

Transcription: RNA Synthesis and Genetic Code

Transcription: RNA Synthesis

Transcription is the process by which DNA direct the synthesis of **mRNA** molecules that carry the coded information needed for protein synthesis. It is carried out by RNA polymerase.

The enzyme couples together the ribonucleoside triphosphates ATP, CTA, GTA and UTP on DNA templates releasing P_{Pi}.

mRNA production via transcription is actually a “two-step” process in which an hnRNA molecule is initially produced and then is “edited” to yield the desired mRNA molecule. The **mRNA** molecule so produced then functions as the carrier of the information needed to direct protein synthesis.

Within a strand of a DNA molecule are instructions for the synthesis of numerous hnRNA/**mRNA** molecules. During transcription, a DNA molecule unwinds, under enzyme influence, at the particular location where the appropriate base sequence is found for the hnRNA/**mRNA** of concern and the “exposed” base sequence is transcribed.

A short segment of a DNA strand so transcribed, which contains instructions for the formation of a particular hnRNA/**mRNA**, is called a gene. A gene is a segment of a DNA strand that contains the base sequence for the production of a specific hnRNA/**mRNA** molecule.

Transcription process

Four steps are involved.

1. A portion of the DNA double helix unwinds, exposing some bases(a gene).
The unwinding process is governed by the enzyme RNA polymerase.

2. Free ribonucleotides, one nucleotide at a time, align along one of the exposed strands of DNA bases, the template strand, forming new base pairs. In this process, U rather than T aligns with A in the base-pairing process. Ribose, becomes incorporated into the new nucleic acid backbone.

3. RNA polymerase is involved in the linkage of ribonucleotides, one by one, to the growing RNA molecule.

4. When the RNA polymerase enzyme encounters a sequence of base that is “read” as a stop signal the **transcription ends**. The newly formed RNA molecule and the RNA polymerase enzyme are released, and the DNA then rewinds to re-form the original double helix.

Genetic code

The nucleotide sequence of an **mRNA** molecule is the informational part of such a molecule. The unit of this base sequence in a given **mRNA** determines the amino acid sequence for the protein synthesized under that mRNA's direction.

The letters **A**, **G**, **T**, and **C** correspond to the nucleotides found in DNA. They are organized into three-letter code words called codons, and the collection of these codons makes up the genetic code. The genetic Code is universal. A codon is a three-nucleotide sequence in an **mRNA** molecule that codes for a specific amino acid. The genetic code is the assignment of the 64 **mRNA** codons to specific amino acids.

One codon, **AUG** codes for the initiation of the protein synthesis and hence called **initiation codon**. Three combinations were termed termination codons-**UAA**, **UGA** and **UAG**. The remaining 60 codons code for 20 amino acids .

| First Nucleotide | Second Nucleotide | | | | Third Nucleotide |
|------------------|-------------------|-----|------|------|------------------|
| | U | C | A | G | |
| U | Phe | Ser | Tyr | Cys | U |
| | Phe | Ser | Tyr | Cys | C |
| | Leu | Ser | Term | Term | A |
| | Leu | Ser | Term | Trp | G |

| | | | | | |
|---|-----|-----|-----|-----|---|
| C | Leu | Pro | His | Arg | U |
| | Leu | Pro | His | Arg | C |
| | Leu | Pro | Gln | Arg | A |
| | Leu | Pro | Gln | Arg | G |
| A | Ile | Thr | Asn | Ser | U |
| | Ile | Thr | Asn | Ser | C |
| | Ile | Thr | Lys | Arg | A |
| | Met | Thr | Lys | Arg | G |
| G | Val | Ala | Asp | Gly | U |
| | Val | Ala | Asp | Gly | C |
| | Val | Ala | Glu | Gly | A |
| | Val | Ala | Glu | Gly | G |

Thus there must be “degeneracy” in the genetic code; i.e., multiple codons must code the same amino acid. Some amino acids are encoded by several codons; e.g. **six** different codons specify **serine**. Other amino acids such as **methionine** and **tryptophan**, have a single **codon**. In general, the third nucleotide in a codon is less important than the other two in determining the specific amino acid to be incorporated, and this accounts for most of the degeneracy of the code. However, for any specific codon, only a single amino acid is indicated; with rare exceptions, the genetic code is unambiguous i.e. given a specific codon, only a single amino acid is indicated.

