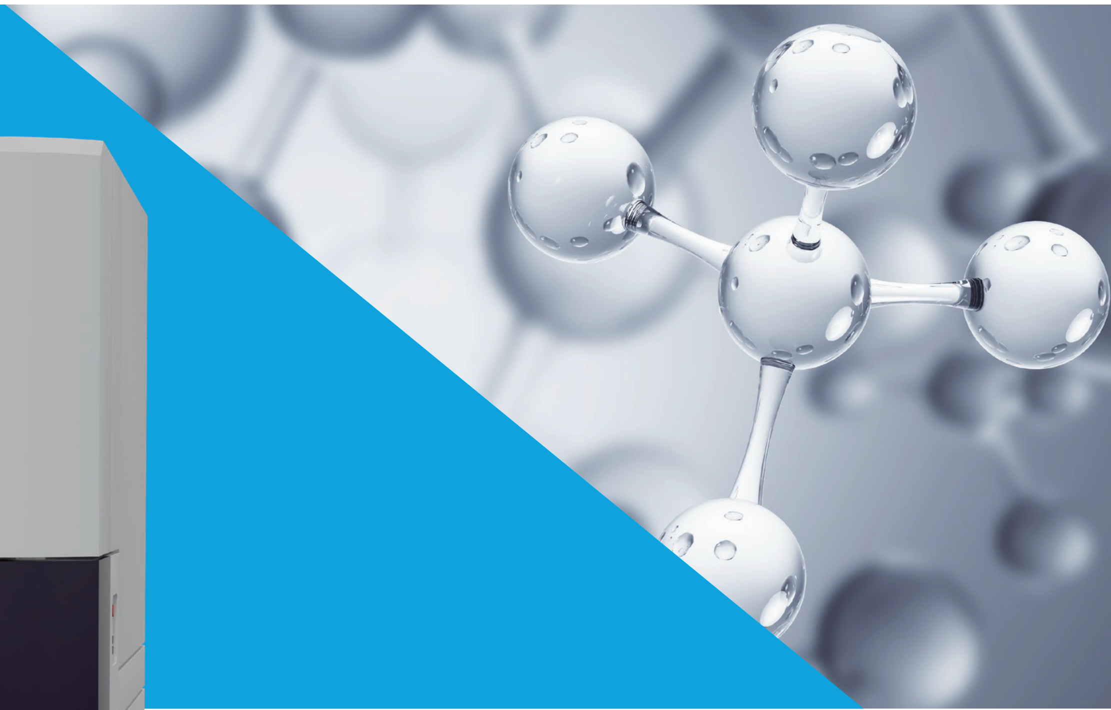
# XtaLAB Synergy-ED

## Fully integrated electron diffractometer




Rigaku

POWERING NEW PERSPECTIVES

# XtaLAB Synergy-ED

## Empowering Crystallographers with 3DED/MicroED

- A dedicated electron diffractometer for nanocrystal structure determination
- Jointly developed by Rigaku and JEOL
- Turnkey, fully integrated hardware + CrysAlis$^{Pro}$-ED workflow

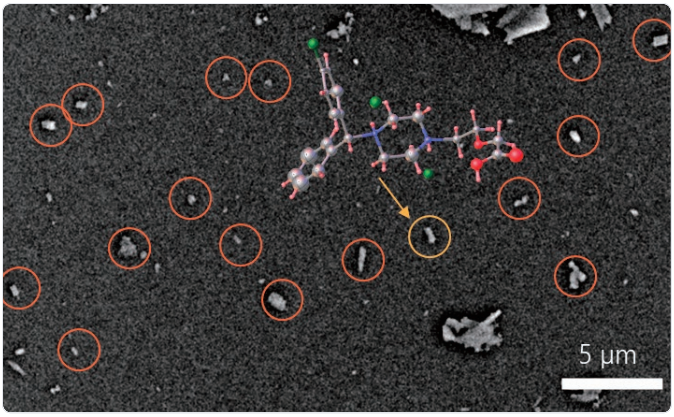

Three-dimensional structure remains the most information-rich analytical result. A single experiment can reveal atomic identity and connectivity, packing, and the intermolecular interactions that underpin properties and performance. Crystal structures explain why compounds behave as they do, how they respond to external stimuli, and they confirm synthetic outcomes with a level of certainty that few other methods can match.

However, many real-world samples sit outside the comfort zone of conventional single-crystal X-ray diffraction: crystals may be too small, form only as microcrystalline powders, or exist as mixtures and transient phases. In these cases, researchers often assemble partial evidence from multiple techniques - adding time in sample preparation, measurement, and data interpretation, and increasing uncertainty compared with a direct diffraction-based structure solution.

3D electron diffraction (3DED/MicroED) closes this gap. It delivers single-crystal structural information from sub-micron grains, directly from a powder, helping you move faster from “unknown solid” to an interpretable 3D structures and composition analysis with far less material than was previously practical. The Rigaku XtaLAB Synergy-ED makes 3DED/MicroED a routine technique. The instrument is designed specifically for diffraction and is controlled through a crystallography-centric workflow in CrysAlis$^{Pro}$-ED, integrating sample screening, data collection, processing, and structure solution so users can be productive without relying on specialist skills and toolchains.

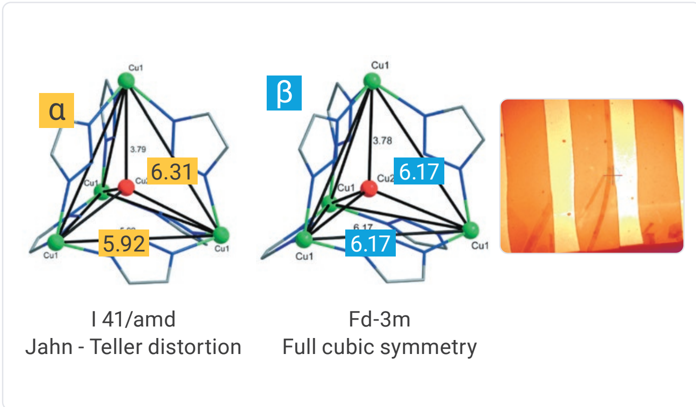
# What can MicroED/3DED do for you?

