

Biology

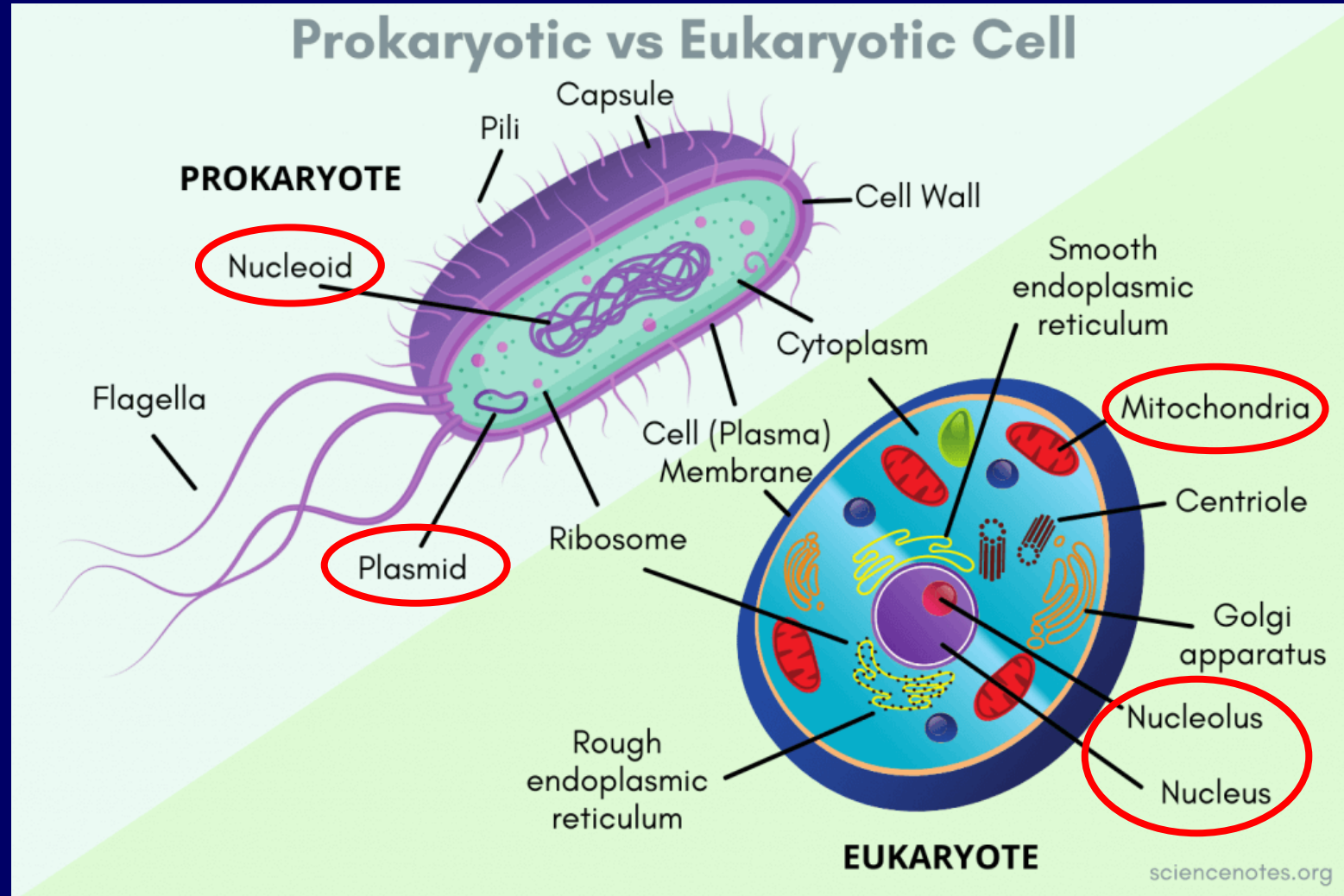
7. Nucleus, cell division, and cell death

Doc. RNDr. Jan Hošek, Ph.D.
hosekj@pharm.muni.cz

Department of Molecular Pharmacy
FaF MU

Genophores

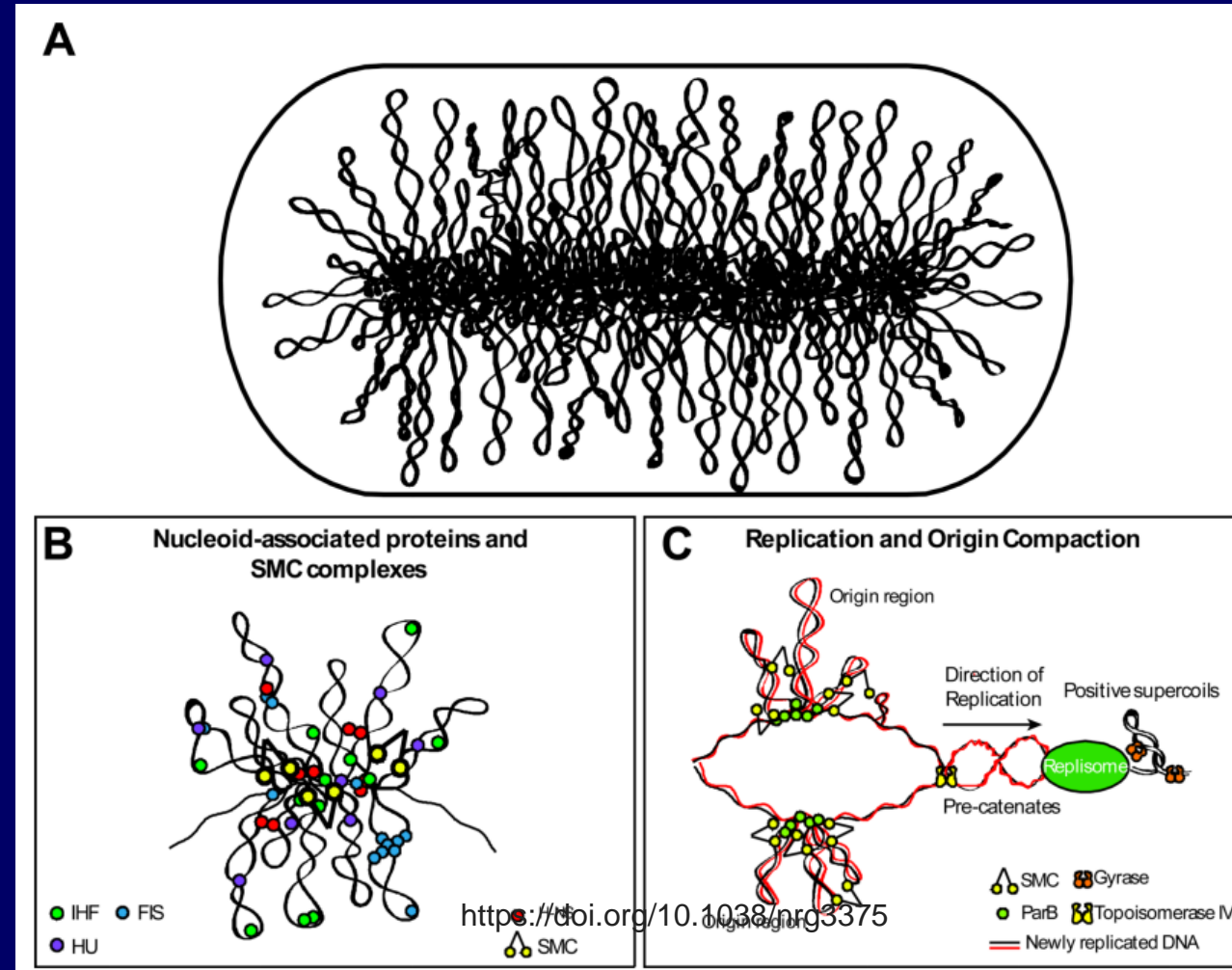
- Nucleoid
- Plasmids
- Nucleus
- Mitochondrial and chloroplast DNA



<https://sciencenotes.org/prokaryotic-vs-eukaryotic-similarities-and-differences/>

Prokaryotic „nucleus“ - nucleoid

- Formed by DNA, RNA and proteins
- It is NOT covered
- Usually 1 circular dsDNA molecule
- DNA is strongly condensated and organised into 3D structure by proteins (Nucleoid-associated proteins - NAPs)

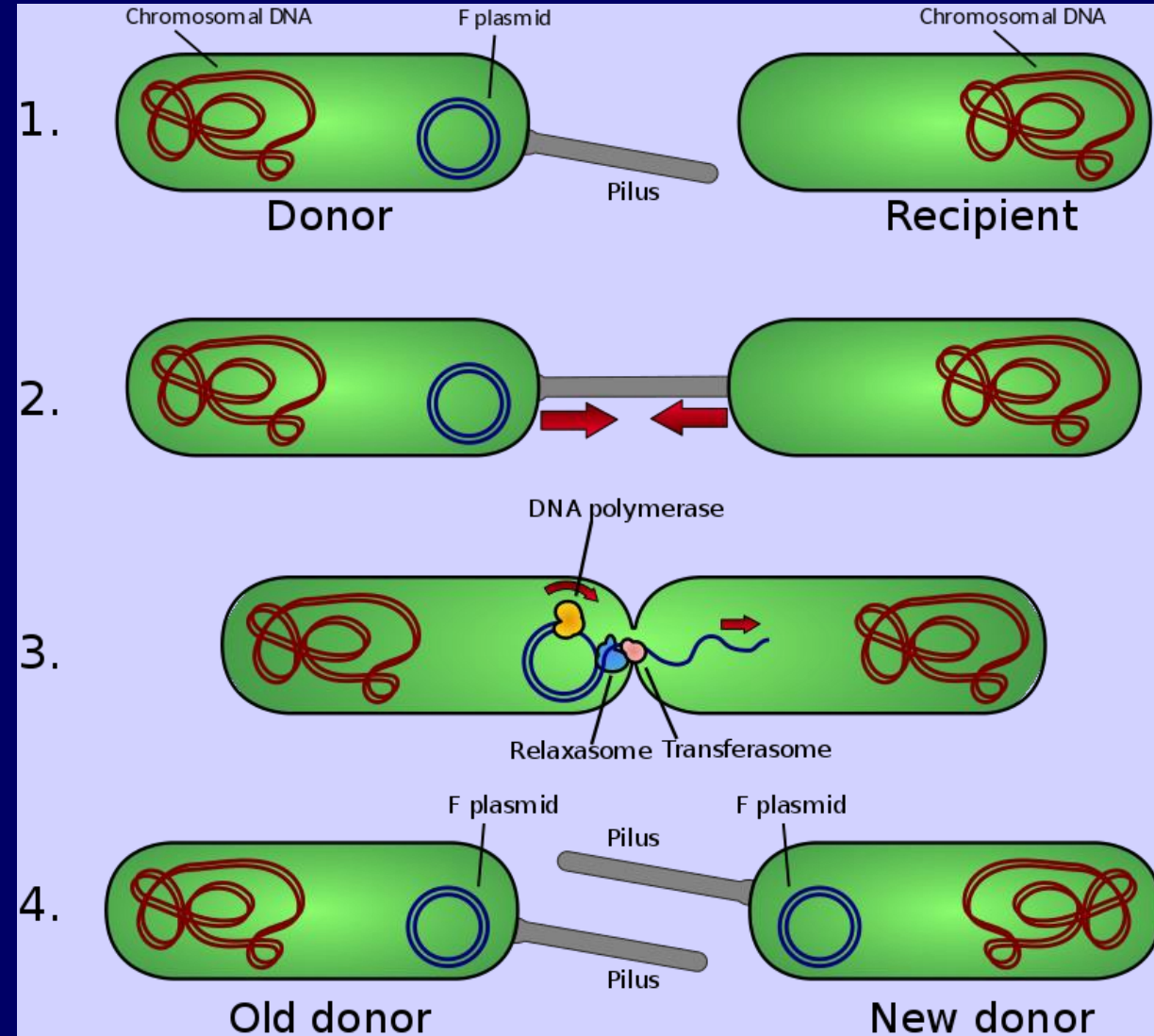


Plasmids

- Extrachromosomal circular dsDNA
- occurrence in many bacterial species
- 1,000 to 200,000 bp in size
- carry only genes encoding secondary features (e.g., resistance to antibiotics)
- autonomous replication
- replication cycle synchronized or unsynchronized
- must contain its origin of replication (*ori* locus)

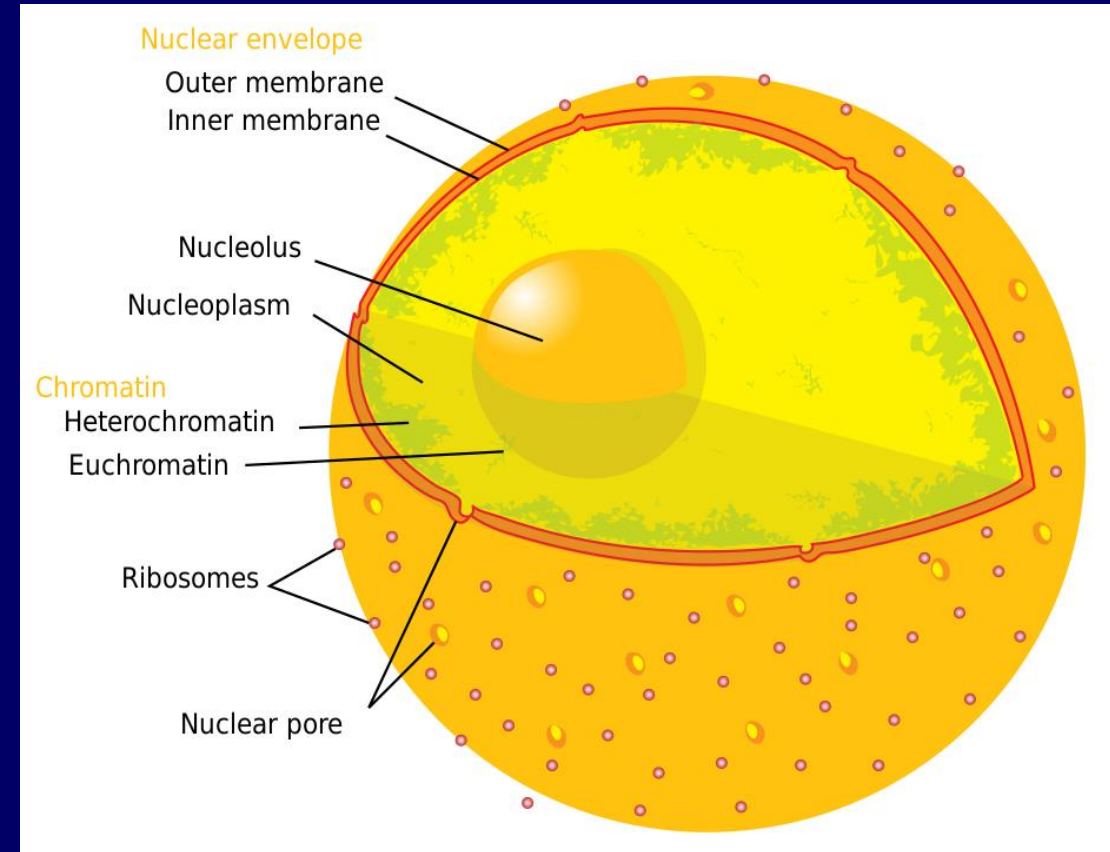
Plasmid types

- **F-plasmid**
 - fertilization plasmid for "sexual" reproduction of bacteria
 - transmitted by conjugation
- **R-plasmid**
 - carries antibiotic resistance genes
- **Col plasmids**
 - they carry genes for the production of bactericidal peptides
- Plasmids with genes for metabolisation of atypical substrates
- Plasmids with genes for virulence



Organisation of eukaryotic nucleus

- Outer membrane – bound on rough ER
- Inner membrane – binds **lamines** – DNA-binding proteins
- Nuclear pores
- Nucleolus
 - Genes for rRNA
 - Functional region formed by sequences of satellites of acrocentric chromosomes
- Nucleoplasm – contains DNA and proteins



https://www.wikiskripta.eu/w/Bun%C4%9B%C4%8Dn%C3%A9_j%C3%A1dro#/media/Soubor:Diagram_human_cell_nucleus.svg

Organisation of eukaryotic nucleus

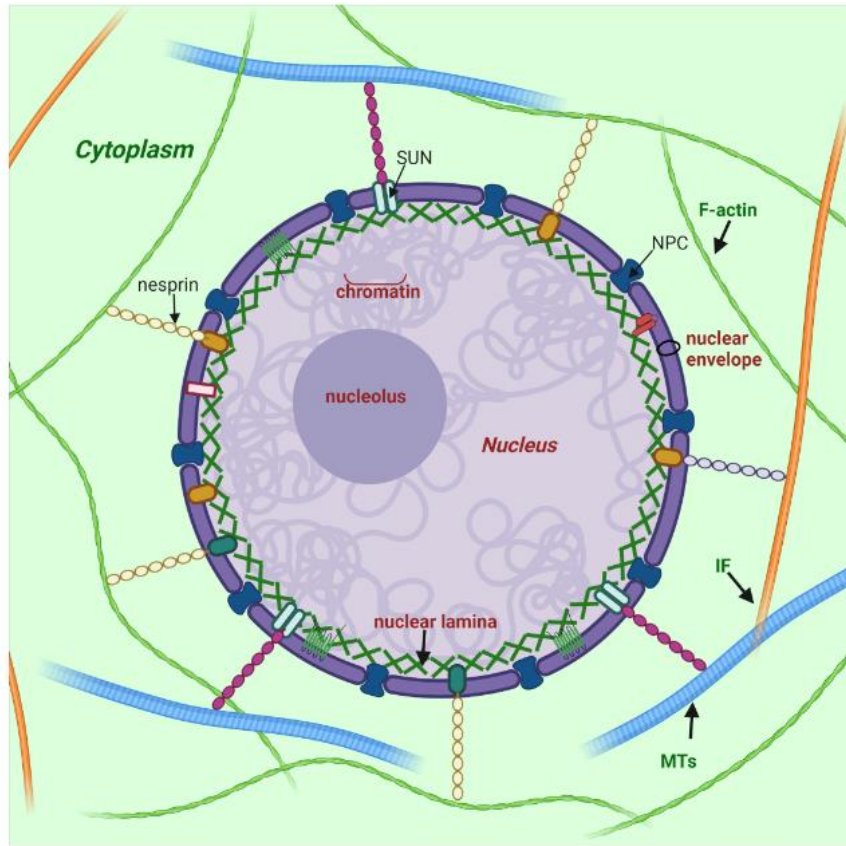


FIGURE 1 | Nuclear lamina position and its interplay with other structures of cell. Nuclear lamina is a stiff meshwork consisting of A-type lamins and B-type localized between the nuclear envelope and chromatin. Nuclear lamins interact with a wide range of nuclear envelope proteins (NEPs). Also, nuclear lamins can interact with the cytoskeleton (filamentous actin – F-actin; microtubules – MTs; and intermediate filaments – IF) via SUN proteins and nesprins. Created with BioRender.com.

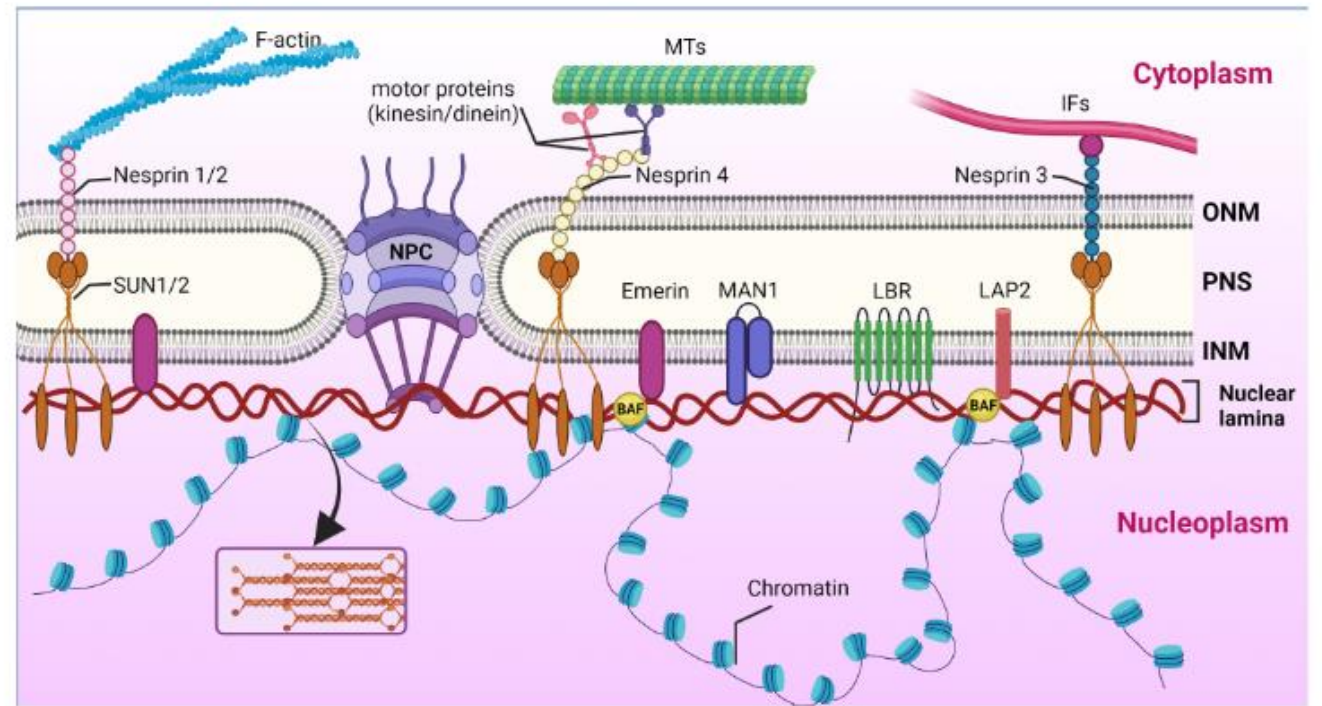


FIGURE 5 | Cooperation of nuclear lamina with nuclear envelope proteins and chromatin. Nuclear lamina is localized between the inner nuclear membrane (INM) and chromatin. Schematic representation of lamin interaction with inner nuclear membrane proteins, the most important of which are MAN1, LAP2, SUN1/2, Emerin, and LBR. The nuclear pore complex (NPC) spans both the inner nuclear membrane (INM) and the outer nuclear membrane (ONM) and mediates macromolecular transport. Via SUN1/2 and the nesprins interacting with them, located in the ONM, lamins cooperate with cytoskeleton components, namely filamentous actin (F-actin), microtubules (MTs), and intermediate filaments (IFs). The space between the ONM and INM is termed the perinuclear space (PNS). Created with BioRender.com.

DOI: 10.3389/fcell.2021.761469

Chromosomes

DNA is divided into sets of chromosomes. Genes are stored on chromosomes linearly in a precise position = locus

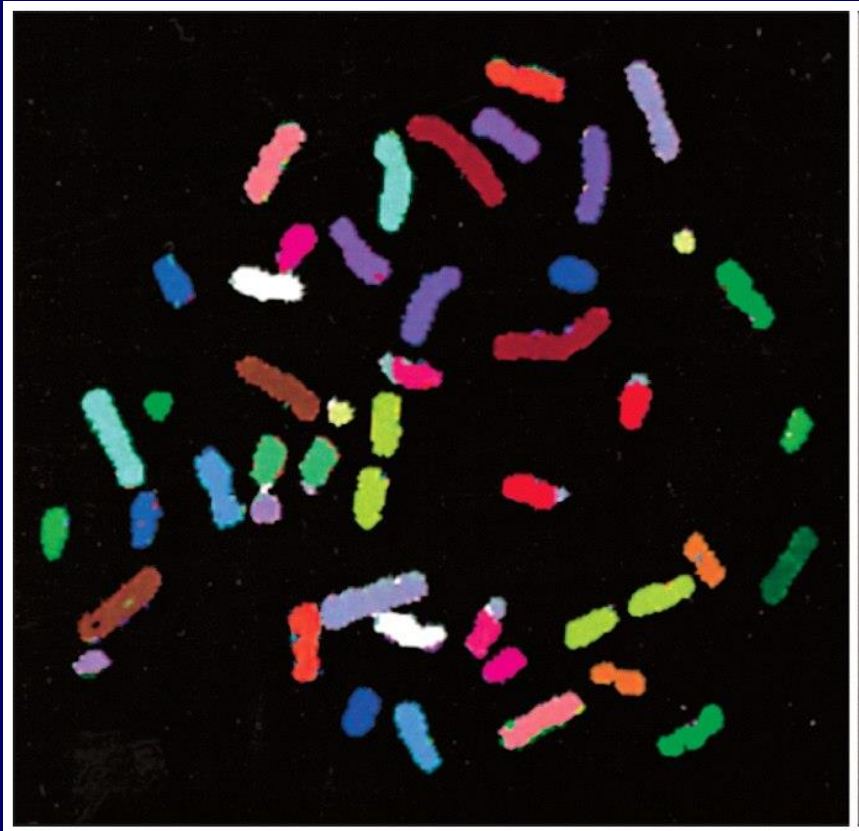
Chromosome consists of chromatin. It is formed:

- ❖ long linear molecule of DNA
- ❖ proteins, which are bound to DNA
 - helps DNA to be packed (histones)
 - participate on gene expression
 - participate on replication and DNA correction

Chromosomes look different in interphase (loose) and mitosis (highly condensed)

Chromosomes

We distinguish between **homologous (autologous) chromosomes** that are paired. Humans have 22 pairs of chromosomes+ **XX** nebo **XY**

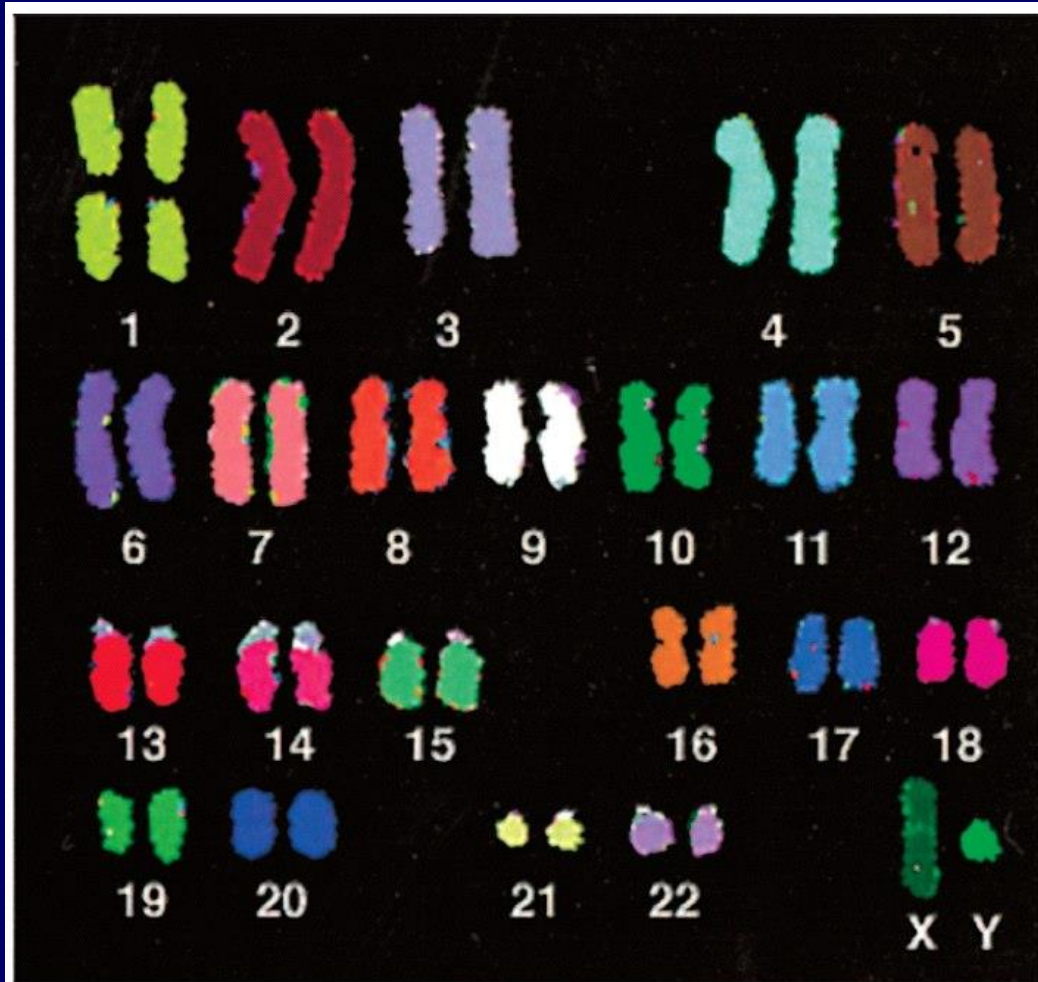


X and Y = sex (non-homologous ; heterologous) **chromosomes**

One chromosome in a pair is always paternal (**P**), the second maternal (**M**)

Human chromosomes in mitosis. The colors used usually distinguish sequences rich in A-T pairs from sequences with C-G pairs.

