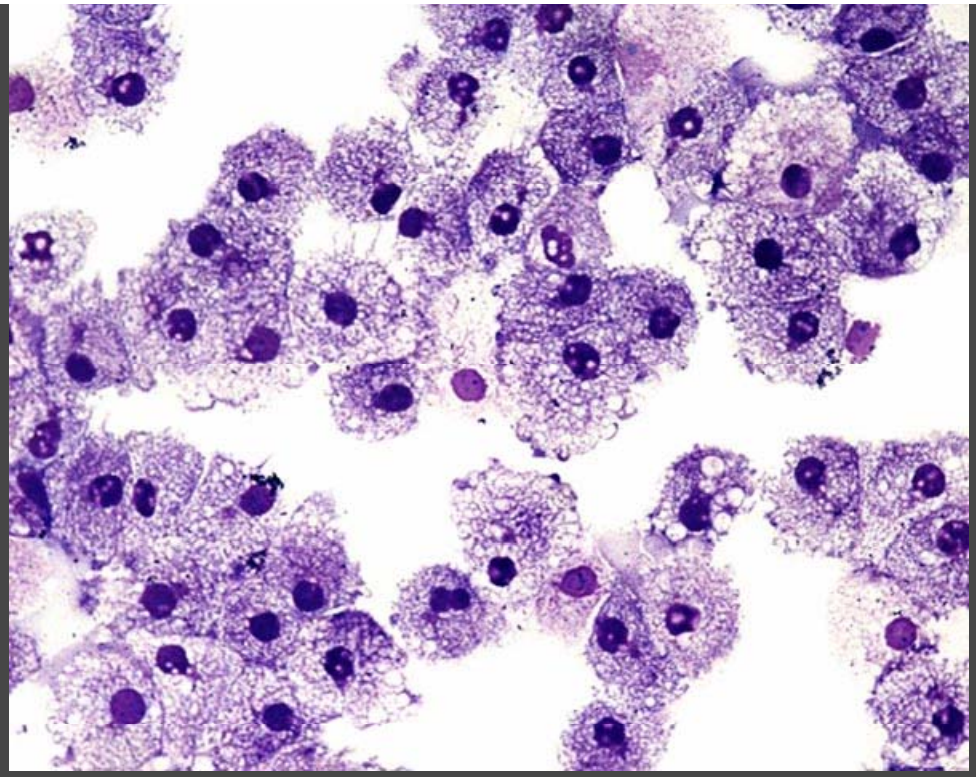
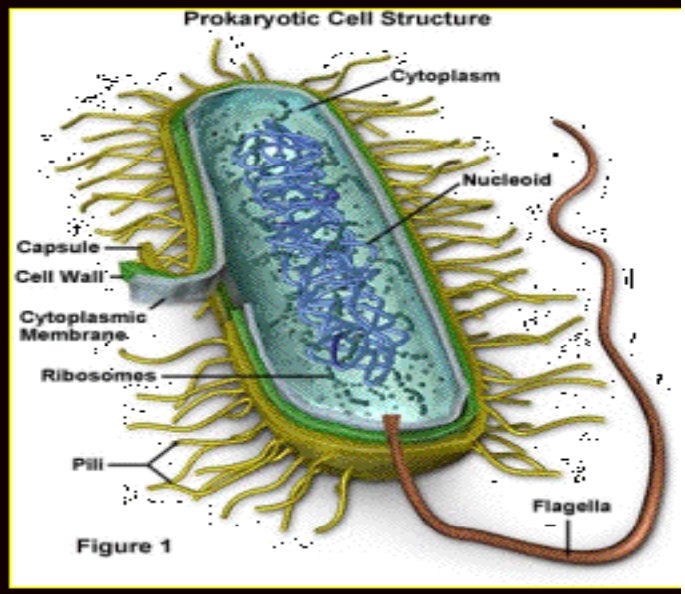


CELL AND CELL DIVISION

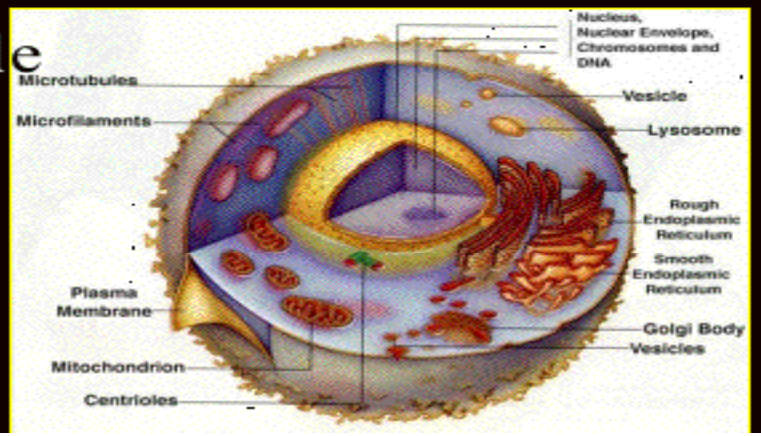
D.HAMMOUDI.MD

Part 1: Cell Division

- Cell division is the cornerstone of life
- ***Genome***: a cell's complete set of an organism's genetic material – (DNA)



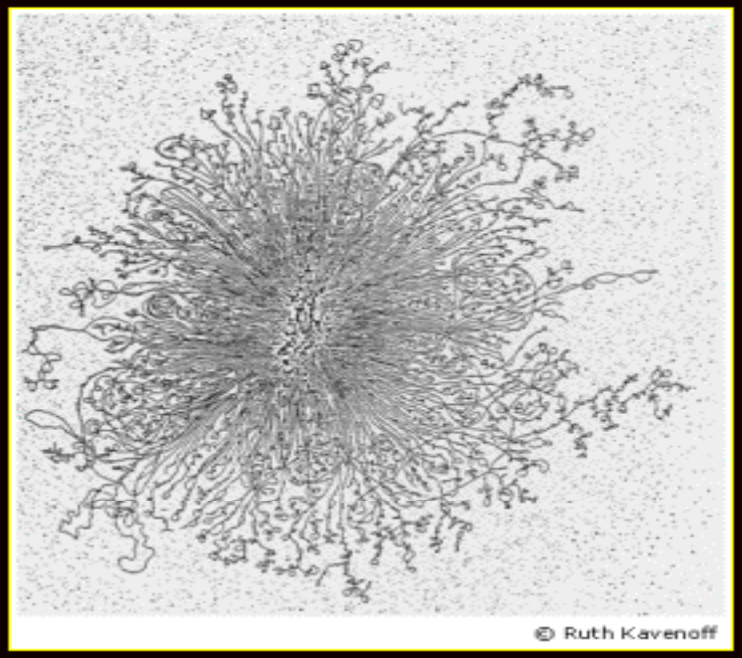
- ***Chromosome***:
  - Bacteria, viruses: DNA molecule w/ most or all DNA
  - Eukaryotes: DNA / protein structure with part of the DNA information



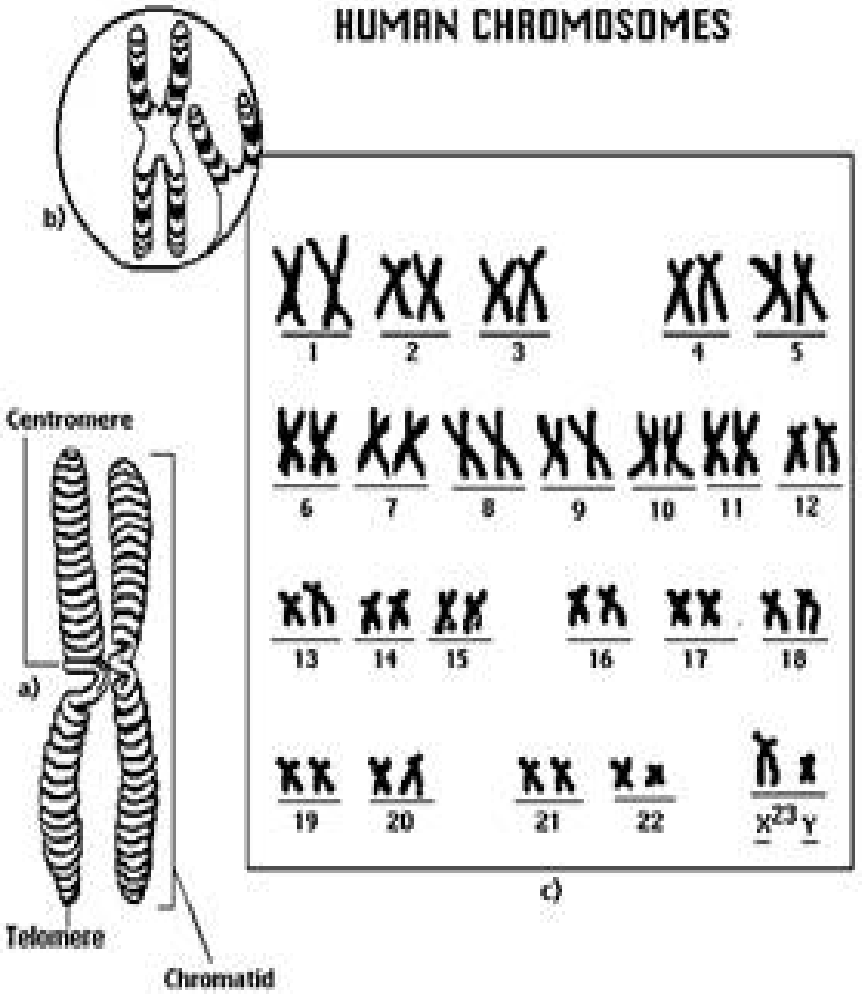
Chromosomes

(colored bodies)

– Prokaryotes have a single, circular chromosome



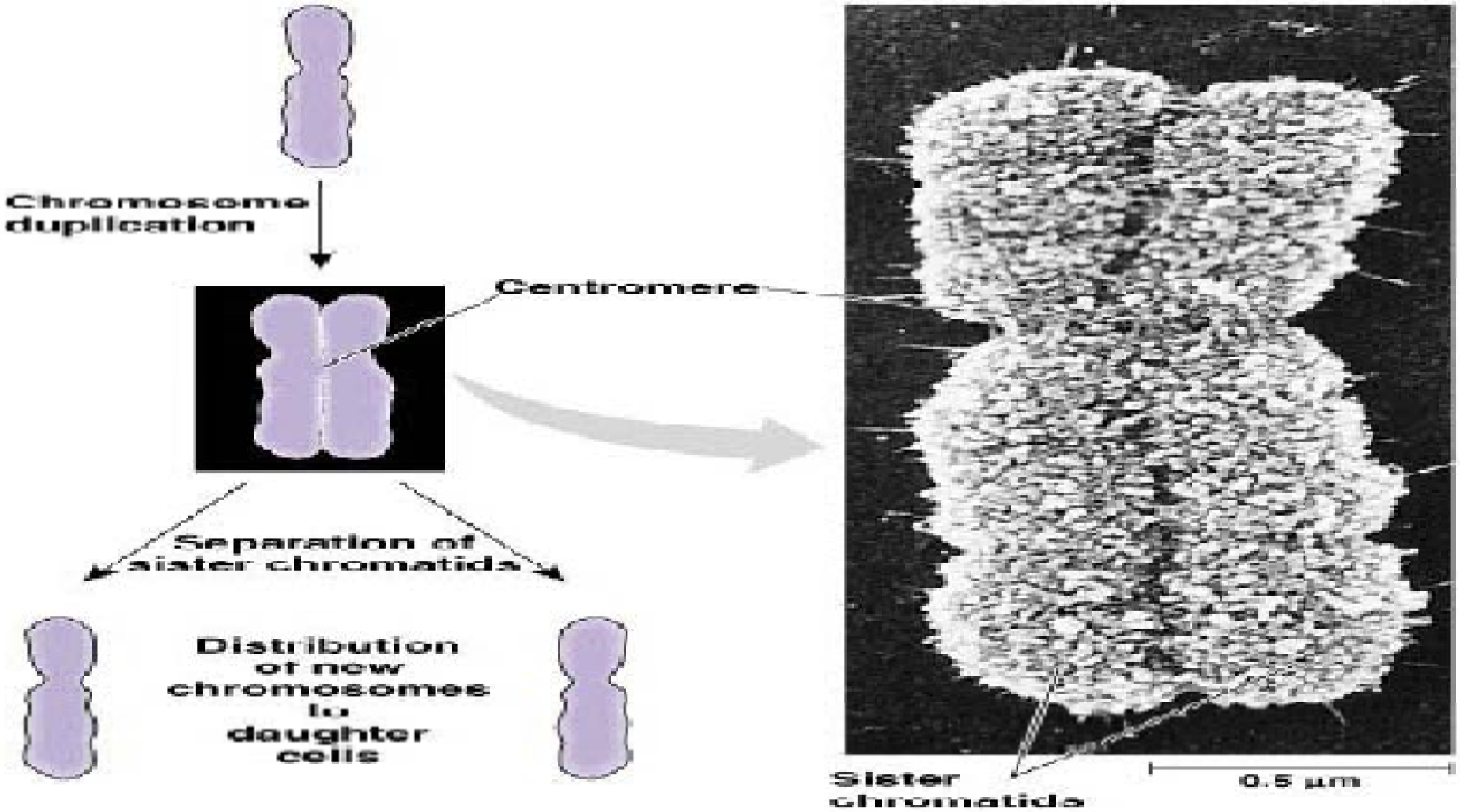
- In animals…
- Somatic cells (cells of the body) are ***diploid***. This means that each cell has two chromosomes of each type. They are in PAIRS.
- Gamete cells (egg, sperm) are ***haploid***. This means that each cell has only one of each type of chromosome.
- Biologists use "**2N**" to symbolize ***diploid***.
- Biologists use "**1N**" to symbolize ***haploid***.



- A ***karyotype*** is a picture showing the arrangement of a full set of human chromosomes.
- Humans have 46 (or 23 pairs) of chromosomes

Cell Division: Key Roles

☐ ☐ Genome: cell's genetic information
☐ ☐ Somatic (body cells) cells
☐ ☐ Gametes (reproductive cells): sperm and egg cells
☐ ☐ Chromosomes: DNA molecules
☐ ☐ Diploid (2n): 2 sets of chromosomes
☐ ☐ Haploid (1n): 1 set of chromosomes
☐ ☐ Chromatin: DNA-protein complex
☐ ☐ Chromatids: replicated strands of a chromosome
☐ ☐ Centromere: narrowing "waist" of sister chromatids
☐ ☐ Mitosis: nuclear division
☐ ☐ Cytokinesis: cytoplasm division
☐ ☐ Meiosis: gamete cell division



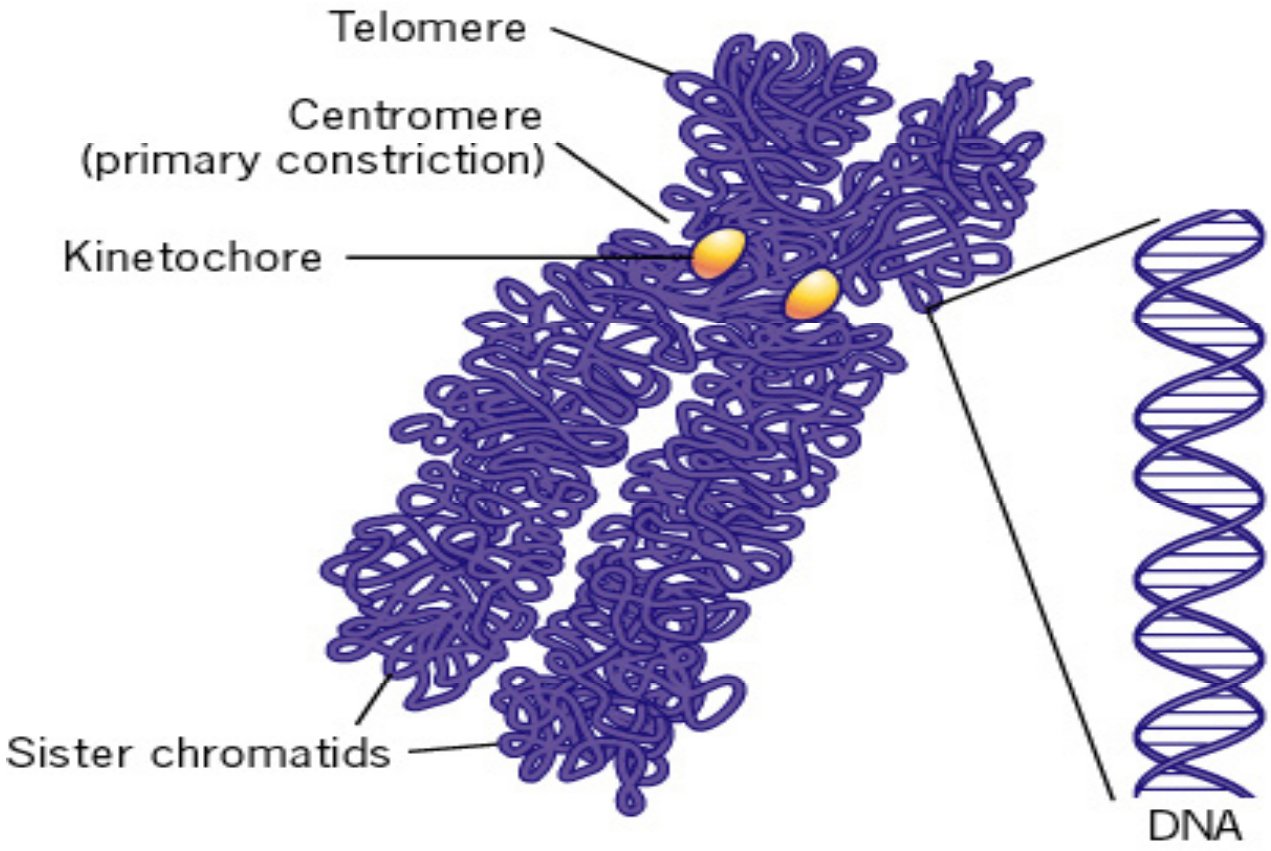
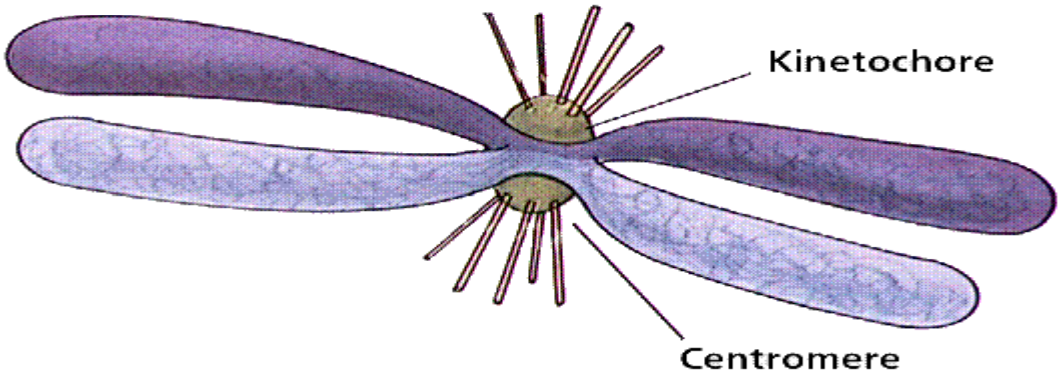


Fig 2.4 The structure of a highly condensed, replicated chromosome.

A Chromosome



Chromosome Structure

Explore the "chromosome viewer" at this site based on information from the Human Genome project (& the source of this figure):

http://www.ornl.gov/sci/techresources/Human_Genome/posters/chromosome/index.shtml

What Exactly is a chromosome?

Chromosomes are the rod-shaped, filamentous bodies present in the nucleus, which become visible during cell division.

They are the carriers of the gene or unit of heredity.

Chromosome are not visible in active nucleus due to their high water content, but are clearly seen during cell division.

- Chromosomes were first described by Strausberger in 1875.
- The term “Chromosome”, however was first used by Waldeyer in 1888.
- They were given the name chromosome (Chromo = colour; Soma = body) due to their marked affinity for basic dyes.
- Their number can be counted easily only during mitotic metaphase.

- Chromosomes are composed of thin chromatin threads called Chromatin fibers.
- These fibers undergo folding, coiling and supercoiling during prophase so that the chromosomes become progressively thicker and smaller.
- Therefore, chromosomes become readily observable under light microscope.
- At the end of cell division, on the other hand, the fibers uncoil and extend as fine chromatin threads, which are not visible at light microscope

Number of chromosomes

- Normally, all the individuals of a **species have the same number** of chromosomes.
- Closely related species usually have similar chromosome numbers.
- Presence of a whole sets of chromosomes is called **euploidy**.
- It includes haploids, diploids, triploids, tetraploids etc.
- Gametes normally contain only one set of chromosome – this number is called **Haploid**
- Somatic cells usually contain two sets of chromosome - **2n : Diploid**

3n – triploid

4n – tetraploid

The condition in which the chromosomes sets are present in a multiples of “n” is **Polyploidy**

When a change in the chromosome number does not involve entire sets of chromosomes, but only a few of the chromosomes - is **Aneuploidy.**

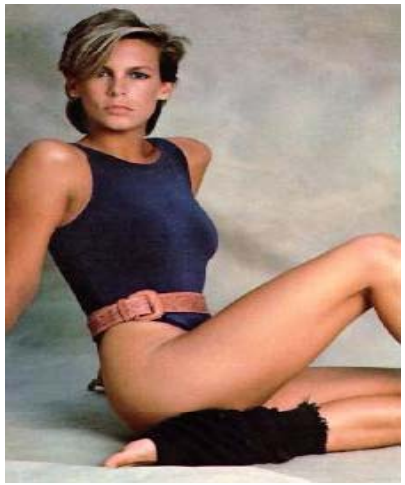
- Monosomics (2n-1)
- Trisomics (2n+1)
- Nullisomics (2n-2)
- Tetrasomics (2n+2)

Sex Determination

- The basic rule: if the Y chromosome is present, the person is male. If absent, the person is female.
- In meiosis, the X and Y chromosomes separate and go into different sperm cells: ½ the sperm carry the X and the other half carry the Y. All eggs have one of the mother's X chromosomes, so when they are fertilized, ½ of the zygotes are XX (female), and ½ are XY (male).
- The Y chromosome has the main sex-determining gene on it, called SRY.
- About 4 weeks after fertilization, an embryo that contains the SRY gene develops testes, the primary male sex organ. The testes secrete the hormone testosterone. Testosterone signals the other cells of the embryo to develop in the male pattern.
- If the embryo does not have the SRY gene, it develops ovaries instead, which secrete estrogen and causes development in the female pattern.

