Lecture Series 5

Cell Cycle & Cell Division

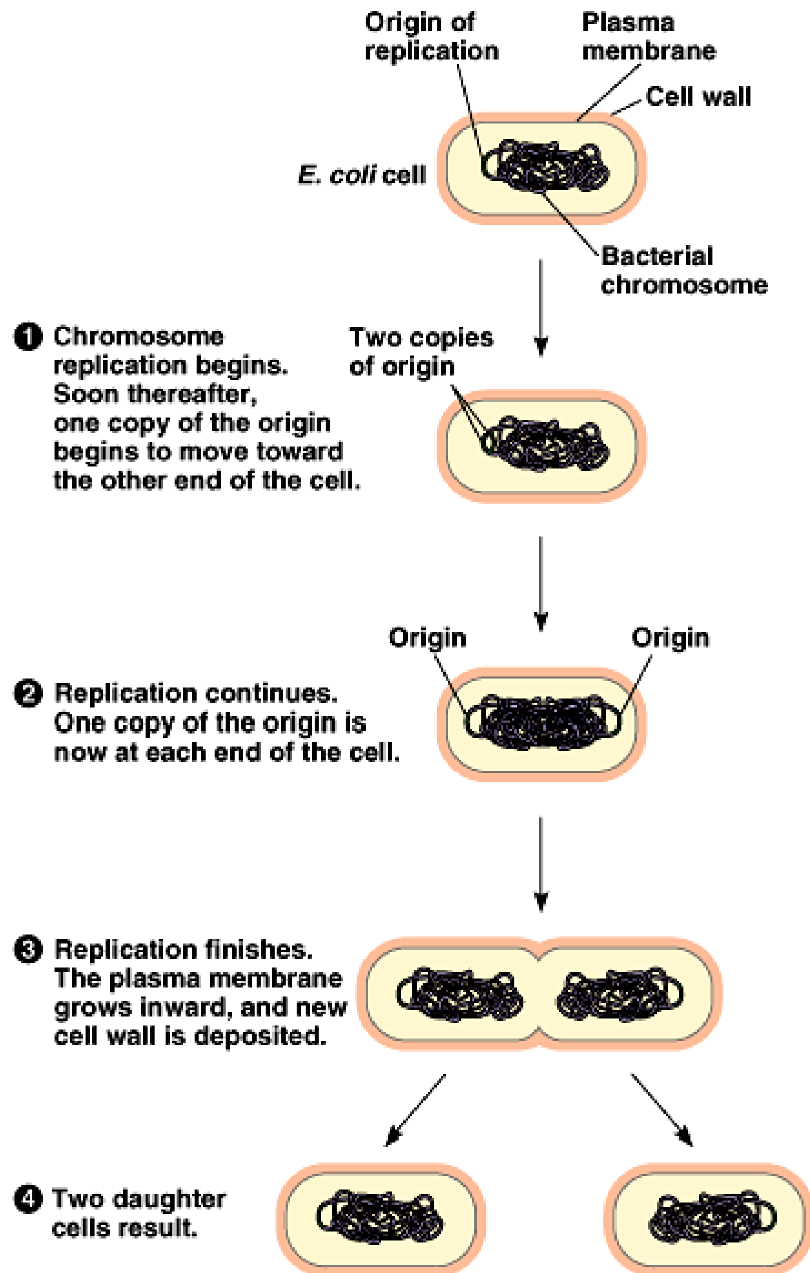
Reading Assignments

- Read Chapter 18
  Cell Cycle & Cell Division
- Read Chapter 19
  pages 651-663 only
  (Benefits of Sex & Meiosis sections – these are in Chapter 20 in 2nd Edition)

A. Systems of Cell Division

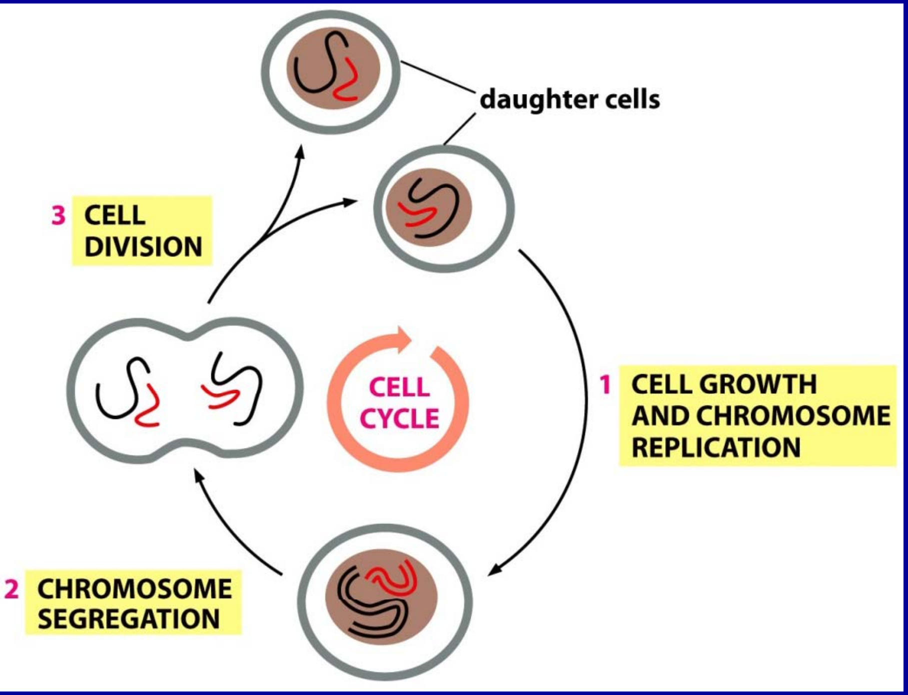
- Cell division is necessary for reproduction, growth, and repair of an organism.
- Cell division must be initiated by three steps: DNA replication, DNA separation, and then division of the cytoplasm.
- In microbes, cellular DNA is a single molecule, or chromosome. Bacteria & Archaea reproduce by binary fission.
- In eucaryotes, nuclei divide by either mitosis or meiosis.

Bacterial cell division (binary fission):



Universal functions of the cell cycle

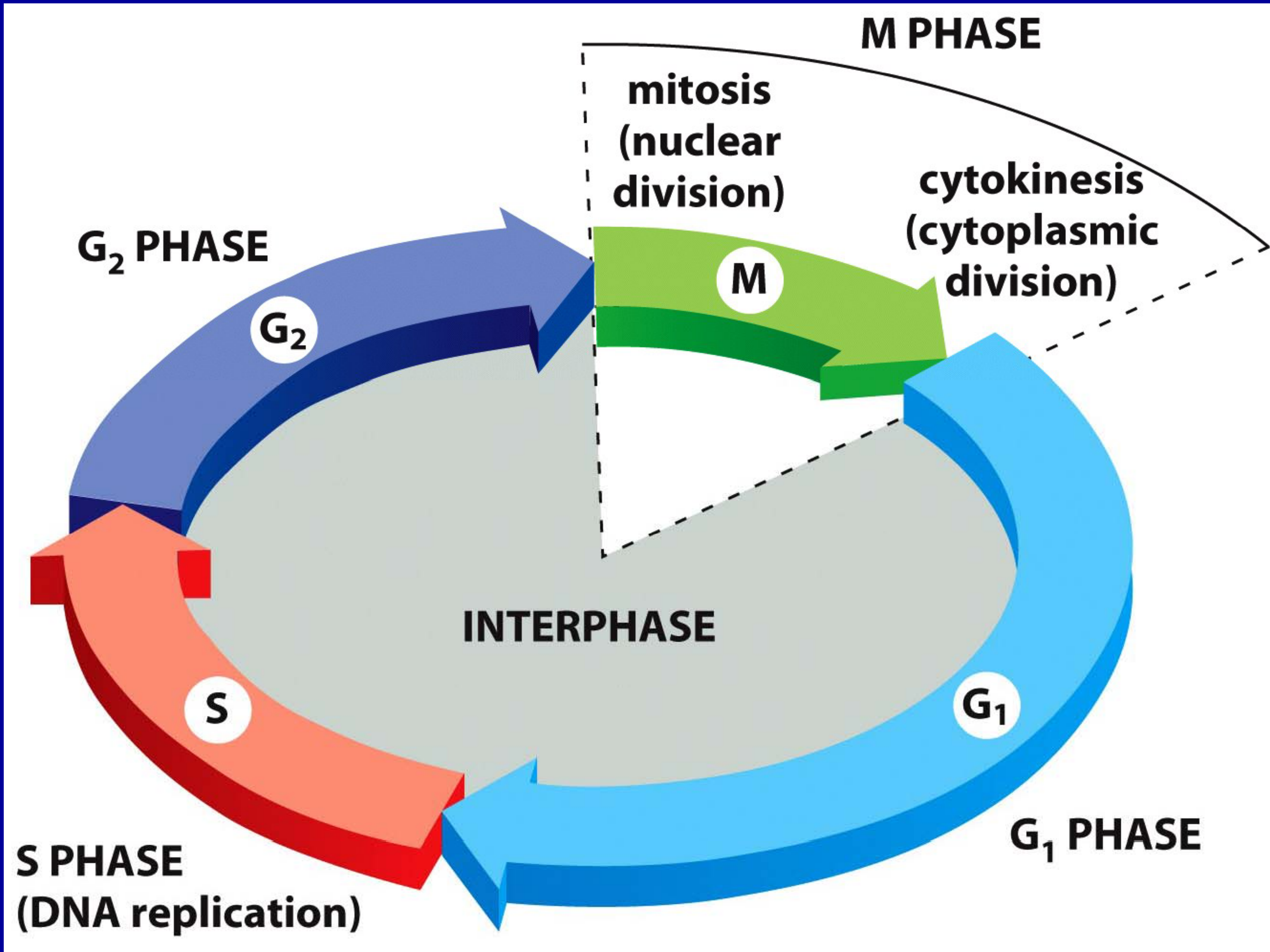
- Replicate the DNA.
- Segregate it into daughter cells.
- Replicate and/or distribute organelles into daughter cells.
- Grow & do it again!



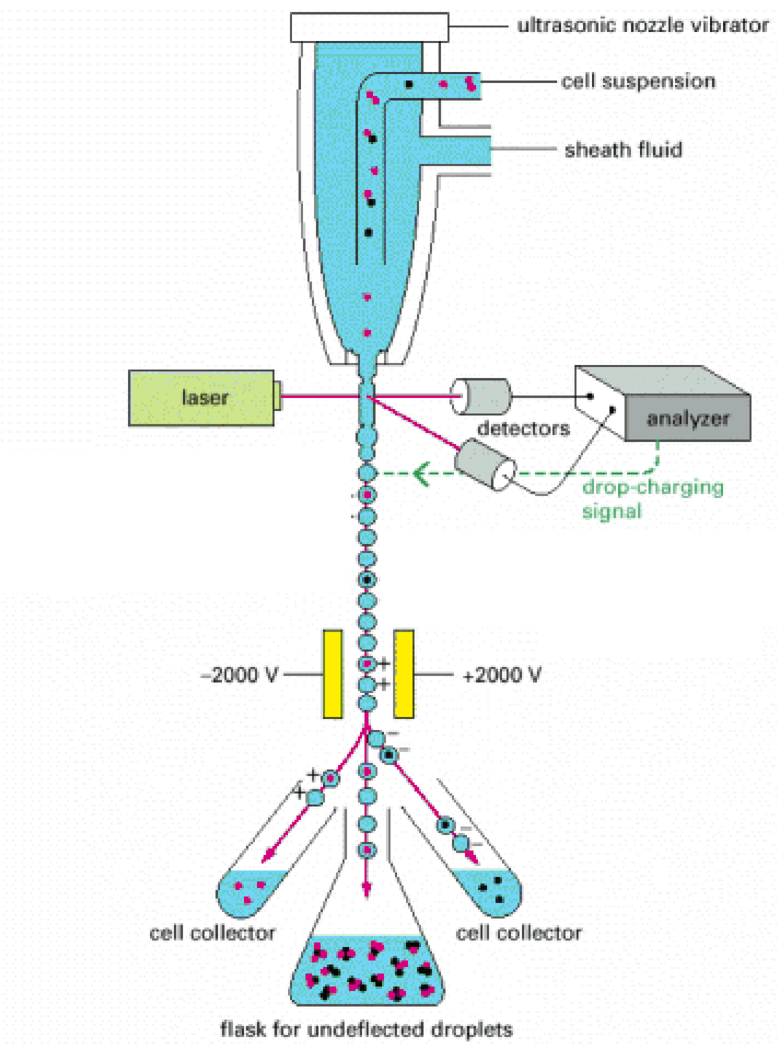
B. Interphase and the Control of Cell Division

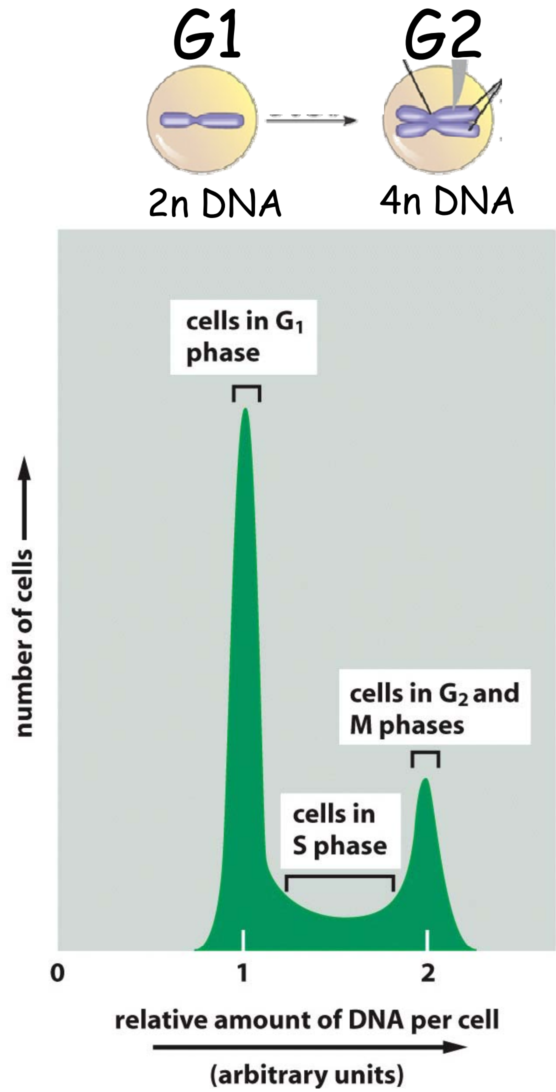
- The mitotic cell cycle has two main phases: interphase and mitosis.
- Interphase is the period between divisions in the cytoplasm.
- During most of the cell cycle the cell is in interphase, which is divided into three subphases: S, G1, and G2.
- DNA is replicated during S phase.

The mitotic cell cycle



FACS analysis (fluorescence-activated cell sorting)

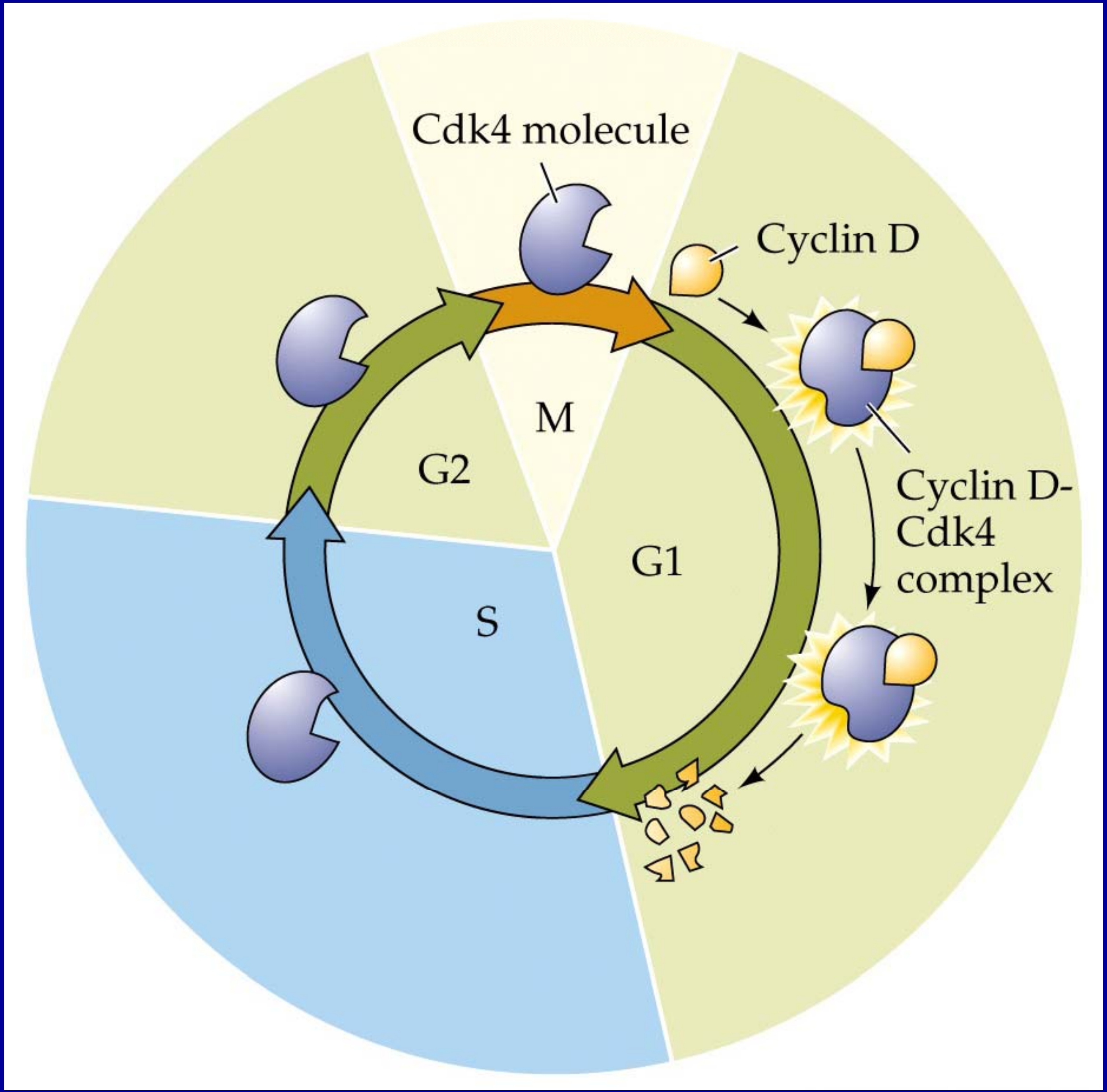




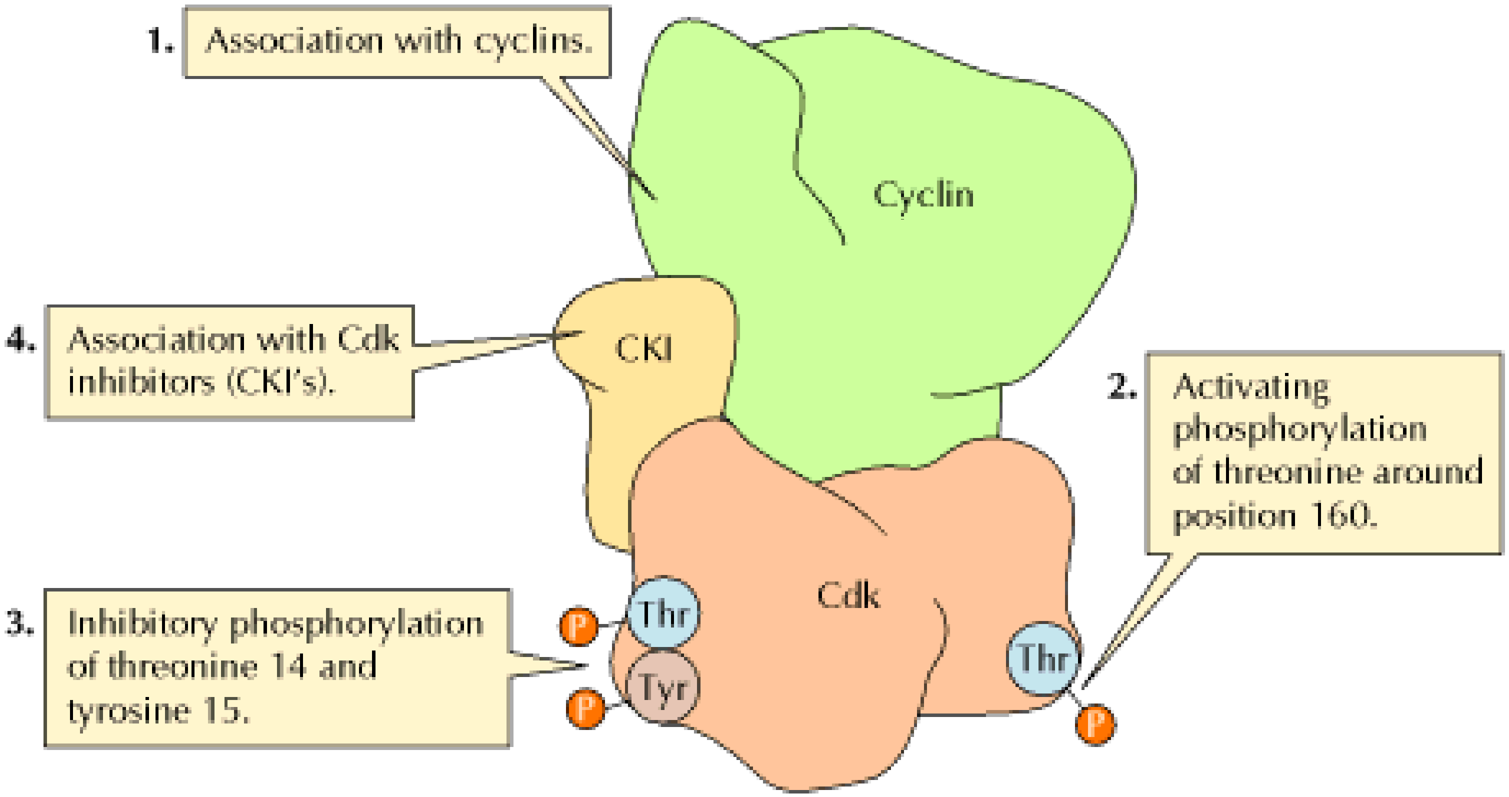
B. Interphase and the Control of Cell Division

- Cyclin-Cdk complexes regulate the passage of cells from G1 into S phase and from G2 into M phase, etc.
- Cyclin binding to Cdk exposes the active site of the protein kinase but breaks down quickly.
- These complexes act as checkpoints regulating the cells progression through the cell cycle.

