Cell division

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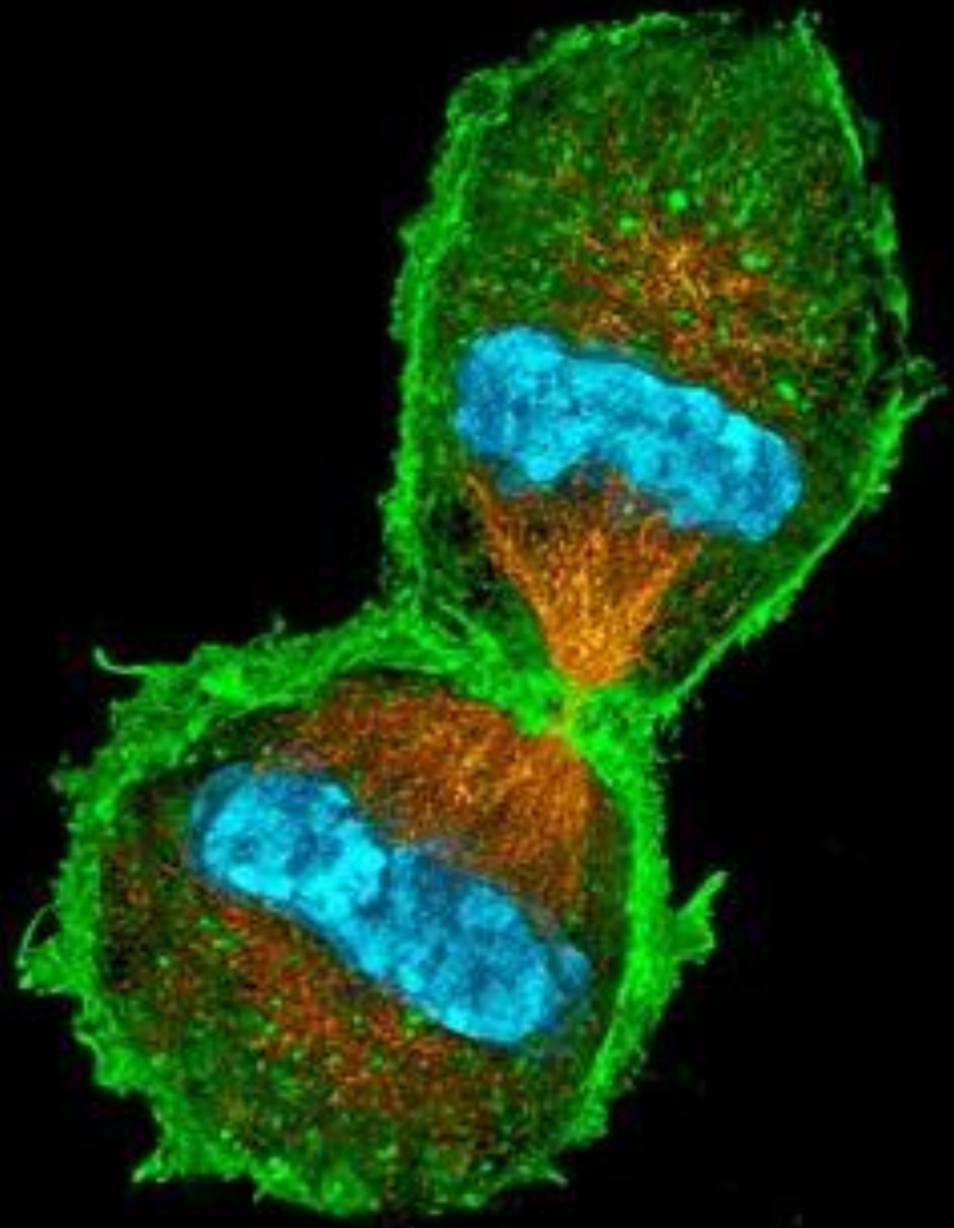
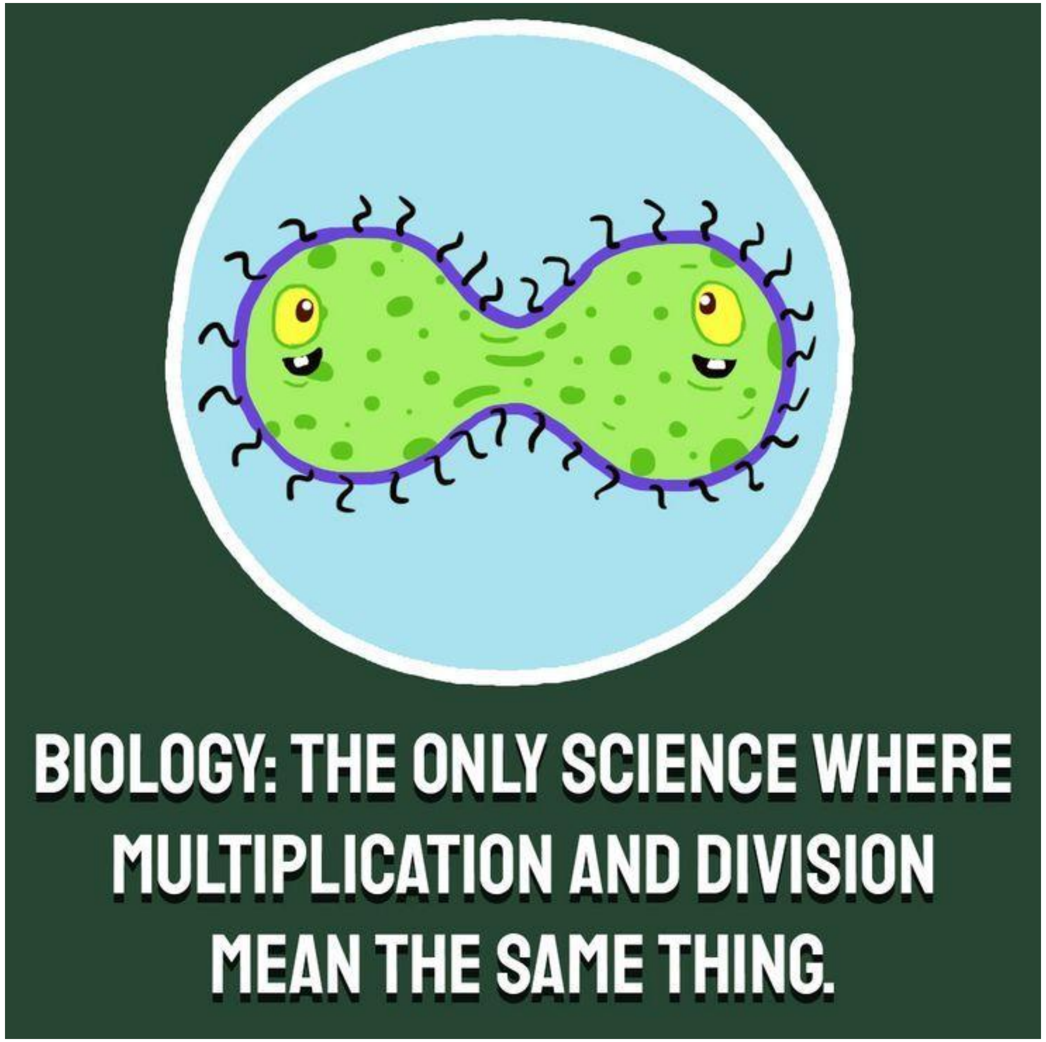


Outline

- Cell division in prokaryotes: binary fission
- Cell division in eukaryotes
- Mitosis
- Cytokinesis
- Meiosis



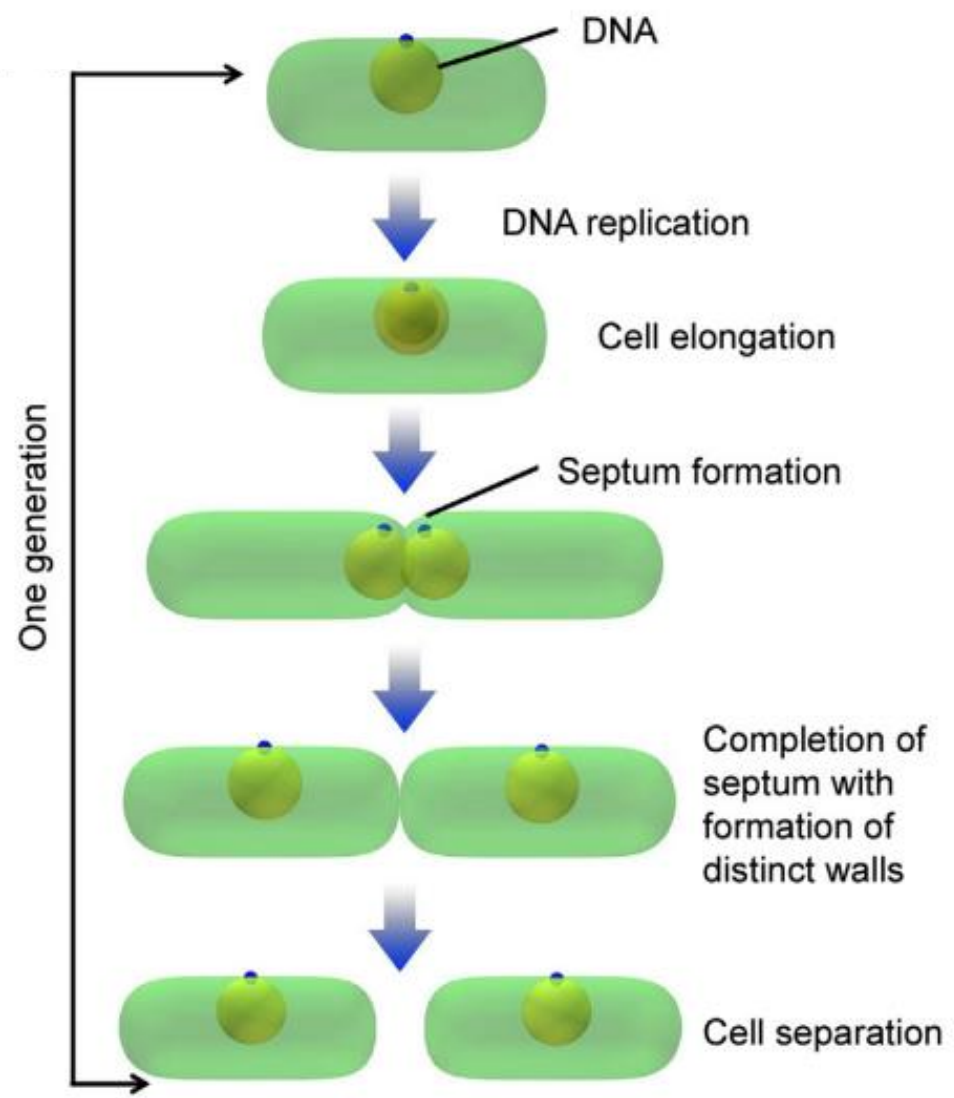
Omnis cellula e cellula

- **Law of cell lineage: *each cell (stems) from another cell***

Cell division in prokaryotes: binary fission

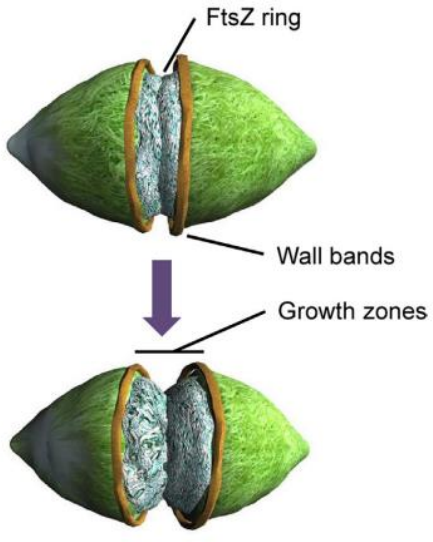
Binary fission

1. Duplication of the chromosome
2. Cell growth/elongation
3. Formation of septum (cross wall)
4. Separation of daughter cells

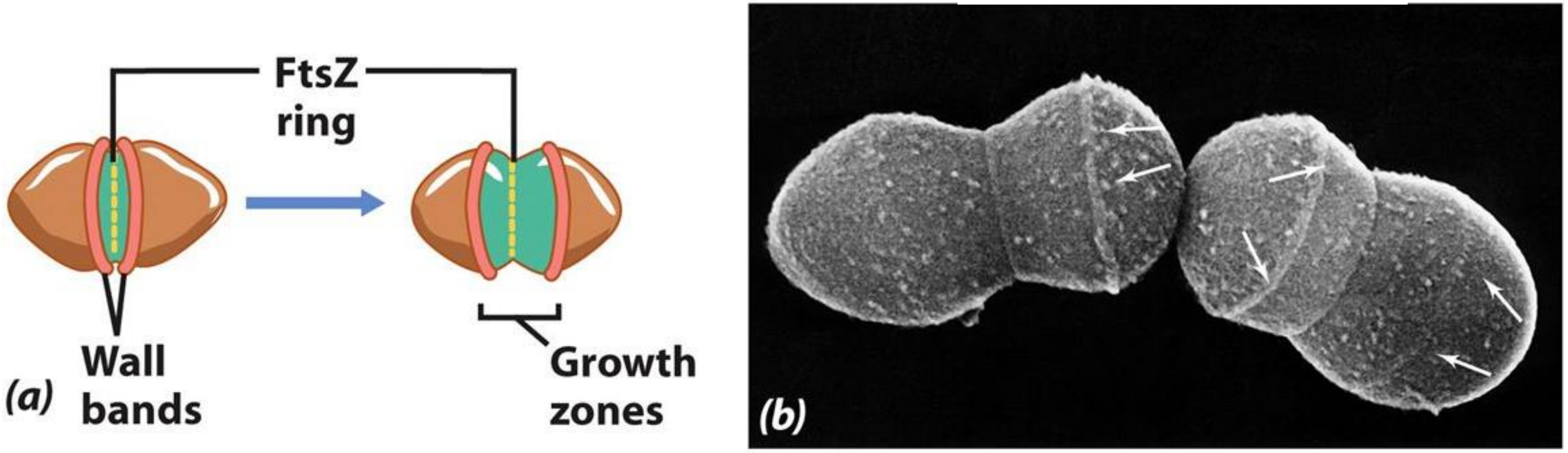


Fission mediated by FtsZ ring

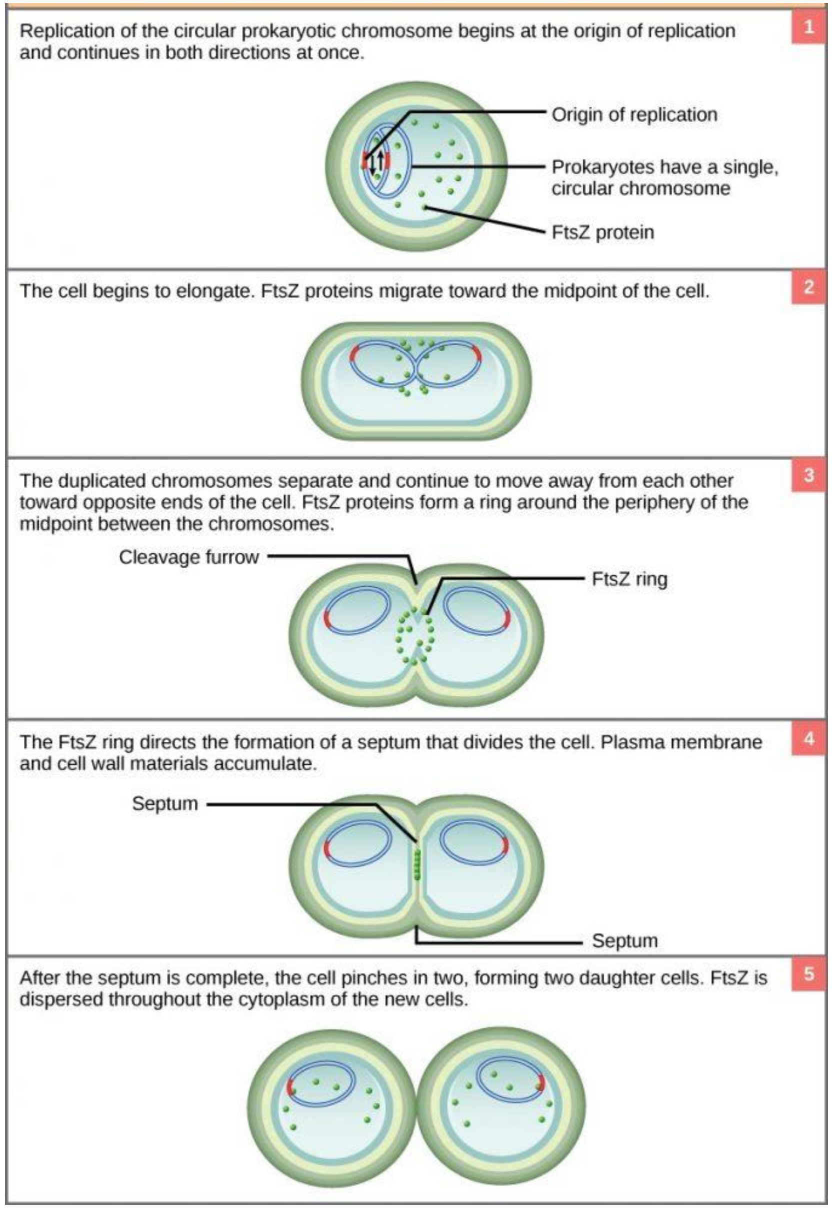
- FtsZ – microtubule homolog
- **Assembles between nucleoids**
- **Directs formation of the septum**
- Recruits the downstream components of the divisome

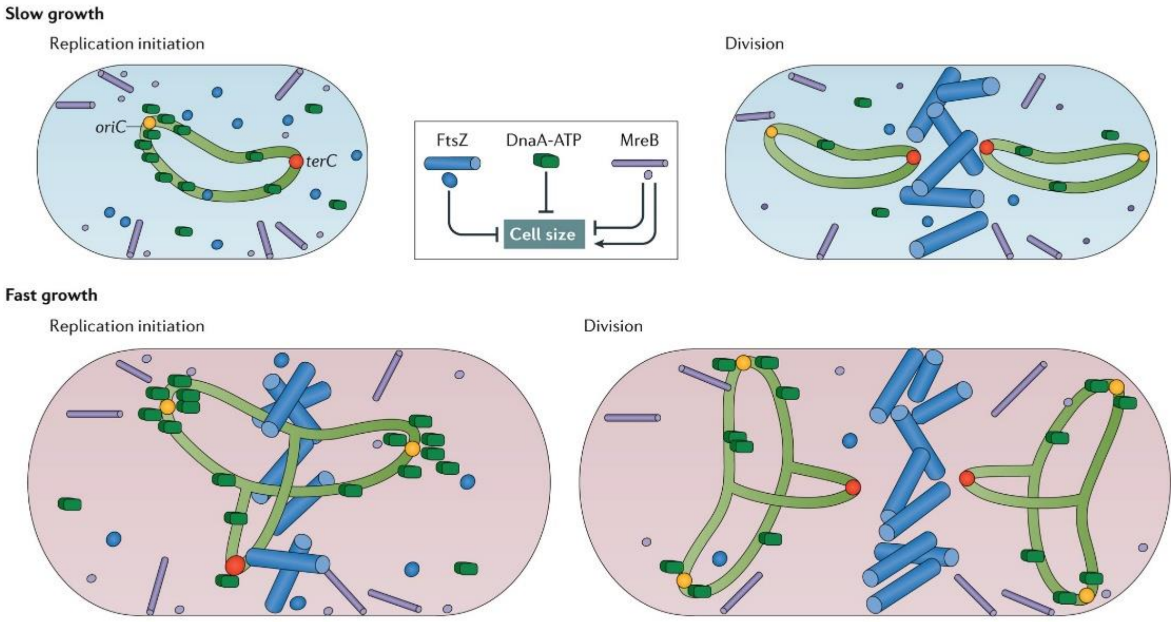


Cell wall synthesis in cocci



FtsZ distribution during the cell cycle

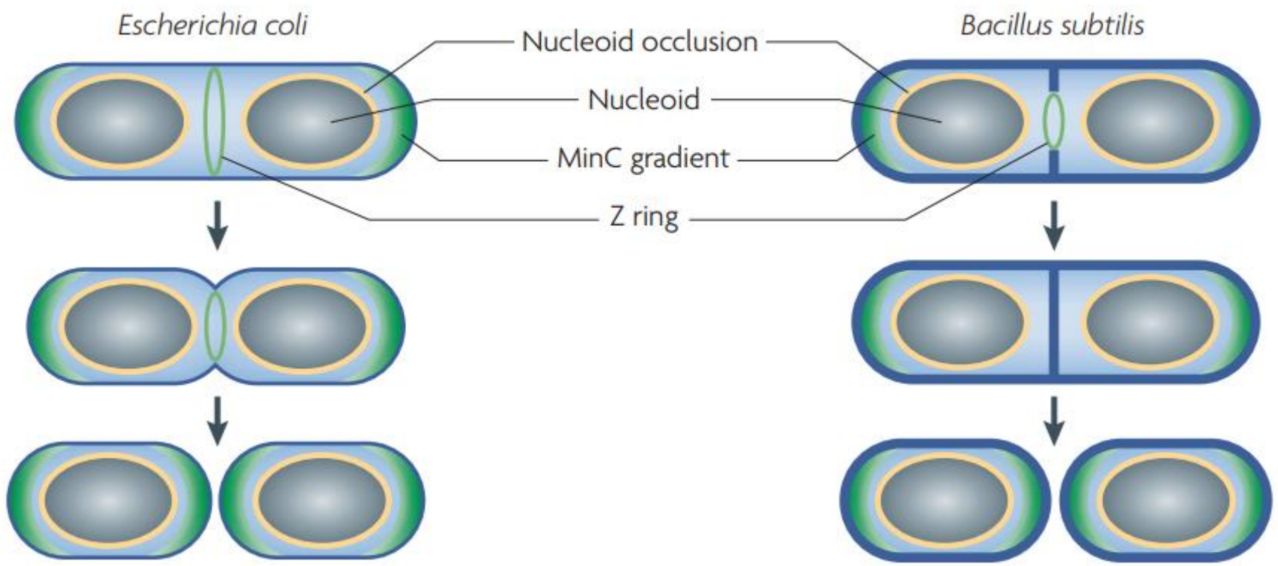


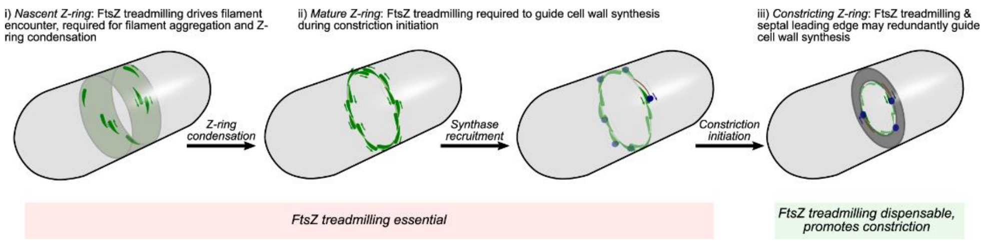


In media that support slow growth, replication initiation and Z-ring assembly occur sequentially (top panel), whereas in media that support fast growth, FtsZ can form the Z-ring a few minutes after cell birth, potentially coinciding with replication initiation (bottom panel).

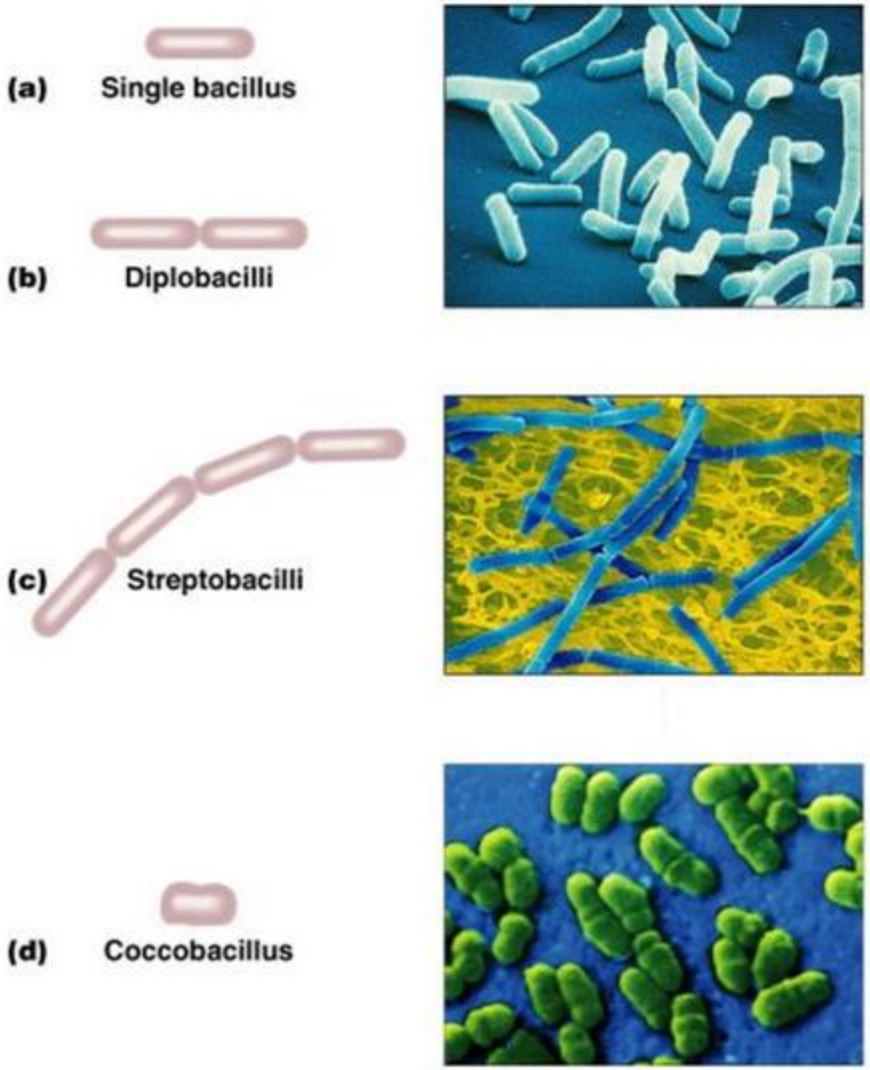
Mechanisms of fission

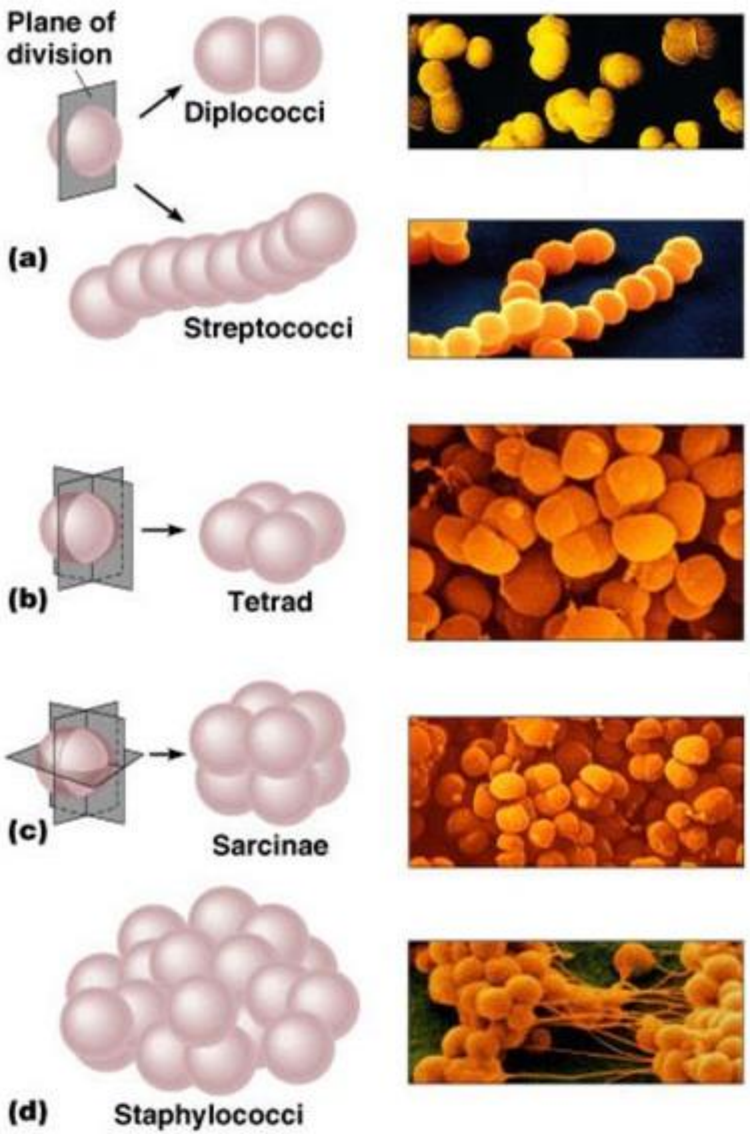
- Gram-negative bacteria: membrane constriction & formation of septum
- Gram-positive bacteria: FtsZ treadmilling & septal cell wall synthesis





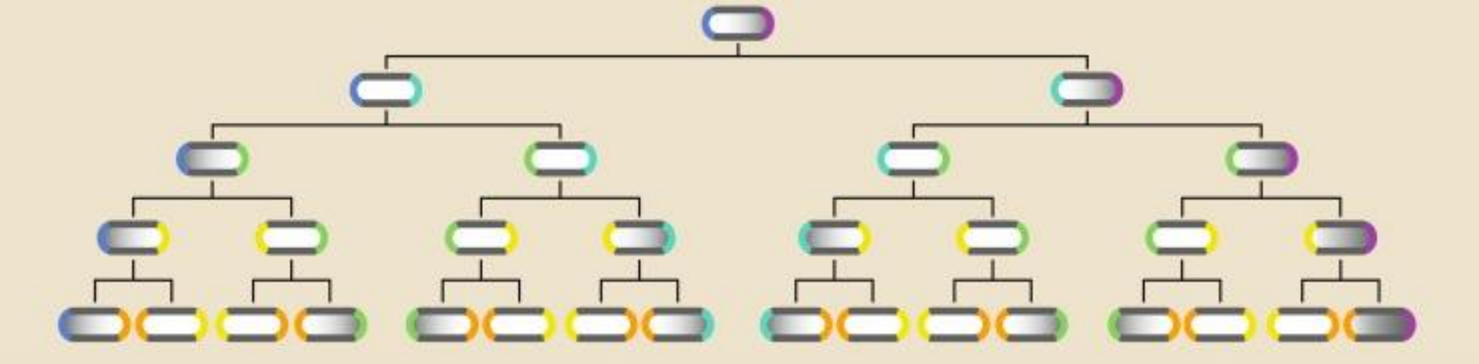
https://doi.org/10.1038/s41467-021-22526-0


