CROSS TOKAI **Experimental Report** J-PARC	承認日 Date of Approval 2017/4/7 承認者 Approver Kaoru Shibata 提出日 Date of Report 2017/4/7
課題番号 Project No. 2014B0156 実験課題名 Title of experiment Changes in the dynamics of Parkinson's disease-related protein alpha-synuclein studied by neutron scattering 実験責任者名 Name of principal investigator Satoru Fujiwara 所属 Affiliation National Institutes for Quantum and Radiological Science and Technology	装置責任者 Name of Instrument scientist Kaoru Shibata 装置名 Name of Instrument/（BL No.） BL02 実施日 Date of Experiment 15/10/28～15/11/01

試料、実験方法、利用の結果得られた主なデータ、考察、結論等を、記述して下さい。（適宜、図表添付のこと）
Please report your samples, experimental method and results, discussion and conclusions. Please add figures and tables for better explanation.

1. 試料 Name of sample(s) and chemical formula, or compositions including physical form.

The following samples were prepared for this experiment.

(1) α-synuclein solution in the D_2O buffer (the concentration of the protein: 7.4 mg/ml)

(2) The D_2O buffer (containing 20 mM HEPES, pD 7.4)

(3) Empty cell

(4) Vanadium standard

2. 実験方法及び結果（実験がうまくいかなかった場合、その理由を記述してください。）
Experimental method and results. If you failed to conduct experiment as planned, please describe reasons.

Human α-synuclein is a protein that is known to form amyloid fibrils, and the formation of the fibrils is thought to be related to the pathogenesis of Parkinson's disease. Elucidation of the mechanism of the amyloid fibril formation of α-synuclein is thus important to understand the mechanism of the pathogenesis of Parkinson's disease. Since the initial process of the fibril formation involves the partial denaturation of the proteins, the dynamic behavior of the protein should be elucidated to understand the process. We have been investigating the dynamic behavior of α-synuclein in the monomeric and fibril states by Quasielastic neutron scattering (QENS). These measurements were carried out at the energy resolution of 12 μeV, corresponding to the measurements of the motions faster than about 55 ps. In order to characterize the dynamic behavior in more detail, slower motions should be characterized as well. In addition, the sample in the monomeric state in the previous measurements contained significant concentration of salt (140 mM NaCl), and such a high concentration of salt could

2. 実験方法及び結果（つづき） Experimental method and results (continued)

affect the dynamic behavior of α-synuclein. We thus prepared the α-synuclein solution in the low salt condition as described above, and the QENS measurements were carried out at the energy resolution of 2.5 μeV. The measurements were done at 300 K. Figure 1 shows examples of the spectra obtained for several Q values.

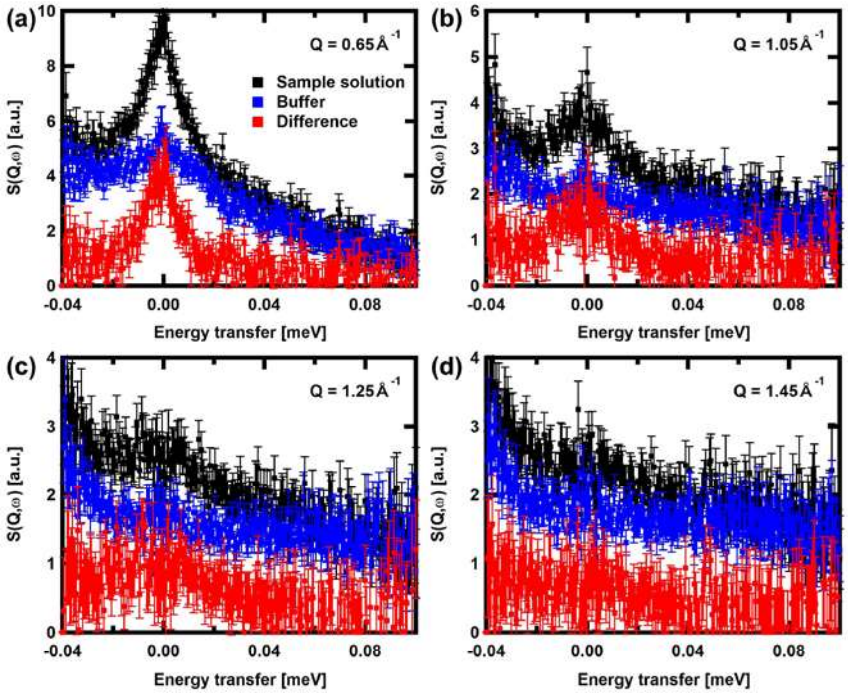

Figure 1. Examples of the QENS spectra of α-synuclein solution, the D_2O-buffer, and the difference spectra, which correspond to the spectra of the protein.

Subtraction of the spectra of the D_2O-buffer from those of the sample solution was adequately performed as shown in Fig.1. Unfortunately, however, the statistics of the spectra was not very good because of the low concentration of the protein, which was necessary to keep the protein in the monomeric state. Fits to the spectra were carried out using the equation containing the Lorentzian function to evaluate the diffusion coefficient of α-synuclein in this state. Figure 2 shows Q^2-dependence of the half widths at half maximum (HWHM) of the Lorentzian function describing the global motions of α-synuclein. The apparent diffusion coefficient can be evaluated from the slope of this curve. It was found that the value is 1.27 ± 0.31 × 10^{-6} cm^2/s. This value is smaller than that obtained from the measurements at the energy resolution of 12 μeV, but still significantly larger than the "true" translational diffusion coefficients, indicating that the diffusion coefficients evaluated by QENS contain the contribution from the segmental motions within the molecules.

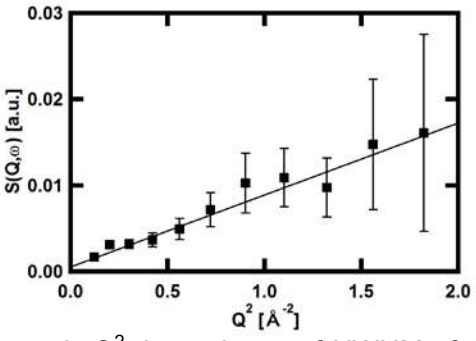

Figure 2. Q^2-dependence of HWHM of the Lorentzian function describing the global motions of α-synuclein.