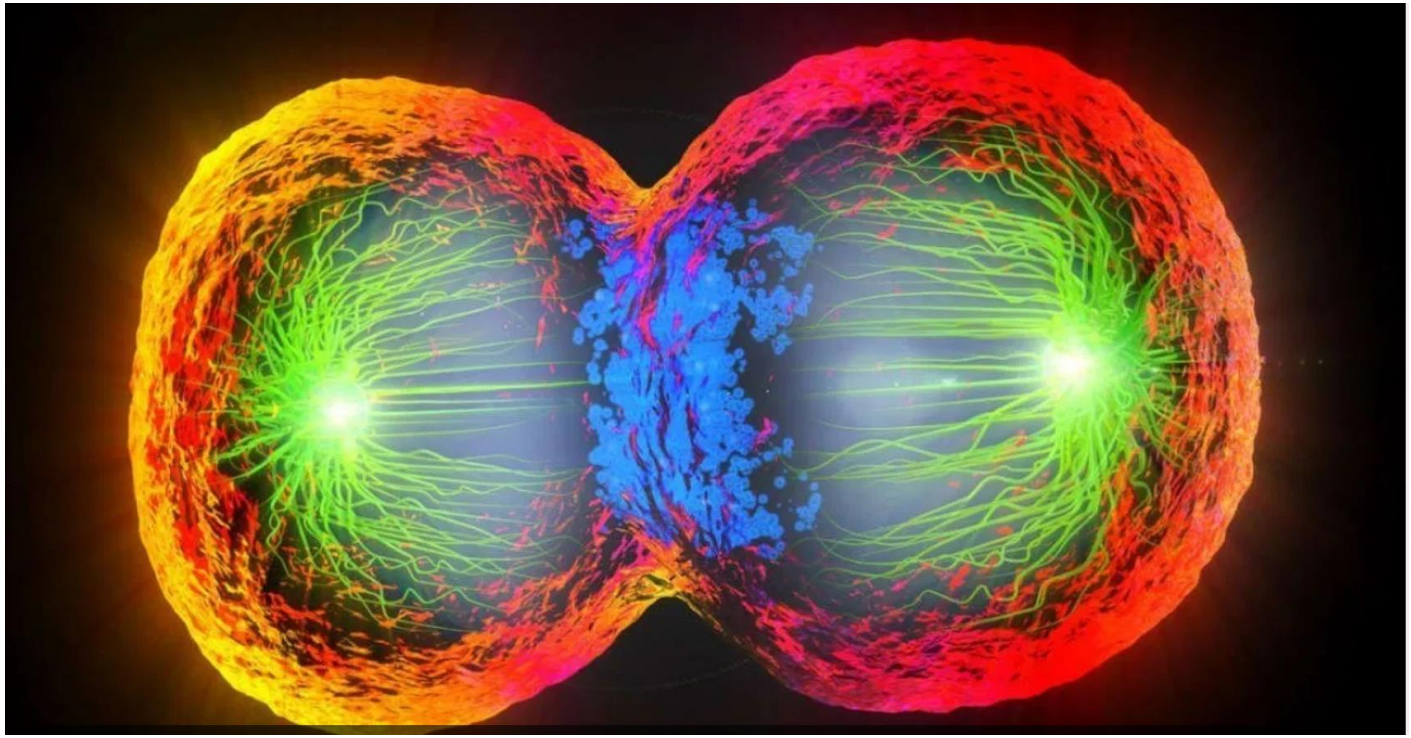
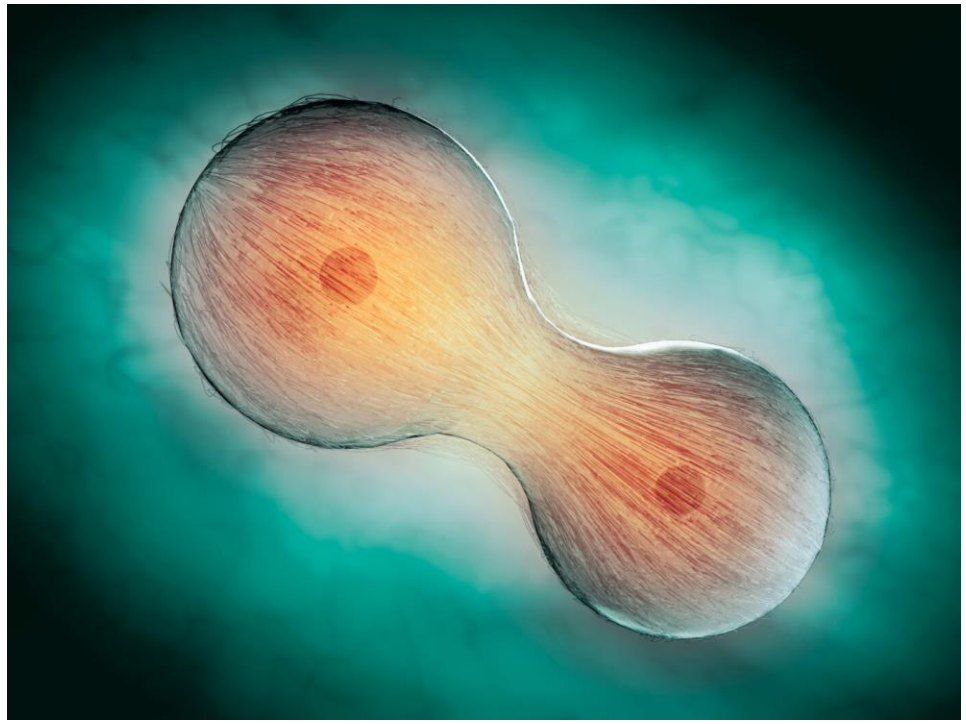
Lesson 8
Cell division



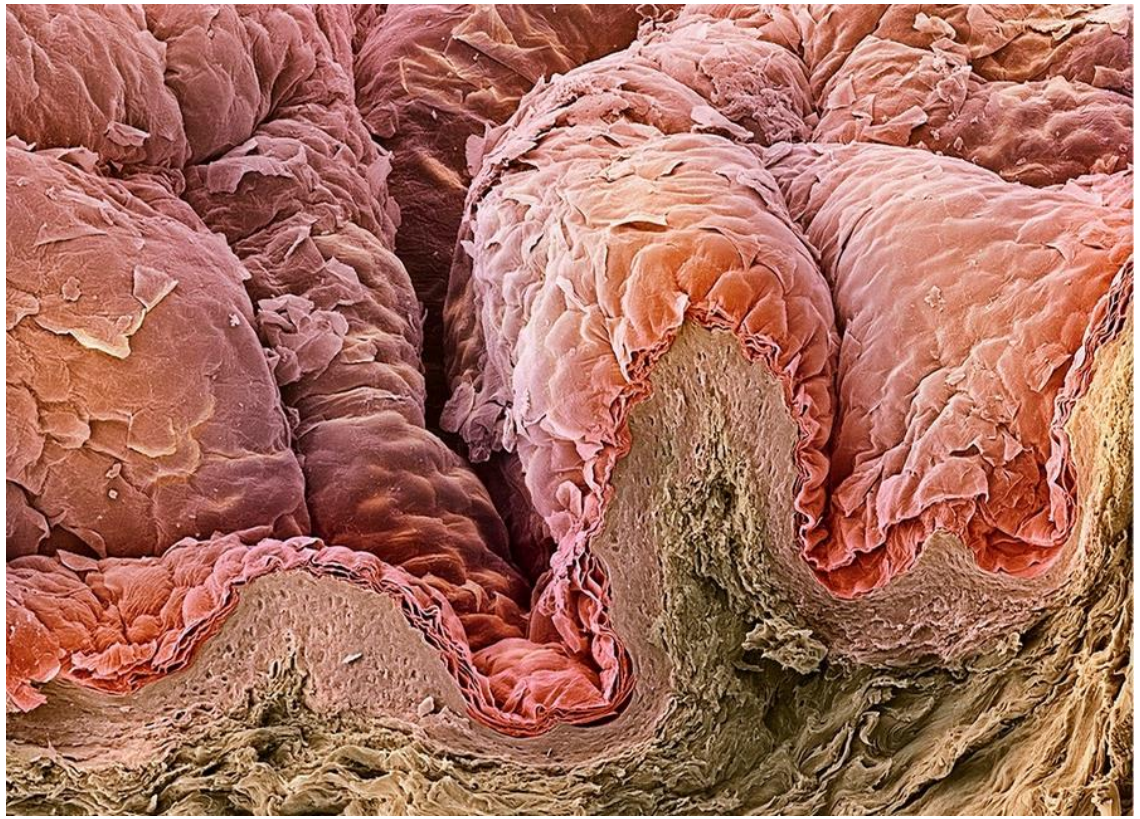
Cell division

- Cells make more cells (copy of themselves)
- Cells make new cells for 3 reasons:
  - Growth → your birth: 1 cell -> 37.2 x 10^{12} cells
  - Repair → cells surrounding a wound will reproduce themselves to repair the tissue
  - Reproduction → asexual reproduction (typical of single-cell organisms)



