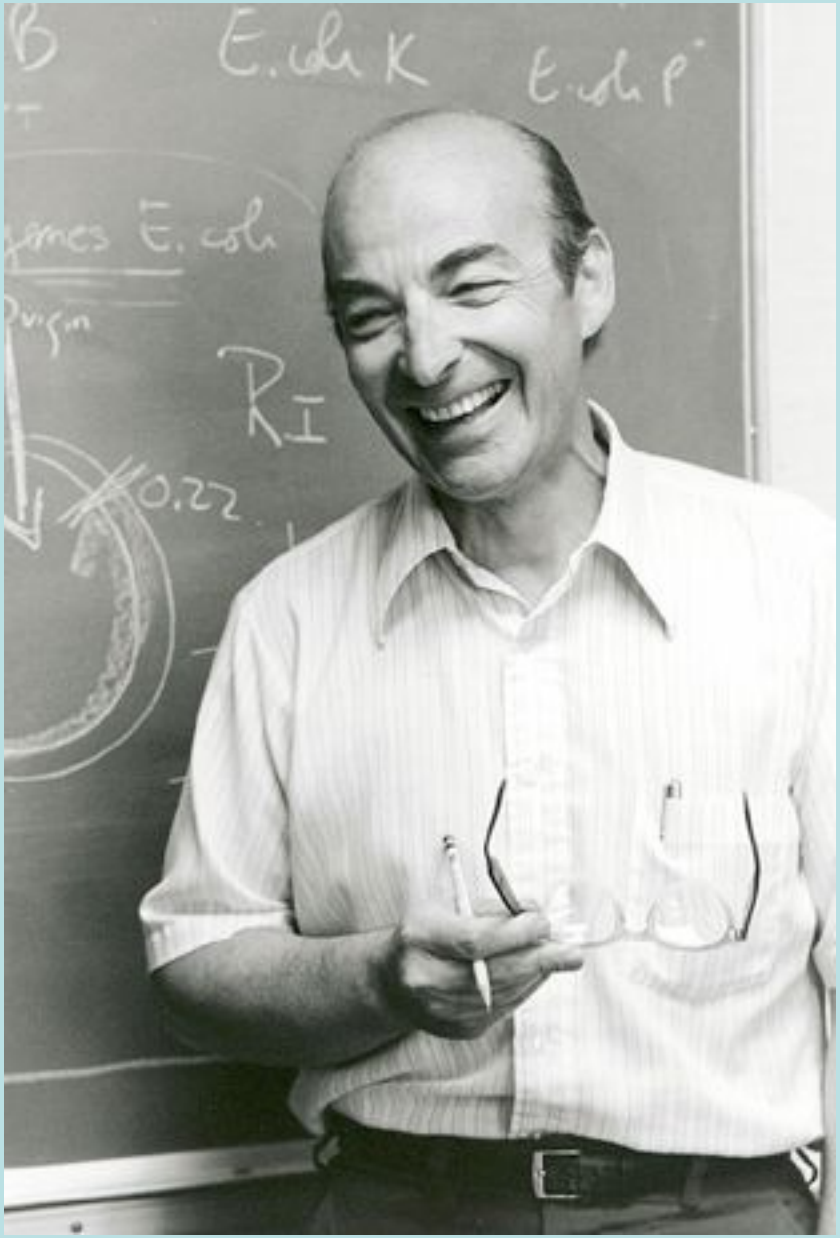
Molecular mechanisms in DNA replication

Replisome: multiprotein structure assembled on the replication fork for synthesis of DNA.

Arthur Kornberg, 1970

Arthur Kornberg was an American biochemist who won the Nobel Prize in Physiology or Medicine 1959 for his discovery of "the mechanisms in the biological synthesis of deoxyribonucleic acid (DNA)" together with Dr. **Severo Ochoa** of New York University.



