# Powder X-ray Diffraction (PXRD) Applications and Sample Preparation

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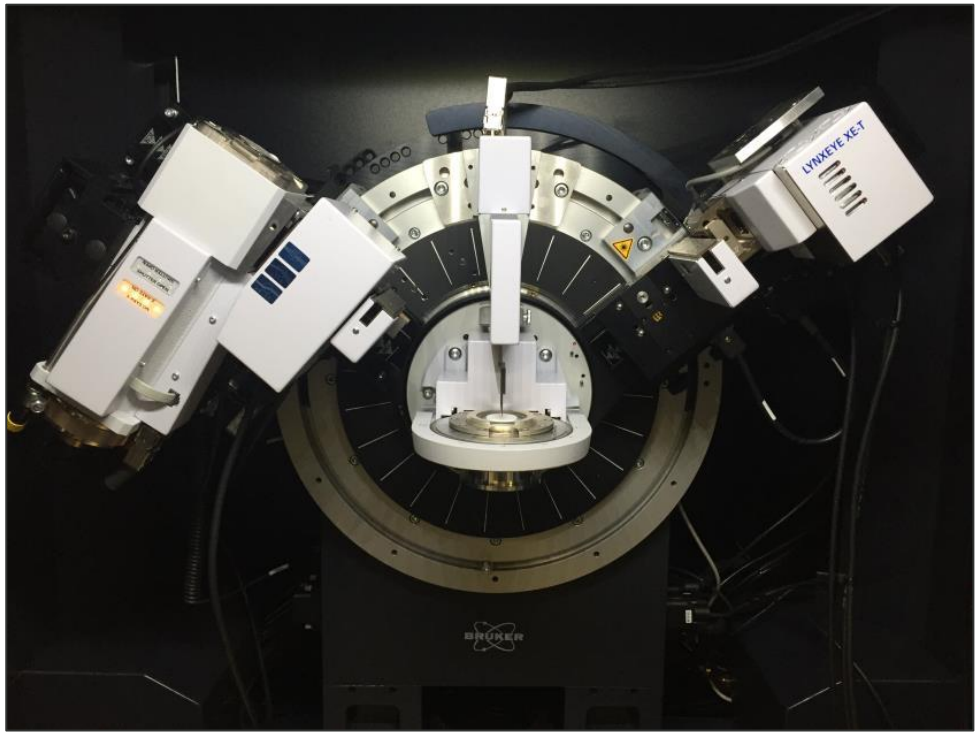
Senior Applications Scientist - XRD

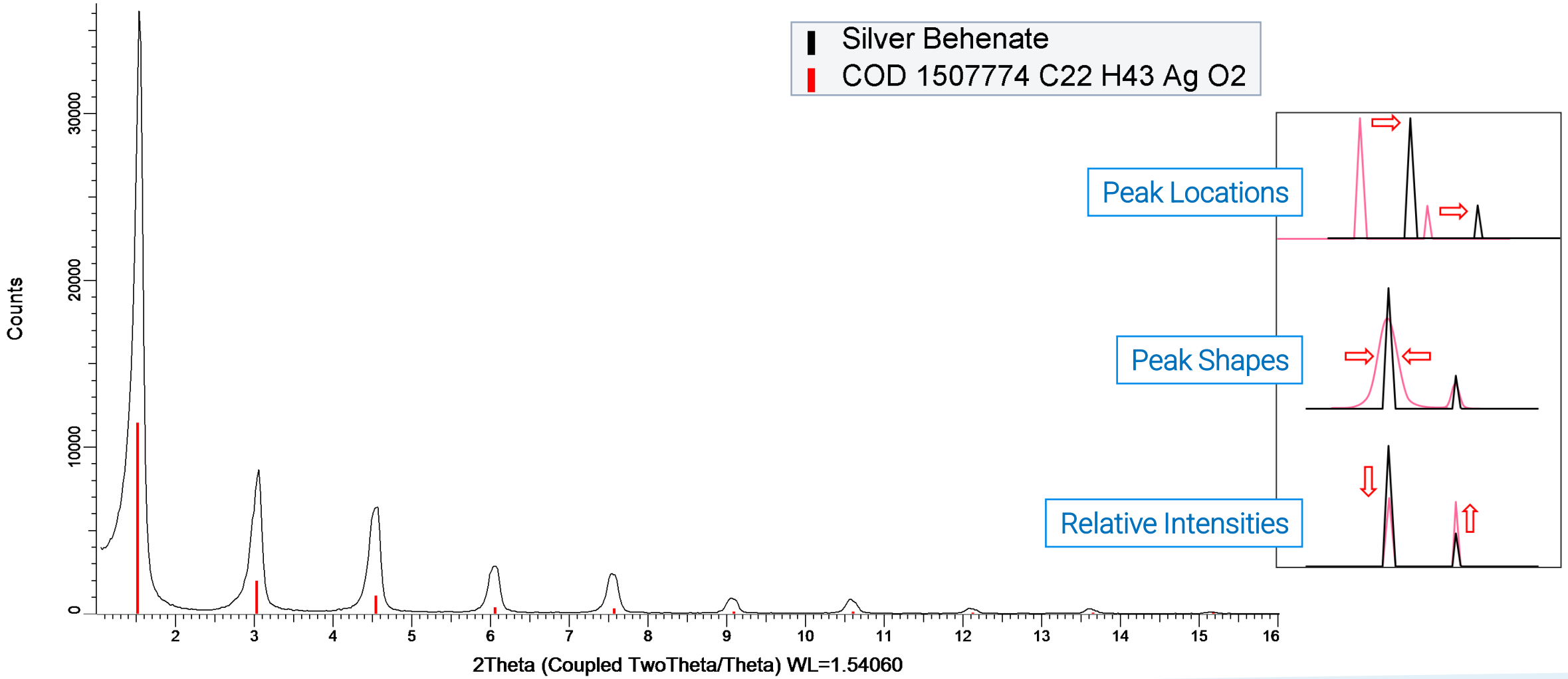
# Technique Overview

## XRPD – Structural Characterization in the Solid State

- Measures characteristic distances crystalline materials
- Crystalline phases possess regular, repeating arrangements of atoms or molecules
- XRPD relies on precise control over incident and diffracted angles of X-ray radiation
- Diffraction signal is observed at specific angles from constructive scattering of the X-ray beam

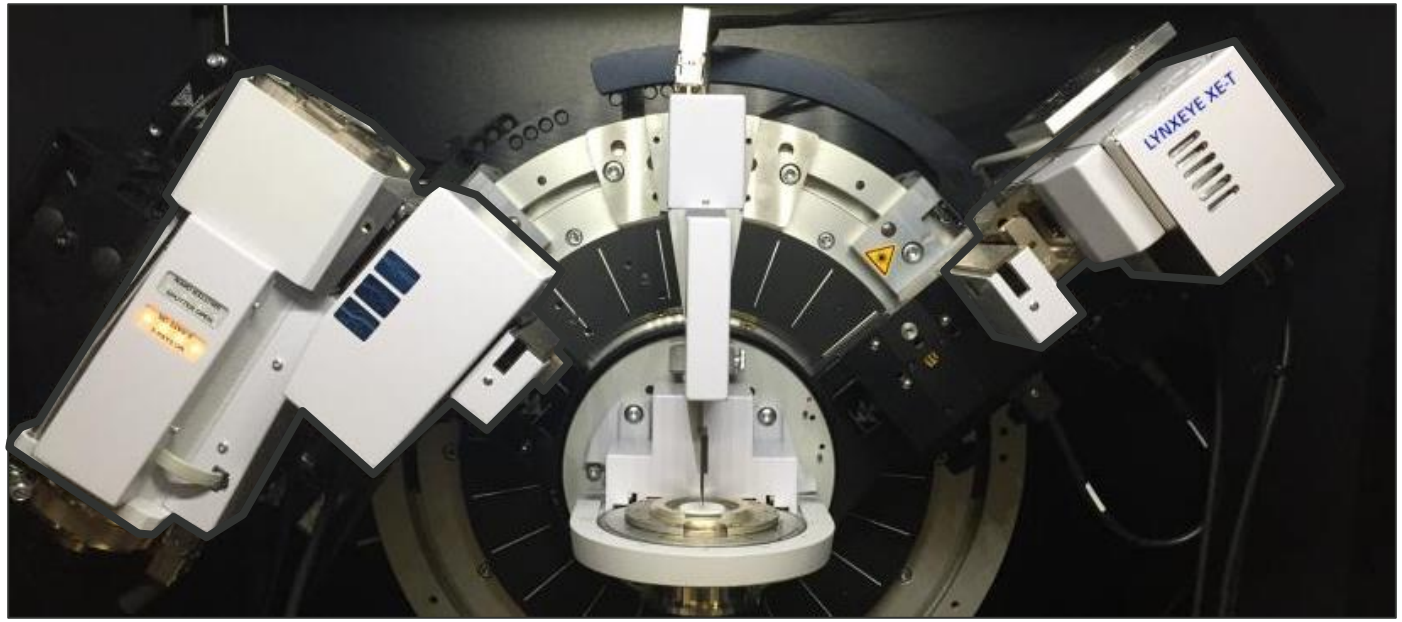


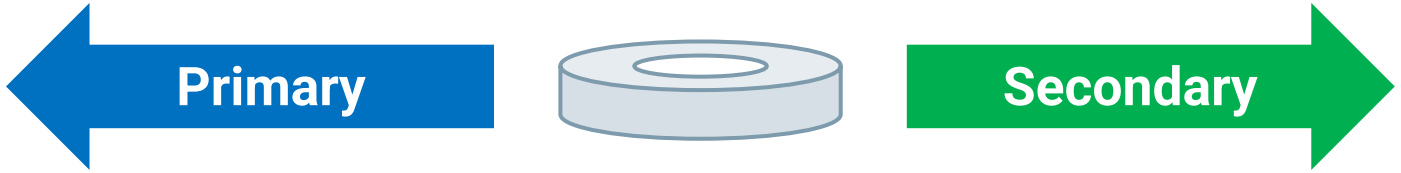
# Technique Overview



# XRPD Instrumentation

# Technique Overview



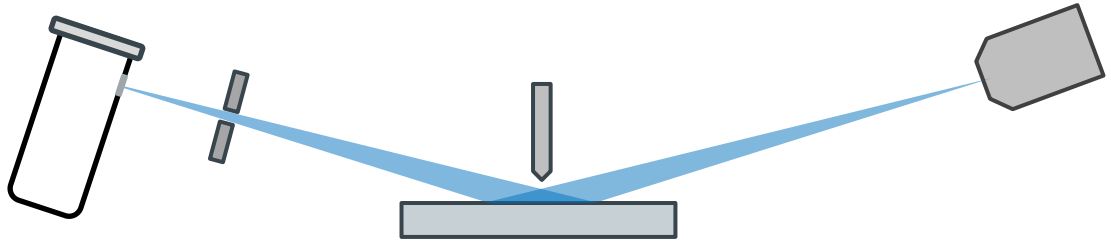




- X-ray Tube
- Divergence Slit
- Goebel Mirror
- Soller Slits

- Air Scatter Slit
- Soller Slits
- Filters/Absorbers
- Detector

# Common Instrument Geometries – Bragg-Brentano (Reflection)

## Line Geometry (1D Detector)

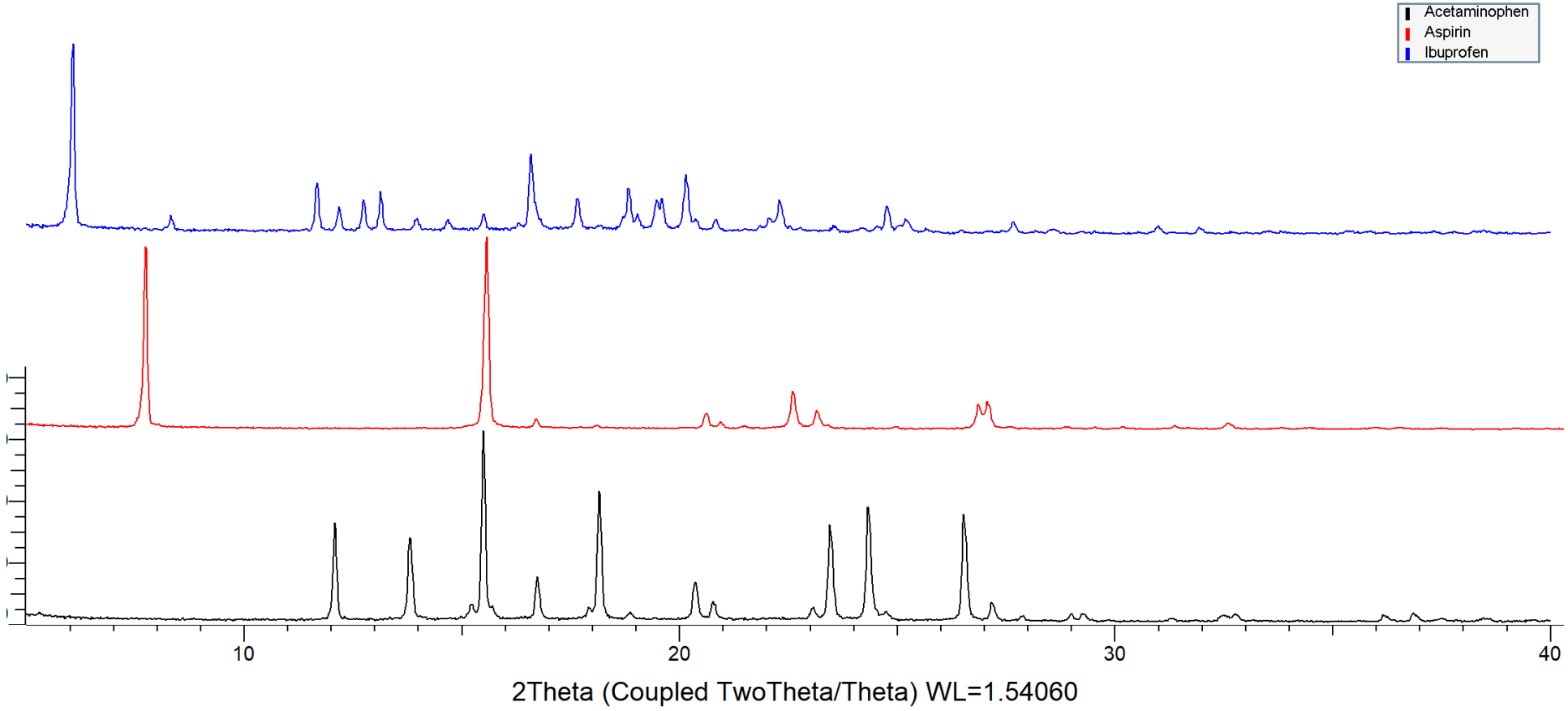


# Applications Overview

- Phase Identification
- Phase Quantification
- Degree of Crystallinity / Percent Amorphous
- Non-Ambient Diffraction
- Structure Solution and Refinement

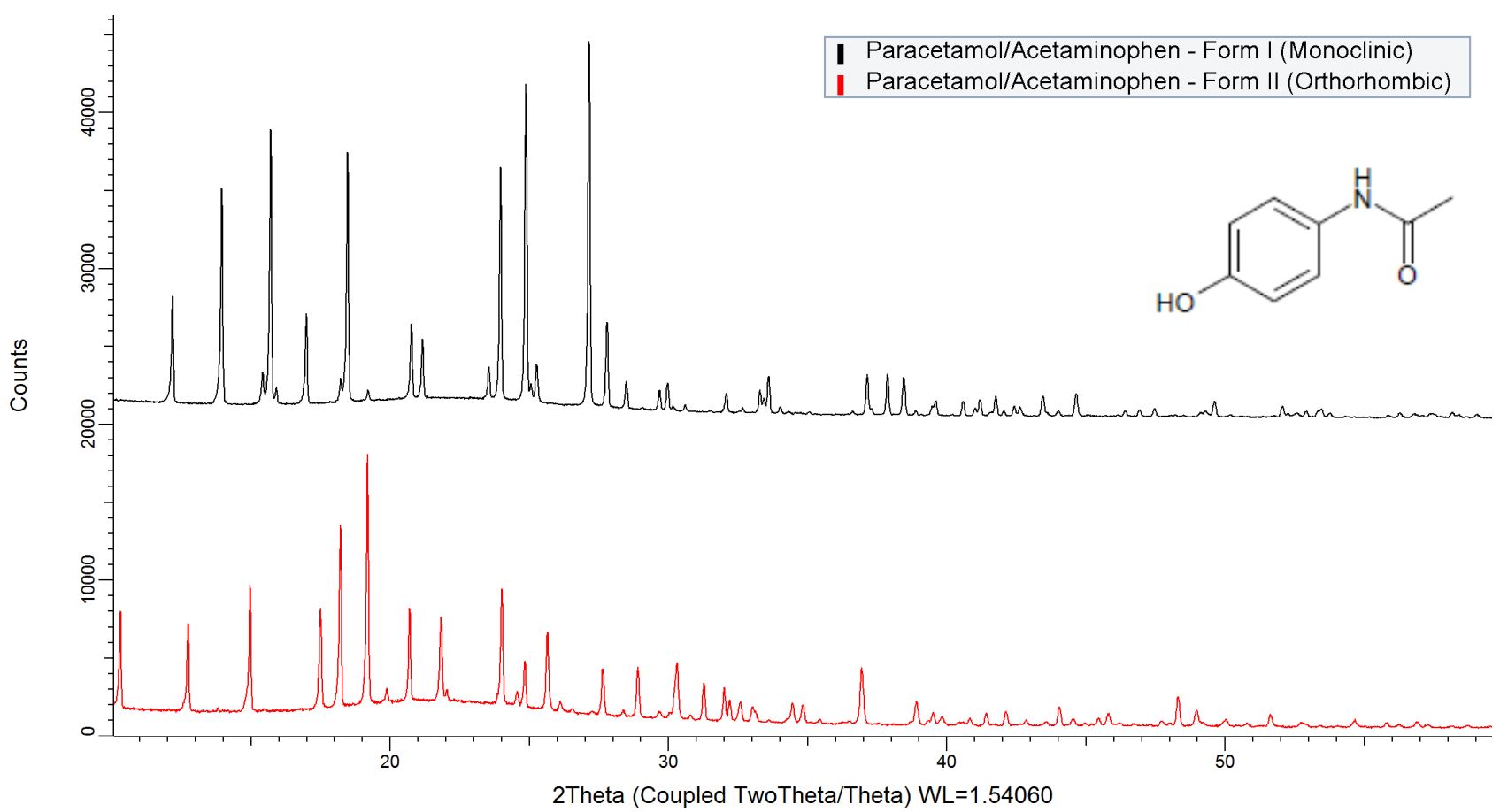
# Qualitative Analysis of Distinct Materials

