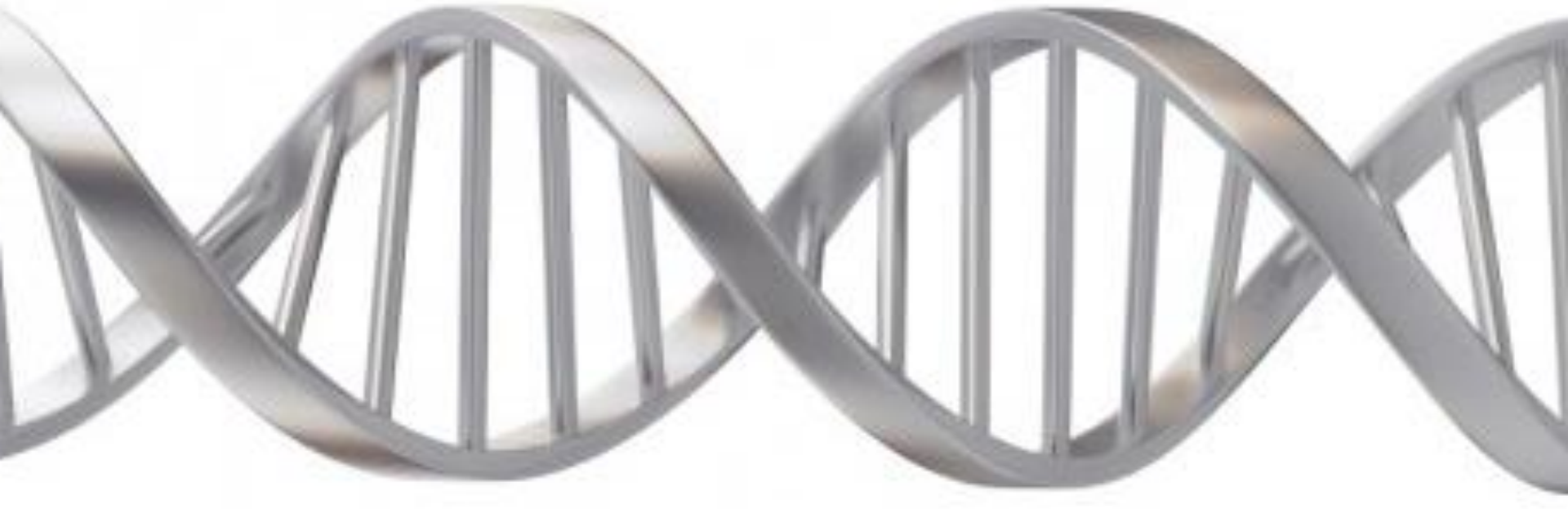
THE MOLECULAR BASIS OF INHERITANCE

Deoxyribonucleic Acid



- https://www.youtube.com/watch?v=5qSrmeiWsuc

DNA = **d**eoxyribo**n**ucleic **a**cid

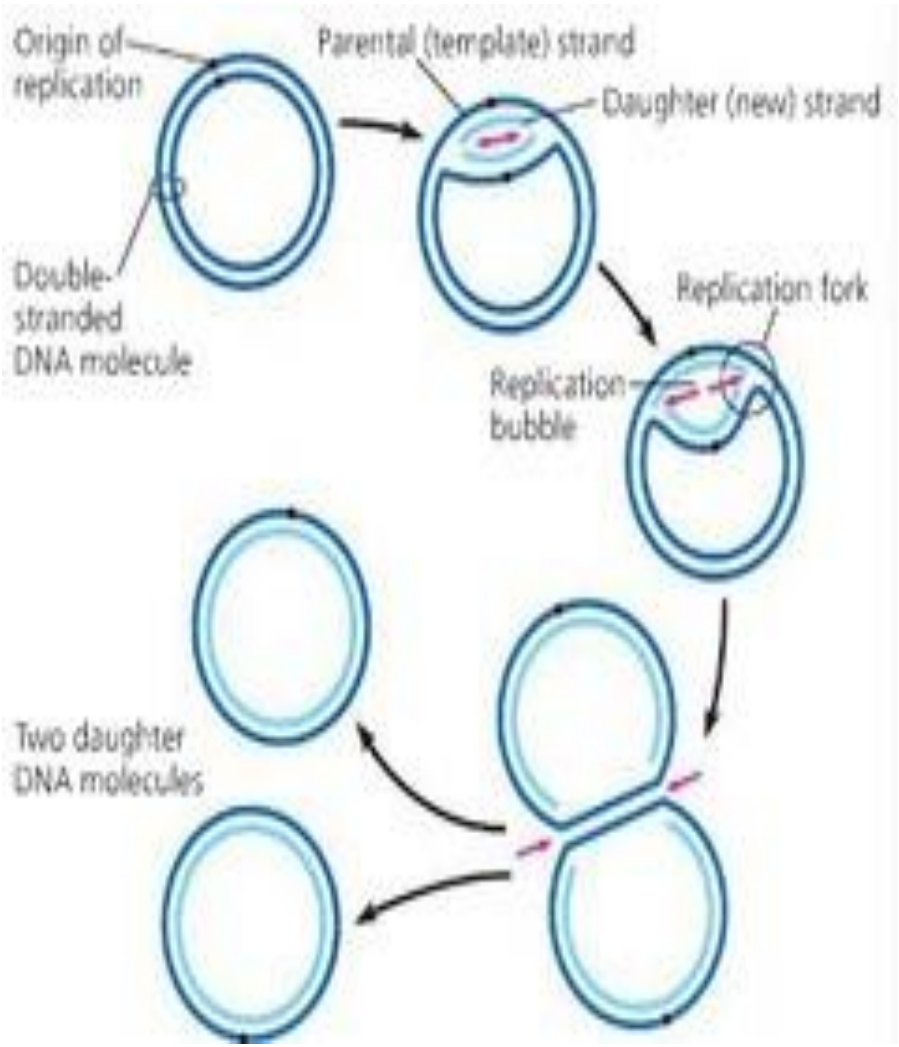
- Consists of a phosphate, sugar backbone and nitrogen bases inside the double helix.
- The sugar (deoxyribose) consists of 5 carbons and 1 oxygen in a ring.
- The carbons are numbered 5', 4', 3', 2', and 1'. Why the "prime"? (naming convention).
- The prime is used to talk about the carbons in the deoxyribose RING, and not the carbons of the nitrogen bases.
- When individual nucleotides link up to make DNA polymers, it is the 3' hydroxyl (OH) that links up with the 5' phosphate group (of the backbone) to form what is known as a **phosphodiester bond**.