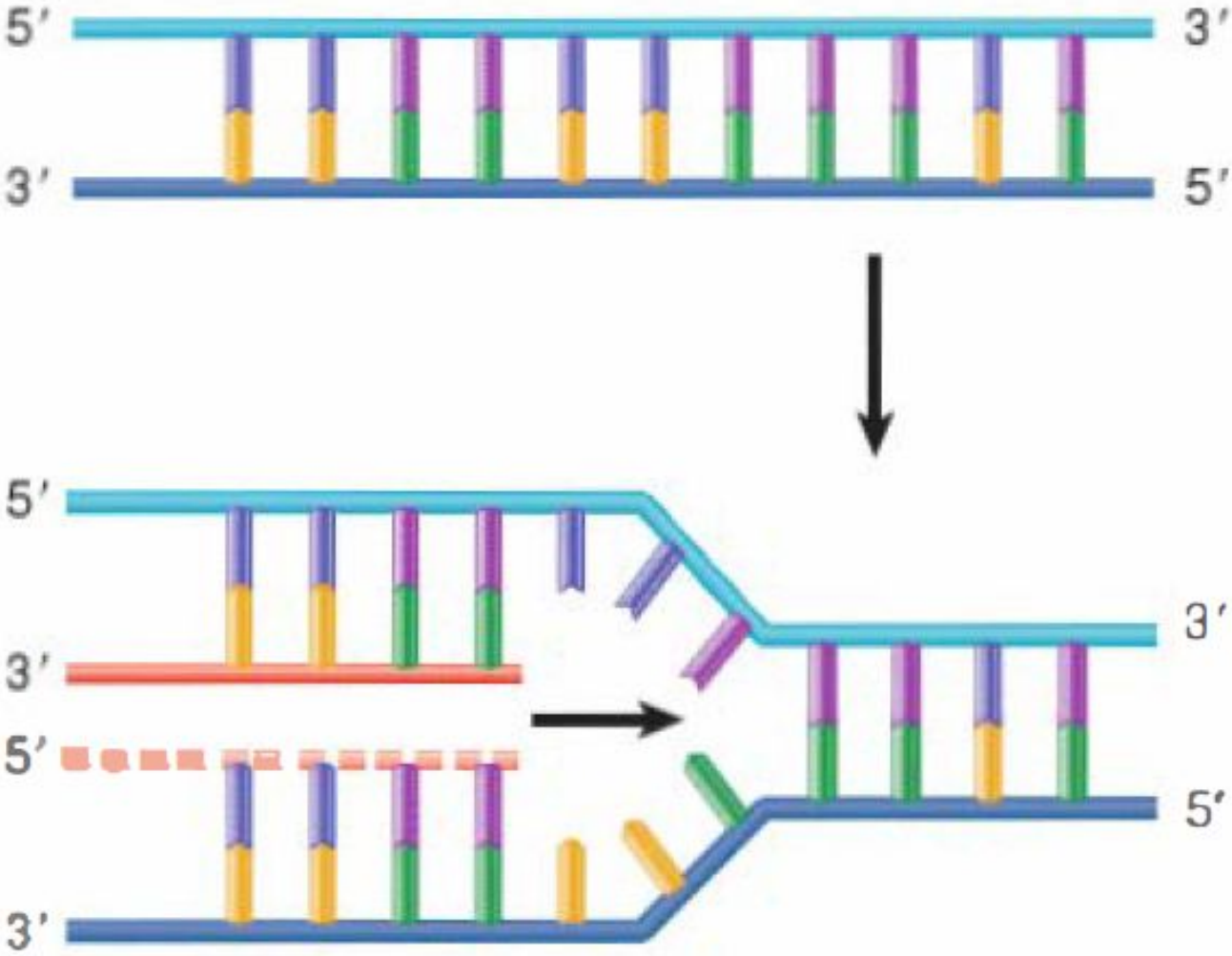


FIGURE 13.2 Semiconservative replication synthesizes two new strands of DNA.

