The principles of cell division, differentiation. Cell cycle, mitosis, meiosis

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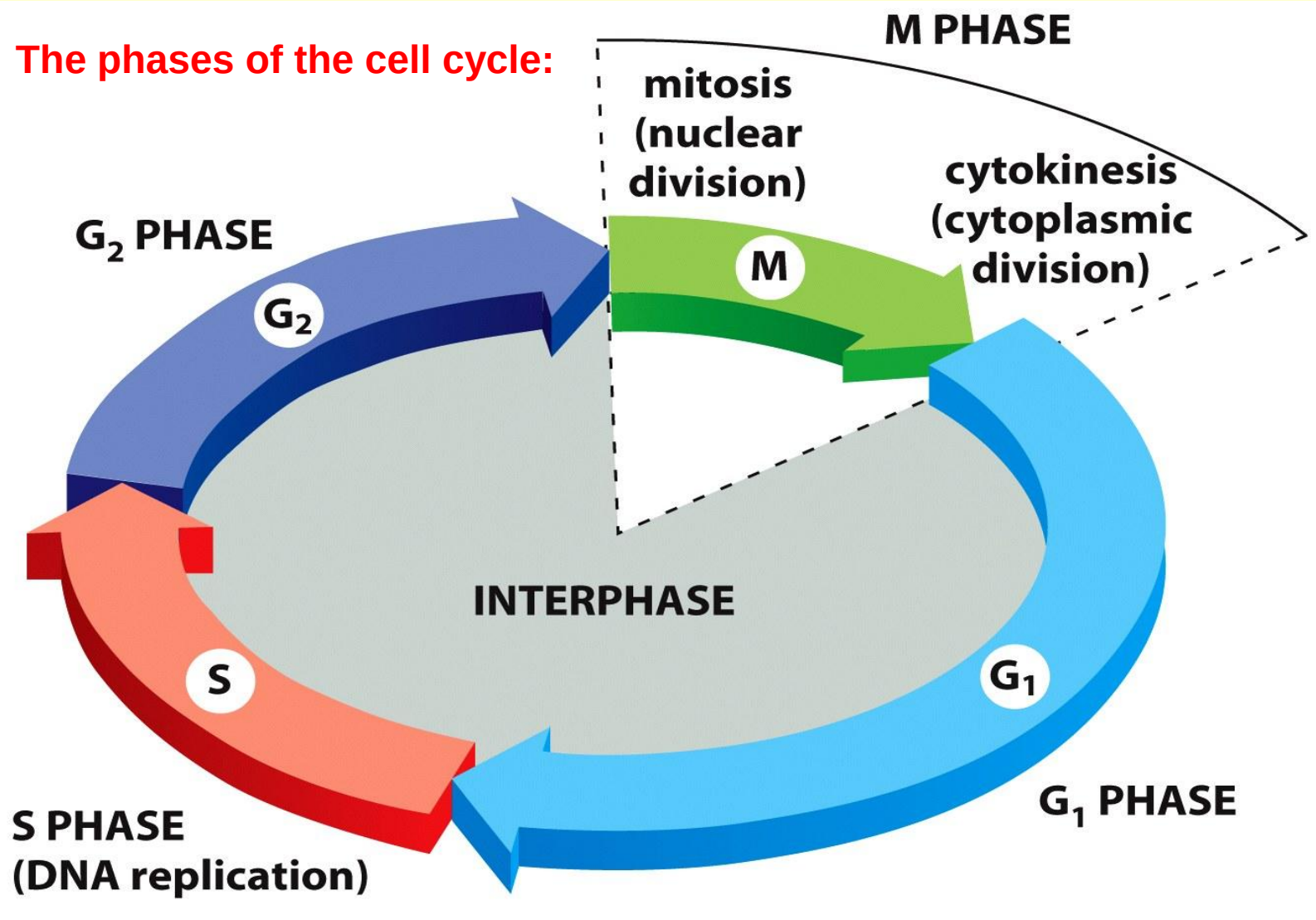
Cell cycle: cell duplication and division

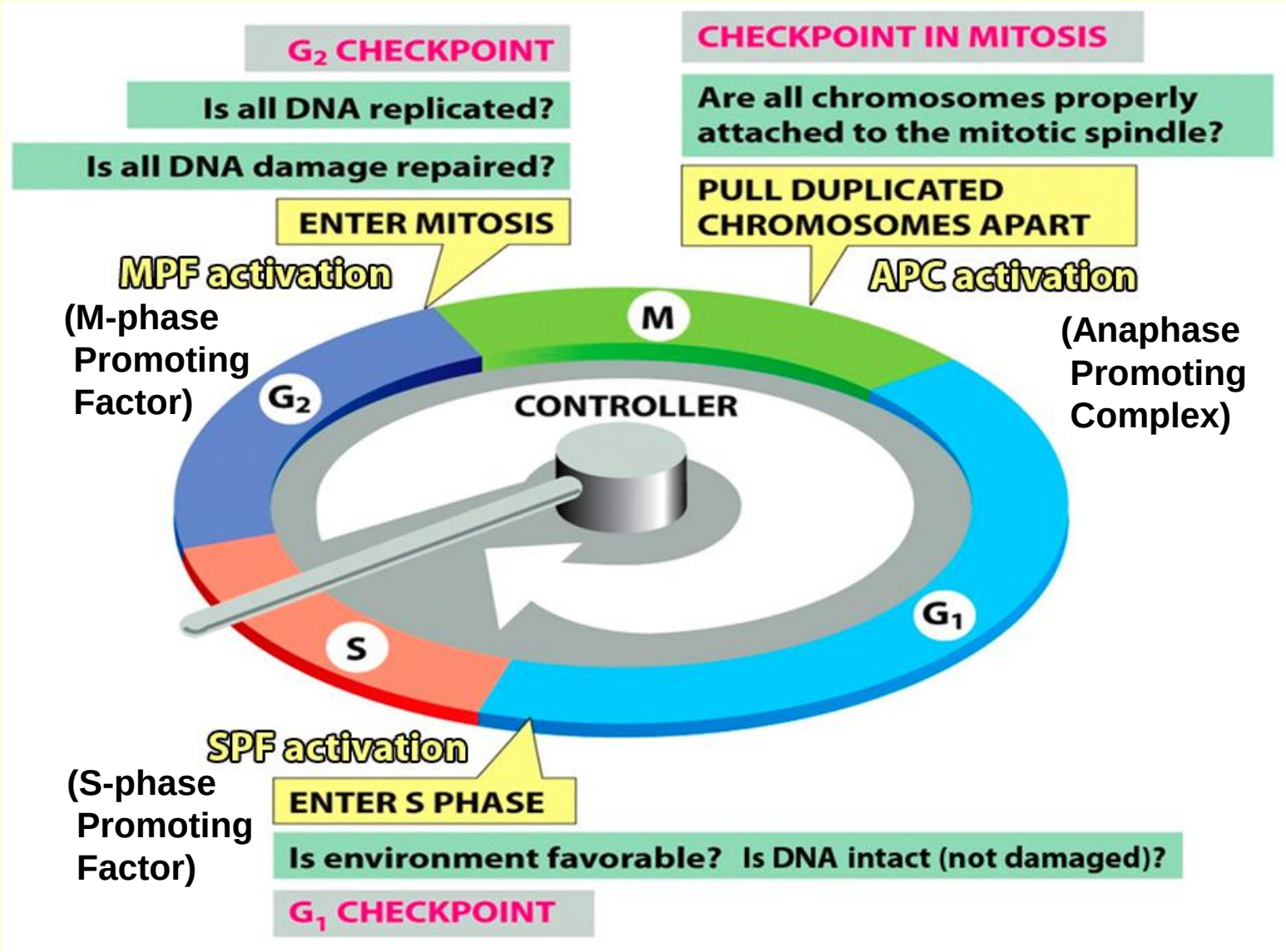


The duration of cell cycle in different eucaryotic cell types

CELL TYPE	CELL-CYCLE TIMES
Early frog embryo cells	30 minutes
Yeast cells	1.5–3 hours
Mammalian intestinal epithelial cells	~12 hours
Mammalian fibroblasts in culture	~20 hours
Human liver cells	~1 year

Table 18-1 *Essential Cell Biology* (© Garland Science 2010)

The check points of the cell cycle



M-phase promoting factor (MPF or M-Cdk) is activated at the G2 checkpoint

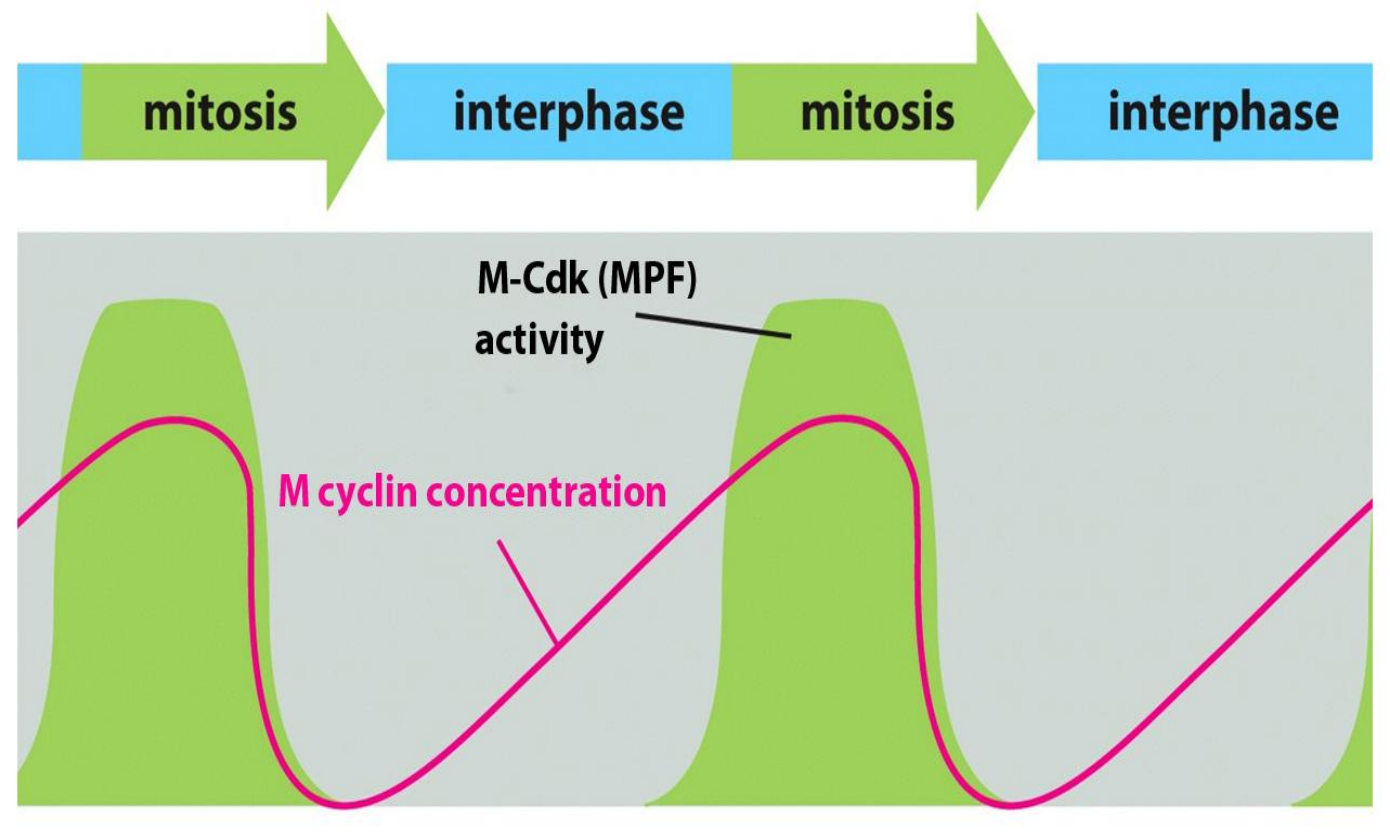
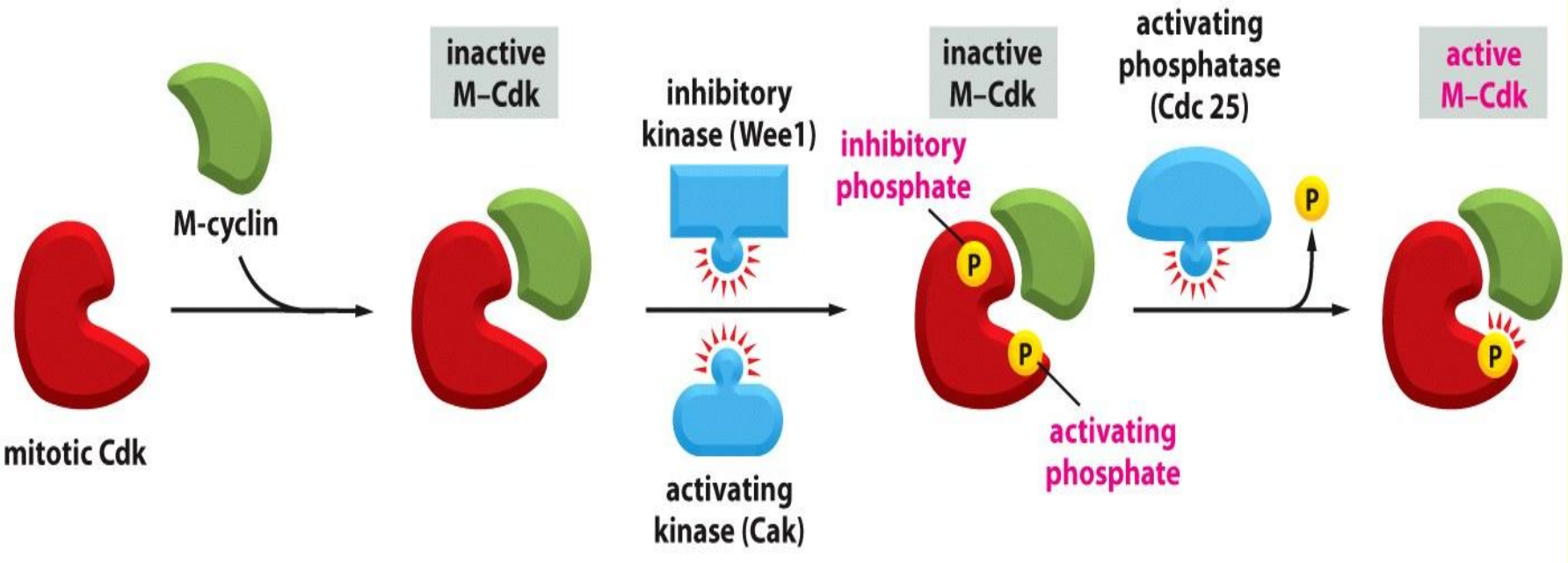


Figure 18-5 *Essential Cell Biology* (© Garland Science 2010)