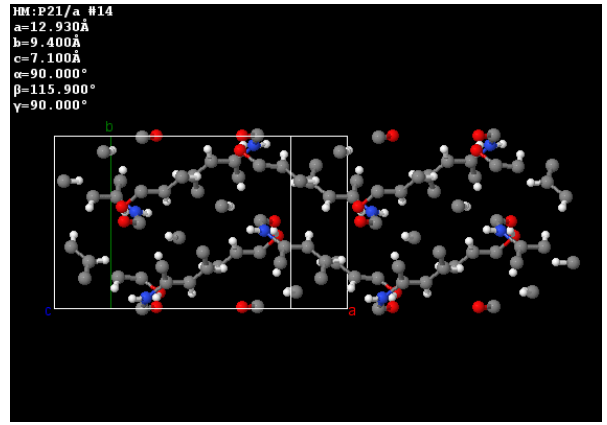
## Diffraction Patterns as a “Fingerprint” for Identification

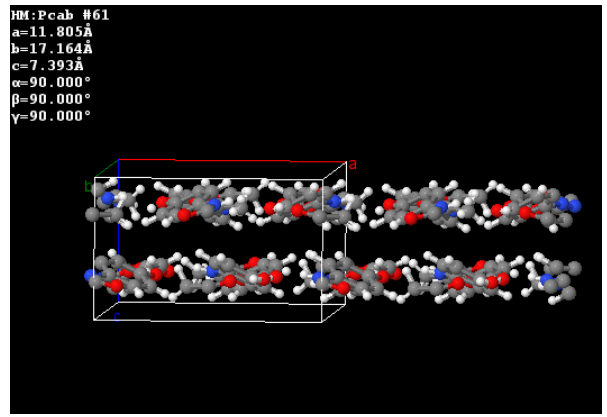


# Structural Polymorphs (Same Molecule, Different Arrangements)

## Polymorphism in acetaminophen affects tableting and granulation

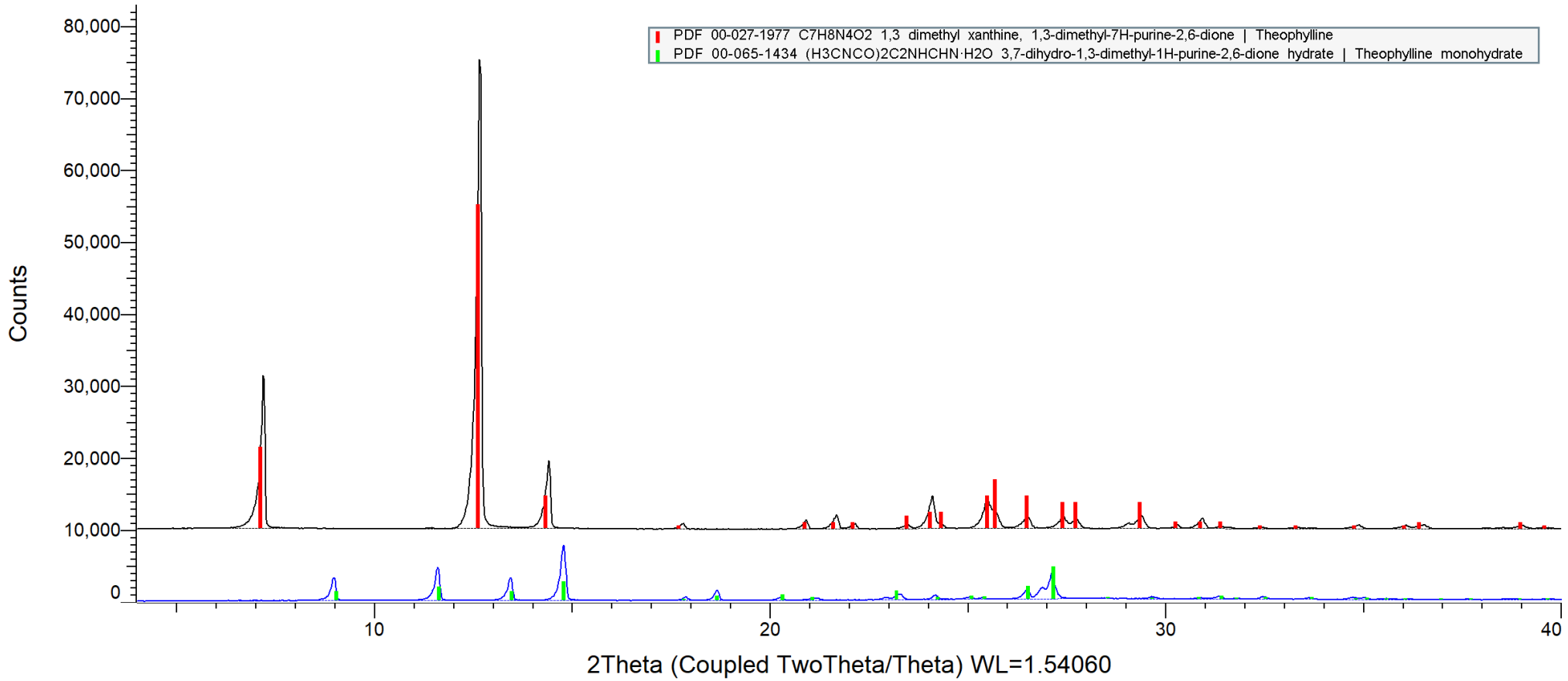


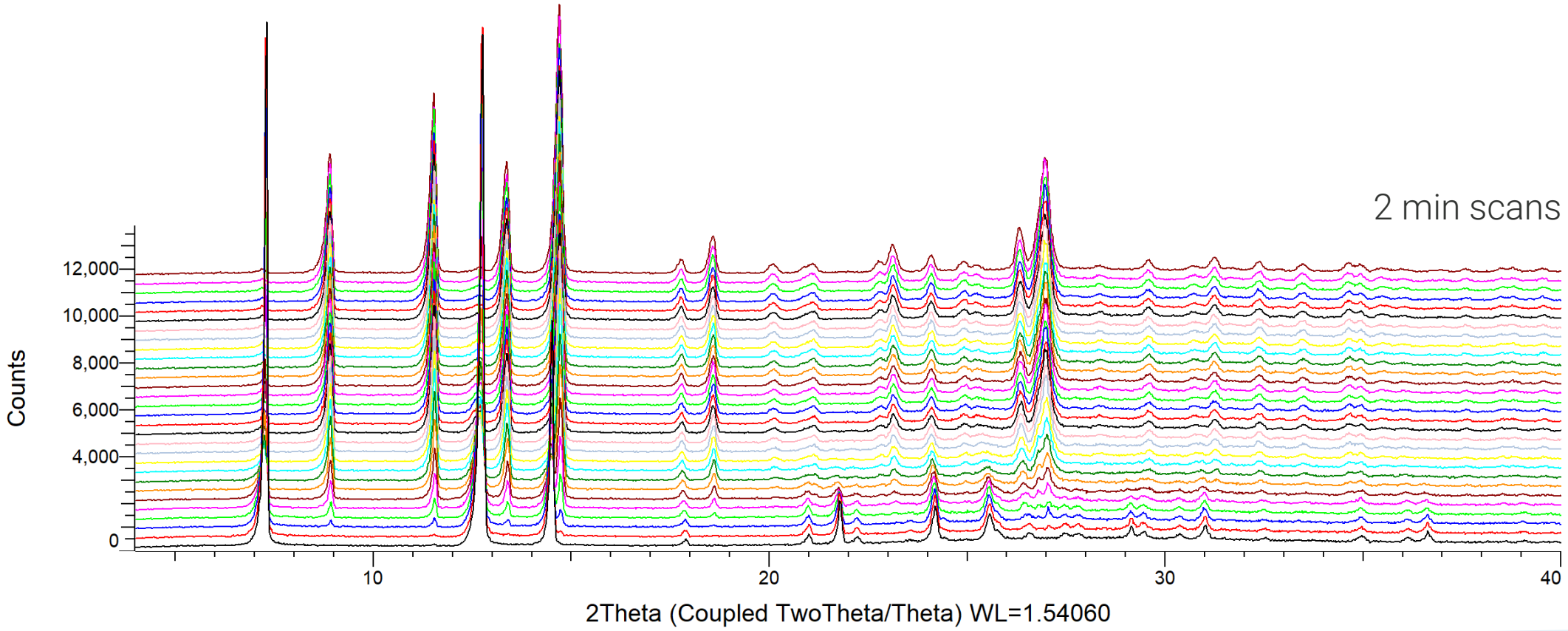
# Solvates and Salt Forms

## Polymorph and salt screening can lead to the formation of distinct crystal structures



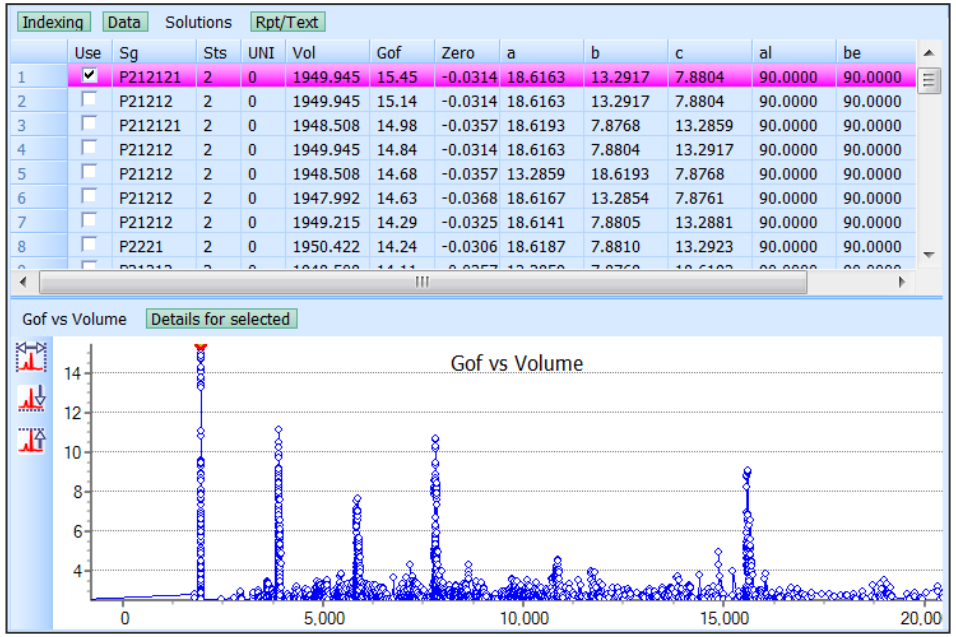
# Solvates and Salt Forms

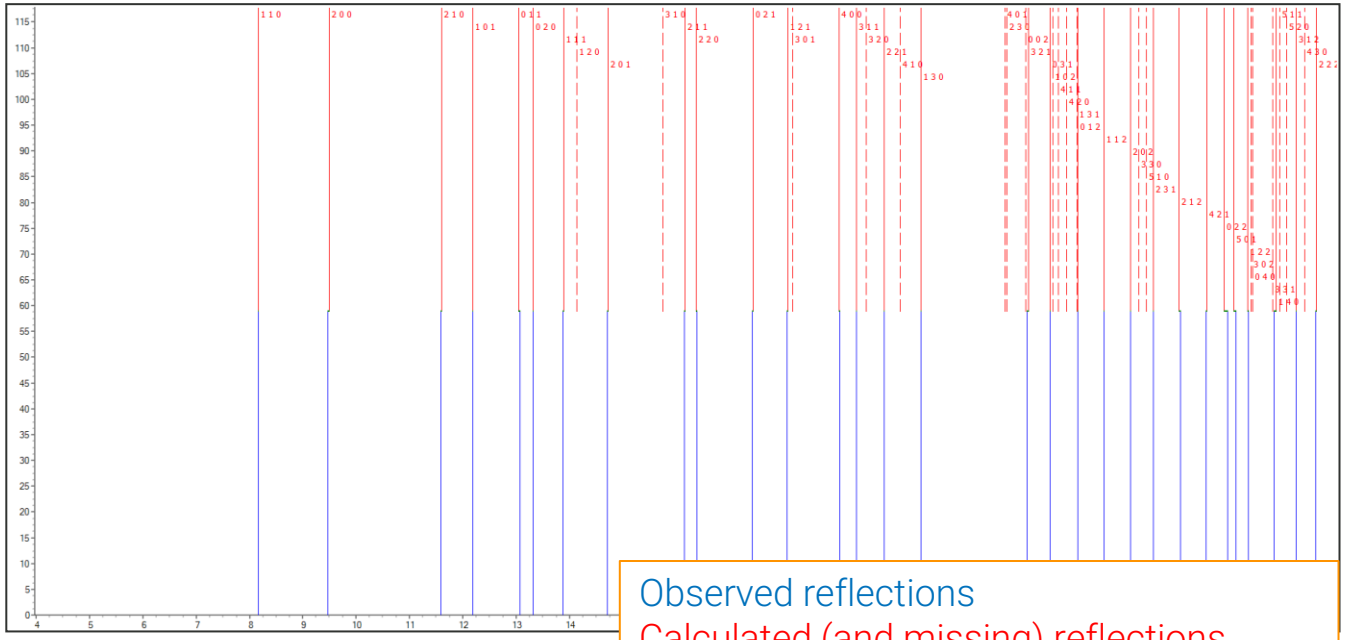
## Time-resolved studies of hydration mechanics with fast scanning (theophylline)



