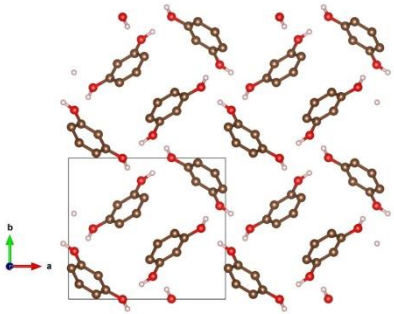
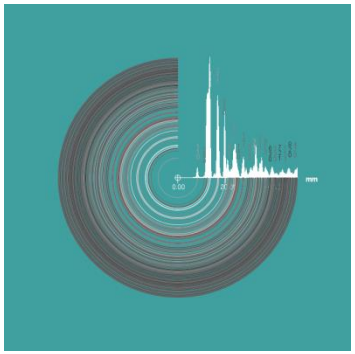
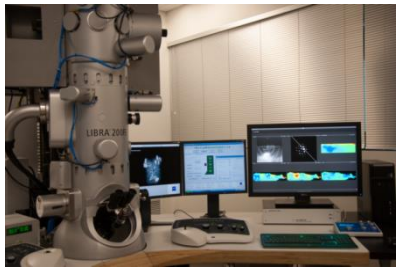
CRYSTAL STRUCTURE ANALYSIS OF PHARMACEUTICALS WITH ELECTRON DIFFRACTION







Dr. Stavros Nicolopoulos

Consultant IUCr Electron Crystallography Comission

Grenoble INP

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www.nanomegas.com

This document was presented at PPXRD - Pharmaceutical Powder X-ray Diffraction Symposium

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SEVENTH FRAMEWORK PROGRAMME

esteem2
european network for electron microscopy

Free transnational access

to the most advanced TEM equipment and skilled operators for HR(S)TEM, EELS, EDX, Tomography, Holography and various in-situ state-of-the-art experiments

X 2 SME participate

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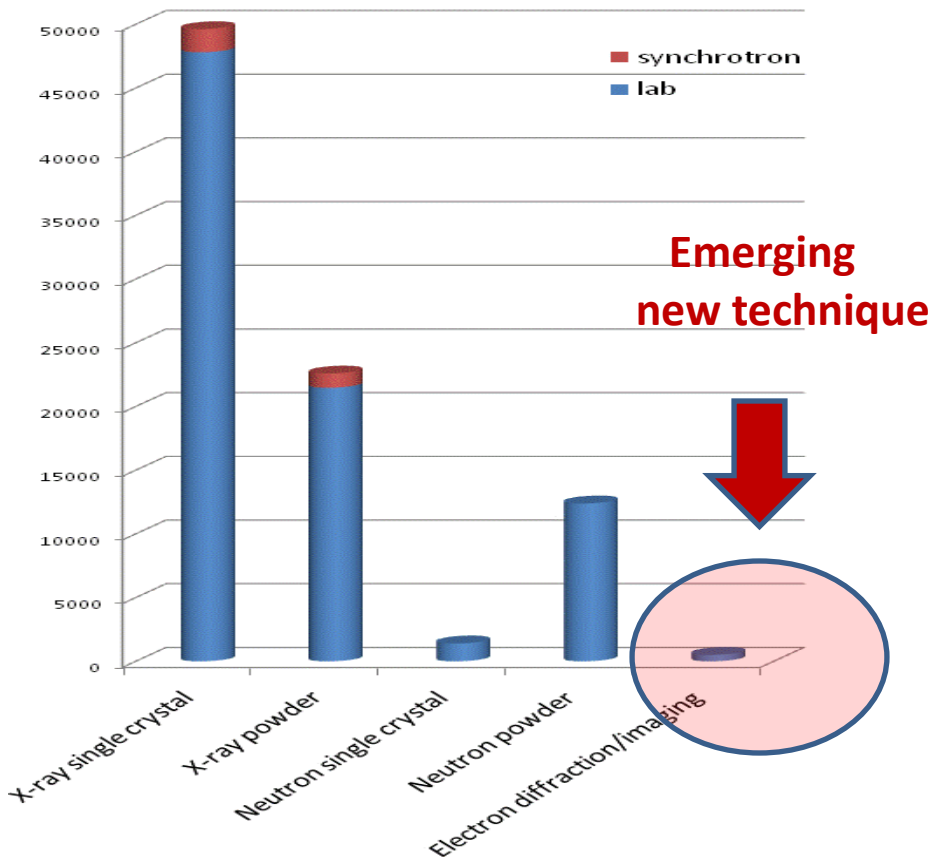
X-ray

Neutron

Electron

Crystallography



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Why electrons?

- **10^{4-5} times stronger interaction with matter compared with X-ray**

  - *single crystal data on powder sample*

  - short data collection time

- Phases are present in high resolution electron microscopy (HREM) images

  - **<u>for nm- and micro-sized crystals</u>**

Comparison X- Ray powder diffraction /electron diffraction: Limitations X-Ray powder

Ovelapping of reflections

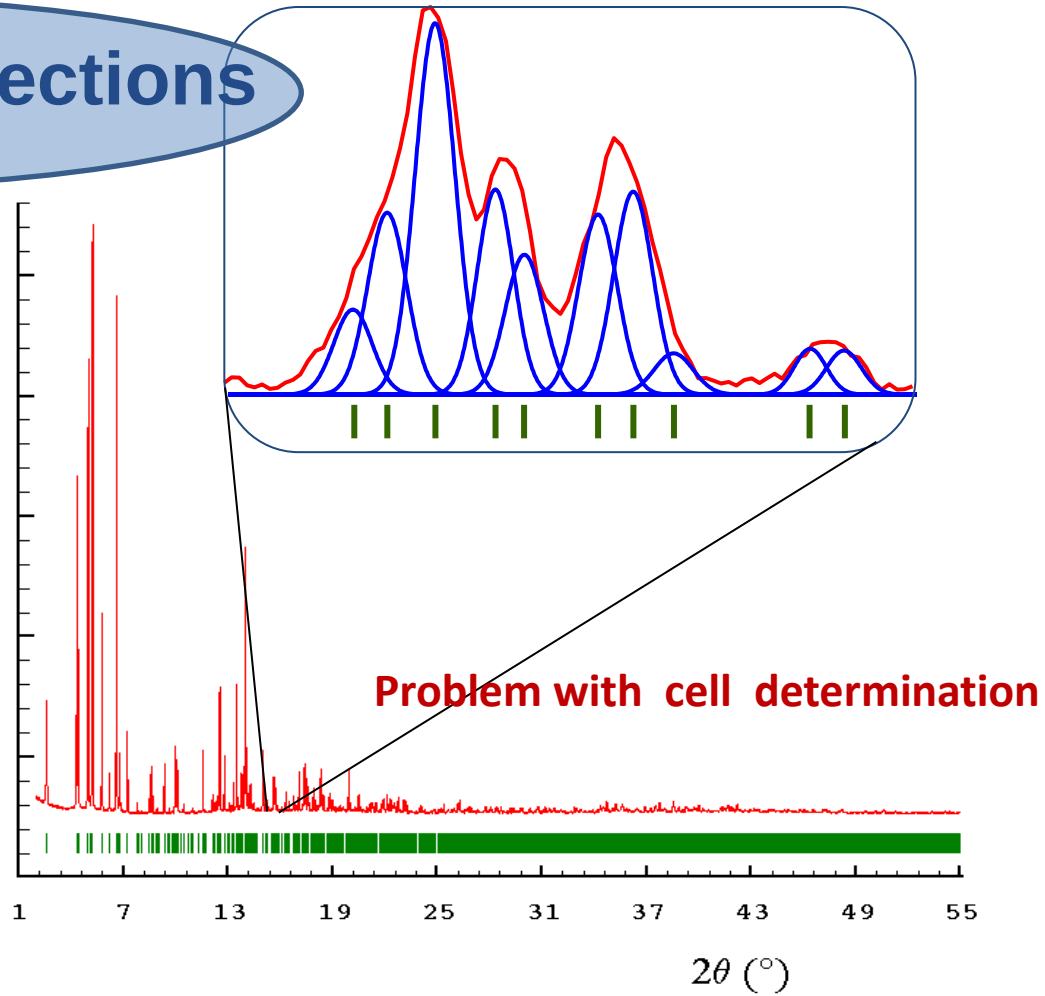
stacking intergrowth

Preferential orientation

Nanocrystals

Impurities

Light atoms (Li, Be)



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X- Ray powder diffraction limitations

overlapping

Stacking intergrowth

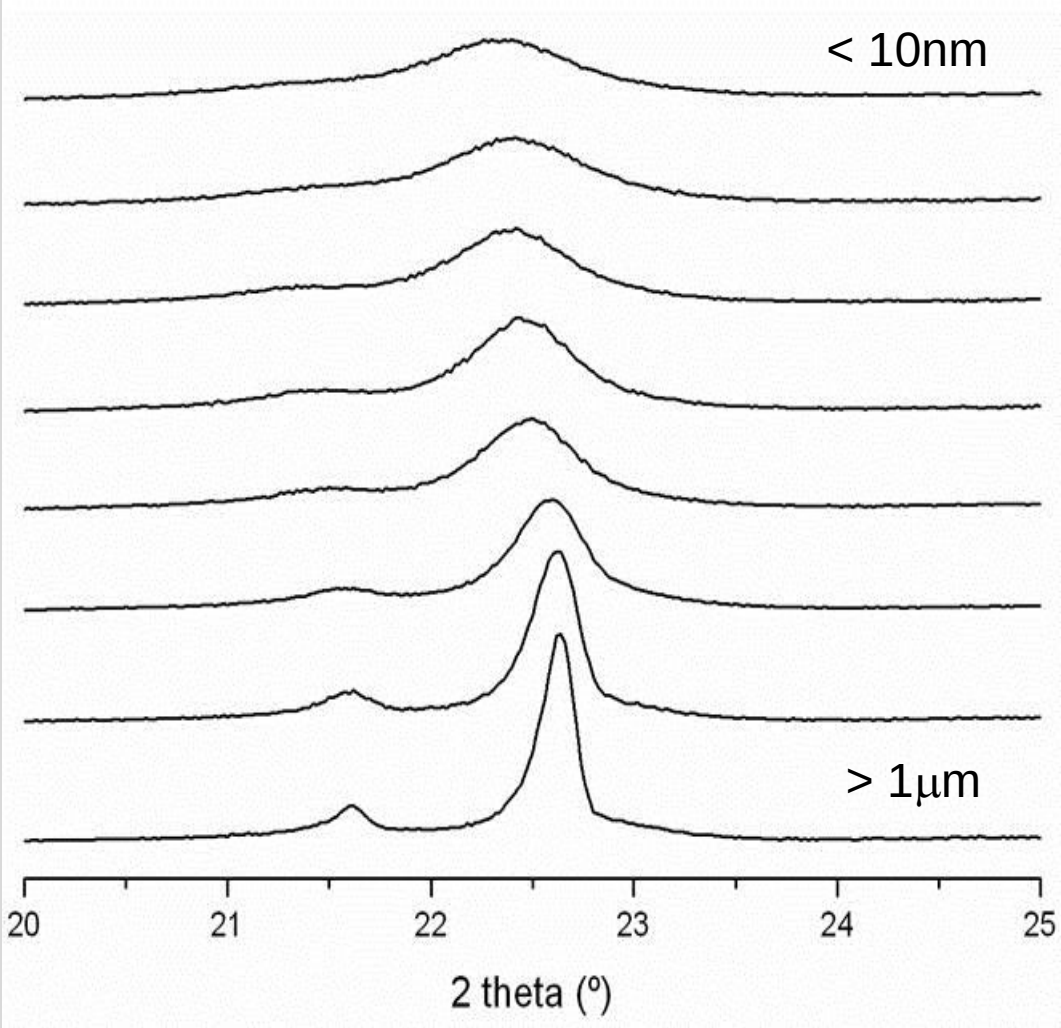
Preferential orientation

Nanocrystals

Impurities

Light atoms (Li, Be)

X-Ray "amorphous"



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Transmission electron microscopy TEM

- Diffraction – selected area, nano- and convergent beam electron diffraction
- Imaging – conventional, high resolution
- Chemical analysis – EDS and EELS

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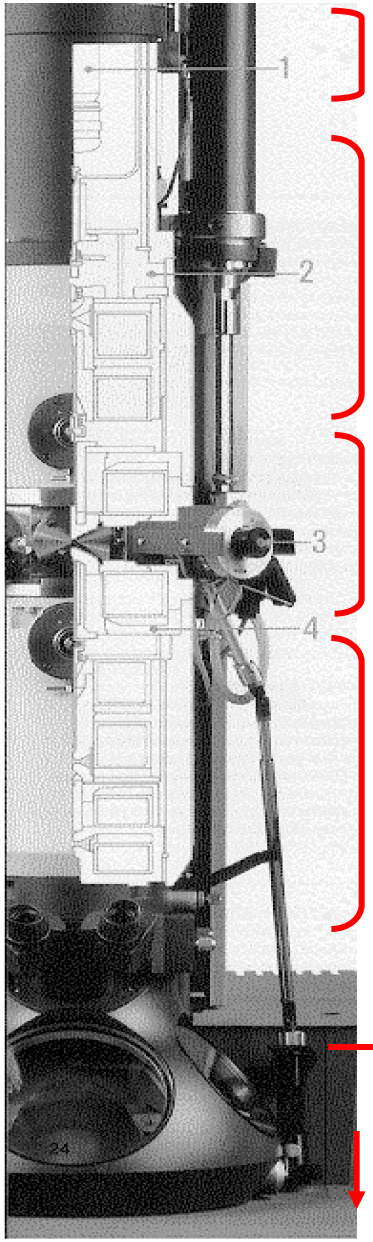

Source (Gun)

Illumination system

Objective Lens

Projection system

Screen

CCD or Photographic plates

TEM : It can be **thermionic** or **field emission**

Two condenser lenses C1 and C2
C1 : different **spot sizes**
C2 : **convrgence** of the beam

It creates the **first image** of the sample

Intermediate lens: to change from **image** mode to **diffraction** mode

Projection lens: to change the **magnification**

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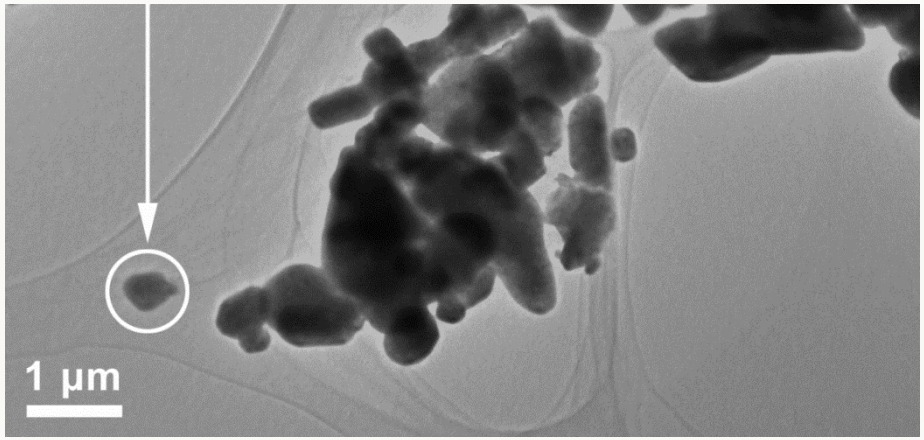
Image courtesy Dr. Mauro Gemmi IIT Italy

TEM : Image resolution

With TEM microscopes we can obtain images of **crystalline materials** with atomic resolution:

Acceleration voltage (kV)	Point resolution (Å)
120	~3
200	2.0
300	1.7

We can see nano-crystals



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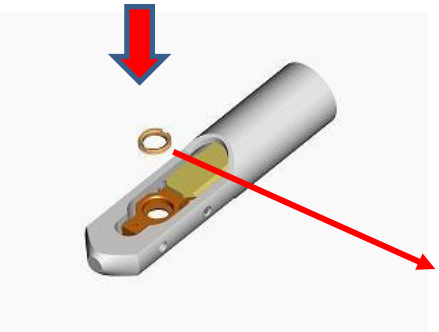
TEM : Brightness and beam size

FEG Guns have a higher brightness (10^3):

we can use beams with a smaller diameter having enough current for obtaining a detectable signal

	Thermionic	FEG
Smallest beam size	10nm	<1nm

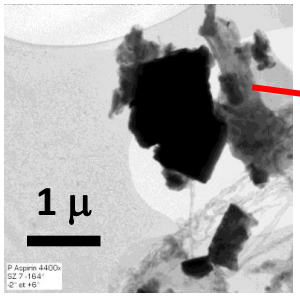
TEM grid
4 mm size



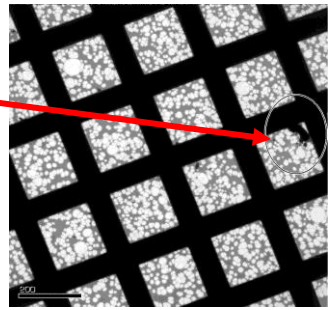
We have a nano-probe!

Very small quantity of sample !

aspirin crystals



TEM grid



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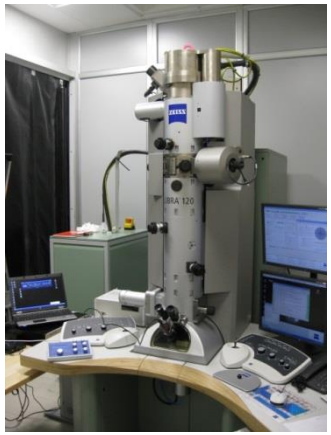
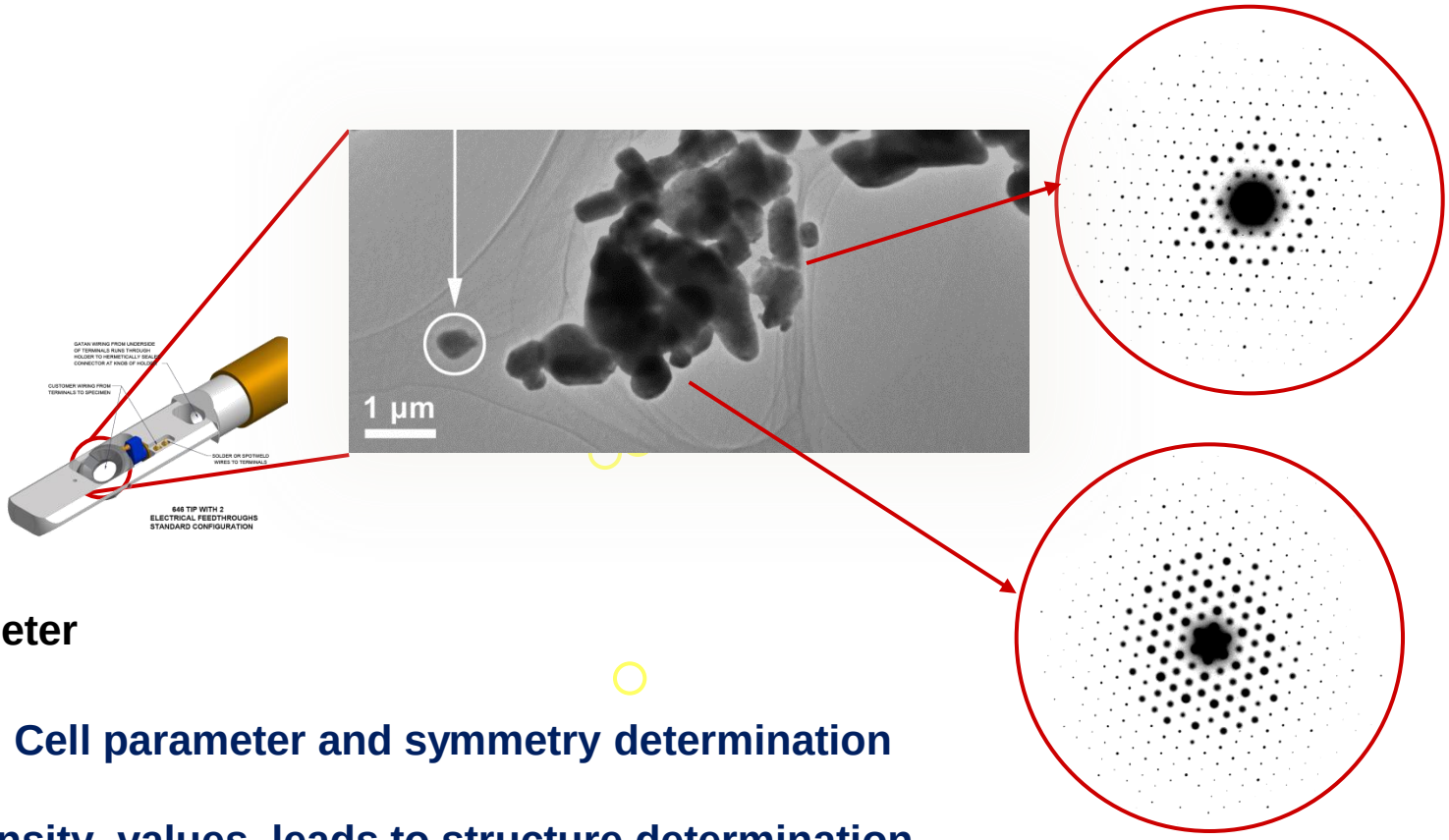
TEM : Electron diffraction advantages



Every TEM (electron microscope) may produce ED patterns and HREM from individual single nanocrystals



TEM goniometer

ED information: Cell parameter and symmetry determination

Measuring intensity values leads to structure determination

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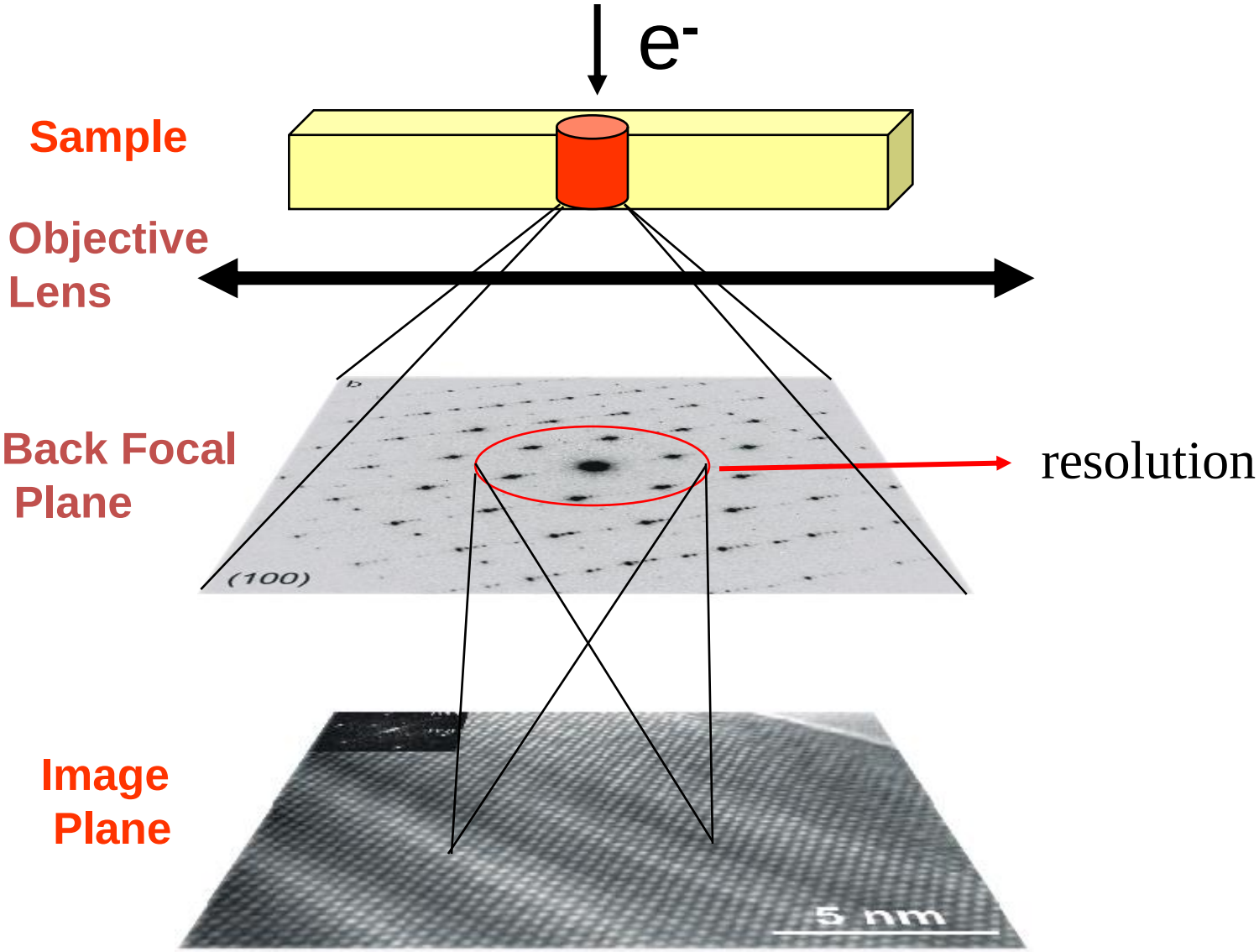
Image formation



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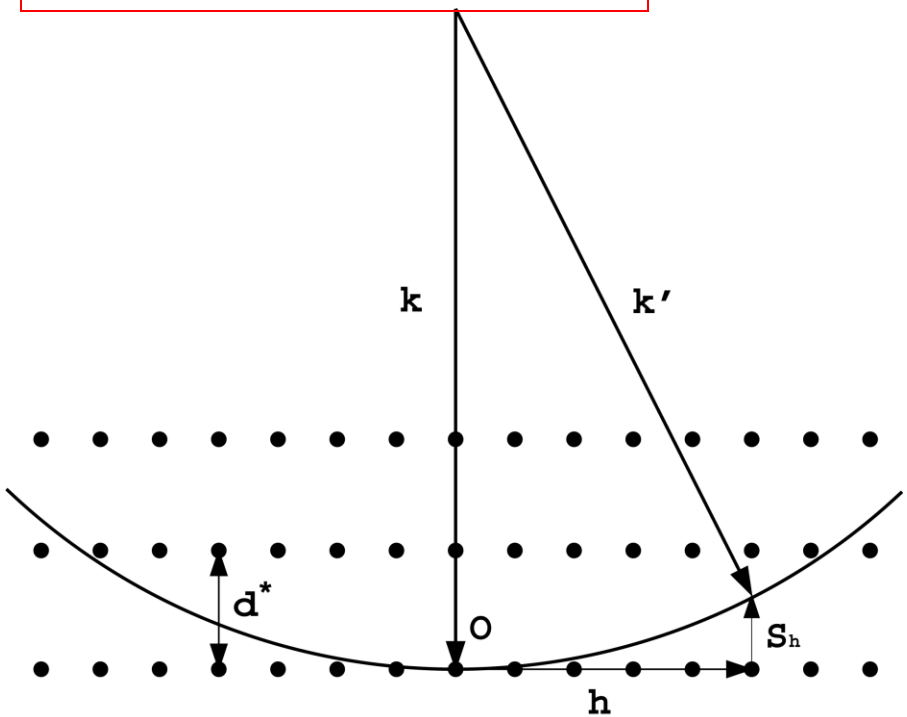
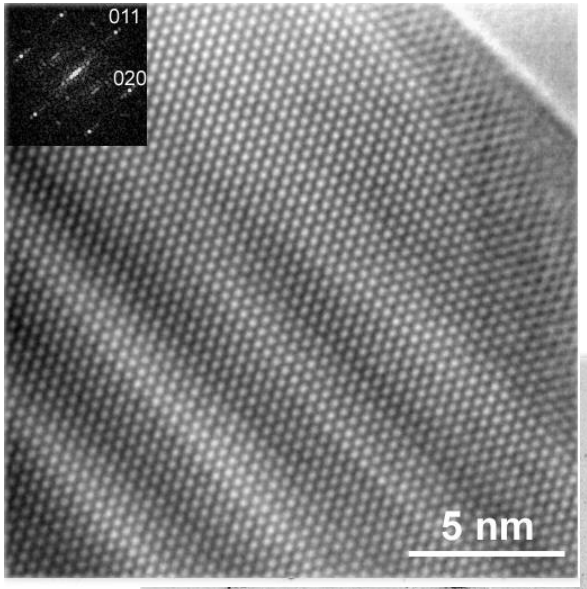
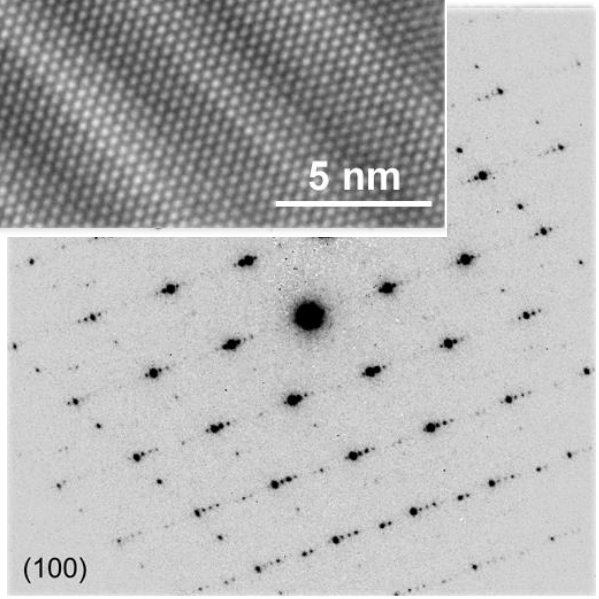
Electron diffraction