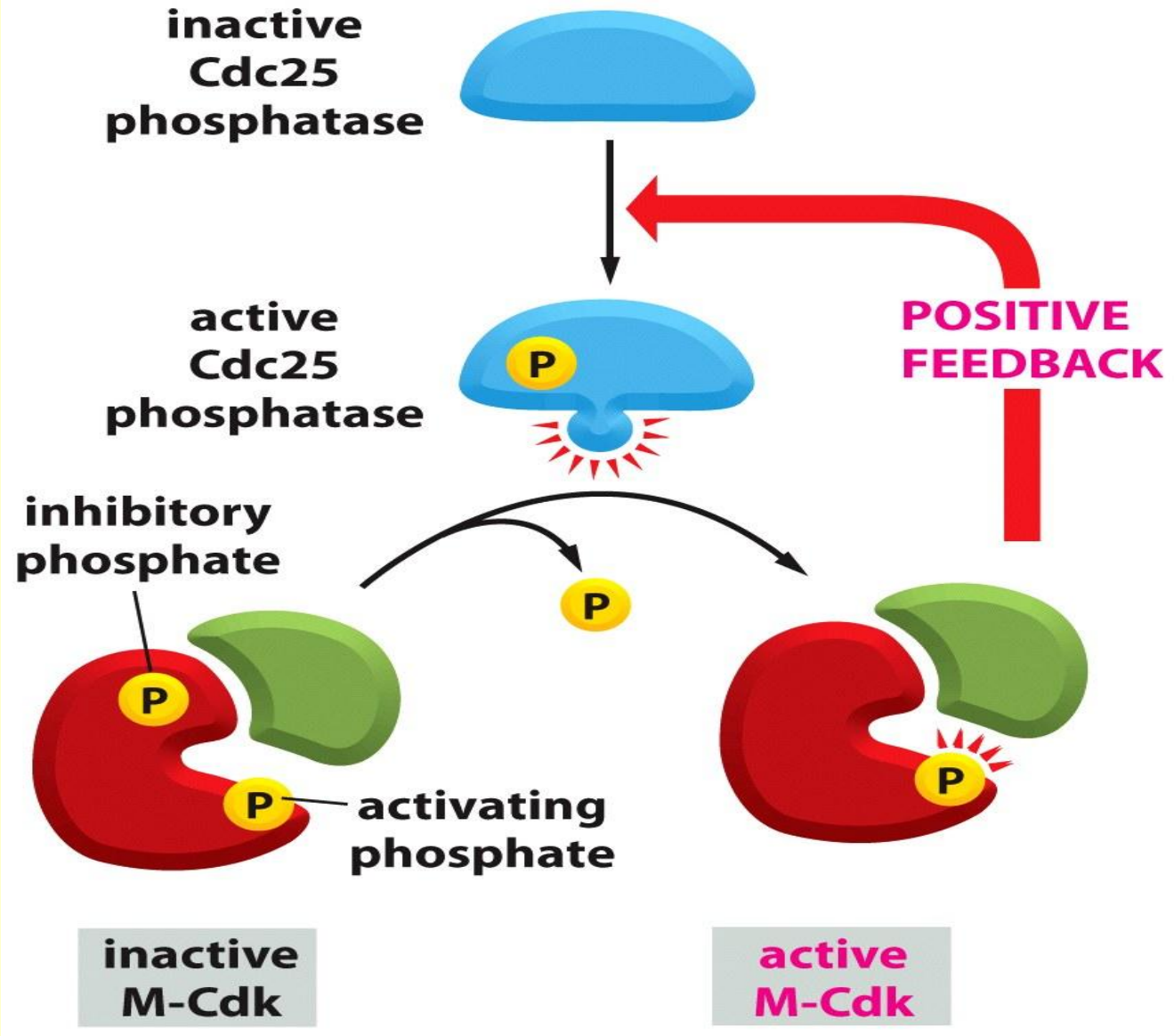
The mechanism of activation of the cyclin-Cdk complexes



Effects of active M-Cdk (MPF):

- termination of gene transcription
- condensation of the chromosomes
- assembly of the mitotic spindle
- breakdown of the nuclear envelope

Positive feedback assures fast activation



The mechanism of inactivation of the cyclin-Cdk complex by APC

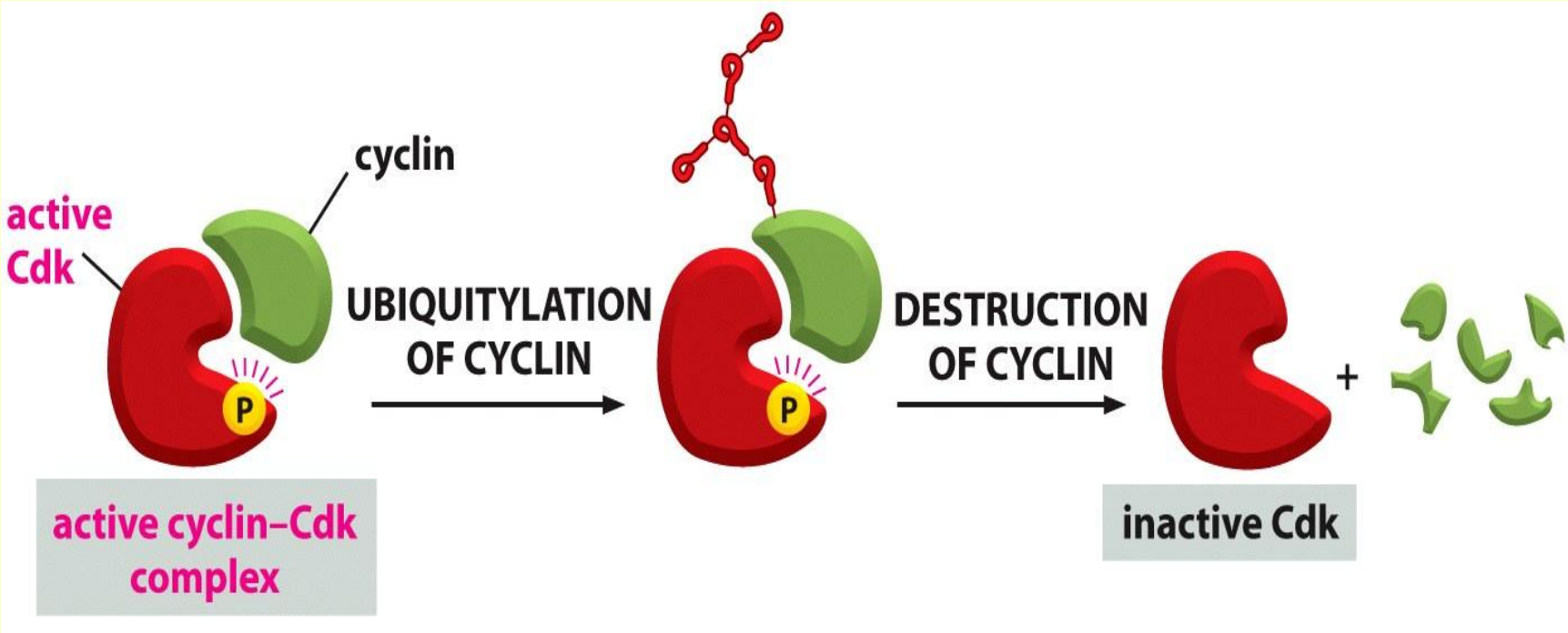


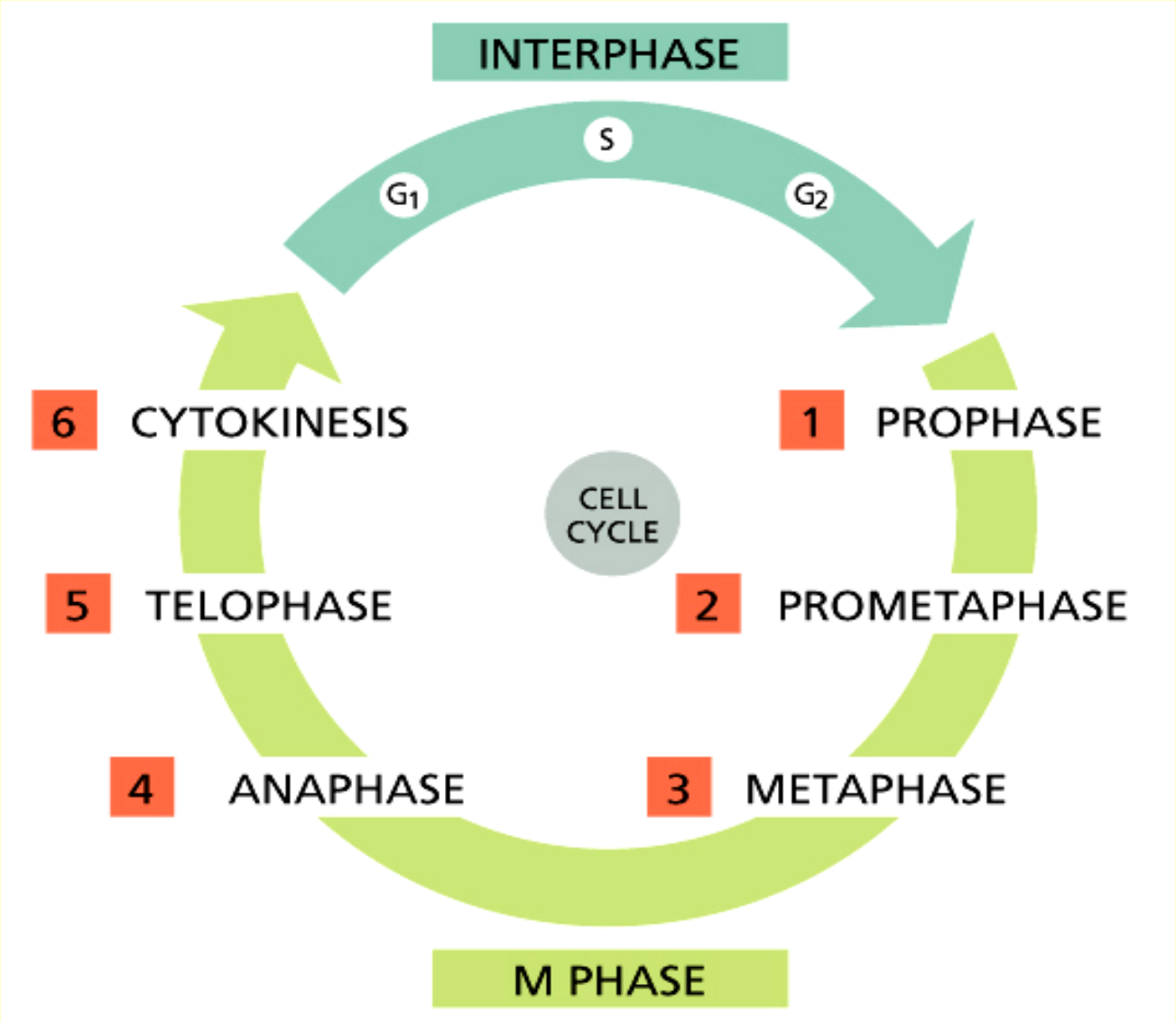
Figure 18-11 *Essential Cell Biology* (© Garland Science 2010)

The major cyclins and cyclin-dependent kinases in vertebrates

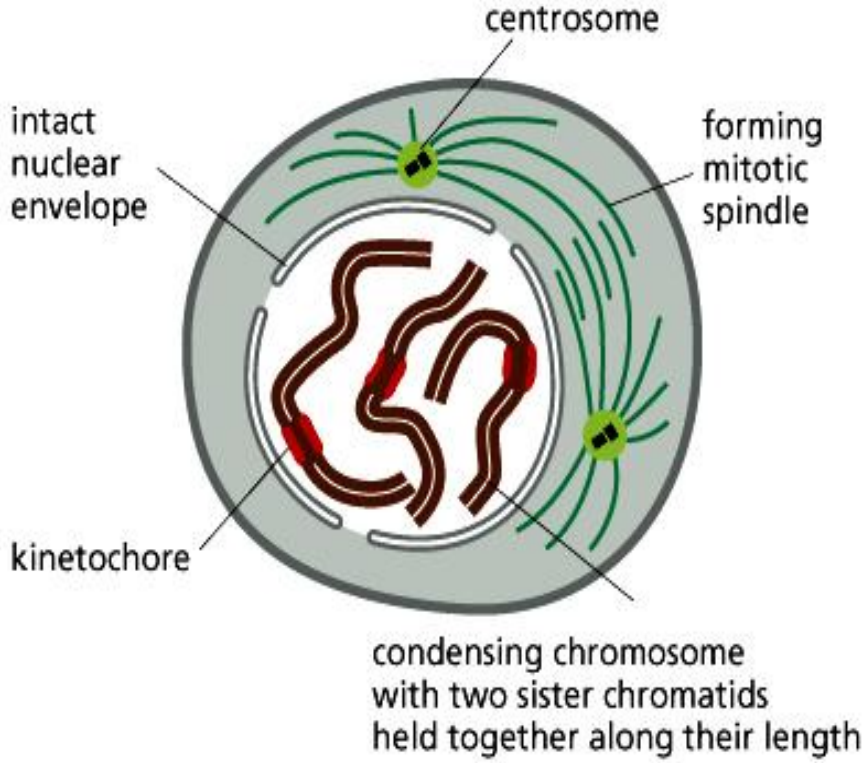
CYCLIN–CDK COMPLEX	CYCLIN	CDK PARTNER
G_1-Cdk	cyclin D* (G1 cyclin)	Cdk4, Cdk6
G_1/S-Cdk	cyclin E (G1/S cyclin)	Cdk2
S-Cdk (SPF)	cyclin A (S cyclin)	Cdk2
M-Cdk (MPF)	cyclin B (M cyclin)	Cdk1

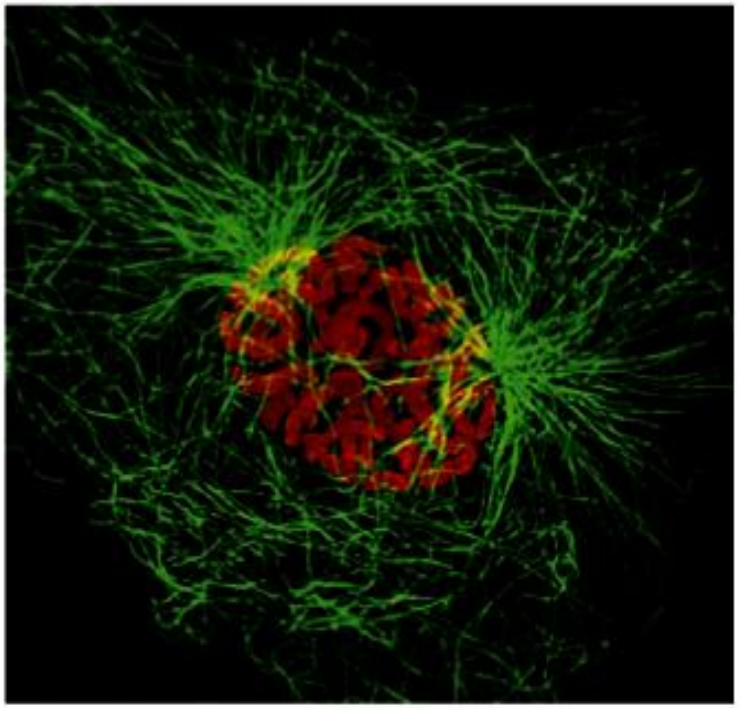
* There are three D cyclins in mammals (cyclins D1, D2 and D3)

Stages of mitosis



1. Prophase





- **The replicated chromosomes condense**
- **The 2 centrosomes begin to move apart**
- **The mitotic spindle assembles outside the nucleus**

