Advanced Methods in Structure Analysis

Lecture 2
Single Crystal Diffraction

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Single Crystal Selection and Mounting

The first step in the determination of a crystal structure by single crystal X-ray diffraction is the growing and selection of a suitable crystal.

Crystal growth is beyond the scope of the present lectures. The size and shape of a suitable single crystal vary depending on the absorption of the crystal and the intensity of the X-ray source.

For a typical crystal using a conventional X-ray source a crystal measuring *ca*. 0.2-0.4 mm in each dimension is ideal.

Crystals are selected under a polarising microscope and mounted on the end of a glass fibre. For low temperature measurements this is carried out using silcone oil which is then frozen. The fibre is then mounted on a goniometer head that allows for adjustment of the crystal position.

UP / DOWN

SIDE-to-SIDE

SIDE-to-SIDE
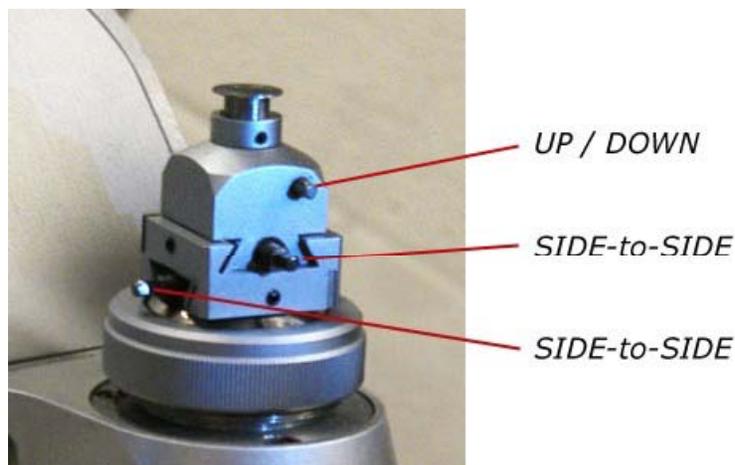
Single Crystal Diffraction

Since von Laue's original experiment several methods of single crystal X-ray diffraction have evolved, including the Laue method, the precession method, the Weissenberg method and four circle diffractometry.

In these lectures we will concentrate on four-circle diffractometry and the two main diffraction geometries used in modern powder diffractometers *viz*. Eulerian geometry and kappa geometry.

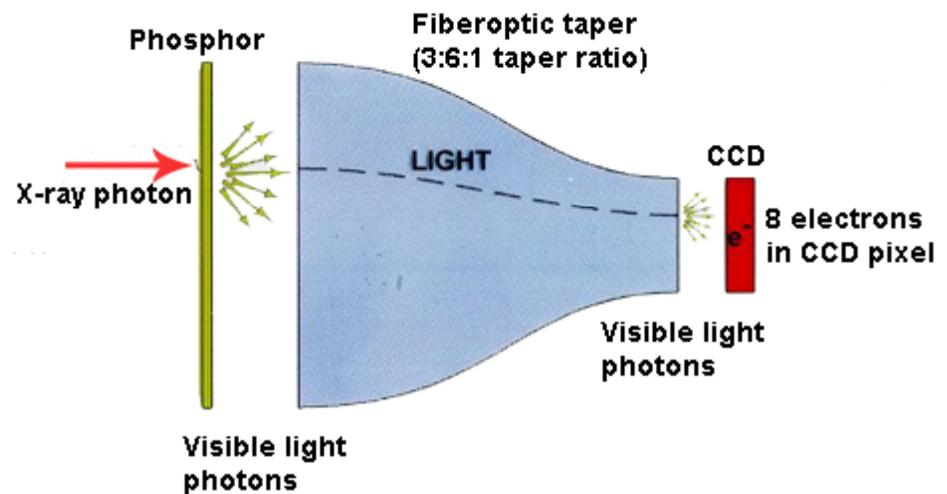In Eulerian geometry the crystal is mounted at the centre of 4 circles: ϕ, χ, ω and 2θ
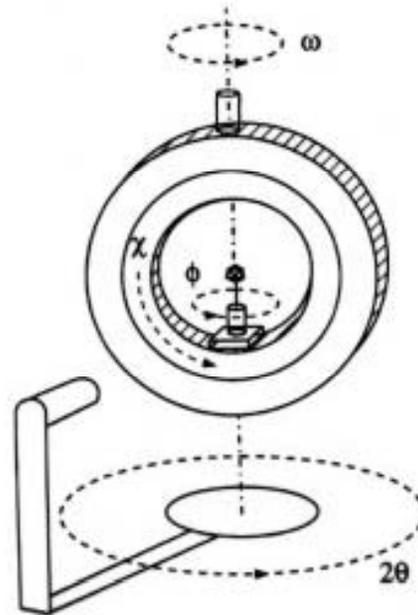
In the case of kappa geometry the χ circle is made up of two other angles κ and ω_κ
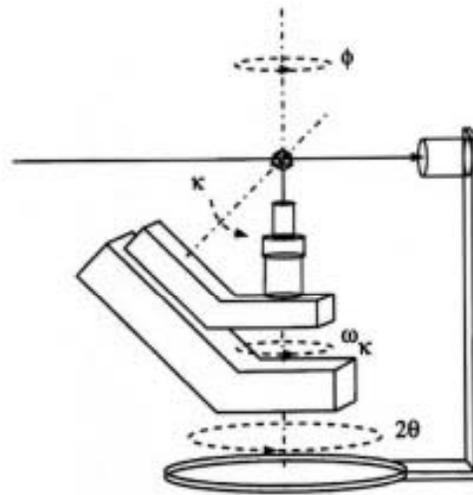
Kappa Geometry