The most obvious advantage of electron diffraction is the ability to study crystals well below 1 µm in size. This can extend structure determination to scarce samples and materials that are difficult to crystallise, where X-ray approaches even at synchrotron sources may struggle to obtain single-crystal data. [1] But it's not just about small samples: In practice, 3DED/MicroED often sits between SCXRD and PXRD: you can solve structures from individual powder grains, while also screening many grains to understand what is really present in a bulk powder.



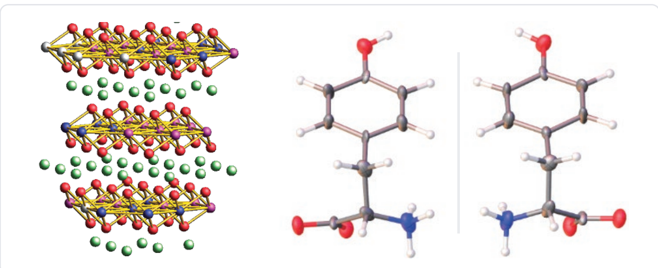

## Multiple grains

A standard 3 mm sample carrier (TEM grid) can host hundreds to thousands of crystalline grains, all accessible in a single loading. Using automated measurements, screen powders for phases and catch low-occupancy forms and contaminants that are hidden by dominant reflections or background in PXRD. For low-symmetry systems, boost completeness by collecting and merging data from multiple grains.



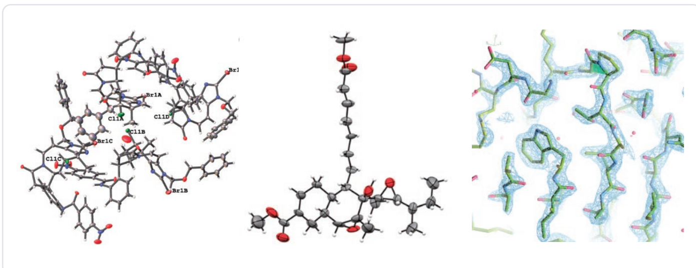

## Flexible environments

Synergy-ED is designed for compatibility with an ecosystem of TEM holders and established preparation methods. Work at room temperature, protect sensitive specimens using cryo-transfer or air-free transfer, apply heating or electrical biasing, expose samples to gases, or follow crystallisation in liquid environments. Optional EDS adds complementary elemental confirmation alongside diffraction.



## Unique insights

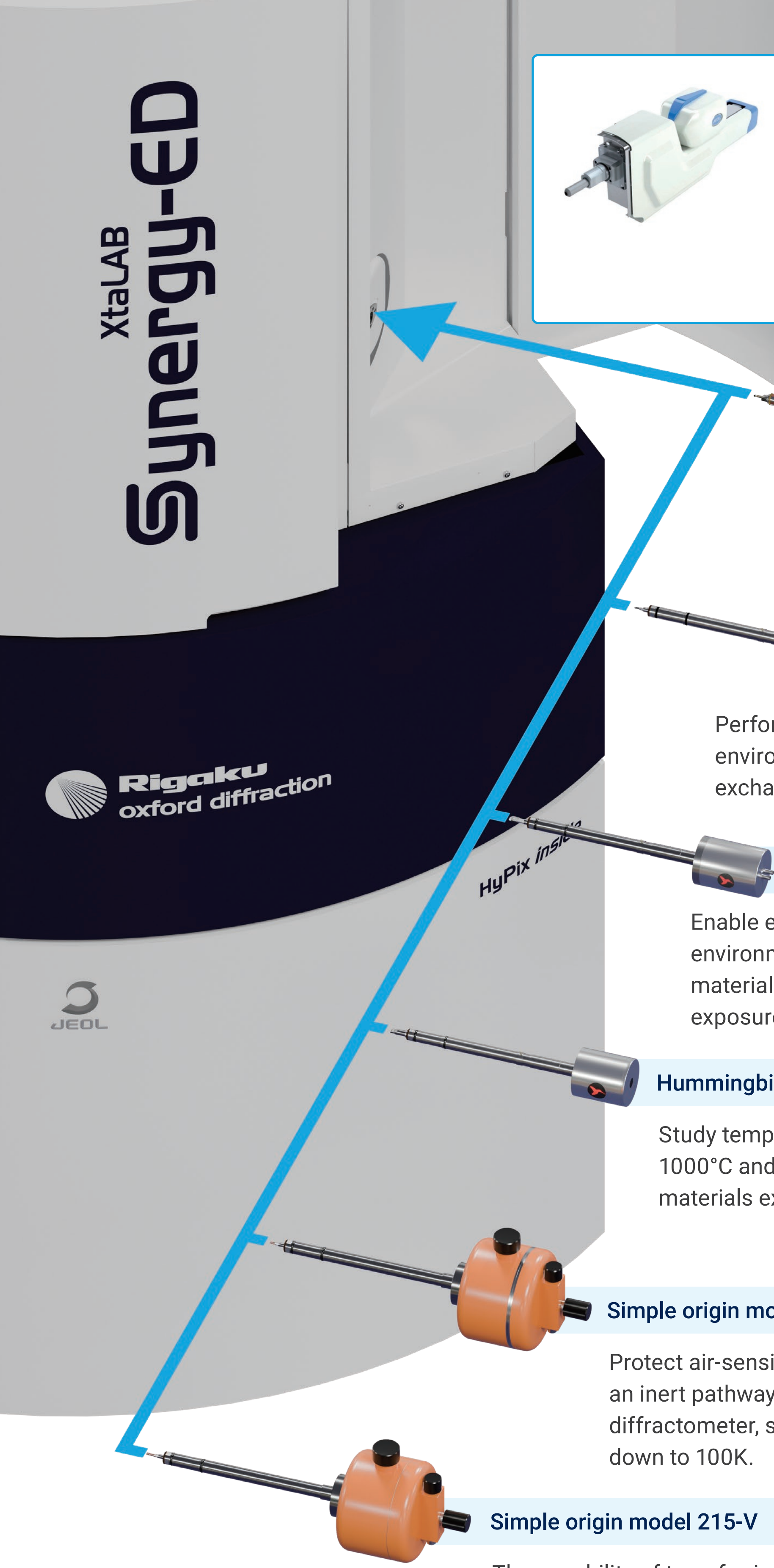
Beyond "just" solving structures, electron scattering enables advanced refinement approaches that can support absolute structure determination and improve treatment of light atoms, disorder, and occupancies - particularly in challenging cases. These workflows are integrated into the Synergy-ED software pathway, making them accessible without building a custom toolchain.



