New Instrumentation For Pharmaceutical XRD/SAXS

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Sponsored by The International Centre for Diffraction Data

PPXRD Website – www.icdd.com/ppxrd ICDD Website - www.icdd.com

2-D XRD/SAXS
Which information can be extracted?

2-D WAXS (XRD)

- Texture
- Crystalline phases
- Strain
- Crystallinity
- Crystallite size
- Amorphous
- …

SAXS and WAXS are **complementary** analysis methods that help better understanding samples or processes, e.g.

- Arrangement of crystals in polymers – types (spherulites, shish …)
- Density distribution between crystal and amorphous zones
- Thermal stability and processability
- Deformation processes

2-D SAXS

- Typical size, size distribution
- Distance between particles
- Arrangement of nano-particles
- Texture of large structures
- Details about system (volume fraction degree of crystallinity)
- Porosity
- Shape and dimensions of nano-particles
- Strain
- …

What does one want in a (home lab) XRD/SAXS system?

- Source
  - Highest flux desired to data collection time and deal with small sample volume, weak diffraction and low concentration
  - Point focus preferred with area detector

- Optics and beam path
  - Suitable to the applications
  - Easy to switch between configurations

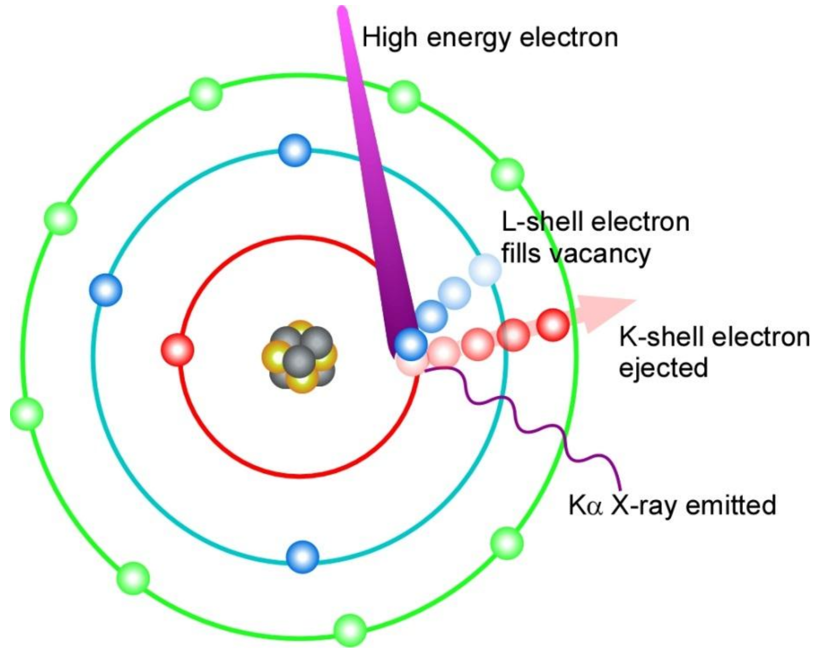
- Detector
  - Must have high quantum efficiency
  - Very low noise, photon-counting detector preferred
  - Larger is better (to see the entire scattering pattern)

- Overall: high reliability, easy use and low maintenance

Sources

Characteristic X-ray generation

- All present day monochromatic home laboratory sources are based on characteristic radiation from a material anode
- The efficiency of this process is very low
  - Approximately 99% of the incident electron power is converted to heat, *not X-rays*
- Dissipation of this waste heat fundamentally limits the brightness of the source

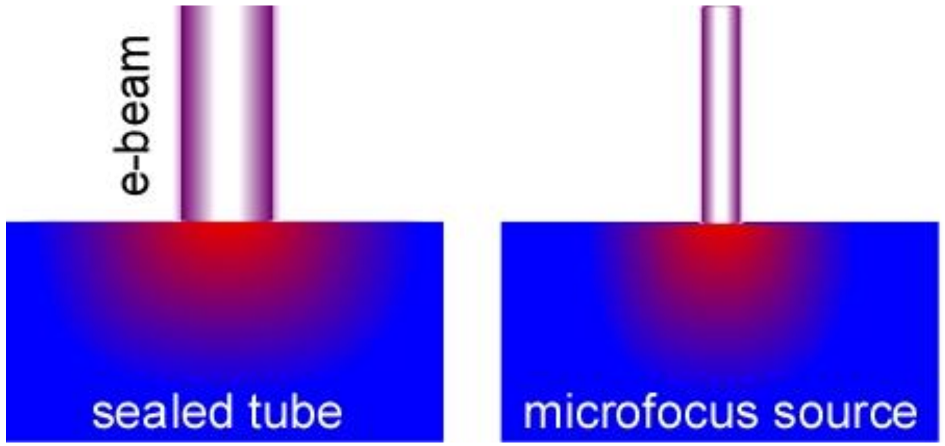


How can one make a source brighter?

- Source performance is ultimately limited by anode melting
  - There are three ways to improve performance
- Make the focus on the anode smaller
  - Allows higher heat extraction efficiency
  - ***Microfocus sources***
- Rotate the anode faster
  - Spreads the heat more efficiently
  - ***Improved rotating anode***
- Use a liquid metal anode
  - Can’t melt (it is already molten!)
  - ***Metal jet sources***

How to make brighter source I: Microfocus sources

- Brightness (***B***) is proportional to power loading (*p*)
- Power loading is higher for *smaller spot focus*



$$p_{\max} = \frac{2\kappa\left(T_m - T_0\right)}{r\sqrt{\pi \ln(2)}}$$

- Large spot
- Quasi-one dimensional heat flow limits power loading

- Small spot
- Two dimensional heat flow (more efficient cooling)
- Relative performance improved by 10 times

IμS microfocus source

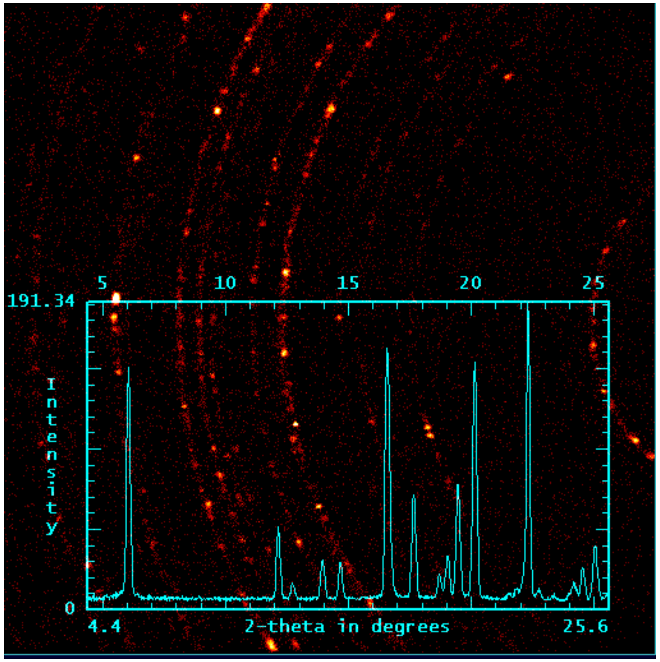
- Intensity $3x10^{10}$ X-rays/mm^2-sec (Cu Kα)
  - 8 times higher than conventional 5.4 kW rotating anode
- Typical lifetime >5 years
  - High reliability
  - 3 year warranty
  - >300 installed
- Air-cooled
- Available in Cr, Cu, Mo, Ag

