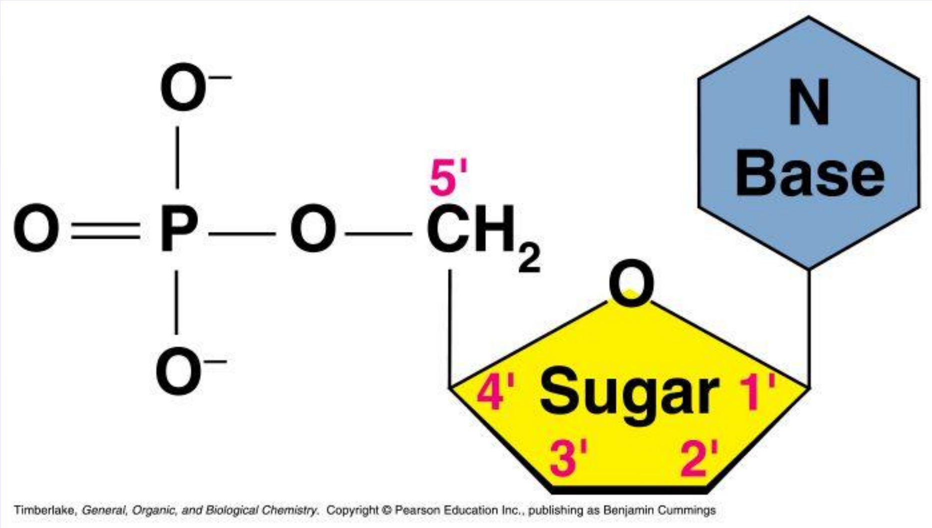
Nucleic Acids

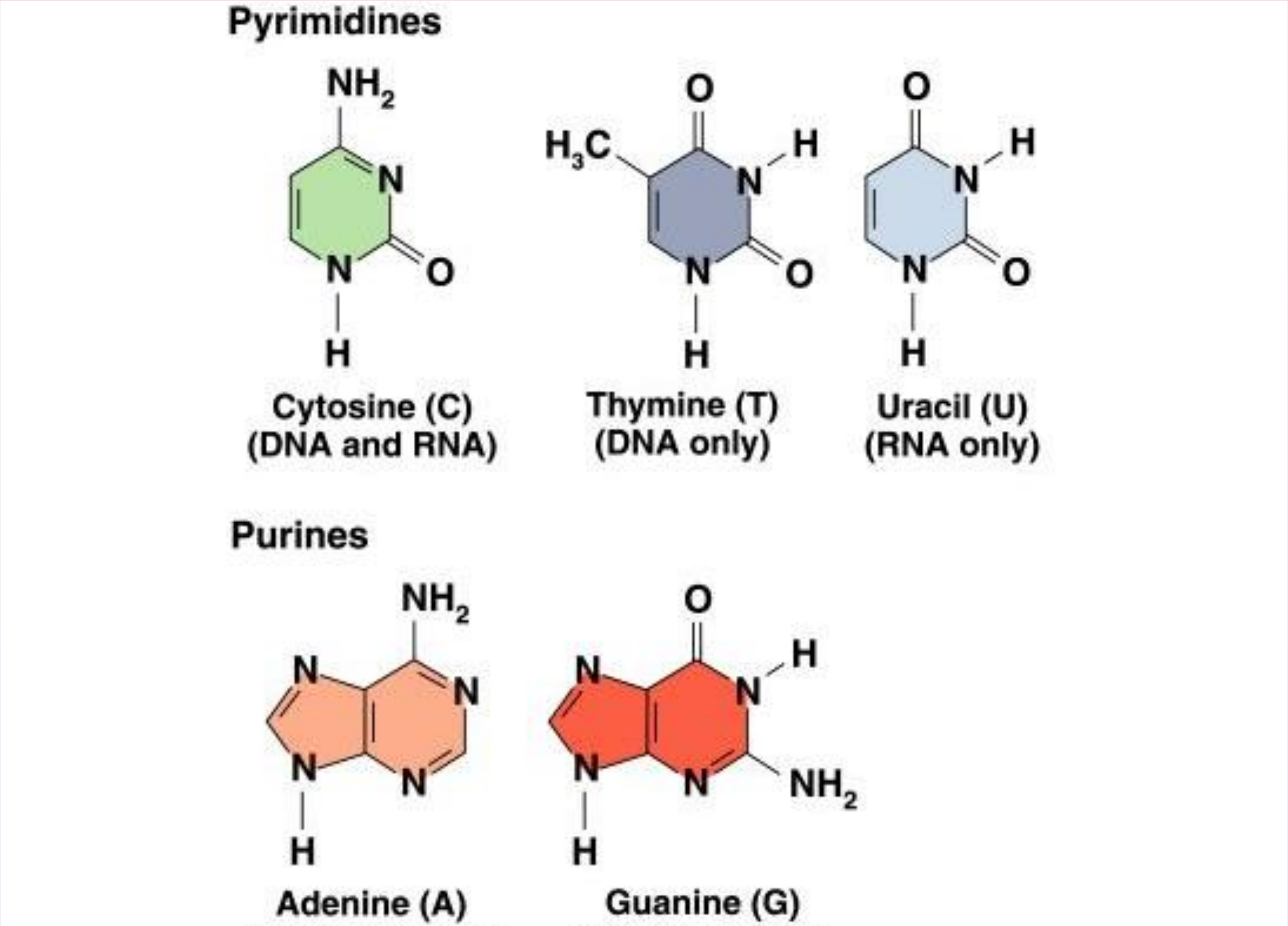
- **Nucleic acids** are molecules that store information for cellular growth and reproduction
- There are two types of nucleic acids:

  - **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**
- These are polymers consisting of long chains of monomers called nucleotides
- A **nucleotide** consists of a nitrogenous base, a pentose sugar and a phosphate group:



