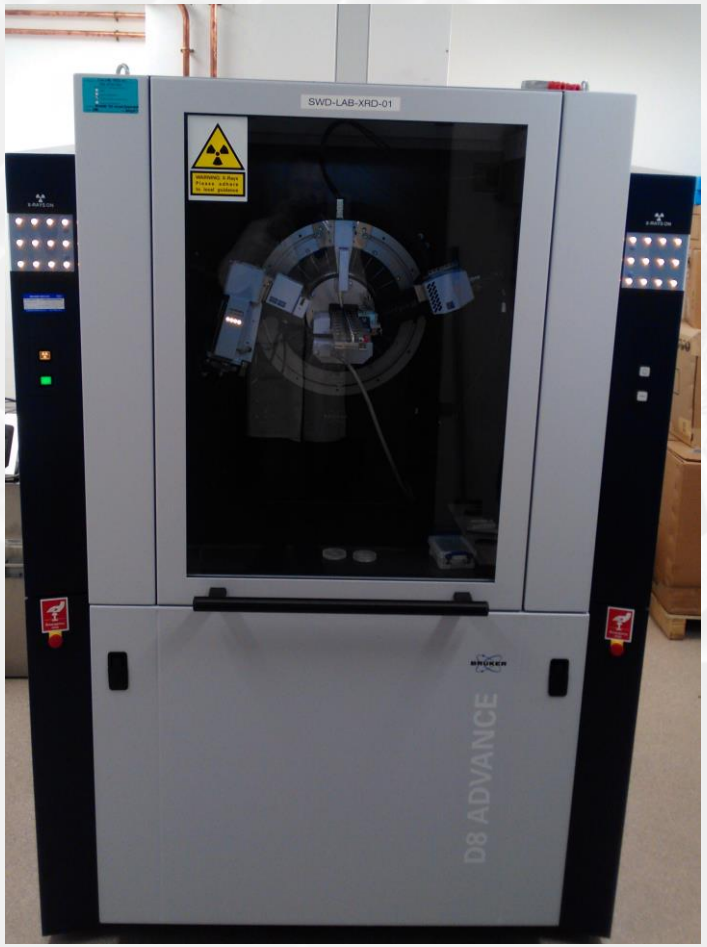
X-Ray Powder Diffraction (XRPD) Analysis

AMPAC Analytical

Synopsis

- Introduction to XRD
- Instrumentation
- Operations of XRD
- Applications
- Case Study



Bruker D8 Advance XRPD

Panalytical Empyrean XRPD

Instrumentation

XRD is a powerful, non-destructive and rapid technique for analysing a wide range of materials (1 µm to 100 mm), including metals, polymers, catalysts, plastics, pharmaceuticals, etc.

Key Features:

- Vital method for investigation and characterization of crystalline materials in the QC and R&D Laboratories
- Best qualitative method for identification of a phase purity of an unknown bulk composition
- Minimal sample preparation required
- The data interpretation is straight forward

X-ray Tube: The main source of X-rays

Incident-Beam Optics: Condition the X-ray beam before it hits the sample

Goniometer: Platform that holds and moves the sample, optics, and detector

Sample Holder: Holds the sample in place and rotates it if required

Air Scatter: Controls the size of the viewed diffracting sample surface, to improve diffraction resolution and minimize cross contamination

Receiving-side Optics: Condition the X-ray beam after it has encountered the sample

