Biology for Engineers and Other Non-Biologists
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Week- 04
Lecture - 22
Translation:
"The Decoding Mechanism"

So, welcome back to the video on translation. Now in the last video when I was talking about transcription we saw how the information which was written in DNA was copied onto an RNA molecule. So RNA molecule was your cue card which then moved, can move from the nucleus into the cytoplasm. So today we are going to (start) starting point of the video is going to be that the mRNA has been already synthesised. Now how is it that this mRNA is read, okay? And having read how is it that the protein is synthesised?

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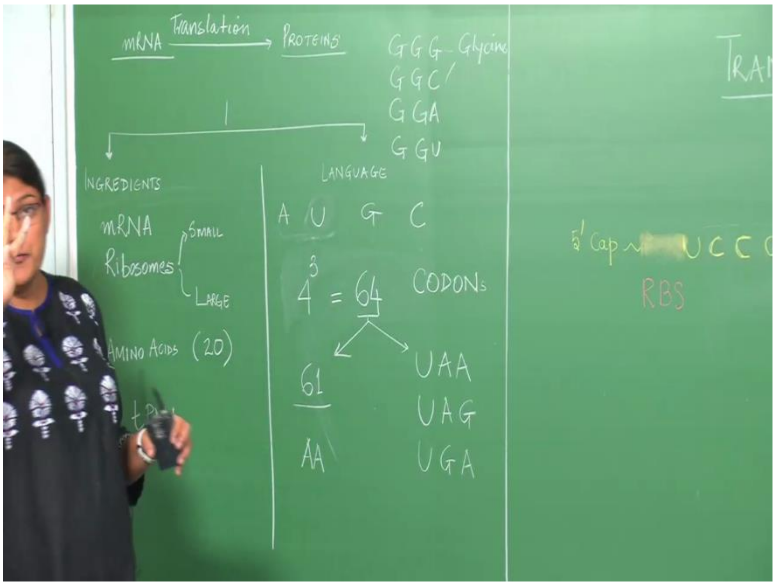

So (f) to understand translation it is important to understand, so translation is the process by which the information which is written in mRNA is finally converted to the product which are the proteins. So that is the process of translation, all right? Now our starting material is this stretch of mRNA molecule which has, you know, meticulously copied all the information which was written in the DNA, so this is now the script which the ribosome needs to read. So we need to understand 2 things in this process of translation, 1; what are the ingredients which are required to make the proteins and 2; how do you read that language? So let us come to the ingredients first.

The first ingredient is the script itself which is in the mRNA molecule, then the chef where this entire synthesis happens which are the ribosomes. The ribosomes have 2 units; there is a small subunit and a large subunit. We will come to this little later again but remember it is a structure made up of 2 units, a small and large unit. So you need the chef, you also need the ingredients (wi) with which the proteins are made and proteins are made up of amino acids. So you need the amino acids.

There are 20 different amino acids and these 20 amino acids arranged in different permutations and combinations because of which you get different proteins. So you have amino acids and then you have a molecule called as the tRNA. It is also called as transfer RNA because this molecule will actually bring in the amino acids to the ribosome, the site of protein synthesis. And this tRNA is (so) you will have different kinds of tRNAs which can then handpick the amino acids and bring them to the ribosomes.

(S) now that is what are the ingredients, you need the messenger RNA which is the script, you need the site of protein synthesis which is the ribosome, you need the basic building blocks of proteins which are the amino acids and these amino acids are ferried to the ribosomes by a molecule called as transfer RNA or tRNA.

Now let us come to the language. Now we know we basically have 4 bases, so you have 4 bases; in case of DNA it is A, T, G and C, okay? But the (wri) script is written in the RNA molecule so (he) instead of a T in case of RNA we are going to have a U, okay? So there are 4 letters or (la) I mean in simpler words the language of DNA has 4 alphabets, A, U, G and C. Now these alphabets have to come together to form words and each word should mean a particular amino acid.