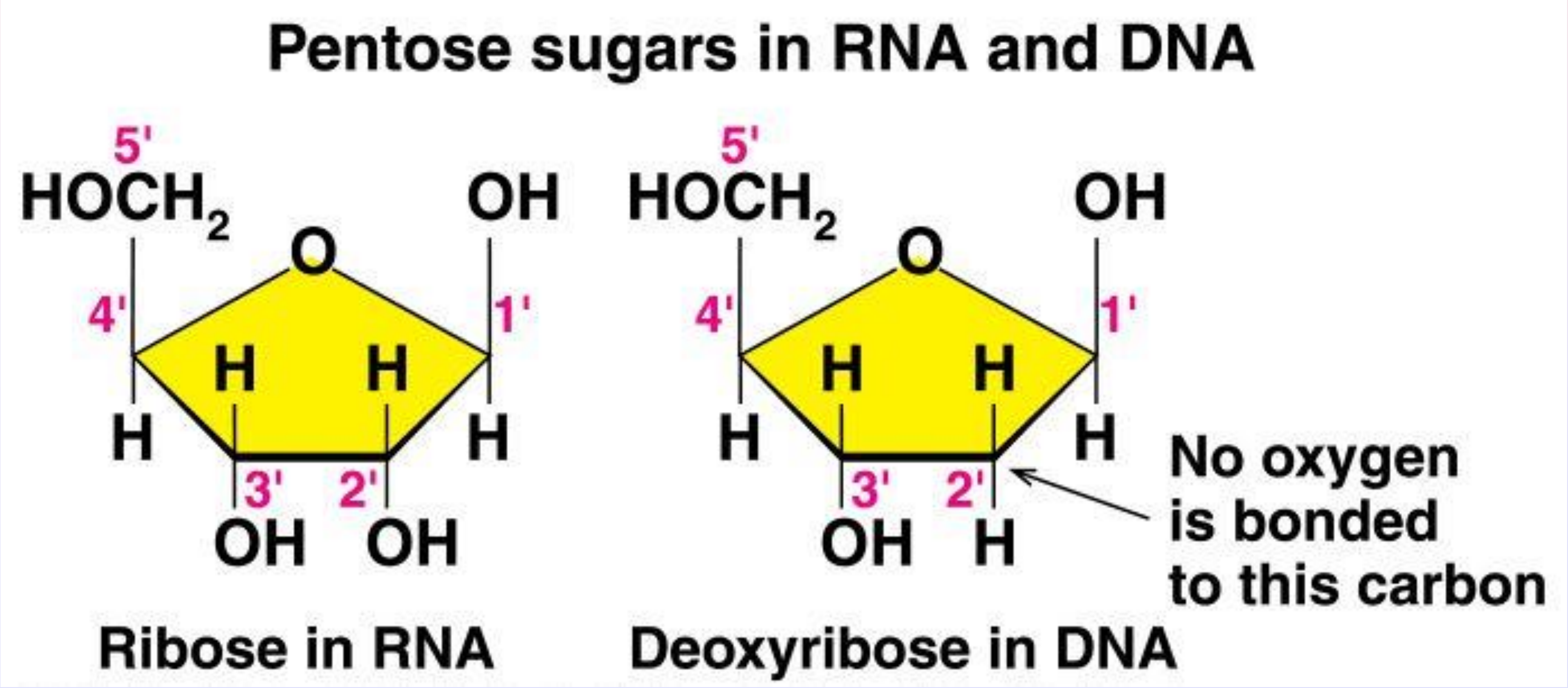
Nitrogen Bases

- The **nitrogen bases** in nucleotides consist of two general types:
  - **purines**: adenine (A) and guanine (G)
  - **pyrimidines**: cytosine (C), thymine (T) and Uracil (U)



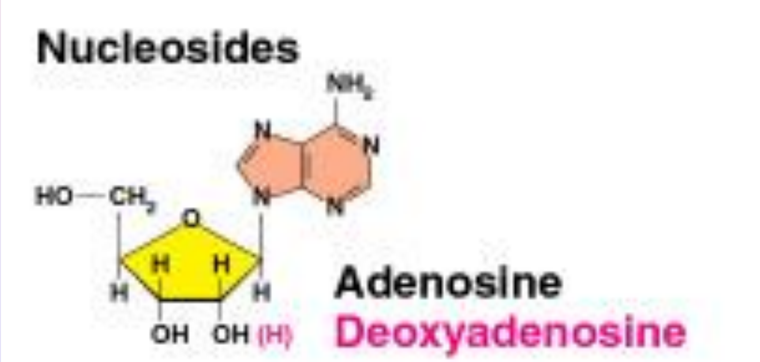
Pentose Sugars

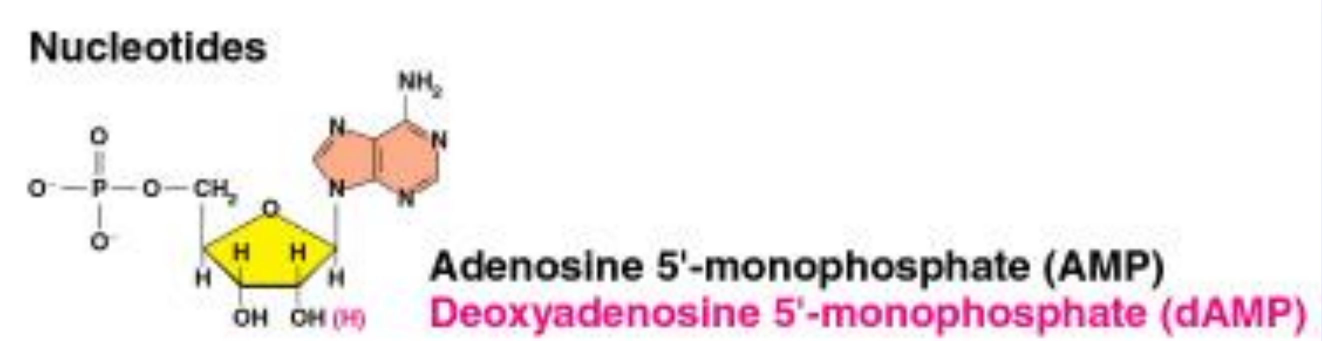
- There are two related **pentose sugars**:
  - RNA contains **ribose**
  - DNA contains **deoxyribose**
- The sugars have their carbon atoms numbered with primes to distinguish them from the nitrogen bases



Nucleosides and Nucleotides

- A nucleoside consists of a nitrogen base linked by a glycosidic bond to C1’ of a ribose or deoxyribose
- Nucleosides are named by changing the nitrogen base ending to *-osine* for purines and *–idine* for pyrimidines
- A nucleotide is a nucleoside that forms a phosphate ester with the C5’ OH group of ribose or deoxyribose
- Nucleotides are named using the name of the nucleoside followed by *5’-monophosphate*



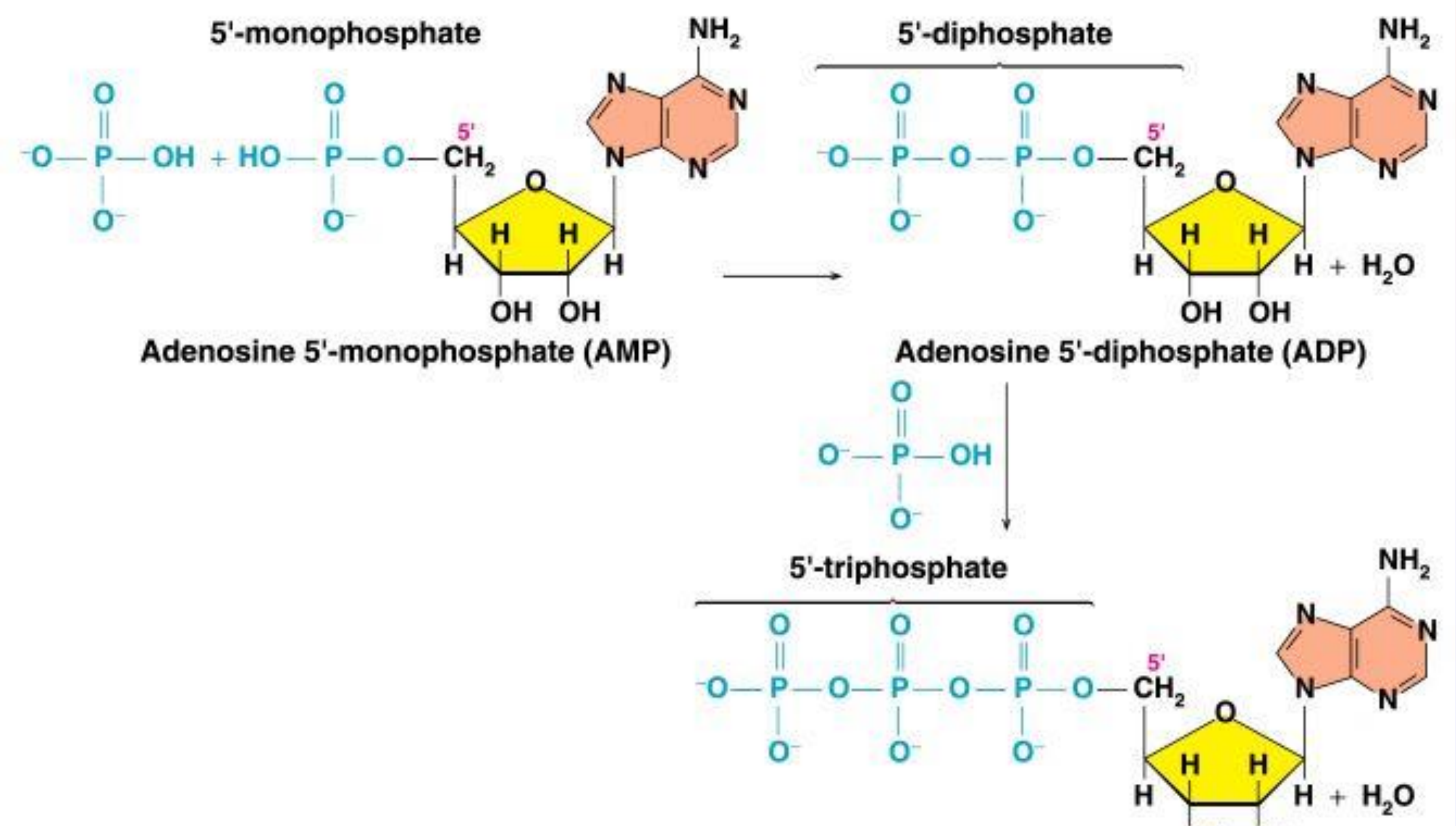


Names of Nucleosides and Nucleotides

Base	Nucleosides	Nucleotides
RNA		
Adenine (A)	Adenosine (A)	Adenosine 5'-monophosphate (AMP)
Guanine (G)	Guanosine (G)	Guanosine 5'-monophosphate (GMP)
Cytosine (C)	Cytidine (C)	Cytidine 5'-monophosphate (CMP)
Uracil (U)	Uridine (U)	Uridine 5'-monophosphate (UMP)
DNA		
Adenine (A)	Deoxyadenosine (A)	Deoxyadenosine 5'-monophosphate (dAMP)
Guanine (G)	Deoxyguanosine (G)	Deoxyguanosine 5'-monophosphate (dGMP)
Cytosine (C)	Deoxycytidine (C)	Deoxycytidine 5'-monophosphate (dCMP)
Thymine (T)	Deoxythymidine (T)	Deoxythymidine 5'-monophosphate (dTMP)