Cell division

- Some cells divide all the time
  - Surface cells (skin or mucous membranes) are constantly renewed

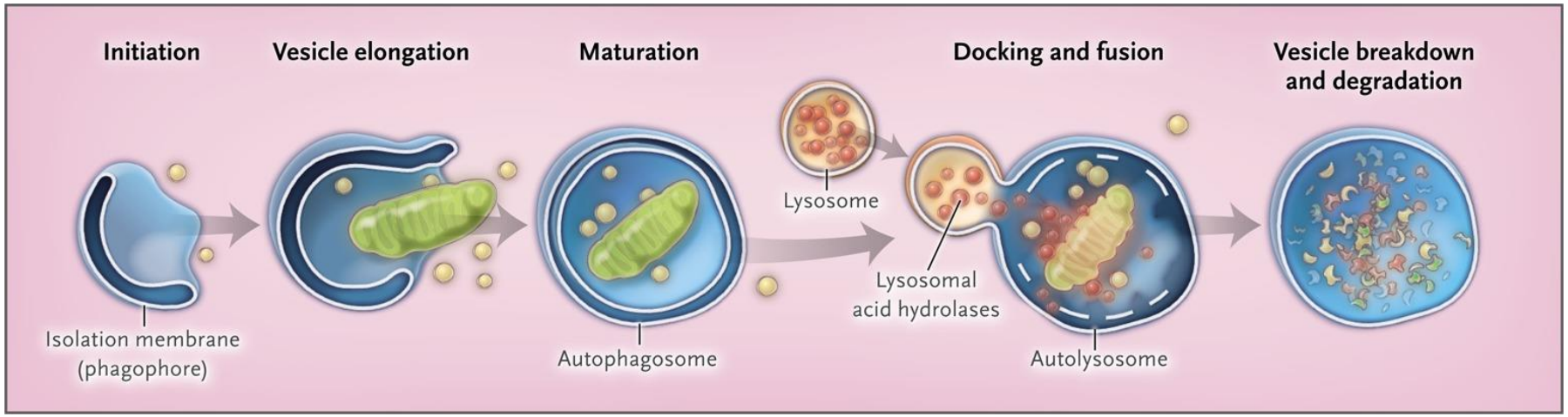


Cell division

- Some cells divide when signaled to divide
  - Liver cells do not normally divide but are triggered to divided upon organ damage
- large yellow ovoid, lower right
  - **nucleus (repository for genetic information, cell control center)**
- fuzzy blue lines, bottom center
  - **RER (contains the ribosomes (the protein synthesis machinery) -> the cell's factory assembly line)**
- blue lines at left of nucleus
  - **SER (shuttles the cell's reaction products to the Golgi apparatus -> the cell's factory shipping department)**
- blue lines at upper left
  - **Golgi apparatus (materials produced by the cell are packed into vesicles and sent to other organelles (for metabolism) or to cell membrane (for excretion) -> The cell factory's postal system)**
- green blobs and spheres
  - **Mitochondria (the cellular power plants where energy is produced. They use food components (mainly carbohydrates) to produce highly energetic molecules (ATP) -> ATP hydrolysis = energy)**
- big yellow spheres
  - **Lysosomes (breaking down cellular components no longer needed/unwanted substances -> they also digest dead organelles (autophagy or autodigestion) -> Can be though of as the call factory's landfill)**
- fat droplets (pale yellow), glycogen (brown) and plasma membranes (pale green)

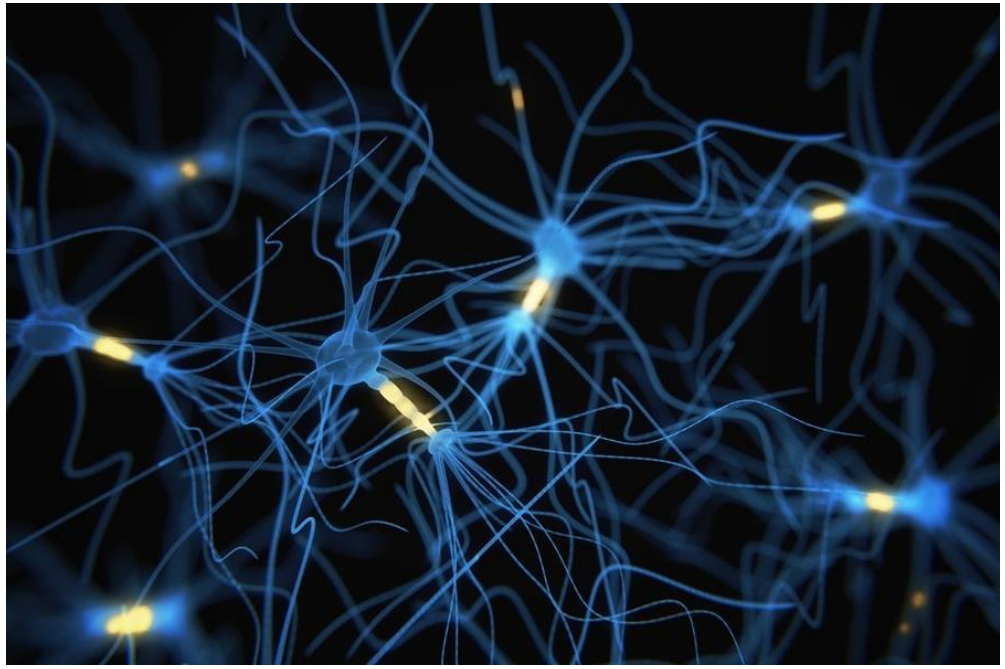
Autophagy

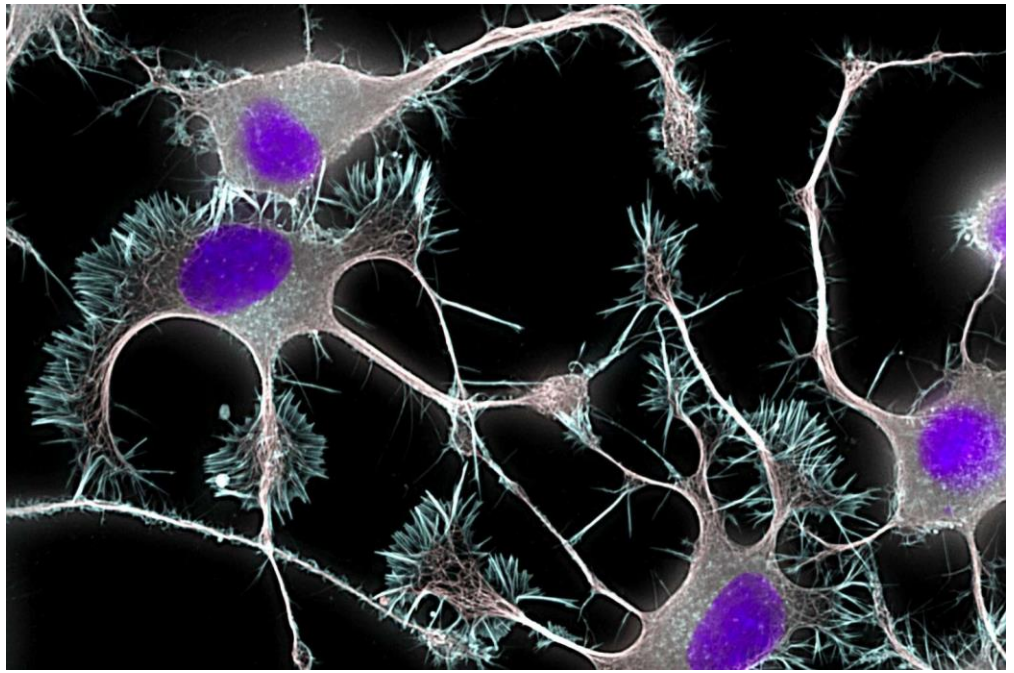
- A cellular self-degradative process fundamental in:
  - balancing sources of energy at critical times in development and in response to nutrient stress
  - housekeeping in removing
    - misfolded or aggregated proteins
    - clearing damaged organelles (mitochondria, ER…)
    - eliminating intracellular pathogens
- **Autophagy is generally thought of as a cellular survival mechanism**



