

Basics of Biology
Professor Vishal Trivedi
Department of Biosciences and Bioengineering
Indian Institute of Technology, Guwahati, Assam, India
Module – XI: Summary and Conclusions
Lecture - 50
Summary (Part-II)

Hello everyone, this is Dr. Vishal Trivedi from Department of Biosciences and Bioengineering IIT, Guwahati and what we were discussing, we were discussing about the properties of the living organisms. And in this course, so far what we have discussed, we have discussed about the different aspects of the living organisms, and I hope that by discussing all these aspects, you could be understood the different properties of the living organisms.

So, if you recall in the previous lecture, we have summarized and discussed some of the important points, what related to this particular course, and why we are doing this, we are doing this because your exams are approaching very fast and the summarizing and revising the content what we have discussed in this particular course, is going to be helpful for the preparing you are preparing for the examinations.

So, in the previous lecture, what we have discussed, we have discussed about the classification of the living organisms, and we have discussed that the different how the different criteria's are being used to classify the different types of organisms and based on these criteria's the, and for to describe these or to explain the classifications, we took the examples of the animal kingdom, where we have discussed about the how the different criteria are being applied.

And that is how the Animalia kingdom is been classified into the different types of phylums, whether it is the Porifera, coelenterata, ctenophora, platyhelminthes and so on. And then subsequent to that, we have also discussed how these different types of organisms are being originated onto the earth and how they are being evolved from the pre-existing animals.

So, that was we have a discussing the evolution and the origin of life. So, we have discussed about the different types of experiments and so on. And then after that, we have also discussed about the different types of the cells, whether it is the prokaryotic cell or the eukaryotic cell.

So, within the prokaryotic cell, we discuss about the cell walls and the different types of properties of the bacterial cells. And within the eukaryotic cell, we discuss about the plant cell and the animal cell. And we discuss about the different types of organelles, we have discussed the structures and the functions of these organelles, we discuss about the mitochondria, chloroplasts, endoplasmic reticulum, Golgi bodies, lysosomes, we discuss about the nucleus and so on.

And while we were discussing about the cells, the cellular activities are being completely being governed by the different types of biomolecules. So, we have also discussed about the different types of biomolecules. So, we discuss about the nucleic acid, we discuss about the carbohydrate, we discuss about the proteins and lipids and what we have discussed while we were discussing about the biomolecule is the structure and the function of these biomolecules in the cellular functions.

So, we discussed about the structure of the carbohydrates, classifications of the carbohydrates, different properties of the carbohydrates, and then we also discuss about how the carbohydrates are contributing into the cellular metabolism. So, while we were discussing about the cellular metabolism, we discussed about the glycolysis and Krebs cycle.

Same, in the same way, we have also discussed about the lipids, the different types of lipids, their classifications, the structure of these lipids, and then we also discuss about the function of these lipids. As far as the protein is concerned, we discuss about the different properties of the proteins, how the proteins are participating into the different functions of the body and so on.

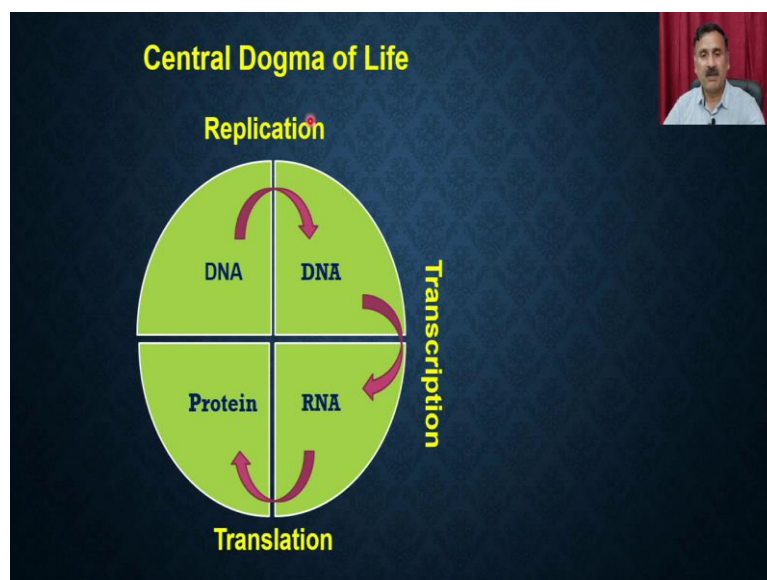
So, now, in today's lecture series, we are going to discuss some more aspects of the, this particular living organisms, and while we were discussing about these aspects, we are also going to revise the content what we have covered in this particular course. So, these biomolecules are participating in the many types of cellular events and the cellular event what we have discussed in this particular course, is the central dogma of life.

So, central dogma of life is a way in which the message is being conveyed from the nucleus into the cytosol. So, in this you have the three different events, one is called as the replication, another is called as transcription and the third is called as a translations. So, what is mean by the replications?

So, DNA dependent DNA synthesis is called as replication and this is being done by the enzyme which is called as the DNA polymerase. Similarly, taking the information from the DNA it has been utilized to synthesize the RNA. So, we can have the different types of RNA whether it is the messenger RNA, tRNA or ribosomal RNA, and this activity is being done by an enzyme which is called as the transcription, it is called as the RNA polymerase.

And then we have the RNA dependent protein synthesis and this event is called as the translation and this process is being governed by the protein machinery of protein synthesis machinery which involves the ribosomes, which involves the different types of RNA species like the messenger RNA, ribosomal RNA, tRNA and it also so, and so, this all these three events are being a part of the central dogma of life. So, let us start discussing with the first event that is the replications.

(Refer Slide Time: 7:12)



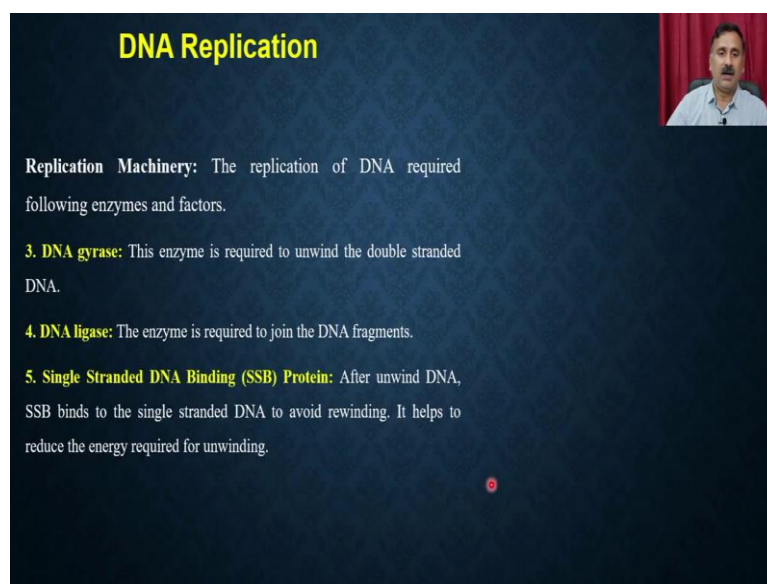
So, as far as the replication is concerned, so, what is mean by the DNA replication, so, duplication or the re-synthesis of the genomic content is essential to maintain the life of an organism. DNA has to be precisely replicate to maintain the sequence identical to the parent DNA and that is very important, because otherwise, there will be mutations and there will be incomplete replication of the DNA.

It will protect the appearance of the potential mutations and resulting the change phenotype. In the current, replication of a DNA fragment has to be performed keeping following point into the concentration. The replication machinery must duplicate the whole fragment what that means is that it should not have the incomplete duplications.

So, if you have the full genome, the whole genome of the organism should be replicated. The replication must be free of the errors, because if there will be errors, it is actually going to change the nucleotides and that will result into the mutation of mutation within the genome and that may result into the malfunctioning of the proteins.

The machinery must amplify the fragment in a given timeframe. So, timeframe is also very important for example, if a cell is dividing in 20 minutes, if a bacterial cell is dividing in 20 minutes, the replication has to be completed in that given timeframe, so, that you cannot have the incomplete replications.

(Refer Slide Time: 8:41)



DNA Replication

Replication Machinery: The replication of DNA required following enzymes and factors.

3. DNA gyrase: This enzyme is required to unwind the double stranded DNA.

4. DNA ligase: The enzyme is required to join the DNA fragments.

5. Single Stranded DNA Binding (SSB) Protein: After unwind DNA, SSB binds to the single stranded DNA to avoid rewinding. It helps to reduce the energy required for unwinding.

DNA replication is a very very complicated process. So, it actually requires a complete machinery. So, in replication machinery, the replication of DNA required the following enzyme and the factor. So, what you require is the DNA gyrase, DNA ligase, single stranded DNA binding protein, you require the DNA polymerase and the primase.

(Refer Slide Time: 9:06)

DNA Replication

1. Identify the site of occurrence: it is difficult to start the replication of circular or very large DNA fragment randomly. Hence, a particular pattern of nucleotide sequence exists on DNA to recognize and facilitates the replication initiation. The difficult task with regard to replication is to denature the double stranded DNA and presence of sequence with low melting temperature will facilitate the event. As discussed in earlier lecture, interaction between adenine and thymine is mediated by 2 hydrogen bonding whereas guanine and cytosine is mediated by three hydrogen bonding. As a result presence of AT rich region will facilitate earlier denaturation and assembly of replication machinery. These sequences are mostly present in a region and known as origin of replication.

Random array of three 13bp sequences, consensus sequence GAUCCNTNTTTT

Binding sites for DnaA protein, six 8bp sequences, consensus sequence TTAATNCAAC

DUE R1 IHF R5 II I2 R2 FIS R3 I3 R4

And how that process is going to happen? So, in the process, so, you are first going to identify the site of the occurrence which is also called as the origin of replications. So, it is difficult to start the replication of a circular or very large DNA fragment randomly. So, you cannot start the replication at any given time.

So, at any given locations. Hence, a particular pattern of nucleotide sequence exists on the DNA to recognize and facilitate the applications. The difficult task with regard to replication is to denature the double stranded DNA and presence of sequence with the low melting temperature is going to facilitate the event. Interaction between the adenine and thymine mediated by the 2 hydrogen bond whereas, the guanine and cytosine is mediated by the 3 hydrogen bonding.

So, as a result the presence of AT rich region will facilitate the earlier denaturation and the assembly of the replication machinery. These sequences are mostly present in a region known as the origin of replication. So, this is the classical example of the origin of replications. After that, we have the, so once you identify it from where you are going to start the replication, then it is actually going to have the three different types of events.

