

D2.1 CELL AND NUCLEAR DIVISION

Ver. 2

Guiding Questions

How can large numbers of genetically identical cells be produced?

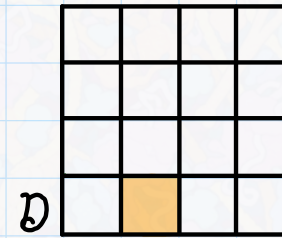
How do eukaryotes produce genetically varied cells that can develop into gametes?

Linking Questions

What processes support the growth of organisms?

How does the variation produced by sexual reproduction contribute to evolution?

2



Theme: Continuity + Change

Level of Organization: Cells

Written and drawn by:

PETER MARIER



SL LEARNING OUTCOMES

D2.1.1	Generation of new cells in living organisms by cell division	In all living organisms, a parent cell—often referred to as a mother cell—divides to produce two daughter cells.
D2.1.2	Cytokinesis as splitting of cytoplasm in a parent cell between daughter cells	Students should appreciate that in an animal cell a ring of contractile actin and myosin proteins pinches a cell membrane together to split the cytoplasm, whereas in a plant cell vesicles assemble sections of membrane and cell wall to achieve splitting.
D2.1.3	Equal and unequal cytokinesis	Include the idea that division of cytoplasm is usually, but not in all cases, equal and that both daughter cells must receive at least one mitochondrion and any other organelle that can only be made by dividing a pre-existing structure. Include oogenesis in humans and budding in yeast as examples of unequal cytokinesis.
D2.1.4	Roles of mitosis and meiosis in eukaryotes	Emphasize that nuclear division is needed before cell division to avoid production of anucleate cells. Mitosis maintains the chromosome number and genome of cells, whereas meiosis halves the chromosome number and generates genetic diversity.
D2.1.5	DNA replication as a prerequisite for both mitosis and meiosis	Students should understand that, after replication, each chromosome consists of two elongated DNA molecules (chromatids) held together until anaphase.
D2.1.6	Condensation and movement of chromosomes as shared features of mitosis and meiosis	Include the role of histones in the condensation of DNA by supercoiling and the use of microtubules and microtubule motors to move chromosomes.
D2.1.7	Phases of mitosis	Students should know the names of the phases and how the process as a whole produces two genetically identical daughter cells.
D2.1.8	Identification of phases of mitosis	Application of skills: Students should do this using diagrams as well as with cells viewed with a microscope or in a micrograph.
D2.1.9	Meiosis as a reduction division	Students should understand the terms “diploid” and “haploid” and how the two divisions of meiosis produce four haploid nuclei from one diploid nucleus. They should also understand the need for meiosis in a sexual life cycle. Students should know the names of the phases and be able to outline the two rounds of segregation in meiosis.
D2.1.10	Down syndrome and non-disjunction	Use Down syndrome as an example of an error in meiosis.
D2.1.11	Meiosis as a source of variation	Students should understand how meiosis generates genetic diversity by random orientation of bivalents and by crossing over.

HL LEARNING OUTCOMES

D2.1.12	Cell proliferation for growth, cell replacement and tissue repair	Include proliferation for growth within plant meristems and early-stage animal embryos as examples. Include skin as an example of cell proliferation during routine cell replacement and during wound healing. Students are not required to know details of the structure of skin.
D2.1.13	Phases of the cell cycle	Students should understand that cell proliferation is achieved using the cell cycle. Students should understand the sequence of events including G1, S and G2 as the stages of interphase, followed by mitosis and then cytokinesis.
D2.1.14	Cell growth during interphase	Students should appreciate that interphase is a metabolically active period and that growth involves biosynthesis of cell components including proteins and DNA. Numbers of mitochondria and chloroplasts are increased by growth and division of these organelles.
D2.1.15	Control of the cell cycle using cyclins	Limit to the concentration of different cyclins increasing and decreasing during the cell cycle and a threshold level of a specific cyclin required to pass each checkpoint in the cycle. Students are not required to know details of the roles of specific cyclins.
D2.1.16	Consequences of mutations in genes that control the cell cycle	Include mutations in proto-oncogenes that convert them to oncogenes and mutations in tumour suppressor genes, resulting in uncontrolled cell division.
D2.1.17	Differences between tumours in rates of cell division and growth and in the capacity for metastasis and invasion of neighbouring tissue	Include the terms “benign”, “malignant”, “primary tumour” and “secondary tumour”, and distinguish between tumours that do and do not cause cancer. Application of skills: Students should observe populations of cells to determine the mitotic index.

D2.1.1 – Generation of new cells in living organisms by cell division. D2.1.2 – Cytokinesis as splitting of cytoplasm in a parent cell between daughter cells. D2.1.3 – Equal and unequal cytokinesis. D2.1.4 – Roles of mitosis and meiosis in eukaryotes. D2.1.5 – DNA replication as a prerequisite for both mitosis and meiosis

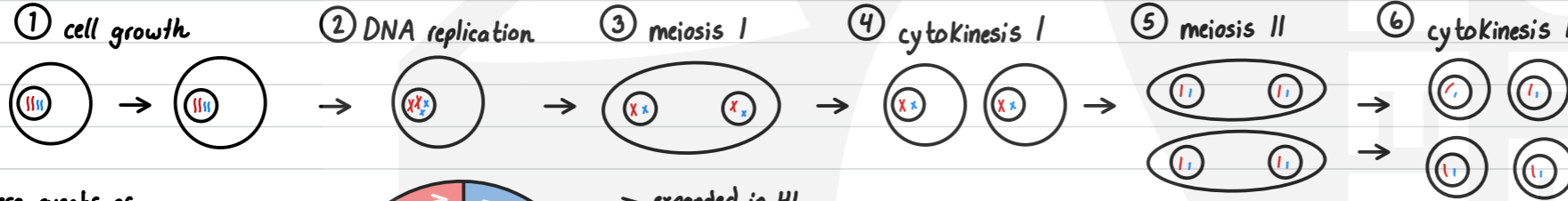
cell division: mother (parent) cell divides to produce two daughter cells ✖ **cell theory**: all living organisms comprise one or more cells which arise from pre-existing cells from cell division **Cell structure A2.2**

process used for asexual reproduction and somatic cell growth in eukaryotes:



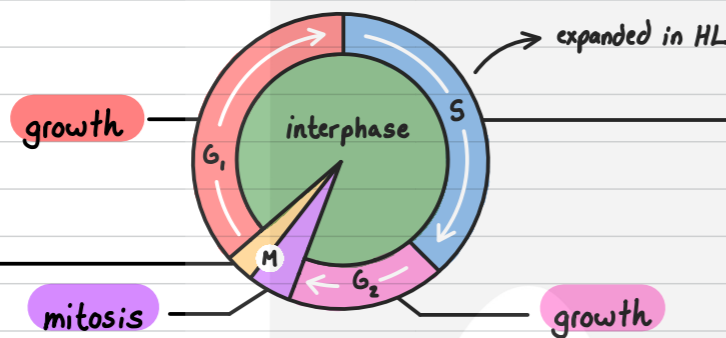
mitosis: nuclear division resulting in 2 identical nuclei is necessary prior to cell division as it ensures each daughter cell has a nucleus with identical chromosome number and composition to parent cell - preserving the genome

process used for gamete formation in sexual reproducing eukaryotes:



meiosis: nuclear divisions resulting in 4 haploid unique nuclei is necessary for gamete formation as it ensures each daughter cell is genetically unique (increasing genetic variation) and contains half the number of chromosomes ensuring the correct chromosome number is maintained after fertilization $n + n \rightarrow 2n$