Detector: Count the number of X-rays scattered by the sample

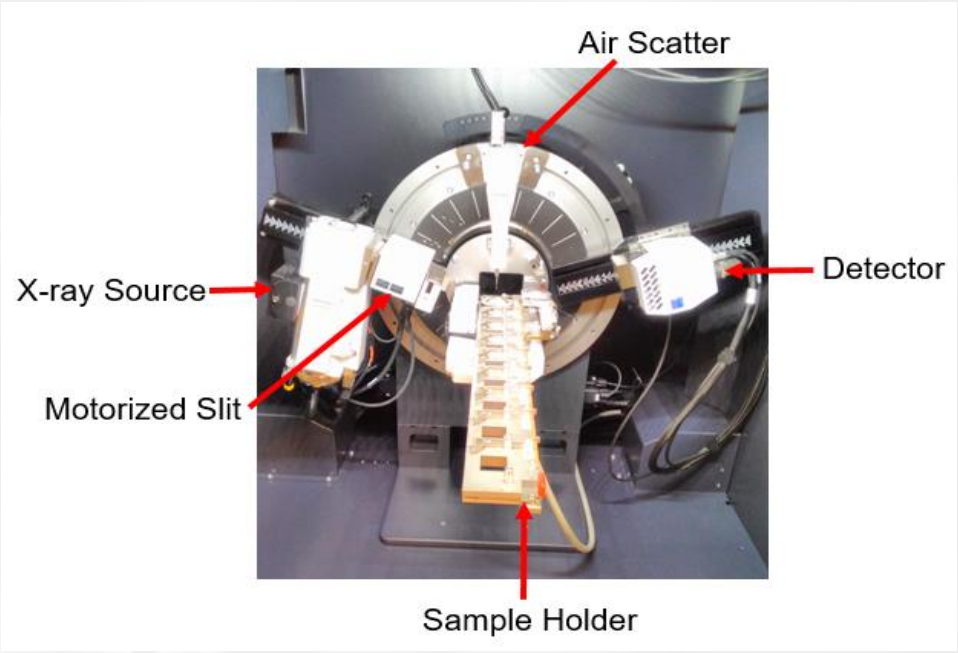


Figure 1: A photo of the Bruker D8 Advance diffractometer

Operations of XRD

- X-rays are generated in a cathode ray tube by heating a filament to produce electrons, accelerating the electrons toward a target by applying a voltage, and bombarding the target material (Cu, λ = 1.54 wavelength) with electrons.
- The generated X-rays are directed towards the sample, and the diffracted rays are collected by the detector (See Figures 2 & 3).
- A key component of all diffraction is the angle between the incident and diffracted rays (2θ). A typical powder patterns data is collected at 2θ from ~5° to 70°, angles that are present in the X-ray scan.
- A detector records and processes this X-ray signal and converts the signal to a count rate which is then output to a device such as a printer or computer monitor.

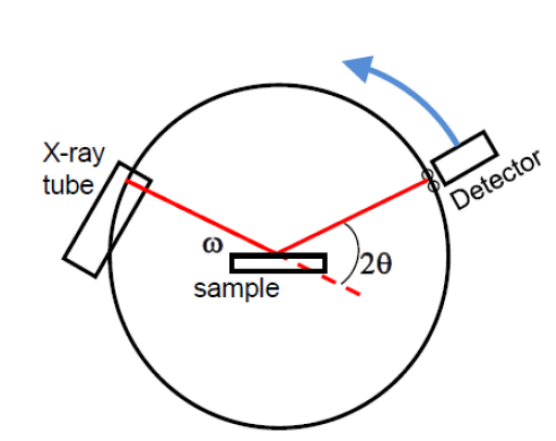


Figure 2: A schematic illustration of operations of XRD main components

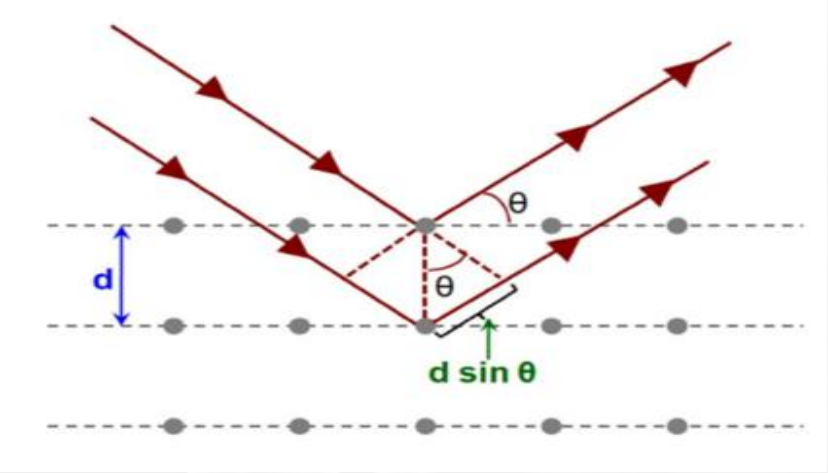


Figure 3: A schematic diagram for coherent diffraction, satisfying Bragg's Law

Applications

Interpretation:

- The peak intensities in the diffractogram are determined by the distribution of atoms within the lattice. As a result, the X-ray diffraction pattern is the fingerprint of periodic atomic arrangement's in a given sample.
- Phases with the same chemical composition can have drastically different diffraction patterns.
- The position and relative intensity of a series of peaks can be used to match experimental data to reference data in a database.

Applications:

- Characterization of Crystalline and Partially Crystalline Solids
- Identification of Crystalline Form, Polycrystalline or Amorphous
- High potency materials can be examined using closed sample holders (Band 4 & 5 materials).

References:

- USP <941> : X-ray diffraction USP monograph, Current Edition.

Case Study – Identification of Polymorphic Forms

Problem Statement: After work up from the reaction mixture, it is possible to get different polymorphic forms of a material.

Impact: Different polymorphs can effect the solubility, dissolution rate, bioavailability and physical stability of the drug substance.

Identification Technique: PXRD is best technique to identify different polymorphic forms in the reaction mixture [USP <941>].

