# Biophysics
# Lectures Three and Four

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# The Atoms and Molecules of Life

Cells are mostly made from the most abundant chemical elements, H, C, O, N, Ca, Mg, Na, K, P, among others.

Such atoms are held together in molecules by covalent and ionic bonds, although molecules bound by ionic bonds are called salts.

Covalent bonds are the strongest kind of chemical bond. A good example is the bond between two hydrogen atoms.

The hamiltonian for two interacting hydrogen atoms is $H = H_0 + W$. The ''free'' hamiltonian $H_0$ is a sum of two isolated-hydrogen-atom hamiltonians

$$H_0 = \frac{\vec{p}_1^{\,2}}{2m} + \frac{\vec{p}_2^{\,2}}{2m} - \frac{e^2}{|\vec{r}_1 - \vec{R}_1|} - \frac{e^2}{|\vec{r}_2 - \vec{R}_2|} \tag{1}$$

where $e$ is the charge of the electron in units with $\alpha = e^2/(\hbar c) \approx 1/137$, and the two protons are located at the classical positions $\vec{R}_1$ and $\vec{R}_2$. The perturbation $W$ is

$$W = \frac{e^2}{|\vec{R}_2 - \vec{R}_1|} + \frac{e^2}{|\vec{R}_2 + \vec{r}_2 - \vec{R}_1 - \vec{r}_1|} - \frac{e^2}{|\vec{R}_2 + \vec{r}_2 - \vec{R}_1|} - \frac{e^2}{|\vec{R}_2 - \vec{R}_1 - \vec{r}_1|}. \tag{2}$$

The hamiltonian is invariant under the interchange of $\vec{r}_1$ and $\vec{r}_2$, and so it commutes with the operator $T$ that interchanges the two electrons. So its eigenstates can be chosen to be eigenstates of $T$ as well as of $H$.

In fact, since electrons are fermions, their physical states must be antisymmetric under the interchange of the two electrons. Now $H$ does not refer to the spin variables, so we can choose the spin state to be either symmetric (spin one) or antisymmetric (spin zero). The space wave-function of the coordinates would then under the interchange of $\vec{r}_1$ and $\vec{r}_2$ be respectively antisymmetric or symmetric.

It is very natural to assume that the space wave-function is antisymmetric. After all, the electrons both have negative charge, and why should they clump together? But in fact the ground state of the hydrogen molecule has a space wave-function that is symmetric. The two electrons actually clump together between the two protons. Hence they attract the two protons to their central clump of negative charge and so hold the two hydrogen atoms together.

The binding energy is about $-4.75$ eV at an interproton separation of $r = |\vec{R}_2 - \vec{R}_1| = 0.74$ Å.

A useful parametrization of the potential energy of the hydrogen molecule as a function of $r$ is

$$V(r) = a e^{-b\,r}\,(1 - c\,r) - \frac{d}{r^6 + e\,r^{-6}}. \tag{3}$$

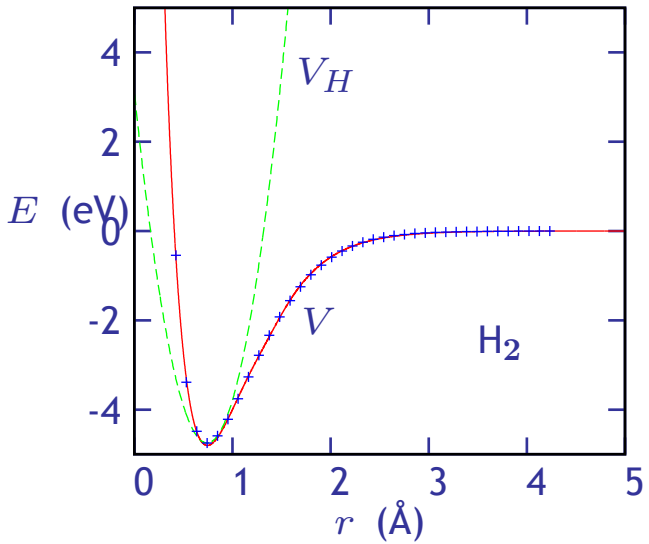



Figure 1: The phenomenological potential (3) with $a = 53.8$ eV, $b = 2.99$ Å$^{-1}$, $c = 2.453$ Å$^{-1}$, $d = C_6 = 3.884$ eV Å$^6$, and $e = 47.6$ Å$^{12}$ (solid, red) is finite, fits the RKR spectral points for molecular hydrogen (crosses, blue), and gives the correct London tail for $r > 3$ Å. The harmonic potential $V_H$ (dashes, green) is accurate only near its minimum.

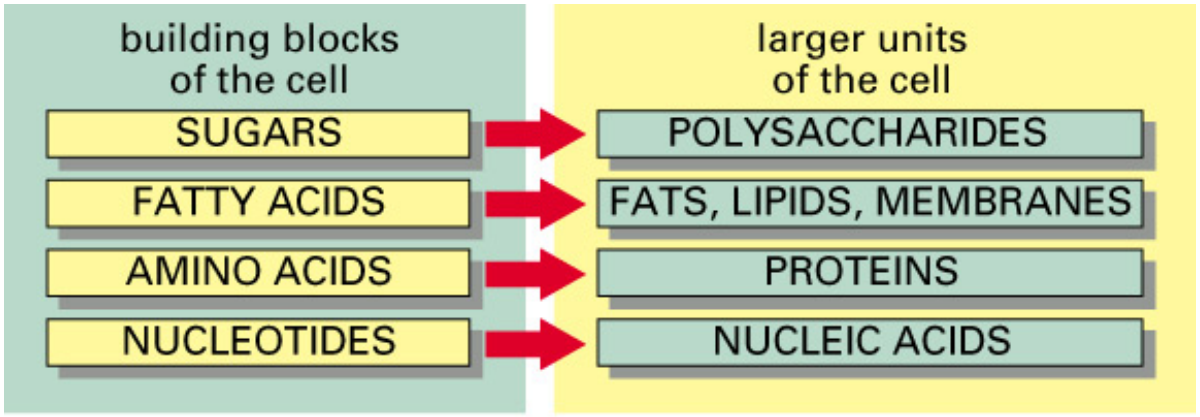



Figure 2–17. Molecular Biology of the Cell, 4th Edition.

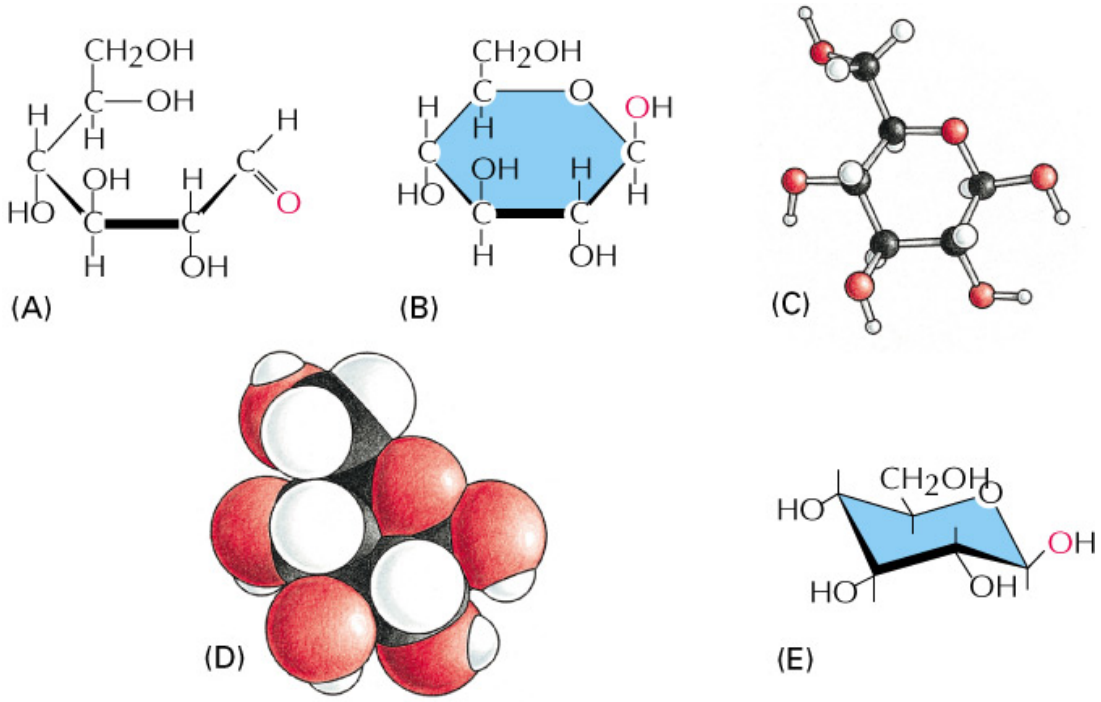



Figure 2–18. Molecular Biology of the Cell, 4th Edition.

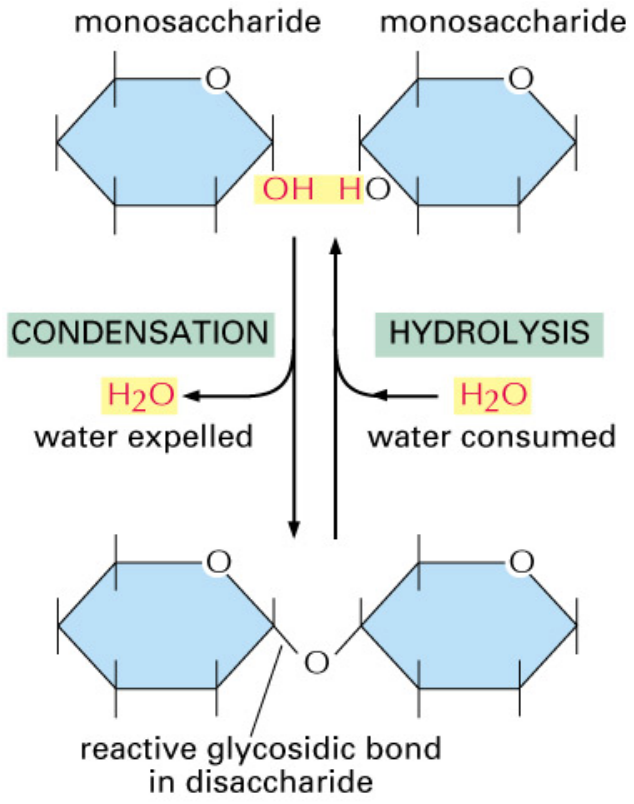



Figure 2–19. Molecular Biology of the Cell, 4th Edition.

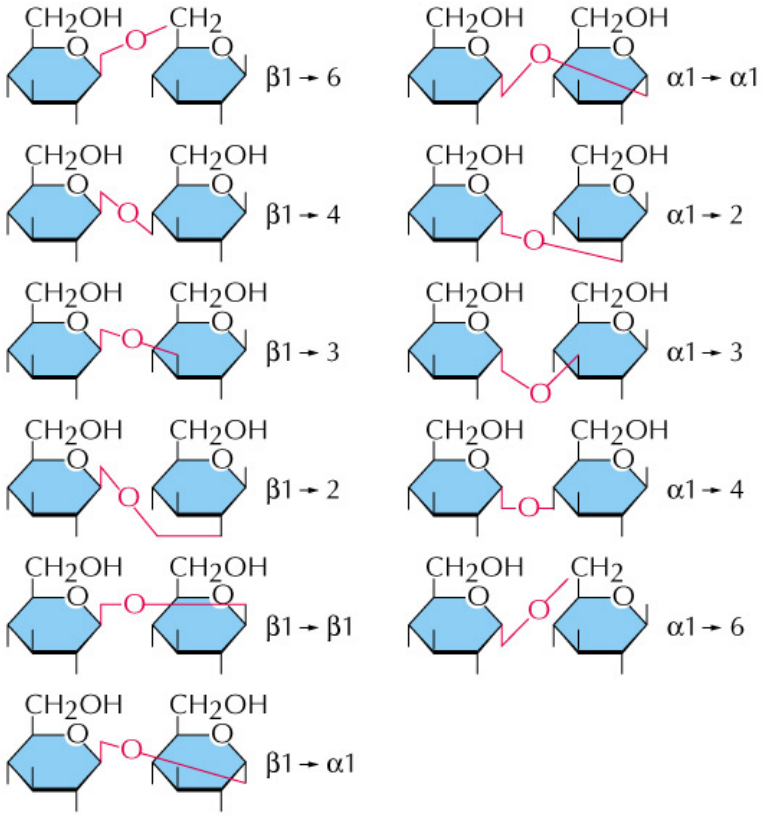



Figure 2–20. Molecular Biology of the Cell, 4th Edition.

Sugars form long polymers with and without branches. Cellulose is a polysaccharide of glucose found in the cell walls of plants; it is the most abundant organic chemical on Earth. The chitin of insect exoskeletons and fungal cell walls is also a polysaccharide. Polysaccharides are the main components of slime, mucus, and gristle. Oligosaccharides covalently linked to proteins are glycoproteins; linked to lipids, they are glycolipids.

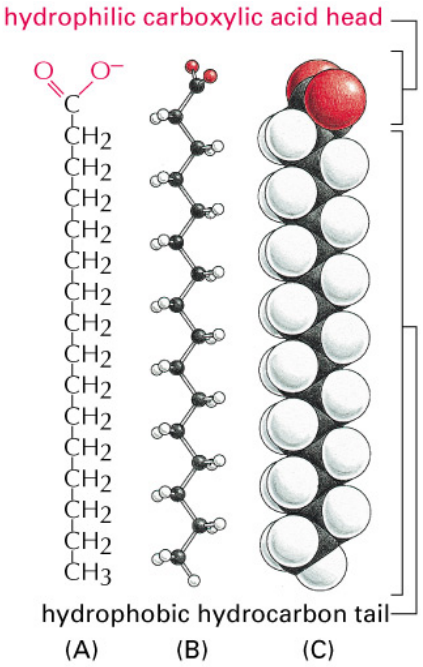



Figure 2–21. Molecular Biology of the Cell, 4th Edition.

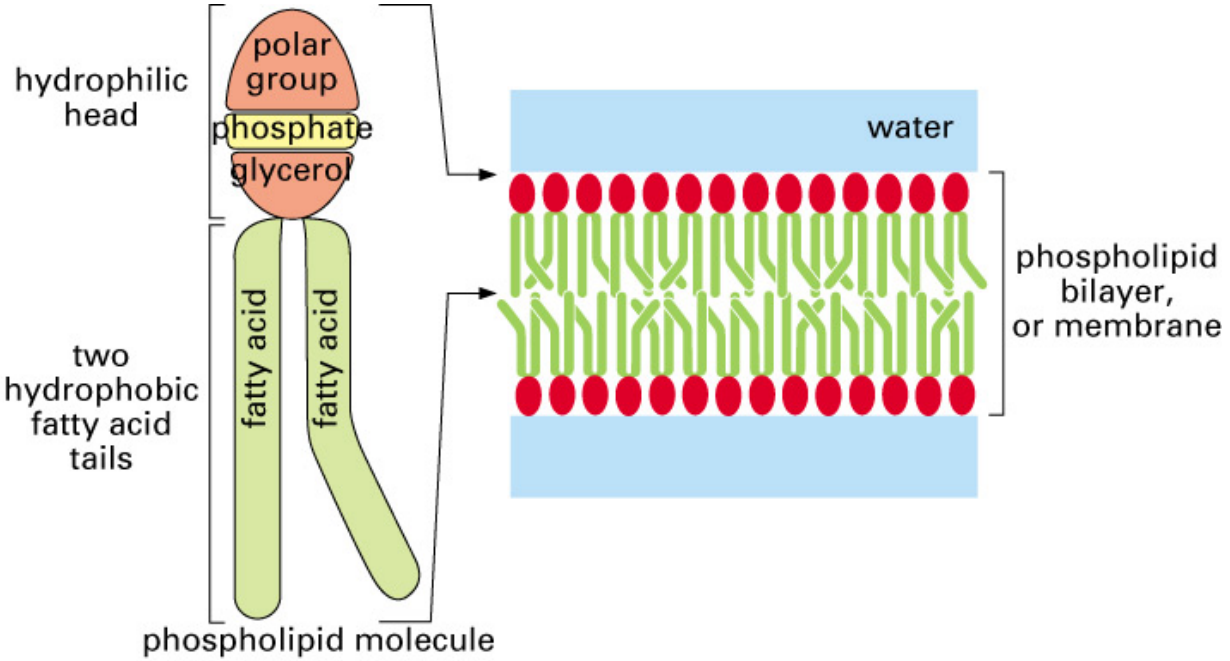



Figure 2–22. Molecular Biology of the Cell, 4th Edition.

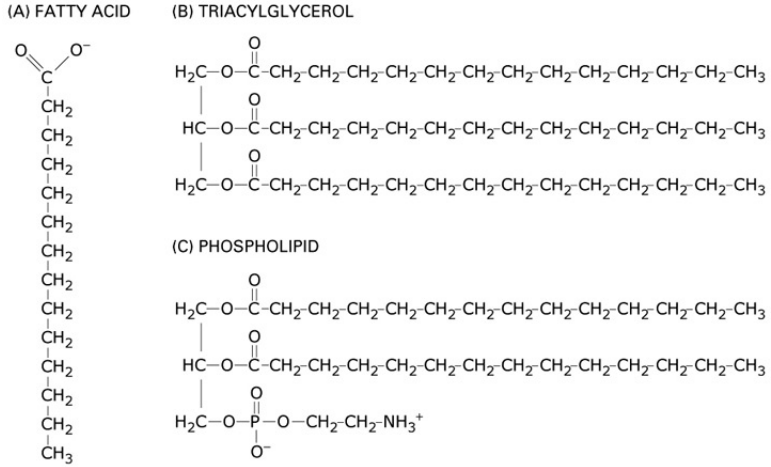
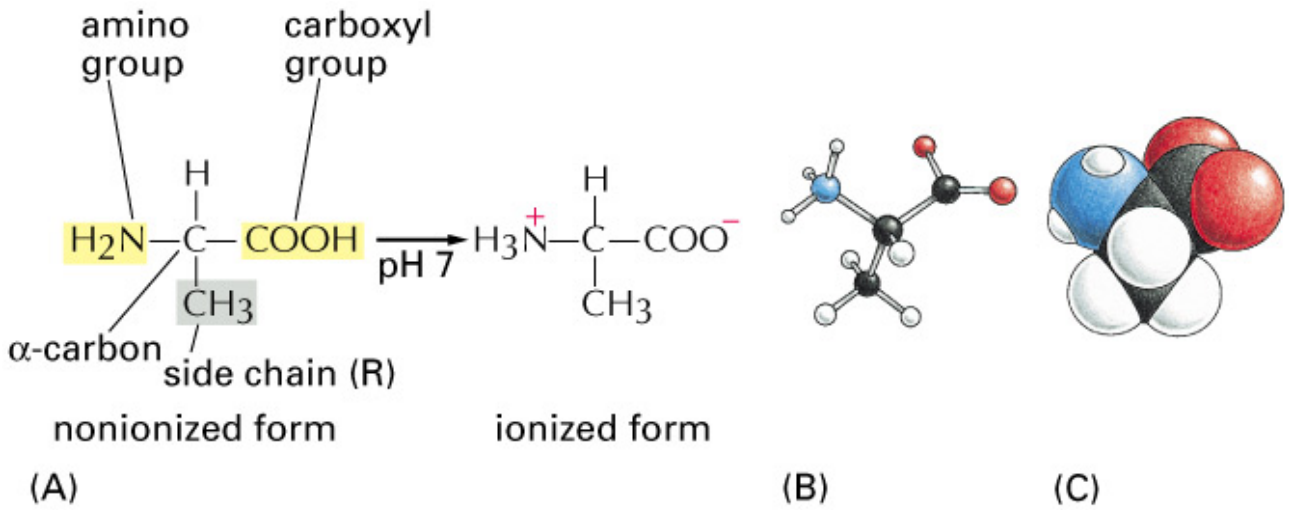



Figure 2-18 MBoC4: A Problems Approach

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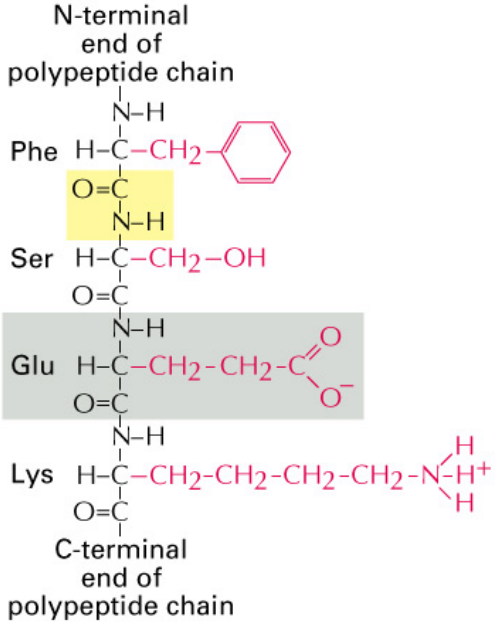



Figure 2–24. Molecular Biology of the Cell, 4th Edition.

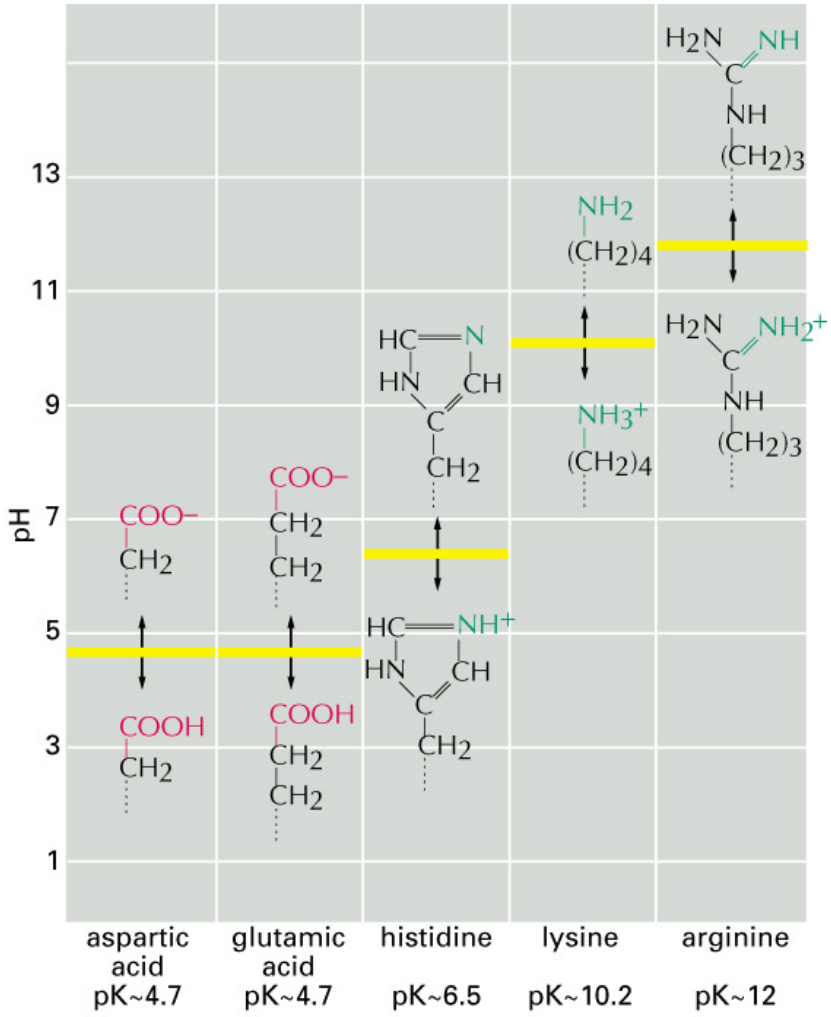



Figure 2–25. Molecular Biology of the Cell, 4th Edition.

The side chains of 5 of the 20 amino acids used in cells are ionized at or close to the nearly neutral pH's found in most parts of cells. In a globular protein, these aa's are usually found on the surface, where they can interact with polar water molecules and with ions.

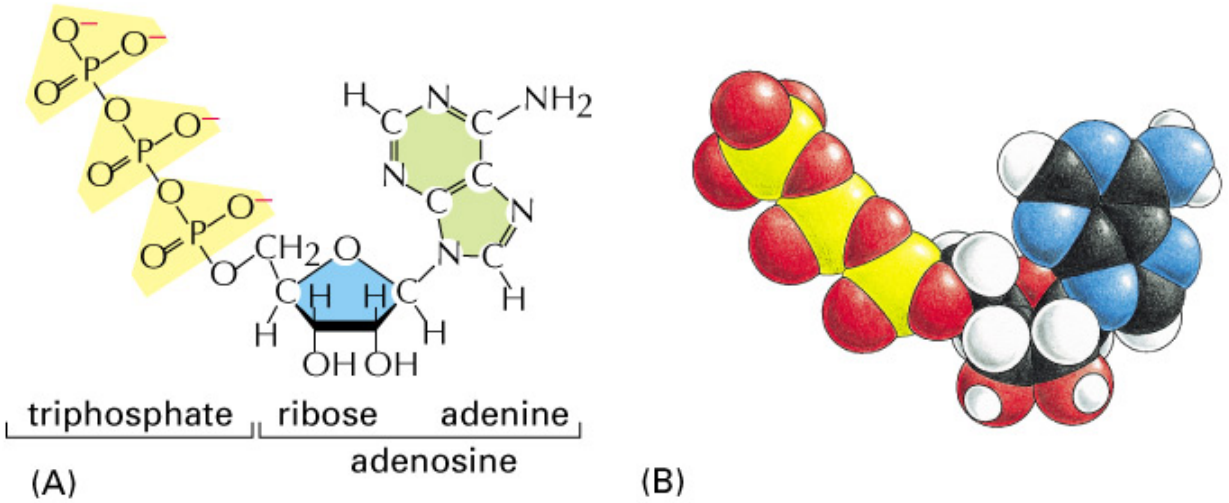



Figure 2–26. Molecular Biology of the Cell, 4th Edition.

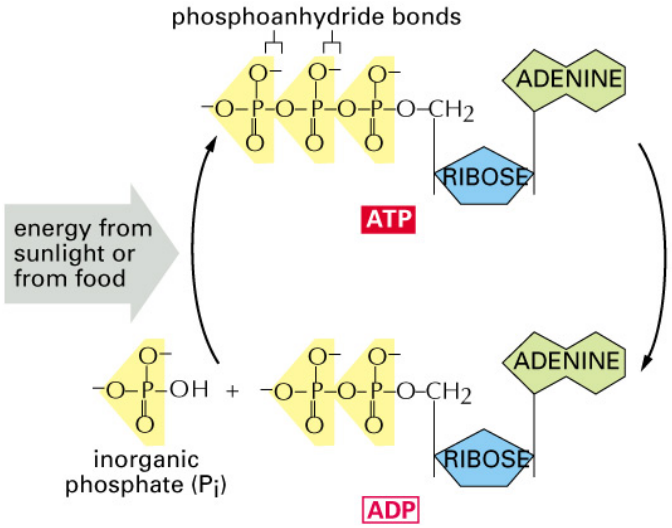



Figure 2–27. Molecular Biology of the Cell, 4th Edition.

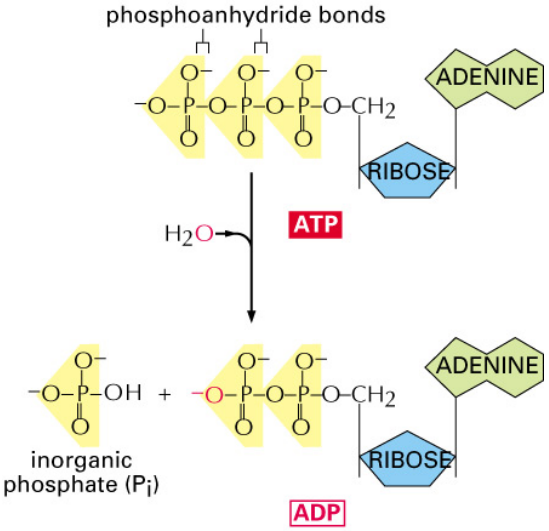



Figure 2–57. Molecular Biology of the Cell, 4th Edition.

