2. آشنایی با مبانی اولیه ژنتیک

اصطلاحات رایج

ژن: واحد وراثت می باشد. بیشتر ژنها اطلاعات مربوط به ساخت پروتئینها را در بر دارند.

ژنوم:کل ماده ژنتیکی موجود در داخل یک سلول می باشد.

ژنوتیپ: اطلاعاتی است که در ژنوم هر یک از سلول‌های موجودات زنده به صورت DNA وجود دارد.

فنوتیپ: به مجموعهٔ صفات ظاهری همچون رنگ چشم و موها فنوتیپ می‌گویند. فنویپ افراد در درجهٔ اول به ژنوتیپ آن‌ها بستگی دارد، ولی تحت تأثیر محیط نیز قرار دارد.

THE UNIVERSAL FEATURES OF CELLS ON EARTH

It is estimated that there are more than 10 million—perhaps 100 million—living species on Earth today. Each species is different, and each reproduces itself faithfully, yielding progeny that belong to the same species.

Most living organisms are single cells; others, such as ourselves, are vast multicellular cities in which groups of cells perform specialized functions and are linked by intricate systems of communication. But in all cases, whether we discuss the solitary bacterium or the aggregate of more than 1013 cells that form a human body, the whole organism has been generated by cell divisions from a single cell. The single cell, therefore, is the vehicle for the hereditary information that defines the species.

All Cells Store Their Hereditary Information in the Same Chemical Code (DNA)

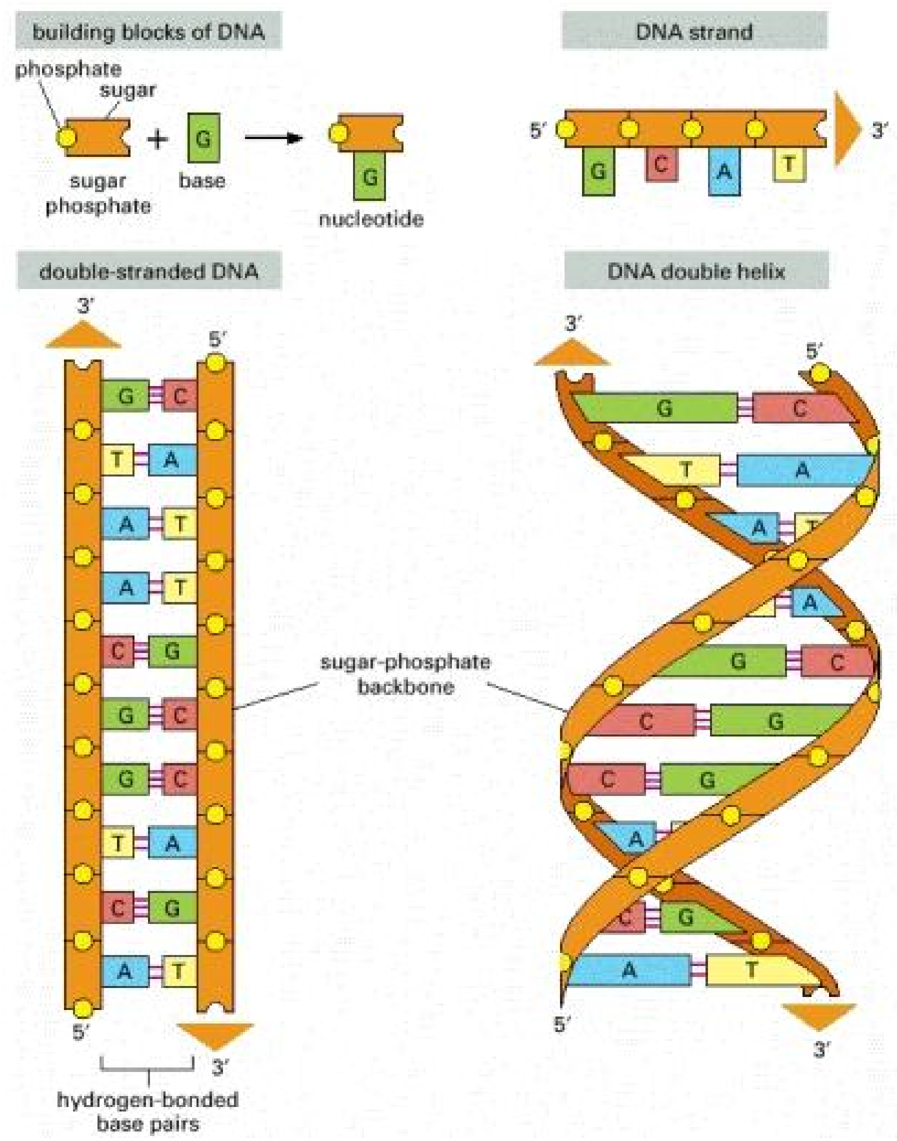
Computers have made us familiar with the concept of information as a measurable quantity—a million bytes (to record a few hundred pages of text or an image from a digital camera), 600 million for the music on a CD, and so on. They have also made us well aware that the same information can be recorded in many different physical forms.

Living cells, like computers, deal in information, and it is estimated that they have been evolving and diversifying for over 3.5 billion years. It is scarcely to be expected that they should all store their information in the same form, or that the archives of one type of cell should be readable by the information-handling machinery of another. And yet it is so. All living cells on Earth, without any known exception, store their hereditary information in the form of double-stranded molecules of DNA—long unbranched paired polymer chains, formed always of the same four types of monomers. These monomers have nicknames drawn from a four-letter alphabet—A, T, C, G—and they are strung together in a long linear sequence that encodes the genetic information, just as the sequence of 1s and 0s encodes the information in a computer file.

All Cells Replicate Their Hereditary Information by Templated Polymerization

The mechanisms that make life possible depend on the structure of the double stranded DNA molecule. Each monomer in a single DNA strand—that is, each **nucleotide—consists of two parts: a sugar (deoxyribose) with a phosphate** group attached to it, and a *base, which may be either adenine (A), guanine (G),* cytosine (C) or thymine (T).

DNA and its building blocks



A Brief History of Genetics

Humans first applied genetics to the domestication of plants and animals between approximately 10,000 and 12,000 years ago. This domestication led to the development of agriculture and fixed human settlements.

Jewish book of religious laws based on oral traditions dating back thousands of years, presents an uncannily accurate understanding of the inheritance of hemophilia. It directs that, if a woman bears two sons who die of bleeding after circumcision, any additional sons that she bears should not be circumcised; nor should the sons of her sisters be circumcised, although the sons of her brothers should. This advice accurately depicts the X-linked pattern of inheritance of hemophilia.

Gregor Mendel (1822–1884) discovered the basic principles of heredity.

Mendel used the pea plant *Pisum sativum in his studies of* heredity.