Comparison: Ibuprofen
IµS & VÅNTEC-2000 vs. Clasical set-up

Sealed Tube

- **0.3 mm collimator**
- **Sample-Detector distance 29 cm**

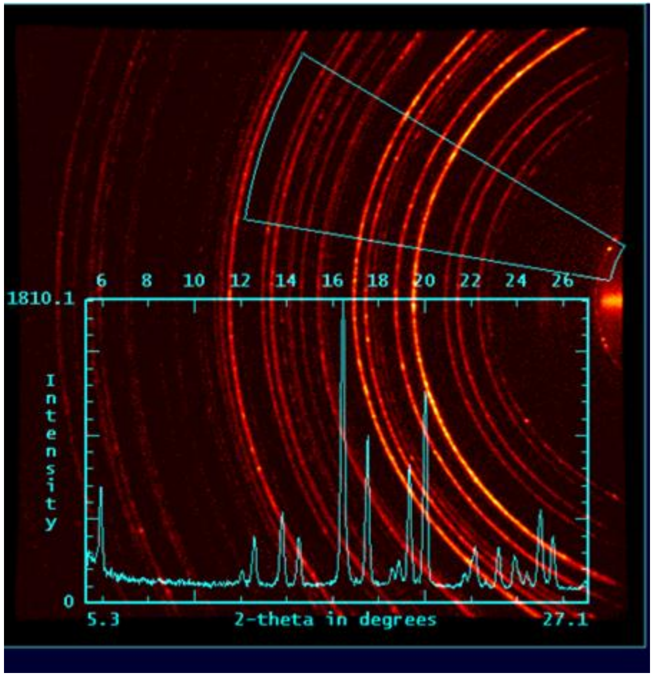
120 sec collection time



IµS – XRD² – foc

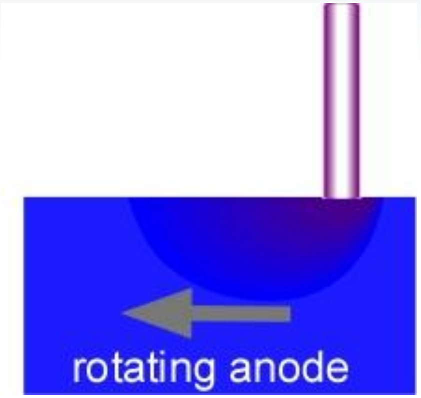
- **2mmX2mm on sample, and 200um spot focused on detector**
- **small slice for integration to obtain better resolution**

15 sec collection time



How to make a brighter source II: Rotating anode sources

- Power loading can be increased by over an order of magnitude by rotating the anode surface to spread out the heat load
  - Power load is also (modestly) increased by smaller spot
- In latest generation rotating anodes angular velocity is 10,000 rpm
- This improves performance by 50 times

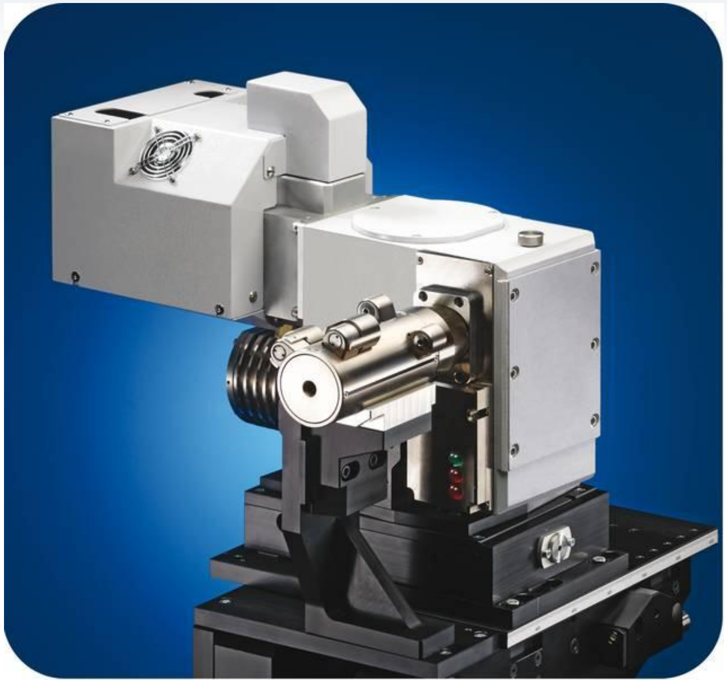


$$p_{\max} \propto \kappa (T_m - T_0) \sqrt{v/w}$$

w=beam width
v=anode velocity

TXS HB High brilliance rotating anode

- Highest intensity rotating anode
  - $2x10^{11}$ X-rays/mm^2-sec Cu $K\alpha$
  - 50 times the intensity of a 5.4 kW classic RAG with multilayer optics
- Cu, Mo, Ag anodes
- Low maintenance
- Easy to align, highly stable mount
  - No alignment base
- Precrystallized, prealigned filaments
  - *No realignment required after filament changes (2X per year)*
- Precision aligned anode
  - *No realignment required after anode exchange (1X per year)*



What are the limits of rotating anode performance?

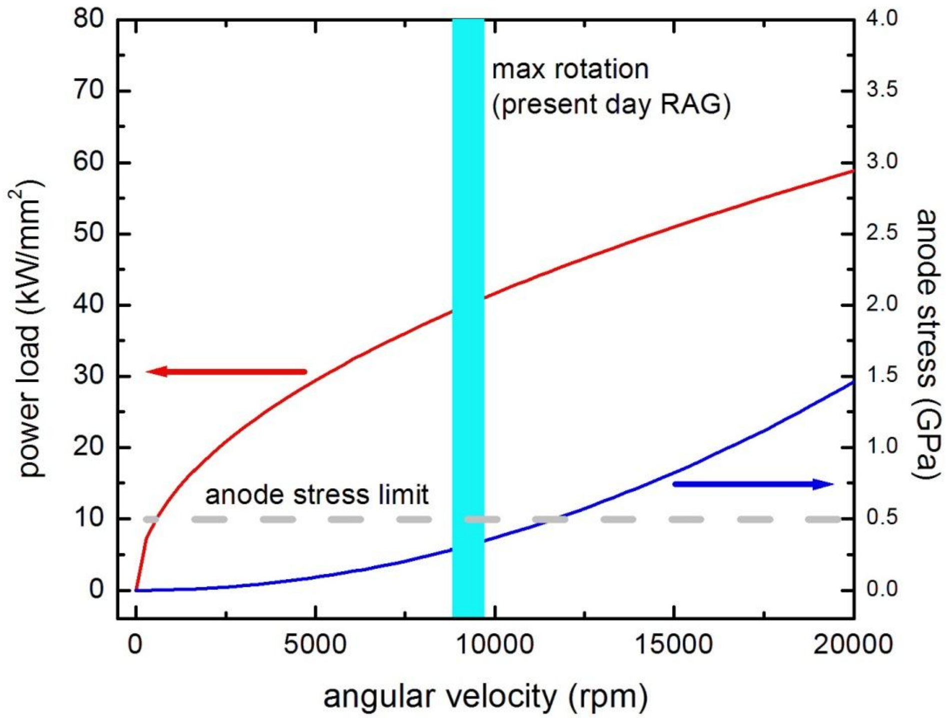
- Faster rotation (ω) allows higher power loading

$$p_{\max} \propto \sqrt{\omega R / w}$$

- However, faster rotation also increases mechanical stress

$$\sigma_h = \frac{PR}{t} = \frac{\rho\omega^2 R^3}{2t} + \rho\omega^2 R^2$$

- State-of-the-art rotating anodes are operated close to mechanical failure limits
  - ***Little room for further improvement***

