DNA Replication & Protein Synthesis

The Discovery of DNA's Structure

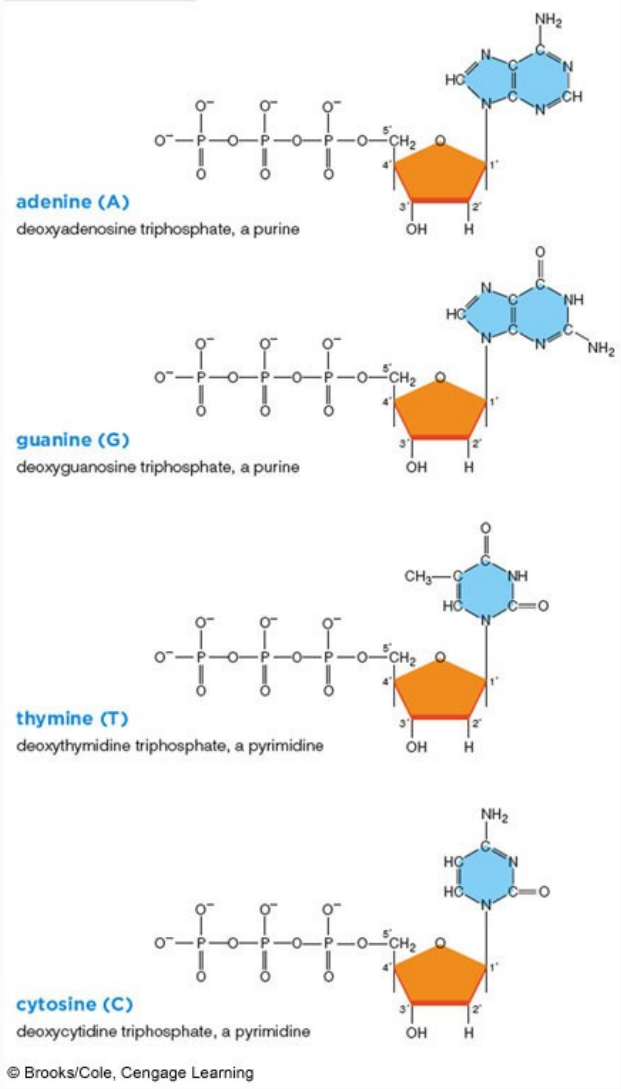
- Watson and Crick's discovery of DNA's structure was based on almost fifty years of research by other scientists

DNA's Building Blocks

- **Nucleotide**
  - A nucleic acid monomer consisting of a five-carbon sugar (deoxyribose), three phosphate groups, and one of four nitrogen-containing bases

- DNA consists of four nucleotide building blocks
  - Two pyrimidines: **thymine** and **cytosine**
  - Two purines: **adenine** and **guanine**

Four Kinds of Nucleotides in DNA



Chargaff's Rules

- The amounts of thymine and adenine in DNA are the same, and the amounts of cytosine and guanine are the same: A = T and G = C

- The proportion of adenine and guanine differs among species

Watson and Crick's DNA Model

- A DNA molecule consists of two nucleotide chains (strands), running in opposite directions and coiled into a double helix

- Base pairs form on the inside of the helix, held together by hydrogen bonds (A-T and G-C)

Patterns of Base Pairing

- Bases in DNA strands can pair in only one way
  - A always pairs with T; G always pairs with C

- The sequence of bases is the genetic code
  - Variation in base sequences gives life diversity

Structure of DNA

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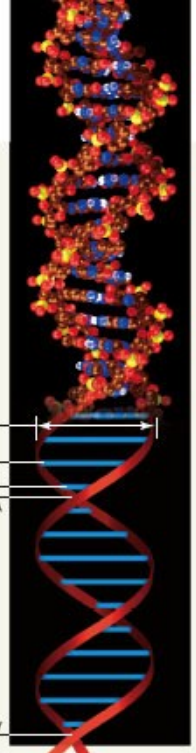
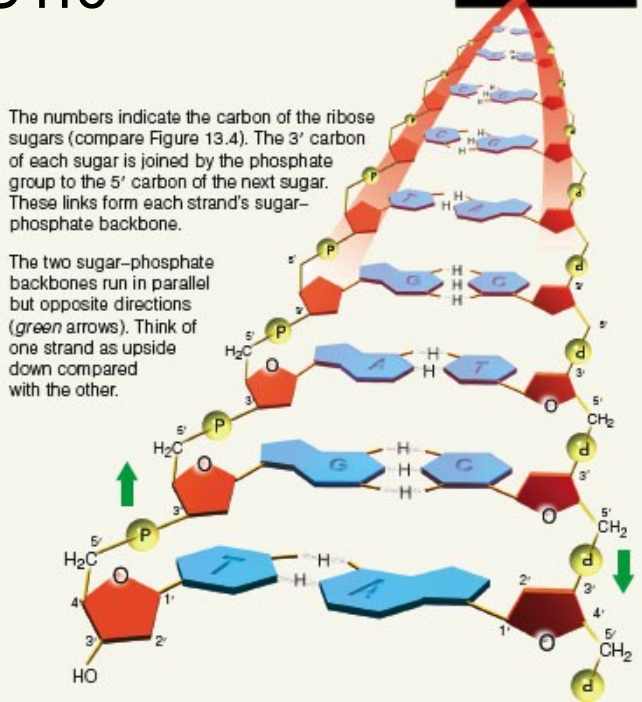
Watson and Crick with their model





Key Concepts

Discovery of DNA's Structure

- *A DNA molecule consists of two long chains of nucleotides coiled into a double helix*
- *Four kinds of nucleotides make up the chains, which are held together along their length by hydrogen bonds*

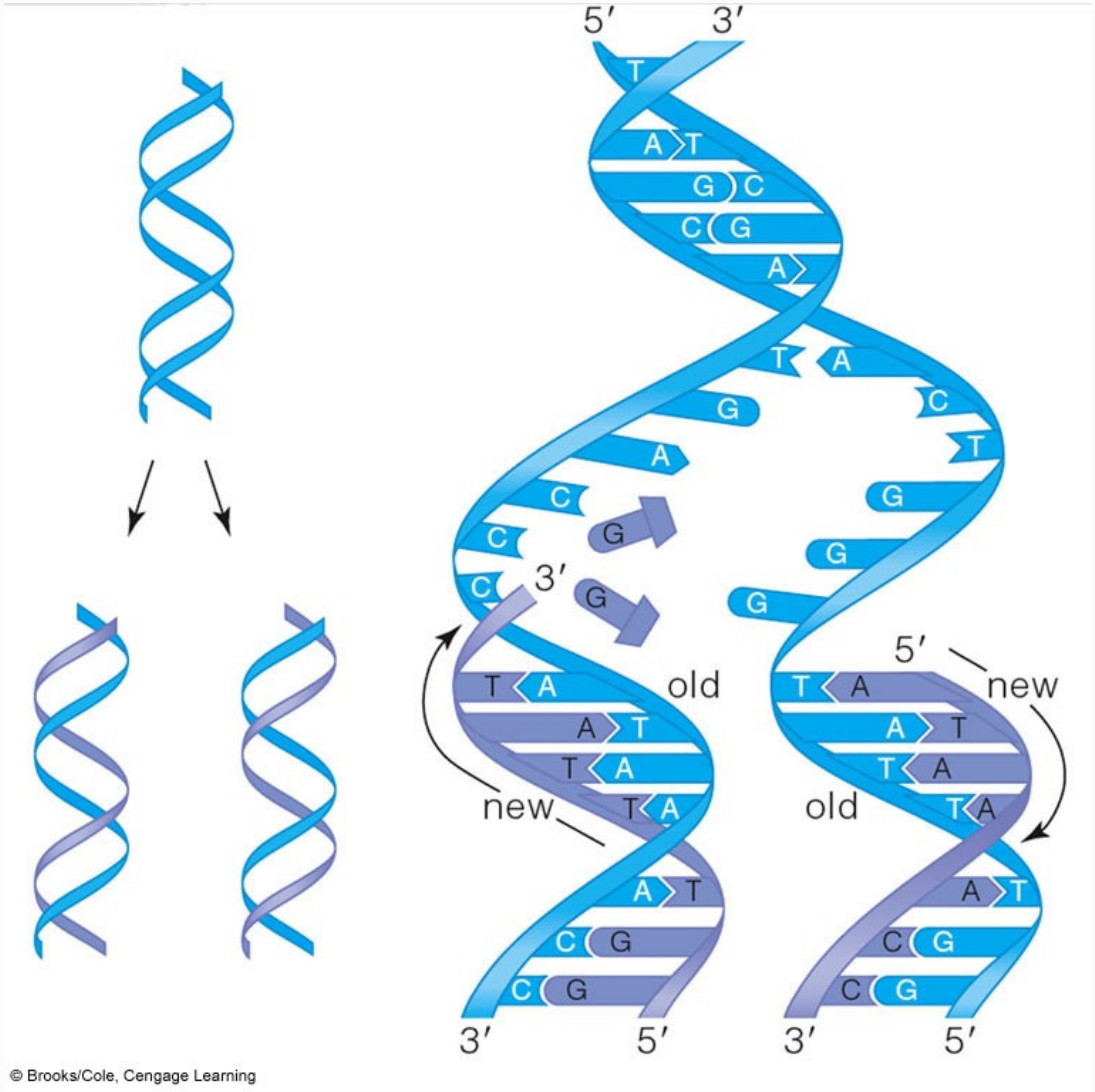
DNA Replication and Repair

- A cell copies its DNA before mitosis or meiosis I
- DNA repair mechanisms and proofreading correct most replication errors