(Refer Slide Time: 10:21)

DNA Replication

2. Initiation: The unzipping of DNA at the origin of replication forms a “Y” shaped structure known as replication fork. A short chain of RNA is formed at the 5' end. This is a RNA primer and synthesized by primase. Synthesis of RNA primer is essential as DNA polymerase cannot perform denovo DNA synthesis.

The diagram illustrates the initiation of DNA replication. A parental DNA double strand is shown being unzipped at a replication fork. Helicases and topoisomerases are indicated at the fork. The leading strand is synthesized continuously towards the fork, while the lagging strand is synthesized discontinuously away from the fork as Okazaki fragments. RNA primers are shown at the 5' ends of both strands. The overall direction of replication is indicated by a red arrow pointing to the left.

It is going to have the initiation, so unzipping of the DNA at the origin or application forms a Y shaped structure known as the replication form. A short chain of RNA is going to form at the five prime end. This is the RNA primer and it is going to be synthesized by an enzyme which is called as the primase.

Synthesis of RNA primer is essential as the DNA polymerase cannot perform the denovo DNA synthesis. So, what is mean by the denovo DNA synthesis is that it is actually require initiation points. It actually requires some synthesis of a DNA, it cannot start without having the second strands.

(Refer Slide Time: 11:02)

DNA Replication

3. Elongation: In the elongation step, DNA polymerase start the synthesis of DNA on the pre-existing short oligomeric nucleotide strand. In this step, an incoming deoxynucleotide triphosphate get joined by hydrogen bonding to the appropriate nitrogen bases of the single DNA chain as per the base pairing rule; A-T, T-A, C-G and G-C. The nucleotide triphosphate joined to each DNA strand, break off their high energy bonds and set free pyrophosphate (P-P) molecules. Pyrophosphate undergoes hydrolysis with the help of an enzyme pyrophosphatase, and release energy and set free inorganic phosphate group 2Pi. The energy released in this process is used to derive the polymerization of nucleoside to form DNA. The released deoxynucleotide monophosphate joined to each single DNA chain become linked together to form new DNA chain. DNA polymerase.

The diagram illustrates the elongation step of DNA replication. The parental DNA double strand is being unzipped at a replication fork. Helicases and topoisomerases are indicated at the fork. The leading strand is synthesized continuously towards the fork, while the lagging strand is synthesized discontinuously away from the fork as Okazaki fragments. RNA primers are shown at the 5' ends of both strands. The overall direction of replication is indicated by a red arrow pointing to the left.

And then it also in the elongation step, in the location step the DNA polymerase start synthesis of DNA on the pre-existing short oligomeric nucleotide strands. And in this step an incoming deoxynucleotide triphosphate get joined by the harmonic appropriate nitrogenous bases of the single DNA as per the base pairing rule like the A to D, D to A, C to G and G to C. The nucleotide triphosphate joined to each DNA strand, break off their high energy bond and set up the free pyrophosphate.

The pyrophosphate undergoes hydrolysis with the help of an enzyme pyrophosphatase and released the energy and set the free inorganic phosphate 2Pi . The energy released in this process is used to derive the polymerization of nucleoside to form the DNA. The release deoxynucleotide monophosphate joined to each other into each single DNA chain become linked together to form the new DNA chain.

(Refer Slide Time: 12:03)

DNA Replication

3. Elongation:

The DNA polymerase can polymerize the deoxyribonucleotides in the 5'-3' direction. As the two DNA strands are antiparallel to each other, the new strand must be formed on the older strand in the opposite direction. The new strand formed continuously in the 5'-3' direction. This strand is known as leading strand. On the other parent DNA, the short DNA strands are synthesized in 5'-3' direction. These short fragments are known as okazaki fragment and these fragments are joined together to give lagging strand. The RNA primer is replaced by deoxyribonucleotide and the gap is joined by the enzyme DNA ligase.

The diagram illustrates the process of DNA replication at a replication fork. A parental DNA double strand is shown being unwound by helicases and topoisomerases. The two strands are antiparallel. The leading strand is synthesized continuously in the 5' to 3' direction. The lagging strand is synthesized discontinuously as Okazaki fragments, each starting with an RNA primer. The overall direction of replication is indicated by a red arrow pointing to the right.

And then we have the elongation steps. So, in the elongation step, the DNA is going to be synthesized with the help of the RNA primers, and next to the RNA primers, you are going to have the addition of the nucleotides based on the base pairing of the nucleotides what is present on to the other strands.

(Refer Slide Time: 12:23)

DNA Replication

4: Termination: The replication fork proceed to the end of the DNA or meet terminal region which contains multiple copies of ter sequences. The Ter sequences are a kind of trap to halt the replication.

Proof reading and DNA repairs: Template nucleotide sequence directs the accurate incorporation of incoming nucleotide and ensured accurate DNA replication. After every round of nucleotide incorporation, DNA polymerase runs in the backward direction and check for accuracy of incorporation. If any error detected, it is corrected at this stage.

The diagram illustrates the replication fork where the parental DNA double strand is being unwound. Helicases and topoisomerases are shown at the fork. The leading strand is synthesized continuously towards the fork, while the lagging strand is synthesized discontinuously away from the fork as Okazaki fragments, each starting with an RNA primer. The overall direction of replication is indicated by a red arrow pointing left.

POLYMERASE CHAIN REACTION

To amplify a lot of double-stranded DNA molecules (fragments) with same (identical) size and sequence by enzymatic method and cycling condition.

The diagram shows a double-stranded DNA template being heated to separate into two single strands. Primers (red and green) bind to the single strands, and DNA polymerase (yellow) synthesizes new strands, creating two double-stranded DNA molecules.

And then we have the termination, so termination is it been done by the, sorry, replication when it pertains to the end of the DNA or meet the terminal region, which contains the multiple copies of the ter sequences. The ter sequence are kind of a trap to hold the replication and that is how it is actually going to undergo those applications. Since the replication is a synthesis of DNA, so it actually should have the proofreading.

So, proofreading you are actually going to ensure that the DNA what you have synthesized is free of errors. Template nucleotide sequence direct the accurate incorporation of incoming nucleotide and ensure accurate DNA replication after every round of nucleotide incorporation, DNA polymerase runs in the backward direction and check for the accuracy of incorporation.

If any error detected, it is corrected at this stage and utilizing the RNA, DNA replication as a technique what has been presented in the cell, the people have also discovered a technique which is called as polymerase chain reaction. And Polymerase Chain Reaction is actually going to be used as a reaction is a technique which have been used to amplify the double standard DNA molecules with the same size and sequence by the enzymatic method and cyclic conditions.

(Refer Slide Time: 13:46)

POLYMERASE CHAIN REACTION

PCR is a repeated cycle reaction that involves mechanism of DNA replication. It results in production of multiple copies of DNA from a single one. The whole process involves three main events, Denaturation, Annealing and Elongation. A DNA fragment of interest is used as a template from which a pair of primers or short oligonucleotides complimentary to the both the double strands of the DNA are made to prime the DNA synthesis where the direction of synthesis or extension is from 5' to 3' as in DNA replication. The number of amplified DNA or the amplicons increases exponentially per cycle thus one molecule of DNA give rise to 2,4,8,16 and so forth

Amount of amplified DNA

$$C = C_0 (1+E)^n$$

Where, C: final amount of DNA, C₀: initial amount of DNA,
E: efficiency, n: number of cycles, e: slope of the exponential phase, (E = 10⁻³³); (E = 1 then e = 3.3219)

The diagram illustrates the PCR process starting with 1 double-stranded DNA molecule. It shows three cycles: 1st Cycle (2 molecules), 2nd Cycle (4 molecules), and 3rd Cycle (8 molecules). The steps are labeled as Denaturation, Primer binding & Elongation, and the number of molecules is shown on the right side of the diagram.

So, how the DNA polymerase is working? So, PCR is a repeated cyclic reaction that involves the mechanism of DNA replication, it results in the production of multiple copies of DNA from a single copy. So, you can imagine that you have a double stranded DNA. In the first step, there will be a denaturation, so both the strands of a template is going to be separate.

And then it will be having a synthesis of the primer binding and the elongations and after that, the DNA polymerase is going to sit and it is going to synthesize. So, that is how you are going to have the two strands. So, you have started with one strand, one template, you are going to have two templates. So, after the first cycle, you are going to have the two molecules.

So, you started with one molecule, after first cycle, you are going to have two molecules. After second cycle, you are going to have four molecules and after the third cycle, you are going to have eight molecules. So, that is why it is actually going to keep giving you the doubling after every cycle. So, that is why if you want to calculate the concentration or the amount of amplified DNA, you can use this formula to calculate.

(Refer Slide Time: 14:54)

POLYMERASE CHAIN REACTION

1. Initial Denaturation: Heating the PCR mixture at 94°C to 96°C for 10min to ensure complete denaturation of template DNA.

A. Denaturation: This is the first step in which the double stranded DNA template is denatured to form two single strand by heating at 95°C for 15-30 secs.

B. Annealing: This is the annealing step where at lower temperature (usually 50-65°C) primers are allowed to bind to template DNA, annealing time is 15-30 secs and it depends on the length and bases of the primers.

C. Elongation: This is the synthesis step where the polymerase perform synthesis of new strand in the 5' to 3' direction using primer and deoxyribonucleoside triphosphates (dNTPs). An average DNA polymerase adds about 1,000 bp/minute. Step 1,2,3 makes one cycle and in general 35-40 such cycles are performed in a typical PCR amplification.

After the cycles are completed, the reaction is held at 70-74°C for several minutes to allow final extension of the remaining DNA to be fully extended.

3. Final Hold.

These are the different steps where you have the initial denaturation, then you have initial denaturation like the 95 degrees Celsius for 5 minutes or 10 minutes. And then we have the cyclic events of the denaturation, annealing and elongations that you have to do for the multiple reaction like for example, this case, it is going to be say the 30 cycles. And then after that, you are going to have the final elongation which is actually at the 72 degrees Celsius for 10 minutes and then the final stop.

