Nanomegas 3D ED/MicroED Solutions and Recent Advances in Precession-Assisted Serial Electron Diffraction

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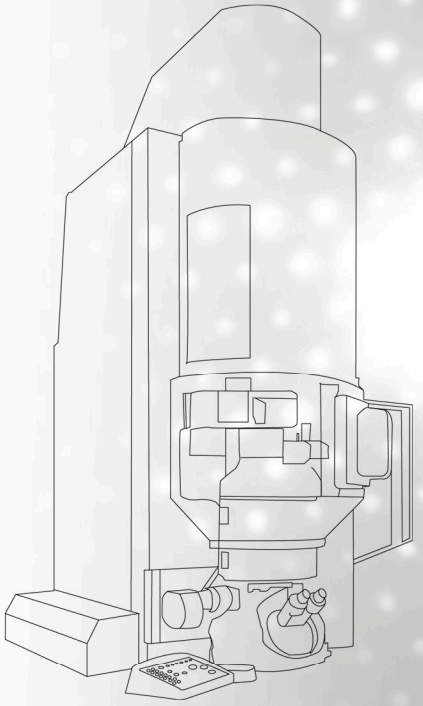
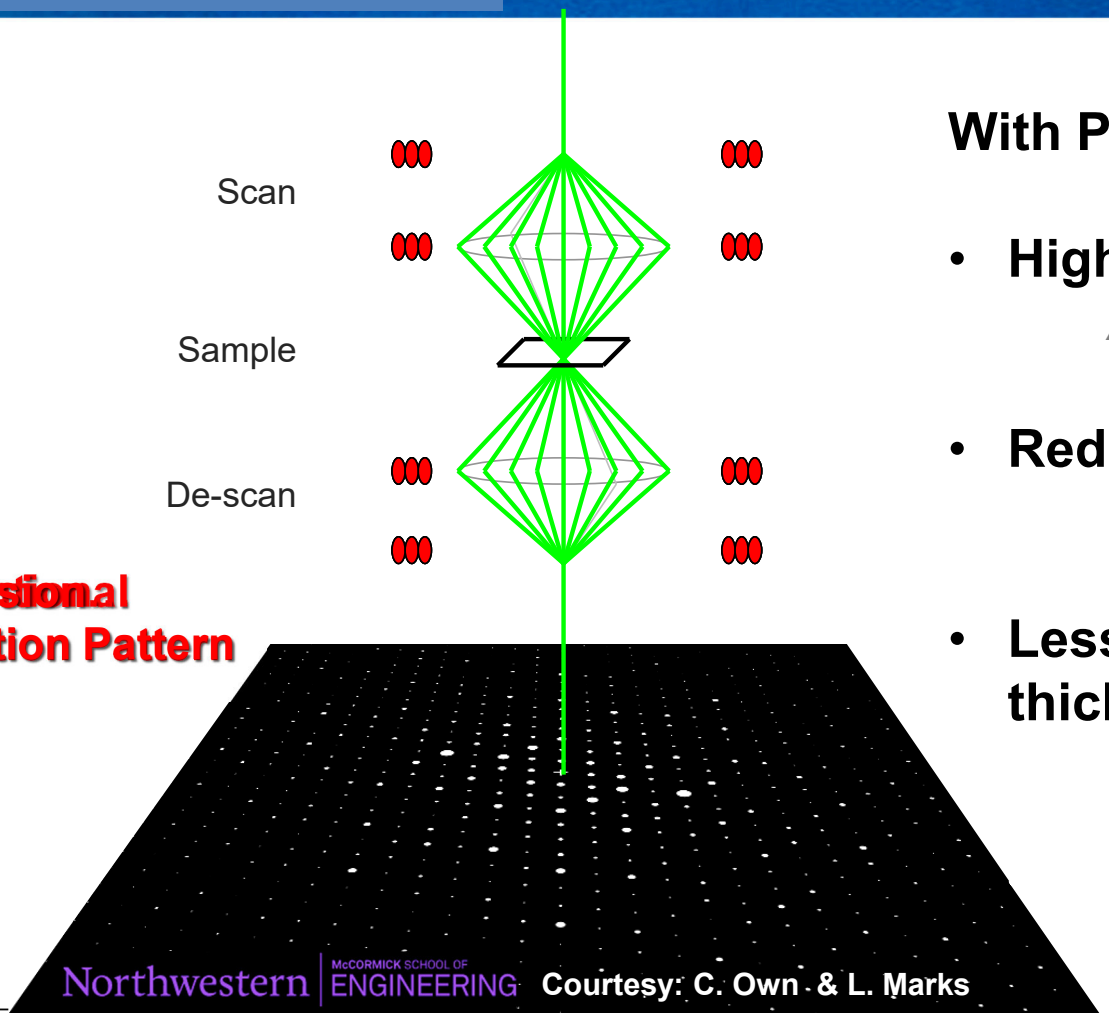


MicroED Short Course
November 3-5, 2025

NanoMEGAS
Advanced Tools for electron diffraction

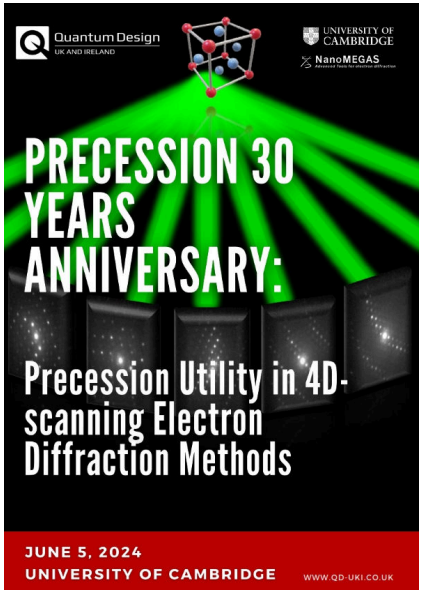
www.nanomegas.com

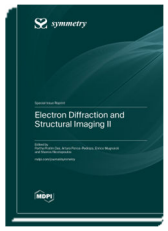
Precession Electron Diffraction



With Precession:

