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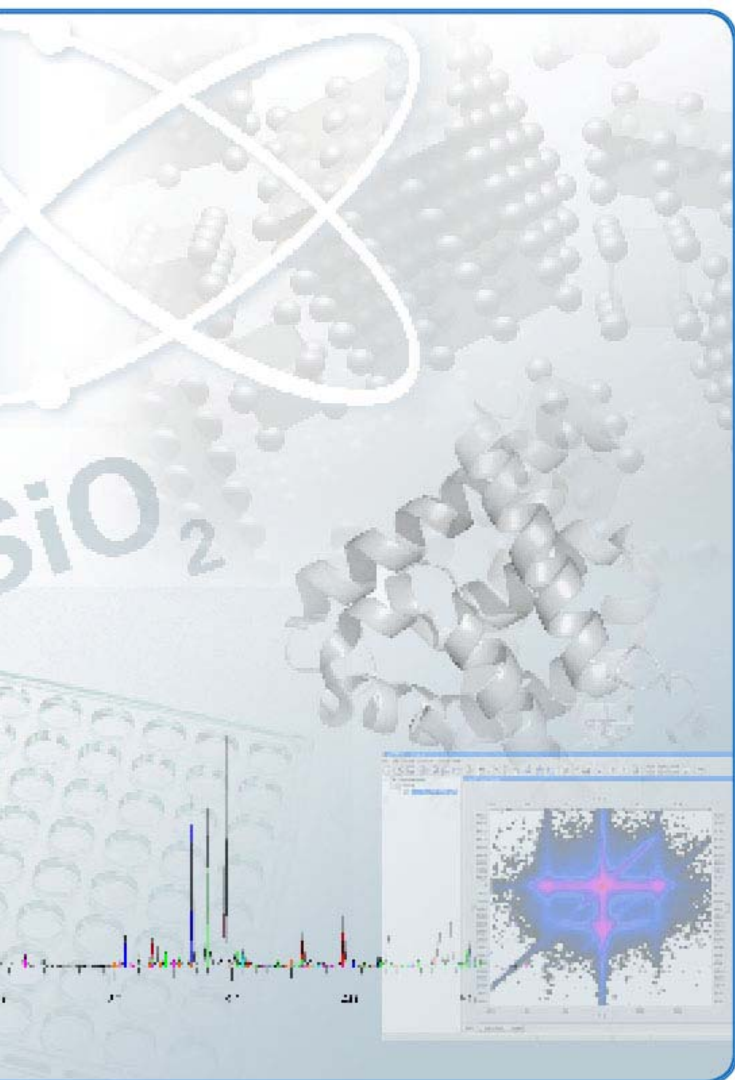

Particle Size Analysis by Two-dimensional XRD

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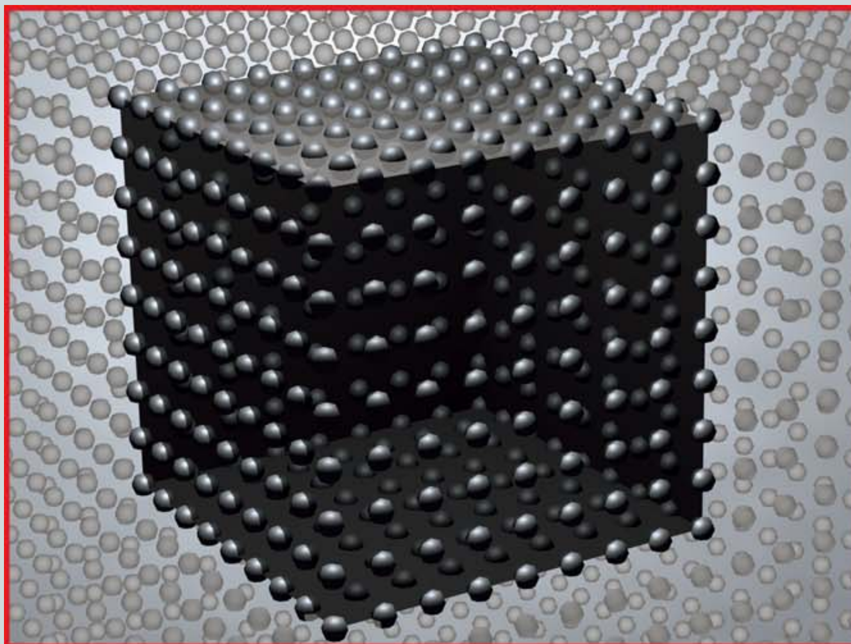
Particle Size Analysis by Two-dimensional XRD

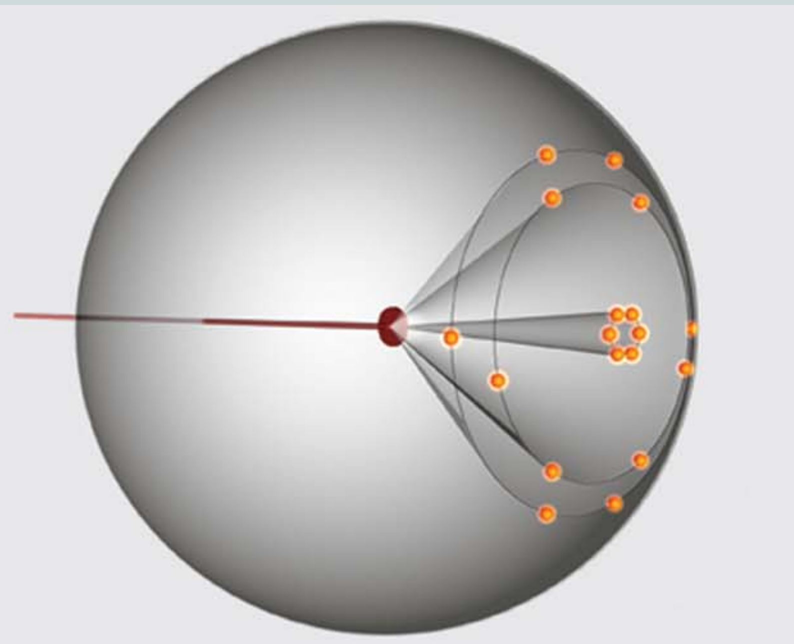
The Eighth Pharmaceutical Powder X-ray Diffraction Symposium
4-7 May 2009 – Glasgow, Scotland, UK

Bob B. He

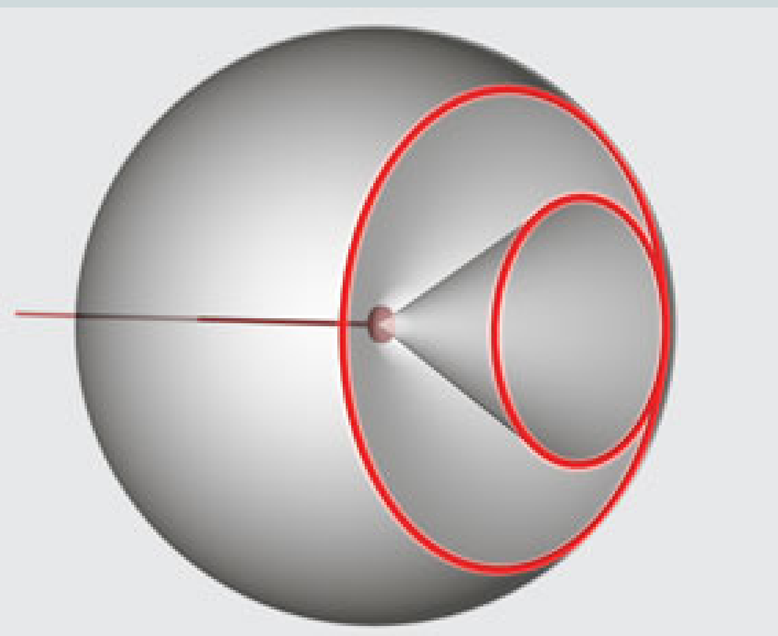
- **Two-dimensional XRD**
- **Particle Size Analysis – conventional methods**
- **Particle Size Analysis –XRD^2 method**