RECORD RECIPROCAL SPACE - TEM



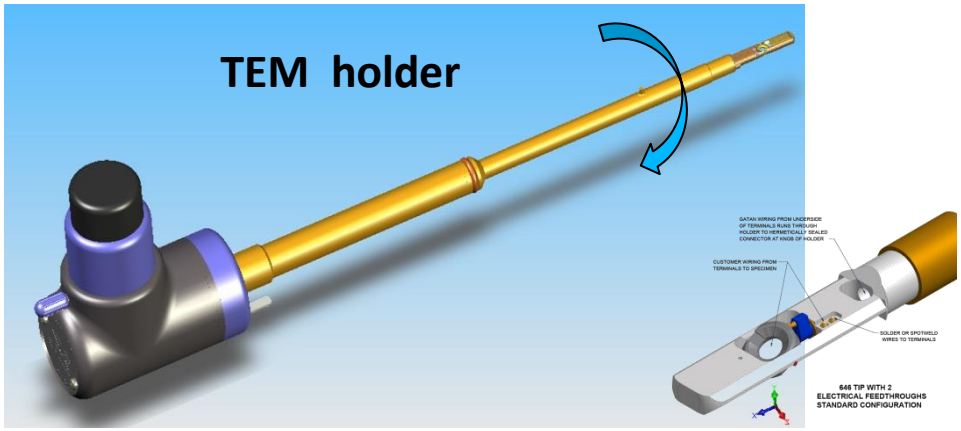
VOLTAGE IN KV	λ IN Å
100	0.0370
300	0.0197
1000	0.0087

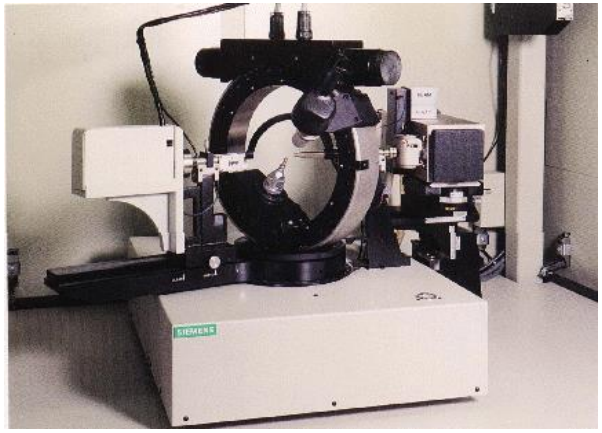




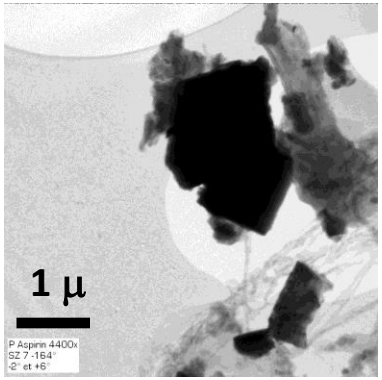
The Ewald sphere is flat! → In one shot we record a reciprocal lattice plane

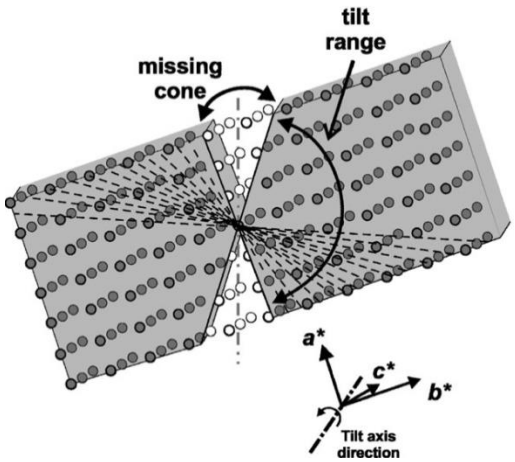
TEM goniometer (single /double tilt, tilt rotation, tomography)

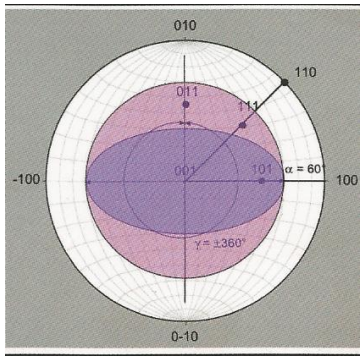




all goniometers work according to same principles, goniometry of direct or reciprocal lattice vectors of individual crystals can be easily treated by matrices and visualized by stereographic projections







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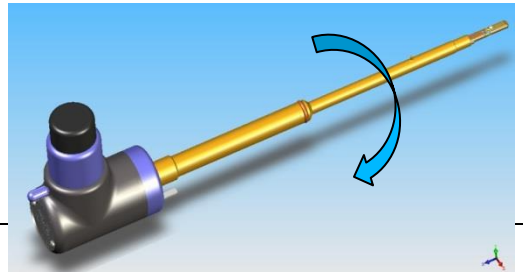
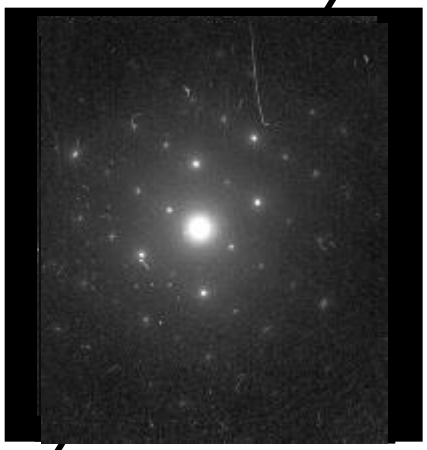
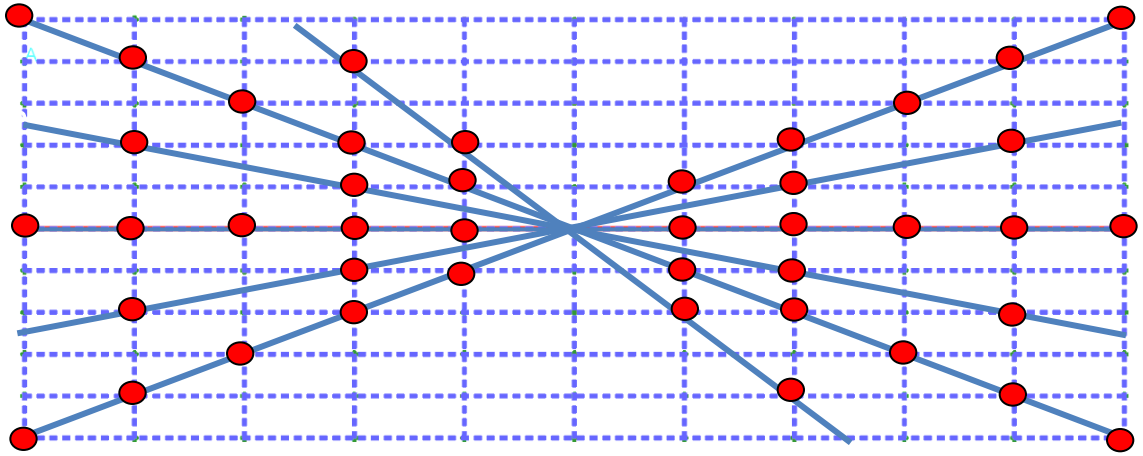
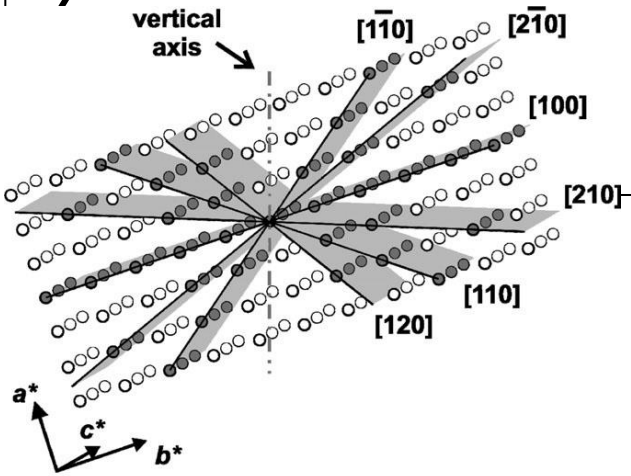
Find crystal cell parameters



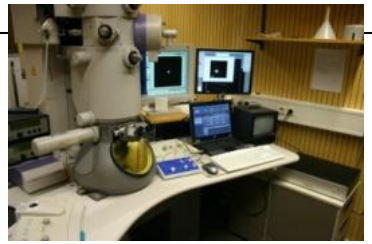
TEM : manual tilt series acquisition



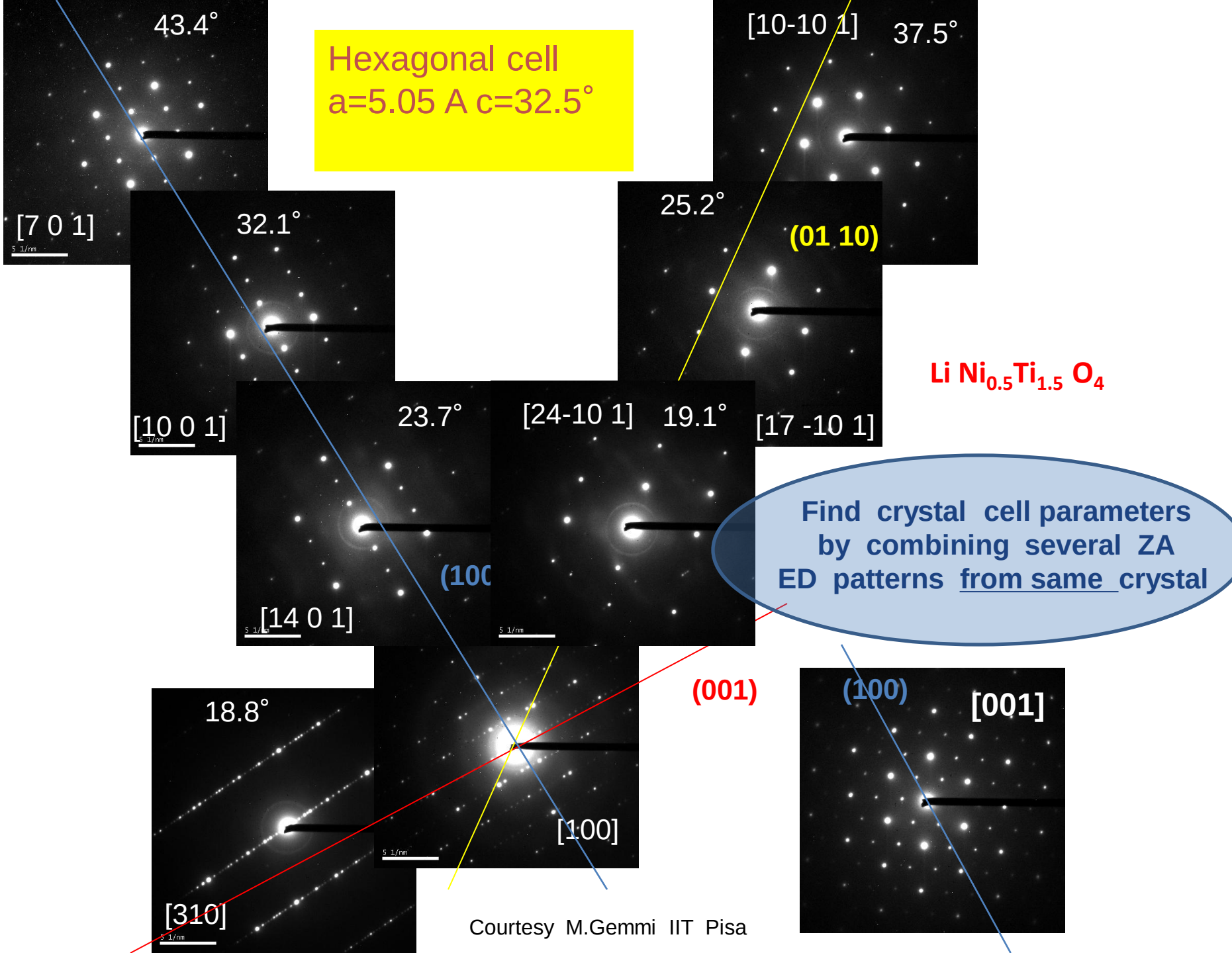




Problem : "missing cone" = lost data

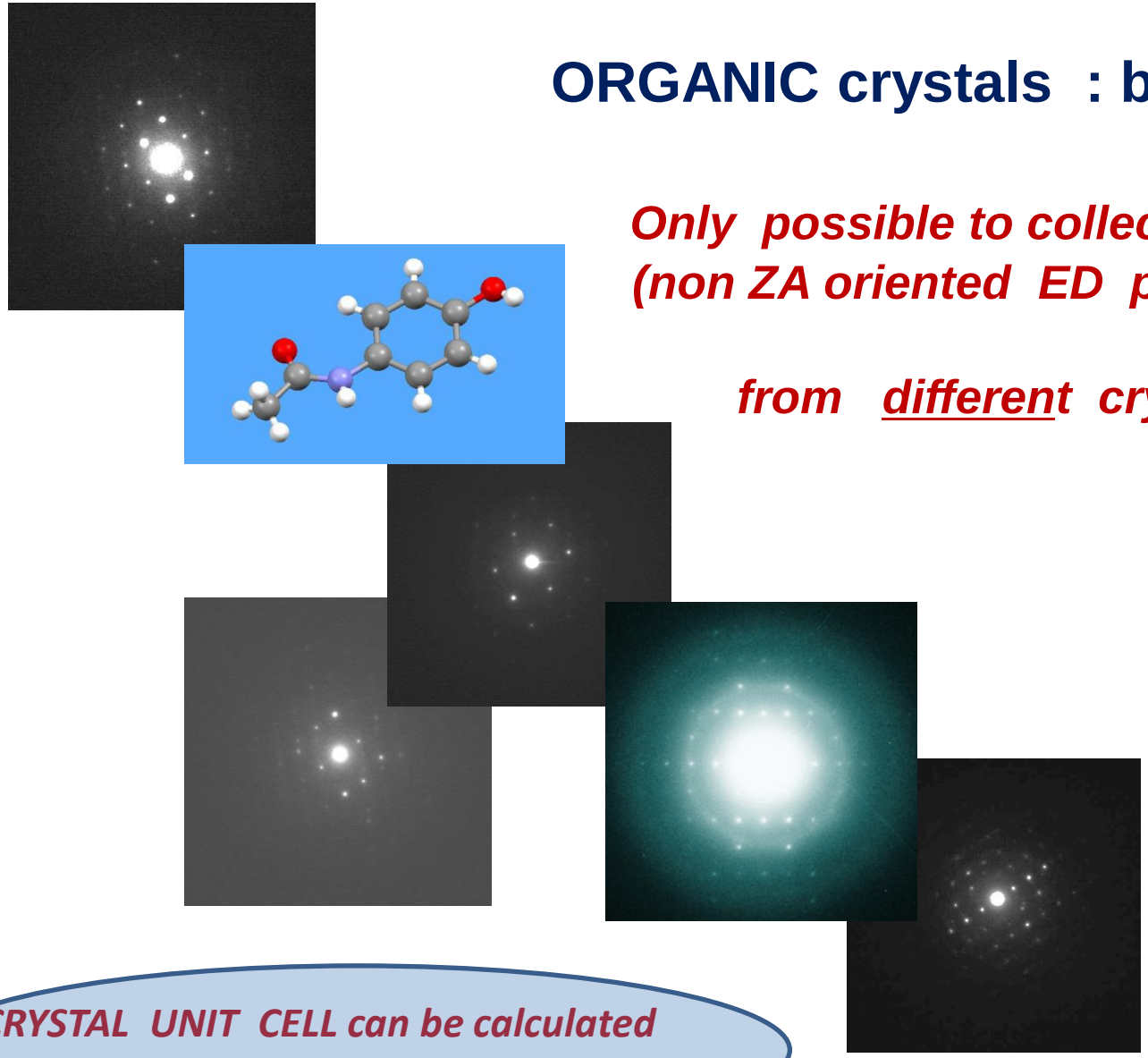


Courtesy : Prof. U Kolb UMainz



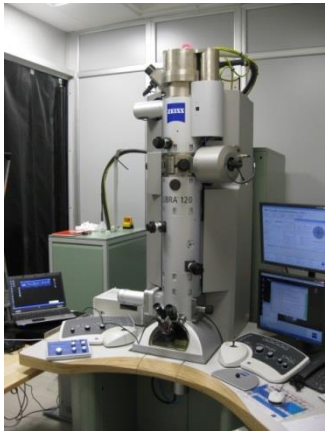
Courtesy M.Gemmi IIT Pisa

ORGANIC crystals : beam sensitive



Only possible to collect several (non ZA oriented ED patterns)

from <u>different</u> crystals



CRYSTAL UNIT CELL can be calculated from several patterns (oriented or not)

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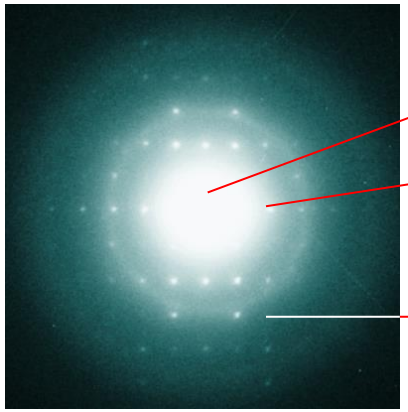
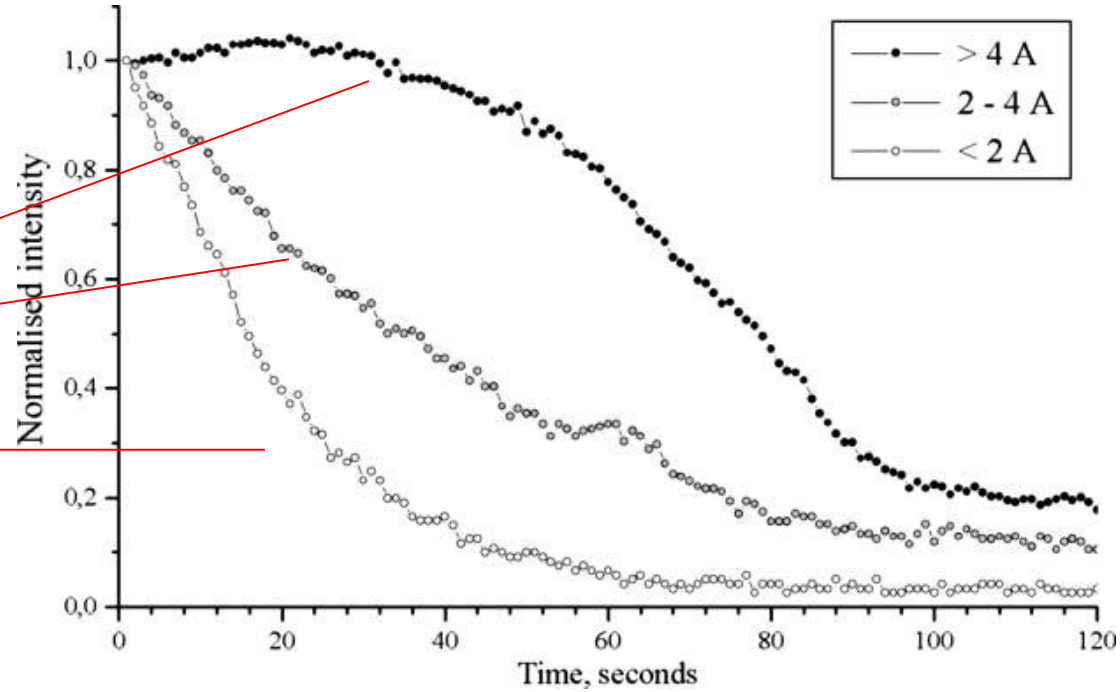
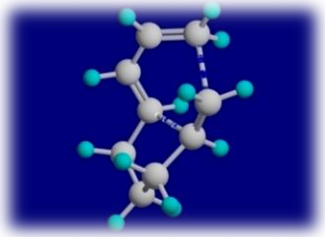
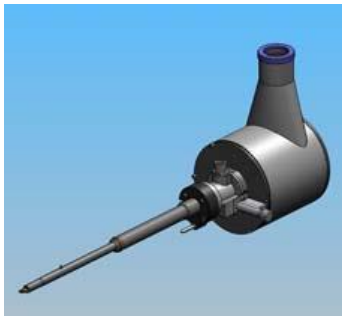
TEM - organic samples
Keeping crystals deep-frozen: cryo techniques







Organic samples degrade fast under the beam – cooling sample at Liquid Nitrogen is mandatory



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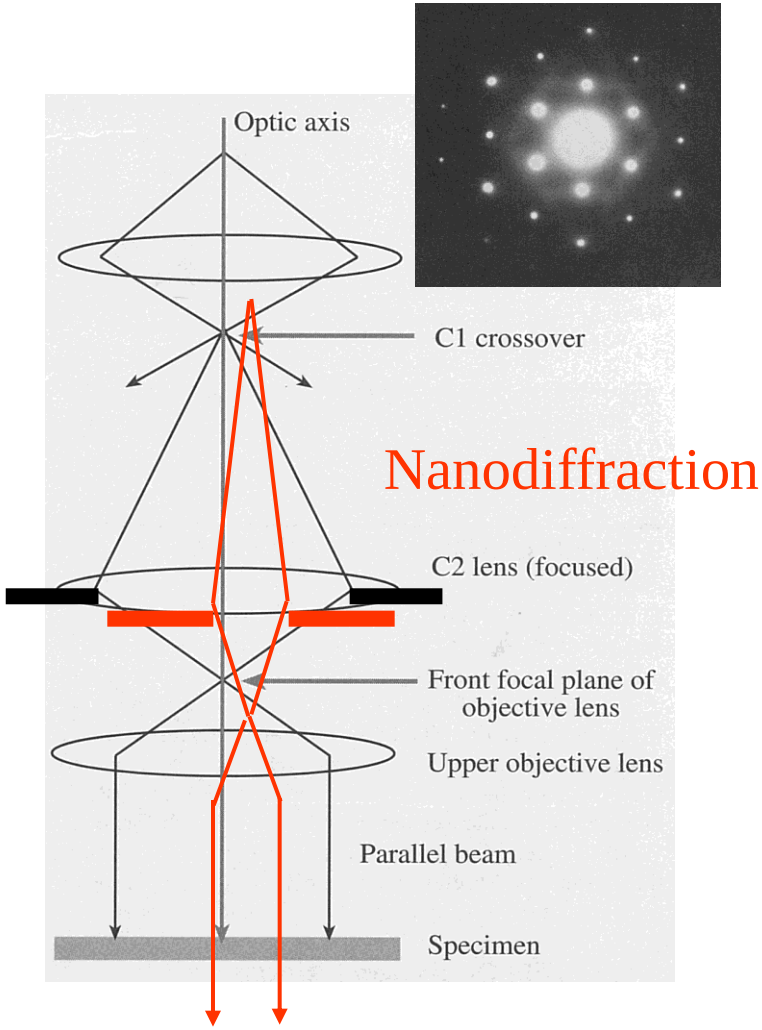
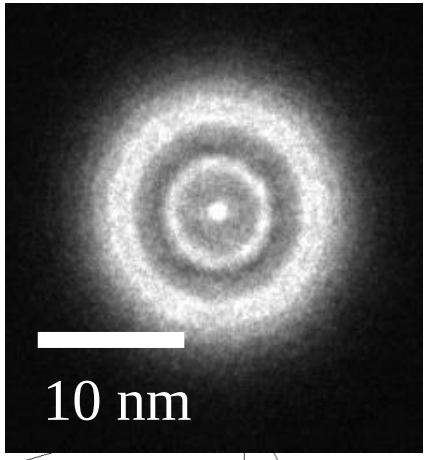
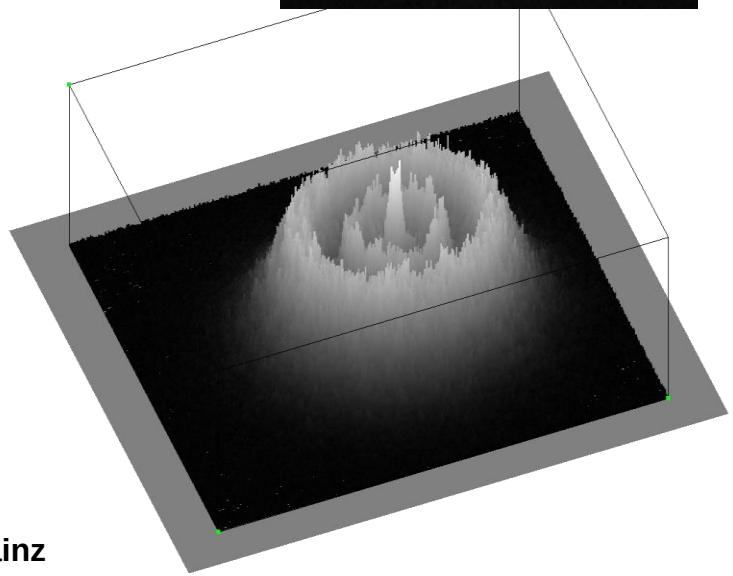
TEM for organic samples : use small probe and low dose



Convergence angle: 0.2 mrad
Electron dose rate: ~ 3 e/A^{2}s





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Courtesy : Prof. U Kolb UMainz

ORGANIC CRYSTALS & ELECTRON DIFFRACTION - EARLY BEGINNINGS 1950-1990

Some electron diffractionists were persistent - Group in Moscow claimed that structures could be solved from e. d. data

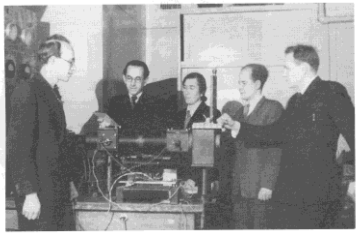
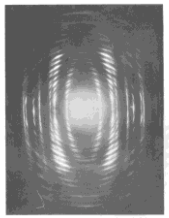


Рис. 1. Коллектив кабинета электронографии (1947 г.) у лабораторного варианта электронографа ЭГ-1. Слева направо: Б.К. Вайнштейн, З.Г. Пинскер, Л.И. Татаринова, Г.И. Дистлер, И.И. Жвани.



