

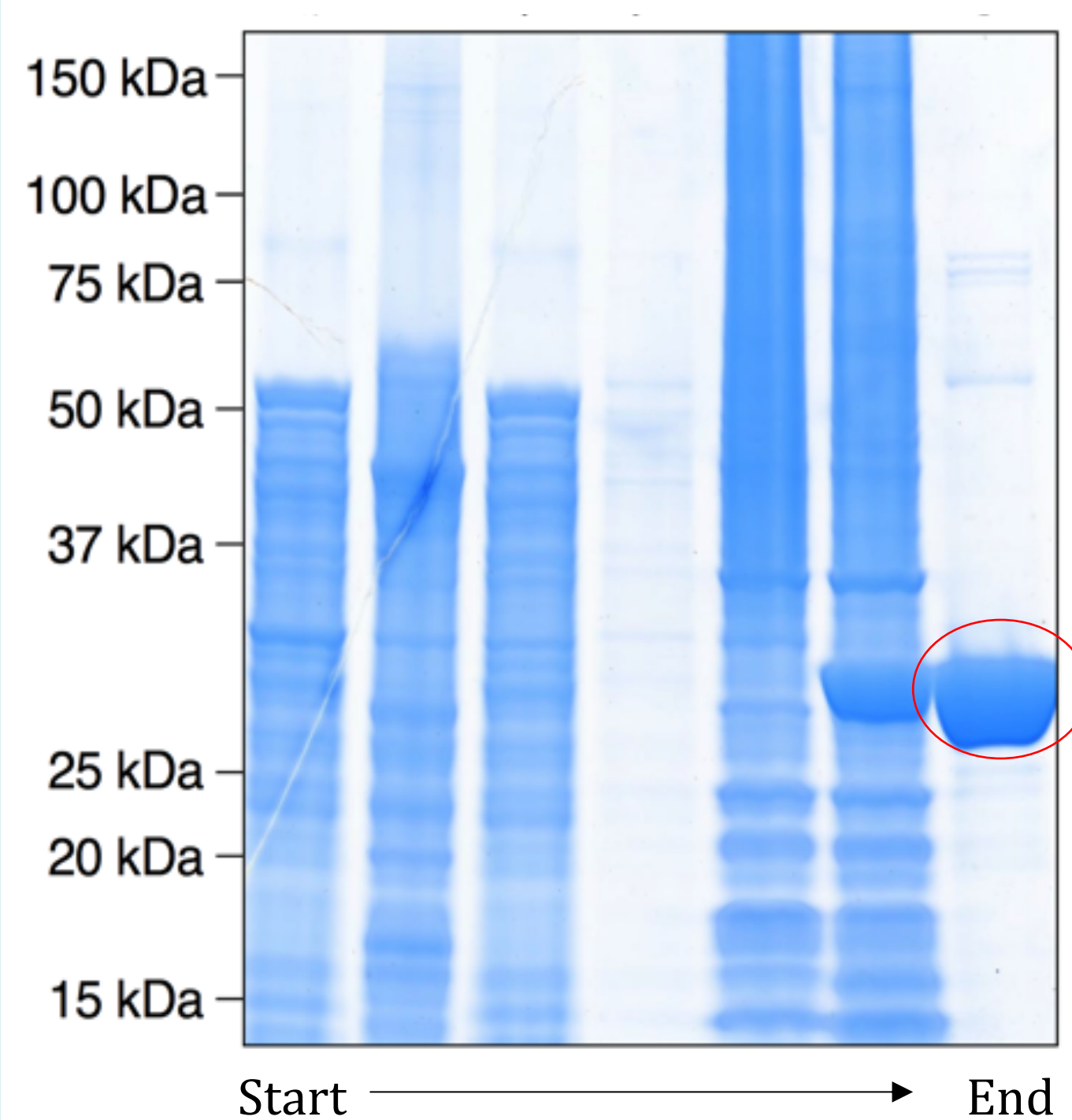
# How to determine a protein structure

## What are proteins?

- Proteins are molecular machines that perform many important tasks within the cell

