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X-Ray Diffraction: Instrumentation and Applications

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X-ray diffraction (XRD) is a powerful nondestructive technique for characterizing crystalline materials. It provides information on structures, phases, preferred crystal orientations (texture), and other structural parameters, such as average grain size, crystallinity, strain, and crystal defects. X-ray diffraction peaks are produced by constructive interference of a monochromatic beam of X-rays scattered at specific angles from each set of lattice planes in a sample. The peak intensities are determined by the distribution of atoms within the lattice. Consequently, the X-ray diffraction pattern is the fingerprint of periodic atomic arrangements in a given material. This review summarizes the scientific trends associated with the rapid development of the technique of X-ray diffraction over the past five years pertaining to the fields of pharmaceuticals, forensic science, geological applications, microelectronics, and glass manufacturing, as well as in corrosion analysis.

Keywords: applications, theory, X-ray diffraction

Introduction

Max von Laue and Co., in 1912, discovered that crystalline substances act as three-dimensional diffraction gratings for X-ray wavelengths similar to the spacing of planes in a crystal lattice (Friedrich et al., 1912).

X-ray diffraction is now a common technique for the study of crystal structures and atomic spacing. X-ray diffraction is based on constructive interference of monochromatic X-rays and a crystalline sample. These X-rays are generated by a cathode ray tube, filtered to produce monochromatic radiation, collimated to concentrate, and directed toward the sample (Figure 1).

The interaction of the incident rays with the sample produces constructive interference (and a diffracted ray) when conditions satisfy Bragg's law:

$$n\lambda = 2d\sin\theta$$

where n is an integer, λ is the wavelength of the X-rays, d is the interplanar spacing generating the diffraction, and θ is the diffraction angle.

This law relates the wavelength of electromagnetic radiation to the diffraction angle and the lattice spacing in a crystalline sample. These diffracted X-rays are then detected, processed, and counted. By scanning the sample through a range of 2θ angles, all possible diffraction directions of the lattice should be attained due to the random orientation of the powdered material. Conversion of the diffraction peaks to d-spacings allows identification of the compound because each compound has a set of unique d-spacings. Typically, this is achieved by comparison of d-spacings with standard reference patterns.

X-ray diffractometers consist of three basic elements: an X-ray tube, a sample holder, and an X-ray detector (Connolly, 2007).

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 with electrons. When electrons have sufficient energy to dislodge inner shell electrons of the target material, characteristic X-ray spectra are produced. These spectra consist of several components, the most common being K_α and K_β.

K_α consists, in part, of $K_{\alpha1}$ and $K_{\alpha2}$. $K_{\alpha1}$ has a slightly shorter wavelength and twice the intensity of $K_{\alpha2}$. The specific wavelengths are characteristic of the target material (Cu, Fe, Mo, Cr). Filtering, by foils or crystal monochrometers, is required to produce monochromatic X-rays needed for diffraction. $K_{\alpha1}$ and $K_{\alpha2}$ are sufficiently close in wavelength such that a weighted average of the two is used. Copper is the most common target material for single-crystal diffraction, with CuK_α radiation $= 1.5418$ Å. These X-rays are collimated and directed onto the sample. As the sample and detector are rotated, the intensity of the reflected X-rays is recorded. When the geometry of the incident X-rays impinging the sample satisfies Bragg's law, constructive interference occurs and a peak in intensity appears. A detector records

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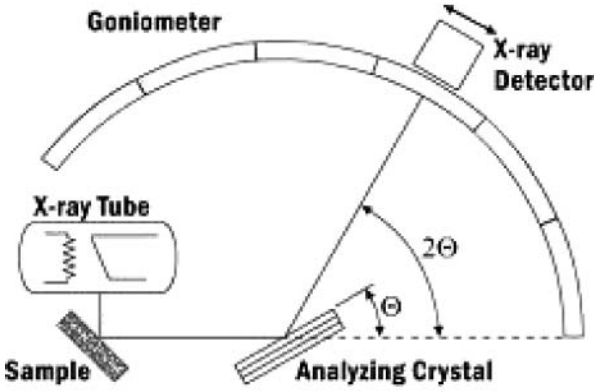

Fig. 1. Schematic diagram of a diffractometer system.

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.

The geometry of an X-ray diffractometer is such that the sample rotates in the path of the collimated X-ray beam at an angle θ while the X-ray detector is mounted on an arm to collect the diffracted X-rays and rotates at an angle of 2θ. The instrument used to maintain the angle and rotate the sample is termed a goniometer.

For typical powder patterns, data are collected at 2θ from 5° to 70°, angles that are preset in the X-ray scan.

X-ray powder diffraction is most widely used for the identification of unknown crystalline materials (e.g., minerals, inorganic compounds). Determination of unknown solids is critical to studies in geology, environmental science, material science, engineering, and biology. Other applications include characterization of crystalline materials, identification of fine-grained minerals such as clays and mixed layer clays that are difficult to determine optically, determination of unit cell dimensions, and measurement of sample purity.

With specialized techniques, X-ray diffraction (XRD) can be used to determine crystal structures by using Rietveld refinement, determine modal amounts of minerals (quantitative analysis), characterize thin film samples, and make textural measurements, such as the orientation of grains, in a polycrystalline sample (Brindley and Brown, 1980).