Oblique texture patterns from mm diameter areas:

Multiple scattering effects supposedly minimized by averaging over several orientations. Dynamical deviations addressed by 2-beam theory, permitting *ab initio* analysis.

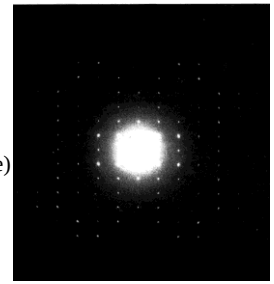
ExxonMobil Research and Engineering

Example 2: Poly(butene-1), polymorph III

Epitaxy by lattice matching is understandable for relatively simple linear polymer chains. However, helical structures can also be oriented with specialized organic substrates - e. g. the polymorphs of isotactic poly(butene-1). (See: S. Kopp, et al., Polymer 35 (1994) 908, 916.)

Form III of this polymer cannot be drawn into a fiber. A powder x-ray determination was constrained by extensive reflection overlap. Electron diffraction data (125 unique) from two orientations were obtained in spacegroup $P2_12_12_1$ after tilting,

a = 12.38, b = 8.88, c = 7.56 Å



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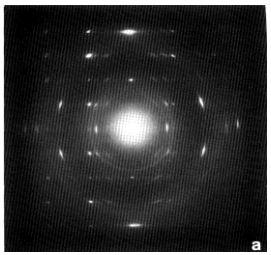


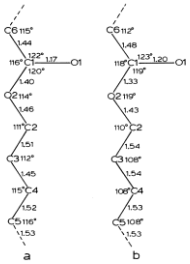
polymer on epitaxial substrate

From D.Dorset lecture ElCryst 2005 Brussels

Application to the determination of linear polymer structures
1. Poly ε-caprolactone

Data from solution-crystallized lamellae and epitaxially oriented material. Space group $P2_12_12_1$, a = 7.48, b = 4.98, c = 17.26 Å, 47 unique data. The analysis used symbolic addition via algebraic unknowns to yield 30 phases. (D. L. Dorset, Proc. Natl. Acad. Sci. USA 88 (1991) 5499.) Potential maps were interpretable. Bond distances and angles agree well with the best x-ray structure.

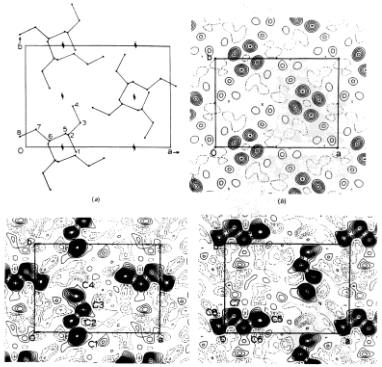
The electron crystallographic determination distinguished between two conflicting powder diffraction models, one with a planar molecular conformation (H. Bittiger, et al., Acta Cryst. B26 (1970) 1923) and the other with a twist around the ester linkage (Y. Chatani, et al., Polym. J. 1 (1970) 555), in favor of the latter. This solution was later verified by a direct methods solution with published powder x-ray data (D. L. Dorset, Polymer 38 (1997) 247.)

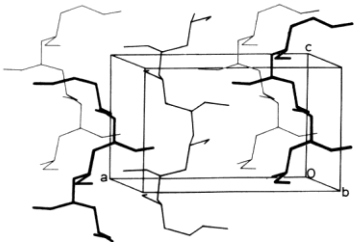


e. d. x-ray

Poly(butene-1), polymorph III

The crystal structure could be determined by a number of direct methods and the atomic positions were observable in potential maps. (D. L. Dorset, M. P. McCourt, S. Kopp, J. C. Wittmann, and B. Lotz, Acta Cryst. B50 (1994) 201.)





3-D chain packing

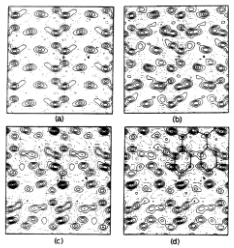
A molecular 4_1 axis was found to be oriented along the space group 2_1 axes in the c-direction. The structure could then be refined by restrained least squares.

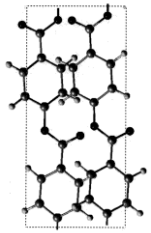
ORGANIC CRYSTALS & ELECTRON DIFFRACTION - EARLY BEGINNINGS 1950-1990

Example 3: Poly (*p*-oxybenzoate)

When epitaxial substrates are not obvious, it is possible sometimes to employ other crystallization techniques to obtain the proper orientation. For example, whiskers are produced from high temperature polymerization in dilute solutions (J. Liu and P. H. Geil, J. Macromol. Sci. Phys. B31 (1992) 163)

possible direct methods solutions





structural model

Whisker crystals of this polymer can be used with normal lamellar preparations for 3-D data collection. The phase 1 form, a = 7.45, b = 5.64, c = 12.47Å, was solved in space group $P2_12_12_1$ by direct methods. (J. Liu, B. L. Yuan, P. H. Geil, and D. L. Dorset, Polymer 38 (1997) 6031.)

Other polymer structure analyses also reported.

Sometimes structure determination difficult despite all measures

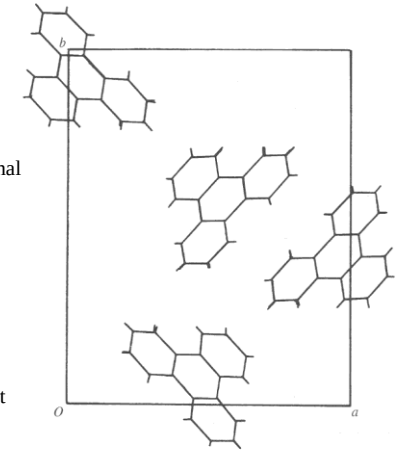
Example 4: triphenylene

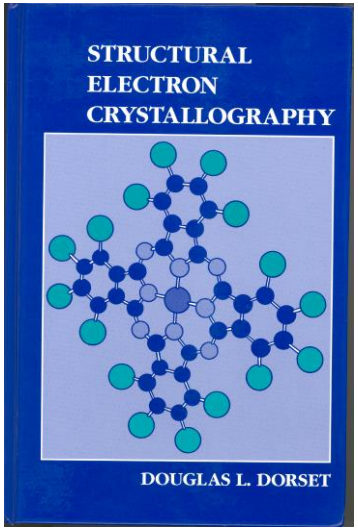
Space group: $P2_12_12_1$
a = 13.20, b = 16.73, c = 5.26 Å

Crystals grown by orientation on naphthalene - also epitaxial view to provide 3-D data set. Crystals flatter than if grown from solution.

Data set very sparse, however. Traditional direct methods not useful. Structure solved by lattice energy minimization. (Dorset, McCourt, Li, Voigt-Martin, J. Appl. Cryst. 31 (1998) 544.)

More recently solved by maximum entropy and likelihood. Only molecular envelope obtained - similar to structures solved by U. Kolb and I. Voigt-Martin at U. Mainz

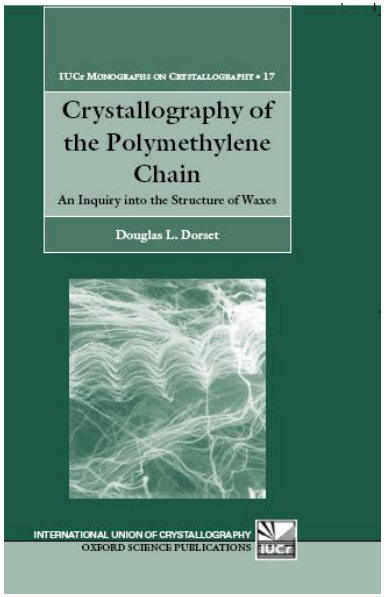




Other structures determined from electron diffraction data:

Light atom inorganics - e. g. boric acid
Lipid bilayers
Linear polymers

Zeolites - accompanying lecture



Major application area of organic electron crystallography:

Structure of polydisperse chain arrays (including chain branching):

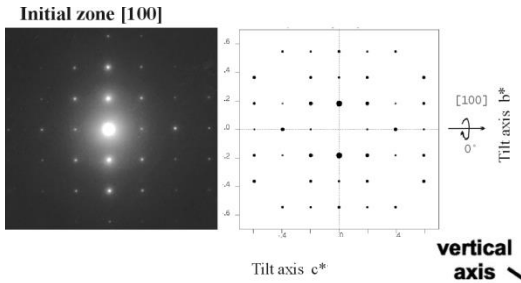
- binary solid solutions
- miscibility gap
- eutectics
- petroleum waxes
- low MW linear polyethylene

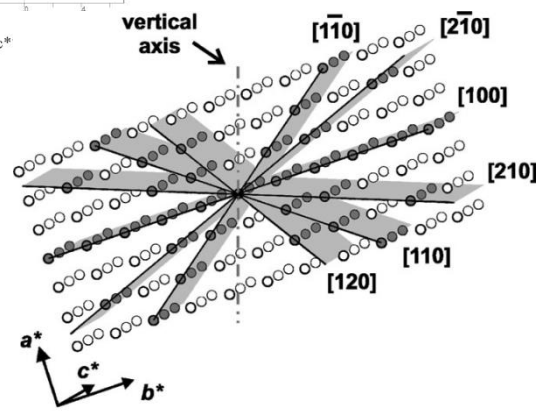
From D.Dorset lecture ElCryst 2005 Brussels

TEM : manual tilt to obtain ED patterns

organic pigments , drugs etc..

ORGANIC CRYSTALS & ELECTRON DIFFRACTION - 1990 - 2000





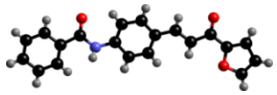
1-(2-furyl)-3-(4-aminophenyl)-2-propene-1-one (FAPPO)

Cell parameter from electron diffraction

a = 28.51 Å

b = 5.043 Å

c = 11.025 Å



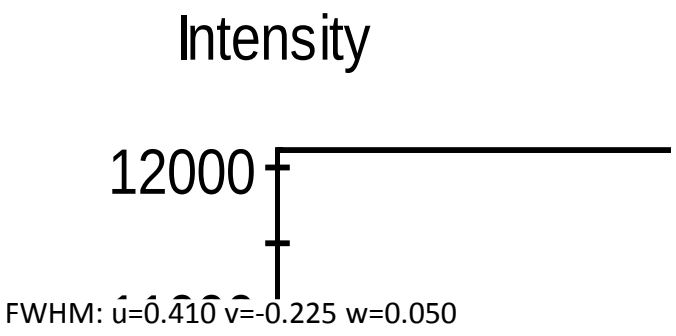
Cell parameter from Pawley Fit:

Rwp= 5.18%, Rp= 3.83%

a = 28.4885 Å

b = 5.0563 Å

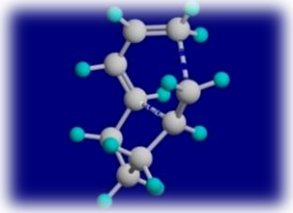
c = 11.0191 Å

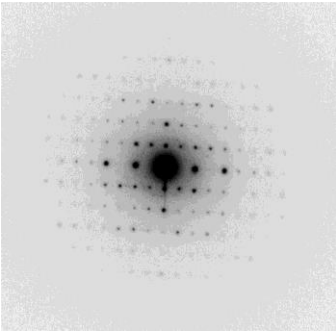


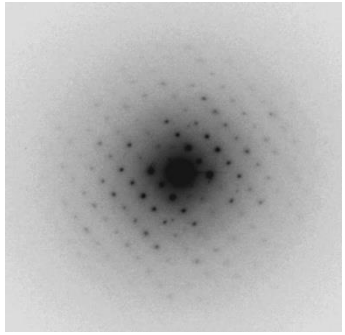
Courtesy : Prof. U Kolb UMainz

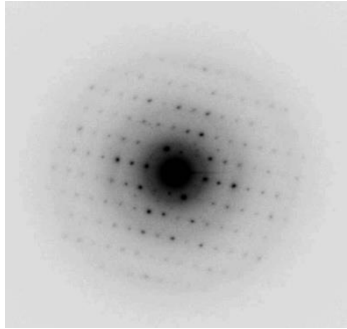
TEM : Manual random search for oriented ED patterns

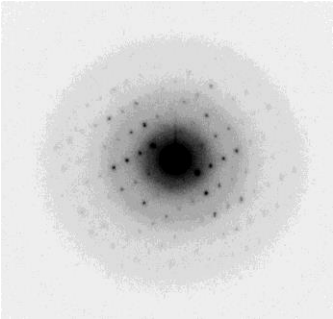
Penicillin G – potassium

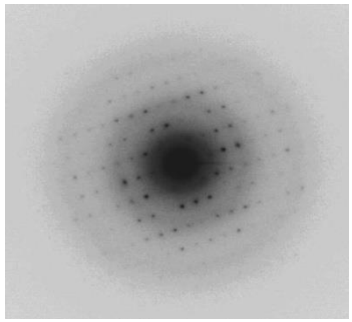


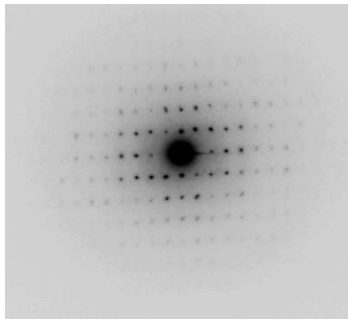












Laue class	Zone axes						
CUBIC CRYSTAL SYSTEM							
m-3m	<111>	<001>	<110>	<uv0>	<uuw>	<uvw>	
WP	3m	4mm	2mm	M	m	1	
ZOLZ	(6mm)	(4mm)	(2mm)	(2mm)	(2mm)	(2)	
m-3	<111>	<001>	<uv0>	<uvw>			
WP	3	2mm	m	1			
ZOLZ	(6)	(2mm)	(2mm)	(2)			
HEXAGONAL CRYSTAL SYSTEM							
6/mmm	<0001>	<11-20>	<1-100>	<uv.0>	<uu.w>	<u-u.w>	<uv.w>
WP	6mm	2mm	2mm	m	m	m	1
ZOLZ	(6mm)	(2mm)	(2mm)	(2mm)	(2mm)	(2mm)	(2)
6/m	<0001>	<uv.0>	<uv.w>				
WP	6	m	1				
ZOLZ	(6)	(2mm)	(2)				
TRIGONAL CRYSTAL SYSTEM							
-3m	<0001>	<11-20>	<u-u.w>	<uv.w>			
WP	3m	2	m	1			
ZOLZ	(6mm)	(2)	(2mm)	(2)			
-3	<0001>	<uv.w>					
WP	3	1					
ZOLZ	6	2					
TETRAGONAL CRYSTAL SYSTEM							
4/mmm	<001>	<100>	<110>	<u0w>	<uv0>	<uuw>	<uvw>
WP	4mm	2mm	2mm	m	m	m	1
ZOLZ	(4mm)	(2mm)	(2mm)	(2mm)	(2mm)	(2mm)	(2)
4/m	<001>	<uv0>	<uvw>				
WP	4	m	1				
ZOLZ	(4)	(2mm)	(2)				
ORTHORHOMBIC CRYSTAL SYSTEM							
mmm	<100>	<010>	<001>	<0vw>	<u0w>	<uv0>	<uvw>
WP	2mm	2mm	2mm	m	m	m	1
ZOLZ	(2mm)	(2mm)	(2mm)	(2mm)	(2mm)	(2mm)	(2)
MONOCLINIC CRYSTAL SYSTEM (unique axis b)							
2/m	<010>	<u0w>	<uvw>				
WP	2	m	1				
ZOLZ	(2)	(2mm)	(2)				
TRICLINIC CRYSTAL SYSTEM							
-1	<uvw>						
WP	1						
ZOLZ	(2)						

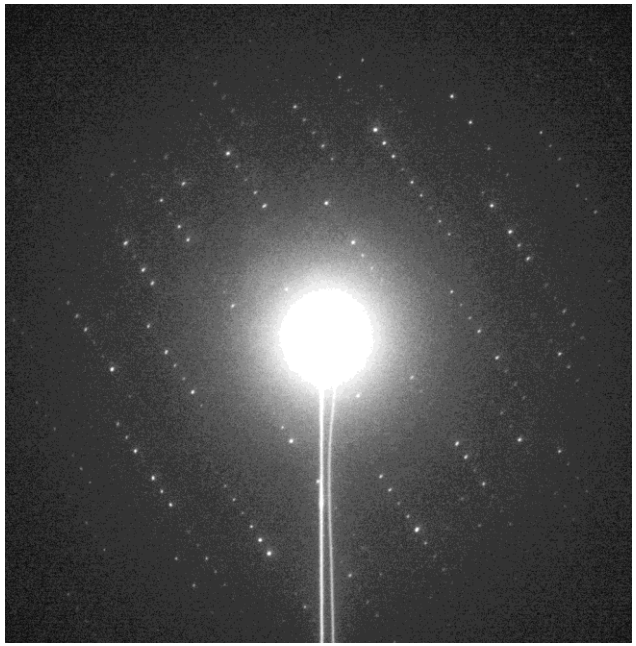
<u>Easier to find crystal cell</u> parameters from "randomly oriented" PED patterns

Orthorombic a = 6.4 A b = 9.4 A c = 30 A

NanoMEGAS
Advanced Tools for electron diffraction

Courtesy JP Abrahams, D.Georguieva Univ Leiden

TEM : high resolution electron diffraction of proteins



- **We can grow sub-micron crystals of different proteins reproducibly**
- **These protein nano-crystals are small enough for electron diffraction**
- **Crystals can be frozen successfully: diffraction so far ~ 2.1 Å**
- **Unit cell parameters can be calculated from the electron diffraction data**
- **Problems:**
  - **limiting factor is the beam damage, BUT electrons are more than 1000 times less damaging than X-rays, so we should be able to do better than synchrotron radiation…**

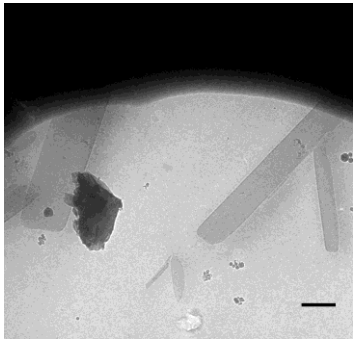
Electron diffraction pattern of a 3D lysozyme nano-crystal recorded on an image plate

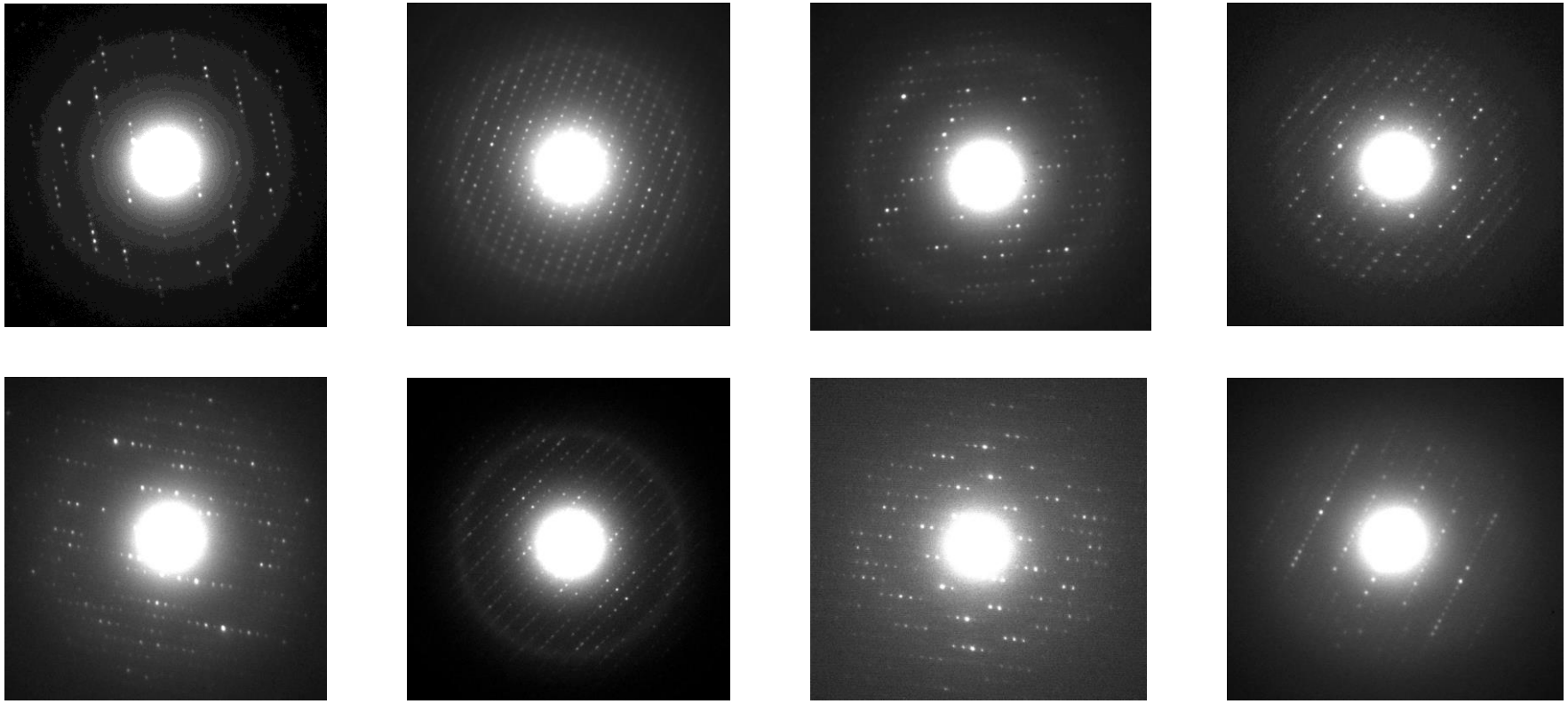
NanoMEGAS
Advanced Tools for electron diffraction

Courtesy JP Abrahams, D.Georguieva Univ Leiden

TEM : manual random search for oriented electron diffraction patterns from lysozyme nanocrystals

$P4_32_12$ a=b=79.2 A c=38.0 A





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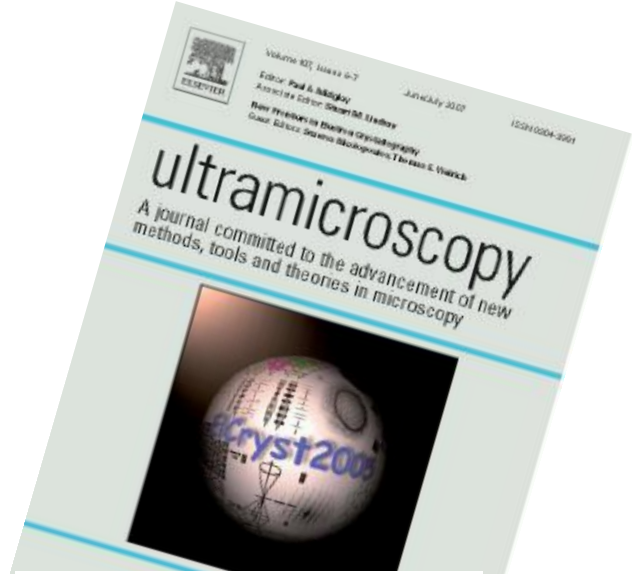
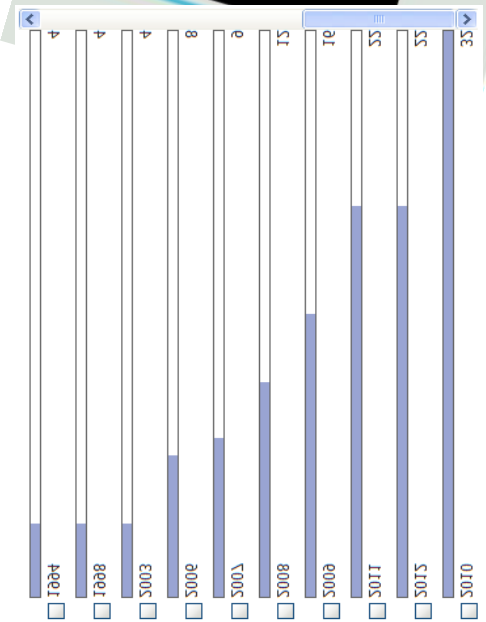
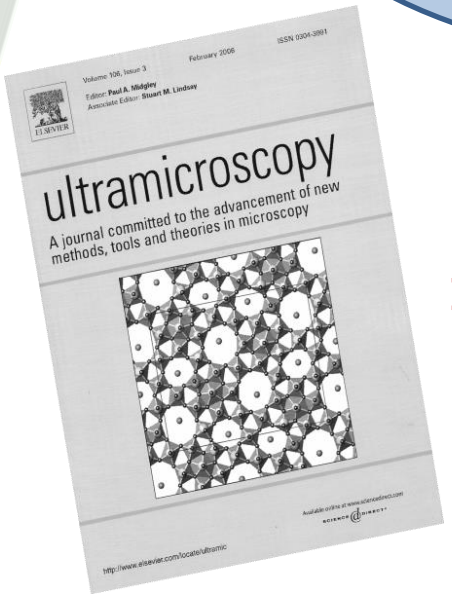
Courtesy JP Abrahams, D.Georguieva Univ Leiden



