ASSESSMENT

TEST 2
MONDAY 23rd OCTOBER 2023
1815 hrs -1930 hrs

Lecture 7 – General Properties of Cells
Lecture 8 – Cell Structure & Function
Lecture 9 – Cell Membranes
Lecture 10 – Respiration
Lecture 11 – Photosynthesis
Lecture 12 – Cell Cycle
Lecture 13 – Cell Division
Lecture 14 – Central Dogma
All Associated Tutorials & Practicals

Central Dogma

Lecture 14
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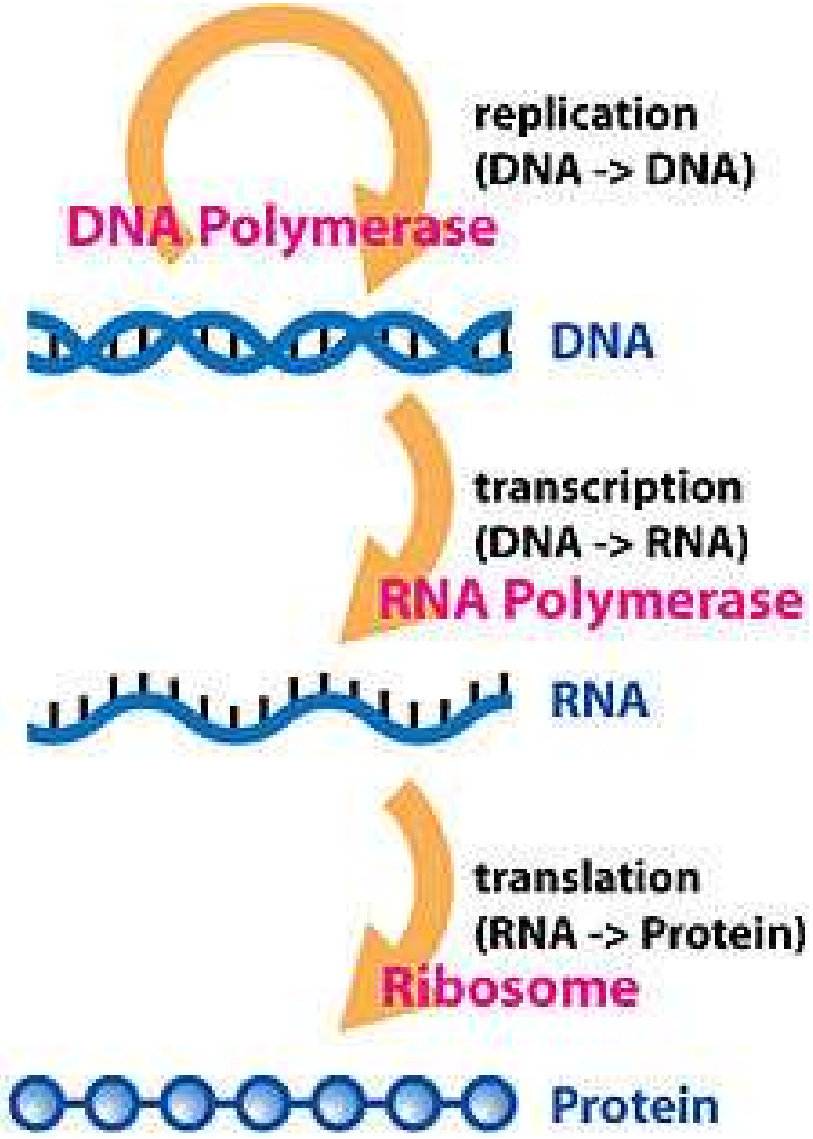


Learning Objectives

- Describe the initiation, elongation, termination steps for DNA replication, transcription, and translation (including the enzymes involved).
- Identify the template and product for DNA replication (DNA to DNA), transcription (DNA to mRNA), and translation (mRNA to protein).
- Describe the difference between the leading and lagging strands during replication
- Describe the difference between the coding and the template strand during transcription.

Exception to the Central Dogma

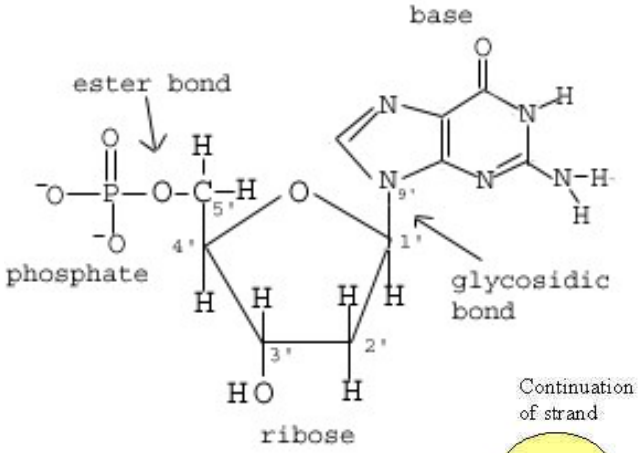
- Retroviruses transcribe RNA into DNA through the use of a special enzyme called reverse transcriptase RNA → DNA → RNA → protein
- Some virus species are so primitive that they use only RNA → proteins, having not developed DNA.
- Prions (misfolded protein) Protein → Protein.