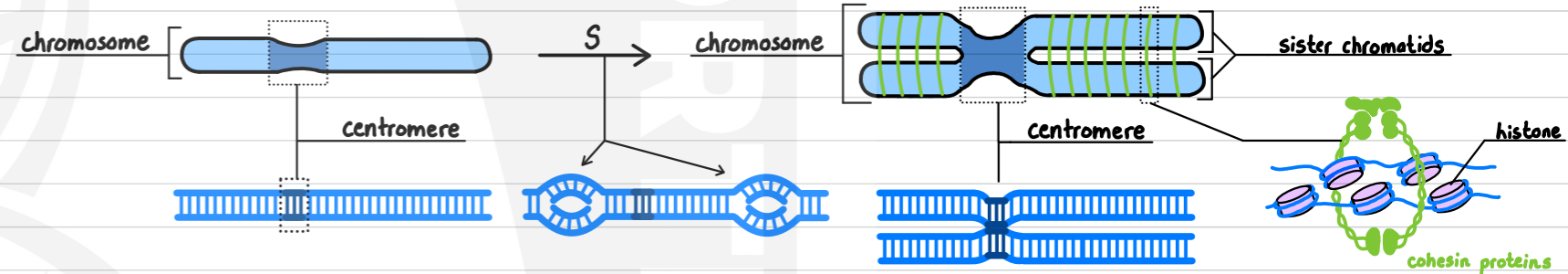
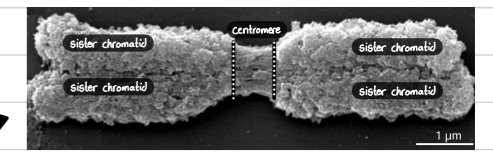
Somatic cells carry out these events as a cycle with **interphase** being the longest as it involves cell growth, gene expression and DNA replication



DNA replication (duplication of genetic material) is a prerequisite for both mitosis and meiosis **DNA replication D1.1**

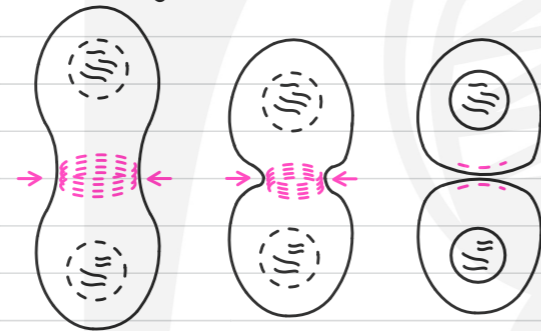
during replication both the DNA and histones duplicate resulting in each chromosome consisting of two identical chromatids ✖ number of chromosomes doesn't change ex. in humans $46 \times 1 \rightarrow 46 \times 2$

sister chromatids are attached together at the centromere region and by **cohesin proteins** ✖ note: chromosomes will not condense and appear as below until prophase

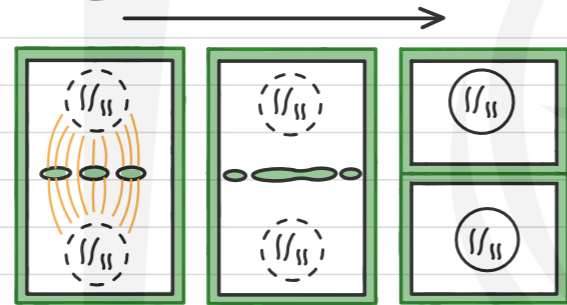


Cytokinesis: the splitting of the cytoplasm in a parent cell into daughter cells

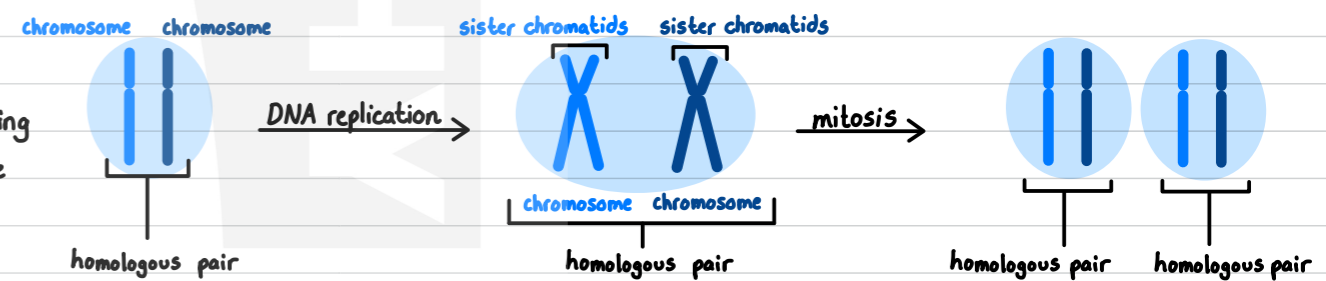
animal cells: contractile ring of **actin** and **myosin** proteins pull cell membrane together forming a cleavage furrow along cell equator. Once it reaches the center, cells pinched apart. Process is centripetal - from outside to inside



plant cells: **microtubules** bring **vesicles** from Golgi to cell equator which fuse together, forming **cell plate**. Cell plate extends outward by further fusion until it reaches original membrane and cell wall - dividing cell. Cellulose is secreted forming new cell walls. Process is centrifugal - from center, moving out

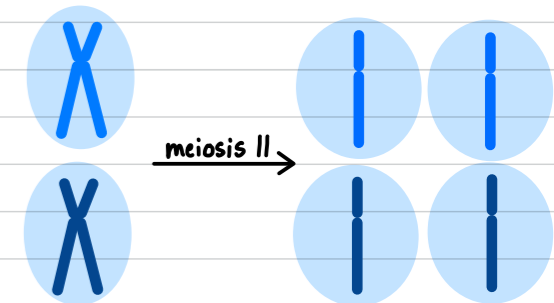


mitosis: separation of identical sister chromatids, resulting in daughter cells which are clones of parent cell



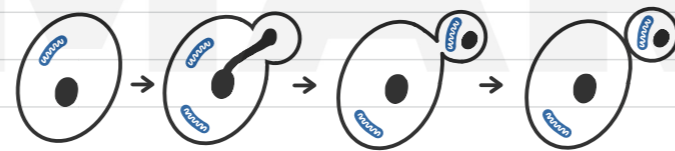
cytokinesis is typically equal where both daughter cells receive roughly equal volume of cytoplasm and at least one mitochondrion (and chloroplast in plant cells) as each can only be made from pre-existing ones

meiosis: meiosis I separates homologous chromosomes, halving the chromosome number ($2n \rightarrow n$). meiosis II separates sister chromatids, halving genetic material