Modern instruments use area detectors such as the charge coupled device or CCD.

Mo Kα radiation (λ = 0.7107 Å) is typically used. The crystal is first centred optically using a microscope at the centre of the four circles.

The crystal is then moved by computer control through the four angles while being irradiated by a monochromatic X-ray beam. This ensures that for any particular combination of *hkl* the correct angle θ can be made with the incident X-ray beam so as to satisfy Bragg's law and exhibit diffraction. Diffracted beams are then detected using an area detector.

Image analysis software is then used to extract the intensities of the diffraction spots on each image.

h0l image of a
monoclinic
crystal
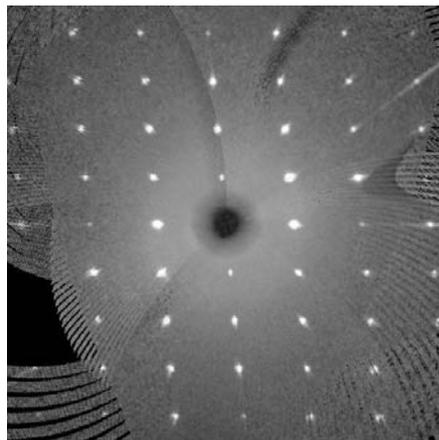
hk0 image of a
monoclinic
crystal
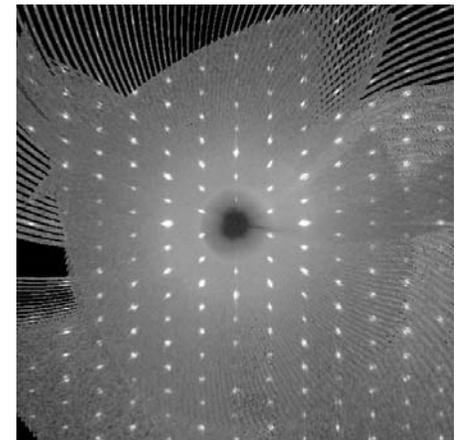
An Initial set of reflections is collected in a systematic ϕ scan (or other angles if requested).

In the case of older diffractometers the initial set consists 25 intense reflections. On newer area detector instruments, 30-40 frames are initially collected and around 200 peaks are "harvested" from these.

These are then indexed (*hkl* assignment) using automatic indexing procedures. These indexed reflections are then used to calculate unit cell parameters and a crystal orientation matrix (UB). The four angle settings for every combination of *hkl* can then be calculated.