There are some strengths and some limitations of X-ray powder diffraction (XRPD):

Strengths

- Powerful and rapid (<20 min) for identification of an unknown mineral
- Provides unambiguous mineral determination in most cases
- Requires minimal sample preparation
- Wide availability of XRD units
- Relatively straightforward data interpretation

Limitations

- Homogeneous and single-phase material is best for identification of an unknown
- Access to a standard reference file of inorganic compounds is required
- Material, in tenths of a gram quantity, must be ground into a powder
- For mixed materials, detection limit is ~ 2% of sample
- For unit cell determinations, indexing of patterns for non-isometric crystal systems is complicated
- Peak overlay may occur and worsens for high angle "reflections"

X-ray diffraction is a high-tech, nondestructive technique for analyzing a wide range of materials including fluids, metals, minerals, polymers, catalysts, plastics, pharmaceuticals, thin-film coatings, ceramics, solar cells, and semiconductors. The technique finds innumerable practical applications in various industries, including microelectronics, power generation, aerospace, and many more. XRD analysis can easily detect the existence of defects in a particular crystal, its resistance level to stress, its texture, its size and degree of crystallinity, and virtually any other variable relating to the sample's basic structure.

The objective of this review is to present the new developments in applications of XRD in different analysis, covering the period between 2009 and 2014. It is useful to give a short introduction to the concept of the XRD, some characteristics of the instruments used, and sample preparation. Quantitative and qualitative determination in different fields of analysis using this technique will be presented.

Xrd Theoretical Aspects

Instrumentation

The instrumentation that is used for powder diffraction measurements has not changed much from that developed in the late 1940s. The major difference found in modern instrumentation is the use of the minicomputer for control, data acquisition, and data processing. Figure 2 illustrates the geometry of the system, showing the layout of a typical diffractometer with system source F, Soller slits P and RP, sample S,

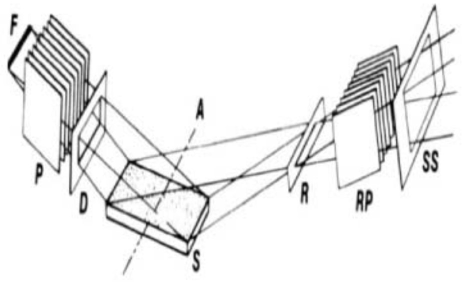

Fig. 2. Geometry of the Bragg-Brentano diffractometer.

divergence slit D, and receiving slit R. The axis of the goniometer is at A.

This geometric arrangement is known as the Bragg-Brentano parafocusing system and is typified by a diverging beam from a line source F, falling onto the specimen S, being diffracted and passing through a receiving slit R to the detector. Distances FA and AR are equal. The amount of divergence is determined by the effective focal width of the source and the aperture of the divergence slit D. Axial divergence is controlled by two sets of parallel plate collimators (Soller slits) P and RP placed between focus and specimen and between specimen and scatter slit, respectively. Use of the narrower divergence slit will give smaller specimen coverage at a given diffraction angle, thus allowing the attainment of lower diffraction angles where the specimen has a larger apparent surface (thus larger values of d are attainable). This is achieved, however, only at the expense of intensity loss.

Choice of the divergence slit, plus its matched scatter slit, is thus governed by the angular range to be covered. The decision as to whether or not the slit size should be increased at a given angle will be determined by the available intensity. A photon detector, typically a scintillation detector, is placed behind the scatter slit and converts the diffracted X-ray photons into voltage pulses. These pulses may be integrated in a rate meter to give an analog signal on an x/t recorder. By synchronizing the scanning speed of the goniometer with the recorder, a plot of degrees 2θ versus intensity, called the diffractogram, is obtained.

A timer/scaler is also provided for quantitative work and is used to obtain a measure of the integrated peak intensity of a selected line(s) from each analyte phase in the specimen. A diffracted beam monochromator may also be used in order to improve signal-to-noise characteristics. The output from the diffractometer is a "powder diagram," essentially a plot of intensity as a function of diffraction angle, which may be in the form of a strip chart or a hard copy from a computer graphics terminal (Brindley and Brown, 1980).

The powder method derives its name from the fact that the specimen is typically in the form of a microcrystalline powder, although, as has been indicated, any material that is made up of an ordered array of atoms will give a diffraction pattern. The possibility of using a diffraction pattern as a means of phase identification was recognized by 1935, but it was not until the late 1930s that a systematic means of unscrambling the superimposed diffraction patterns was proposed by Hanawalt, Rinn, and Frevel (1986).

Sample Preparation

Proper sample preparation is one of the most important requirements in the analysis of powder samples by X-ray diffraction. This statement is especially true for soils and clays that contain finely divided colloids, which are poor reflectors of X-rays, as well as other types of materials such as iron oxide coatings and organic materials that make characterization by XRD more difficult.

Sample preparation includes not only the right sample treatments to remove undesirable substances, but also appropriate techniques to obtain desirable particle size, orientation, thickness, and other parameters. Several excellent books are available that deal with appropriate sample preparation techniques for clays and soils (Bish and Post, 1989; Iyengar et al., 1997; Jackson, 1979; Moore and Reynolds, 1989).

Analysis of powders by XRD requires that they are extremely fine grained to achieve good signal-to-noise ratio (and avoid fluctuation in intensity), avoid spottiness, and minimize preferred orientation. Reduction of powders to fine particles also ensures enough particle participation in the diffraction process. The recommended size range is around 1–5 μm (Cullity, 1978; Klug and Alexander, 1974), especially if quantification of various phases is desired.

For routine qualitative evaluation of mineral components, the samples are usually ground to pass through a 325-mesh sieve (45 μm). Grinding is accomplished either through hand grinding or in a mechanical grinder. The effects of excessive grinding include lattice distortion and possible formation of an amorphous layer (Beilby layer) outside the grains.

There are two types of mounts normally employed depending on the nature of crystallite orientation required.

