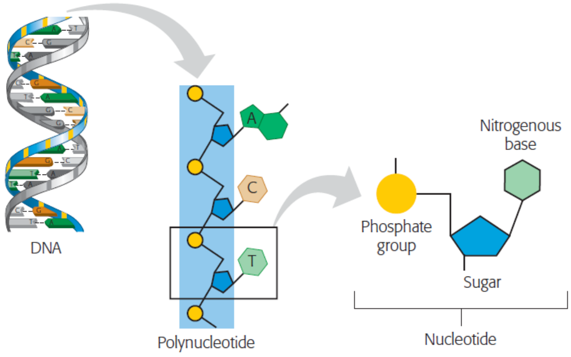
Chapter 10 The Structure and Function of DNA

1. DNA: Structure and Replication

- **DNA and RNA Structure**
  - Nucleotides (monomers)→Polynucleotides (polymers)
  - **sugar-phosphate backbone**/ Sugar-phosphate-sugar-phosphate repeating pattern by **covalent bonds**
  - **Compare** the chemical components of **DNA and RNA**

    Both are polymers of nucleotides (a sugar + a nitrogenous base + a phosphate group). In RNA, the sugar is ribose; in DNA, it is deoxyribose. Both RNA and DNA have the base A, G, C, but DNA has T and RNA has U
  - **Watson and Crick' s Discovery of the Double Helix**

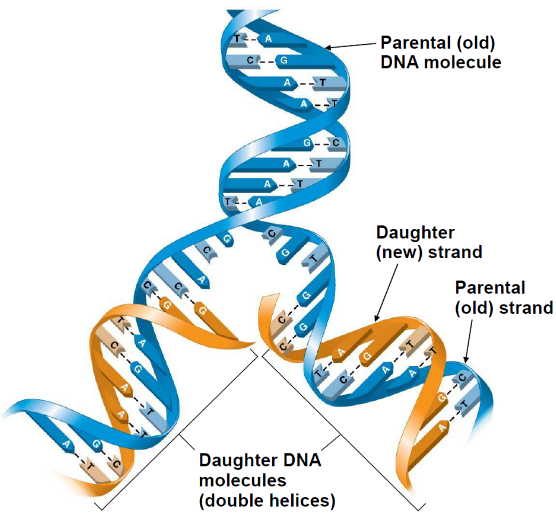
    Watson and Crick worked out the three-dimensional structure of DNA: two polynucleotide strands wrapped around each other in a **double helix**. **Hydrogen bonds** between bases hold the strands together. Each base pairs with a **complementary** partner: A with T, and G with C.



DNA	*deoxyribonucleic acid*
RNA	*ribonucleic acid*
T	*Thymine*
C	*cytosine*
A	*Adenine*
G	*guanine*
U	*uracil*

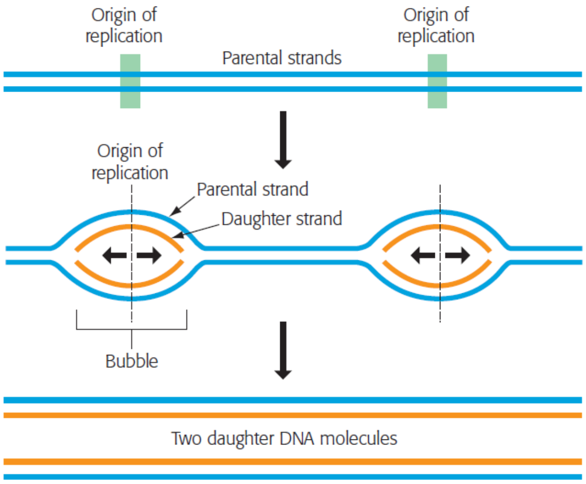
	DNA	RNA
Nitrogenous base	C G A T	C G A U
Sugar	Deoxy-ribose	Ribose
Number of strands	2	1

- **DNA Replication**
  - Parental DNA separate→ nucleotides lined up in accordance with the **base-pairing** rules→ **DNA polymerases** link the nucleotides to form new DNA strands.