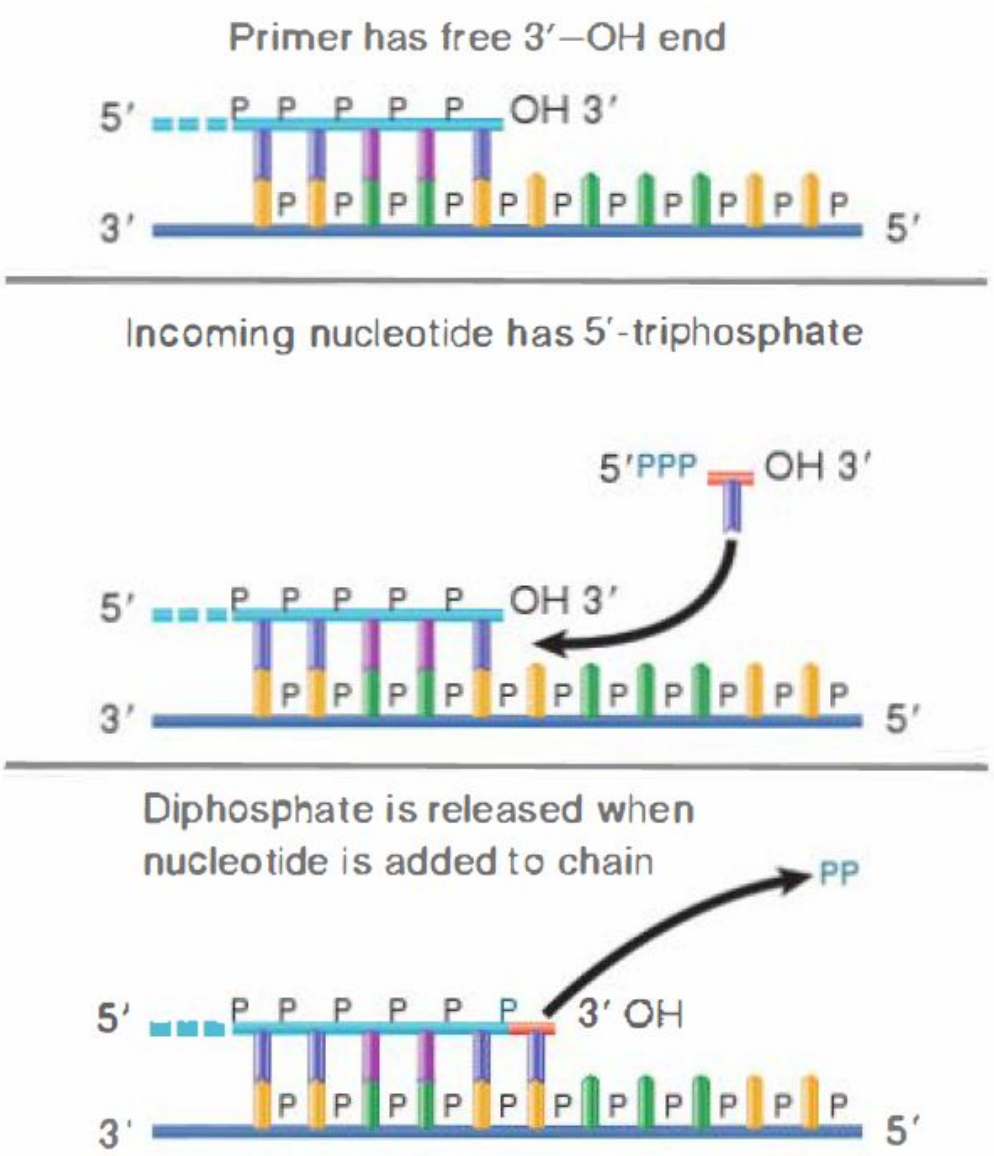
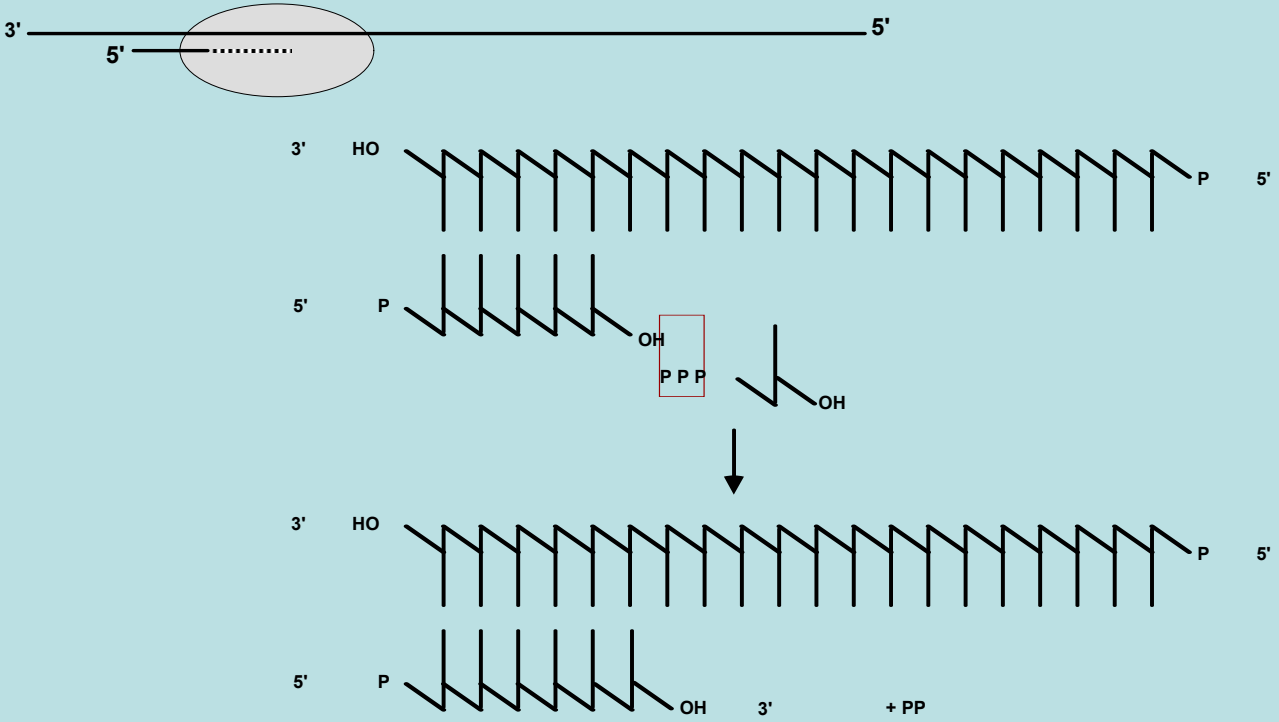


