Chapter 3: Duplicating the DNA-Replication

Double helix separation

New strand synthesis

I've missed more than 9000 shots in my career. I've lost almost 300 games. 26 times, I've been trusted to take the game winning shot and missed. I've failed over and over and over again in my life. And that is why I succeed.


MICHAEL
JORDAN
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Chapter 10 Opener Principles of Genetics, 4/e

Seven pairs of identical twins: No instructions regarding how to pose.

People often explain nearly identical phenotypes of monozygotic twins like Merry and Sherry by stating that "they contain the same genes."

Of course, that is not true. To be accurate, the statement should be that identical twins contain progeny replicas of the same parental genes.

A human life emerges from a single cell, a tiny sphere about 0.1 mm in diameter.

65 trillion (65,000,000,000,000) cells.

So, DNA replication has to be..

Fast

+

Accurate

Which step does DNA replication occur?

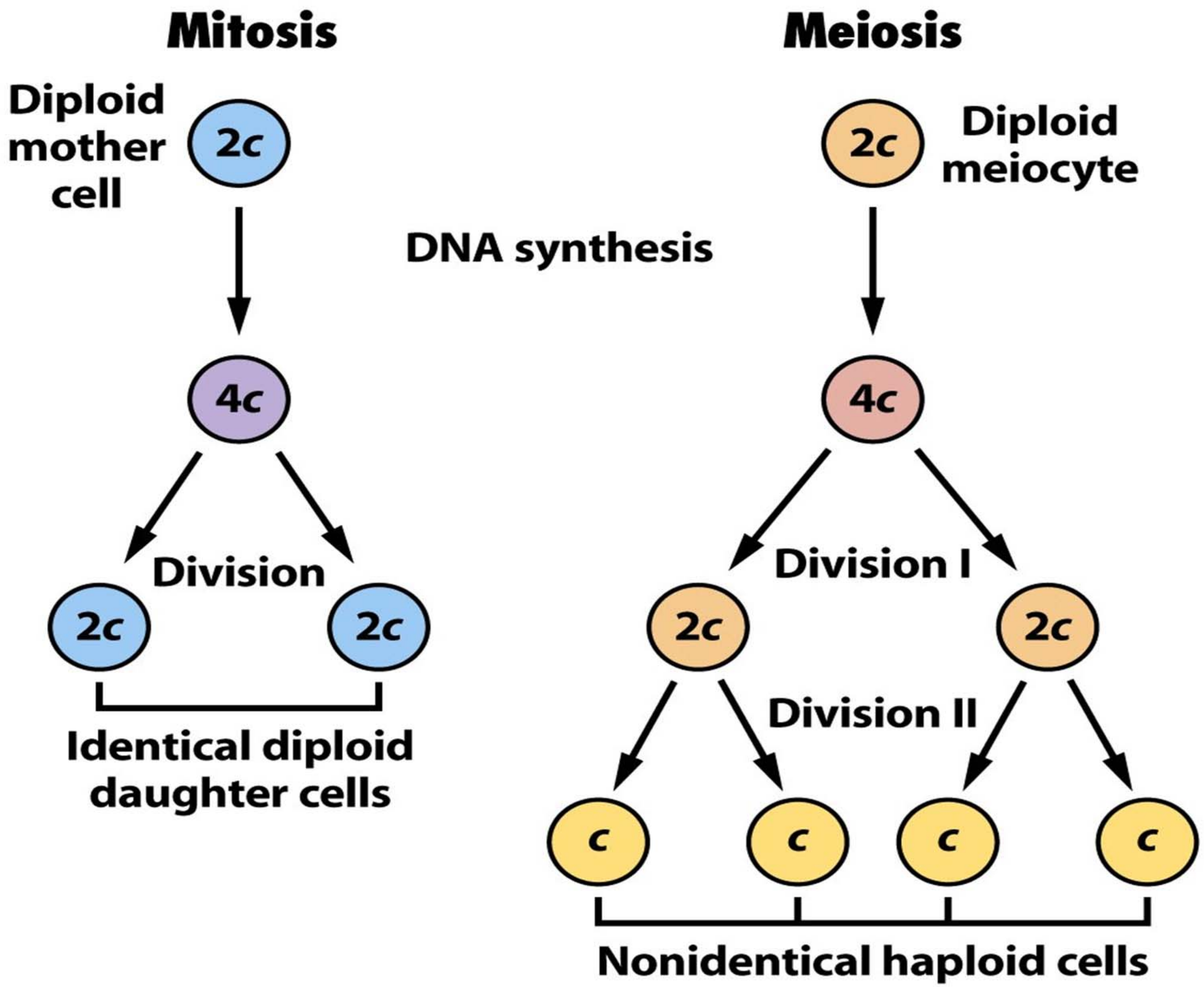


Figure 2-10 Principles of Genetics, 4/e

Replicated DNA(chromosomes)

Sister chromosome? Homolgous chromosome?

Figure 2-3b Principles of Genetics, 4/e

Light micrograph of human chromosomes during cell division.

Double helix separation

- <u>Replication</u>: the process that DNA of original, or mother cell is duplicated to give two identical copies
- For replication, the two strands of the DNA double helix separate and build a complimentary strand on each of the two original strands
- <u>Semi-conservative replication</u>: replication of DNA in which each daughter molecule gets one of the two original strands and one new complimentary strand (=each of the progeny conserves half of the original DNA molecule)

Semiconservative Replication (Meselson and Stahl)

Each of the parental strands is conserved and serves as a template for the synthesis of a new complementary strand; that is, the base sequence in each progeny strand is determined by the hydrogen-bonding potentials of the bases in the parental strand.

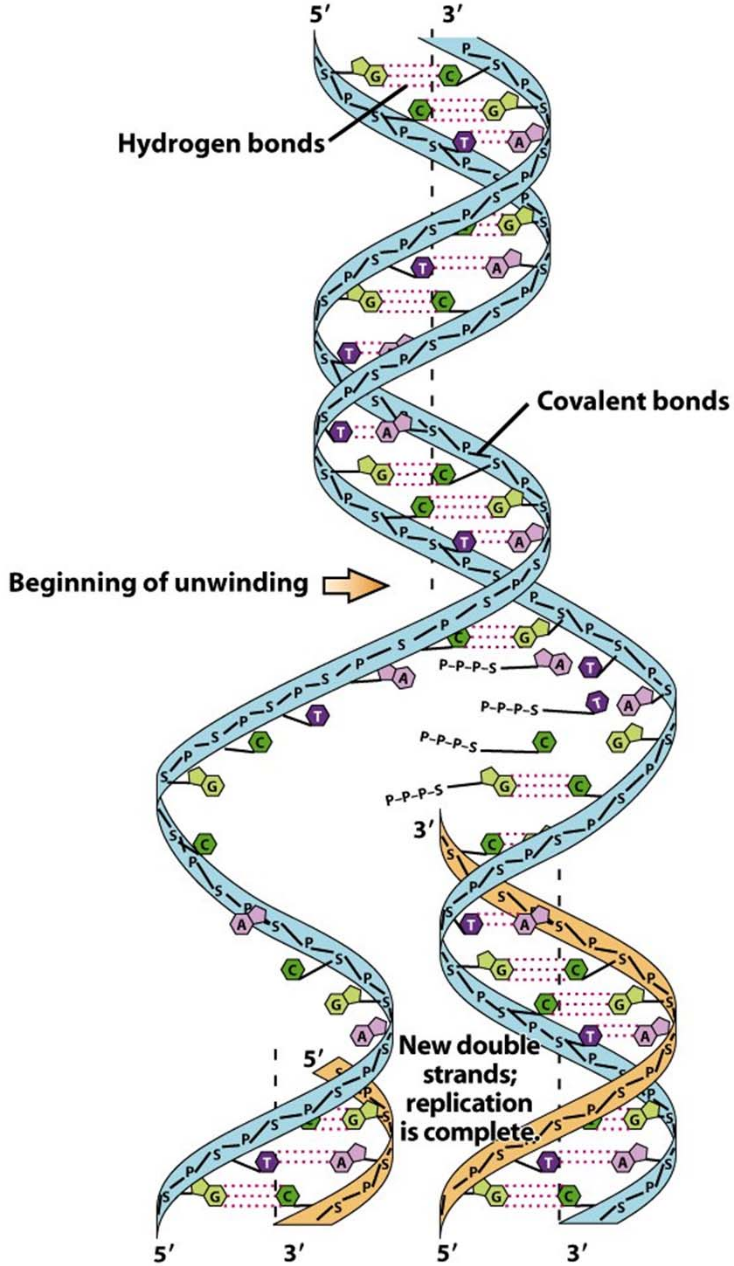


Figure 10-1 Principles of Genetics, 4/e

Semiconservative Replication (Meselson and Stahl)

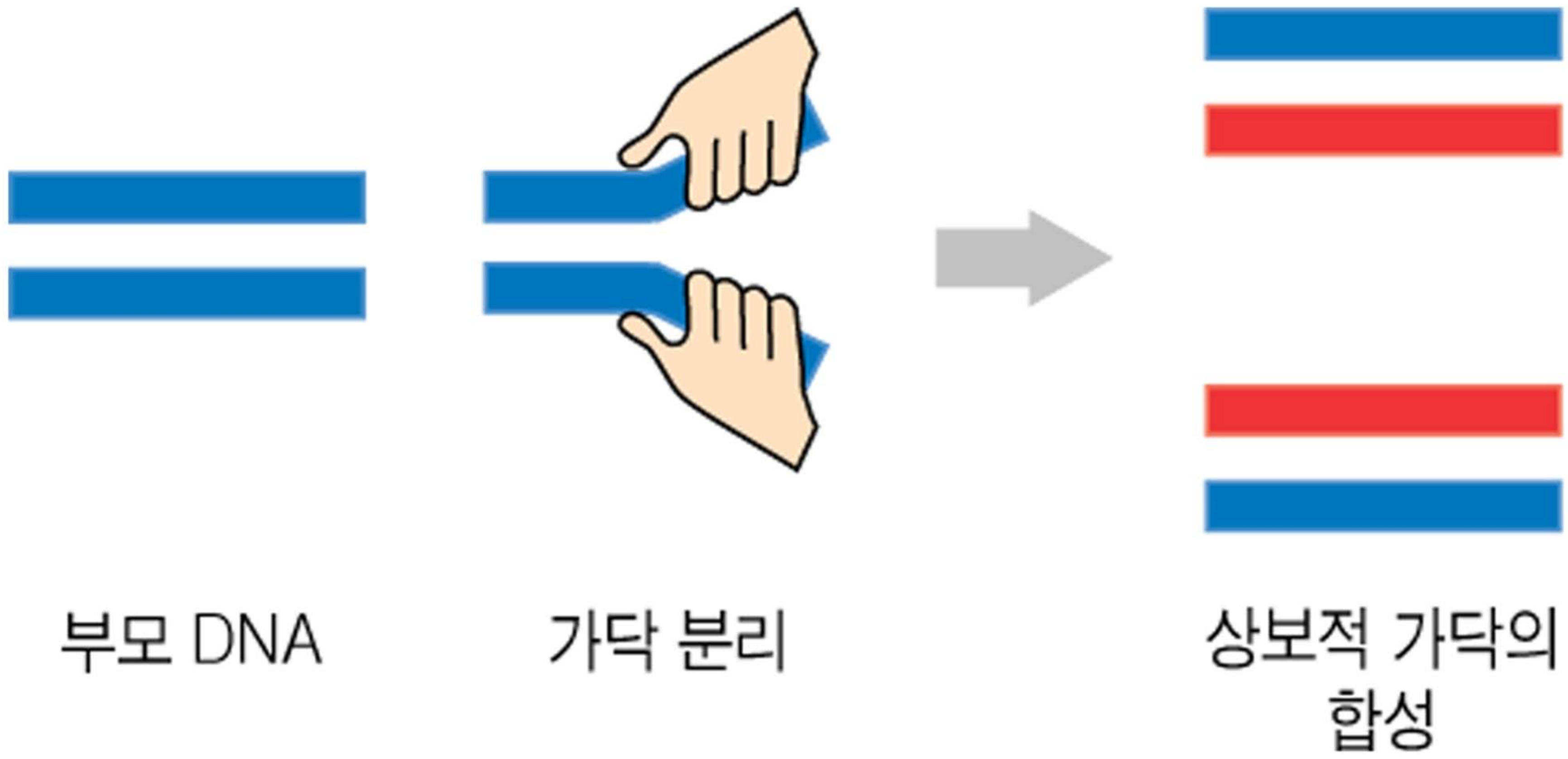
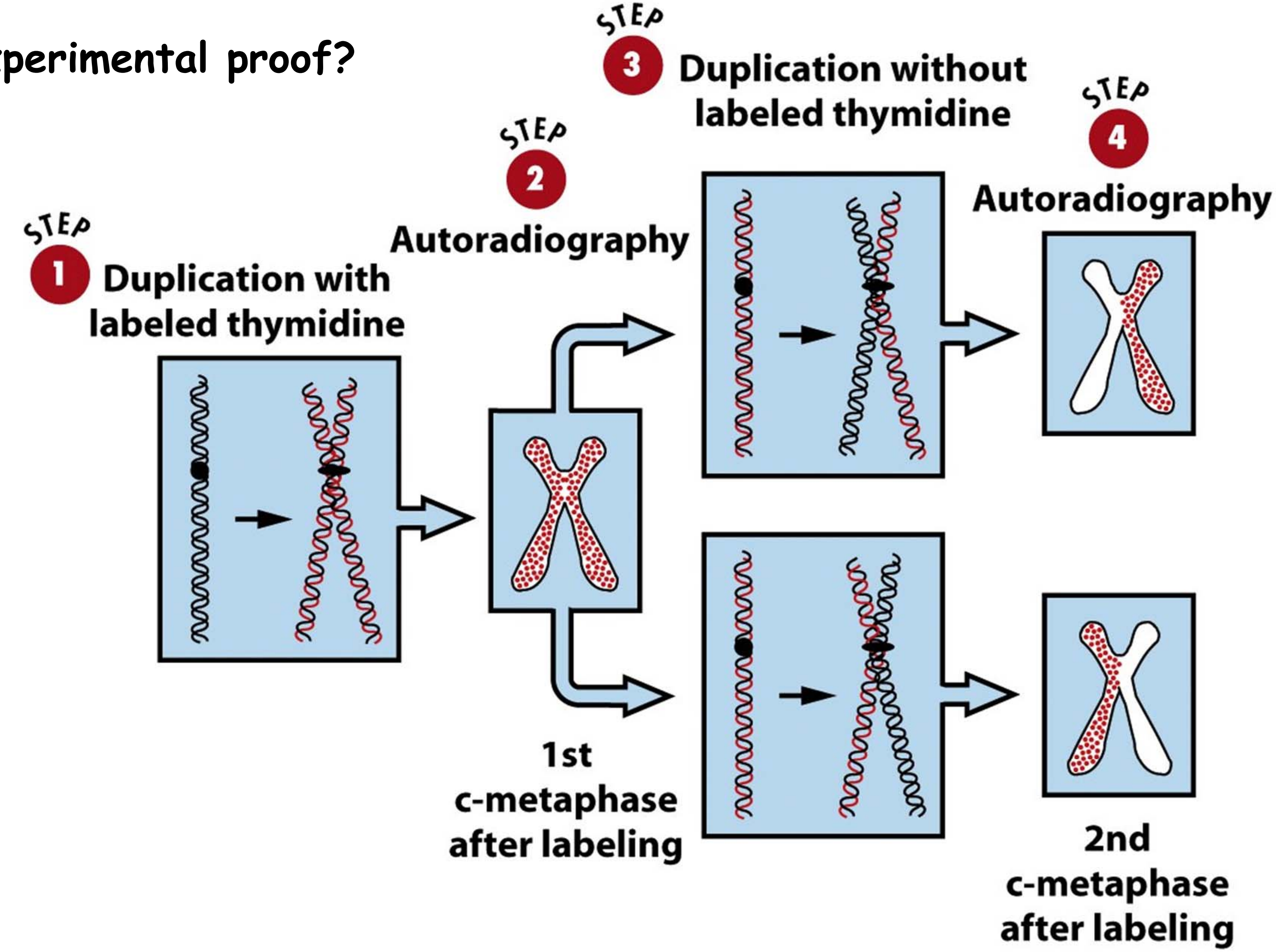