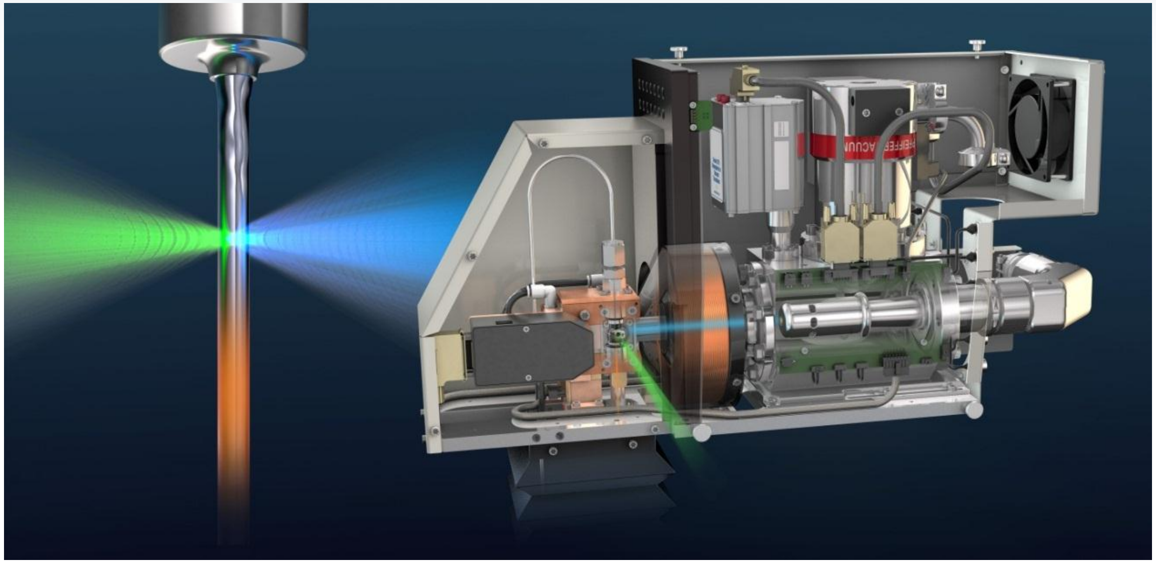


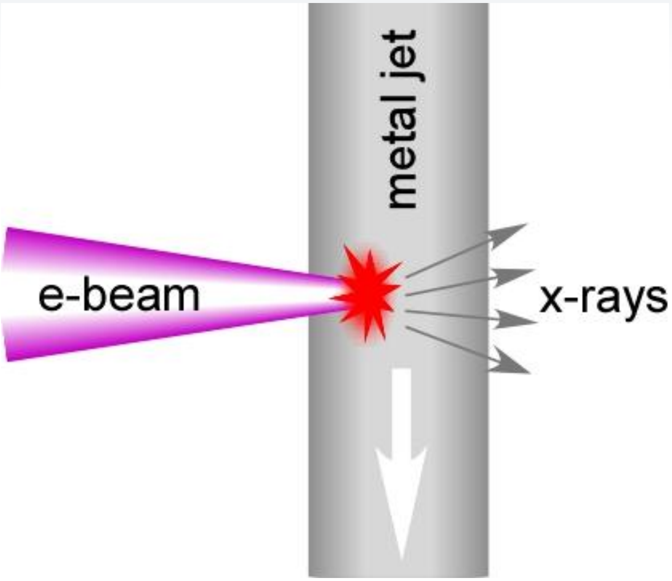
Source Comparisons

Source	Beam size (μm)	Intensity (X-rays/sec/mm^2)	Relative Intensity
Classic 5 kW RAG	300	$4x10^9$	1
IμS microfocus	110	1.3×10^{10}	8
TXS rotating anode	180	2×10^{11}	50

- Home lab sources intensities have significantly improved
  - Microfocus sources now up to 8 times the intensity of a classic 5 kW RAG
  - Latest microfocus RAGs up to 50 times the intensity of a classical 5 kW RAG
- However, beamlines still more than two orders of magnitude brighter!
- *Is it possible to produce a true synchrotron-class source in the home lab?*

NEW: Liquid metal sources





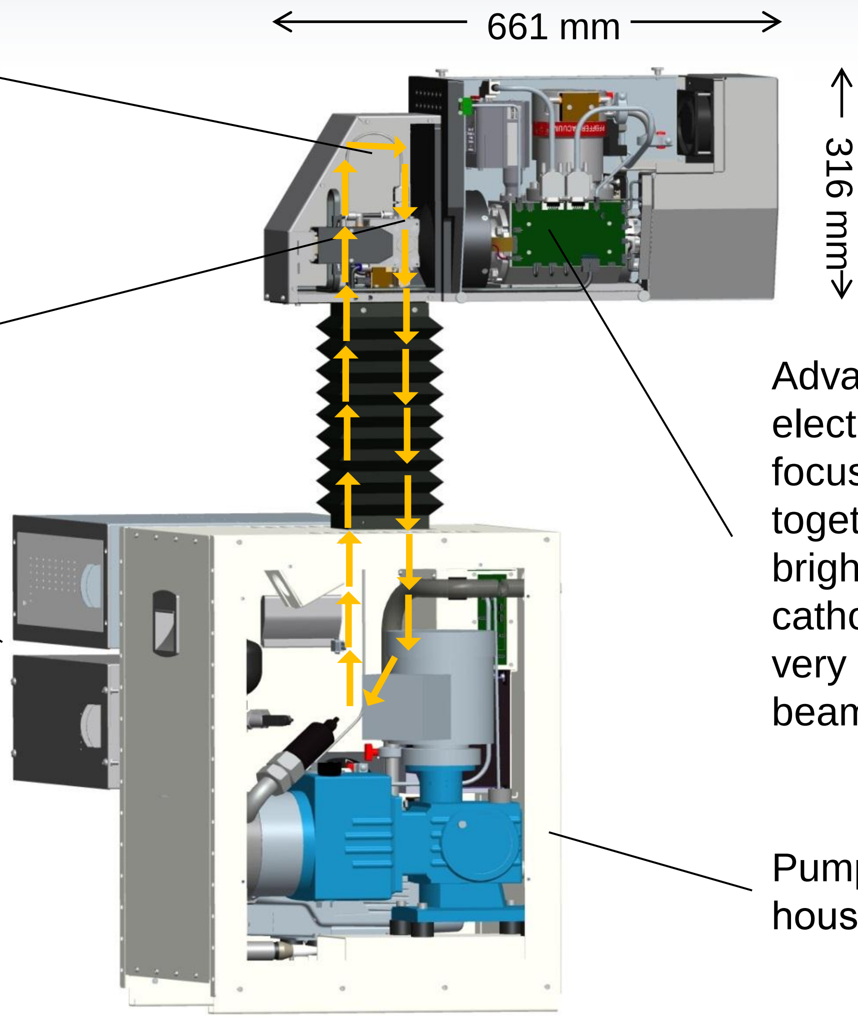
- High-speed liquid-metal-jet anode
- Anode is regenerative
- No longer limited by melting
- >500 kW/mm^2 e-beam power density
  - Rotating anode limited to maximum 50 kW/mm^2

MetalJet Source Details

The path of the continuously recycled liquid metal alloy.

X-rays are emitted from the interaction point between the metal jet and the e-beam.

Electronics is housed in two 19” boxes.

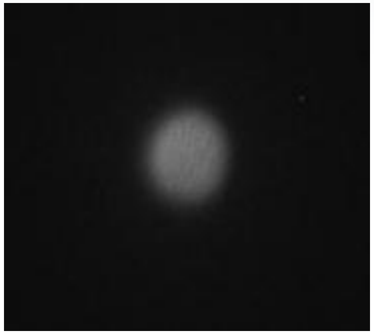


Advanced electromagnetic focusing optics together with a high brightness LaB6 cathode results in a very high quality e-beam focus.

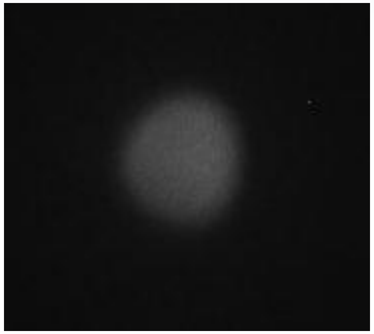
Pumps etc. are housed in a 19” box.

