quasielastic neutron scattering measurements on HEWL in solution containing various concentrations of ethanol. The measurements were carried out using a high resolution near-backscattering spectrometer, BL02 (DNA), at MLF/J-PARC, Tokai, Ibaraki, Japan, at the energy resolution of 12 μeV. Differences in the amplitudes and rates of the internal motions were observed between HEWL in different conditions. The results obtained showed that HEWL becomes more flexible towards the formation of amyloid fibrils. This abnormal flexibility of the protein should be related to the mechanism of amyloid fibril formation.

Reference

[1] S. Fujiwara, T. Yamada, T. Matsuo, N. Takahashi, K. Kamazawa, Y. Kawakita, and K. Shibata, Jpn. J. Appl. Phys. **82**, SA019 (2013).