(Refer Slide Time: 15:29)

APPLICATIONS OF PCR

- Molecular Identification**
 - Molecular Archaeology
 - Molecular Epidemiology
 - Molecular Ecology
 - DNA fingerprinting
 - Classification of organisms
 - Genotyping
 - Pre-natal diagnosis
 - Mutation screening
 - Drug discovery
 - Genetic matching
 - Detection of pathogens
- Sequencing**
 - Bioinformatics
 - Genomic Cloning
 - Human Genome Project
- Genetic Engineering**
 - Site-directed mutagenesis
 - Gene Expression Studies

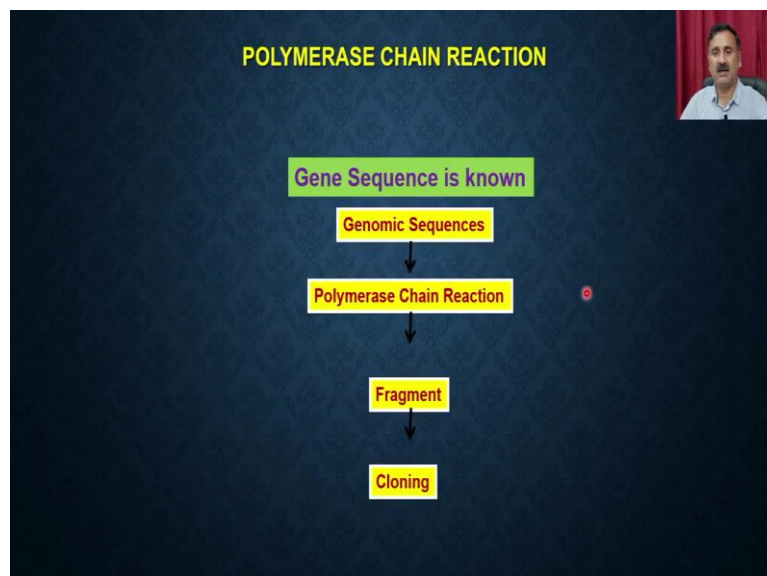
Polymerase Chain Reaction is being applied in the different fields. So, it can be used for the molecular identification, it has been used for the sequencing and it also used in the genetic engineering. In the molecular identification, the PCR is being used for the many different

types of fields like molecule archeology, molecule epidemiology, molecular ecology, DNA fragmentation.

It also been used in the classification of the organisms like the genotyping, prenatal diagnostics, mutation screening, drug discovery and so on. Within the sequencing that PCR is extensively been used to provide the sequences of the different types of genomes, so it can be used, it has been used very successfully for the Human Genome Project and genome projects of the other organisms.

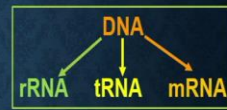
As far as the lab is concerned, the PCR is being used very extensively for generating the site-directed mutagenesis and as well as for the gene expression studies and how we are going to do a PCR?

(Refer Slide Time: 16:33)

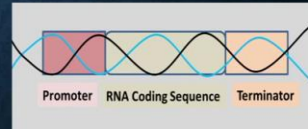


TRANSCRIPTION

Every cell mainly contains three types of RNA-transfer RNA (t-RNA), ribosomal RNA (rRNA), messenger RNA (mRNA). Synthesis of RNA from DNA templates with the help of DNA dependent RNA polymerases is known as transcription. It occurs unidirectionally in which chain is synthesized in 5' to 3' direction. The segment which is transcribed from DNA is known as **Transcription unit**.



In eukaryotes **monocistronic** transcription unit occur in which coding sequence presents for only one polypeptide. But in prokaryotes **polycistronic** transcription unit occurs in which coding sequence presents for more than one polypeptide.



For the doing a PCR you require a gene sequence, you require the PCR fragments and cloning. So, this is the way you actually can be used the PCR into the laboratory conditions. Subsequent to the replications, we also discussed about the transcription. So, transcription means with the sequence what is present on the DNA, you can be able to synthesize the three different types of RNA whether it is the ribosomal RNA, tRNA and messenger RNA.

And the, so every cell contains the three different types of RNA, transfer RNA, ribosomal RNA, messenger RNA and synthesis of RNA from the DNA template with the help of the DNA dependent RNA polymerase is known as the transcription. It occurs unidirectionally in which the chain is synthesized in 5 prime to 3 prime direction.

Segment which is transcribed from DNA is called as the transcription unit. So, this is the transcriptional unit. So, in a in eukaryotes, the monocistronic transcriptional unit occurs in which the coding sequence present for only one polypeptide whereas, in the prokaryotes it has the polycisronic transcriptional unit and that codes for more than the one protein.

(Refer Slide Time: 17:48)

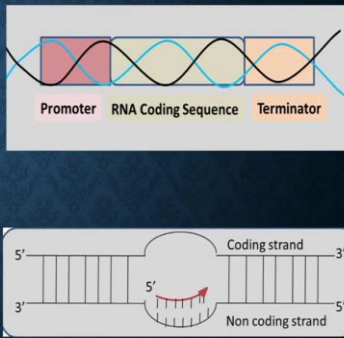
TRANSCRIPTION

Start Point – It is the first base pair from where transcription starts and is called **start site**. RNA polymerase moves from start point along with template, synthesize RNA up to terminator sequence.

Upstream –It is nontemplate nucleotide in 5' end or minus direction; sequence before start point.

Downstream–It is nucleotide in 3' end or plus direction; sequence after start point.

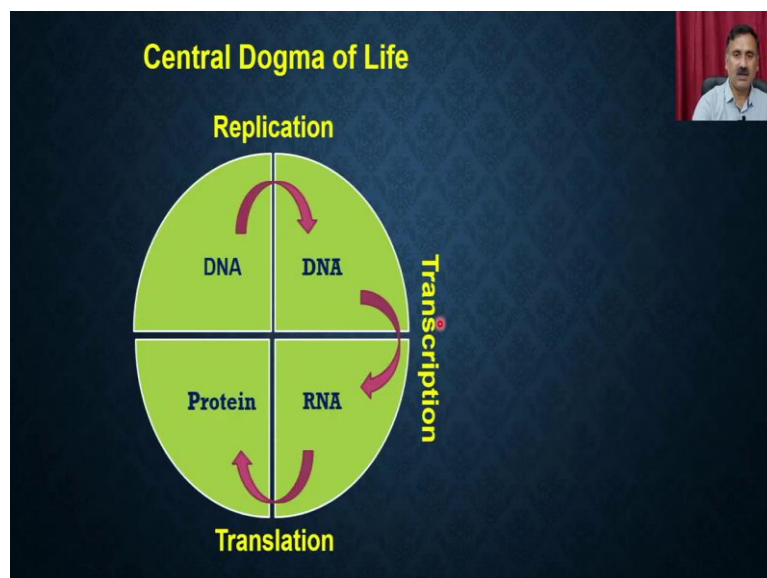
DNA is a double stranded structure. During transcription only one strand is transcribed so that transcribed sequence is identical with one strand of DNA, known as **Coding or sense strand** and other complementary strand is known as **template or antisense strand**.



The diagram illustrates the components of a transcription unit and the transcription process. The top diagram shows a DNA double helix with three regions highlighted: a red 'Promoter' region, a yellow 'RNA Coding Sequence' region, and an orange 'Terminator' region. The bottom diagram shows a DNA double helix with one strand being transcribed into a red RNA strand. The transcribed strand is labeled 'Coding strand' with 5' and 3' ends, and the complementary strand is labeled 'Non coding strand' with 3' and 5' ends.

In an individual transcriptional unit, you have the start points, you have upstream and downstream factors and then also require the coding as well as the, or the sense strand and the template or the antisense strands. And then we also discuss about the mechanism of transcriptions and so on.

(Refer Slide Time: 18:07)



POST-TRANSCRIPTIONAL MODIFICATION

m-RNA: Steps in RNA processing:

- (1) Add a cap to the 5' end,
- (2) Add a poly-A tail to the 3' end,
- (3) splice out introns

POST-TRANSCRIPTIONAL MODIFICATION

r-RNA: Steps in RNA processing:

Processing of rRNA: Eukaryotes have 80s ribosomes and prokaryotes have 70s ribosomes. Ribosomal RNAs are transcribed as long precursor sequence which is then modified at specific bases and cleaved to give mature products. In both bacteria and eukaryotes rRNA processing involves two basic steps of cleavage and base modification.

So, this is what we have discussed so far, we have discussed about the replications where we have discussed about the DNA dependent DNA synthesis and then we also discuss about the transcription which is the DNA dependent RNA synthesis and then, we are also going to discuss, so once we discuss about the transcription.

We are also going to discuss about the post translational modifications and in the post-transcriptional modifications, we discuss about the post translational modification of the messenger RNA. So, in the messenger RNA, three steps or three different types of modifications what we have discussed, we have discussed about the adding a cap to the 5 prime end or adding a poly-A tail or the splicing of the different types of introns.

I am not going to discuss in detail about these steps because that we have already discussed in that that particular relevant module. Then we also discuss about the post translational

modification of the ribosomal RNA. So, in the processing of ribosomal RNA, eukaryotes have the 80s ribosomes, whereas the prokaryotes have 70s ribosome. So, the ribosomal RNAs are going to complex with the protein and that is how they are going to be formed the ribosomes.

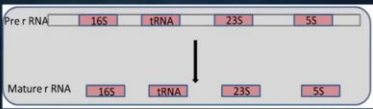
So, you can have the two different types of ribosome, small subunit and the large subunit. And eukaryotes have the 80s ribosome whereas the prokaryotes have the 70s ribosomes and the kind of modifications, what are present in the ribosomal RNA? In ribosomes, ribosomal RNA in both bacteria and eukaryotes, ribosomal processing involves a two basic steps, the cleavage as well as the base modifications.

(Refer Slide Time: 19:54)

POST-TRANSCRIPTIONAL MODIFICATION

r-RNA: Steps in RNA processing:

rRNA processing in Bacteria: rRNA precursor in bacteria is a 30s rRNA which modified and cleaved to give 23s rRNA, 16s rRNA, 5s rRNA and some t-RNA segments in between are also there sometimes. **30s pre- rRNA transcript** consist of 16s rRNA sequence followed by spacer which may have t-RNA sequence in some cases and then there is 23s rRNA sequence followed by 5s rRNA sequence near to 3' end. At times there is one more t-RNA sequence after 5s rRNA sequence at 3' end. There are seven different genes for rRNA in E.coli, they are essentially similar in sequence of rRNA segments but differ with number and sequence of t-RNA segments. Maturation process involves methylation of 30s rRNA precursor at specific sites occurring at 2'hydroxyl groups of bases. Some bases such as uridine is modified to pseudouridine or dihydrouridine. Further cleavage process is carried out using enzymes RNase III, RNase P, and RNase E at sites 1, 2 and 3 respectively. Intermediate products are formed namely 17s, tRNA, 23S and 5S. These are acted on by certain nucleases to give final products of 16s, tRNA, 23s, 5s rRNA respectively.