## Sample integrity

Beam damage is always a consideration at nanoscales. Because electrons generate strong diffraction signal from very small volumes, useful data can often be collected at low dose. Synergy-ED leverages a noise-free counting detector and dose-aware workflows to keep exposure as low as practical while maintaining data quality.

[1] Pearce. N et al, Nat Commun 13, 415 (2022) https://doi.org/10.1038/s41467-022-28022-3




### JEOL JED-2300 EDS/EDX spectrometer

Analyse sample composition alongside diffraction. Use electron-beam-induced X-ray emission to confirm which elements are present and assess relative quantities—particularly helpful for mixtures, impurities, and phase screening workflows.

### Tomography holder

Room temperature experiments with a wide tilt range (± 80°)

### Insight chips 4 channel liquid nano-channel holder

Perform experiments under a liquid environment. Flow-cell options enable solvent exchange *in situ* while monitoring structure.

### Hummingbird scientific gas holder

Enable electron diffraction under controlled gaseous environments - useful for humidity studies, porous materials research, and experiments where gas exposure is central to the experiment.

### Hummingbird scientific heating and biasing holder

Study temperature-dependent behaviour up to 1000°C and apply electrical biasing for functional materials experiments.

### Simple origin model 216-V

Protect air-sensitive samples during transfer, maintaining an inert pathway into the diffractometer. Inside the diffractometer, sample temperature can be controlled down to 100K.

### Simple origin model 215-V

The capability of transferring samples at low temperature is essential to protect samples from solvent loss during transfer into vacuum, and to mitigate radiation damage. Two grids can be loaded in one session - reducing changeover time and maximising throughput.

# The Workflow

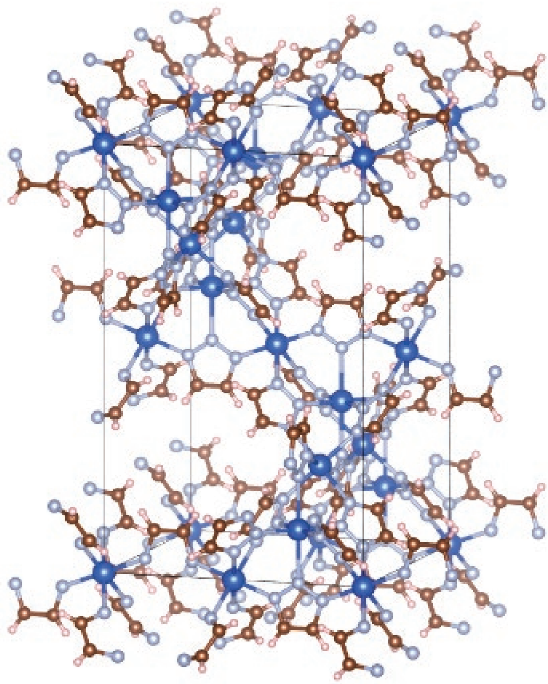
Electron diffraction took time to reach the mainstream of analytical techniques because routine success historically demanded atypical skills: transmission electron microscope (TEM) reconfiguration, operation and alignment, specialised acquisition tools, and convoluted data processing and structure determination pipelines. These requirements created a steep training burden and limited productivity for users whose primary expertise was X-ray diffraction and traditional crystallography.

With the XtaLAB Synergy-ED, these barriers fall. The platform delivers a crystallography-centric approach to 3 DED/ MicroED, allowing productive researchers from day one. All steps of the measurement pipeline, from instrument control and data collection to data processing and structure refinement, are integrated into the industry-standard CrysAlis$^{Pro}$ software, where crystallographers will feel right at home. No interaction with low-level electron optical components or regular complex alignment procedures are required.

- Familiar, crystallography-centred operation
- Guided, intuitive workflow in CrysAlis$^{Pro}$-ED
- Leverage your X-ray expertise

XtaLAB Synergy-ED is controlled by CrysAlis$^{Pro}$-ED to provide a unified experience aligned with Rigaku Oxford Diffraction X-ray diffractometers. For existing CrysAlis$^{Pro}$ users, the learning curve is minimal - so you can focus on rapid data collection, phase screening, and structure solution rather than microscope complexity. CrysAlis$^{Pro}$-ED extends the familiar workflow with electron-diffraction tools for screening, automation, and batch analysis across entire powder samples.