DNA – *The nucleic acid with all the genes*

What we know about DNA

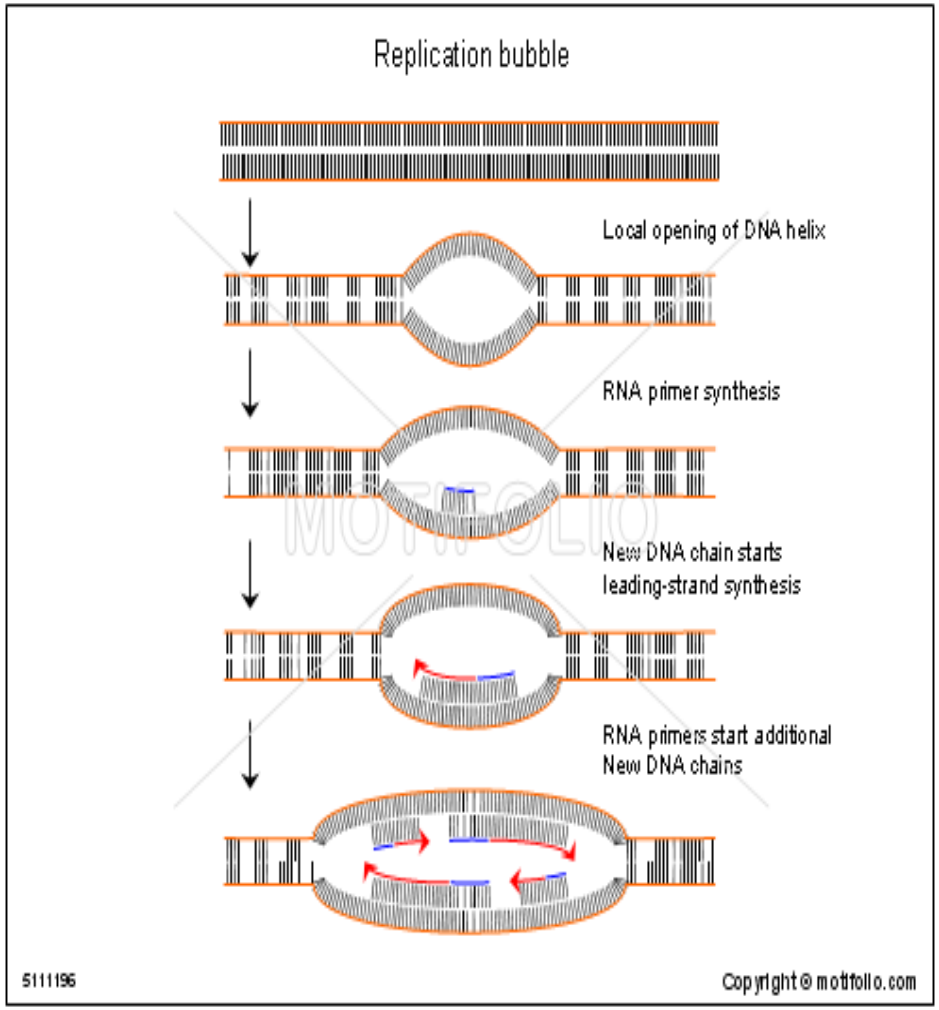
- Sugar, P backbone
- Nucleotides: A,T, G, C
- Base pair rule: A&T, G&C
- H-bonds between ????
- Anti-parallel, complementary strands
- 3D structure = ????

Prokaryotic DNA Replication



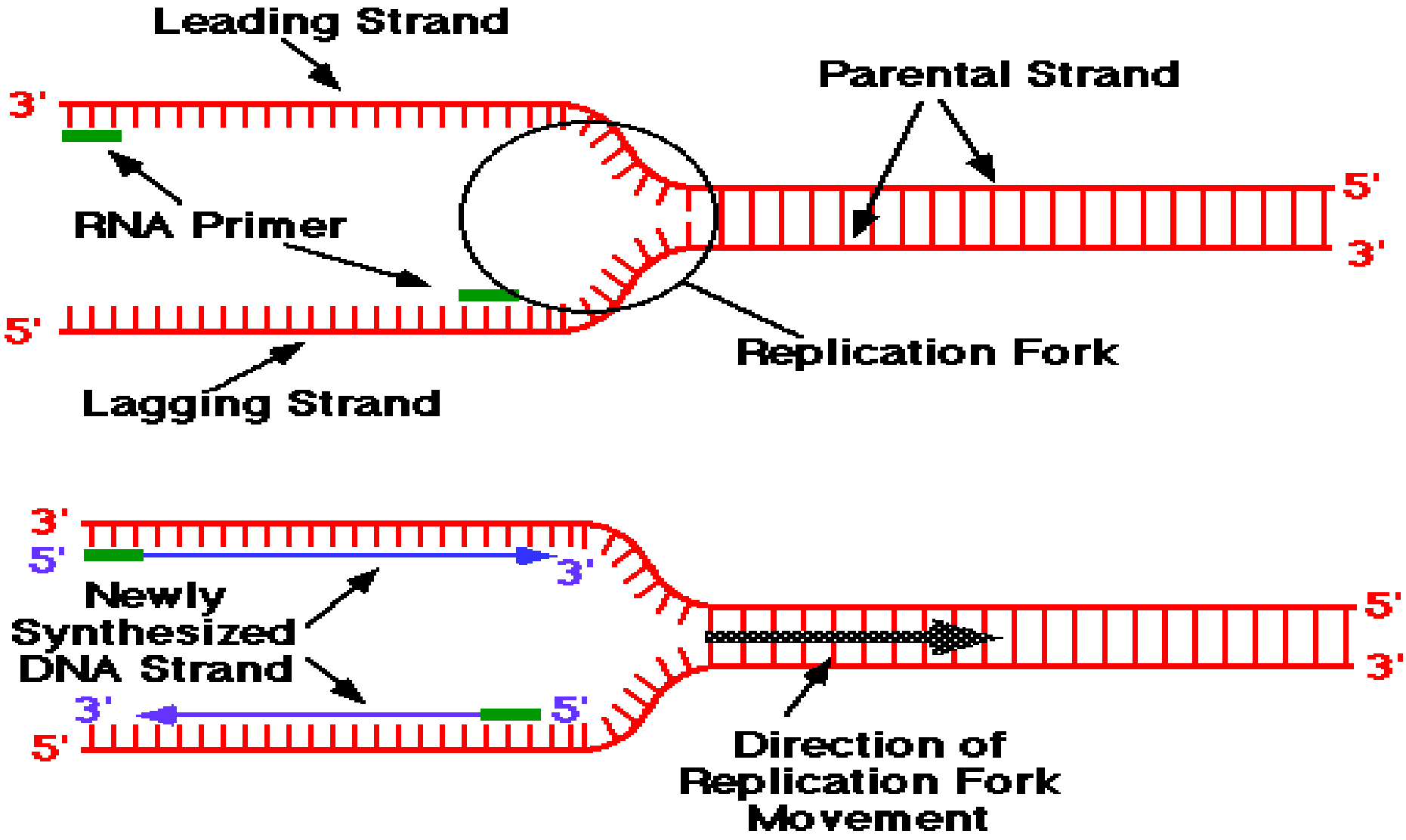
- Over 100 enzymes are involved in process of DNA replication with E. coli (bacteria).
- Using a **single replication origin** and two replication forks moving in opposite directions, a growing E. coli can replicate its ~4,700,000 base pairs of DNA in ~40 minutes.

