

POWDER DIFFRACTION CRYSTALLOGRAPHY: 98 YEARS AS PLAN B?

Brian H. Toby

Advanced Photon Source, Argonne National Laboratory, Argonne, Illinois 60539 (USA)

Preface: *This essay was written in 2014, which was celebrated as the centenary for crystallography, to accompany a talk provided for the Transactions Symposium, “100 Years of Crystallography” at that year’s American Crystallographic Association annual meeting ([on line here](#)). Both the talk and essay were intended to show that powder diffraction has a history almost as long as that of single-crystal diffraction; that its invention was motivated from many of the same goals, though it can be argued in hindsight that powder diffraction provides more types of information than its older sibling. I explored this through my own perspective on the highlights of nearly a century’s advances.*

While historical events do not change, our interpretation of them sometimes does. Since that time, there have been significant discussions on the history behind what is now known as Rietveld Analysis. It is certainly true that in the mid-1960’s crystallographic analysis from powder diffraction was to see a major advance when a group at the Reactor Centrum Nederland in Petten comprised of Bert Loopstra, Bob van Laar and later Hugo Rietveld considered the peak overlap problem (1). Building on initial Italian work in describing how peak widths changed for constant-wavelength (CW) neutron diffractometers (2), they deployed “profile decomposition” [using the nomenclature of Young (3)] to determine intensities of overlapped reflections (4), which led the development of a method for the fitting of crystallographic parameters, as well as experimental and sample parameters that dictate peak shapes (5). However, it was Hugo Rietveld who developed a computer program (6) to implement crystallographic model fitting specifically to neutron powder diffraction patterns, which was rapidly adopted by the Petten group in their crystallographic work (7, 8). Rietveld would later redevelop his code to be more accessible and he documented it and distributed it widely. While that later work was never reported in the literature, this code was used as a starting point for the work of many others, for example for fitting to x-ray diffraction (9) and to pulsed-neutron diffraction (10, 11). As discussed further in the International Tables (12), I use the term Rietveld Analysis intentionally and in tribute to a kind and gracious scientist who I am proud to have met, but alas on too few occasions. Hugo died in 2016. BHT 12/2020.

ABSTRACT: Powder diffraction patterns were used for structure solution almost contemporaneously with the Bragg’s initial single-crystal determinations. Structures have continued to be determined from powders, in the subsequent century. There has been a nearly explosive growth in this technique since the 1970’s. This was initially driven by neutron diffraction, which prompted the invention of Rietveld analysis, but synchrotrons have gone on to have at least as large an impact. There is no apparent upper limit to the scale of systems that can be structurally studied with powder diffraction; novel protein structures have been determined. When short-range ordering or disordered regions of a material are of interest, the Fourier transform of a powder diffraction pattern, the pair distribution function can be modeled.

INTRODUCTION

Within the context of this discussion, the term powder diffraction crystallography is intended to cover where structural analysis is performed from diffraction measurements from a polycrystalline specimen, that is composed of a large number of crystals, as opposed to diffraction from an individual single-crystal specimen or a small number of twins.

In this centenary celebration of crystallography, it is worth noting that powder diffraction is almost as old as single-crystal diffraction. In fact, as will be discussed below, one can argue that powder diffraction actually goes back to the initial experiments of Friedrich, Knipping and Laue. Certainly true: the first crystallographic structure determinations from powder diffraction trailed those of the Braggs by only a few years. While powder diffraction has a great many applications outside of crystallography, it was invented for structural determination. The techniques utilized for structural study from single crystals have evolved in a steady fashion over this last century; we have seen an explosion of new capabilities for powder diffraction structural study just in the most recent decades. The instrumental and analysis technique improvements in this period have resulted in a significant increase in the complexity of materials characterized with powder diffraction, as well as the number of structures determined. This article will provide a very subjective history of powder diffraction crystallography, focusing on some of the developments with which this author is most familiar. For a more comprehensive history of powder diffraction, the reader is recommended to Chapter 4 of H. Klug and L. Alexander's book or the excellent comprehensive historical article by W. Paszkowicz (13, 14). It should also be noted that electron diffraction has advanced considerably in the last few years as a method for structure determination, both as a standalone technique and combined with more traditional methods (15). This area warrants a separate review.

THE EARLY DAYS

As is well known, single-crystal diffraction was first demonstrated by Max von Laue (then Max Laue) and co-workers in 1912 (16). Almost immediately, news of this experiment reached the father-and-son team of W.H. and W.L. Bragg. They replicated the experiment, but with the improvement of a monochromatic x-ray source, thanks to the availability of Bragg senior's x-ray spectrometer. By the next year, the structures of materials were first demonstrated (17, 18). Shortly after, during the early days of World War I, Peter Debye and his student Paul Scherrer in Germany and early industrial scientist Albert Hull in the United States began looking at diffraction from powder specimens and both used this technique to determine structures of materials where they could not obtain single crystals. However, even in the initial Friedrich-Knipping-Laue experiment, diffraction from a single crystal was compared to that from a powdered sample to show that the characteristic single crystal reflection spots were a physical effect from the crystal rather than a chemical effect. Since that initial experiment used polychromatic x-rays, the characteristic powder diffraction rings arising from the projection of cones of scattering either were not seen or not noted, although those researchers did note rings in

subsequent early experiments. While working in Germany during the war, Debye and Scherrer had the fortune to be Dutch and Swiss citizens, respectively, or they most likely would have been called to a battlefield, where they might have met with the same fate as Robert Bragg, son/brother of WH and WL, who died in combat in 1915. The now eponymous form of powder diffraction developed by Debye and Scherrer utilized a ring of x-ray film surrounding a sample in a rotating capillary tube. (19). They used such data to determine the structure of LiF.

In the US, Albert Hull, who was employed by General Electric's research laboratories, developed a somewhat similar powder diffraction camera and used the resulting data to study structures of metals important in his work. The ethos at GE was not supportive of publication, so Hull wrote up his work in his off-hours. He published his work unaware of the Debye paper, due to the embargoes from the war (20). There is some irony in this delay, in that some decades later, GE became a major player in the commercial powder diffraction market with their XRD-5 powder diffraction instrument. Hull reported that his initial attempt to solve the crystal structure of Fe from powder diffraction failed, but later he found an assistant's arithmetic error and he did complete that study (along with many other metals of interest to GE) (21). Hull later went on to invent a number of types of important vacuum tubes including the magnetron (22); an updated version of that became very important for Radar during World War II and can be found in every kitchen, in the now ubiquitous microwave oven. The Braggs, in memory of Robert, were never happy with attributing powder diffraction to a German laboratory and always referred to it as the Hull technique.