So if you have each alphabets coding for one amino acid you have only 4 possibilities. Let us say if 2 of them at a time are coding for one amino acid, A can code with U or A can combine with G, or A can combine with C, then you will have 4 to the power 2, about 16 different possibilities in which these combinations can happen. So you can essentially, will have 16 different words. But that is still falling short because you have about 20 amino acids.

So what we know now is that actually there are 3 of them who come together at a time and then they code for a word. So if you have 4 bases (an) which you are (co) combining in (gr) groups of 3, then you have about 4 to power 3, about 64 different possibilities. You have 64 different words, each word meaning something. Now each, so in biology the (al) alphabets are 4, but these alphabets arrange in groups of 3 to form a code which is called as the codon, okay? And there are 64 codons in our system out of which, 61 of them code for amino acids, while 3 of them do not code for any amino acid.

For example you will have UAA, UAG and then UGA. Now these 3 codons, they do not code for any amino acid but you have 61 of them which are coding for amino acid. Now that is, again brings one interesting point; you have 61 codons, all right, but you have only 20 amino acids. Now there is seen, there is seen that (the) more than 1 codon can code for an amino acid. For example you will have an amino (acics) say GGG, can code for an amino acid. The (same), let us say this codes for glycine, for example, all right?

Now the same amino acid can also be coded by another codon, like GGC. This code also codes for glycine. So you can have multiple codons for the same amino acid but a single codon cannot code for 2 different amino acids. Let me make this clear again. So let us say the amino acid is a glycine, the glycine can be coded by GGG or GGC. So the glycine can be coded by more than 1 codon, okay? In fact glycine is coded by 4 different codons, (u) all right?

So there are 4 different codons which code for the same amino acid which is glycine, but it is not possible that the GGG will code (flaw) glycine will also code for alanine, that is not allowed, okay? So the genetic languages, the 3 nucleotides come together to form one word which is the codon and each word codes for a specific amino acid. You can have more than one word for a particular amino acid. But (a) meaning of the word is unambiguous, it is, it means if it is GGG it will always code for a glycine, it cannot code for any other amino acid.

So that is the language, and now that language is there in that language is sitting on the mRNA molecule. But that language has to be read and interpreted, right? Now that interpretation of the language is done in part, right, by the tRNA molecule. Now tRNA is a very interesting RNA molecule. If one were to look at its two-dimensional structure, it has a clover leaf structure, I mean; it looks like the cloves, right?And what you find is this tRNA molecule which is usually about 80 nucleotides long, so there are different tRNAs; each tRNA has a region which is called as the anticodon or anticodon.

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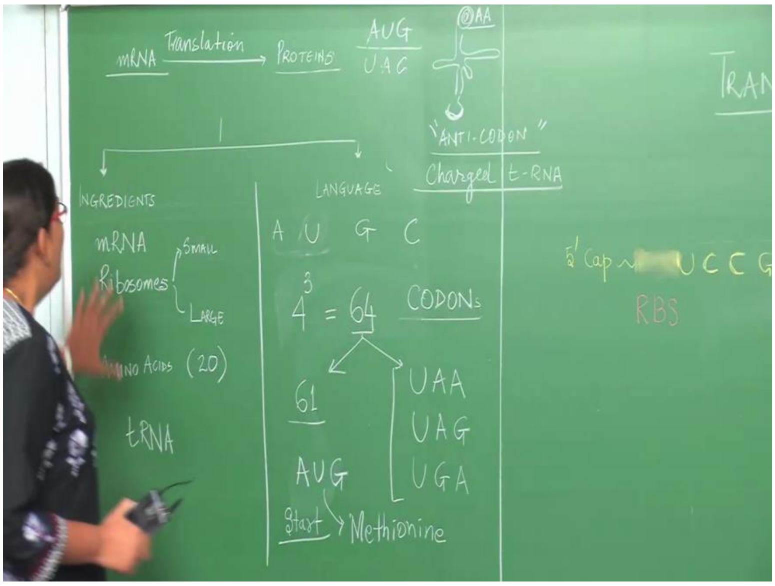

So if you have, let us say a codon AUG; now this codon has to be read by the anticodon. So the anticodon will be complimentary to the codon, which will, in this case will be UAC, right, because A will not, there is no thymine so you will have a uracil; this is again an RNA it is not a DNA. The uracil will always pair with an adenine and guanine will always pair with a cytosine; that is the complementarity.

