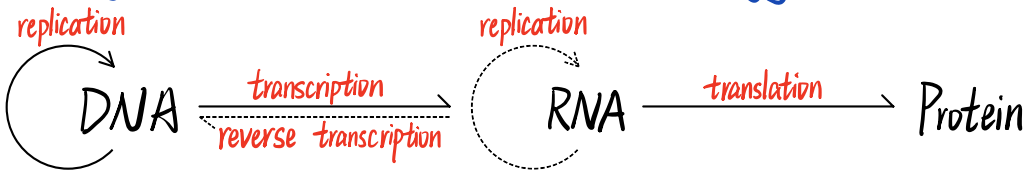
The Structure and Function of DNA (Slide 15)

§1 Central Dogma (中心法则) of Molecule Biology



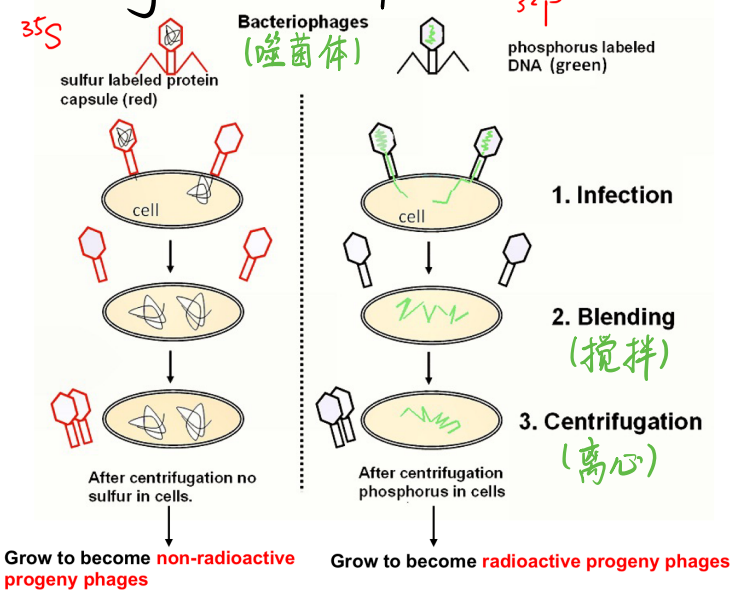
§2 The Discovery about DNA

1. The discovery of hereditary material (遗传物质)

1° The process of discovery

- **DNA was known to be a chemical component of cells by the late 1800s.**
- **By the late 1930s, experimental studies had convinced most biologists that one specific kind of molecule is the basis of inheritance.**
- **By the 1940s, scientists knew that chromosomes consist of two types of chemicals:**
  1. **DNA and**
  2. **protein.**
- **By the early 1950s, a series of discoveries had convinced the scientific world that DNA was the molecule that acts as the hereditary material.**
  - **This breakthrough ushered in the field of molecular biology, the study of heredity at the molecular level.**

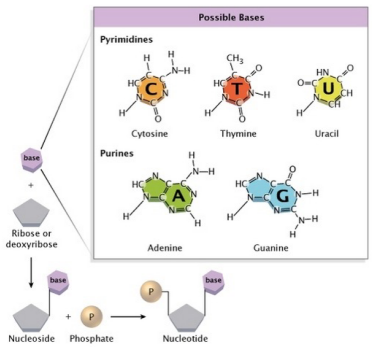
2° Hershey-Chase Experiment (赫尔希-蔡斯实验)

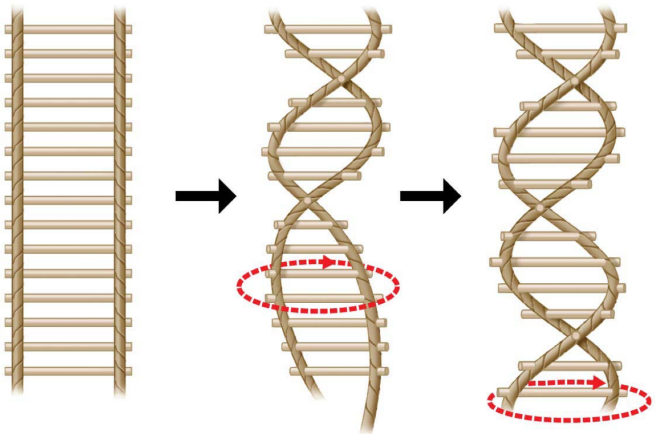


2. The discovery of double helix structure

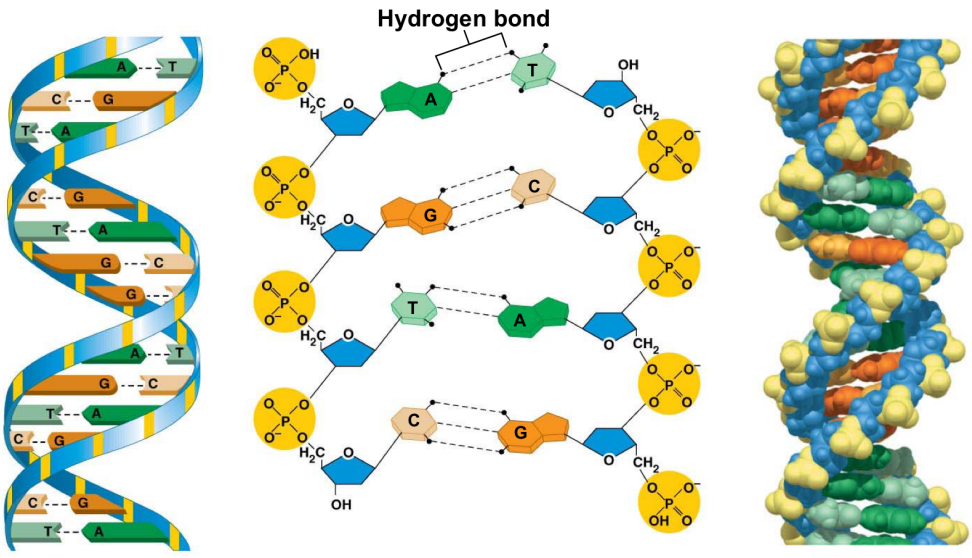
1° James Watson and Francis Crick determined that DNA is a double helix (双螺旋)