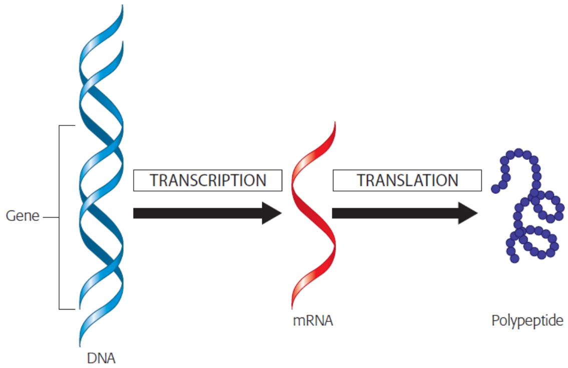
- DNA replication begins at some specific sites **(origin of replication)** simultaneously in **both directions**, creating **replication "bubbles"**. Eventually, all the bubbles merge, yielding two completed double-stranded daughter DNA molecules.

Figure 10.7 Multiple "bubbles" in replicating DNA.

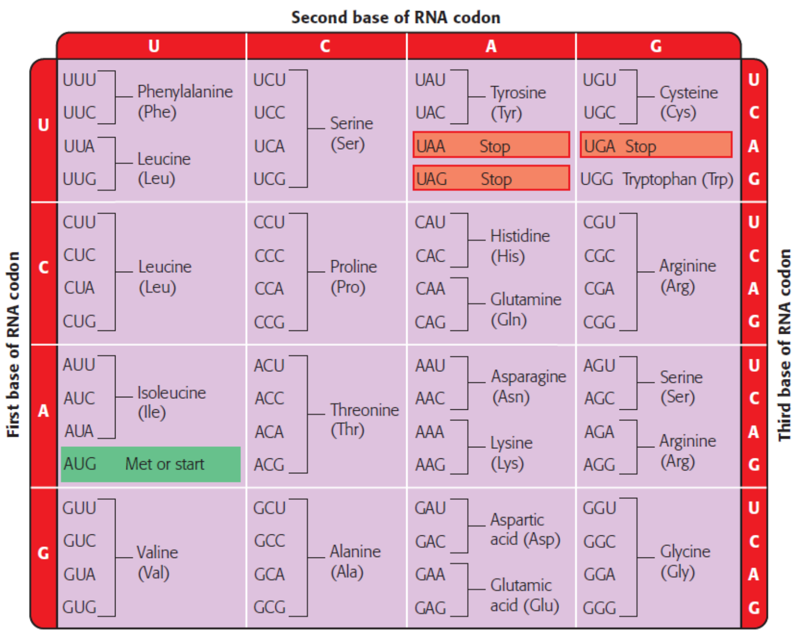


2. From DNA to RNA to Protein

- **How an Organism' s Genotype Determines Its Phenotype**
  - The information constituting an organism' s genotype is carried in the sequence of its DNA bases. The genotype controls phenotype through the expression of proteins.



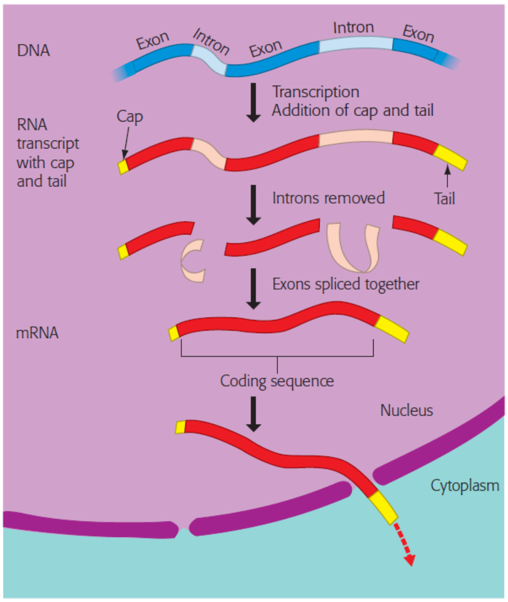
  - The genetic instructions for the amino acid sequence of a polypeptide chain are written in DNA and RNA as a series of three-base words called **codons**（密码子）--**a triplet code**
- **The Genetic Code**
  - **Genetic code** is the set of rules that convert a nucleotide sequence in RNA to an amino acid sequence.
  - Of the **64 triplets**, **61 code for amino acids and 3 are stop codons**:
    - AUG: methionine (abbreviated **Met**) and **start codons**
    - UAA, UAG, and UGA: **stop codons**
  - The genetic code is redundant: There is more than one codon for most amino acids.
  - The genetic code is nearly universal, shared by organisms from the simplest bacteria to the most complex plants and animals.