So every codon, likewise all 61 codons will have the complementary anticodons. So each tRNA molecule in itself will have a complimentary anticodon and at the other end will also have an amino acid attached to it. Now such a tRNA molecule which for a given codon carries that specific amino acid is also called as a charged tRNA.

Now I am not going to get into details of how all this charging happens because then it becomes too mind-boggling and I do not want to bother you with all those details. Just remember that the codes are the codons, the 3 letter codes and each (c) code codes for a specific amino acid, and then the code is decoded by the tRNA because of the anticodon which is complementary to the codon, okay? And each tRNA will then bring in the respective amino acid.

Now among the codons as I told you, 3 of them are stop codons, so for UAA, UAG and UGA there is no tRNA molecule available, okay? And for the AUG you have, this is always the start codon. It is also the first codon so it is like you are writing a script, right, if you are writing on a letter and you start with a capital T for the, right, so the first word is always a AUG which codes for methionine. So out of the 64 codons 4 codons are special; the start codon which is AUG and the terminator codons which areUAA, UAG and UGA. So I hope till here you have understood what are the ingredients and how the language is read in translation.

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Now let us look at the actual process of translation. So what I have done here is I have drawn a mRNA molecule. So this mRNA molecule has a 5 prime cap. It has a 3 prime poly-A tail, okay? And now this mRNA is sitting in the cytoplasm. And then it has this whole sequences, we need to make sense of this sequence, okay? So now each RNA molecule also has a specific signature which is called as the ribosome binding site, okay? So it is around here in this ribosome when (a) so let us say you have these 2 subunits, I told you, right? Ribosome has a small subunit and a large subunit, okay?

So the ribosome binding site is kind of scanned by this small subunit and wherever the small subunit will see this, the ribosomes will start assembling, okay? (Sorry let me draw this little properly). So the ribosome will recognise this and the small subunit of ribosome will then start assembling, okay, (the) this is the small subunit of ribosome.

Now, in this sequence if you see carefully, what is the start codon? The start codon is AUG. So if you look at the sequence this is UCC, right? Then you have GAU, but then if you read a little carefully this becomes AUG. Now this is your start codon. So there is another important aspect in the reading of language that you have to understand is about punctuations. I am (p) really simplifying this. So AUG becomes the first code, the next code is always read without any break in sets of 3. So this becomes your second codon, right? Then this becomes, (so let me just) so this becomes the (first) second codon, this becomes the first codon which is always AUG; first codon, second codon.

Then again you read the next triplet without the break, so this becomes your third codon and then you have the fourth codon and then you come to the fifth codon. If you notice the fifth codon is a UAA which is nothing but the stop codon, isn't it? So here the process will stop, okay? So (the) this is the RNA molecule and by just looking and scanning through it you can understand that it has AUG followed by GGG then the (n) third codon then the fourth codon and then you bump into a stop codon. So let us look at translation.

Now translation has 3 stages; the first stage is initiation, the second stage is elongation and the third stage is termination, okay? So (we) let us look at the first stage which is initiation. What is happening in initiation is the ribosome, the small subunit of ribosome scans this mRNA and attaches itself based on ribosome binding site and then here is a start codon. Wherever there is a start codon the first tRNA which will have the complementary anticodon, right so let us say this is the anticodon site, will come and bind, so I am just drawing this like a clamp like (structure) just a hook like structure. So this is the amino acid it is bringing which is nothing but methionine, all right?

So the first tRNA has come and it has dogged itself onto the start codon, the small subunit of ribosome has come in sitting, and now when this happens, this is the first step during the process of initiation. Once these are juxtaposed and are put together only then (then) the large subunit of ribosome comes and sits. So this is the large subunit of the ribosome which is sitting, okay? So, it is like this; you have the RNA molecule, let us say this represents the RNA molecule, the small subunit comes and binds and then the big subunit will come and sit on top.