- **James Watson and Francis Crick determined that DNA is a double helix（双螺旋), a helix (spiral) with a uniform diameter made up of two polynucleotide strands.**



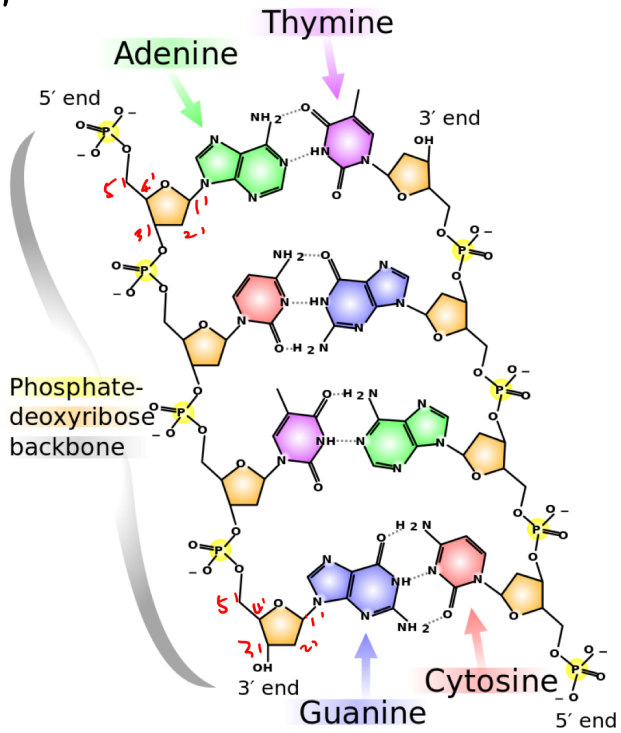


Twist



(a) Ribbon model (b) Atomic model (c) Computer model

2° Double-stranded DNA is an antiparallel molecule. The 5' end (phosphate-bearing end) of one strand aligns with the 3' end (hydroxyl-bearing end) of its partner, and vice versa.



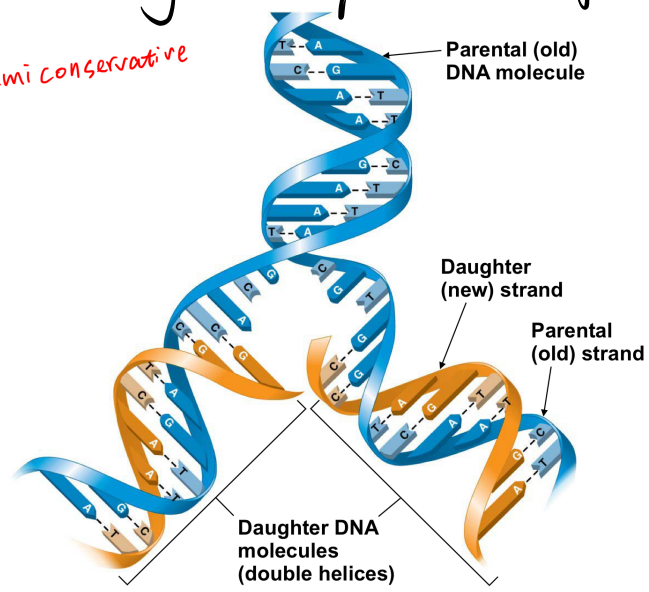
§3 Structure / Function: DNA Replication

1. Semi-conservative (半保留复制)

1° When a cell reproduces, it must duplicate (复制) this information, providing one copy to the new offspring cell while keeping one copy for itself.

2° Each DNA strand serves as a mold, or template (模板) to guide reproduction of the other strand.

Semi conservative



2. DNA polymerases (DNA聚合酶)

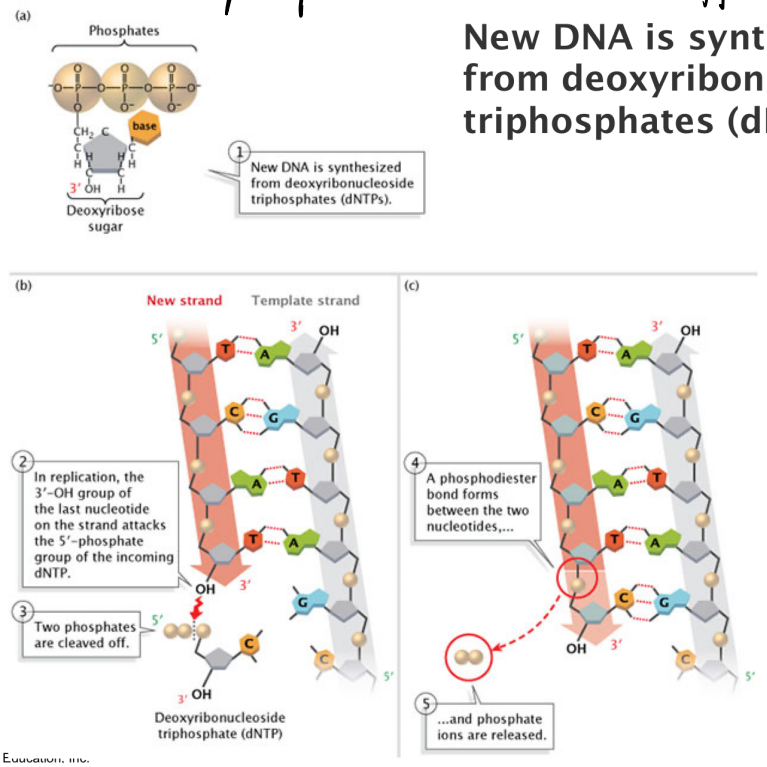
1° DNA polymerases are enzymes that make the covalent bonds between the nucleotides of a new DNA strand.