A few oddities

- It is possible to be XY and female. Two ways this can happen:
- 1. the SRY gene can be inactivated by a mutation. If SRY doesn't work, testes don't develop and the embryo develops as a normal female.
- 2. In a condition called "androgen insensitivity", the person is XY with a functional SRY gene, but her cells lack the testosterone receptor protein, so the cells don't ever get the message that the testosterone is sending. Testes develop in the abdominal cavity, and no ovaries, fallopian tubes, or uterus develop. At puberty, the internal testes secrete testosterone, which gets converted into estrogen and the body develops as a normal (but sterile) adult female.



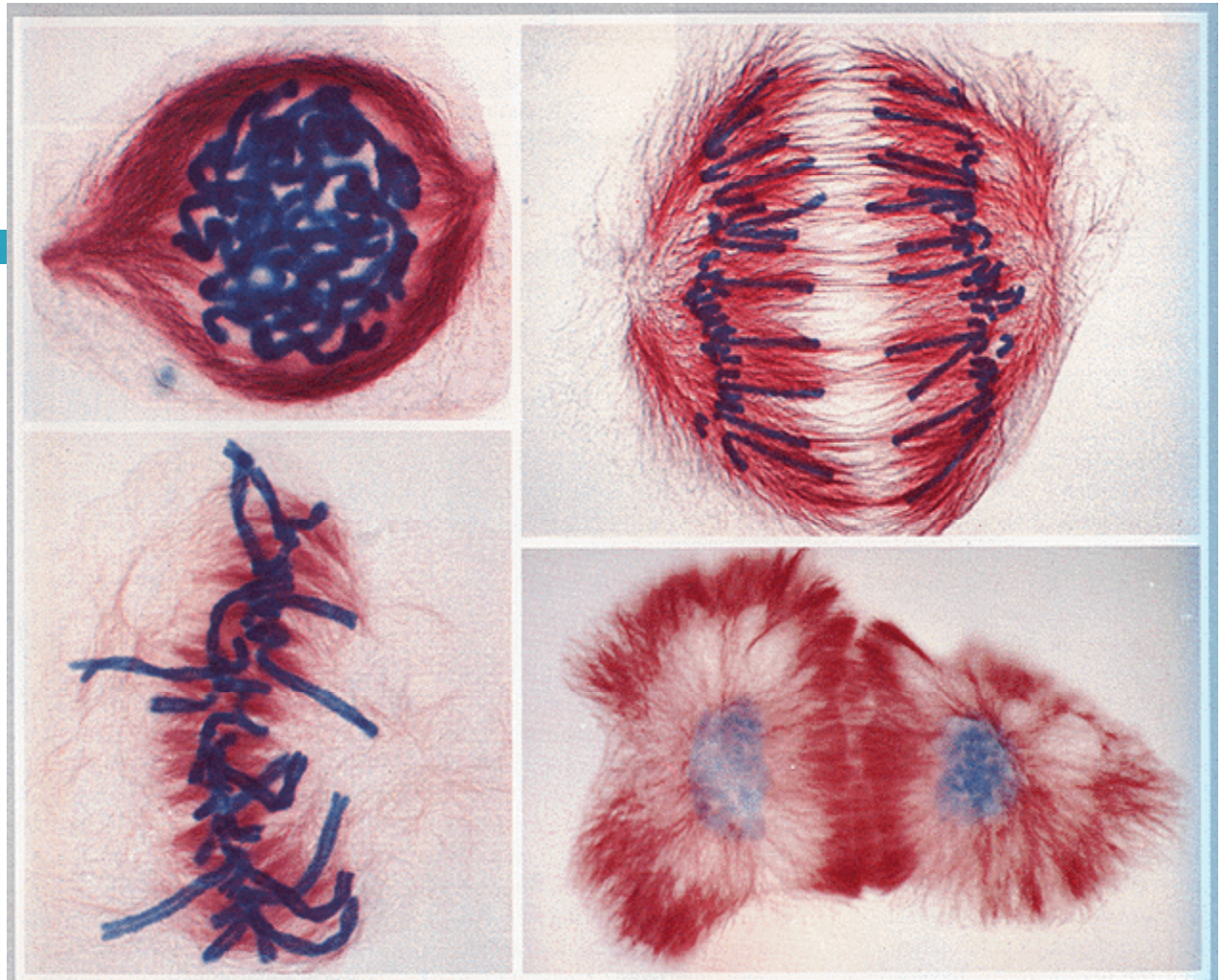
Hermaphrodites

In some cases, androgen insensitivity is only partial: the cells respond a little bit to testosterone produced by the testes. The embryo develops with ambiguous genitalia, neither completely male not completely female. Such a person is sometimes called a "hermaphrodite".

Another condition, congenital adrenal dysplasia, causes the adrenal glands to produce an abnormally large amount of testosterone in a female embryo, This can also cause development of ambiguous genitalia, a hermaphrodite.

- Another rare condition: a chimera occurs when two separate embryos fuse together. This can result in a person with some XX cells and some XY cells. Such a person can have both testes and ovaries, a "true" hermaphrodite. This condition is extremely rare: more people say they have it than actually do.

Cell division



Plat cells in various stages of mitosis: (a) prophase; (b) metaphase; (c) anaphase; (d) telophase (all magnified about 2,700 times).

INTERPHASE - DNA replicates

PROPHASE - diffuse chromatin condenses into discrete chromosomes

PROMETAPHASE - chromosome movement toward the "equatorial plane"

METAPHASE - chromosomes are lined up at the equatorial plane (also called the metaphase plate)

ANAPHASE - Sister chromatids disjoin and migrate to opposite poles.

TELOPHASE - chromosomes decondense and a cleavage furrow begins to form in the middle of the cell. Finally, the cell divides in two, this is called *cytokinesis.*

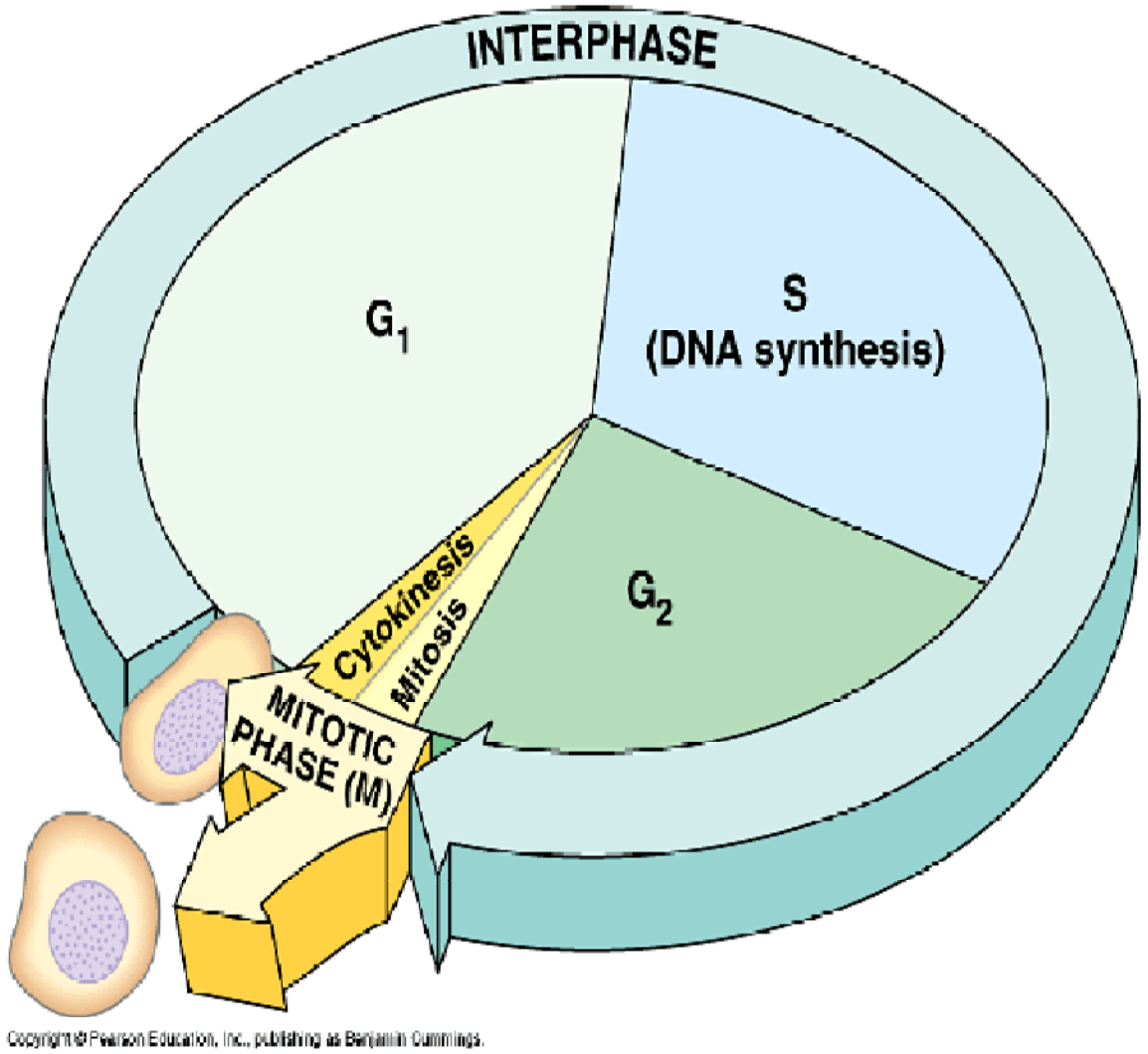
The Cell Cycle

☐ ☐ Interphase (90% of cycle)

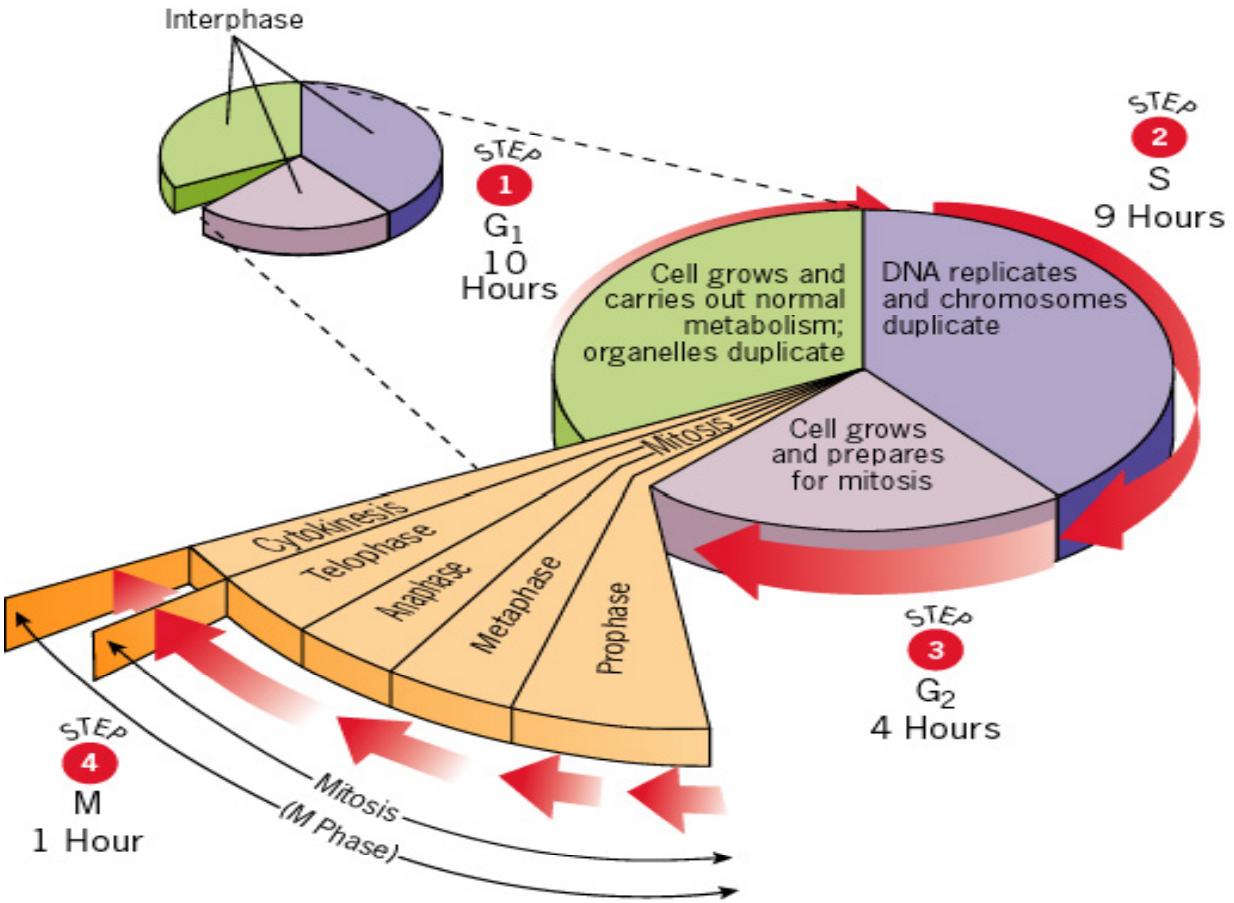
- G1 phase~ growth
- S phase~ synthesis of DNA
- G2 phase~ preparation for cell division

☐ ☐ Mitotic phase

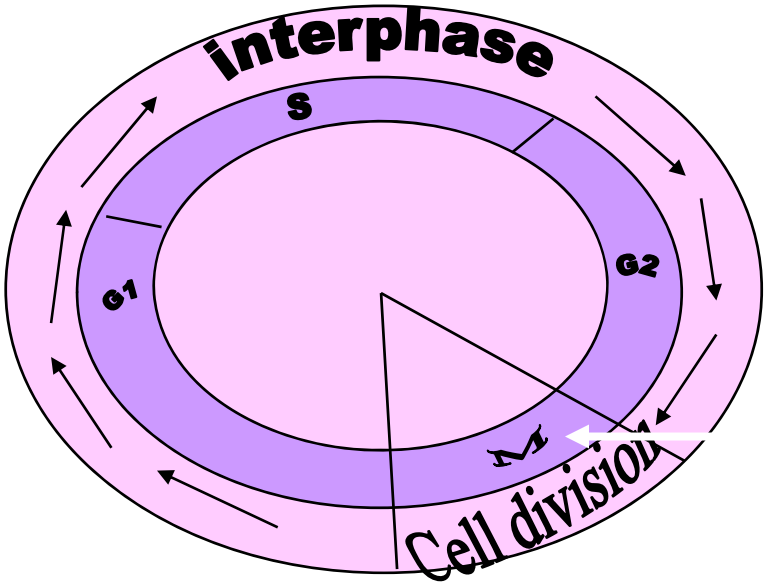
- Mitosis~ nuclear division
- Cytokinesis~ cytoplasm division



The cell cycle.



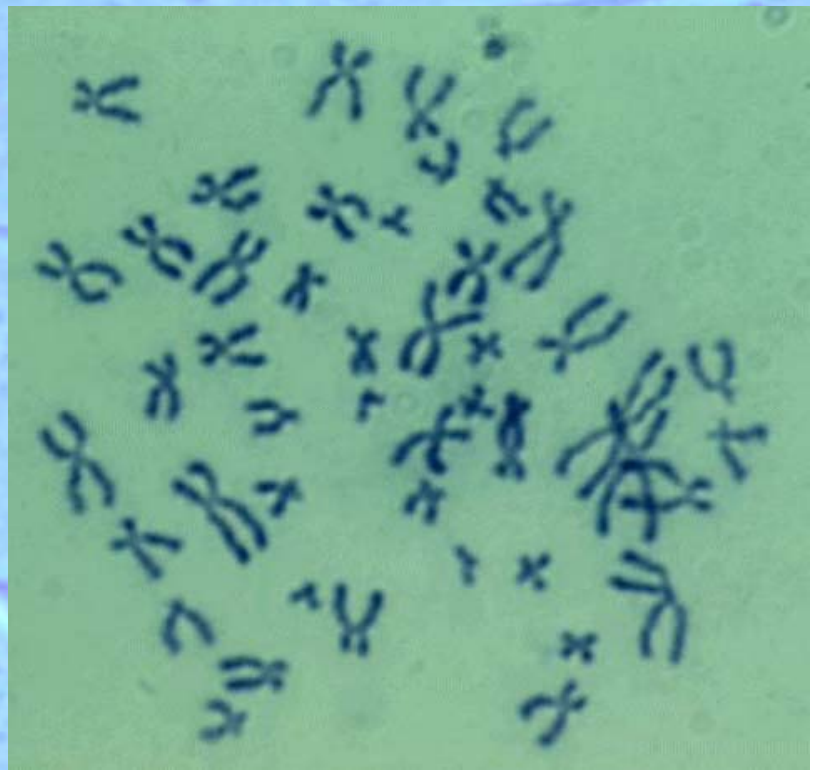
The Stages of the Cell Cycle

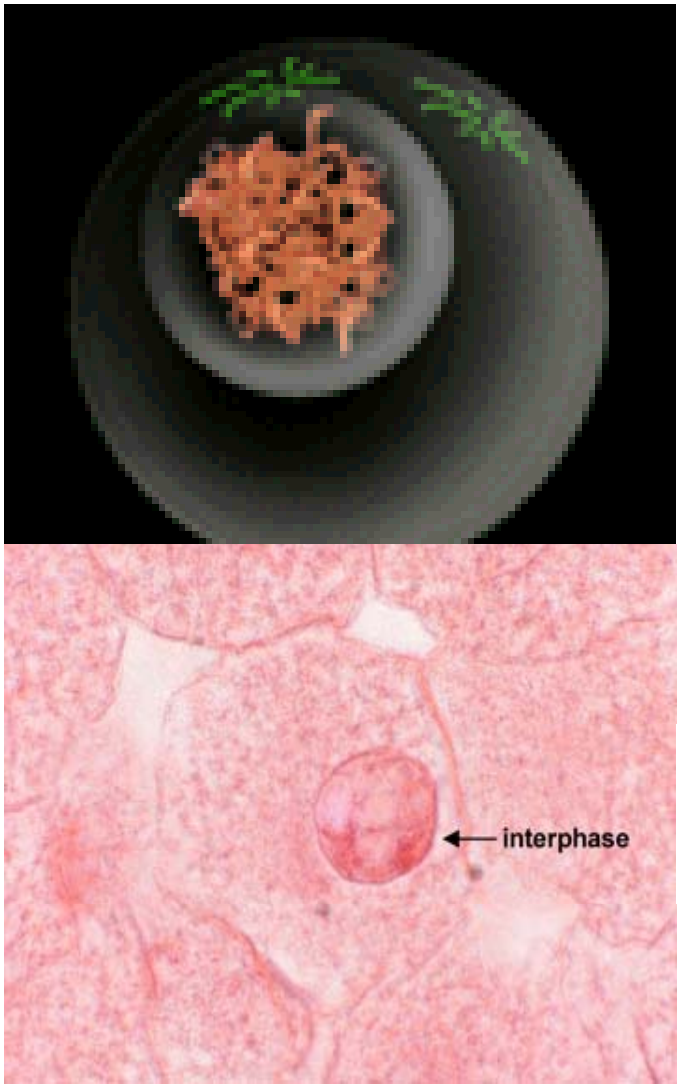


Mitosis

BASIC GENETICS

- Each cell in the human body contains two sets of 23 chromosomes
- Mitosis identically replicates this information
- Each cell therefore has the same genetic material
- Reproductive cells only have one set of chromosomes. These combine to make a new person with different genetic material to both parents





Interphase

The cell is engaged in metabolic activity and performing its prepare for mitosis (the next four phases that lead up to and include nuclear division).

•Chromosomes are not clearly discerned in the nucleus, although a dark spot called the nucleolus may be visible.

