The Molecular Nature of the Genetic Material

- Mendel published his work in 1865.
- That work was lost until *ca.* 1900.
- With the "rediscovery" of Mendel's conceptual work the hunt was on for the physical nature of the gene.
- What was it and how did it function?
- These questions were largely answered from 1940's through the 1960's and lead to the biotech revolution beginning of the 1970's.

Bacterial transformation implicates DNA as the substance of genes

- 1928 – Frederick Griffith – experiments with smooth (S), virulent strain *Streptococcus pneumoniae*, and rough (R), nonvirulent strain
  - Bacterial transformation demonstrates transfer of genetic material
- 1944 – Oswald Avery, Colin MacLeod, and MacIyn McCarty – determined that DNA is the transformation material

Griffith experiment

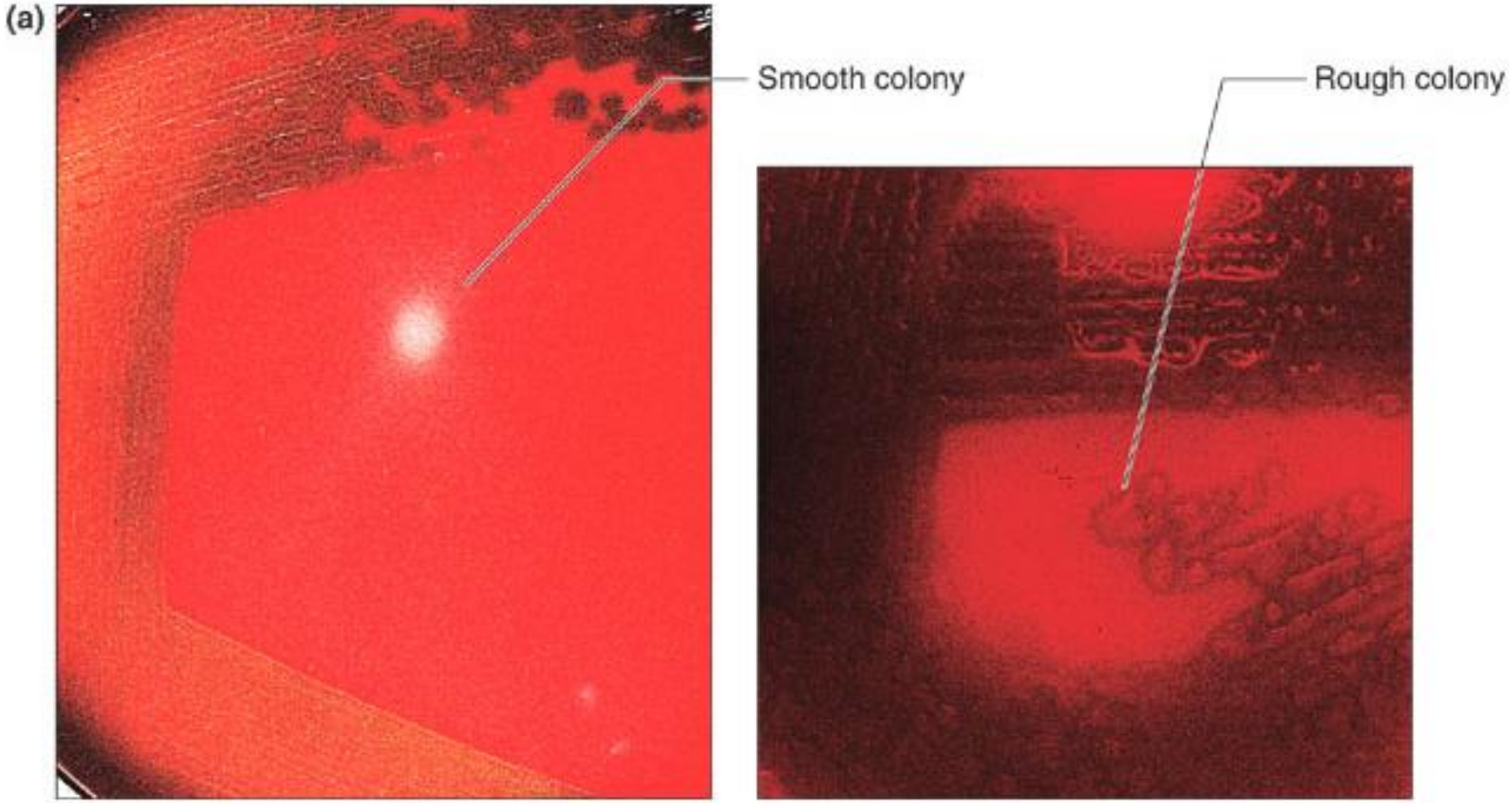


Fig. 6.3

Griffith experiment

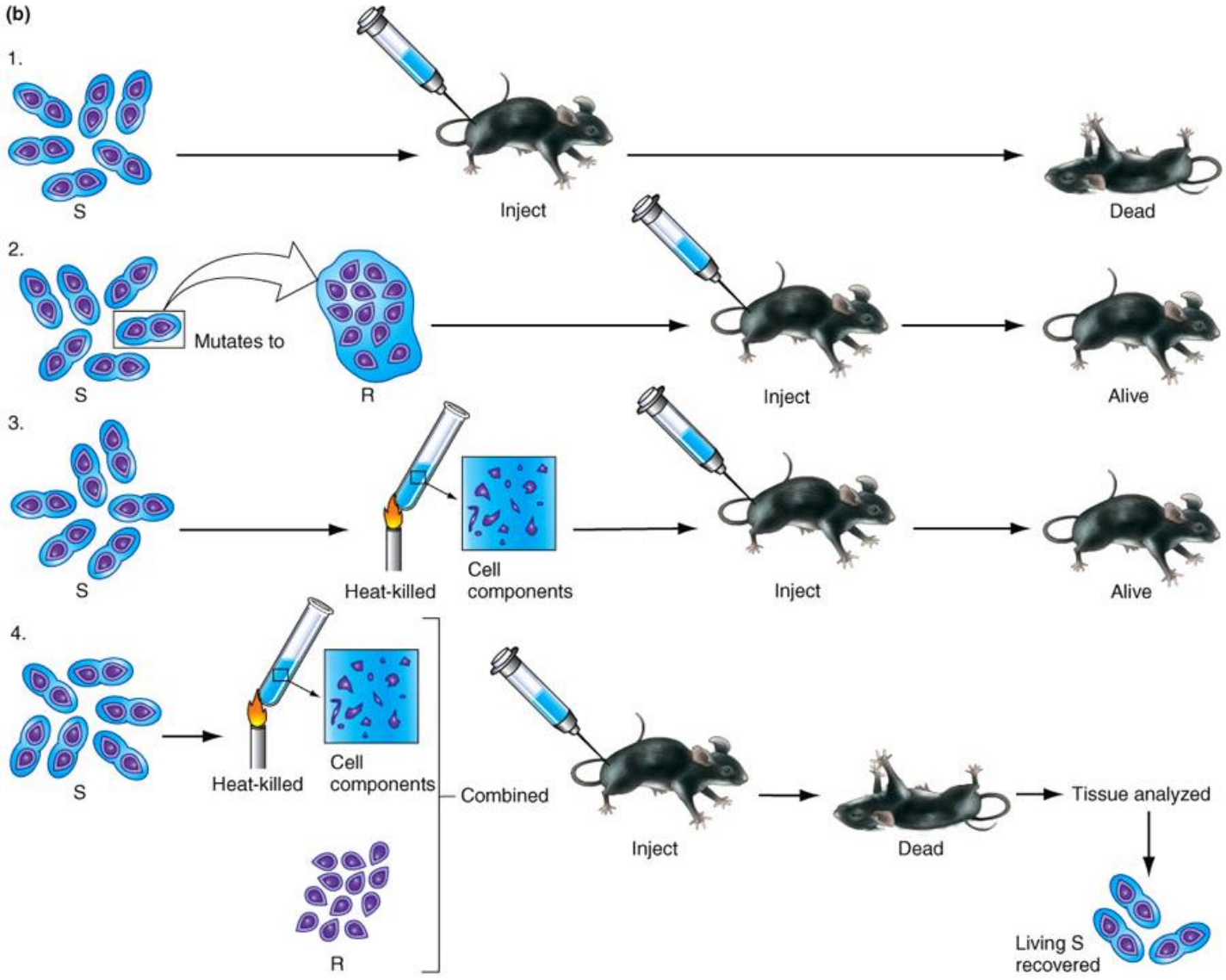
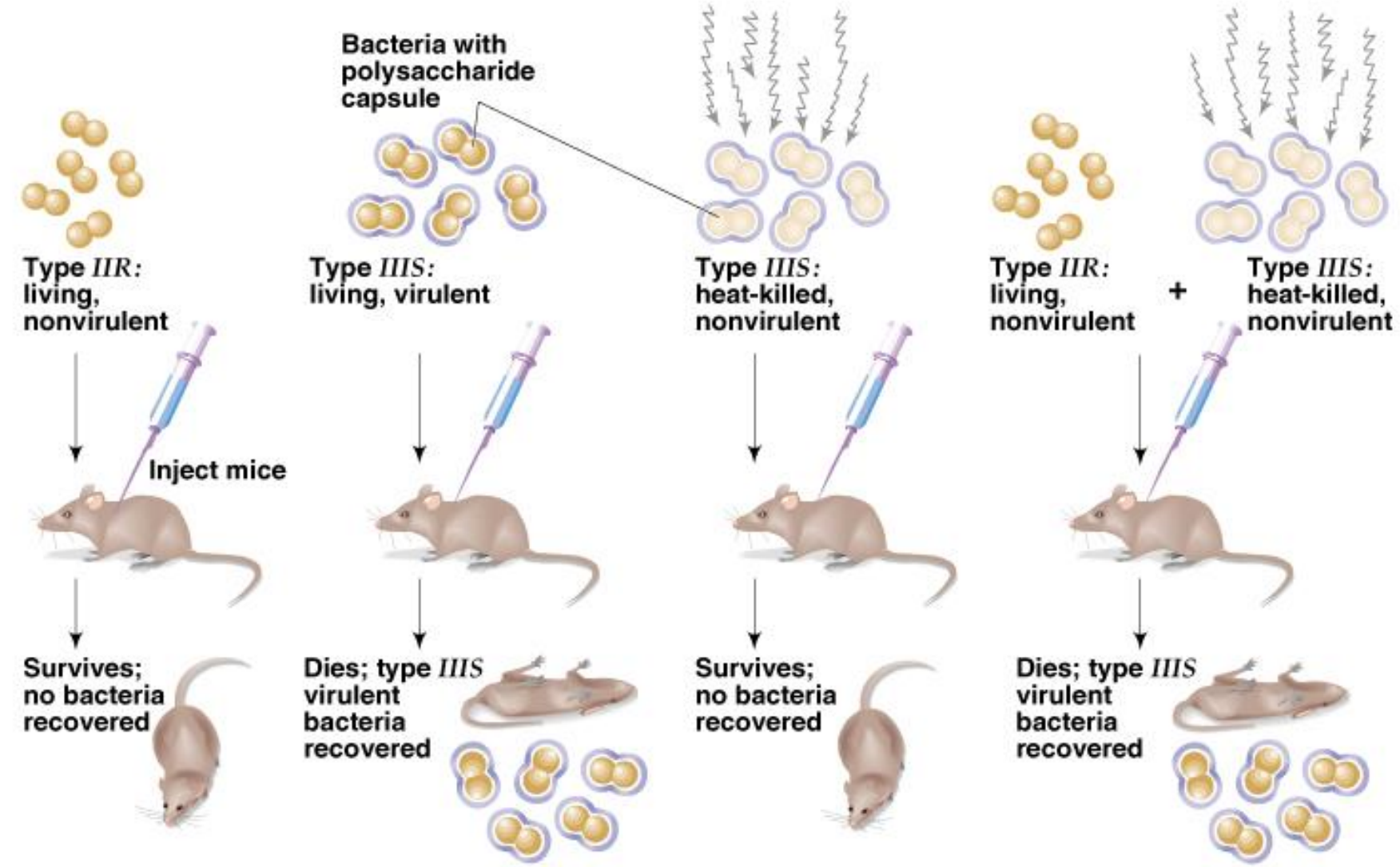


Fig. 6.3 b

Fig. 2.2 Griffith's transformation experiment



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Avery, MacLeod, McCarty Experiment

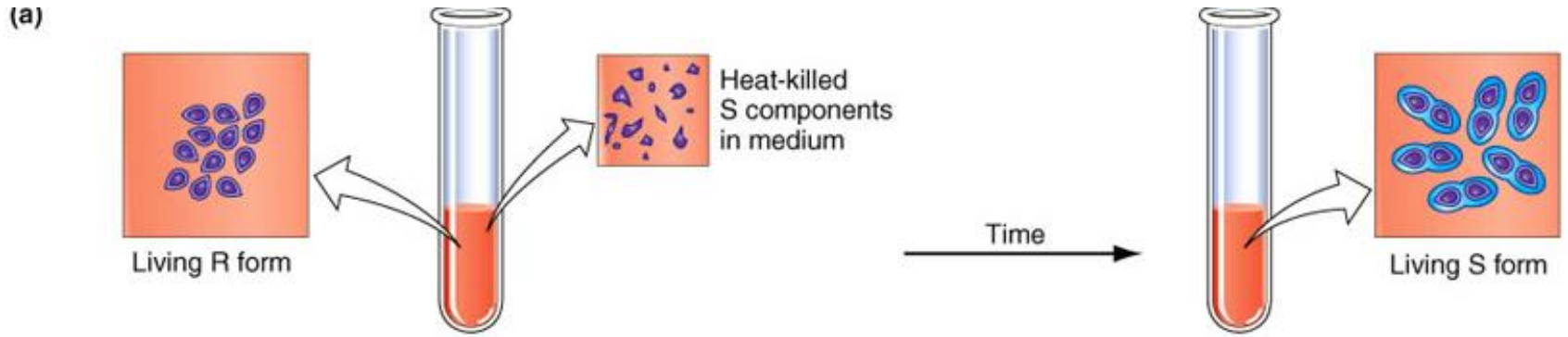
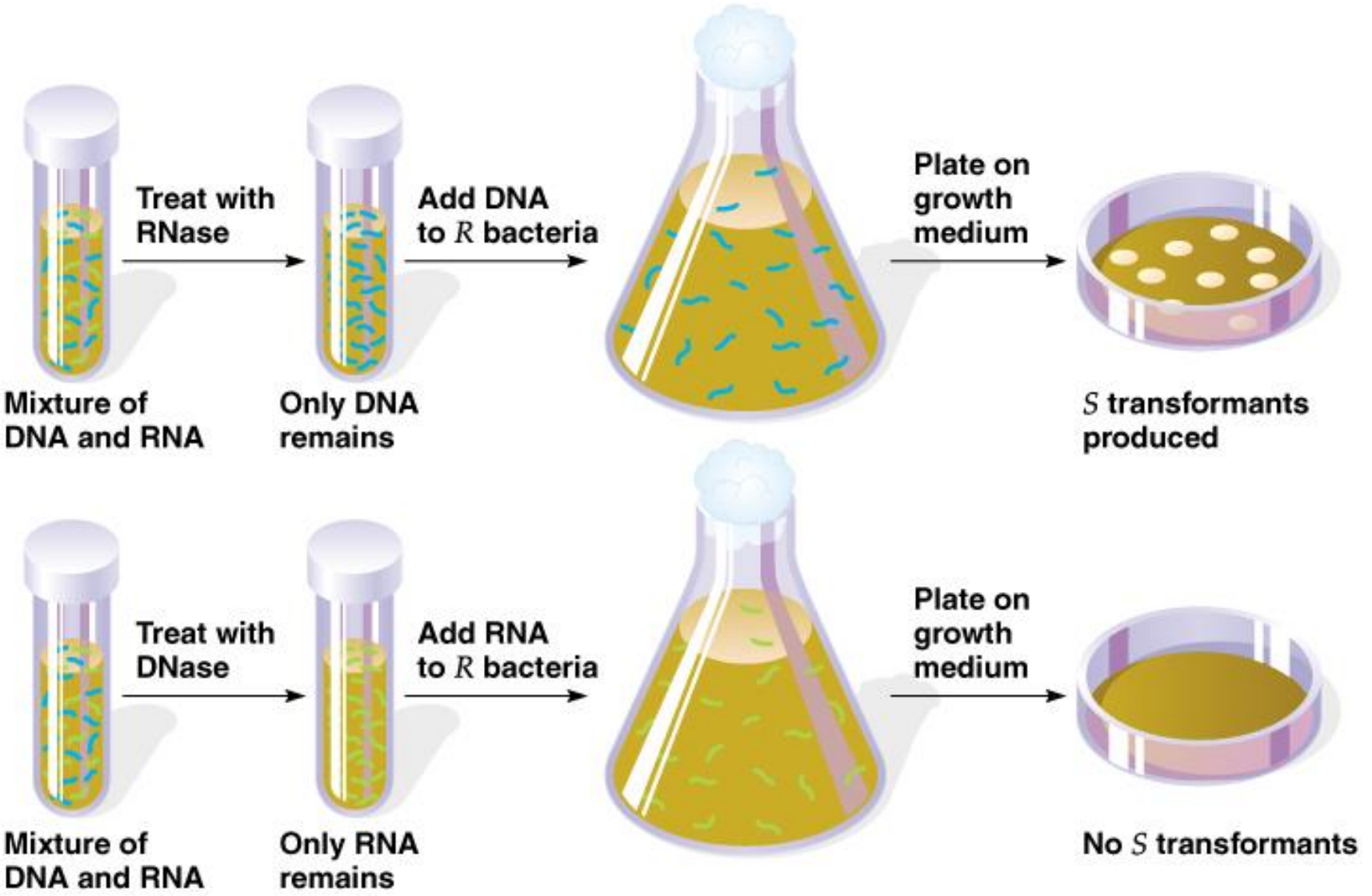


Fig. 6.4 a

Fig. 2.3 Experiment that showed that DNA, not RNA, was the transforming principle



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Avery, MacLeod, McCarty experiment