▲ **Figure 10.10 The dictionary of the genetic code, listed by RNA codons.** Practice using this dictionary by finding the codon UGG. (It is the only codon for the amino acid tryptophan, Trp.) Notice that the codon AUG (highlighted in green) not only stands for the amino acid methionine (Met), but also functions as a signal to "start" translating the RNA at that place. Three of the 64 codons (highlighted in red) function as "stop" signals that mark the end of a genetic message, but do not encode any amino acids.

- Transcription: From DNA to RNA
    - **Initiation of transcription**: the attachment of RNA polymerase to the promoter and the start of RNA synthesis.

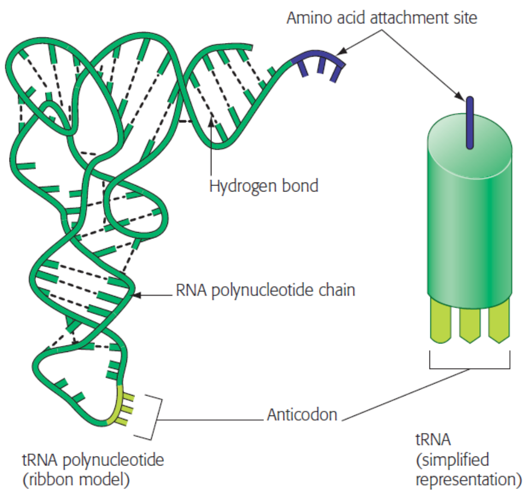
      Promoter: located in the DNA at the beginning of the gene and a specific place where RNA polymerase attaches.
    - **RNA Elongation**: the RNA grows longer and the RNA strand peels away from its DNA template, allowing the two separated DNA strands to come back together in the region already transcribed.
    - **Termination of transcription**: RNA polymerase reaches a special sequence of bases in the DNA template called a **terminator**, signaling the end of the gene, polymerase detaches from the RNA and the gene, and the DNA strands rejoin.
- The Processing of Eukaryotic RNA
    - Addition of extra nucleotides (**cap** and **tail**) to the ends of the RNA transcript, protect the RNA from attack by cellular enzymes and help ribosomes recognize the RNA as mRNA.
    - Noncoding nucleotides-**introns**（内含子）, that interrupt the nucleotides that actually code for amino acids. coding regions—the parts of a gene that are expressed—are **called exons**（外显子）.
    - **RNA splicing**（RNA 剪接）: Before the RNA leaves the nucleus, the introns are removed and the exons are joined to produce an mRNA molecule with a continuous coding sequence.



▲ **Figure 10.13 The production of messenger RNA (mRNA) in a eukaryotic cell.** Note that the molecule of mRNA that leaves the nucleus is substantially different from the molecule of RNA that was first transcribed from the gene. In the cytoplasm, the coding sequence of the final mRNA will be translated.

- **Translation**
  - Convert the three-letter words (codons) of nucleic acids to the amino acid words of proteins- **Transfer RNA (tRNA)**.
  - tRNA molecules must carry out two distinct functions: pick up the appropriate amino acids and recognize the appropriate codons in the mRNA.
  - **Structure of tRNA** molecules enables them to perform both tasks.
    - At one end, the **anticodon** recognizes a particular codon on the mRNA by using base-pairing rules.
    - At the other end is a site where one specific kind of amino acid attaches.
    - tRNA molecules for each amino acid are similar but slightly different.

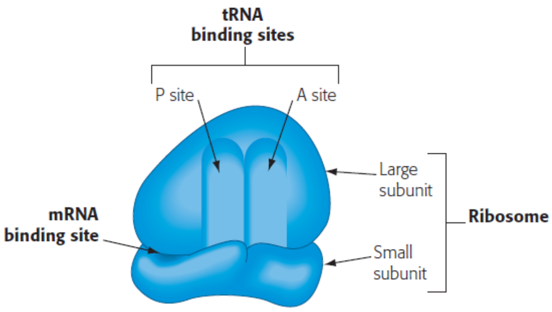
▼ **Figure 10.14 The structure of tRNA.** At one end of the tRNA is the site where an amino acid will attach (purple), and at the other end is the three-nucleotide anticodon where the mRNA will attach (light green).