Chromosomes

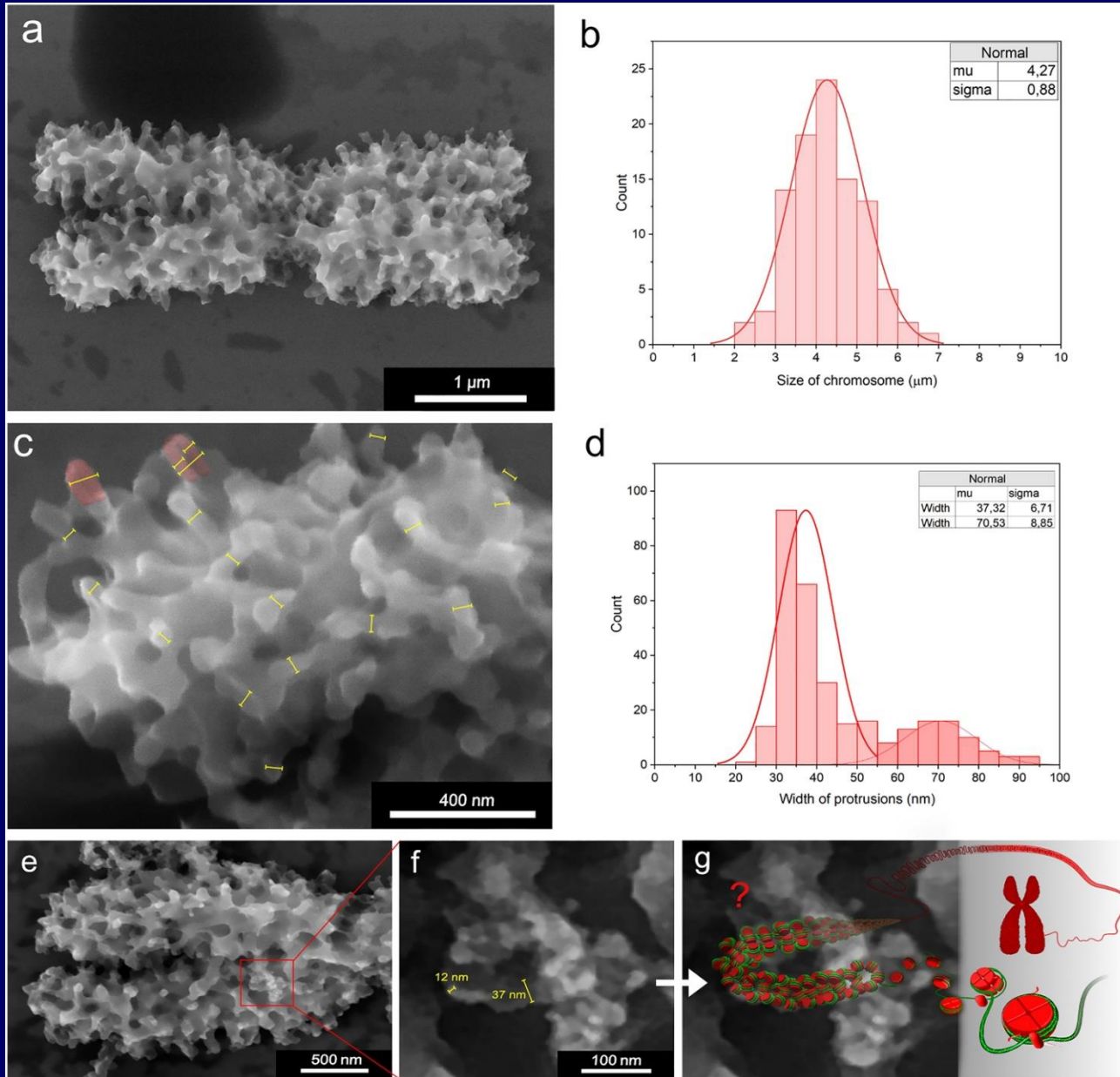


(B)

10 μm

Artificially arranged
chromosomes of one cell
into pairs =
KARYOTYPE

How chromosomes look like? – update VI/2024



Barley (*Hordem vulgare*) mitotic metaphase chromosomes observed by A-ESEM, secondary electron detector. (a) Overview of a chromosome with protrusions covering its entire body, including centromeric region, top view. (b) Histogram of chromosome length distributions as determined using A-ESEM (95 measurements). (c) Detailed view of the protrusions on the terminal telomeric chromosome region, with the sizes of the protrusions indicated (yellow bars). (d) Histogram of the protrusion widths (183 measurements). (e) Close-up of a chromosome region showing ~ 12 nm features, which may represent nucleosome fibers. (f,g) The ~ 12 nm features form ~ 37 nm structures (yellow bars), whose molecular composition is not clear (see the text for more details).

Article | [Open access](#) | Published: 06 June 2024

Advanced environmental scanning electron microscopy reveals natural surface nano-morphology of condensed mitotic chromosomes in their native state

[Vilém Neděla](#) , [Eva Tihlaříková](#), [Petr Cápál](#) & [Jaroslav Doležel](#)

[Scientific Reports](#) 14, Article number: 12998 (2024) | [Cite this article](#)

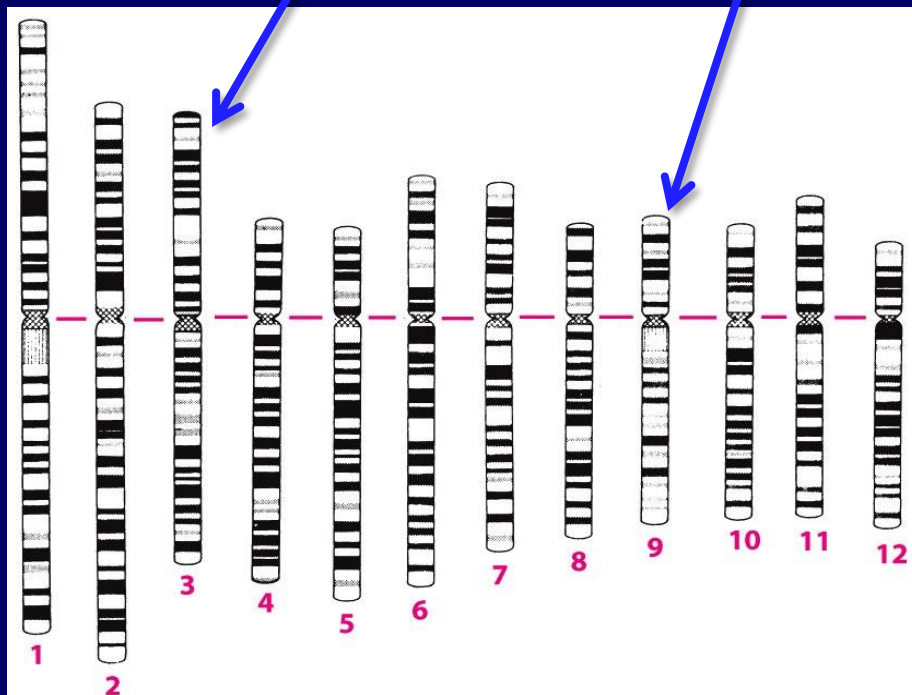
Human chromosome banding

Chromosomes are stained in early stage of mitosis (condensed)

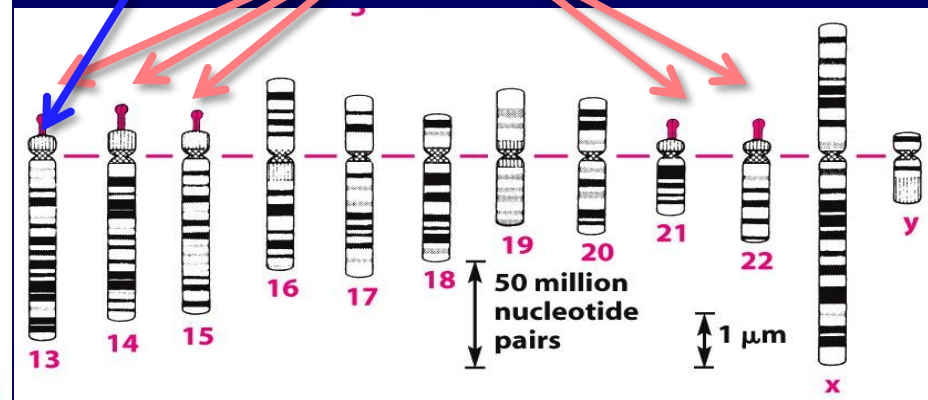
Based on the centromere position we distinguish: metacentric; submetacentric; acrocentric

Short arm = *p* (*petit*)

Long arm = *q* (*queue*)



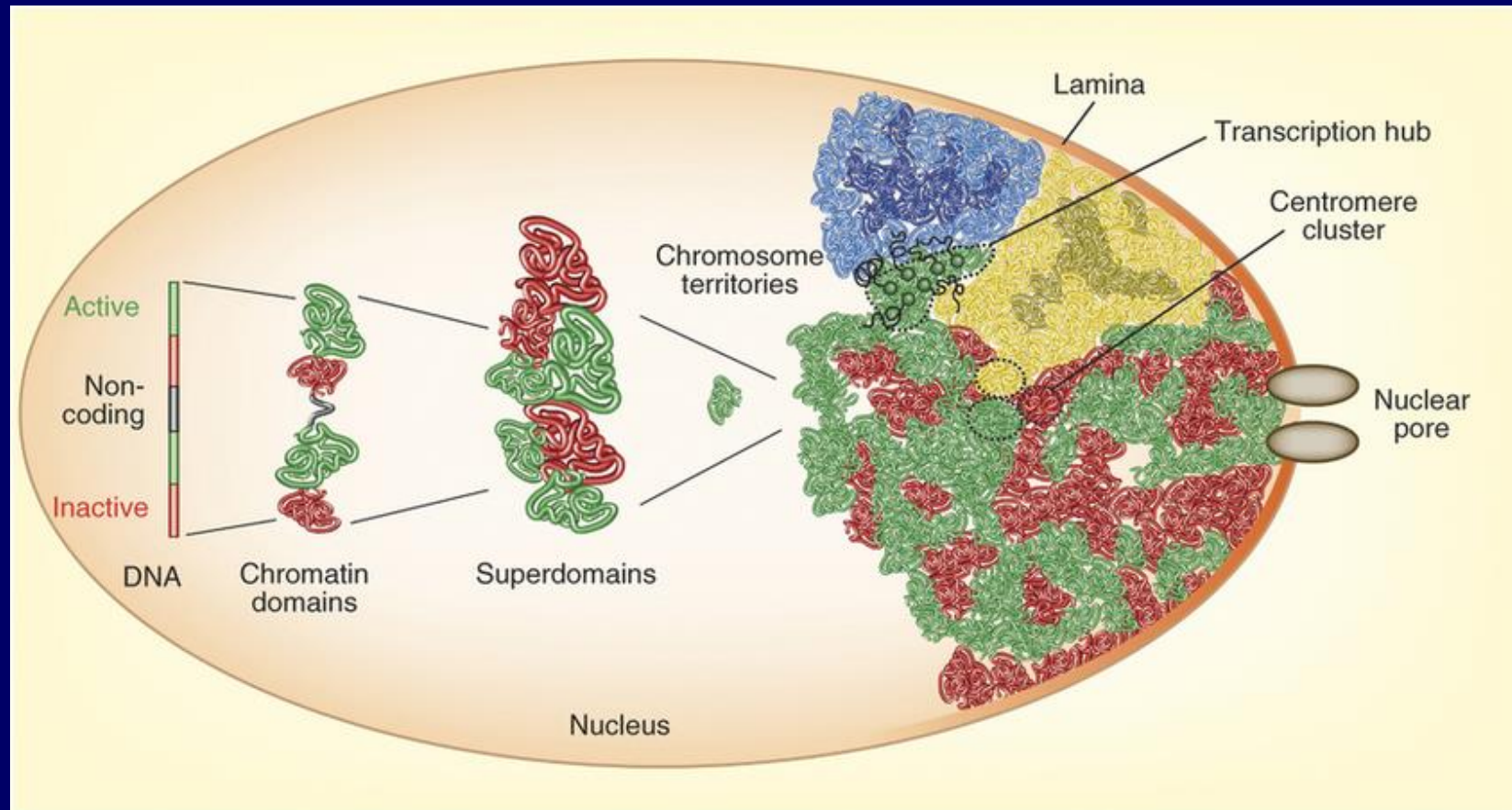
The protrusions contain genes for large ribosomal RNA (rRNA)



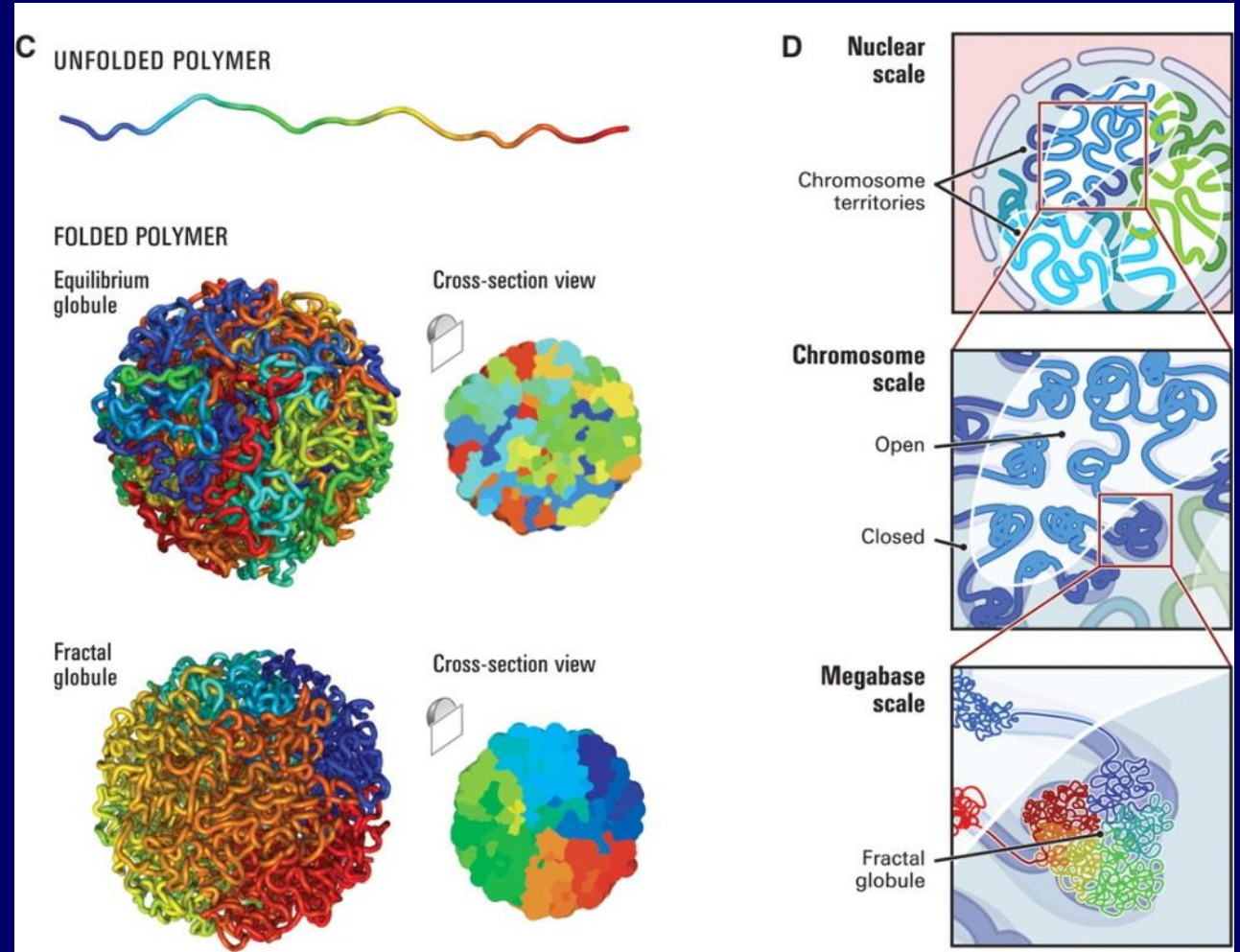
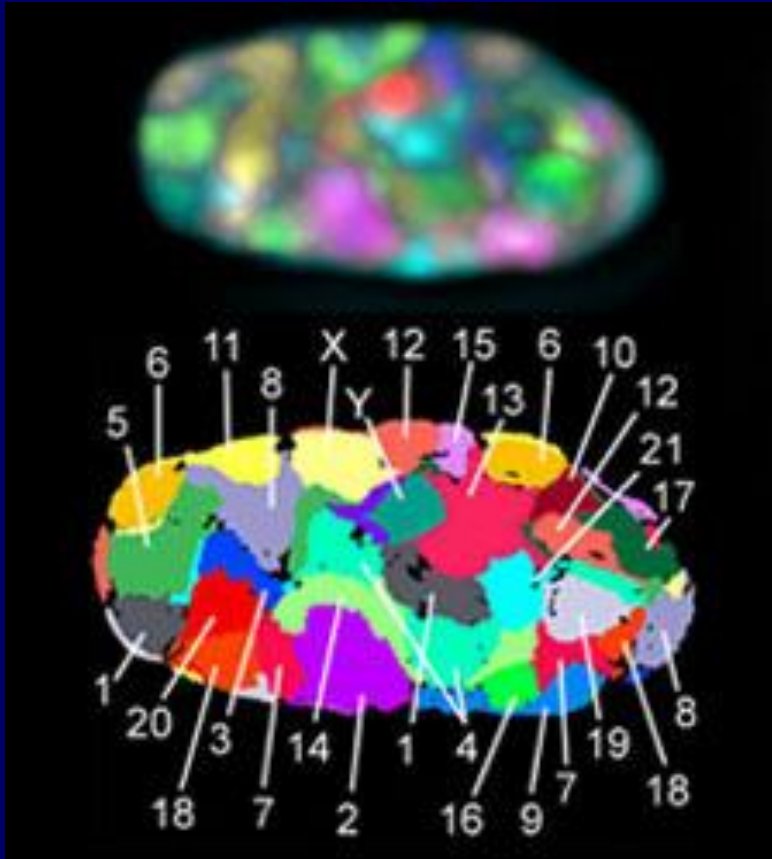
Giemsa staining . Dark bands = high content of A-T base pairs

Chromatin organisation in nucleus

- Location of chromosomes in the nucleus is not random
- Clustering of areas with the same function and activity



Chromatin organisation in nucleus – fractal globule



E. Lieberman-Aiden et al., *Science* 326, 289-293 (2009)

Cell cycle

A cell reproduces by carrying out an ordered sequence of reactions = **CELL CYCLE**

It is the basic mechanism by which all living things reproduce.

Each cell comes from only one other cell.

Cell doctrine R. Virchow 1858

The cell cycle includes the events that occur:

- ❖ doubling of cell mass
- ❖ cell genome replication
- ❖ own division of the mother cell into two daughter cells



**This is how genetic information is transferred
to the next generation of cells**

Cell division in multicellular organisms does not only occur during the formation of a new individual, but also during life, with different types of cells at different rates

They usually do not divide at all: nerve, muscular cells

Minimal rate of division: hepatocytes (1x per year)

They divide intensively: gut epithelial cells, blood stem cells (more than 1x a day), cells of hair folikul

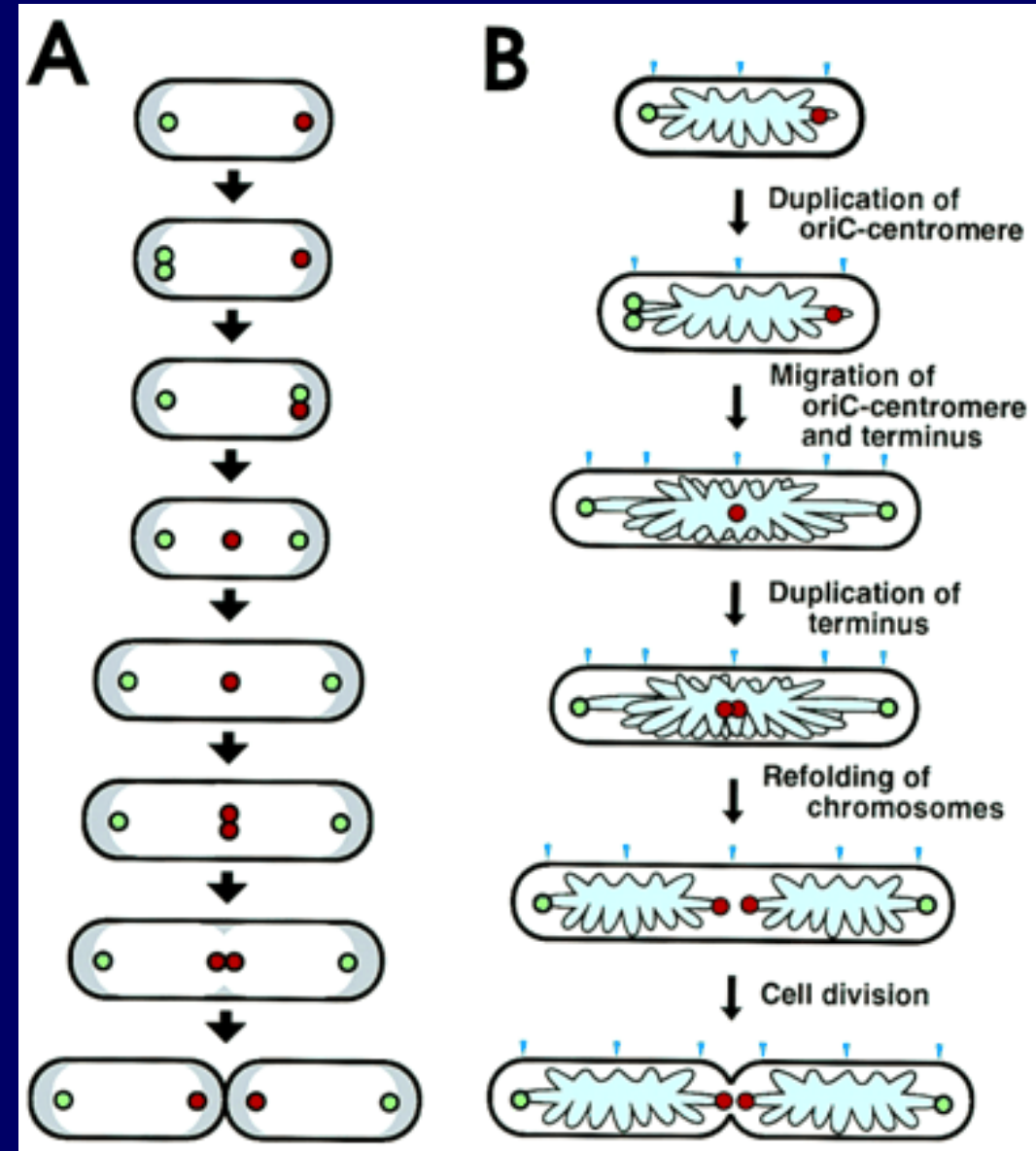
Each of us creates a million new cells every second, the stop dividing leads to death.

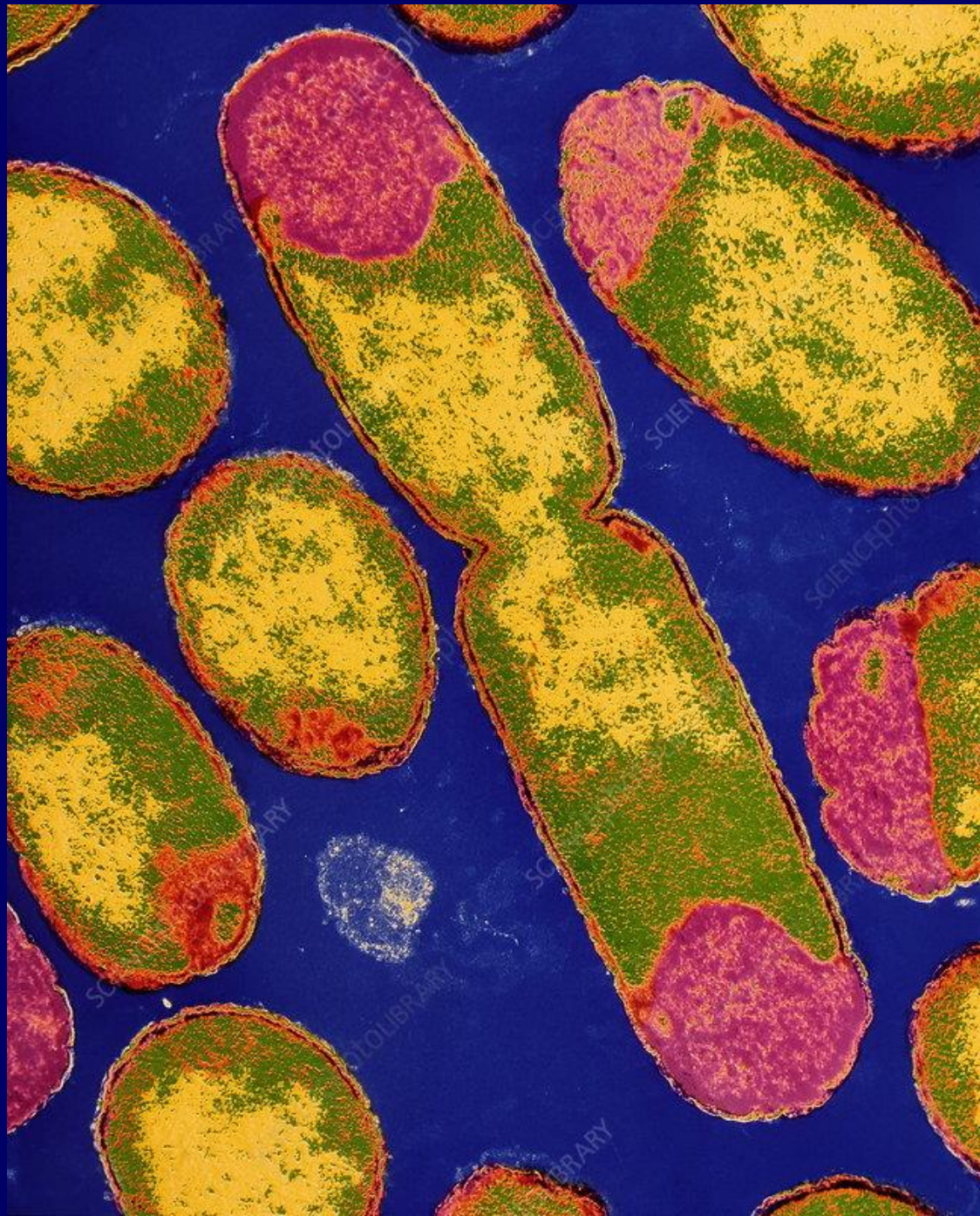
Bacterial cell division (*E. coli*)

It has a single circular chromosome that is attached to the plasma membrane and remains attached during chromosome replication.

Both chromosomes are separated by cell growth. The cell wall and the plasma membrane are inserted between the two chromosomes → two cells are formed.