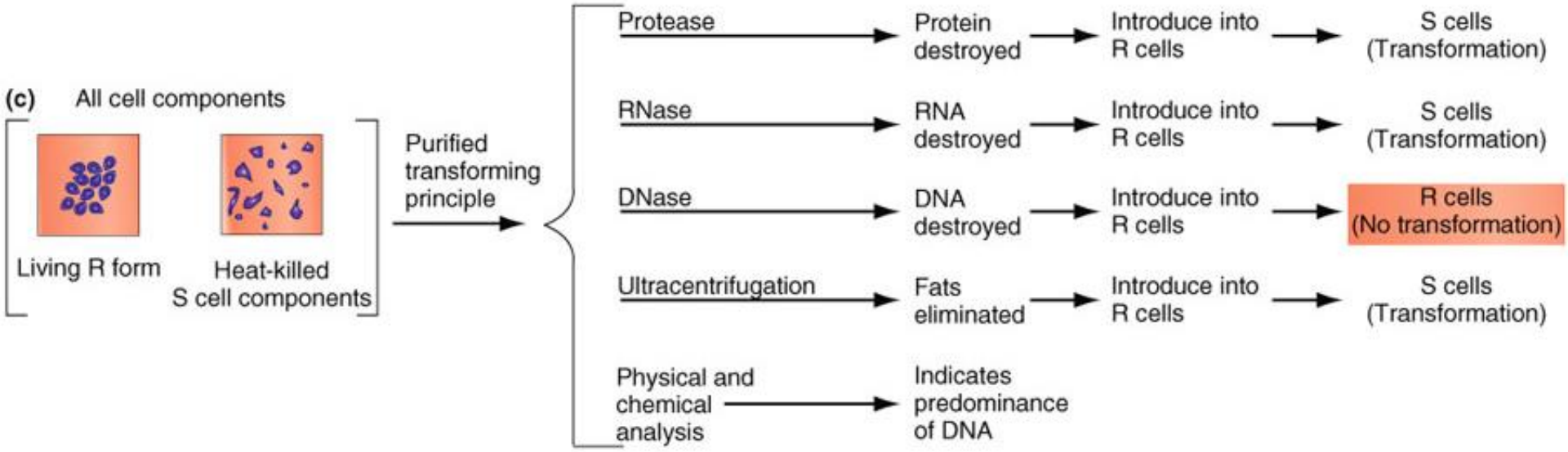

Fig. 6.4 c

Hershey and Chase experiments

- 1952 – Alfred Hershey and Martha Chase provide convincing evidence that DNA is genetic material
- Waring blender experiment using T2 bacteriophage and bacteria
- Radioactive labels ^{32}P for DNA and ^{35}S for protein

Fig. 2.4 Bacteriophage T2

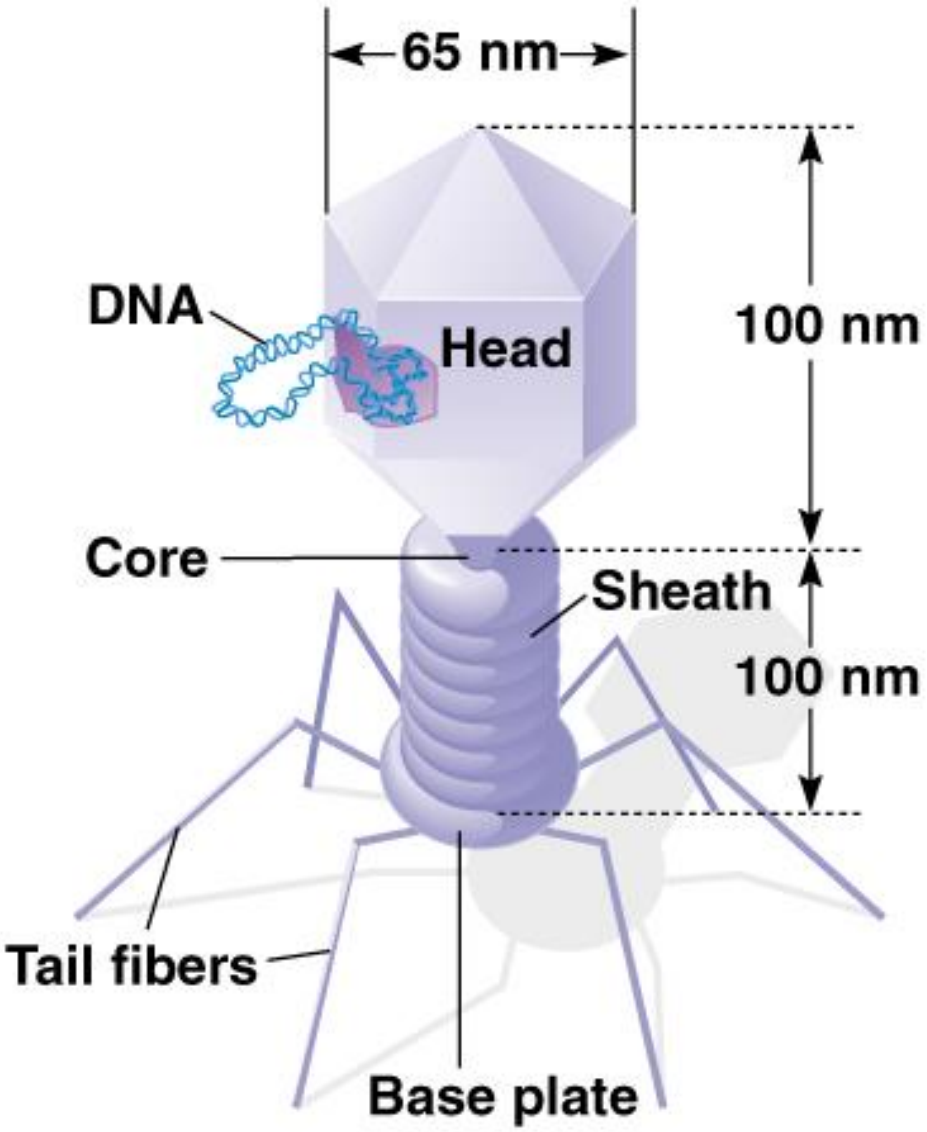

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Fig. 2.5 Lytic life cycle of a virulent phage, such as T2

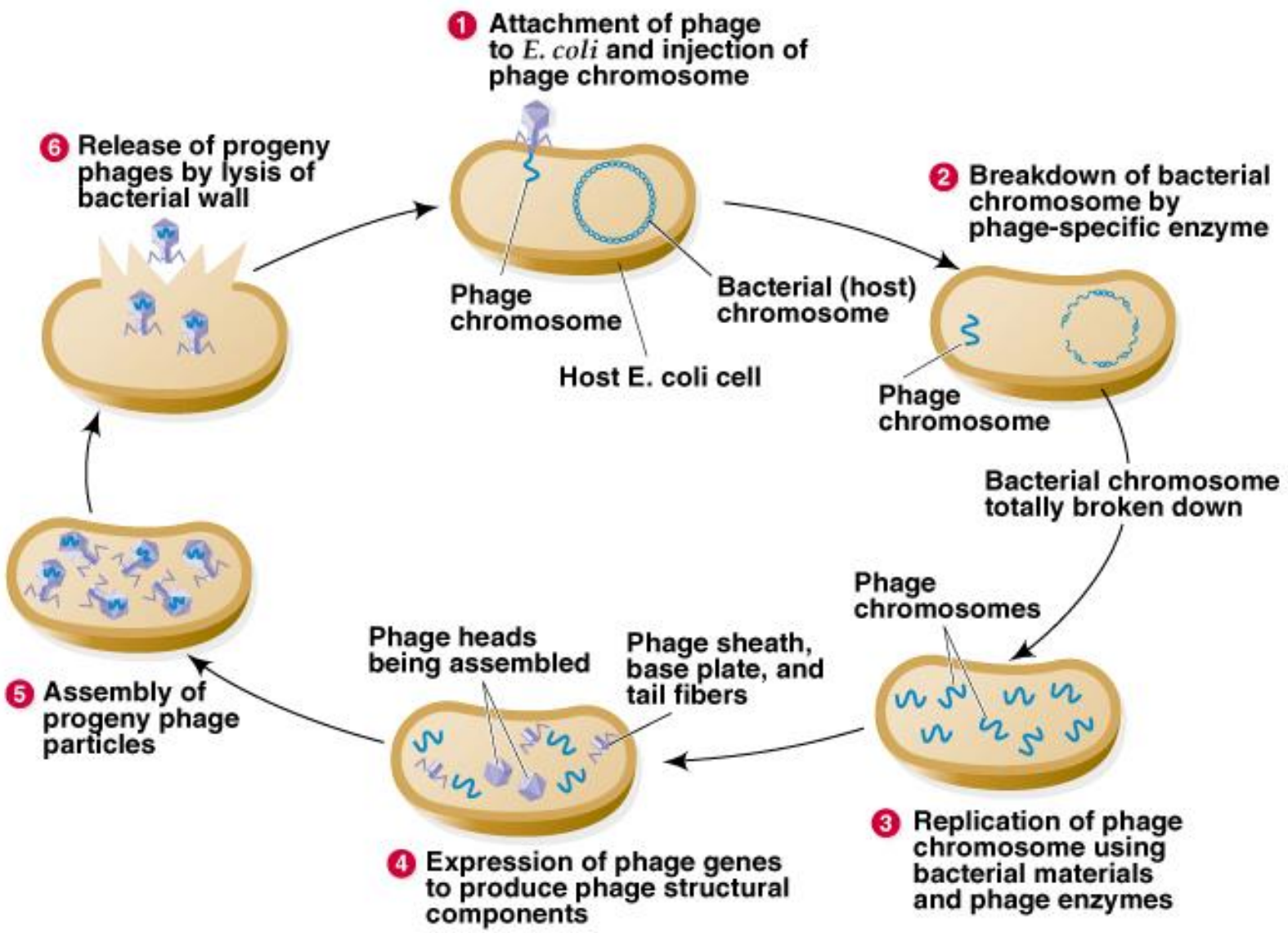

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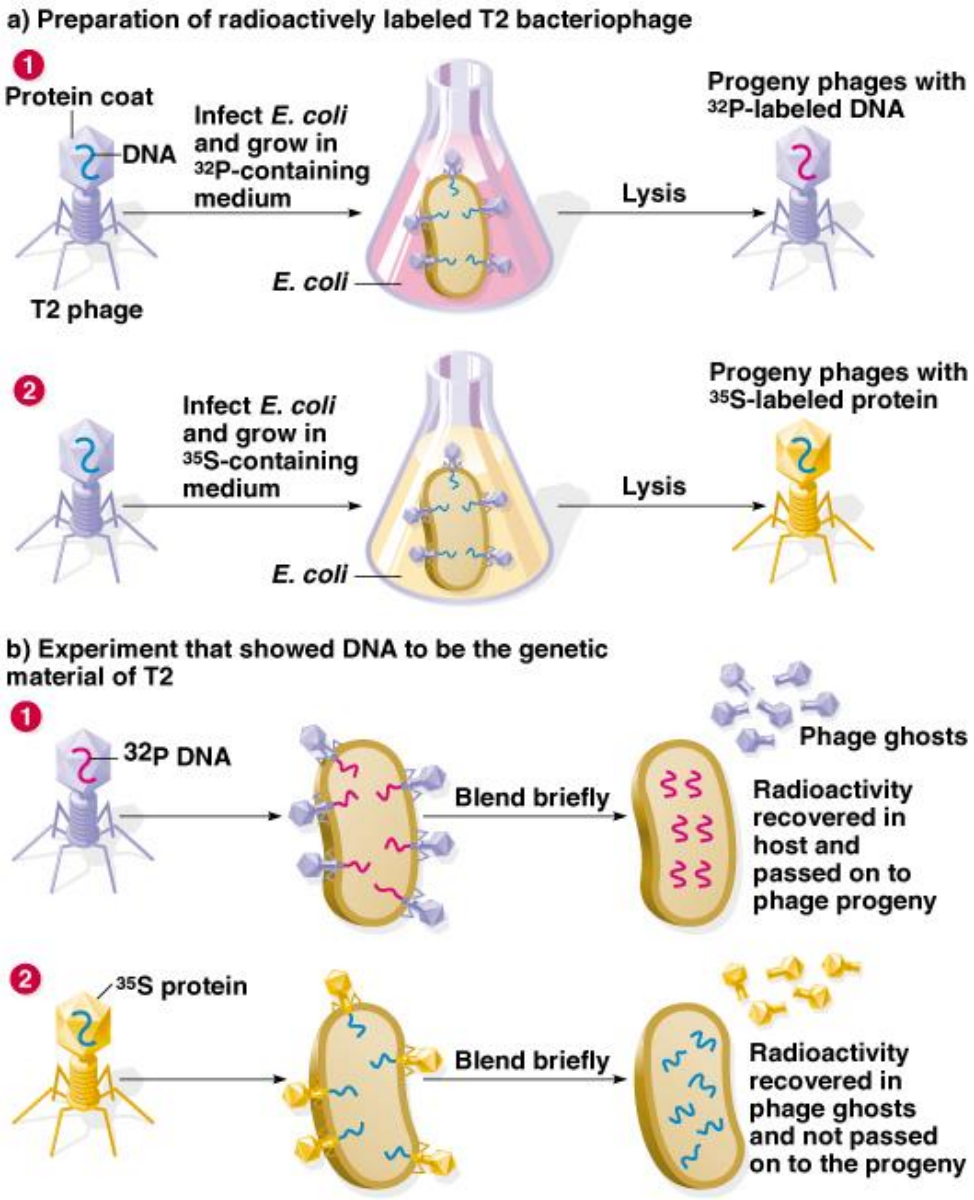
Fig. 2.6 Hershey-Chase experiment demonstrating DNA is genetic material



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Chargaff's ratios

TABLE 6.1 **Chargaff's Data on Nucleotide Base Composition in the DNA of Various Organisms**

	Percentage of Base in DNA				Ratios	
Organism	*A*	*T*	*G*	*C*	*A:T*	*G:C*
Staphylococcus afermentams	12.8	12.9	36.9	37.5	0.99	0.99
Escherichia coli	26.0	23.9	24.9	25.2	1.09	0.99
Yeast	31.3	32.9	18.7	17.1	0.95	1.09
*Caenorhabditis elegans**	31.2	29.1	19.3	20.5	1.07	0.96
*Arabadopsis thaliana**	29.1	29.7	20.5	20.7	0.98	0.99
Drosophila melanogaster	27.3	27.6	22.5	22.5	0.99	1.00
Honeybee	34.4	33.0	16.2	16.4	1.04	0.99
Mus musculus (mouse)	29.2	29.4	21.7	19.7	0.99	1.10
Human (liver)	30.7	31.2	19.3	18.8	0.98	1.03

*Data for *C. elegans* and *A. thaliana* is based on that for close relative organisms.
Note that even though the level of any one nucleotide is different in different organisms, the amount of A always approximately equals the amount of T, and the level of G is always similar to that of C. Moreover, as you can calculate for yourself, the total amount of purines (A plus G) nearly always equals the total amount of pyrimidines (C plus T).

DNA's chemical constituents

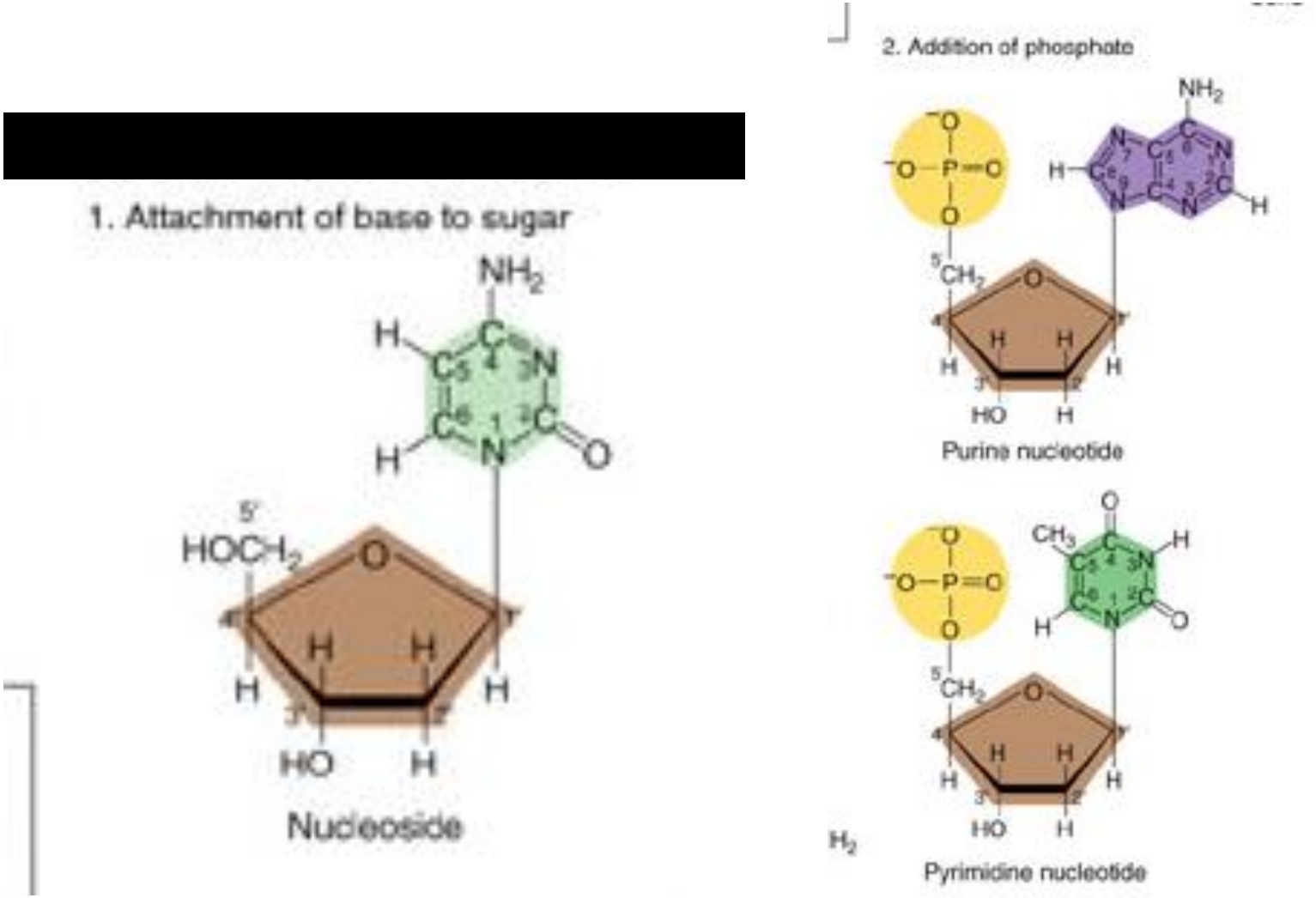
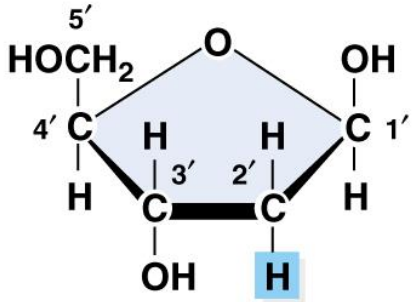
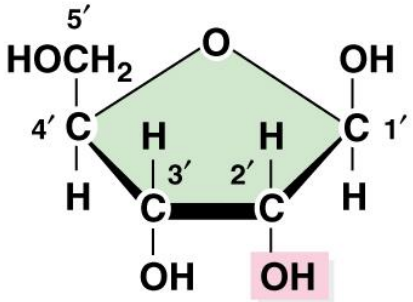


