Medicinal Chemistry
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Tutorial 05 – Nucleic acids, and Basics of Molecular Biology

So welcome to the tutorial session. So in today's session we are going to look at the topics of RNA mediated protein synthesis. So we will start with the first question.

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The first question is, explain the process of translocation in protein synthesis? So again we have looked at protein synthesis in some bit of detail. And so here translation is a very important part of protein synthesis.

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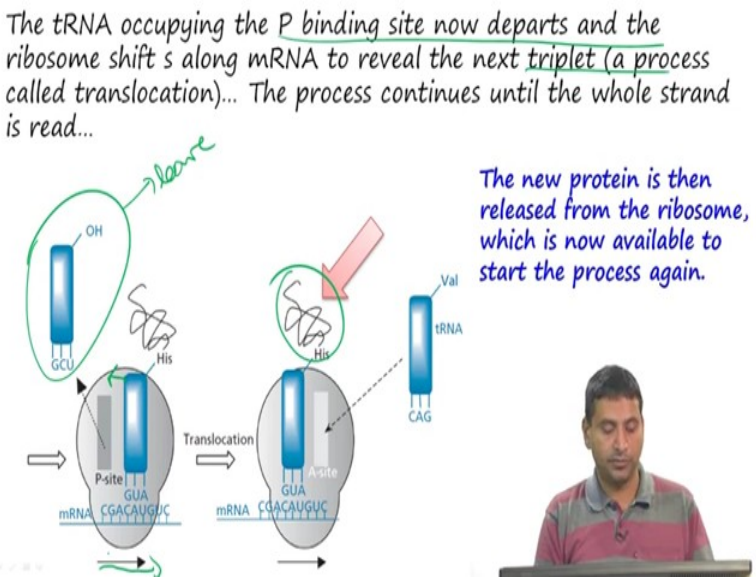

So what happens is that, once the tRNA occupies the P binding site and after it does, it forms the peptide bond and then it departs. The tRNA, the P binding site departs and the ribosome shifts along the mRNA. So in this process this tRNA is going to leave and a new tRNA should come and bind to the A binding site. But this molecule should shift. So in order for this to shift, you have the mRNA moving in one direction and this process wherein it moves or shifts and reveals the next triplet code is called translocation. So this is a very critical component of a protein synthesis because once the new protein is formed, it will be shifted out when the final stop codon shows up. But until then you need this process to happen in a very smooth manner and the translocation is an important part of this entire process.

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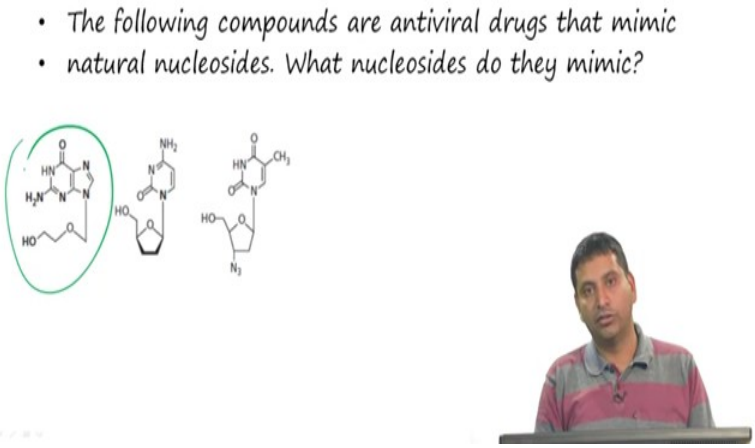

The next question, the following compounds are antiviral drugs, and they mimic the natural nucleosides. So they are shown over here, what nucleosides do they mimic? So here is, we look at in detail some of these examples of how these drugs work in the later part of the course. But let's, the question here is asking us to understand which nucleosides that they mimic.