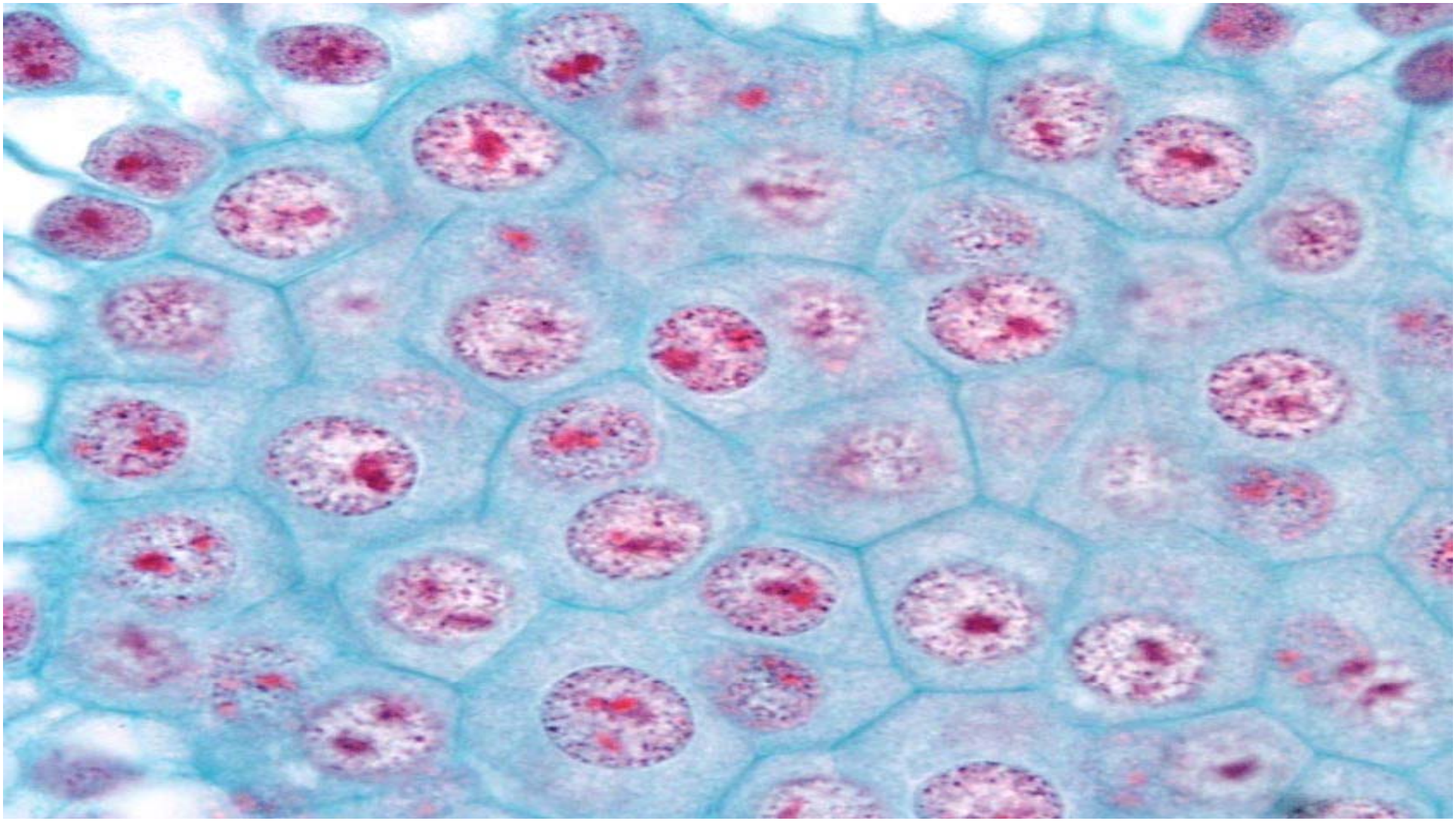
•The cell may contain a pair of centrioles (or microtubule organizing centers in plants) both of which are organizational sites for microtubules.

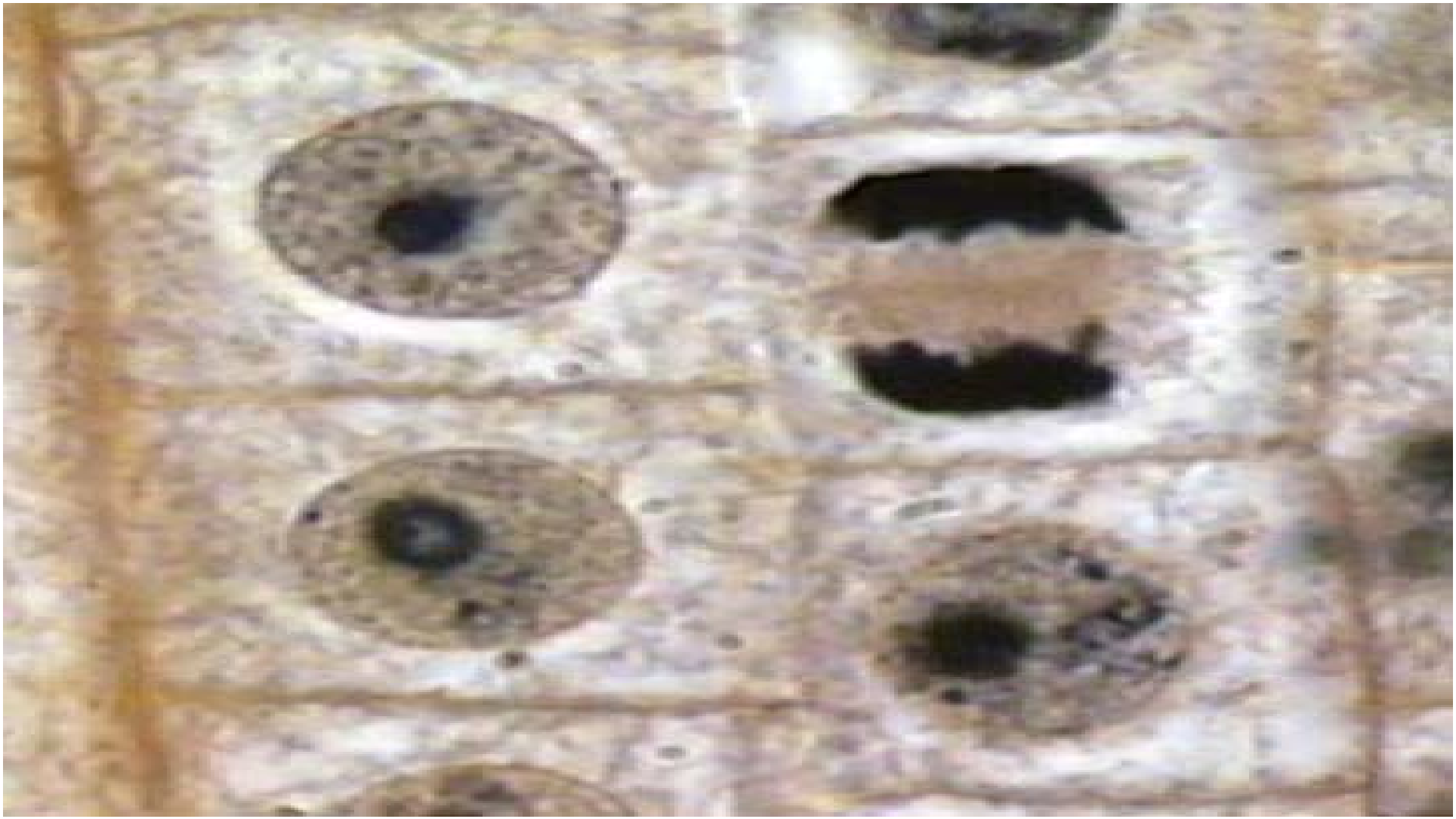
•

Ninety percent or more of the cell cycle is spent in interphase.

•During interphase, cellular organelles double in number, the DNA replicates, and protein synthesis occurs.

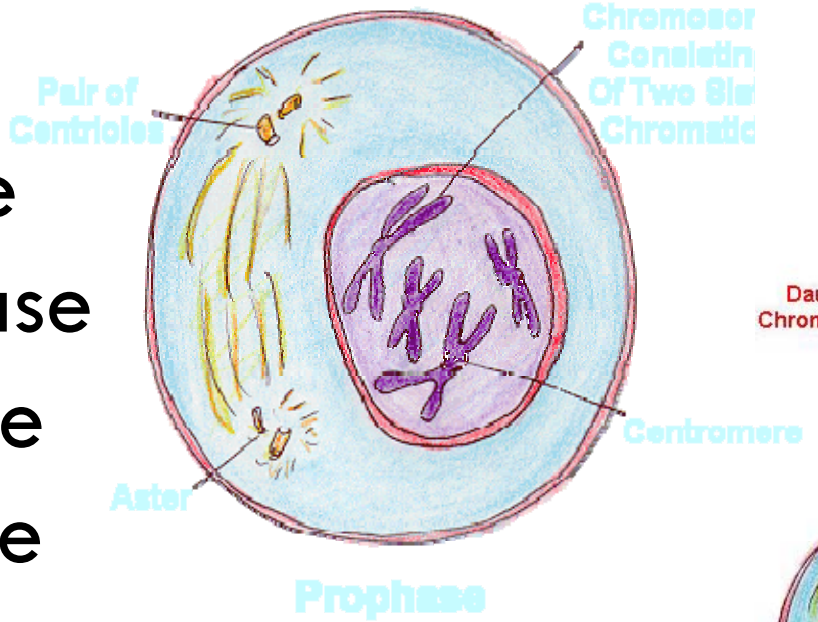
•The chromosomes are not visible and the DNA appears as uncoiled chromatin.

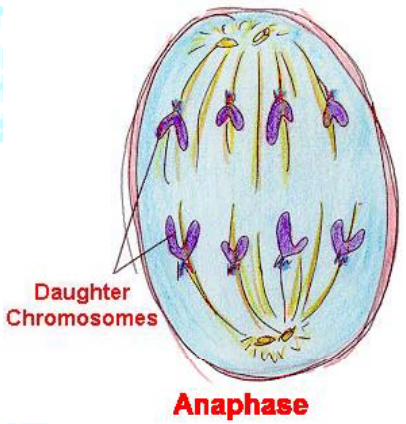


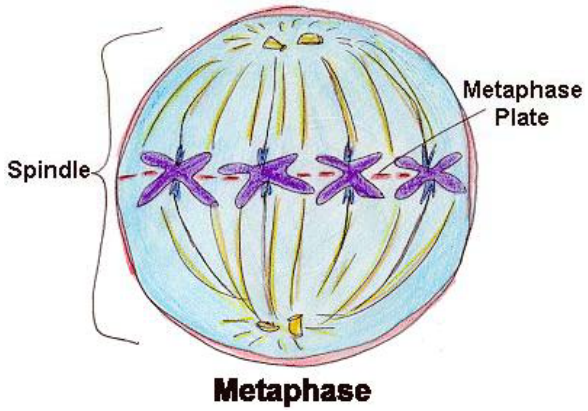


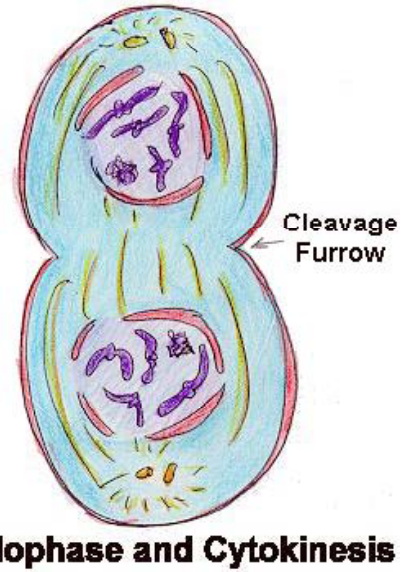
Mitosis

- ☐ ☐ Prophase
- ☐ ☐ Metaphase
- ☐ ☐ Anaphase
- ☐ ☐ Telophase



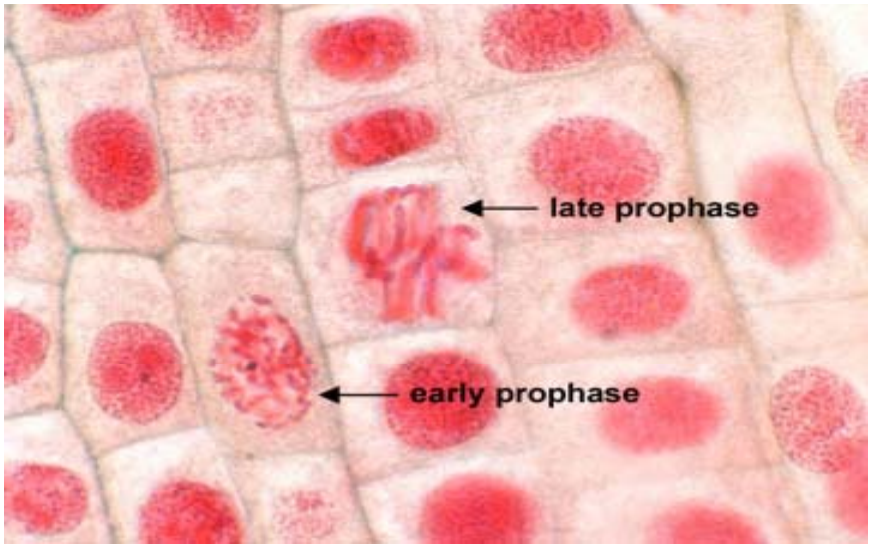


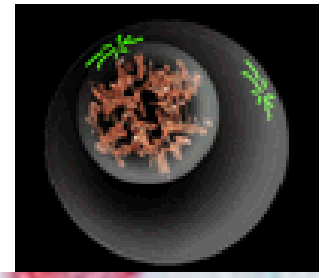


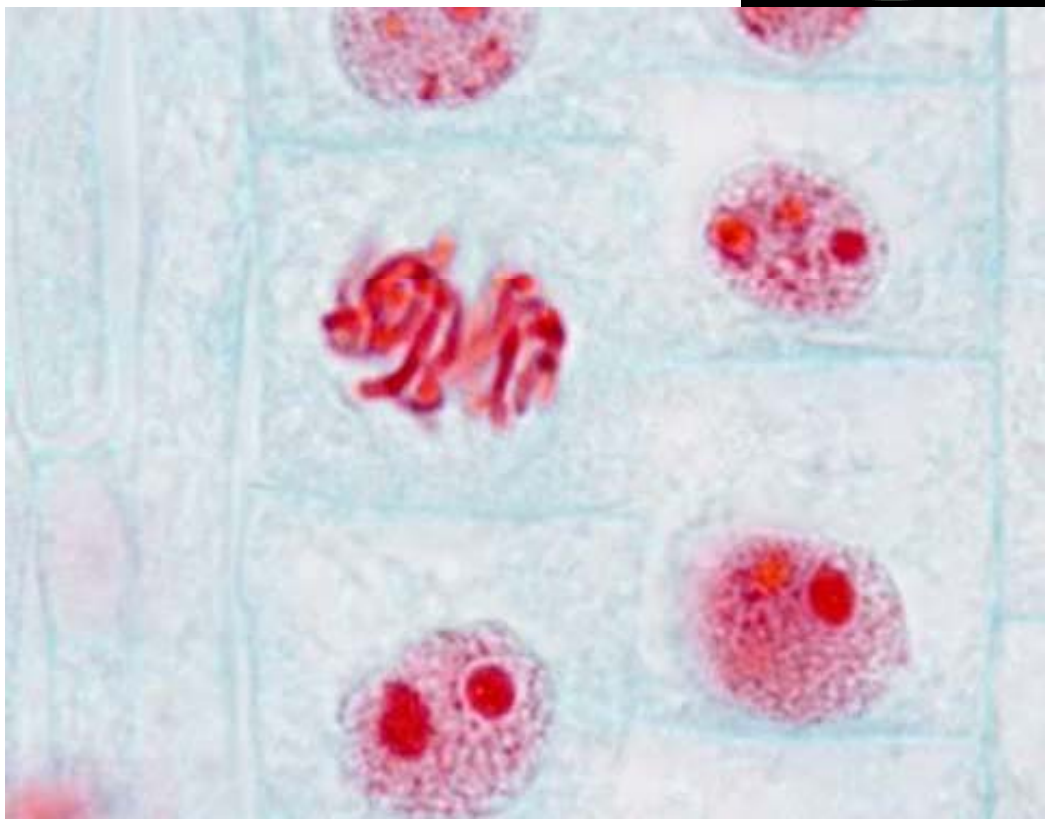


Prophase

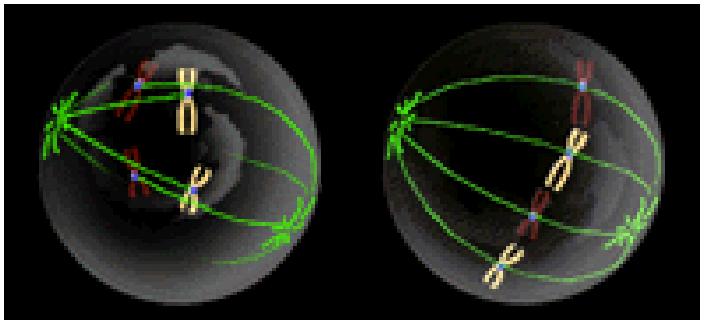
- ☐ ☐ Chromosomes visible
- ☐ ☐ Nucleoli disappear
- ☐ ☐ Sister chromatids
- ☐ ☐ Mitotic spindle forms
- ☐ ☐ Centrosomes move



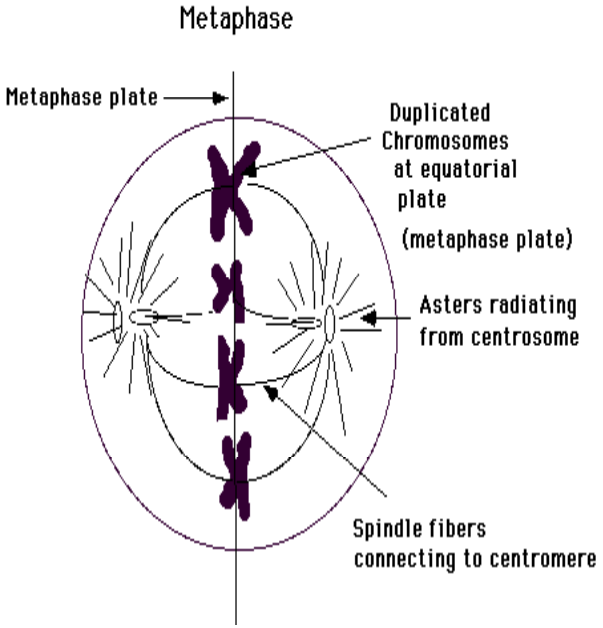


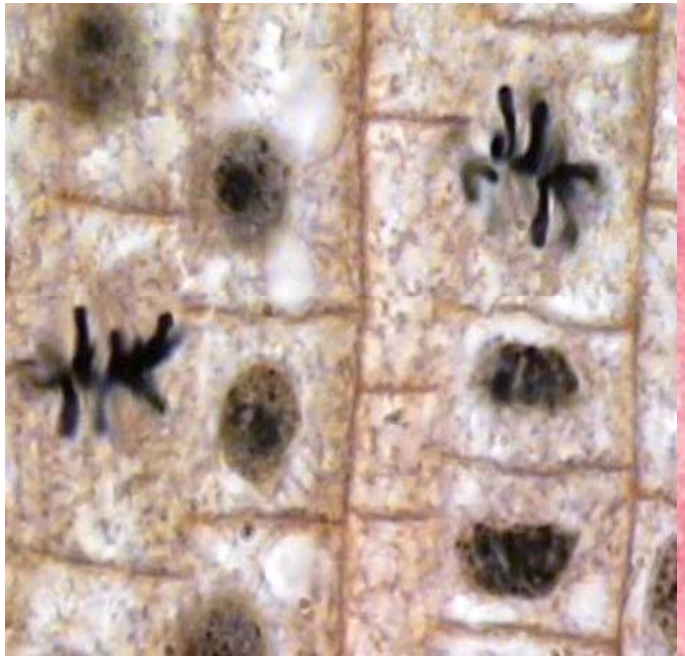


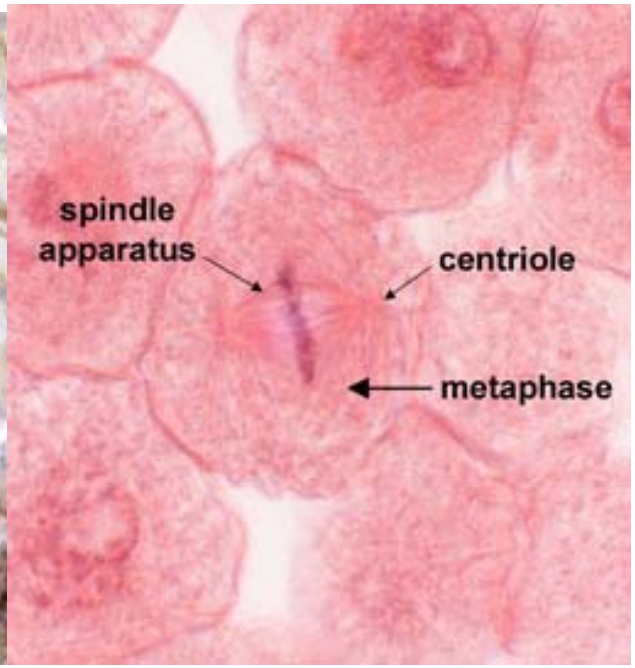
Metaphase



- ☐ ☐ Centrosomes at opposite poles
- ☐ ☐ Centromeres are aligned
- ☐ ☐ Kinetochores of sister chromatids attached to spindle

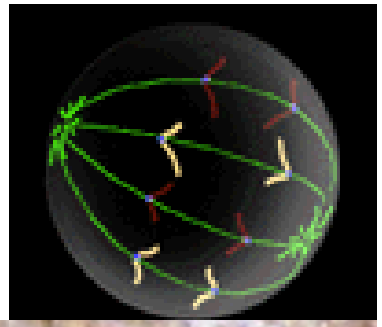


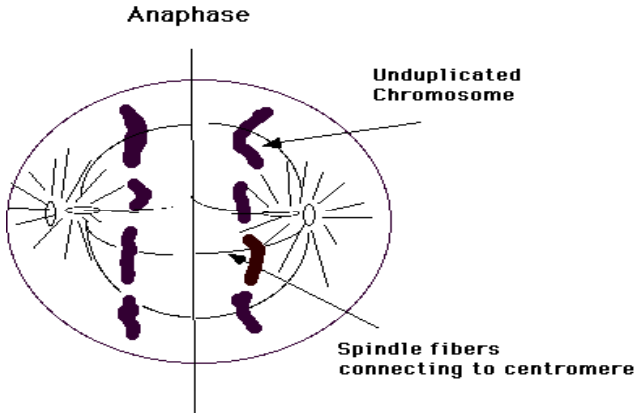


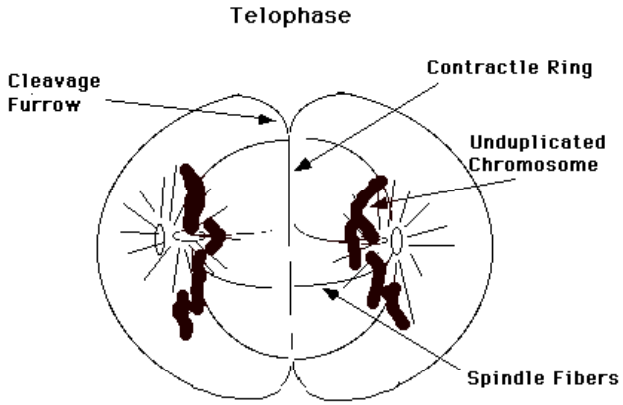


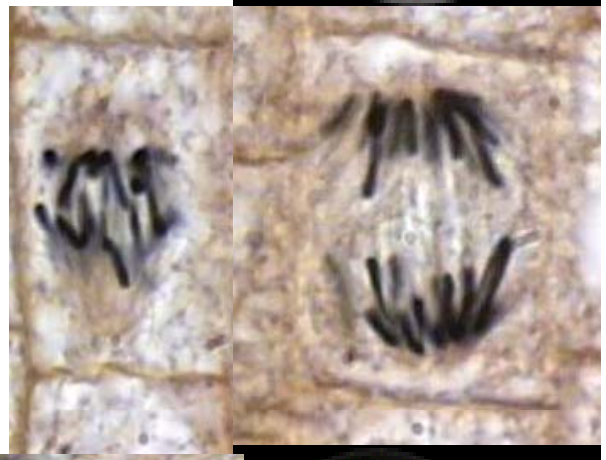
Anaphase

- ☐ ☐ Paired centromeres separate; sister chromatids liberated
- ☐ ☐ Chromosomes move to opposite poles
- ☐ ☐ Each pole now has a complete set of chromosomes