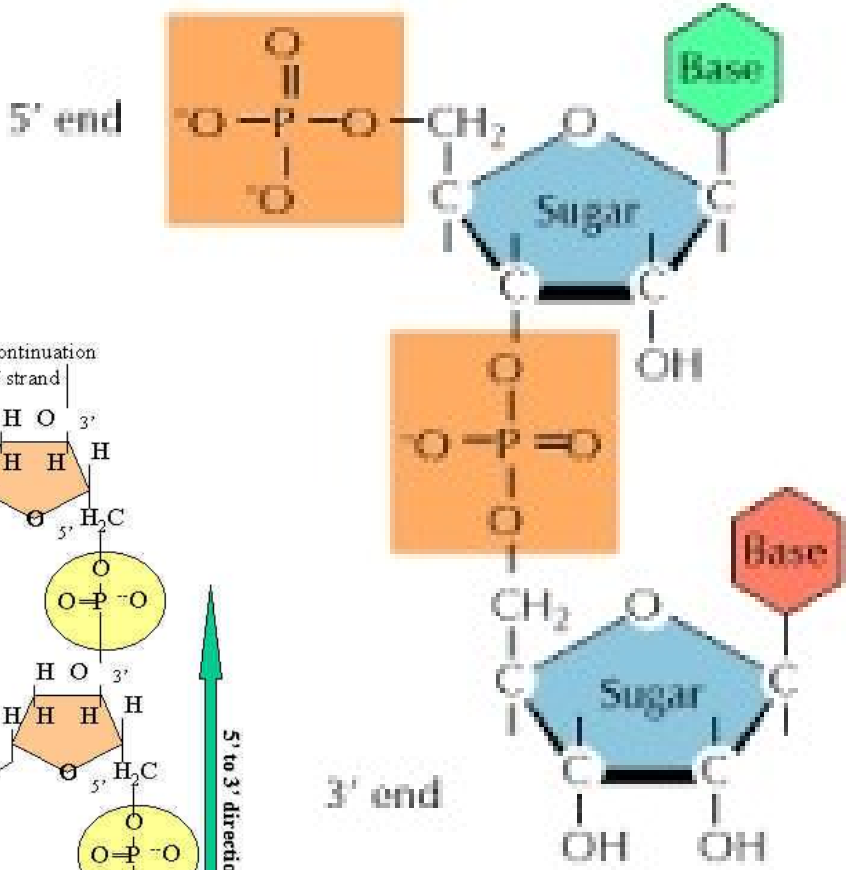
Gene Expression and Control

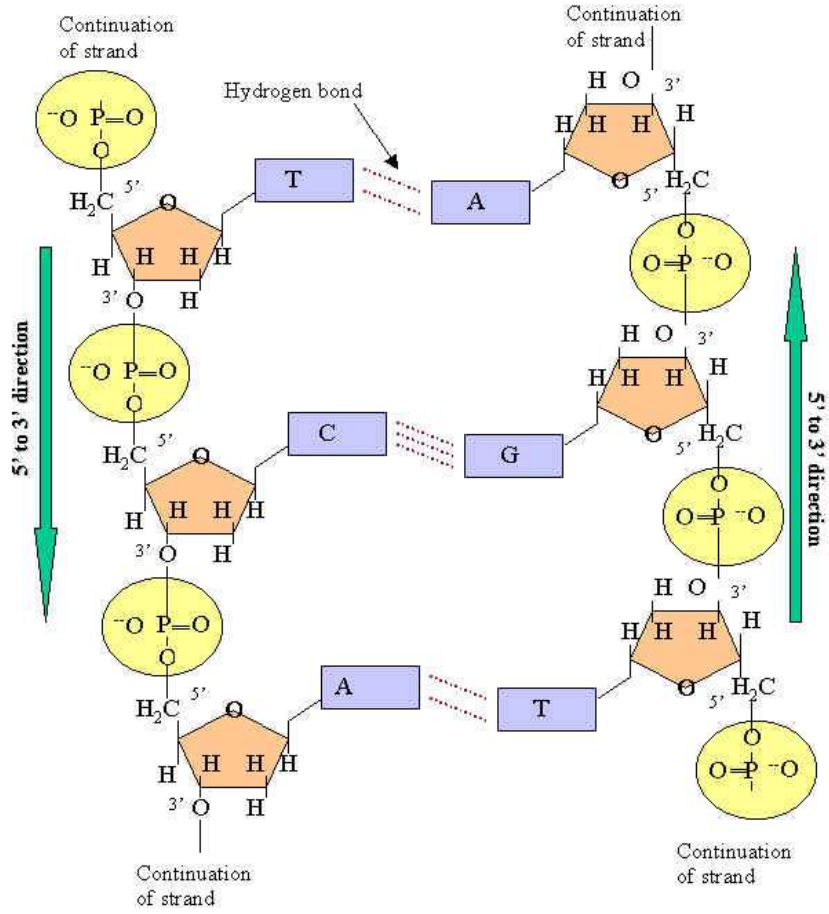
Tutorial Presentations will cover an example of how genes are expressed and controlled in bacteria

This lecture focuses on how information encoded by a gene becomes converted to the gene's product (RNA or protein)