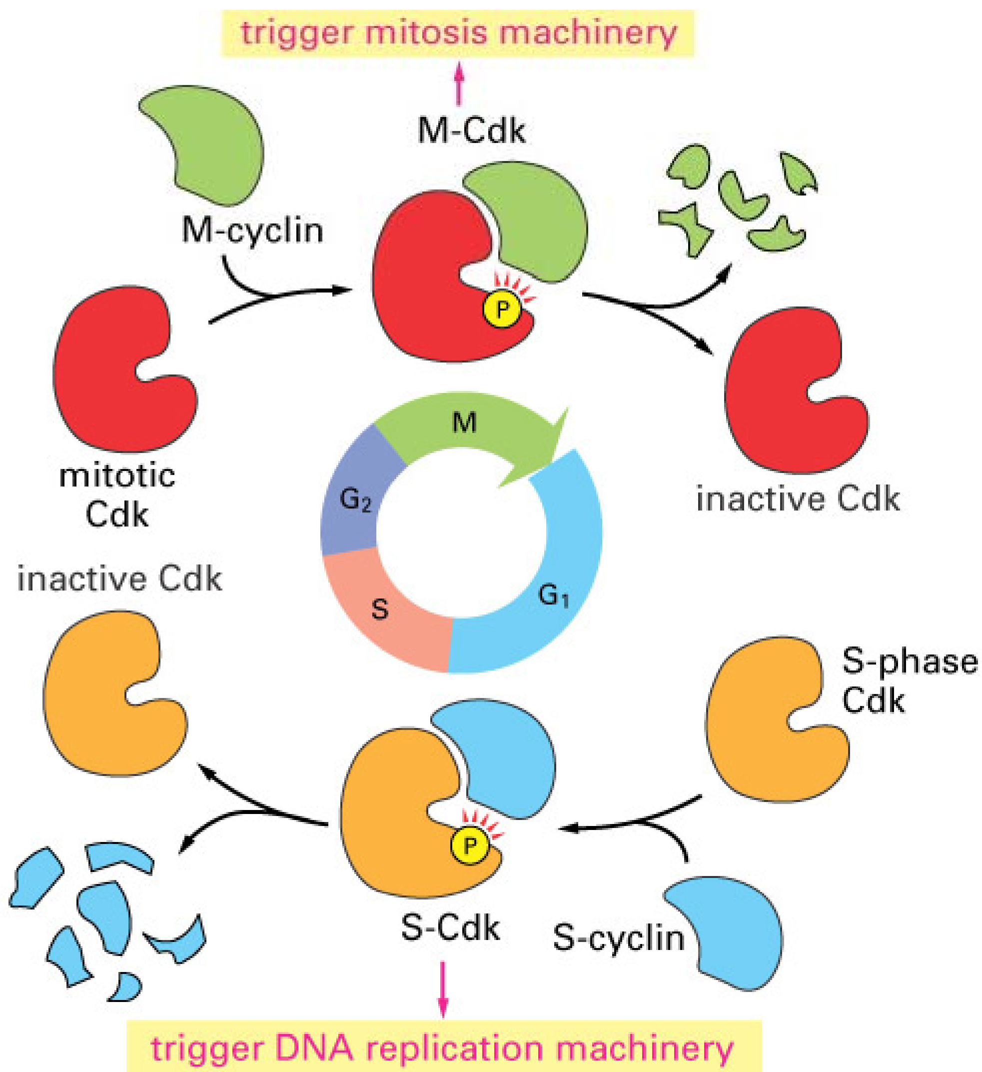
G1 into S phase:



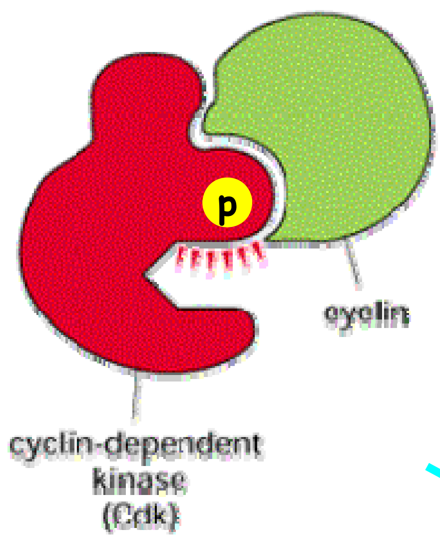
Cyclin dependant kinases



Cyclin dependant kinases bind to different cyclins



Processes regulated by Cyclin dependant kinases



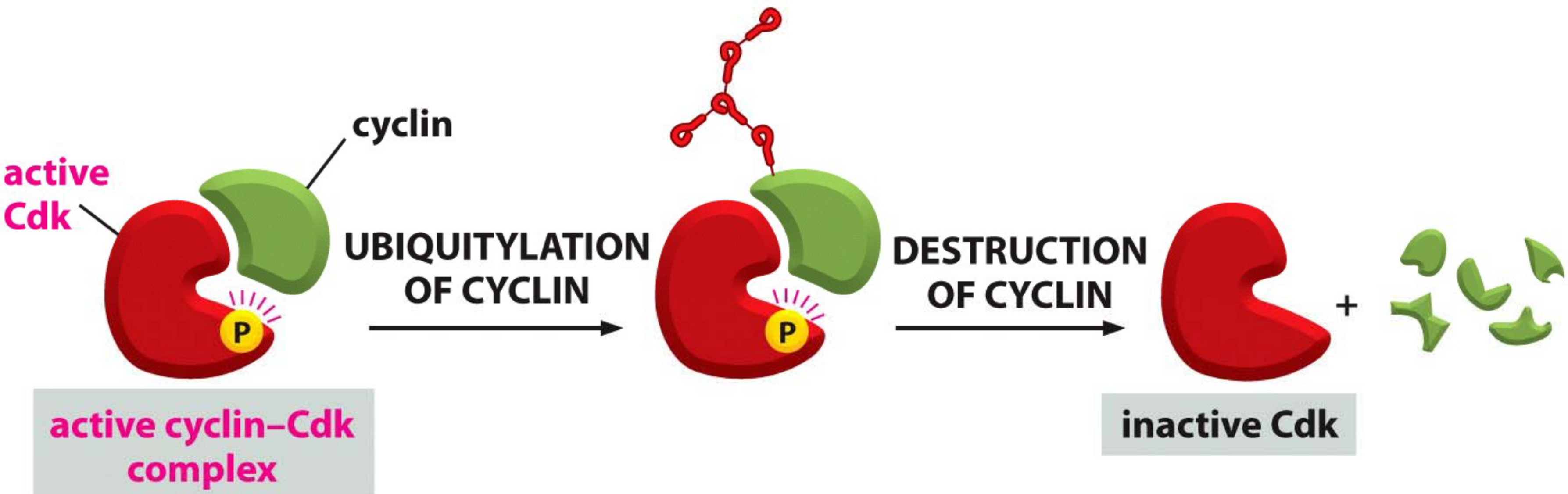
G1 → Cell Growth

S → DNA Synthesis

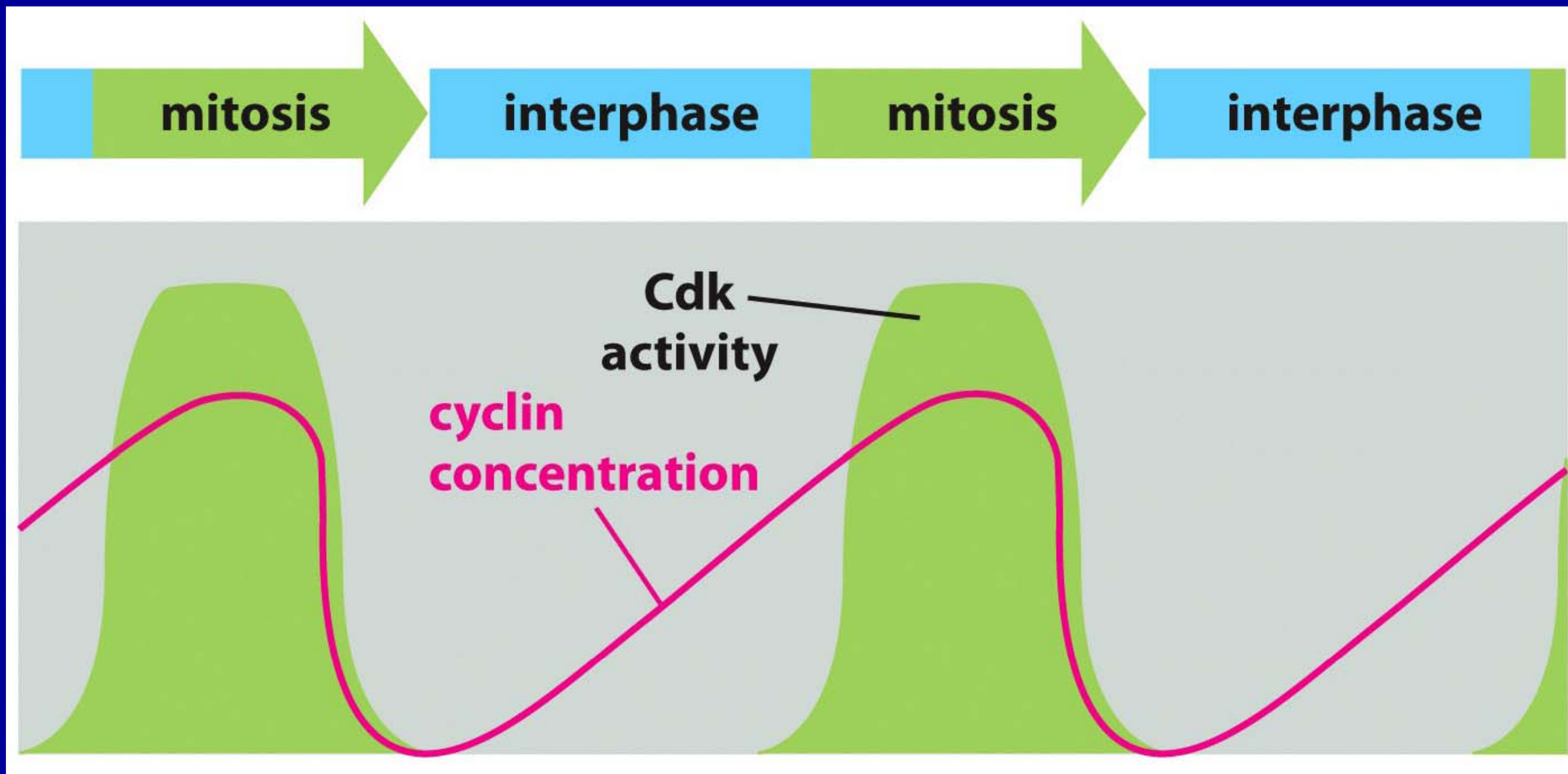
G2 → Spindle Formation

M → Chromosome Condensation

Activity is regulated by Cyclin degradation



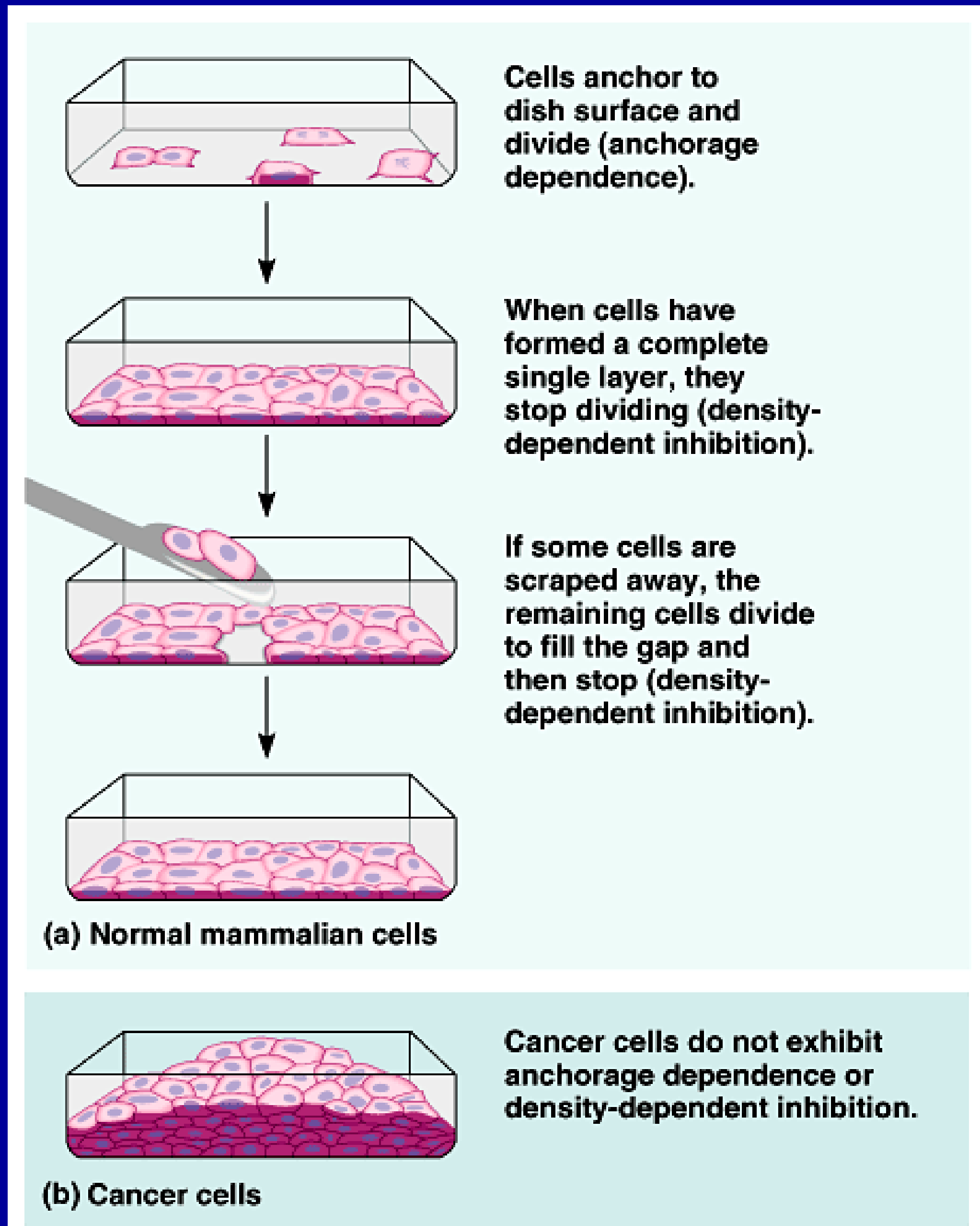
Targeted destruction in Proteosomes


mitosis
interphase
mitosis
interphase
Cdk
activity
cyclin
concentration

B. Interphase and the Control of Cell Division

- In addition to the **internal** cyclin-Cdk complexes, **external** controls to the cell, such as growth factors and hormones, can also stimulate a division cycle.
- Cancer cells often have defective Cyclin-Cdk complexes or lose external control over their growth factors.

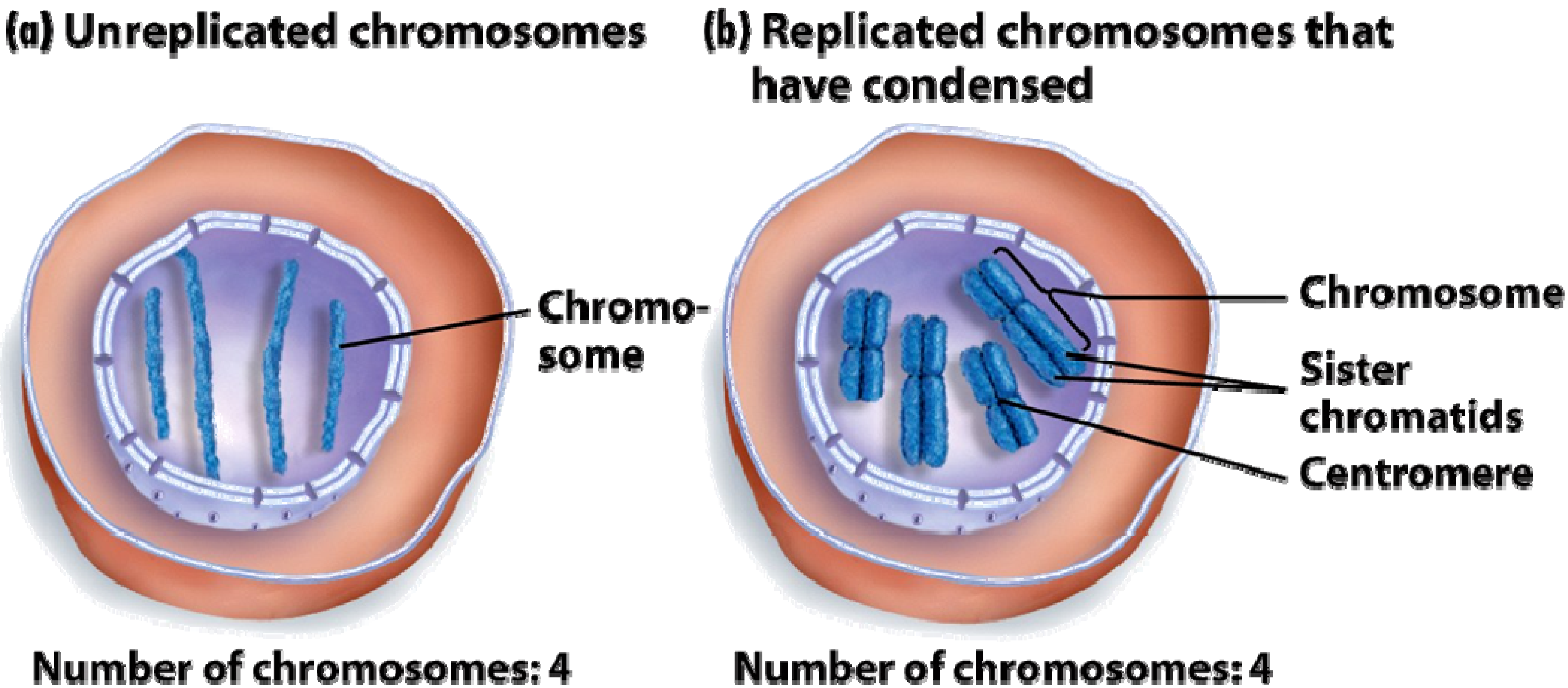
Density-dependent inhibition of cell division



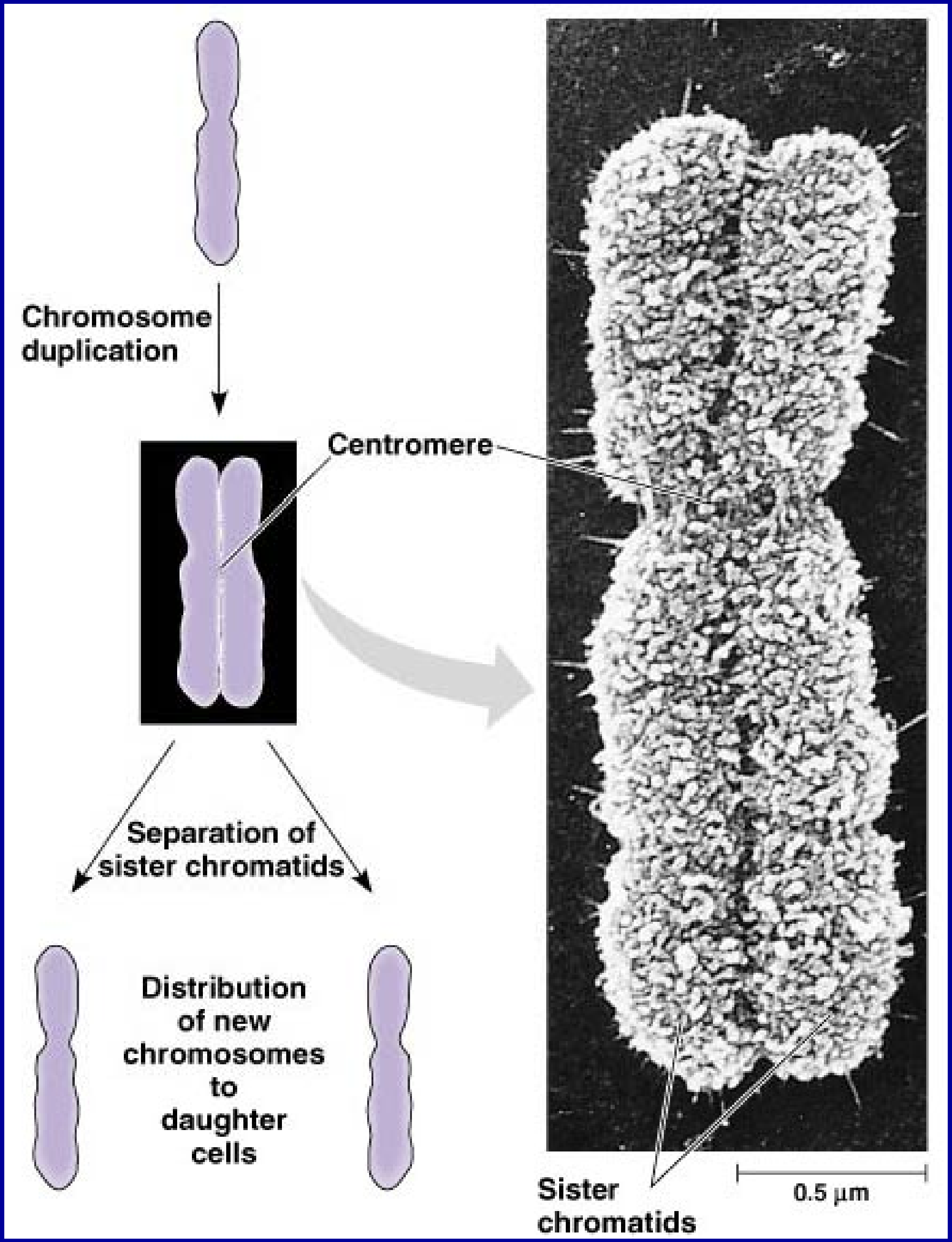
C. Eucaryotic Chromosomes

- Chromosomes contain DNA and proteins. At mitosis, chromosomes initially appear double because two sister chromatids are held together at the centromere.
- Each sister chromatid consists of one double-stranded DNA molecule complexed with proteins and referred to as chromatin.