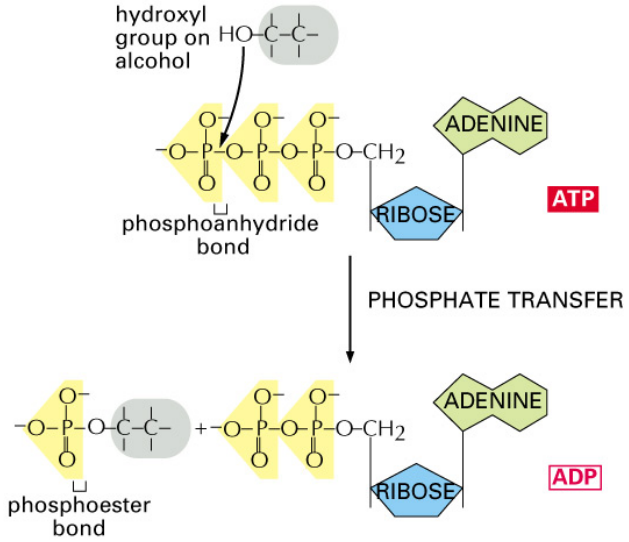



Figure 2–58. Molecular Biology of the Cell, 4th Edition.

The hydrolysis of the terminal phosphate of ATP yields $\approx 12$ kcal/mol.

This ATP is one of the four nucleotides used to make DNA:

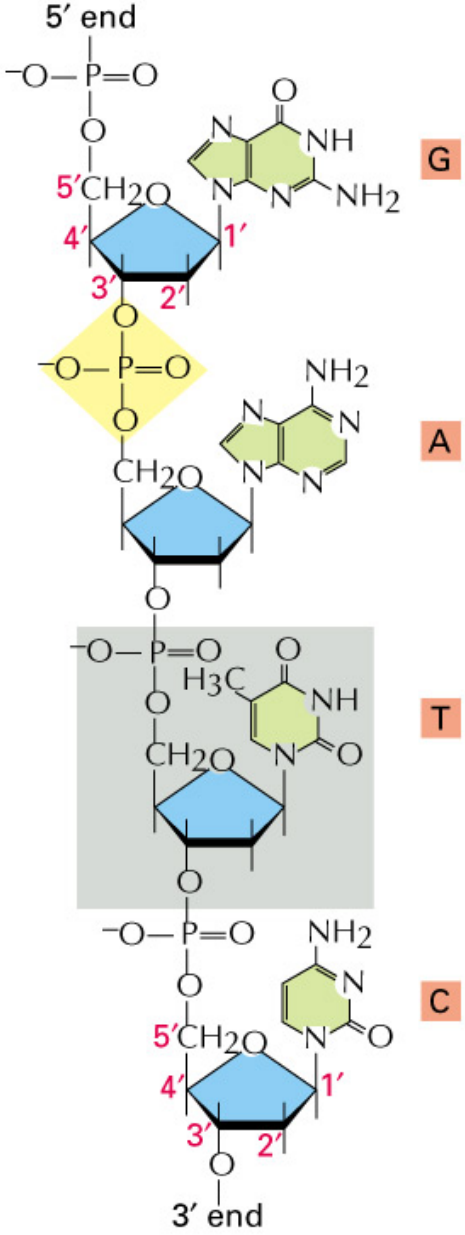



Figure 2–28. Molecular Biology of the Cell, 4th Edition.

CTP, GTP, and TTP are also used to make DNA and RNA:

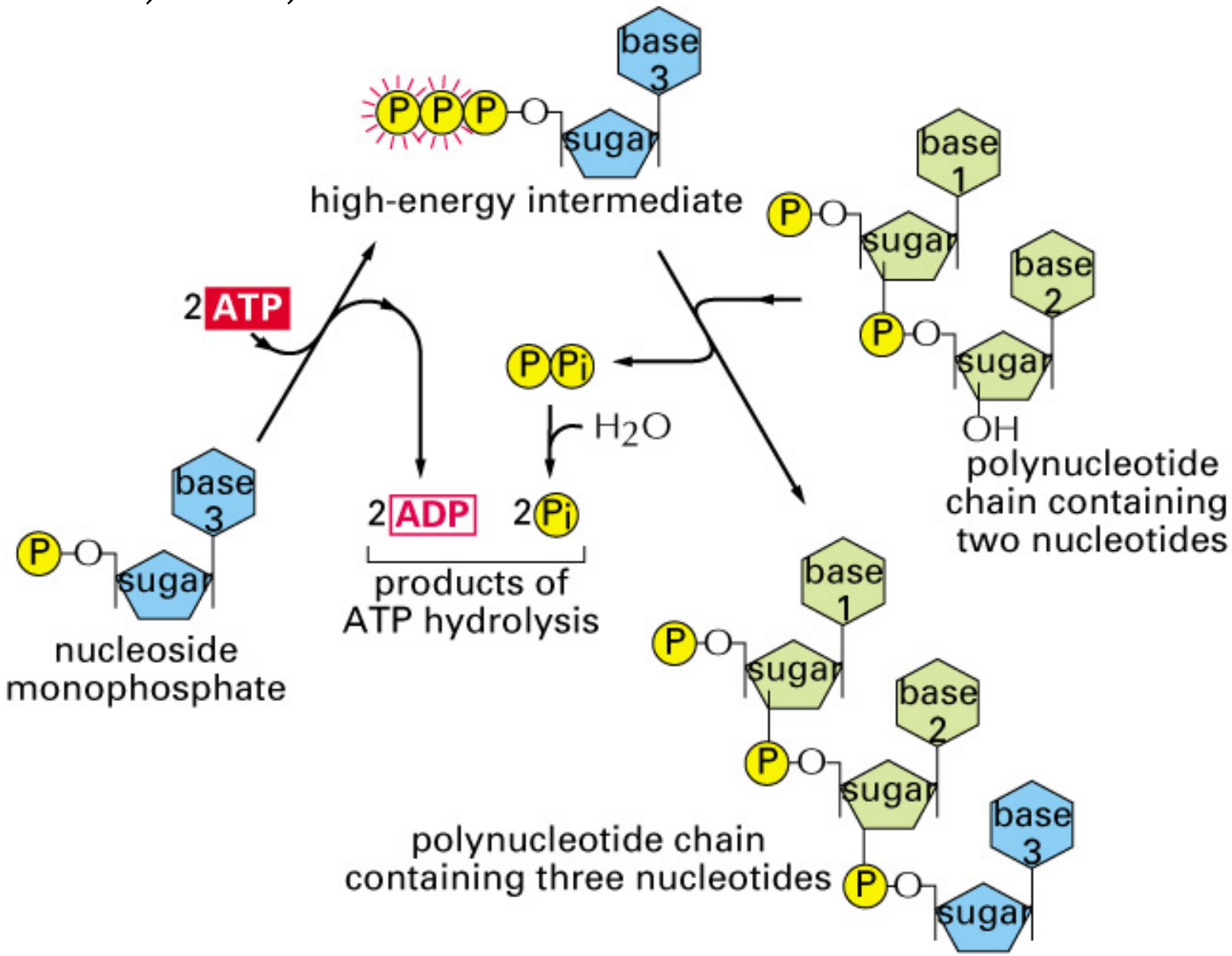
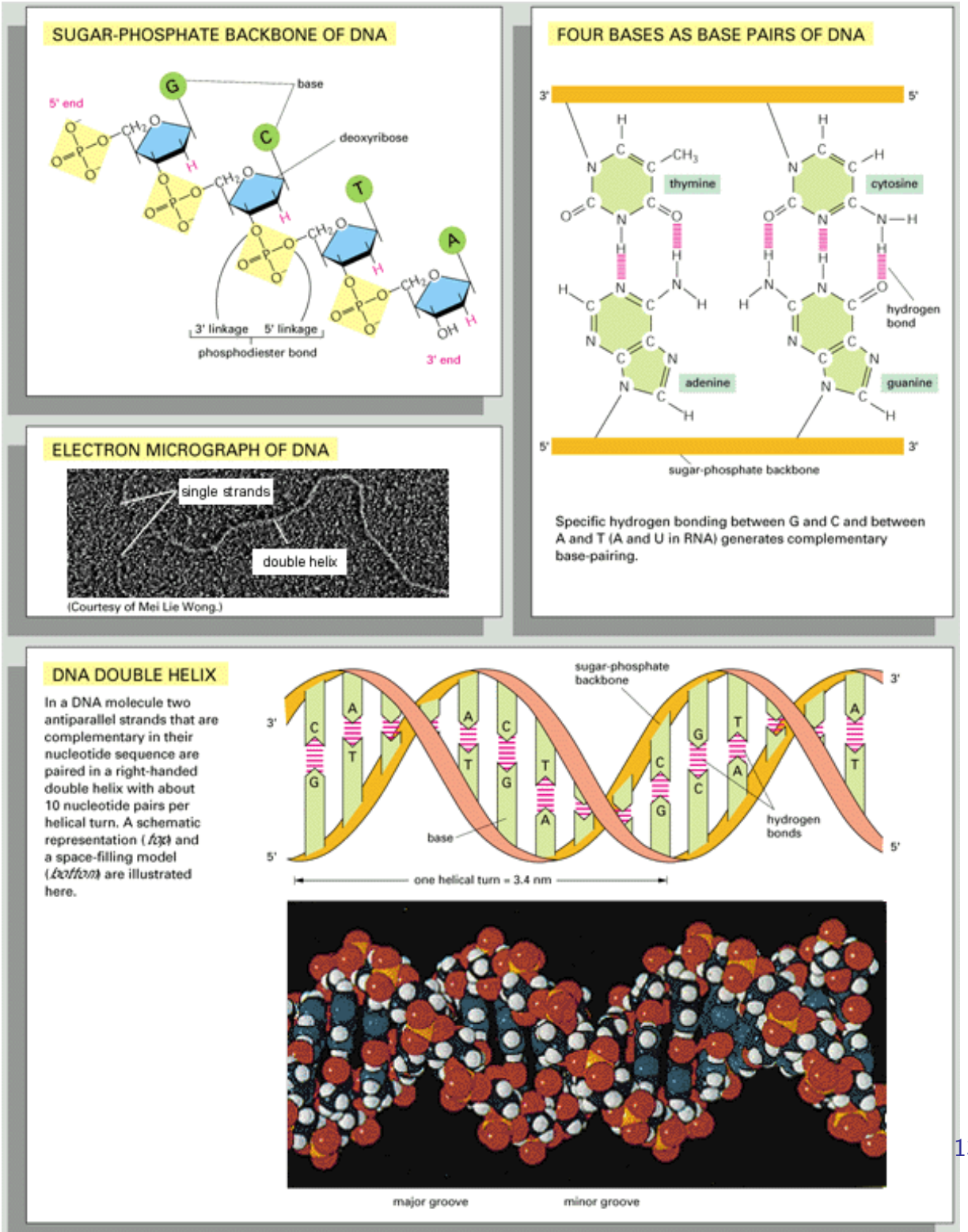
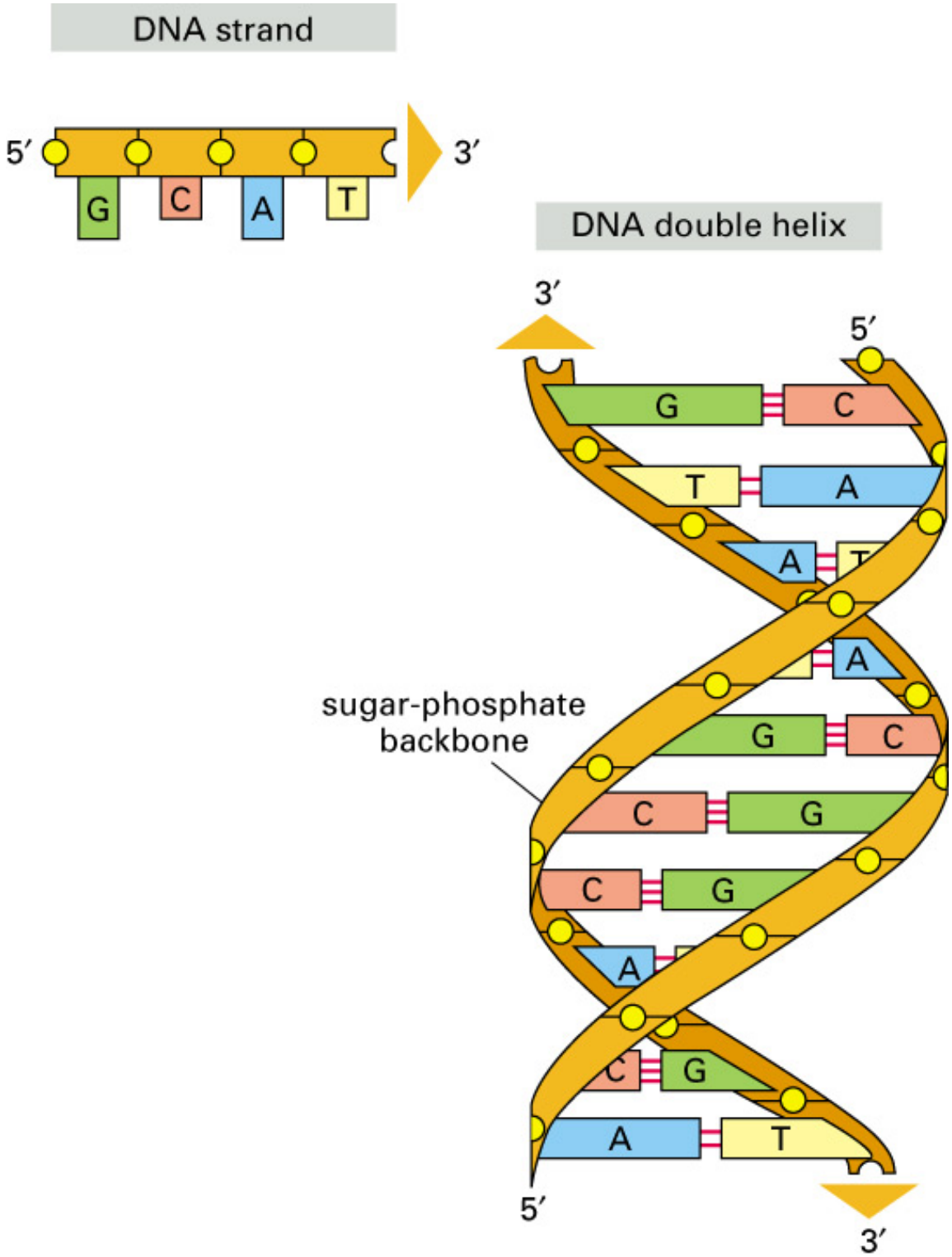



Figure 2–67. Molecular Biology of the Cell, 4th Edition.

Cells are digital, run by programs written in the four-letter code – A, C,T, G – of DNA.
Digital control is simple and precise.
Hence, gene therapy is possible.
Human DNA has $3.2 \times 10^9$ base pairs.
It is 109 cm. long.




DNA strand
5′
3′
G
C
A
T
DNA double helix
3′
5′
sugar-phosphate
backbone
5′
3′

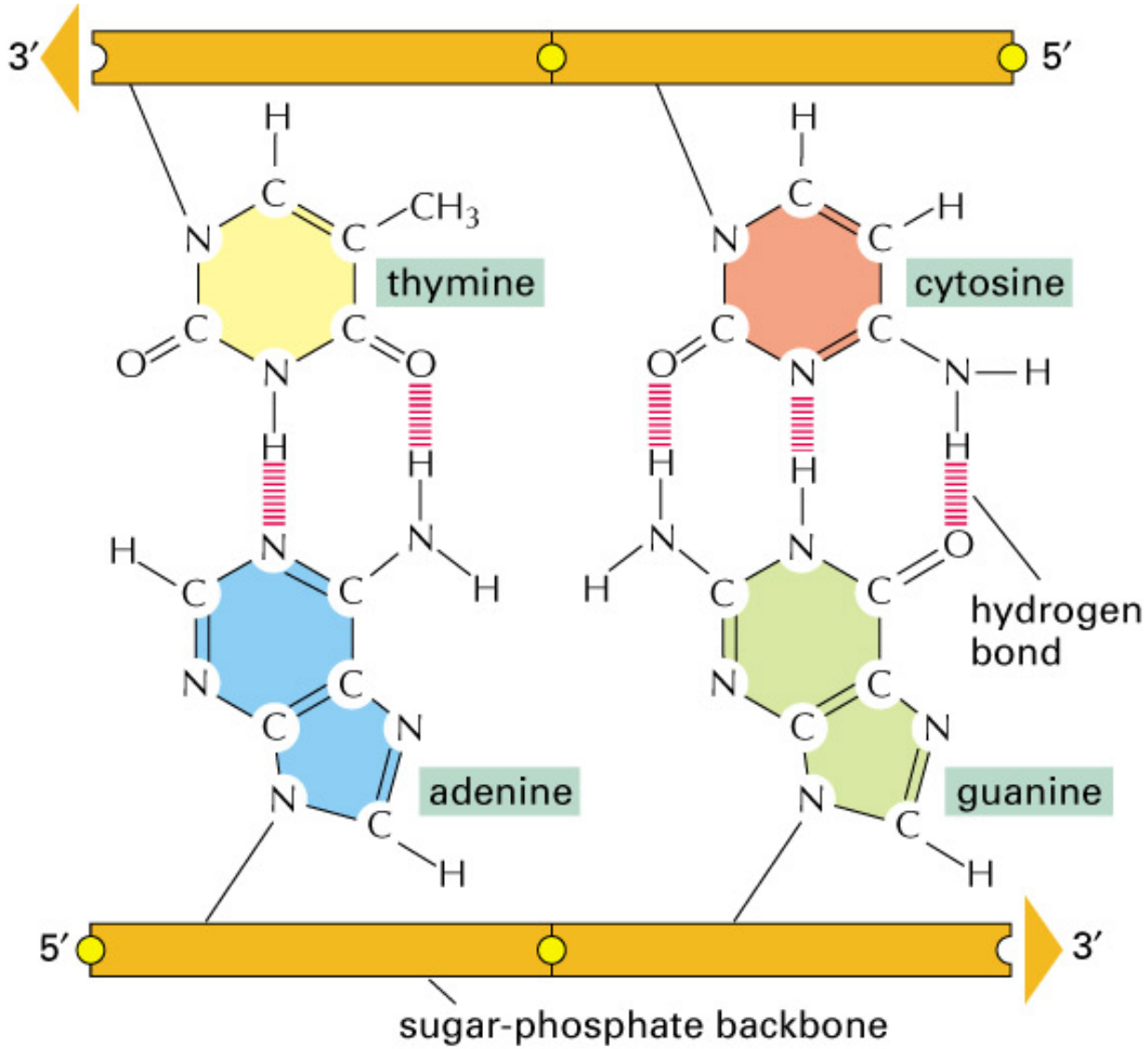



Figure 4–4. Molecular Biology of the Cell, 4th Edition.

Watson-Crick pairing: A=T has two H-bonds, but $\mathrm{C} \equiv \mathrm{G}$ has three.

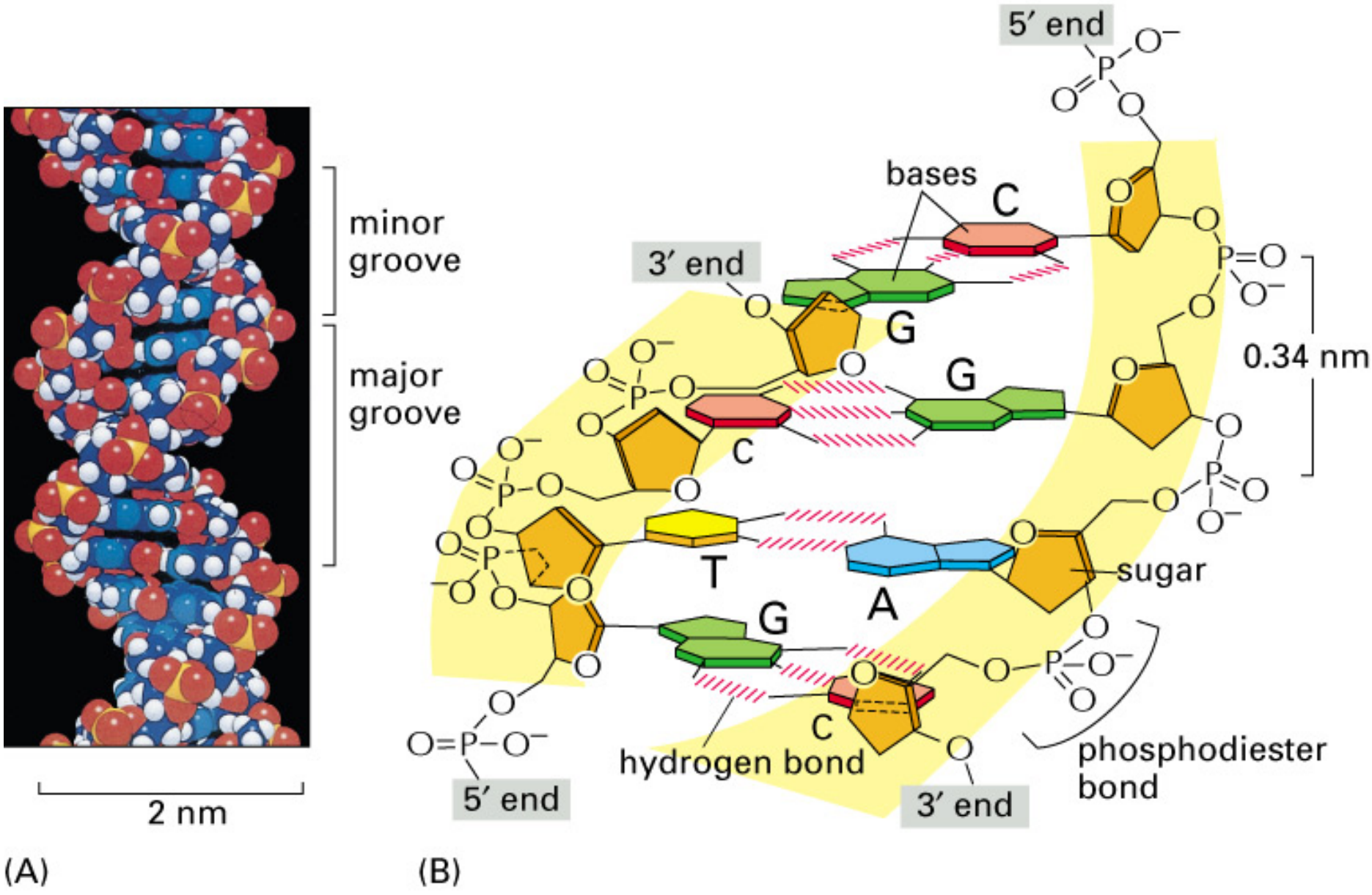



Figure 4–5. Molecular Biology of the Cell, 4th Edition.

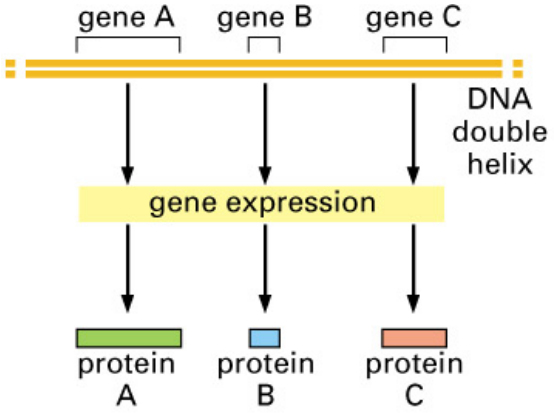



Figure 4–6. Molecular Biology of the Cell, 4th Edition.

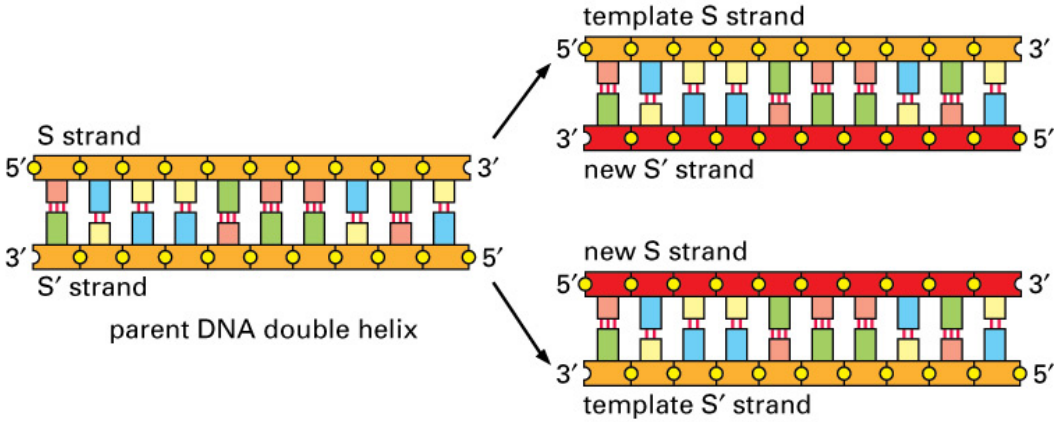



Figure 4–8. Molecular Biology of the Cell, 4th Edition.

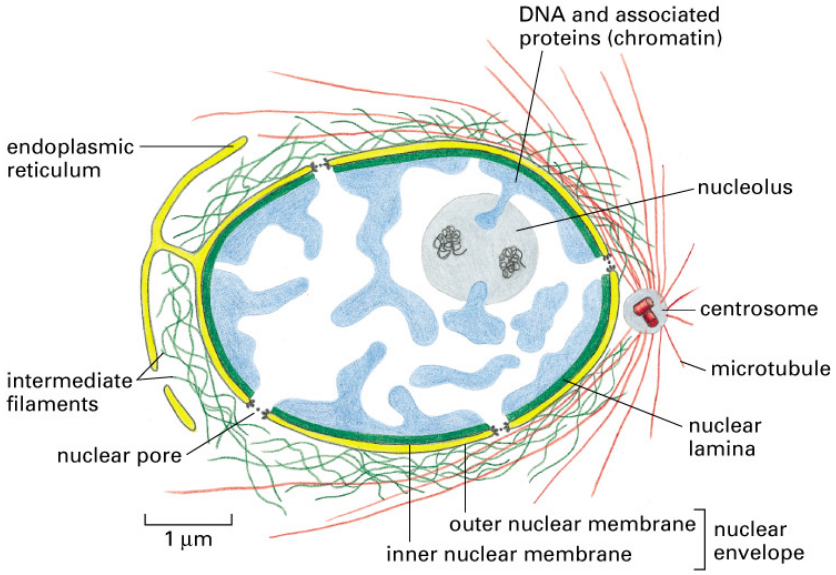



Figure 4–9. Molecular Biology of the Cell, 4th Edition.

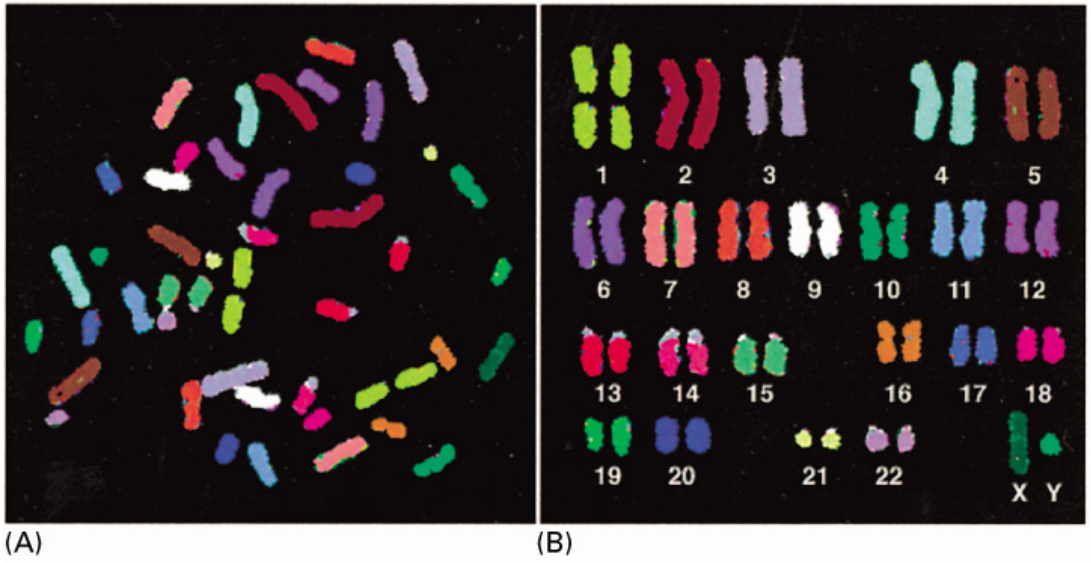



Figure 4–10. Molecular Biology of the Cell, 4th Edition.