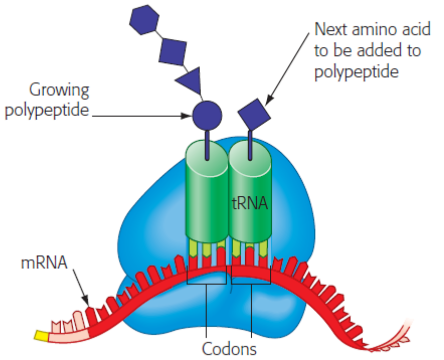
  - **Structures of Ribosomes and "players" of Translation**
    - Two subunits: Proteins + ribosomal RNA (rRNA).
    - mRNA binding site on small subunit and tRNA binding site on large subunit.
    - P site, holds the tRNA carrying the growing polypeptide chain, while A site, holds a tRNA carrying the next amino acid to be added to the chain.

- The subunits holding the tRNA and mRNA molecules close together. The ribosome can then connect the amino acid from the tRNA in the A site to the growing polypeptide

Figure 10.15 The ribosome.



(a) A simplified diagram of a ribosome. Notice the two subunits and sites where mRNA and tRNA molecules bind.



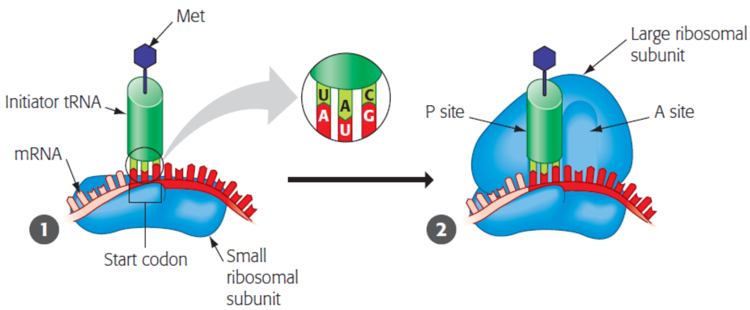
(b) The "players" of translation. When functioning in polypeptide synthesis, a ribosome holds one molecule of mRNA and two molecules of tRNA. The growing polypeptide is attached to one of the tRNAs.

- **The Process of translation**

<u>Initiation</u>:

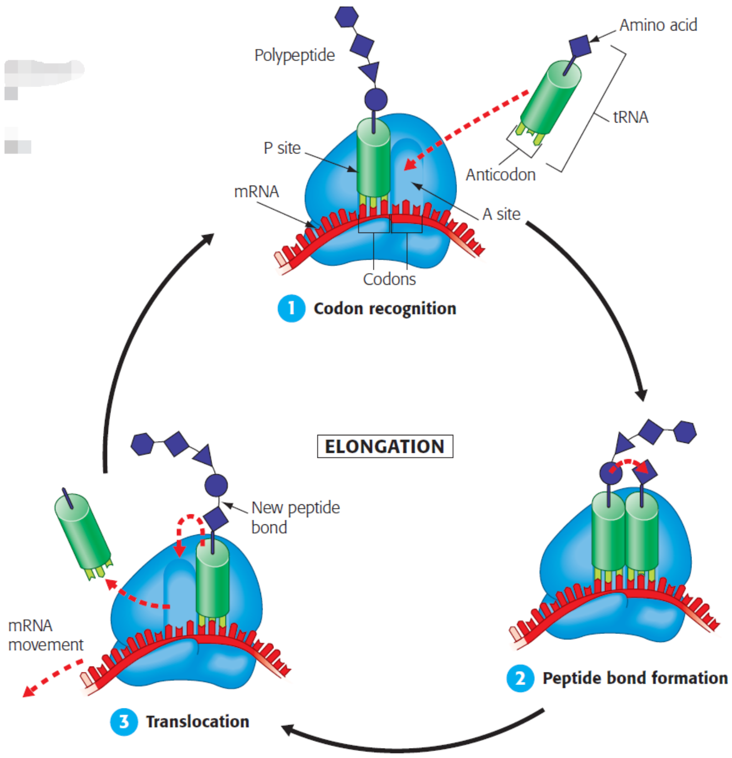
- An mRNA molecule binds to a small ribosomal subunit, tRNA binds to the start codon（起始密码子）
- A large ribosomal subunit binds to the small one, creating a functional ribosome.

Figure 10.17 The initiation of translation.