Now if I were to take a cross-section, this is (I am), this is a 2-D (f) diagram unfortunately, it will become clearer in some animation videos which I will show you (la) I cannot show you but I will definitely give you the links for those. So when you cut it across and see a cross-section, when this entire large subunit and the small subunit along with mRNA in between; so there is a groove here in (the) through which the RNA is passing through, you, the whole assembly is ready for translation.

Now this site, so this, once the large subunit arranges the largest subunit has 3 sites (so I am just going to rub this off, here), it has 3 sections; it has a section which is called as the E-site or the empty site, the P-site and the A-site, all right? Now, so this is, now the system is ready to bring in the next amino acids. The first amino acid is methionine. Now the next tRNA comes, again it binds with the help of its anticodon sequence, right, and it will bring in the next amino acid, let us say amino acid 2; I think GGG we discussed codes for glycine so this comes in as the second. Now the incoming tRNA is coming at the A-site.

Once this has happened, now the 2 tRNAs are next to each other you will have the process of formation of peptide bonds; remember to amino acids are joined by the process of peptide bonds. So this methionine will be passed on to the second amino acid through the formation of peptide bond. And once this happens, so what will happen then is that this entire ribosome will shift by one codon to the right, okay? So this now will shift by one codon to the right.

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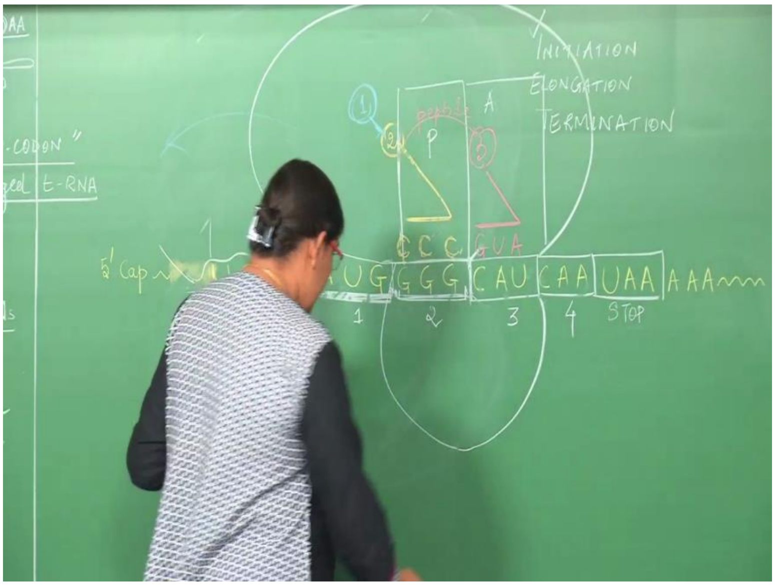

(Sorry just rubbing this off again, right). So now it has, methionine has been passed on and methionine is now linked to this tRNA. Now this entire ribosome shifts and what happens is now the ribosome small subunit is sitting here, right, and the large subunit is sitting here. So what was the A-site in the first round now becomes the P-site. AUG is the exit site, so now the tRNA is empty; it has donated its methionine. So from here the tRNA which had brought in the methionine is free, so this tRNA will go out from the E-site.

This becomes the P-site and now this is the codon which is now ready to be read against sitting at the A-site. So now at this site the third tRNA will come which will read the codon through its anticodon and will bring the third amino acid. Again there will be a peptide bond formation between these 2 and then this tRNA becomes empty and then this tRNA also moves out of the E-site. So this is how the process of translation happens and the ribosome keeps sliding one codon at a time and along the mRNA template and reads it, brings in the corresponding tRNA and every time the charged tRNA comes, it then forms of peptide bond with the previous tRNA and hence the polypeptide chain keeps on getting elongated.

