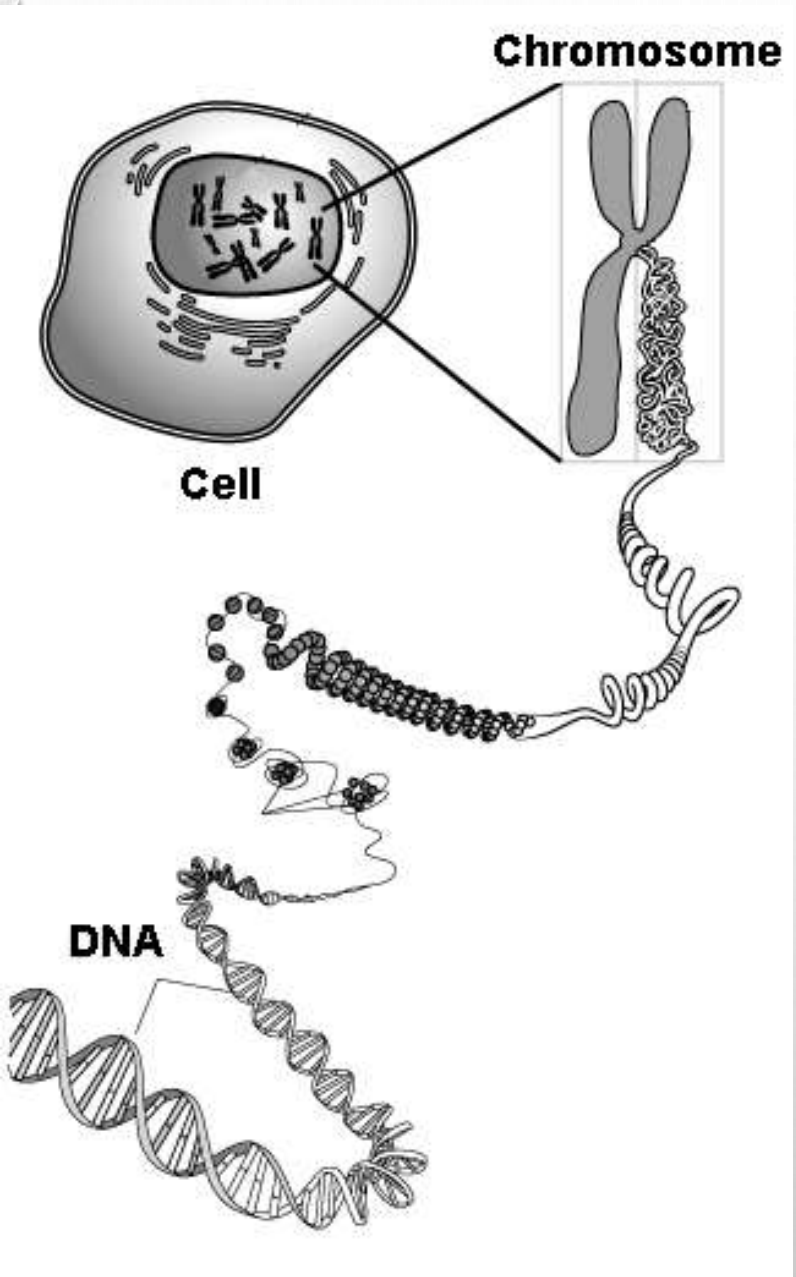
DEOXYRIBONUCLEIC ACID



Nucleus

Chromosomes

Genes

Segments of DNA

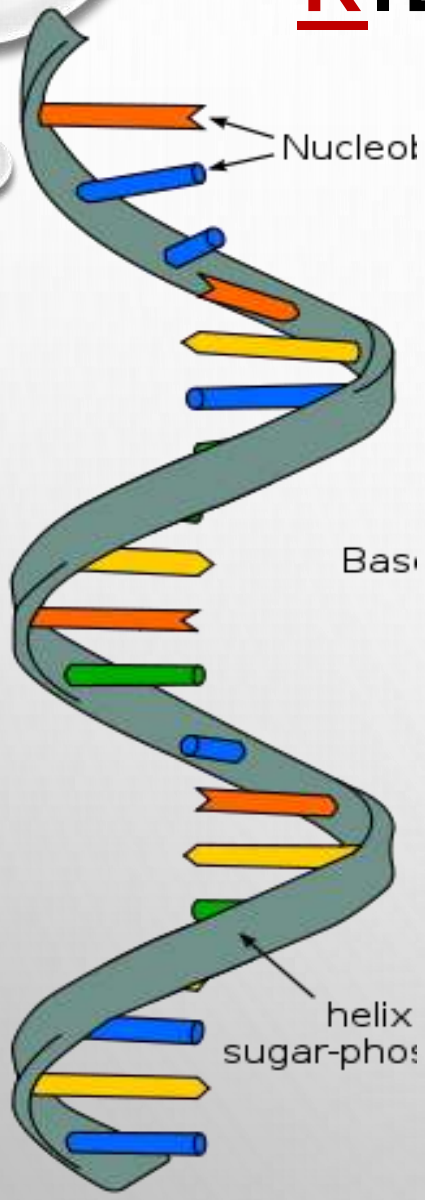
Portions of DNA are called genes.

DNA is tightly wound into chromosomes and located in the nucleus of cells.

DNA cannot leave the nucleus.

DNA is **DOUBLE STRANDED(2** sides)

RIBONUCLEIC ACID



RNA
Ribonucleic acid

RNA is **SINGLE STRANDED** and does not have to stay in the nucleus!

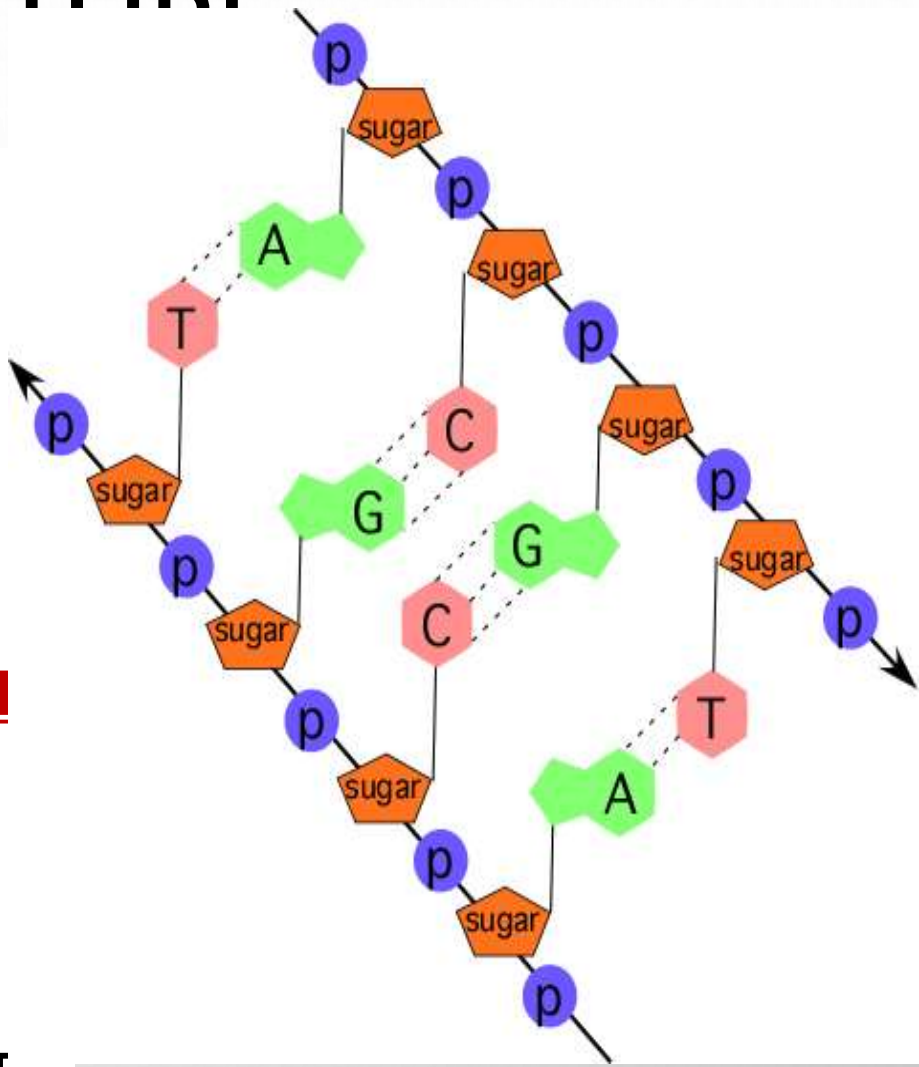
RNA is not found in chromosomes because it does not carry the genetic code, however it can read the **DNA code and take the information out of the nucleus.**

RNA's main job is to build proteins!

DNA STRUCTURE

- THE BUILDING BLOCKS OF DNA ARE CALLED NUCLEOTIDES.

- ONE NUCLEOTIDE IS MADE OF 3 IMPORTANT THINGS:
  - 1. 5-CARBON SUGAR **DEOXYRIBOSI**
  - 2. PHOSPHATE
  - 3. NITROGEN BASE
  - THERE ARE 4 NITROGEN BASES IN DNA: ADENINE, GUANINE, CYTOSINE, AND **THYMINE** THAT PAIR TOGETHER)