- **Higher resolution**
  Access to higher order reflections
- **Reduction of dynamical effect**
  Close to kinematical reflections
- **Less sensitivity to specimen thickness / bending**





Special Issue On Electron Diffraction
19 Invited Articles

Established in 2004 in Brussels, Belgium: Electron Diffraction Solutions for TEM

> 1000 articles in 21 years based on the provided solutions

Scientific and Research Activities

innoviris .brussels
empowering research

Innovative electron diffraction solutions for amorphous materials and electrochemistry

esteem3

MUMMERING

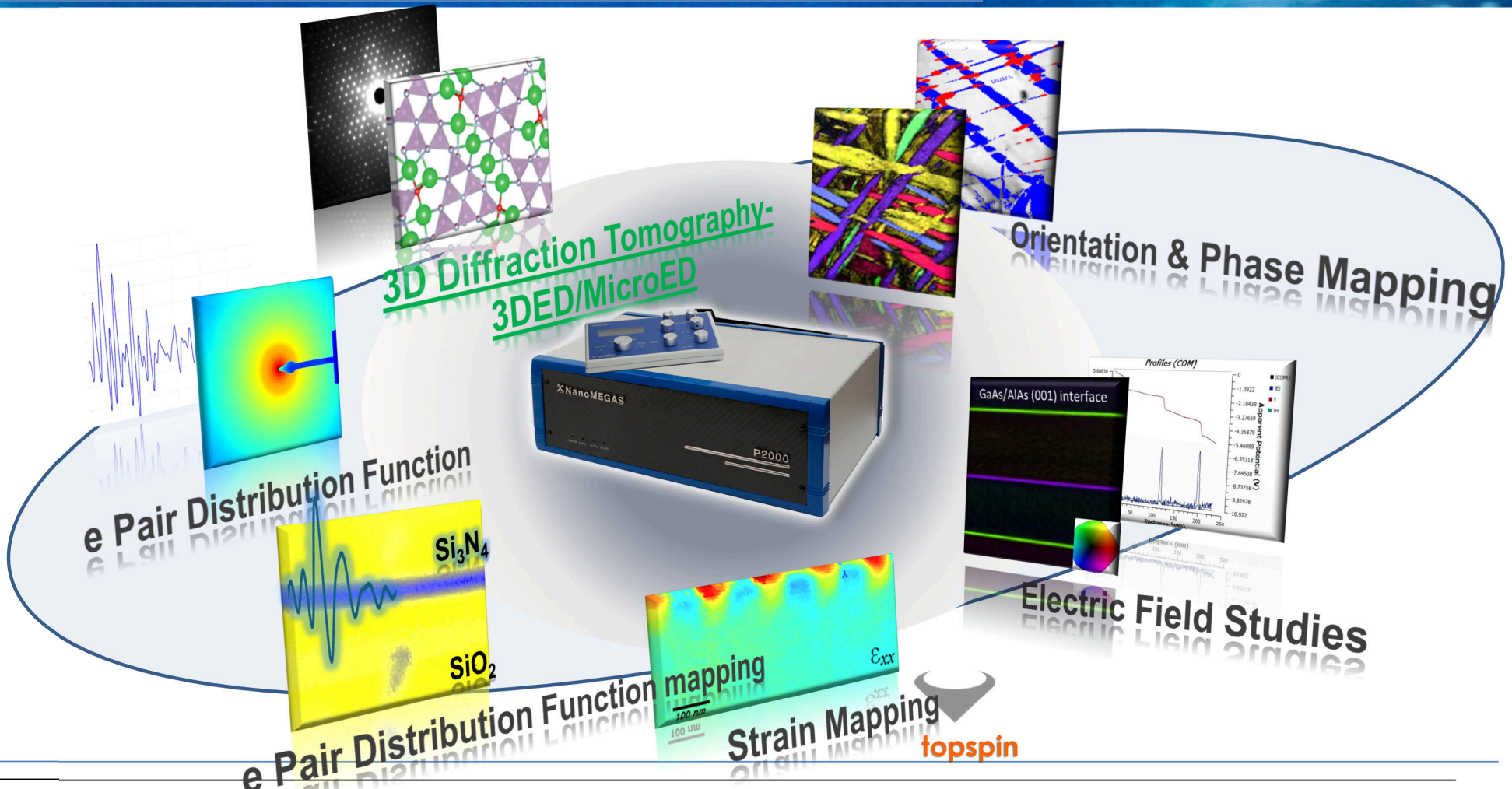
NanED

Partner

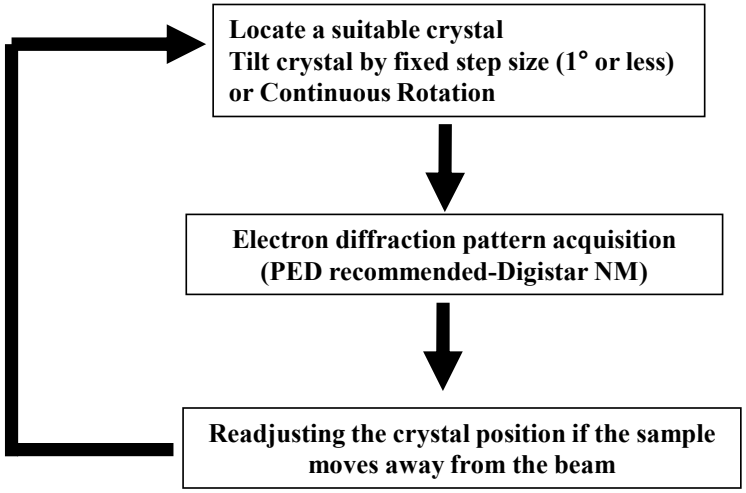
NanoMEGAS
Advanced Tools for electron diffraction