In its early years, powder diffraction was used much the same as single crystal diffraction, where diffraction was recorded on film and intensities were estimated as weak, medium, strong, etc. Models were constructed by *ansatz*: where a scientist shows that a model matches experimental measurements without any justification or derivation of the model. By the needs of the day, agreement was largely qualitative rather than quantitative. A variety of advances such as point-detector diffractometers, Beevers-Lipson strips, mechanical, analog and later digital computers, and least-squares refinements allowed single-crystal structure analysis to become a quantitative comparison between experiment and model, the gold-standard technique it is today. Structure solution techniques such as Patterson maps and direct methods allowed for derivation of models from data rather than exclusively from the crystallographer's imagination and experience, allowing increasingly complex problems to be attacked. In contrast, techniques for powder diffraction crystallography lagged behind. Powder diffraction did see increasingly wider use and the techniques did improve. The development of the Guinier camera provided much higher resolution data than the original Debye-Scherrer device. The invention of the Bragg-Brentano parafocussing diffractometer (23), allowed collection of diffraction patterns in hours and the instrument design of William Parish for Norelco (Philips) brought down the cost of powder diffraction instrumentation considerably (24). The use of a point detector in the diffractometers allowed users to bypass the delays of the darkroom before seeing results. This would turn out to be of great value decades later, when computerized data collection became common.

Even though powder diffraction became a common laboratory measurement, the main application of these instruments was for phase identification and for quantitative phase analysis, not for crystallography. These latter applications drove scientists at Dow Chemical Company to develop a tabulation of powder diffraction patterns for materials of interest to them. In the late 1930's through the American Society for Testing Materials (ASTM) a Joint Committee for Powder Diffraction Standards was developed which created and distributed the "JCPDS" powder diffraction database as an expansion of the donated Dow catalog. Cam Hubbard, Judy Stalick and others at the National Institute for Standards and Technology (then NBS) developed the AIDS-83 computer format and data entry software program for entries in both the JCPDS and NBS-Crystal Data databases and convinced the somewhat recalcitrant successor organization to the JCPDS, the International Centre for Diffraction Data (ICDD), to place their previously on-paper database into this format. This move left the ICDD primed to provide an electronic product just as laboratory minicomputers were becoming widely available. Later, with the advent of the compact disk, the ICDD was one of the early pioneers of that format (CD-ROM) for product distribution.

NEUTRON DIFFRACTION

Nuclear reactors were developed in the 1940's as part of the World War II Manhattan Project to develop atomic weapons. While diffraction of neutrons had been observed earlier using radioactive sources, once the much greater flux from reactor sources was available, diffraction was pursued by Ernest Wollan and Harold Zinn, initially as a mechanism for separation of neutrons by wavelength (25); Wollan and Zinn went on to have influential roles as administrators at Oak Ridge and Argonne National Laboratories, respectively. Wollan, soon joined by a young Clifford Shull, began to perform crystallographic measurements with neutrons in the mid-1940s.

For neutron work, powder diffraction had several key advantages over single-crystal diffraction. Neutron single crystal measurements, until recently, required centimeter-scale crystals, which very much limited the materials accessible for study. Also, while a single-crystal measurement might require a month or two of data collection time from a very scarce instrumental resource, a powder diffraction dataset required closer to a day. It is easier to perform powder diffraction measurements under extreme conditions (temperature, pressure, chemical environment, etc.) in comparison to measurements with single crystals. Many types of these experiments, most notably with non-ambient temperatures, are still greatly facilitated by neutron probes, where metal shields are "transparent."

As is true now, powder diffraction was widely used in the early days of neutron studies. Landmark papers from Shull and coworkers demonstrate magnetic scattering – neutrons being scattered by ordered unpaired electrons due to the neutron-electron spin interaction -- were presented with powder diffraction data (26, 27). Regrettably, Wollan did not live long enough for the potential to share the 1994 Nobel Prize for neutron scattering with Bertram Brockhouse and Shull, which this discovery helped engender.

The 1960's saw a huge growth in the number of neutron sources across the world – though at no point could it be claimed these techniques became easily accessible – and virtually all such facilities included a powder diffractometer. These instruments were carefully designed, engineered to balance diffraction resolution against data collection time through use of highly mosaic monochromators and Soller collimation. This resulted in instruments with good resolution, but more importantly with highly regular Gaussian peak shapes, which will turn out to enable the next major advance in powder diffraction crystallography.

RIETVELD REFINEMENT

By the 1960's the level of single-crystal crystallographic analysis had risen to where least-squares optimization and other calculations were commonly performed, thanks to the physically massive electronic computers of the day, (which offer a tiny fraction of the memory and computing speed to be found in a contemporary mobile phone.) Crystallographers wishing to perform the same types of analyses from powder diffraction data were often stymied by overlapped reflections. The intensities of well-resolved reflections could be estimated by peak-fitting techniques, but when peaks are closely (or worse still, exactly) overlapped, all that one can estimate is the sum of intensity arising from two or more reflections. Crystallographers would most often simply omit these overlapped reflections from their analyses, a painful choice due to the paucity of reflections from data with longer wavelength sources and smaller unit cells. On occasion, motivated scientists would rewrite analysis software, where the overlap conditions for the project at hand would be explicitly integrated into the code, so that the integrated intensity for groups of reflections could be input.

Hugo Rietveld then changed everything. Initially, he demonstrated that the peak profiles from neutron powder diffraction could be well modeled (5). Shortly later, in 1969, he developed the fitting method that now bears his name, which optimized the crystallographic parameters for a model, as well as a number of experimental ones, to best fit a computed powder diffraction pattern to match the observed one (6). While many crystallographers immediately grasped the major advantage of directly fitting to an experimental measurement, others noted that the resulting parameters values and their uncertainties did not match those obtained by the tried-and-true integrated intensity methods validated by single crystal diffraction. This led some to reject this new approach. This controversy persisted until Ted Prince at the NBS (now NIST) Reactor demonstrated that the Rietveld method results were indeed correct; the parameter and uncertainty estimate differences were due to a neglect of parameter correlation with the original integrated intensity analyses. If the covariance matrix from the intensity integration were appropriately included within the secondary fit, the Rietveld analysis results were duplicated (28).