(a) Single bacillus
(b) Diplobacilli
(c) Streptobacilli
(d) Coccobacillus


Plane of division
Diplococci
(a)
Streptococci
(b)
Tetrad
(c)
Sarcinae
(d)
Staphylococci

Inheritance of cell poles

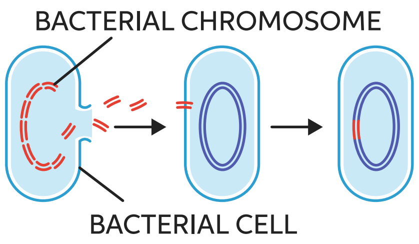
- *E. coli*: symmetrically dividing
- **Inheritance of old poles: allows asymmetric segregation** of proteins or other cellular components during cell divisions



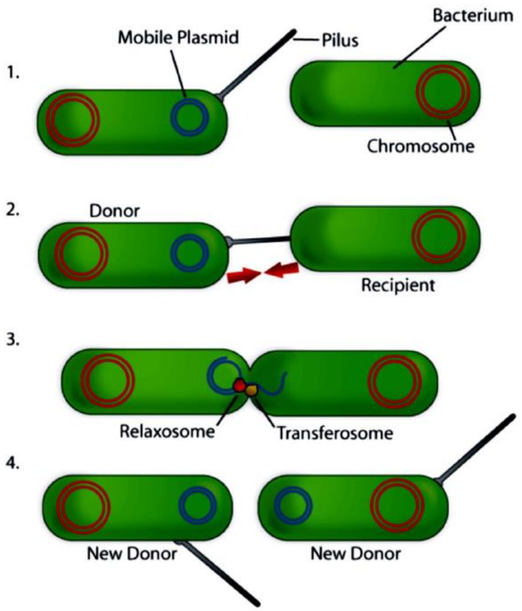
- **Aging in unicellular organisms:** cells with exhibits a diminished growth rate, decreased offspring production, and an increased incidence of death
- **Lineage survival:** cells with new poles maintain fitness

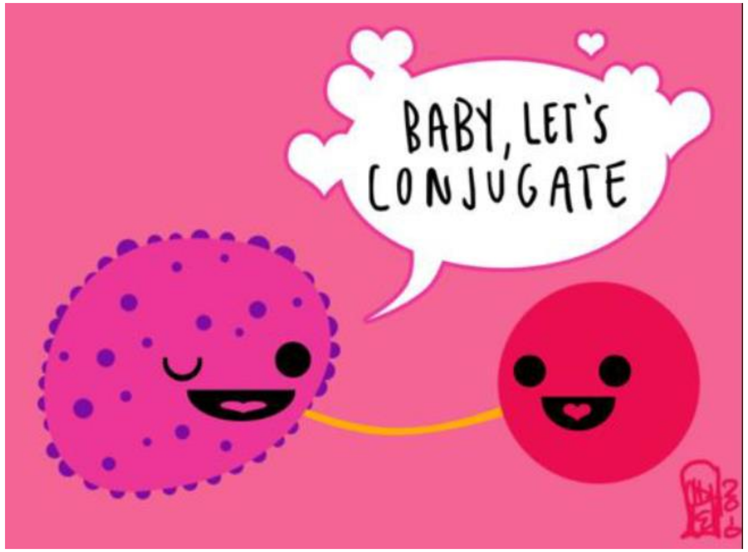
Bacterial transformation and conjugation

- **Transformation**: incorporation of foreign DNA



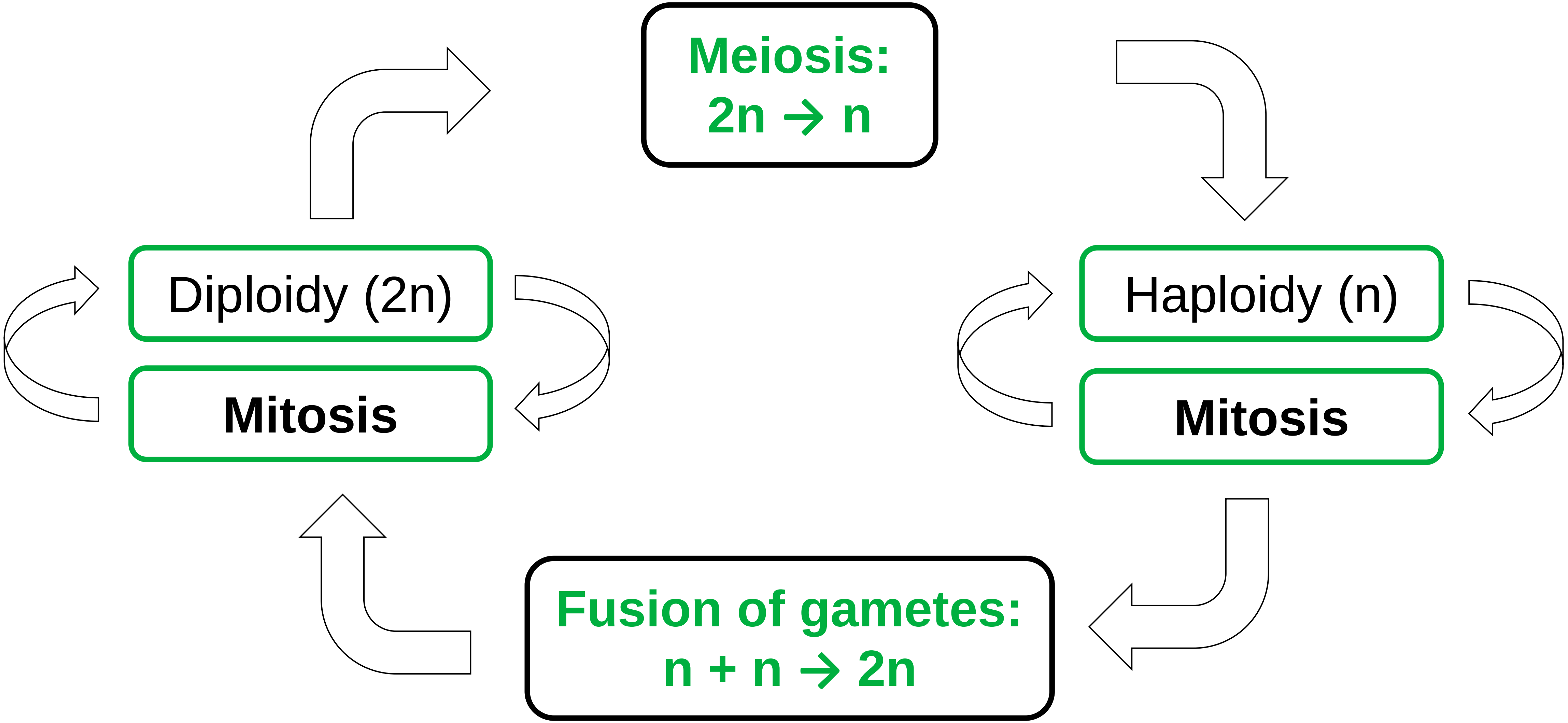
- **Conjugation: exchange of genetic material** (mobile plasmids, retained as plasmids)



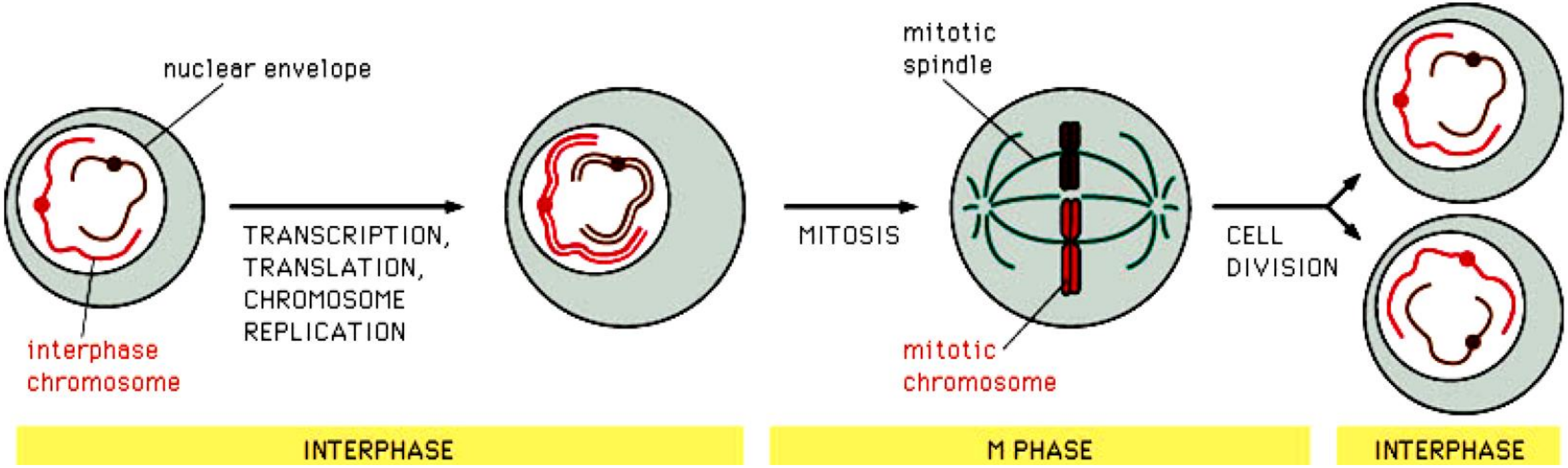


Does not involve cell division!
No sexual reproduction in bacteria!

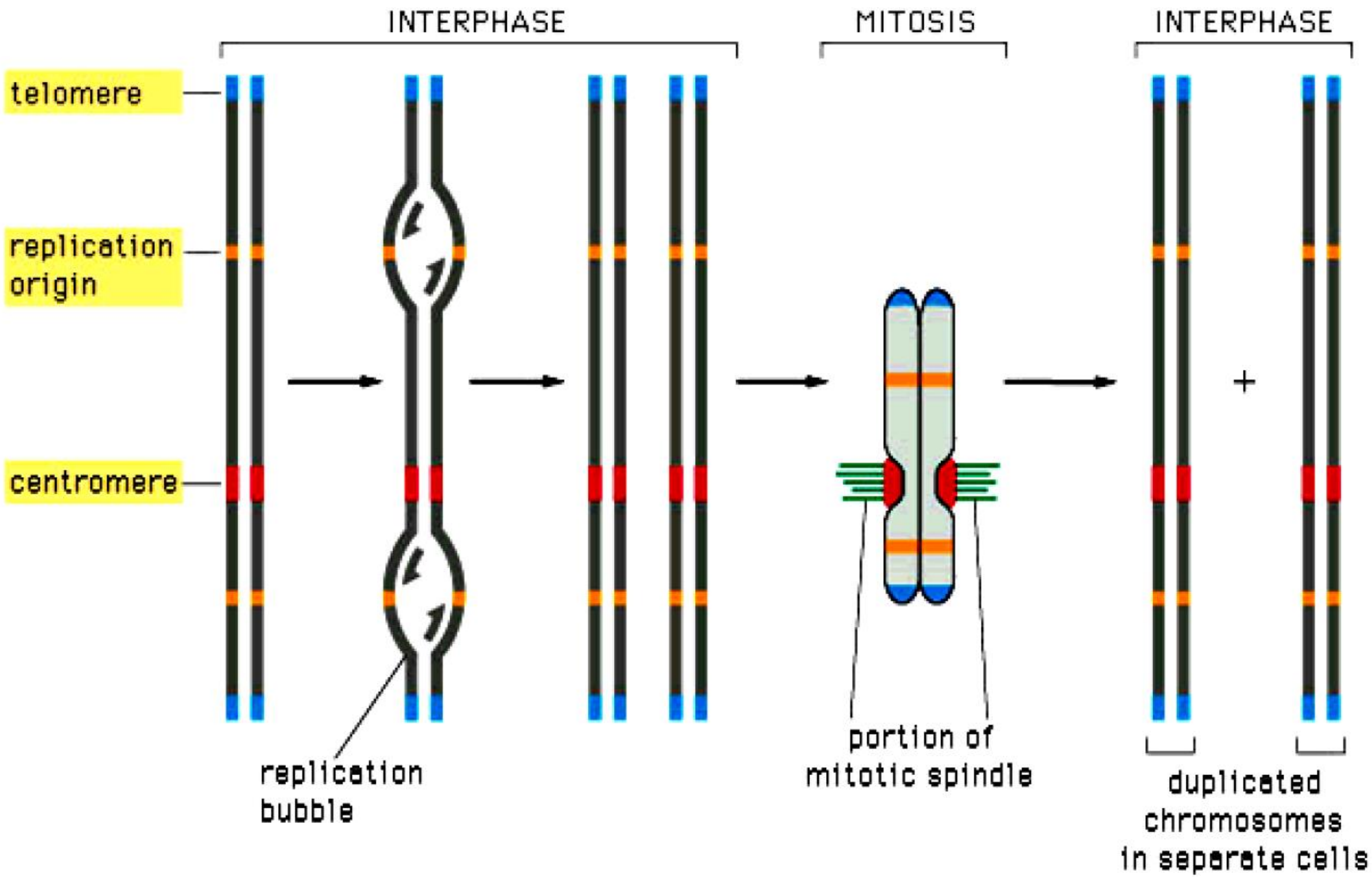
Cell division in eukaryotes


Meiosis:
2n → n
Diploidy (2n)
Mitosis
Haploidy (n)
Mitosis
Fusion of gametes:
n + n → 2n

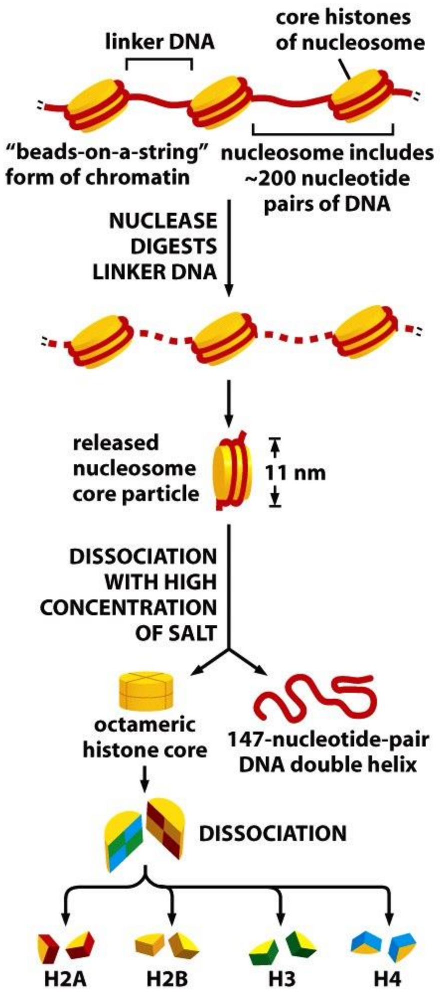
Chromatin organization during the cell cycle



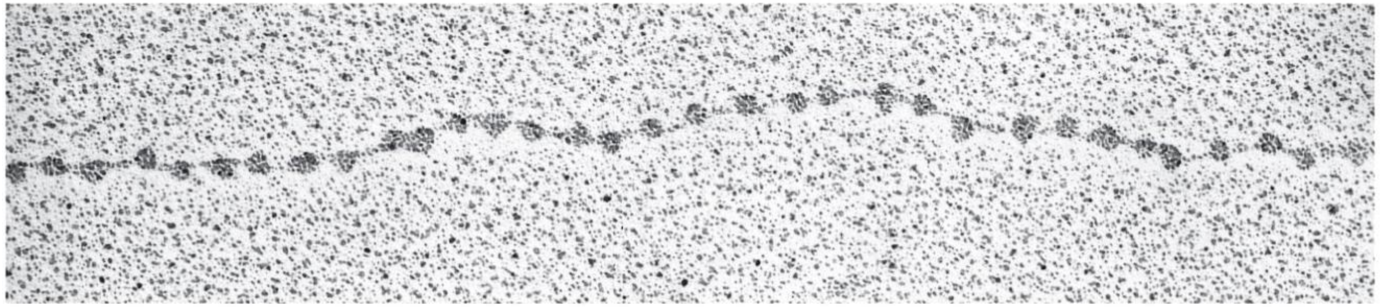
Duplication of genetic material: S-phase



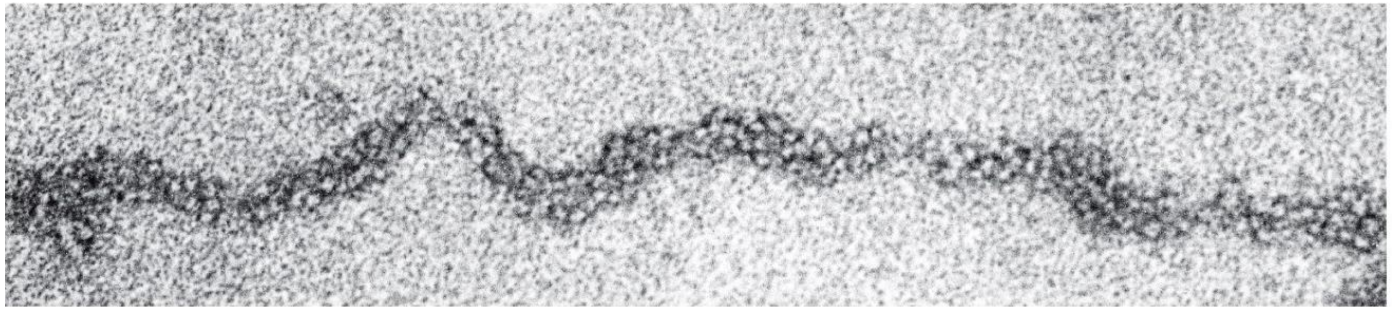
Chromatin organization



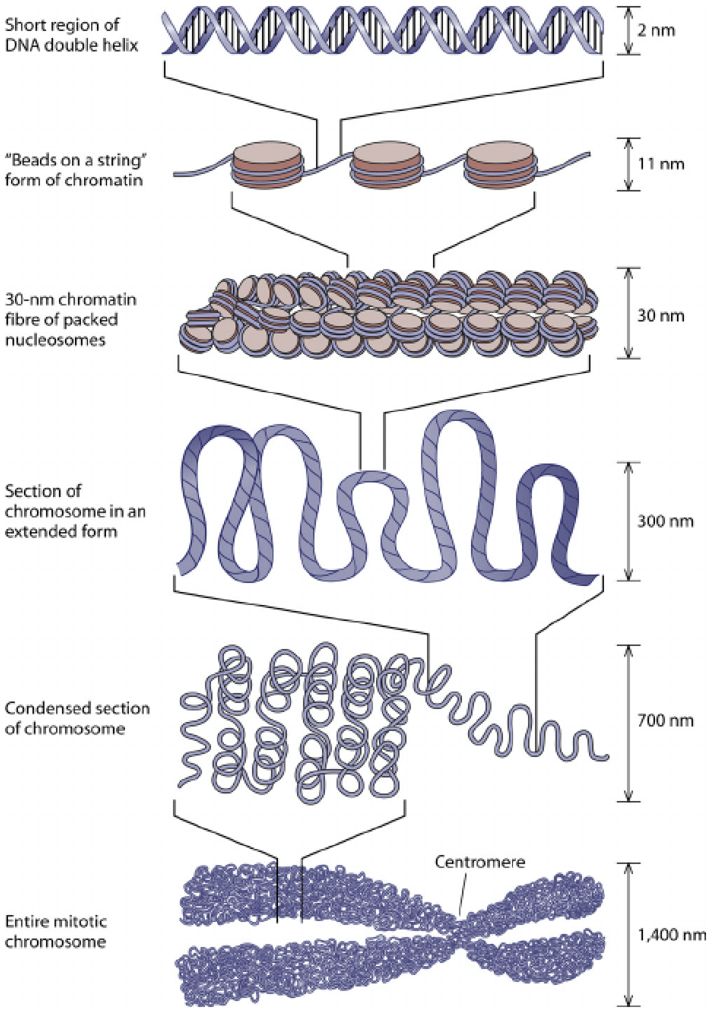
- **Nucleosomes → „beads on a string"** /11 nm fibre

