The Molecular Basis of Inheritance

Overview: Life's Operating Instructions

- In 1953, James Watson and Francis Crick introduced an elegant double-helical model for the structure of deoxyribonucleic acid, or DNA
- DNA, the substance of inheritance, is the most celebrated molecule of our time
- Hereditary information is encoded in DNA and reproduced in all cells of the body
- This DNA program directs the development of biochemical, anatomical, physiological, and (to some extent) behavioral traits

Fig. 16-1

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Additional Evidence That DNA Is the Genetic Material

- It was known that DNA is a polymer of nucleotides, each consisting of a nitrogenous base, a sugar, and a phosphate group
- In 1950, Erwin Chargaff reported that DNA composition varies from one species to the next
- Chargaff’s rules state that in any species there is an equal number of A and T bases, and an equal number of G and C bases

Fig. 16-5

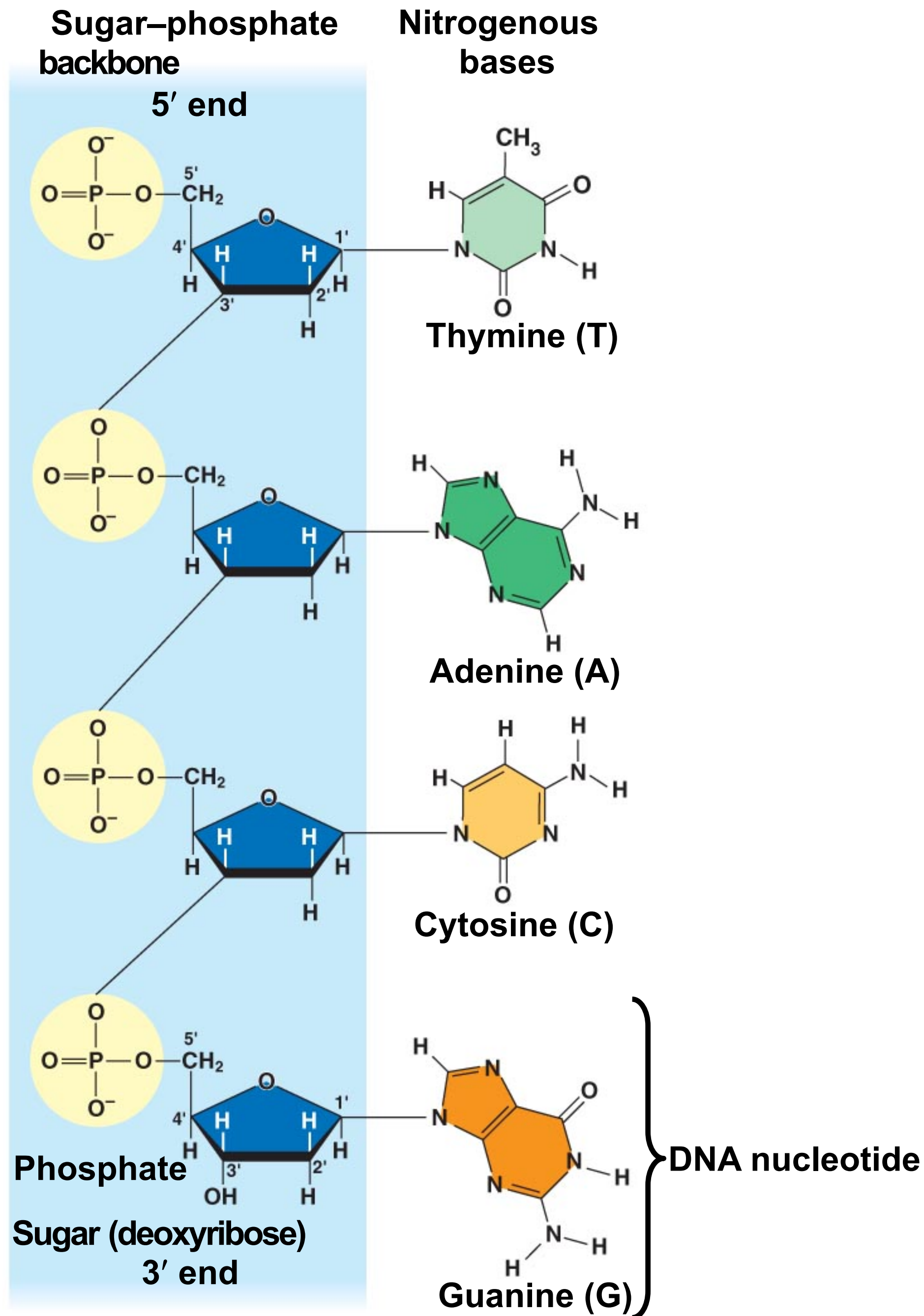

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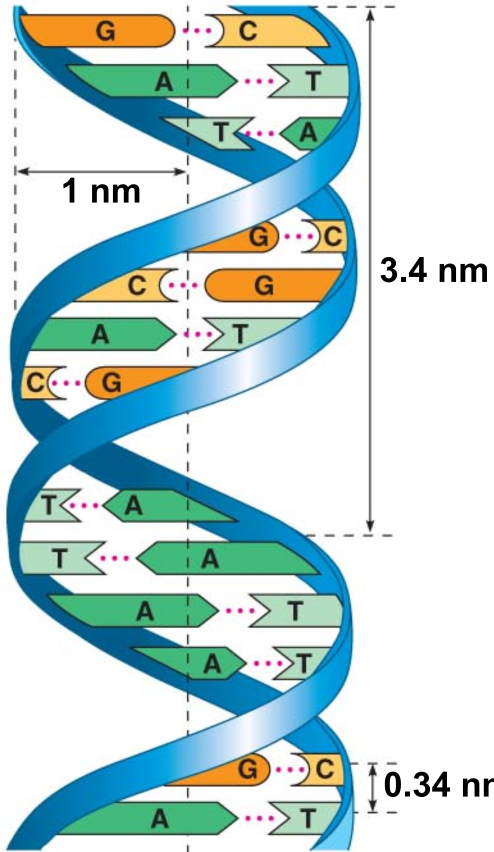
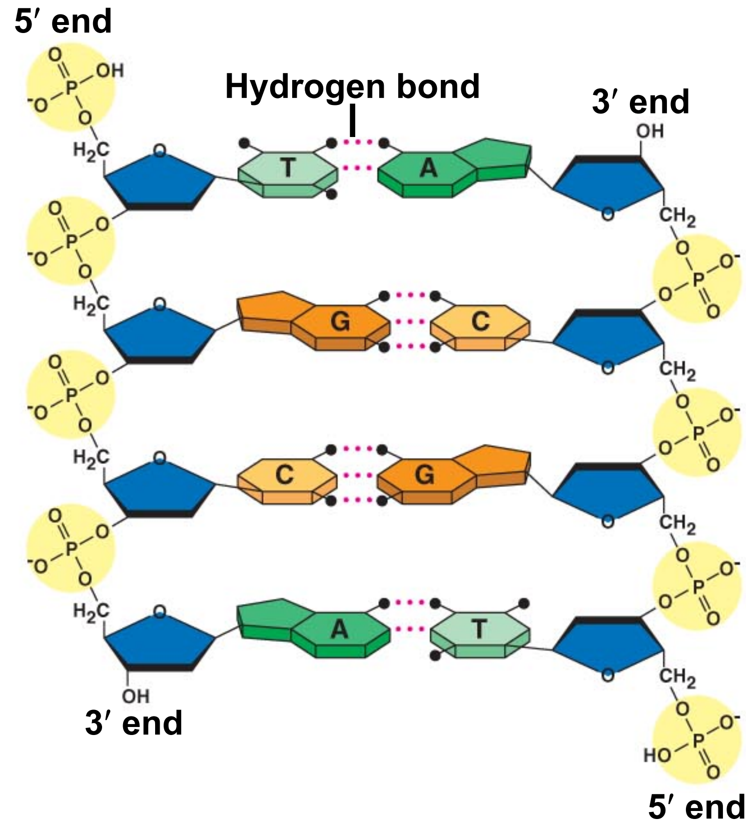
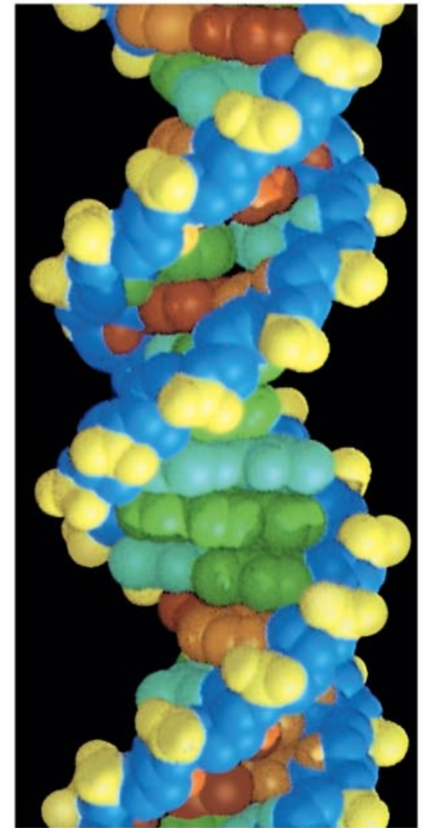
Fig. 16-7