그림 5-1

Experimental proof?



Interpretation of the autoradiographs above in terms of semiconservative replication.

Figure 10-2c Principles of Genetics, 4/e

Double helix separation

- Before replication DNA double helix separate into strands by DNA *gyrase* (unwind supercoils) and DNA helicase (unwind double helix)

- After separation, DNA strands are kept apart by single strand binding protein (SSB)

DNA Replication in Prokaryote

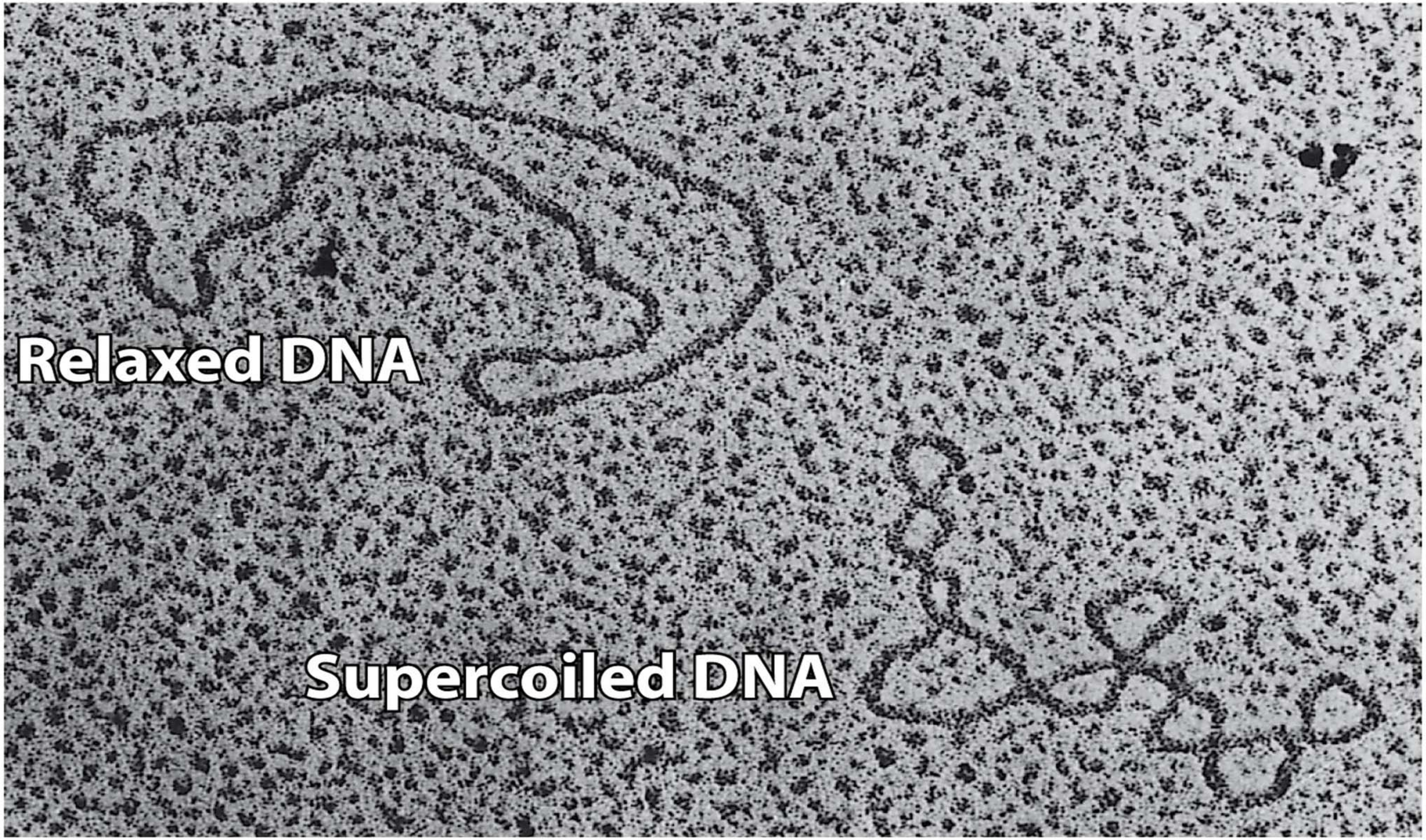
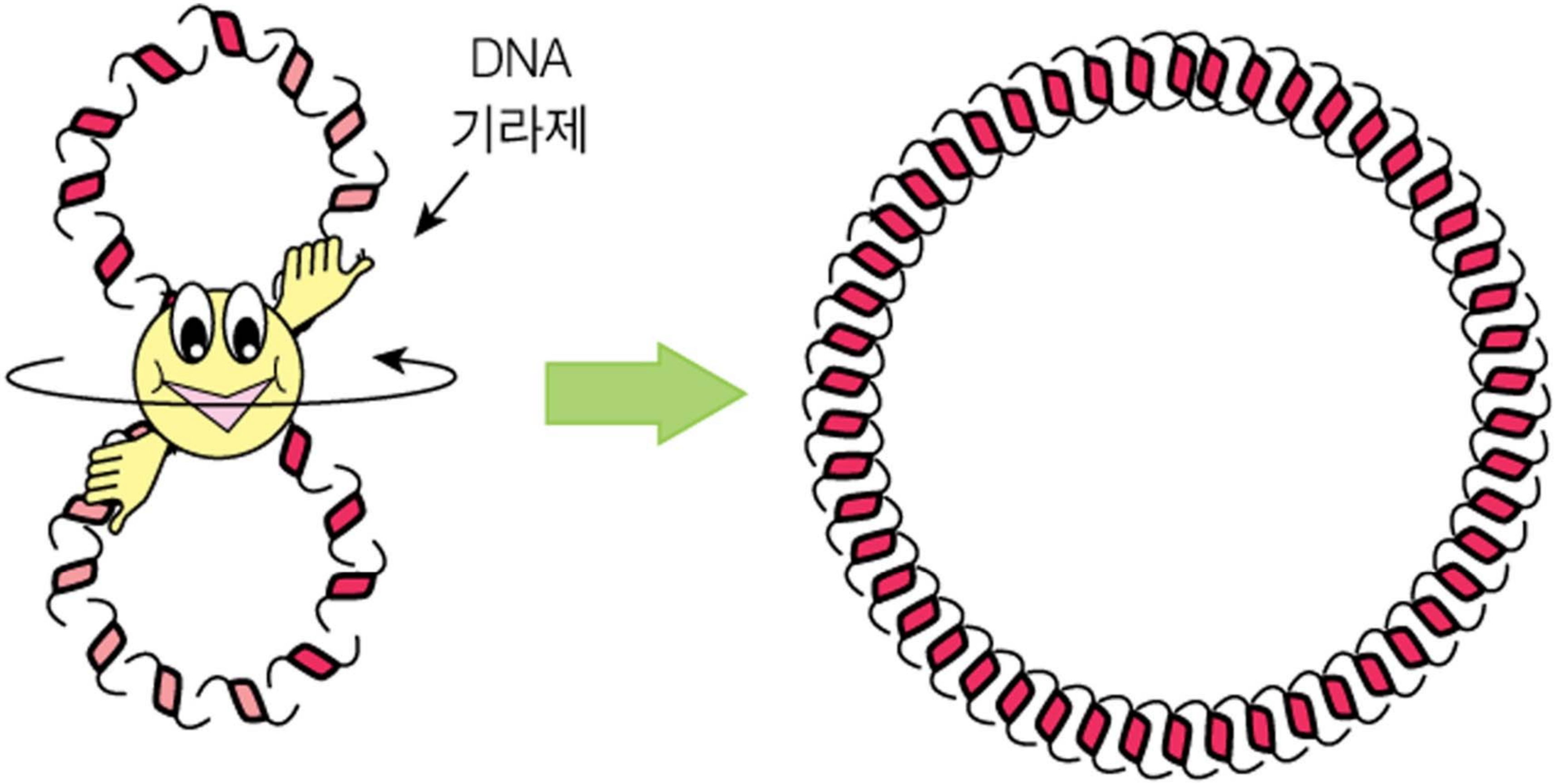


