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SynergyUltra opens a new era with digits of different performances and capabilities in protein crystallography; 4s-4m-40m

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The accurate protein structures and their complex targets compounds are necessary and critical for designing and developing effective medicines and potent substances. To date, massive numbers of these structures have been determined by single-crystal X-ray diffraction (SC-XRD) analysis. Other new technologies like single-particle analysis using a Cryo-electron microscope or, more recently, utilization of three-dimensional electron diffraction (3D-ED) are emerging to overcome the difficulty of crystallization and hence to be thought the enhancement in the speed.

The geometry of the atoms defines interactions among the molecules, and some of those are highly sensitive to the directions and/or distances; thus, the accurate and precise structural information of the molecule is an indispensable firm base for successful drug design processes. In this context, SC-XRD is still the best approach if it could be performed as its necessity.

Meanwhile, it has still been widely believed that SC-XRD requires considerable time and effort to crystalize the target molecules and other efforts to collect the datasets and phasing.

This presentation introduces our next-generation instrument that opens a new era of protein SC-XRD with laboratory instruments formats. Ultra-fast and accurate measurements of protein crystals using our latest system SynergyUltra will be presented. The following numbers characterize the power of SynergyUltra.

- 4 seconds, the whole data collection for the molecular replacement phasing:
  The 4 seconds in total data collection fulfilling the 1.8Å resolution range. The obtained results were accurate enough for molecular replacement phasing employing Alpha Fold 2 deduced structure as a searching model. As a result, detailed electron densities were obtained, in which disorder of the sidechain can be modeled and refined for their population. Utilizing the SynergyFlow robotics system enables to obtain the unique crystal structures every several minutes that enable curtain bombing (carpet bombing) structure analyses of mutant proteins and/or its s complexes with various candidates.

- 4 minutes, the whole data collection good for SAD phasing:
  The 4 minutes in total data collection fulfilling the 1.75Å resolution range. This measurement allows obtaining highly even and redundant data sets that are accurate enough for successful S-SAD phasing. 97% of residues were automatically modeled and refined to yield the detailed electron densities. 4 minutes measurements would be useful unless above 4 seconds MR experiments did not work well.

- 40 minutes, the whole data collection for ultra-high resolution data collection.
  The 40 minutes in total data collection fulfilling the 1.40Å resolution range. This measurement allows obtaining further precise and highly accurate electron density that shows the spherical shapes for each atom similar to those obtained in small-molecule crystallography in that atom types can be identified by their density.