Fig. 6.7

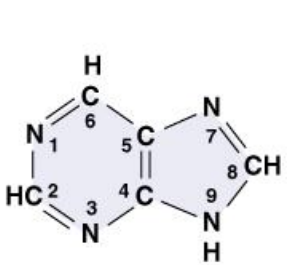
Figs. 2.9, 2.10 Structures of deoxyribose and ribose, and of the nitrogenous bases in DNA and RNA



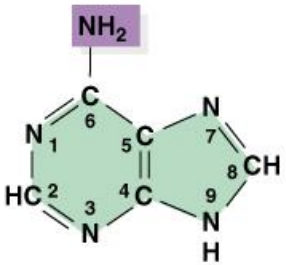
Deoxyribose



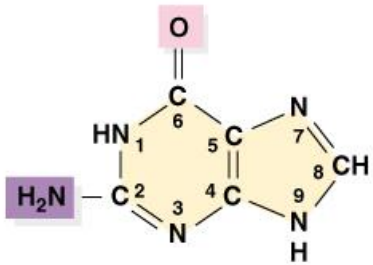
Ribose



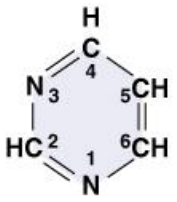
Purine (parent compound)



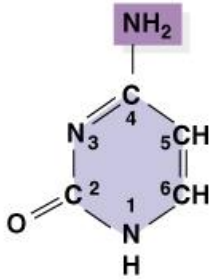
Adenine (A)



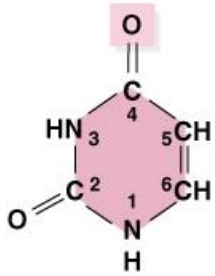
Guanine (G)



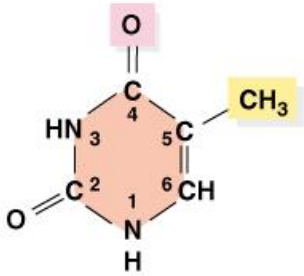
Pyrimidine (parent compound)



Cytosine (C)



Uracil (U) (found in RNA)



Thymine (T) (found in DNA)

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The Watson-Crick Model: DNA is a double helix

- 1951 – James Watson learns about x-ray diffraction pattern projected by DNA
- Knowledge of the chemical structure of nucleotides (deoxyribose sugar, phosphate, and nitrogenous base)
- Erwin Chargaff's experiments demonstrate that ratio of A and T are 1:1, and G and C are 1:1
- 1953 – James Watson and Francis crick propose their double helix model of DNA structure

X-ray diffraction patterns produced by DNA fibers – Rosalind Franklin and Maurice Wilkins

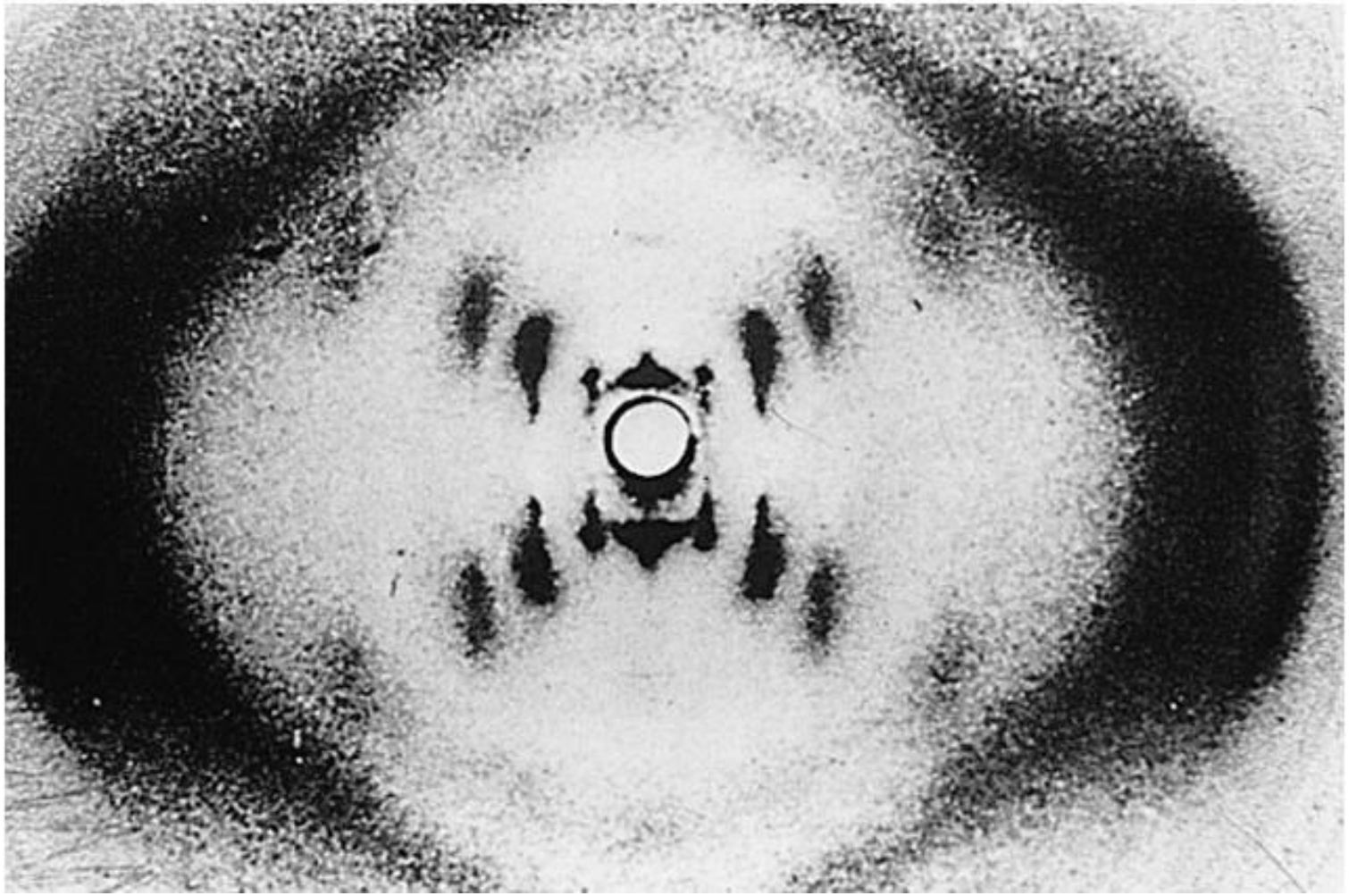
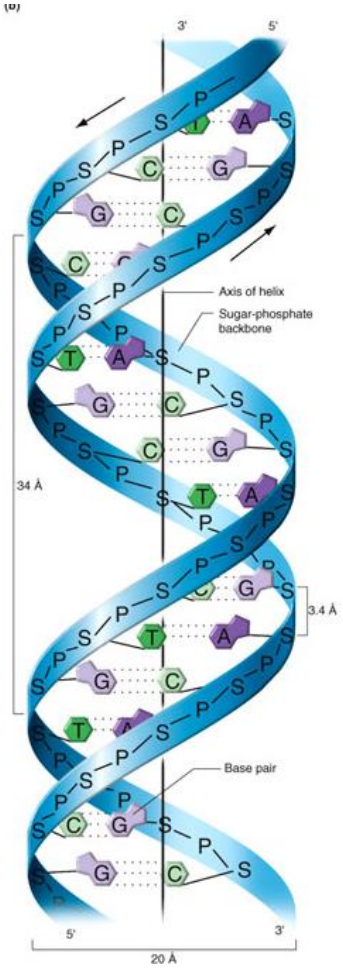
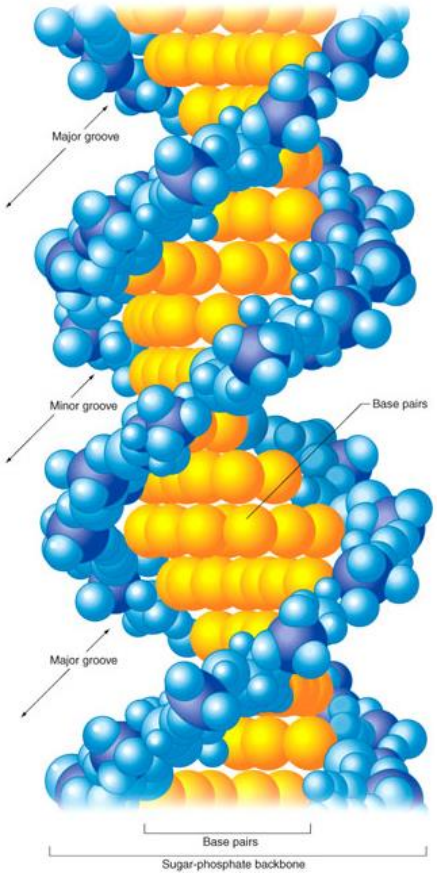


Fig. 6.6

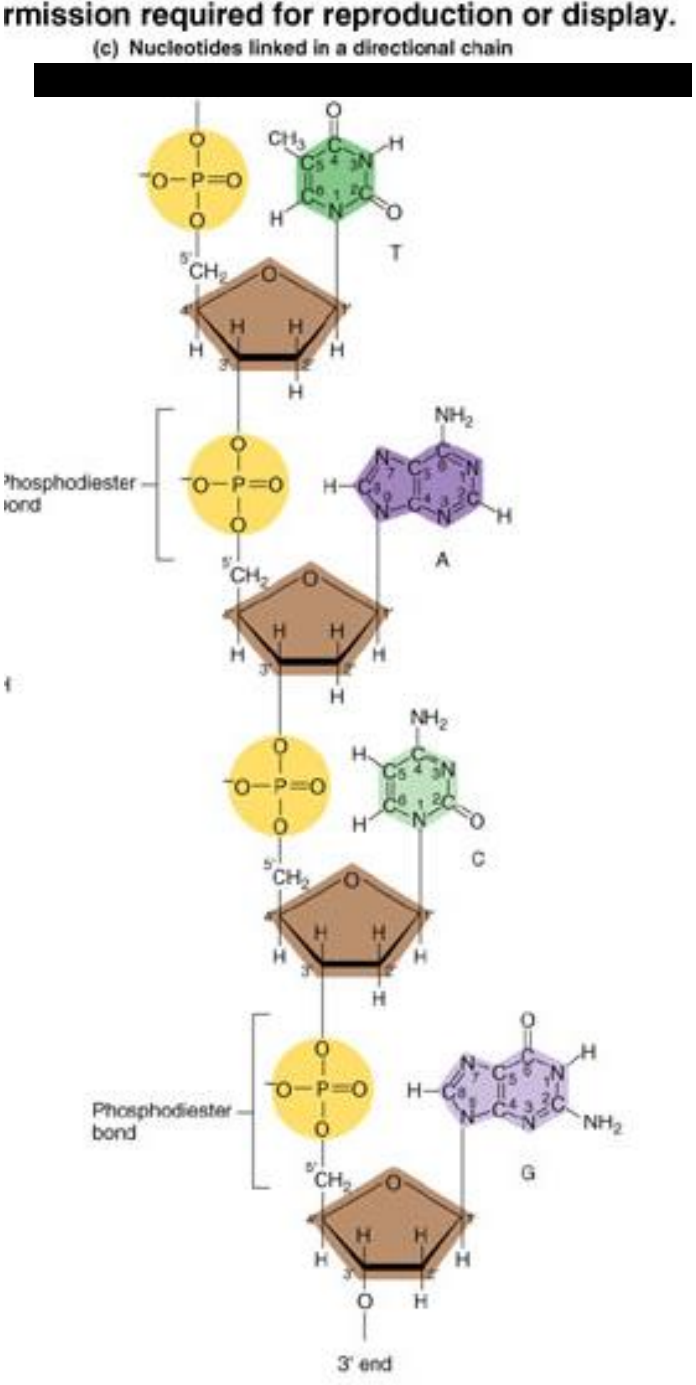




- DNA is double helix
- Strands are antiparallele with a sugar-phosphate backbone on outside and pairs of bases in the middle
- Two strands wrap around each other every 30 Angstroms, once every 10 base pairs
- Two chains are held together by hydrogen bonds between A-T and G-C base pairs

Fig. 6.9

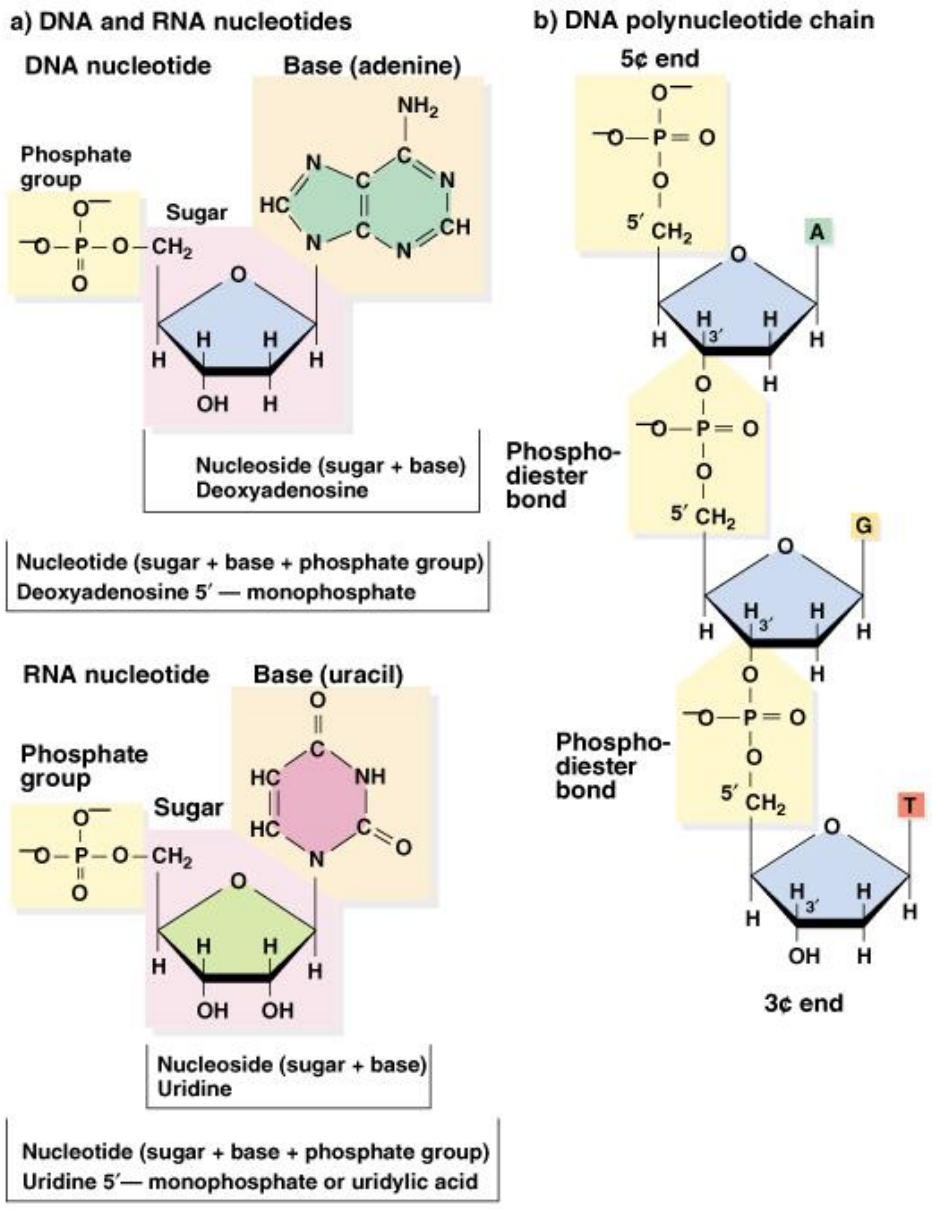
rmission required for reproduction or display.



