(0:23) This is a three dimensional structure of a protein called lysozyme. It represents the order of nature, and I feel awed when I look at it. (0:35) It's an enzyme that's in our tears, saliva and mucus, and helps us fight bacteria. And knowing this three dimensional structure helps us to understand the mechanism of action of this enzyme and therefore how it helps fight bacteria in our bodies. (0:55) Unfortunately, the size of the molecule is such that is far too small for us to see under a light microscopy or with our naked eye, because the wavelength of light is much, much larger than the size of this tiny molecule. For that reason, we have to use radiation that is much smaller in wavelength, and we use x-rays to look at this molecules.

(1:30) These are protein crystals. Locked within each crystal are millions of protein molecules, all arranged in a ordered, grid-like structure. By firing x-rays at these and measuring how they scatter, we can work out the molecular structure of nearly any crystallized sample. It's through this method, know as x-ray crystallography, that some of the most important biological structures have been obtained, from the double-helix of DNA to numerous proteins, vitamins and drugs. (2:07) But getting from a crystal to something like this, the structure, is not at all trivial, and it can take a long time to grow suitable crystals.

(2:26) Now we are in the protein production and purification lab, because before we can set up crystallization trials, we need to produce enough protein for that process. We do this by genetically modifying E. coli bacteria, which then act as a little factory to produce our protein in large flasks of broth, which we incubate. Once that's happened, we break open the cells, extract the protein and then purify it ready for the crystallization process.

(3:01) So, why do we need to grow crystals of our protein molecules before we can shine x-rays at them and try and find the three dimensional structure of them? If we imagine this string of beads is a protein molecule made up of twenty different aminoacids - different colored beads - that are found in nature, this folds up in a very complex, complicated manner, in a three dimensional shape, like this. And if we look at one of these, a true biological molecule here, real one, what this metal model represents is the string through the beads. And we can see it starts at this end and follows a pretty torturous path going around here, that you'd never imagine when you just look at this string of aminoacids. And the other end of it comes out here. (3:47) Now it turns out if I take a tube here with my protein in it that I've purified and prepared, there are millions and millions of protein molecules in there, and if I shine x-rays at it, the x-rays will scatter off in all sorts of random directions and I won't get any information about the shape of the molecule within the tube. However, if I can get the protein molecules to line up in an ordered array, such as in a crystal, where they are all lined up in the same orientation, when the x-rays scatter from the crystal, then I can get enough information, the signal is strong enough for me to get the three dimensional structure of the protein.

(4:38) We've now come down to the crystallization lab to look at how we crystallize proteins. In this Petri dish, I've got some supersaturated sodium acetate and that means there are so many molecules crowded in this solution, it's almost not holding the molecules and it wants to solidify. And if I hit it with this spatula here, you can see that it crystallizes. We get a fantastic pattern as it crystallizes across the dish.

(5:17) Essentially, this is what we try to do with our protein, which is to produce supersaturated solution of the protein, and we dehydrate in a very controlled manner. (5:32) The proteins we work on here, unfortunately, can be sometimes really difficult to crystallize, so we load small volumes of the protein into trays like this with different additives, but we have robots that help us do that, by pipetting small volumes into these trays. Once we have the tray with the protein and additives in, we take it to this crystal hotel, which holds the tray for several weeks at 4°C and also monitors whether we have crystals or not, by photographing the tray drops regularly.

(6:20) But that is only part one of the story, because once we finally manage to grow a protein crystal, we then have to take it for x-ray analysis. And from the data we obtain, we try to generate a structure of our protein molecule, such as this one of lysozyme. (6:40) The protein structures we work on today are far more complex and they can produce very small and delicate crystals. So to study them, we have to take them to extremely powerful x-ray sources at specialist facilities, such as the Diamond Light Source. It's only once we get our crystals there, that the next stage of our journal can truly begin.