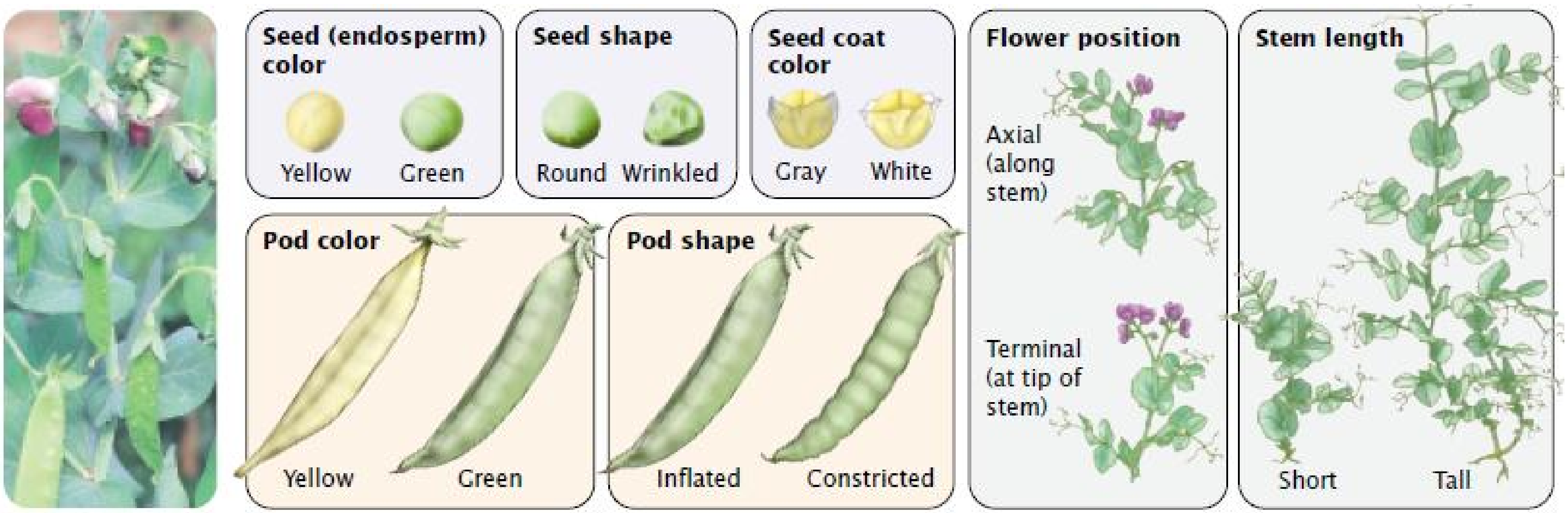
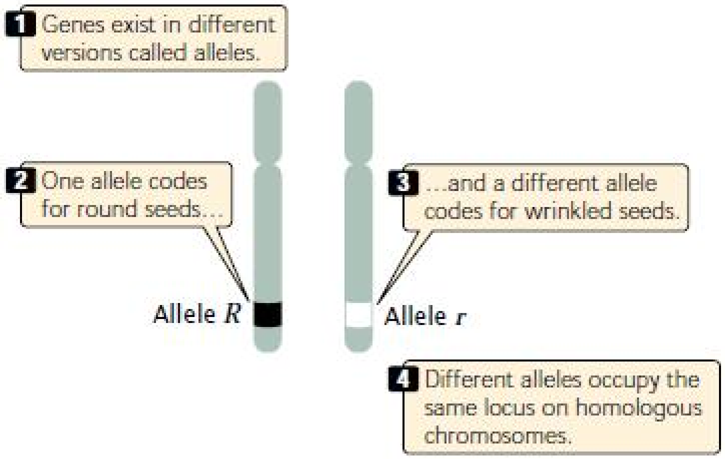
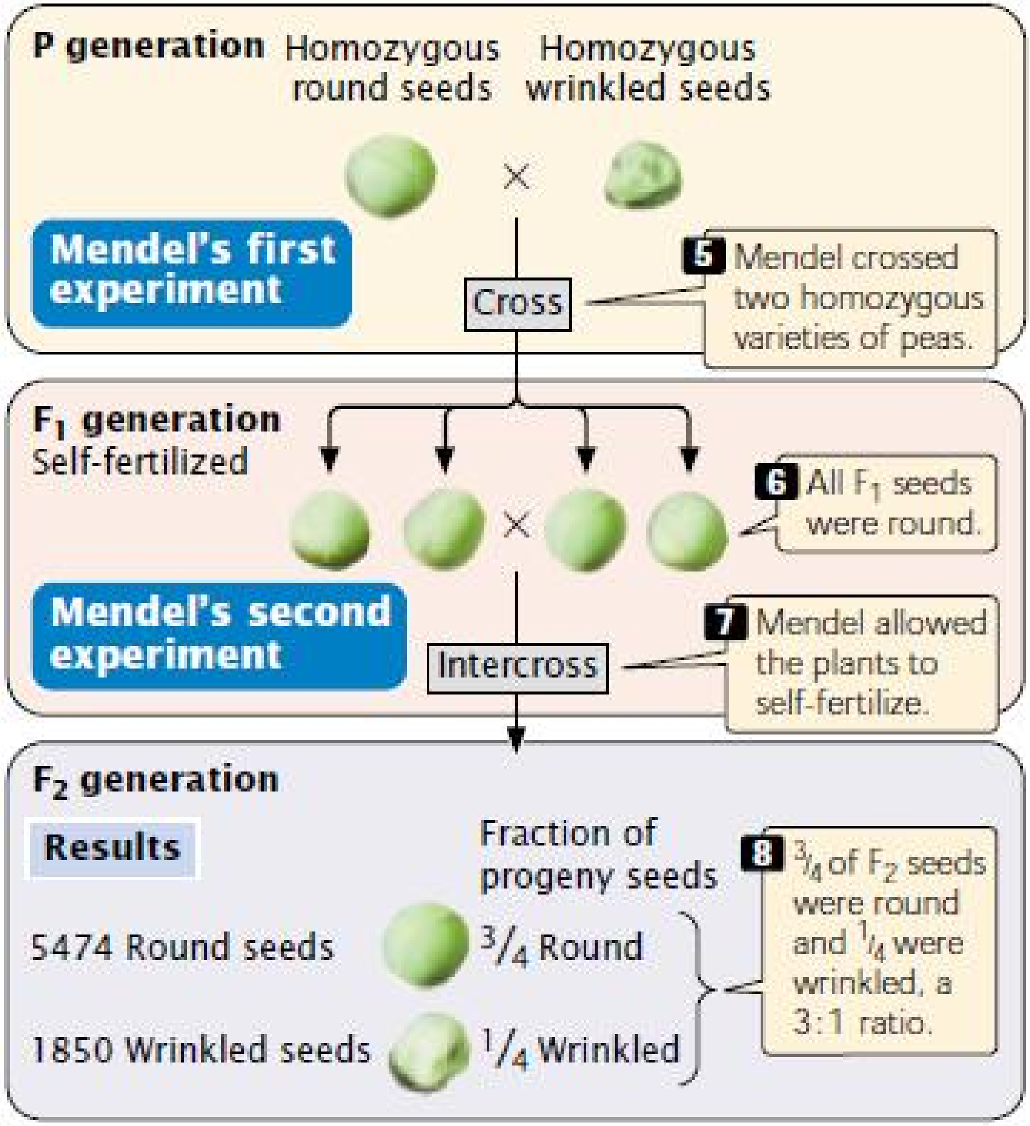


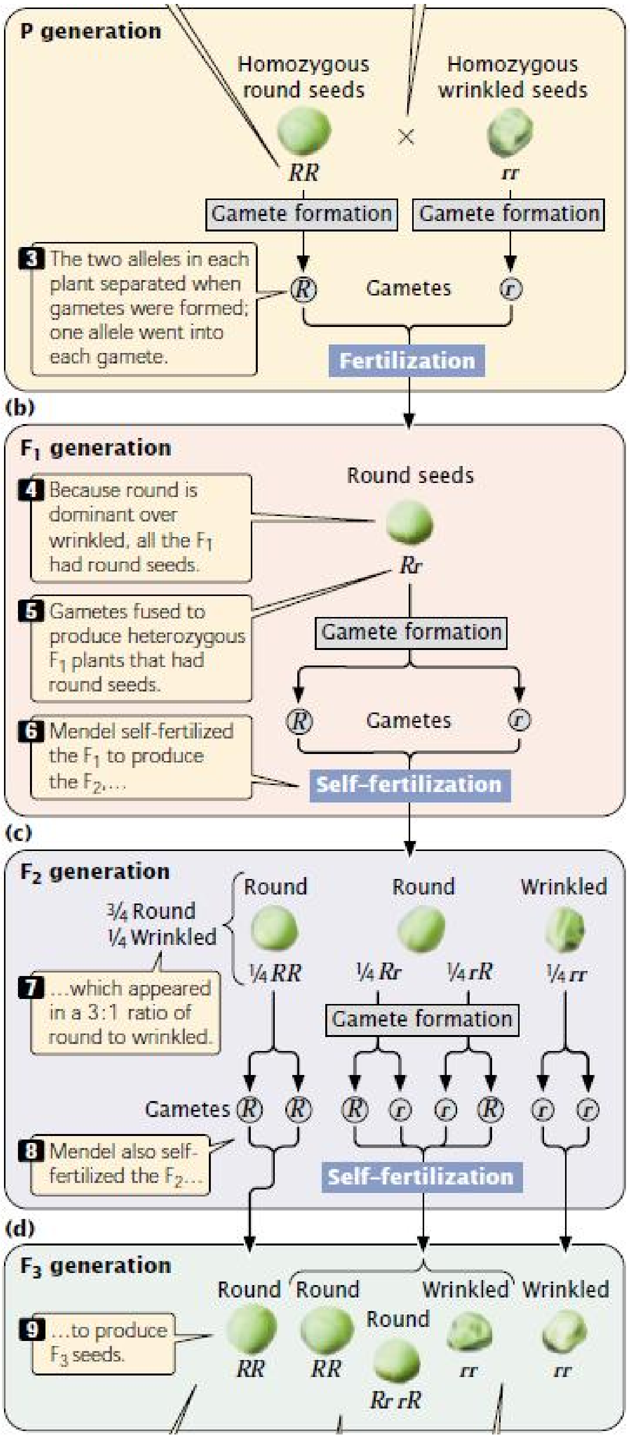
Table 3.1 Summary of important genetic terms