Semiconservative DNA Replication

- Each strand of a DNA double helix is a template for synthesis of a complementary strand of DNA
- One template builds DNA continuously; the other builds DNA discontinuously, in segments
- Each new DNA molecule consist of one old strand and one new strand

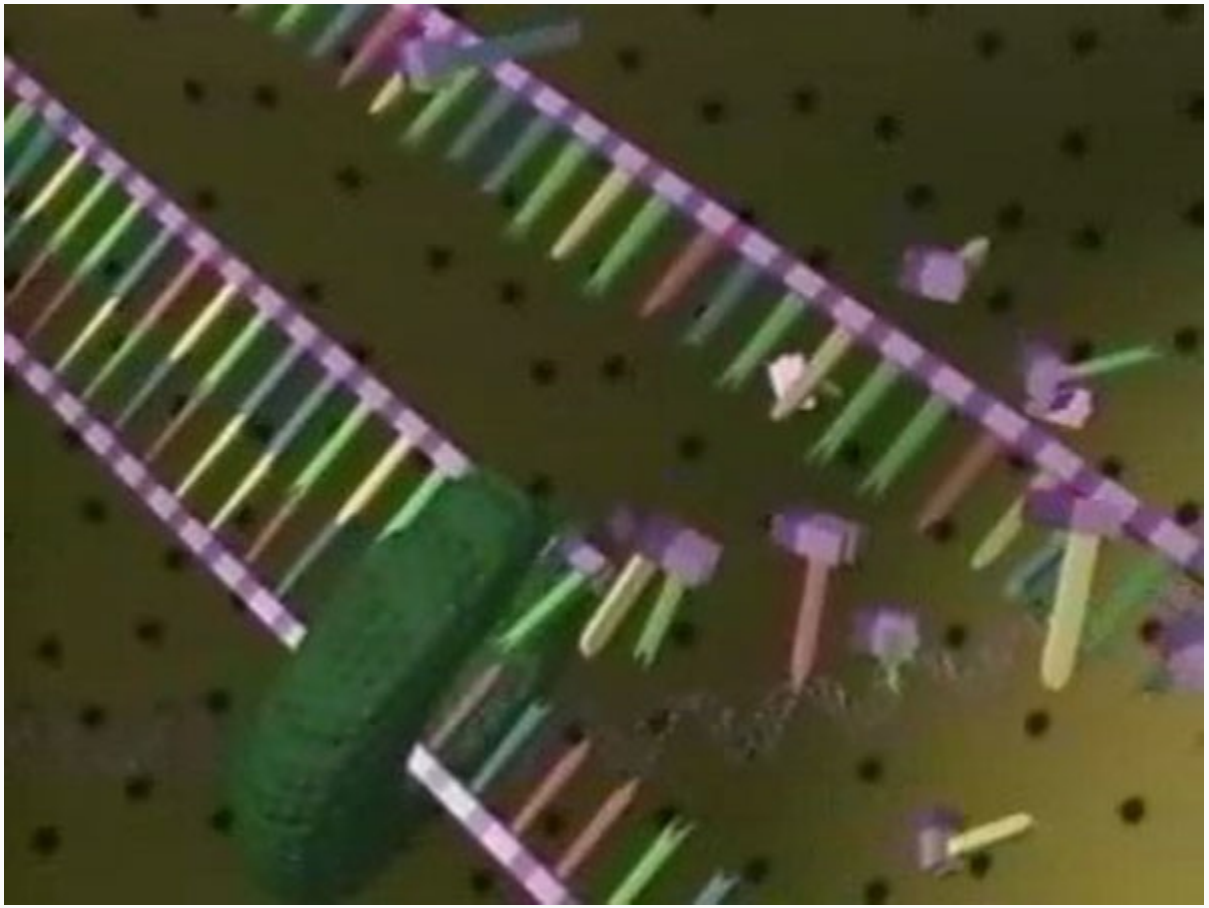
Semiconservative Replication of DNA



Enzymes of DNA Replication

- **DNA helicase**
  - Breaks hydrogen bonds between DNA strands
- **DNA polymerase**
  - Joins free nucleotides into a new strand of DNA
- **DNA ligase**
  - Joins DNA segments on discontinuous strand

Animation: DNA replication



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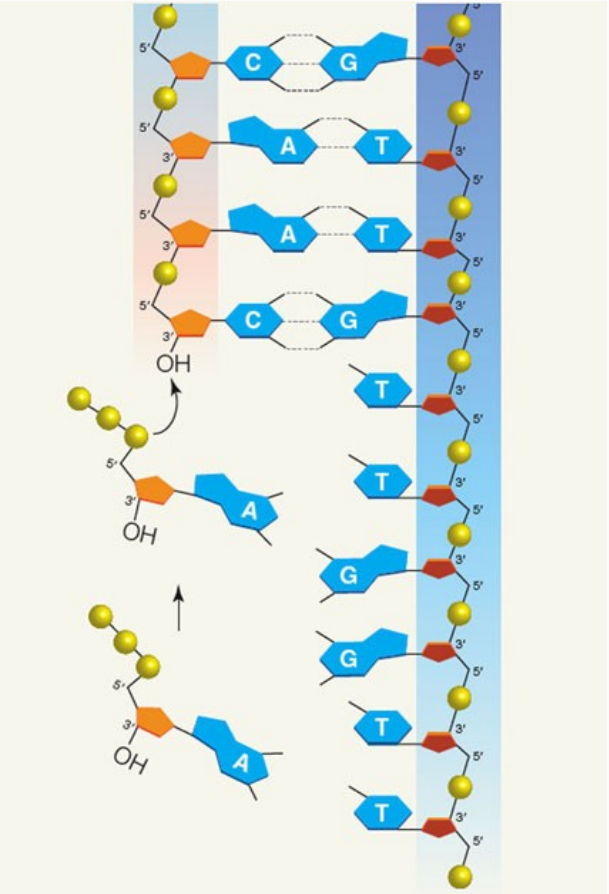
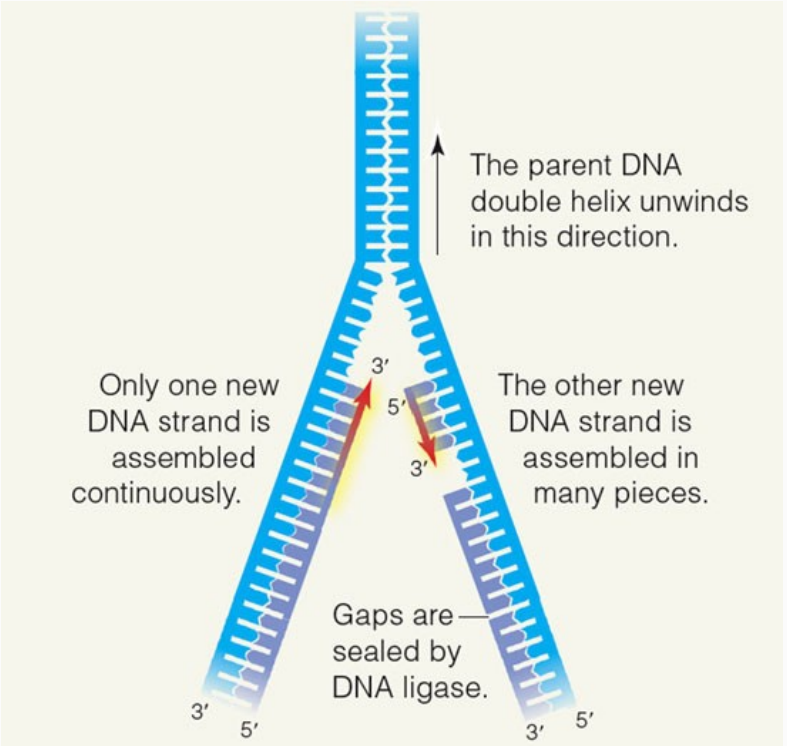
Discontinuous Synthesis of DNA



A Each DNA strand has two ends: one with a 5′ carbon, and one with a 3′ carbon. DNA polymerase can add nucleotides only at the 3′ carbon. In other words, DNA synthesis proceeds only in the 5′ to 3′ direction.

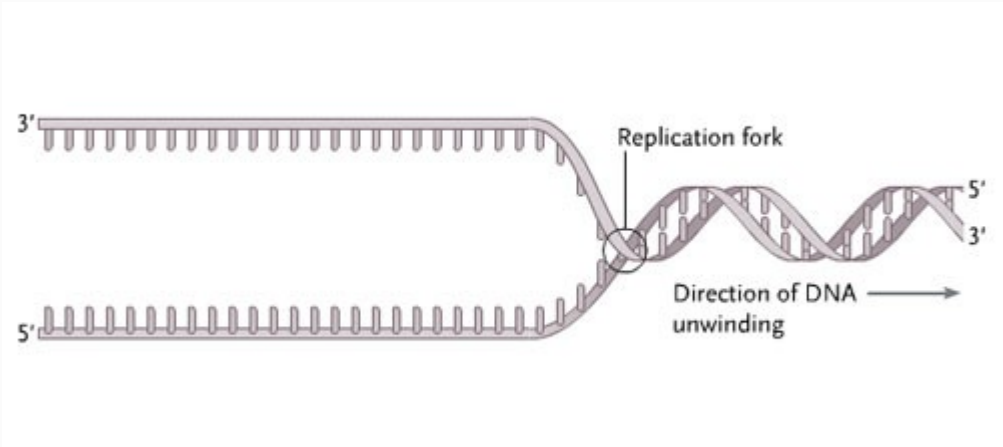


B Because DNA synthesis proceeds only in the 5′ to 3′ direction, only one of the two new DNA strands can be assembled in a single piece.