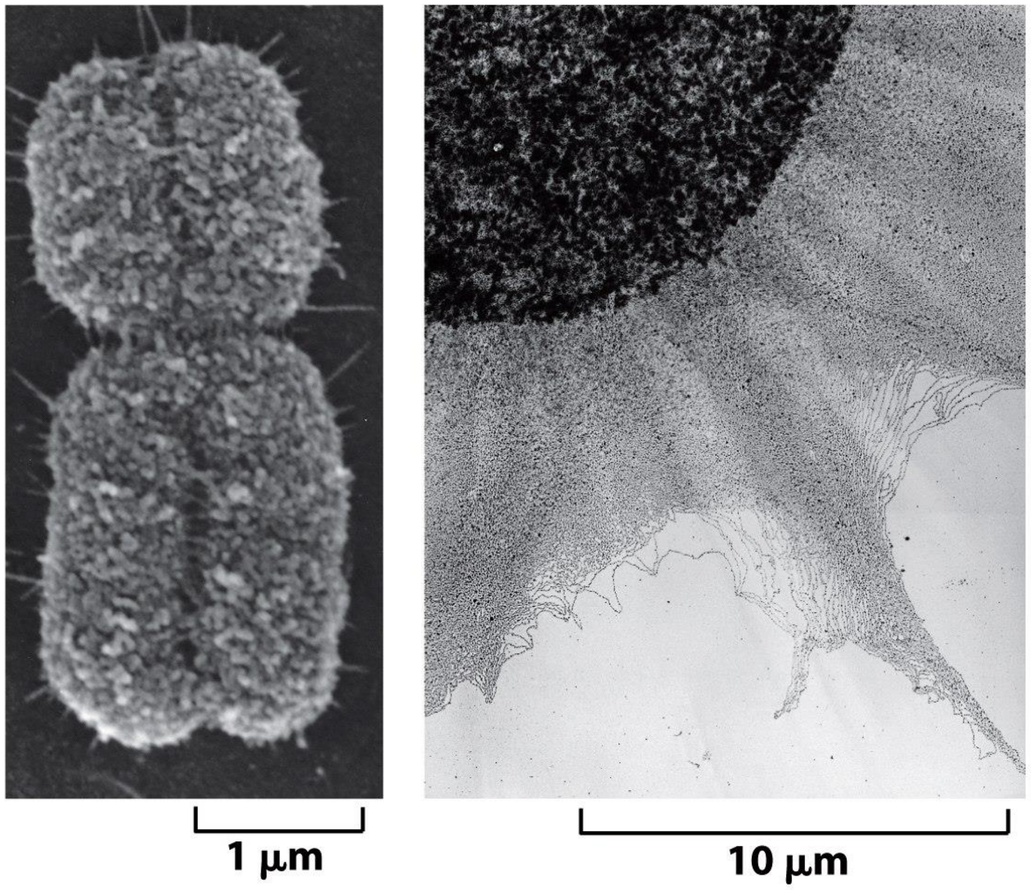


- **30 nm fibre (solenoid)**



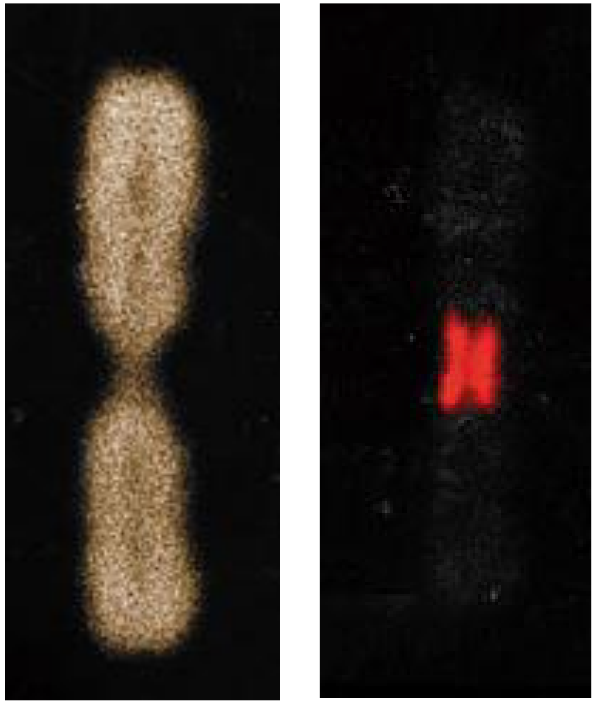
Chromatin organization

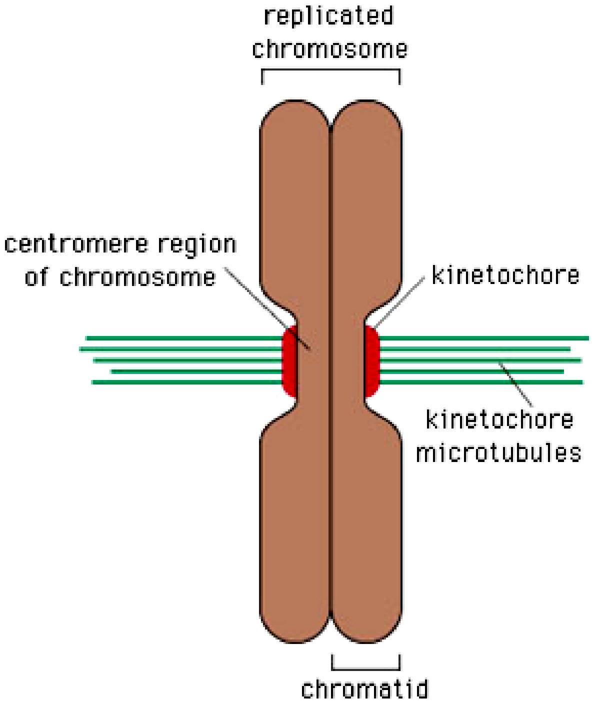


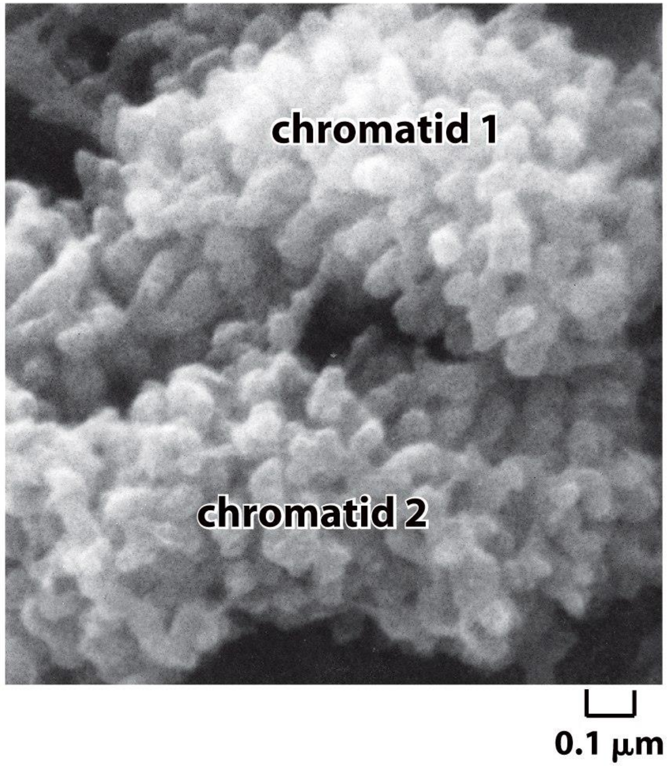


Metaphase chromosome structure

– Monocentric chromosomes

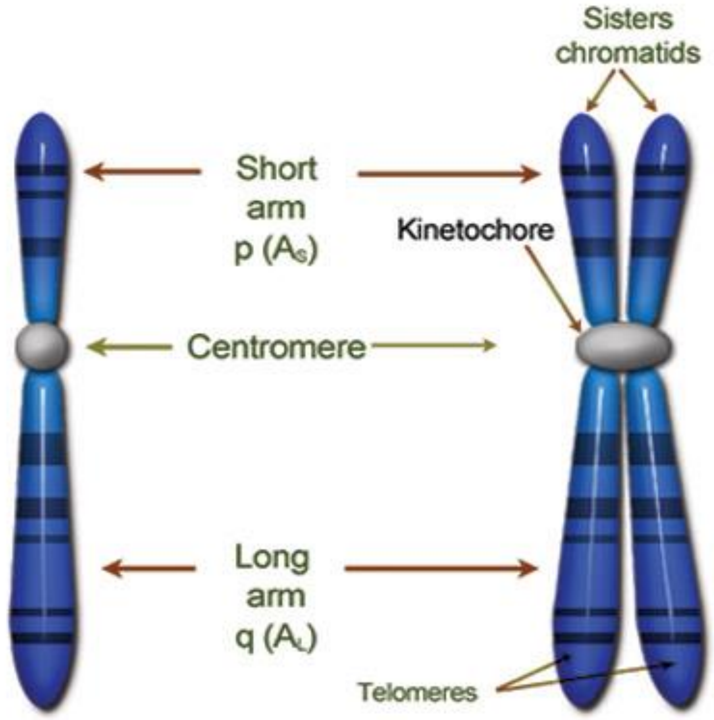


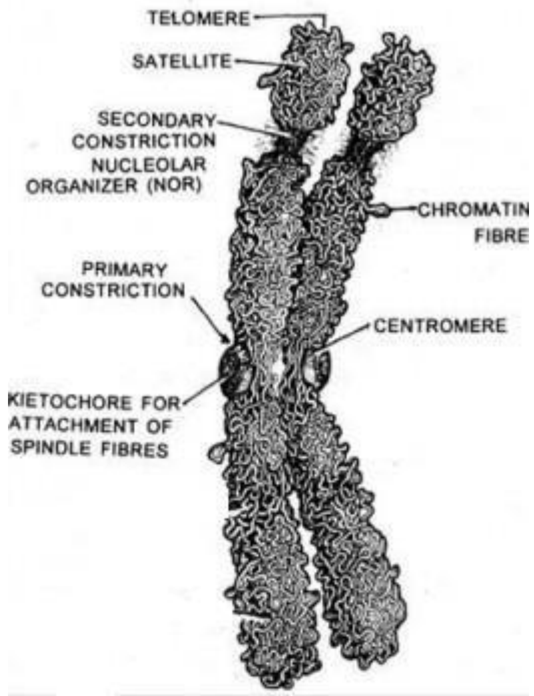


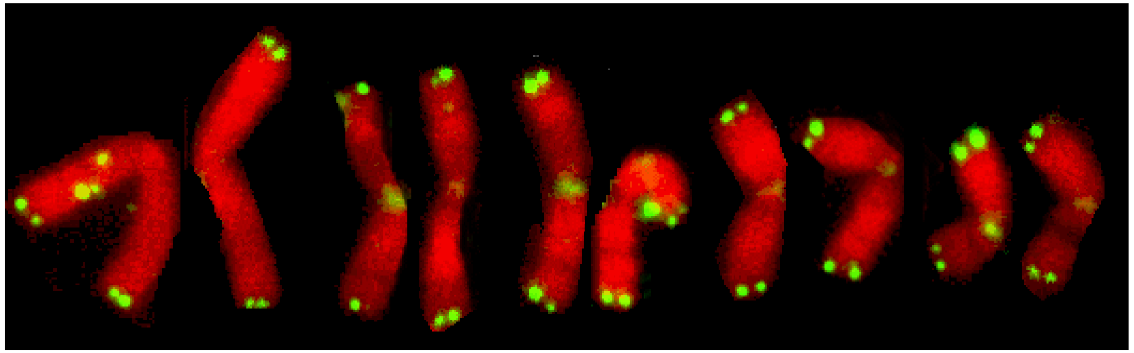


Metaphase chromosome structure

– **Monocentric chromosomes**

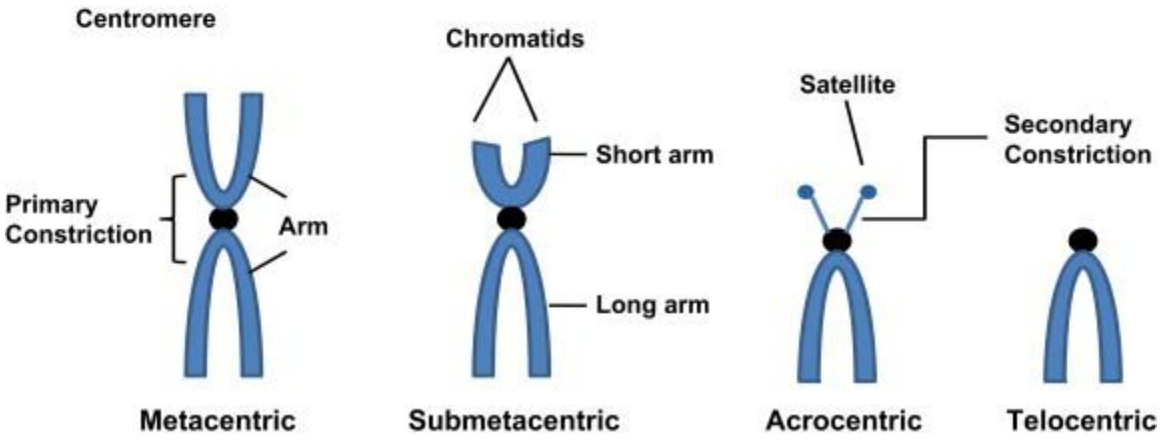


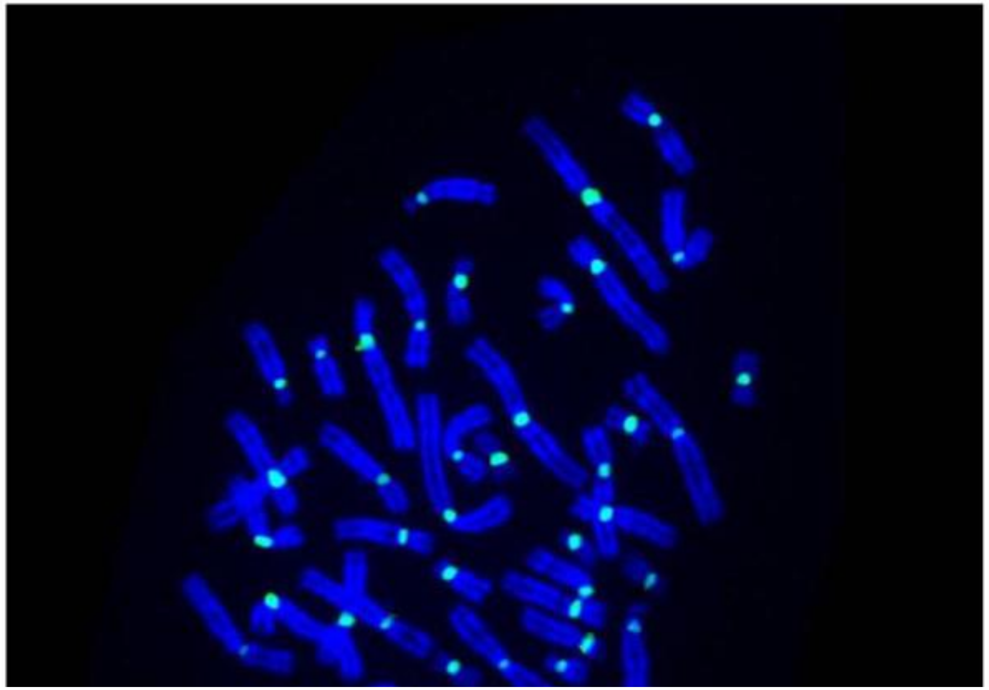




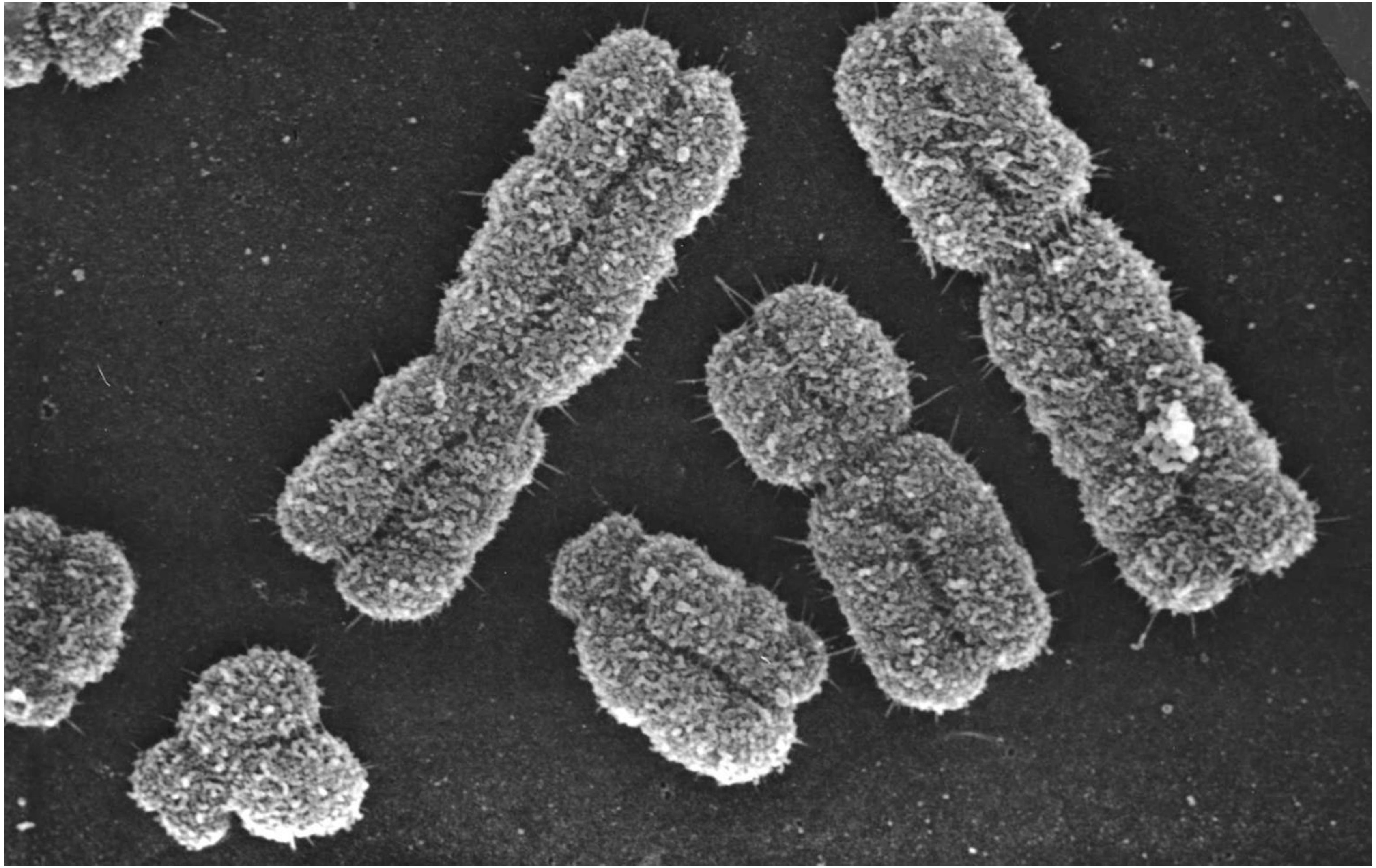
Metaphase chromosome structure

- **Monocentric chromosomes**

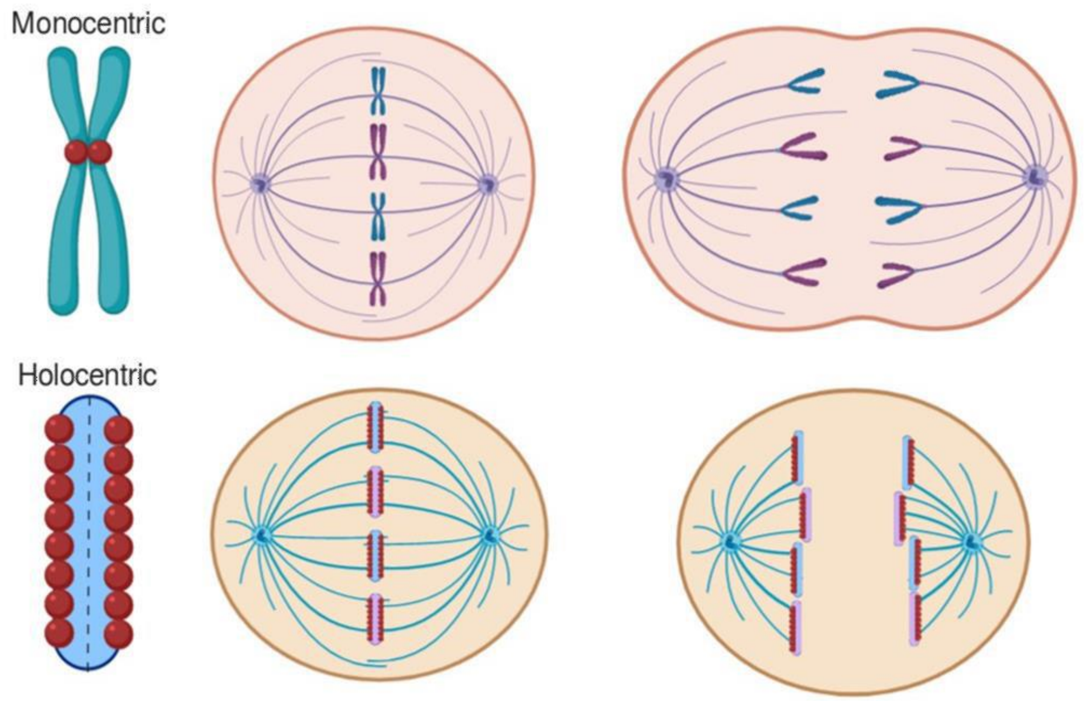




- Classified according the centromere position

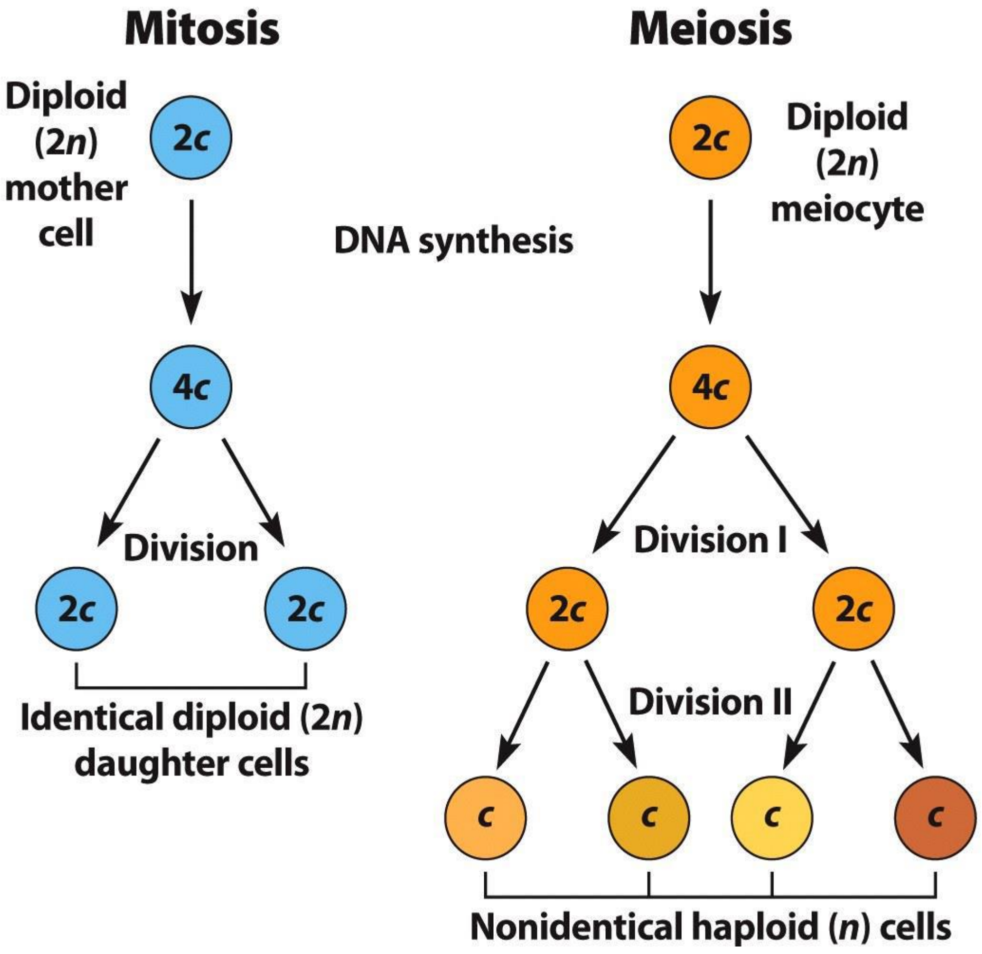


Monocentric versus holocentric chromosomes



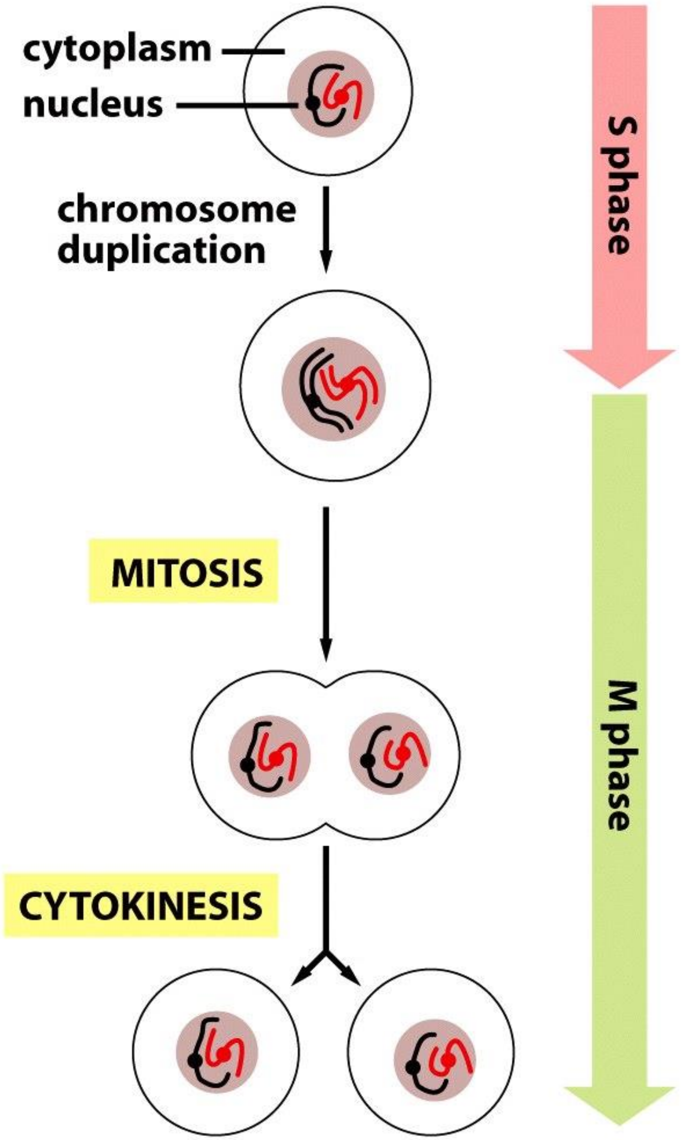
- **Monocentric: one kinetochore**
- **Holocentric: multiple kinetochores**
  - Lack primary constriction
  - Microtubules bind one chromatid at multiple sites (kinetochores)
  - Chromatids move in parallel (not V-shape)
  - Present in some insects, plants, arachnids, and nematodes
  - Further reading

DNA content – cell cycle and division



- ***c* = DNA mass of one (haploid) set of chromosomes** when each chromosome is formed by one chromatid
- *n* = haploid number – chromosomes in a gamete
  - half of the usual complete sets of chromosomes in somatic cells
- *x* = chromosome number – one complete set of chromosomes

Mitosis



Mitosis

Fundamental role

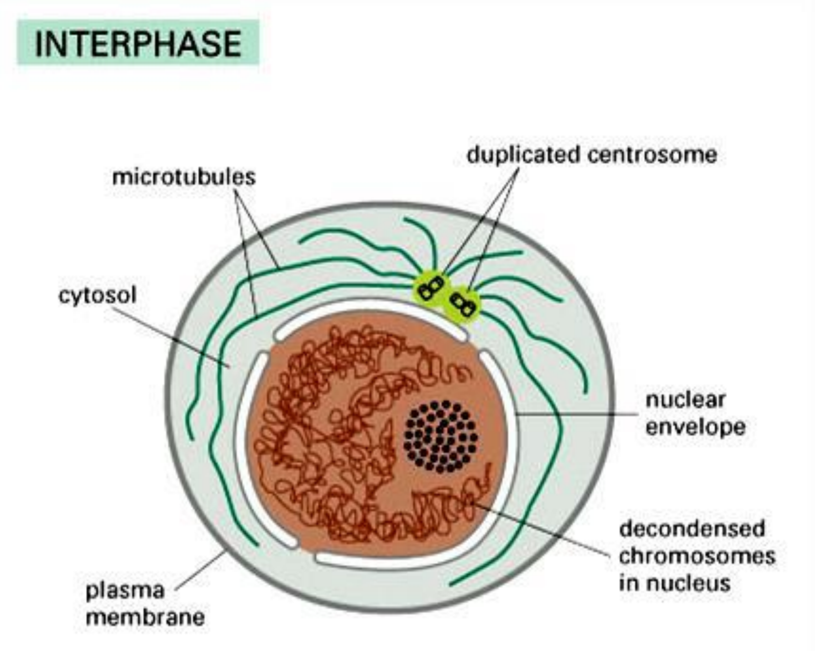
- Passing the identical genetic information to the next generation of cells

Stages of mitosis

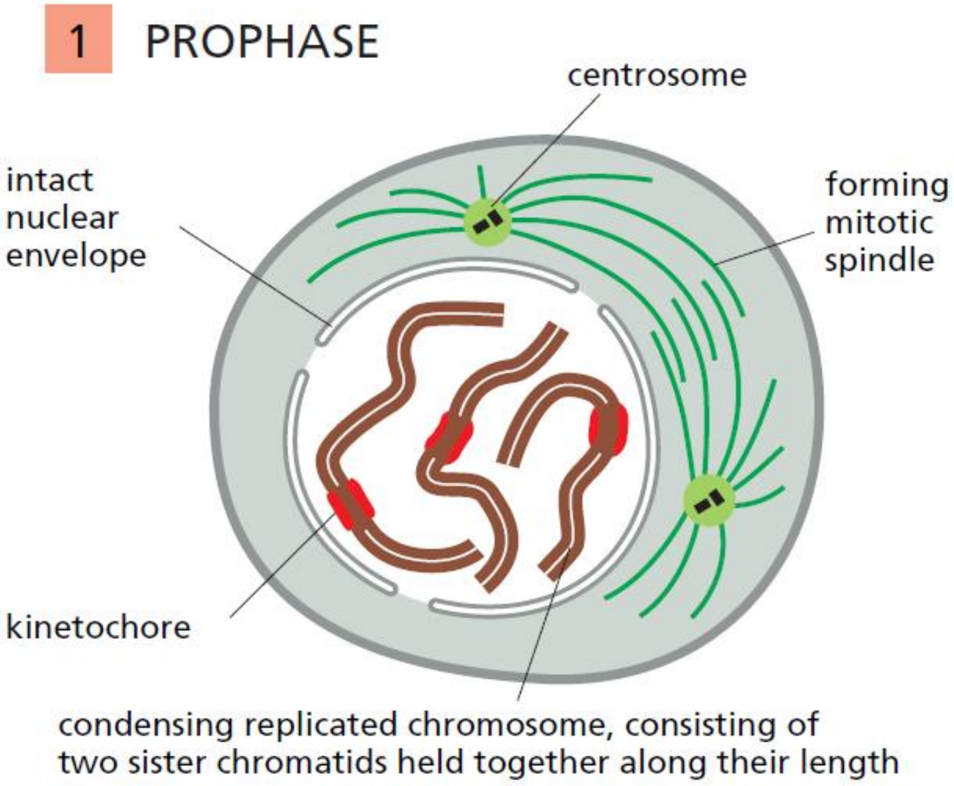
- **Initiated after progression through the G2/M checkpoint**
  - Fully replicated undamaged DNA?, sufficient cell size?, (animal cells: duplicated centrosomes?)

- **Prophase**
- **Prometaphase**
- **Metaphase**
- **Anaphase**
- **Telophase**

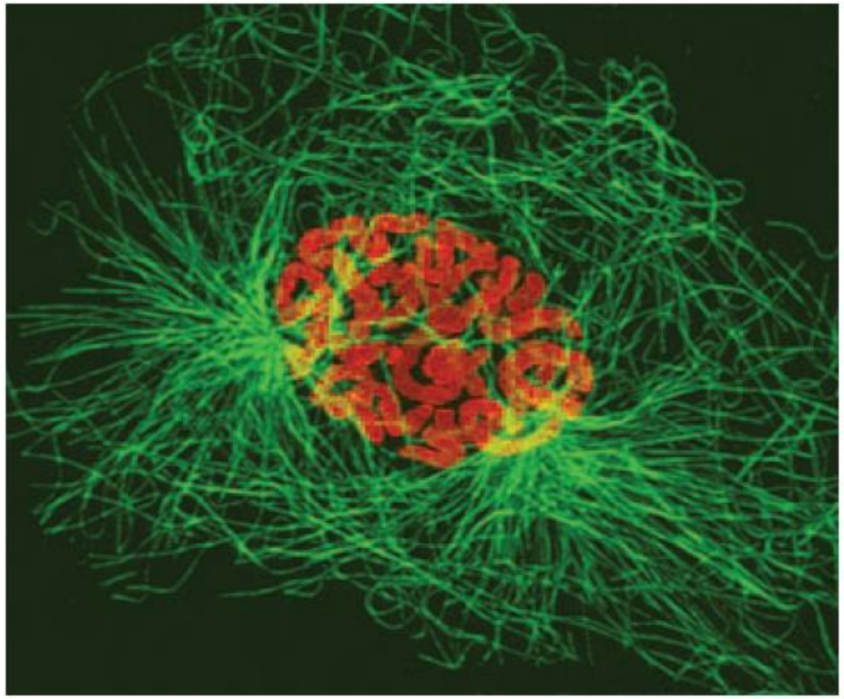
vs.



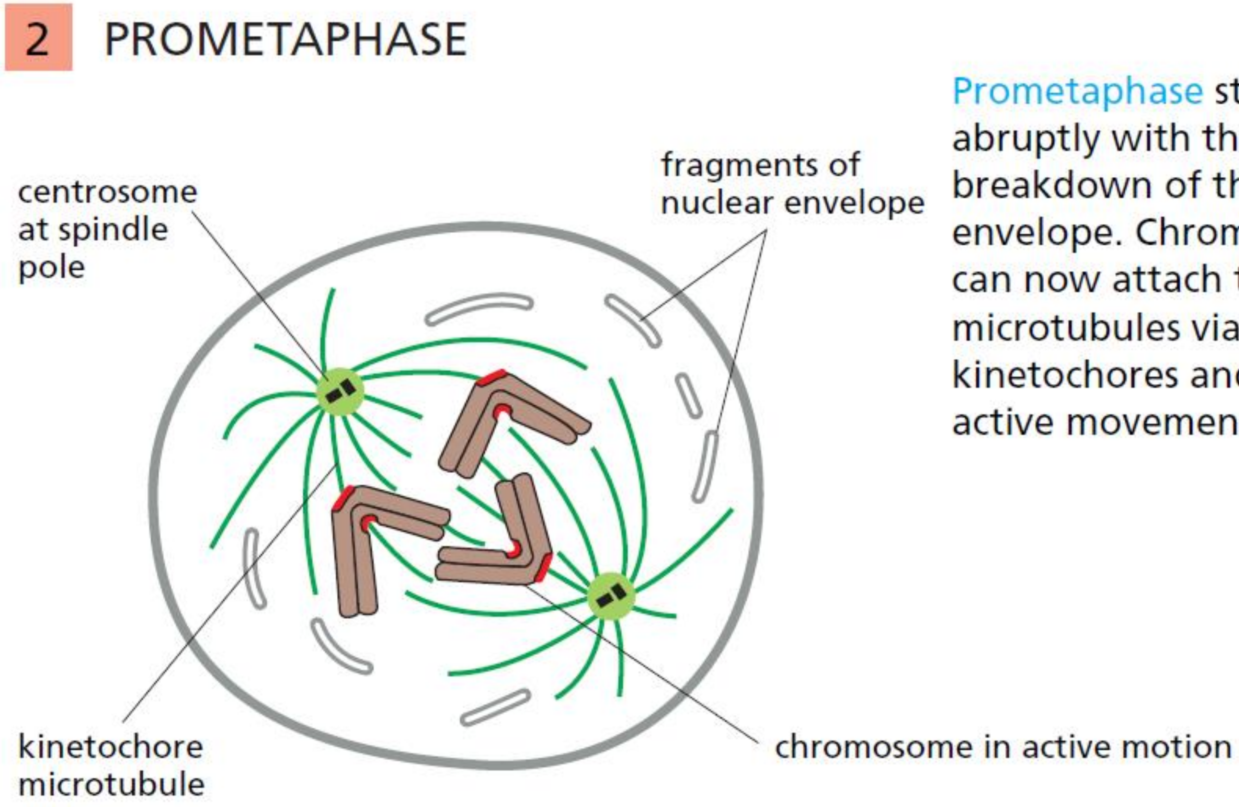
Prophase



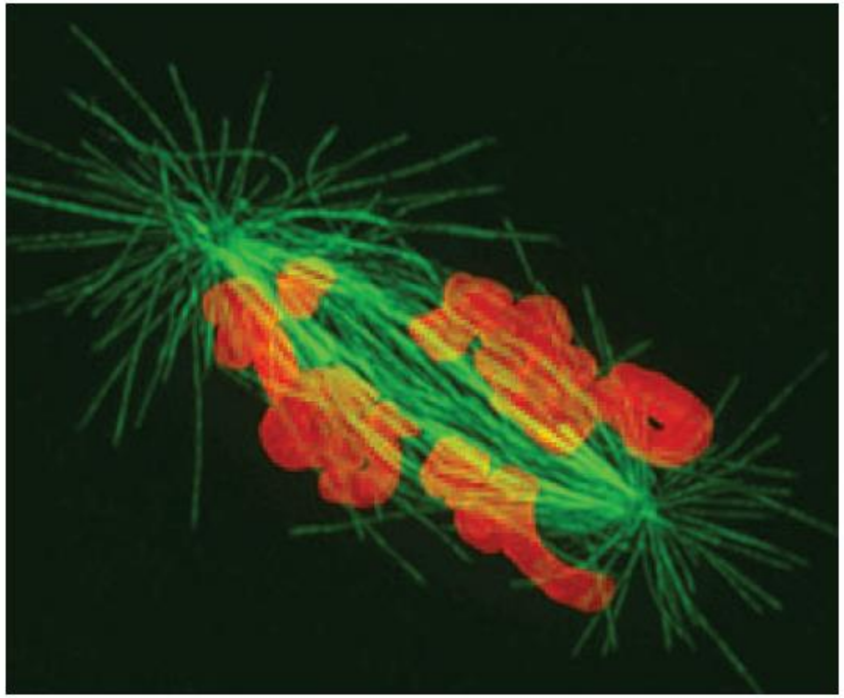
At prophase, the replicated chromosomes, each consisting of two closely associated sister chromatids, condense. Outside the nucleus, the mitotic spindle assembles between the two centrosomes, which have replicated and moved apart. For simplicity, only three chromosomes are shown. In diploid cells, there would be two copies of each chromosome present. In the photomicrograph, chromosomes are stained *orange* and microtubules are *green*.



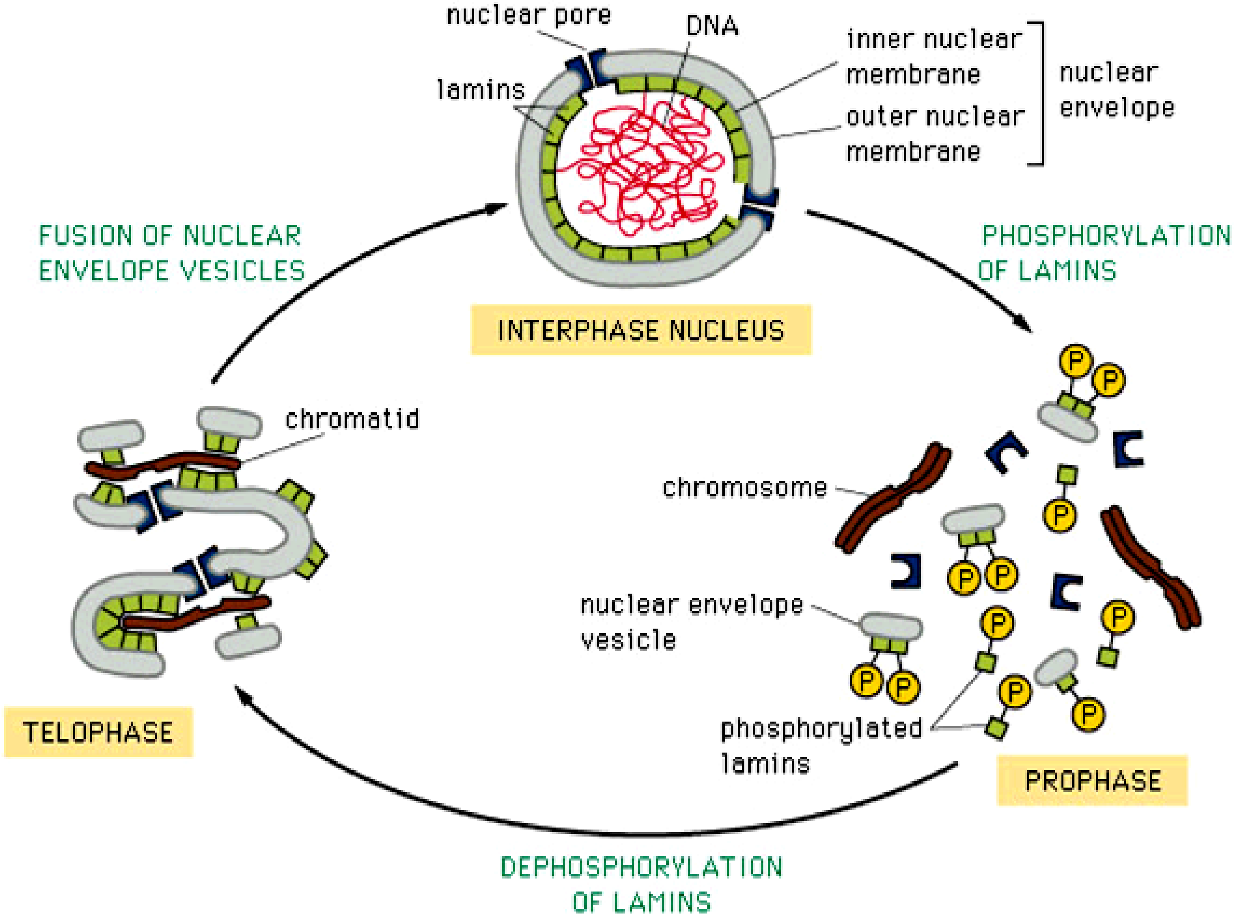
Promethaphase



Prometaphase starts abruptly with the breakdown of the nuclear envelope. Chromosomes can now attach to spindle microtubules via their kinetochores and undergo active movement.