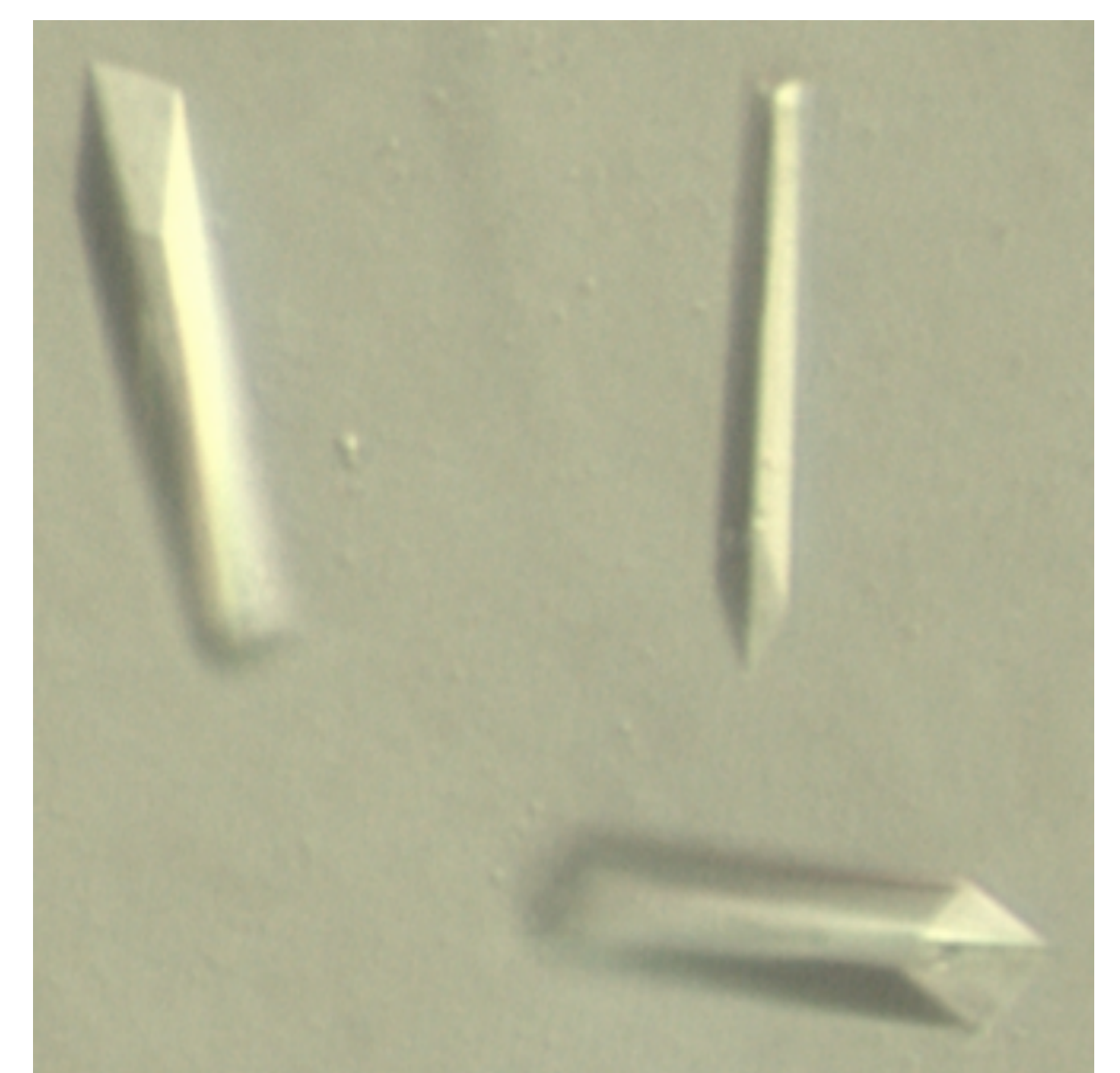
## Why determine a protein structure?