# Structure Determination and Refinement

## Indexing gives a list of potential candidates for unit cells (repeating structural building block)

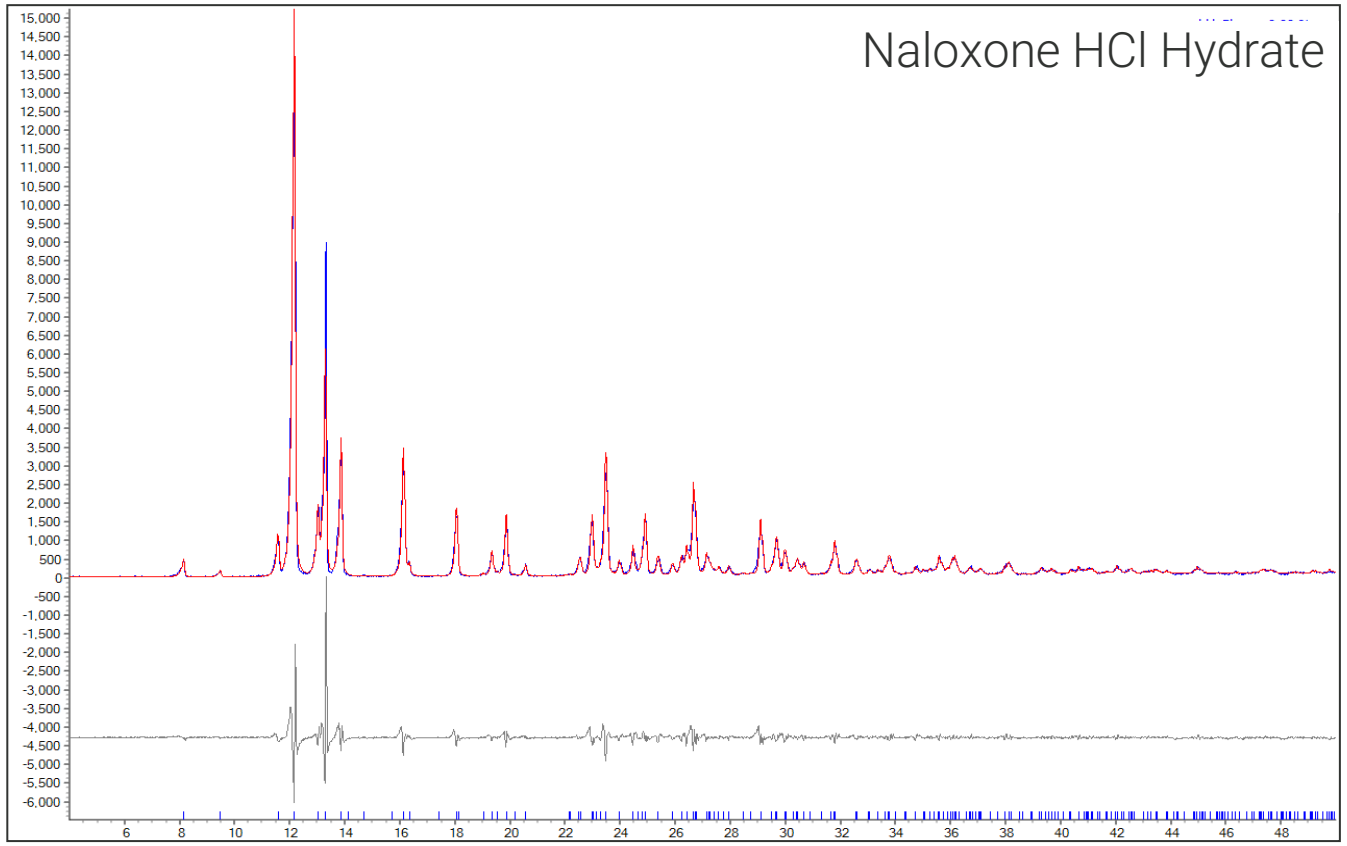


Observed reflections
Calculated (and missing) reflections

# Structure Determination and Refinement

## Whole pattern fitting (Pawley or LeBail) provides refined unit cell parameters



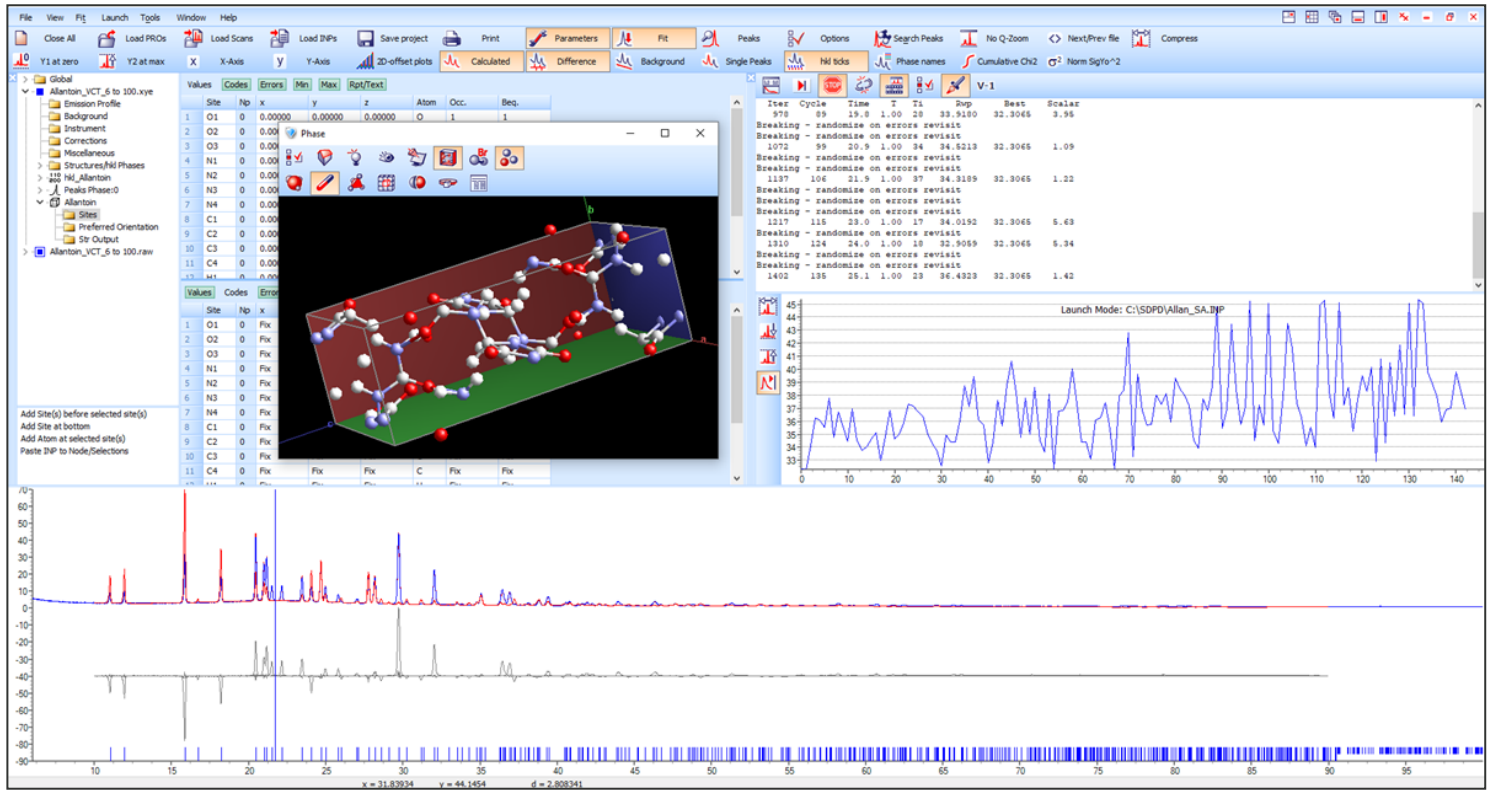

ICDD Calculated Parameters
Space Group: P212121 (19)
Molecular Weight: 399.87 g/mol
Crystal Data ▼

| | | |
|---|---|---|
| a: 13.185 Å | α: 90.00° | Volume: 1917.77 Å³ |
| b: 18.569 Å | β: 90.00° | Z: 4.00 |
| c: 7.833 Å | γ: 90.00° | |

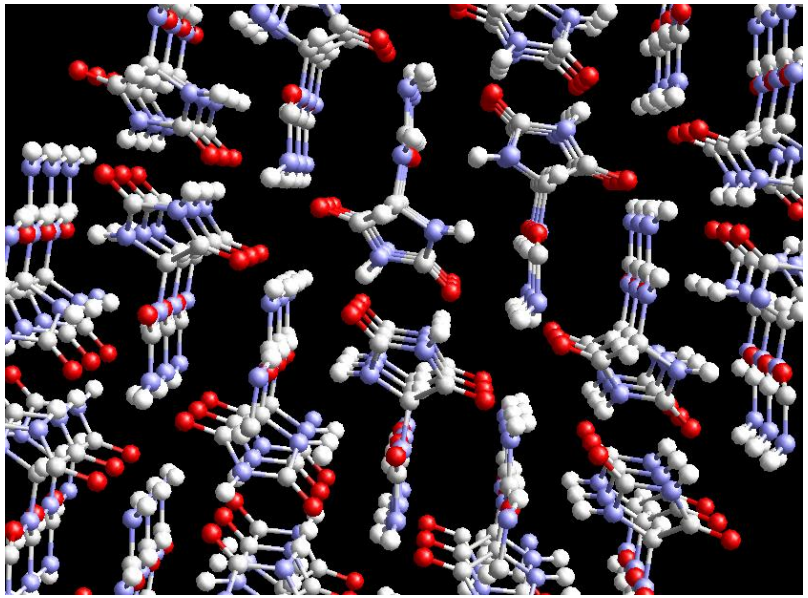
| | | |
|---|---|---|
| Spacegroup | P212121 | |
| a (Å) | 18.635495 | @ |
| b (Å) | 13.304927 | @ |
| c (Å) | 7.8940452 | @ |

# Structure Determination and Refinement

## Structure solution from powder diffraction (confirm or supplement single crystal XRD studies)

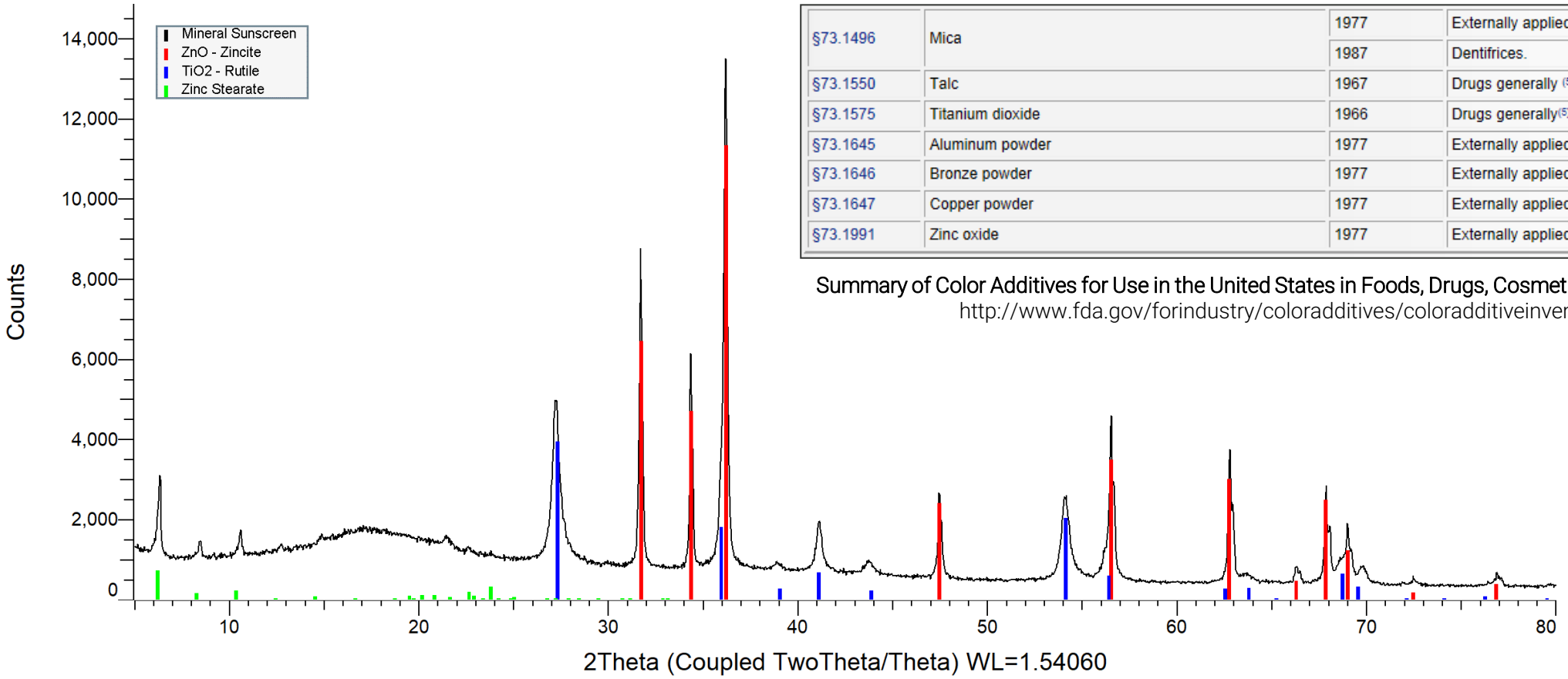


Allantoin



# Colorants, Dyes, and Pigments

## Titanium and zinc oxides are commonly used white pigments

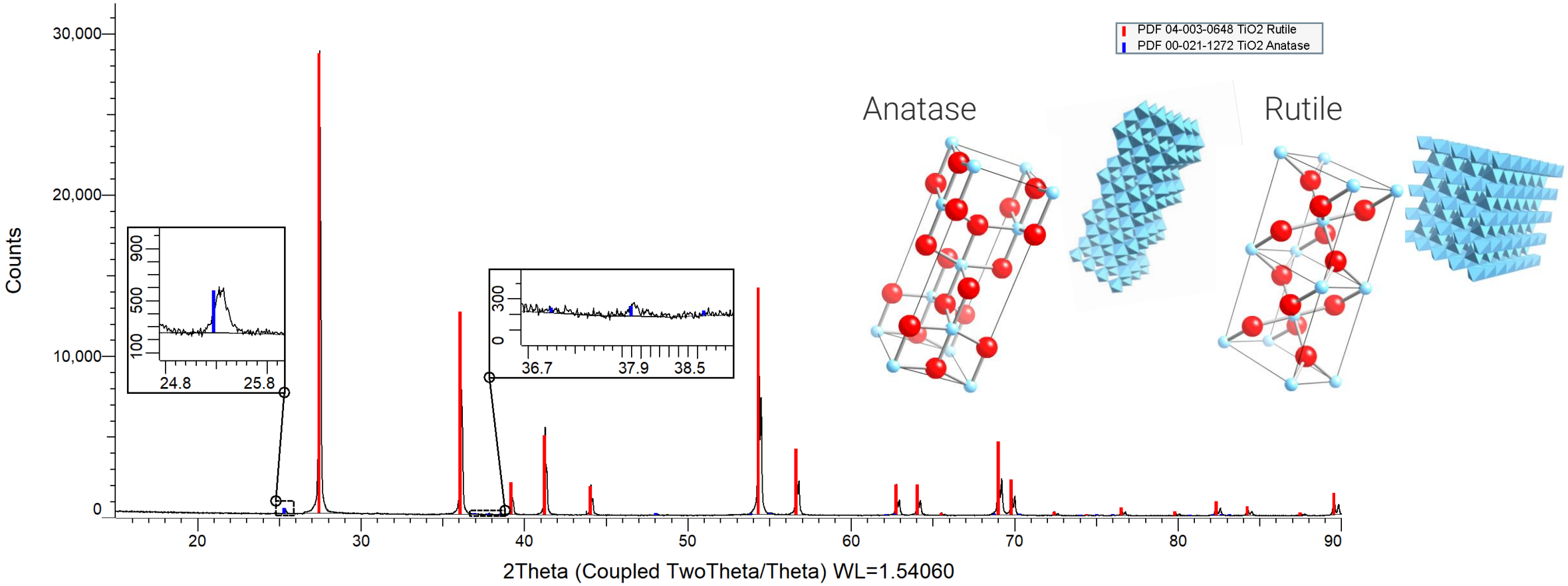



| | | | |
|---|---|---|---|
| §73.1496 | Mica | 1977 | Externally applied drugs[6] including eye area use. |
| | | 1987 | Dentifrices. |
| §73.1550 | Talc | 1967 | Drugs generally [5]. |
| §73.1575 | Titanium dioxide | 1966 | Drugs generally[5] including eye area use . |
| §73.1645 | Aluminum powder | 1977 | Externally applied drugs[6] including eye area use. |
| §73.1646 | Bronze powder | 1977 | Externally applied drugs[6] including eye area use. |
| §73.1647 | Copper powder | 1977 | Externally applied drugs[6] including eye area use. |
| §73.1991 | Zinc oxide | 1977 | Externally applied drugs[6] including eye area use. |

Summary of Color Additives for Use in the United States in Foods, Drugs, Cosmetics, and Medical Devices
http://www.fda.gov/forindustry/coloradditives/coloradditiveinventories/ucm115641.htm