On older instruments, the diffractometer is then set to collect an initial set of diffraction data between certain limits of *hkl*. Using these data a new set of intense reflections are selected to provide a more accurate unit cell refinement.

The *hkl* limits are then increased so that a full data set can be collected. From the crystal system and the known intensity relationships for that system only a fraction of the total sphere of reciprocal lattice needs to be collected. These are known as the **unique reflections**.

On modern instruments a full data collection is carried out using a ϕ or ω scan with a few images from ϕ/χ scans. Almost the whole of the limiting sphere of reflection can be collected in a relatively short time.

Data Reduction

The data require a number of corrections, such as for geometric and polarisation factors.

$$I_{hkl} = I\frac{1}{Lp}$$

Where L is the Lorentz factor and p is the polarisation factor and is given by:

$$p = \frac{1+\cos^2 2\theta}{2}$$

Note the equation for p varies if a monochromator is used. The Lorentz factor is purely geometric and varies with diffractometer.

The areas of each diffraction peak are subtracted from the background to give a corrected intensity. Absorption corrections can also be applied at this stage. The I_{hkl} data are directly proportional to the square of F_{hkl}.

$$sF_{hkl}^{2} = I_{hkl}$$

Where s is a scaling factor dependent on beam intensity and crystal size etc and is refined during structure analysis. F_{hkl} here is therefore termed the observed structure factor, F_{obs}

The final results are essentially:

$$a, b, c, \alpha, \beta, \gamma \qquad h, k, l, F_{obs}^{2}, \sigma(F_{obs}^{2})$$

Absorption

Absorption correction is usually carried out prior to structure analysis. Corrections are required since the path length traveled by the X-ray beam is different due to the morphology of the crystal.

The most rigorous method is to index the faces of the crystal and calculate the path length for each reflection.

However, a number of empirical methods have evolved and on modern instruments these are fairly routine.

For Bruker CCD instruments the SADABS program is typically used (SADABS User Manual Bruker AXS).

Other absorption correction software include:

DIFABS - N. Walker and D. Stuart, Acta Crystallogr., Sect A 1983, 39, 158-166.

PSISCANS - A. C. T. North, D. C. Phillips and F. S. Mathews, Acta. Crystallogr. Sect A, 1968, 24, 351-359.

Crystal Structure Analysis

Crystal structure analysis is carried out in a systematic way and can be divided into the following basic steps.

(1)   Cell parameter and crystal system determination
(2)   Data collection
(3)   Data reduction
(4)   Space group determination (systematic absences)
(5)   Obtain starting model (Structure Solution)
(6)   Calculate structure factors for model
(7)   Least Squares refinement of model to minimise difference
        between observed and calculated structure factors.
(8)   Calculate electron density maps to locate new atom positions
(9)   Repeat steps 6 to 8 until a satisfactory model is obtained

Information from structure analysis

(1)   Unit cell parameters a, b, c, α, β, γ
(2)   Crystal system and space group
(3)   Atomic parameters for every atom in the unit cell (x, y, z, thermal parameters and fractional occupancy)
(4)   Bond lengths and angles
(5)   Molecular structure
(6)   Crystal structure (how the molecules pack together eg. The extent of H- bonding).

Crystal structure analysis can therefore be divided into two main parts:

Structure determination
The *ab initio* determination of the initial model

Structure refinement
The least squares refinement of the model to yield an acceptable fit.

Structure Determination

X-ray data collection yields I_{hkl} which is proportional to Fo^2. Unfortunately we can only determine the magnitude of Fo not its phase (sign). In order to model the structure we require the phase of Fo as well as its magnitude. There are a number of ways to solve the phase problem. The three main methods are as follows:

(1) By analogy with isostructural solids

(2) Patterson vector density methods (heavy atom methods)

(3) Direct methods

Structural analogy

This method is rarely used with single crystal analysis, but is common for structure analysis from powders.. It is best illustrated using an example:

NiO has a diffraction pattern that can be indexed on a cubic cell with a = 4.178Å. A space group of Fm3m is consistent with systematic absences in the data. The structure is therefore likely to be analogous to rocksalt. The starting model can therefore be derived from the rocksalt structure:

NaCl   NiO

a = 5.628 Å a = 4.178Å

Na 0,0,0   Ni 0,0,0

Cl ½, ½, ½   O ½, ½, ½

Patterson methods

This method is important for unknown structures, where a heavy atom is present among lighter atoms. The method works by producing a vector density map. ρ_{uvw} is the vector density at point u,v,w in the vector map and is given by:

$$\rho_{uvw} = \frac{1}{V} \sum_{hkl} I_{hkl} e^{-2\pi i (hu+kv+lw)}$$

Every peak in the vector map corresponds to a pair of peaks in the real unit cell. The height of the peak is proportional to the product of the atomic numbers. Each peak in the Patterson map is located at a distance and in a direction from the origin (0,0,0) corresponding to the vector between a pair of atoms in the real unit cell.

$P\bar{1}$

x,y,z

q

0

-x, -y, -z

Real Cell

u,v,w

q

0
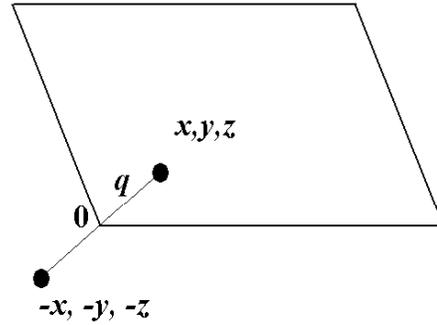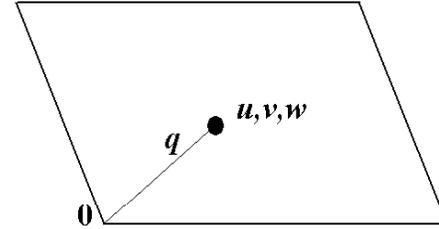
Patterson Cell

Generally, for the vector between atoms at points x, y, z and x_1, y_1, z_1

$u = x_1 - x;$ $v = y_1 - y;$ $w = z_1 - z$

Patterson cells generally have higher symmetry than the real cell. They are always centrosymmetric, since there will always be 2 vectors between atom pairs of equal magnitude but opposite in direction (*i.e.* u,v,w and $-u,-v,-w$)

Determining a structure from Patterson maps is not always easy. In 1935 David Harker suggested a method to locate atoms by looking for special lines and planes within the map.

e.g. a crystal in space group *Pm* will have atoms related by

$$x, y, z \equiv x, -y, z$$

This means in the Patterson map there will be a predominance of peaks of the type $0,2y,0$. This is called a Harker line.

Similarly in space group $P2_1$ in the real cell atoms will be related by.

$$x, y, z \equiv -x, \tfrac{1}{2} + y, -z$$

This will result in Patterson peaks of the type $2x, \tfrac{1}{2}, 2z$ (a Harker Plane).

Since the height of the vector peaks is proportional to the product of the atomic numbers, the vector map will be dominated by vectors between heavy atoms.

Therefore this method is particularly suitable for locating heavy atoms in metal organic type structures. The heavy atom is located first and used for the initial phasing of structure factors.

Patterson Map searching is now fully automatic in programs such as SHELX-S.

Direct methods
Direct methods represent an alternative to Patterson maps when there is no single heavy atom present or when there a number of heavy atoms that give too many vectors. It is particularly important for organic structures.

The process involved is complex but can be broken down into the following basic steps.

(1) Normalization of structure factors

Since the scattering factor and hence the magnitude of the structure factor vary with Bragg angle θ, in order to compare F_{obs} independent of Bragg angle it is necessary to use a normalized structure factor E_{hkl}

$$E_{hkl}^2 = \frac{F_{hkl}^2}{x \sum_n f_n^2}$$

x is the Debye Waller factor.

Tentative phases are then assigned to E_{hkl} using the magnitude of the structure factors.

(2) A series of phase relationships is set up between the most intense reflections.

We shall briefly consider some of these phase relationships in a qualitative way. For a more detailed description see for example:

An Introduction to direct methods. The most important phase relationships and their application in solving the phase problem. H. Schenk, IUCR, electronic edition 2001.