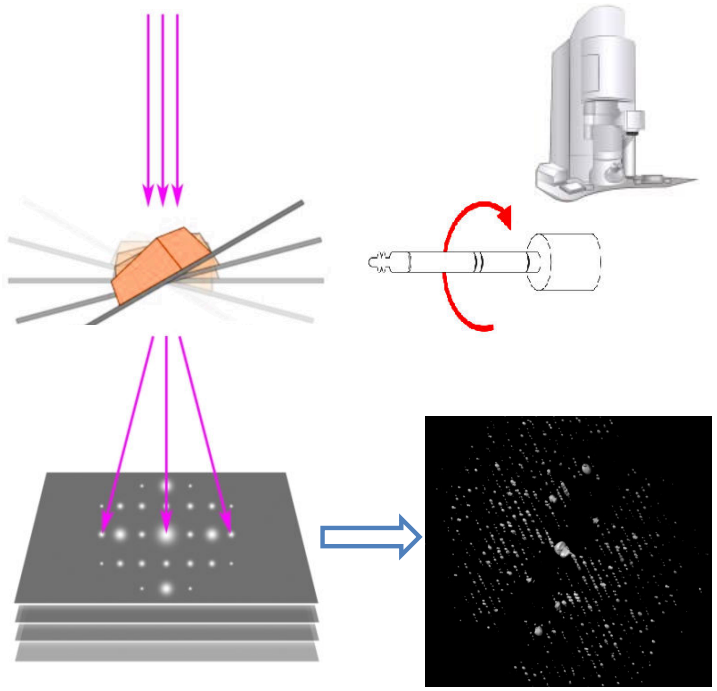
www.nanomegas.com

NanoMEGAS Electron Diffraction Solutions – 330+ installations



3D ED Data Acquisition in TEM





ADT U. Kolb et al., *Ultramicroscopy* 107, 507 -513 (2007)

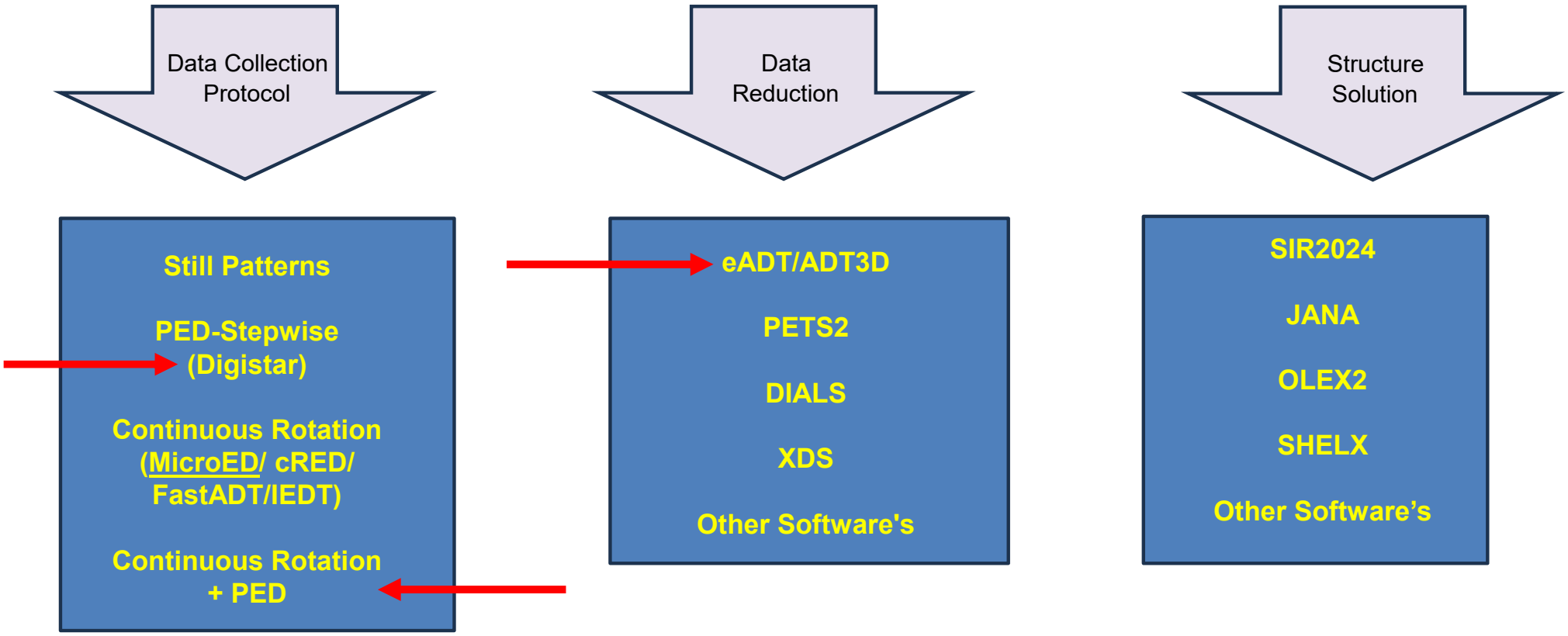
PEDT Mugnaioli et al., *Ultramicroscopy* 109, 758 -765 (2009)