Pre-r RNA	16S	tRNA	23S	5S
Mature r RNA	16S	tRNA	23S	5S

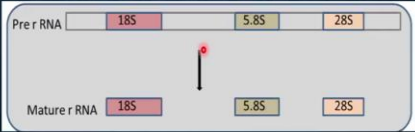
And this is what is the modification what has been done in the ribosomal RNA, so, ribosomal RNA processing in bacteria where you can have the pre-ribosomal RNA, where you have a big ribosomal RNA and that it is going to be chunked it is going to be cleaved off to give you the 16s ribosomal RNA, 33s and say 5s.

(Refer Slide Time: 20:20)

POST-TRANSCRIPTIONAL MODIFICATION

r-RNA: Steps in RNA processing:

rRNA processing in Vertebrates (Eukaryotes): In Eukaryotes nucleolus is the centre of processing ribosomal RNA. A 45s precursor is formed by RNA polymerase I and processed in 90s **preribosomal nucleolar complex** to give 18s, 28s, and 5.8s rRNA. There is tight coupling of RNA processing with ribosomal assembly. 5s rRNA is transcribed by RNA polymerase III from a separate gene. Precursor RNA undergoes methylation at more than 100 bases from 14000 nucleotides at 2' hydroxyl group. Furthermore there is modification of bases such as uridine to pseudouridine etc. followed by series of cleavage reaction. Cleavage and modifications are guided by **snoRNAs (small nucleolar RNA)**. In yeast, entire processing involves pre-rRNA, 170 non-ribosomal protein, 70 snoRNA and 78 ribosomal proteins. snoRNA are supposed to be remnant of spliceosomes.



Then we have the RNA processing in vertebrates or the eukaryotes. So, in the eukaryotes, you can have the mature ribosomal RNA. So, this is the RNA transcripts, and that is going to be cleaved, and that is how you are going to have mature ribosomal RNA of 18s, 5.8s and 28s.

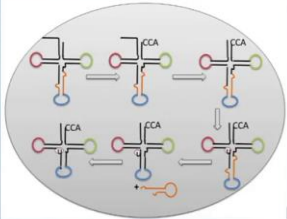
(Refer Slide Time: 20:41)

POST-TRANSCRIPTIONAL MODIFICATION

t-RNA: Steps in RNA processing:

Processing of t-RNA: In both Eukaryotes and prokaryotes t-RNA processing occurs. It is transcribed as long precursor; sometimes single primary transcripts carry more than one t-RNA segments which are separated by cleavage.

Processing of pre tRNA involves cutting off of extra sequences by **endonucleases** such as **RNase P** at 5' end and **RNase D** at 3' end. RNase P is a ribozyme with RNA exhibiting catalytic activity. After removal of sequences from 3' end, CCA sequence is added via enzyme tRNA nucleotidyltransferase. This enzyme binds to CCA sequence at its active site and **phosphodiester bond** is formed with 3' end. Furthermore, there is base modification occurring simultaneously such as methylation, deamination or reduction; in case of pseudouridine, uracil is removed and reattached to sugar through C5.



And then we have the post transcriptional modification of the tRNA. So, processing of tRNA in both eukaryotes and prokaryotes, the tRNA processing occur it is transcribed as a long precursors and processing of tRNA involves a cutting off an extra sequence by the endonucleus such as RNase P at the 5 prime end, and RNase D at the 3 prime end.

RNase P is a ribozyme with the RNA exhibiting catalytic activity. So, after removal of sequence from the 3 prime end, CCA sequences added by the enzyme tRNA nucleotidyltransferase. This enzyme binds to the CCA sequence at the, at its active site and phosphodiester bond is formed with the 3 prime end.

Furthermore, there is a base modification occurring simultaneously such as methylation, deimination, induction and in case of the psuedouridine, uracil is removed and attached to the sugar through the C5 ounce. So, these are some of the post translational modifications what we have discussed in this particular course.

(Refer Slide Time: 21:45)

The slide is titled "TRANSLATION" in yellow text on a dark blue background. In the top right corner, there is a small video inset of a man with a mustache. The main content consists of a bulleted list of topics in yellow and green text, and a diagram on the right. The diagram shows "DNA" at the top, with three arrows pointing down to "rRNA", "tRNA", and "mRNA".

- Structure of Translation Machinery
- Genetic Code
- Mechanism of Translation
- Activation of Amino acid
- Initiation
- Elongation
- Termination
- Post-Translational Modification

Now, let move on to the, this we have also discussed about the translation. So, in within the translation what we have discussed, we have discussed about the structure of the translational machinery, whether it is a prokaryotic machinery or the eukaryotic machinery, we discuss about the genetic codes, we discuss about the mechanism of translation. So, within the mechanism of translation, we discuss about the activation of amino acids, initiation, elongation and termination.


And all these mechanisms we have discussed in detail about the prokaryotic system as well as the eukaryotic system and what are the different proteins are involved in governing the different events, whether it is the activation of amino acids, initiation, elongation and terminations. And then we also discuss about the post translational modifications.

(Refer Slide Time: 22:33)

TRANSLATION

Post-Translational Modification

Phosphorylation: Phosphorylation is an important post-translational modification. It is prevalent from bacteria to higher eukaryote sustaining as mainly two types. First it acts to functionally regulate the catalytic activity of the protein by defining a rigid and permanent 3-D protein structure. Secondly, temporarily phosphorylate proteins serve as anchors for other protein substrates in signal transduction pathways. As, such it acts as a key-player in the regulation of many cellular processes like cell-cycle, cell growth, apoptosis and regulation of signal transduction pathways.

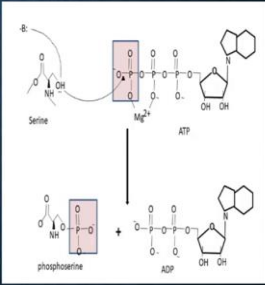


TRANSLATION

Post-Translational Modification

Phosphorylation:

Mechanism of phosphorylation: In eukaryotic cells, phosphorylation is known to occur only at the side chains of three amino acids, serine, threonine and tyrosine. This is because these amino acids harbour a nucleophilic (-OH) group. The terminal phosphate group (γ -PO₃²⁻) on the universal phosphoryl donor adenosine triphosphate (ATP) serves as the point of nucleophilic attack from that -OH group, which results in the transfer of the phosphate group to the amino acid side chain. Magnesium (Mg²⁺) ions acts as catalyst by chelating the γ - and β -phosphate groups resulting in lowering of the threshold for phosphoryl transfer to the nucleophilic (-OH) group



So, post translational modifications, these are the post translational modifications what we have discussed, so, we discuss about the phosphorylations. We discuss about the mechanism of phosphorylation where the phosphate is being transferred from the ATP to the serine. And that is how it is actually going to form the phosphoserine.

(Refer Slide Time: 22:55)

Post-Translational Modification

Phosphorylation:

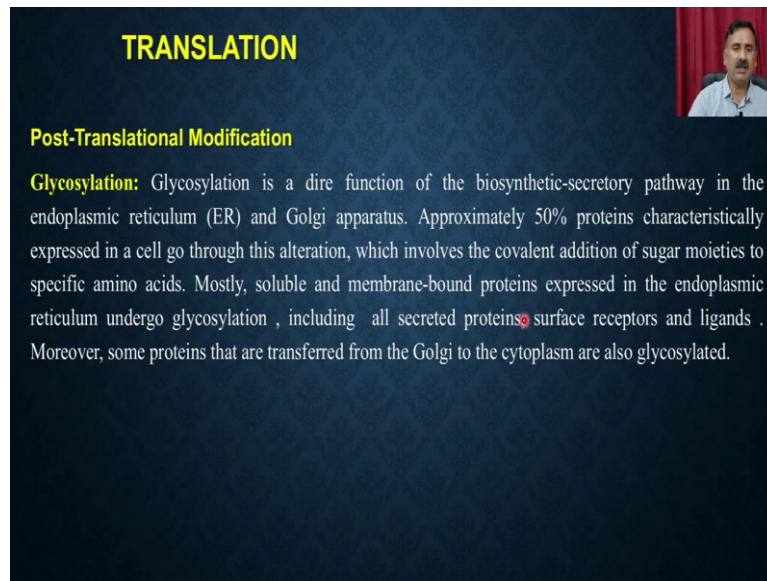
These conformational changes can affect the protein in two different ways; (1) Phosphorylation causing conformational changes in the phosphorylated proteins, These conformational changes stimulate the catalytic activity of protein, so any protein can be activated or inactivated by the phosphorylation. (2) Phosphorylated proteins employ the neighbouring proteins which have structurally conserved domains that distinguish and bind to phosphomotifs. These domains are specific for diverse amino acids. Protein phosphorylation is a reversible Post translation modification which is carried by kinases which phosphorylate and phosphatases which dephosphorylate to substrates. These two type of enzymes make possible the dynamic nature of phosphorylated proteins. So the balance concentration of kinase and phosphatase is very important for the cell and it is also important for the catalytic efficiency of a particular phosphorylation site.

```
graph TD; SignalIn[Signal in] --> Kinase[Kinase]; Kinase --> Inactive[Inactive enzyme]; Inactive --> Active[Active enzyme]; Active --> SignalOut[Signal out]; Active --> Phosphatase[Phosphatase]; Phosphatase --> Inactive; Active -- Off --> Inactive; Inactive -- On --> Active; Kinase --- Pi((Pi)); Phosphatase --- Pi2((Pi));
```

We discuss about the relevance of the this particular modification like the phosphorylations. So, phosphorylation causes the conformational changes in the phosphorylated protein and these conformational changes stimulate the catalytic activity of proteins. So, any protein can be activated or inactivated by the phosphorylations. Number two, phosphorylated protein employs the neighboring protein which have a structurally conserved domain that distinguish and bind to the phosphomotifs.

So, these domains are specific for diverse amino acids. Protein phosphorylation is a reversible post translational modification which is carried out by the kinases, which phosphorylate and it is and the phosphatase, which is dephosphorylated to the substrate. This means the protein phosphorylation is a reversible event and that is how it is actually going to regulate the activity of the different types of enzymes.