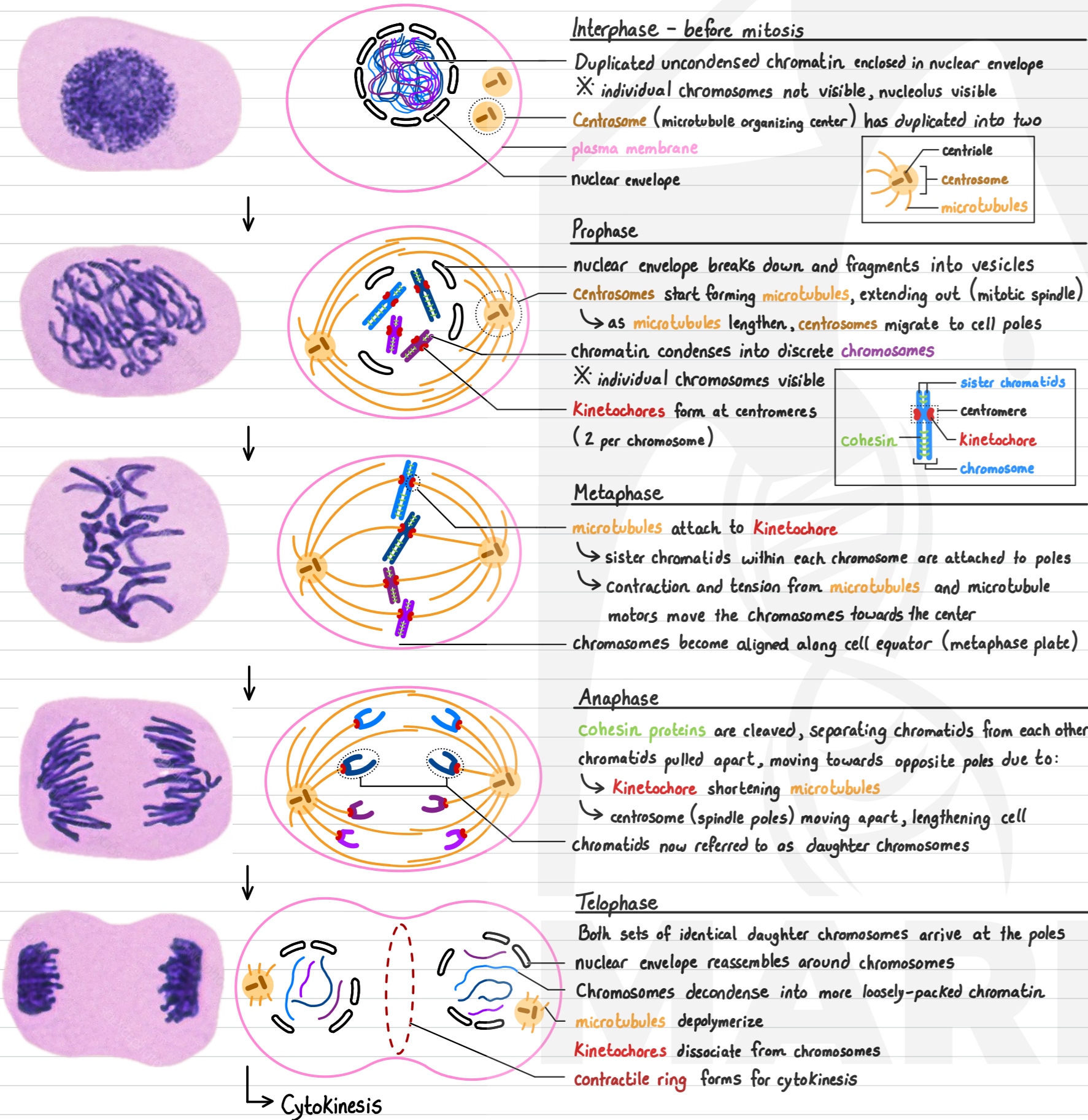


✖ **Unequal cytokinesis in oogenesis** (after meiosis I and II) results in small **polar bodies** which degenerate and not used. large cell with most of cytoplasm matures into nutrient-rich **ovum**.

✖ **Unequal cytokinesis in yeast budding** (asexual reproduction) much smaller daughter cells bud off from large mother cell

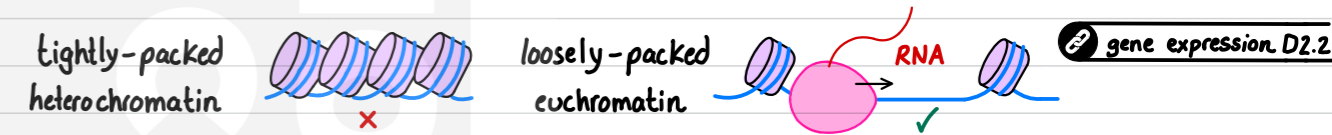


Mitosis (nuclear division) occurs after interphase and consists of 4 main phases: Prophase → Metaphase → Anaphase → Telophase. Afterwards the cytoplasm divides via cytokinesis forming daughter cells



Eukaryotic DNA is wrapped-around histone proteins forming chromatin nucleic acids A1.2

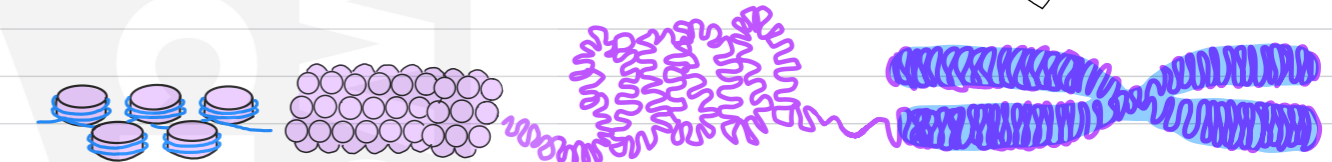
↳ helps organize and control the relative compaction and gene expression in specific sections



↳ during interphase chromatin is less condensed overall to allow for replication and gene expression

✗ Both mitosis and meiosis require chromatids to be separated and for chromosomes to move to opposite poles - this cannot occur reliably if DNA is decondensed

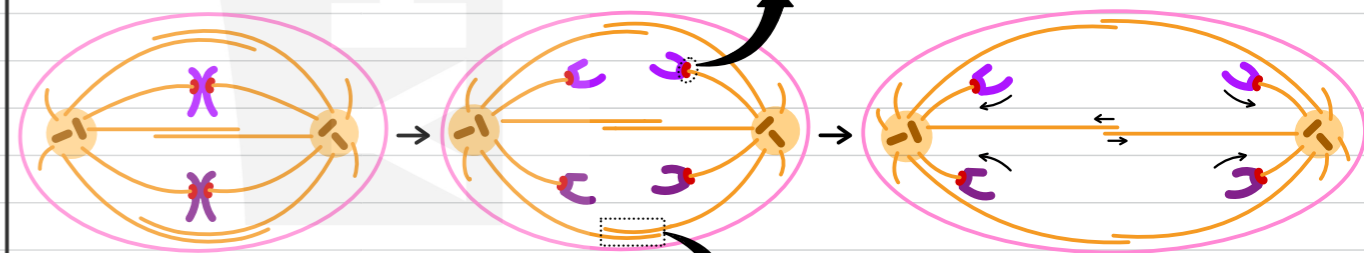
↳ chromatin becomes supercoiled into very compact chromosomes facilitating and organizing chromosome migration - like compressing files



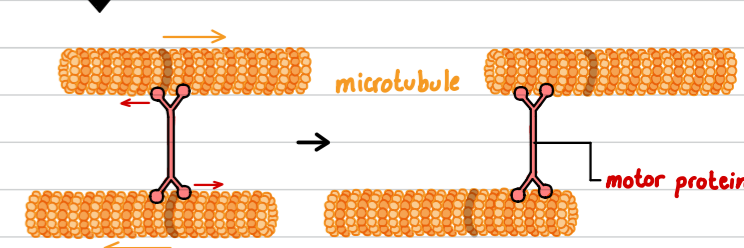
ex: in an average condensed chromosome there is 50,000µm of DNA packed within 5µm → 10,000:1

During mitotic and meiotic phases, chromosomes don't move independently but are pulled using microtubules and motor proteins allowing them to align and segregate to opposite poles

↳ The Kinetochores are bound to microtubules extending from the centrosomes at the pole. Kinetochores motor proteins depolymerize microtubules by removing tubulin protein subunits from end (shortening microtubule) and 'walks' along it, moving chromosome towards the pole



↳ motor proteins are bound in between overlapping microtubules. They move toward the microtubule ends in a stepwise 'walking' motion, generating force which moves microtubules towards the poles - moving poles apart and lengthening cell (contributing to chromosome movement)



Meiosis (reduction division) occurs after interphase and consists of 2 rounds of division - meiosis I and meiosis II, each consisting of 4 phases followed by cytokinesis

