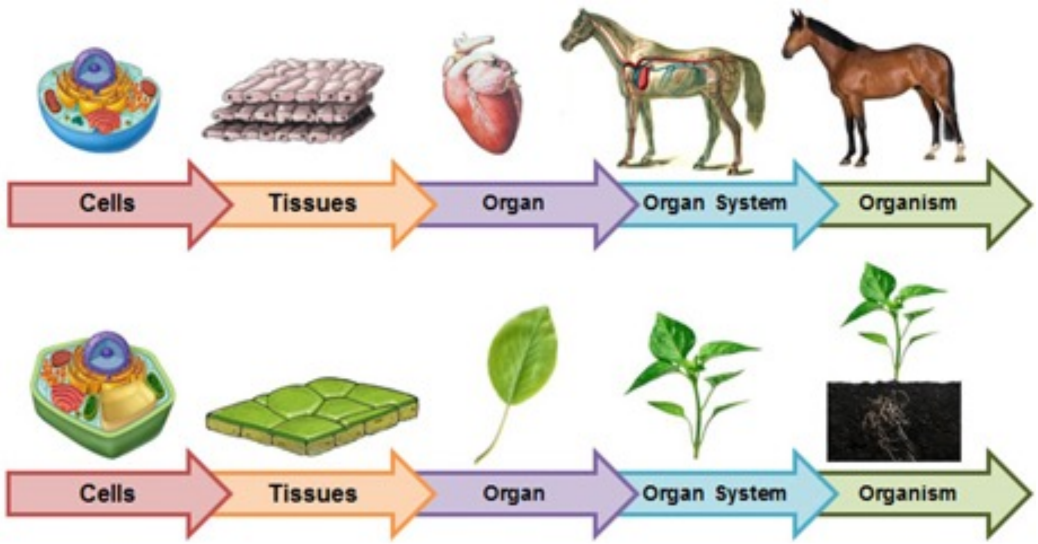
LSM1301



DNA & Heredity

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Reminders

- Laboratory assignment 4 is due tomorrow (23rd March, 23.59 hrs)
  - Make sure to check the Similarity Report

- Practical 5 is this Thursday (24th March)
  - Please wear long pants and shoes
  - Bring labcoat or purchase one
  - Read the handout before coming to lab

Lecture Topics and Assignments

This is a temporary plan, and is subject to change.

- Introduction (1 Lecture Session)

- Dr. NP Lectures/labs/Museum (5 Lects, 2 Labs, 1 Museum, 3 Tutorials)
  - Total Assignments (25%)

- Chemistry of Life (1 Lect session)
- Cell Structure and Function (1 Lect)
- Energy and Life (1 Lect)
- DNA and Gene Expression (2 lect, DNA and Heredity; Gene Expression)
- Biotechnology (1 Lect)
- Summary & Tutorial (1 Session)
  - Total Assignments 25%= 4 lab assignments (25%)

Today

Learning Plan (DNA and Heredity)

Topic	Learning outcomes for the WK	Activities for online session	Activities for face-to-face session	Assignments/ Assessments
DNA and Heredity	• *Describe the compositions and structure of DNA and RNA* • *Explain how DNA was proven to be genetic materials* • *Explain why there is a leading strand and lagging stranding during DNA replication* • *Describe the enzymes required for DNA replication* • *Explain the information flow from genes to proteins* • *Connect DNA replication with cell division, and explain how DNA integrity is maintained* • *Analyse possible consequences of DNA mutation*	• *Read lecture notes to gain an overall picture about this topic* • *Watch video: What is DNA? https://www.youtube.com/watch?v=q6PP-C4udkA (11 min)* • *Watch video: DNA replication http://www.youtube.com/watch?v=FBmO_rmXxIw (11 min)* • *Participate discussion on LumiNUS forum via posting questions and answering questions (peer learning)* • *Practice more questions on DNA Replication, Gene Expression, and Gene Regulation via online resources https://highered.mheducation.com/sites/0073031208/student_view0/chapter14/multiple_choice.html (optional)* • *Practice exam (http://study.com/academy/exam/topic/dna-replication-processes-and-steps.html)*	• *Practice questions on DNA replication* • *Explain template strand and non-template strand; sense strand and antisense strand* • *Discuss various mutations and consequences* • *Practice questions on gene expression*	• *Enhance understanding with Track-learning MCQs* • *Complete assignments related to lab sessions* • *Watch webcast lecture if needed*

Case study: Similarities in both physical and behavioral traits

Could the term of “like mother, like son” be true?


- Like mother, like daughter
- The apple doesn’t fall far from the tree

Nature vs. Nurture Debate

Nature:

Our genetics determine our behavior. Our personality traits and abilities are in our "nature."

Nurture:

Our environment, upbringing, and life experiences determine our behavior. We are "nurtured" to behave in certain ways.

Some commonly spread myths

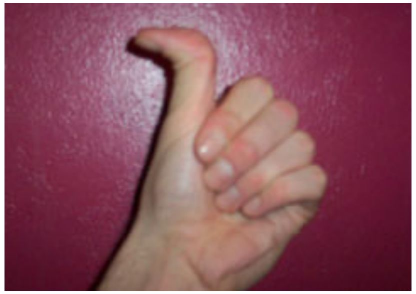
Ability to roll tongue

(recessive)

There is little laboratory evidence supporting the hypothesis that tongue rolling is inheritable and dominant.

No Hitchhiker's thumb **(dominant)**

Hitchhiker's thumb **(recessive)**



- Dominant genes are most often expressed as observable
- Recessive gene can be masked by a dominant gene. In order to have a trait that is expressed by a recessive gene, such as Hitchhiker's thumb, you must get the gene from both parents

Cleft chin **(dominant)**

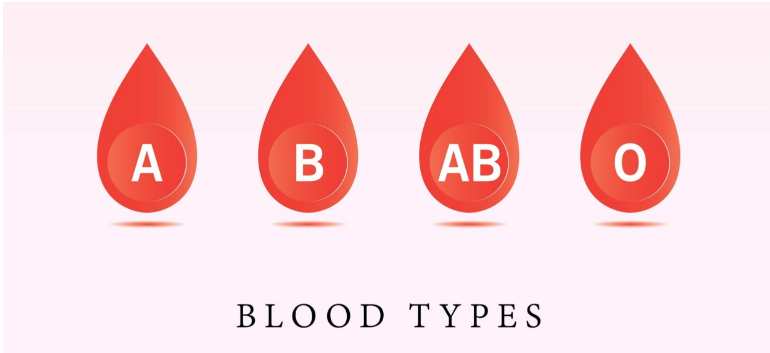
Chin without a cleft **(recessive)**

Face freckles (dominant)

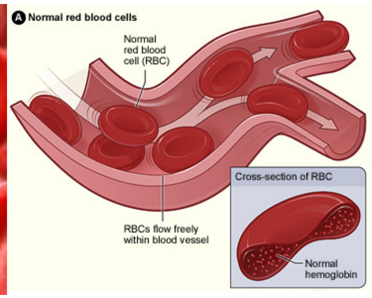
No face freckles (recessive)

Blood type A/B (dominant)

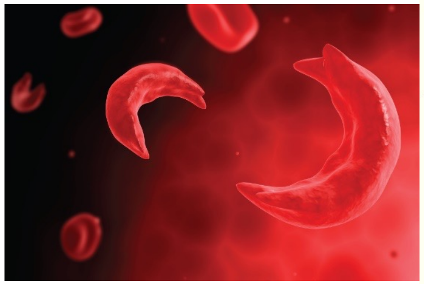
Blood type O (recessive)

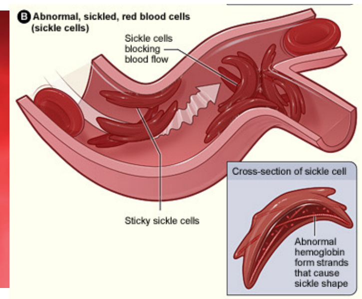


Normal red blood cells (dominant)



Sickle blood cells (recessive)





Intended Learning Outcomes

At the end of this class, the student should be able

- To describe the experiments to demonstrate that DNA is the genetic material of living organisms, and to relate the experiments to concepts acquired in the topics of ‘Science of Biology’ and ‘Chemistry of Life’
- To describe the molecular structure of DNA, and to relate the structure to the process of DNA replication
- To apply the principles that underpin DNA replication to DNA sequencing
- To describe the processes of binary fission, mitosis and meiosis, and to relate the processes to DNA replication and concepts acquired in the topic of ‘Cell Structure and Function’

Case study: Canine Morphology

Researchers studying the dog genome have a new understanding of why domestic dogs vary so much in size, shape, coat texture, color and patterning

March 2, 2010 issue of *PLoS Biology*

Case study: Mining coronavirus genomes for clues to the outbreak's origins

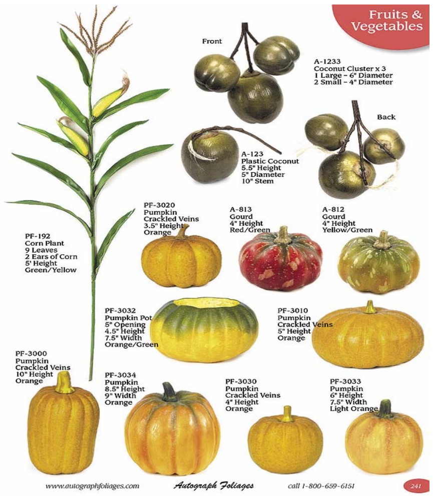
COVID-19

SARS-CoV-2

https://www.sciencemag.org/news/2020/01/mining-coronavirus-genomes-clues-outbreak-s-origins

Genetics

- Genetics: **the scientific study of inheritance and its underlying mechanisms.**
- Genetics: **The study of the structure and function of genes and the transmission of genes from parents to offspring.**



Outline

- Genetic Material
  - Johannes Friedrich Miescher
  - Frederick Griffith
  - Avery, MacLeod and McCarty
  - Alfred Hershey and Martha Chase
- DNA Nucleotides
  - Erwin Chargaff
- DNA Structure
  - Rosalind Franklin
  - Maurice Wilkins
  - James Watson and Francis Crick
  - Watson-Crick model
- DNA Replication
- Cell Division
  - Binary fission
  - Eukaryotic cell division
  - Eukaryotic cell cycle
  - Eukaryotic chromosomes
  - Mitosis
  - Cytokinesis
  - Meiosis
- Mutations

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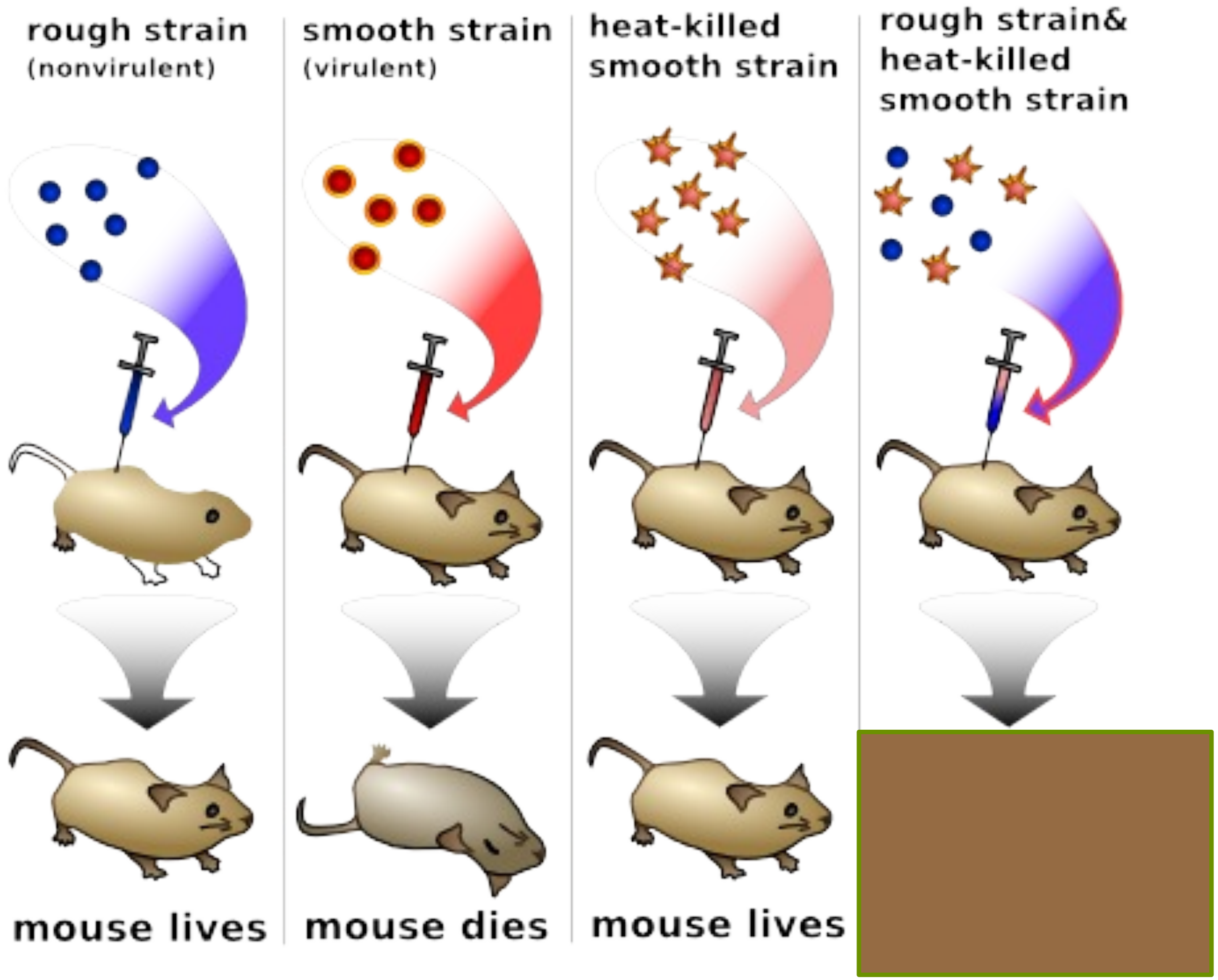
Johannes Friedrich Miescher

- In late 1860s, investigated chemical composition of nuclei
  - From white blood cells found in pus from discarded bandages
- Found substance that was different from proteins
  - Resistant to protein-digesting enzymes
  - Rich in phosphorus
  - Also found in sperms of different animals
- Substance called nuclein

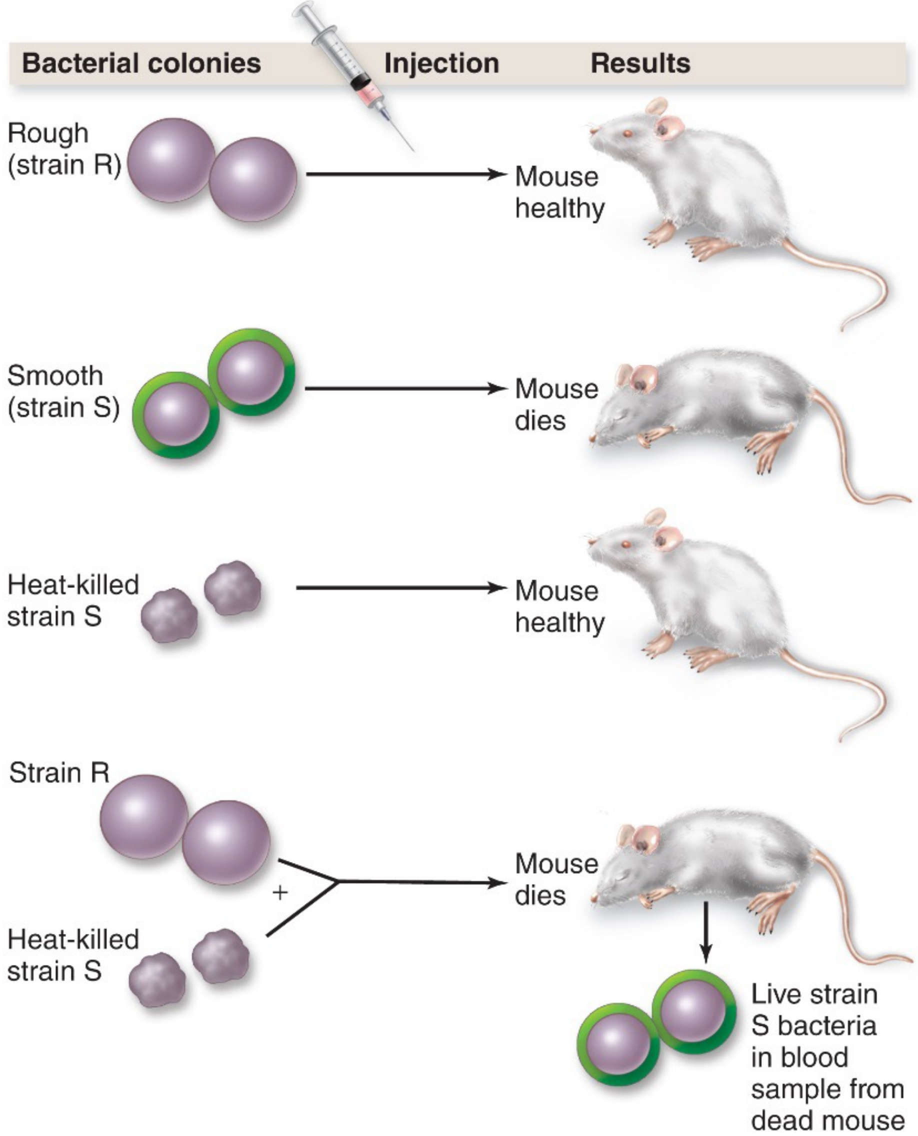
Frederick Griffith

Frederick Griffith's transformation experiment using *Streptococcus pneumoniae* in 1928



Avery, MacLeod and McCarty

- To rule out the possibility that a protein contaminant was actually causing the transformation, Avery treated samples with **protein-destroying enzymes (protease)** and still induced transformation
- When **DNA-destroying enzymes (DNase)** were added to the samples, transformation did not occur
- This suggested that the transforming molecule from the S-strain was DNA, not protein



How did scientists explain Griffith's transformation experiment?

The experiments can be explained if DNA is the transforming agent

- Heating S-strain cells killed them but did not completely destroy their DNA
- When killed S-strain bacteria were mixed with living R-strain bacteria, fragments of DNA from the dead S-strain cells was absorbed and incorporated into the chromosome of the R-strain bacteria
- If these fragments of DNA contained the genes needed to cause disease, an R-strain cell would be transformed into an S-strain cell
- Thus, Avery, MacLeod, and McCarty concluded that genes are made of DNA.