Process of DNA replication



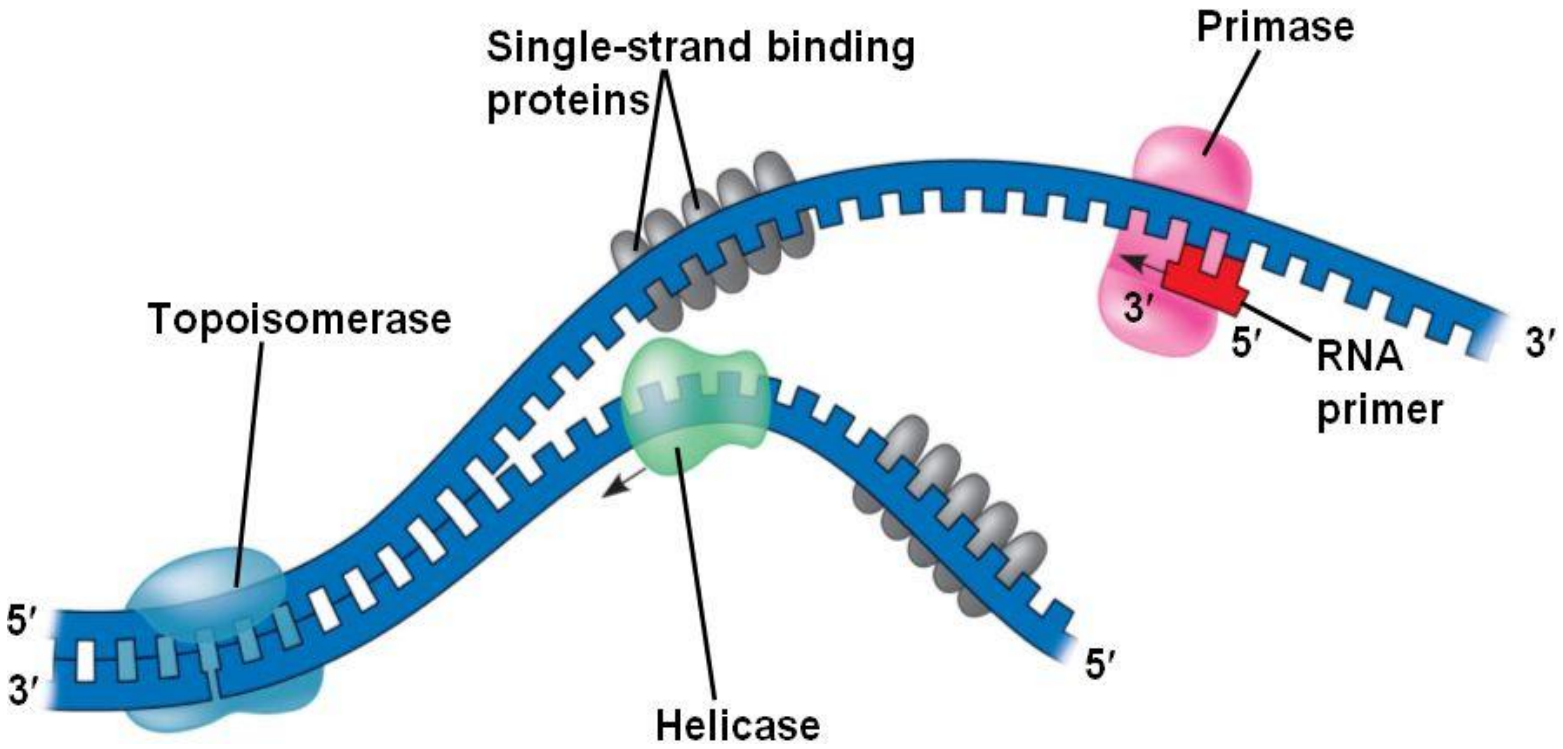
- 1st step= formation of…..
- Replication Bubble: the DNA splits apart and the process of replication begins.
- Replication or synthesis of a new strand occurs in the 5’ to 3’ direction.

DNA REPLICATION



DNA replication enzymes

- **Helicase**: *Unwinds DNA (double helix)*
- **Topoisomerase**: *relieves tension on DNA strands, near replication fork*
- **Primase**: *initiates nucleotide additions … HOW?*