PRECESSION ELECTRON DIFFRACTION

NEW structure analysis technique for TEM

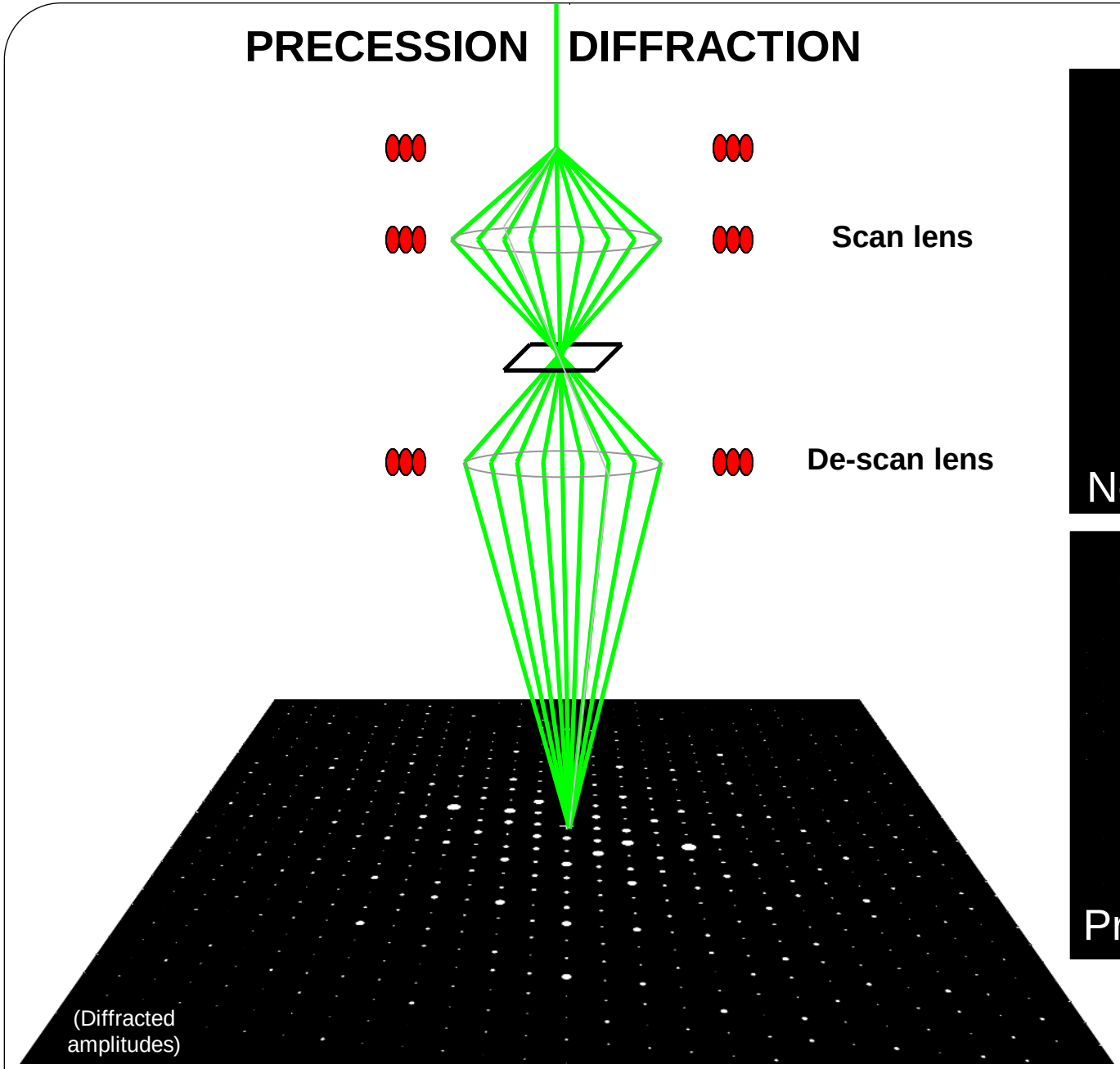


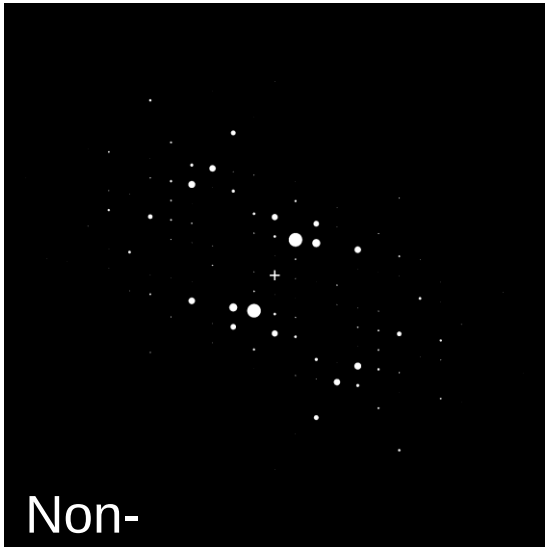


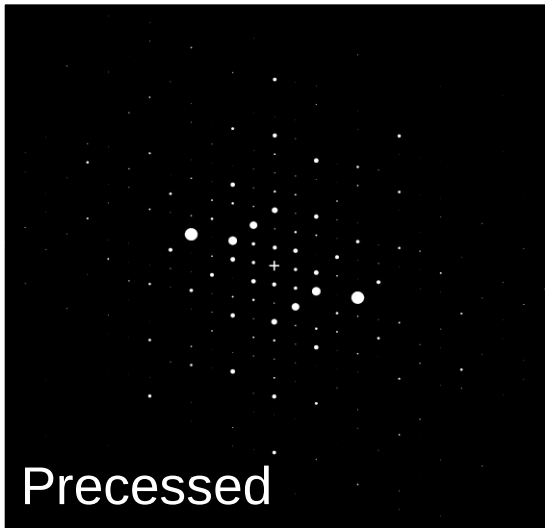
> 150 articles in 8 years

> 75 installations world-wide in TEM

NanoMEGAS
Advanced Tools for electron diffraction



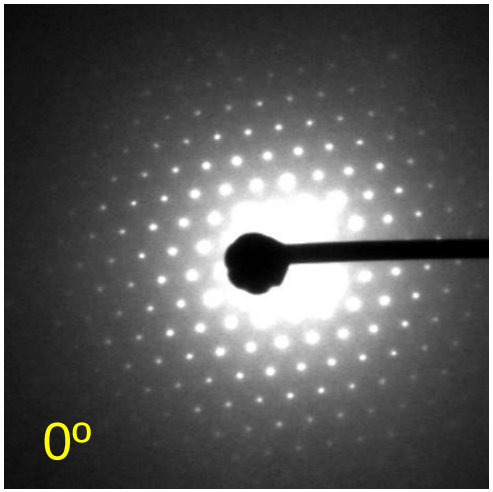


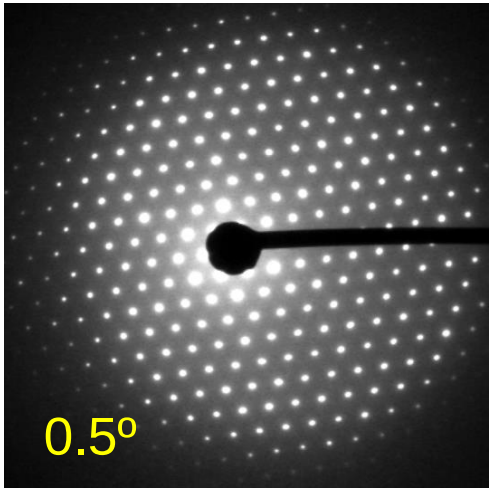


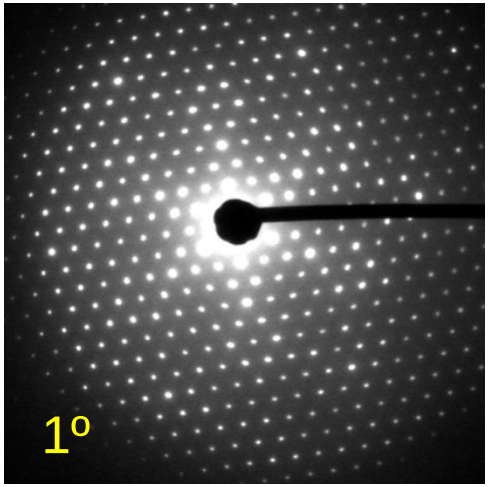
Precession…

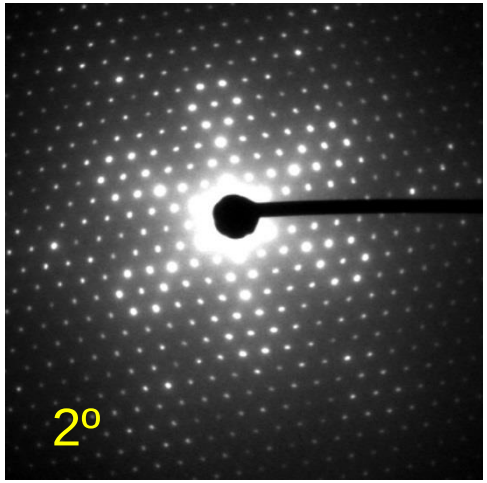
Courtesy Northwestern Univ USA (ref. C.S.Own , L.Marks)

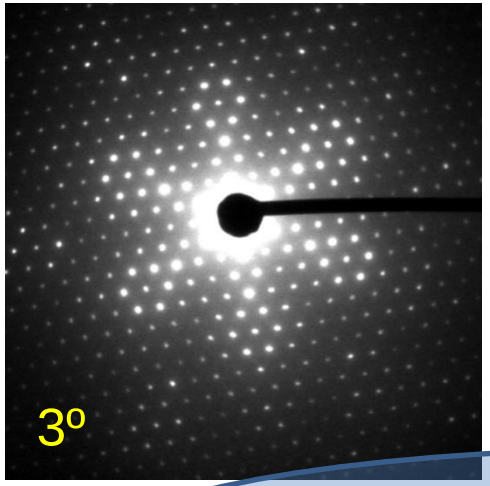
TEM : with precession electron diffraction (PED) ED intensity data are closer to kinematical values (X-Ray like)











As the precession angle increases from 0º to 3º, the diffraction pattern goes to higher resolution (i.e. more diffraction spots are seen).

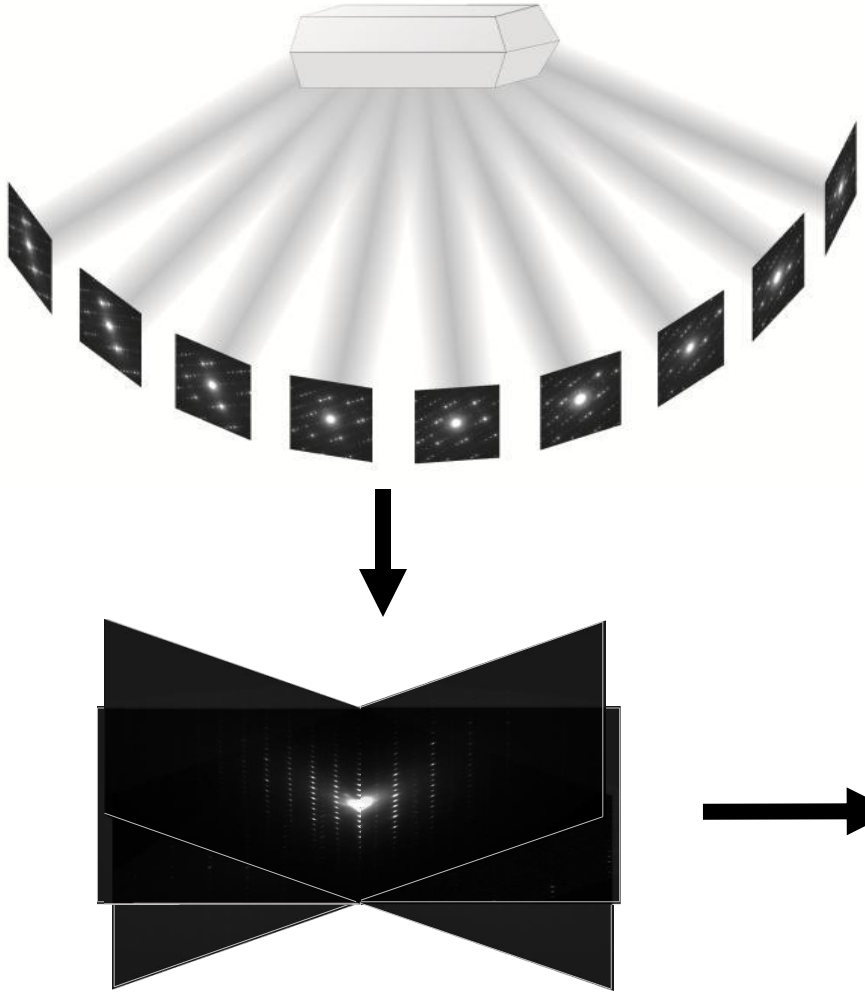
Mayenite $Ca_{12}Al_{14}O_{33}$

Cubic a = 11,89 A

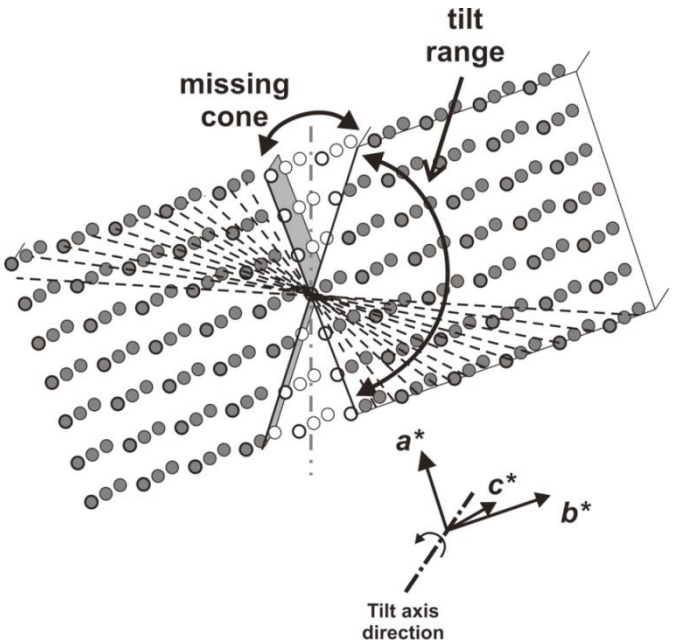
WE CAN USE PED DATA TO SOLVE STRUCTURES !

NanoMEGAS
Advanced Tools for electron diffraction

New Technique for cell & structure determination : Automatic precession diffraction tomography (ADT 3D)



Data analysis by ADT3D
3D reconstrucution of diffraction space



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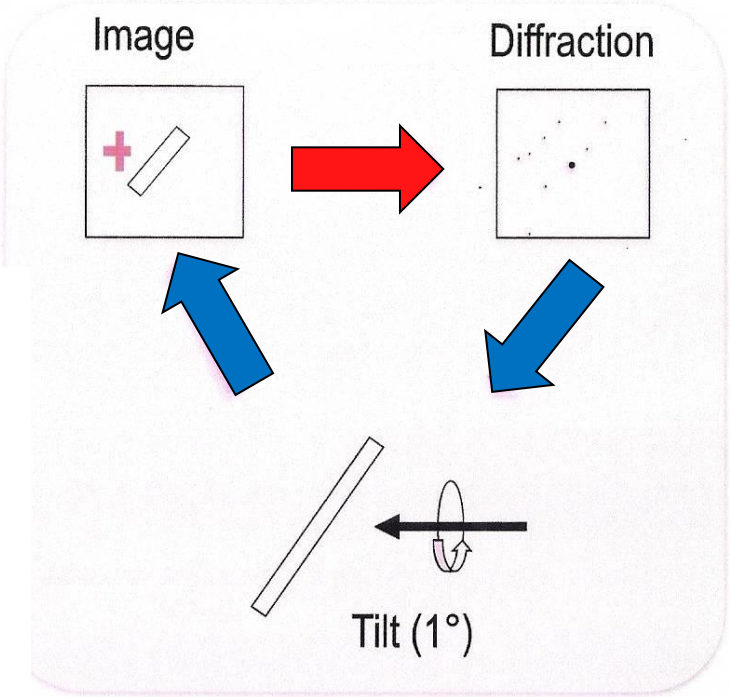
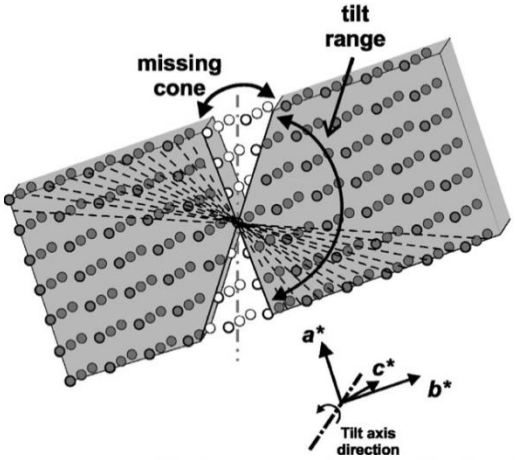
Courtesy : Prof. U Kolb UMainz

TEM - ADT3D : 3D sampling of reciprocal space

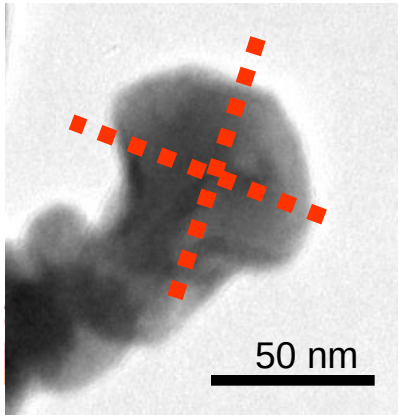
Select a crystal



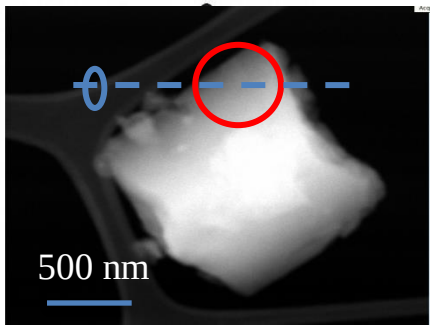
Tilt series



Arbitrary axis: Less dynamical effects,
More reflections
Easier to learn



Data collection: Any TEM using SAED or NED,
~30° for unit cell parameter
≥ 100° for structure solution

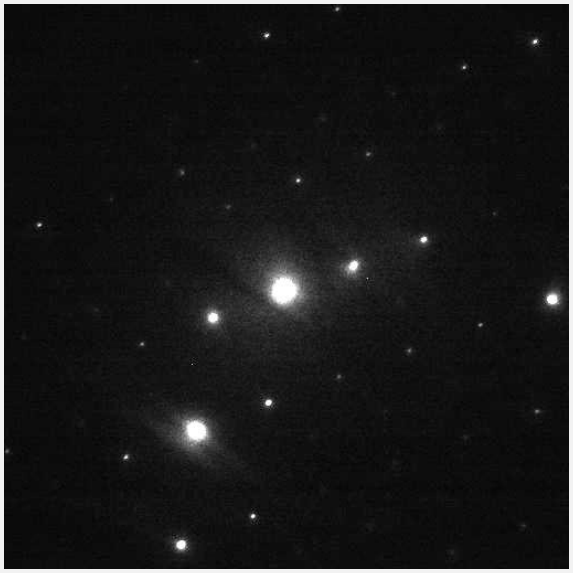


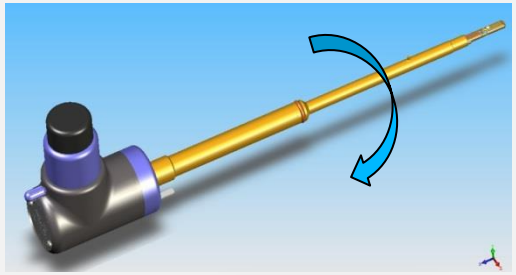
Courtesy : Prof. U Kolb UMainz

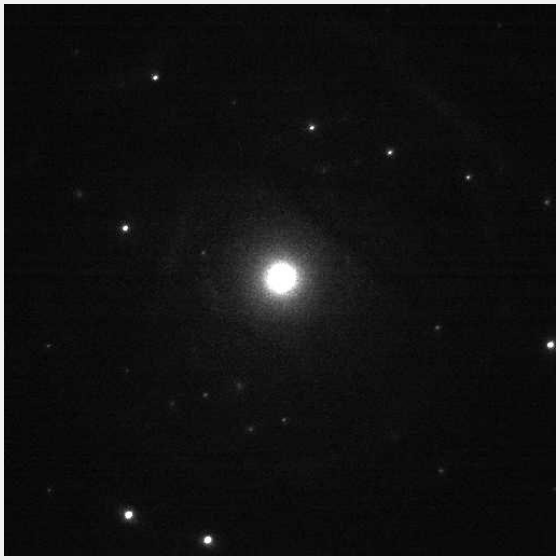
3D sampling of reciprocal space

Tilt angle ±30° (max. ±70°)

In steps of 1°







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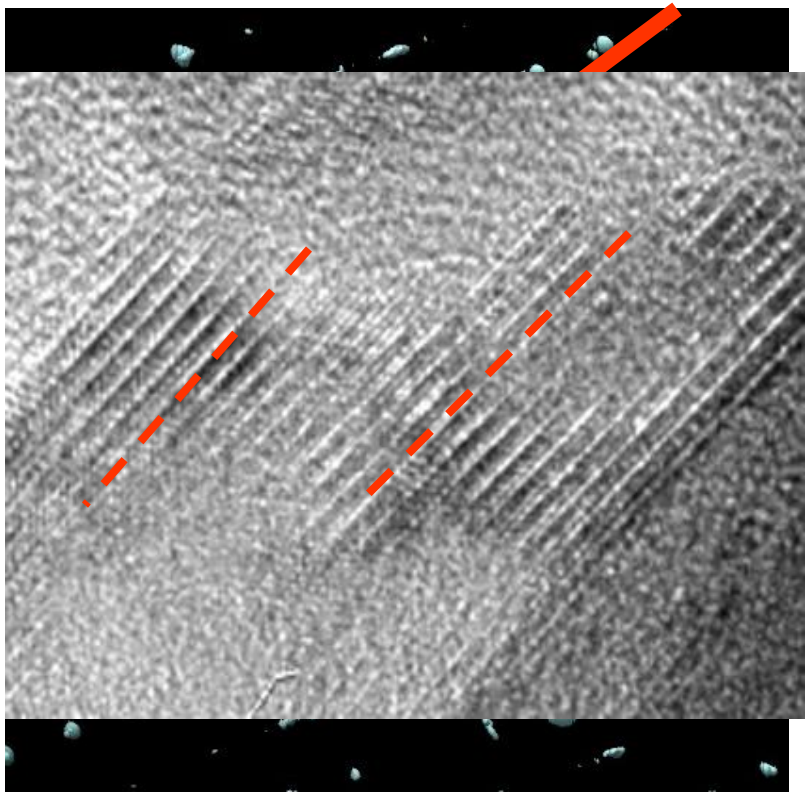
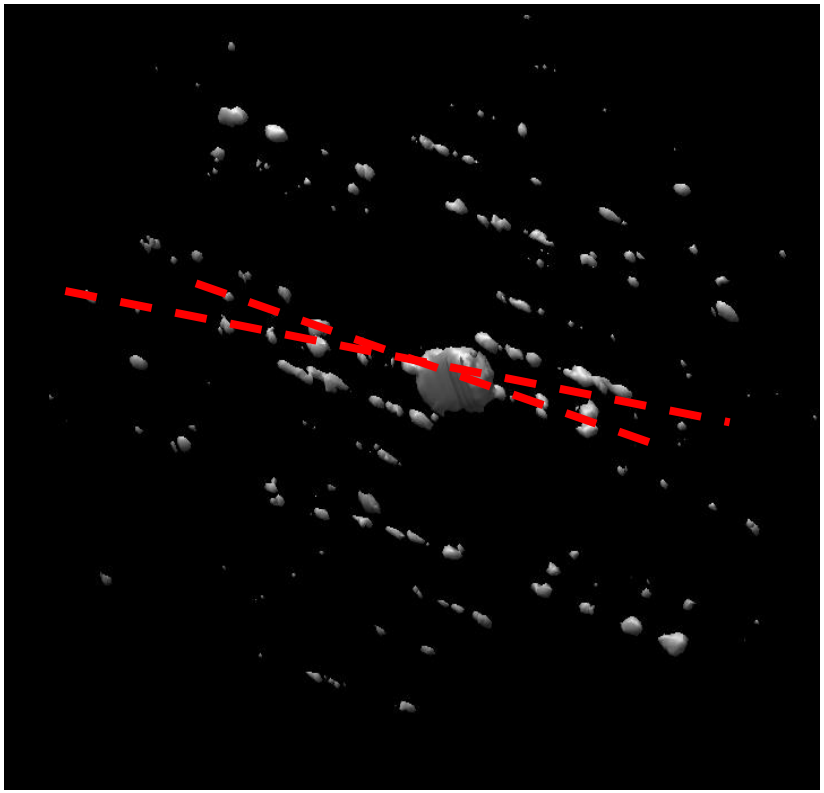
Advanced Tools for electron diffraction

Register intensities with CCD camera

TEM ADT3D : Disorder & polycrystallinity





DISORDER

$0kl$: k = 2N+1

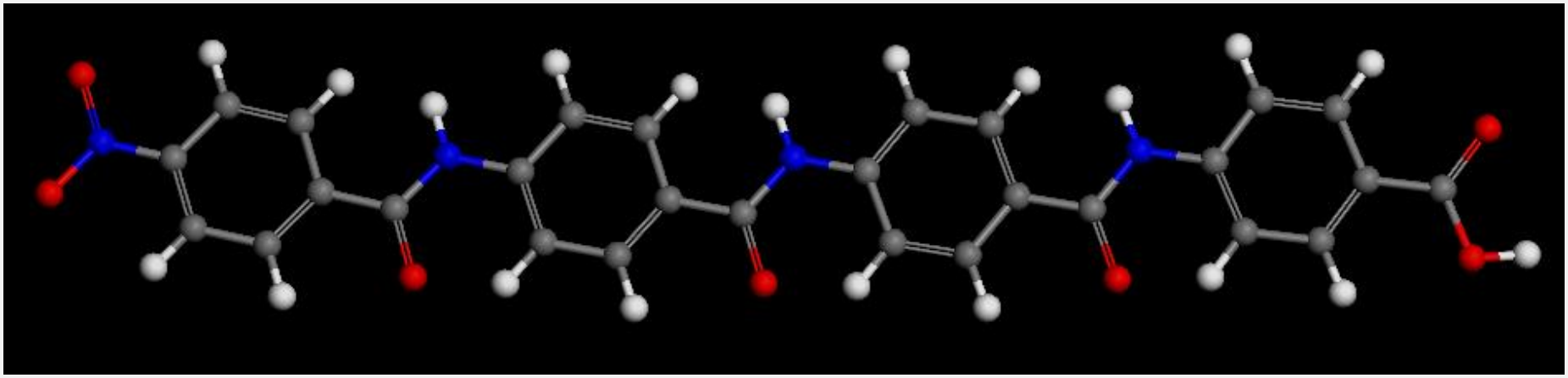
POLYCRYSTALS

c* tilted ~ 3°

Courtesy : Prof. U Kolb UMainz

Results

ADT-3D solving organic (polymer) compounds NS4



a=56.3Å b=5.8Å c=18.8Å β=75.53°

Unit cell content (asymm unit, Z=4)
28 C, 4 N, 7 O
Tilt range: ±60° **0.8031Å Angstrom resolution**

9410 total reflections 3818 independent reflections

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Advanced Tools for electron diffraction

Crystal Structures solved from ADT[1,2] data (new structures are marked with *)

	Space group	N° ind. reflections	N° ind. atoms	Volume (Å³)	Completeness (%)
Phosphates					
SrP_3N_5O[3]*	Pnam	1790	25	1900	86
$Ba_6P_{12}N_{17}O_9Br_3$*	$P6_3/m$	1343	11	1530	99
Tungstates					
$Na_2W_4O_{13}$[4]	P-1	738	10	262	69
$Na_2W_2O_7$	Cmce	454	9	1264	91
$K_{20}Al_4W_{24}O_{88}$*	C2	1307	36	1983	84
Layered materials					
Sodium titanate ($Na_2Ti_6O_{13}$)[5]	C2/m	517	11	510	72
Sodium titanate ($NaTi_3O_7OH{\cdot}2H_2O$)[6]*	C2/m	628	13	670	79
Hydrous silicate*	P-4m2	121	8	540	84
Ca-compounds					
Calcite ($CaCO_3$)[7]	R-3c	106	3	120	97
Calcium silicate hydrate ($Ca_5Si_6O_{17}{\cdot}5H_2O$)*	Cm	689	19	930	69
High pressure phases					
Hydrous Al-pyroxene ($Mg_2Al(OH)_2AlSiO_6$)[8]*	C2/c	498	8	560	87
Minerals					
Barite ($BaSO_4$)[9]	Pnma	355	5	350	82
Mullite ($Al_6Si_2O_{13}$)	Pbam	213	5	180	86
Charoite_96($(K,Sr)_{16}(Ca,Na)_{32}[(Si_{70}(O,OH)_{180})](OH,F)_4{\cdot}nH_2O$)[10]*	$P2_1/m$	3353	89	4430	96
Charoite_90($(K,Sr)_{16}(Ca,Na)_{32}[(Si_{70}(O,OH)_{180})](OH,F)_4{\cdot}nH_2O$)[11]*	$P2_1/m$	2878	90	4450	97
Metal Organic Frameworks (MOF)					
MFU_4large ($Cl_4Zn_5N_{18}C_{36}O_6H_{12}$)[12]*	Fm-3m	655	8	32770	100
Basolite ($C_6H_4CuO_5$)	Fm-3m	384	7	18640	99
Bi-MOF*	$Pca2_1$	1158	34	3560	67
Inorganic nanophases					
Intermetallic nanoparticles (ZnSb)[13]	Pbca	106	2	440	70
Intermetallic nanoparticles (Zn_8Sb_7)[13]*	P-1	3651	30	1610	57
Intermetallic matrix (NiTe)	$P6_3/mmc$	37	2	150	93
Intermetallic nanodomains (Ni_3Te_2)*	$P6_3mc$	57	5	300	95
Semiconductor 6H-SiC	P6mm	52	6	130	100
Pseudo-spinel ($Li_2Ti_3NiO_8$)[14]	P-3c1	187	11	720	91
Zeolites					
ZSM-5 ($Na_xAl_xSi_{96-x}O_{192}$)	Pnma	2288	39	5490	79
IM-5 ($Si_{288}O_{576}$)	Cmcm	2170	71	16380	68
Natrolite ($Na_2Al_2Si_3O_{10}{\cdot}2H_2O$)[5]	Fdd2	719	10	2250	92
ITQ-43 ($Si_{92}O_{184}$)[15]*	Cmmm	2735	39	14040	91
ECS-3 ($(Na,K)_3Al_3Si_4C_{12}H_8O_{12}{\cdot}nH_2O$)[16]*	Cc	4417	62	5040	72
Organic					
NLO-active material 10-CNBA ($C_{29}NH_{17}$)[17]	$P2_1/c$	1871	30	2000	90
Oligo p-benzamide OPBA3[18]	$P2_1/c$	3078	30	1755	81
Oligo p-benzamide OPBA4[18]*	C2/c	3576	39	4545	77

