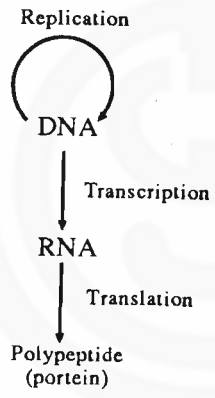
# UNIT 14 PROTEIN BIOSYNTHESIS

## Structure



## 14.1 INTRODUCTION




Genetic information is stored as the sequence of bases in DNA, rewritten into the sequence of nucleotides in RNA, and finally expressed as the sequence of amino acids in a polypeptide.

In the units 4 and 5, you have learnt about nucleic acids and proteins. You must be familiar with their constituents, structures and functions. In this unit, we will learn how proteins are synthesised in the living organisms and the role of nucleic acids.

DNAs i.e. the genes, contain coded instructions for specific sequences of amino acids in various proteins. These are first "copied", i.e. transcribed, in the form of specific sequences of bases in a special RNA, called messenger RNA or mRNA. The latter combines with ribosomes where the coded instructions are decoded, i.e. "**translated**" into amino acid sequence in proteins with the help of another type of RNA, called transfer RNA or tRNA. There are a large number of different tRNAs, each specific for one amino acid. These carry the amino acids to the ribosomes and align them properly in accordance with the coded message on mRNA. This is achieved by specific interaction of some bases on tRNA which form base-pairs with those on the mRNA. Relationship between the base sequence on mRNA and the amino acides specified by them is called **genetic code**. The RNA specific synthesis of polypeptides and proteins is called "**translation**". This process is complex and requires the participation of a large number of different macromolecules.

In this Unit, we will first give an overview of protein synthesis and then discuss the various stages in some detail. We will also briefly study how this process is regulated according to cell needs. This will be followed by a description of the molecular basis of the action of antibiotics. At the end we will study the biochemistry of cancer. You are advised to go through Unit 4 again before proceeding on with this unit.

### Objectives

After studying this unit, you should be able to :

- describe the genetic code,
- explain the role of ribosomes,
- list the different steps in protein biosynthesis and describe their significance in the process,
- describe different factors and constraints governing the protein synthesis in a cell,
- explain the principle of antibiotic drug action, and
- describe cellular basis of cancer.

## 14.2 OVERVIEW OF PROTEIN SYNTHESIS

Protein synthesis occurs on ribosomes. Each ribosome particle consists of RNA molecules and about 52 different protein molecules and carries the enzymes system needed to form peptide bonds between amonio acids. Ribosomes provide a site for binding the mRNA and sites for bringing in and aligning the amino acids in preparation for their assembly into the finished polypeptide chain. Amino acids themselves are unable to interact with the ribosome and cannot recognise bases in the mRNA molecule. There exists a collection of "carrier molecules" described in the Unit 4, namely, the tRNA. These molecules contain a site for amino acid attachment and a region called the anticodon that recognises the appropriate base sequence (the codon) in the mRNA (Fig. 4.3 Unit 4). Proper selection of the amino acids for assembly is determined by the positioning of the tRNA molecules, which in turn is determined by hydrogen-bonding or base pairing between the anticodon of each tRNA molecule and the corresponding codon of the mRNA. When an amino acid is attached to a tRNA molecule, the tRNA is said to be aminoacylated or charged. This linking of an amino acid to its corresponding tRNA is catalysed by the enzyme aminoacyl-tRNA synthetase and requires ATP. For each amino acid, there is at least one kind of tRNA and aminoacyl-tRNA synthetase.

Actual protein synthesis takes place in three stages: initiation, chain elongation, and termination. There are two sities on a ribosome for binding the charged tRNA molecule, called the **P site** and **A site**. The **initiation** involves the binding of the initiator tRNA (bearing methionine) to the start codon of mRNA on the P site of ribosome. This is followed by the binding of the appropriate aminoacyl-tRNA to the next codon of mRNA on the A site of ribosome. A peptide bond is then formed by transfer of the first amino acid (the one on the initator tRNA) to the second amino acid (the one attached to the tRNA in the A site). The first tRNA molecule, which is now free, is then ejected from the P site and the dipeptide amino acyl tRNA molecule shifts from the A site to the P site. The aminoacyl-tRNA corresponding to the third codon now binds the A site to start another round of elongation, which proceeds as described above. **Termination** occurs when a stop codon on the mRNA has occupied the A site. Then, the completed polypeptide chain is released from the ribsome. Before we study the protein biosynthesis in detail, let us learn about genetic code, and the structure and role of ribosome.

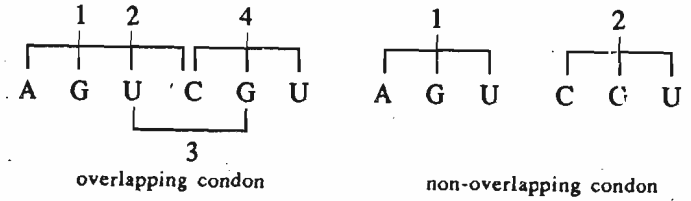
## 14.3 GENETIC CODE

We have been using the terms codons, anticodons, and codes in this unit and in previous units. It is now appropriate to define these terms more precisely. The genetic material is the DNA molecule (except in a few RNA viruses, where RNA is the genetic material). It has now been established that the genetic information is carried in the form of specific in sequences of bases (**codon**) in DNA. Different segments of DNA function as genes, i.e. code for specific proteins by specifying the sequence of amino acids. The relationship between the sequence of bases in DNA, or its RNA-transcript (i.e. messenger RNA), and the sequence of amino acids in proteins specified by them is called the **genetic code**.

As you know already, proteins contain 20 different amino acids which are to be coded for by the four bases present in a DNA molecule. It is obvious that if a single base is to code for one amino acid, then only four amino acids can be coded for. Simple arithmetic shows that if a combination of two bases coded for one amino acid, the maximum number of such pairs is only sixteen (i.e $4^2$). This is not adequate explanation for the twenty amino acids found in the proteins. Therefore it was realised that minimum code size would be triplet of bases. Number of different triplets made from four bases is sixty four (i.e. $4^3$), which are sufficient to code all the amino acids. Later on by genetic experiments, it was confirmed that indeed the **genetic code is triplet of bases: three adjacent nucleotides specify an amino acid**. The first codon to be identified was UUU which codes for phenylalanine.

Each amino acid is usually represented by a three-letter abbreviation
Phenylalanine = Phe
Lencine = Leu
Methionine = Met; etc.

The genetic code possesses certain characteristics such as non-overlapping and degeneracy. By **non-overlapping** we mean that any base can be part of one triplet (codon) and is not used in another codon. Thus, each base is "read" only once.



Degeneracy refers to one amino acid being coded for by more than one triplet. Only methionine and tryptophan are coded for by a single triplet each which are, AUG and UGG, respectively. For all other amino acids, there are more than one triplet codons. It may stressed, however, that any triplet codes for a single amino acid only. Further more, a given triplet codes for the same amino acid in all the species. The only exceptions are in the protein biosynthesis in mitochondria where small differences are observed. Thus, the code is not universal but applicable to almost all species. It is referred to as the "standard" genetic code and is shown in Table 14.1.

**Table 14.1: The "Standard" Genetic Code; Codon Assignments**

| First base | Second base | | | | Third base |
|---|---|---|---|---|---|
| | U | C | A | G | |
| U | UUU | UCU | UAC | UGU | |
| | Phenylalanine | Serine | Tyrosine | Cysteine | U |
| | UUC | UCC | UAC | UGU | |
| | Phenylalanine | Serine | Tyrosine | Cysteine | C |
| | UUA | UCA | UAA | UGA | |
| | Leucine | Serine | CT* | CT* | A |
| | UUG | UCG | UAG | UGG | |
| | Leucine | Serine | CT* | Tryptophan | G |
| C | CUU | CCU | CAU | CGU | |
| | Leucine | Proline | Histidine | Arginine | U |
| | CUC | CCG | CAC | CGC | |
| | Leucine | Proline | Histidine | Arginine | C |
| | CUA | CCA | CAA | CGA | |
| | Leucine | Proline | Glutamine | Arginine | A |
| | CUG | CCG | CAG | CGG | |
| | Leucine | Proline | Glutamine | Arginine | G |
| A | AUU | ACU | AAU | AGU | |
| | Isoleucine | Threonine | Asparagine | Serine | U |
| | AUC | ACC | AAC | AGC | |
| | Isoleucine | Threonine | Asparagine | Serine | C |
| | AUA | ACA | AAA | AGA | |
| | Isoleucine | Threonine | Lysine | Arginine | A |
| | AUG (Start)** | ACG | AAG | AGG | |
| | Methionine | Threonine | Lysine | Arginine | G |
| G | GUU | GCU | GAU | GGU | |
| | Valine | Alanine | Aspartic acid | Glycine | U |
| | GUC | GCC | GAC | GGC | |
| | Valine | Alanine | Aspartic acid | Glycine | C |
| | GUA | GCA | GAA | GGA | |
| | Valine | Alanine | Glutamic acid | Glycine | A |
| | GUG | GCG | GAG | GGG | |
| | Valine | Alanine | Glutamic acid | Glycine | G |

The codon CT* is a signal codon for chain-termination.
AUG functions as a signal for chain initiation or starting point for translation.
Note that the codes are given for messenger RNA. In DNA, U will be replaced by T.

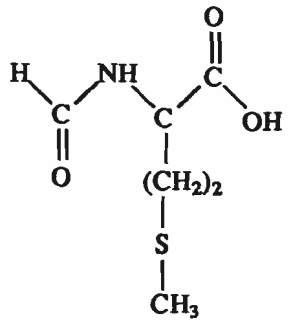
Each amino acid is usually represented by a three-letter abbreviation : Phenylalanine = Phe; Lencine = Leu; Methionine = Met; etc.

Today we know all codes for all amino acids (Table 14.1). Out of the 64 ($4^3$ = 64) possible triplets from four bases, only 61 triplets have been known to code for specific amino acids. The other three, namely, UAA, UAG and UGA, do not code for any amino acide. These function as chain terminator or stop signals. The triplet AUG (coding for methionine) also serves as the initiator codon, i.e. for starting the synthesis of a new polypeptide. Let us discuss these codons in some details.