Figure 9-13 Principles of Genetics, 4/e

DNA Structure: Negative Supercoils *In Vivo*

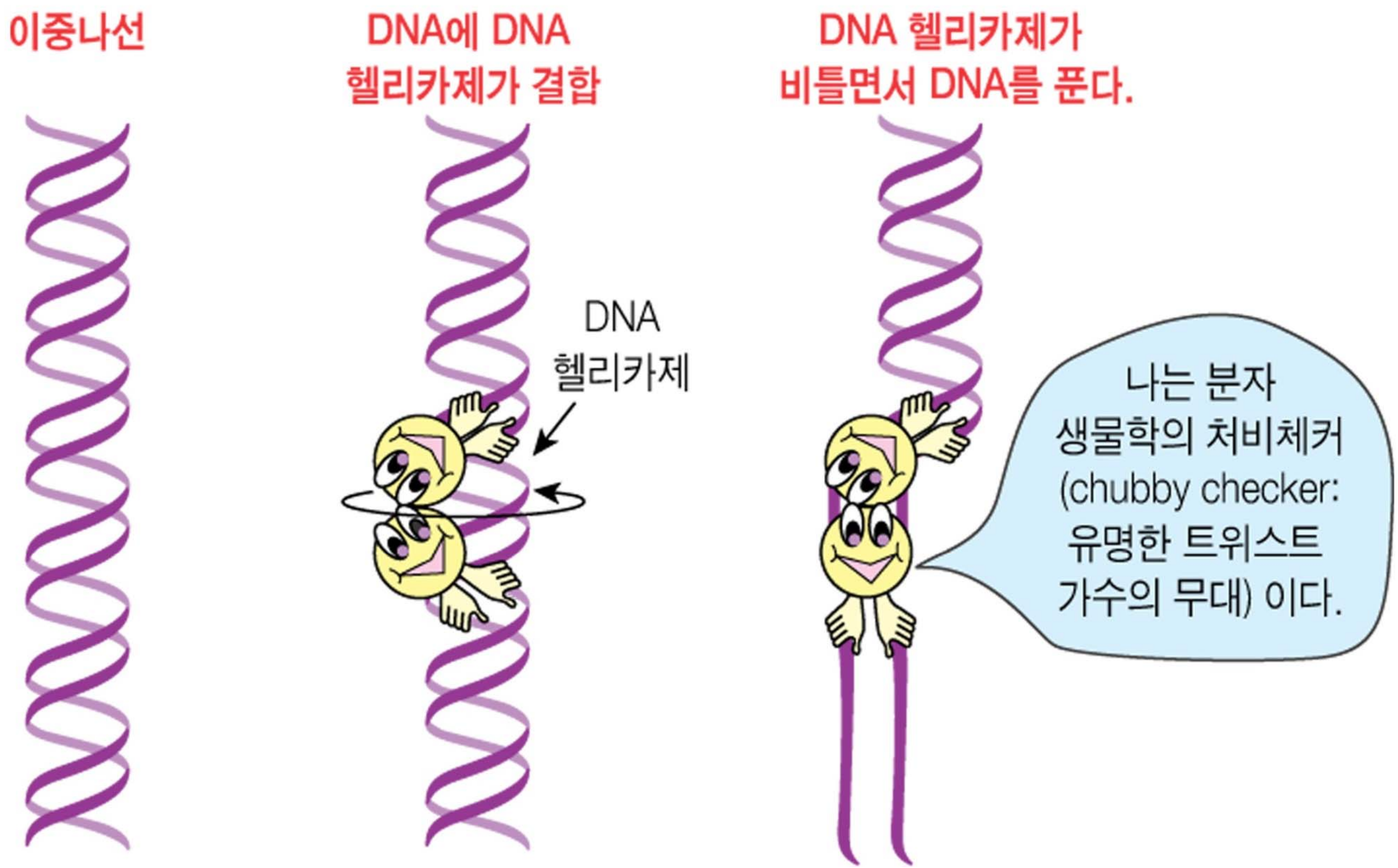
Three enzymes are needed for double helix separation



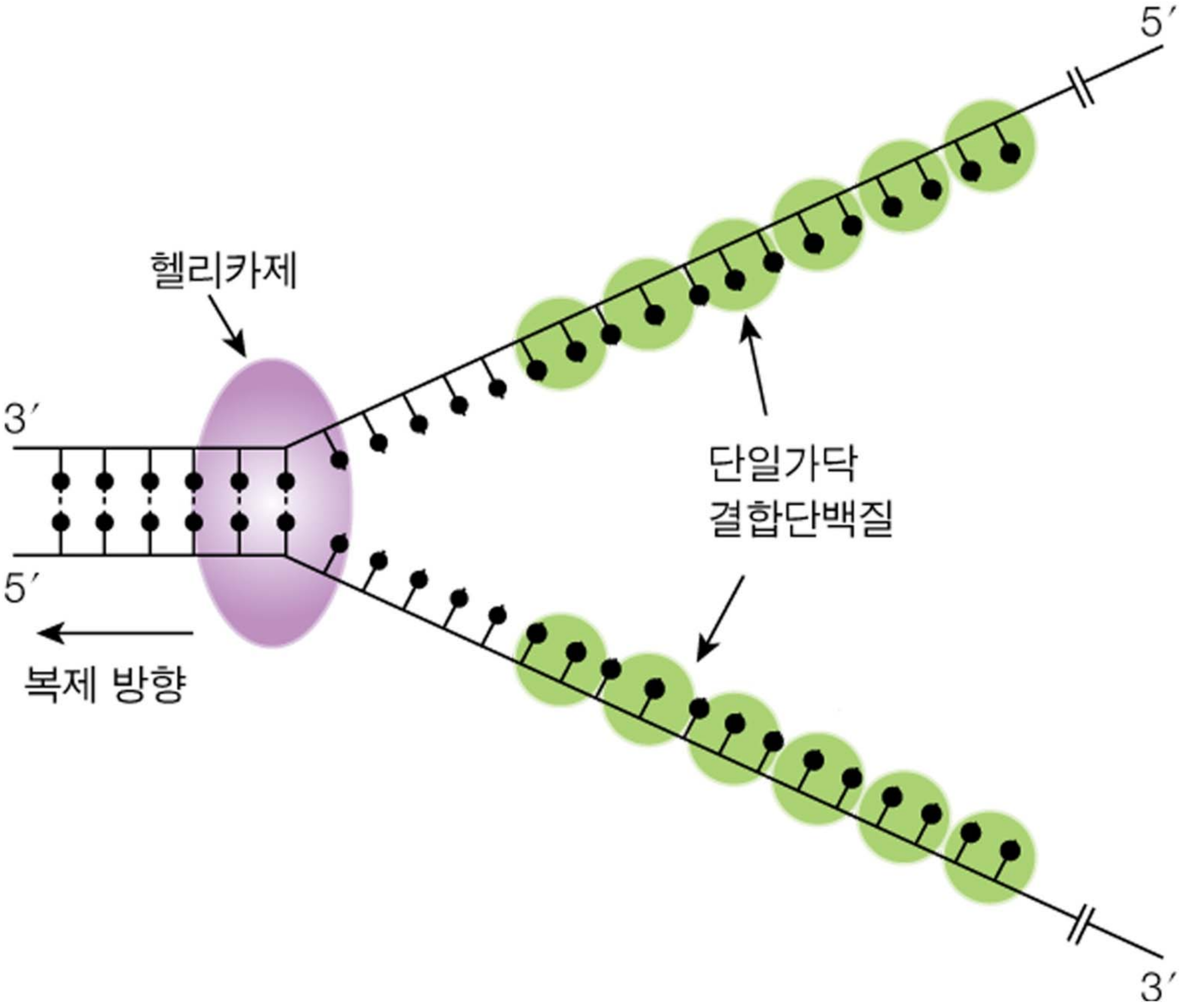
음성의 슈퍼코일 DNA

슈퍼코일이 없는 원형 DNA

Three enzymes are needed for double helix separation



Three enzymes are needed for double helix separation



Single-strand DNA-binding (SSB) protein keeps the unwound strands in an extended form for replication.

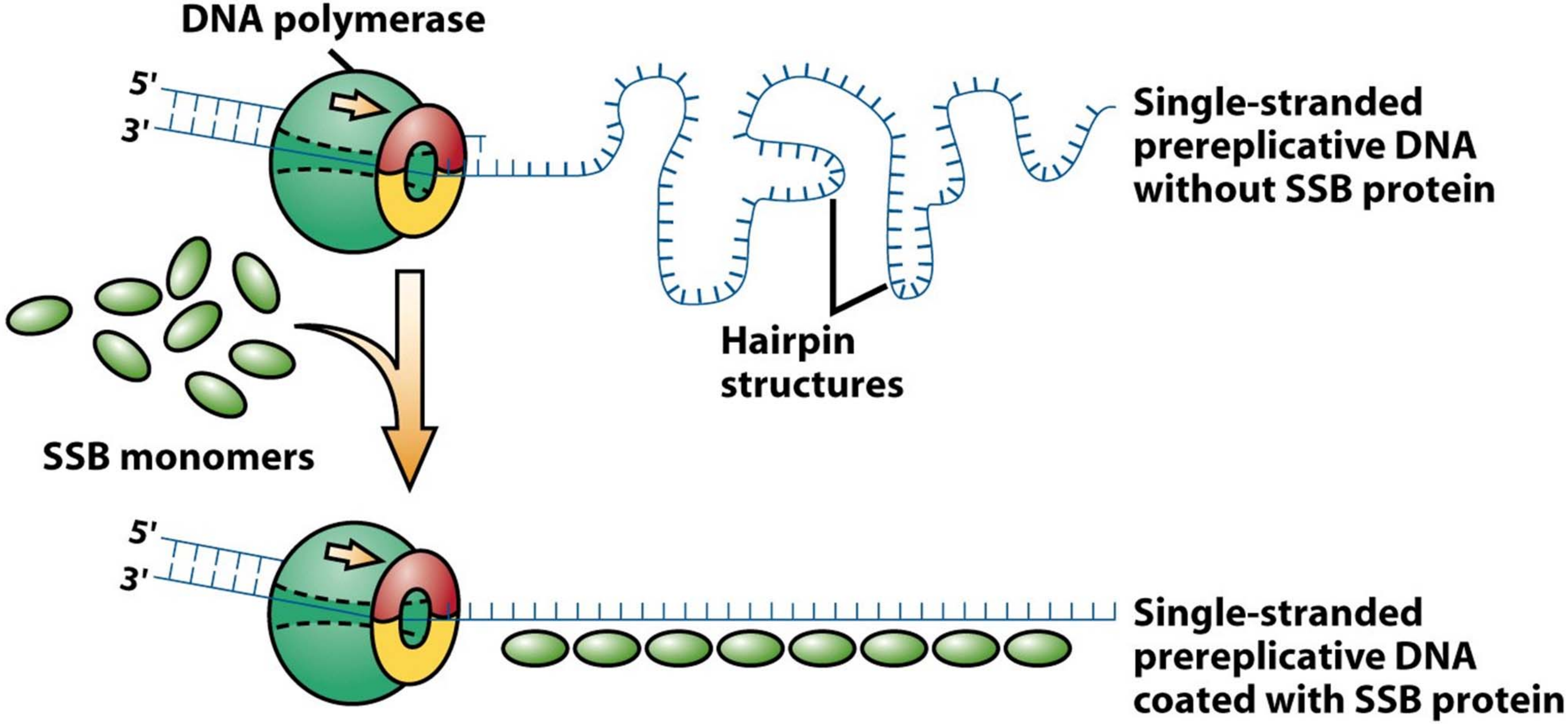


Figure 10-21b Principles of Genetics, 4/e

New strand synthesis

- Separated parental strands serves as template strands and the synthesis of new complimentary strands starts by base-paring
- DNA polymerase III (Pol III) is responsible for synthesizing new complementary strand DNA and for correcting the mismatched base pairs
- Pol III has two subunits, synthetic subunit and sliding clamp subunit
- New DNA strands always start at the 5' end and grow in the 3' direction