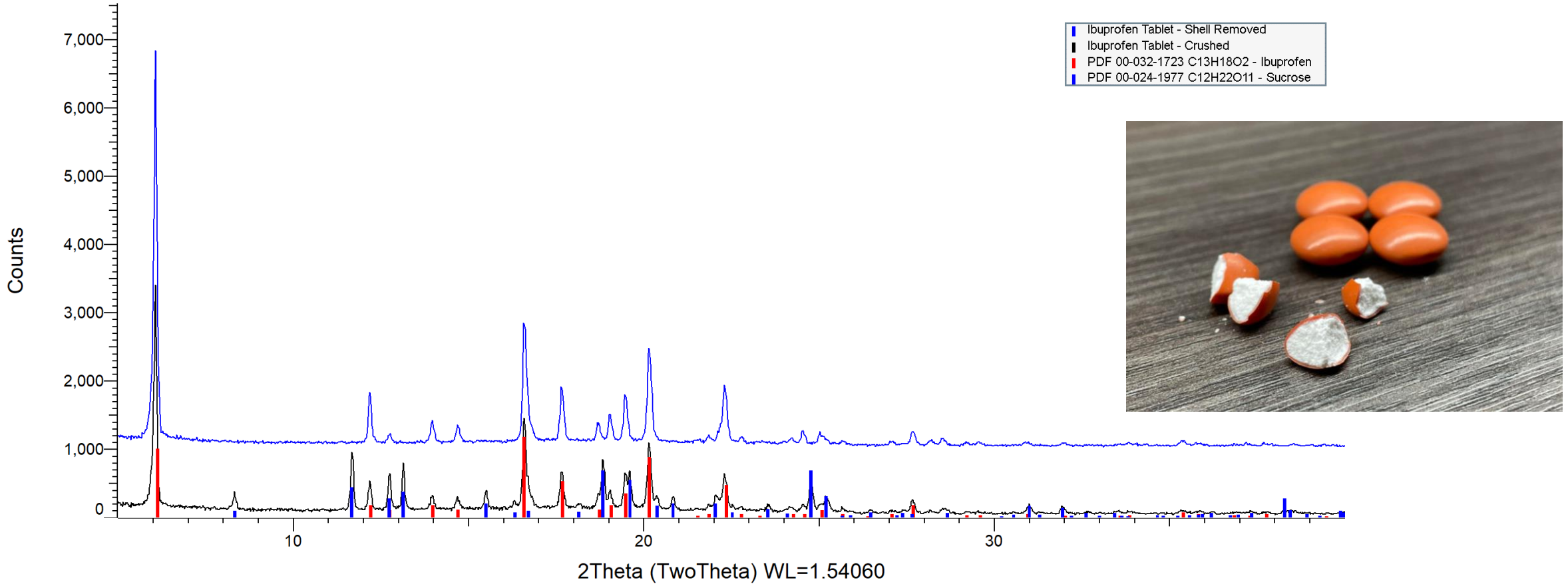
# Colorants, Dyes, and Pigments

## Polymorphs of $TiO_2$ have different optical properties



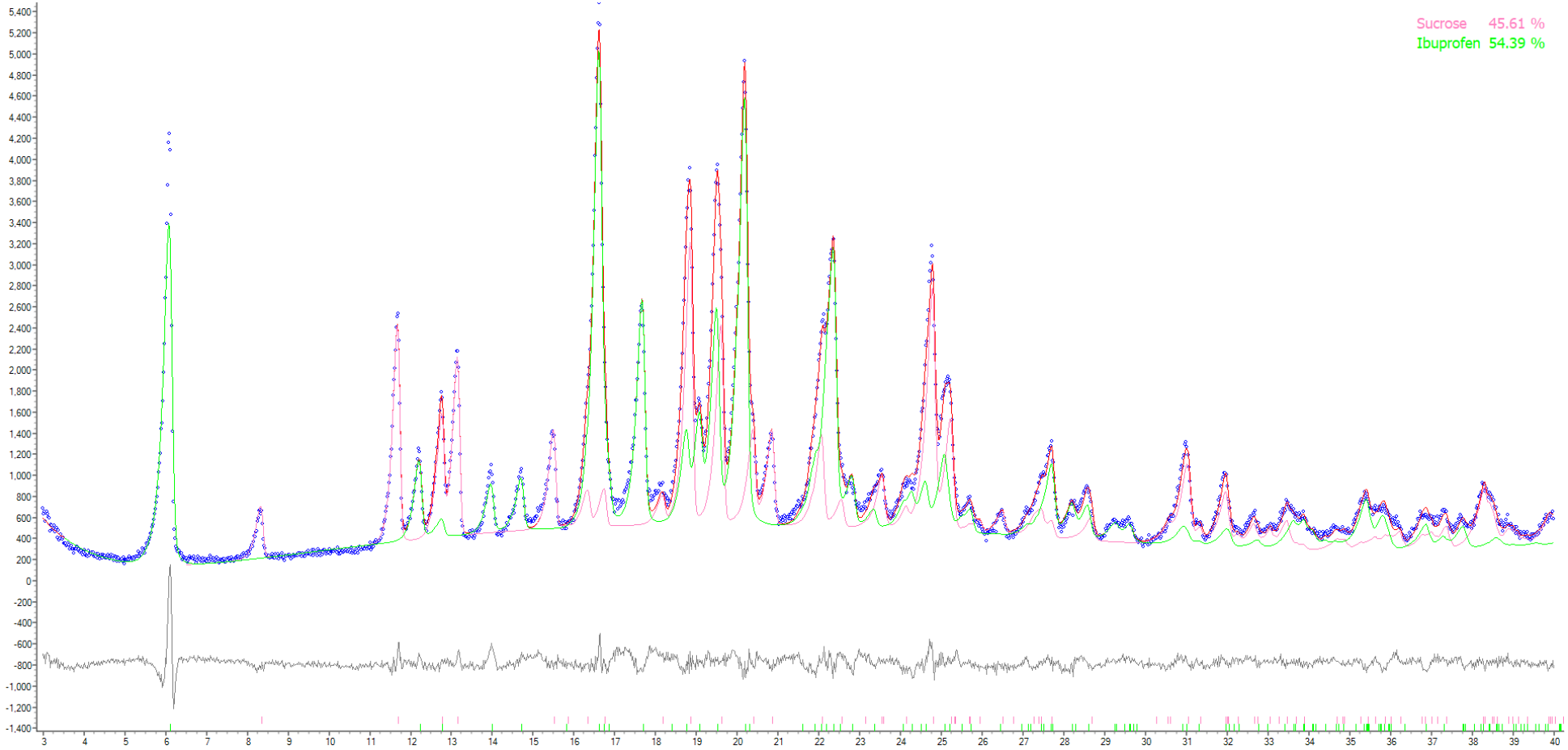
# Formulations and Excipients

## Pill and tablet engineering for masking bitter tastes or controlling release



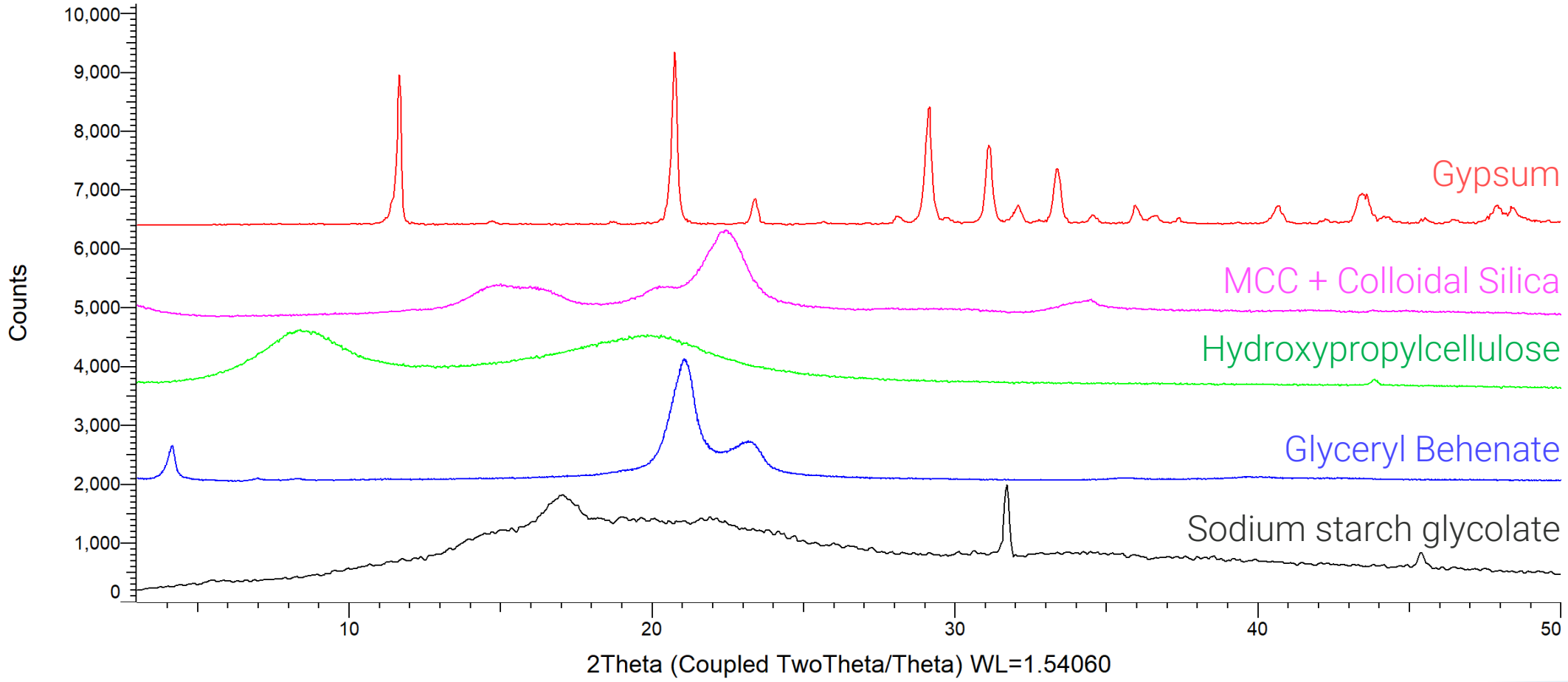
# Formulations and Excipients

## Quantification with Rietveld refinement (modeling with known crystal structures)



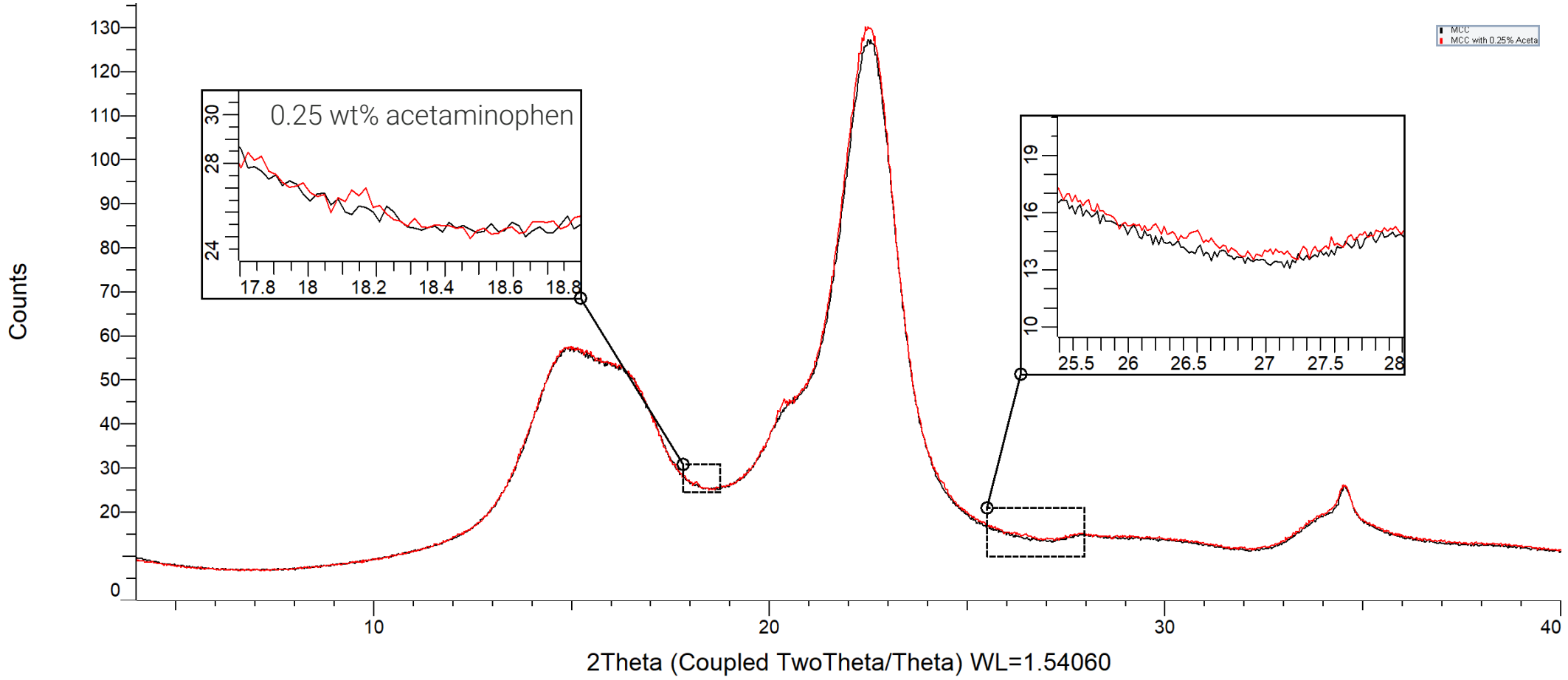
# Formulations and Excipients

## Excipient phases can be crystalline or amorphous



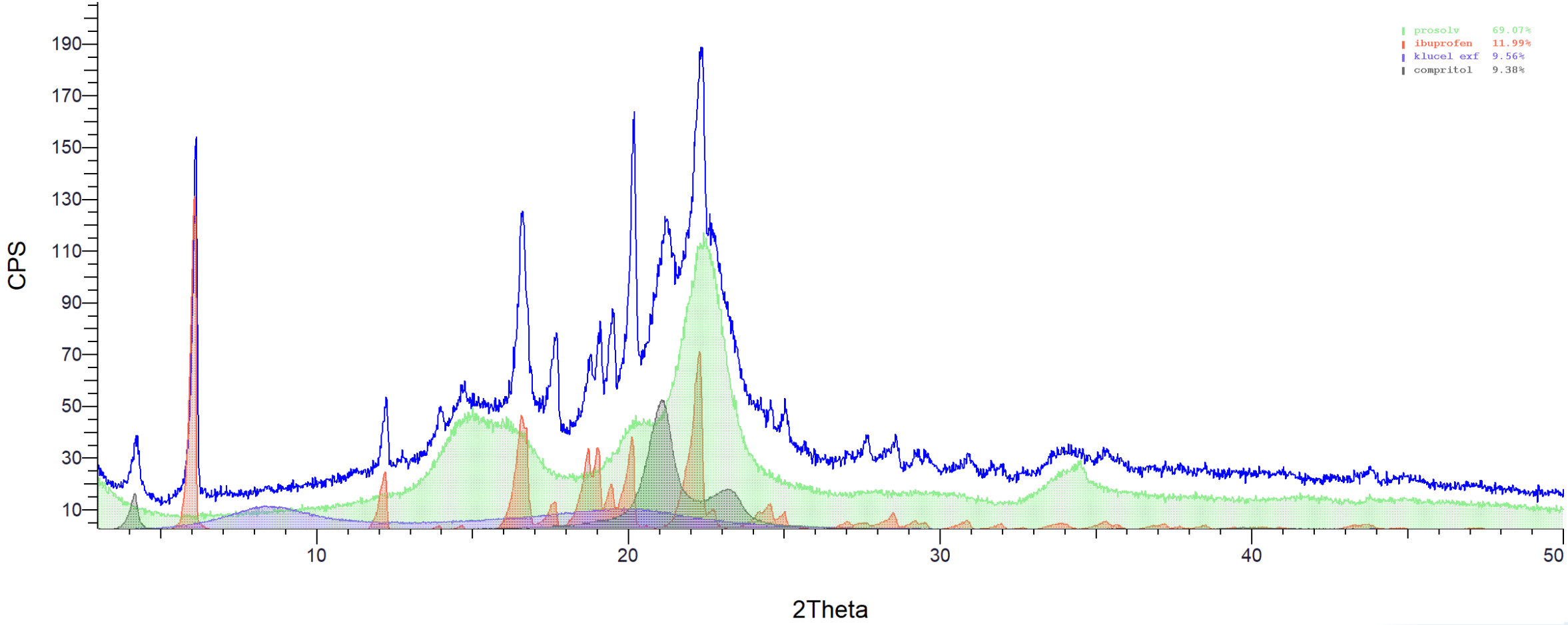
# Crystalline versus Amorphous Content

## Small amounts of crystalline can be detected in predominantly amorphous data



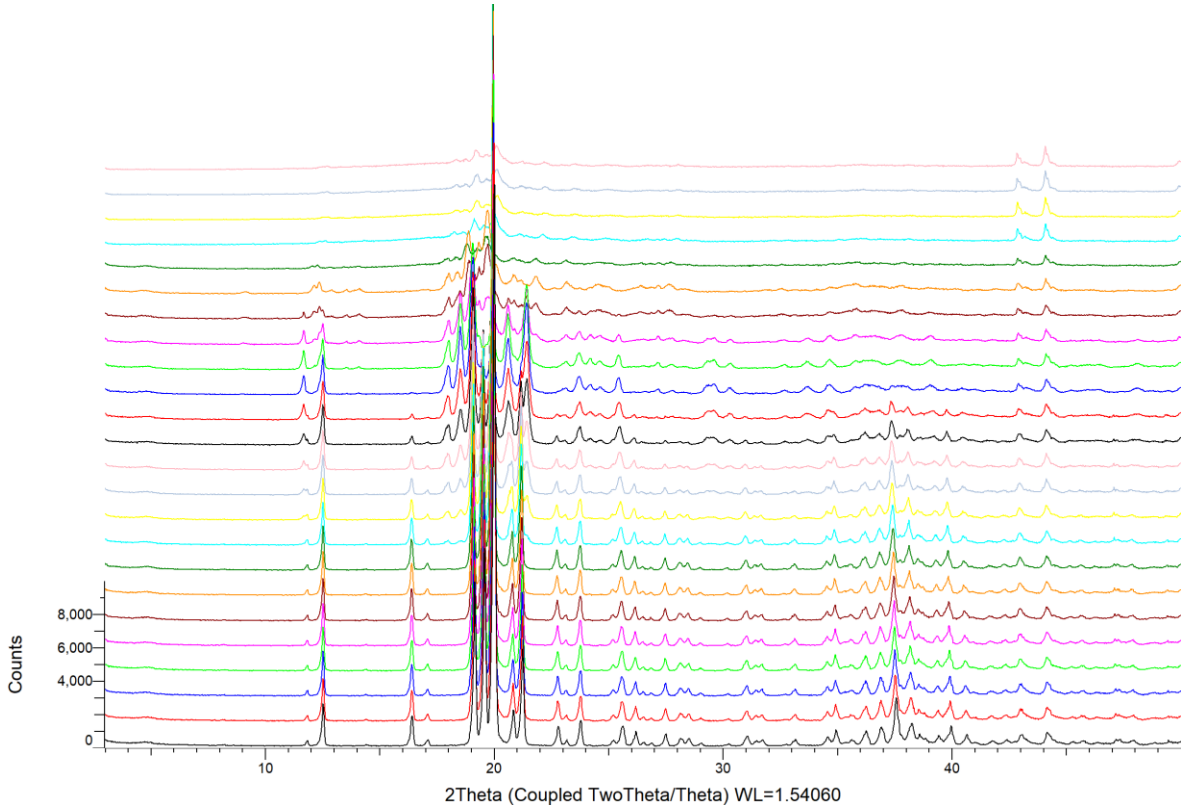
# Crystalline versus Amorphous Content

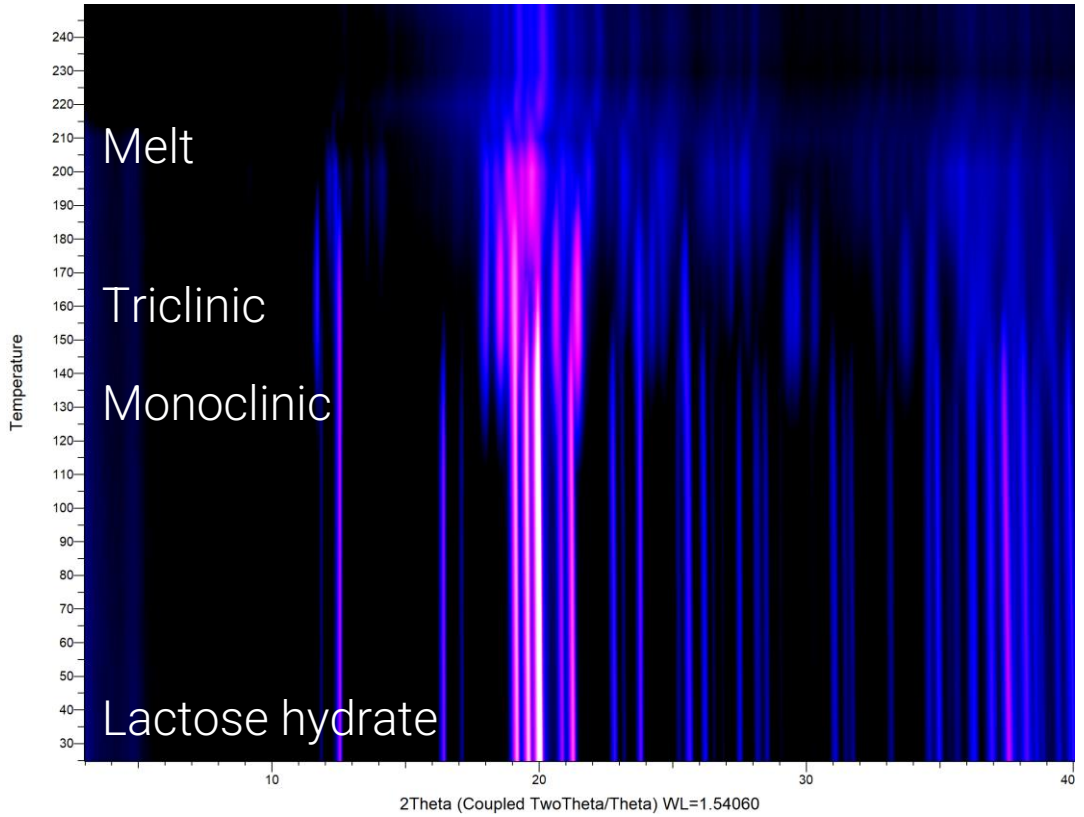
## Quantification of amorphous phases with whole pattern fitting



