

Fourier syntheses

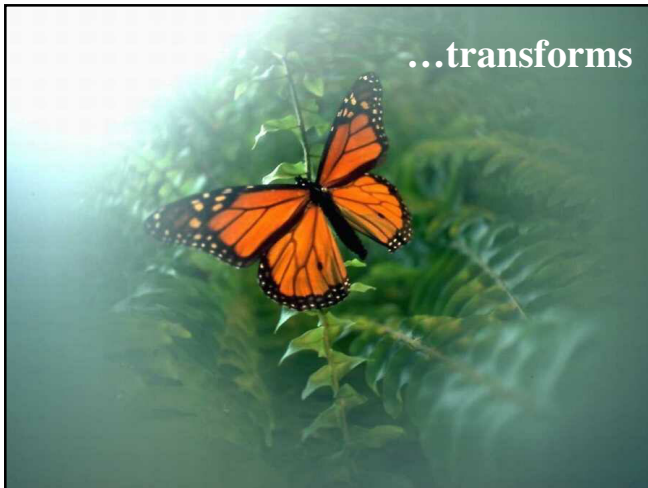
Bill Clegg

CCG course 2005

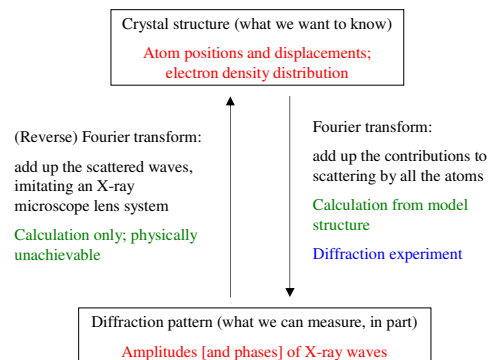
Furrier...



...transforms



7.1 The relationship between a crystal structure and its diffraction pattern



Models of a crystal structure

Electron density: a continuous function with a single value at each point in the unit cell
 $\rho(x,y,z)$

A collection of atoms: each would be a spherical electron density distribution at rest, but is smeared out by displacements (vibration, disorder,...)

Parameters to describe this:

Atomic scattering factors (how each atom scatters X-rays)
 $f_j(\sin\theta/\lambda)$, for $j = 1 \dots N$ with N atoms in the unit cell
known functions, tabulated

Atomic displacement parameters (smearing out of the atomic electron density over a larger volume)

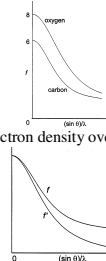
isotropic (one parameter per atom)
anisotropic (usually six parameters per atom)

Modify the atomic scattering factors f_j , reducing them, especially at higher angles

Atomic positions: coordinates as fractions of the unit cell axis lengths (pure numbers, no units)

x_j, y_j, z_j

Note: adding or subtracting any integer is equivalent to moving into another unit cell



7.2 Forward and reverse Fourier transforms

Some basic notation

For each single wave, $F = A + i B$

where i is a special symbol that just means "keep the i-terms and non-i-terms apart"; this is just a way of writing two orthogonal coordinates (similar to the National Grid for specifying places in Britain).

$$\begin{aligned} F &= |F| \cos \phi + i |F| \sin \phi \\ &= |F| (\cos \phi + i \sin \phi) \\ &= |F| e^{i\phi} \quad \text{by a standard property of complex numbers} \end{aligned}$$

In full: $F(hkl) = |F(hkl)| \exp[i \phi(hkl)]$ for each diffracted wave with indices h,k,l

'structure factor' amplitude phase

The forward Fourier transform (the diffraction experiment, which can also be modelled by calculation)

Diffraction pattern = Fourier transform of electron density

$$F(hkl) = \text{FT} [\rho(xyz)]$$

In full mathematical form:

$$F(hkl) = \int_{\text{cell}} \rho(xyz) \cdot \exp[2\pi i(hx + ky + lz)] dV$$

What does this mean?

To calculate the **structure factor (amplitude and phase)** of a reflection in a particular direction (specified by h,k,l), take the value of the **electron density at each point in the unit cell**, multiply by a **complex number** that combines xyz (the structure in 'real space') with hkl (the diffraction pattern in 'reciprocal space'), and add up all these values (**integrate over the whole cell volume**).

As well as representing what happens in the experiment, this calculation can also be done to imitate the experimental process, giving a set of calculated structure factors (one sum for each diffracted beam or reflection), each with an amplitude $|F(hkl)|$ and phase $\phi(hkl)$. In the actual experiment, only amplitudes are measured; phases are lost.

$$F(hkl) = \int_{\text{cell}} \rho(xyz) \cdot \exp[2\pi i(hx + ky + lz)] dV$$

Note that every bit of the structure contributes to every reflection.

