

Sine Ydun Larsen (1943–2025)

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Figure 1
Sine at the IUCr Congress in 2008, the year she was elected as President of the IUCr.

1. A picture of Sine Larsen

There is a picture of Sine Larsen, shovel in hand and a broad smile on her face, celebrating the ground-breaking for the first building for the Partnership for Structural Biology, the CIBB. This is the perfect image of Sine – she is in the midst of things as Science Director at the ESRF, joining forces with the ILL the EMBL and the IBS to strengthen life science in Grenoble and indeed in Europe as a whole. She is smiling, ever positive and seeing possibilities where others might only see challenges and she is preparing for hard, manual labour. If she had not been stopped, she would have dug out the entire foundations by herself. She was not afraid of work, coming from hardy, Danish farmer's stock.

Those of us who were there that day with her also know that she was in a hurry. Not because she really needed to finish the foundations before sundown, but because this was the 8th of June 2004 and she was loath to miss the transit of Venus across the face of the sun that was taking place concurrently. Sine was



Figure 2
Sine breaking ground for the first building for the Partnership for Structural Biology (CIBB).

first and foremost a scientist, and regardless of the fact that her chosen fields were crystallography and chemistry, her curiosity was boundless and this chance to take part in a scientific once-in-a-lifetime event was not one she was willing to miss, so she finished her digging and had us all enjoy the celestial happening.

Starting her career as an inorganic chemist and then switching to structural biology gave her an ideal background for someone so integral to the IUCr. She knew how diverse structural science is, and she took great pride in having published in most of the IUCr journals, if not all.

Sine was long in the service of the IUCr. She was appointed General Secretary and Treasurer in 1995, following the death of her predecessor, Asbjörn Hordvik, and she was then elected and reelected to that same post 1996, 1999 and 2002, serving ten years as GS&T and on the Executive Committee of the IUCr. In 2008, she was elected President of the IUCr and served another six years on the Executive Committee, first as President and then as Immediate Past President. For us who worked with her, there are precious memories of her no-nonsense competence, her energy, her enthusiasm and her great hospitality when she would host lavish dinners for the entire Finance Committee during our meetings in Copenhagen.

She had a rare combination of scientific, managerial and people skills that made her singularly well suited for our community. Seemingly effortless, she would navigate the crowds at the gatherings during Congress and General Assembly. She knew everyone and remembered the names of everyone, stopping for a quick word. She saw people and

made people feel being seen, whether they'd be IUCr staff, university professors or young and hopeful graduate students.

Sine was kind and considerate, but she was no softie. In her capacities as scientific director at the ESRF and as general director at the MAX IV synchrotron in Lund as well as during her work for the IUCr, she showed that she was capable of making hard decisions when needed. She did not take on executive duties in order to become loved. That happened anyway.

She is much missed. The crystallographic community is poorer without her.

Sven Lidin, former President and General Secretary and Treasurer of the IUCr.

2. IUCr activity

Sine Larsen's death has deeply saddened all those of us who have had the privilege to work with her on the IUCr's Finance Committee. She was elected to the Executive Committee as its General Secretary and Treasurer in 1996. In this role, which placed her firmly on the Finance Committee as well, she had responsibility not only for the overall financial health of the Union but also the operation of its Chester Office, a dual role that she fulfilled admirably for nine years. There is no doubt that the wellbeing of the IUCr became her passion and its mission to support crystallographers around the globe was close to her heart. She rapidly learned the many financial intricacies of our scientific journal publishing business, which provides the Union's livelihood. She brought in an analysis of the finances of each journal by instituting activity-based accounting, whereby relevant costs were apportioned to each journal individually and set against its revenue stream. Then it became obvious where gains and losses occurred and therefore what action was needed. This clarity was most helpful in guiding the development of the journals.