XRD² & Single Crystals

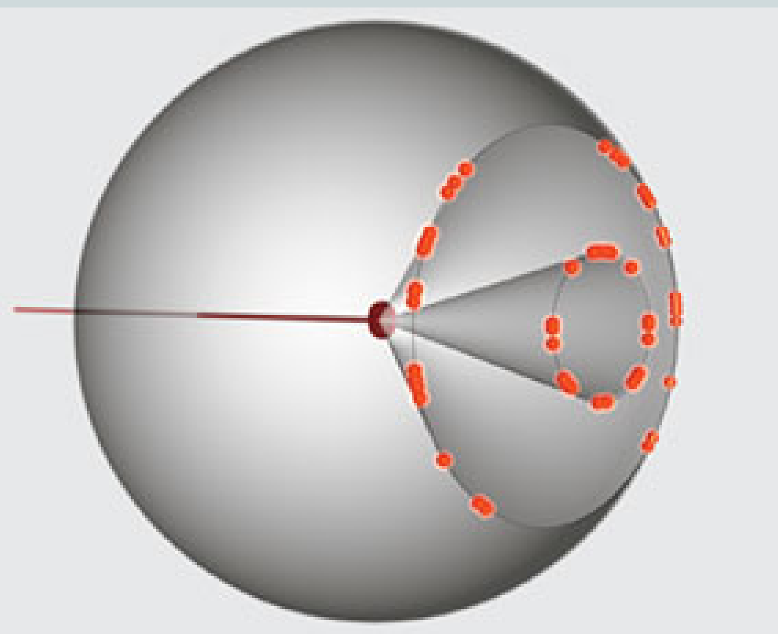




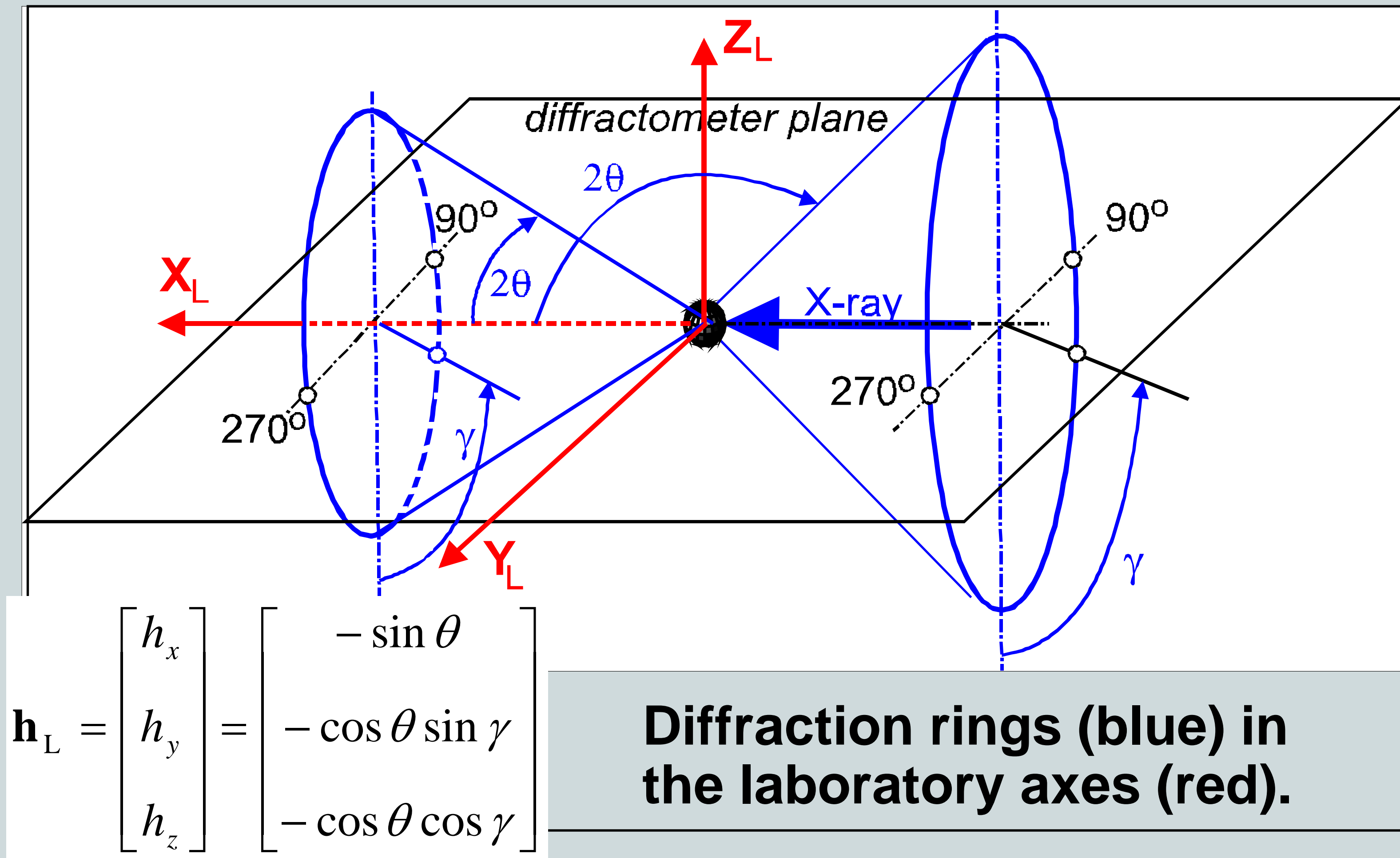
XRD² & Powders



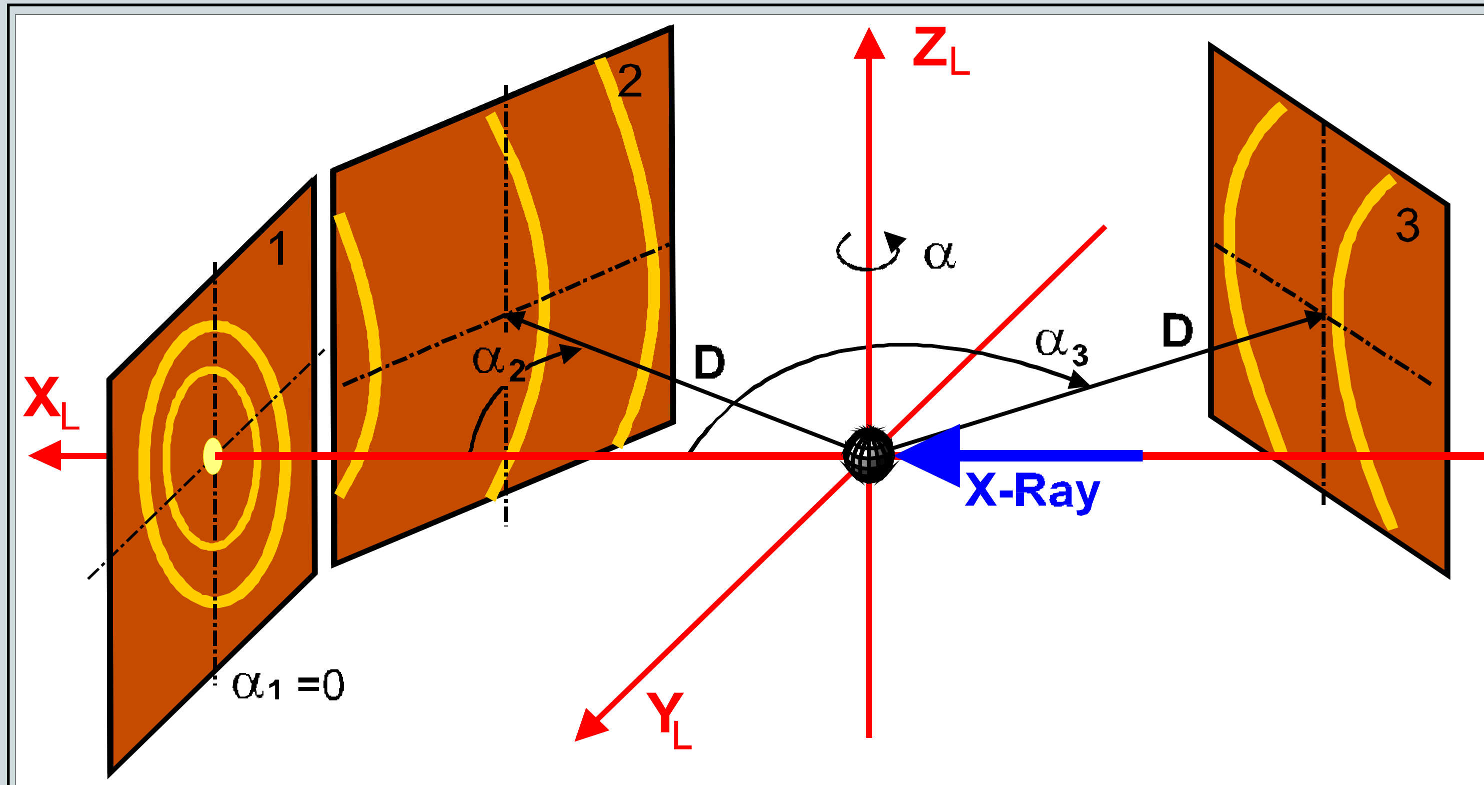
XRD² & Micro Samples or Large Grains



XRD^2: Geometry Convention (1) - Diffraction Space

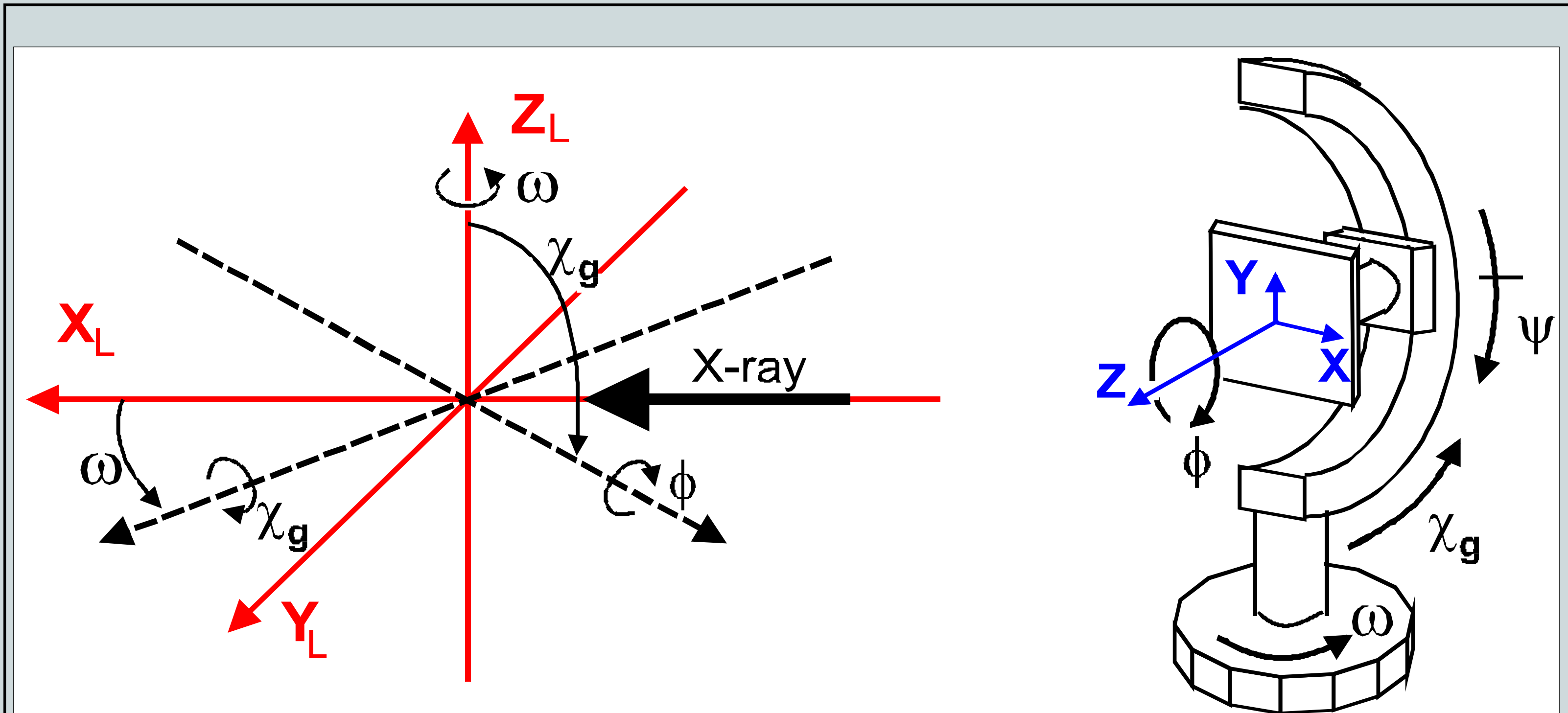