What essential process happens in S phase? DNA Replication!

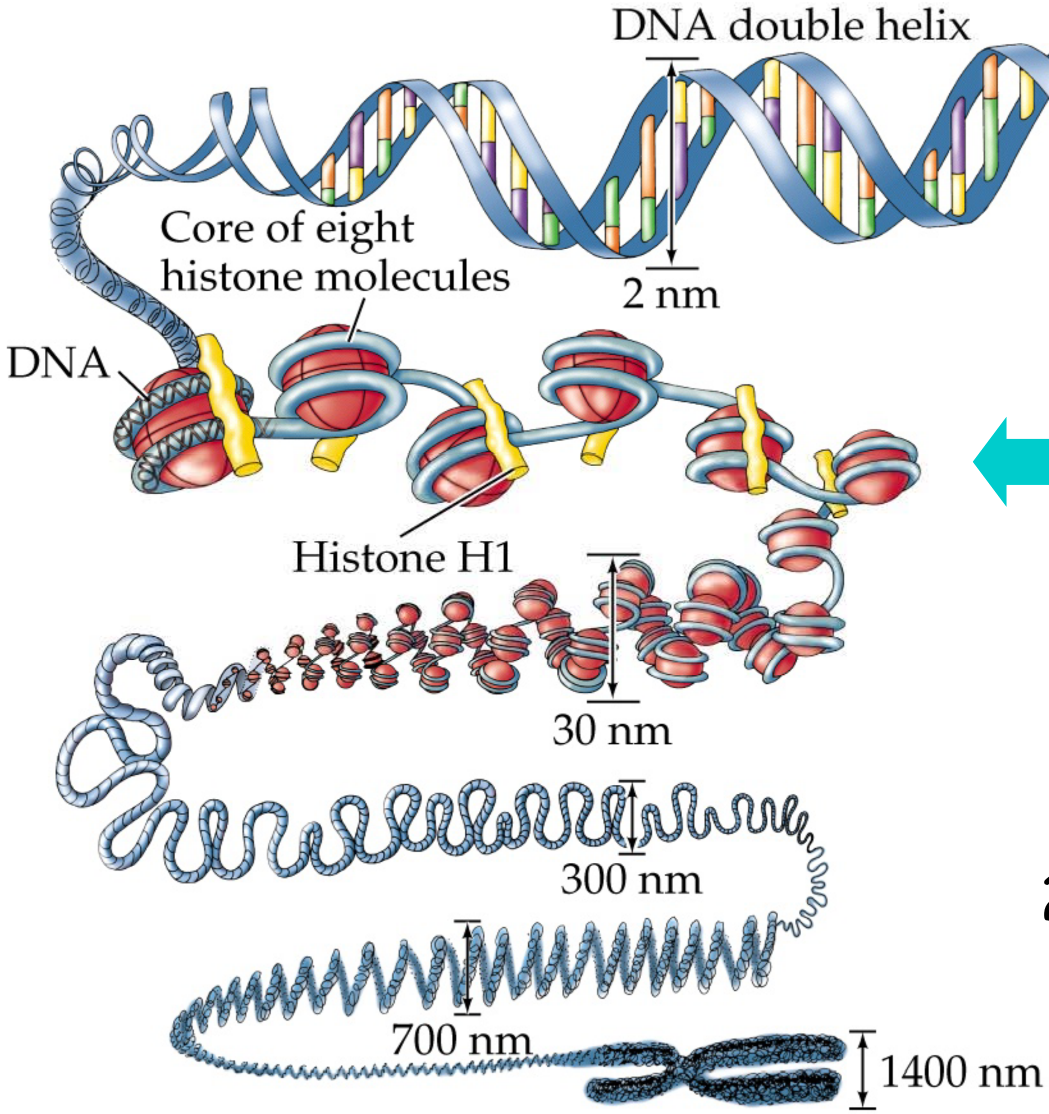


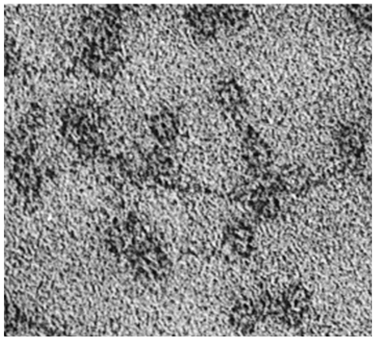
Chromosome duplication and distribution during mitosis



C. Eucaryotic Chromosomes

- During interphase, DNA in chromatin is wound around histone core proteins to form nucleosomes.
- DNA folds repeatedly, packing within the nucleus. When mitotic chromosomes form, it supercoils and condenses even more.

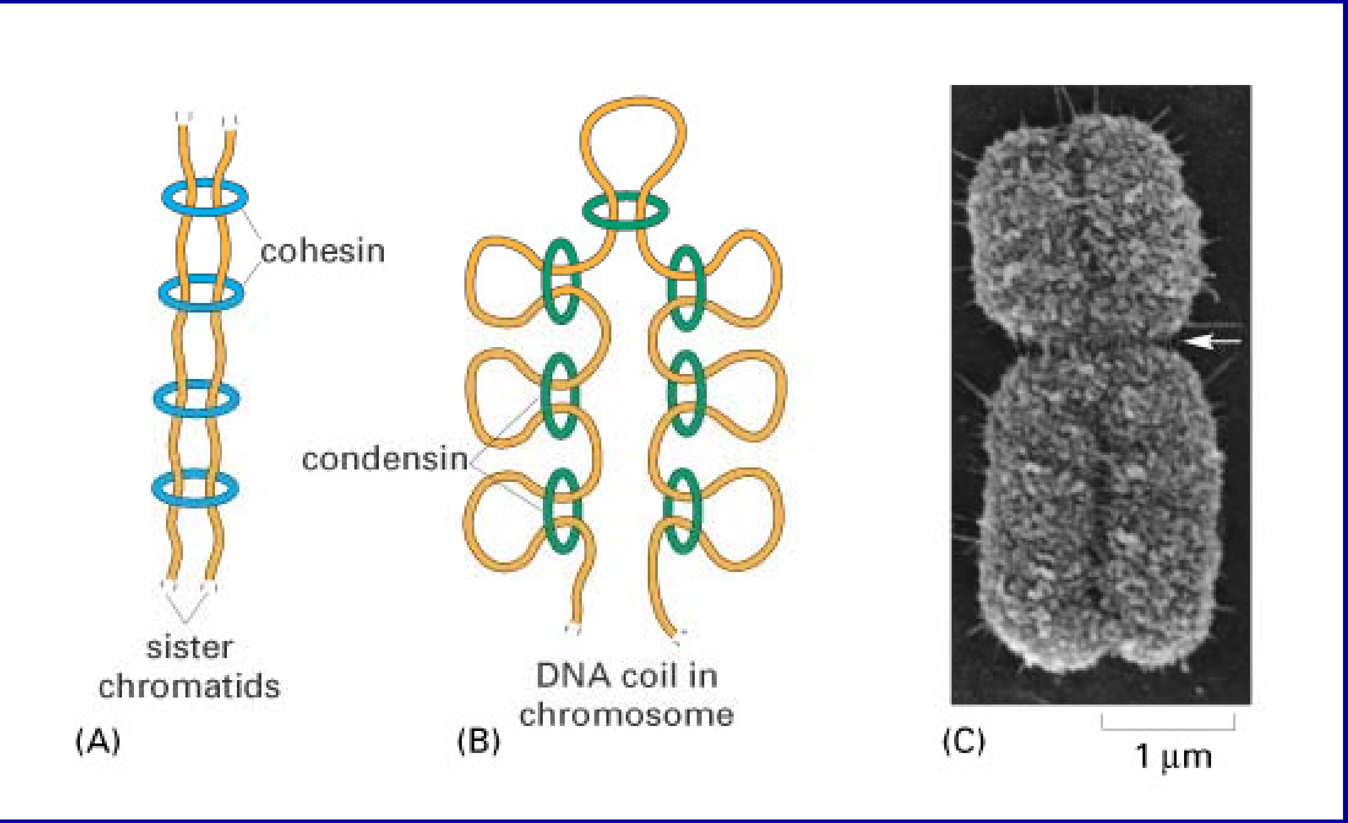




Nucleosomes aka
"beads on a string"

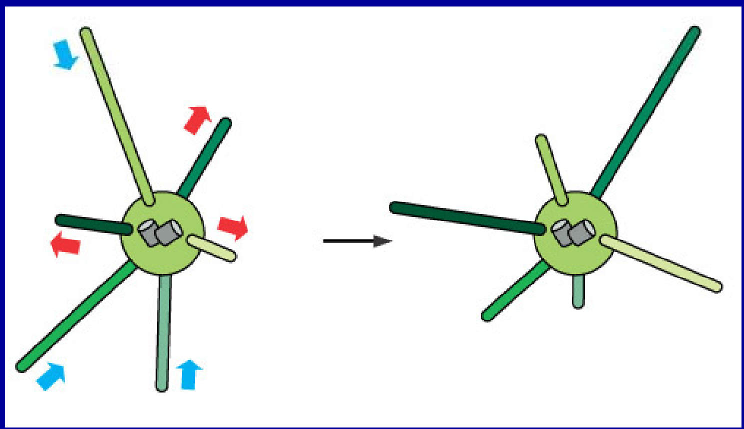
2 meter long molecule
into 5 μm nucleus!

Cohesins and condensins help prepare replicated chromosomes for mitosis.

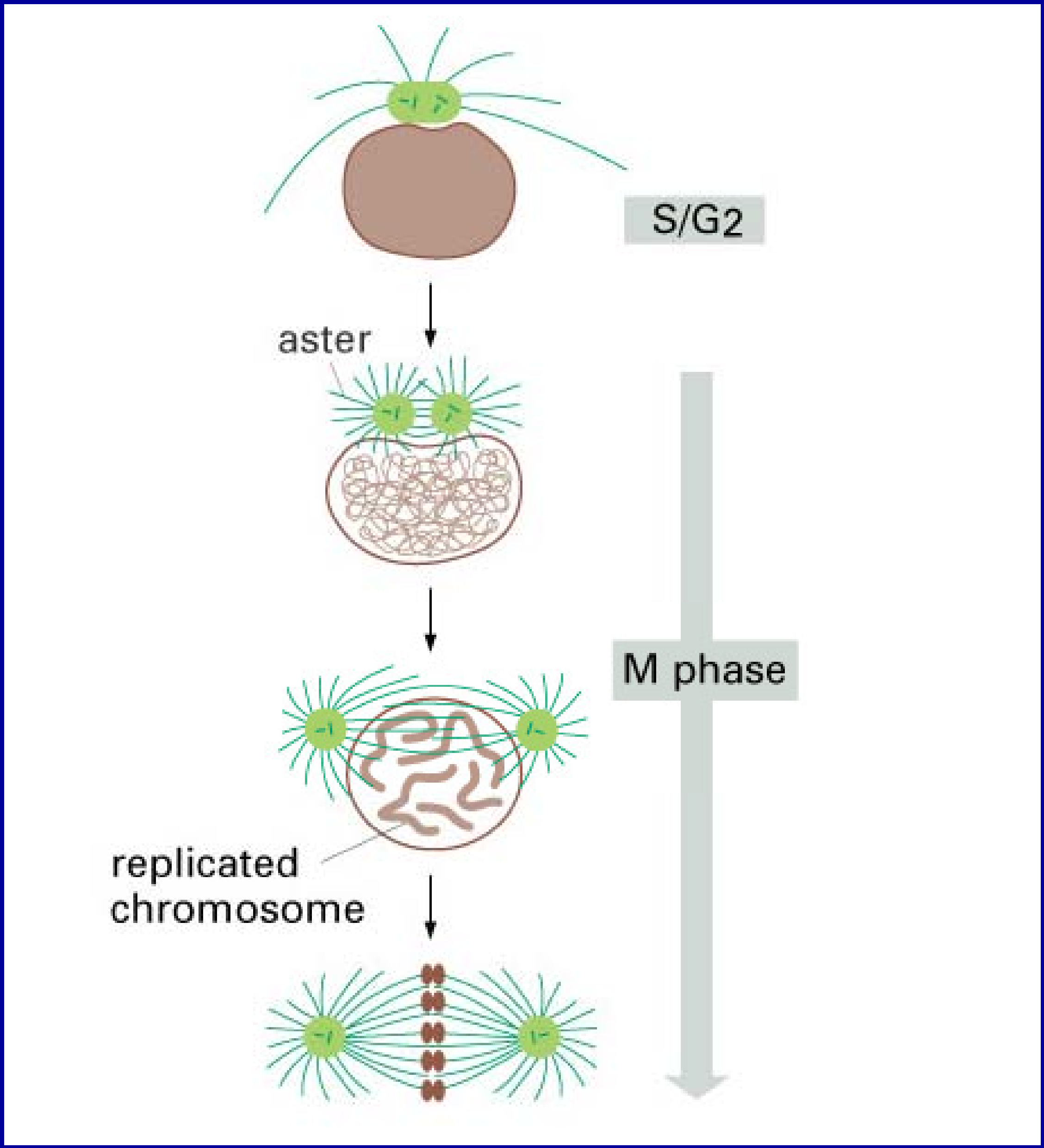


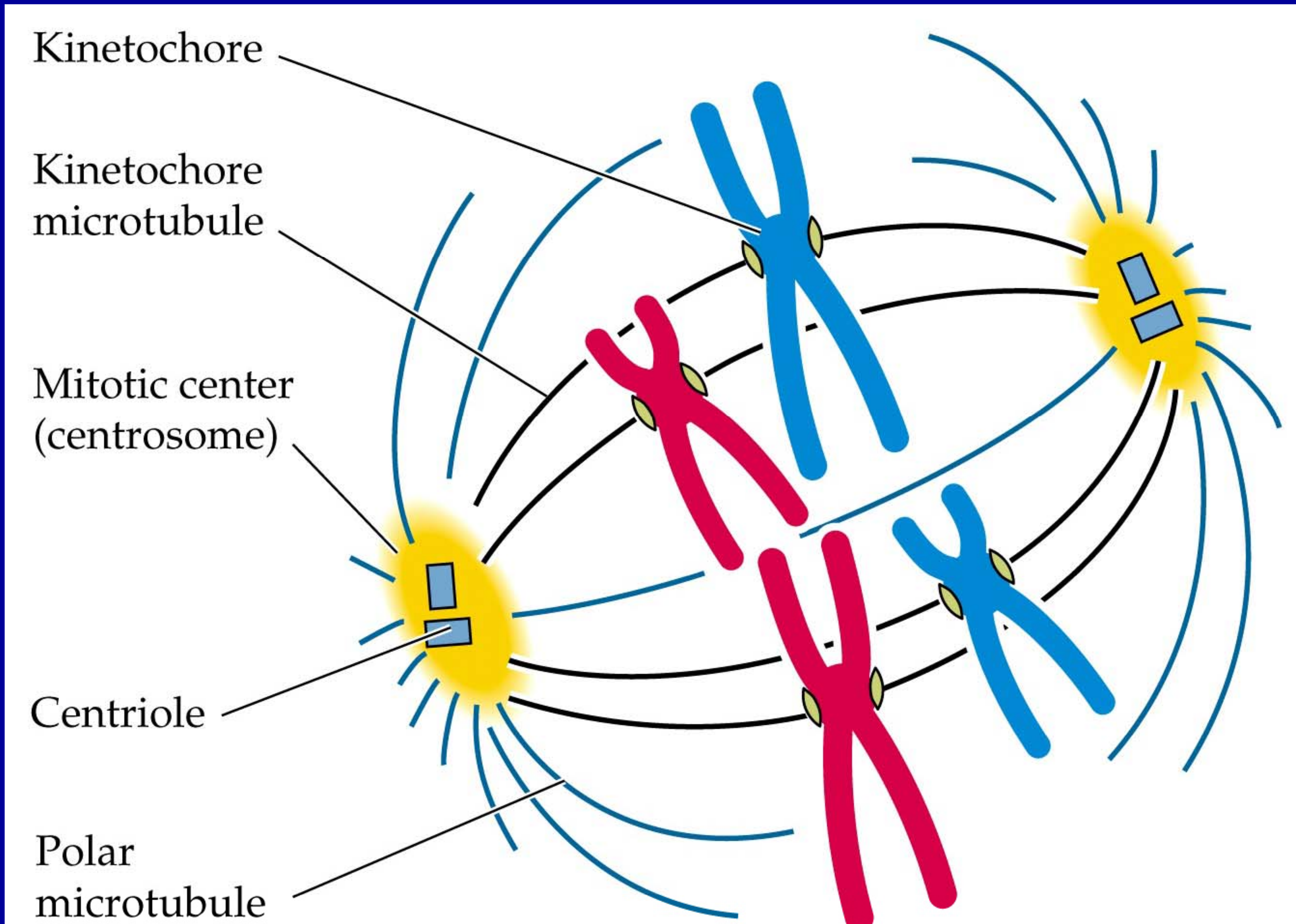
D. Mitosis: Distributing Exact Copies of Genetic Information

- After DNA is replicated during S phase, the first sign of mitosis is the duplication of the centrosome, which initiates microtubule formation for the spindle.
- Rem: dynamic instability.

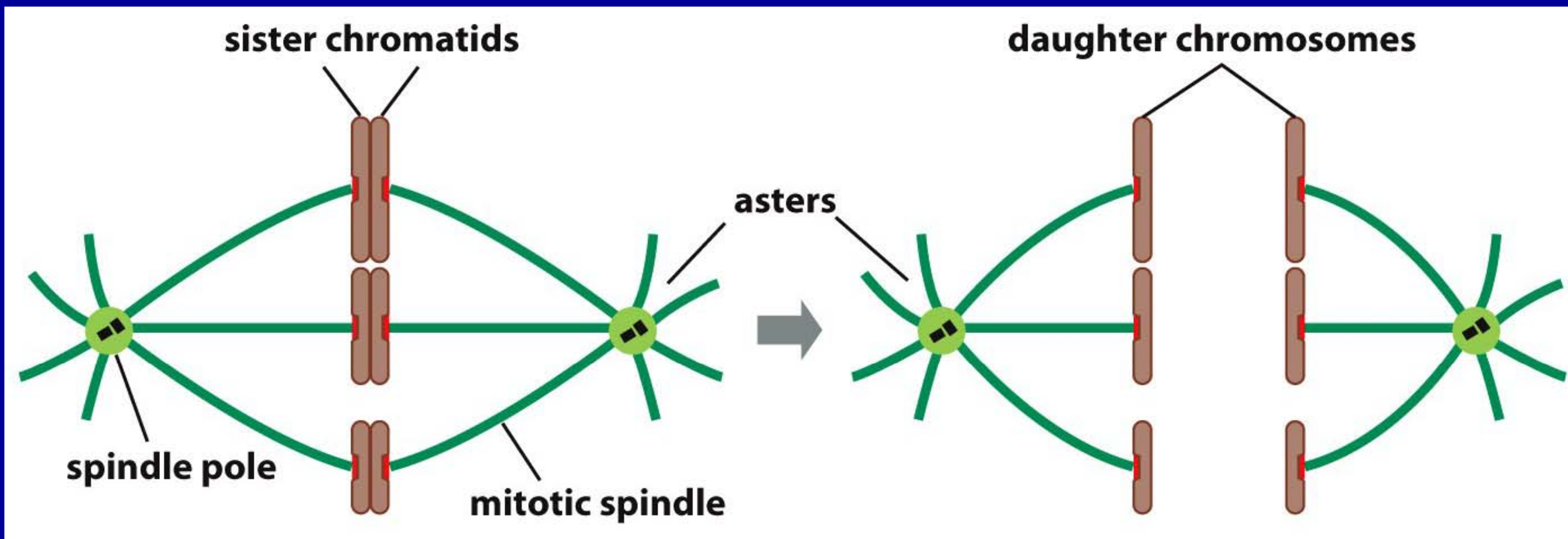


The centrosome duplicates to form the two poles of a mitotic spindle.