Structure of Nucleic Acids



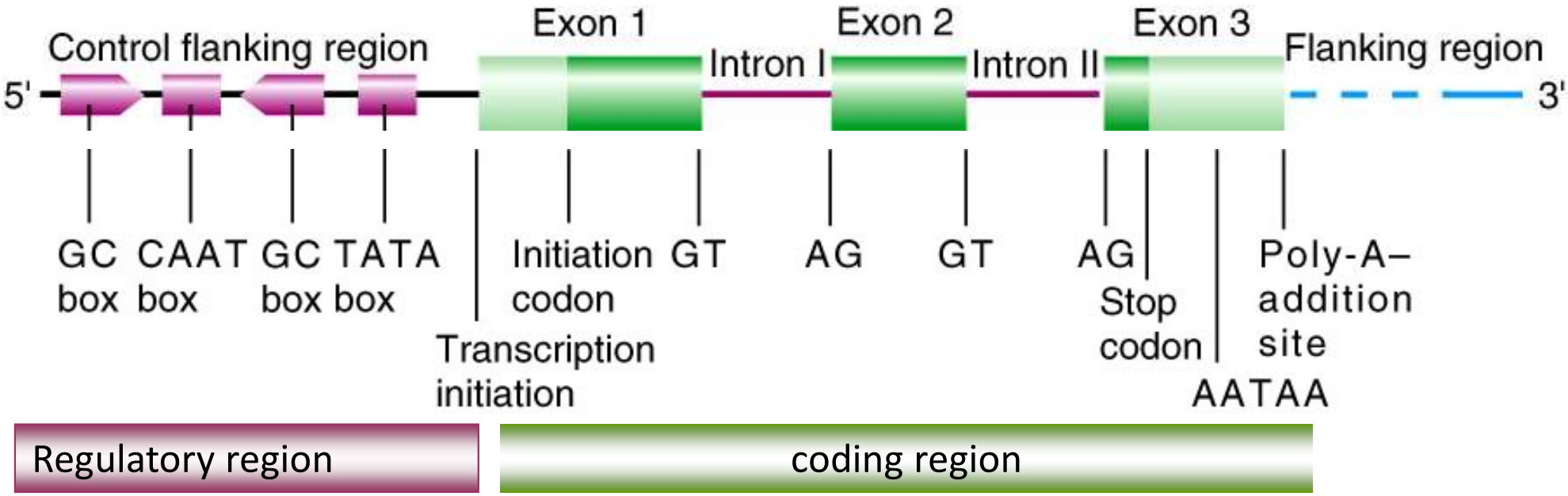




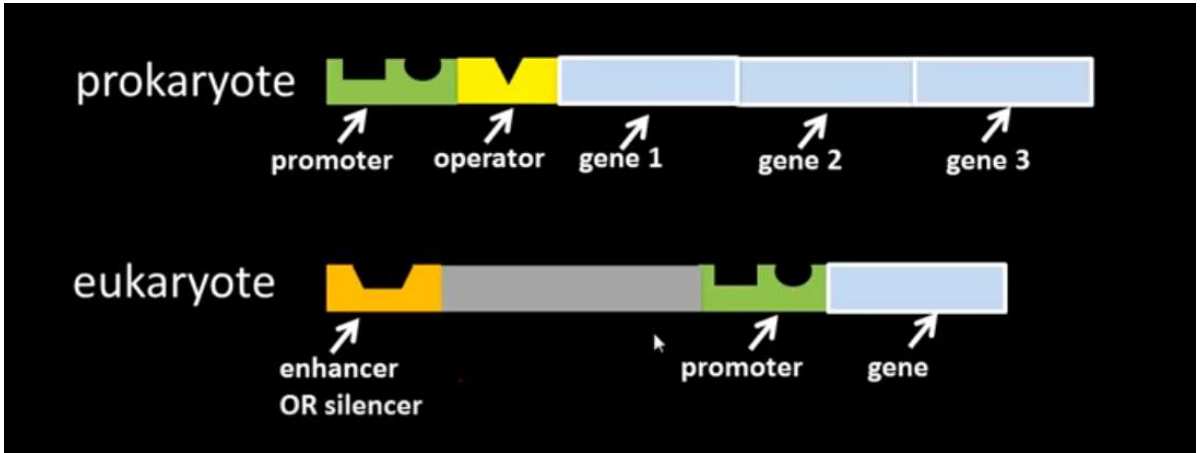
The Nature of Genetic Information

- DNA carries all genetic information and instructions.
- A strand of DNA is a chain made up of four kinds of nucleotides in what is known as a DNA sequence.
- Part of the information carried occurs in subsets called **genes**.
- A cell uses the sequence of a gene to build an RNA or a protein product.
  - The process begins with **transcription** (enzymes use the DNA sequence of a gene as a template to assemble a strand of RNA. In essence, what is being made is an RNA copy of a gene.

Basic Structure of a Gene



In most eukaryotic genes, coding regions (**exons**) are interrupted by noncoding regions (**introns**). During transcription, the entire gene is copied into a pre-mRNA, which includes **exons** and **introns**. During the process of RNA splicing, **introns** are removed and **exons** joined to form a contiguous coding sequence.



- RNA has structural similarities and differences to DNA. Their functions however are different!

- DNA's only role is to store a cell's heritable information.

- RNAs are encoded by DNA. There are different kinds of RNA and they each have different functions.

- **Messenger RNA (mRNA) is the only kind of RNA that carries a protein-building message.**

- The message is encoded within the mRNA itself in sets of 3 bases (codon)

- This genetic series forms a meaningful parcel of information – the sequence of amino acids of a protein.

- The protein-building information in an RNA is translated into a sequence of amino acids in a process called translation. The result is a polypeptide that twists and folds into a protein.

- Transcription and translation are part of gene expression in which genetic information flows from DNA to RNA to protein.
  - Proteins (enzymes) take part in lipid and carbohydrate assembly, replication of DNA, synthesis of RNA and the performance of many functions that keep the cell alive.

DNA Replication

- A cell replicates its DNA before it divides. This means that one double helix becomes two double helices.
- Each strand in the double helix serves as a template for synthesis of a new complementary strand of DNA.
- During replication an enzyme (DNA **helicase**) breaks the hydrogen bonds that hold the double helix together so that the two strands can unwind
- Unwound strands are kept apart by single strand binding proteins (SSBP)