FIGURE 13.4 DNA is synthesized by adding nucleotides to the 3′-OH end of the growing chain, so that the new chain grows in the 5′ to 3′ direction. The precursor for DNA synthesis is a nucleoside triphosphate, which loses the terminal two phosphate groups in the reaction.

DNA polymerase activity

- Semiconservative replication
- Repair reactions



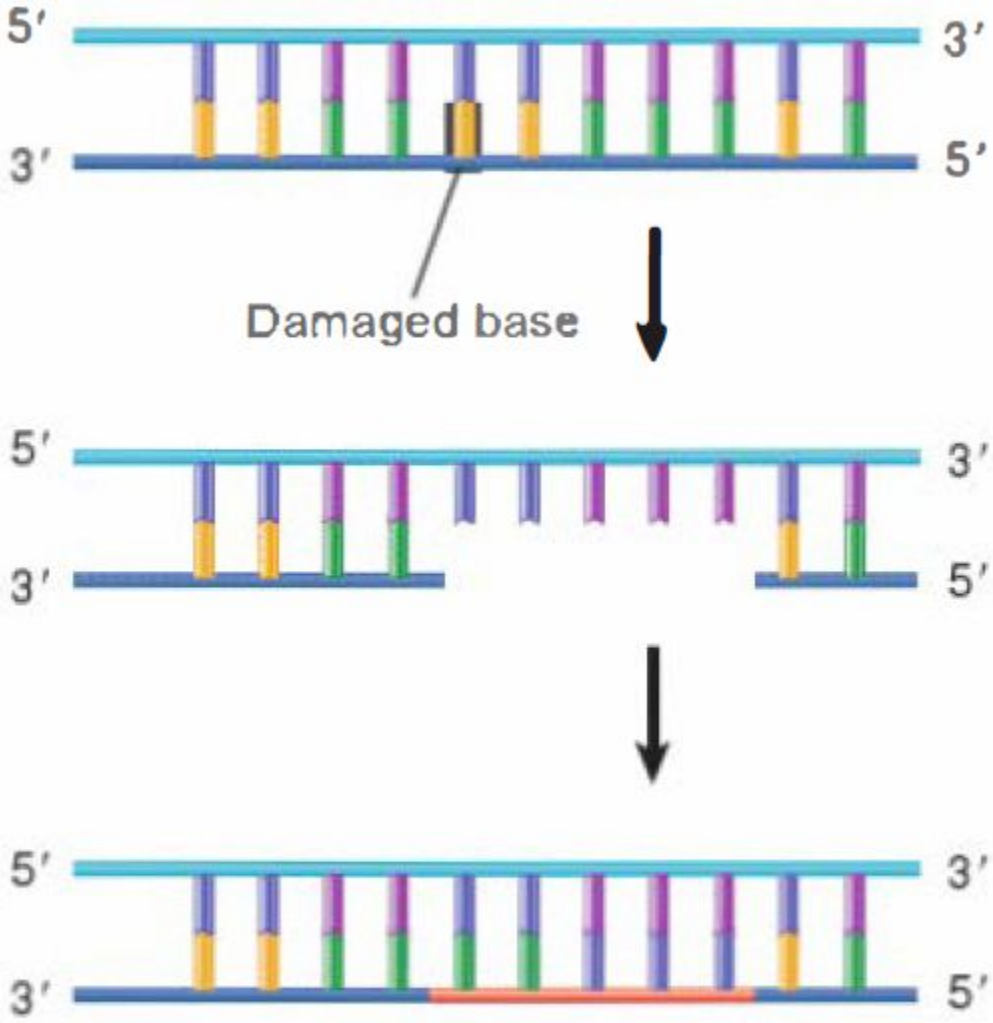


FIGURE 13.3 Repair synthesis replaces a short stretch of one strand of DNA containing a damaged base.