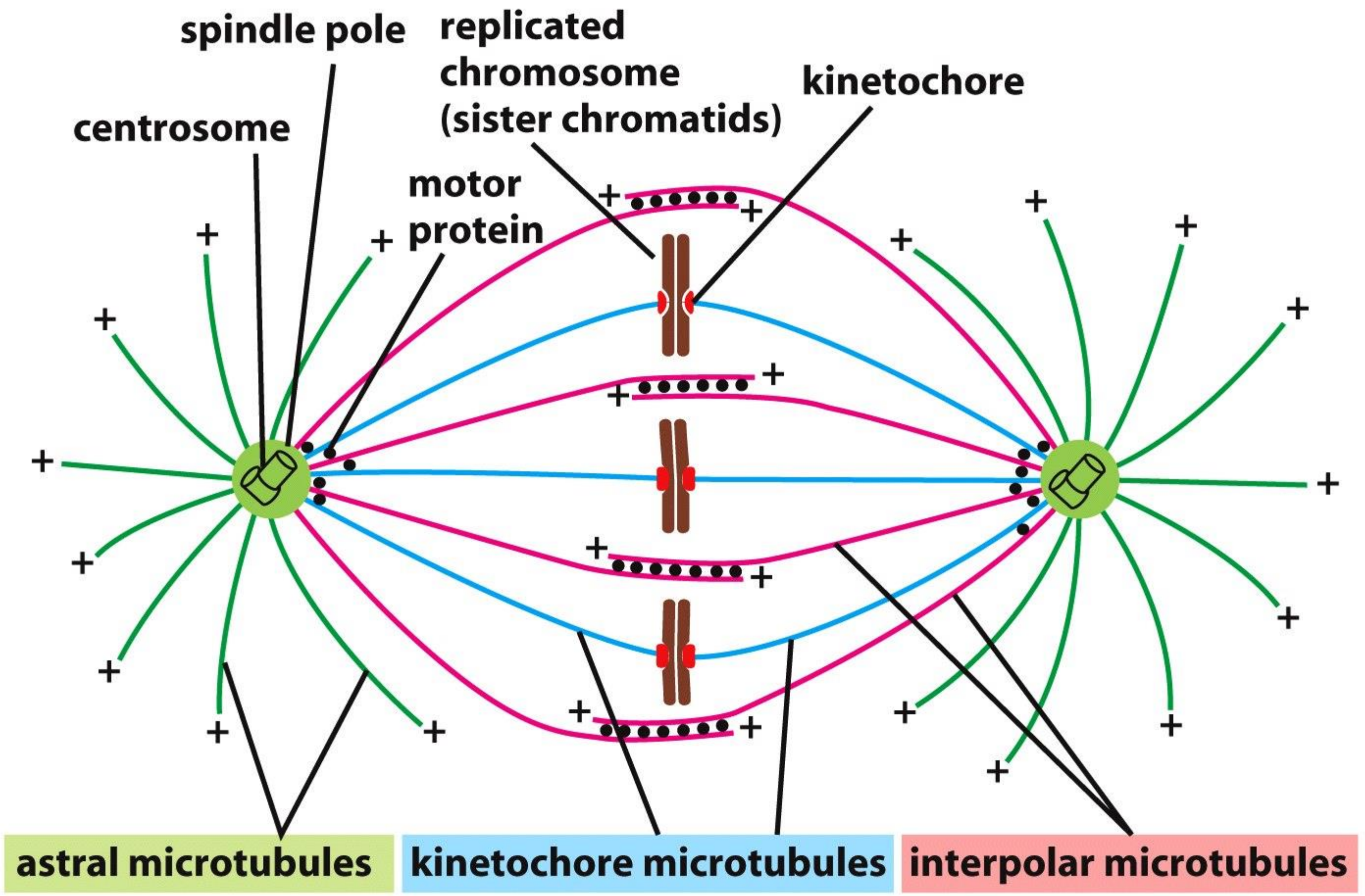


Nuclear envelope breakdown

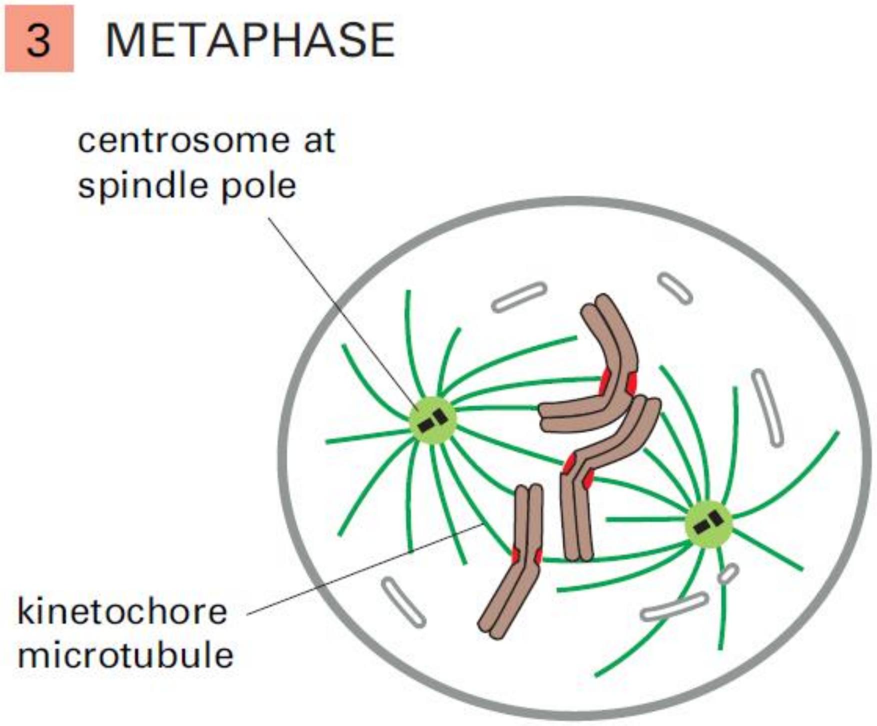


– **Progressive phosphorylation of lamins** by active M-Cdk (cycline B-Cdk1; progression through the G2/M checkpoint)

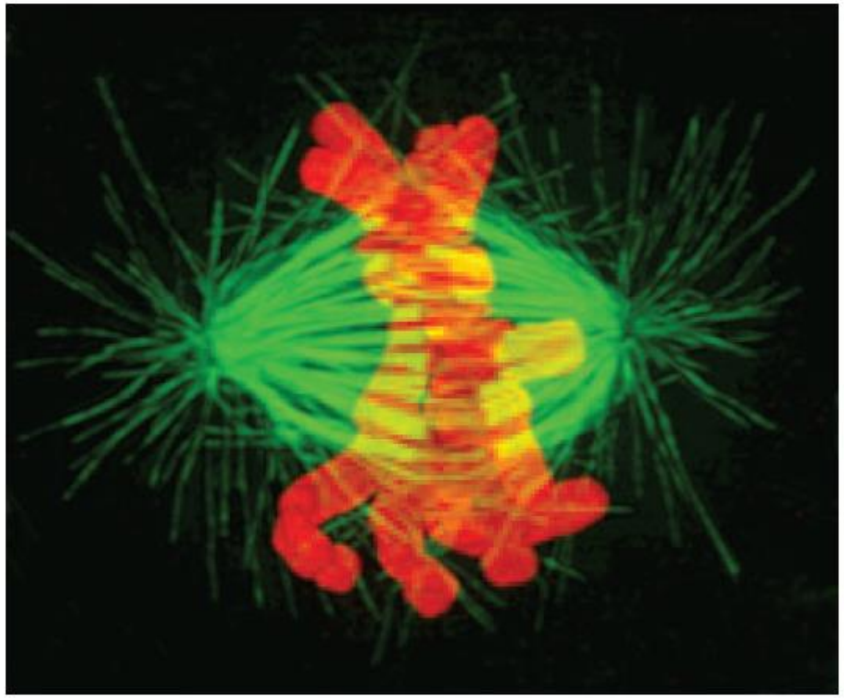
Mitotic spindle – three types of microtubules



Metaphase

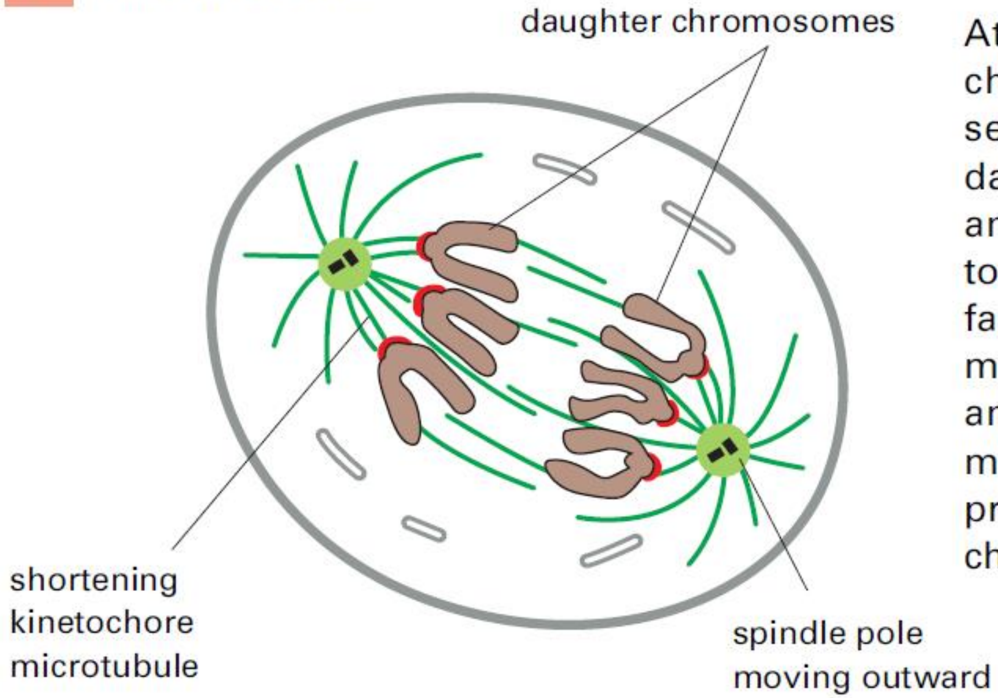


At metaphase, the chromosomes are aligned at the equator of the spindle, midway between the spindle poles. The kinetochore microtubules attach sister chromatids to opposite poles of the spindle.

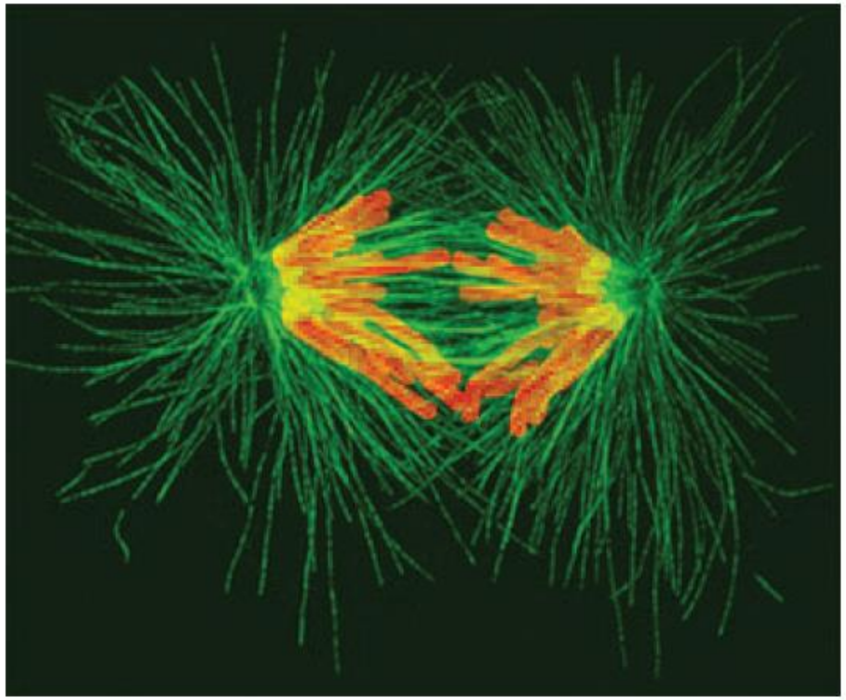


Anaphase

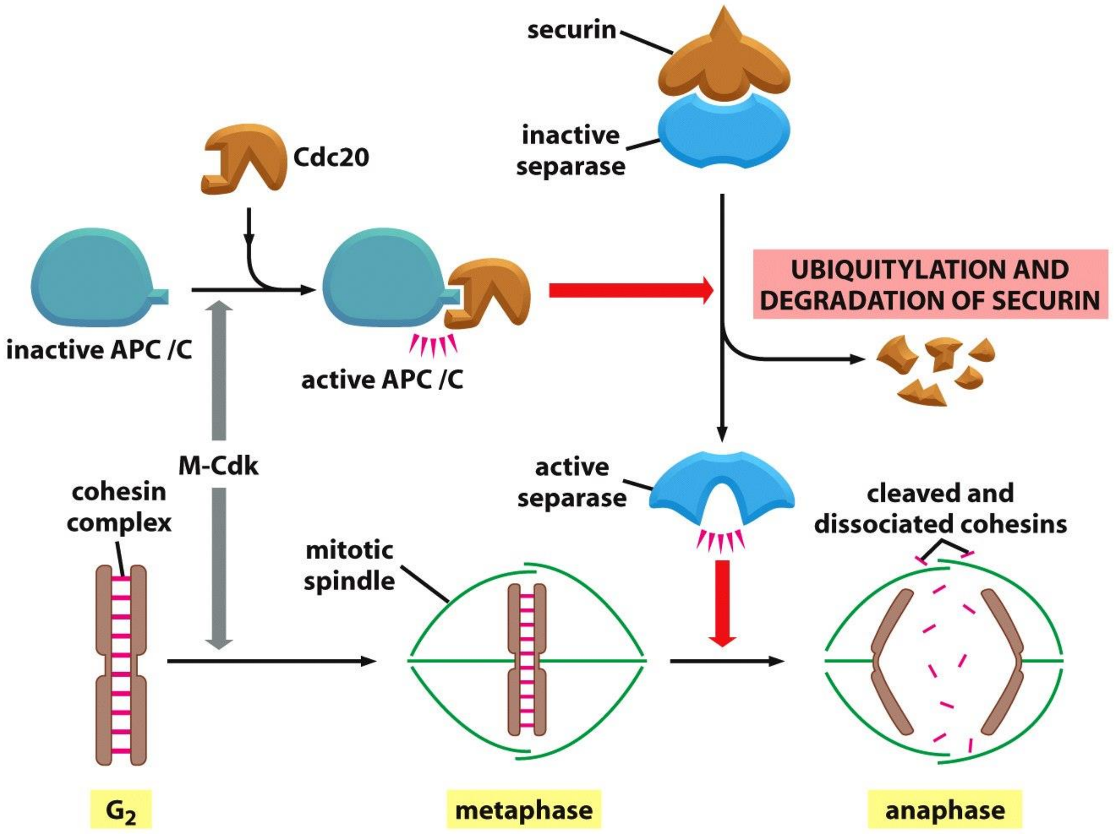
4 ANAPHASE



At anaphase, the sister chromatids synchronously separate to form two daughter chromosomes, and each is pulled slowly toward the spindle pole it faces. The kinetochore microtubules get shorter, and the spindle poles also move apart; both processes contribute to chromosome segregation.



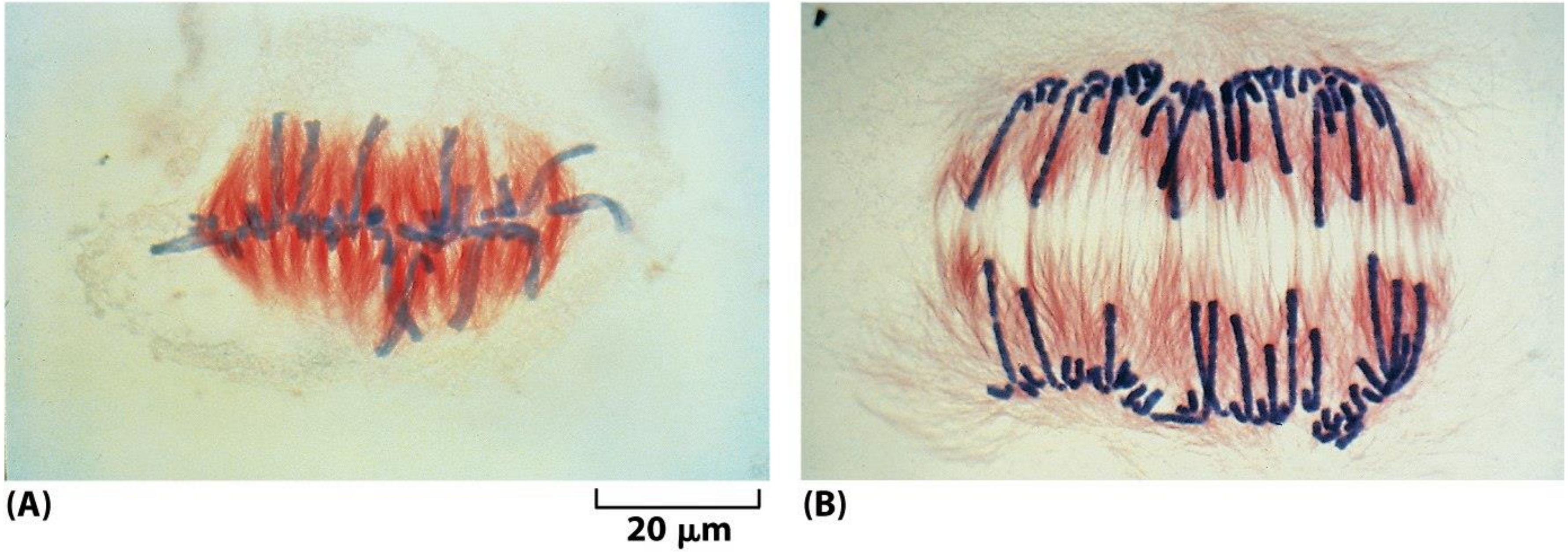
Anaphase: sister-chromatid separation



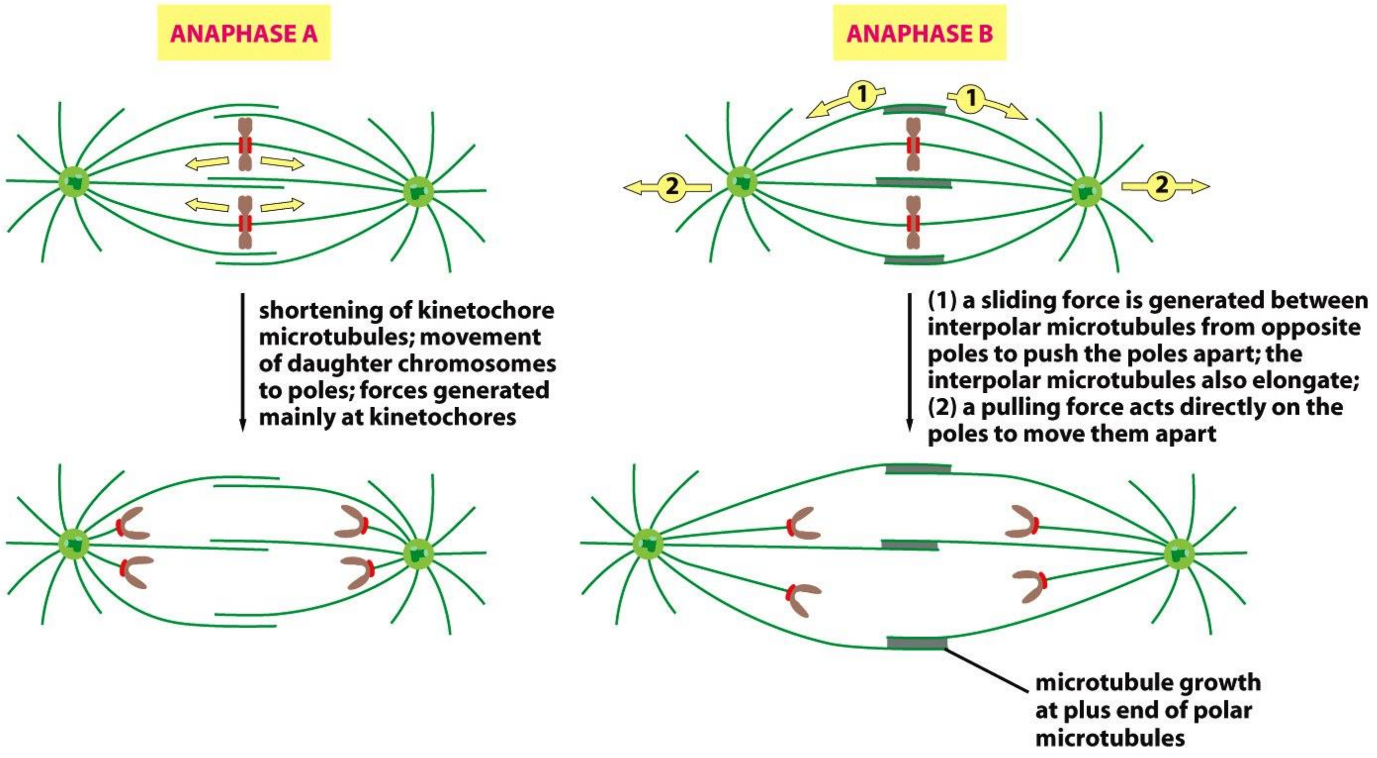
- **Separase cleaves cohesins**
- Allows sister-chromatid separation
- Normally **prevented by securin**

- **Spindle checkpoint:** securin is a **target of APC/C** ubiquitin ligase

Anaphase: sister-chromatid separation



Anaphase: sister-chromatid separation

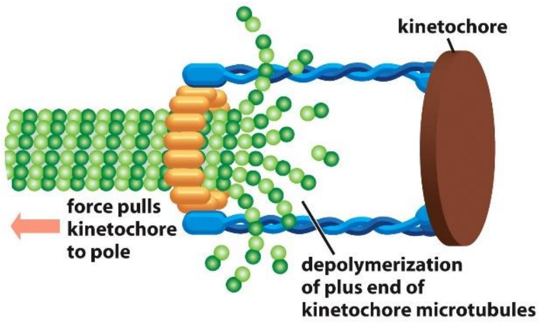


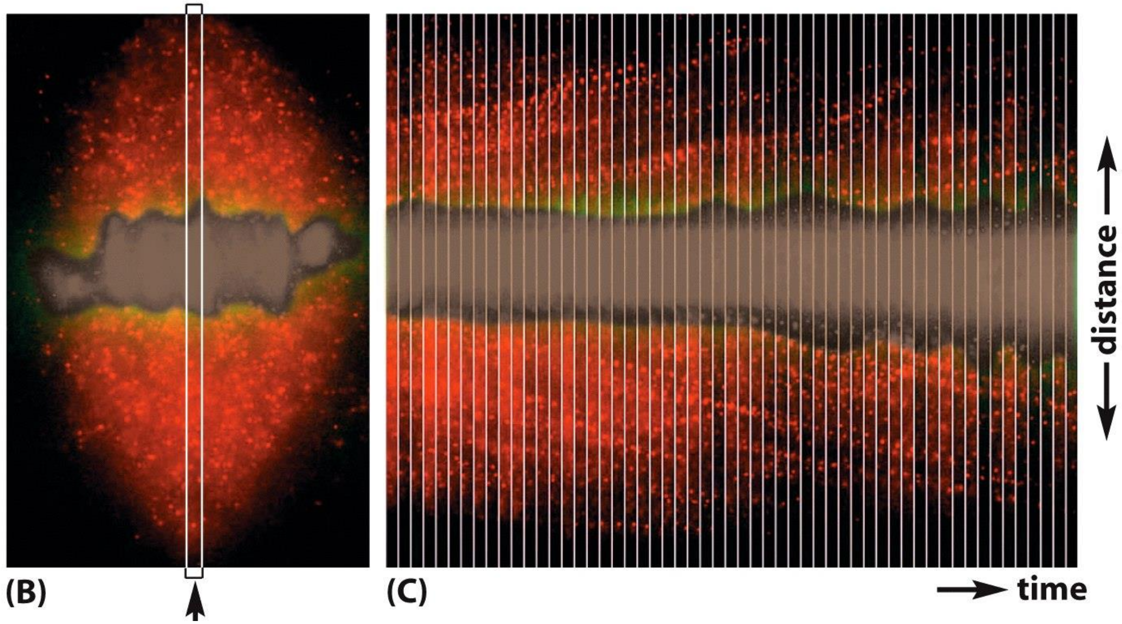
Synergy between:

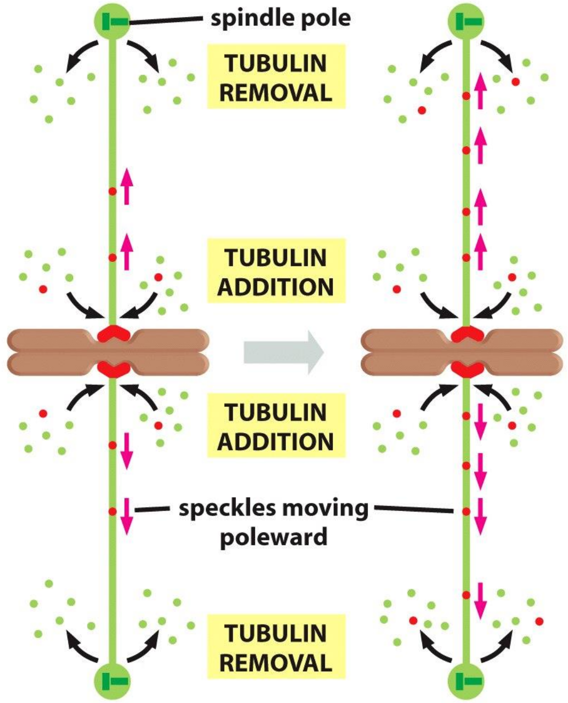
- **Anaphase A**
  - **Kinetochore microtubules shortening**
  - Microtubule flux (depolymerization at both ends)
- **Anaphase B**
  - **Growth of interpolar microtubules** from opposite poles interconnected by motor proteins

Spindle microtubule flux

- Depolymerization of spindle microtubules can occur at both + & - end
  - Poorly understood, mediated by motor proteins



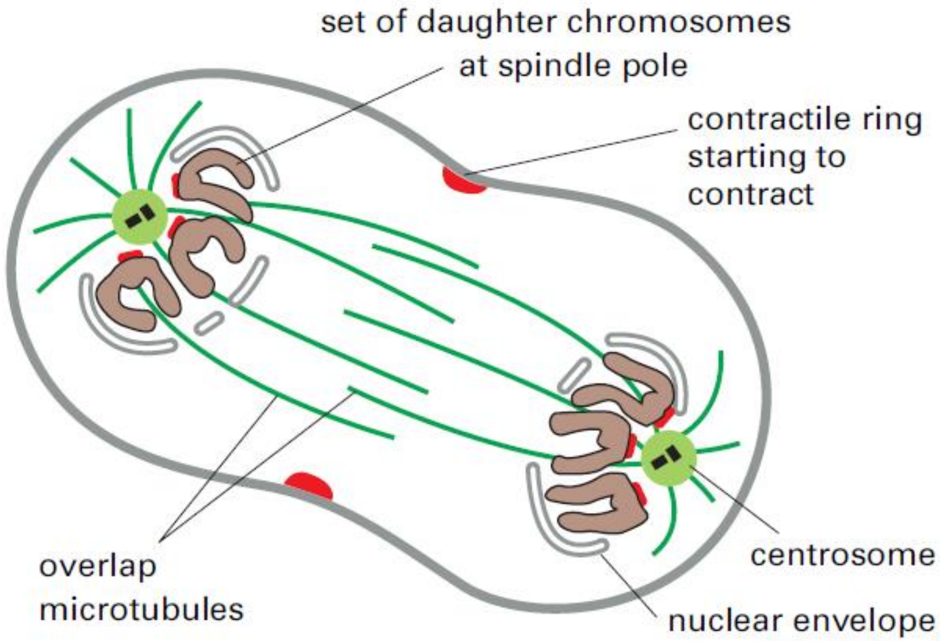




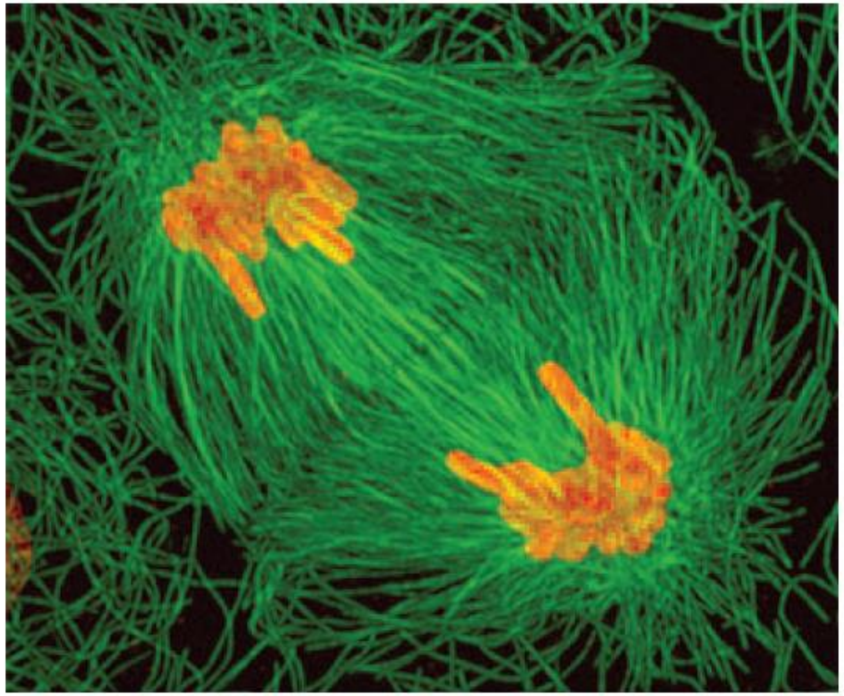
Fluorescent tubulin time-lapse microscopy

Telophase

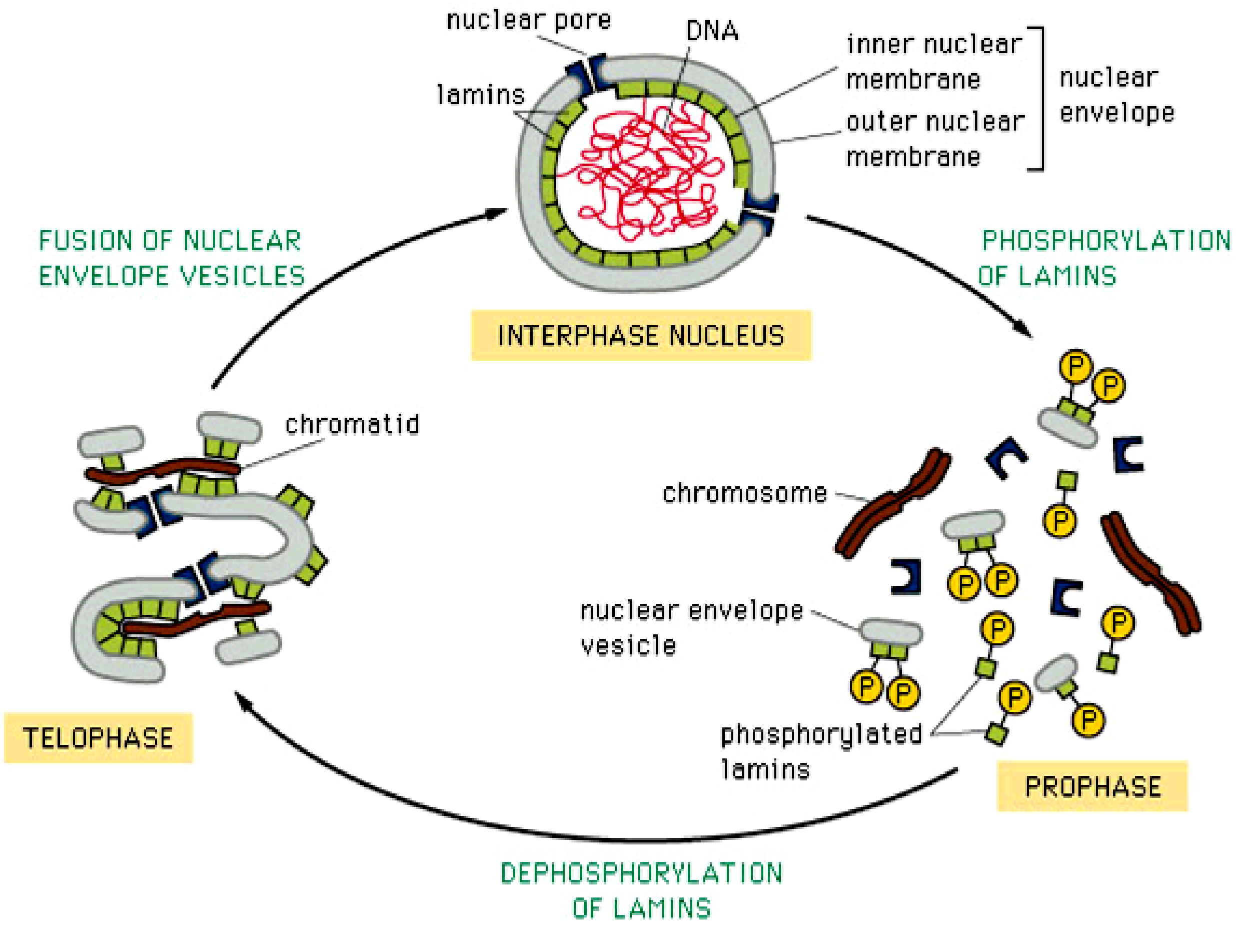
5 TELOPHASE



During telophase, the two sets of daughter chromosomes arrive at the poles of the spindle and decondense. A new nuclear envelope reassembles around each set, completing the formation of two nuclei and marking the end of mitosis. The division of the cytoplasm begins with contraction of the contractile ring.