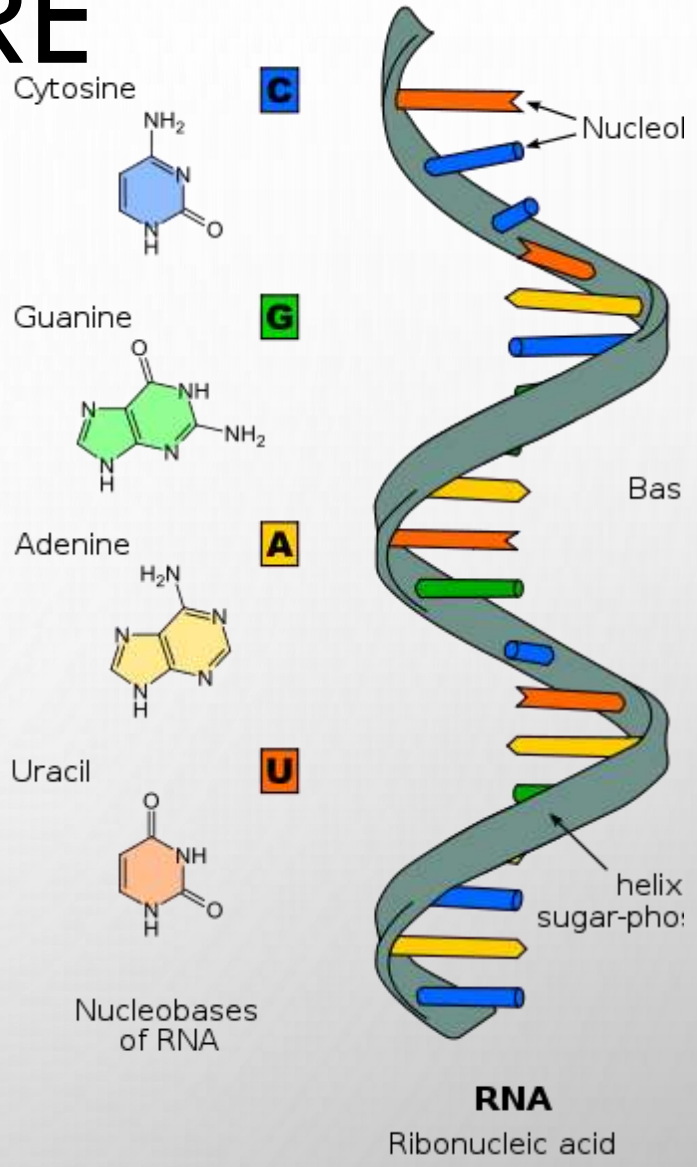
- A → T C → G

RNA STRUCTURE

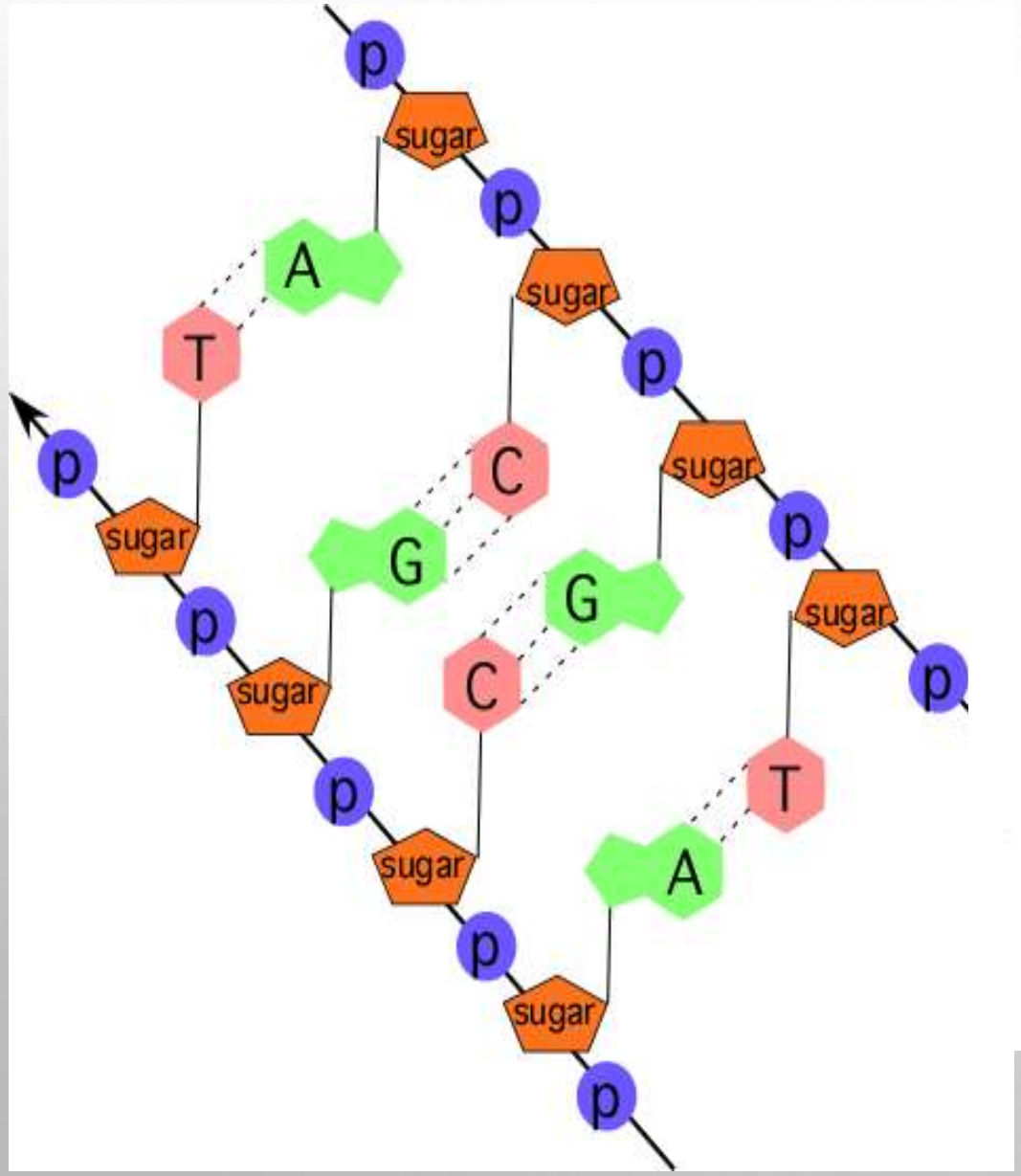
- THE BUILDING BLOCKS OF RNA ARE NUCLEOTIDES, JUST LIKE DNA.

- A NUCLEOTIDE IN RNA IS STILL MADE OF 3 IMPORTANT THINGS:
  - 1. 6-CARBON SUGAR - **RIBOSE** (INSTEAD OF DEOXYRIBOSE)
  - 2. PHOSPHATE
  - 3. NITROGEN BASE
  - THERE ARE 4 NITROGEN BASES IN RNA, A,G,C, AND **U** THAT PAIR TOGETHER)

- A → **U** C →G



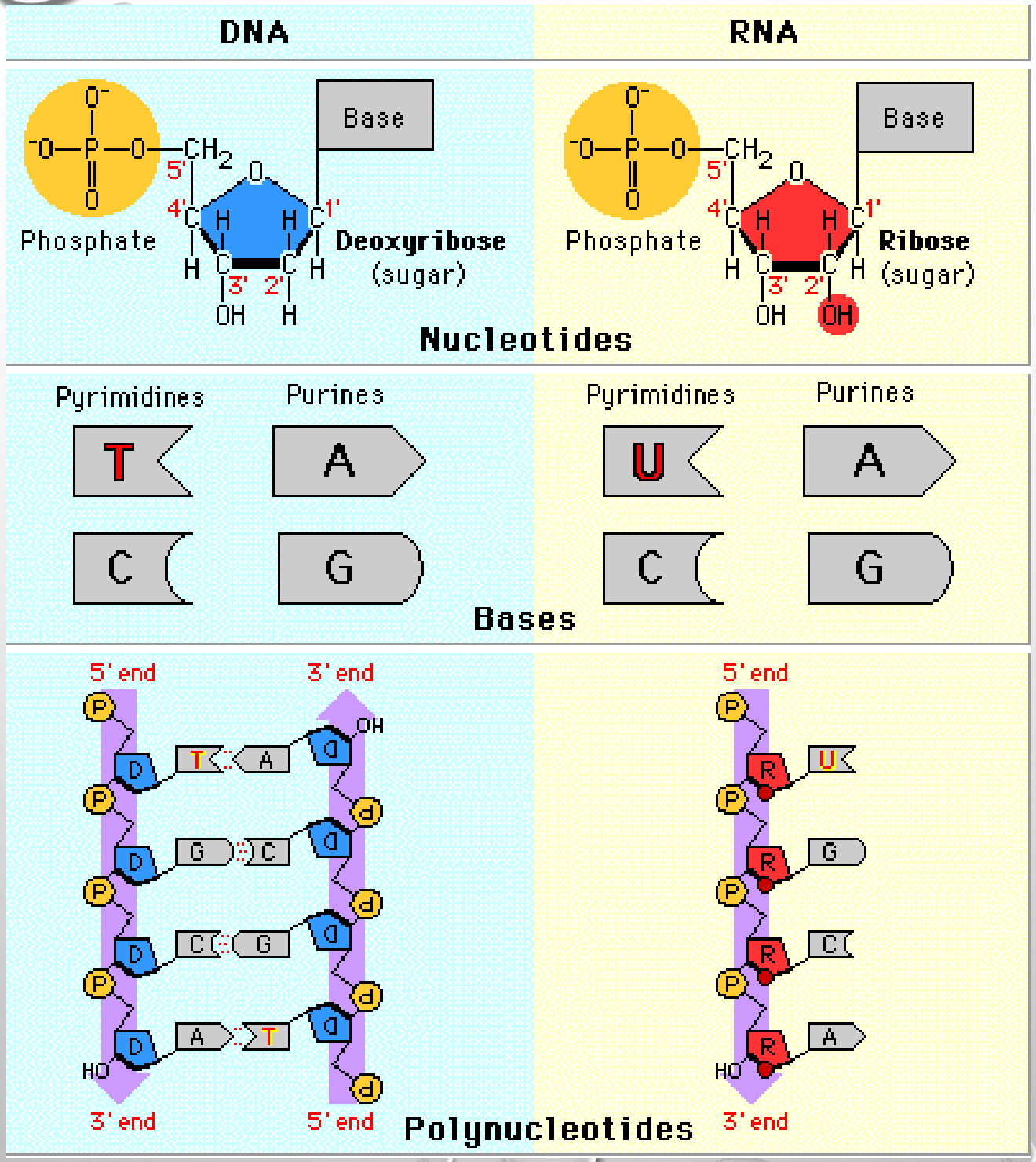
DNA

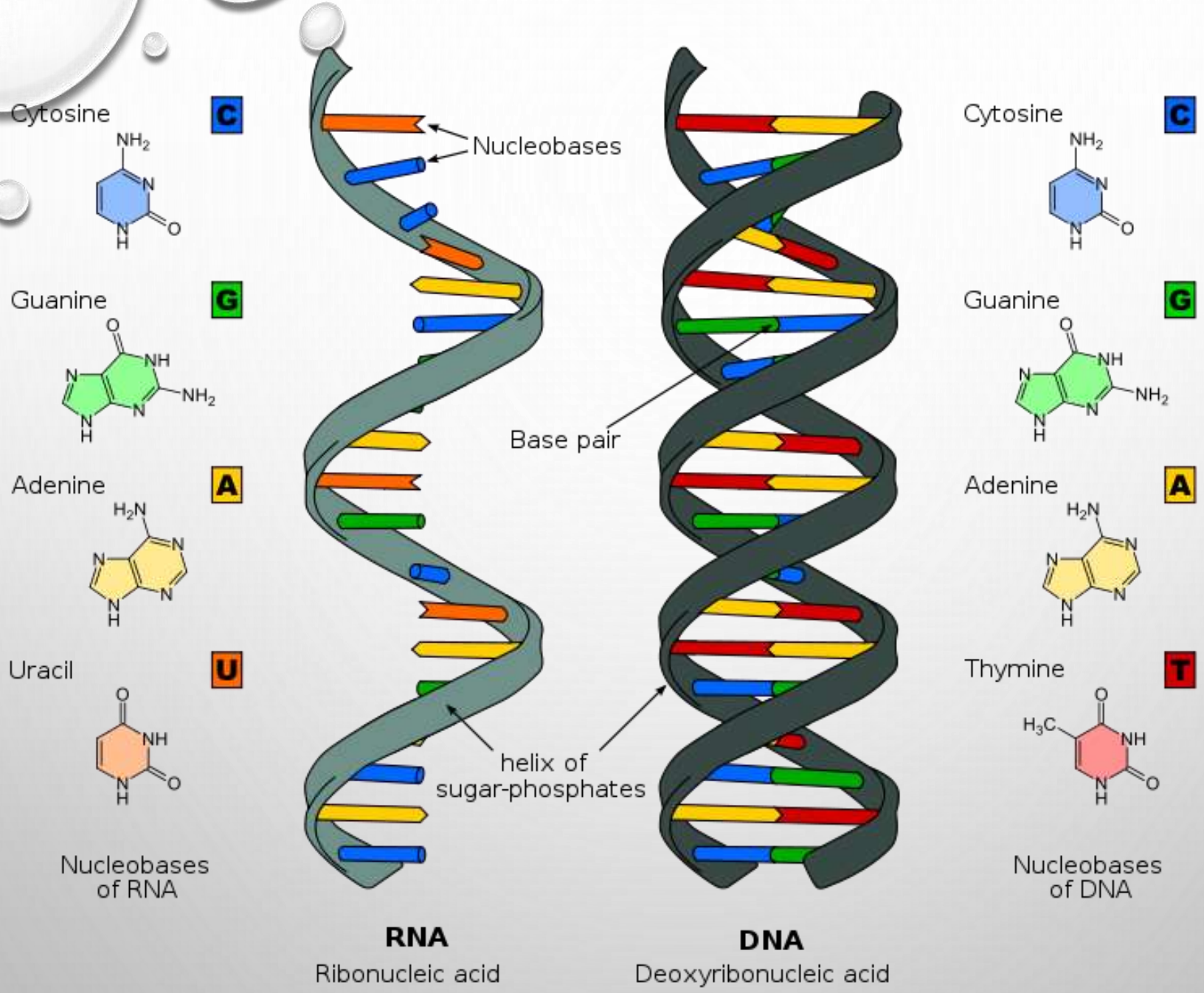


RNA

Both DNA and RNA:

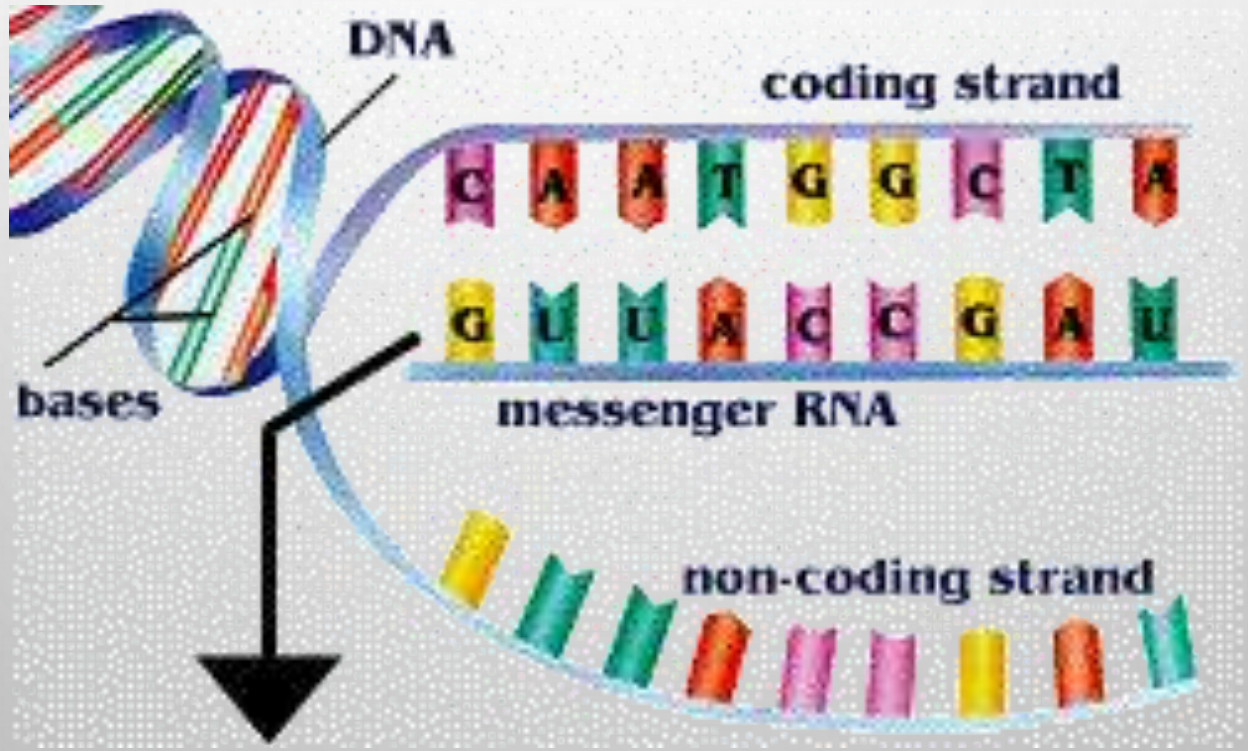
a. are single stranded
b. contain the same four nitrogenous bases
c. have the same five carbon sugars
d. contain phosphate groups