The initial computer code developed by Hugo Rietveld was written in Algol, which he later recoded in Fortran, which had then, as now, a wide following in science. That code was passed from researcher to researcher, gaining new capabilities in the process. For example, Rietveld analysis pioneer Alan Hewat introduced additional sophistication by implementing anisotropic

displacement parameters into the models (29). The extension of Rietveld analysis to x-ray powder diffraction would seem straightforward, but in truth was difficult due to the complexities of x-ray diffraction peak shapes. This was completed more than a decade later, in a program that included considerable code in the lineage that could be traced back to the original Fortran code from Hugo Rietveld (30). After this, it would still take yet than another decade before Rietveld analysis would be widely adopted by the x-ray community. Over the last decade or two, we have seen a change in the utilization of Rietveld analysis from technique used by crystallographic experts, to a tool widely used by researchers in a variety of fields for many different types of studies (31). The quality of the scientific literature has not always benefited from this change.

In the 1970's through the end of the century, many different laboratories developed their own Rietveld analysis codes, for a variety of motivations. As one example, when the NBS neutron diffractometer with 5 detectors was commissioned, a Rietveld code was developed to fit models to these overlapping datasets directly without merging (32). The RIETAN code was developed in Japan and continues to be widely used in that region (33). In this author's view, the most notable developments were: (1) the GSAS package, developed at Los Alamos National Laboratory, which allowed a set of crystallographic models to be fitted to combinations of both single-crystal and powder data, with both neutrons and x-rays (34). GSAS was one of the first time-of-flight neutron analysis implementations and may have been. GSAS may also be the first Rietveld code rewritten completely from scratch -- not recycling any of the original Fortran from Rietveld. Further, GSAS extended the power of the techniques for complex problems by allowing combined use of x-ray and neutron powder data, for problems where each one alone was inadequate, or combined used of x-ray single-crystal and neutron powder data where each was advantageous for different aspects of the structure (35, 36). (2) The FullProf program, initially from Saclay, France was designed to provide a sophisticated mechanism for determination of magnetic structures and has continued to advance the state of the art for this work (37). (3) For development of models for modulated structures, the Jana system was developed; this has proven popular even for systems where modulation is not present (38). (4) An alternate approach for fitting profiles in x-ray diffraction, known as fundamental parameters, where reflection profiles are computed directly from convolutions of various contributing effects was demonstrated (39). From this approach, the TOPAS Rietveld code was developed in the late 1990's (40). This code is also widely used, but more for its flexibility and versatility than due to an interest in fundamental parameter instrument descriptions. Rietveld analysis is commonly used for quantitative phases analysis or for accurate lattice parameter determination. (5) One widely used code, MAUD, deals specifically with the accurate determination of texture in minerals and machined materials where the crystallographic phases (often more than one) are already well known (41, 42).

This author's most highly cited work (by about an order of magnitude) is a computer program that offers only minor new capabilities, but greatly simplifies the tasks of installing, learning and using the GSAS software suite, particularly for the non-expert crystallographer (43). It is

humbling to note that this paper, with no new “science,” is one of the 50 most cited works under the keyword crystallography and is the second most highly cited paper produced by NIST. To better address the needs of non-experts performing powder diffraction crystallographic analysis, the GSAS-II package has been initiated to replace GSAS/EXPGUI (44). It is an exciting (though sometimes frustrating) project to design and develop a 21st century code for this purpose.

TIME OF FLIGHT NEUTRON POWDER DIFFRACTION

While reactor-based instruments continued to be developed and improved, most notably at the *Institut Laue-Langevin* in Grenoble, France, only a few new reactor sources were constructed since the 1970's. In contrast, another method for generation of neutrons was first proposed by Glenn Seaborg in his Ph.D. thesis, where he named this process spallation. This was first done for neutron experimentation in the early 1960's with a commercial electron accelerator, as well as in the 1970's with the Nimrod accelerator at the Rutherford Lab (Harwell, UK). The next major improvement was to switch to a proton accelerator, which was prototyped with the ZING-P and ZING-P' sources at Argonne National Lab. The first dedicated accelerator driven pulsed-neutron source was the IPNS facility at Argonne, which recycled much major equipment from the ZGS high-energy physics source and the ZING-P prototypes. IPNS operated from 1982 through 2008, never with better than modest (or perhaps starvation-level) funding, but nonetheless was always highly productive. In Britain on the Harwell site, the Isis facility was designed much more ambitiously and started operation in 1984. The courage and force of will that went into creation of that facility is amazing to me in retrospect. I heard much from friends about the meager prospects for science in U.K. in the 1970's, which, ironically, only got worse when crystallographically-trained Margaret Thatcher (a student of Dorothy Hodgkin) became prime minister through all of the 1980s. Yet, somehow, Isis was built, was operated, has been upgraded and continues to this day to be world-leading, even though it too incorporated some hardware from the 1950's era Nimrod accelerator.

Spallation is the growth direction for neutron sources. The world's two newest neutron sources, the recently completed Spallation Neutron Source (SNS) at Oak Ridge National Lab is the leading US facility and the European Spallation Source, currently under construction in Sweden, promise to be the “next big things” in neutrons.

Spallation sources deliver neutrons in short bursts (pulses) and at high energy. These neutrons must then be stripped of most of their energy (moderated). As these neutrons travel from the source to the sample, the highest energy (shortest wavelength) neutrons arrive first and the lowest energy ones later (but one hopes before the high-energy neutrons arrive from the next pulse.) This provides a different way to perform a diffraction experiment: It was shown as far back as the 1960's that one can collect an entire section of a diffraction pattern with a single detector, as intensity versus wavelength (which is measured from time it takes for the neutron to arrive) at fixed 2θ , rather than the more traditional intensity versus 2θ at fixed wavelength mode

(45). However, Rietveld refinement of such data required developing quantitative corrections for diffraction intensities (accounting for both source spectrum and detector sensitivity) as well as a model for the highly asymmetric peak shapes generated by the neutron moderator. This was demonstrated successfully with ZING-P' data just as the workhorse SEPD and GPPD diffractometers were made available at IPNS (11). These instruments did not offer terribly high resolution data, compared to other contemporary instruments, but the combination of rapid data collection, data over a wide range in Q, excellent environmental systems and an extremely motivated staff caused these instruments to be amongst the most productive in the world.