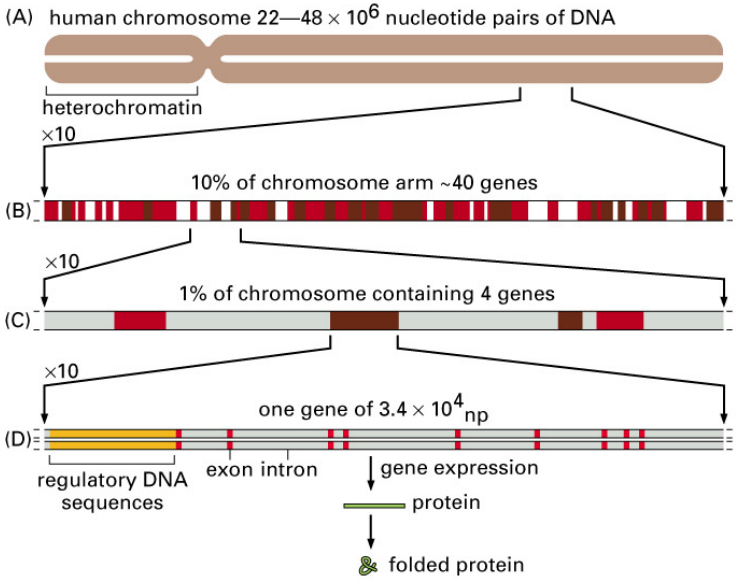
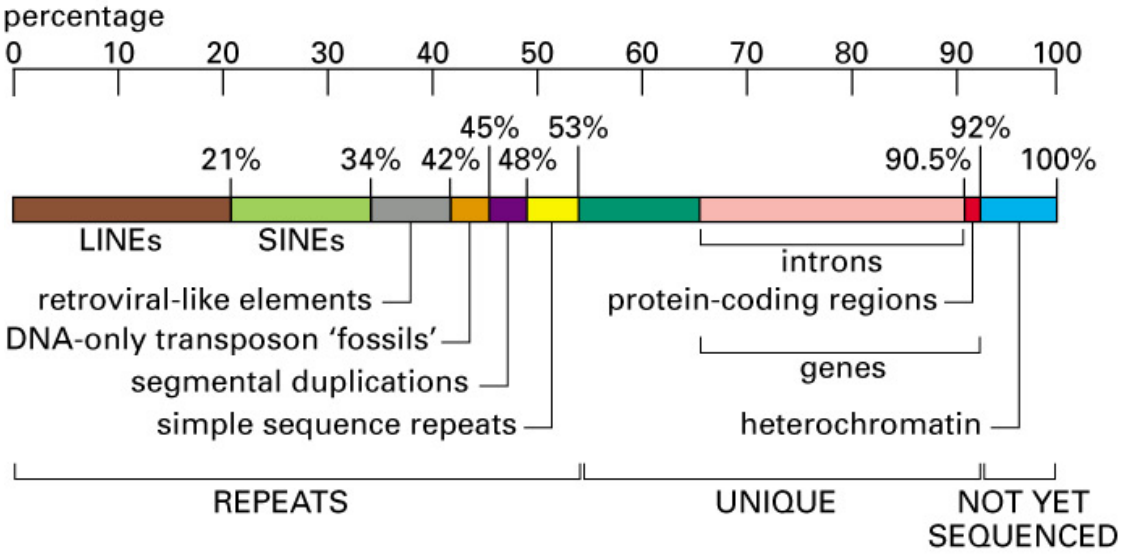



Figure 4–15. Molecular Biology of the Cell, 4th Edition.

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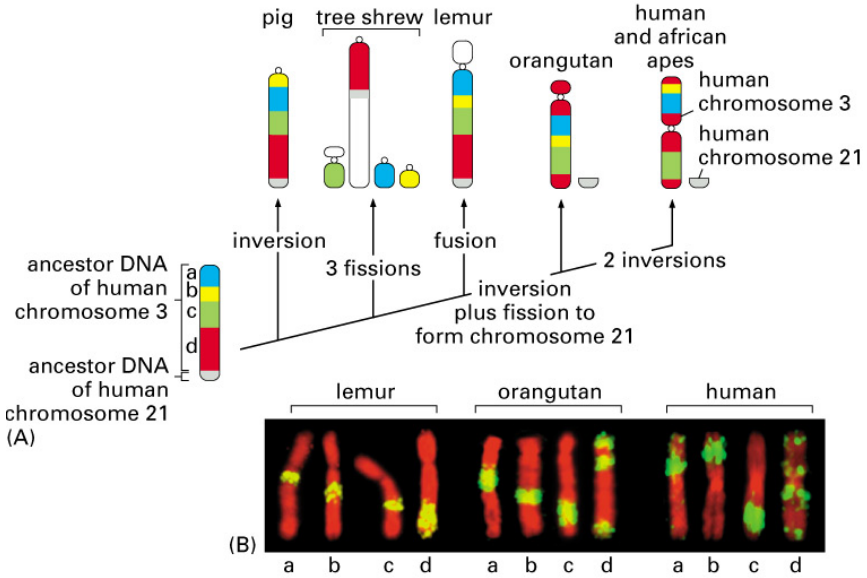



Figure 4–19. Molecular Biology of the Cell, 4th Edition.

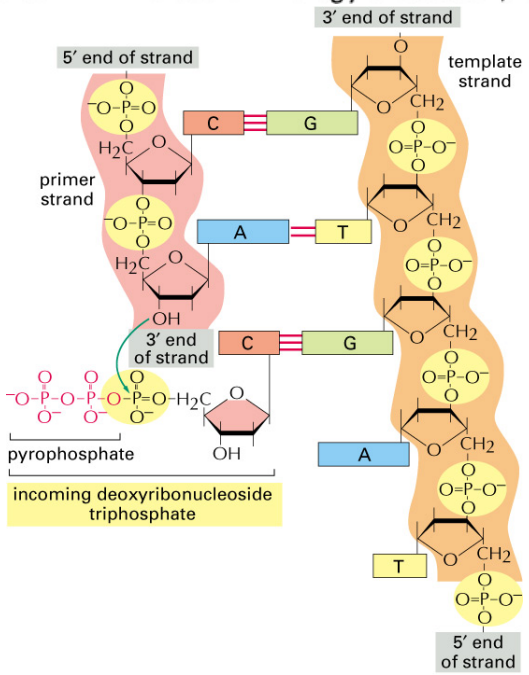



Figure 5–3. Molecular Biology of the Cell, 4th Edition.

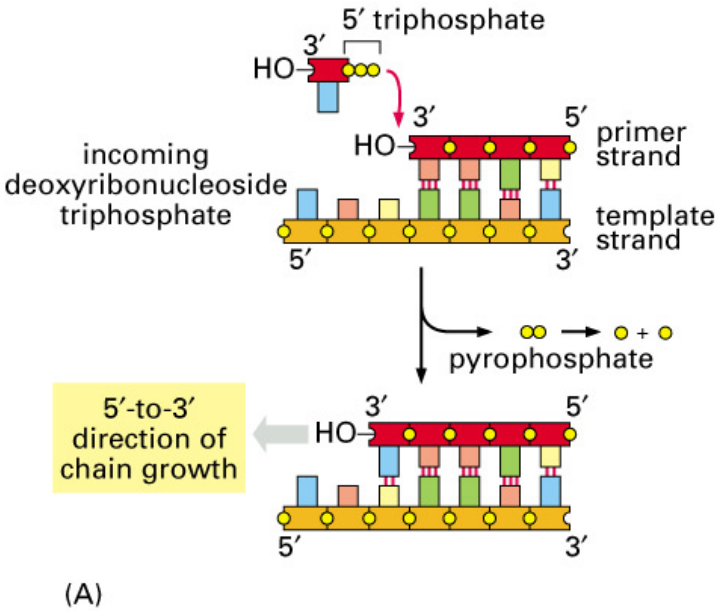
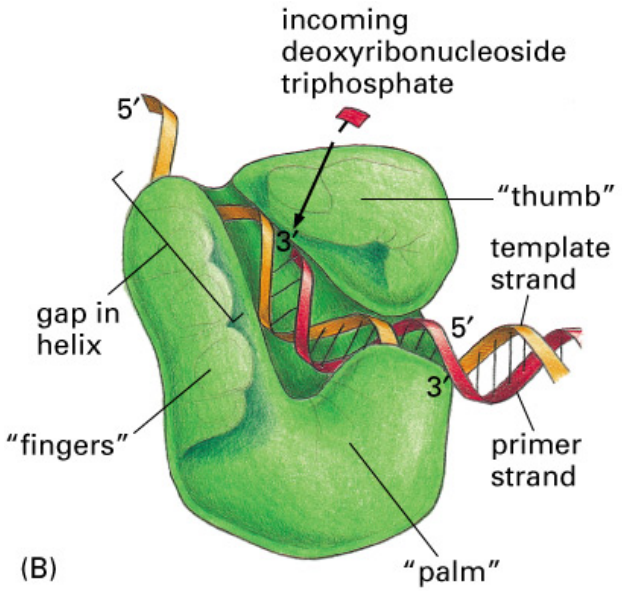



Figure 4–5 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

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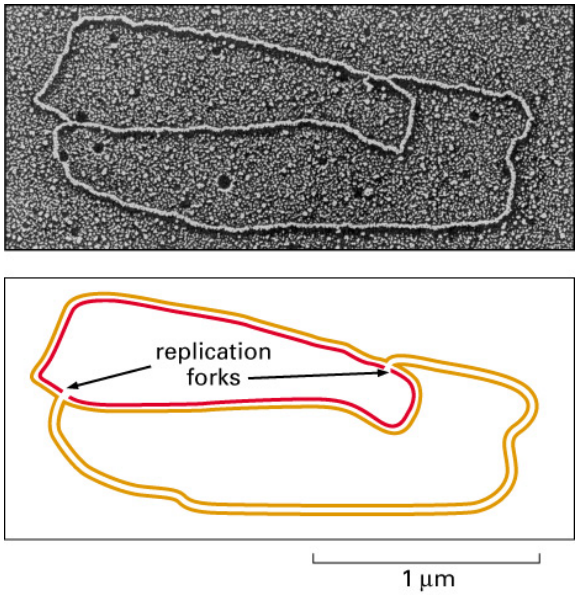


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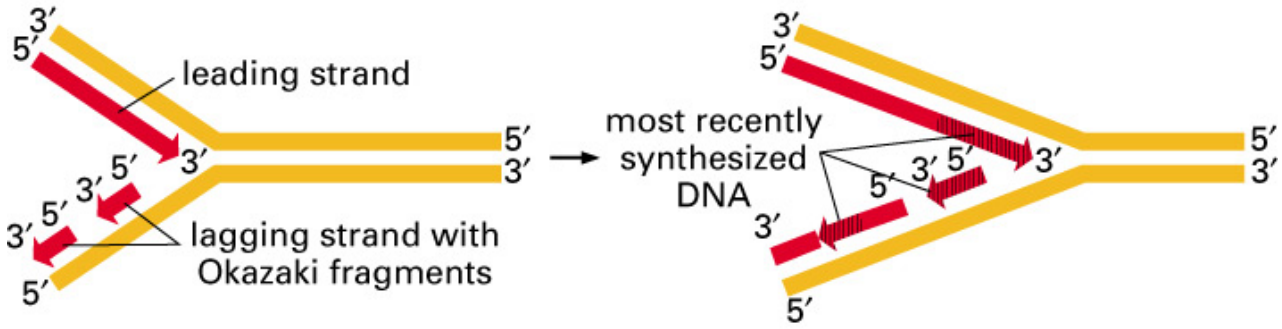


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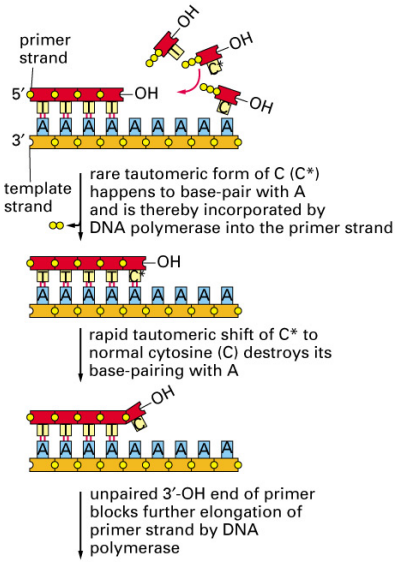


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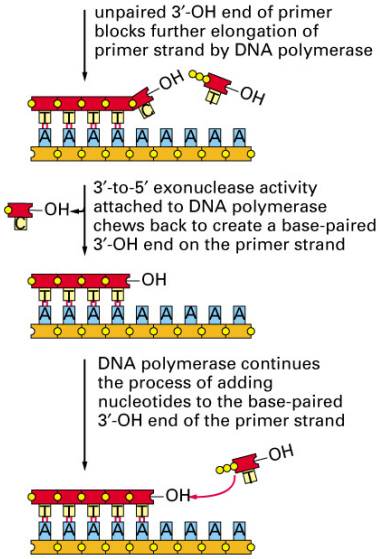


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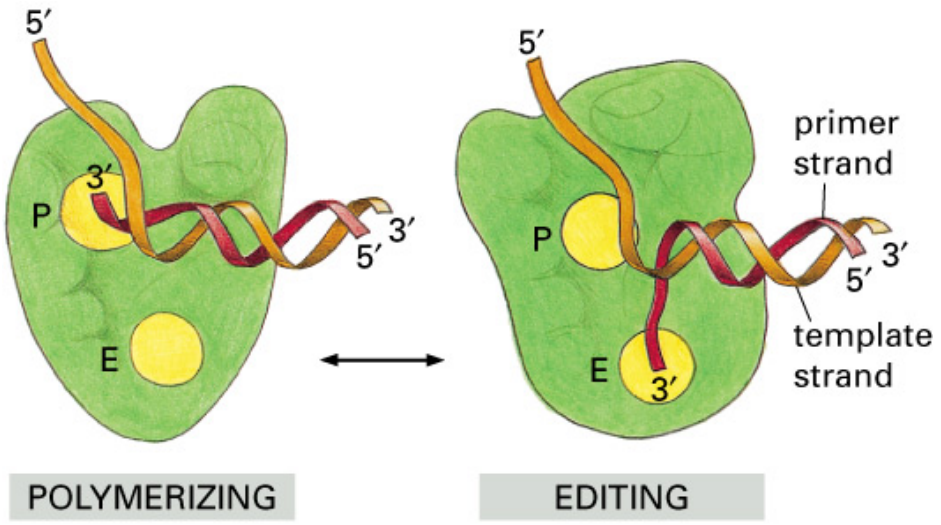


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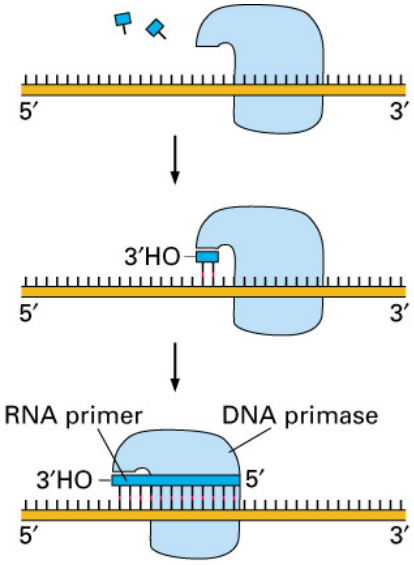



Figure 5–12. Molecular Biology of the Cell, 4th Edition.

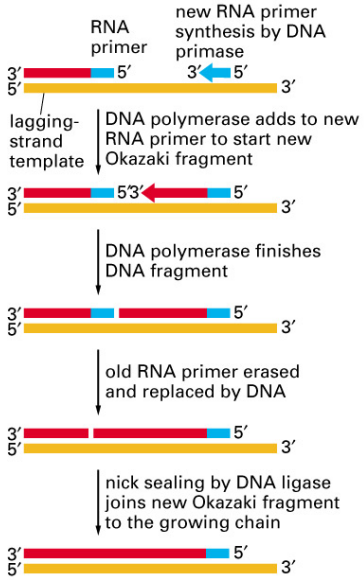



Figure 5–13. Molecular Biology of the Cell, 4th Edition.

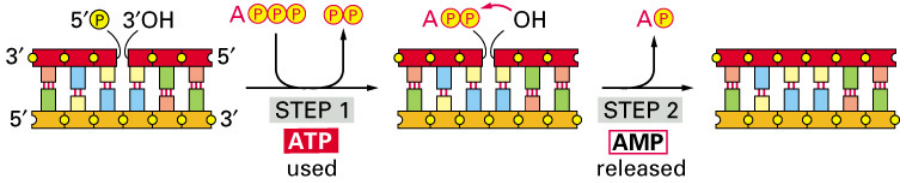
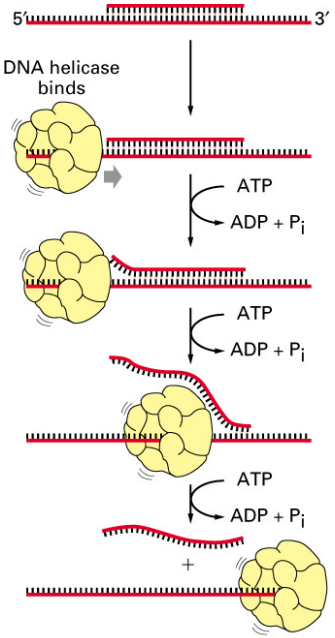



Figure 5–14. Molecular Biology of the Cell, 4th Edition.

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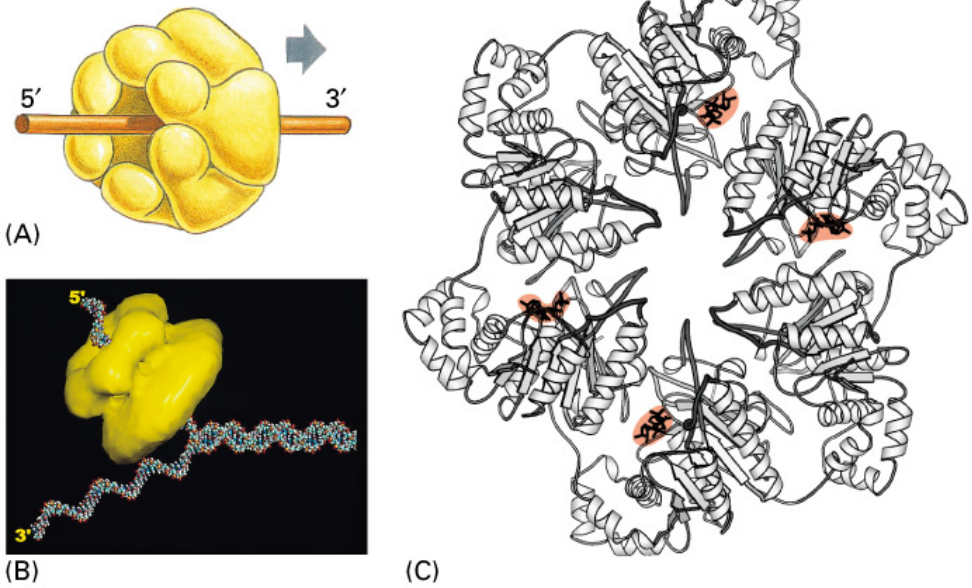



Figure 5–16. Molecular Biology of the Cell, 4th Edition.

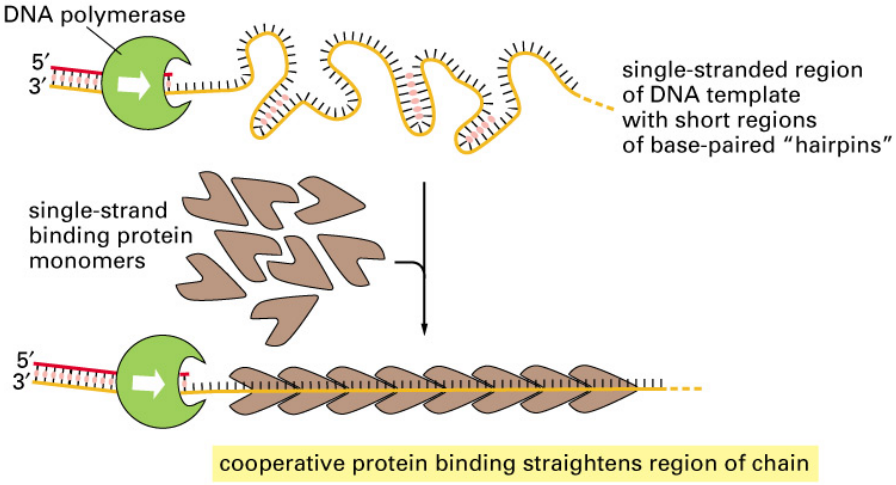



Figure 5–17. Molecular Biology of the Cell, 4th Edition.

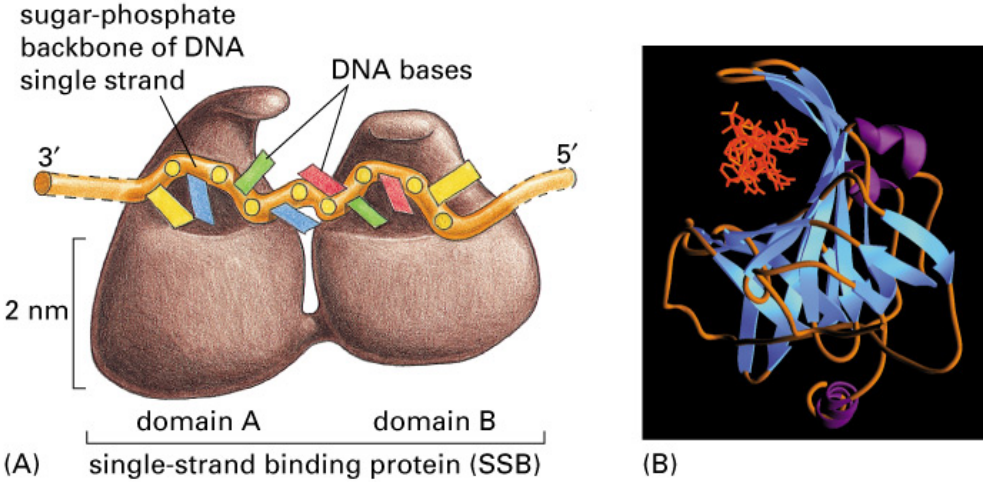
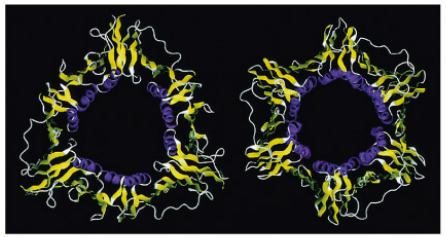


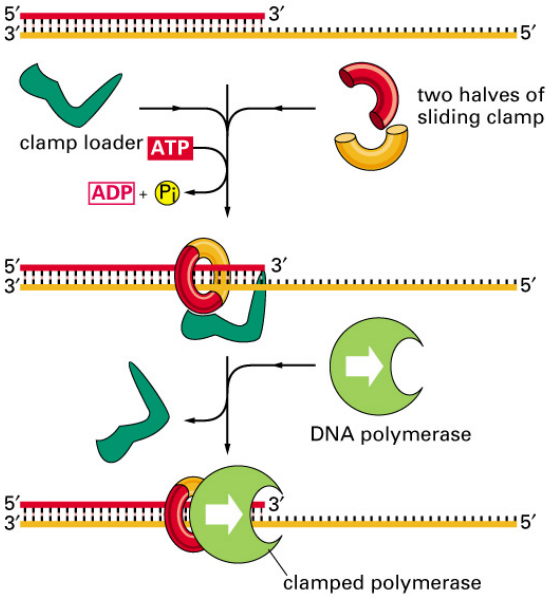

Figure 5–18. Molecular Biology of the Cell, 4th Edition.

(A)



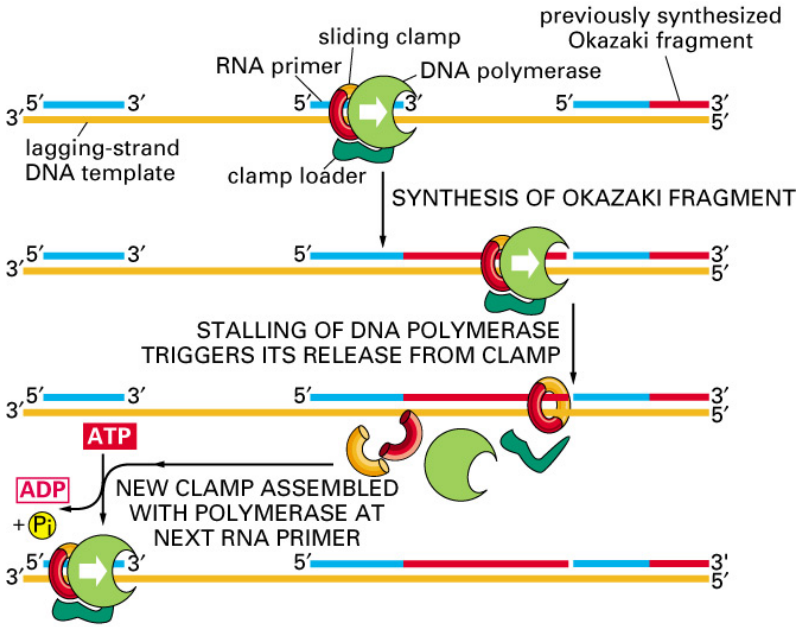
(B)

Figure 5–19 part 1 of 2. Molecular Biology of the Cell, 4th Edition.