(a) Key features of DNA structure



(b) Partial chemical structure



(c) Space-filling model

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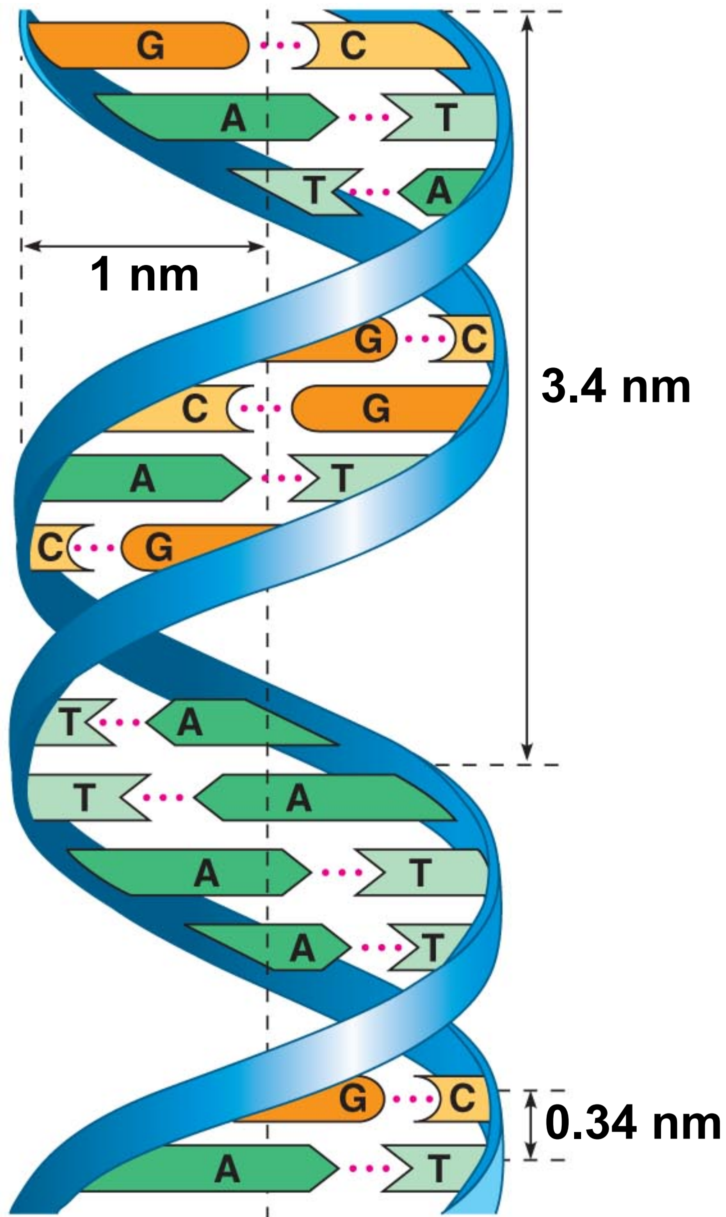
Fig. 16-7a



(a) Key features of DNA structure

5′ end
Hydrogen bond
3′ end
OH
H_2C
T
A
G
C
C
G
A
T
CH_2
OH
3′ end
HO
5′ end

(b) Partial chemical structure

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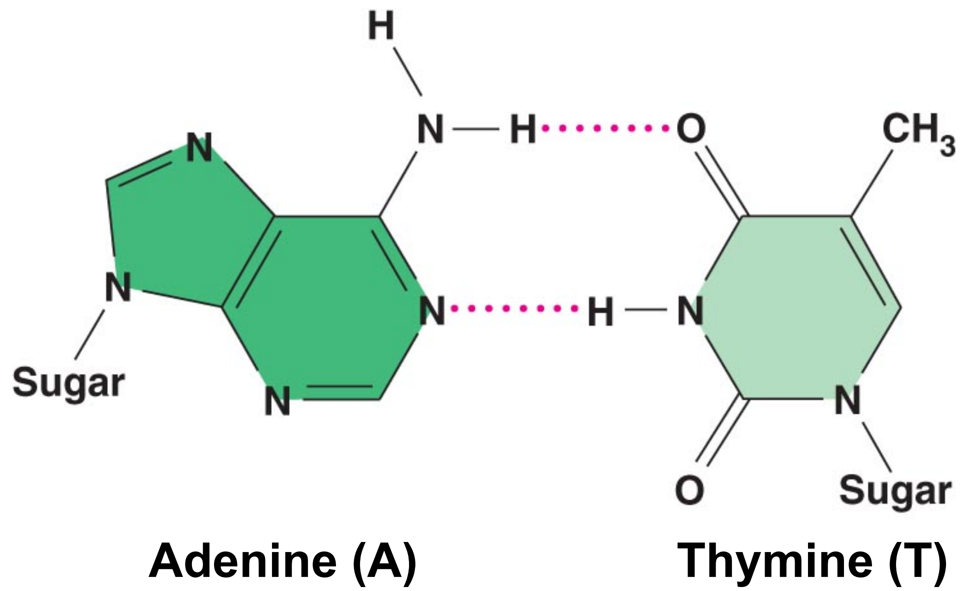
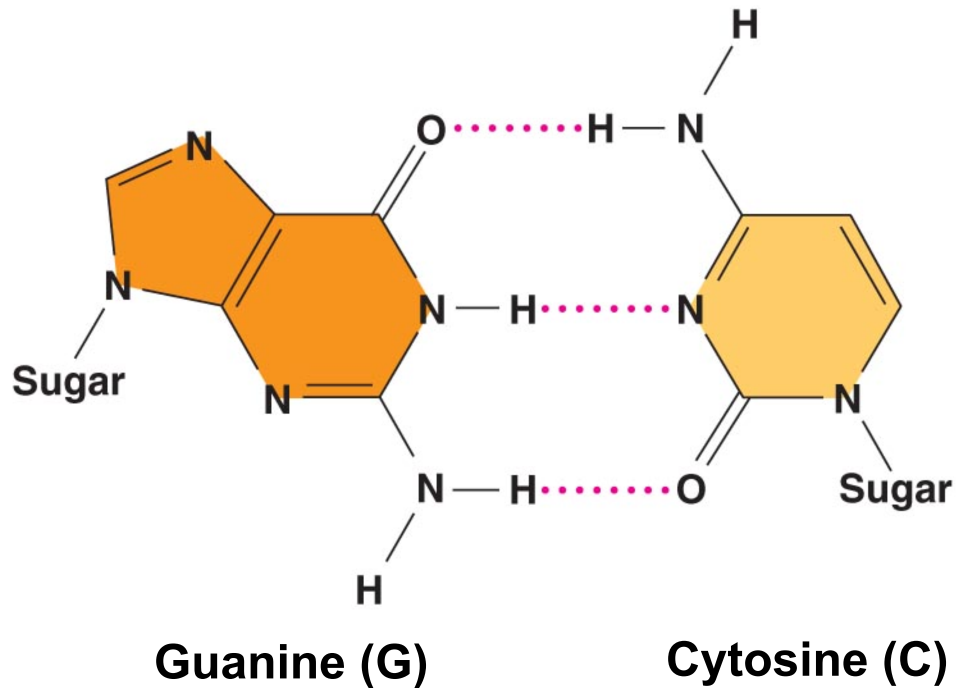
Fig. 16-8





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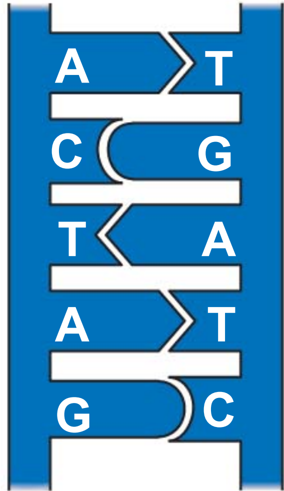
The Basic Principle: Base Pairing to a Template Strand

- Since the two strands of DNA are complementary, each strand acts as a template for building a new strand in replication
- In DNA replication, the parent molecule unwinds, and two new daughter strands are built based on base-pairing rules

