Development History of the PDXL Structure Analysis Package

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1. First attempt

It was in 1999 that we tried crystal structure analysis from powder diffraction data ("SAPD") for the first time. At that time, we used strong X-rays generated from a rotating anode X-ray tube, a multilayer mirror and a parallel slit analyzer (PSA) with an extremely small aperture angle (0.057 deg) to create parallel beam optics, and collected diffraction data from a glass capillary filled with polycrystalline samples. The measurement took more than 60 hours. We believed that the data, which had a FWHM smaller than 0.1 deg, was some of the highest resolution data taken from laboratory-use diffractometers at the time. We used several third-party programs such as JADE[(1)], ITO[(2)], EXPO[(3)], to analyze the data.

We chose two organic compounds with very simple molecular structures, taurine and *p*-benzoquinone, as our target samples for SAPD. The space group of taurine and *p*-benzoquinone is $P2_1/c$. The asymmetric unit of *p*-benzoquinone structure consisted of half of the molecule (Z'=0.5). Today you would be able to obtain SAPD results for both compounds comparable to results from single crystal ("SC") structure analysis, but at that time the results were just good enough. The molecular structures were distorted as shown in Figure 1. In Europe, several people had successfully used SAPD to analyze organic compounds with more complicated molecular structures[(4)]. By contrast, in Japan at that time only a handful of researchers had found success using SAPD with organic compounds[(5)]. Because of this, even our results from taurine and *p*-benzoquinone could be presented at the annual conference of Crystallographic Society of Japan in 1999.

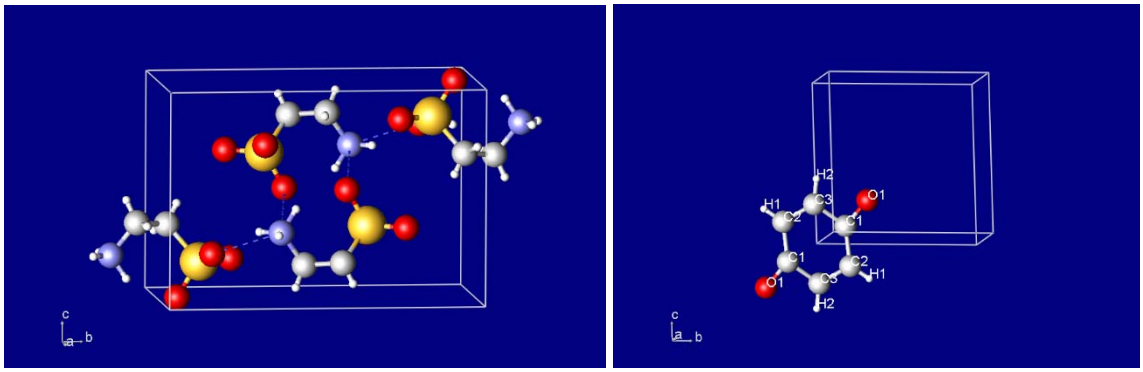

Figure 1. Crystal structure results in 1999. Left: Taurine, Right: p-Benzoquinone.

2. Reorganization of the software development department

For a while thereafter, we continued our experiments with high-resolution optics, but we didn't do any software development related to SAPD. Eventually the manager of one of the software

development groups proposed that we try developing some SAPD software and senior management gave his proposal the green light. The software development department was reorganized and several key members got together in one group. Everyone in that team had been in the SC structure analysis group, and they had been involved in the development of SC structure analysis software (teXsan[6], and CystalStructure[7]). It was a great opportunity to start the development of SAPD software.

Trying to perfect SAPD has been anything but easy since then. Even those who had experience with SC structure analysis needed to put in considerable time and effort to learn the steps and specific know-how required for SAPD. One of the chief reasons for this was that SAPD required several steps, and they had to use different programs for each step. It was a lengthy and annoying process to create input files for analysis conditions, and moreover, to run a program at each step and then check the results at each step using a text editor or a structure display program such as Mercury[8]. If the result was not satisfying, they had to manually edit the input file and run the program again. This tedious process was considered to be one of the main reasons that the SAPD technique was not widely practiced at the time. We decided that we should develop a program that implemented all the steps.

3. Enhancements on PDXL

Many of the functions required for SAPD had already been implemented in PDXL[9], Rigaku's integrated powder X-ray analysis software that launched in October, 2007. You were be able to do SAPD using nothing but PDXL after adding initial structure determination algorithms, a molecular structure modeling tool, and so forth. While doing maintenance work on PDXL Ver.1, we started to develop ideas and plans specific to SAPD software, then prototyped and tested it repeatedly. In April, 2009, when the PDXL maintenance work settled down, the development of SAPD software product started in earnest, and all the required features were added over the next six months. As initial structure determination algorithms, direct-space methods (parallel tempering method[10]), a charge flipping algorithm[11], and a hybrid method were implemented. The hybrid method optimizes the positions and orientations of molecules using direct-space methods by fitting the molecule to the electron density distribution map obtained by the charge flipping algorithm. In addition, direct methods from EXPO(3) were made available in PDXL thanks to collaboration with the Prof. Carmelo Giacovazzo and Prof. Angela Altomare's group at Bari University in Italy. In October, 2009, PDXL Ver.1.5 was released to market, and you have been able to take all the steps required for SAPD with nothing but PDXL since then. By then, a decade had passed since we presented our SAPD results at the conference of the Crystallographic Society of Japan.