<u>Elongation</u>:

- **Codon recognition**: tRNA molecule pairs with the mRNA codon in the A site.
- **Peptide bond formation**: The polypeptide leaves the P site tRNA and attaches to (peptide bond) the amino acid on the A site tRNA, amino acid+1.
- **Translocation**: The P site tRNA leaves, ribosome moves tRNA (carrying the growing polypeptide) to P site together with mRNA.

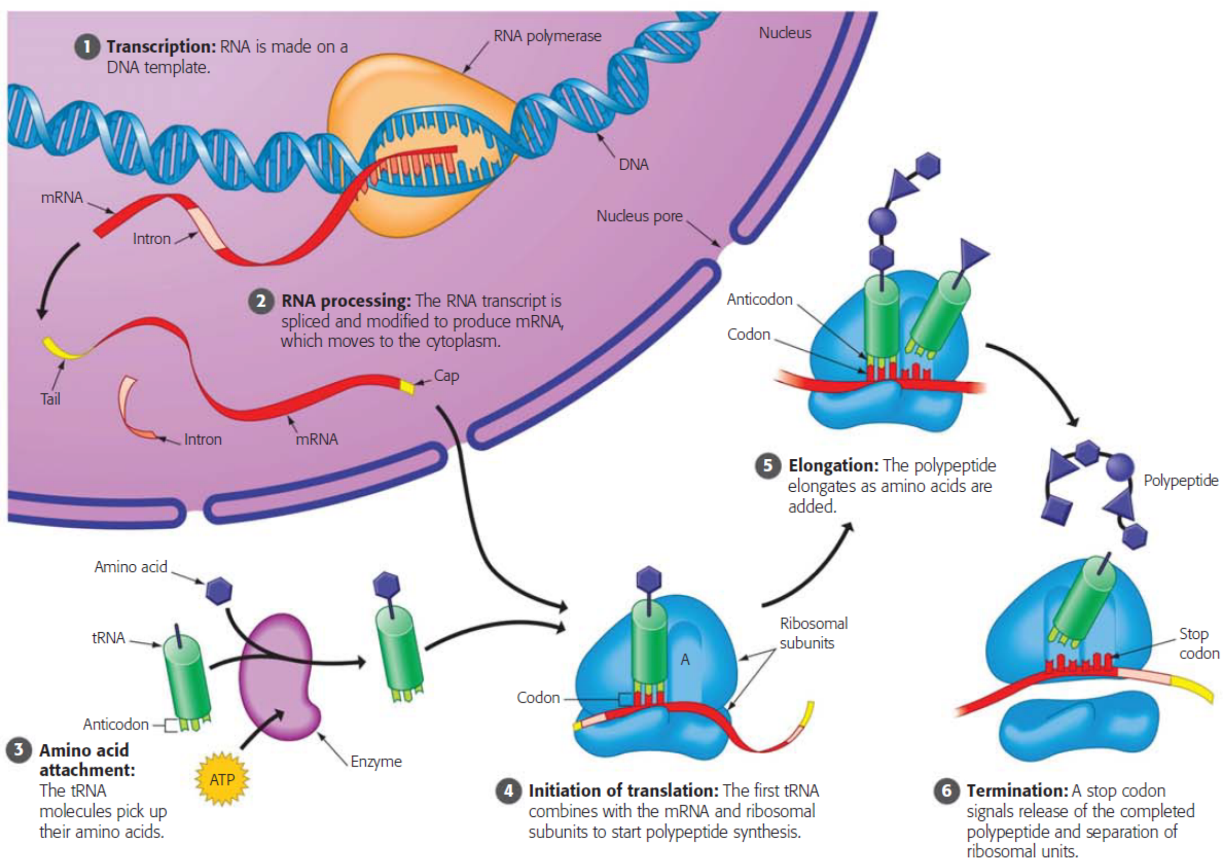


<u>Termination</u>

- ➢ a stop codon（终止密码子）reaches the ribosome’ s A site,
- ➢ The completed polypeptide is freed, and
- ➢ The ribosome splits back into its subunits.

- **Review: DNA → RNA → Protein**

Figure 10.19 A summary of transcription and translation. This figure summarizes the main stages in the flow of genetic information from DNA to protein in a eukaryotic cell.



- **Mutations**
  - ■ Mutations are changes in the DNA base sequence, caused by errors in DNA replication or

recombination or by mutagens. Substituting, deleting, or inserting nucleotides in a gene has varying effects on the polypeptide and organism.