Fig. 16-9-1



(a) Parent molecule

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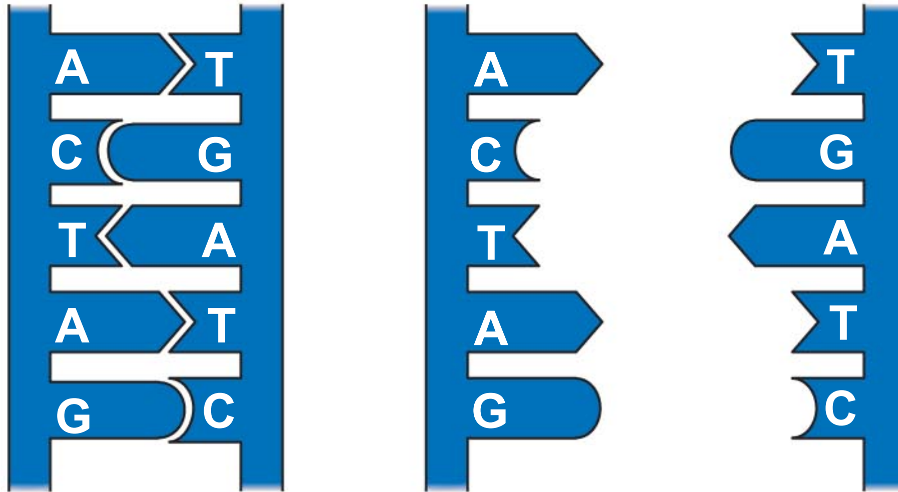
Fig. 16-9-2



(a) Parent molecule

(b) Separation of strands

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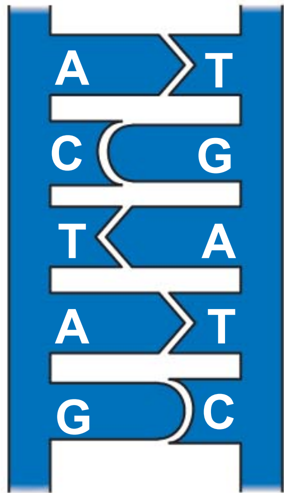
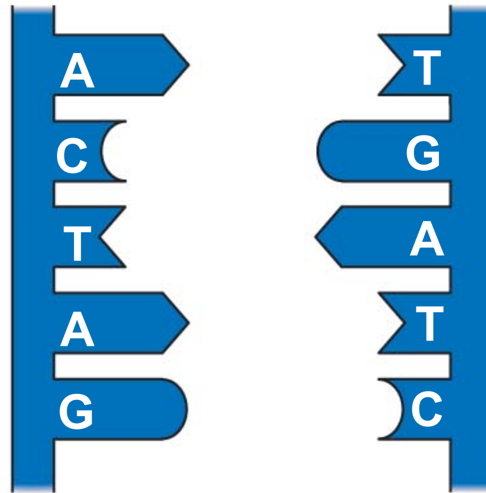
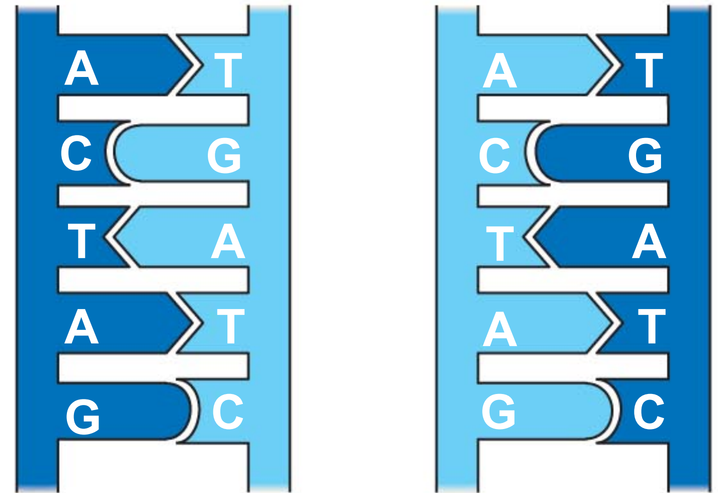
Fig. 16-9-3



(a) Parent molecule



(b) Separation of strands



(c) "Daughter" DNA molecules, each consisting of one parental strand and one new strand

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DNA Replication: *A Closer Look*

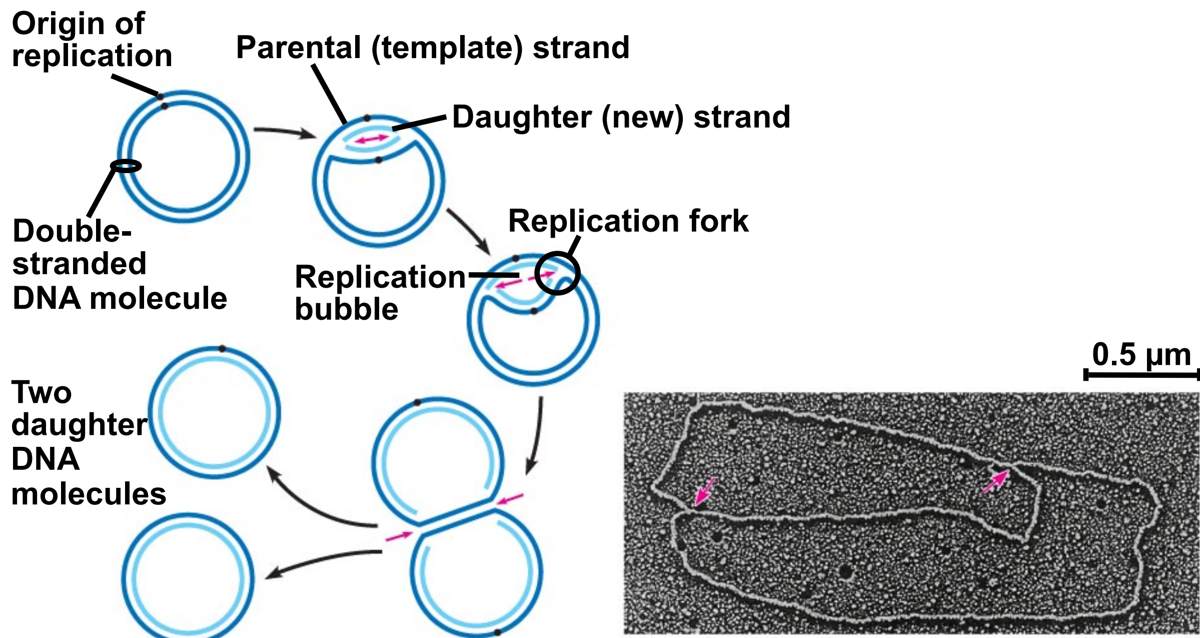
- The copying of DNA is remarkable in its speed and accuracy
- More than a dozen enzymes and other proteins participate in DNA replication

Circular (mitochondria)
versus
linear DNA (nucleus)

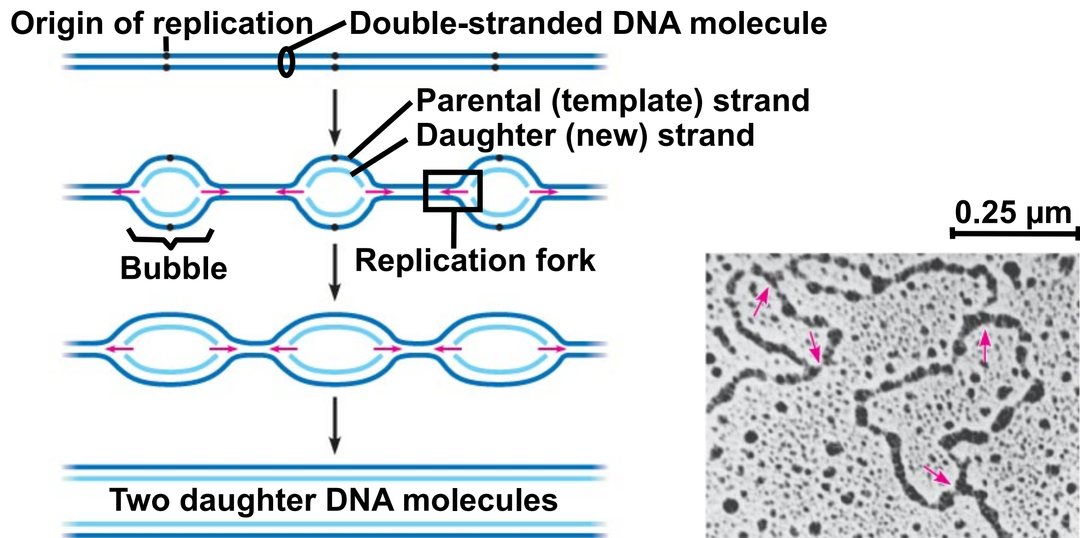
Getting Started

- Replication begins at special sites called **origins of replication**, where the two DNA strands are separated, opening up a replication "bubble"
- A eukaryotic chromosome may have hundreds or even thousands of origins of replication
- Replication proceeds in both directions from each origin, until the entire molecule is copied

Fig. 16-12



(a) Origins of replication in *E. coli*



(b) Origins of replication in eukaryotes

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- At the end of each replication bubble is a **replication fork**, a Y-shaped region where new DNA strands are elongating
- **Helicases** are enzymes that untwist the double helix at the replication forks
- **Single-strand binding protein** binds to and stabilizes single-stranded DNA until it can be used as a template
- **Topoisomerase** corrects "overwinding" ahead of replication forks by breaking, swiveling, and rejoining DNA strands