The Isis facility set its aim at a much higher target. Bill David, Richard Ibberson and others constructed an instrument named (with typical British understatement) the High Resolution Powder Diffractometer (HRPD). To achieve resolution that is still unmatched a quarter of a century after initial commissioning, the instrument was placed in a separate building, 100 m from the neutron source. This distance is long enough that the distance that longer wavelength neutrons fall due to gravity during the time they need to reach the sample becomes a design constraint. The spectacular and complex datasets from this instrument provide a real challenge to non-expert users, but offer enough observations to take on some extremely complex studies.

TOF powder diffractometers tend to have large numbers of detectors surrounding the sample, to take best advantage of the relatively small number of neutrons that arrive at the instrument. This in turn is highly advantageous for measurement of texture in materials and several instruments have been built dedicated to that. Likewise, since TOF instrumentation can offer excellent resolution, this makes the technique beneficial for measurement of small lattice shifts due to strain, or broadening due to residual stress. Again, dedicated instrumentation for these measurements is advantageous.

SYNCHROTRON POWDER DIFFRACTION

The x-rays produced by electron beam accelerators, particularly those where the electron beam was magnetically deflected to send the beam in a circular path, were initially considered as a nuisance. Starting in the 1970's synchrotrons (now more correctly termed storage rings) began to be used intentionally for x-ray production. This was led in the U.S. by two high-energy physics facilities, the Stanford linear accelerator (SLAC), and the Cornell high-energy synchrotron source (CHESS). Both were constructed for high-energy physics experimentation, but were later made available for so-called "parasitic operation" as x-ray sources, particularly when this did not inconvenience the high-energy physics program and could bring in extra revenue. During these early days, several powder diffraction experts including William Parrish (by then at IBM) and David E. Cox of Brookhaven began making powder diffraction measurements at synchrotron facilities. These were difficult endeavors, because in a matter of days, the experimenters needed to bring in all instrumentation, assemble and align it, diagnose and fix problems and then complete desired measurements; sleep was at best optional.

Some of the benefits of synchrotron sources were obvious. Synchrotrons offer a wide range of accessible wavelengths, allowing scattering experiments near selected absorption edges. Their high intensity and highly collimated beams held the potential for superb statistical accuracy in measurements. David Cox, perhaps due to his neutron scattering background, where monochromator mosaicity would be increased to provide the desired resolution, also foresaw that use of a perfect crystal monochromator *and* a perfect crystal analyzer would offer the ultimate in diffraction resolution, as well as offer complete rejection of fluorescence and scattering other than in the region of the sample. In effect, the narrow Darwin width of a perfect-crystal analyzer can be considered as a very narrow Soller collimator that also provides energy discrimination.

When a synchrotron facility was constructed specifically as a dedicated x-ray source, *i.e.* the National Synchrotron Light Source (NSLS) at Brookhaven, Dave Cox lead a team of academic and industrial scientists in the construction of the first dedicated synchrotron powder diffractometer (46). This operated in two modes, one with a broad spectrum of x-rays (“white-beam”) for energy-dispersive diffraction, most valuably from samples at high pressures inside diamond anvil cells and the other mode with a monochromatic beam and an analyzer crystal for very high-resolution data. The disadvantage of this latter technique is that nearly all of the x-rays are rejected by the optics, so that a single scan required close to a day. One approach to improve upon this was to replace the analyzer crystal and point detector with a position-sensitive linear detector (47). With a very small diameter sample, excellent resolution could still be obtained, but the background rejection from the analyzer was lost.

The highly productive NSLS powder diffraction instruments inspired a new generation of dedicated perfect-crystal optic powder diffractometers. This was done first at the European Synchrotron Radiation Facility (ESRF) in Grenoble, France with nine analyzer-detectors operating in parallel, as well as with a brighter source, to bring down data collection times (48, 49). That design concept has now been repeated for instruments in England, Switzerland, Australia, Spain and the United States. The US instrument can be operated in a highly automated fashion, allowing experimenters to simply ship their samples to the synchrotron rather than travel there to perform the measurement, without creating significant demands on beamline staff (50). This mail-in data collection mode greatly opens access to the facility for the research community and has allowed the high-resolution powder diffraction instrument to achieve the highest publication rate of any instrument in that synchrotron.

Electronic area detection revolutionized single-crystal diffraction as soon as it became available, greatly improving data collection times in comparison to point detectors. In contrast, it took longer for powder diffraction to adopt area detection. Geometric resolution demands for single crystal work are relatively minimal, since the reflections are spread out effectively in three dimensions. However, when large and well pixelated area detectors became available, starting with the Mar345 image plate detector, a complete low resolution powder diffraction pattern could be collected in a few minutes, where most of that time was spent reading out the image,

rather than recording the diffraction (51). These detectors have largely been replaced at synchrotrons by large amorphous-silicon based direct readout detectors (52). The amorphous-silicon detectors, originally developed for medical imaging, can be read out multiple times per second, which makes them superb for *in situ* and *operando* powder diffraction measurements, where phase changes may occur very quickly. Since area detectors offer significantly lower resolution data than analyzer-crystal measurements, linear or curved position-sensitive detectors are in general preferred for crystallography (53-55), but as will be discussed later, have revolutionized x-ray pair distribution function work. However, a scanned area detector design has been demonstrated to outperform position-sensitive detection for crystallographic applications (56).

STRUCTURE SOLUTION

As noted, determination of structures of novel materials from powder diffraction was practiced for most of the last century. However, it has not become the routine process that is often true for single crystal diffraction analysis. Two steps are usually needed to determine a structure for a novel material from its diffraction pattern. The first is to index the diffraction pattern, thus determining the material's unit cell and the second is to determine an approximate model for the structure, at which point Rietveld refinement and difference-Fourier analysis, etc. become possible.