4. Structure Analysis Guidance becomes available

We realized that it was no longer just academic researchers that perform SAPD. In order to promote more widespread adoption of the SAPD technique, we would have to develop user-friendly software closer to a typical Windows experience — something that everyone can use. We decided to make a Wizard that would help less experienced users navigate each step in the SAPD technique.

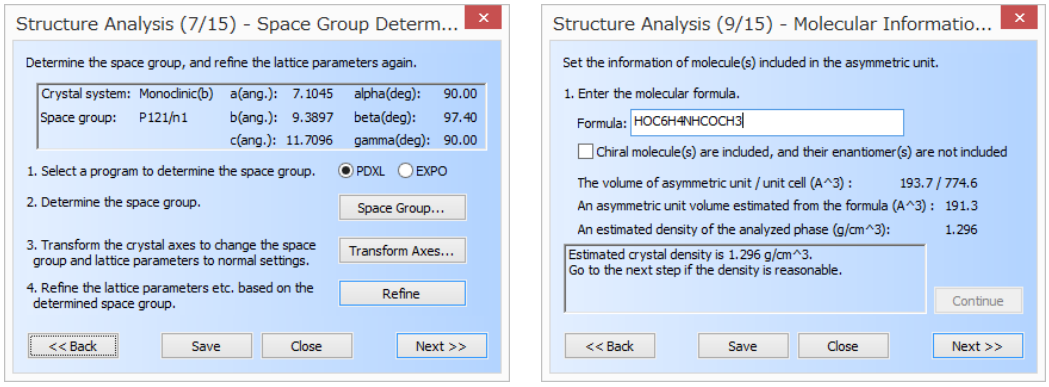

Figure 2. Structure Analysis Guidance

As an aside, the development team called this wizard *Neko*, which means cat in Japanese. In Japan, we have a saying that translates as “I’ll take any help I can get, even from a cat!” to express that we are incredibly busy to the point of being overwhelmed. So, we gave this wizard the pet name Neko, which implied that it would help you out when you are really busy. In other words, Neko would help you with SAPD when you are in trouble. Every time we made improvements to the Wizard, we would laugh and say, “The cat is getting smarter again!”

Neko, the Structure Analysis Wizard consists of 15 pages/steps. It gives you good advice at each step, from loading data through creating a report and CIF. If it finds something that’s clearly an error, the Wizard keeps you from going on to the next step until the error is corrected. At the important step of assessing the obtained structure, it tells you how to evaluate the structure using various tools prepared in PDXL. When you get to structure refinement, it considers how the refinement should be performed, and normally it gives you much better fitting results than you would get by yourself. Neko is a smart adviser who teaches you how to do SAPD using PDXL.

Thanks to Neko, I was also able to solve the crystal structure of an organic compound that I had wanted to solve for quite some time. During my days as a PhD student in university [12], I had tried SC structure analysis of the compound many times, but never succeeded. The biggest reason for the failure was because the compound sublimates in atmosphere. Today the sublimation problem can be avoided with good sampling technique for single crystals, however, when I tried to collect data, single crystals of the compound became smaller even though they were sealed in a glass capillary. With powder samples, changes in crystal size are not problematic if the single crystal state is kept. The sublimation of the compound seemed to be minimized by filling the glass capillary with a powder of the compound. I was able to solve the crystal structure without any trouble thanks to PDXL and Neko. It took 15 years to get it, but it was a great result.