# Non-Ambient Diffraction

## *In situ* diffraction studies reveal phase changes and can supplement DSC/TGA data



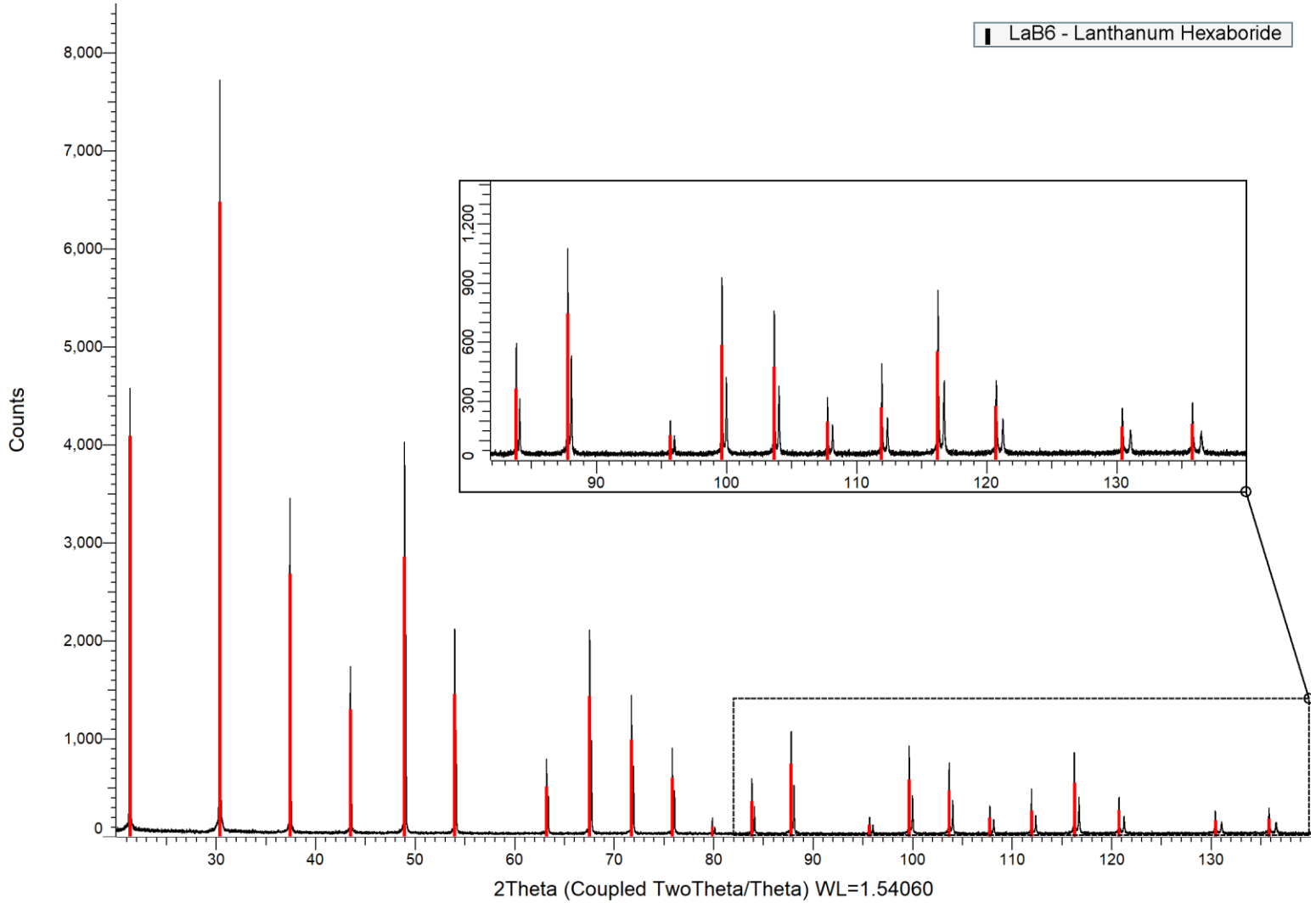



XRD FUNDAMENTALS

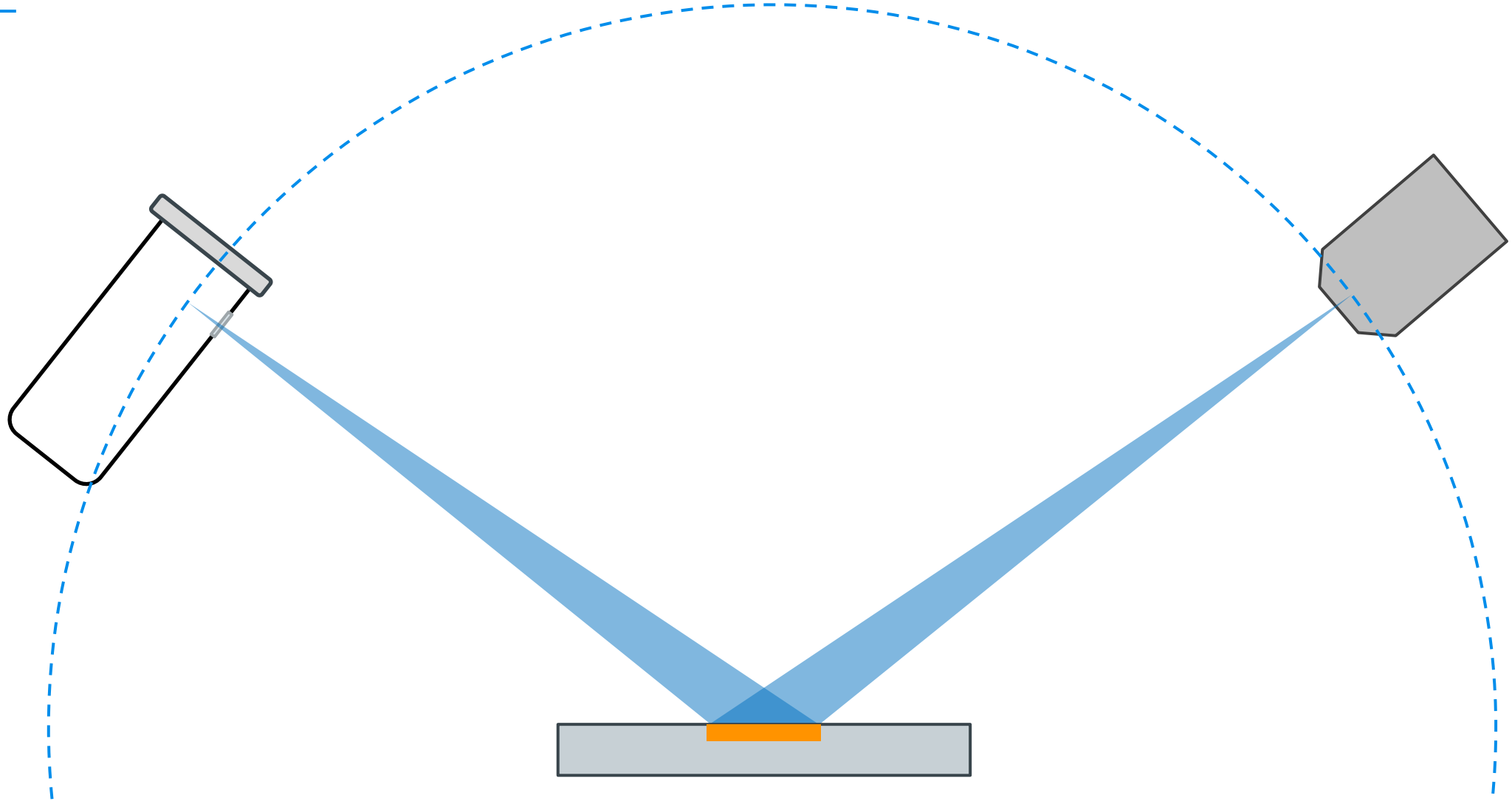
# Powder XRD Sample Preparation

# Data Quality from an Ideal Sample

- Sharp, clearly resolved peaks
- High peak-to-background
- High signal-to-noise
- Accurate relative peak intensities



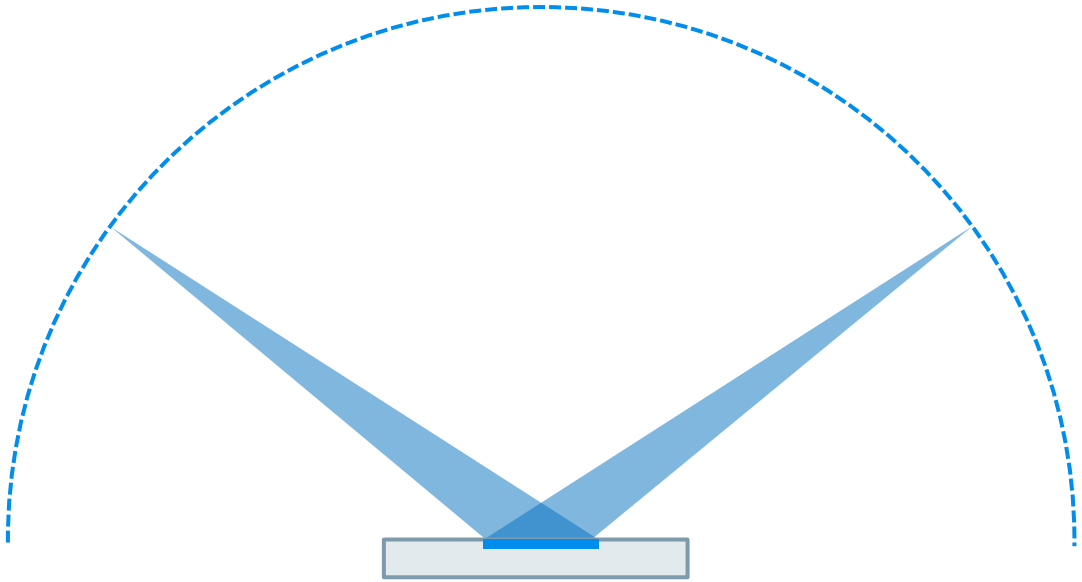
# Bragg-Brentano Geometry

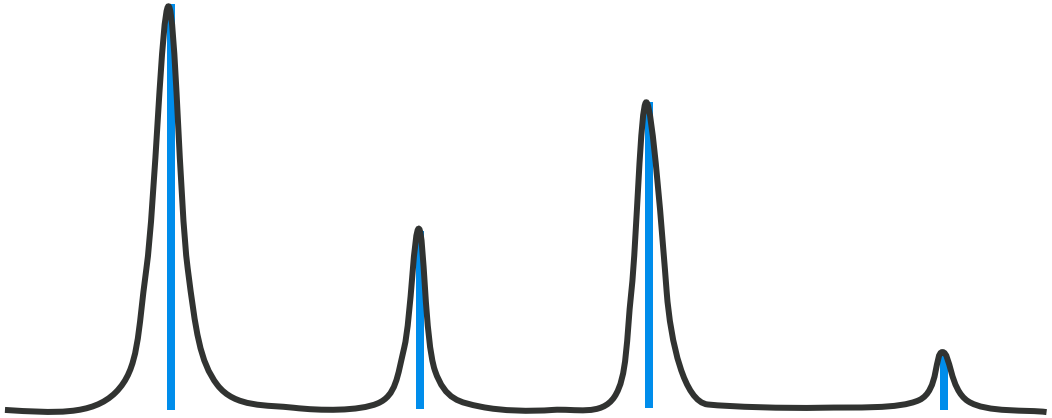


# Ideal Sample for Bragg-Brentano Geometry

- Flat
  - Sample is level with top surface of holder
  - Affected by sample displacement (sample height)
- Smooth
  - Powder is smooth and fine-grained
  - Affected by graininess (rough or coarse powder with large grains)
- Random
  - Completely randomize crystallite statistics
  - Affected by preferred orientation (over- or under-represented diffraction planes)