Cell division

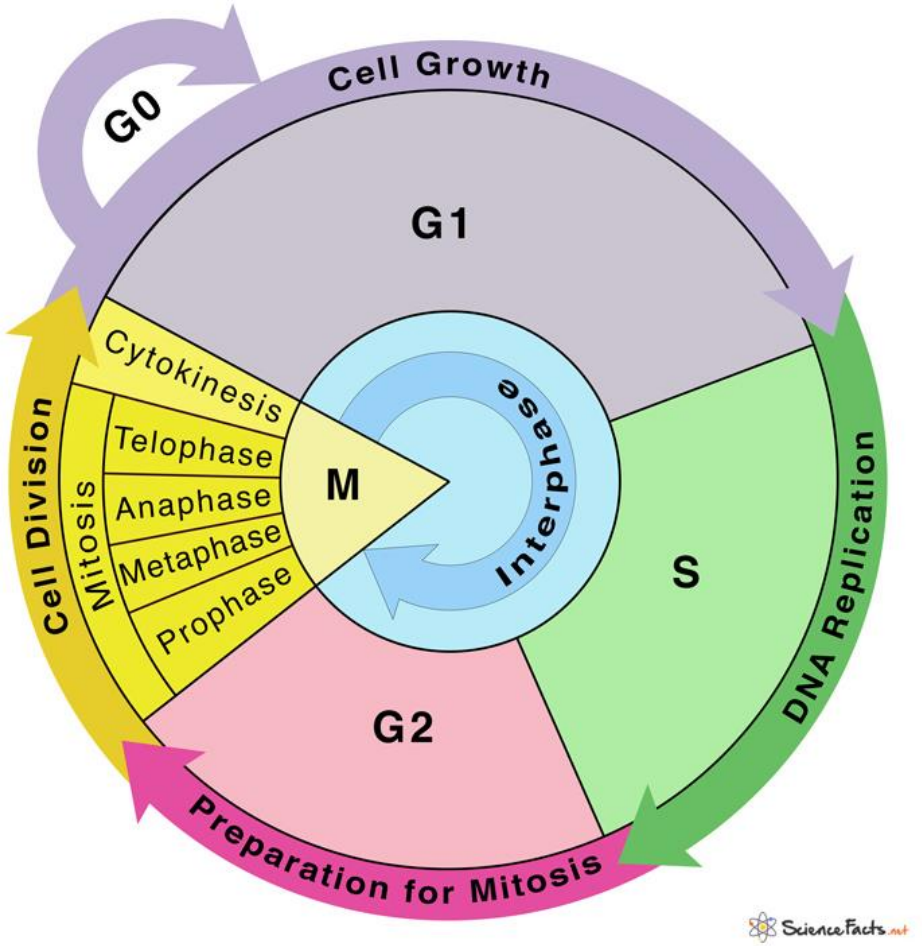
- Some cells divide all the time
  - Surface cells (skin or mucous membranes)
- Some cells divide when signaled to divide
  - Liver cells do not normally divide but are triggered to divided upon organ damage
- Some cells do not divide
  - Your brain neurons and most cells in the nervous tissue do not divide at all
    - When brain and spine nerves are damaged, they cannot be repaired





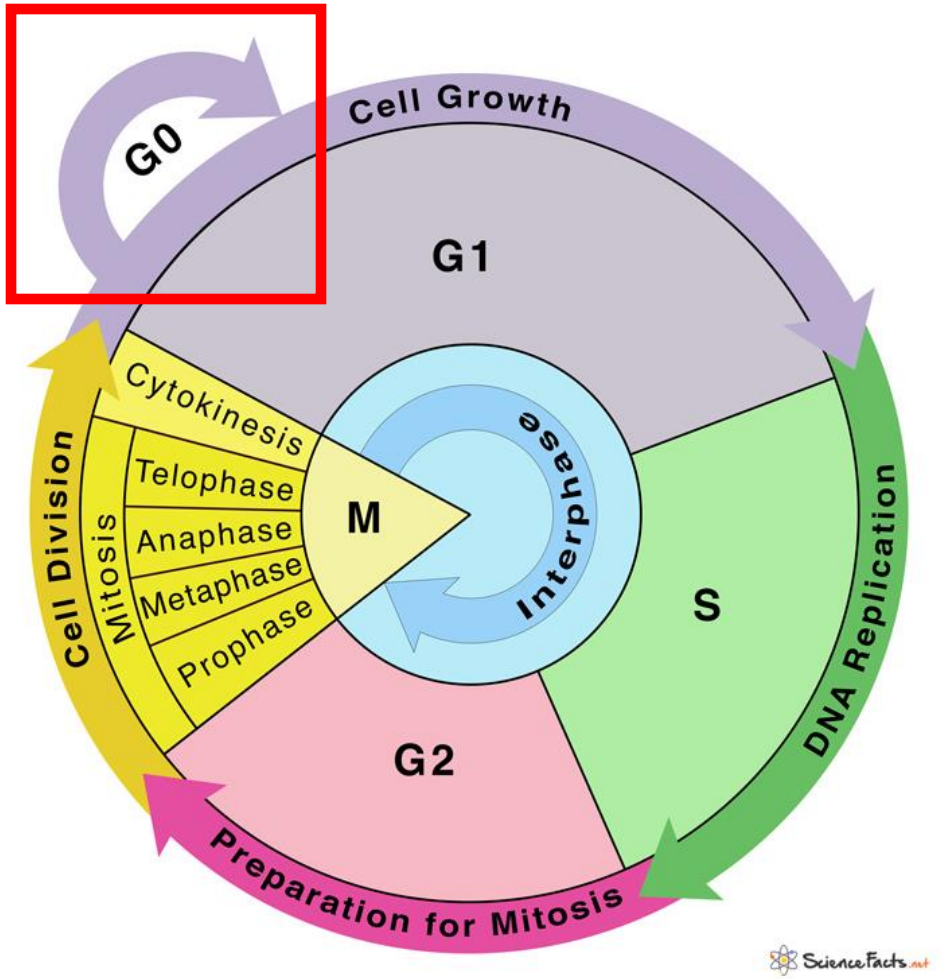
Cell cycle: the cell's traffic light

- Somatic cells (all cells except germ cells) divide via mitosis (later)
- The non-dividing phase of the cell cycle = interphase
  - Three subphases:
    - G1, S and G2
- **Cells spend most of their time in G1**
  - The cell factory is in full swing and cells copy all their content except DNA



