STRUCTURAL CHEMISTRY
ISSN 2053-2296

Data collection is your last experiment

Tim Gruene*

Institute of Inorganic Chemistry, Faculty of Chemistry, University of Vienna, Austria. *Correspondence e-mail: tim.gruene@univie.ac.at

Received 5 June 2024
Accepted 5 June 2024

The title is a quote from Dauter (1999).

Keywords: chemical crystallography; MicroED; 3D ED; electron diffraction.

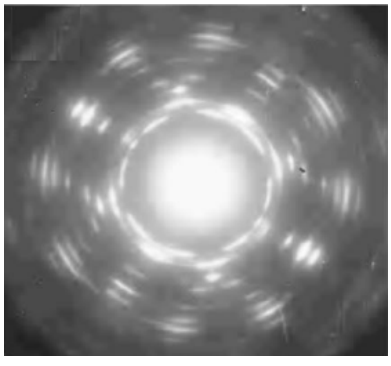
Exciting developments are unfolding in the realm of chemical crystallography, especially with the profound impact of electron diffraction and the remarkable progress it has witnessed in recent years. The perception that structure determination through electron diffraction is solely an academic pursuit or a niche area no longer holds true. It has become increasingly practical and feasible, mirroring the wealth of information attainable through X-ray crystallography. One of the most important milestones in that respect is determination of absolute configuration (Brázda *et al.*, 2019).

The forthcoming special edition of *Acta Crystallographica Section C: Structural Chemistry* features two noteworthy studies on natural products, underscoring the maturation of electron diffraction in this field (Gurung *et al.*, 2024; Decato *et al.*, 2024).

Key to the success of electron diffraction are the similarities in experiment execution and data collection processes between X-ray and electron diffraction, rendering electron diffraction an innovative frontier for experienced X-ray crystallographers. The surge in the acceptance of electron diffraction can be attributed, in part, to the availability of dedicated electron diffractometers, such as Rigaku's Synergy-ED and ELDICO's ED-1. Quite a respectable number of these instruments have been installed at least in Europe and other regions are catching up. Prior to the availability of dedicated electron diffractometers, TEM manufacturers have been offering software packages (microED packages) as add-ons to their normal software. In my experience, sharing a TEM for imaging with other groups means cutting back instrument time for diffraction studies, hence good planning should precede the decision of what type of instrument is being purchased.

In addition to the logistic advantage that there will be no debate whether the next experiment will be for electron microscopy or for electron diffraction, these new electron diffractometers have great technological advantages.

ELDICO Scientific developed an intriguing design, a horizontal flight tube – many doubted that a horizontal flight tube would at all be possible, because electron microscopes have always been vertical – like light microscopes. This design makes the instrument very much akin to an X-ray in-house diffractometer. The instruments interfaces with familiar integration packages, like the Bruker *APEX* suite, as well as the specialized *PETS*, and also *DIALS* or *XDS* can be used. Not only is the design appealing, the sample chamber is one of the stand-out characteristics of the ED-1. The horizontal flight tube has a vertical rotation axis as a consequence, which does not have to fight for gravity and thus feature a very stable rotation with a very small sphere of confusion. Unlike electron microscopes, the sample chamber is large, giving much freedom in the sample holder, and the sample changing mechanism.



Rigaku and JEOL teamed up to bring the Synergy-ED to the market. Rigaku is a well-established manufacturer of in-house X-ray diffractometers. Rigaku joined forces with JEOL to create the Synergy-ED, based on a slightly modified electron microscope, with an improved goniometer, and a lens system better suited for diffraction studies than conventional TEMs. Unnecessary to mention: both instruments sport hybrid pixel detectors that reduce noise and show the direct beam without the need for a beamstop, which is of aid for data processing.

For both instruments, crystallographic software guarantees a smooth workflow for sample selection and data collection, and offers many different routes downstream for structure solution and refinement, including the use of *PETS*, which is currently the only route to determine the absolute structure from electron diffraction data (Palatinus *et al.*, 2015).

