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Editorial

Approach of Serial Crystallography II

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Abstract: Serial crystallography (SX) is an emerging X-ray crystallographic method for determining macromolecule structures. It can address concerns regarding the limitations of data collected by conventional crystallography techniques, which require cryogenic-temperature environments and allow crystals to accumulate radiation damage. Time-resolved SX studies using the pump-probe methodology provide useful information for understanding macromolecular mechanisms and structure fluctuation dynamics. This Special Issue deals with the serial crystallography approach using an X-ray free electron laser (XFEL) and synchrotron X-ray source, and reviews recent SX research involving synchrotron use. These reports provide insights into future serial crystallography research trends and approaches.

Serial crystallography (SX) experiments using an X-ray free electron laser (XFEL) with a short pulse width, or short time X-ray (<100 ms) exposure in a synchrotron, minimize radiation damage to crystals compared with traditional X-ray crystallographic methods [1,2]. Moreover, SX data collection at room temperature provides more biologically reliable data on structural dynamics in macromolecules compared to cryo-crystallographic techniques [3–5]. In addition, in SX data collection, if a crystal sample is stimulated with a pump, such as an optical laser or a ligand/inhibitor solution, and then diffraction data are collected by exposure to X-rays after a selected time delay. This can time-resolve molecular mechanisms of macromolecules [6,7]. Thus, SX techniques provide more biologically reliable structural information than conventional X-ray crystallography and can provide detailed information on their mechanisms of action.

Each XFEL facility or synchrotron capable of performing SX can provide unique X-ray characteristics (photon flux, X-ray size, repetition rate, jitter, etc.) and different experimental environments (vacuum, helium or ambient, temperature, etc.), as well as a diverse array of preferred sample delivery techniques (injection, fixed-target scanning, hybrid methods, etc.) [8]. Accordingly, SX experimental approaches will be diverse, and they will depend on the facility, target samples, and desired information [5,8,9]. In this Special Issue, we discuss approaches to serial crystallography. Specifically, we cover two SX research articles and one review, as follows:

Gorel et al. reported shock damage analysis in serial femtosecond crystallography data collected at MHz XFEL [10]. When the MHz XFEL beam penetrates the liquid jet, supersonic shock waves are generated at the XFEL transmission point. The effect of these shock waves on the next crystal sample was investigated. The results of these investigations confirm that there was no damage to the crystal sample due to the characteristics of the XFEL used. This approach provides data acquisition efficiency in SFX experiments with MHz XFEL pulses. In addition, it is useful for verifying the reliability of data collected when a supersonic shock wave is generated.

Park et al. reported fixed-target serial synchrotron crystallography using a nylon mesh and an enclosed film-based sample holder [11]. This sample delivery method was derived from a previously developed fixed-target sample delivery method applied in serial femtosecond crystallography (SFX) studies [12], but the sample holder was re-designed to be suitable for a beamline instrument at a synchrotron, and this method was used to

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determine the crystal structures of model samples while changing exposure time and oscillation parameters. This approach can be applied in existing macromolecular beamline instruments without the installation of a special device.

Martin-Garcia provided a timely review of the recent time-resolved SX studies conducted in synchrotrons [13]. In their review, the importance of time-resolved SX is summarized comprehensively as the target samples and data collection environments of 41 successful SSX studies are discussed. Furthermore, notable sample delivery methods, including viscous jets, the hit-and-return (HARE) system, the liquid application method for time-resolved analysis (LAMA) system, the mix-and-diffusion device, and microfluidics devices have been covered.

During the drafting of this Special Issue, various SX technologies have continued to further develop. Although these studies are not addressed in this Special Issue, they provide useful information for maintaining an optimal environment specific to each facility [14–19] or target sample delivery method [20–35]. All articles in this Special Issue discussing SX approaches and recently developed SX techniques will provide great opportunities to better understand macromolecular functions in greater depth.

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