XRD^2: Geometry Convention (2) - Detector Space



Detector position in the laboratory coordinates is determined by the detector distance D and swing angle α.

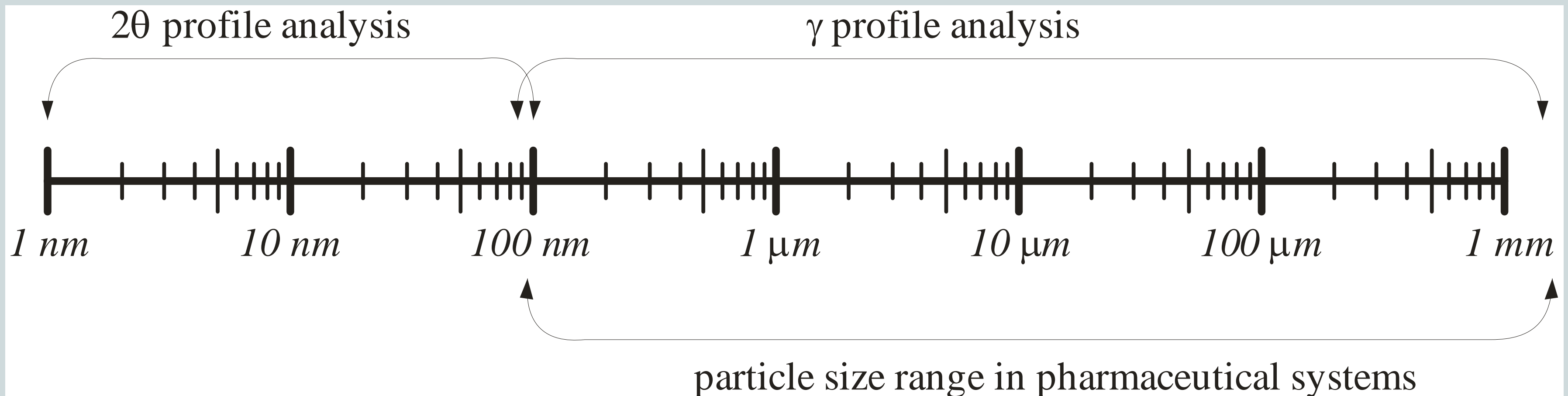
XRD^2: Geometry Convention (3)- Sample Space



Rotation axes ω, φ, χ_g and the laboratory axes $X_L Y_L Z_L$ (red).