- Proteins have a defined three dimensional structure. Knowing what the protein looks like in three dimensional space can help us understand how they work, and what happens when they go wrong
- How can we work out what these vital molecular machines look like?
- One of the best methods is X-ray crystallography



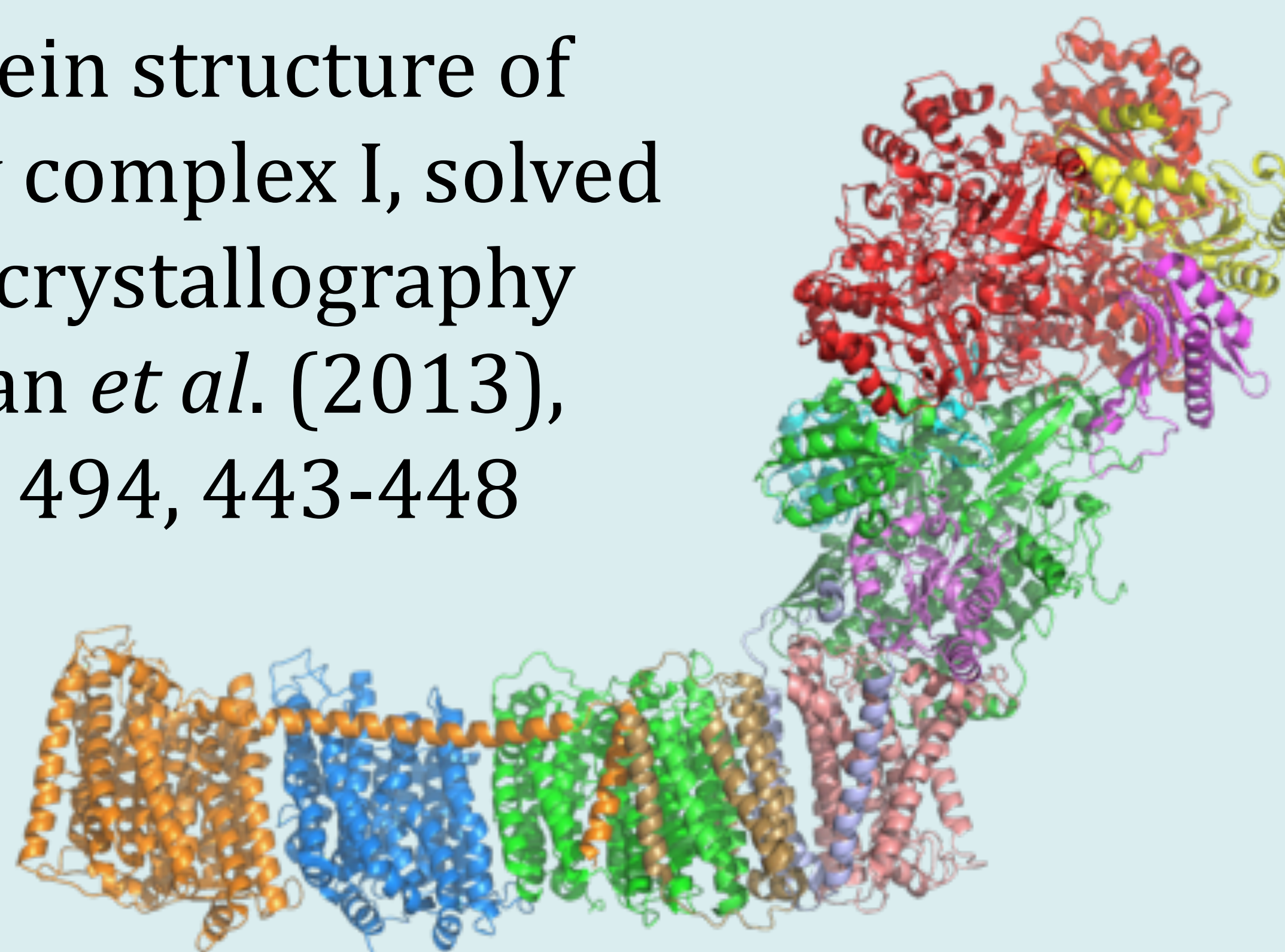
- Cells contain thousands of different proteins
- We first need to purify the protein of interest from the rest of the proteins in the cell!

- We crystallize the protein; crystals are ordered, three-dimensional arrays of individual protein molecules
- These crystals are only 0.1 mm long!



