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Structures of Biological Macromolecules from Multi-crystal Native SAD Phasing

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Native metalloproteins have been routine subjects for mutli- and single-wavelength anomalous diffraction (respectively MAD and SAD) analyses for some time; however, despite notable early successes, native molecules without heavy atoms ($Z \geq 25$) have only recently become routinely accessible. Crystals of native proteins and nucleic acids have substantial contents of light elements (P, S, Cl, K, Ca) of potential for use in SAD phasing. Anomalous signals from such elements can be enhanced by using a lower than usual x-ray energy; nevertheless, typical Bijvoet differences usually still remain at a level comparable to noise. We have devised robust SAD procedures to study native, light-atom-only biological structures. We have so far used a modestly low energy (6 - 7 keV), but we further enhance the signal-to-noise in anomalous diffraction by combining data from multiple crystals chosen to be statistically equivalent. We have applied our multi-crystal native SAD approach in several structure determinations (1,2) at sizes up to 1200 ordered residues per asymmetric unit and at resolutions so far as low as 3.2 Å. Our tested practices can be replicated readily, and we plan further improvements in computing protocols and in instrumentation.

[1] *Q. Liu, T. Dahmane, Z. Zhang, et al. (2012). Structures from Anomalous Diffraction of Native Biological Macromolecules. Science 336, 1033-1037.,* ***[2]*** *Q. Liu, Q. Liu and W.A. Hendrickson (2013). Robust Structural Analysis of Native Biological Macromolecules from Multi-crystal Anomalous Diffraction Data. Acta Cryst. D 69, 1314-1332.*

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