Condensins help to coil the mitotic chromatids into compact chromosomes

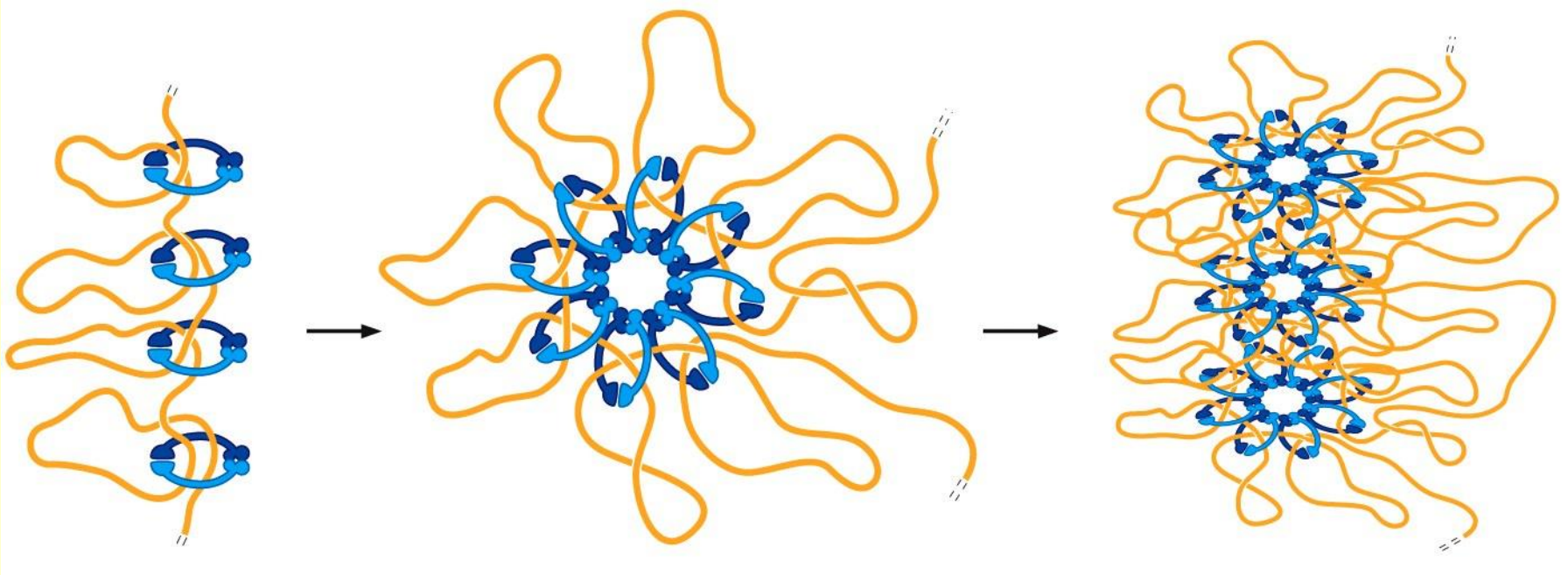
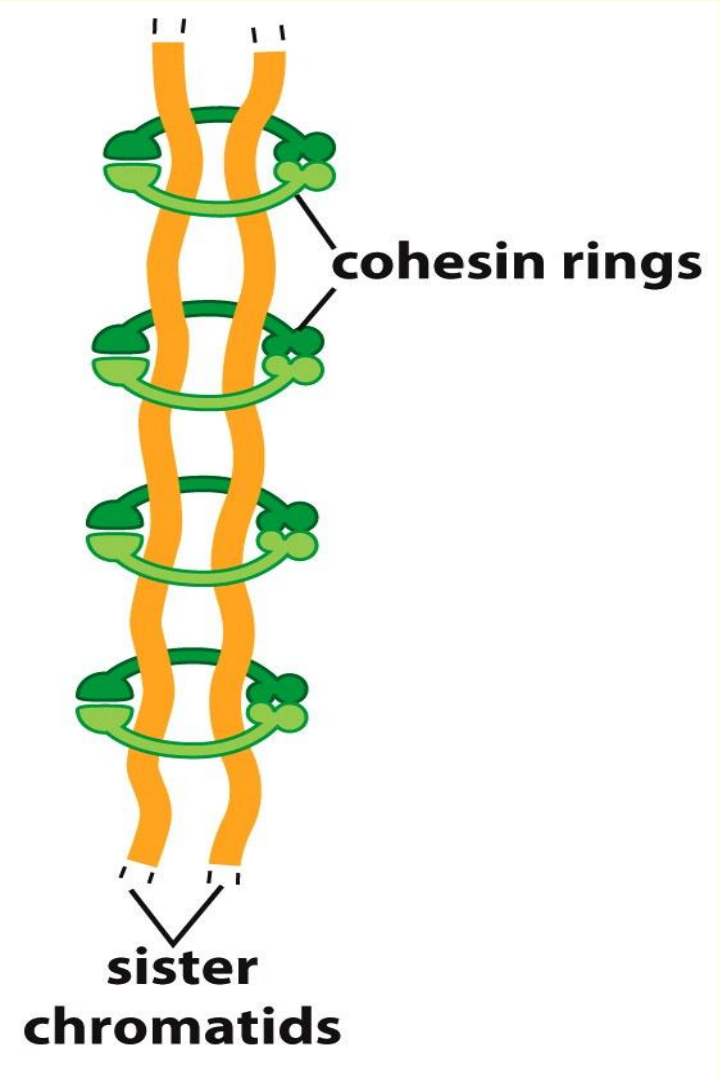
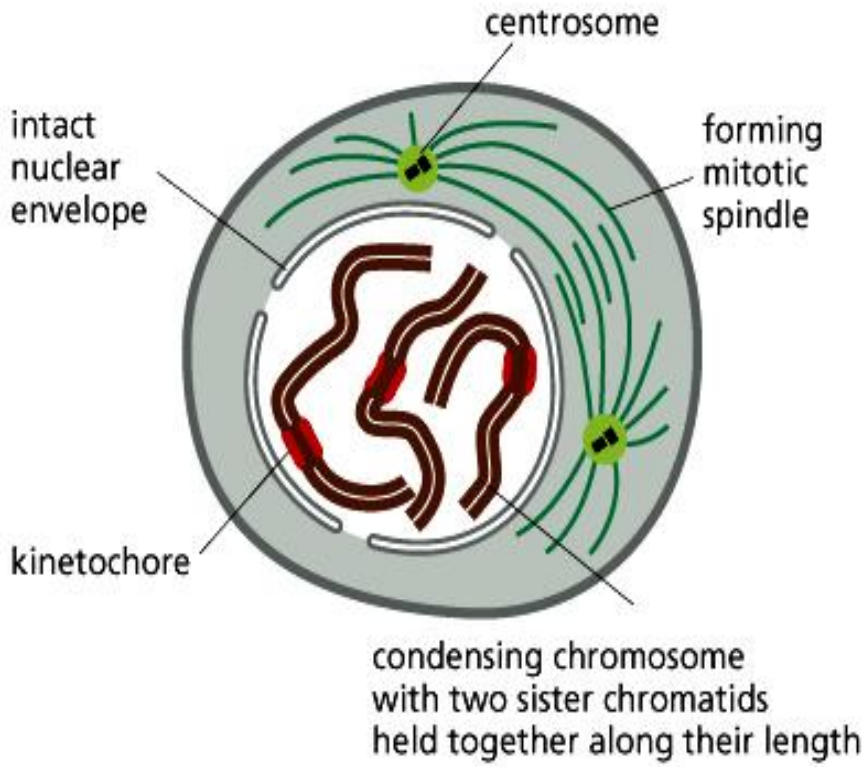


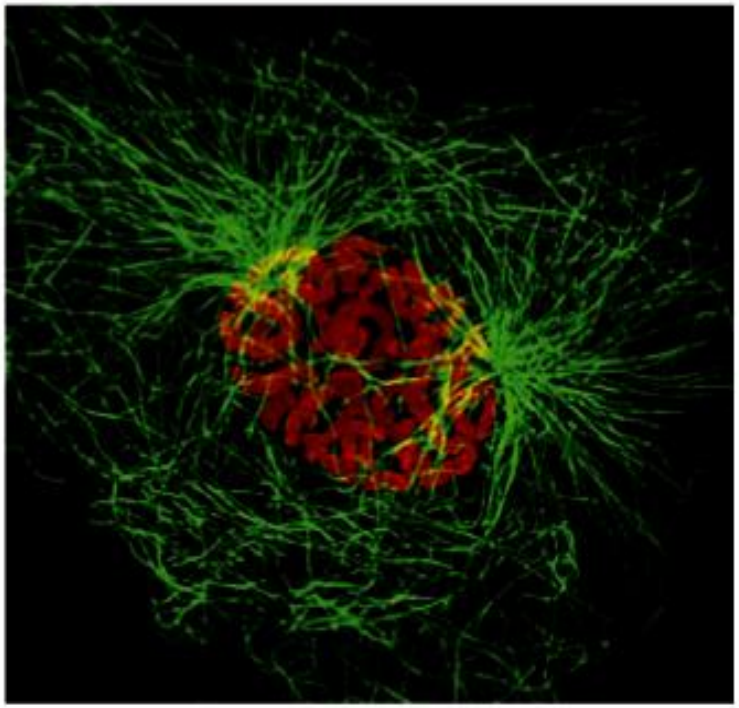
Figure 18-19a *Essential Cell Biology* (© Garland Science 2010)

Cohesins tie together sister chromatids in replicated chromosomes



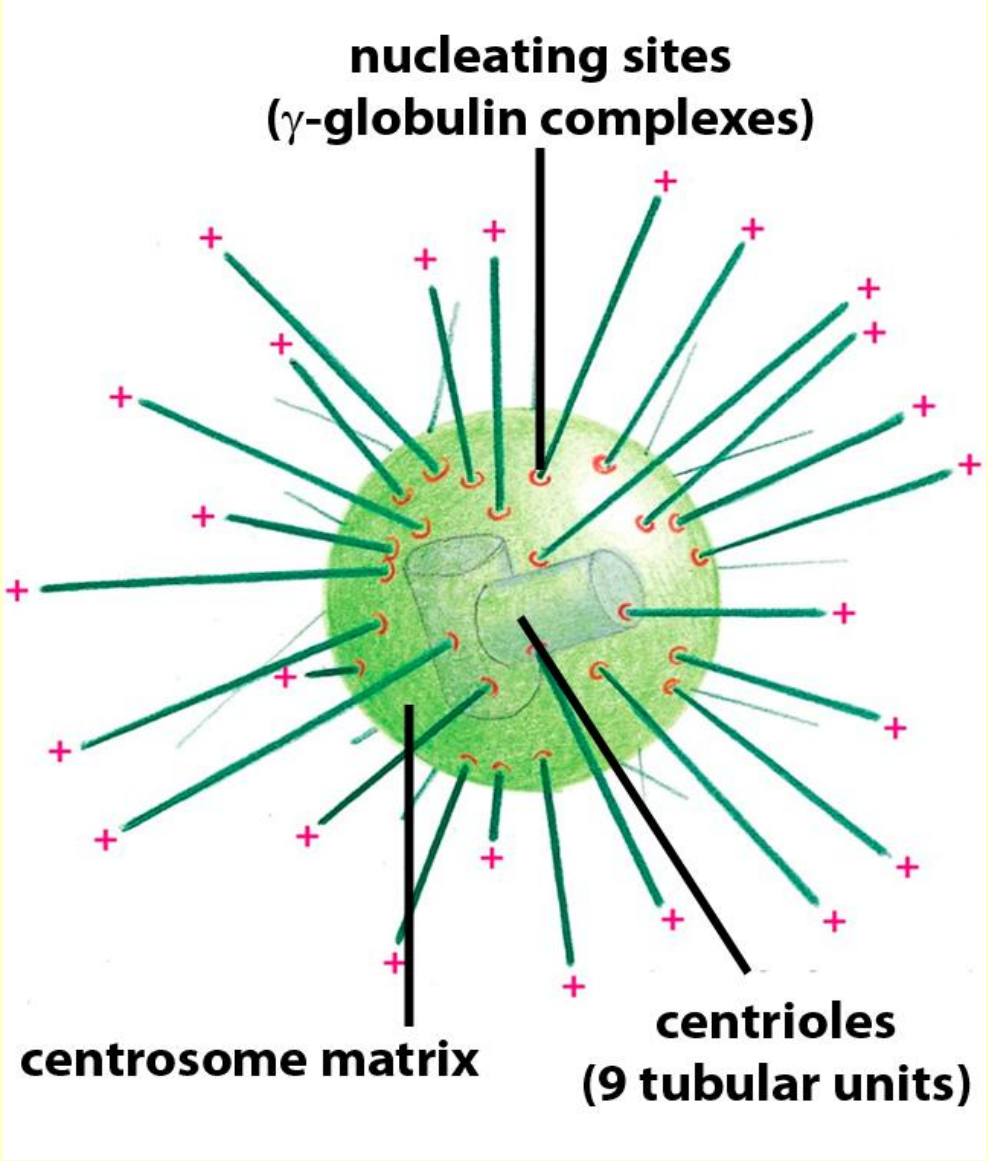
1. Prophase

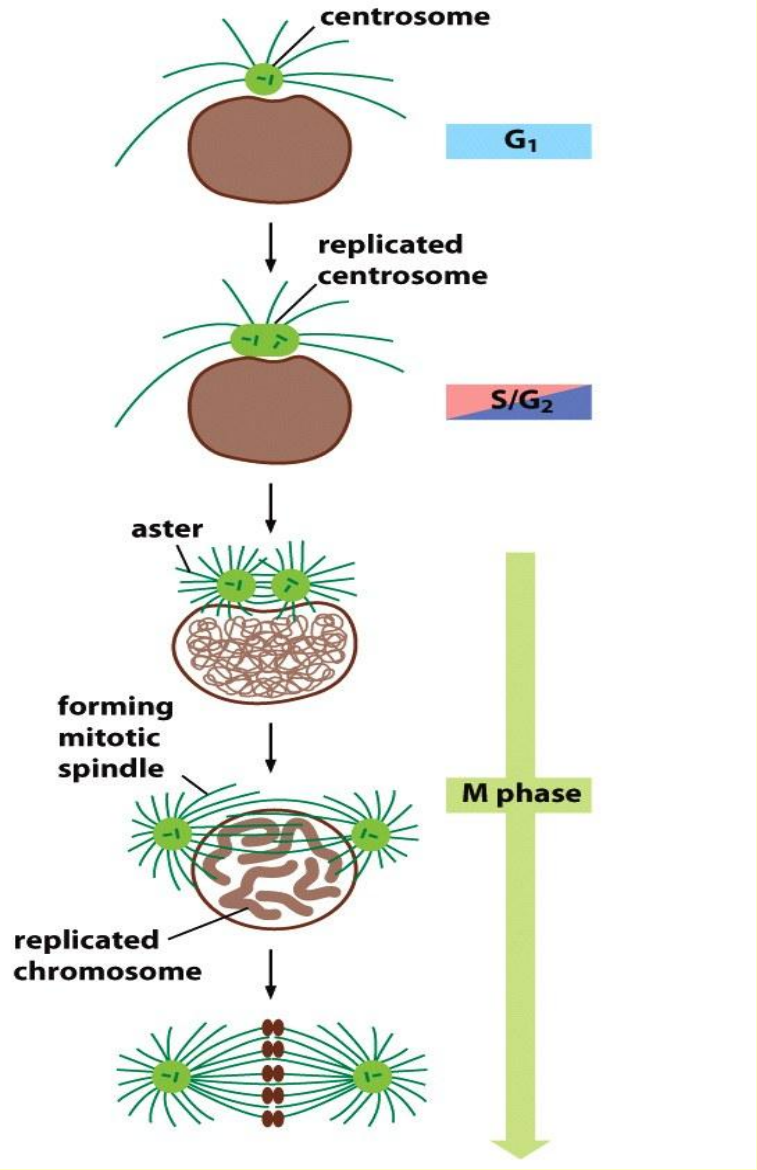




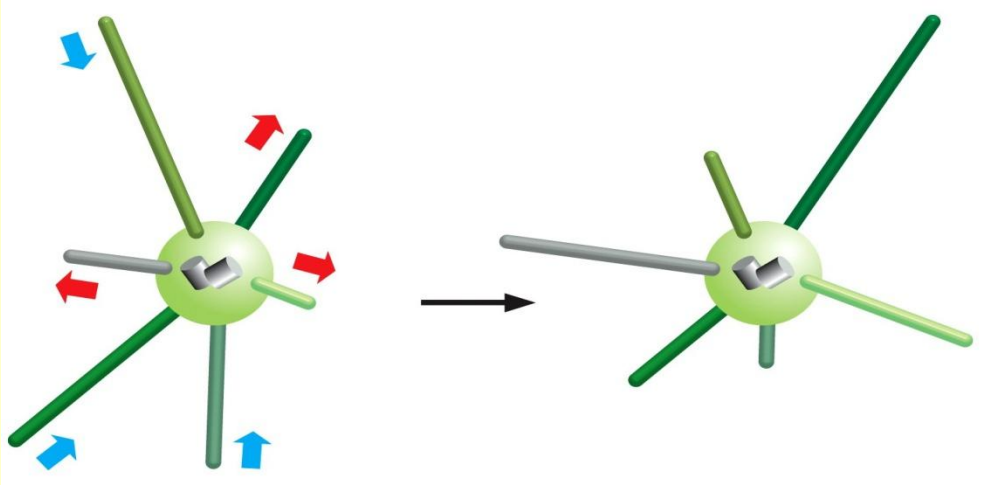
- **The replicated chromosomes condense**
- **The 2 centrosomes begin to move apart**
- **The mitotic spindle assembles outside the nucleus**