All unit cells are identical, so the calculation is done just for the contents of one cell.

If a structure is known, these calculations should give a set of calculated amplitudes that agree with the observed ones except for a simple overall scale factor.

However, this is not a convenient form for calculation, because of the integration and the continuous function for the electron density. It is easier to describe the structure in terms of individual atoms. So we need to modify this equation.

Using the atomic description instead of continuous electron density, the forward Fourier transform equation becomes

$$F(hkl) = \sum_j f_j(\theta) \cdot \exp(-8\pi^2 U_j \sin^2 \theta / \lambda^2) \cdot \exp[2\pi i(hx_j + ky_j + lz_j)]$$

1 2 3 4 5

What does this mean?

Every atom scatters X-rays falling on it (**terms 3 and 4**). In any particular direction, specified by (h,k,l) , these separate scattered waves from each atom have different relative phases that depend on the relative positions of the atoms (**term 5**). The total diffracted wave in this direction (**term 1**, what we want to know) is just the sum (**term 2**) of all the X-rays scattered by the individual atoms. This fearsome looking equation just represents the combination or addition of many waves, with the correct relative amplitudes and phases, to give one resultant wave in each direction.

This calculation must be done for each diffracted beam (different h,k,l values). Every atom ($j = 1, 2, \dots$) in the unit cell contributes one term to the sum, with the appropriate scattering factor f_j , displacement parameter U_j , and position (x_j, y_j, z_j) .

Note that there is a wave $F(000)$, for which $h = k = l = 0$ and $\theta = 0$. It can't be measured experimentally, because it is coincident with the undiffracted X-rays. However, from the equation we can see that $F(000)$ is the sum of all atomic scattering factors at zero Bragg angle, which is the sum of the atomic numbers for all atoms in the unit cell, i.e. the total number of electrons in the unit cell. It represents all the electrons scattering together in phase. All other $F(hkl)$ values are smaller than this.

The reverse Fourier transform (the recombination of diffracted beams, which can not be carried out experimentally)

Electron density = Fourier transform of diffraction pattern
 $\rho(xyz) = \text{FT} [F(hkl)]$

In full mathematical form:

$$\rho(xyz) = \frac{1}{V} \sum_{h,k,l} F(hkl) \cdot \exp[-2\pi i(hx + ky + lz)]$$

$$\rho(xyz) = \frac{1}{V} \sum_{h,k,l} |F(hkl)| \cdot \exp[i\phi(hkl)] \cdot \exp[-2\pi i(hx + ky + lz)]$$

The term $1/V$ is just to give the correct units (electron density is in electrons per cubic Å, but structure factors F are in electrons). Note an extra minus sign in the final term compared with the forward Fourier transform.

We need to include all reflections in this sum, also $F(000)$. In practice, we measure reflections only up to some chosen maximum Bragg angle, but higher angle reflections are weaker (because of the atomic scattering factors and atomic vibrations), so they contribute little to the sum anyway.

$$\rho(xyz) = \frac{1}{V} \sum_{h,k,l} |F(hkl)| \cdot \exp[i\phi(hkl)] \cdot \exp[-2\pi i(hx + ky + lz)]$$

1 2 3 4 5

What does this mean?

The image of the electron density (**term 1**, what we want to know) is obtained by adding together (**term 2**) all the diffracted waves, with their correct amplitudes (**term 3**) and correct relative phases (terms **4** and **5**). **Term 4** is the intrinsic phase of each diffracted wave, and **term 5** is also needed in order to add up the effects of the waves at different places in the unit cell.

Term 3 is the observed amplitudes, from the experiment.

Term 5 can be calculated.

But **term 4** is the unknown phases: the Phase Problem.

The sum is carried out for lots of different positions (xyz) covering the unit cell (in practice, we only need to cover the asymmetric unit, and the rest is generated by symmetry). For each position, there is a contribution from every diffracted wave.

So every observed diffracted beam contributes to the electron density at every position.

All waves consist of equal positive and negative parts, and thus they make no net contribution to the total electron density in the unit cell when added to the Fourier synthesis. Only $F(000)$ makes a net contribution, equal to the total number of electrons in the unit cell.

A Fourier synthesis may be thought of as smearing out the correct total number of electrons uniformly throughout the unit cell (this is the $F(000)$ term), and then redistributing this density by successive addition of other waves, each of which will reduce the density in some regions and increase it in others by the same amount.