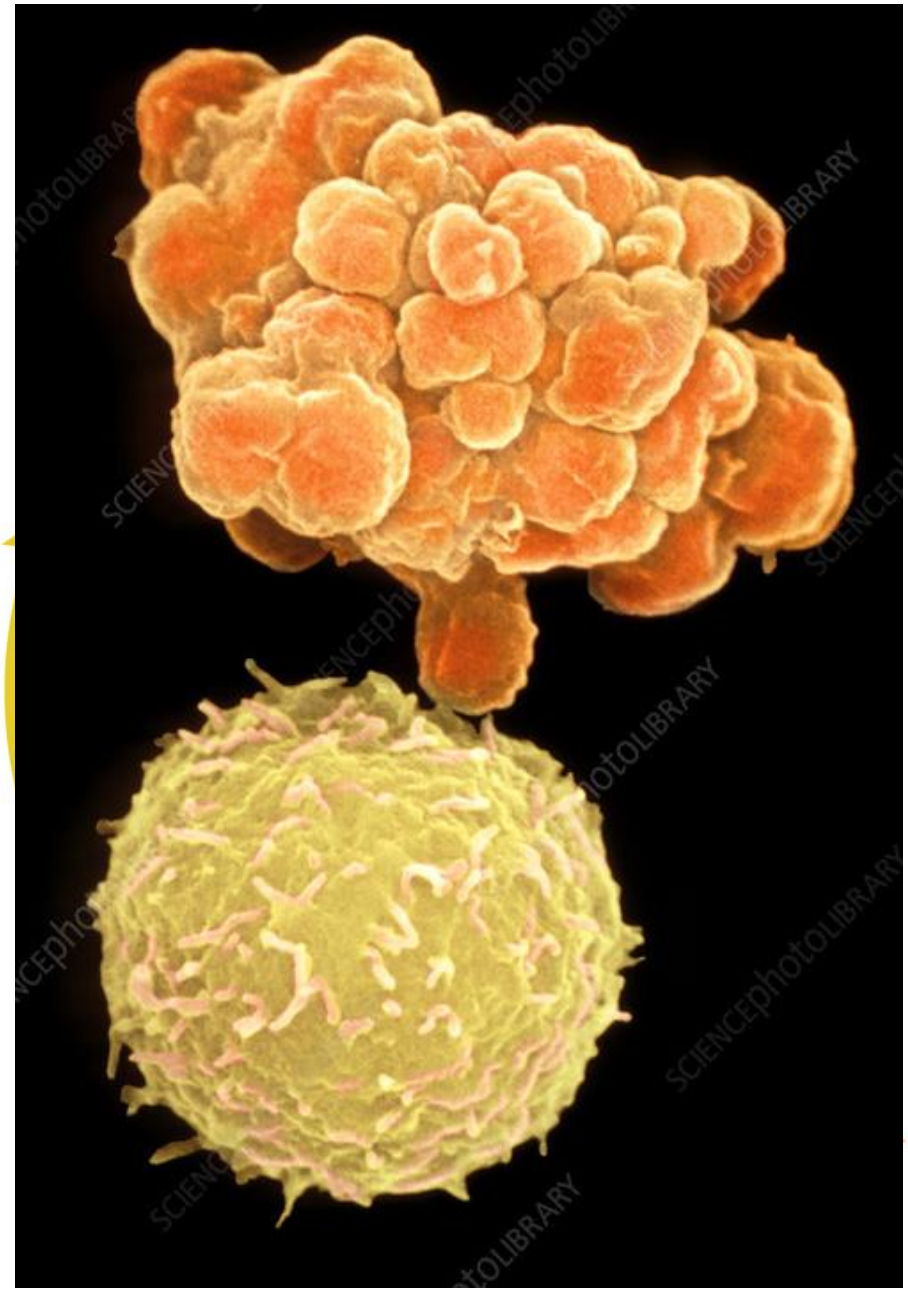
G0: a cellular state outside the replicative cycle

- Cells were thought to enter G0 primarily due to environmental factors (*e.g.*, starving)
  - limited resources for proliferation
    - was thought of as a resting phase
- G0 is a normal resident form of non-dividing cells
  - Neuronal cells (among the most metabolically active cells) reside in a terminal G0 phase as a part of their developmental program



The cell G1 checkpoint

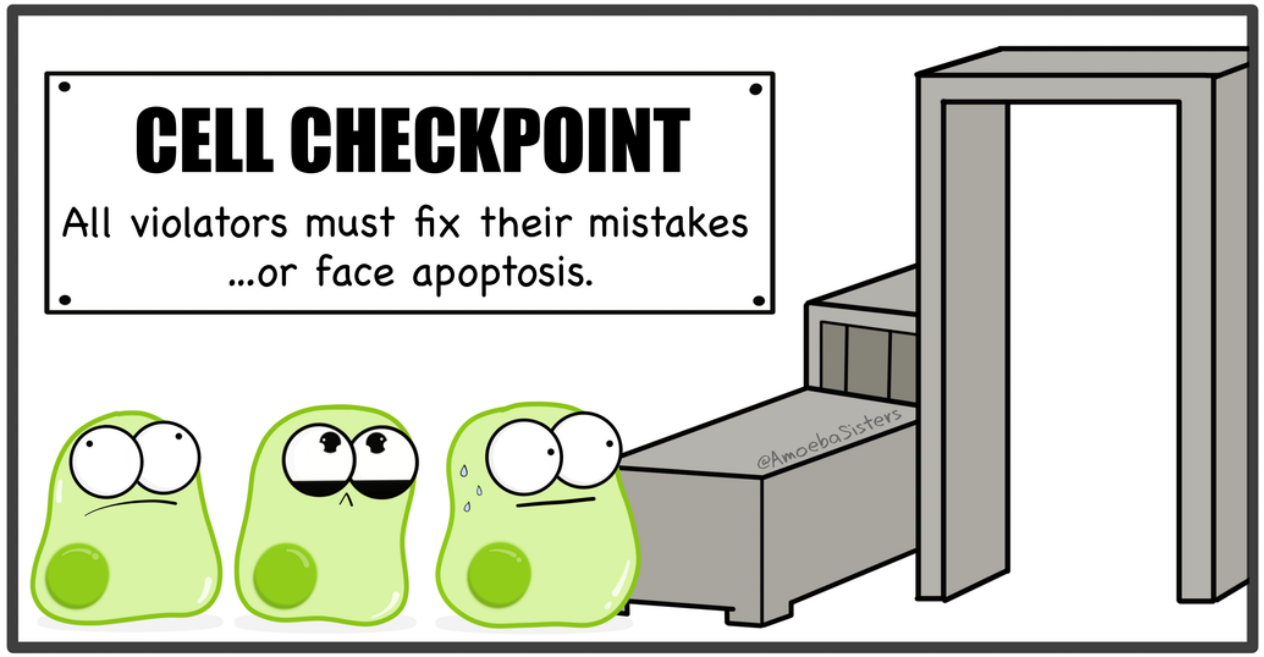
- Before exit G1, dividing cells must pass an integrity test called **checkpoint**
- If checkpoint is negative, repair is attempted
  - **Repair successful** → proceed to next interphase stage (S phase)
  - **Repair unsuccessful** →cell is signaled to commit suicide (**apoptosis = programmed cell death**)



The cell checkpoint

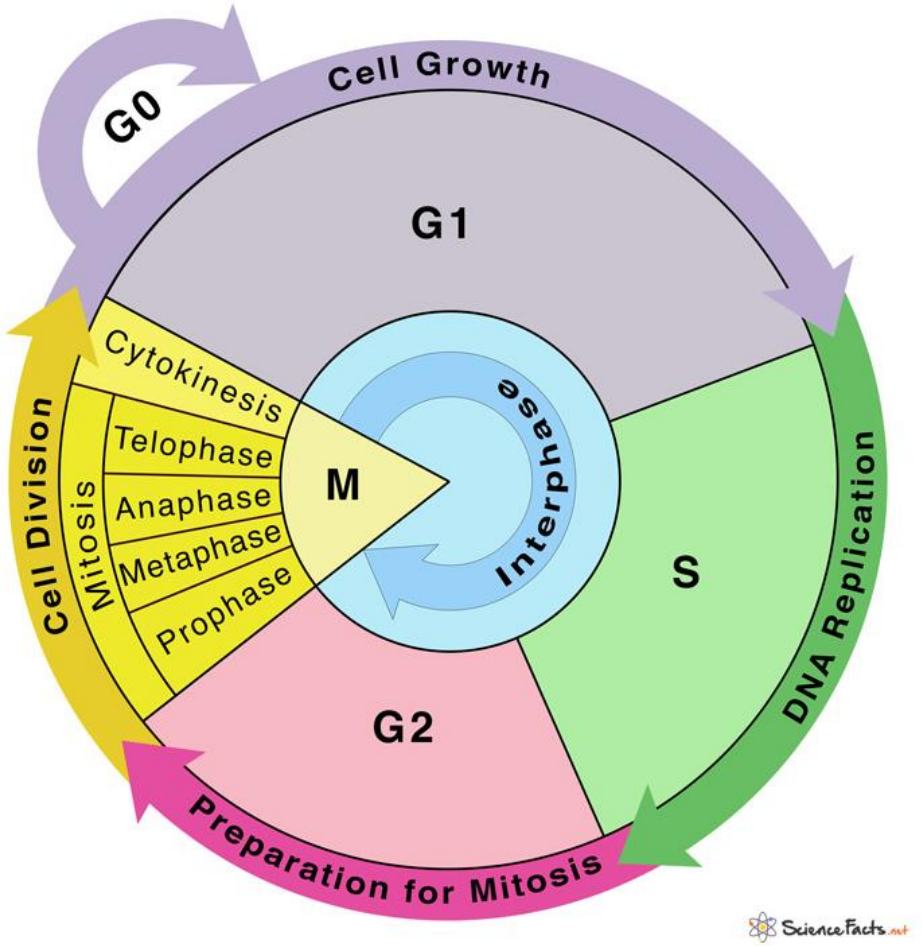
- Criteria for G1 checkpoint pass:

1. Signals tell cells to divide
2. Cells must have plenty of nutrients
3. The DNA must be in optimal conditions
4. Cells must have the right size and shape to divide