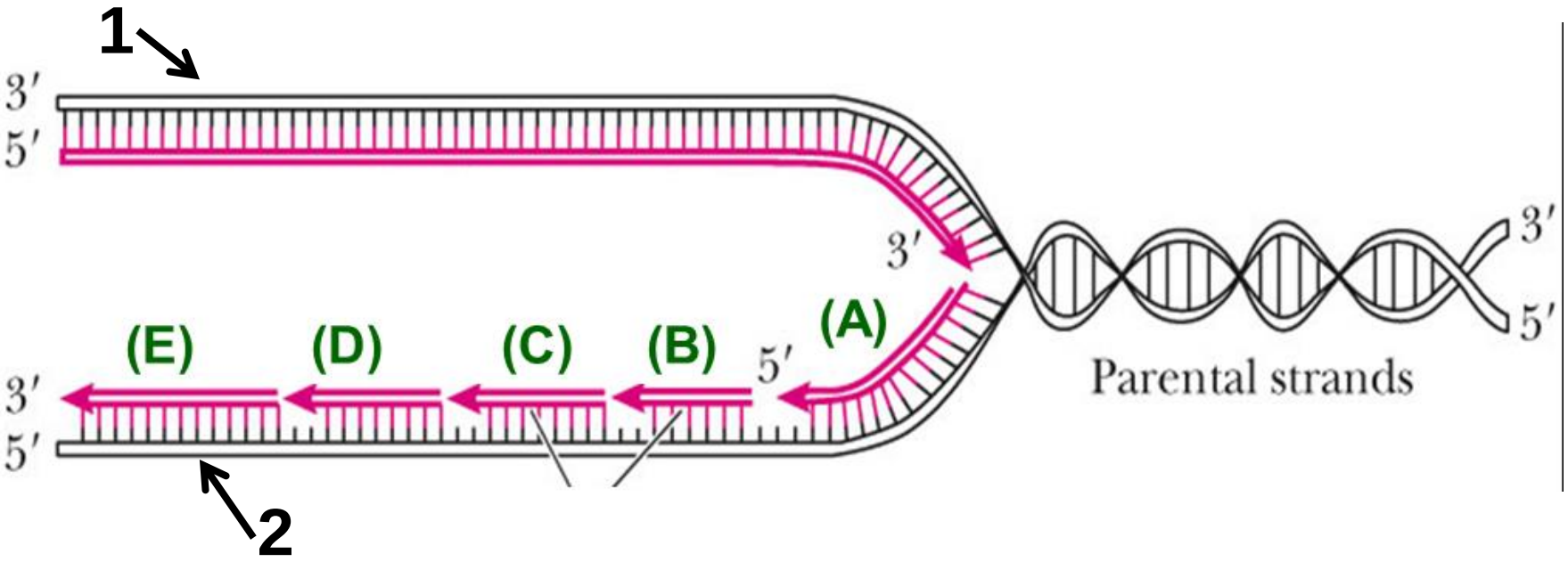


DNA REPLICATION

What do we KNOW?

- Both strands act as templates during replication
  - Leading and lagging strands
- Synthesis is DIRECTIONAL
- Requires enzymes
- Requires proteins
- Requires RNA primers!

1) Which Okazaki fragment was synthesized the earliest? (A~E)
2) Which strand is leading strand? (**1** or **2**)



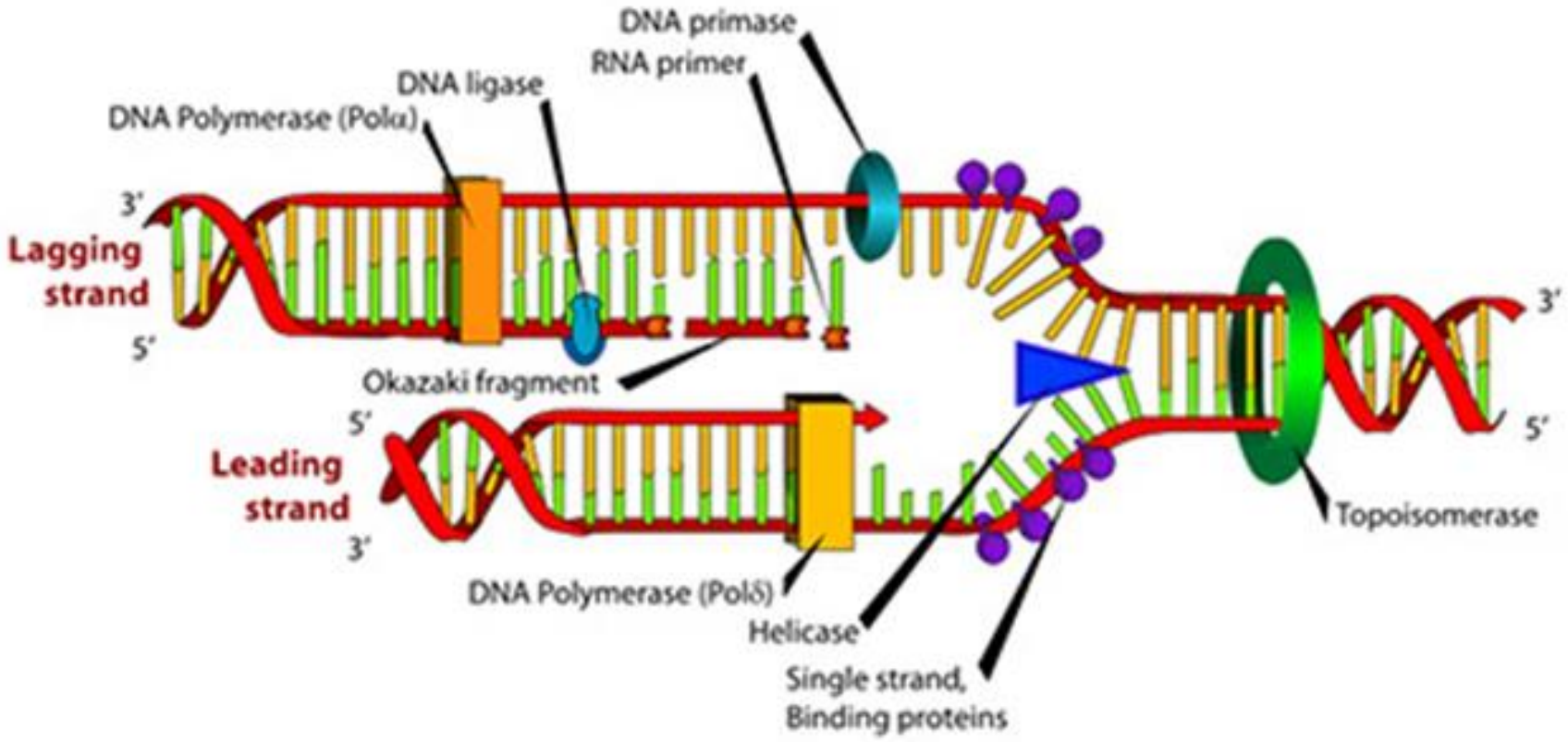
movement of the replication fork

MORE ENZYMES! DNA polymerase III

- Catalyzes the synthesis of new DNA by adding nucleotides to a preexisting chain.
  - Can add up to 1,000 new base pairs / second to open strand of DNA.
- Synthesizes the ???? strand **continuously**
- Only ONE primer is needed by DNA Pol III
- Forms *hydrogen bonds* between the nitrogen base on the parent strand and the complementary nitrogen base of the new daughter nucleotide
- Forms *covalent bonds* between the 3' end of the previous daughter nucleotide and the 5' end of the new daughter nucleotide (hence 5' to 3' direction)

DNA Polymerase

- DNA polymerase is notorious for its astounding **accuracy** in DNA replication.
  - ONLY makes a mistake every 4,000-5,000 base pairs (bp).