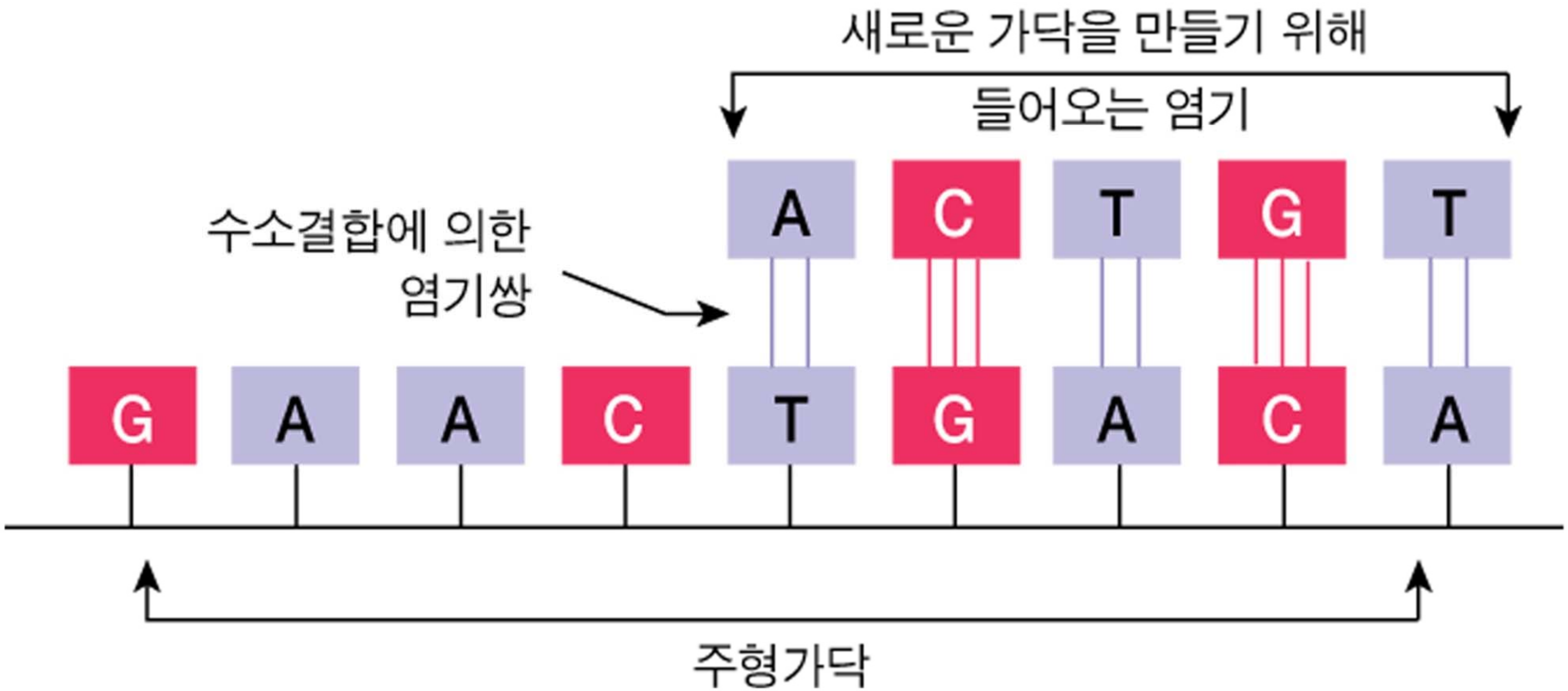
New strand synthesis

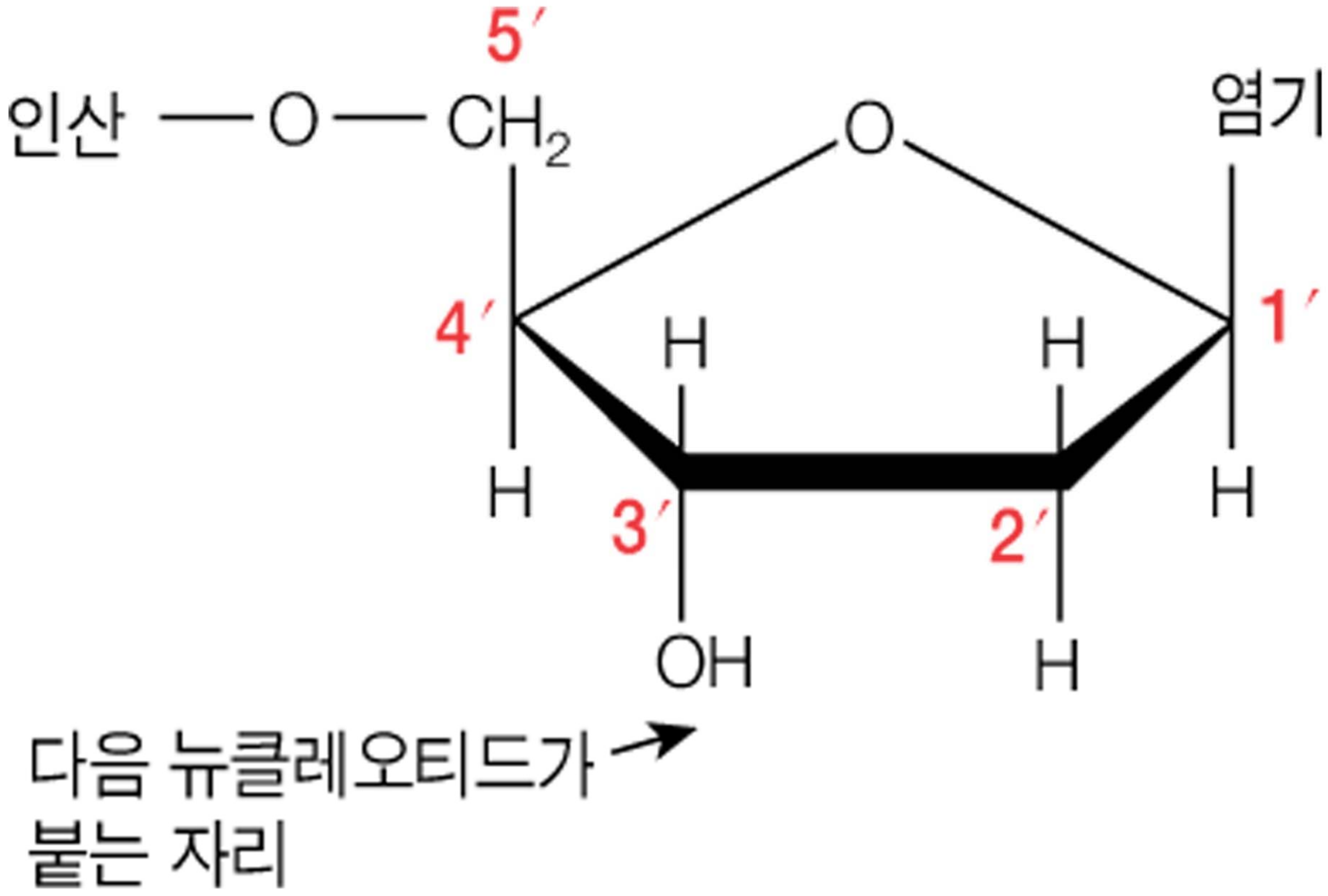
- Replication fork: region where the enzymes replicating a DNA molecule are bound to untwisted, single strand DNA

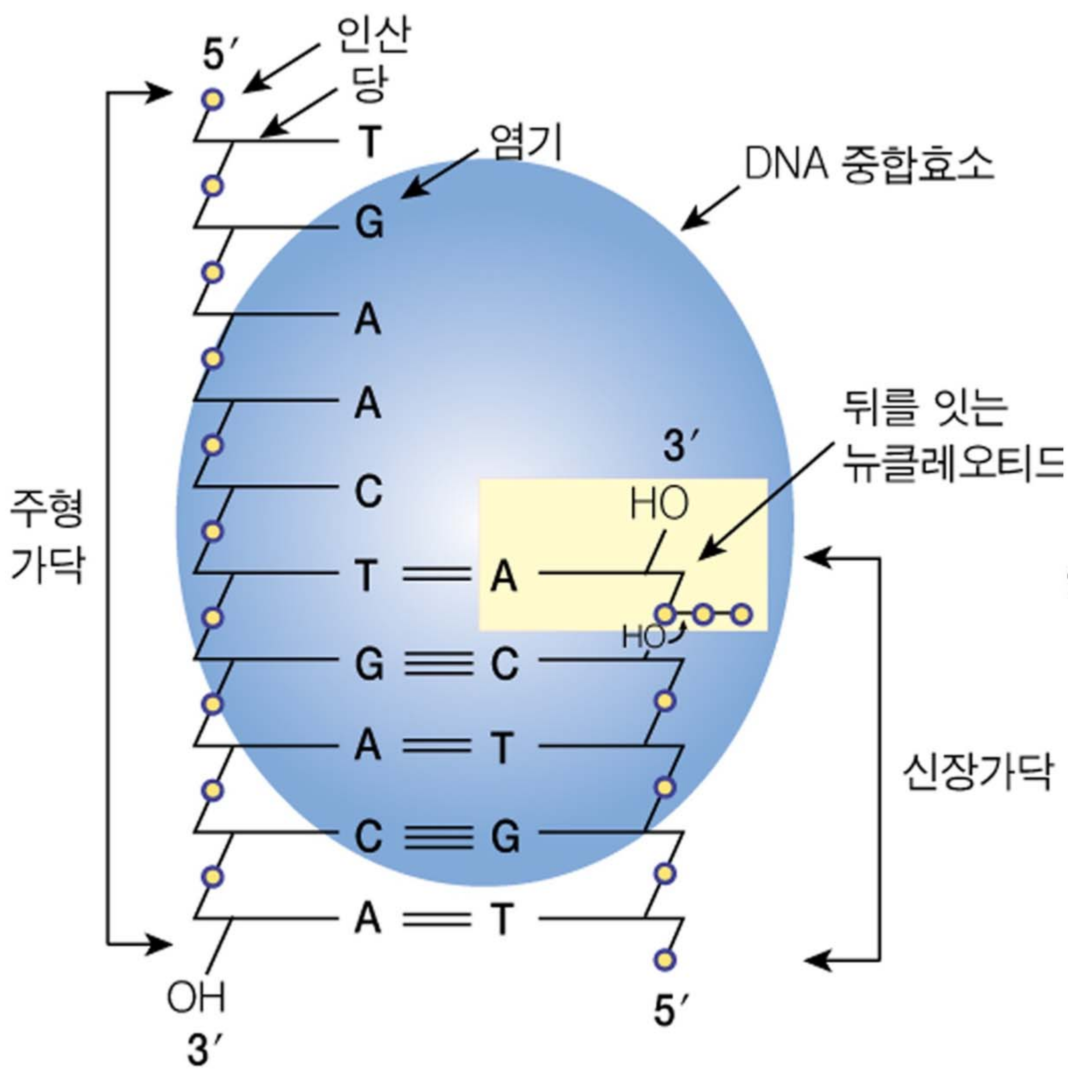
- In replication fork, one strain is made continuously (leading strand) and the other strand can be only made in short segments (lagging strand)

- Lagging strands consist of Okazaki fragments, which joined together to give a complete strand by DNA polymerase I and DNA ligase

New strand synthesis by 'Strong bond' & 'Weak bond'




5′
인산
O
CH2
O
염기
4′
H
H
1′
H
H
3′
2′
OH
H
다음 뉴클레오티드가
붙는 자리



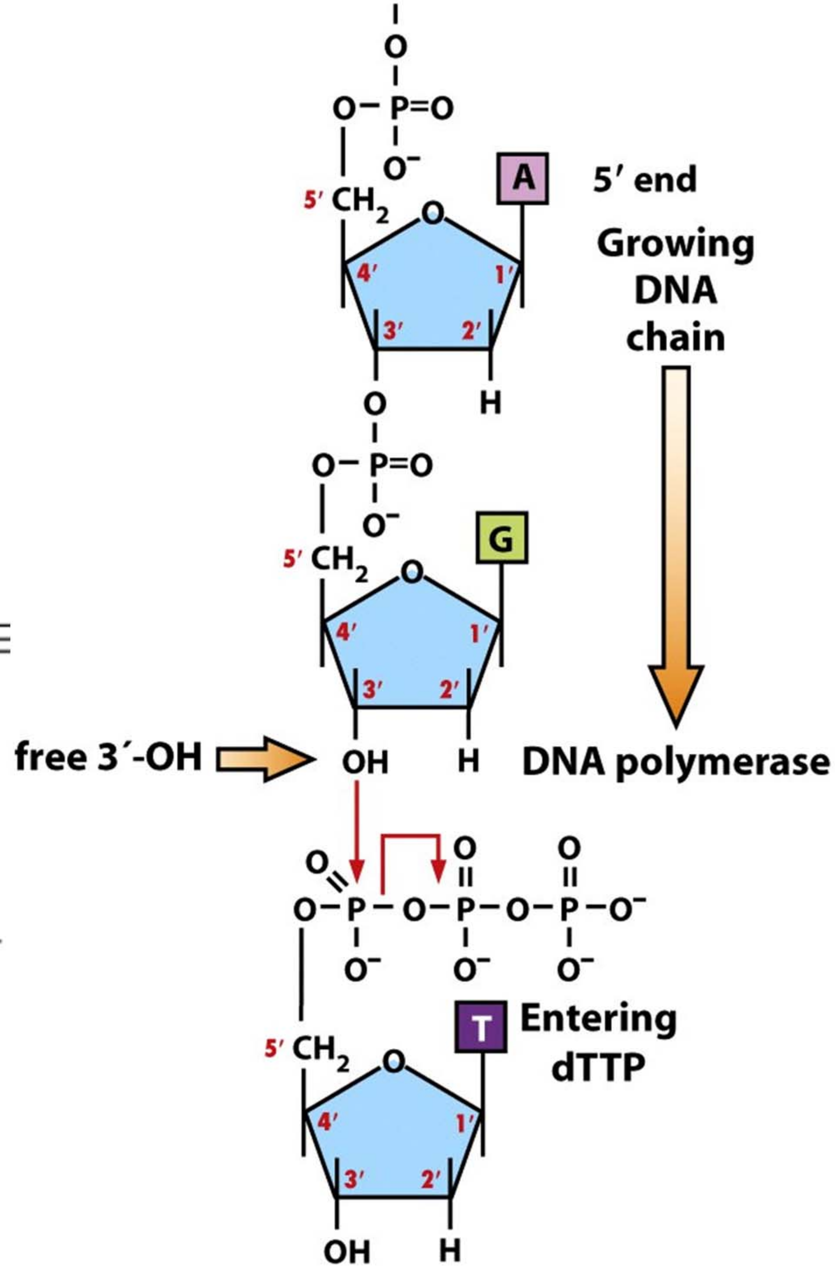
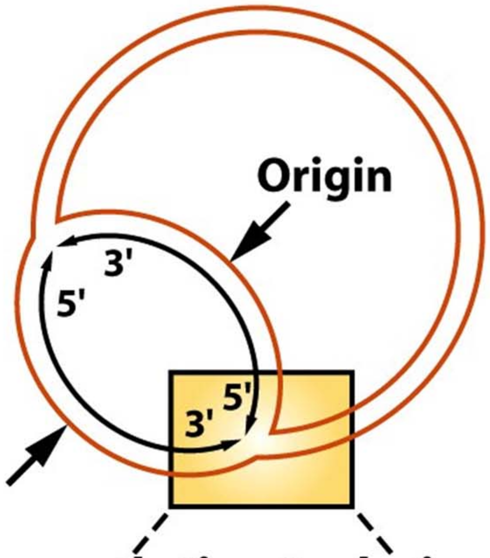


Figure 10-11 Principles of Genetics, 4/e



Relatively low-resolution techniques such as autoradiography and electron microscopy show that at the macromolecular level both nascent DNA chains are extended in the same overall direction at each replication fork.