Type of Mutation	Effect
Substitution of one DNA base for another	**Silent** mutations result in no change to amino acids.
	Missense mutations swap one amino acid for another.
	Nonsense mutations change an amino acid codon to a stop codon.
Insertions or **deletions** of DNA nucleotides	Frameshift mutations can alter the triplet grouping of codons and greatly change the amino acid sequence.

- **Mutagen**
  - Physical mutagen: high-energy radiation, such as X-rays and ultraviolet (UV) light.
  - Chemical mutagens are of various types. (e.g.chemicals that are similar to normal DNA bases but that base-pair incorrectly when incorporated into DNA.)

3. Viruses and Other Noncellular Infectious Agents

Viruses are infectious particles consisting of genes packaged in protein. A virus cannot reproduce on its own. It can multiply only by infecting a living cell and directing the cell' s molecular machinery to make more viruses.

- **Bacteriophages**
  - Viruses that attack bacteria are called **bacteriophages** ("bacteria-eaters"), or **phages**
  - DNA enclosed within proteins.
  - **The lytic cycle** (裂解周期) and **The lysogenic cycle** (溶原周期) (**Difference**: with or without phage production or the death of the cell)

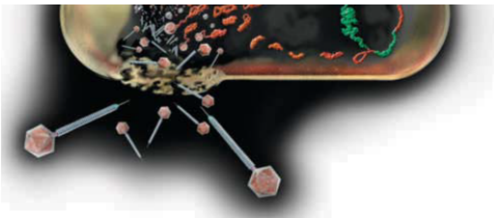
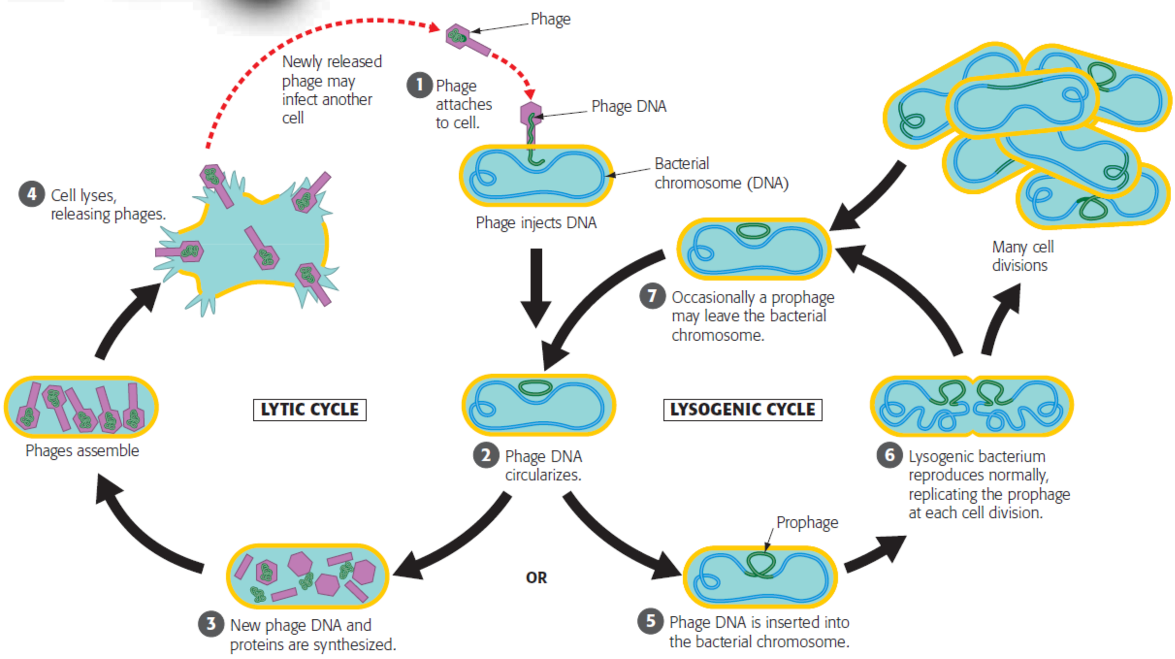


Figure 10.25 Alternative phage reproductive cycles. Certain phages can undergo alternative reproductive cycles. After entering the bacterial cell, the phage DNA can either integrate into the bacterial chromosome (lysogenic cycle) or immediately start the production of progeny phages (lytic cycle), destroying the cell. Once it enters a lysogenic cycle, the phage's DNA may be carried in the host cell's chromosome for many generations.