Random mounts are preferred when identification of phases in a specimen is required. In this type of mount, particles ground to 1–5 μm are packed to a flat surface onto a sample holder to assume different orientations and ensure reflections from various planes (hkl).

Oriented mounts are used when analyzing clay minerals, which rarely show strong diffraction effects from Bragg planes other than the (001). In general, these are prepared by making a slurry of the sample with distilled water. The water is then allowed to evaporate until the slurry is smeared into a sample holder (a glass slide or ceramic tile).

Important factors in sample preparation are:

- Sample properties also influence the quality of a powder pattern by either reducing intensities or distorting intensities.
- Preferred orientation or texture: Texture means that the powder particles do not have an arbitrary shape but a strongly regular anisotropic shape, typically platelets or needles. On preparation these are then preferably oriented along the sample surface massively changing the peak intensities. Several techniques may be employed to minimize this effect:
- The most efficient way is to form a slurry in a highly viscous liquid such as nail varnish. In such a liquid, the random orientation is retained on drying.
- Alternatively, the anisotropic particle shape can be reduced by grinding in a ball mill. This should be done with great care as excessive grinding can easily break down the particle size to nanometer size and lead to amorphization. It is recommended to try the effect of subsequent 5 min grinding intervals to optimize the process on respective samples. In the case of coatings or thin films preferred orientation is often a desired effect. In this case Rietveld refinement can be used to determine the degree of texture.
- Crystallite size and strain: the broadness of a diffraction peak corresponds to the mean crystallite size in a reciprocal

manner. The smaller the average crystallite size, the broader the reflections and the lower the absolute intensities. This effect becomes visible below an average crystallite size of less than 200 nm. Related to crystallite size broadening is strain broadening. Strain broadening occurs due to the presence of defects in crystals. Such strain can be introduced by substitution of constituting atoms but also by special thermal treatment. It is possible to distinguish strain broadening from size broadening as the angle dependence is much larger than in the latter case (He, 2009).

- Sample preparation height: Rotating sample holders improve the measurement statistics and thus provide the best results. However, they are not available for all machines. The most serious error during sample preparation is to fill the sample holder too high or too low. Both result in a significant shift of peak positions, which can make the interpretation difficult.

Applications

5/6 lines of each points

Pharmaceutical Industry

The pharmaceutical industry is one of the most successful in the technology sector, and its ability to innovate has seen it launch nearly 1,400 new chemical entities as human therapeutics over the past 30 years. Despite this success, the research and development (R&D) process to bring a drug successfully to market remains challenging. Drug development is a risky and expensive process in order to increase demand for more available and affordable drugs (generic drugs) and to propose adapted new drug products.

In the drug design, discovery, development, and formulation process, X-ray powder diffraction can help to establish a formulation by discovering the morphology and the degree of crystallinity, providing unique polymorph identification, and determining the quantity of each in mixture. With XRD, nonambient analysis can also be performed to study moisture influence on physical properties of drugs.

Drugs come in a variety of forms (tablets, pills, capsules, aerosol sprays) and with a variety of formulations. A single drug may be formulated in dozens of ways to enhance the ability of the drug to enter the body (fast action or long-lasting action) and be delivered to a targeted area (skin cream, nasal spray, anti-itch, anticancer). A formulation could help shelf life, provide buffering capability in the stomach, make the medicine taste better, or be part of a design for time release of the drug into the blood stream. The first question to ask is what problem are you trying to solve? Do you want to identify the ingredients or understand the effectiveness of a drug coating or packaging material? Are you trying to determine effective shelf life? X-ray diffraction analyses are used in all these applications.

XRD can be used to unambiguously characterize the composition of pharmaceuticals. An XRD pattern is a direct result of the crystal structures that are present in the pharmaceutical under study. As such, the parameters typically associated with crystal structure can be simply accessed. For example, once an active drug has been isolated, an indexed X-ray powder diffraction pattern is required to analyze the crystal structure, secure a patent, and protect the company's investment. For multicomponent formulations, the actual percentages of the active ingredients in the final dosage form can be accurately analyzed in situ, along with the percentage of any amorphous packing ingredients used.

XRPD continues to be an indispensable analytical technique supporting a wide variety of pharmaceutical development activities. XRD has a broad range of applications in various stages of drug development and manufacturing, such as active pharmaceutical ingredient (API) characterization and identification. API characterization is more commonly applied during drug development, while API identification is directed more towards manufacturing, regulatory aspects, and intellectual property (Ivanisevic et al., 2010).

Solid form screening, the activity of generating and analyzing different solid forms of API, has become an essential part of drug development. The multistep screening process needs to be designed, performed, and evaluated carefully, since decisions made based on the screening may have consequences on the whole life cycle of a pharmaceutical product. The selection of the form for development is made after solid form screening. The selection criteria include not only pharmaceutically relevant properties, such as therapeutic efficacy and processing characteristics, but also intellectual property (IP) issues (Aaltonen et al., 2009). Basic principles of solid form screening are reviewed, including the methods used in experimental screening (generation, characterization, and analysis of solid forms, data mining tools, and high-throughput screening technologies) as well as basics of computational methods. Differences between solid screening strategies between brand and generic pharmaceuticals by various manufacturers are discussed by Aaltonen et al. (2009).

Solid form screening is commonly performed to find a candidate with optimal properties for early development or to find a form with different properties to improve a formulation in later development. A variety of screens can be performed including polymorph, salt, co-crystal, amorphous, and amorphous dispersion. XRPD is commonly used at various stages of screening to identify and characterize new forms. It is also used to help evaluate other properties, such as physical stability and manufacturability, in order to choose the best form for development (Newman, 2011). The author discusses the use of XRPD during screening and form selection of pharmaceutical materials.