Firstly let us consider why larger F_{obs} values are important. Larger F_{obs} values are obtained where the atoms lie close to the lattice planes. Conversely smaller F_{obs} values are obtained where the atoms are further away from the planes.

Larger F_{obs}

Smaller F_{obs}
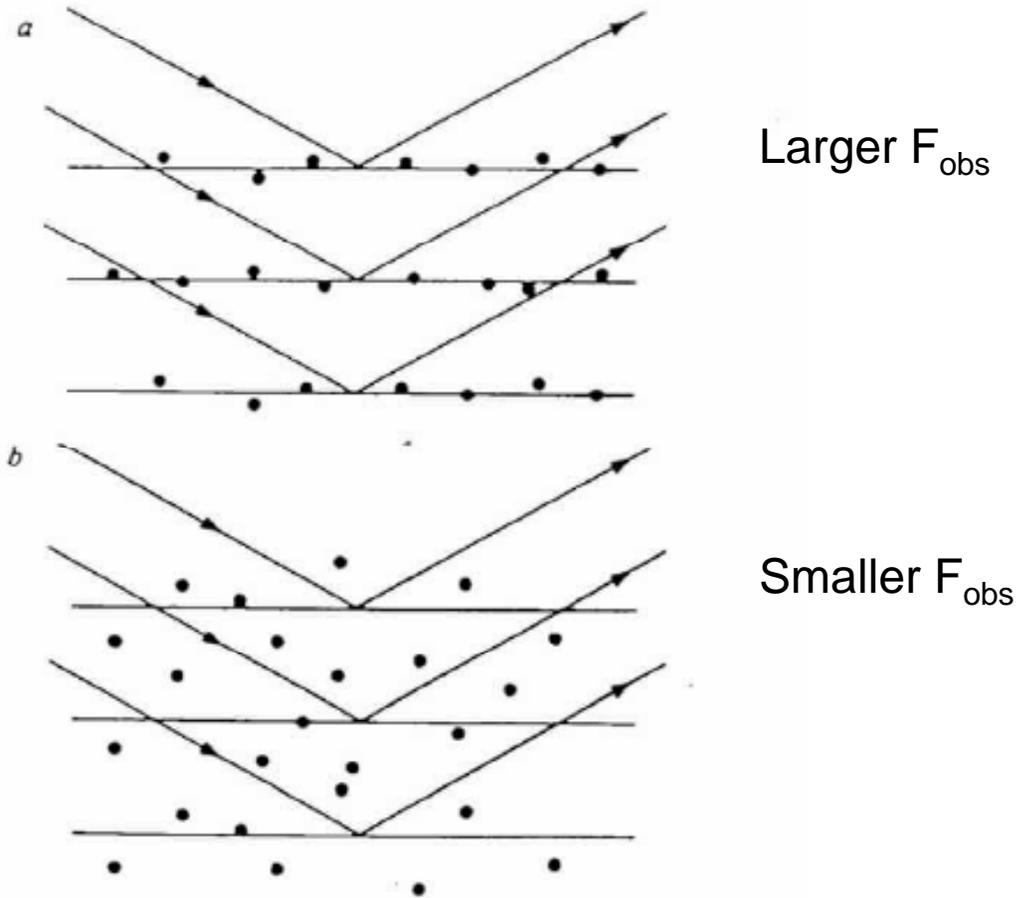
The Σ_1.phase relationship

The Σ_1.phase relationship estimates the phase of E_{2h2k2l} from the magnitudes of E_{hkl} and E_{2h2k2l} in centrosymmetric structures. In centrosymmetric structures only phases of 0 and π are possible.