Micro-ED/ cRED/FADT/IEDT Nederlof et al., *Acta Crystallogr. D 69, 1223-1230 (April, 2013); Shi et al. eLife eLifee01345 (Nov, 2013)*

ACS Cent. Sci. 2019, 5, 1315−1329

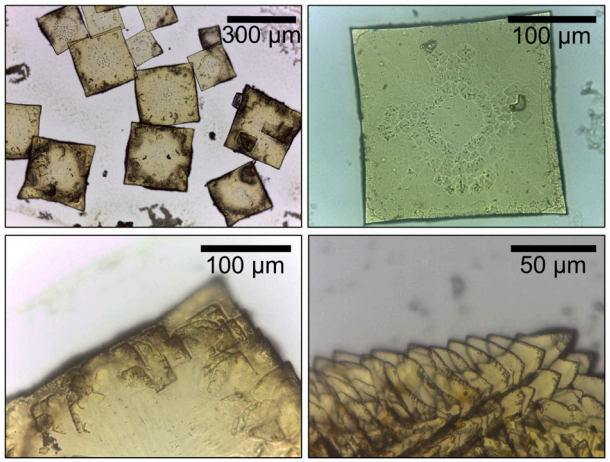
3D ED/Micro ED

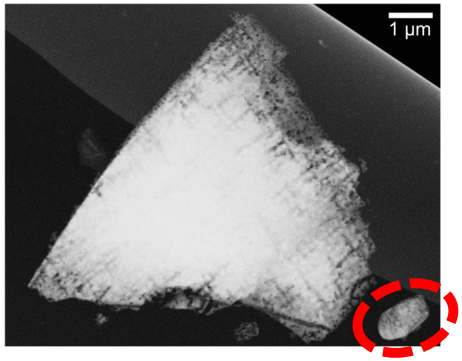
Data Collection to Structure Solution Where NM Solution Helps



One Example Among Many Structures Solved with Stepwise Precession Assisted 3DED

Structure of Orthocetamol ($C_8H_9NO_2$)- Its structure was still unknown in 2019!

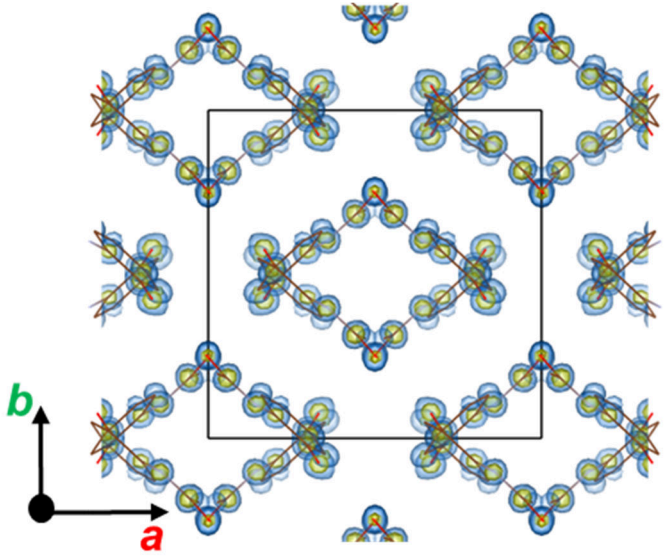




The Crystal Structure of Orthocetamol Solved by 3D Electron Diffraction.
Andrusenko et al. *Angew Chem Int Ed* **58**, 10919 (2019).

a = 10.56Å, b = 10.39Å,
c = 13.72Å, β = 93.11°

*C*2/*c*



Resolution = 0.9Å, Coverage (ind. refl.) = 97%, $R_{int}(F)$ = 28.45%

Kinematical refinement converged at $R1(4\sigma)$ = 37.31%

After the introduction of a rotational **twinning** that exchanges ***a*** and ***b***, refinement converged at $R1(4\sigma)$ = 32.70%
(twinning contribution 34%)

Stepwise PED was used for data acquisition due to the small domain size.
The twinned domains are smaller than the 150 nm diameter beam used for 3D ED data acquisition

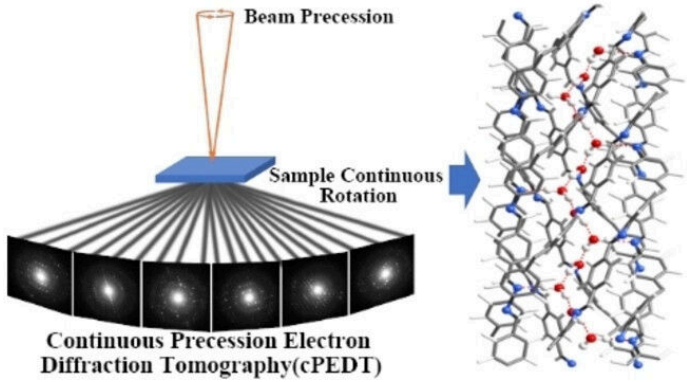
Combination of PED + Continuous Rotation – Example 1

Locating Hydrogen Positions for COF-300 by Cryo-3D Electron Diffraction

Sun *et al.* (*Angew Chem. Int. Ed.*, 2023)

Comparison of the data collected between Continuous Rotation + PED VS Continuous Rotation Only