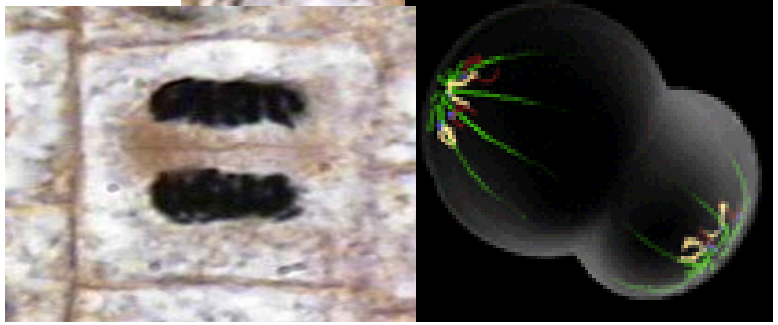






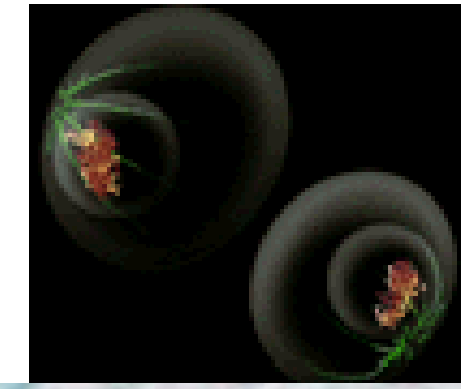
Telophase

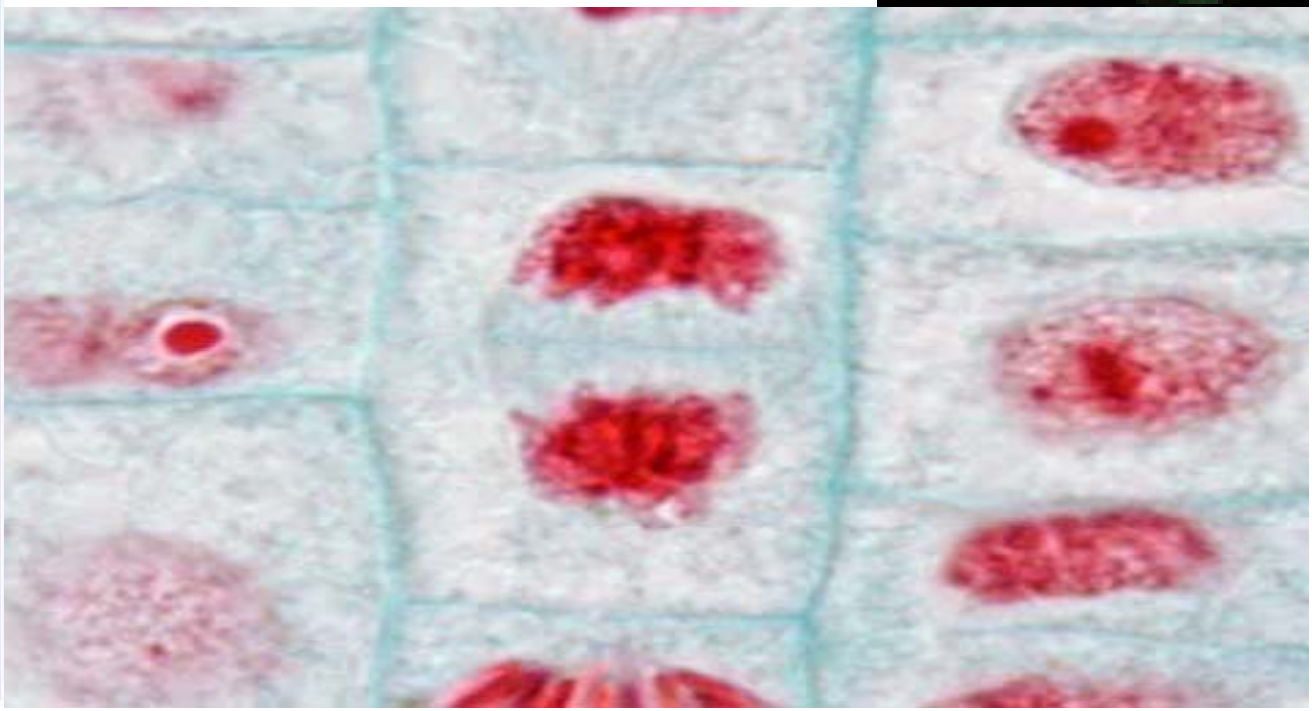
- ☐ ☐ Daughter nuclei form
- ☐ ☐ Nuclear envelopes arise
- ☐ ☐ Chromatin becomes Less coiled
- ☐ ☐ Two new nuclei complete mitosis

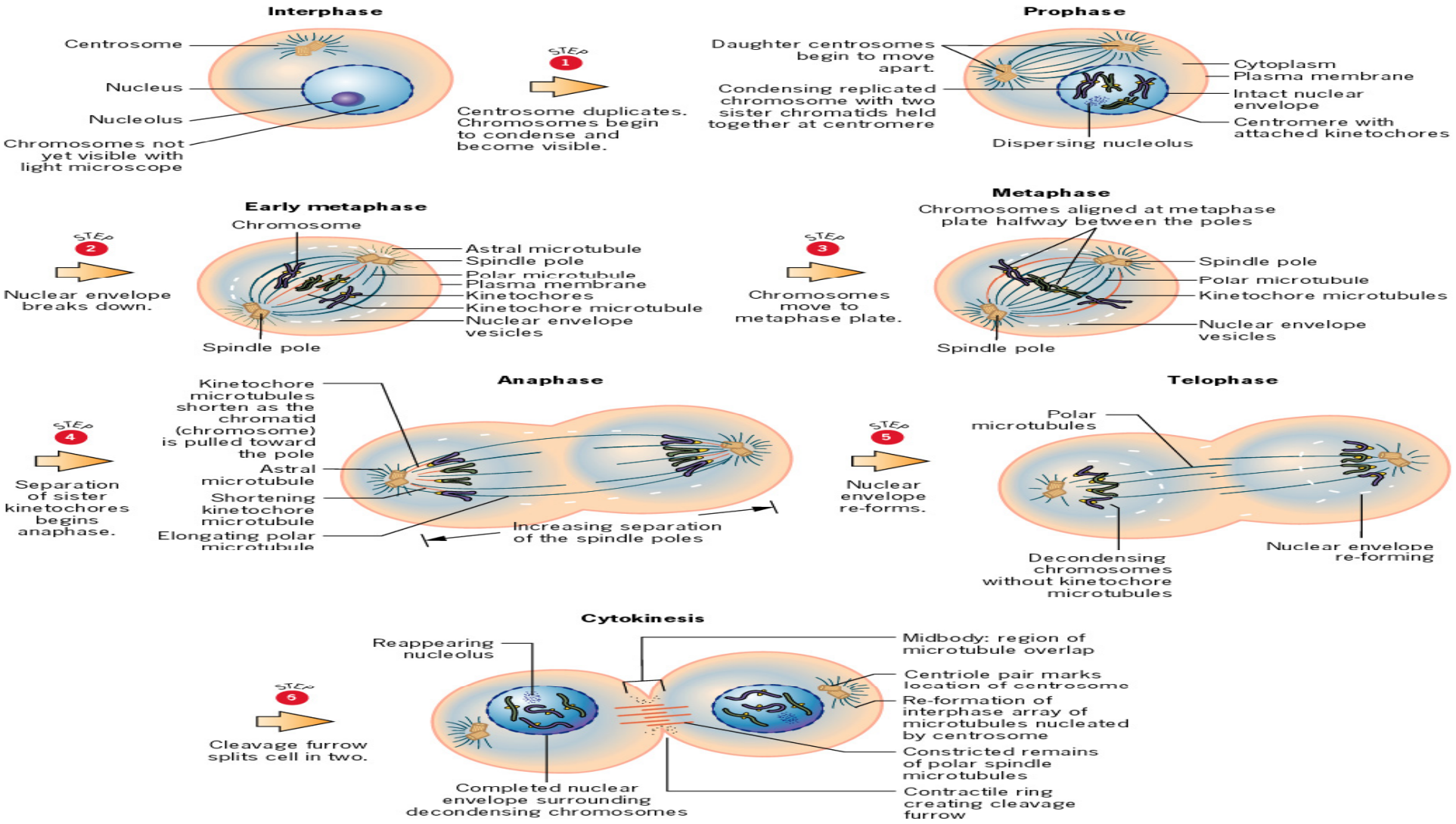


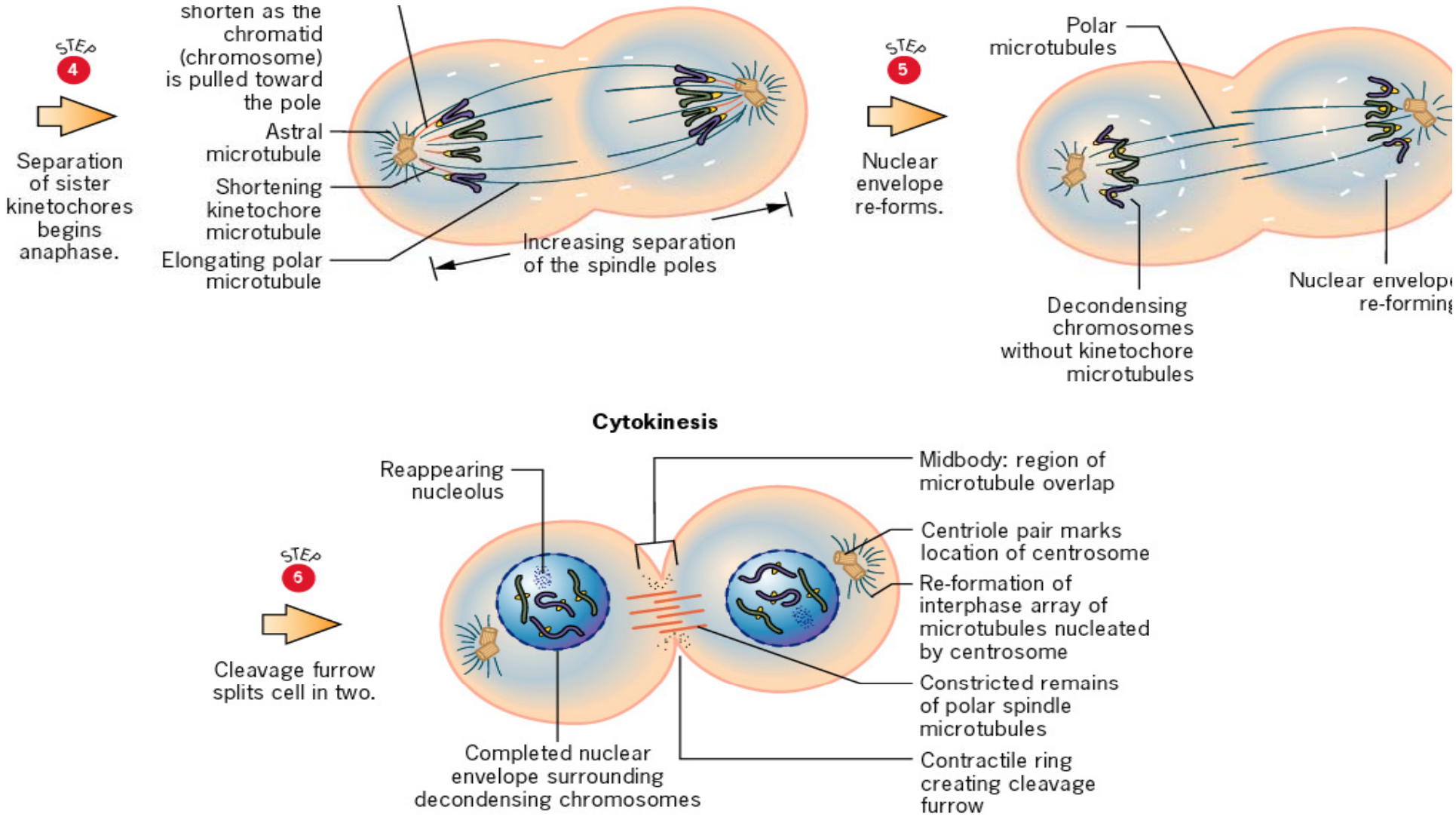
Cytokinesis

- ☐ ☐ Cytoplasmic division
- ☐ ☐ Animals: cleavage furrow






Interphase
Centrosome
Nucleus
Nucleolus
Chromosomes not yet visible with light microscope
STEP 1
Centrosome duplicates. Chromosomes begin to condense and become visible.
Prophase
Daughter centrosomes begin to move apart.
Condensing replicated chromosome with two sister chromatids held together at centromere
Cytoplasm
Plasma membrane
Intact nuclear envelope
Centromere with attached kinetochores
Dispersing nucleolus
STEP 2
Nuclear envelope breaks down.
Early metaphase
Chromosome
Astral microtubule
Spindle pole
Polar microtubule
Plasma membrane
Kinetochores
Kinetochore microtubule
Nuclear envelope vesicles
Spindle pole
STEP 3
Chromosomes move to metaphase plate.
Metaphase
Chromosomes aligned at metaphase plate halfway between the poles
Spindle pole
Polar microtubule
Kinetochore microtubules
Nuclear envelope vesicles
Spindle pole
STEP 4
Separation of sister kinetochores begins anaphase.
Anaphase
Kinetochore microtubules shorten as the chromatid (chromosome) is pulled toward the pole
Astral microtubule
Shortening kinetochore microtubule
Elongating polar microtubule
Increasing separation of the spindle poles
STEP 5
Nuclear envelope re-forms.
Telophase
Polar microtubules
Decondensing chromosomes without kinetochore microtubules
Nuclear envelope re-forming
STEP 6
Cleavage furrow splits cell in two.
Cytokinesis
Reappearing nucleolus
Midbody: region of microtubule overlap
Centriole pair marks location of centrosome
Re-formation of interphase array of microtubules nucleated by centrosome
Constricted remains of polar spindle microtubules
Contractile ring creating cleavage furrow
Completed nuclear envelope surrounding decondensing chromosomes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Astral microtubule
Shortening kinetochore microtubule
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Decondensing chromosomes without kinetochore microtubules
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Cleavage furrow splits cell in two.
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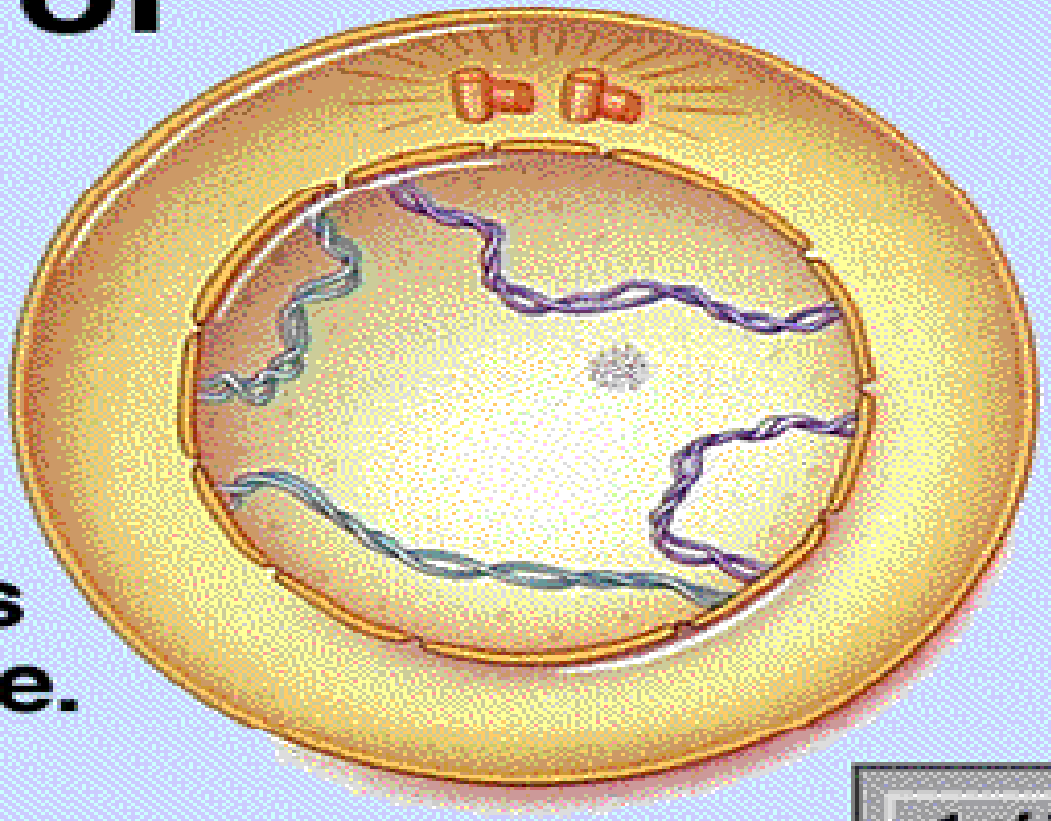
Midbody: region of microtubule overlap
Centriole pair marks location of centrosome
Re-formation of interphase array of microtubules nucleated by centrosome
Constricted remains of polar spindle microtubules
Contractile ring creating cleavage furrow
Completed nuclear envelope surrounding decondensing chromosomes

Stages of Mitosis

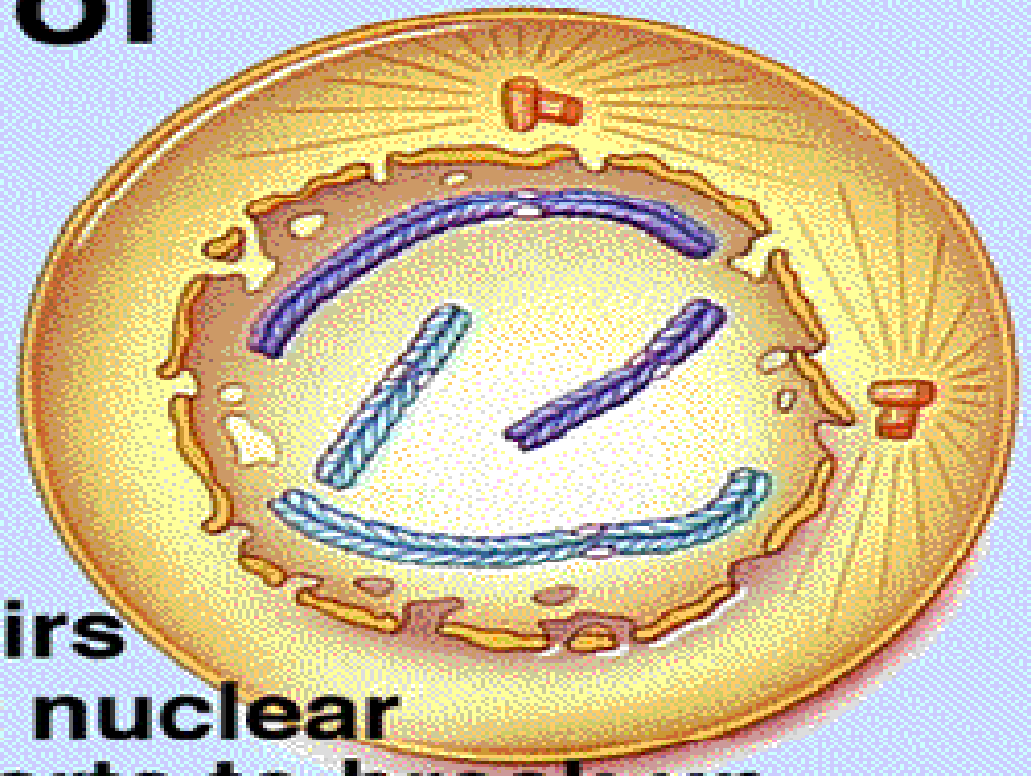
Early Prophase

DNA begins to condense.