Kinetochore
Kinetochore microtubule
Mitotic center (centrosome)
Centriole
Polar microtubule

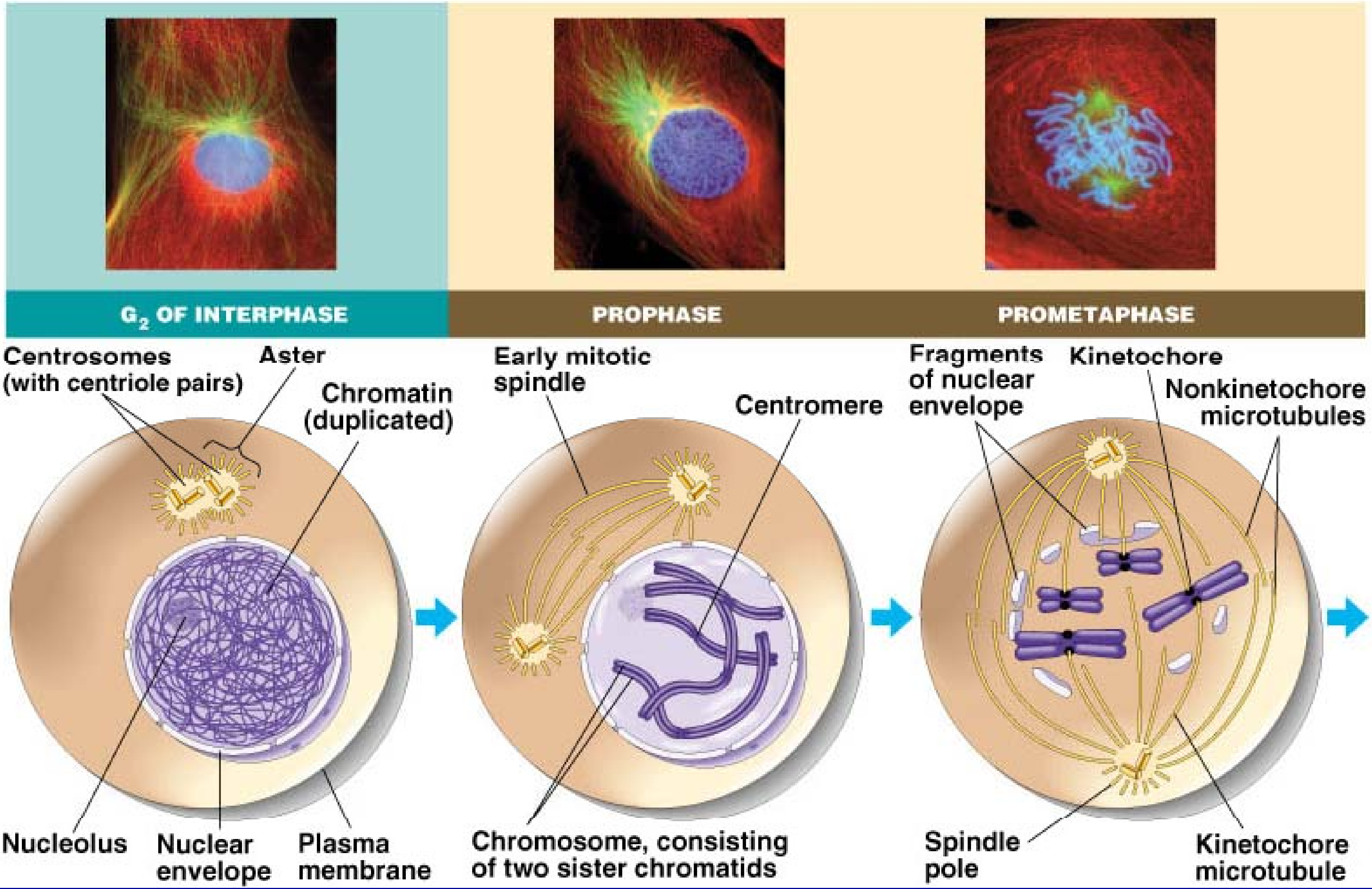
Each pair of sister chromatids separates to become two daughter chromosomes.



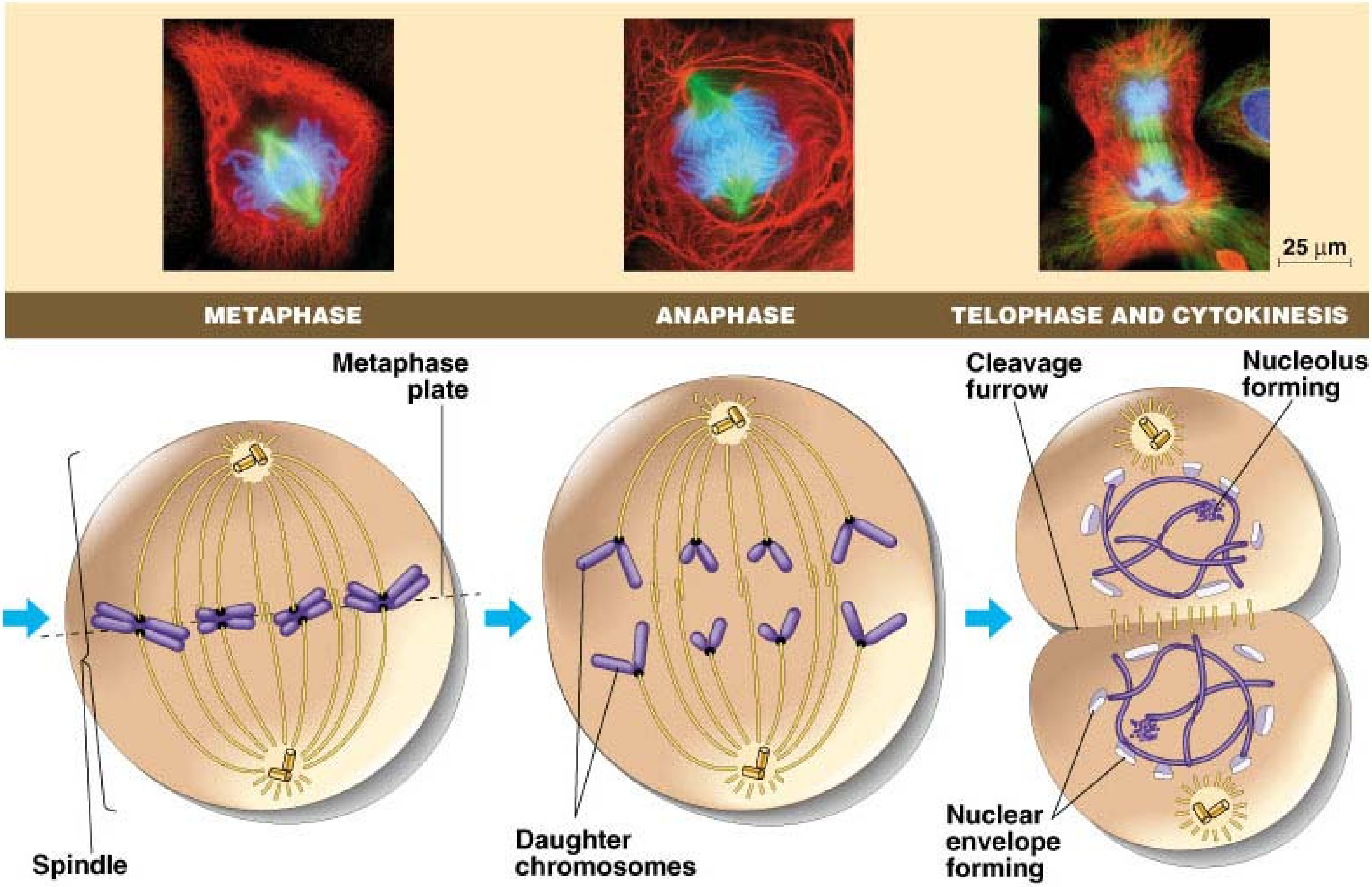
D. Mitosis: Distributing Exact Copies of Genetic Information

- Mitosis is continuous, but can be divided into 5 stages: prophase, prometaphase, metaphase, anaphase, and telophase.
- Cytokinesis occurs in the 6th stage, overlapping with the end of mitosis.

Mitotic cell division stages (animal cell): prophase; prometaphase.



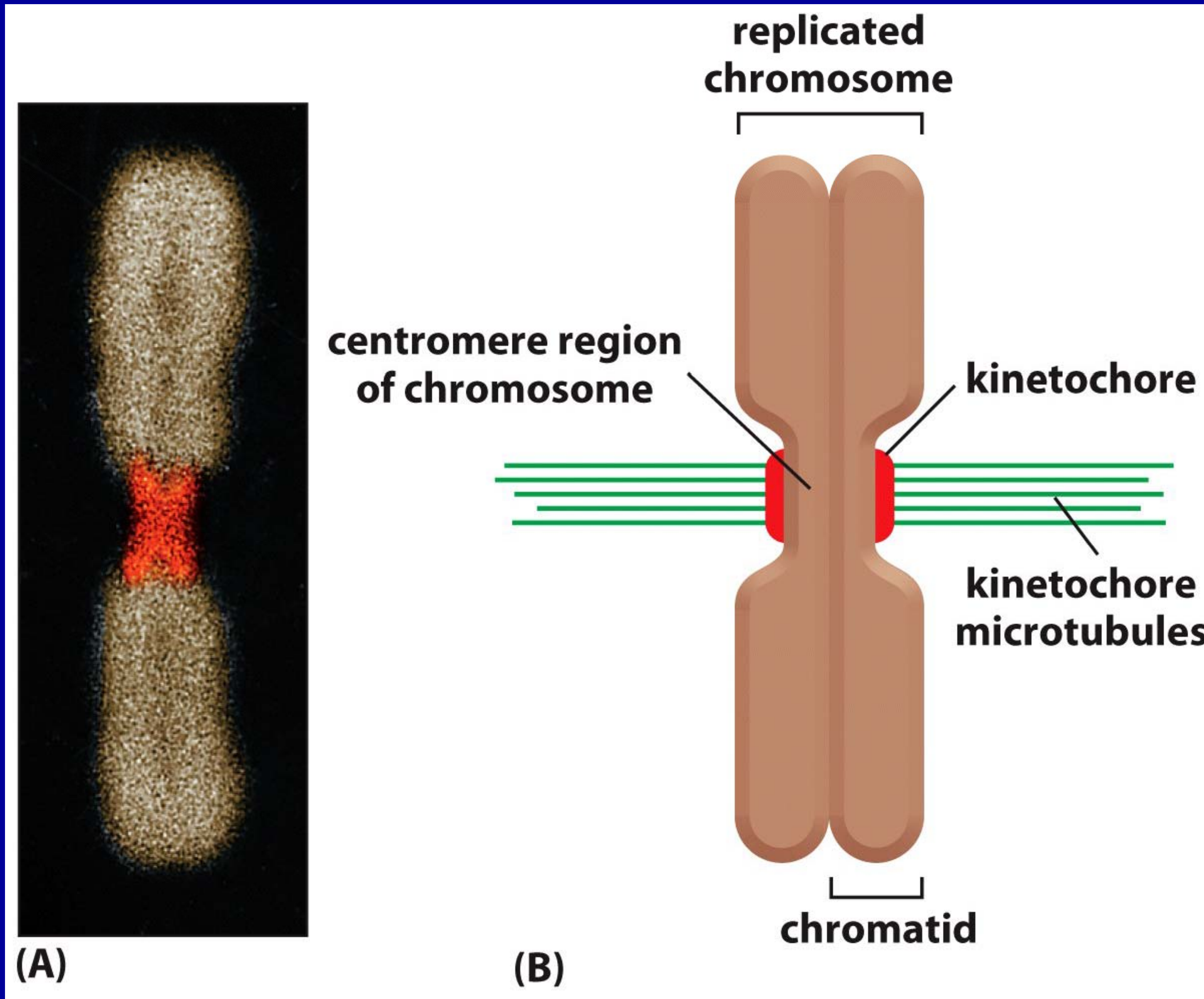
Mitotic cell division stages (animal cell): metaphase; anaphase; telophase.

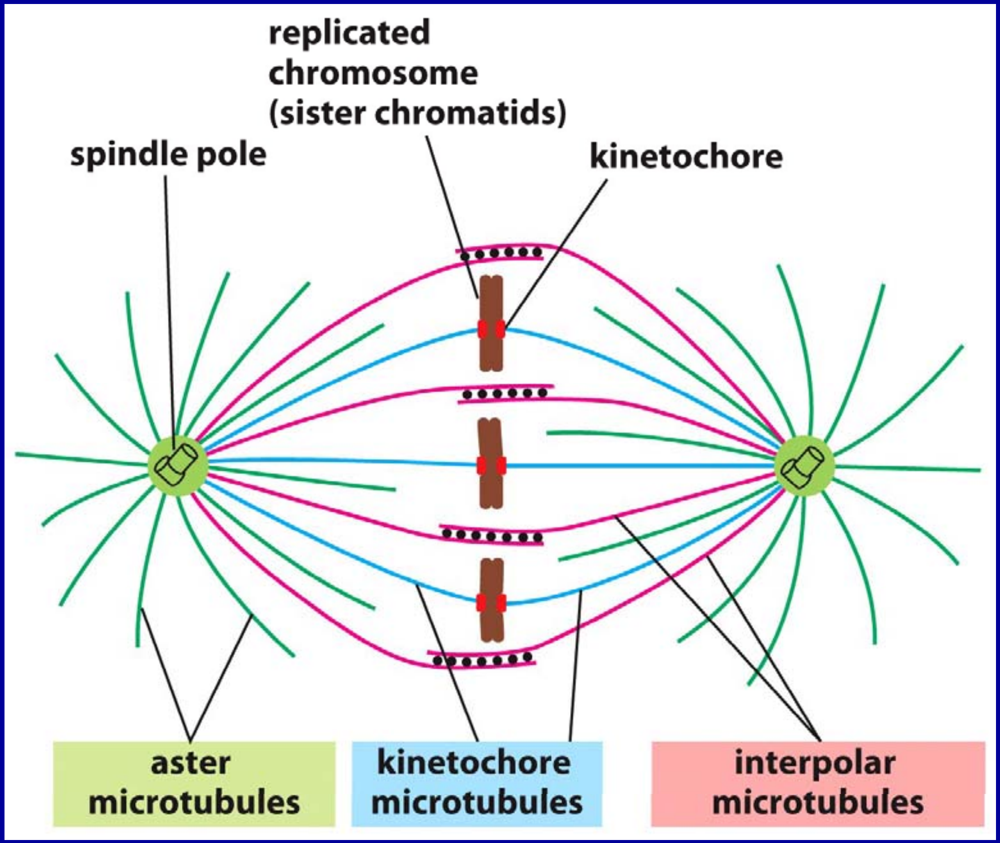


D. Mitosis: Distributing Exact Copies of Genetic Information

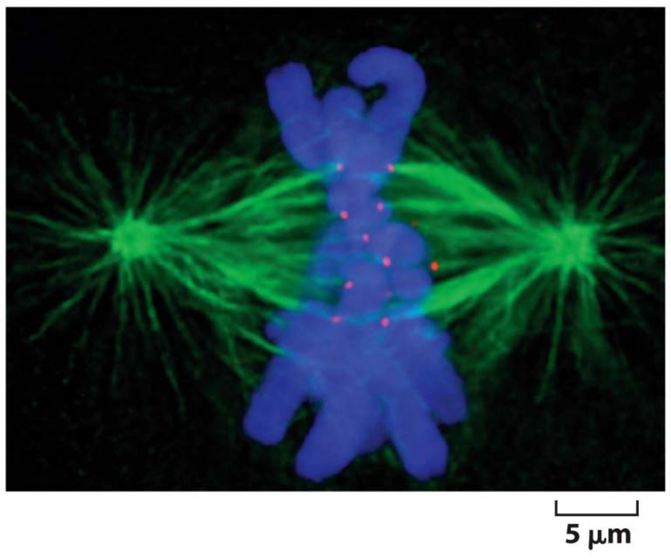
- During prophase, the chromosomes condense and appear as paired chromatids.
- During prometaphase, the chromosomes move toward the middle of the spindle. The nuclear envelope breaks down. Kinetochore microtubules appear and attach the kinetochores to the centrosomes.

The centromere region of a chromosome





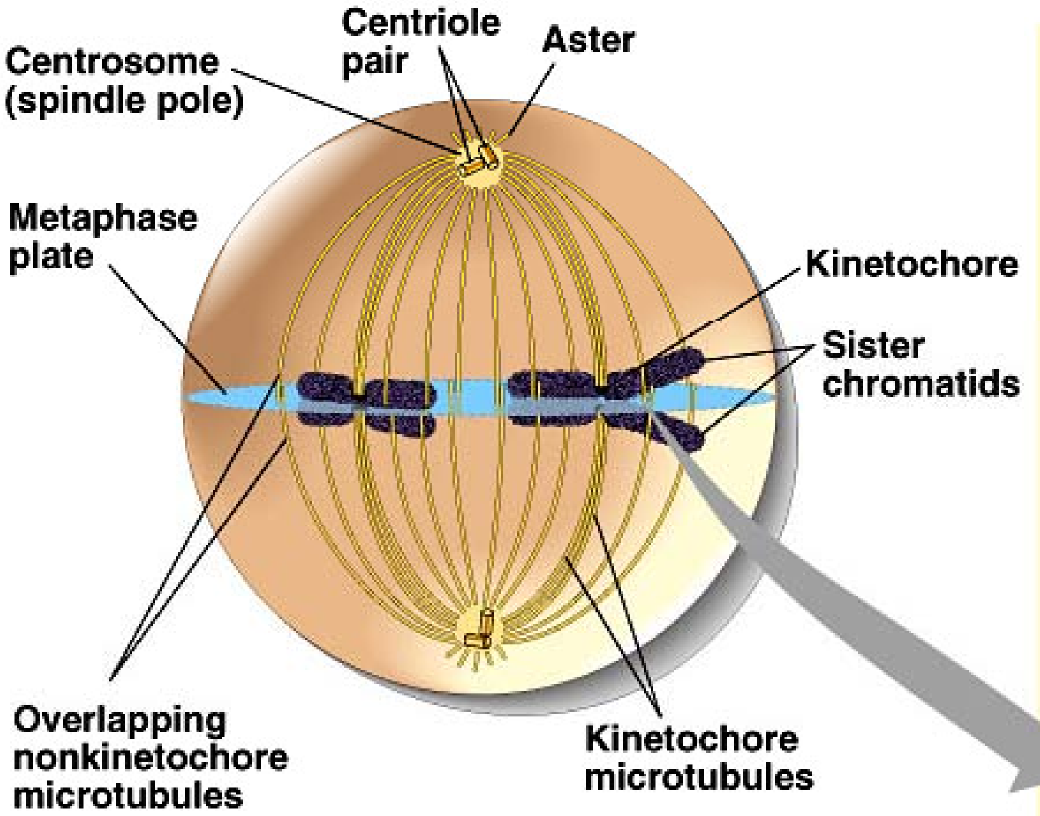
Three classes of microtubules make up
the mitotic spindle



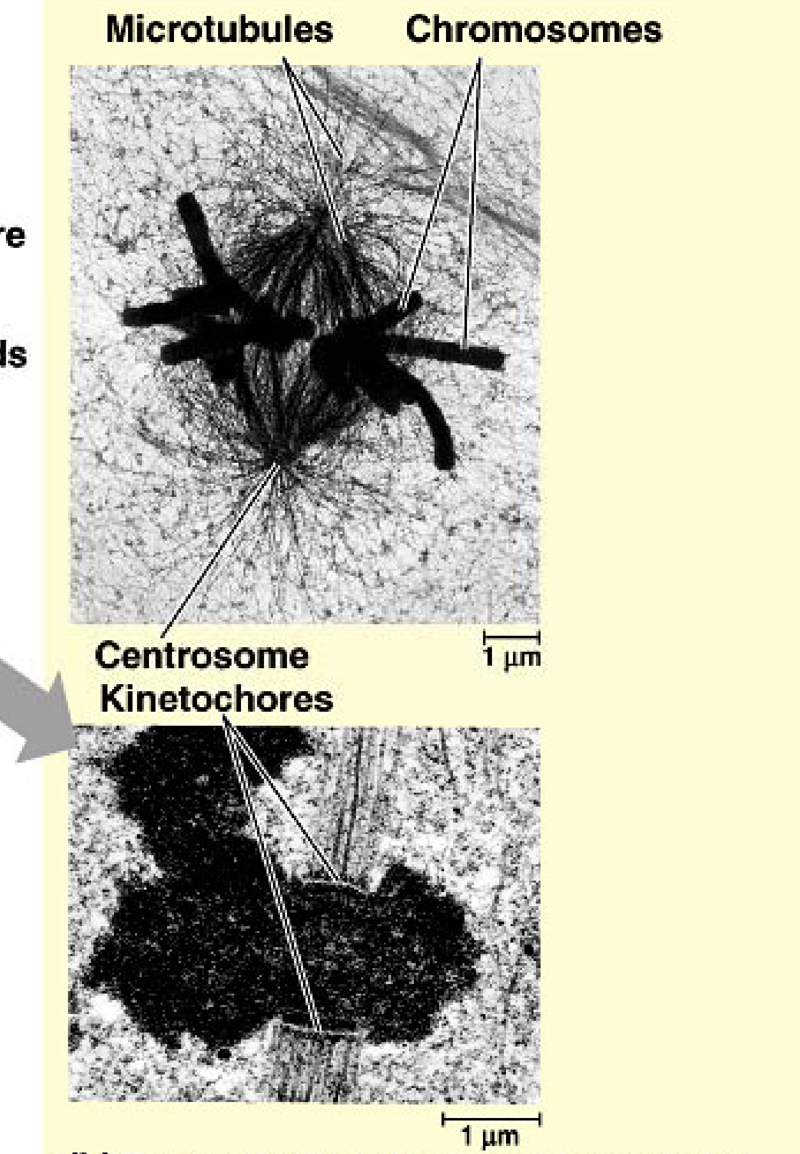
D. Mitosis: Distributing Exact Copies of Genetic Information

- In metaphase, chromatids gather at the middle of the cell, their centromeres on the metaphase plate.
- In anaphase, the centromeres holding the chromatid pairs together separate. Each member of the pair, now called a daughter chromosome, migrates to its pole along the microtubule track.