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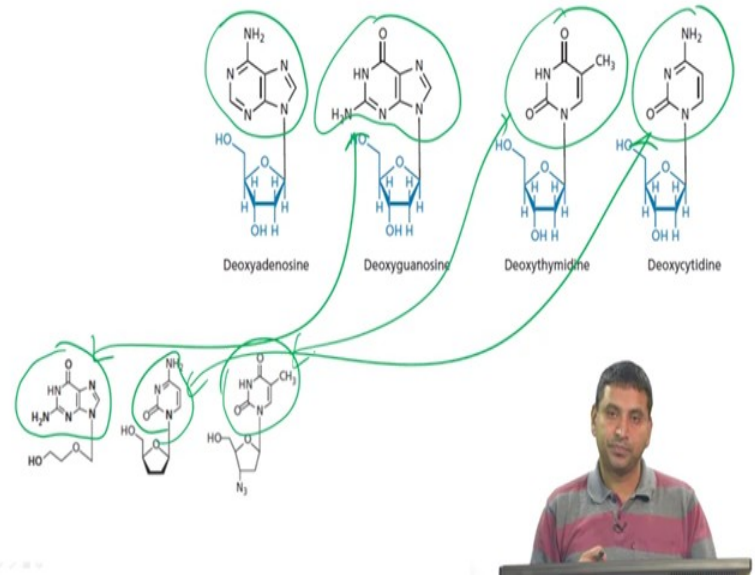

So in order to answer this question, let us first draw out the natural nucleosides that are present. So we see here that this is the structure of adenine, this is the structure of guanine, this is the

structure of thymine and this is the structure of cytidine. So let us start with the first example. So here this compound to me looks like guanine. So this mimics guanine as shown here. And this compound here has a cytidine like molecule. So here is the how we would match this.

And the last compound is mimicking thymine. So what we would expect with these antiviral molecules is that since they have an identical structure to the base, then the hydrogen bonding that would occur between the complimentary bases would be similar. So antiviral drugs act in this manner. We will look at this in more detail towards the later part of the course.

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- Why is supercoiling important/essential?

Why is supercoiling important or essential?

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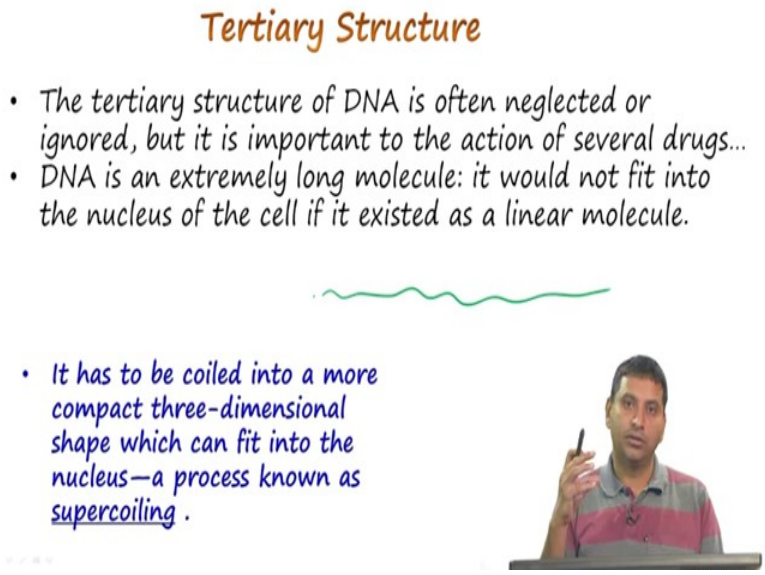

So DNA supercoiling is very important because it helps with the tertiary structure of DNA. Now DNA is extremely long molecule and it would not fit in the nucleus of the cell if it existed as a linear molecule. So if you take DNA to be a linear molecule, it is extremely long. So what happens is that it is coiled into a more compact 3-dimensional shape which can fit into the nucleus. And this process is known as supercoiling. So therefore, supercoiling is very important to be able to fit the genetic material in the nucleus.

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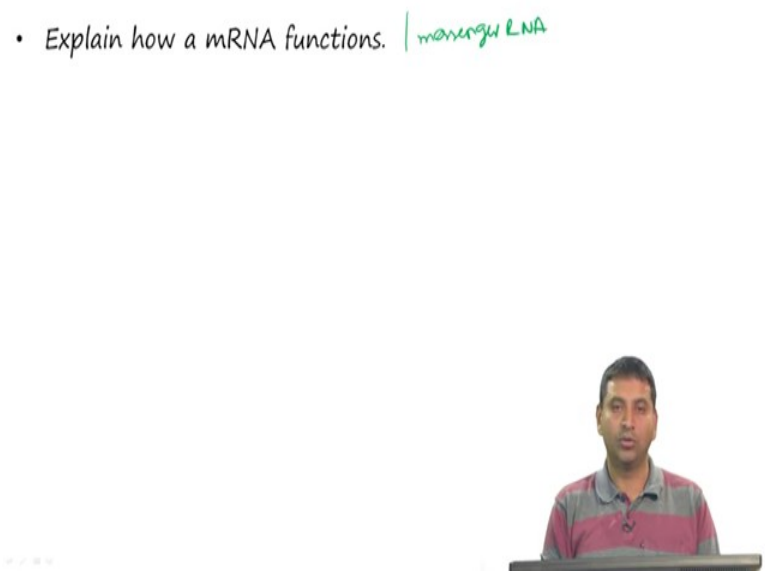

Next question is, explain how mRNA functions? So mRNA as we know is basically messenger RNA and in order to understand what messenger RNA is, messenger RNA takes a message from DNA to the protein synthesis machinery.