Alfred Hershey and Martha Chase

- Worked with bacteriophage
  - Virus that **infects bacteria**
- Infected Escherichia coli bacteria with viruses
  - Protein coats of viruses, labelled with 35S, stayed outside bacteria
  - DNA of viruses, labelled with 32P, entered bacteria
  - Showed that DNA, not protein, is genetic material

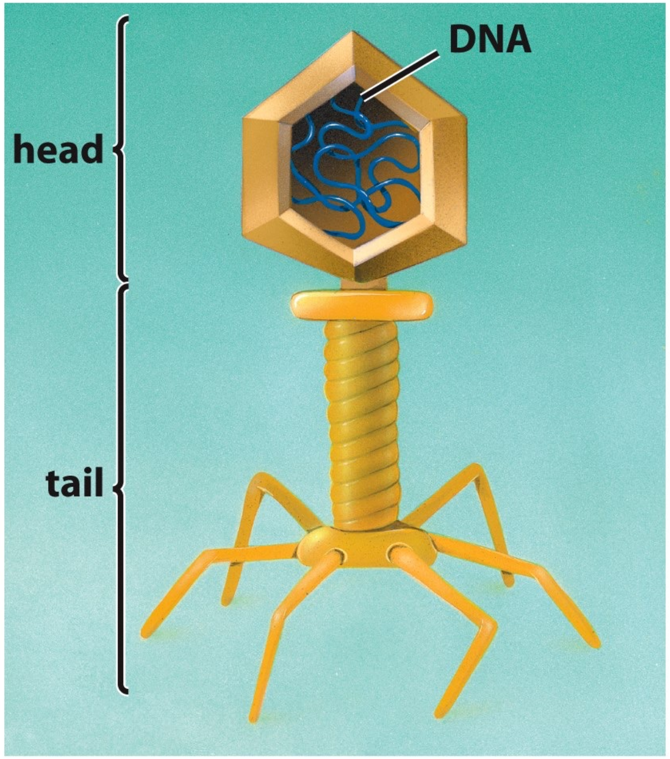
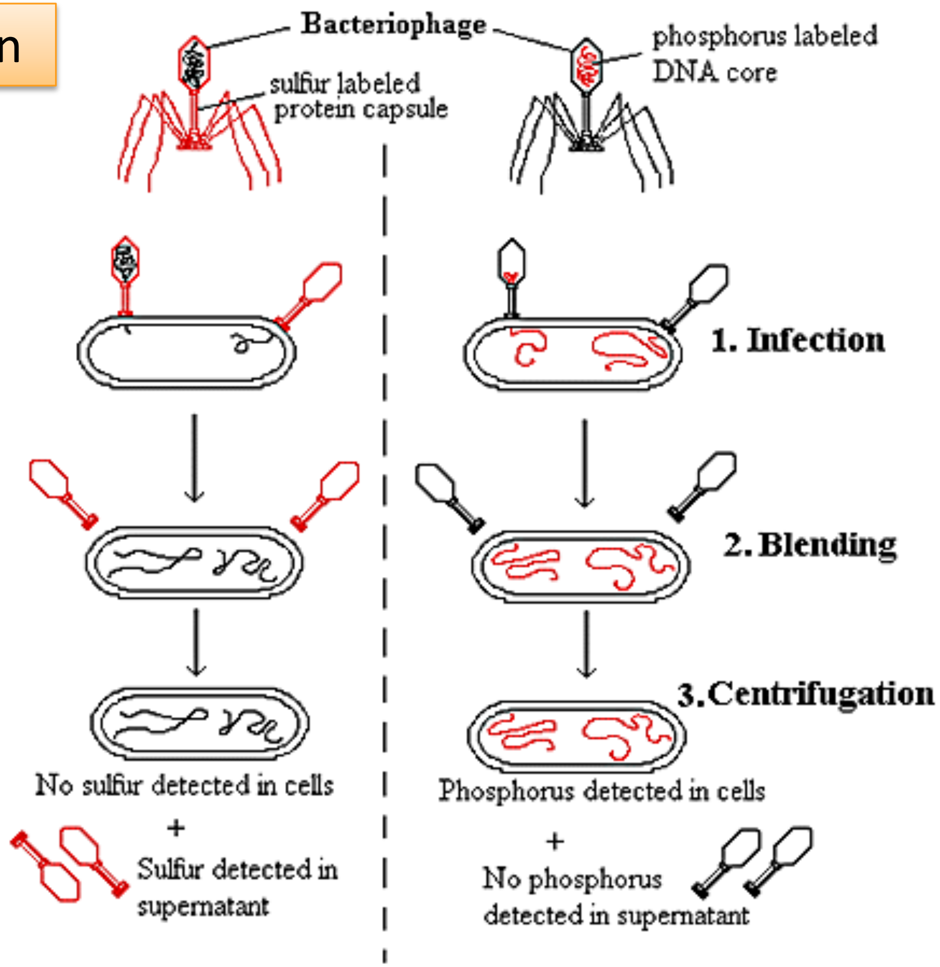


Figure E9-1a Biology: Life on Earth, 8/e

T2

^{35}S to track protein

^{32}P to track nuclei acid



The Hershey-Chase Experiment

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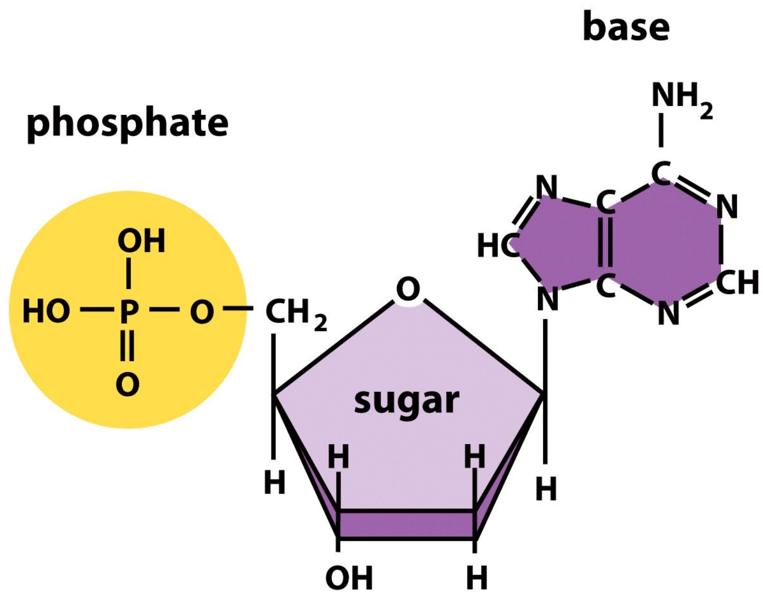
DNA

DeoxyriboNucleic Acid or DNA is a long chain of nucleotides

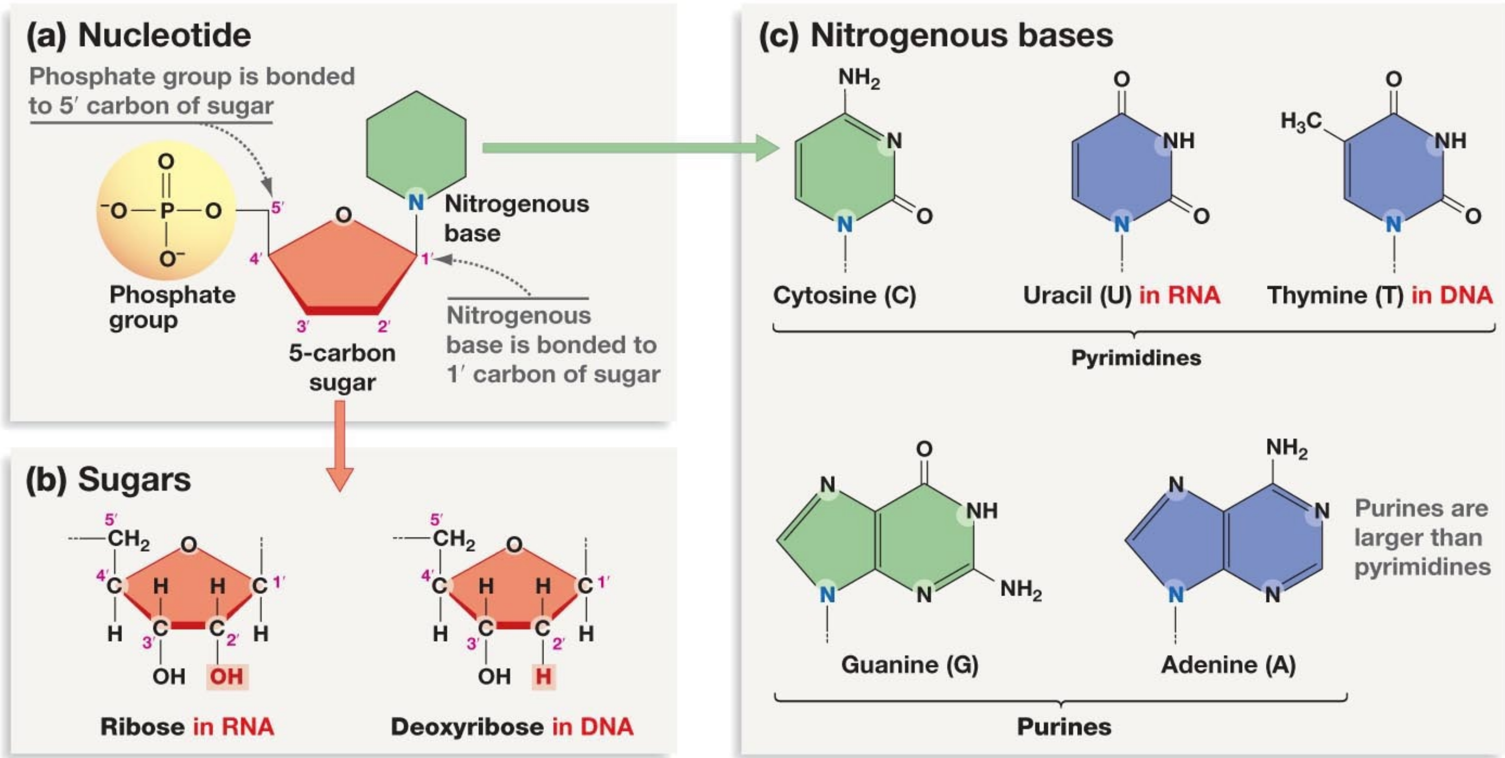
– Nucleotides are the monomers (building block) of nucleic acid chains

– All nucleotides are made of three parts:

  - Phosphate group
  - Five-carbon sugar
  - Nitrogen-containing **base**



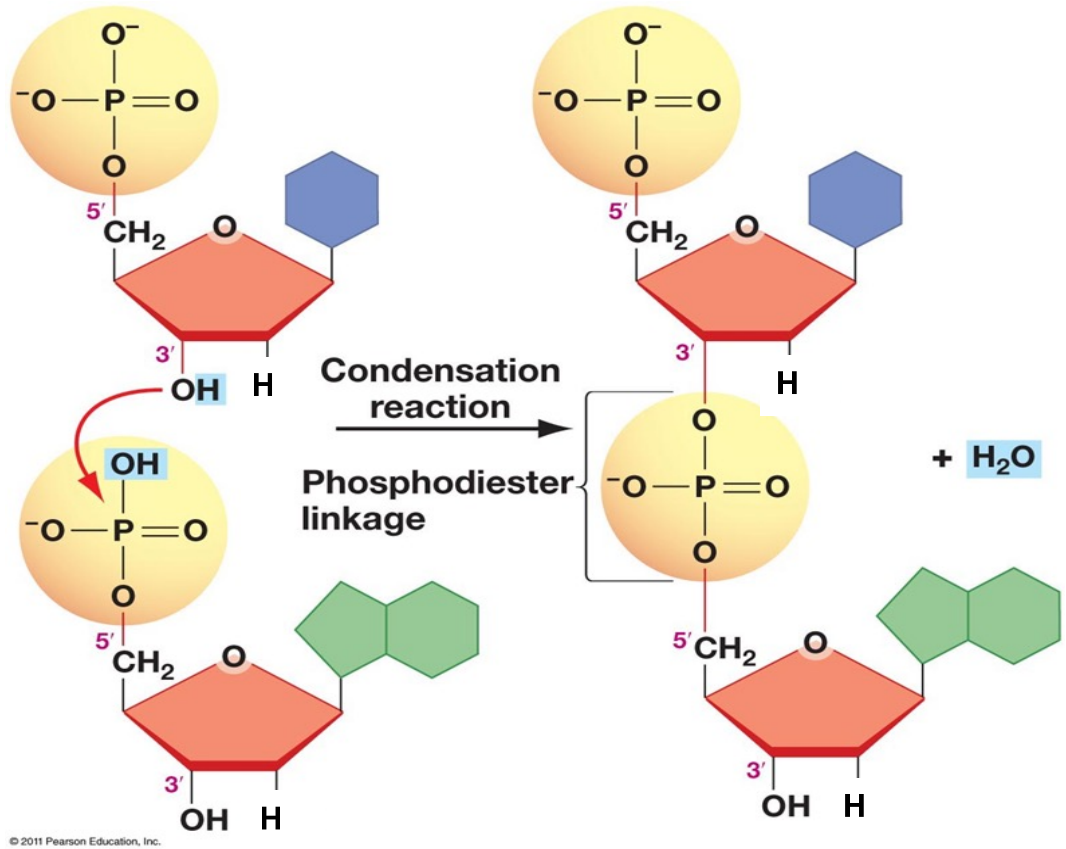
Nucleotides in DNA & RNA



DNA: DeoxyriboNucleic Acid
RNA: RiboNucleic Acid

DNA Chain Formation

DNA chain are formed by condensation



Erwin Chargaff (1905-2002)

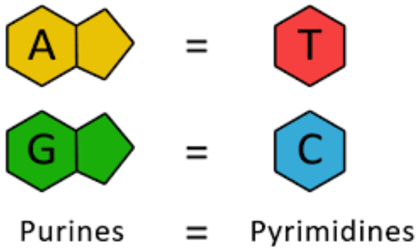
- In 1950s, analysed amounts of four bases in DNA from different organisms
- For the same species
  - Amounts of A, T, G and C are constant
  - Amounts of A and T are equal
  - Amounts of G and C are equal
- For different species, amounts of A, T, G and C are different
- Finding called Chargaff's rules

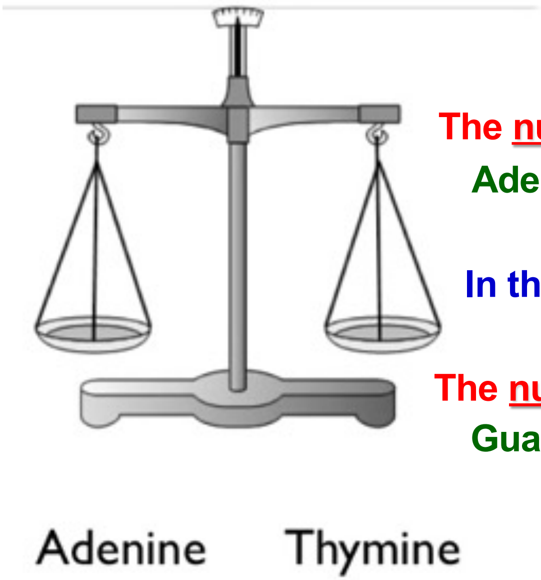
Organism	% Adenine	% Thymine	% Cytosine	% Guanine
Octopus	33.2	31.6	17.6	17.6
Sea Urchin	32.8	32.1	17.3	17.7
Rat	28.6	28.4	20.5	21.4
Grasshopper	29.3	29.3	20.7	20.5
Human	29.3	30.0	20.0	20.7

Chargafff's Rules

Rule 1

for a dsDNA





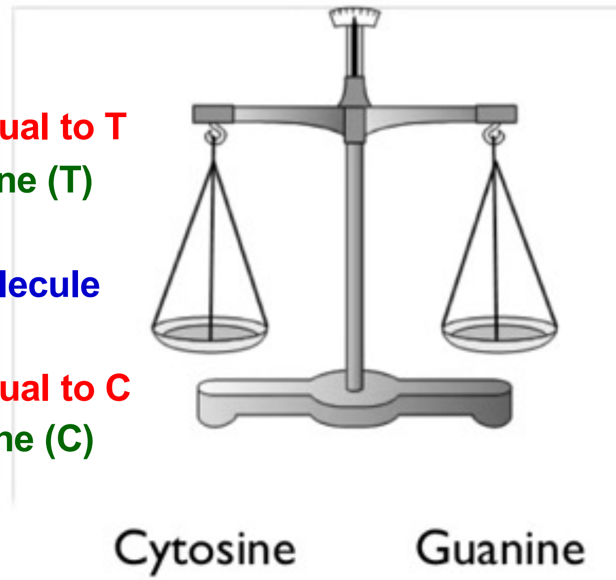
The <u>number</u> of A is equal to T

Adenine (A)= Thymine (T)

In the same DNA molecule

The <u>number</u> of G is equal to C

Guanine (G)=Cytosine (C)



Rule 2

The relative amounts of A, G, T, and C bases in a DNA molecule varies from one species to another (i.e. differs in different DNA molecules)

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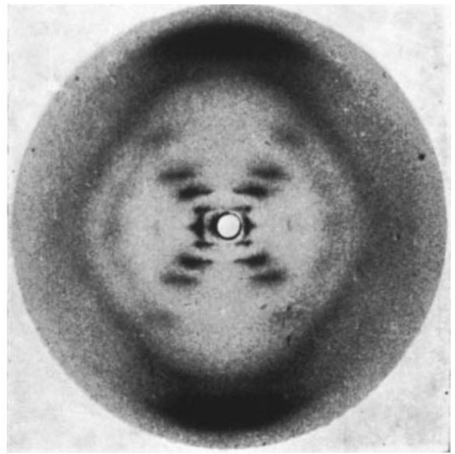
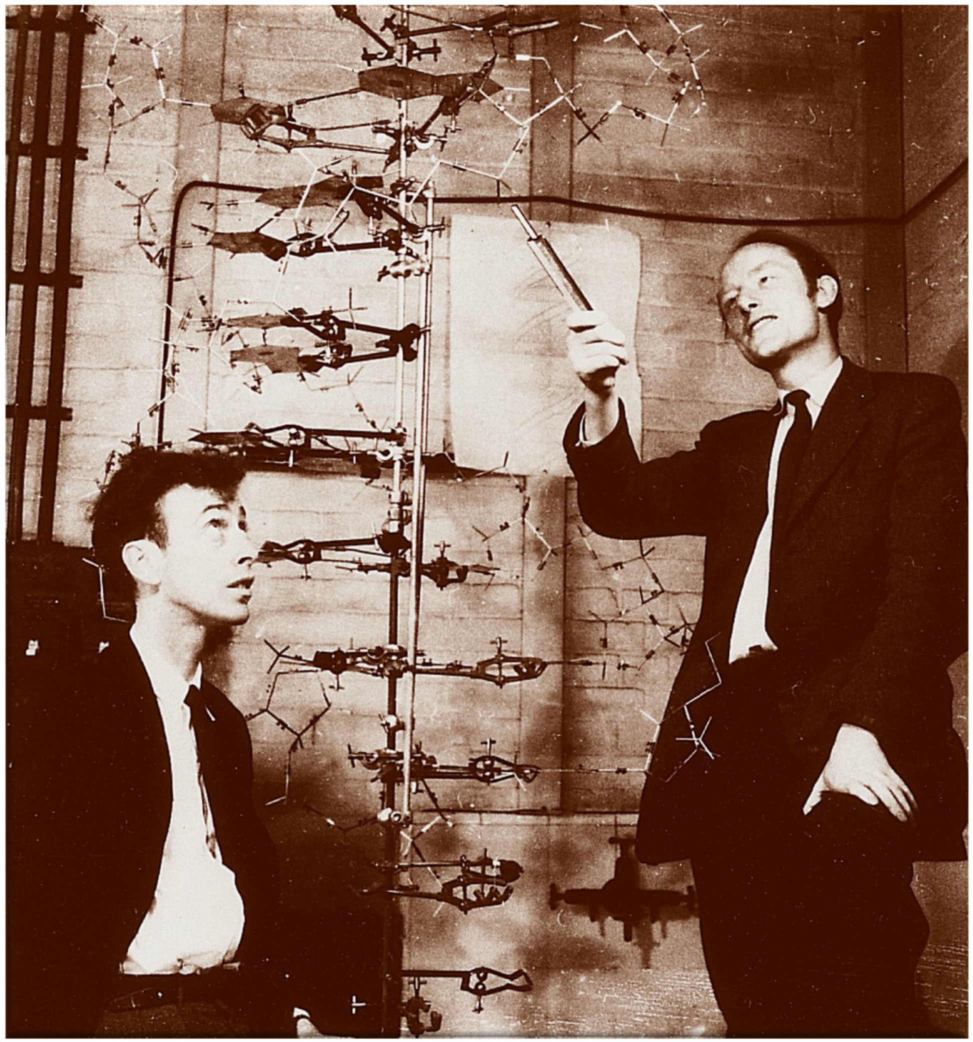
Rosalind Franklin

- In early 1950s, studied structure of DNA using X-ray diffraction
  - DNA has two chains twisted into double helix
  - Regularly repeating structure of nucleotides
  - Phosphate groups on outside of helix
  - Dimensions of DNA was calculated



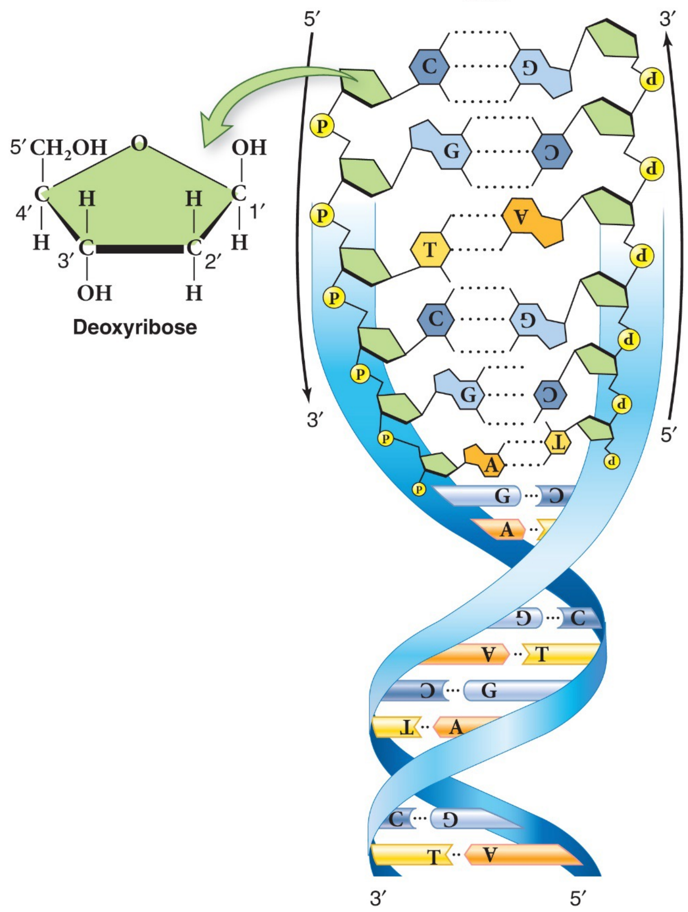
James Watson and Francis Crick

- In early 1950s, constructed models of DNA to fit
  - Franklin’s X-ray data
  - Chargaff’s rules
  - Knowledge of chemical bonds
- Did not sufficiently cite Franklin’s data



Watson-Crick Model

- DNA consists of two nucleotide strands (chains)
  - In opposite directions – anti-parallel
  - One chain ends in 3' carbon, the other ends in 5' carbon
  - Coiled into double helix
- Each nucleotide strand (chain)
  - Deoxyribose sugars and phosphate groups linked together alternately
  - Forms sugar-phosphate backbone



How Does DNA Encode Information?