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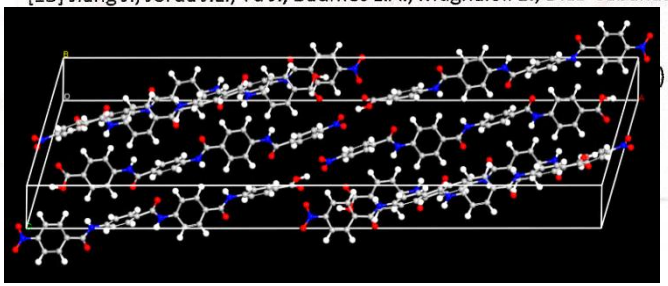

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3D diffraction tomography
Example on pharma API sample

API sample Nateglinide Form B

X-RAY DATA (from Synchrotron powder diffraction)

B: $P2_1$ with a=38.68198 Ang, b=57.94722 Ang, c=8.03988 Ang and beta=95.15785 deg

work in colllaboration with Dr. F.Gozo Excelsius Brussels

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Unit cell Naterglinide

- **Data set 1: a = 55.59Å, b=37.13Å, c=4.99Å, alpha=90.1, beta=88.5, gamma=90.2**

- **Data set 2: a = 56.7Å, b=38.4Å, c=4.92Å, alpha=89.2, beta=90.7, gamma=88.85**

- **X-RAY DATA**

  B: $P2_1$ with a=38.68198 Ang, b=57.94722 Ang, c=8.03988 Ang and beta=95.15785 deg

Work on progress
data consistent with X-Ray

Unpublished work , analysis with EDT software
by Dr. Oleynikov Stockholm University

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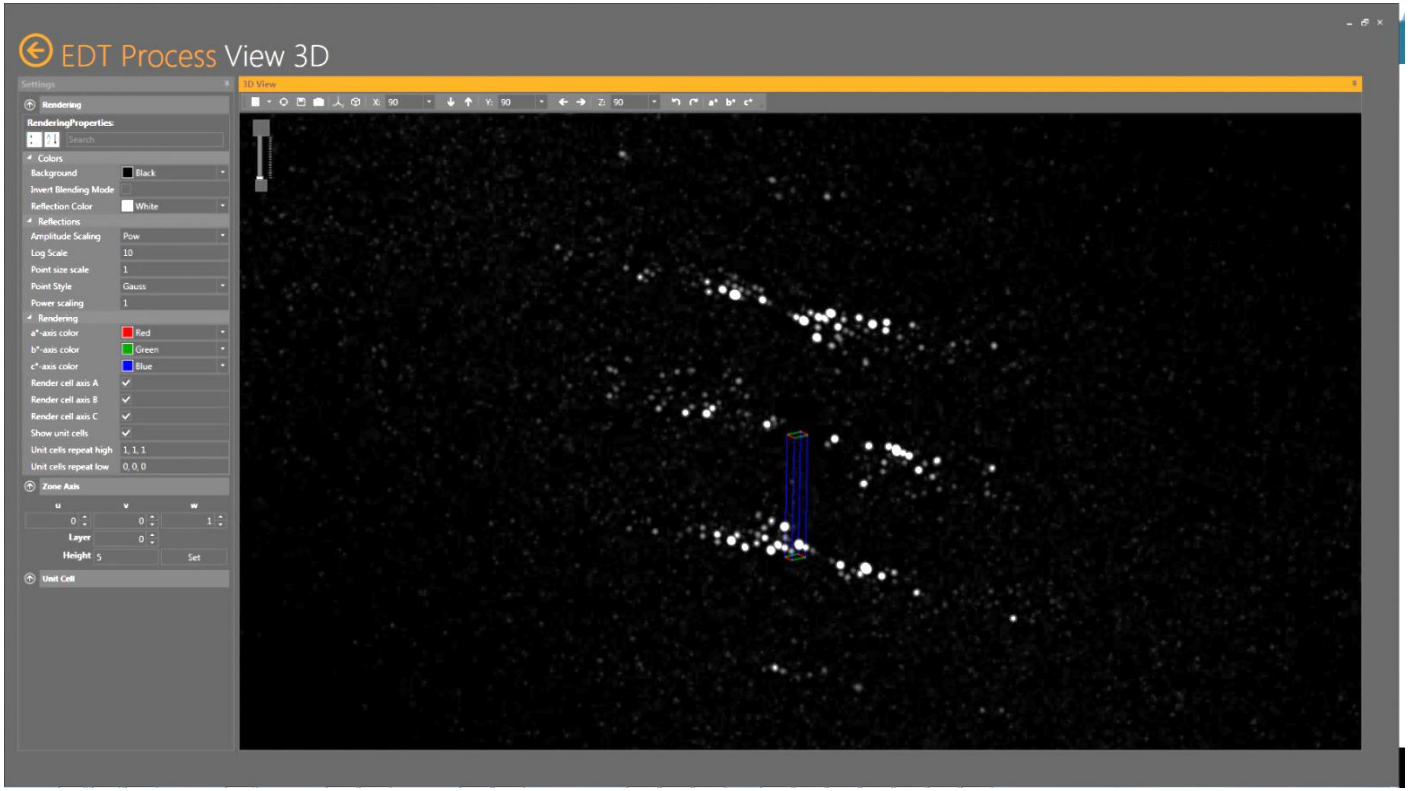
RESULTS 3D diffraction tomography
on a single Naterglinide nanocrystal



Unpublished work , analysis with EDT software by Dr. Oleynikov Stockholm University

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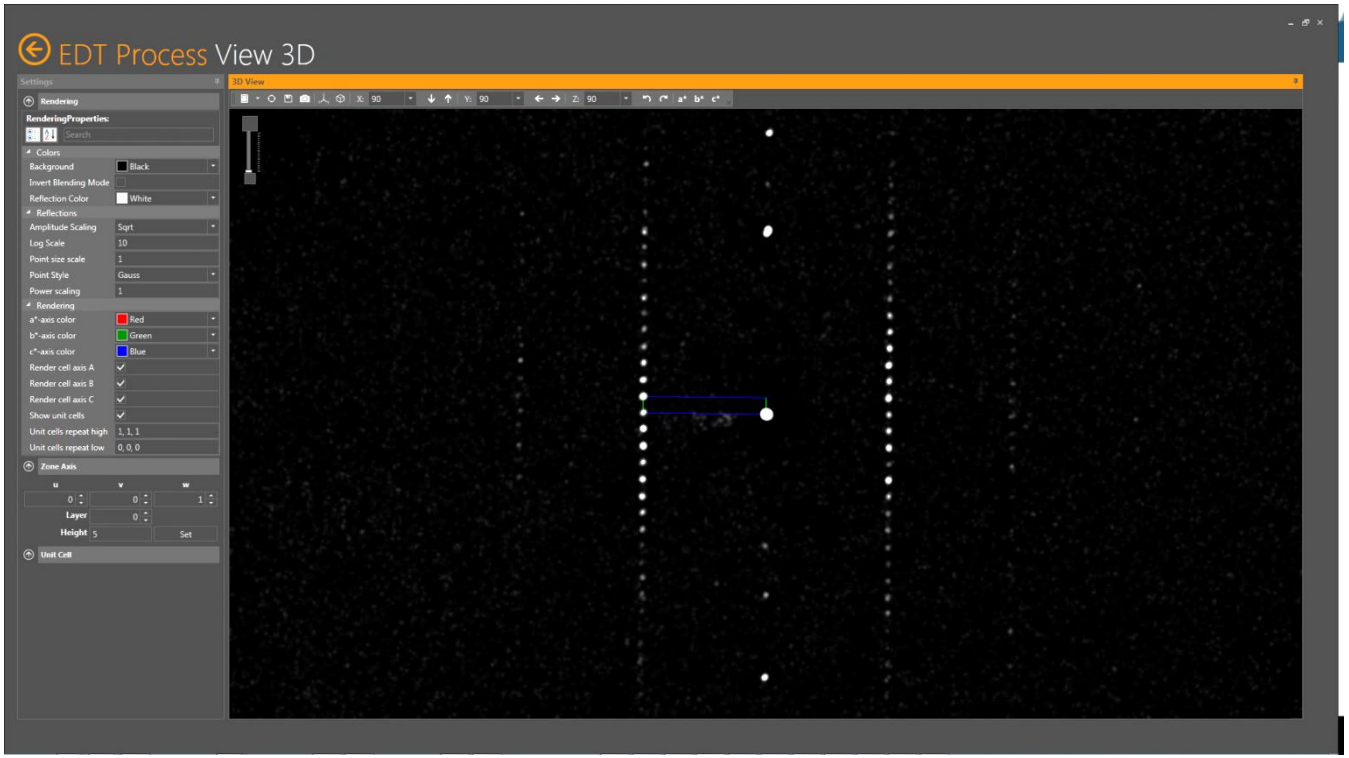
RESULTS 3D diffraction tomography
on a single Naterglinide nanocrystal



Unpublished work , analysis with EDT software by Dr. Oleynikov Stockholm University

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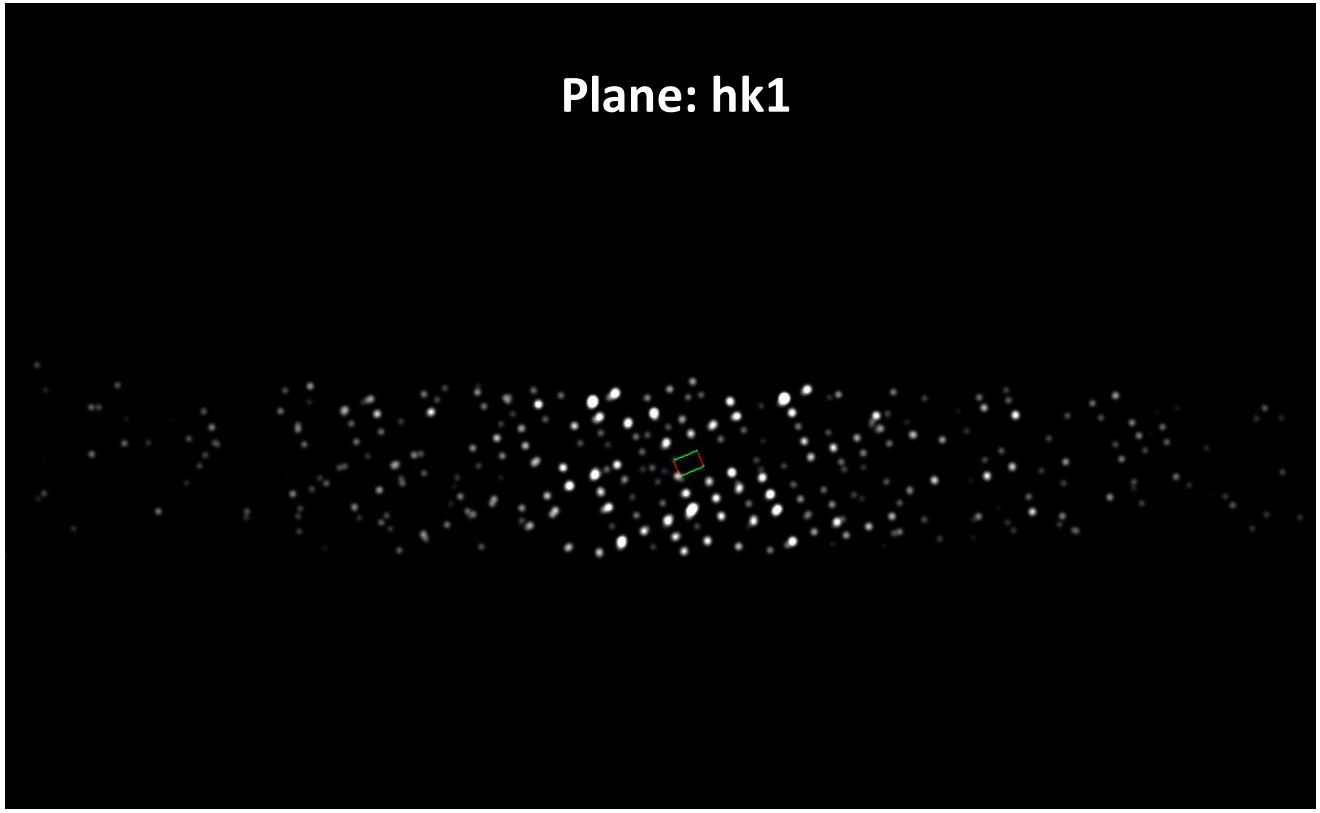
RESULTS 3D diffraction tomography
on a single Naterglinide nanocrystal



Unpublished work , analysis with EDT software by Dr. Oleynikov Stockholm University

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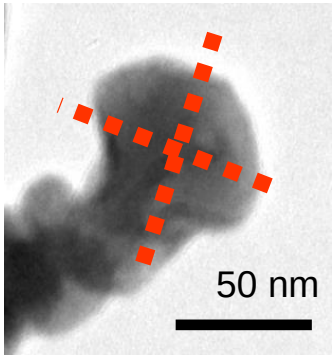
Automatic 3D precession diffraction tomography ADT-3D



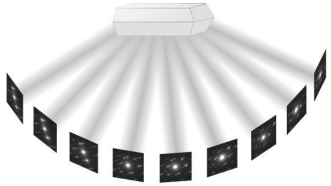
Access to single nano-crystals with TEM

Data collection in 90-120 min

Reveal Unit cell & crystal symmetry
though 3D automatic reciprocal space acquisition and reconstruction

Solve ab-initio structures using 3D precession intensities

ADT 3D for beam sensitive samples (pharma) should be used with cryo-techniques



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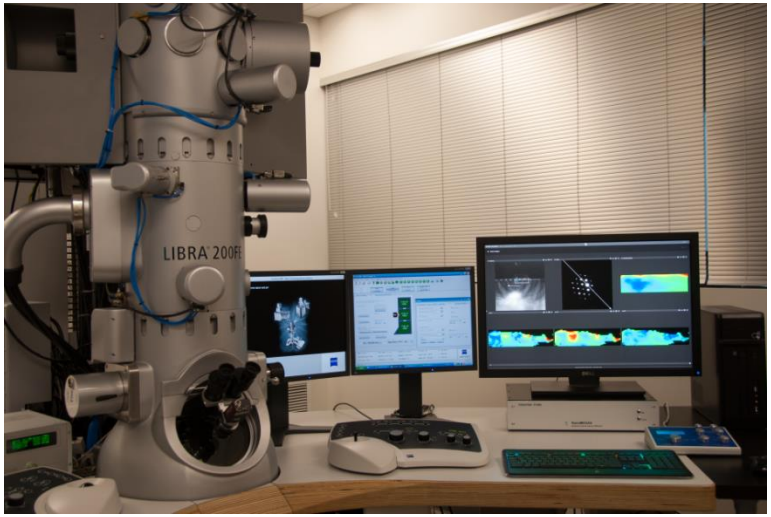
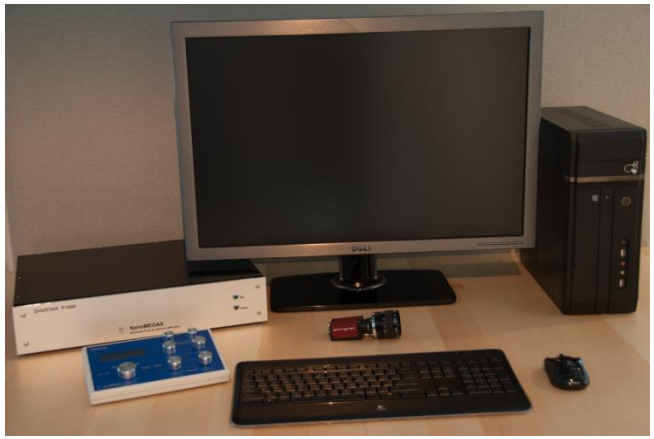
ORGANIC CRYSTALS : THE RANDOM TOMOGRAPHY METHOD





The challenge :

- **FIND CRYSTAL TEXTURE & amorphous content**
- **FIND UNIT CELL PARAMETER from thousands of nanocrystallites**
- **FIND CRYSTAL STRUCTURE from unknown crystals**

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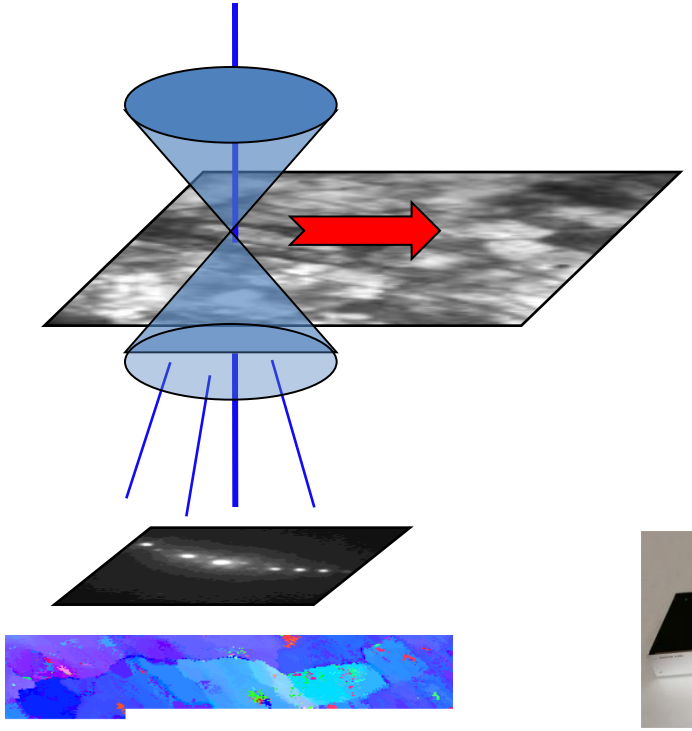
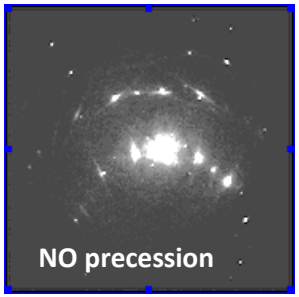
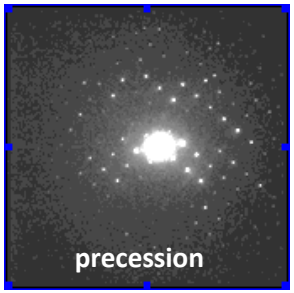
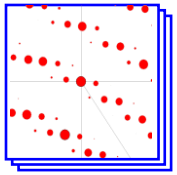
ASTAR (Orientation and phase imaging in TEM)



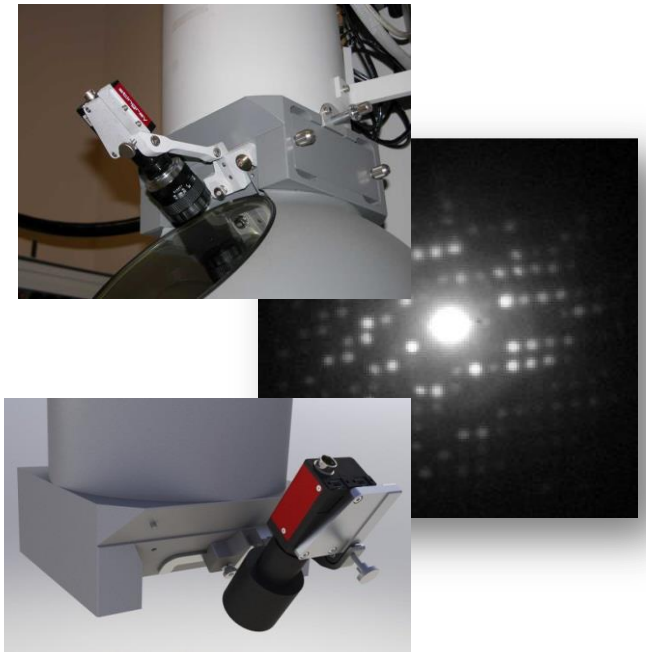
Orientation map







Using precession diffraction the number of ED spots observed increases (almost double) ; correlation index map becomes much more reliable when compared with templates



Scanning the TEM beam in precession mode
Step size 0.1 nm -100 nm
Dedicated CCD with > 100 frames /sec
Typical area 5 x 5 microns
Scanning times (typical) 5-10 min

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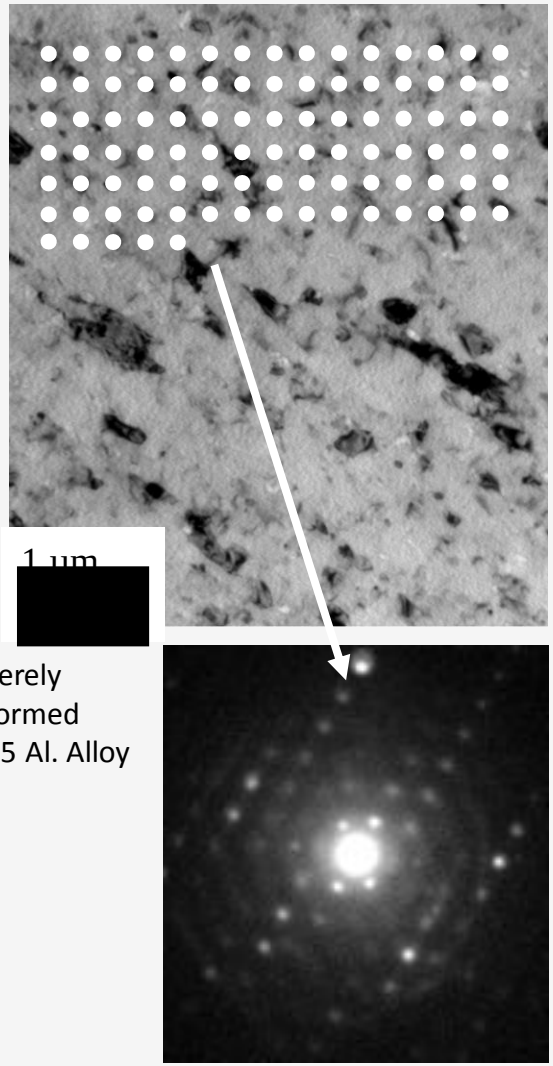
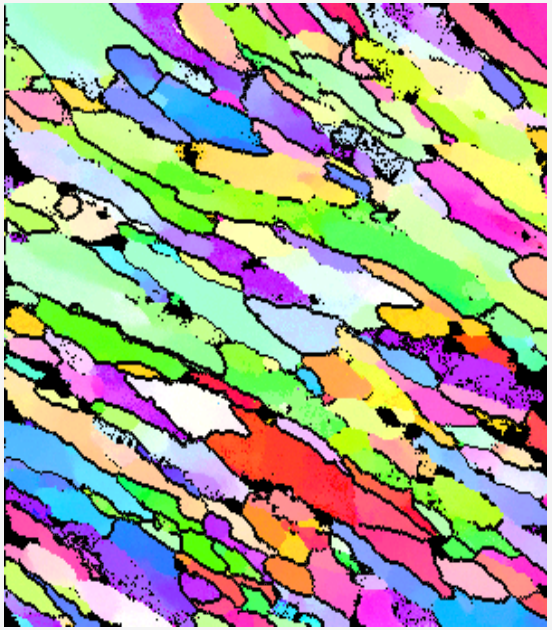
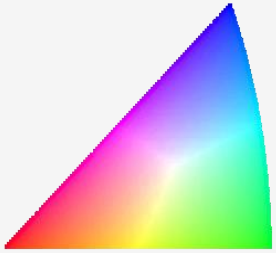
ASTAR : Automated Crystal Orientation Mapping



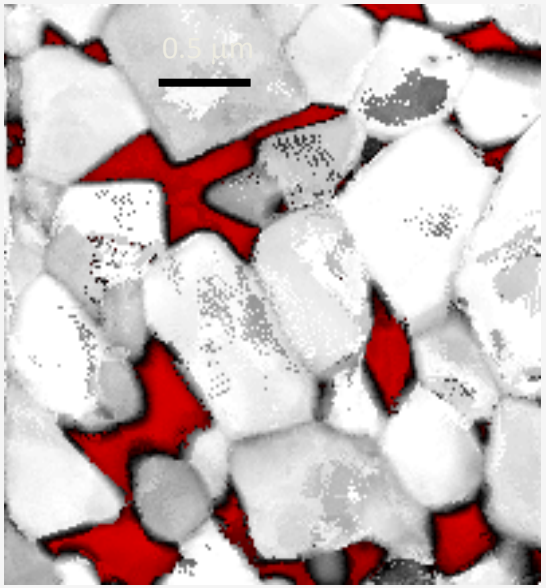
Severely deformed 7075 Al. Alloy



Orientation map



WC-Co



Phase map

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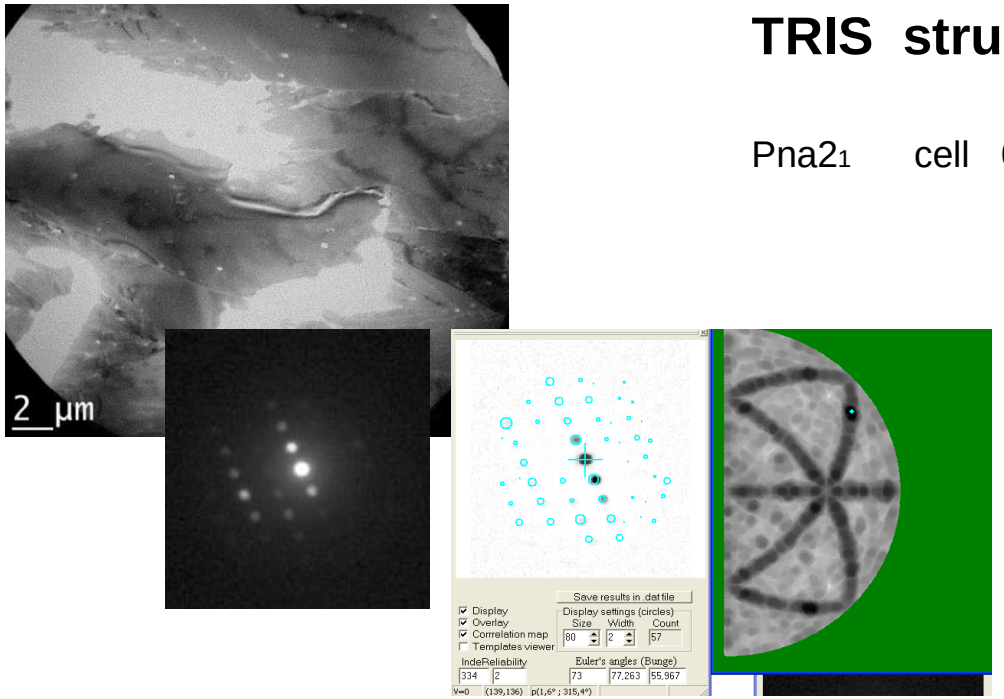
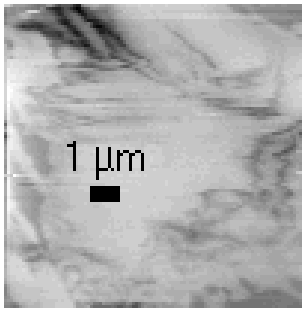
ASTAR : texture of organic structures