2° can help repair DNA that has been damaged by toxic chemicals or high-energy radiation, such as X-rays and ultraviolet light.

3. 5′→3′ replication

1° New DNA is synthesized from deoxyribonucleoside triphosphate (dNTPs) (脱氧核苷三磷酸)

2° In replication, the 3′-OH group of the last nucleotide on the strand attacks the 5′-phosphate group of the incoming dNTP. Then, two phosphates are cleaved off.



3° 3′→5′ is unstable

3′ HO-Ap Cp Tp Gp Cp Tp 5′

5′ ←— pppA pC pG pA-OH 3′

↳ unstable

4. Error correction

1° Step 1: 5′→3′ polymerization activity.

error rate: $1/10^3$

2° Step 2: 3′→5′ exonuclease (外切) activity. (take stuff out)
It's called the proofreading function. It will correct recent work.
error rate: $1/10^5 \sim 10^6$

3° Step 3: Mismatch repair system (错配修复)
Cuts, removes, replaces after replication
error rate: $1/10^8 \sim 10^9$

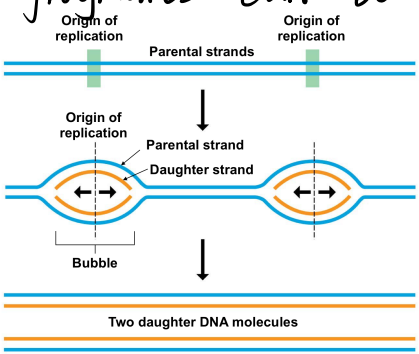
5. The process of replication

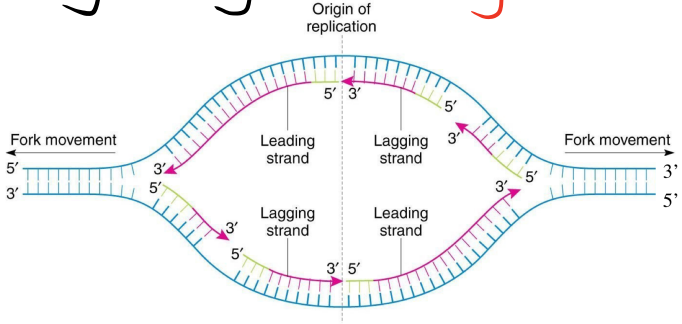
1° Begins on a double helix at specific sites, called origins of replication (复制原点)
Circular DNA (prokaryotes): one origin of replication
Linear DNA (eukaryotes): multiple origins of replication

2° Proceeds in both directions (bidirectional), creating what are called replication "bubbles" (复制泡)

3° Needs RNA primer (引物) which is produced by primase (引发酶), the primer will finally be removed

4° Forms leading strands (前导链) and lagging strands (后随链).
Lagging strands are not continuous, they are called Okazaki fragment (冈崎片段). The ligation of Okazaki fragments can be catalyzed by DNA ligase (DNA连接酶)

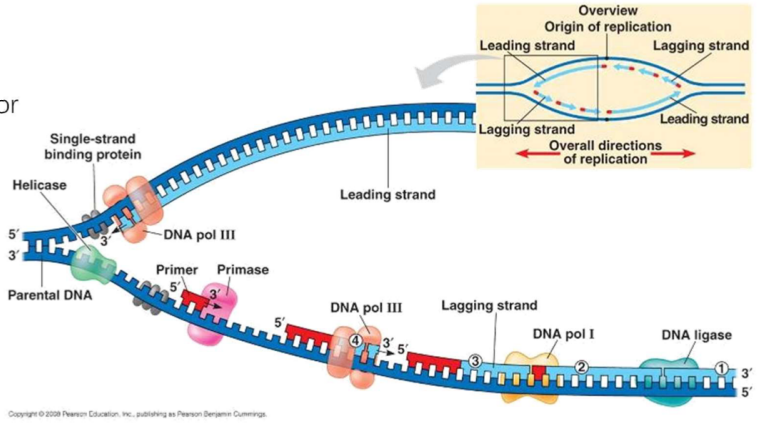




DNA replication (enzymes involved)

- DNA helicase: open the double helix for further replicating.
- DNA primase: form RNA primer at the start of DNA replication.
- DNA polymerase: elongation of new DNA strand; cleavage of wrong added nucleotide.
- DNA ligase: ligation of Okazaki fragments

* Ribonuclease H: remove RNA primer.



§4. Information Flow: From DNA to RNA to Protein

1. Genotype (基因型) and phenotype (表现型)

1° An organism's genotype, its genetic make up, is the heritable information contained in the sequence of nucleotide bases in its DNA.

2° The phenotype, the organism's physical traits, arises from the actions of a wide variety of proteins.

2. DNA specifies the synthesis of proteins

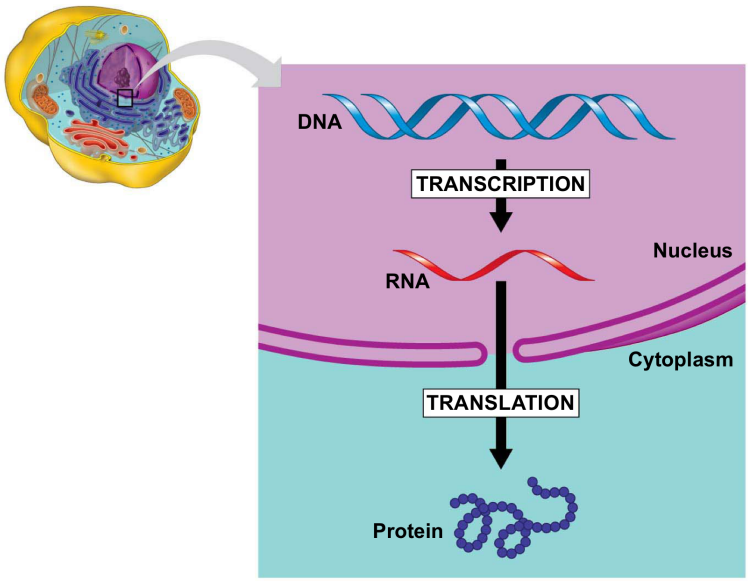
1° Transcription (转录)

The transfer of genetic information from DNA into an RNA molecule.