(Refer Slide Time: 23:50)



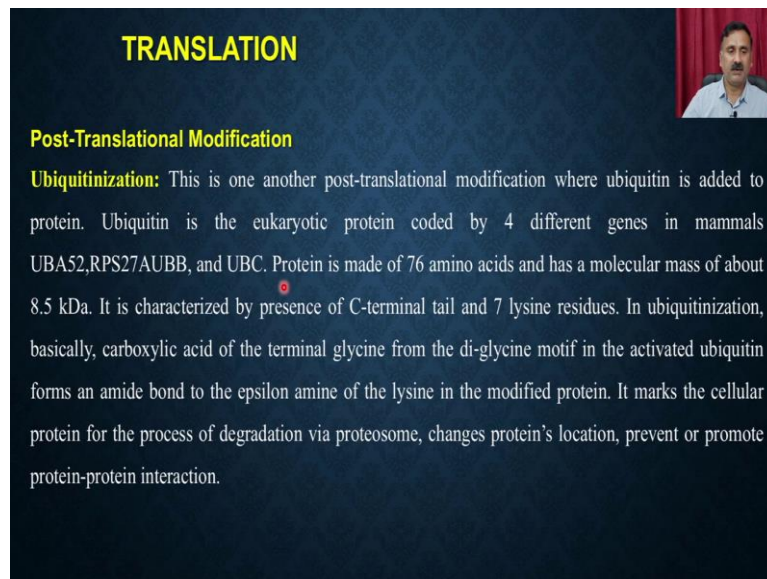
TRANSLATION

Post-Translational Modification

Glycosylation: Glycosylation is a dire function of the biosynthetic-secretory pathway in the endoplasmic reticulum (ER) and Golgi apparatus. Approximately 50% proteins characteristically expressed in a cell go through this alteration, which involves the covalent addition of sugar moieties to specific amino acids. Mostly, soluble and membrane-bound proteins expressed in the endoplasmic reticulum undergo glycosylation , including all secreted proteins, surface receptors and ligands . Moreover, some proteins that are transferred from the Golgi to the cytoplasm are also glycosylated.

And then we also discussed about the glycosylation. And we also discuss about a different component or different mechanisms of the glycosylations.

(Refer Slide Time: 24:01)



TRANSLATION


Post-Translational Modification

Ubiquitination: This is one another post-translational modification where ubiquitin is added to protein. Ubiquitin is the eukaryotic protein coded by 4 different genes in mammals UBA52, RPS27AUBB, and UBC. Protein is made of 76 amino acids and has a molecular mass of about 8.5 kDa. It is characterized by presence of C-terminal tail and 7 lysine residues. In ubiquitination, basically, carboxylic acid of the terminal glycine from the di-glycine motif in the activated ubiquitin forms an amide bond to the epsilon amine of the lysine in the modified protein. It marks the cellular protein for the process of degradation via proteasome, changes protein's location, prevent or promote protein-protein interaction.

And then we also discuss about the ubiquitinations and ubiquitination is being governed by the complete ubiquitylation machinery where you have the different steps.

(Refer Slide Time: 24:12)

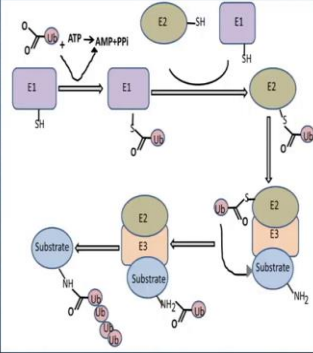
TRANSLATION




Post-Translational Modification

Steps

Activation of Ubiquitin: It occurs in a two-step reaction process. At first, ubiquitin interacts with ATP and forms ubiquitin-adenylate intermediate. In the next step, ubiquitin is transferred to E1 active site containing cysteine residue. This causes formation of thioester linkage between the C-terminal carboxyl group of ubiquitin and the E1 cysteine sulfhydryl group.



TRANSLATION

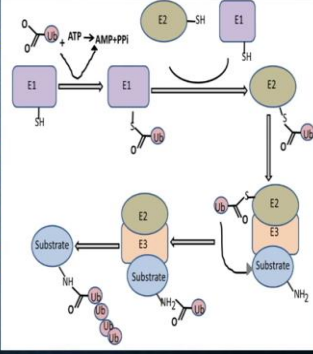


Post-Translational Modification

Steps

Transfer of Ubiquitin from E1 active site to E2 active site via trans-esterification reaction occurs.

In the last step of the ubiquitylation cascade there is formation of an isopeptide bond between a lysine of the target protein and the C-terminal glycine of ubiquitin via activity of one of the hundreds of E3 ubiquitin-protein ligases. In E1-E2-E3 cascade, one E1 molecule causes binding to several E2 which in turn bind to hundreds of E3 in hierarchical fashion.

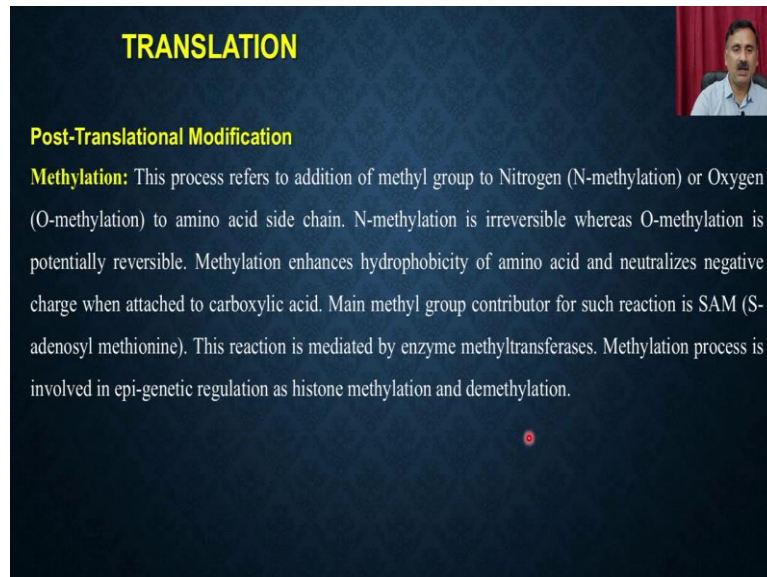


So, in the step one, you have the activation of ubiquitin. And so it occurs in a two-step reaction. At first the ubiquitin interacts with the ATP and forms the ubiquitin-adenylate intermediate. And in the second step, the ubiquitin is transferred to the E1 active site containing the cysteine residue.

And this causes formation of thioester linkage between the C-terminal carboxyl group of ubiquitin and the E1 cysteine sulfhydryl group. Once the activation is done then you can actually be having the transfer of a ubiquitin. And in the last step, the ubiquitin is actually going to be added to the target proteins and that is how you are actually going to have either the mono ubiquitylation or the poly ubiquitylation.

So, this is the mono ubiquitylations and once these events are going to be done for the multiple rounds, then it is actually going to form the polyubiquitylations.

(Refer Slide Time: 25:08)



TRANSLATION

Post-Translational Modification

Methylation: This process refers to addition of methyl group to Nitrogen (N-methylation) or Oxygen (O-methylation) to amino acid side chain. N-methylation is irreversible whereas O-methylation is potentially reversible. Methylation enhances hydrophobicity of amino acid and neutralizes negative charge when attached to carboxylic acid. Main methyl group contributor for such reaction is SAM (S-adenosyl methionine). This reaction is mediated by enzyme methyltransferases. Methylation process is involved in epi-genetic regulation as histone methylation and demethylation.

Apart from that we also discuss about the methylation. So, this process refers to the adding of methyl group to the nitrogen or the oxygen to form the amine to amino acid side chain and methylation is irreversible whereas, O-methylation is potentially reversible. Methylation enhances the hydrophobicity of the amino acid and utilizes the negative charge when attached to the carboxylic acid.

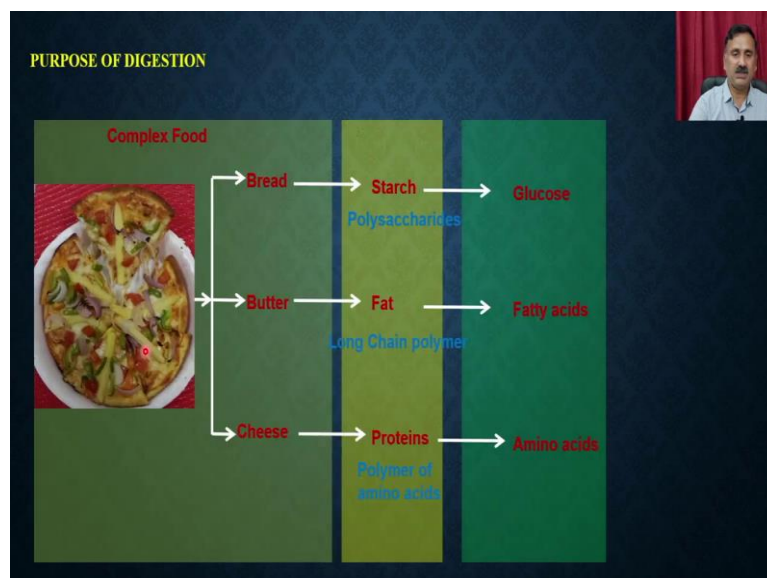
So, many methyl group contributor for such reaction is SaAm, which is called as the S-adenosyl methogege. And this reaction is mediated by an enzyme which is called as the methyltransferases. Methylation process is involved in epigenetic regulation as histone methylation and demethylations. So, methylation is also very crucial in terms of regulating the many types of activities of the different proteins.

(Refer Slide Time: 26:02)



Subsequent to this, we also discuss about the human physiology and within the human physiology, we discuss about the digestion, circulatory system, muscular system, nervous system, and then we discuss about the homeostasis and within the homeostasis, we discuss about the endocrine system and the excretory system.

(Refer Slide Time: 26:23)

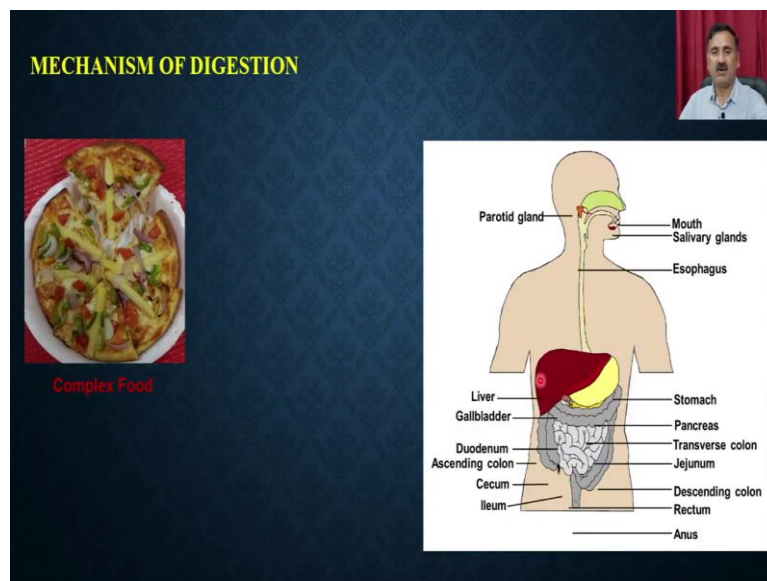


So, when we talk about the digestion, so, digestion, the what is the purpose of the digestion, the purpose of retention is that it actually going to simplify the complex foods. So, we have taken an example of the pizza, so pizza is made up of the three components, one is bread, butter and cheese, and bread is nothing but a starch which is actually a polysaccharide.