Different DNA Polymerases in *E.coli*

Enzyme	Gene	Function
I	*polA*	major repair enzyme
II	*polB*	replication restart
III	*polC*	replicase
IV	*dinB*	translesion replication
V	*umuD'$_2$C*	translesion replication

FIGURE 13.5 Only one DNA polymerase is the replication enzyme. The others participate in repair of damaged DNA, restarting stalled replication forks, or bypassing damage in DNA.

DNA polymerase	Function	Structure
	High fidelity replicases	
α	Nuclear replication	350 kD tetramer
δ	Lagging strand	250 kD tetramer
ε	Leading strand	350 kD tetramer
γ	Mitochondrial replication	200 kD dimer
	High-fidelity repair	
β	Base excision repair	39 kD monomer
	Low-fidelity repair	
ζ	Base damage bypass	heteromer
η	Thymine dimer bypass	monomer
ι	Required in meiosis	monomer
κ	Deletion and base substitution	monomer

FIGURE 13.24 Eukaryotic cells have many DNA polymerases. The replication enzymes operate with high fidelity. Except for the β enzyme, the repair enzymes all have low fidelity. Replication enzymes have large stuctures, with separate subunits for different activities. Repair enzymes have much simpler structures.

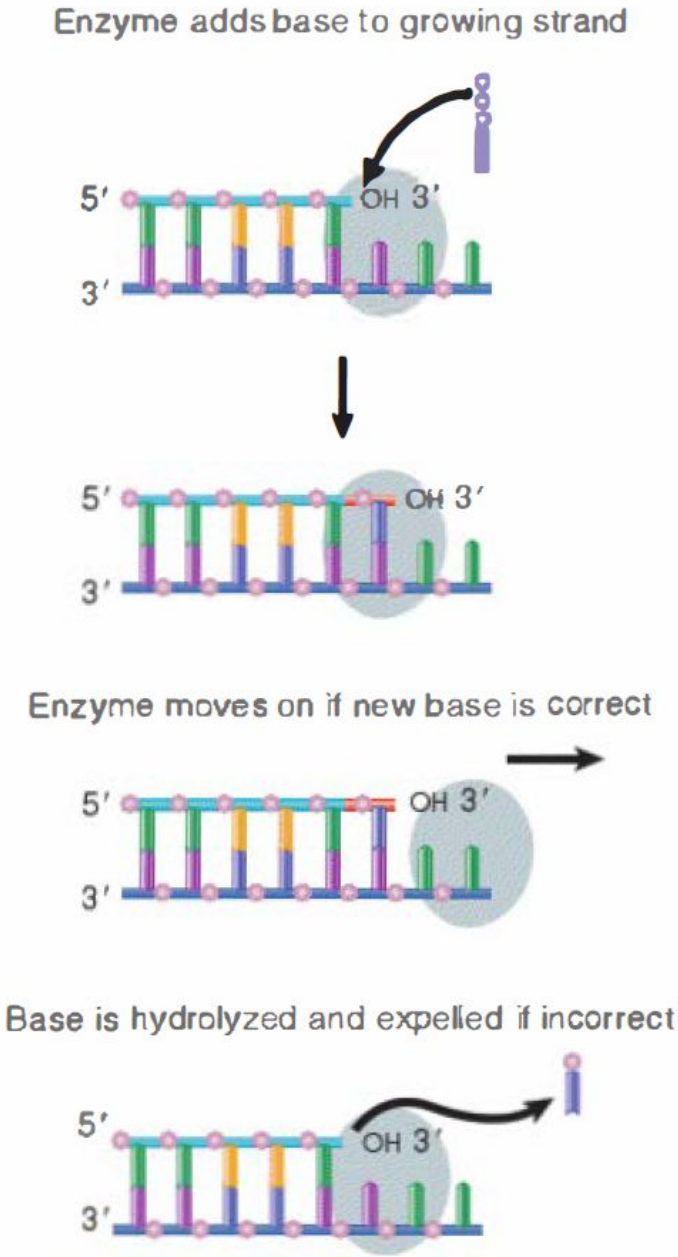


FIGURE 13.7 DNA polymerases scrutinize the base pair at the end of the growing chain and excise the nucleotide added in the case of a misfit.