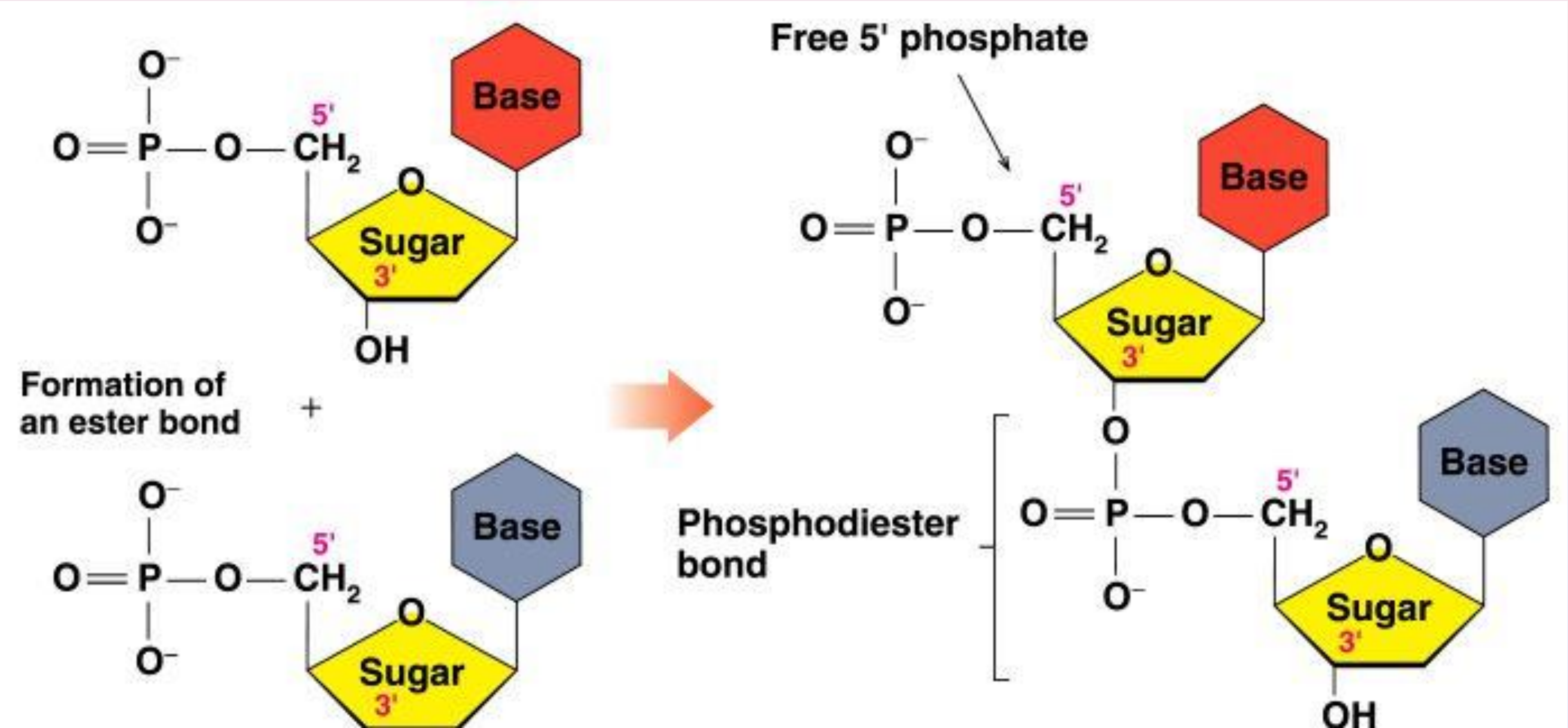
AMP, ADP and ATP

- Additional phosphate groups can be added to the nucleoside 5'-monophosphates to form **diphosphates** and **triphosphates**
- **ATP** is the major energy source for cellular activity



Primary Structure of Nucleic Acids

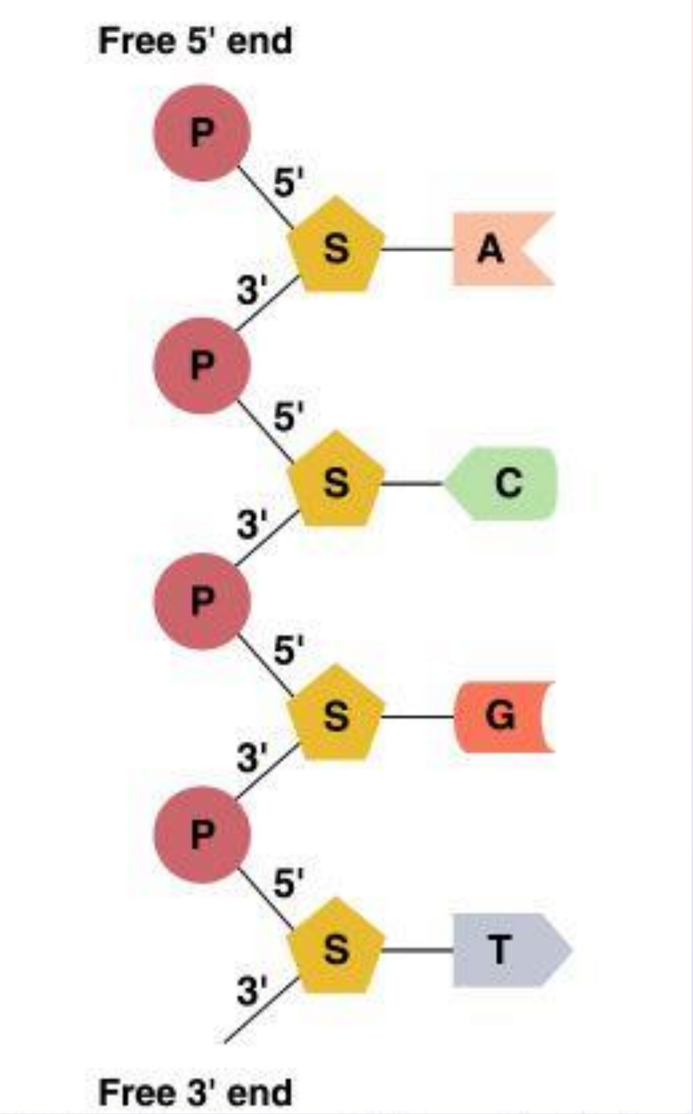
- The **primary structure** of a nucleic acid is the nucleotide sequence
- The nucleotides in nucleic acids are joined by phosphodiester bonds
- The 3'-OH group of the sugar in one nucleotide forms an ester bond to the phosphate group on the 5'-carbon of the sugar of the next nucleotide