(C)

Figure 5–19 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

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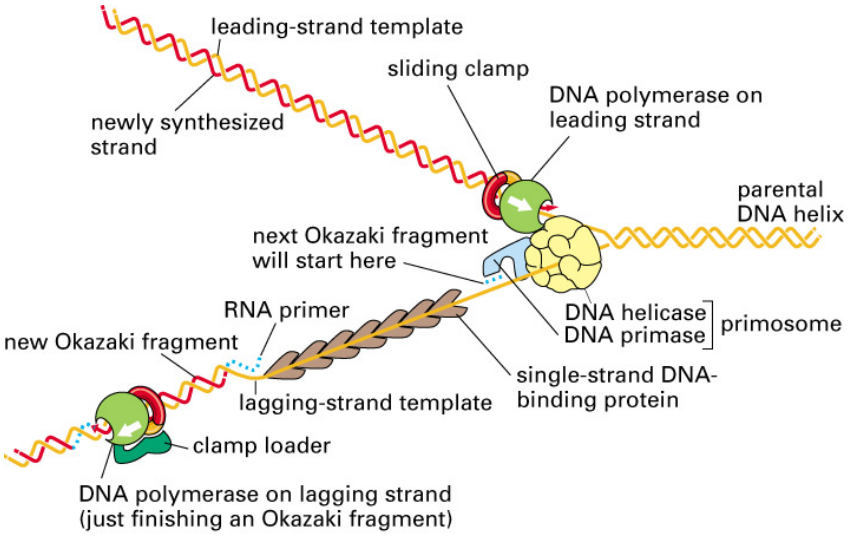


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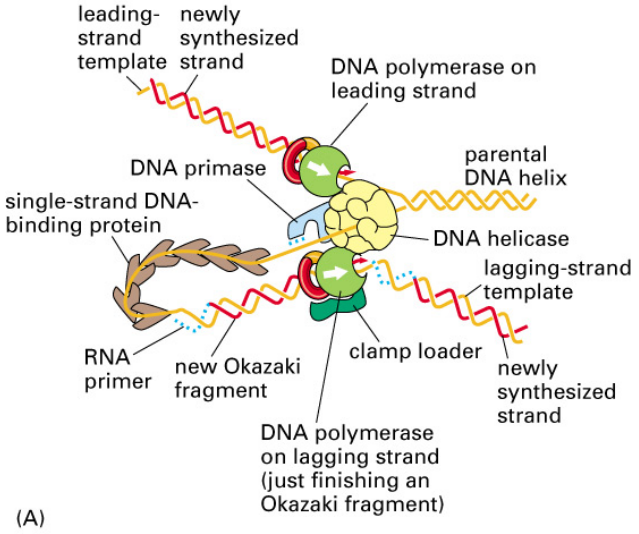


(A)

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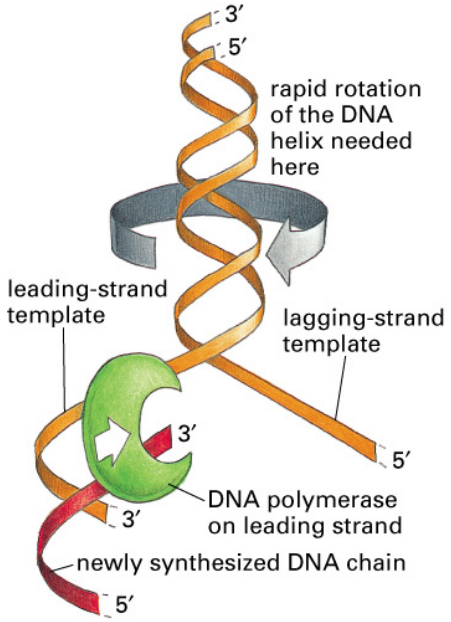


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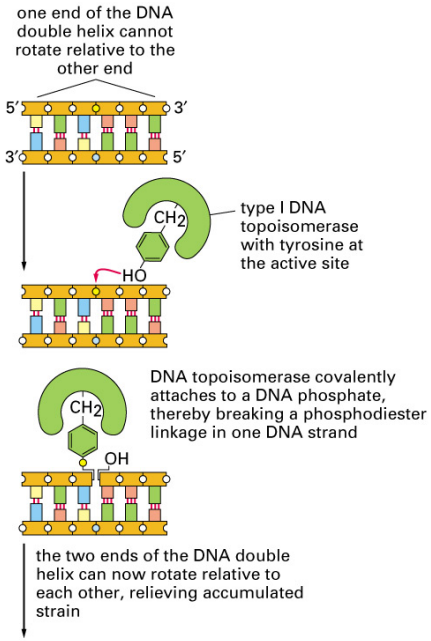


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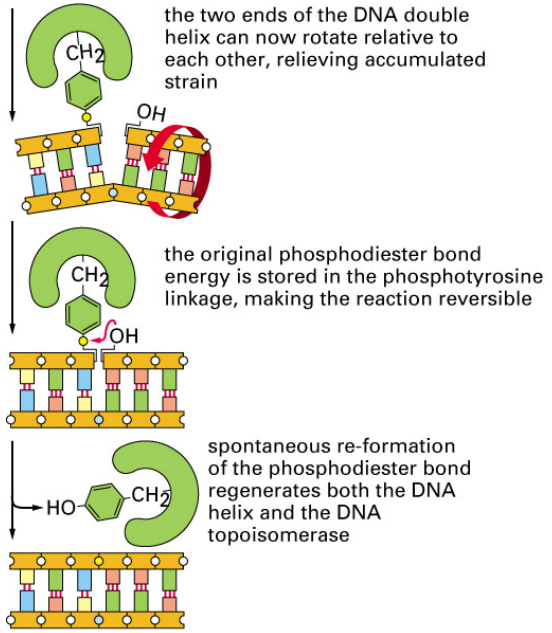



Figure 5–25 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

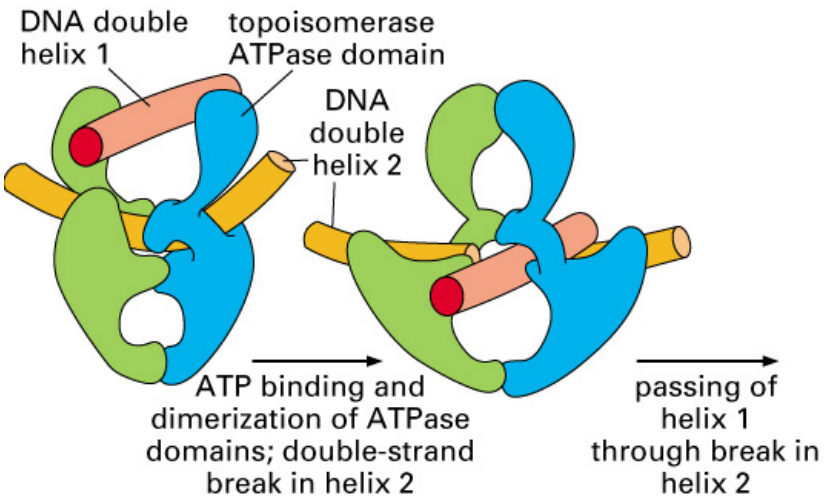



Figure 5–26 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

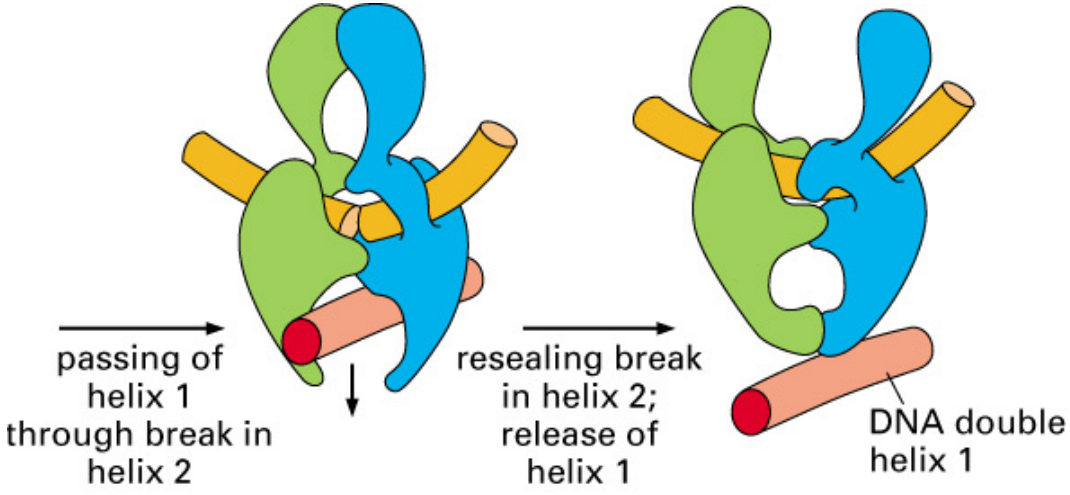



Figure 5–26 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

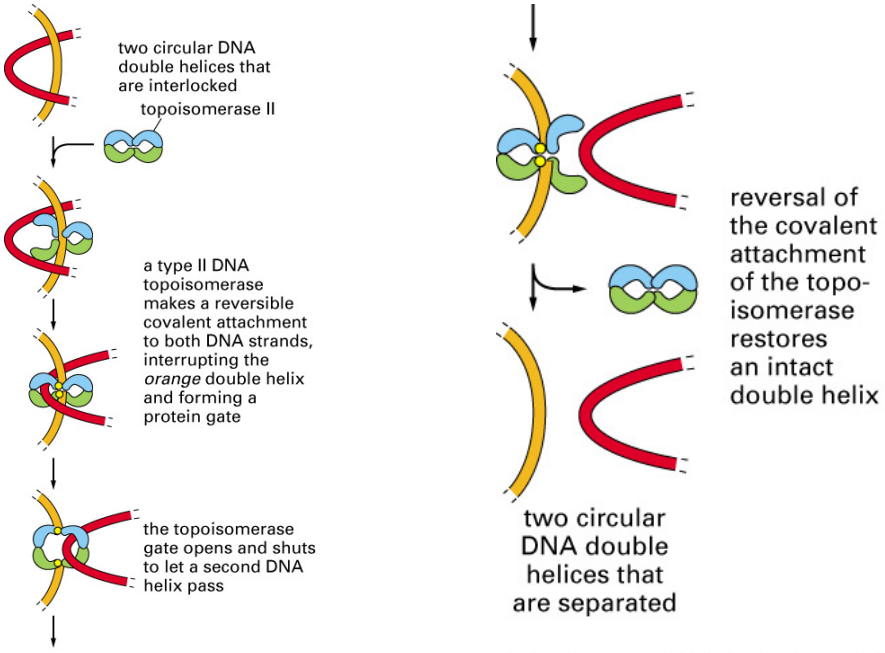



Figure 5–27 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

Figure 5–27 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Mammalian DNA polymerase is like prokaryotic DNA polymerase.
It differs from it in three minor ways.
It uses two different DNA polymerases on the lagging strand.
Its DNA primase is a subunit of one of the lagging-strand DNA polymerases.
And because eukaryotic genomes are so much longer than prokaryotic ones, many DNA holoenzymes work together when duplicating a eukaryotic genome.

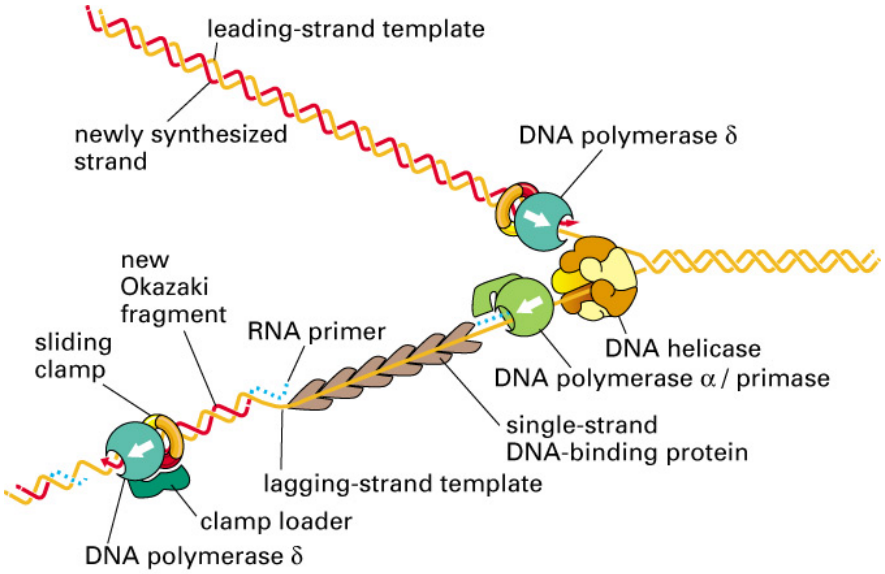



Figure 5–28. Molecular Biology of the Cell, 4th Edition.

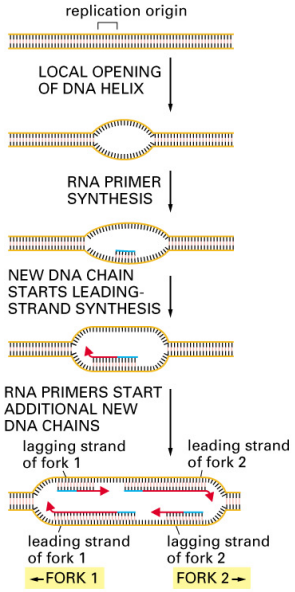
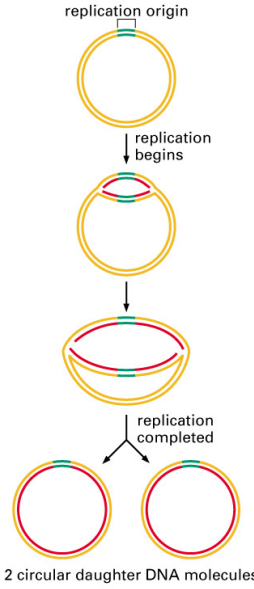



Figure 5–29. Molecular Biology of the Cell, 4th Edition.

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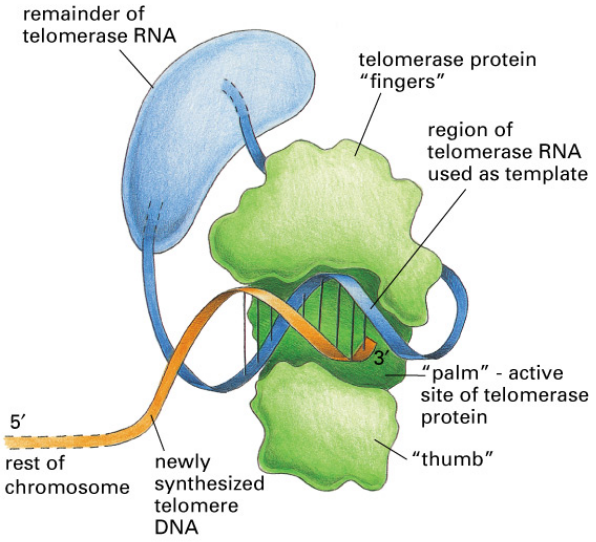



Figure 5–42. Molecular Biology of the Cell, 4th Edition.

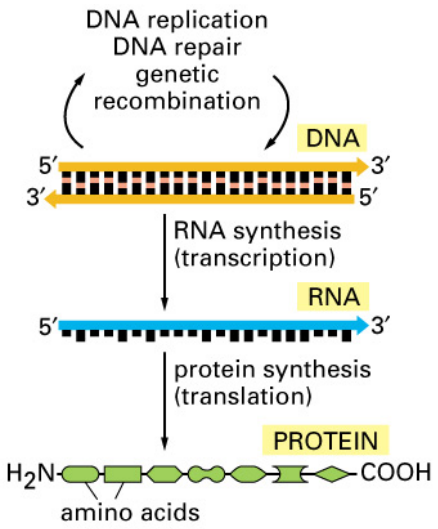



Figure 6–2. Molecular Biology of the Cell, 4th Edition.

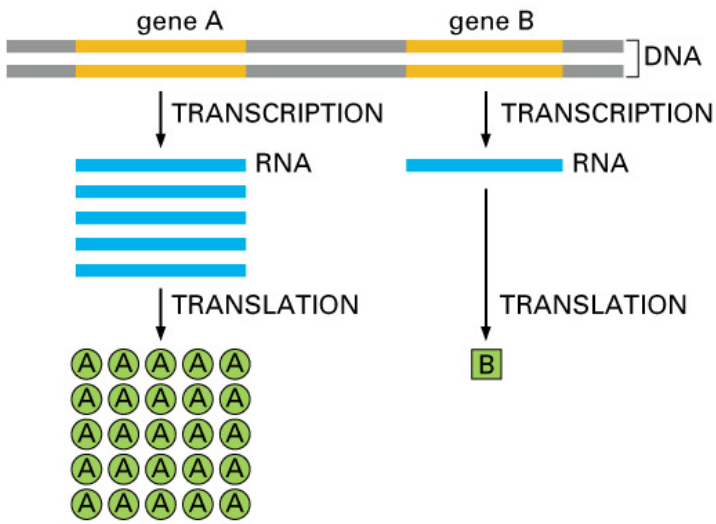



Figure 6–3. Molecular Biology of the Cell, 4th Edition.

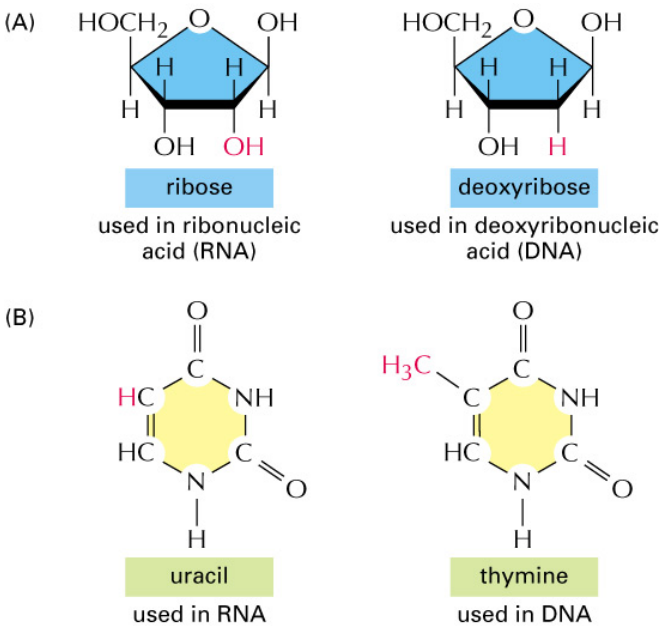



Figure 6–4 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

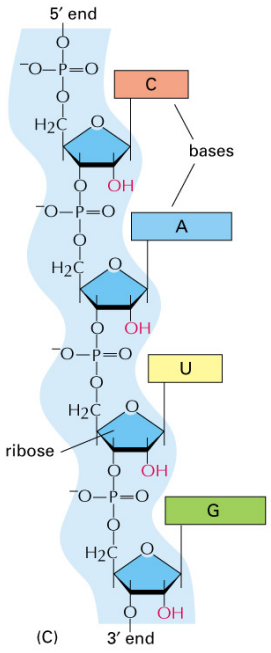



Figure 6–4 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

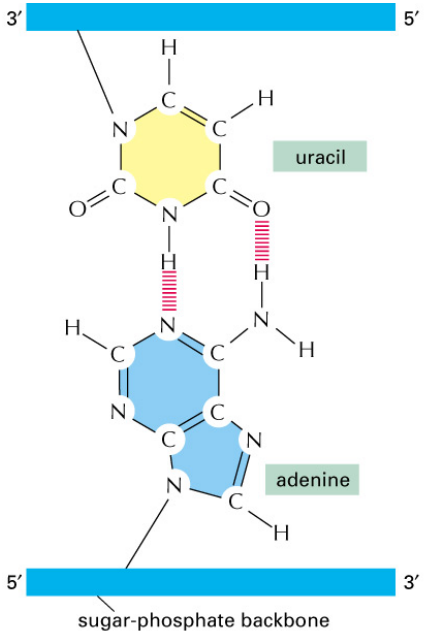



Figure 6–5. Molecular Biology of the Cell, 4th Edition.

Deoxyribose lacks an oxygen atom. Uracil lacks a methyl group.

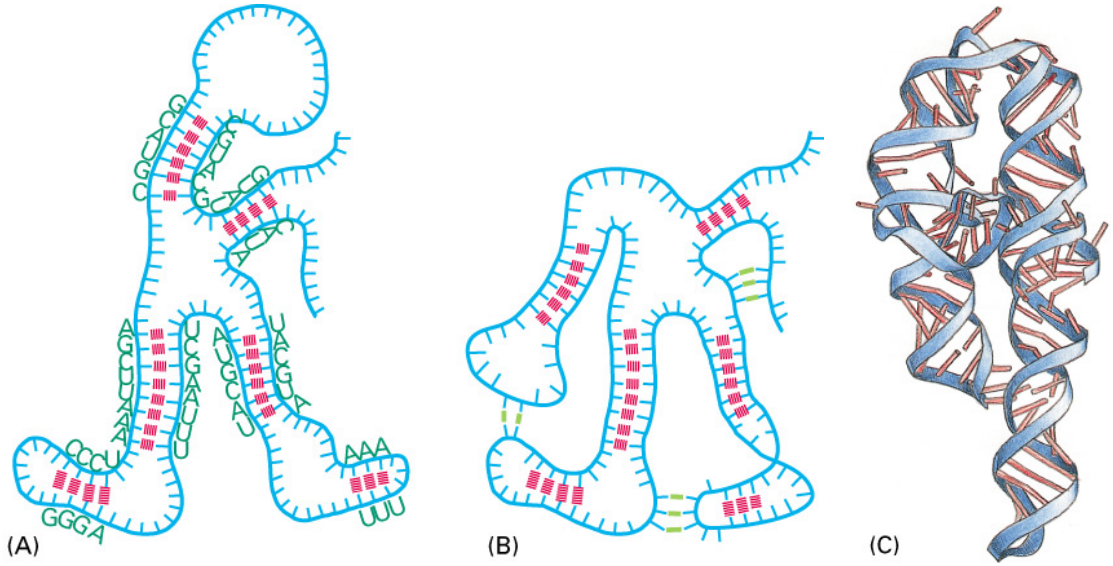
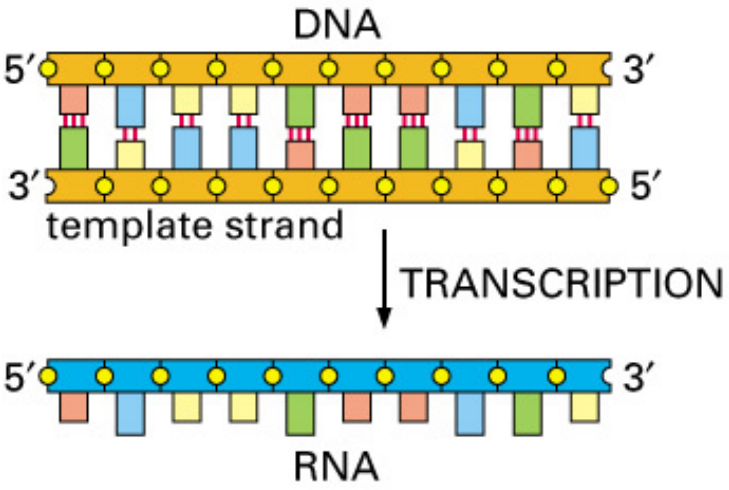



Figure 6–6 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

Figure 6–6 part 2 of 2. Molecular Biology of the Cell, 4th Edition.



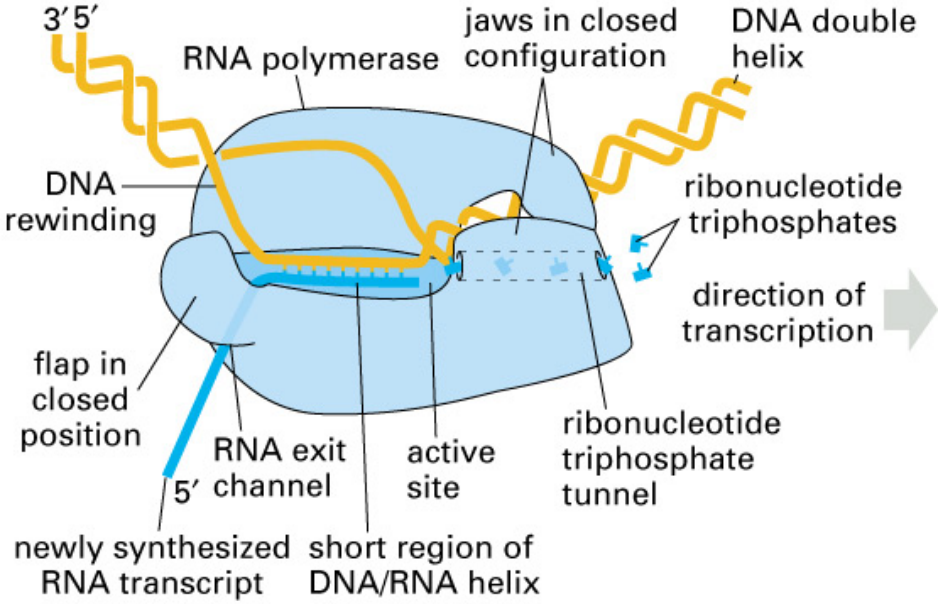




Figure 6–7. Molecular Biology of the Cell, 4th Edition.

Figure 6–8. Molecular Biology of the Cell, 4th Edition.

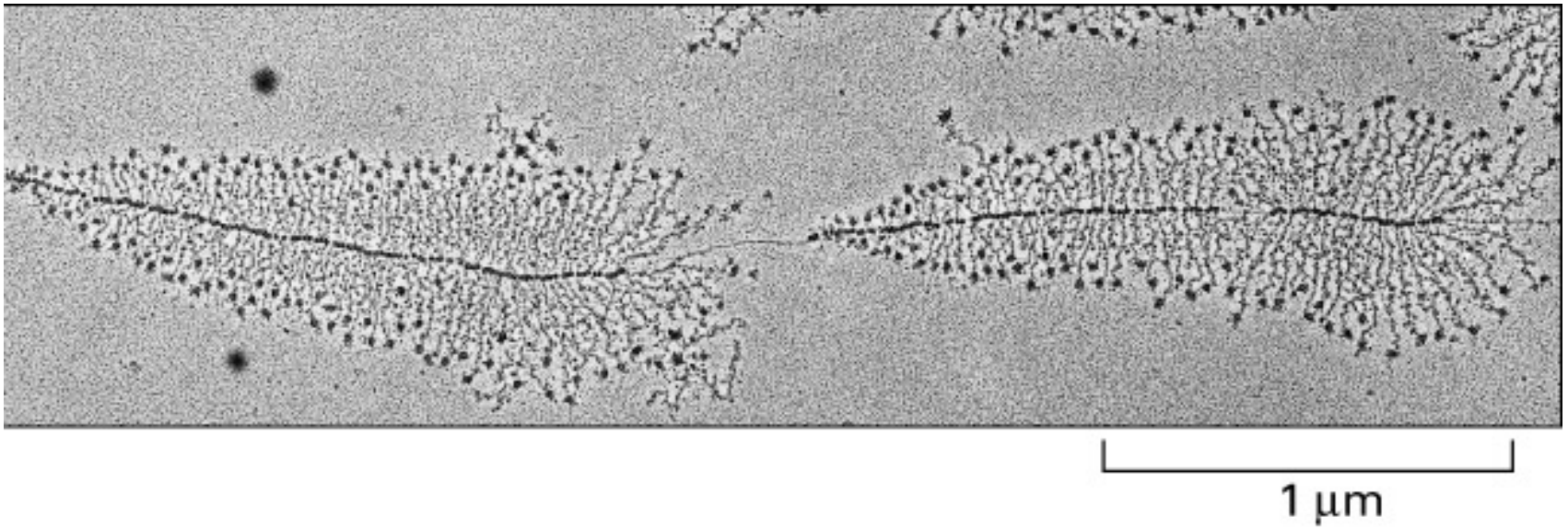



Figure 6–9. Molecular Biology of the Cell, 4th Edition.