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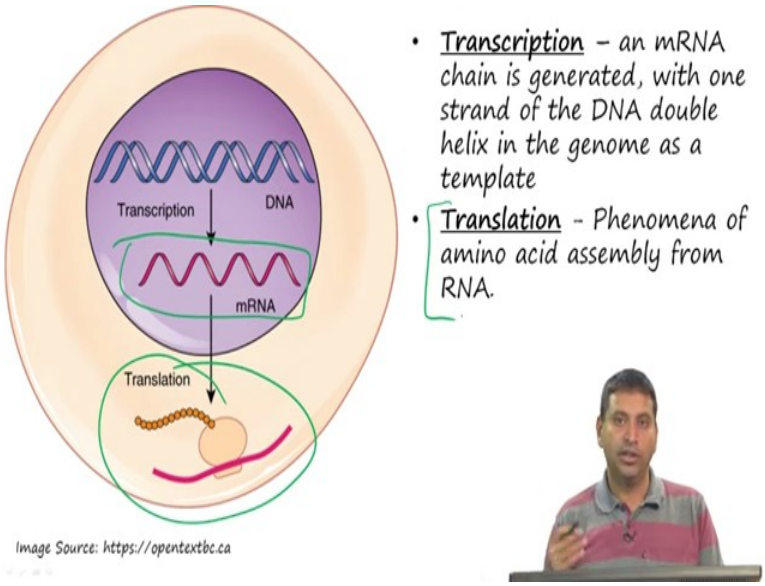

So this process is called as transcription. Transcription is the process by which a mRNA is produced using the code from DNA and this allows us to transfer the information in DNA and send it to the ribosome or endoplasmic reticulum where the protein synthesis is occurring. So protein synthesis, the process is called translation where this code that mRNA is carrying with it goes to the endoplasmic reticulum and the ribosome there and that is converted using the machinery to produce a protein.

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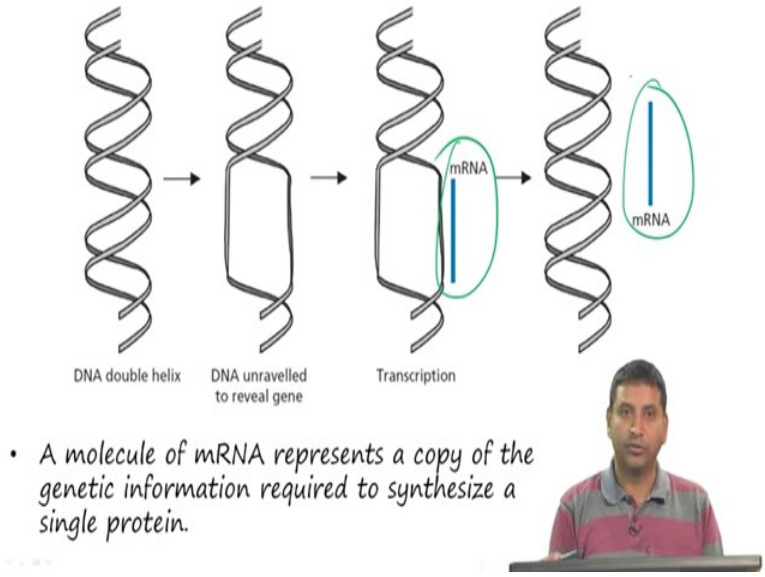

So mRNA works, the transcription happens first by exposing the gene and then the mRNA is synthesized over here and then mRNA is produced.