Now this keeps on happening till the ribosome encounters the stop site, okay? So let me just rub this off, I hope you have understood how this is happening. There are some very nice videos on you tube, I will give you links to those, it will make it even clearer to you. So by the time it reaches the stop codon what has happened is, the ribosome is sitting, right?

This becomes the A-site in the ribosome; this is where is the peptidal site, right? So there will be a corresponding tRNA which would have its fourth amino acid which was connected to the third amino acid which in turn was connected to the second amino acid and then the first amino acid which was the methionine. So you are getting a chain of amino acids getting synthesised and now the ribosome has bumped into a position which is the stop codon.

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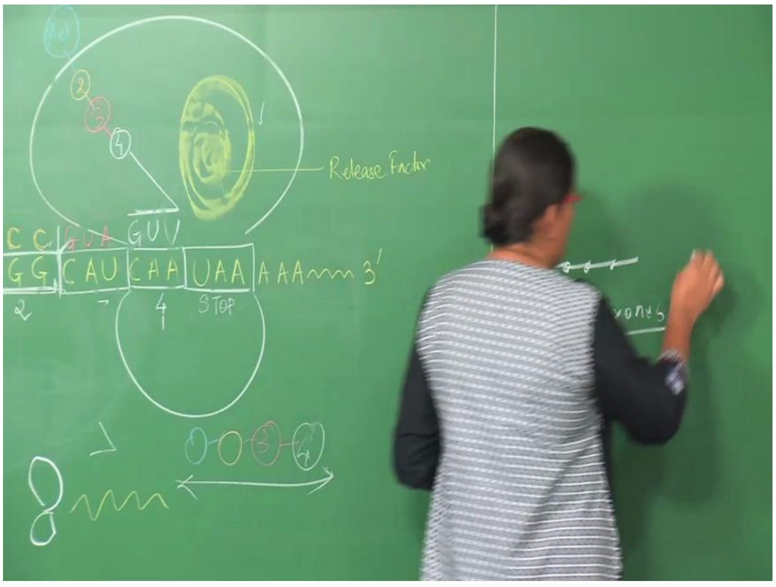

Now there is no tRNA for the stop codon. So instead of a tRNA whenever the ribosome hits this stop codon (a) what is called as a release factor comes, a release factor, it is a protein which comes and binds to this A-site, it is called as the release factor. And once this release better comes and binds to the A-site, it basically causes the dissociation of this entire complex. So at the end of it everything gets dissociated, the small subunit, the large subunit, the ribosomes come apart, the mRNA comes apart, the tRNA becomes free again, the last tRNA and then you are left with just the polypeptide chain.

So you have the methionine, the second amino acid, the third amino acid, right, and the final the fourth amino acid. Now you have got a peptide (change), right? This is a polypeptide, okay? So this has happened as what you have seen here is, you started with the start codon on the mRNA, assembly of the ribosomes, coming in of methionine, coming in of a second tRNA again through base pairing with anticodon. And then the amino acids keep on getting added onto this growing chain of polypeptide.

Now this is just a polypeptide chain, it is just a linear arrangement of amino acids but in reality the proteins are much more folded and that is possible because after this process of translation has happened, the termination will stop because of the binding of release factor. So once the translation has happened, polypeptide chain is ready.

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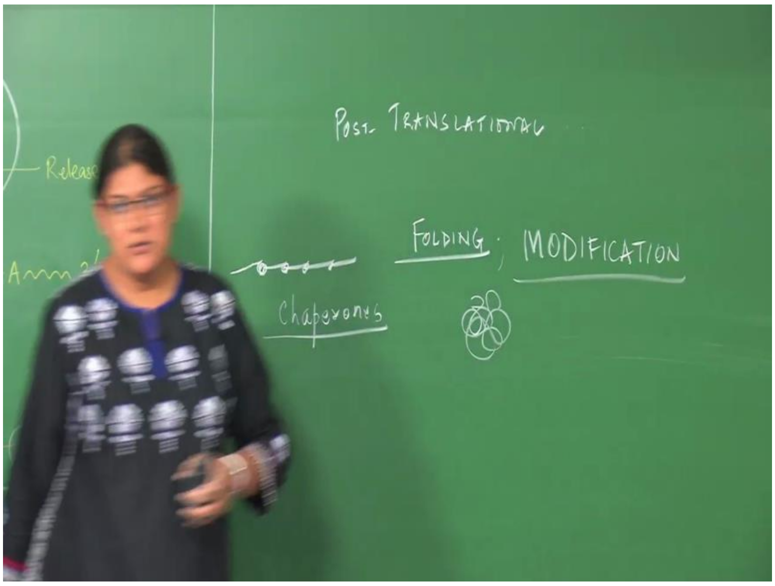