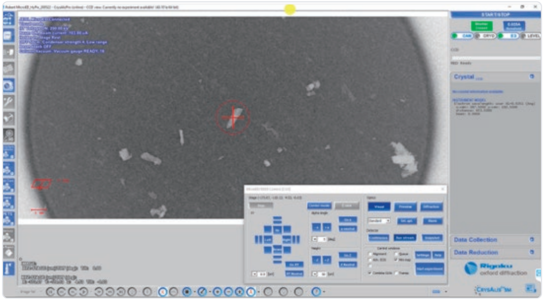
With many grains available on a single grid, throughput matters. CrysAlis$^{Pro}$-ED can run queues of manually or automatically selected crystals with minimal user intervention. Innovative cluster analysis and dataset-merging tools help group datasets by unit cell/phase, choose candidates for merging, and accelerate downstream structure determination.



## Prepare

Sample preparation can be as simple as sprinkling some powder onto a grid but approaches exist (slurries, cruching, cryo, air-free transfer, and more).

**Scan the QR code** for practical sample preparation guidance and best practices.



## Visualise and select

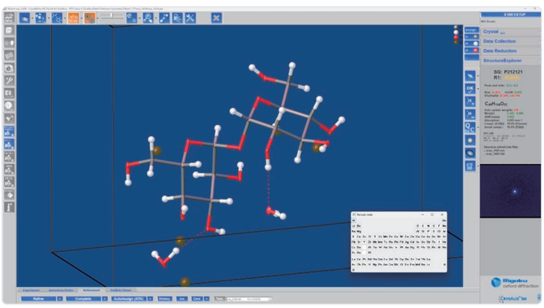
Navigate the grid in real time and identify candidate crystals at a glance. Select grains with a click (or use AI-assisted selection). Centre on the rotation axis for data collection automatically or with an intuitive semi-automatic routine.

## Queue or collect

Collect immediately, or add positions and parameters to a queue for unattended sequential measurements - ideal for screening powders, capturing minor phases, and increasing completeness via multi-crystal merging.

## Process

As with our X-ray diffractometers, data can be processed automatically as you collect. CrysAlis$^{Pro}$-ED provides ED-specific tools such as unit-cell clustering and dataset-merging utilities, with a streamlined path into AutoChem for structure solution.

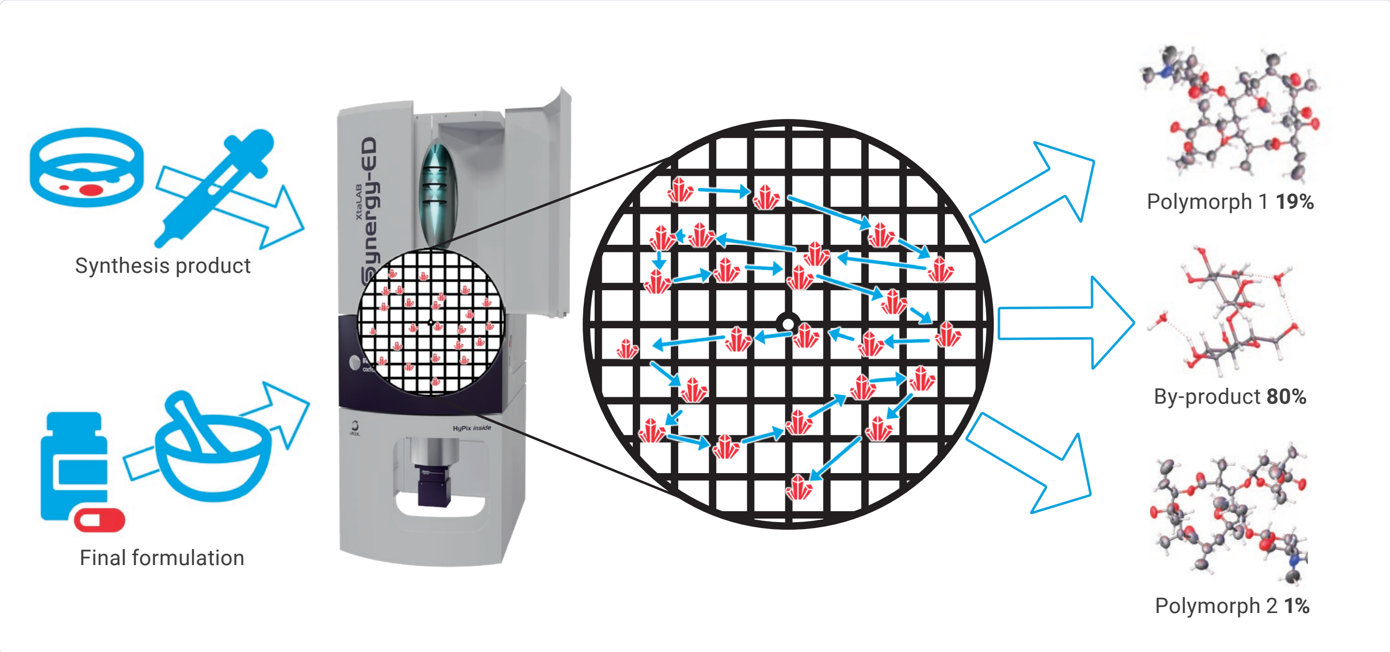


## Solve

AutoChem supports electron-appropriate scattering factors and (when needed) dynamical refinement workflows, providing a robust path from ED data to solved and refined structures—including support for absolute structure determination. Visualise results directly in CrysAlis$^{Pro}$ via Structure Explorer.

# XtaLAB Synergy-ED for pharma

Electron diffraction is increasingly valuable in pharmaceutical research because it enables rapid structural analysis of extremely small crystals that are often unavailable in sufficient size for traditional X-ray diffraction. This makes it particularly effective for polymorph screening, where detecting and differentiating crystalline forms early can influence drug efficacy, stability, and intellectual property. It also supports the identification of potentially harmful impurities and side products, ensuring safer formulations. Moreover, electron diffraction allows researchers to characterize patentable active pharmaceutical ingredients (APIs) at early R&D stages, accelerating innovation and protecting IP. Its ability to extract structural data from low-availability or scarce materials further enhances its utility, making it a powerful and highly valuable complement to conventional techniques in pharmaceutical development.