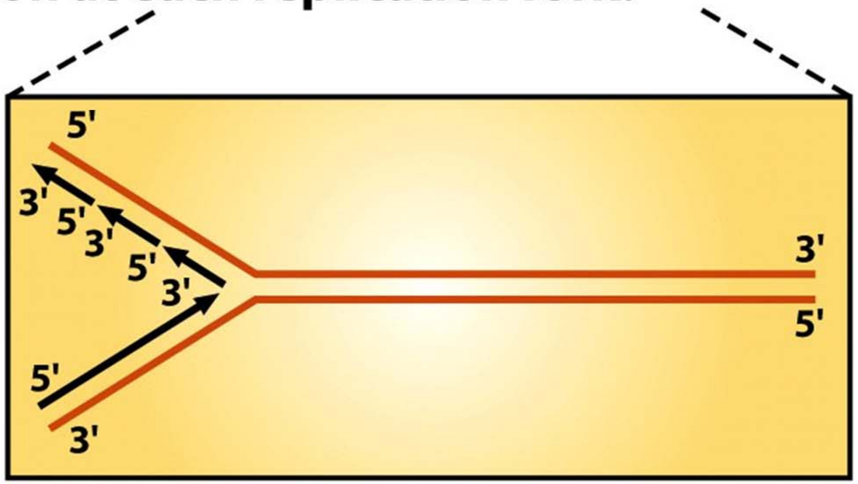
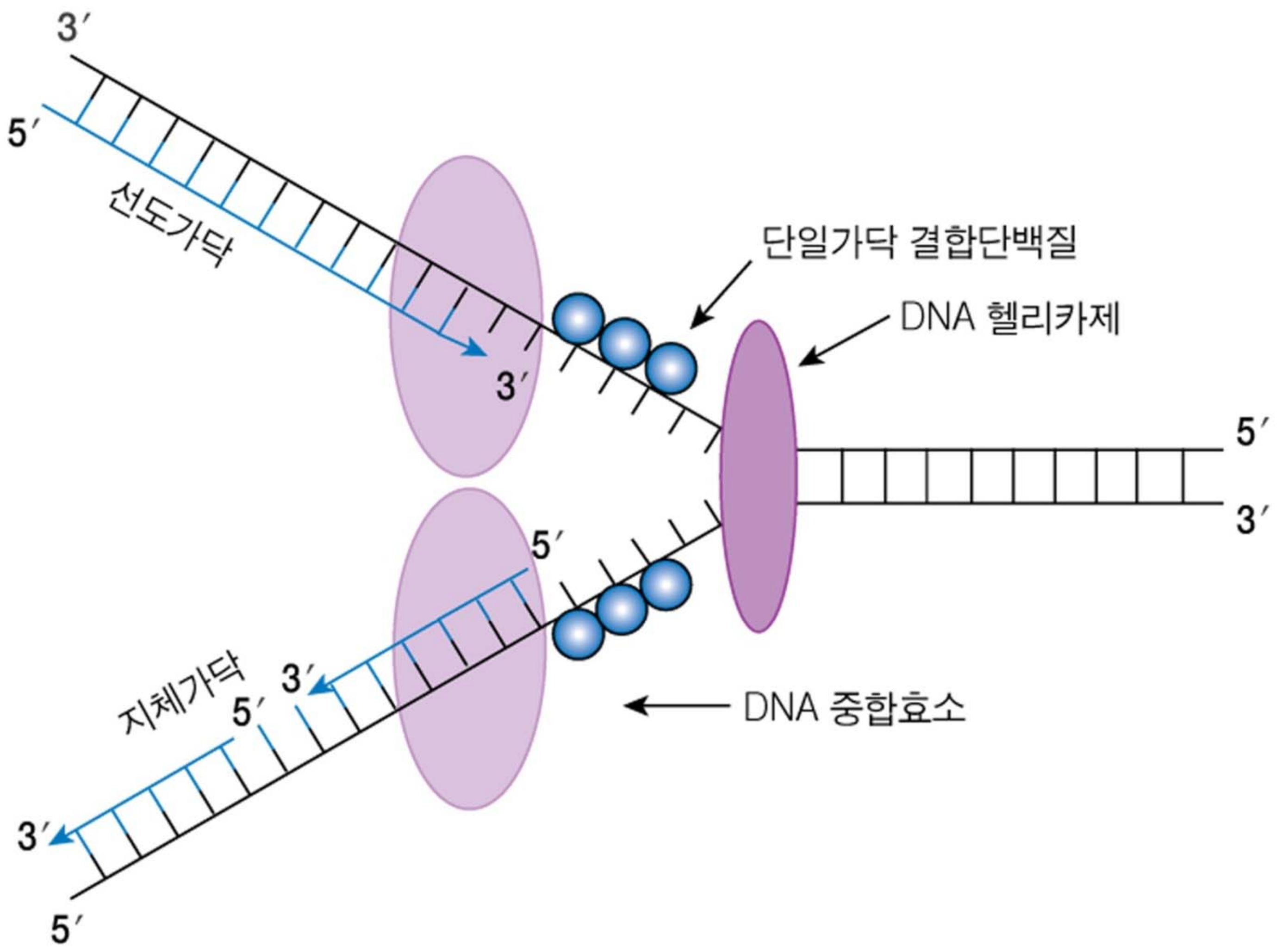


Figure 10-17a Principles of Genetics, 4/e

New strand synthesis

- Short RNA pieces called primers get a new strand started for both leading and lagging strand, and primers are made by primase
- The bacterial chromosome is circular and replication proceeds in both directions at an origin around the circle (one origin, one replication fork)
- Eukaryotic chromosome is linear, several replication forks are scattered and start at a separate origin of replication (replication bubble)
- Eukaryotic cell cycle is subdivided into four phases:
  - G1 (gap1), S (DNA synthesis), G2 (gap2), M (mitosis)
- Mitosis of eukaryotic cells is subdivided into four phases:
  - prophase, metaphase, anaphase, telophase

Replication Fork



Proofreading Activities of DNA Polymerases

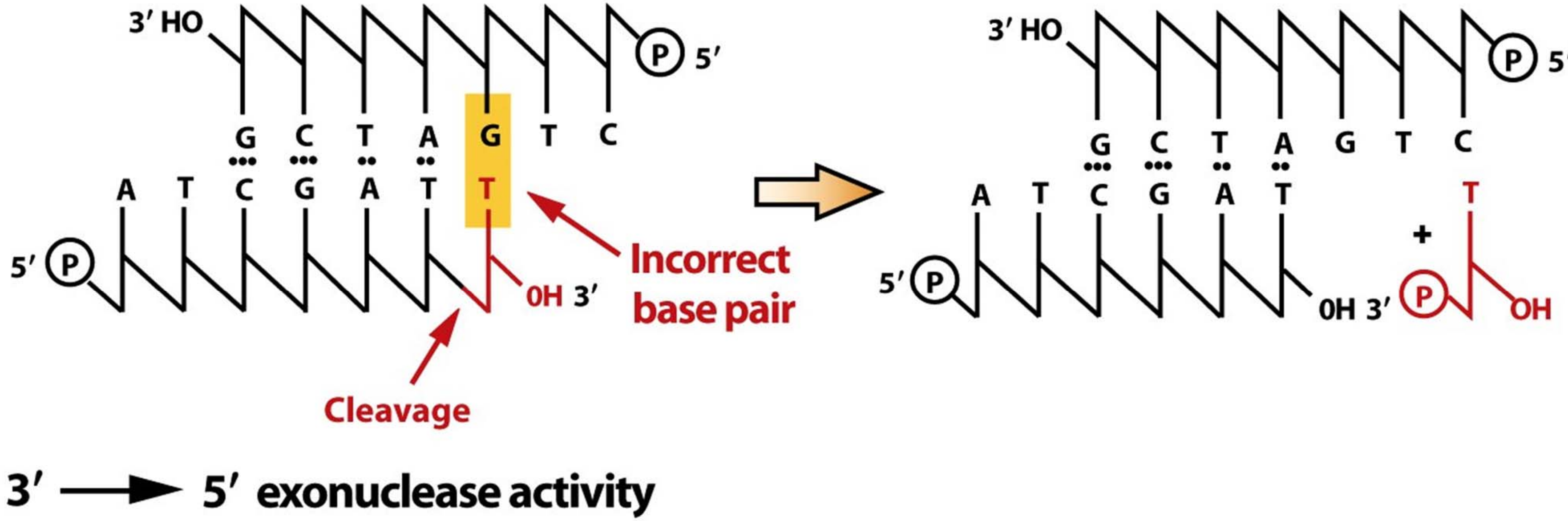
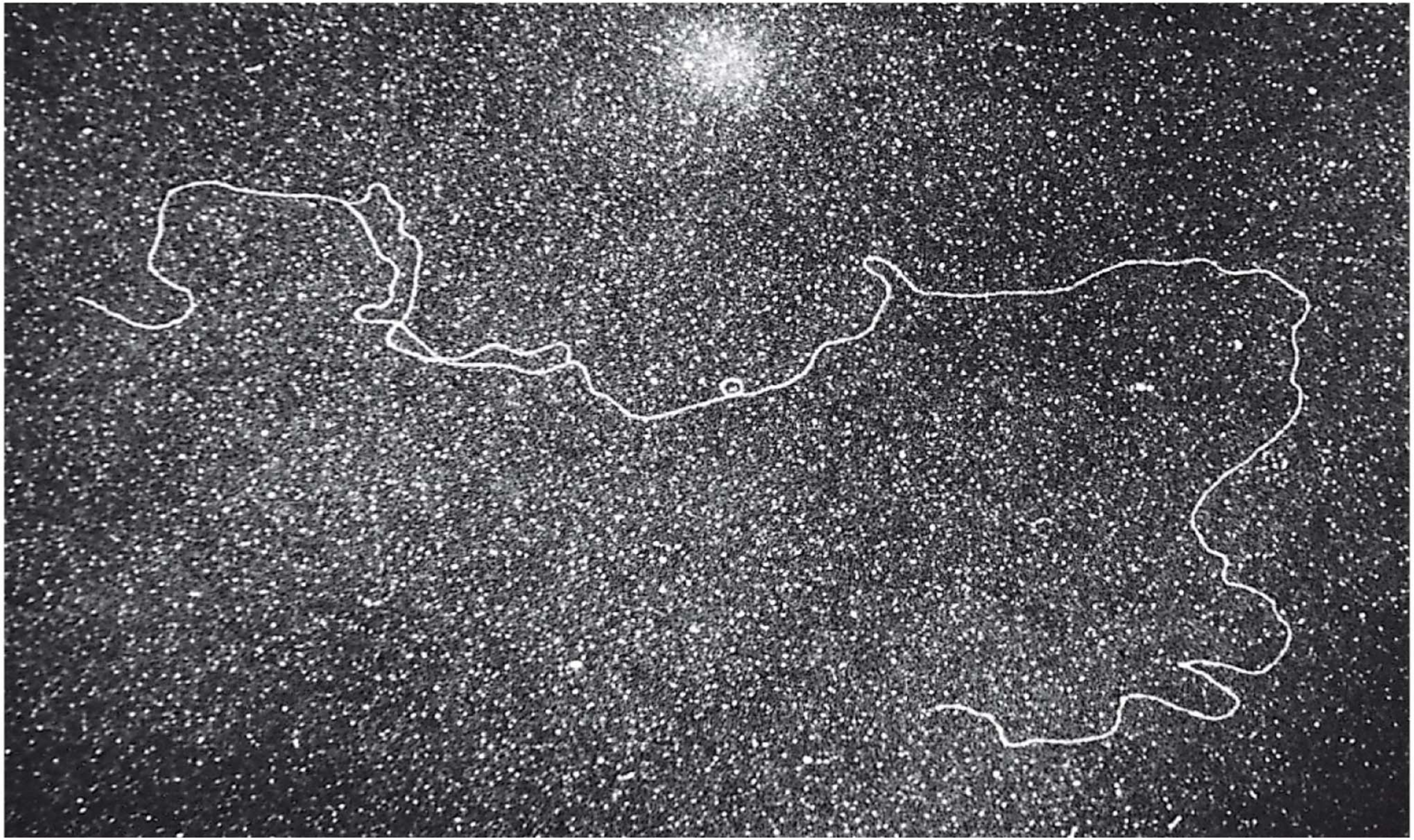
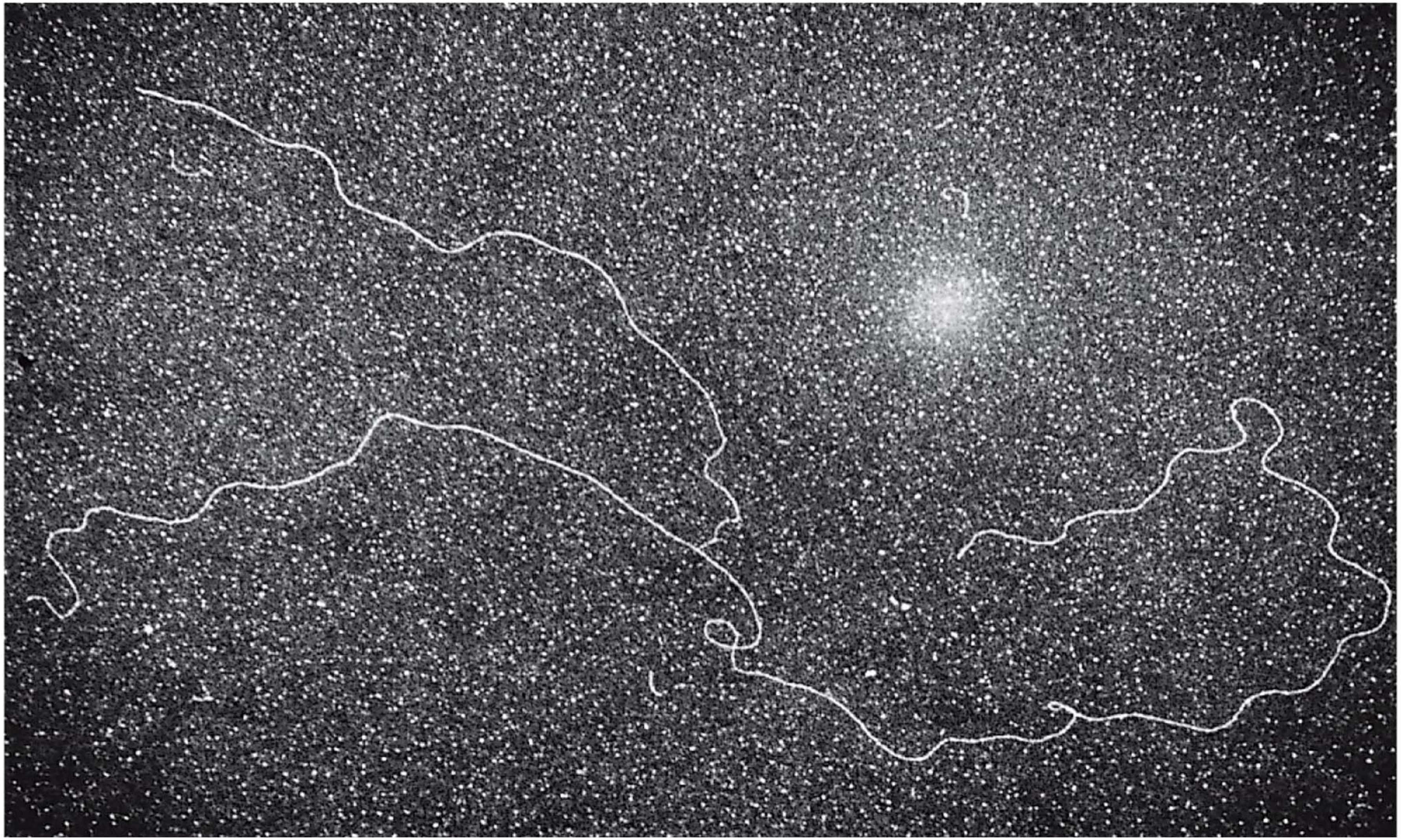