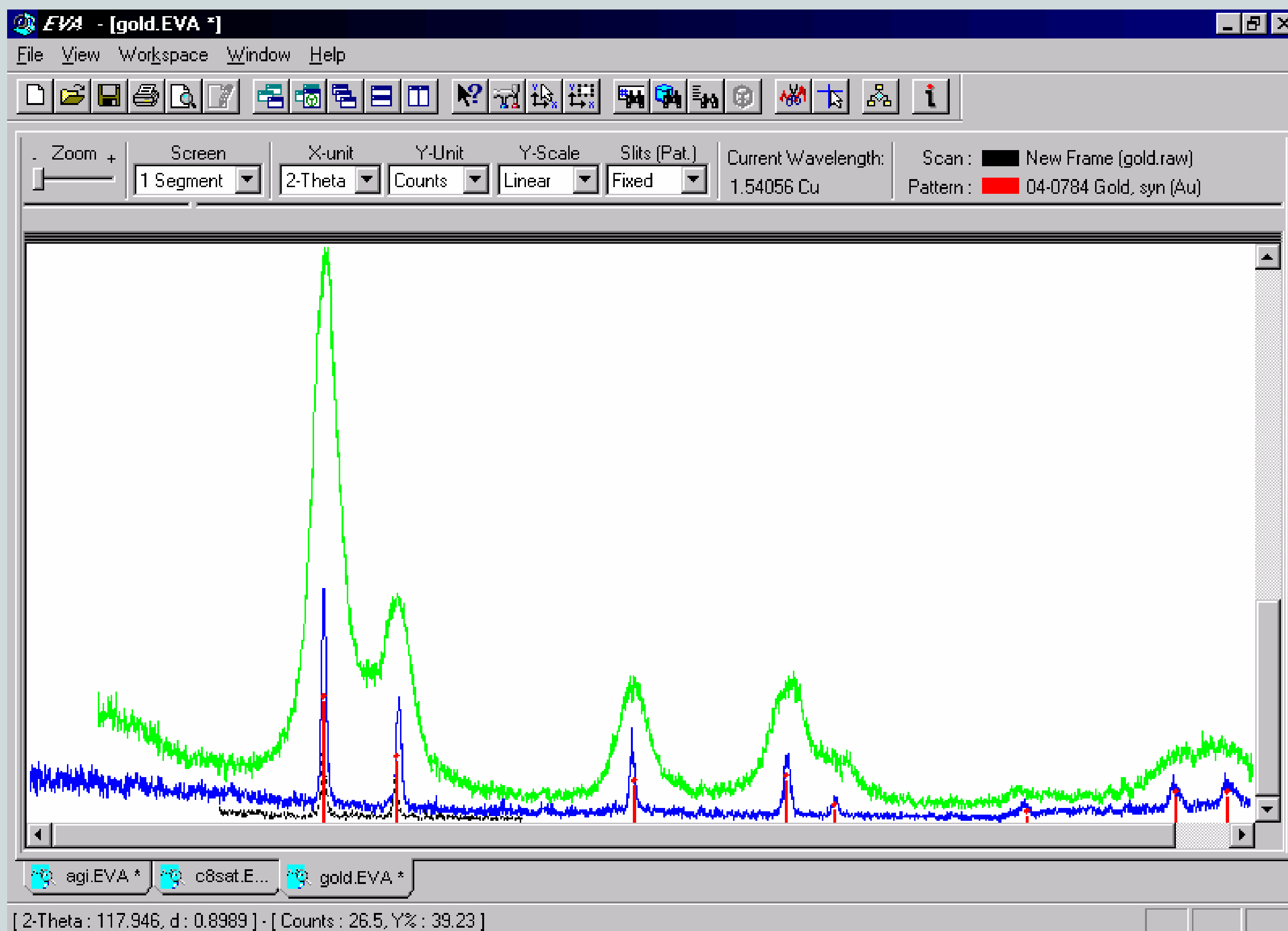
Rotation axes ω, φ, $\chi_g(\psi)$ and translation axes XYZ (blue).

XRD²: Particle Size Analysis by X-ray Diffraction:



- 2θ profile analysis, including measurement from peak FWHM by Scherrer equation, or profile analysis by Stokes and Wilson, is suitable for particle size below 100 nm.
- γ profile analysis, based on sampling statistics, is suitable for particle size from sub-micrometer to a few millimeters.
- The particle size range of pharmaceutical substances is from sub-micrometer to a few millimeters.

XRD²: Peak broadening-gold Nanoparticles



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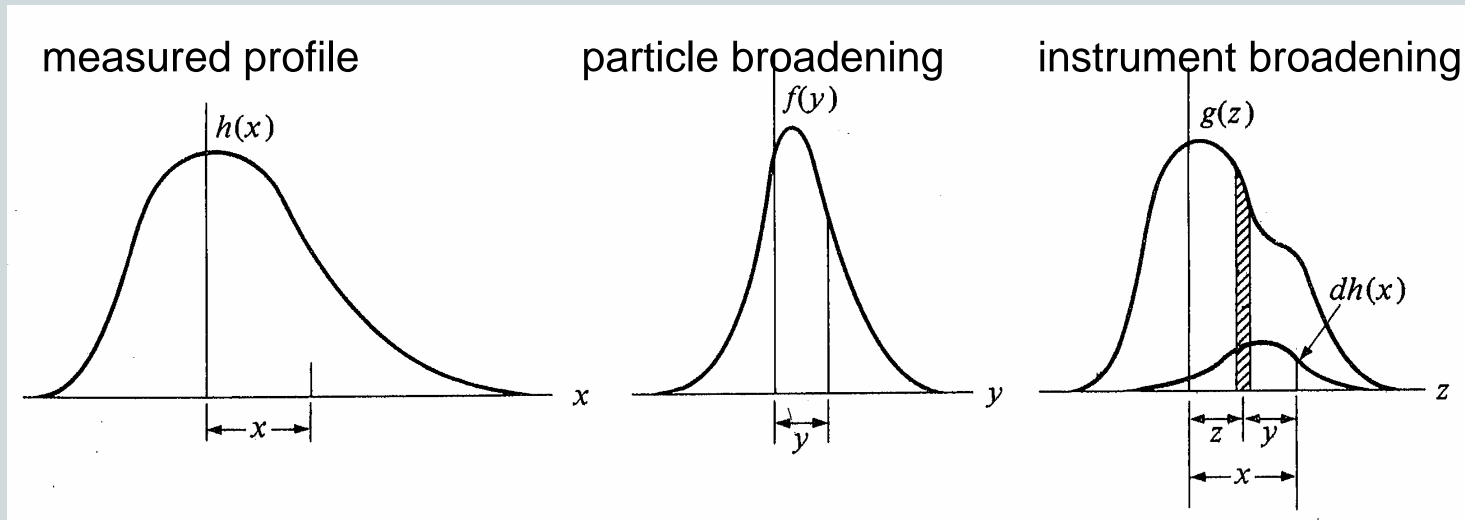
XRD²: Particle size and instrument broadening:



The measured profile is a convolution of the functions representing particle-size broadening and instrument broadening

$$h(x) = \frac{1}{A}\int g(z) f(x-z) dz$$

where *A* is the area of the *f(y)* curve and *y=x-z.*

Ref: B. E. Warren, *X-ray Diffraction*, Dover Publications, Inc. New York, 1990.

XRD²: Particle size calculation:

Scherrer equation:

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

where λ is wavelength (Å), B is FWHM (radians) corrected for instrument broadening, θ is Bragg angle, C is a crystal shape factor from 0.9~1.

For Gaussian profiles,

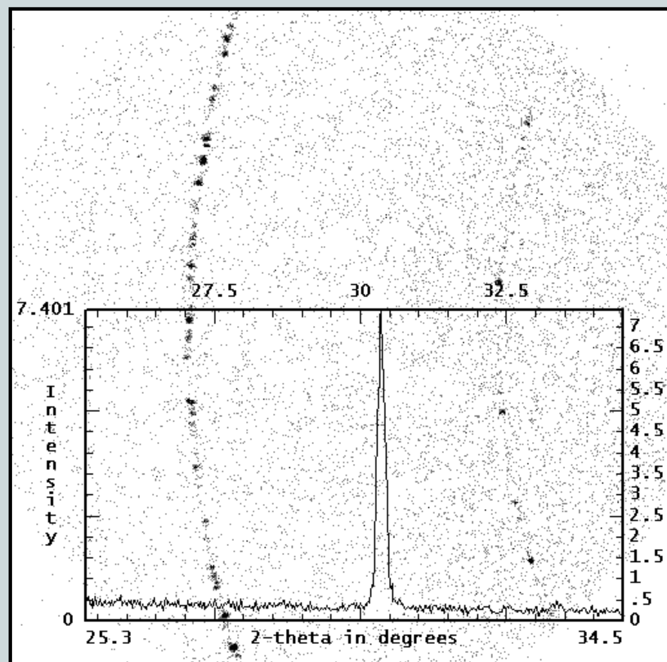
$$B^2 = U^2 - S^2$$

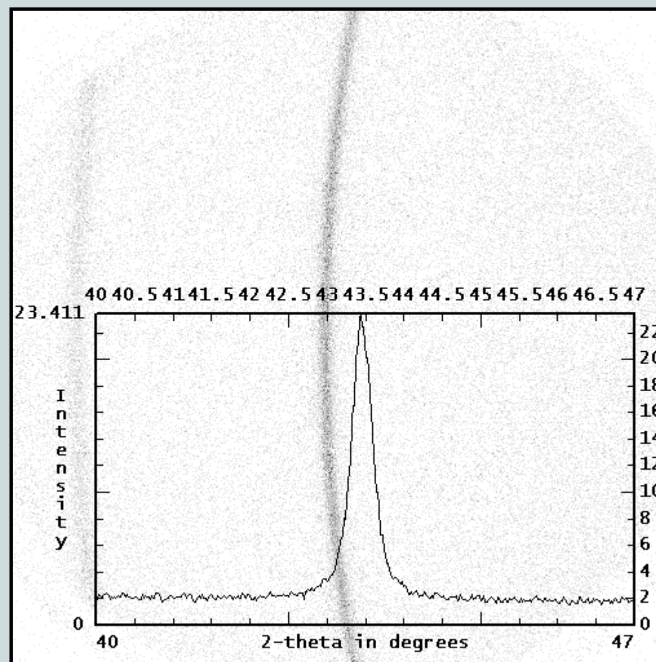
while for Cauchy profiles,

$$B = U - S$$

where *B* is the corrected FWHM for crystallite size calculation by Scherrer equation, and *U* and S are the FWHM's of the unknown and standard peaks, respectively.