Spot Size

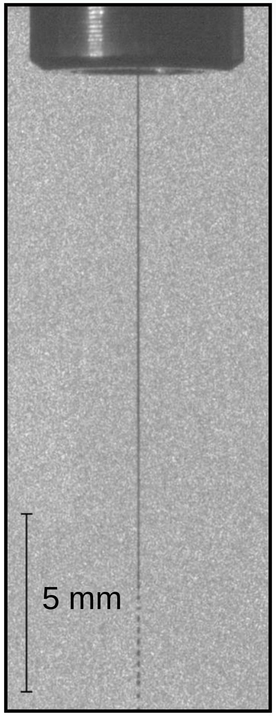
5 µm



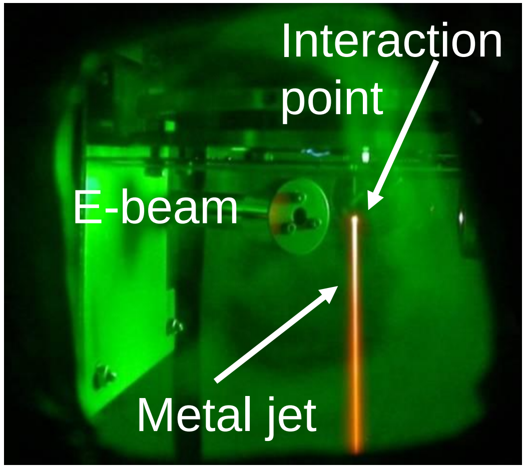
10 µm



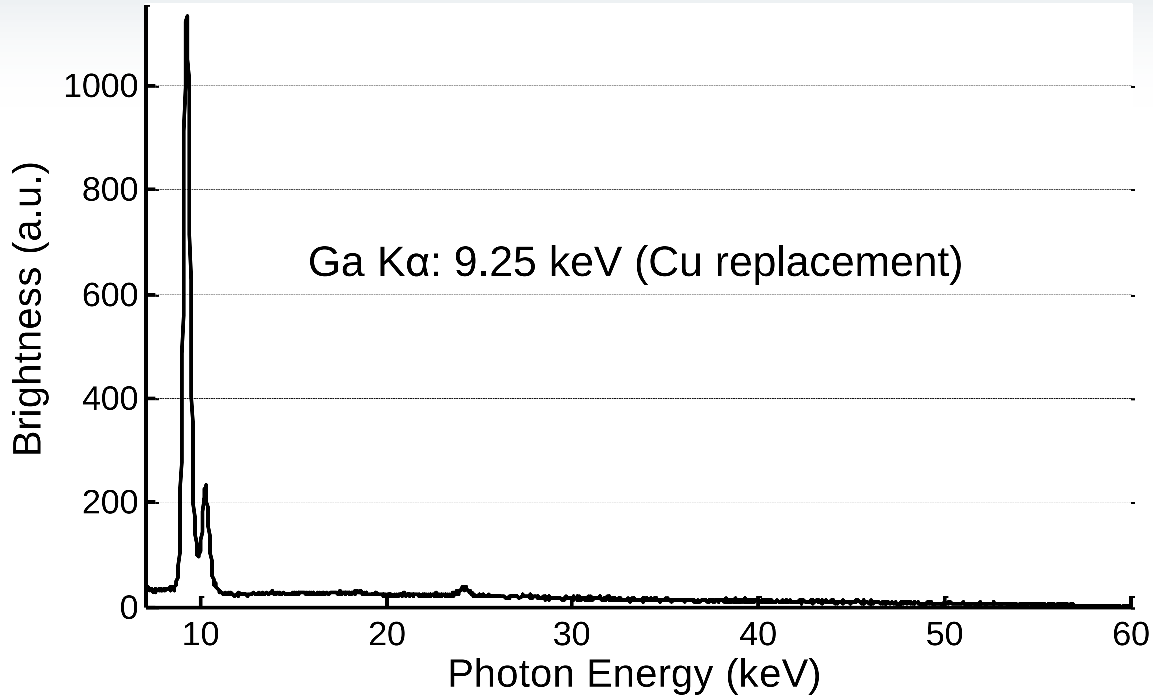
20 µm



- Variable spot size: 5-20 µm



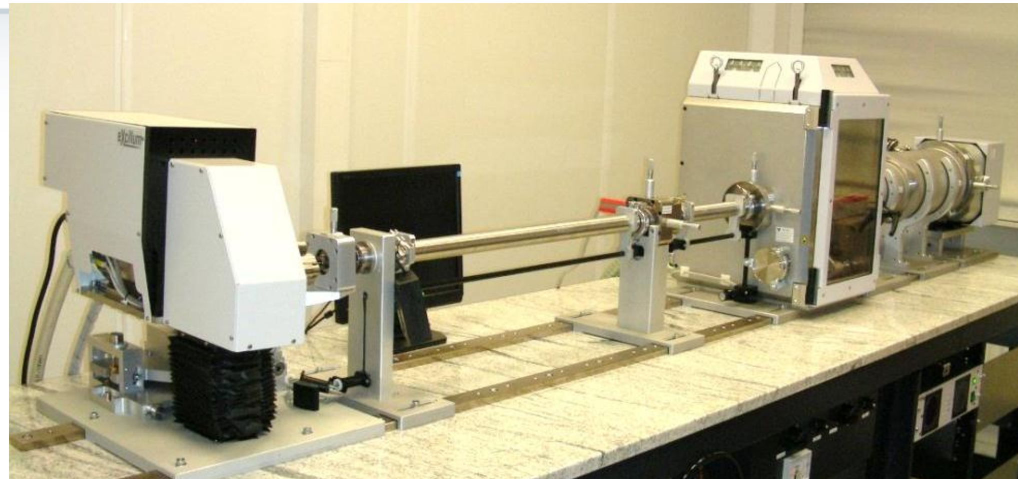
Source Spectrum and Brightness



Spot size [µm, FWHM]	**Voltage** [kV]	**Power** [W]	**Ga Kα Brightness** [Photons/(s × mm² × mrad² × line]
5	60	50	1.5×10^{11}
10	60	100	7.6×10^{10}
20	60	200	3.8×10^{10}

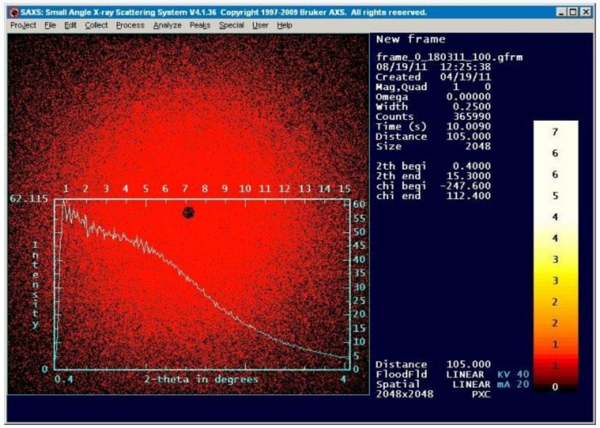
NANOSTAR with MetalJet

- Extraordinary flux, *comparable to synchrotron beamlines*
  - Up to $5x10^9$ cps
- q range 0.005-0.45 A^{-1}
- High flexibility
  - Isotropic or anisotropic samples
- Easy maintenance
  - Comparable to standard rotating anode
- Optional WAXS attachment (IP)
- Rat tail tendon



Flux comparison from glassy carbon

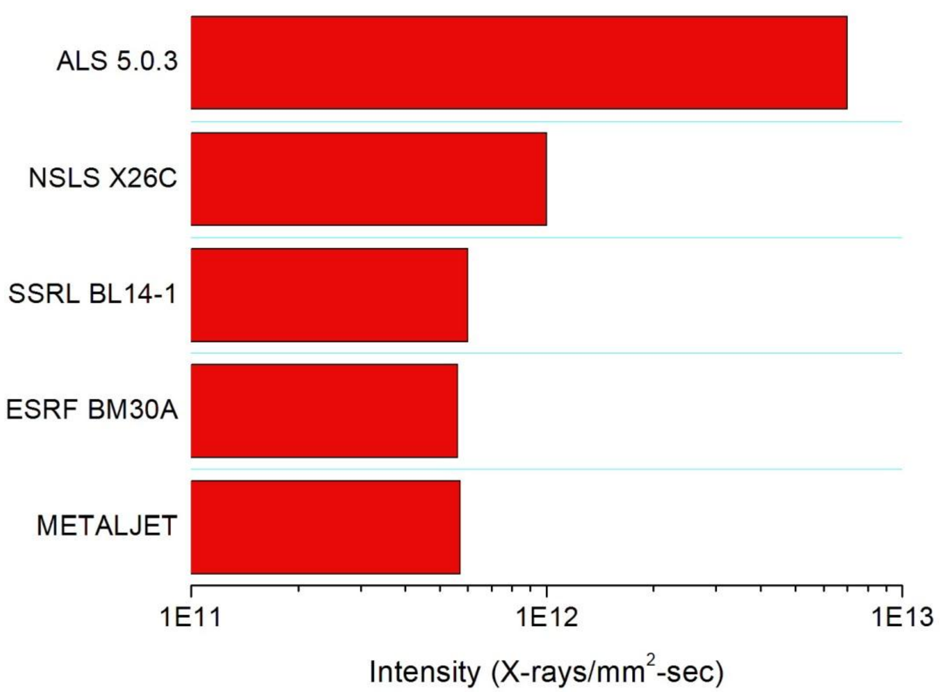
	Microfocus Cu-IμS	Rotating anode HB-TXS	MetalJet JXS-D1
Glassy Carbon			
Flux (cps)	1,50E+05	7,00E+05	4,00E+06



- Signal from glassy carbon 6 times higher than the brightest available rotating anode (HB-TXS)
  - ***>140 times*** higher intensity than classical rotating anode (5 kW)

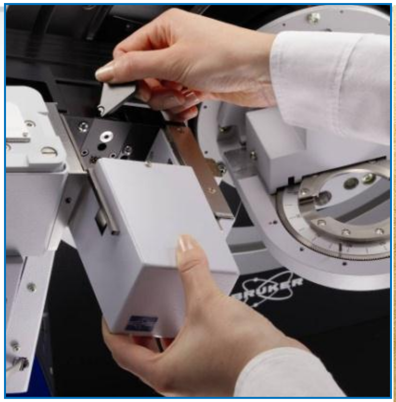
So, is it possible to put a synchrotron beamline on a table top?