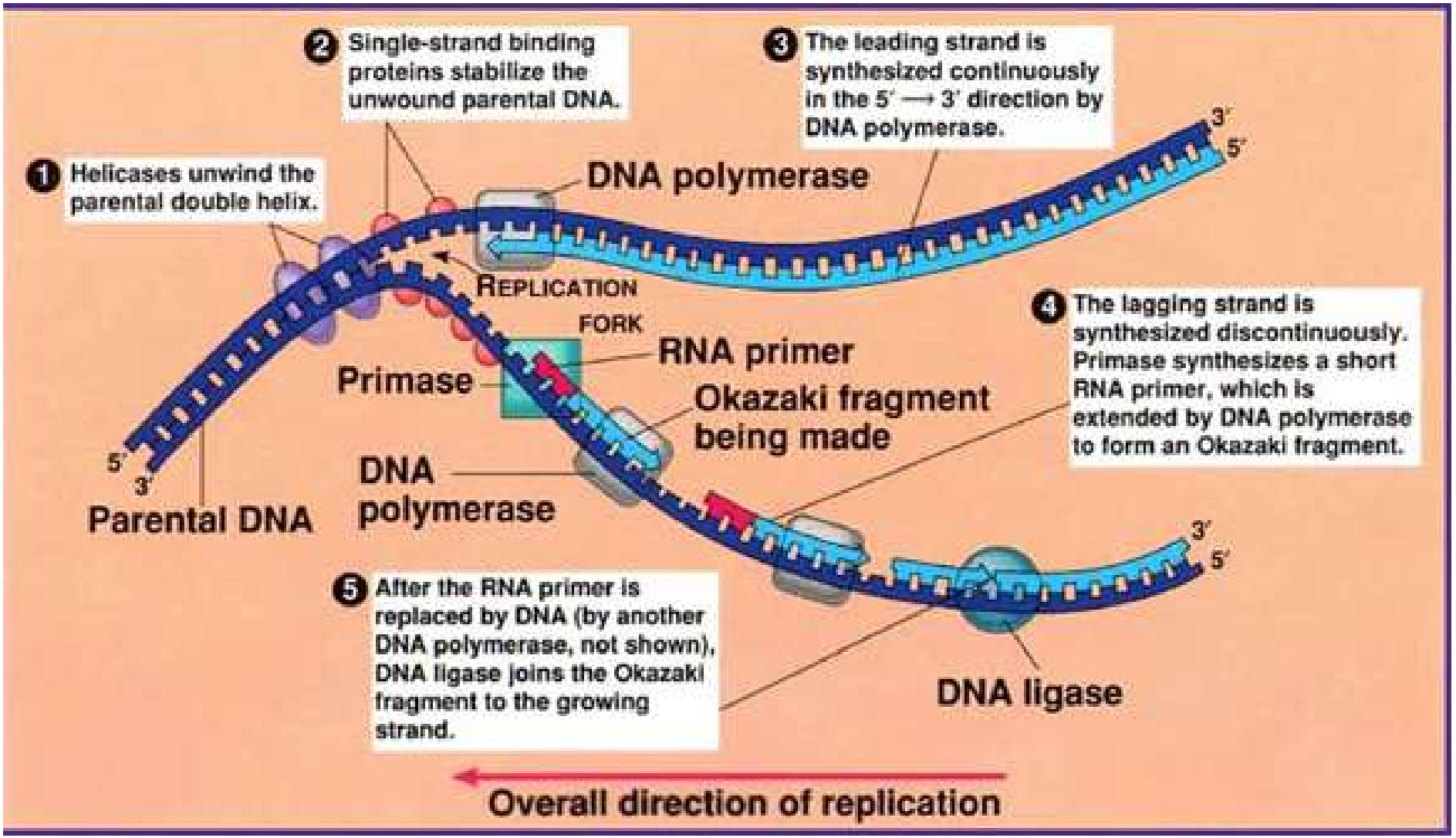
- Another enzyme called **DNA polymerase** assembles a complementary strand of DNA on each of the parent strands from free nucleotides using base pairing rules. *The synthesis depends on RNA primers made by DNA **primase**

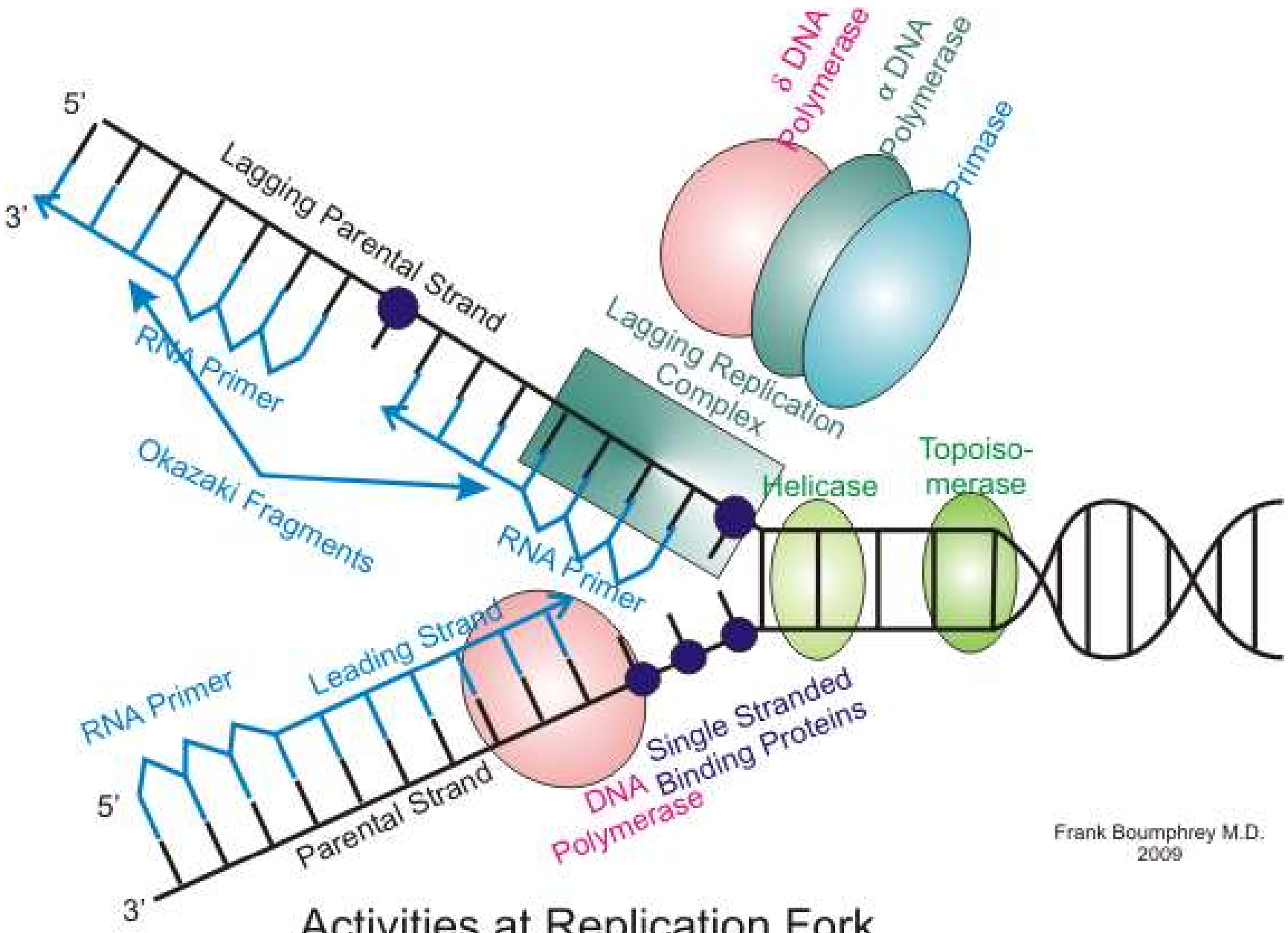
  (There are different types of DNA polymerase that perform different functions)