The other new DNA strand forms in short segments, which are called Okazaki fragments after the two scientists who discovered them. DNA ligase joins the fragments into a continuous strand of DNA.

It jumps back! It has to be assembled at the unwinding!

Animation: Semidiscontinuous DNA replication



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Checking for Mistakes

- **Because so much DNA is being replicated in the many cells of the body, there is a potential for errors to occur!**

- **DNA repair mechanisms**
  - DNA polymerases proofread DNA sequences during DNA replication and repair damaged DNA

- When proofreading and repair mechanisms fail, an error becomes a **mutation** – a permanent change in the DNA sequence.
  - Can alter the genetic message and affect protein synthesis

Mutations

- Mutations in germ cells
  - Passed to future generations
  - Important for evolutionary change

- Mutations in somatic cells
  - Not passed to future generations but passed to all other somatic cells derived from it

Key Concepts
How Cells Duplicate Their DNA

- *Before a cell begins mitosis or meiosis, enzymes and other proteins replicate its chromosome(s)*
- *Newly forming DNA strands are monitored for errors*
- *Uncorrected errors may become mutations*

From DNA to Protein – Transcription and Translation

The Nature of Genetic Information

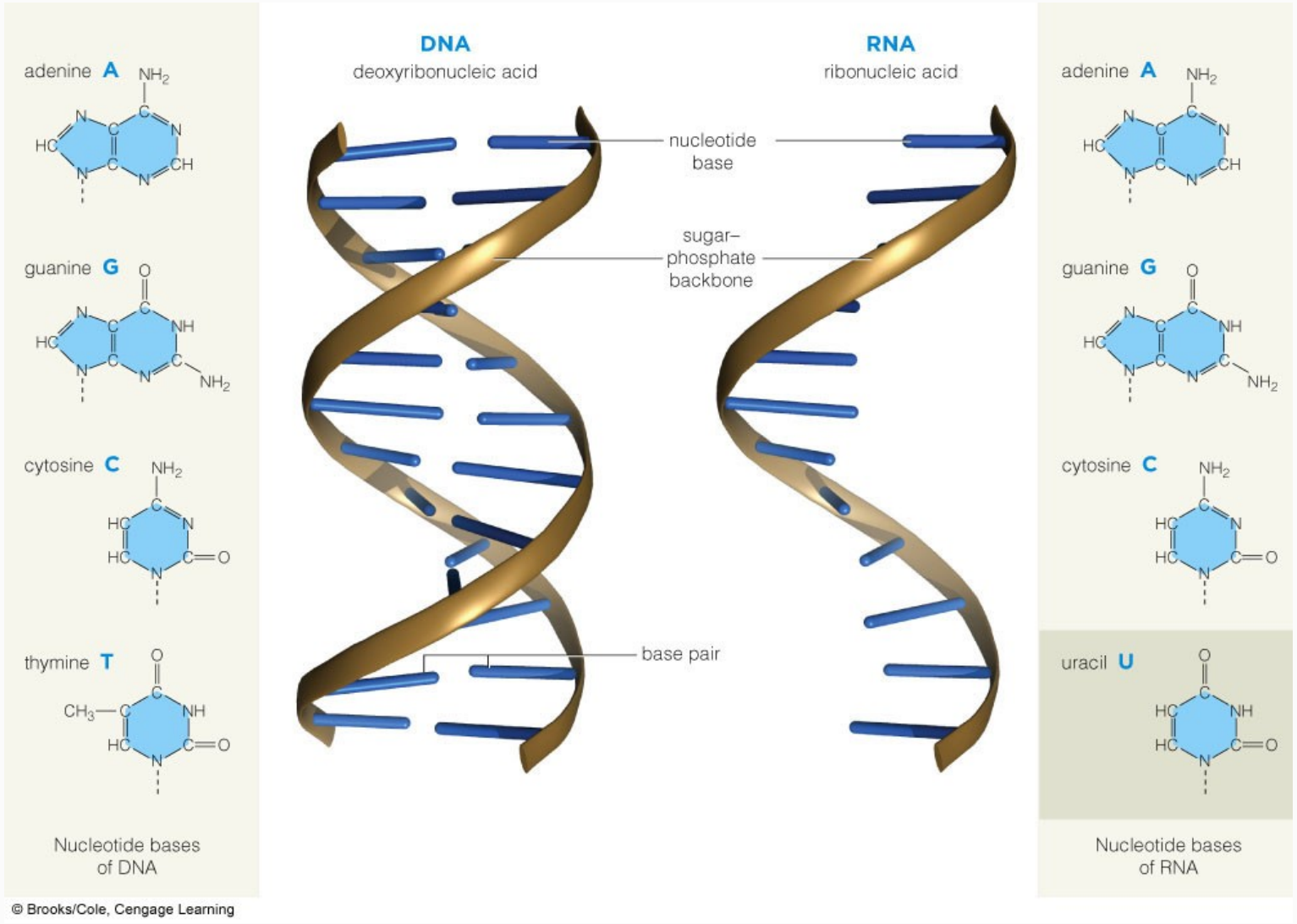
- Each strand of DNA consists of a chain of four kinds of nucleotides: A, T, G and C
- The sequence of the four bases in the strand is the genetic information
- Transcription and translation are used to turn the DNA strand's base sequence into a protein

Converting a Gene to an RNA

- **Transcription**
  - Enzymes use the nucleotide sequence of a gene to synthesize a complementary strand of RNA

- DNA is transcribed to RNA
  - Most RNA is single stranded
  - RNA uses uracil in place of thymine
  - RNA uses ribose in place of deoxyribose

DNA and RNA



RNA in Protein Synthesis

- **Messenger RNA (mRNA)**
  - Contains information transcribed from DNA
- **Ribosomal RNA (rRNA)**
  - Main component of ribosomes, where polypeptide chains are built
- **Transfer RNA (tRNA)**
  - Delivers amino acids to ribosomes

Converting mRNA to Protein

- **Translation**
  - The information carried by mRNA is decoded into a sequence of amino acids, resulting in a polypeptide chain that folds into a protein

- mRNA is translated to protein
  - rRNA and tRNA translate the sequence of base triplets in mRNA into a sequence of amino acids

Key Concepts
DNA to RNA to Protein

- *Proteins consist of polypeptide chains*
- *The chains are sequences of amino acids that correspond to sequences of nucleotide bases in DNA called genes*
- *The path leading from genes to proteins has two steps: transcription and translation*

Transcription: DNA to RNA

- RNA polymerase assembles RNA by linking RNA nucleotides into a chain, in the order dictated by the base sequence of a gene

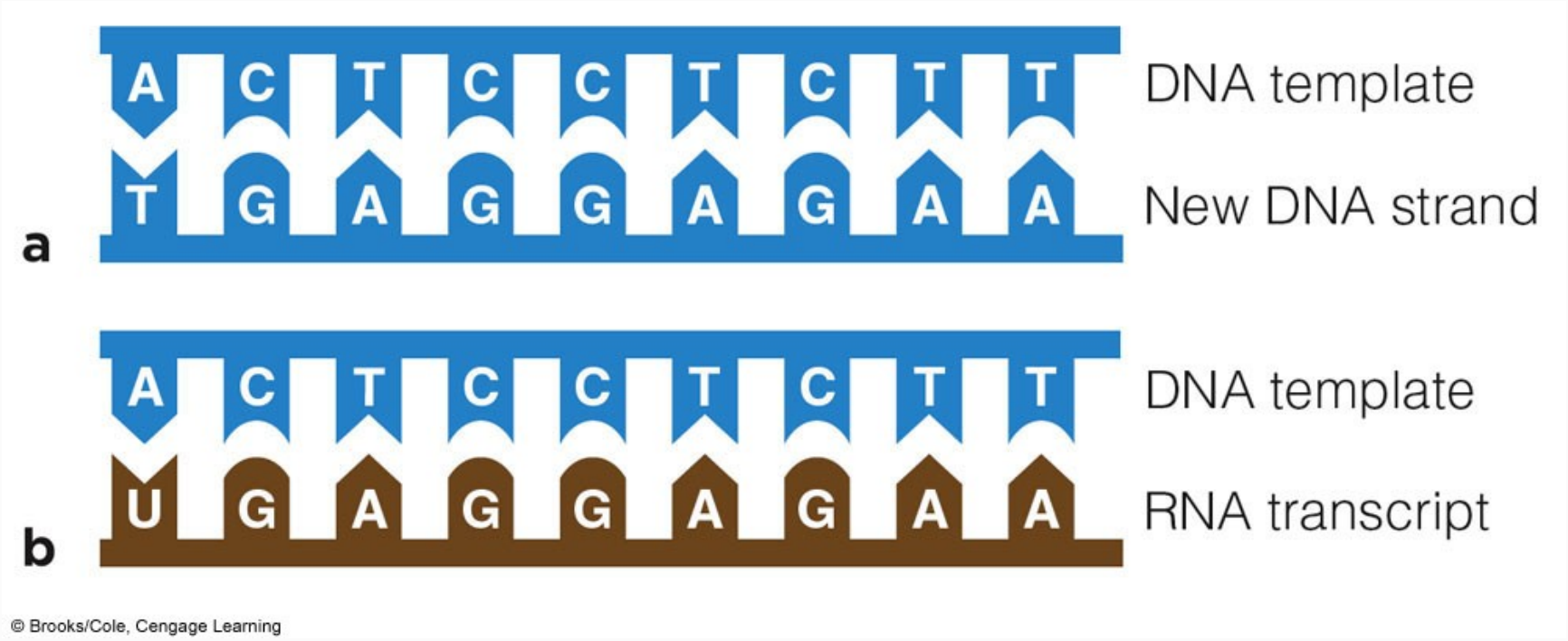
- A new RNA strand is complementary in sequence to the DNA strand from which it was transcribed