2° Translation (翻译)

The transfer of information from RNA into a polypeptide (多肽)

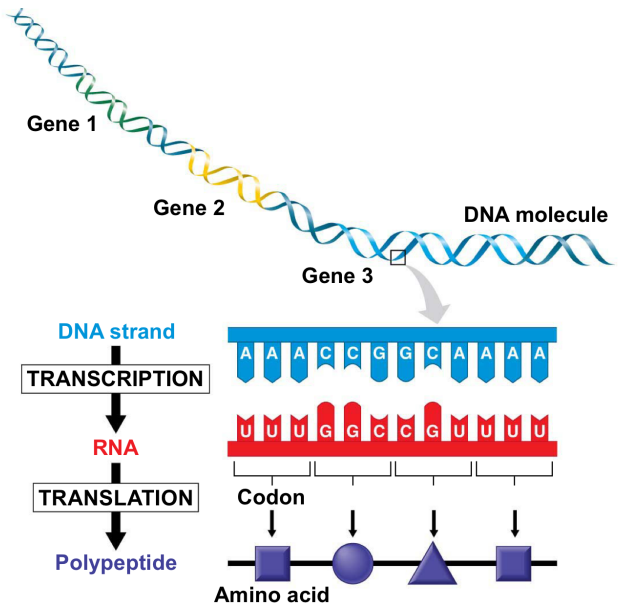
3° The function of a DNA gene is to dictate the production of a polypeptide.



3. The genetic code

1° The flow of information from gene to protein is based on a triplet code called codons (密码子)

- **Three-base codons in the DNA are transcribed into complementary three-base codons in the RNA.**
- **Then the RNA codons are translated into amino acids that form a polypeptide.**



2° The genetic code is the set of rules that convert a nucleotide squence in RNA to an amino acid sequence.

3° Of the 64 triplets (三联体)

① 61 code for amino acids

② 3 are stop codons, instructing the ribosomes to end the polypeptide (UAA, UAG, UGA)

Second base of RNA codon

First base of RNA codon	U	C	A	G	Third base of RNA codon
U	UUU Phenylalanine (Phe) UUC UUA Leucine (Leu) UUG	UCU Serine (Ser) UCC UCA UCG	UAU Tyrosine (Tyr) UAC UAA Stop UAG Stop	UGU Cysteine (Cys) UGC UGA Stop UGG Tryptophan (Trp)	U C A G
C	CUU Leucine (Leu) CUC CUA CUG	CCU Proline (Pro) CCC CCA CCG	CAU Histidine (His) CAC CAA Glutamine (Gln) CAG	CGU Arginine (Arg) CGC CGA CGG	U C A G
A	AUU Isoleucine (Ile) AUC AUA AUG Met or start	ACU Threonine (Thr) ACC ACA ACG	AAU Asparagine (Asn) AAC AAA Lysine (Lys) AAG	AGU Serine (Ser) AGC AGA Arginine (Arg) AGG	U C A G
G	GUU Valine (Val) GUC GUA GUG	GCU Alanine (Ala) GCC GCA GCG	GAU Aspartic acid (Asp) GAC GAA Glutamic acid (Glu) GAG	GGU Glycine (Gly) GGC GGA GGG	U C A G

4° The genetic code is nearly universal.

- **Because diverse organisms share a common genetic code, it is possible to program one species to produce a protein from another species by transplanting DNA.**
- **This allows scientists to mix and match genes from various species—a procedure with many useful genetic engineering applications in agriculture, medicine, and research.**

§5 Transcription: From DNA to RNA

1. Transcription

1° Eukaryotes: DNA → pre-mRNA → mRNA

Prokaryotes: DNA → mRNA

2° Only one of the DNA strands serves as a template (模板) for the newly forming RNA molecule. The other strand is unused.

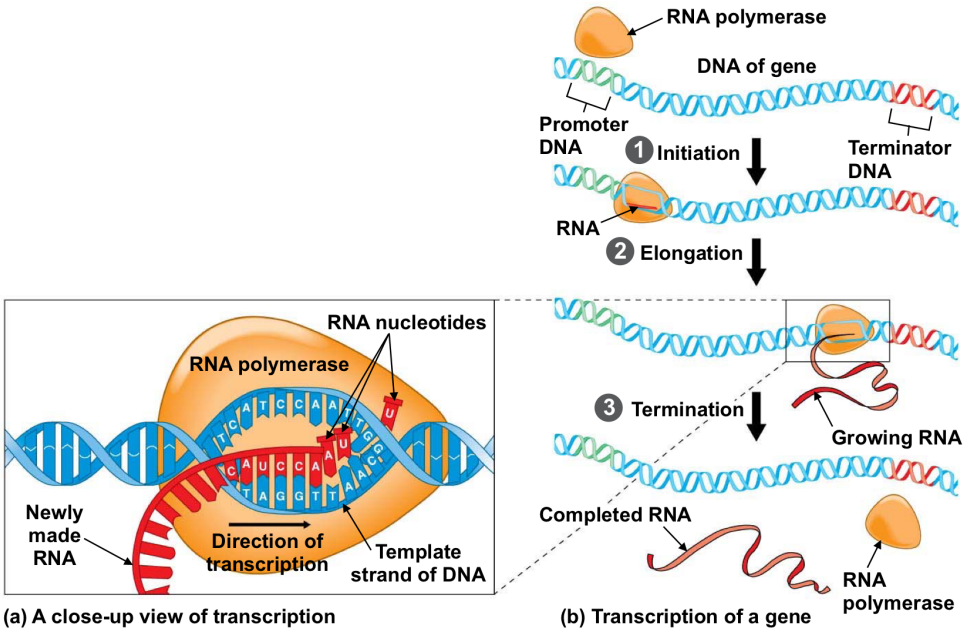
3° The nucleotides that make up the new RNA molecule take their place one at a time along the DNA template strand by forming hydrogen bonds with the nucleotide bases there.

