"APEX3 software provided the final breakthrough, enabling us to determine the absolute configuration of a pharmaceutically-relevant sample from synchrotron data."

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Case Study 3
Hunting the Elusive Absolute Configuration

Executive Summary

At the Swiss Light Source (SLS), a PILATUS 2M-F detector and the multi-axis PRIGo goniometer obtained data good enough to determine the absolute configuration of a pharmaceutically-relevant molecule. Bruker's APEX3 was able to interpret the anomalous data correctly, while all other attempts thus far—using laboratory systems or other software—had failed to obtain this elusive result.

Challenges

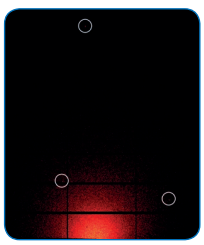
A synchrotron beamline's most important advantage over a laboratory X-ray source is its brilliance, which can be over a billion times greater than a conventional laboratory source. In theory, higher brilliance lets us see more detail in the crystals we study (e.g., better accuracy and precision in the anomalous signal that is necessary to determine an absolute configuration).

However, hardware alone is not sufficient. Advanced software is needed to accurately process the dataset and preserve its superb quality: APEX3.

Product Benefits

APEX3, the most advanced and most trusted software for small molecules in home laboratories, is now also available for the most important synchrotron data formats, including PILATUS frames.

- Easy frame conversion of PILATUS frames
- Accurate and precise data integration
- The best scaling and error models



Frame from a PILATUS-2M-F detector converted to .sfrm format using APEX3. Three reflections (barely visible to the naked eye) are marked with white circles. The upper reflection is at 1.15 Å of resolution.

Results, Return on Investment, and Future Plans

A pentapeptide compound with the formula $C_{26}H_{36}N_6O_6$ was successfully crystallized by Crystallise! within a few weeks of receiving the sample. Other companies had carried out trials for months—and even years—without success. The µm-sized crystals obtained by Crystallise! were investigated at the SLS. The first measurement carried out yielded a crystal structure, but a lack of anomalous dispersion signal hindered any conclusions about the absolute configuration.

Further data sets were collected, and careful data processing with APEX3 drastically improved the anomalous signal. The final criteria parameters for the Hooft Y = 0.01(16) were reliable enough to confirm the absolute configuration. (furthermore, chiral HPLC provided a 99% ee for this compound).

Advanced software will be of great help in the elucidation of absolute configurations for µm-sized crystals of small molecules containing only light atoms. For these types of experiments, we have found the winning combination: SLS synchrotron data with APEX3, and we are looking forward to many more challenging samples.