Introduction to Cell Biology
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Central Dogma: The DNA structure Part 3

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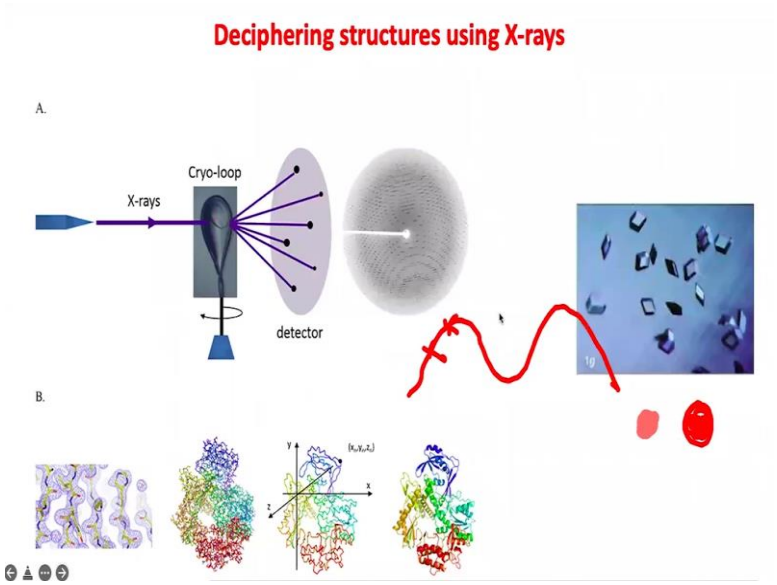

Is there any question at this point?

Student: Sir, what happens after the X-rays fall on the detector I did not get that, can you repeat?

Professor: So, imagine the detector like a TV screen. Imagine that you take a piece of paper with lots of holes in it, this is again not completely accurate, and you shine the light. And as shown over here, let us say the light goes through these holes and diffract. So, that you get spots on the TV screen.

Now, the TV screen will have detector will have will basically be pixelated in a way where each pixel will detect the light and transfer the information to a computer. Then the whole the pixels which have been which have received the light and which are activated will be erased and you will get a blank screen, the crystal will be turned by one degree and X-ray which will be shot through the crystal again.

You take an image, you turn the crystal, again, you erase the screen and you take another picture. So, you take a few thousand pictures like this, all of them looking approximately like the picture shown here, then all these images are collated, the intensities of each spot is

measured. And the patterns you see over here are based on the symmetry of what is called as a unit cell inside the crystal.

So, these are all very complicated concepts. And which you will learn as I said in third year, what you need to know is if you have a crystal of which is a regular crystalline array, you shine X-rays which have a very low wavelength, you will get a pattern and the pattern can be used to decipher electron density map. The electron density map, once you fit your model inside the electron density map will give you an atomic resolution structure of the macro molecule that you are trying to solve. Is that clear?

Student: Thank you, sir.

Student: Sir, could you explain the phase issue with crystallography you spoke about?

Professor: Not in this class. It is too complicated. Just remember that your there is something called as a phase problem, and you are losing the phase and effectively if you think of a beam of light. So, basically, the phase information is where the light is in phase, here or here.

So, you are losing this information, all you are getting is each spot which is very intense, or you have a spot which is less intense. So, you have intensity, but you are losing the phase information and in it, because we cannot detect, we do not have an ability to detect the phase. If we knew the phase, then we could solve the structure even more quickly.

Student: Sir, I had a doubt. Sir, what is A and B type of DNA?

Professor: I will come to it. That is all, I am doing things in a stepwise manner, I will come A and B type of DNA.