The mitotic spindle at metaphase



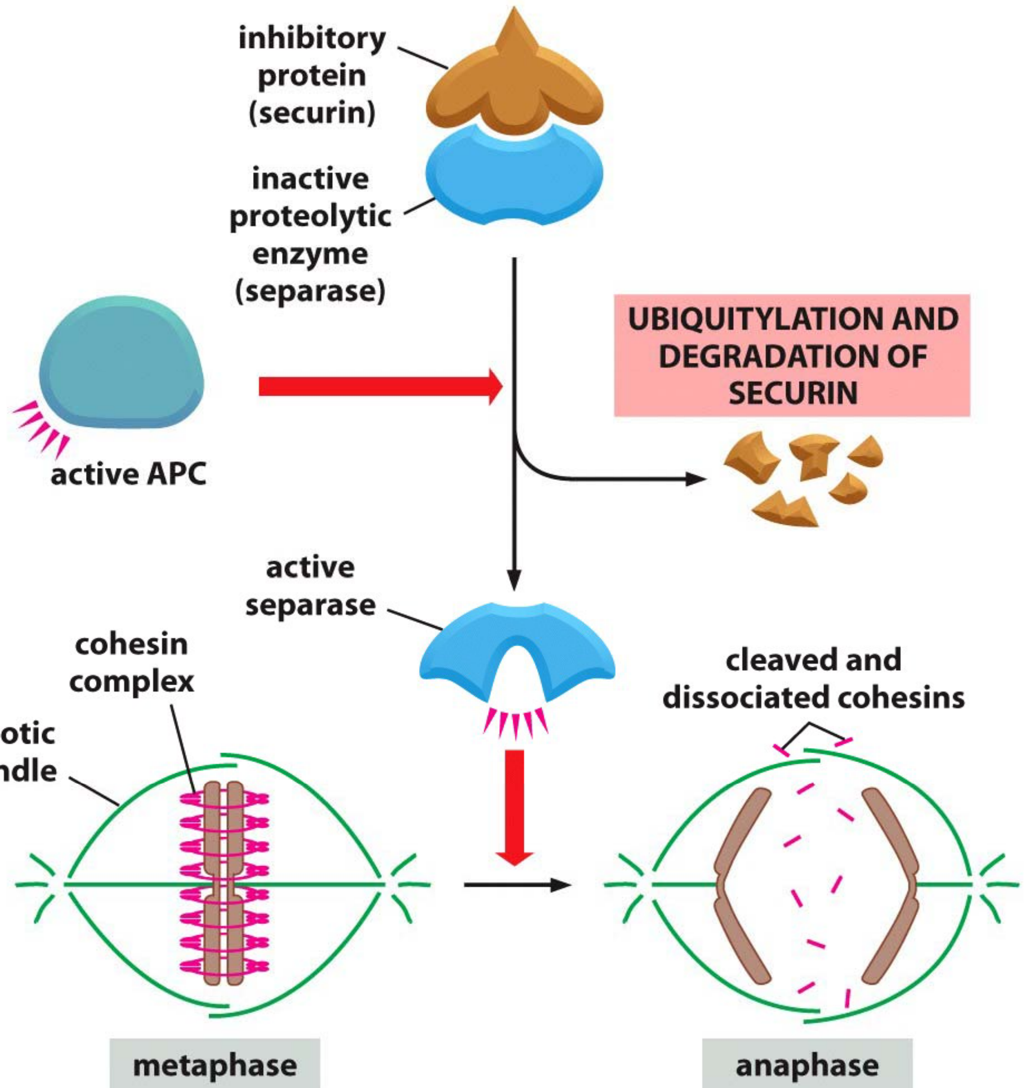
(a) Diagram of two duplicated chromosomes arrayed at the metaphase plate



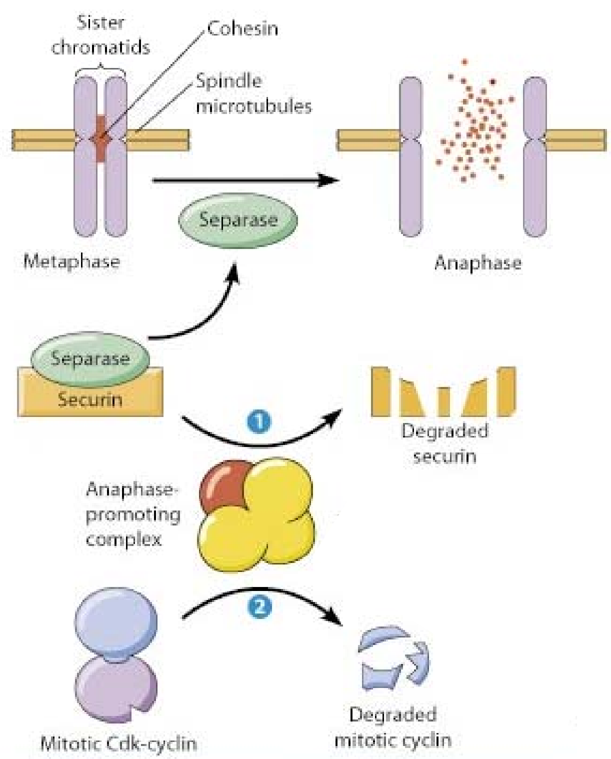
(b) Transmission electron micrographs

From Dr. Matthew Schibler, *Photoplasma* 137 (1987):29–44. Reprinted by permission of Springer-Verlag.

Anaphase Promoting Complex (APC)

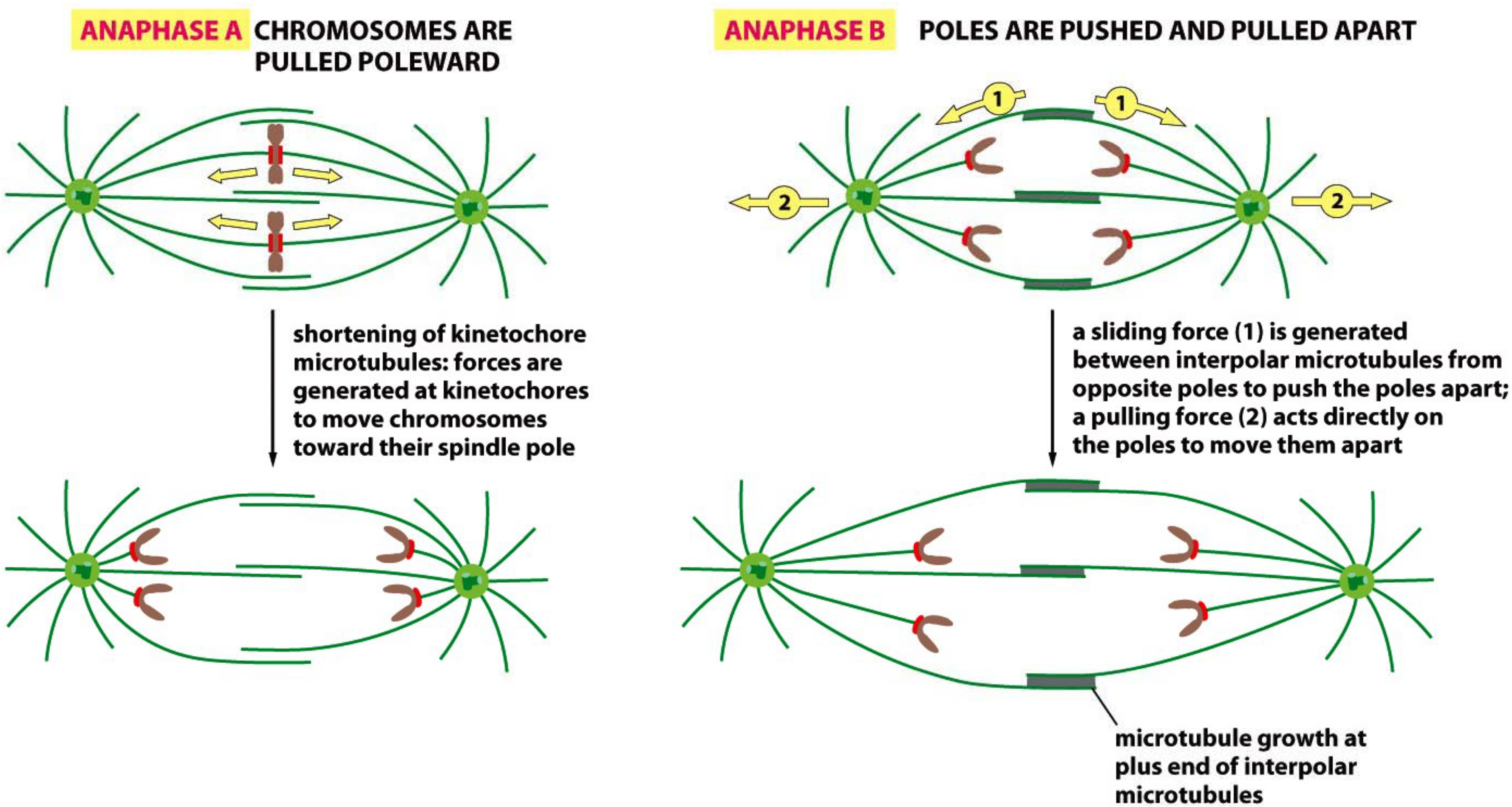


Anaphase Promoting Complex (APC)



(a) **The anaphase-promoting complex** targets securin and mitotic cyclin for degradation. ❶The destruction of securin allows separase to cleave the cohesins that hold sister chromatids together, thereby initiating anaphase. ❷The degradation of mitotic cyclin depresses mitotic Cdk activity, leading to cytokinesis, chromosome decondensation, and nuclear envelope reassembly.

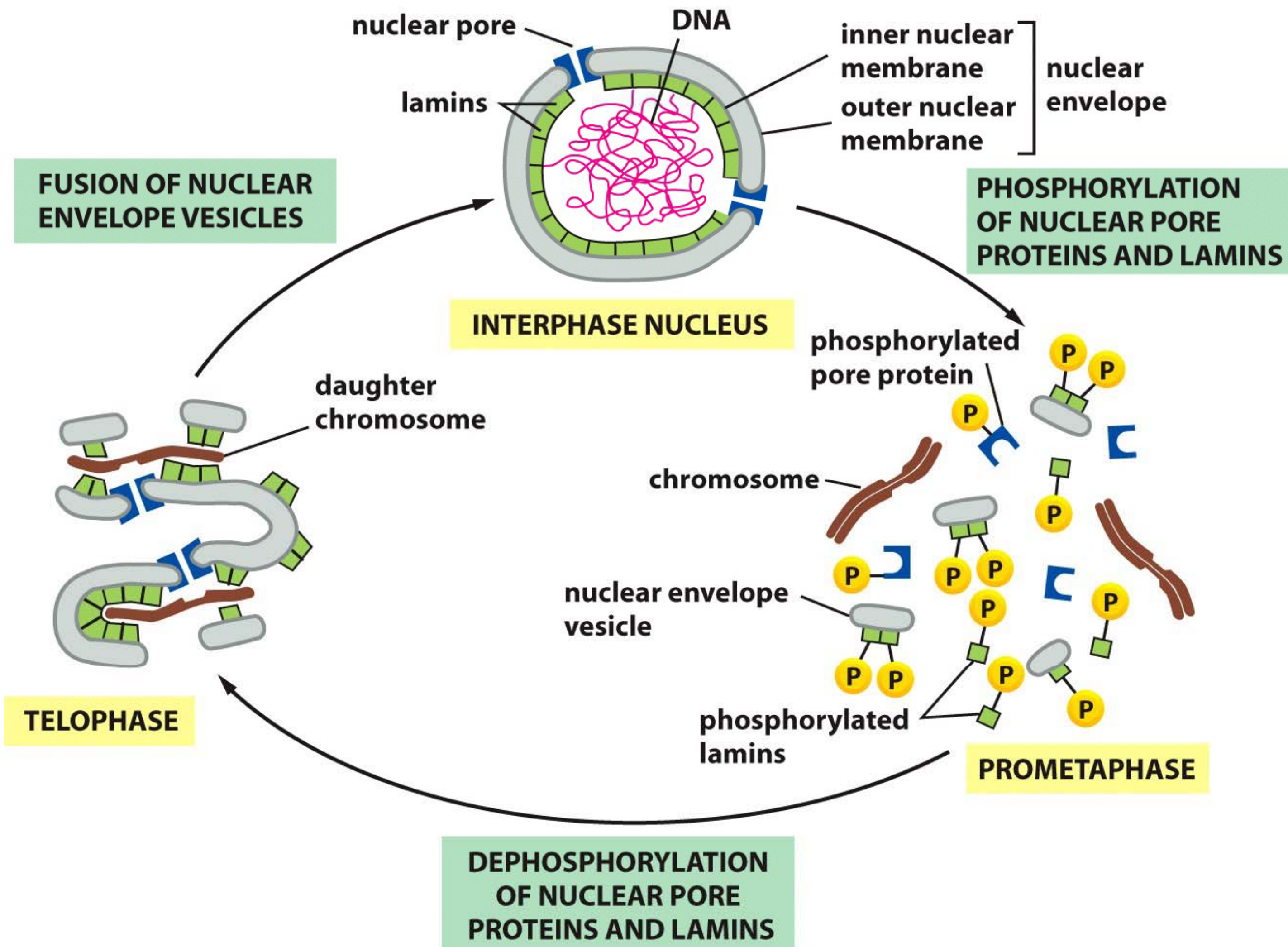
What drives the movements at anaphase?



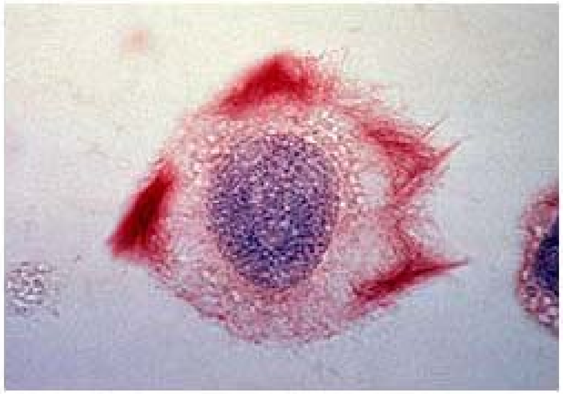
D. Mitosis: Distributing Exact Copies of Genetic Information

- During telophase, the chromosomes become less condensed. The nuclear envelopes and nucleoli re-form, producing two nuclei whose chromosomes are identical to each other and to those of the cell that began the cycle.

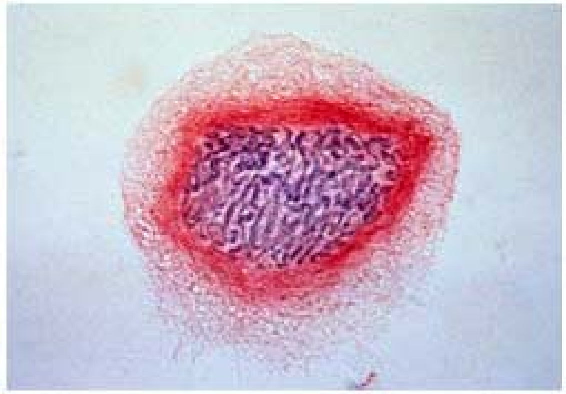
Nuclear envelope reassembly



Mitosis in a plant cell (sans centrosome)

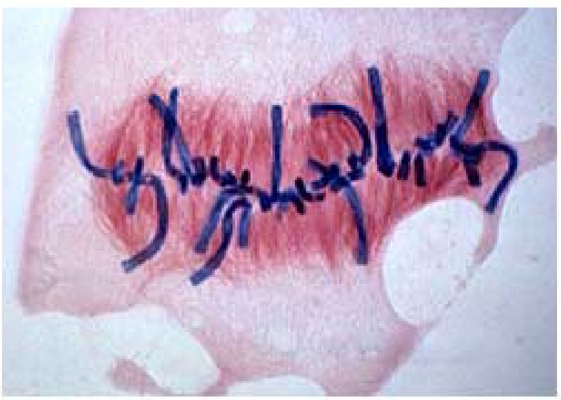


Interphase

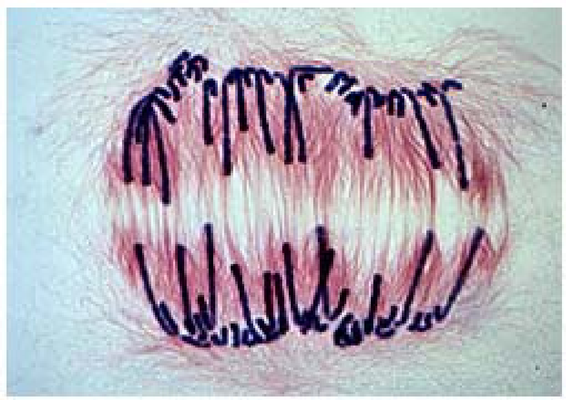


Prophase

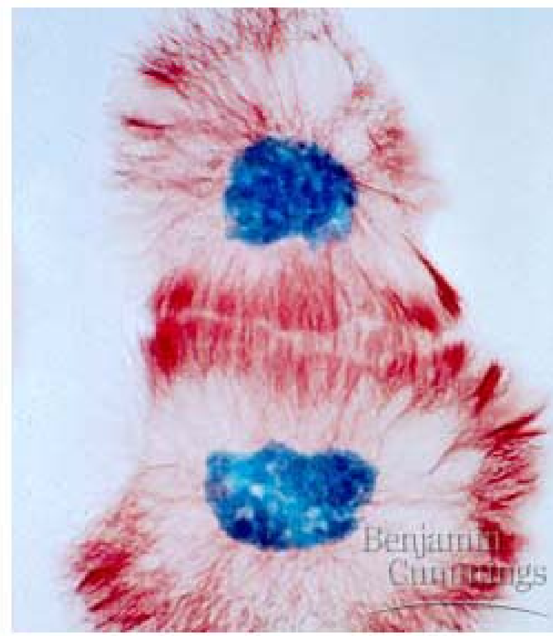
Prometaphase



Metaphase



Anaphase

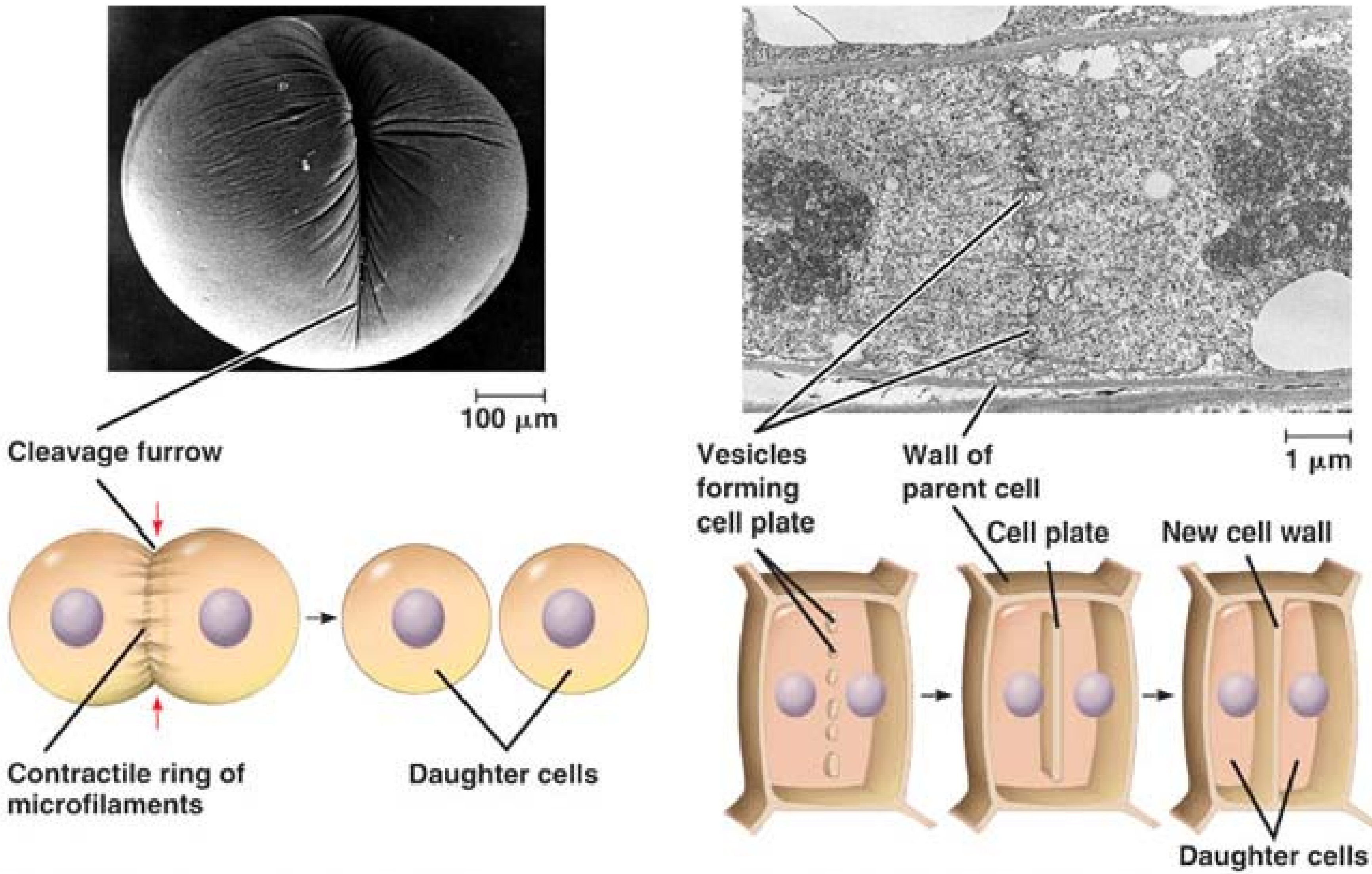


Telophase

E. Cytokinesis: The Division of the Cytoplasm

- Cytokinosis usually follows nuclear division. Animal cell cytoplasm usually divides by plasma membrane furrowing caused by contraction of cytoplasmic actin filaments.
- In plant cells, cytokinesis is accomplished by vesicle fusion and the synthesis of new cell wall material by phragmoplast.