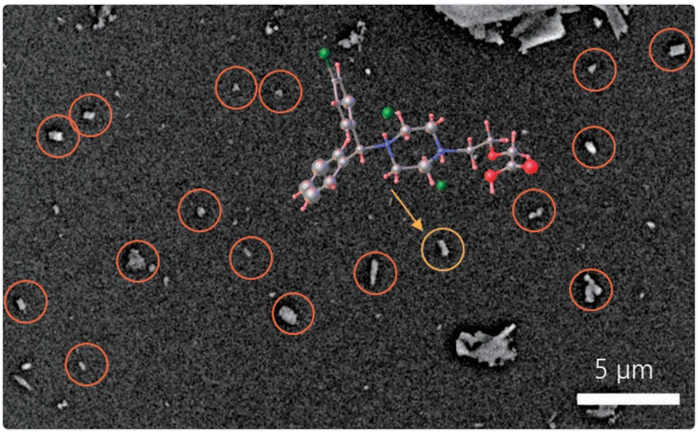



### Levocetirizine

(Karothu et al., Angew. Chem. Int. Ed.2023, 62, e20230376)

When attempting to identify polymorphs, racemates, or APIs within a mixture, electron diffraction proves especially powerful. Because a single grid can typically accommodate many crystal grains, it is ideally suited for samples with unknown composition or variable ratios of different forms.

For example, in the experiment described here, a sample containing both an excipient and the API was analyzed to demonstrate how electron diffraction can readily uncover the 'needle in the haystack. Among all the grains collected on the grid, only one belonged to the API, levocetirizine. Despite this low API-to-excipient ratio, the full crystal structure was successfully determined.




https://doi.org/10.1002/anie.202303761


## More pharmaceutical examples

### **De-risk polymorph mixtures**—without perfect separation

(Nakai et al., Cryst. Growth Des. 2025, 25, 24, 10619–10626)

When “Form A + Form B” refuses to separate, you still need answers. 3D ED/MicroED targets micron-scale single-crystal domains within mixed powders to:

- Confirm the presence of multiple polymorphs experimentally in a sample dominated by one form
- Solve and refine structures even in challenging cases (e.g., twinning)
- Convert “mixture uncertainty” into actionable structural evidence for solid-form strategy

https://doi.org/10.1021/acs.cgd.5c01477

### **Unlock elusive PROTAC Structures**

(Screen et al., J. Am. Chem. Soc. 2025, 147, 31, 28056–28072)

ROTAC drug candidates can be exceptionally difficult to characterize in the solid state because they are large, flexible molecules that often yield only very small crystals. In this study, 3D ED / MicroED enabled structure determination after extensive screening, revealing how these complex molecules pack in the solid state and which intermolecular interactions dominate.

https://doi.org/10.1021/jacs.5c07977

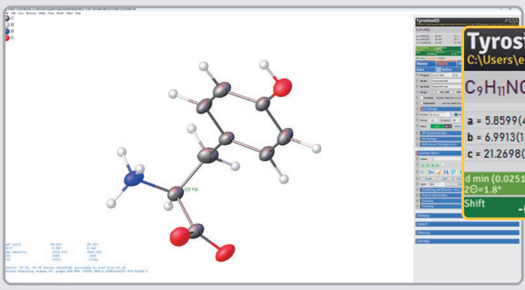
### **Resolve nitrosamine drug substance related impurities (and others)**—fast, from microcrystals

(Nakai et al., Org. Process Res. Dev. 2025, 29, 12, 3115–3125)

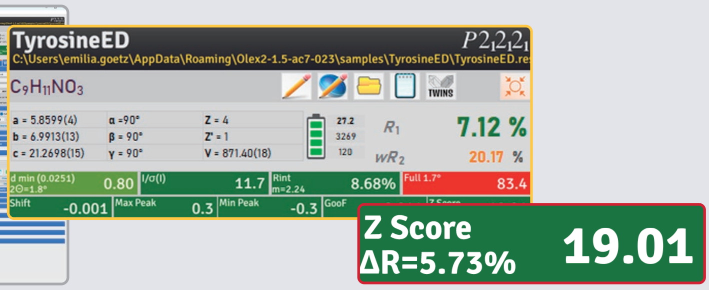
When an impurity triggers a risk assessment, structure clarity matters. 3D ED/MicroED supports:

- Structure determination across diverse nitroso compounds, demonstrating practical scope
- Confident structure assignment using electrostatic potential refinement (including hydrogen-related residual potential where informative)
- A direct path from “unknown crystalline impurity” to defensible structural evidence for decision-making

https://doi.org/10.1021/acs.oprd.5c00236



Dynamical refinement using n-beam algorithm




Z-score indicating confidence in chirality

As the proteins in our bodies are chiral so are many of the APIs that bind to them and chirality can affect drug action and efficacy. Determining the chirality of potential APIs is therefore of huge importance. Electron diffraction offers the possibility to determine the absolute structure via dynamical diffraction effects. Now CrysAlis$^{Pro}$ and Olex2 introduce a simpler, easy to use approach for dynamical diffraction, enabling absolute structure determination — n-beam refinement.

# XtaLAB Synergy-ED for porous materials

Electron diffraction is especially valuable for porous materials because many of the most important framework solids exist only as nanocrystalline powders, intergrown phases, or transient states that are difficult to characterize by conventional single-crystal X-ray diffraction. In these systems, small structural differences can control adsorption, selectivity, flexibility, and stability.