Let us look at the 110 and 220 reflections as an example. If the phase of E_{110} is 0 then the maxima in electron density are found on these planes (I) and the minima halfway between them (II).
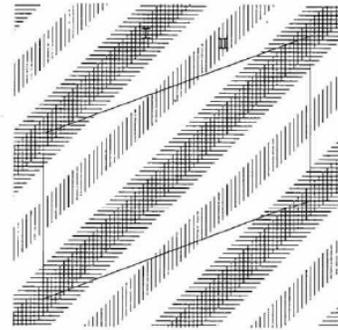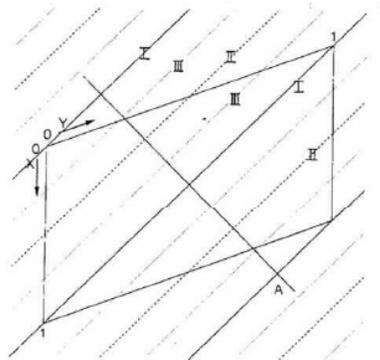
If the phase of E_{220} is zero then its maxima lie at I and II. reflections as an example. If the phase of E_{110} is 0 then the maxima in electron density are found on these planes and the minima halfway between them. Combining these we can predict the electron density maxima. Similar diagrams can be drawn for phases = π.

Similar methods can be used for other phase relationships and these form the basis of modern direct methods programs.

(3) The space group symmetry is used to determine which of the phase relationships are important. This process is called convergence.

(4) Using these relationships a number of reflections are selected for multiple starting points in phase determination.

(5) Phases are determined using a weighted multiple tangent algorithm.

(6) From the phased *hkl* data, electron density maps can be generated in order to locate atoms.

Electron Density Maps

After assigning phases to the structure factors, it is necessary to relate the structure factors back to the atoms in the unit cell. This is done by electron density maps created through a Fourier summation

$$\rho_{xyz} = \frac{1}{V} \sum_{hkl} Sc F_o e^{-2\pi i(hx+ky+lz)}$$

ρ_{xyz} = electron density at point *xyz*
V = volume of unit cell
Sc calculated phase of structure factor
F_o = observed structure factor

A more useful map is the difference Fourier map, which plots the residual scattering density. It is used to locate the remaining atoms after refinement of a partial initial model, *e.g.* after using Patterson methods.

$$\Delta\rho_{xyz} = \frac{1}{V} \sum_{hkl} (F_o - F_c) e^{-2\pi i(hx+ky+lz)}$$

Normally a computerised grid search is carried out to locate the maxima.

R-Factors

Least square refinement is carried out minimising the difference between the observed and calculated structure factors. There are a number of different R-factors used to establish the quality of the fit.

$$wR2 = \left\{ \Sigma \left[w(F_o^2 - F_c^2)^2 \right] / \Sigma \left[w(F_o^2)^2 \right] \right\}^{1/2}$$

$$R1 = \Sigma \left| |F_o| - |F_c| \right| / \Sigma |F_o|$$

$$GooF = S = \left\{ \Sigma \left[w(F_o^2 - F_c^2)^2 \right] / (n-p) \right\}^{1/2}$$

Where n is the number of reflections and p is the number of parameters.

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┌─────────────────────────────┐          ┌──────────────────────┐
│ 1. Select crystal           │─────────▶│ Deduce unit cell and │
│ 2. Mount on goniometer      │          │ crystal system       │
│ 3. Collect 25 reflections   │          └──────────────────────┘
│ 4. Derive unit cell         │
│    parameters               │                    ┌──────────────────────────┐
└─────────────────────────────┘                    │ Look for intensity       │
        │                                           │ relationships and general│
        ▼                                           │ systematic absences      │
┌────────────┐    ┌──────────────────────┐          │                          │
│ Flaw in    │◀───│ Collect data in      │          │ Preliminary deduction of │
│ crystal    │    │ defined hkl range    │          │ space group.             │
└────────────┘    │ gives I_hkl &        │          └──────────────────────────┘
                  │ background intensity │
                  └──────────────────────┘
┌──────────────────────────────────┐
│ Data reduction, i.e. subtract    │
│ background from I_hkl,            │   ┌────────────────┐ ┌───────────────┐ ┌──────────────┐
│ correct for geometrical and      │   │ Obtain initial │ │ Obtain initial│ │ Obtain heavy │
│ polarisation factors, correct    │   │ model by       │ │ model by      │ │ atom position│
│ for absorption, produce          │   │ structure      │ │ direct methods│ │ by Patterson │
│ h,k,l, F_O^2, σ(F_O^2)           │   │ analogy with   │ │               │ │ methods      │
└──────────────────────────────────┘   │ isostructural  │ │               │ │              │
                                        │ solid          │ │               │ │              │
                                        └────────────────┘ └───────────────┘ └──────────────┘
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Using initial model calculate structure factors F_C using

$$F_{hkl} = \sum f_i \, e^{2\pi i (hx_i + ky_i + lz_i)}$$

Obtain intial phases of structure factors S_C

Calculate electron density maps using the modulus of F_O and the phase of the F_C (S_C).