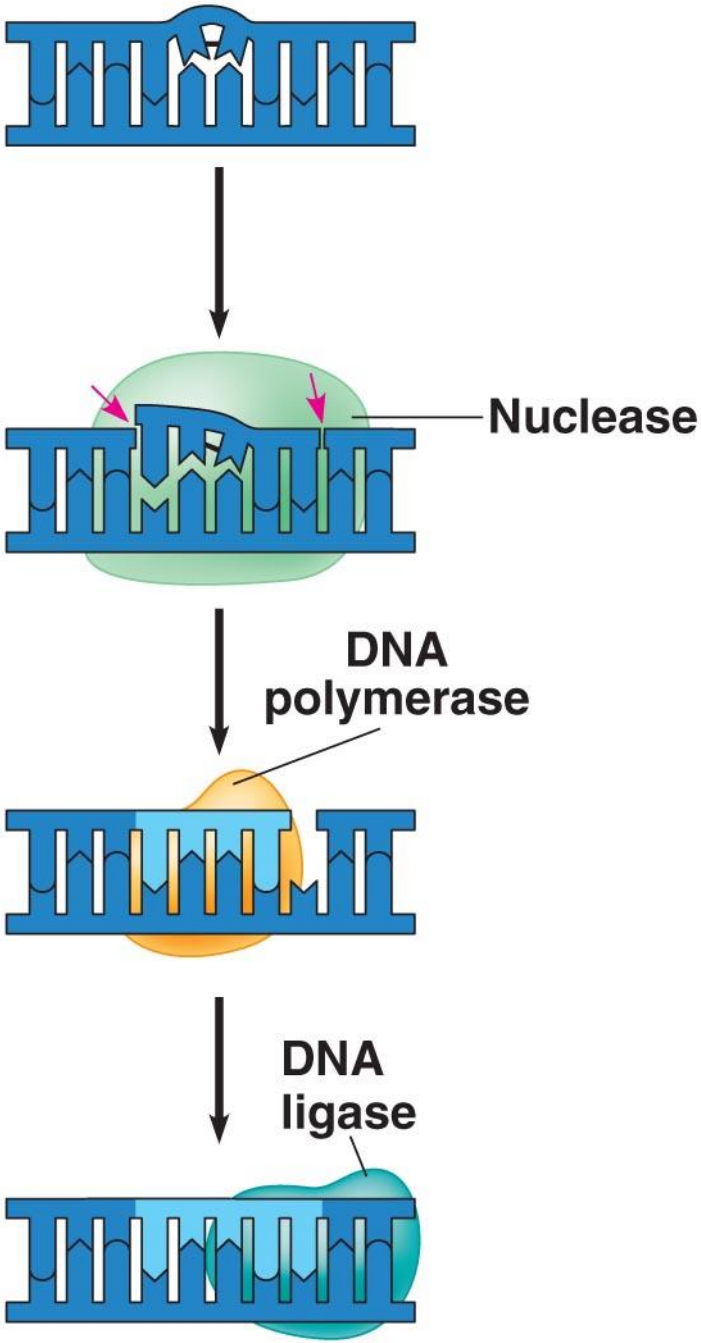
DNA Polymerase

This process is very efficient!

- DNA polymerases are good proofreaders… a mistake is made only in 1 of every 10 000 nucleotide parings…

– DNA polymerases need help… **mismatch repair**!

- Ex: **nucleotide excision repair** in which the enzyme **nuclease** cuts the damaged segment so that DNA replication “tries again.”

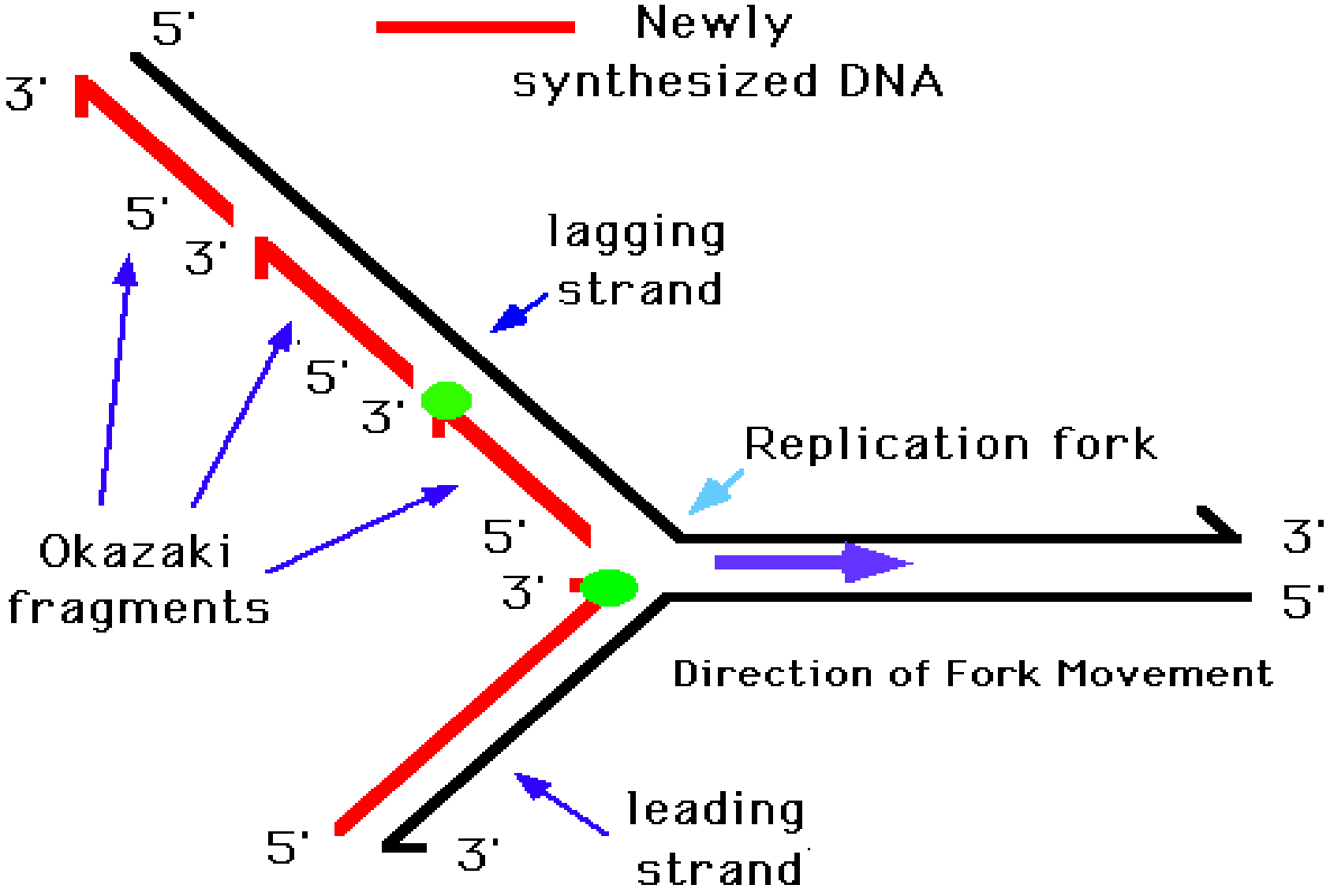


MORE on DNA Pol III

- Synthesizes the **lagging** strand *AWAY from* the replication fork in the mandatory 5' → 3' direction.
- The lagging strand is synthesized **discontinuously** as a series of fragments called …