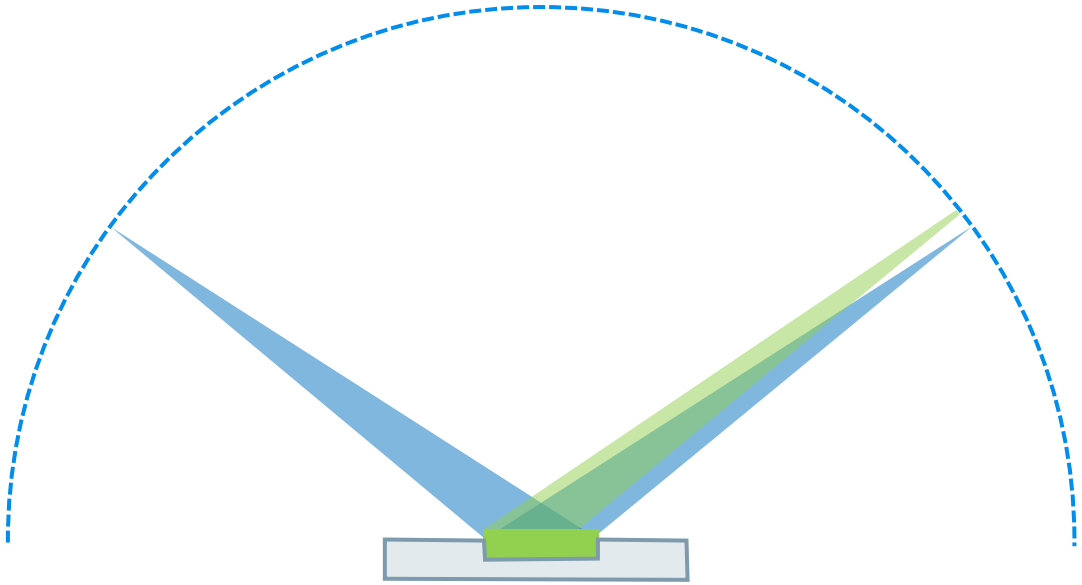
# Sample Displacement

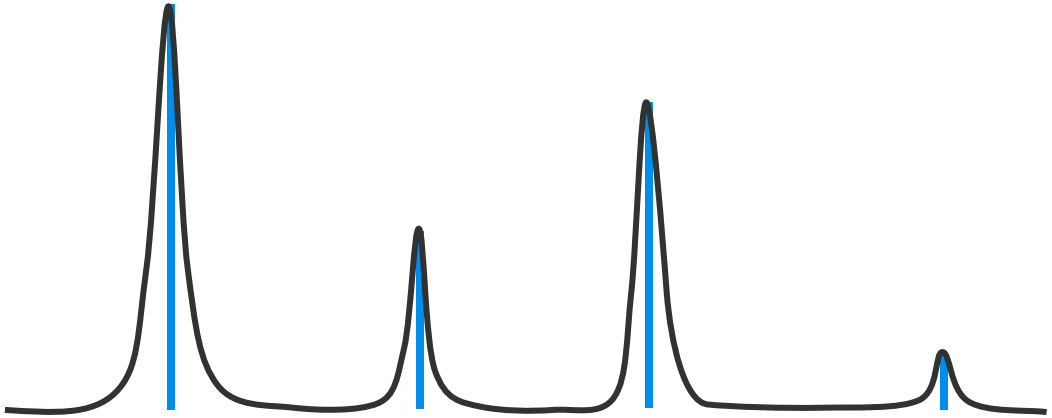




Correct sample height leads to correct observed peak positions

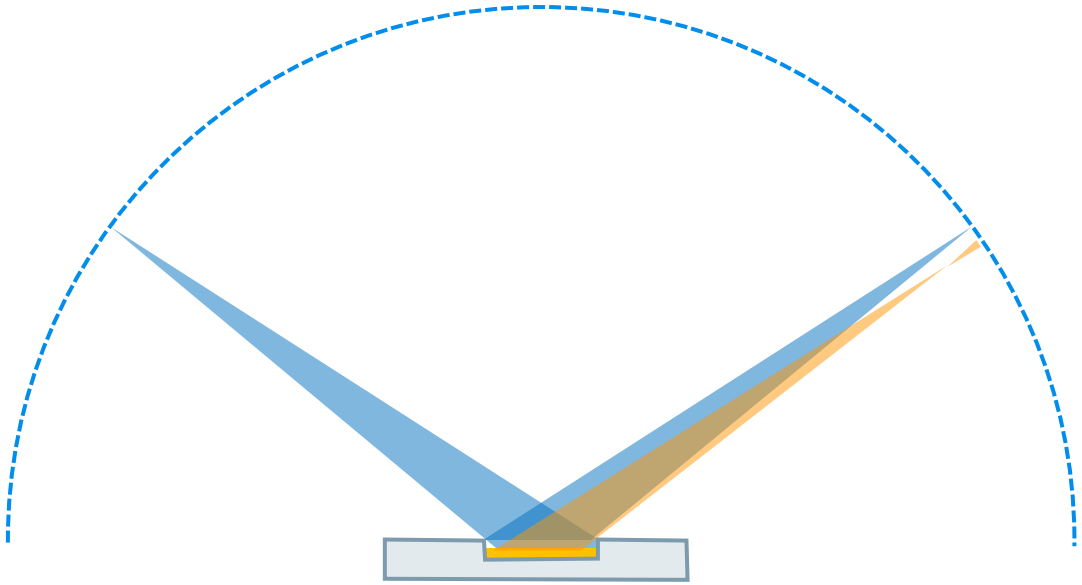
# Sample Displacement

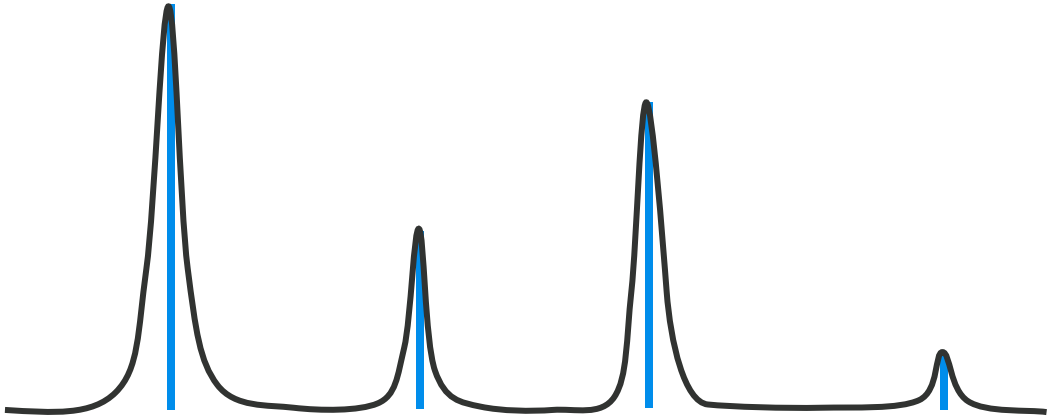




If the sample is too high, peaks will shift to higher 2Theta positions

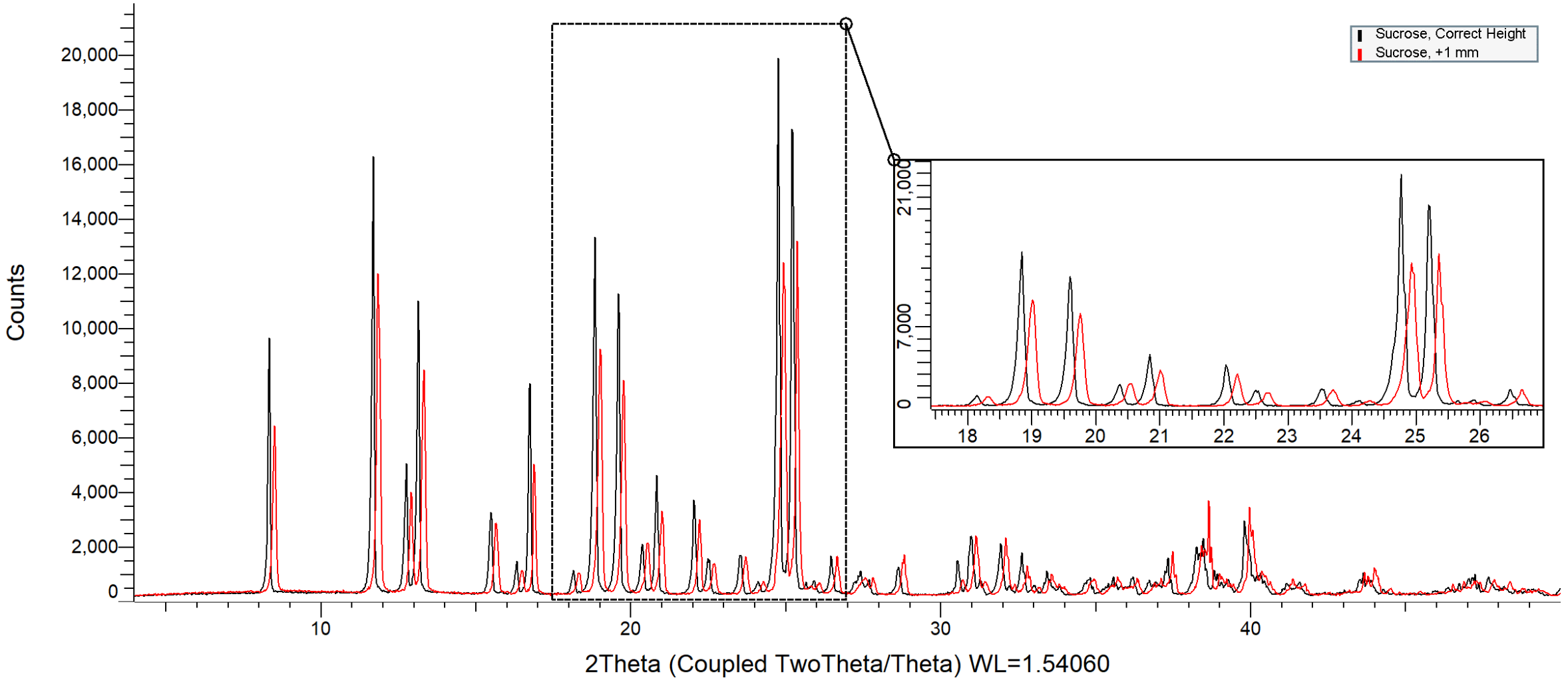
# Sample Displacement



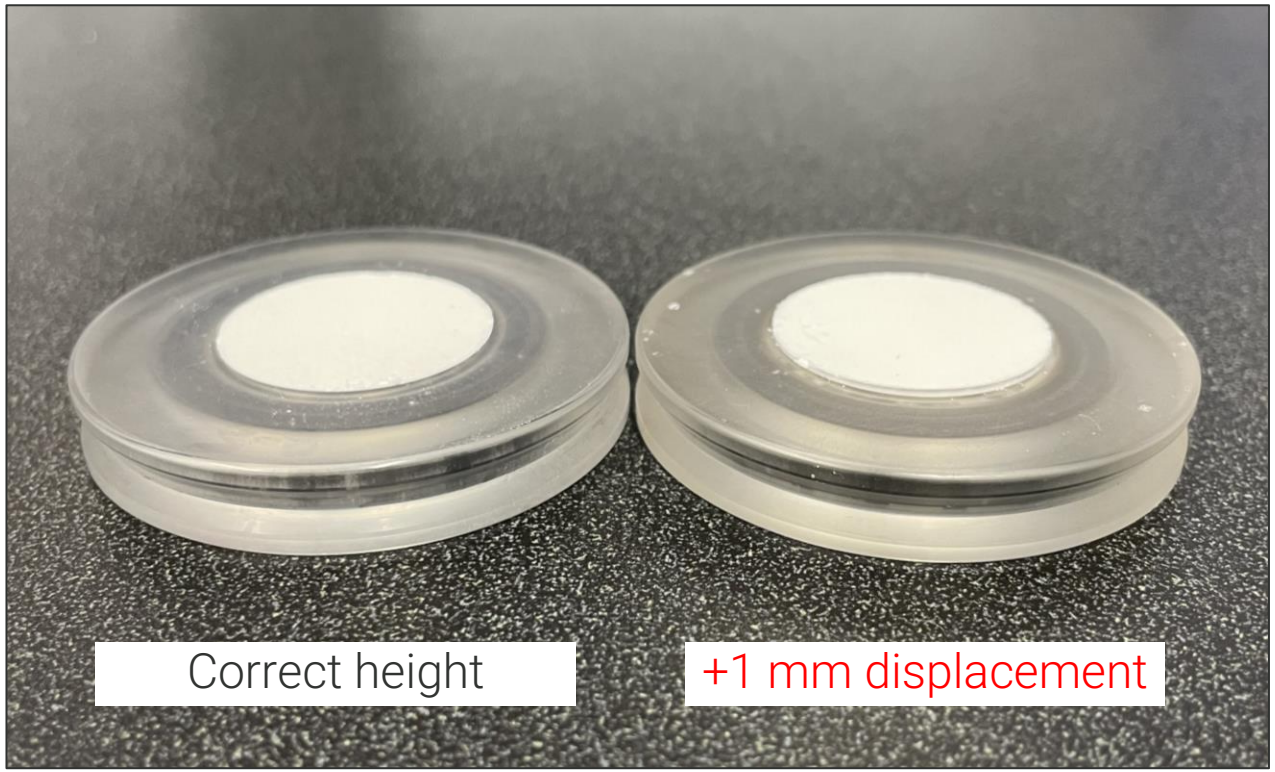


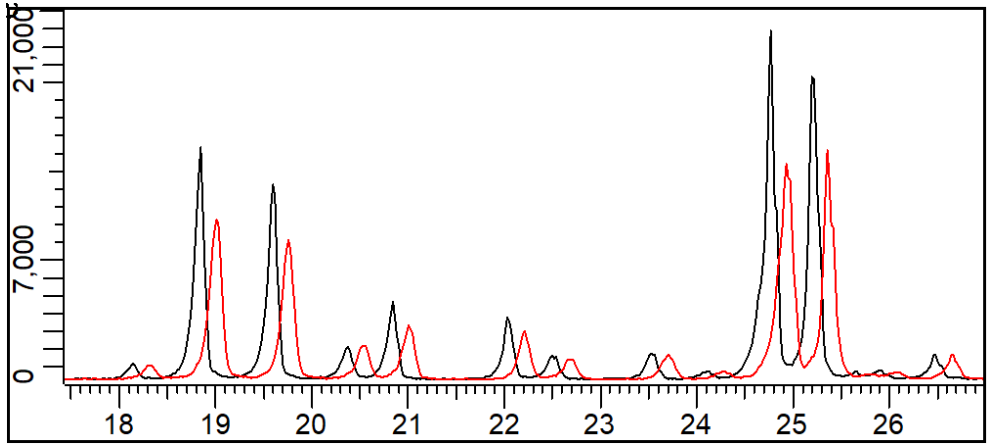
If the sample is too low, peaks will shift to lower 2Theta positions

# Sample Displacement (Sucrose)

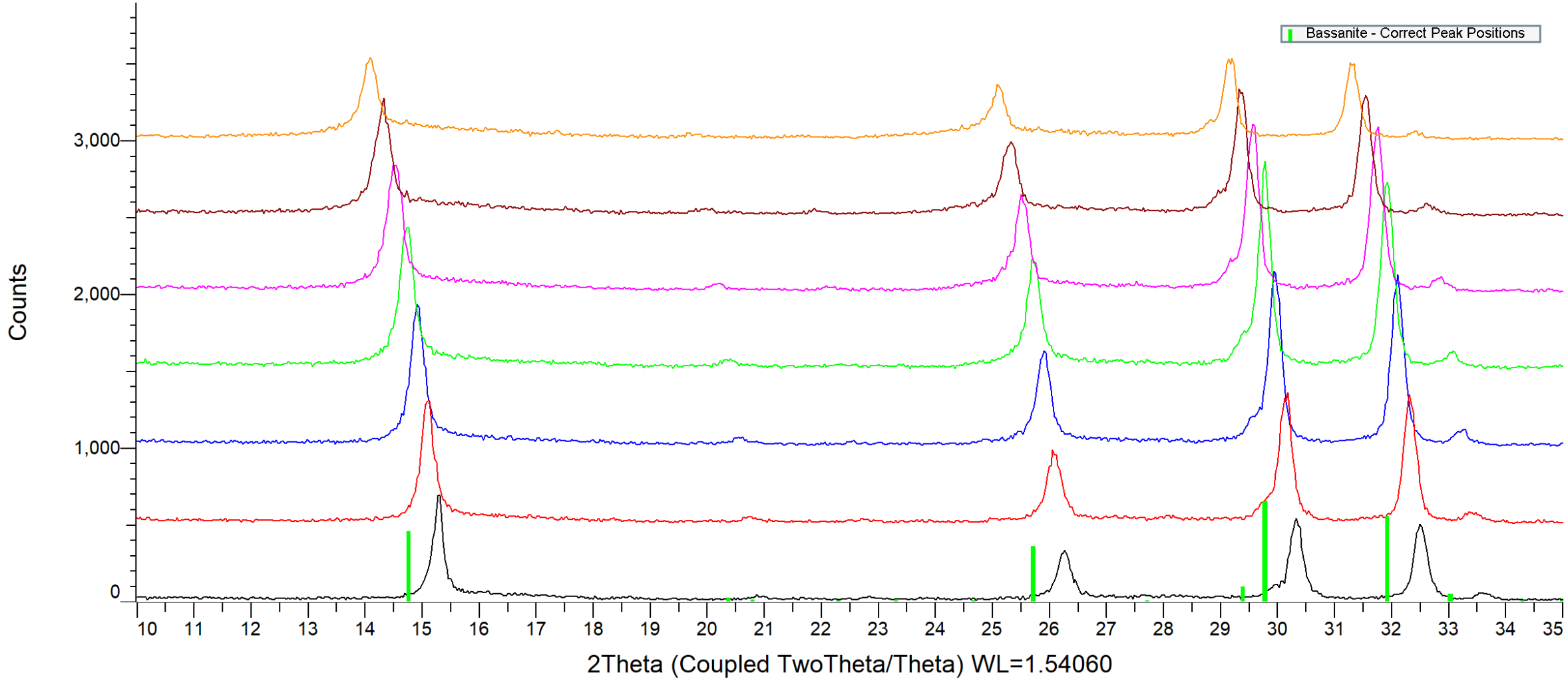


# Sample Displacement (Sucrose)

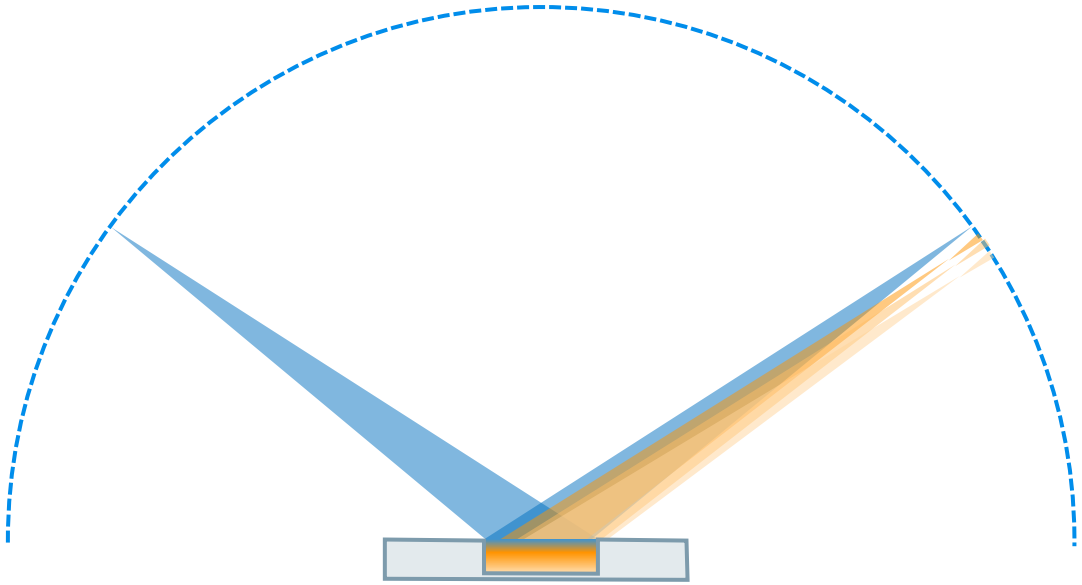


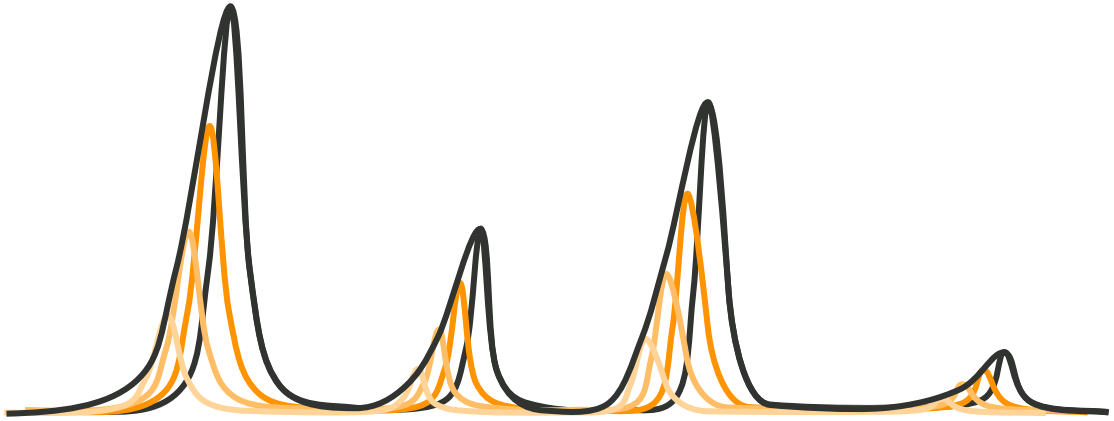



# Sample Displacement (Bassanite)



# Sample Transparency (Light Elements)





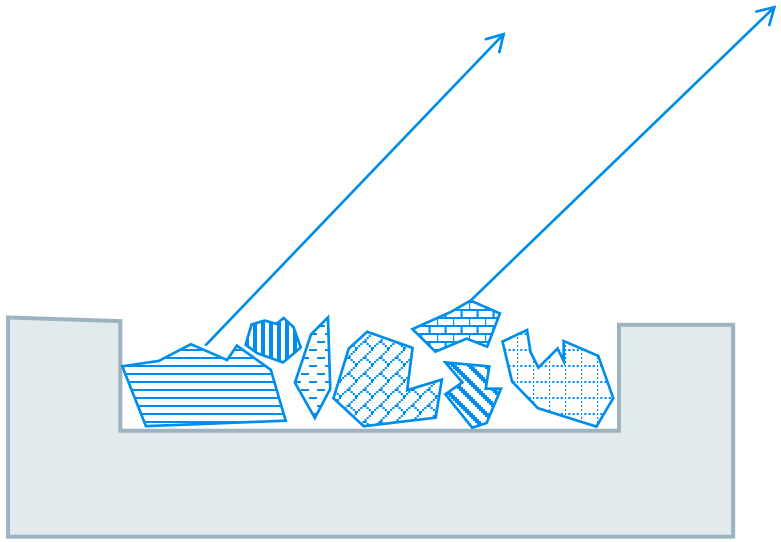
Highly transparent samples can lead to peak asymmetry
due to a gradient of weaker diffraction from inside the sample

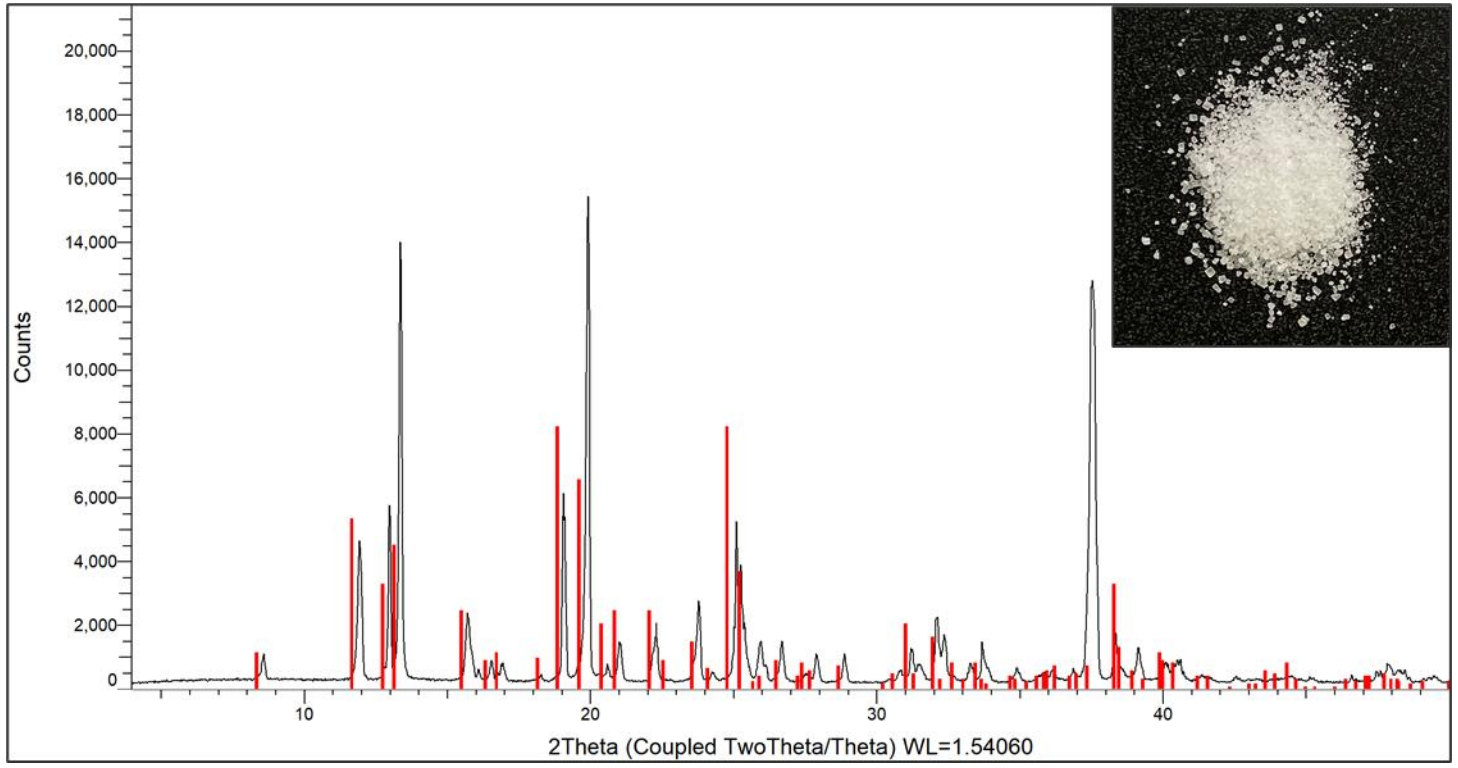
# Ideal Sample for Bragg-Brentano Geometry