The loss of three-dimensional information from the projection of the Fourier transform of a crystal structure into a single-dimensional powder diffraction pattern makes the process of reconstruction of the unit cell difficult. The fact that some observed peaks may arise from an impurity and thus will not fit the unit cell also makes this a much more difficult problem. This is further confounded by the problem that unavoidable small errors in placement of the sample in a Bragg-Brentano diffractometer shift the peaks, adding an additional fitting parameter. Synchrotron diffraction has improved on the latter, by eliminating the sample displacement problem, but it is fair to say that most crystallographers who perform indexing on a regular basis will utilize a collection of software – some quite old -- since single one approach seems to work for all problems (57-61). A comprehensive review of the many successful approaches to the problem of indexing of powder diffraction patterns would be quite lengthy, indeed, but still this is an area of open research: At present, there are no algorithms that will find the two unit cells from a mixture of two novel phases present in reasonably comparable amounts.

Once a pattern is indexed, a refinement is usually performed to determine a set of reflection intensities. These intensities cannot provide structure factor estimates for reflections that are closely overlapped in the powder pattern, but will provide an intensity sum for the overlapped group. A number of different methods are commonly used to determine approximate structures (62). Again, no one approach seems to satisfy all needs. The development of direct methods has, of course, revolutionized single-crystal crystallography. It has been a more difficult problem for powder diffraction, but the group of Carmelo Giacovazzo in Bari, Italy, through much effort

from Angela Altomare and co-workers, has produced an ever-improving set of tools for direct-methods structure solution from powder diffraction data (63-65). An alternate and somewhat related algorithm, called charge-flipping, determines an approximate electron (or nuclear density) map through an iterative approach to assigning phases to reflections (66, 67). This has proven to be quite successful (68, 69). The maximum-entropy method is another approach for generation of density maps that has not been used as frequently for powder diffraction, but perhaps as larger-scale computing becomes more routine, this may change (70, 71). A completely different approach to structure solution, known as rigid-body simulated annealing, involves placing molecular fragments into random positions in the unit cell and using a Metropolis Monte Carlo algorithm to find a trial structure. This has been quite successful (72-74). The software for this has come a long way from this author's initial attempt in this area, when his collaborator Clive Freeman commandeered all of the Silicon Graphics workstations at Biosym, Inc. to find three independent molecular bodies to fit a set of poorly resolved synchrotron data with jury-rigged software (75). Despite the success of various approaches to computational structure solution, the process is far from rigorous and there is still a role for "stealth and guile" (*ansatz*) for suggesting likely models.

PROTEIN POWDER DIFFRACTION

This author feels compelled to confess his initial rampant skepticism when hearing of work to study protein structures to diffraction data using Rietveld analysis; clearly there are some problems too tough for powders. In fact, crystals that are much too small for single-crystal diffraction can still offer very sharp diffraction patterns. In fact, proteins produce some of the highest resolution and certainly the most information-rich powder diffraction patterns ever recorded. Robert Von Dreele was able to demonstrate that with synchrotron powder diffraction data, protein structures can be refined quite adequately (76). Later he demonstrated that novel macromolecular structures could even be solved from powder diffraction (77). Other groups have gone on to embrace this technique with new studies every year or two (78, 79). Perhaps someday there might even be a synchrotron instrument dedicated to automated pharmaceutical-protein binding studies using powder diffraction. Since many proteins are available in very small amounts and can be notoriously difficult to form into usable single crystals, such an instrument could mix the ligand and protein, precipitate a powder (without a need to screen for usable crystals), prepare a specimen and measure a powder pattern. It might even be possible to repurify and recycle the protein for binding with another pharmaceutical. Crystallographic analysis could also be simplified, since most complexes would be isomorphous with the parent protein. To reduce the number of crystallites needed for a reliable measurement, Gandolfi-style randomization could be used (80).

MICROCRYSTAL DIFFRACTION FROM POLYCRYSTALLINE MATERIALS

Another area made possible by synchrotrons as well as by electron microscopes, is microbeam diffraction, where only a small number of domains, or perhaps even only a single crystal,

contribute to the diffraction pattern. With x-rays, two different approaches have been used to index and measure diffraction intensities from individual reflections from small numbers of superimposed diffracting crystallites in a bulk polycrystalline material (81, 82). More use of these techniques have been made for relating materials properties to meso-scale rather than atomic structure (83). However, it is also possible to use these approaches for crystallographic structure determination (84). The technique of precession electron diffraction uses averaging to significantly reduce the impact of dynamic scattering effects (85). This has allowed electron diffraction to become a much more promising technique for structure determination from polycrystalline materials (86).

PAIR DISTRIBUTION FUNCTION ANALYSIS

If a powder diffraction pattern is collected over a very wide Q range, is corrected appropriately, and has a Fourier transform applied, the resulting pattern is a 1-dimensional atom-atom correlation function, analogous to a radially averaged Patterson function. This is called a pair distribution function (PDF), or earlier a radial distribution function. Such determinations started in the 1930's and have been a mainstay for study of amorphous materials, where crystallographic analysis is not possible (87, 88). Wright coined the term "total scattering" to describe these measurements, because the entire pattern including diffuse scattering, is used to obtain the PDF. Initially, researchers sometimes fit models to such data, but they were large ensembles that were not expected to show realistic detailed atomic structure. In the 1980's, to examine local ordering that was not reflected in the long-range crystallographic ordering of high T_c superconductors, the author had the opportunity to develop a crystallographic type of modeling by fitting to a PDF (89). In this, the contents of a small unit cell, with symmetry reduced from that of the crystallographic structure, was shown to fit the measured PDF well. In the intervening years, modeling of PDFs has become a widely-used technique (90). This has been much aided by the development of a technique for very rapid (now <1 sec) measurement of PDFs via synchrotron diffraction data at very short x-ray wavelengths (91). Since crystallographic order may not capture the chemically important aspect of short-range order in some interesting materials, this is a quite valuable technique with a growing user base.

CONCLUSIONS

Powder diffraction has been used for crystallographic study almost as long as its better-developed sibling, single-crystal diffraction. While the latter has seen a systematic development in capabilities over the past century, most of the major advances in powder diffraction have come in the most recent few decades. Single crystal diffraction will always be preferable when: (1) suitable crystals are available, (2) the measurement under the desired chemical/physical environmental conditions is possible, and (3) the measurement can be performed with the time available for use of the facility or before the sample decays, etc. Any one of these conditions frequently prompts the need for "plan B." To date, all scales of problems, from simple salts to complex proteins have been successfully structurally characterized using powder diffraction. The

technique is rapidly advancing; it may well be that the second century of powder diffraction will see more advances than the first.