The S phase, G2 and G2 checkpoint

- The **S phase**: **where DNA is replicated** (later)
  - S stands for synthesis (DNA “synthesis”)
    - Cells are making new DNA
- When DNA replication is over, cells enter **Gap 2** (**G2**) stage
  - they undergo another **checkpoint** (G2 checkpoint) to verify DNA replication before entering the last phase (**division**)

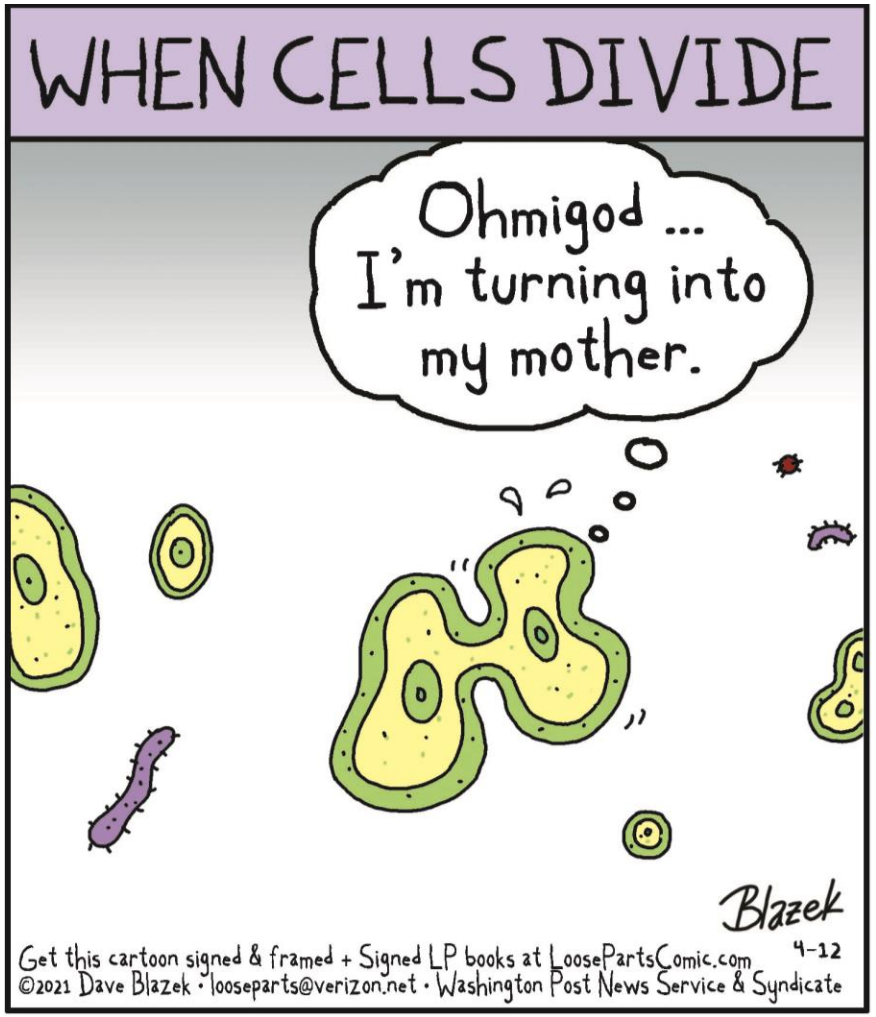


The cell G2 checkpoint

- Criteria for G2 checkpoint pass:

1. DNA is not damaged
2. Cells have copied all the chromosomes
3. Signals tell the cell to proceed into mitosis

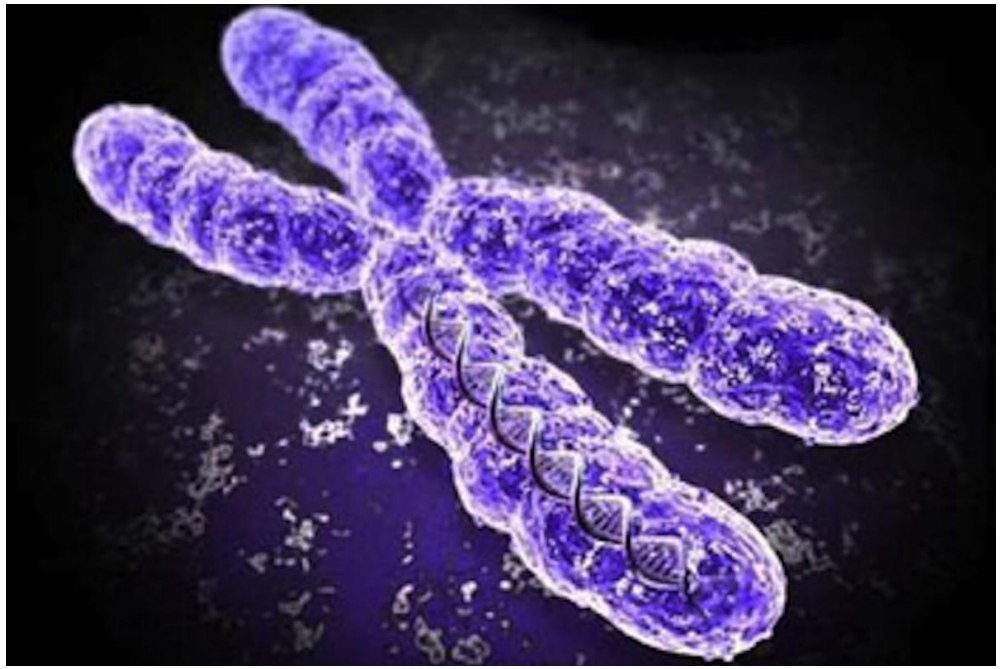
- If checkpoint is not successful
  - Cells will be stuck in G2
    - DNA repair is attempted
      - If **successful** → proceed to division
      - If **not successful** → apoptosis



Cell division

1. DNA replication → make two sets of genes (DNA)
2. DNA partitioning between daughter cells

- Genes (DNA) are organized in chromosomes (chrs)



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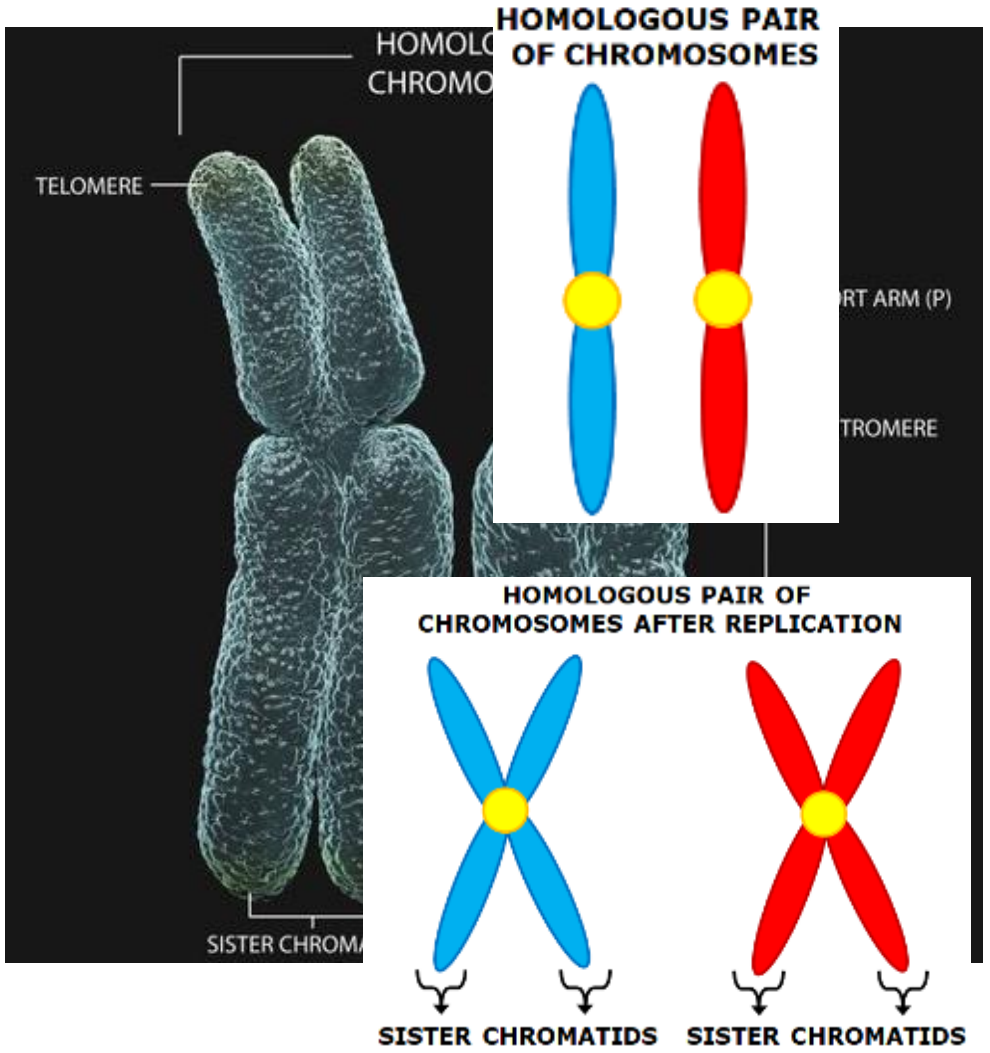
- Genes (DNA) are organized in chromosomes (chrs)
- Body (**somatic**) cells contain 2 of each chrs
  - somatic cells are **diploid** (2n)
- Each matching couple of chrs are called homologs or homologous chrs