- Flat
  - Sample is level with top surface of holder
  - Affected by sample displacement (sample height)
- Smooth
  - Powder is smooth and fine-grained
  - Affected by graininess (rough or coarse powder with large grains)
- Random
  - Completely randomize crystallite statistics
  - Affected by preferred orientation (over- or under-represented diffraction planes)

# Coarse or Grainy Powders

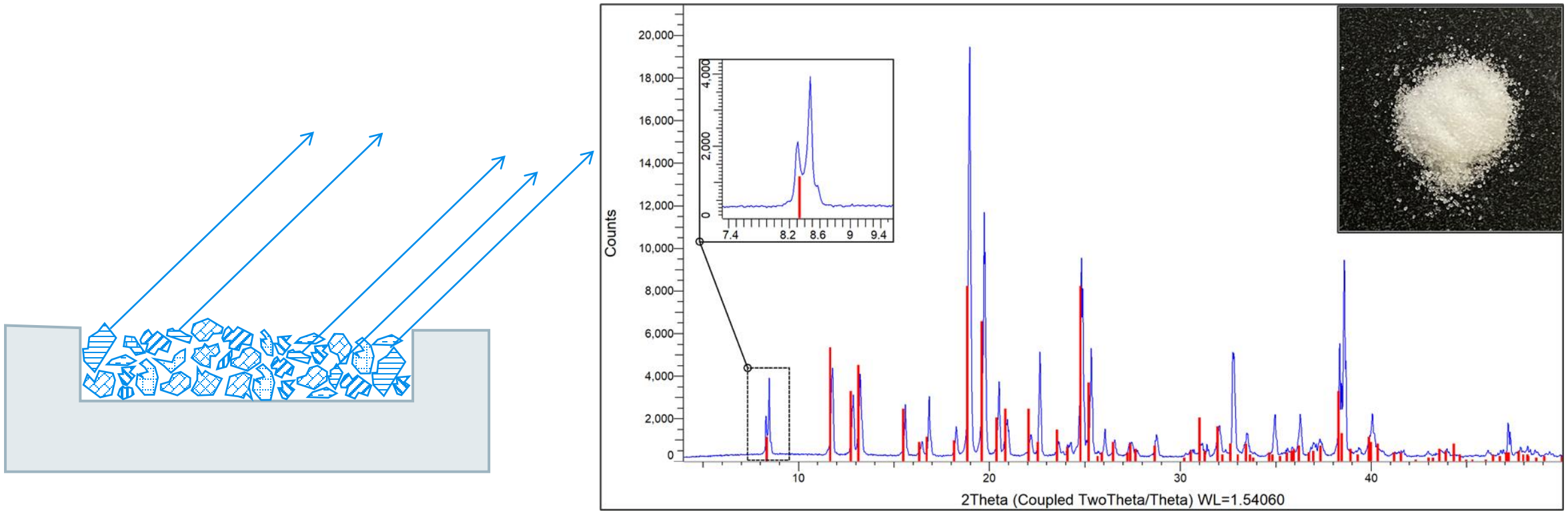
# Coarse or Grainy Powders





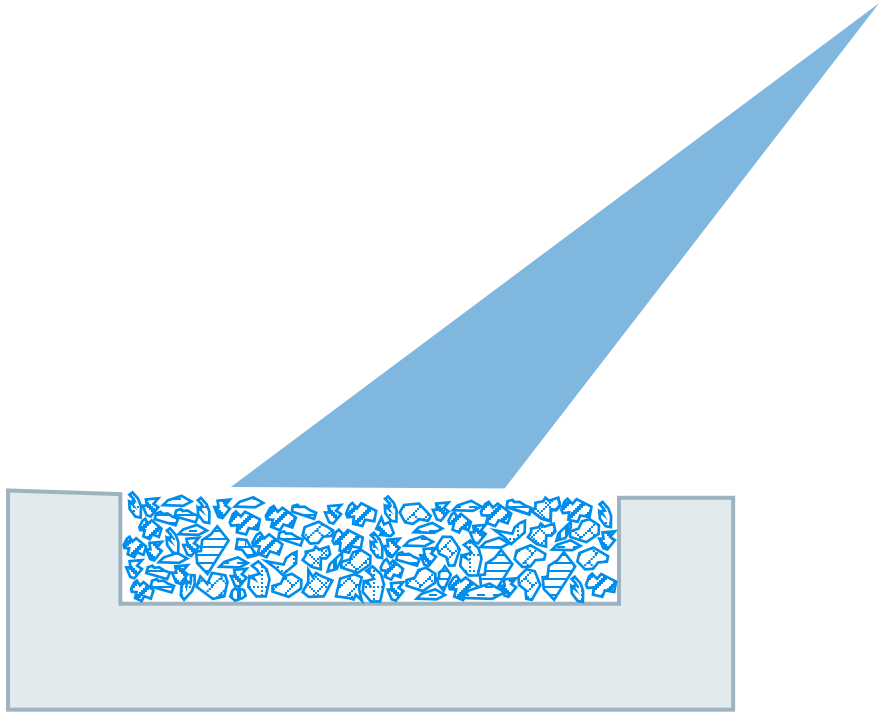

Samples with large grains have a limited number of crystals
in the correct orientation for diffraction to occur (wrong intensities)

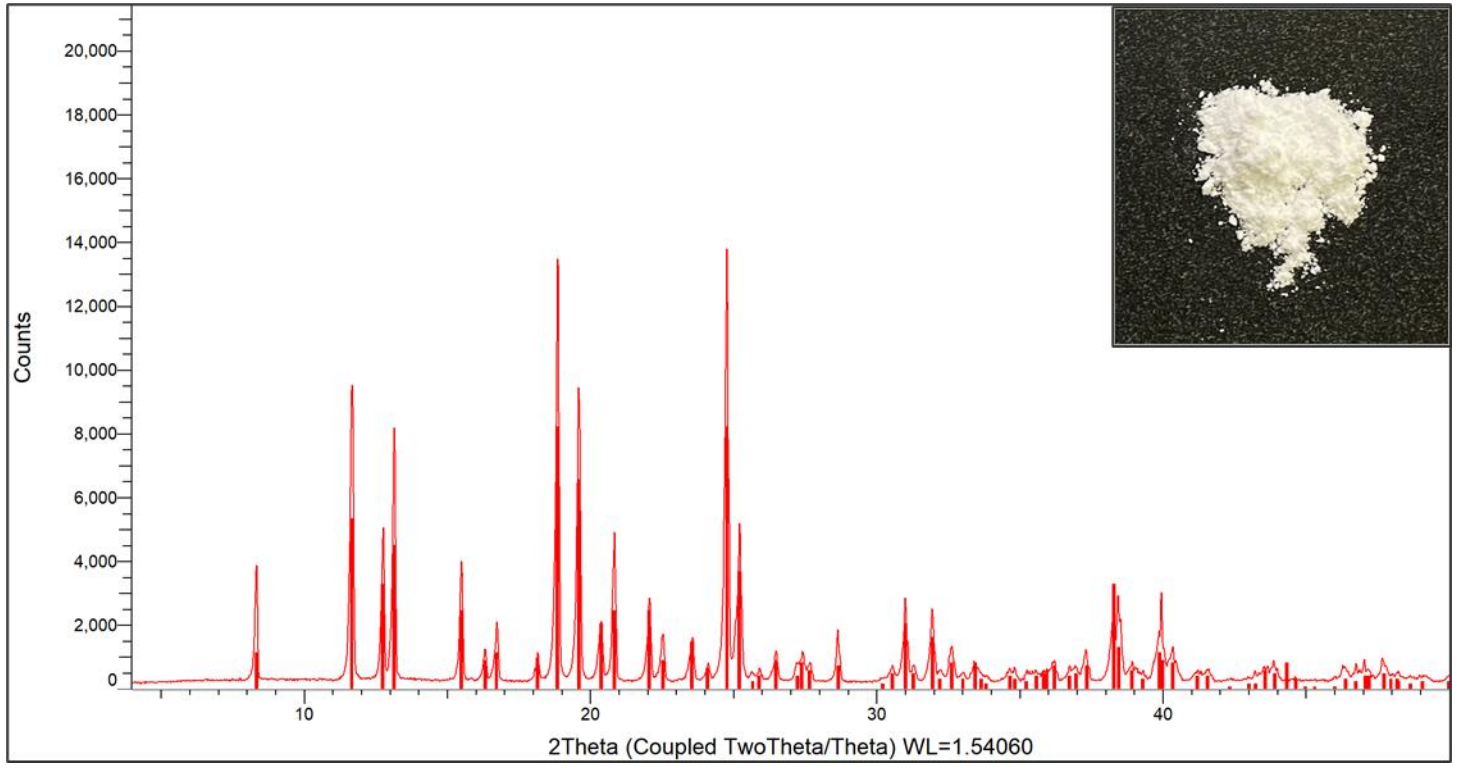
# Coarse or Grainy Powders




Grainy samples are difficult to pack evenly, leading to surface roughness and multiple sample heights (peak shifting or doubling)

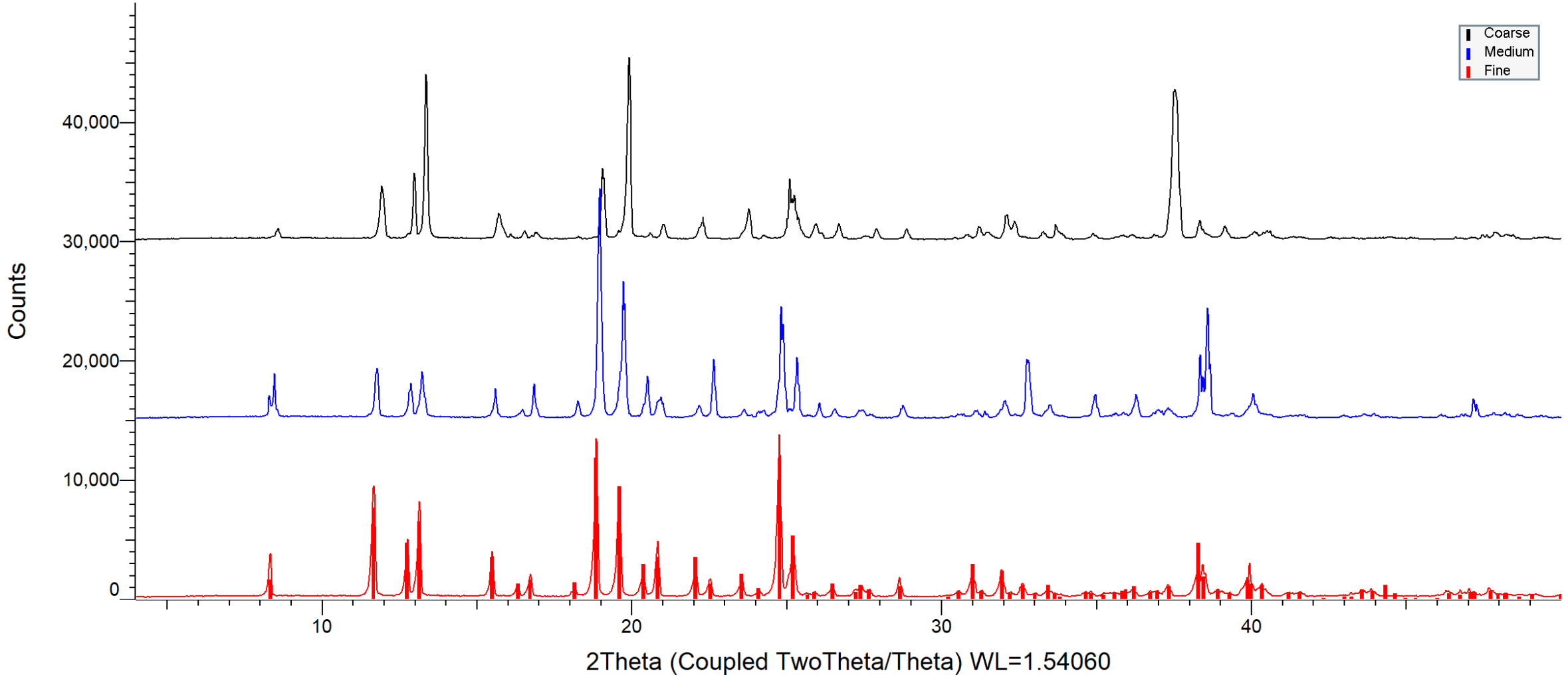
# Coarse or Grainy Powders



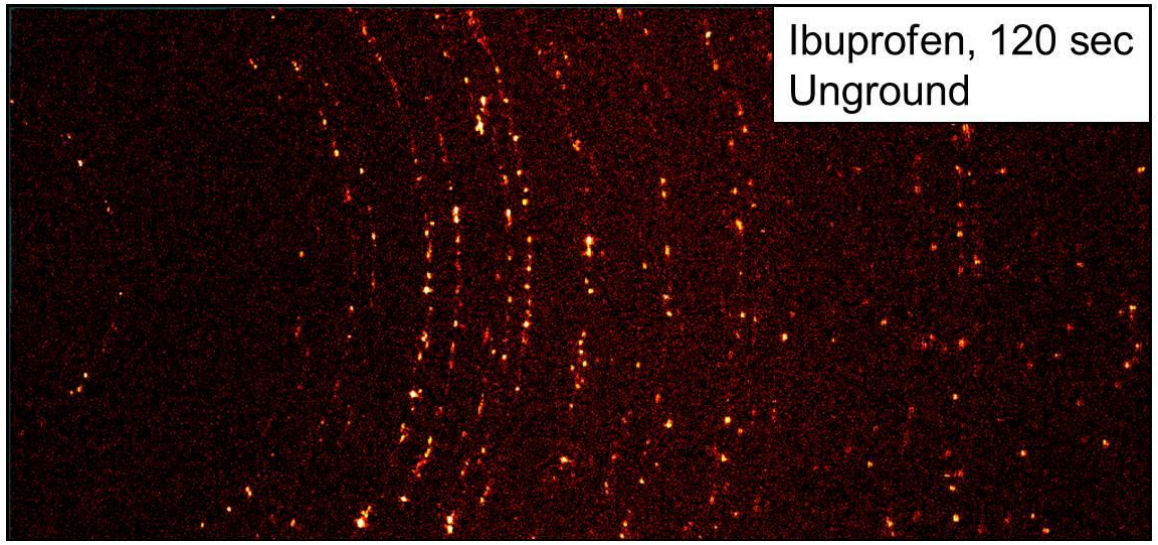


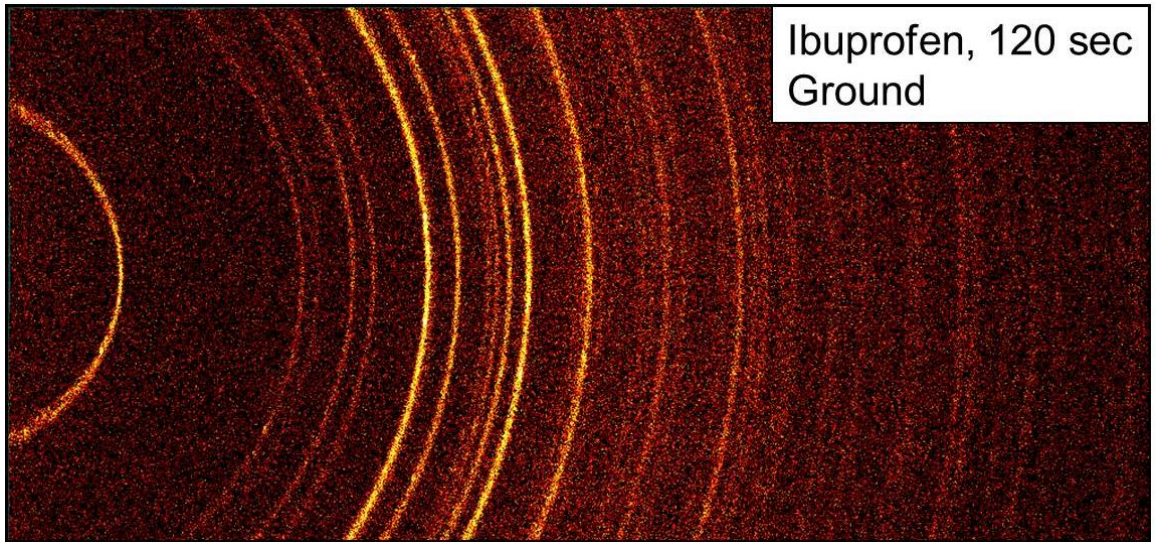

Fine powders are easier to prepare as a smooth surface and have large enough statistics to observe each crystal orientation

# Coarse or Grainy Powders (Sucrose)



# Coarse or Grainy Powders (Ibuprofen)




Large grains = spotty diffraction
Fine powder = correct intensities and peak shapes