DNA's chemical constituents

Fig. 6.7c

Fig. 2.11 Chemical structures of DNA and RNA



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- Stucturally, purines (A and G pair best with pyrimadines (T and C)
- Thus, A pairs with T and G pairs with C, also explaining Chargaff's ratios

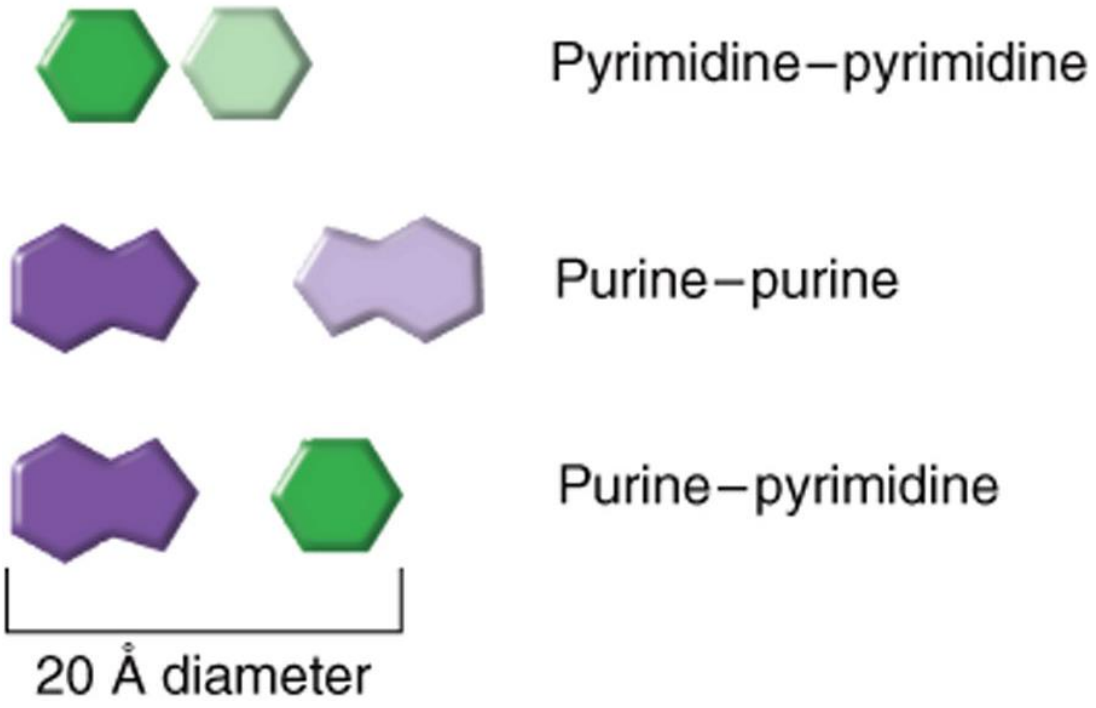

Fig. 6.9 d

Complementary base pairing by formation of hydrogen bonds explain Chargaff's ratios

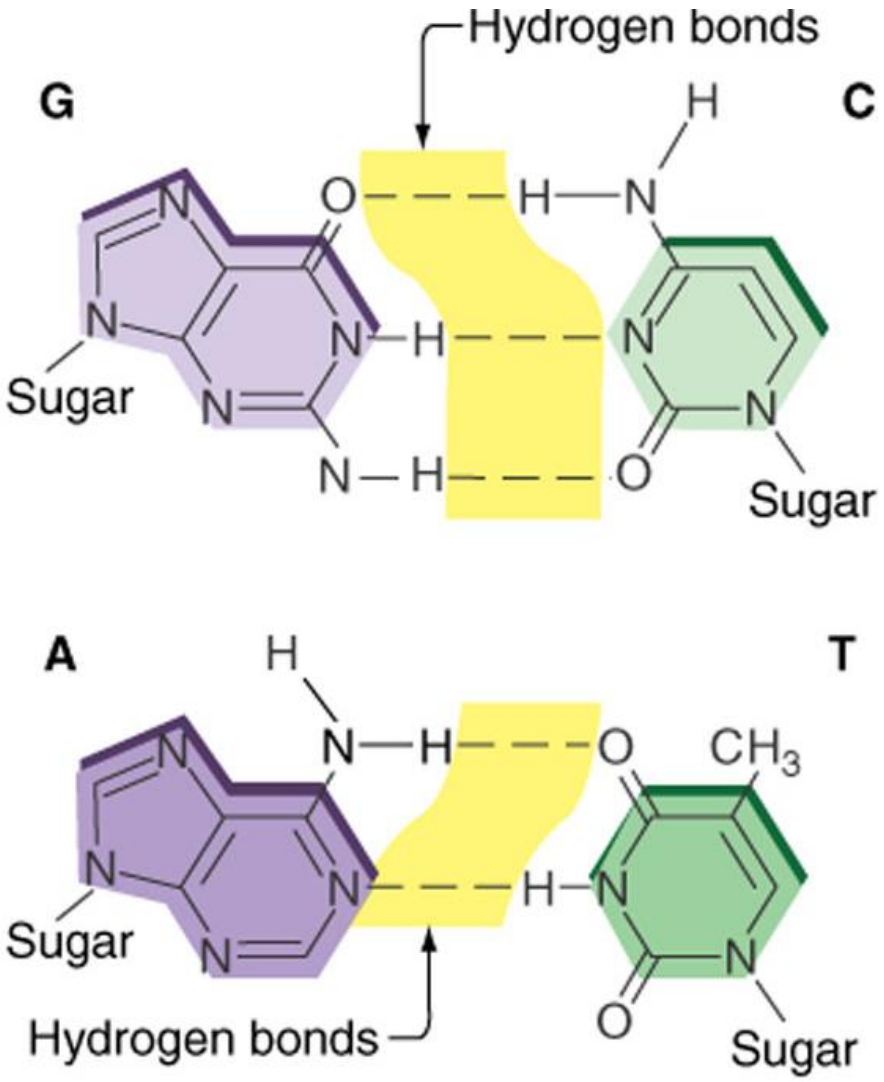

Fig. 6.8

Fig. 2.15 Structures of the complementary base pairs found in DNA

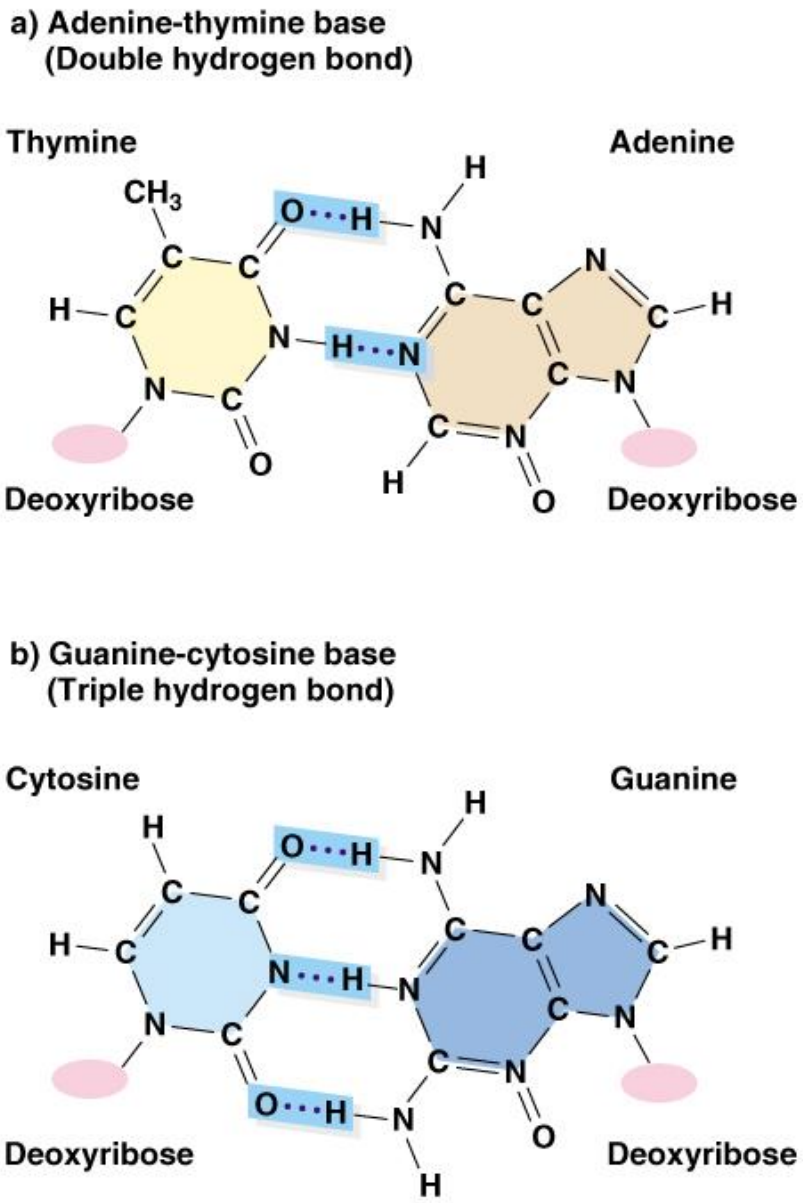

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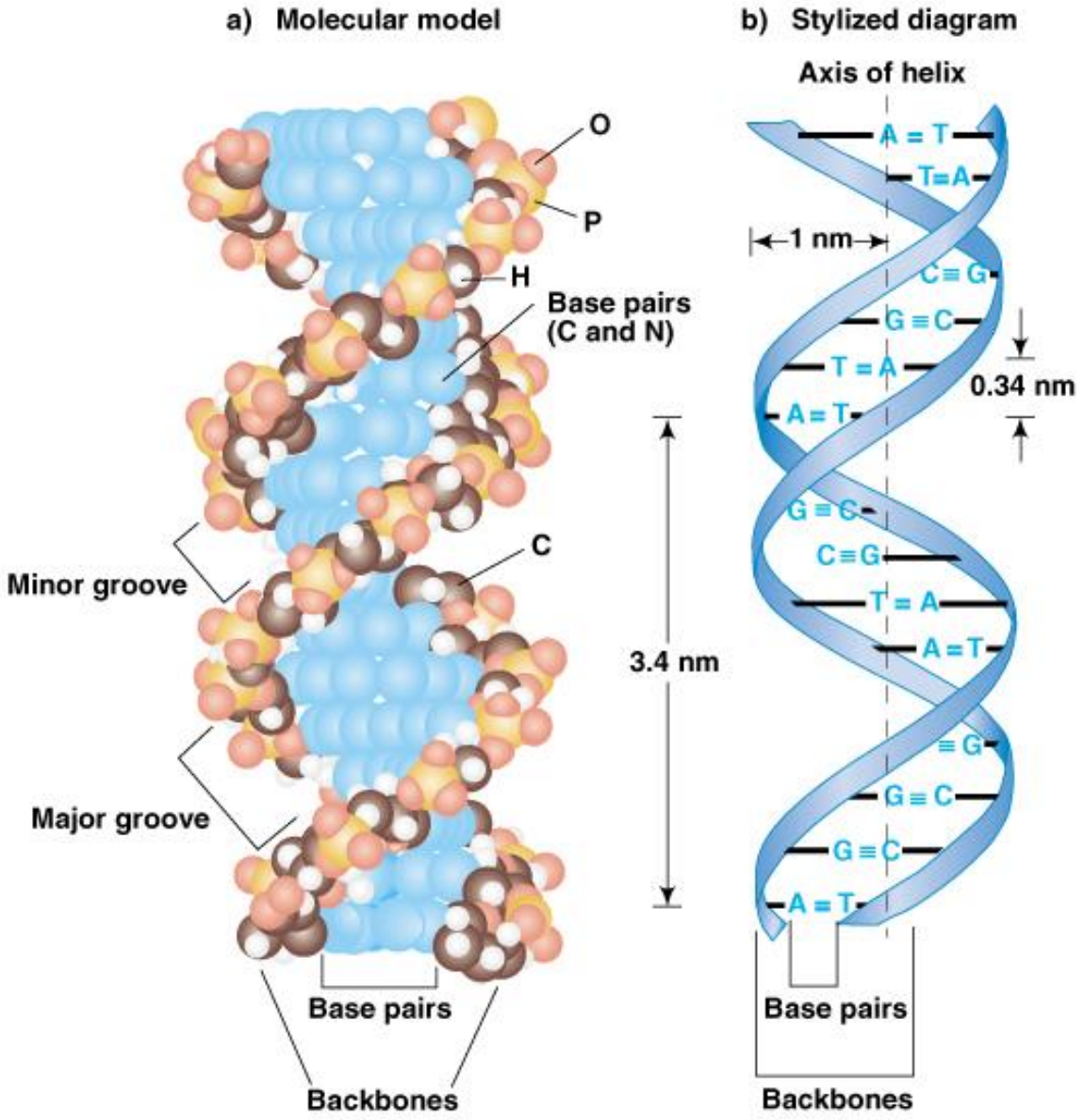
Fig. 2.14 Molecular structure of DNA



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Double helix may assume alternative forms

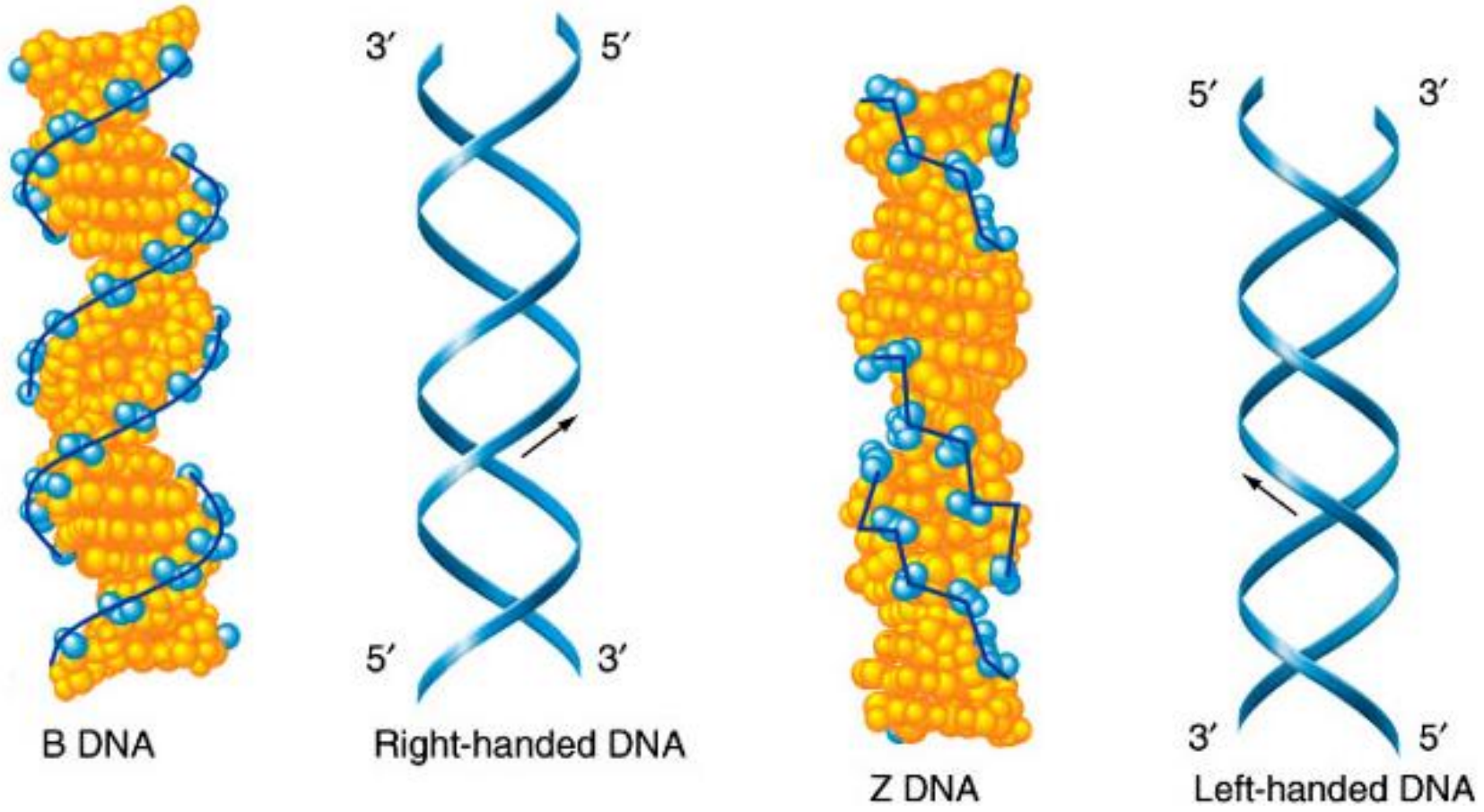

Fig. 6.10

Meselson-Stahl experiments confirm semiconservative replication

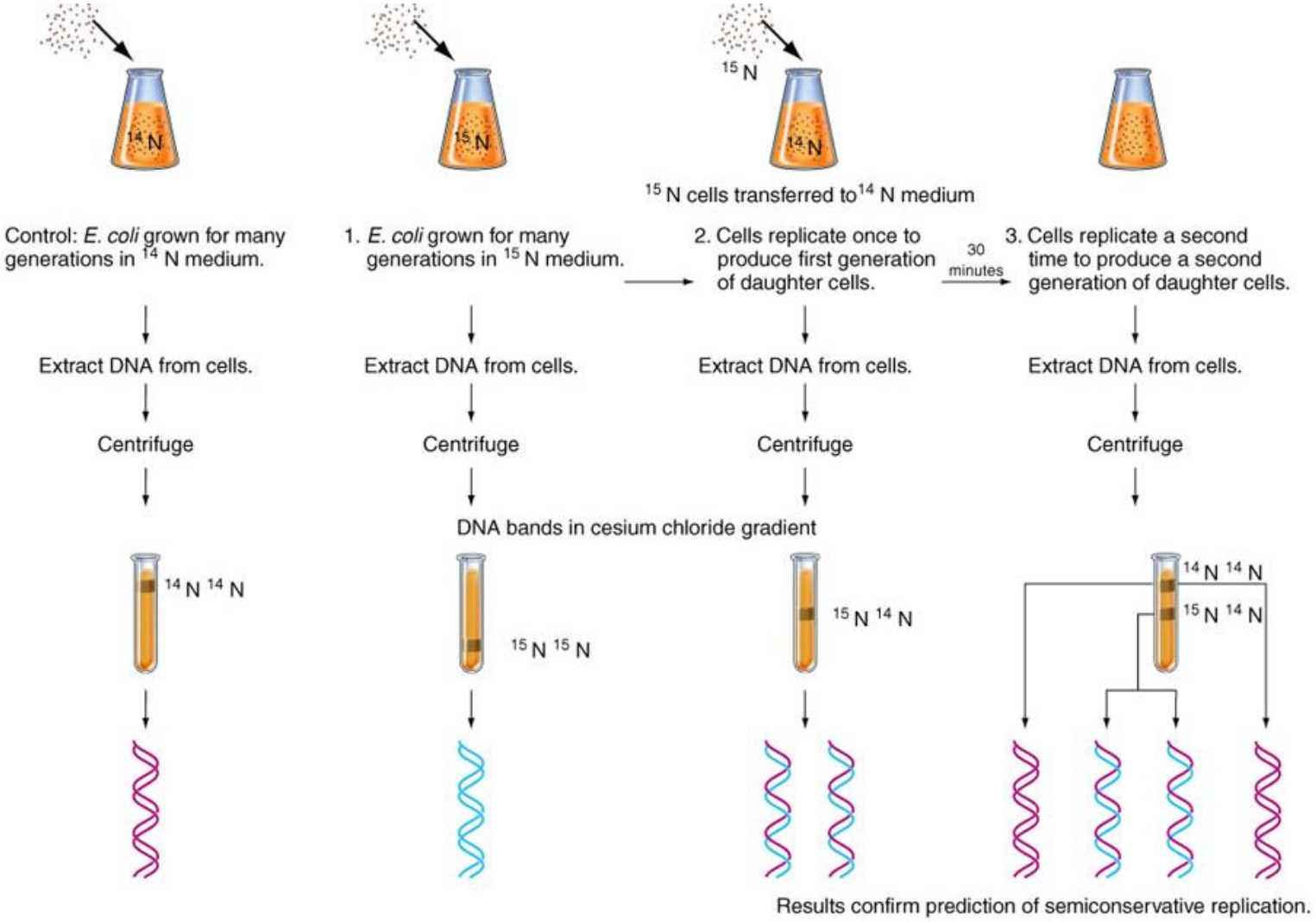

Fig. 6.16

DNA replication: Copying genetic information for transmission to the next generation

