



## Particle Size Analysis by Two-dimensional XRD

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### Particle Size Analysis by Twodimensional XRD



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

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Two-dimensional XRD

Particle Size Analysis – conventional methods

Particle Size Analysis –XRD<sup>2</sup> method







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# XRD<sup>®</sup> & Micro Samples or Large Grains





## XRD<sup>2</sup>: Geometry Convention (1) - Diffraction Space





## XRD<sup>2</sup>: Geometry Convention (2) - Detector Space





## XRD<sup>2</sup>: Geometry Convention (3)- Sample Space





## XRD<sup>2</sup>: 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.



2) EVA - [gold.EVA *]
<u>File View Workspace Window H</u> elp
Zoom + Screen X-unit Y-Unit Y-Scale Slits (Pat.) Current Wavelength: Scan : New Frame (gold.raw)   Image: Screen Image: Science Image: Science Image: Science Image: Science Image: Science Science Science Image: Science Image: Science Image: Science Image: Science Science Image: Science </td
[2-Theta : 117.946, d : 0.8989] - [ Counts : 26.5, Y% : 39.23 ]



### XRD<sup>2</sup>: 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.



### **XRD<sup>2</sup>:** Particle size calculation:

Scherrer equation:

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

where  $\lambda$  is wavelength (Å), B is FWHM (radians) corrected for instrument broadening,  $\theta$  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.



#### XRD<sup>2</sup>: 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.





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## XRD<sup>2</sup>: 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.



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:

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

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,  $v_i = \pi d_i^3/6$ 





For XRD<sup>2</sup>, the instrumental window  $\Omega$  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 (≈1/µ).

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

05.05.2009



#### **Sealed Tube**

- 0.3 mm collimator
- Sample-Detector distance 29 cm

#### 120 sec collection time



#### IµS – XRD<sup>2</sup> – focus

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

#### 15 sec collection time





For XRD<sup>2</sup> 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  $\mu$  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.



For XRD<sup>2</sup> in reflection mode, the particle size is given by

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

where k is the instrumental calibration factor or can be calculated

from  $k = \left(\frac{3\beta}{8\pi}\right)^{\frac{1}{3}}$  if the instrument broadening in 20 direction is known.

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

$$d = k \left\{ \frac{p_{hkl_i} b^2 t \arcsin[\cos\theta\sin(\Delta\gamma/2)]}{N_s} \right\}^{\frac{1}{3}}$$
  
e instrumental calibration factor or  $k = \left(\frac{3\beta}{4\pi}\right)^{\frac{1}{3}}$ 

where k is the instrumental calibration factor or





- The frame was collected from a SRM660a (LaB6) sample in transmission mode and Cu-Kα x-rays.
- The 2D detector (Hi-Star<sup>™</sup>) 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.





- The 2θ-integrated plots (γprofiles) 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 2<sup>nd</sup> order polynomial trend line is fitted to each γ-profile as a threshold line.
- Every two intersections of γprofile with the threshold line represents a crystallite.



Calibration Results:

(hkl)	$P_{hkl}$	20	Δω	N <sub>s</sub>	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.



The measurement range of crystallite size and  $\gamma$  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  $\gamma$ -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  $k_n = n^{\frac{1}{3}}k$  n is the number of the targets.
- The standard material may be diluted by light and amorphous materials. For example, a diluted LaB<sub>6</sub> sample with various linear absorption coefficients or matching thickness for profile analysis can be made by mixing with different amounts of starch.





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



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