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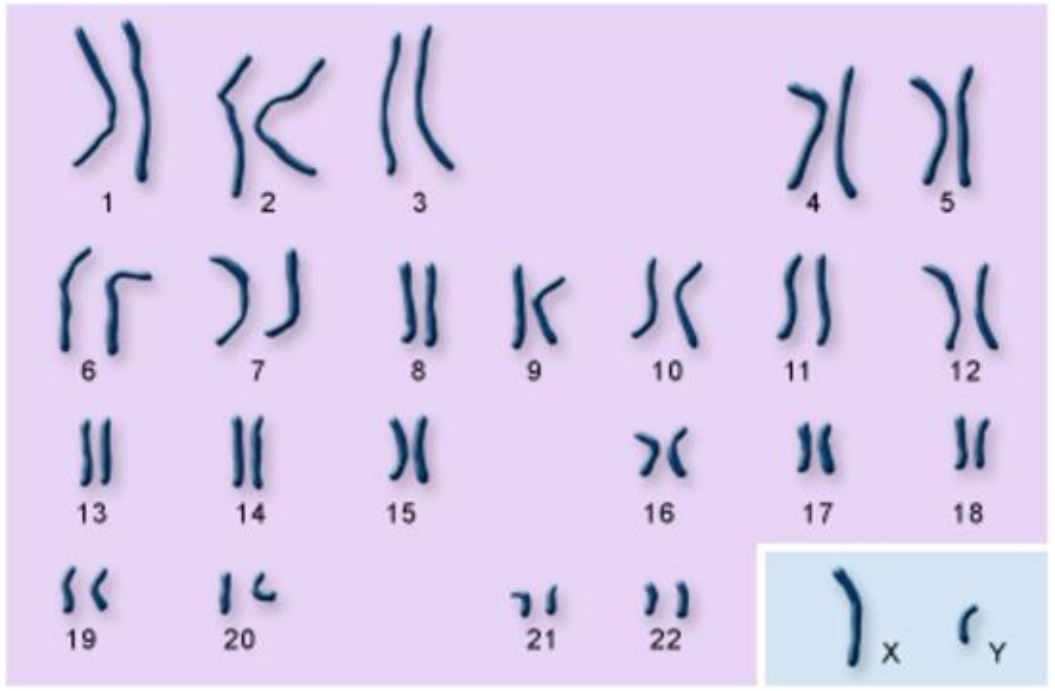
- Normal somatic cells have 23 couples of chrs
  - That makes 46 chrs in total
  - One chrs couple is the sex chr (XX or XY)
  - The remaining 22 couples (aka autosomes) look the same in M/F

Karyotype



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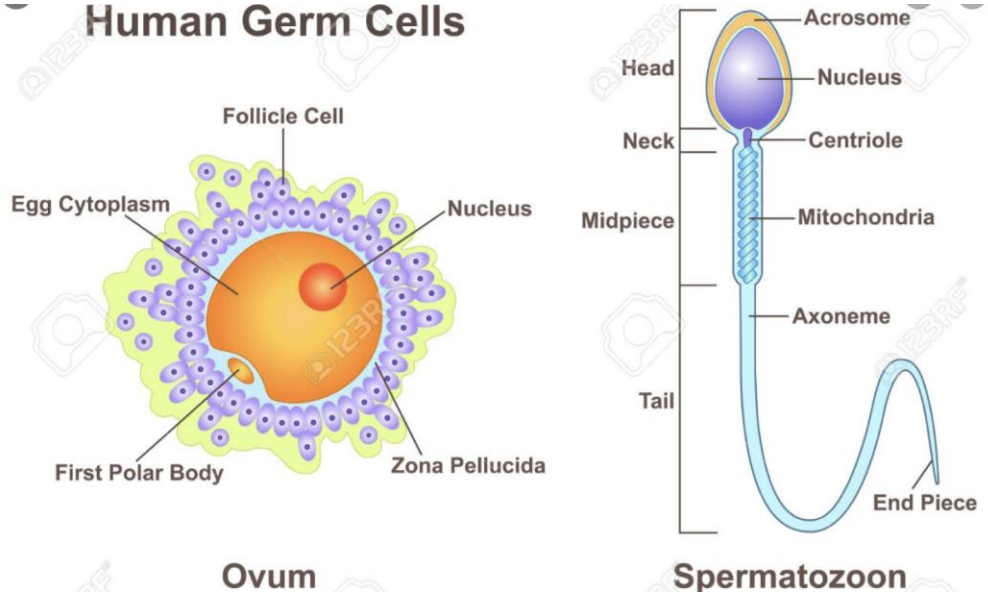
  - That makes 46 chrs in total
  - One chrs couple is the sex chr (XX or XY)
  - the remaining 22 couples (aka autosomes) look the same in M/F
- **Germ** cells (2n) generate **gametes** = egg/sperm
  - Gametes contain 1 of each chrs
  - Gametes are **haploid** (n) cells



Cell division

- Two types of cell division
  - **Mitosis**
  - **Meiosis**

Cell division - MITOSIS

- **Mitosis** occurs in **somatic** cells
- Outcome = **2** daughter cells **identical** to the parent cell (**2n**)
- The mitotic process in brief:
  - Chrs (DNA) replicate → **sister chromatids**
  - Sister chromatids line up on a special structure called **mitotic spindle**
  - Sister chromatids segregate
    - One copy of each chr is partitioned to each daughter cell (2n)
  - Cell membrane partitions the two daughter cells

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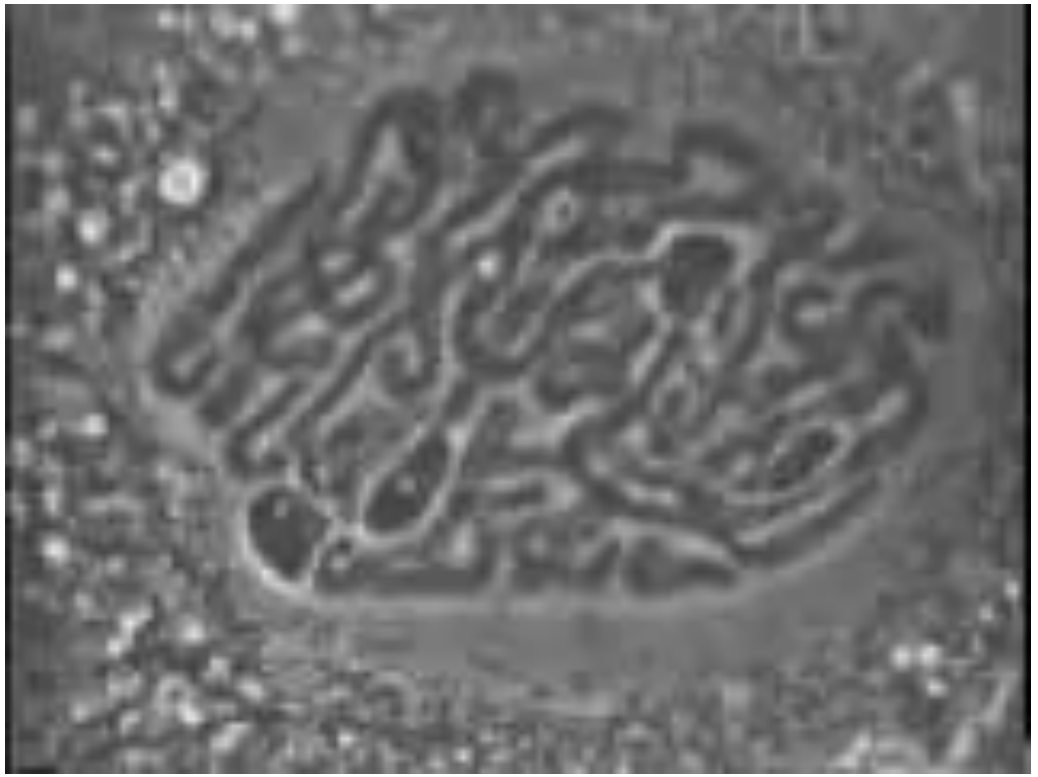
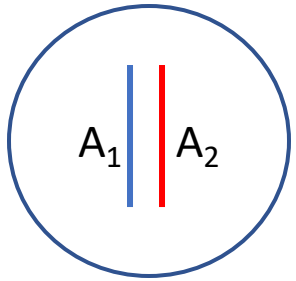
- **1 diploid mother cell (2n) → 2 diploid daughter cells (2n)**