For both instruments, a rule of thumb applies: the learning curve for a crystallographer is steep to operate an electron diffractometer, since there are many analogies, and only a few extra bits need to be acquired. One paradigm is shifting from macromolecular crystallography to chemical crystallography: The dose (as in energy per mass unit) that a particle can take before it gets seriously damaged depends linearly on the volume of the particle. Hence, with samples being several orders of magnitude smaller in volume, care should be taken to avoid radiation damage. the crystallographer needs to assess the stability of the crystal in the beam and adjust the data collection strategy accordingly: accept a single large data set at reduced intensity and thus at reduced maximum resolution, or collect data at strong intensity and merge data from several crystals. There is no one-rule-fits-all, and it is easy to sacrifice one or two crystals to find out and adjust.

Electron crystallography has been a get-together for scientists with a great variety of backgrounds. With its origin in materials science, ED attracted attention from people in mineralogy and the research of inorganic compounds, in chemical crystallography, structural biology, and nearly all disciplines of crystallography. This issue of *Acta Crystallographica Section C: Structural Chemistry* also reports the broad interest from structural biologists with background in electron microscopy (Aragon *et al.*, 2024). Methods developers are motivated, and data quality is making great leaps forward.

Crystallography has a long tradition as a guardian of quality, and critical assessment of structural quality has been emphasized across the broad field. Now, with many newcomers drawing their attention to crystallography, it is important to maintain our high level of quality assessment. Newcomers may not be familiar with the high degree of openness at with scientific questions are handled, discussed and shared on mailing lists (examples being the CCP4 Bulletin Board, https://legacy.ccp4.ac.uk/ccp4bb.php, and the Bruker mailing list, bruker-axs@g-groups.wisc.edu). Crystallography has been one of the main pillars of open data science (Brink *et al.*, 2024; Giess *et al.*, 2023), with many programs being open source, or available free of charge for academic use, and excellent training opportunities with expert teaching.[1]

Acknowledgements

The author used ChatGPT to improve the language in the article.

References

Aragon, M., Bowman, S. E. J., Chen, C.-H., de la Cruz, M. J., Decato, D. A., Eng, E. T., Flatt, K. M., Gulati, S., Li, Y., Lomba, C. J., Mercado, B., Miller, J., Palatinus, L., Rice, W. J., Waterman, D. & Zimanyi, C. M. (2024). *Acta Cryst.* C**80**, 179–189.

Brázda, P., Palatinus, L. & Babor, M. (2019). *Science*, **364**, 667–669.

Brink, A., Bruno, I., Helliwell, J. R. & McMahon, B. (2024). *IUCrJ*, **11**, 9–15.

Dauter, Z. (1999). *Acta Cryst.* D**55**, 1703–1717.

Decato, D., Palatinus, L., Stierle, A. & Stierle, D. (2024). *Acta Cryst.* C**80**, 143–147.

Giess, T., Itzigehl, S., Range, J., Schömig, R., Bruckner, J. R. & Pleiss, J. (2023). *J. Appl. Cryst.* **56**, 565–575.

Gurung, K., Šimek, P., Jegorov, A. & Palatinus, L. (2024). *Acta Cryst.* C**80**, 56–61.

Palatinus, L., Petříček, V. & Corrêa, C. A. (2015). *Acta Cryst.* A**71**, 235–244.

[1] CCP4 developers have been holding CCP4 workshops worldwide for a very long time (see https://www.CCP4.ac.uk/workshops; visited on 31/05/2024), the Erice Crystallography Workshop has been running since 1974 (see https://crystalerice.org/2024; visited on 31/05/2024) and Dr Michael Bodensteiner and colleagues organized the 1st Munich Crystallography Workshop in 2023 (see https://www.crc.tum.de/crc/events/workshops/munich-crystallography-workshop; visited on 31/05/2024).