10.5: Multiwavelength anomalous diffraction (MAD)

An approach to solving the phase problem in protein structure determination by comparing structure factors collected at different wavelengths, including the absorption edge of a heavy-atom scatterer. Also known as **multiple-wavelength anomalous diffraction** or **multiwavelength anomalous dispersion**.

Discussion

The 'normal' atomic scattering factor f^0 describes the strength of X-rays scattered from the electrons in an atom assuming that they are free oscillators. Because the scattering electrons are in fact bound in atomic orbitals, they act instead as a set of damped oscillators with resonant frequencies matched to the absorption frequencies of the electron shells. The total atomic scattering factor *f* is then a complex number, and is represented by the sum of the normal factor and real and imaginary 'anomalous' components:

$$f = f^0 + f' + if''.$$

A consequence of the wavelength dependence of anomalous dispersion is that the structure factors will be significantly perturbed, both in amplitude and in phase, by resonant scattering off an absorption edge. Hence, if diffraction is carried out at a wavelength matching the absorption edge of a scattering atom, and again at a wavelength away from the absorption edge, comparison of the resulting diffraction patterns will allow information to be extracted about the phase differences. For suitable species, the effect is of comparing a native molecule with a strictly isomorphous derivative (and in such cases phase determination and improvement are similar to isomorphous replacement methods).

The technique, often using tunable synchrotron radiation, is particularly well suited to proteins where methionine residues can be readily replaced by selenomethionine derivatives; selenium has a sufficiently strong anomalous scattering effect that it allows phasing of a macromolecule.

History

This technique was introduced by W. Hendrickson (Hendrickson, W. A., 1991, *Determination of macromolecular structures from anomalous diffraction of synchrotron radiation*. *Science*, **254**, 51–58.)

See also

MAD and MIR. J. L. Smith, W. A. Hendrickson, T. C. Terwilliger and J. Berendzen. *International Tables for Crystallography* (2006). Vol. F, ch. 14.2, pp. 299-309

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