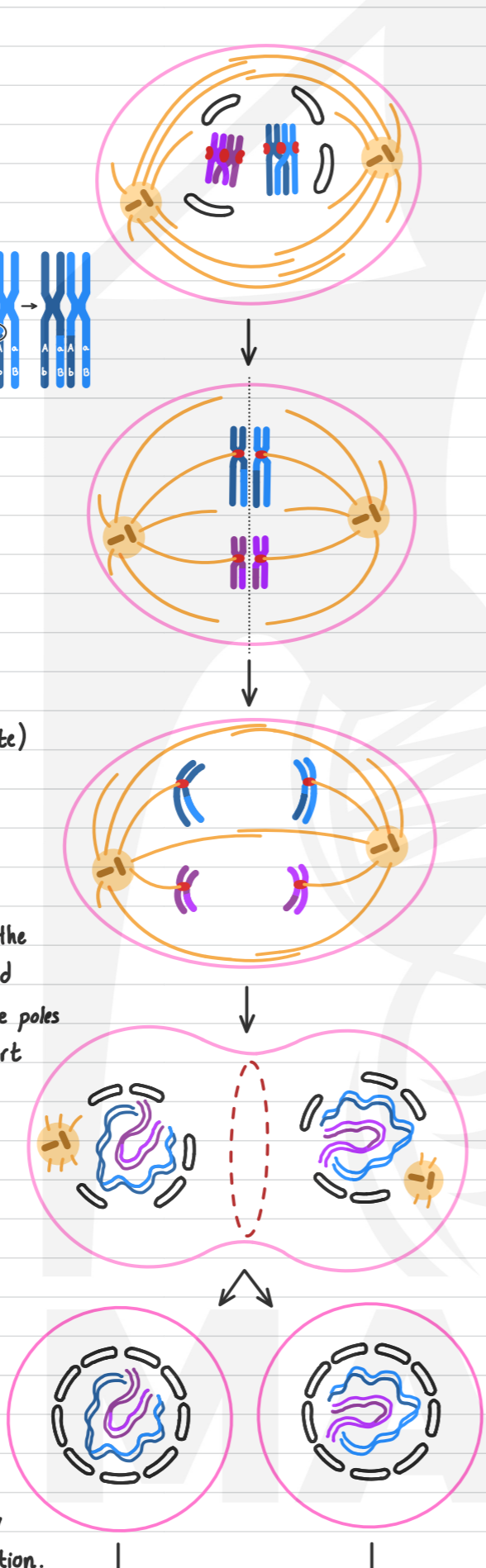
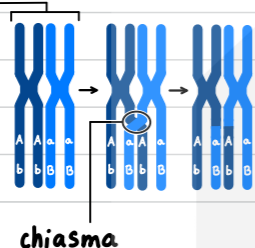
very similar process to mitosis

Meiosis I - separation of homologous chromosomes

Meiosis II - separation of sister chromatids

Prophase I

nuclear envelope breaks down and fragments into vesicles
 centrosomes form **microtubules** (spindle) and migrate to cell poles
 chromatin condenses into discrete **chromosomes**
 homologous chromosomes pair up, forming **bivalents**
 genetic recombination: non-sister chromatids crossover at random points (chiasmata) and exchange alleles - sister chromatids no longer identical → increases genetic variation



Metaphase I

The 2 **Kinetochores** on the sister chromatids of a chromosome are linked together by proteins - acting like a single **Kinetochores**
Microtubules attach to the **Kinetochores** of chromosomes (both chromatids of 1 chromosome attached to 1 pole)
 contraction and tension from **microtubules** and microtubule motors align bivalents along cell equator (metaphase plate)
 orientation of each bivalent along equator is random and independent of the other → increases genetic variation

Prophase II

nuclear envelope breaks down and fragments into vesicles
 centrosomes form **microtubules** and migrate to cell poles
 chromatin condenses into discrete **chromosomes**

Metaphase II

microtubules attach to **Kinetochores**
 sister chromatids within each chromosome are attached to poles
 contraction and tension from **microtubules** and microtubule motors align chromosomes along metaphase plate

Anaphase I

cohesin proteins are cleaved along chromatid arms but not at the centromere - separating bivalent but keeping sister chromatids joined
 homologous chromosomes are separated, moving towards opposite poles
Kinetochores shorten **microtubules** and centrosome move apart

Anaphase II

cohesin proteins at centromere are cleaved, separating chromatids from each other
 chromatids pulled are separated, moving towards poles
Kinetochores shorten **microtubules** and centrosome move apart
 chromatids now referred to as chromosomes

Telophase I

1 of each homologous chromosome arrives at each pole
 each chromosome consists of 2 non-identical sister chromatids
 nuclear envelope reassembles around chromosomes
 Chromosomes decondense into more loosely-packed chromatin
microtubules depolymerize
contractile ring forms for cytokinesis

Telophase II

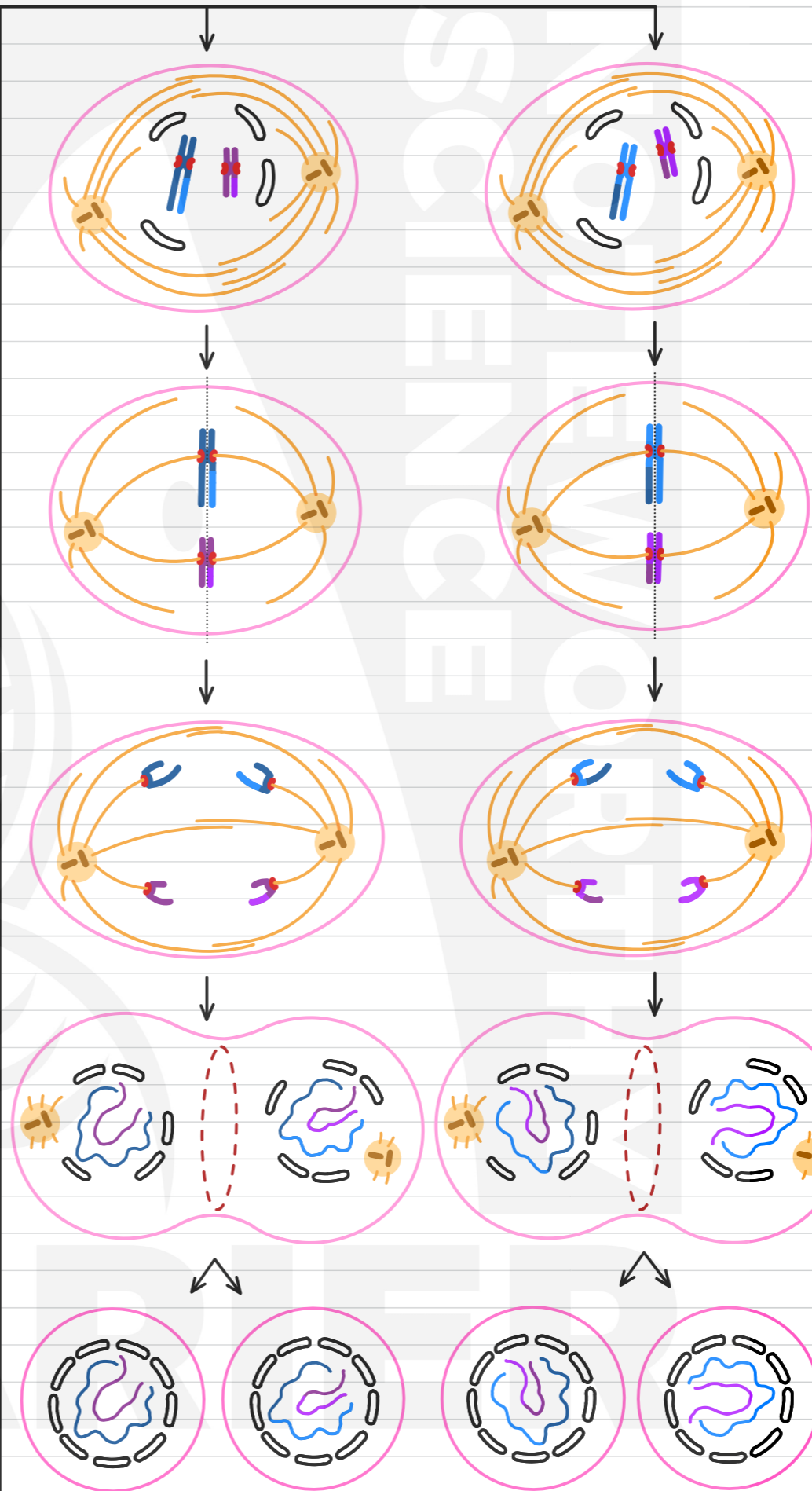
1 of each chromosome arrive at the poles
 nuclear envelope reassembles around chromosomes
 Chromosomes decondense
microtubules depolymerize
contractile ring forms for cytokinesis

Cytokinesis I

Cytoplasm and cell divides. Division is equal in spermatogenesis and unequal in oogenesis, forming large cell and small polar body
 both cells are haploid and genetically unique. No DNA replication.