- Complementary base pairing produces semiconservative replication
  - Double helix unwinds
  - Each strand acts as template
  - Complementary base pairing ensures that T signals addition of A on new strand, and G signals addition of C
  - Two daughter helices produced after replication

Fig. 3.1 Three models for the replication of DNA

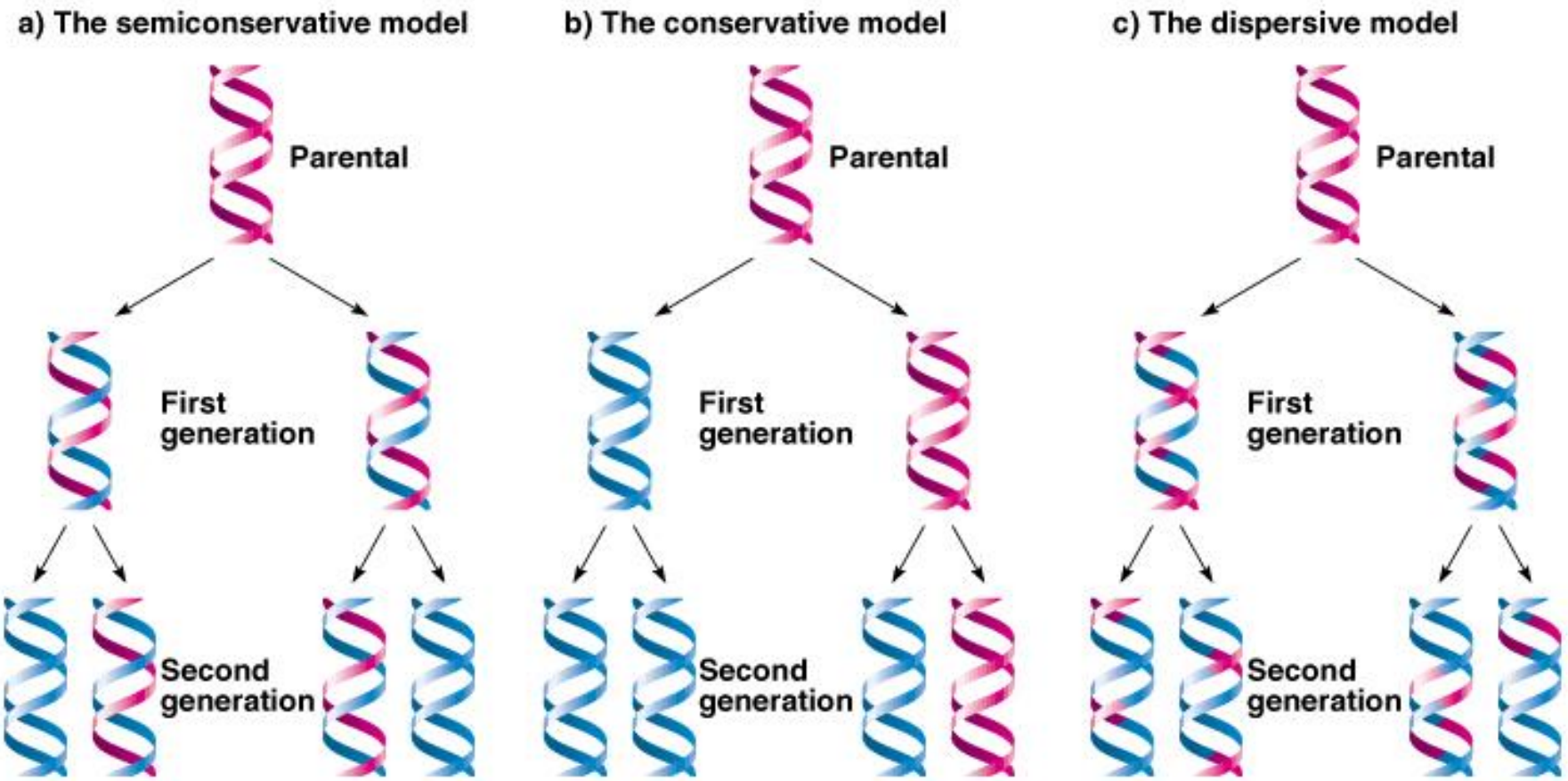

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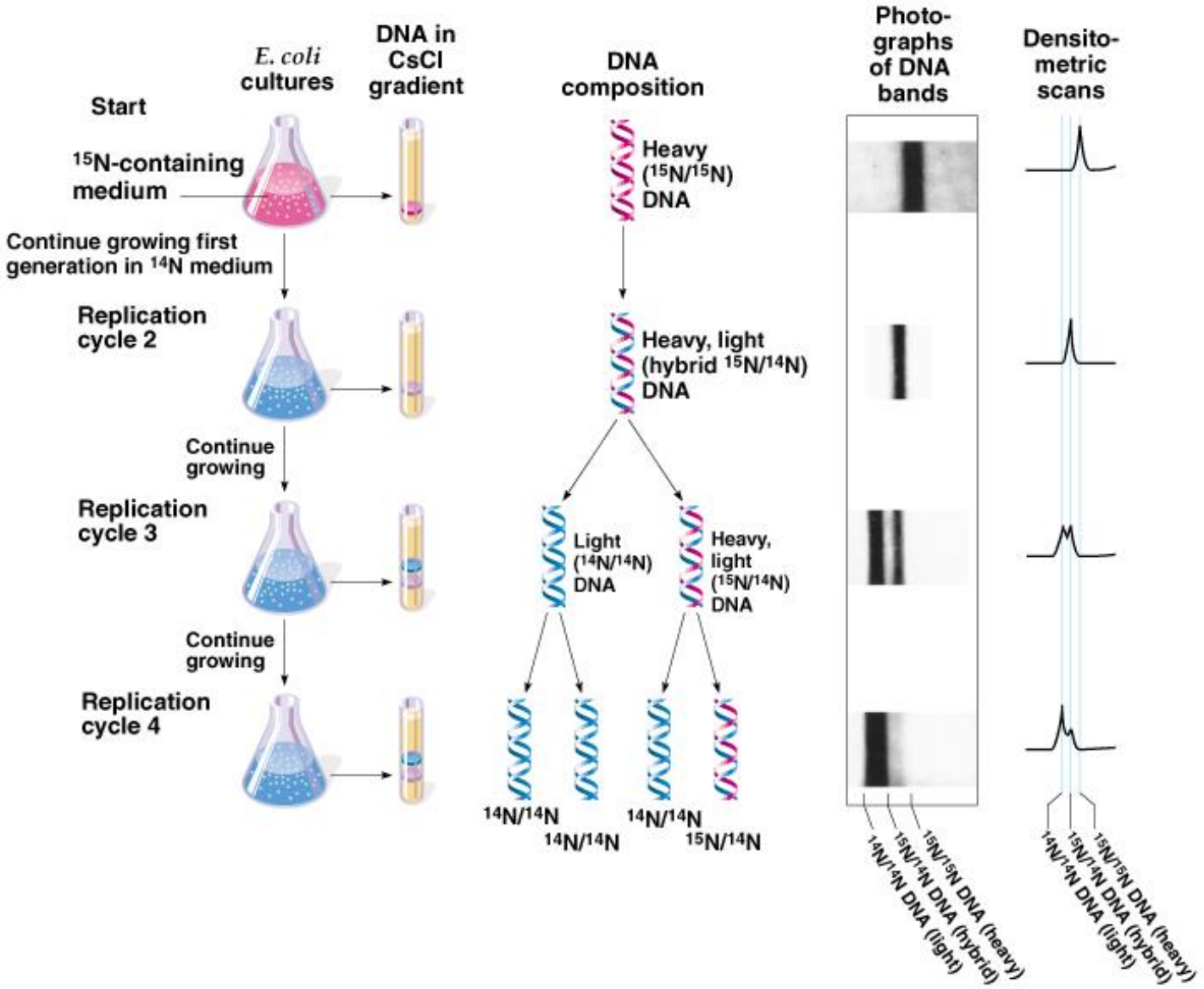
Fig. 3.2 The Meselson-Stahl experiment, which showed that DNA replicates semiconservatively



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Box Fig. 3.1 Equilibrium centrifugation of DNA of different densities in a cesium chloride density gradient

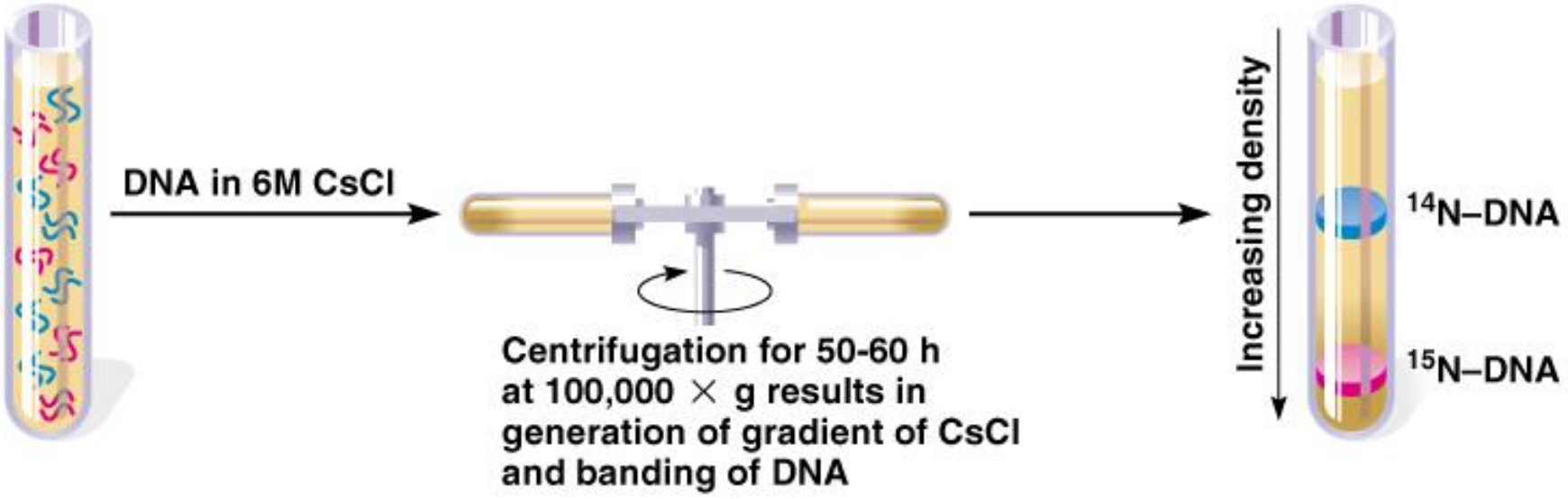

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Fig. 3.4a DNA chain elongation catalyzed by DNA polymerase

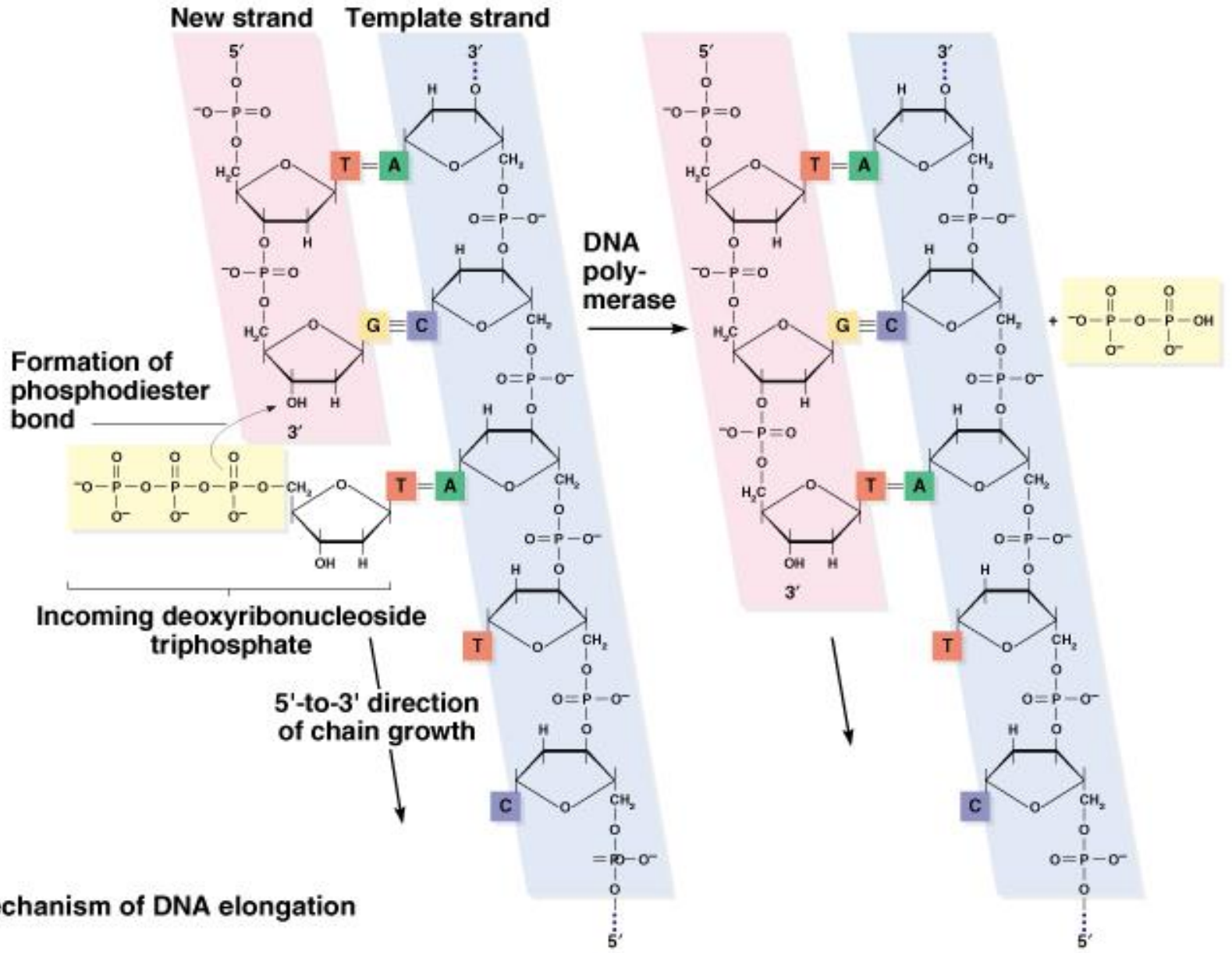

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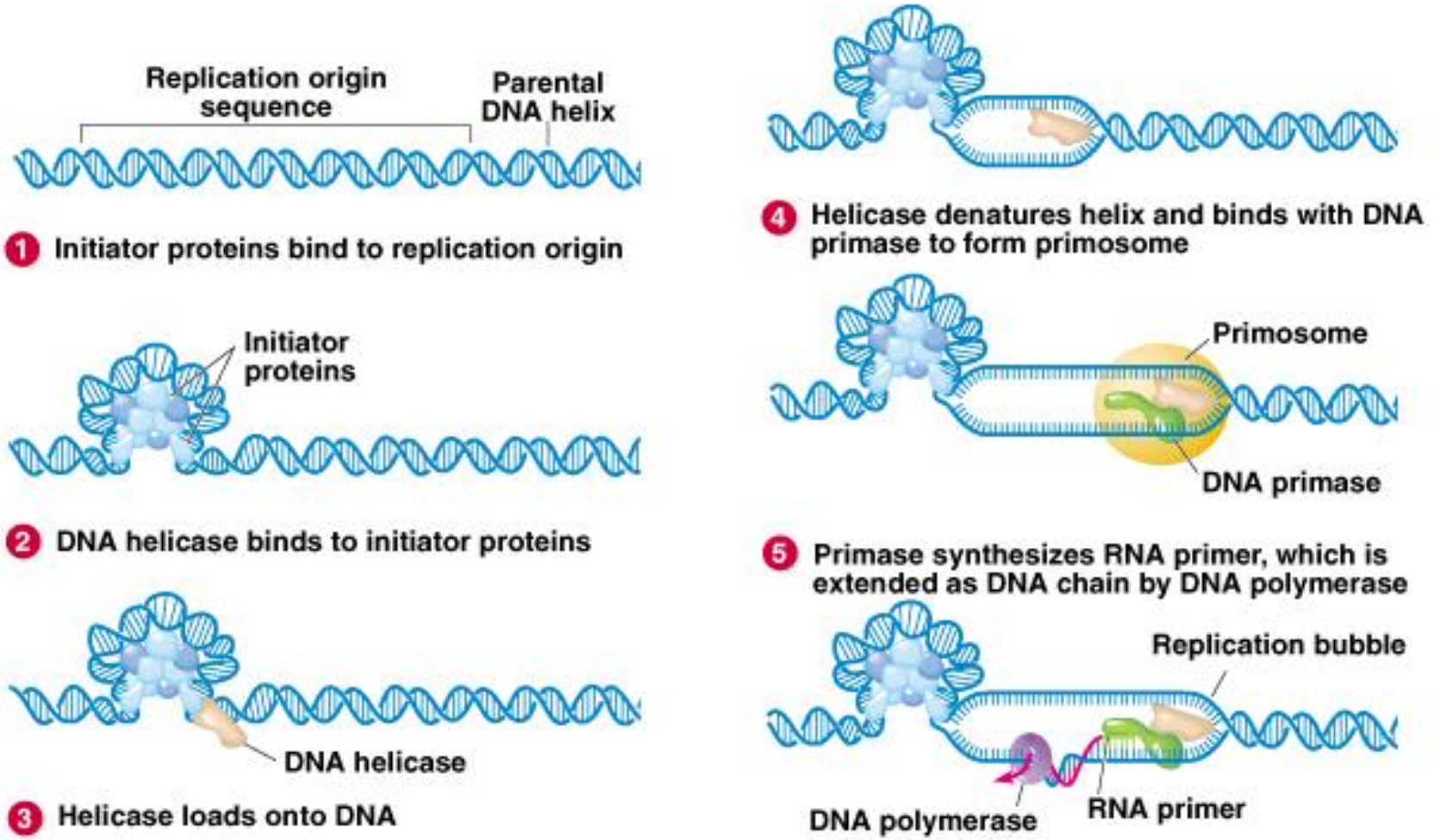
Fig. 3.5 Model for the formation of a replication bubble at a replication origin in *E. coli* and the initiation of the new DNA strand