How can a molecule with only four simple parts be the carrier of genetic information?

- The key lies in the sequence of nucelotides
- Within a DNA strand, the four types of nucleotides can be arranged in any linear order, and this sequence is what encodes genetic information
- The genetic code is analogous to languages, where small sets of letters combine in various ways to make up many different words
- The sequence of only four nucleotides can produce many different combinations

A 10-nucleotide sequence can code for more than 1 million different combinations of the four bases

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DNA Replication

- Begins when DNA unwinds and unzips into two strands
  - By DNA helicases, that pull apart the parental DNA double helix at the hydrogen bonds between the complementary base pairs.
  - Hydrogen bonds between bases broken
  - Formation of replication bubbles and replication forks

DNA Replication

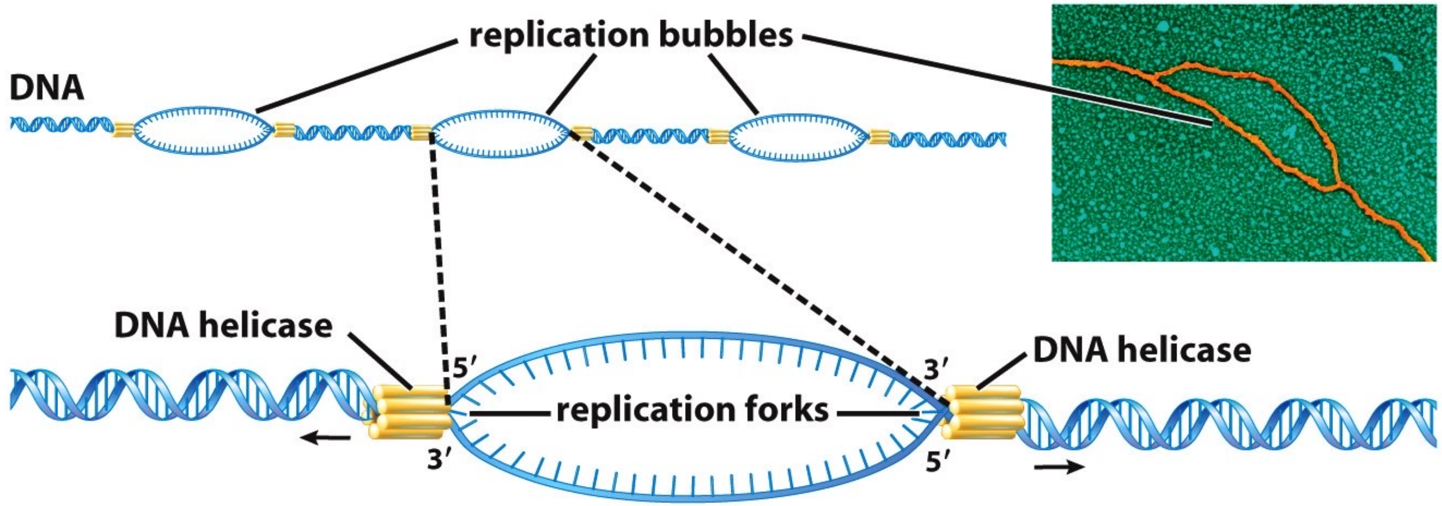


Figure E9-7ab Biology: Life on Earth, 8/e

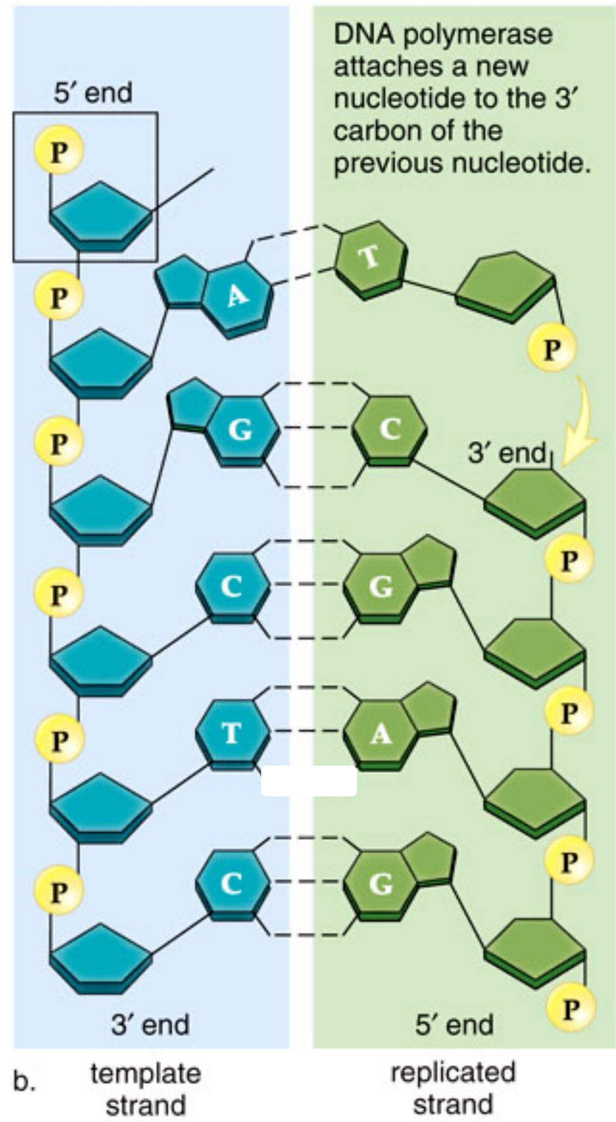
A replication bubble is an unwound and open region of a DNA helix where DNA replication occurs.

DNA Replication

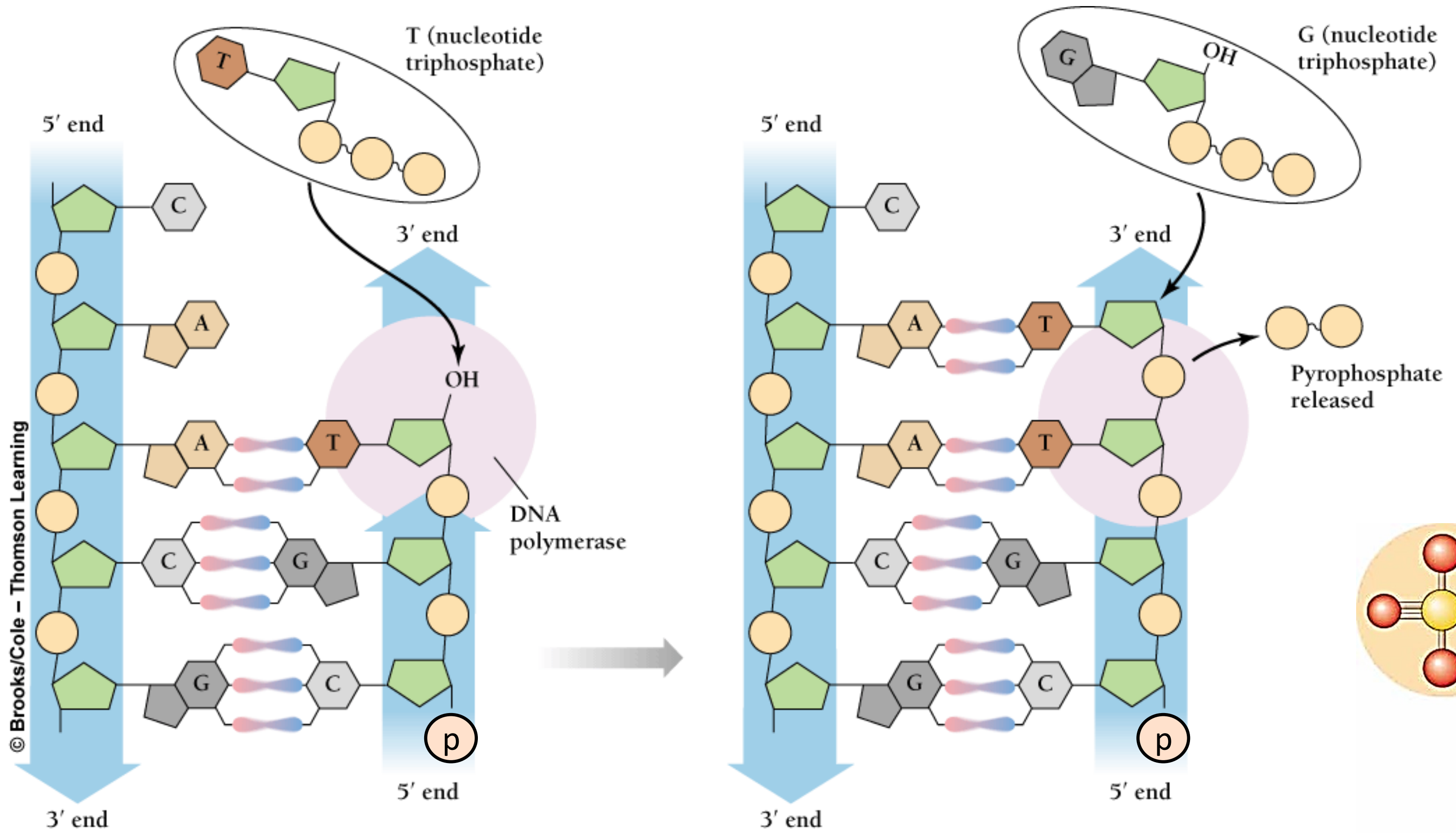
- Short RNA primer synthesised first to provide 3′ end for DNA polymerase
  - Primer is synthesized by RNA polymerase (Primase)
  - A typical primer is about five to ten nucleotides long. The primer primes DNA synthesis, i.e., gets it started.
- Each old strand serves as template for synthesis of new strand
  - By DNA polymerases
  - Based on complementary base-pairing rule

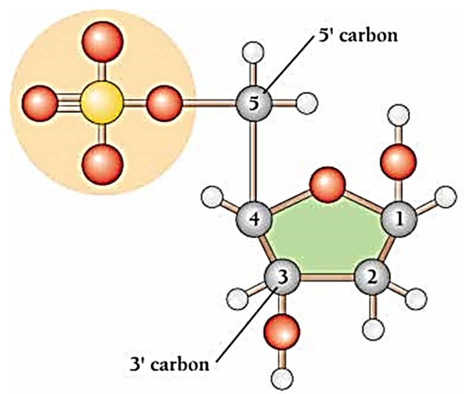
DNA Replication

- DNA polymerase adds nucleotides in 5′ to 3′ direction only
  - Can only join new nucleotide to free 3′ end of previous nucleotide



New strand is synthesized in 5' to 3' direction





Template strand

Replicated strand

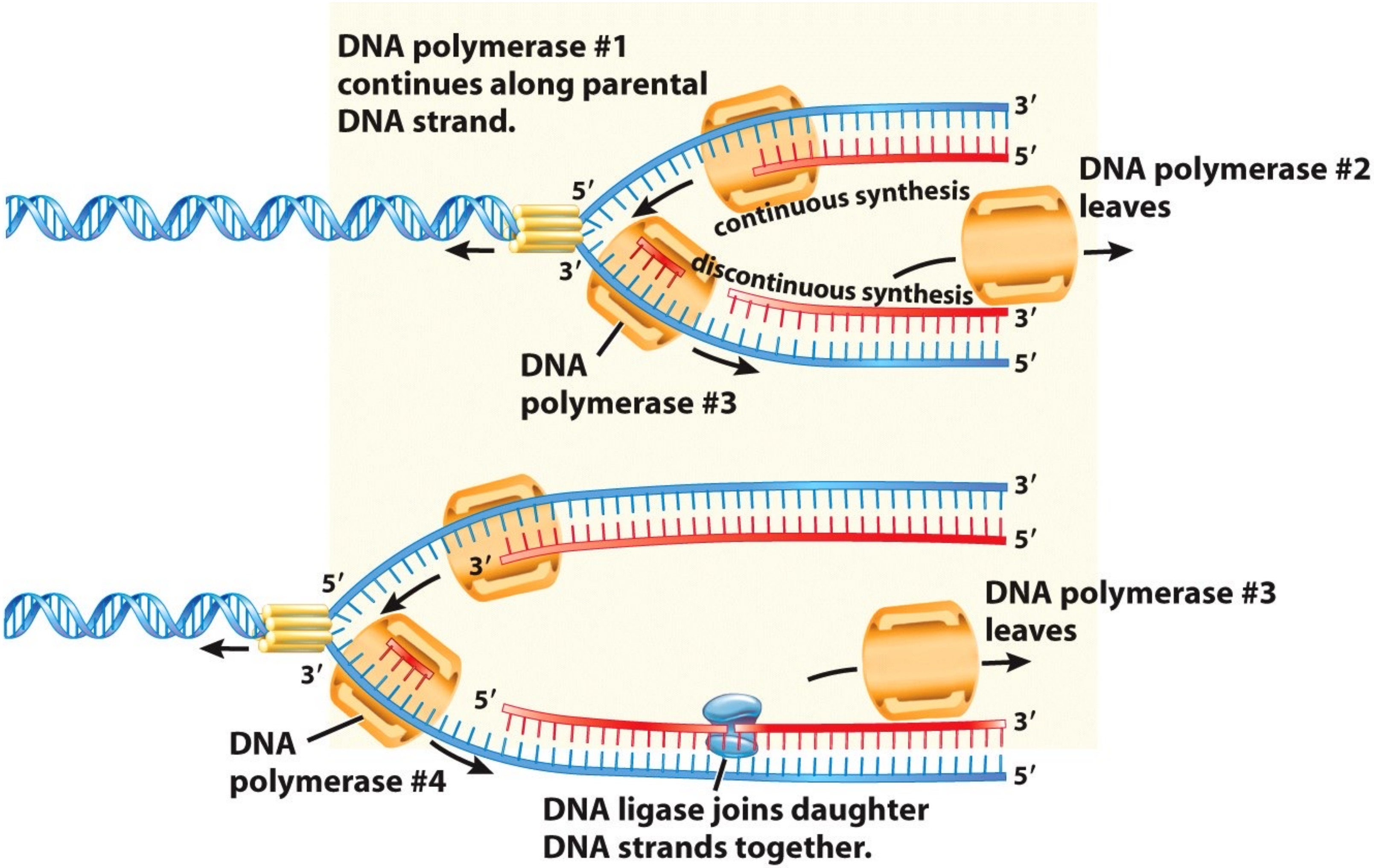
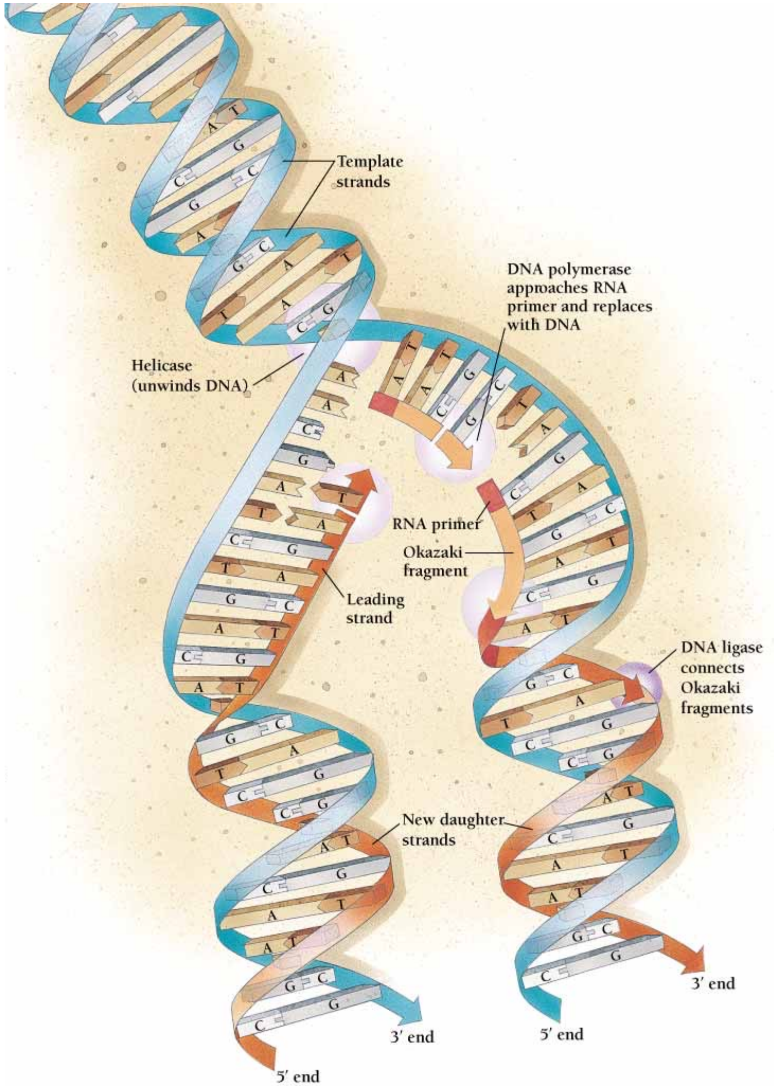


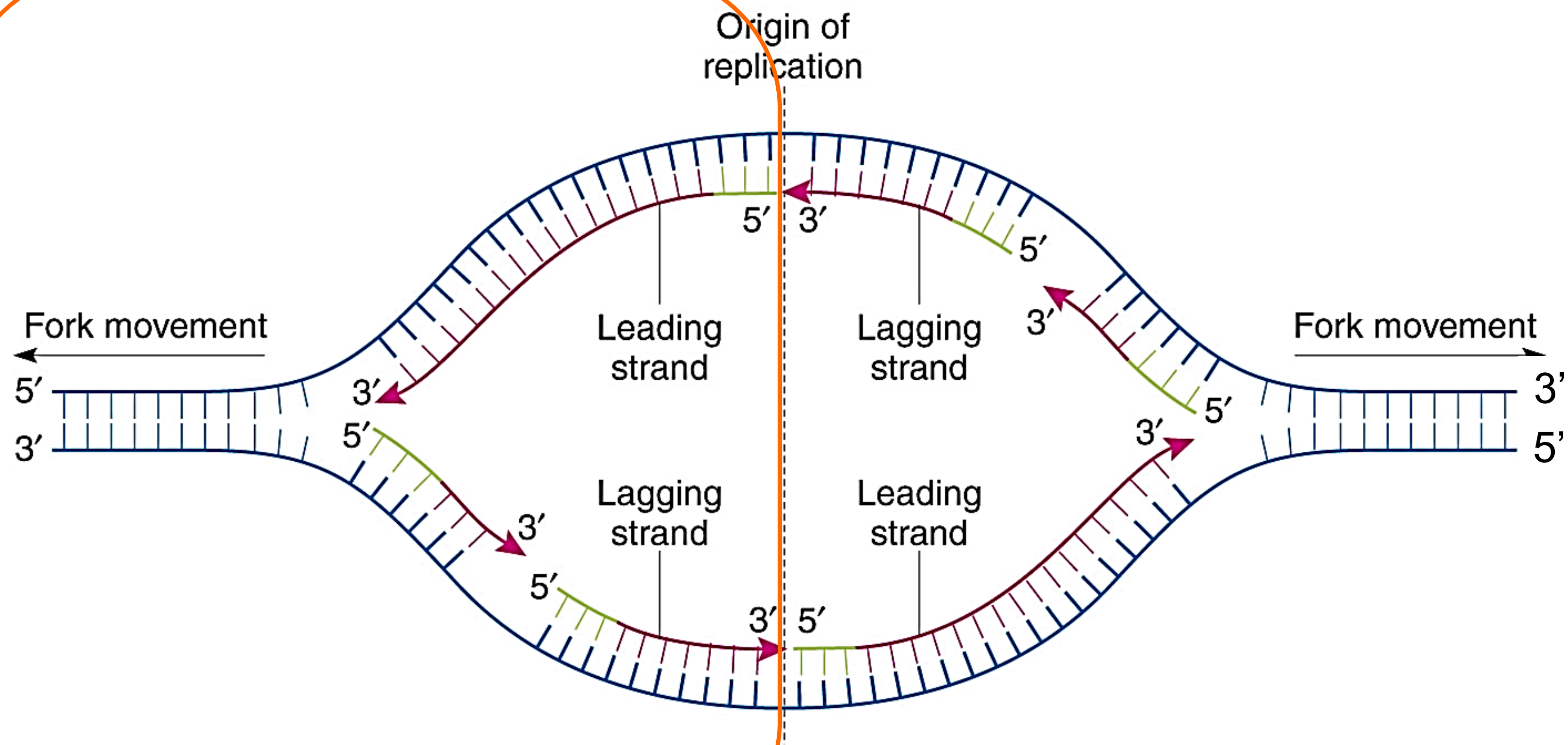
Figure E9-7de Biology: Life on Earth, 8/e

