Chapter one shows that a diffraction pattern measured in the far-field can under certain approximations be considered as the Fourier transform of the object. The next step in the experiment is to record the diffraction pattern, so that we can hopefully back calculate the structure of the object that we have injected. Since radiation can be considered as a wave, two parameters describe it at any point: the amplitude of the wave, and the phase phi (where is the wave in its oscillation). In equation we can see F(s) as the amplitude and Sr as the phase. Experimentally it is not possible to measure the phase of X-rays directly, it varies at times shorter than an attosecond. How to deal with this missing data will be described in a later section. The amplitude can be measured by measuring the intensity of the wave at a certain point (I = |A|2).

The problem of unknown phases is well known and is called the phase problem. There are many ways to overcome it: for example in crystallography the anomalous scattering of heavy atoms is exploited to retrieve phases (these techniques are named SAD or MAD). Holography uses the interference between two wave fields to obtain the phases. Ptychography uses the precisely known overlap and high redundancy between many exposures to solve the phase problem.

CXI has a different and neat way to retrieve phases. To understand the method we should look back at crystallography. In crystallography a molecule, say haemoglobin, is packed in a regular lattice structure (this is the infamous crystallization step). Mathematically this can be described by C = H \* L. Where C denotes the crystal, H is the electron density of hemoglobin, L is the lattice structure of the crystal, and \* denotes the convolution. Convolution just places a copy of H at each point in L. The diffraction pattern of crystal can be described as: F(C) = F(H \* L) = F(H) F(L). Here we used the convolution theorem in Fourier theory. A derivation of this equality can be found in (). The Fourier transform of a lattice structure gives another lattice structure with inverse lattice dimensions. This means that the Fourier transform of hemoglobin F(H), also known as the molecular transform, is sampled at discrete points F(L), the so called Bragg peaks (SBragg). In contrast, in CXI F(H) is sampled at the much finer pixel grid of the pnCCD detector (SCXI).

In 1952 Sayre noticed that sampling F(H) at the F(Lattice) is sampling at the critical sampling rate (see Shannon 1949). This means that knowing the phases belonging to the Bragg peaks is just enough to back calculate the structure of hemoglobin. If the sampling rate of F(H) SCXI is finer than twice SBragg, it is theoretically possible to retrieve the phase information from the measured intensities alone. This situation is called oversampling.

In practice there are many ways of actually retrieving the phase information, but one of the most common phase retrieval techniques are based on convex optimization algorithms. In the next section the general idea behind convex optimization is explained.

Convex optimization

As can be seen in Figure oversampling in Fourier space implies that there is an area the size of dL around the object for which we know the electron density is zero. This forms a constraint on the data. We know that a correct choice of phases would make the corresponding rho(r) be zero in this area. The area that can contain positive electron density is called the support. Furthermore, we know the recovered Fourier amplitudes should agree with the measured intensities. In general an optimization algorithm tries to find a solution for which the distance to both these constraints is maximal or minimal (minimal in our case). An iterative approach to find the solution that minimizes the disagreement of both constraints can be described as follows:

1. Assign random phases to each pixel
2. Inverse Fourier transform F(s)
3. Set all electron density outside of S to zero, keep other electron density.
4. Fourier transform rho(r)
5. Make sure all amplitudes match the measured intensities. Keep the phases.
6. Go back to step 2.

A way to formally write down the constraint of step 3 and 5 can be found in equations.

Two error metrics can be associated with both constraints; the fourier error (Ef) and the real space error Er.

Convex optimization means that there is only one solution. A most straightforward implementation of the above-described algorithm is called Error Reduction, invented in by Gerchberg, Saxton.

Often our constraint sets are not convex, which means that there are multiple solutions (minima). In this case ER will likely not find the global minimum, thus other algorithms were invented. Historically an algorithm named HIO was one of the first. In this algorithm step 5 is slightly adjusted.

Shrinkwrap

Effect of missing data

Simulation of phase contrast methods