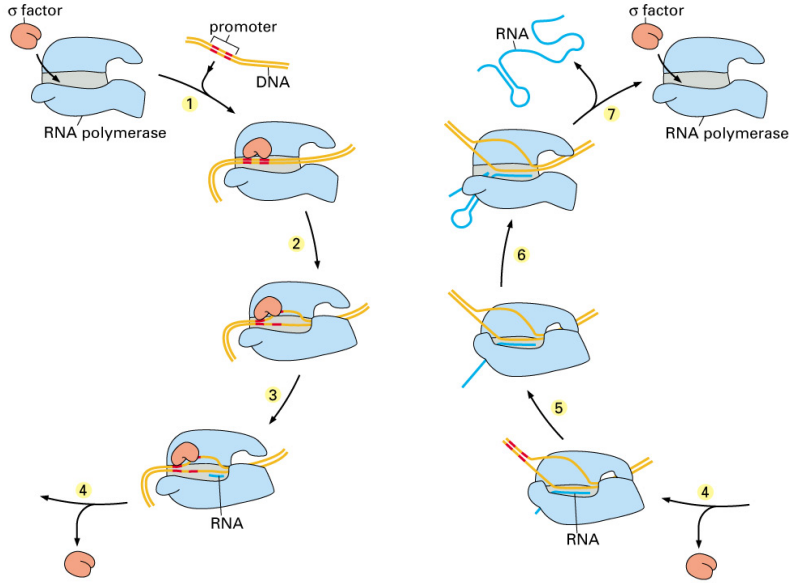



Figure 6–10 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

Figure 6–10 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

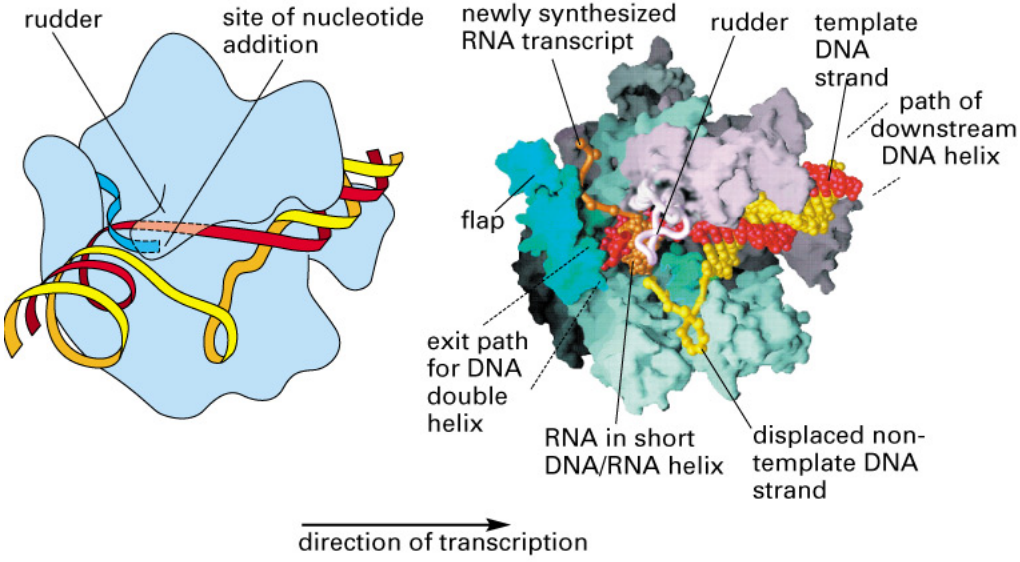
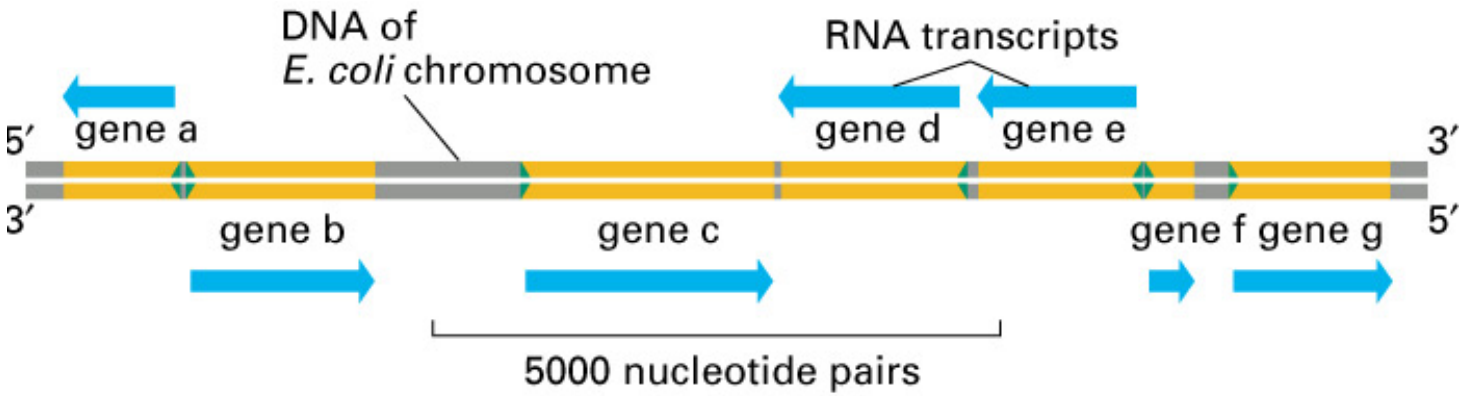



Figure 6–11. Molecular Biology of the Cell, 4th Edition.

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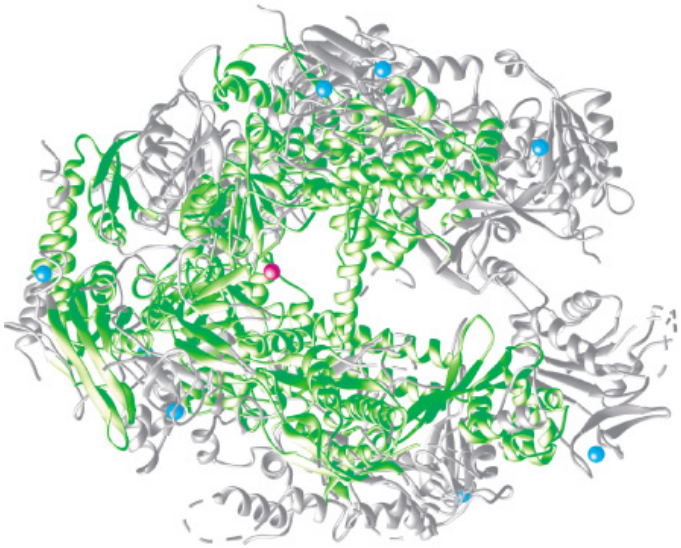


Figure 6–15. Molecular Biology of the Cell, 4th Edition.

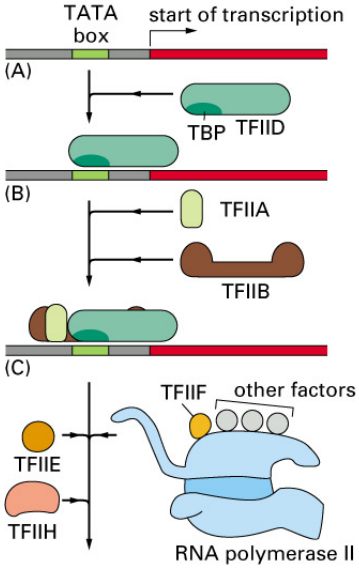



Figure 6–16 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

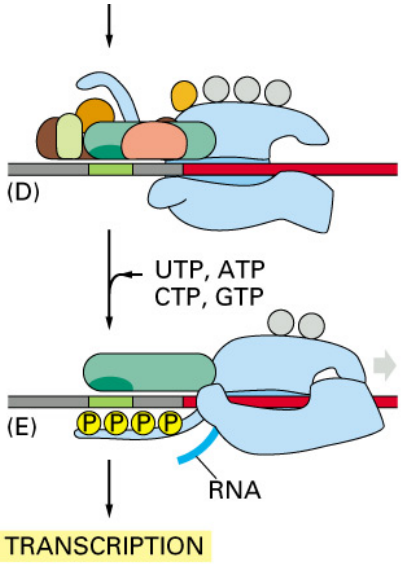



Figure 6–16 part 2 of 2. Molecular Biology of the Cell, 4th Editic

Eukaryotes have 3 RNA polymerases; prokaryotes only 1. Eukaryotic RNA poly II has 12 subunits; prokaryotic RNA poly has 5. The TATA box is a promoter.

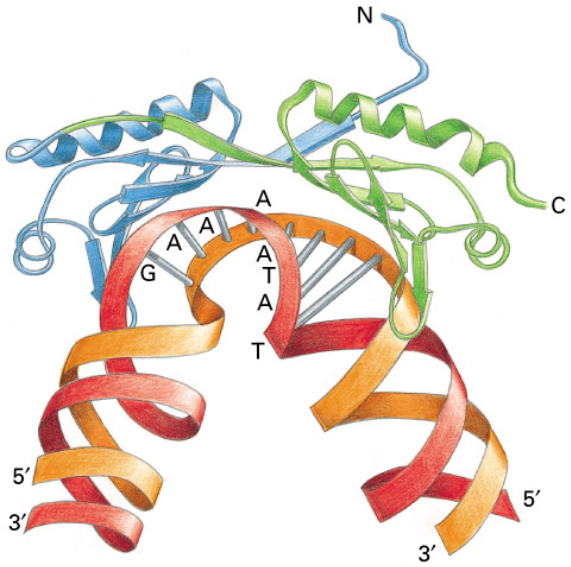



Figure 6–18. Molecular Biology of the Cell, 4th Edition.

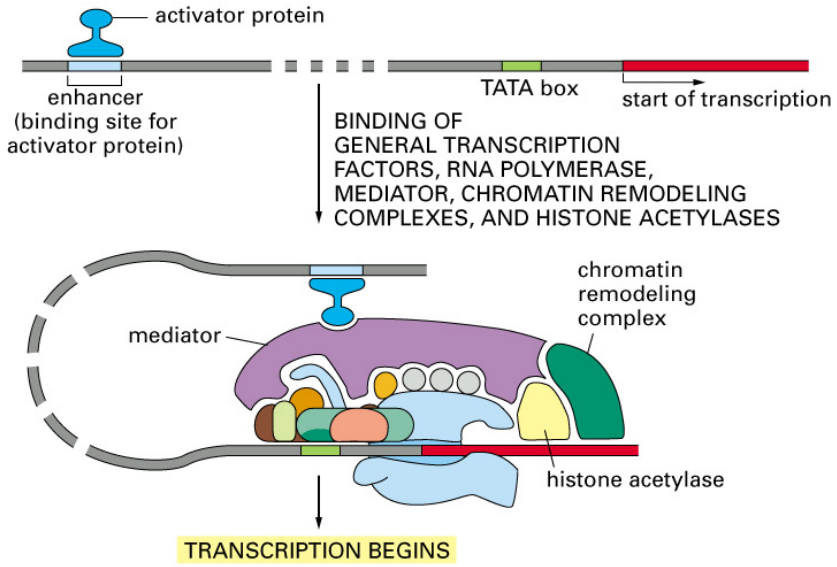
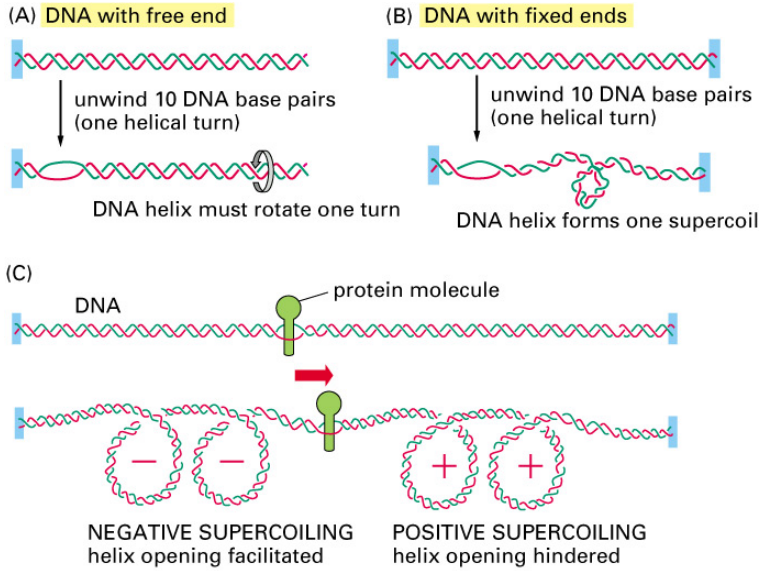



Figure 6–19. Molecular Biology of the Cell, 4th Edition.

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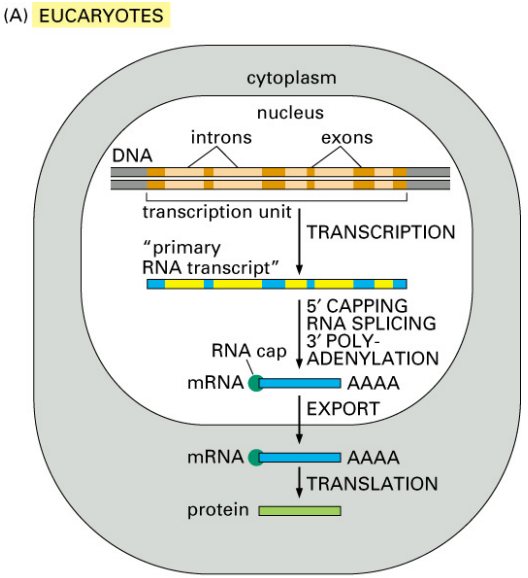



Figure 6–21 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

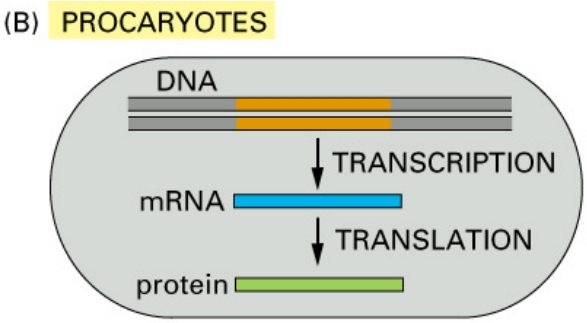
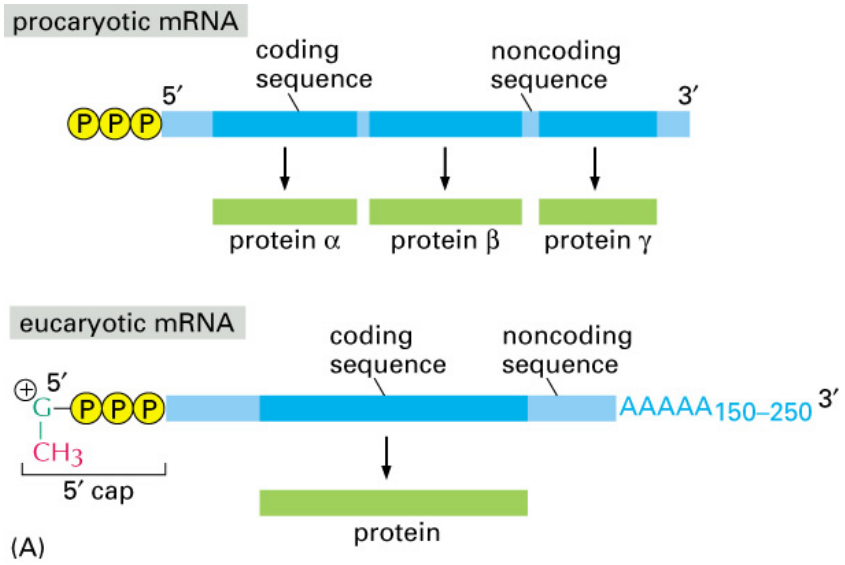



Figure 6–21 part 2 of 2. Molecular Biology of the Cell

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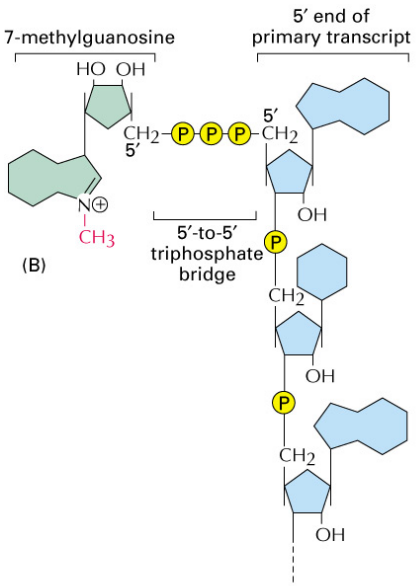


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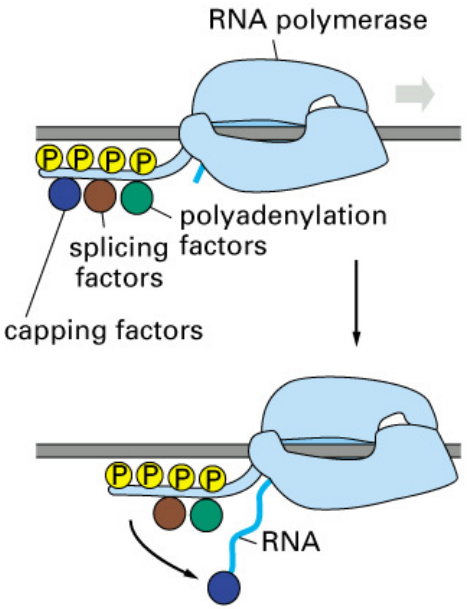


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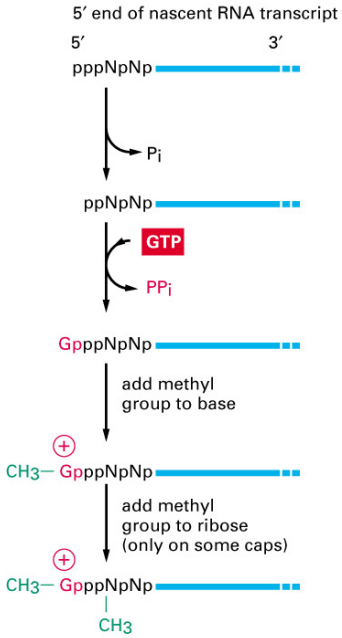



Figure 6–24. Molecular Biology of the Cell, 4th Edition.

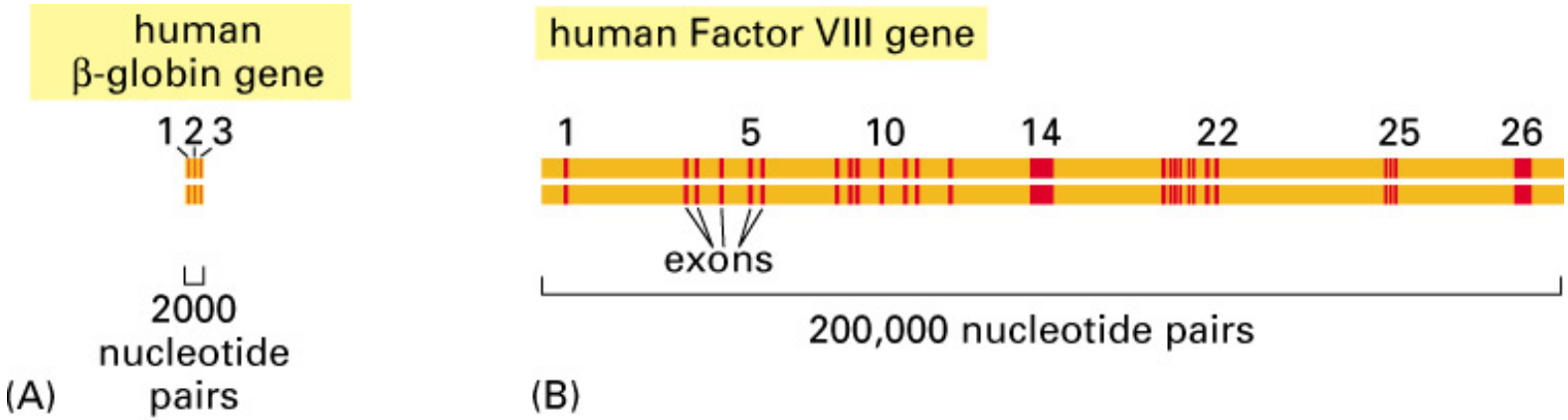



Figure 6–25. Molecular Biology of the Cell, 4th Edition.

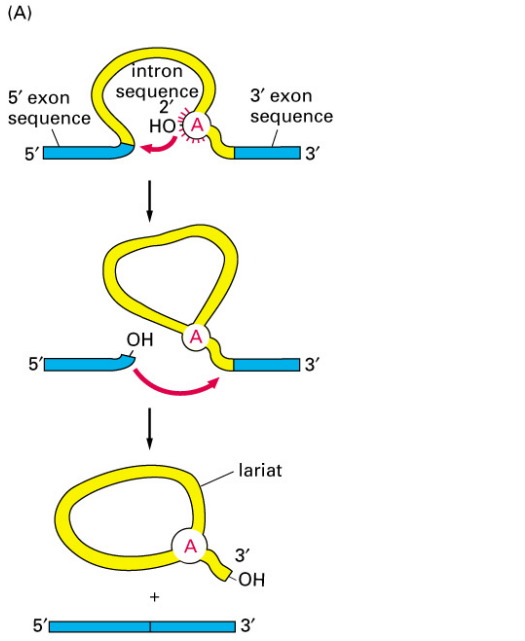
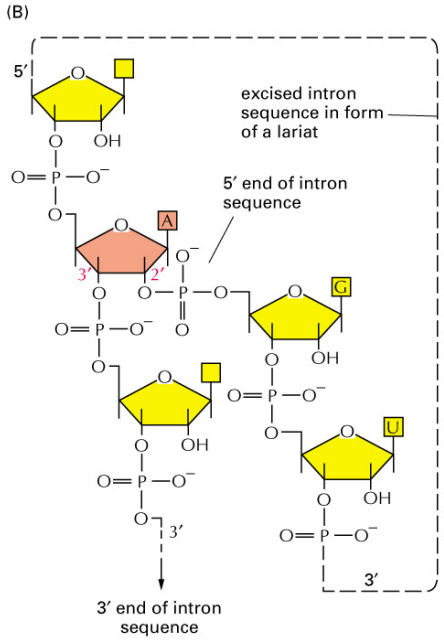



Figure 6–26 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

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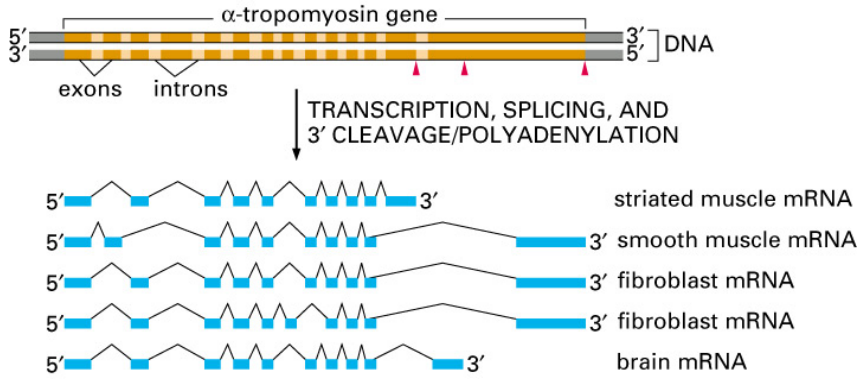



Figure 6–27. Molecular Biology of the Cell, 4th Edition.

Alternative splicing increases the stability of the eukaryotic genome.

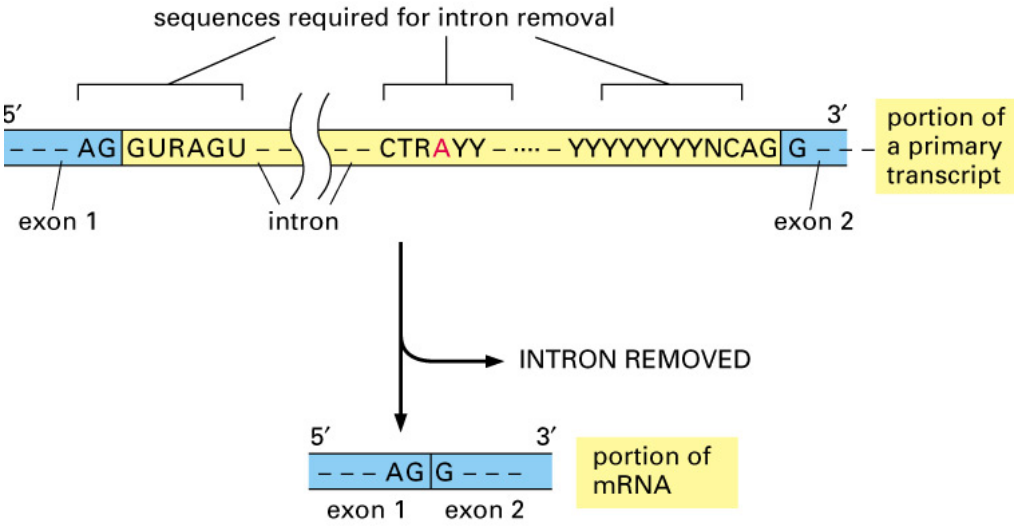



Figure 6–28. Molecular Biology of the Cell, 4th Edition.

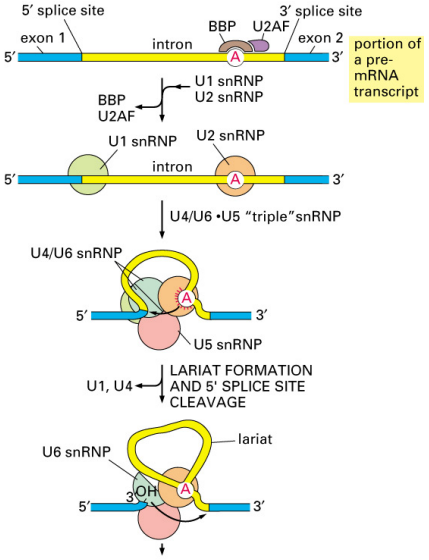



Figure 6–29 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

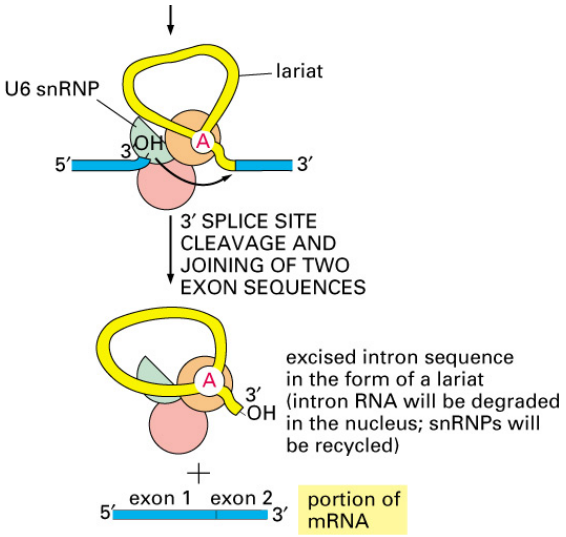



Figure 6–29 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

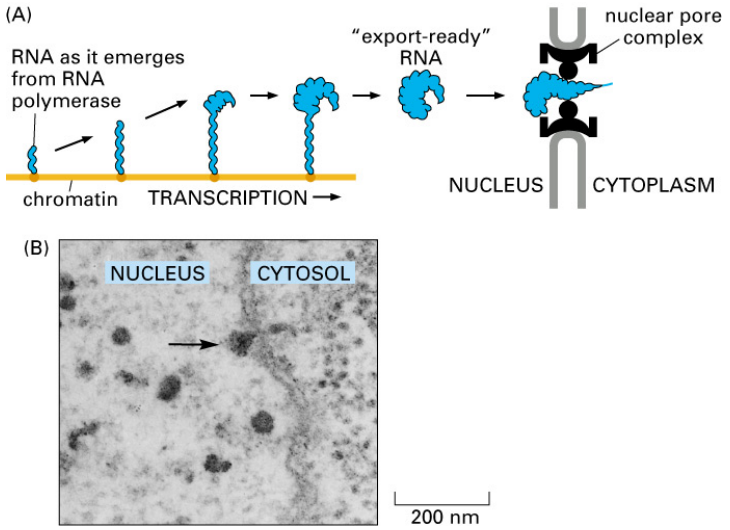



Figure 6–39. Molecular Biology of the Cell, 4th Edition.

AG|GURAGU (R = A or G) signals the start of many human introns.

Figure 6–41. Molecular Biology of the Cell, 4th Edition.

# Transcribed genes are separated by untranscribed spacers.

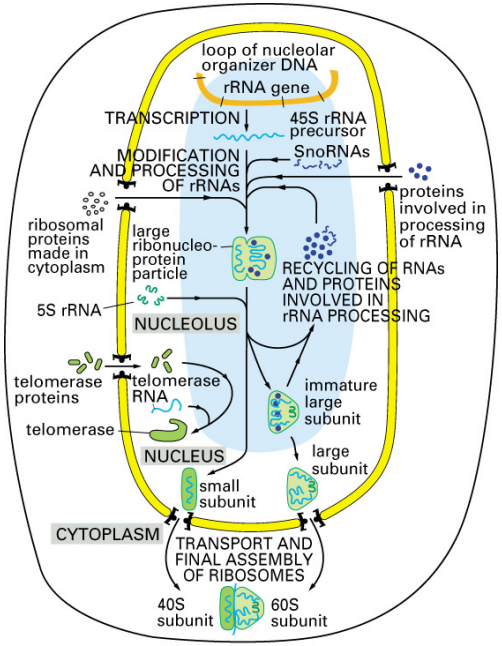



Figure 6–47. Molecular Biology of the Cell, 4th Edition.

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| GCA<br>GCC<br>GCG<br>GCU | AGA<br>AGG<br>CGA<br>CGC<br>CGG<br>CGU | GAC<br>GAU | AAC<br>AAU | UGC<br>UGU | GAA<br>GAG | CAA<br>CAG | GGA<br>GGC<br>GGG<br>GGU | CAC<br>CAU | AUA<br>AUC<br>AUU | |
| Ala | Arg | Asp | Asn | Cys | Glu | Gln | Gly | His | Ile | |
| A | R | D | N | C | E | Q | G | H | I | |
| UUA<br>UUG<br>CUA<br>CUC<br>CUG<br>CUU | AAA<br>AAG | AUG | UUC<br>UUU | CCA<br>CCC<br>CCG<br>CCU | AGC<br>AGU<br>UCA<br>UCC<br>UCG<br>UCU | ACA<br>ACC<br>ACG<br>ACU | UGG | UAC<br>UAU | GUA<br>GUC<br>GUG<br>GUU | UAA<br>UAG<br>UGA |
| Leu | Lys | Met | Phe | Pro | Ser | Thr | Trp | Tyr | Val | stop |
| L | K | M | F | P | S | T | W | Y | V | |

Figure 6–50. Molecular Biology of the Cell, 4th Edition.