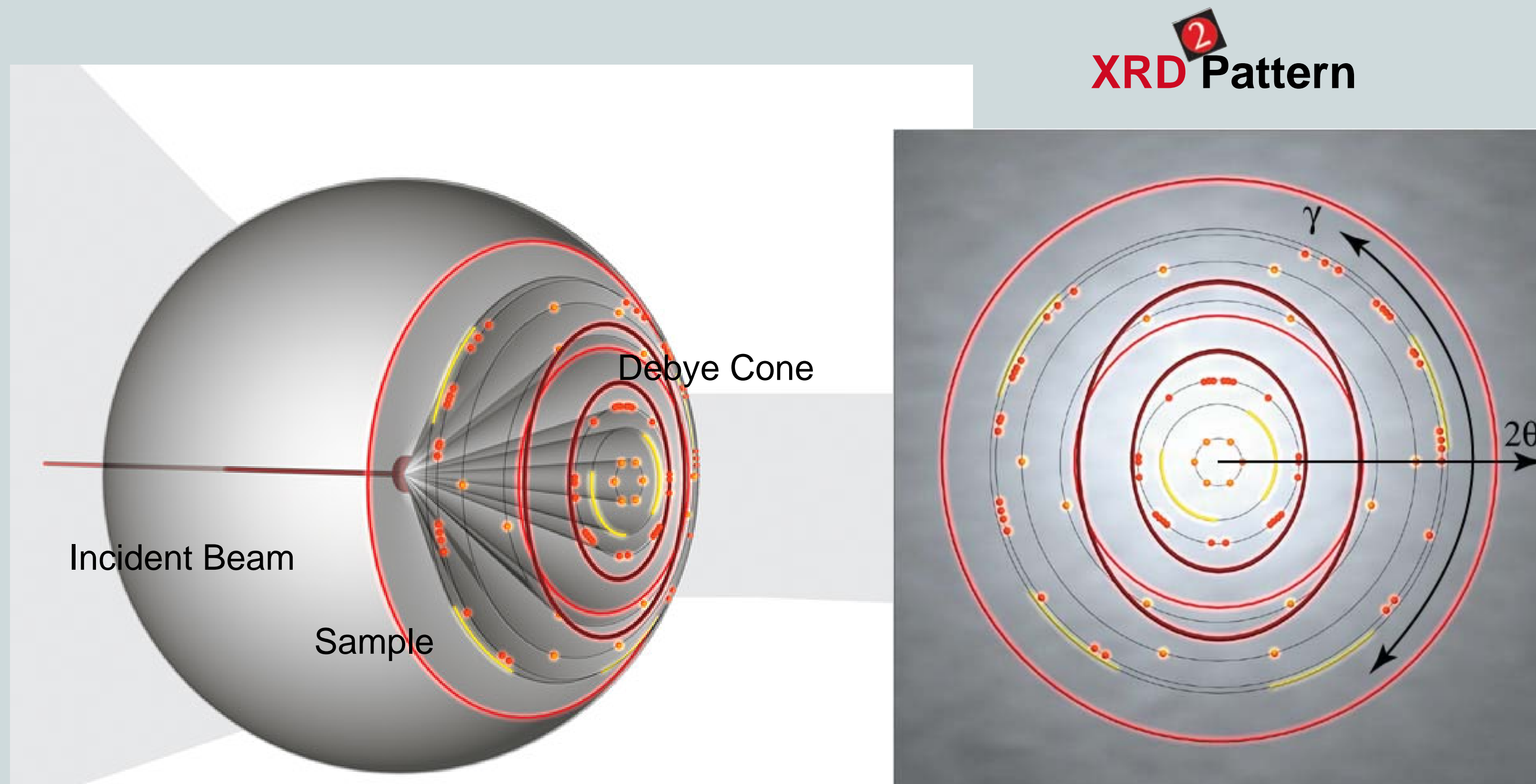
XRD²: Particle size calculation by Scherrer equation:





- Left: NIST SRM 660, LaB6. Profile fitting of the peak shown gives a FWHM of 0.162° with a Gaussian profile and 0.133° with a Cauchy.
- Right: Cu (111) peak from a semiconductor tab tape. Profile fitting with a Cauchy function for a peak at 43.455° 2θ gives a FWHM of 0.300°.
- Using LaB6 as an instrumental broadening standard with a Cauchy FWHM of 0.133°, the corrected FWHM is 0.167°, and the Scherrer equation gives a crystallite size of 512 Å.

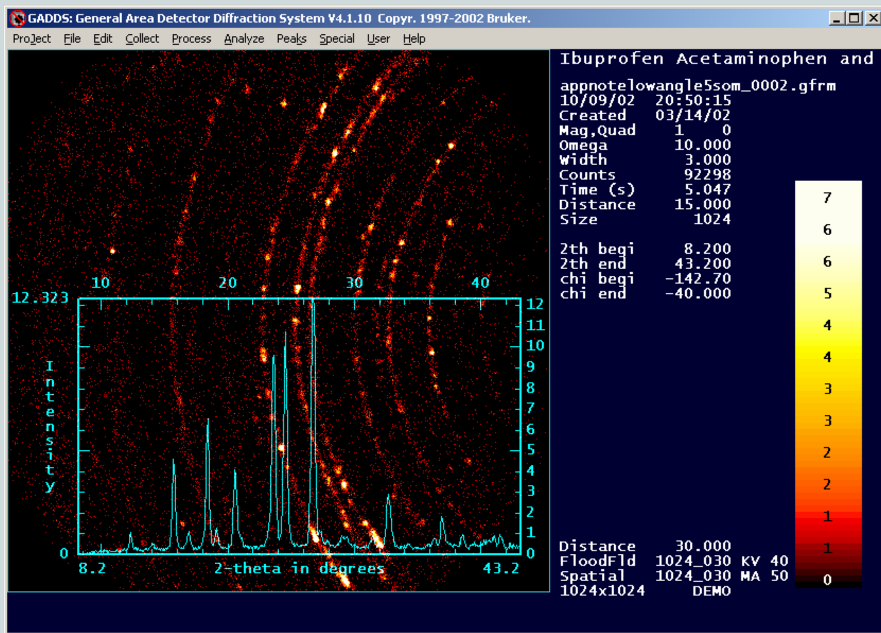
XRD²: Particle size measurement by γ profile analysis:



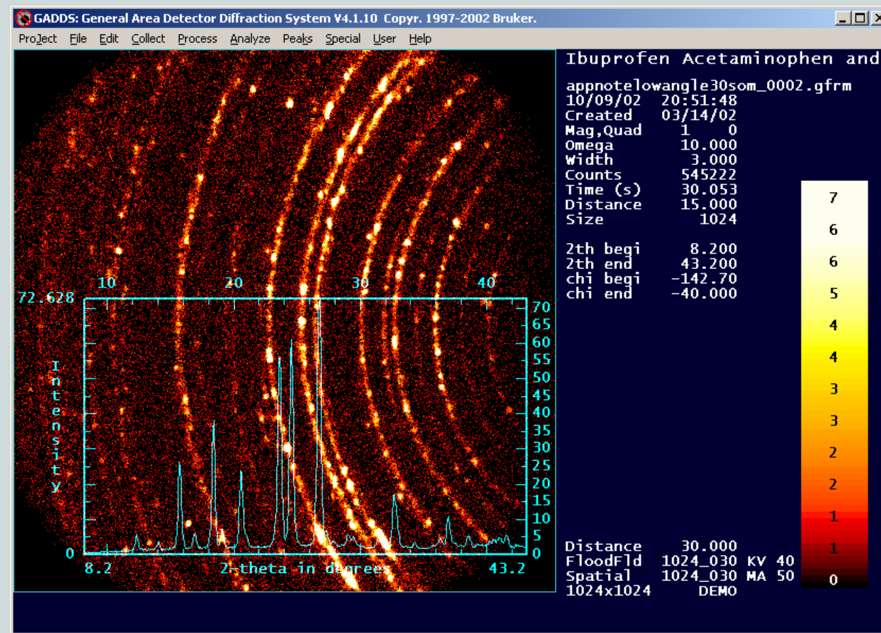
XRD²: Data Collection:

Acetaminophen powder

5 second data collection



30 second data collection



- 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.