Translation or Protein Synthesis

Translation: Protein synthesis

Translation is the process by which [mRNA](#) codons are deciphered and a particular protein molecule is synthesized. The substances needed for the translation phase of protein synthesis are [mRNA](#) molecules, ribosomes, tRNA molecules, amino acids, and a number of enzymes. A ribosome is an rRNA-protein complex that serves as the site for the translation phase of protein synthesis.

There are five general steps to the translation process:

- (1) Activation of tRNA,
- (2) Initiation
- (3) Elongation
- (4) Termination, and
- (5) Post-translational processing.

Translation or Protein synthesis Initiation

The initiation of protein synthesis in human cells begins when [mRNA](#) attaches itself to the surface of a **small ribosomal subunit** such that its first codon, which is always the initiating codon AUG, occupies a site called the **P site** (peptidyl site).

An activated tRNA molecule with anticodon complementary to the codon AUG attaches itself, through complementary base pairing the AUG codon.

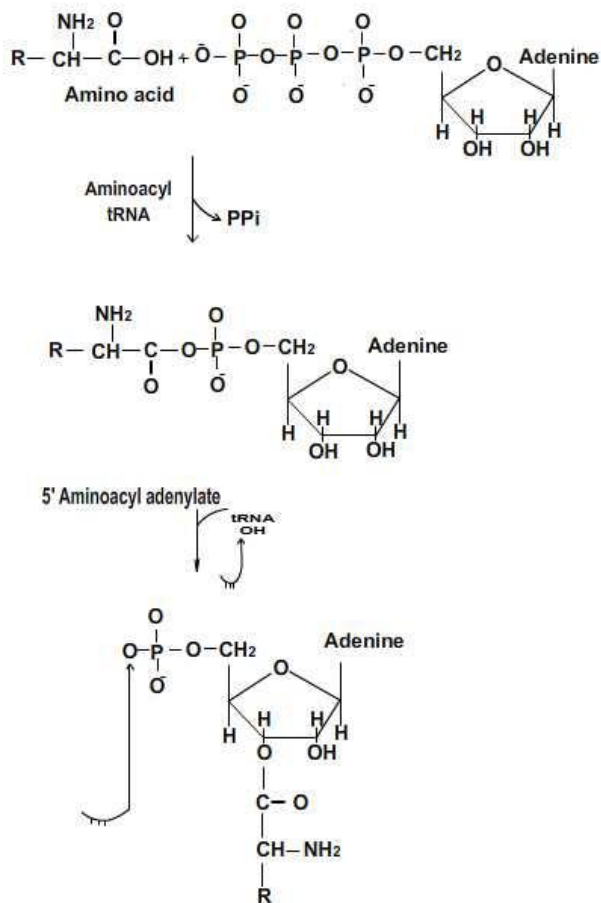
The resulting complex then interacts with a **large ribosomal subunit** to complete the formation of an initiation complex. Since the initiating codon AUG codes for the amino acid methionine, the first amino acid in a developing protein chain will be **N-formyl methionine**.

Activation of tRNA

There are two steps involved in tRNA activation.

Step I: An amino acid interacts with an activator molecule(ATP) to form a highly energetic complex.

Step II: This complex then reacts with the appropriate tRNA molecule to produce an activated tRNA molecule, a tRNA molecule that has an amino acid covalently bonded to it at its 3' end through an ester linkage.



Elongation

Elongation is a cyclic process consisting of three steps catalysed by elongation factors (eEF)

1. Binding of aminoacyl tRNA to the A site

Next to the P site in an [mRNA](#)-ribosome complex (80s ribosome) is a second binding site called the A site(aminoacyl site). At this second site the next [mRNA](#) codon is exposed, and a tRNA with the appropriate anticodon binds to it. eEF-1alpha and GTP are needed.