Solid phase transitions such as polymorph interconversions are routinely examined by XRPD using variable temperature sample stages (VT-XRPD). Both sub-ambient and elevated temperature stages are available. While thermal techniques such as differential scanning calirometry (DSC) and thermogravimetric analysis (TGA) are also widely used for these studies, VT-XRPD permits the direct identification of crystalline phase as a function of temperature. Most pharmaceutical laboratories rely on both technologies. Indeed, instruments are available that permit simultaneous XRPD and DSC sample analyses (Kishi, 2011).

VT-XRPD is also widely used to study the thermal stabilities of pharmaceutical hydrates. Borghetti et al. (2012) characterized the flavonoid quercetin obtained from three different commercial suppliers by a variety of analytical techniques including VT-XRPD. Three samples of quercetin raw materials were characterized employing VT-XRPD, scanning electron microscopy (SEM), Raman spectroscopy, simultaneous thermogravimetry and infrared spectroscopy, and differential scanning calorimetry, in order to determine their physicochemical properties, specially thermal stability in the solid state. The results demonstrated that the raw materials of quercetin analyzed present distinct crystalline structures, ascribed to the different degree of hydration of their crystal lattice. The thermal stability of these quercetin raw materials in the solid state was highly dependent on their degree of hydration, where quercetin dihydrate (QCT) was thermodynamically more stable than the other two samples.

XRPD is also commonly used to investigate the structure of variable hydrates, which are crystalline species that contain non-stoichiometric amounts of water held within channels present in the crystal lattice. The amount of water present in a variable hydrate is typically a function of the relative humidity (RH) environment of the sample. Since the XRPD peak positions are directly related to the dimensions of the unit cell, subtle changes in the size of the unit cell due to the presence of water may be evaluated by comparison of XRPD patterns collected for the species under different RH environments. In certain systems, an increase in a particular lattice parameter may be a direct function of the amount of water present in the hydrated structure (Vogt and Williams, 2010).

Suzuki et al. (2012) used XRPD along with with other techniques to determine the structure of the variable hydrate of sitafloxacin hydrate. Sitafloxacin (STFX) hydrate is a non-stoichiometric hydrate. The hydration state of STFX hydrate varies non-stoichiometrically depending on the relative humidity and temperature, although XRPD of STFX hydrate was not affected by storing at low and high relative humidities. The detailed properties of crystalline water of STFX hydrate were estimated in terms of hygroscopicity, thermal analysis combined with X-ray powder diffractometry, crystallography, and density functional theory (DFT) calculation. Single-crystal X-ray structural analysis showed that two STFX molecules and four water molecule sites were contained in an asymmetric unit.

XRPD may also be used to probe the hydration states of noncrystalline materials. For example, the structure of the common excipient poly(vinylpyrrolidone) (PVP) was analyzed by XRPD after equilibration under various RH environments (Teng et. al., 2010). To examine the effects on molecular scale structure due to polymer chain length and water sorption, different molecular weights of PVP were studied at ambient temperature and different controlled relative humidities. Sorption of water determined gravimetrically on drying and changes to the glass transition temperature (T_g) measured by modulated differential scanning calorimetry (mDSC) were found to be consistent with previous reports. The XRPD results show that the position of the high- and low-angle halos for PVP change with the sorption of water. The corresponding characteristic scattering distances display a strong correlation with the measured water content and to T_g. Chemometric analysis was also performed to extract water content information from XRPD data and the results obtained were correlated with the values measured gravimetrically, which lends support to the apparent clustering of water in PVP drawn by other techniques.

Recent advances in the performance of XRPD instrumentation (particularly with respect to peak resolution) permit the use of data obtained from conventional laboratory diffractometers. In addition, the development of direct-space methods for structure solution require only that the XRPD peak shape and width functions of the XRPD patterns be accurately defined (Harris, 2012).

These techniques were also applied to obtain crystal structures for three out of five polymorphs of *m*-aminobenzoic acid (Williams et al., 2012). Given the importance of the phenomenon of polymorphism from both fundamental and applied perspectives, there is considerable interest in the discovery of new systems that exhibit abundant polymorphism. The preparation strategies and structural properties of three new polymorphs of *m*-aminobenzoic acid (*m*-ABA) were reported, elevating this system to the rare class of polymorphic systems with at least five known polymorphs. The crystal structures of the three new polymorphs were determined directly from powder X-ray diffraction data, using the direct-space genetic algorithm technique for structure solution followed by Rietveld refinement, demonstrating the opportunities that now exist for determining crystal structures when crystals of sufficient size and quality for single-crystal X-ray diffraction are not available. The assignment of the tautomeric form in each polymorph was confirmed by X-ray photoelectron spectroscopy.

Forensic Science

Chemical analysis of forensic "specimens" usually means identification and/or comparison. However, the specimens differ from most of those encountered in other situations in that they constitute evidence, and as such should be preserved. Powder diffraction is a nondestructive process, and is therefore well suited to forensic analysis. It is also versatile and can be used for analyzing organic, inorganic, and metallic specimens, and, qualitatively and quantitatively, mixtures of these materials.