4° RNA polymerase (RNA聚合酶) grows RNA from 5' to 3'.

using UTP, ATP, GTP, CTP.

5° Doesn't need primer.

6° Error rate is $1/10^4$



2. The first phase: initiation of transcription

1° The "start transcription" signal is a nucleotide sequence called a promoter (启动子)

2° Promoter is

① located in the DNA at the beginning of the gene

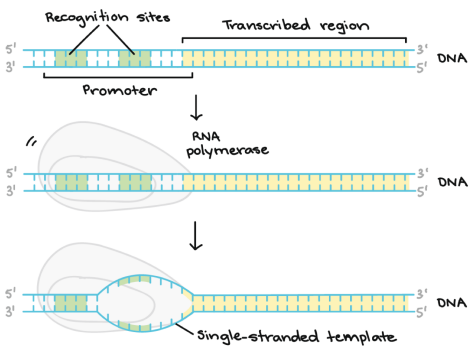
② a specific place where RNA polymerase attaches.

3° The first phase of transcription, called initiation, is

① the attachment of RNA polymerase to the promoter

② the start of RNA synthesis.

Initiation



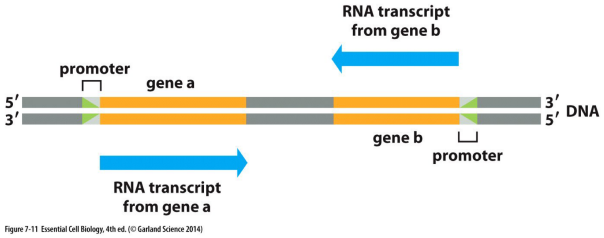


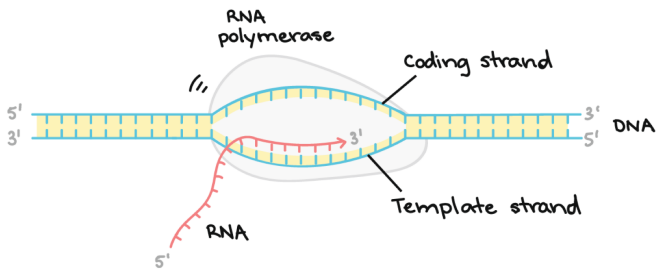
Figure 7-11 Essential Cell Biology, 4th ed. (© Garland Science 2014)

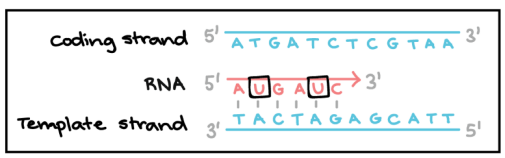
3. The second phase: RNA elongation (延伸)

1° The RNA grows longer

2° The RNA strand peels away from its DNA template, allowing the two separated DNA strands to come back together in the region already transcribed.

Elongation





4. The third phase: termination of transcription

1° RNA polymease reaches a special sequence of bases in the DNA template called a terminator (终止子), signalling the end of the gene.

2° Polymerase detaches from the RNA and the gene.

3° The DNA strands rejoin.

5. The processing of eukaryotic RNA

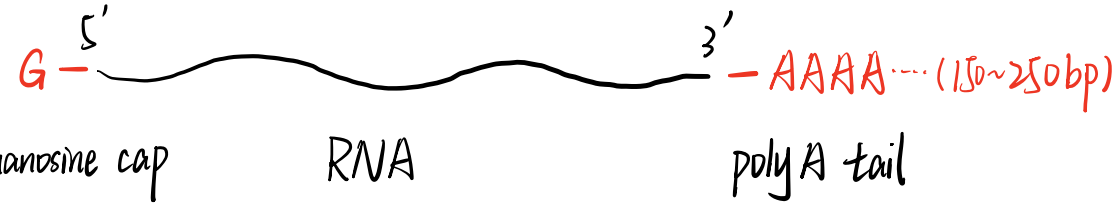
1° The eukaryotic cell modifies, or processes, the RNA transcripts in the nucleus before they move to the cytoplasm for translation.

2° Kind one: the addition of cap and tail to the ends of the RNA.

① stablize mRNA

② markers for the nuclear transport

③ promote translation (help ribosomes recognize the RNA as mRNA.



3° Kind two: RNA splicing (RNA剪接)

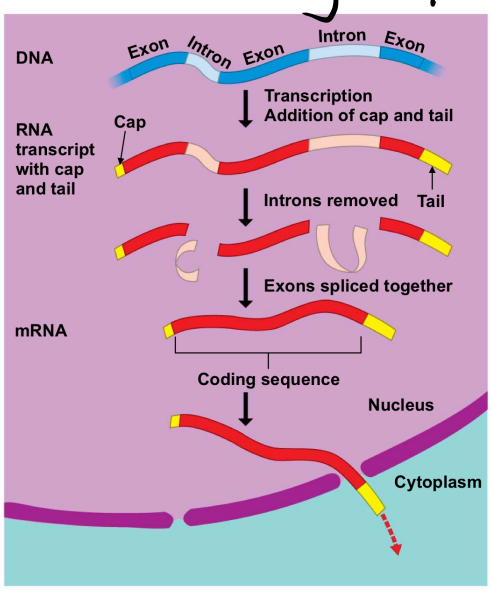
① 98% genes of plants and animals include such internal noncoding regions, which are called introns (内含子)

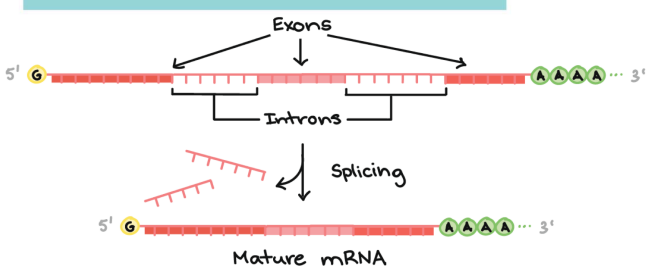
② 2% genes are coding regions which are called exons (外显子)

Before the RNA leaves the nucleus,

① the introns are removed

② the exons are joined to produce an mRNA molecule with a continuous coding sequence.