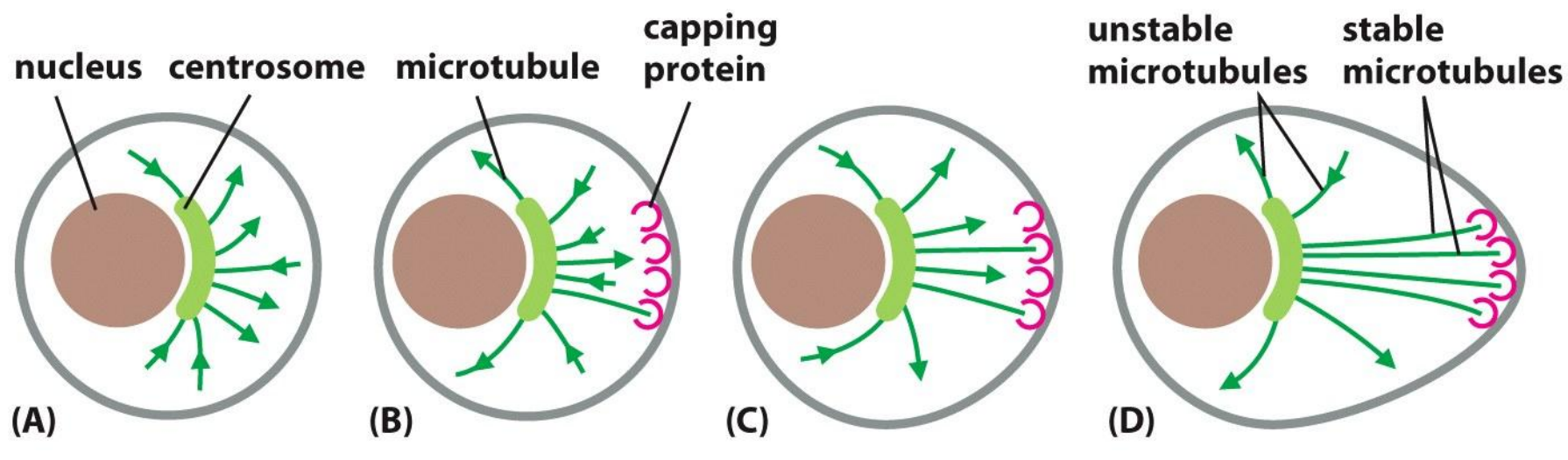
Centrosomes and their duplication





Dynamic instability of microtubules and their stabilization by capping





Microtubules form mitotic spindles during mitosis

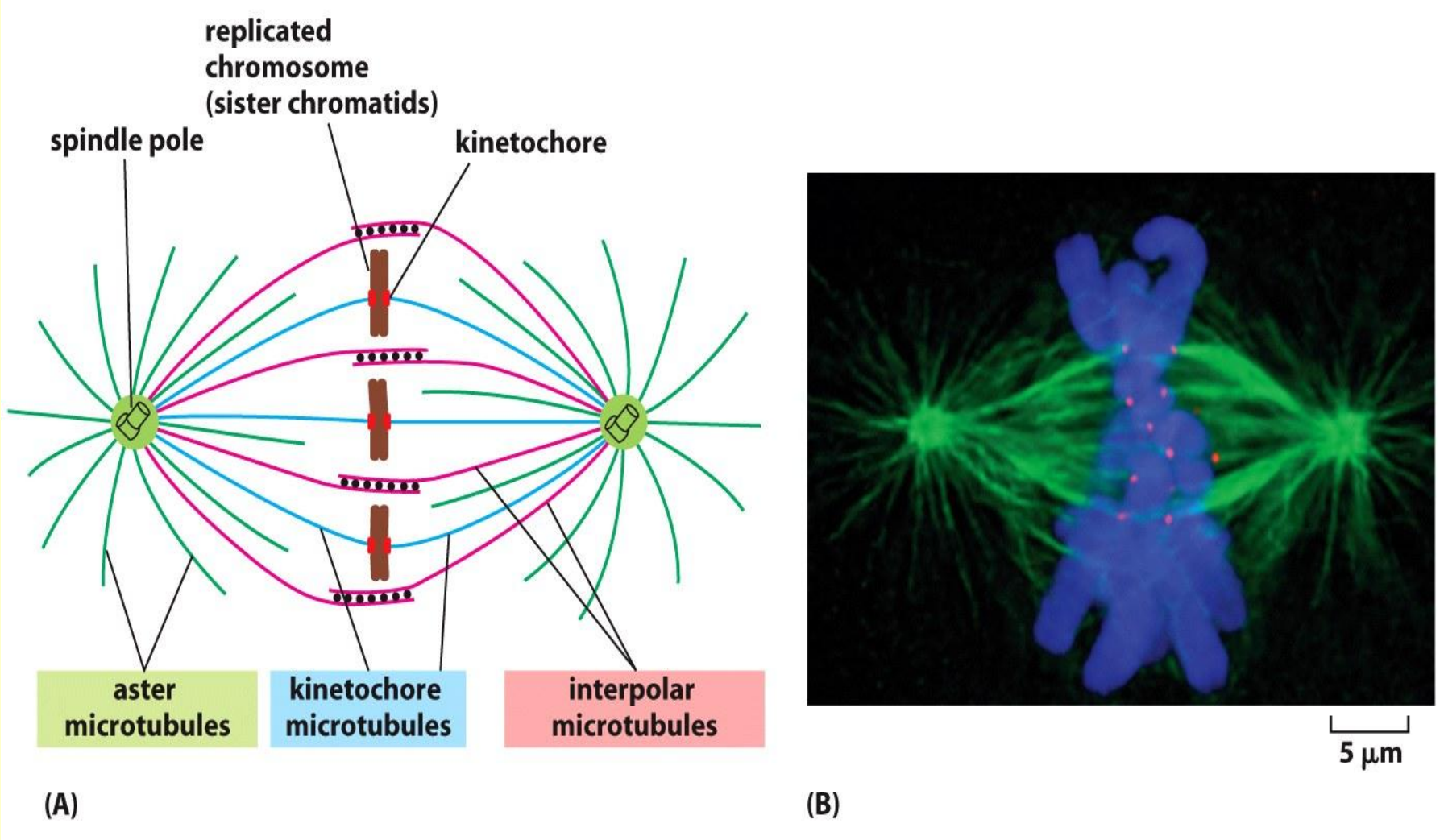
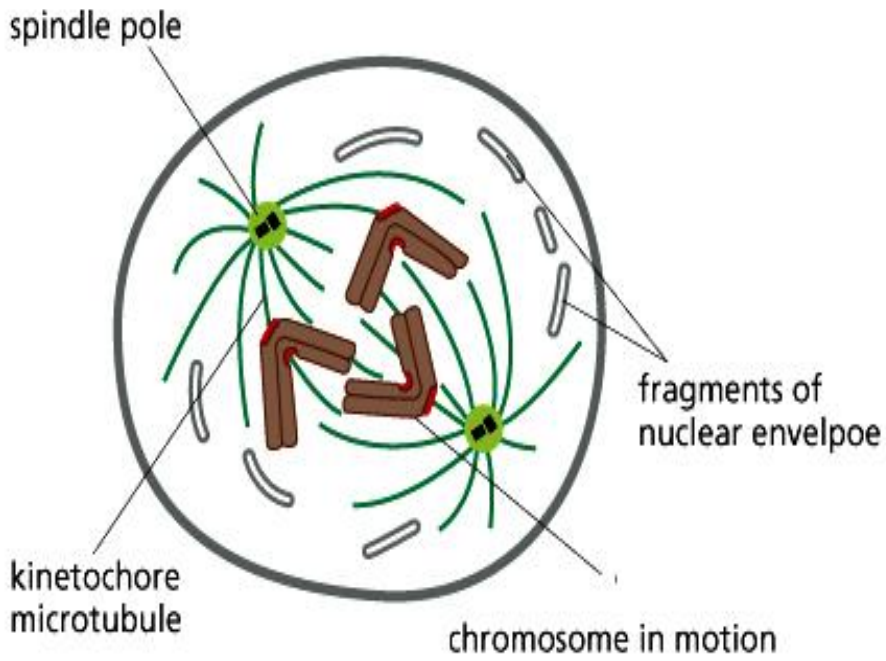
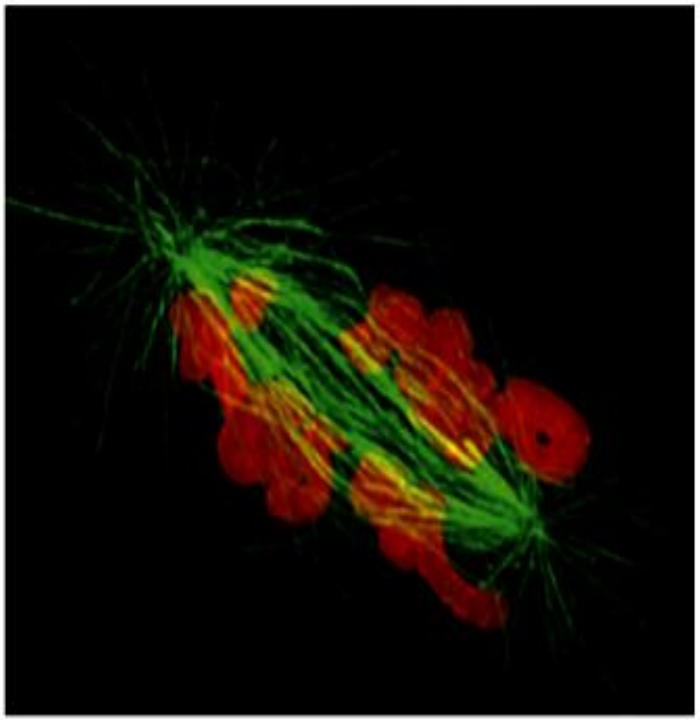


Figure 18-21 *Essential Cell Biology* (© Garland Science 2010)

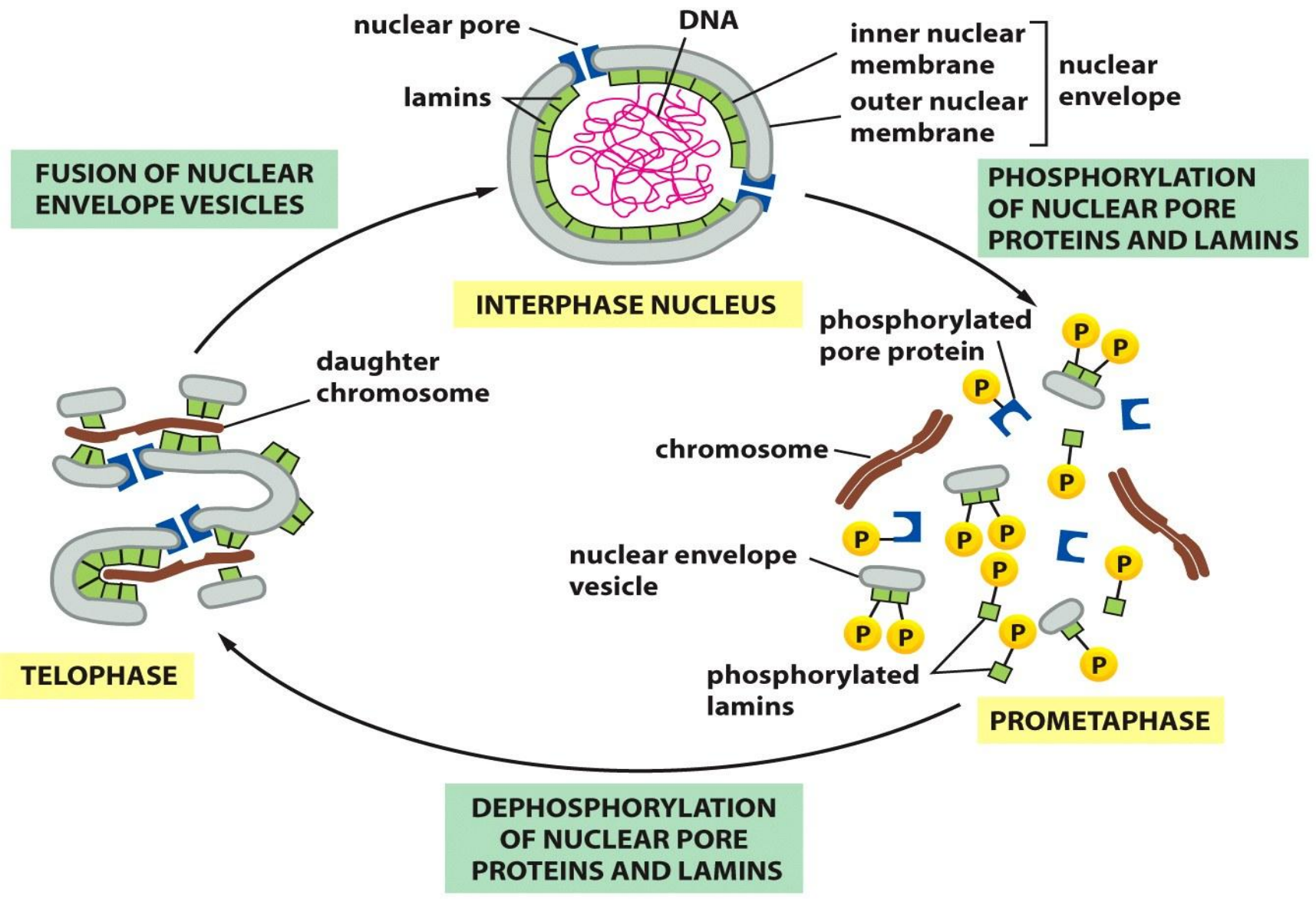
2. Prometaphase



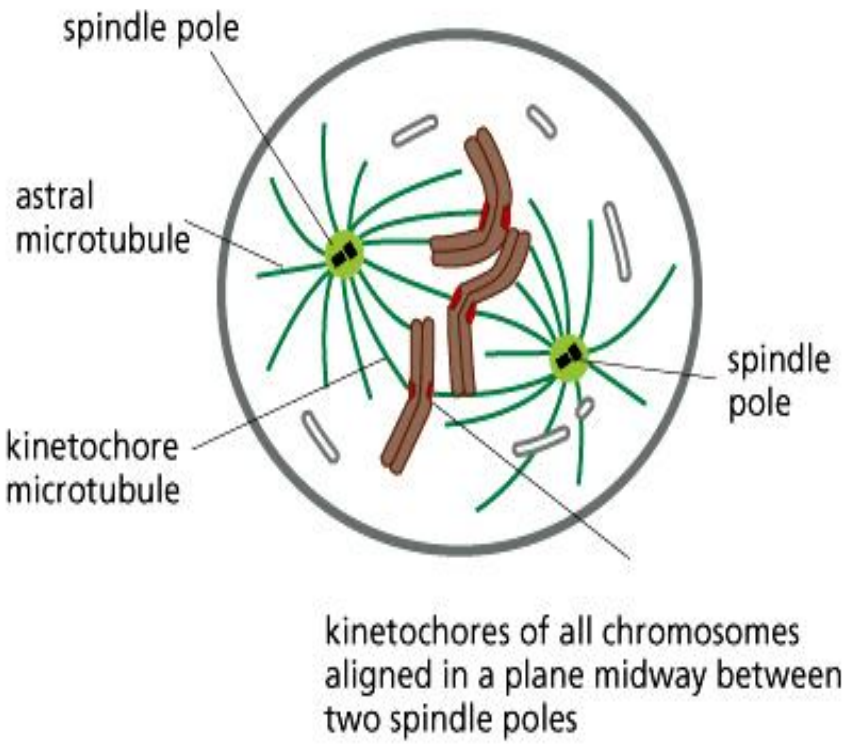


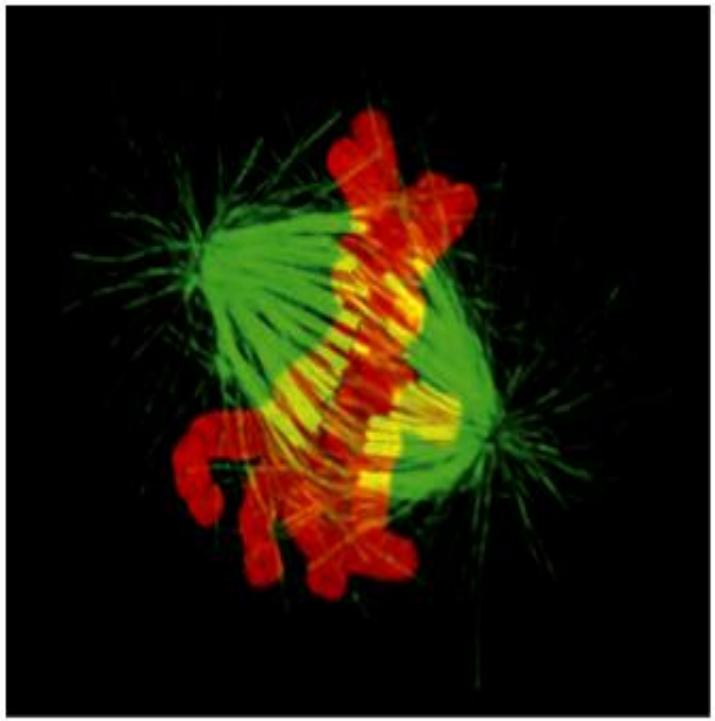
- **The nuclear envelope breaks down**
- **Chromosomes attach to spinde microtubulues**