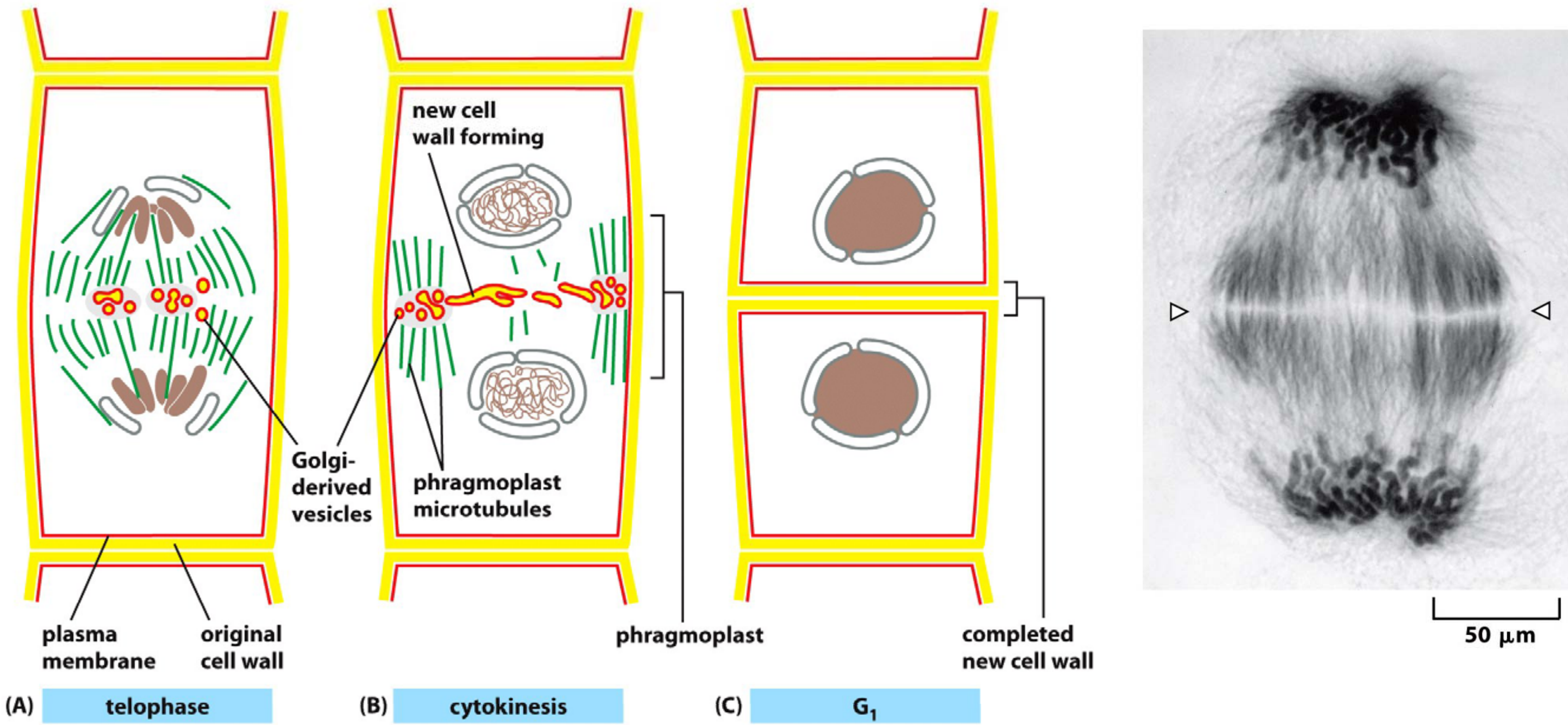
Cytokinesis in animal and plant cells



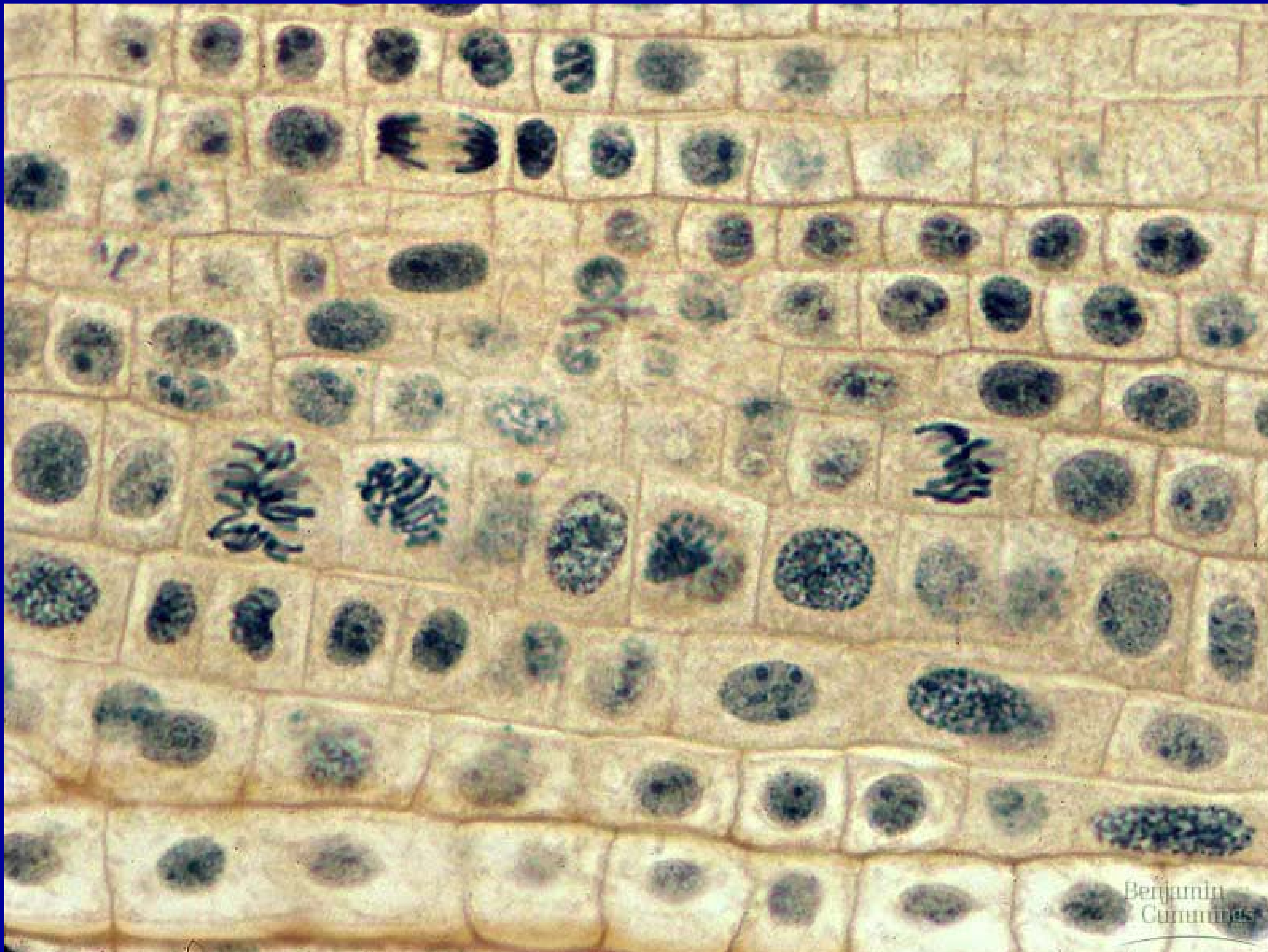
(a) Cleavage of an animal cell (SEM)

(b) Cell plate formation in a plant cell (TEM)

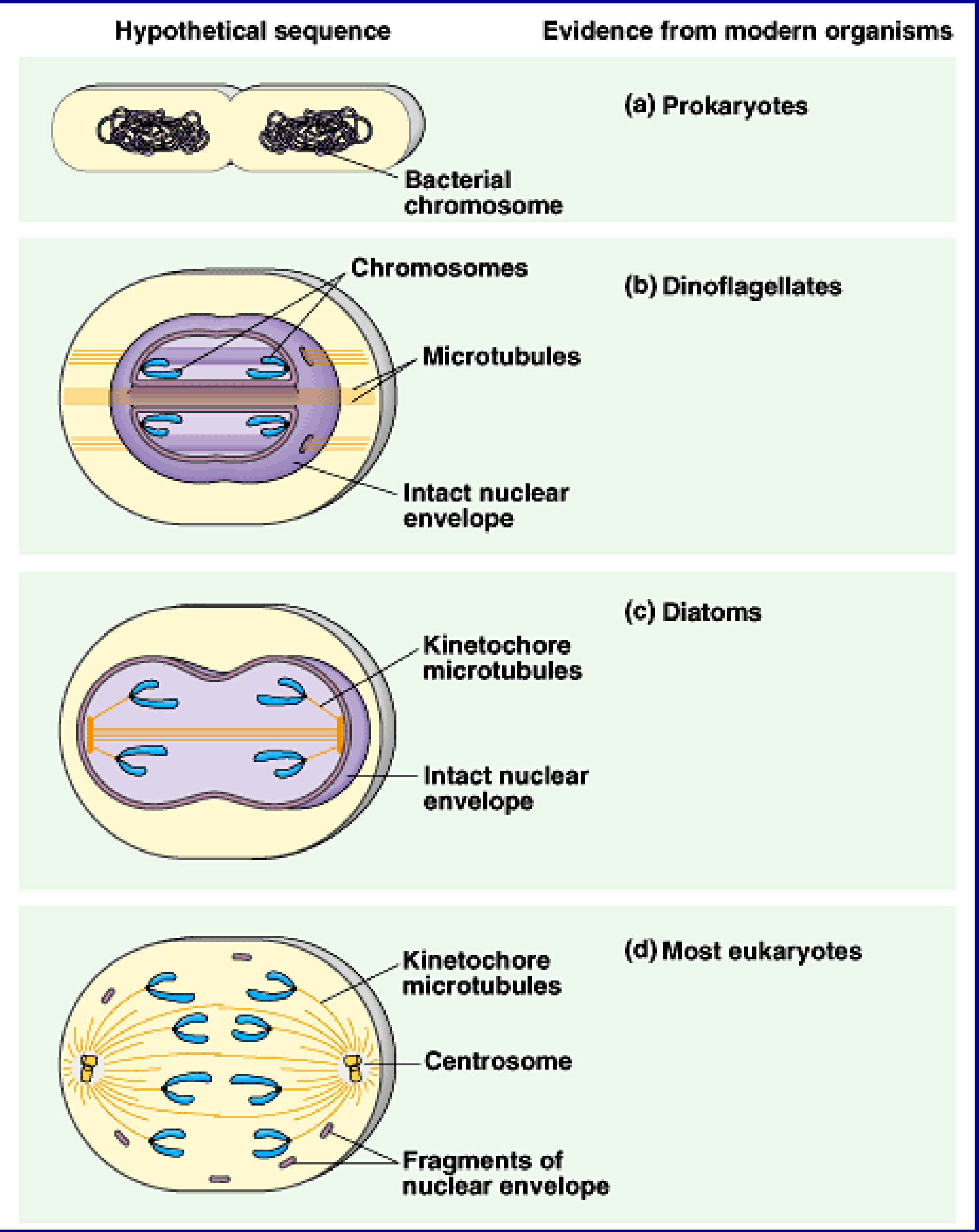
Cytokinesis in plant cells is guided by microtubule-based phragmoplast.



Mitosis in an onion root



A hypothesis for the evolution of mitosis



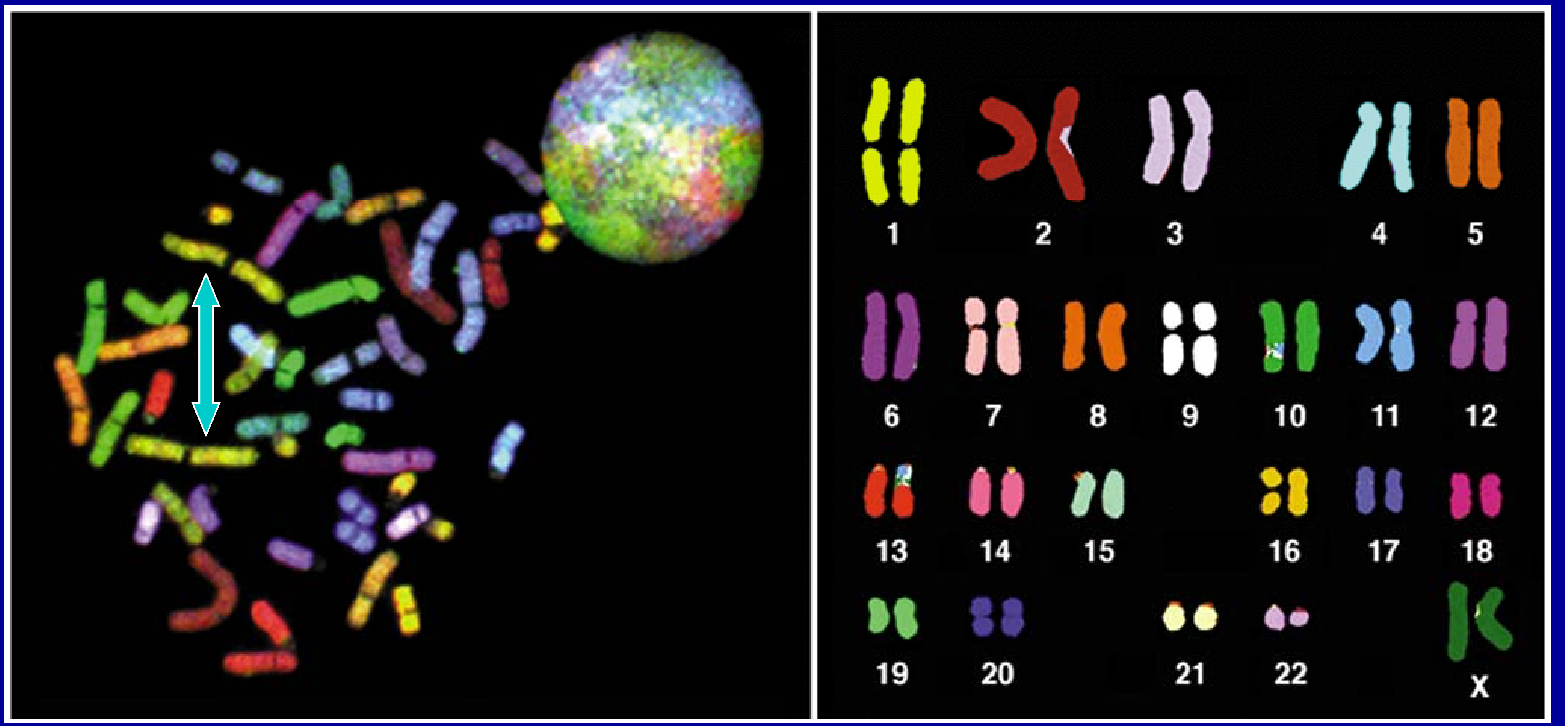
E. Cytokinesis: The Division of the Cytoplasm

- The cell cycle can repeat itself many times, forming a clone of genetically identical cells.
- Asexual reproduction produces an organism genetically identical to the parent. Any genetic variety is the result of mutations.

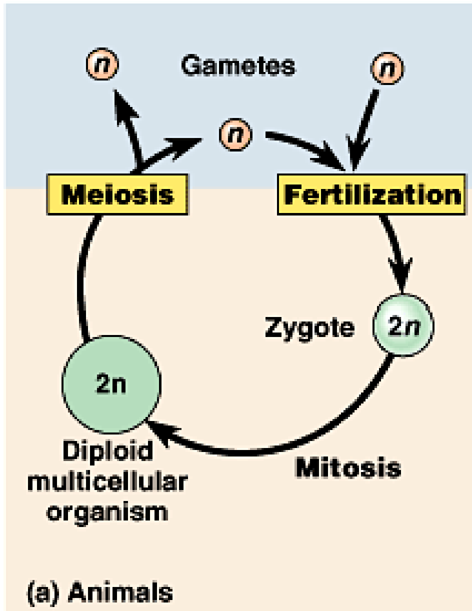
F. Meiosis: Sexual Reproduction and Diversity

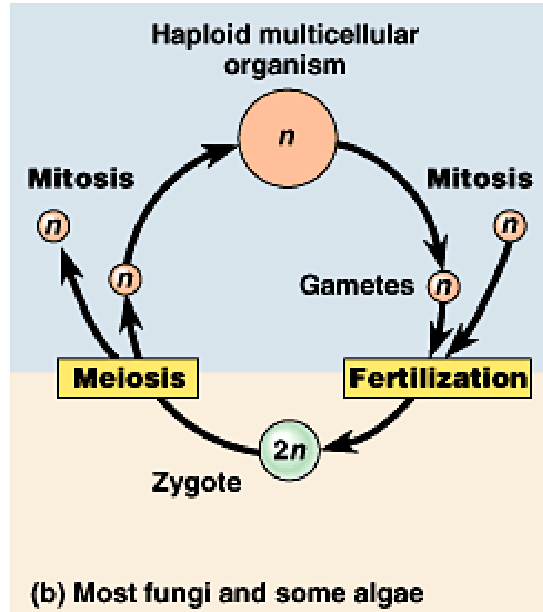
- In sexual reproduction, two haploid gametes—one from each parent—unite in fertilization to form a genetically unique, diploid zygote.
- The number shape and size of metaphase chromosomes constitute a karyotype.
- The more chromosome pairs there are in a diploid cell, the greater the diversity of chromosome combinations generated by meiosis.
- Humans have 23 pairs of chromosomes.

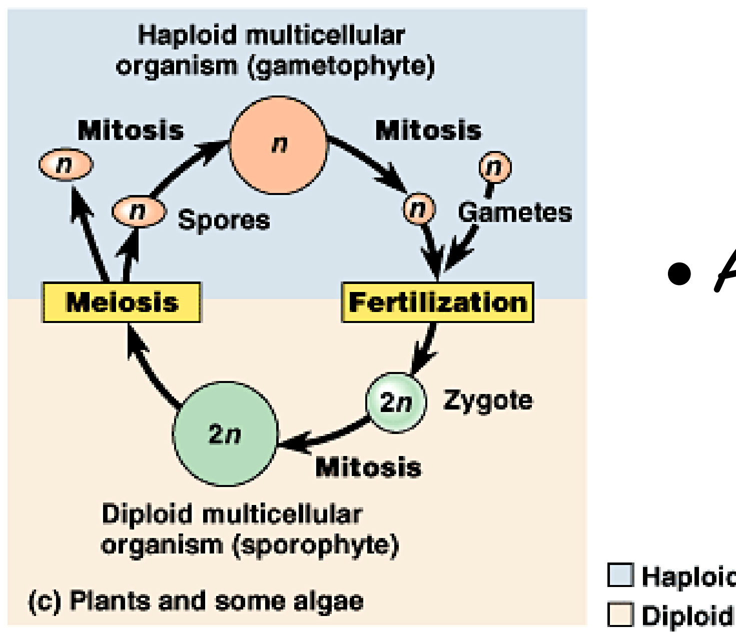
Chromosome Painting and respective Karyotype



Three sexual life cycles differing in the timing of meiosis and fertilization (syngamy)