Sine also cared deeply about the staff who worked in Chester: there was rarely a working day when she did not ring in from Denmark to enquire about the state of play, according to Mike Dacombe, then IUCr's Executive Secretary. She also visited Chester regularly and during those visits she made it her business to talk to the staff and uncover whether there were any problems that needed addressing. Sine and Erik's hospitality to the Finance Committee when it met annually in Copenhagen was legendary: she regarded us all as part of her global family. She was indeed a most caring General Secretary and Treasurer, and when she became President in 2008 she continued in the same vein. Sine worked so hard to secure a healthy future for the Union, one in which we had sufficient funds for crystallographers from around the world to benefit from IUCr support, for example for attendance at international schools and conferences. She was also fully involved in creating a viable financial basis for IUCr's major initiatives such as the 'electronification' of the journals and the establishment of new journals. She supported the journals in other ways too and acted as an Editor on its flagship journal *IUCrJ*.

In everything she did, her knowledgeable advice and sound judgement were always much valued. We all respected her

greatly, not only as an internationally-leading individual scientist and research director but also as a wise and very approachable friend. She is sorely missed by all of us.

Malcolm Cooper, Convenor, IUCr Finance Committee.

3. Sine at the ESRF

Professor Sine Ydun Larsen came to Grenoble, France in 2003 to take up her role as ESRF Director of Research for Chemistry, Life and Medical Sciences and Soft Matter Science. She stayed until late 2009, when she decided to return to her position as Professor at the University of Copenhagen. During this period of almost seven years, she worked side-by-side with Dr Francesco Sette, who was serving as Director of Research for Physical Sciences until the end of 2008, while Professor W. G. Stirling was ESRF Director General (DG). For the remainder of her time at the ESRF, Sine worked with Dr Harald Reichert, who became Director of Research for Physical Sciences in early 2009, and with Francesco who started to serve as DG.

This was a very exciting time at the ESRF, and many projects that were crucial to ensure the full exploitation of the facility and to prepare for the future benefitted enormously from Sine's work: her enthusiasm, scientific knowledge, and ability to listen and to inspire contributed decisively to the ESRF of today, and to forging a new generation of ESRF users and scientists – especially in the biological sciences, soft matter research and novel cultural heritage disciplines based on synchrotron radiation.

Sine was instrumental in stabilizing the structural biology programme at the ESRF, which, since the late 1990s, was starting to fully exploit undulator radiation to study protein crystals with exceptionally large unit cells and increasingly smaller size. Under her leadership, and in close collaboration with the neighbouring institutes EMBL Grenoble and the Institut de Biologie Structurale (IBS), the ESRF led the way to today's modern macromolecular crystallography (MX) with outstanding innovations: the realization of the first fully automated MX beamlines with robotic sample changers, ultra-high-precision micro- and mini-diffractometers, large-area silicon-based 2D detectors, and advanced automated control of crystal harvesting, alignment, data collection and processing. This orders-of-magnitude increase in throughput and performance brought unprecedented quality to MX data and set a new standard for MX worldwide. This has led to reliable and massive contributions to the Protein Data Bank (PDB), a reliable and a highly sought-after commercial service for pharmaceutical companies, and a fantastic science-based cooperation among structural biology users with the introduction of the MX beamtime Block Allocation Groups (BAGs) concept. These advances were pivotal in shaping what MX is today, and led directly to the Nobel Prizes in Chemistry in 2009 (structure of the ribosome), 2012 (structure of the cell-membrane G-protein-coupled receptors, GPCRs) and 2024 (AI-assisted protein structure prediction). During this period, Sine was also directly involved in the launching and expansion



Figure 3
Sine on the footbridge of the Experimental Hall, ESRF. Photograph by E. Bouy.

of the Partnership for Structural Biology (PSB), an on-campus partnership among EMBL, ESRF, IBS and the Institut Laue-Langevin (ILL), promoting cutting-edge science and technological pipelines for the advancement of integrated structural biology, benefitting both on-site scientists and ESRF and ILL users worldwide. This fantastic adventure, today more active than ever, supports over twenty specialized platforms covering the entire protein research pipeline: starting from protein identification, production, purification, crystallization and biophysical characterization, to structure determination with the most advanced techniques using synchrotron X-rays, neutrons and electron microscopy, including state-of-the-art data analysis and storage for on-site users and users worldwide. Beyond these cutting-edge technologies, the PSB has contributed to the graduation of more than 400 PhD students, the research and training of 300 postdoctoral researchers, and more than 650 publications involving several PSB partners, which in turn benefitted greatly from Sine's unparalleled ability to inspire and motivate students and young scientists. The PSB model, a pioneering framework for coordinating and optimizing resources within a local science- and technology-driven ecosystem, has become an example and a gold standard for scientific collaboration in Europe and worldwide. We are grateful to Sine for her foresight and formidable engagement at the beginning of the PSB adventure, which required uniting hundreds of people – from the ESRF, the EPN Science Campus, the user community at large and the ESRF governing bodies – to work effectively together on a complex and multifaceted project.