Fig. 16-13

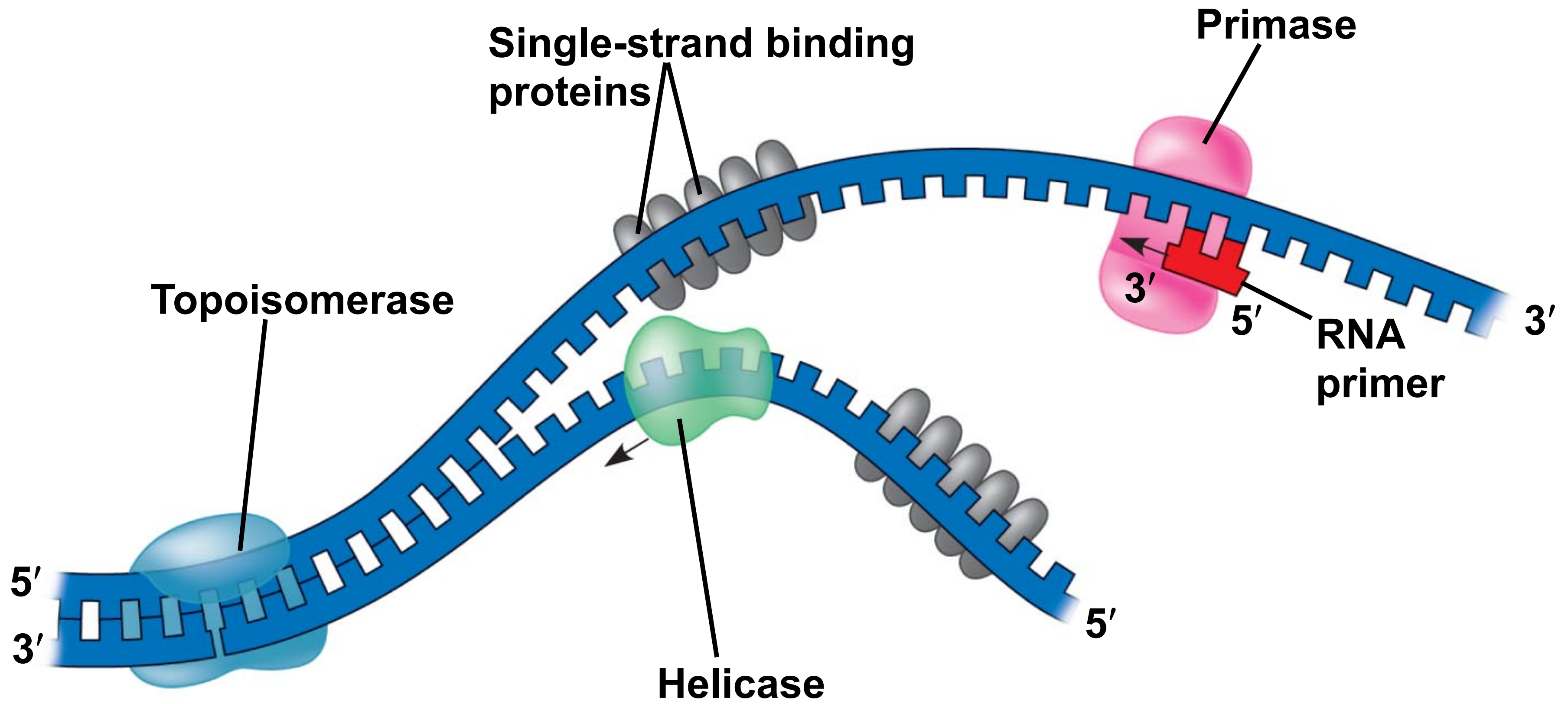

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Fig. 16-14

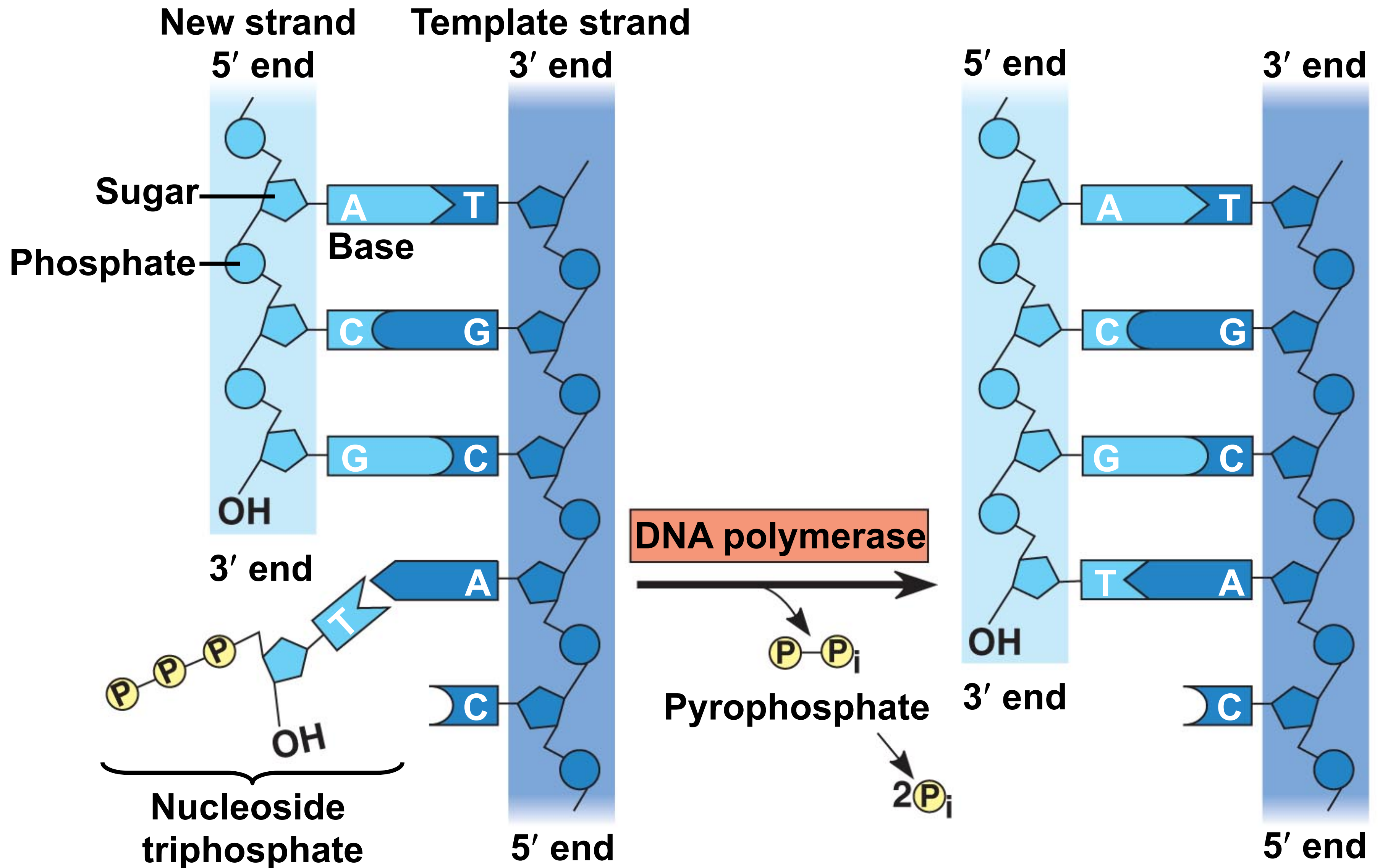

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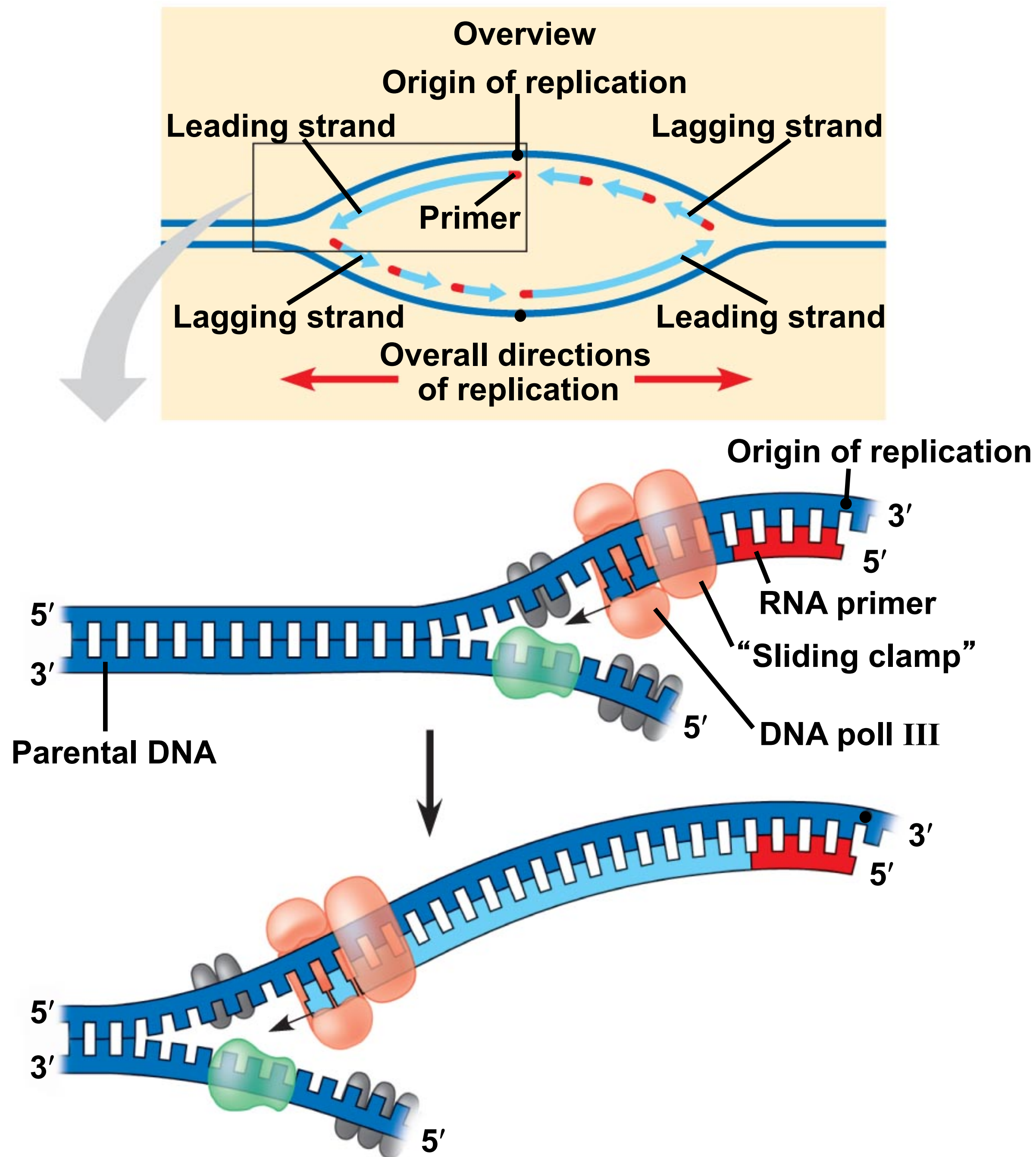
Fig. 16-15



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- To elongate the other new strand, called the **lagging strand**, DNA polymerase must work in the direction away from the replication fork
- The lagging strand is synthesized as a series of segments called **Okazaki fragments**, which are joined together by **DNA ligase**

Fig. 16-16

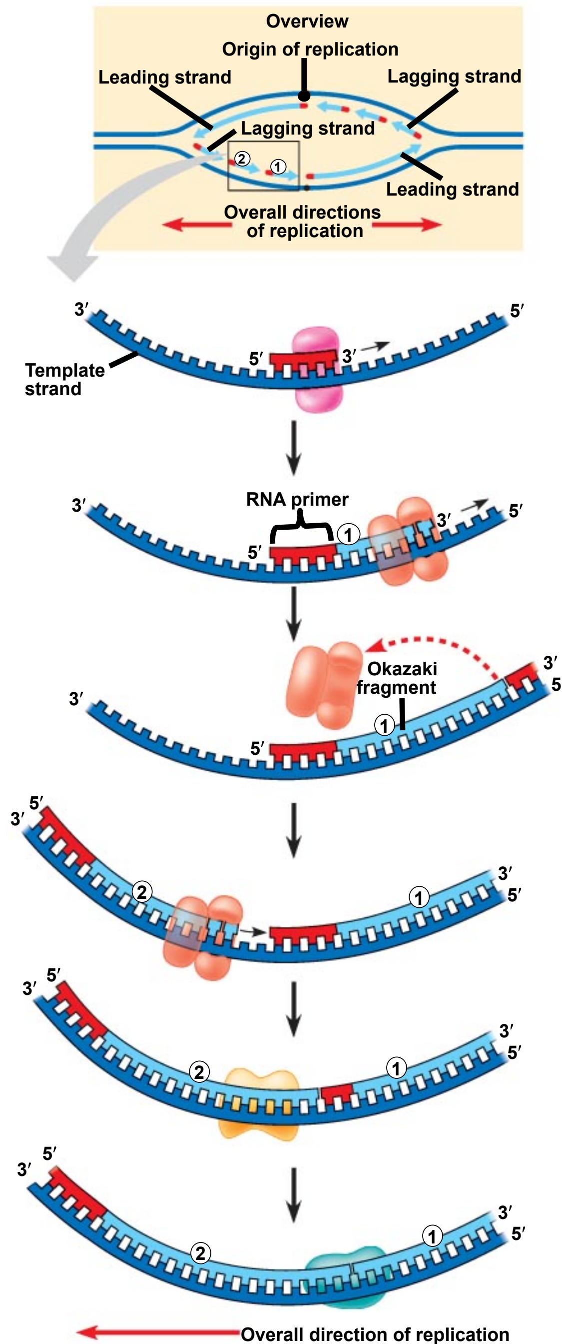

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Fig. 16-16a

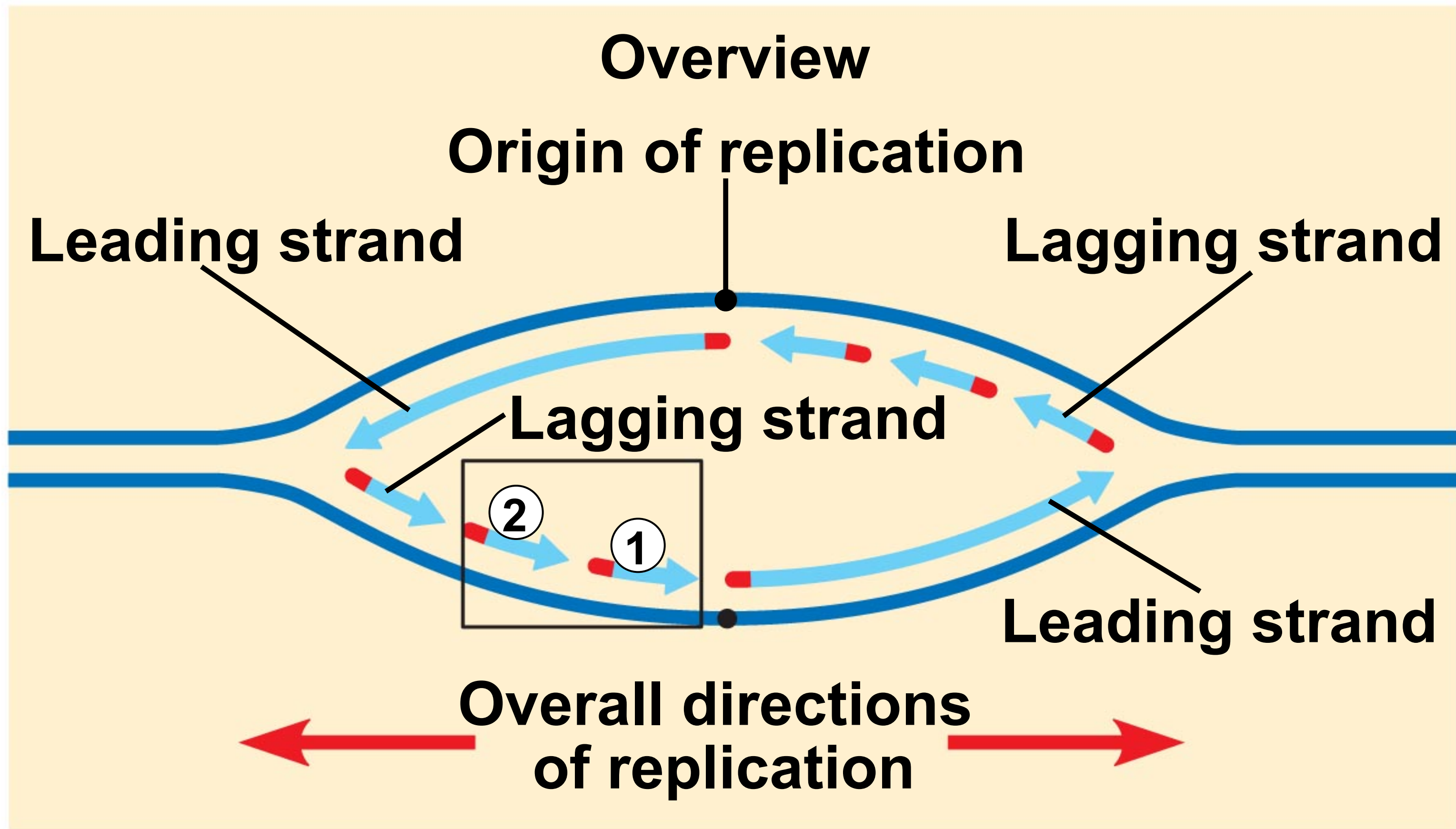

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Table 16-1

Table 16.1 Bacterial DNA Replication Proteins and Their Functions

Protein	Function
Helicase	Unwinds parental double helix at replication forks
Single-strand binding protein	Binds to and stabilizes single-stranded DNA until it can be used as a template
Topoisomerase	Relieves "overwinding" strain ahead of replication forks by breaking, swiveling, and rejoining DNA strands
Primase	Synthesizes an RNA primer at 5′ end of leading strand and of each Okazaki fragment ofl agging strand
DNA pol III	Using parental DNA as a template, synthesizes new DNA strand by covalently adding nucleotides to the 3′ end of a pre-existing DNA strand or RNA primer
DNA pol I	Removes RNA nucleotides of primer from 5′ end and replaces them with DNA nucleotides
DNA ligase	Joins 3′ end of DNA that replaces primer to rest of leading strand and joins Okazaki fragments of lagging strand