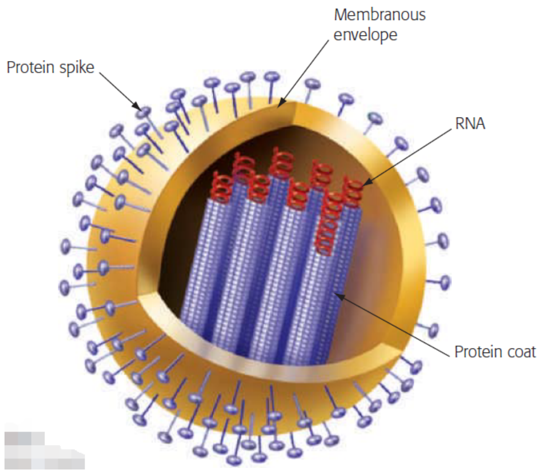
- **Plant viruses**

  Viruses that infect plants can be a serious agricultural problem. Most have RNA genomes. Viruses enter plants via breaks in the plant' s outer layers.

- **Animal Viruses**
  - **Influenza（流感）(flu) virus**

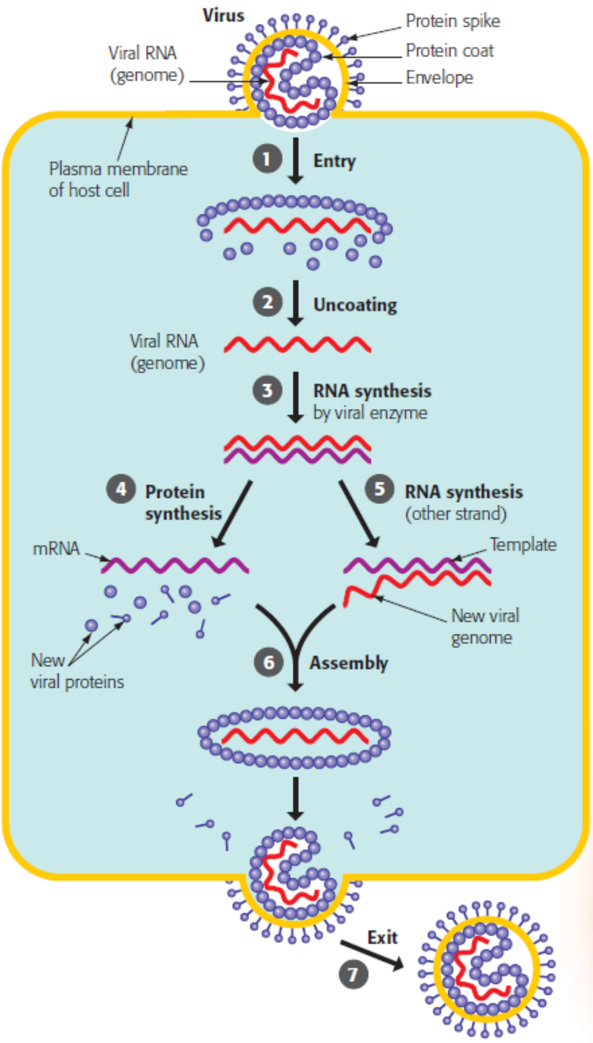
    Like many animal viruses, this one has an **outer envelope** made of **phospholipid membrane**, with projecting spikes of **protein**. The envelope enables the virus to enter and leave a host cell.

Diseases Caused by RNA and DNA Virus	
RNA Viruses	DNA Viruses
Flu	hepatitis（肝炎）
common cold	chicken pox（水痘）
measles（麻疹）	herpes（疱疹）
mumps（流行性腮腺炎）	shingles（带状孢疹）
AIDS	cold sores（唇孢疹）
polio（小儿麻痹症）	genital herpes（生殖器孢疹）



  - **The reproductive cycle of an enveloped virus**
    - The viral envelope fuses with the cell’ s membrane, allowing the protein-coated RNA to enter the cytoplasm.
    - Enzymes then remove the protein coat. An enzyme that entered the cell as part of the virus uses the virus’ s RNA genome as a template for making complementary strands of RNA. The new strands have two functions:
    - They serve as mRNA for the synthesis of new viral proteins, and
    - they serve as templates for synthesizing new viral genome RNA. The new coat proteins assemble around the new viral RNA.
    - Finally, the viruses leave the cell by cloaking themselves in plasma membrane. In other words, the virus obtains its envelope from the cell, budding off the cell without necessarily rupturing it.
  - **Herpesviruses**, which cause chicken pox, shingles（带状孢疹）, cold sores（唇孢疹）, and genital herpes（生殖器孢疹）, are enveloped DNA viruses that reproduce in a host cell’ s **nucleus** and get their envelopes from the cell’ s nuclear membrane. they remain **dormant**（休眠）and until some sort of stress, such as a cold, sunburn, or emotional stress, triggers virus production and they can remain **latent** inside cells for long periods.