= **BINAR DIVISION**



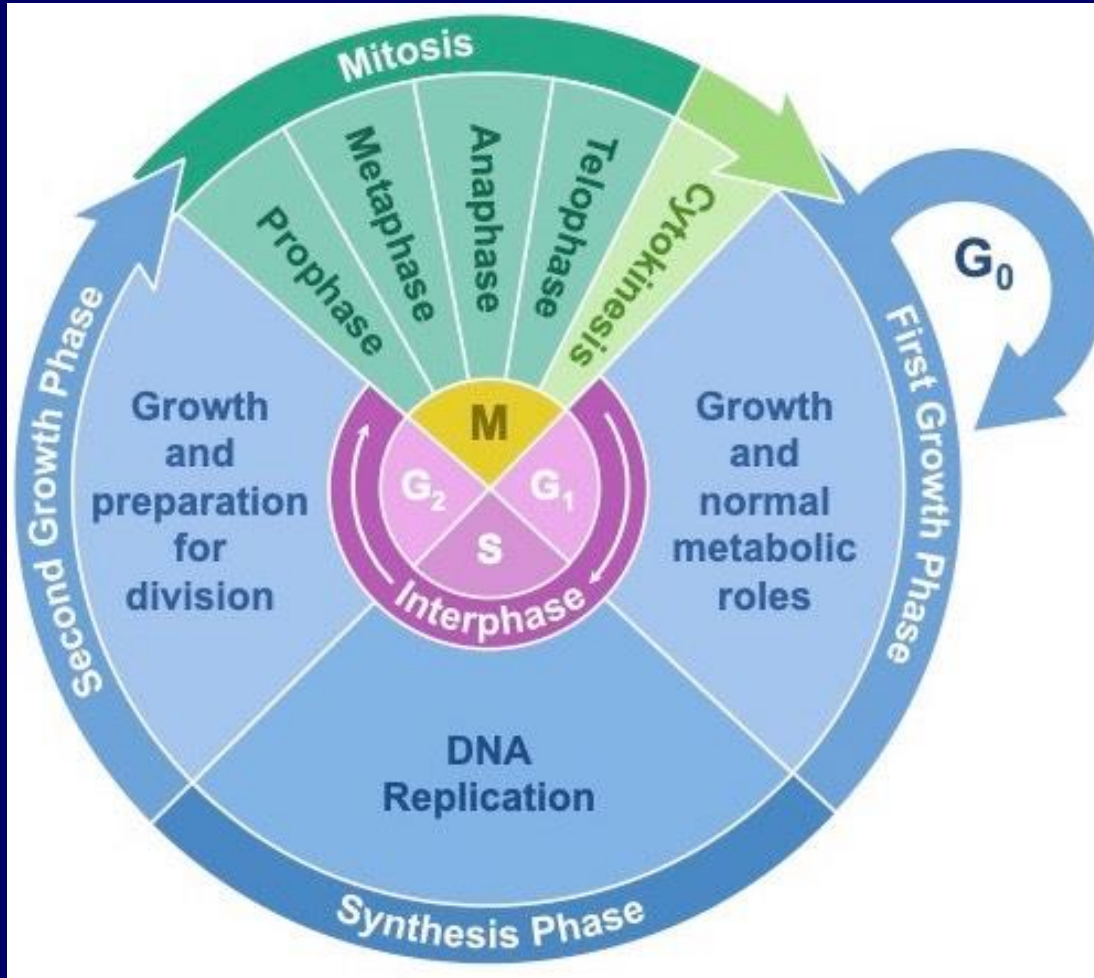


[https://www.sciencephoto.com/
media/12477/view/tem-of-
dividing-e-coli-bacterium](https://www.sciencephoto.com/media/12477/view/tem-of-dividing-e-coli-bacterium)

Cell cycle of eukaryotic cells

M-PHASE + INTERPHASE (G_1 , S, G_2)

<https://www.vce.bioninja.com.au/unit-one/area-of-study-1-cell-develo/cell-cycle.html>



STAGES OF THE CELL CYCLE

INTERPHASE:

- G_1 – Growth and metabolic roles
- S – Replication of DNA occurs
- G_2 – Growth and more preparation

MITOSIS:

- P – Chromosomes are condensed
- M – Chromosomes align at cell centre
- A – The duplicated DNA segregates
- T – Chromosomes are decondensed

CYTOKINESIS

Cell splits into two daughter cells

RESTING PHASE (G_0)

Cells may leave interphase and enter into a non-dividing quiescent phase

G_1 and G_2 phases

are the phases when the cell grows and the cytoplasmic organelles duplicate

Cell cycle of eukaryotic cells



INTERPHASE

G₁-phase (presyntetic)

duplication processes of ribosomes, ER, mitochondria, synthesis of enzymes, nucleotides take place

S-phase (syntetic)

- ❖ nuclear DNA replication
- ❖ histone synthesis

G₂-phase (postsyntetic)

- ❖ proteins, RNA synthesis

❖ **G₀-phase** (quiescent)

- ❖ only basal metabolism maintained
- ❖ It occurs only in some types of cells, especially those that are already terminally differentiated (neurons, erythrocytes)

The length of the cell cycle varies

Cell type	Length of cell cycle
Cells of an early frog embryo	30 min
Yeast cells	1,5 – 3 h
Intestinal epithelial cells	12 h
Mammalian fibroblasts in culture	20 h
Human hepatocyte	1 year

Control of cell division and cell growth

Cell division and growth is regulated by extracellular signaling molecules (usually peptides), which mediate their effect through specific receptors.

These proteins can be divided into three main classes:

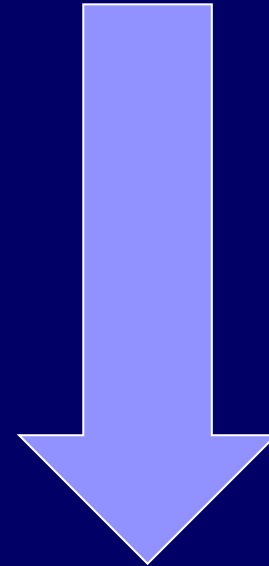
- ❖ **Mitogens**
- ❖ **Growth factors**
- ❖ **Survival factors**

❖ **Mitogens** – stimulate cell division by triggering G1/S-Cdk activity, which "unlocks" intracellular negative control mechanisms that block cell division without these mitogens.

❖ **Growth factors** – they stimulate cell growth (increase the cell mass) by promoting the synthesis of proteins and other macromolecules and inhibiting their degradation.

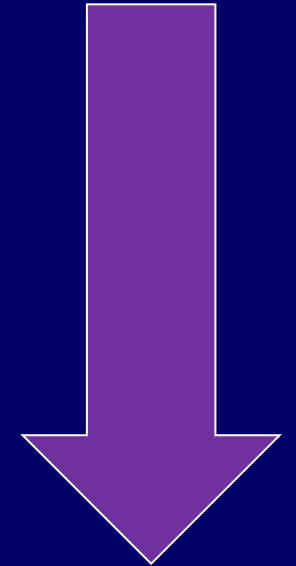
❖ **Survival factors** – they help the cell to survive by suppressing events leading to apoptosis.

**Presence of
mitogens and
growth factors**



**ENTRANCE TO
G₁ PHASE**

**Presence only of
growth factors**



**ENTRANCE TO G₀
PHASE**

The cell cycle must be well regulated and coordinated in a multicellular organism → ensuring continuity and sequence of individual steps and processes

- ❖ activate and inactivate the relevant enzymes
- ❖ enable cell cycle regulation through chemical signals (signal molecules)
- ❖ use of so-called **molecular brakes** (Rb-protein, p53, p21) to stop the cell cycle at so-called **checkpoints**

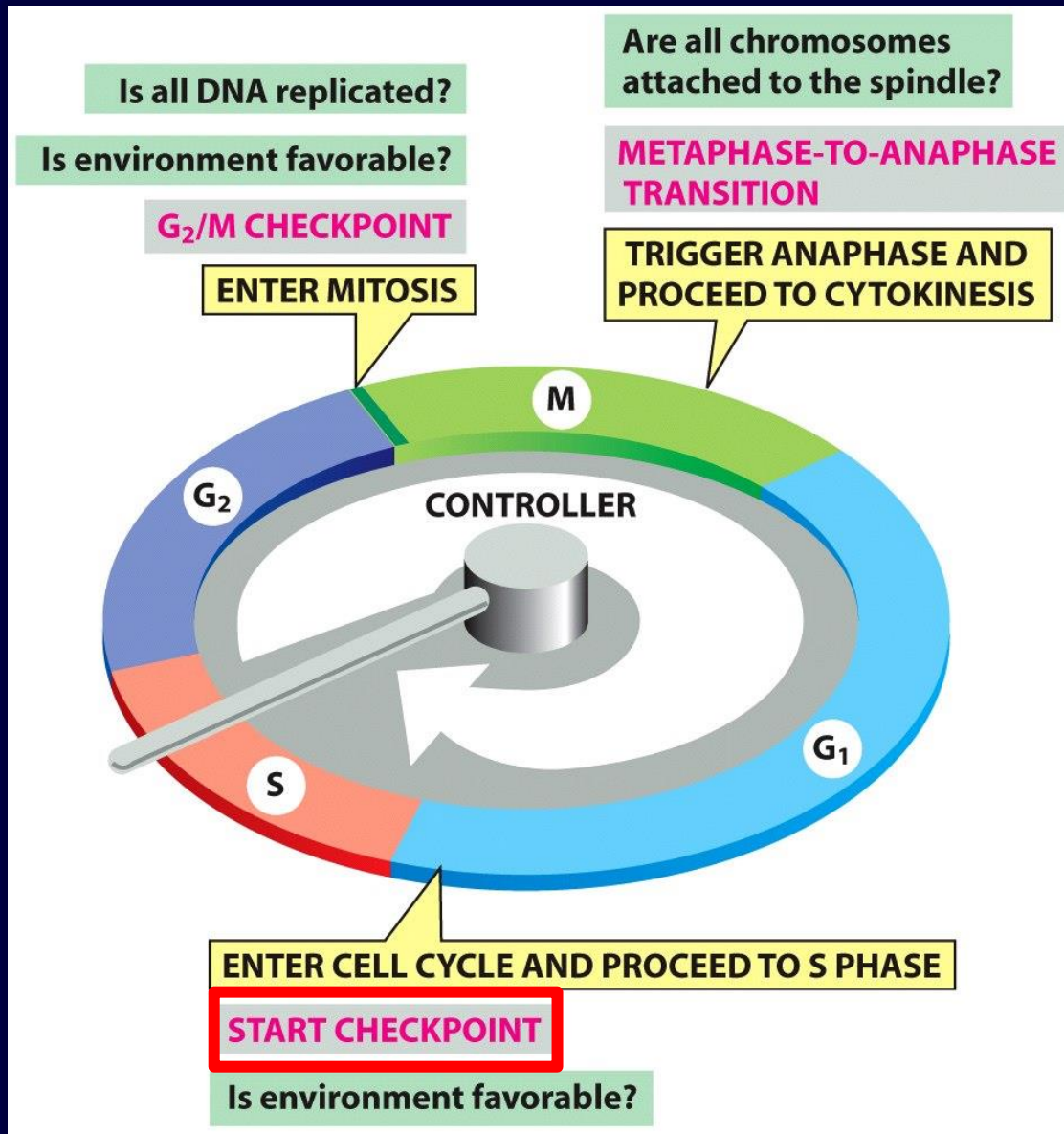
Animal cells have an intrinsically limited number of cell divisions they can go through

This phenomenon is called cellular senescence, and the length varies from cell type to cell type. Even though the relevant factors are present, the cell stops responding to them.

The gradual shortening of telomeres (small structures at the end of chromosomes) with each cell division is considered the most important cause of cell aging. A cell is unable to replicate telomeres without the enzyme telomerase.

Some cells do not have this enzyme at all, or its activity may change due to age.

Checkpoints of cell cycle

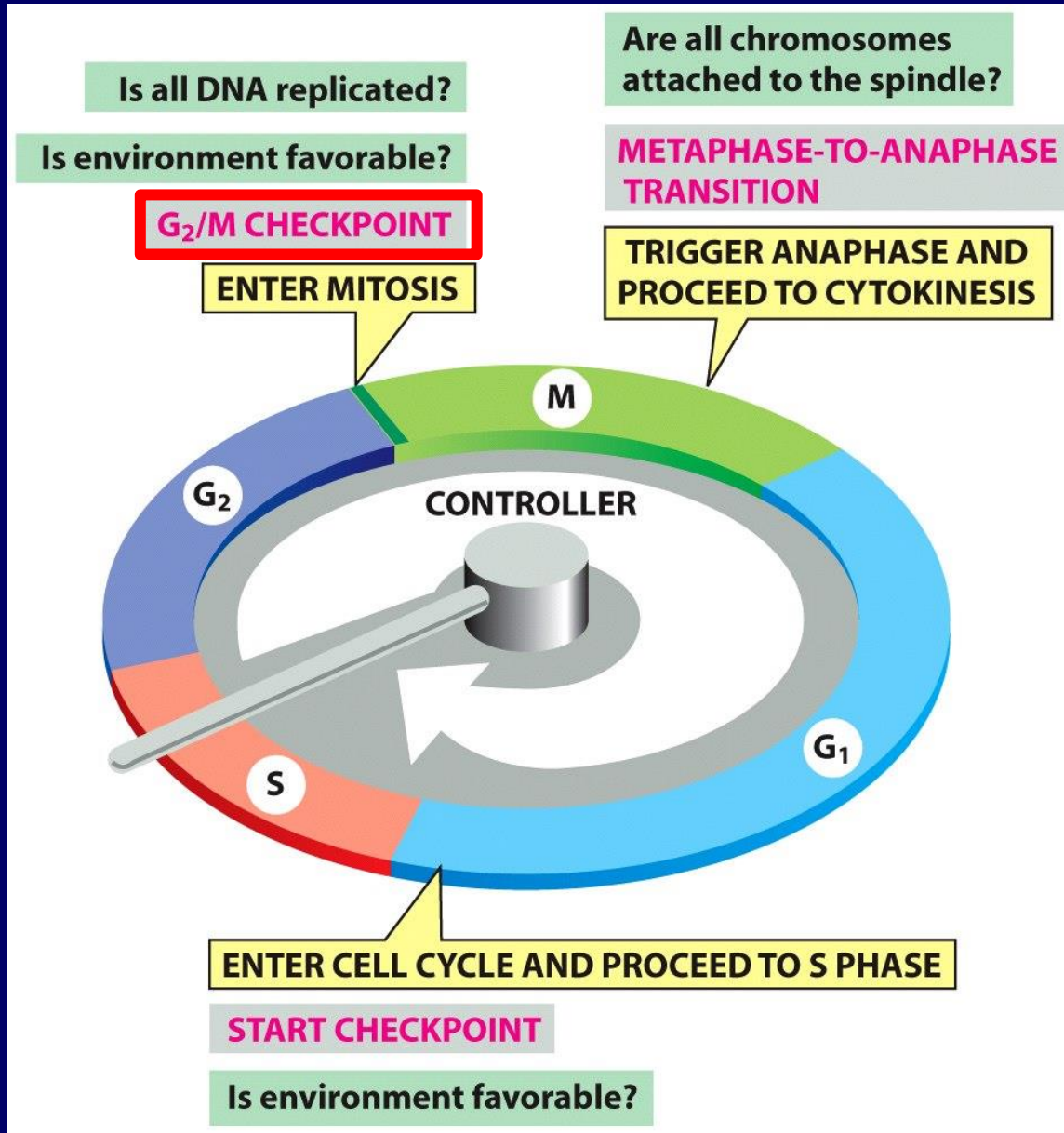


Cell cycle control is ensured by **three checkpoints**:

- 1) before entering S-phase
= initiation of DNA replication
→ **DNA REPLICATION**

Is the environment hospitable?
Is the cell big enough?
Isn't the DNA damaged?

Checkpoints of cell cycle



Cell cycle control is ensured by **three checkpoints**:

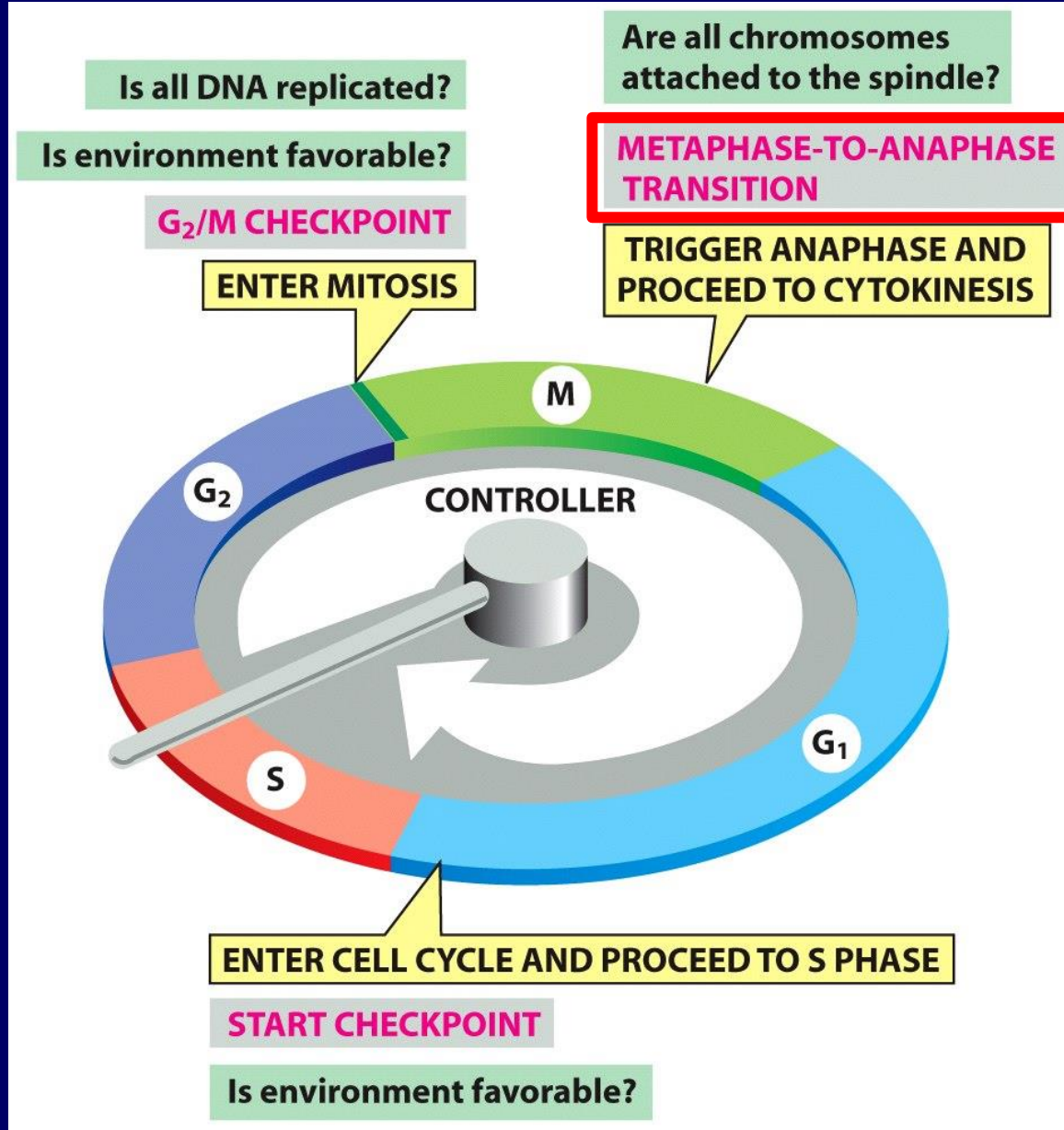
2) before entering M-phase

= mitosis initiation →

FORMATION OF THE MITOTIC SPINDLE

Is the environment hospitable?
Is all DNA replicated?

Checkpoints of cell cycle



Cell cycle control is ensured by **three checkpoints**:

3) At the interface of metaphase / anaphase = anaphase initiation → completion of **DIVISION** of the nucleus and subsequently the cell

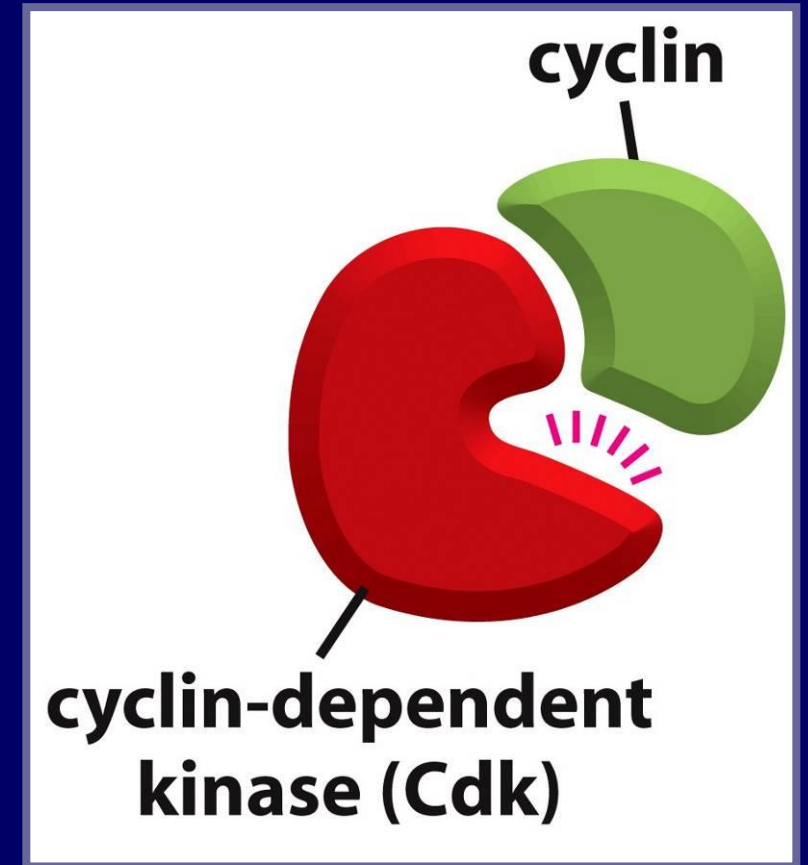
Are all chromosomes attached to the spindle?

Cell cycle control

It is done by **activating and deactivating** the respective **CYCLIN-DEPENDENT KINASES**.

They are activated by regulatory proteins „**CYCLINES**“

These activated kinases then catalyze the phosphorylation of the respective proteins and control the passage of the cell through the phases of the cycle.

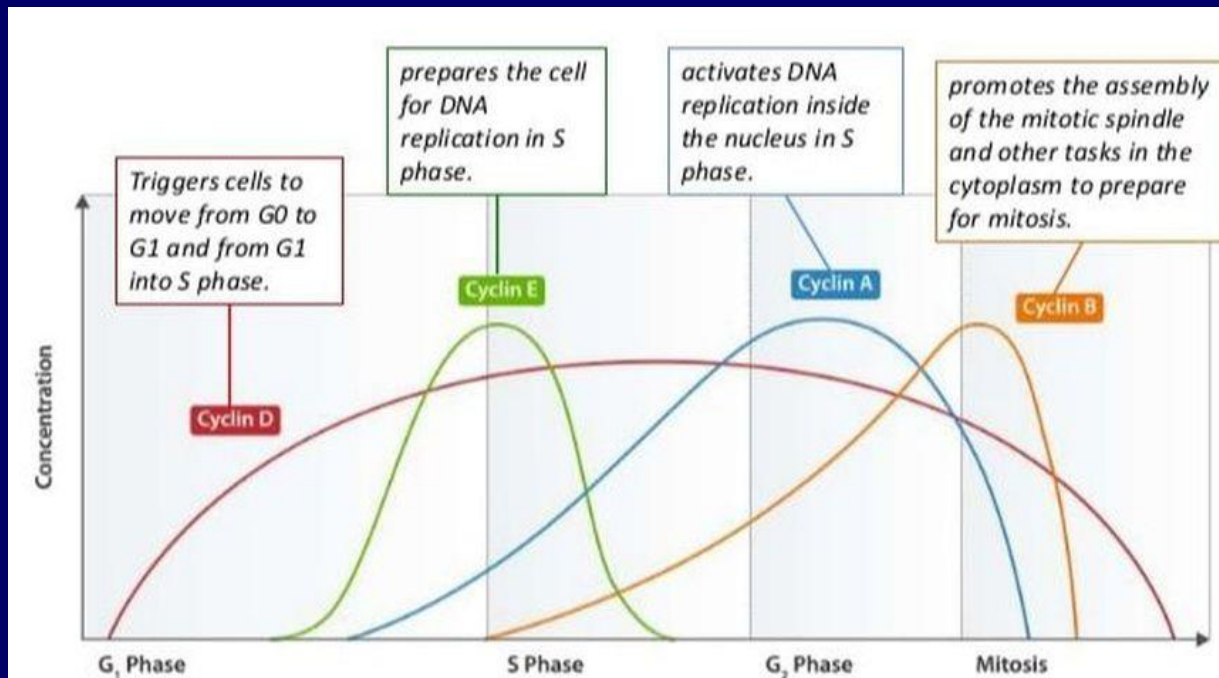


After cyclins form a complex with Cdk, **the kinase is activated and able to initiate the appropriate part of the cell cycle.**

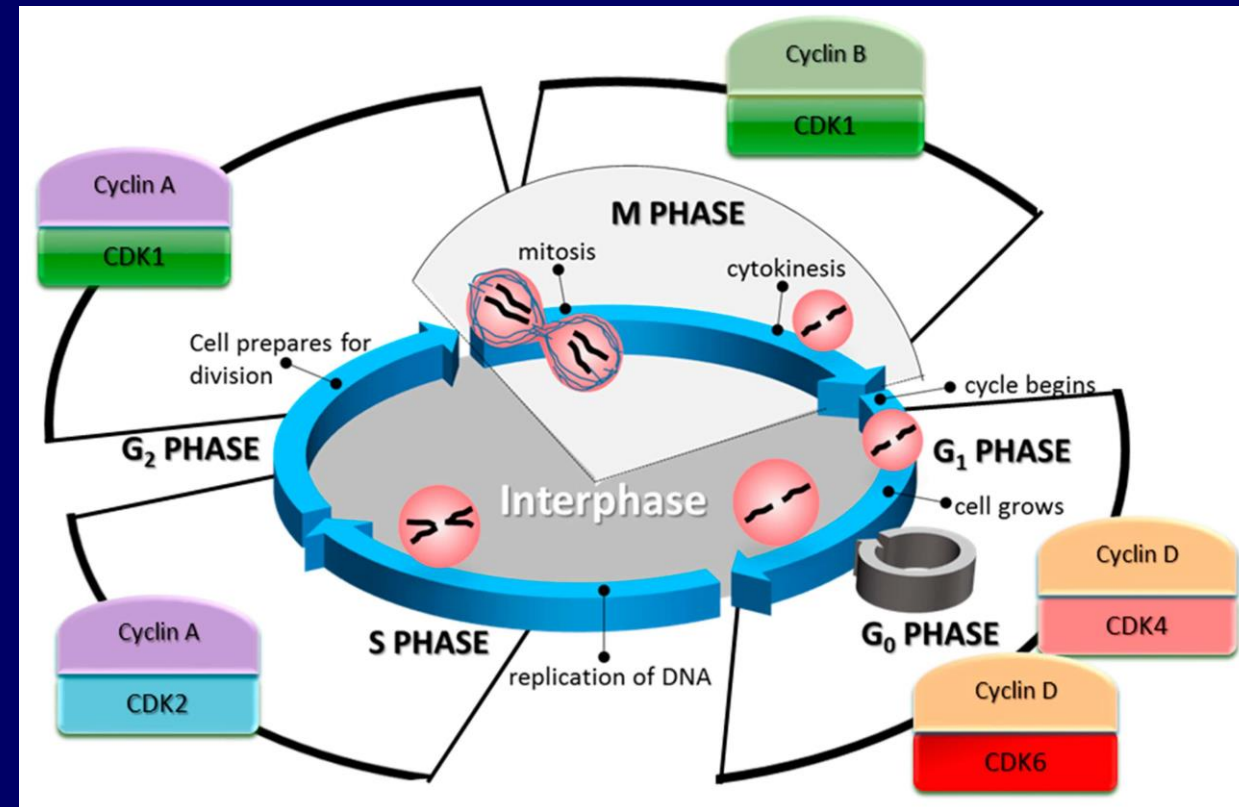
Without cyclins, Cdk is inactive.