XRD[2]: Particle size measurement by γ profile analysis:

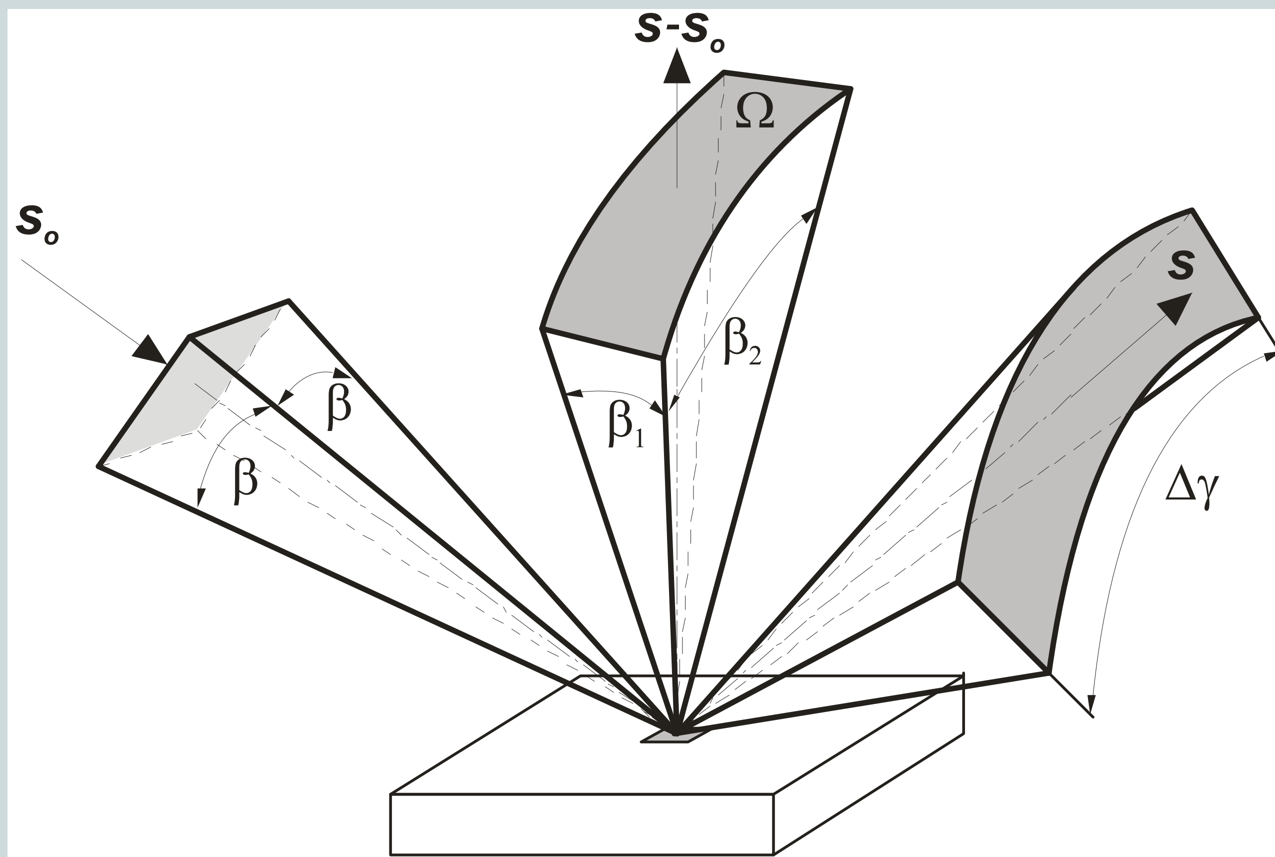
The sampling statistics are determined by both the sample structure and instrumentation. For a perfect random powder sample, the number of contributing crystallites for a measured diffraction line can be given by:

$$N_s = p_{hkl} \cdot \frac{Vf_i}{v_i} \cdot \frac{\Omega}{4\pi}$$

where p_{hkl} is the multiplicity of the diffracting planes,
V is the effective sampling volume,
f_i is the volume fraction of the crystallites being measured and $f_i = 1$ for single phase materials,
v_i is the volume of individual crystallites and
Ω is the angular window of the instrument in solid angle.

The factor Vf_i / v_i is the number of the crystallites being measured within the effective volume. The factor $\Omega / 4\pi$ is the ratio of the effective volume satisfying the Bragg condition. Assuming sphere-shaped particles, $v_i = \pi d_i^3 / 6$

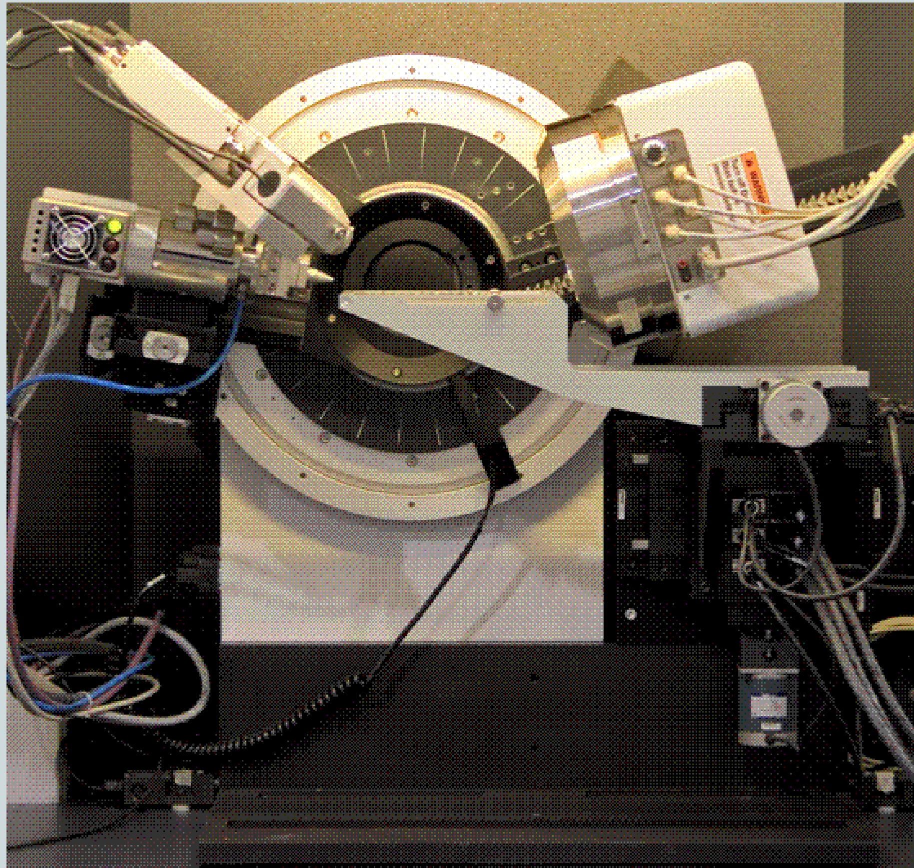
XRD²: Particle size measurement by γ profile analysis:

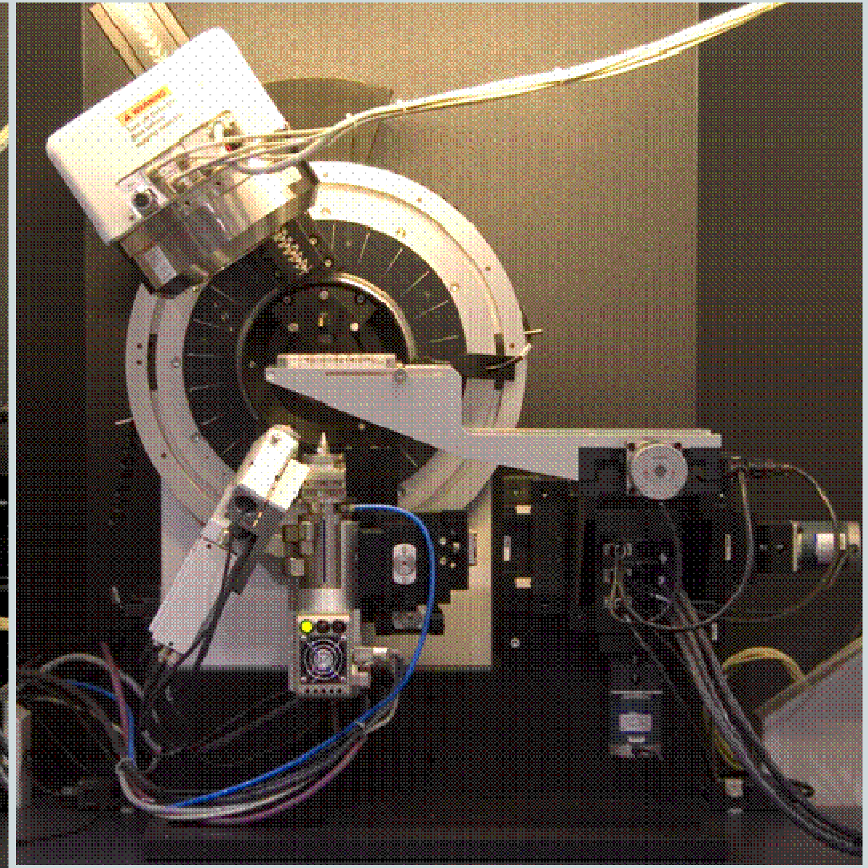


For XRD², the instrumental window Ω is given by

$$\Omega = \beta_1 \beta_2 = 2\beta \arcsin[\cos\theta \sin(\Delta\gamma/2)]$$

D8 DISCOVER with GADDS HTS (IµS):
Crystallite size by Reflection & Transmission





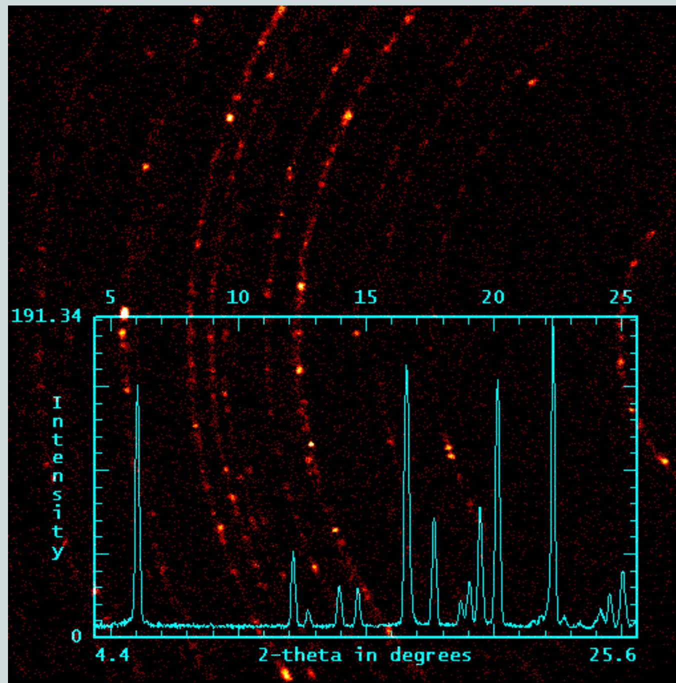
- Reflection mode: Effective diffraction volume is determined by the beam size and μ.
- Transmission mode: Effective diffraction volume is determined by the beam size and t ($\approx 1/\mu$).

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

Sealed Tube

- 0.3 mm collimator
- Sample-Detector distance 29 cm

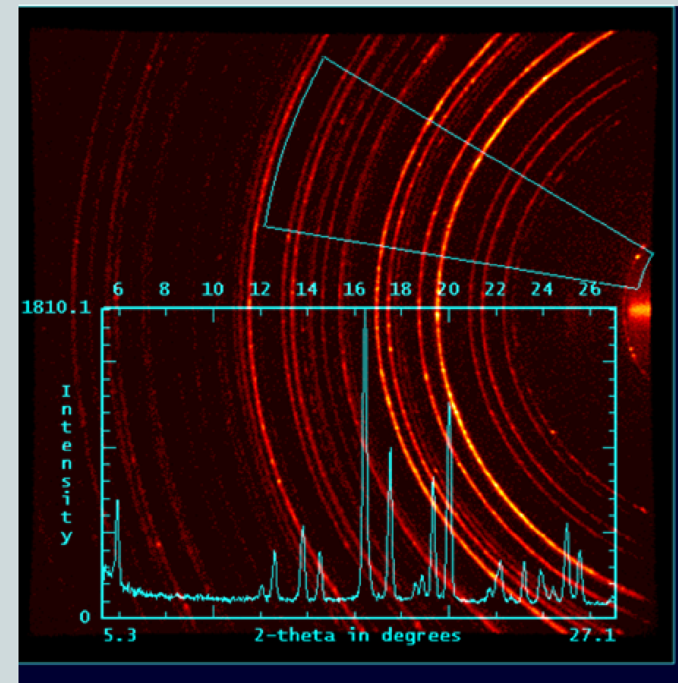
120 sec collection time



IµS – XRD^2 – focus

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

15 sec collection time



XRD^2: Particle size measurement by γ profile analysis:

For XRD^2 in reflection mode, the effective sampling volume is given by

$$V = \frac{A_0 \cos\eta}{\mu(\cos\eta + \cos\zeta)} = \frac{\pi b^2 \cos\eta}{4\mu(\cos\eta + \cos\zeta)}$$

With $\cos\eta = \sin\omega\cos\psi$

and $\cos\zeta = -\cos 2\theta \sin\omega\cos\psi - \sin 2\theta \sin\gamma\cos\omega\cos\psi - \sin 2\theta \cos\gamma\sin\psi$

Where A_0 is the cross section of the incident x-ray beam and μ is the linear absorption coefficient.

For transmission mode with the incident beam perpendicular to the sample surface, we have the effective sampling volume

$$V = \frac{\pi b^2 \cos 2\theta \left[\exp(-\mu t) - \exp\left(-\frac{\mu t}{\cos 2\theta}\right)\right]}{4\mu(1 - \cos 2\theta)}$$

where t is the thickness of the sample.

XRD²: Particle size measurement by γ profile analysis:

For XRD² in reflection mode, the particle size is given by

$$d = k\left\{\frac{p_{hkl}b^2 \arcsin[\cos\theta \sin(\Delta\gamma/2)]}{\mu N_s}\right\}^{1/3}$$

where *k* is the instrumental calibration factor or can be calculated

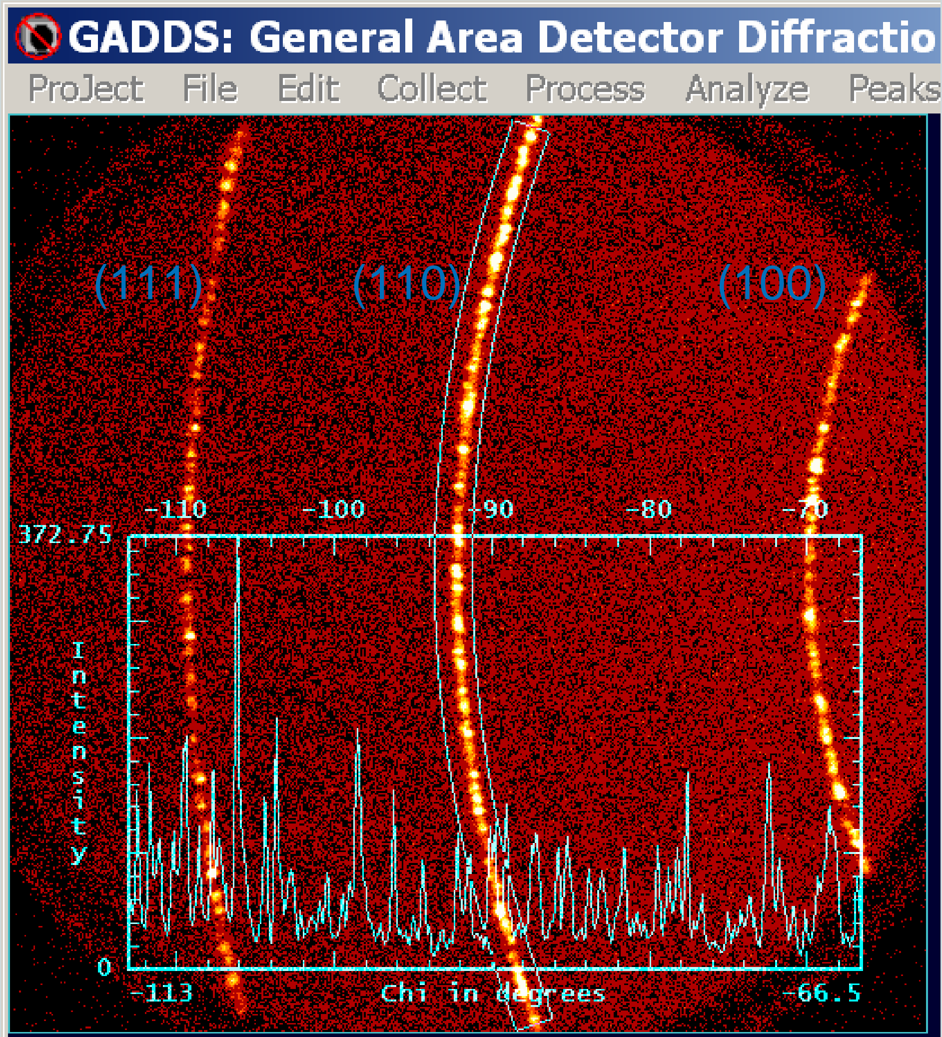
from $k = \left(\frac{3\beta}{8\pi}\right)^{1/3}$ if the instrument broadening in 2θ direction is known.