DNA Replication

- Leading strand synthesised continuously
- Lagging strand synthesised in short fragments
  - Okazaki fragments
  - Joined together by DNA ligase

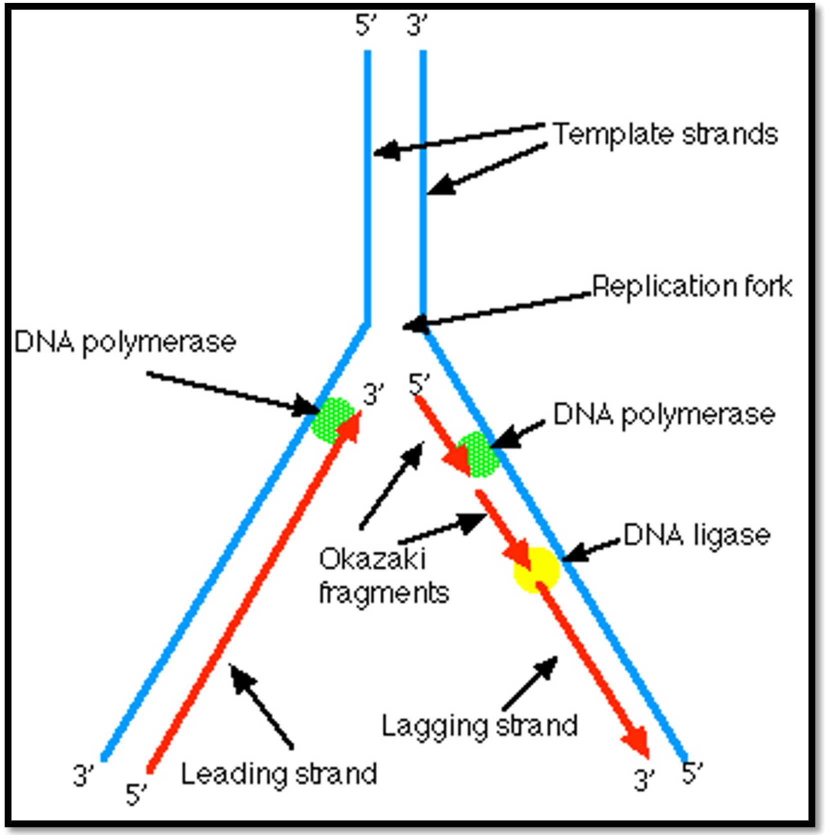


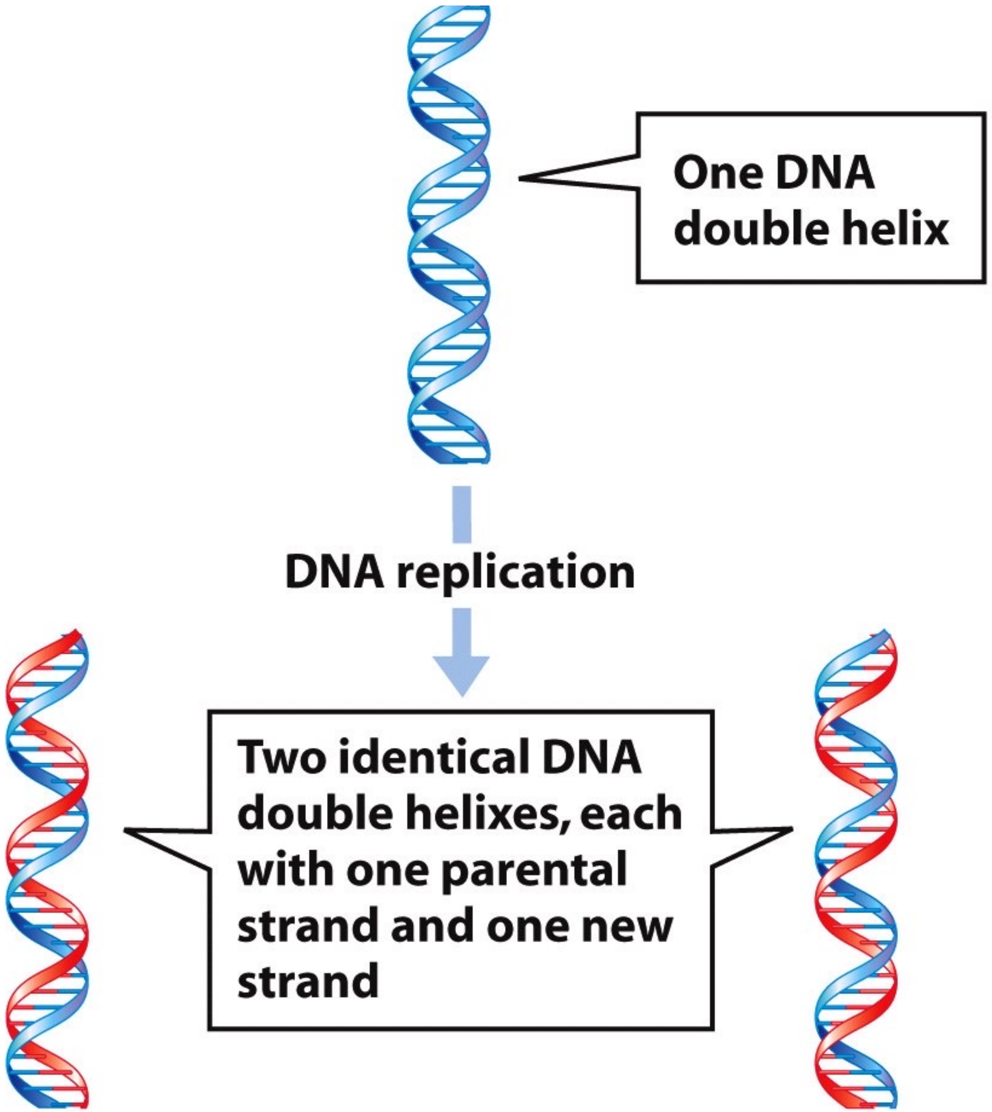
One Replication Bubble and Two Forks



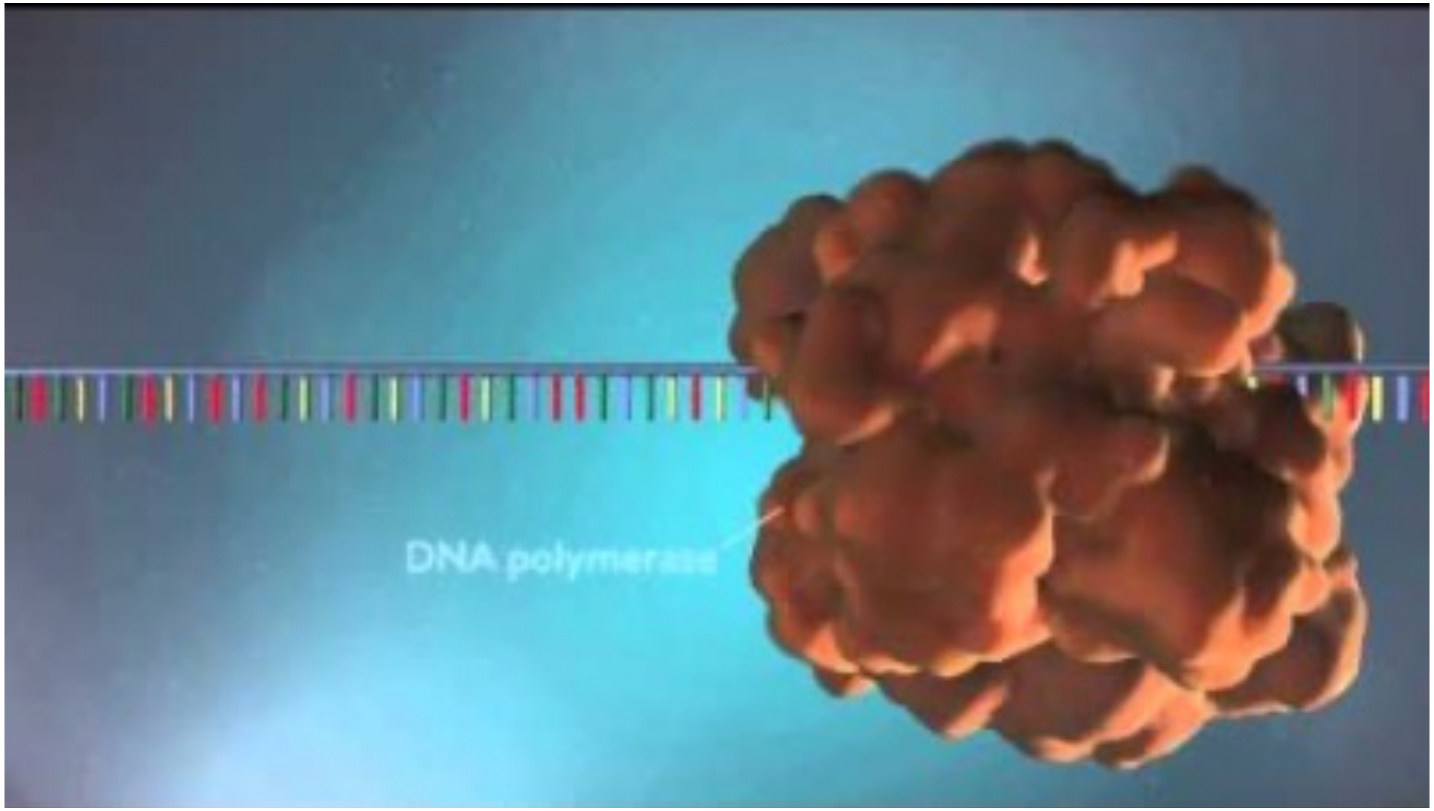
DNA Replication

- Semi-conservative replication
- Each strand of double helix acquires a new strand
  - Each "old" parent strand serves as template for complementary "new" daughter strand
- Each new DNA molecule is half "old" and half "new"




One DNA double helix
DNA replication
Two identical DNA double helixes, each with one parental strand and one new strand

DNA Replication (video)



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

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  - Cytokinesis
  - Meiosis
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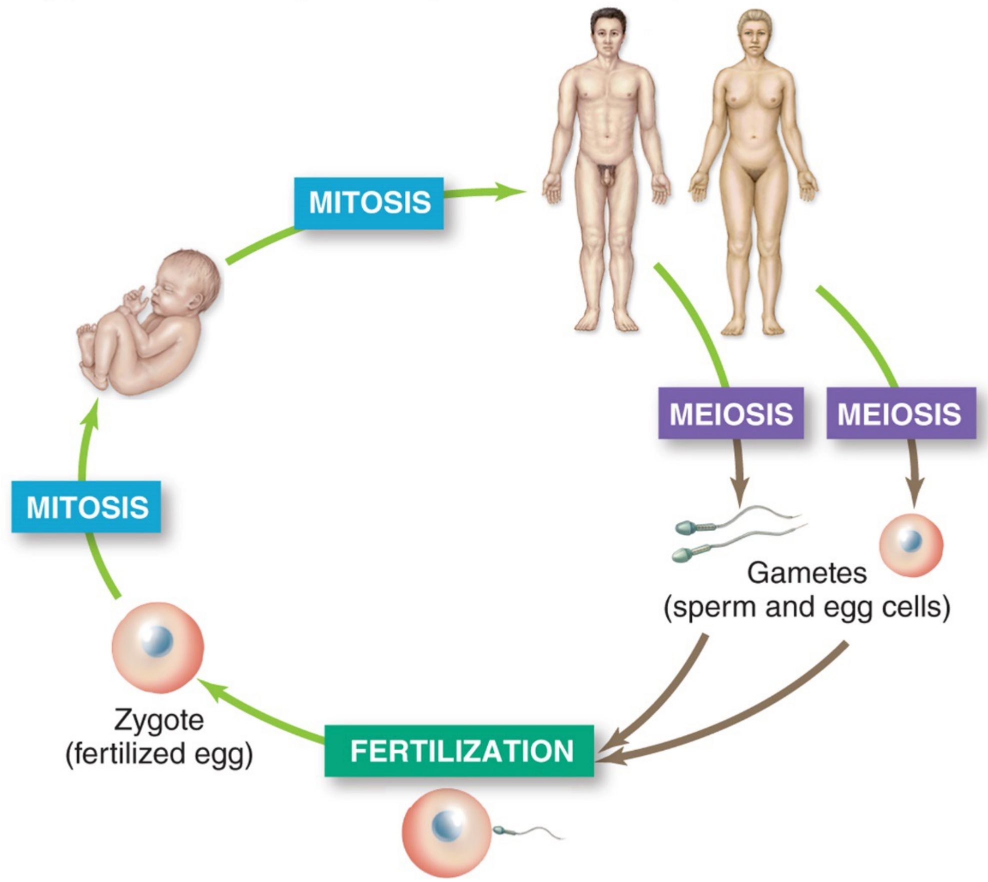
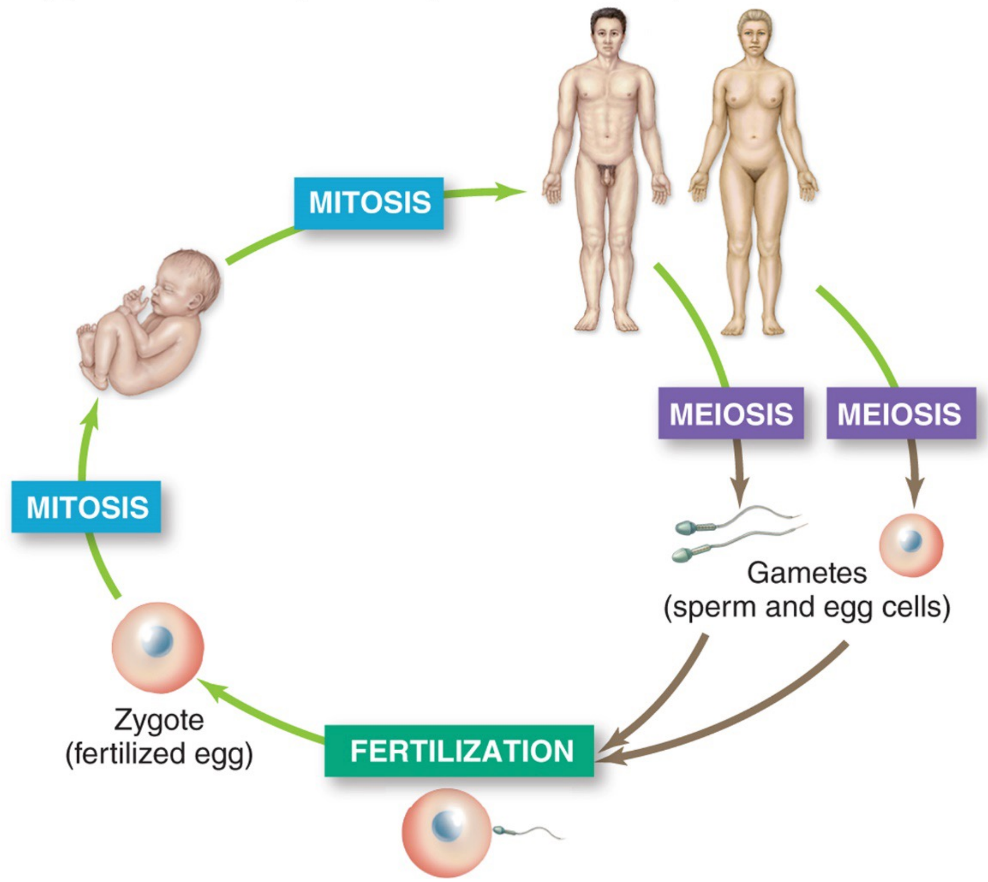
Cell Division

- Cells reproduce by cell division
  - One parent cell results in two daughter cells
  - Each daughter cell receives one identical set of hereditary information, via DNA replication, from parent cell
- Mitosis
  - Cell division of eukaryotic cells
  - Results in growth and increase in number of cells



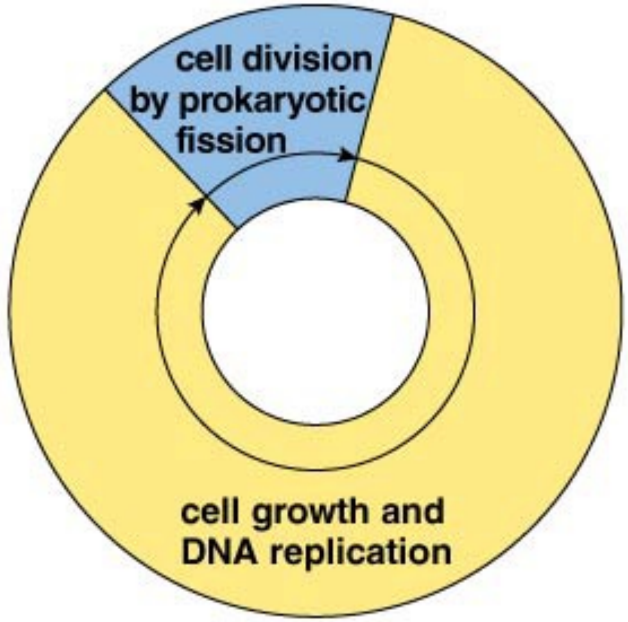
Cell Division

- Sexual reproduction in eukaryotes
  - Offspring produced by fusion of sex cells (gametes) from two adults at fertilisation
- Meiosis
  - Specialised type of cell division in adult's reproductive system
  - Results in half the genetic information of parent cells



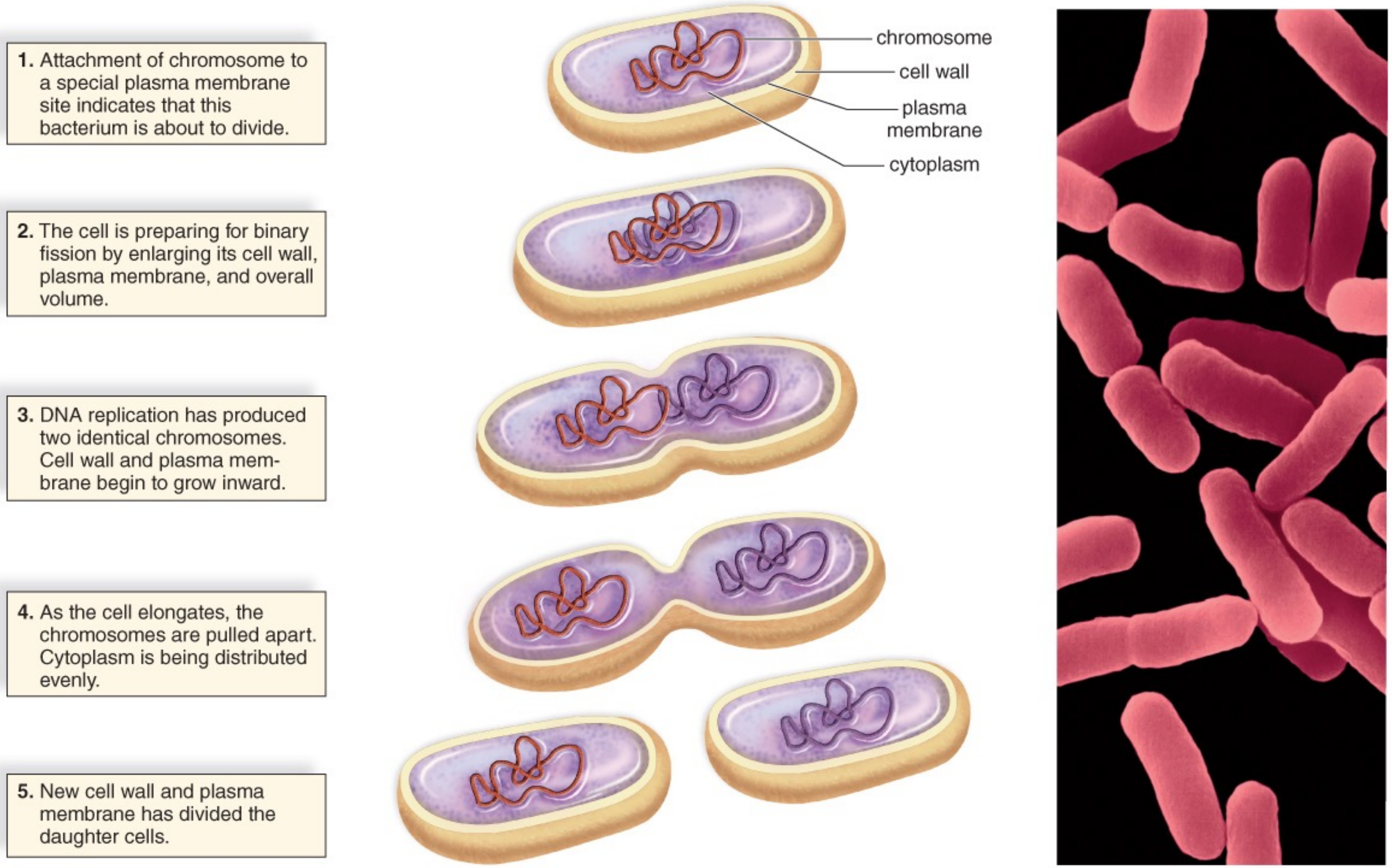
Binary Fission

- Reproduction in prokaryotes
  - Occurs by binary fission
- Binary fission (splitting in two)
  - Asexual process
  - DNA replicated and distributed to two identical daughter cells
- Prokaryotic DNA
  - One single, circular chromosome
  - About 1–2 mm in circumference ≈ 1,000 times of length of cell
- Prokaryotic cell cycle
  - Relatively long period of growth followed by binary fission



