Single-crystal X-ray crystallography

The most common experimental means of obtaining a detailed picture of a large molecule like a protein.

Allows the resolution of individual atoms.

Not an imaging technique!

Interpretation of the scattering (diffraction) of X-rays from many identical molecules in an ordered array like a crystal.

Creation of a molecule’s image from a crystal has similarities to creating an image with a lens
Why do we use x-rays?

• The features we’re trying to see are on the order of the distance between atoms: $10^{-10}$ meters.

• To “see” the atoms, we need to use light with a wavelength that is close to this distance.

• X-Rays (x-ray light) have a suitable wavelength.

What is a crystal?

• A crystal is a periodic arrangement of objects (molecules) repeating in two or three dimensions.

• The repeating unit is a parallelepiped (in 3-D) or a parallelogram (in 2-D).

• A crystal of a typical protein will be half a mm on a side and contain $10^{15}$ molecules.
Why do we use crystals when we’d like to see one molecule?

• We can’t focus enough X-rays into a small enough volume to “see” a molecule.

• Even if we could, the X-rays would burn up the molecule.

• Even if that would work, we don’t have a lens for the X-rays.

• A single molecule is a weak scatterer for X-rays. Diffraction from a periodic arrangement of molecules (crystal) results in an amplified signal.

Growing crystals

• Slow, controlled precipitation from aqueous solutions that do not denature the protein

• Precipitants: ionic compounds (salts), organic solvents, polymers like polyethylene glycol.
Q: How do we perform the second interference step in the functioning of the lens -- to reconstruct the image of the original object?
A: We will have to calculate it.

Q: How will we represent that object?
A: The x-rays are scattered from electrons in the atoms of the crystal.

Therefore: for us, the “image” is going to be a representation of the electron density.
Electron-density maps

- Because protein molecules are in an ordered array in the crystal, electron density can be described mathematically by a periodic function, or as a Fourier series.
- Using the mathematical Fourier transforms the diffraction pattern can be converted to electron density maps.
- Computer programs are then used to come up with 3-d spatial coordinates.

What is the concept of “resolution?”
Another example.

The famous Taylor and Lipson rubber ducky.

From crystals to X-ray diffractometer, computer, electron density maps, and molecular models.