

5.15: Structure determination

Structure determination in crystallography refers to the process of elaborating the three-dimensional positional coordinates (and also, usually, the three-dimensional anisotropic displacement parameters) of the scattering centers in an ordered crystal lattice. Where a crystal is composed of a molecular compound, the term generally includes the three-dimensional description of the *chemical* structures of each molecular compound present.

Experimental techniques

Owing to the highly ordered arrangement of atoms as scattering centers in a crystal lattice, most structure determination techniques involve the diffraction of electromagnetic or matter waves of wavelengths comparable to atomic dimensions. Bragg's law specifies the condition for plane waves to be diffracted from lattice planes. The diffracted radiation passing through a crystal emerges with intensity varying as a function of scattering angle. This variation arises from constructive and destructive interference of scattered beams from the planes associated with the different atoms present in the lattice. The result is seen by an imaging detector as a pattern of diffraction spots or rings.

Among diffraction-based techniques are:

- single-crystal X-ray diffraction
- X-ray powder diffraction
- X-ray fiber diffraction
- neutron powder diffraction
- neutron single-crystal diffraction
- polymer electron diffraction

Other techniques for three-dimensional structure determination that are complementary to diffraction methods include

- electron microscopy
- nuclear magnetic resonance spectroscopy (used largely for biological macromolecules in solution)

Methodology

The following summary applies to single-crystal X-ray diffraction. A crystal, mounted on a goniometer, is illuminated by a collimated monochromatic X-ray beam, and the positions and intensities of diffracted beams are measured. The measured intensities I_{hkl} (corresponding to scattering from a lattice plane with Miller indices h,k,l) are reduced to structure amplitudes F_{hkl} by the application of a number of experimental corrections:

$$F_{hkl}^2 = I_{hkl} (kLpA)^{-1}$$

where k is a scale factor, Lp the Lorentz-polarization correction, and A the transmission factor representing the absorption of X-rays by the crystal. The structure amplitude represents the amplitude of the diffracted wave measured relative to the scattering amplitude of a single electron.

However, the diffracted wave is completely described by the structure factor F_{hkl} :

$$\begin{aligned} \mathbf{F}_{hkl} &= F_{hkl} \exp(i\alpha_{hkl}) = \sum_j f_j \exp[2\pi i (hx_j + ky_j + lz_j)] \\ &= \sum_j f_j \cos[2\pi (hx_j + ky_j + lz_j)] + i \sum_j f_j \sin[2\pi (hx_j + ky_j + lz_j)] \\ &= A_{hkl} + iB_{hkl} \end{aligned}$$

where the sum is over all atoms in the unit cell, x_j, y_j, z_j are the positional coordinates of the j th atom, f_j is the scattering factor of the j th atom, and α_{hkl} is the phase of the diffracted beam.

The atomic scattering factor can be worked out from the physical properties of the atom species, but the phase cannot be determined by direct experimental observation. If the phases can be derived in some way, then the positional coordinates can be calculated from the expression above. The phase problem represents the major obstacle to constructing an initial structural model, and is addressed through a number of techniques, such as direct methods, Patterson synthesis, heavy-atom method, isomorphous replacement *etc.*

Once an initial structural model has been calculated, it is usually necessary to conduct an iterative refinement procedure to improve the agreement between the structural model and the experimental diffraction intensities. The most common approach is to perform

a least-squares minimization between the experimental structure factors and those calculated by varying the adjustable parameters of the structural model. These normally include atomic positions, anisotropic displacement parameters, occupancies, chemical bond lengths and angles, and other geometric characteristics of a molecule. Some metric, such as the residual R factor

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is used to indicate improvements or reductions in the quality of fit between model and observation. In the expression above (the 'conventional' R factor), F_{obs} and F_{calc} are the observed and calculated structure amplitudes, and the deviations are summed over all experimentally recorded intensities. There is considerable discussion on the most appropriate statistical metric to use for this purpose.

Other refinement techniques, such as maximum likelihood and maximum entropy, are also used.

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