(a) The prokaryotic cell cycle

Binary Fission

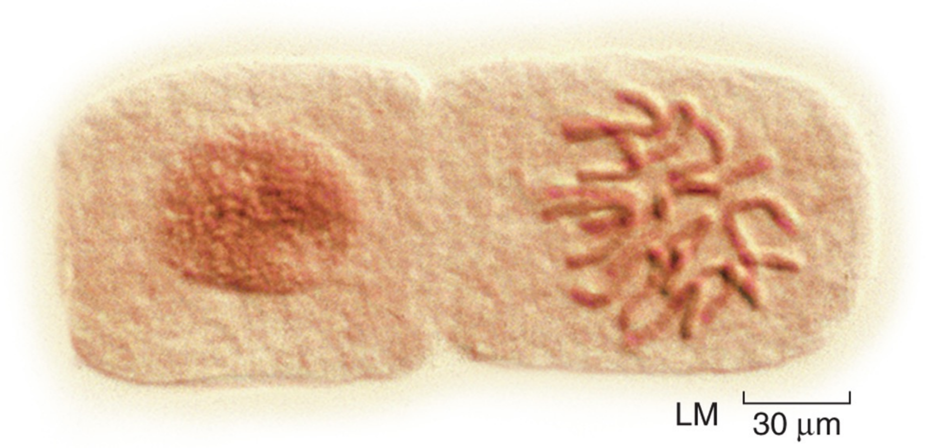


SEM 2,345×

(right): © Dennis Kunkel Microscopy, Inc./Visuals Unlimited

Eukaryotic cell division

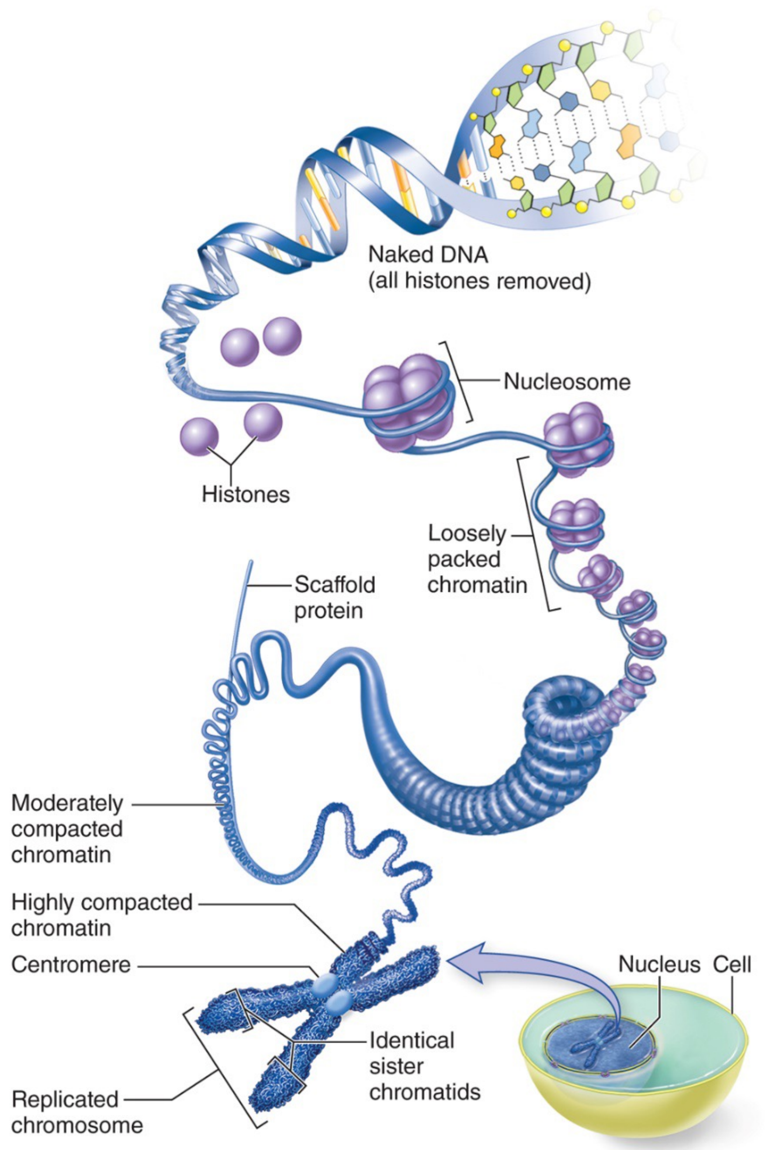
- When DNA is loosely packed
  - DNA replication and protein synthesis occur
- When DNA has condensed into visible chromosomes
  - Cell division occurs



©Clouds Hill Imaging Ltd./Corbis

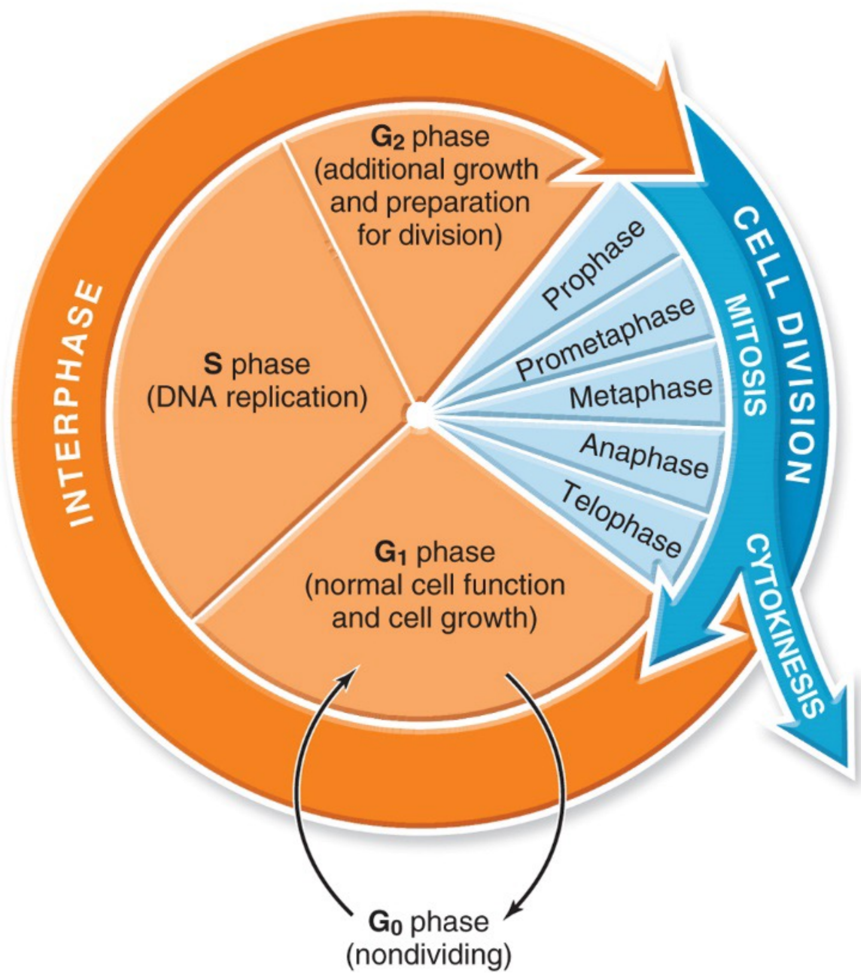
Eukaryotic cell division

- Eukaryotic cells have multiple chromosomes
- Each eukaryotic chromosome
  - Linear DNA double helix bound to proteins called histones
  - DNA-histone spools further folded into coils
  - Coiled strand then folded into loops, then attached to protein scaffolding
  - Resulting in chromosome being 1,000 times shorter than extended DNA molecule
- During cell division
  - More proteins fold up DNA and histones –10 times shorter than resting state



Eukaryotic Cell Cycle

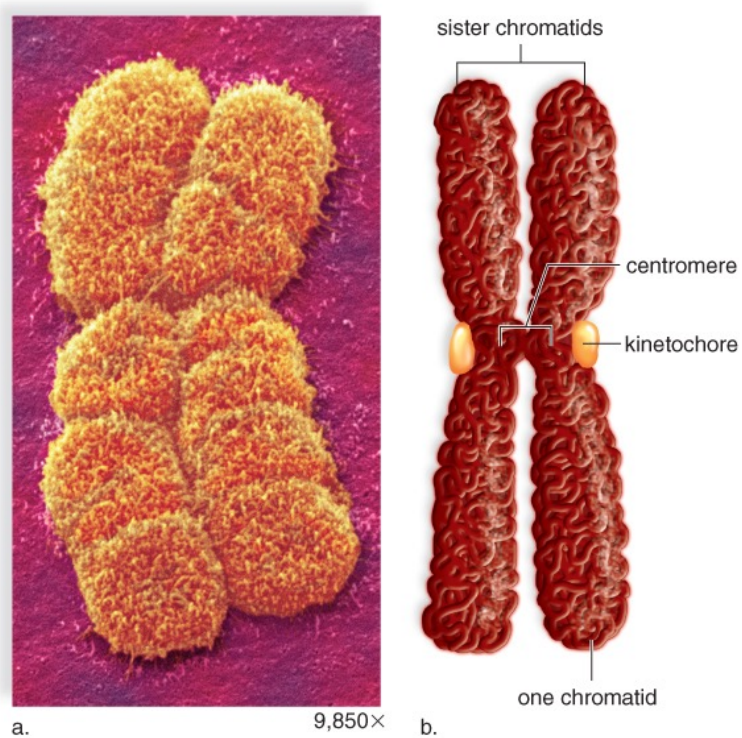
- Cell cycle
  - Orderly sequence of stages from one cell division to next
- Two major stages of cell cycle
  - Interphase (includes several phases)
  - Mitotic cell division (includes mitosis and cytokinesis)



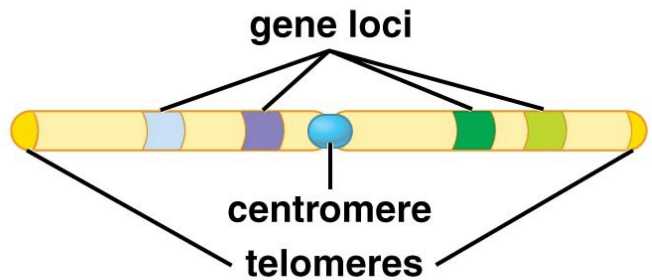
Eukaryotic Cell Cycle

- Interphase consists of three phases
  - G1 (growth phase 1) – acquisition of nutrients and materials, protein synthesis, cell grows in size
  - S (synthesis phase) – DNA synthesis (replication)
  - G2 (growth phase 2) – synthesises proteins necessary for cell division
- G0 phase
  - Cell continues to function
  - But does not replicate DNA or divide
  - Most cells in G0 phase
- Checkpoint mechanisms
  - Work at certain points in cell cycle

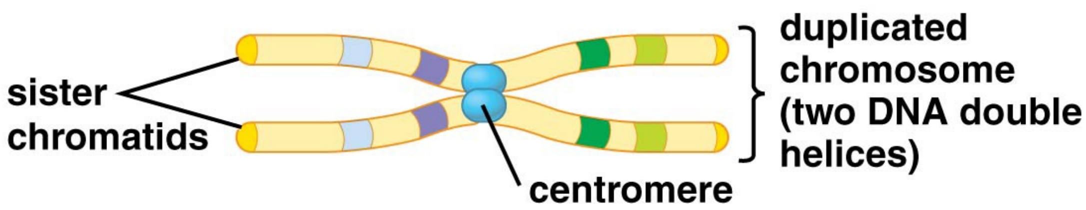
Eukaryotic Chromosomes



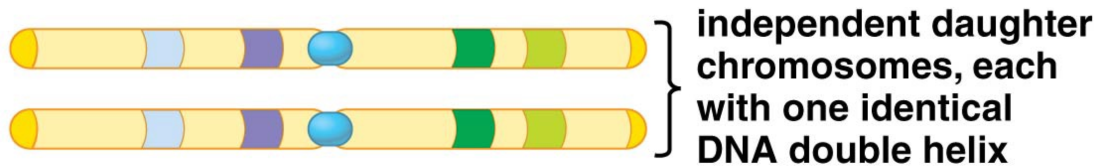
a: © Andrew Syred/Photo Researchers, Inc.



(a) A eukaryotic chromosome (one DNA double helix) before DNA replication

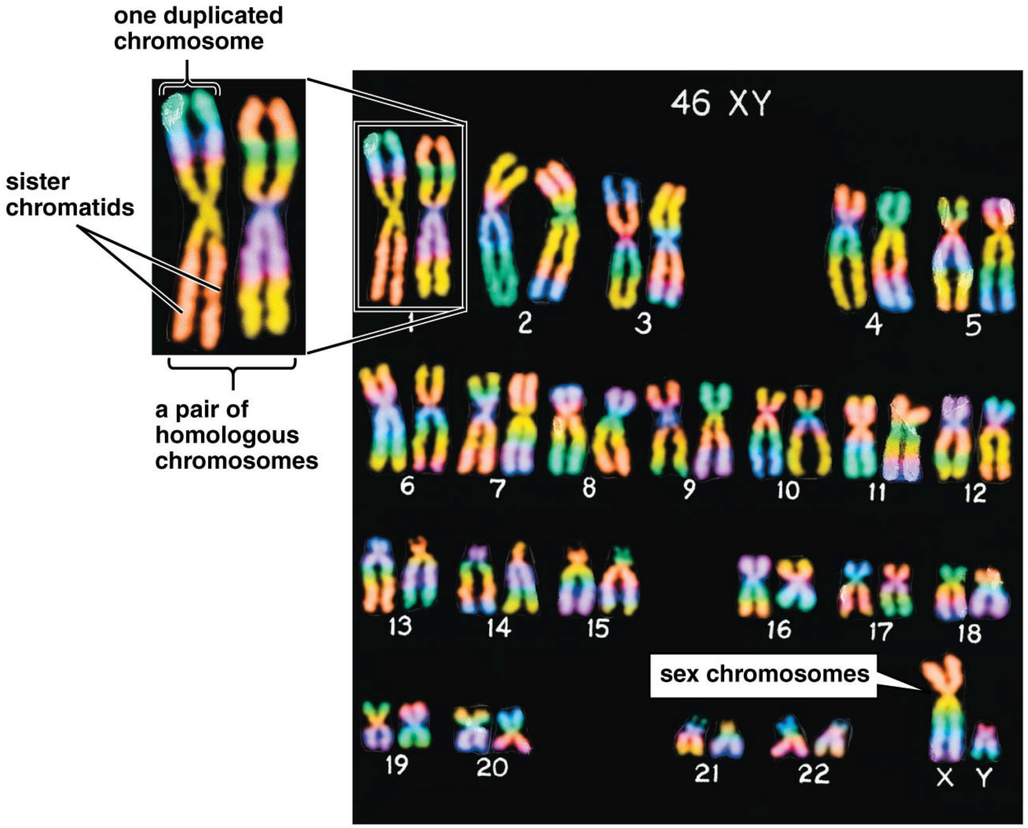


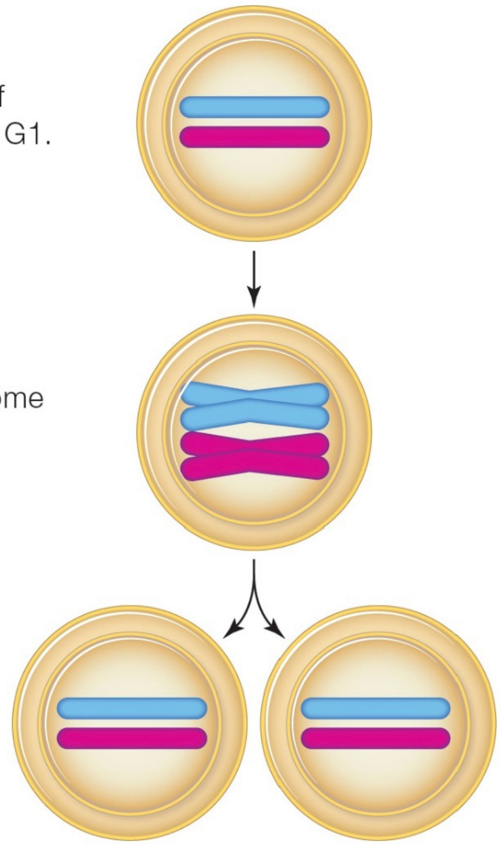
(b) A eukaryotic chromosome after DNA replication



(c) Separated sister chromatids become independent chromosomes

Eukaryotic Chromosomes





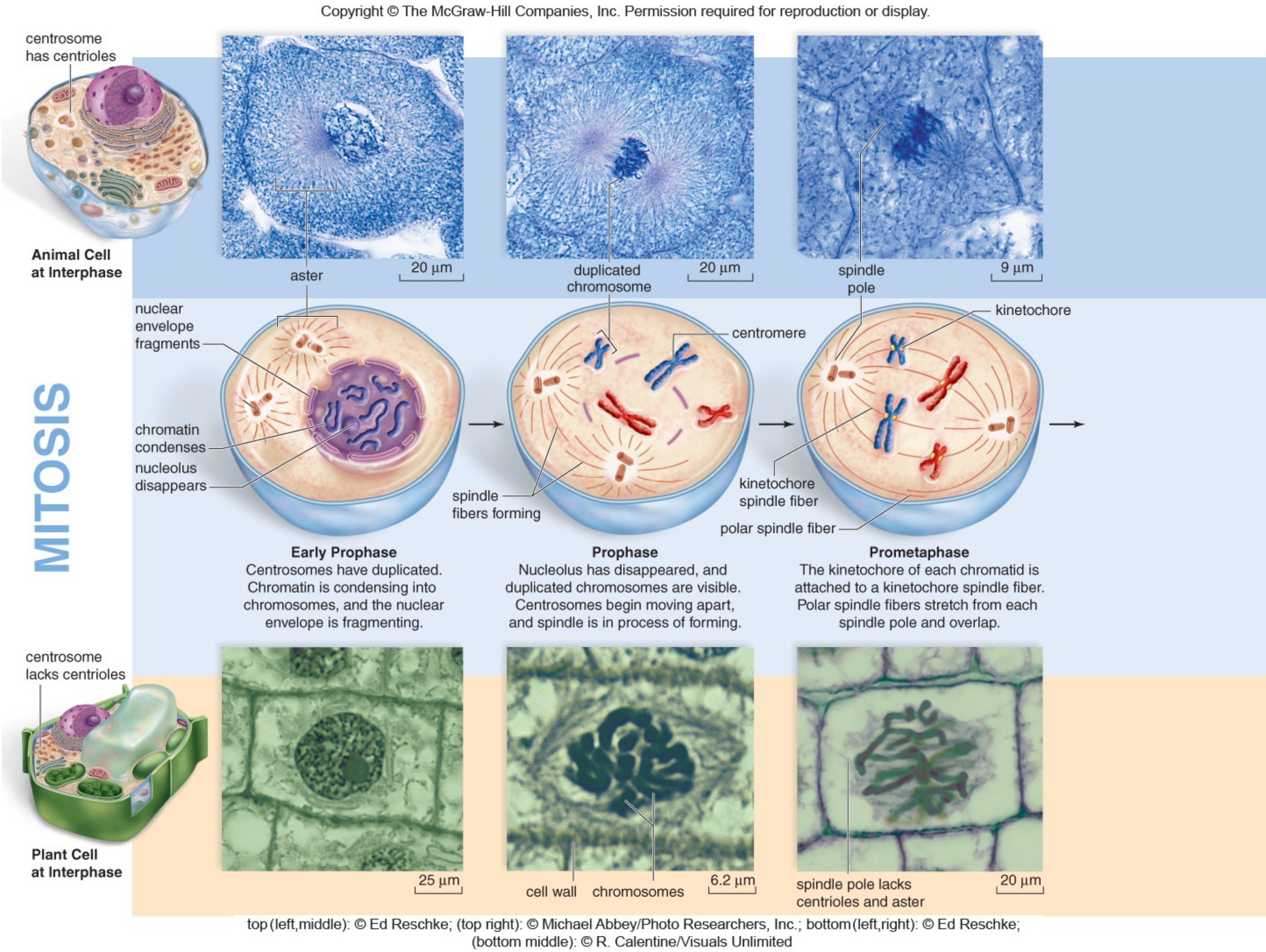
A An unduplicated pair of chromosomes in a cell in G1.