DNA Replication and Transcription

- DNA replication and transcription both synthesize new molecules by base-pairing

- In transcription, a strand of mRNA is assembled on a DNA template using RNA nucleotides
  - Uracil (U) nucleotides pair with A nucleotides
  - **RNA polymerase** adds nucleotides to the transcript

Base-Pairing in DNA Synthesis and Transcription

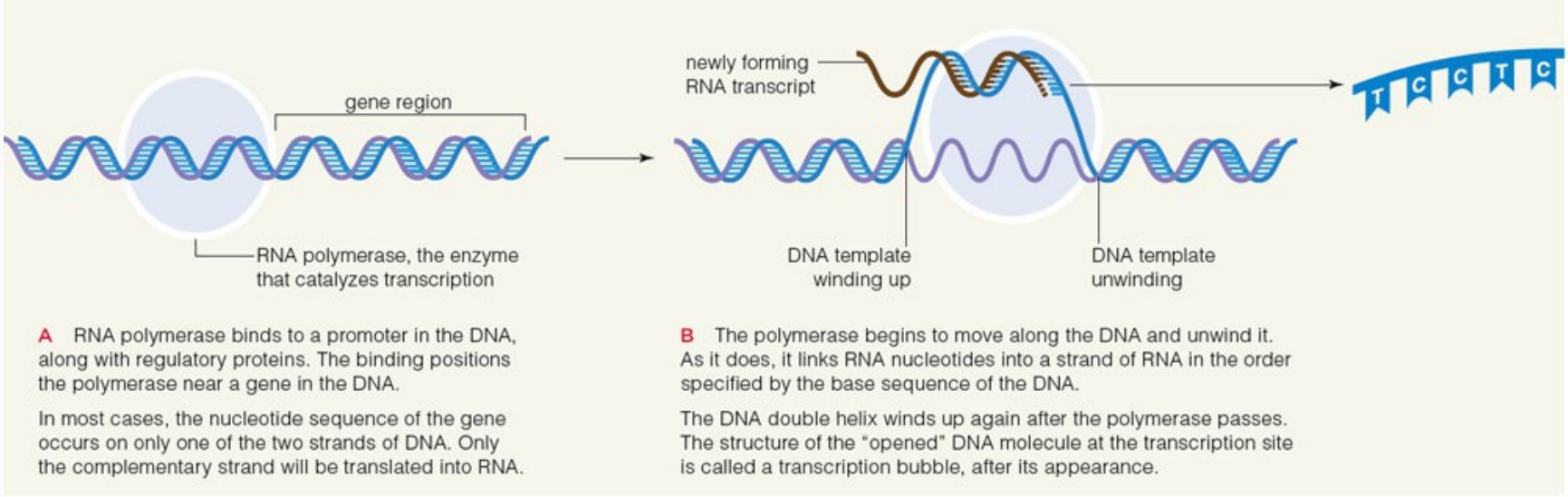


The Process of Transcription

- RNA polymerase and regulatory proteins attach to a **promoter** (a specific binding site in DNA close to the start of a gene)

- RNA polymerase moves over the gene in a 5' to 3' direction, unwinds the DNA helix, reads the base sequence, and joins free RNA nucleotides into a complementary strand of mRNA

Transcription



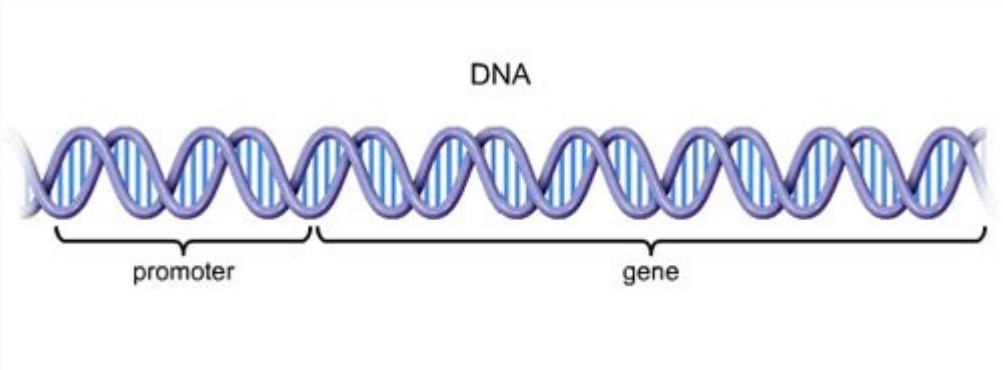
A RNA polymerase binds to a promoter in the DNA, along with regulatory proteins. The binding positions the polymerase near a gene in the DNA.

In most cases, the nucleotide sequence of the gene occurs on only one of the two strands of DNA. Only the complementary strand will be translated into RNA.

B The polymerase begins to move along the DNA and unwind it. As it does, it links RNA nucleotides into a strand of RNA in the order specified by the base sequence of the DNA.

The DNA double helix winds up again after the polymerase passes. The structure of the "opened" DNA molecule at the transcription site is called a transcription bubble, after its appearance.