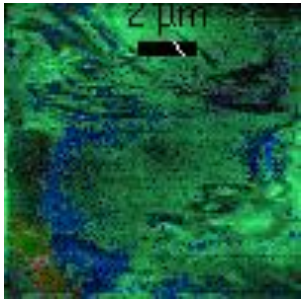


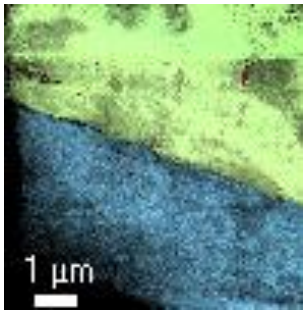
TRIS structure $C_{16}H_{48}N_4O_{12}$

$Pna2_1$ cell 0.7768 X 0.8725 X 0.8855 nm

Fast scanning > 100 fps prevent crystal instant beam damage







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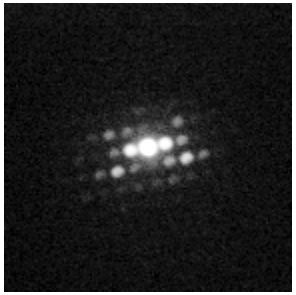
Collaboration Dr. Winnie Li IBS Grenoble

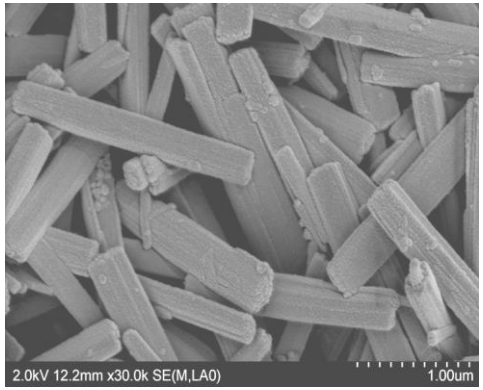
Grenoble INP

ASTAR : texture of organic nanomagnets

Organic matter : $[Fe(Htrz)_2(trz)].BF_4$



Jeol 3010, 100fps,
spot 25nm,



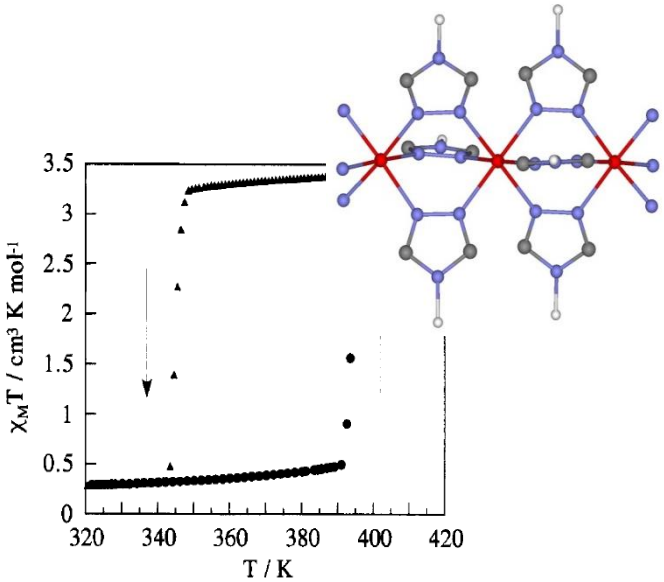
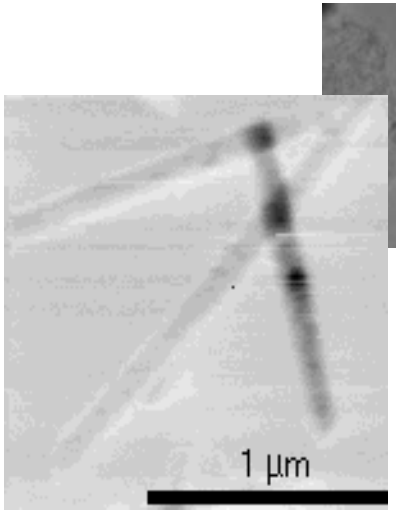
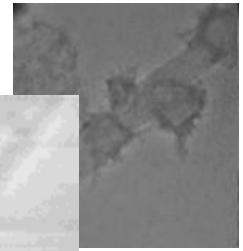
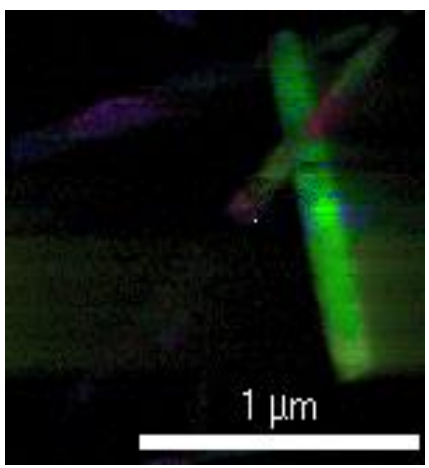
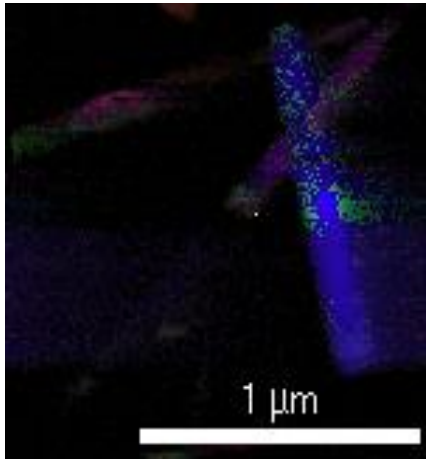


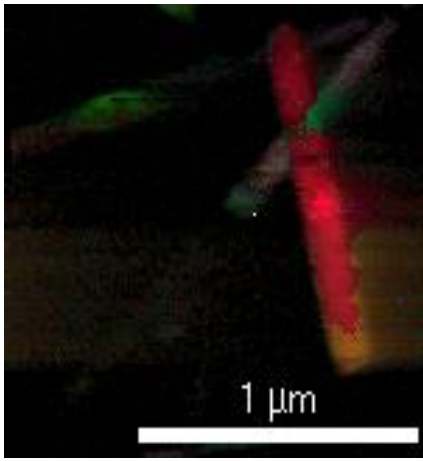
Figure 1. $\chi_M T$ versus T plots in the warming and cooling modes for $[Fe(Htrz)_2(trz)](BF_4)$ (**1a**).











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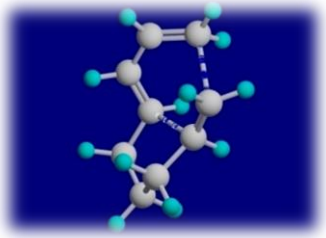
Courtesy:Sebastien Pillet, Univ of Nancy France

What about the amorphous content in a sample ?



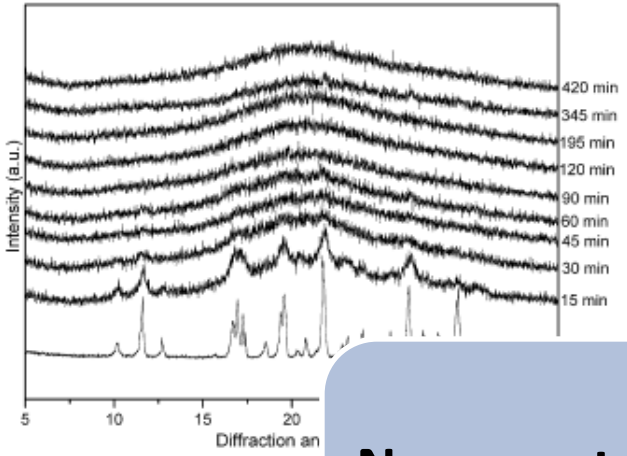
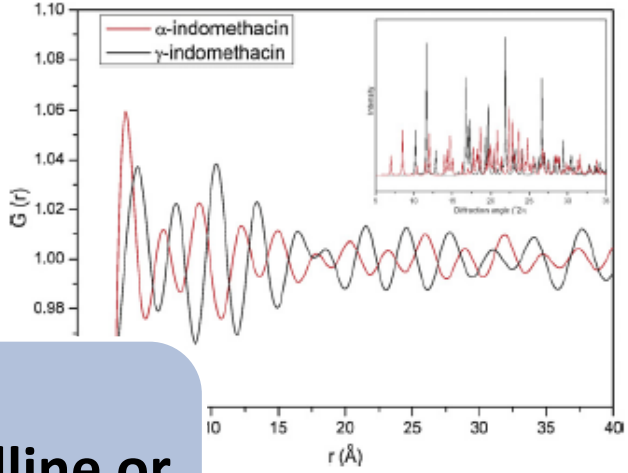


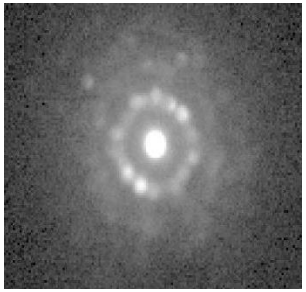
Fig. 2. XRPD diffractograms of the cryo-m
for different times (time in the figure corre

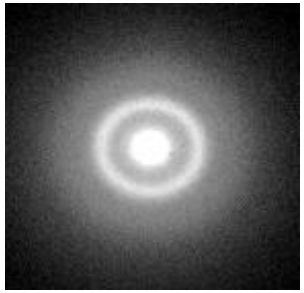


and α-form of indomethacin. XRPD diffractograms of γ-
ethacin are shown in the inset.

Nanocrystalline or Amorphous ?

ED pattern from overlapping nanocrystals < 10 nm





ED pattern from amorphous area

both may show "X-ray amorphous" pattern

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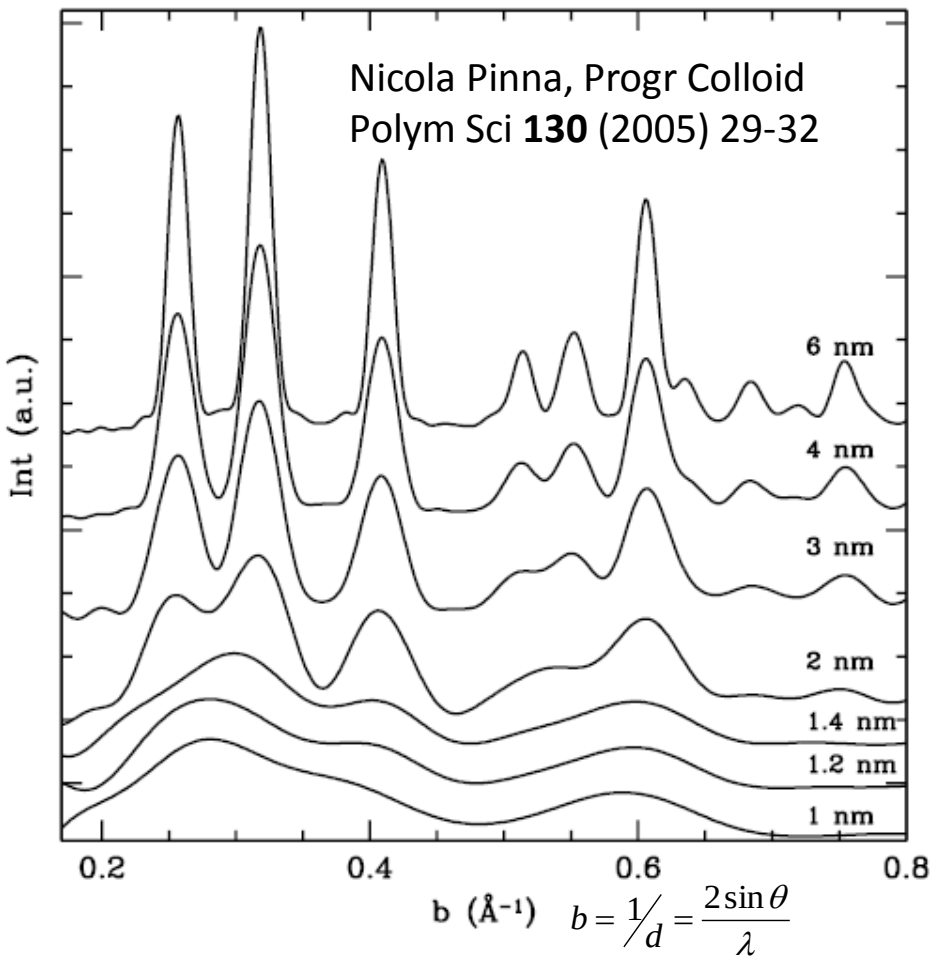
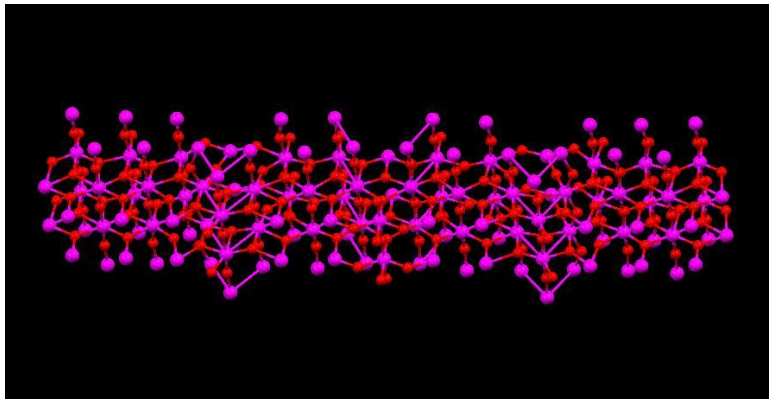
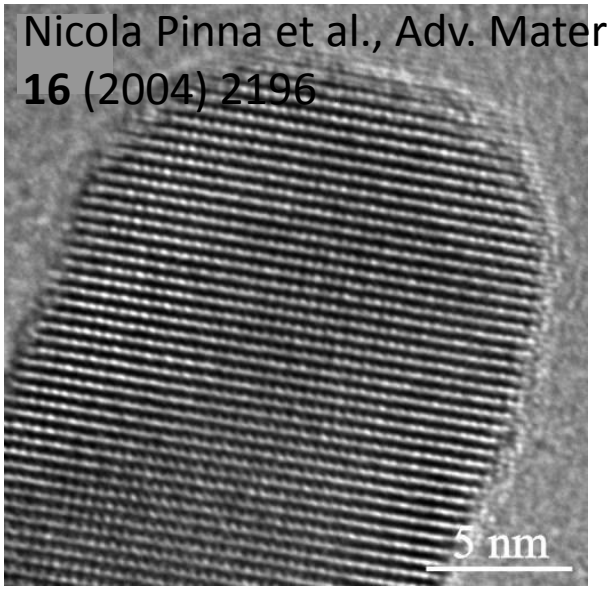




Ta_2O_5

tantite



Crystals < 5 nm look like "X-Ray amorphous"

but we can see them in TEM !

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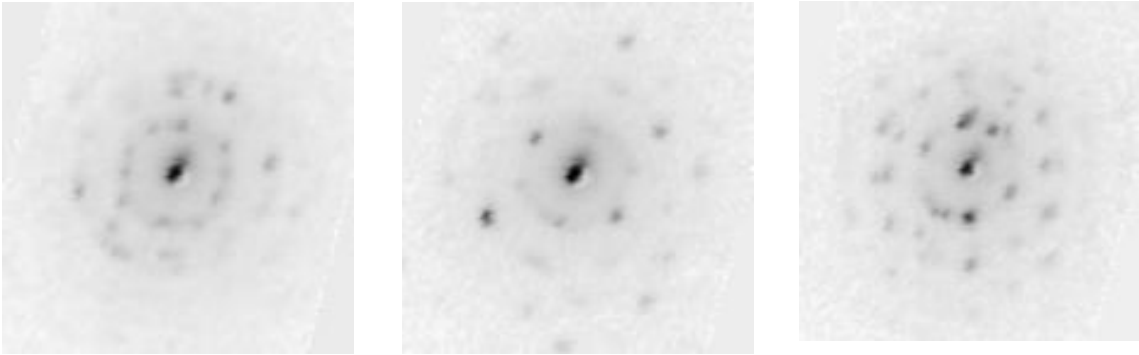
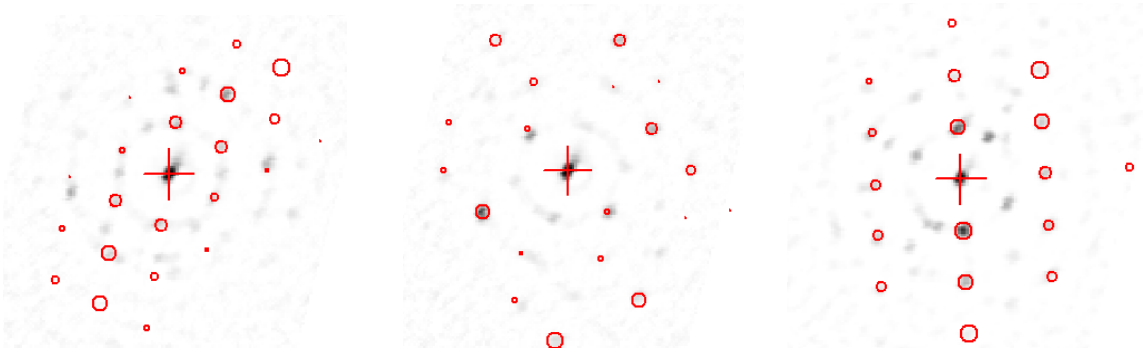
Nanocrystalline or Amorphous ?

Example: Polycrystalline thin film of Ni-Fe nanocrystals (average size 5-20 nm)

Data taken with JEOL JEM 2200F operating at 200 kV spot size 1-8 nm



ASTAR can index even overlapping diffraction patterns from polycrystalline sample



Data taken with JEOL JEM 2200F operating at 200 kV spot size 1-8 nm

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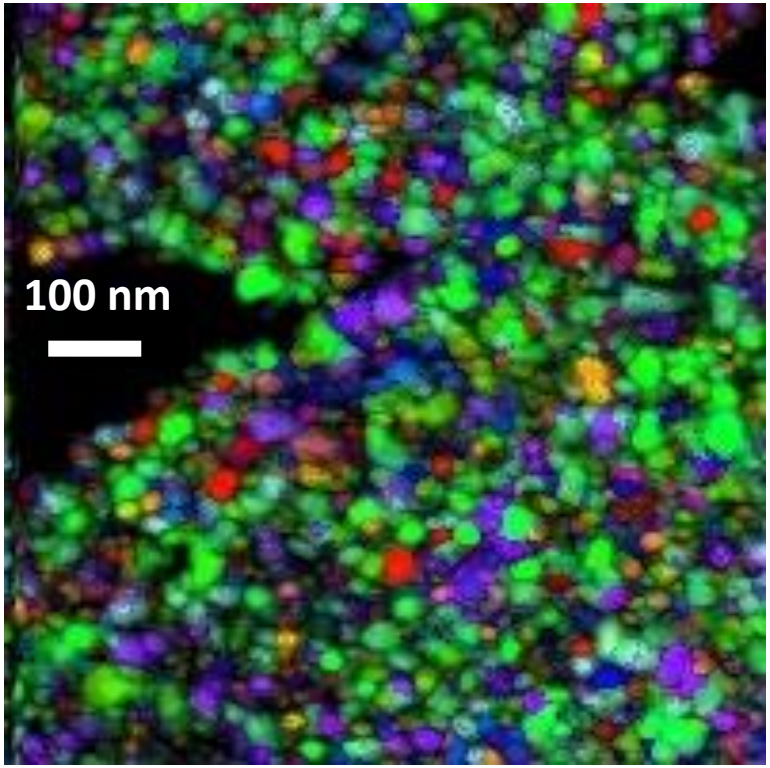
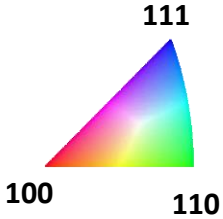
Results courtesy Prof. Dr. E.Rauch CNRS Grenoble

they are polycrystalline !





Orientation map (z)

ASTAR orientation image showing individual Ni-Fe orientations

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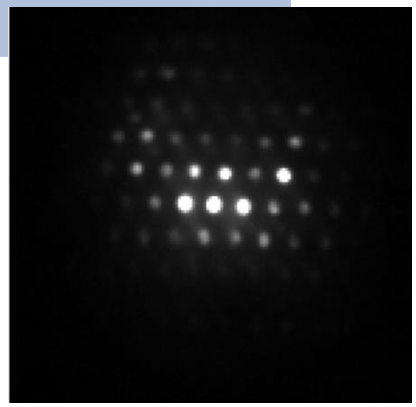
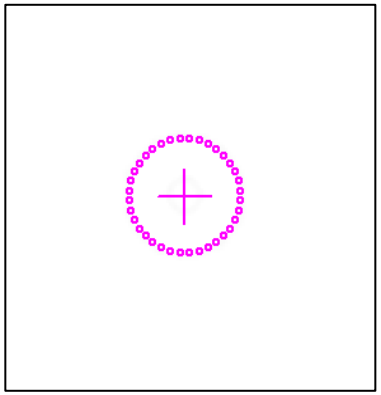
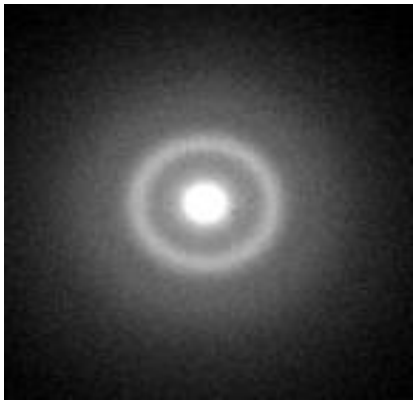
JEOL 2200 FS 200 KV, Humboldt Univ Berlin

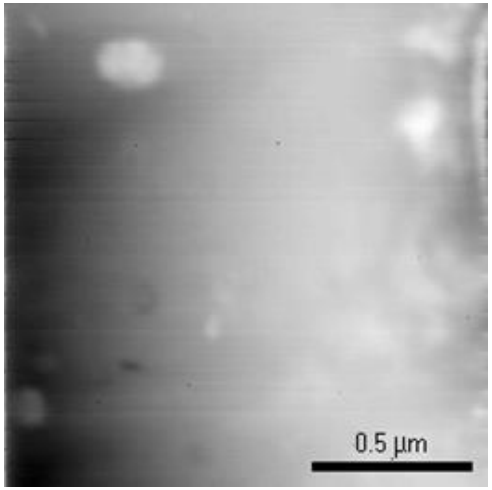
Nanocrystalline or Amorphous ?

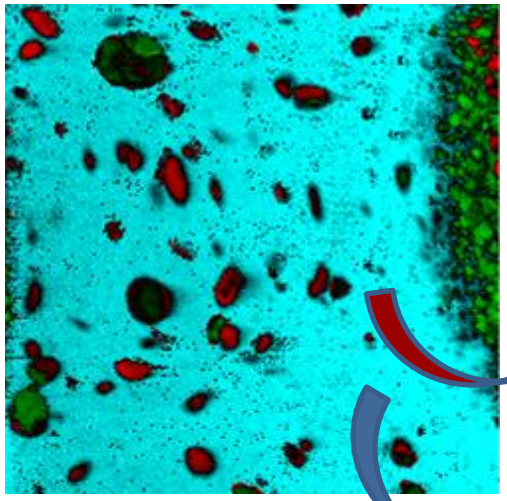
Example : Mg-Cu-Gd partly recrystallized metallic glass with Mg_2Cu and Cu_2Gd crystalline precipitates











crystalline

amorphous

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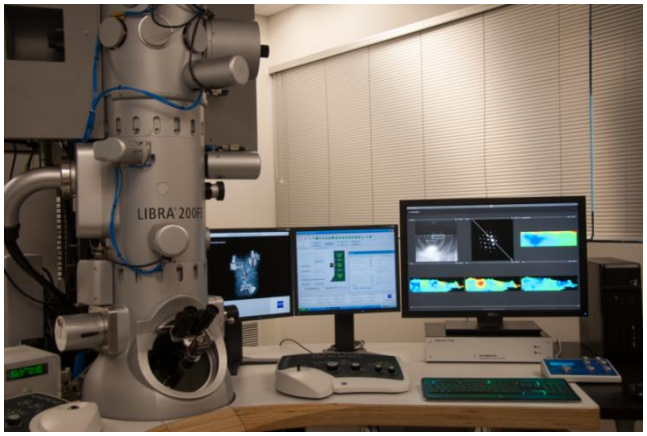
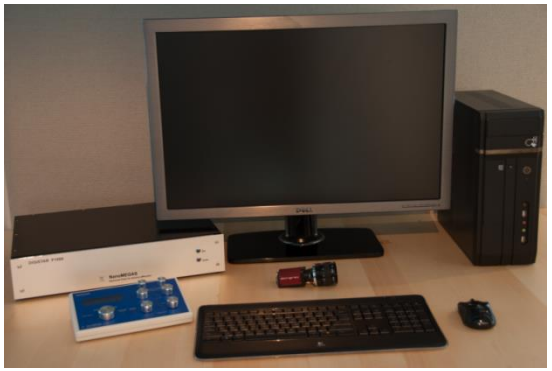
PHARMA CRYSTALS : THE RANDOM TOMOGRAPHY METHOD





The challenge :

FIND CRYSTAL TEXTURE & amorphous content

FIND UNIT CELL PARAMETER
from thousands of nanocrystallites

FIND CRYSTAL STRUCTURE
from unknown crystals

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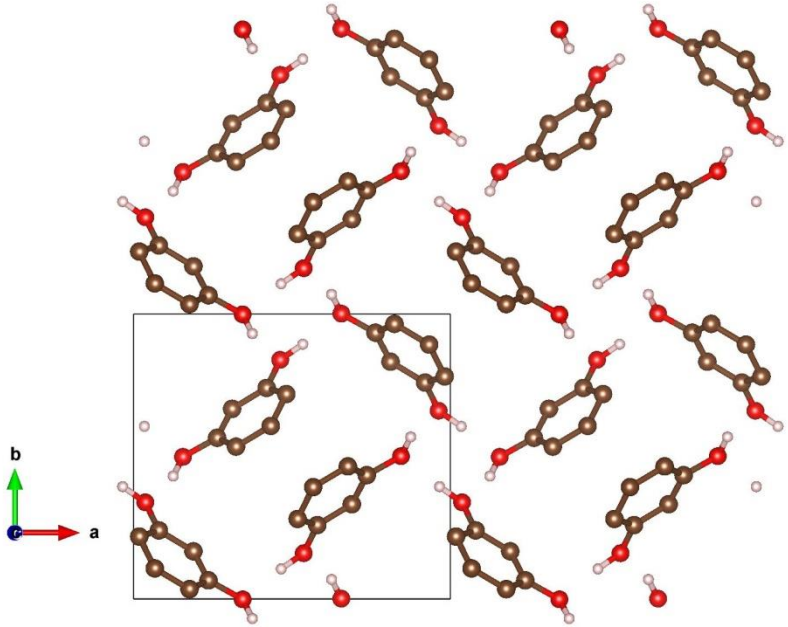
RESORCINOL crystal structure

1,3-Dihydroxybenzene.