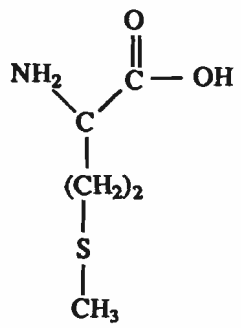
## Initiation Codons

mRNA is generally polycistronic, i.e. it carries message for the synthesis of several different proteins. It is, therefore, necessary that it should also have "start" and "stop" signals, so that message or information for each protein is well demarcated and separated from that for another proteins. As shown in Table 14.1, such signals do exist in the genetic code. The triplet AUG functions both as the codon for methionine, when it occurs in the interior of the message, and also for chain initiation when it occurs in the beginning of the message. In the latter case, it codes for N-formyl methionine and not for free methionine.

Truly functional genetic unit, gene or cistron, is one that specifies the synthesis of one polypeptide chain. Recall that some proteins are made up of a single polypeptide chain whereas others contain more than one identical or different such chains held together by noncovalent interactions (subunits). If the subunits are chemically different, more than one cistrons are required to specify the complete protein.



N-Formyl methionine (FMet)



Methionine (Met)

There are two types of tRNAs for methionine, namely $tRNA^{FMet}$ and $tRNA^{Met}$. They have the same anticodon but are specific for formyl-methionine and methionine, respectively. They combine with mRNA at AUG codon at the start and in the interior of the message, respectively. Because of this, each nascent polypeptide chain has a methionine residue at the N-terminal. In some cases, the triplet GUG functions as the start signal. In eukaryotes, the initiating methionine is not formylated.

### Termination Codons

Three triplets do not code for any amino acid. These are UAA, UAG and UGA. They are called **termination** or **stop** or **release** or **nonsense codons**. These codons are not read by any aminoacyl-tRNA (aa-tRNA) but instead are recogonized at the appropriate stage (termination) in translation by specific proteins called release factors, consequently a completed polypeptide is released. It has been observed that in some cases, the release codon works singly whereas in others two successive stop codons do the job of chain termination (Fig. 14.1).

| | |
|---|---|
| Human hemoglobin a chain mRNA | 5' AAAUACCGUUAAGCU... |
| *E. Coli* lactose repressor mRNA | 5' GAAAGCGGCGAGUGACCGCAAGGCAAUUAA. |
| MS2 "A" portein mRNA | 5' CGGCUCUCUAGAUAGAGCCCUCAA... |
| MS2 Coat protein mRNA | UCCGGCAUCUACUAAUAGACGCCG... |

**Fig. 14.1 : The bold triplet indicates the termination codons.**

## SAQ 1

Which of the following is not true of the genetic code?

a) There are three nucleotides per codon

b) Each codon codes for only one kind of amino acid

c) The codons are carried on mRNA

d) There is just one codon for each type of amino acid.

# 14.4 STRUCTURE AND ROLE OF RIBOSOME

The locus of protein biosynthesis are ribosomes. These are large complexes of protein and ribosomal RNA (rRNA) (Fig.14.2). They consist of two subunits – one "large" and one "small", whose relative sizes are generally given in terms of their sedimentation coefficients,

A ribsome is composed of two irregularly shaped subunits, which fit together snugly. The two subunits do move apart slightly during translation.

or S values. The *E. Coli* ribosomes have a particle mass of approximately $2.5 \times 10^6$ daltons and sedimentation coefficient equal to 70S and their subunits are 50S and 30S. Subunits can be further split into their constituent proteins and RNAs. The 30S subunit contains 21 different proteins and a 16S RNA molecule. The 50S subunit contians 32 different proteins and two RNA molecules, 5S RNA and 23S RNA. Eukaryotic ribosomes are larger, namely 80S. These have subunits of 40S and 60S. Small subunit has one 18S RNA molecule and 33 different protein. The larger subunit contians three RNA molecules (28S, 5.8S and 5S) and 45 different proteins. There is no functional difference between the prokaryotic ribosome and eukaryotic ribosome.

Specific ribosomal proteins are directly involved in binding mRNA and tRNA. rRNA apparently does not participate directly in these binding sites but serves as a structual polymer holding the multiplier particles in a **compact configuration**.

The dalton is a unit of mass nearly equivalent to the mass of a single hydrogen atom, the terms dalton and molecular weight are use interchangeable.

The ribosome has two binding sites for tRNA molecules, the A (aminoacyl) and P (peptidyl) sites; each extends over both subunits (see Figure 14.3). Together, they cover two neighbouring codons of mRNA. During translation, the A site on the ribosome binds an incoming aminoacyl-tRNA as specified by the codon currently occupying this site. This codon specifies the next amino acid to be added to the growing peptide chain. The P site codon is occupied by the growing chain peptidyl-tRNA. This tRNA carries the chain of amino acids that has already been synthesised. See Figure 14.4 for an illustration of the role of the A and P site in translation.

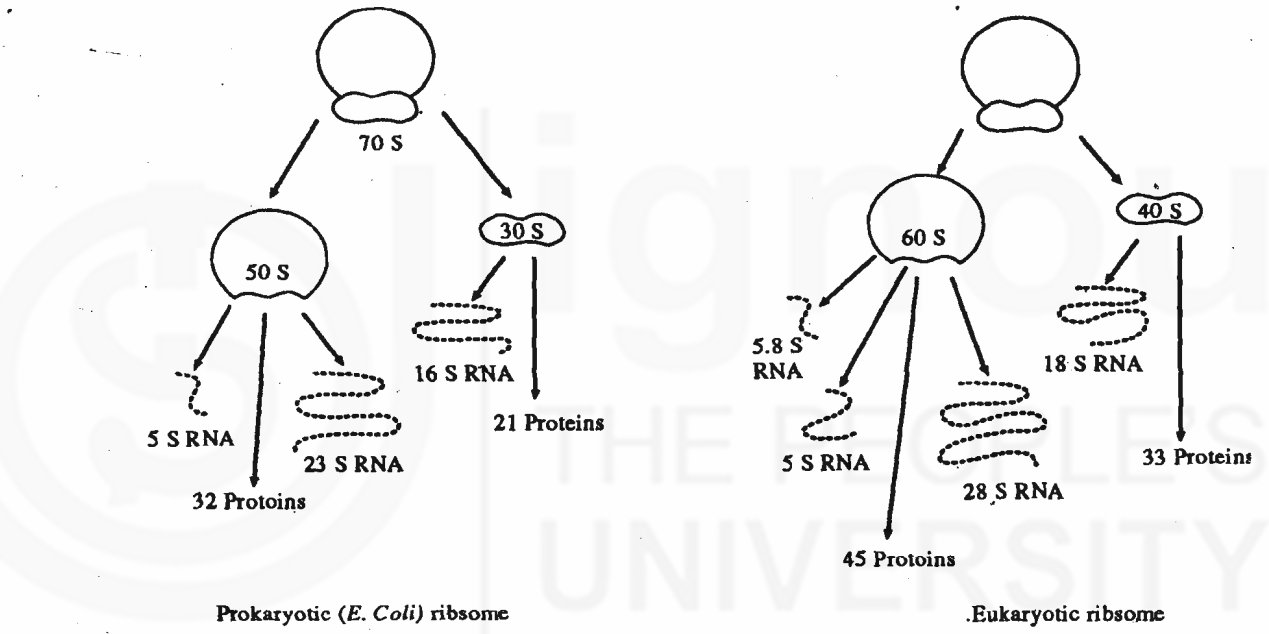



**Figure 14.2 : Ribosomal composition**

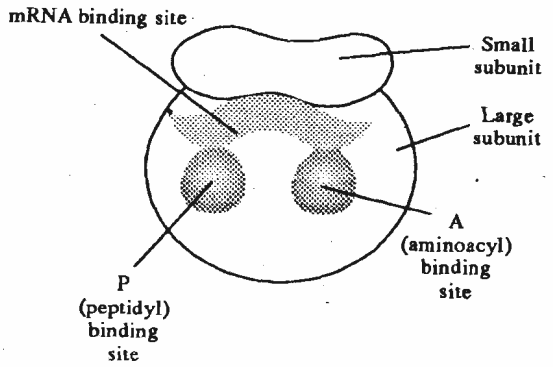



**Figure 14.3 : The binding site of a ribosoma are located mainly on the large submit.**

# 14.5 MECHANISM OF PROTEIN SYNTHESIS

We shall now describe the complex sequence of reactions in which tRNA, mRNA, ribosomes, enzymes and proteins are involved. There are four broad steps in the synthesis of a protein

i) activation of amino acid,

ii) initiation of polypeptide chain formation

iii) elongation of the polypeptide chain

iv) termination of polypeptide chain formation

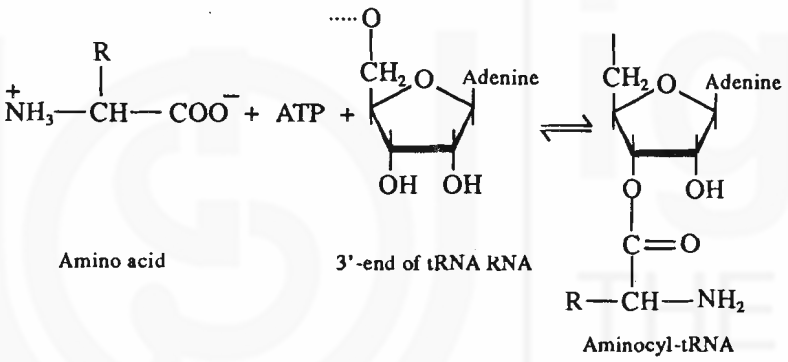
The process is summarised in Figure 14.4

The triplet base sequence at anticodon is directly related to the amino acid carried by that tRNA molecule.

## 14.5.1 Activation of Amino Acids

Thermodynamically, peptides are less stable than free amino acids. Therefore, the latter must be "activated" by expenditure of energy so that the peptide synthesis becomes thermodynamically feasible. Secondly, the amino acids have no specificity for the bases of mRNA codons therefore, they do not recognise them. In protein biosynthesis, both these "problems" are solved by attaching amino acids to their specific tRNAs. This reaction requires ATP and is referred to as activation of amino acids. The resultant amino acyl-tRNA (aa-tRNA) then participates in the protein biosynthesis.