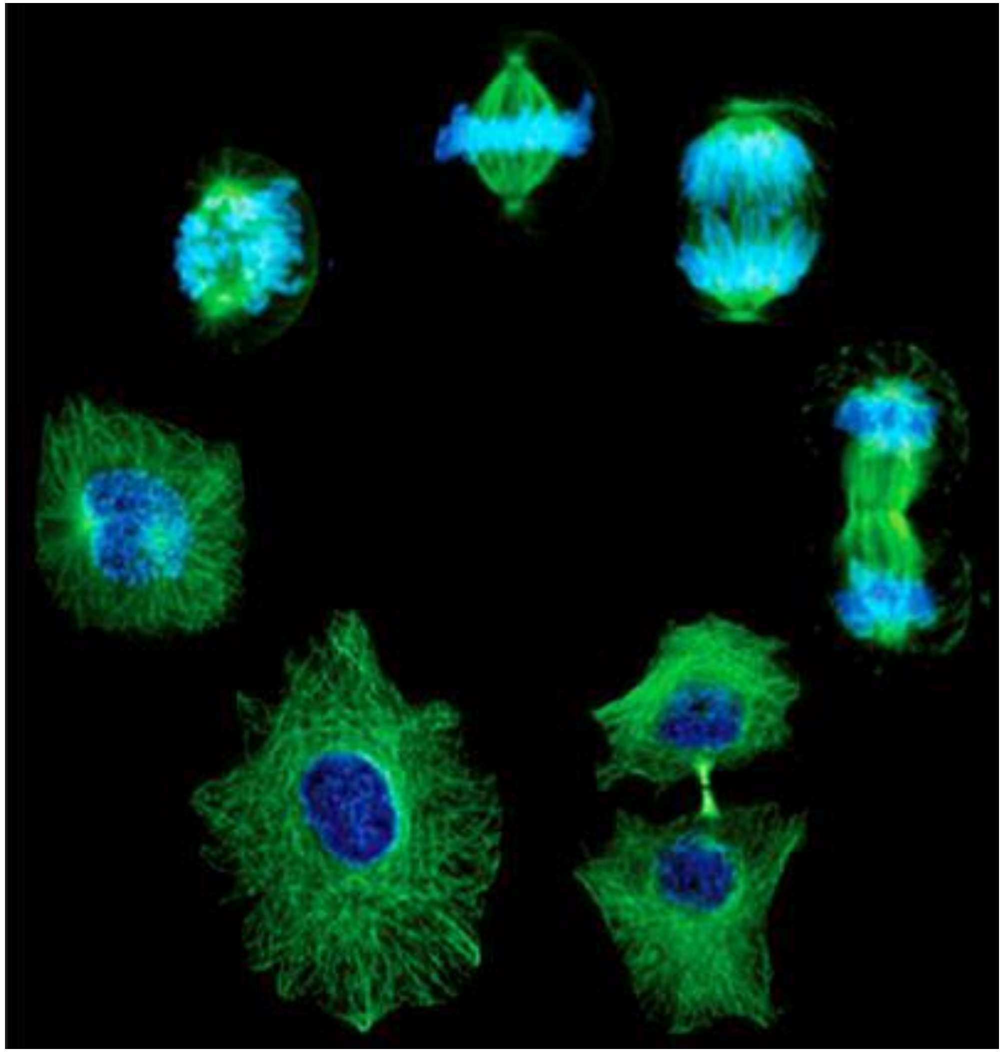


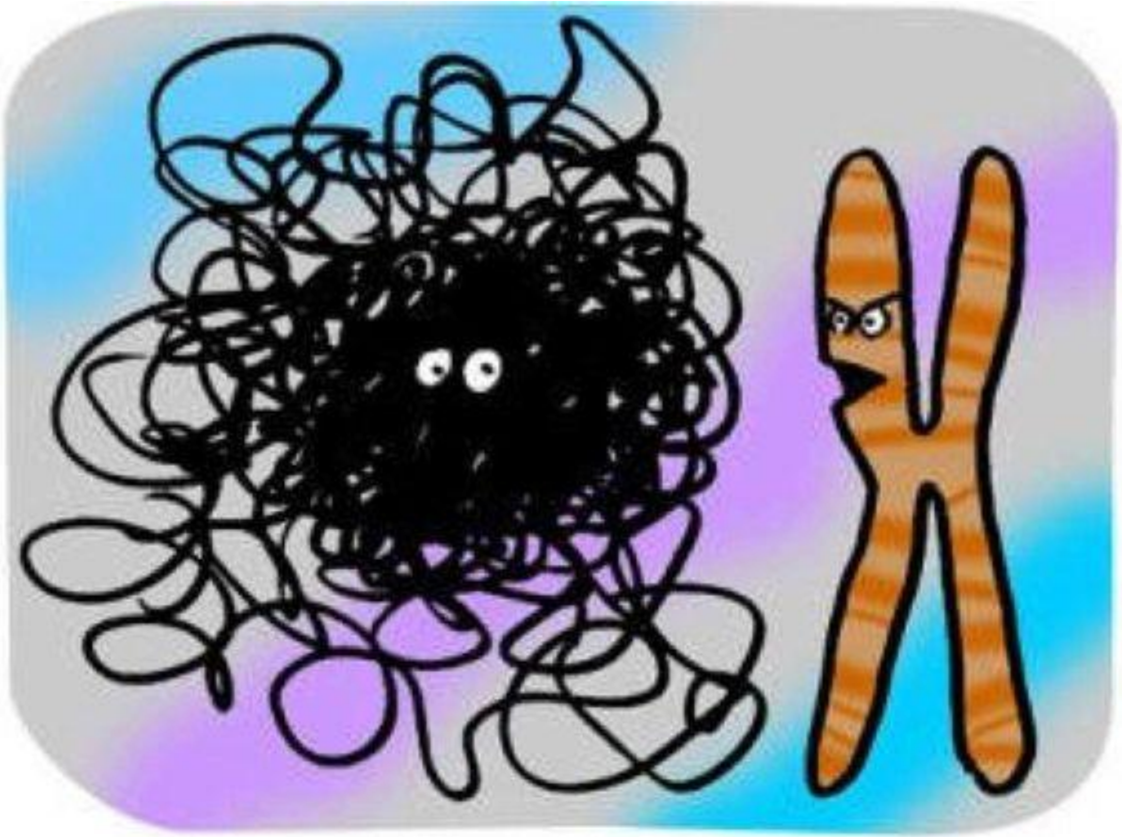
Nuclear envelope reassembly



- **Dephosphorylation of lamins** by protein phosphatases
  - Protein phosphatase 1 (PP1), PP2A
  - Active due to the deactivation of Cdks (degradation of cyclins by APC/C)

Microtubules / DNA

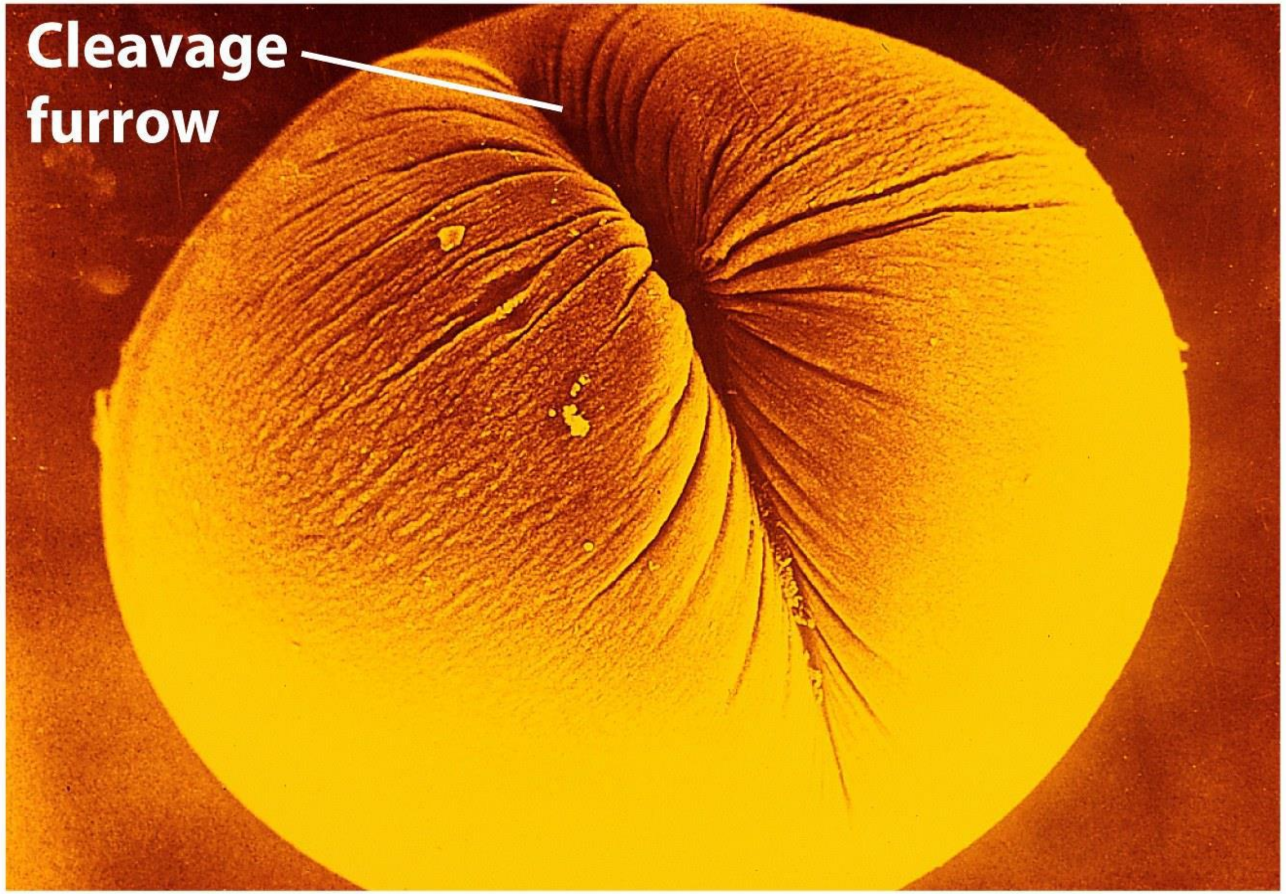




Dude, mitosis starts in five minutes...
I can't believe you're not condensed yet.

Cytokinesis

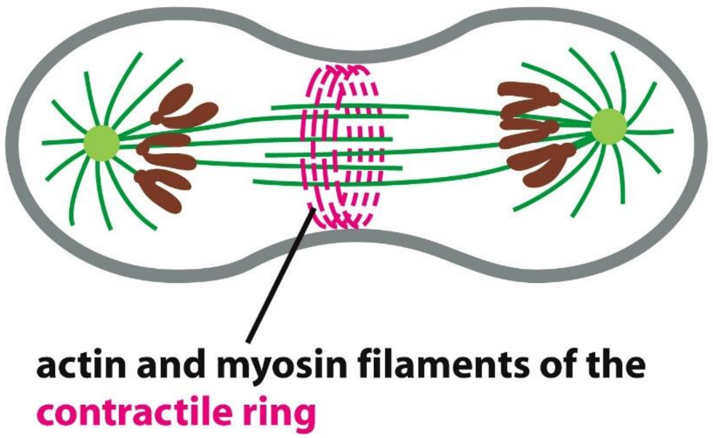
Cytokinesis in an animal cell (zygote)

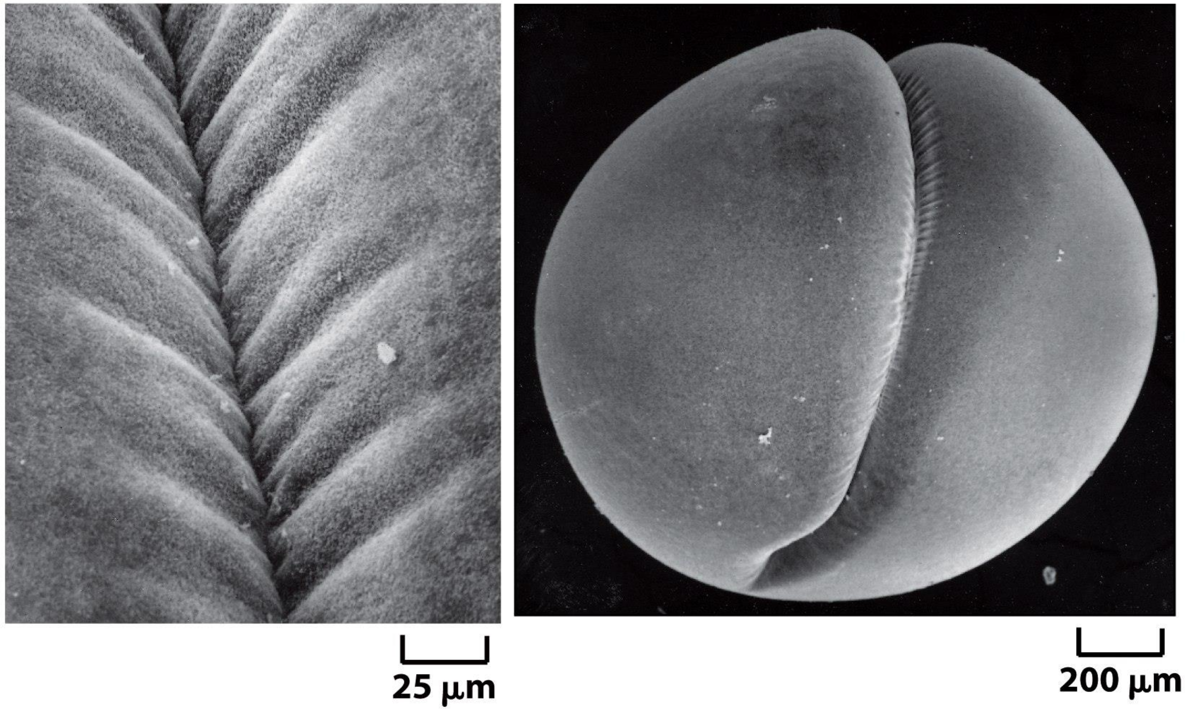


(mag × 30)

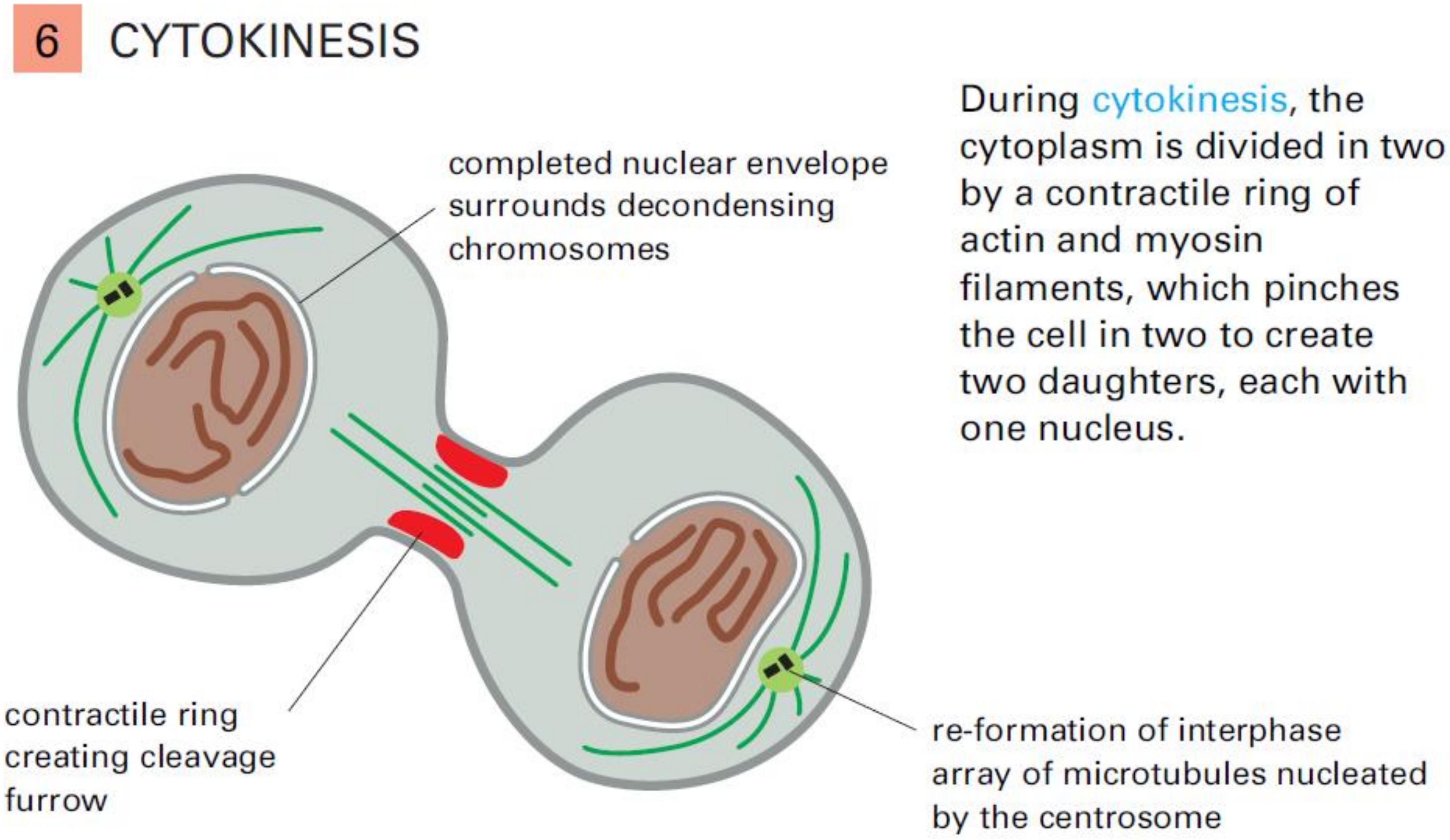
Cytokinesis – animal cells

- **Contractile ring** at the original equatorial plane
- **Actin and myosin movement**

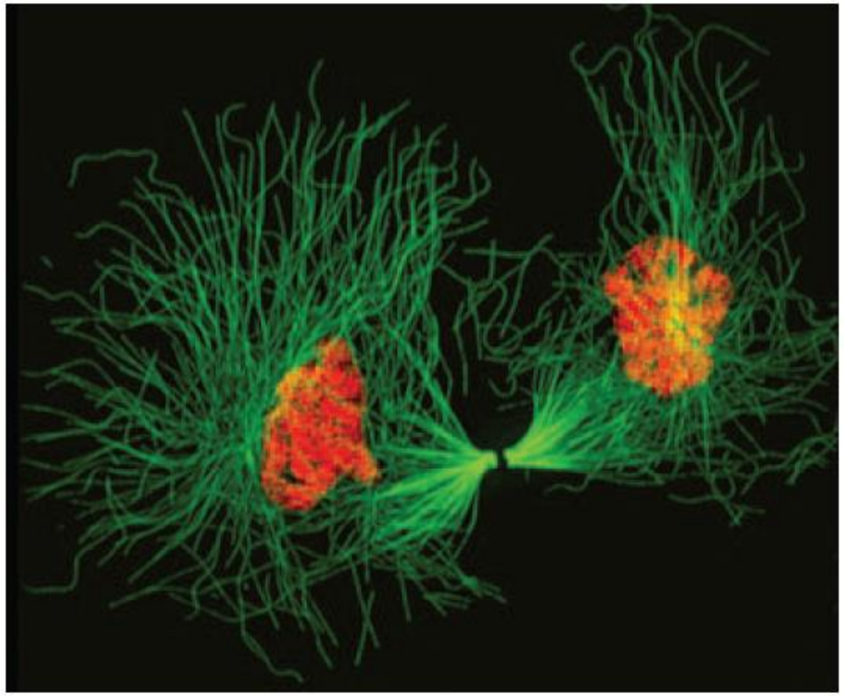




Cytokinesis – animal cells



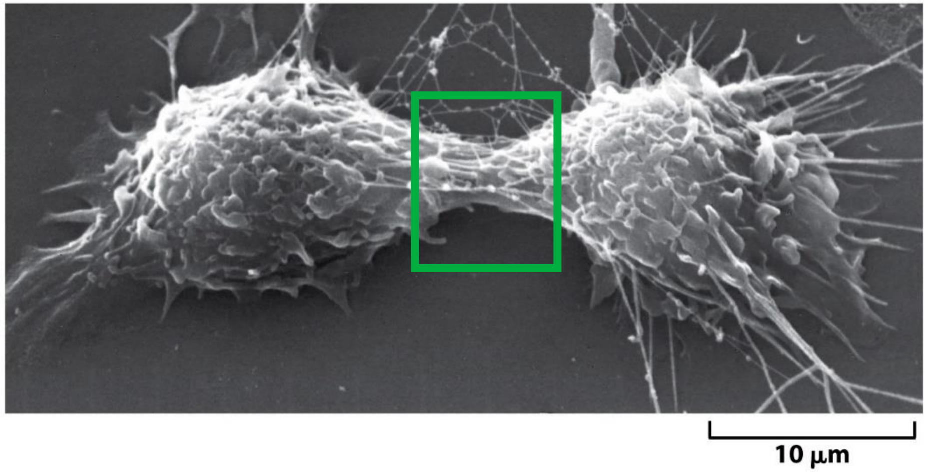
During cytokinesis, the cytoplasm is divided in two by a contractile ring of actin and myosin filaments, which pinches the cell in two to create two daughters, each with one nucleus.

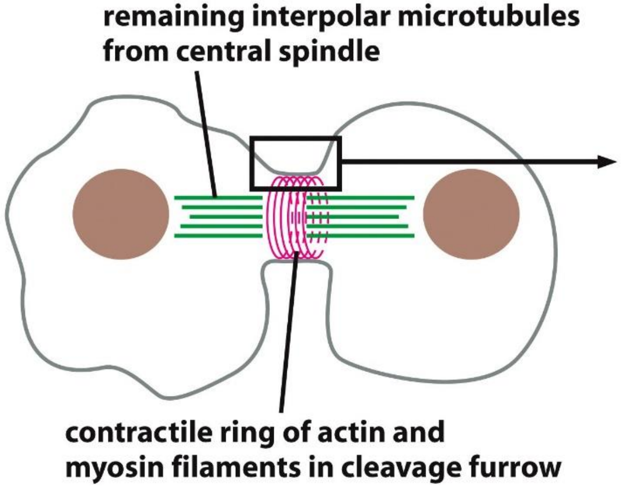


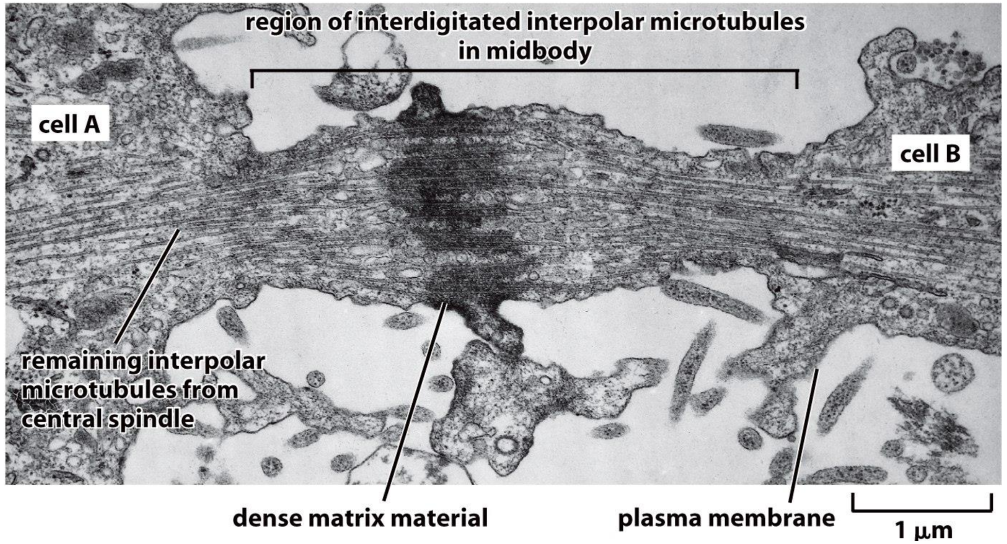
Cytokinesis – animal cells

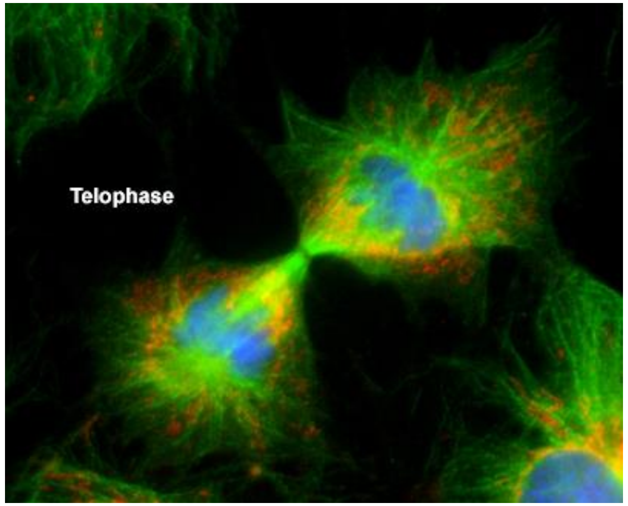
– Midbody

- Tether between dividing cells
- After complete separation – signaling functions, cell polarization