§6 Translation: The Players

1. Messenger RNA (mRNA)

1° Produced by transcription

2° Once it is present, the machinery used to translate mRNA molecules requires enzymes and sources of chemical energy, such as ATP.

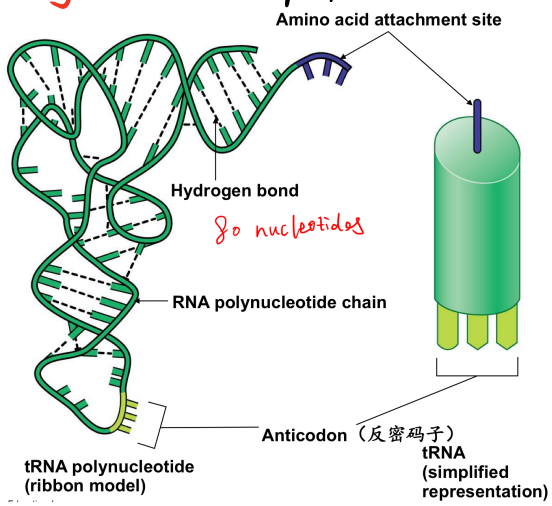
2. Transfer RNA (tRNA)

1° An interpreter to convert the three-letter words (codons) of nucleic acids to the amino acid words of proteins.

2° tRNA carries two distinct functions:

① pick up the appropriate amino acids

② recognize the appropriate codons in the mRNA



3° At one end of the tRNA is a special triplet of bases called an anticodon (反密码子)

① The anticodon triplets is complementary to a codon triplet on mRNA.

② The anticodon recognizes a particular codon by using base-pairing rules.

4° One specific kind of amino acid attaches to the other end.

3. Ribosomes

1° A ribosome consists of two subunits. Each subunit is made up of

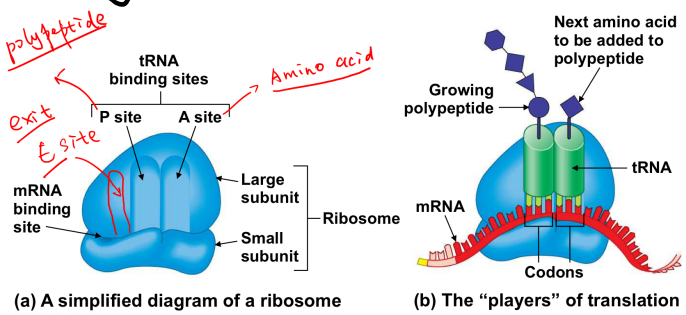
① a protein

② a considerable amount of another kind of RNA, ribosomal RNA (rRNA)

2° A fully assembled ribosome has

① a binding site for mRNA on its small subunit.

② binding sites for tRNA on its large subunit.

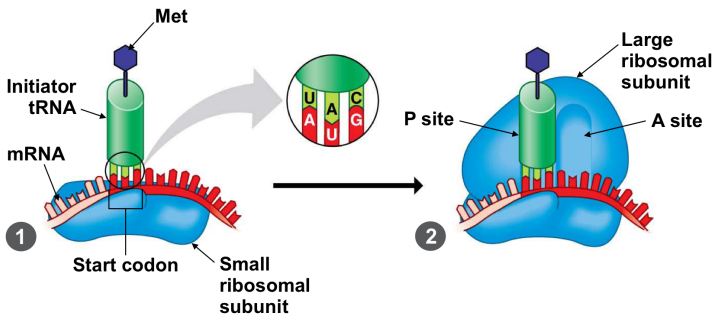


(a) A simplified diagram of a ribosome (b) The "players" of translation

4. The first phase: initiation

1° An mRNA molecule binds to a small ribosomal subunit, then a special initiator tRNA binds to the start codon (起始密码子)

2° A large ribosomal subunit binds to the small one, creating a functional ribosome.



5. The second phase: elongation

Once initiation is complete, amino acids are added one by one to

the first amino acid. Each addition occurs in the three-step elogation process.

① Step 1: Codon Recognition

The anticodon of an incoming tRNA molecule pairs with the mRNA codon in the A site of the ribosome.

② Step 2: Peptide bond formation.

(1) The polypeptide leaves the tRNA in the P site and attaches to the amino acid on the tRNA in the A site

(2) The ribosome creates a new peptide bond.

③ Step 3: Translocation

(1) The P site tRNA moves to E site and then leaves the ribosome, and the ribosome moves the remaining tRNA, carrying the growning polypeptide, to the P site.

(2) The mRNA and tRNA move as a unit.

b. Termination

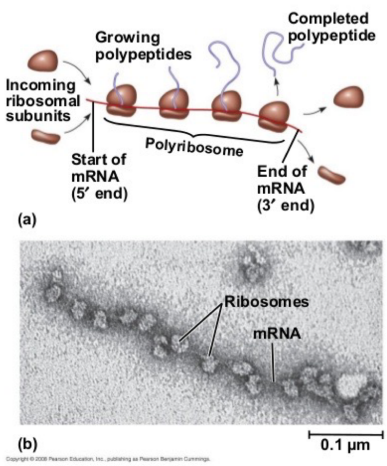
Elongation continues until

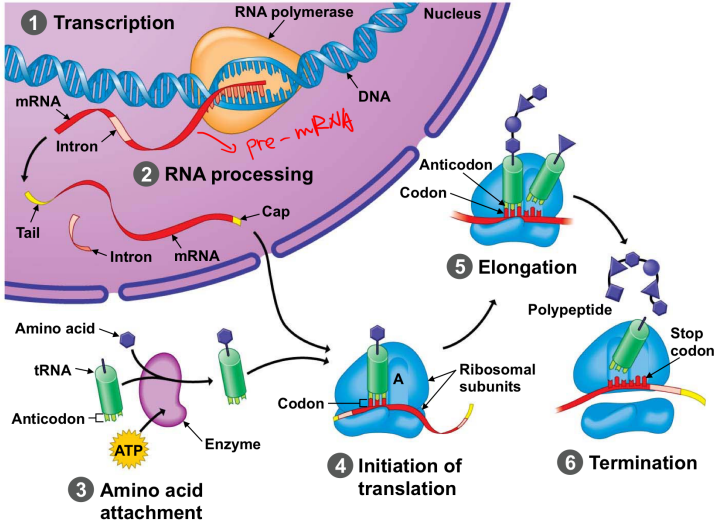
1° a stop codon (终止密码子) reaches the ribosome's A site.