Formation of aa-tRNA is catalysed by specific enzymes called aminoacyl-tRNA synthetases. This help in establishing an ester linkage betwen 3' - OH group of the terminal ribose of tRNA and amino acid. The overall reaction requires ATP and may be represented as:




The reaction is driven to completion by hydrolytic removal of pyrophosphate ion (PPi) catalysed by inorganic pyrophosphatase. Thus, the activation of amino acids for protein biosynthesis resembles that of fatty acids in the biosynthesis of fats (Unit 8). As in the latter, the activation of amino acids is also a two-step process with enzyme-bound aminoacyl-AMP as an intermediate.

1) Activation of the aminoacid by the enzyme (aminoacyl tRNA synthetase)

$$\text{Aminoacid} + \text{ATP} \underset{\text{synthetase}}{\overset{\text{amino acyl- tRNA}}{\rightleftharpoons}} \text{aa- AMP} + \text{PPi}$$

2) The transfer of the aminoacid from aa-AMP to the specific tRNA

$$\text{aa- AMP} + \text{tRNA} \underset{\text{synthetase}}{\overset{\text{aminoacyl- tRNA}}{\rightleftharpoons}} \text{aa- tRNA} + \text{AMP}$$

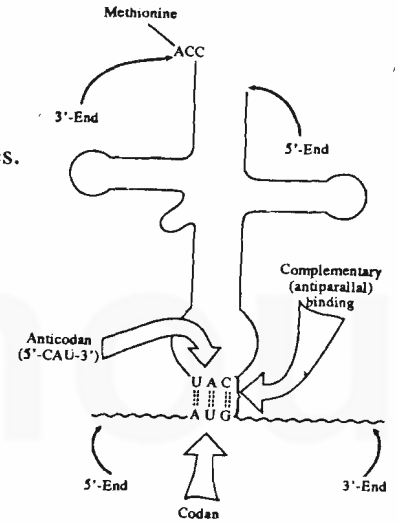
An aa-tRNA is also referred to as a "charged" tRNA.

The aa-tRNA synthetases are remarkably specific, they recognize not only the correct amino acid from the cellular amino acid pool containing amino acids with very similar structures (e.g. Ile, Val, Phe, Tyr, etc.), but also the appropriate tRNA molecule from the whole range of tRNAs. The process is strikingly error-free.

## 14.5.2 Initiation of Polypeptide Chain Formation

The activated aminoacid, i.e., aminoacyl-tRNAs diffuse to the ribosomes, which are the sites of polypeptide formation. The polypeptide synthesis never takes place in the solution but instead always requires ribosomes, that orient the aa-tRNA and the mRNA for accurate alignment in accordance with the genetic code. Methionine is invariably the peptide initiating residue in eukaryotes, and as N-formylmethionine (FMet) in prokaryotes.

In *E. coli*, initiation begins by the attachment of FMet-tRNA to the same alter submit of sibosome (305), which has the initiator proteins and mRNA molecules already bonded.




Complementary binding of the anticodon of methiongl-tRNA (CAU) to mRNA codon for methionine (AUG). Amino acid attachment sileis also shown.

The initiating Met-tRNA$^{Met}$ and F-Met-tRNA$^{fMet}$ are the only aminoacyl-tRNAs which go directly to the P site. All other aminoacyl-tRNA enter through the A site of the ribosome.

Initiation complex - an aggregate composed of mRNA, an intact ribsome, and the initial aminoacyl tRNA adduct.

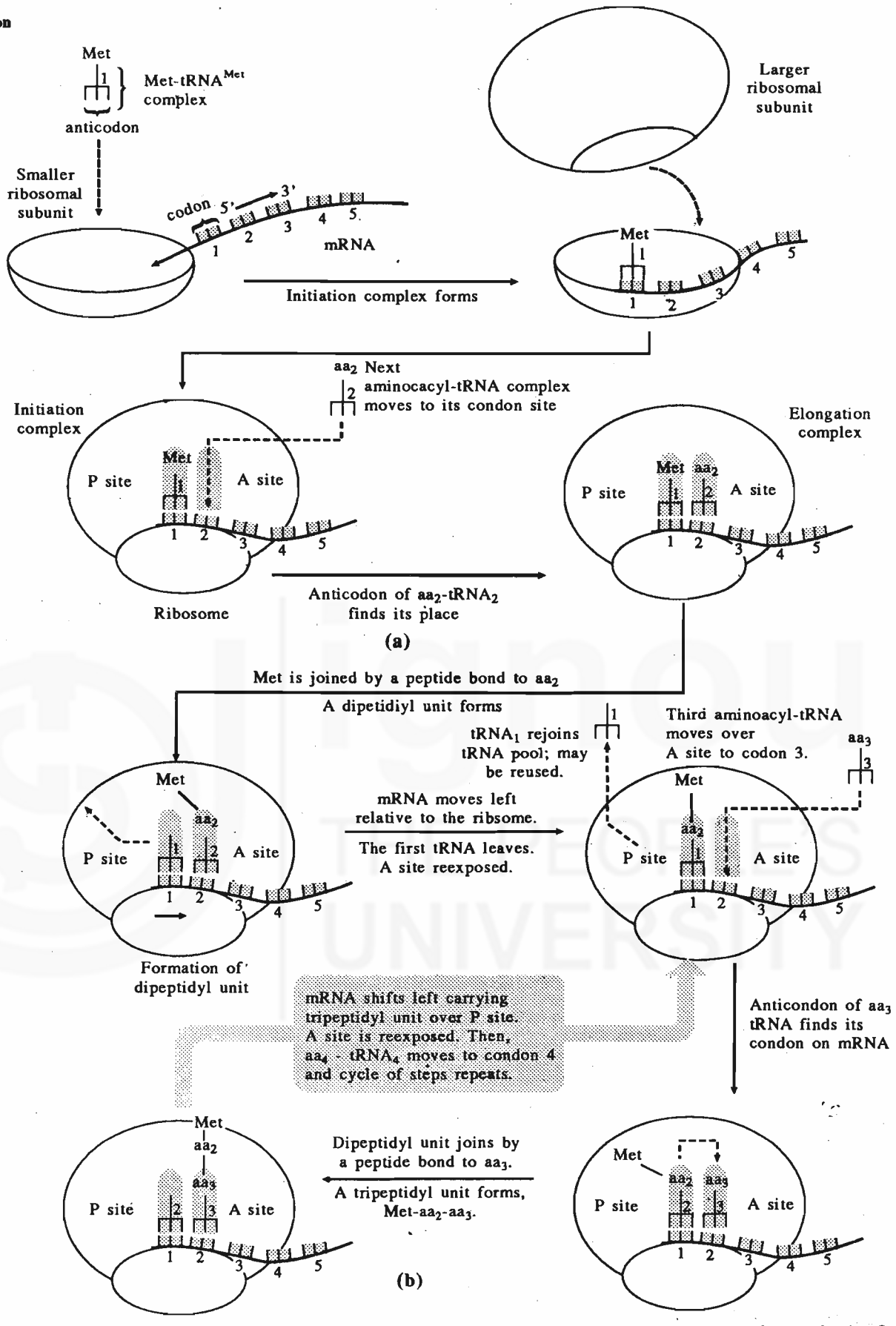


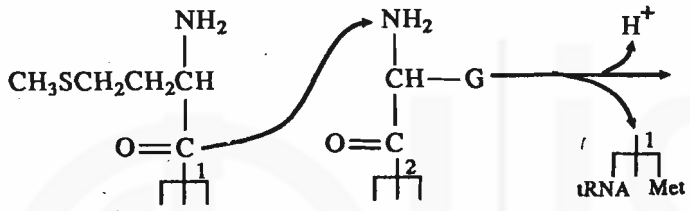

**Figure 14.4 (a) : Formation of the elongation complex at the beginning of the synthesis of a polypeptide.**

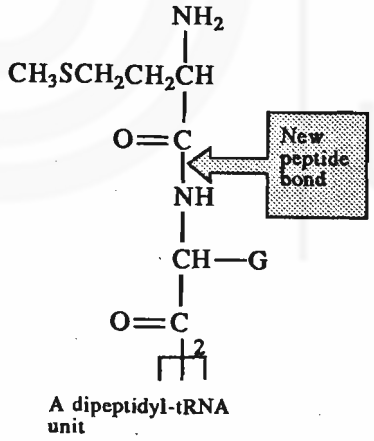
**(b) : The elongation steps in the synthesis of a polypeptide. The dipeptidly unit, Met-aa$_2$, formed by the process of (a) now has a third amino acid residue, aa$_3$, added to it.**

The formyl group is introduced and removed enzymatically. In *E. coli*, initiation begins by the attachment of FMet-tRNA to the smaller submit of ribosome (30S), which has the initiator proteins and mRNA molecule already bonded, see Fig. 14.4 a. The mRNA molecule bonds to the P site, of the ribosome. At the P site, all of the necessary enzymes for translation are present. The anticodone of the FMet-tRNA (CAU) bonds to the codon (AUG) on the mRNA. To complete the initiation stage, the larger ribosomal unit bonds to the complex and produces the initiation complex. Now the second aa-tRNA$_1$ unit, tRNA having aminoacyl group aa$_2$, binds to the matching codon at site A, i.e. aminoacyl binding site. Consequently, the aminoacyl units lie side by side and peptide bond formation (chain elongation) starts.

## 14.5.3 Elongation of the Polypeptide Chain

The first charged tRNA, i.e. tRNA$_1$ transfers its amino acid (Met) to the aa$_2$ amino acid of the second charged tRNA (tRNA$_2$), forming an amide (peptide) bond. The process is catalysed by certain enzymes, called **peptidyl transferases**. The freed tRNA (tRNA$_1$) on the P site leaves the mRNA and mRNA moves one codon over. The third charged tRNA (tRNA$_3$) finds its anticodon matching on the third codon over the A-site vacated by leftward movement of one codon. The elongation takes place by transferring the dipeptide Met-aa$_2$ to the aa$_3$ amino acid and mRNA shifts one codon leftward from A-site to P-site as the free tRNA (tRNA$_2$) dissociates. The process is repeated over and over again till the required chain length is reached.