DNA
RNA
Base
Phosphate
Deoxyribose
(sugar)
Base
Phosphate
Ribose
(sugar)
Nucleotides
Pyrimidines
Purines
T
A
C
G
Pyrimidines
Purines
U
A
C
G
Bases
5' end
3' end
3' end
5' end
Polynucleotides
5' end
3' end


Cytosine
C
Guanine
G
Adenine
A
Uracil
U
Nucleobases of RNA
Nucleobases
Base pair
helix of sugar-phosphates
RNA
Ribonucleic acid
DNA
Deoxyribonucleic acid
Cytosine
C
Guanine
G
Adenine
A
Thymine
T
Nucleobases of DNA

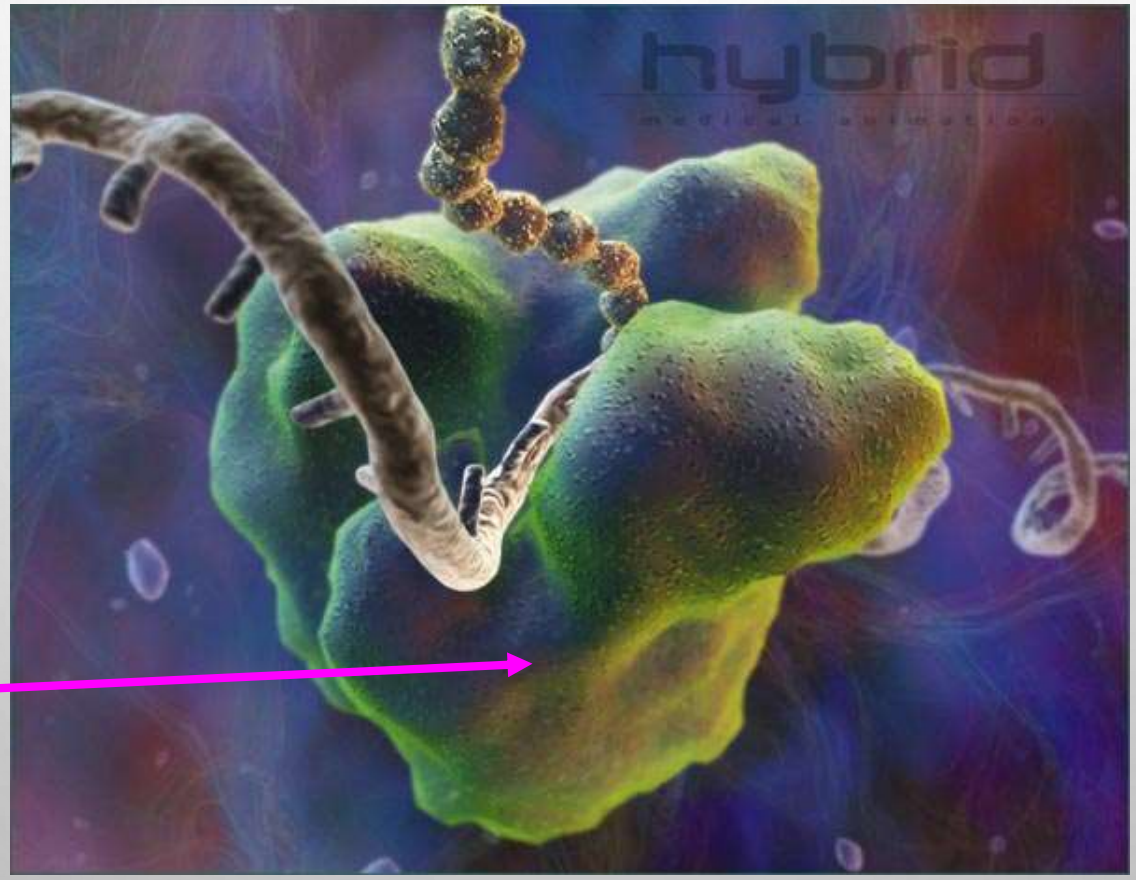
THREE MAIN TYPES OF RNA

- 1. <u>MESSENGER RNA (MRNA)</u> - CARRIES COPIES OF INSTRUCTIONS FOR THE ASSEMBLY OF AMINO ACIDS INTO PROTEINS FROM DNA TO THE REST OF THE CELL (SERVE AS “MESSENGER”)



THREE MAIN TYPES OF RNA

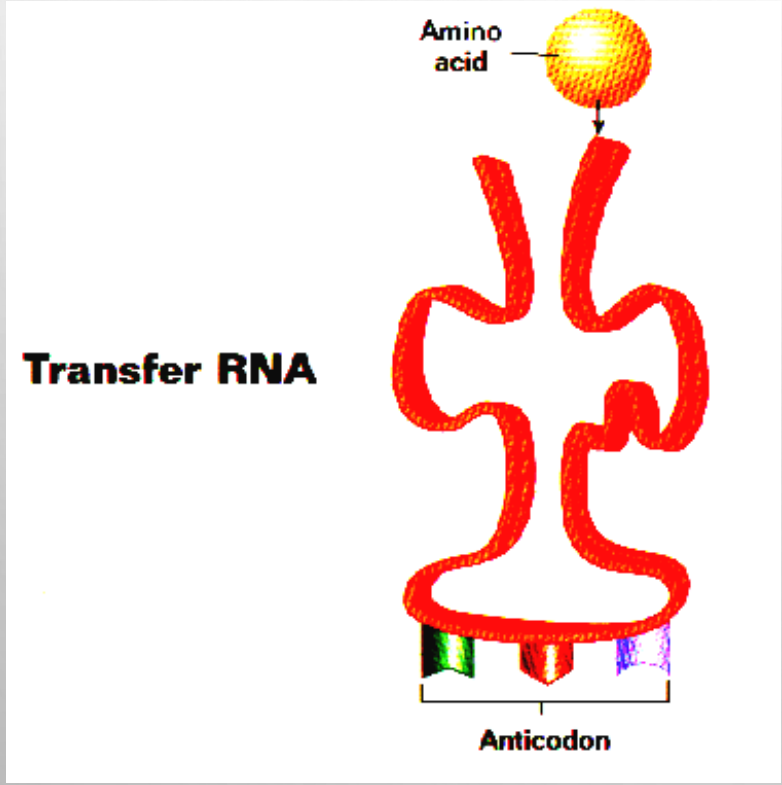
2. <u>RIBOSOMAL RNA (RRNA)</u> – MAKES UP THE MAJOR PART OF RIBOSOMES, WHICH IS WHERE PROTEINS ARE MADE.

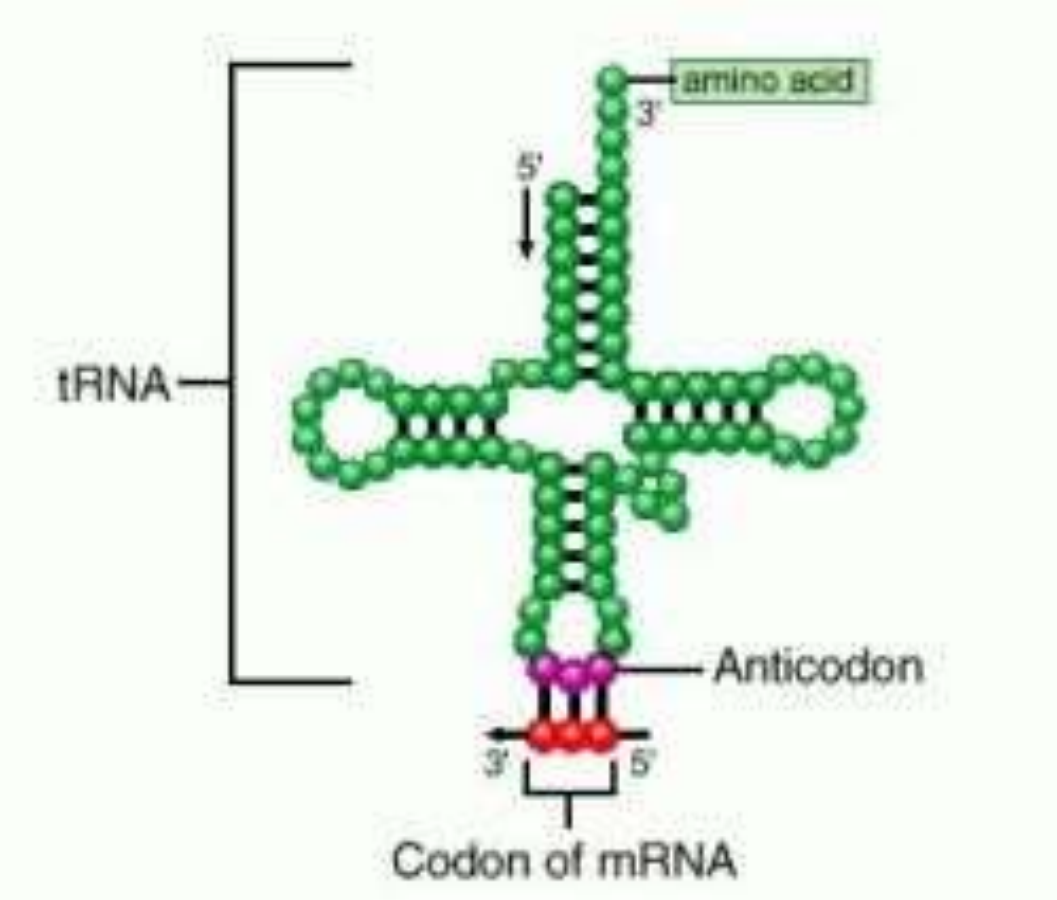


Ribosomal RNA

THREE MAIN TYPES OF RNA

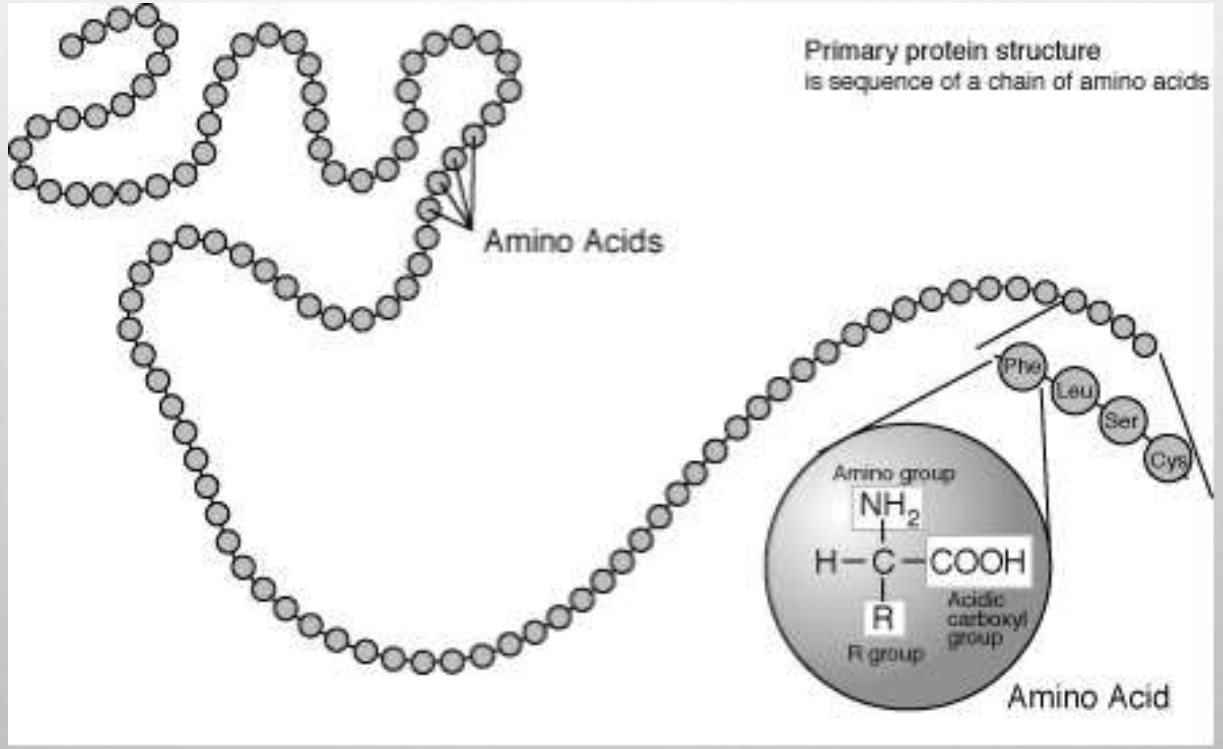
3. TRANSFER RNA (TRNA) - TRANSFERS AMINO ACIDS TO RIBOSOMES DURING PROTEIN SYNTHESIS