Stages of Mitosis

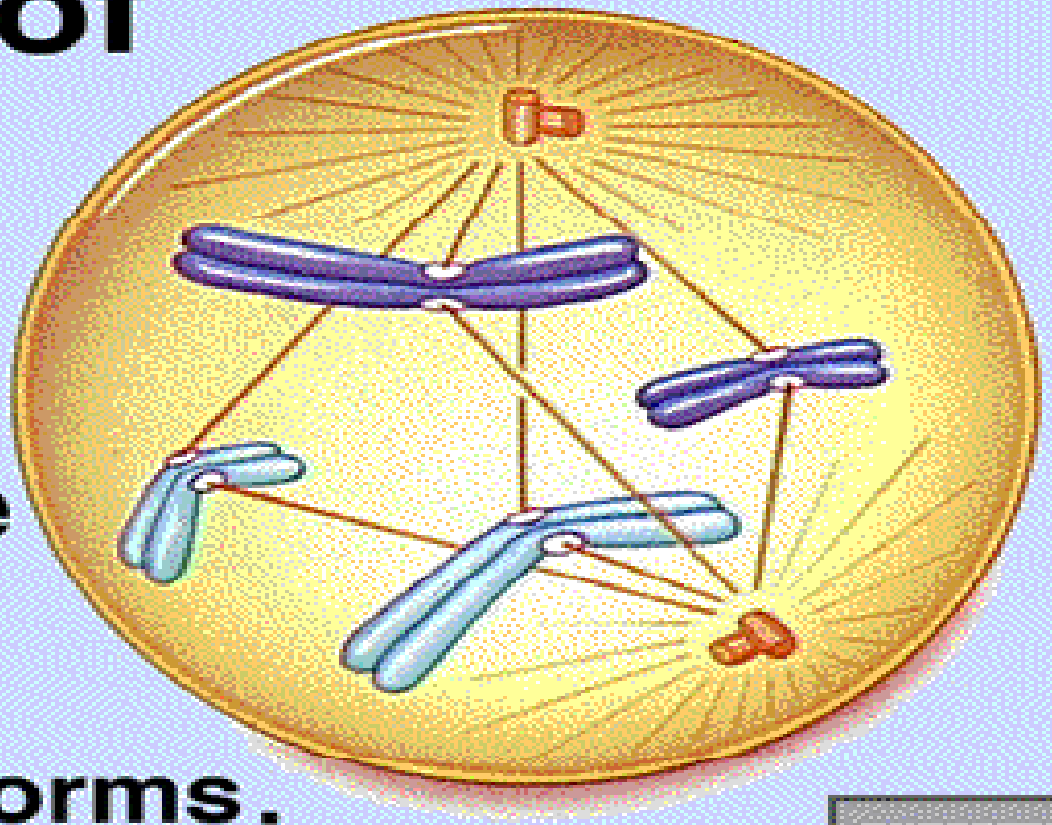
Late Prophase



Centriole pairs move apart; nuclear envelope starts to break up.

Stages of Mitosis

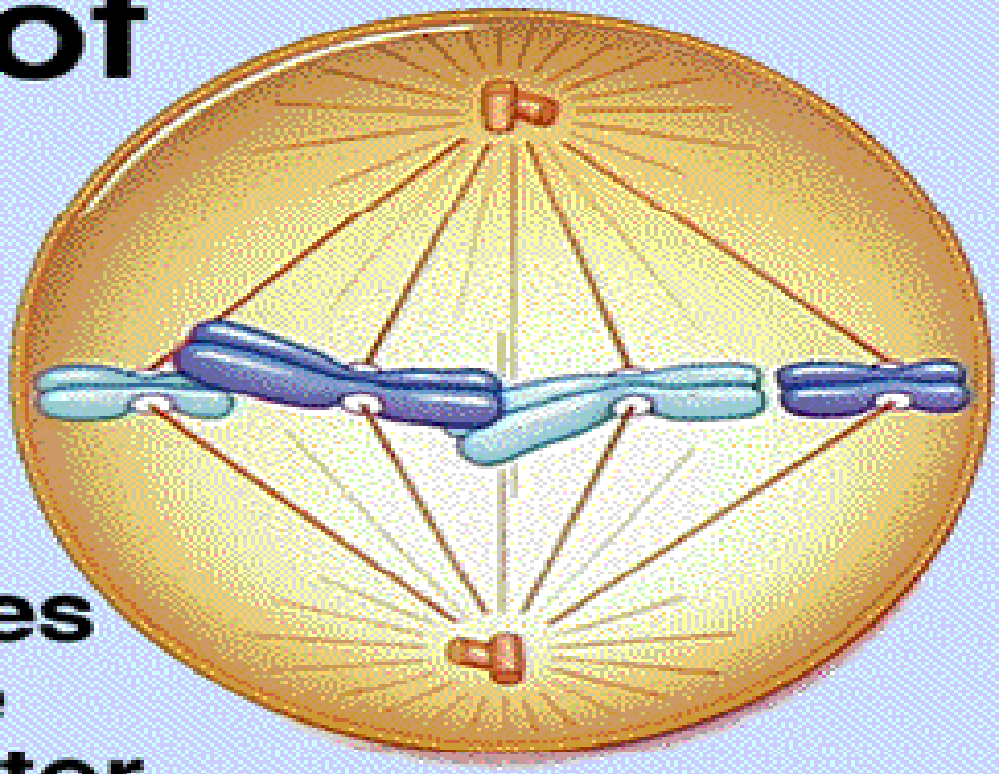
Transition to Metaphase



Spindle apparatus forms.

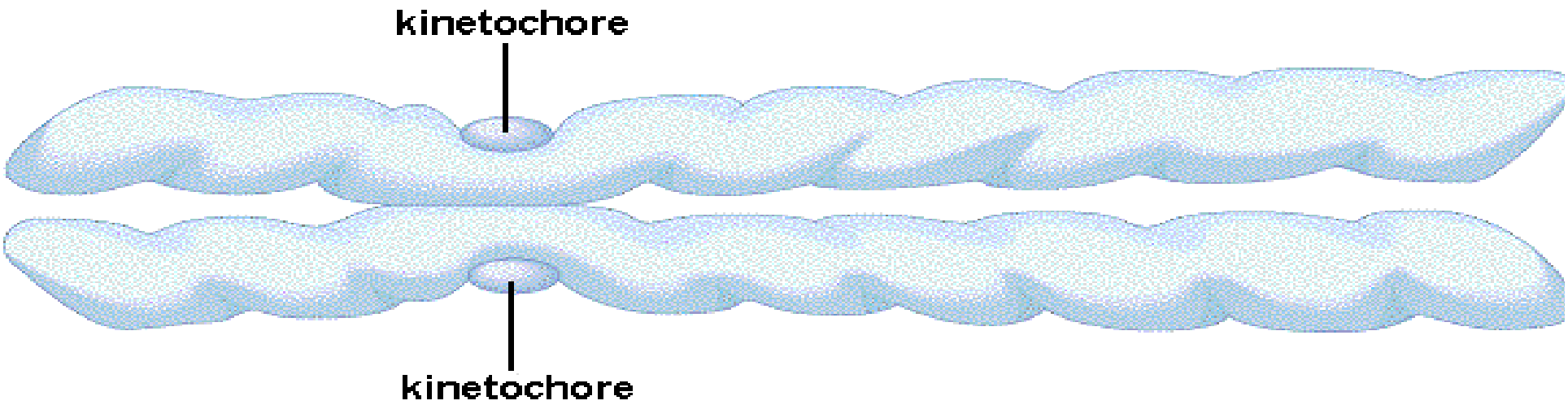
Stages of Mitosis

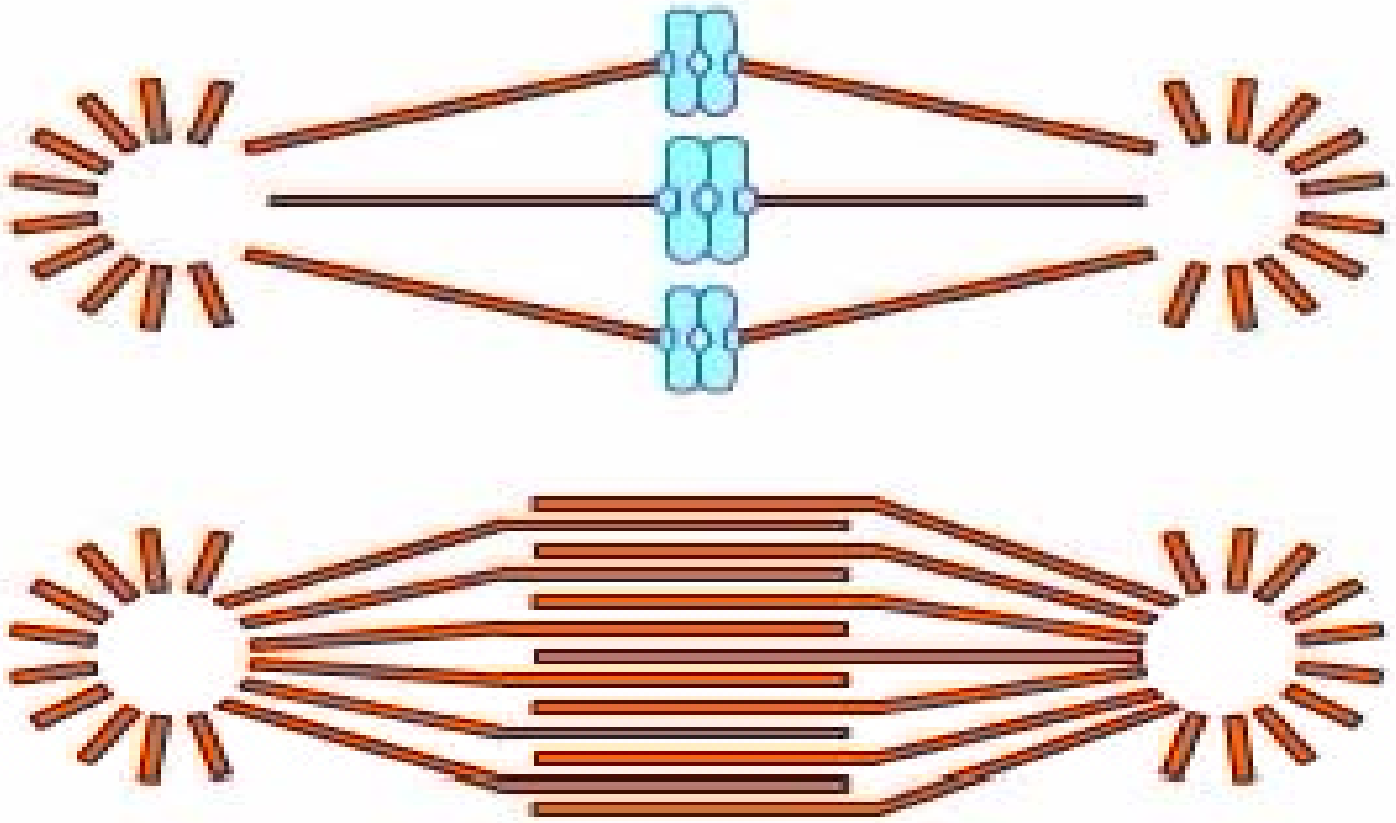
Metaphase



Chromosomes line up at the spindle equator.

Kinetochore (centromere)

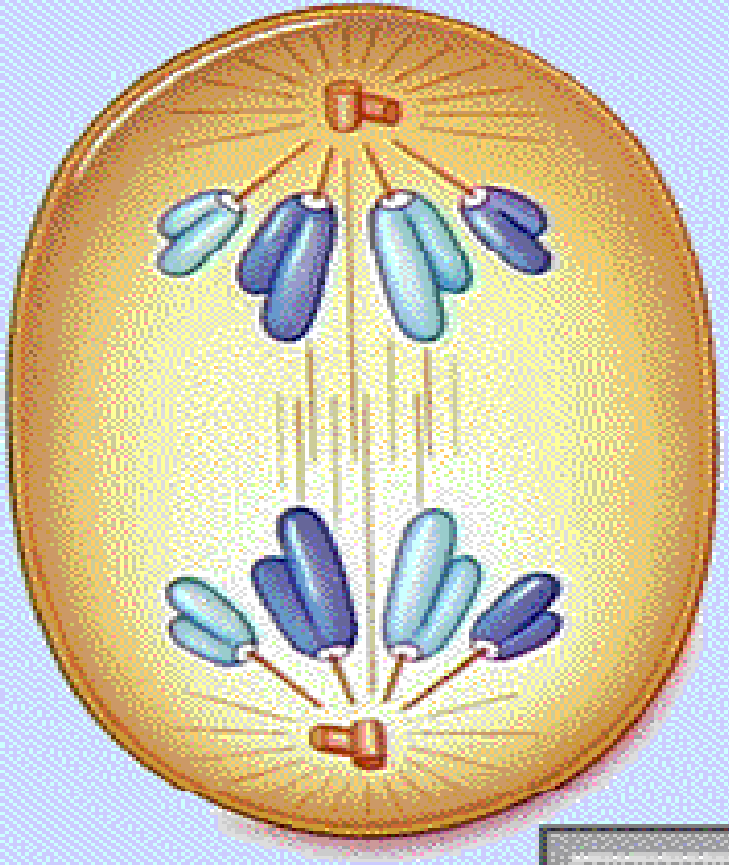


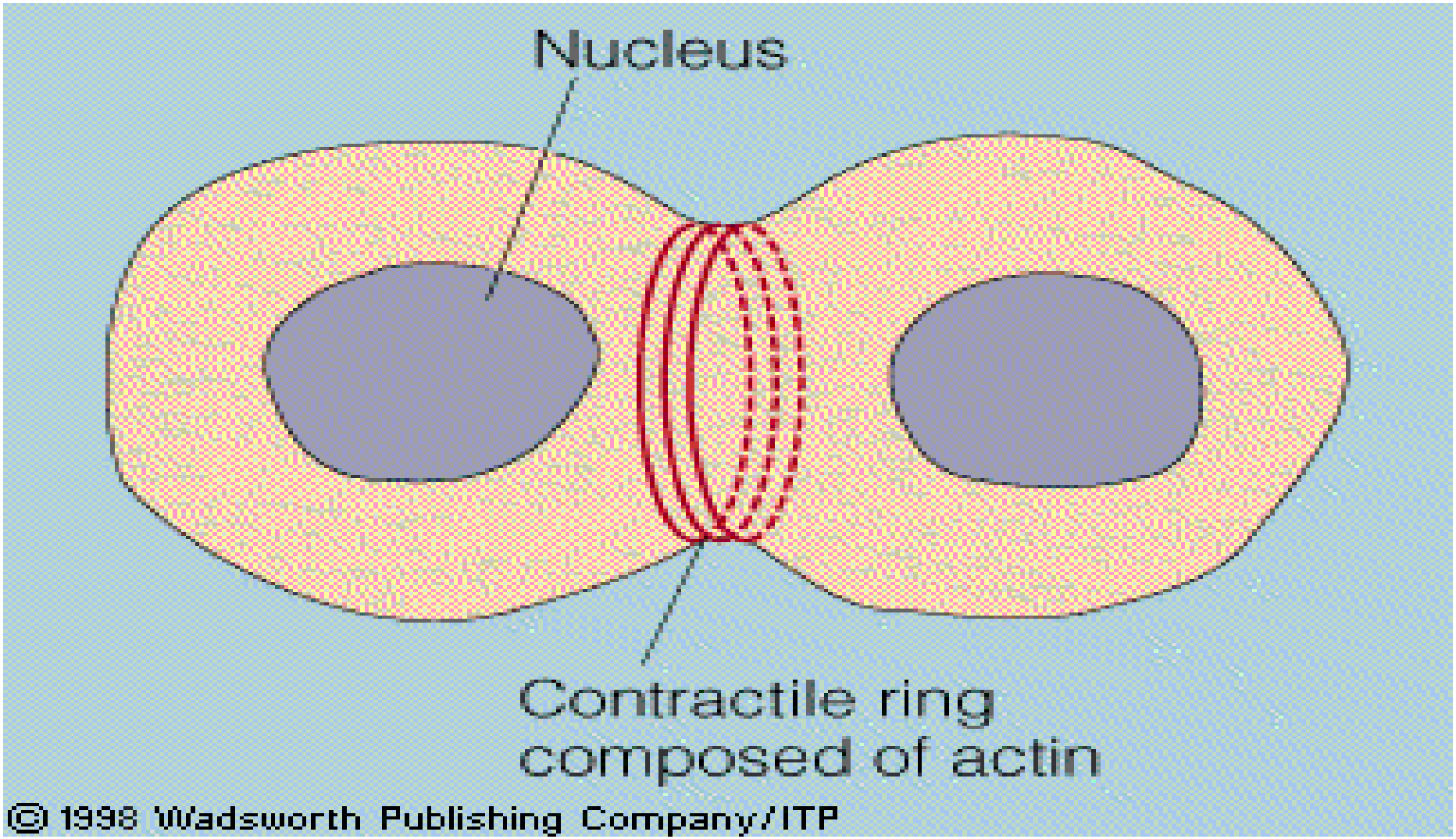


Stages of Mitosis

Anaphase

Sister chromatids move apart.

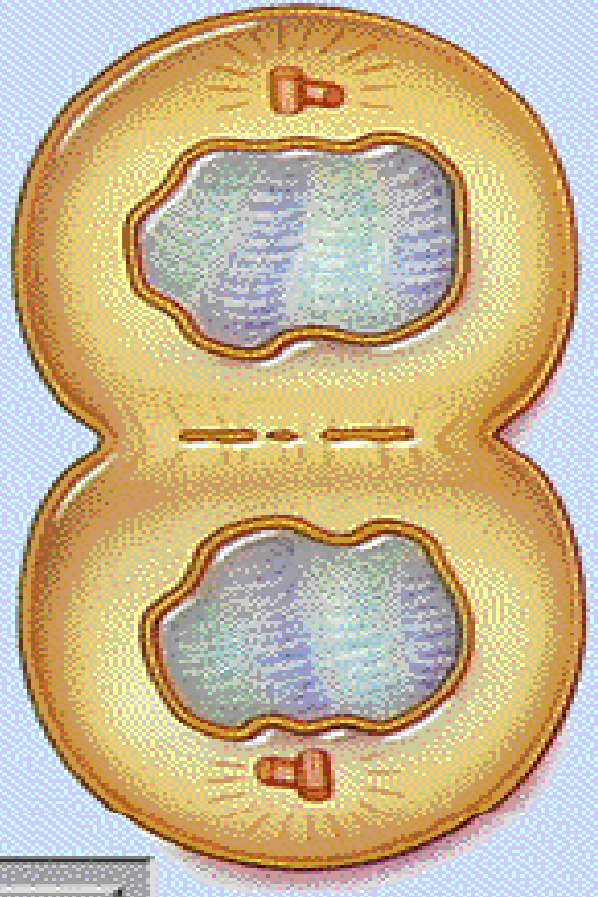



Nucleus
Contractile ring
composed of actin
© 1998 Wadsworth Publishing Company/ITP

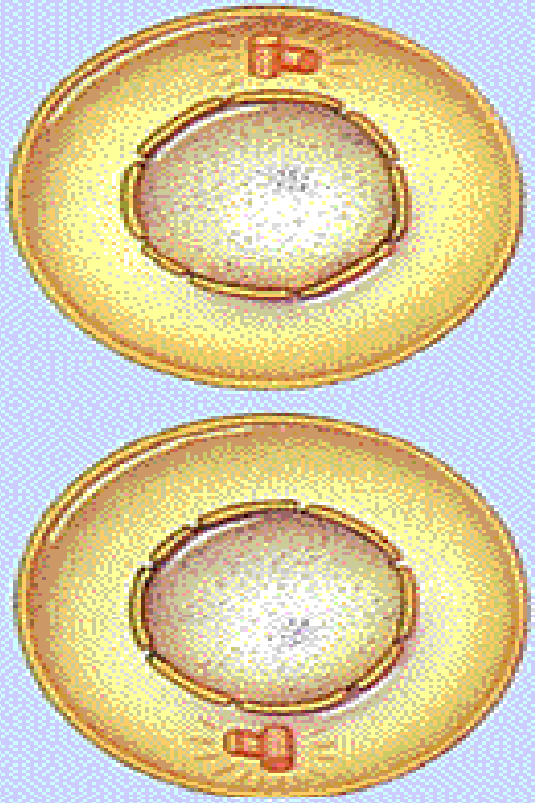
Stages of Mitosis

Telophase

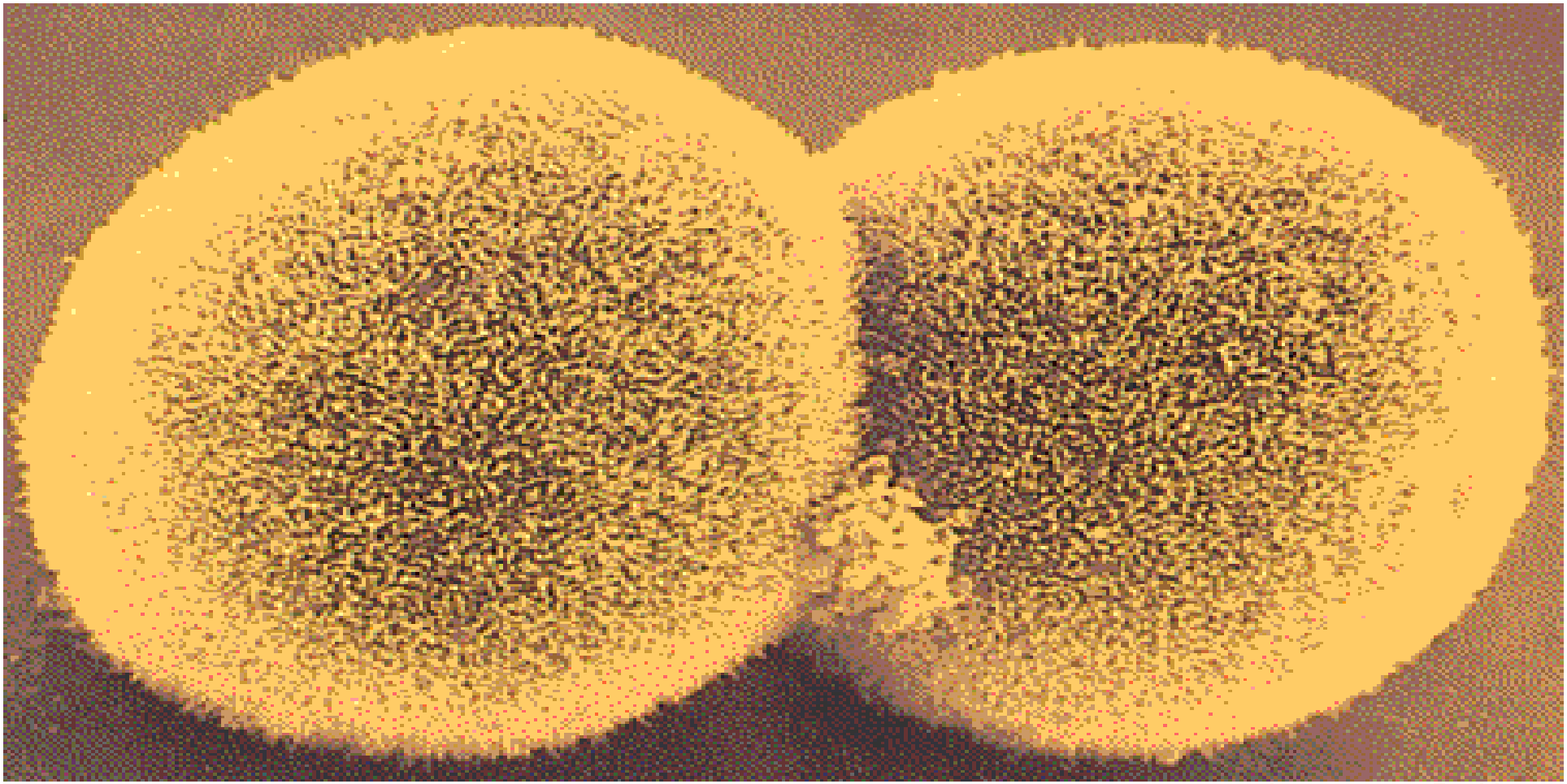
Cytoplasmic division occurs.