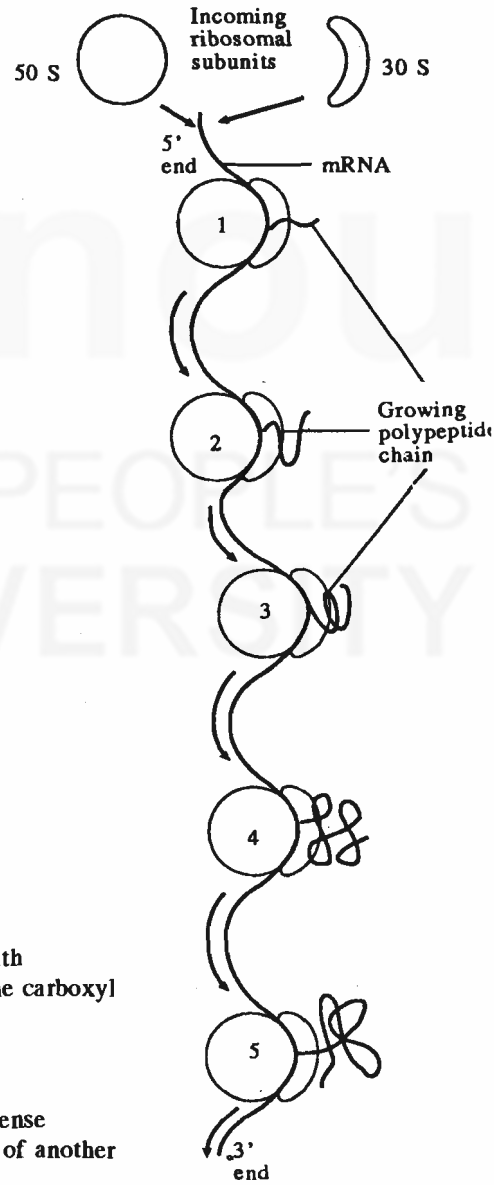

It is very important to realise at this point that the peptide chain grows stepwise with addition of a single amino acid starting with the amino terminal and ending with the carboxyl terminal. The codons of mRNA are "read" from 5'- to the 3'-end.

## 14.5.4 Termination of Polypeptide Chain Formation

Once the ribosome has moved down to one of the chain terminating codons (nonsense codons), the polypeptide is released and the ribosome can be reused for synthesis of another protein of polypeptide chain.

As the polypeptide chain leave the ribosome it assumes its unique secondary, tertiary and quaternary structures (Unit 5).

Each strand of mRNA may be used to make multiple copies of a particular protein. A number of ribosomes - as many 10 or 20 usually bind to a single strand of mRNA, each ribosome independently producing a polypeptide. The entire complex is called a polyribosome.




A polyribsome

Several details have been left out in this simplified description of protein biosythesis. For example, the role of various "initiation factors" in the formation of initial Met-tRNA$^{FMet}$-mRNA-ribosome complex has not been described. Similarly details of GTP-requiring movement of ribosome along mRNA and release factors which bring about release of completed polypeptide chain have been omitted. Interested students may consult any advanced text book of biochemistry for these details.

## SAQ 2

The elongation of polypeptide chain takes place at

a) A-site b) P-site

c) between A and P site d) both at A and P sites

## 14.6 REGULATION OF PROTEIN BIOSYNTHESIS

Requirements for various proteins in a living organism vary according to its physiological state and environments. Also, some proteins must be synthesised in larger amounts than others. Still others are synthesised mainly in response to the prevailing environments. When not required, such proteins are either not sythesised or their exceedingly small amounts are formed. It is said that the concerned gene is not expressed under these conditions.

Concentration of any protein in the cell depends on the rates of its synthesis and degradation. In this section, we will consider only the regulation of the rate of protein biosynthesis. As you must have learned by now, there are two major steps in protein biosynthesis process, namely, transcription (Unit 13) and translation (this unit). In prokaryotes, the control operates mostly at the transcriptional level. In the eukaryotes, on the other hand, the protein biosynthesis is regulated mostly at the translational level. Changes in the transcriptional patterns in eukaryotes occur during cell defferentiation.

A well known example illustrating the principle of synthesis of proteins as and when required in prokaryotes is the induction of β-galactosidase (also called lactase) of *Escherichia coli.* These bacteria grow very well in media containing glucose as the engery and carbon source. Under these conditions, the bacteria synthesise very small amounts of β-galactosidasa. If the same bacteria are transferred to a lactose containing medium in the absence of glucose, they start synthesising β-galactosidase and grow equally well. Lactose is said to be an inducer and β-galactosidase an induciable enzyme as against others, e.g. glycolytic enzymes, which are synthesised under all conditions. The latter enzymes are called constitutive enzymes. Induction of β-galactosidase is also caused by other β-galactosides. Most commonly used inducer is isopropyl thiogalactoside. Since it is not hydrolysed by the enzyme, its concentration remains constant in the growth medium. If the bacteria growing on lactose are harvested, washed and transferred to a glucose medium, the synthesis of β-galactosidase is again reduced to a minimal level. This ability of the bacteria to synthesise a set of enzymes as and when required is important for the cellular economy and provides adaptiability to grow in a variety of environments and utilise the available nutrients. At the same time, the cell does not have to synthesise such proteins which are not required. An outline of the mechanism of this switching on and off of the enzyme synthesis as per requirements is given below.

Similar to lactose, their are certain compounds which causes a decrease in the amount of certain enzymes. Such compunds are called corepressors.

Operon are composed of a group of structural genes that are transcribed as a single massage plus their associated control elements. An operon is controlled by a single repressor.

Several structural genes, i.e. genes specifying separate polypeptide chain, are found to be continuously arranged on the bacterial ribosome. Collection of these genes and their control elements, to be discussed below, is referred to as an **"Operon"**, e.g. the lac operon in the above case. The **lac operon** is responsible for the synthesis of three enzymes, namely β-galactosidase, galactoside permease and thiogalactoside transacetylase. The corresponding three structural genes are continuously located and referred to as Z, Y and A

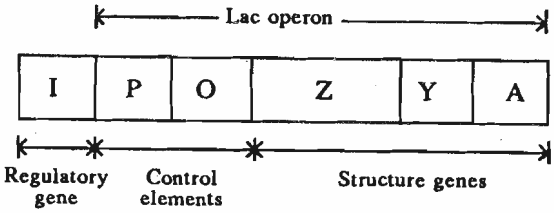



**Fig. 14.5 : Genetic map of *E.Coli* lac operon, i.e. the genes encoding proteins of lactose metabolism and the control site which regulates thei expression.**

genes, respectively. They are immediately preceded by the control elements, namely the O (operator) and P (promotor) genes. Together, these five genes constitute the lac operon which is responsible for the synthesis of proteins, mediating lactose metabolism and control thereof. Close to it lies another gene - the regulatory or the "I" gene. (Fig. 14.5)

The regulatory "I" gene produces its corresponding mRNA, called I-mRNA which on combination with ribosomes and translation causes the synthesis of a specific protein called Repressor. This protein has a high affinity for, and binds specifically to the O gene. The binding prevents transcription of the lac operon. Thus, the synthesis of the lactose metabolism is prevented (Fig. 14.6 a). This situation prevails in the absence of an inducer, e.g. when the bacteria are growing in glucose medium. When an inducer is present, it binds specifically to the repressor to give rise to an inducer-repressor complex. The latter has no affinity for the O gene. In the absence of repressor binding to the operator (O gene), the structual genes are transcribed to give lac-mRNA and regulating in the synthesis of specific proteins (Fig. 14.6 b).

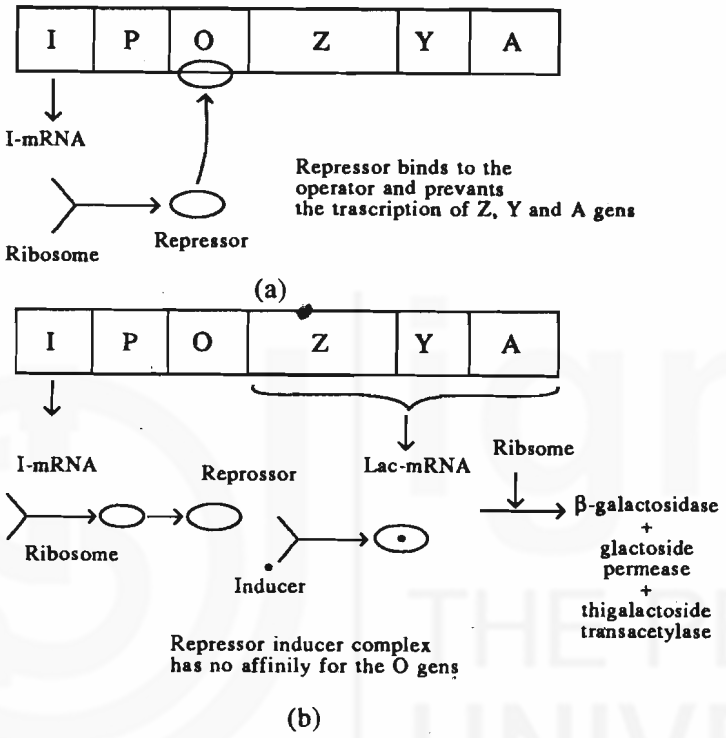



**Fig. 14.6 : Expression of lac-operon of E. Coil**
**(a) in the absence of inducer and**
**(b) in the presence of inducer.**

Note that the inducer-repressor interaction is reversible.

$$\text{Inducer} + \text{Repressor} \rightleftharpoons \text{Inducer-repressor complex}$$

If the concentration of inducer decreases, the complex dissociates. Free repressor is able to bind to the operator and switch off transcription of the lac operon. The bacterial mRNAs are short lived, average life span being 2-3 min. Therefore, the existing lac-mRNA is rapidly degraded and β-galactosidase synthesis is stopped in a couple of minutes.

Regulation of protein biosynthesis in eukaryotes is more complicated. As mentioned above, it operates at the translation level. It involves reversible activation/deactivation of initiation factors which are required for starting the synthesis of a new polypeptide chain. This regulation is achieved by phosphorylation and dephosphorylation of the initiation factor, in a similar manner as described under regulation of enzyme activity by reversible covalent modification of the enzyme protein. Another mechanism, which operates mostly at embryonic stage, involves "masking" of mRNA by associated with some protein and consequent stoppage of its translation.

# 14.7 ANTIBIOTICS INHIBITION OF PROTEIN BIOSYNTHESIS

The protein biosynthesis is the integral part of the life of any organism. In a way if protein synthesis is some how stopped the organism cannot sustain life any longer. This fact has been exploited in some antibiotics ation.

An antibiotic is defined as a compound produced by a micro-organism that inhibits the growth and metabolism of other micro-organism at small concentration. Antibiotics have been widely used both clinically and as research reagents for unravelling the detail of protein synthesis and DNA and RNA synthesis. Table 14.2 lists a few out of hundreds of antibotics that prohibit protein synthesis in bacteria. Some of them have only limited clinical usefulness because they also inhibit the growth of animal cells and hence are toxic to both bacterium and host.