- The energy for the attachment of the nucleotides is provided by phosphate group transfers.

- DNA **ligase** seals any gaps as the strand grows.

- The new strand forms a helix with the template strand as the template strand grows.


2 Single-strand binding proteins stabilize the unwound parental DNA.
3 The leading strand is synthesized continuously in the 5′ ⟶ 3′ direction by DNA polymerase.
1 Helicases unwind the parental double helix.
DNA polymerase
3′
5′
REPLICATION FORK
RNA primer
Primase
Okazaki fragment being made
4 The lagging strand is synthesized discontinuously. Primase synthesizes a short RNA primer, which is extended by DNA polymerase to form an Okazaki fragment.
5′
3′
Parental DNA
DNA polymerase
3′
5′
5 After the RNA primer is replaced by DNA (by another DNA polymerase, not shown), DNA ligase joins the Okazaki fragment to the growing strand.
DNA ligase
Overall direction of replication



Activities at Replication Fork

- DNA replication is a fast process that does not always have perfect accuracy.

- Sometimes the wrong base is added, bases get lost or extra ones get added resulting in less than perfect complementarity.

- Some errors are due to damage by radiation or chemicals.

- DNA repair mechanisms can sometimes repair the errors or damage. DNA polymerases can have proof-reading capability and there are other mechanisms to stop the cell from dividing.

- When proof-reading and repair mechanisms fail, an error becomes a mutation. The outcome can be harmful or silent.
  - Mutations are a source of variation in traits.

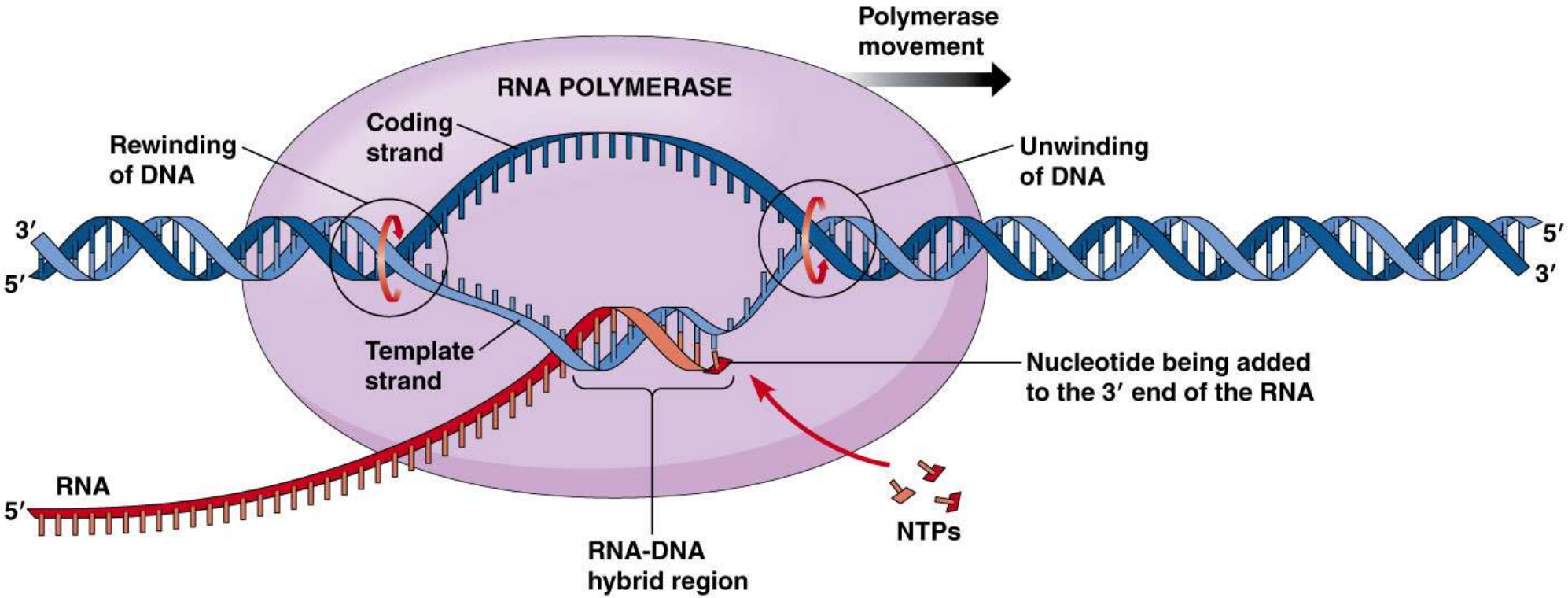
Transcription: DNA to RNA

- In transcription part of one strand of DNA serves as a template for synthesis of an RNA strand. The enzyme **RNA polymerase** adds nucleotides to the end of the growing strand.