B By G2, each chromosome has been duplicated.

C Mitosis and cytoplasmic division package one copy of each chromosome into each of two new cells.

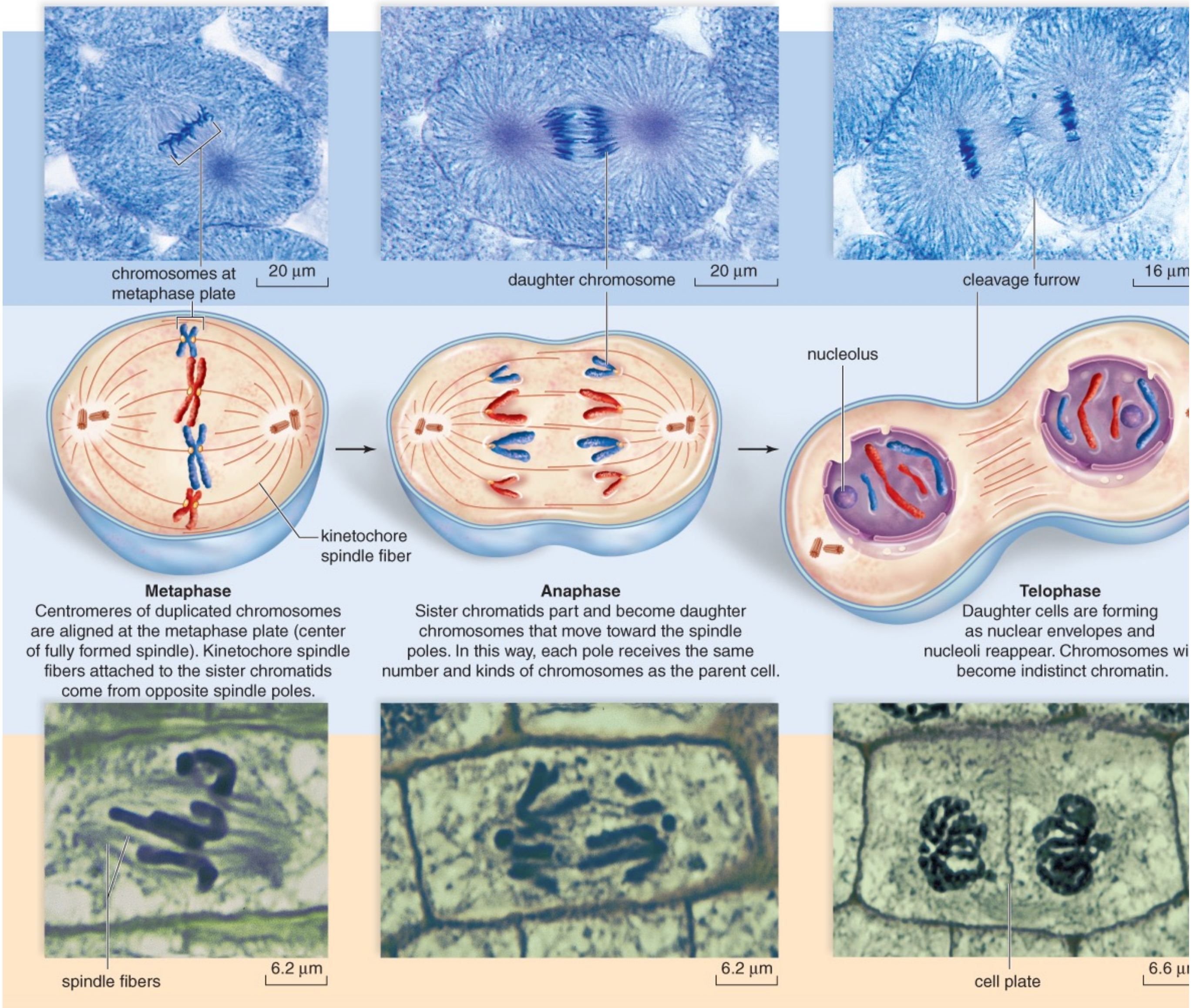
Mitosis

- In animal cells, centrosome contains two barrel-shaped centrioles (9 triplets of microtubules arranged in cylinder)
- Centromere of each chromosome develops two kinetochores (specialised protein complex)



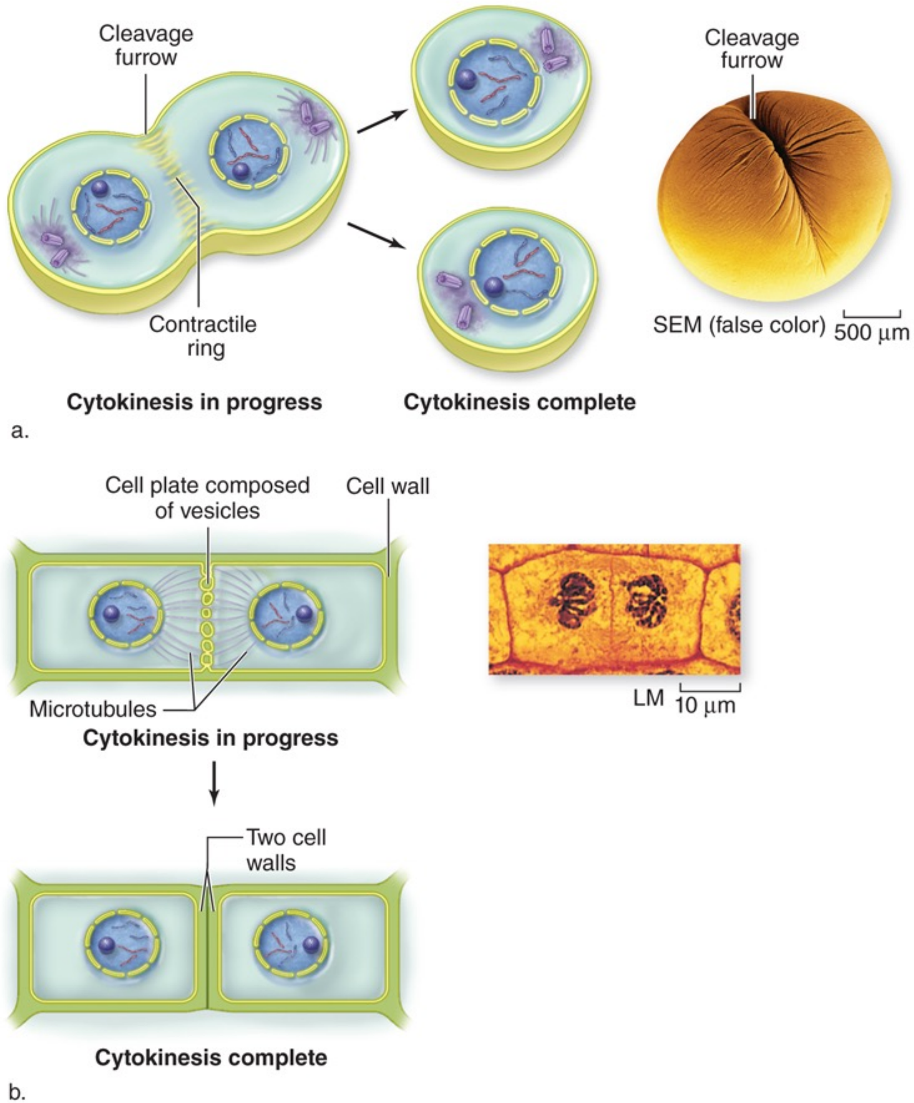
Mitosis

- Spindle – dynamic network of microtubules
- Equatorial plane of the cell – metaphase plate – plane through which parent cell will be divided



Cytokinesis

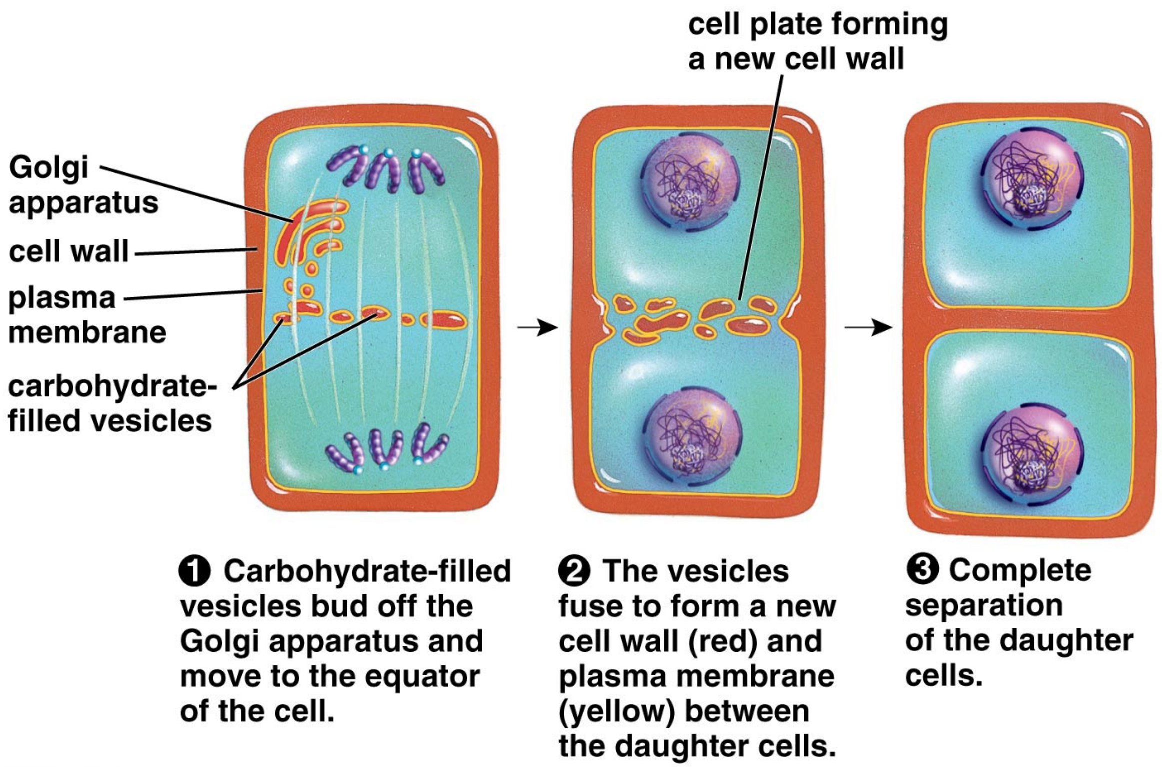
- Division of cytoplasm
  - Often between late anaphase and end of telophase
- In animal cells
  - Band of microfilaments (actin filaments) form contractile ring around equator of cell
  - Results in cleavage furrow that contracts and pinches cytoplasm in two



a: ©Dr. David M. Phillips/Visuals Unlimited; b: ©R. Calentine/Visuals Unlimited

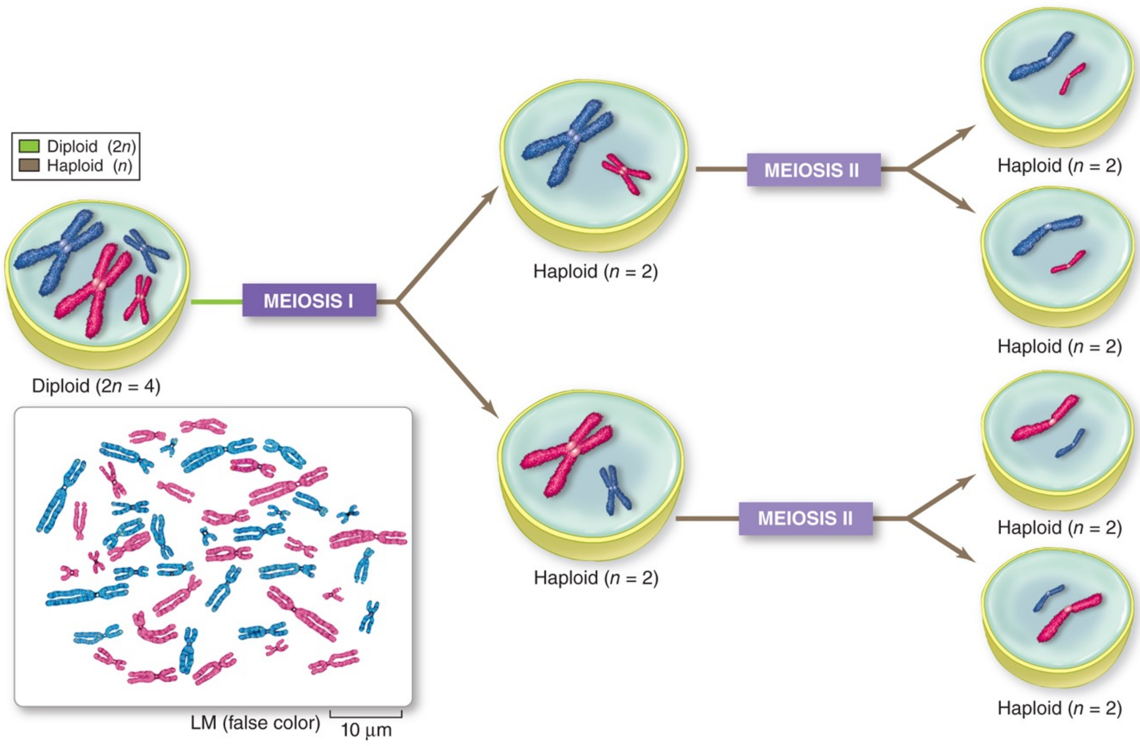
Cytokinesis

- In plant cells
  - Cell plate formed by fusion of small carbohydrate-filled vesicles assemble along equator of cell into continuous flattened vesicle
- Membrane of cell plate become plasma membrane of daughter cells



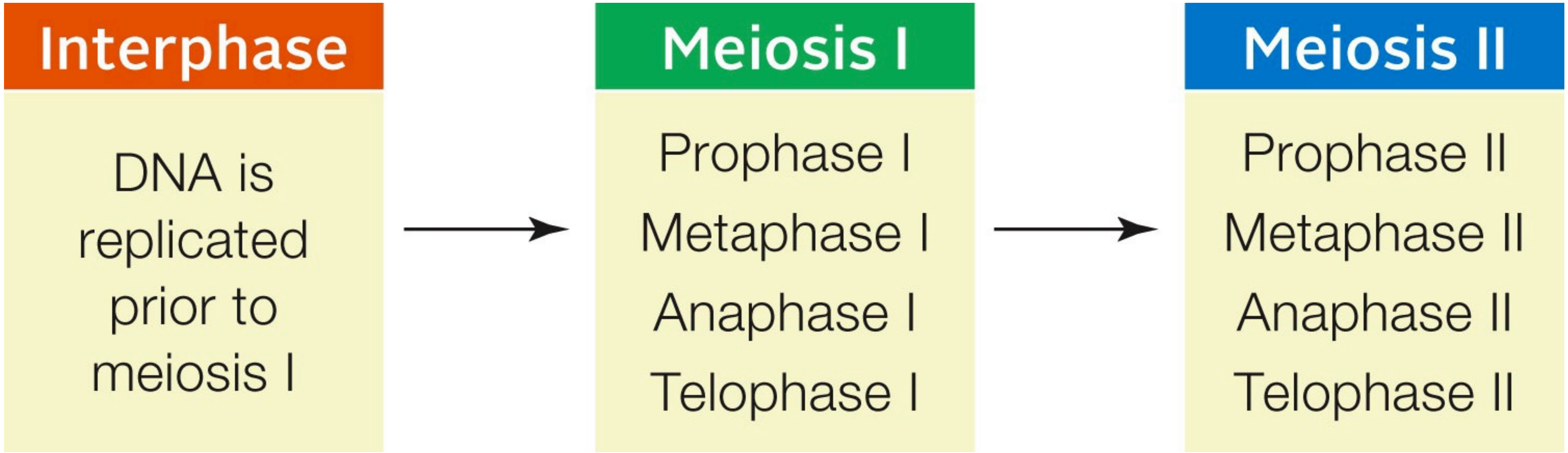
Meiosis

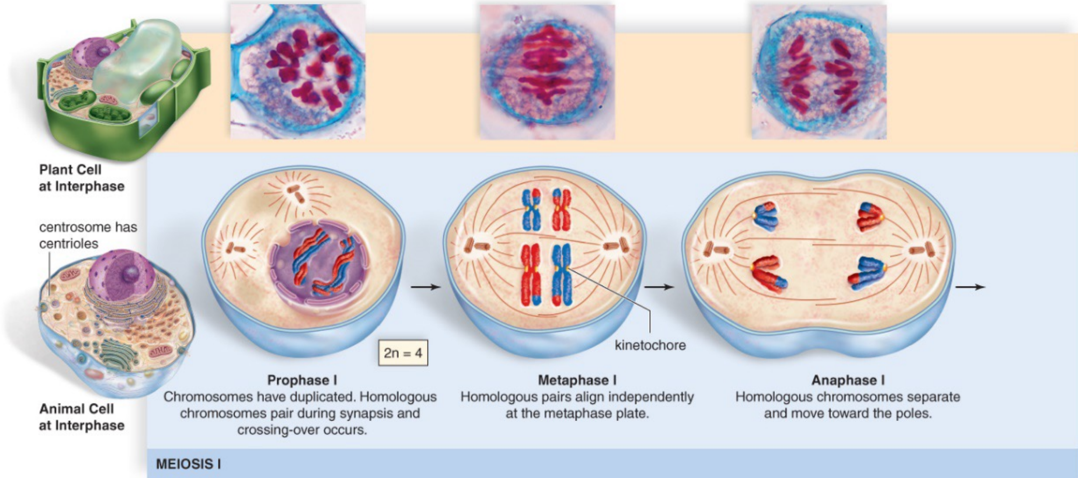
- Halves chromosome number prior to fertilisation
  - Produces haploid (one set of chromosomes) gametes
- During fertilisation
  - Gametes fuse to form diploid (two sets of chromosomes) zygote



Meiosis

- Consists of one round of DNA replication
  - But followed by two rounds of nuclear divisions





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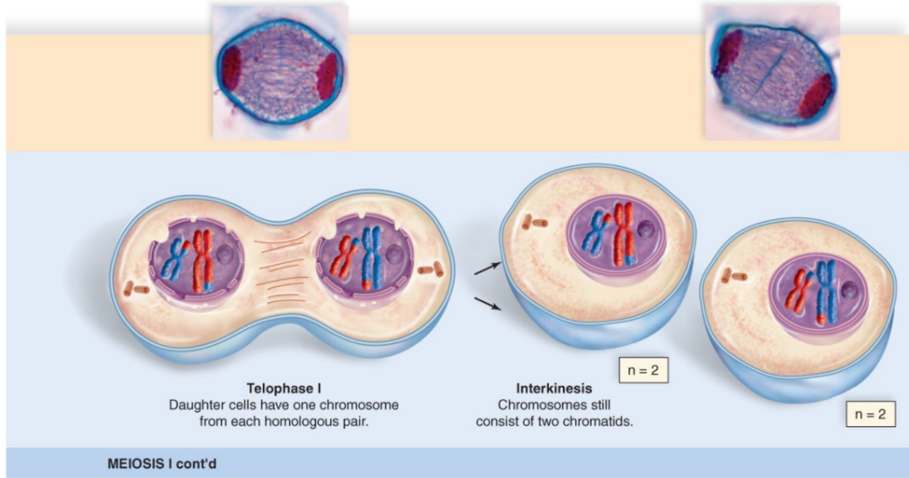