Similarly, immediately after the launch of the PSB, under Sine's impulse, the ESRF and the ILL created the Partnership for Soft Condensed Matter (PSCM), a new endeavour that mirrors the PSB in terms of organization and user support with research-driven technology platforms, training objectives for the next generation, and coordination of the user community. Indeed, today the PSCM continues its mission to support the soft matter research community on-site and across the user organizations of the ESRF and ILL partner countries

by providing ancillary platforms to the ESRF and ILL beamlines that are required for the preparation and characterization of soft matter samples before and after X-ray and neutron experiments. Again, the continued and growing success of the PSCM can be measured by the numerous European academic institutions associated with it, and a very productive community performing experiments made possible by the expertise and infrastructure of the PSCM.

During the first decade of the new millennium, the ESRF broadened its scientific horizons to address new areas of exploitation of synchrotron radiation by developing new interest in coupling established X-ray techniques with emerging microscopy and imaging capabilities, including exploitation of beam transverse coherence. Sine provided a major impulse in this direction in activities that were just coming to life at that time. The most striking example is the development of analytical studies based on the use of X-ray and infrared spectro-microscopy in the field of cultural heritage. What was once truly in its infancy gained enormous growth, and Sine's commitment, motivation and support of the internal staff involved in this new endeavour, as well as her ability to build up a network of users in Europe, Israel and Cyprus, was simply outstanding. Much like her contributions to the PSB and the PSCM, it is also thanks to Sine's engagement, vision and ability to bring many people working together from many different disciplines that nowadays the use of synchrotron radiation has become an indispensable tool for studying the most subtle and complex issues in the analysis of precious artefacts at the ESRF, as well as at almost every synchrotron laboratory in the world.

The ESRF Upgrade Programme Phase I, whose conception began in 2004 with a first paper by Francesco Sette and José Goulon, benefitted greatly from Sine's contributions, particularly in the fields of structural biology, biomedical sciences, soft matter research, and X-ray imaging and microscopy. She contributed directly and indirectly to the process, establishing the ESRF Upgrade Programme as a reference for future synchrotron-radiation research in Europe and worldwide. This influence was evident in its inclusion as the only synchrotron-based project on the ESRFI Roadmap since its inception in 2006, and in the drafting of the ESRF Purple Book, the launch of which, in late 2007, enabled the ESRF Council to approve the funding and implementation of the ESRF Upgrade Programme in 2008, during its June meeting in Bad Zurzach (Switzerland).

A distinguished figure in the field of crystallography, with major contributions to both structural biology and structural chemistry documented in 300 peer-reviewed publications, and the recipient of the 2018 Max Perutz Prize from the European Crystallographic Association, Sine was an outstanding scientist. But Sine was much more than that, and her legacy is huge from many points of view! She was a visionary leader who made possible many outstanding developments for synchrotron-radiation research and the optimal operation of synchrotron facilities, thanks to her remarkable ability to inspire people, especially the younger generation of researchers, to unite them, to make each of them a unique

collaborator, and to build mutual trust through her genuine care for others, and by giving each of us who had the privilege of knowing her, her unique smile.

Itziar Echeverria, Head of the Director General Office, Directorate, ESRF; Montserrat Soler Lopez, Head of the Structural Biology Group, Experiments Division, ESRF; Francesco Sette, Senior Scientist, Experiments Division (former Director General and former Director of Research), ESRF.