Reading Primary Structure

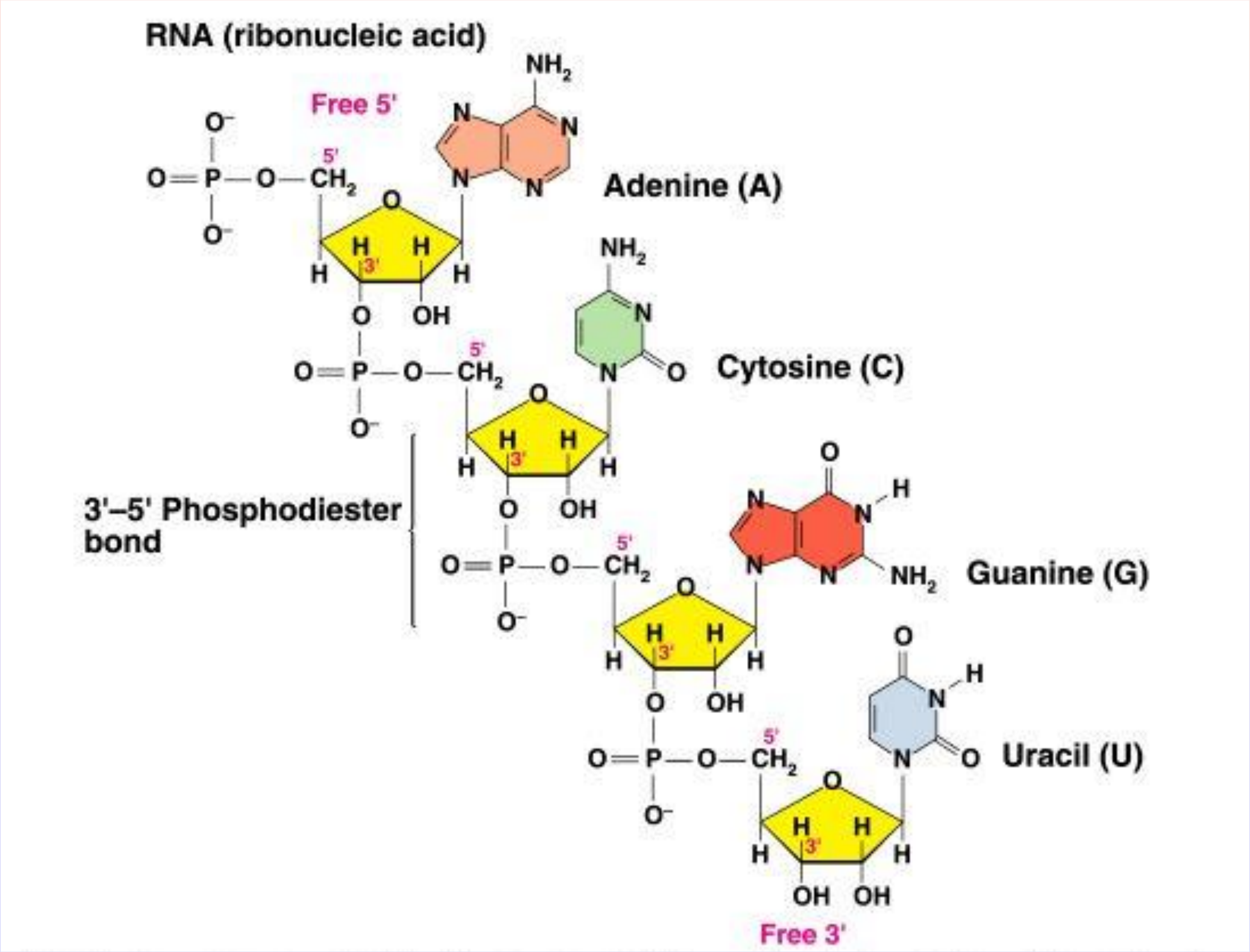
- A nucleic acid polymer has a free 5’-phosphate group at one end and a free 3’-OH group at the other end
- The sequence is read from the free 5’-end using the letters of the bases
- This example reads

  5’—A—C—G—T—3’



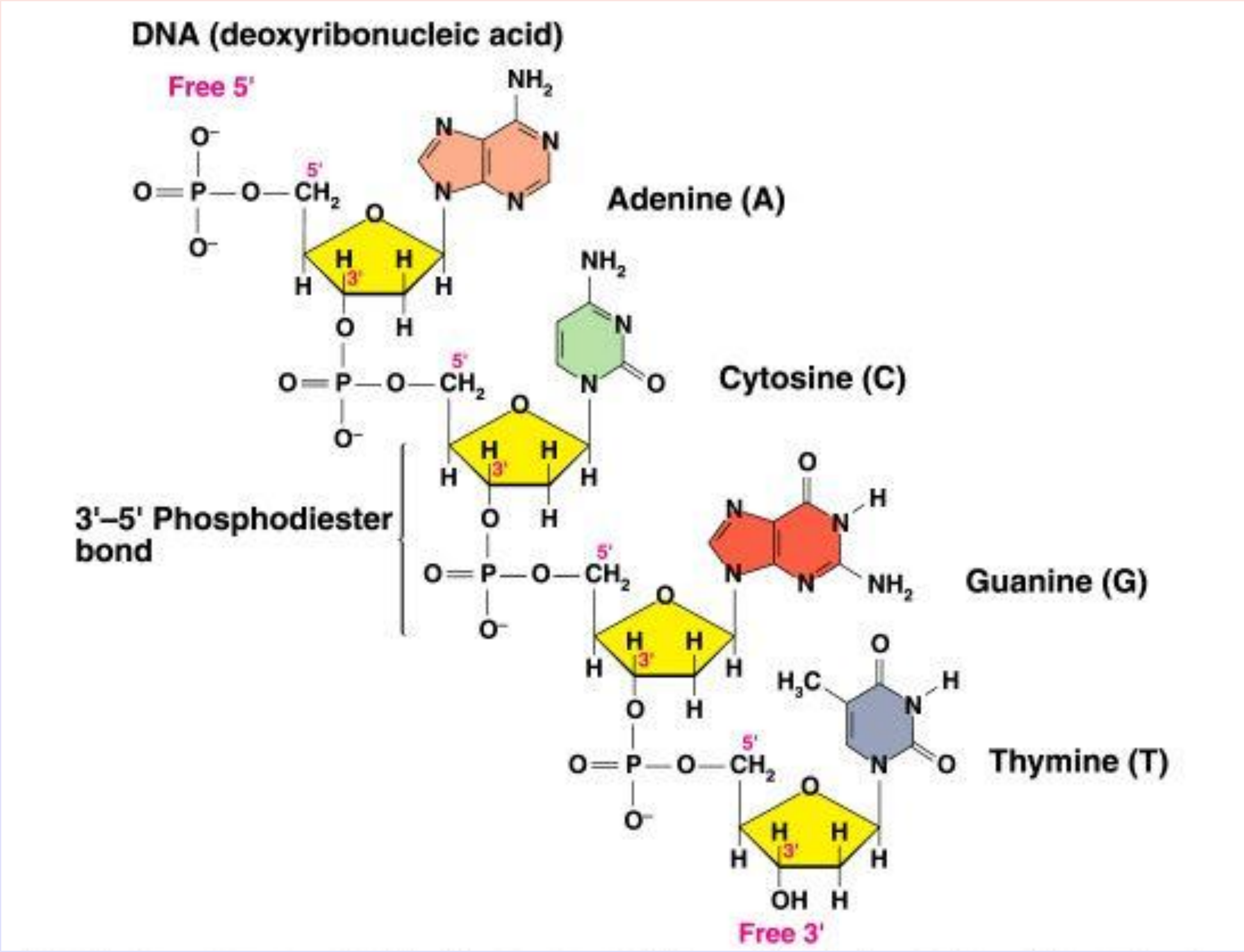
Example of RNA Primary Structure

- In RNA, A, C, G, and U are linked by 3'-5' ester bonds between ribose and phosphate



Example of DNA Primary Structure

- In DNA, A, C, G, and T are linked by 3'-5' ester bonds between deoxyribose and phosphate



Secondary Structure: DNA Double Helix

- In DNA there are two strands of nucleotides that wind together in a **double helix**