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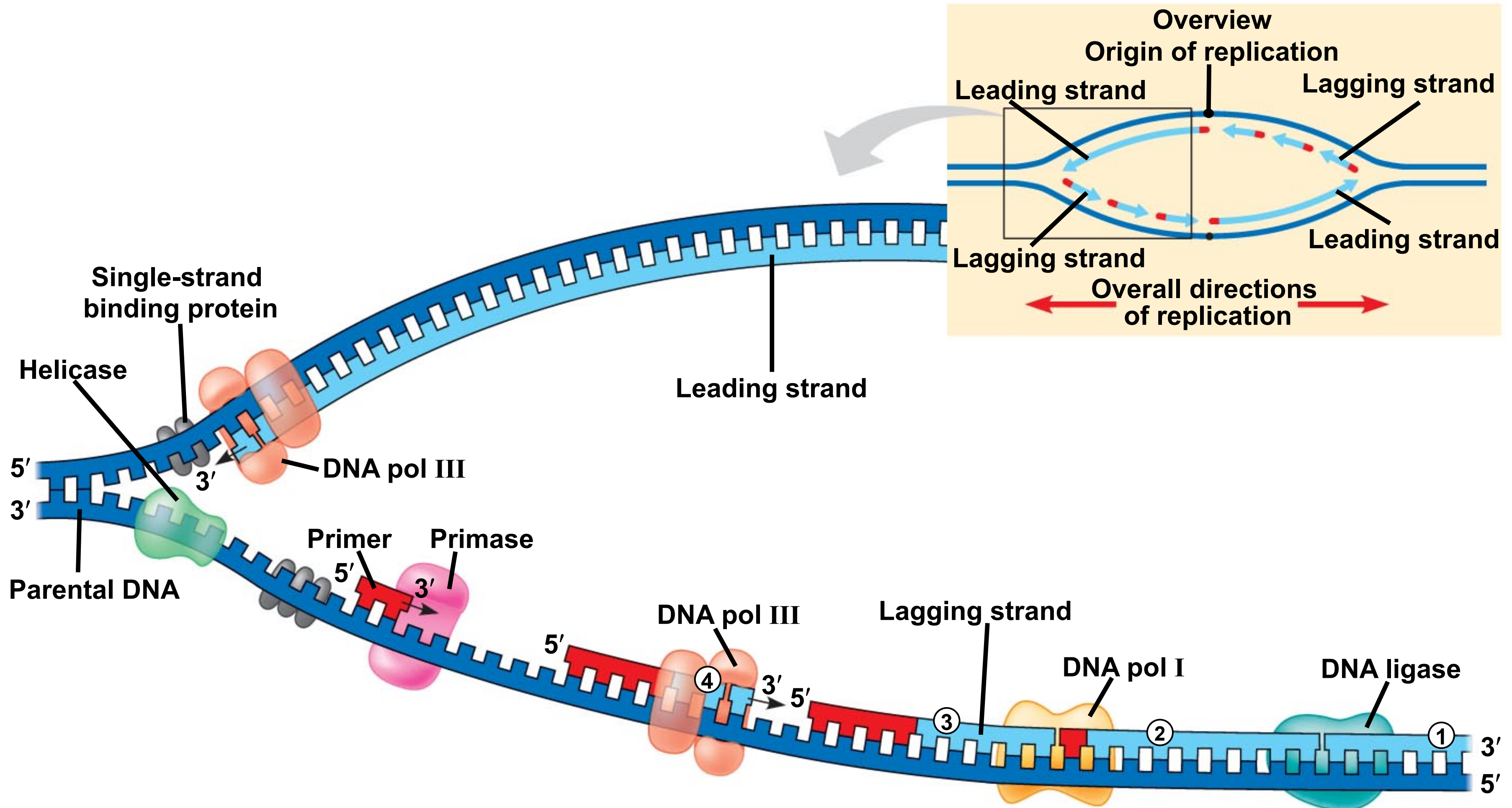
Fig. 16-17



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Concept 16.3 A chromosome consists of a DNA molecule packed together with proteins

- The bacterial chromosome is a double-stranded, circular DNA molecule associated with a small amount of protein
- Eukaryotic chromosomes have linear DNA molecules associated with a large amount of protein
- In a bacterium, the DNA is "supercoiled" and found in a region of the cell called the **nucleoid**

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- **Chromatin** is a complex of DNA and protein, and is found in the nucleus of eukaryotic cells
- **Histones** are proteins that are responsible for the first level of DNA packing in chromatin

