

Combining isomorphous-replacement with the direct-methods origin-free modulus sum function in powder diffraction

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In the last time there have been significant advances towards the application of the isomorphous replacement technique to powder diffraction data of proteins. This progress is in part due to the small intrinsic peak widths of small protein crystals and to the combination of brilliant X-ray sources with parallel beam geometry and high-quality analyser crystals that allow increasing spectacularly the angular resolution [1]. Also important has been the development of intensity extraction software for proteins taking advantage of the information contained in multiple powder patterns affected by variable anisotropic unit cell distortions [2]. These advances together with the fact that the low angle portion of a powder pattern is less affected by peak overlap, result in a considerable amount of reliably estimated individual intensities.

For simple heavy atom substructures, the heavy atoms can be located by direct interpretation of the Patterson function computed from the intensity differences between heavy atom derivative and native protein crystals. For more complicated substructures, direct-methods are better suited for solving the Patterson function of the substructure. To gain expertise with powder data, the isomorphous replacement technique and the direct-methods origin-free modulus sum function (S) [3,4] were combined to solve a complex centrosymmetrical zeolite structure [5]. This was, however, a special case since here both large and weak contributions of the heavy atom substructure (i.e. the template) are available from the experiment. The simplicity with which the template substructure could be solved at 3.2 Å resolution encouraged us to solve the two principal drawbacks that still exists for the application of the S function to protein data:

- i. the large number of reflections to be processed;
- ii. due to the non-centrosymmetry of protein crystals, the estimation of the weak contributions from the set of experimentally accessible large contributions.

While work to overcome the second drawback is still in progress, the first one was solved recently. It consists on the maximisation of the S function with a more accurate and easy-to-implement new procedure called S-FFT that only uses Fourier transforms [6]. As will be shown one major advantage of the S-FFT procedure is that it is largely independent of the number of reflections to be processed.

References

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