- Yes, at least the equivalent of a typical present generation bending magnet beamline

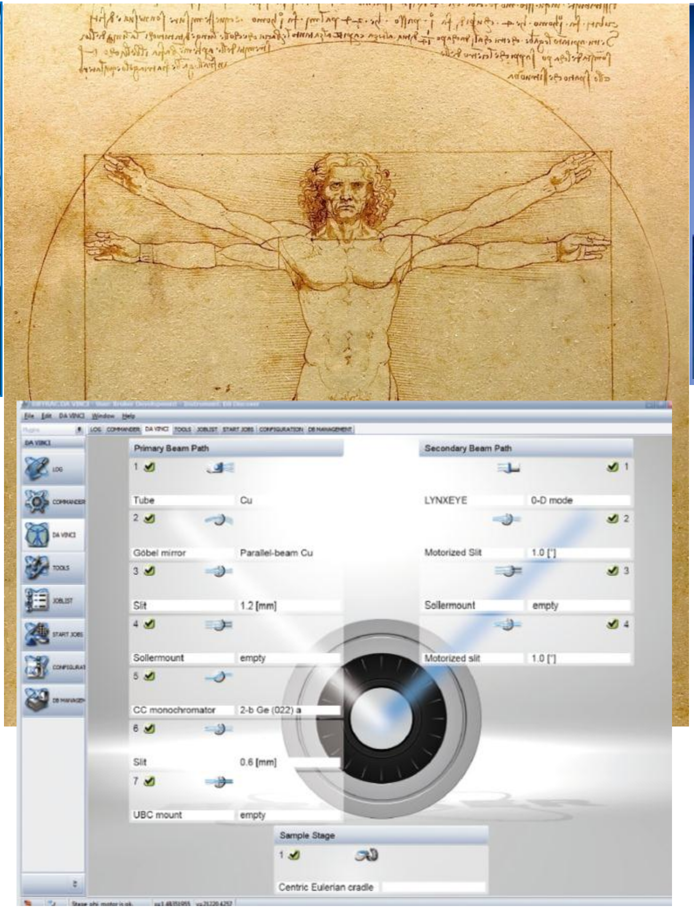


Optics and beam collimation

DAVINCI Innovations



DIFFRAC.SNAP-LOCK



DIFFRAC."Da Vinci"

"The virtual goniometer"

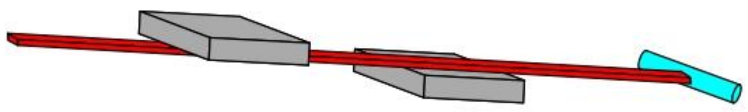
DIFFRAC.MODE

No barrier between 0D/1D/2D

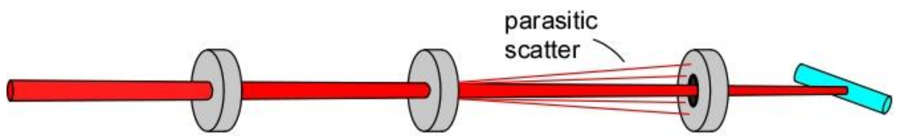
Vertical theta-theta, CEC for microdiffraction/stress/texture

SAXS beam collimation

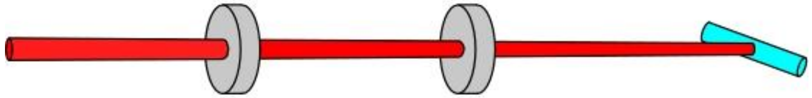
- Kratky camera
  - Advantages: Higher flux (for a given source), compact
  - Disadvantages: Half of scattered flux is lost, desmearing required.
- 3 pinhole
  - Advantages: uniform beam, no desmearing required, anisotropic samples
  - Disadvantages: lower flux, physically longer
- 2 pinhole
  - Apertures made of material that *does not scatter X-rays* (see Y. Li et al, App. Crys. 26, 2008, p1134)



Kratky



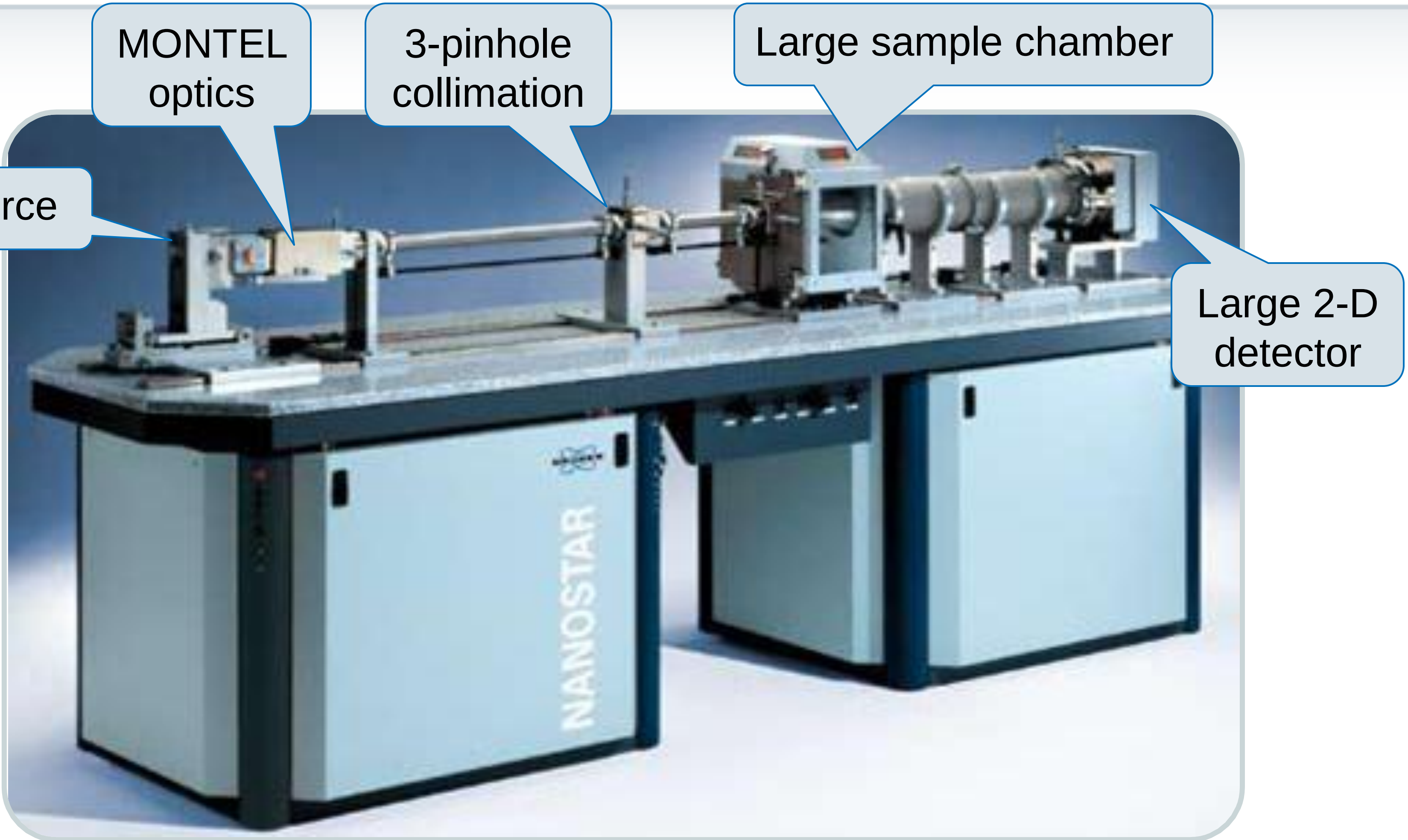
3 pinhole



Introducing the Bruker MICROpix, and MICROcalix

- Low cost
- High flux at sample
  - 1.4×10^8 cps
- High resolution
  - $q = 0.0056-0.45\ A^{-1}$
- Compact 2-D Kratky camera
  - Proven Hecus technology
- 50 W ImS source
  - Air-cooled
  - Low maintenance: 5 years tube life typical (3 years guaranteed)
- Air-cooled VANTEC detector
  - Quantum-limited sensitivity, small pixels, lowest noise
- SAXS/WAXS options

NANOSTAR


MONTEL optics
3-pinhole collimation
Large sample chamber
X-ray source
Large 2-D detector
NANOSTAR