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Replication is bidirectional

- Replication forks move in opposite directions
- In linear chromosomes, telomeres ensure the maintenance and accurate replication of chromosome ends
- In circular chromosomes, such as *E. coli*, there is only one origin of replication.
- In circular chromosomes, unwinding and replication causes supercoiling, which may impede replication
- Topoisomerase – enzyme that relaxes supercoils by nicking strands

Fig. 3.6a, b Model for the events occurring around a single replication fork of the *E. coli* chromosome

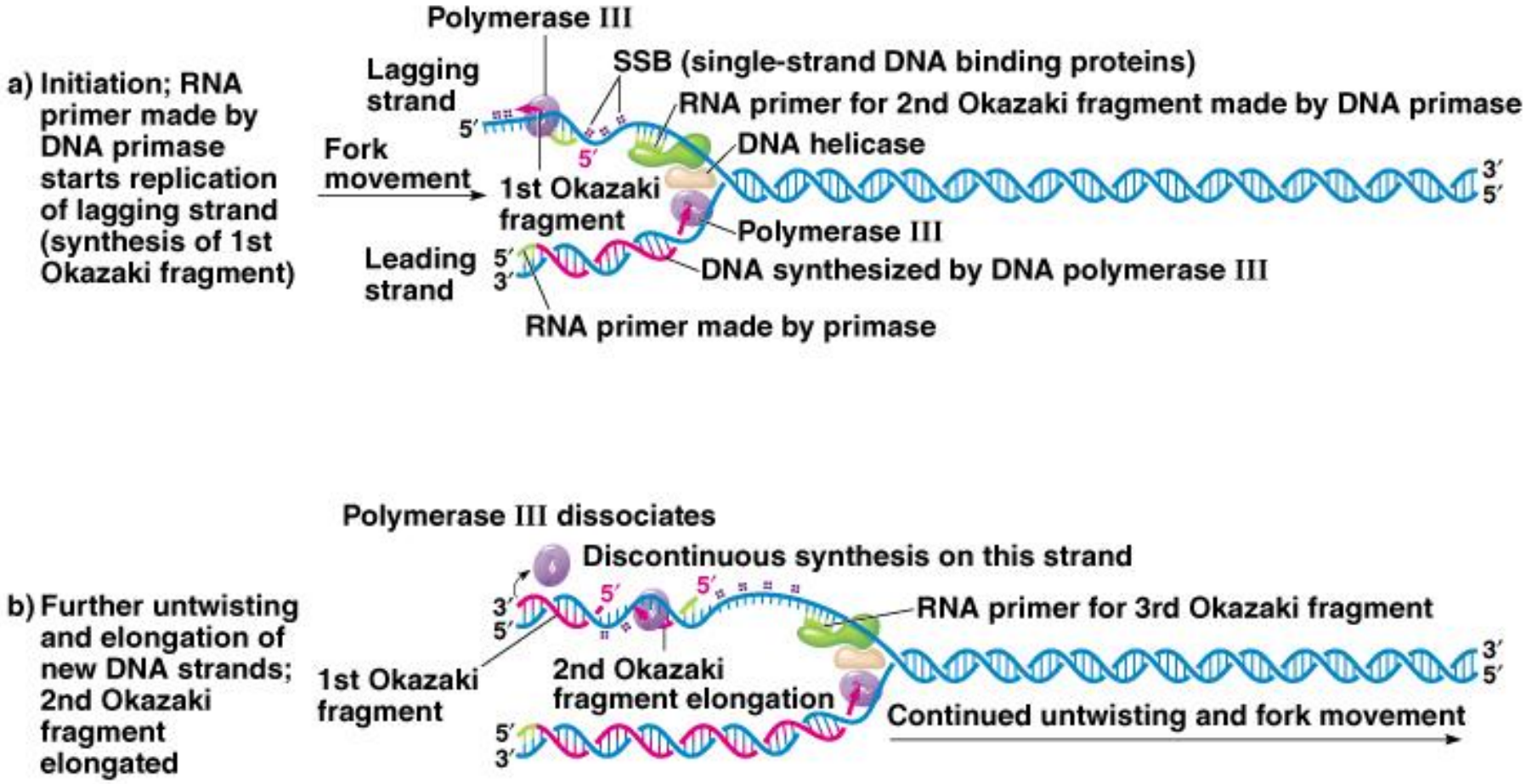

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Fig. 3.6c-e Model for the events occurring around a single replication fork of the *E. coli* chromosome

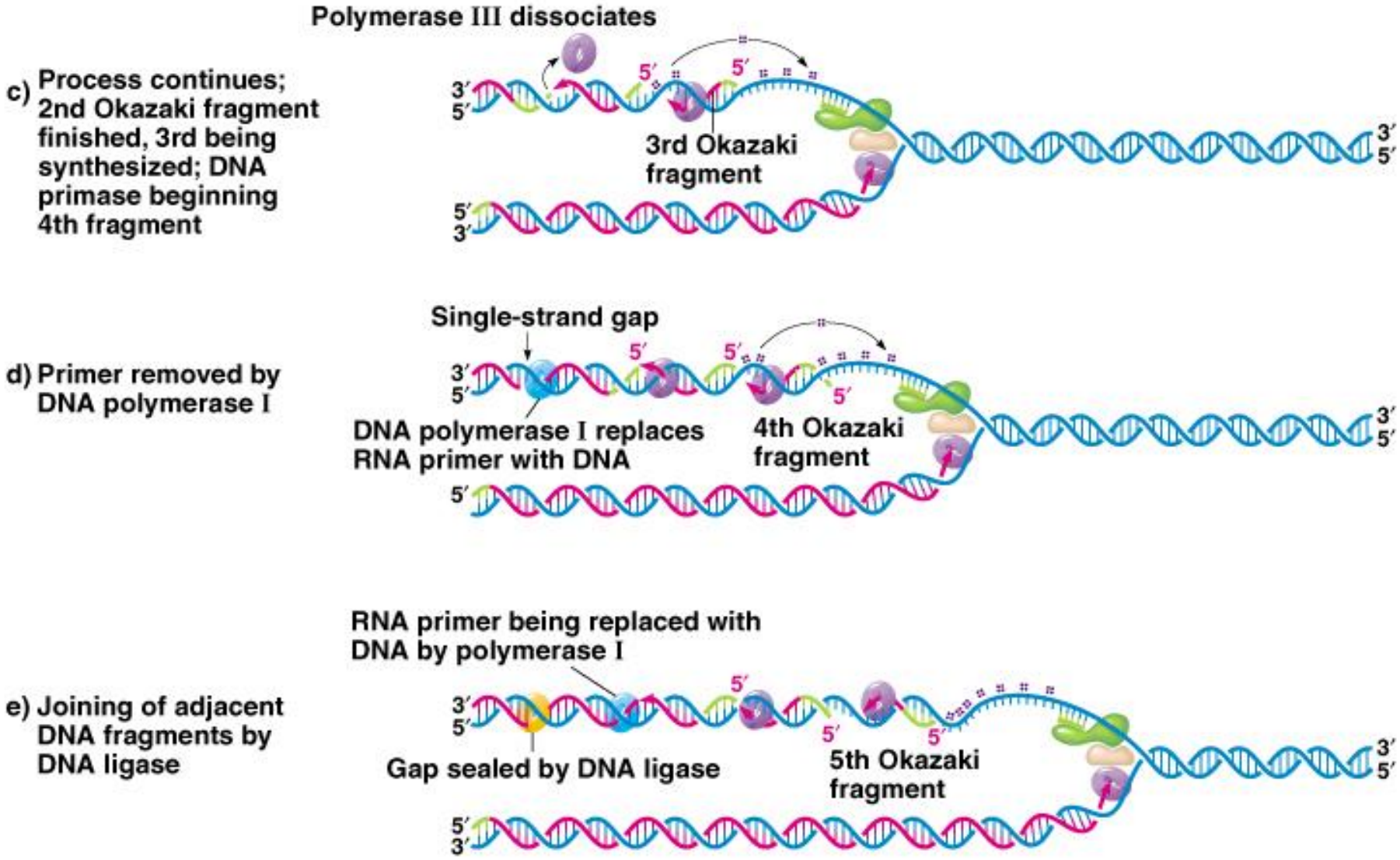

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Fig. 3.7 Action of DNA ligase in sealing the gap between adjacent DNA fragments to form a longer, covalently continuous chain

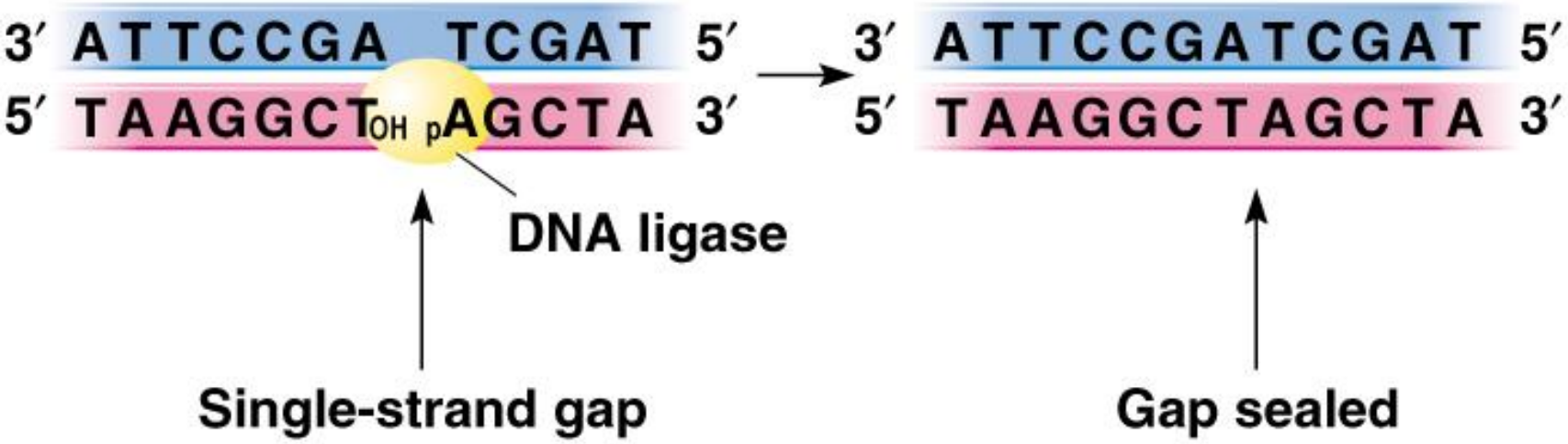

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Fig. 3.8 Model for the "replication machine," or replisome, the complex of key replication proteins, with the DNA at the replication fork

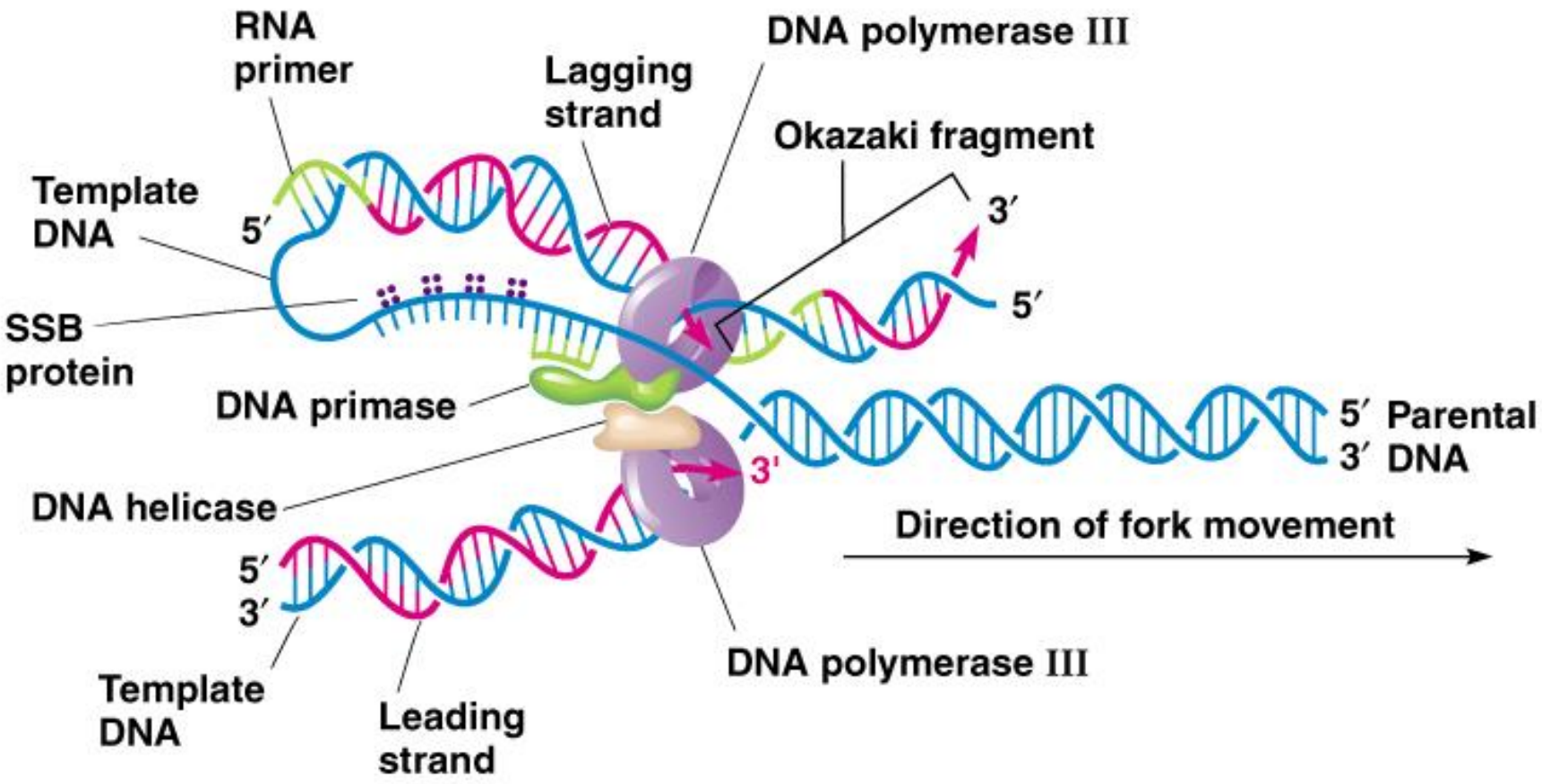

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Fig. 3.9 Diagram of the formation at a replication origin sequence of two replication forks that move in opposite directions

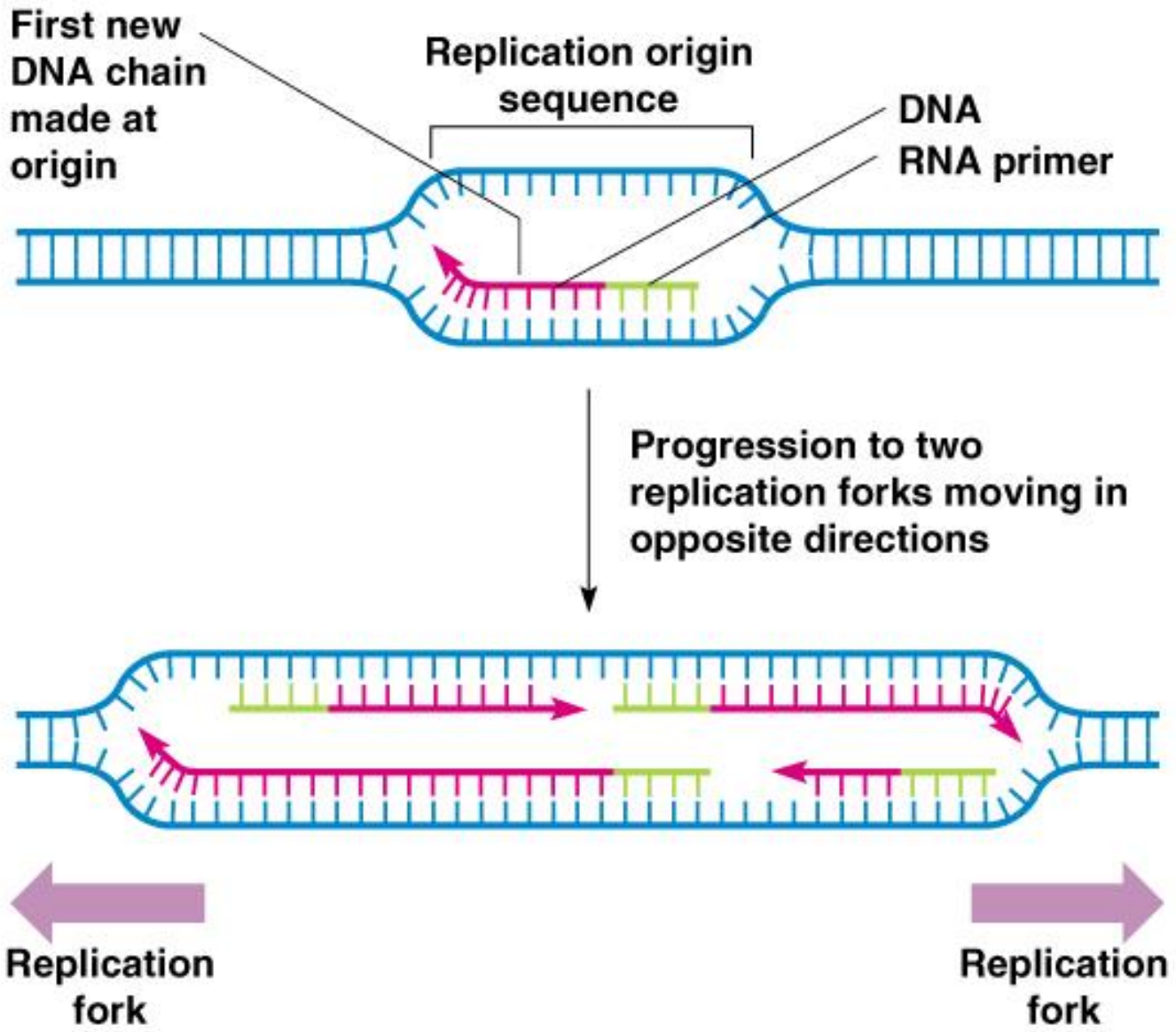

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Fig. 3.10 Bidirectional replication of circular DNA molecules