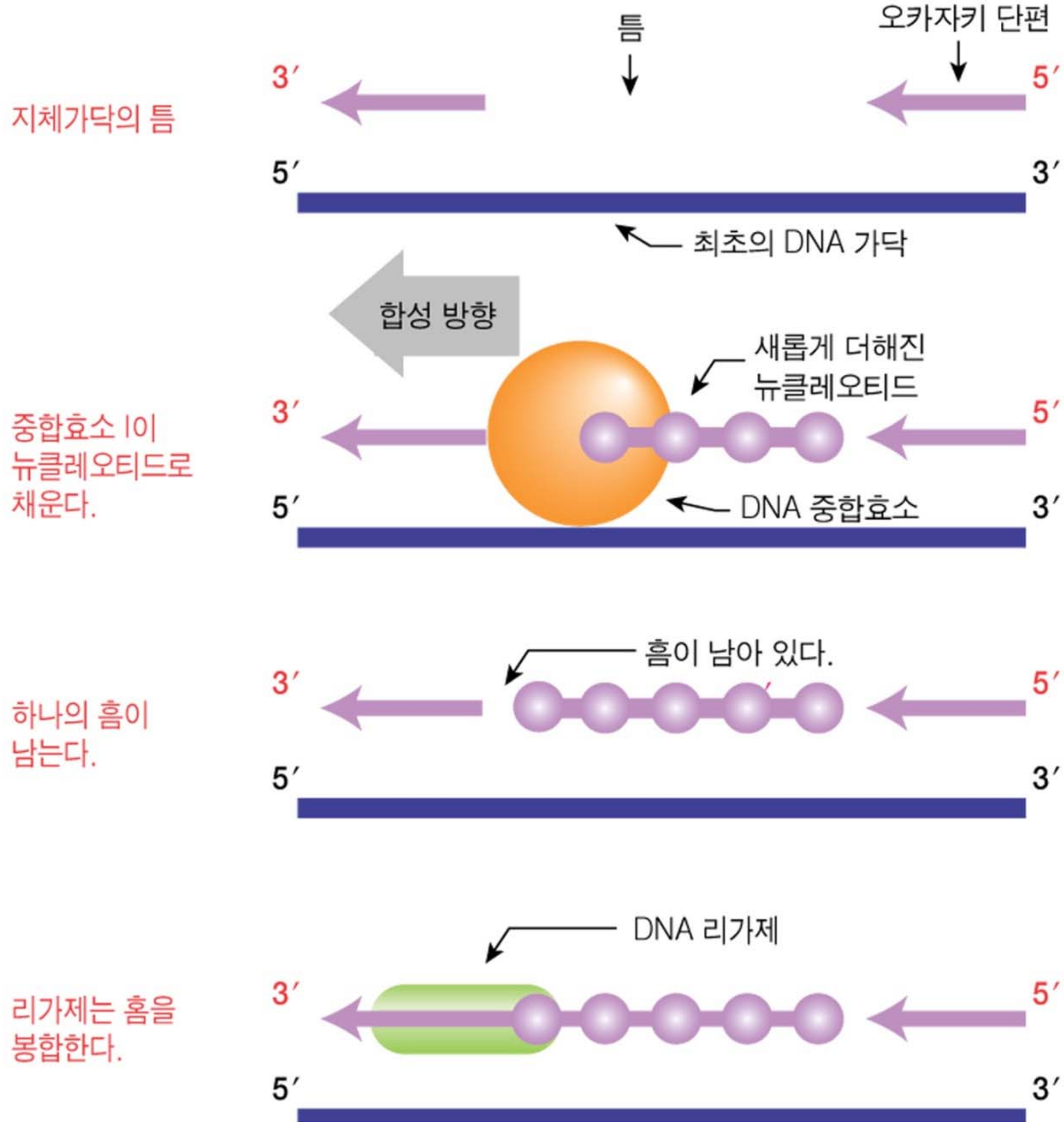
Figure 10-12c Principles of Genetics, 4/e



Electron micrographs of replicating bacteriophage T7 chromosomes. The phage T7 chromosome, unlike the *E. coli* and phage λ chromosomes, replicates as a linear structure.



Replication proceeds bidirectionally from the origin until the fork moving in a leftward direction reaches the left end of the molecule, yielding a Y-shaped structure such as that shown in (*b*).



틈
오카자키 단편
지체가닥의 틈
3′
5′
5′
3′
최초의 DNA 가닥
합성 방향
새롭게 더해진
뉴클레오티드
중합효소 I이
뉴클레오티드로
채운다.
3′
5′
DNA 중합효소
5′
3′
흠이 남아 있다.
하나의 흠이
남는다.
3′
5′
5′
3′
DNA 리가제
리가제는 흠을
봉합한다.
3′
5′
5′
3′