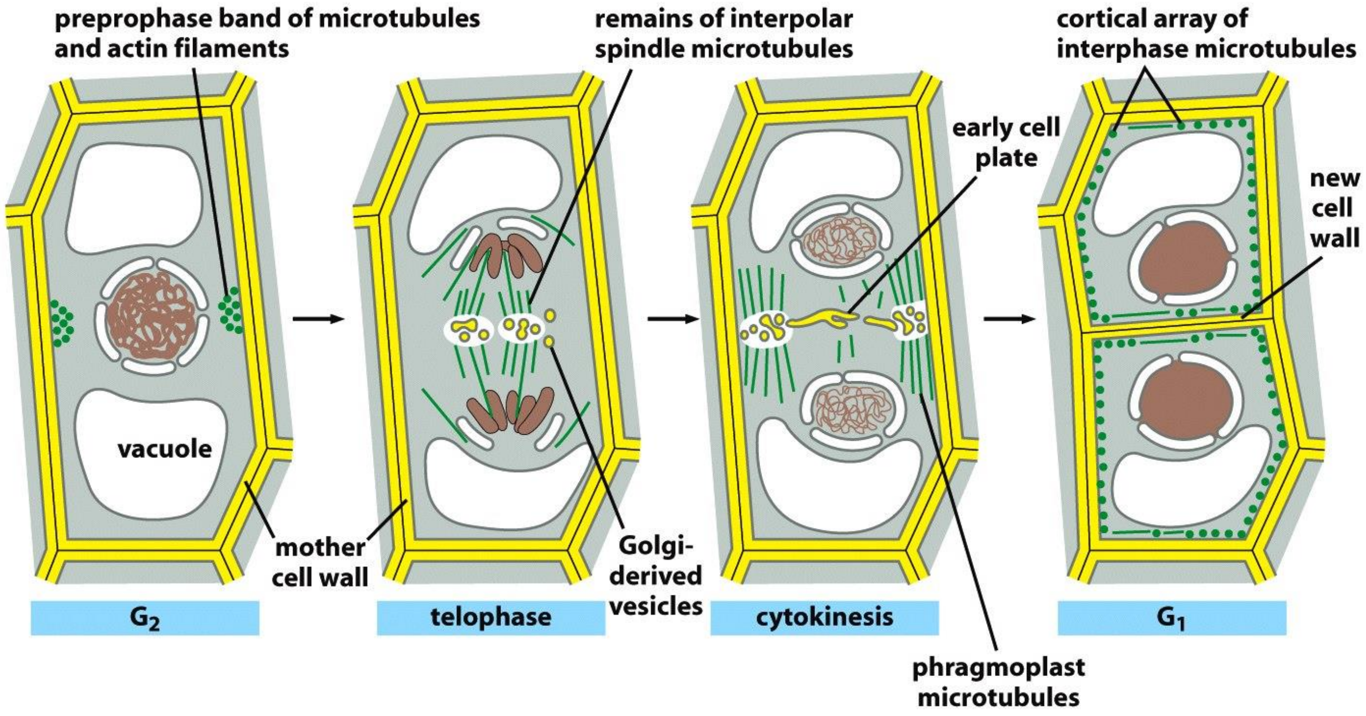






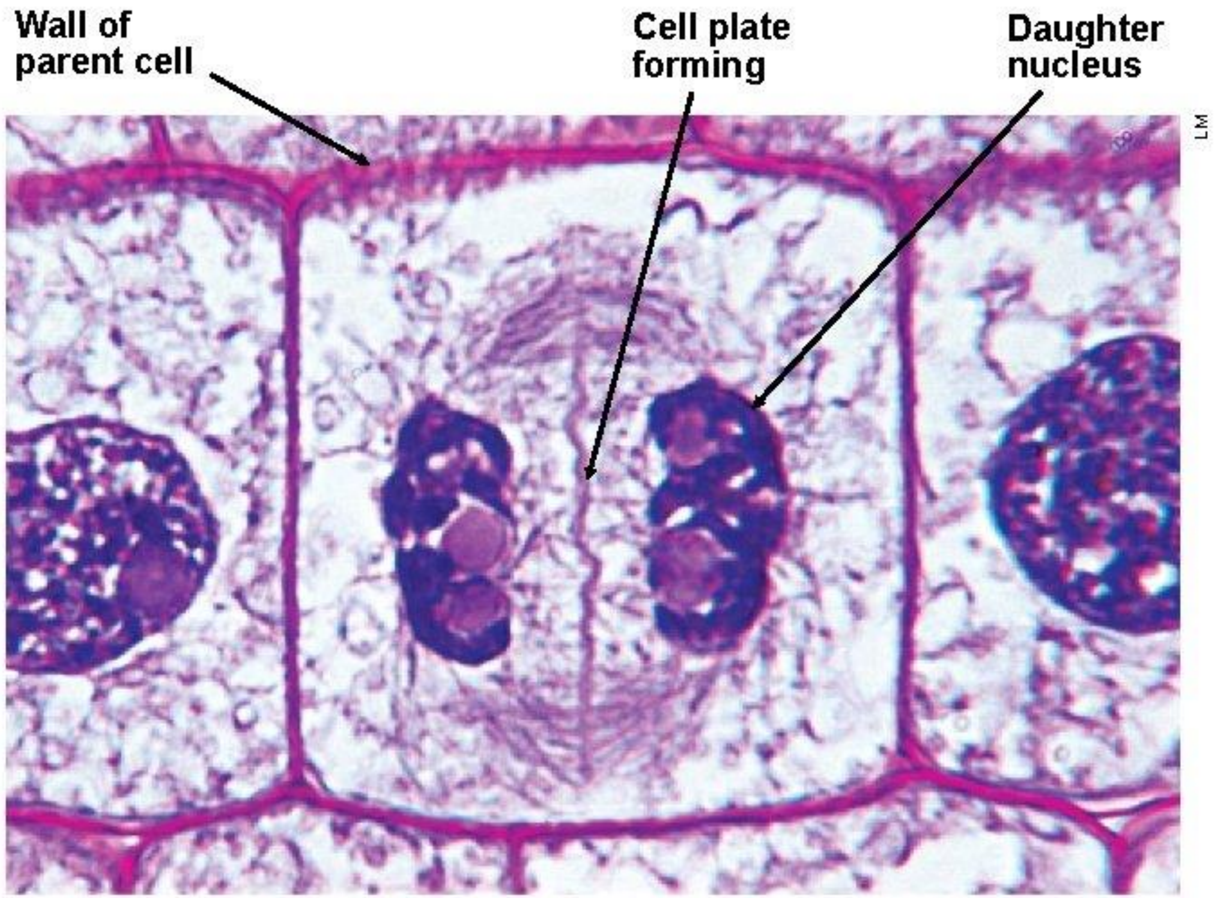


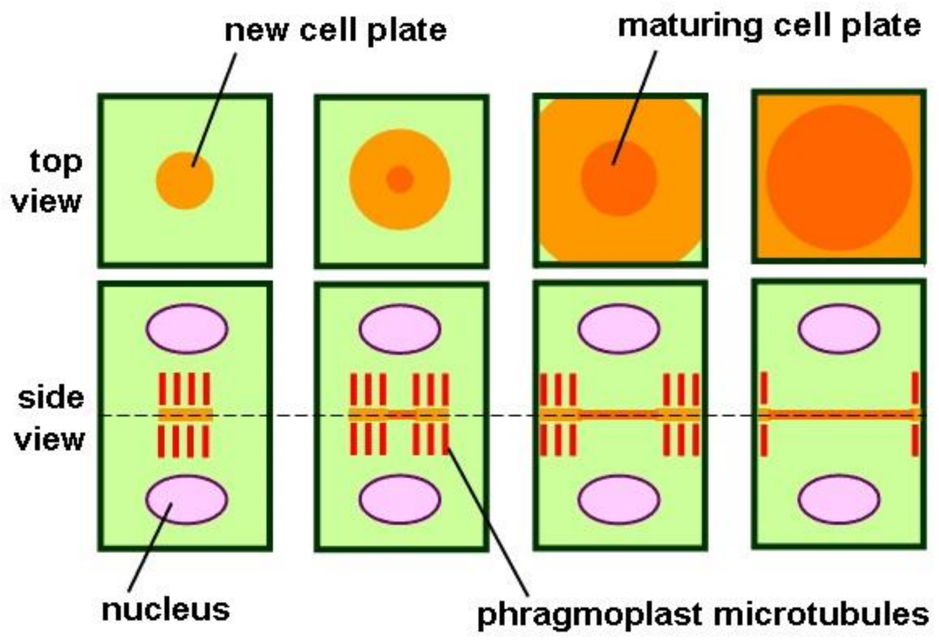
Cytokinesis – plant cells



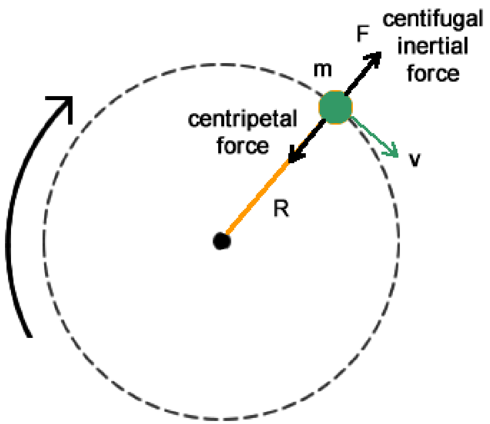
- **Phragmoplast** guides assembly of the **cell plate** (new cell wall)
- GA-derived vesicles filled with polysaccharides and glycoproteins
- Fusion – outward growth of the early cell plate

Cytokinesis – plant cells



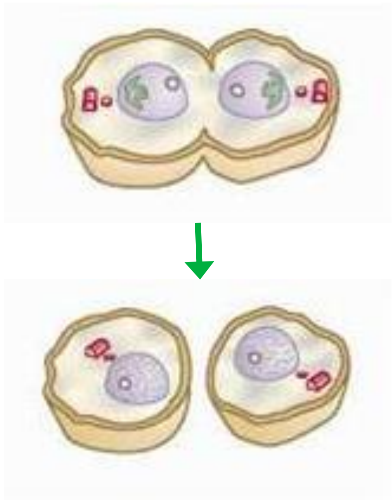


Cytokinesis – centripetal vs. centrifugal



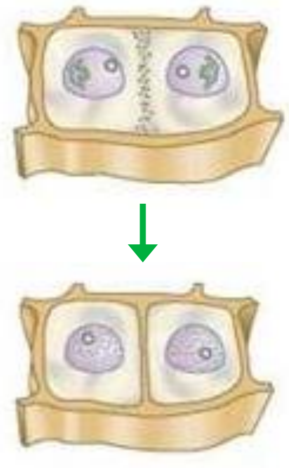
Animal cells

- **Centripetal division**
- Cleavage furrow



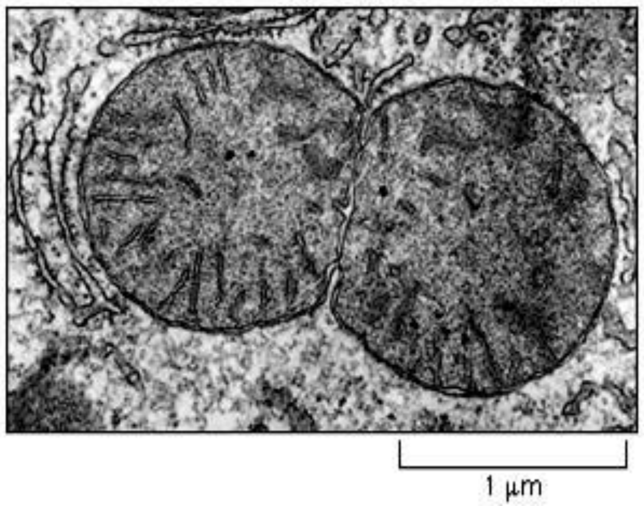
Plant cells

- **Centrifugal division**
- Central early cell plate growth

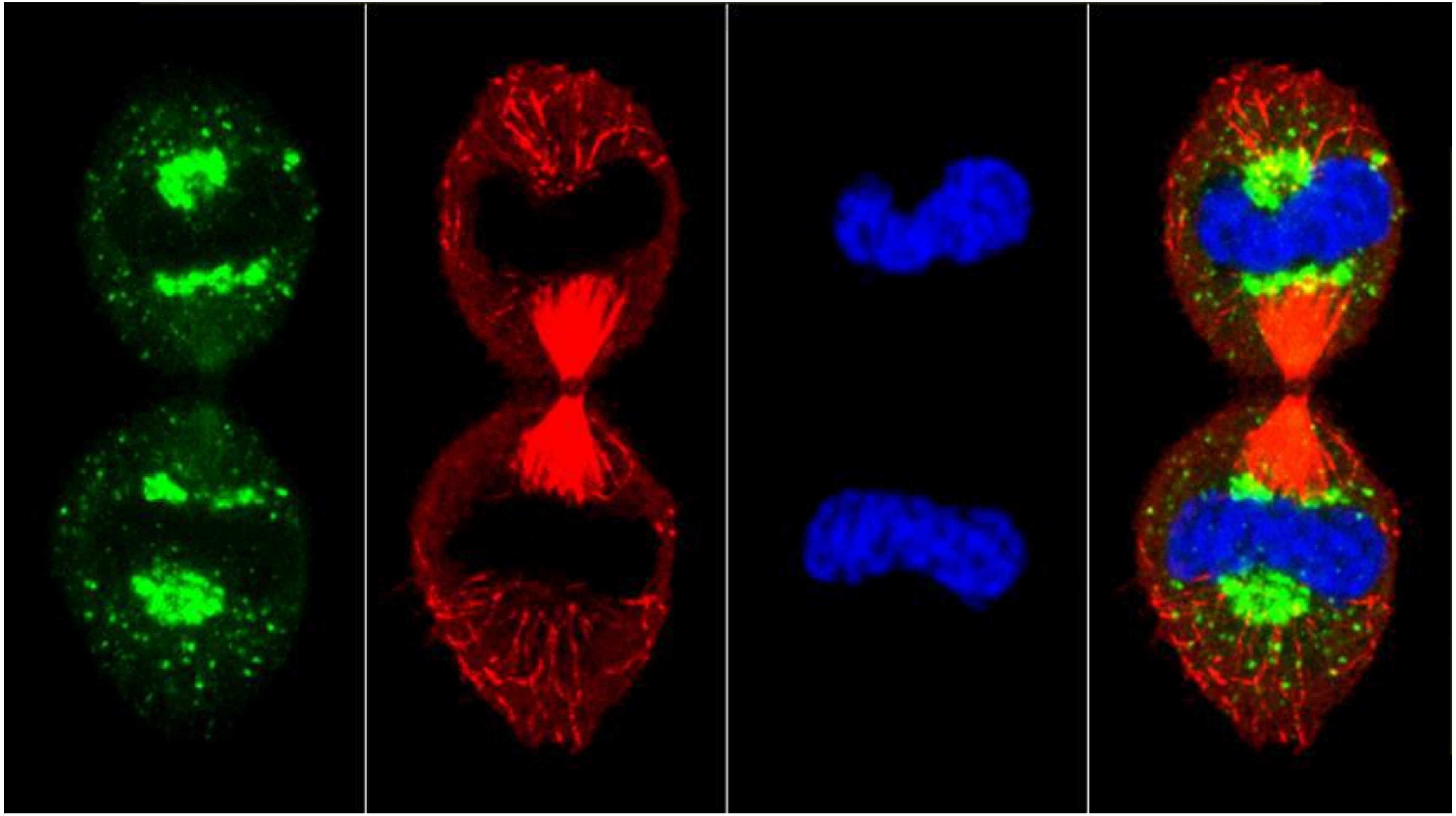


Distribution of organelles into daughter cells

- Most organelles are not synthesized *de novo*
  - Recent studies: GA, ER, peroxisomes, lysosomes, vacuoles may form *de novo*
  - Mitochondria cannot be synthesized de novo
- **Biosynthesis and fragmentation / fission of pre-existing organelles**
- Equal distribution during mitosis



Mitochondrion fission



ER microtubules DNA merge

Meiosis

Reproduction of eukaryotes

Asexual reproduction

- The offspring inherit the full set of genes of their single parent

Sexual reproduction

- Involves **fusion of gametes**
- Original sets of genes of both parents are **reshuffled and combined** in a **genetically unique offspring**
- Selective advantage in a rapidly changing environment

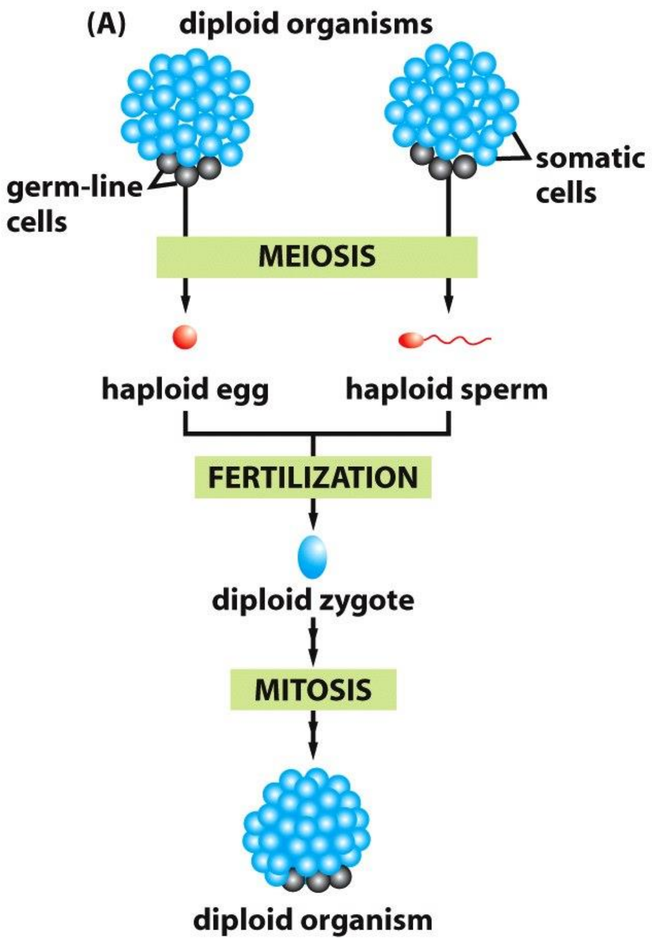
Meiosis

- Two subsequent cell divisions with only one round of DNA replication:
- **Meiosis I** (heterotypic division)
- **Meiosis II** (homotypic division)

Function

- Reduction of chromosomes: haploid gametes from germ cells
- Independent assortment of the maternal and paternal homologs: 2^n combinations
- Recombination of genes: crossing-over of homologous chromosomes

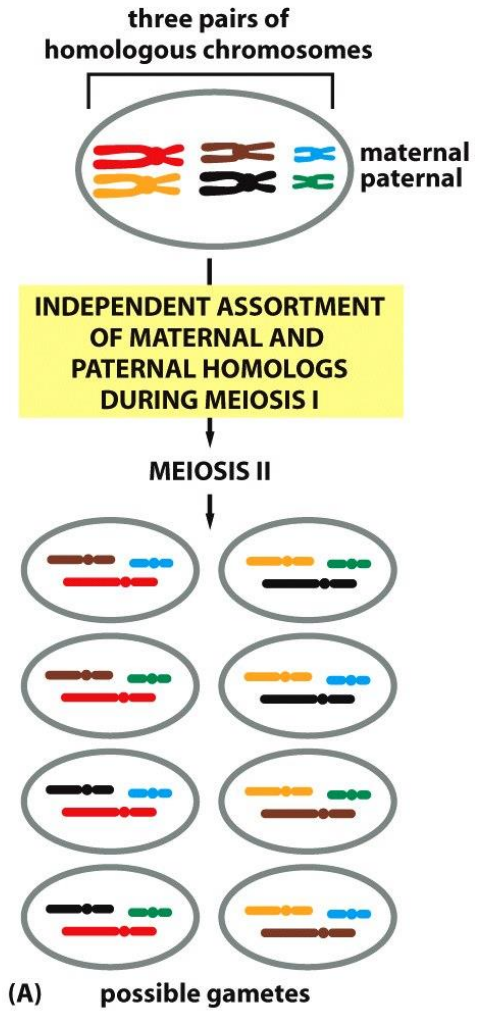
Three major roles of meiosis



– **Reduction of the sets of chromosomes**

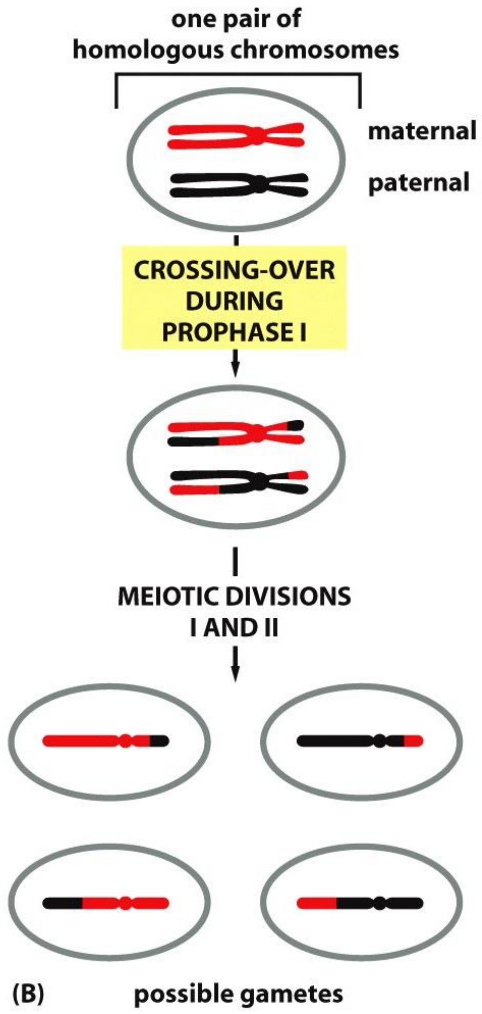
– **Haploid gametes** from **diploid germ-line cells**

Three major roles of meiosis



- **Independent assortment of the maternal and paternal homologous chromosomes**
- **Genetic variability: 2^n combinations**
- Humans: 2^{23} = 8,388,608 different combinations (different gametes)
  - Further variability: one of these gametes of one parent fuses with one from the possible combinations from the other parent
  - Further variability: genetic recombination during crossing-over

Three major roles of meiosis



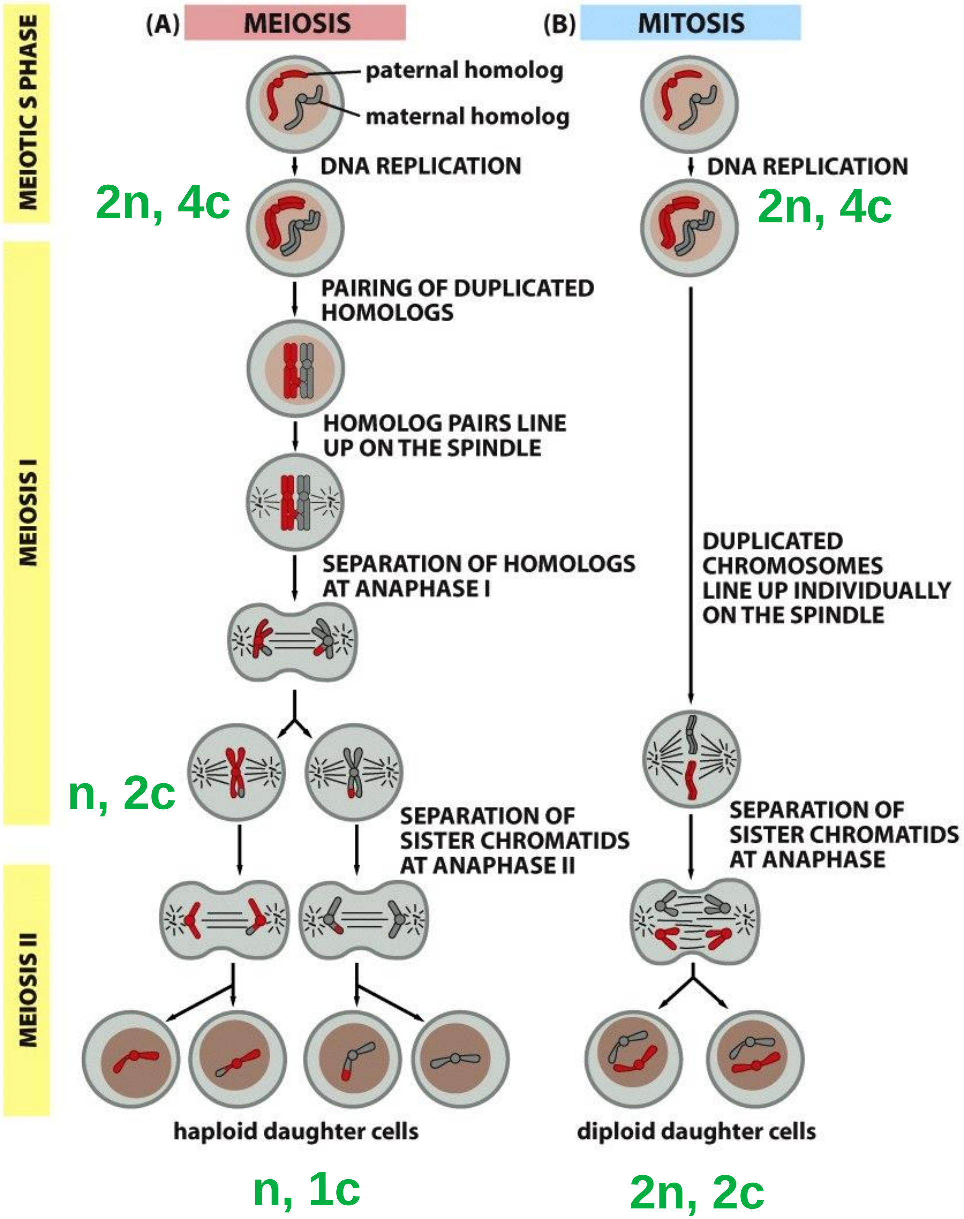
- **Recombination of genes**: exchange of genetic material between homologous chromosomes during crossing over
- Shuffles DNA regions of maternal and paternal chromosomes

- **Increases genetic variability of gametes**

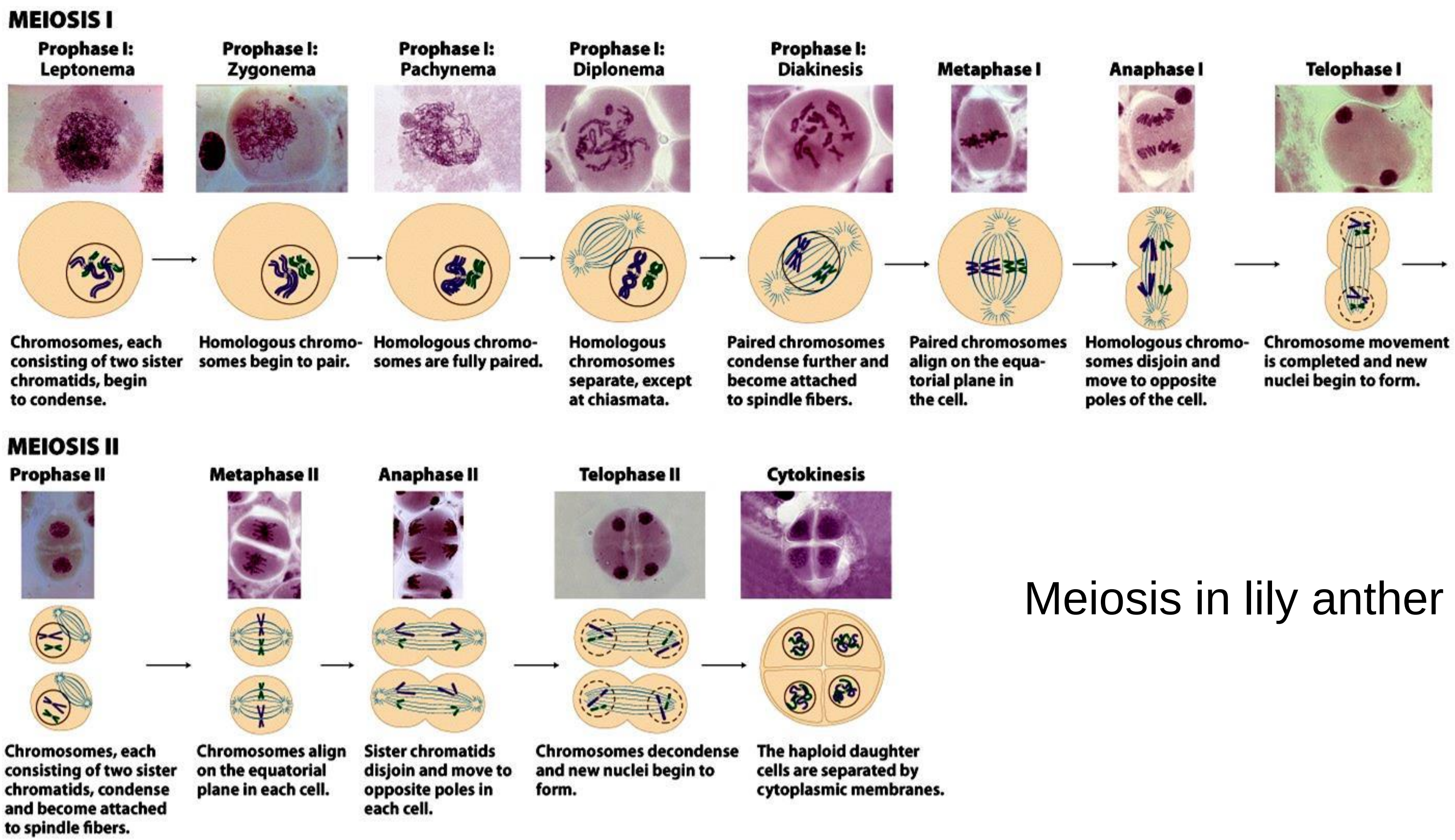
Stages of meiosis

- Premeiotic interphase
- **Meiosis I – heterotypic**
  - **Prophase I**
    - Leptotene
    - Zygotene
    - Pachytene: crossing-over
    - Diplotene
    - Diakinesis
  - **Metaphase I**
  - **Anaphase I:** separation of homologs
  - **Telophase I & Cytokinesis**
- **Meiosis II – homotypic**
  - **Prophase II**
  - **Metaphase II**
  - **Anaphase II:** separation of chromatids
  - **Telophase II & Cytokinesis**