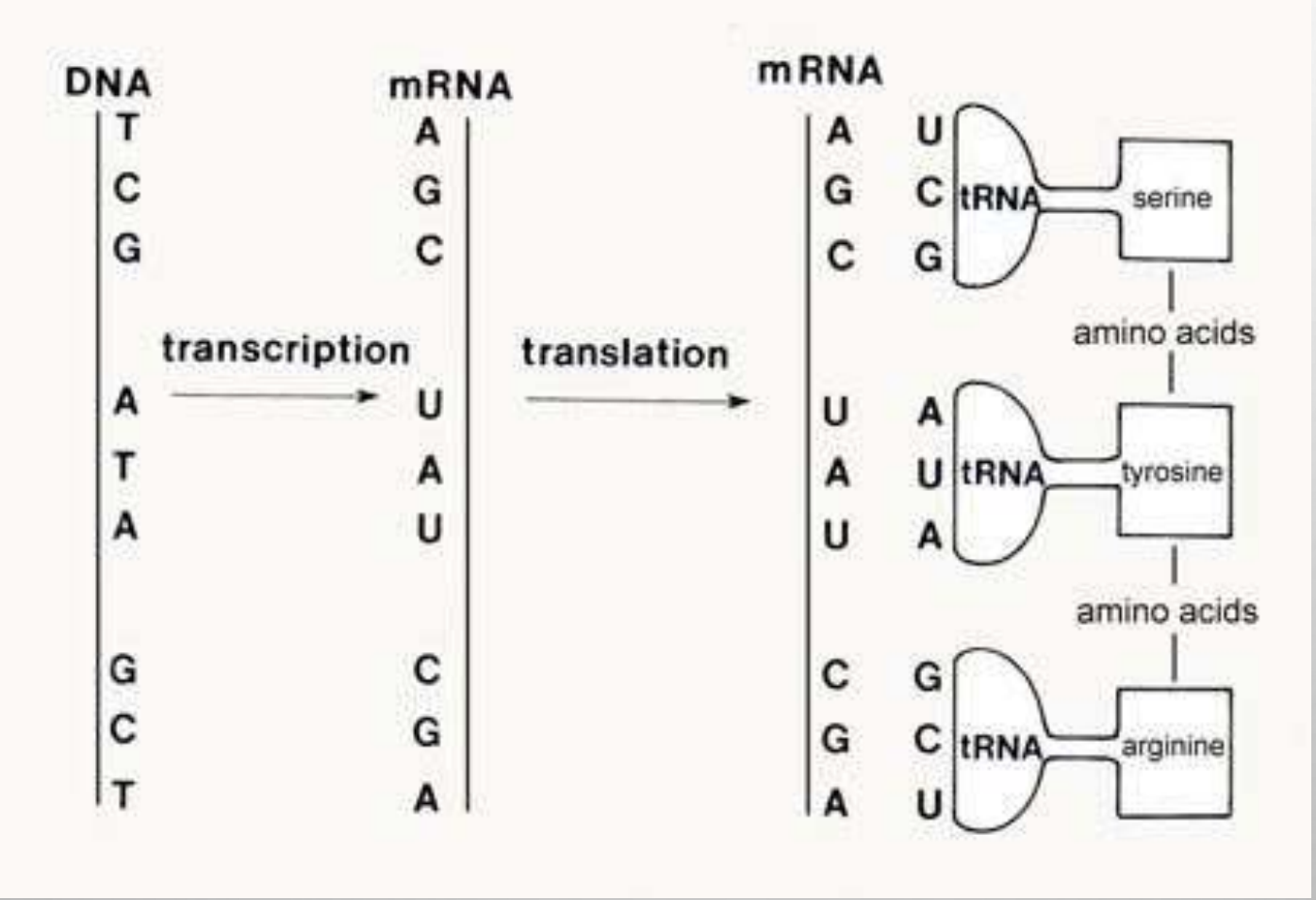
PROTEINS

- PROTEINS ARE MADE UP OF A CHAIN OF AMINO ACIDS.
- PROTEINS ARE ENZYMES, WHICH CATALYZE AND REGULATE CHEMICAL REACTIONS.



2 STEPS TO MAKE A PROTEIN

1. TRANSCRIPTION
   - DNA → RNA
2. TRANSLATION
   - RNA → PROTEIN (CHAIN OF AMINO ACIDS)



- WHEN TRANSCRIPTION NEEDS TO TAKE PLACE, DNA MUST PROVIDE THE CODE IN ORDER TO CREATE AN MRNA STRAND.

- MRNA WILL BE ABLE TO LEAVE THE NUCLEUS AND NOW IT HAS THE CODE TRANSCRIBED INSIDE IT'S BASE PAIRS!

- PRACTICE:

- DNA STRAND: TTA ACG GGT CTA
- MATCHING DNA STRAND: AAT TGC CCA GAT
- MRNA: UUA ACG GGU CUA

DNA REPLICATION:

- Copying genetic information for transmission to the next generation
- Occurs in S phase of cell cycle
- Process of DNA duplicating itself
- Begins with the unwinding of the double helix to expose the bases in each strand of DNA
- Each unpaired nucleotide will attract a complementary nucleotide from the medium
  - will form base pairing via hydrogen bonding.
- Enzymes link the aligned nucleotides by phosphodiester bonds to form a continuous strand.

DNA REPLICATION:

- First question asked was whether duplication was semiconservative or conservative

  - Meselson and Stahl expt

  - Semiconservative -
    - one strand from parent in each new strand

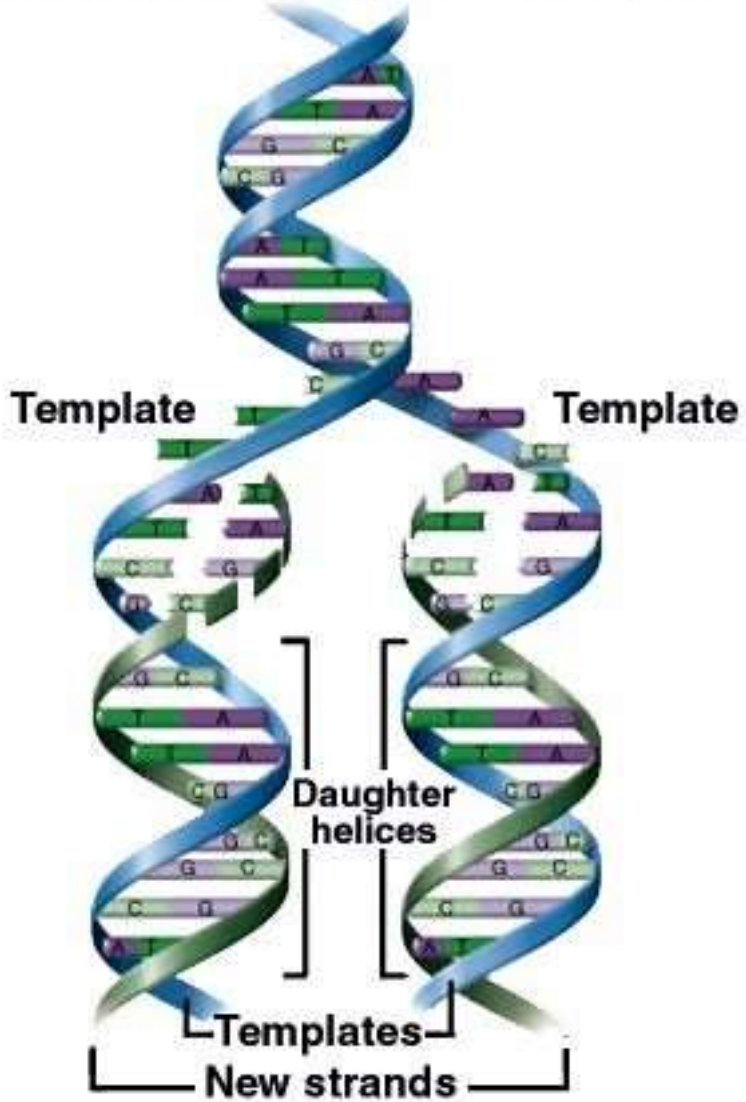
  - Conservative-
    - both strands from parent and other is all new strands

DNA REPLICATION:

- 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

DNA replication: an overview

1. Original double helix
2. Strands separate
3. Complementary bases align opposite templates
4. Enzymes link sugar-phosphate elements of aligned nucleotides into a continuous new strand

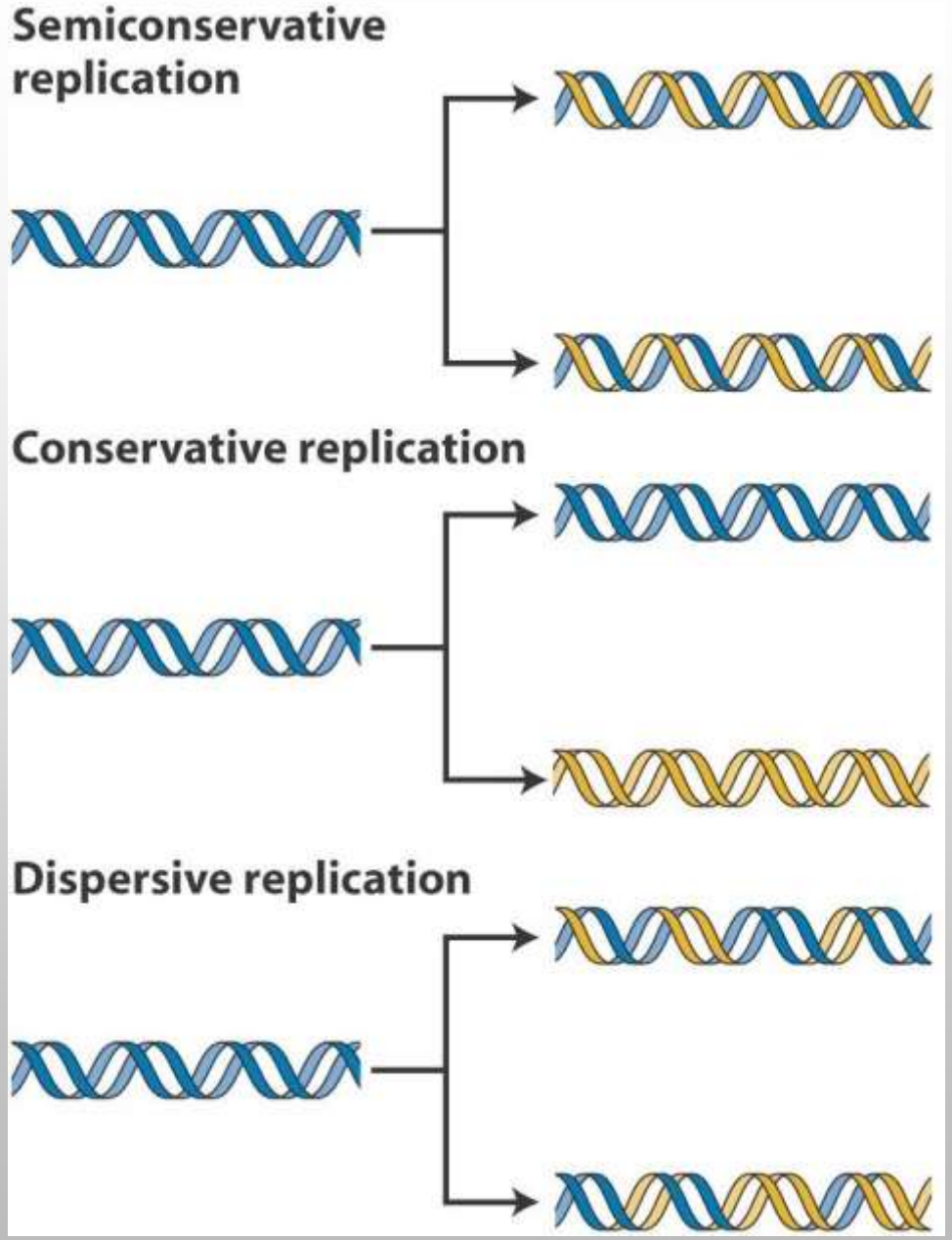


EXPERIMENTAL PROOF OF SEMICONSERVATIVE REPLICATION – THREE POSSIBLE MODELS

- Semiconservative replication –
  - Watson and Crick model

- Conservative replication:
  - The parental double helix remains intact;
  - both strands of the daughter double helix are newly synthesized

- Dispersive replication:
  - At completion, both strands of both double helices contain both original and newly synthesized material.