Particle name	The type of data collection	R_{int}/ %	The number of hydrogen atoms found	R_1 value/ %
1	cPEDT	15.39	7	19.87
	cRED	27.83	7	20.28
2	cPEDT	14.87	6	22.52
	cRED	16.44	5	22.55
3	cPEDT	27.30	3	21.92
	cRED	38.62	3	26.39
4	cPEDT	43.02	1	31.87
	cRED	49.26	1	27.60
5	cPEDT	22.33	5	25.30
	cRED	43.34	3	29.30



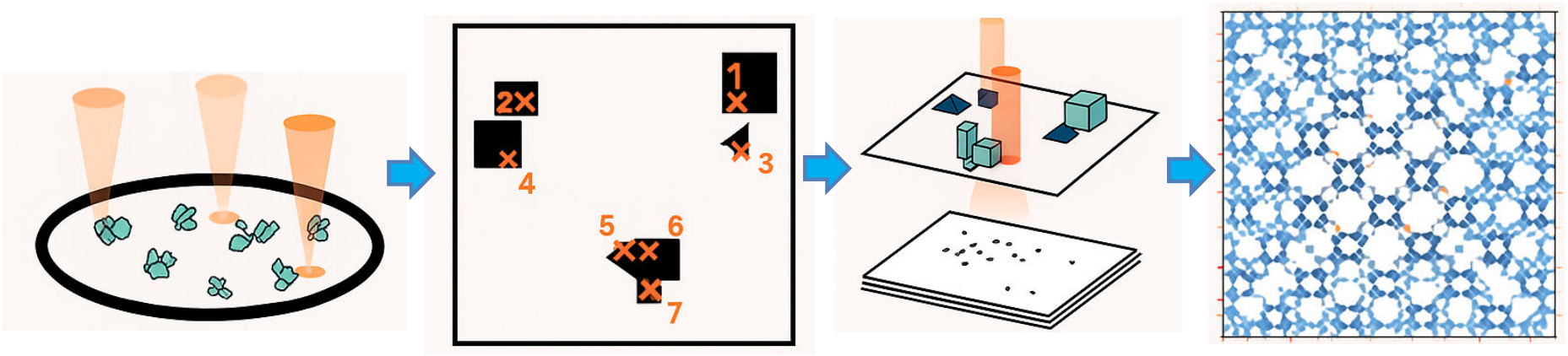
Lower R(int), More No of H atoms found during Kinematic refinement, Lower Refined R value with Continuous Rotation + PED data

Combination of PED + Continuous Rotation – Example 2

Crystal	10			07			13			09		11		12	
	Continuous Rotation + PED VS Continuous Rotation														
Acquisition Method	Cont	Prec&Cont	Prec&Cont	Cont	Prec&Cont	Prec&Cont	Cont	Prec&Cont	Prec&Cont	Prec&Cont	Prec&Cont	Prec&Cont	Prec&Cont	Prec&Cont	Prec&Cont
Integration Method	Profile fit	Profile fit	Integration	Profile fit	Profile fit	Integration	Profile fit	Profile fit	Integration	Profile fit	Integration	Profile fit	Integration	Profile fit	Integration
Tilt range (°)	109	122		114	97		118	120		112		103		96	
N. of stitched tilt series	3	2		3	2		2	4		2		2		1	
Cell Parameter a (Å)	26.85(1)	26.62(1)		26.77(1)	26.74(1)		26.816(1)	26.721(1)		26.77(1)		26.736(1)		26.866(1)	
Cell Parameter c (Å)	7.553(4)	7.652(3)		7.538(5)	7.589(3)		7.601(5)	7.618(3)		7.587(3)		7.633(3)		7.622(5)	
N. reflections	12926	18701	18784	17148	15033	15319	17579	17972	18289	17151	17455	15239	15504	14104	14374
N. independent reflections	6038	6825	6832	6185	6096	6211	7352	7376	7415	6067	6186	6918	6986	6022	6138
N. reflecton > 2σ	507	3178	5539	998	2663	4811	1109	1280	3072	2912	5021	2352	3900	1556	2613
R_{int}	1.0831	0.3164	0.2690	0.5957	0.2766	0.2629	0.6955	0.5874	0.3926	0.4186	0.3816	0.3682	0.3321	0.3952	0.4026
R1(all)	0.7256	0.4200	0.3847	0.5667	0.4759	0.4018	0.6170	0.5835	0.4881	0.5206	0.4482	0.5093	0.4330	0.5039	0.4528
R1(obs)	0.6565	0.3375	0.3716	0.3492	0.4216	0.3882	0.4905	0.3944	0.4108	0.4898	0.4404	0.4119	0.3686	0.3719	0.3652
wR2(all)	0.8863	0.6221	0.6477	0.7188	0.6802	0.6661	0.8053	0.7319	0.7095	0.7334	0.7006	0.6995	0.6650	0.7171	0.6955
wR2(obs)	0.8185	0.5865	0.6389	0.6225	0.6520	0.6477	0.7324	0.6473	0.6729	0.7162	0.6954	0.6548	0.6386	0.6573	0.6471
Atoms (C,N) found ab-initio	no solution	20	20	no solution	no solution	18	no solution	no solution	17	no solution	no solution	19	20	no solution	19

It is considered the structure is solved when one can recognize most of the C and N atoms (total 20). Group of 10 B atoms is difficult to recognize ab-initio and it is very distorted, so it was not used as a criteria. *(To be Published Das et al.)*

A New Method For Data Collection and Structure Solution - *Serial Electron Diffraction*



Low Magnification Sample Screening in STEM Mode

Identify Regions of Interest (Manual/automatic targeting, or full-grid acquisition)