$$\rho_{xyz} = \frac{1}{V} \sum S_C |F_O| e^{-2\pi i (hx_i + ky_i + lz_i)}$$

Calculate difference Fourier maps to locate missing atoms

$$\Delta\rho_{xyz} = \frac{1}{V} \sum |F_O - F_C| \, e^{-2\pi i (hx_i + ky_i + lz_i)}$$

Obtain positions of missing atoms add to model

Obtain new model

Calculate structure factors using refined model

Refine by least squares refinement in 3D. This varies x,y,z and U in order to minimise the difference between F_O and F_C

Are the R-factors low ?
Are the ESDs low ?
Are all the atoms located ?

Calculate R-factors and estimated standard deviations

$$R_1 = \frac{\sum |F_O - F_C|}{\sum |F_O|}$$

$$wR_2 = \sqrt{\frac{\sum w(F_O^2 - F_C^2)^2}{\sum w(F_O^2)^2}}$$

where w is a scale factor

Calculate bond lengths and angles

Does the model make chemical sense ?

Obtain final tables of atomic parameters bond lengths and angles
Molecular and crystal structure projections

Typical processes involved in single crystal structure determination

Thermal parameters

Scattering by an atom is dependent not only on its atomic number (size), but also on how much it vibrates.

At room temperature and above atoms show significant thermal vibration, which means that their electron density will be spread out over a larger volume.

If this vibration is considered to be the same in every direction it is termed isotropic and is described by a single parameter. The scattering is modified by:

$$e^{-B(\sin\theta)\lambda^2}$$

Where B is the isotropic thermal parameter:

$$B = 8\pi^2\overline{U}^2$$

$\overline{U}^2$ is the mean square vibrational amplitude. Both B and $\overline{U}^2$ have units of Å^2

The isotropic vibrational analysis is somewhat simplified. In real molecular structures atomic vibration is not the same in every direction.
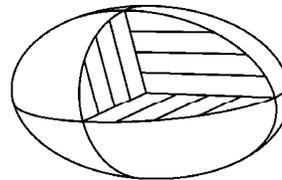
The vibration is therefore better described as anisotropic and requires six parameters.

$$\exp[-2\pi i^2 (U_{11}h^2a*^2 + U_{22}k^2b*^2 + U_{33}l^2c*^2$$

$$+ 2U_{12}hka*b* + 2U_{13}hla*c* + 2U_{23}klb*c*)]$$

The parameters U_{11} U_{22} U_{33} U_{12} U_{23} and U_{13} are known as anisotropic thermal parameters
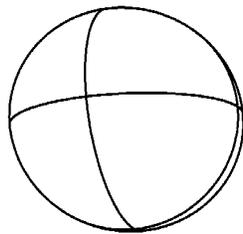
Isotropic vibration
(sphere)

Anisotropic vibration
(ellipsoid)

Bond Lengths and Angles

Generally for a triclinic cell, bond length l is given by:

$$l = \left\{ \begin{array}{l} (a(x_1 - x_2))^2 + (b(y_1 - y_2))^2 + (c(z_1 - z_2))^2 \\ -2ab(x_1 - x_2)(y_1 - y_2)\cos\gamma \\ -2ac(x_1 - x_2)(z_1 - z_2)\cos\beta \\ -2bc(y_1 - y_2)(z_1 - z_2)\cos\alpha \end{array} \right\}^{\frac{1}{2}}$$

For angle θ between atoms A, B and C separated by distances AB, AC and BC

$$\theta = \cos^{-1}\left(\frac{(AB)^2 + (AC)^2 - (BC)^2}{2(AB)(AC)} \right)$$