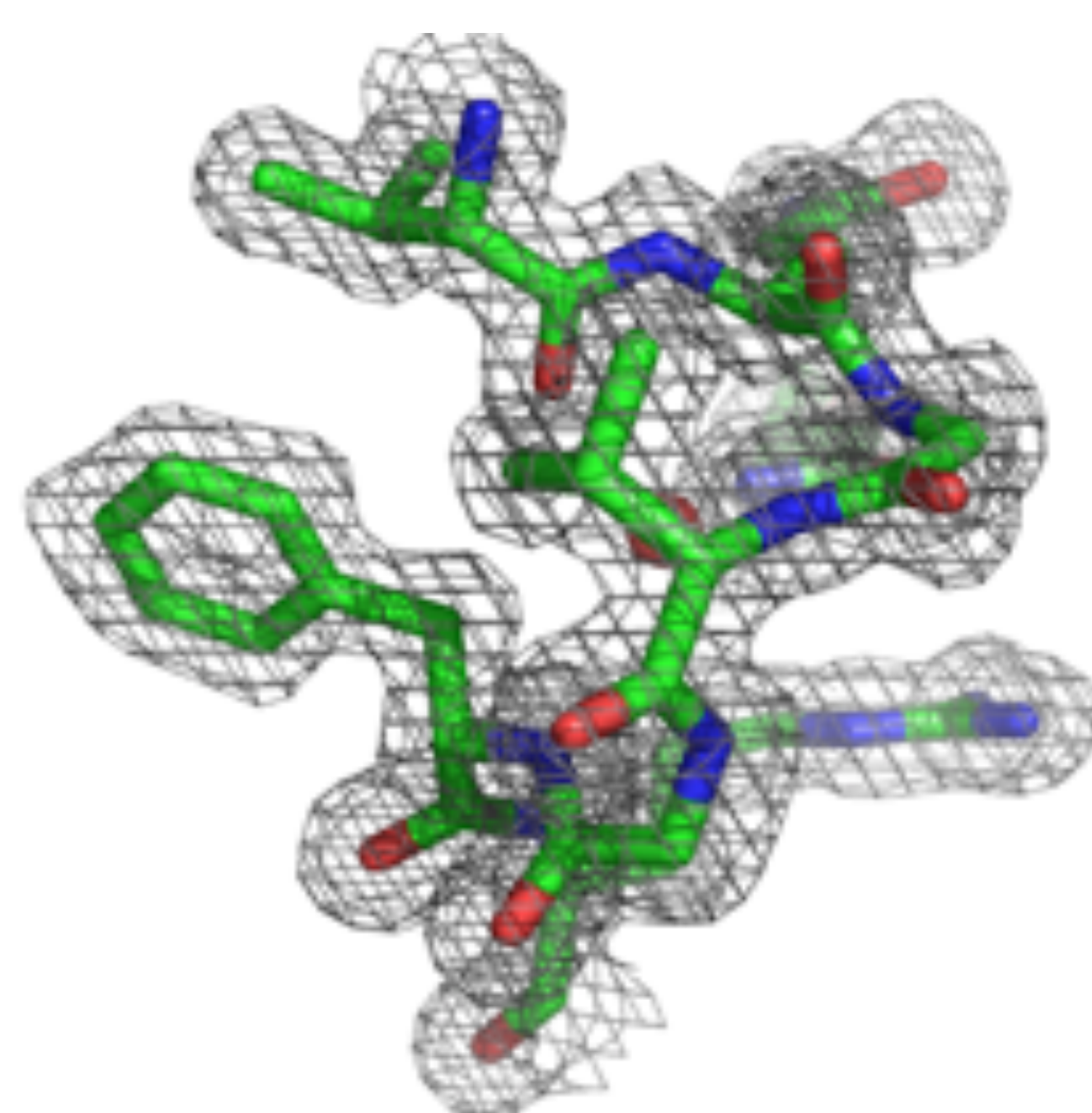
### Step 1: Purify the protein!

