End-condition for solution small angle X-ray scattering measurements by kernel density estimation

H. Sekiguchi¹, N. Ohta¹, H. Ishibashi², H. Hino³, M. Mizumaki¹

Center for Synchrotron Radiation Research, Japan Synchrotron Radiation Research Institute, Sayo-cho, Japan, Graduate School of Life Science and Systems Engineering, Kyusyu Institute of Technology, Kitakyusyu, Japan, Department of Statistical Modeling, The Institute of Statistical Mathematics, Tachikawa, Japan

sekiguchi@spring8.or.jp

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Small-angle X-ray scattering (SAXS) is an effective structural characterization method on the nano- to micrometer scale in various research fields, including biomacromolecules. The use of a high-brilliance synchrotron radiation (SR) sources offers significant advantages in terms of the measurements timescale and small sample requirements; SR-SAXS is a reasonable tool for large-scale structural studies due to the automation of sample changers, scattering experiments, data processing and interpretation of scattering profiles. Although high-flux X-rays are beneficial, their damage must be considered when dealing with bio- or soft-materials. Since the damage sensitivity varies from sample to sample, users routinely collect time-series data and then determine the X-ray exposure time that comprises identical information for each sample. For samples with the insignificant effect of X-ray damage, the X-ray exposure time can be longer than necessary to obtain the information, resulting in low-throughput experiments. Therefore, to perform X-ray scattering experiments efficiently and adequately on various samples, an experienced specialist is usually required to optimize the X-ray exposure time for each sample. Considering the recent trend toward automated sample exchange and data acquisition where a large variety of samples are to be measured, it would not be possible to devote the human resources to optimize the exposure time for each sample in most cases.

In order to efficiently carry out SR-SAXS measurements for a large number of samples with various X-ray damage sensitivity, we investigate whether it is possible to reduce the X-ray exposure time in order to extract information from SAXS data and to estimate the minimum exposure time using statistical and mathematical approaches, not by experienced specialist. We applied the kernel density estimation (KDE) approach [1] to accelerate and optimize the measurement. This approach has already been employed to make effective use of the neutron scattering data obtained [2], where signals are depleted. We apply a statistical inequality to estimate the kernel density estimation method’s error to determine the minimum X-ray exposure time for protein solution scattering experiments (Fig. 1) and evaluate the method’s validity using the results of Guinier analysis as an indicator [3,4]. We find that the KDE makes it possible to find a benchmark that eliminates unnecessary X-ray exposure time. To meet the increasing demand for automatic measurement, we believe our approach would be useful to construct a meaningful automatic measurement system.

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**Figure 1.** Derivation of the optimal / minimum X-ray exposure time by kernel density estimation

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[4] Python scripts for KDE calculation and one of datasets used in this work (https://doi.org/10.5281/zenodo.7045445).