Term	Definition
Gene	A genetic factor (region of DNA) that helps determine a characteristic
Allele	One of two or more alternate forms of a gene
Locus	Specific place on a chromosome occupied by an allele
Genotype	Set of alleles that an individual possesses
Heterozygote	An individual possessing two different alleles at a locus
Homozygote	An individual possessing two of the same alleles at a locus
Phenotype or trait	The appearance or manifestation of a character
Character or characteristic	An attribute or feature



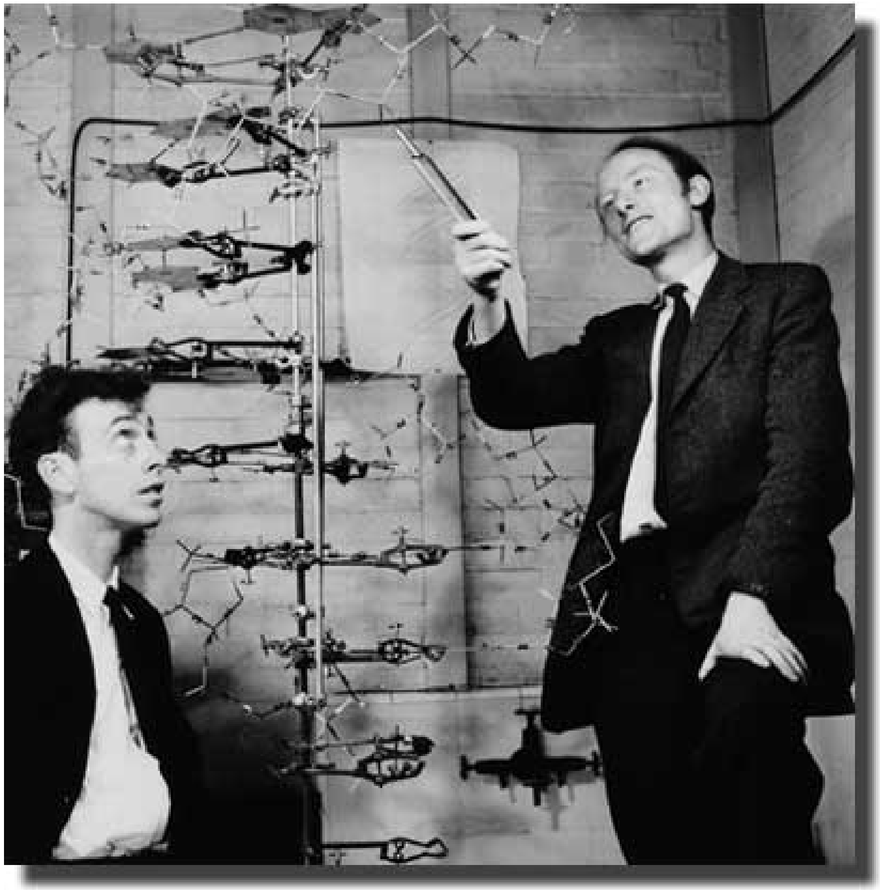


Conclusion: The traits of the parent plants do not blend. Although F_1 plants display the phenotype of one parent, both traits are passed to F_2 progeny in a 3:1 ratio.



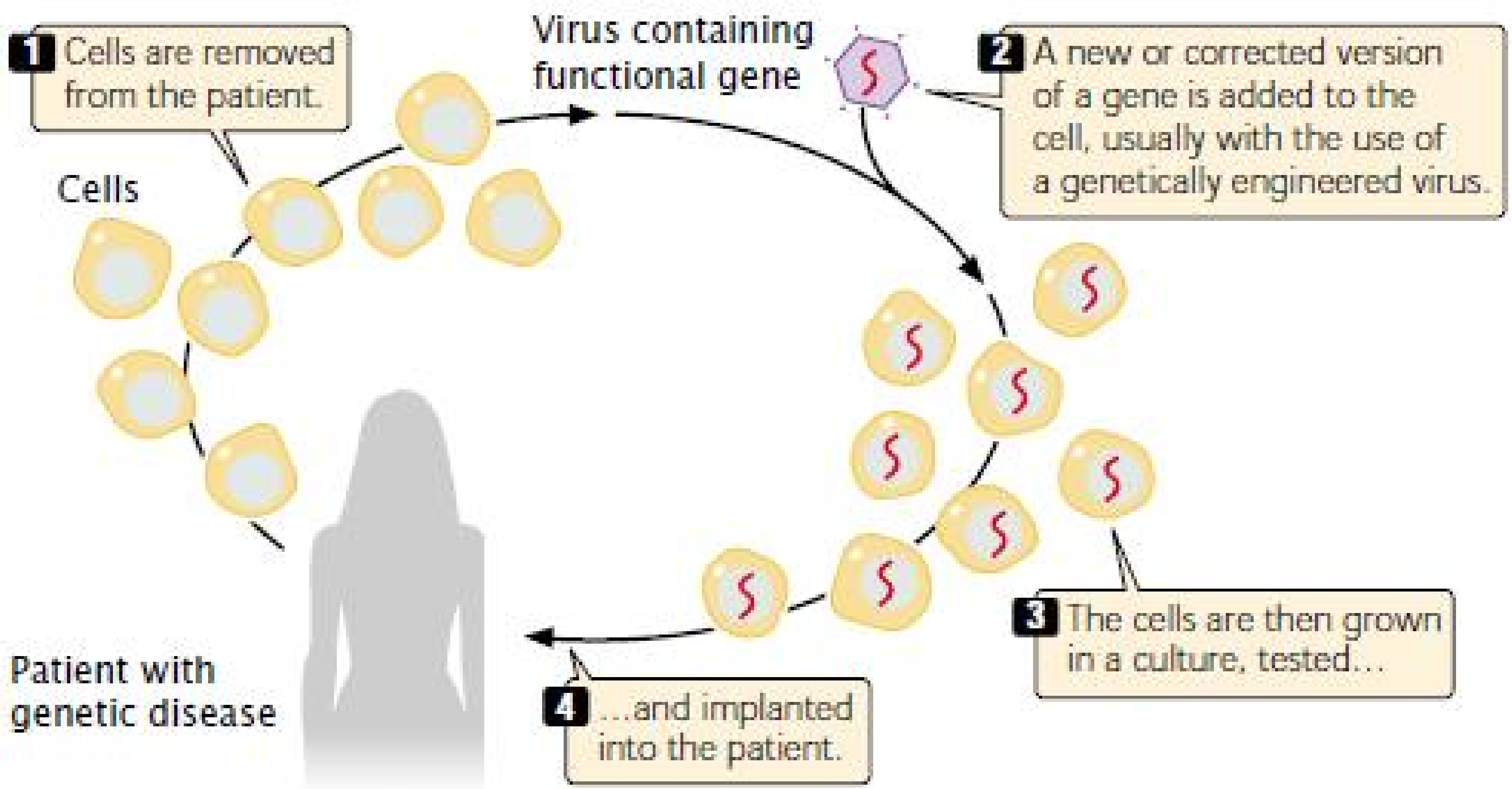
The principle of segregation states that each individual organism possesses two alleles coding for a characteristic. These alleles segregate when gametes are formed, and one allele goes into each gamete. The concept of dominance states that, when dominant and recessive alleles are present together, only the trait of the dominant allele is observed.