7.3 Some mathematical and computing considerations

Illustration by a relatively small crystal structure

Unit cell $10 \times 10 \times 10 \text{ \AA}$, containing 60 atoms

7000 reflections ($\theta < 25^\circ$ with $\text{MoK}\alpha$ radiation)

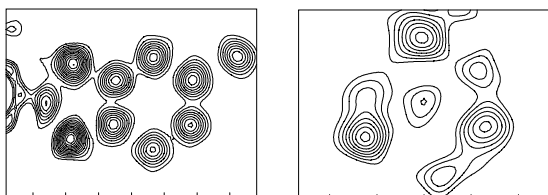
Forward FT to obtain F_c (ignoring symmetry effects): 7,000 sums, in each of which there are 60 terms; 420,000 calculations.

Reverse FT to obtain electron density at points 0.3 \AA apart: 37,000 points in the unit cell, so 37,000 sums, in each of which there are 7,000 terms; about 260 million calculations.

Remember: reflection phases can take any value between 0 and 360° for non-centrosymmetric structures, but must be either 0 or 180° for centrosymmetric structures, considerably simplifying the mathematics.

In small-molecule crystallography, electron density maps are not often looked at (though they can be very revealing!). Instead, automatic peak-finding routines locate the centres of the lumps of electron density (atoms) and just provide coordinates of proposed atoms.

Since electron density is three-dimensional, planar sections are often represented as contour maps.



7.4 Uses of different kinds of Fourier syntheses

$$\rho(xyz) = \frac{1}{V} \sum_{hkl} |F(hkl)| \exp[i\phi(hkl)] \exp[-2\pi i(hx + ky + lz)]$$

$ F(hkl) $	measured amplitudes
$\exp[i\phi(hkl)]$	unknown phases
$\exp[-2\pi i(hx + ky + lz)]$	easily calculated

Different kinds of Fourier syntheses use different coefficients instead of the observed amplitudes $|F|$ in this equation; they may also apply weights, so that reflections contribute more or less strongly to the sum.

Patterson syntheses

Use $|F_0|^2$ instead of $|F_0|$

Set all phases to zero

All necessary information is known

The result is not the desired electron density!

But it is related to it in a potentially useful way

...see later! (today)

E-maps

Use $|E_0|$ instead of $|F_0|$ (normalized structure factors)

— equivalent to point atoms at rest

Use only the largest $|E_0|$ values (fewer phases needed)

Unknown phases estimated by 'direct methods'

E-maps tend to contain sharper peaks

but also more noise (peaks not corresponding to genuine atoms)

... see later! (Peter Main)

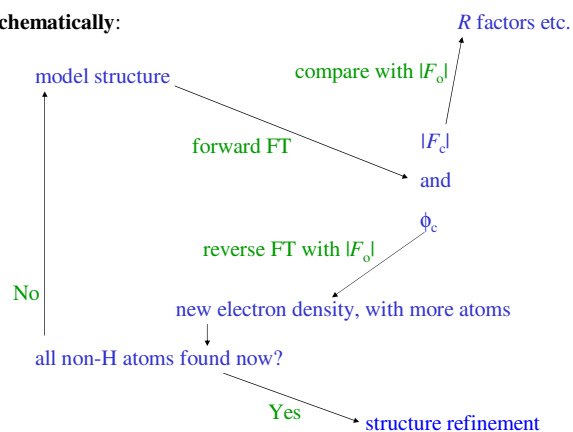
F_o syntheses

Use $|F_o|$ from the diffraction experiment

Phases are estimated from a model structure

The map contains model structure atoms plus new atoms
(and spurious peaks)

Schematically:



Difference syntheses

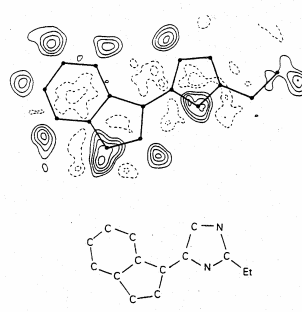
Use $|F_o - F_c|$ instead of $|F_o|$

Phases are estimated from a model structure

The map contains new atoms (and spurious peaks)
and *corrections* to model structure atoms

$|F_o|$ and $|F_c|$ must be on the same scale

Weights may be used, since some reflections (especially weak ones) are likely to have relatively large uncertainties



Top: difference map, with contours, and with model structure atoms and bonds superimposed.

Bottom: provisional assignment of atom types in the model structure.