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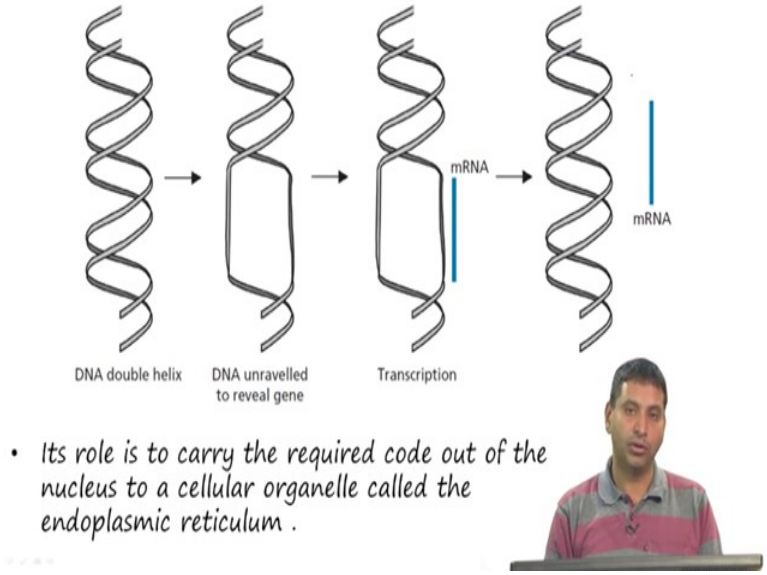

So its role, as we discussed earlier, is to carry the required code out of the nucleus to a cellular organelle known as endoplasmic reticulum.

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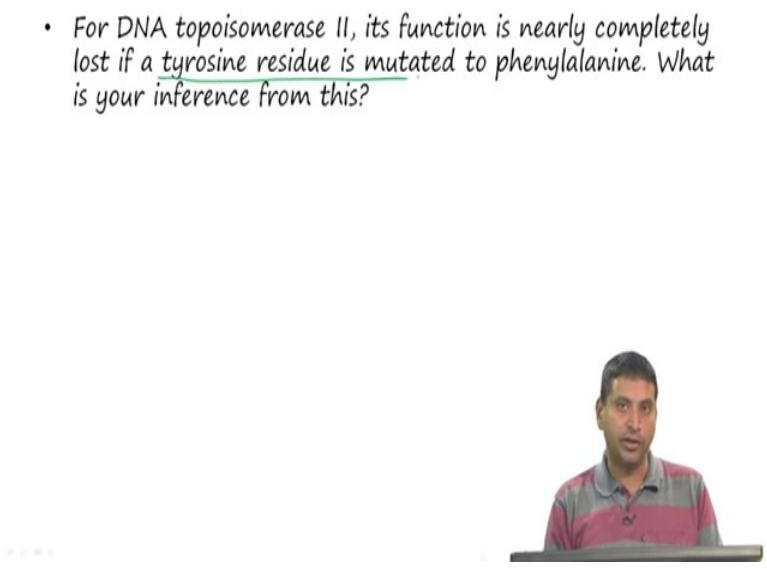

For DNA topoisomerase II, its function is nearly completely lost if a tyrosine residue is mutated to a phenylalanine. What is your inference from this? So again going along what we have looked at in the previous classes, the way in which we would understand the function of a protein, in this

case DNA topoisomerase II, would be to carry out what is known site-directed mutagenesis. And this site-directed mutagenesis basically replaces a protein, an amino acid residue with other amino acid residue.

So if the tyrosine here is replaced with a phenylalanine, then the activity of DNA topoisomerase II is almost completely lost. So therefore the tyrosine residue must be a very important part of DNA topoisomerase II activity.

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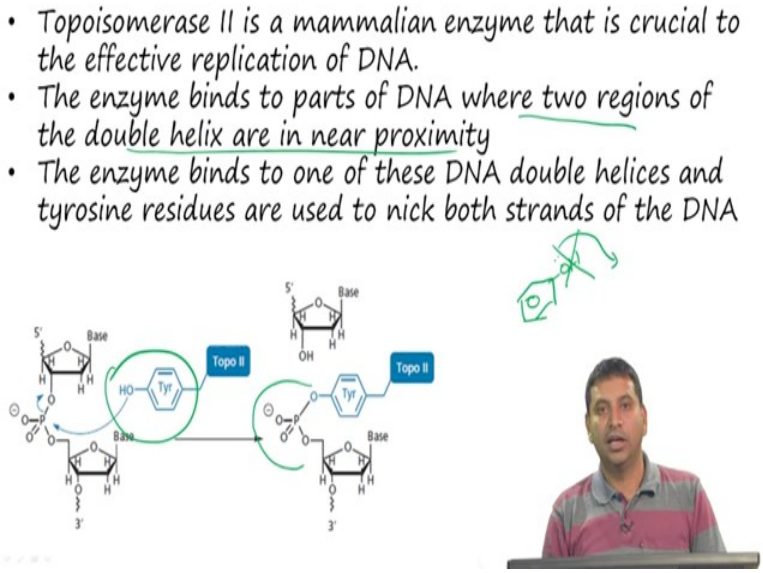