- This process occurs in the nucleus

The Process of Transcription

- At transcription initiation, RNA polymerase and other regulatory proteins bind to the promoter region of a gene.
- The polymerase starts moving along the DNA over the gene.
- As it moves the polymerase unwinds the double helix a little bit at a time creating what is called a transcription bubble and ‘reading’ the base sequence of the **non-coding strand.**
- During this time, the polymerase joins free RNA nucleotides into a chain in an order dictated by the DNA sequence.
- At the end of the gene (terminator sequence), the polymerase and the new RNA strand (RNA copy of a gene) are released



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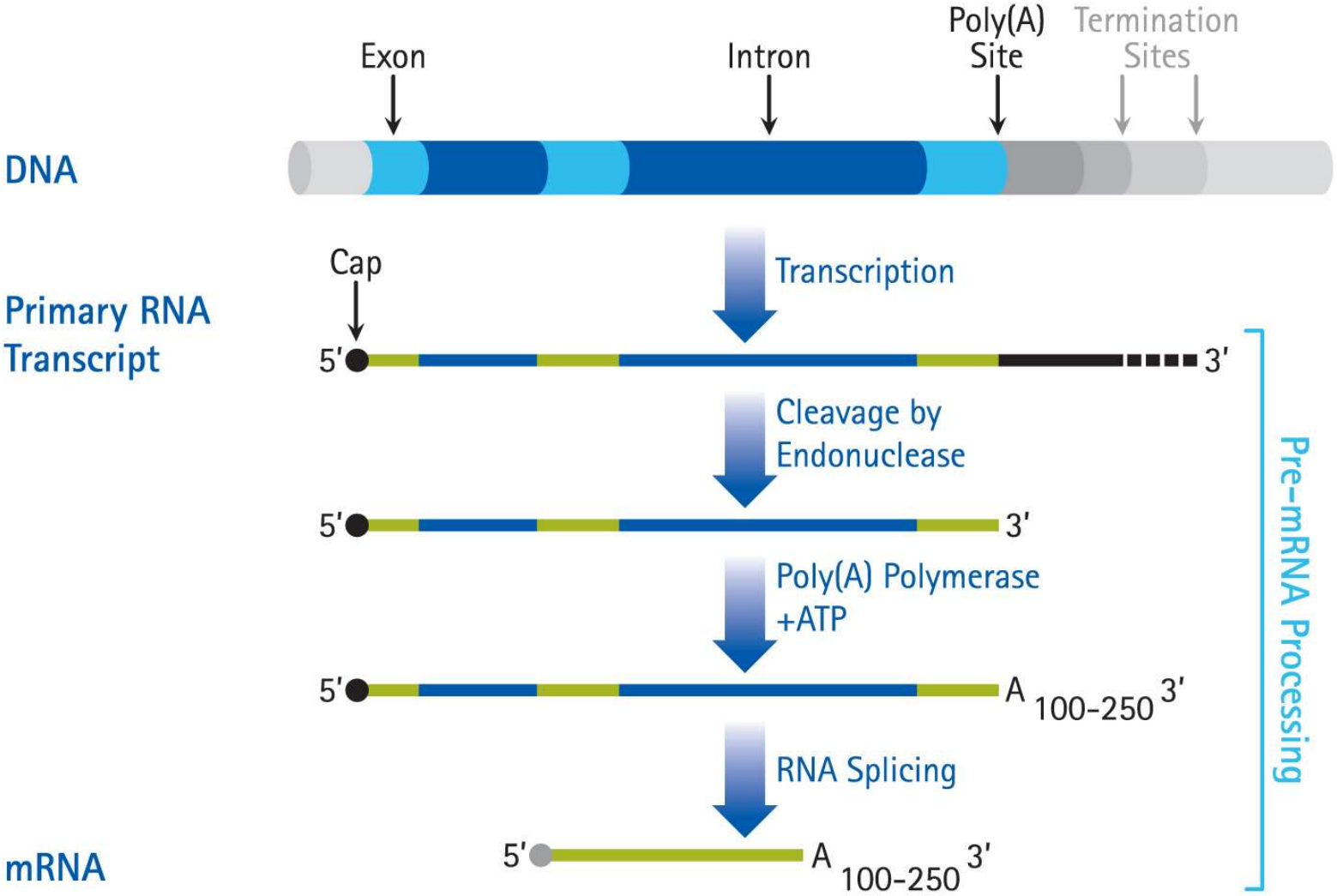
- Some modifications are made to the RNA transcript before translation.

- The 5’ end gets a modified guanine cap (protection, ribosome recognition) while the 3’ end gets polyadenylated (protection, recognition and transport)

- The non-coding regions of the gene (introns) are removed from the transcript in a process called splicing.

