STRUCTURAL BIOLOGY

ISSN 2059-7983

# Diffraction Structural Biology 2025: introductory overview

**Kristina Djinović Carugo,[a]* Atsushi Nakagawa[b]* and John R. Helliwell[c]***

[a]European Molecular Biology Laboratory (EMBL) Grenoble, Grenoble, France, [b]Institute for Protein Research, The University of Osaka, Suita, Japan, and [c]Department of Chemistry, University of Manchester, Manchester, United Kingdom. *Correspondence e-mail: kristina.djinovic@embl.org, atsushi@protein.osaka-u.ac.jp, john.helliwell@manchester.ac.uk

**Keywords:** structural biology; International Symposium on Diffraction Structural Biology.

This virtual issue of articles in *Acta Crystallographica Section D* comprises a collection of a selected group of presentations submitted in the context of the seventh International Symposium on Diffraction Structural Biology (ISDSB) 2025. Taken together, these articles provide a snapshot of a field that has expanded considerably since the first ISDSB meeting more than two decades ago: not only in the range and capabilities of its experimental techniques, but also in the biological questions that structural biology now seeks to address.

The ISDSB series of symposia was initiated in 2003 by the Japan Society for the Promotion of Science (JSPS) and specifically by the University–Industry Cooperative Research Committee (#169) (169th Committee) chaired by Professor Noriyoshi Sakabe. The phrase 'Diffraction Structural Biology' was proposed by Professor Sakabe and colleagues in association with the 169th Committee, and has shown the world the importance of research on structural biology mainly by X-ray, neutron, electron and other diffraction techniques, as well as stimulating the interface of basic research and industrial applications. In 2003 the 1st International Symposium on Diffraction Structural Biology (ISDSB 2003) was held in Tsukuba hosted by the 169th Committee, followed by the 2nd International Symposium (ISDSB2007) in Tokyo in 2007 (a special issue was published in *Journal of Synchroton Radiation*; https://journals.iucr.org/s/issues/2008/03/00/), ISDSB2010 in Paris (a special issue was published in *Journal of Synchroton Radiation*; https://journals.iucr.org/s/issues/2011/01/00/), ISDSB2013 in Nagoya (a special issue was published in *Journal of Synchroton Radiation*; https://journals.iucr.org/s/issues/2013/06/00/), ISDSB2016 in Knoxville (a special issue was published in *Acta Crystallographica Section D*; https://journals.iucr.org/d/issues/2018/08/00) and ISDSB2019 in Osaka (a virtual issue was compiled of articles published in *Acta Crystallographica Sections D* and *F*; https://journals.iucr.org/special_issues/2021/ISDSB2019/).

The Seventh International Symposium on Diffraction Structural Biology (ISDSB2025) was held from 5 to 7 May 2025 at the European Photon and Neutron Science (EPN) Campus in Grenoble, France, providing a particularly fitting setting for the meeting. The EPN Campus brings together EMBL, ESRF, ILL and IBS, combining expertise and infrastructure in X-ray, neutron, electron and complementary approaches and exemplifying the increasingly integrative nature of contemporary structural biology.

The scientific program reflected the remarkable expansion of the field since the first ISDSB meeting, encompassing dynamic and four-dimensional structural biology, tomography




 https://doi.org/10.1107/S2059798326011307 

and correlative approaches, electron diffraction, neutron diffraction and scattering, structure-based drug discovery, integrative structural biology, and the rapidly expanding contributions of artificial intelligence, software and structural databases. Rather than being centred on a single experimental technique, the programme highlighted how different experimental, computational approaches and scales of observation are increasingly combined to address biological questions that cannot be resolved by any one method alone.

The breadth of modern diffraction structural biology is well illustrated by the articles assembled in this ISDSB2025 Collection. They span developments in X-ray, electron and neutron diffraction, small-angle X-ray scattering, experimental facilities and computational structural biology. Collectively, they illustrate an important shift in emphasis: from determining individual molecular structures towards describing conformational ensembles, dynamics, interactions and increasingly complex biological assemblies, and towards connecting molecular structure with biological function across spatial and temporal scales.

The contributions to this collection illustrate an important evolution in the meaning of Diffraction Structural Biology. X-rays, neutrons and electrons remain powerful and complementary physical probes of biological matter. Their impact is increasingly amplified by their integration with scattering, cryo-electron microscopy, tomography, NMR, spectroscopy, imaging and computational approaches. The boundaries between individual structural techniques are consequently becoming less important than the biological questions they can address together.