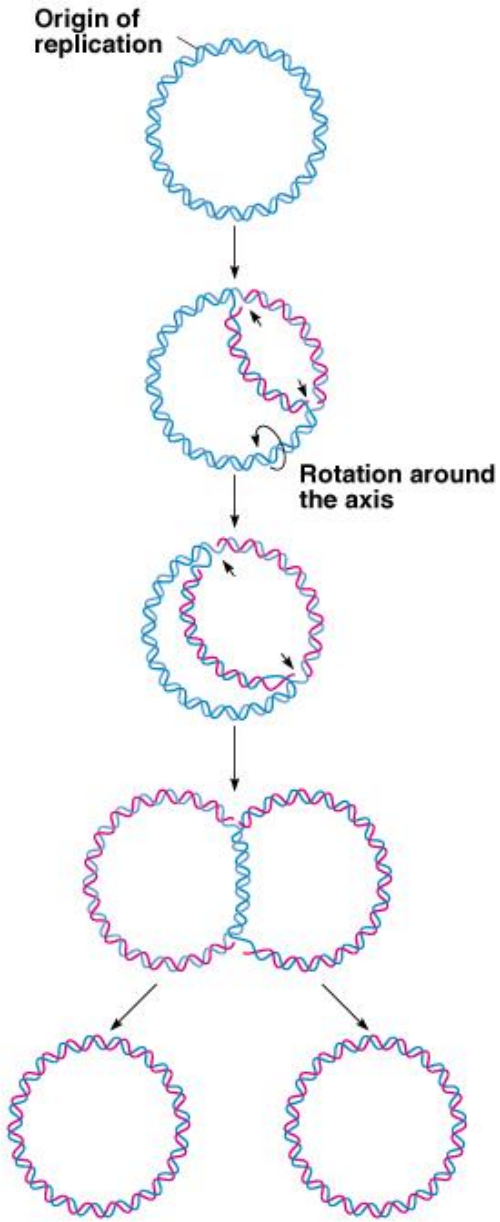

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Fig. 3.11b Diagram showing the unreplicated, supercoiled parent strands and the portions already replicated

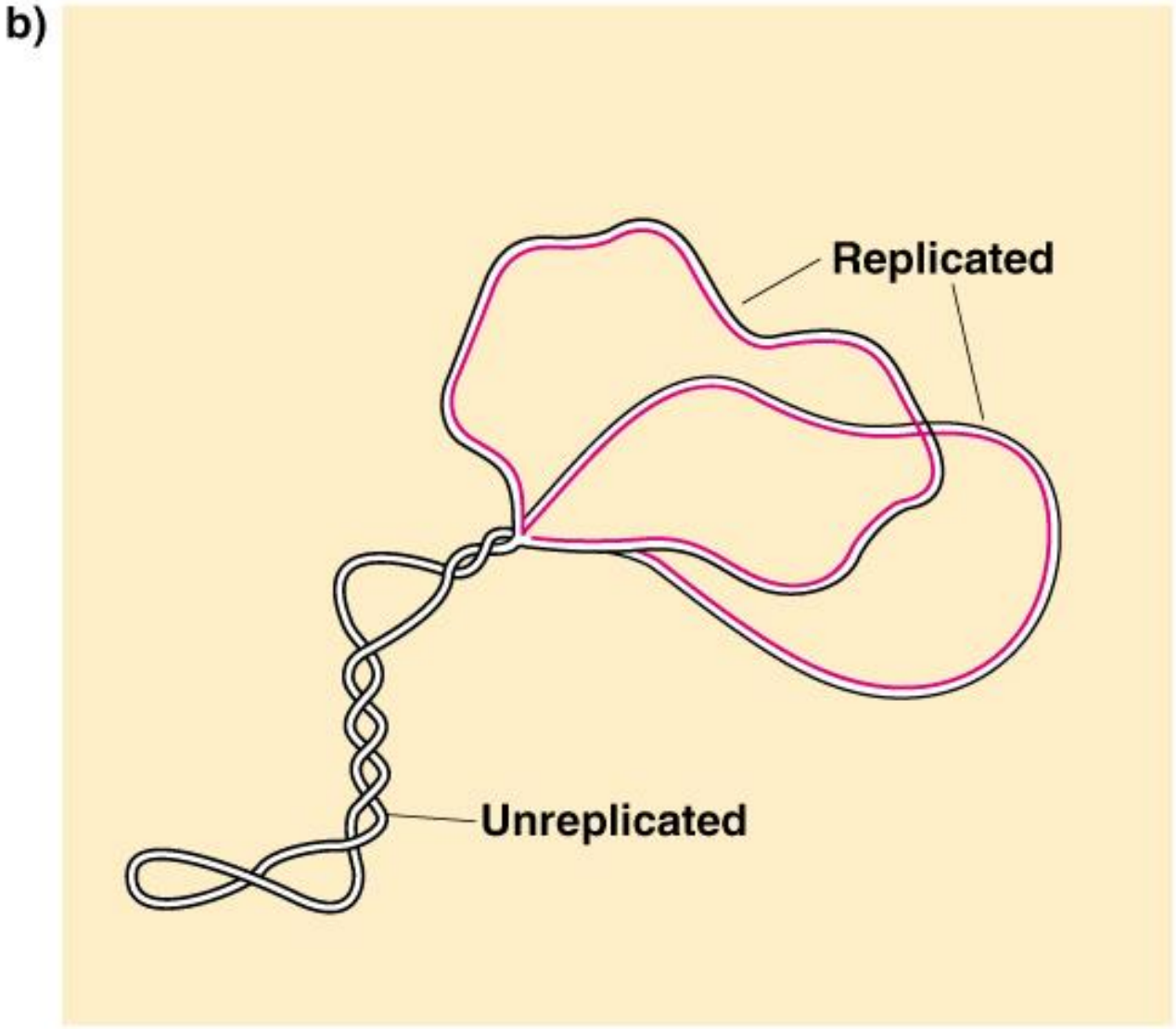

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Fig. 3.12 The replication process of double-stranded circular DNA molecules through the rolling circle mechanism

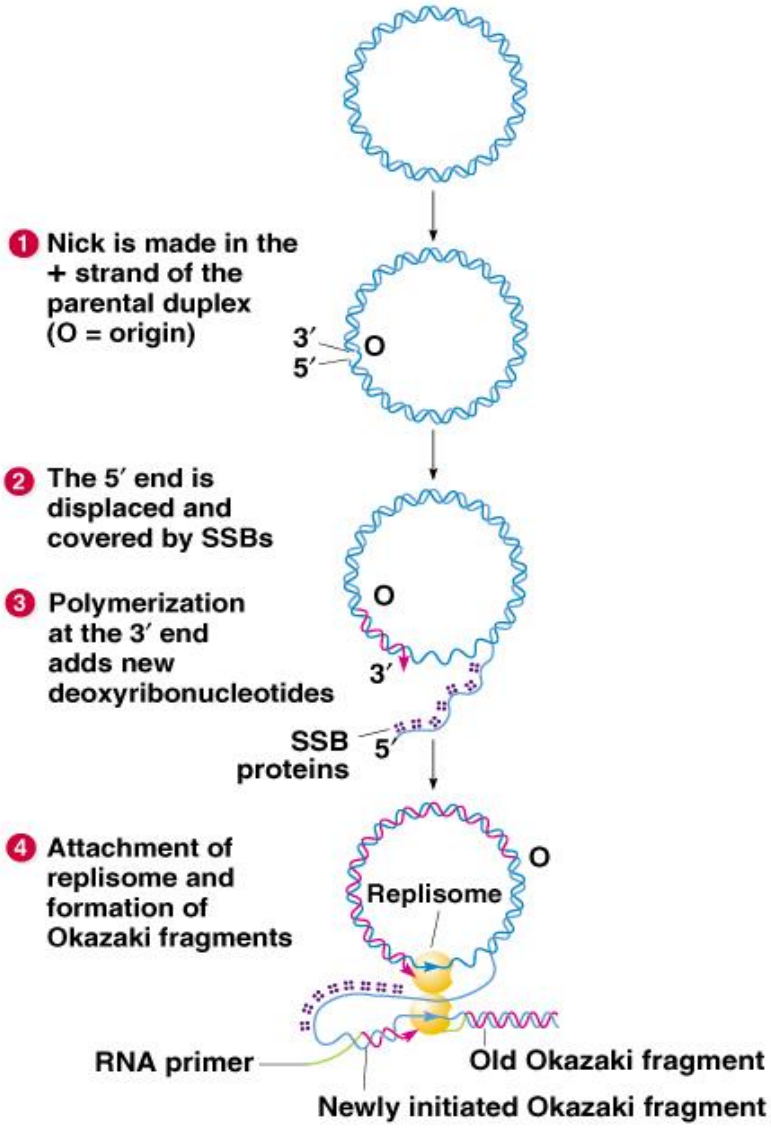

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Fig. 3.17 Temporal ordering of DNA replication initiation events in replication units of eukaryotic chromosomes

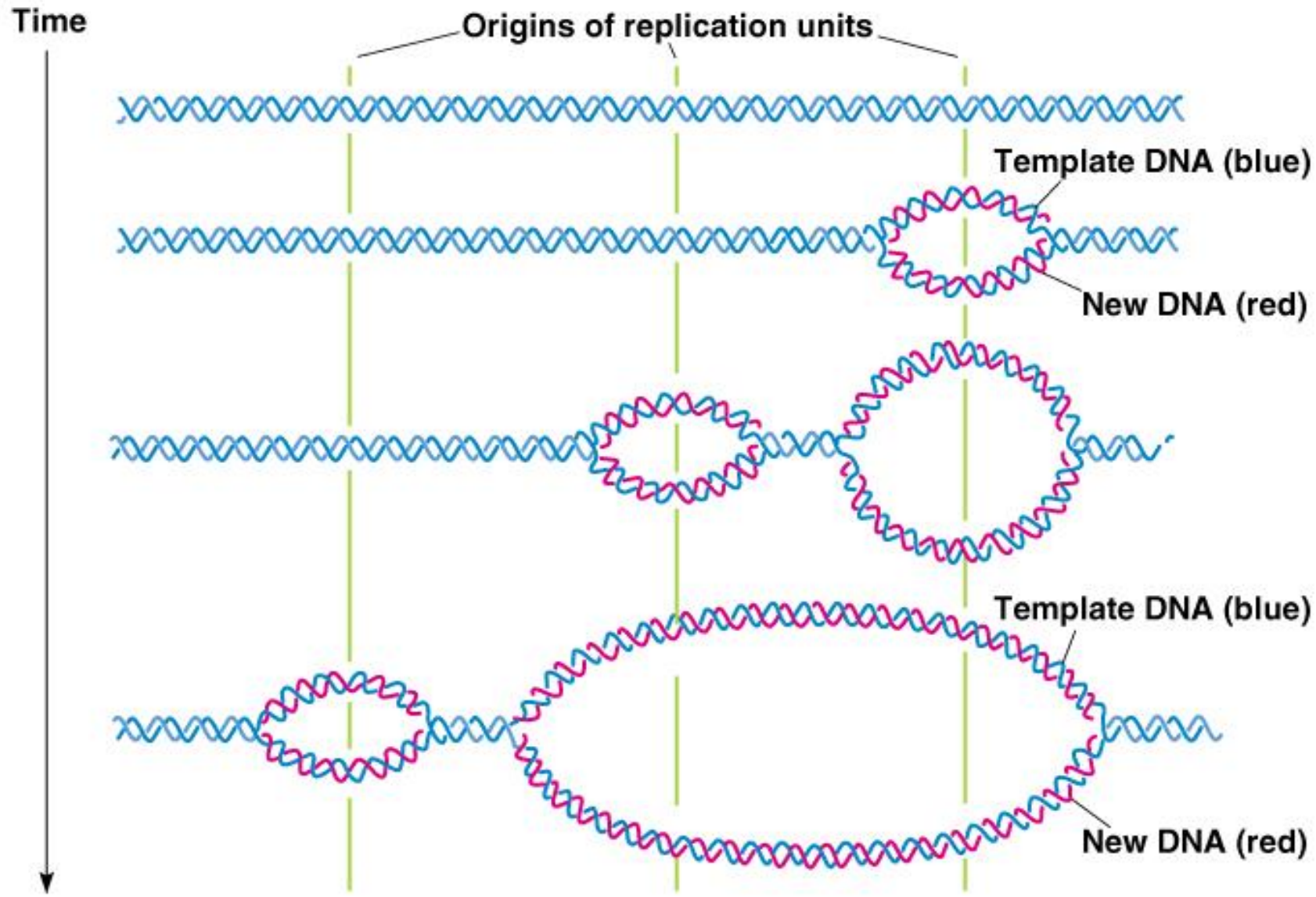

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Fig. 3.18 The problem of replicating completely a linear chromosome in eukaryotes

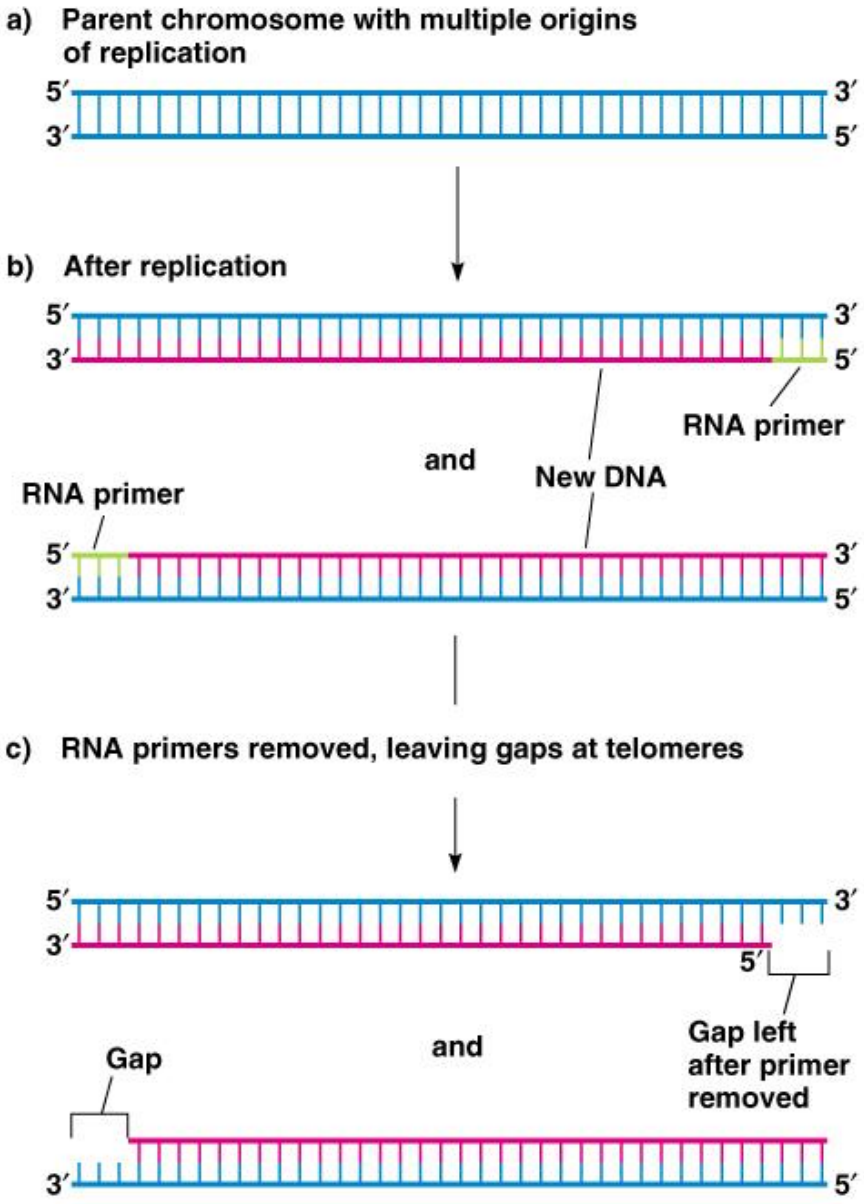

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Fig. 3.19 Synthesis of telomeric DNA by telomerase