A prime example of its value is in the analysis and comparison of street narcotics seizures, which, in addition to the drug itself, will invariably contain excipients or adulterants. Some of these compounds will have been added deliberately by the dealer in order to render the drugs more palatable and of course to maximize profit. In doing so, however, he is creating an analytical "signature" or profile that can be useful in tracing individual drug seizures to a common source—the dealer. The more chemical components identified in an individual seizure, the greater the evidential value of a match between numbers of chemically identical seizures. In addition, many drugs, and certain excipients or adulterants, exist in different polymorphic forms, hydrated forms, and optically active or racemic forms, and each variation may be successfully differentiated by powder diffraction, adding to the evidential value of the analysis. The opium poppy

Papaver somniferum is the source of the narcotic analgesics morphine and codeine. Salutaridine reductase (SalR; EC 1.1.1.248) reduces the C-7 keto group of salutaridine to the C-7 (*S*)-hydroxyl group of salutaridinol in the biosynthetic pathway that leads to morphine in the opium poppy plant. *P. somniferum* SalR was overproduced in *Escherichia coli* and purified using cobalt-affinity and size-exclusion chromatography. Hexagonal crystals were obtained using ammonium sulfate as precipitant and diffracted to a resolution of 1.9 Å (Higashi et al., 2010).

The result of cooperation between a police forensic laboratory and an academic institution highlights the possibility of applying single-crystal X-ray diffraction analysis as an effective method of identifying designer drugs in forensic analysis. The description of the relationship between the geometrical parameters of moieties and the analysis of intermolecular interactions occurring in crystals of the title compounds extends knowledge about the synthetic derivatives of cathinone and may play a role in future studies, leading to a better understanding of their characteristic properties (Trzybinski et al., 2013).

The possibility of discriminating between sheets of paper can be of considerable importance in questioned document examinations. Nineteen similar types of office paper were characterized by infrared spectroscopy and X-ray diffraction to determine the most discriminating features that could be measured by these techniques. The discriminating value associated with them was also assessed. By using a sequence of these two techniques, all the samples could be differentiated (Causin et al., 2010).

Powder X-ray diffraction (PXRD) is used widely in forensic science laboratories with the main focus on qualitative phase identification and validation of PXRD in the field of forensic sciences. According to the standard EN ISO/IEC 17025, the method has to be tested for several parameters. Trueness, specificity, and selectivity of PXRD were tested using certified reference materials or a combination thereof. All three tested parameters showed the secure performance of the method. Sample preparation errors were simulated to evaluate the robustness of the method. These errors were either easily detected by the operator or nonsignificant for phase identification. In case of the detection limit, a statistical evaluation of the signal-to-noise ratio showed that a peak criterion of three sigma is inadequate, and recommendations for a more realistic peak criterion are given (Eckardt et al., 2012).

XRD in forensic science is used mainly in contact trace analysis. Examples of contact traces are paint flakes, hair, glass fragments, soils, stains of any description, and loose powdered materials. Identification and comparison of trace quantities of material can help in the conviction or exoneration of a person suspected of involvement in a crime.

Soils may constitute evidence that connects a person or object to a particular location. The value of soil stems from its ubiquity and transferability to objects or persons. Due to the complexity of soil, the analysis of its inorganic and organic components can provide complementary and independent types of information about its geological origin, dominant vegetation, management, and environment. Dawson and Hillier (2010) present an overview of a range of soil characterization methods including chemical analysis, mineralogy, and palynology, along with new approaches such as DNA profiling and profiling of other digital data such as that obtained from X-ray powder diffraction, infrared spectroscopy, and organic marker analysis. Individual analytical techniques have different scales of resolution and relevance depending on the nature of the criminal case and context. Each method has its strengths and weaknesses. As more methods have become digital and quantitative, their use in combination as digital profiles will help to characterize soils more accurately and at different scales.

These new approaches can be tested using existing soil databases, and database development and use will help to refine and narrow probable origin of a questioned sample in police intelligence, as well as giving increasingly robust sample comparisons for evidence (Dawson and Hillier, 2010).

In view of the difficulties in extracting quantitative information from burned bone, a study suggested a new and accurate method of determining the temperature and duration of burning of human remains in forensic contexts (Piga et al., 2009). Application of powder X-ray diffraction to a sample of human bone and teeth allowed their microstructual behavior, as a function of temperature (200°–1000°C) and duration of burning (0, 18, 36, and 60 min), to be predicted. The experimental results from the bones and teeth determined that the growth of hydroxylapatite crystallites is a direct and predictable function of the applied temperature, which follows a nonlinear logistic relationship. This will allow the forensic investigator to acquire useful information about the equilibrium temperature brought about by the burning process and to suggest a reasonable duration of fire exposure (Piga et al., 2009).

Conservation science relies on measurements of physical and chemical properties. In Europe in recent decades, noninvasive (integrity of the object is preserved, no sampling is necessary) and nondestructive microanalytical (sample is taken, but analyzed as is, not consumed or modified) methods have been widely tested in the cultural heritage field, especially in the case of paintings. This growing trend can easily be demonstrated by the increasing number of publications in top-impact analytical journals. Current developments can be divided into two directions:

- Developments in physical principles and instrumentation, e.g., portable instruments (Grieten and Casadio 2010; Miliani et al., 2010).
- Developments in measuring and interpretation strategies, including unconventional approaches (Cardell et al., 2009; Palmieri et al., 2011).

The uniqueness and limited amounts of forensic samples and samples from objects of cultural heritage together with the complexity of their composition require the application of a wide range of microanalytical methods that are nondestructive to the samples, because these must be preserved for potential later revision. Laboratory powder

X-ray micro-diffraction (micro-XRD) is a very effective nondestructive technique for direct phase analysis of samples smaller than 1 mm containing crystal constituents. It complements optical and electron microscopy with elemental microanalysis, especially in cases of complicated mixtures containing phases with similar chemical composition. However, modification of X-ray diffraction to the microscale together with its application for very heterogeneous real samples leads to deviations from the standard procedure (Švarcová et al., 2010).