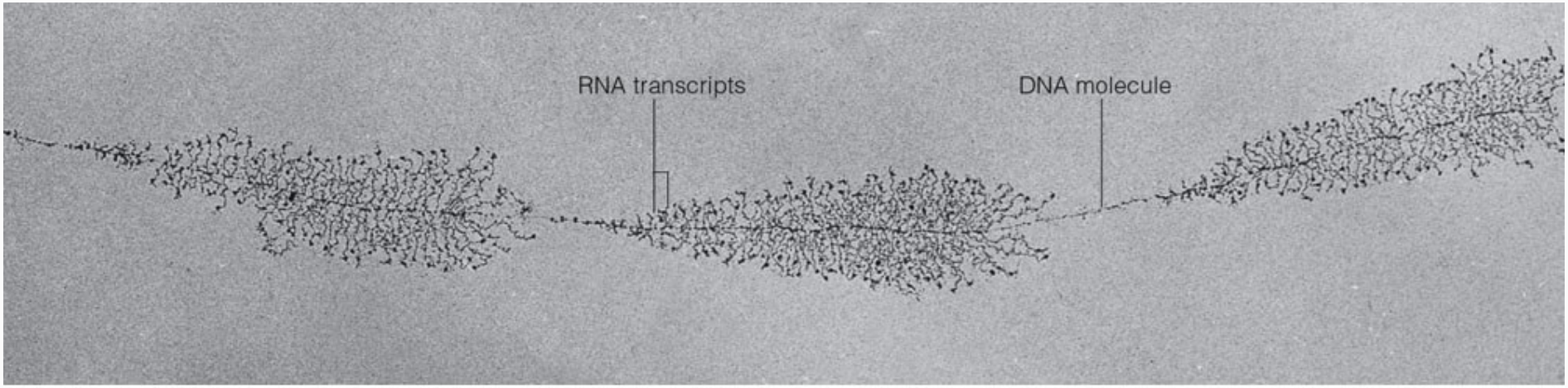
Animation: Gene transcription details



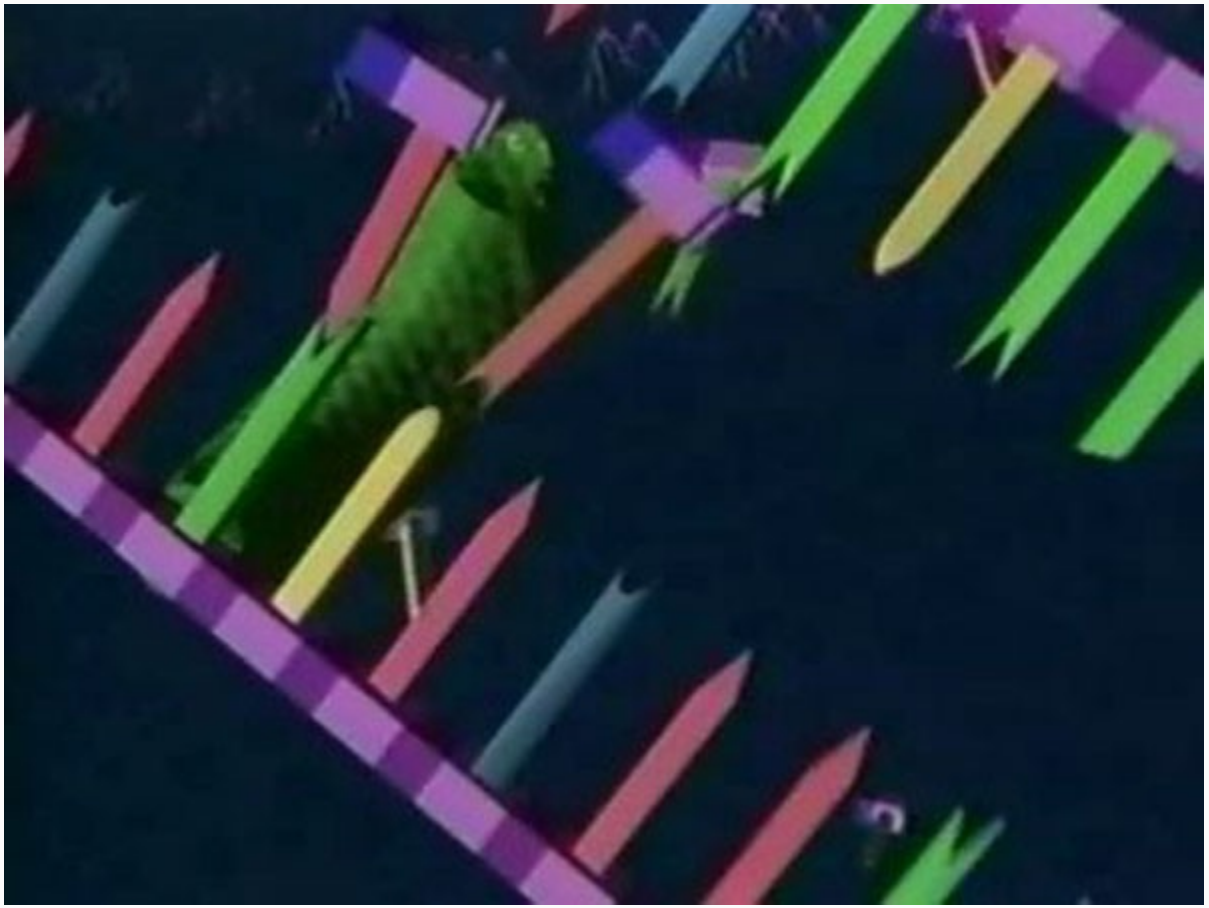
http://www.youtube.com/v/vJSmZ3DsntU

Transcription

- Many RNA polymerases can transcribe a gene at the same time



Animation: Transcription



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Key Concepts
DNA to RNA: Transcription

- *During transcription, one strand of a DNA double helix is a template for assembling a single, complementary strand of RNA (a transcript)*

- *Each transcript is an RNA copy of a gene*

RNA and the Genetic Code

- Base triplets in an mRNA are words in a protein-building message
- Two other classes of RNA (rRNA and tRNA) translate those words into a polypeptide chain

Post-Transcriptional Modifications

- In eukaryotes, RNA is modified before it leaves the nucleus as a mature mRNA

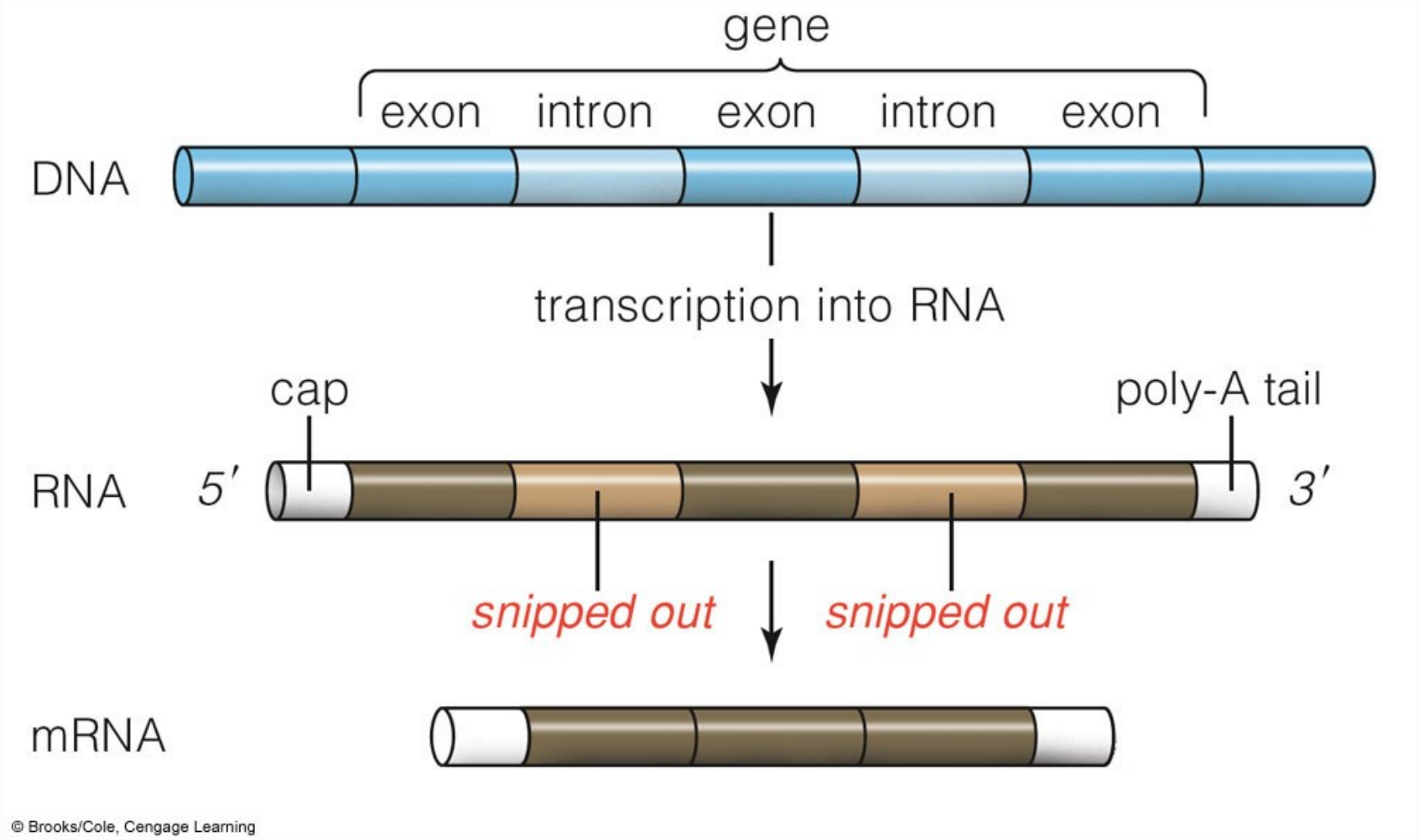
- **Introns**
  - Nucleotide sequences that are removed from a new RNA

- **Exons**
  - Sequences that stay in the RNA

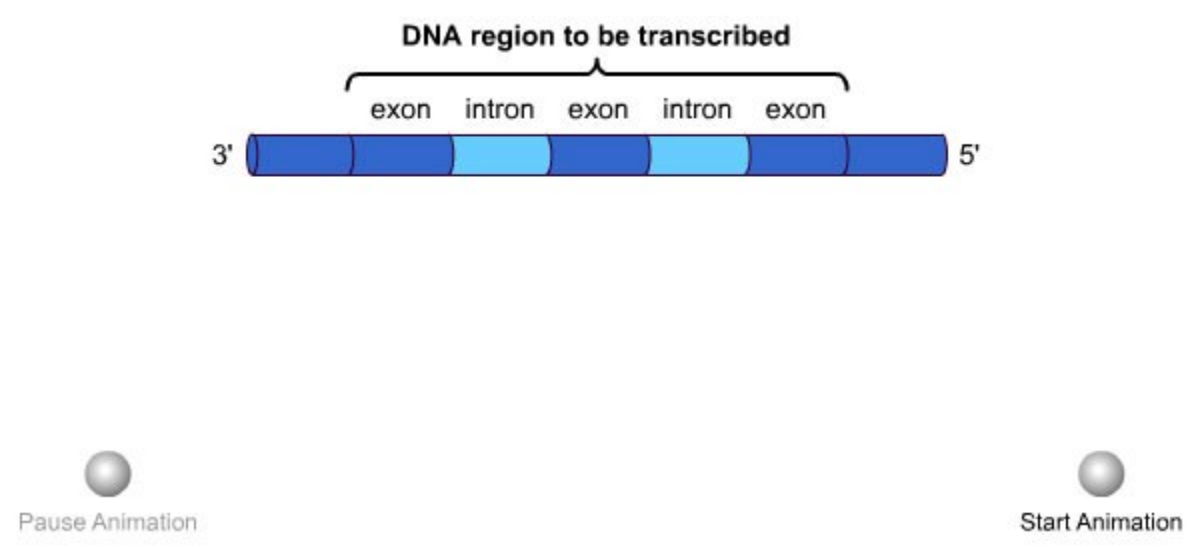
Alternative Splicing

- **Alternative splicing**
  - Allows one gene to encode different proteins
  - Some exons are removed from RNA and others are spliced together in various combinations