Heterotypic vs. homotypic division

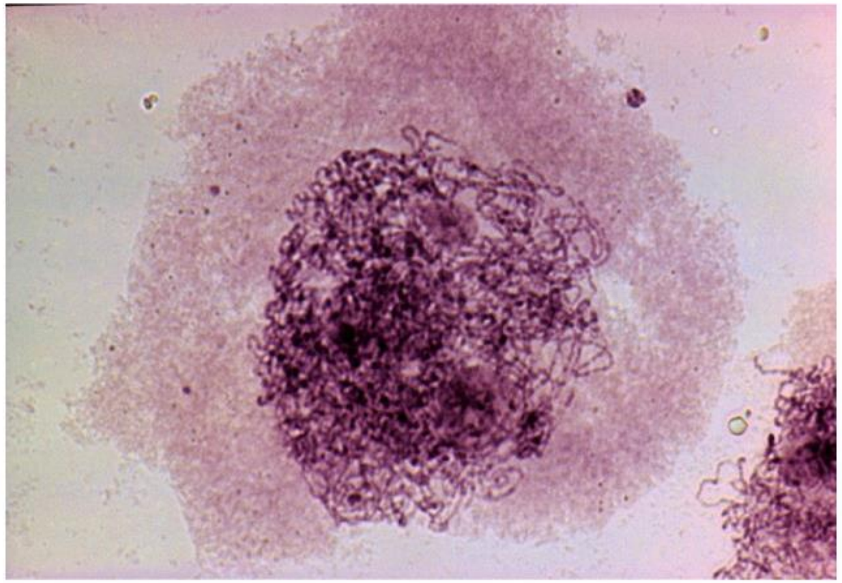


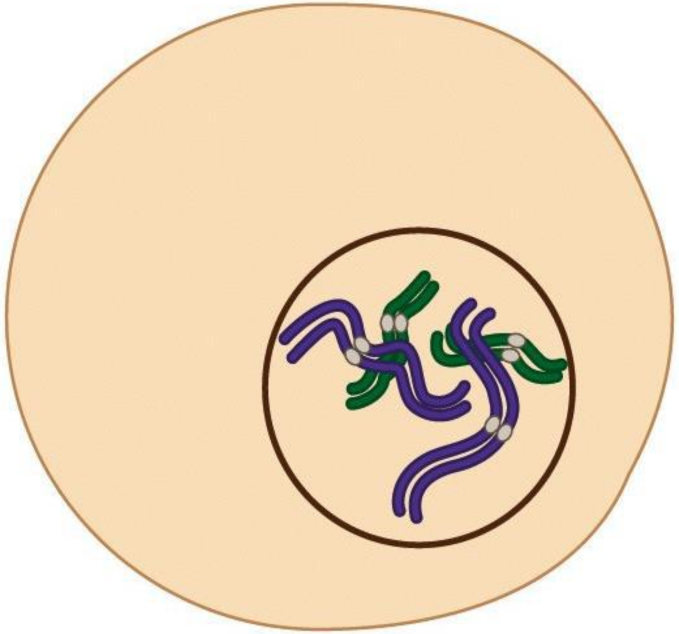
Stages of meiosis



Meiosis in lily anther

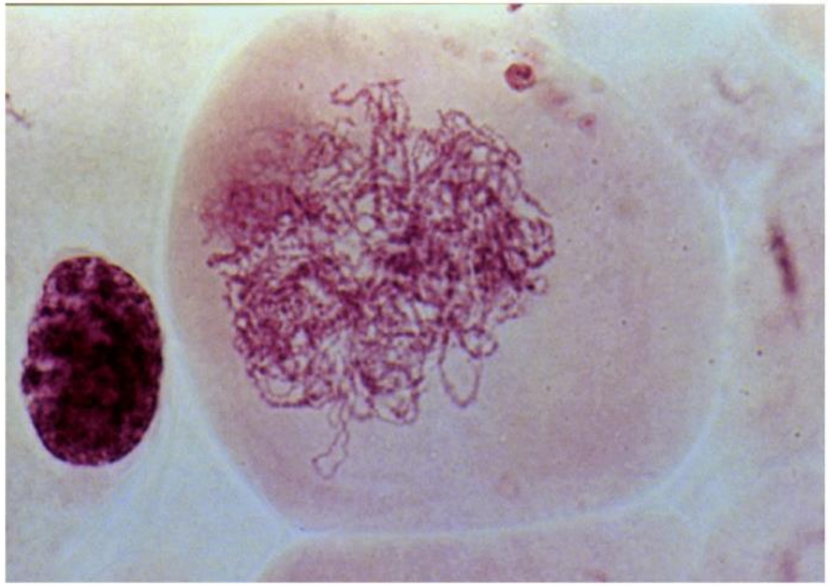
Meiosis I: Prophase I – Leptotene

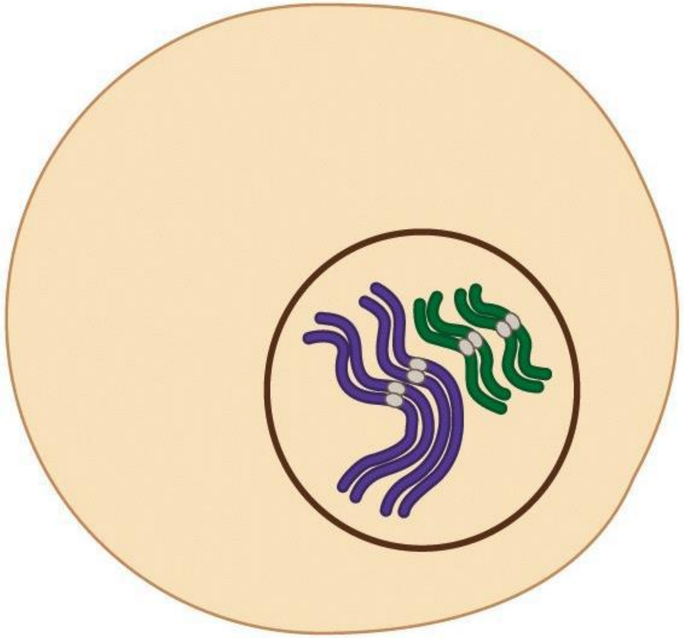




– Condensation of chromosomes – each formed by two chromatids

Meiosis I: Prophase I – Zygotene

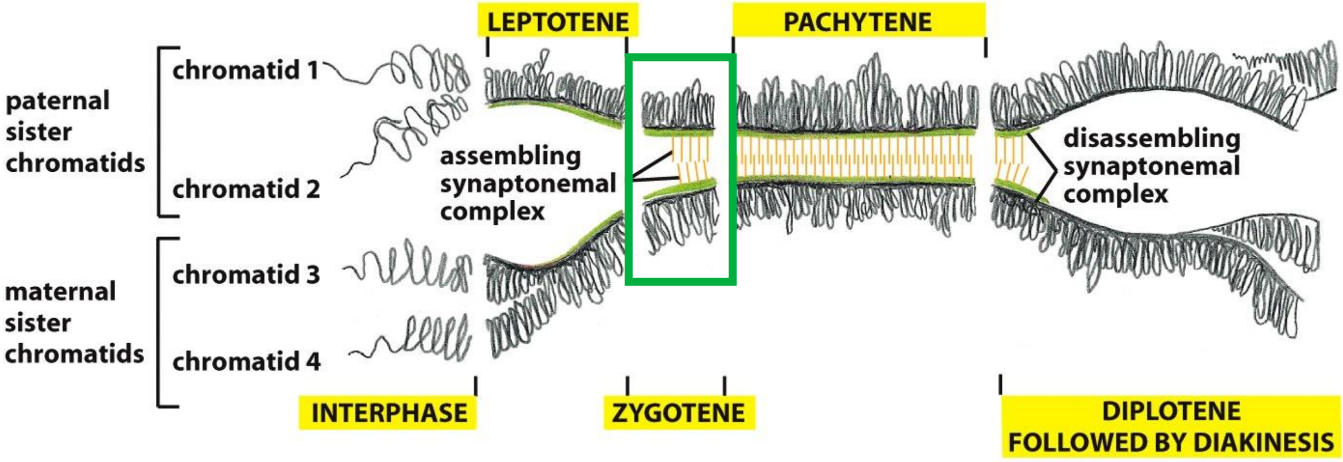


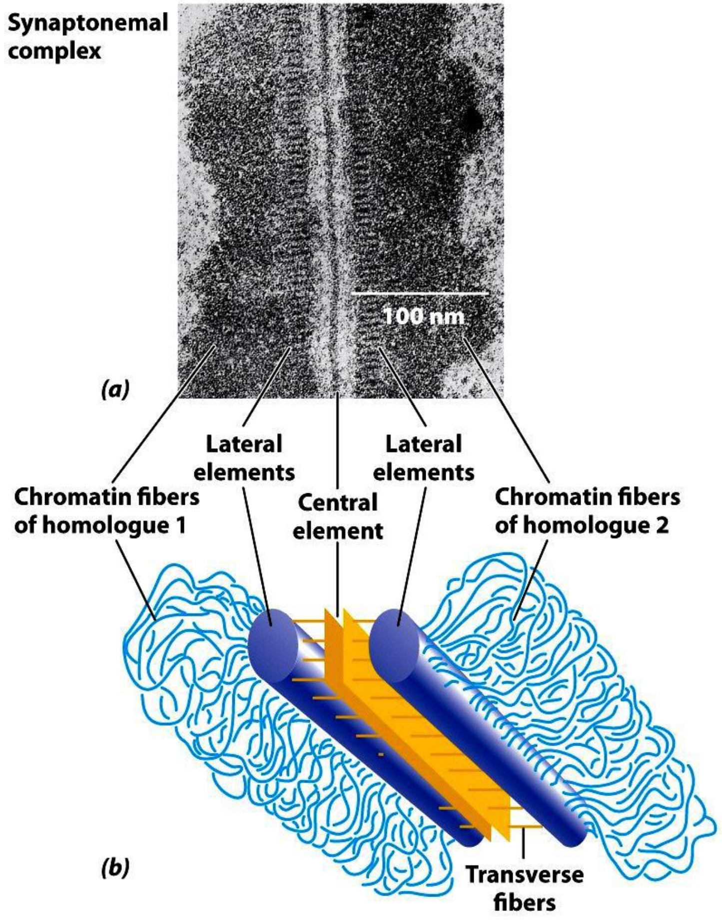


– Homologous chromosomes begin to pair

Meiosis I: Prophase I – Zygotene

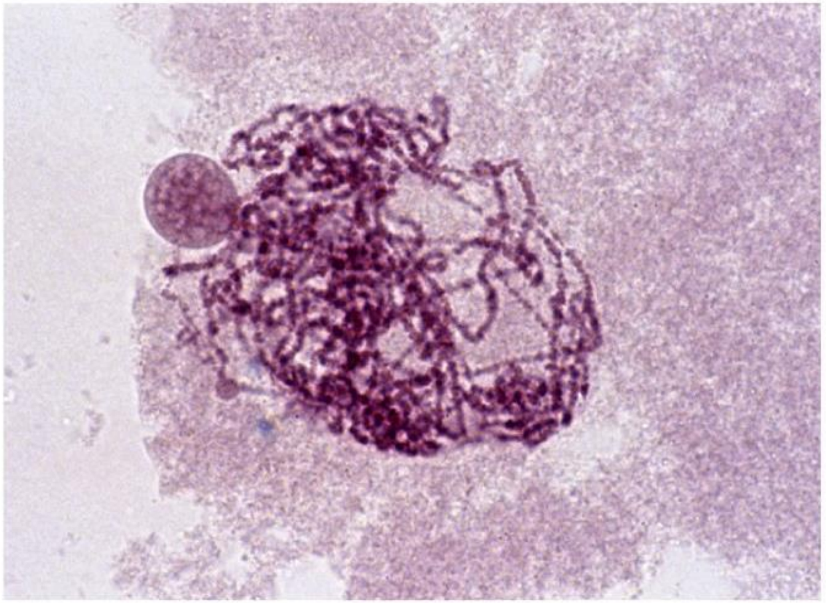
- **Formation of synaptonemal complex**

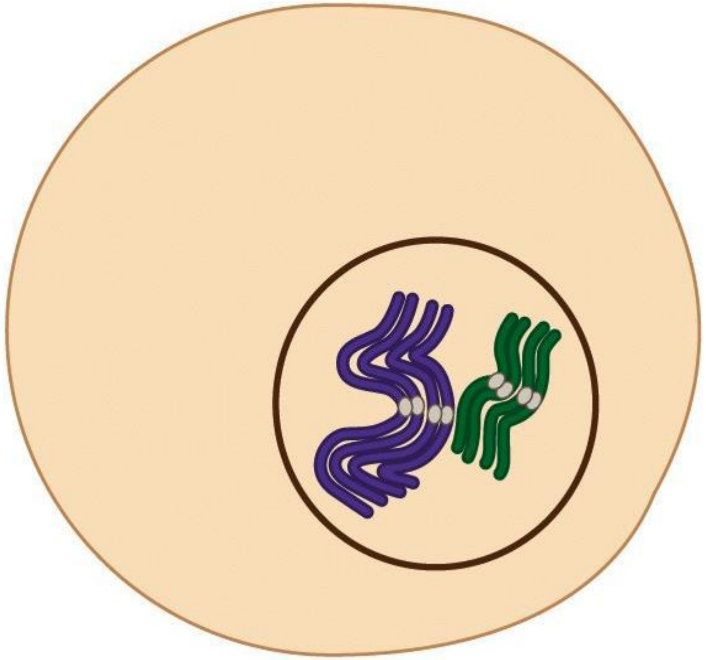




- Specific protein complexes forming:
  - Central element
  - Transverse filaments
  - Lateral elements

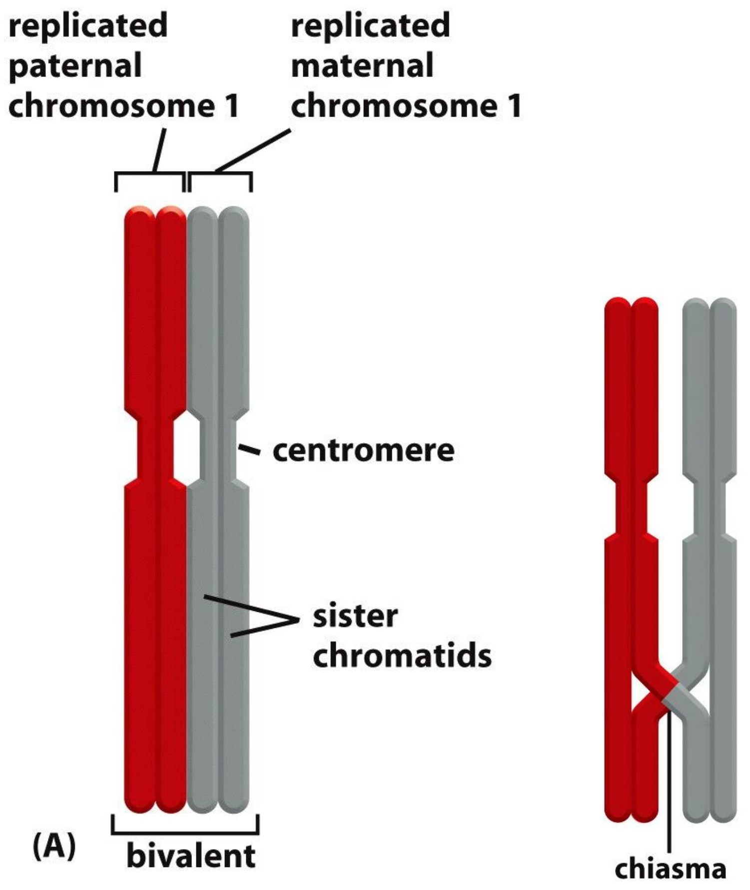
Meiosis I: Prophase I – Pachytene



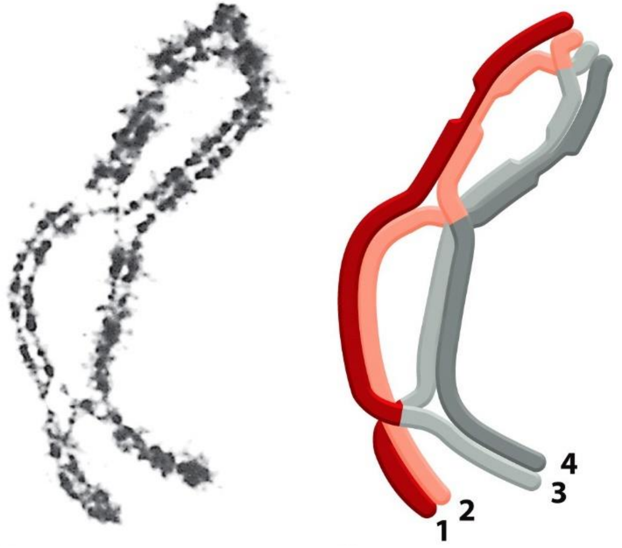


– Homologous chromosomes are fully paired

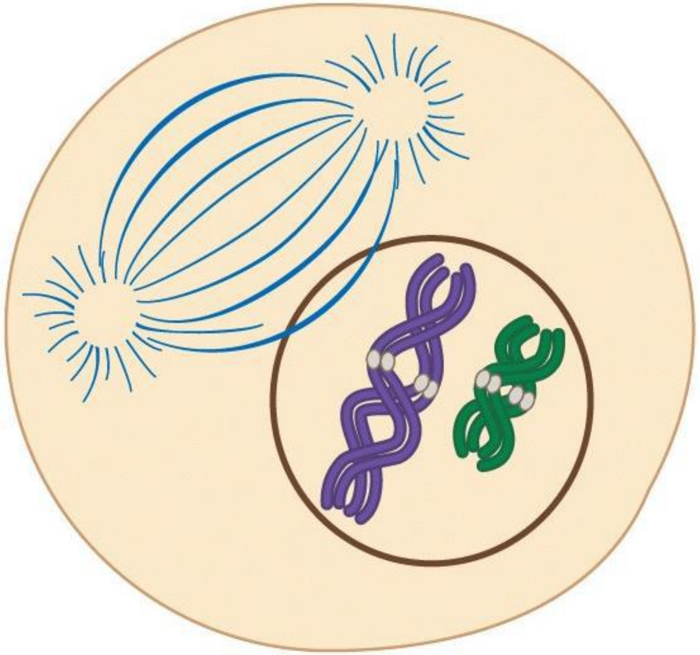
Meiosis I: Prophase I – Pachytene



- Formation of **bivalents** (= **tetrads** referring to chromatids)
- **Crossing-over** between chromatids of homologous chromosomes
- Results in **chiasmata**



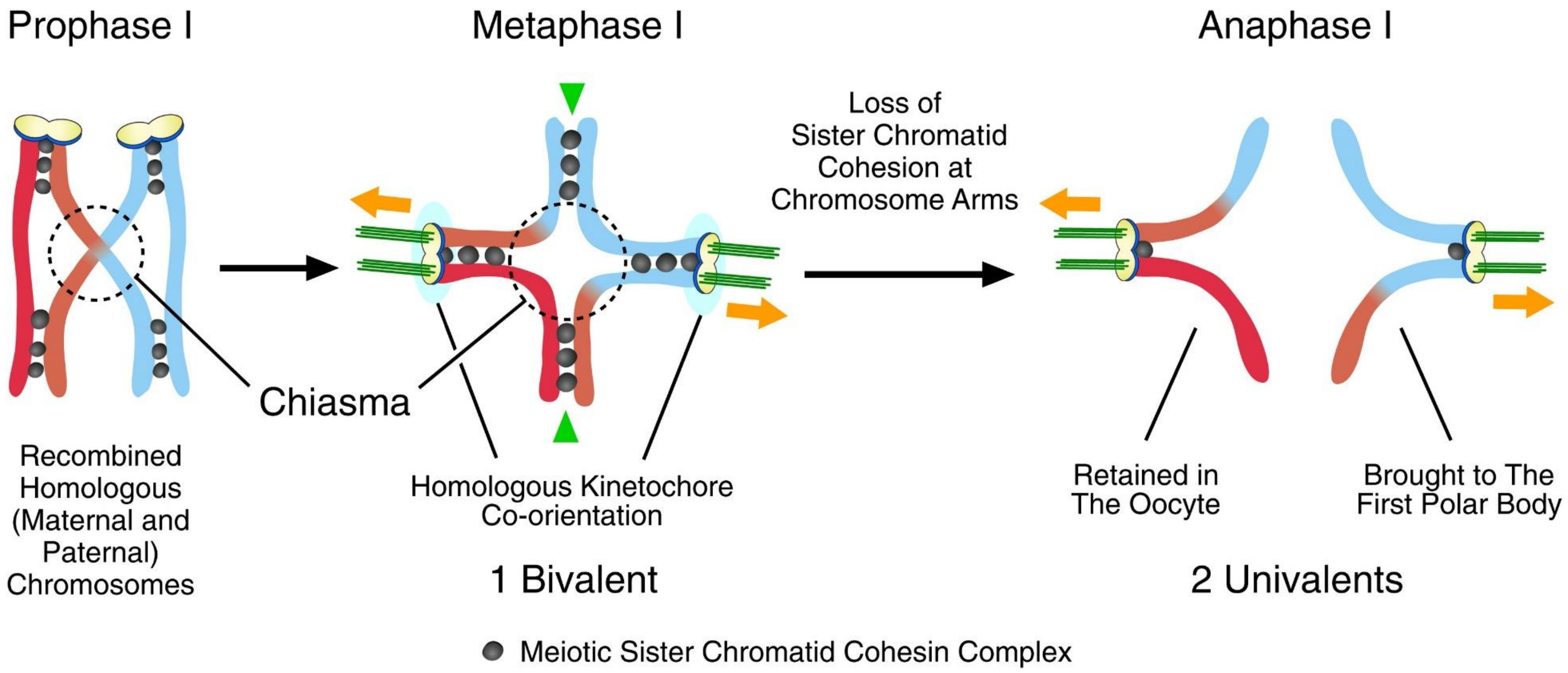
Meiosis I: Prophase I – Diplotene



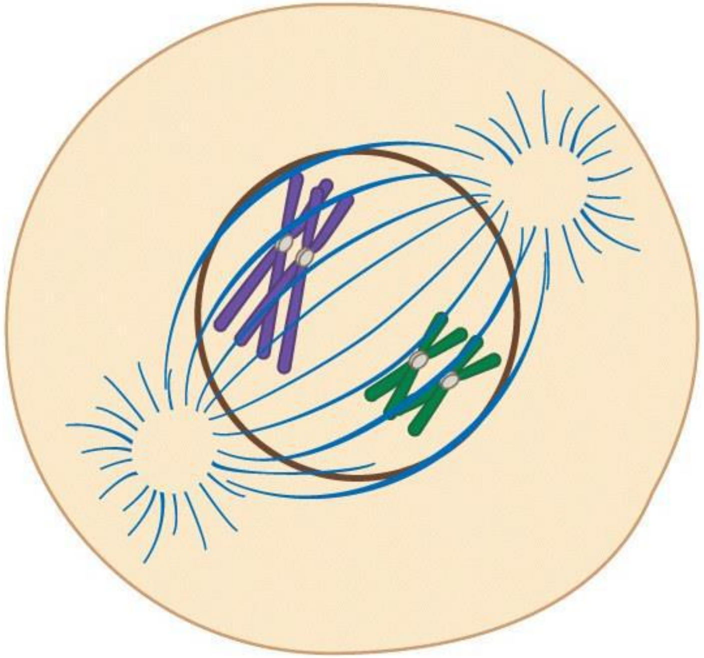
– Homologous chromosomes separate, except at chiasmata

Resolution of chiasmata

- **Fully resolved during Anaphase I**

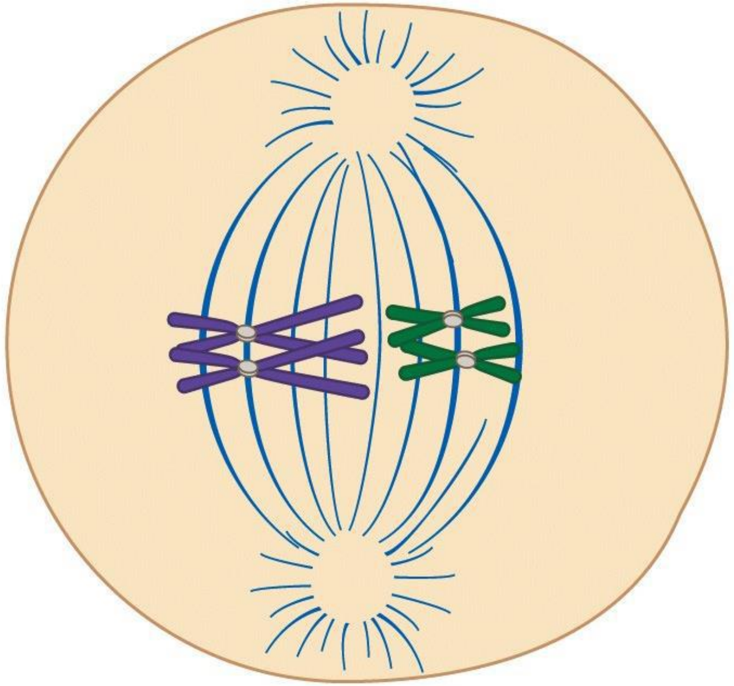


Meiosis I: Prophase I – Diakinesis



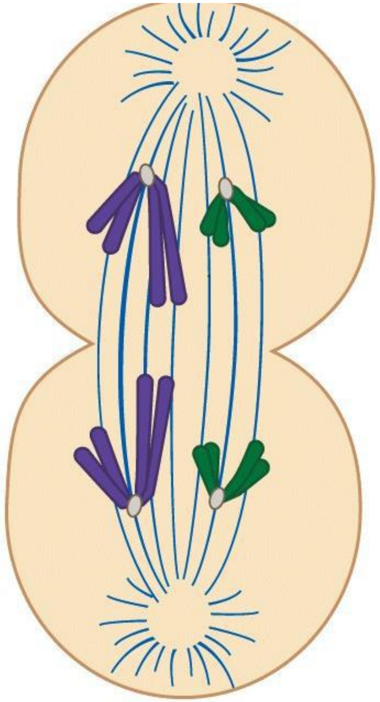
- Further condensation of paired chromosomes and their attachment to spindle microtubules

Meiosis I: Metaphase I



– Paired chromosomes align at the equatorial plane in the cell

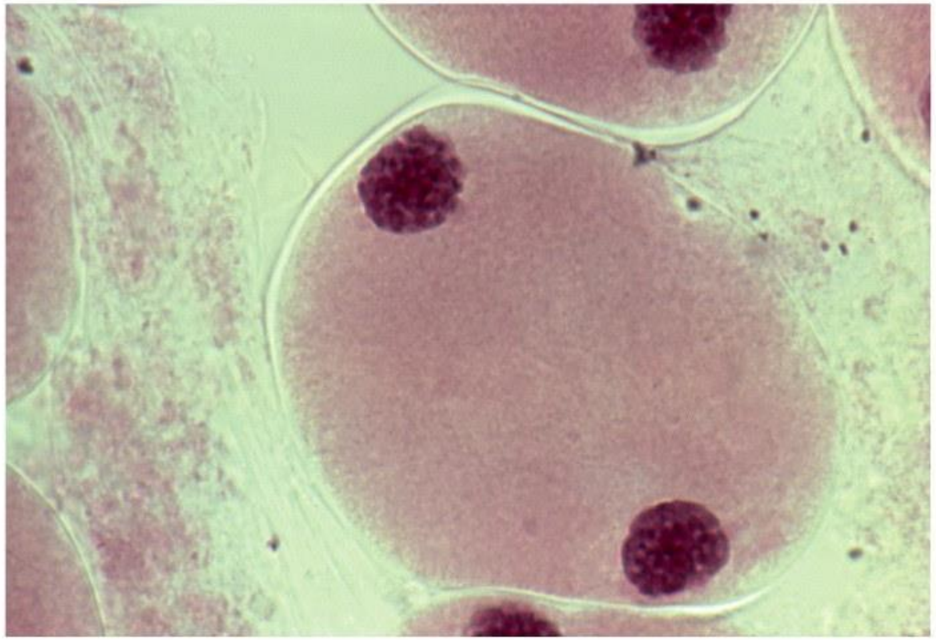
Meiosis I: Anaphase I

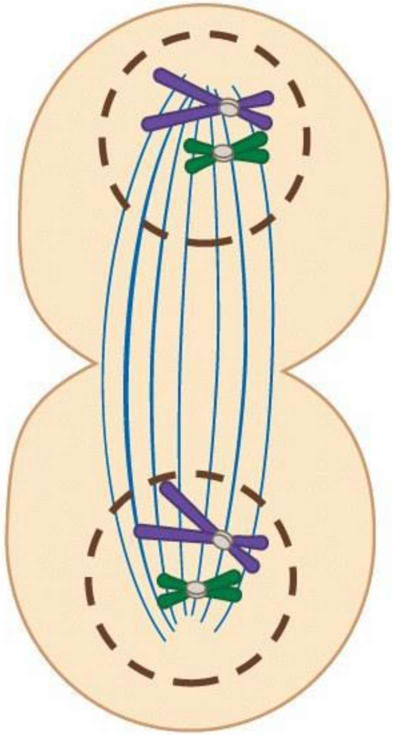


– **Reduction of chromosome sets: haploid cells**

– **Homologous chromosomes** separates (chiasmata resolved) and are moved to opposite poles of the cell – independent assortment

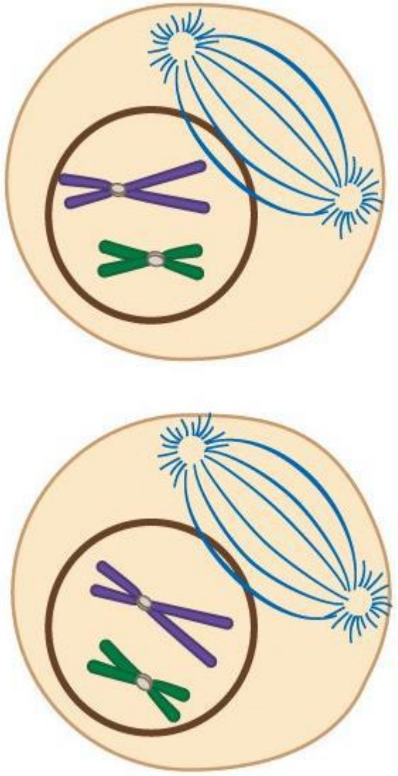
Meiosis I: Telophase I





- Chromosome movement is completed, formation of new nuclei
- Followed by Cytokinesis I

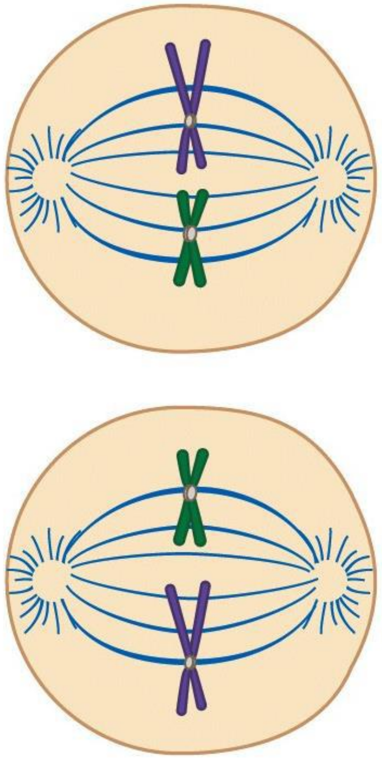
Meiosis II: Prophase II



- Haploid cells
- Each chromosome consists of two chromatids (some with recombined regions)

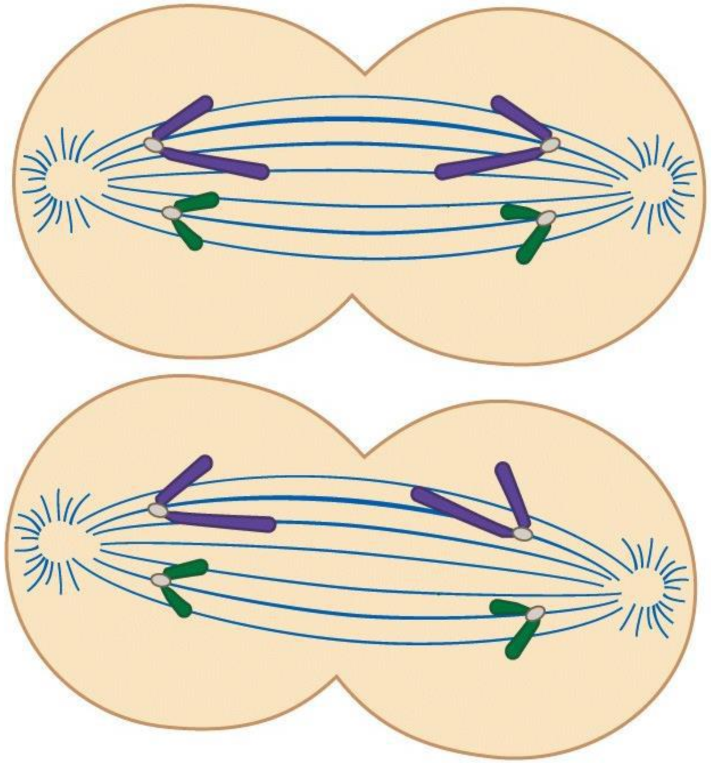
- Chromosomes condense and become attached to spindle microtubules