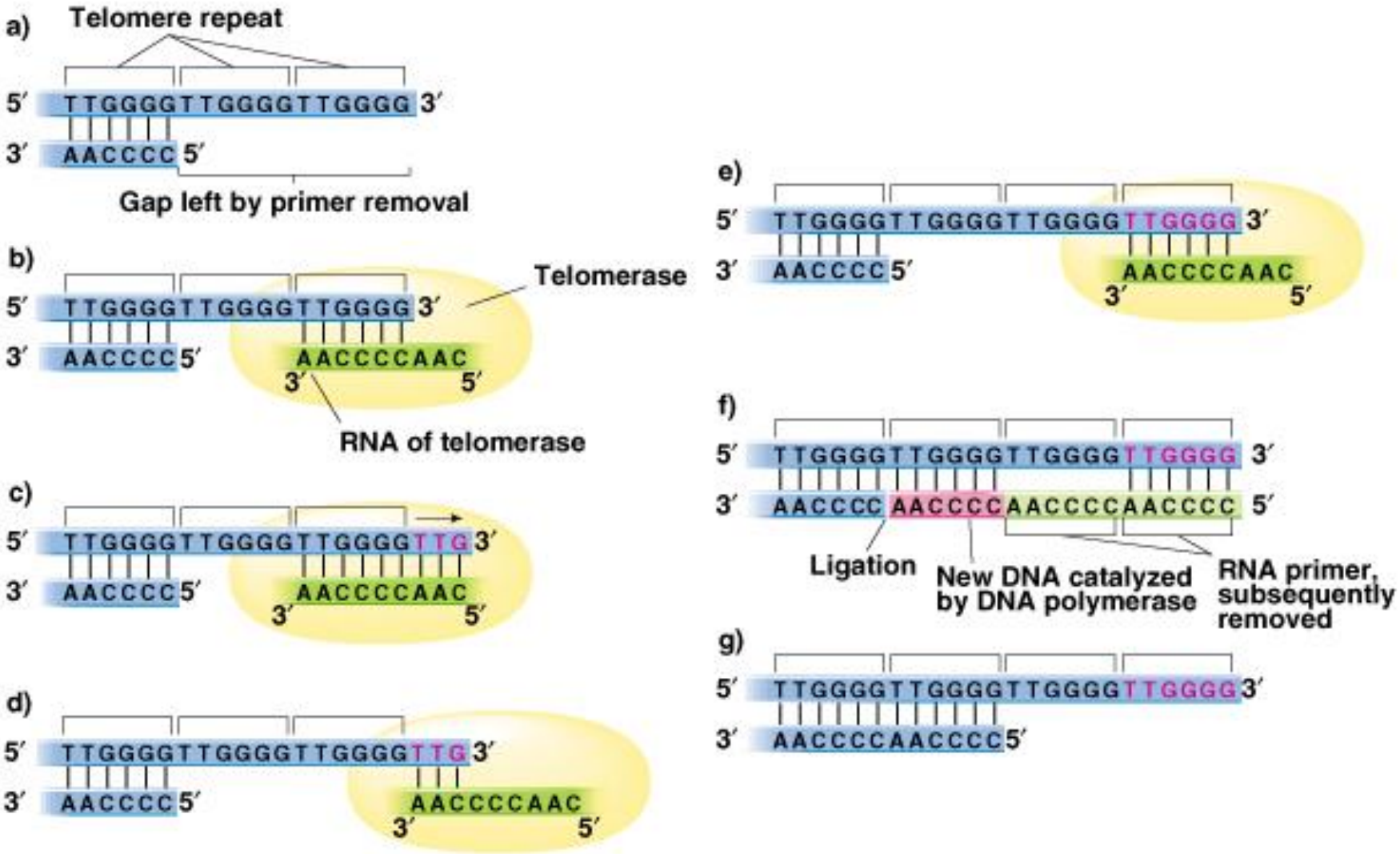

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Fig. 2.25 A possible nucleosome structure

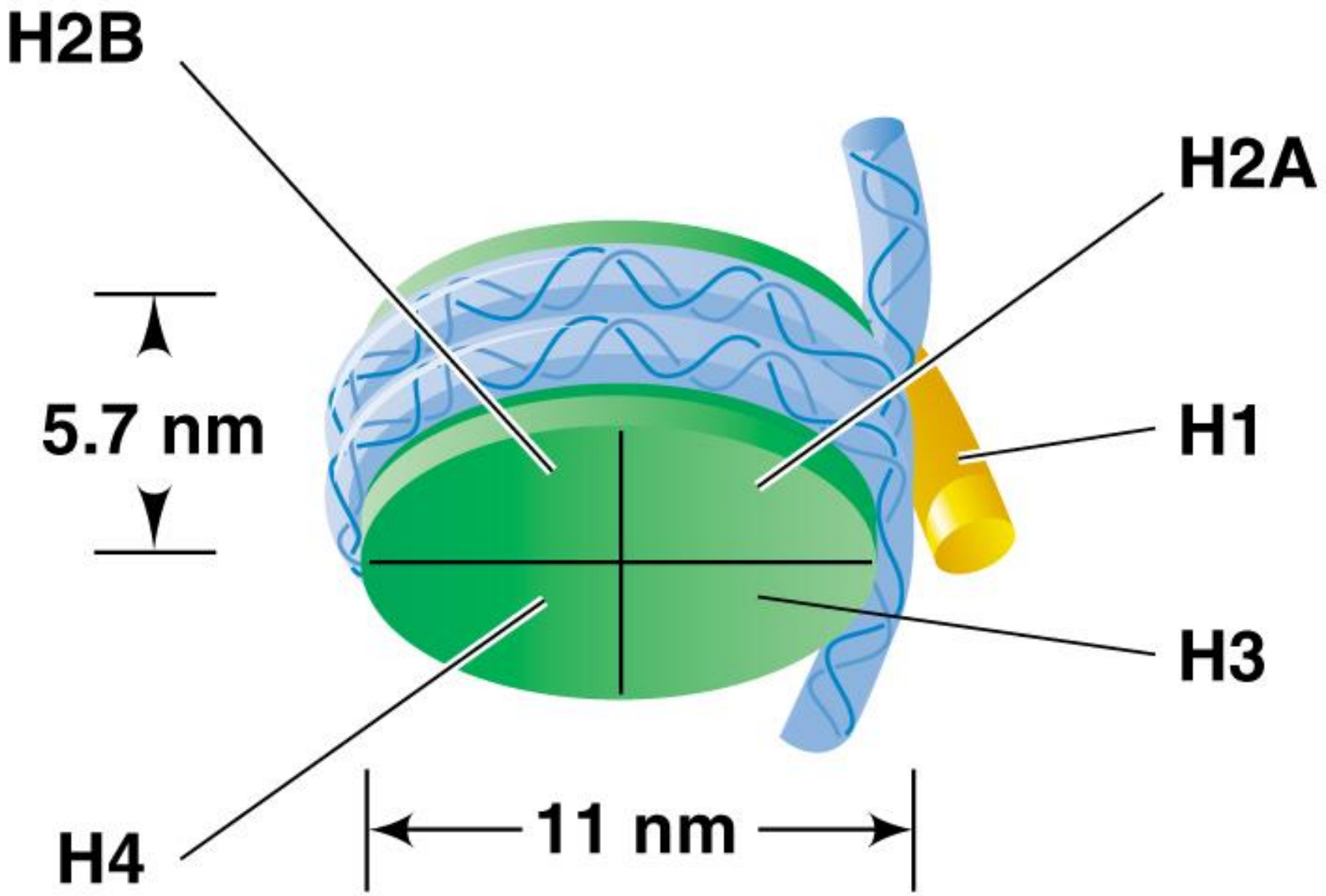

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Fig. 2.26 Nucleosomes connected together by linker DNA and H1 histone to produce the "beads-on-a-string" extended form of chromatin

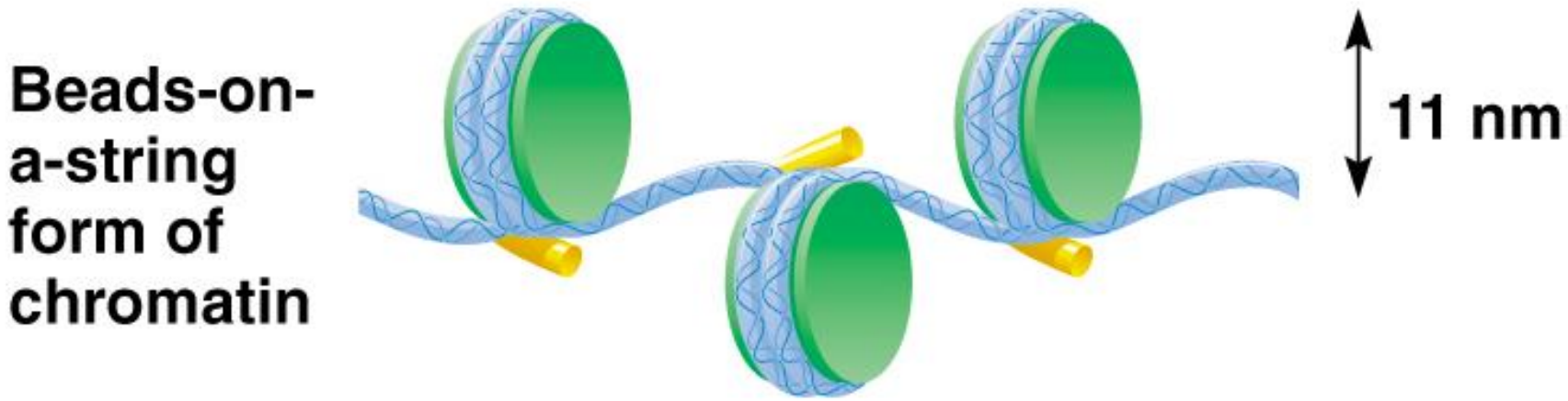

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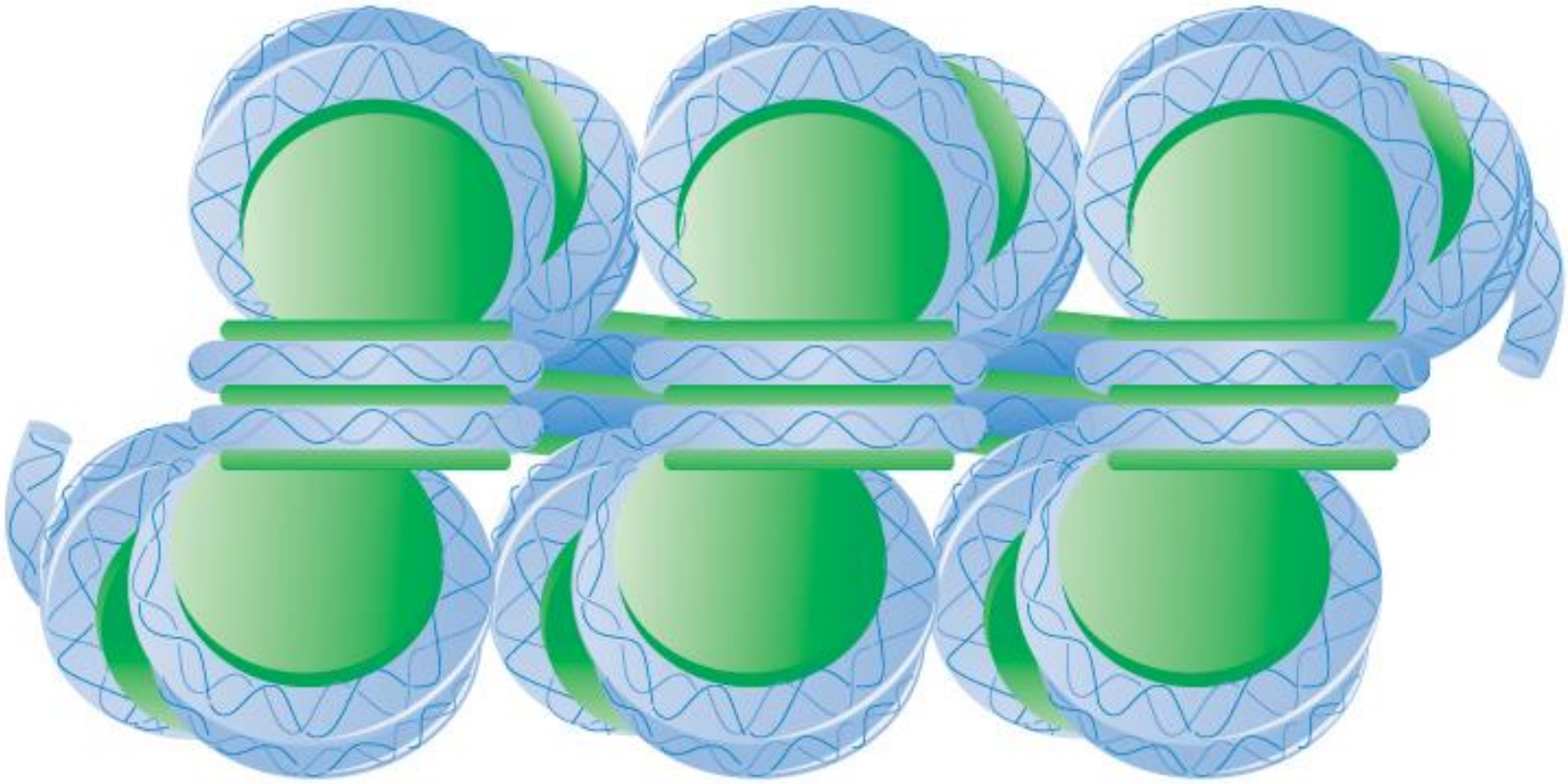
Fig. 2.28b Packaging of nucleosomes into the 30-nm chromatin fiber



b)

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Fig. 2.29 Model for the organization of 30-nm chromatin fiber into looped domains that are anchored to a nonhistone protein chromosome scaffold

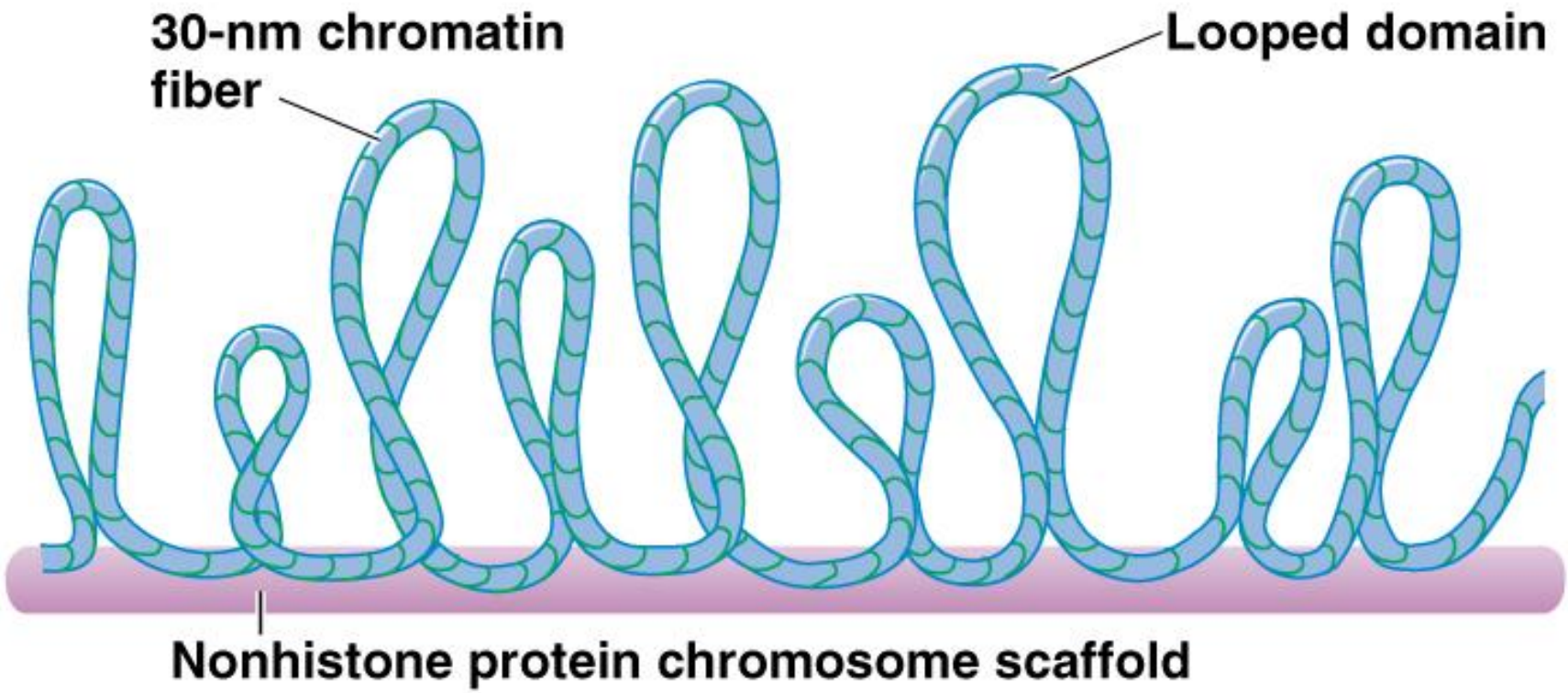

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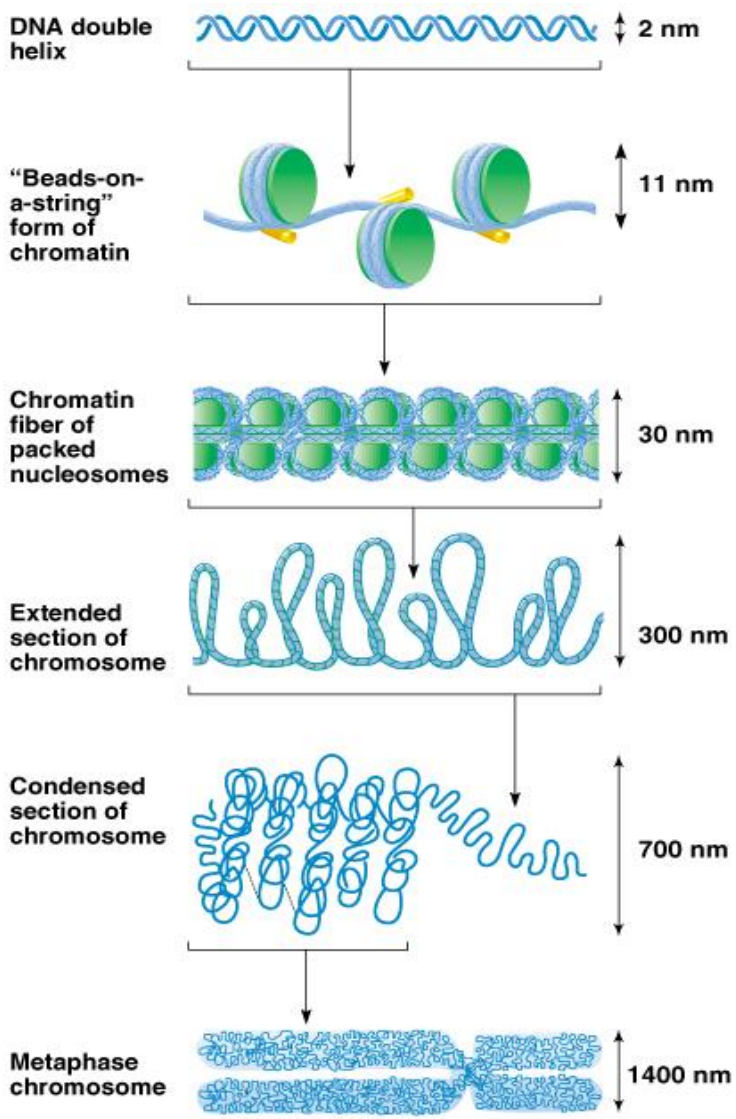
Fig. 2.31 The many different orders of chromatin packing that give rise to the highly condensed metaphase chromosome



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