Semiconservative replication
Conservative replication
Dispersive replication

MESELSON-STAHL EXPERIMENTS CONFIRM SEMICONSERVATIVE REPLICATION

- Experiment allowed differentiation of parental and newly formed DNA.
- Bacteria were grown in media containing either normal isotope of nitrogen (^{14}N) or the heavy isotope (^{15}N).
- DNA banded after equilibrium density gradient centrifugation at a position which matched the density of the DNA:
  - heavy DNA was at a higher density than normal DNA.

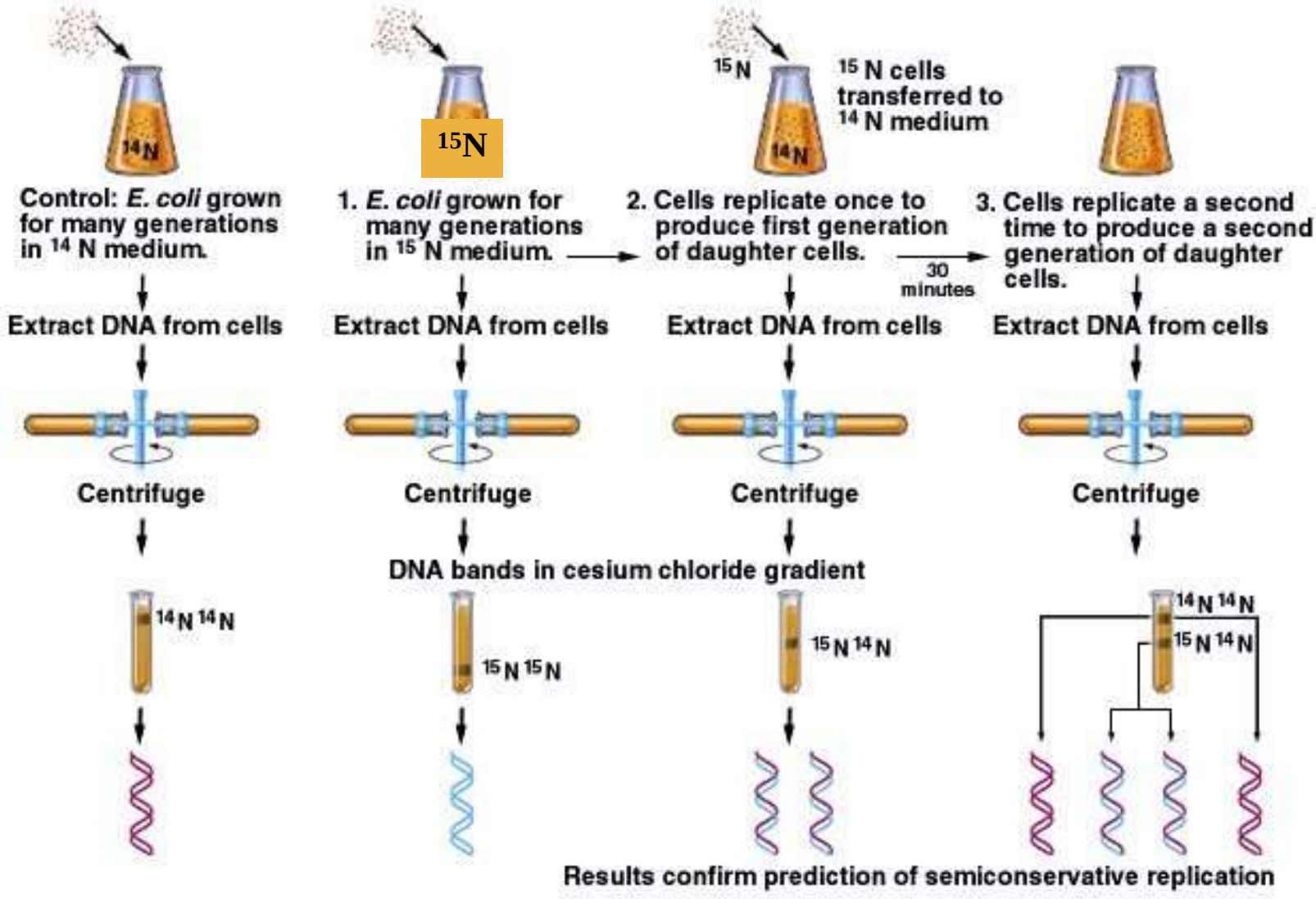
Fig. 6.16

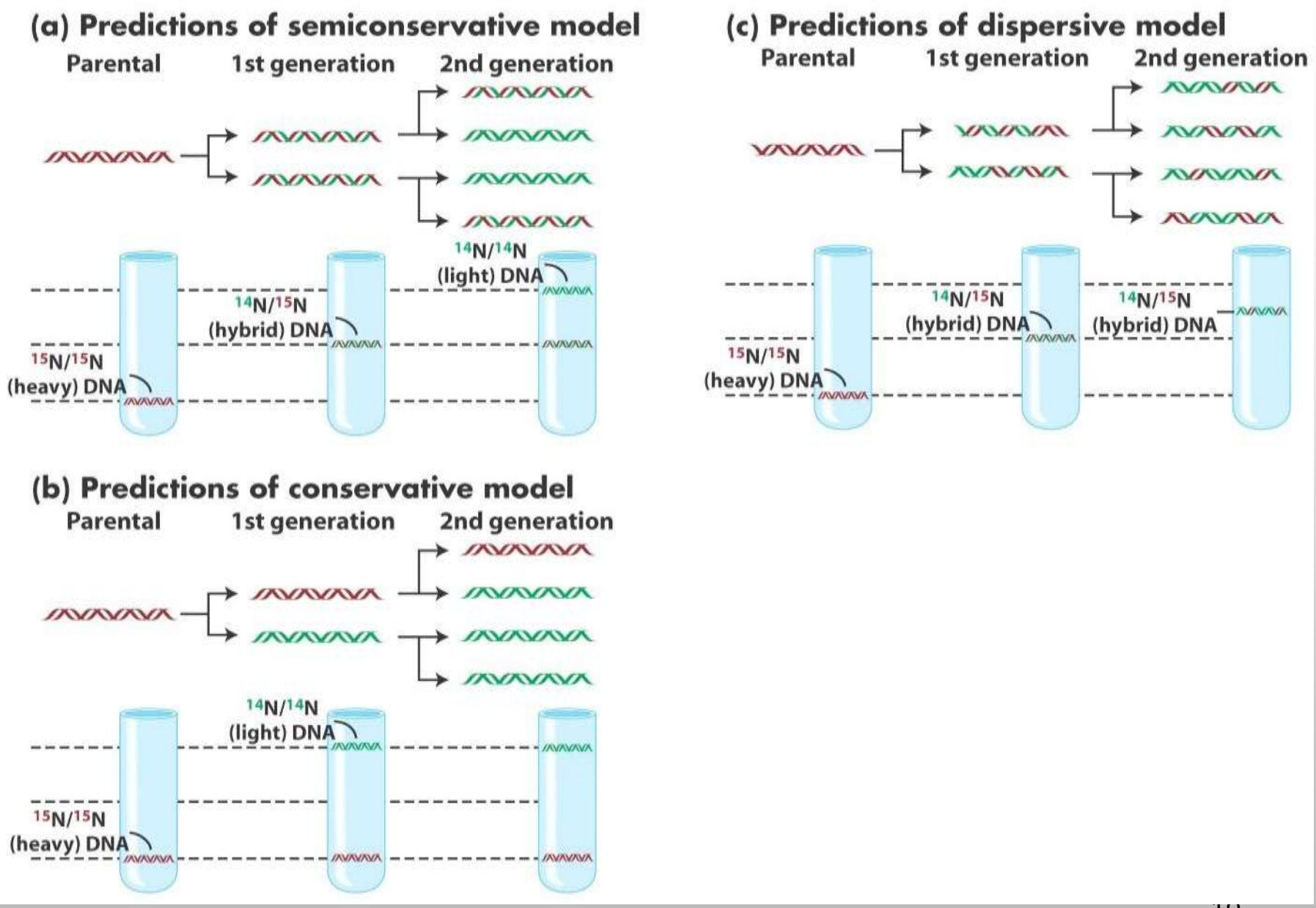
MESELSON-STAHL EXPERIMENTS CONFIRM SEMICONSERVATIVE REPLICATION

- When bacteria grown in ^{15}N were transferred to normal ^{14}N containing medium,
  - the newly synthesized DNA strand had the ^{14}N while the parental strand had ^{15}N.

- They checked the composition of the resulting DNA molecules by density gradient centrifugation,
  - found an intermediate band,
  - indicating a hybrid molecule
  - containing both ^{14}N and ^{15}N DNA.

The Meselson-Stahl experiment




(a) Predictions of semiconservative model
Parental
1st generation
2nd generation
14N/14N
(light) DNA
14N/15N
(hybrid) DNA
15N/15N
(heavy) DNA
(b) Predictions of conservative model
Parental
1st generation
2nd generation
14N/14N
(light) DNA
15N/15N
(heavy) DNA
(c) Predictions of dispersive model
Parental
1st generation
2nd generation
14N/15N
(hybrid) DNA
14N/15N
(hybrid) DNA
15N/15N
(heavy) DNA

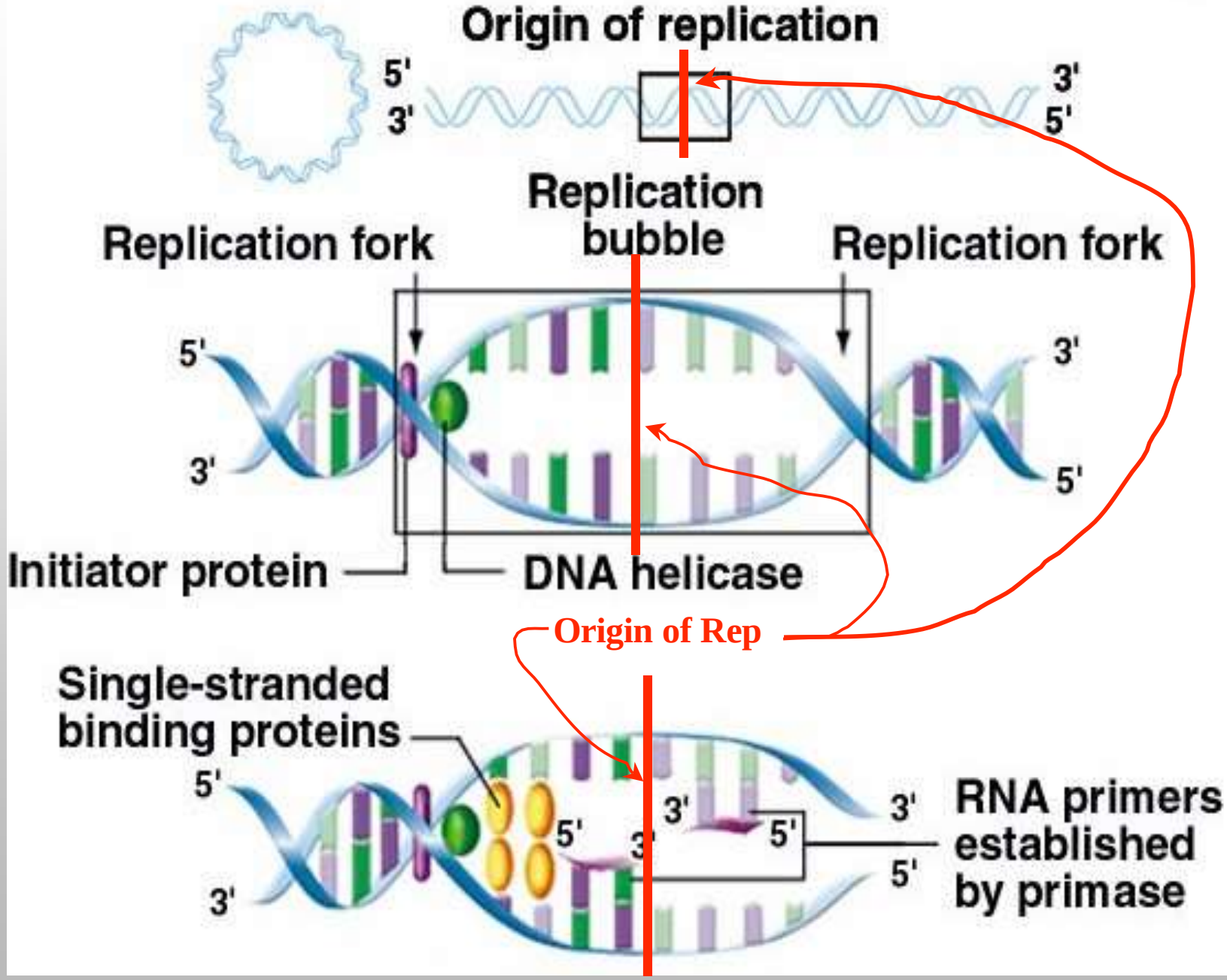
THE MECHANISM OF DNA REPLICATION

- Tightly controlled process,
  - occurs at specific times during the cell cycle.
- Requires:
  - a set of proteins and enzymes,
  - and requires energy in the form of ATP.
- Two basic steps:
  - Initiation
  - Elongation.
- Two basic components:
  - template
  - primer.