Cell cycle control

- Entry into the individual phases of the cell cycle is determined by the concentration of cyclins and the activity of CdK

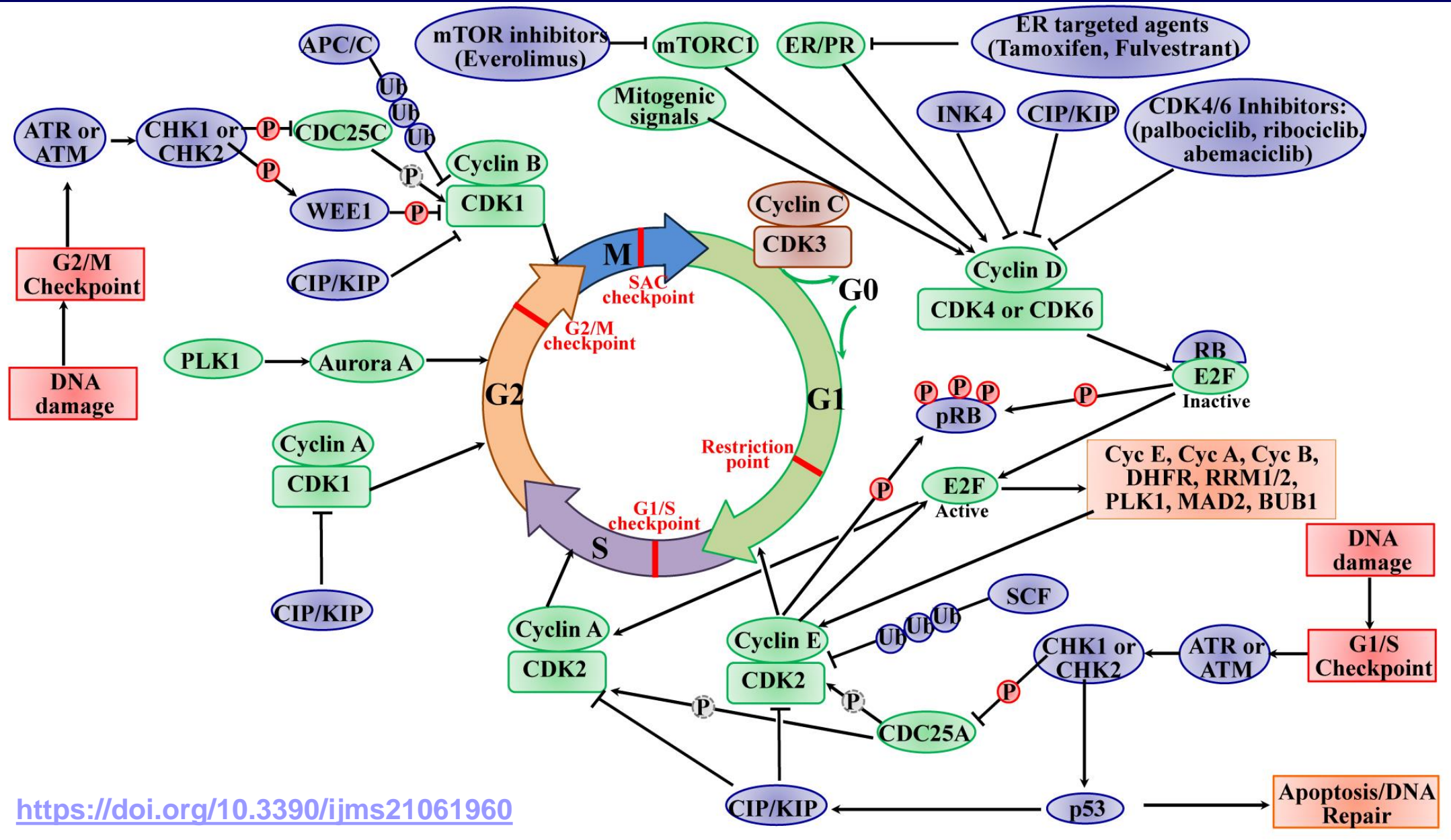


<https://mysciencesquad.weebly.com/ib-hl-16u5.html>

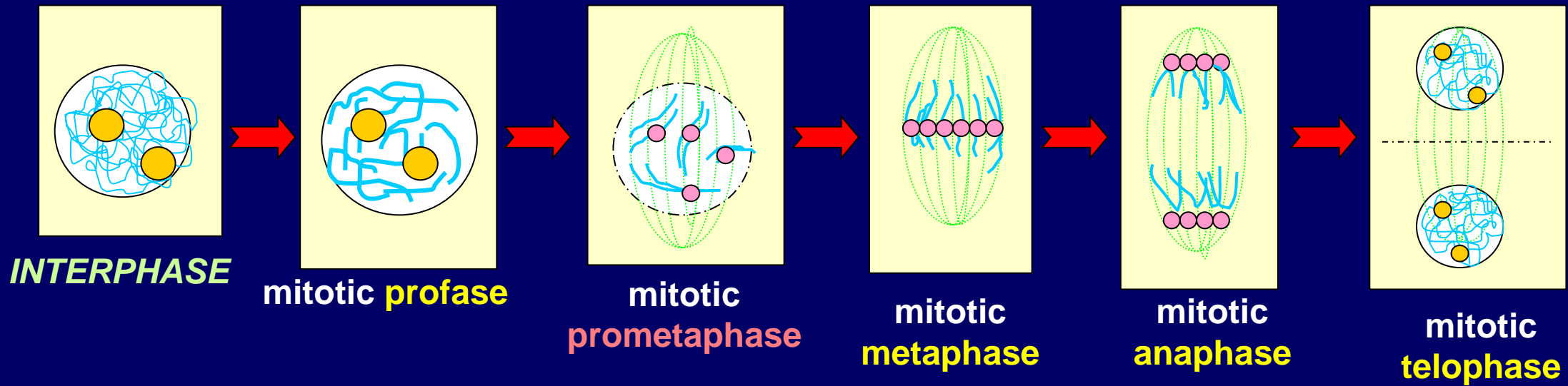
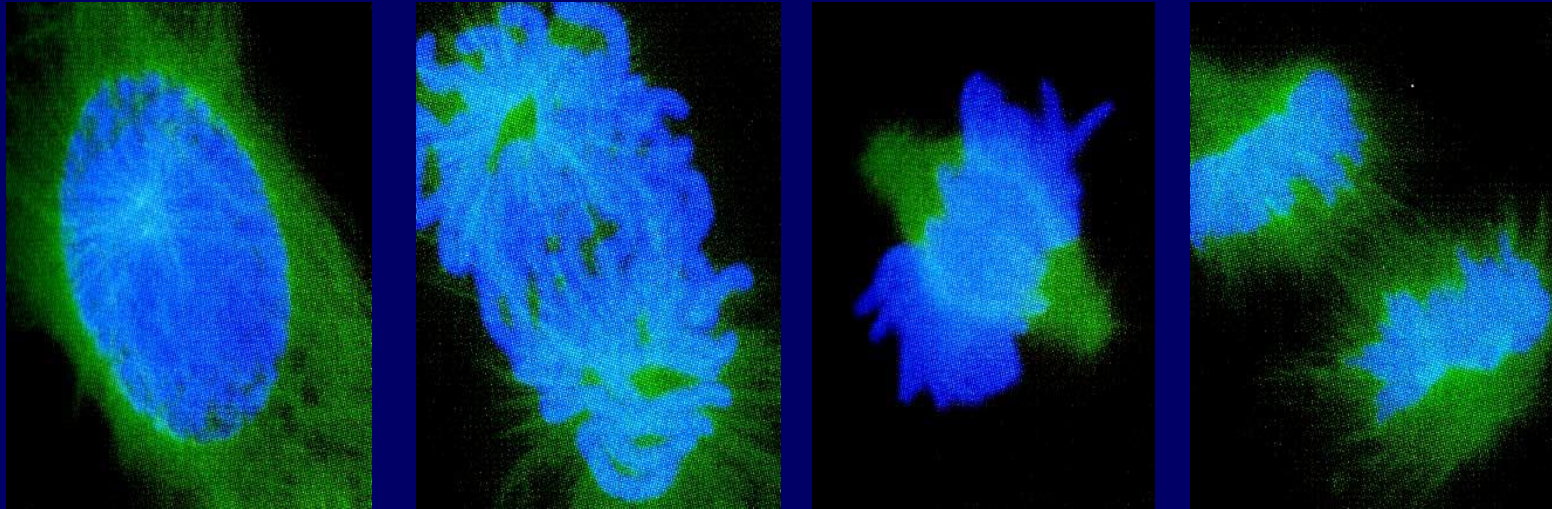


<https://facts.net/science/biology/15-astounding-facts-about-cyclin-dependent-kinases-cdks/>

Cell cycle control

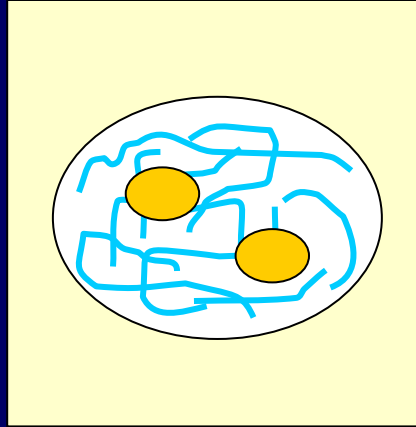


MITOSIS – individual phases



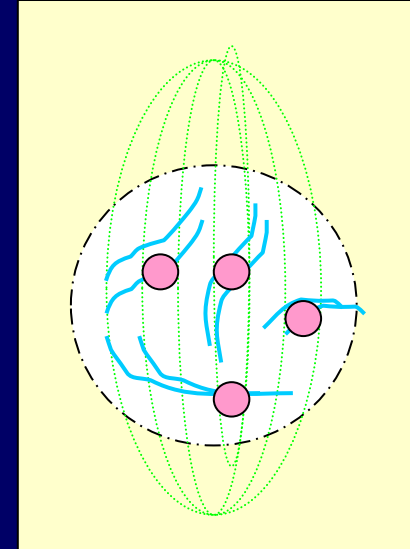
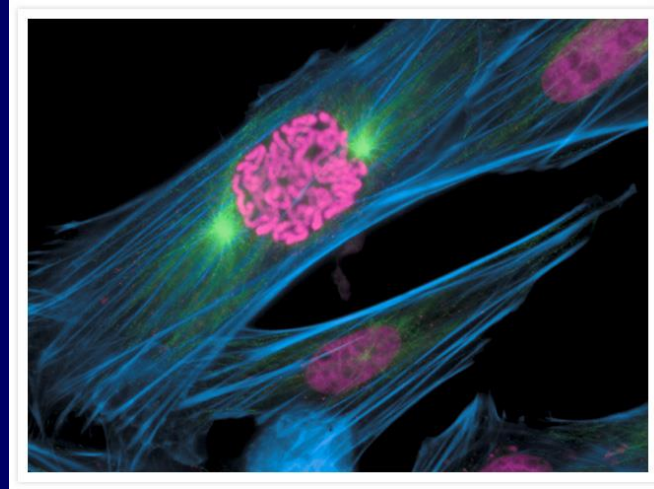
Briefly about the individual phases of mitosis

Prophase



early mitotic
prophase

Condensation of
chromosomes occurs

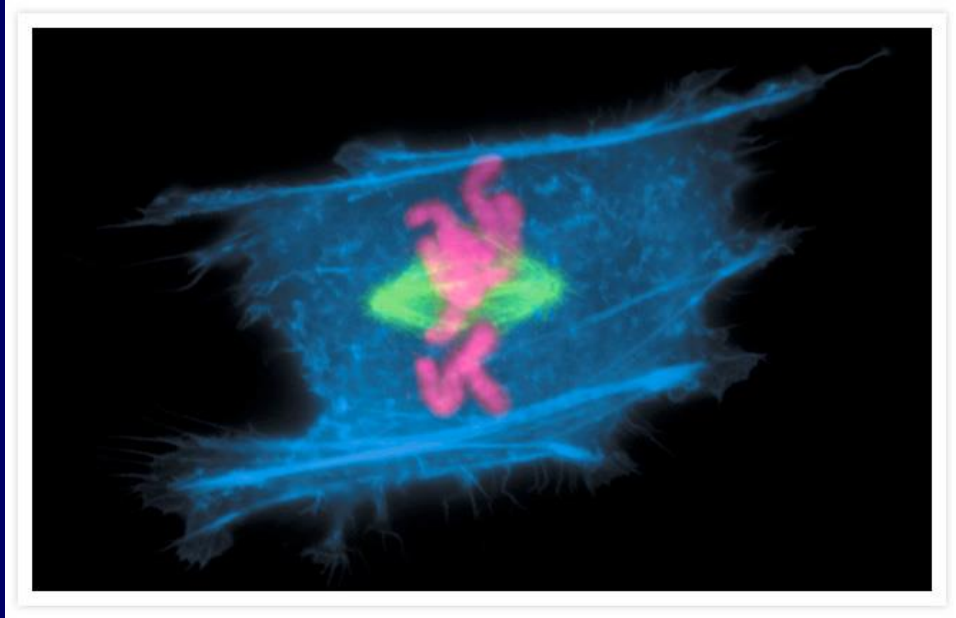
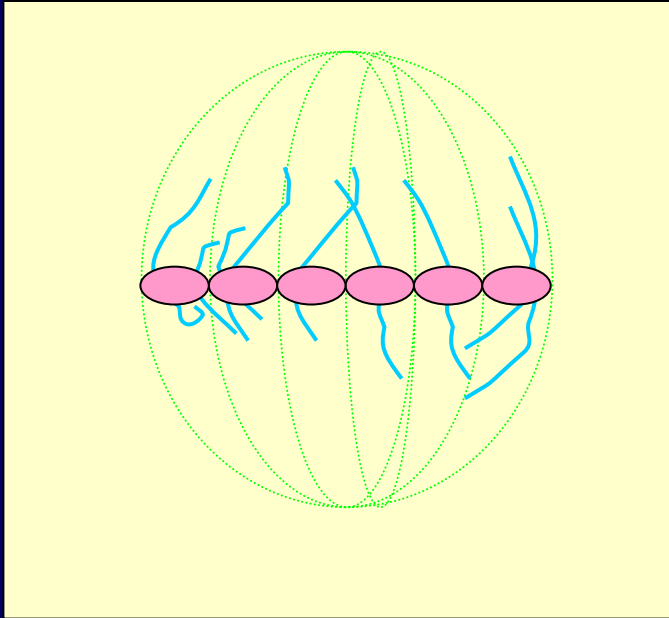


late mitotic **prophase**
(**prometaphase**)

A mitotic spindle begins to
form outside the nucleus

Briefly about the individual phases of mitosis

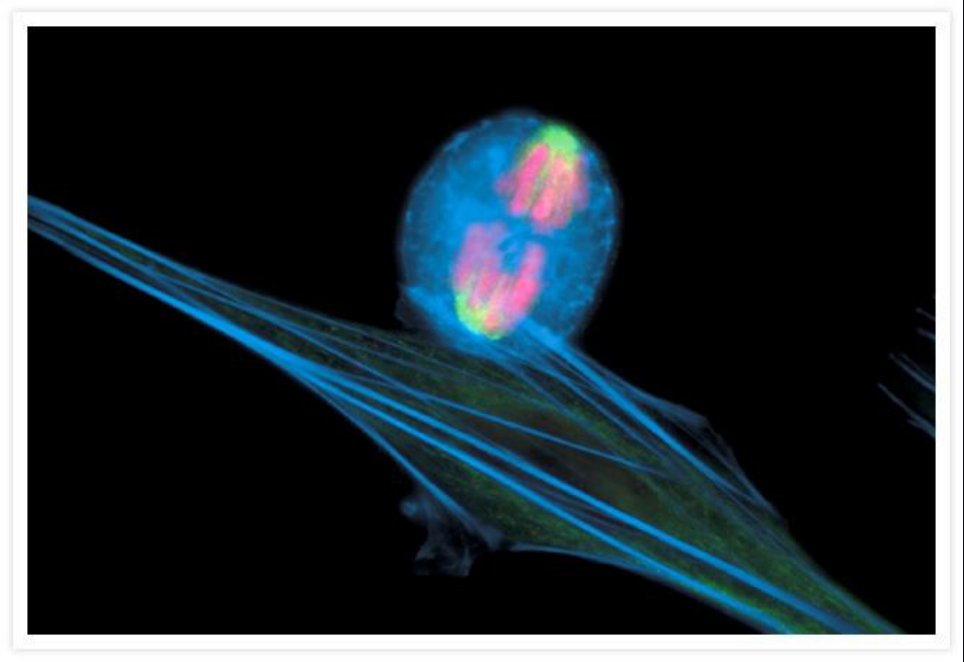
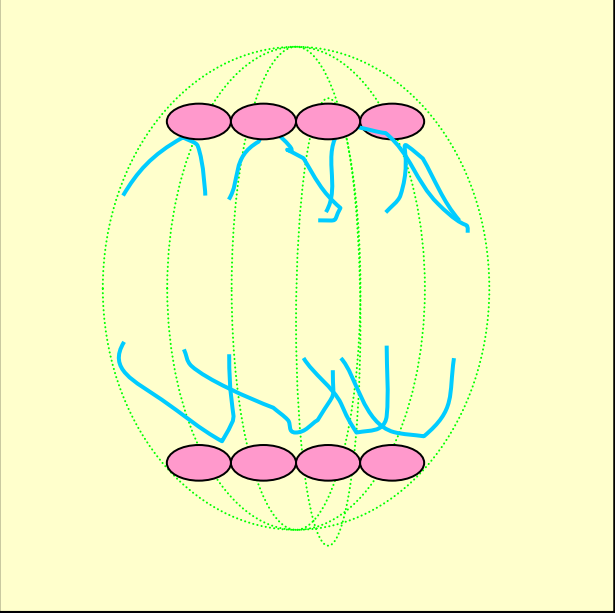
Metaphase



Chromosomes group together in the equatorial plane and thus form the metaphase plate.

Briefly about the individual phases of mitosis

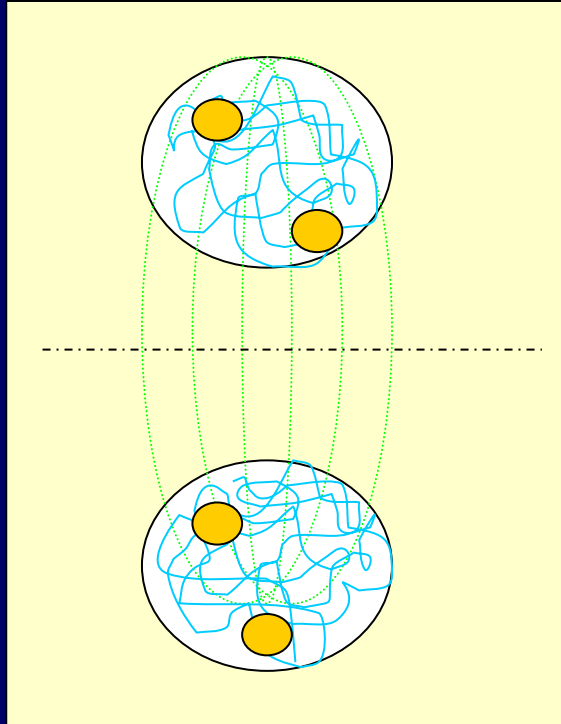
Anaphase



Sister chromatids are separated

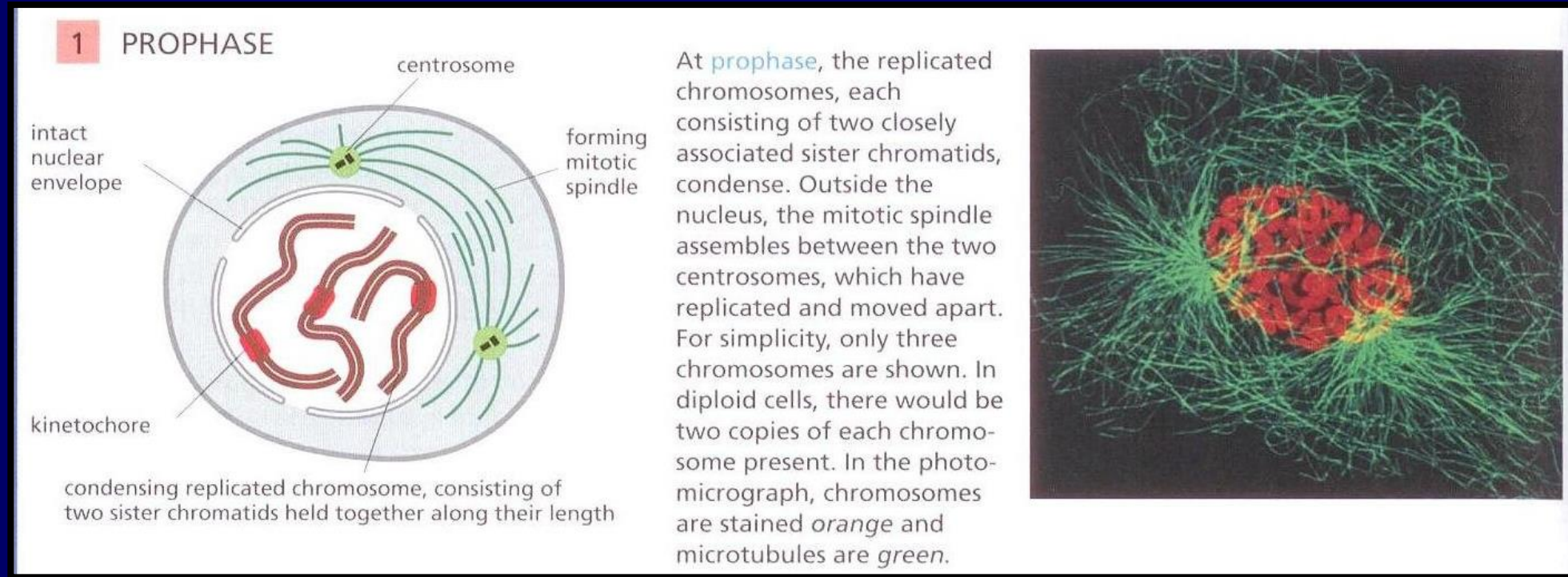
Briefly about the individual phases of mitosis

Telophase



A new nuclear envelope forms around each set of chromosomes and two daughter nuclei are formed

Prophase

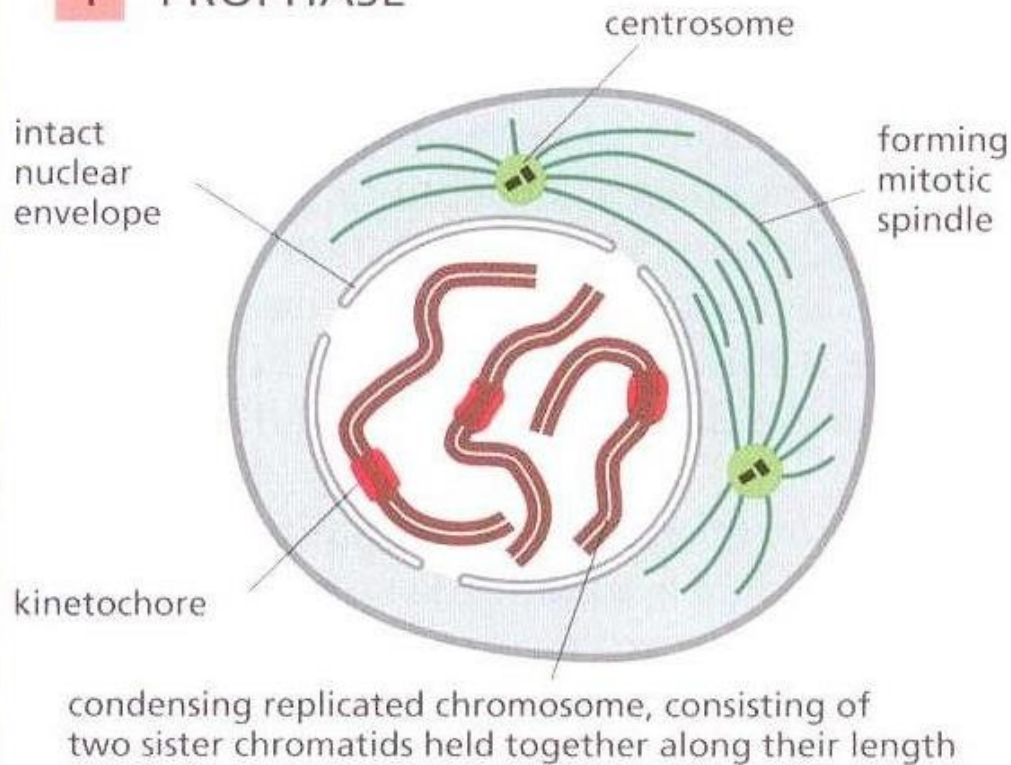


1. At the end of S-phase, DNA replication is finished, the centrosome is also duplicated (first they are together at one pole)
2. Condensation and spiralization of chromosomes (50,000x shortening). Sister chromatids are joined together along their entire length.

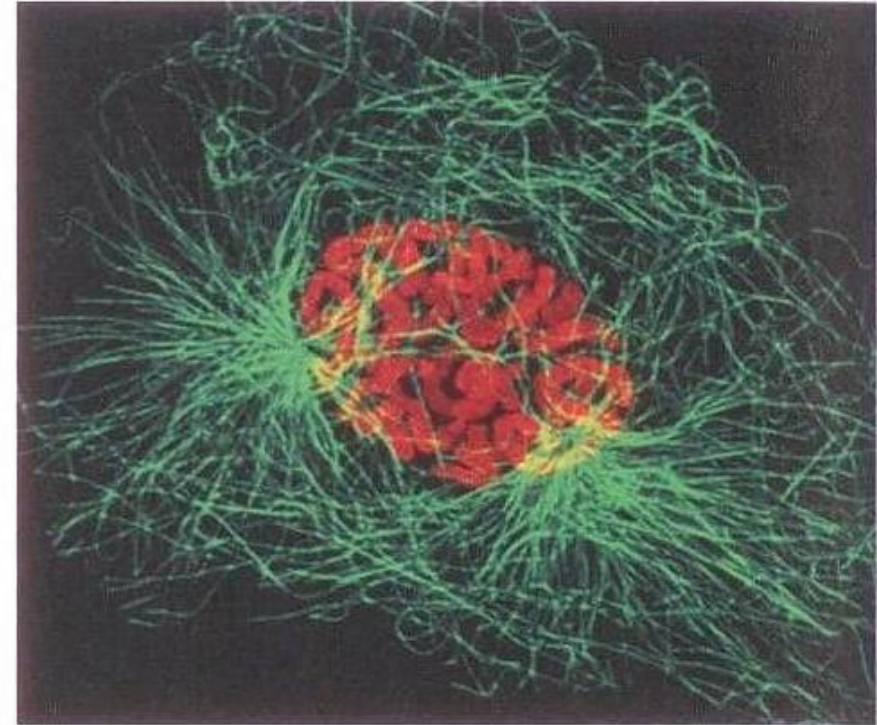
Participation of the structure of the cytoskeleton: centrosome, microtubules, kinetochore and **molecular motors: kinesin, dynein**

Prophase

1 PROPHASE

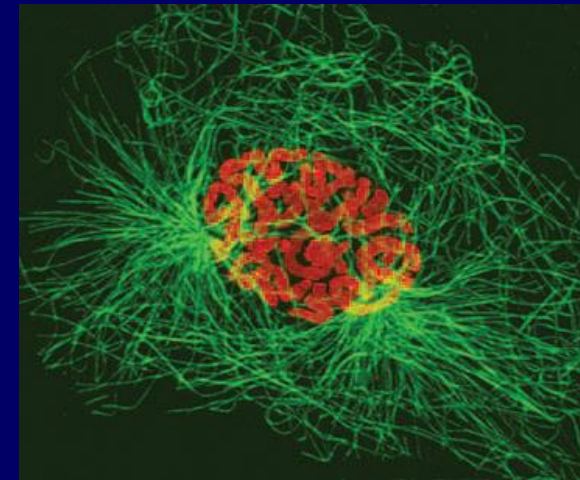
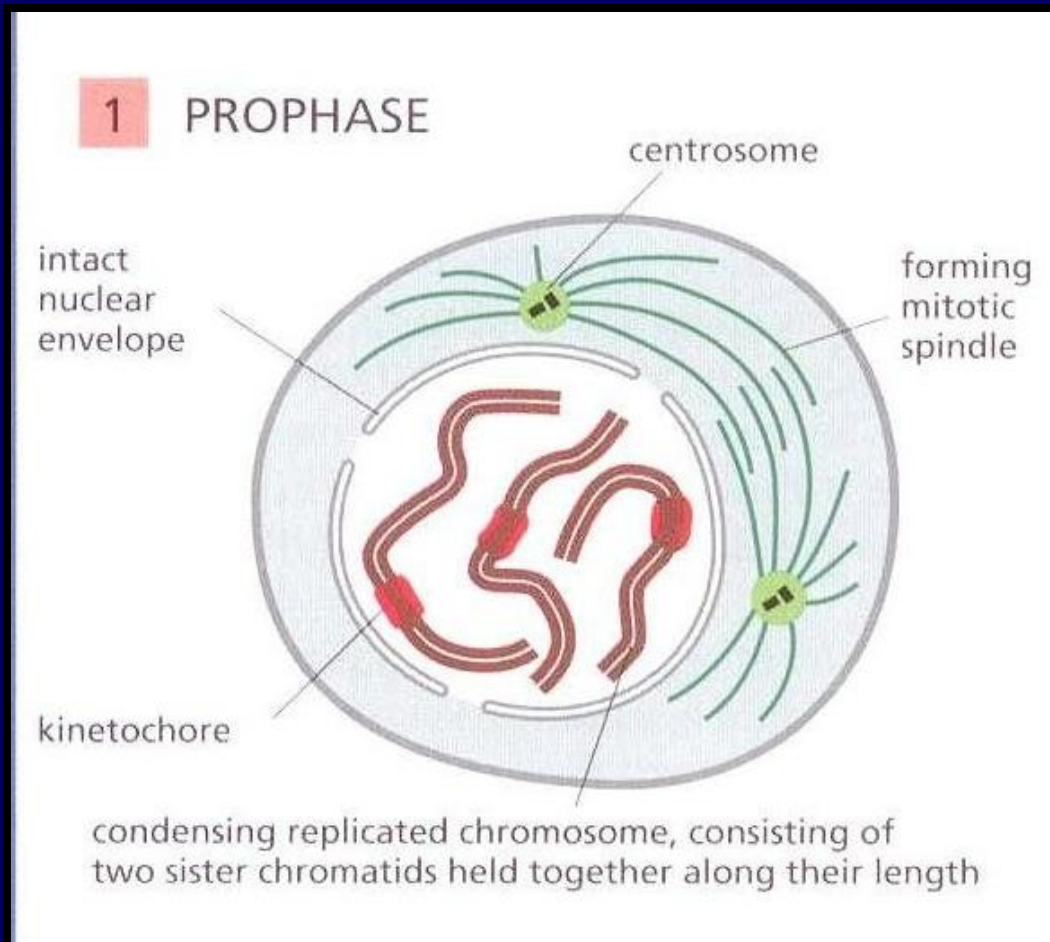


At **prophase**, the replicated chromosomes, each consisting of two closely associated sister chromatids, condense. Outside the nucleus, the mitotic spindle assembles between the two centrosomes, which have replicated and moved apart. For simplicity, only three chromosomes are shown. In diploid cells,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



- Both centrosomes begin to move to opposite poles of the nucleus – the movement occurs along microtubules and is controlled by molecular motors. ATP is consumed in the process.