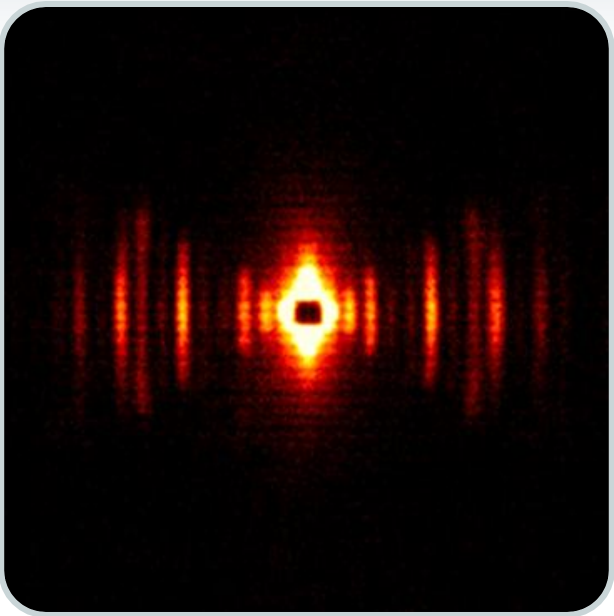
Detector

VÅNTEC-2000 - 2-D MIKROGAP™ X-Ray Detector

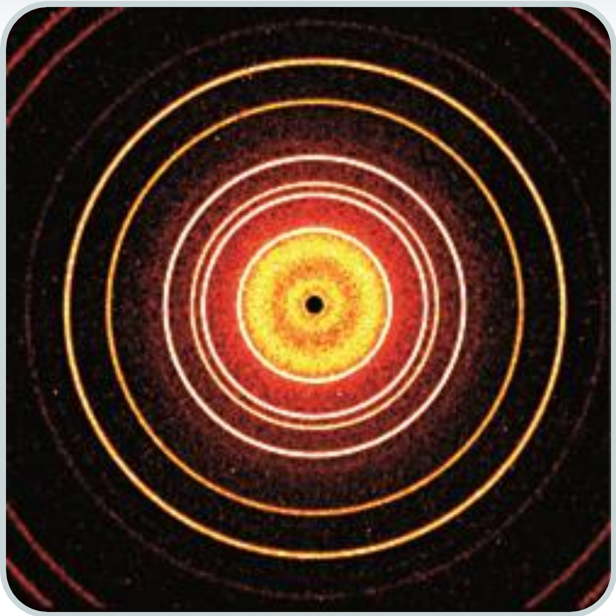
US Patent 6,340,819

- 140mm x 140mm detector window
  - Covering large Q-range
- True photon counter
  - Real time data collection and display
- No intrinsic detector noise
  - High sensitivity and low background
- High Local and Global Count Rate
- Extended Dynamic Range
  - > 10^8 (local max. count rate / local noise rate
- High Spatial Resolution
  - 68 µm x 68 µm pixel size
- Proven radiation-hardness
- No maintenance required

2-D SAXS/WAXS
Typical Data



2-D SAXS pattern of collagen fibrils



2-D WAXS pattern of Al_2O_3

- A 2-D detector is essential for measuring anisotropic data, but also enhances sensitivity for isotropic data
- Data evaluation is done on integrated 1-D data

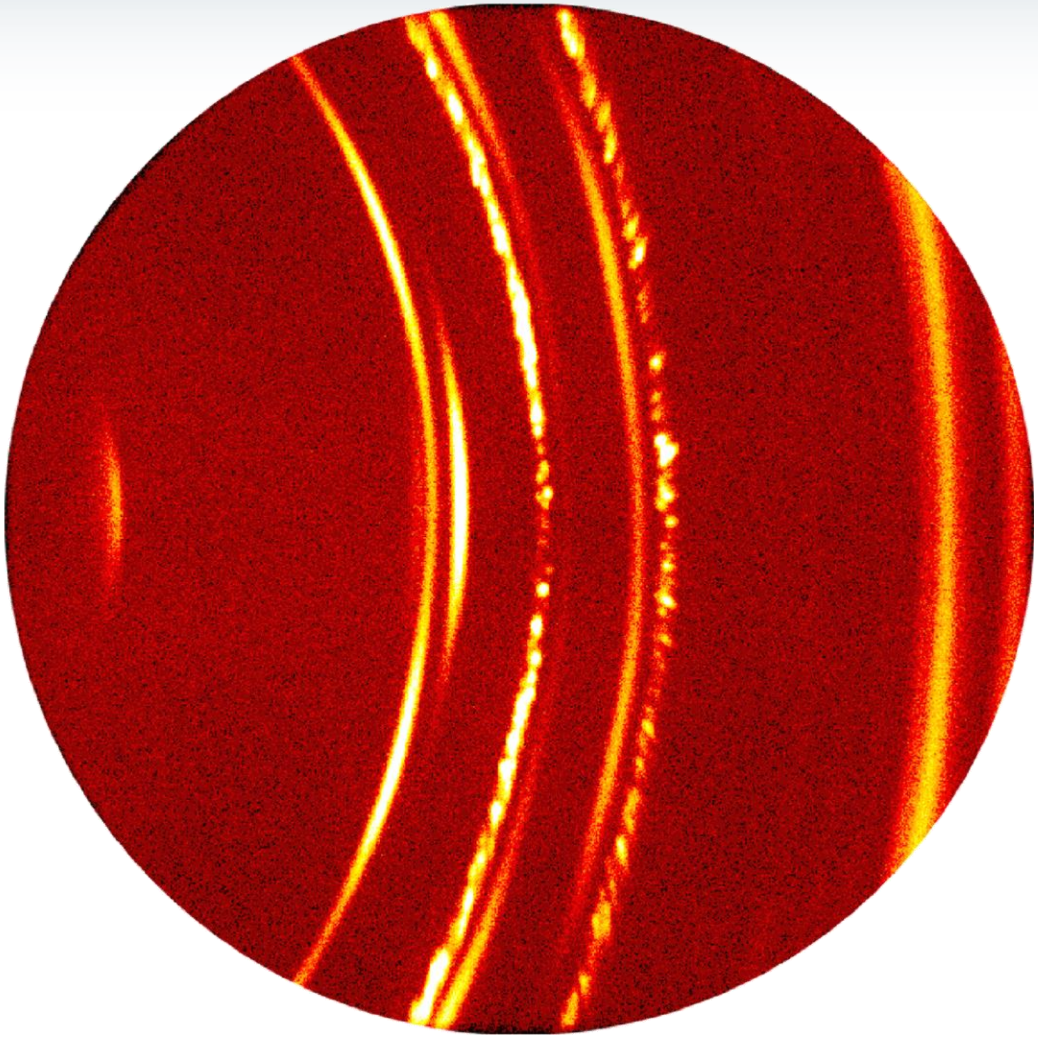
VÅNTEC-500 – Outperforms all previous gaseous detectors.

Detector geometry:

- Be-window opening 140 mm in dia.
- Frame size:
  2048 x 2048 pixels
  1024 x 1024 pixels
  512 x 512 pixels
- Pixel size:
  68 μm x 68 μm
  136 μm x 136 μm
  272 μm x 272 μm
- Detector working distance:
  5~30 cm in D8 DISCOVER enclosure
- 2θ range in a single frame:

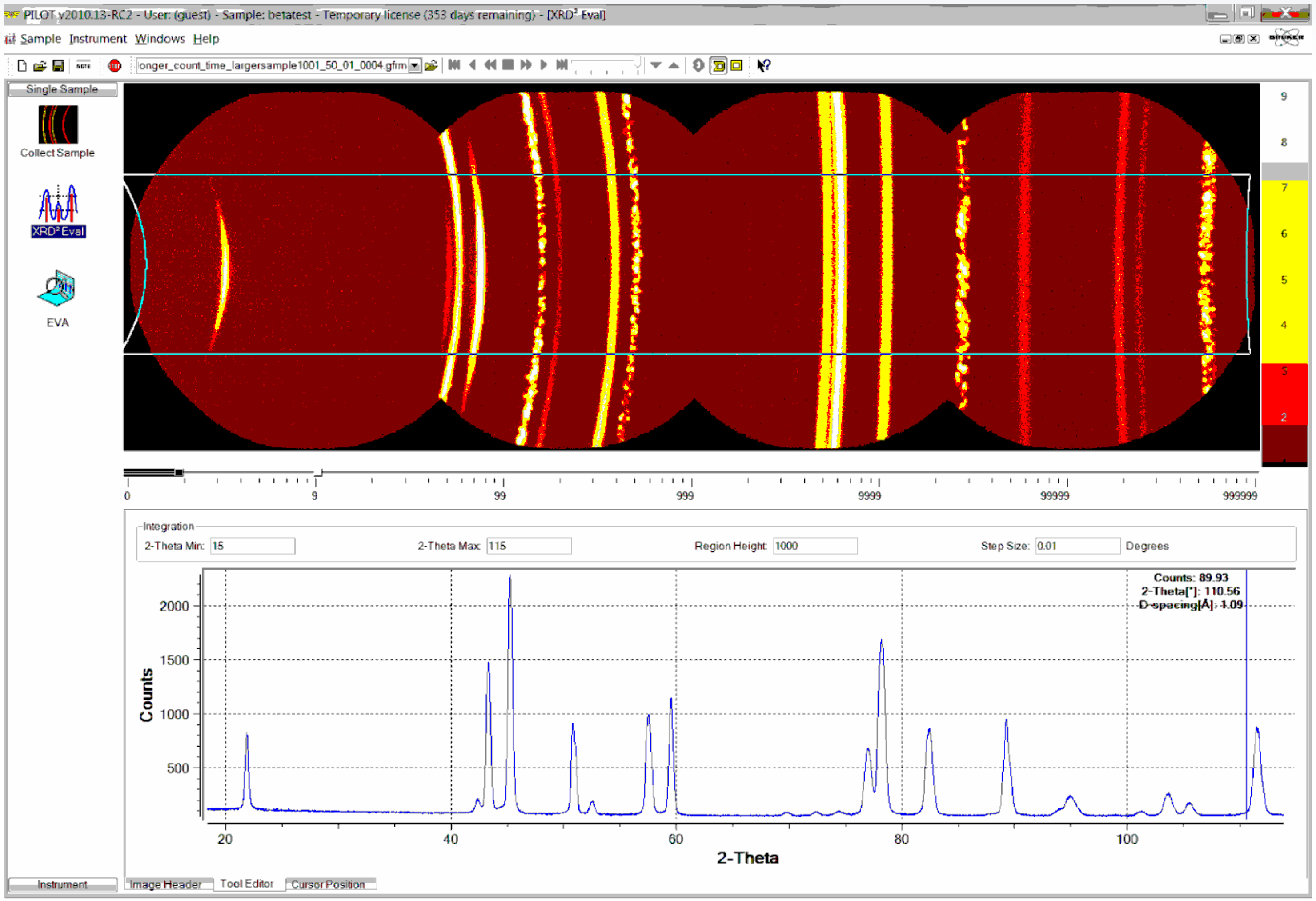
5 cm	83°
10 cm	56°
15 cm	42°
20 cm	33°
25 cm	27°
30 cm	23°

XRD²: Single Frame Covering All



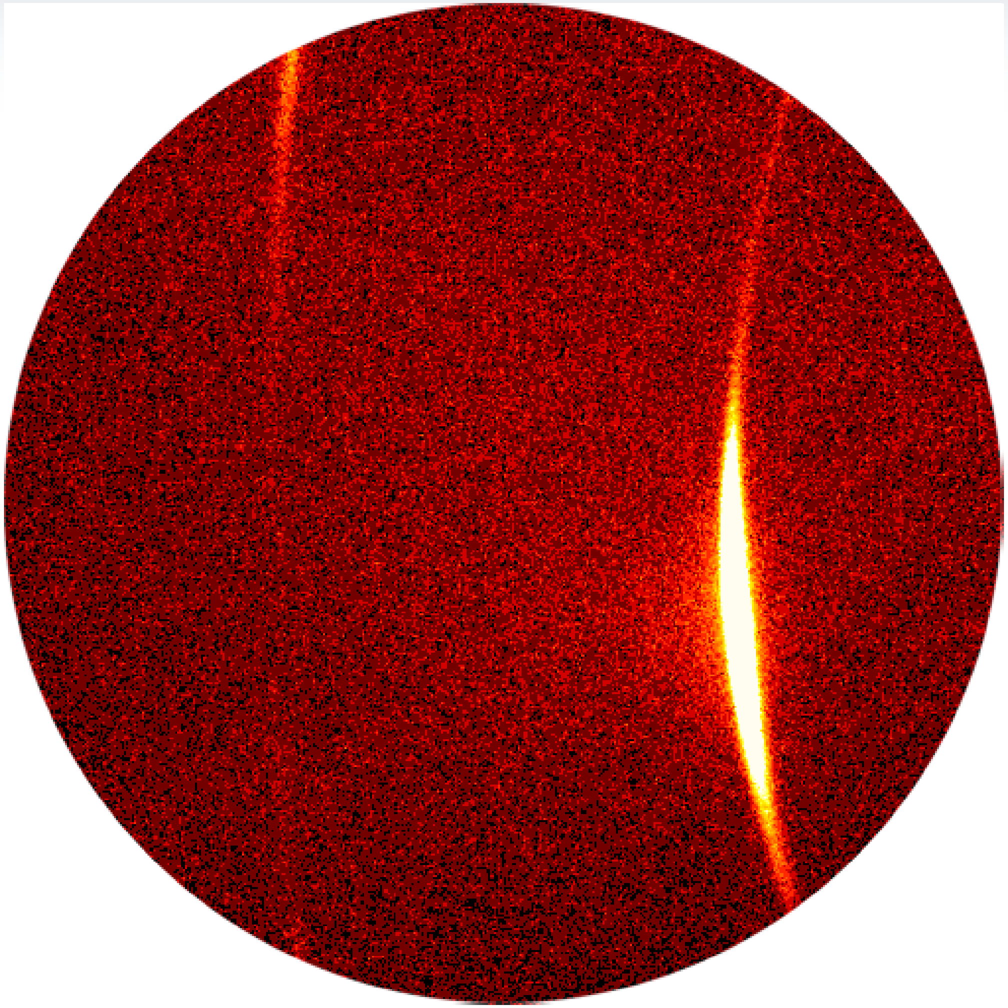
- 2θ coverage: 70° at 8 cm detector distance
- In-situ measurement for chemical reaction, phase transformation or other real-time physical changes.
- Sample with strong texture and large grain

XRD²: Frame Merge and Integration

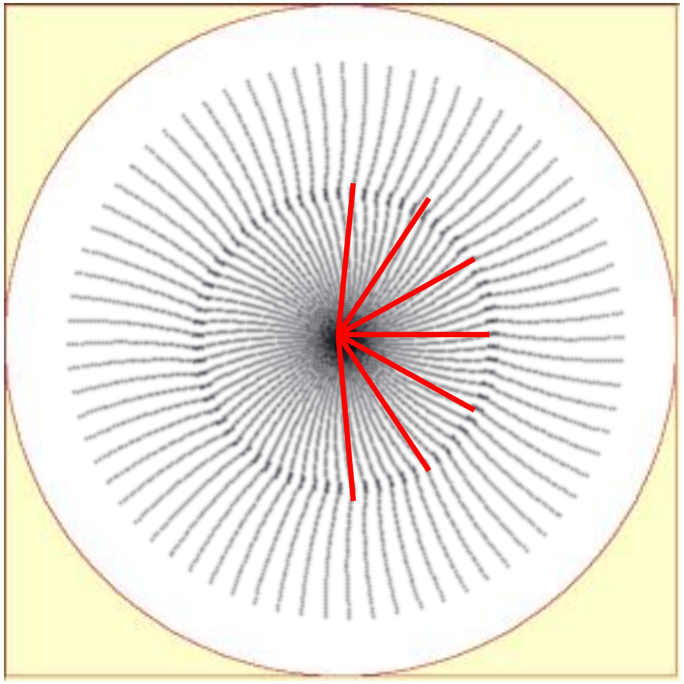


- 4 frames at 20 cm
- Merged frames 2θ coverage: 100°
- Integrated profile for phase ID search/match