- The transcript (mature mRNA) is now ready for export to the **cytosol.**

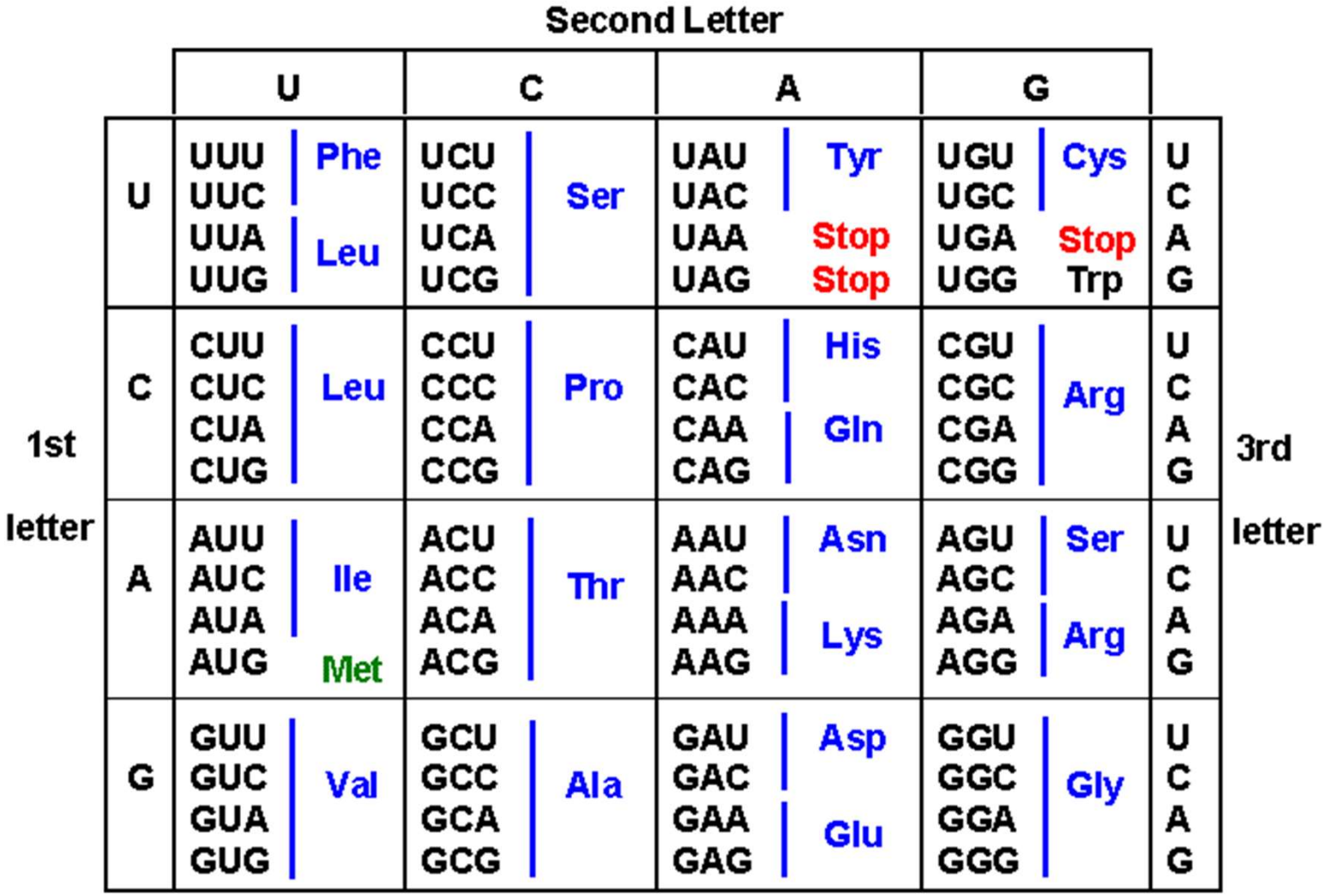

Exon
Intron
Poly(A) Site
Termination Sites
DNA
Cap
Transcription
Primary RNA Transcript
5′
3′
Cleavage by Endonuclease
5′
3′
Poly(A) Polymerase +ATP
5′
A 100-250 3′
RNA Splicing
5′
A 100-250 3′
mRNA
Pre-mRNA Processing

mRNA & the Genetic Code

- mRNA is a disposable copy of a gene. Its role is to carry the protein building information to the other two types of RNA; rRNA and tRNA for translation.

- The protein building information is encoded within the mRNA in sets of 3 bases (codon).

- There are 64 codons that make up the genetic code and each of them code for an amino acid. (There is a redundancy in the genetic code)


Second Letter
U
C
A
G
1st letter
3rd letter
U
UUU Phe
UUC
UUA Leu
UUG
UCU
UCC Ser
UCA
UCG
UAU Tyr
UAC
UAA Stop
UAG Stop
UGU Cys
UGC
UGA Stop
UGG Trp
C
CUU
CUC Leu
CUA
CUG
CCU
CCC Pro
CCA
CCG
CAU His
CAC
CAA Gln
CAG
CGU
CGC Arg
CGA
CGG
A
AUU
AUC Ile
AUA
AUG Met
ACU
ACC Thr
ACA
ACG
AAU Asn
AAC
AAA Lys
AAG
AGU Ser
AGC
AGA Arg
AGG
G
GUU
GUC Val
GUA
GUG
GCU
GCC Ala
GCA
GCG
GAU Asp
GAC
GAA Glu
GAG
GGU
GGC Gly
GGA
GGG

Translation

- One codon follows the next along a length of mRNA so the order of codons in a mRNA determines the order of amino acids in the polypeptide that will be translated from it.

  gene DNA sequence -> mRNA sequence -> amino acid sequence

rRNA & tRNA – The Translators

- Ribosomes and tRNA interact to translate an mRNA into a polypeptide. The translation process has an initiation, elongation and termination step.

- Ribosomes are made up of a small and large subunit which consist of proteins and rRNA. rRNA is the main component of the subunits.

Initiation

- rRNA does not contribute any genetic material. It has binding sites that allow the mRNA to interact with tRNA. mRNA first binds to the small subunit

- tRNA is actually what translates nucleotides to amino acids.

- On one end of the tRNA is an amino acid, on the other end are three nitrogenous bases (anti-codon) that correspond to that amino acid.