And the purpose of the digestion is that it should convert the starch into the glucose and that glucose is being absorbed by the human body and that is how it is actually going to be taken up for the nutrition. Similarly, the butter, butter is made up of the fat or fat or the fatty acids and that is going to be converted into the fatty acid and that fatty acid is going to be absorbed into the blood and it is going to be utilized for the energy production.

Then we have the cheese and the cheese is made up of the proteins and this protein is made up of the polymer of amino acids, and the protein is going to be digested to produce the amino acid and these amino acids are going to be absorbed.

(Refer Slide Time: 27:31)



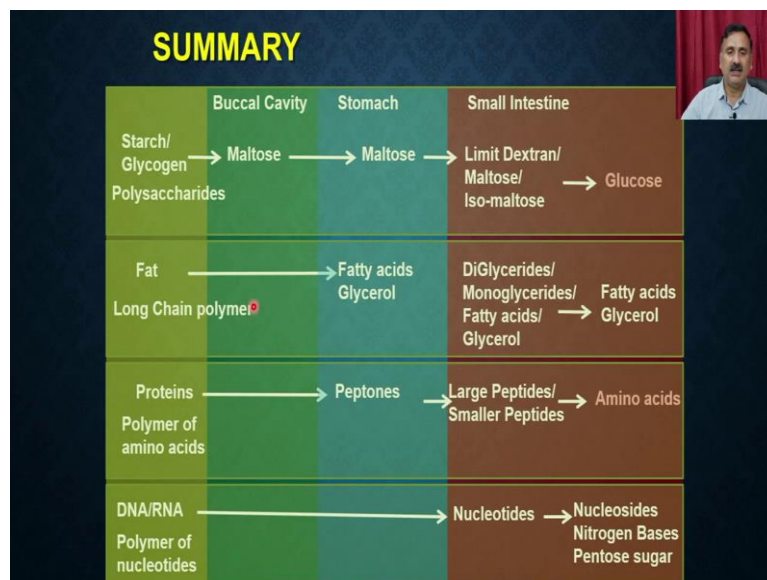
Now, what is the mechanism of digestion? So, mechanism of digestion is that you are going to have a complex food, so, you are going to take up the food through your mouth. There are so many glands water present in the mouth also buccal cavity that is going to help the swallowing of the food then it will enter into the esophagus.

And after that it is going to enter into the stomach and from the stomach it is going to enter into the small as well as the large intestine and in this chamber the reaction is going to take place with the help of the different types of enzymes. So, what are different enzymes?

(Refer Slide Time: 28:06)

Enzymes Secreted in Alimentary Canal

List of digestive enzymes in human		
Enzyme	Substrate	Site of action
Ptyalin (salivary amylase)	Starch	Mouth
Pepsin	Proteins	Stomach
Gastric Lipase	Little amount of fats	
Renin	Casein	Child's stomach
Pancreatic amylase	Starch	
Trypsin	Proteins	
Chymotrypsin	Proteins	
Elastase	Protein (Elastin)	
Carboxypeptidase	Large peptides	
Pancreatic lipase	Fats (Triglycerides)	
Nuclease	Nucleic acids (DNA, RNA)	Small Intestine
Enterokinase	Trypsinogen	
Aminopeptidase	Large peptides	
Dipeptidase	Dipeptides	
Disaccharidase	Disaccharide	
Intestinal lipase	Fats	
Nucleotidase	Nucleotide	
Nucleosidase	Nucleoside	



We have the different enzymes like the ptyalin, which is going to be act on the starch and is going to be present in the mouth or the buccal cavity. Then we have the couple of enzymes what is present in the stomach. And then we also have the couple of enzymes what is present in the small intestine and their target protein.

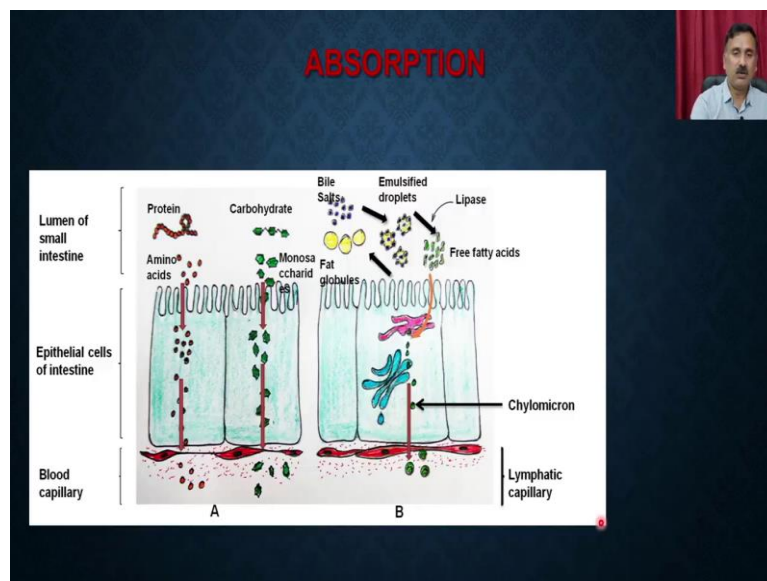
So, ultimately what is going to be achieved by the end of the digestion is that the starch or the polysaccharides are actually going to be converted into the maltose into the buccal cavity, it is going to be remain undigested within the stomach. So, there will be no further digestion in the stomach and then maltose is going to be converted into first into the limit dextran, maltose or iso-maltose.

And then ultimately it is going to be digested into the glucose in the small intestine and from there, it is going to be absorbed into the small intestine. Similarly, for the fat which is actually a long chain polymer is going to be digested into the fatty acid and glycerol in the stomach and from stomach it will move into the small intestine where it is going to be digested into the diglycerides, monoglyceride, fatty acids and glycerol.

And ultimately it is going to be converted into fatty acid and glycerol and in this particular fatty acid and glycerol is going to be absorbed by the body. Similarly, for the proteins, protein there will be no digestion in the buccal cavity it is going to be converted into the peptones then large peptide and a small peptide into the small intestine and ultimately, it is going to be converted into amino acid and it is going to be absorbed.

Then for the DNA or RNA it is going to be converted into nucleotide in the small intestine and from nucleotide it will actually form the first the nucleosides, the nitrogen bases and the pentose sugar and all these are actually going to be absorbed into the blood.

(Refer Slide Time: 30:07)



So, there is a discreet mechanism through which the absorption take place into the micro villi. And that is how the nutrition as well as the water and all these materials are going to be absorbed into the body into the small intestine, water is going to be absorbed in the large intestine and undigested material is actually going to be stored into the rectum in the form of feces and that is going to be a waste material and going to be removed from the body.

(Refer Slide Time: 30:39)



Subsequent to digestion we also discuss about the circulatory system. So, within the circulatory system, we discuss about the structure and the function of heart, we have discussed about the how the heart is connected to throughout the body with a complex network of the arteries and the vein and what are the differences between the artery and the vein.

And what is the function of the blood in providing the protection against the infectious organisms and subsequent to the muscular circulatory system we also discuss about the muscular system. So, within the muscular system, we discuss about the different types of muscles, whether it is the involuntary muscles, voluntary muscles or the cardiac muscles. And then we also discuss about the mechanism of the molecular mechanism how the muscle cells are contracting.

(Refer Slide Time: 31:34)

Molecular mechanism:

Muscle contraction mechanism is described by sliding filament theory. This theory described by Andrew F Huxle, Rolf Niedergerke, Hugh Huxley and Jean Hanson in 1954. Muscle contraction is a cyclic repetitive process. In which, actin filament slide over myosin and generate tension in the muscle.

Action potential from CNS reaches neuromuscular junction and release the acetylcholine near to muscle fibre. Acetylcholine diffuse the synapse where it binds to the nicotinic acetylcholine receptors. After binding, receptors get activated on neuromuscular junction and it lead to the opening of the sodium/potassium channel. It results in sodium influx and potassium outflow from the cell. Sodium/potassium movement from the muscle cell generate an action potential which leads to the depolarization of the inner muscle fibre.

The diagram illustrates the molecular mechanism of muscle contraction. It shows a cycle starting from a 'Muscle resting condition' where actin and myosin filaments are not interacting. A 'Nerve signal generated action potential initiation of muscle contraction' triggers the 'Release of Ca²⁺ from Sarcoplasmic Reticulum & bind to troponin'. This causes the 'Movement of troponin & ATP lysing', leading to 'Actin - myosin binding & contraction of actin filament'. This is followed by 'ATP binding to myosin' and 'Release of Ca²⁺ from troponin & moving to the sarcoplasmic reticulum', returning the system to the resting state.

So, within the molecular mechanisms, so muscle contraction mechanism is described by a sliding filament theory. And this theory is described by the Andrew Huxle or, and Rolf Niedergerke and the Huge Huxley and the Jene Hanson in the year of 1954. The muscle contraction is a cyclic repeated process in which the actin filaments light over the myosin and generate tension in the muscles.

And the action potential from the brain is the initial stimulus and that is how it is actually going to have the, these are the cyclic reactions and that is how the muscles are actually going to contract.

(Refer Slide Time: 32:13)

NERVOUS SYSTEM

It co-ordinate physiological functions in human. Nervous tissue originates from ectoderm and is specialized for receiving stimuli and transmitted message.

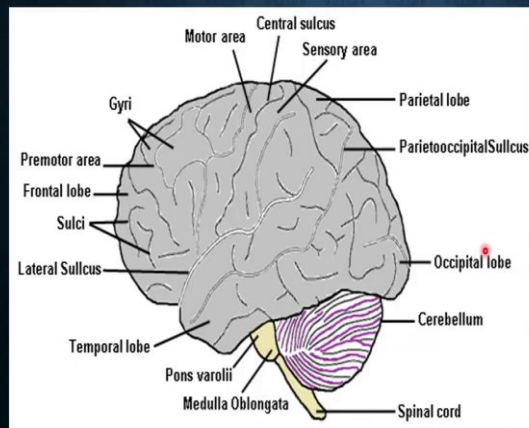
The origin of human nervous system is ectodermal. The whole nervous system is divided into three parts.

```
graph TD;
  NS[Nervous System] --> CNS[Central Nervous System];
  NS --> PNS[Peripheral Nervous System];
  NS --> ANS[Autonomic Nervous System];
  CNS --> Brain;
  CNS --> SpinalCord[Spinal Cord];
  PNS --> CranialNerve[Cranial Nerve];
  PNS --> SpinalNerve[Spinal Nerve];
  ANS --> Sympathetic;
  ANS --> Parasympathetic;
```

The flowchart shows the hierarchy of the Nervous System. It is divided into three main parts: Central Nervous System, Peripheral Nervous System, and Autonomic Nervous System. The Central Nervous System includes the Brain and Spinal Cord. The Peripheral Nervous System includes Cranial Nerve and Spinal Nerve. The Autonomic Nervous System includes Sympathetic and Parasympathetic.