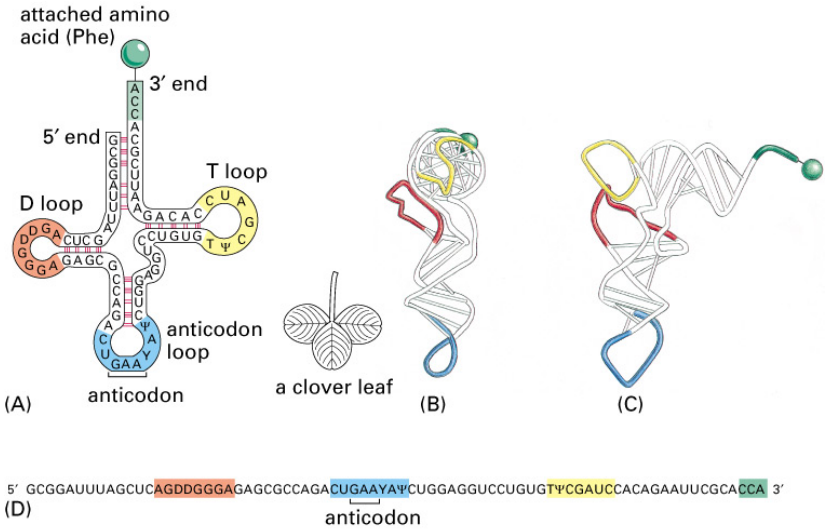
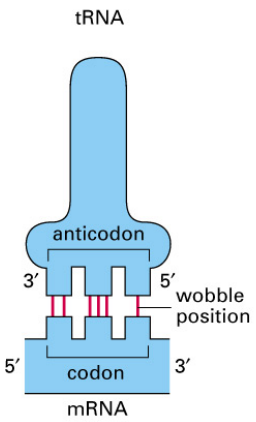



Figure 6–52. Molecular Biology of the Cell, 4th Edition.




bacteria

| wobble codon base | possible anticodon bases |
|---|---|
| U | A, G, or I |
| C | G or I |
| A | U or I |
| G | C or U |

eucaryotes

| wobble codon base | possible anticodon bases |
|---|---|
| U | G or I |
| C | G or I |
| A | U |
| G | C |

Figure 6–53. Molecular Biology of the Cell, 4th Edition.

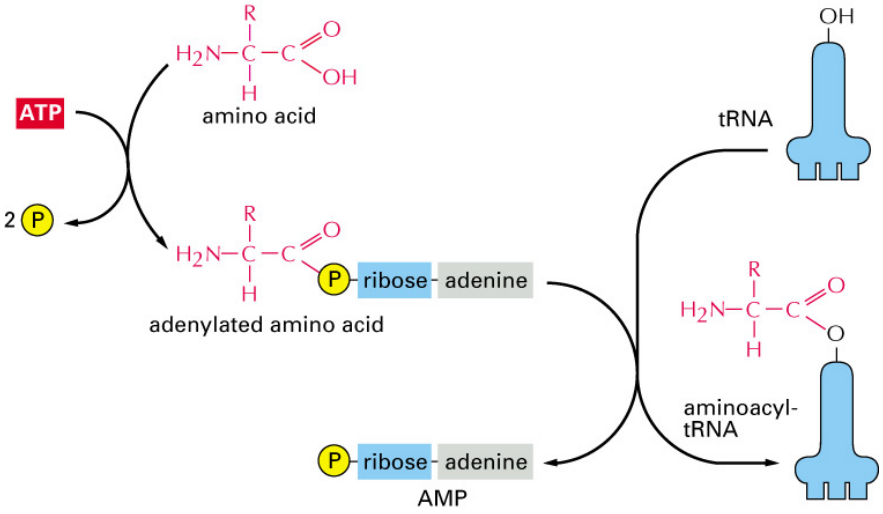



Figure 6–56. Molecular Biology of the Cell, 4th Edition.

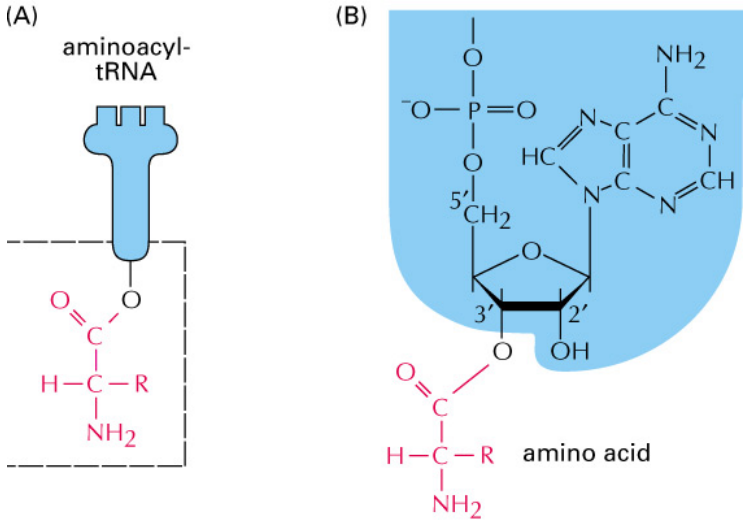



Figure 6–57. Molecular Biology of the Cell, 4th Edition.

Most cells have 20 aminoacyl-tRNA synthetases. They charge tRNA's with their aa's.

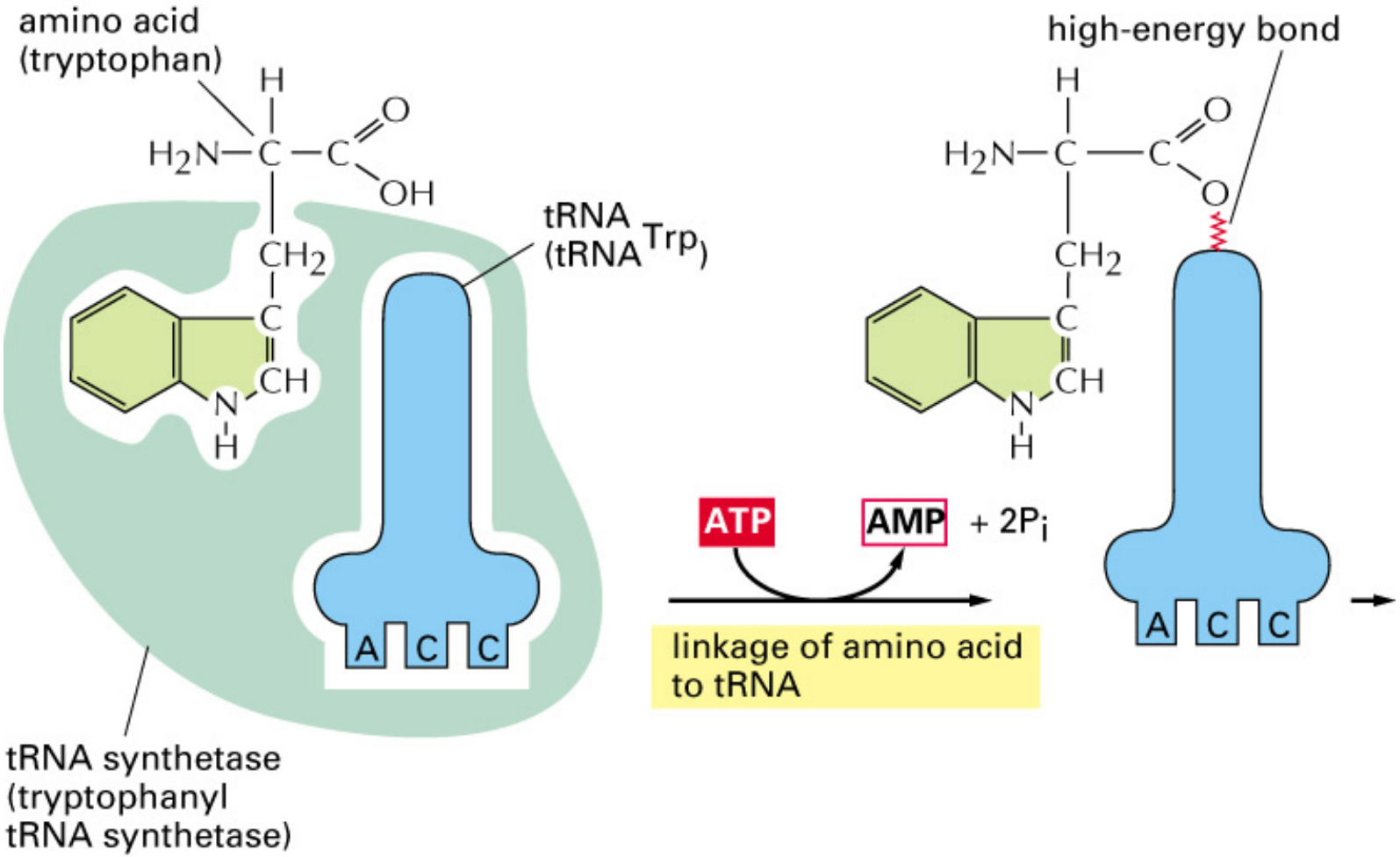



Figure 6–58 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

A tRNA synthetase adds W to $tRNA^W$.

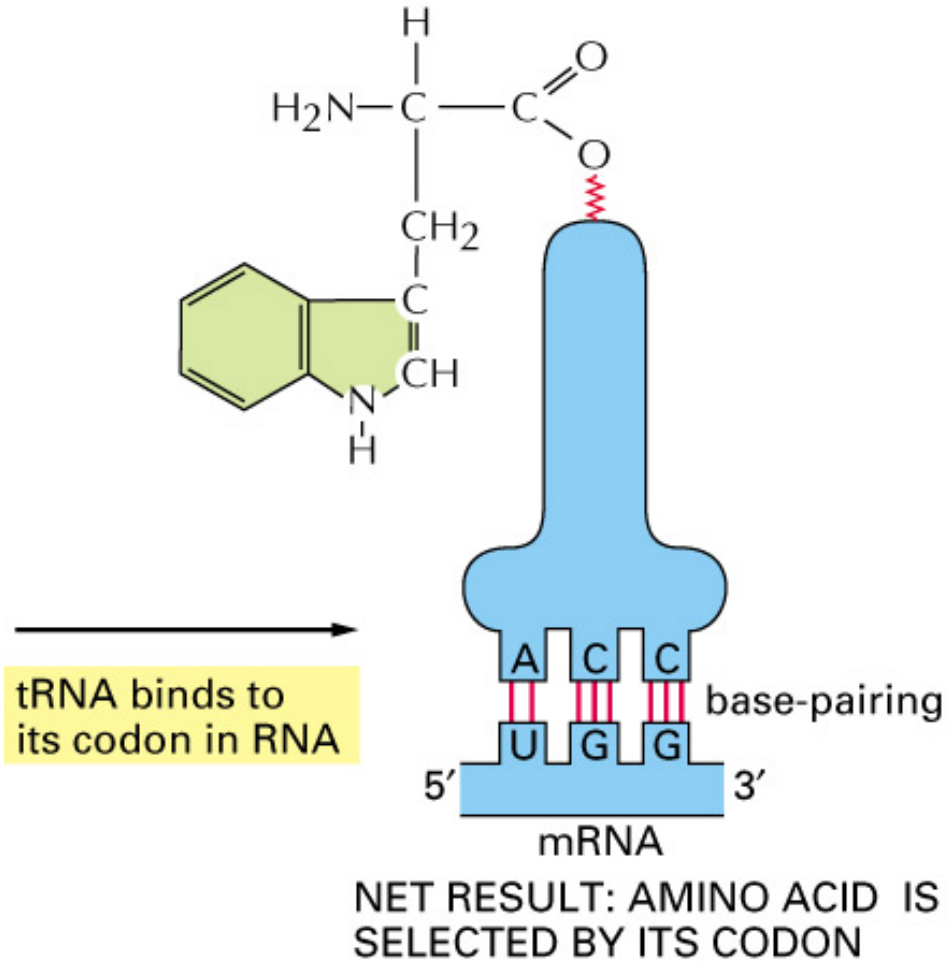



Figure 6–58 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Later the $\text{tRNA}^{W}$ charged with W binds to its codon in RNA.

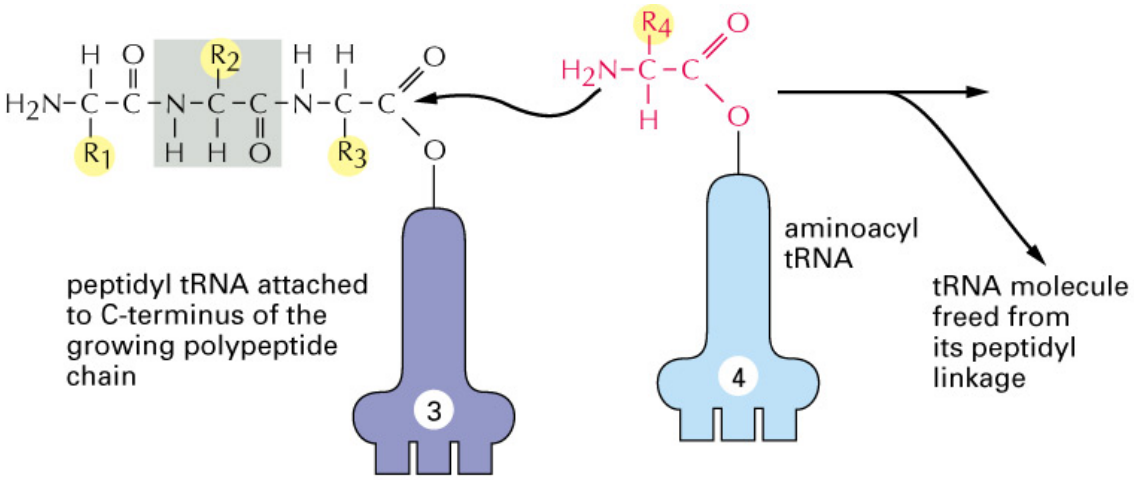



Figure 6–61 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

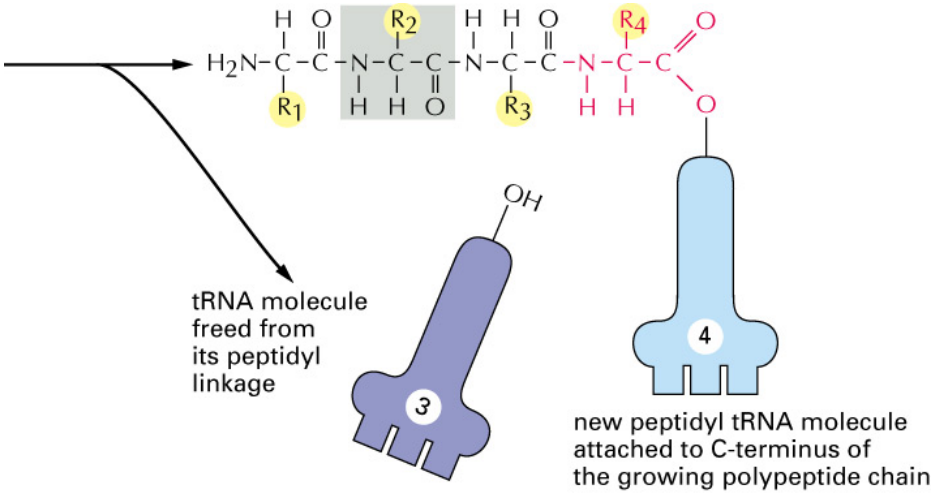



Figure 6–61 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

How a ribosome takes aa's from tRNA's and makes a protein.

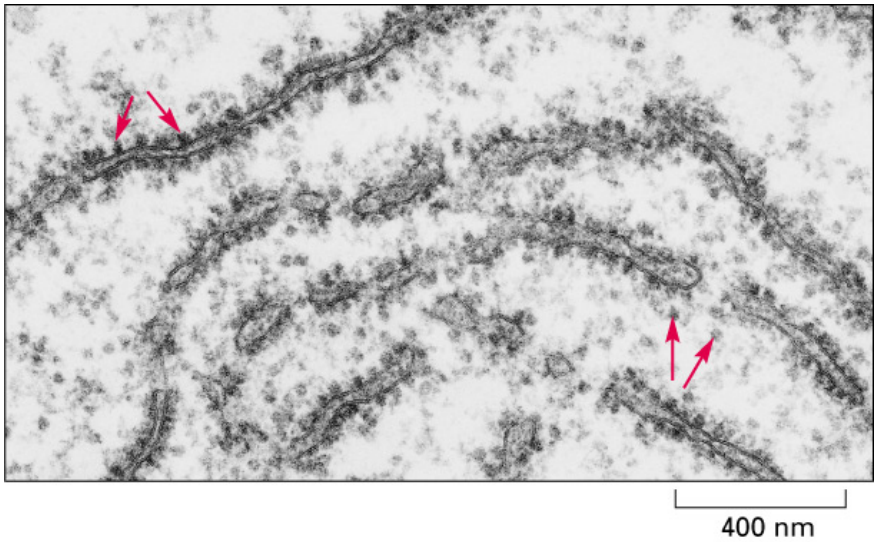



Figure 6–62. Molecular Biology of the Cell, 4th Edition.

Ribosomes in the cytoplasm of a eucaryotic cell. Some are free in the cytosol (the main fluid of the cell); others are attached to membranes of the endoplasmic reticulum (the ER, which is an outgrowth of the membrane of the nucleus).

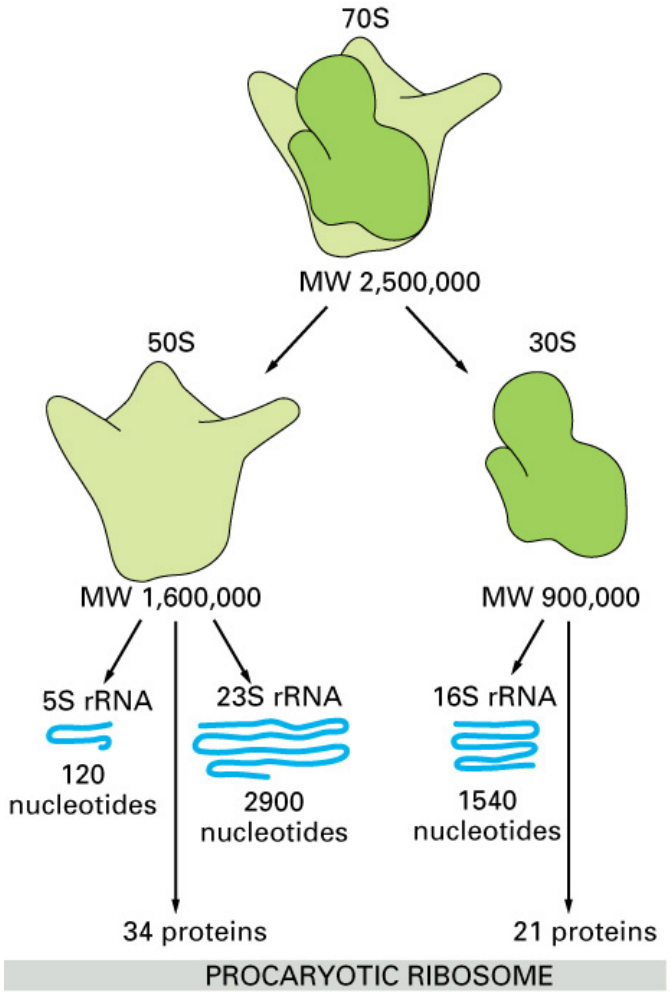



Figure 6–63 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

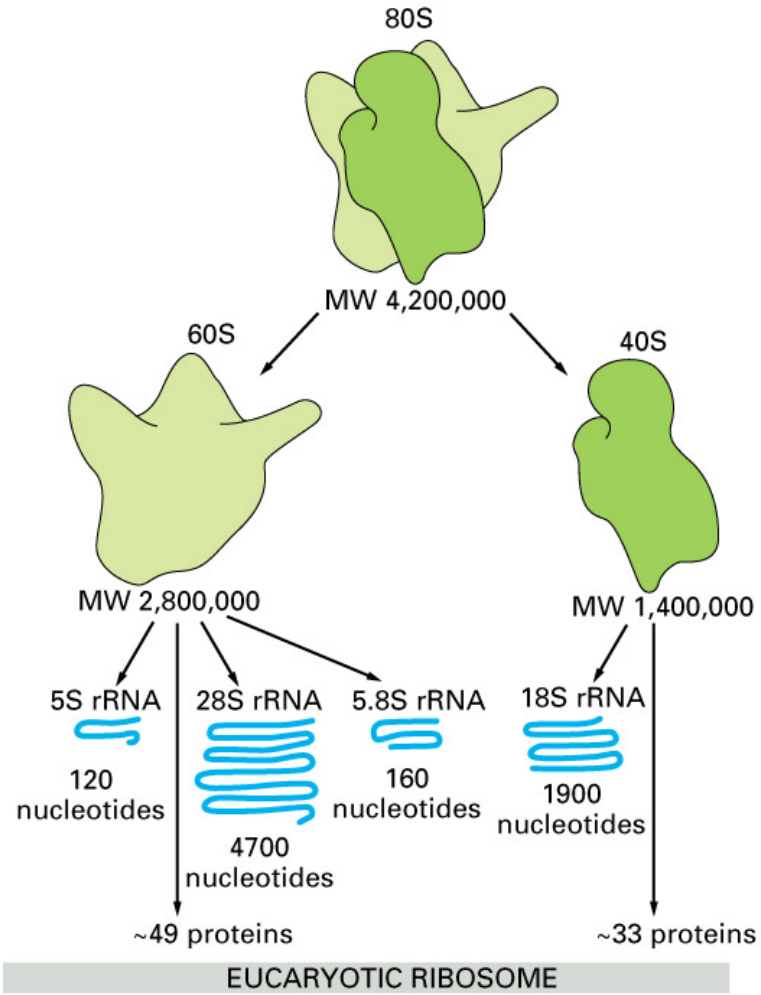



Figure 6–63 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

The ''S values'' are determined by rates of sedimentation and are a measure of the size of a molecule.

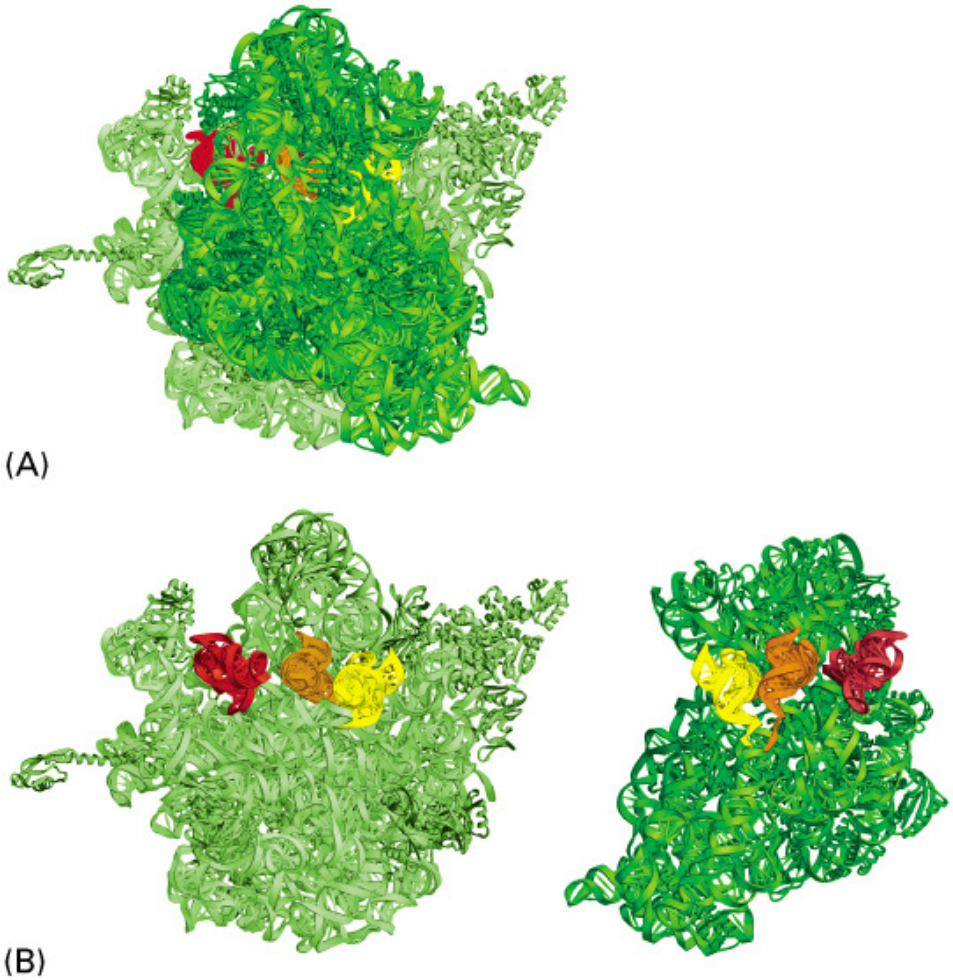



Figure 6–64 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

A bacterial ribosome. The tRNAs are shown bound in the E-site (red, eject), the P-site (orange, peptidyl), and the A-site (yellow, acceptor). In B, the ribosome is opened like a book.

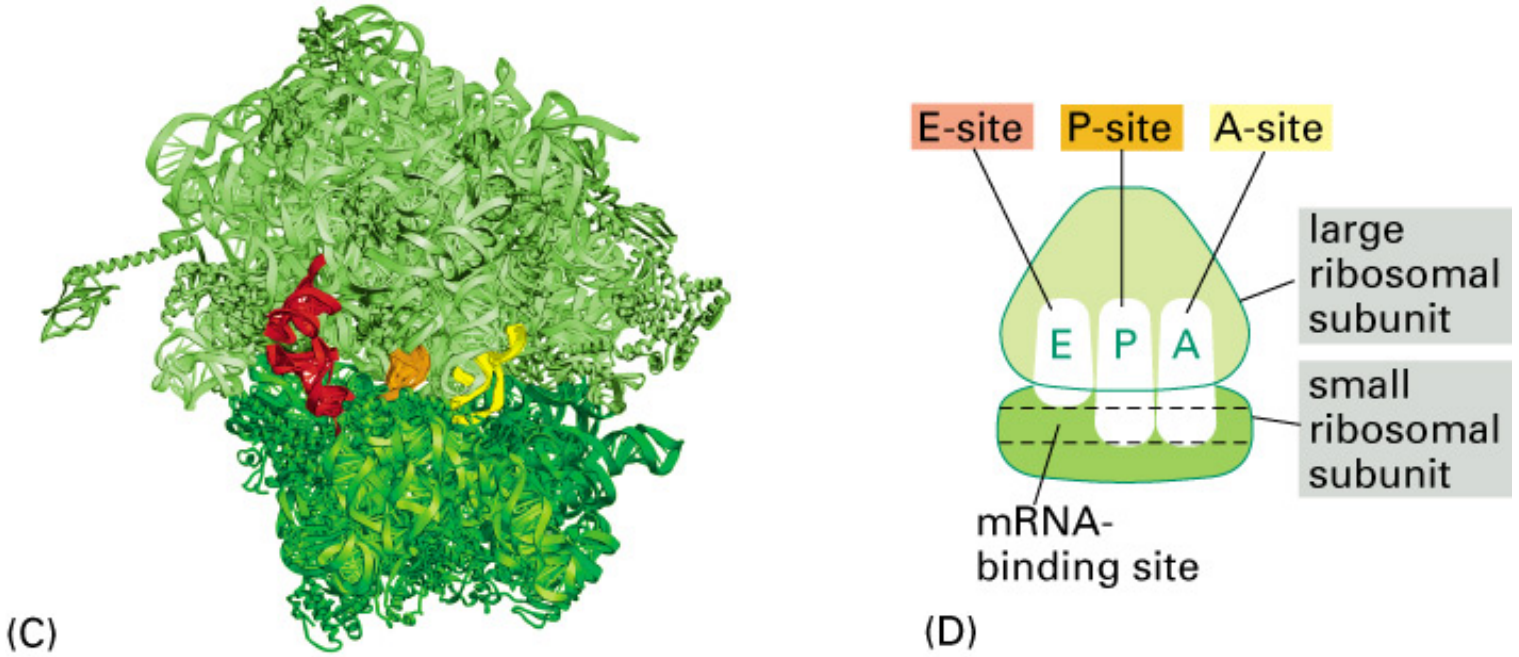



Figure 6–64 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Top view.