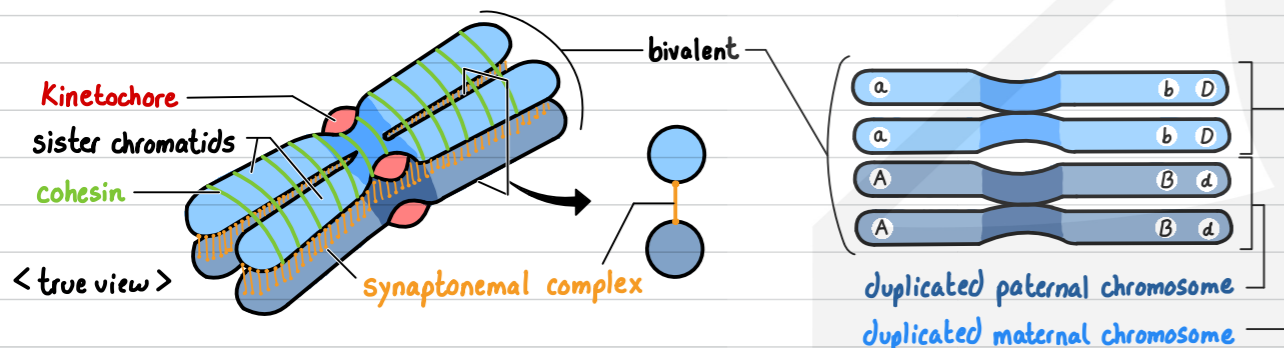
Cytokinesis II

Cytoplasm and cell divides (equally or unequally)
 Each cell (gamete):
 haploid nucleus, 1 copy of each chromosome (n)
 genetically unique from each other and parent
 will specialize into sex cell (sperm or ovum)

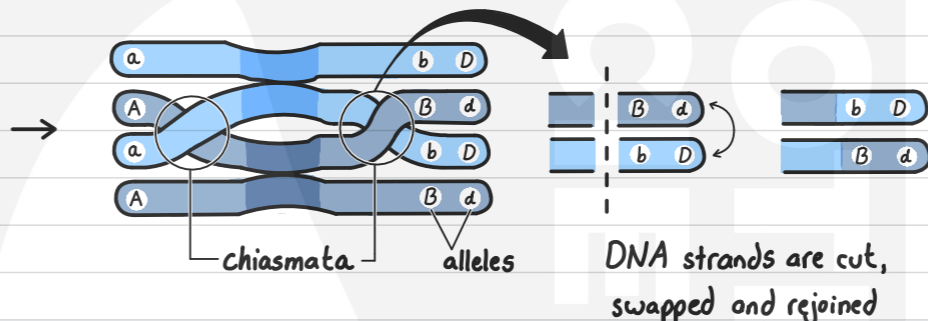


Crossing over (intrachromosomal recombination) between two homologous chromosomes' non-sister chromatids results in recombinant chromosomes; increasing genetic variation. Occurs in Prophase I

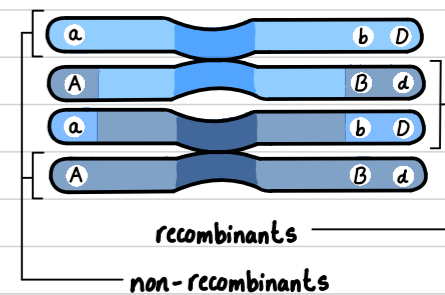
① **Synapsis**: pairing up and joining of homologous chromosomes forming a bivalent



② **Crossing-over**: non-sister chromatids exchange alleles at points along the chromatids (chiasmata). The location and number of chiasmata is random



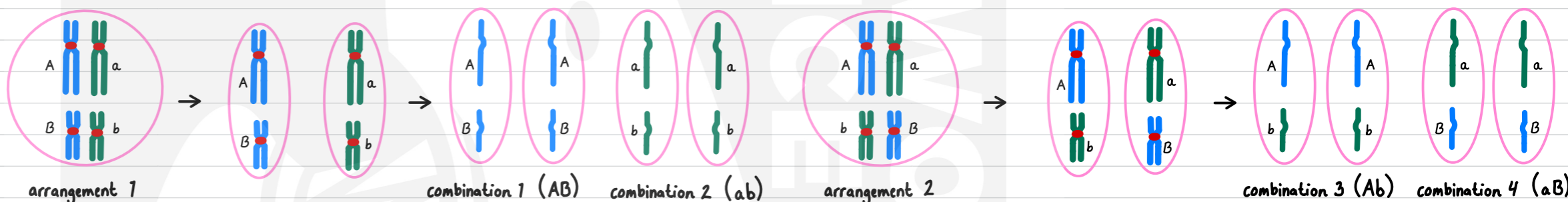
③ Chromatids that crossed over are recombinants. Sister chromatids of chromosome non-identical



Random orientation (interchromosomal recombination) of pairs of homologous chromosomes (bivalents) at equator results in independent assortment of alleles (for non-linked genes). Occurs in Metaphase I **Inheritance D3.2**

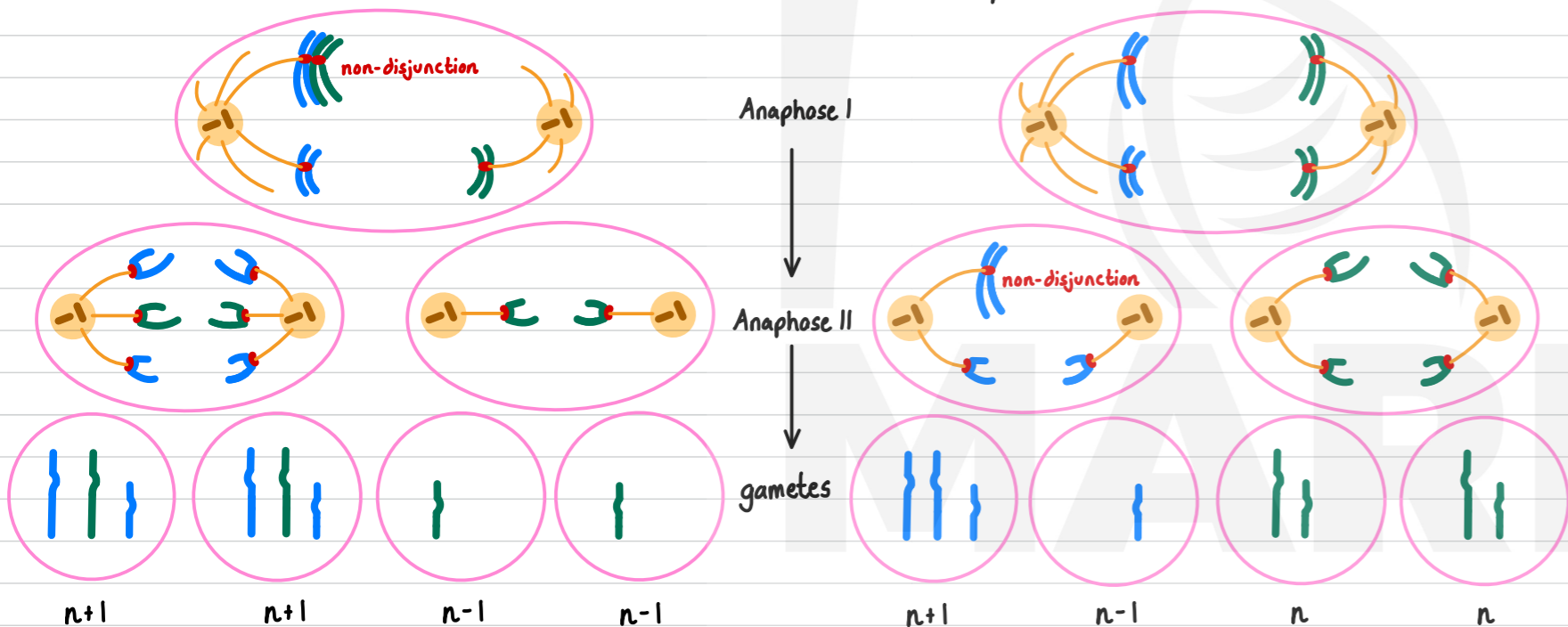
The orientation of one bivalent is random and independent of other bivalents
 $\therefore 2^n$ possible ways of arranging chromosomes where n is the number of bivalents