Replication fidelity

- Presynthetic check
- Proofreading

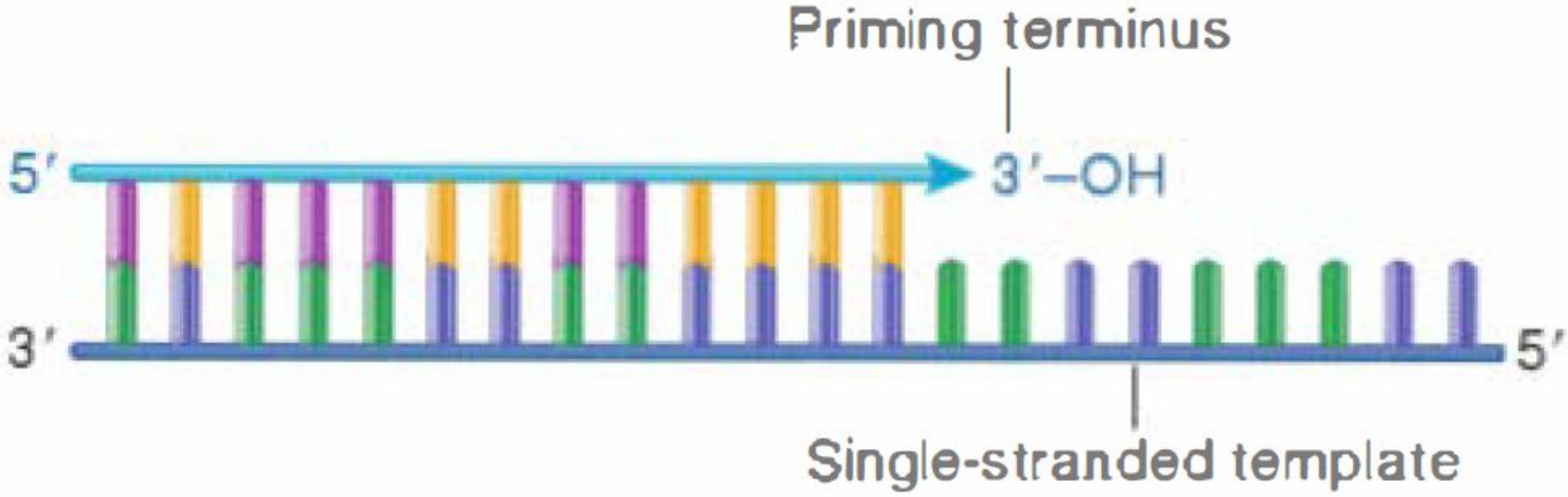


FIGURE 13.12 A DNA polymerase requires a 3′–OH end to initiate replication.