THE MECHANISM OF DNA REPLICATION (PROKARYOTIC)

- DNA polymerase
  - the enzyme that extends the primer;
  - Pol III –
    - produces new stands of complementary DNA
  - Pol I –
    - fills in gaps between newly synthesized Okazaki segments
- additional enzymes/proteins
  - i) DNA helicase –
    - unwinds double helix
  - ii) Single-stranded binding proteins –
    - keep helix open
  - iii) Primase –
    - creates RNA primers to initiate synthesis
  - iv) Ligase –
    - welds together Okazaki fragments

Mechanism of DNA replication, 1



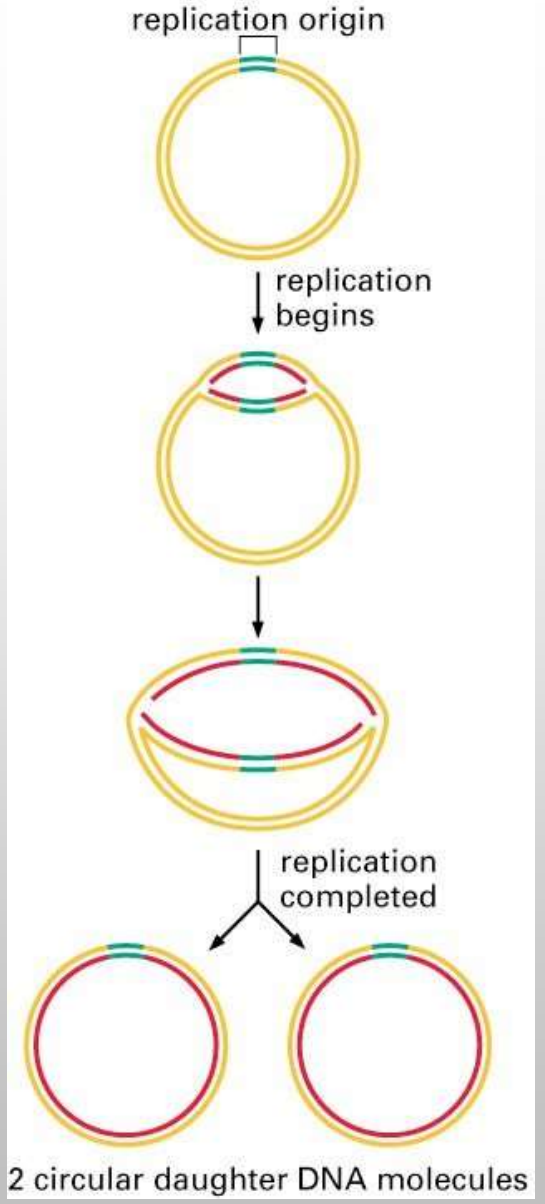
ORIGINS OF REPLICATION

- Replication proceeds in both directions (bidirectionally) from a single origin of replication on the prokaryotic circular chromosome

- Replication proceeds in both directions (bidirectionally) from hundreds or thousands of origins of replication on each of the linear eukaryotic chromosomes.

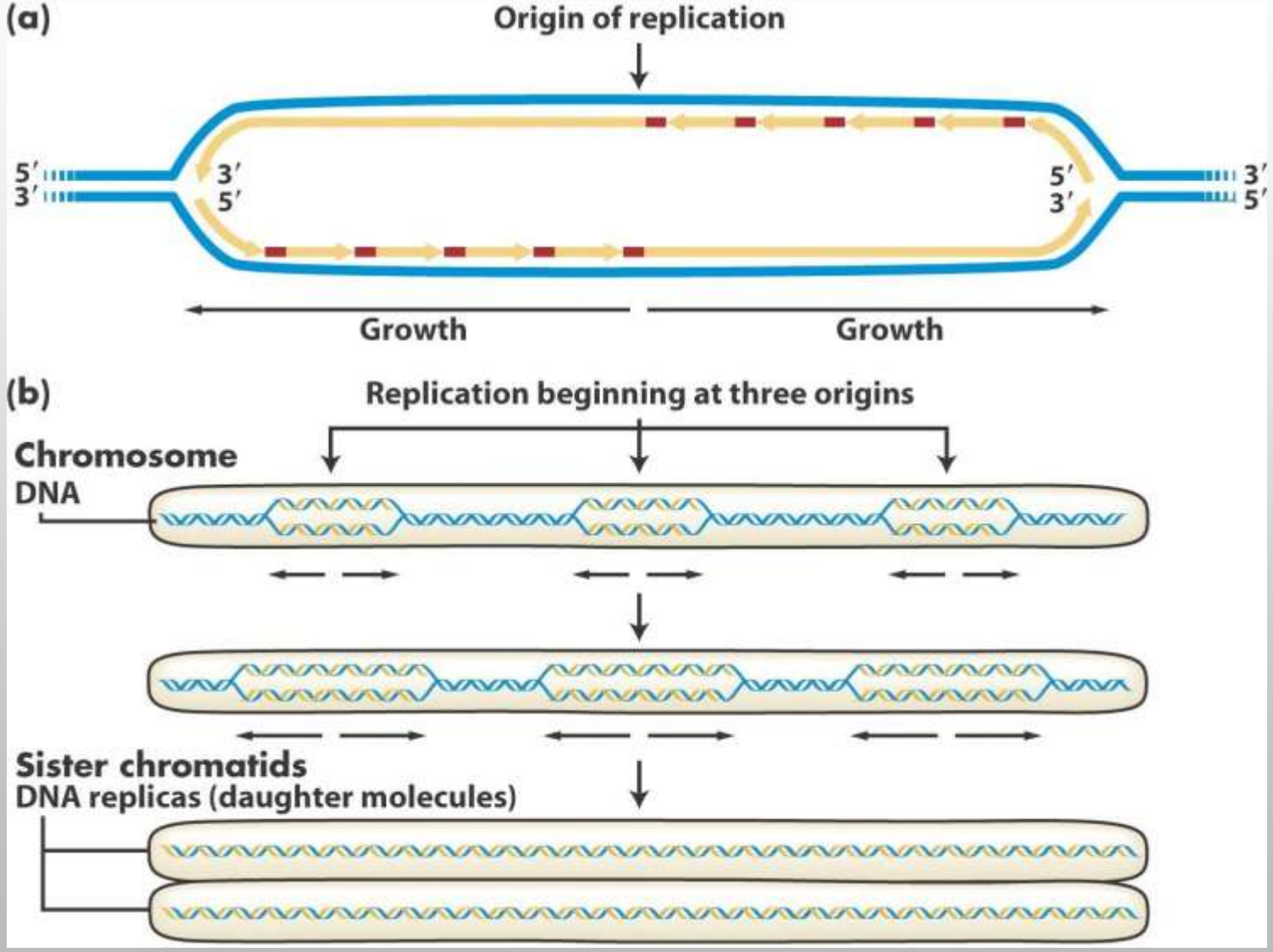
ORIGINS OF REPLICATION

- Bacteria have 1 origin of replication per one chromosome
- They only have one chromosome = 1 origin!

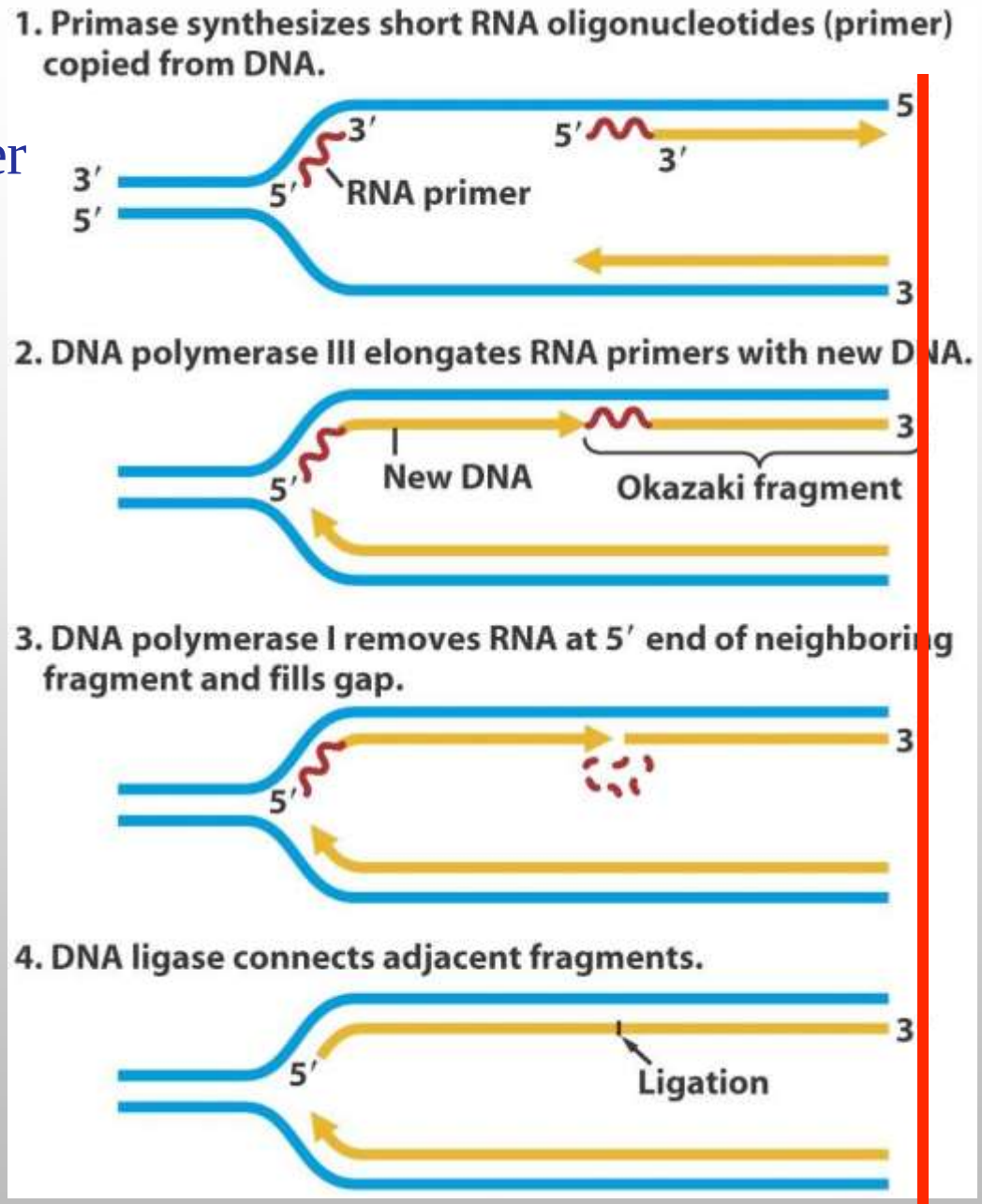


Molecular Biology of the Cell, 4th Edition.