2° the completed polypeptide is freed

3° the ribosome splits back into its subunits.

Fig. 17-20





§7 Mutations

1. Mutations (突变)

1° Mutations can involve

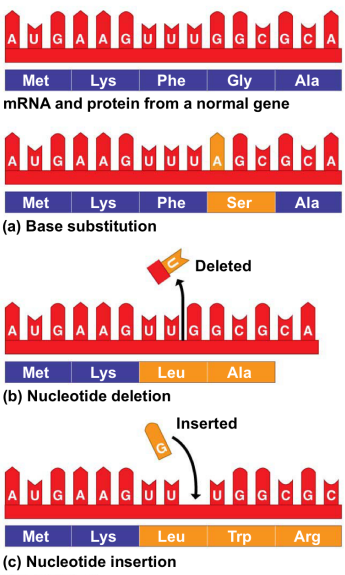
① large regions of a chromosome

② just a single nucleotide pair

2° General categories:

① nucleotide substitutions (替换)

② nucleotide deletions (缺失) or insertions (插入)



2. Types of mutation

1° Missense mutations (错义突变)

involve a single nucleotide and change the amino

acid coding

2° Nonsensing mutations (无义突变)

change an amino acid codon into a stop codon

3° Frameshift mutations (移码突变)

Mutations involving the deletion or insertion of one or more nucleotides in a gene.

Most often produces a non-functioning polypeptide.

3. Mutagens (诱突变剂)

1° Physical mutagens: X-rays and UV light ……

2° Chemical mutagens

3° Many mutagens can act as carcinogens (致癌物)

4° Mutagens are one source of the rich diversity of genes in the living world, a diversity that makes evolution by natural selection possible.

5° Cancer can also be caused by mutations in

① Genes that stimulate the cell division

(proto-oncogene (原癌基因) ⟶ oncogene (致癌基因))

② Genes that stop cell division.

(tumor-suppressor gene (抑癌基因) ⟶ oncogene)

③ Genes that repair other damaged genes.

④ Genes that tell a cell to die.

§8 Viruses and Other Nonecellur Infectious Agents

1. Virus

1° A virus is generallu not consider alive because it

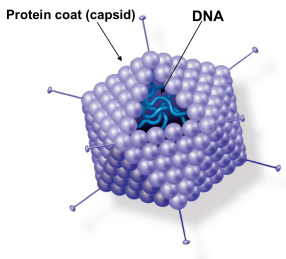
① is not cellular

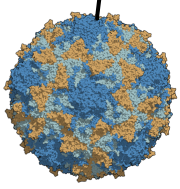
② cannot reproduce on its own.

2° A virus is

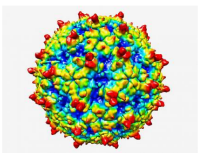
① a bit of nucleic acid (DNA or RNA; Both DNA and RNA may be single or double-stranded), wrapped in a protein coat (capsid (衣壳))

② In some cases, a lipid envelope of membrane.





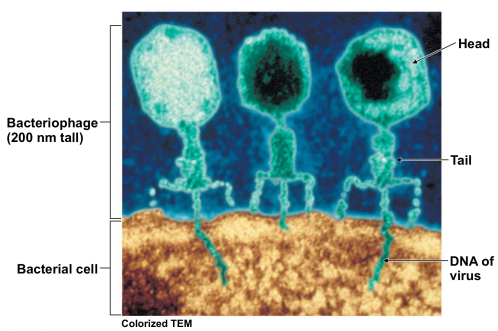
poliovirus



rhinoviruses
Rhino: nose

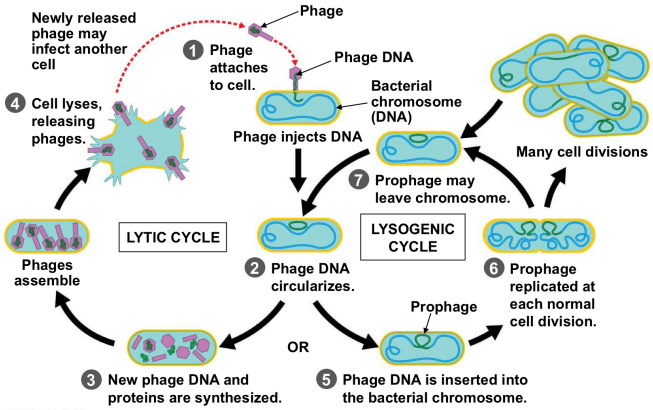
2. Bacteriophages / Phages (噬菌体)

1° The phage consists of a molecule of DNA enclosed within an elaborate structure made of proteins.



2° Once they infect a bacterium, most phages enter a reproductive cycle called the lytic cycle (裂解周期)

3° Some viruses can also reproduce by an alternative route —— the lysogenic cycle (溶原周期), in which viral DNA replication occurs without phage production or the death of the cell.