ACKNOWLEDGEMENTS

I would like to thank Dr. Robert Von Dreele and Dr. Diane Toby for reading a draft of this paper. Many people have taken the time to talk to me over the years about their own early experiences, but I would particularly like to thank Dr. David Cox. I would also like to thank Prof. Cliff Shull for buying me a beer after an ACA session, as well as for his memories. The entire field has benefitted greatly from my employer and our sponsor: use of the Advanced Photon Source, an Office of Science User Facility operated for the U.S. Department of Energy (DOE) Office of Science by Argonne National Laboratory, was supported by the U.S. DOE under Contract No. DE-AC02-06CH11357.

REFERENCES

1. van Laar B, Schenk H. The development of powder profile refinement at the Reactor Centre Netherlands at Petten. *Acta Crystallogr A*. 2018;74(2):88-92.
2. Cagliotti G, Paoletti A, Ricci FP. Choice of collimators for a crystal spectrometer for neutron diffraction. *Nucl Instrum*. 1958;3:223.
3. Young RA. Introduction to the Rietveld Method. In: Young RA, editor. *The Rietveld Method*. Oxford: Oxford University Press; 1993. p. 1-38.
4. van Laar B. Multi-Spin-Axis Structure for CoO. *Physical Review*. 1965;138(2A):A584-A7.
5. Rietveld HM. Line Profiles of Neutron Powder-Diffraction Peaks for Structure Refinement. *Acta Crystallogr*. 1967;22:151-2.
6. Rietveld HM. A Profile Refinement Method for Nuclear and Magnetic Structures. *J Appl Crystallogr*. 1969;2:65-71.
7. Loopstra BO, Rietveld HM. The structure of some alkaline-earth metal uranates. *Acta Crystallographica Section B*. 1969;25(4):787-91.
8. Loopstra BO, Rietveld HM. Further refinement of the structure of WO₃. *Acta Crystallographica Section B*. 1969;25(7):1420-1.
9. Young RA, Mackie PE, von Dreele RB. Application of the pattern-fitting structure-refinement method of X-ray powder diffractometer patterns. *J Appl Crystallogr*. 1977;10(4):262-9.
10. Worlton TG, Jorgensen JD, Beyerlein RA, Decker DL. Multicomponent profile refinement of time-of-flight neutron diffraction data. *Nuclear Instruments and Methods*. 1976;137(2):331-7.
11. Von Dreele RB, Jorgensen JD, Windsor CG. Rietveld refinement with spallation neutron powder diffraction data. *J Appl Crystallogr*. 1982;15(6):581-9.
12. Toby BH. Chapter 4.7 Rietveld refinement. In: Gilmore CJ, Kaduk JA, Schenk H, editors. *International Tables for Crystallography Volume H: Powder diffraction*. Hoboken, N.J.: Wiley; 2019. p. 465-72.
13. Klug HP, Alexander LE. *X-ray Diffraction Procedures: For Polycrystalline and Amorphous Materials*. New York: Wiley-Interscience; 1974.
14. Paszkowicz W. Ninety Years of Powder Diffraction: from Birth to Maturity. *Synchrotron Radiation in Natural Science*. 2006;10(1-2):115-26.
15. Xie D, Baerlocher C, McCusker LB. Combining precession electron diffraction data with X-ray powder diffraction data to facilitate structure solution. *J Appl Crystallogr*. 2008;41(6):1115-21.

16. Friedrich W, Knipping P, Laue M. Interference phenomena with Röntgen rays. *K Bayer Akad Wiss Sitzber, Math-Phys Kl.* 1912;10:303-22.
17. Bragg WH, Bragg WL. The Structure of the Diamond. *Proceedings of the Royal Society of London Series A.* 1913;89(610):277-91.
18. Bragg WL. The Structure of Some Crystals as Indicated by Their Diffraction of X-rays. *Proceedings of the Royal Society of London Series A.* 1913;89(610):248-77.
19. Debye P, Scherrer P. Interferenz an regellos orientierten Teilchen im Röntgenlicht I. . *Physikalische Zeitschrift* 1916;17:277-83.
20. Hull AW. A New Method of X-ray Crystal Analysis. . *Physical Review.* 1917;10:661.
21. Hull AW. The crystal structure of iron. *Journal of the Franklin Institute.* 1917;184(3):447-8.
22. Hull AW. Autobiography. In: Ewald PP, editor. *Fifty Years of X-ray Diffraction.* Utrecht: International Union of Crystallography; 1962.
23. Brentano J. Focussing method of crystal powder analysis by X-rays. *Proc Phys Soc Lond.* 1925;37:184-93.
24. Parrish W. X-ray powder diffraction analysis film and Geiger counter techniques. *Science.* 1949;110:368-71.
25. Mason TE, Gawne TJ, Nagler SE, Nestor MB, Carpenter JM. The early development of neutron diffraction: science in the wings of the Manhattan Project. *Acta Crystallogr A.* 2013;69:37-44.
26. Shull CG, Smart JS. Detection of Antiferromagnetism by Neutron Diffraction. *Physical Review.* 1949;76(8):1256-7.
27. Shull CG, Strauser WA, Wollan EO. Neutron Diffraction by Paramagnetic and Antiferromagnetic Substances. *Physical Review.* 1951;83(2):333-45.
28. Prince E. Comparison of profile and integrated-intensity methods in powder refinement. *J Appl Crystallogr.* 1981;14(3):157-9.
29. Hewat A. The Rietveld computer program for the profile refinement of neutron diffraction powder patterns modified for anisotropic thermal vibrations. UKAERE Harwell Report RRL. 1973;73:897.
30. Wiles DB, Young RA. A new computer program for Rietveld analysis of X-ray powder diffraction patterns. *J Appl Crystallogr.* 1981;14(2):149-51.
31. McCusker LB, Von Dreele RB, Cox DE, Louer D, Scardi P. Rietveld Refinement Guidelines. *J Appl Crystallogr.* 1999;32:36-50.