NERVOUS SYSTEM

Central Nervous System: It comprises the brain and the spinal cord.

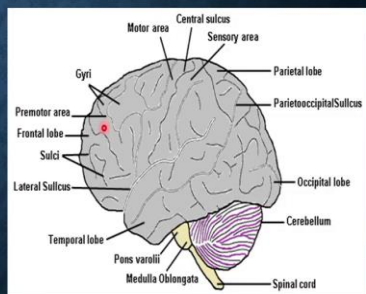


NERVOUS SYSTEM

Central Nervous System: It comprises the brain and the spinal cord.

Table 14.1: Different areas of brain and their functions

Name of Area	Location	Function
Prefrontal cortex	Frontal lobe	Site of intelligence, knowledge and memory
Premotor area	Frontal lobe	Writing centre, associated movement of eye, head & body, control complex movement of jaw, tongue, pharynx and larynx
Motor area	Frontal lobe	Analysis of all type of voluntary muscle
Frontal eye field	Frontal lobe	Opening and closing of eyelid and conjugate movement of eye
Broca's area or motor speech area	Frontal lobe	Analysis for speak
Auditory area	Temporal lobe	Analysis for sound
Olfactory area	Temporal lobe	Analysis for smell
Wernicke's area	Temporal lobe	Analysis for communication
Gustatory area	Parietal	Analysis for taste
Somesthetic area	Parietal	Analysis for touch, pain, pressure etc.
Angular gyrus	Parietal	Analysis for writing (associated with speech)
Occipital area	Occipital	Analysis for vision



Subsequent to the muscle system, we also discuss about the nervous system. So, within the nervous system, we have said that the nervous system can be divided into three main parts. It can be central nervous system, peripheral nervous system or the autonomic nervous system, within the central nervous system, we have the two components like the brain and the spinal cord.

Whereas the peripheral nervous system is actually going to take up the message from the brain or the spinal cord, and that is being done by the cranial nerves or the spinal nerve, whereas in the autonomic nervous system, you can have the sympathetic autonomic nervous system or the parasympathetic nervous system.

So, within the nervous system, while we were discussing about the nervous system, we discussed about the structure of the brain, and we also discuss about the distribution of the

cranial nerves, from the brain and their role in the different types of activities. So, we discussed about like the, in what area of the brain the nerves are originating, and what is their function.

(Refer Slide Time: 33:19)

NERVOUS SYSTEM

List of human cranial nerves

Name	Origin	Distribution	Nature	Function
Olfactory	Olfactory epithelium	From olfactory lobe to temporal lobe	Sensory	Smell
Optic	Retina	Leads to occipital lobe	Sensory	Sight
Oculomotor	Midbrain	Four eye muscle	Motor	Movement of eyeball
Trochlear	Midbrain	Superior oblique eye muscle	Motor	Rotation of eyeball
Trigeminal	Pons varolii	Skin of nose, eyelid, forehead, scalp, conjunctiva, lachrymal gland.	Mixed	Sensory supply to concerning part
a. Ophthalmic	-	-	Sensory	-
a. Maxillary	-	Mucous membrane of cheeks and upper lip and lower eyelid	Sensory	-
a. Mandibular	-	Lower jaw, lower lip, pinna.	Mixed	Muscle of mastication
Abducens	Pons varolii	Lateral rectus eye muscle	Motor	Rotation of eyeball
Facial	Pons varolii	Face, neck, taste buds, salivary gland	Mixed	Taste (anterior 2/3 part of tongue), facial expression, saliva secretion
Auditory	Pons varolii	Internal ear	Sensory	Hearing and equilibrium
Glossopharyngeal	Medulla oblongata	Muscle and mucous membrane of pharynx and tongue.	Mixed	Taste (posterior 1/3 part of tongue), saliva secretion
Vagus	Medulla oblongata	Larynx, lungs, Heart, stomach, intestines	Mixed	Visceral sensations and movements
Accessory spinal	Medulla oblongata	Muscles of pharynx and larynx	Motor	Movement of pharynx and larynx
Hypoglossal	Medulla oblongata	Muscles of tongue	Motor	Movement of tongue.

NERVOUS SYSTEM

A neuron is mainly divided into two parts:

- 1) Cell body or cyton and
- 2) Cell process.

Cyton: It is broader part of neuron which contains uninucleated cytoplasm. Except centriole, all type of cell organelles is found in cytoplasm. Due to absence of centrioles, neurons can't divide. Some other cells organelles like *neurofibril* and *nissl's granule* found in neuron, which help in transfer of impulse to cyton. Nissl's granule is formed by coiling of endoplasmic reticulum around the ribosome.

And so, these are the different types of cranial nerves, what is going to be originated from the different parts of the brain and what is their function. And we also discuss about the function the structure and the function of the individual neuron cells because the brain is made up of the different types of neuron cells. And in neuron cell is mainly been divided into two parts, cell body or cyton and the cell processes.

So, cyton, it is a broader part of the neuron. So, this is the cyton which contains the unit nucleated cytoplasm, except centriole, all types of cell organelle is found into the cytoplasm.

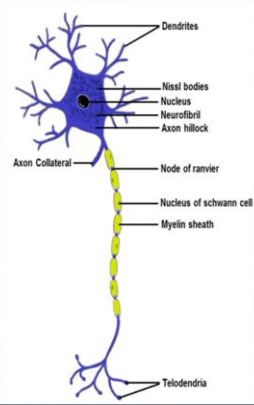
Due to the absence of centrioles, neurons cannot divide. Some other cell organelles like the neurofibril and Nissl's granules are found in the neuron which helps in the transfer of impulse to cyton. Nissl granule is formed by the coiling of the endoplasmic reticulum around the ribosomes.

(Refer Slide Time: 34:18)

NERVOUS SYSTEM

Cell process: Dendron and axon are cell process of neuron. Fine branches of Dendron called dendrites, contains some receptor points, so that Dendron receive the stimuli and produce centripetal conduction. Axon is the longest cell process of neuron. Axon is covered by axolemma. Part where axon arises from cyton called *axon hillock*. Cytoplasm of axon is called axoplasm which only contains neurofibrils and mitochondria. The terminal end of axon is branched and vesicular, called *telodendria*.

Some neurons are covered by layer of sphingomyelin (a phospholipid) called as *myelin sheath* or *medulla*. Myelin sheath is covered by thin cell membrane which is called as *neurilemma* or *schwan cell*. Myelin sheath act as insulator and prevent leakage of ions.



And then we have the cell processes. So, Dendron and axon are the cell processes of the neurons and they will actually going to convey the message.

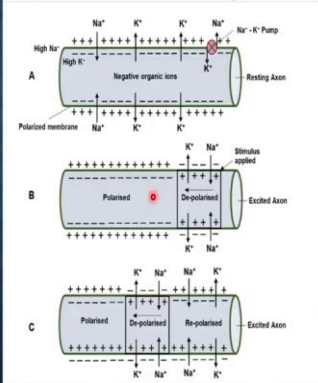
(Refer Slide Time: 34:29)

NERVOUS SYSTEM

The resting membrane potential

The cell membrane of nerve cell is said to be polarized when negative potential exists more inside the cell with respect to outside. The potential difference across the cell membrane at rest is called resting membrane potential and it is approx. -65 mV.

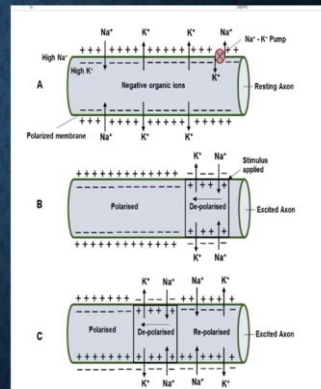
The resting membrane potential is maintained by active transport of ions against their electrochemical gradient by sodium potassium pump and also by passive diffusion of ions. For active transport, there are carrier proteins located in the cell surface membrane. They are driven by energy supplied by ATP and coupled by removal of three sodium ions from the axon with the help of uptake of two potassium ions. The passive diffusion of ions opposes the active movement of ions.



NERVOUS SYSTEM

The resting membrane potential

The rate of diffusion depends on the permeability of the axon membrane for the ions. Potassium ions have more permeability than that of sodium ions. Therefore loss of potassium ions is more than the gain of sodium ions. This leads to the net loss of potassium ions from the axon and generation of negative charge within the membrane.

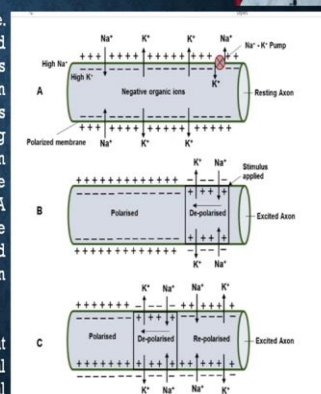


NERVOUS SYSTEM

Action Potential or exciting stage

The event of depolarisation initiates a nerve impulse or spike. This nerve impulse is also known as *Active potential*, generated by change in sodium ion channel. These channels are known as voltage gated channel. At resting stage these channels remain close due to binding of calcium ions. An action potential is generated by a sudden opening of the sodium gates. Opening of gate increases the permeability of membrane for sodium which then enters inside by diffusion. This increase in positive ions inside the axon drops the negative potential inside axon. A change of -10 mV in potential difference from resting membrane potential is known as spike potential, sufficient to trigger a rapid influx of sodium ions; which leads the generation of action potential.

First, the negative resting potential is cancelled out, at this point the membrane is completely depolarised then the potential difference is developed across the membrane. The potential difference at 30 mV is corresponds to the maximum concentration of sodium inside the axon.