EUKARYOTIC ORIGINS OF REPLICATION



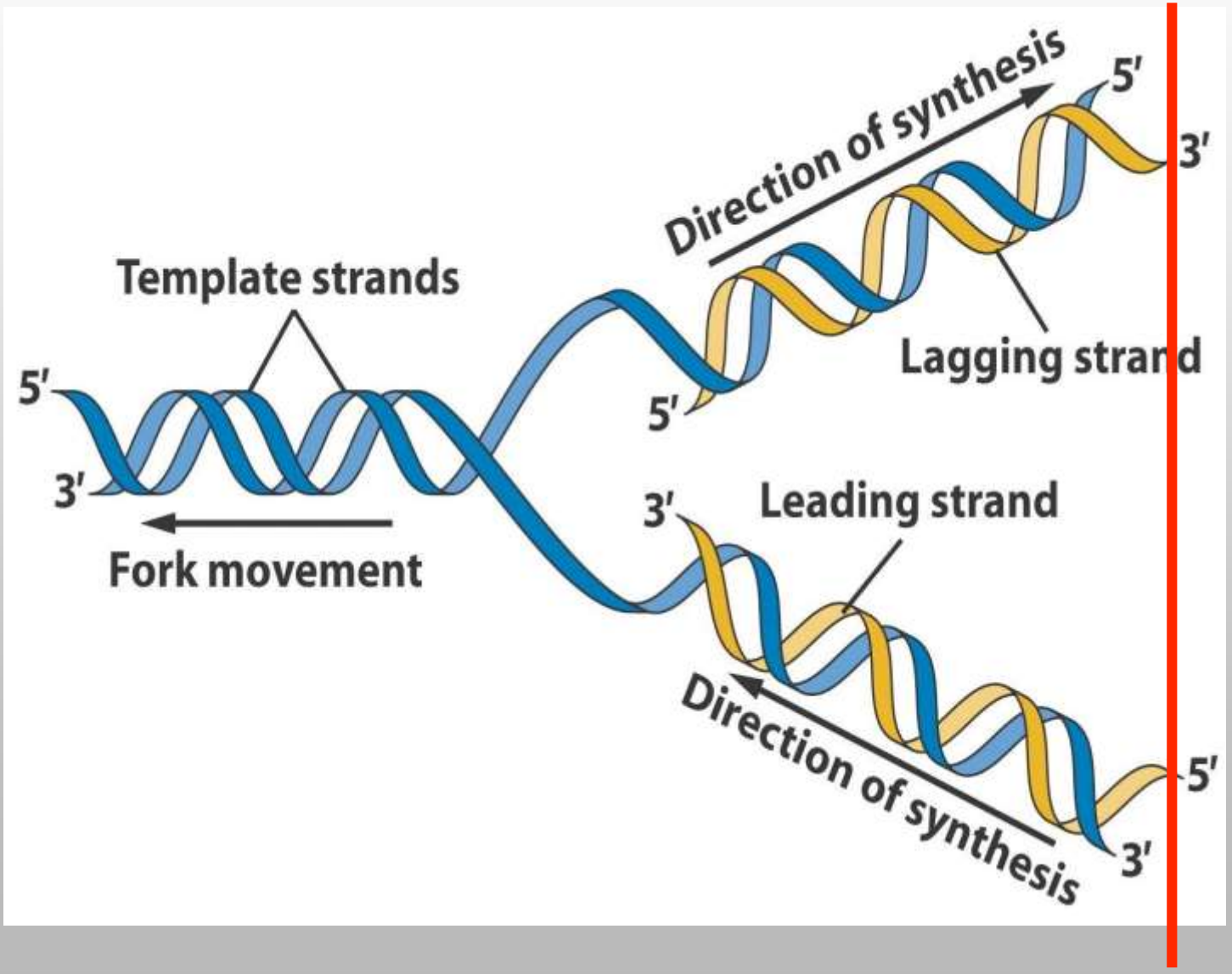
- Replication Initiation:
  - Primase and the RNA Primer
- Replication Elongation:
  - DNA polIII
    - Must have 3' to add to
- Replication is Finished:
  - DNA polI removes primer
  - Fills gap using 3'ends
  - DNA ligase connects frags
    - Uses 5' ends!



Origin of Rep

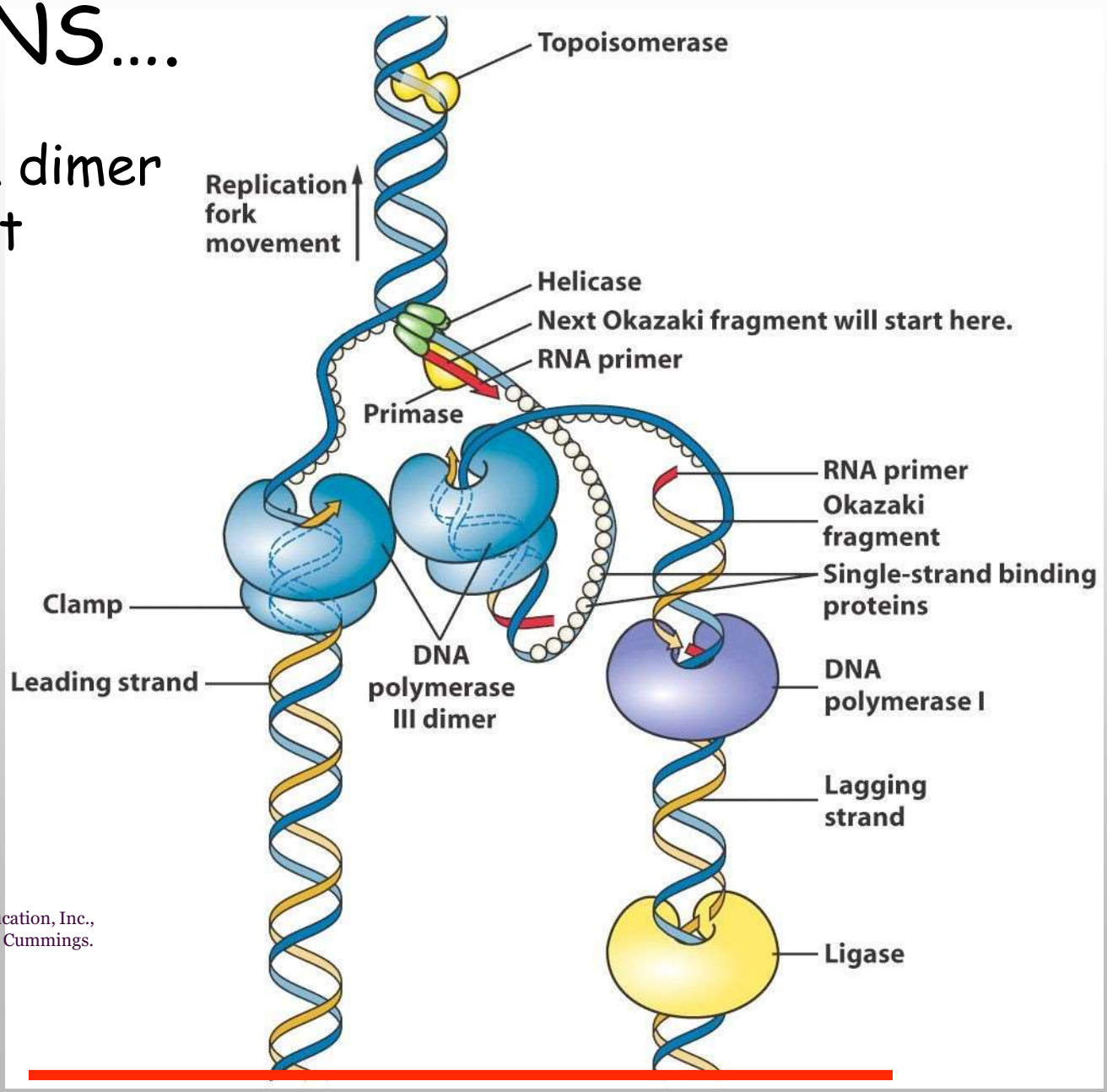
REPLICATION FORK

Origin of Rep



WHAT REALLY HAPPENS….

DNA pol works as a dimer
Lagging strand must loop around to accommodate dimerization

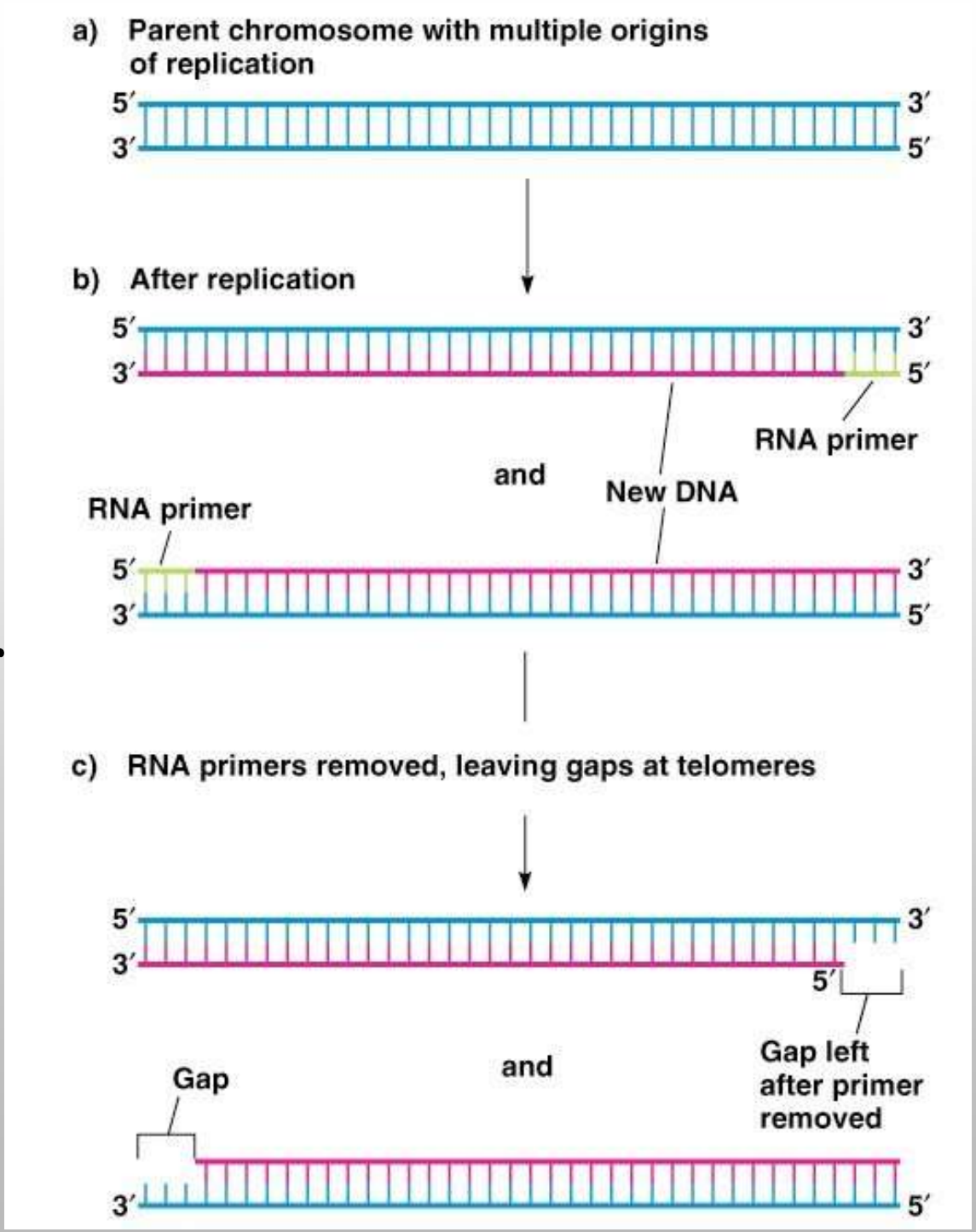


REPLICATION TERMINATION

- THE ENDS OF CHROMOSOMES (TELOMERES) CANNOT BE REPLICATED ON THE LAGGING STRAND BECAUSE THERE IS NO PRIMER AVAILABLE.
- **TELOMERASES**
  - ENZYMES THAT CONTAIN RNA PRIMERS WHICH EXTEND THE ENDS OF CHROMOSOMES (NOT NORMALLY EXPRESSED IN SIGNIFICANT LEVELS)
    - TELOMERES FORM A SORT OF SINGLE STRANDED CAP AROUND THE CHROMOSOME ENDS TO PROTECT THEM FROM BEING DEGRADED
  - CHROMOSOME ENDS ARE PROGRESSIVELY SHORTENED WITH EACH ROUND OF REPLICATION.
  - "OLD" CELLS WITH SHORTENED TELOMERES UNDERGO APOPTOSIS
    - No death signal
    - PROTECTIVE FOR NORMAL CELLS
    - KILL THE OLD AND POSSIBLY MUTATED