Disassembly of the nuclear envelope during mitosis



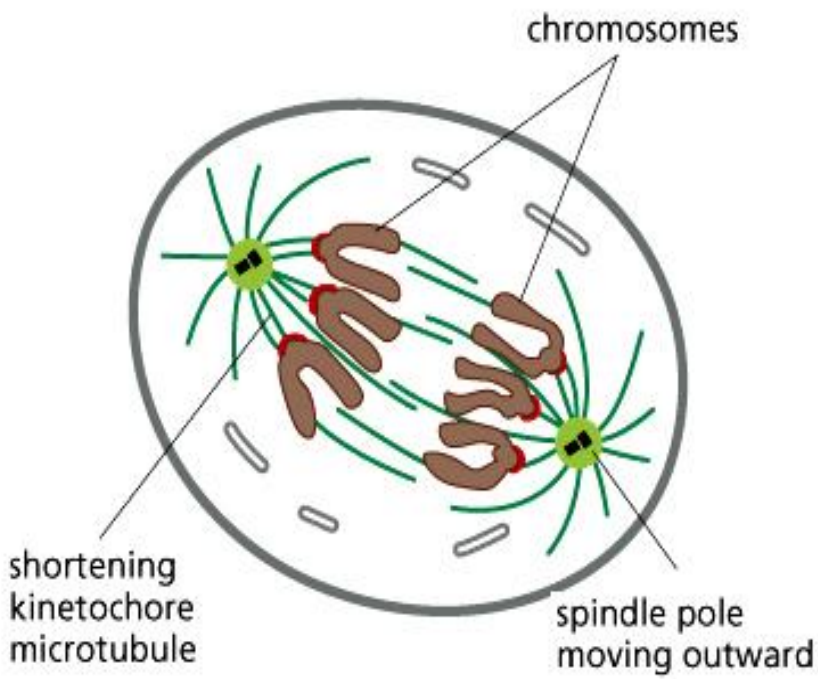
3. Metaphase

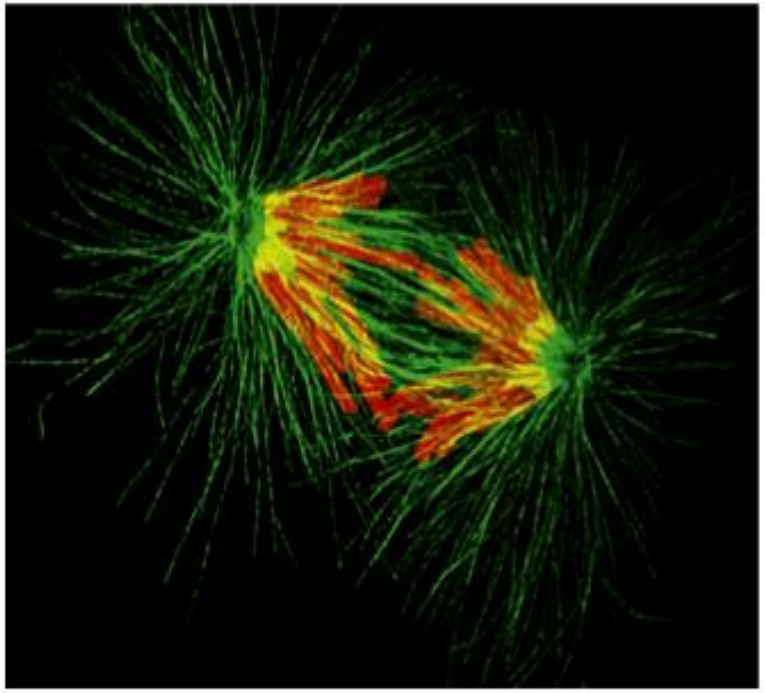




- **The chromosomes align at the equator of the spindle**

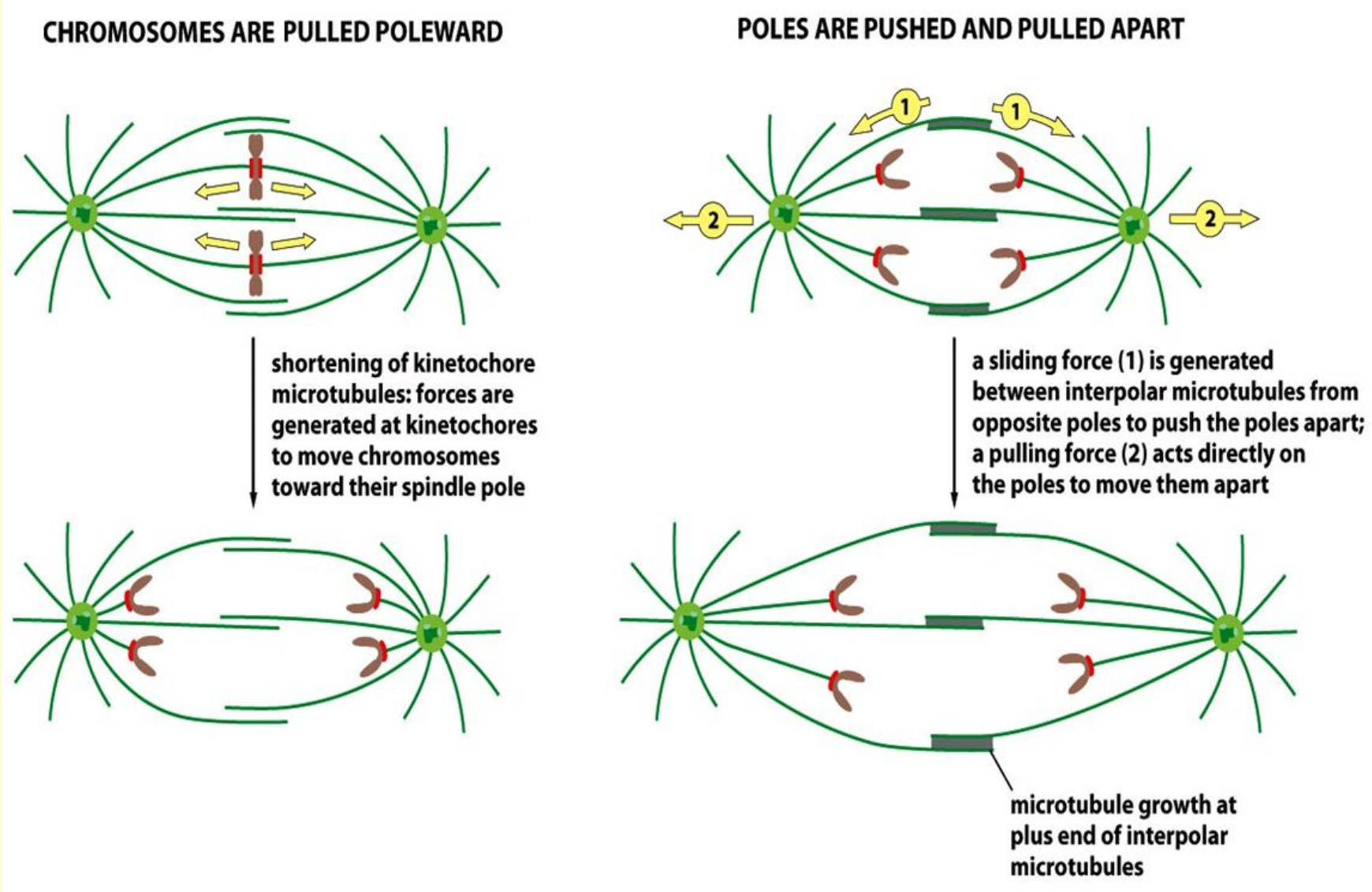
4. Anaphase



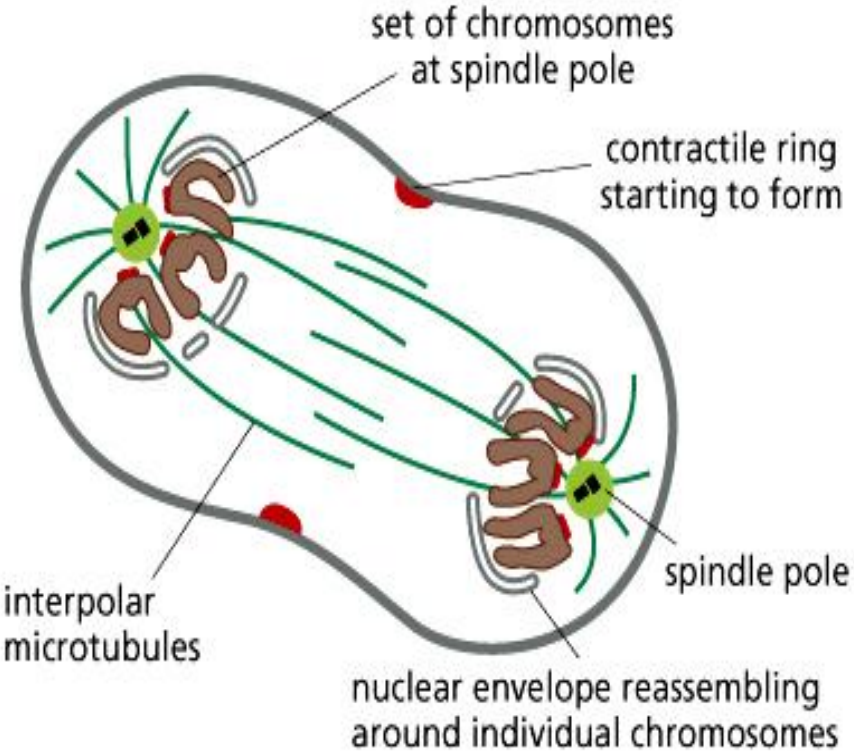


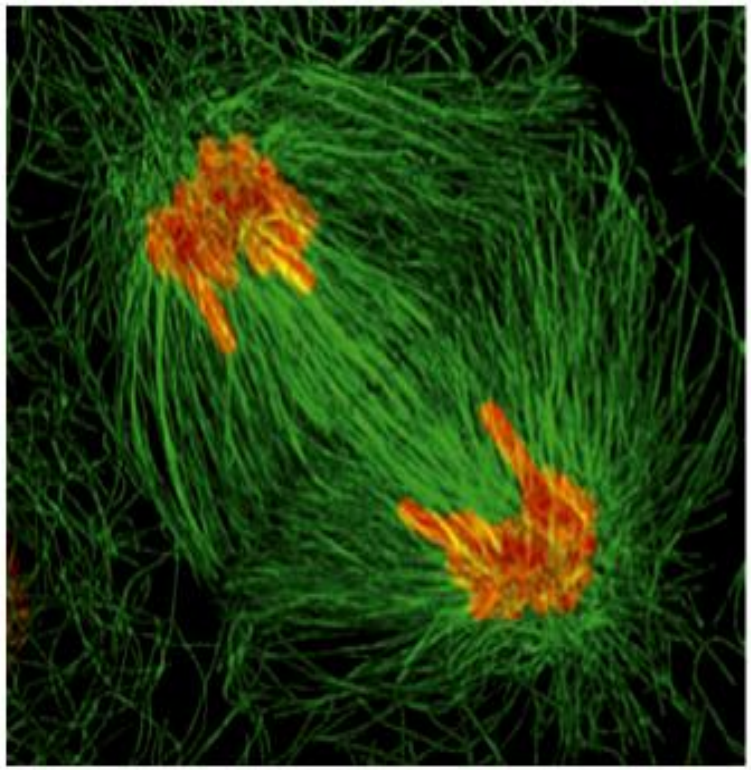
- **Anaphase promoting complex (APC), a ubiquitin kinase, degrades M cyclin thereby terminating the activity of MPF**
- **APC degrades cohesins allowing the separation of sister chromatides**
- **The kinetochor microtubules get shorter and pull chromatides towards the spindle poles**
- **The spindle poles move apart**