α-phase a=10.447 Å, b=9.356 Å, c=5.665 Å Pna2$_1$

β-phase: a=7.811 Å b= 12.615 Å , c=5.427 Å Pna2$_1$



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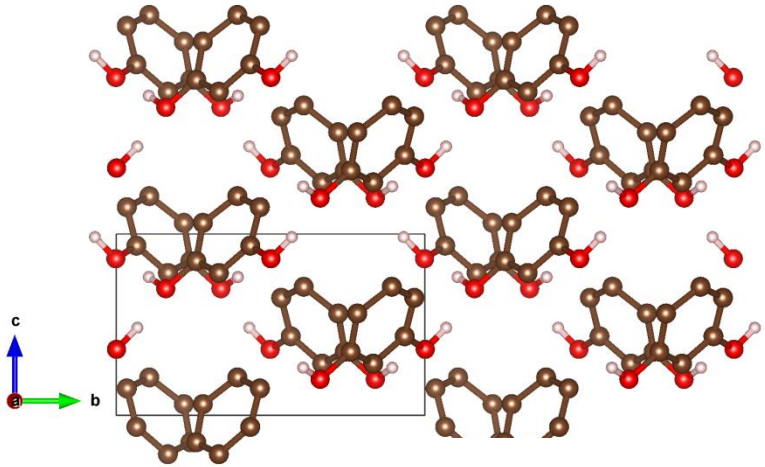
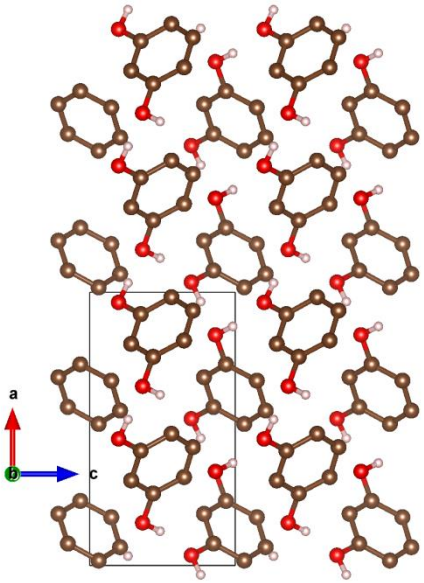
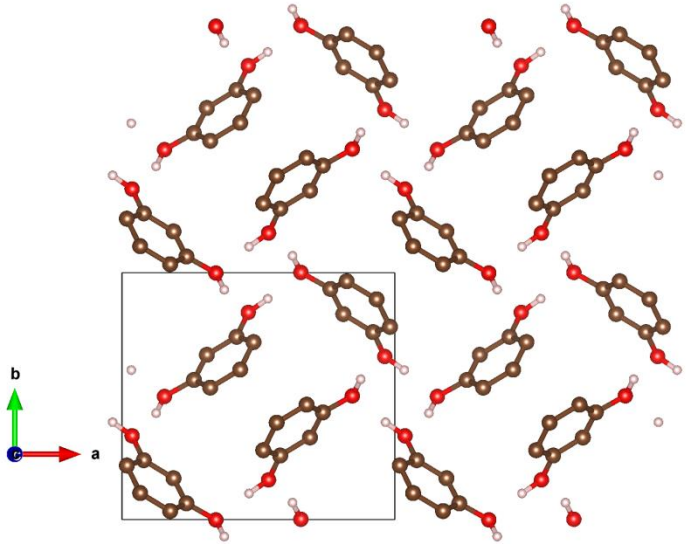
RESORCINOL crystal structure







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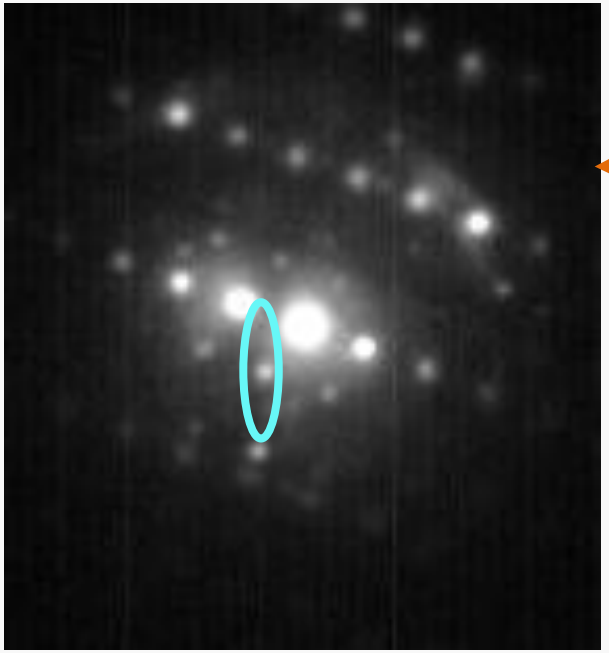
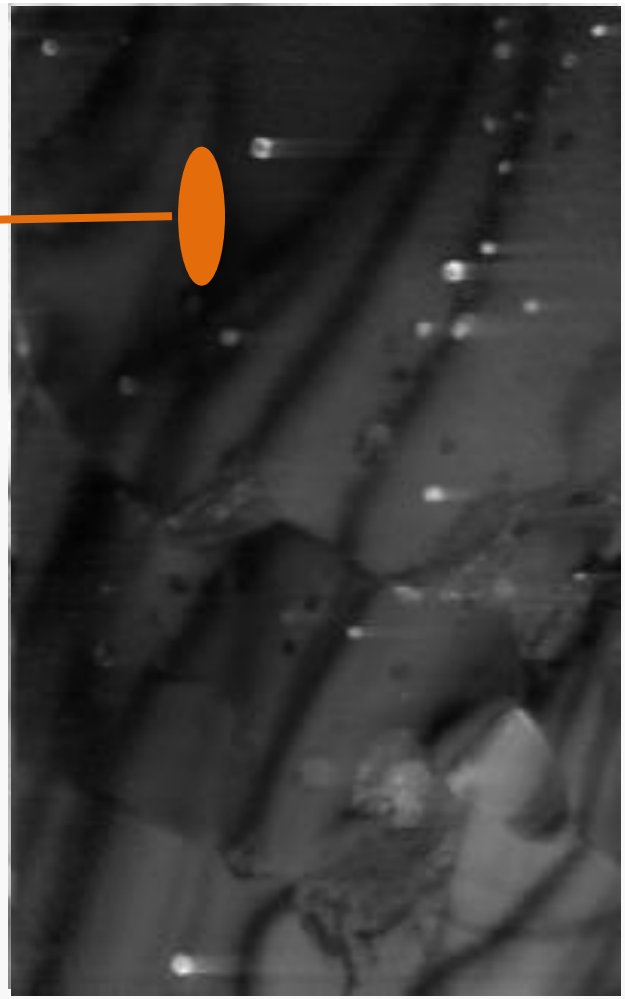
ASTAR : create virtual dark (VDF) maps from digital images

Diffraction pattern



Dark field image



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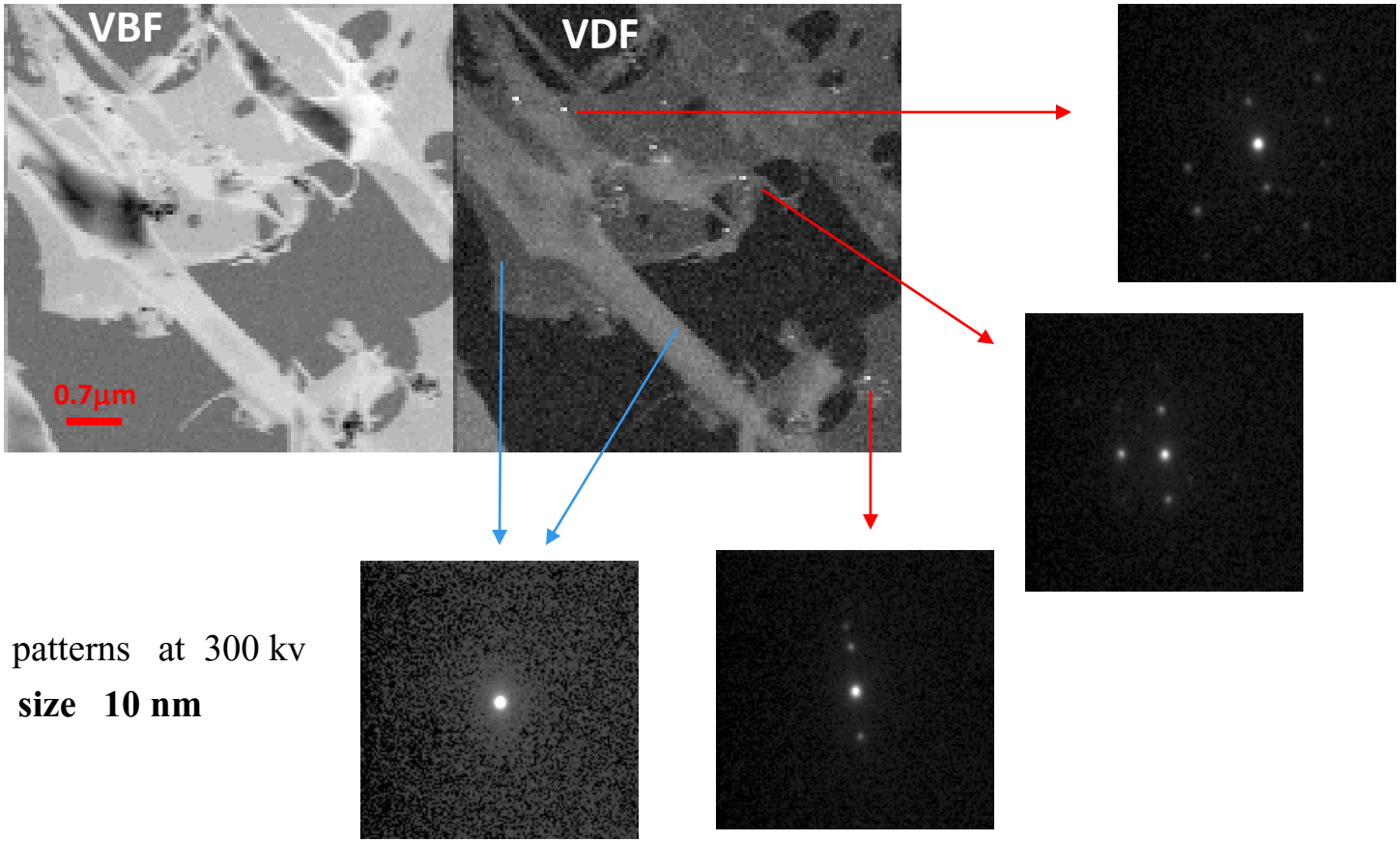
ASTAR : Reveal crystalline – amorhous content



PED patterns at 300 kv
spot size 10 nm

Crystals of resorcinol < 10 nm clearly revealed on amorphous background !

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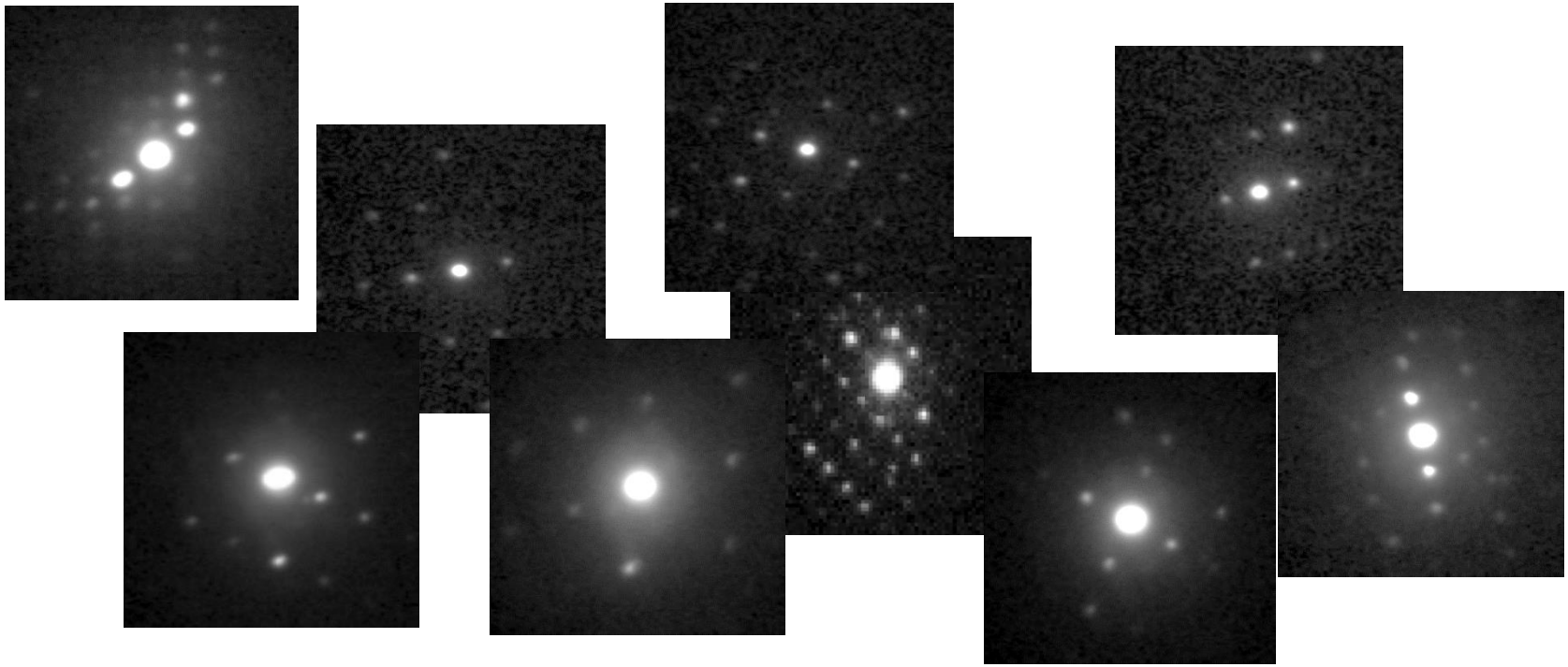
ASTAR : Random precession diffraction tomography

UNIT CELL DETERMINATION

Collection of 12 random "quasi- oriented" PED patterns at 300 kv **spot size 10 nm**
scanning at high speed rates > 50 fps



EDiff software after collection of 9 random PED patterns
reveals the correct unit cell parameter of α phase
5.615 9.195 10.05 90 90 90

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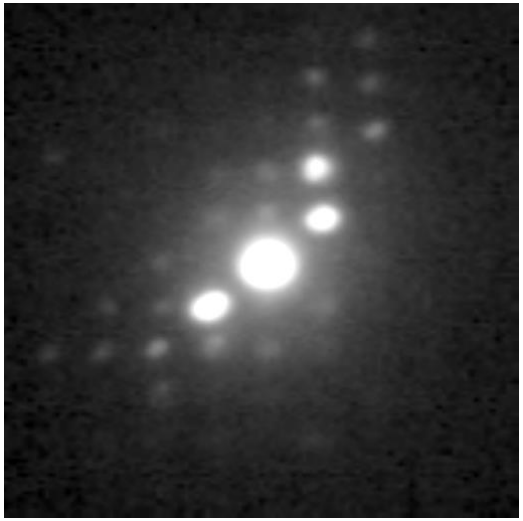
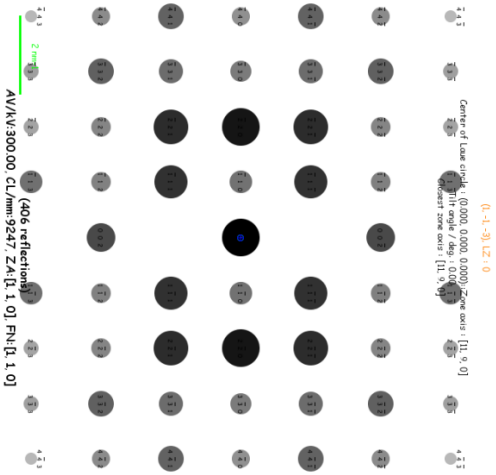
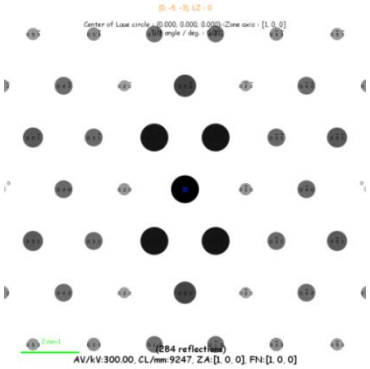
ASTAR : Random precession diffraction tomography

UNIT CELL DETERMINATION

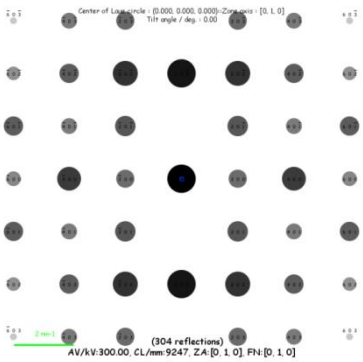


ZA 110

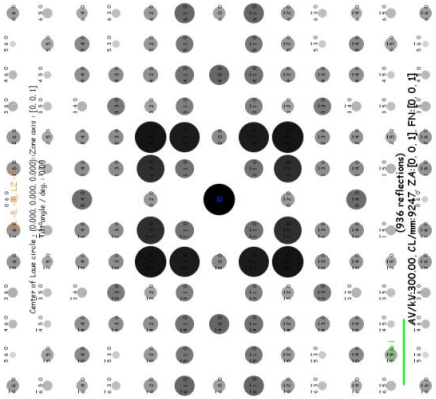




ZA 100



ZA 010



ZA 001

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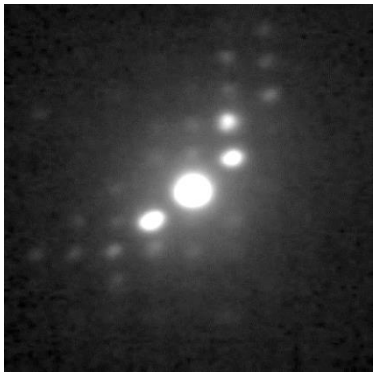
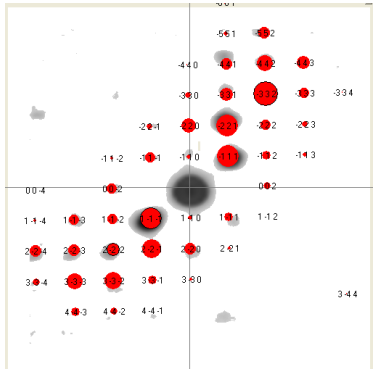
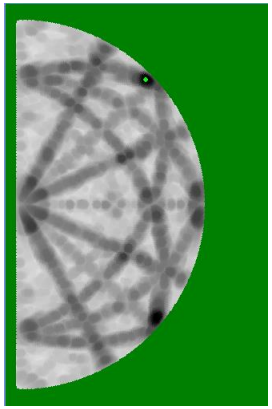
Diffraction simulation confirms correct ZA index

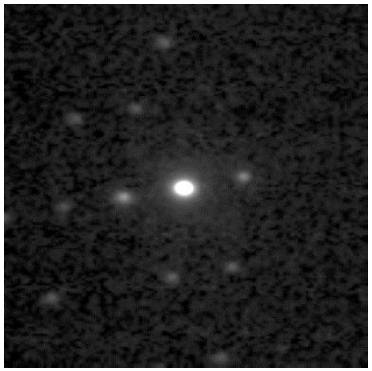
ASTAR : Random precession diffraction tomography

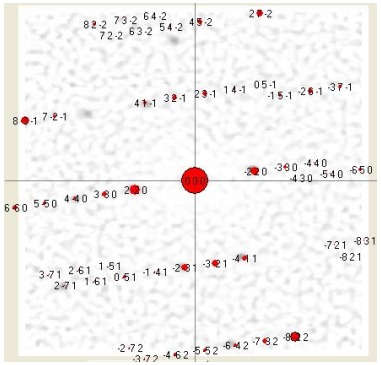


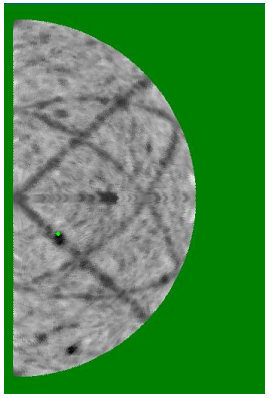




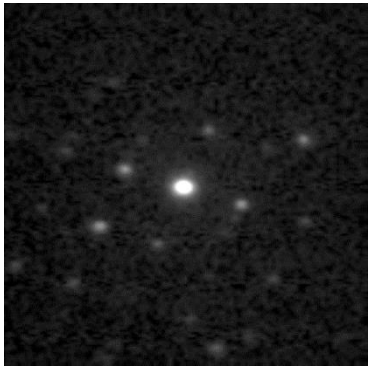
Zone axis close to [110]

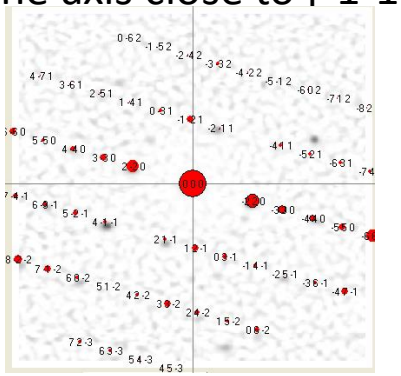


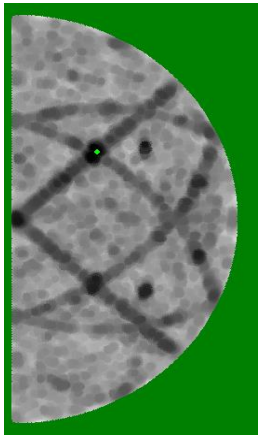




Zone axis close to [-1-1-5]

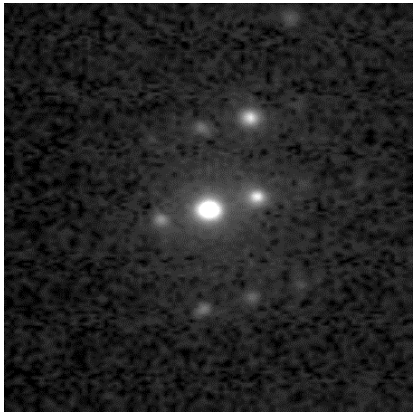


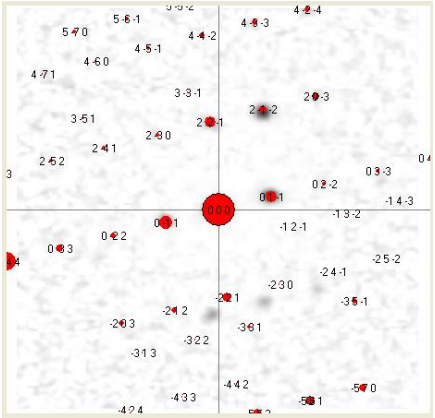


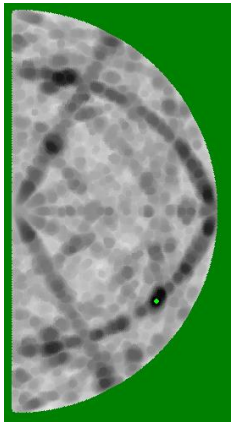


ASTAR : Random precession diffraction tomography

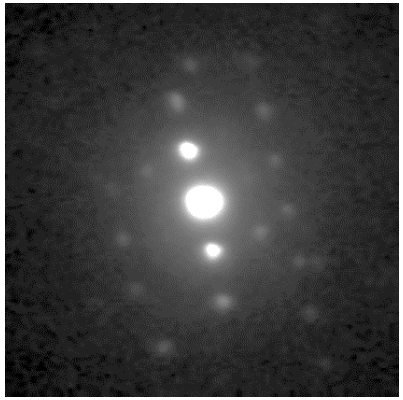
ZA close to [-7 -7 -5]

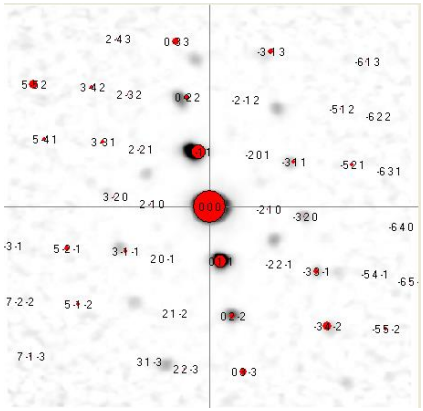


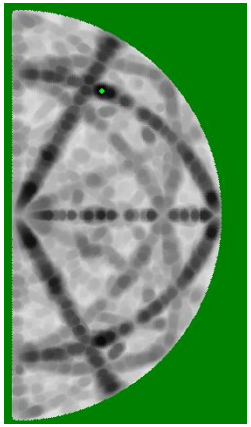




ZA close to [5 8 8]







UNIT CELL DETERMINATION - SOLVE CRYSTAL STRUCTURE

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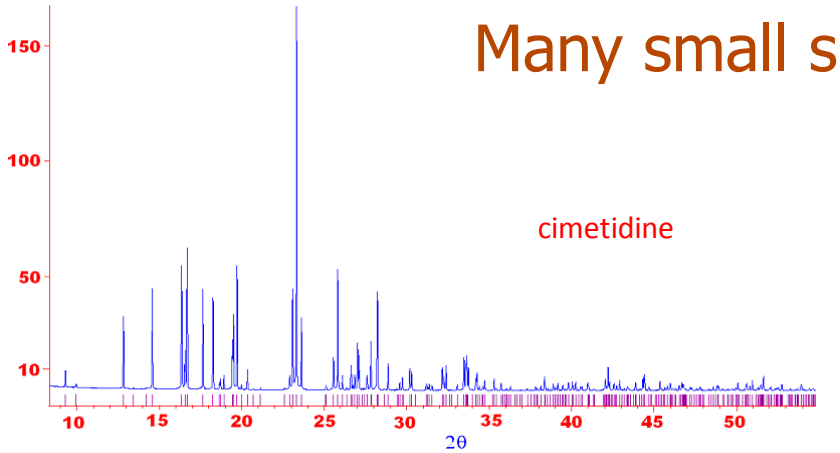
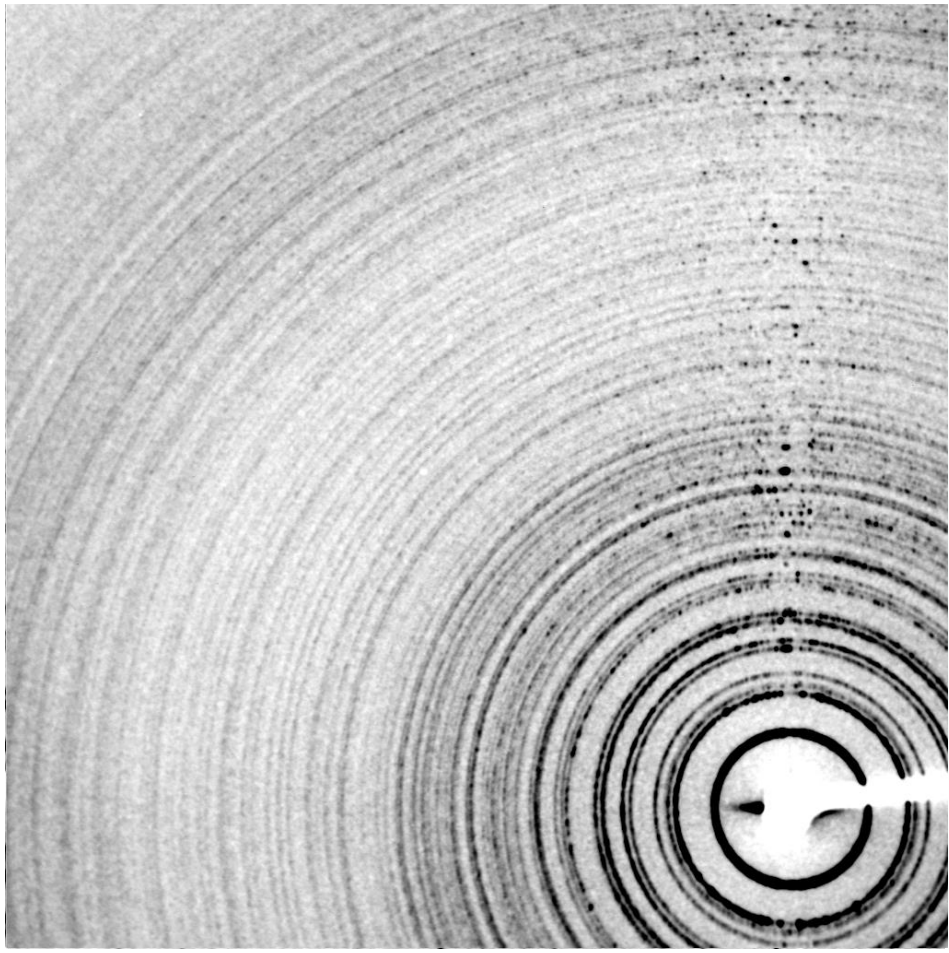
Many small single crystals make a powder