Geological Applications

XRD is the key tool in mineral exploration. Mineralogists have been among the foremost in developing and promoting the new field of X-ray crystallography after its discovery. Thus, the advent of XRD has literally revolutionized the geological sciences to such a degree that they have become unthinkable without this tool. Nowadays, any geological group actively involved in mineralogical studies would be lost without XRD to unambiguously characterize individual crystal structures. Each mineral type is defined by a characteristic crystal structure, which will give a unique X-ray diffraction pattern, allowing rapid identification of minerals present within a rock or soil sample. The XRD data can be analyzed to determine the proportion of the different minerals present.

The surface layer of soil, consisting of a mixture of mineral and organic matter, reflects the nature and properties of the soil. Weathering of the minerals of the earth's crust originally derived most of the substances, including plant nutrients. Among various substances, clay is an important soil constituent that controls its properties and also influences its management and productivity. In addition to commercial applications of clay minerals, they have great potential to fix pollutants such as heavy metal organics and play an important role in cleansing the biosphere. Despite the fact that excess clay induces unfavorable properties and requires more energy for tillage operation, clay immensely improves soil fertility. Thus, it is important to carry out quantitative and qualitative analysis of clay minerals in soil. X-ray diffraction has shown to be one of the best tool for the identification and quantification of minerals present in soil (Shrivastava, 2009).

In another study the sand deposits from River Niger in Anambra State, southeastern Nigeria, were characterized for their potential utilization as industrial raw materials for ceramics and enamel wares. Physical, chemical, and mineralogical characteristics of the sand sample were determined. XRD was used in the mineralogical characterization. Results obtained were analyzed using the Bragg-Wolf equation and International Centre for Diffraction Data software. The results showed that the sample contained phyllosilicate minerals of the mica group and was identified as shirozulite (KMn_3 $[Si_3Al]O_{10}[OH]_2$), a new manganese with dominant monoclinic arrangement. The physicochemical analysis of the deposits confirmed the XRD results. It was concluded that the samples could be utilized as industrial raw materials for ceramics and enamel wares (Eunice et al., 2013).

X-ray diffraction analysis of black shale of the Upper Triassic Member Chang 7 of the Yanchang Formation in the southeastern Ordos Basin, China, showed that black shales were deposited in brackish, strongly reducing, semi-deep/deep lacustrine facies and were mainly composed of quartz, feldspar, carbonate (dolomite), clay minerals (illite and illite/smectite), and a certain amount of pyrite. The mineral composition characteristics of this set of black shales are similar to those of highly productive shale gas in North America, for example, shallow burial, low clay mineral and abundant brittle mineral, so the strata are conducive to the development of cracks and fractures. Thus, this area is favorable for shale oil/gas exploration and development (Yao et al., 2014).

Andreeva et al. (2011) studied Middle Devonian (Givetian) dolomites occurring in three well sections, OP-2 Mihalich, R-119 Kardam, and R-1 Vaklino (northeastern Bulgaria). Two general genetic dolomite groups were distinguished and interpreted on the basis of performed XRD analyses and petrographic observations. The first group is represented by early diagenetic crypto- to microcrystalline dolostones that are characterized by nearly stoichiometric composition (from 51.0 to 51.7 mole % $CaCO_3$) and degree of order ranging from 0.50 to 0.91. They were interpreted as products of rapid precipitation in an arid peritidal (sabkha) environment with hypersalinity of the water milieu and elevated Mg/Ca ratio of the dolomitizing solutions. The second group includes late diagenetic medium crystalline dolostones that have almost stoichiometric composition (from 50.0 to 51.3 mole % $CaCO_3$) and higher degree of order (from 0.77 to 1.18), indicating a possible slow crystallization process and precipitation from dilute solutions at elevated temperatures in an open diagenetic system. A part of them might have also resulted from neomorphic alteration of precursor metastable dolomite phases.

Microelectronics Industry

Since the microelectronics industry uses silicon and gallium arsenide single-crystal substrates in integrated circuit production, there is a need to fully characterize these materials using XRD. XRD topography can easily detect and image the presence of defects within a crystal, making it a powerful nondestructive evaluation tool for characterizing industrially important single-crystal specimens.

The engineering of strained semiconductor materials represents an important aspect of the enhancement of complementary metal-oxide semicondictor (CMOS) device performance required for current and future generations of microelectronic technology. An understanding of the mechanical response of the silicon (Si) channel regions and their environment is key to the prediction and design of device operation. Because of the complexity of the composite geometries associated with microelectronic circuitry, in situ characterization at a submicron resolution is necessary to verify the predicted strain distributions. Of the measurement techniques commonly used for strain characterization, synchrotron-based X-ray microbeam diffraction represents the best nondestructive method to provide spatially resolved information. The mapping of strain distributions in silicon-on-insulator (SOI) features induced by overlying silicon nitride structures and embedded heteroepitaxial features adjacent to SOI device channels were presented (Murray et al., 2010). The interaction regions of the SOI strain were observed to extend large distances from the SOI/stressor interfaces leading to significant overlap in the strain distributions at technically relevant dimensions. Experimental data were also compared to several mechanical models to assess their validity in predicting these strain distributions.

Recent development of bright X-ray sources, reliable X-ray focusing optics, large X-ray detectors, and X-ray data modeling and processing have improved X-ray techniques to the point where many are being introduced in metal-on-silicon (MOS) transistor manufacturing lines as new metrology methods. The fudamental physical properties of X-rays, such as their small wavelength and their weak interaction with solid-state matter, satisfy basic in-line metrology requirements: nondestructiveness, speed, accuracy, reliability, and long-term stability. The capability of X-ray–based metrology methods to monitor critical 65 and 45 nm processes such as ion implant, nitrided SiO_2 gate dielectrics, NiSi, Cu/porous low-κ interconnects, and metal-insulator-metal (MIM) capacitors was highlighted (Wyon, 2010).