The protein structure of respiratory complex I, solved by X-ray crystallography Baradaran *et al.* (2013), Nature, 494, 443-448



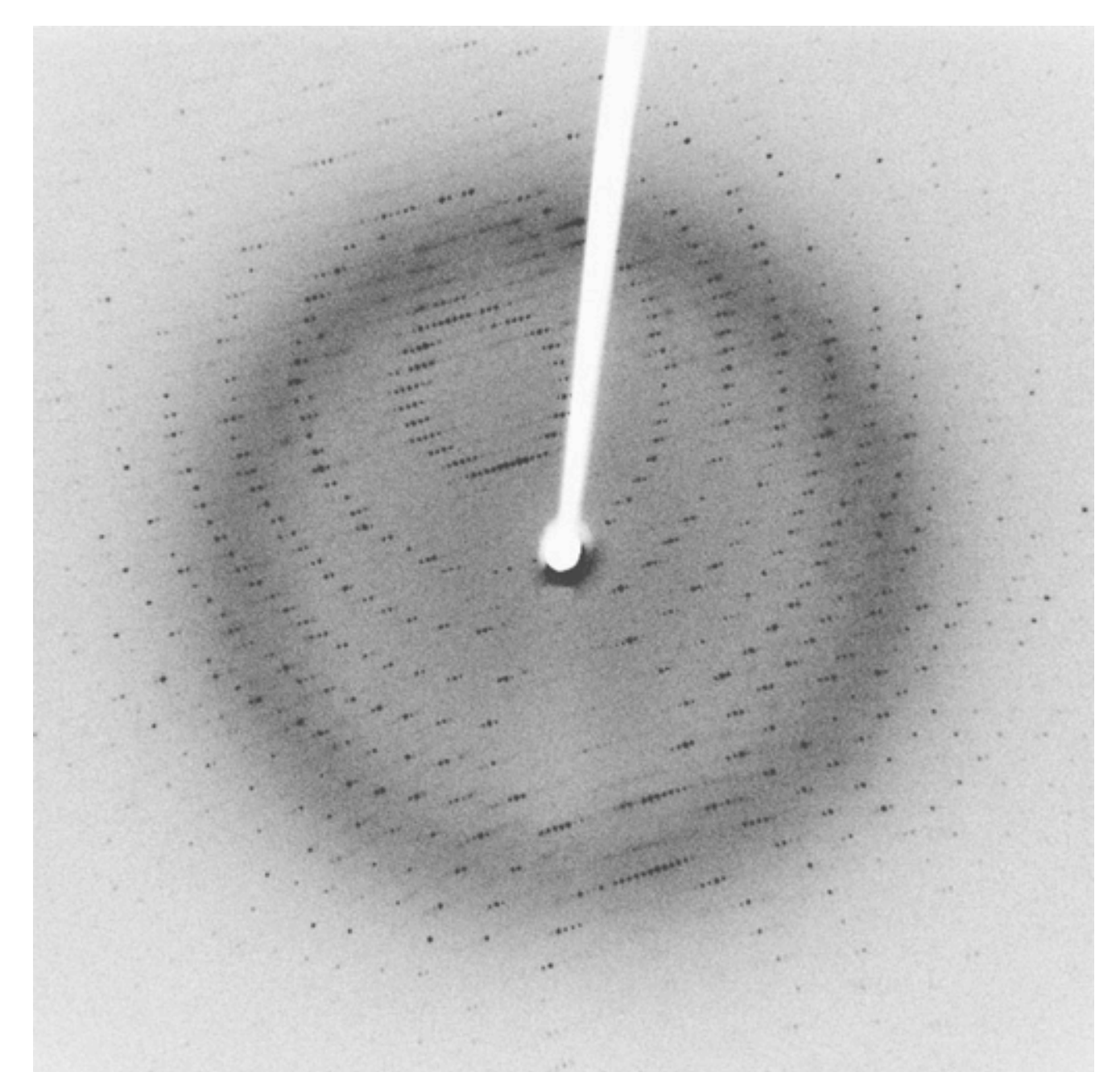
### Step 2: Crystallize the protein!

### Step 4: Determine the structure!



- Using complex mathematics, we can estimate where the electrons are within the crystal
- We can then model where the atoms are within the protein!

- We 'shoot' the crystals with X-rays!
- The electrons around the atoms diffract (or 'bend') the X-rays; this produces a diffraction pattern!



### Step 3: Shoot the crystals with X-rays!

- Determining a protein structure can take years (or even decades) of research!
- Over 100,000 protein structures have been determined using X-ray crystallography!
- These are all freely available to look at on the internet ([www.rcsb.org](http://www.rcsb.org))!