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| Erythromycin | Binds to the 50S subunit and inhibits translocation (procaryotes) |
| Puromycin* | Causes premature chain termination by acting as an analog of aminoacyl-tRNA (procaryotes and eucaryotes) |

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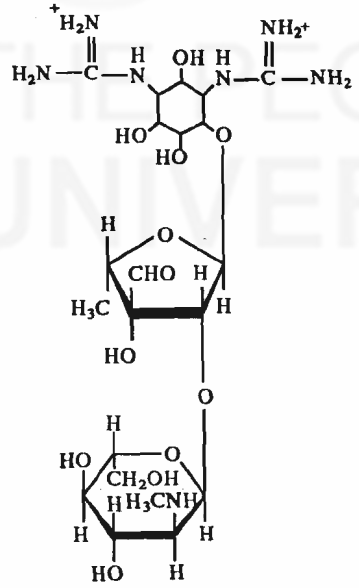


Streptomycin

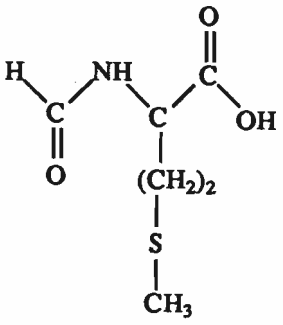
Streptomycin, for example interferes with the binding of Met-tRNA to the P site and thereby inhibits the initiation of synthesis of a polypeptide chain. It also leads to a misreading of mRNA. This brings about inhibition of initiation and elongation steps. The frequent error incorporated is the insertion of isoleucine (AUU) in place of phenylalanine (UUU).

Tetracycline too inhibits the aminoacyl - tRNA binding to the ribosome inhibiting the polysome formation and protein synthesis.

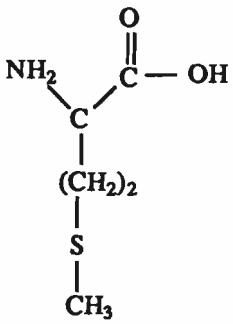
## Initiation Codons

mRNA is generally polycistronic, i.e. it carries message for the synthesis of several different proteins. It is, therefore, necessary that it should also have "start" and "stop" signals, so that message or information for each protein is well demarcated and separated from that for another proteins. As shown in Table 14.1, such signals do exist in the genetic code. The triplet AUG functions both as the codon for methionine, when it occurs in the interior of the message, and also for chain initiation when it occurs in the beginning of the message. In the latter case, it codes for N-formyl methionine and not for free methionine.

Truly functional genetic unit, gene or cistron, is one that specifies the synthesis of one polypeptide chain. Recall that some proteins are made up of a single polypeptide chain whereas others contain more than one identical or different such chains held together by noncovalent interactions (subunits). If the subunits are chemically different, more than one cistrons are required to specify the complete protein.



N-Formyl methionine (FMet)



Methionine (Met)

There are two types of tRNAs for methionine, namely $tRNA^{FMet}$ and $tRNA^{Met}$. They have the same anticodon but are specific for formyl-methionine and methionine, respectively. They combine with mRNA at AUG codon at the start and in the interior of the message, respectively. Because of this, each nascent polypeptide chain has a methionine residue at the N-terminal. In some cases, the triplet GUG functions as the start signal. In eukaryotes, the initiating methionine is not formylated.

### Termination Codons

Three triplets do not code for any amino acid. These are UAA, UAG and UGA. They are called **termination** or **stop** or **release** or **nonsense codons**. These codons are not read by any aminoacyl-tRNA (aa-tRNA) but instead are recogonized at the appropriate stage (termination) in translation by specific proteins called release factors, consequently a completed polypeptide is released. It has been observed that in some cases, the release codon works singly whereas in others two successive stop codons do the job of chain termination (Fig. 14.1).

| | |
|---|---|
| Human hemoglobin a chain mRNA | 5' AAAUACCGUUAAGCU... |
| *E. Coli* lactose repressor mRNA | 5' GAAAGCGGCGAGUGACCGCAAGGCAAUUAA. |
| MS2 "A" portein mRNA | 5' CGGCUCUCUAGAUAGAGCCCUCAA... |
| MS2 Coat protein mRNA | UCCGGCAUCUACUAAUAGACGCCG... |

**Fig. 14.1 : The bold triplet indicates the termination codons.**

## SAQ 1

Which of the following is not true of the genetic code?

a) There are three nucleotides per codon

b) Each codon codes for only one kind of amino acid

c) The codons are carried on mRNA

d) There is just one codon for each type of amino acid.

# 14.4 STRUCTURE AND ROLE OF RIBOSOME

The locus of protein biosynthesis are ribosomes. These are large complexes of protein and ribosomal RNA (rRNA) (Fig.14.2). They consist of two subunits – one "large" and one "small", whose relative sizes are generally given in terms of their sedimentation coefficients,

A ribsome is composed of two irregularly shaped subunits, which fit together snugly. The two subunits do move apart slightly during translation.

or S values. The *E. Coli* ribosomes have a particle mass of approximately $2.5 \times 10^6$ daltons and sedimentation coefficient equal to 70S and their subunits are 50S and 30S. Subunits can be further split into their constituent proteins and RNAs. The 30S subunit contains 21 different proteins and a 16S RNA molecule. The 50S subunit contians 32 different proteins and two RNA molecules, 5S RNA and 23S RNA. Eukaryotic ribosomes are larger, namely 80S. These have subunits of 40S and 60S. Small subunit has one 18S RNA molecule and 33 different protein. The larger subunit contians three RNA molecules (28S, 5.8S and 5S) and 45 different proteins. There is no functional difference between the prokaryotic ribosome and eukaryotic ribosome.

Specific ribosomal proteins are directly involved in binding mRNA and tRNA. rRNA apparently does not participate directly in these binding sites but serves as a structual polymer holding the multiplier particles in a **compact configuration.**

The dalton is a unit of mass nearlyequivalent to the mass of a single hydrogen atom, the terms dalton and molecular weight are use interchangeable.

The ribosome has two binding sites for tRNA molecules, the A (aminoacyl) and P (peptidyl) sites; each extends over both subunits (see Figure 14.3). Together, they cover two neighbouring codons of mRNA. During translation, the A site on the ribosome binds an incoming aminoacyl-tRNA as specified by the codon currently occupying this site. This codon specifies the next amino acid to be added to the growing peptide chain. The P site codon is occupied by the growing chain peptidyl-tRNA. This tRNA carries the chain of amino acids that has already been synthesised. See Figure 14.4 for an illustration of the role of the A and P site in translation.