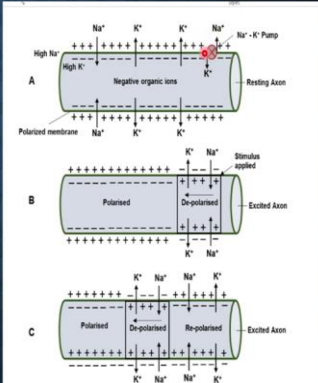
And then we have also discussed about how the mechanism through which the signal is traveling from the one end of the neuron to the other part of neuron. So, where we have discussed about the resting membrane potential, we have discussed about the action potential and then we also talk about the repolarization potentials. And we discussed in mechanism also that how the different events are happening and responsible for relaying the signal from one end of the neuron to the other part of the neuron.

(Refer Slide Time: 35:03)

NERVOUS SYSTEM

Repolarisation

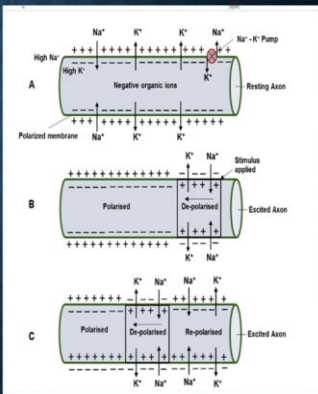
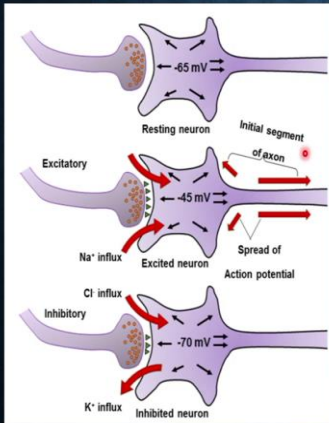
A fraction of second after the sodium gates open, depolarisation of membrane causes opening of potassium gates therefore potassium diffused out of the axon. This causes less positive charge inside with respect to outside. Thus due to repolarisation, potential changes from 30 mV to -65 mV. The neuron is now prepared for receiving another stimulus and to conduct as described before. Now it's necessary to restore normal resting potential by expelling sodium ions out and taking potassium ions inside. The time taken for restoration is called *refractory period* because during this period membrane can't receive another impulse.



And this is what we have summarized in this particular picture that we have the resting neurons, excited neuron and as well as the repolarization neurons and these are the things that is going to happen. After this at the end in the previous module, we have also discussed about the homeostasis so, what is homeostasis?

(Refer Slide Time: 35:22)

NERVOUS SYSTEM



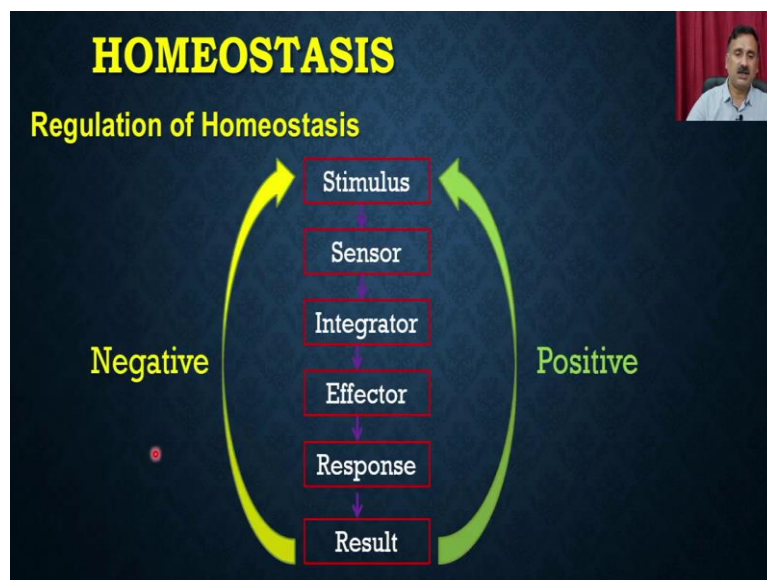
Homeostasis means the home like environment and it is the environment which you do not like to change. So, you always feel most comfortable when you are in your home. And that is why the homeostasis is very important for the any organism to remain healthy and to grow.

So, homeostasis what is mean by the homeostasis is that it is actually going to keep the conditions or the parameters unchanging, it is maintaining a relatively stable internal environment regardless of the external conditions and it allows the changes within the narrow limit and it is under that dynamic equilibrium which means the different parameters are actually going to affect each other, but it will remain within the dynamic equilibriums.

(Refer Slide Time: 36:13)

HOMEOSTASIS

- “Unchanging”
- Maintaining a relatively stable internal environment, regardless of external conditions.
- Allows changes within narrow limits.
- “Dynamic Equilibrium”



These are the machines part of the homeostatic machinery where you have the stimulus, sensors, integrator, effector, responses and results and what is the role of the stimulus, it is actually going to respond when there will be a deviation of the parameter from the set point and the error is measured by the sensor.

Once it measure that there is a deviation then the sensor is actually going to sense that particular signal and it is actually going to give that the integrator and the effectors. So, effectors are usually in an organ or tissue. So, they will actually say okay, what could be the effect what is going to form, and then it is going to result into the response and that result in response is actually going to either decrease the stimulus or increase the stimulus.

So, under what condition it is actually going to decrease the stimulus. So, when you have the negative feedback mechanism, it is the result is going to decrease the stimulus which means it is actually going to reverse the effects whereas, when the results are going to increase the stimulus then it is going to be called as the positive feedback mechanisms.

(Refer Slide Time: 37:25)

Negative feedback homeostasis:

- It occurs when a change in one direction produces a change in the other. It is the opposite feedback mechanism of positive feedback which is responsible for reversing the stimulus by activating the opposite responses and leads to reduced productivity of the stimulus.
- Most important for maintaining constant internal environment.
- **Examples:**
 - Regulation of body temperature
 - Blood pH
 - Hormone levels
 - Oxygen/Carbon dioxide balance
 - Blood sugar levels
 - Blood pressure
 - Acid/base balance
 - Osmoregulation
 - Calcium homeostasis
 - Energy balance

Fig: Body temperature regulation

Fig: Negative feedback loop

So, what is mean by the negative feedback mechanism? It occurs when the change in one direction produces a change in the other, this. It is the opposite feedback mechanism of the positive feedback which is responsible for reversing the stimulus by activating the opposite responses and leads to the reduced productivity of the stimulus, most important for maintaining the constant internal environment.

So, one of the classical example is the regulation of body temperature, blood pH, hormones, oxygen, carbon dioxide, sugar, blood pressure, acid, osmoregulation, calcium homeostasis and the energy balance. This is a classical example, I have shown how the body is maintaining the constant temperature of 37.

(Refer Slide Time: 38:13)

Positive feedback homeostasis:

- In response to an output variation, causes the output to vary even more in the direction of initial deviation. So, it promotes the change to proceed further and change amplifies until the removal of the stimulus.
- Reinforcement of particular stimulus in the body.

Examples:

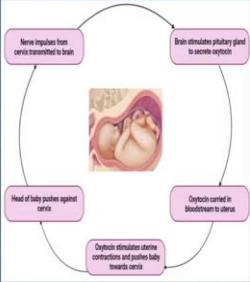
Childbirth: The pushing of the child's head downwards induces the release of oxytocin, that stimulates further contractions of the cervix, where it creates a pressure on it. These contractions continue to stimulate the release of oxytocin until the baby is born.

Lactation: Stimulation of milk production by breastfeeding, that causes further feeding and continues until the baby stops feeding.

Ovulation: The release of estrogen by dominant follicle inside the ovary, that stimulates the release of FSH and LH, which further stimulates for the growth of the follicle.

Blood clotting: The activated platelets release the clotting factors which stimulates the aggregation of more platelets at the site of injury.

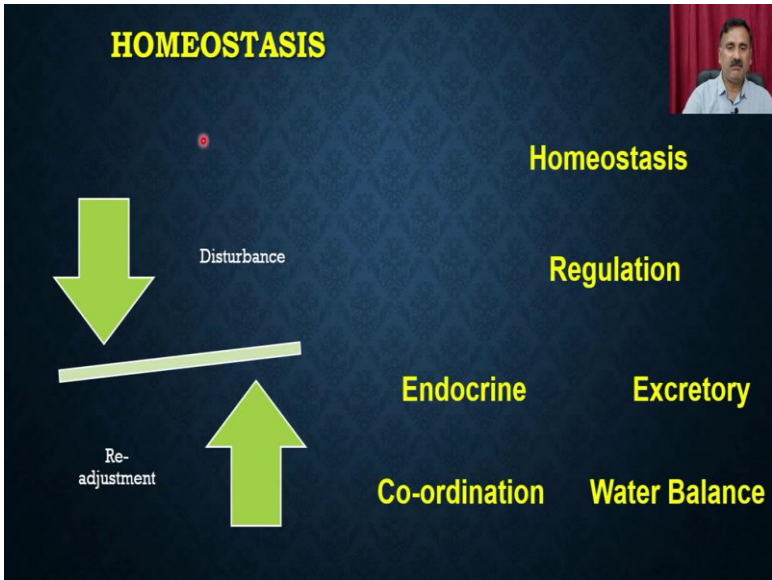
Fruit ripening: Ethylene is released by ripened fruits, which further stimulates the ripening of the nearby fruits.



And then we have the positive feedback homeostasis. So, in response to an output variation, the, it promotes the chain to proceed further and changes amplify until the removal of the stimulus. So, it is rare, but it is occurring in the special circumstances. So, what are the special circumstances, you can have the childbirth, lactation, evolutions, blood clotting and as well as the fruit ripening. So, these are some of the classical events in which the positive feedback homeostasis is actually going to play a crucial role.

(Refer Slide Time: 38:49)

HOMEOSTASIS



Homeostasis

Regulation

Endocrine **Excretory**

Co-ordination **Water Balance**

So, what is mean by the homeostasis is that there are factors which are actually going to disturb the homeostasis and but once this happens, it could be because of the positive or the

negative feedback mechanism it is actually going to reverse these changes and that is all the homeostasis would be under the dynamic equilibrium.

And homeostatic regulation required the activity of the endocrine system which is going to coordinate the different types of events or coordinate the activities between the different types of organs and whereas the excretory system it is actually going to maintain the water balance.

(Refer Slide Time: 39:25)



So, within the human physiology, what we have discussed, we have discussed about the digestions, regulatory system, muscular system, nervous system, and we have also discussed about the endocrine system and as well as the excretory system to understand their role into the homeostasis. So, in this particular course, what we have discussed so far, we have discussed many aspects related to the living organisms.

Whether it is related to classifications, evolutions and biomolecules, cellular processes or the human physiology. So, with this I would like to conclude my lecture here and I hope the summarizing and as well as revising the content in this particular module is going to be helpful for you to prepare for your forthcoming exams. So, with this I would like to conclude my lecture here. Thank you.