FIG.
11.14

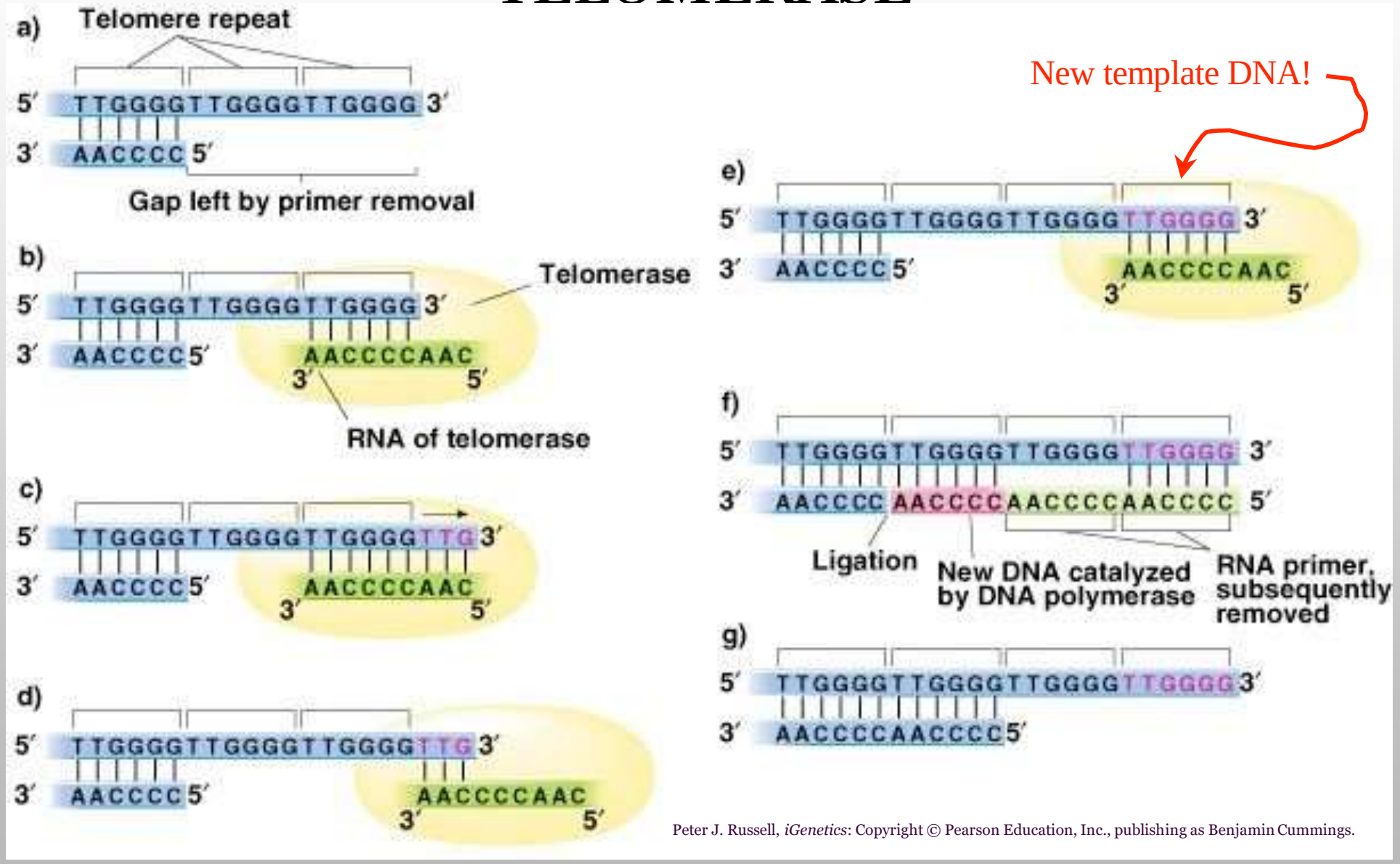
The problem of replicating completely a linear chromosome in eukaryotes



REPLICATING THE ENDS OF CHROMOSOMES

- telomerase adds an RNA primer complementary to telomere sequences
  - chromosomal replication proceeds by adding to the 3’ end of the primer
- Fills the gap left behind by replication
- Telomerase enzyme can also add DNA basepairs to the TEMPLATE DNA
  - complementary to the RNA primer basepairs
  - Using an RNA template to make DNA, telomerase functions as a reverse transcriptase called TERT (telomerase reverse transcriptase).
    - This goes against the Central Dogma….
    - Evolutionarily thought to be derived from a Retrovirus

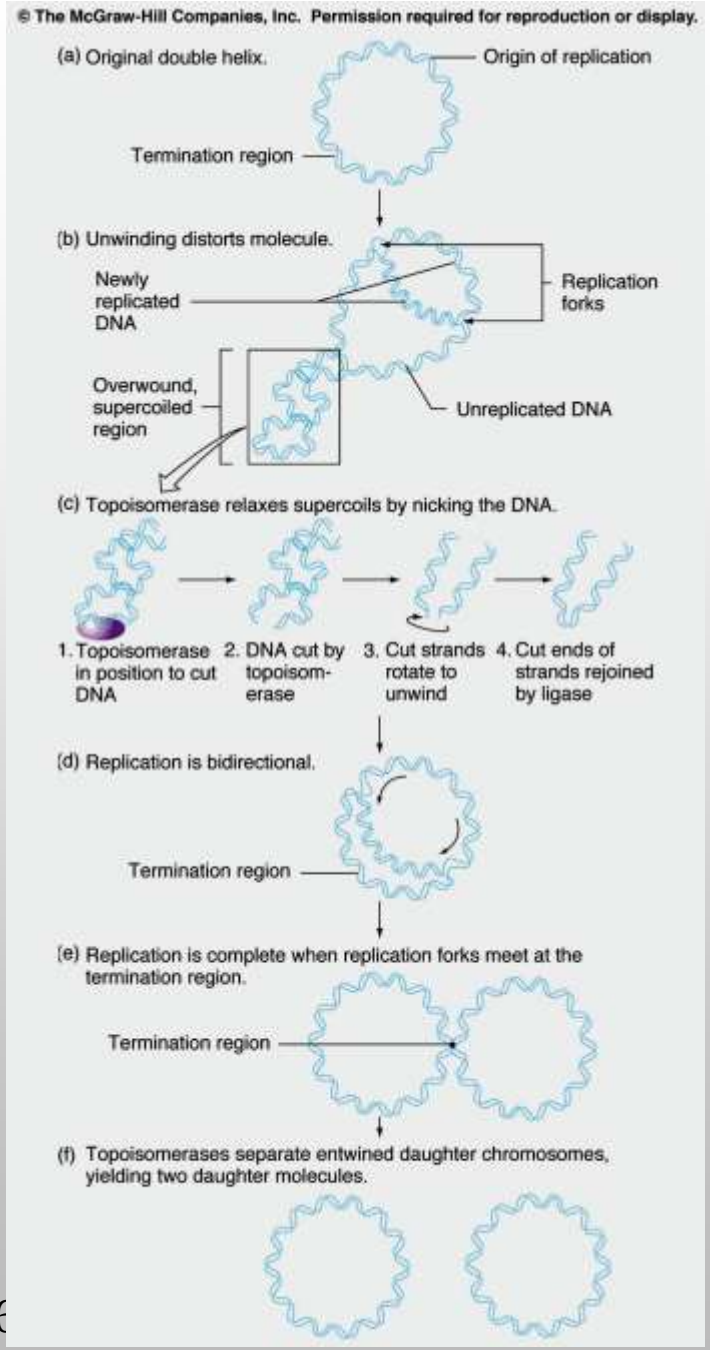
FIG. 3.19
SYNTHESIS OF TELOMERIC DNA BY TELOMERASE



REPLICATION AT THE CHROMOSOMAL LEVEL

- Replication is bidirectional.
- For circular DNA (and linear chromosomes)
  - the unwinding at the replication forks causes supercoiling.
- **DNA topoisomerases**
  - enzymes that help relax the DNA by nicking the strands
  - releasing the twists
  - then rejoining the DNA ends.
  - Example is DNA gyrase

THE BIDIRECTIONAL REPLICATION OF A CIRCULAR CHROMOSOME (PROKARYOTIC)



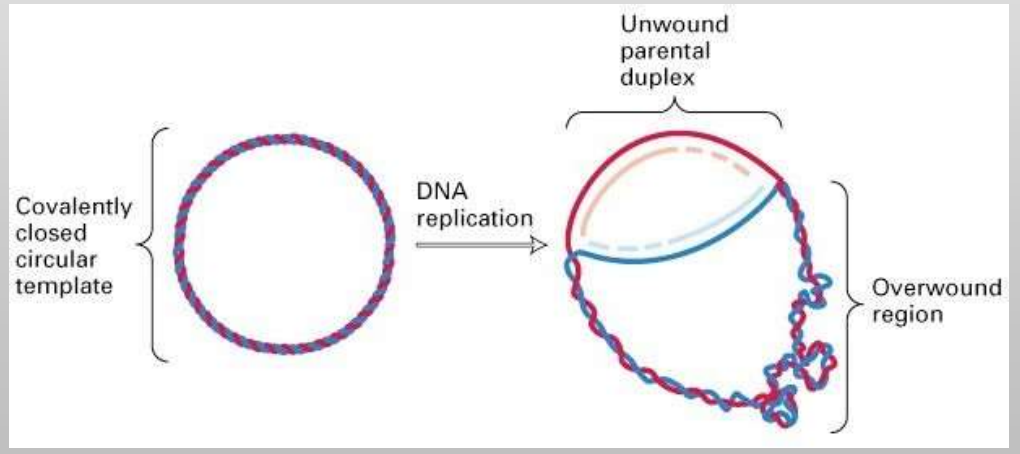
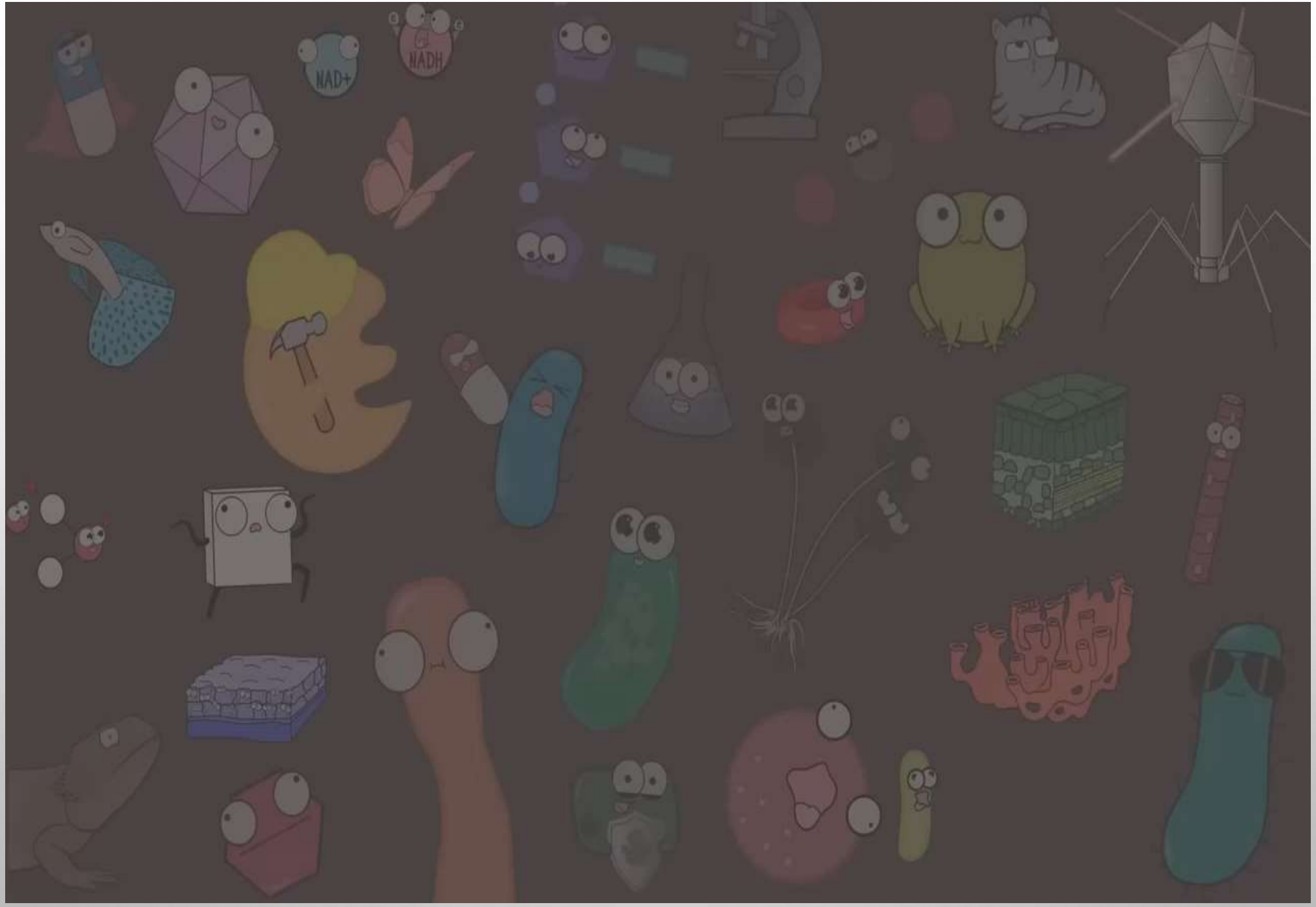


Fig. 6


NAD+
NADH

ASSEMBLING NEWLY REPLICATED DNA INTO NUCLEOSOMES

- When eukaryotic DNA is replicated, it complexes with histones.
  - This requires synthesis of histone proteins and assembly of new nucleosomes.

- Transcription of histone genes is initiated near the end of G1 phase, and translation of histone proteins occurs throughout S phase.

- Assembly of newly replicated DNA into nucleosomes is shown in Figure 11.16.

THE ASSEMBLY OF NUCLEOSOMES AFTER REPLICATION