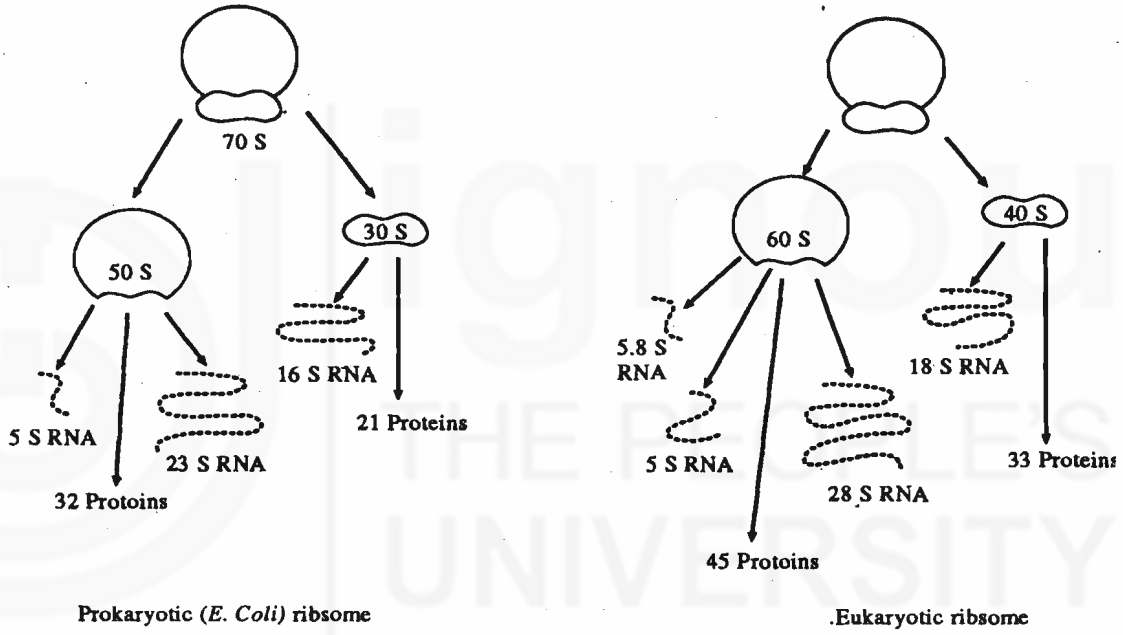



**Figure 14.2 : Ribosomal composition**

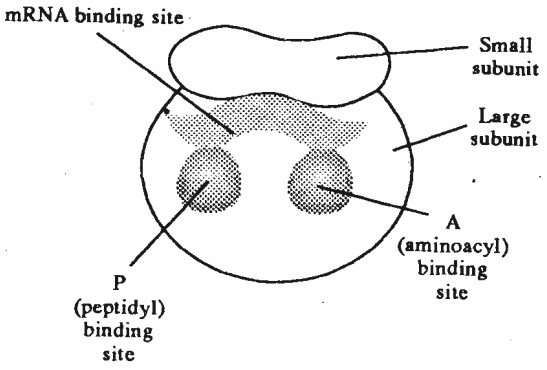



**Figure 14.3 : The binding site of a ribosoma are located mainly on the large submit.**

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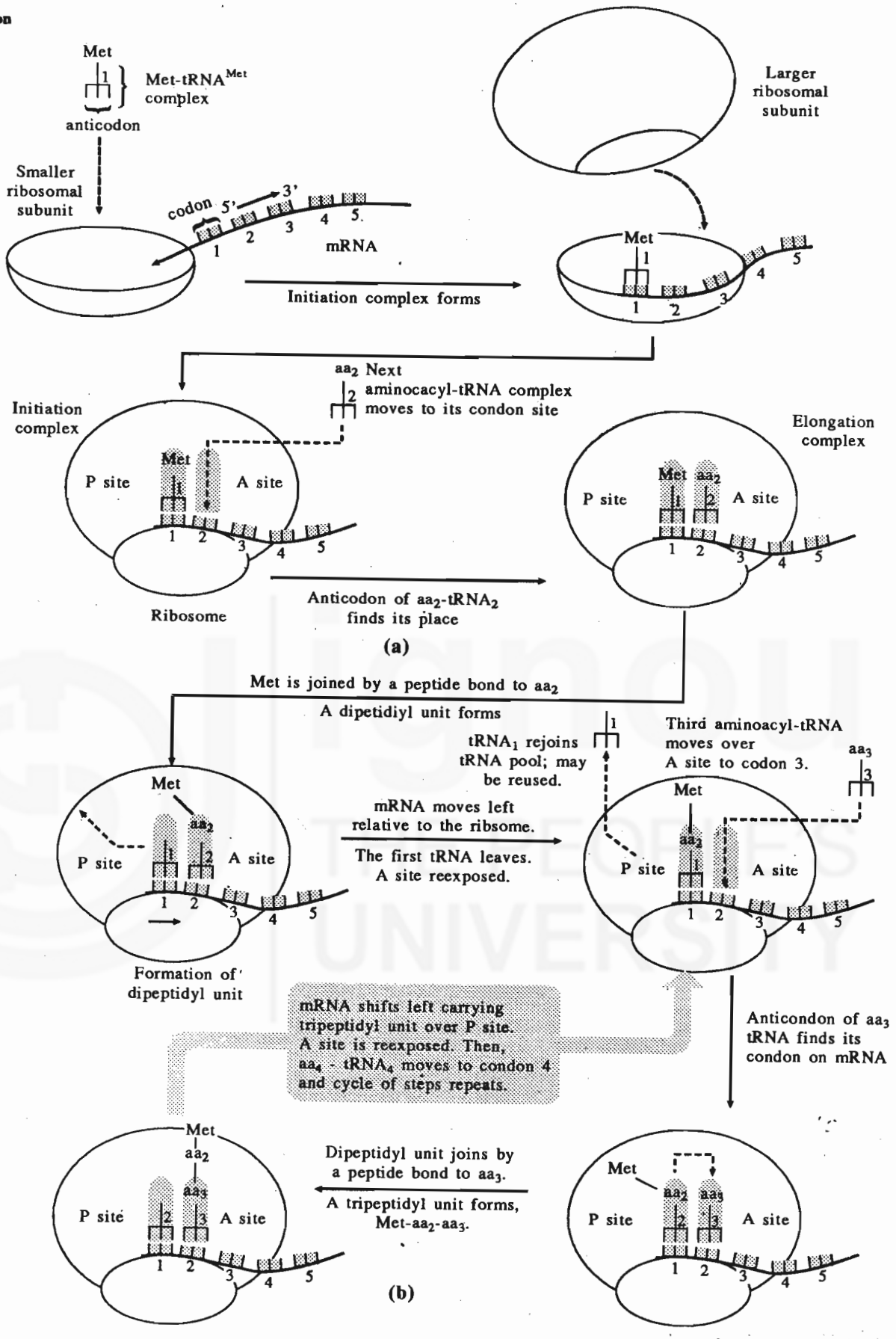


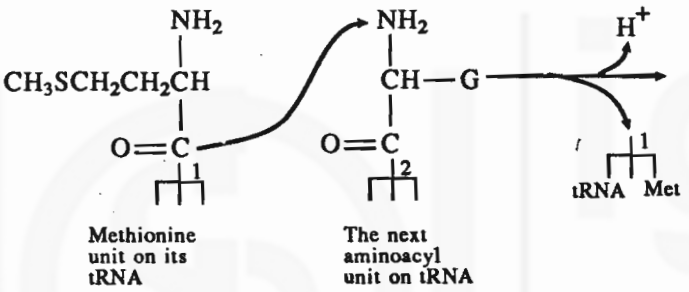

**Figure 14.4 (a) : Formation of the elongation complex at the beginning of the synthesis of a polypeptide.**

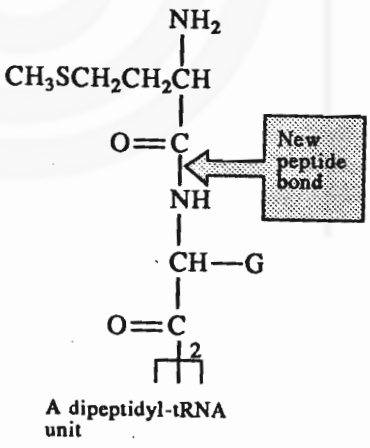
**(b) : The elongation steps in the synthesis of a polypeptide. The dipeptidly unit, Met-aa$_2$, formed by the process of (a) now has a third amino acid residue, aa$_3$, added to it.**

The formyl group is introduced and removed enzymatically. In *E. coli*, initiation begins by the attachment of FMet-tRNA to the smaller submit of ribosome (30S), which has the initiator proteins and mRNA molecule already bonded, see Fig. 14.4 a. The mRNA molecule bonds to the P site, of the ribosome. At the P site, all of the necessary enzymes for translation are present. The anticodone of the FMet-tRNA (CAU) bonds to the codon (AUG) on the mRNA. To complete the initiation stage, the larger ribosomal unit bonds to the complex and produces the initiation complex. Now the second aa-$tRNA_1$ unit, tRNA having aminoacyl group $aa_2$, binds to the matching codon at site A, i.e. aminoacyl binding site. Consequently, the aminoacyl units lie side by side and peptide bond formation (chain elongation) starts.

## 14.5.3 Elongation of the Polypeptide Chain

The first charged tRNA, i.e. $tRNA_1$ transfers its amino acid (Met) to the $aa_2$ amino acid of the second charged tRNA ($tRNA_2$), forming an amide (peptide) bond. The process is catalysed by certain enzymes, called **peptidyl transferases**. The freed tRNA ($tRNA_1$) on the P site leaves the mRNA and mRNA moves one codon over. The third charged tRNA ($tRNA_3$) finds its anticodon matching on the third codon over the A-site vacated by leftward movement of one codon. The elongation takes place by transferring the dipeptide Met-$aa_2$ to the $aa_3$ amino acid and mRNA shifts one codon leftward from A-site to P-site as the free tRNA ($tRNA_2$) dissociates. The process is repeated over and over again till the required chain length is reached.



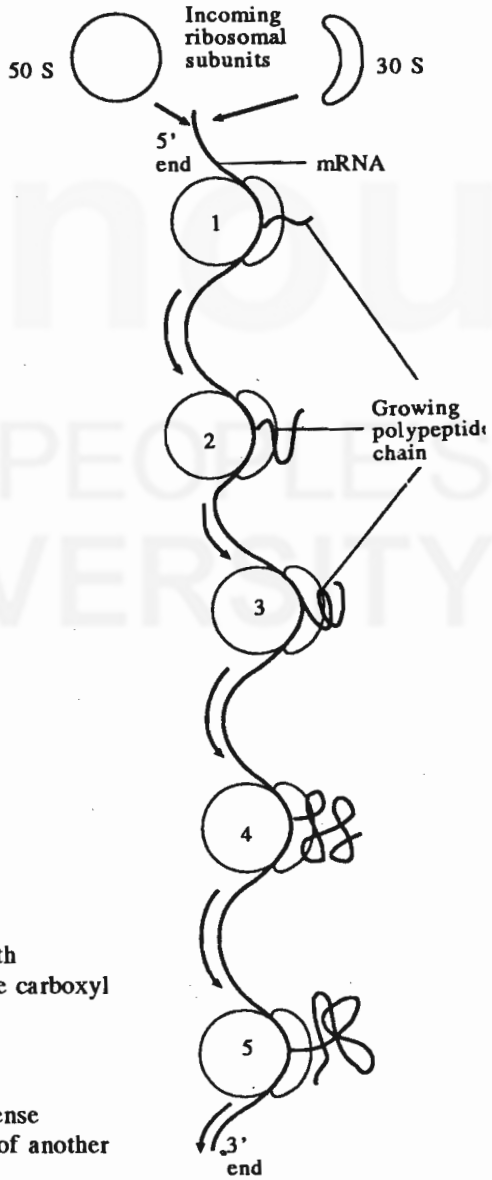

It is very important to realise at this point that the peptide chain grows stepwise with addition of a single amino acid starting with the amino terminal and ending with the carboxyl terminal. The codons of mRNA are "read" from 5′- to the 3′-end.

## 14.5.4 Termination of Polypeptide Chain Formation

Once the ribosome has moved down to one of the chain terminating codons (nonsense codons), the polypeptide is released and the ribosome can be reused for synthesis of another protein of polypeptide chain.

As the polypeptide chain leave the ribosome it assumes its unique secondary, tertiary and quaternary structures (Unit 5).

Each strand of mRNA may be used to make multiple copies of a particular protein. A number of ribosomes - as many 10 or 20 usually bind to a single strand of mRNA, each ribosome independently producing a polypeptide. The entire complex is called a polyribosome.




A polyribsome

Several details have been left out in this simplified description of protein biosythesis. For example, the role of various "initiation factors" in the formation of initial Met-tRNA$^{FMet}$-mRNA-ribosome complex has not been described. Similarly details of GTP-requiring movement of ribosome along mRNA and release factors which bring about release of completed polypeptide chain have been omitted. Interested students may consult any advanced text book of biochemistry for these details.

## SAQ 2

The elongation of polypeptide chain takes place at

a) A-site b) P-site

c) between A and P site d) both at A and P sites

## 14.6 REGULATION OF PROTEIN BIOSYNTHESIS

Requirements for various proteins in a living organism vary according to its physiological state and environments. Also, some proteins must be synthesised in larger amounts than others. Still others are synthesised mainly in response to the prevailing environments. When not required, such proteins are either not sythesised or their exceedingly small amounts are formed. It is said that the concerned gene is not expressed under these conditions.