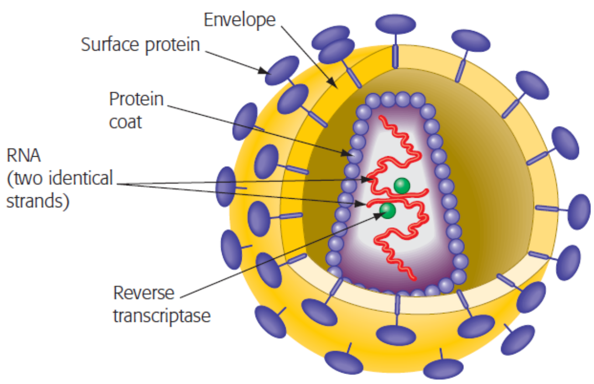
Figure 10.28 The reproductive cycle of an enveloped virus. This virus is the one that causes mumps. Like the flu virus, it has a membranous envelope with protein spikes, but its genome is a single molecule of RNA.



- We usually recover completely from colds because our **respiratory tract**（呼吸道）tissue can efficiently replace damaged cells. In contrast, the **poliovirus**（脊髓灰质炎病毒；小儿麻痹病毒）attacks **nerve cells**, which are **not usually replaceable**. The damage to such cells by polio is permanent. In such cases, the only medical option is to prevent the disease with **vaccines**（疫苗）.

- **HIV, the AIDS Virus**
  - **AIDS** (acquired immunodeficiency syndrome)
  - **HIV** (human immunodeficiency virus), HIV is a retrovirus（逆转录酶病毒）,
  - **Reverse Transcription:** The synthesis of DNA on an RNA template catalyzed by **reverse transcriptase**（逆转录酶）

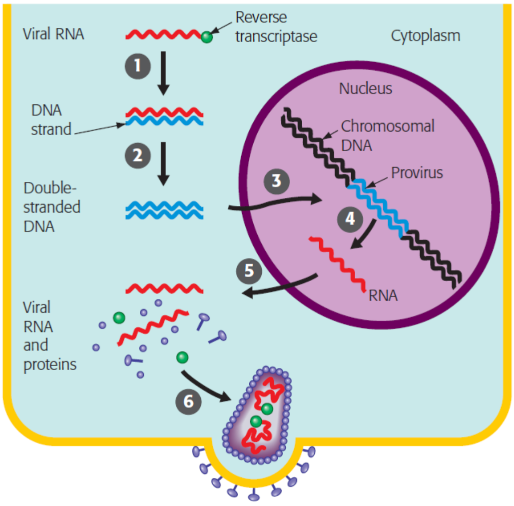
Figure 10.30 HIV, the AIDS virus.



  - **The standard reproductive cycle for retroviruses**

- The reverse transcriptase (green) uses the RNA as a template to make a DNA strand and then
- adds a second, complementary DNA strand.
- The resulting double-stranded viral DNA then enters the cell nucleus and inserts itself into the chromosomal DNA, becoming a provirus. Occasionally, the provirus is
- transcribed into RNA and translated into viral proteins.
- New viruses assembled from these components eventually leave the cell and can then infect other cells.

Figure 10.31 The behavior of HIV nucleic acid in an infected cell.



- **Anti-HIV drugs**
  - The first type inhibits the action of enzymes called proteases（蛋白酶）
  - The second type (drug AZT) inhibits the action of the **HIV enzyme reverse transcriptase**.
- **Drug cocktail**: contains reverse transcriptase inhibitors and protease inhibitors. (more effective)

- Viroids (类病毒) and **Prions** (阮病毒)
  - **Viroids** are small, circular RNA molecules that infect plants.
  - **Prions** are thought to be a misfolded form of a protein normally present in brain cells.