3. Plant viruses

1° Many known plant viruses have RNA rather than DNA as their genetic material

e.g. tobacco mosaic virus (TMV) (烟草花叶病毒)

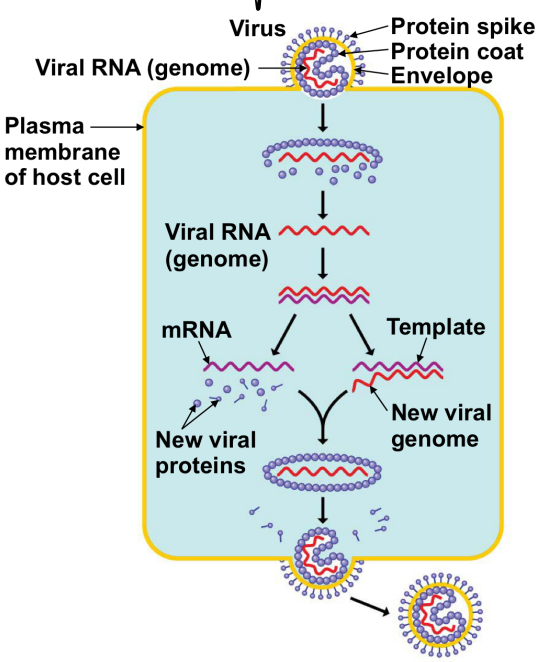
2° There is no cure for most viral plant diseases.

4. Animal viruses

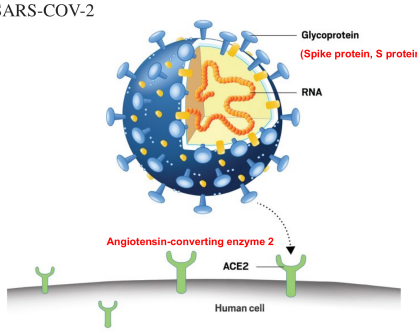
1° Influenza (flu) virus (流感) has an outer envelop made of phospholipid membrane, with projecting spikes of protein.

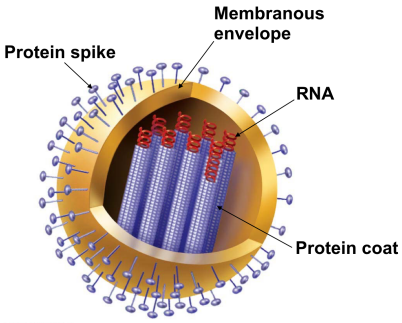
2° RNA viruses: flu, common cold, measles (麻疹), mumps (流行性腮腺炎), AIDS, and polio (小儿麻痹症)

3° DNA viruses: hepatitis (肝炎), chicken pox (水痘) and herpes (疱疹) infection



SARS-COV-2

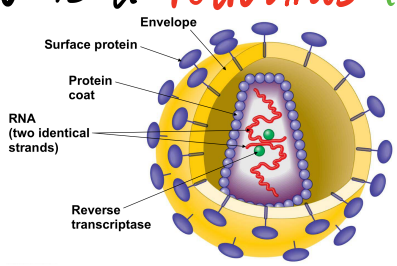




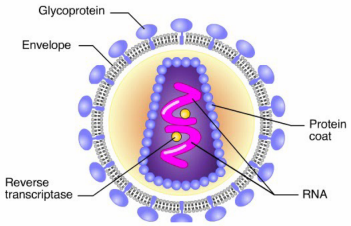
- **Not all animal viruses reproduce in the cytoplasm.**
- **For example, herpesviruses, which cause chicken pox, shingles（带状孢疹）, cold sores（唇孢疹）, and genital herpes（生殖器孢疹）, are enveloped DNA viruses that reproduce in a host cell's nucleus and get their envelopes from the cell's nuclear membrane.**
- **The amount of damage a virus causes the body depends partly on how quickly the immune system responds to fight the infection and partly on the ability of the infected tissue to repair itself.**
  - **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）.**

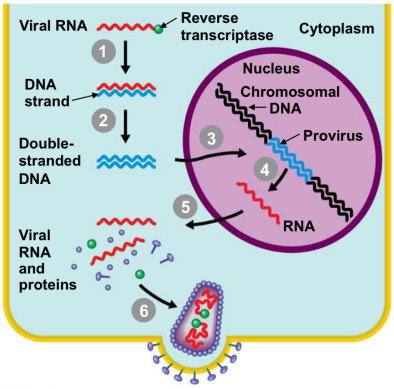
5. HIV, the AIDS virus

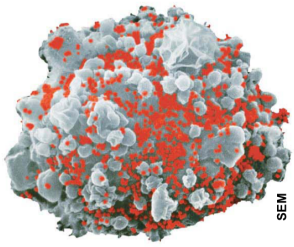
1° HIV is a retrovirus (逆转录病毒)



2° These viruses carry molecules of an enzyme called reverse transcriptase (逆转录酶), which catalyzes reverse transcription: The synthesis of DNA on an RNA template.







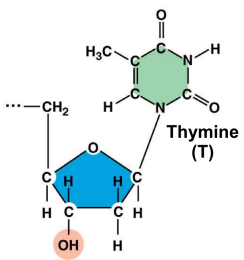
HIV (red dots) infecting a white blood cell

3° Two types of inhibitions

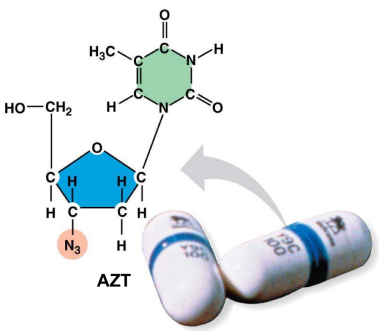
① protease (蛋白酶) inhibitors

② reverse transcriptase inhibitors (AZT)

- **The first type inhibits the action of enzymes called proteases（蛋白酶）, which help produce the final versions of HIV proteins.**
- **The second type, which includes the drug AZT, inhibits the action of the HIV enzyme reverse transcriptase.**



Part of a T nucleotide



AZT

- **In fact, the death rate from HIV infection can be lowered by 80% with proper treatment.**
- **However, even in combination, the drugs do not completely rid the body of the virus.**
- **Because AIDS has no cure yet, prevention (namely, the avoidance of unprotected sex and needle sharing) is the only healthy option.**