

## Development of a drug screening pipeline at SPring-8 macromolecular crystallography beamlines

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SPring-8 beamlines BL32XU, BL41XU, and BL45XU provide users with automated measurements that do not require a visit using the automated data collection system ZOO [1]. Among these beamlines, BL45XU is specialized in automated measurement, and the automated data collection system is used in most data collection schemes. By using the automated data collection system, 200 sets of diffraction data from single crystals of biomacromolecules can be obtained within 24 hours. It is also possible to automatically acquire small-wedge data from membrane protein crystals grown in LCP. Taking advantage of the throughput of this automated measurement system, pharmaceutical companies and CROs in Japan and overseas regularly collect large amounts of data at SPring-8 today.

At SPring-8, we are developing a facility that enables compound screening for drug discovery using a wide variety of compounds by taking advantage of the throughput of the automated data collection system. The introduction of compounds into crystals of drug target proteins is performed by adding compound solutions directly to the drop on the crystallization plate where crystals are obtained using the acoustic liquid handler ECHO 650T, based on the method developed by XChem at the Diamond Light Source [2]. The crystals are soaked in the compound solution and fished with a cryoloop. The diffraction data are acquired by the automated data collection system. Data processing is performed by KAMO, an automated data processing pipeline developed at SPring-8 [3]. An automated structural analysis system is currently under construction for large-volume structural analysis. Furthermore, a feasibility study on compound screening by *in situ* plate diffraction measurement system at room temperature has been conducted. The *in situ* plate diffraction measurement system installed at BL26B1, SPring-8, can acquire small-wedge data and we can obtain the complete data necessary for structural analysis by merging the data. We have shown that the acoustic liquid handler ECHO can be used to screen compounds at room temperature by directly injecting compounds into a drop on the crystallization plate and collecting small-wedge data [4].

In the presentation, we will report on various compound screening methods combined with SPring-8 beamline technologies and their examples for use.

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