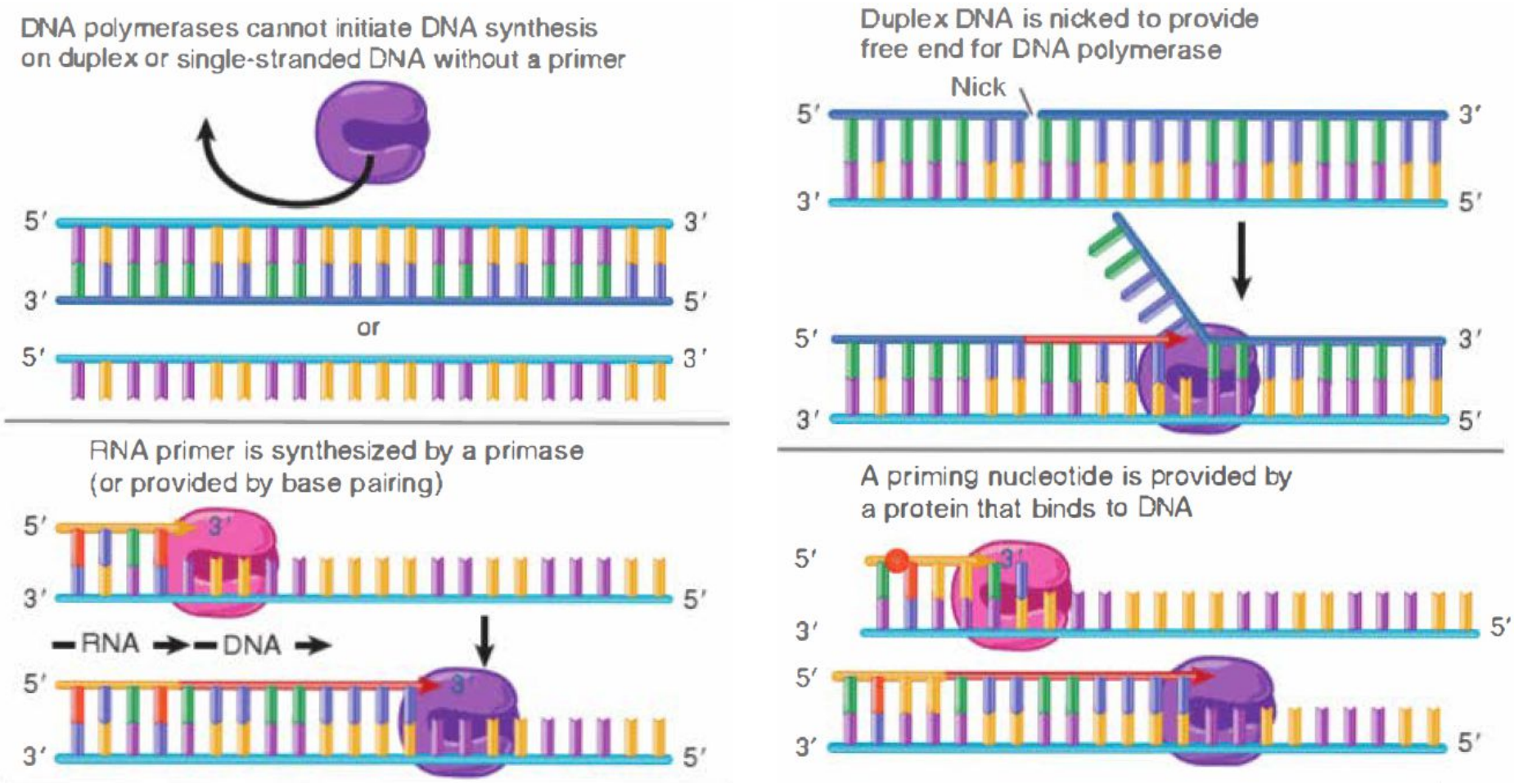


FIGURE 13.13 There are several methods for providing the free 3′–OH end that DNA polymerases require to initiate DNA synthesis.