# Ideal Sample for Bragg-Brentano Geometry

- Flat
  - Sample is level with top surface of holder
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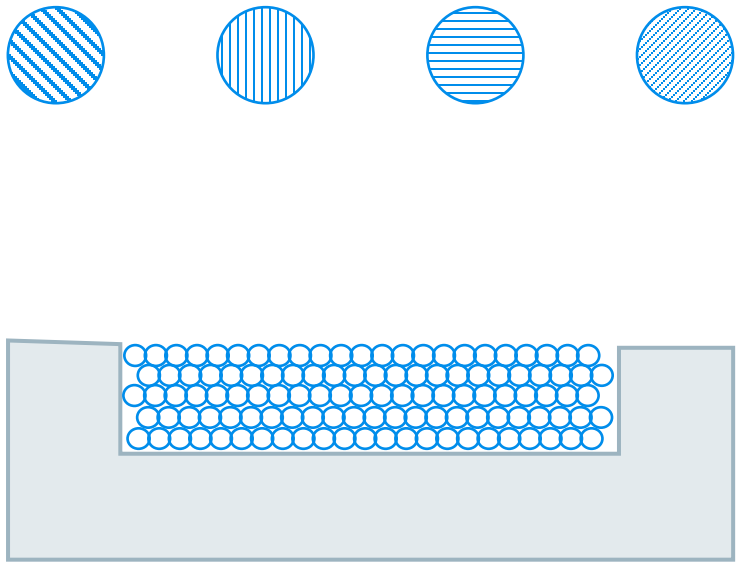
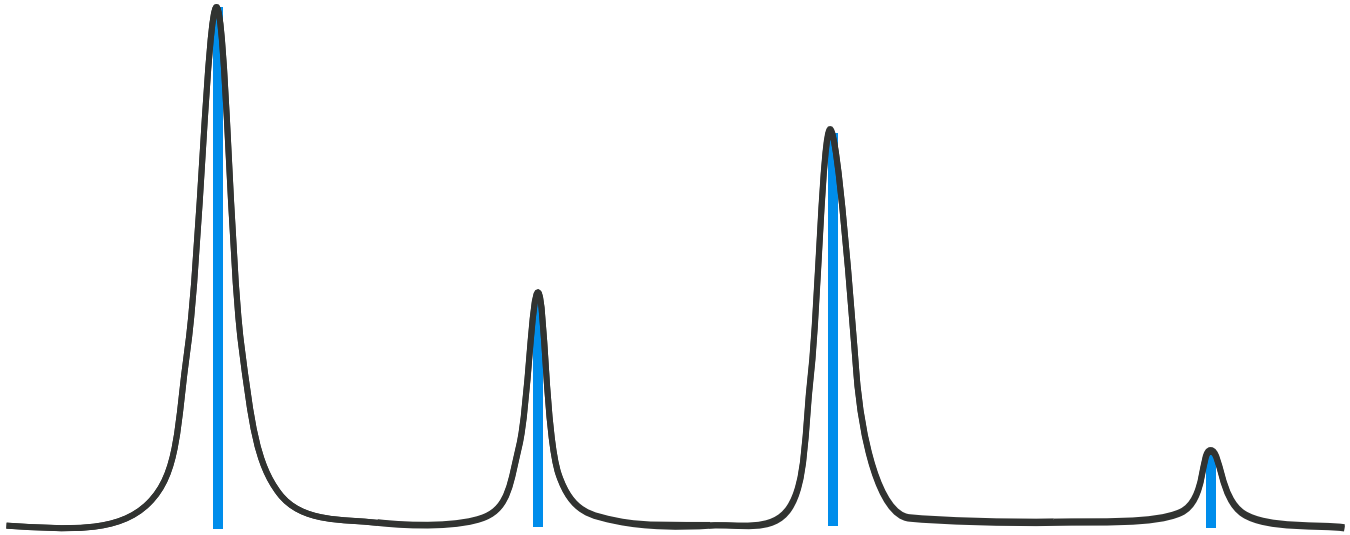
- Smooth
  - Powder is smooth and fine-grained
  - Affected by graininess (rough or coarse powder with large grains)
- Random
  - Completely randomize crystallite statistics
  - Affected by preferred orientation (over- or under-represented diffraction planes)

# Preferred or Non-Random Orientation





An ideal powder has particle shapes
that are conducive to random orientations

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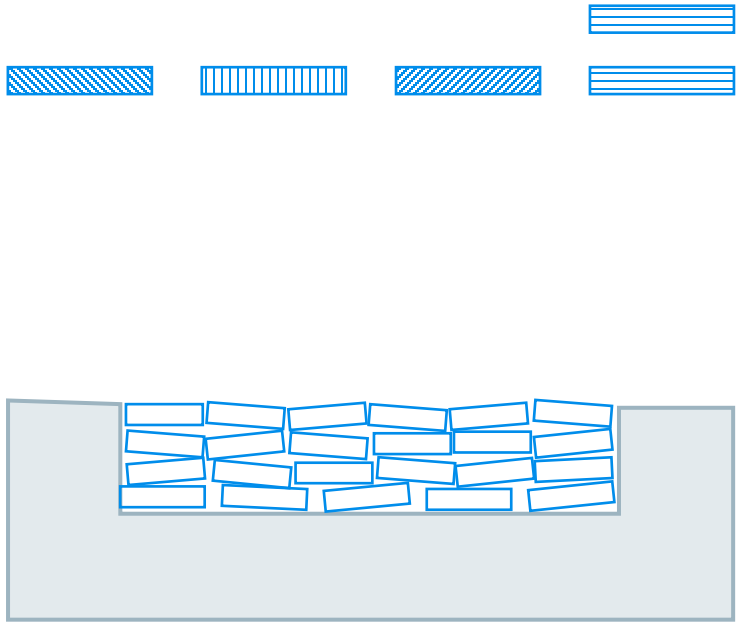

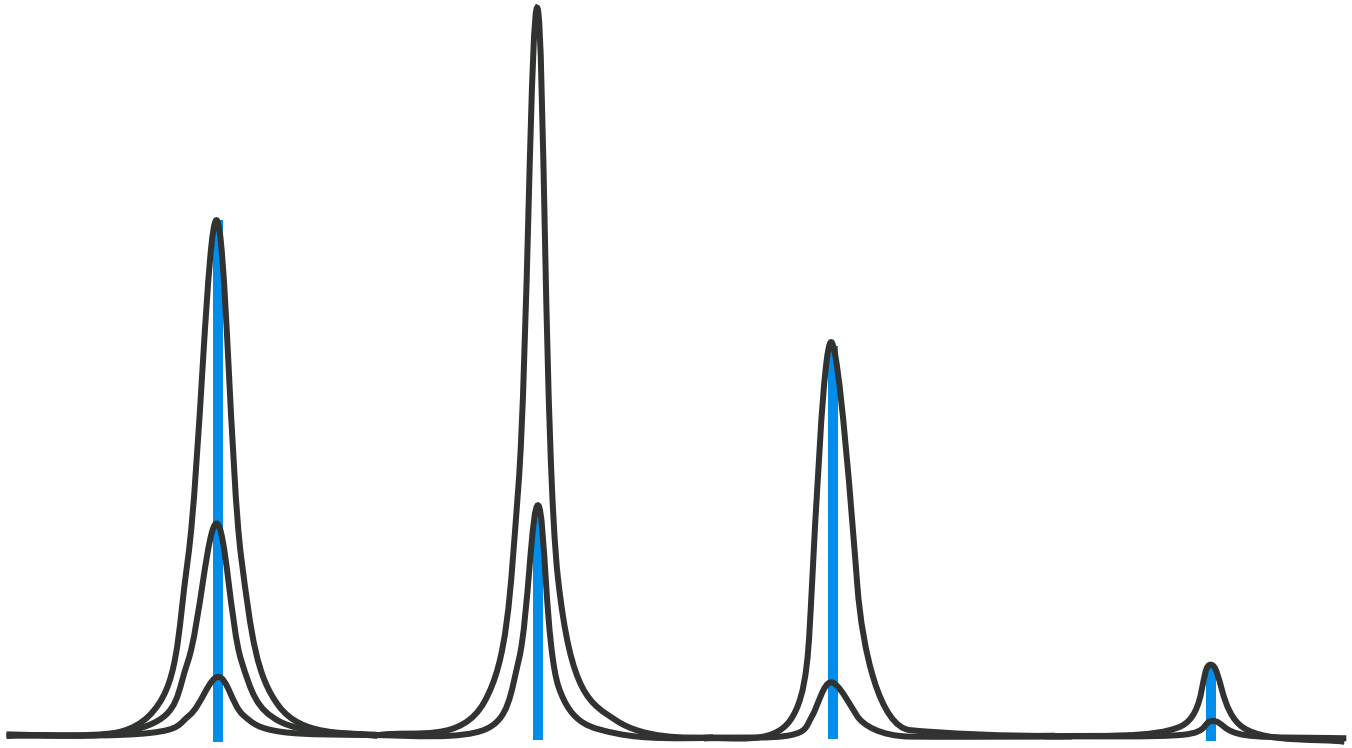

If a material has particles that are shaped like plates or needles,
certain crystal orientations can be overrepresented (wrong intensity)

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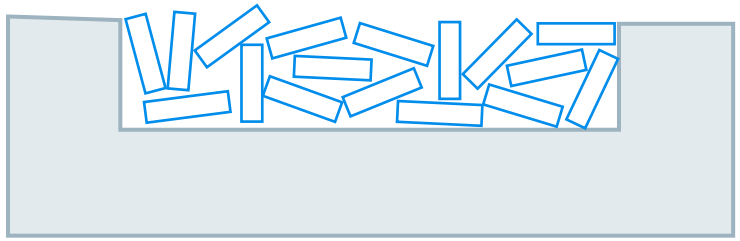
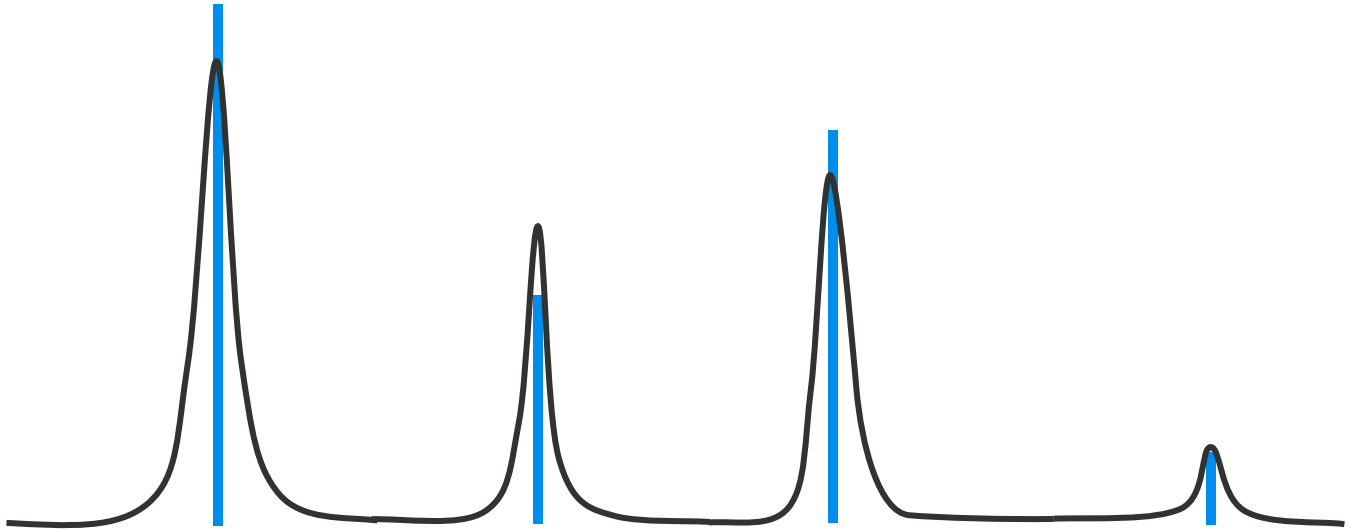
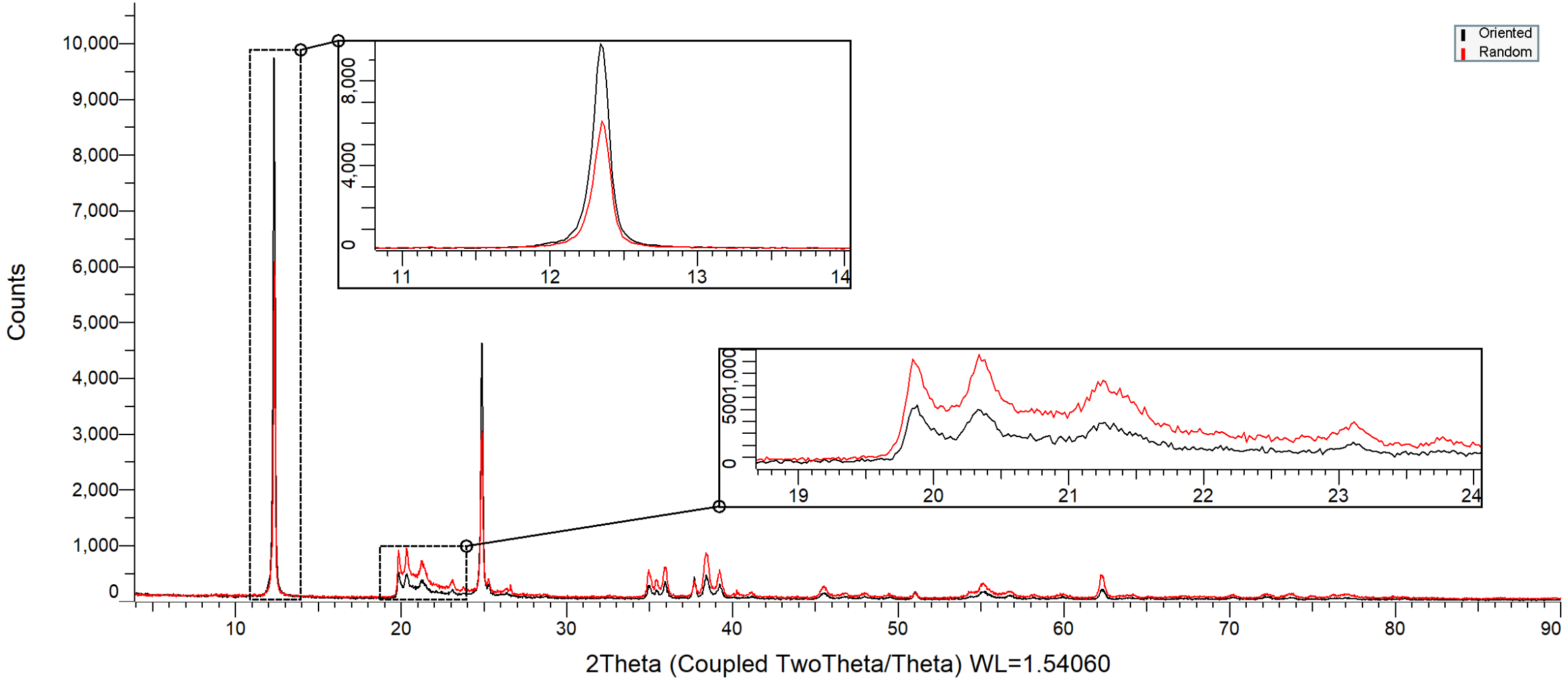


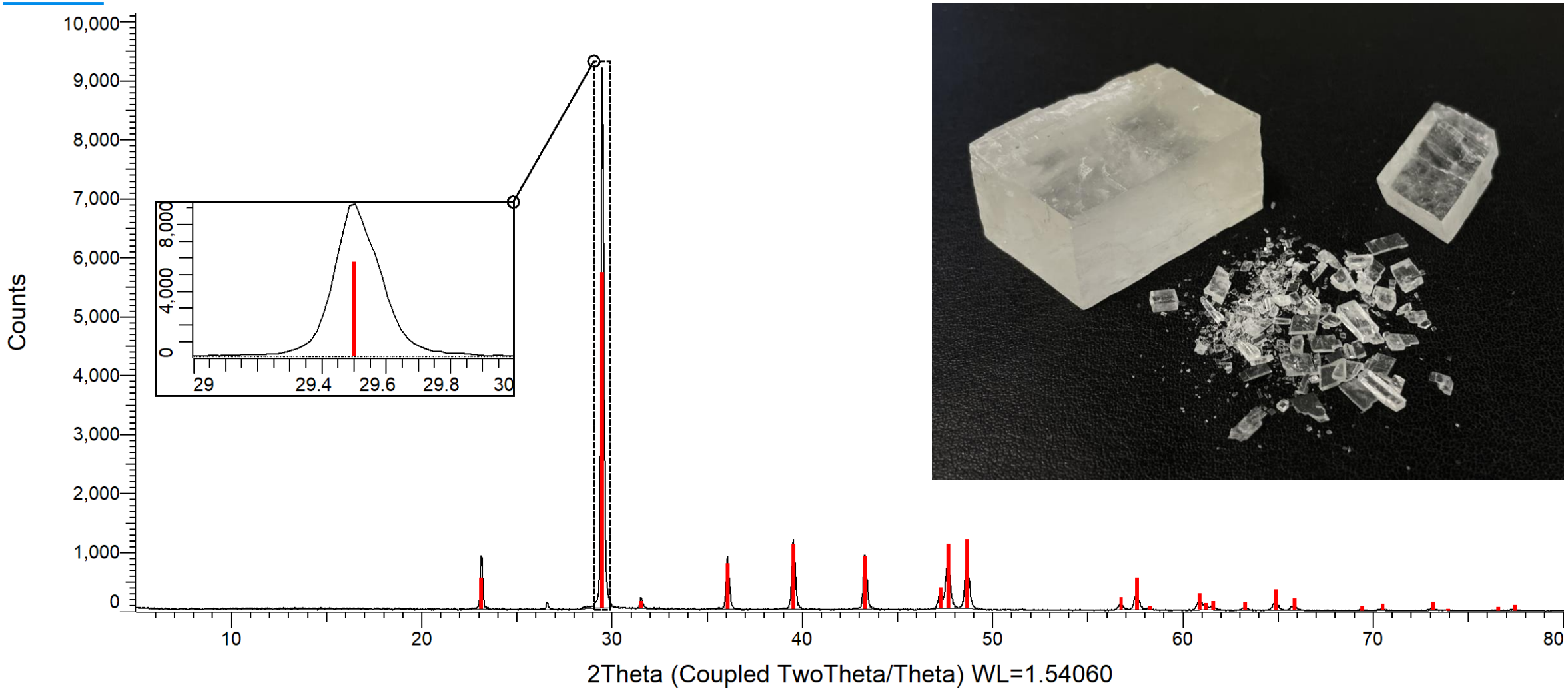


If a material tends to orient, try to increase randomization during sample preparation (gentle packing, back- or side-loading)

# Preferred or Non-Random Orientation (Kaolinite)



# Preferred or Non-Random Orientation (Calcite)

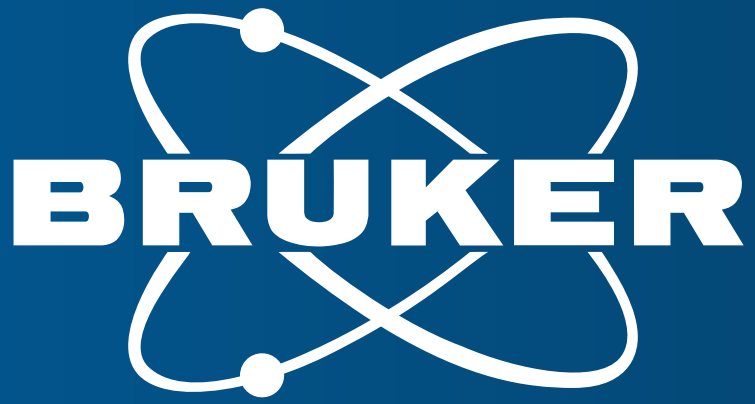


# Summary

- The ideal diffraction specimen is flat, smooth, and random
  - Sample displacement affects observed peak positions
  - Graininess affects peak intensities and shapes
  - Preferred orientation affects relative peak intensities

- Accurate, high-quality diffraction data is achieved through careful sample preparation

- Phase identification, phase quantification, and structural refinement are all improved with better quality data

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