Francis Crick and James Watson, discoverers of the DNA molecular structure. One of the most important biological discovery in the 20th century.



Molecular biology + Genetics = Genetic engineering

Twentieth-century genetic engineering



Future genetic engineering

Generating different human organs including heart, eye, leg, etc to transplant

Curing all genetic disorders

Producing genetical ID cards

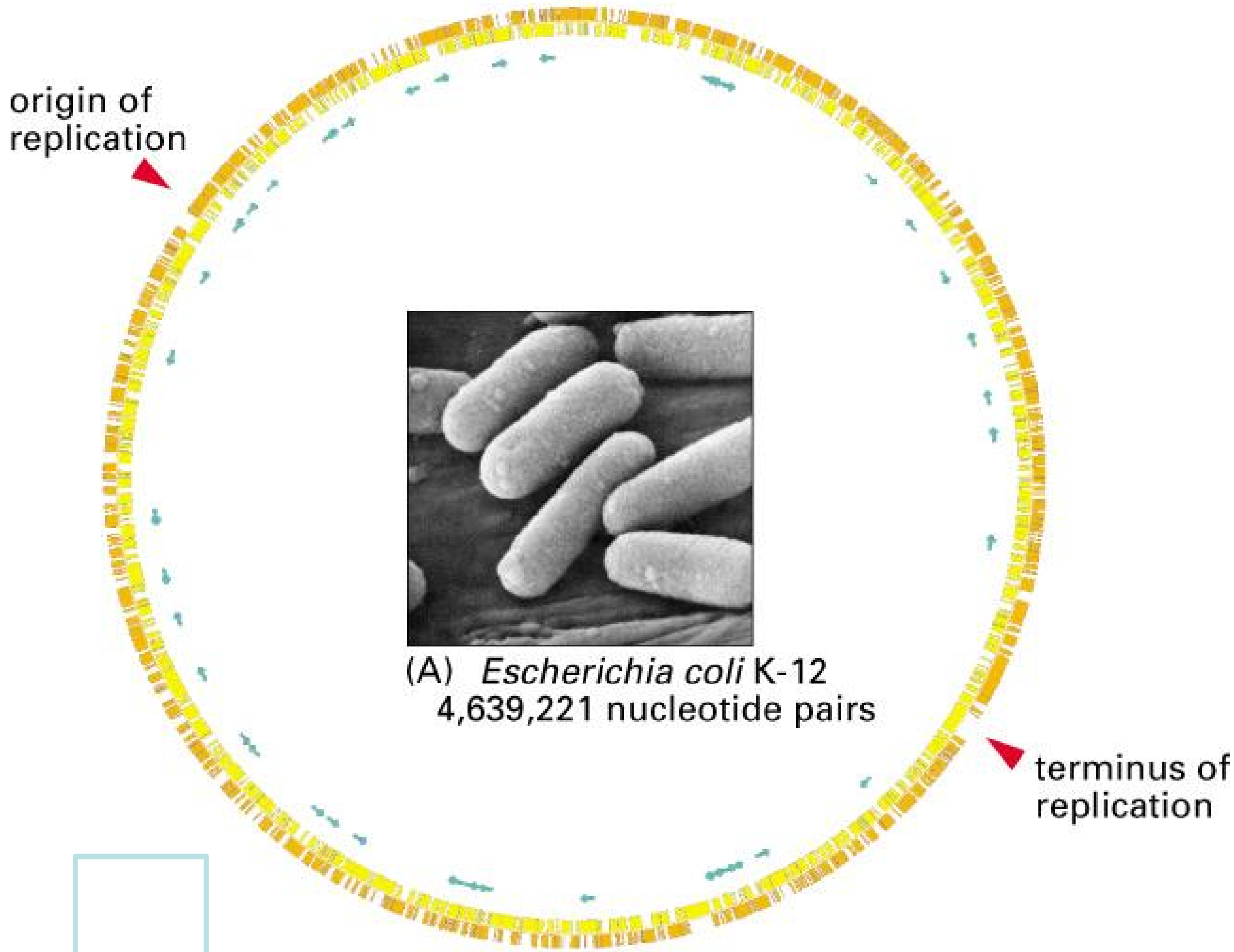
Increasing growth rate of different creatures including plants and animals

etc…

Genome organization in Prok. and Euk.

- Prokaryotes
  - Circular DNA
- Eukaryotes
  - Linear DNA

Prokaryotic DNA



Prokaryotic DNA

The genetic information of a bacterial cell is contained not only in the main chromosome but also in extrachromosomal DNA elements called plasmids.

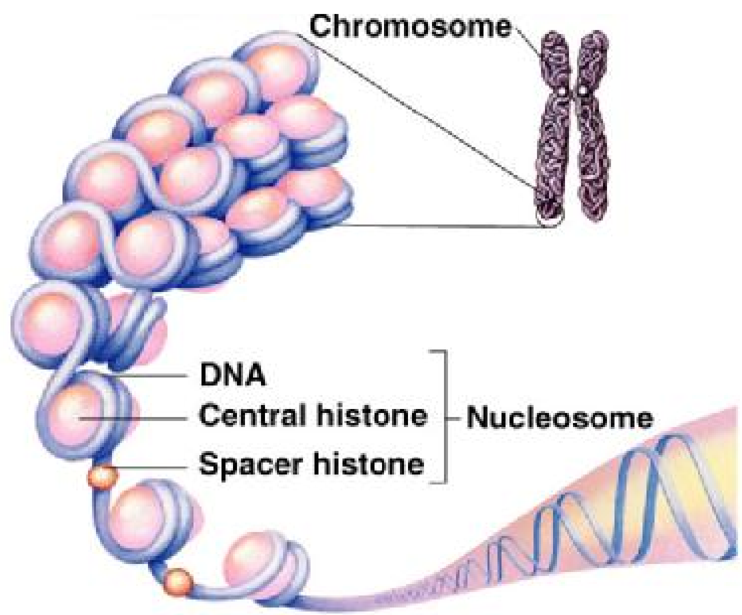
Plasmids are self-replicating within a cell, and many plasmids have a block of genes that enable them to move from one bacterial cell to another. Loss of its plasmids has no effect on the essential functions of a bacterial cell.
Consequently, the cell is seen to act as *host to the plasmids. Similar to* bacterial chromosomes, but much smaller, plasmids are circular double-stranded DNA molecules.