* humans: $2^{23} = > 8$ million possible combinations



Non-disjunction: a failure of separation of chromosomes during meiosis, resulting in a gamete with one chromosome too many, n+1 (trisomy) or too few, n-1 (monosomy). Error occurs in either Anaphase I or Anaphase II

Down Syndrome (trisomy 21) occurs when a gamete that had a non-disjunction of chromosome 21 participates in fertilization. The fetus will have 47 chromosomes (24+23) and 3 copies of chromosome 21



	Mitosis	Meiosis
DNA replication	in interphase before Mitosis	in interphase before Meiosis I not Meiosis II
number of divisions	1 round including: Prophase, Metaphase, Anaphase, Telophase and cytokinesis	2 rounds, each including: Prophase, Metaphase, Anaphase, Telophase and cytokinesis
formation of bivalents	does not occur	occurs in Prophase I along with crossing over between homologous non-sister chromatids, forming chiasmata
segregation	sister chromatids in anaphase	homologous chromosomes in anaphase I sister chromatids in anaphase II
resulting daughter cells	2 - genetically identical same chromosome number as parent	4 - genetically unique haploid
role in animals, plants, fungi	produces cells for growth, repair, and in some cases asexual reproduction	produces unique haploid gametes for sexual reproduction

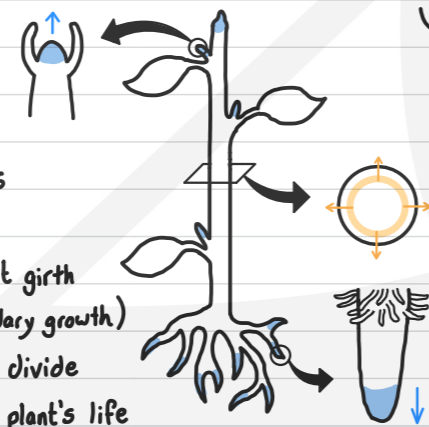
Cell proliferation: overall increase in number of cells due to rate of cell growth and division > rate of cell death. Required in animals and plants for 3 primary reasons:

↳ **Growth**: increase in body size / mass

ex: **growth plates** at end of bones are active in juveniles enabling rapid growth

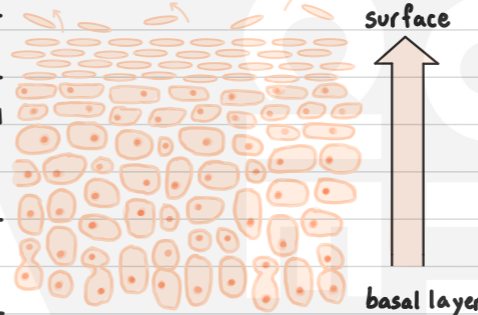
ex: **early-stage animal embryos**
Cell specialization B2.3

ex: **apical meristems** in plant shoot and root tips lengthens plant (primary growth)
lateral meristems causes plant girth to widen and strengthen (secondary growth)
* meristems retain ability to divide and differentiate throughout plant's life



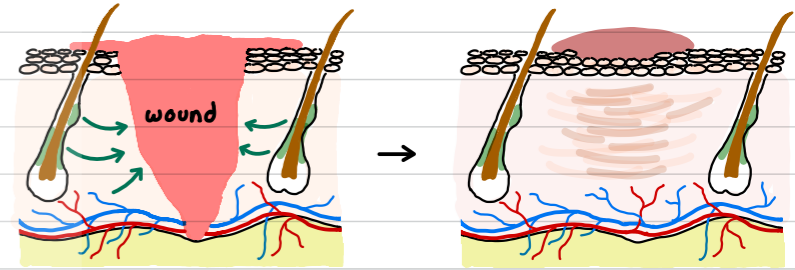
↳ **Cell replacement**: routine replacement of cells with limited lifespan

ex: dead skin cells — new cells replace dead cells being shed — rapidly dividing cells

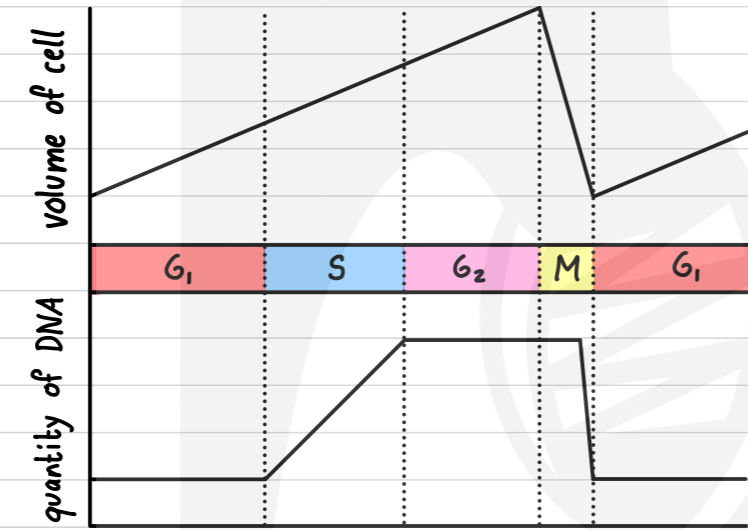
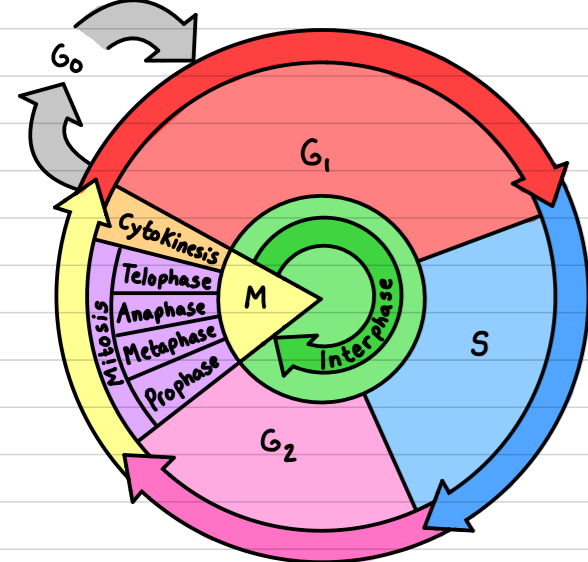


↳ **tissue repair**: healing after loss or damage to tissues

ex: **Hair follicle stem cells** can divide and differentiate to repair skin tissue



Cell cycle: series of events that takes place in a cell as it grows and divides, enabling cell proliferation — Controlled by a cell cycle control system - cyclically operating set of cellular molecules that triggers and regulates key events