For transmission mode with the incident beam perpendicular to the sample surface, the particle size is given by

$$d = k\left\{\frac{p_{hkl_i}b^2 t \arcsin[\cos\theta \sin(\Delta\gamma/2)]}{N_s}\right\}^{1/3}$$

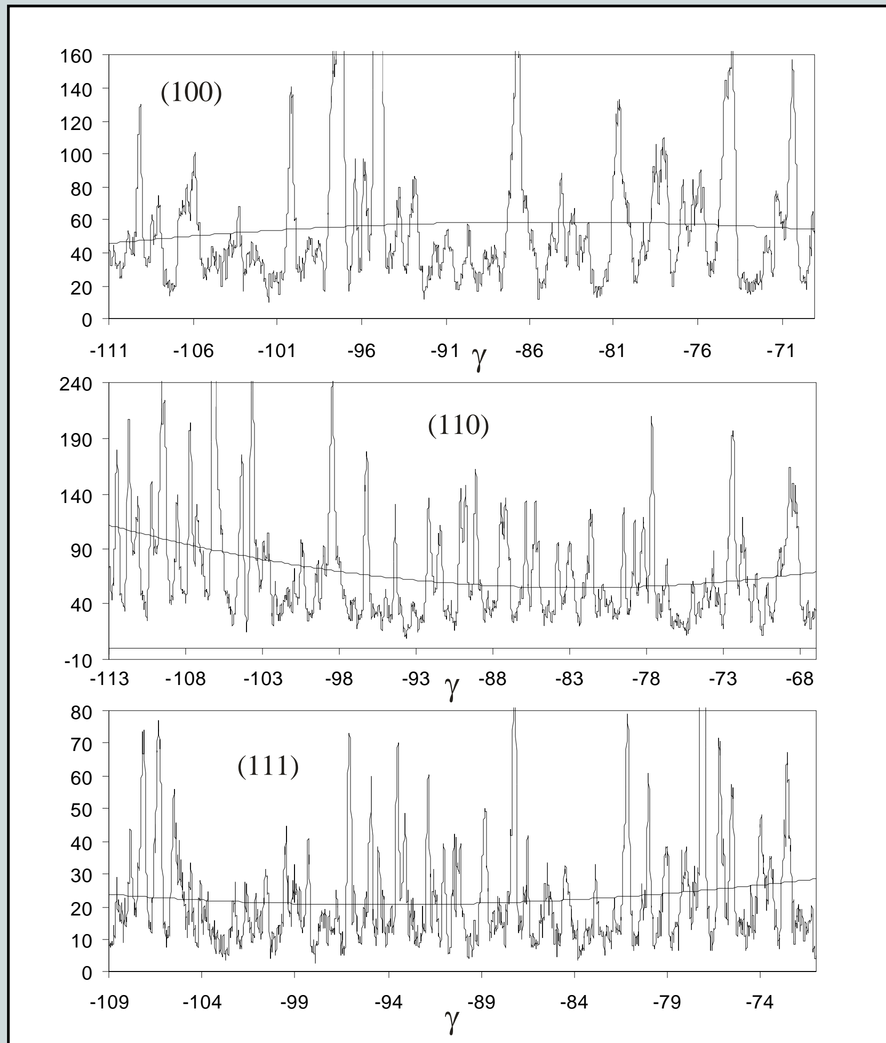
where *k* is the instrumental calibration factor or $k = \left(\frac{3\beta}{4\pi}\right)^{1/3}$

XRD²: Particle size measurement by γ profile analysis:



- The frame was collected from a SRM660a (LaB6) sample in transmission mode and Cu-Kα x-rays.
- The 2D detector (Hi-Star™) is set at 23.75 cm from the instrument center.
- The beam (collimator pinhole) size *b* is 200 μm.
- The sample thickness *t* is 7.0 μm, based on the calculated μ of 1138 cm-1 and the measured transmission of 0.45.

XRD²: Particle size measurement by γ profile analysis:



- The 2θ-integrated plots (γ-profiles) of three rings from (100), (110) and (111) planes are displayed.
- The number of crystallites is counted from the number of intersections of the γ-profile with a threshold line.
- To cancel out the effects of the overall intensity fluctuation (texture, etc.), a 2nd order polynomial trend line is fitted to each γ-profile as a threshold line.
- Every two intersections of γ-profile with the threshold line represents a crystallite.

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XRD²: Particle size measurement by γ profile analysis:

Calibration Results:

(hkl)	P_{hkl}	2θ	$\Delta\omega$	N_s	k
(100)	6	21.36	38	23	0.1217
(110)	12	30.38	46	41	0.1106
(111)	8	37.44	42	38	0.1281

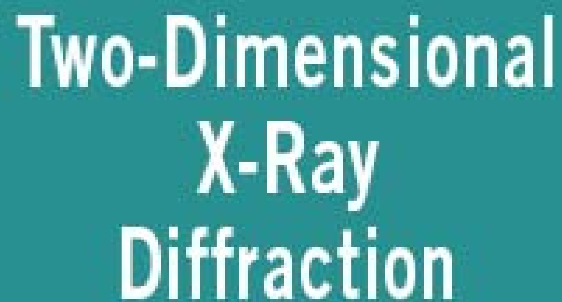
- The average scaling factor *k* is 0.12 in this calibration. The system can then be used to measure the crystallite size of unknown materials if the data can be collected in approximately the same condition.
- It is always necessary to calibrate the system with a known standard, preferably with a comparable sample geometry and crystallite size.
- For reflection mode, it is critical to have a standard with a comparable linear absorption coefficient so as to have similar penetration.

XRD^2: Particle size measurement by γ profile analysis:

The measurement range of crystallite size and γ resolution:

- The γ-resolution on crystal spots can be improved by using a long sample-to-detector distance.
- Reducing the x-ray beam size, beam divergence and sample thickness can reduce the number of spots along the γ-profile so as to reduce the demand for γ-resolution.
- Using a low multiplicity ring also reduces the demand for γ-resolution.
- In cases where too few diffraction spots can be observed (i.e. large grains) in the diffraction ring, a large beam size or sample oscillation (by rotation or translation) may improve the sampling statistics. However, the system should be calibrated in the same condition with a known sample having comparable crystallite size.
- Multi-target integration can deal with large grain size without new calibration. Only replace the calibrated *k* by k_n
  n is the number of the targets.

  $$k_n = n^{1/3} k$$
- The standard material may be diluted by light and amorphous materials. For example, a diluted LaB_6 sample with various linear absorption coefficients or matching thickness for profile analysis can be made by mixing with different amounts of starch.



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- B. B. He, Introduction to two-dimensional X-ray diffraction, *Powder Diffraction*, *Vol. 18, No 2*, June 2003.

http://www.wiley.com/WileyCDA/WileyTitle/productCd-0470227222.html