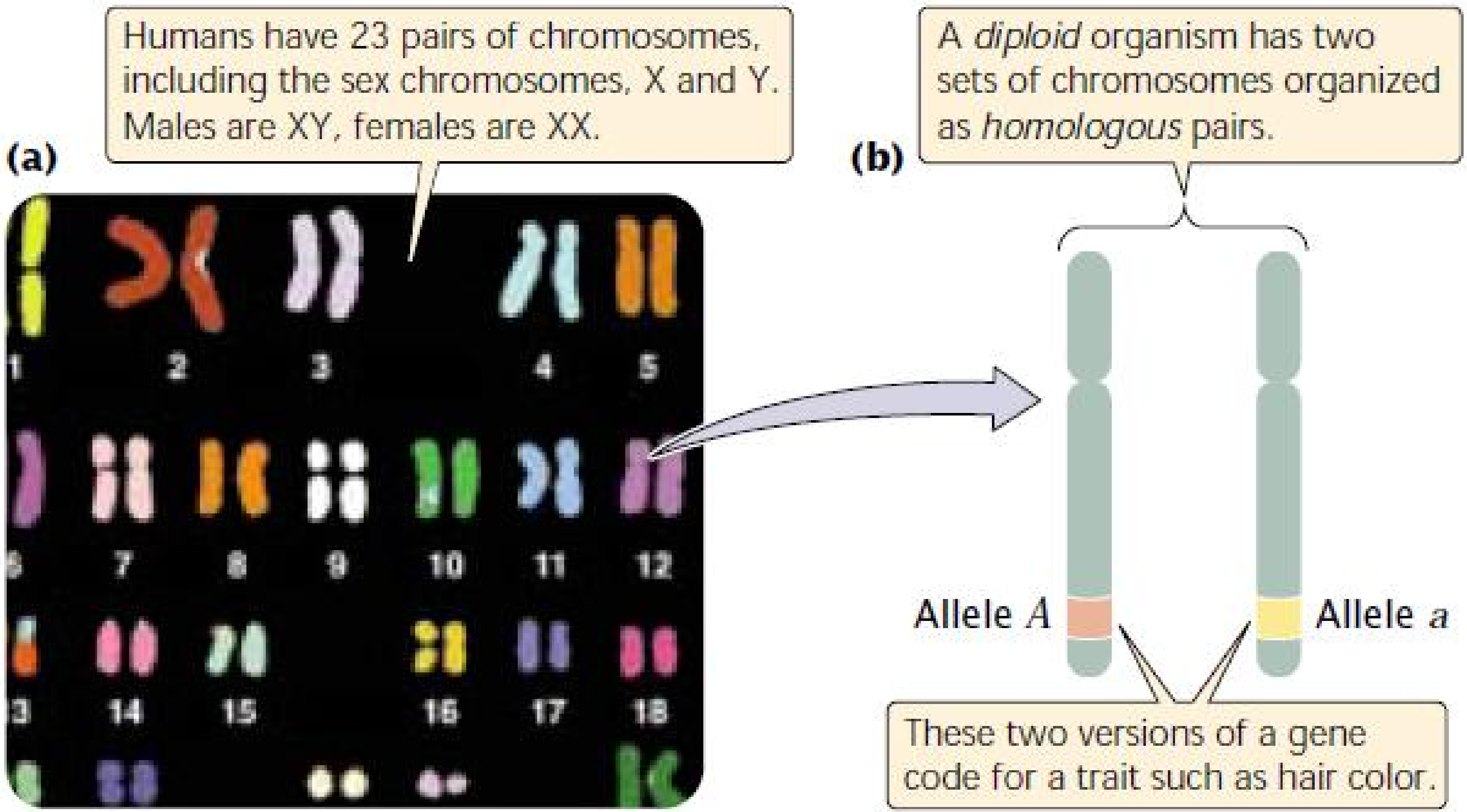
Some plasmids encode resistance to certain antibiotics or heavy metal ions or to ultraviolet radiation. Some plasmids have the ability to transfer themselves from one bacterial host cell into another.

The ability of plasmids to replicate themselves has been utilized in the construction of cloning vectors, many of which contain a replication function derived from plasmids and can therefore be maintained indefinitely in the cytoplasm of the host bacteria.

Eukaryotic DNA

- Eukaryotic DNA is packaged into chromatin which is a complex combination of DNA and proteins.
- Chromatin structure is directly related to the control of gene expression.
- Chromatin structure begins with the organization of the DNA into nucleosomes.
- Nucleosomes may block RNA polymerase II from gaining access to promoters.




Humans have 23 pairs of chromosomes, including the sex chromosomes, X and Y. Males are XY, females are XX.
(a)
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
(b)
A *diploid* organism has two sets of chromosomes organized as *homologous* pairs.
Allele A
Allele a
These two versions of a gene code for a trait such as hair color.