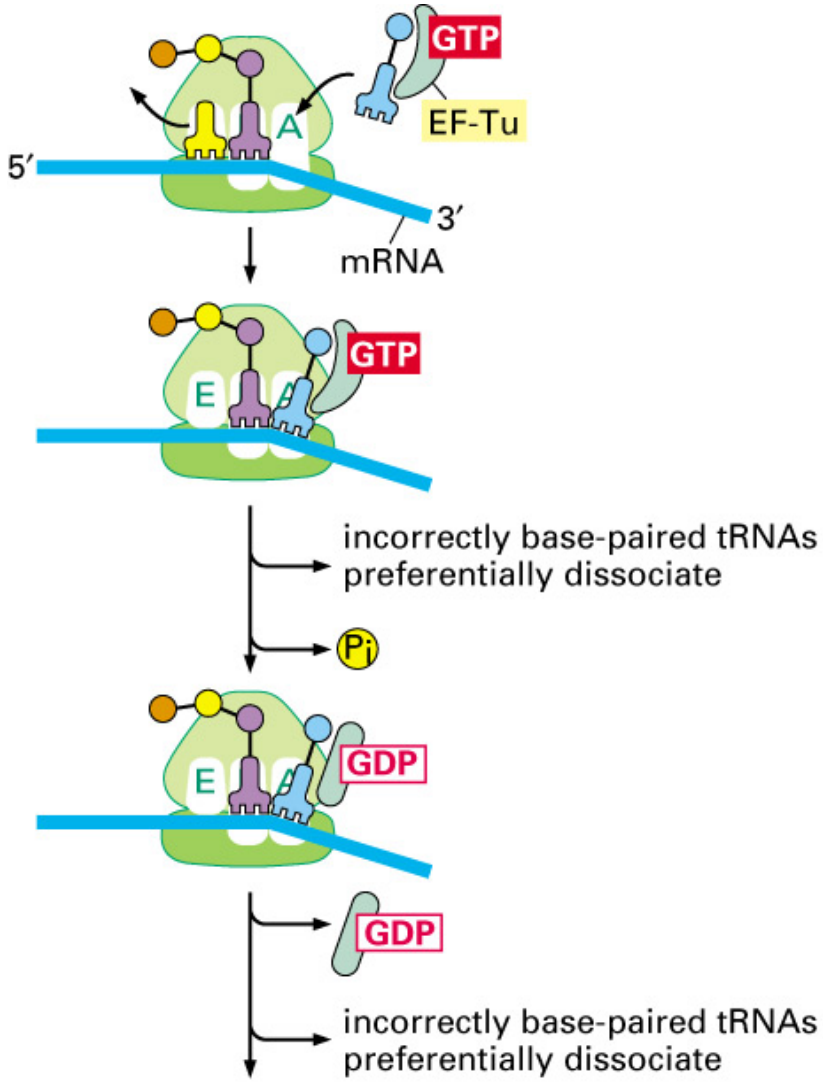



Figure 6–66 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

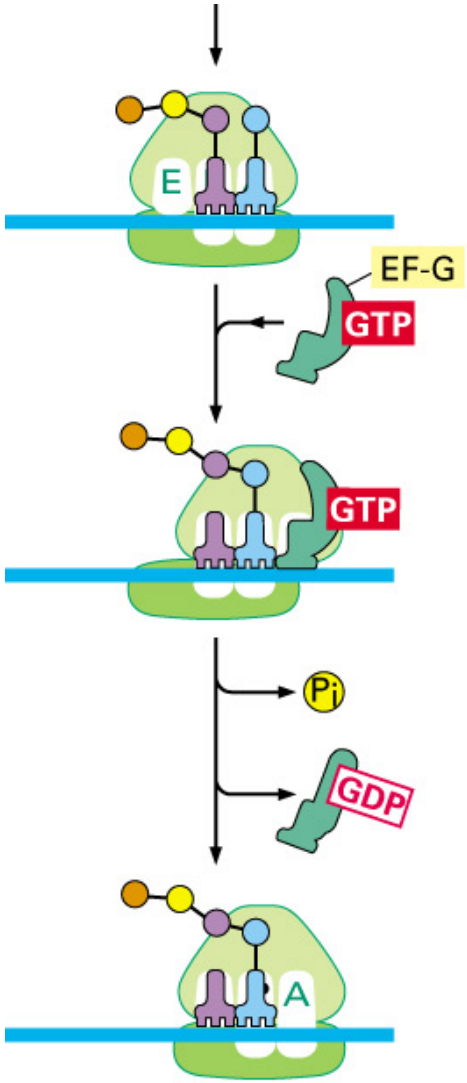



Figure 6–66 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

What happens in the 3 sites of a ribosome.

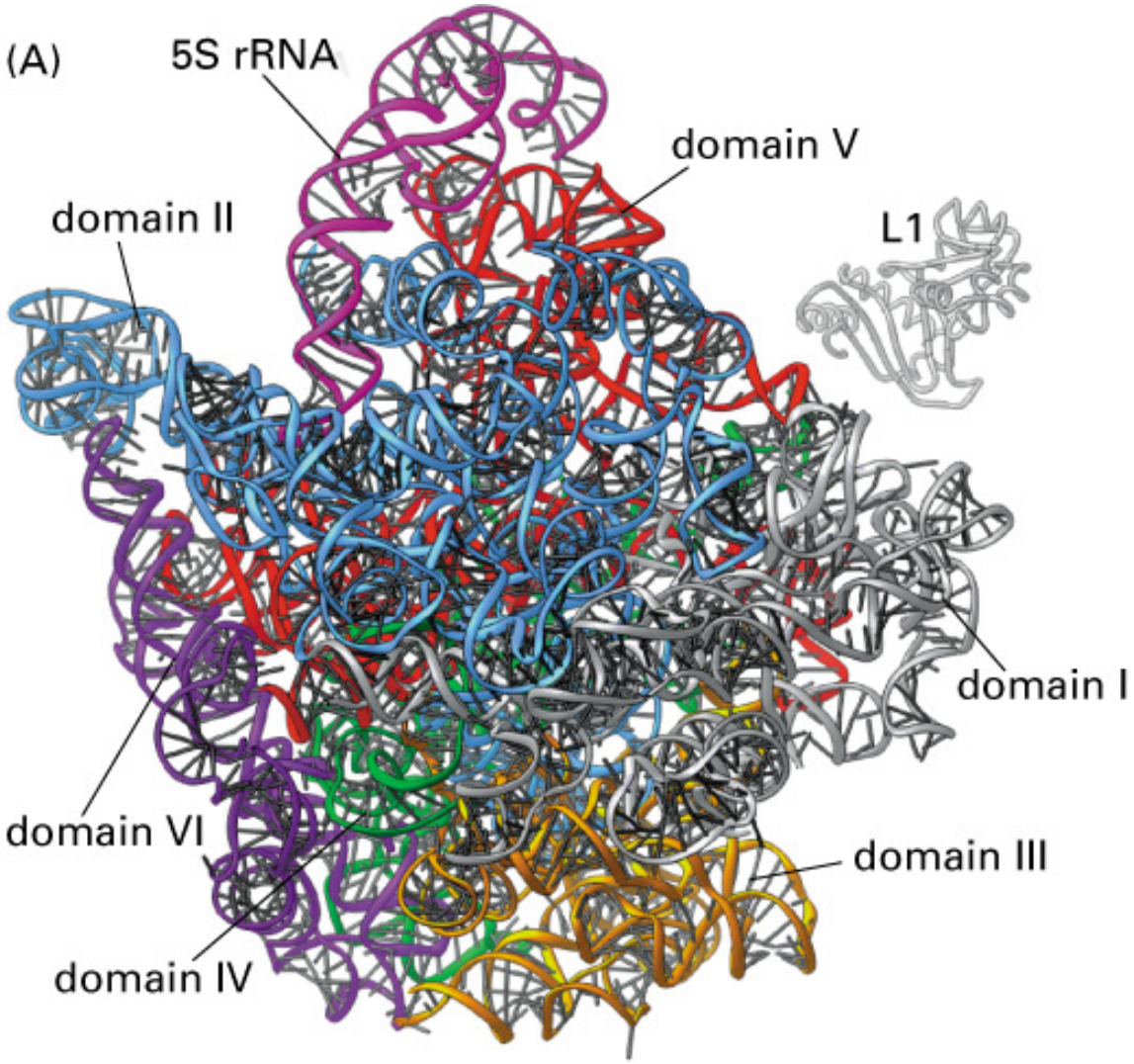



Figure 6–67 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

X-ray structure of a bacterial ribosome.

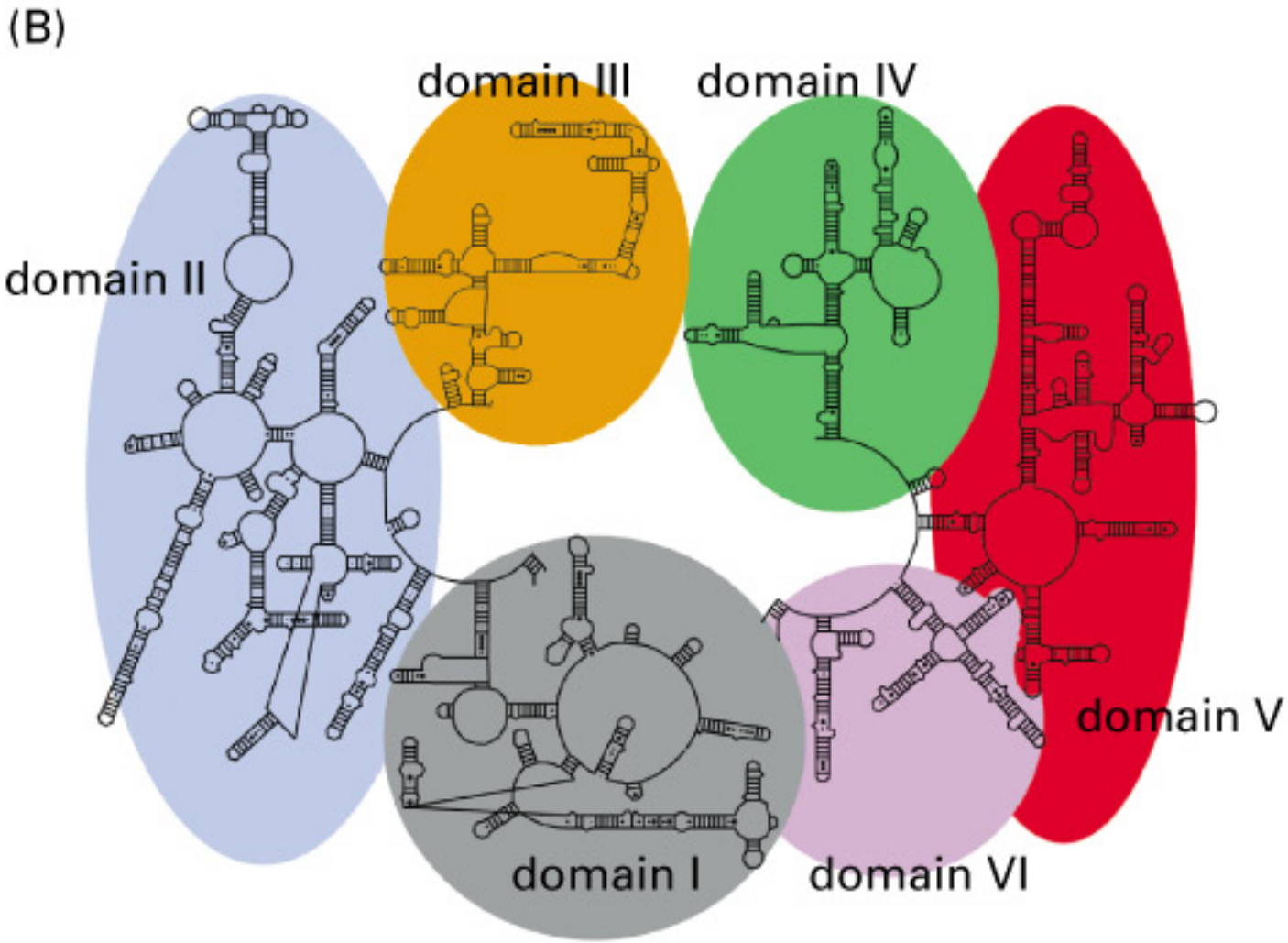



Figure 6–67 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Secondary structure of a bacterial ribosome.

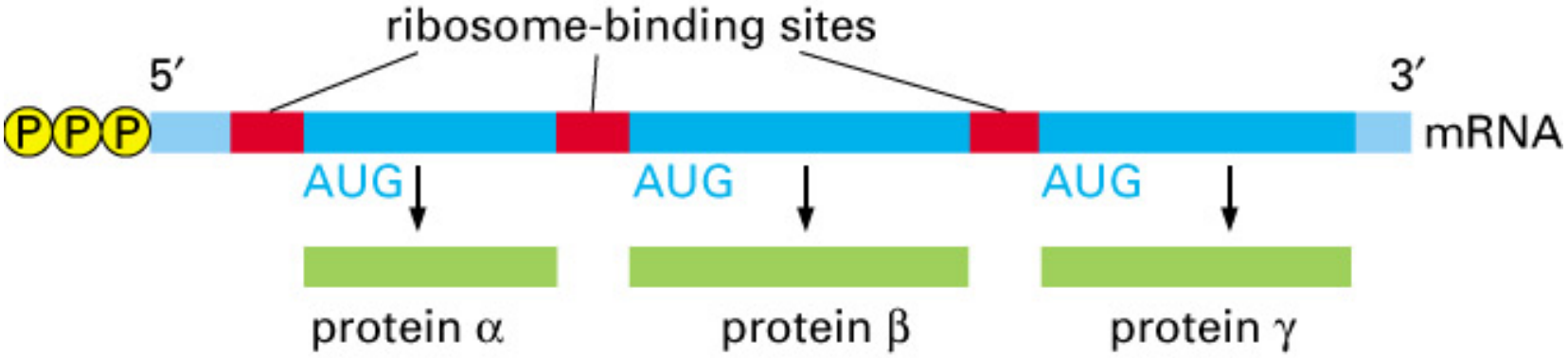



Figure 6–72. Molecular Biology of the Cell, 4th Edition.

A single molecule of procaryotic mRNA can carry several genes. AUG is the codon for the aa M.

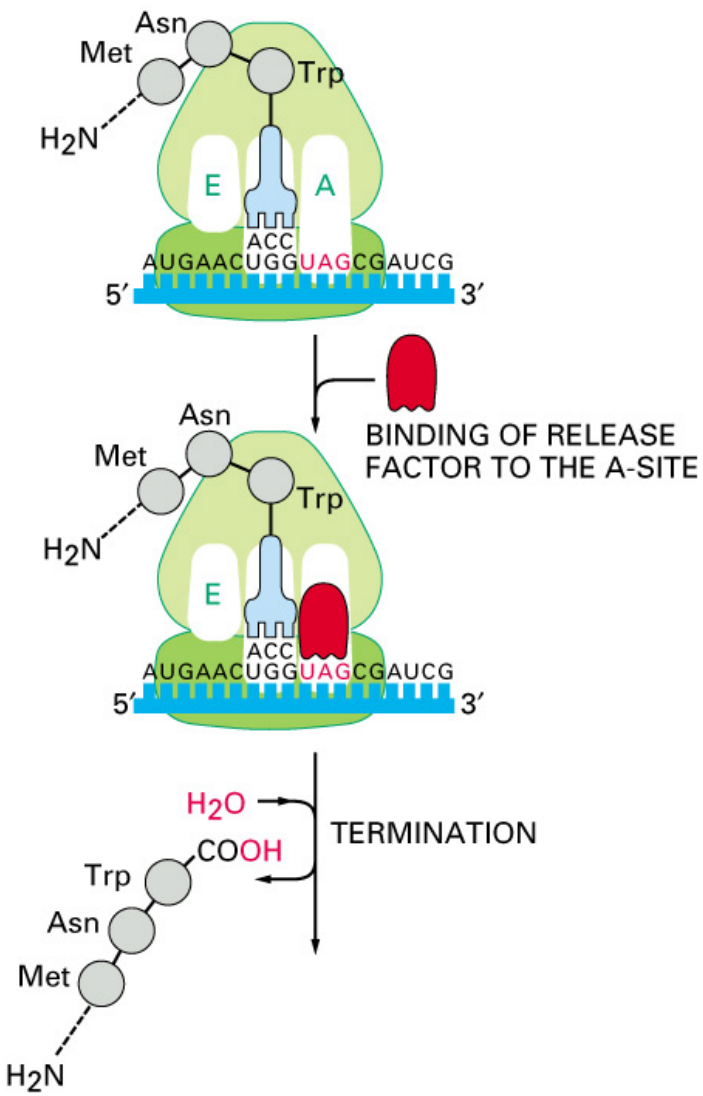



Figure 6–73 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

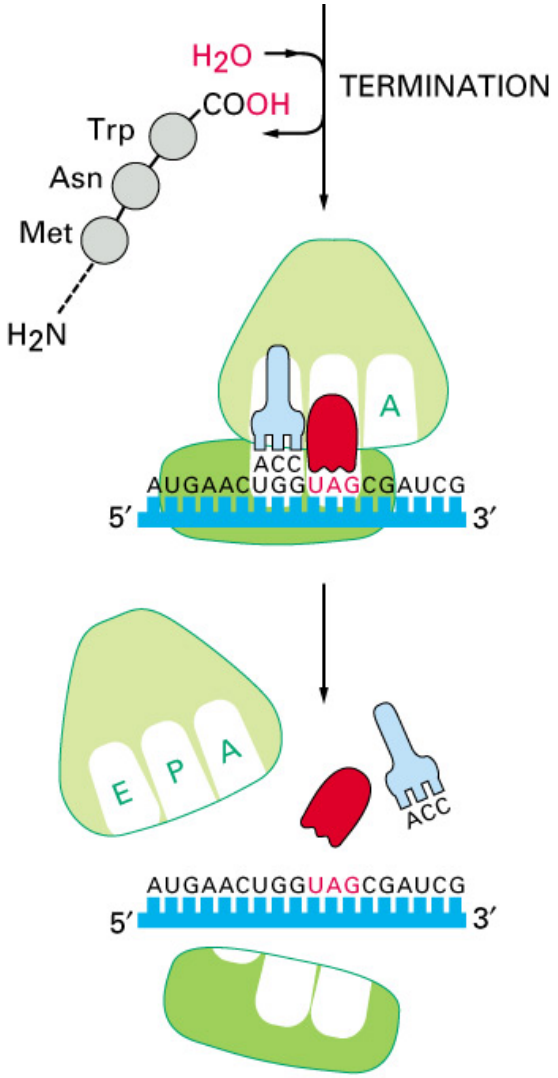



Figure 6–73 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

UAG is one of 3 stop codons.

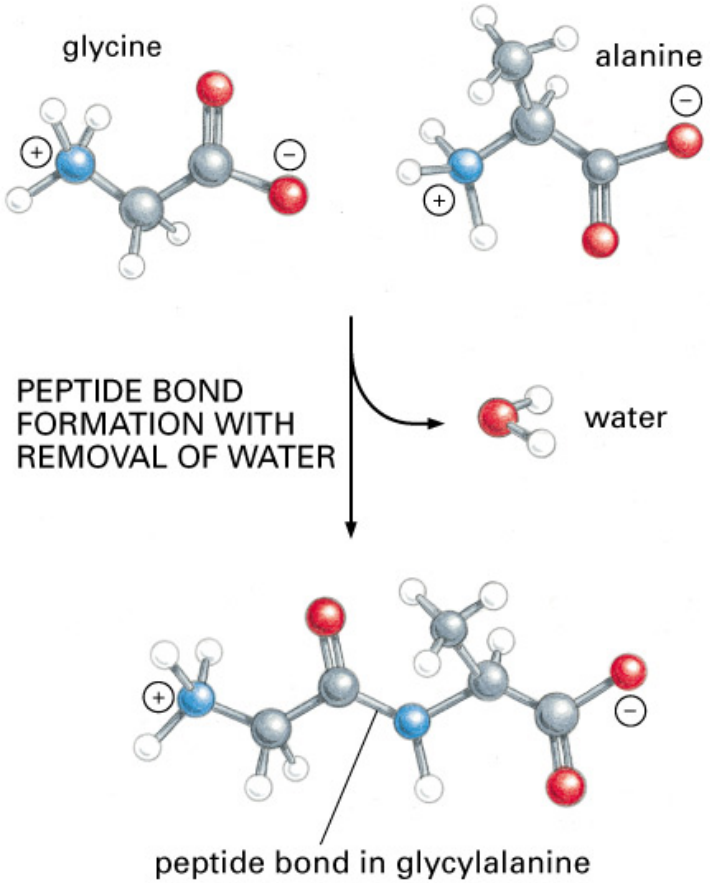



Figure 3–1. Molecular Biology of the Cell, 4th Edition.

This bond is made by the ribosome.

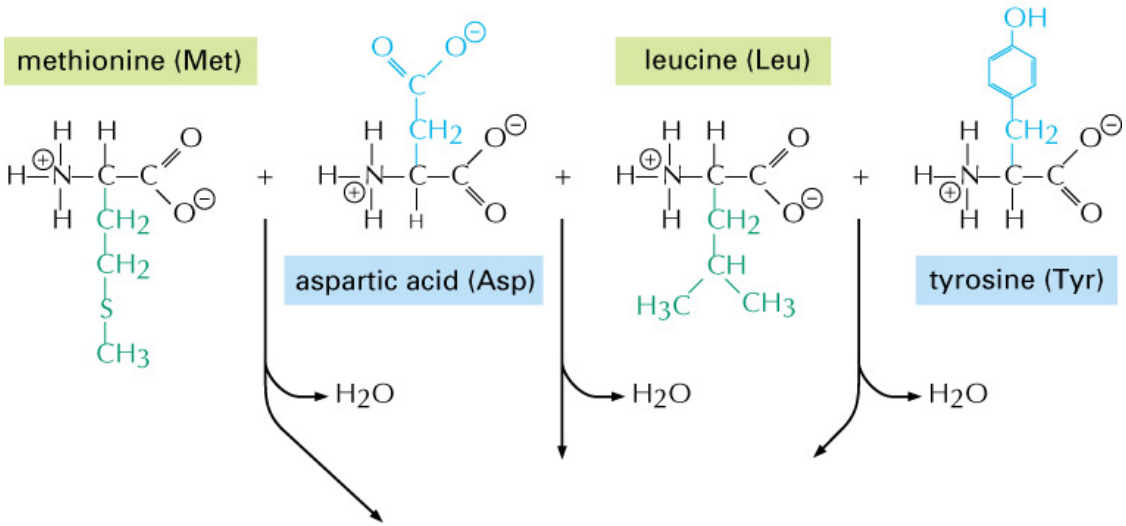



Figure 3–2 part 1 of 3. Molecular Biology of the Cell, 4th Edition.

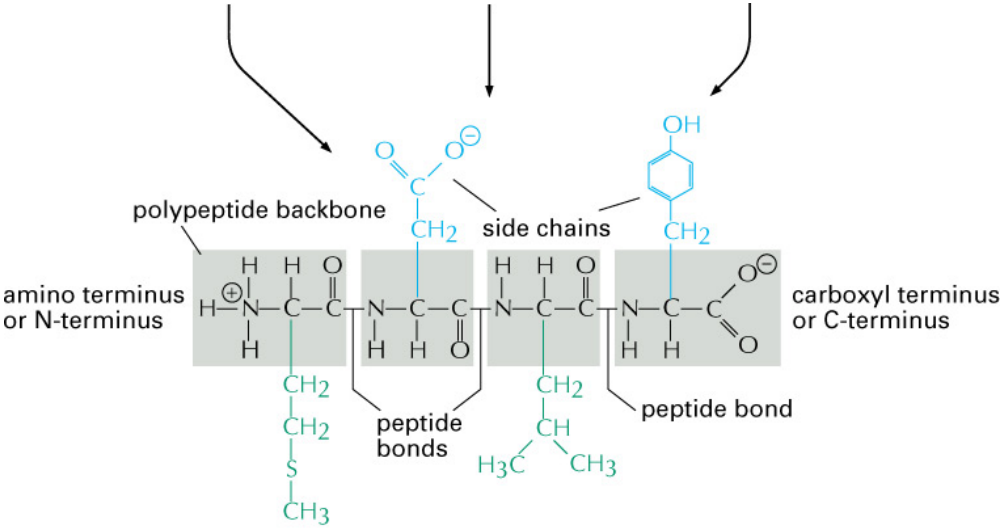



Figure 3–2 part 2 of 3. Molecular Biology of the Cell, 4th Edition.

These bonds are made by the ribosome.

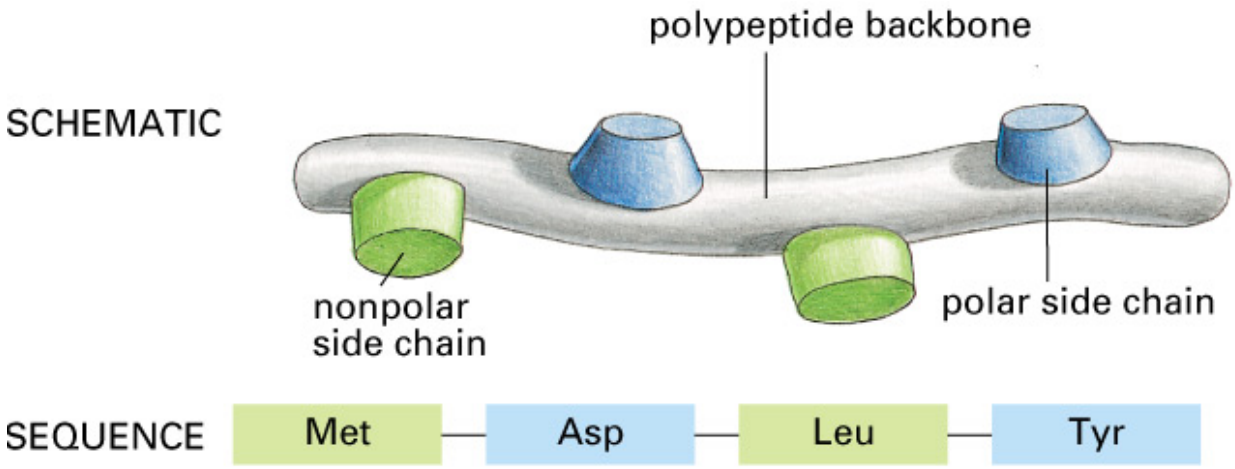



Figure 3–2 part 3 of 3. Molecular Biology of the Cell, 4th Edition.

| AMINO ACID | | | SIDE CHAIN |
|---|---|---|---|
| Aspartic acid | Asp | D | negative |
| Glutamic acid | Glu | E | negative |
| Arginine | Arg | R | positive |
| Lysine | Lys | K | positive |
| Histidine | His | H | positive |
| Asparagine | Asn | N | uncharged polar |
| Glutamine | Gln | Q | uncharged polar |
| Serine | Ser | S | uncharged polar |
| Threonine | Thr | T | uncharged polar |
| Tyrosine | Tyr | Y | uncharged polar |

POLAR AMINO ACIDS

| AMINO ACID | | | SIDE CHAIN |
|---|---|---|---|
| Alanine | Ala | A | nonpolar |
| Glycine | Gly | G | nonpolar |
| Valine | Val | V | nonpolar |
| Leucine | Leu | L | nonpolar |
| Isoleucine | Ile | I | nonpolar |
| Proline | Pro | P | nonpolar |
| Phenylalanine | Phe | F | nonpolar |
| Methionine | Met | M | nonpolar |
| Tryptophan | Trp | W | nonpolar |
| Cysteine | Cys | C | nonpolar |

NONPOLAR AMINO ACIDS

Figure 3–3. Molecular Biology of the Cell, 4th Edition.