Prophase

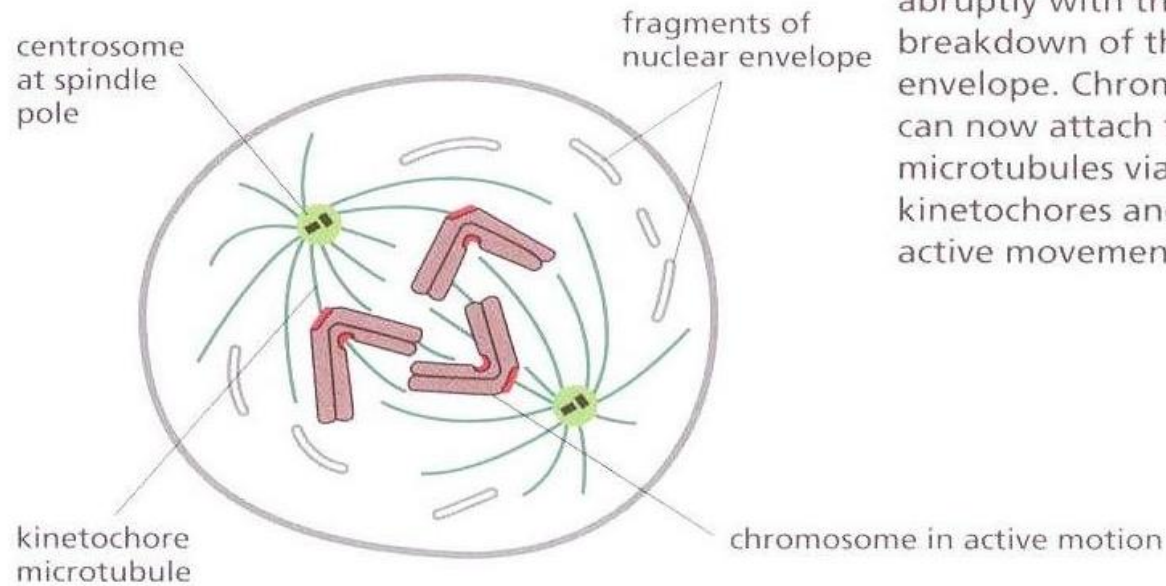


4. A bundle of microtubules is organized around each centrosome (at each pole). These interact to form the mitotic spindle.

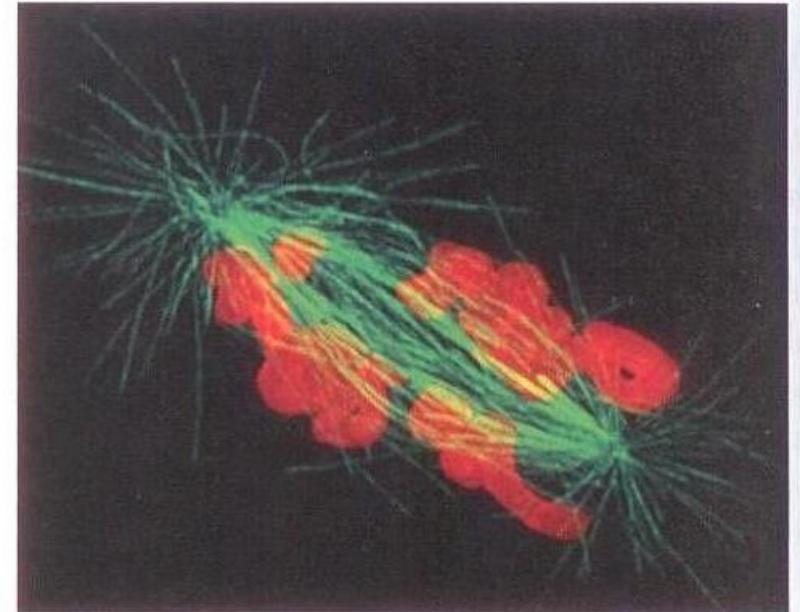
Kinetochore = the protein structure through which the chromosomes are attached to the mito. spindle – is completed in prometaphase

Prometaphase (late prophase)

2 PROMETAPHASE



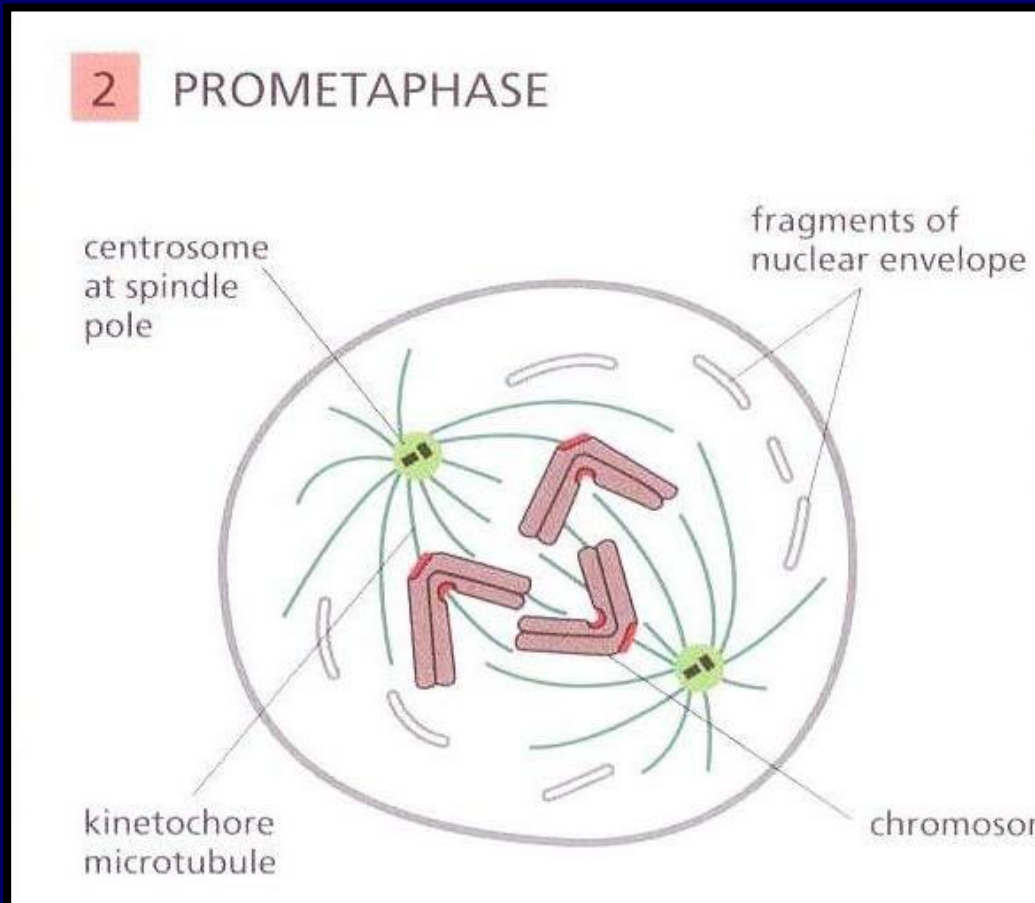
Prometaphase starts abruptly with the breakdown of the nuclear envelope. Chromosomes can now attach to spindle microtubules via their kinetochores and undergo active movement.



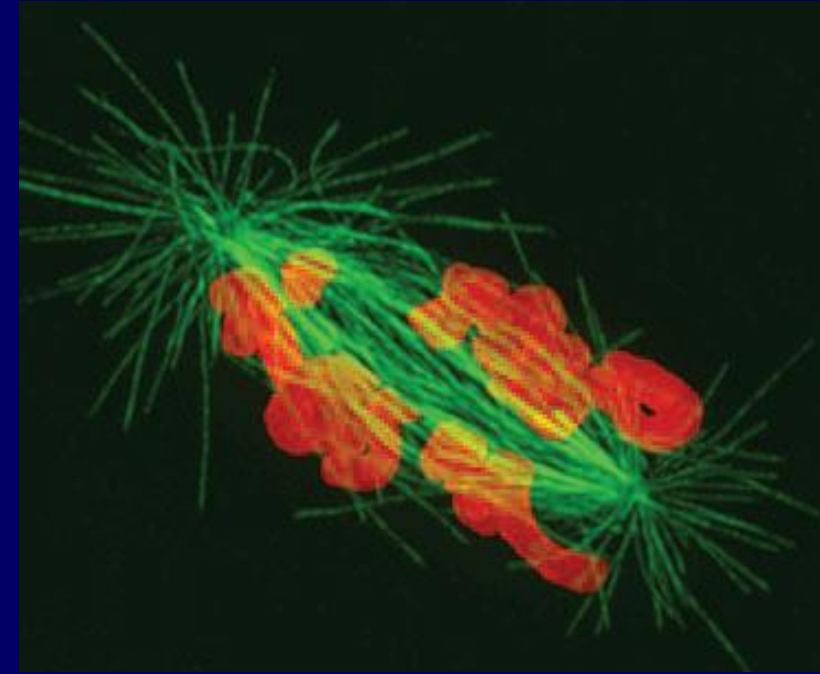
1. Breakdown of the nuclear envelope into membrane vesicles.

It begins with the **phosphorylation of nuclear lamins** (= protein subunits of intermediate filaments) and the subsequent disintegration of the nuclear lamins. Nuclear lamins are located under the nuclear envelope (stabilize it). This brings the spindle microtubules into contact with the chromosomes.

Prometaphase

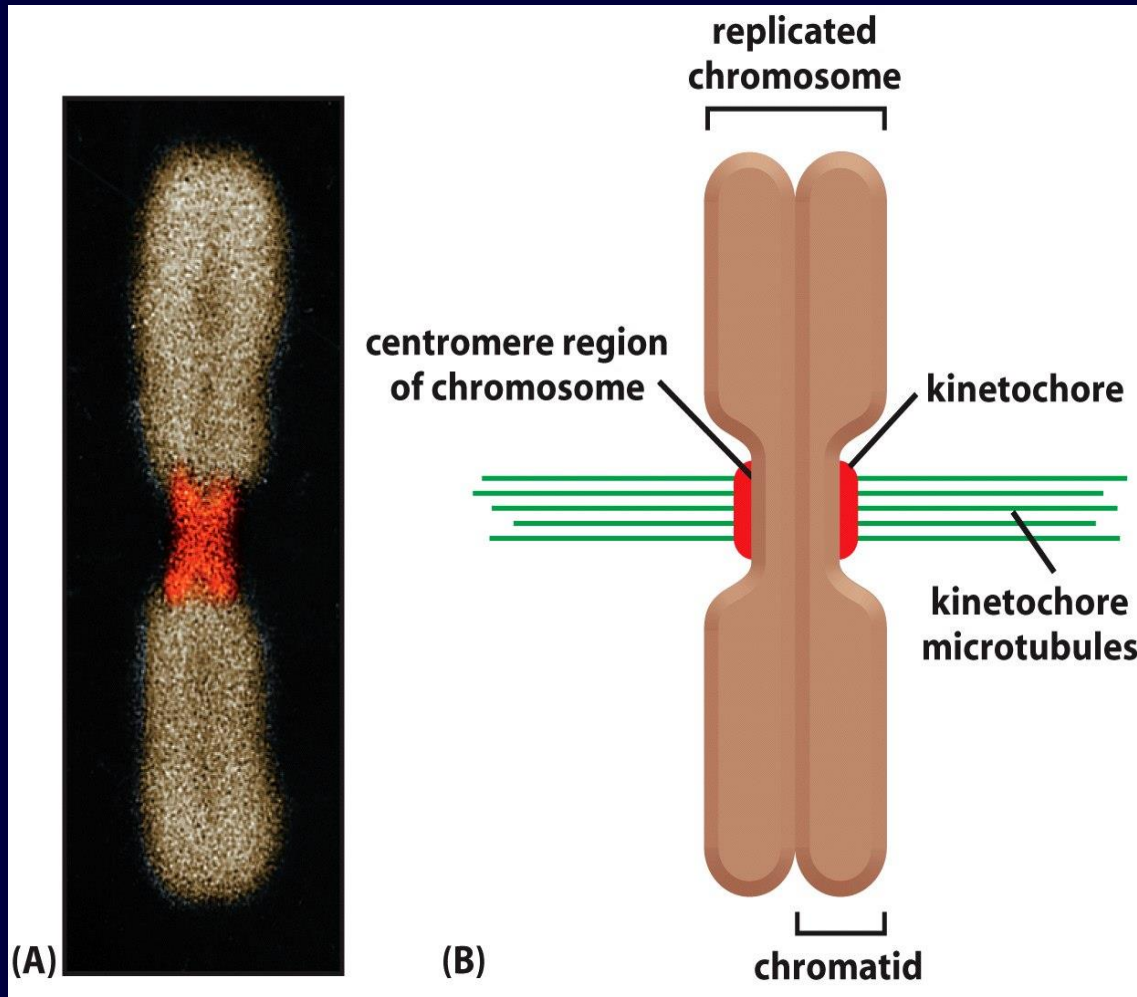


Kinetochores form on chromosomes during late prophase.



2. Chromosomes attach to the microtubules of the mitotic spindle

Microtubules attach to chromosomes via special protein complexes called **kinetochores**.



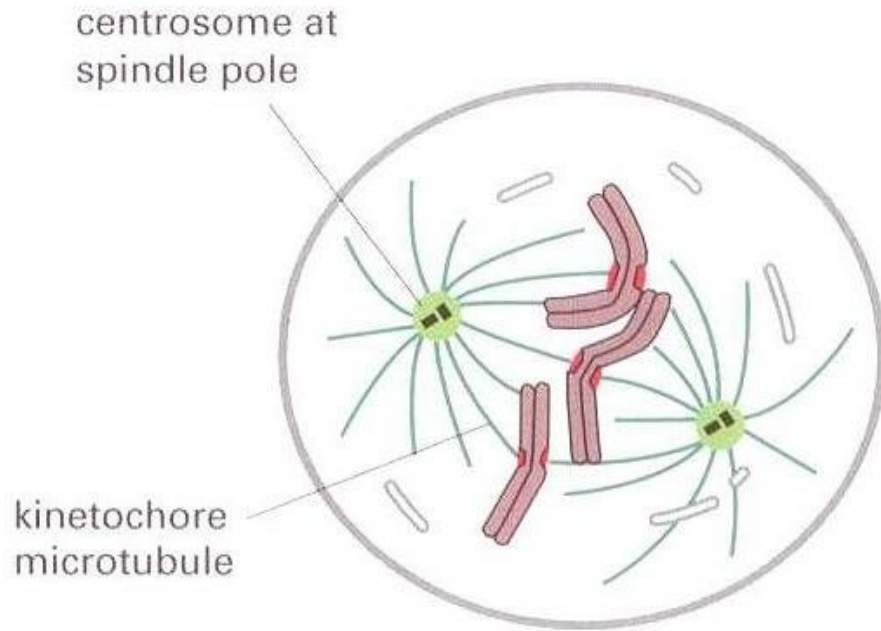
20-40 microtubules
are attached to the
human kinetochore

Each sister chromatid has its own kinetochore in the region of the centromere, which connects it to the kinetochore microtubule.

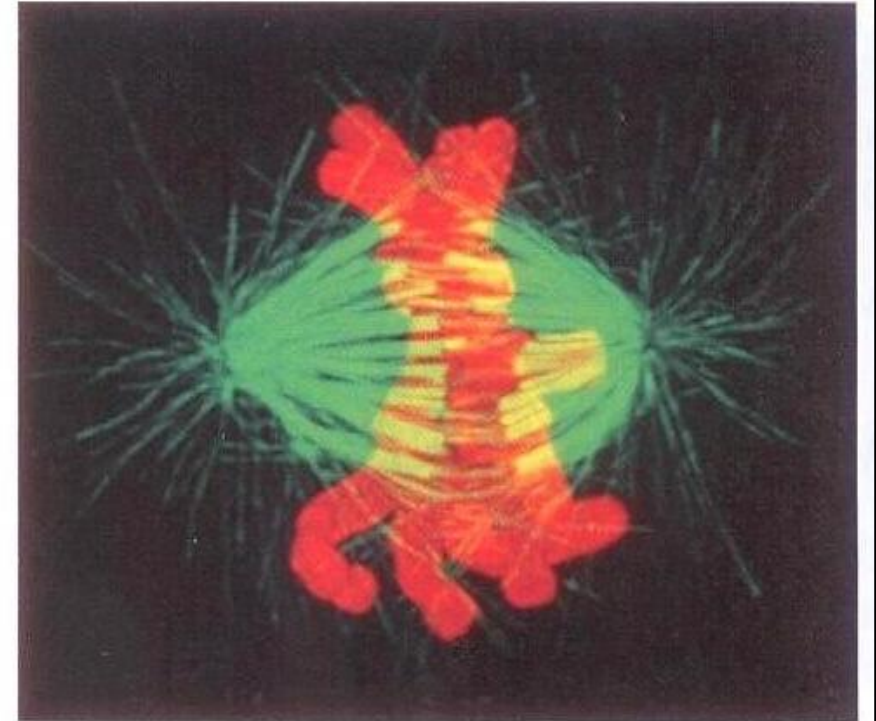
The kinetochore is encoded by a special centromere DNA sequence. Its removal means that kinetochores cannot form and chromosomes cannot segregate correctly during mitosis

Metaphase

3 METAPHASE



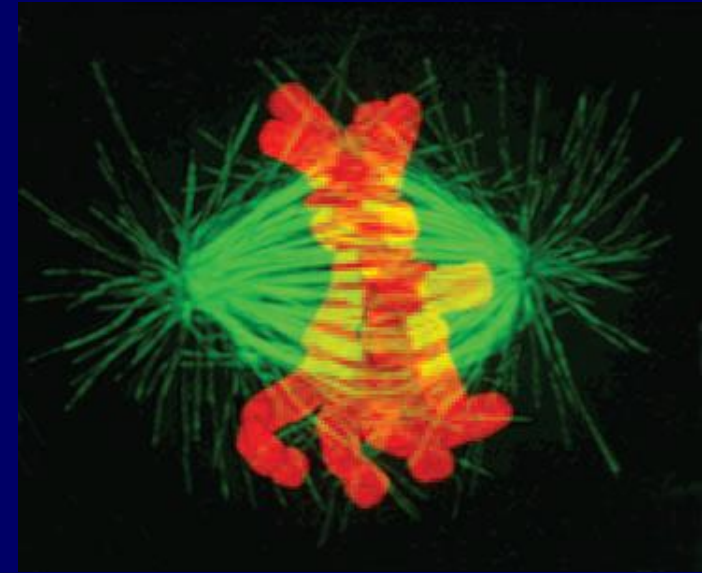
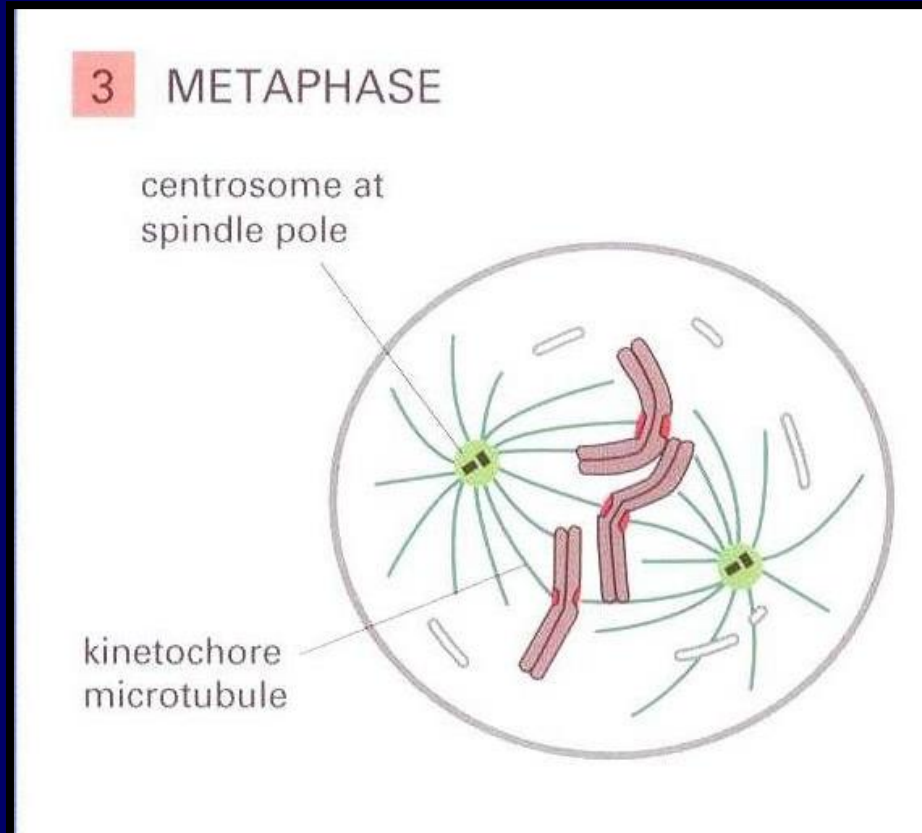
At **metaphase**, the chromosomes are aligned at the equator of the spindle, midway between the spindle poles. The kinetochore microtubules attach sister chromatids to opposite poles of the spindle.



1. The beginning of metaphase is defined by the formation of the metaphase plate.

Chromosomes are aligned in the equatorial plane between the poles. Also, the kinetochores of all chromosomes are aligned in a plane.

Metaphase



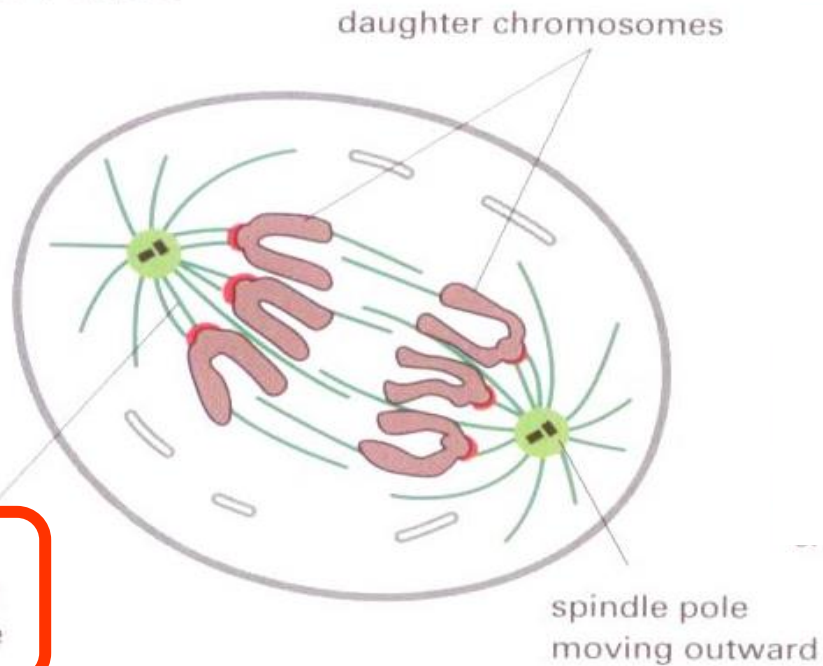
2. The chromosomes in the metaphase plate are held together by considerable force.

Both microtubular molecular motors (motor proteins) and the gradual growth and degradation of microtubules (tubulin units are either added or removed, leading to movement) are involved in the creation and maintenance of this state.

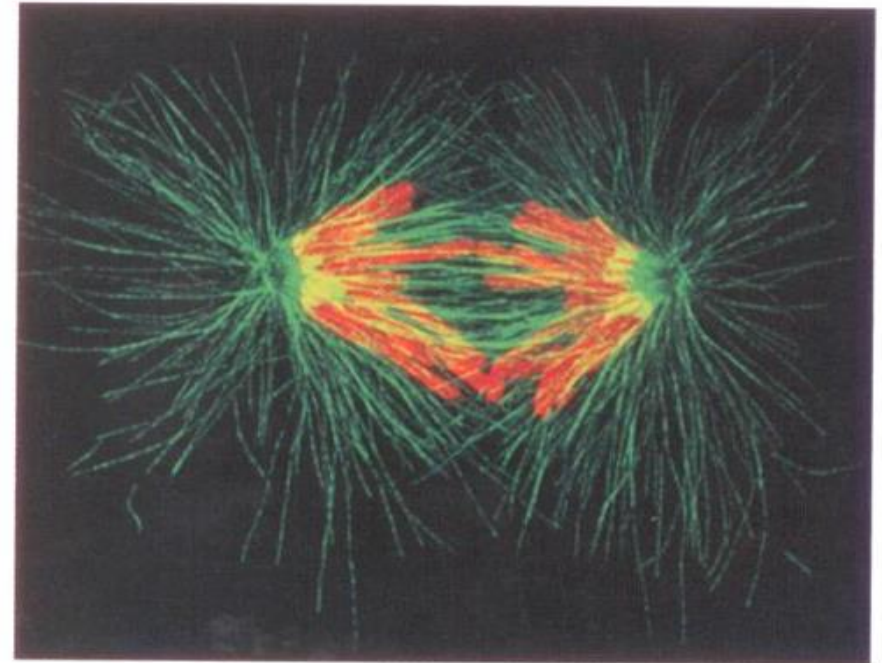
Colchicine = mitotic spindle poison blocks the addition of microtubule subunits

Anaphase

4 ANAPHASE



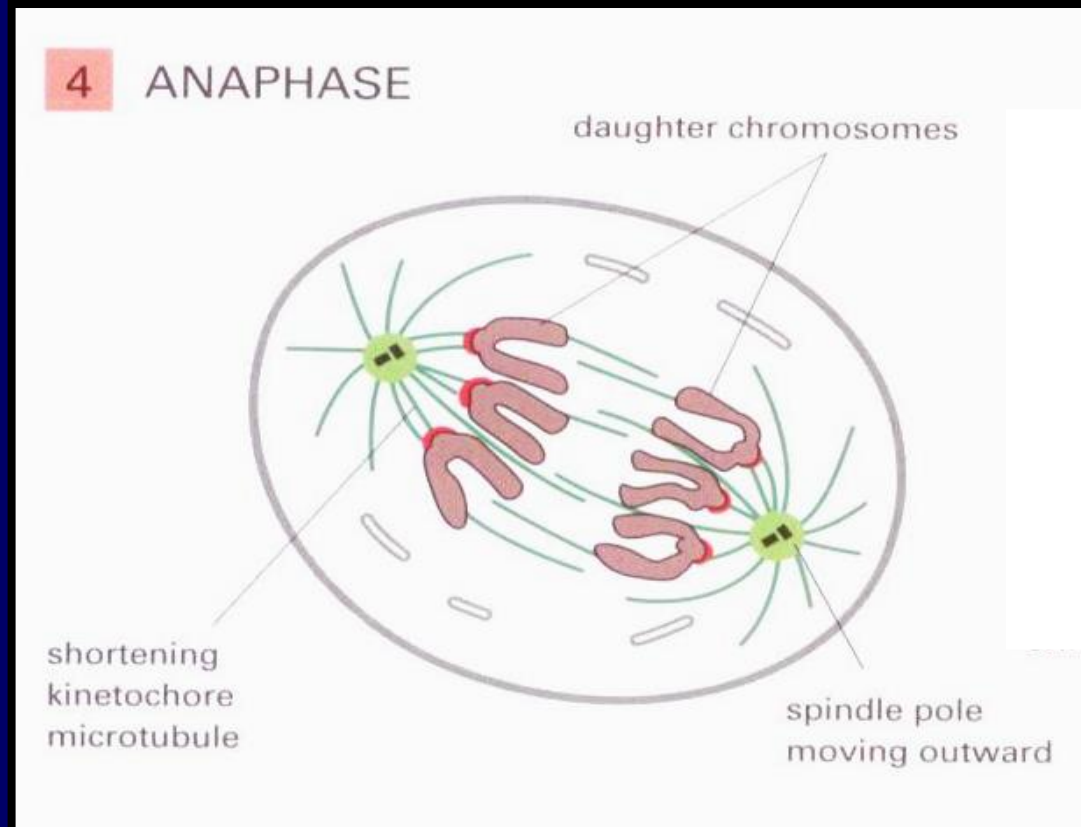
In anaphase, the sister chromatids synchronously separate to form two daughter chromosomes, each is pulled slowly toward the spindle pole it sees. The kinetochore microtubules get shorter, and the spindle poles also move apart; both processes contribute to chromosome segregation.