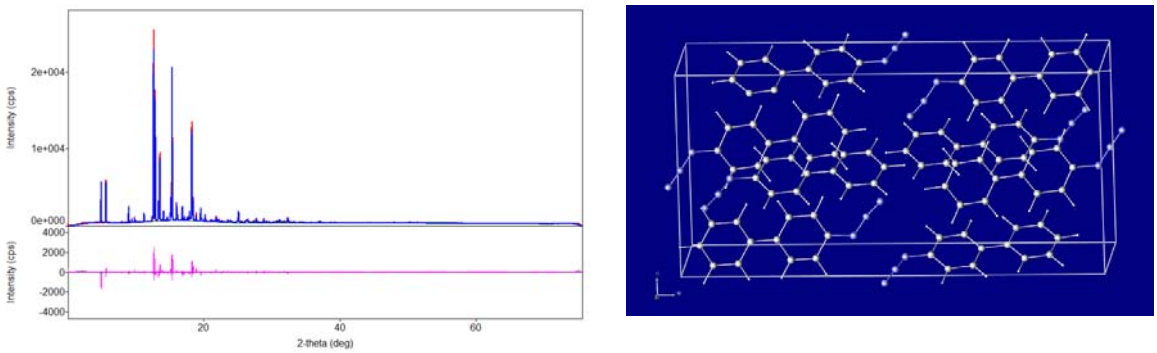

Figure 3. SAPD of p-azidobiphenyl

5. Promotion activities

After some time, the Structure Analysis Wizard came to be called Structure Analysis Guidance. Structure Analysis Guidance made SAPD much more accessible. Needless to say, those who have experiences with SC structure analysis are able to use it, but now even inexperienced users without SC structure analysis and/or powder X-ray diffraction analysis backgrounds are able to perform SAPD. All they need is chemical knowledge of molecular structures, intermolecular interactions, etc. PDXL's Structure Analysis Guidance teaches the user how to do it!

In the beginning, we ran promotional activities focusing on Japanese pharmaceutical companies, many of which purchased the PDXL Structure Analysis Package. Some of the customers presented their own analysis results at conferences such as Annual Meetings of the Pharmaceutical Society of Japan and Academy of Pharmaceutical Science and Technology, Japan. We also make presentations on SAPD at conferences in Japan and elsewhere around the world almost every year. Table 1 shows the timeline of our major presentations.

This year, notably, we will make a presentation on SAPD at the IUCr 2017 conference[13] held in Hyderabad, India. Our approach for restraint and another useful feature obtained as a result of collaboration with CSD[14] will be introduced.

Table 1. Major presentations.

Month, Year	Conference	Presentation title
Aug, 2009	ECM 25 (Turkey)	Compact Multi-Analyzer and its Applications to Structure Analysis
May, 2010	Academy of Pharmaceutical Science & Technology, Japan	Characterization of Polymorphs of Furosemide Nicotinamide Cocrystals
Aug, 2010	ECM 26 (Germany)	Structure Determination of Flufenamic Acid Cocrystals from Laboratory X-ray Powder Diffraction data
Oct, 2010	AsCA 2010 Satellite Meeting (South Korea)	High-quality powder diffraction data obtained with in-house diffractometer
Oct, 2010	AsCA 2010 (South Korea)	Ab Initio Structure Analysis of Solid-State Photodimerized Methoxyazachalcone from Powder Diffraction Data
Jan, 2011	Seminar of Crystallographic Society of Japan	Crystal Structure Analysis from Powder Diffraction Data obtained by Laboratory-use Diffractometers
Oct, 2012	Japan Society of Coordination Chemistry Conference	Phase Transition Behavior of Ni-Diamine Complexes by Dehydration, Hydration and Heating
Sep, 2012	Synchrotron Seminar, Chemical Society of Japan	Crystal Structure Analysis from Powder X-ray Diffraction Data
Mar, 2013	Annual meeting of Chemical Society of Japan	Transition Behavior of Ni(II)-Diamine Complex Exhibits Reversible Acetonitrile Adsorption-Desorption
Jun, 2014	EXPO/SIR Workshop (Italy)	PDXL as a complementary package to EXPO
Oct, 2014	Symposium of Crystallo-graphic Society of Japan	Advanced tools for crystal structure analysis from powder diffraction data
Jun, 2016	EPDIC 15 (Italy)	Crystal structures and transition behaviors of Ni-complexes based on powder crystal structure analysis
Dec, 2016	AsCA 2016 Satellite Meeting (Vietnam)	Rietveld refinement (Part 2)

6. Going forward

First we focused on SAPD of organic compounds because two of the development team members were well-versed in SC structure analysis of organic compounds. Of course, we have also been implementing some tools for SAPD of inorganic compounds recently. Even though PDXL has the great assistant called Structure Analysis Guidance, several hints and a fair amount of know-how are required to solve the structure of particularly complicated molecules. Rigaku holds a user meeting for the PDXL Structure Analysis Package once or twice a year, where we give lectures that teach our users best practices and the in-depth functionality of the package. Sometimes we also give SAPD seminars to help build awareness of the SAPD technique. At present, these activities are only in Japan, but we will likely start to hold the user

meetings and the SAPD seminars in other regions in the near future.

The first choice for crystal structure analysis is still the SC structure analysis technique. We would like SC users to consider the SAPD technique a second choice that they can turn to if they cannot find a good quality single crystal. The possibilities presented by SAPD make it more than just a feature of powder diffraction software. We are going to improve PDXL further, and we will be very happy if both those familiar with SAPD and more inexperienced people come to recognize it as a good tool for crystal structure analysis from now on.

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