» 1
» 2
» 3
» 5
» 10
» 20
» 50

- Spots cover spheres in 3D reciprocal space

- 2D area detector takes a slice
- (on Ewald sphere)
- 1D powder scan measures distance from origin



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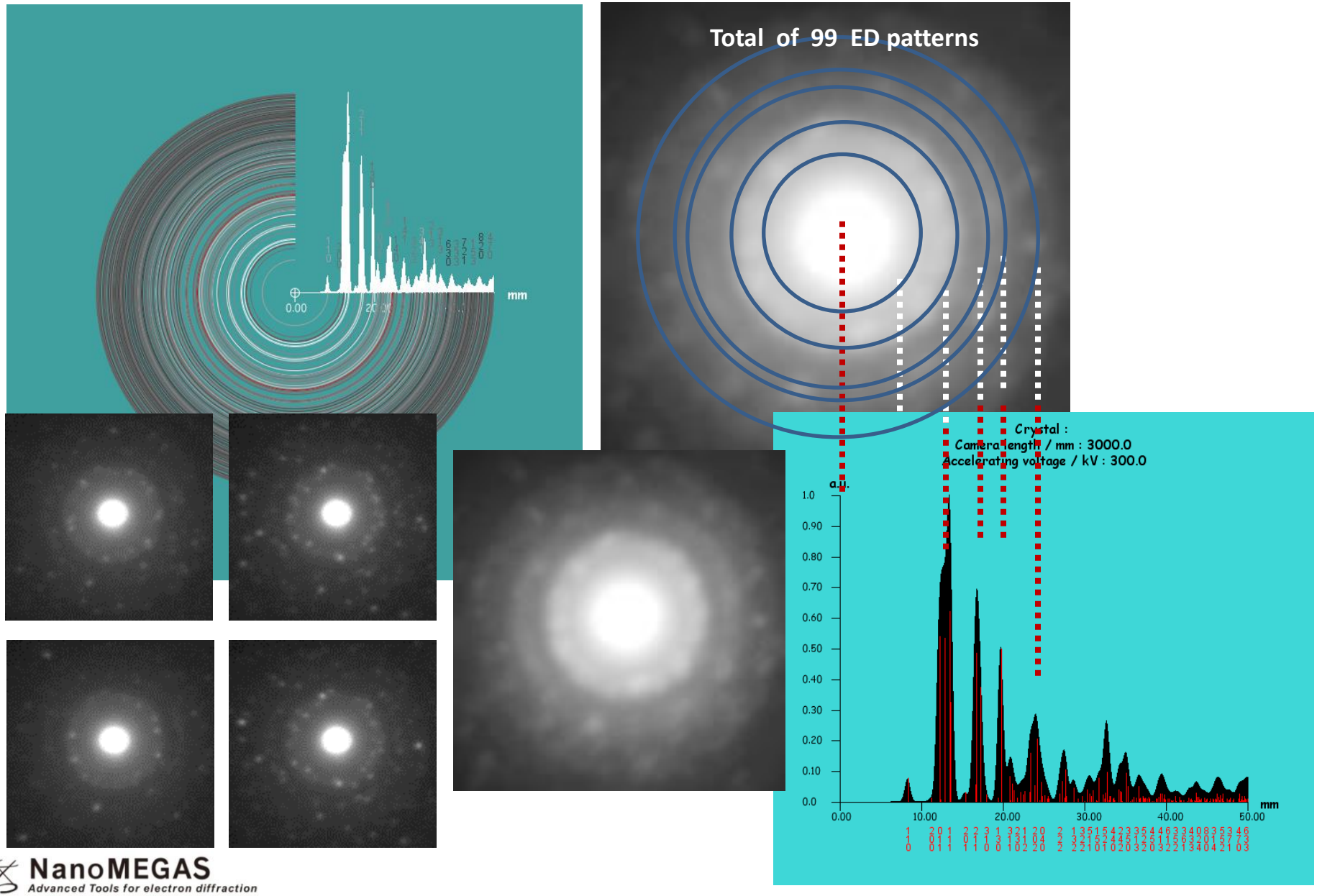
Courtesy I.Margiolaki ESRF Grenonble

ASTAR : Adding random PED patterns to form a powder



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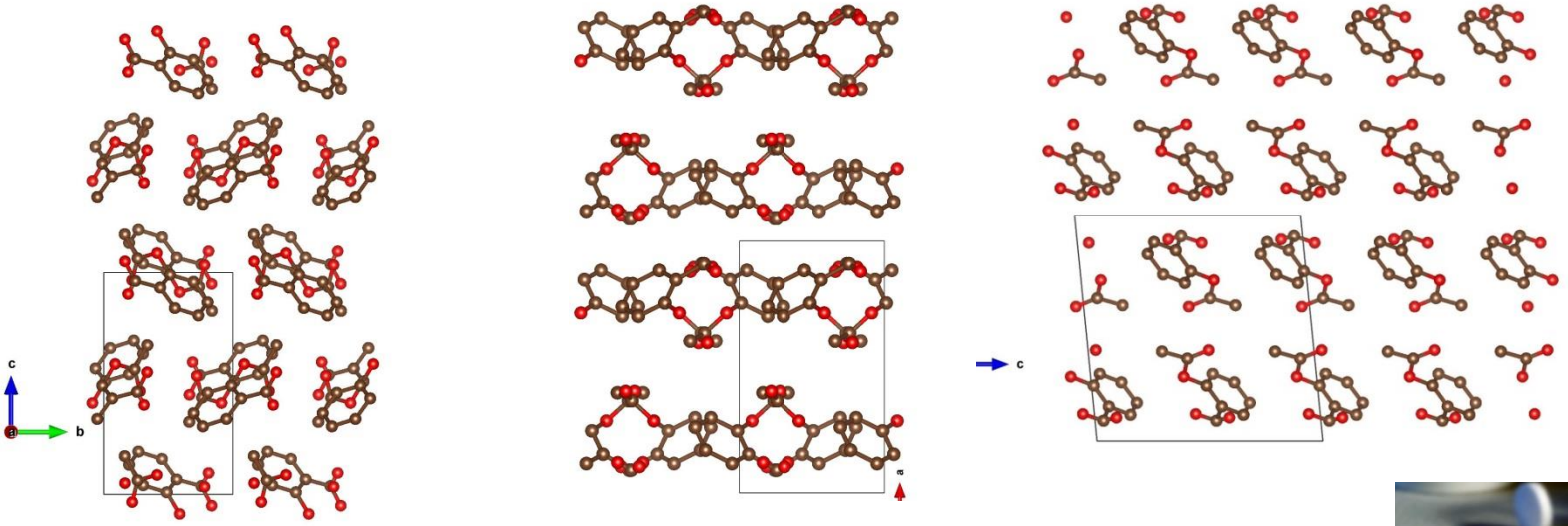
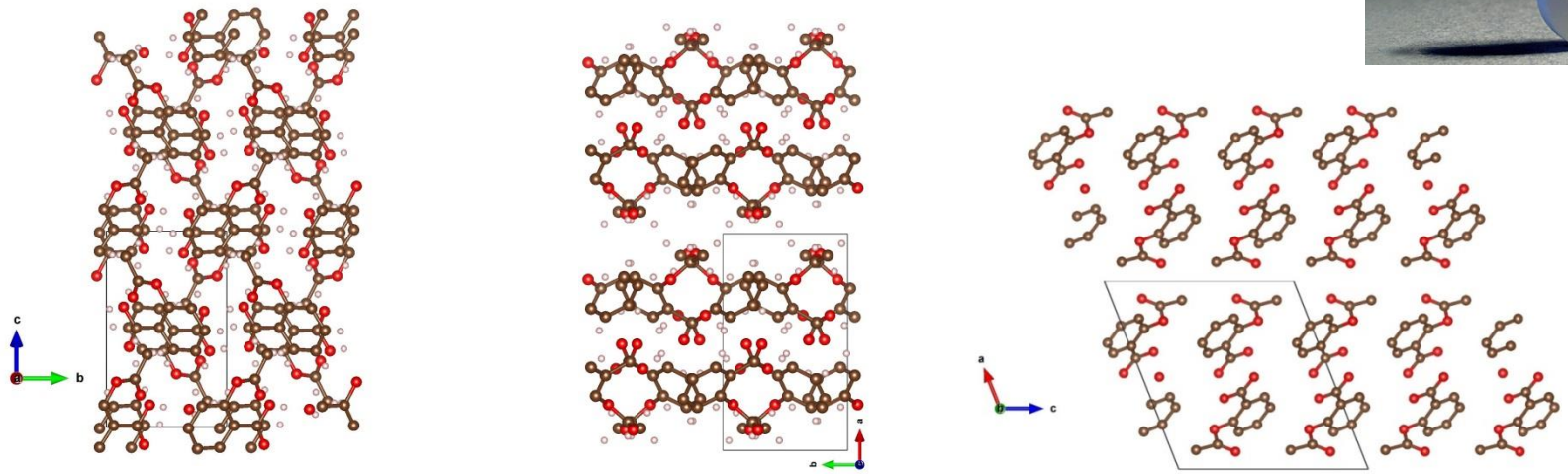
ASPIRIN

form I (P21/c): a=11.233(3) Å, b=6.544(1) Å, c=11.231(3) Å, â = 95.89(2)°



form II (P21/c): a=12.095(7) Å, b=6.491(4) Å, c=11.323(6) Å, â=111.509(9)°



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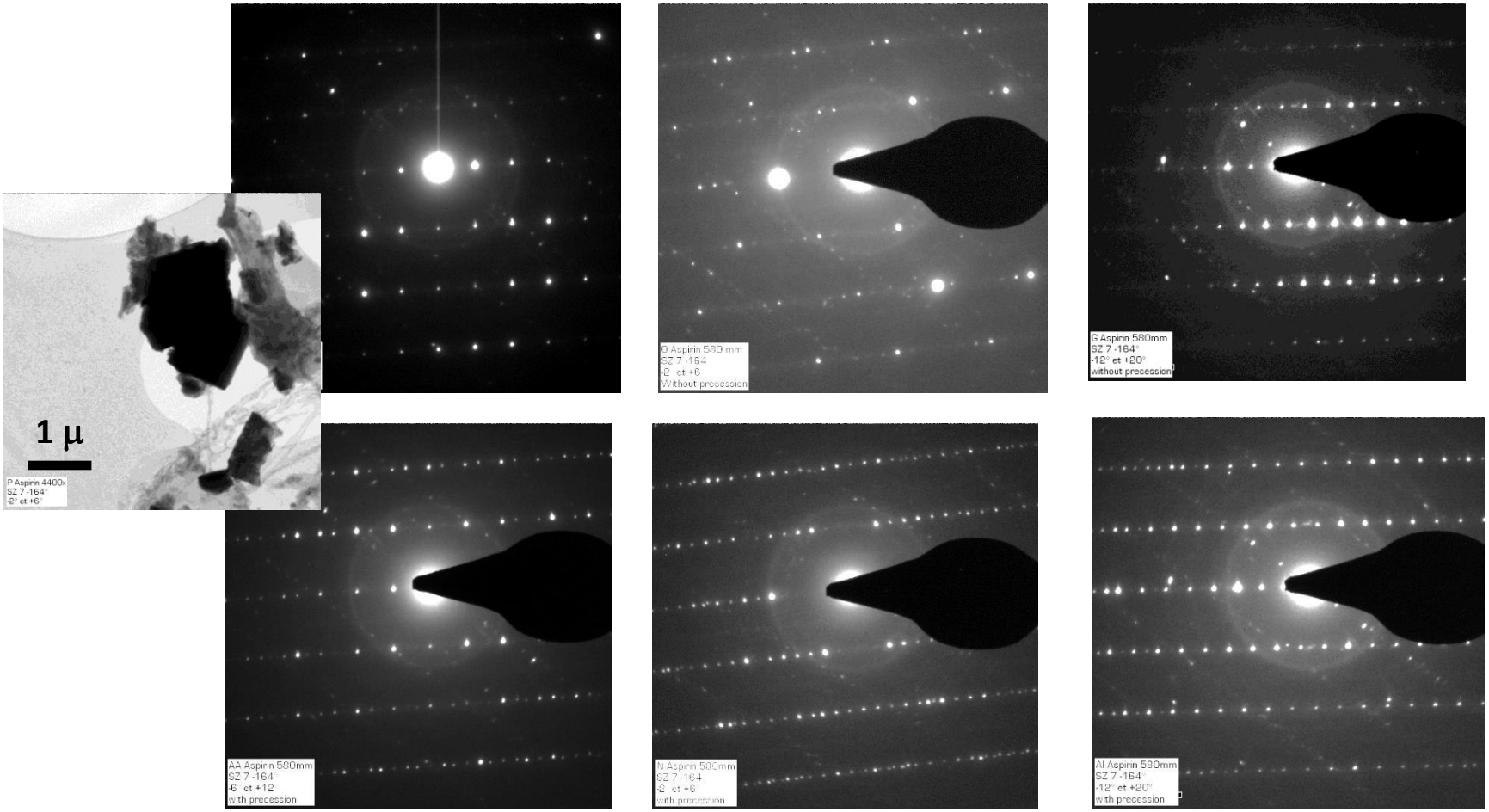
ASPIRIN

PED patterns improvement with precession



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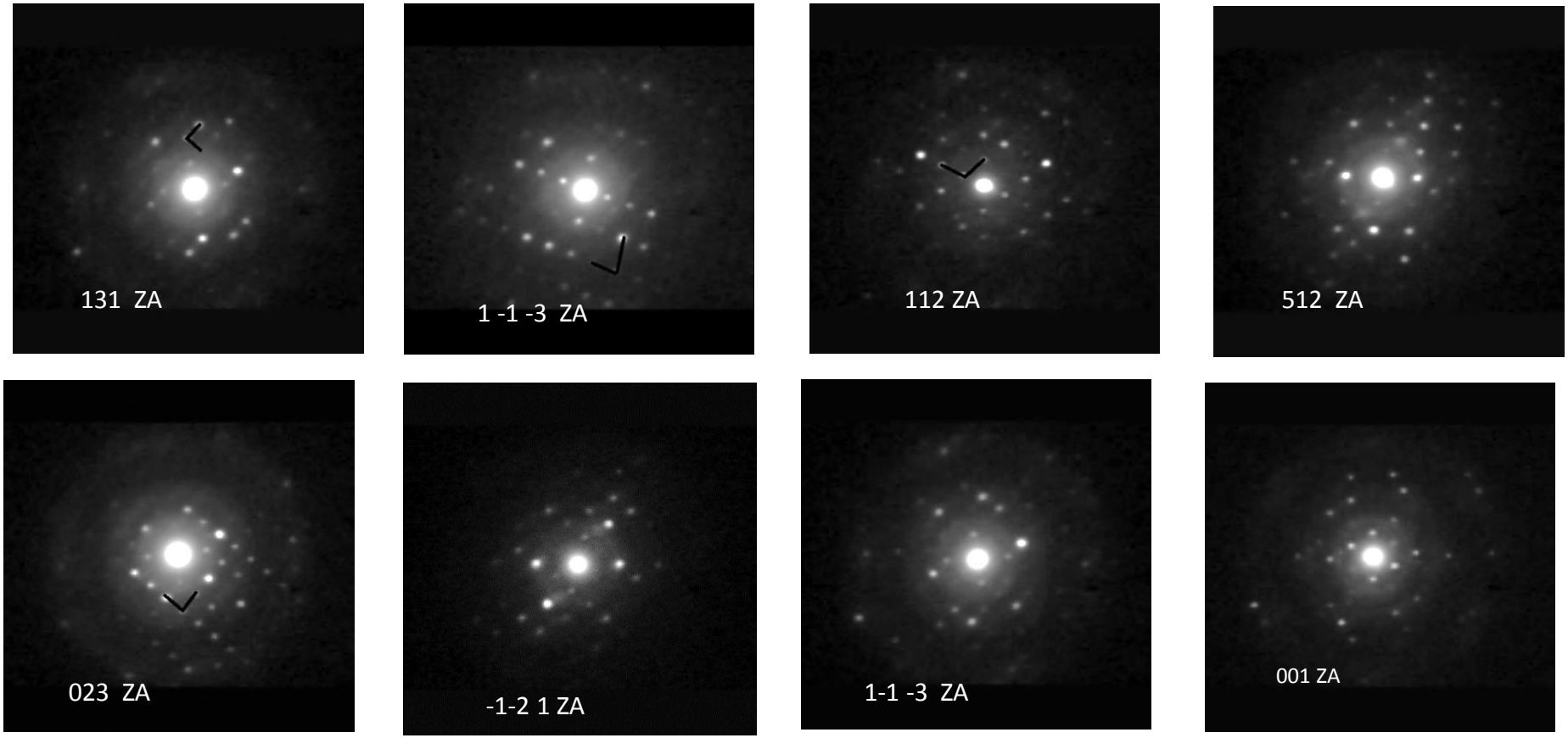
ASTAR : Random precession diffraction tomography



EDIff software : cell parameters are found from 11 random PED patterns

a	b	c	alpha	beta	gamma
6.663	**10.68**	**11.75 97.5**	**89.3**	**91**	**95.000**

Data collected with 120 kv TEM IIT Pisa

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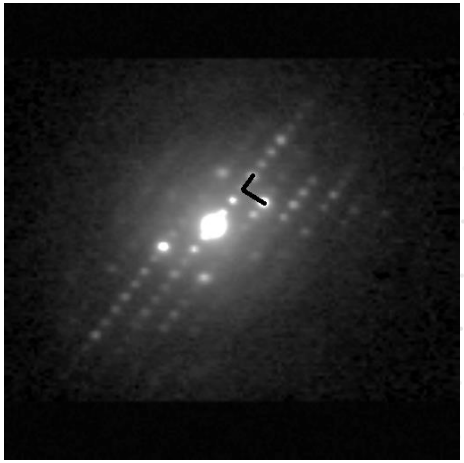
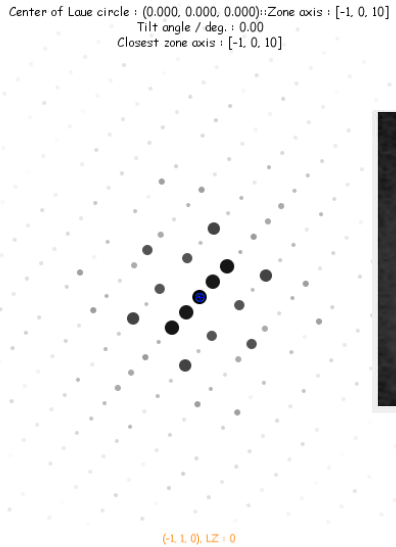
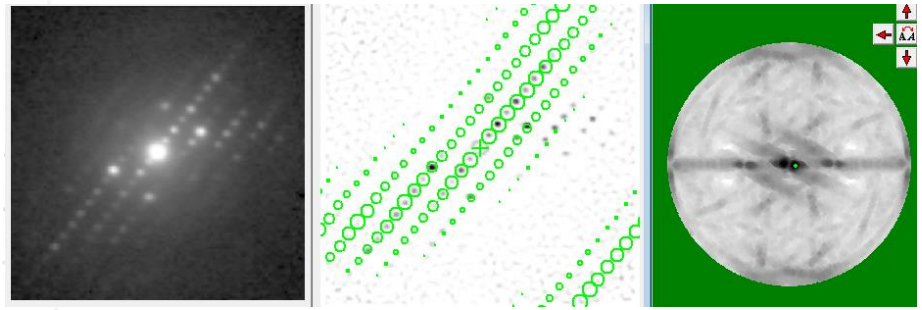
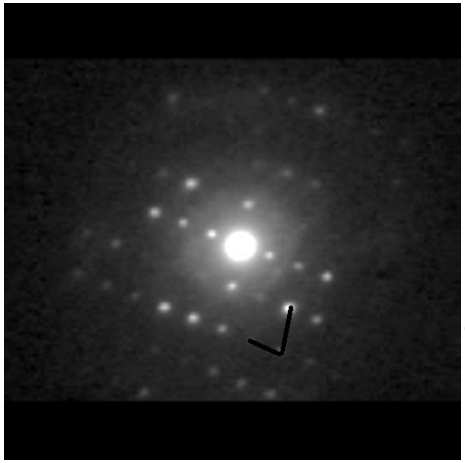
ASTAR : Random precession diffraction tomography

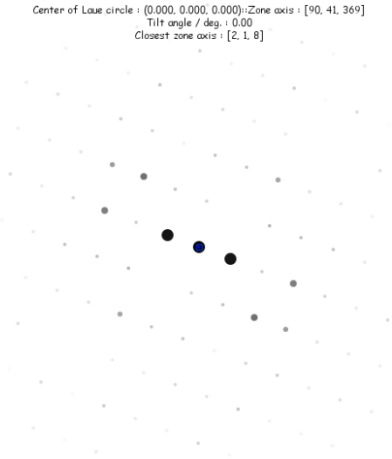


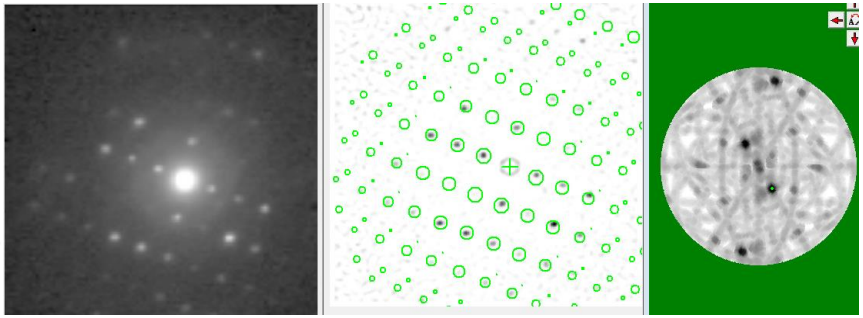




ZA 001, Best match







ZA 113 Best Match

5 nm-1

UNIT CELL DETERMINATION - SOLVE CRYSTAL STRUCTURE

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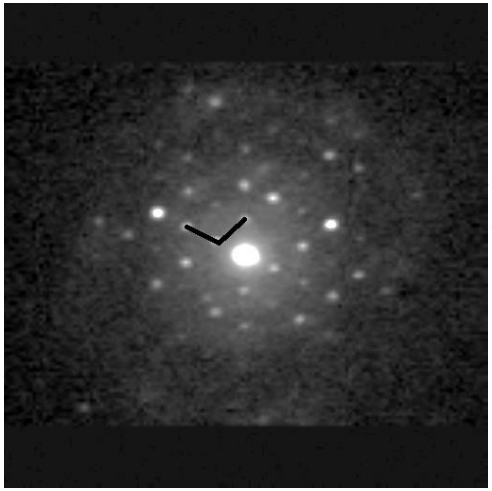
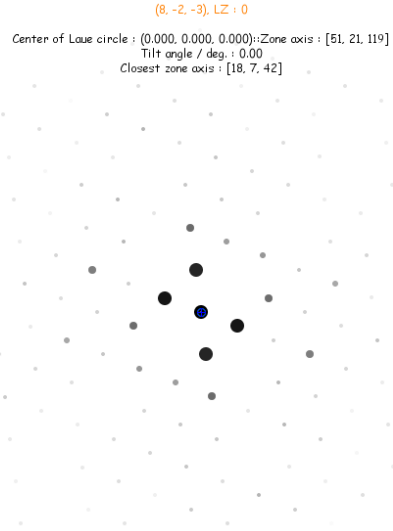
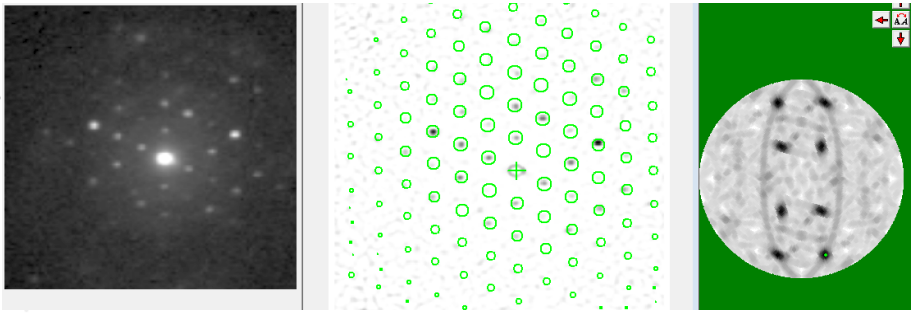
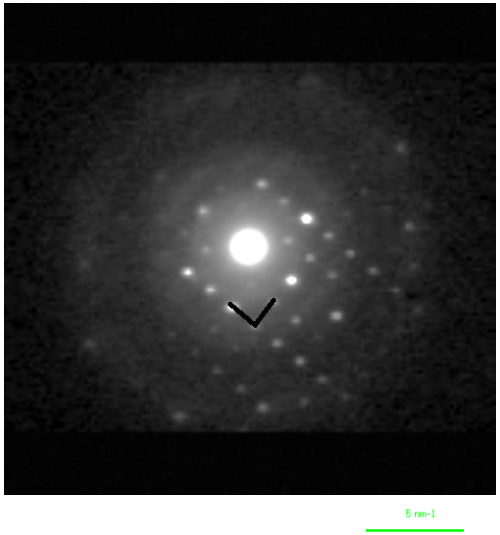
ASTAR : Random precession diffraction tomography

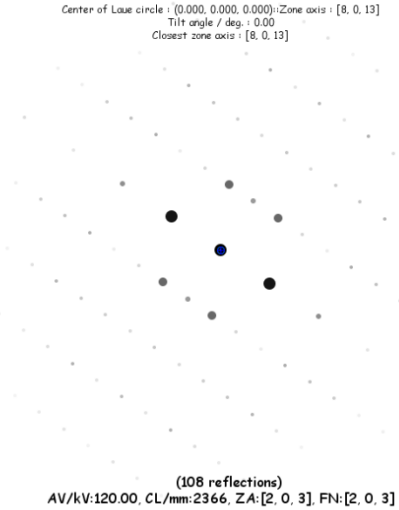


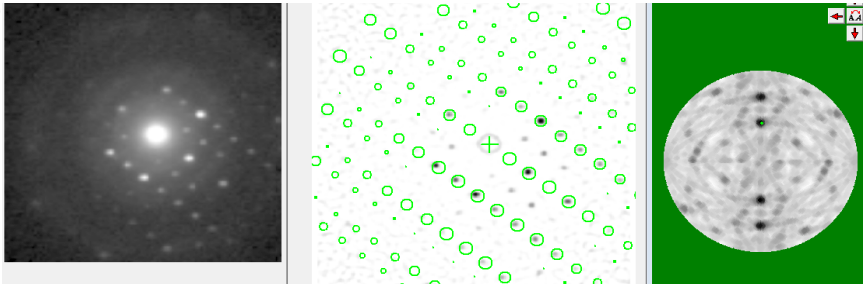




ZA 112 Best Match







ZA 203 , Best Match

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UNIT CELL DETERMINATION - SOLVE CRYSTAL STRUCTURE

CONCLUSIONS

Try electron diffraction !

Contact us at

info@nanomegas.com

www.nanomegas.com

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Advanced Tools for electron diffraction

CONCLUSIONS

Most important reasons to use Electron Diffraction

- Nanocrystalline samples that give poor X-Ray patterns
- Inconclusive cell determination /crystal structure from X-Ray
- Detailed overview over crystalline vs amorphous content
- Solve crystal structures ab-intio from < 50 nm crystals

How Electron Diffraction can be used ?

- Use any TEM (120, 200, 300 kv LaB6 or FEG) with cryoholder
- 3D precession diffraction tomography (ADT-3D) can help to find ab-initio the unit cell /crystal structure of any unknown crystal > 50 nm
- Random precession diffraction tomography (ASTAR) to find unit cell and crystal structure by reconstructing reciprocal space from quasi-oriented PED patterns
- Reveal detailed local amorphous vs crystalline part in samples

NanoMEGAS team

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