Meiosis II: Metaphase II



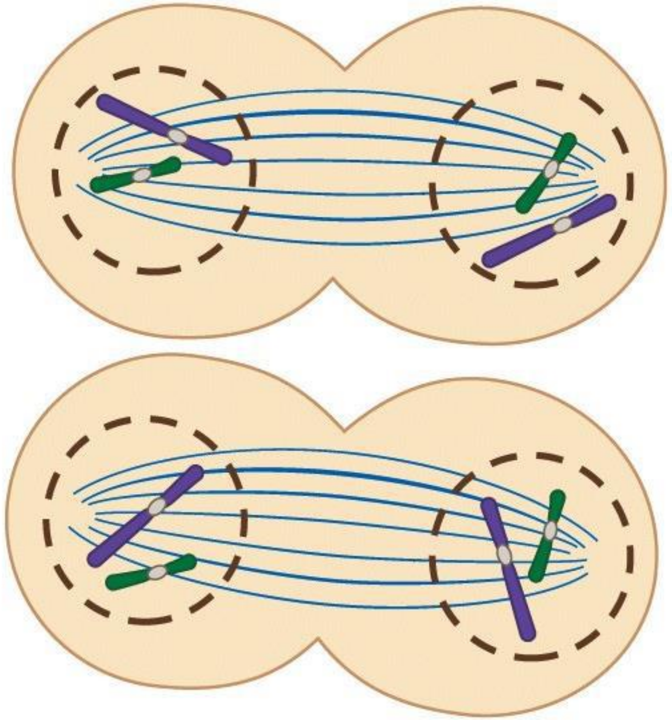
- Chromosomes align at the equatorial plane in each cell

Meiosis II: Anaphase II



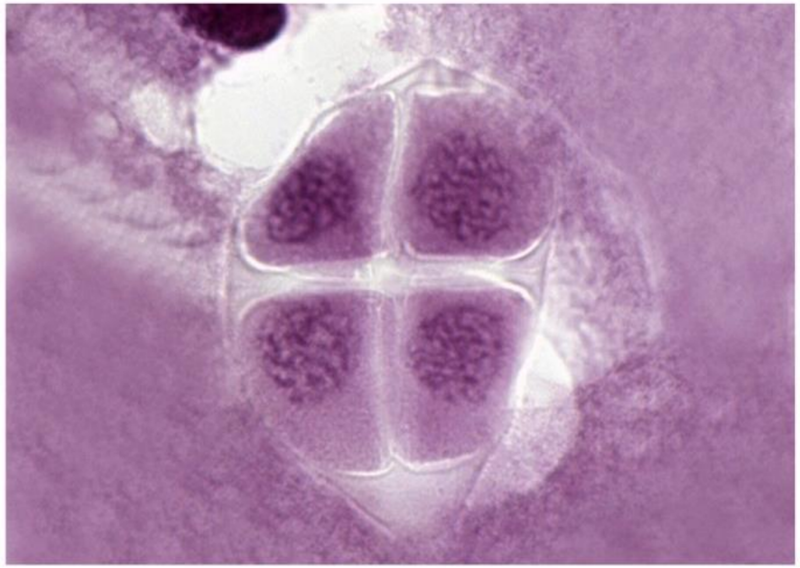
- **Sister chromatids** separate and are moved to opposite poles of the cells

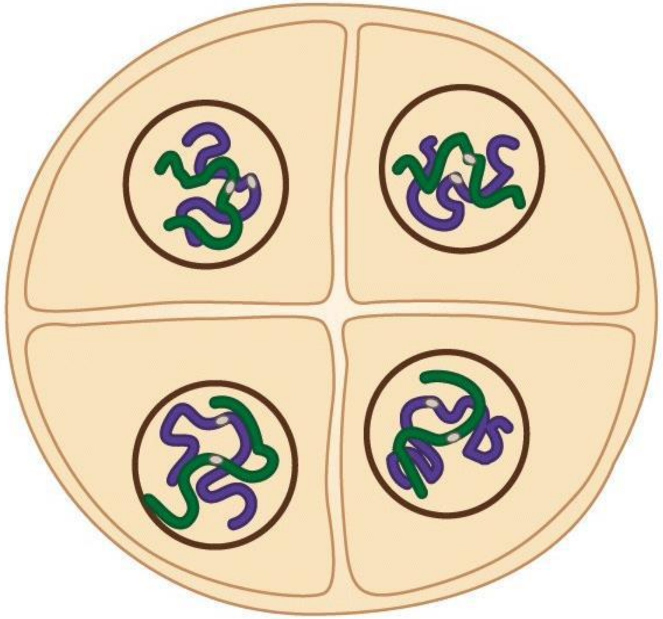
Meiosis II: Telophase II



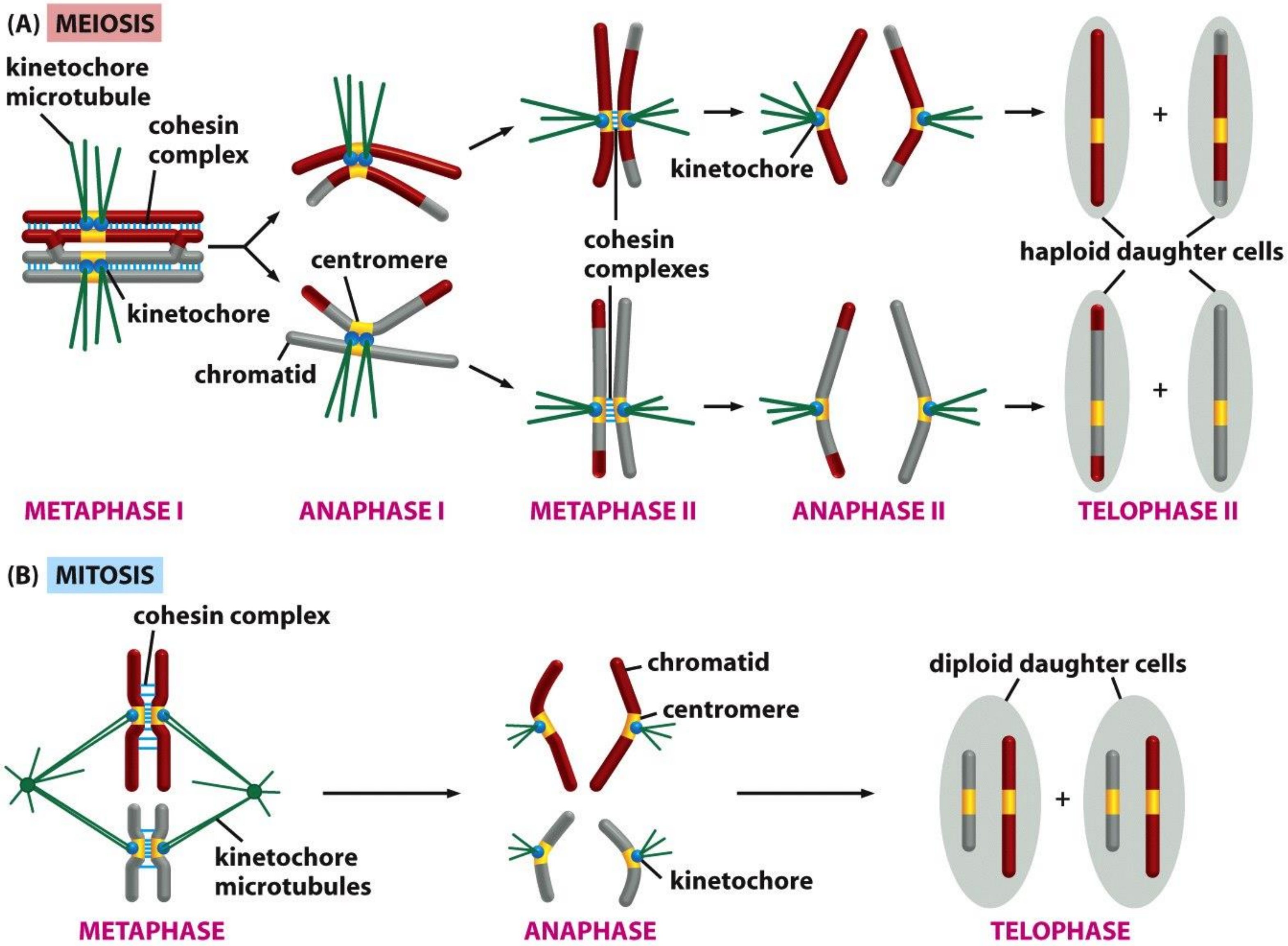
– Chromosomes decondense, formation of new nuclei
– Followed by Cytokinesis II

Meiosis endpoint



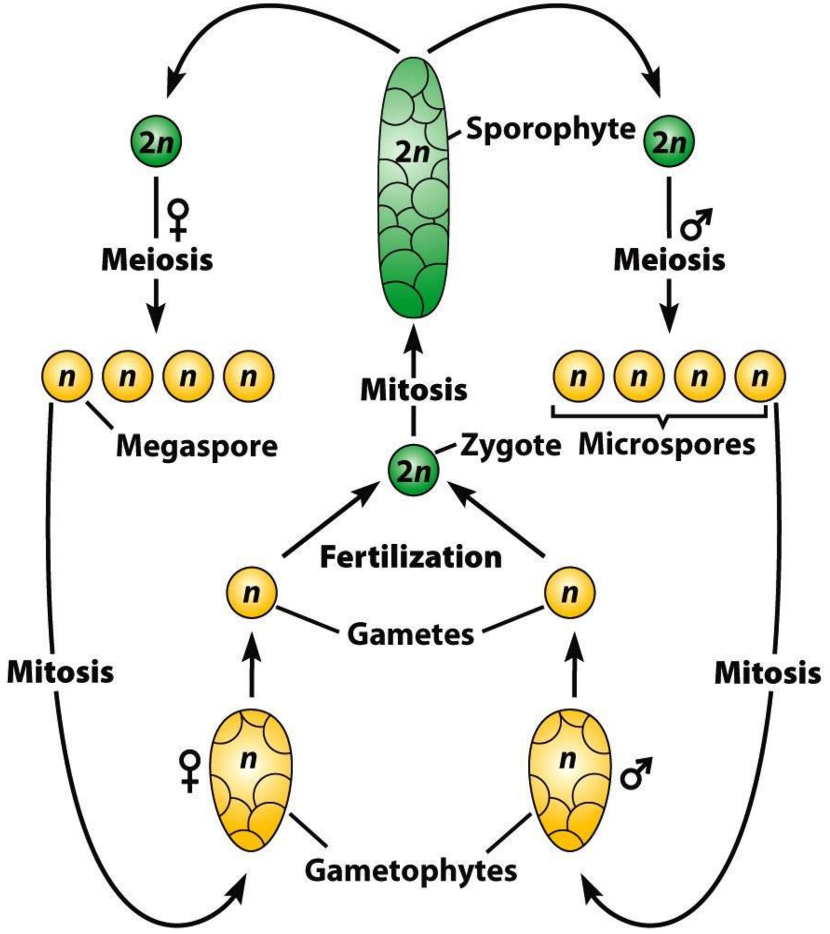


- **4 haploid cells**
- separated by plasma membranes, + cell walls in plants/fungi

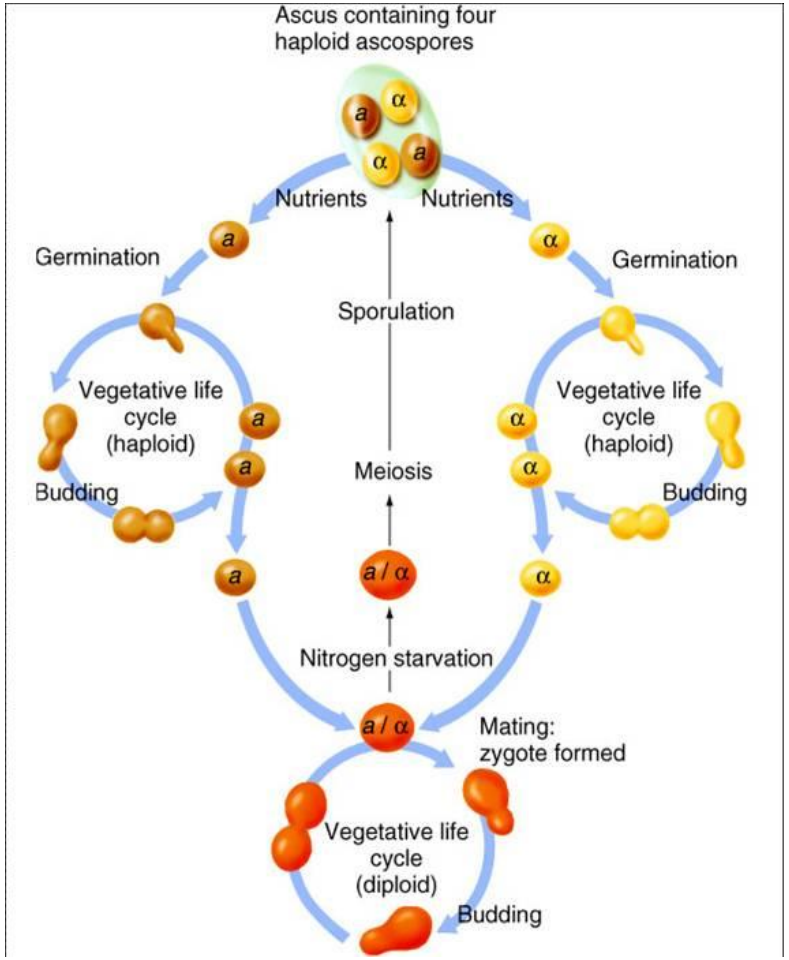

(A) MEIOSIS
kinetochore microtubule
cohesin complex
kinetochore
centromere
chromatid
kinetochore
cohesin complexes
haploid daughter cells
+
+
METAPHASE I
ANAPHASE I
METAPHASE II
ANAPHASE II
TELOPHASE II
(B) MITOSIS
cohesin complex
kinetochore microtubules
chromatid
centromere
kinetochore
diploid daughter cells
+
METAPHASE
ANAPHASE
TELOPHASE

Alteration of generations in plants and algae

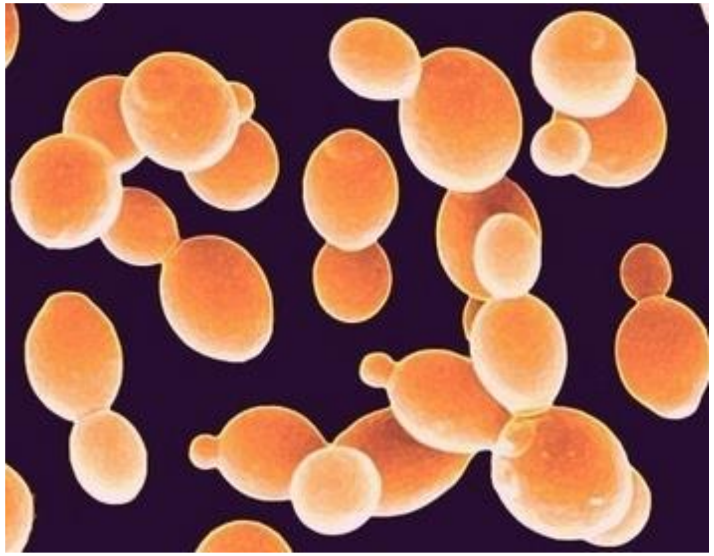
- **Sporophyte (2n)** produces haploid spores by meiosis
- Spores grow into haploid **gametophytes (n)** that produce gametes by mitosis

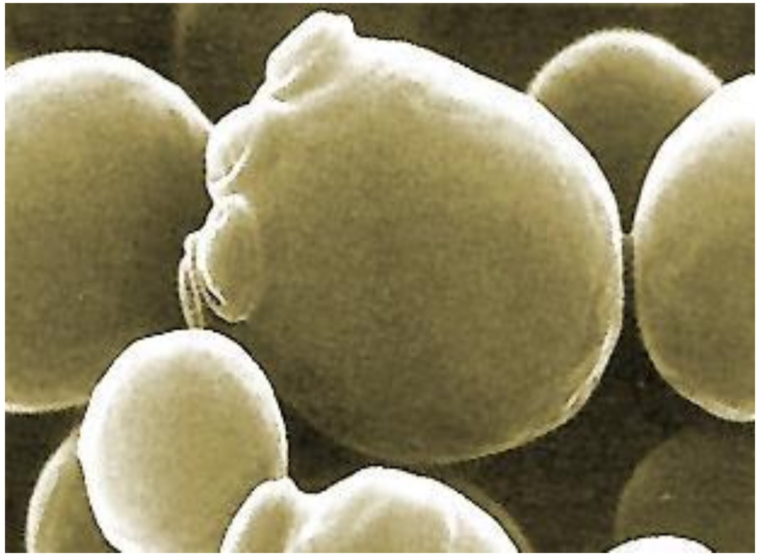


Yeast mating: *Saccharomyces cerevisiae*

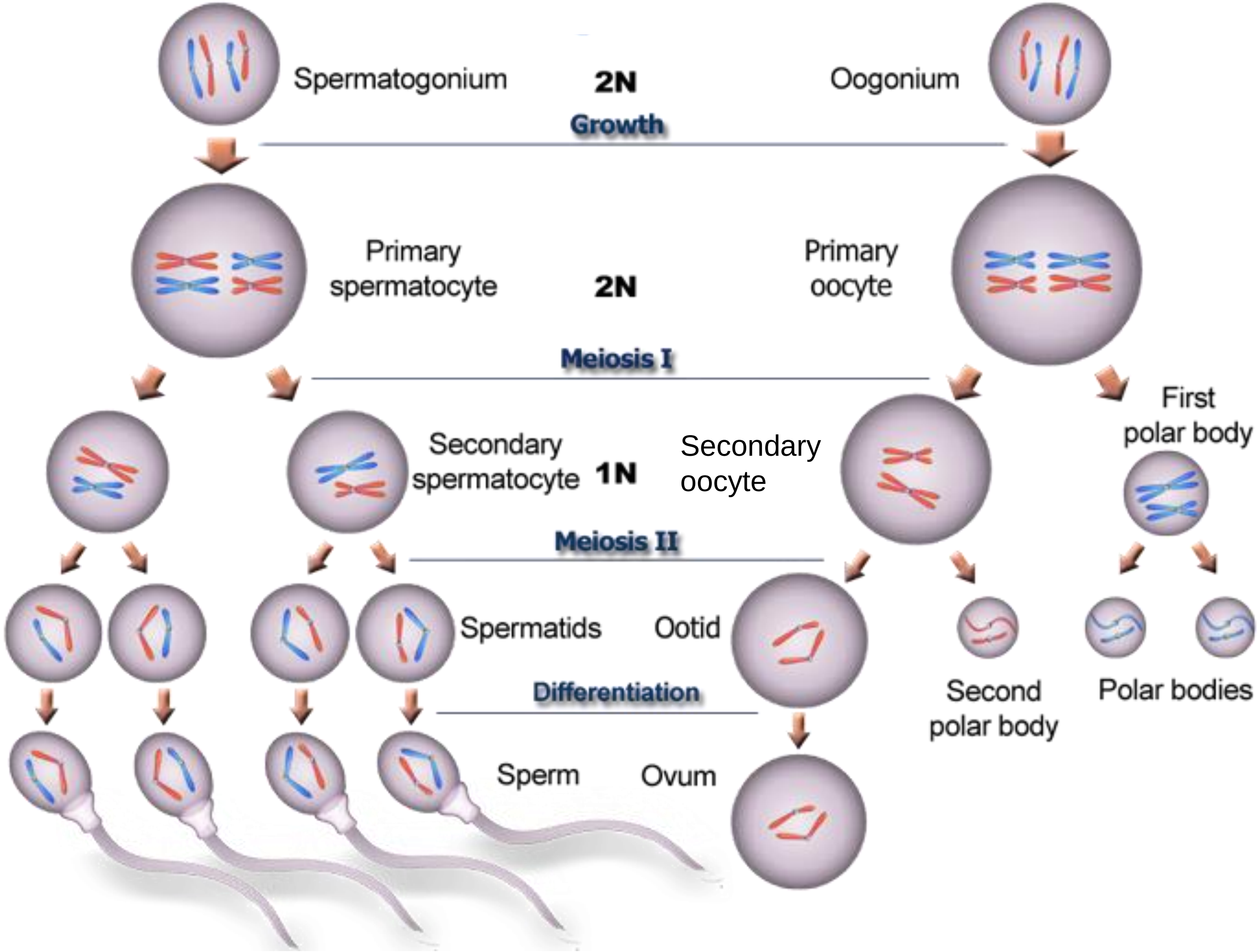


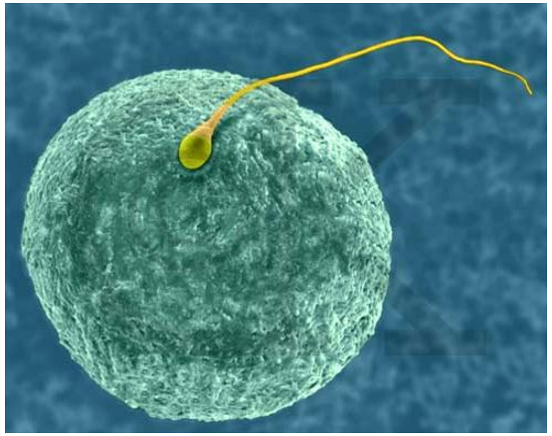
- Switch between haploid & diploid life cycle based on conditions
- Meiosis initiated upon nutrient starvation

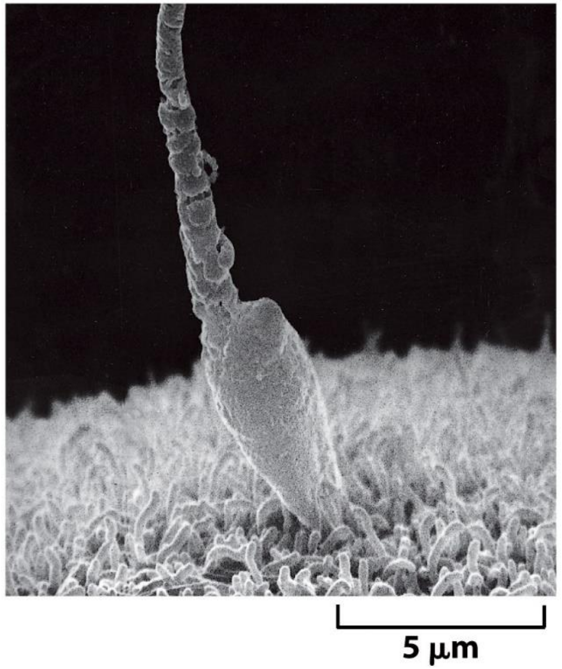




Gametogenesis in animals







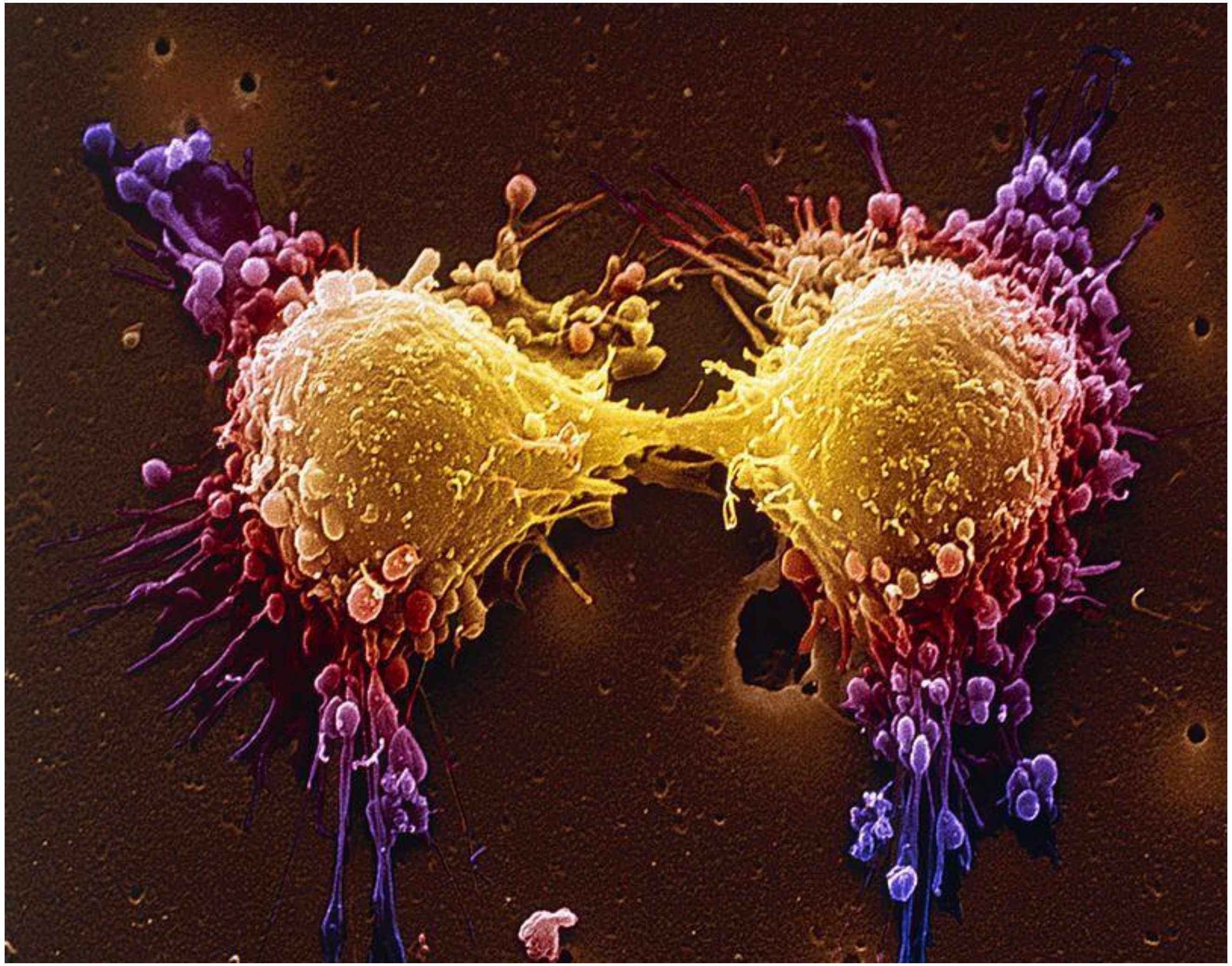
Meiotic aberrations and genetic consequences

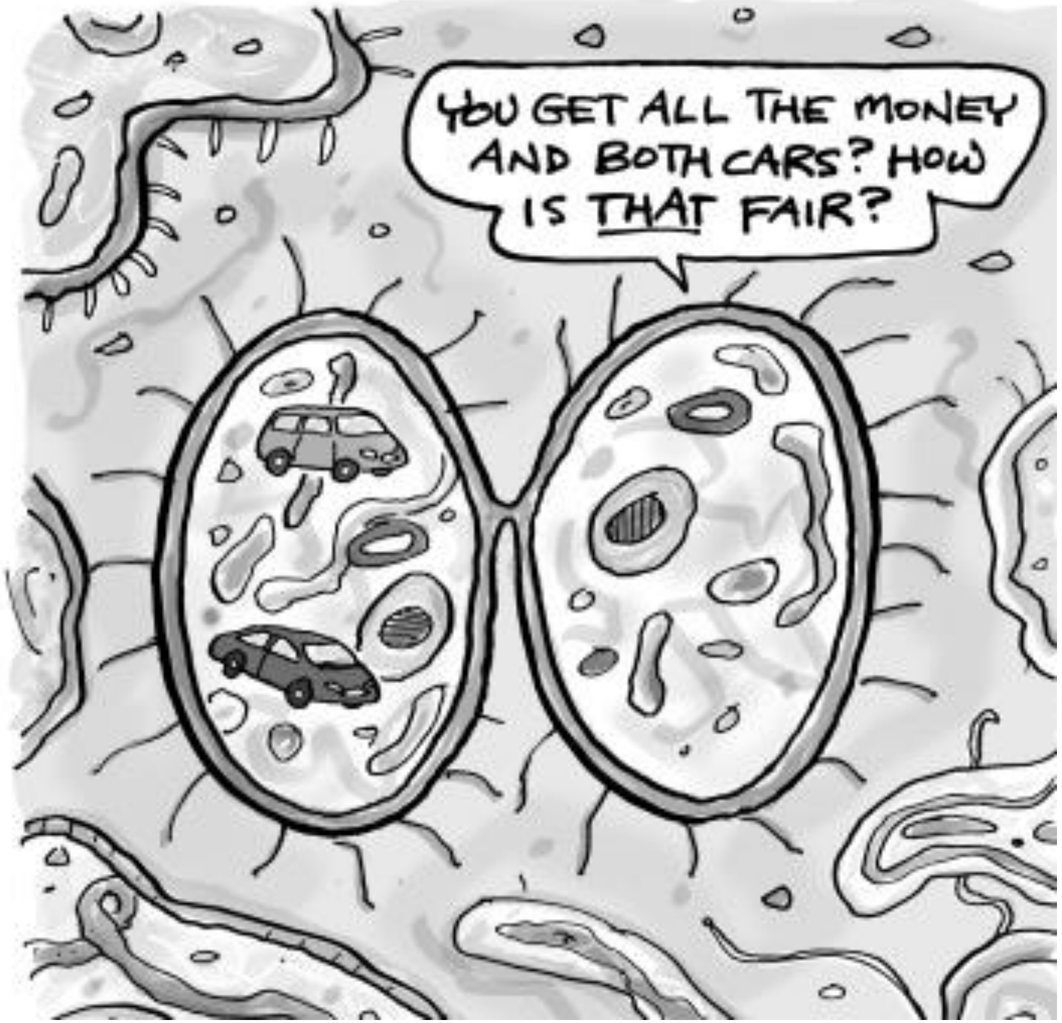
Unequal crossing-over

- **Prophase I**: loss (**deletion**) of genetic material in one chromatid and gain (**duplication**) in other

Nondisjunction

- Homologue chromosomes (**Anaphase I**) or sister chromatids (**Anaphase II**) fail to separate, e.g., aberrations in spindle apparatus or centromeres
- Leads to **aneuploidy**: monosomy or trisomy syndromes




YOU GET ALL THE MONEY AND BOTH CARS? HOW IS THAT FAIR?