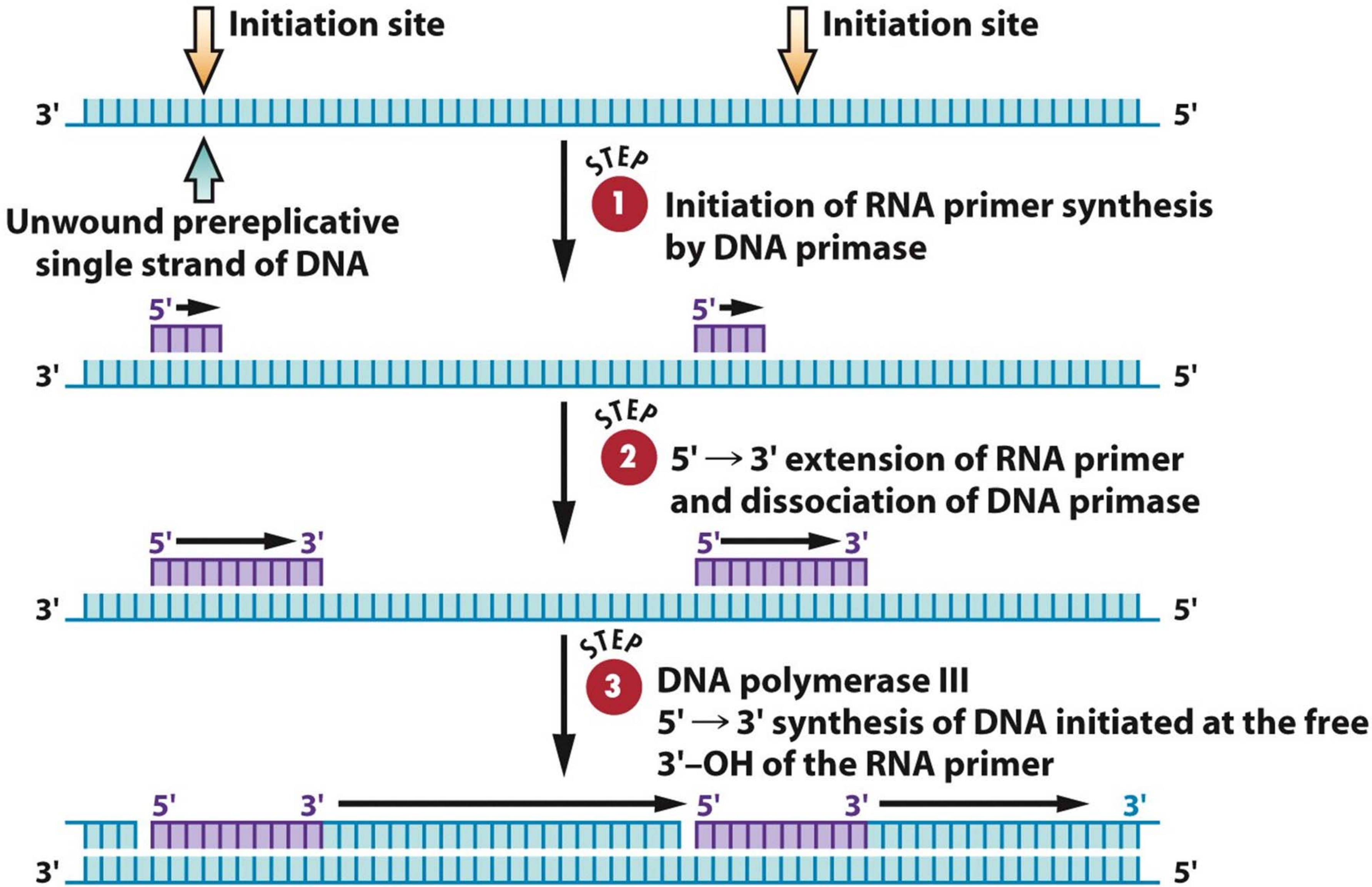


Figure 10-20 part 1 Principles of Genetics, 4/e

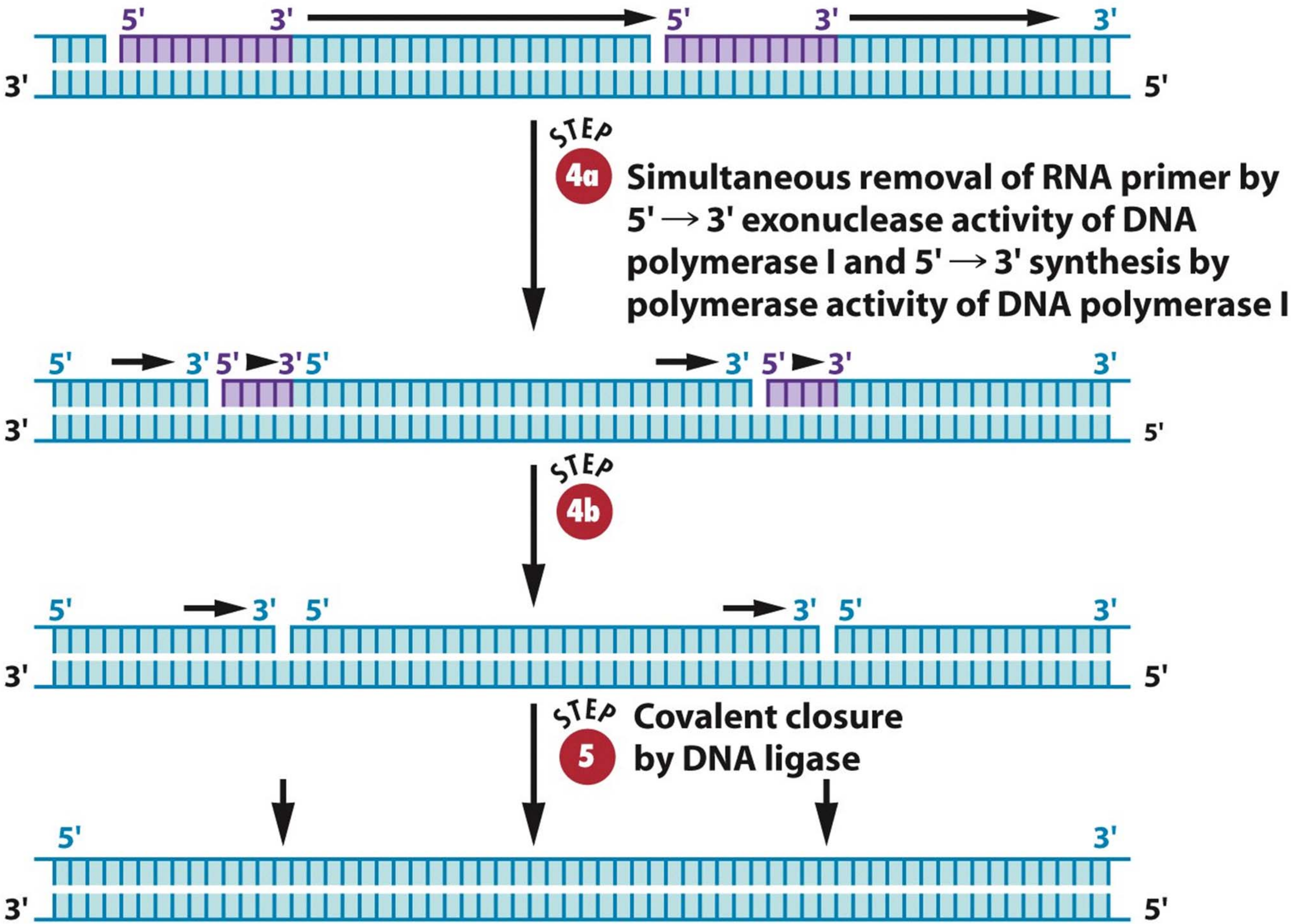
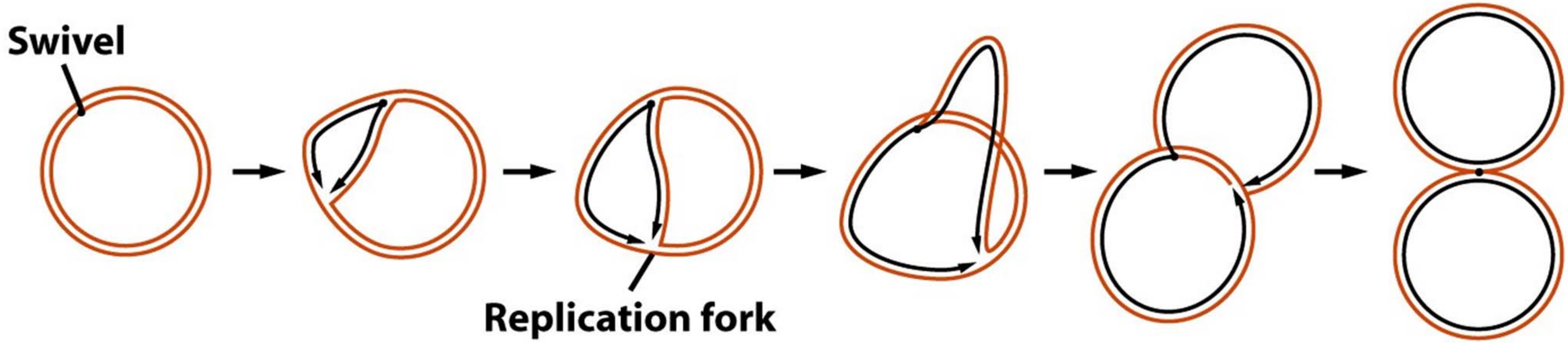
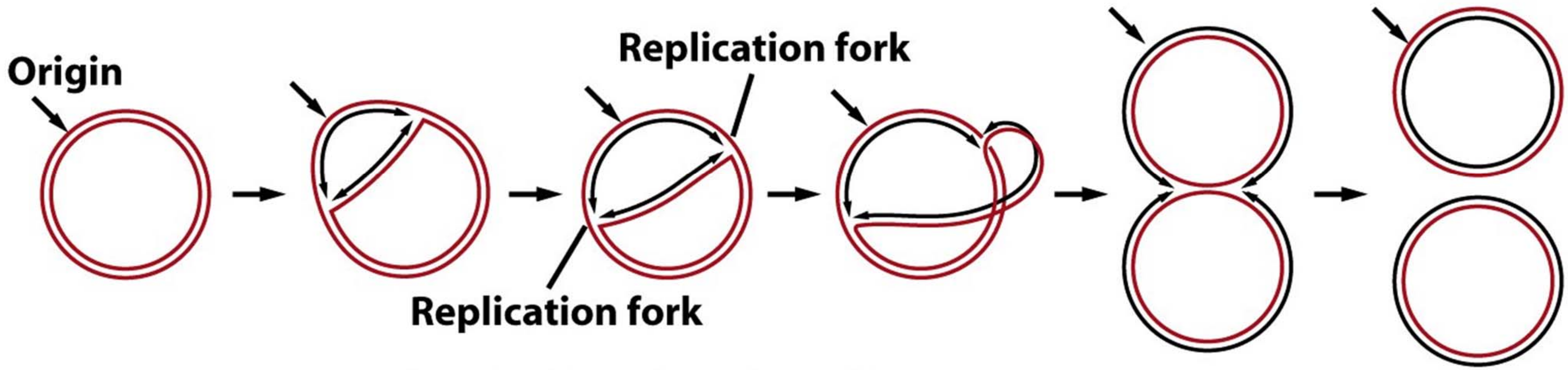


Figure 10-20 part 2 Principles of Genetics, 4/e

DNA replicates bidirectional



Original interpretation: unidirectional replication.



Correct interpretation: bidirectional replication.

Figure 10-3bc Principles of Genetics, 4/e

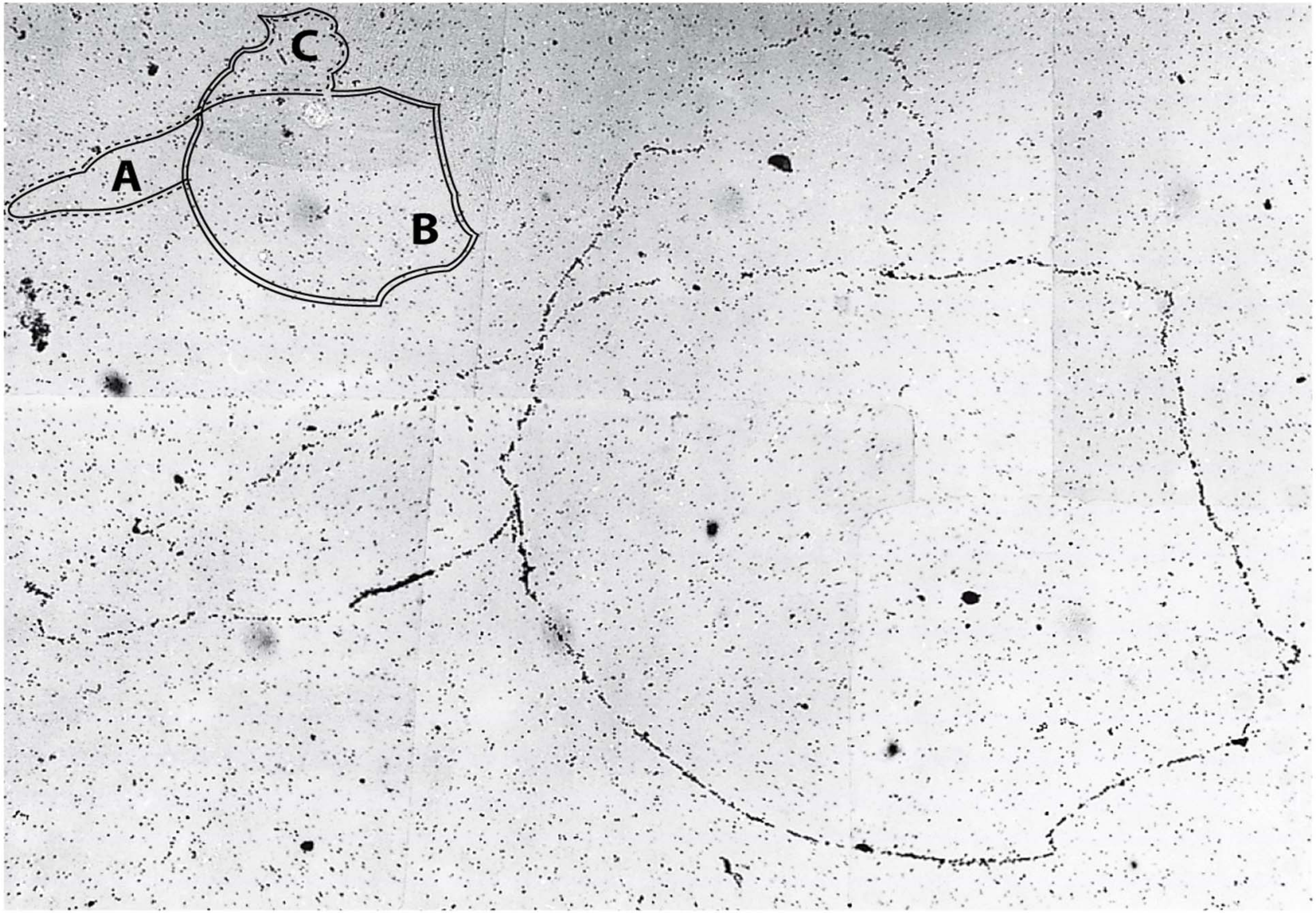
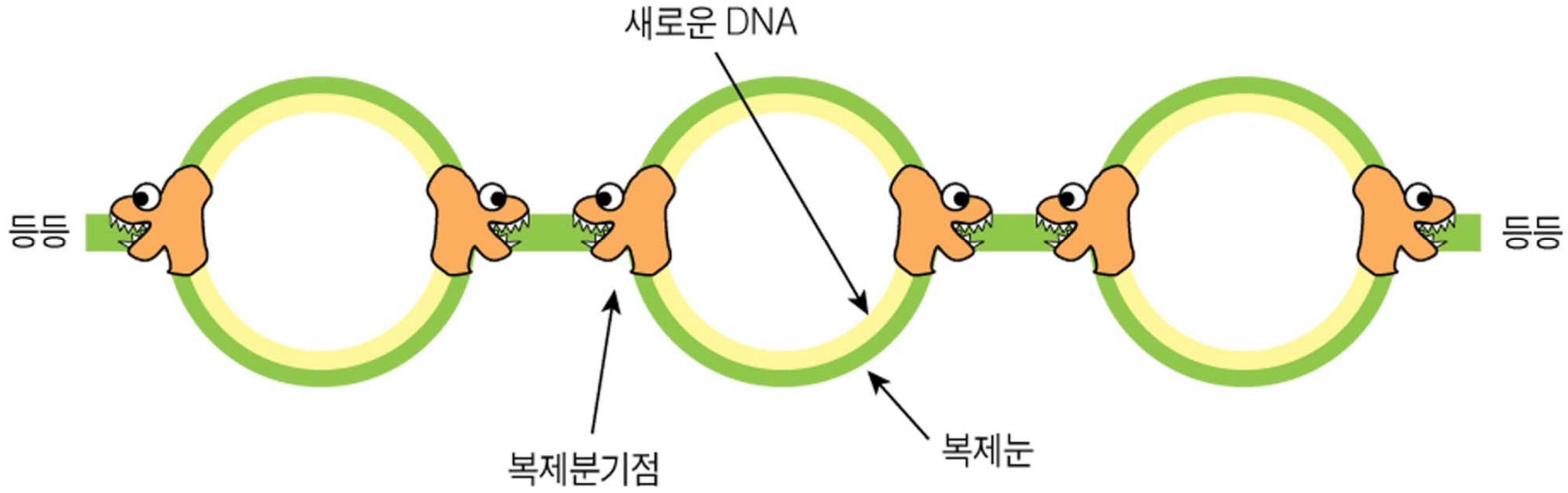