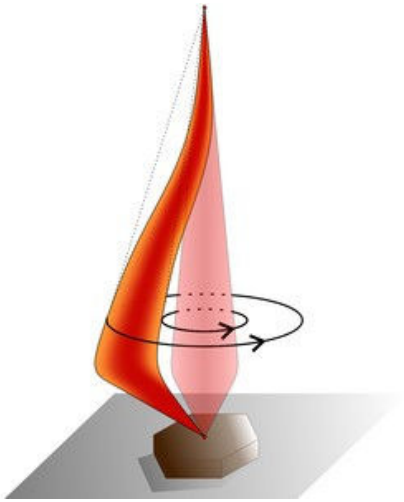
Serial ED Data Acquisition

Structure Solution

Smeets et al., J Appl Cryst, 2018, Bücker et al., Nature Commun. 2020, Hogan-Lamarre et al., IUCrJ, 2024

New Trend - Precession-Assisted Serial Electron Diffraction

- **Precession** can help achieve better **integration of reflections**
- It **reduces dynamical effects**, leading to more reliable intensity measurements
- This enables ***structure analysis with fewer diffraction patterns***
- It may also allow **dynamical refinement** for improved structural accuracy



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On the use of beam precession for serial electron crystallography

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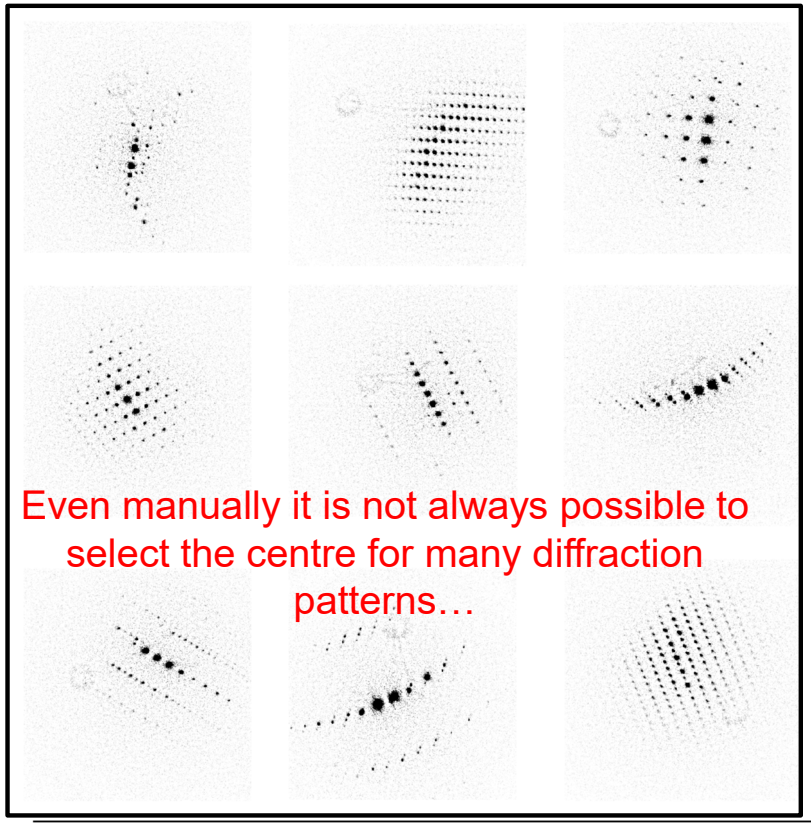
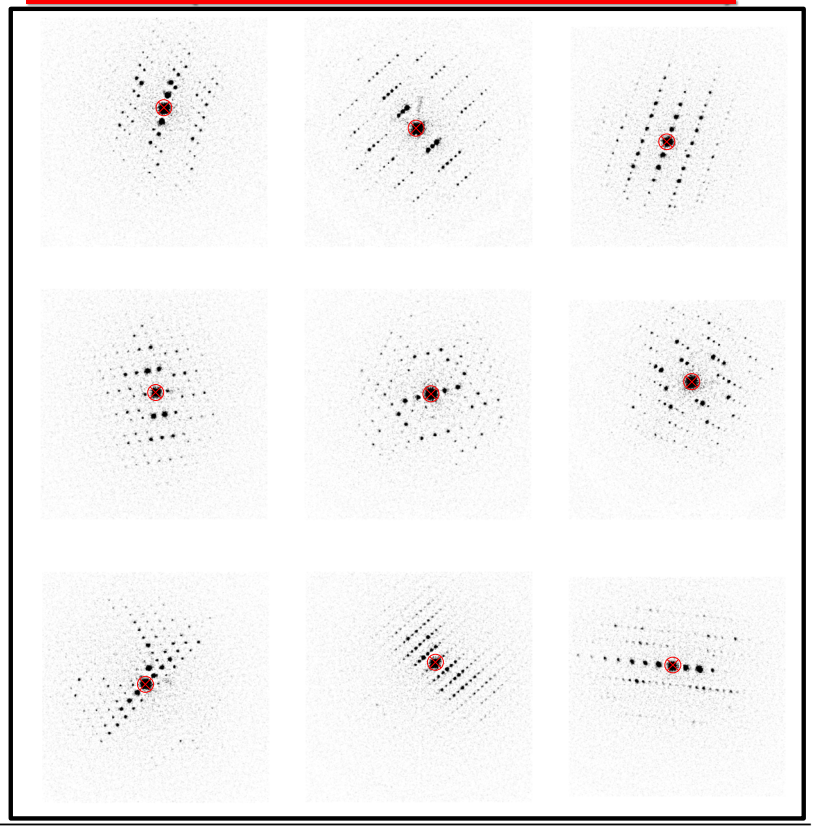
A Case Study – Carbamazepine – Precession Assisted Serial ED