Fig. 16-21a

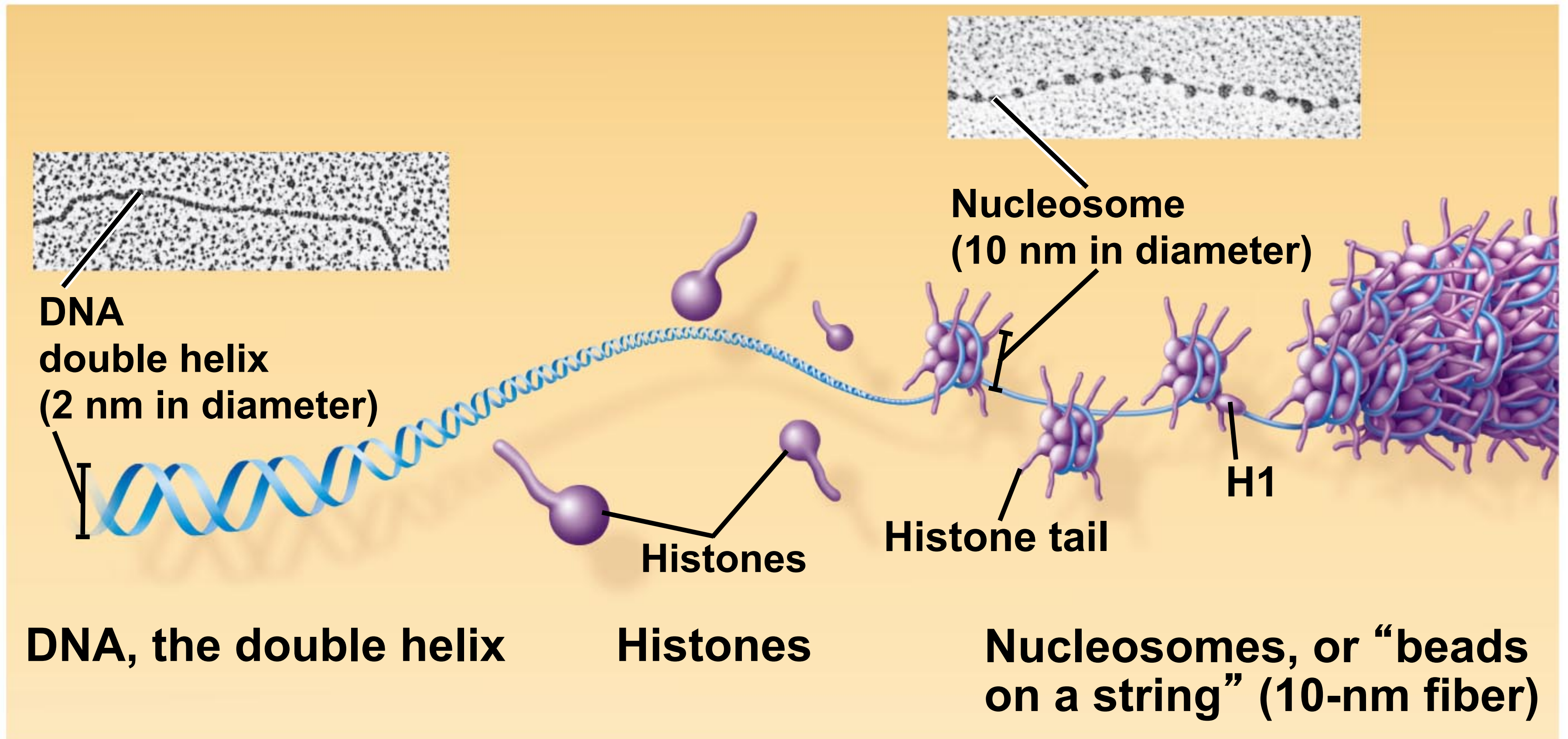

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Fig. 16-21b

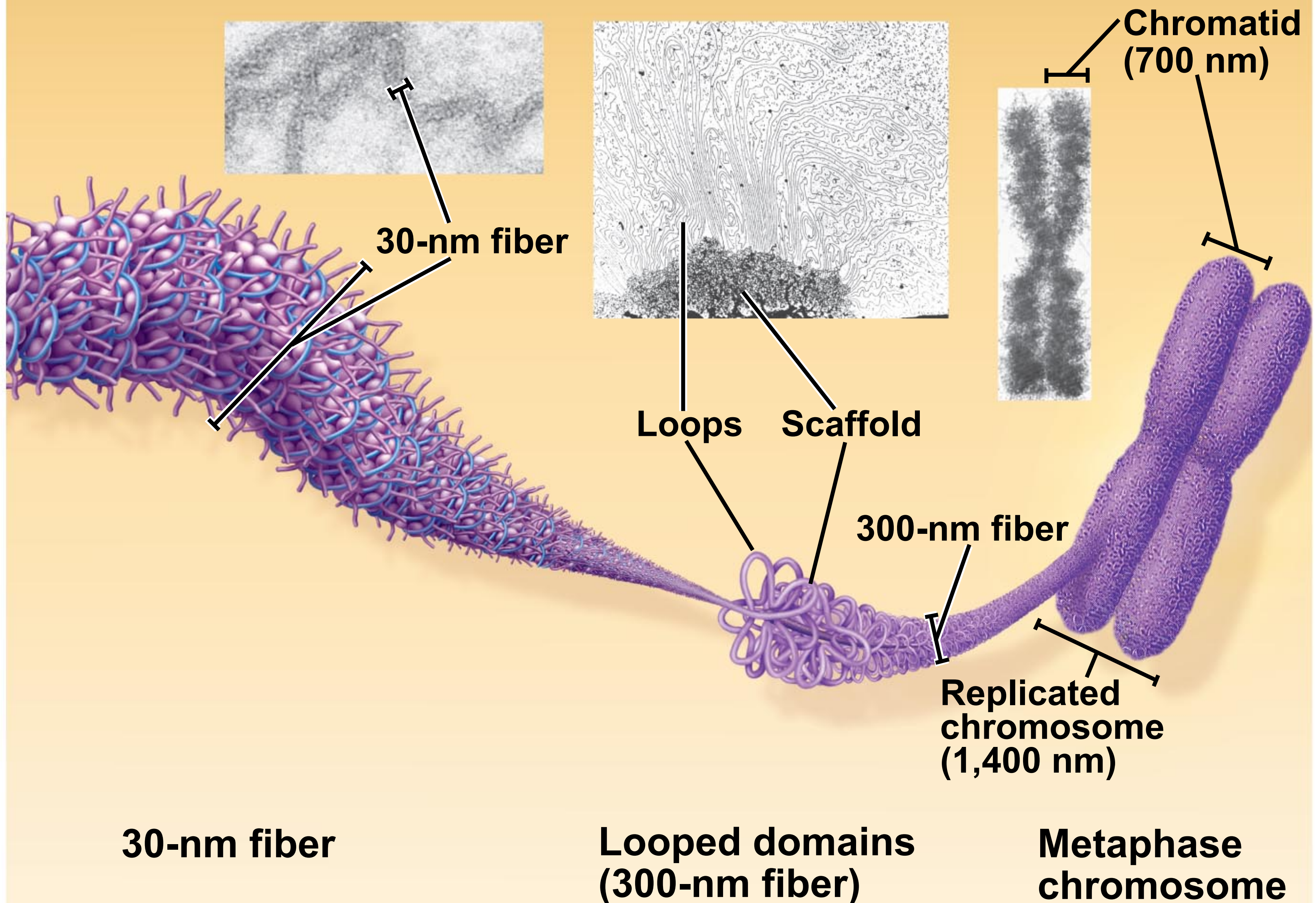

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Fig. 16-UN2

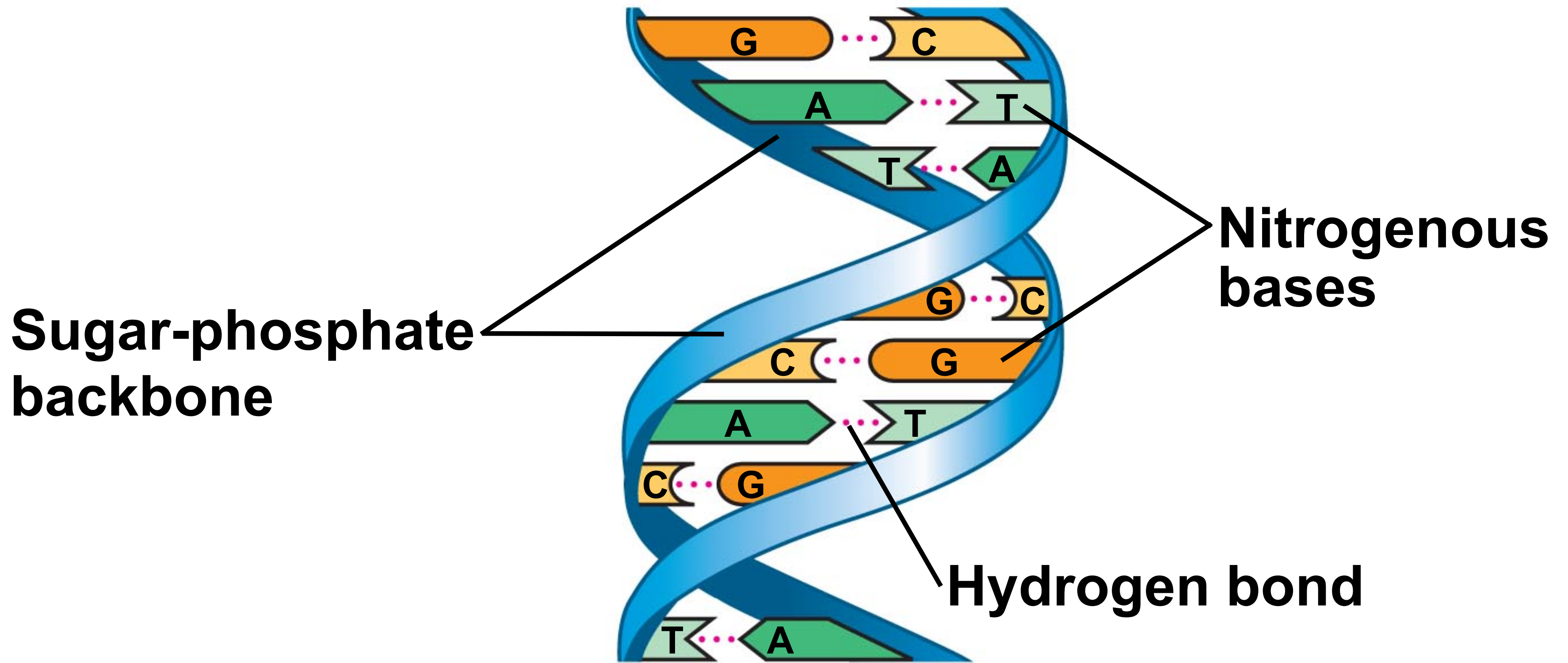

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Fig. 16-UN3

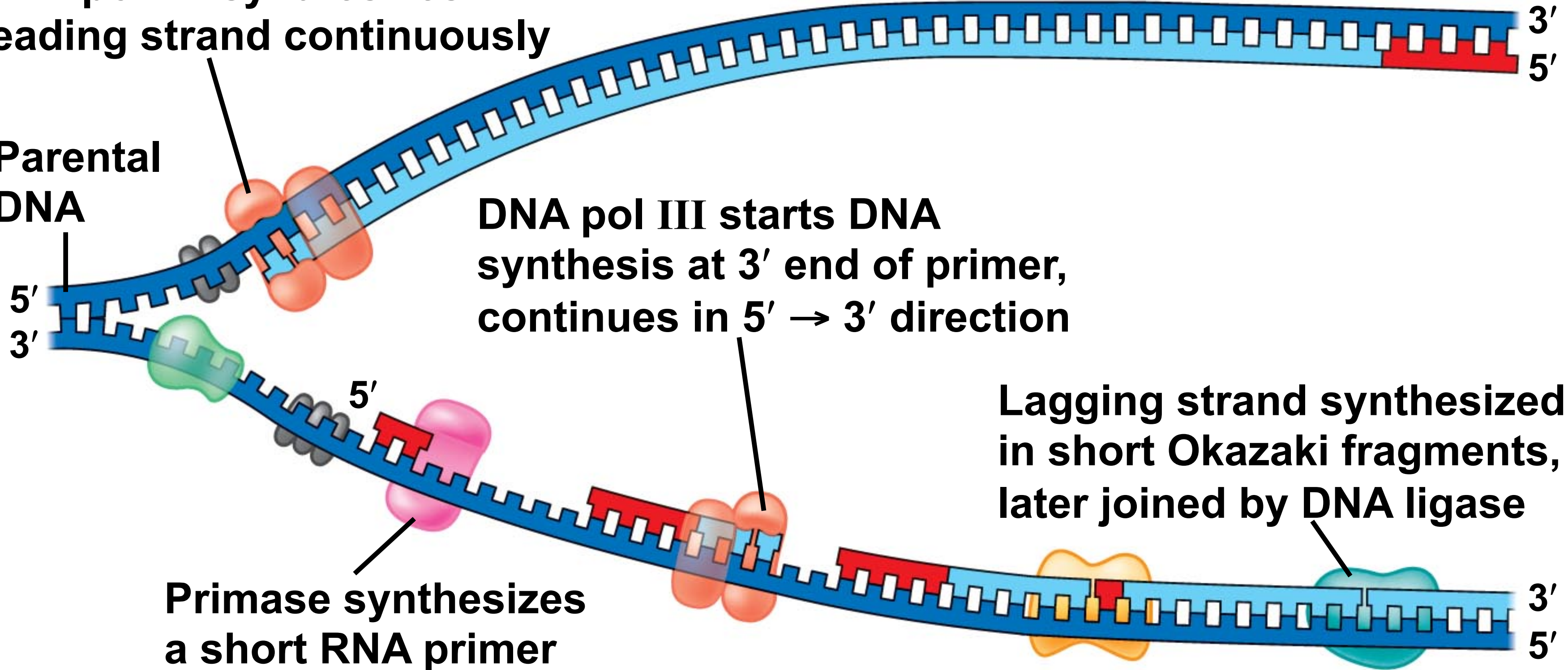

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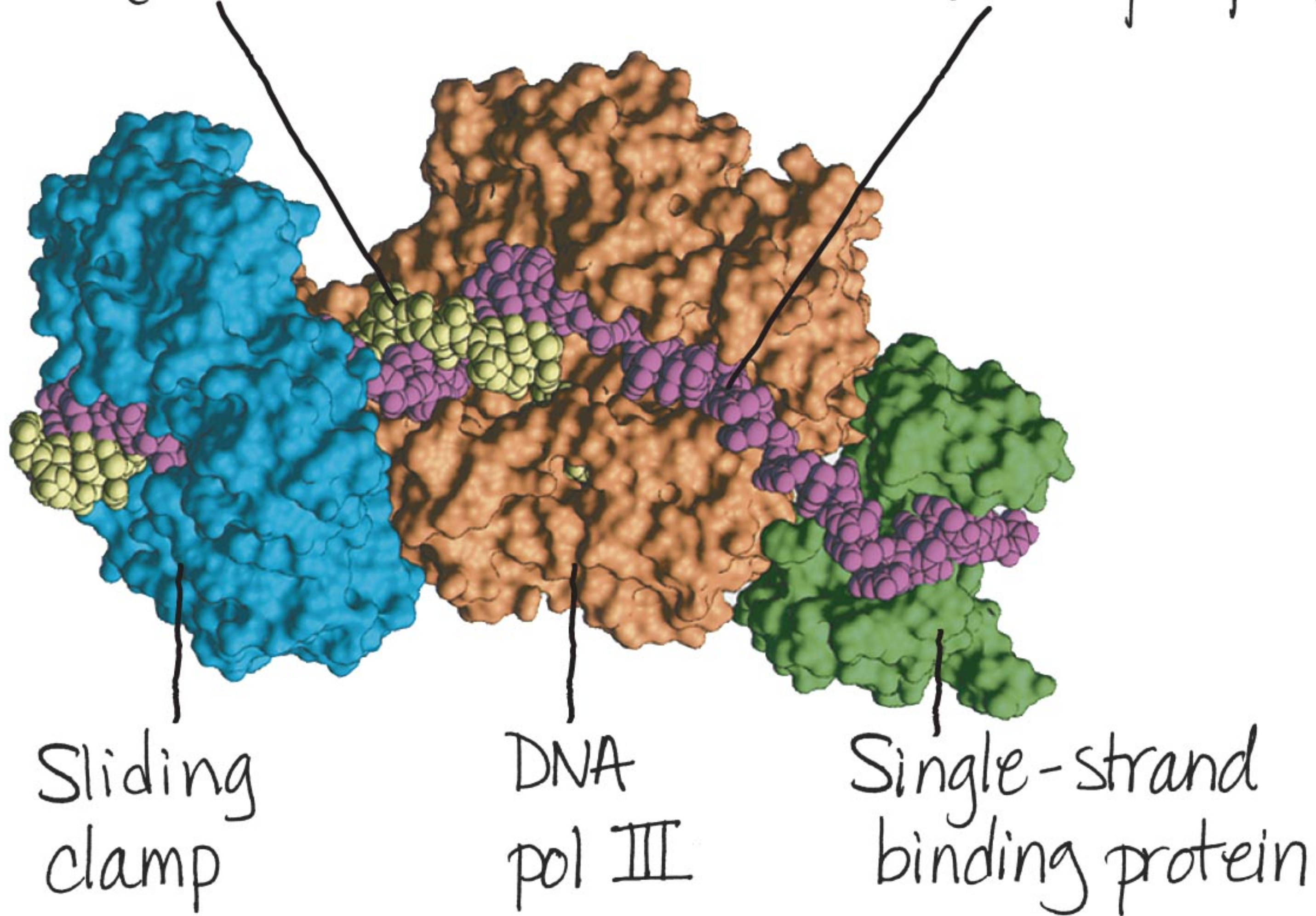
Fig. 16-UN5



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PCR_28June2016_jw.xls

C40 hold at 4°C

Row	A	B	C
1			no. of reactions
2	40µl RX	**µl**	
3			**13**
4	water	15.8	205.4
5	5X PCR buffer	8	104
6	dNTPs	4	52
7	MgCl2	4	52
8	DMSO	0	0
9	**LCO1490M13**	2	26
10	**HCO2198M13**	2	26
11	TAQ enzyme	0.2	2.6
12			
13		36	
14			
15	template (unless indicated otherwise)	1	
16	**species/ specimen**	**tube #s**	**sample quantity 4.0 µl**
17	2426	1	
18	2427	2	
19	2428	3	
20	2429	4	
21	2430	5	
22	2431	6	
23	2432	7	
24	2433	8	
25	2434	9	
26	2435	10	
27	2436	11	
28	2437	12	
29	blank	13	
30			
31	Load 10 µl on 1.0% agarose at 90 milliamps for ~30 minutes (use 7 µl 1kb plus ladder).		