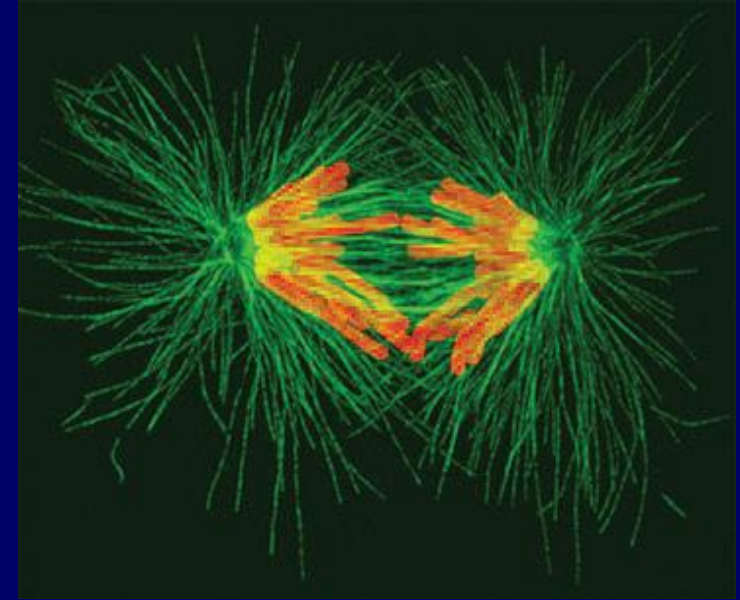
1. The connection between sister chromatids is broken by proteolytic enzymes.

Each chromatid (daughter chromosome) moves toward the spindle pole to which it is attached.

Anaphase

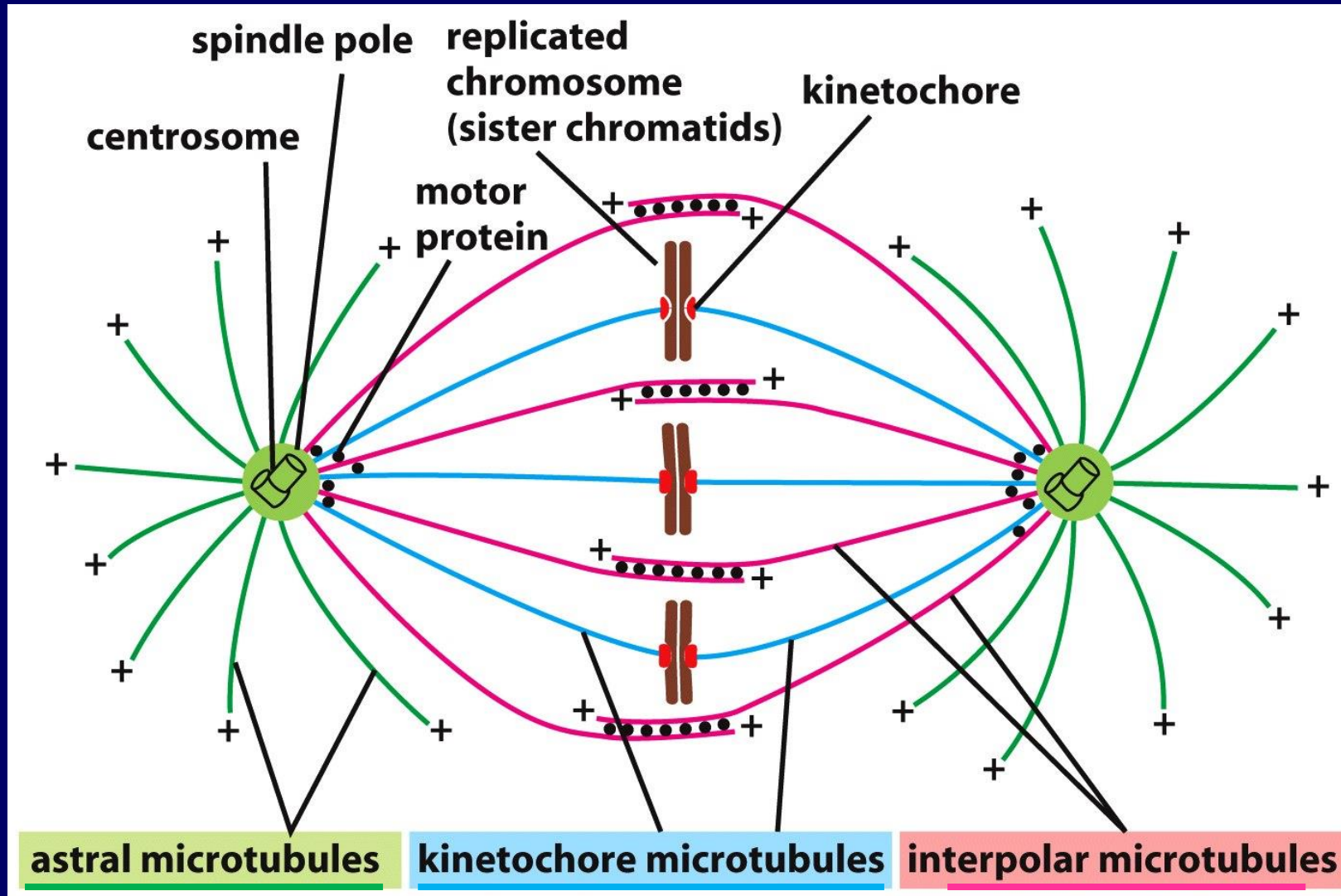


Chromosome movement speed $1\mu\text{m}$ per minute.
Movement is the result of **two independent processes (anaphase A - anaphase B)**



2. This segregation of chromosomes leads to the division of chromosomes into two identical sets at opposite ends of the mitotic spindle.

Three types of mitotic spindle microtubules

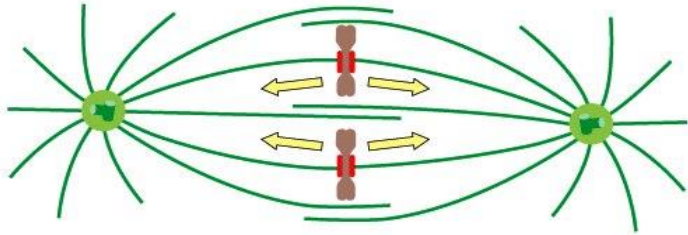


Kinetochore microtubules connect chromosomes to both poles

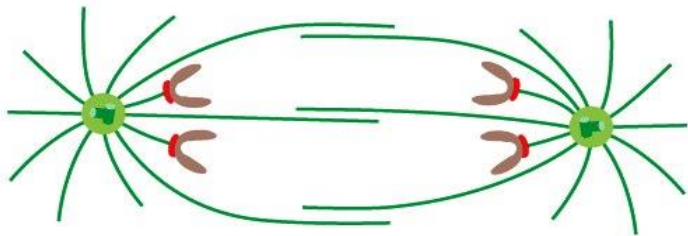
Chromosomes are pulled forward

The poles move away from each other

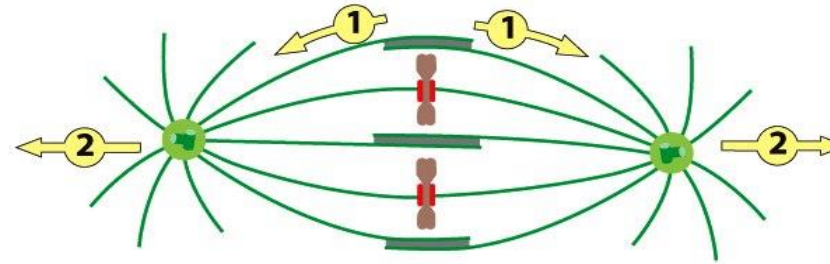
ANAPHASE A



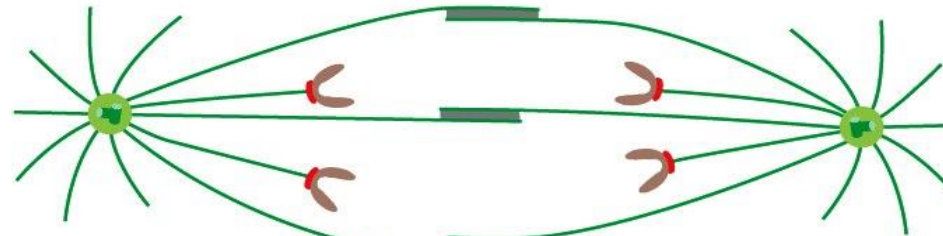
shortening of kinetochore microtubules; movement of daughter chromosomes to poles; forces generated mainly at kinetochores



ANAPHASE B



(1) a sliding force is generated between inter-polar microtubules from opposite poles to push the poles apart; the inter-polar microtubules also elongate; (2) a pulling force acts directly on the poles to move them apart



microtubule growth at plus end of polar microtubules

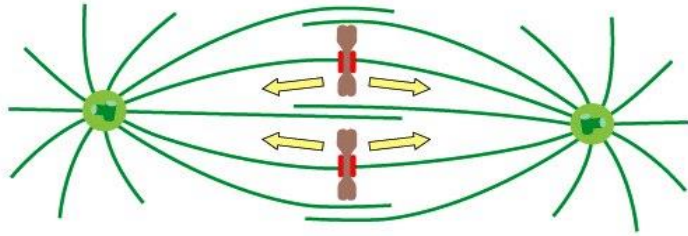
A: Molecular motors (motor proteins) of the kinetochore "walk" even with the attached chromosome along the kinetochore microtubule

Chromosomes are pulled forward

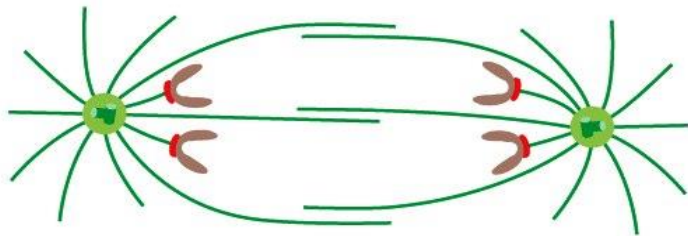
they are on long polar microtubules

The poles move away from each other

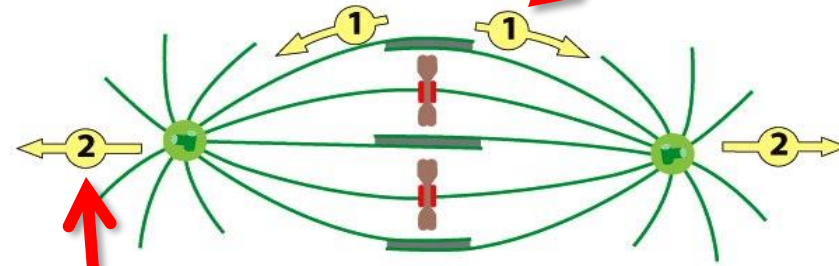
ANAPHASE A



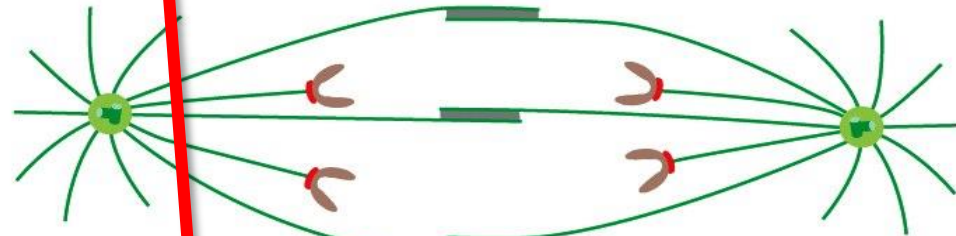
shortening of kinetochore microtubules; movement of daughter chromosomes to poles; forces generated mainly at kinetochores



ANAPHASE B



(1) a sliding force is generated between interpolar microtubules from opposite poles to push the poles apart; the interpolar microtubules also elongate; (2) a pulling force acts directly on the poles to move them apart



microtubule growth at plus end of polar microtubules

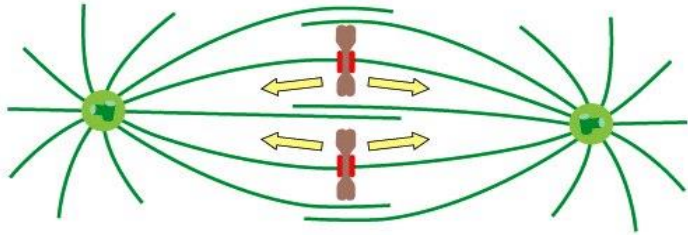
B: Motive forces provided by sets of "molecular motors"

they are on microtubules extending from the spindle pole

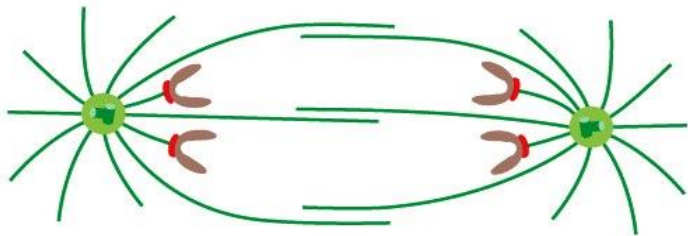
Chromosomes are pulled forward

The poles move away from each other

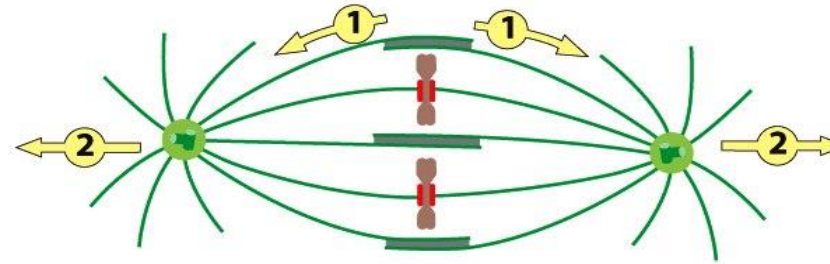
ANAPHASE A



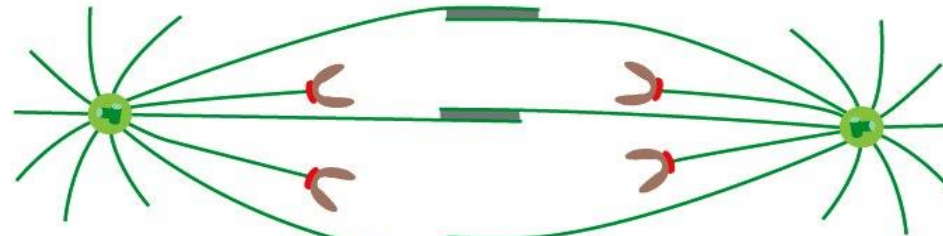
shortening of kinetochore microtubules; movement of daughter chromosomes to poles; forces generated mainly at kinetochores



ANAPHASE B



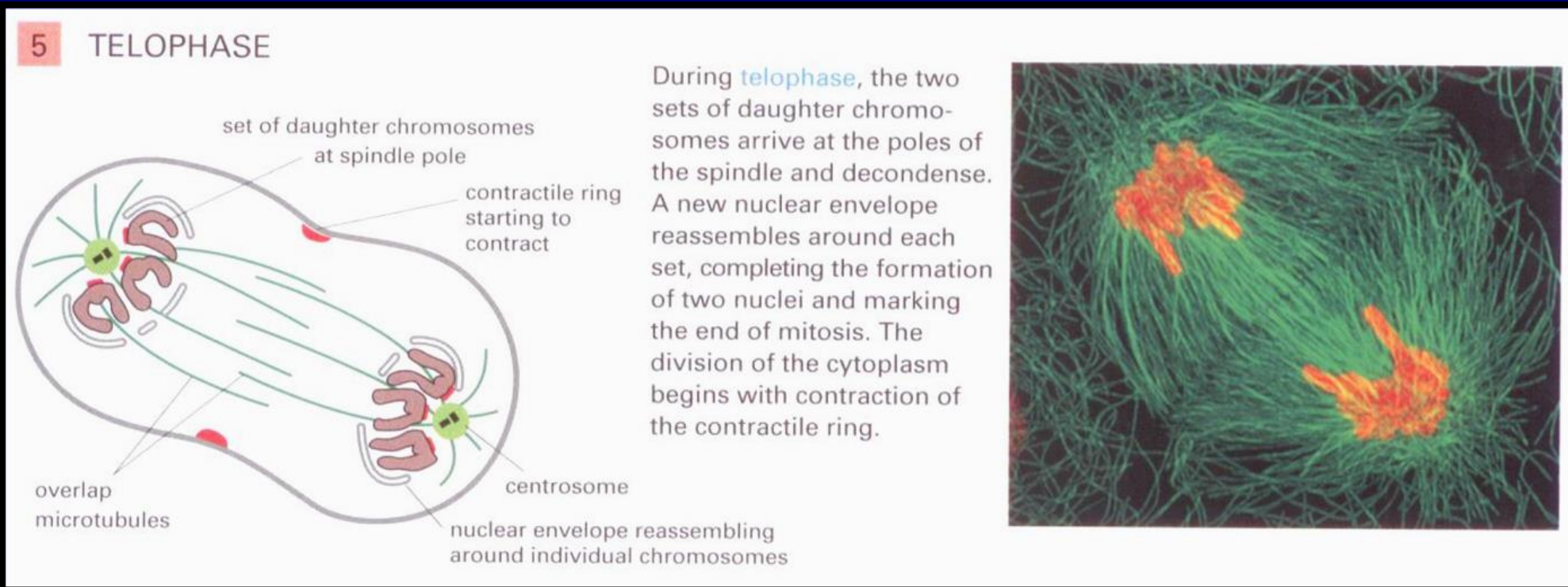
(1) a sliding force is generated between inter-polar microtubules from opposite poles to push the poles apart; the inter-polar microtubules also elongate; (2) a pulling force acts directly on the poles to move them apart



microtubule growth at plus end of polar microtubules

B: The spindle poles move away is accompanied by the elongation of the polar microtubules - at their plus ends, new subunits polymerize

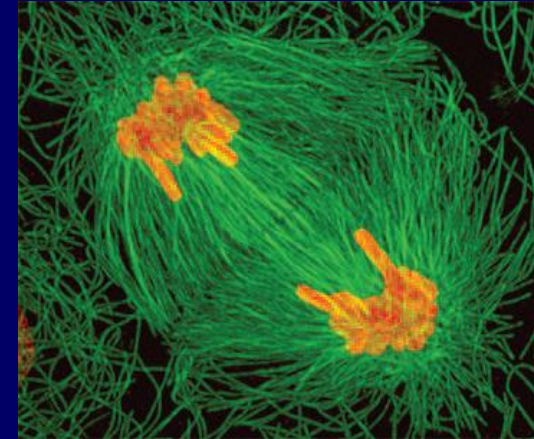
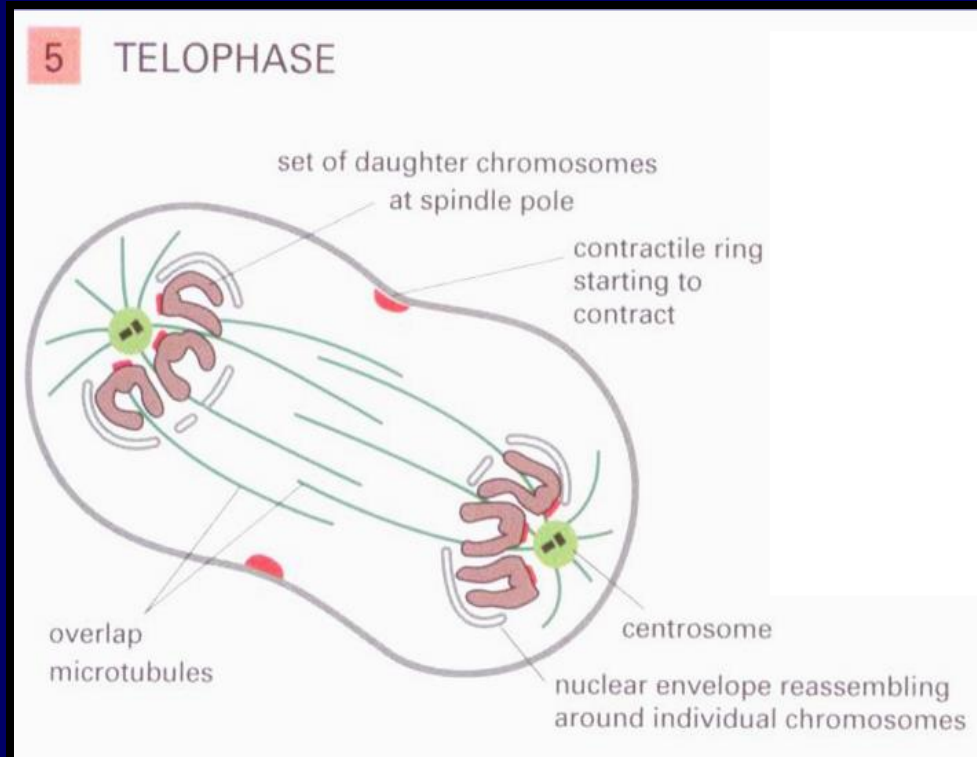
Telophase



A new nuclear envelope begins to form around each set of chromosomes and two daughter nuclei are formed.

Vesicles of the nuclear membrane cluster around individual chromosomes and then fuse to form the nuclear envelope. Nuclear lamins that were phosphorylated in prometaphase are dephosphorylated and reassociate back into the nuclear lamin, which is under the nuclear envelope (has an inner and outer nuclear membrane)

Telophase

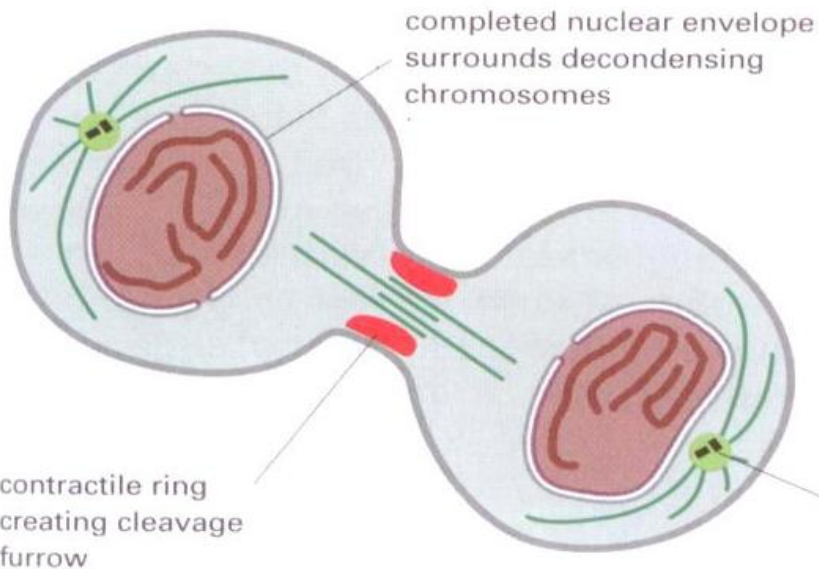


Additional nuclear proteins enter the nucleus through pores in the newly formed nuclear envelope and the nucleus grows.

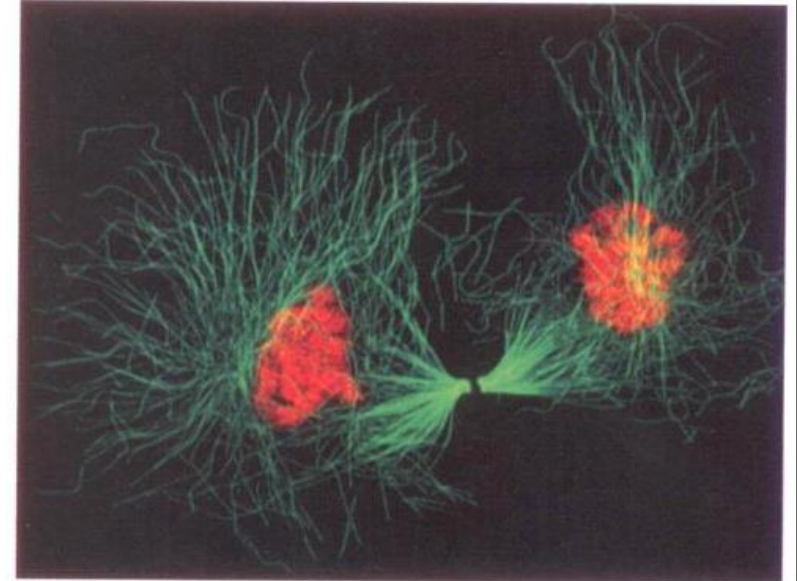
Chromosomes decondense into the so-called interphase state, so gene transcription can resume. Mitosis ends.

Cytokinesis

6 CYTOKINESIS

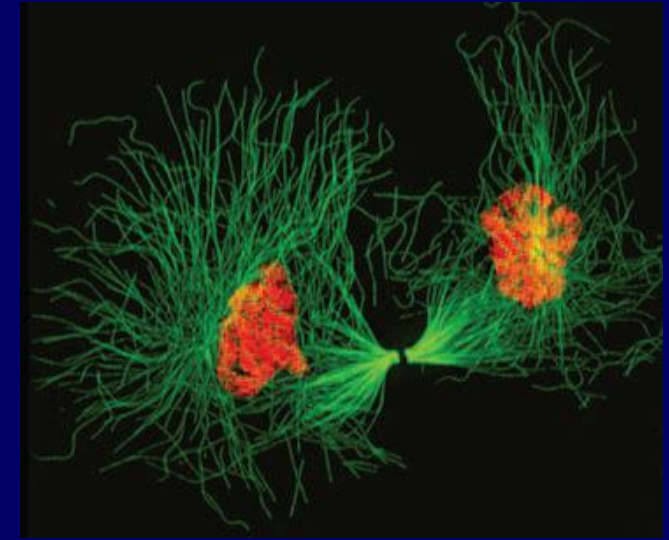
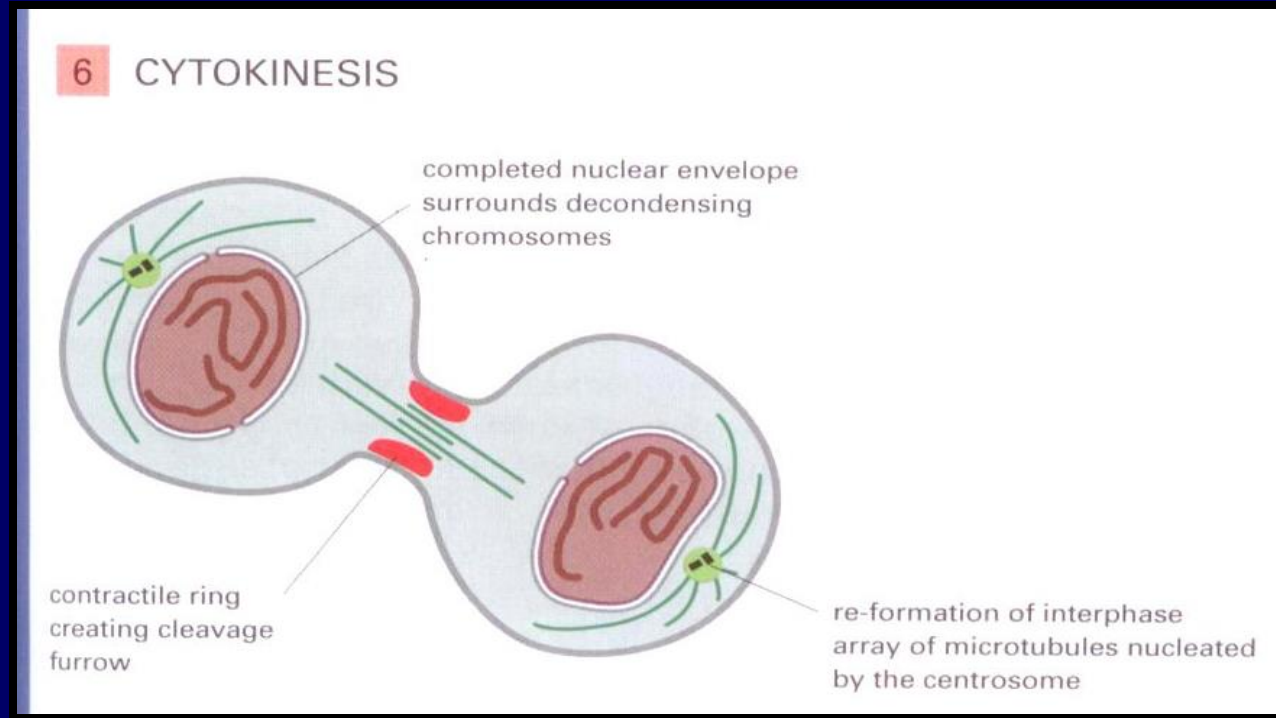


During **cytokinesis**, the cytoplasm is divided in two by a contractile ring of actin and myosin filaments, which pinches the cell in two to create two daughters, each with one nucleus.



