Solving structures with native SAD on laboratory X-ray sources

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The solving of macromolecular structures by intrinsic anomalous signal (native SAD) critically depends on the quality of the diffraction data. Radiation damage, all but unavoidable at modern synchrotrons, quickly makes the observed anomalous differences unreliable. While ways exist to mitigate damage at synchrotrons, it can also be tackled at the source. We show that laboratory X-ray sources with their limited flux in combination with noise-free photon counting detectors are excellent environments to solve structures by experimental phasing.

In a first set of experiments performed with a microfocus Cu source, we show how accurate anomalous data can be collected from native crystals even at room temperature with doses as low as 30 kGy. Not only does this result in structures of macromolecules as close to their physiological state as crystallography can provide, it also increases throughput in the laboratory by eliminating the time-consuming screening of cryo-conditions.

Next, we show that intrinsic anomalous signal sufficient for structure determination can be detected even in data collected with a Ga source. Thanks to the shorter wavelength of the Ga radiation, datasets complete to 1.2 Å can be collected in a single sweep while accurately measuring the anomalous differences between low-resolution Bijvoet pairs.

It is ironic that in times of abundant beamtime at synchrotron facilities and a quest for ever brighter beams, the humble home source proves such a powerful instrument. As long as the diffraction data are measured with the highest accuracy, e.g. on PILATUS or EIGER R series detectors, phasing of native macromolecular crystals is routinely achievable.