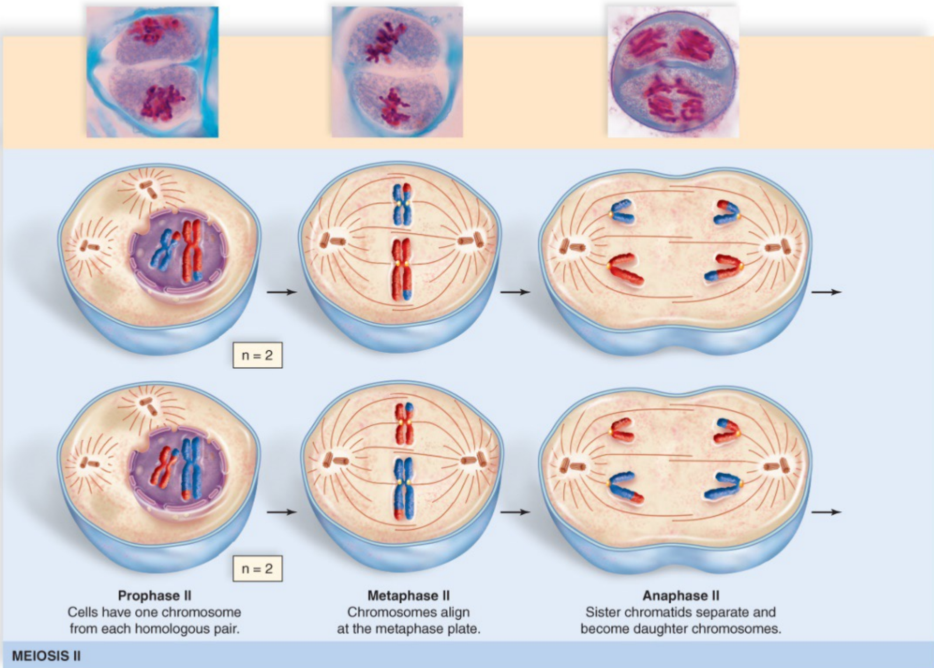

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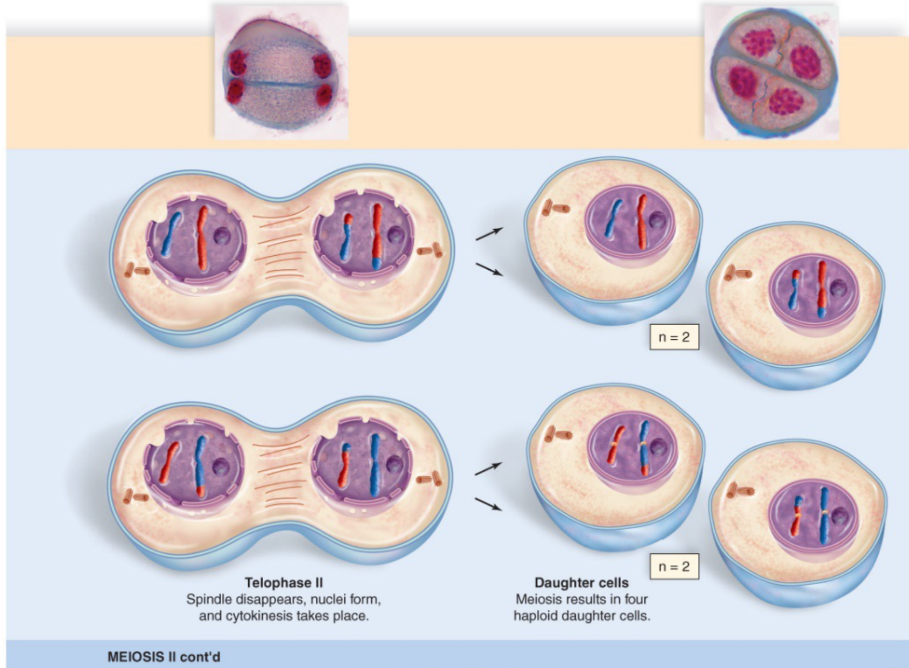

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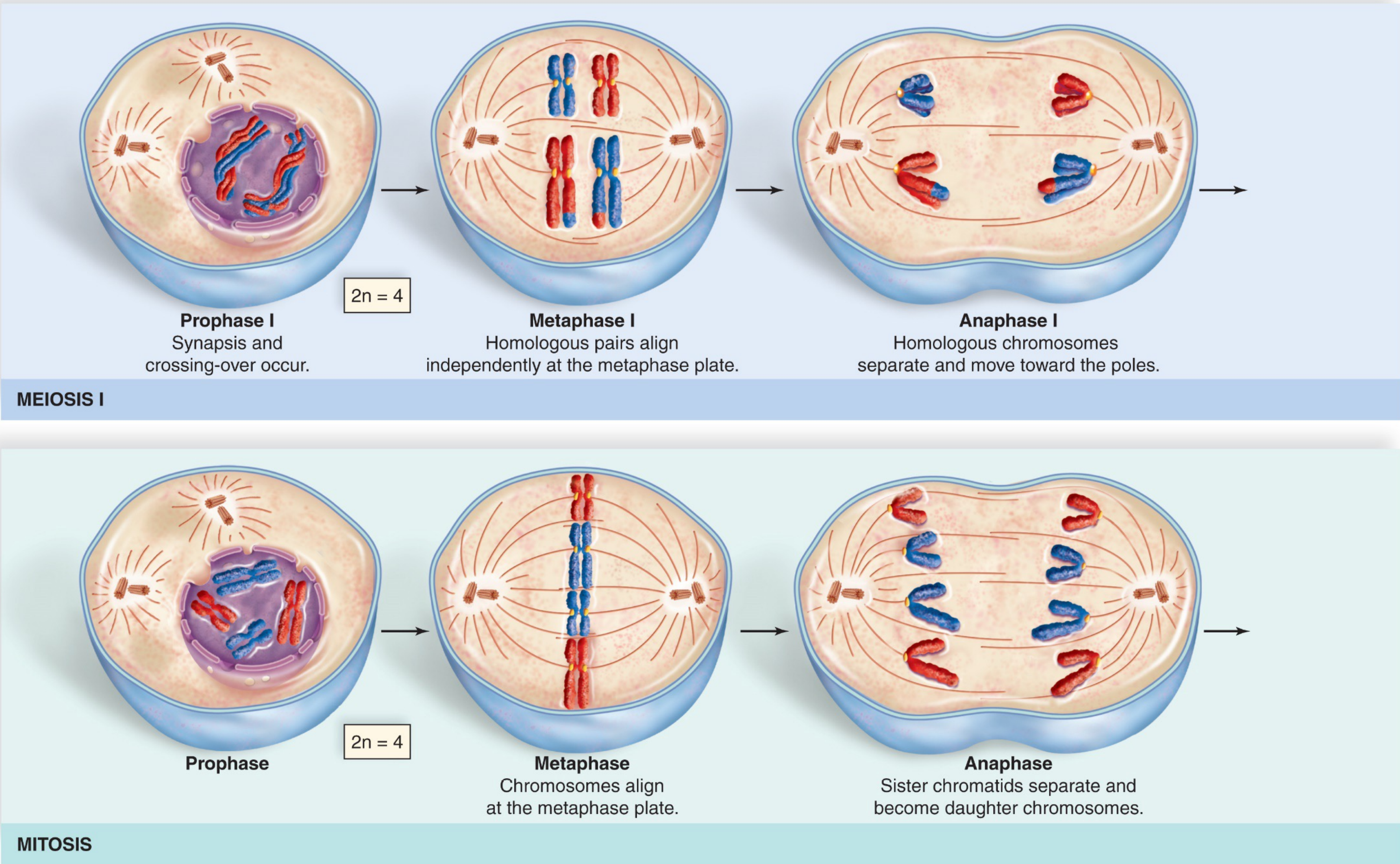
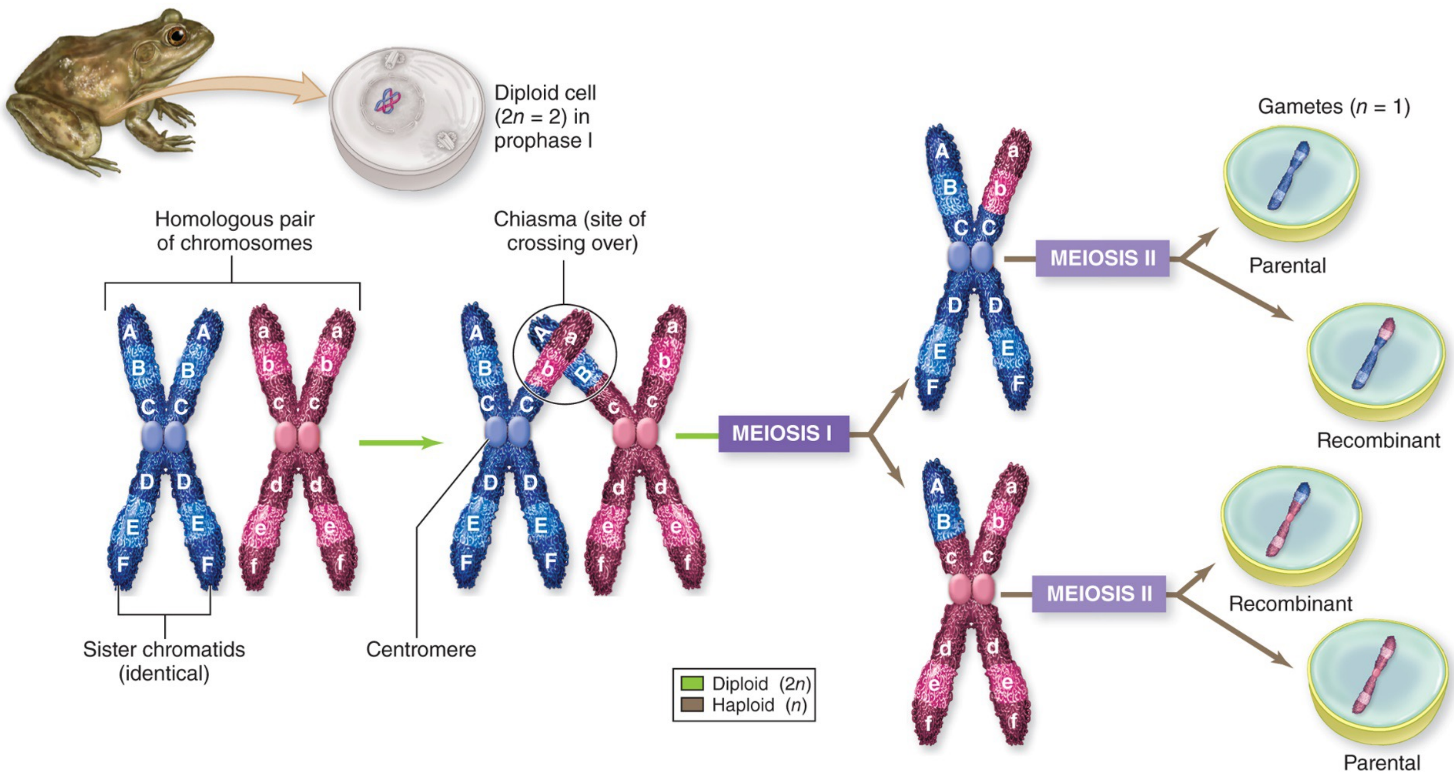

2n = 4
Prophase I
Synapsis and
crossing-over occur.
Metaphase I
Homologous pairs align
independently at the metaphase plate.
Anaphase I
Homologous chromosomes
separate and move toward the poles.
MEIOSIS I
2n = 4
Prophase
Metaphase
Chromosomes align
at the metaphase plate.
Anaphase
Sister chromatids separate and
become daughter chromosomes.
MITOSIS

Meiosis

- Prophase I
  - Homologous chromosomes pair up and physically align themselves against each other side by side – synapsis
  - Synapsed homologues – bivalent (two homologues) or tetrad (four chromatids)
  - Synapsis aligns DNA of non-sister chromatids, allowing non-sister chromatids of paternal chromosome and maternal homologues to exchange genetic material – crossing-over
  - During crossing-over, enzymes cut through DNA of paired homologues, then graft cut-ends together, often switching paternal and maternal ends

Meiosis

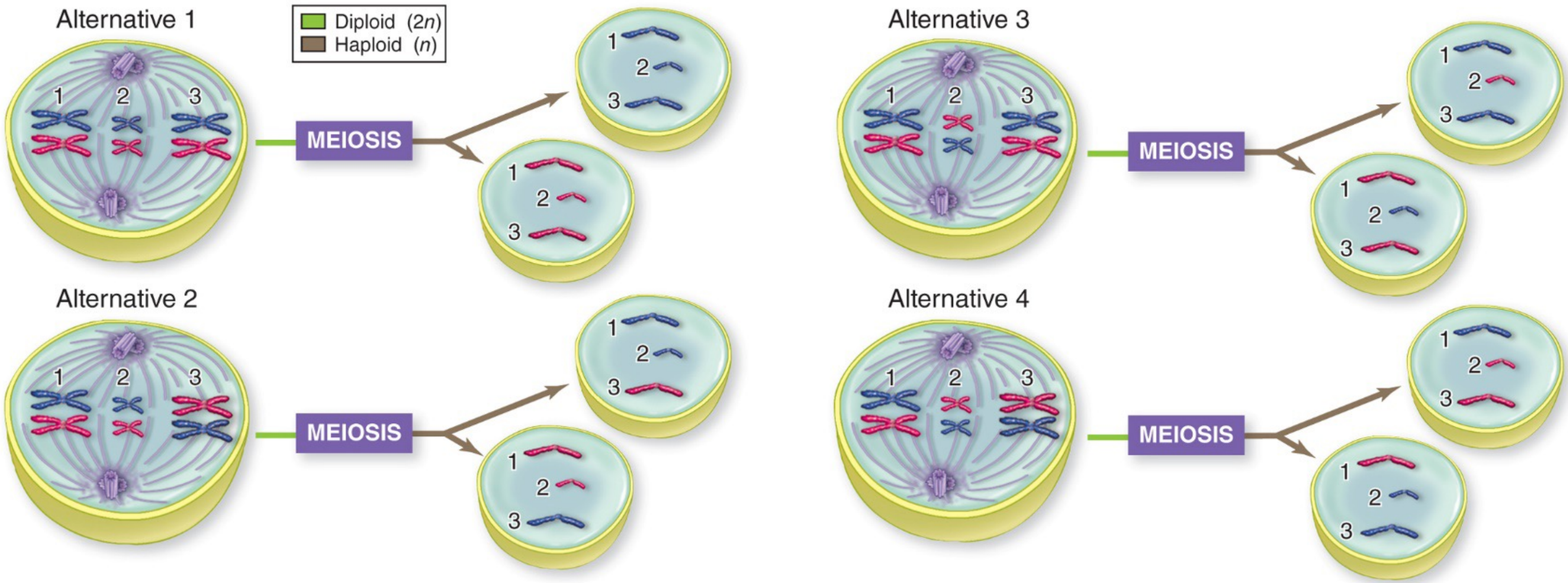


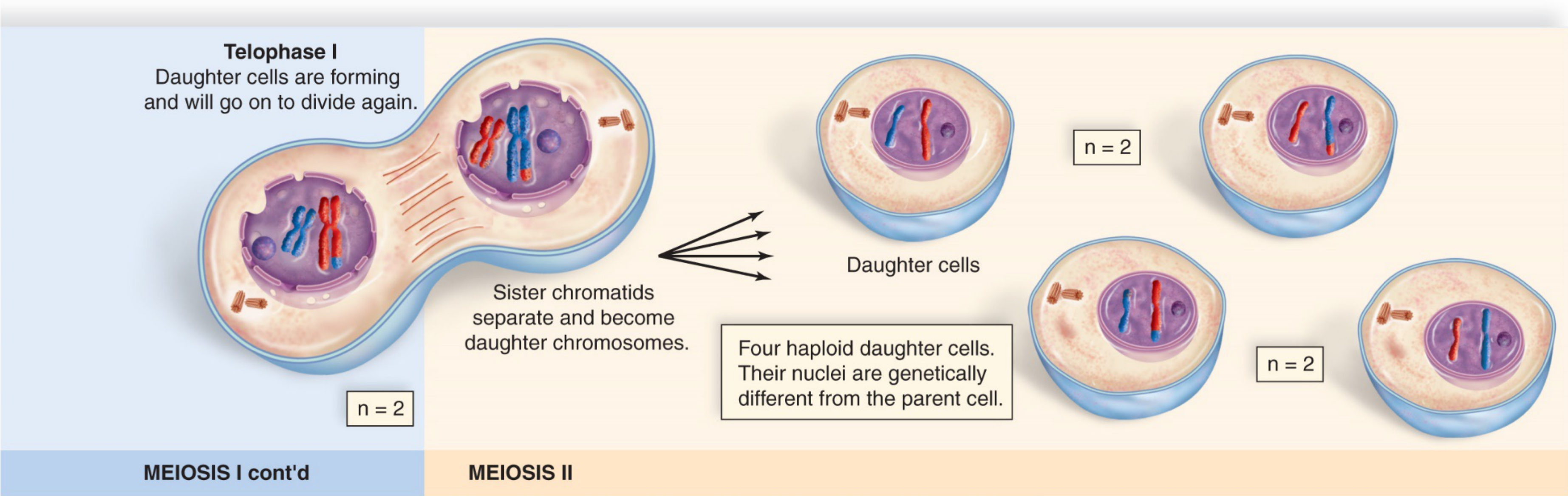
Diploid cell
(2n = 2) in
prophase I
Gametes (n = 1)
Homologous pair
of chromosomes
Chiasma (site of
crossing over)
MEIOSIS I
MEIOSIS II
MEIOSIS II
Parental
Recombinant
Recombinant
Parental
Sister chromatids
(identical)
Centromere
Diploid (2n)
Haploid (n)
A
B
C
D
E
F
a
b
c
d
e
f

Meiosis

- Metaphase I
  - Homologous pairs align at metaphase plate
  - Bivalents aligned independently of one another
  - Paternal or maternal homologue may be oriented toward either pole of parent cell
  - Daughter cell can receive any combination of maternal and paternal homologues
  - Random combining of paternal and maternal homologues – independent assortment
  - Results in random mixing of blocks of alleles into gametes

Meiosis


Alternative 1
Diploid (2n)
Haploid (n)
MEIOSIS
Alternative 2
MEIOSIS
Alternative 3
MEIOSIS
Alternative 4
MEIOSIS


Telophase I
Daughter cells are forming and will go on to divide again.
n = 2
Sister chromatids separate and become daughter chromosomes.
Daughter cells
n = 2
n = 2
Four haploid daughter cells. Their nuclei are genetically different from the parent cell.
MEIOSIS I cont'd
MEIOSIS II

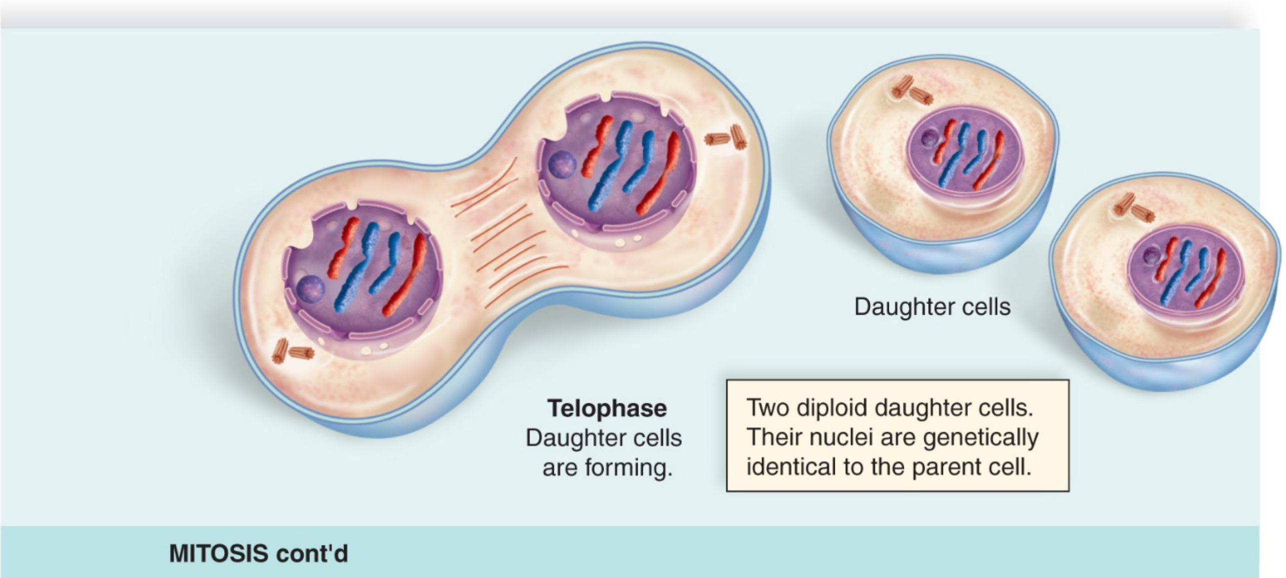

Daughter cells
Telophase
Daughter cells are forming.
Two diploid daughter cells. Their nuclei are genetically identical to the parent cell.
MITOSIS cont'd

Table 10.1 Meiosis I Compared to Mitosis

Meiosis I	Mitosis
Prophase I	**Prophase**
Pairing of homologous chromosomes	No pairing of chromosomes
Metaphase I	**Metaphase**
Bivalents at metaphase plate	Duplicated chromosomes at metaphase plate
Anaphase I	**Anaphase**
Homologues of each bivalent separate and duplicated chromosomes move to poles	Sister chromatids separate, becoming daughter chromosomes that move to the poles
Telophase I	**Telophase**
Two haploid daughter cells, not identical to the parent cell	Two diploid daughter cells, identical to the parent cell

Table 10.2 Meiosis II Compared to Mitosis

Meiosis II	Mitosis
Prophase II	**Prophase**
No pairing of chromosomes	No pairing of chromosomes
Metaphase II	**Metaphase**
Haploid number of duplicated chromosomes at metaphase plate	Diploid number of duplicated chromosomes at metaphase plate
Anaphase II	**Anaphase**
Sister chromatids separate, becoming daughter chromosomes that move to the poles	Sister chromatids separate, becoming daughter chromosomes that move to the poles
Telophase II	**Telophase**
Four haploid daughter cells, not genetically identical	Two diploid daughter cells, identical to the parent cell

Outline

- Genetic Material
  - Johannes Friedrich Miescher
  - Frederick Griffith
  - Avery, MacLeod and McCarty
  - Alfred Hershey and Martha Chase
- DNA Nucleotides
  - Erwin Chargaff
- DNA Structure
  - Rosalind Franklin
  - Maurice Wilkins
  - James Watson and Francis Crick
  - Watson-Crick model
- DNA Replication
- Cell Division
  - Binary fission
  - Eukaryotic cell division
  - Eukaryotic cell cycle
  - Eukaryotic chromosomes
  - Mitosis
  - Cytokinesis
  - Meiosis
- Mutations

Mutations

- A **mutation** is a change in a cell's DNA sequence, either in a protein coding gene or in a noncoding regulatory region.