Interphase



After mitosis, two diploid daughter cells have formed.

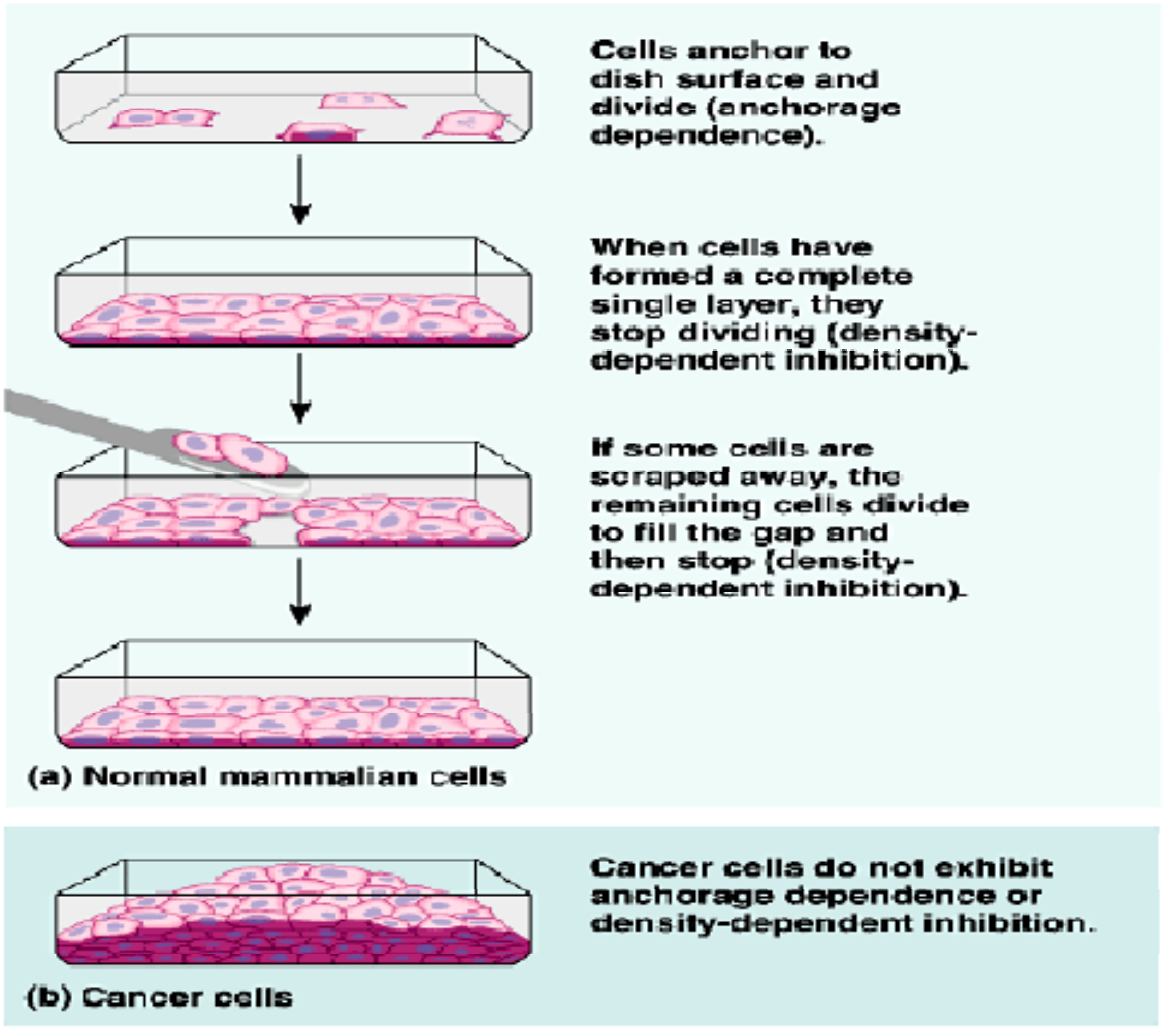


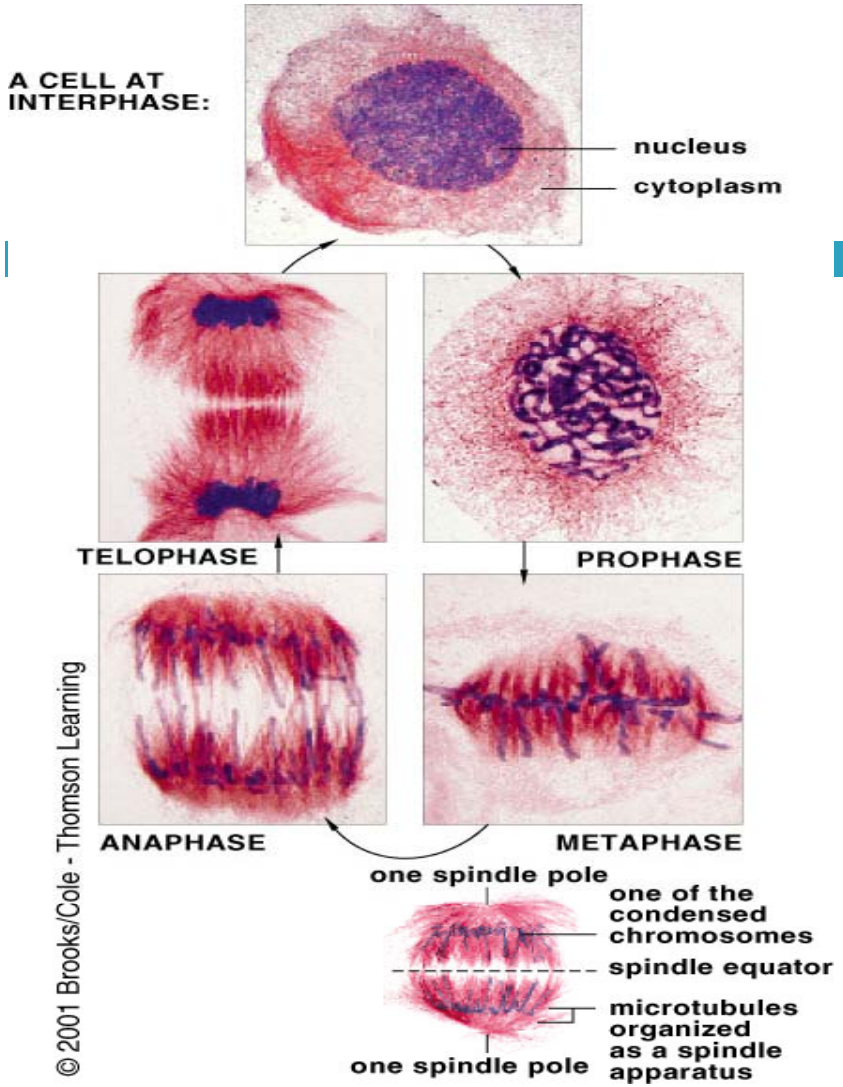
Cell Cycle regulation

☐ ☐ Growth factors

☐ ☐ Density-dependent inhibition

☐ ☐ Anchorage dependence



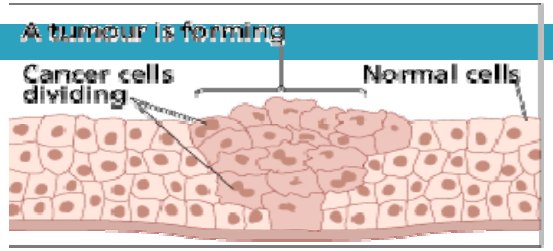


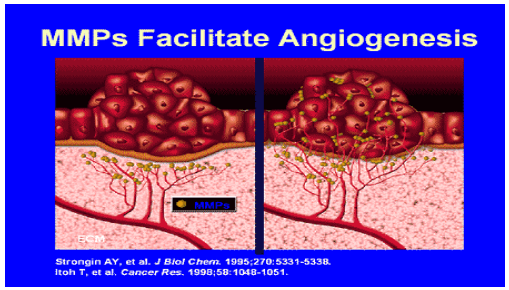
Importance???

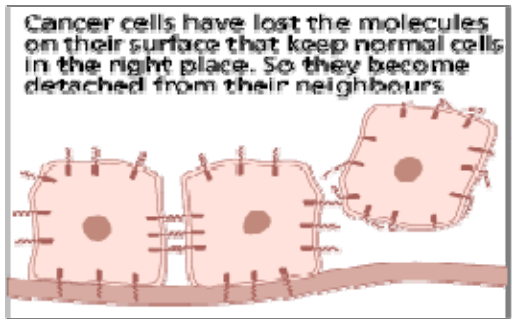
- Growth
- Replacement
- Cancer
- Regeneration of…

Cancer Progression

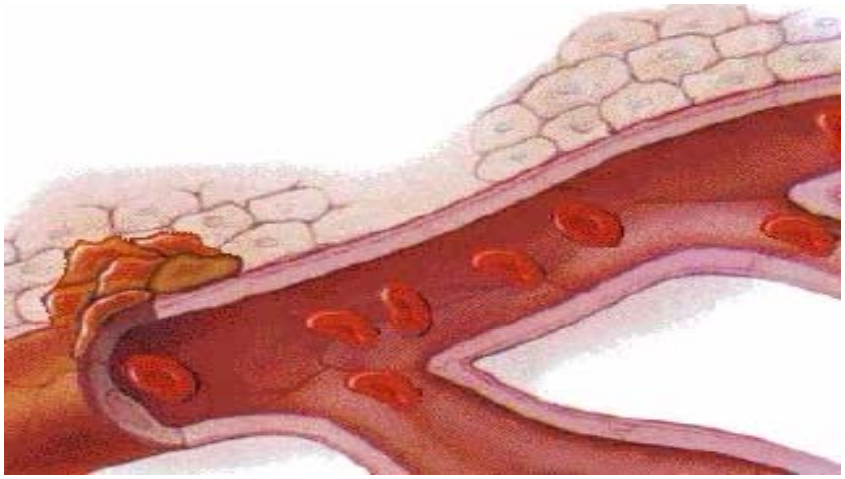
- There are many different forms of cancer, affecting different cell types and working in different ways. All start out with mutations in specific genes called "oncogenes". The normal, unmutated versions of the oncogenes provide the control mechanisms for the cell. The mutations are caused by radiation, certain chemicals (carcinogens), and various random events during DNA replication.
- Once a single cell starts growing uncontrollably, it forms a tumor, a small mass of cells. No further progress can occur unless the cancerous mass gets its own blood supply. "Angiogenesis" is the process of developing a system of small arteries and veins to supply the tumor. Most tumors don't reach this stage.
- A tumor with a blood supply will grow into a large mass. Eventually some of the cancer cells will break loose and move through the blood supply to other parts of the body, where they start to multiply. This process is called metastasis. It occurs because the tumor cells lose the proteins on their surface that hold them to other cells.







Cancer?



- Unregulated mitosis
- Benign
- Malignant/ metastasis
- How does it begin?

Normal cycle controls

- Internal signals
- External signals:
  growth factors
  fibronectin,etc
  carcinogens
- Apoptosis
- Immune functions
- And…

Cell immortilization!!

- Hayflick limit??
- Hela cells
- Contact inhibition
- Increased telomerase activity
- = immortalization!

Immortalization???

- If you replaced…
- Why not??…look at your shoestrings?
- Telomerase & telomeres & …?
- Recently…
- Implications???

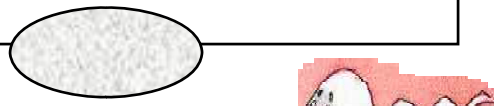
MEIOSIS

When gamete (sperm or egg) cells reproduce themselves the process is called MEIOSIS.

During meiosis, a single diploid cell divides and produces FOUR haploid reproductive cells.

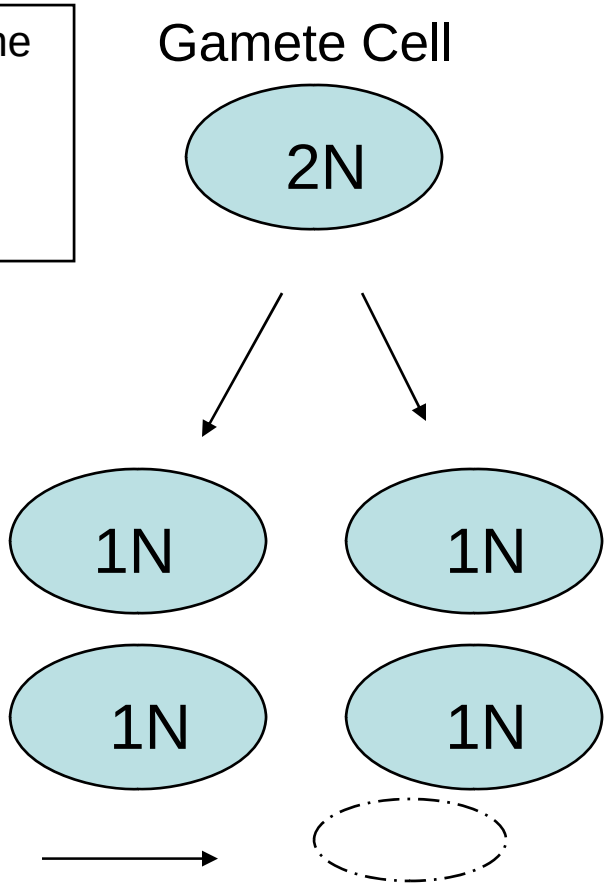
In Meiosis there is one chromosome duplication followed by two cellular divisions (into four cells) so Meiosis is broken down into Meiosis I and Meiosis II.

Upon <u>fertilization</u>, a 1N sperm meets a 1N egg and a zygote (2N) is formed.



1 N egg

1 N sperm



Meiosis – key differences from mitosis

- Meiosis **reduces the number of chromosomes by half**.
- **Daughter cells differ from parent**, and each other.
- Meiosis involves **two divisions**, Mitosis only one.
- Meiosis I involves:
  - **Synapsis** – homologous chromosomes pair up. **Chiasmata** form (*crossing over* of non-sister chromatids).
  - In Metaphase I, **homologous pairs line up** at metaphase plate.
  - In Anaphase I, *sister chromatids do NOT separate*.
  - Overall, **separation of homologous pairs of chromosomes,** rather than sister chromatids of individual chromosome.

Mitosis vs. Meiosis

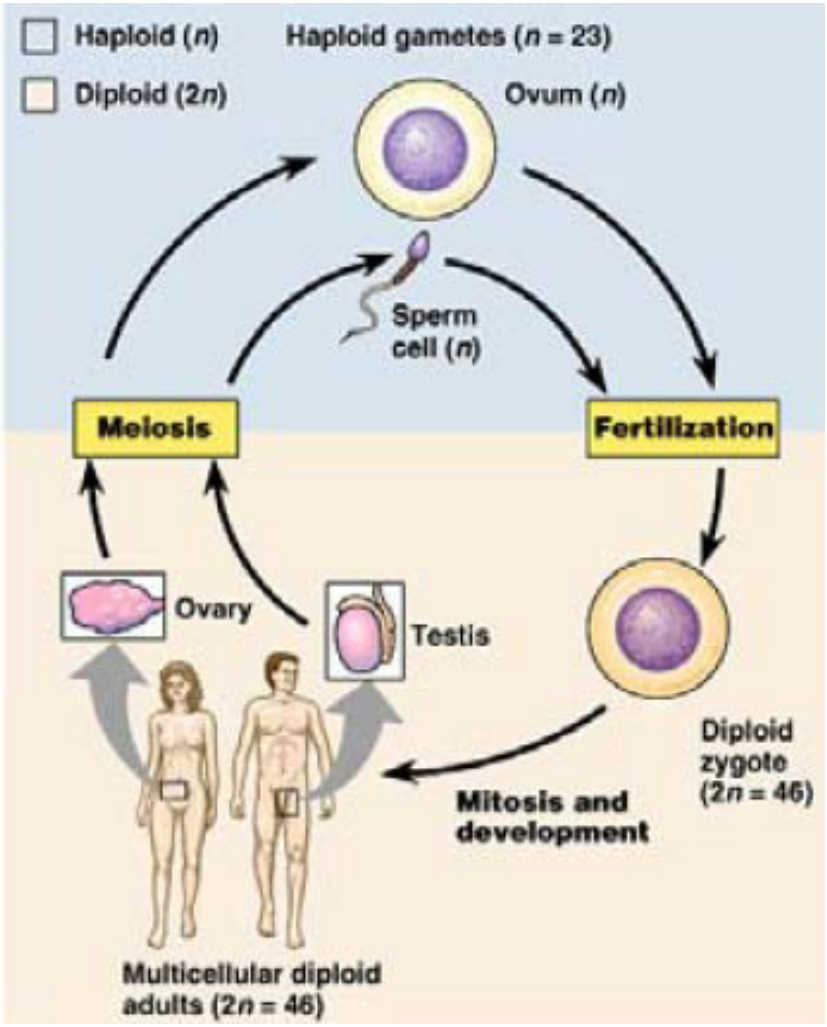
asexual reproduction

- one parent; all genes come from one parent
- offspring are identical to parent
- division of somatic cells

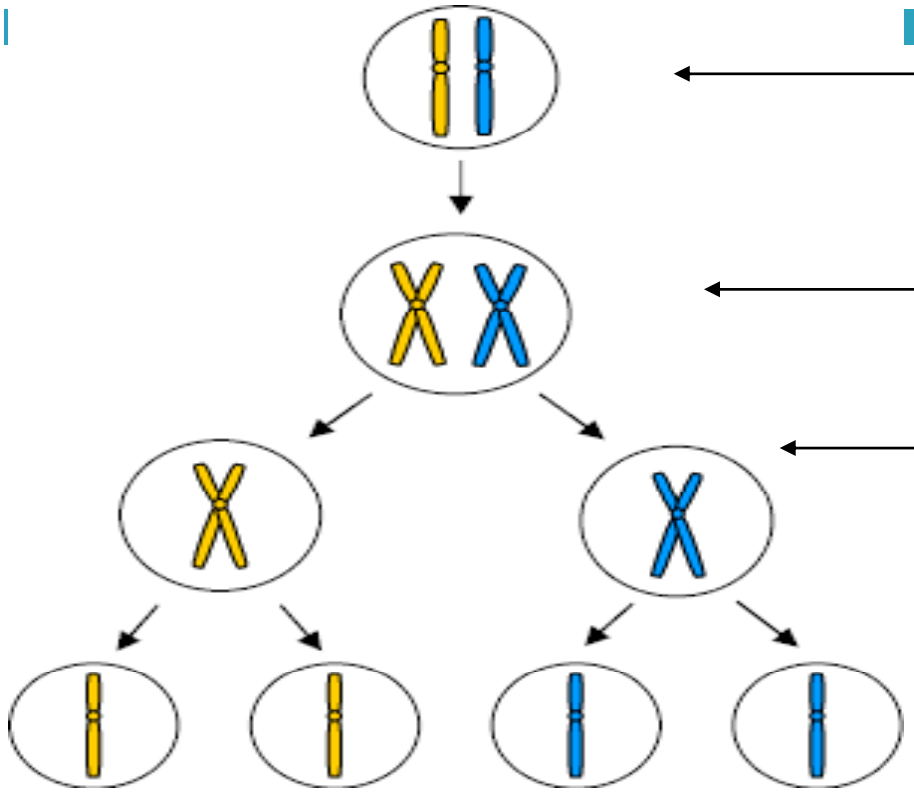
sexual reproduction

- two parents; each donates half of total genes
- offspring is unique
- division of germ cells