  - the strands run in opposite directions

  - the bases are arranged in step-like pairs

  - the **base pairs** are held together by hydrogen bonding

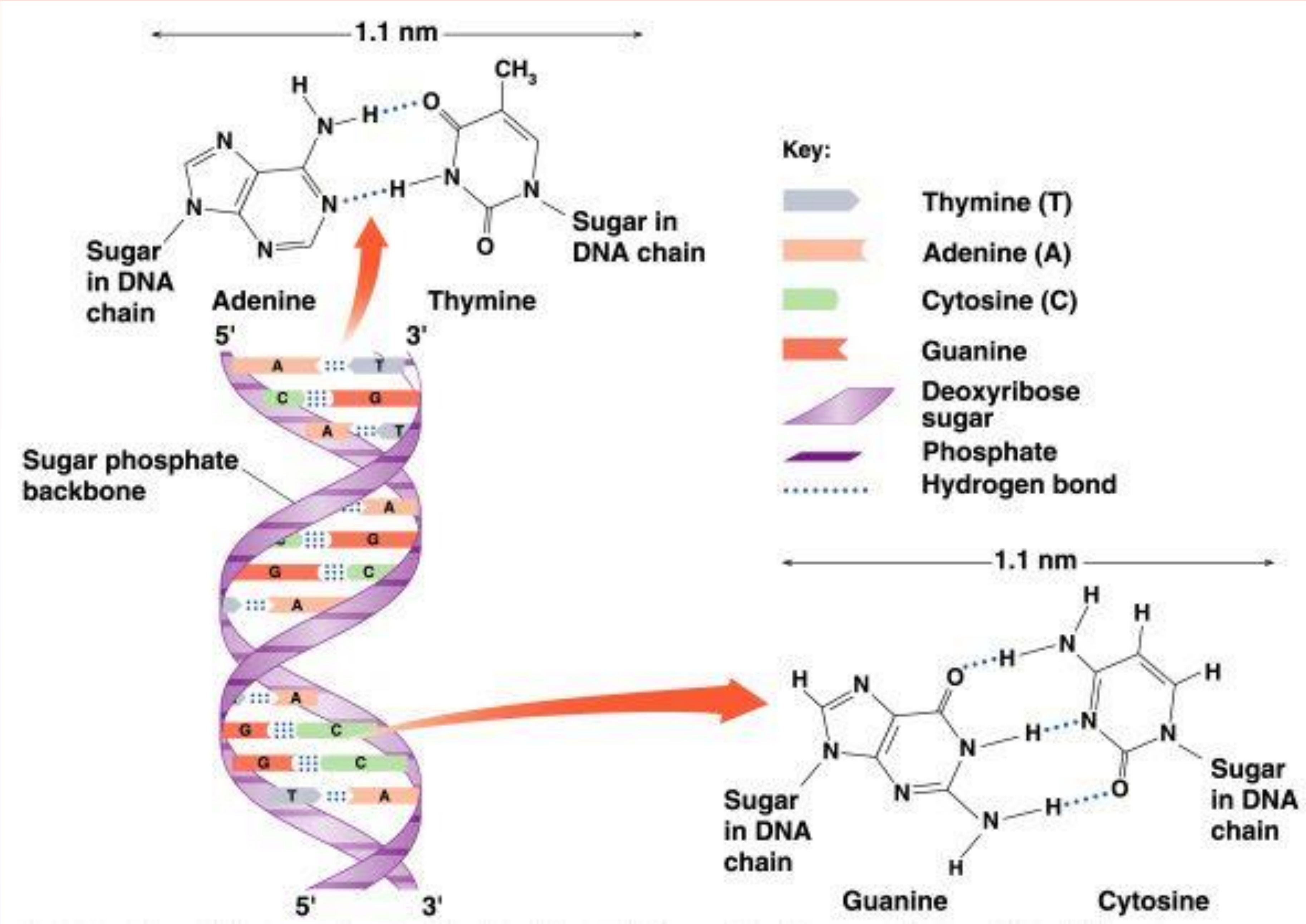
- The pairing of the bases from the two strands is very specific
- The **complimentary base pairs** are **A-T** and **G-C**

  - two hydrogen bonds form between A and T

  - three hydrogen bonds form between G and C

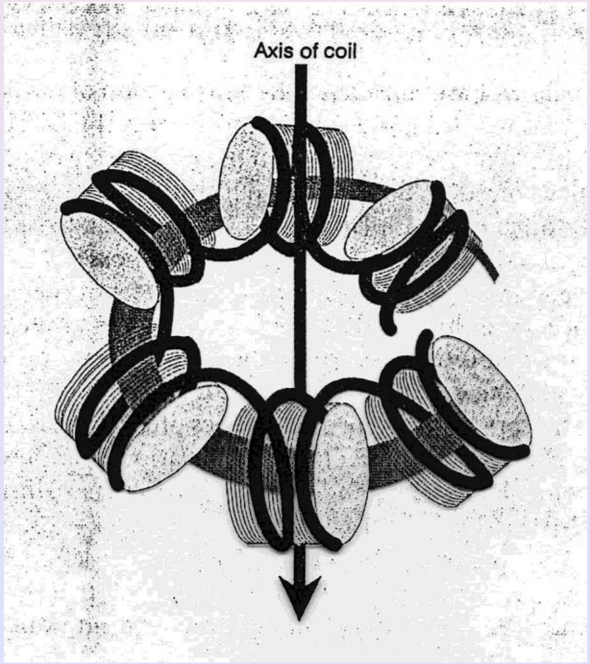
- Each pair consists of a purine and a pyrimidine, so they are the same width, keeping the two strands at equal distances from each other

Base Pairing in the DNA Double Helix



Storage of DNA

- In **eukaryotic** cells (animals, plants, fungi) DNA is stored in the **nucleus**, which is separated from the rest of the cell by a semipermeable membrane
- The DNA is only organized into **chromosomes** during cell replication
- Between replications, the DNA is stored in a compact ball called **chromatin**, and is wrapped around proteins called **histones** to form **nucleosomes**



DNA Replication

- When a eukaryotic cell divides, the process is called **mitosis**

  - the cell splits into two identical daughter cells

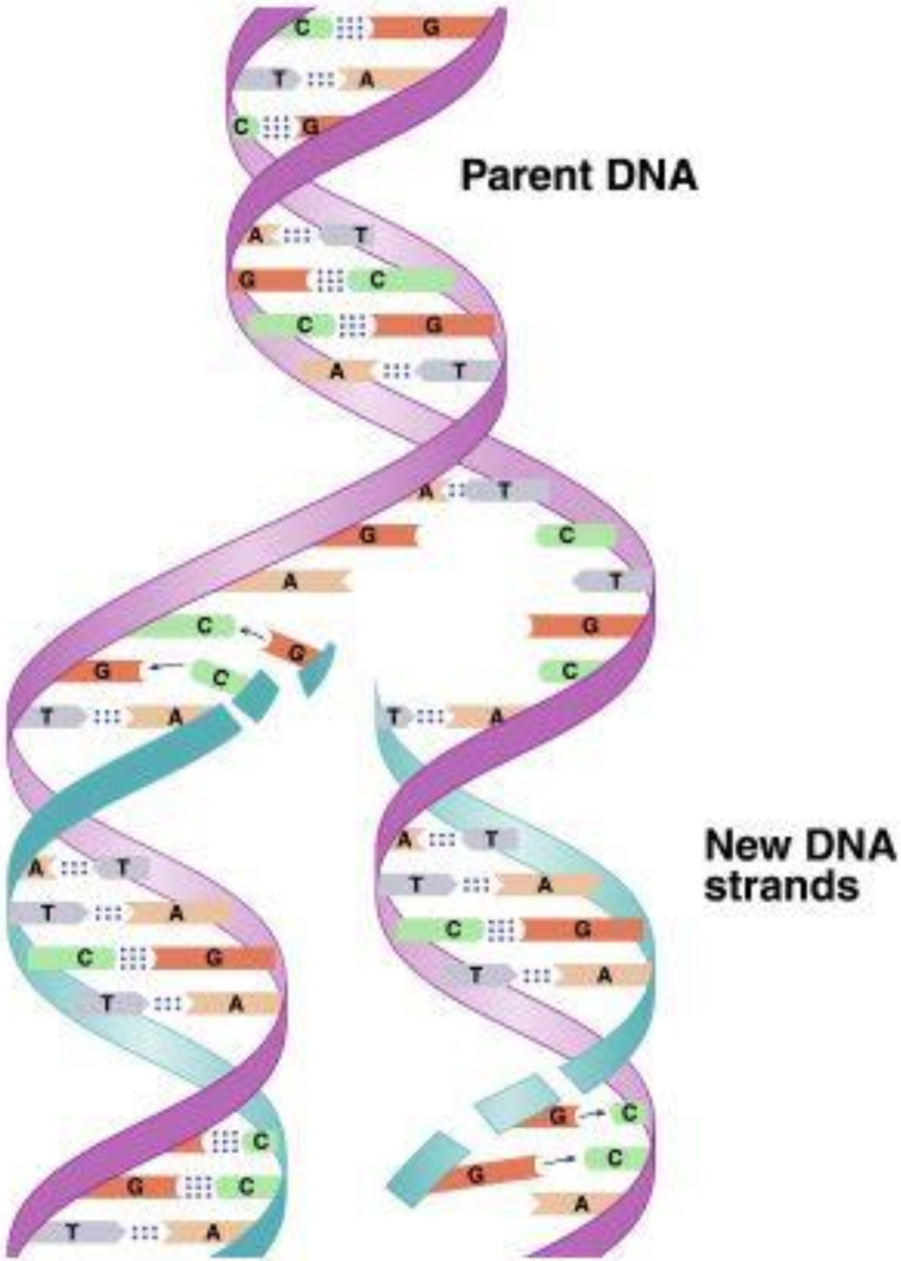
  - the DNA must be replicated so that each daughter cell has a copy
- **DNA replication** involves several processes:

  - first, the DNA must be unwound, separating the two strands

  - the single strands then act as templates for synthesis of the new strands, which are complimentary in sequence

  - bases are added one at a time until two new DNA strands that exactly duplicate the original DNA are produced
- The process is called **semi-conservative replication** because one strand of each daughter DNA comes from the parent DNA and one strand is new
- The energy for the synthesis comes from hydrolysis of phosphate groups as the phosphodiester bonds form between the bases

Semi-Conservative DNA Replication



Ribonucleic Acid (RNA)

- RNA is much more abundant than DNA
- There are several important differences between RNA and DNA:
  - the pentose sugar in RNA is ribose, in DNA it's deoxyribose
  - in RNA, uracil replaces the base thymine (U pairs with A)
  - RNA is single stranded while DNA is double stranded
  - RNA molecules are much smaller than DNA molecules
- There are three main types of RNA:
  - ribosomal (rRNA), messenger (mRNA) and transfer (tRNA)

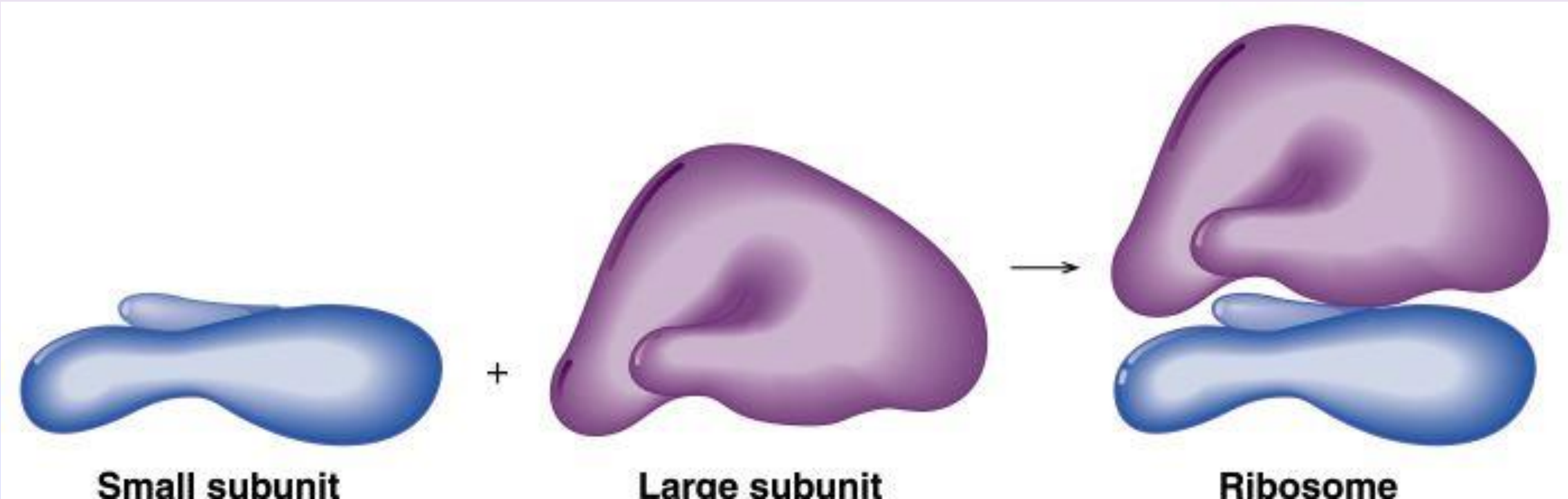
Types of RNA

Table 22.3 Types of RNA Molecules

Type	Abbreviation	Percentage of Total RNA	Function in the Cell
Ribosomal RNA	rRNA	75	Major component of the ribosomes
Messenger RNA	mRNA	5–10	Carries information for protein synthesis from the DNA in the nucleus to the ribosomes
Transfer RNA	tRNA	10–15	Brings amino acids to the ribosomes for protein synthesis

Ribosomal RNA and Messenger RNA

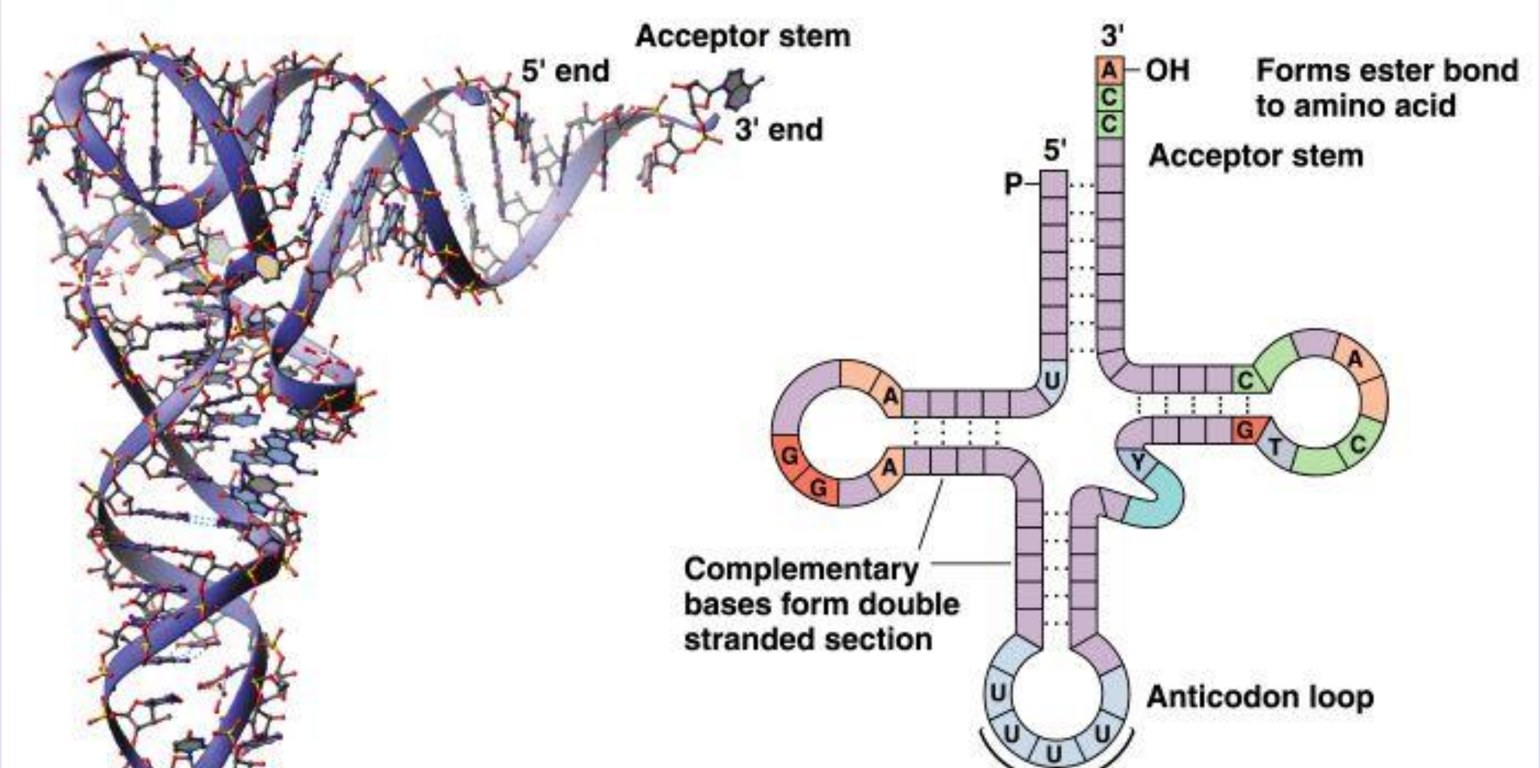
- **Ribosomes** are the sites of protein synthesis
  - they consist of **ribosomal DNA** (65%) and proteins (35%)
  - they have two subunits, a large one and a small one
- **Messenger RNA** carries the genetic code to the ribosomes
  - they are strands of RNA that are complementary to the DNA of the gene for the protein to be synthesized