- During translation, the two ribosomal subunits converge as an intact ribosome on a mRNA in an initiation step

- The anti-codon of an initiator base pairs with the first AUG codon of the mRNA and the initiation step is concluded by the large ribosomal subunit joining the small subunit.

Elongation

- The ribosome assembles the polypeptide chain as it moves along the mRNA. After the first methionine, another tRNA brings the second amino acid to the complex as its anti-codon base-pairs with the second codon in the mRNA.

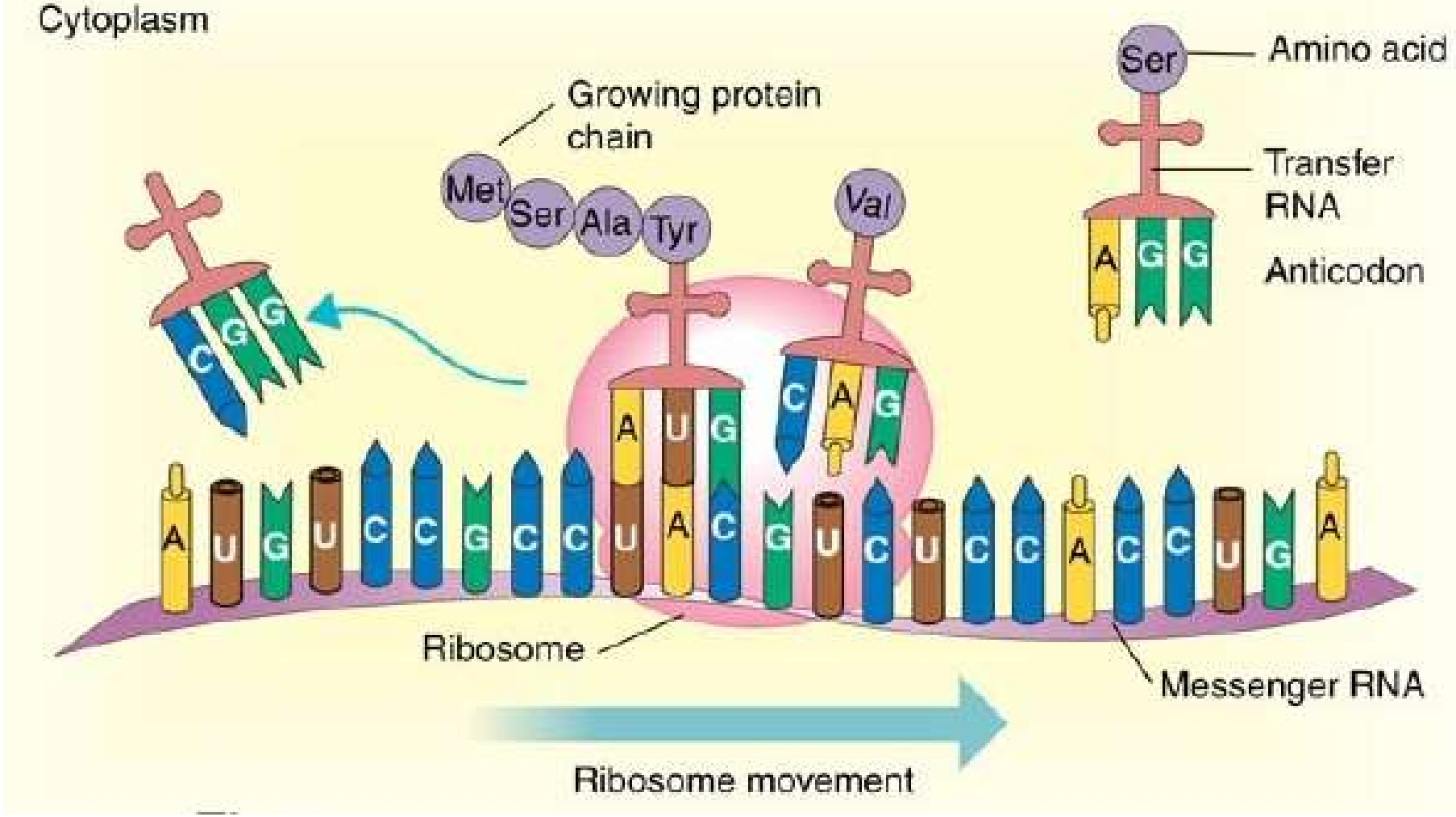
- The ribosome joins the first two amino acids via a peptide bond.

- The first tRNA is released and the ribosome moves to the next codon. Another tRNA brings the third amino acid to the complex where there is base pairing and peptide bond formation

- The elongation of the polypeptide is facilitated by successive tRNAs.

Termination

- Termination occurs when the ribosome reaches a stop codon in the mRNA.
- The RNA and the polypeptide detach from the ribosome and the ribosomal units separate.
- Translation is now complete. The new polypeptide can now remain in the cytoplasm or enter the rough ER of the endomembrane system.


Cytoplasm
Growing protein chain
Met
Ser
Ala
Tyr
Val
Ser
Amino acid
Transfer RNA
Anticodon
Ribosome
Messenger RNA
Ribosome movement

Mutated Genes & Their Products

- Mutations are changes in the sequence of a cell's DNA. An altered gene product can result despite the safety net provided by the redundancy in the genetic code.

- Types of mutations include deletions, insertions or base pair substitutions.

- Defects in gene products can be seen in disease states such as sickle cell anaemia or beta thalassemia.

What Causes Mutations?

- Spontaneous errors during DNA replication. Uncorrected errors can become mutations

- Insertions can be caused by the activity of transposable elements (segments of DNA that can insert themselves anywhere in a chromosome.

- Ionizing radiation can break chromosomes or generate free radicals that damage DNA.

Thank You

- Please complete the online course evaluation

Next Lecture

- Mendelian Genetics

- Make time to try out some exercises on this link

http://www.pbs.org/wgbh/aso/tryit/dna/