2. [Peptide](#) formation

With amino acids in place at both the **P** and the **A sites**, the enzyme **peptidyl transferase** of the 60 ribosomal [subunit](#) effects the linking of the P site amino acid to the A site amino acid to form a dipeptide. This peptide bond formation leaves the tRNA at the P site empty and the tRNA at the A site bearing the dipeptide.

The empty tRNA at the P site now leaves that site and is free to pick up another molecule of its specific amino acid. Simultaneously with the release of tRNA from the P site, the ribosome units shift along the [mRNA](#).

3. Translocation

The shift puts the newly formed dipeptide at the P site, and the third codon of [mRNA](#) is now available, at site A, to accept a tRNA molecule whose anticodon complement this codon. The movement of a ribosome along a [mRNA](#) molecule is called translocation. Translocation is the part of translation in which a ribosome moves down a [mRNA](#) molecule three base positions (one codon) so that a new codon can occupy the ribosomal A site. The elongation factor 2 eEF-2)and GTP are responsible for this.

Now this process is repeated. The third codon, now at the A site, accepts an incoming tRNA with an accompanying amino acid; and then the entire dipeptide at the P site is transferred and bonded to the A site amino acid to give a tripeptide. The empty tRNA at the P site is released and then the ribosome shifts along the [mRNA](#), and the process continues.

Termination

The polypeptide continues to grow by way of translocation until all necessary amino acids are in place and bonded to each other.

Appearance in the [mRNA](#) codon sequence of one of the three stop codons(UAA,UAG, or UGA) terminates the process. No tRNA has an anticodon that can base-pair with these stop codons. The polypeptide is then cleaved from the tRNA through hydrolysis.

Post-Translation Processing

Some modification of proteins usually occurs after translation. For example, most proteins do not have Met(the initiation codon) as their first amino acid. Cleavage of N-terminal Met is post-translation processing. Formation of S-S bonds between cysteine units is another example of post-translation processing.

Efficiency of mRNA Utilization

Many ribosomes can move simultaneously along a single [mRNA](#) molecule. In this highly efficient arrangement, many identical protein chains can be synthesized almost at the same time from a single strand of [mRNA](#). This multiple use of [mRNA](#) molecules reduces the amount of resources and energy that the cell expends to synthesize needed protein. Such complexes of several ribosomes and [mRNA](#) are called polyribosomes or polysomes. A polysome is a complex of [mRNA](#) and several ribosomes.

Mutations

A **mutation** is an error in base sequence in a gene that is reproduced during DNA replication. Such errors alter the genetic information that is passed on during transcription. The altered information can cause changes in amino acid sequence during protein synthesis. Sometimes, such changes have a profound effect on an organism.

A mutagen is a substance or agent that causes a change in the structure of a gene. Radiation and chemical agents are two important types of mutagens.

Radiation: Radiation, in the form of ultraviolet light, X rays, radioactivity, and cosmic rays, has the potential to be mutagenic. Ultraviolet light from the sun is the radiation that causes sunburn and can induce changes in the DNA of the skin cells. Sustained exposure to ultraviolet light can lead to serious problems such as skin cancer.

Chemical agents: Chemical agents can also have mutagenic effects. Nitrous acid(HNO_2) is a mutagen that causes deamination of heterocyclic nitrogen bases. e.g. HNO_2 can convert [cytosine](#) to uracil. [Deamination](#) of a [cytosine](#) that was part of an [mRNA](#) codon would change the codon; for example CGG would become UGG.

A variety of chemicals—including nitrites, nitrates, and nitrosamines—can form nitrous acid in the body. The use of nitrates and nitrites as preservatives in foods such as bologna and hot dogs is cause of concern because of their conversion to nitrous acid in the body and possible damage to DNA.

Fortunately, the body has repair enzymes that recognize and replace altered bases. Normally, the vast majority of altered DNA bases are repaired, and mutations are avoided. Occasionally, however, the damage is not repaired, and the mutation persists.