4. Sine and the Danish protein crystallography community

Sine studied chemistry at the Department of Chemistry, University of Copenhagen (UCPH) and obtained a degree in small molecule crystallography in 1968. It was during her time in the USA as a postdoc at MIT that Sine first became interested in protein crystallography before she returned to Denmark and became employed at the Department of Chemistry as Associate Professor. Apart from a few stints at the ESRF and MAXIV – during which Sine was still affiliated with and maintained an active group at UCPH – she remained associated with the department for a total of 55 years.

In the early years, Sine was one of the few female faculty members and also the first woman to take up a full professorship at the Department of Chemistry of UCPH, and she therefore became a very important role model, particularly for female students and younger colleagues. Sine's research focused primarily on structural analysis of small molecules using X-ray crystallography. However, with the establishment of a centre of excellence funded by the Danish National Research Foundation in 1993, the aptly named Centre for Crystallographic Studies, she took a leading role in Danish protein crystallography. This led to close and fruitful long-term collaborations with another centre of excellence led by Professor Kaj Frank Jensen, who was studying nucleotide metabolism enzymes, as well as with several major Danish biotech companies – especially focusing on the structure and function of carbohydrate modifying enzymes with potential for bioconversion.

In general, Sine was exceptionally good at attracting and supporting a large number of students in her group, some of whom met her through high school projects, others through regular teaching in their second year BSc physical chemistry course. This success was largely due to Sine's amazing ability to convey excitement for her research, as well as a genuine interest in students and young researchers as human beings. Sine truly distinguished herself by remembering all the students she had taught by name and often even those she had met outside her regular teaching.

The Centre for Crystallographic Studies quickly made Sine's group the largest at the department at that time. The group worked with both small molecules and proteins, on topics ranging from very fundamental to applied projects, from charge-density studies and hydrogen bonds to allosteric regulation of enzymes and protein engineering. Sine managed to create a truly attractive and international environment for

students and young researchers, with strong support for family life embedded within the spirit of the laboratory. This included a room for changing a large number of babies' diapers and a lively atmosphere late into the evening. Indeed, Sine was often so busy that if you needed to talk with her, it often became very late.

Sine remained active until the end. She returned from a European Crystallography Meeting in 2021 inspired by the recent advances in user-accessible electron diffraction instruments and immediately got the department's potential stakeholders involved – because UCPH had to have one! In 2024, we inaugurated the department's new electron diffractometer, granted to Professor Jesper Bendix by the Novo Nordisk Foundation. Sine was invited as a special guest and the instrument is named after her.

Community spirit, farming and glögg. Along with colleagues from Lund and Aarhus University, Professor Anders Liljas and Jens Nyborg, Sine was essential in establishing and maintaining a larger community of young protein crystallographers in Denmark and Southern Sweden, particularly through the CoLuAA (Copenhagen–Lund–Aarhus) annual protein crystallography meeting. This meeting series – lasting close to three decades – was centered on a strong focus on students and early researchers, and an informal inclusive atmosphere where every project was good enough for a talk. This provided an excellent training ground for young researchers in the field to present their projects and practice their presentation skills in front of a friendly audience. The meeting series also created a strong network of both young

and established researchers in the field across southern Scandinavia.

Sine prioritized and managed to gather the whole group – and collaborators – for large social events which forged friendship and collaborations across generations of group members. Two traditions that stand out are the summer parties and the Christmas events. Typically, at least 100 people gathered for the summer parties, held at Sine and her husband Erik's working farm, and the weather was almost always excellent (not at all a given in Denmark). Christmases were marked by glögg parties (glögg is the Danish version of mulled wine), which took place at the department. The last Christmas glögg party was held only a couple of years ago in 2022. And even then, many years after Sine officially retired, over 50 former students and postdocs (and their students!) gathered with their families. A similar number joined many more family members, friends and former colleagues for a last goodbye – Sine's last party? – at Lillerød church on the 14 January this year. The connections she helped establish as a mentor will last many more generations. In recognition of her remarkable achievements to science and the scientific community, the University has dedicated one of its new gardens in the Niels Bohr Building, the newly inaugurated future home of several departments of the Faculty of Science at UCPH, to Sine Larsen.

Head of Department Pernille Harris and Professor Leila Lo Leggio, Department of Chemistry, University of Copenhagen, on behalf of the Danish protein crystallography community.