The D8 DISCOVER with DAVINCI
VÅNTEC-500 for texture measurement



- Steel can
- (200) & (110) rings
- Intensity variation during ϕ scan

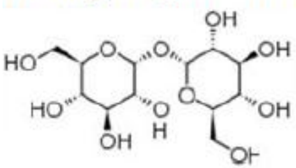


XRD²: Crystal Size by γ profile analysis: Organic glass for food & drugs

Food

Bio-preservation

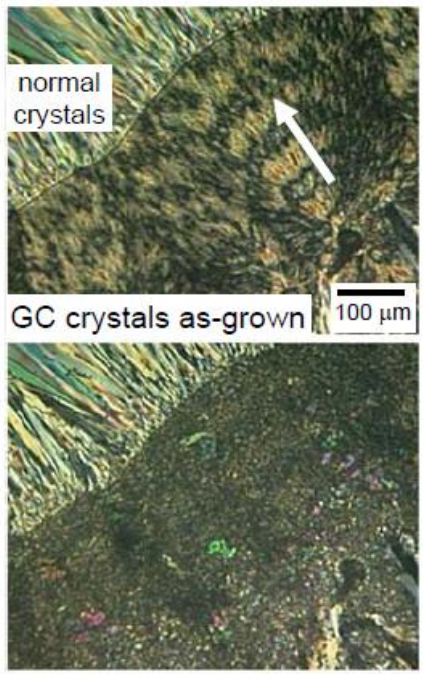
In sugar glasses



In amber

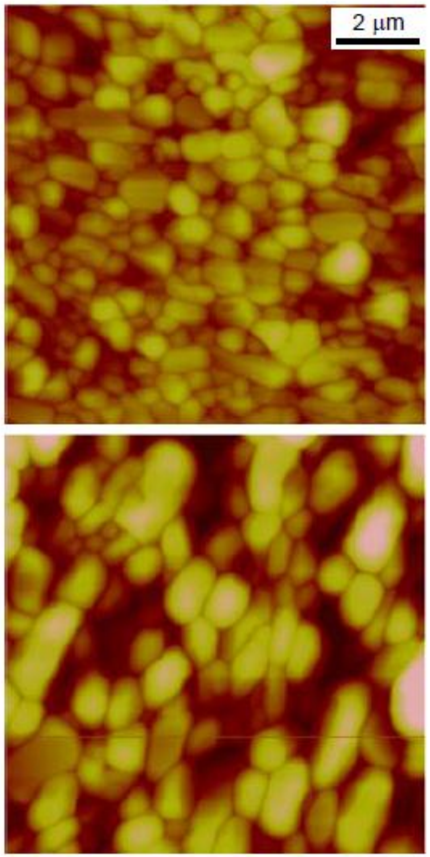
Annealing of GC crystals

LM



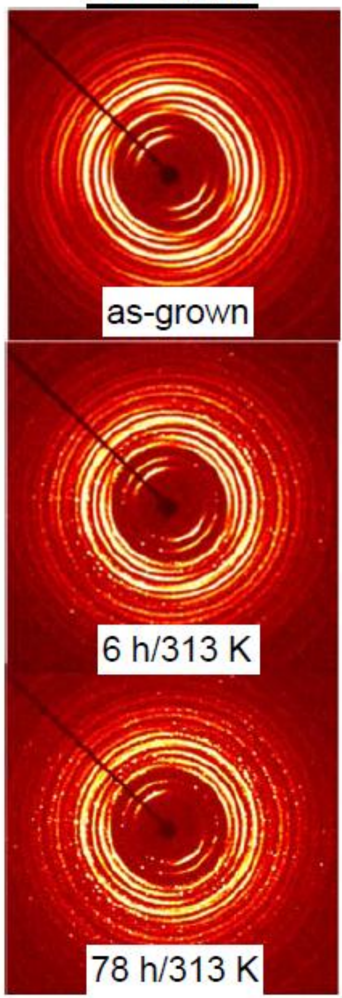
50 min/313 K

AFM



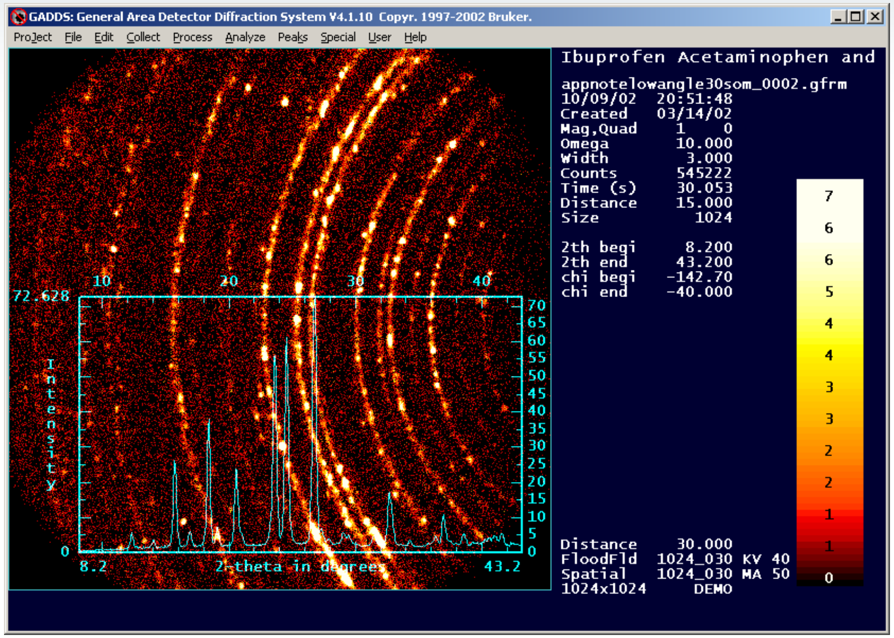
30 min/313 K

2D XRD



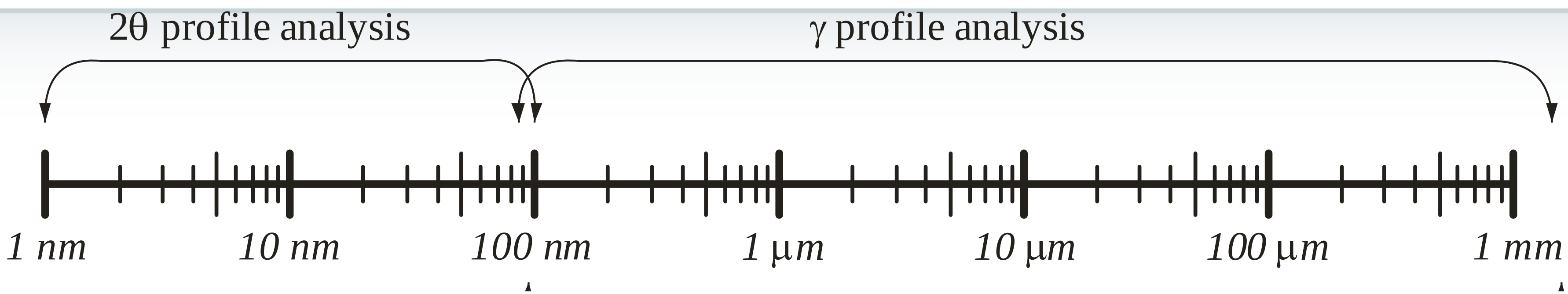
*Courtesy of Prof. Lian Yu, U. of Wisconsin - Madison

XRD²: Crystal Size by γ profile analysis: Acetaminophen powder



- The spotty diffraction ring is due to the large crystallites compared to the sampling volume (beam size).
- The number of spots on the ring is determined by crystallite size, instrumental window (γ-range), multiplicity of the crystal plane, and effective diffraction volume.
- The size of jelly beans and candy bin determines how many you can fill.

XRD[2]: Particle Size Analysis



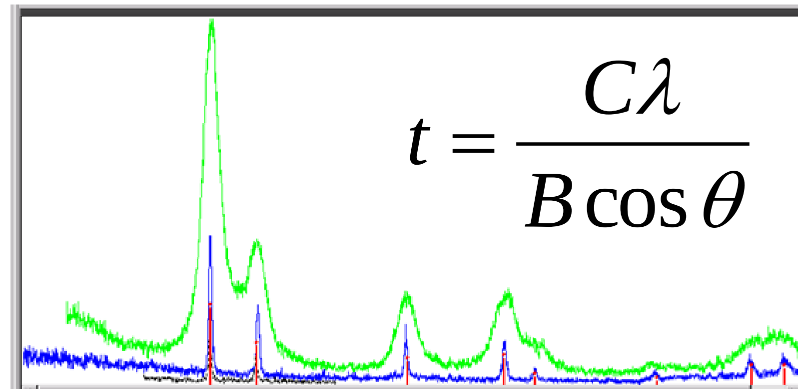
- 2θ profile analysis, suitable for <100 nm. Scherrer equation:

where B is FWHM corrected

for instrument broadening,

C is 0.9~1 (crystal shape).

$$t = \frac{C\lambda}{B\cos\theta}$$



Gold nano-particle

- γ profile analysis is suitable for particle size from sub-micrometer to a few millimeters.

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Thanks for your attention