XtaLAB Synergy-ED makes it possible to solve structures directly from individual nanocrystals, revealing framework states and heterogeneity that bulk diffraction can average out.

## In situ MOF growth

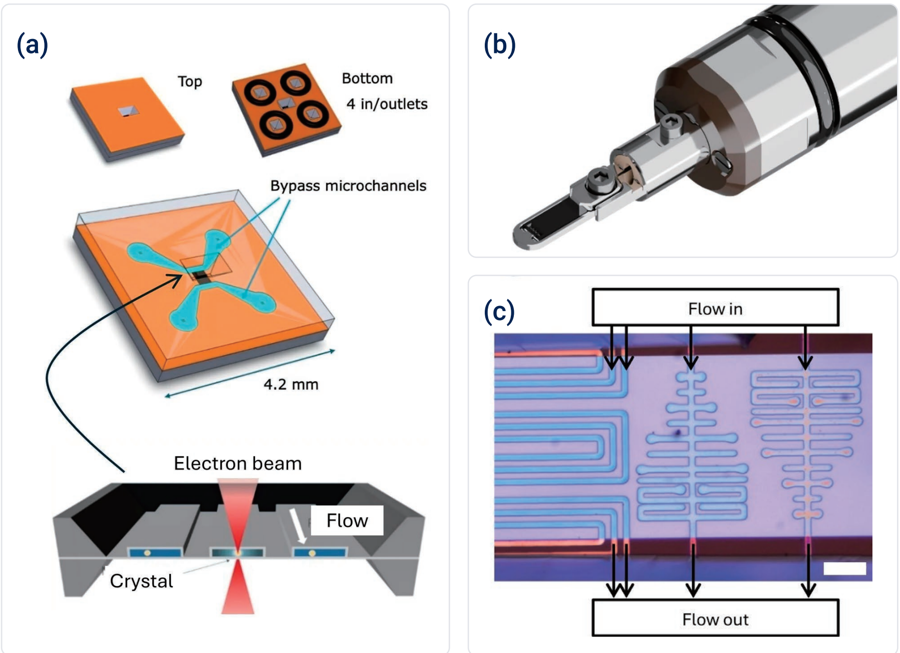
Many important materials crystallize only under liquid conditions or form extremely small crystals during synthesis. Traditional crystallography typically requires crystals to be grown separately, isolated, and transferred for analysis—often losing critical information about how the material forms.

Using XtaLAB Synergy-ED together with the Insight Chips liquid nano-channel sample holder, researchers can grow nanocrystals directly inside microfluidic channels and immediately collect electron diffraction data from the same sample. In the demonstrated experiment, nanocrystals of the metal–organic framework ZIF-8 were grown in situ within the chip and successfully analyzed by electron diffraction, producing data of sufficient quality for full structure determination.

This integrated approach enables researchers to:

- Grow and analyze crystals directly from solution inside nano-channels
- Perform electron diffraction on crystals that form during synthesis
- Study crystal nucleation and growth processes in real time
- Obtain structural information from nanocrystals too small for conventional methods

By combining controlled liquid environments with the capabilities of XtaLAB Synergy-ED, researchers gain a powerful tool for investigating crystal formation mechanisms and challenging materials that only exist as nanoscale crystals.



## Published examples

### In situ breathing states in flexible MOFs

(Liddle et al., Small, 21, no. 50 (2025): e09071)

Capture transient breathing states in flexible frameworks

MIL-53 in situ breathing-state study

Flexible MOFs do not always transform in a simple one-step manner. In this study, single-crystal 3D ED resolved transient intermediate states in MIL-53-type materials and revealed particle-to-particle heterogeneity during breathing transitions.

This shows how electron diffraction can uncover framework behaviour that would otherwise remain hidden in bulk measurements.

When porous frameworks transform through multiple intermediate states, bulk diffraction can hide the details. 3D ED / MicroED enables:

- Structure determination of transient framework states
- Detection of particle-to-particle heterogeneity
- Clearer understanding of breathing mechanisms in flexible porous materials

https://doi.org/10.1002/smll.202509071

### Solve single-crystalline sp²-carbon-linked COFs

(Li et al, Nature Chemistry, 17 (2025) 226-232)

For many covalent organic frameworks, the synthetic challenge does not end with making the material — it extends to proving its structure. In particular, sp²-carbon-linked COFs are highly attractive because of their stability and electronic properties, but obtaining crystals large and well ordered enough for conventional single-crystal X-ray diffraction is extremely difficult.

3D ED / MicroED overcame this bottleneck by enabling direct structure determination from the very small crystals that could actually be obtained, providing the structural proof needed to confirm framework connectivity and packing.

- Structure determination from crystals too small for SCXRD
- Direct validation of framework connectivity and packing
- Stronger structure–property claims for advanced porous materials

https://doi.org/10.1038/s41557-024-01690-y

### Reveal entirely new structures—not just known ones

(Qiu et al, Angew. Chem. Int. Ed. 2025, 64, e202421571)

Some new crystalline phases are recognized long before they are structurally understood because they form only as very small crystals, preventing definitive characterization by conventional single-crystal diffraction. In the case of orange phosphorus, this meant the material could be observed and discussed, but its crystal structure remained unresolved.