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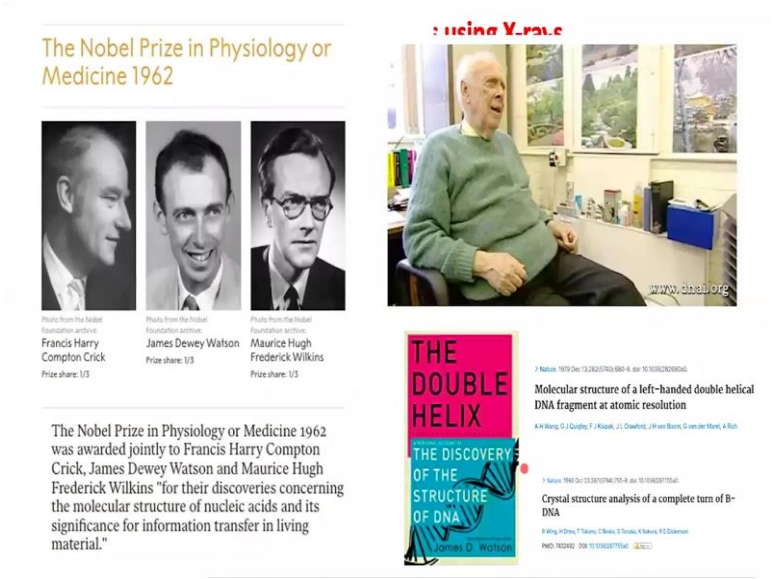

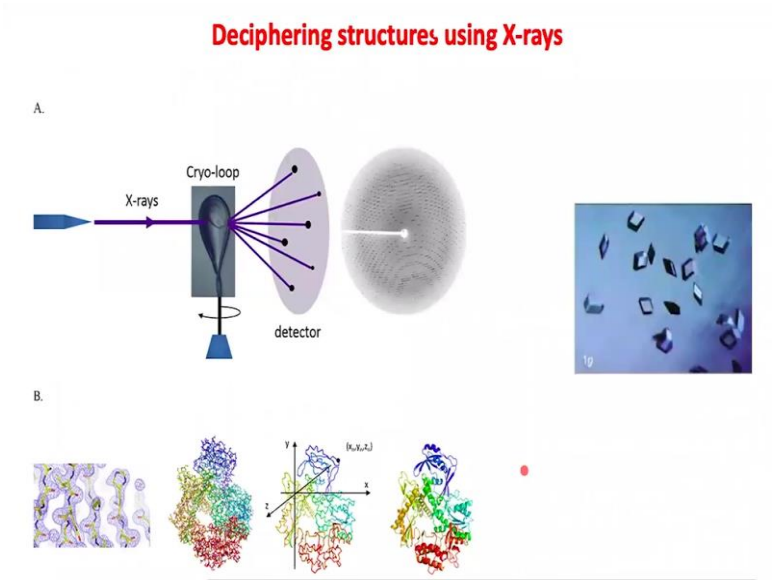

Student: Sir, in the electron density map can we fine each and every atom with the help of electron density map?

Professor: Yes, so it depends on so different crystals. Crystals are nothing but crystalline arrays, which we have made right after purifying macromolecules with proteins being the most common. Now all crystals which we grow in the lab, PhD students do that regularly are not of the same quality.

There is huge reasons for variation in quality. So, some crystals give diffraction patterns, which are very high resolution, which means we can get as much as 1.5-1 angstrom

resolution. I will explain what an angstrom is, that is one tenth of a nanometer. But some crystals do not.

But yes, the answer to your question is we can get atomic resolution electron density maps, which then can be used to extrapolate to a model, which is a atomic level model for using X-ray crystallography.

Student: Sir, it is still not clear to me why the fourth spot was missing in the DNA picture?

Professor: The question you are asking is literally a PhD third year question. Especially because you are asking something related to fiber diffraction, which frankly, I do not really understand. So, it turns out from what I can read is that if you do have the missing fourth spot seem to indicate to Watson and Crick and to Rosalind Franklin that they were two strands in the DNA not a single strand and you are right I even I do not understand at this point why that is so, this is one of the questions I cannot answer unfortunately.

I can answer some questions about spots on crystals but fiber diffraction I have never done and I have no experience.

Student: Sir, can you repeat how James Watson's book created controversy?

Professor: So, it created controversy because before he published his book, nobody publicly ever said that they had gone to King's College London, they had gone to Rosalind's lab in her absence. And Maurice Wilkins have shown her photograph and shown them photograph 51. And it was the photograph 51, which suddenly created neuronal firing in their brain, which led to the structure.