Mitotic spindles segregate daughter chromosomes



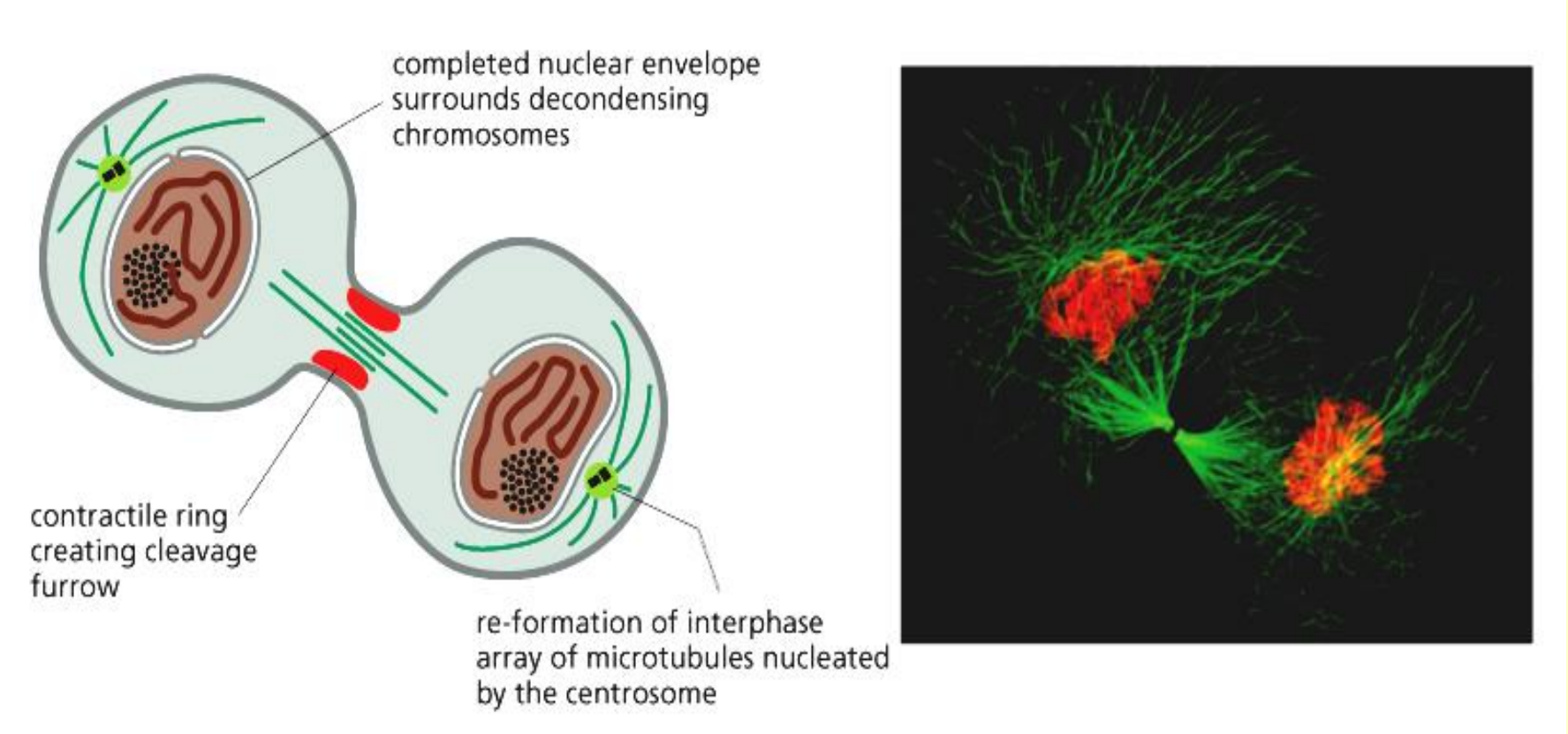
5. Telophase





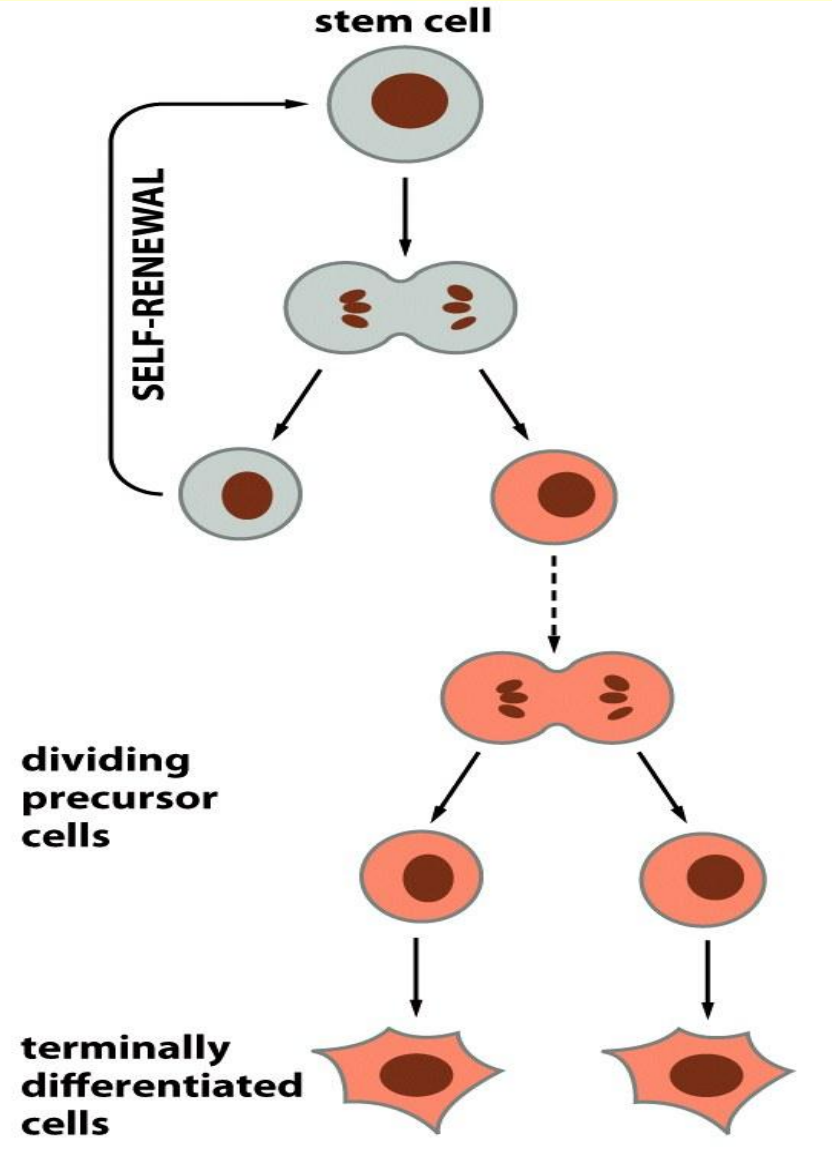
- **The two sets of chromosomes arrive at the spindle poles**
- **Two nuclear envelopes are reassembled**

6. Cytokinesis



- **The cytoplasm is divided into two by a contractile ring formed by actin and myosin**

Cell types of mitosis: stem cells and progenitor cells

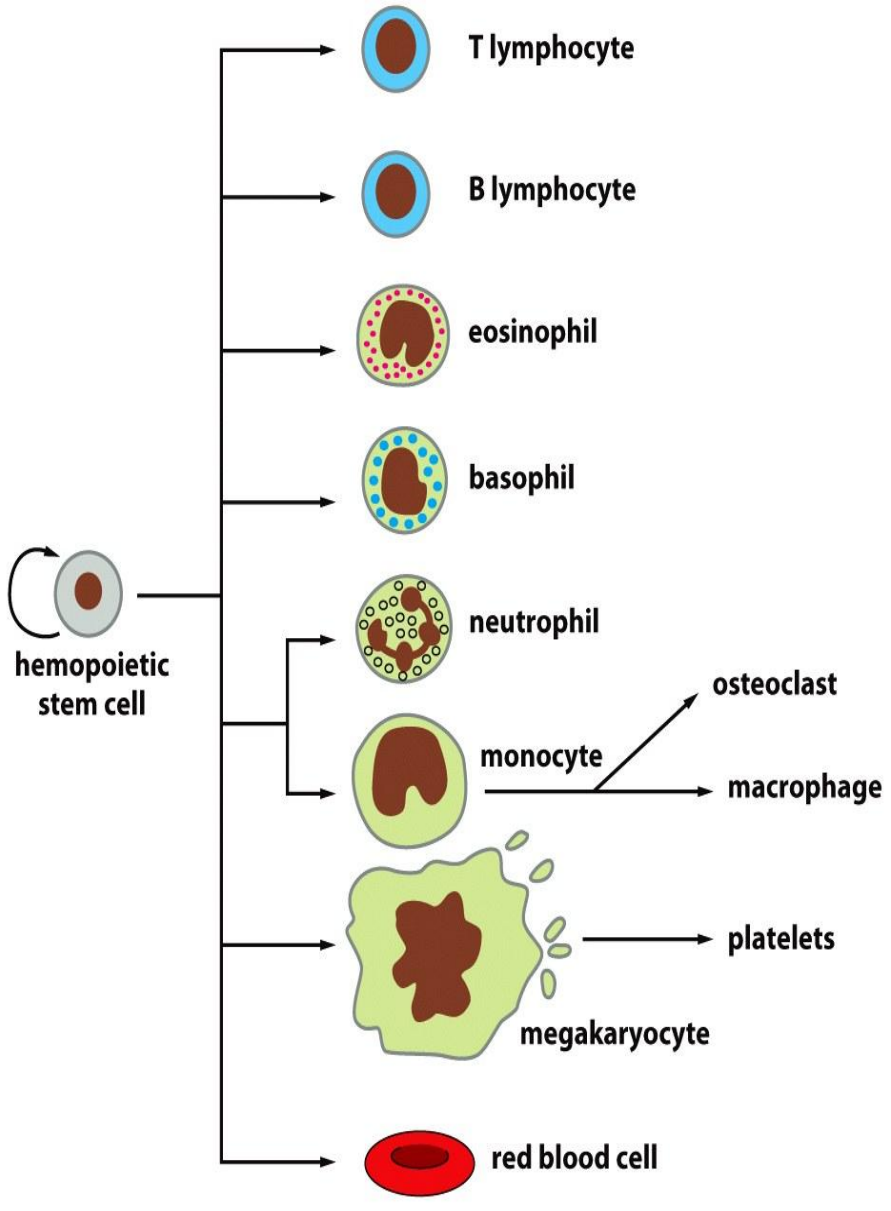


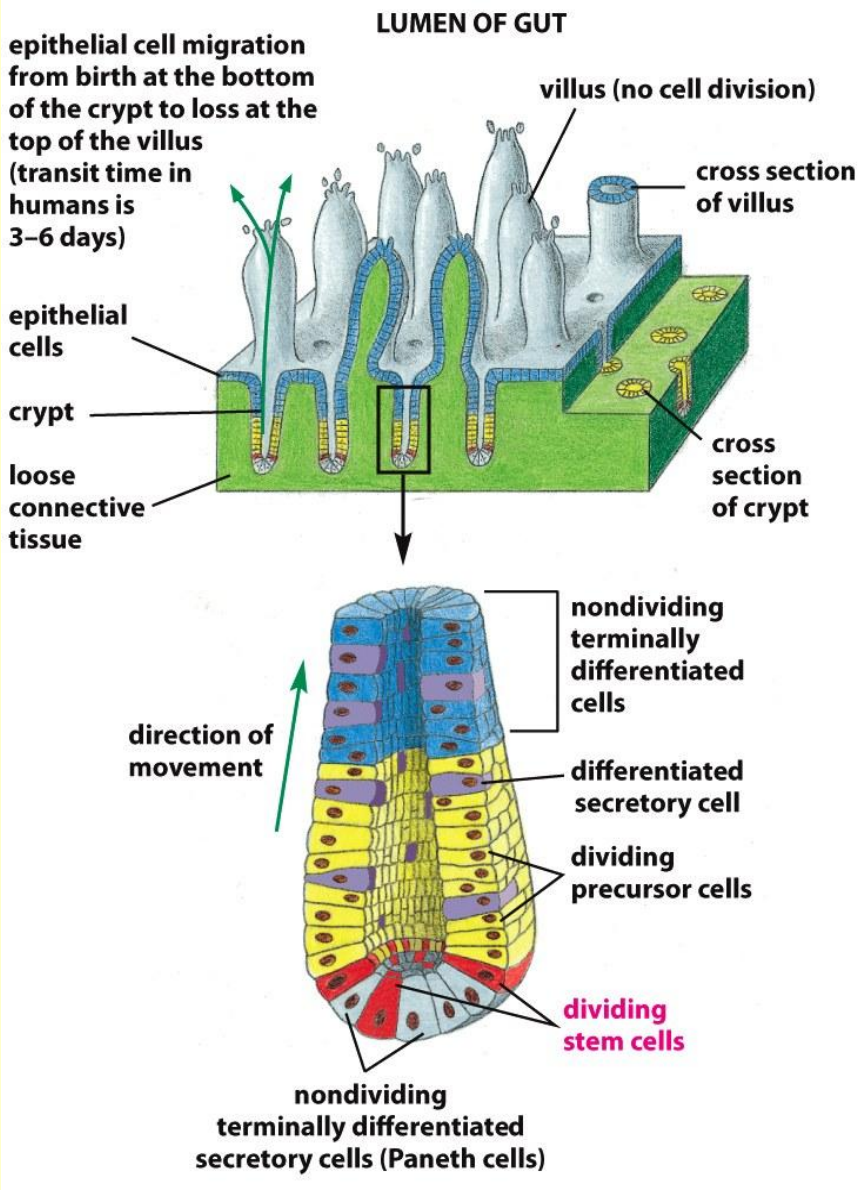
Stem cells
At least one of the daughter cells is identical with the mother cell, the other may differentiate to a progenitor cell.
The number of their mitosis is not limited.

Progenitor (precursor) cells
Transitory amplifiers: they divide into 2 identical daughter cells without self-renewing.
Differentiation into determined cell types.
The number of mitosis is limited.

Hayflick limit: cultured cells can undergo no more than 50 mitosis, probably because of insufficient telomerase activity.