So we already have learned in the class that topoisomerase II is a mammalian enzyme that is crucial for effective replication of DNA. So this enzyme binds to parts of DNA where two regions of the double helix are in near proximity. Then the enzyme binds to one of these DNA double helices and the tyrosine residues are used to nick both the strands of DNA. So this tyrosine residue over here what it does is, it reacts with this phosphodiester bond here and produces a nick because you now have the separation of the single strand to, there is a nick that is produced.

So therefore if you have now mutate this tyrosine residue which is this hydroxyl group is very crucial, if you remove this and only use phenylalanine, then there is no possibility of this reaction occurring and therefore the enzyme loses its activity.

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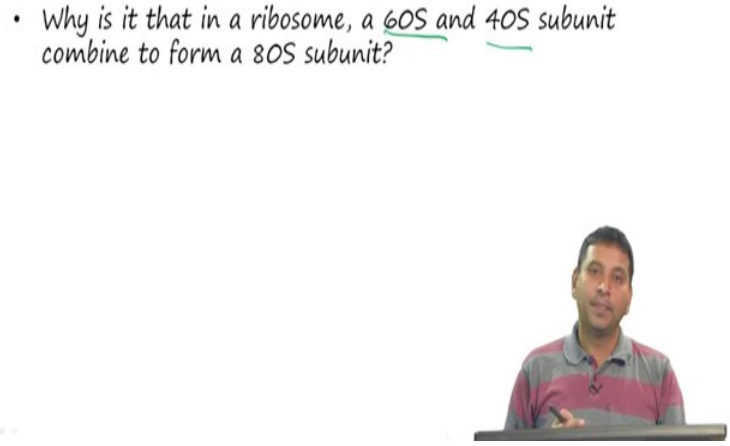

Next question is, why is it that in a ribosome a 60S subunit and a 40S subunit combine to from a 80S subunit? That means if I combine a 60S and 40S, I should get a 100S, but I actually get 80S.

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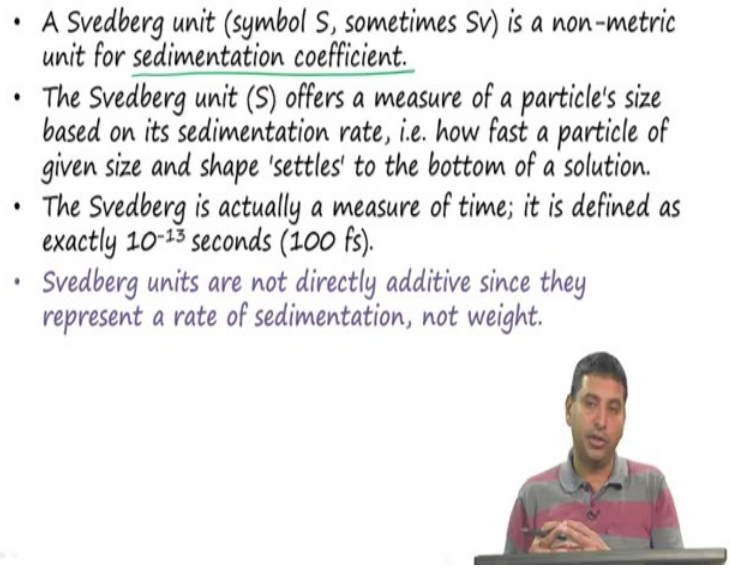

So the answer to this is that the S stands for Svedberg. So Svedberg unit is a non-metric unit which is known as a sedimentation coefficient. So Svedberg offers a measure of a particle size based on the sedimentation rate. That is, how fast a particle of a given size and shape settles down to the bottom of the solution. So Svedberg is actually a measure of time and it is defined in, it is defined as exactly 10 to the power minus 13 seconds, which is actually 100

femtoseconds. So Svedberg units are not directly additives since they represent a rate of sedimentation and not weight.

And so it is quite logical that a 60S subunit and a 40S subunit combine and form a new subunit which can sediment at a rate which is higher than these two, because they are probably larger, but it has nothing to do with, it is not, this property is not an additive property in that 60 and 40 will have to add to give 100.