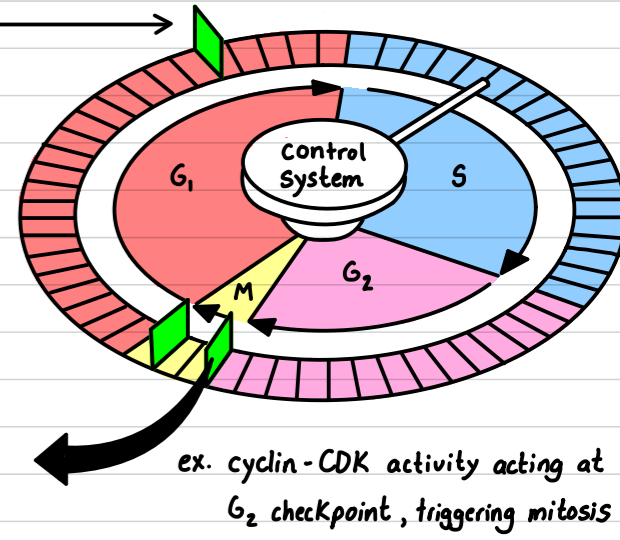
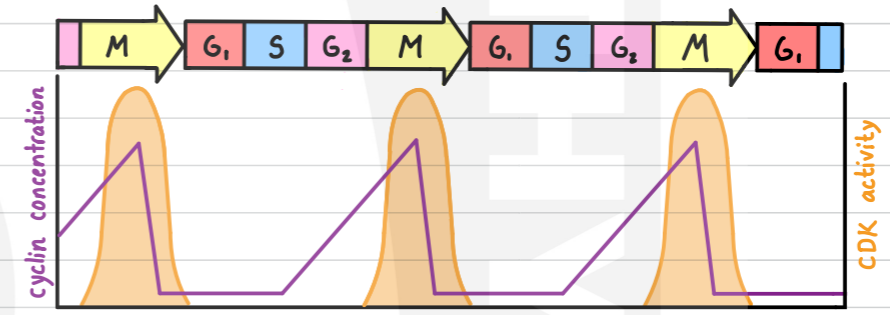


↳ **cyclin-dependent Kinases (CDK)**: enzymes which activate or inactivate proteins involved in cell cycle activities by phosphorylating them. Their concentration is constant throughout cycle but are only active when bound to a specific cyclin, forming a cyclin-CDK complex



↳ **cyclins**: proteins which regulate the progression of the cell cycle by binding to and activating CDKs, triggering processes. Cyclin concentrations rise and fall throughout cycle, thereby impacting CDK activity and the cell cycle

↳ Between different phases there are **checkpoints**. These act as control points to ensure key events have taken place and environment is suitable before proceeding to next phase
* at each checkpoint a cyclin threshold concentration is required



ex: cyclin-CDK activity acting at G₂ checkpoint, triggering mitosis

Interphase: very active and longest phase when most of cellular activities and metabolic reactions occur

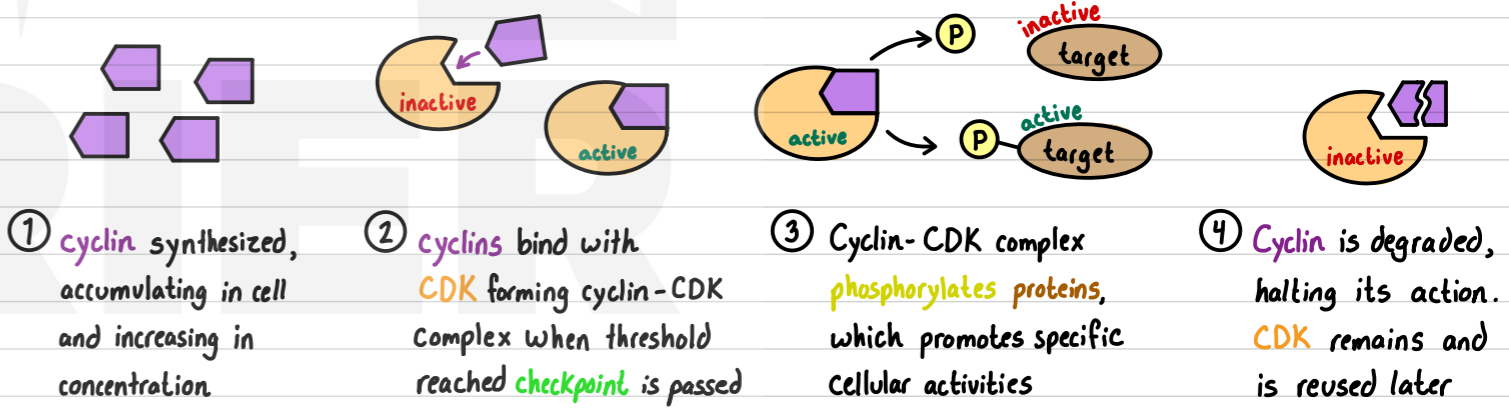
- **Gap 1 (G₁) Phase**: protein synthesis, cell grows larger, cytoplasm volume increases, organelles duplicate
- **Synthesis (S) Phase**: DNA is replicated as chromatids; doubling total amount (chromosome number unchanged)
- **Gap 2 (G₂) Phase**: cell resumes growth and protein synthesis. Organelles duplicate.

↳ mitochondria and chloroplasts self-replicate

Mitotic (M) Phase: the division of the nucleus and cell.

- **Mitosis**: the division of the nucleus. Subdivided into 4 phases: Prophase, Metaphase, Anaphase, Telophase
- **Cytokinesis**: the division of the cytoplasm and cell as a whole, producing 2 daughter cells

* some cells may leave cell cycle during G₁ and enter **Gap 0 (G₀) Phase** where cells differentiate and no longer divide



gene mutation: permanent structural changes to genes at the molecular level (i.e. change in DNA nucleotide base sequence) Mutations D1.3

↳ if a mutation alters a gene involved in cell cycle control it can lead to abnormal cells and accelerated growth rates, potentially resulting in **tumours** (mass of proliferating cells, dividing out of control)

- **proto-oncogene**: code for proteins which promote cell cycle progression and cell proliferation.
 - * the 'gas pedal' of cell cycle progression ex: RAS, MYC



↳ **mutation** in proto-oncogenes results in **overactive/over expressed** forms called **oncogenes**

* mutation is genetically dominant: only one of the pairs in a diploid cell needs to be mutated

↳ as gene is **overactive**, an overabundant amount of cell cycle regulating proteins are synthesized resulting in **increased cell cycle progression and excessive cell division/growth**

- **tumour-suppressor gene**: code for proteins which halt cell cycle progression to correct an error and repair DNA or promote apoptosis (controlled cell death) when an irreparable error is detected
 - * the 'brake' of cell cycle progression ex: p53



↳ **mutation** in tumour-suppressor gene results in **inactivation/under expression**

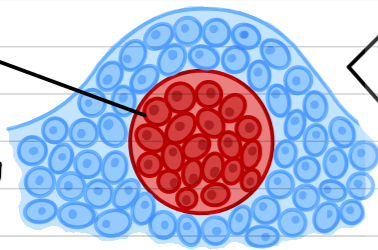
* mutation is genetically recessive: both tumour-suppressor genes in a diploid cell need to be mutated

↳ as gene is **inactive**, proteins which cause cell arrest, DNA repair, and apoptosis no longer synthesized resulting in cells with increased errors and overall increase in cell cycle progression

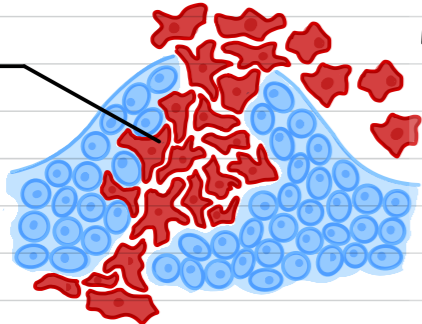
NO BRAKES



benign tumour
grow slowly and do not metastasize or spread - remaining together, encapsulated within normal tissue
* not cancer-causing



malignant tumour
rapidly growing, invading nearby tissues and can metastasize, spreading around the body
* cancer-causing