Interfacial microstructures of thermosonic Au wire bonding to the Al pad of a die were investigated first by high-resolution transmission electron microscopy (HRTEM) and X-ray micro-diffractometry. The equal-thickness interference structures were observed by HRTEM due to diffusion and reaction activated by ultrasonic and thermal methods at the Au/Al bond interface. X-ray diffraction results showed that three different interplanar crystal spacings ("d" value) of the interfacial microstructures were 2.2257, 2.2645, and 2.1806 Å respectively from the high intensity of diffraction to the low intensity of diffraction. These indicated that the intermetallic phase $AlAu_2$ formed within a very short time. It would be helpful to further research wire bonding technology (Li et al., 2011).

The manufacture of ultra-large-scale integration technology can impose significant strain within the constituent metallization because of the mismatch in coefficients of thermal expansion between metallization and its surrounding environment. The resulting stress distributions can be large enough to induce voiding within Cu-based metallization, a key reliability issue that must be addressed. The interface between the Cu and overlying capping layers is a critical location associated with void formation. By combining conventional and glancing-incidence X-ray diffraction, depth-dependent stress distributions that develop in Cu films and patterned features were investigated. In situ annealing and as-deposited measurements revealed that strain gradients were created in capped Cu structures, where an increased in-plane tensile stress was generated near the Cu/cap interface. The interplay between plasticity in Cu and the constraint imposed by capping layers dictates the extent of the observed gradients. Cu films possessing caps deposited at temperatures where Cu experienced only elastic deformation did not exhibit depth-dependent stress distributions. However, all capped Cu samples exposed to temperatures that induce plastic behavior developed greater tensile stress at the Cu/cap interface than in the bulk Cu film after cooling, representing a clear concern for the mitigation of metallization voiding (Murray et al., 2012).

Glass Industry

While glass is X-ray amorphous and does not itself give X-ray diffraction patterns, there are still manifold uses of XRD in the glass industry. They include identification of crystalline particles that cause tiny faults in bulk glass and measurements of crystalline coatings for texture, crystallite size, and crystallinity.

The effects of high pressures on the structure of silica glass have been elucidated using high-energy X-ray diffraction up to 43.5 GPa. A decrease in the first two peak positions in the real-space pair-distribution functions up to 15 GPa indicates initial shrinkage of the tetrahedral units. Above this threshold pressure the Si-O bond peak shape becomes asymmetric and the average Si-O bond length and coordination number both increase linearly with pressure. Also, strained geometries in the O—O correlations lead to a pronounced topological rearrangement of the second and third nearest neighbors (Benmore et al., 2010).

The crystallization behavior of aluminosilicate glasses of lanthanum, yttrium, and scandium was studied by differential thermal analysis (DTA), XRD, scanning electron mscroscopy-energy dispersive X-ray (SEM-EDX), and electron probe microanalysis (EPMA). Young's modulus E and hardness H were measured by using nano-indentation and elastic modulus C_{11} and C_{44} by Brillouin scattering. The Young's modulus measured by nano-indentation agreed with those determined by Brillouin scattering and those calculated using Makishima-Mackenzie and Rocherullé model's. The results of DTA analysis indicated that (a) the glass transition temperatures T_g are higher for yttrium- and scandium-containing glasses than for their lanthanum counterparts, the melting observed in the yttrium glasses and recently in the scandium glasses correspond to the ternary eutectic Ln_2O_3-Al_2O_3-SiO_2 (Ln = Y, Sc) and (b) the thermal stability is strongly related to the ionic radii of the rare earth. The last results obtained on scandium-containing glasses confirmed this hypothesis. The XRD results showed that the nature of the observed crystallized phases is consistent with the phase diagrams (Sadiki et al., 2010).

Molecular dynamics simulations and complementary neutron and X-ray diffraction studies were carried out within the single-phase glass-forming range of $(Y_2O_3)_x(Al_2O_3)_{(100-x)}$ for $x = 27$ and 30. An R-factor analysis showed that the simulation models agreed to within ~6% of the diffraction data in both cases. The Al–O polyhedra are dominated by four- and fivefold species, and the Y–O local coordinations are dominated by six-, seven-, and eightfold polyhedra. Analysis of the oxygen environments revealed a large number of combinations, which explains the high entropy of single-phase yttrium aluminate glasses and melts. Of these, the largest variation between $x = 27$ and 30 was found in the number of aluminum oxygen triclusters (oxygens bonded to three Al) and oxygens surrounded by three Y and a single Al. The most abundant connections are between the AlO_x and YO_y polyhedra, of which 30% are edge shared. The majority of AlO_x–AlO_x connections were found to be corner shared (Du et al., 2009).

A high-energy X-ray diffraction study was carried out on a series of $0.5Li_2S + 0.5[(1 - x)GeS_2 + xGeO_2]$ glasses with $x = 0.0$, 0.1, 0.2, 0.4, 0.6, and 0.8. Structure factors were measured to wave vectors as high as 30 Å^{-1} resulting in atomic pair distribution functions with high real space resolution. The three dimensional atomic-scale structure of the glasses was modeled by reverse Monte Carlo simulations based on the diffraction data. Results from the simulations show that at the atomic-scale $0.5Li_2S + 0.5[(1 - x)GeS_2 + xGeO_2]$ glasses may be viewed as an assembly of independent chains of $(Li^{+-}S)_2GeS_{2/2}$ and $(Li^{+-}O)_2GeO_{2/2}$ tetrahedra as repeat units, where the Li ions occupy the open space between the chains. The new structure data may help understand the reasons for the sharp maximum in the Li^+ ion conductivity at $x \sim 0.2$ (Messurier et al., 2009).