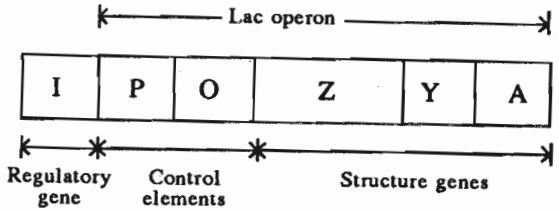
Concentration of any protein in the cell depends on the rates of its synthesis and degradation. In this section, we will consider only the regulation of the rate of protein biosynthesis. As you must have learned by now, there are two major steps in protein biosynthesis process, namely, transcription (Unit 13) and translation (this unit). In prokaryotes, the control operates mostly at the transcriptional level. In the eukaryotes, on the other hand, the protein biosynthesis is regulated mostly at the translational level. Changes in the transcriptional patterns in eukaryotes occur during cell defferentiation.

A well known example illustrating the principle of synthesis of proteins as and when required in prokaryotes is the induction of β-galactosidase (also called lactase) of *Escherichia coli.* These bacteria grow very well in media containing glucose as the engery and carbon source. Under these conditions, the bacteria synthesise very small amounts of β-galactosidasa. If the same bacteria are transferred to a lactose containing medium in the absence of glucose, they start synthesising β-galactosidase and grow equally well. Lactose is said to be an inducer and β-galactosidase an induciable enzyme as against others, e.g. glycolytic enzymes, which are synthesised under all conditions. The latter enzymes are called constitutive enzymes. Induction of β-galactosidase is also caused by other β-galactosides. Most commonly used inducer is isopropyl thiogalactoside. Since it is not hydrolysed by the enzyme, its concentration remains constant in the growth medium. If the bacteria growing on lactose are harvested, washed and transferred to a glucose medium, the synthesis of β-galactosidase is again reduced to a minimal level. This ability of the bacteria to synthesise a set of enzymes as and when required is important for the cellular economy and provides adaptiability to grow in a variety of environments and utilise the available nutrients. At the same time, the cell does not have to synthesise such proteins which are not required. An outline of the mechanism of this switching on and off of the enzyme synthesis as per requirements is given below.

Similar to lactose, their are certain compounds which causes a decrease in the amount of certain enzymes. Such compunds are called corepressors.

Operon are composed of a group of structural genes that are transcribed as a single massage plus their associated control elements. An operon is controlled by a single repressor.

Several structural genes, i.e. genes specifying separate polypeptide chain, are found to be continuously arranged on the bacterial ribosome. Collection of these genes and their control elements, to be discussed below, is referred to as an "**Operon**", e.g. the lac operon in the above case. The **lac operon** is responsible for the synthesis of three enzymes, namely β-galactosidase, galactoside permease and thiogalactoside transacetylase. The corresponding three structural genes are continuously located and referred to as Z, Y and A

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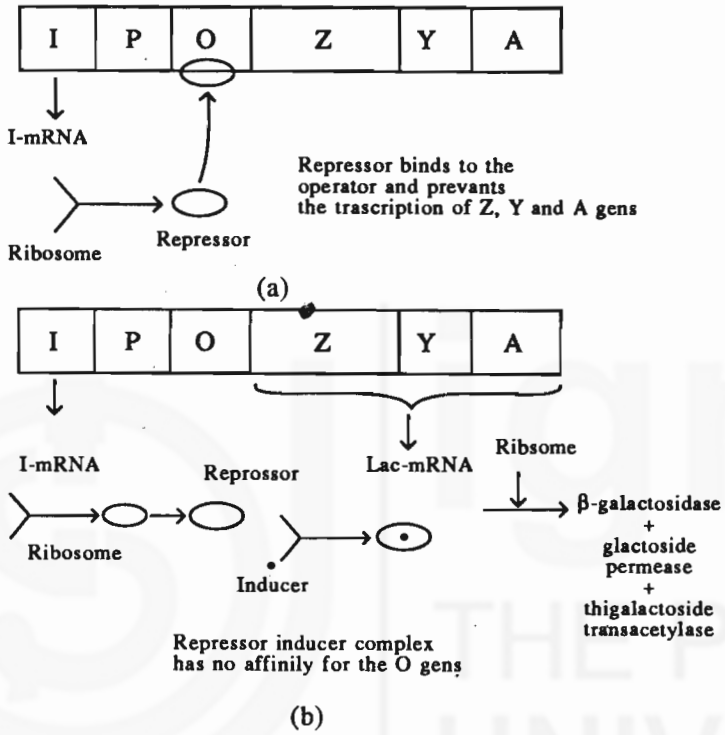


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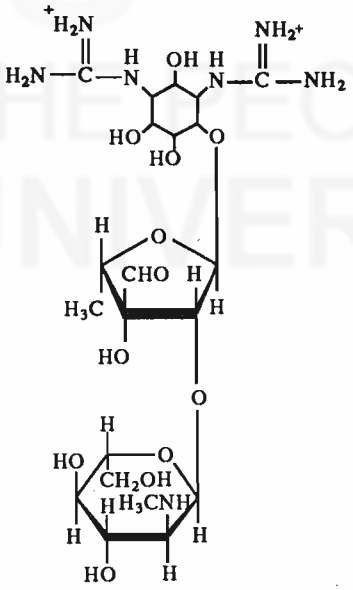

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Tetracycline too inhibits the aminoacyl - tRNA binding to the ribosome inhibiting the polysome formation and protein synthesis.

**SAQ 3**

Streptomycin acts by

a) disrupting mRNA synthesis

b) deactivating tRNAs

c) inhibiting initiation and causing misreading of mRNA

d) activating the enzymes

## 14.8 CANCER BIOCHEMISTRY

Normally, the development and growth of body cells is vigorously controlled. The cycle of cell multiplication begins when a cell is "born" (i.e. when its present cells divides into two identical cells) and is completed when it divides into two daughter cells. This requires doubling of each cellular constituent, including its DNA inside and outside its nucleus (e.g. in mitochondria and chloroplasts). Duplication of cellular constituents does not take place uniformally throughout its life span, but take place at different stages (also called phases of cell growth). First stage in the life of the cell is called $G_1$ (gap 1), during which many biomolecules including enzymes ae formed. This is followed by S-phase (S for synthesis) when DNA is duplicated. Another segment $G_2$ (gap 2) separates the S-phase from mitosis or the M-phase. Separation of the DNA copies and cell division takes place in the M-phase, after which another cycle of cell growth starts. This is illustrated in Fig. 14.7. Normal cells can enter a resting state $G_0$ from $G_1$ when further growth or multiplication is not required. They can revert to $G_1$ when growth is desired.

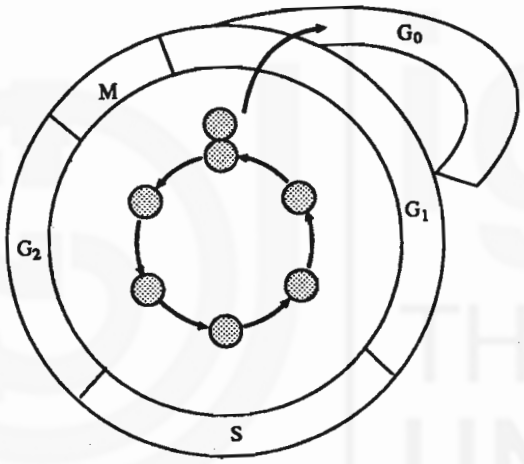



**Fig. 14.7 : Different phases of growth and multiplication of a normal cell**

Most adult body cells remains in $G_0$ phase. It is not exactly known what makes a cell go into $G_0$ phase or revert to $G_1$ phase. One of the signals apparently involves cell-cell contact. For example, if normal vertebrate cells are grown in tissue culture (grown in container) they adhere to the container surface and cover it with a single layer of cells. They stop growing when the container surface is fully covered (Fig. 14.8). Normal cells do not pile on top of each other.

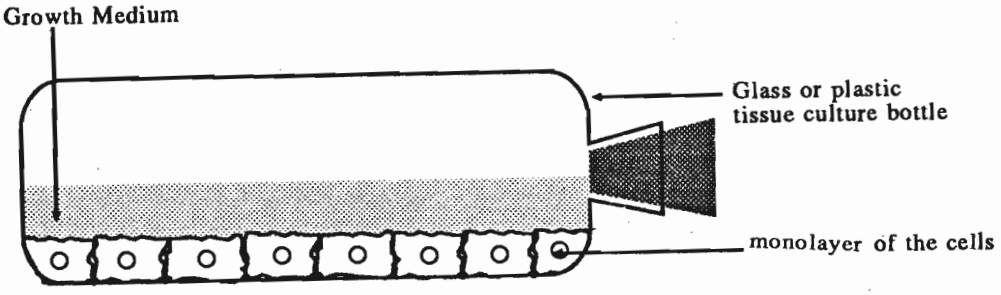



**Fig. 14.8 : Growth of normal vertebrated cells in tissue culture**

Occasionally, some cells lose their developmental controls and continue to grow and multiply in an unregulated manner. In tissue culture, such cells grow ever after the container surface is fully covered. They pile upon each other (Fig. 14.9)

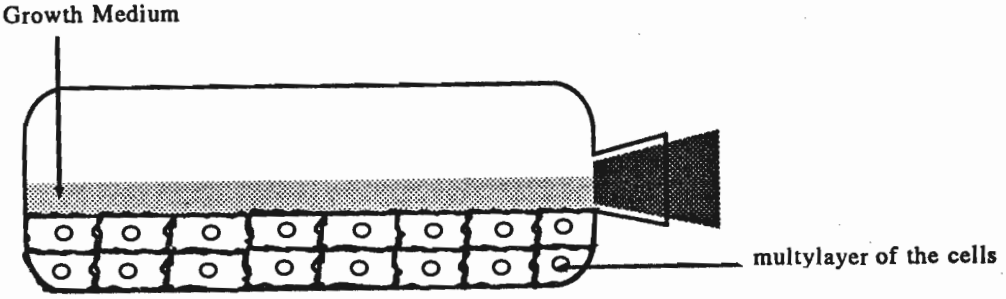
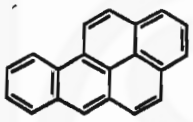



**Fig. 14.9 : Growth of altered cells which have lost developmental control, in tissue culture.**

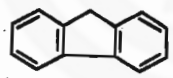
Loss of developmental control causes excessive multiplilcation of the altered cells and growth of a tumour, i.e. abnormal growth of cells. Tumours are of two types:

1) Benign ('kind') tumour tends to grow slowly, and its cells stay together. Benign tumours are often encapsulated in a layer of connective tissue. Warts and moles are common examples. These are rarely life threatening unless they grow in restricted space, e.g. brain, or secrete excessive amounts of certain hormones.