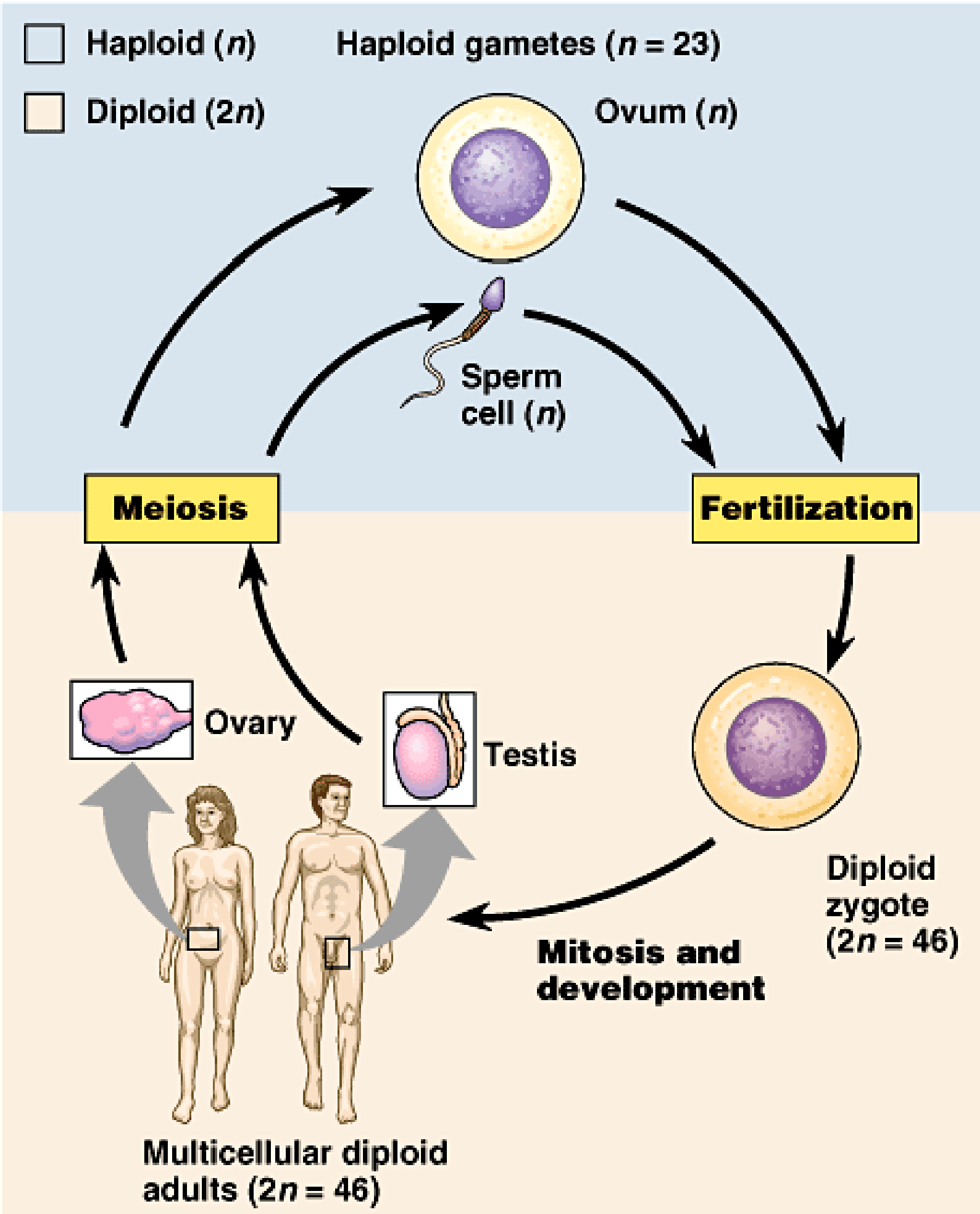






- Alternation of generations

The human life cycle



- **Random** Fertilization

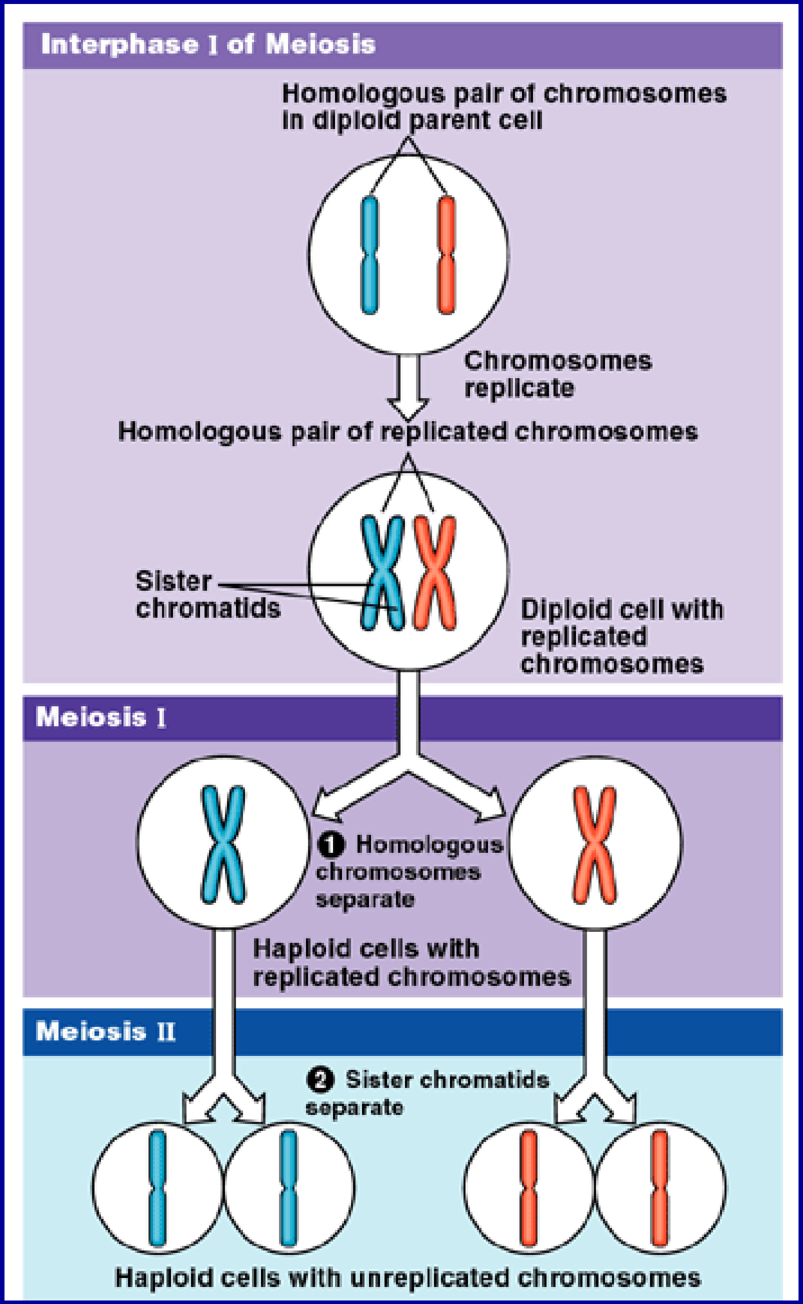
F. Meiosis: Sexual Reproduction and Diversity

- In sexually reproducing organisms, certain cells in the adult undergo meiosis, whereby a diploid cell produces haploid gametes.
- Each gamete contains a random mix of one of each pair of homologous chromosomes from the parent.
- Zygotes are formed by random fertilization which increases diversity.

G. Meiosis: A Pair of Nuclear Divisions

- Meiosis reduces the chromosome number from diploid to haploid and ensures that each haploid cell contains one member of each chromosome pair. It consists of two nuclear divisions.
- We often refer to meiosis as <u>reduction-division</u>.

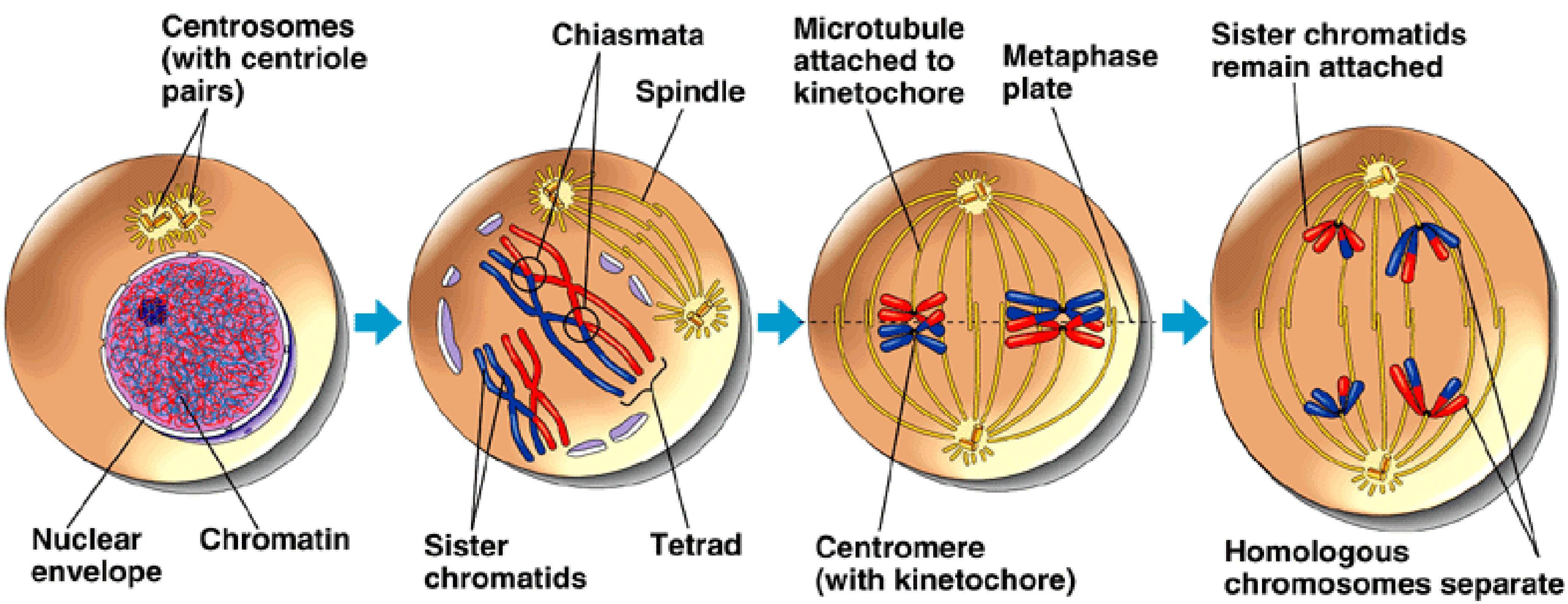
Overview of meiosis: how meiosis reduces chromosome number



The stages of meiotic cell division: Meiosis I

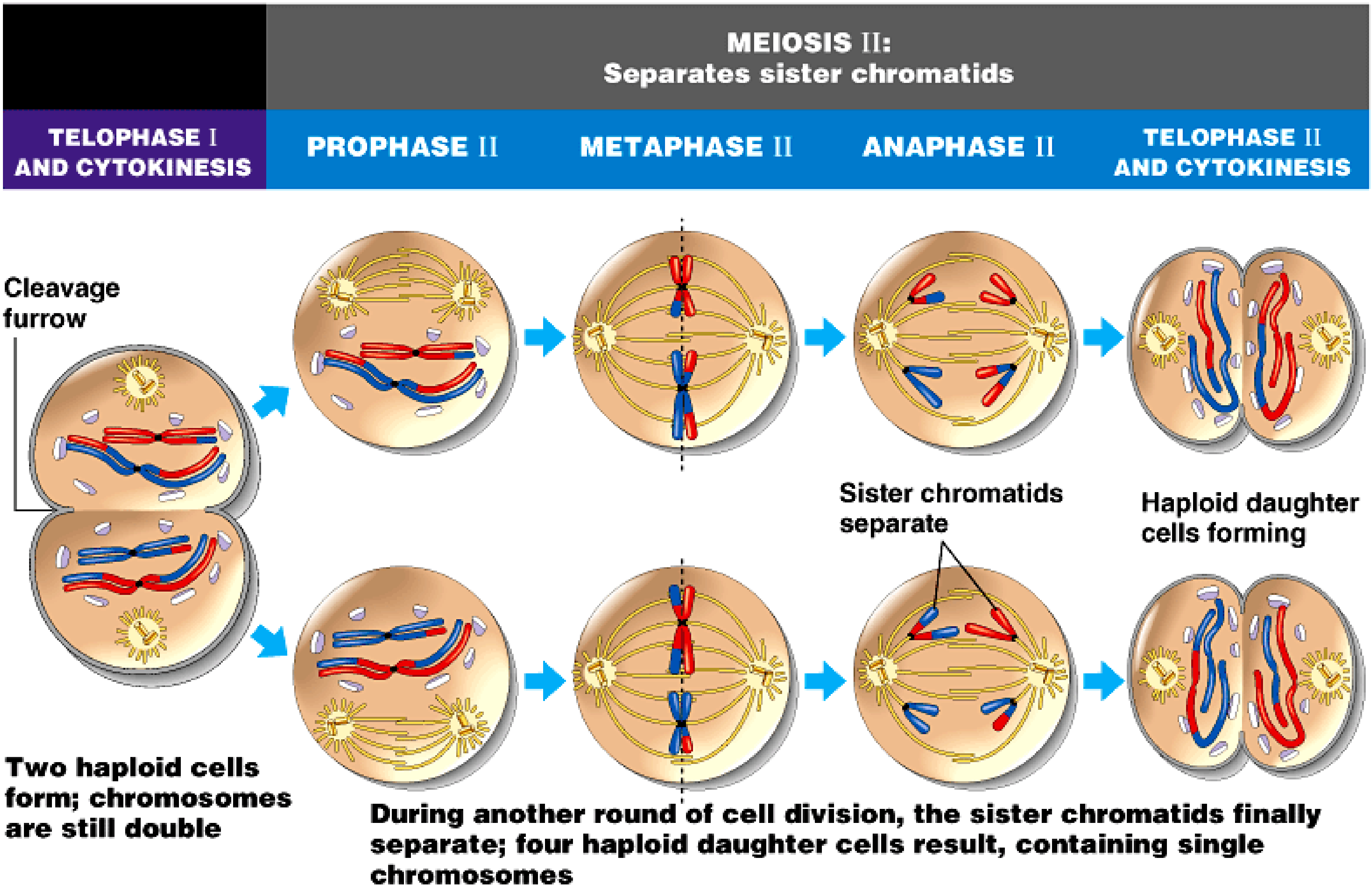
MEIOSIS I:
Separates homologous chromosomes

INTERPHASE	PROPHASE I	METAPHASE I	ANAPHASE I



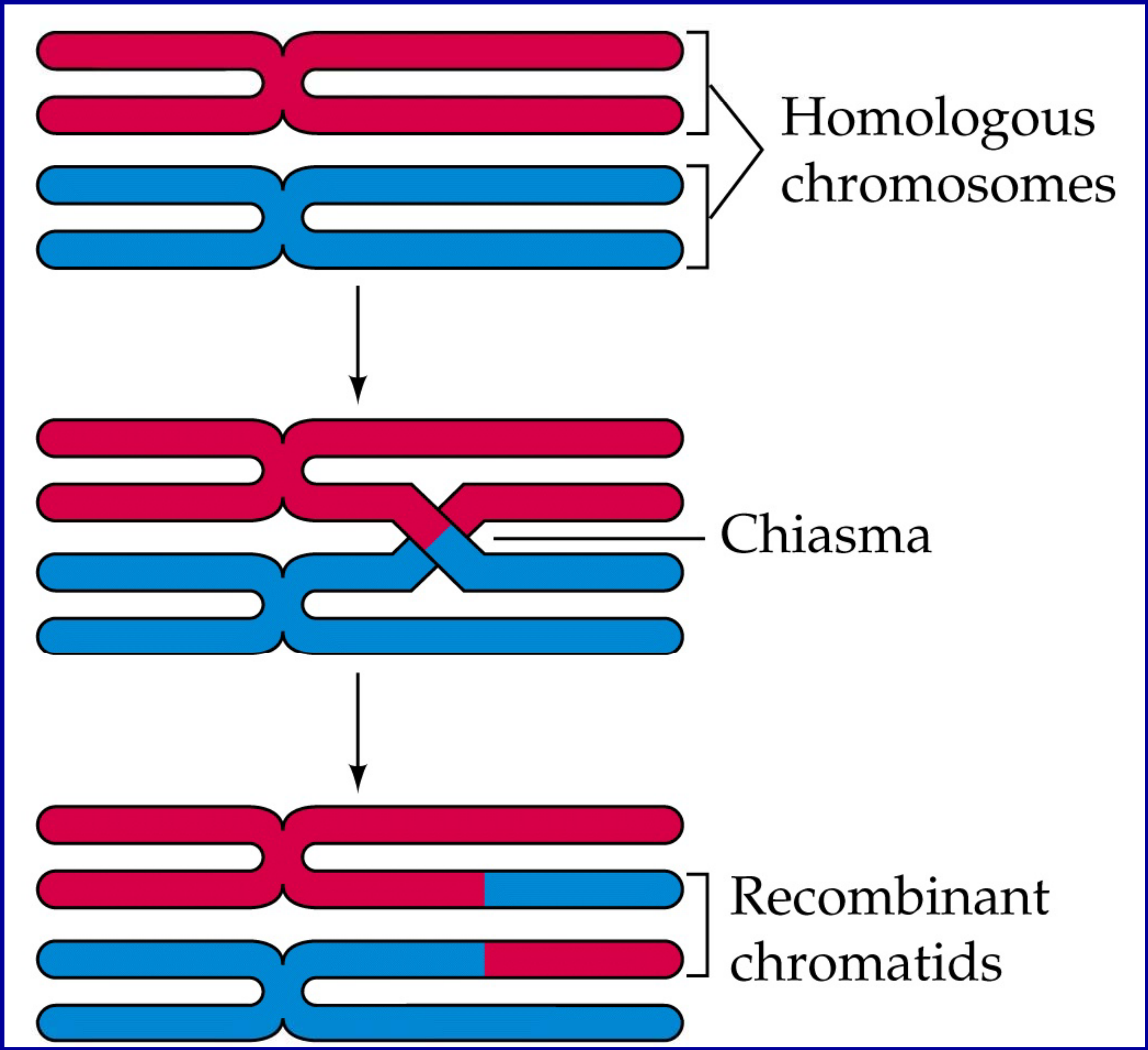
Chromosomes duplicate	Homologous chromosomes pair and exchange segments	Tetrads line up	Pairs of homologous chromosomes split up

The stages of meiotic cell division: Meiosis II



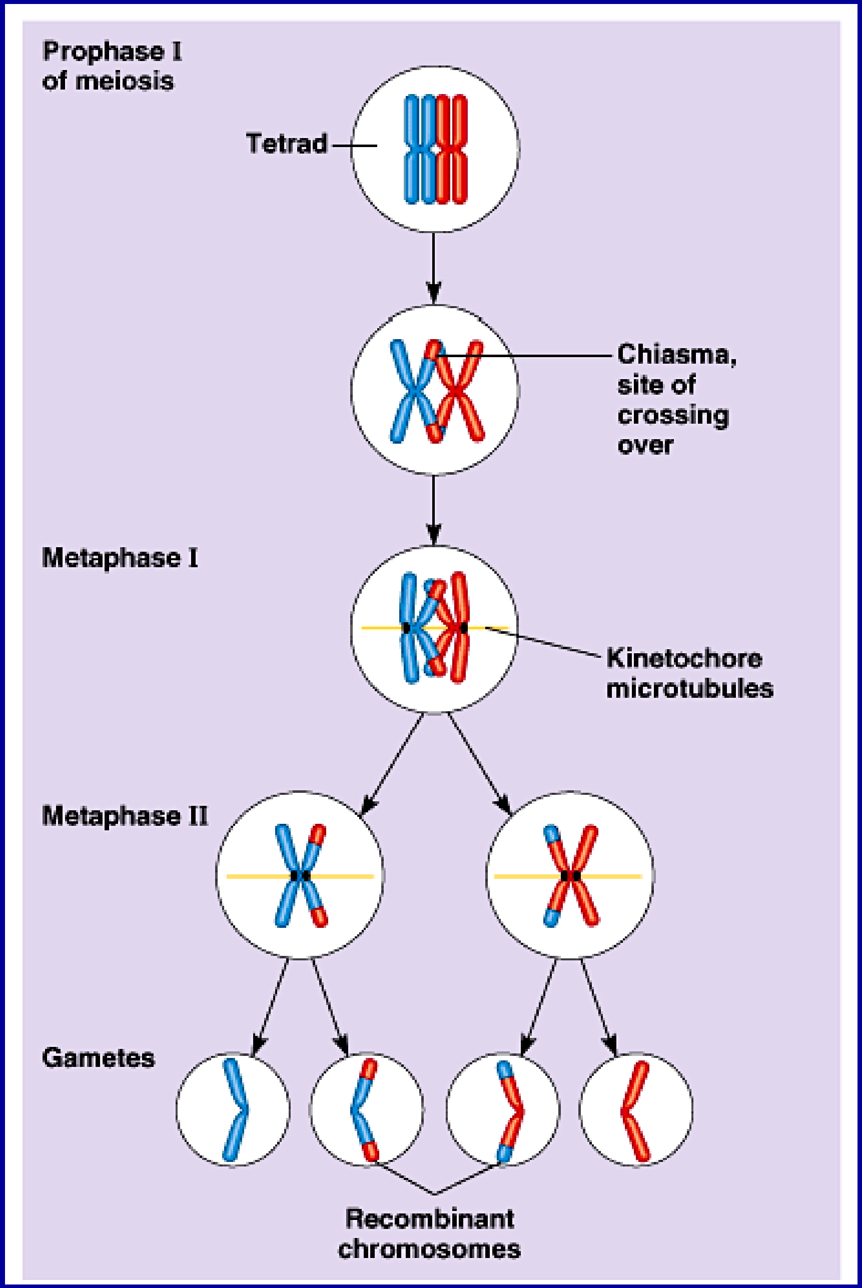
G. Meiosis: A Pair of Nuclear Divisions

- During prophase I of the first meiotic division, homologous chromosomes pair, and material may be exchanged by <u>crossing over</u> between nonsister chromatids of two adjacent homologs.
- In metaphase I, the paired homologs gather at the equatorial plate. Each chromosome has one kinetochore and associates with polar microtubules for one pole.
- In anaphase I, entire chromosomes, each with two chromatids, migrate to the poles. By the end of meiosis I, there are two nuclei, each with the haploid number of chromosomes but with two sister chromatids.



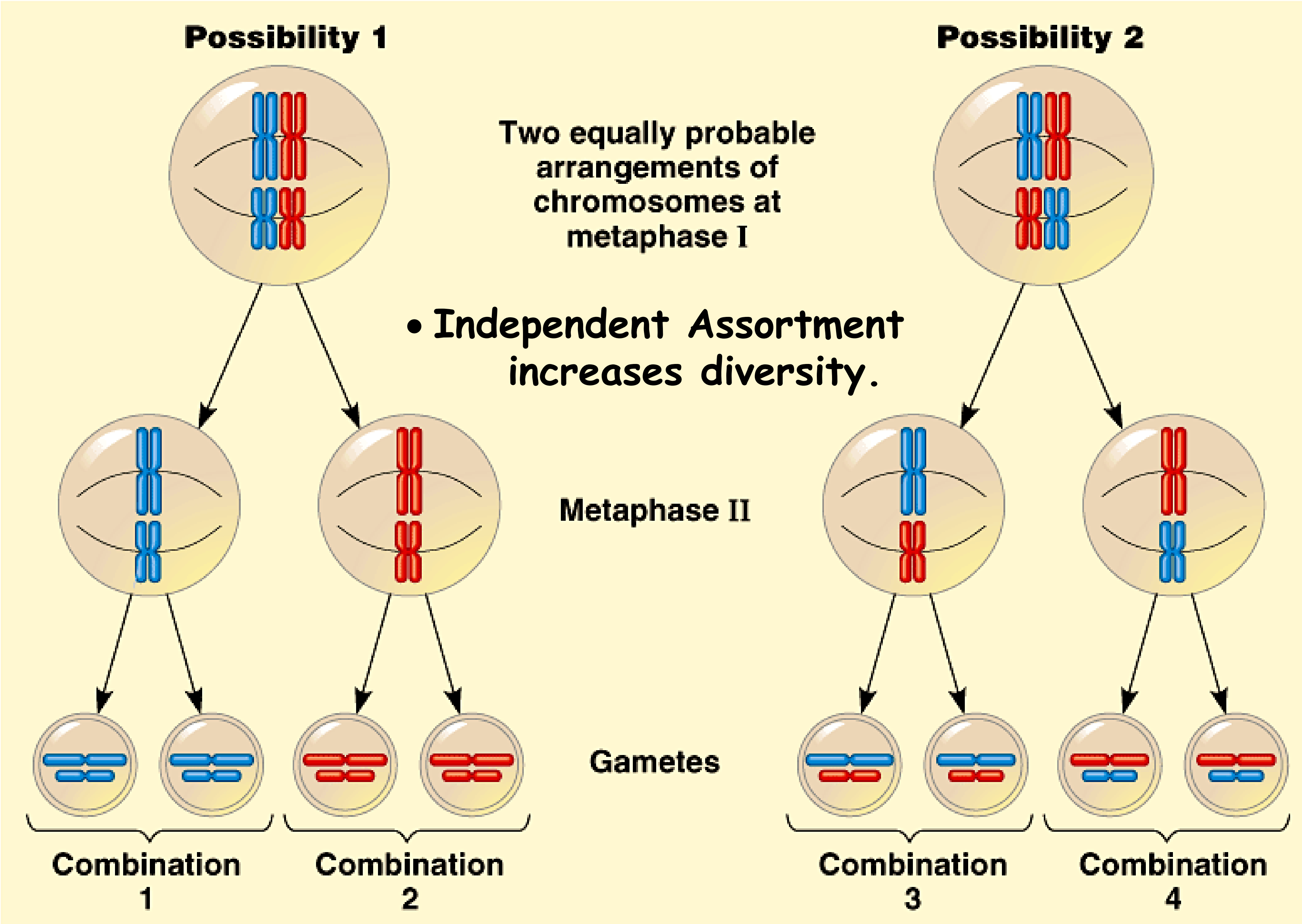
Synapsis: Crossing over of nonsister chromatids.