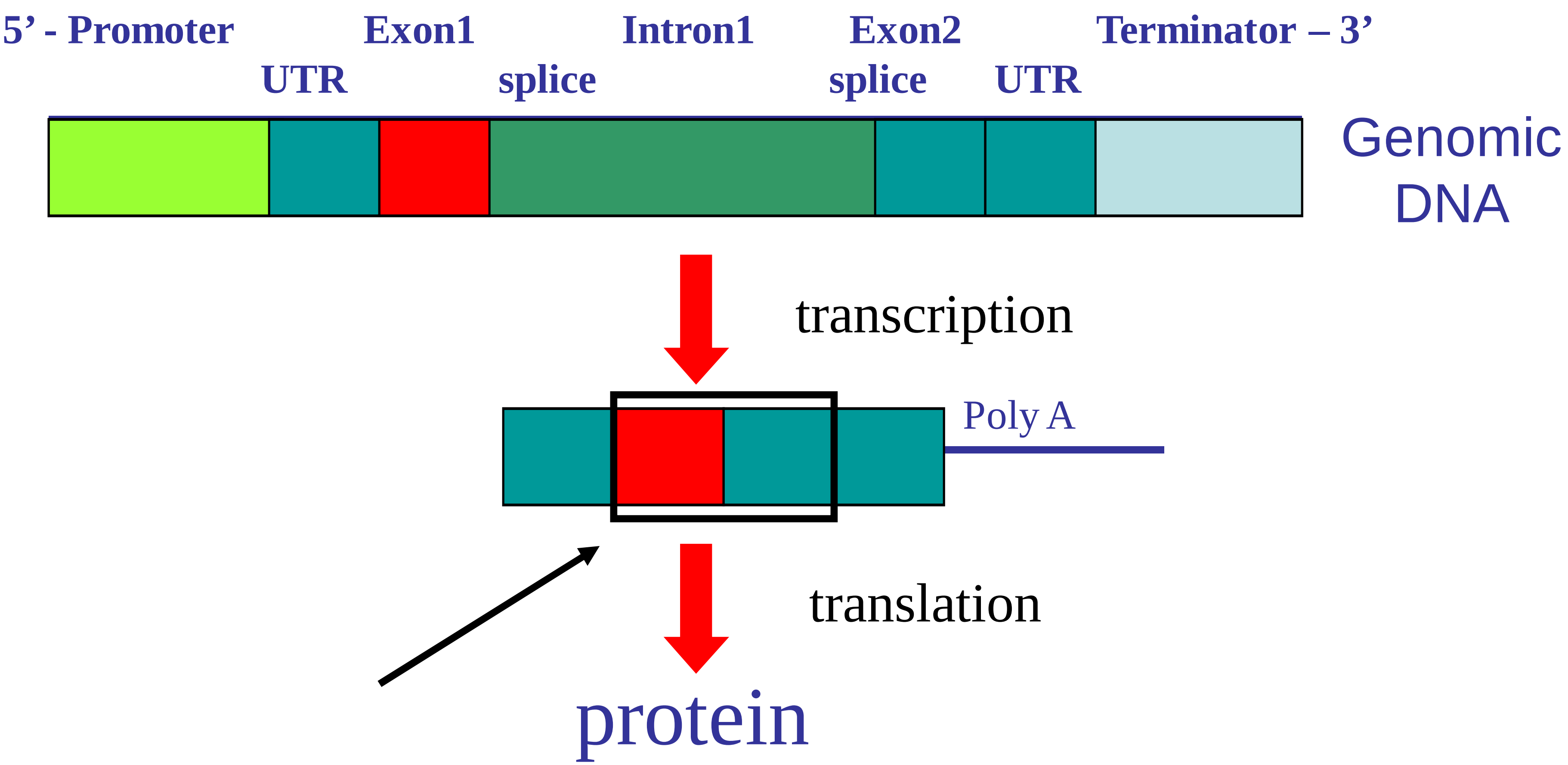
Gene Structure

– Promoter: regions of DNA which promote transcription

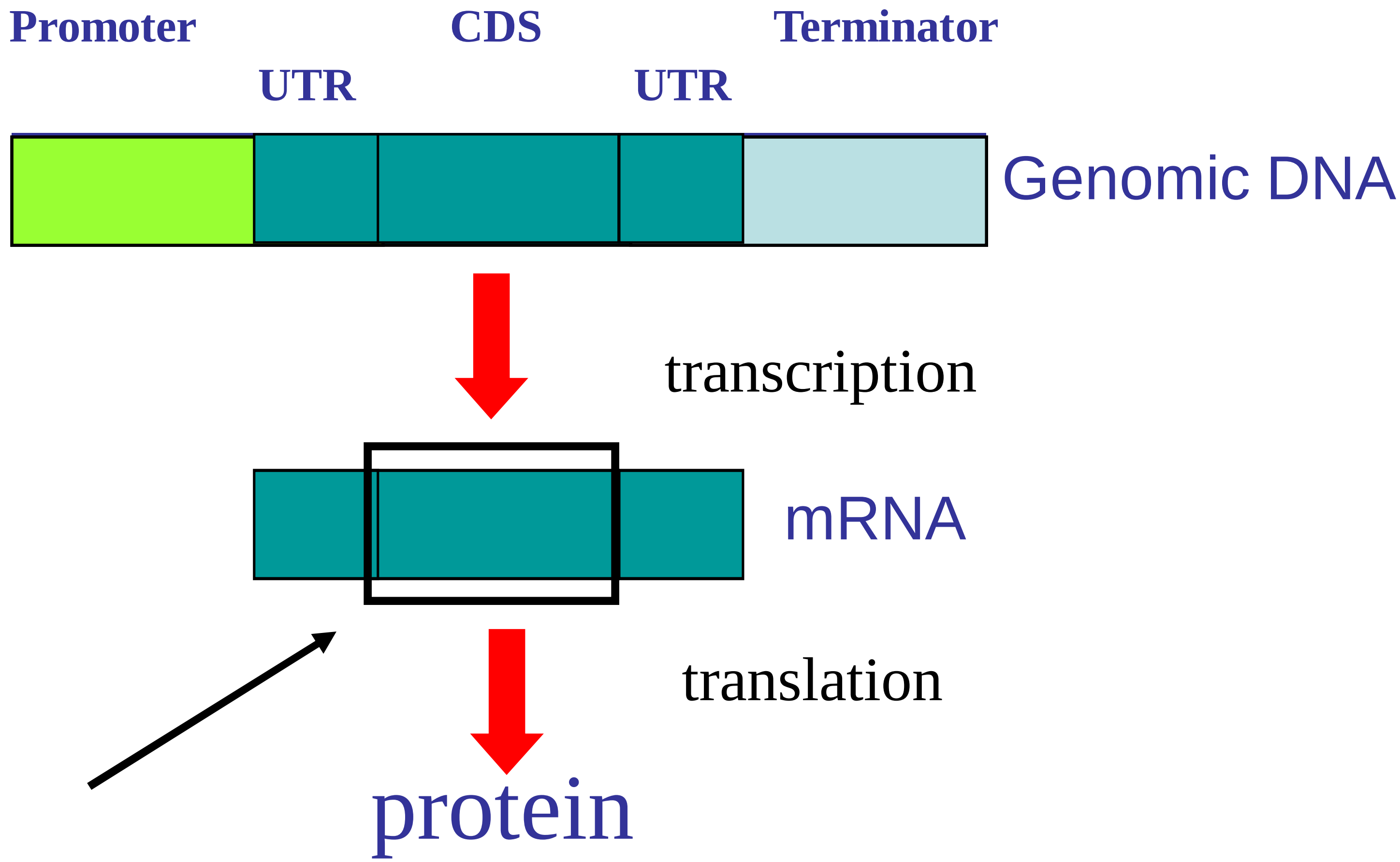
– Terminator: regions of DNA which terminate transcription

– Splice site (Eukaryotics only)

Eukaryotic Gene Structure

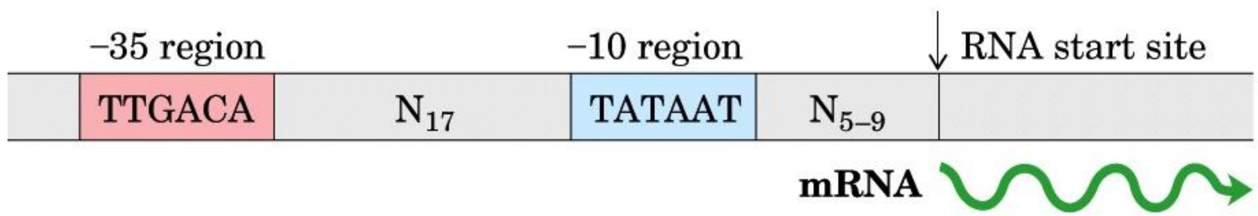


Prokaryotic Gene Structure



Prokaryotic Promoter

- One type of RNA polymerase.
- Pribnow box located at –10 (6-7bp)
- –35 sequence located at -35 (6bp)



Eukaryote Promoter

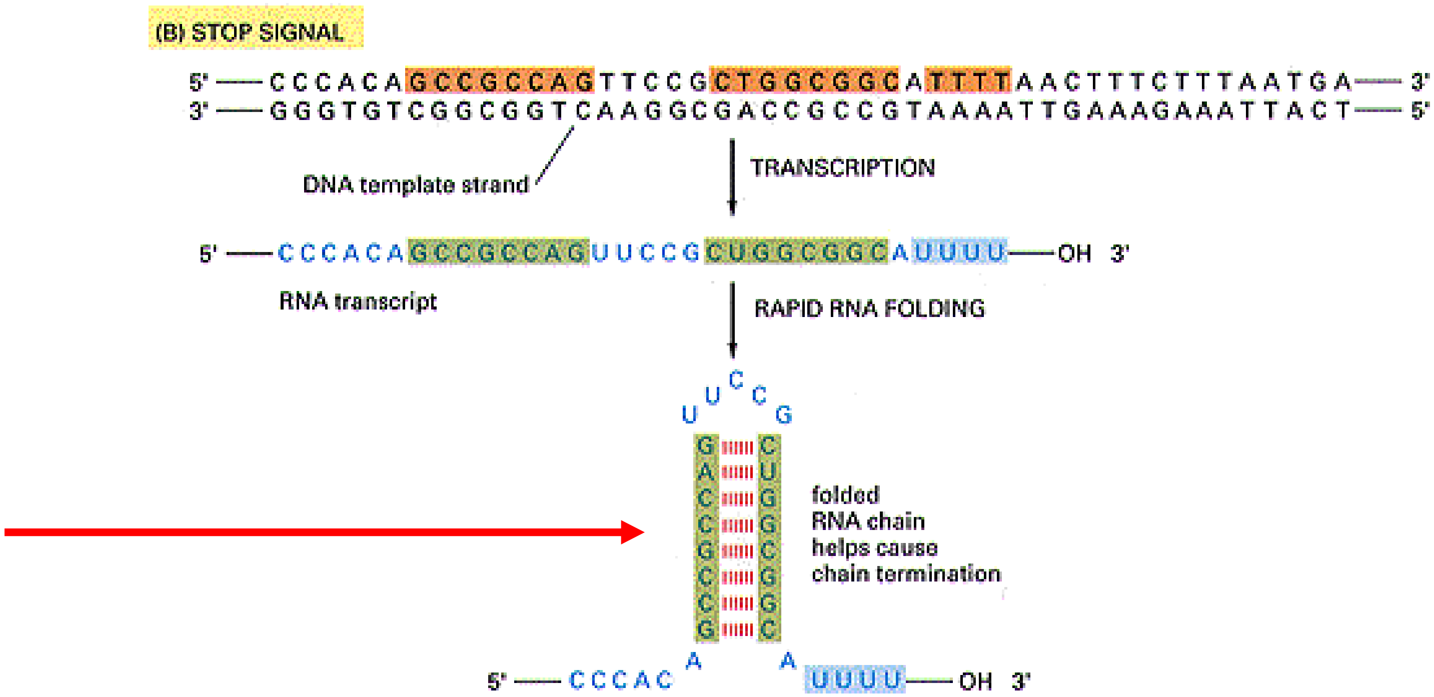
- 3 types of RNA polymerases are employed in transcription of genes:
  - RNA polymerase I transcribes rRNA
  - RNA polymerase II transcribes all genes coding for polypeptides
  - RNA polymerase III transcribes small cytoplasmatic RNA, such as tRNA.

Eukaryote Promoter

- Goldberg-Hogness or TATA located at –30
- Additional regions at –100 and at –200
- Possible distant regions acting as enhancers or silencers (even more than 50 kb).