Post-Transcriptional Modifications



Animation: Pre-mRNA transcript processing



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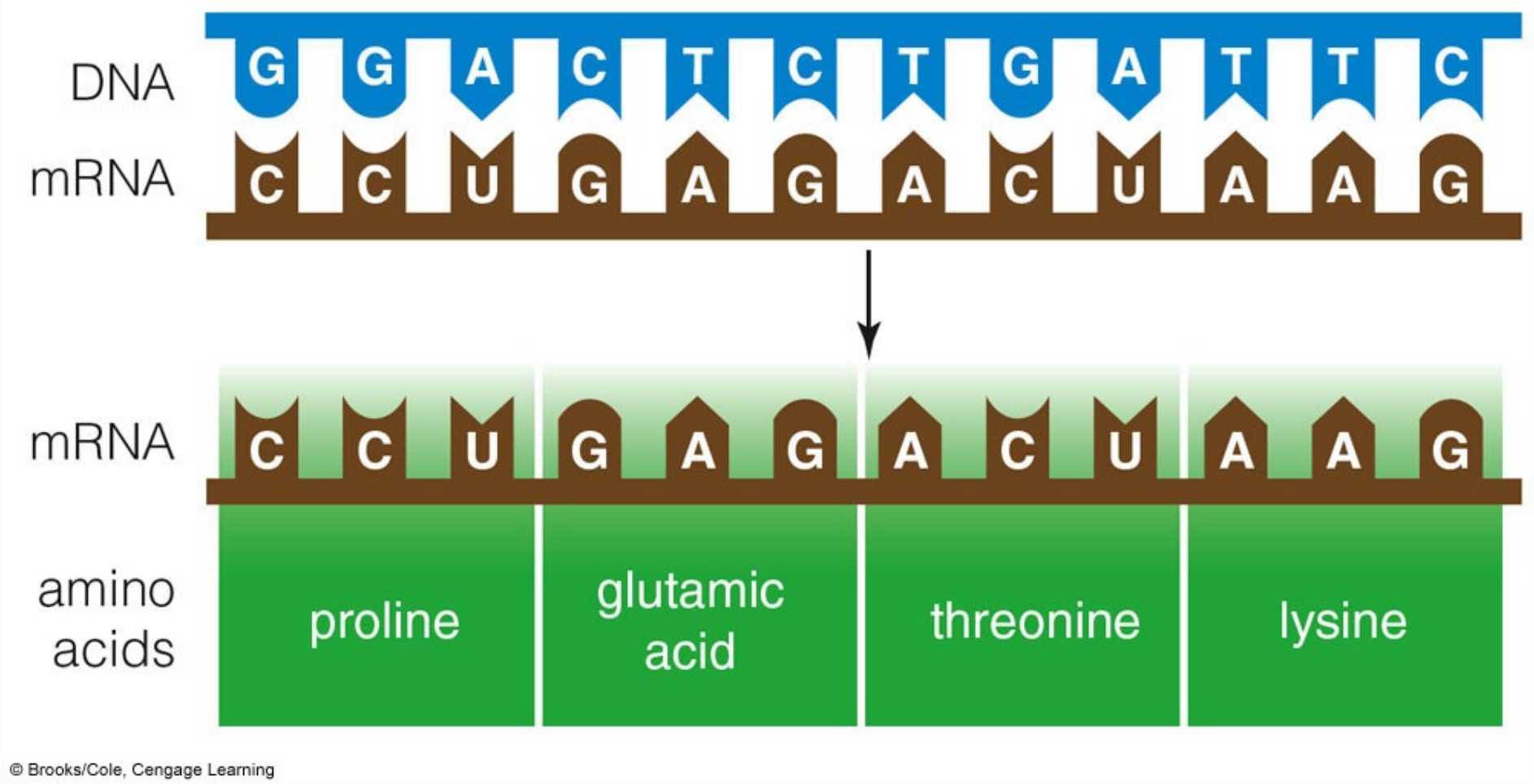
mRNA – The Messenger

- mRNA carries protein-building information to ribosomes and tRNA for translation

- **Codon**
  - A sequence of three mRNA nucleotides that codes for a specific amino acid
  - The order of codons in mRNA determines the order of amino acids in a polypeptide chain

Genetic Information

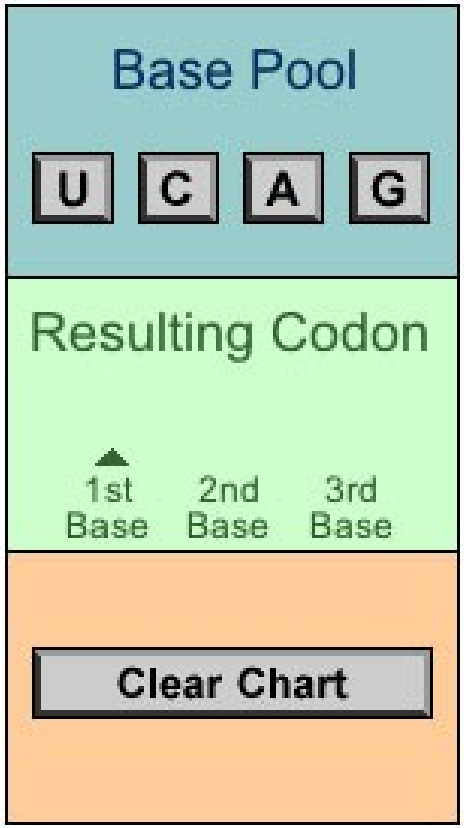
- From DNA to mRNA to amino acid sequence



Genetic Code

- **Genetic code**
  - Consists of 64 mRNA codons (triplets)
  - Some amino acids can be coded by more than one codon
- Some codons signal the start or end of a gene
  - AUG (methionine) is a start codon
  - UAA, UAG, and UGA are stop codons

The Genetic code



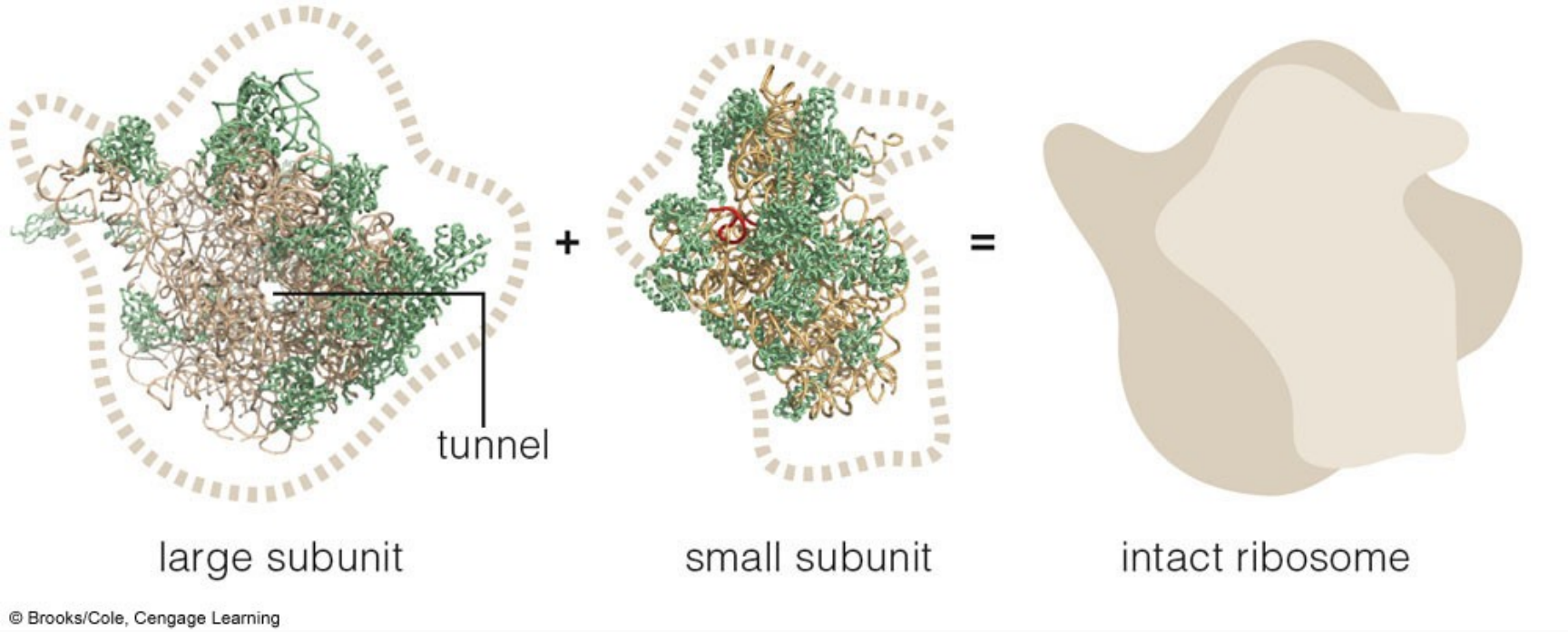
	U	C	A	G	
U	phenylalanine	serine	tyrosine	cysteine	U
	phenylalanine	serine	tyrosine	cysteine	C
	leucine	serine	stop	stop	A
	leucine	serine	stop	tryptophan	G
C	leucine	proline	histidine	arginine	U
	leucine	proline	histidine	arginine	C
	leucine	proline	glutamine	arginine	A
	leucine	proline	glutamine	arginine	G
A	isoleucine	threonine	asparagine	serine	U
	isoleucine	threonine	asparagine	serine	C
	isoleucine	threonine	lysine	arginine	A
	methionine (start)	threonine	lysine	arginine	G
G	valine	alanine	aspartate	glycine	U
	valine	alanine	aspartate	glycine	C
	valine	alanine	glutamate	glycine	A
	valine	alanine	glutamate	glycine	G