- Mutations may have **varying effects** on function
  - Mutations are often **harmful**, and an organism inheriting them may quickly die
  - Some mutations may **have no functional effect**
  - Some mutations may **be beneficial** and provide an advantage to the organism in certain environments
    - These advantageous mutations may be favored by natural selection and are the **basis for evolution** of life on Earth

How Do Mutations Occur?

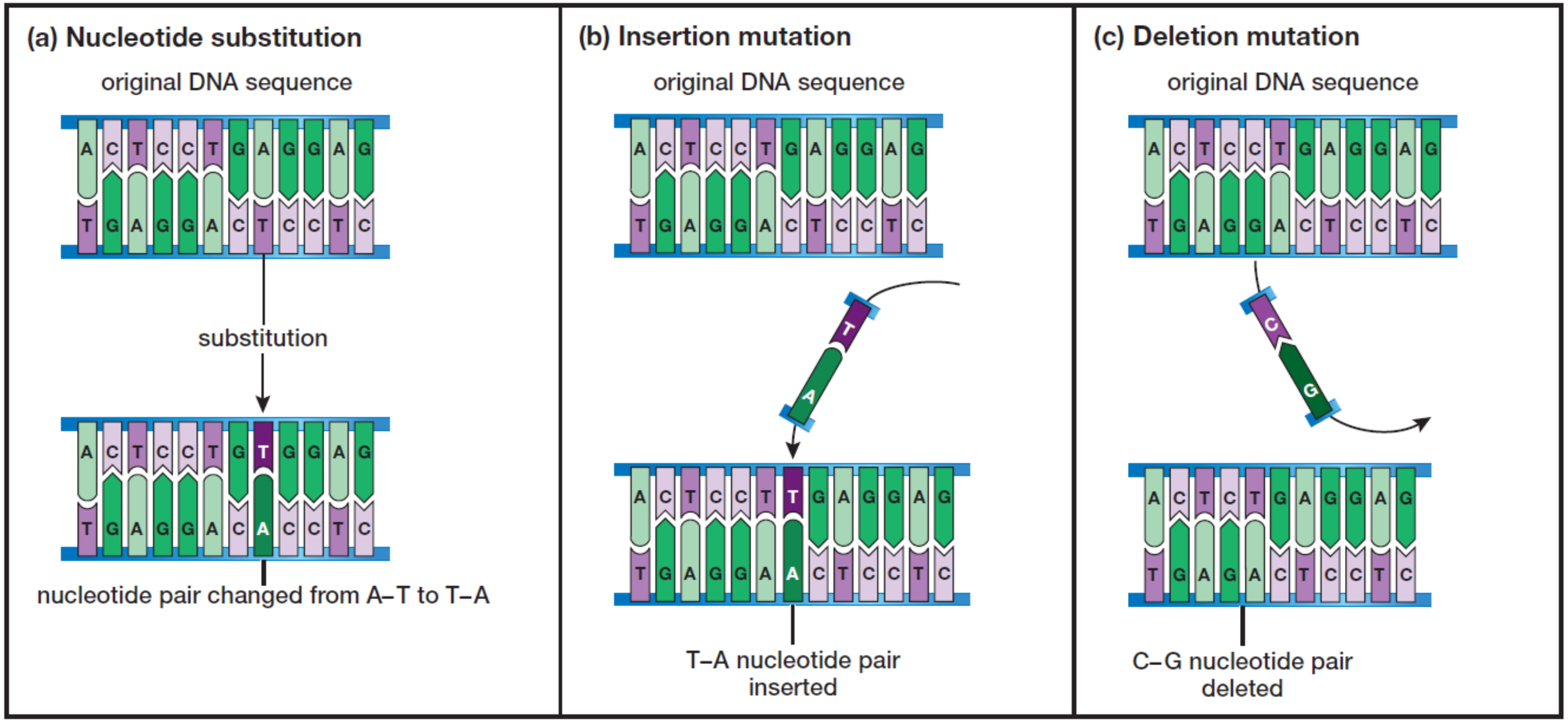
Mistakes do happen: DNA is altered or damaged in a number of ways

- Mistakes are made during normal DNA replication

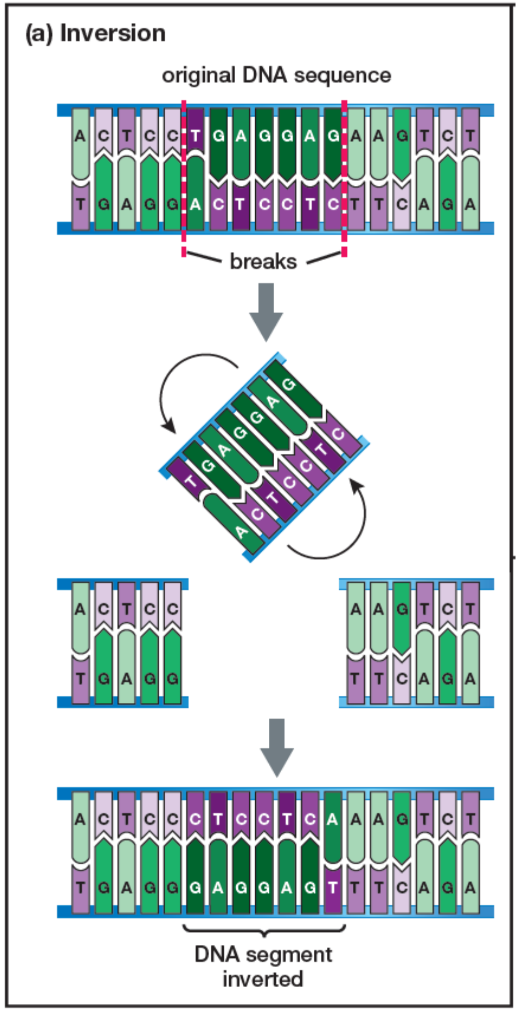
  Replicated DNA strands usually contain only about one mistake in every 100 million to 1 billion base pairs

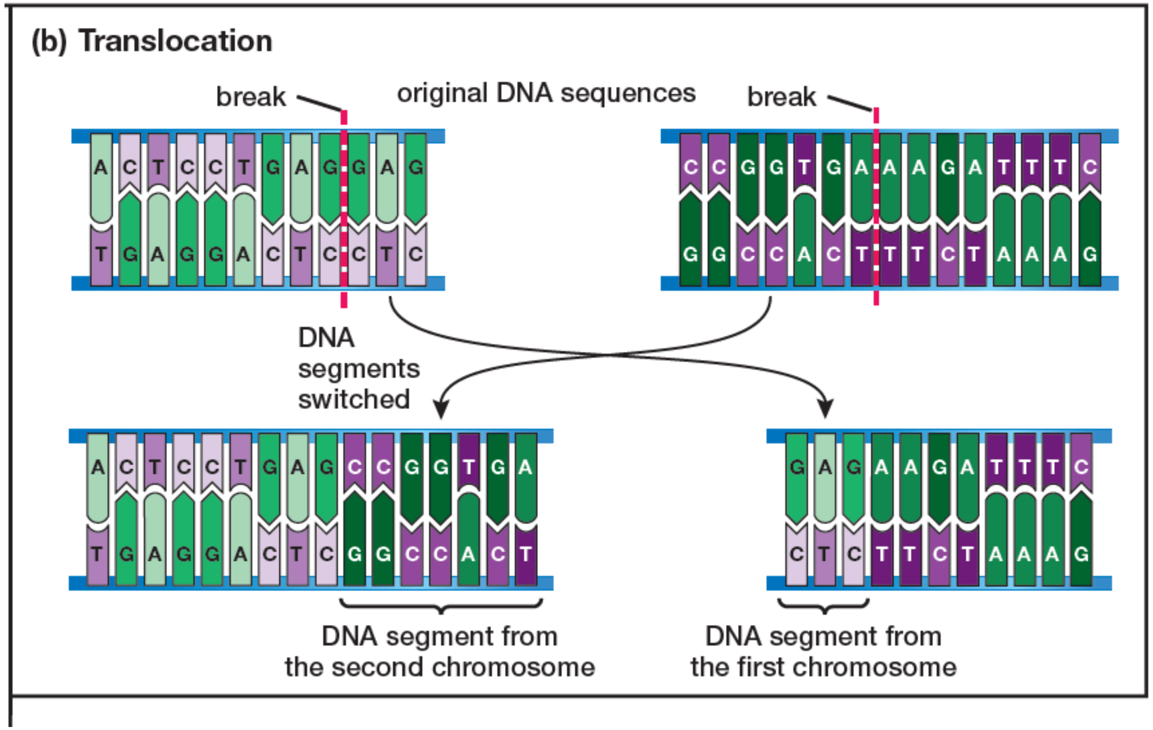
- Certain chemicals (some components of cigarette smoke, for example) increase DNA errors during and after replication
- Ultraviolet radiation or X-rays contribute to incorrect base pairing

Types of mutations



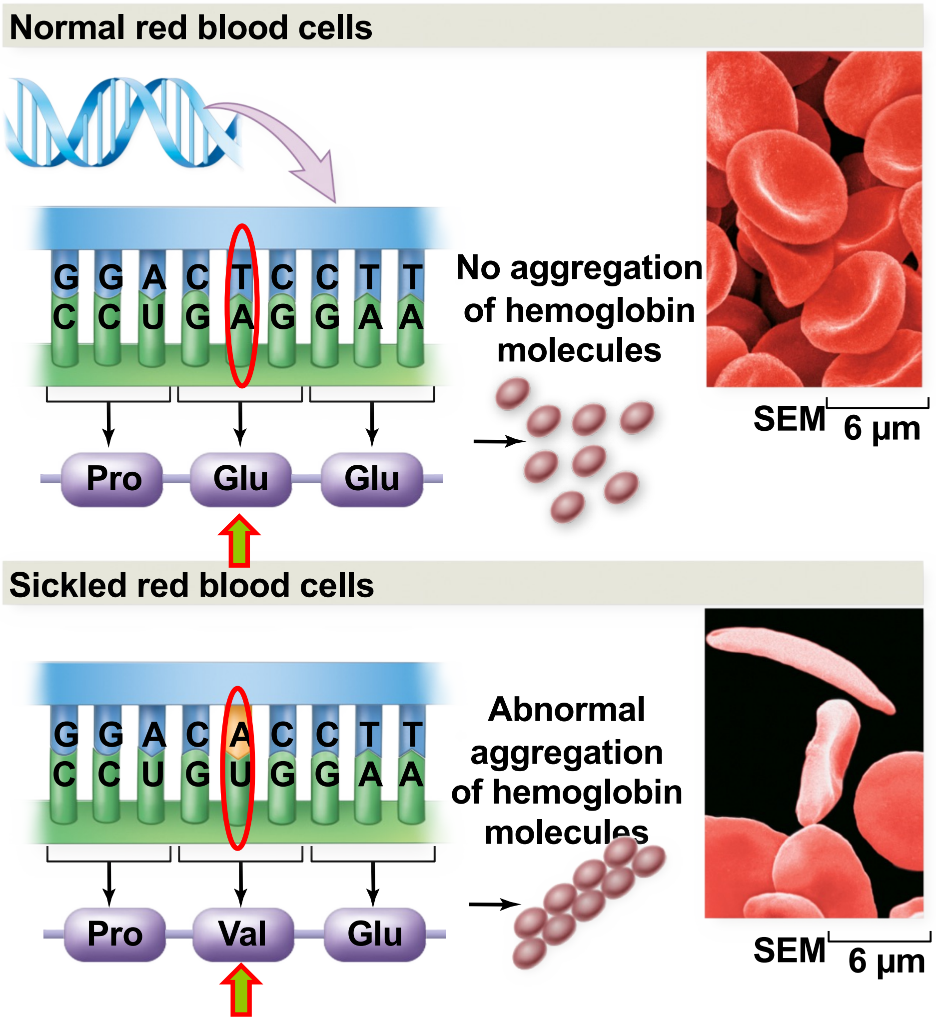
Types of mutations





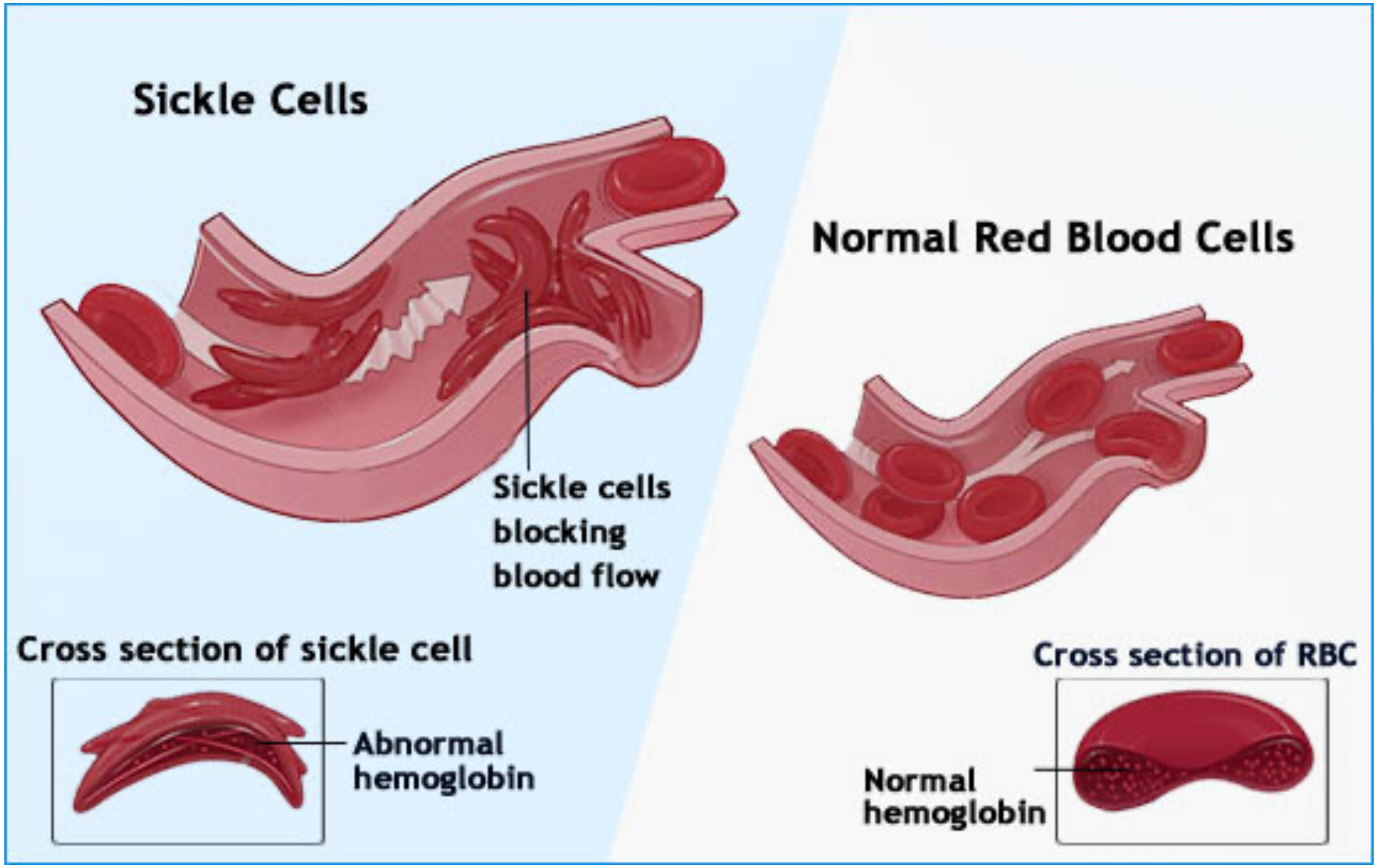
Mutations in DNA (video)

Case study: Sickle cell disease



A single base substitution in a hemoglobin gene causes blood cells to form abnormally, leading to sickle cell disease.

Case study: Sickle cell disease



Outline

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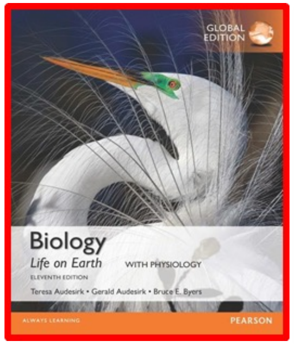
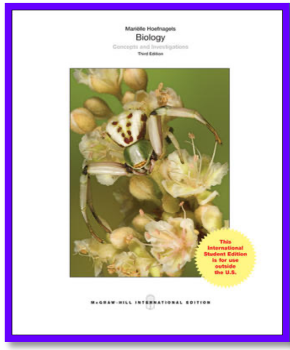
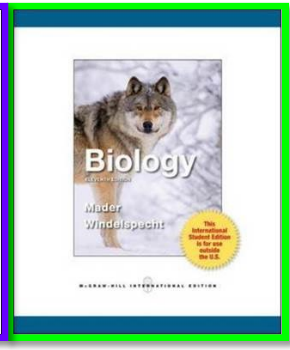
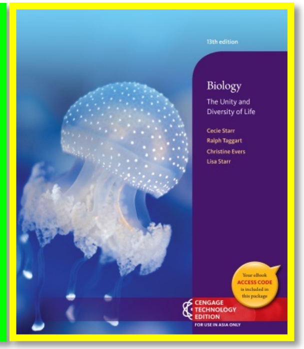
  - Binary fission
  - Eukaryotic cell division
  - Eukaryotic cell cycle
  - Eukaryotic chromosomes
  - Mitosis
  - Cytokinesis
  - Meiosis
- Mutations

Text Books/References









This Lecture: DNA

Chapters 12 | Chapter 3, 7, 8 | Chapters 3,12 | Chapter 3, 8

Next Lecture: Gene Expression

Chapter 13 | Chapters 3, 7, 8 | Chapters 13 | Chapters 9, 10

Reminders

- Laboratory assignment 4 is due tomorrow (23rd March, 23.59 hrs)
  - Make sure to check the Similarity Report
- Practical 5 is this Thursday (24th March)
  - Please wear long pants and shoes
  - Bring labcoat or purchase one
  - Read the handout before coming to lab