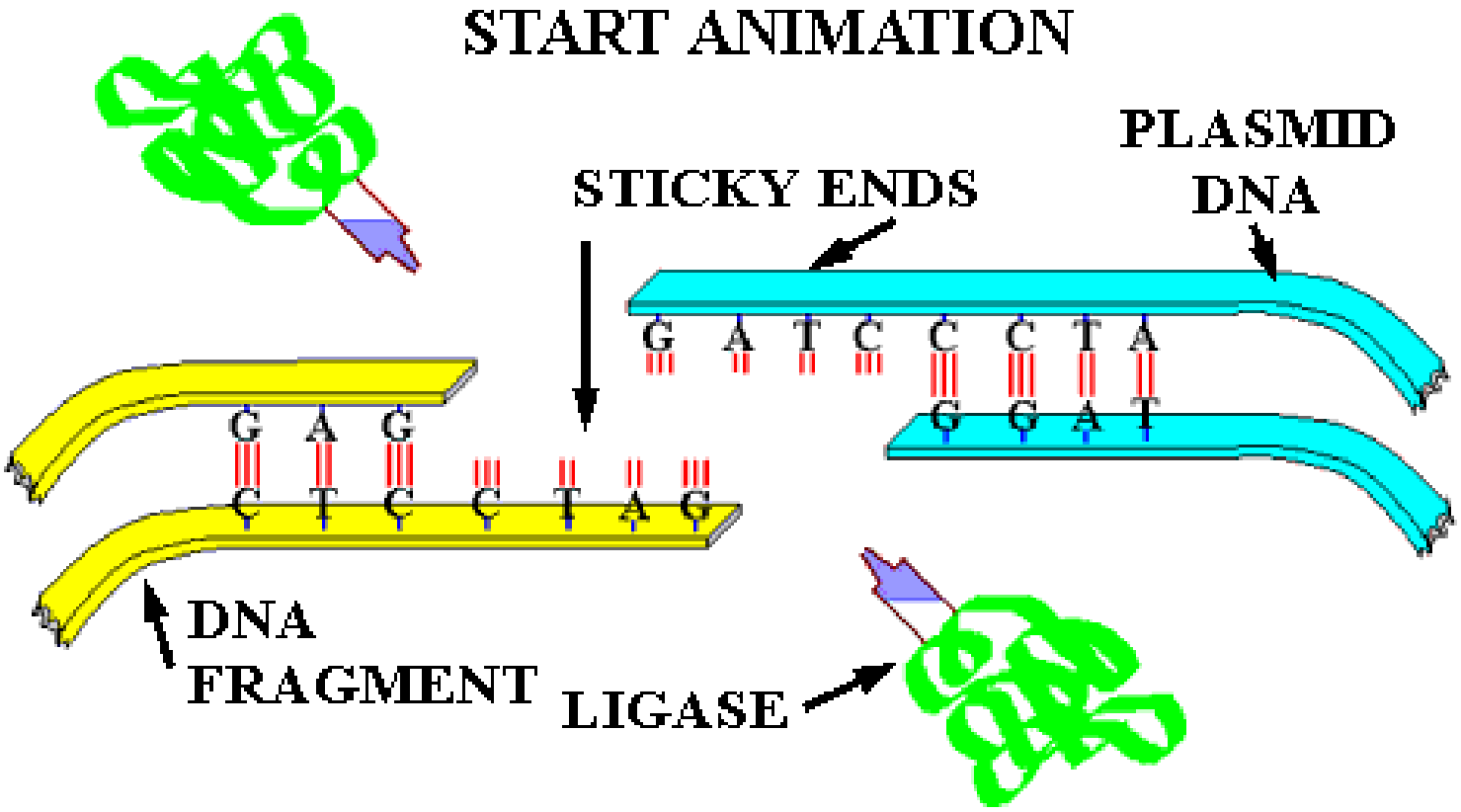
Okazaki fragments!

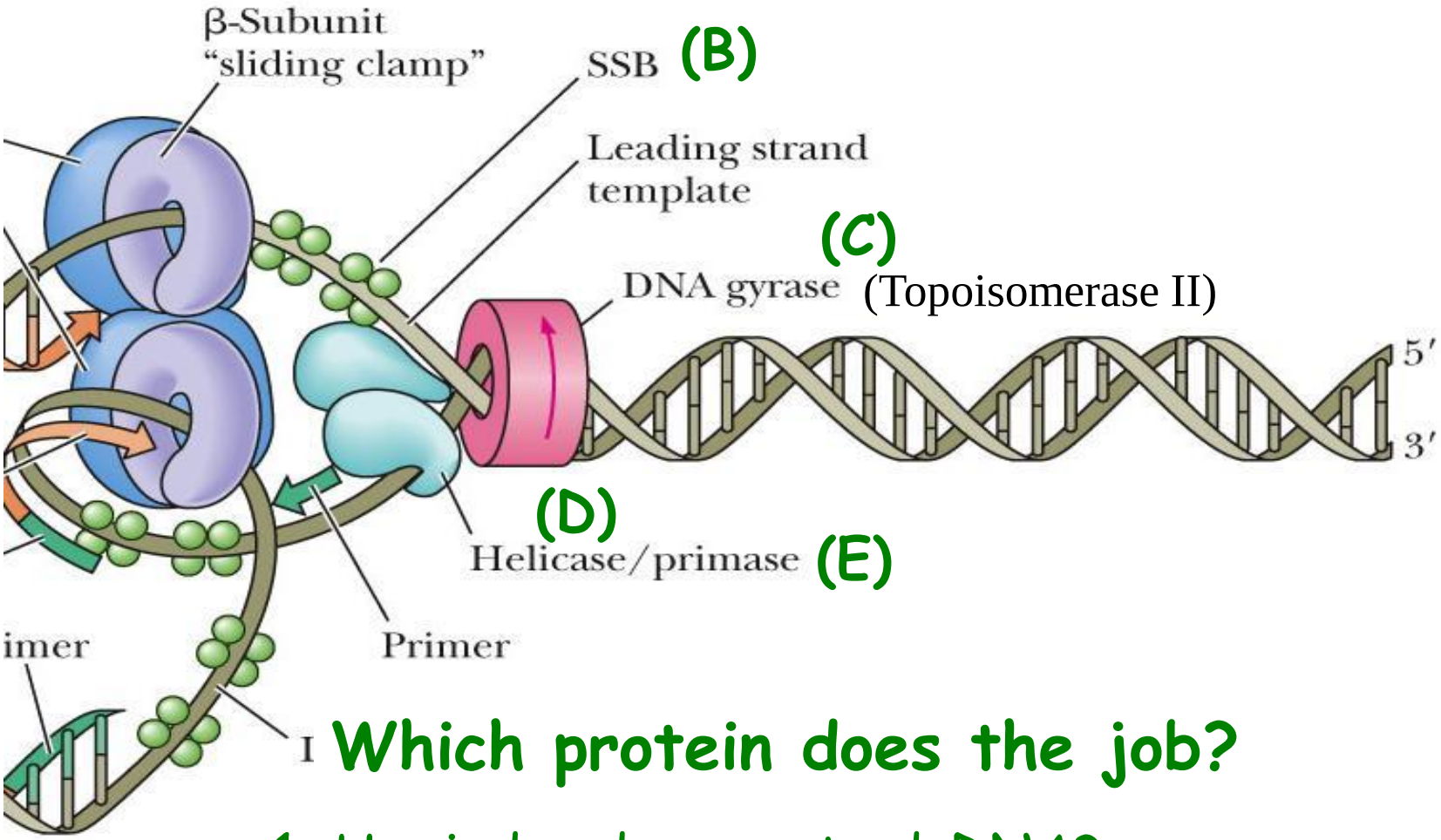
- The short synthesized DNA fragments , formed on the lagging strand.
- Enzymes can only work in one direction along parent DNA (synthesizing 5’ → 3’) on the leading strand.
- The fragments are created on the lagging strand because synthesis can not occur in the normal direction and therefore synthesis is discontinuous.
- On the leading strand (3’ to 5’) the 5’ to 3’ synthesis is continuous, therefore okazaki fragments are NOT necessary.