32. Finger LW, Prince E. A system of FORTRAN IV computer programs for crystal structure computations. Washington DC: National Bureau of Standards; 1975. Report No.: 854.
33. Izumi F, Ikeda T. A Rietveld-analysis program RIETAN-98 and its applications to zeolites Mater Sci Forum. 2000;321-3:198-203.
34. Larson AC, Von Dreele RB. General Structure Analysis System (GSAS). Los Alamos National Laboratory; 2004. Report No.: LAUR 86-748.
35. Vitale G, Bull LM, Morris RE, Cheetham AK, Toby BH, Coe CG, et al. Combined Neutron and X-Ray-Powder Diffraction Study of Zeolite CaLSX and A ¹H NMR Study of its Complex with Benzene. Journal of Physical Chemistry. 1995;99(43):16087-92.
36. Grohol D, Huang QZ, Toby BH, Lynn JW, Lee YS, Nocera DG. Powder Neutron Diffraction Analysis and Magnetic Structure of Kagome-type Vanadium Jarosite NaV₃(OD)₆(SO₄)₂. Physical Review B. 2003;68(9):094404.
37. Rodríguez-Carvajal J. Recent Advances in Magnetic Structure Determination by Neutron Powder Diffraction. Physica B. 1993;192(1-2):55-69.
38. Petricek V, Dusek M, Palatinus L. Jana2006. The crystallographic computing system. Praha, Czech Republic. : Institute of Physics 2006.
39. Cheary RW, Coelho A. A fundamental parameters approach to X-ray line-profile fitting. J Appl Crystallogr. 1992;25(2):109-21.
40. Coelho A. TOPAS: General Profile and Structure Analysis Software for Powder Diffraction Data. Karlsruhe, Germany: Bruker AXS GmbH; 2007.
41. Lutterotti L, Matthies S, Wenk H-R. MAUD: a friendly Java program for material analysis using diffraction. Newsletter of the Commission on Powder Diffraction. 1999:14-5.
42. Wenk HR, Lutterotti L, Vogel SC. Rietveld texture analysis from TOF neutron diffraction data. Powder Diffraction. 2010;25(3):283-96.
43. Toby BH. EXPGUI, a Graphical User Interface for GSAS. J Appl Crystallogr. 2001;34:210.
44. Toby BH, Von Dreele RB. GSAS-II: The Genesis of a Modern Open-Source All-Purpose Crystallography Software Package. J Appl Crystallogr. 2013;46:544-9.
45. Buras B, Leciejewicz J. A New Method for Neutron Diffraction Crystal Structure Investigations. Physica Status Solidi (b). 1964;4(2):349-55.
46. Cox DE, Toby BH, Eddy MM. Acquisition of Powder Diffraction Data with Synchrotron Radiation. Australian Journal of Physics. 1988;41(2):117.

47. Lehmann MS, Christensen AN, Nielsen M, Feidenhansl R, Cox DE. High-Resolution Synchrotron X-ray-powder Diffraction with a Linear Position-Sensitive Detector. *J Appl Crystallogr.* 1988;21:905-10.
48. Fitch AN. The high resolution powder diffraction beam line at ESRF. In: Cernik RJ, Delhez R, Mittemeijer EJ, editors. *European Powder Diffraction: EPDIC IV, Pts 1 and 2. Materials Science Forum.* 228. Zurich-Uetikon: Transtec Publications Ltd; 1996. p. 219-21.
49. Hodeau JL, Bordet P, Anne M, Prat A, Fitch AN, Dooryhee E, et al. Nine crystal multi-analyzer stage for high resolution powder diffraction between 6 keV and 40 keV. *Proc SPIE - Int Soc Opt Eng.* 1998;3448:353-61.
50. Toby BH, Huang Y, Dohan D, Carroll D, Jiao X, Ribaud L, et al. Management of metadata and automation for mail-in measurements with the APS 11-BM high-throughput, high-resolution synchrotron powder diffractometer. *Journal of Applied Crystallography.* 2009;42(6):990-3.
51. Cerenius Y, Stahl K, Svensson LA, Ursby T, Oskarsson A, Albertsson J, et al. The crystallography beamline I711 at MAX II. *Journal of Synchrotron Radiation.* 2000;7:203-8.
52. Lee JH, Almer J, Aydiner C, Bernier J, Chapman K, Chupas P, et al. Characterization and application of a GE amorphous silicon flat panel detector in a synchrotron light source. *Nuclear Instruments & Methods in Physics Research Section a-Accelerators Spectrometers Detectors and Associated Equipment.* 2007;582(1):182-4.
53. Suard E, Hewat A. The Super-D2B project at the ILL. *Neutron News.* 2001;12(4):30-3.
54. Patterson BD, Brönnimann C, Maden D, Gozzo F, Groso A, Schmitt B, et al. The materials science beamline at the Swiss Light Source. *Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms.* 2005;238(1-4):224-8.
55. Bergamaschi A, Cervellino A, Dinapoli R, Gozzo F, Henrich B, Johnson I, et al. The MYTHEN detector for X-ray powder diffraction experiments at the Swiss Light Source. *Journal of Synchrotron Radiation.* 2010;17(5):653-68.
56. Toby BH, Madden TJ, Suchomel MR, Baldwin JD, Von Dreele RB. A scanning CCD detector for powder diffraction measurements. *Journal of Applied Crystallography.* 2013;46(4):1058-63.
57. Visser JW. A fully automatic program for finding the unit cell from powder data. *J Appl Crystallogr.* 1969;2:89-95.
58. Werner PE, Eriksson L, Westdahl M. TREOR, a semi-exhaustive trial-and-error powder indexing program for all symmetries. *J Appl Crystallogr.* 1985;18:367-70.
59. Boultif A, Louer D. Indexing of powder diffraction patterns for low-symmetry lattices by the successive dichotomy method. *J Appl Crystallogr.* 1991;24:987-93.
60. Coelho A. Indexing of powder diffraction patterns by iterative use of singular value decomposition. *J Appl Crystallogr.* 2003;36(1):86-95.