Serial ED
Carbamazepine
NO PED (1011 Patterns – 573 used)

Ongoing Collaboration Work with Enrico Mugnaioli and Iryna Andrusenko - University of Pisa, Italy



Serial ED
Carbamazepine
PED 1° (1005 Patterns – 573 used)



A Case Study – Carbamazepine – Precession Assisted Serial ED

Serial ED
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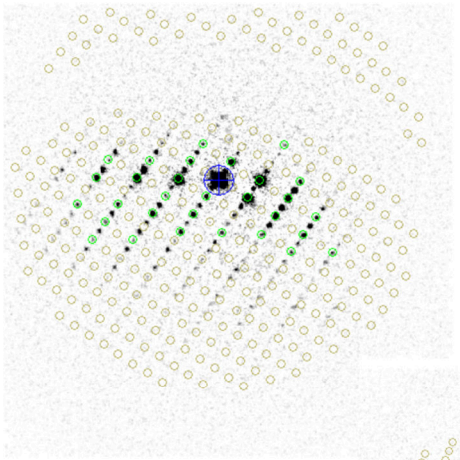
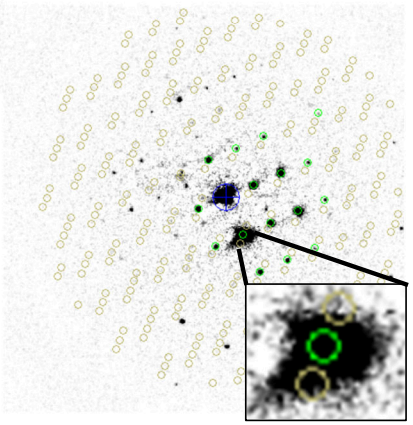
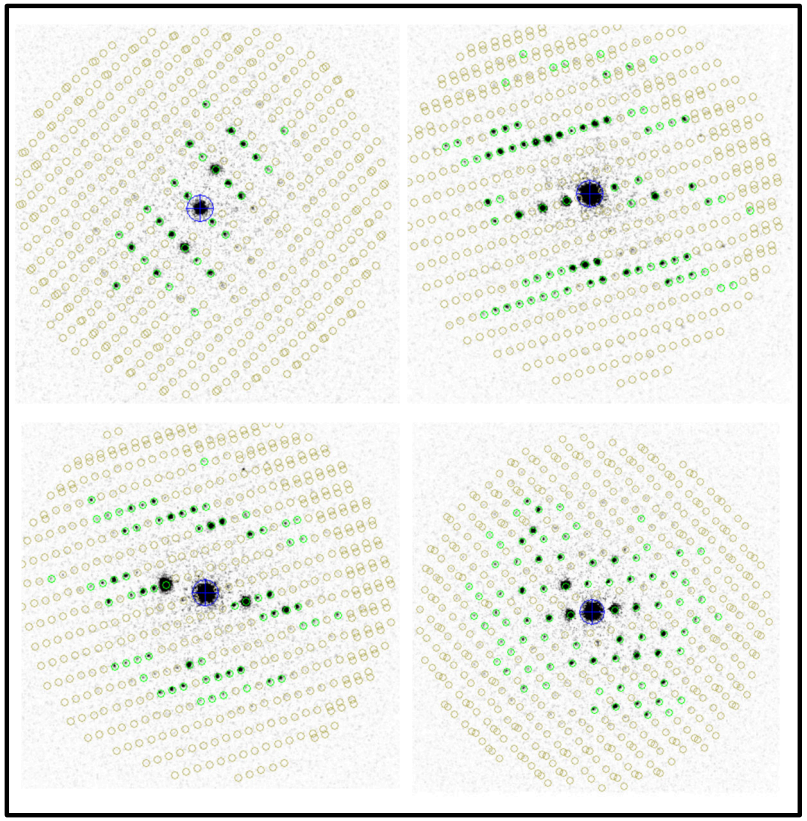


Indexing the diffraction pattern could be challenging!



Two-beam condition that makes some of the reflections oversaturated!

Serial ED
Carbamazepine
PED 1°



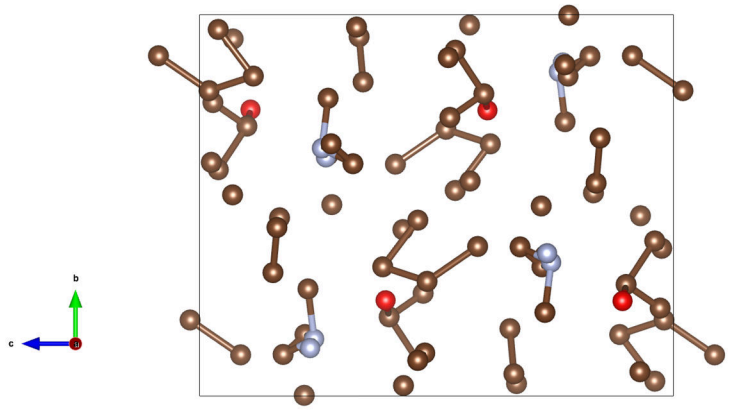
A Case Study - Carbamazepine – Precession Assisted Serial ED

Serial ED
Carbamazepine
NO PED

***Ab-initio* structure solution in $P2_1/n$**

Res 1.0 Å
R_{int} 32.89 %

No structure solution at all!