Results: Comparison of sample diffractogram with the Ref Std diffractograms confirmed that the sample is present in Form D (For more details, see Figure 4). The agreement in the 2θ-diffraction angles between the sample and the Ref Std is within 0.2°. Peak relative intensities between sample and Ref Std may vary considerably due to preferred orientation effects.

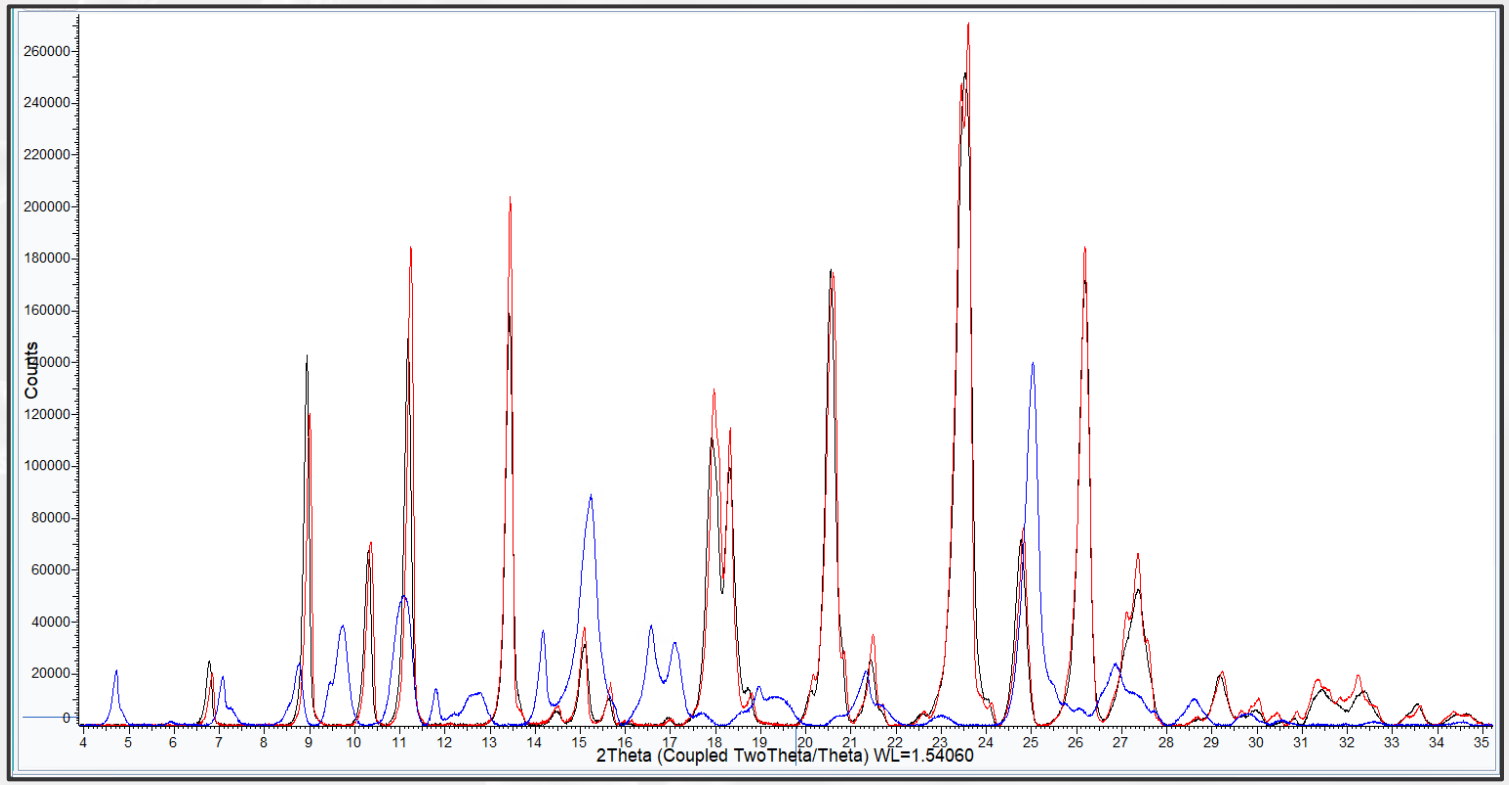


Figure 4: **Ref Std Form D** (red line); **Ref Std Form B** (blue line); **Sample** (black line)

Case Study – In Process Production Support

XRD analysis can be used for production support to confirm the correct form is being produced

- Conversion from Form 2 to preferred Form 1 occurs during drying; XRD testing was performed as an "In-Process" test to confirm complete conversion to Form 1
- Red arrow point out to undesired Form 2; present in the First Drying Sample and not present in Final Drying Sample