Sexual Life Cycles of Animals



Meiosis



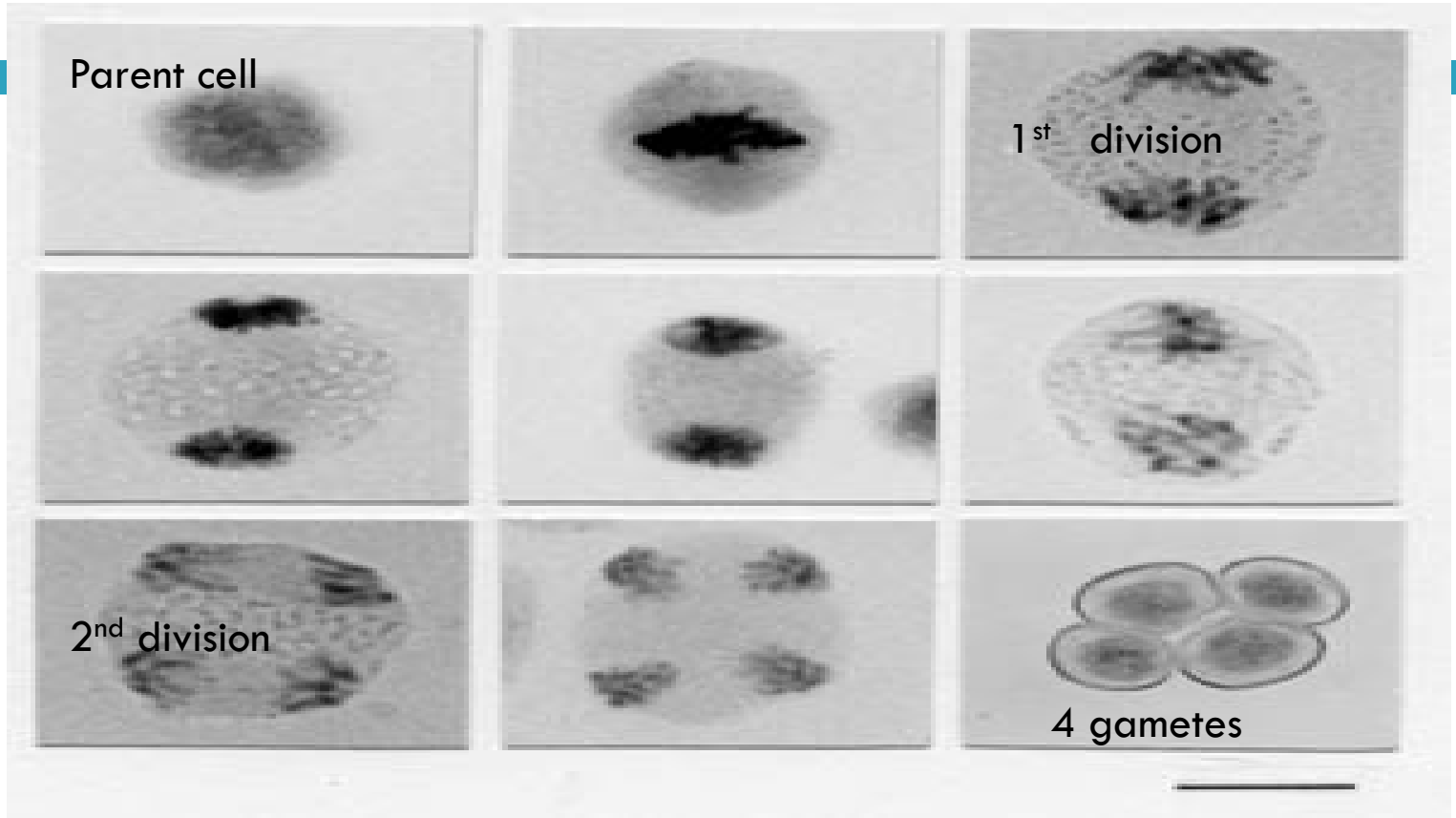
Parent cell – chromosome pair

Chromosomes copied

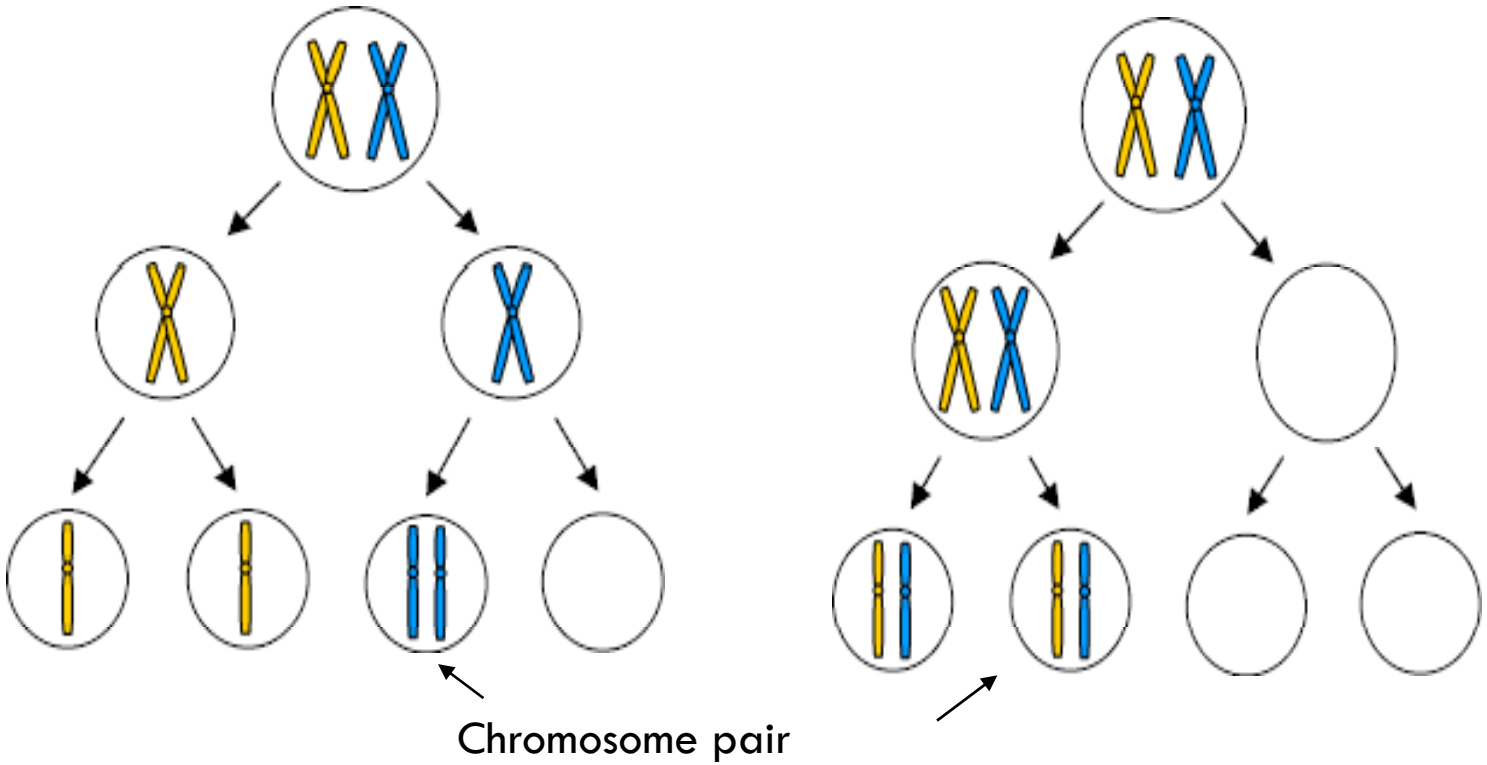
1st division - pairs split

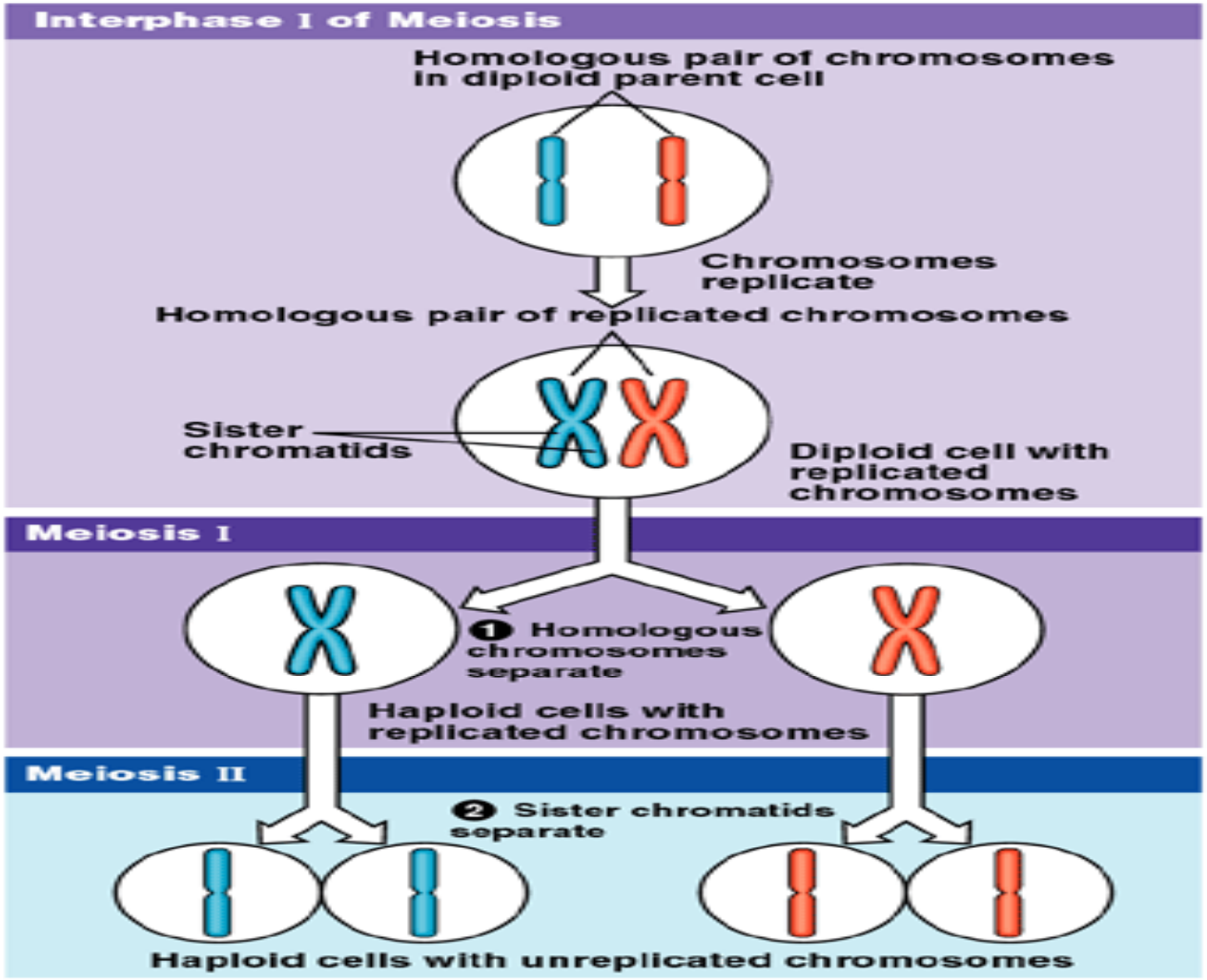
2nd division – produces 4 gamete cells with ½ the original no. of chromosomes

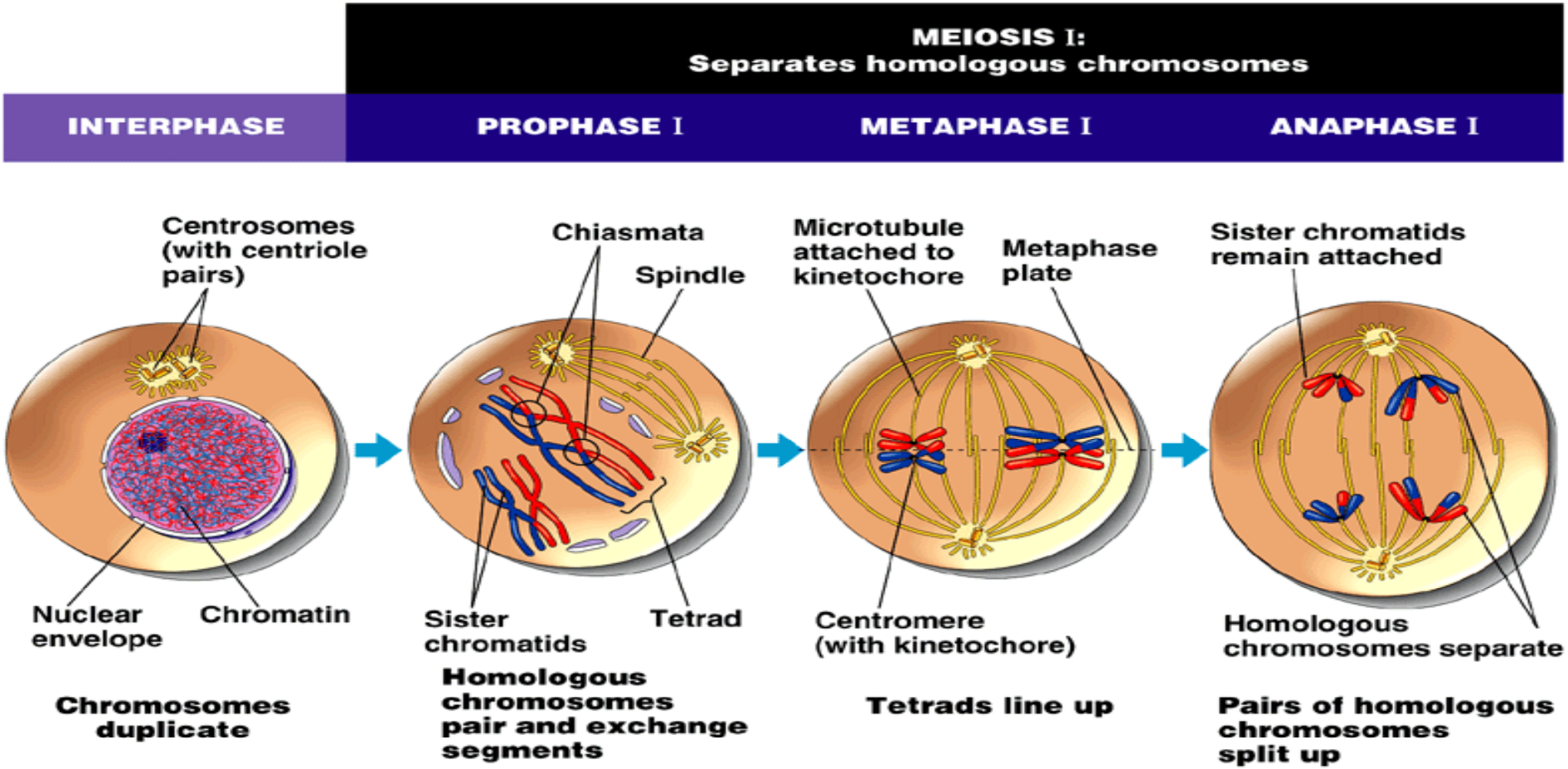
Meiosis – mouse testes

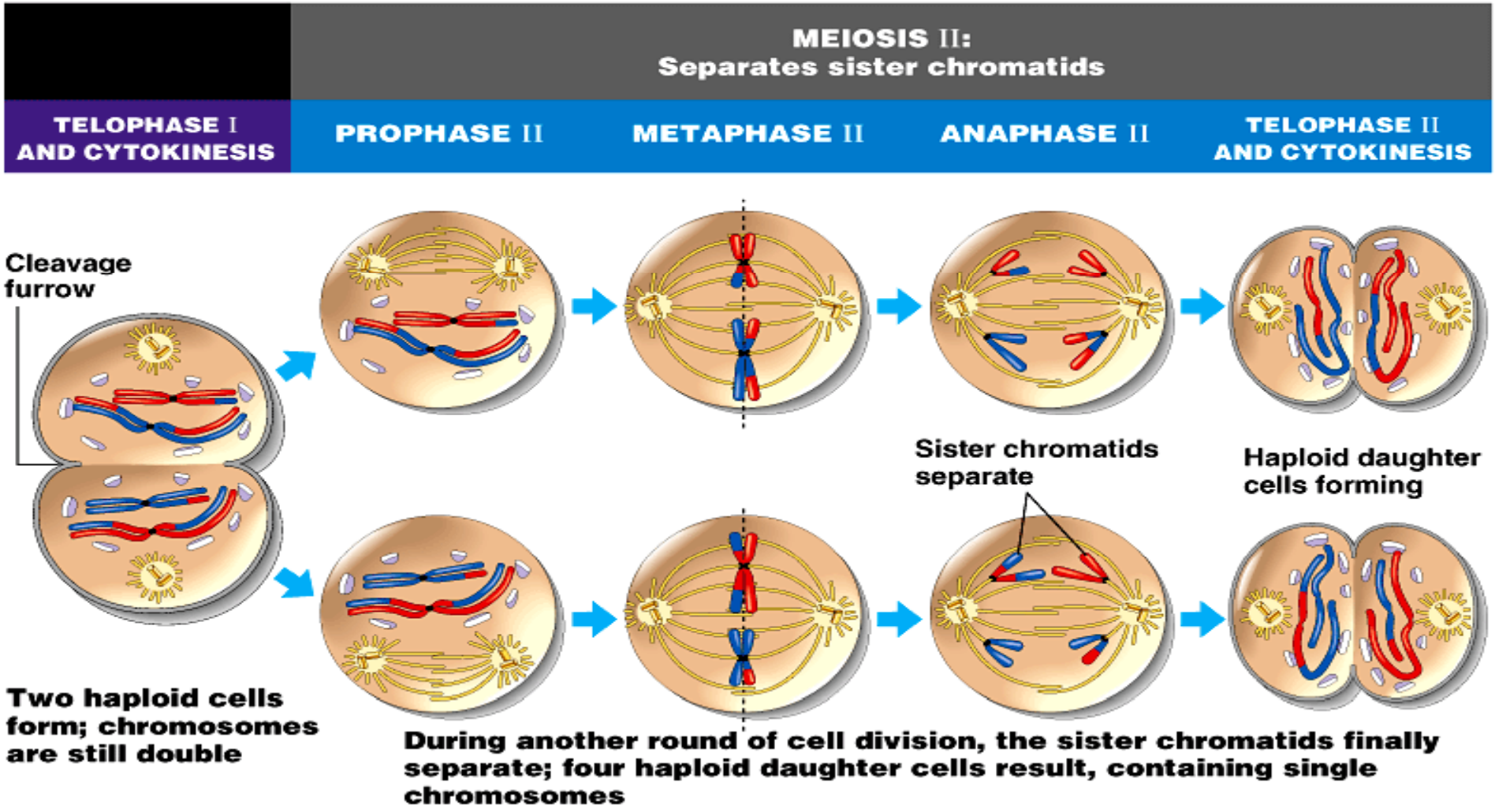


Meiosis – division error

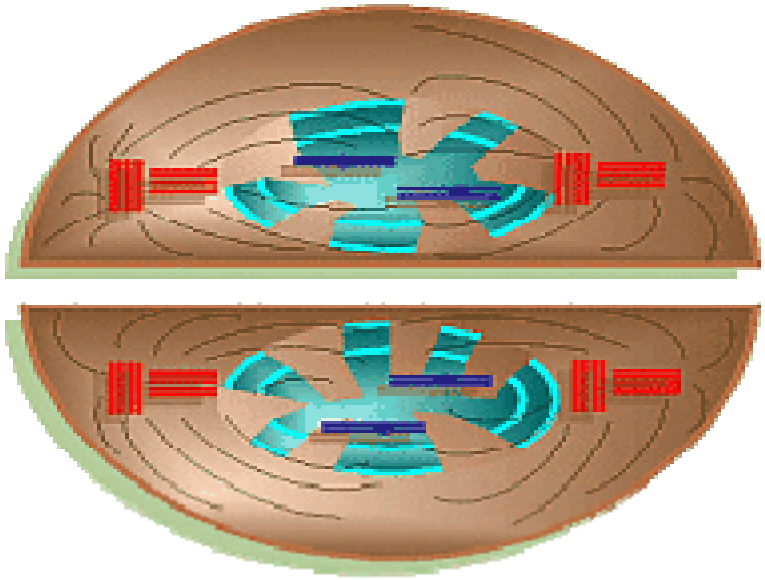


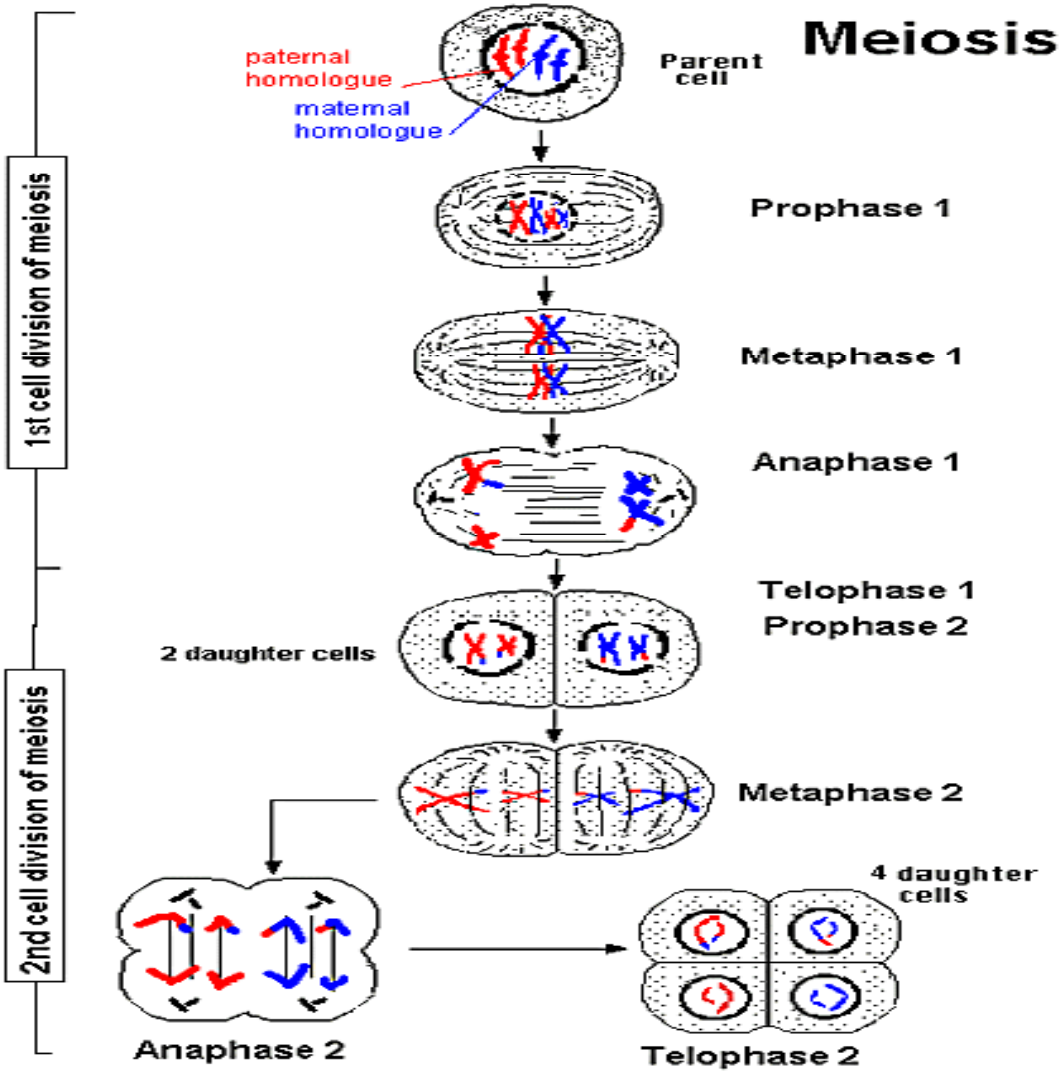






Animation




Meiosis
paternal homologue
maternal homologue
Parent cell
Prophase 1
Metaphase 1
Anaphase 1
Telophase 1
Prophase 2
2 daughter cells
Metaphase 2
4 daughter cells
Anaphase 2
Telophase 2
1st cell division of meiosis
2nd cell division of meiosis