Nasu et al. (2009) investigated the micro-mechanism of deformation behavior of metallic glasses. The authors reported the results of direct observations of short-range and medium-range structural change during tensile deformation of metallic glasses by the high energy X-ray diffraction method. $Cu_{50}Zr_{50}$ and $Ni_{30}Zr_{70}$ metallic glass samples in a ribbon shape (1.5 mm width by 25 μm) were made using the rapid quenching method.

Tensile deformation added to the sample was made by using special equipment adopted for measuring the high energy X-ray diffraction. The peaks in pair distribution function g(r) for $Cu_{50}Zr_{50}$ and $Ni_{30}Zr_{70}$ metallic glasses moved in a zigzag into the front and rear during tensile deformation. These results of direct observation on atomic distribution change for $Cu_{50}Zr_{50}$ and $Ni_{30}Zr_{70}$ metallic glass ribbons during tensile deformation suggest that micro-relaxations occur.

Corrosion Analysis

XRD is the only analytical method that readily provides information about the phase composition of solid materials.

The most important, versatile, and widely used method for corrosion protection of steelwork is by paint or organic coatings. Information on the microscopic level for a protective coating is essential to understand the basic determinants of its attributes and improvement requirements. Bitumen has been an important material for the protection of steelwork in the world's petroleum and other chemical and water industries. Bitumen is, however, attended with some undesirable characteristics, and it can vary widely in quality from one source to another. Results show that about 3.75 to 4.847% of each coating is constituted of 5 to 7 of 14 listed different mineral phases, and there is variation in quantity and types of these phases even in coatings produced at the same temperature with bitumen from the same source (Guma et al., 2012).

Three bronze vessels from the ancient Chinese art collection at the Art Institute of Chicago were examined with the advanced noninvasive characterization capabilities of high-energy synchrotron X-ray diffraction performed at the Advanced Photon Source of Argonne National Laboratory to create a comprehensive overview of each object's manufacture as well as subsequent corrosion processes. Findings were also complemented with traditional noninvasive characterization techniques, including optical imaging, X-ray radiographic imaging, and X-ray fluorescence (XRF) spectrometry. The results, obtained without sampling, allow a clear distinction between genuinely ancient Chinese bronzes and those with modern restorations and "archaistic" objects made many centuries later in emulation of ancient styles (Young et al., 2010).

The inhibition behavior of *Momordica charantia* seeds extract (MCSE) as an environmentally benign corrosion inhibitor for J55 steel was investigated in 3.5 wt.% NaCl saturated with CO_2 solution by means of polarization curve, AC impedance, and XRD. The results showed that MCSE can inhibit the corrosion of J55 steel. The maximum inhibition efficiency was achieved when MCSE concentration was 1000 ppm by weight in this study. The adsorption of the studied inhibitor obeyed the Langmuir adsorption isotherm (Singh et al., 2013).

Corrosion ID can help to locate the origin of corrosion in a facility and, at the same time, provide solutions to the problem. The formation of scale deposits (e.g., corrosion deposits, formation materials, reaction products, catalysts, and refractory materials) in sulfur recovery unit process equipment is one of the major operational problems in the oil and gas industry. Thick deposits of various types of mineral scale can grow within these units. Subsequently, these deposits end up adversely affecting the production rate and quality. Zaidi et al. (2012) conducted a study of 13 types of scale deposits that built up in different regions of the equipment (converter, condenser, and vessel) using XRD, which is the best available technique for the identification and quantification of all compounds present in deposits. Additionally, the recent application of the Rietveld refinement method in XRD quantitative phase analysis has produced great advantages over conventional methods, such as the reference intensity ratio method, in accuracy and convenience. The refinement results showed that while iron oxide (magnetite and hematite) corrosion products were found in the steam drum, several case studies show that sulfates (iron, sodium, and ammonium) are the major deposit compounds built up in the condenser. A high weight percentage of hematite indicated the presence of dissolved oxygen in the boiler feed water. The deposits accumulated in the converter are titanium and aluminum oxide, which indicates the leakage of a catalyst. Sulfur and carbon were also detected from the line. The findings will help engineers to overcome the problems by devising the right corrective procedures.

Conclusion

X-ray diffraction (XRD) is an analytical technique used to characterize crystalline phases of a wide variety of materials, typically for mineralogical analysis and identification of unknown materials. Powder diffraction data are fundamentally derived by the atomic and molecular arrangements explained by the physics of crystallography.

There are several advantages of XRD techniques in science laboratories:

- Nondestructive, fast, and easy sample preparation
- High-accuracy for d-spacing calculations
- Can be done in situ
- Allows characterizing single crystal, poly, and amorphous materials
- Standards are available for thousands of material systems

In the past few years, powder XRD systems have become more and more efficient for the pharmaceutical industry due to innovations and improvements in detection and source emission technology. X-ray diffraction methods are especially significant for the analysis of solid materials in forensic science. They are often the only methods that allow a further differentiation of materials under laboratory conditions.

Minerals are the building blocks of the solid Earth. Some minerals are readily recognized by their distinctive colors or crystal forms, but in most cases, powder X-ray diffraction is the primary and most definitive method used to identify minerals. The high flux and density of X-rays produced at synchrotrons provide the microelectronics industry with a powerful probe of the structure and behavior of a wide array of solid materials that are being developed for use in devices of the future. X-ray diffraction studies are also used to obtain information on the short and intermediate range structure of glasses.

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