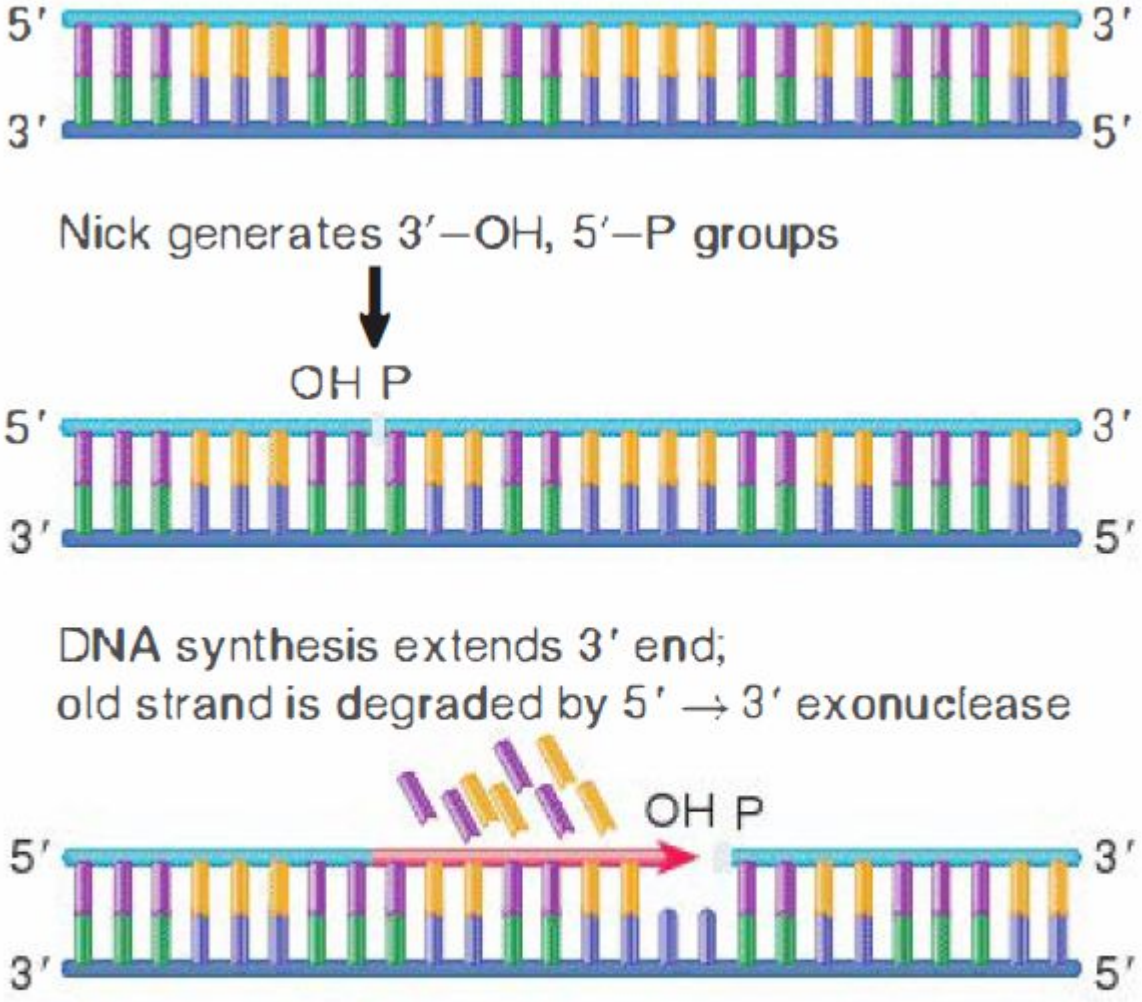


FIGURE 13.6 Nick translation replaces part of a preexisting strand of duplex DNA with newly synthesized material.

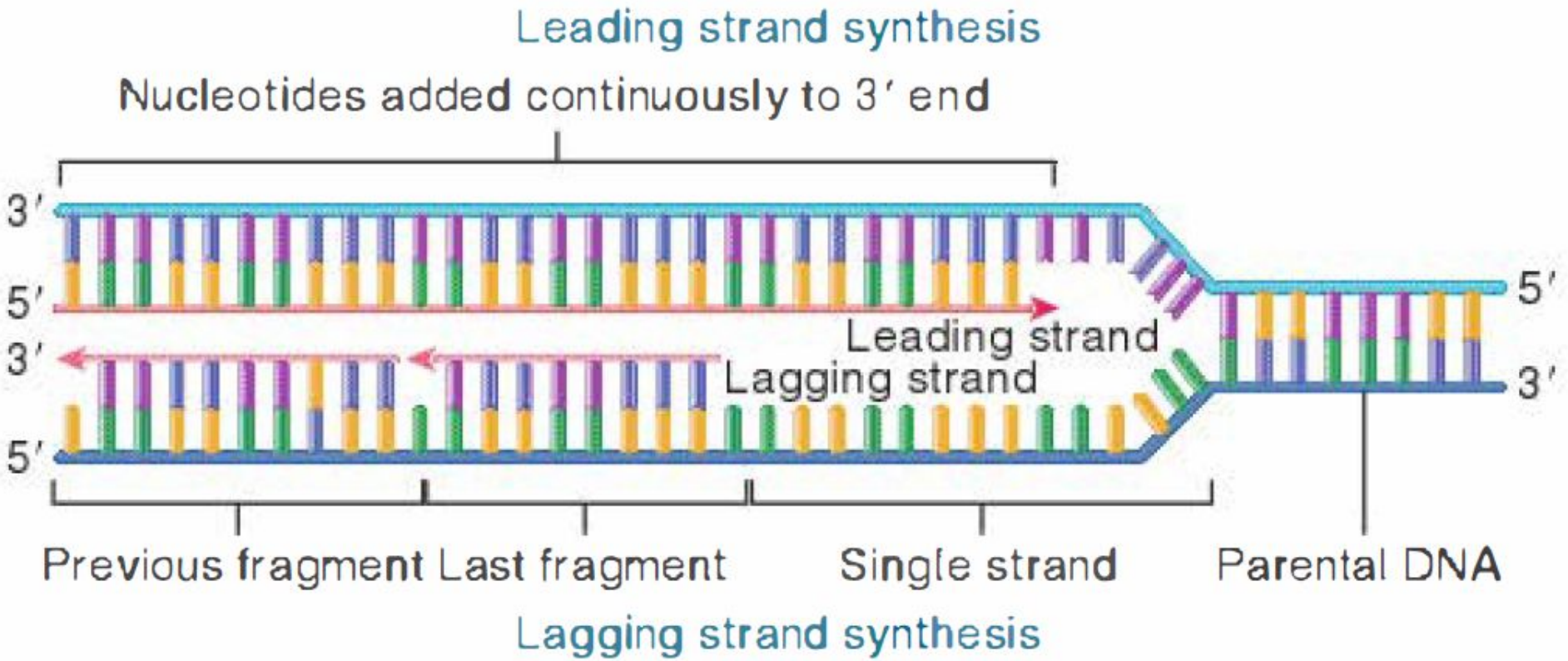


FIGURE 13.10 The leading strand is synthesized continuously, whereas the lagging strand is synthesized discontinuously.