This polypeptide chain; so let us say this is now the polypeptide chain, right, this polypeptide chain will undergo folding, okay? It is like I take this thread and then try to (w) wind it and you know form it into a ball of thread. So, that processing happens inside special structures which are called as chaperones.

So, chaperone proteins bring about what is called as protein folding. So after the amino acids have joined in the range, they have to be folded, so protein folding happens and this gets completely into a 3-D structure and if further required as it happens in endoplasmic reticulum and the Golgy complex in eukaryotes this folded protein will get further processed and then secreted or sent to its appropriate target.

So this is, this protein folding and specific other required modifications, I am not going into them because of simplicity; these modifications are called as post-translational modifications, okay? So let me just wind up this video by talking about and summarising what we studied in this video. We saw how mRNA, the script which is written on mRNA is decoded by the tRNA and the script is written into 3 letter words which are called as the codons.

The codons are read and interpreted by tRNA by the means of complementary anticodon. It is the tRNA which in response to a specific codon will bring in the specific amino acid and this entire adding of amino acid happens codon by codon in the ribosome, with the help of ribosome. And then once the ribosome and the entire translational machinery bumps into a stop codon the release factor comes every things gets dissociated, the peptide chain gets separated from the rest of the complex and this peptide chain will then undergo the process of post-translational modification.

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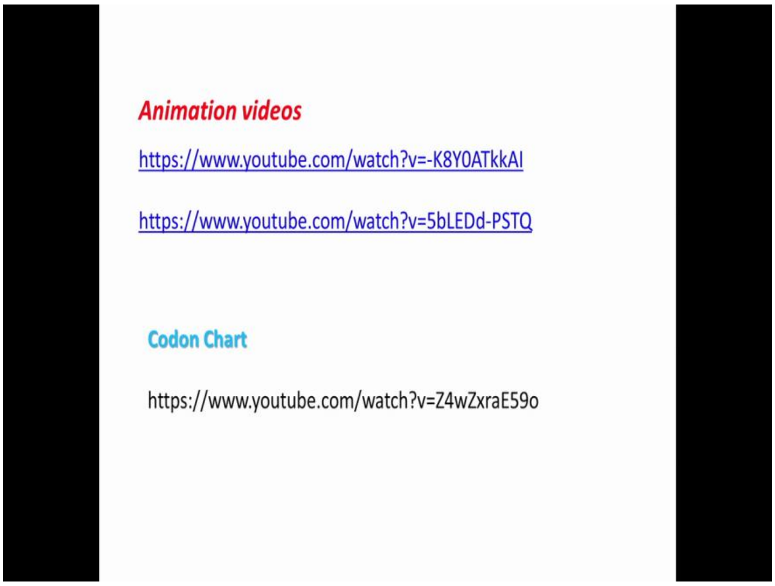

I hope this video has helped you understand the concept of how the message is decoded and I would like you to really go through these animation videos. They are really very nice. They (in) just 7 to 10 minutes, they exactly show you how the process is happening. So whatever I could not do it on the blackboard will be easily (understand) understood by you when you watch this particular video.

And if you really want to know all the 64 codons and what they really code for and how to read the there is another video on codon chart you can have a look at that too. So thank you and hopefully you have enjoyed this series of videos; I do understand there have been a few mistakes here and there, we will try to correct them and if you have any confusions (it) please write back to us and we will try to clarify your confusions. Thank you.