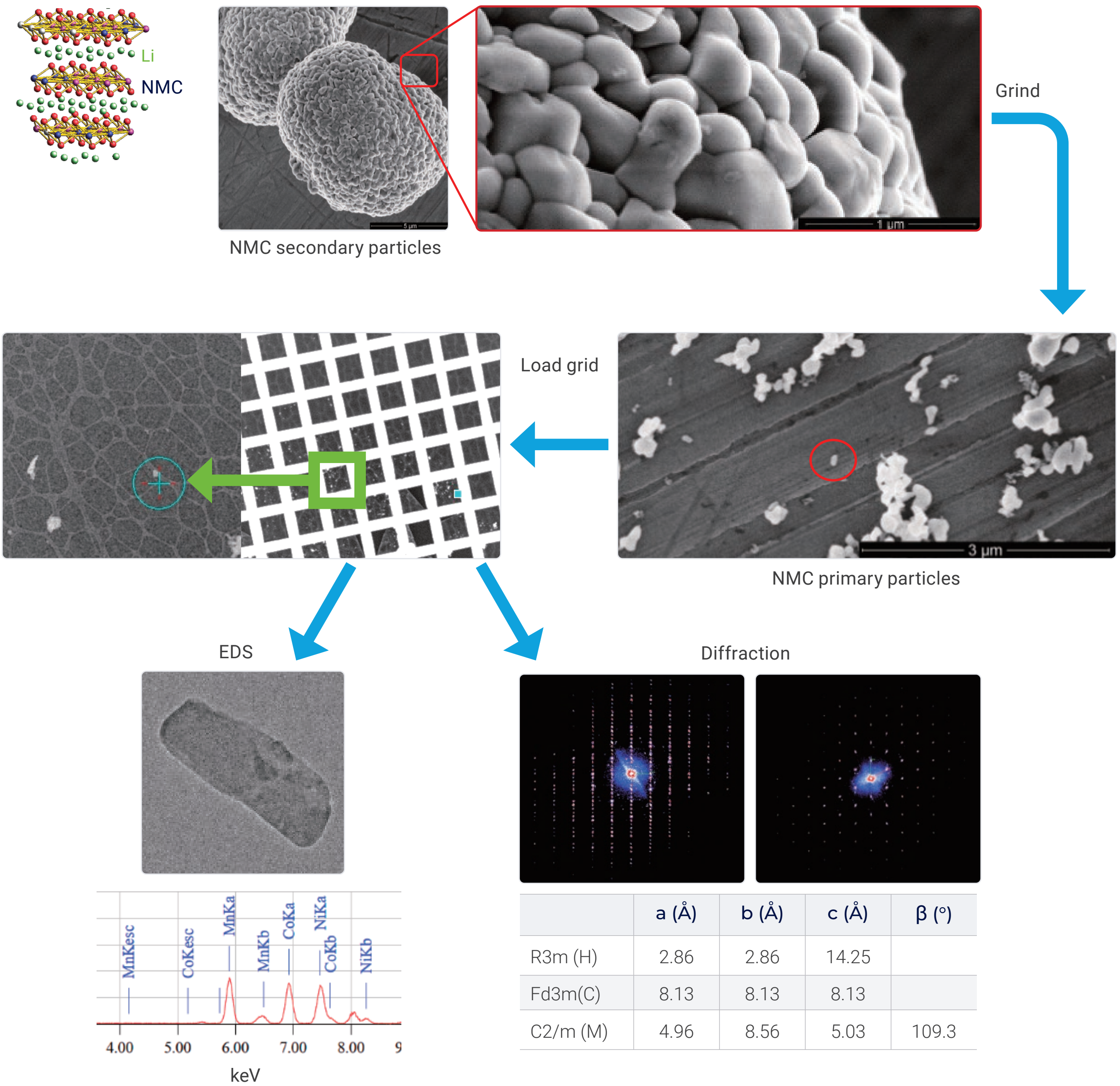
3D ED / MicroED overcame this bottleneck by enabling direct structure determination from nanocrystals, turning an uncertain phase into a fully characterized new allotrope.

- Definitive structure solution from crystals too small for SCXRD
- Structural proof of a previously unresolved phosphorus phase
- Faster progress from new phase discovery to crystallographic understanding

https://doi.org/10.1002/anie.202421571

# XtaLAB Synergy-ED for battery

Battery materials can be difficult to adequately study from a structural perspective since they are often recovered from cells in the form of nanocrystalline or polycrystalline powders after cycling. These small, disordered domains make conventional single-crystal X-ray diffraction impractical, but electron diffraction can reveal detailed structural information at this scale. Understanding the phases present within cycled materials is critical, since subtle structural changes directly affect electrochemical performance, stability, and degradation pathways. By identifying phase transformations, metastable intermediates, and degradation products, electron diffraction enables researchers to pinpoint mechanisms of capacity loss, guide materials optimization, and accelerate the design of next-generation energy storage systems.




| | a (Å) | b (Å) | c (Å) | β (°) |
|---|---|---|---|---|
| R3m (H) | 2.86 | 2.86 | 14.25 | |
| Fd3m(C) | 8.13 | 8.13 | 8.13 | |
| C2/m (M) | 4.96 | 8.56 | 5.03 | 109.3 |

## Published examples

### Improved solid electrolytes

(Kinzhybalo et al, J. Mater. Chem. C, 2024,12, 11347-11351)

Solid electrolytes are central to the development of safer, higher-performance batteries, but many promising ionic conductors form only as fine microcrystalline powders. XtaLAB Synergy-ED overcomes this challenge by enabling crystal structure determination directly from sub-micron crystals using electron diffraction.

With access to accurate structural models, researchers can identify the atomic pathways that enable ion transport and evaluate how composition and structure affect conductivity. This capability supports faster discovery of advanced solid electrolytes and helps drive innovation in solid-state battery technologies designed for safer and more efficient energy storage.

https://doi.org/10.1039/D4TC01216J

### Improved electrodes

(Desai et al., Chem. Commun., 2025,61, 11433-11436)

Next-generation battery materials often crystallize only as extremely small particles, making their structures difficult to determine with conventional crystallography. XtaLAB Synergy-ED enables three-dimensional electron diffraction analysis from micro- and nanocrystals, providing the structural insight needed to guide materials development.