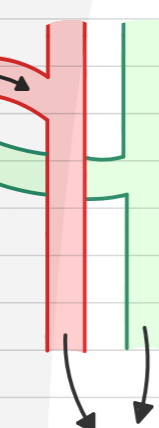


primary tumour: mass of cells growing at the site where mutation first occurred i.e. the initial tumour that was formed



metastasis: spread of cancer cells to locations distant from the original site. This can occur when some of the tumour cells break off and enter the **blood** or **lymph** vessels, transporting them to new tissues or organs

secondary tumour: mass of cells growing at a site different from the primary tumour. Results from a malignant tumour breaking off, metastasizing and successfully establishing in a new tissue or organ
ex: primary tumour in the breast spreading to the lungs or brain forming secondary tumours



Cancer: uncontrolled cell division of abnormal cells in a part of the body. Involves malignant tumours and metastasis leading to damage

↳ cancer itself arises from mutations in a somatic cell during an individual's lifetime and thus isn't passed on (i.e. cannot pass lung cancer to offspring)

* some genes may contain mutations which increases cancer susceptibility (i.e. inherited mutation can raise lung cancer risk)

Application of Skills

$$\text{Mitotic index} = \frac{\text{number of cells in mitosis (Prophase + Metaphase + Anaphase + Telophase)}}{\text{total number of cells (Interphase + Mitosis)}}$$

↳ a measure of cellular proliferation. The higher the mitotic index, the greater the proportion of cells undergoing mitosis and cell division.

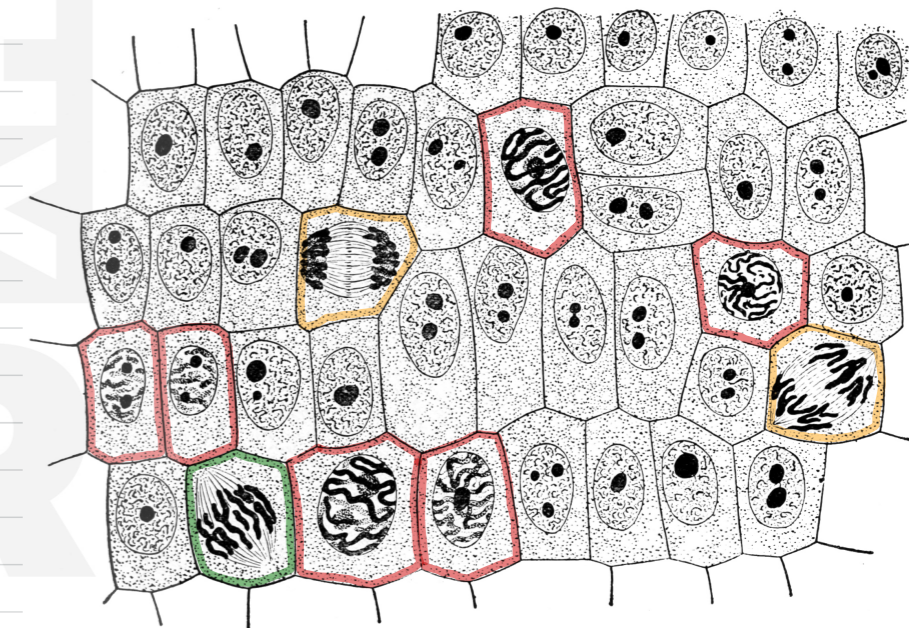
↳ the mitotic index may be used in the diagnosis of cancer by comparing the value of a potentially cancerous tissue to normal tissue. If the value is significantly higher, it may indicate cancer as the cells are dividing more than expected

ex: Calculate mitotic index:

Cells in Prophase	6
Cells in Metaphase	1
Cells in Anaphase	2
Cells in Telophase	0
Total number of cells	40

$$\text{Mitotic index} = \frac{6 + 1 + 2 + 0}{40} = 0.225$$

* only count cells where you can clearly see nucleus

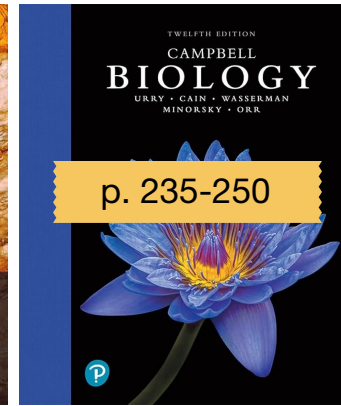
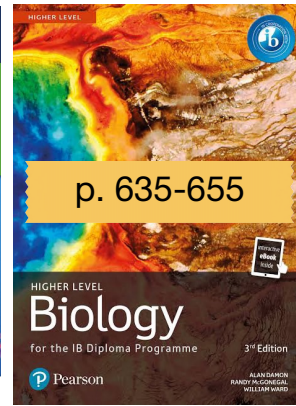
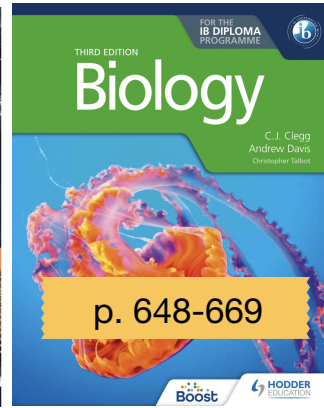
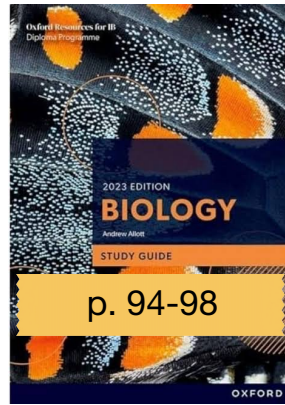
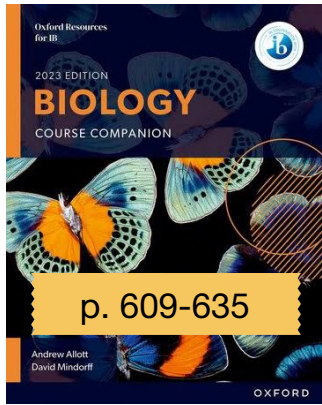


Resource Links

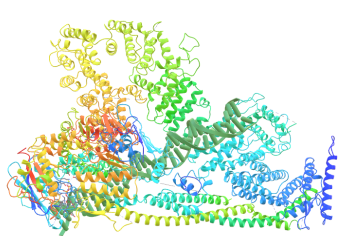
each resource is hyperlinked



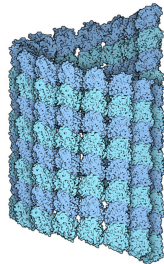
Textbooks



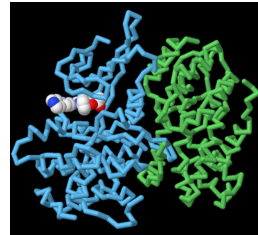
3D models



Cohesin complex



Microtubule



Cyclin/CDK

Articles

Brown, G. (2021). Oncogenes, Proto-Oncogenes, and lineage restriction of cancer stem cells. *International Journal of Molecular Sciences*, 22(18), 9667. <https://doi.org/10.3390/ijms22189667>

Debela, D. T., et.al. (2021). New approaches and procedures for cancer treatment: Current perspectives. *SAGE Open Medicine*, 9. <https://doi.org/10.1177/205031212111034366>

Muller, P. a. J., & Vousden, K. H. (2013). p53 mutations in cancer. *Nature Cell Biology*, 15(1), 2–8. <https://doi.org/10.1038/ncb2641>

Musacchio, A., & Desai, A. (2017). A Molecular view of kinetochore assembly and function. *Biology*, 6(1), 5. <https://doi.org/10.3390/biology6010005>

Ohkura, H. (2015). Meiosis: An Overview of Key Differences from Mitosis. *Cold Spring Harbor Perspectives in Biology*, 7(5), a015859. <https://doi.org/10.1101/cshperspect.a015859>

Simulators / Interactives