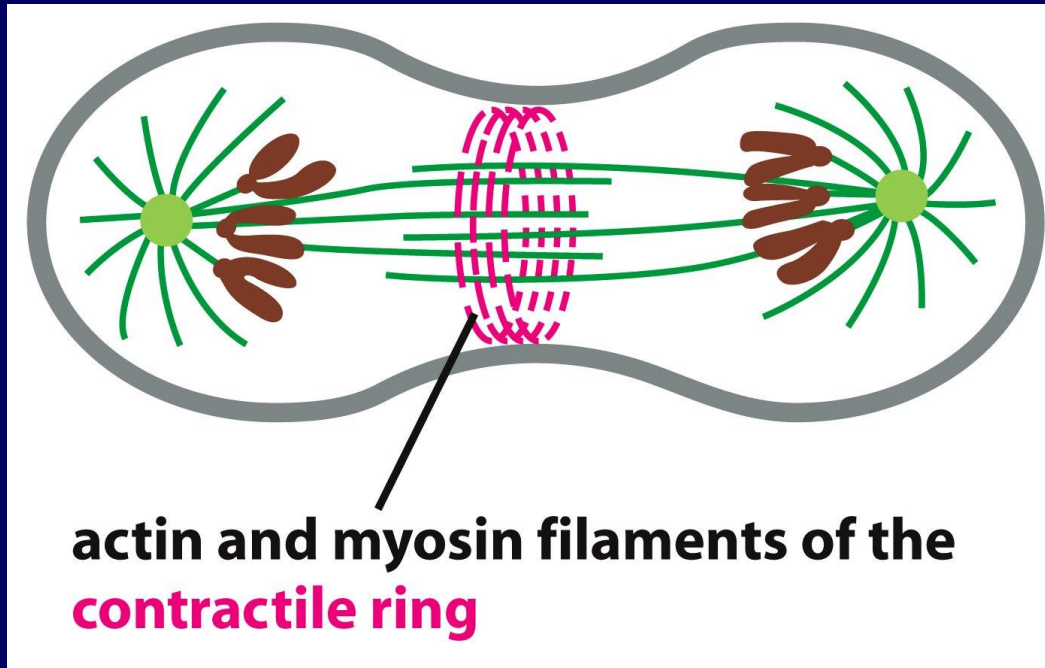
Cytokinesis is the division of the cytoplasm and all its components. It starts already in anaphase - a dividing groove is formed perpendicular to the longitudinal axis of the mitotic spindle. In anaphase, the contractile ring also begins to form.

Cytokinesis



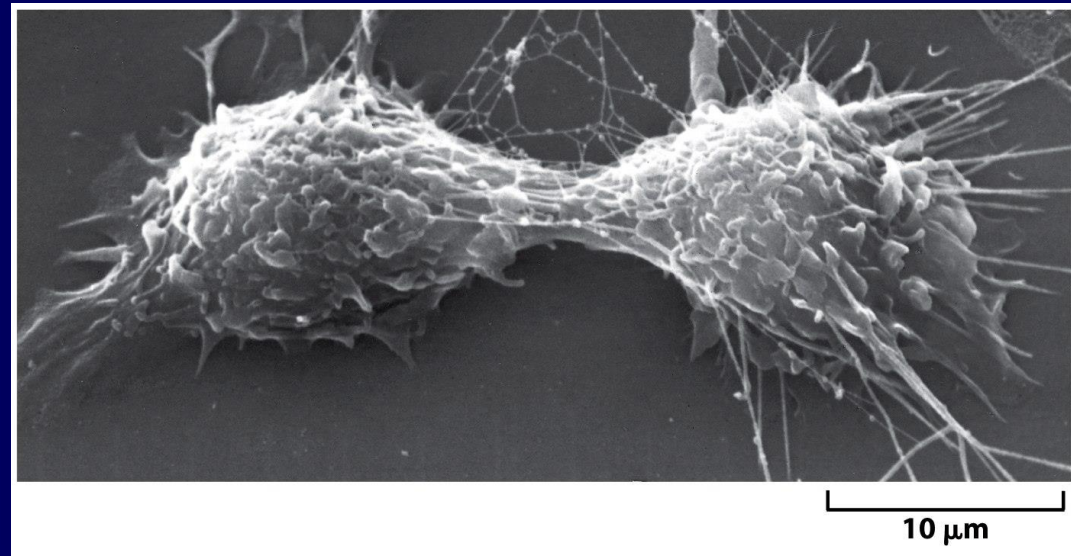
The contractile ring is formed from bundles of actin and myosin filaments. It is attached to proteins associated with the inner side of the membrane and is able to exert a great force.

The movement of actin filaments against myosin filaments is similar to the contraction of a muscle. However, the ring structure is only temporary !! It disappears.



During rapid division,
sometimes
cytokinesis does not
immediately follow
mitosis, the so-called
SYNCYTIUM
(multinucleated cell)

Membranes are then formed
simultaneously in coordinated
cytokinesis =
CELLULARISATION



Cells in animal tissues are usually in firm adhesive contact with their neighbors, flattened and adhered to the substrate.

As soon as the cell enters the M-phase, the **phosphorylation of integrins** (responsible for the mutual cohesion of cells in tissues) and the weakening of these interactions and bonds, the cell becomes rounded.

After cytokinesis is completed, the cells flatten again and mutual adhesion forces are restored. The cell has thus rearranged its contacts with neighboring cells - this allows the incorporation of new cells into the tissues.

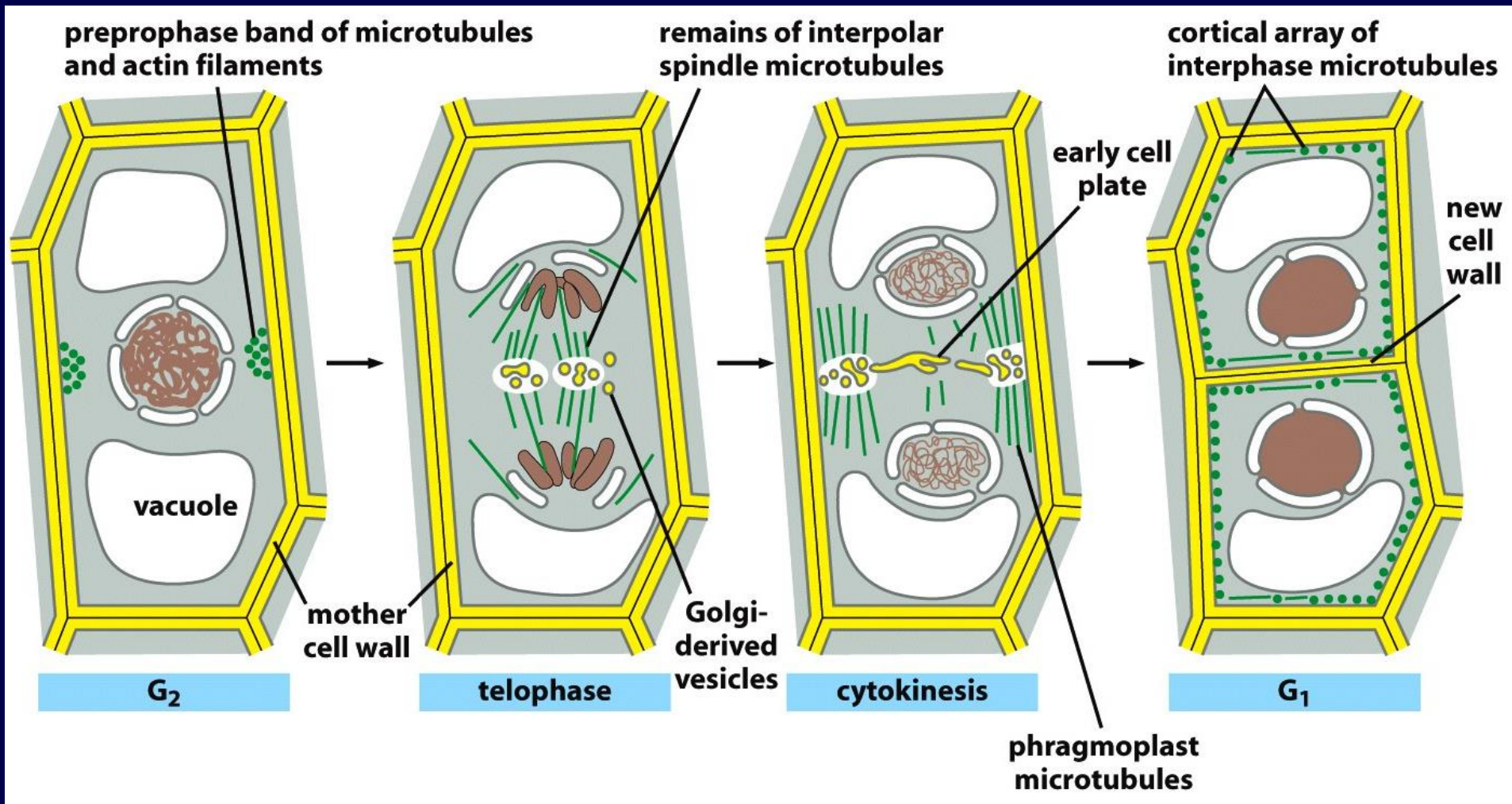
Differences in cytokinesis in plants

A plant cell not only has a plasma membrane, but also a solid cell wall.

Daughter cells are not separated by a contractile ring, but by a newly forming cell wall.

It begins to form at the **beginning of telophase** and its formation is controlled by a structure called **FRAGMOPLAST**.

It is formed from the remnants of polar microtubules in the equatorial plane of the mitotic spindle.



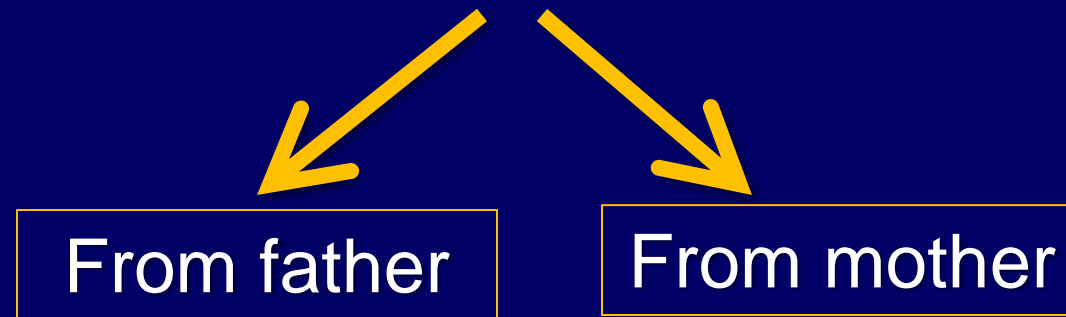
Small membrane-bound vesicles derived from the Golgi apparatus with polysaccharides and glycoproteins travel along the microtubules to the phragmoplast. They are necessary for the formation of the cell wall.

Meiosis

It was described in 1883. Meios = decreasing

It is cell division that takes place during the formation of gametes (specialized cells intended for reproduction).

Gametes are **HAPLOID** = have only one set of chromosomes. Other human cells are **DIPLOID** = have two sets of chromosomes.



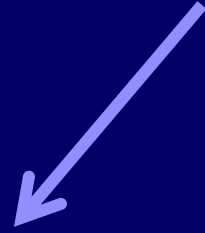
Difference between meiosis and mitosis



- 1) The replicated chromosomes line up randomly at the metaphase plate
- 2) The sister chromatids then separate from each other to form separate chromosomes.
- 3) The resulting daughter cells each have one copy of each maternal and one copy of each paternal chromosome.

= DAUGHTER CELLS ARE DIPLOID AND GENETICALLY IDENTICAL

Difference between meiosis and mitosis



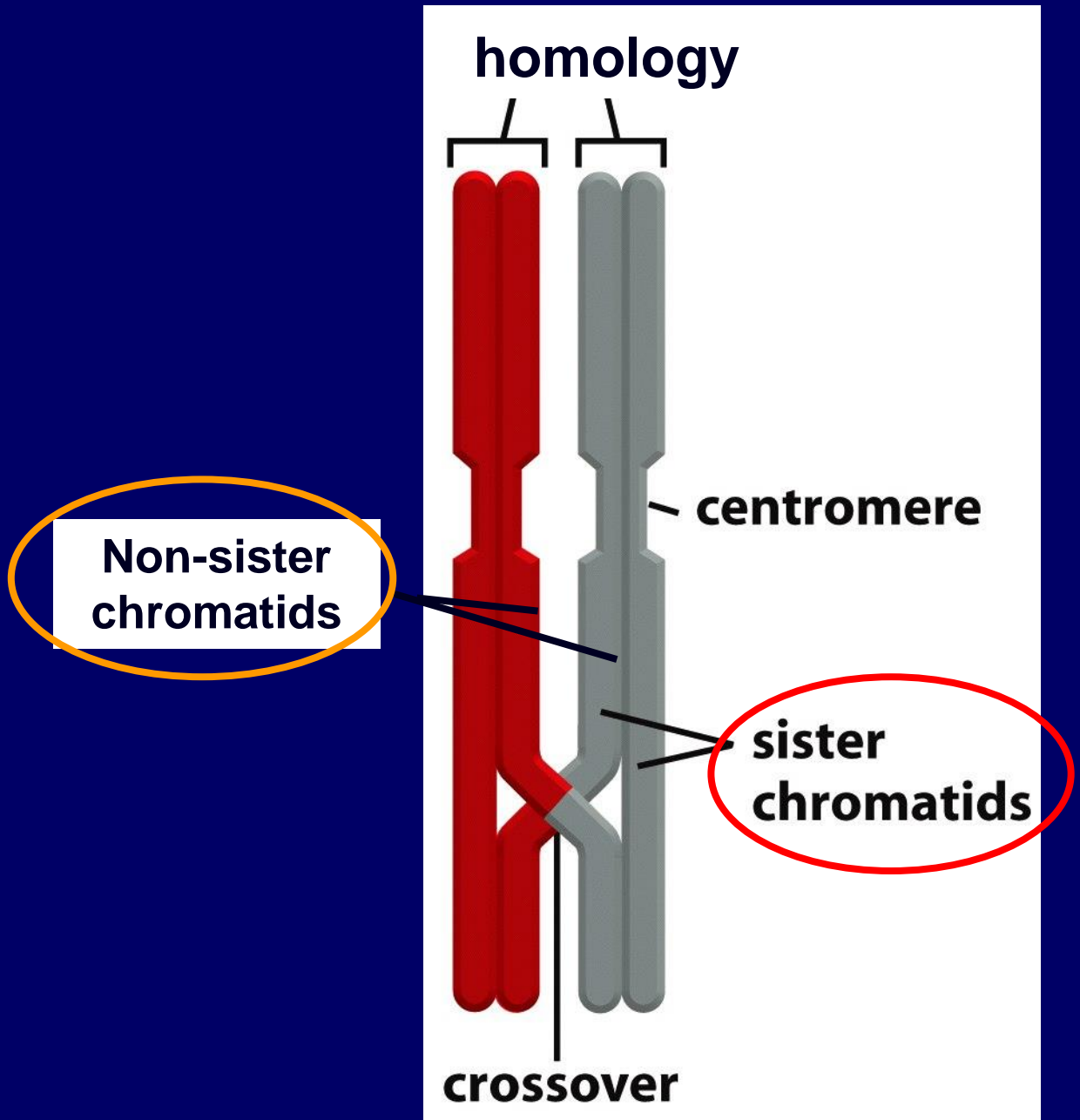
- 1) The replicated chromosomes pair with their homologue before being arranged in the metaphase plate and create structures = bivalents, which therefore contain four chromatids (2x2)
- 2) The formation of a bivalent enables genetic recombination between the paternal and maternal parts of the same chromosome = **CROSSING OVER**
- 3) Bivalents diverge towards the poles

Difference between meiosis and mitosis

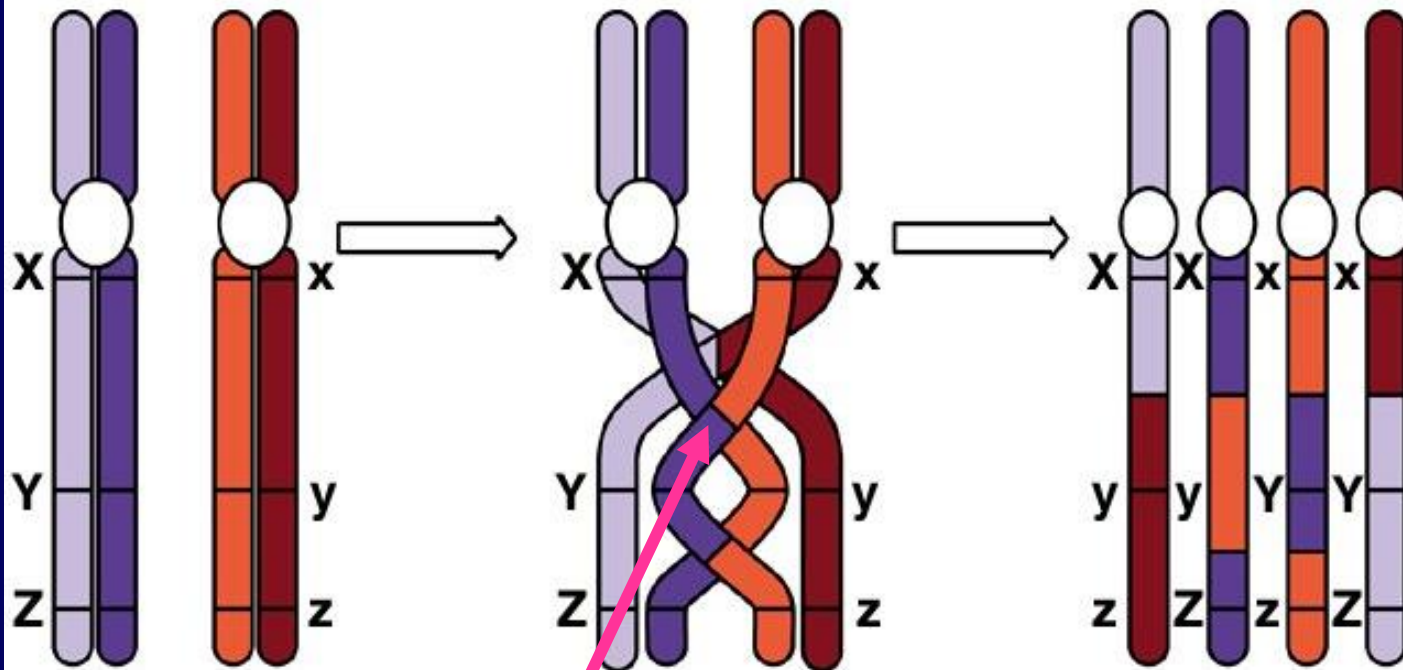


- 1) Before the second **meiotic division**, there is no DNA replication, nor is interphase present.
 - 2) Sister chromatids separate in the normal way as in mitosis.
- = **A TOTAL OF FOUR HAPLOID CELLS ARE FORMED, WHICH MAY NOT CARRY COMPLETELY IDENTICAL GENETIC MATERIAL.**

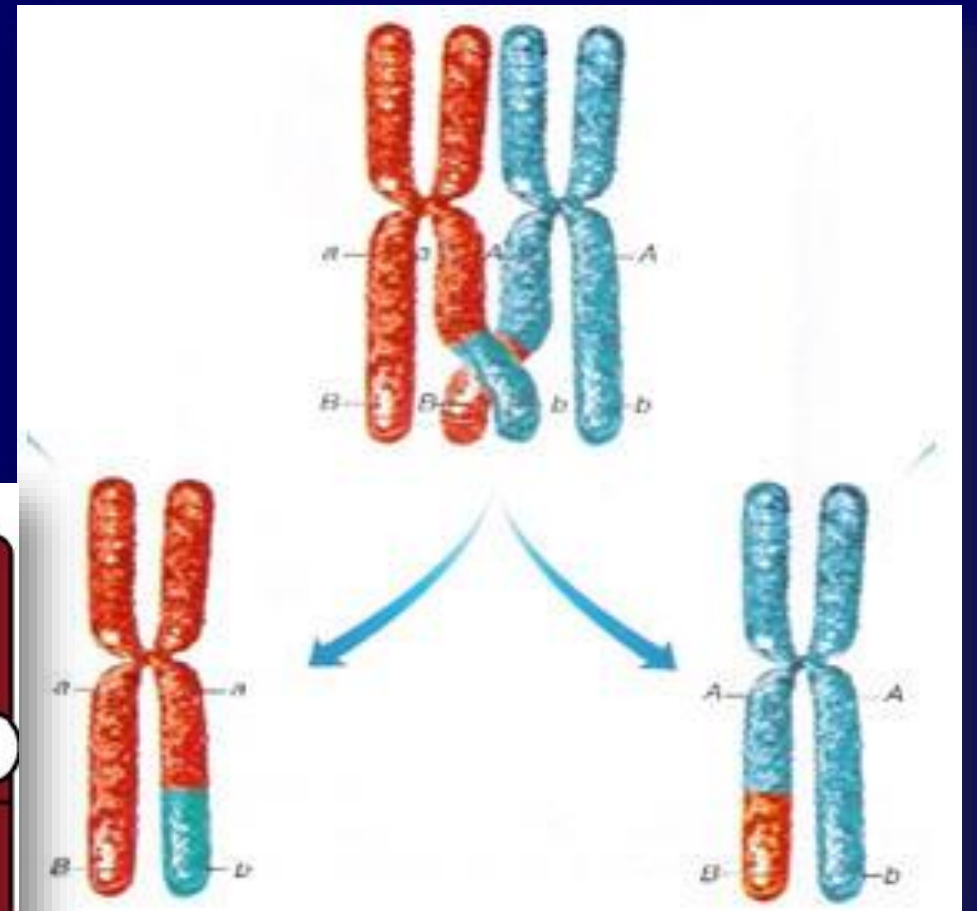
Thanks to crossing-over, the father's and mother's genes are mixed.



Result crossing-over



Chiasmats



Meiosis

Meiosis involves two cell divisions:

1st and 2nd meiotic division.

(prophase, prometaphase, metaphase, anaphase, telophase)

DNA replication occurs before the first meiotic division (S-phase), but not before the second.

Meiosis

1st MEIOTIC DIVISION

The longest stage is **prophase**, when bivalents are formed. This stage can last for many years. We therefore distinguish 5 stages of the first prophase: **leptotene, zygotene, pachytene, diplotene and diakinesis**

At the end of prophase, the nuclear envelope breaks down, signaling the beginning of prometaphase.

The remaining stages already take place quickly and similarly to mitosis.

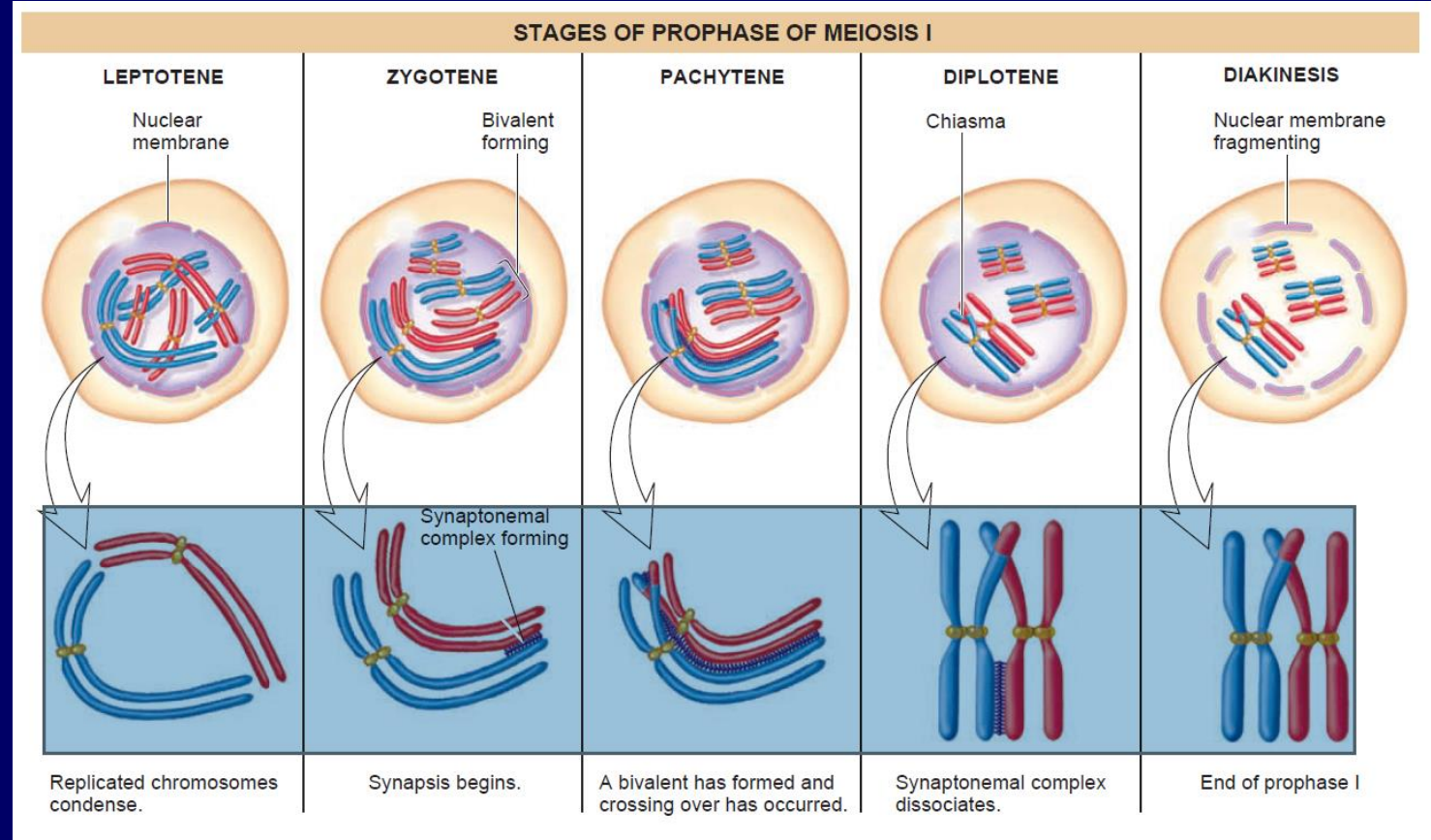
LEPTOTENE: spiralization of DNA strands and chromosome differentiation.

ZYGOTENE: homologous chromosomes move closer to each other and with the help of a special protein, **bivalents are created**

PACHYTENE: chromosomes complete spiralization and bivalents are observable as so-called tetrads (4-chromatid complexes). Non-sister chromatids intertwine - the formation of chiasmata (knots). In this phase, the so-called **crossing-over** occurs.

DIPLTENE: protein bonds between homologous chromosomes loosen and gradually move apart. Non-sister chromatids still connected by chiasmata (knots).

DIKINEZE: there is a rearrangement and **separation of homologous chromosomes**. Chiasmata move to the end of chromatids where they disappear (chiasmata terminalization).



Meiosis

1st MEIOTIC DIVISION (heterotypic division)

Replicated cells diverge into daughter cells homologues (bivalents).

Haploid cells are formed.

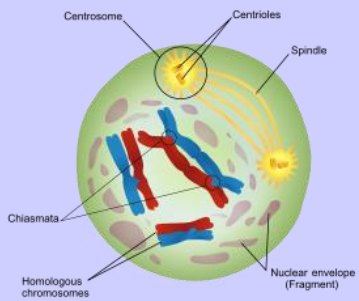
If the homologues do not separate from each other (= nondisjunction), at the end of the gamete arise, where one is missing and the other a certain chromosome resides.

Sister chromatids remain connected (behave as one unit) at all times.

2nd MEIOTIC DIVISION (homotypic division)

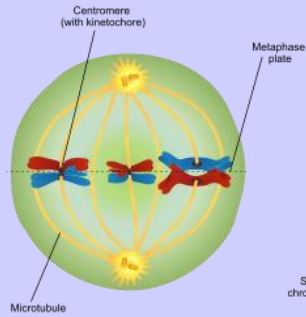
Sister chromatids separate into daughter cells only during the second meiotic division.

Prophase I



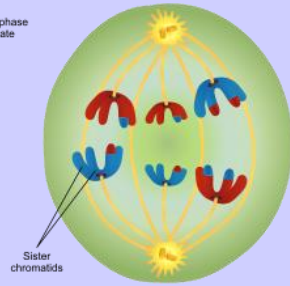
The chromosomes condense, and the nuclear envelope breaks down. Crossing-over occurs.

Metaphase I



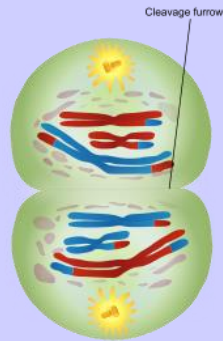
Pairs of homologous chromosomes move to the equator of the cell.

Anaphase I



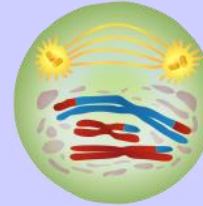
Homologous chromosomes move to the opposite poles of the cell.