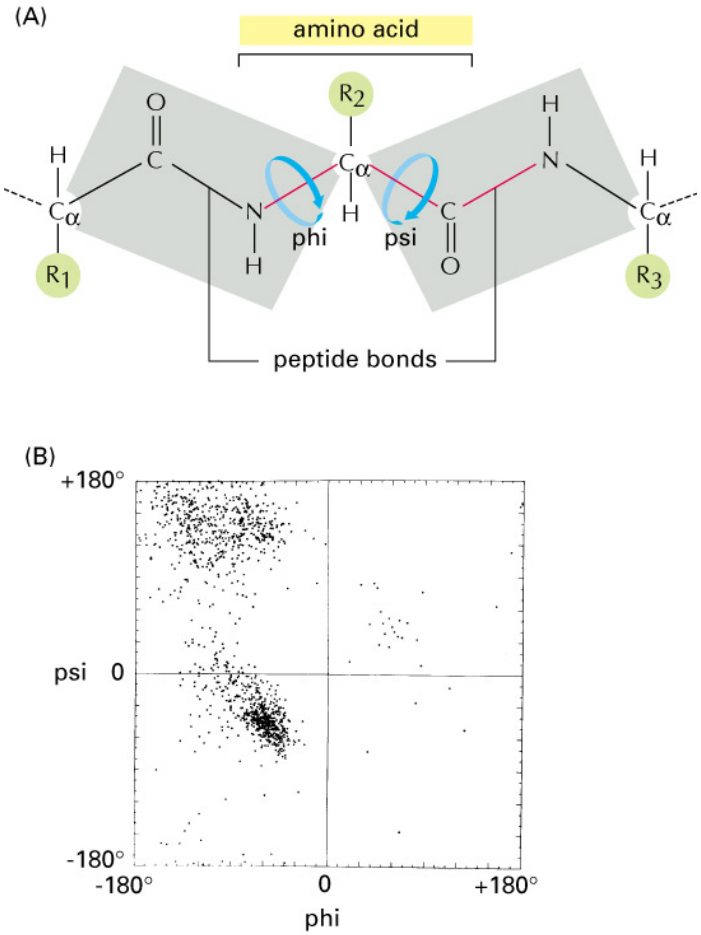


Figure 3–4. Molecular Biology of the Cell, 4th Edition.

The upper region leads to $\beta$-strands, which are $\beta$-helices and form $\beta$-sheets, and the lower region leads to $\alpha$-helices.

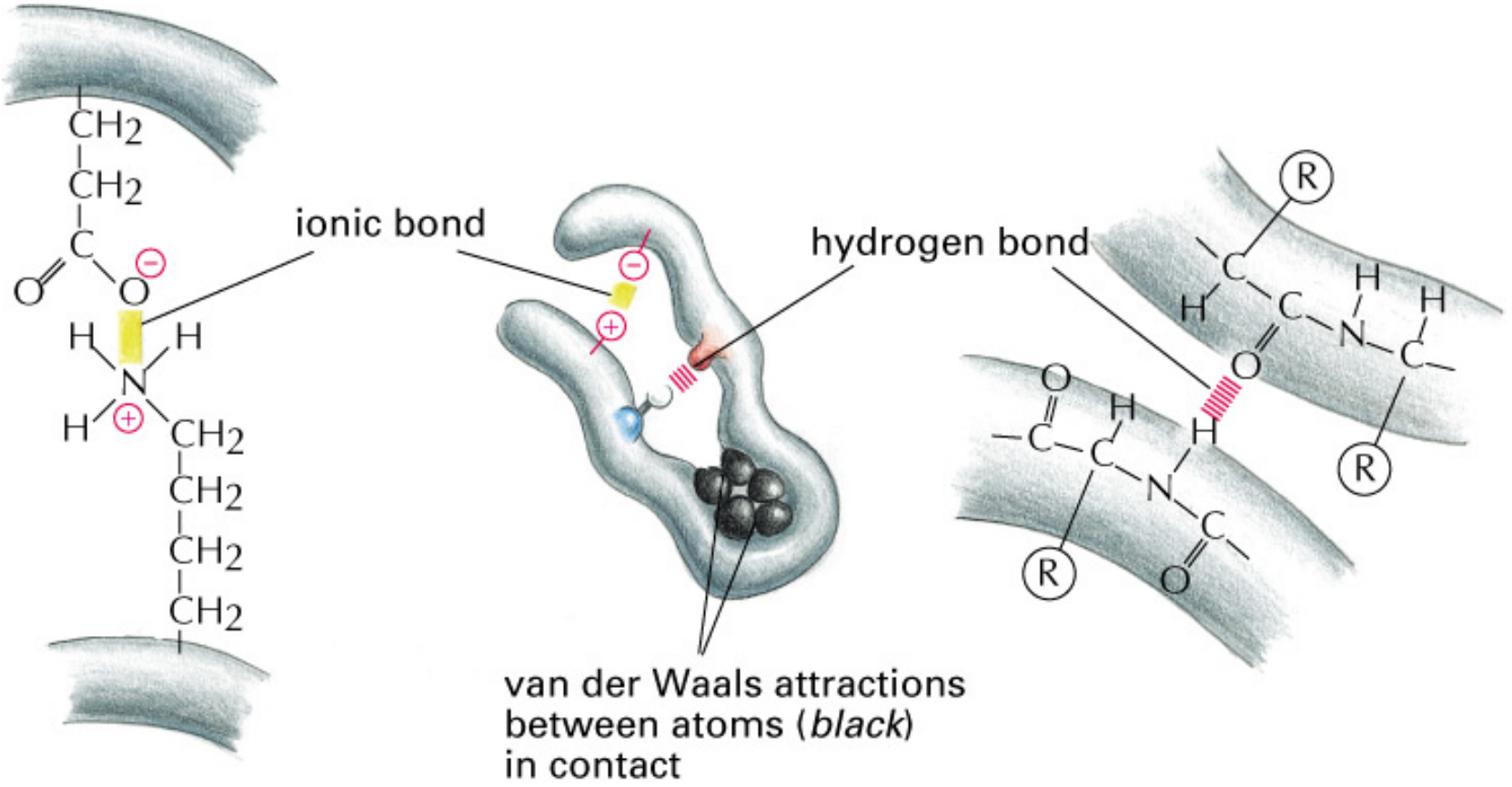



Figure 3–5. Molecular Biology of the Cell, 4th Edition.

The H-bonds hold $\alpha$-helices and $\beta$-sheets together.

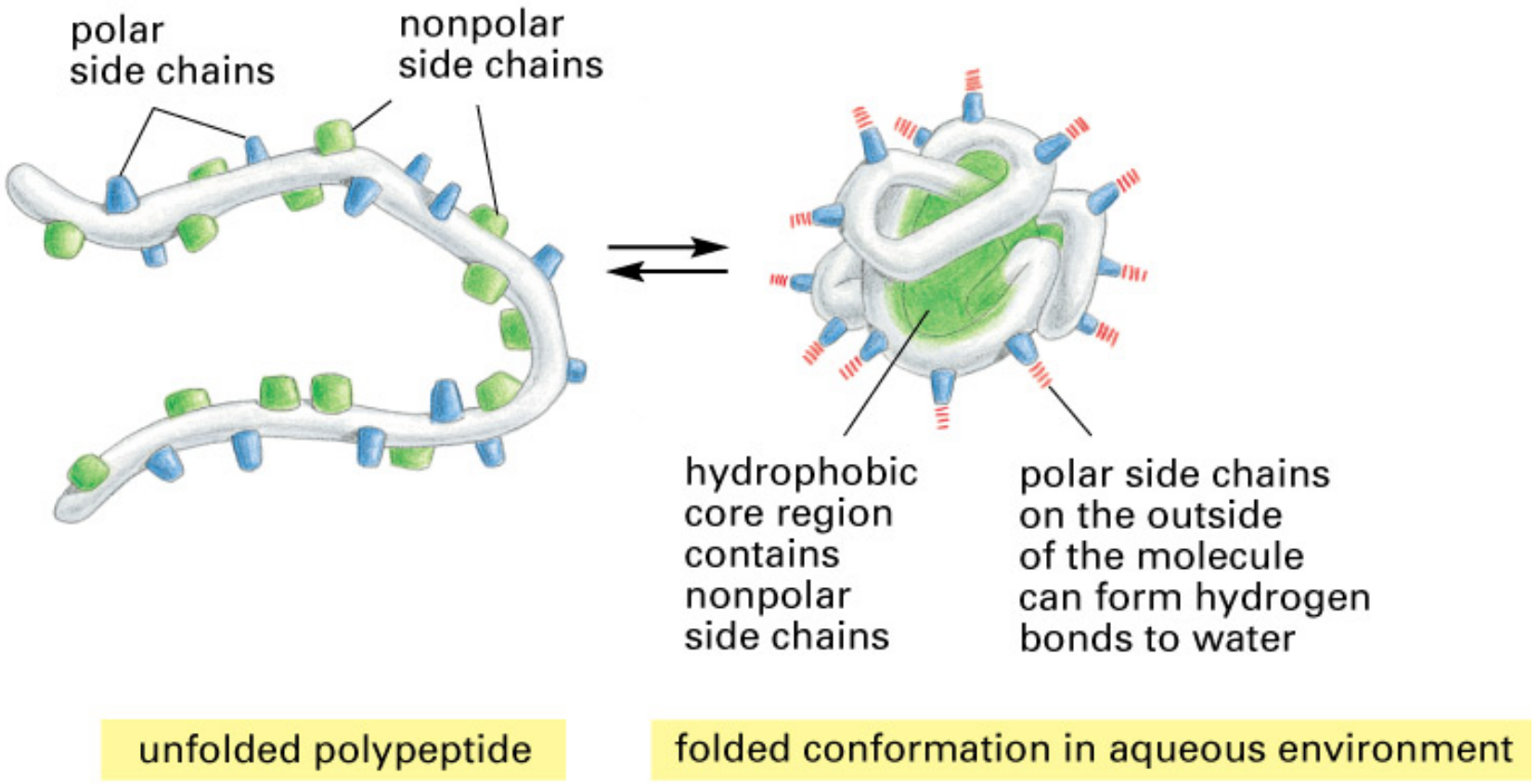



Figure 3–6. Molecular Biology of the Cell, 4th Edition.

Polar water molecules repel non-polar aa side-chains and attract polar and charged aa side-chains.

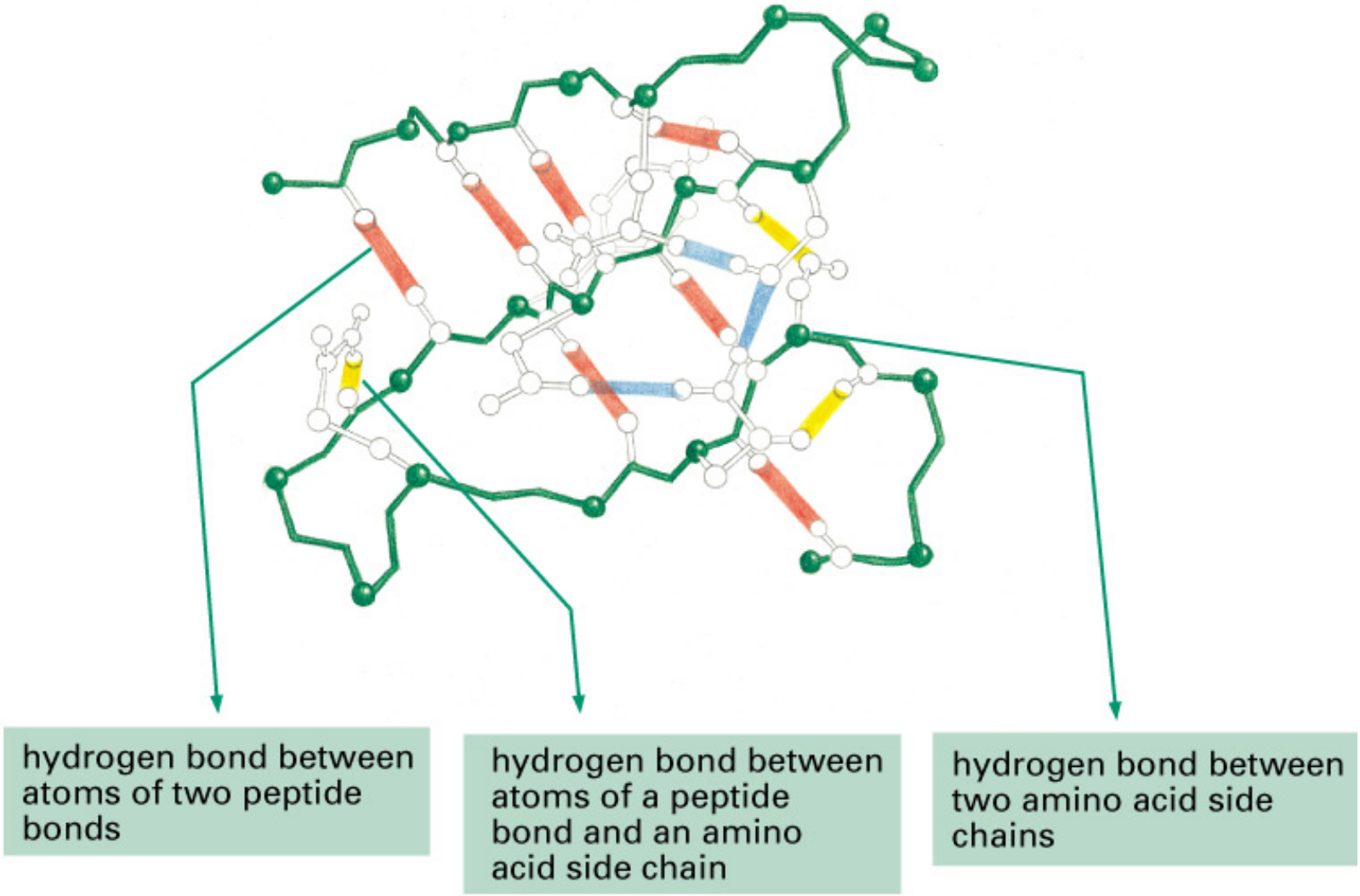



Figure 3–7. Molecular Biology of the Cell, 4th Edition.

H-bonds often run between the O of C=O and the N of N-H; the N is the donor atom and the O is the acceptor atom.

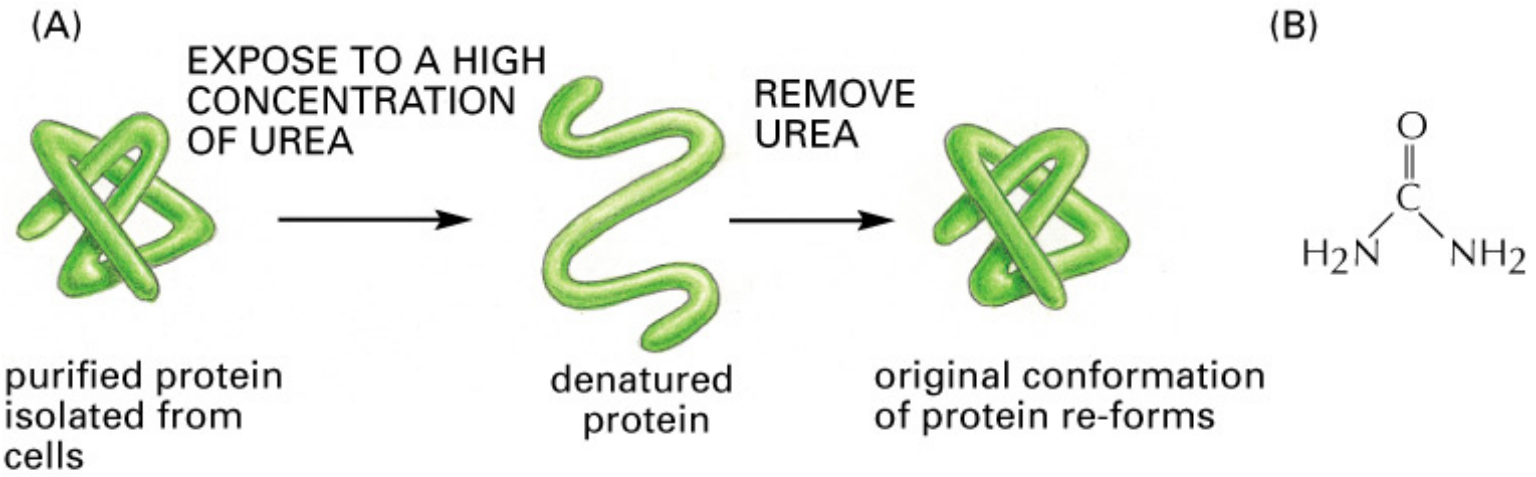



Figure 3–8. Molecular Biology of the Cell, 4th Edition.

Urea denatures proteins, which can fold back into their native structures when placed in their natural solvent, typically that of the cytosol.

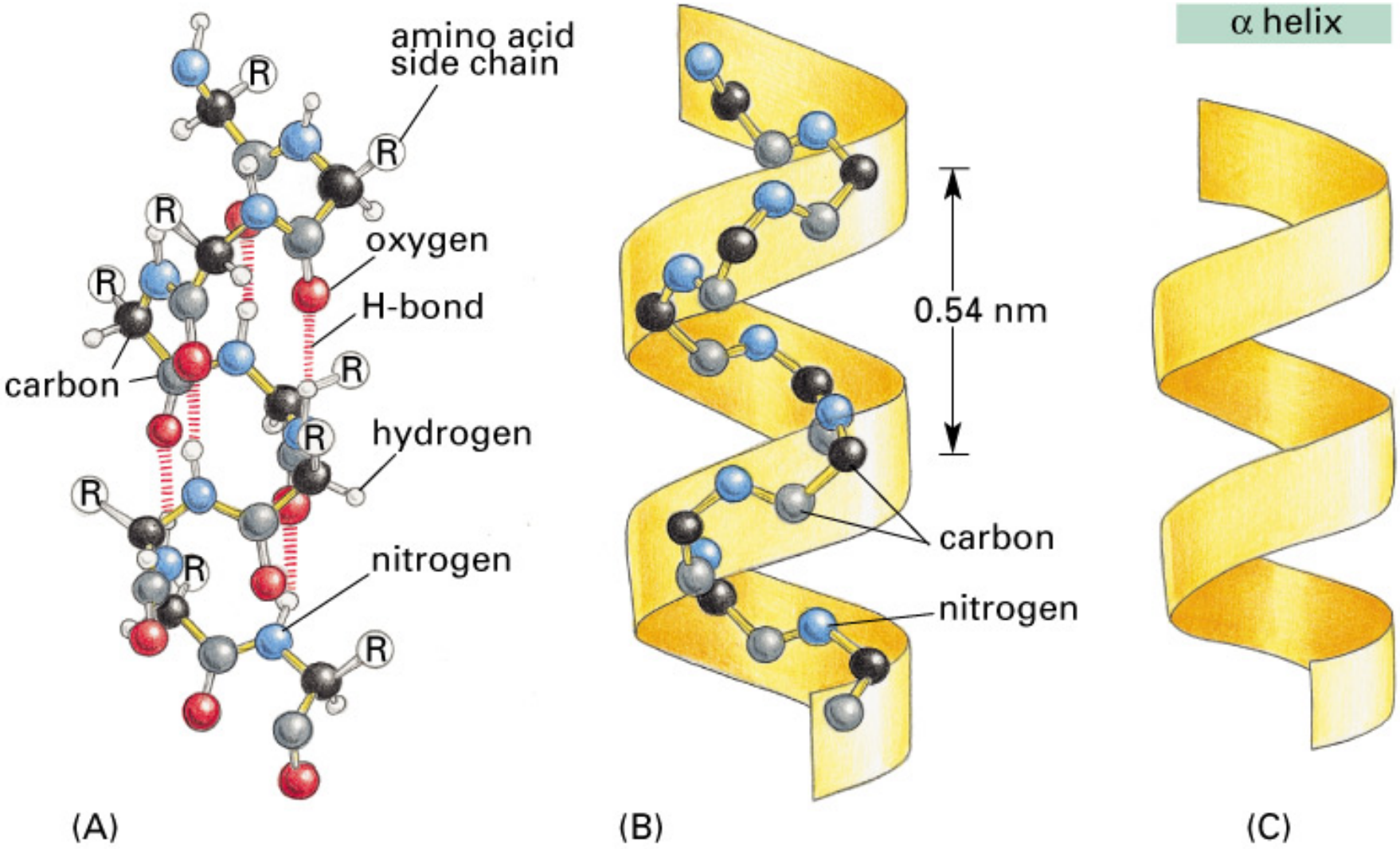



Figure 3–9 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

Linus Pauling's $\alpha$-helix.

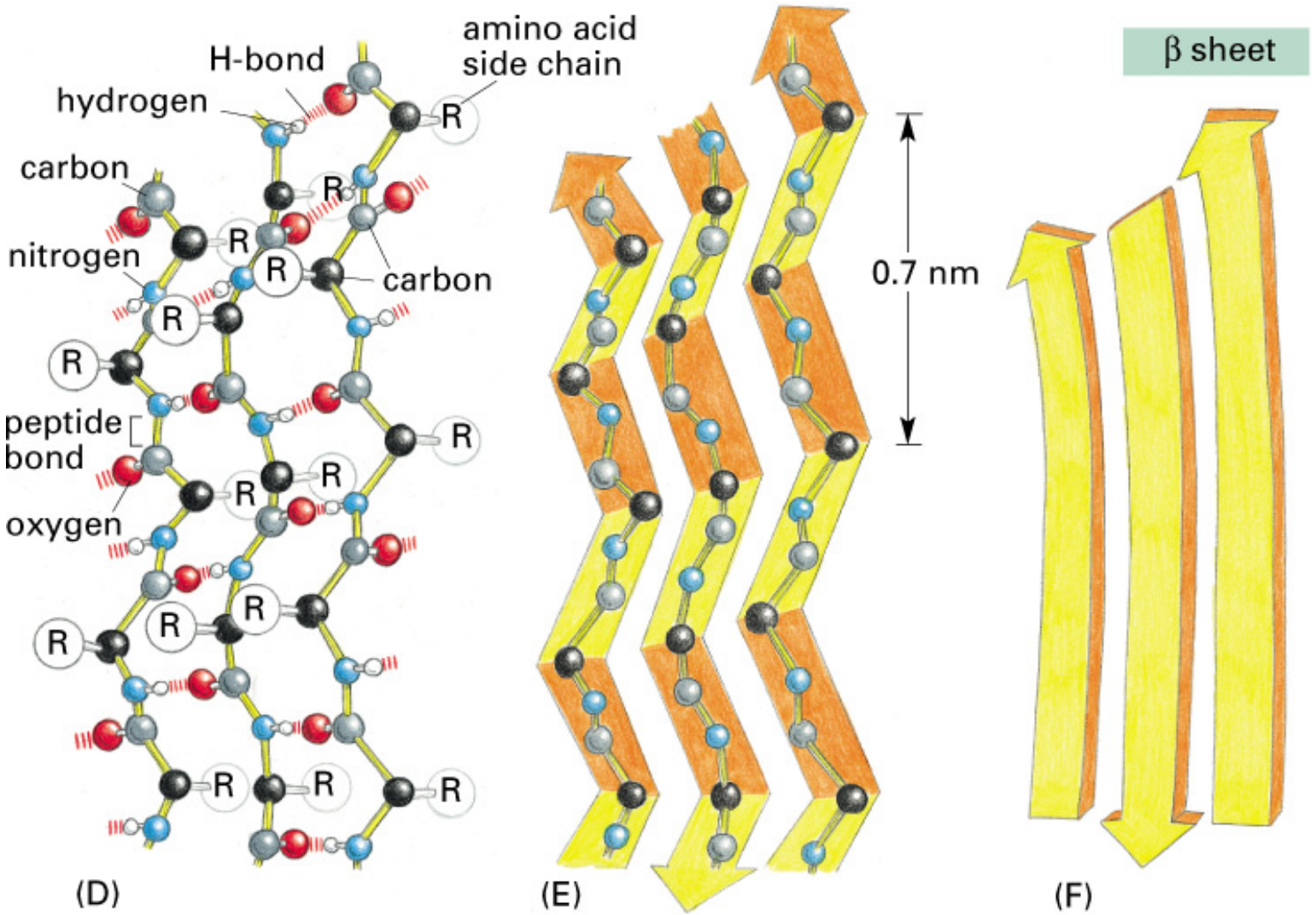



Figure 3–9 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

A $\beta$-sheet.

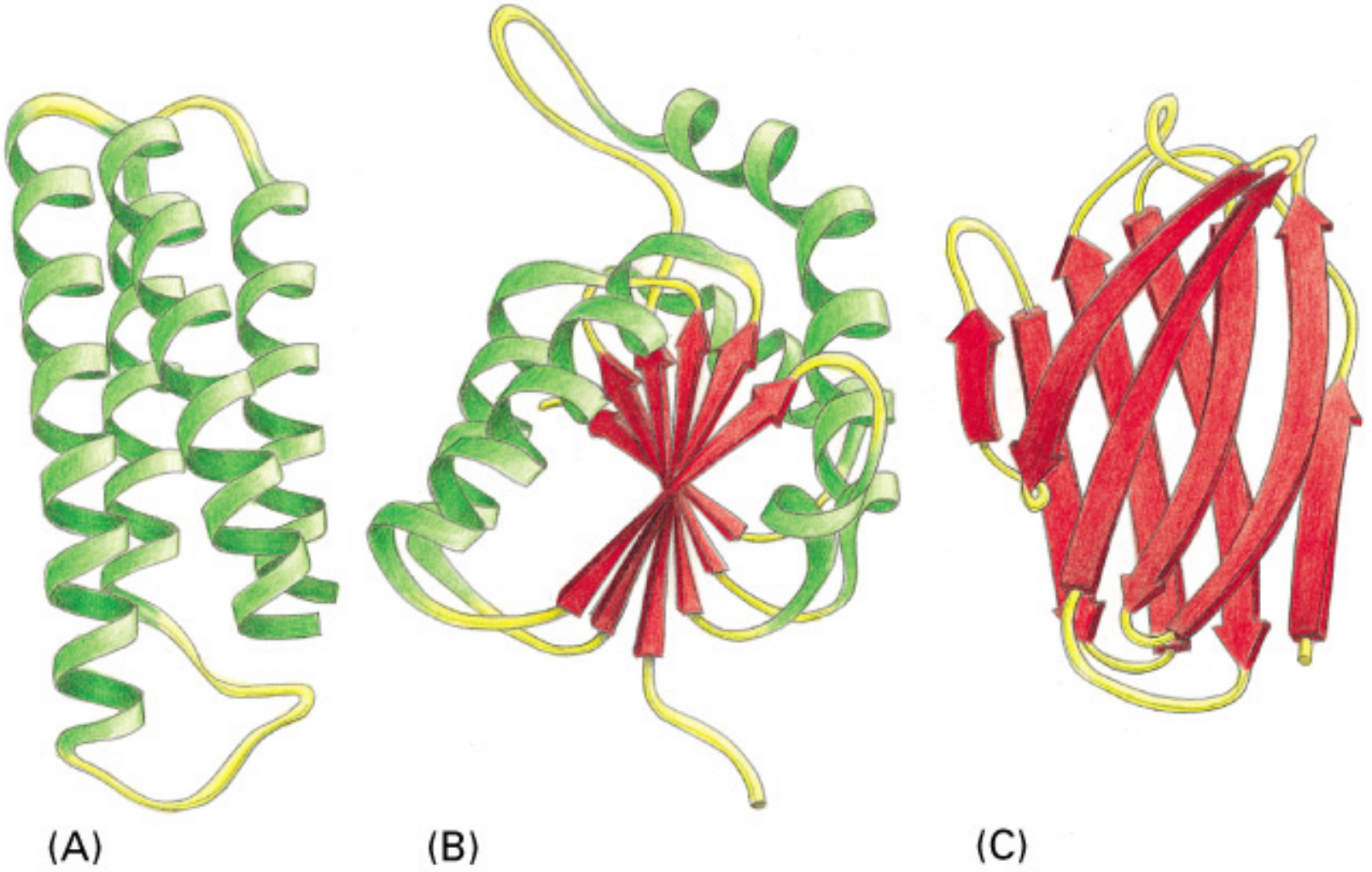



Figure 3–13. Molecular Biology of the Cell, 4th Edition.

Ribbon models of 3 protein domains. (A) is cytochrome $b_{562}$; (B) is the NAD-binding domain of lactic dehydrogenase; and (C) is an IG domain.