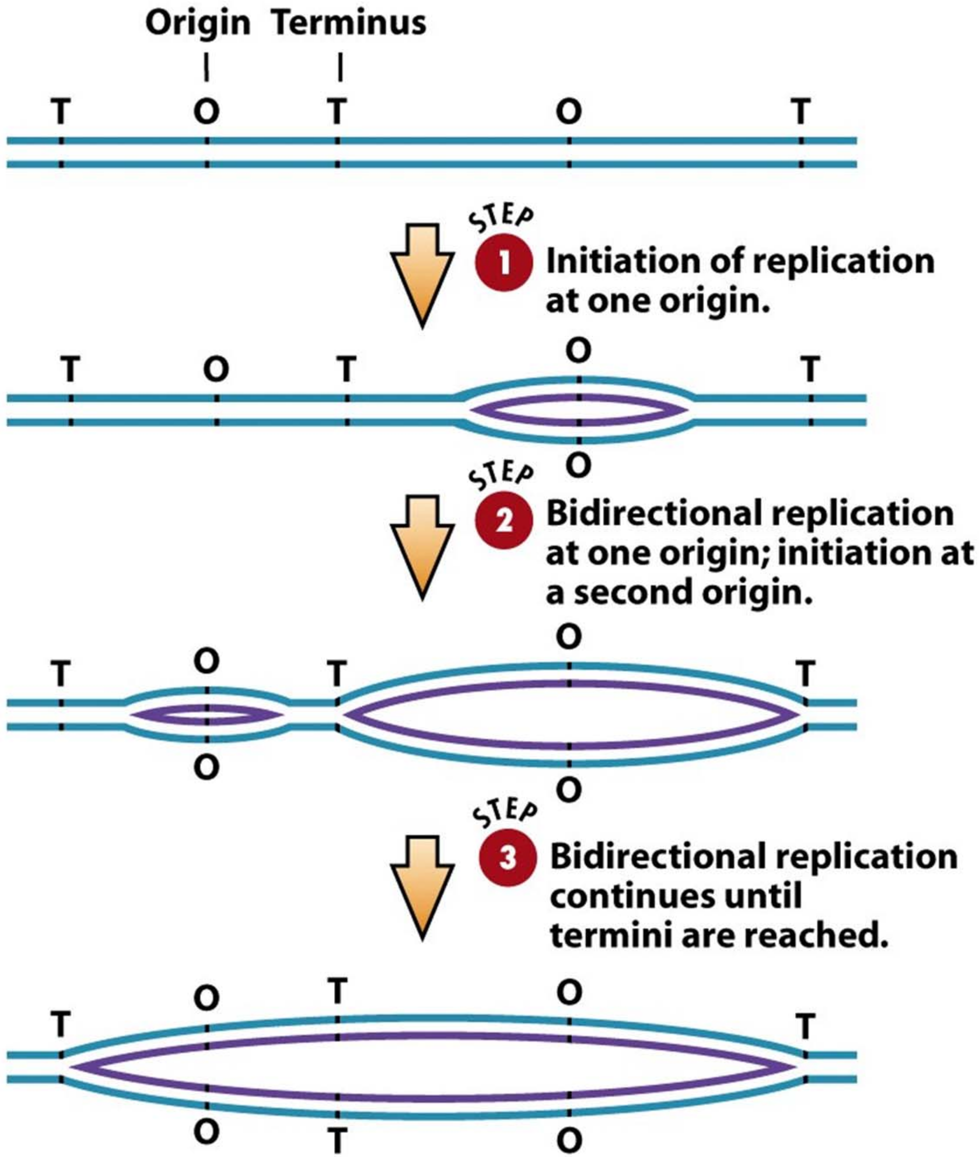
Figure 10-3a Principles of Genetics, 4/e

θ-shaped replicating chromosome

For fast DNA replication?



Replication bubbles in eukaryotes



Diagrammatic interpretation of the replication of the DNA molecules visualized above.

Figure 10-29c Principles of Genetics, 4/e

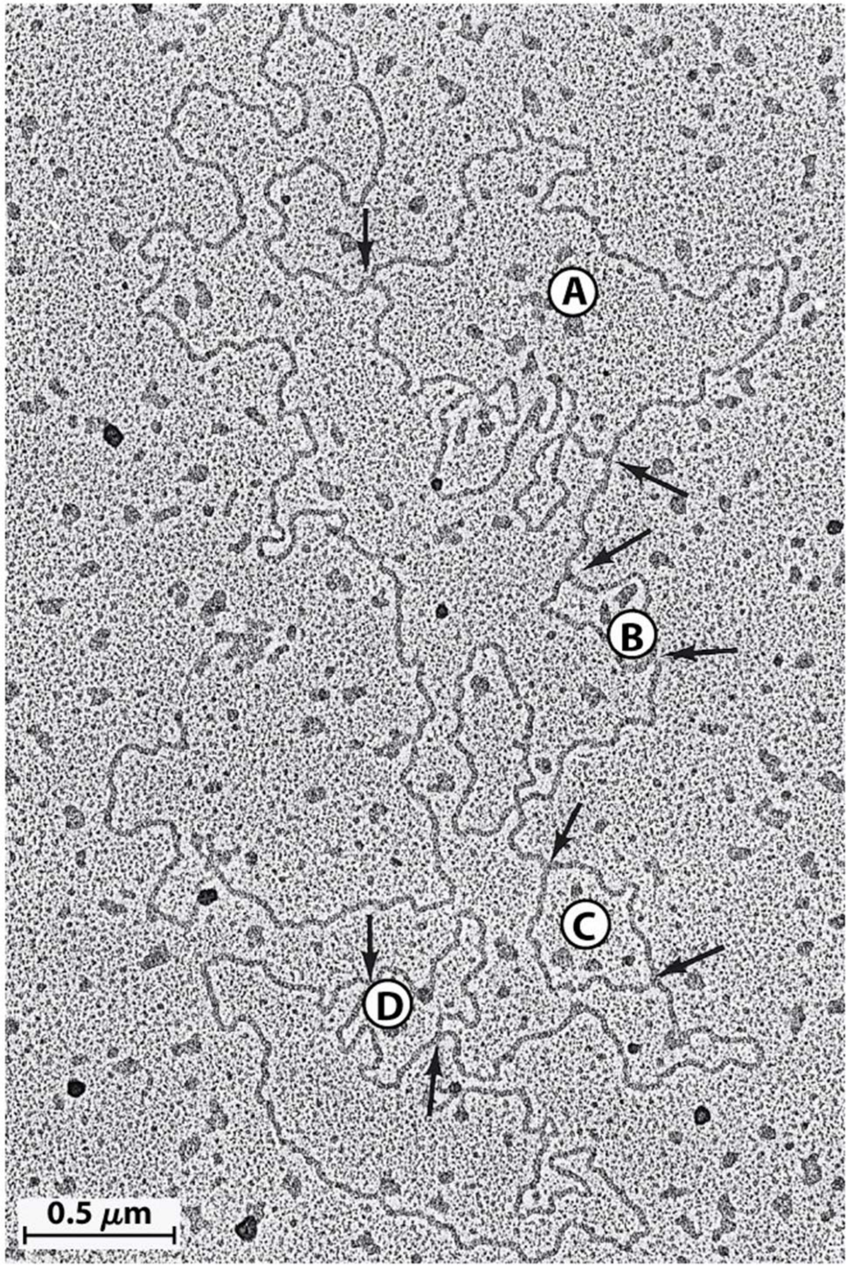


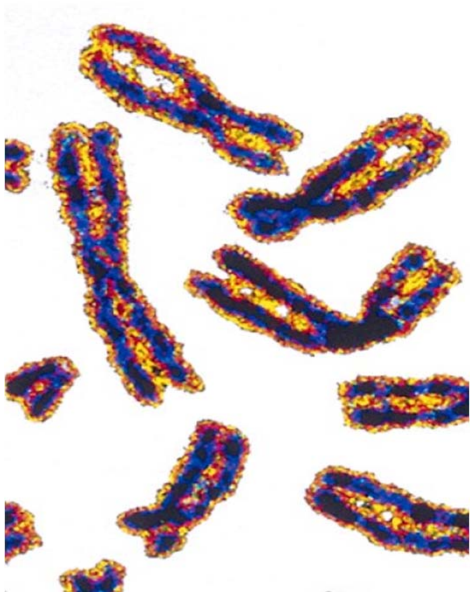
Figure 10-30 Principles of Genetics, 4/e

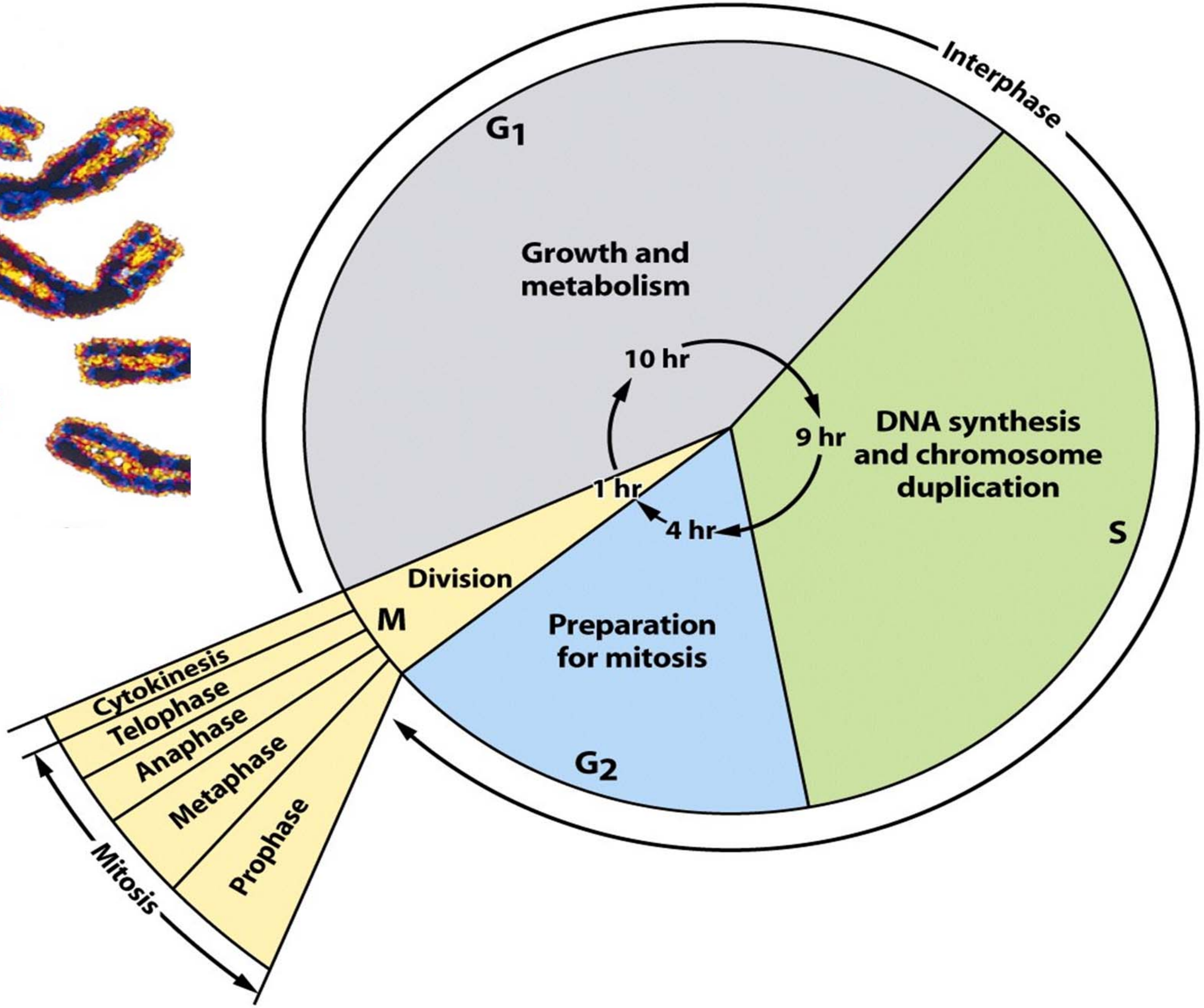
Electron micrograph of a DNA molecule in *D. melanogaster* showing multiple sites of replication.

Four eye-shaped replication structures (labeled A-D) are present in the segment of the DNA molecule shown.

The arrows show the positions of replication forks.

All these happen where?





DNA replication, telomere, telomerase, and aging !