Telophase I & cytokinesis

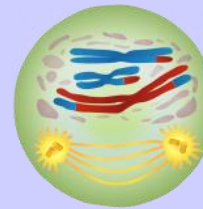


Chromosomes gather at the poles of the cells. The cytoplasm divides.

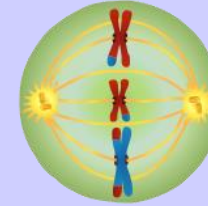
Prophase II



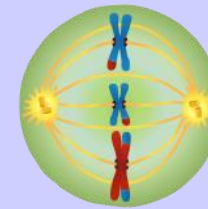
A new spindle forms around the chromosomes.



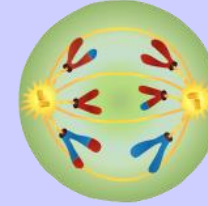
Metaphase II



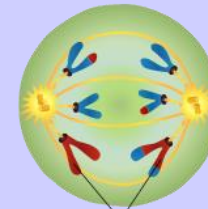
Metaphase II chromosomes line up at the equator.



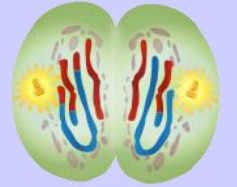
Anaphase II



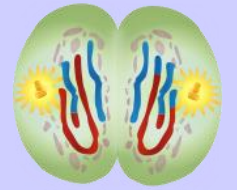
Centromeres divide. Chromatids move to the opposite poles of the cells.



Telophase II & cytokinesis



A nuclear envelope forms around each set of chromosomes. The cytoplasm divides.

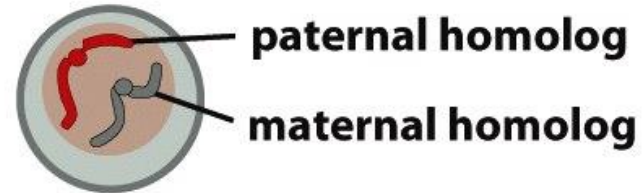


https://en.wikipedia.org/wiki/Meiosis#/media/File:Meiosis_Stages.svg

Meiotic S-phase

MEIOTIC S PHASE

(A) MEIOSIS



↓ DNA REPLICATION



(B) MITOSIS

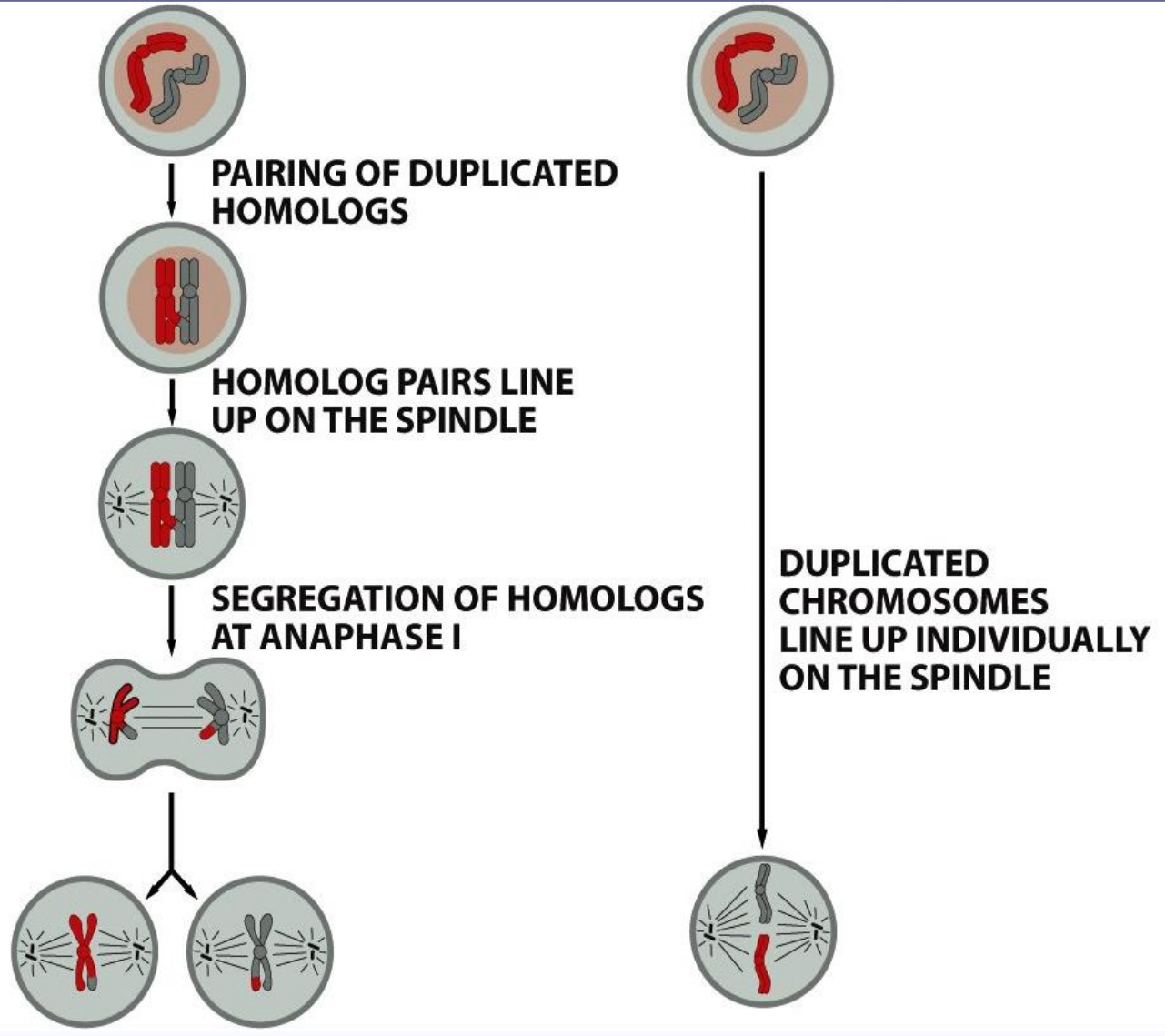


↓ DNA REPLICATION



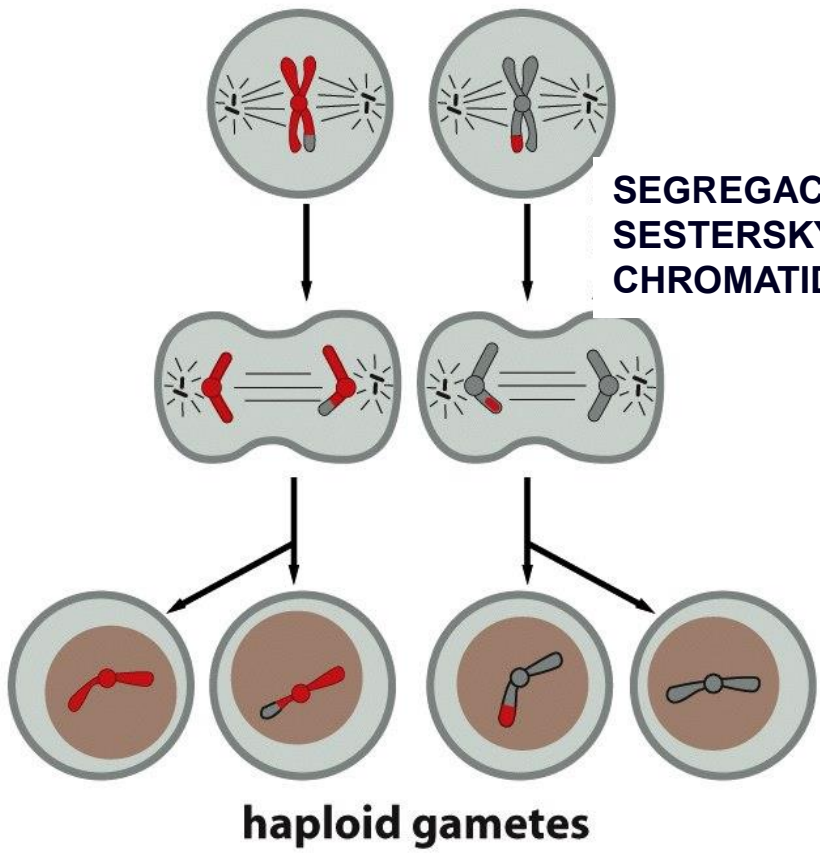
(A) MEIOSIS

(B) MITOSIS

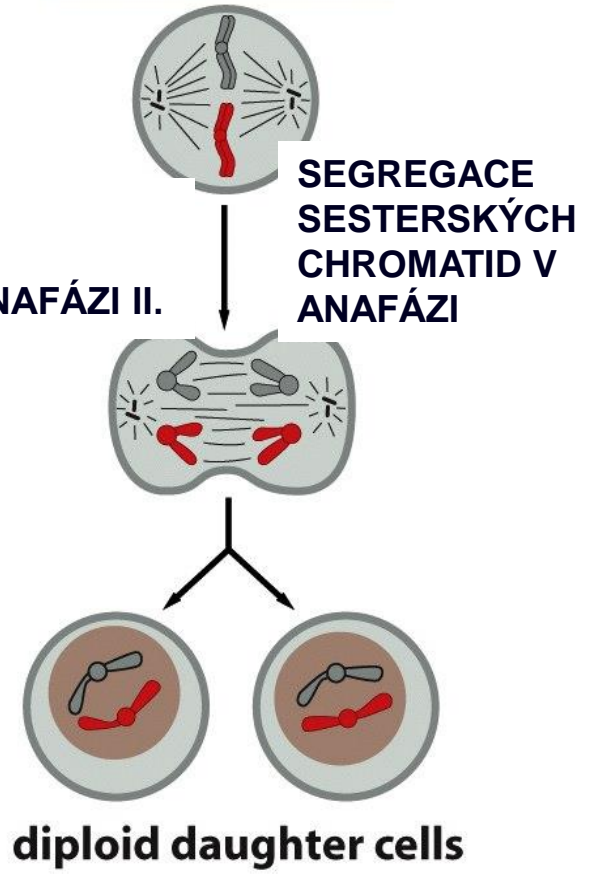


MEIOSIS II

(A) MEIOSIS



(B) MITOSIS



SEGREGACE
SESTERSKÝCH
CHROMATID V
ANAFÁZI II.

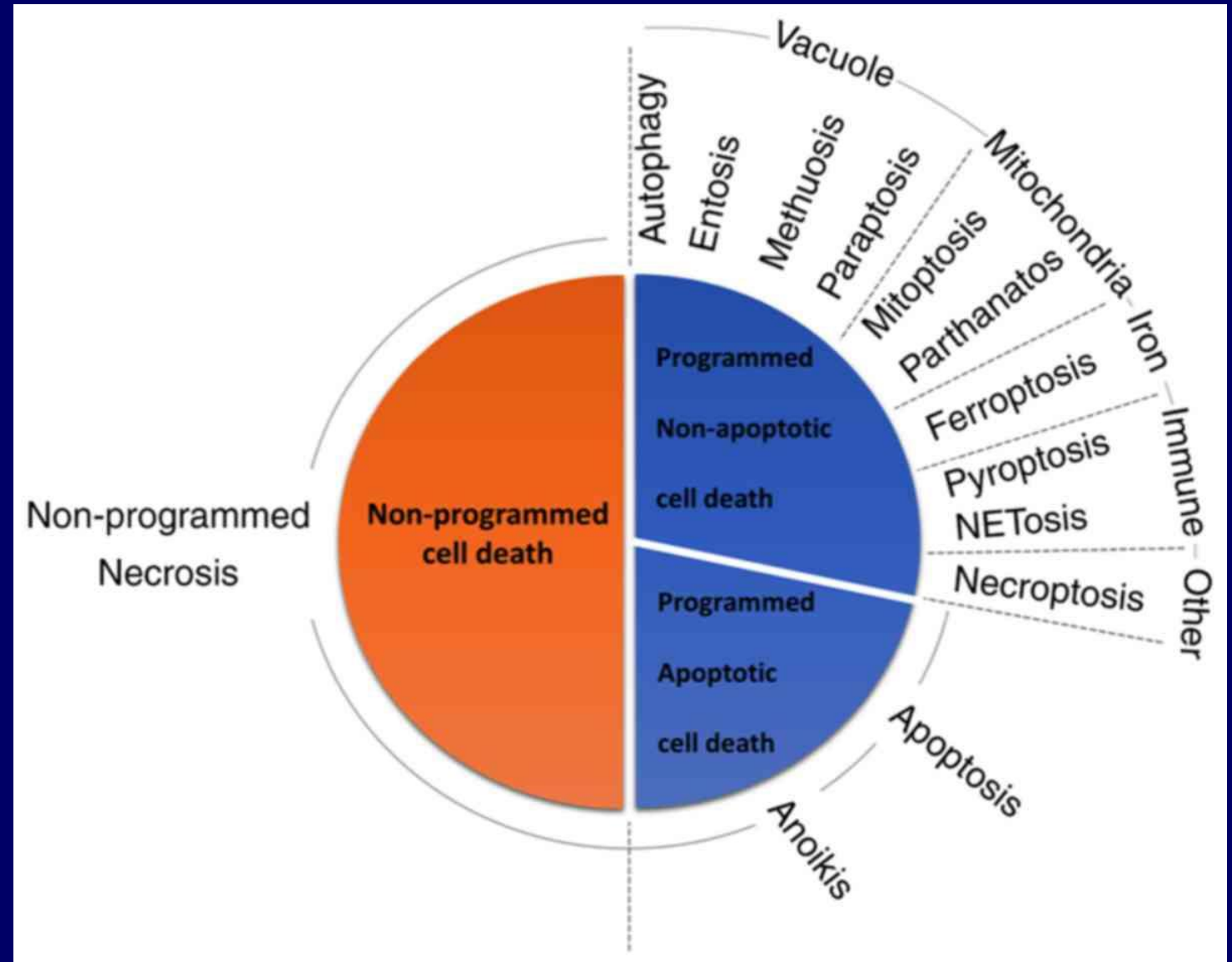
SEGREGACE
SESTERSKÝCH
CHROMATID V
ANAFÁZI

haploid gametes

diploid daughter cells

Cell death

- **Programmed cell death** – controlled and planned cell death
- **Unprogrammed cell death** – necrosis, cell death due to significant stress



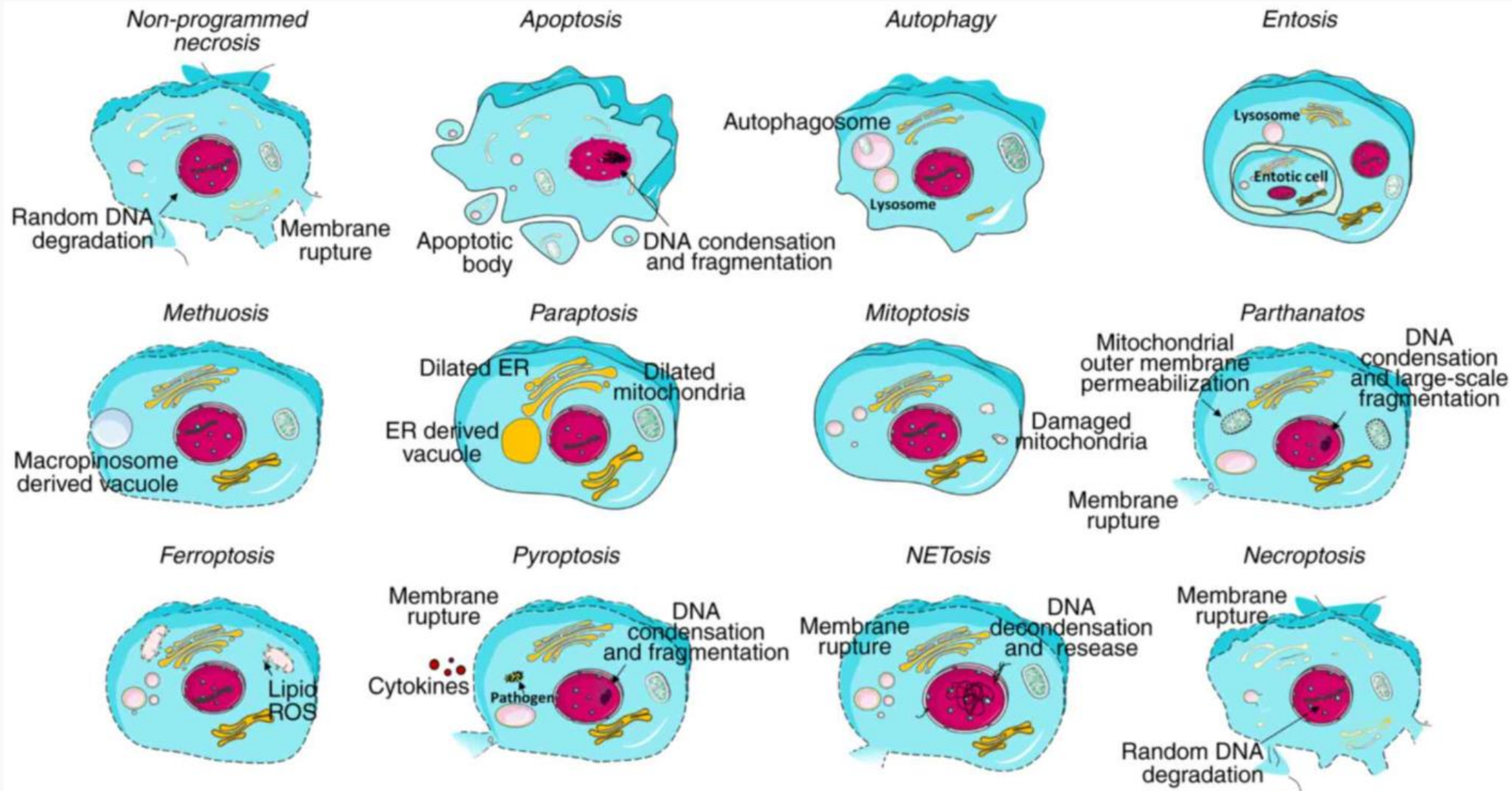
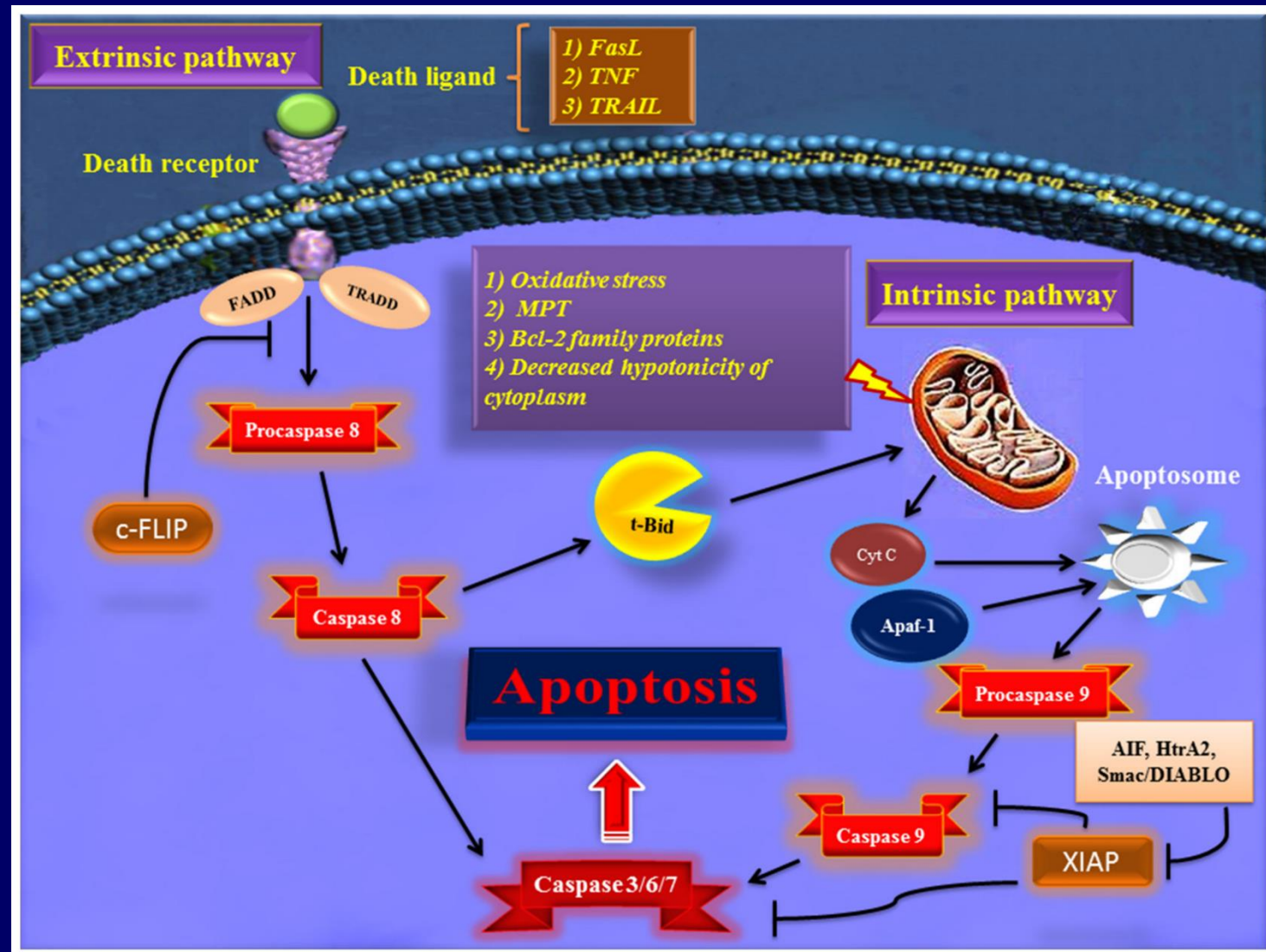
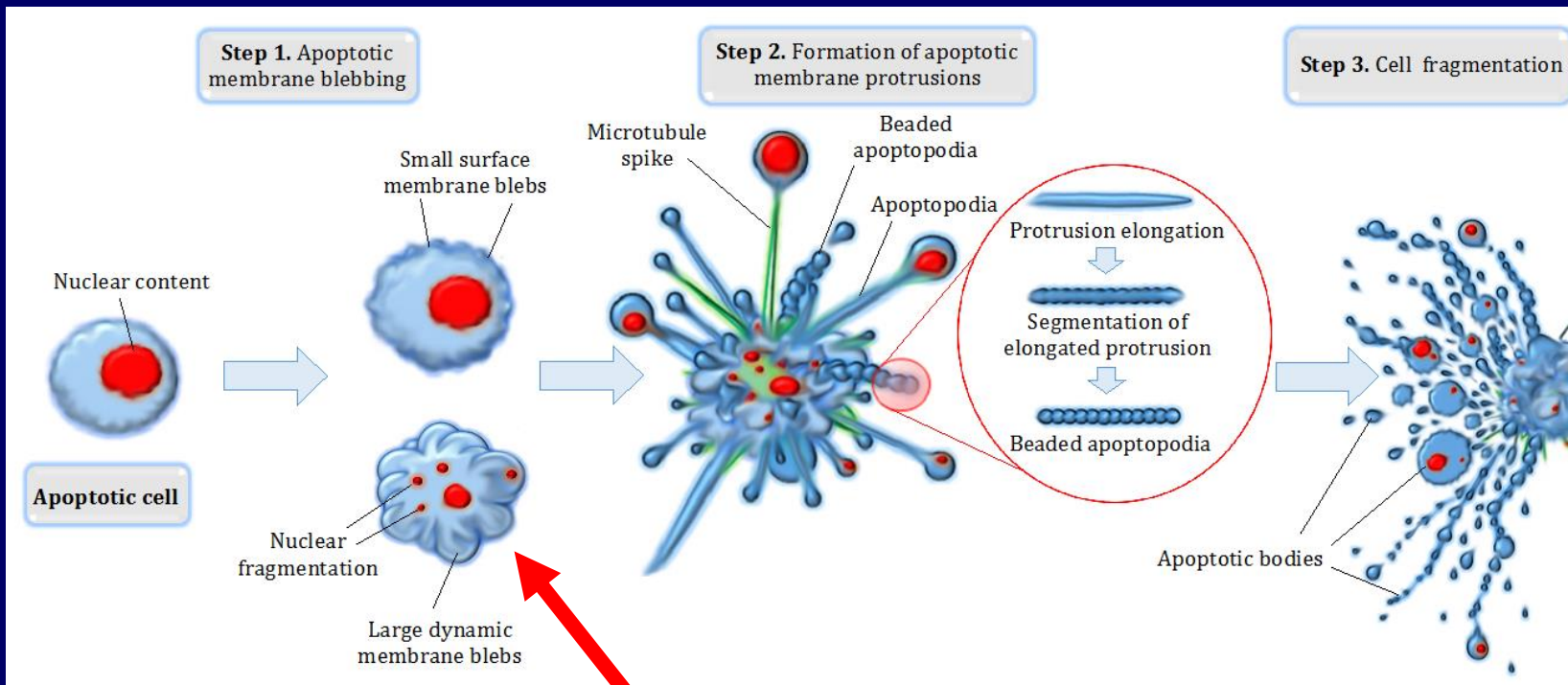


Figure 2 - Typical morphology of each cell death. The morphological alteration focuses on cell size, membrane integrity, chromatin density, organelle arrangement and presence of vacuoles.

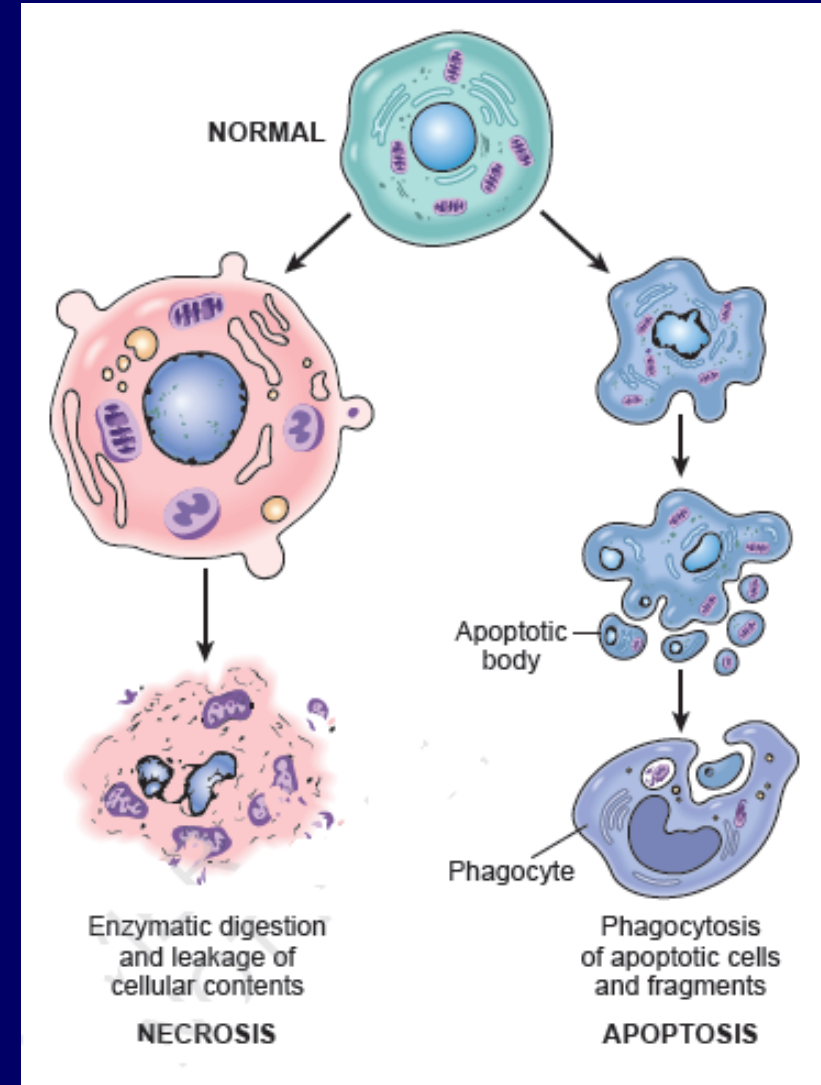
Apoptosis

- Controlled cell death - after the "DIE" signal, the cell initiates a sequence of steps leading to the death of the cell
- Extrinsic pathway – signal outside the cell (e.g. immune cells)
- Intrinsic pathway – signal inside the cell (e.g. DNA damage)
- Important role of caspases (cysteinyl aspartate specific protease)





Condensation and breakdown of chromatin



https://plos.figshare.com/articles/figure/_Confirmation_of_apoptosis_mediated_cell_death_in_HSC_4_cells_through_observation_of_A_DNA_laddering_using_DNA_fragmentation_assay_on_cells_treated_with_CEB4_for_12_and_24_h_followed_by_analysis_of_extracted_DNA_on_0_1_w_v_agarose_gel_electrophoresis_Smea/416013