Meiosis 1

First division of meiosis

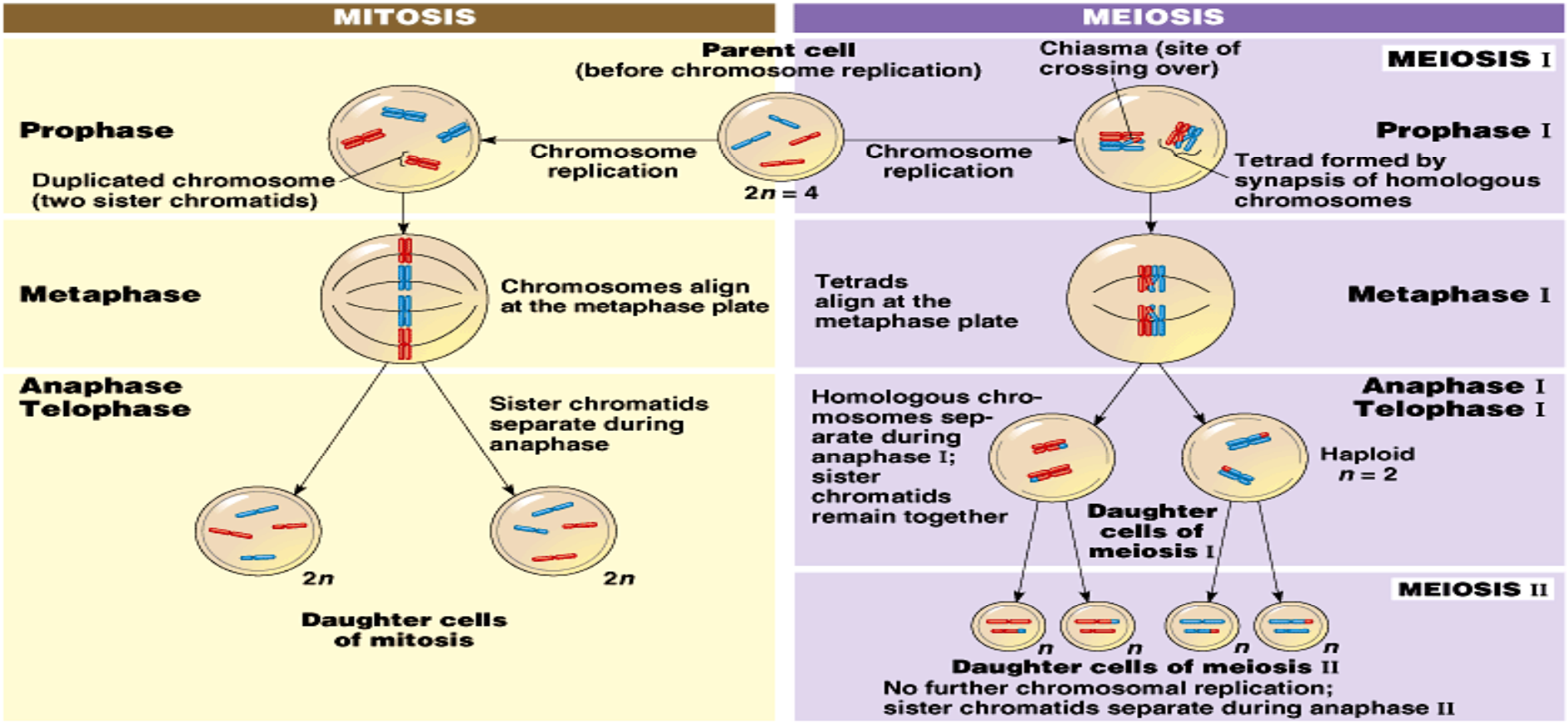
- **Prophase 1:** Each chromosome dupicates and remains closely associated. These are called sister chromatids. Crossing-over can occur during the latter part of this stage.
- **Metaphase 1**: Homologous chromosomes align at the equatorial plate.
- **Anaphase 1**: Homologous pairs separate with sister chromatids remaining together.
- **Telophase 1**: Two daughter cells are formed with each daughter containing only one chromosome of the homologous pair.

Meiosis II

Second division of meiosis: Gamete formation

- **Prophase 2**: DNA does not replicate.
- **Metaphase 2**: Chromosomes align at the equatorial plate.
- **Anaphase 2**: Centromeres divide and sister chromatids migrate separately to each pole.
- **Telophase 2**: Cell division is complete. Four haploid daughter cells are obtained.

Mitosis vs. meiosis



SUMMARY

Event	Mitosis	Meiosis
DNA replication	Occurs during interphase before nuclear division begins	Occurs once, during the interphase before meiosis I begins
Number of divisions	One, including prophase, metaphase, anaphase, and telophase	Two, each including prophase, metaphase, anaphase, and telophase
Synapsis of homologous chromosomes	Does not occur	Synapsis is unique to meiosis: During prophase I, the homologous chromosomes join along their length, forming tetrads (groups of four chromatids); synapsis is associated with crossing over between nonsister chromatids
Number of daughter cells and genetic composition	Two, each diploid ($2n$) and genetically identical to the parent cell	Four, each haploid (n), containing half as many chromosomes as the parent cell; genetically nonidentical to the parent cell and to each other
Role in the animal body	Enables multicellular adult to arise from zygote; produces cells for growth and tissue repair	Produces gametes; reduces chromosome number by half and introduces genetic variability among the gametes

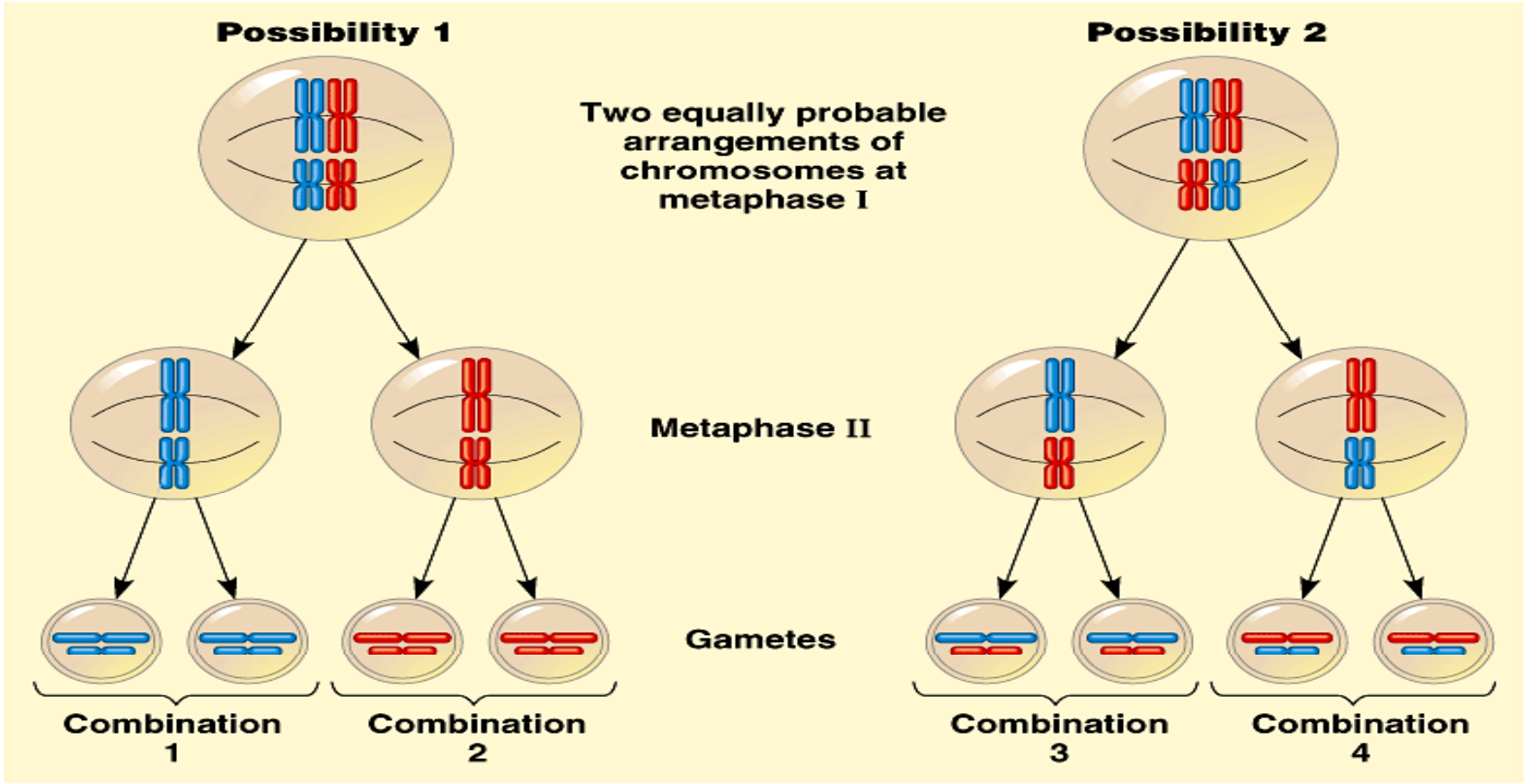
Meiosis creates genetic variation

- During normal cell growth, ***mitosis*** **produces daughter cells identical to parent cell** (2n to 2n)
- *Meiosis* results in **genetic variation** by **shuffling** of maternal and paternal chromosomes and **crossing over.**

  No daughter cells formed during meiosis are genetically identical to either mother or father

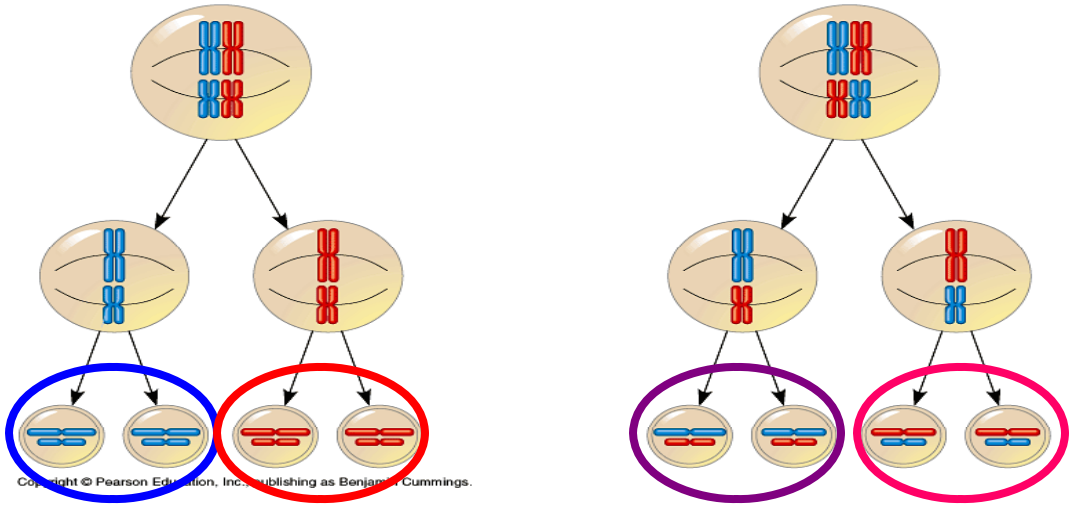
  During sexual reproduction, fusion of the unique haploid gametes produces truly unique offspring.

Independent assortment



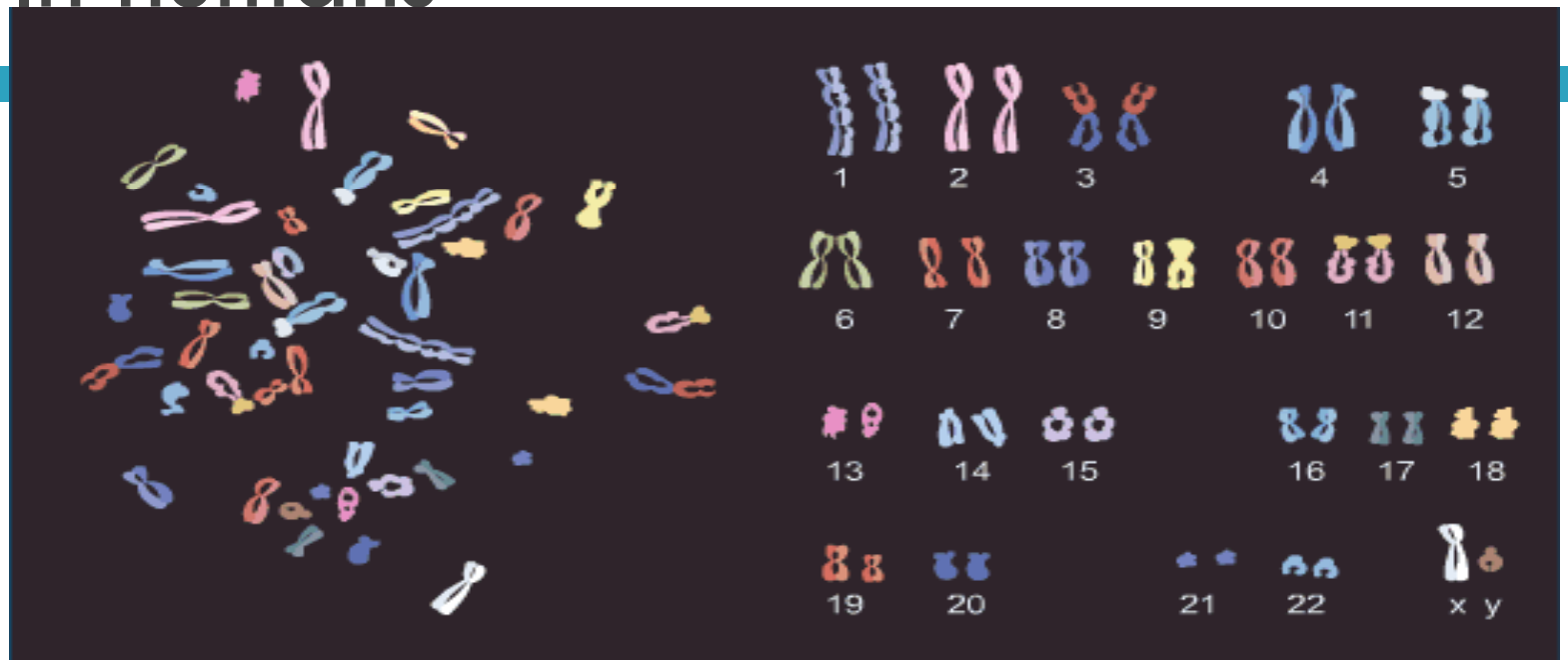
Independent assortment

Number of combinations: 2^n



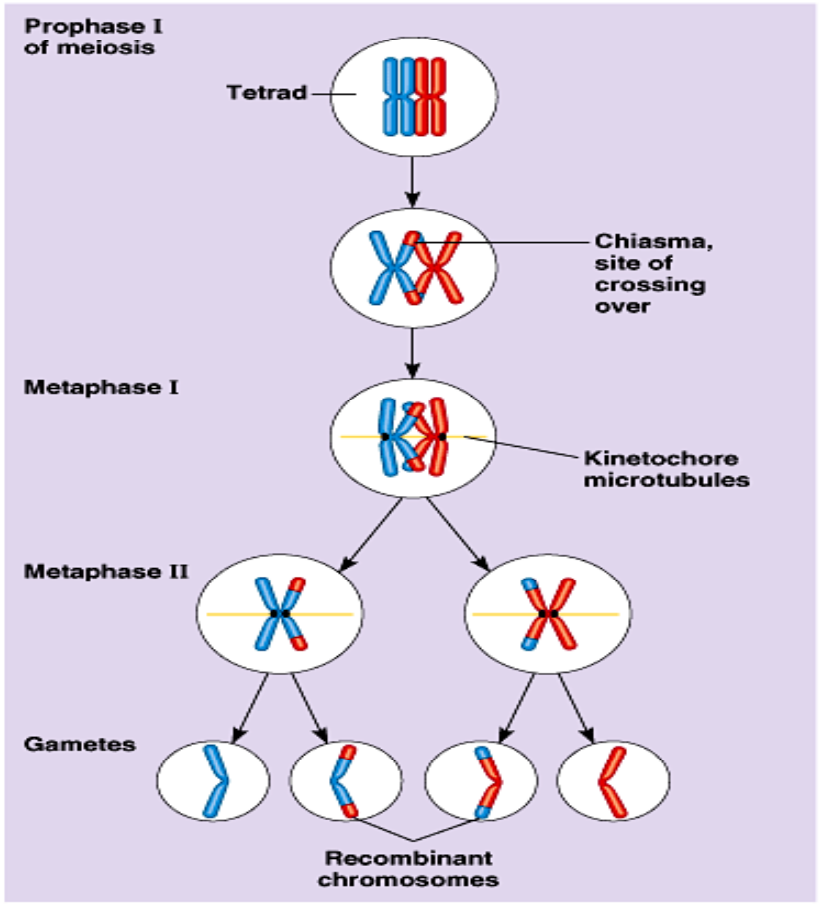
e.g. 2 chromosomes in haploid
2n = 4; n = 2
$2^n = 2^2 = 4$ possible combinations

In humans



e.g. 23 chromosomes in haploid
2n = 46; n = 23
$2^n = 2^{23}$ = ~ 8 million possible combinations!

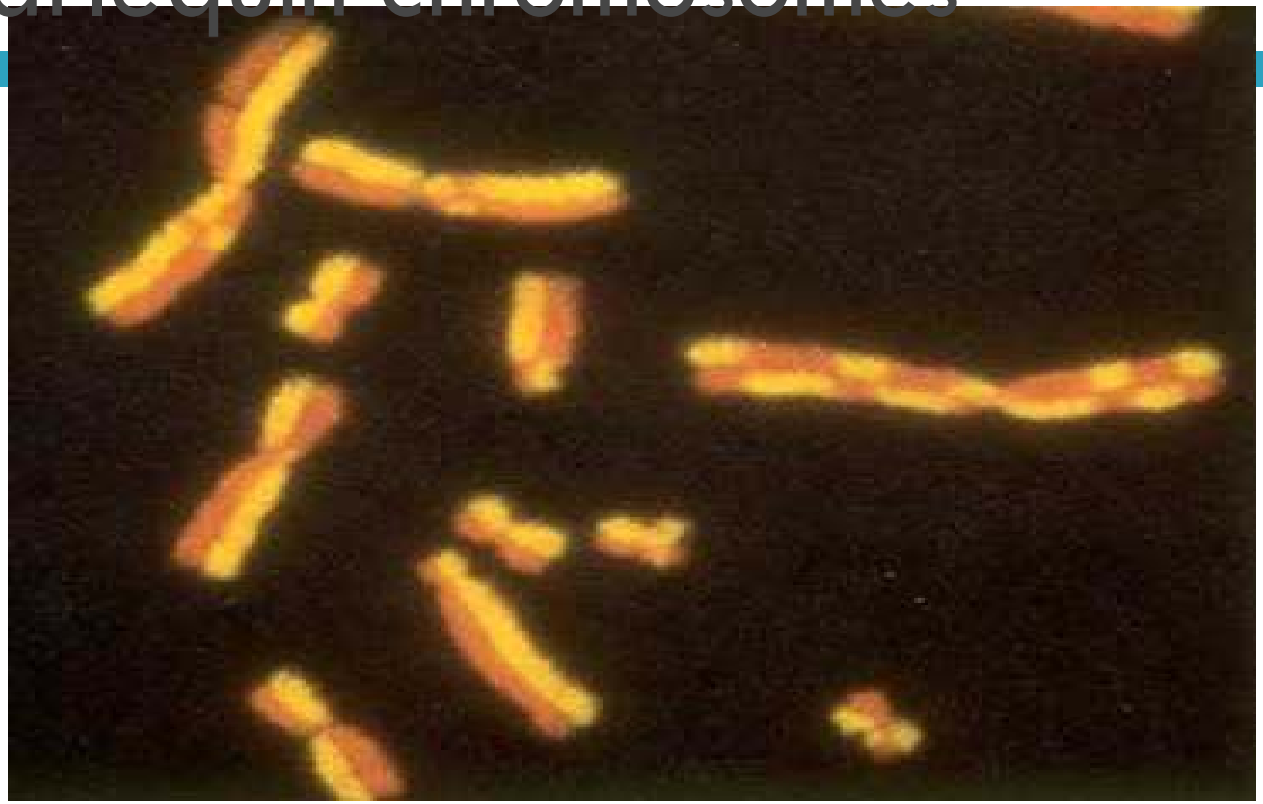
Crossing over



Chiasmata – sites of crossing over, occur in **synapsis**. Exchange of genetic material between non-sister chromatids.

Crossing over produces **recombinant chromosomes**.

Harlequin chromosomes



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http://edweb.sdsu.edu/ltca/Mitosis_Meiosis_files/frame.htm