32	100ml of TE buffer, 1g agarose, 4ul of safeview		
33		step time temp. (°C)	
34		1	2 min. 94°C
35		2	15 sec. 94°C
36		3	30 sec. 54°C
37		4	2 min. 72°C
38		5	step 2 to step 4 (x30)
39		6	2 min. 72°C
40		7	hold at 4°C

Sheet1 Sheet2 Sheet3

Normal View Select destination and press ENTER or choose Paste

PCR_21July2016_FORM*****.xls

PCR: 21 July 2016 COI

Name:

		no. of reactions
40µl RX	**µl/rxn**	
		10
water	15.8	158
5X PCR buffer	8	80
dNTPs (10 mM)	4	40
MgCl2 (50 mM)	4	40
DMSO	0	0
LCO1490M13 (20 µM)	2	20
HCO2198M13 (20 µM)	2	20
TAQ enzyme (2000 units/ml)	0.2	2
	36	
template (unless indicated otherwise)	4	
species/ specimen	**tube #s**	**sample quantity 4.0 µl**
	1	
	2	
	3	
	4	
	5	
	6	
	7	
	8	

Load 10 µl on 1.0% agarose at 100 milliamps for ~30 minutes (use 7 µl 1kb plus ladder).

100 ml of TE buffer, 1 g agarose, 5 µl of safeview

step	time temp. (°C)
1	2 min. 94°C
2	15 sec. 94°C
3	30 sec. 54°C
4	2 min. 72°C
5	step 2 to step 4 (x30)
6	2 min. 72°C
7	hold at 4°C

PCR Animations

https://www.youtube.com/watch?v=3XPAp6dgl14

https://www.youtube.com/watch?v=eEcy9k_KsDI

Preview YouTube video How #2A57

Preview YouTube video Poly#2A58