In this respect, the original concept of Diffraction Structural Biology contained many principles that are now widely referred to as integrative structural biology. The emphasis on bringing together different probes, methodologies and scientific communities remains as relevant today as it was when the ISDSB series began. What has changed is the extraordinary range and power of the available approaches: synchrotron radiation and X-ray free-electron lasers, next-generation neutron sources, electron diffraction, cryo-electron microscopy, NMR, hybrid approaches of these techniques, advanced detectors and sample environments. At the same time, advances in computational modelling and artificial intelligence now provide complementary tools that are changing both how structural data are interpreted and how experimental questions are formulated, opening windows onto biological structure across an unprecedented range of spatial and temporal scales.

More than twenty years after the first ISDSB meeting, the challenge for structural biology is therefore no longer simply to determine molecular structures precisely with ever higher resolution. Increasingly, studies revolve around which structural states are biologically relevant; how molecules change, interact and assemble; how these processes depend on their environment and evolve with time; and how information obtained from different experimental and computational approaches can be combined into coherent, testable models of biological mechanism. An equally important challenge is to understand the accuracy, uncertainty and limitations associated with these models, albeit no doubt as precise as possible, particularly as experimentally determined and computationally predicted information become increasingly intertwined. Combining the outcomes from different individual methods on a single macromolecule or complex is needed to separate out the method-dependent aspects of their individual models to bring us as close as possible to the truth of the living cell.

The contributions collected from ISDSB2025 illustrate several important steps in this continuing evolution, including a PDB survey article of body-temperature biological macromolecule crystal structures and their ligands for pharmaceutical applications (Brink *et al.*, 2026), the design (Bertelsen *et al.*, 2026) and development (Yamada *et al.*, 2026) of new macromolecular crystallography beamlines, advanced techniques for structural biology (Shaikhqasem *et al.*, 2026; Guillotin *et al.*, 2026; Paknia *et al.*, 2026) and a wide sample of the range of the ISDSB 2025 subjects (Hutin *et al.*, 2026); the full range of topics covered is listed at the conference website (https://www.psb-grenoble.eu/isdsb2025/).

One particularly striking message emerging from ISDSB2025 is therefore that 'Diffraction Structural Biology' has become broader rather than less relevant. Diffraction remains at its core, but increasingly forms part of a continuum of experimental and computational observations spanning atoms, molecules, assemblies and cellular structures, and extending from static structural descriptions towards dynamic biological mechanisms.

We hope that this collection conveys both the vitality of diffraction-based structural biology and its increasing integration with the wider landscape of structural science. In the spirit in which the ISDSB series was established, we also hope it will stimulate further interactions among researchers using X-rays, neutrons, electrons, scattering, spectroscopy, imaging and computational approaches, and help to develop new experimental and conceptual connections capable of addressing increasingly complex questions in biology and medicine. We look forward to the next ISDSB.

## References


Bertelsen, M., Willendrup, P. K., Yoo, S., Meligrana, A., McDonagh, D., Bergmann, J., Oksanen, E. & Finke, A. D. (2026). *Acta Cryst.* D**82**, 751–760.

Brink, A., Helliwell, J. R. & Jacobs, F. J. F. (2026). *Acta Cryst.* D**82**, 1–10.

Guillotin, A., Hutin, S., Masselot-Joubert, L., Hammani, K., Zubieta, C. & Nanao, M. (2026). *Acta Cryst.* D**82**, 421–433.

Hutin, S., Filho, P. L. O., Popov, A. M., Pernot, P., Zubieta, C. & Tully, M. D. (2026). *Acta Cryst.* D**82**, 940–946.

Paknia, E., Flensburg, C., Chodkiewicz, M. L., Fogh, R. H., Keller, P., Vonrhein, C., Schulze-Briese, C., Dominiak, P. M., Bourenkov, G., Bricogne, G. & Chari, A. (2026). *Acta Cryst.* D**82**, 1044–1055.

Shaikhqasem, A., Hamdi, F., Machner, L., Parthier, C., Breithaupt, C., Kyrilis, F. L., Feller, S. M., Kastritis, P. L. & Stubbs, M. T. (2026). *Acta Cryst.* D**82**, 11–22.

Yamada, Y., Sakurai, K., Fukuda, A., Yamane, H., Hatano, T., Nakamura, T., Ueno, G., Masunaga, T., Yamamoto, M. & Nango, E. (2026). *Acta Cryst.* D**82**, 23–29.