So, it is almost as if they had not seen the photograph, they might not have made the model. And even if they had made the model, it would have been much later rather than earlier, they would have to wait till they saw the picture in a paper which Rosalind was publishing in nature. So, literally, they got information about the patterns, which fibers of DNA were giving in advance, there is nothing wrong in that.

But Rosalind did not know about it, then Watson is a kind of an interesting guy. I will show you why he is an interesting guy. He also made a few comments about personal comments about people in the field, which was not appreciated. So, by the way you can just do a Google

search of all of this and these are controversies which have been talked about again and again and again. So, it is very easy information to get.

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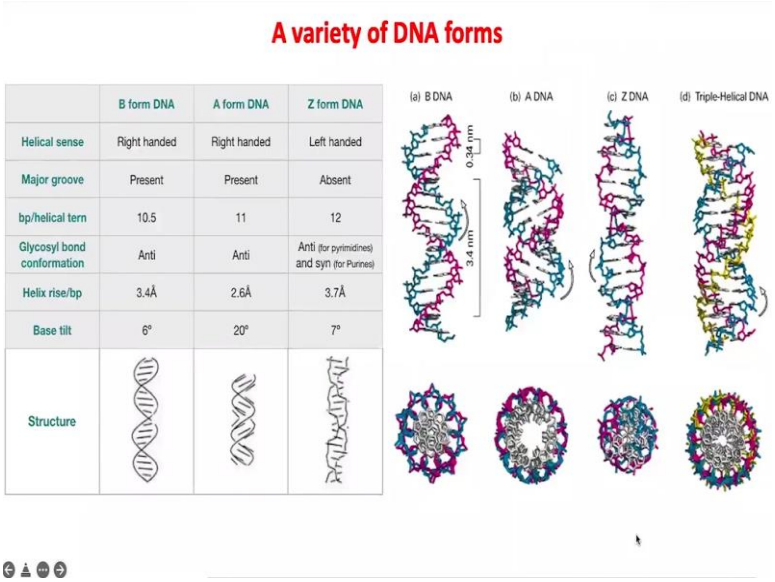

Student: Sir, the basic nucleotide, what is arrangement or basic nucleotide structure is the same in all forms of DNA?

Professor: Yes.

Student: So, like in all forms of DNA, it will be like one phosphate, one sugar and one base?

Professor: Yes.

Student: Sir, then why do these different shapes arise?

Professor: Shapes are biologically functional. It is like saying, if you again, a strange analogy, why would you make screws, for example, in different shapes is not one screw enough, each screw which is used for fitting a door or fitting a cupboard or fitting a table has its own, they are long screws, they are short screws, there are functional significance.

Similarly, these different forms of DNA, which are believed to be found inside the cell, they are not just artifacts of humidity and salt, have been clearly shown to have functional roles. In fact, the triple helical part and the four helical part have more functional roles than we ever realize. So, more interesting question is, four stranded DNA, why is it very important?

And it turns out, they have very important biological roles, more than let us say Z form versus A form of DNA.

Student: Also sir, they did not like Francis and Crick, disprove the triple helical DNA cannot exist. So, why is it existing?

Professor: No, so you see, all in the 1950s. Especially before 1953, there was not much data about what this molecule looked like. There was data for proteins, but DNA was people were clueless about whether it was single standard double standard, triple helical. And the B form of DNA is definitely a double helical antiparallel structure.

But it is only 10 years, 20 years later, that we realized that other forms of DNA, especially triple helical do exist. So, it is not as if the idea of triple helix is wrong. It is just that even the structure which Linus Pauling grew, or the model he made in 1953, early 1953, the even the model was wrong.

So, the current triple helical form of DNA is completely correct, because the model is correct. And we have structures of triple helical forms of DNA. And for it to be accurate, the three dimensional location of each nucleotide should be correct. And Linus Pauling was nowhere near the correct structure at that point of time.

Student: They basically disproved the model. Not the idea of triple helical DNA?

Professor: Yes, basically. So their model was wrong. They, for the first 10 years that the idea was that they could not be a triple helix. But today we know there is a triple helix.

Student: Sir, where is this triple helical DNA found?

Professor: It is found inside the cell.

Student: Sir, all cells?

Professor: Inside all cells, inside your cells also.

Student: Thank you, sir.