Max-Planck-Innovation

Technology Offer

Max-Planck-Innovation GmbH
Amalienstr. 33
80799 Munich
Germany

Phone: +49 (89) 29 09 19 - 0
Fax: +49 (89) 29 09 19 - 99
info@max-planck-innovation.de
www.max-planck-innovation.de

Contact:
Dr. Matthias Stein-Gerlach
Tel.: 089 / 290919-18
Stein-gerlach@max-planck-innovation.de

Synchrotron Serial Snapshot Crystallography of Biological Nanocrystals carried in Microscopic, Ultra-Slow, High Viscosity Free-Streams

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An apparatus and method allowing high throughput collection of X-ray diffraction data at room temperature.

Background

Nearly all structure determination of biological macromolecules is carried out via crystallographic measurements at synchrotrons. The conventional practice to immobilize the crystals and mitigate radiation damage is to work with cryo-cooled samples. Even at cryogenic temperatures, though, the resistance of biological samples to x-ray damage is limited and a new sample must be mounted, manually or robotically, at regular intervals.

Moreover, given that virtually all biological processes take place at or near room temperature, the ability to measure at ambient temperature would not just be of considerable practical convenience, but also of fundamental scientific relevance, since meaningful time-resolved experiments could then be performed.

Technology

Scientists at the Arizona State University and the Max Planck Institute for Medical Research have developed an apparatus and methodology for room temperature biological structure determination, using x-ray diffraction from randomly oriented biological microcrystals carried in a flowing microscopic stream. The use of this slowly flowing stream for crystal delivery resulted in extremely high-throughput delivery of crystals into the X-ray beam.

Moreover, by embedding the crystals in the high-viscosity carrier stream, high-resolution room-temperature studies could be conducted at atmospheric pressure using the unattenuated X-ray beam, thus permitting the analysis of small or weakly scattering crystals. This has been achieved thanks to a high-viscosity extrusion injector, especially developed for that purpose. The method and apparatus have been used to record diffraction images from serial x-ray exposures of 100 ms duration at 10 per second (still images) or 1 per second (rotation images) from micron-sized lysozyme crystals, embedded in a 35 um diameter fluid free stream of lipidic cubic phase, flowing through an x-ray spot of the Swiss Light Source, using less than half a milligram of protein crystals.

In summary, our scientists have developed an apparatus and methodology, which allow high throughput collection of x-ray diffraction data at room temperature. We are now looking for a licensing partner for this technology.

Patent Information

PCT application filed: PCT/EP2015/000208; US application Nr. 15/112,350

Publication

Botha S., Nass K., Barends T.R., Kabsch W., Latz B., Dworkowski F., Foucar L., Panepucci E., Wang M., Shoeman R.L., Schlichting I., Doak R.B. (2015): Room-temperature serial crystallography at synchrotron X-ray sources using slowly flowing free-standing high-viscosity microstreams. *Acta Crystallogr D Biol Crystallogr.* **71(Pt 2)**:387-97. doi: 10.1107/S1399004714026327.