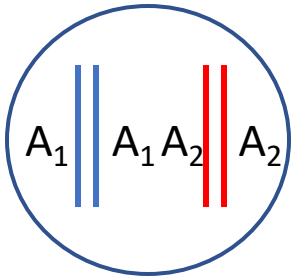
Cell division - MITOSIS

Diploid (2n) cell with 1 homolog

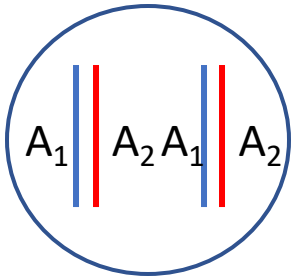


DNA REPLICATION

Sister chromatid

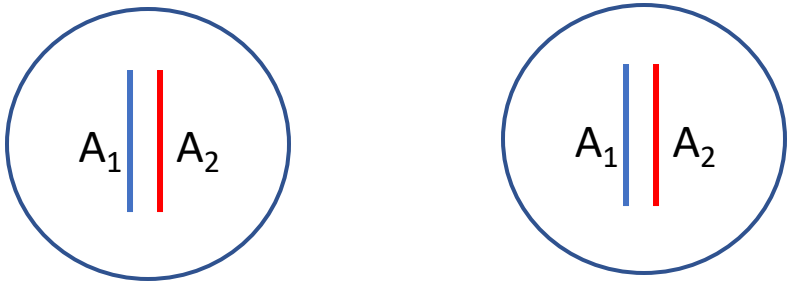


SISTER CHROMATID SEGREGATION

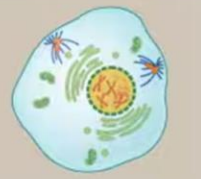
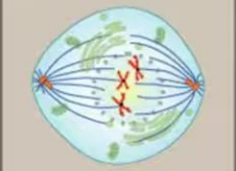
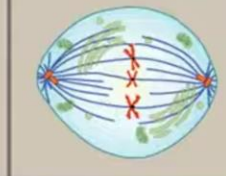
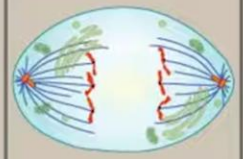
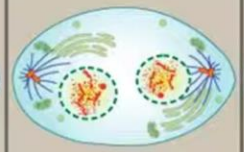
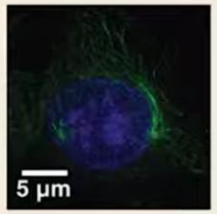
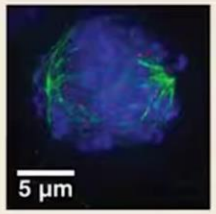
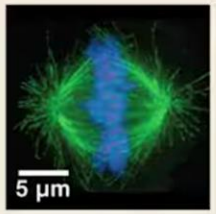
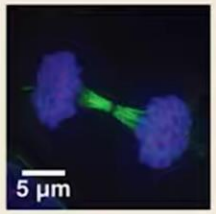
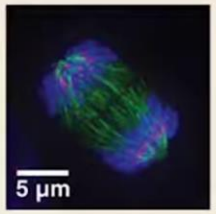


Homologs partitioning into daughter cells

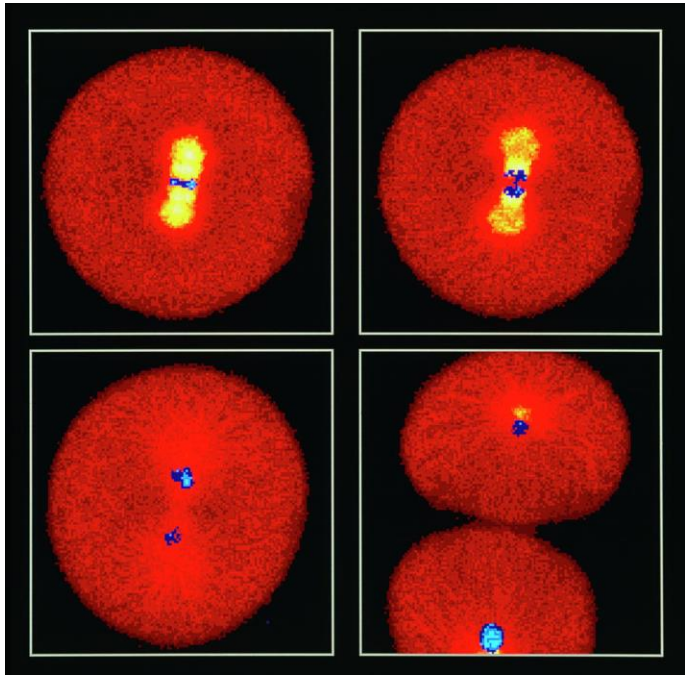
Two diploid (2n) daughter cells identical to the parent cell

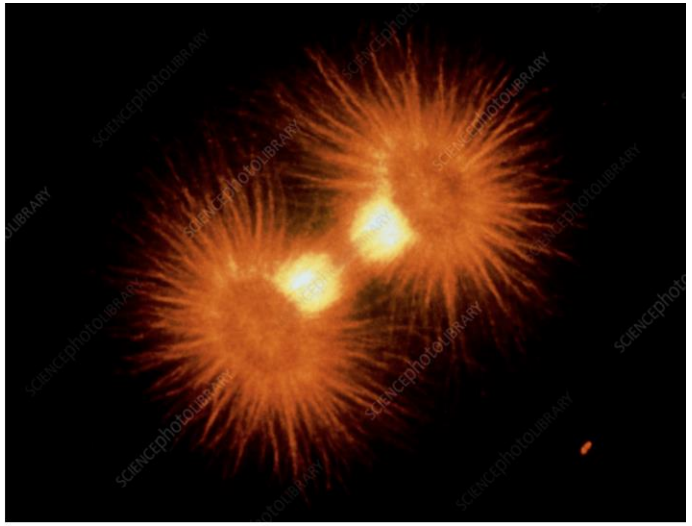


Cell division - MITOSIS

Prophase	Prometaphase	Metaphase	Anaphase	Telophase	Cytokinesis
					
• Chromosomes condense and become visible • Spindle fibers emerge from the centrosomes • Nuclear envelope breaks down • Centrosomes move toward opposite poles	• Chromosomes continue to condense • Kinetochores appear at the centromeres • Mitotic spindle microtubules attach to kinetochores	• Chromosomes are lined up at the metaphase plate • Each sister chromatid is attached to a spindle fiber originating from opposite poles	• Centromeres split in two • Sister chromatids (now called chromosomes) are pulled toward opposite poles • Certain spindle fibers begin to elongate the cell	• Chromosomes arrive at opposite poles and begin to decondense • Nuclear envelope material surrounds each set of chromosomes • The mitotic spindle breaks down • Spindle fibers continue to push poles apart	• Animal cells: a cleavage furrow separates the daughter cells • Plant cells: a cell plate, the precursor to a new cell wall, separates the daughter cells
					