5'
Newly
synthesized DNA
3'
5'
3'
lagging
strand
5'
3'
Replication fork
Okazaki
fragments
5'
3'
3'
5'
Direction of Fork Movement
5'
3'
leading
strand

DNA **lig**ase

Anatomy: Think about a **lig**ament which joins 2 bones together. Ligase joins two exposed ends of DNA together.

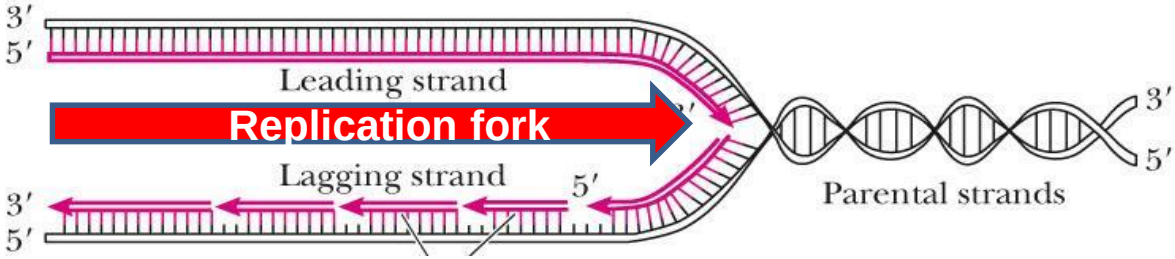




Which protein does the job?

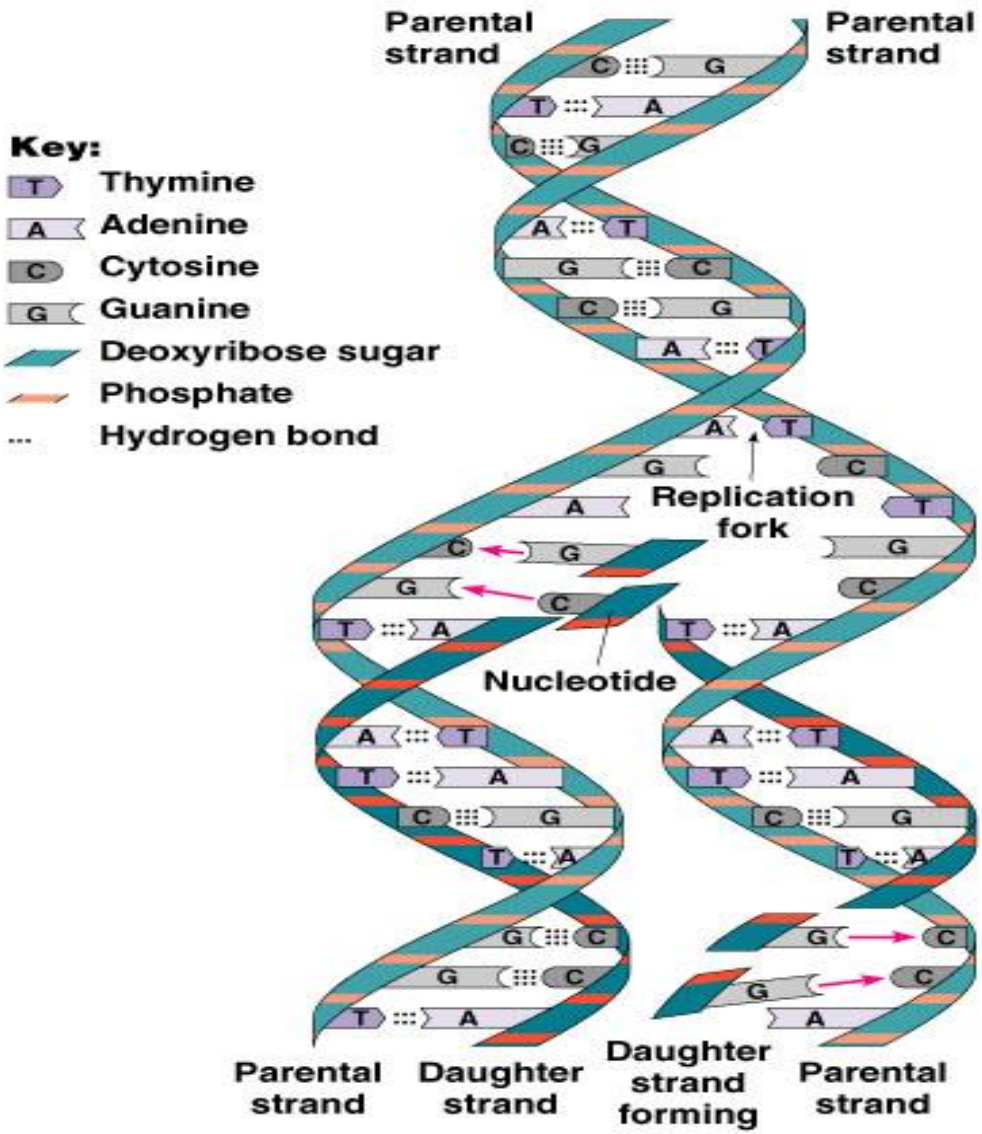
1. Unwind and separate dsDNA?
2. Protect ssDNA?
3. Remove overwound DNA region (positive supercoils) ahead of replication fork?
4. Synthesize RNA primer?