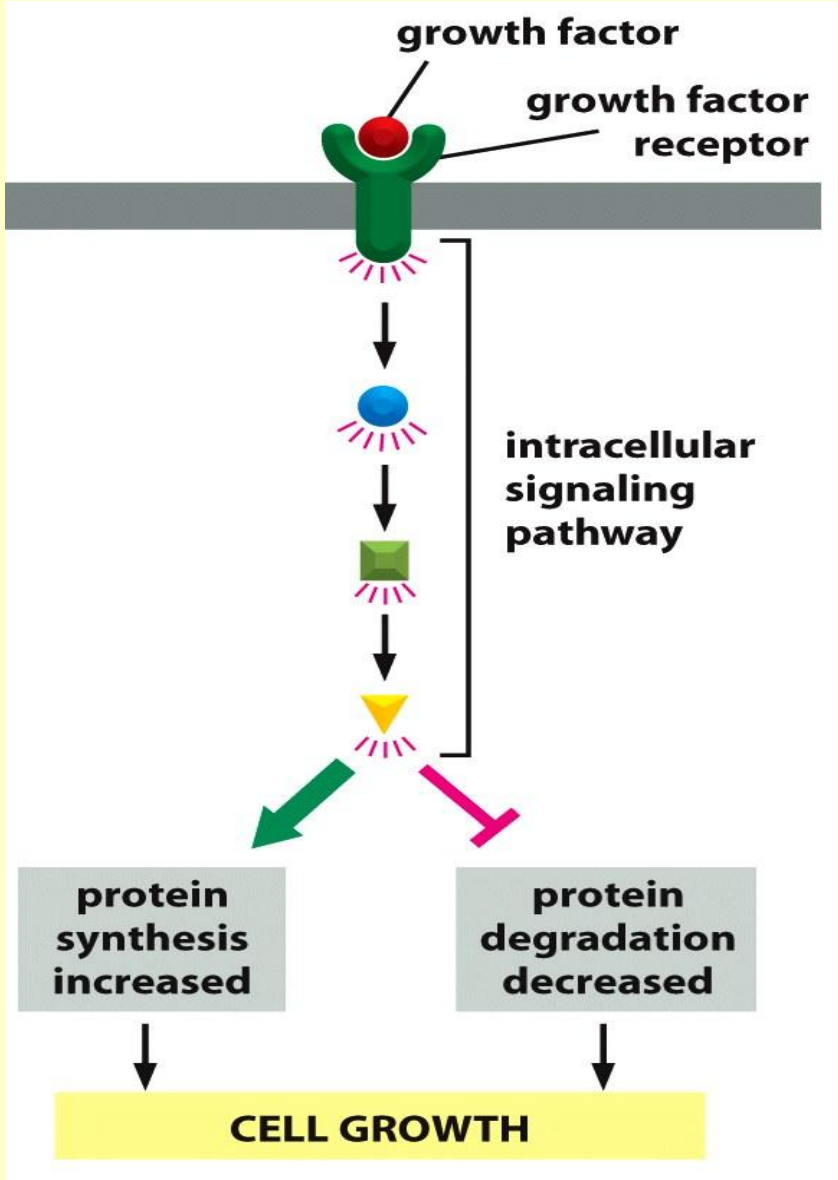
Examples of stem cells



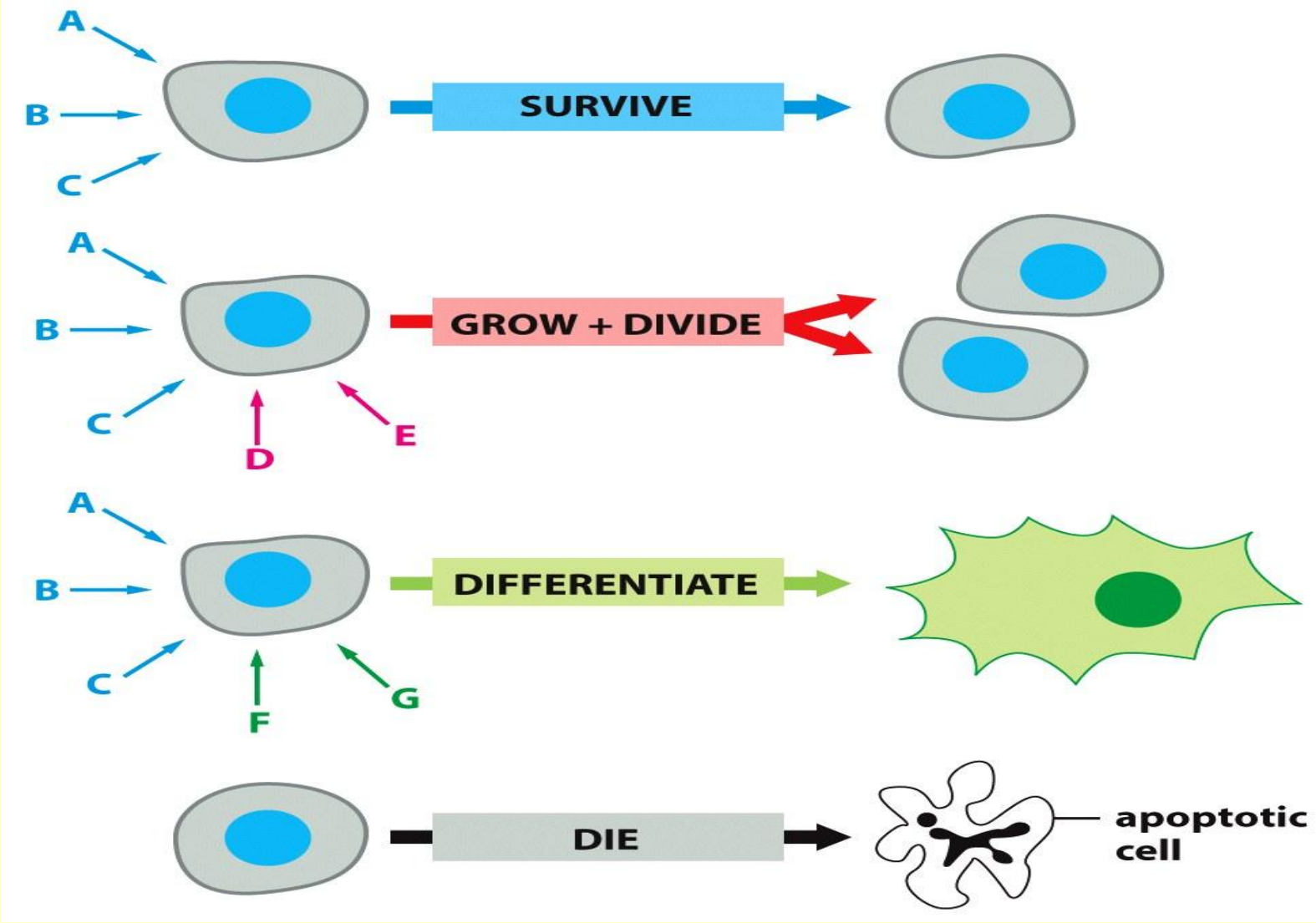


Extracellular control of the cell cycle in multicellular organisms

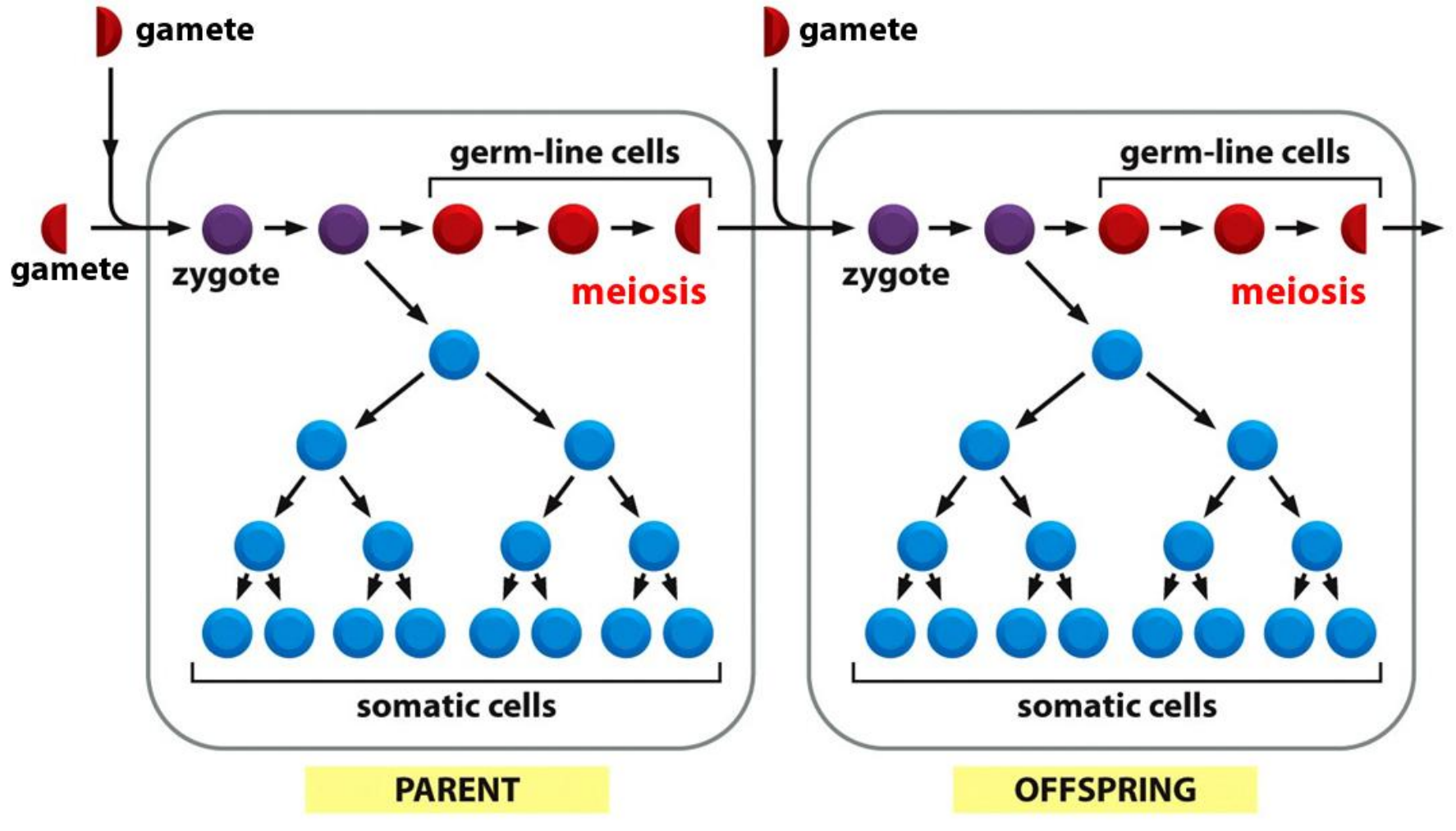
1. Growth factors regulate cell size
2. Mitogens regulate proliferation
3. To divide, most cells require surface attachment to focal contacts (laminin or fibronectin)
4. Contact inhibition: most cells stop proliferation when they already form a continuous layer
5. Factors resulting in differentiation are often also called growth factors. Growth factors, which promote differentiation usually inhibit proliferation



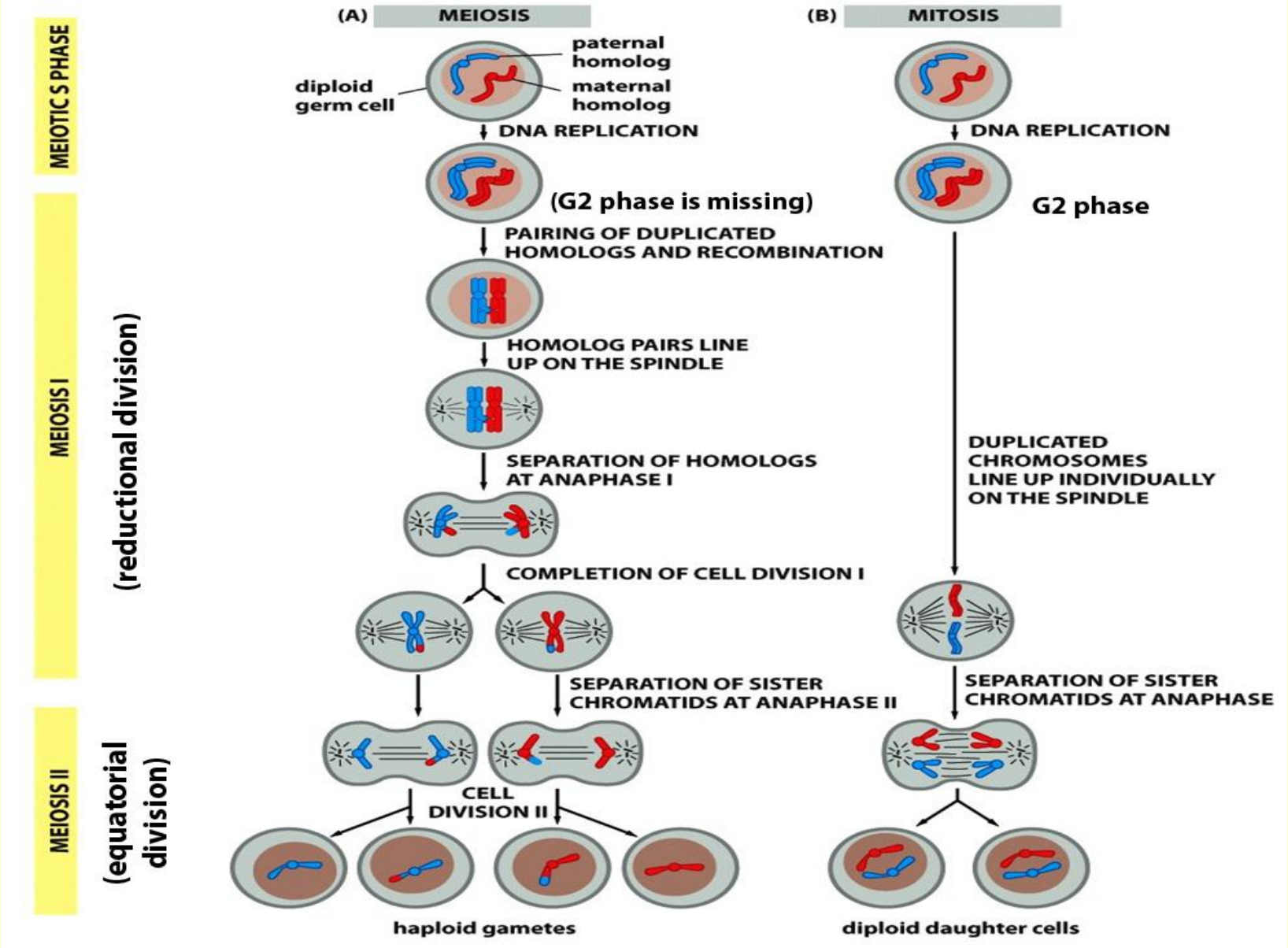
The general functions of growth factors



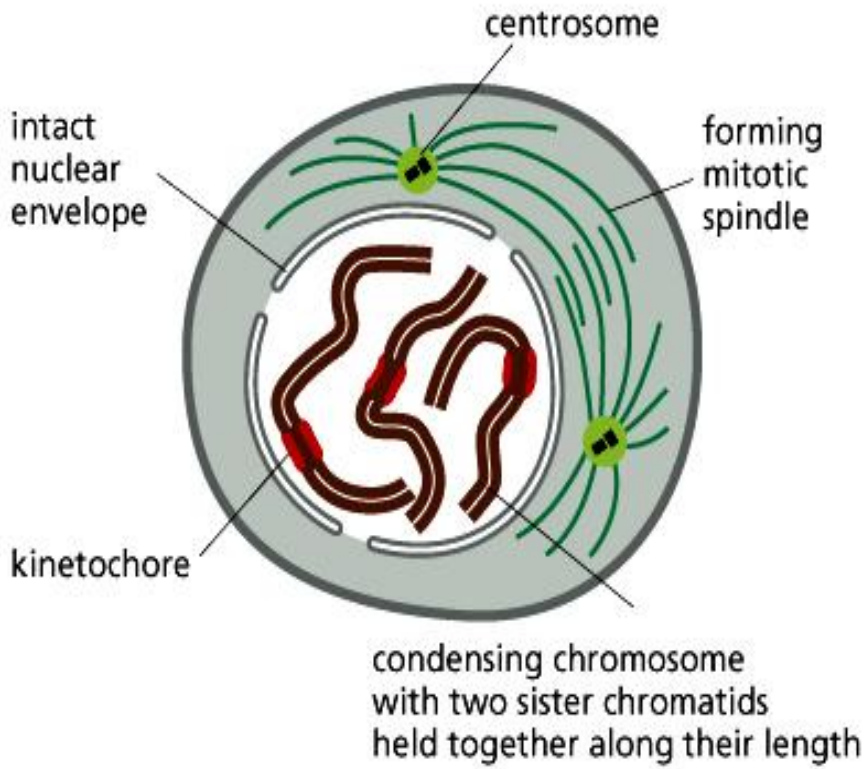
Propagation of genetic information in sexually reproducing animals

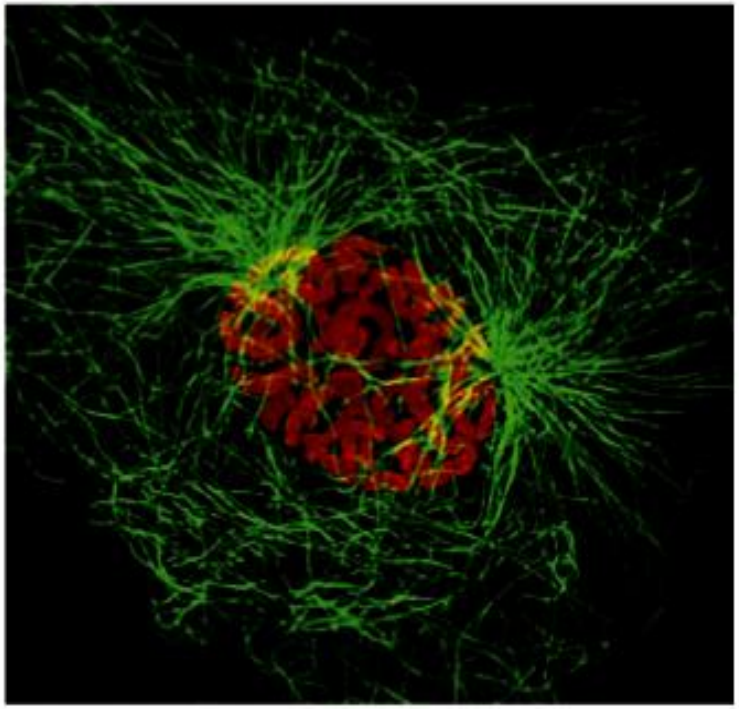


Meiotic cell division: comparison with mitosis



Prophase of mitosis



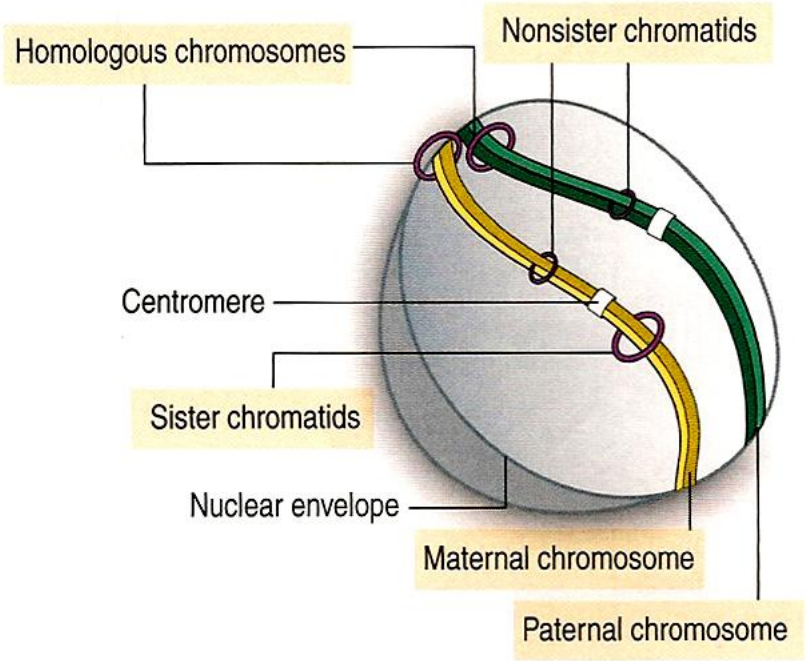


- **The replicated chromosomes condense**
- **The 2 centrosomes begin to move apart**
- **The mitotic spindle assembles outside the nucleus**