This capability has been applied to sodium-ion battery electrode materials, where precise structural information helps reveal how atomic arrangements influence ion storage and transport. By enabling structure determination from crystals too small for traditional methods, XtaLAB Synergy-ED accelerates the discovery and optimization of lower-cost battery chemistries that support renewable energy storage and electrification.

https://doi.org/10.1039/D5CC03175C

# XtaLAB Synergy-ED for materials

In broader materials research, the ability to resolve atomic structures from crystal grains only a few hundred nanometers across opens up new opportunities across fields where traditional single-crystal X-ray diffraction is not feasible. Quickly acquiring multiple structures across a range of grains enables better understanding of the processes going on during their synthesis and use. Many advanced materials are synthesized as nanocrystalline powders, or heterogeneous mixtures, making structural analysis particularly challenging. By accessing this size regime, researchers can uncover phase relationships, hidden impurities, and transient intermediates that govern material performance. This capability is especially valuable for systems where scarcity of sample, disorder, or complex multi-phase behavior limit the use of conventional methods. As a result, electron diffraction has become a powerful complement to established structural tools, driving deeper insights into the design and optimization of functional materials across chemistry, physics, and engineering.

## Catalysis

Catalyst discovery suffers when active sites are heterogeneous or poorly characterized. This paper demonstrates a route to chemically well-defined Pd cluster nodes locked into a crystalline framework—and crucially, shows that continuous-rotation 3D ED can unambiguously solve the structure of a nanocrystalline, organometallic polymer network at high completeness. For catalyst and functional materials teams, Synergy ED enables confident structural models from crystals far below the single-crystal X-ray size regime—supporting clearer links between active-site geometry, stability, and reactivity.

# Features of the XtaLAB Synergy-ED

## Designed for diffraction

High-quality electron diffraction data requires a stable, reproducible instrument. Synergy-ED hardware and control systems are configured specifically for diffraction, with electron optics and operating routines designed to deliver reliable performance across a wide range of experimental conditions (crystal size, unit-cell dimensions, and beam intensity). Because the instrument is diffraction-dedicated, you avoid the reconfiguration, alignment, and calibration burden typical of general-purpose TEM workflows and obtain consistent performance from experiment to experiment.

## 200 keV electron gun

Higher accelerating voltage improves sample penetration, supporting a broader crystal-thickness range and increasing the likelihood of successful experiments across real-world powders and microcrystalline samples.

## Post-sample optics

Adjust diffraction-pattern magnification (virtual detector distance) to match unit-cell size and resolution requirements - supporting both large unit cells and high-resolution data, and helping resolve closely spaced reflections (e.g., in twinned or highly mosaic samples). An optical design using weak lenses minimises optical distortions and leaves ample space around the sample for complex sample holders and high tilt range.

## HyPix-ED

The HyPix-ED uses proven HyPix technology to provide noise-free, electron-counting performance without any practical restrictions on speed or dynamic range. In contrast to imaging-focused electron cameras, the HyPix-ED will consistently provide you with the highest data quality even at the lowest attainable electron fluxes.

## Compatibility with an ecosystem of TEM holders

We fully support and certify the compatibility of TEM sample holders for heating, cooling, electrical biasing, cryo-transfer, gas and liquid environments or air-sensitive samples. Thanks to TEM holder compatibility being a core design principle and our close collaboration with leading holder manufacturers, the list of supported sample environments is growing all the time.

## Integrated crystallographic workflow

Every step of your experiment from sample selection and visualisation through to getting that all important structure is conducted in our user-friendly and user-inspired software, CrysAlisPro-ED. Use software designed for a smooth diffraction workflow and top quality analysis of diffraction data instead of assembling a multi-software toolchain that is hard to maintain and may impact data quality and metadata integrity. Benefit from cutting-edge new developments, and future-proof your investment by enjoying lifetime free upgrades.

### Peer reviewed publications

Publications from electron diffraction are taking off. The XtaLAB Synergy-ED has now produced over 150 peer reviewed publications. **Scan the QR code** to see a comprehensive list of Synergy-ED publications and discover how electron diffraction can boost your reseach.


**JEOL JEM-2300ED**

200 KV gun/beamline designed for ED, real-space capabilities, selectable (virtual) detector distance.

**Sample stage**

Allowing x,y,z sample alignment and rotation (tilt) about a single axis. Cryo-transfer, cooling, heating, inert-transfer, etc. options are available.

**Rigaku HyPix-ED**

Single-electron sensitive, zero-background, continuous-collection, hybrid-pixel detector.


**Rigaku CrysAlis$^{Pro}$**

Software for instrument control, sample screening, data collection and reduction, and structure solution. Supports workflows and automatic data processing.

| | | Comments |
|---|---|---|
| Source energy | 200 keV | Excellent sample penetration with reasonable instrument complexity. |
| Post sample optics (virtual XtD) | Yes | Enables study of both large unit cells and highest-resolution data. |
| Detector technology | Hybrid-pixel counter | Accurate and noise-free data even at very short exposure, hardware event counting, and true shutterless data collection. |
| Supported sample holders types: | Cryo-transfer | Protects samples from vacuum, dehydration, solvent loss, and radiation damage. Multi-grid versions available. |
| | Air-free transfer | Provides a full workflow from glovebox to diffractometer without exposure to air. Liquid-nitrogen cooling version available. |
| | MEMS chip heating and biasing | Allows fast and accurate temperature control up to 1000°C and electrical biasing. |
| | MEMS chip gas cell and heating | Keeps sample in gas or vapour environments at variable temperatures, including gas exchange and mixing. |
| | Nano-channel chip holder | Enables measurement in liquid environment and real-time study of crystal growth. |
| Available supplementary techniques | X-ray spectroscopy (EDS) | Gain elemental composition information on a single-grain basis with full automation. |

# XtaLAB Synergy-ED

Fully integrated electron diffractometer

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