The results of crossing over during meiosis



- Crossing over increases diversity.

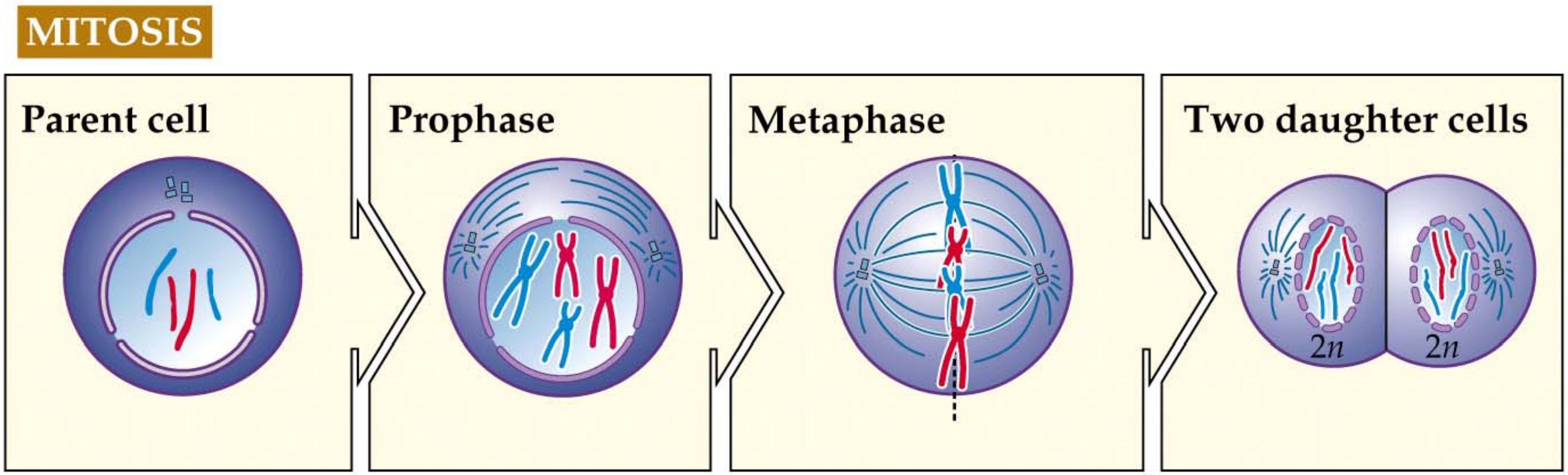
The results of alternative arrangements of two homologous chromosome pairs on the metaphase plate in meiosis I aka Independent Assortment



- Independent Assortment increases diversity.

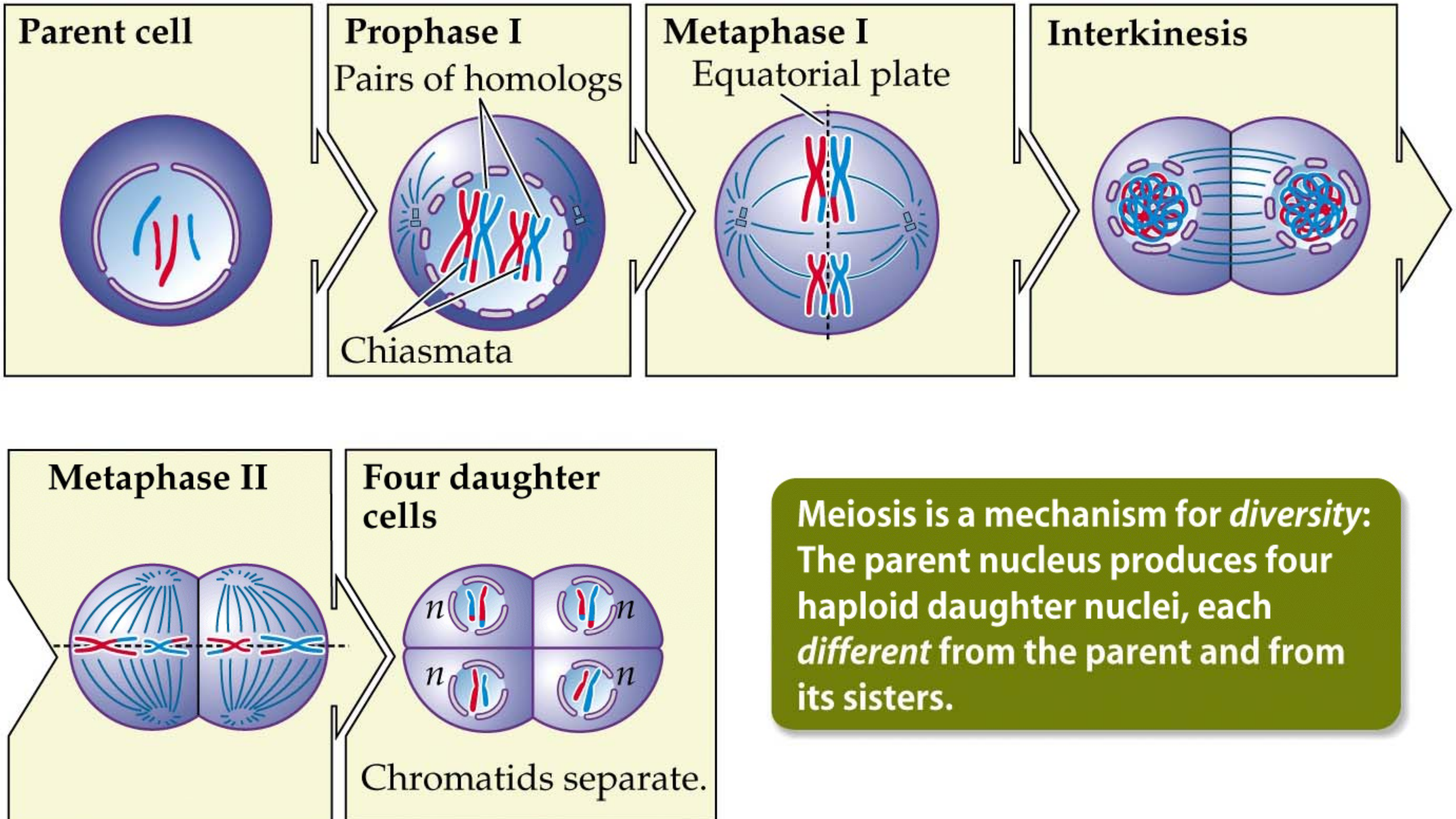
G. Meiosis: A Pair of Nuclear Divisions

- In meiosis II, the sister chromatids separate. No DNA replication precedes this division, which in other aspects is similar to mitosis. The result of meiosis is four cells, each with a haploid chromosome content.



Mitosis is a mechanism for *constancy*: The parent nucleus produces two daughter nuclei, *identical* to the parent and to each other.

MEIOSIS


Parent cell
Prophase I
Pairs of homologs
Chiasmata
Metaphase I
Equatorial plate
Interkinesis
Metaphase II
Four daughter cells
n
n
n
n
Chromatids separate.
Meiosis is a mechanism for *diversity*: The parent nucleus produces four haploid daughter nuclei, each *different* from the parent and from its sisters.

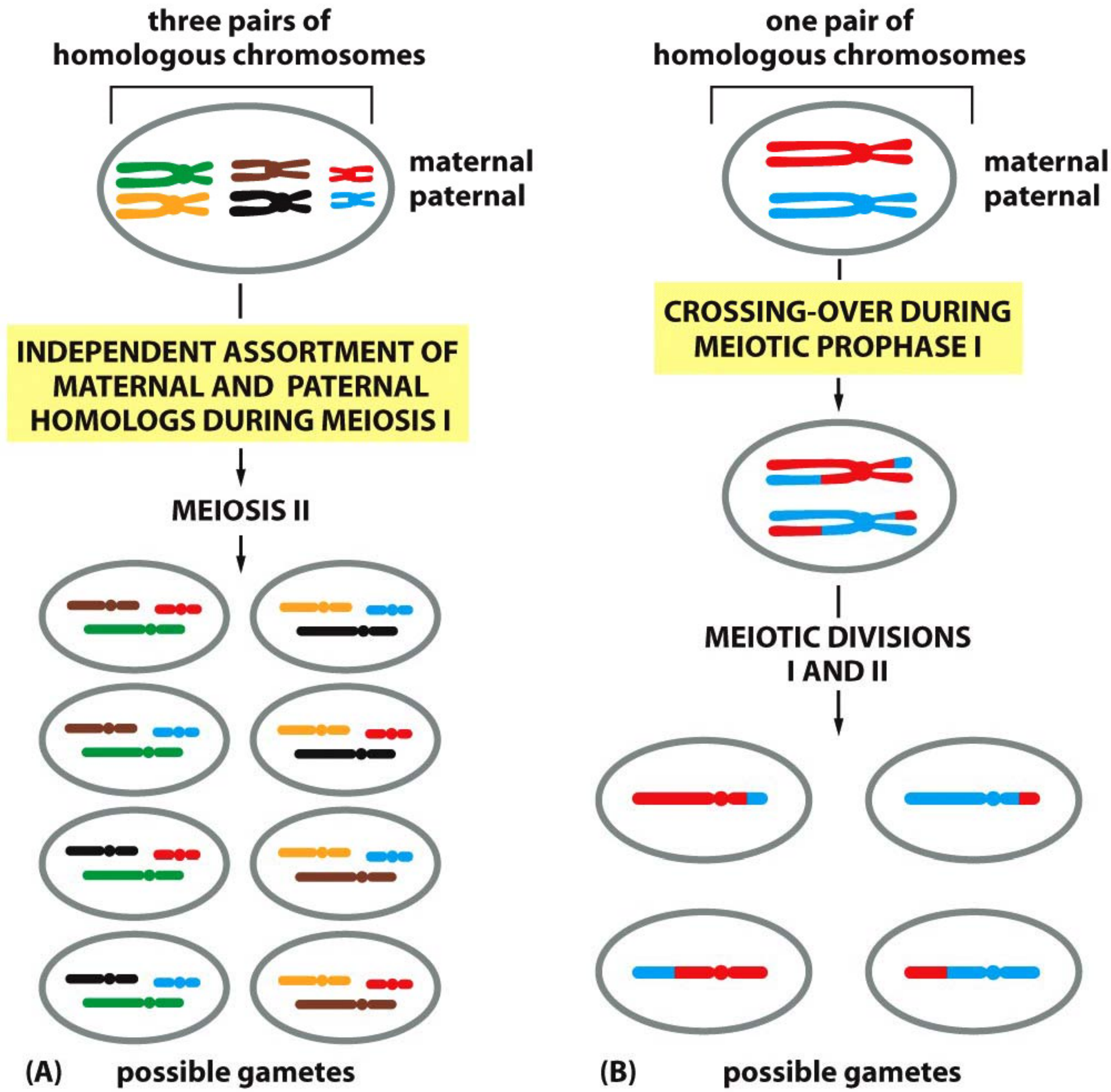
H. Origins of Genetic Variation Among Offspring

- Mutations
  - Are the original source of genetic variation.
- Sexual Reproduction
  - Produces new combinations of variant genes, adding more genetic diversity.

H. Origins of Genetic Variation Among Offspring

- In species that produce sexually, the behavior of chromosomes during meiosis AND fertilization is responsible for most of the variation that arises each generation. Genetics = Applied Meiosis!

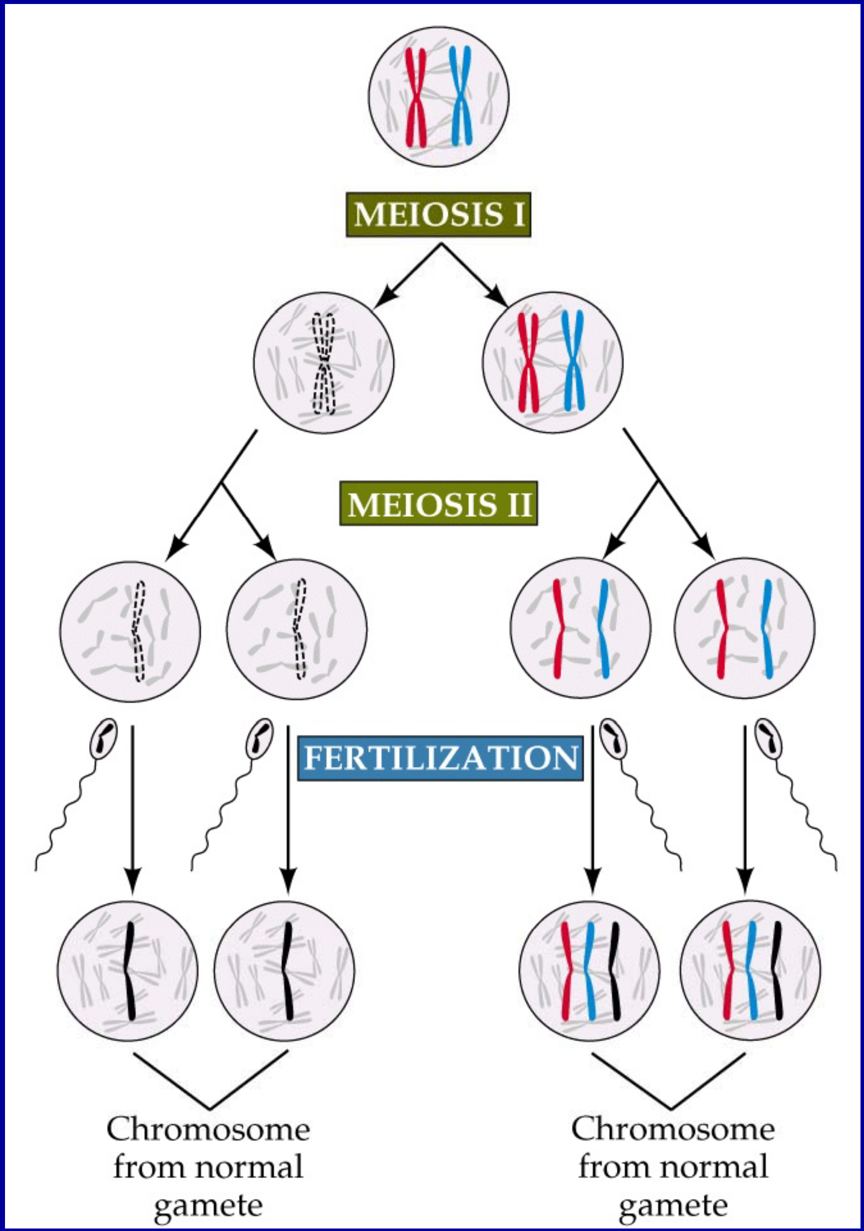
  - *Independent Assortment of Chromosomes*
    - Homologous pairs of chromosomes orient randomly at metaphase I of meiosis.
  - *Crossing over*
    - Produces recombinant chromosomes that carry genes derived from two different parents during prophase I of meiosis.
  - *Random Fertilization*
    - The fusion of gametes will produce a zygote with any of about 64 trillion diploid combinations.



Combos: 2^n where n = # chromosome pairs

I. Meiotic Errors: Source of Chromosomal Disorders

- In nondisjunction, one member of a homologous pair of chromosomes fails to separate from the other, and both go to the same pole. This event leads to one gamete with an extra chromosome and another other lacking that chromosome.
- Fertilization with a normal haploid gamete results in aneuploidy and genetic abnormalities that are invariably harmful or lethal to the organism.



Nondisjunction in gamete

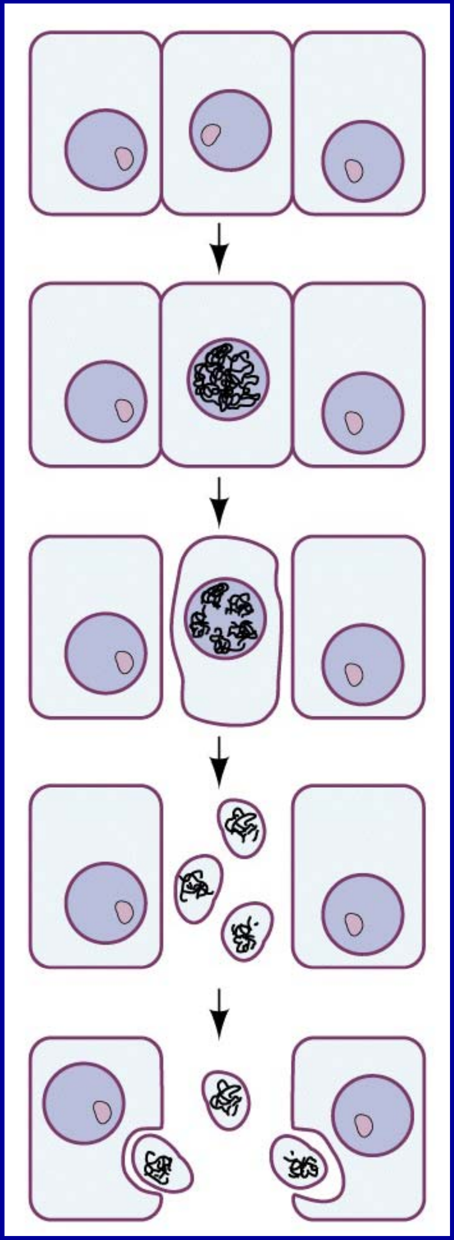
Aneuploidy in zygote

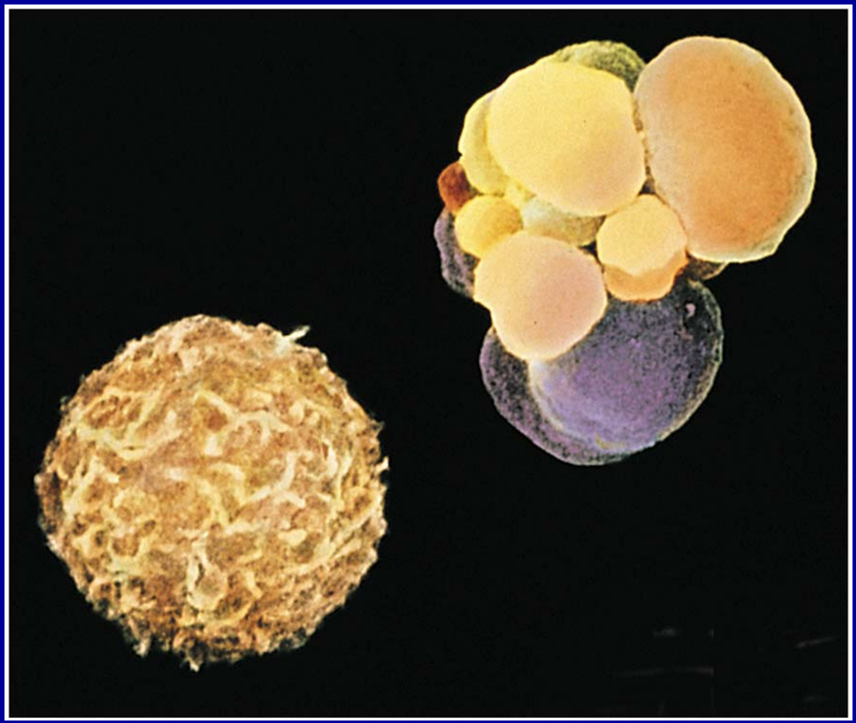
J. Cell Death

- Cells may die by necrosis or may self-destruct by apoptosis, a genetically programmed series of events that includes the detachment of the cell from its neighbors and the fragmentation of its nuclear DNA.

9.2 *Two Different Ways for Cells to Die*

	NECROSIS	APOPTOSIS
Stimuli	Low O_2, toxins, ATP depletion, damage	Specific, genetically programmed physiological signals
ATP required	No	Yes
Cellular pattern	Swelling, organelle disruption, tissue death	Chromatin condensation, membrane blebbing, single-cell death
DNA breakdown	Random fragments	Nucleosome-sized fragments
Plasma membrane	Burst	Blebbed
Fate of dead cells	Ingested by phagocytes	Ingested by neighboring cells
Reaction in tissue	Inflammation	No inflammation





Membrane "Blebbing"
by a WBC via apoptosis.