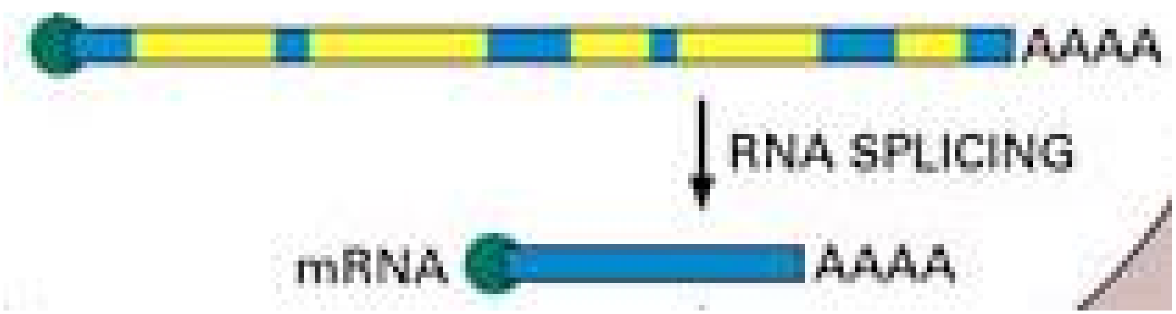
Termination Sites

- A disassociation signal at the end of the gene that stops elongating, dissociate RNA and releases RNA polymerase.
- The terminator region pauses the polymerase and causes disassociation.



Splice Sites

- Eukaryotics only
- Removing internal parts of the newly transcribed RNA.
- Takes place in the cell nucleus

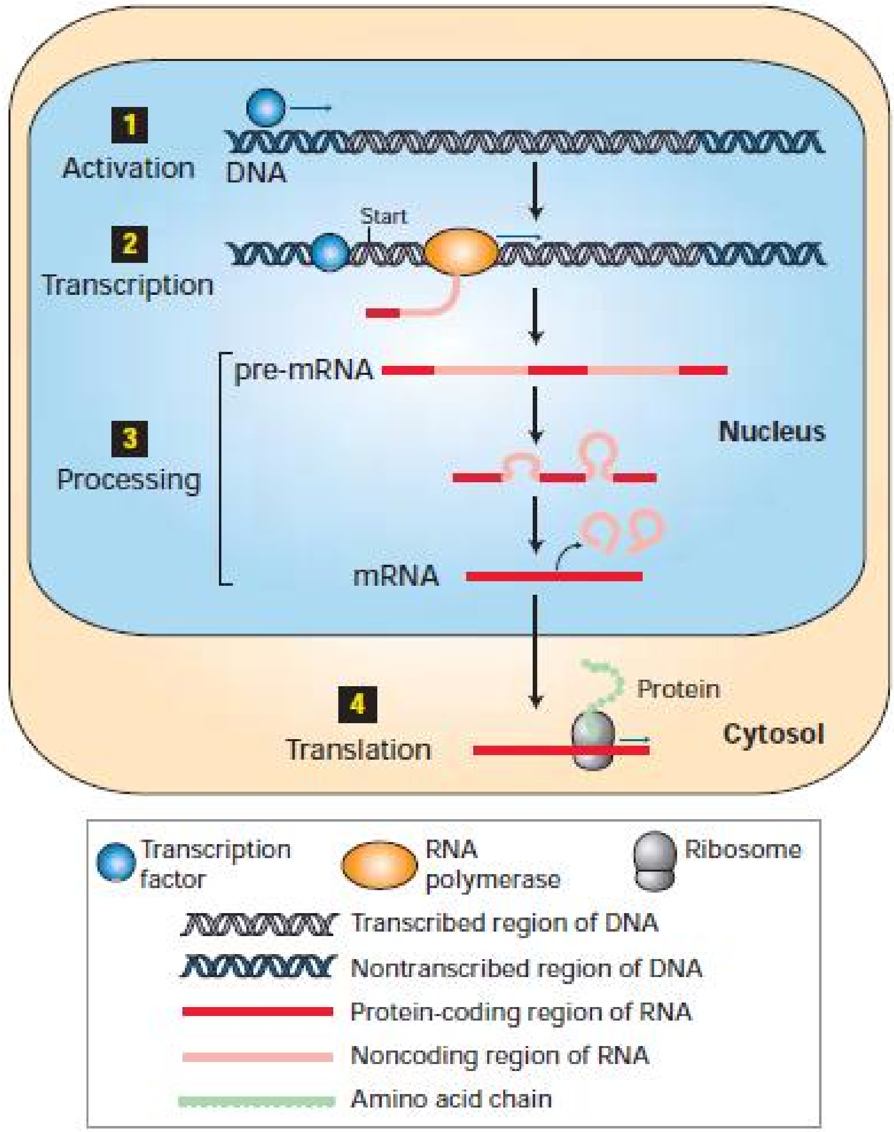


How does the gene express? (from DNA to protein)

I. Transcription

II. RNA Processing

III. Translation

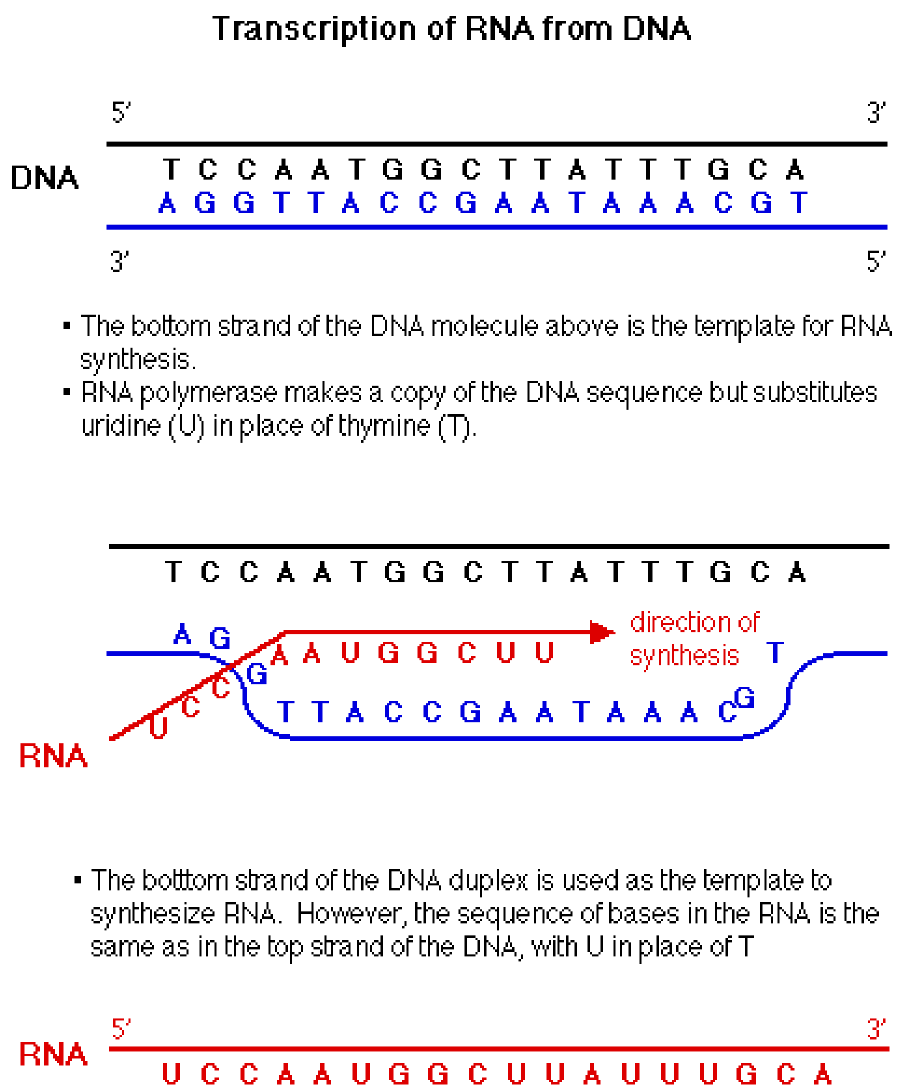


Transcription

- Generation of single stranded RNA from a DNA template (gene)
- Catalysed by RNA Polymerases
- Generates:
  - mRNA - messenger RNA
  - tRNA - transfer RNA
  - rRNA - ribosomal RNA
- Occurs in prokaryotes and eukaryotes by essentially identical processes

Transcription

DNA is always read 5' to 3', just like we read from left to right. But RNA is written from 3' to 5' to the corresponding "anti-sense" DNA strand.