rRNA and tRNA – The Translators

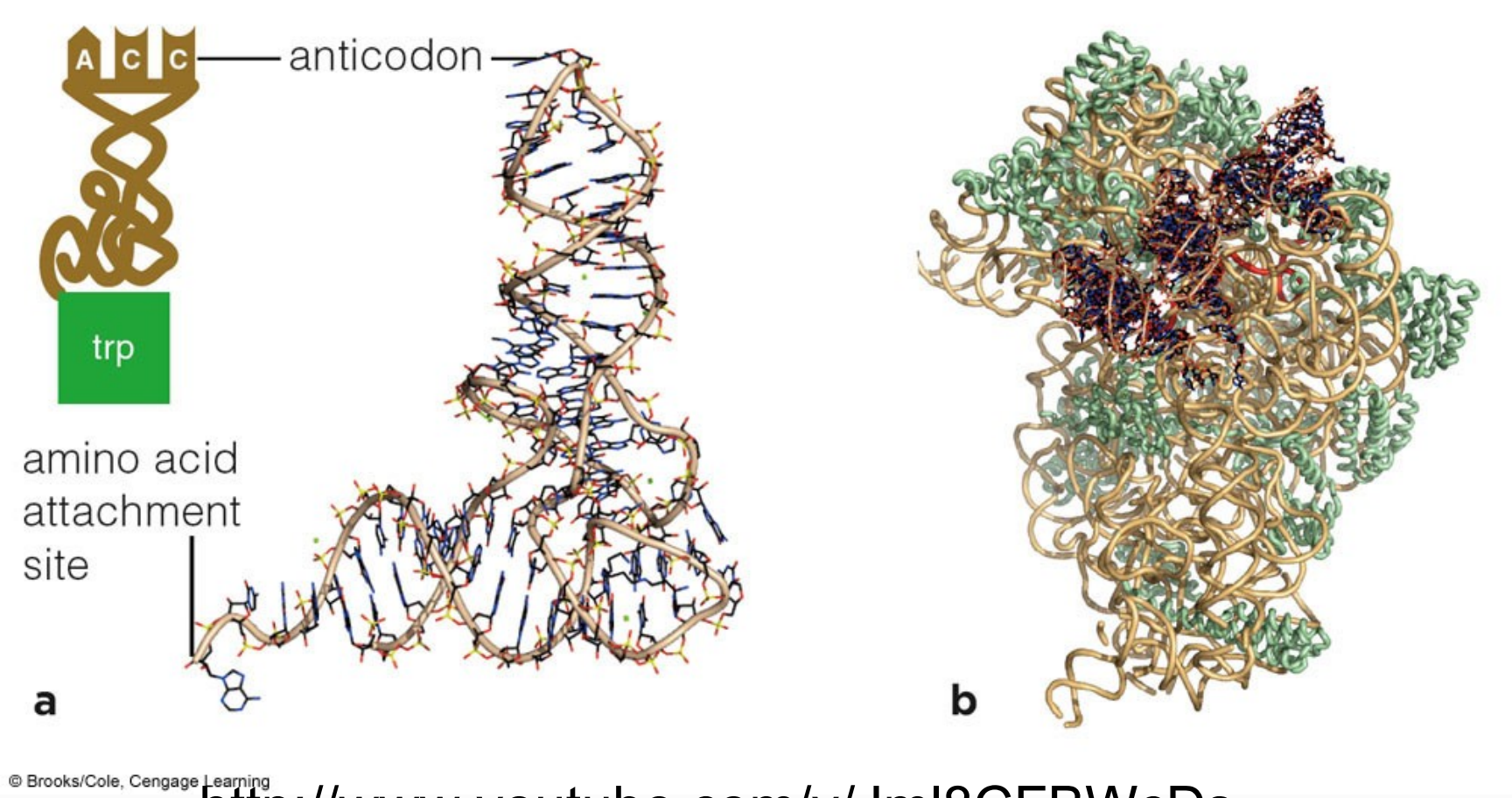
- tRNAs deliver amino acids to ribosomes
  - tRNA has an **anticodon** complementary to an mRNA codon, and a binding site for the amino acid specified by that codon

- Ribosomes, which link amino acids into polypeptide chains, consist of two subunits of rRNA and proteins

Ribosomes



tRNA



http://www.youtube.com/v/Jml8CFBWcDs

Key Concepts
RNA

- *Messenger RNA carries DNA's protein-building instructions*
- *Its nucleotide sequence is read three bases at a time*
- *Sixty-four mRNA base triplets—codons—represent the genetic code*
- *Two other types of RNA interact with mRNA during translation of that code*

Translation: RNA to Protein

- Translation converts genetic information carried by an mRNA into a new polypeptide chain
- The order of the codons in the mRNA determines the order of the amino acids in the polypeptide chain

Translation

- Translation occurs in the cytoplasm of cells
- Translation occurs in three stages
  - Initiation
  - Elongation
  - Termination

Initiation

- An initiation complex is formed
  - A small ribosomal subunit binds to mRNA
  - The anticodon of initiator tRNA base-pairs with the start codon (AUG) of mRNA
  - A large ribosomal subunit joins the small ribosomal subunit

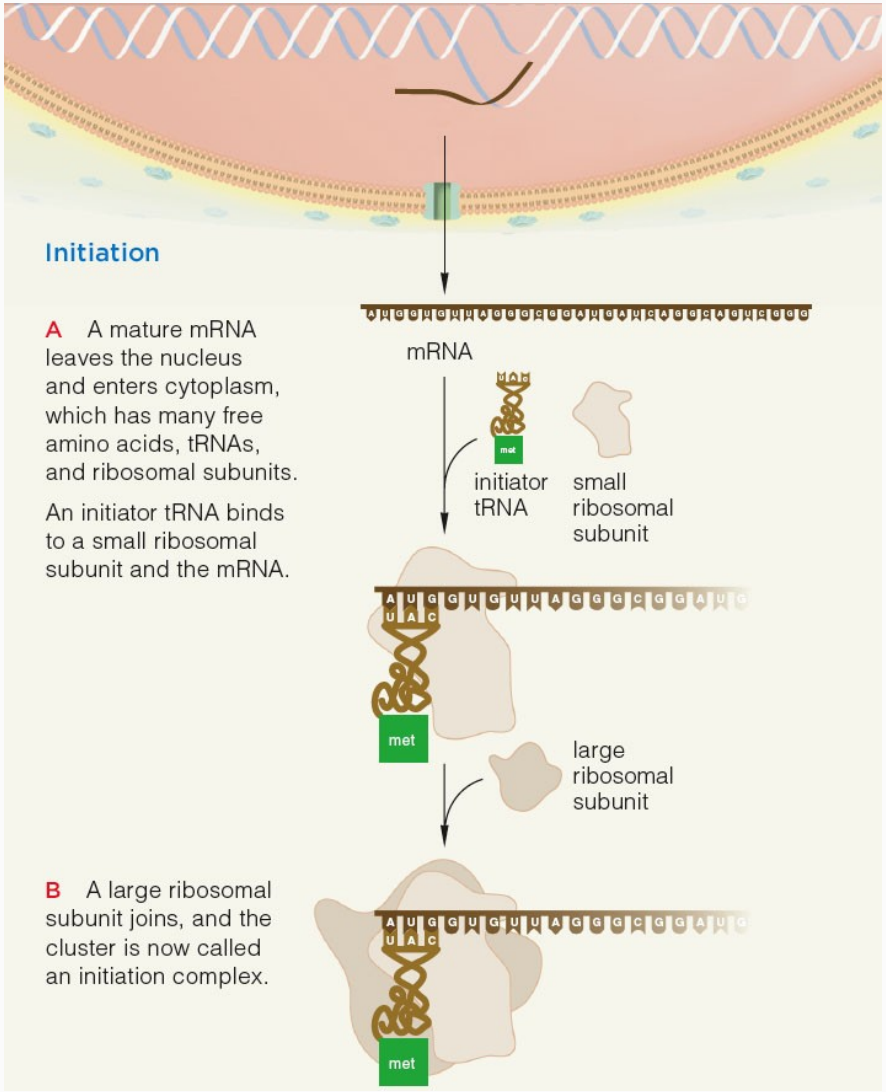
Elongation

- The ribosome assembles a polypeptide chain as it moves along the mRNA
  - Initiator tRNA carries methionine, the first amino acid of the chain
  - The ribosome joins each amino acid to the polypeptide chain with a peptide bond