61. Boultif A, Louer D. Powder pattern indexing with the dichotomy method. *J Appl Crystallogr.* 2004;37:724-31.
62. David WIF, Shankland K. Structure determination from powder diffraction data. *Acta Crystallogr A.* 2008;64:52-64.
63. Cascarano G, Favia L, Giacovazzo C. SIRPOW.91-a direct-methods package optimized for powder data. *J Appl Crystallogr.* 1992;25:310-7.
64. Altomare A, Burla MC, Camalli M, Carrozzini B, Cascarano GL, Giacovazzo C, et al. EXPO: a program for full powder pattern decomposition and crystal structure solution. *J Appl Crystallogr.* 1999;32:339-40.
65. Altomare A, Cuocci C, Giacovazzo C, Moliterni A, Rizzi R. COVMAP: a new algorithm for structure model optimization in the EXPO package. *J Appl Crystallogr.* 2012;45:789-97.
66. Oszlanyi G, Suto A. Ab initio structure solution by charge flipping. *Acta Crystallogr A.* 2004;60(2):134-41.
67. Palatinus L, Chapuis G. SUPERFLIP - a computer program for the solution of crystal structures by charge flipping in arbitrary dimensions. *J Appl Crystallogr.* 2007;40:786-90.
68. Baerlocher C, McCusker LB, Palatinus L. Charge flipping combined with histogram matching to solve complex crystal structures from powder diffraction data. *Z Kristallog.* 2007;222(2):47-53.
69. Xie D, McCusker LB, Baerlocher C. Structure of the Borosilicate Zeolite Catalyst SSZ-82 Solved Using 2D-XPD Charge Flipping. *Journal of the American Chemical Society.* 2011;133(50):20604-10.
70. Sakata M, Sato M. Accurate Structure-Analysis By The Maximum-Entropy Method. *Acta Crystallogr A.* 1990;46:263-70.
71. Kumazawa S, Kubota Y, Takata M, Sakata M, Ishibashi Y. MEED: a program package for electron-density-distribution calculation by the maximum-entropy method. *J Appl Crystallogr.* 1993;26:453-7.
72. Favre-Nicolin V, Cerny R. FOX, 'free objects for crystallography': a modular approach to ab initio structure determination from powder diffraction. *J Appl Crystallogr.* 2002;35(6):734-43.
73. Stephens PW, Huq A. PSSP: An open source powder structure solution program for direct space simulated annealing. *Trans Am Crystallogr Assoc.* 2002;37:125-42.
74. David WIF, Shankland K, van de Streek J, Pidcock E, Motherwell WDS, Cole JC. DASH: a program for crystal structure determination from powder diffraction data. *J Appl Crystallogr.* 2006;39(6):910-5.

75. Ramprasad D, Pez GP, Toby BH, Markley TJ, Pearlstein RM. Solid-State Lithium Cyanocobaltates with A High-Capacity for Reversible Dioxygen Binding - Synthesis, Reactivity, and Structures. *Journal of the American Chemical Society*. 1995;117(43):10694-701.
76. Von Dreele R. Combined Rietveld and stereochemical restraint refinement of a protein crystal structure. *J Appl Crystallogr*. 1999;32(6):1084-9.
77. Von Dreele RB, Stephens PW, Smith GD, Blessing RH. The first protein crystal structure determined from high-resolution X-ray powder diffraction data: a variant of T3R3 human insulin-zinc complex produced by grinding. *Acta Crystallogr D*. 2000;56(12):1549-53.
78. Helliwell JR, Bell AMT, Bryant P, Fisher SJ, Habash G, Helliwell M, et al. Time-dependent analysis of K₂PtBr₆ binding to lysozyme studied by protein powder and single crystal X-ray analysis. *Z Kristallog*. 2010;225(12):570-5.
79. Margiolaki I, Giannopoulou AE, Wright JP, Knight L, Norrman M, Schluckebier G, et al. High-resolution powder X-ray data reveal the T-6 hexameric form of bovine insulin. *Acta Crystallogr D*. 2013;69:978-90.
80. Gandolfi G. Discussion upon methods to obtain X-ray 'powder patterns' from a single crystal. *Mineral Petrogr Acta*. 1967;13:67-74.
81. Larson B, Yang W, Ice G, Budai J, Tischler J. Three-dimensional X-ray structural microscopy with submicrometre resolution. *Nature*. 2002;415(6874):887-90.
82. Poulsen HF. *Three-dimensional X-ray diffraction microscopy: mapping polycrystals and their dynamics*: Springer; 2004.
83. Levine LE, Larson BC, Yang W, Kassner ME, Tischler JZ, Delos-Reyes MA, et al. X-ray microbeam measurements of individual dislocation cell elastic strains in deformed single-crystal copper. *Nature materials*. 2006;5(8):619-22.
84. Schmidt S, Poulsen HF, Vaughan GBM. Structural refinements of the individual grains within polycrystals and powders. *J Appl Crystallogr*. 2003;36(2):326-32.
85. Vincent R, Midgley PA. Double Conical Beam-Rocking System For Measurement Of Integrated Electron-Diffraction Intensities. *Ultramicroscopy*. 1994;53(3):271-82.
86. Palatinus L, Jacob D, Cuvillier P, Klementova M, Sinkler W, Marks LD. Structure refinement from precession electron diffraction data. *Acta Crystallogr A*. 2013;69(2):171-88.
87. Warren BE, Gingrich NS. Fourier integral analysis of x-ray powder patterns. *Physical Review*. 1934;46:368-71.
88. Wright AC, Leadbetter AJ. *Diffraction Studies of Glass Structure. Physics and Chemistry of Glasses*. 1976;17(5):122-45.

89. Dmowski W, Toby BH, Egami T, Subramanian MA, Gopalakrishnan J, Sleight AW. Short-Range Ordering Due to Displacements of Thallium and Oxygen Atoms in Superconducting $Tl_2Ba_2CaCu_2O_8$ Observed by Pulsed-Neutron Scattering. *Physical Review Letters*. 1988;61(22):2608-11.
90. Egami T, Billinge SJL. *Underneath the Bragg Peaks: Structural Analysis of Complex Materials*. London: Pergamon; 2003.
91. Chupas PJ, Qiu XY, Hanson JC, Lee PL, Grey CP, Billinge SJL. Rapid-acquisition pair distribution function (RA-PDF) analysis. *J Appl Crystallogr*. 2003;36:1342-7.