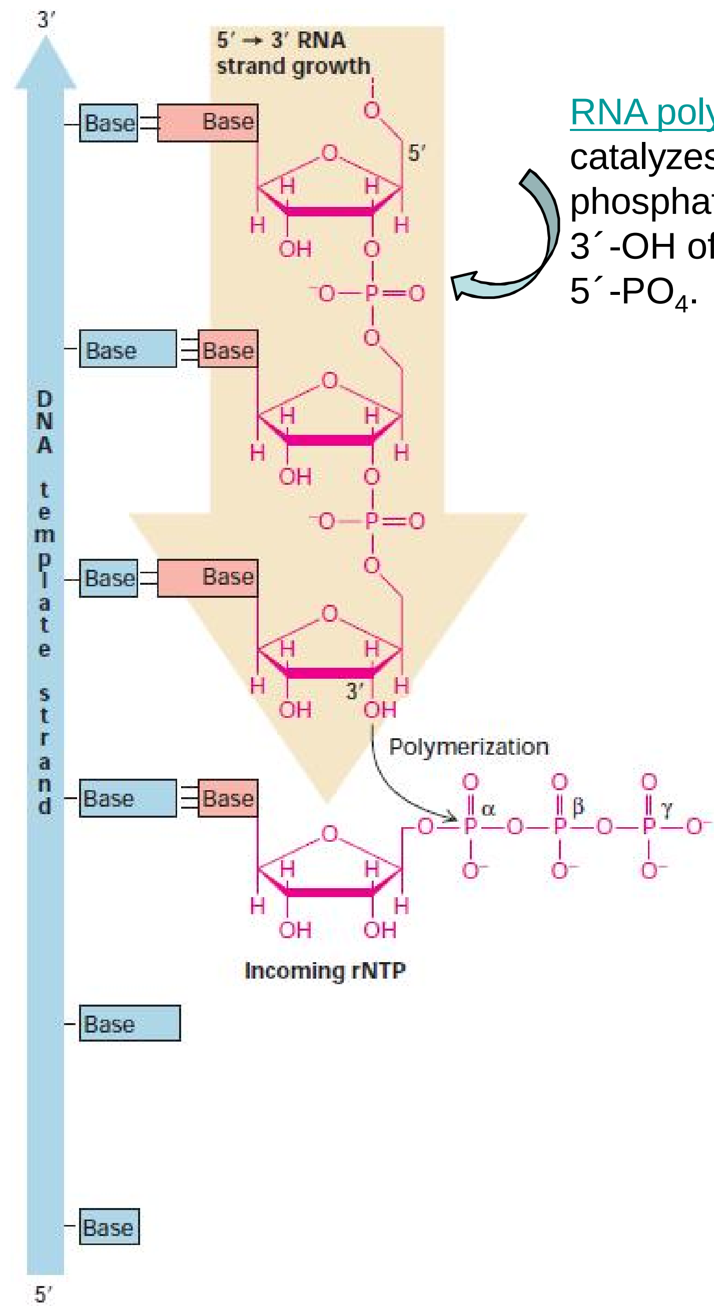
Sense strand of DNA

Antisense strand of DNA

Transcription of antisense strand

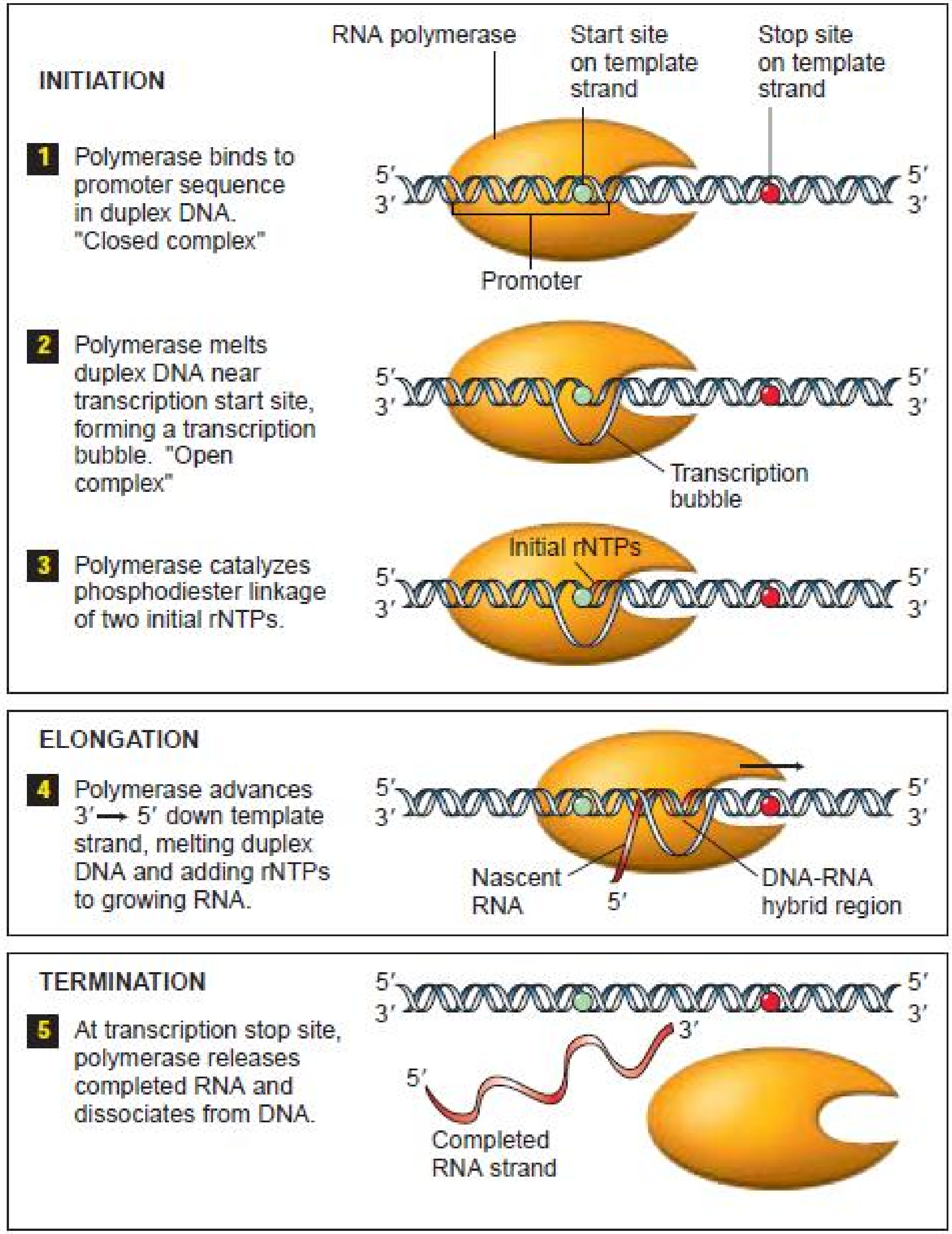
Polymerization of ribonucleotides by RNA polymerase during transcription:

The ribonucleotide to be added at the 3 end of a growing RNA strand is specified by base pairing between the next base in the template DNA strand and the complementary incoming ribonucleoside triphosphate (rNTP). A phosphodiester bond is formed when RNA polymerase catalyzes a reaction between the 3 O of the growing strand and the phosphate of a correctly base-paired rNTP. RNA strands always are synthesized in the 5n3 direction and are opposite in polarity to their template DNA strands.



RNA polymerase catalyzes sugar-phosphate bond between 3´-OH of ribose and the 5´-PO_4.

Three stages in transcription



RNA synthesis (summary)

- Catalysed by RNA Polymerase
- Cycle requires initiation, elongation and termination
- Initiation is at the Promoter sequence
- Regulation of gene expression is at the initiation stage
- Transcription factors binding to the promoter regulate the rate of initiation of RNA Polymerase