The correct formula is $C_{13}H_{12}N_2O$

$2F_o - F_c$ syntheses

Use $2|F_o| - |F_c|$ instead of $|F_o|$

Phases are estimated from a model structure

This combines features of full and difference syntheses

Uses of difference syntheses at different stages

Location of hydrogen atoms
(down-weight high-angle data?)

Confirmation of completeness of refined structure
(all data, no weights)
should contain no significant features

Weighted Fourier syntheses

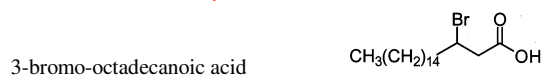
$$\rho(xyz) = \frac{1}{V} \sum_{hkl} w(hkl) |F(hkl)| \exp[i\phi(hkl)] \exp[-2\pi i(hx + ky + lz)]$$

Choose weights w to alter the relative contributions of different reflections for various reasons

- emphasise certain features (see H atoms above)
- compensate for expected errors in phases

The final difference synthesis must be unweighted!

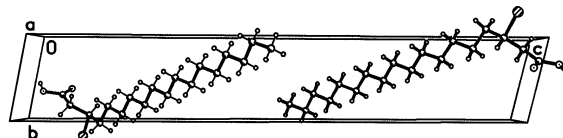
Illustration of Fourier syntheses with a 'one-dimensional structure'



a long thin molecule with a single heavy atom

Crystallises with 2 molecules in a triclinic unit cell, related to each other by inversion symmetry (asymmetric unit is half the unit cell)

Unit cell is also long and thin: $a \sim b \ll c$



We can use a much simplified version of the Fourier transform equation here.

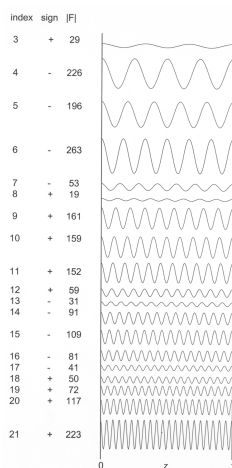
1. Use only $(00l)$ reflections to obtain information about the structure only along the c axis (find only z coordinates), because the molecule lies mainly in this direction.
2. Because of the inversion symmetry, all reflection phases must be either 0 or 180° ; no other values are possible. This is true for ALL centrosymmetric structures. Choosing a phase now just means choosing either a positive or a negative sign for each term in the sum: do we add the wave 'the right way up' or 'upside down'?
3. The inversion symmetry also turns the final exponential term into a simpler cosine.

$$\rho(z) = \frac{1}{c} \sum_l |F(l)| \cdot \text{sign}[F(l)] \cdot \cos[2\pi(lz)]$$

wanted known +1 or -1 easily calculated

We have 19 measured amplitudes, for $l = 3$ to 21 (others not accessible in this 1966 experiment). So there are 2^{19} possible answers for different combinations of signs of waves; this is over one million!

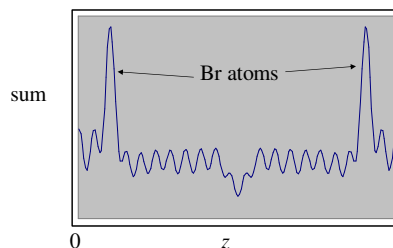
Look at the contributions the 19 individual waves can make to the sum; larger amplitudes mean a bigger contribution. The final cosine term means that reflections with small l (low Bragg angle) contribute low resolution information, and those with large l (high Bragg angle) contribute high resolution information.



All the contributions are shown here with zero phase (positive sign). The correct signs are listed on the left; of course, we do not know these to begin with!

Adding up all 19 waves with the correct signs gives a clearly recognisable one-dimensional structure: the two large peaks are the Br atoms of the two molecules in the unit cell, and the smaller peaks, approximately equally spaced, are C and O atoms (which overlap each other in pairs along this direction).

Other possible combinations of signs for the waves are explored in an [Excel spreadsheet](#) (using all waves with $l = 0$ to 21).



Summary of points from spreadsheet use

1. Adding waves with random (or wrong) signs gives nothing helpful.
2. Adding waves with correct signs gives easily recognised structure.
3. Waves with small amplitudes can be omitted and this makes little difference; this reduces the number of phases to be found.
4. The Br atoms can be found easily from a Patterson synthesis.
5. Adding waves with signs obtained from a model structure consisting only of the Br atoms gives close to the right answer.
6. A difference synthesis shows the missing C/O atoms without the dominant electron density of the known Br atoms.
7. The structure can also be used to illustrate direct methods!