MITOSIS

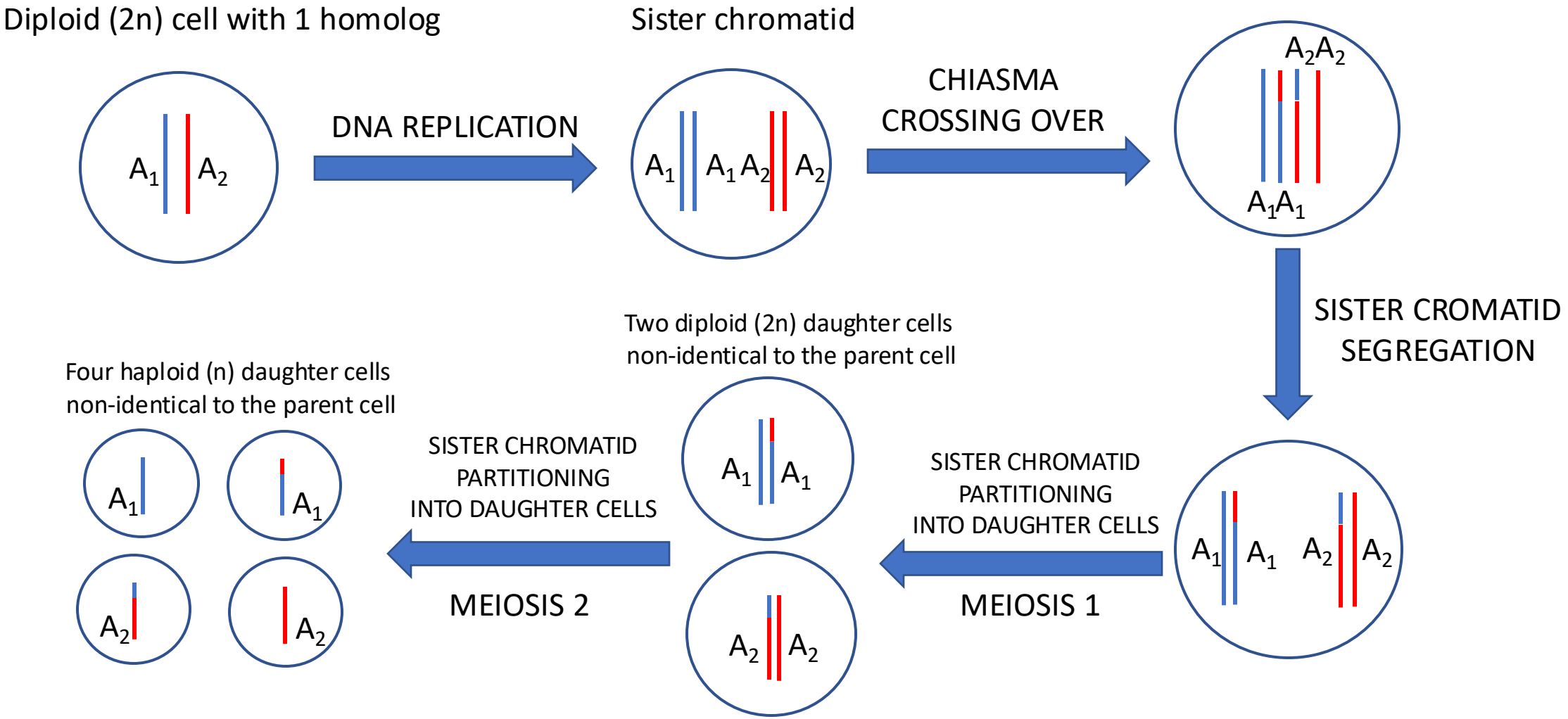




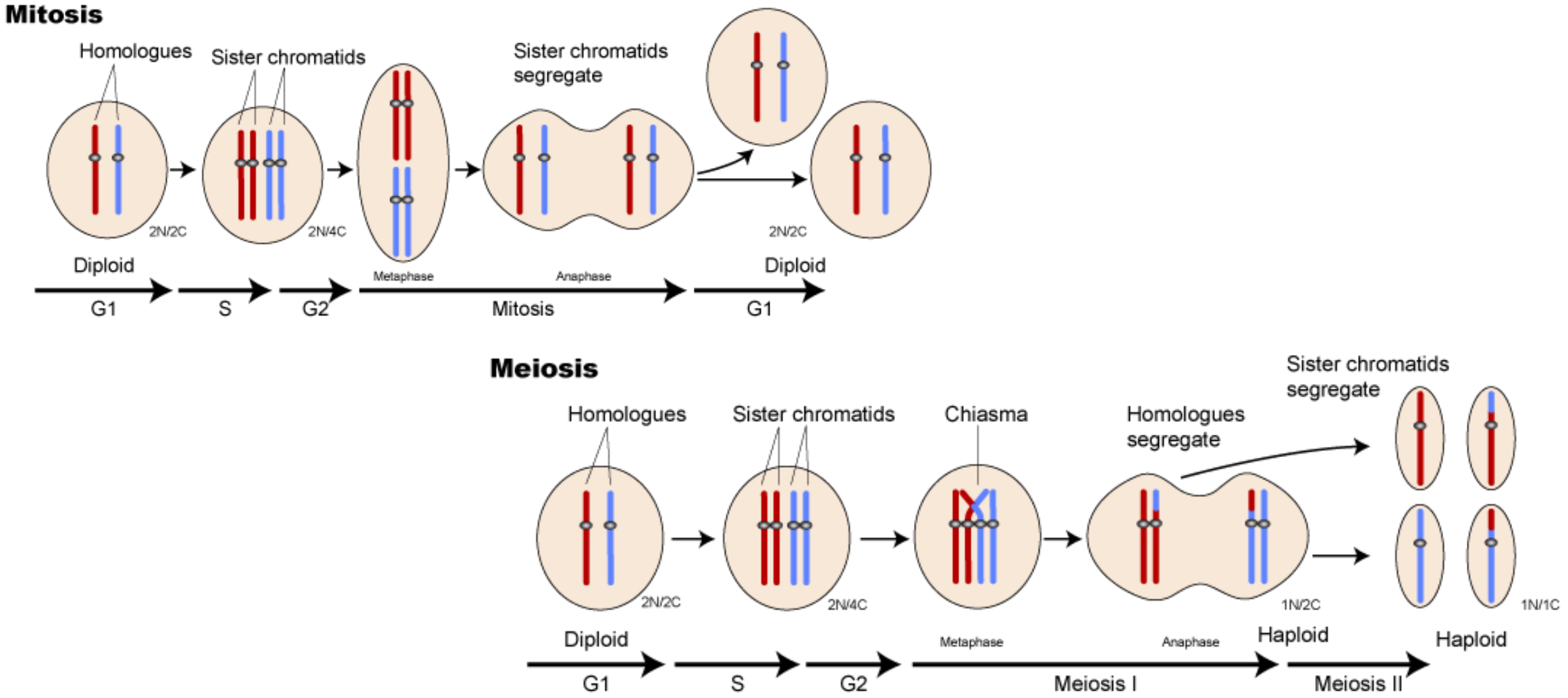
Cell division - MEIOSIS

- Goal of meiosis: production of gametes (egg/sperm, haploid) from diploid germ cells
- Outcome:
  - **4** cells
  - **non-identical to the parent**
  - each daughter cell (egg/sperm) is **haploid** → n = 1 copy of each chr
- The meiotic process in brief:
  - Chrs (DNA) replicate → **sister chromatids**
  - Sister chromatids come close one another and exchange DNA segments (**chiasma**, **crossing-over**)
    - Ensures individual genetic variability
  - Meiosis 1
    - Each replicated homologous chr pair goes to daughter cells
    - Output is two diploid cells
  - Meiosis 2
    - The two daughter cells divide again
    - Single homolog goes to each new daughter cell
    - Output is 4 haploid cells

Cell division - MEIOSIS



Cell division – Mitosis *vs*. Meiosis



A big mistake - Nondisjunction

- Meiosis must sort the chromosomes very carefully to ensure each gamete gets a complete set of chrs (via many checkpoints)
- Sometimes, chrs fail to separate and travel together = **nondisjunction**
- If this happens during meiosis I and then meiosis II proceeds regularly
  - Output = two gametes having an extra copy of one of the chrs and two gametes missing one of the chrs
- If this happens during meiosis II
  - Output = two normal gametes, one gamete having an extra copy of one chr and one gamete missing one of the chr
- When a gamete with an abnormal number of chrs is fertilized, the result is an aneuploid individual
  - A person who has the wrong number of chrs in her/his cells

When more is less – Trisomy 21 (or Dawn Syndrome)

- In humans, very few aneuploid events are compatible with life
- One of these is also the most common chromosomal defect among humans (1/733 births)
- Originates from the aneuploidy condition of having 3 copies of chromosome 21 and normal gametes
- Problems of Trisomy 21
  - Increased risk of heart diseases
  - Alzheimer's disease
  - Childhood leukemia
  - Impaired respiratory and thyroid conditions
  - Mild to moderate mental impairment
- Trisomy 21 risk increases with mother age (rises quicky after age 35)
- Current research is focused on discovery the gene(s) leading to DS and to correct these faulty genes with gene therapy