Replication of DNA must be discontinuous on at least one strand because



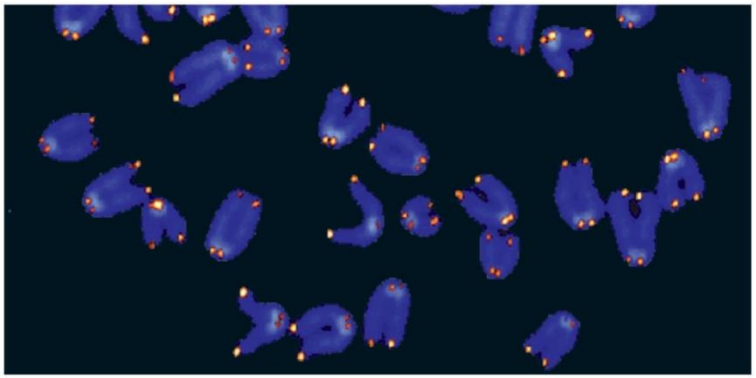
(A) nicks are required for the unwinding of supercoils.
(B) the 5' exonuclease continually introduces nicks in the new DNA.
(C) the direction of polymerization is always 5' to 3′ while the two strands being copied in the replication fork are antiparallel.
(D) fork movement is bidirectional.
(E) RNA primers are used.

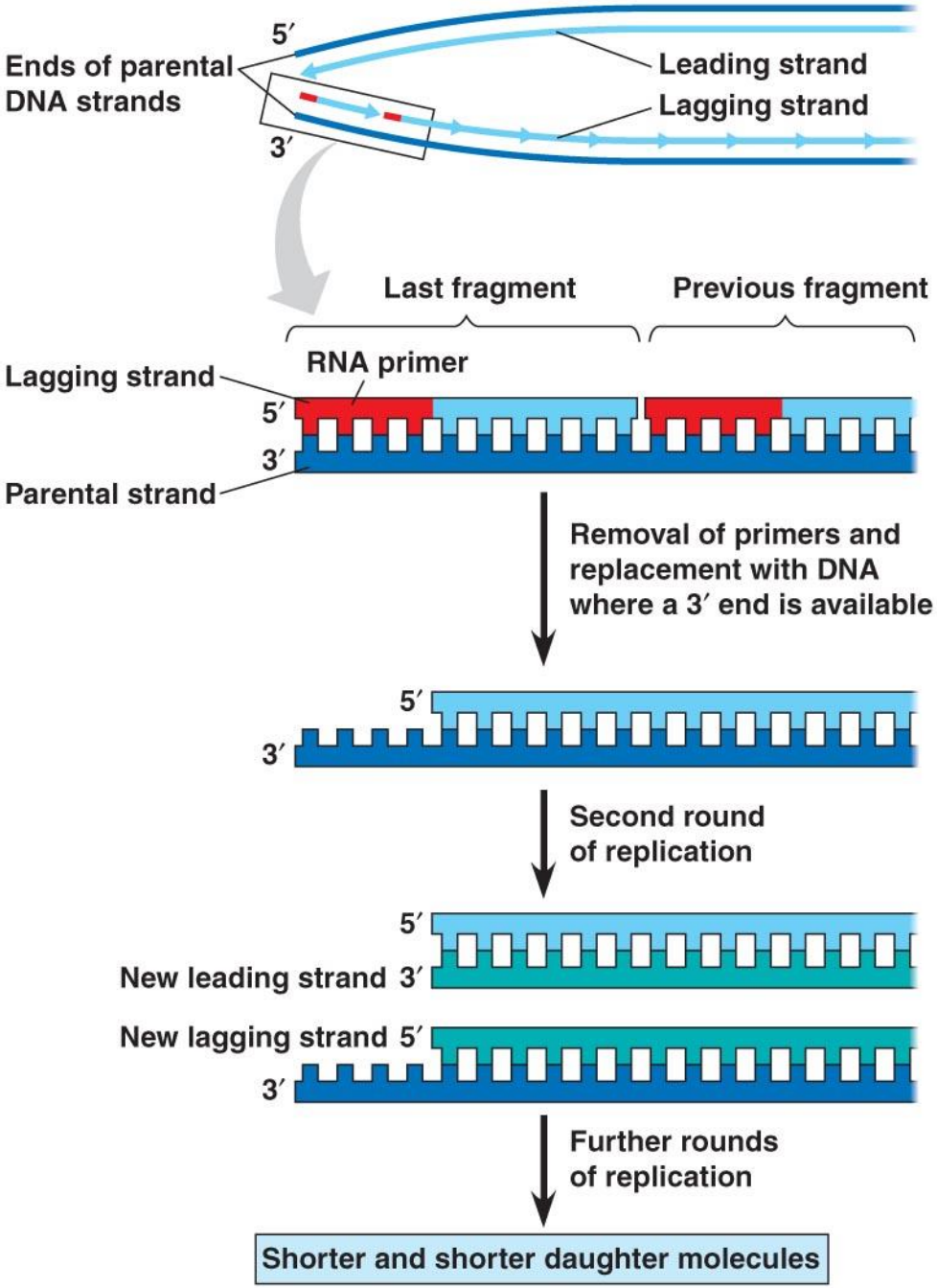
Completed: DNA parent & daughter strand structure



Telomeres

– At the ends of chromosomal DNA are special sequences called **telomeres**.
  - Telomers get shorter with every round of RNA replication
  - In some embryonic tissue, **TELOMERASE** lengthens the telomers, restoring their original length
  - Not a problem with circular prokaryotic DNA





Website for overview of DNA replication.

- http://nitro.biosci.arizona.edu/courses/EEB105/lectures/DNA_replication/DNA_rep.html

Website/youtube showing DNA synthesis- ridiculously fast!!!

- http://www.youtube.com/watch?v=4jtmOZaIvS0&feature=player_embedded