Transfer RNA

- **Transfer RNA** translates the genetic code from the messenger RNA and brings specific amino acids to the ribosome for protein synthesis
- Each amino acid is recognized by one or more specific tRNA
- tRNA has a tertiary structure that is L-shaped

  - one end attaches to the amino acid and the other binds to the mRNA by a 3-base complimentary sequence



Differences between RNA and DNA

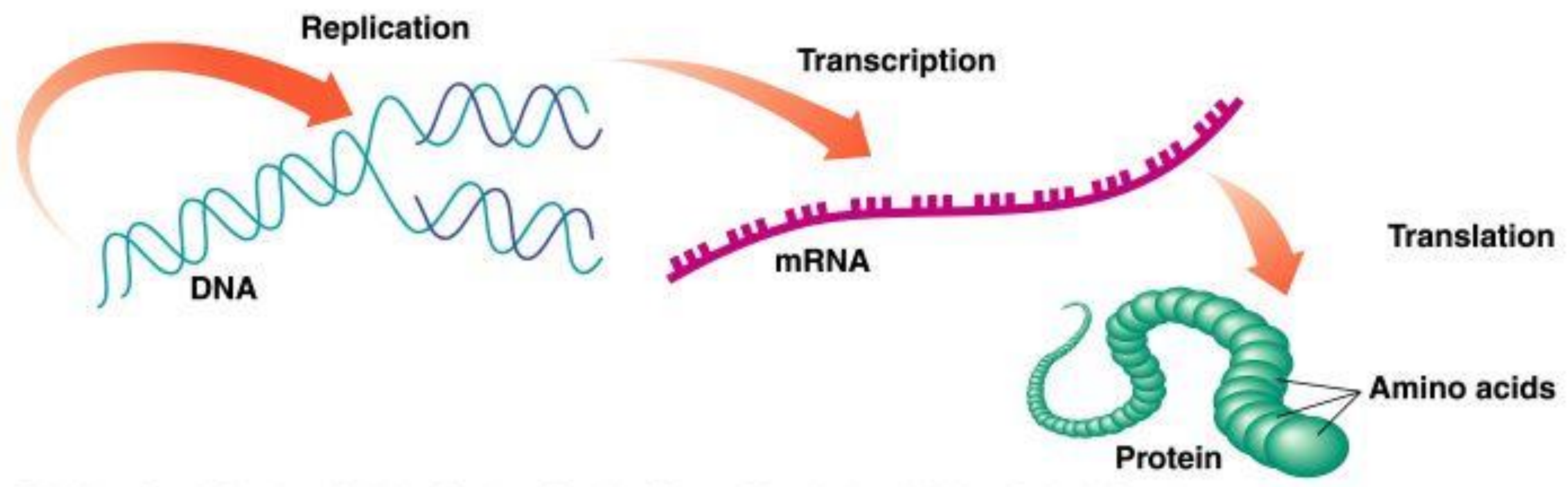
Both have adenine, guanine and cytosine. Both have nucleotides linked by phosphodiester bond, in 3’-5’direction.
Both have important role in protein synthesis.

	DNA	RNA
1. Uracil	absent	Present
2. Sugar	Deoxyribose	Ribose
3. Site	Nucleus, mitochondria but never in cytosol	Nucleus, ribosome, cytosol,

4. Strands	Two helical strands	Single strand
5. Types	Major forms are A,B &Z	t-RNA ,m-RNA,r- RNA,
6. Carries genetic information		Only m-RNA carries genetic information
7. DNA can synthesize RNA by transcription		Usually RNA can’t form DNA except by reverse transcriptase.
8. Number of Bases	equal	Not equal
9. Thymine	Present	Absent

Protein Synthesis

- The two main processes involved in **protein synthesis** are
  - the formation of mRNA from DNA (**transcription**)
  - the conversion by tRNA to protein at the ribosome (**translation**)
- Transcription takes place in the nucleus, while translation takes place in the cytoplasm
- Genetic information is transcribed to form mRNA much the same way it is replicated during cell division



Transcription

- Several steps occur during **transcription**:

  - a section of DNA containing the gene unwinds

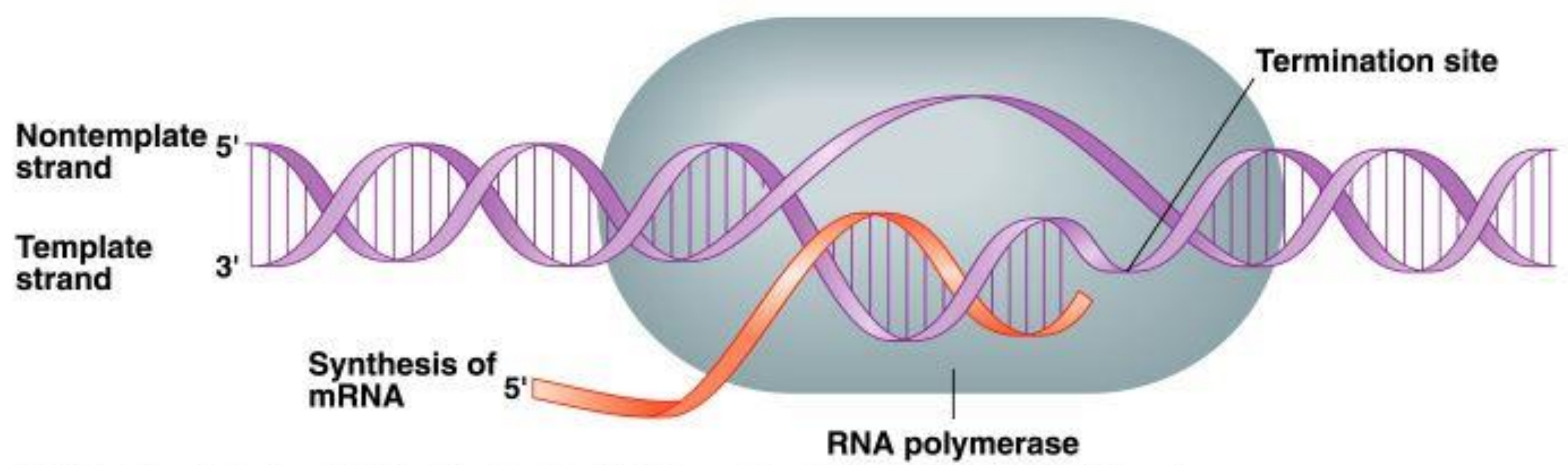
  - one strand of DNA is copied starting at the initiation point, which has the sequence TATAAT

  - an mRNA is synthesized using complementary base pairing with uracil (U) replacing thymine (T)

  - the newly formed mRNA moves out of the nucleus to ribosomes in the cytoplasm and the DNA re-winds