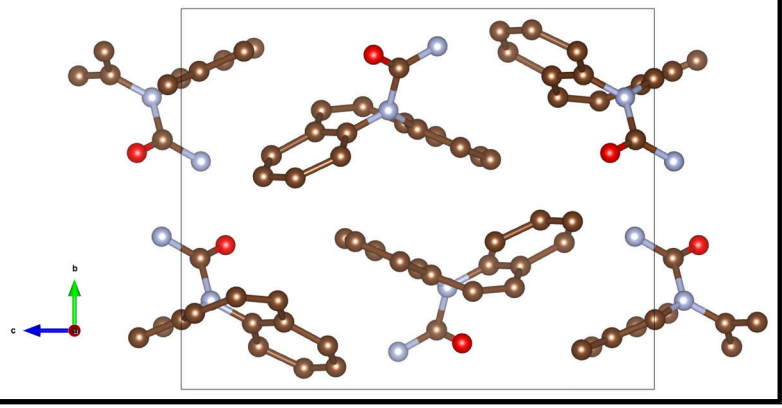


Serial ED
Carbamazepine
PED 1°

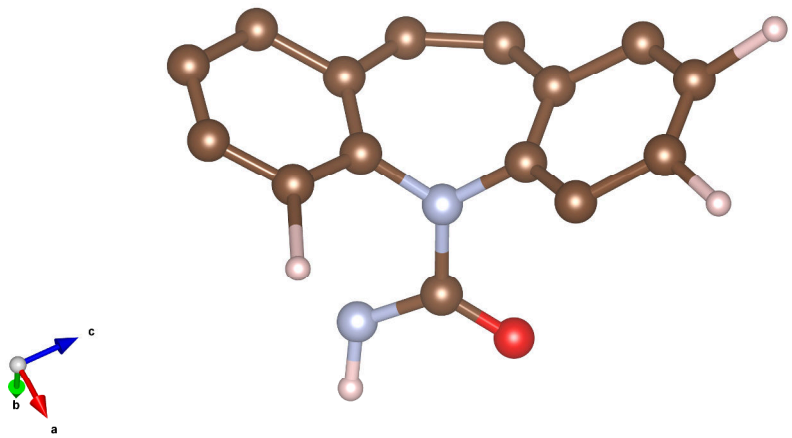
***Ab-initio* structure solution in $P2_1/n$**

Res 1.0 Å
R_{int} 13.60 %
Completeness 94%
u(iso) 0.00865 Å^2
Final R 21.80%

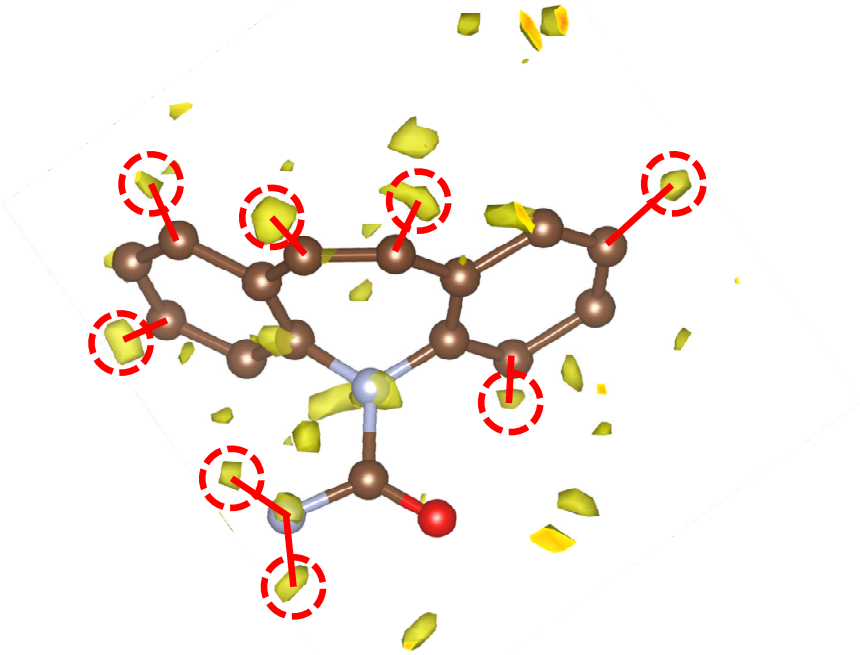
Just perfect!



High Quality Structure – Precession Assisted Serial ED



4 hydrogen atoms are spotted in the *ab-initio* solution



8 hydrogen atoms are determined from the first difference Fourier map, without performing any refinement

Ongoing Collaboration Work with Enrico Mugnaioli and Iryna Andrusenko - University of Pisa, Italy

Conclusions:

1. NanoMEGAS provides a precession system where the precession angle can be varied over a wide range, depending on the application, and operated at high frequencies.

2. The precession mode can be used for both stepwise 3DED and continuous 3DED experiments.

3. The NanoMEGAS precession and scanning synchronization system, integrated with many popular camera (CCD, CMOS and Direct Electron Detector e.g. QD, ASI, Dectris, Direct Electron etc..) platforms, enables precession assisted 4D-STEM applications.

4. We are developing precession assisted Serial Electron Diffraction (Serial ED) for high-quality structure determination of beam-sensitive materials.

Photo from NanoMEGAS annual meeting, Brussels, June 2025

Thanks for your attention !!!

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Serial ED
Carbamazepine
PED 1°

Manual data collection in STEM mode
CL 250 (resolution in real space up to 0.7Å)
PED 1°
Total **1005** frames
Exposition time 200 ms / frame
Acquisition time – half day
Size 0.99 GB

Used **573** frames

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Carbamazepine
NO PED

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