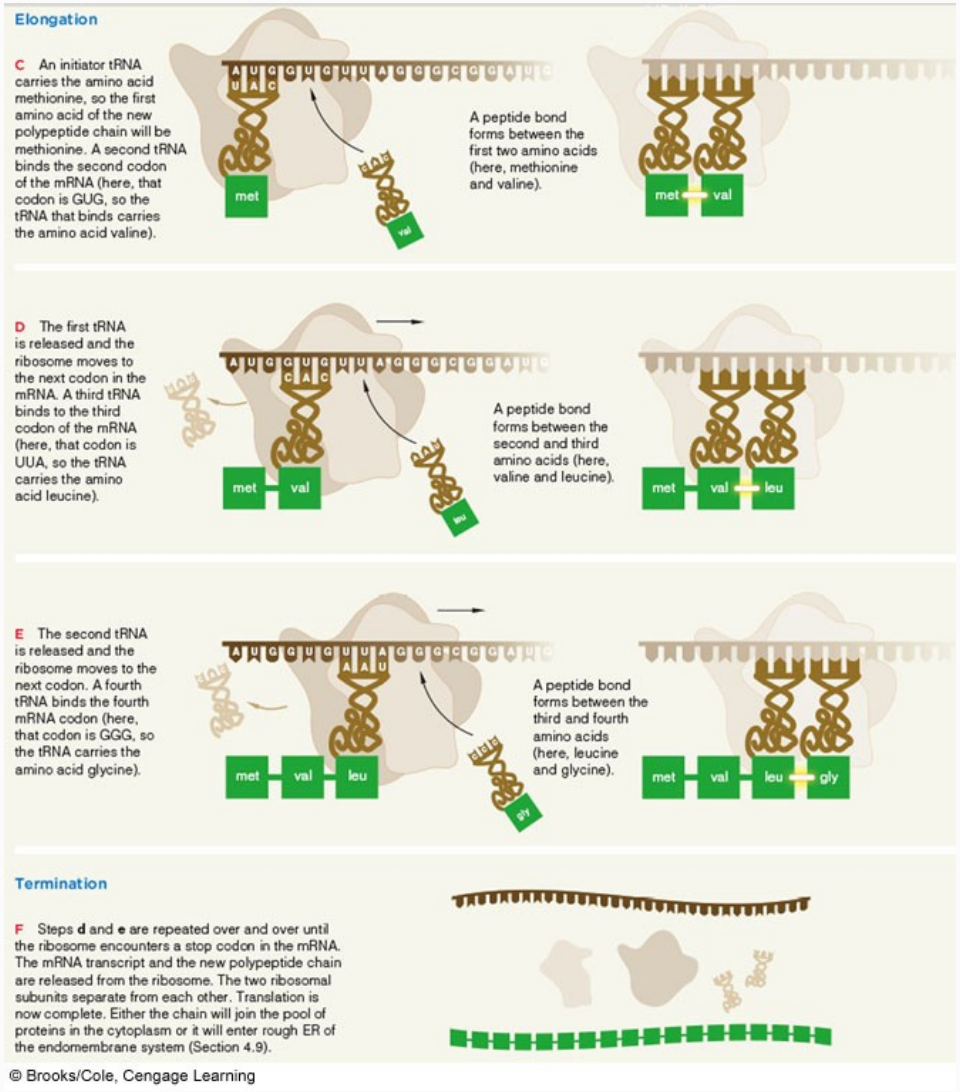
Termination

- When the ribosome encounters a stop codon, polypeptide synthesis ends
  - Release factors bind to the ribosome
  - Enzymes detach the mRNA and polypeptide chain from the ribosome

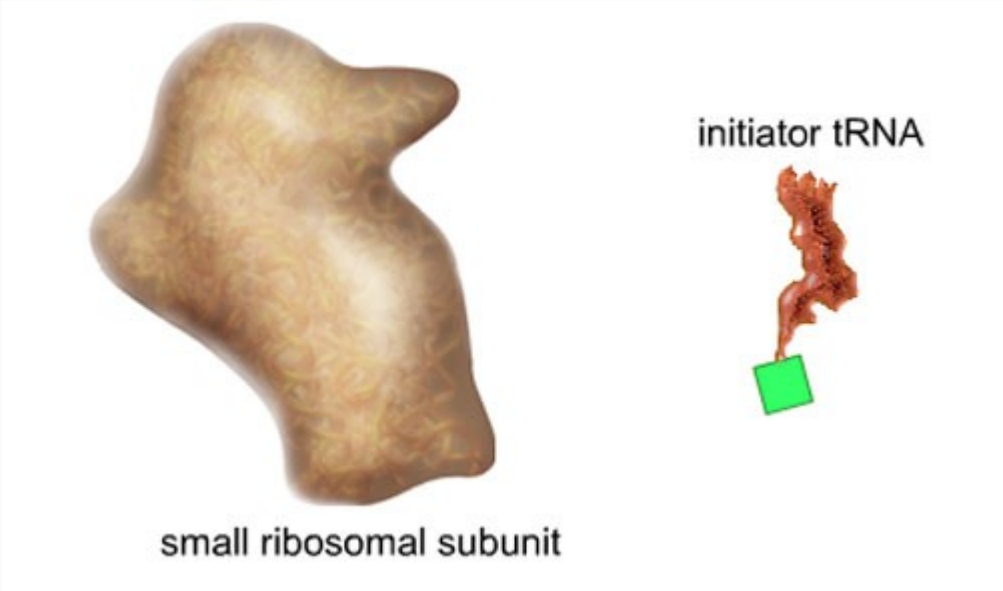
Translation in Eukaryotes



Translation in Eukaryotes



Animation: Translation



- http://www.youtube.com/watch?v=D5vH4Q_tAkY

Key Concepts
RNA to Protein: Translation

- *Translation is an energy-intensive process by which a sequence of codons in mRNA is converted to a sequence of amino acids in a polypeptide chain*

Mutated Genes and Their Protein Products

- If the nucleotide sequence of a gene changes, it may result in an altered gene product, with harmful effects

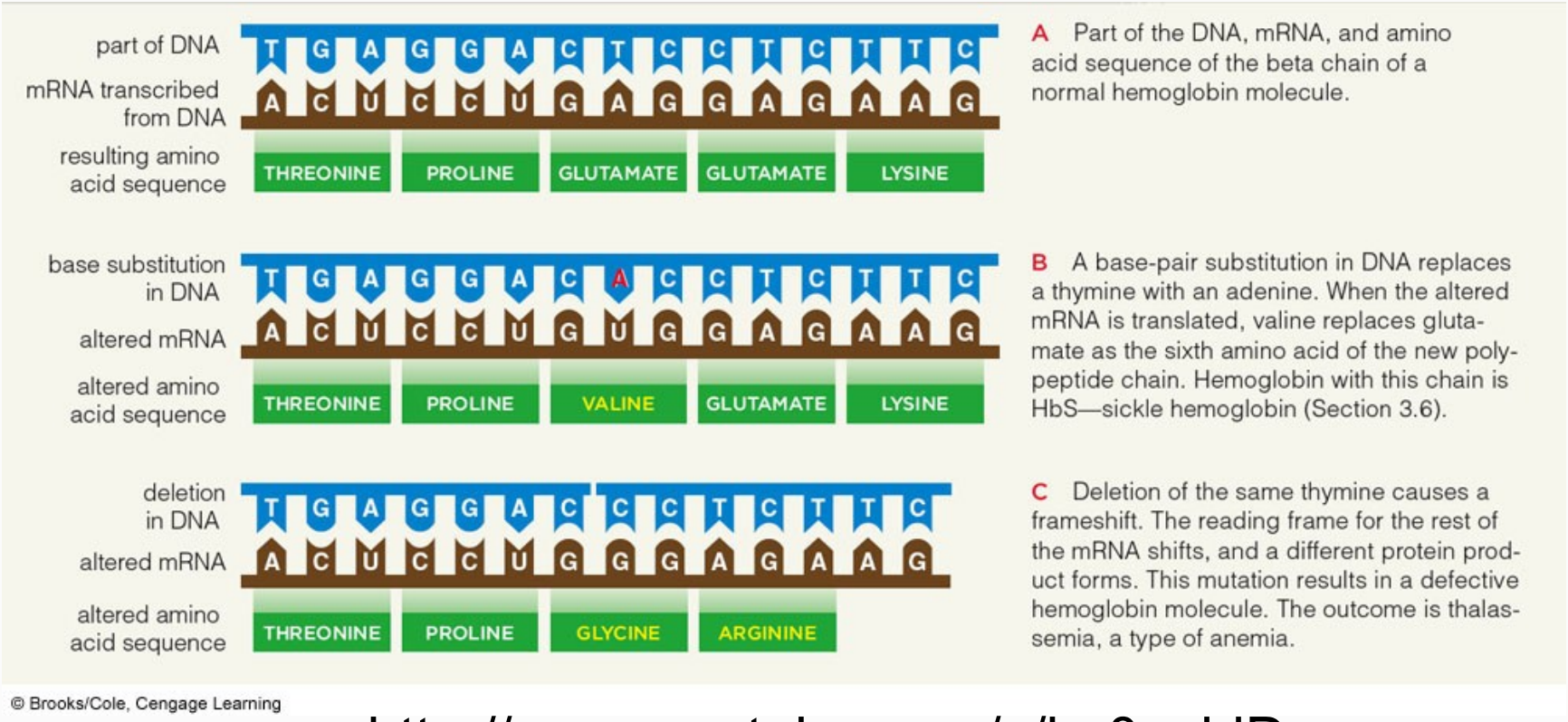
- **Mutations**
  - Small-scale changes in the nucleotide sequence of a cell's DNA that alter the genetic code

Common Mutations

- **Base-pair-substitution**
  - May result in a premature stop codon or a different amino acid in a protein product
  - *Example:* sickle-cell anemia

- **Deletion** or **insertion**
  - Can cause the reading frame of mRNA codons to shift, changing the genetic message
  - *Example:* Huntington's disease

Common Mutations



http://www.youtube.com/v/kp0esidDr-c

What Causes Mutations?

- **Transposable elements**
  - Segments of DNA that can insert themselves anywhere in a chromosomes
- Spontaneous mutations
  - Uncorrected errors in DNA replication
- Harmful environmental agents
  - Ionizing radiation, UV radiation, chemicals

Key Concepts
Mutations

- *Small-scale, permanent changes in the nucleotide sequence of DNA may result from replication errors, the activity of transposable elements, or exposure to environmental hazards*

- *Such mutation can change a gene's product*

Summary:
Protein Synthesis in Eukaryotic Cells