2) Malignant('wicked') tumours or cancers grow in an invasive manner and are not encapsulated. Consequently, some of these cells may escape from the tumour to colonise other sites in the body to give rise to secondary tumors (metastasis). Malignant tumours are invariably life-threatening if left untreated.



Benzpyrene



cetylaminofluorene

About one hundred different types of human cancers have been described. A common feature of all of these is uncontrolled growth. The cells have been altered or transformed in some ways which are not fully understood. Cancer cells are inmortal in the sense that they can be grown in tissue culture flasks to infinity by transfering to containers containing fresh growth medium. This is in contrast to the normal cells which die after some transfers from one flask to the other. Thus, immortality and uncontrolled growth are characteristic features of cancer cells. Note that cancer is a cellular disease and not a disease of the tissue or organ where the tumour may appear. Also cancer is a disease of multi-cellular species only. Cancer is known to be produced by a variety of agents, called carcinogens. These may be ionising radiations like ultraviolet or X-rays (physical carcinogens), chemical substances e.g., polycylic aromtic compunds, e.g. benzpyrene and acetylamino fluorene (chemical carcinogens) or viruses.

Almost each malignant tumour arises from a single transformed cell. Transformation may be caused by any one or a combination of various carcinogens. Considering that the human body has around $10^{14}$ cells, transformation must be rare occurrence indeed. It appears that production of a transformed cell requires that it or its ancestors must have undergone several independent carcinogeic changes. These changes may accumulate in a cell thus increasing the probability of appearance of cancer with advancing age. This is actually observed. For example, in U.S.A where more reliable statistical data are avilable number of deaths from cancer per year increase from less than one per million population at 22 years age to about a hundred per million population at 62 years age. Further, the transformed cells exhibit some marked changes in their chromosomes. Thus, the transformation from normal to malilgnant cells can be traced to changes in cell DNA (mutation).

Ionising radiations may damage the cellular DNA by bringing about chemical alteration(s) in its bases. The chemical carcinogens may combine with DNA or insert between its bases. This will produce errors in DNA replication and also alter reading frame of the messenger RNA and thus produce altered proteins.

Actions of chemical carcinogens may be promoted by some other non-carcinogenic chemicals. They latter by themselves do not produce cancer. This was demonstrated by various experiments on laboratory animals. For example, when rats were fed small (essentially non-carcinogenic) doses of acetylamino fluorene for three weeks, only a small percentage of the animals developed tumours. Similarly, feeding the sedative phenobarbital to rats produced no tumours at all. If the rats were first fed small doses of acetylamino fluorene for three weeks and latter phenobarbital only (no acetylamino fluorene), many liver

tumours were observed. Many chemicals in our environments, e.g. cigaratte smoke, may contain such promoting factors. Further, some of the so called chemical carcinogens may be harmless by themselves but are converted inot active carcinogens as a result of cellular metabolism.

Studies on virus-produced cancers have provided some interesting information. An example in Rons sarcoma virus, which produces sarcoma (i.e. malignant tumour in connective tissue) in chicken. It is a "retrovirus" or an "RNA virus". It carries its genetic information on RNA. In the host, it is copied on a newly synthesised DNA (reverse transcription, hence the name retro virus) before a messenger RNA is synthesised. It has a small genome, consisting of four genes only. Three of these code for viral proteins required to reproduce more virus particles. The fourth gene is involved in cell transformation. It is referred to as V-scr (virus sarcome gene). Hybridisation experiments have shown that V-src has considerable homology (identity of base sequence) with a normal cellular gene of the host. The latter has been refferred to as C-src (C for cellular). The gene V-src has been referred to as an "oncogene" i.e. one which mediates host cell transformation and C-src is called "proto-oncogene", i.e. normal cellular analogue of the oncogene.

Cancer causing genes are called oncogene

Viral oncogene products, i.e. proteins synthesised according to its genetic information, mimic the effect of normal polypeptide growth factors hormones of the host. This may possibly be related to the uncontrolled growth of the cancer cells. However, the exact mechanism of transformation is not yet known.

## SAQ 4

Fill in the blanks :

a) The.....division and growth of cells result in cancer.

b) Compounds causing cancer are termed.....

c) Chemical carcinogens may combine with ..... or ..... between its bases.

## 14.9 SUMMARY

The genetic code is inscribed on the mRNA in form of triplet of bases. Each code is unique and codes for one amino acid only. The genetic code is degenerate and non-overlapping. There is a codon which initiate the polypeptide synthesis process (AUG). Other than the initiation codon, there are three other codons UAA, UAG and UGA. They are often referred to as nonsense or release or termination codons.

Aminoacid does not have affinity towards the RNA and are required to be activated. The activation is achieved by the complexation of the amino acid with the specific tRNA, the process is catalysed by a set of enzymes, very specific and remarkably efficient called aminoacyl synthetase. The engery for the process of activation is provided by ATP.

In protein synthesis, the ribosomes plays the vital role of site for protein synthesis. They also provide site for binding the mRNA. The tRNA having a closer leaf like structure carries the anticodons complementary to the codons on the mRNA. It brings the amino acid to the site of polypeptide synthesis. The process is remarkably error free and aminoacids are attached to the processing polypeptide chain in the sequence coded by the codons on the mRNA. The terminating codons couse the chain termination and the completed polypeptide is released. It has been established that smaller polypeptides are synthesised in translation and these then unite to give the resultant proteins.

The process of protein synthesis is regulated by a number of factors in order that proteins are synthesilsed in required amounts. In prokaryotes, the control operates mostly at the transriptional level. In the eukaryotes, on the other hands, the protein biosynthesis is regulated mostly at the translational level.

There are some anitibiotics, which inhibit prokaryotic (bacteria) protein synthesis.

Abnormal growth of cells is called tumours. They are two tyes. (i) Benign tumours are often encapsulated in a layer of connective tissues. They are rarely life threatening. Malignant tumours or cancers grow in an invasive manner and are not encapsulated. They are invariably life threatening if left untreated. Cancer is known to be produced by a variety of agents, called carcinogens. These may be radiations like UV or X-rays (physical carcinogens), chemical substances i.e., polycyclic aromatic compounds (chemical carcinogens) or viruses.

## 14.10 TERMINAL QUESTIONS

1) What is the significance of genetic code?

2) Explain briefly, what do you understand from the terms codons and anticodons.

3) Illustrate the importance of initiation and termination codons.

4) Give a brief account of the steps involved in protein biosynthesis.

5) Explain the terms

a) operons b) operators

c) inducer

6) "Antibiotics interfere in the protein biosynthesis in prokaryotes". Explain with illustrations.

7) What do you understand by the terms:

a) cancer b) carcinogen

## 14.11 ANSWERS

**Self Assesment Questions**

1) d) - One amino acid may be coded by more than one triplet of bases.

2) a)

3) c)

4) a) uncontrolled ; b) carcinogenic

c) DNA, insert

**Terminal Questions**

1) See Section 14.2

2) Codons : The genetic code is a dictionary that gives the correspondence between a sequence of bases (nucleotide bases) and a sequence of amino acids. The individual words in the code are each composed of three nucleotide bases. These genetic words are called codons.

Anticodons : The selection of a particular amino acid from the pool of cellular amino acids is dicted by set of three bases in the tRNA which are called anticodons and are complementary to the codons on the mRNA.

3) Refer to subsection 14.2.1 & 14.2.2.

4) i) Charged tRNAs i.e. aminoacyl-tRNAs diffuse to the ribosome.
ii) mRNA attaches to a ribosome.
iii) Changed tRNA brings the first amino acid (FMet) and binds to the first start codon mRNA on the ribosome surface at P site.
iv) Another charged tRNA brings the second amino acid ($aa_2$) and binds to the second codon of mRNA at A site of ribosome.
v) The first amino acid is joined to the second amino acid on the second tRNA.
vi) The empty first tRNA leaves and the mRNA and second tRNA move on the ribosome, bringing the third codon into A site on the ribosome.
vii) The charged tRNA bearing the amino acid specified by the third codon binds to the A site.
viii) Steps 5 to 7 are repeated with each amino acid until a "Stop" codon on the mRNA is reached.

5) a) Operon : A set of functionally-related structural genes toghther with a promoter and an adjacent operator which controls their activity. The genes are transcribed as a single mRNA unit.

b) Operator : The site in an operon to which a regulatory protein binds.

c) Inducer : It has been found that addition of certain substance into the growth medium cause an increase in the amount of the enzyme, such compounds or substrates are called inducers.

6) Refer to Section 14.5

7) a) Cancer : It is uncontrolled growth and division of certain cells. The cancerous cells lose their ability to control their growth and division, the cells divide at times and sites, where they should not.

b) Carcingoens : Anything that may lead to cancer is called carcinogens, Examples :

Radiation like UV or X-rays (physical carcinogens, chemical substances i.e., polycyclic aromatic compounds (chemical carcinogens) and viruses.

# UNIT 15 BIOTECHNOLOGY

## Structure



## 15.1 INTRODUCTION

So far in this course we have described the various types of biomolecules present in living organisms, their chemistry and involvement in metabolism and generation of energy and principles of molecular biology. In this unit, we will show you how this basic knowledge of biochemistry can be deliberately exploited in a number of ways. This exploitation is increasing rapidly and forms the basis of a current revolution in industry that has come to be known as biotechnology. It is expected to transform the ways in which we produce many vital commodities, including food, chemicals and energy. The success of biotechnology owes much to an increasing knowledge of genetics - which enables us to manipulate the genes of organism to our own ends, the science of genetic engineering.

In this unit first we will give a broad overview of biotechnology, its origin, current status and potential and then examine in more detail some major aeas of biotechnology.

### Objectives :

After reading this unit you should be able to :

- explain and describe the meaning of biotechnology and its importance,
- explain the basis of

(i) genetic engineering,

(ii) enzyme engineering and

(iii) describe fermentation technology.

## 15.2 WHAT IS BIOTECHNOLOGY ?

Man has been trying too understand,reproduce and modify the natural facts and phenomena of the mother nature since his existence on Earth. The knowledge gathered by observation, experimentation, systematic and critical testing is referred to as science. Technology, on the other hand is referred to as the useful application of science in industry or elsewhere and it plays an important role in daily life. When a technology is dependent on living cells or their constituents, it is referred to as biotechnology.

The biotechnologica' processes were started long ago. These include many traditional processes such as brewing, baking, wine making, cheese making and production and preservation of food materials. However, the newly acquired biological knowledge, specially