RNA Polymerase

- During transcription, RNA *polymerase* moves along the DNA template in the 3’-5’direction to synthesize the corresponding mRNA
- The mRNA is released at the termination point



Regulation of Transcription

- A specific mRNA is synthesized when the cell requires a particular protein
- The synthesis is regulated at the transcription level:

  - **feedback control**, where the end products speed up or slow the synthesis of mRNA

  - **enzyme induction**, where a high level of a reactant induces the transcription process to provide the necessary enzymes for that reactant
- Regulation of transcription in eukaryotes is complicated and we will not study it here

The Genetic Code

- The **genetic code** is found in the sequence of nucleotides in mRNA that is translated from the DNA
- A **codon** is a **triplet** of bases along the mRNA that codes for a particular amino acid
- Each of the 20 amino acids needed to build a protein has at least 2 codons
- There are also codons that signal the “start” and “end” of a polypeptide chain
- The amino acid sequence of a protein can be determined by reading the triplets in the DNA sequence that are complementary to the codons of the mRNA, or directly from the mRNA sequence
- The entire DNA sequence of several organisms, including humans, have been determined, however,

  - only primary structure can be determined this way

  - doesn’t give tertiary structure or protein function

mRNA Codons and Associated Amino Acids

Second Letter

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

[a] Codon that signals the start of a peptide chain.
STOP codons signal the end of a peptide chain.

Reading the Genetic Code

- Suppose we want to determine the amino acids coded for in the following section of a mRNA

  5’—CCU —AGC—GGA—CUU—3’

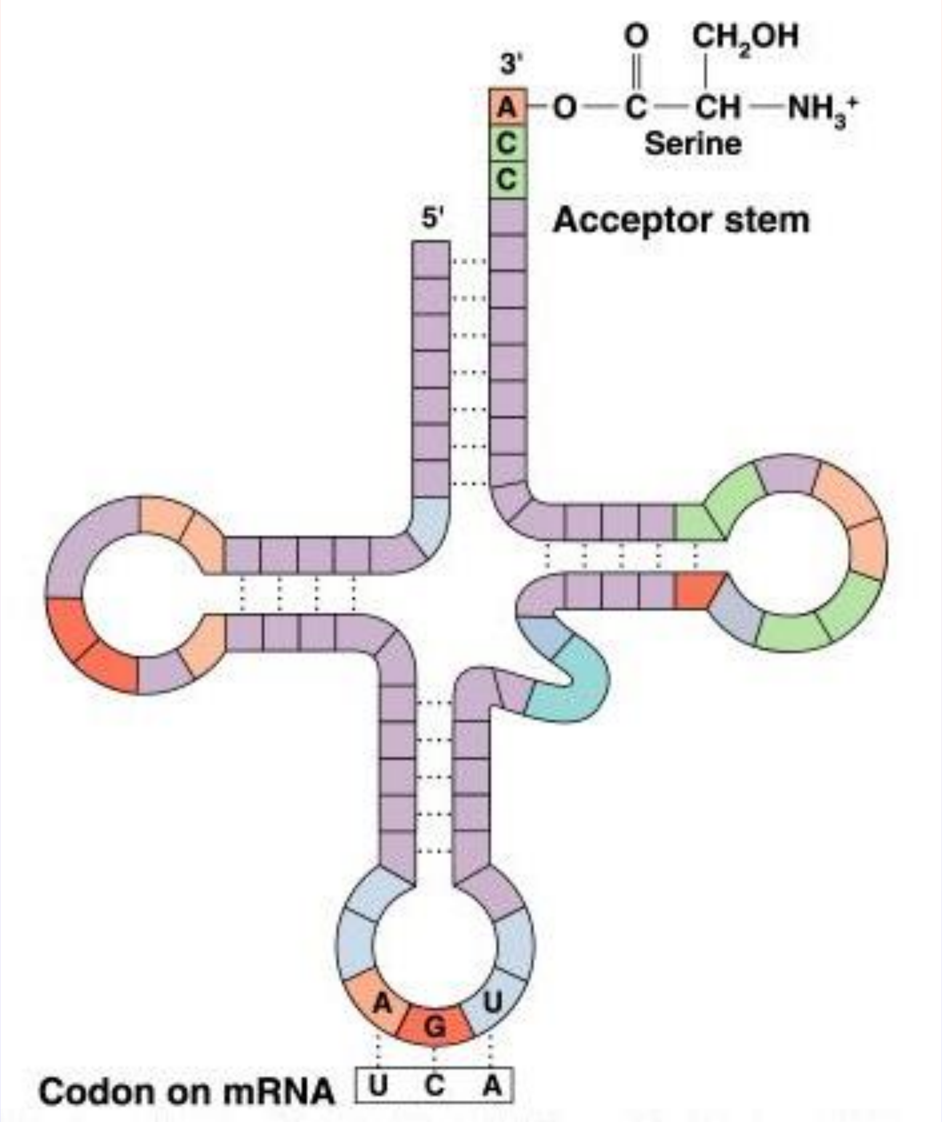
- According to the genetic code, the amino acids for these codons are:

CCU = Proline	AGC = Serine
GGA = Glycine	CUU = Leucine

- The mRNA section codes for the amino acid sequence of Pro—Ser—Gly—Leu

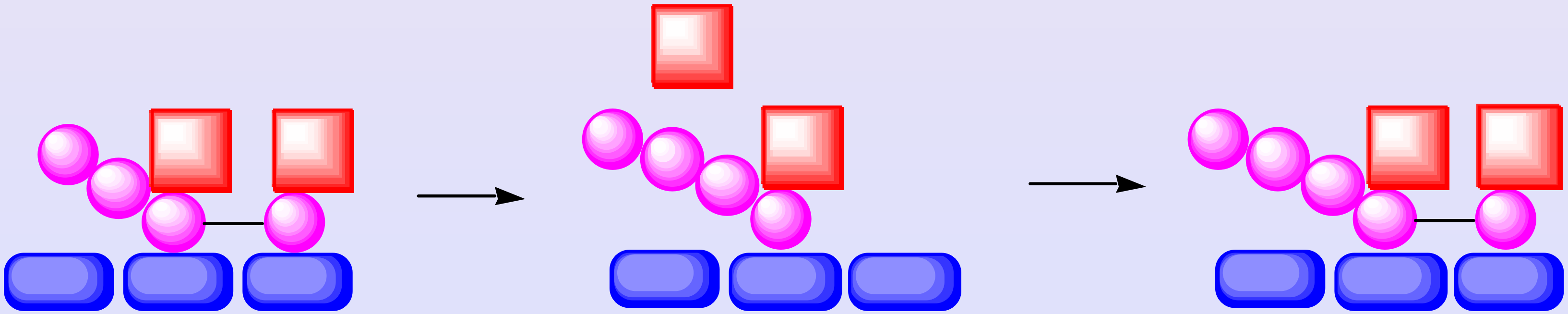
Translation and tRNA Activation

- Once the DNA has been transcribed to mRNA, the codons must be tranlated to the amino acid sequence of the protein
- The first step in **translation** is activation of the tRNA
- Each tRNA has a triplet called an **anticodon** that complements a codon on mRNA
- A *synthetase* uses ATP hydrolysis to attach an amino acid to a specific tRNA



Initiation and Translocation

- Initiation of protein synthesis occurs when a mRNA attaches to a ribosome
- On the mRNA, the **start codon (AUG)** binds to a tRNA with methionine
- The second codon attaches to a tRNA with the next amino acid
- A peptide bond forms between the adjacent amino acids at the first and second codons
- The first tRNA detaches from the ribosome and the ribosome shifts to the adjacent codon on the mRNA (this process is called **translocation**)
- A third codon can now attach where the second one was before translocation



Termination

- After a polypeptide with all the amino acids for a protein is synthesized, the ribosome reaches the the **“stop” codon**: UGA, UAA, or UAG
- There is no tRNA with an anticodon for the “stop” codons
- Therefore, protein synthesis ends (**termination**)
- The polypeptide is released from the ribosome and the protein can take on it’s 3-D structure

  (some proteins begin folding while still being synthesized, while others do not fold up until after being released from the ribosome)