Stages 1 and 2 of prophase in meiosis I

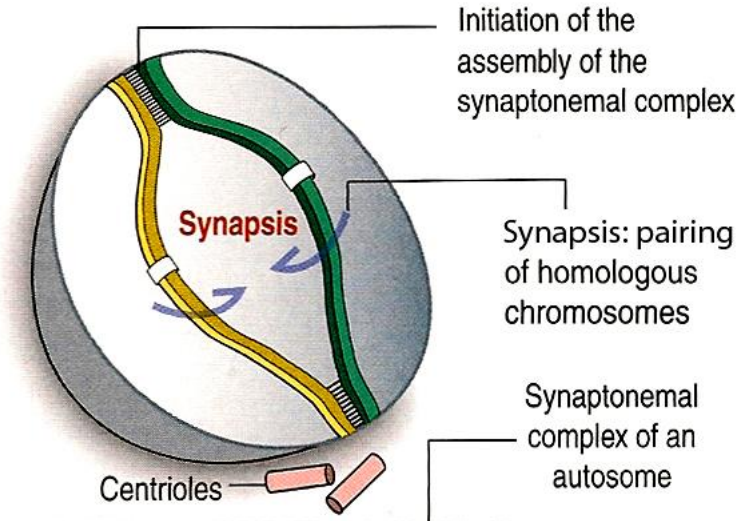
A Leptotene (thin threads)

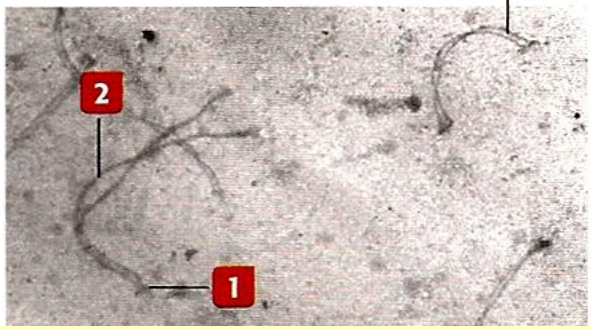
Each homologous chromosome consists of two **sister** chromatids. Chromosomes attach to the inner membrane of the nuclear envelope.



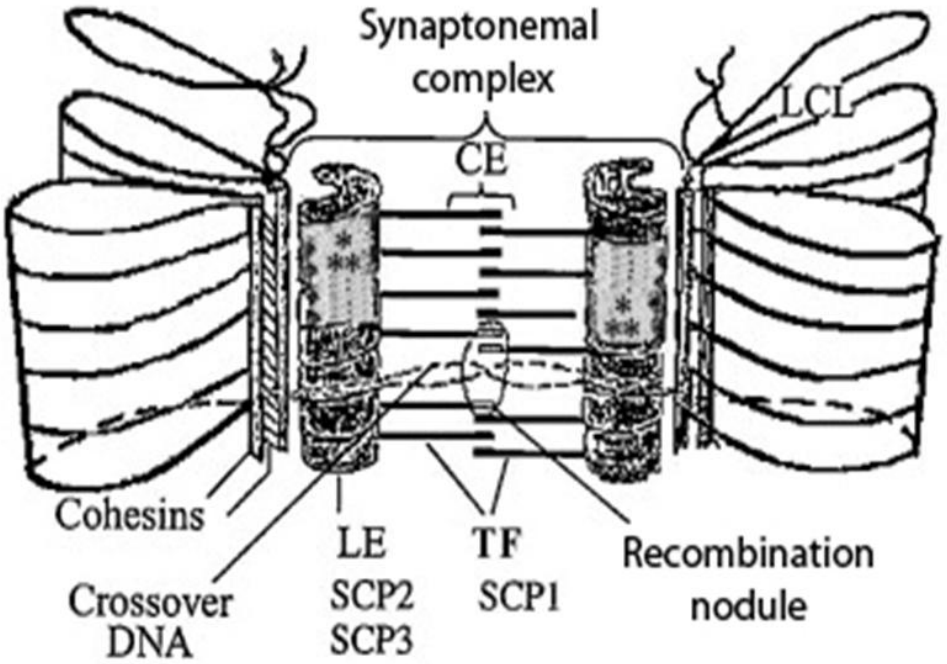
B Zygotene (paired threads)

Synapsis of homologous chromosomes starts. Starting from nuclear envelope attachment points, a synaptonemal complex develops between the homologous chromosomes.





The molecular structure of the synaptonemal complex



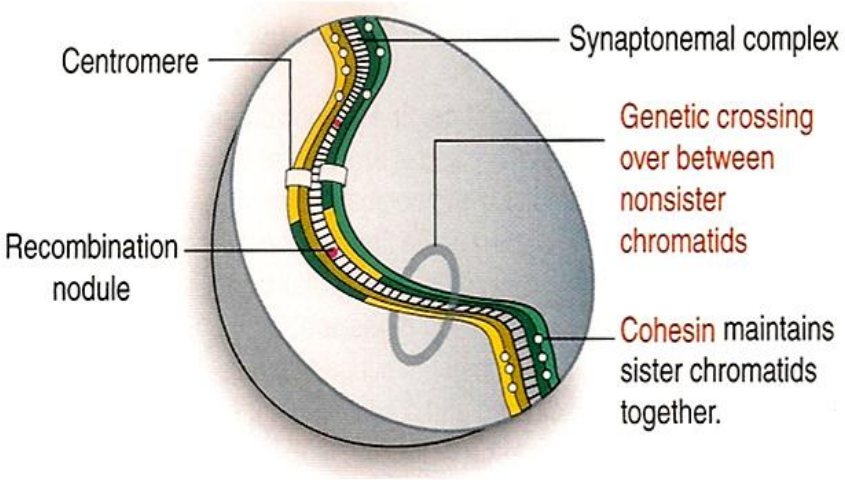
CE: central element; LE: lateral element; TF: transverse filament
SCP: synaptonemal complex protein

Stages 3 and 4 of prophase in meiosis I

C Pachytene (thick threads)

When each homologous chromosome becomes entirely linked by a synaptonemal complex, synapsis is complete. Cohesin stabilizes the association between sister chromatids.

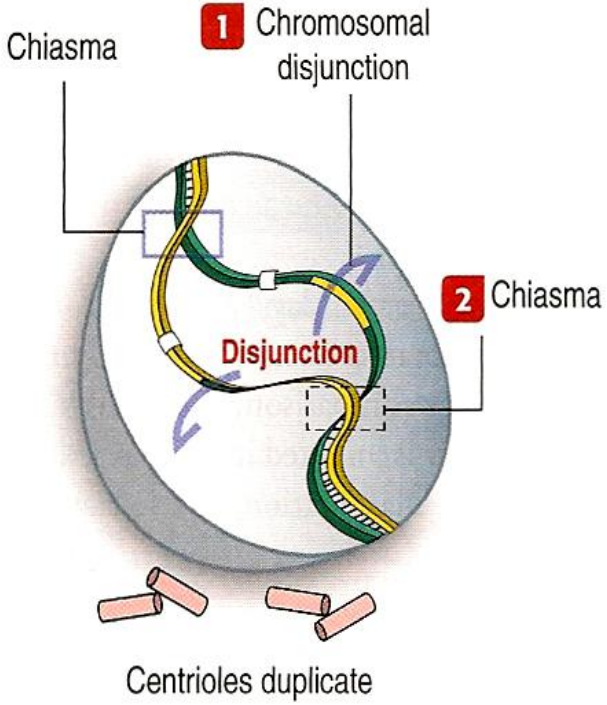
Homologous stretches of paternal and maternal DNA are in register with each other and crossing over between nonsister chromatids starts.



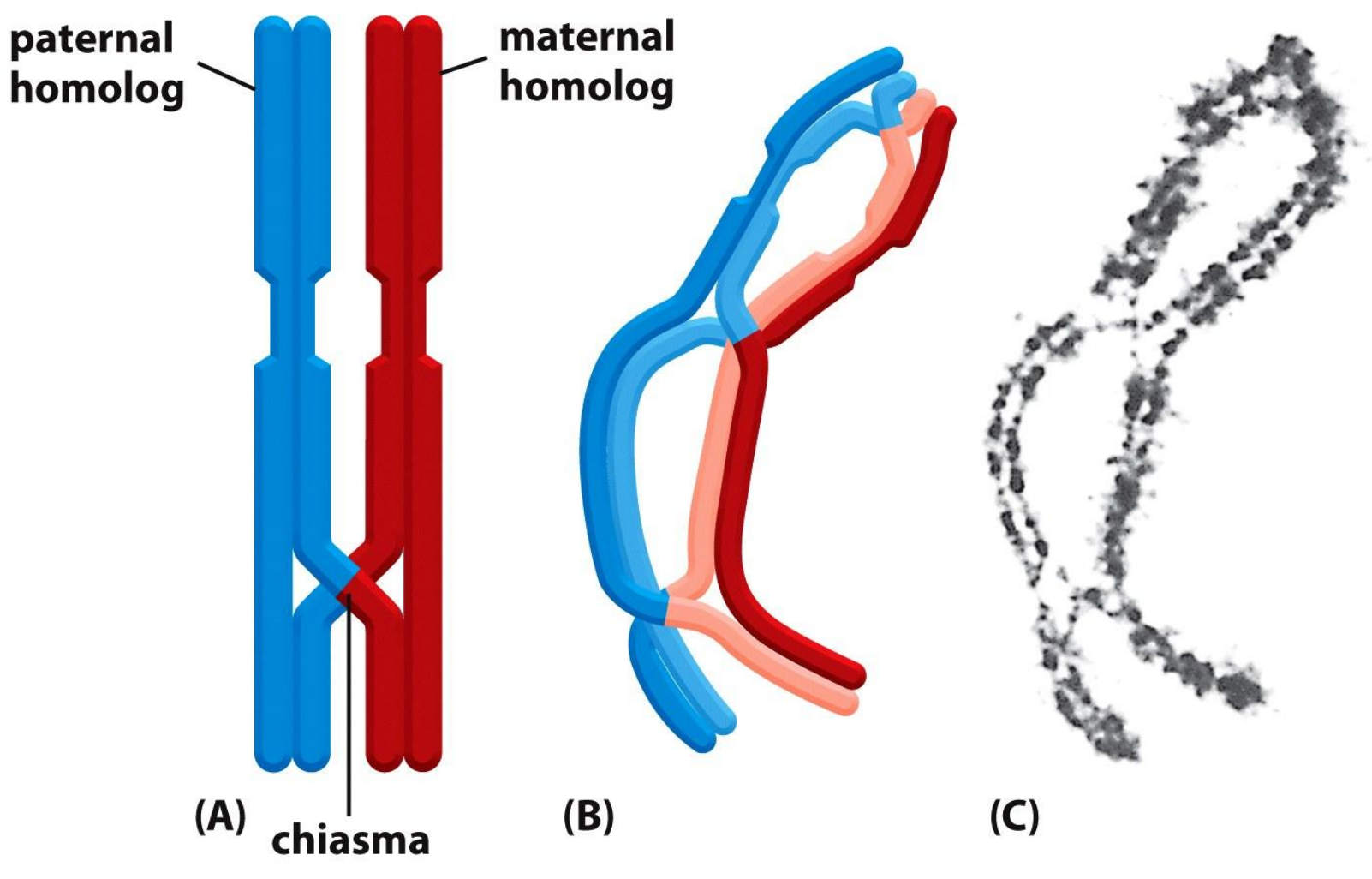
D Diplotene (two threads)

Disjunction of homologous chromosomes takes place when crossing over terminates. Chromosomes remain connected by one or more **chiasmata**, or crossing points.

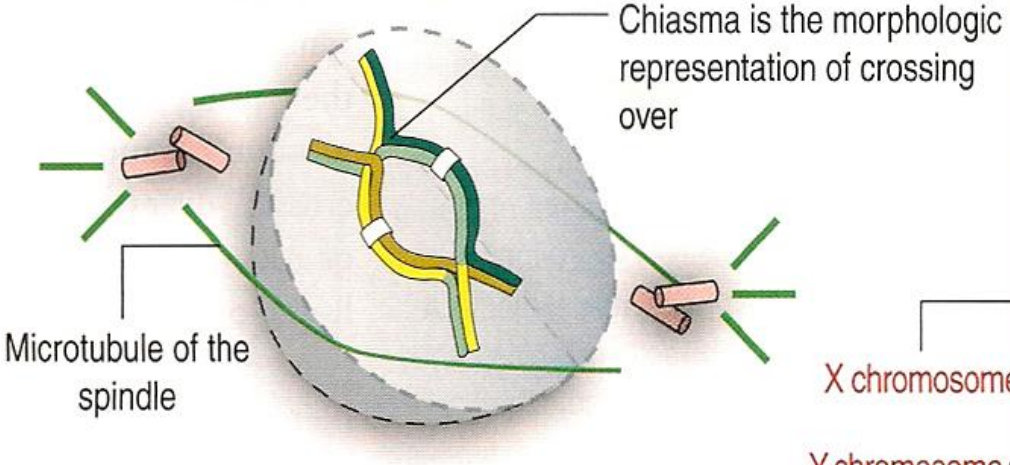
Centrioles duplicate in preparation for metaphase.

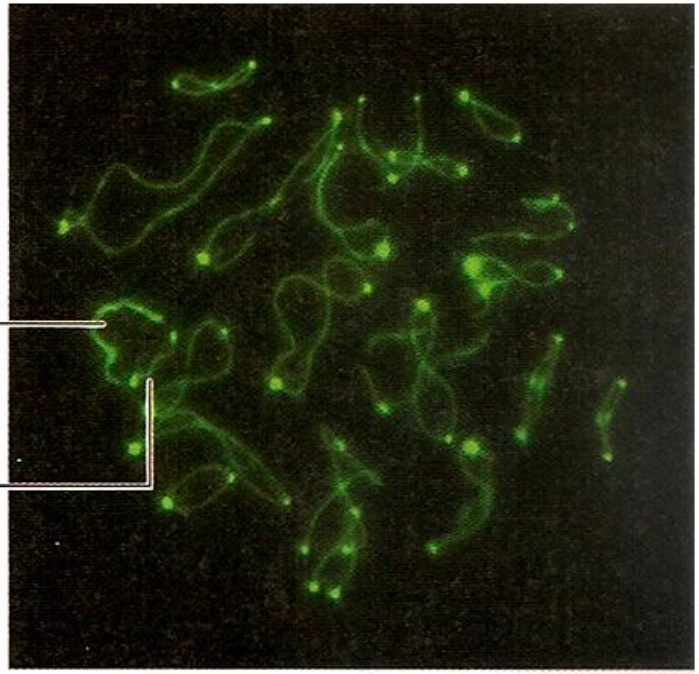


Homologous recombination takes place in pachytene stage of prophase only in meiosis I



Stage 5 of prophase in meiosis I





E **Diakinesis (moving through)**

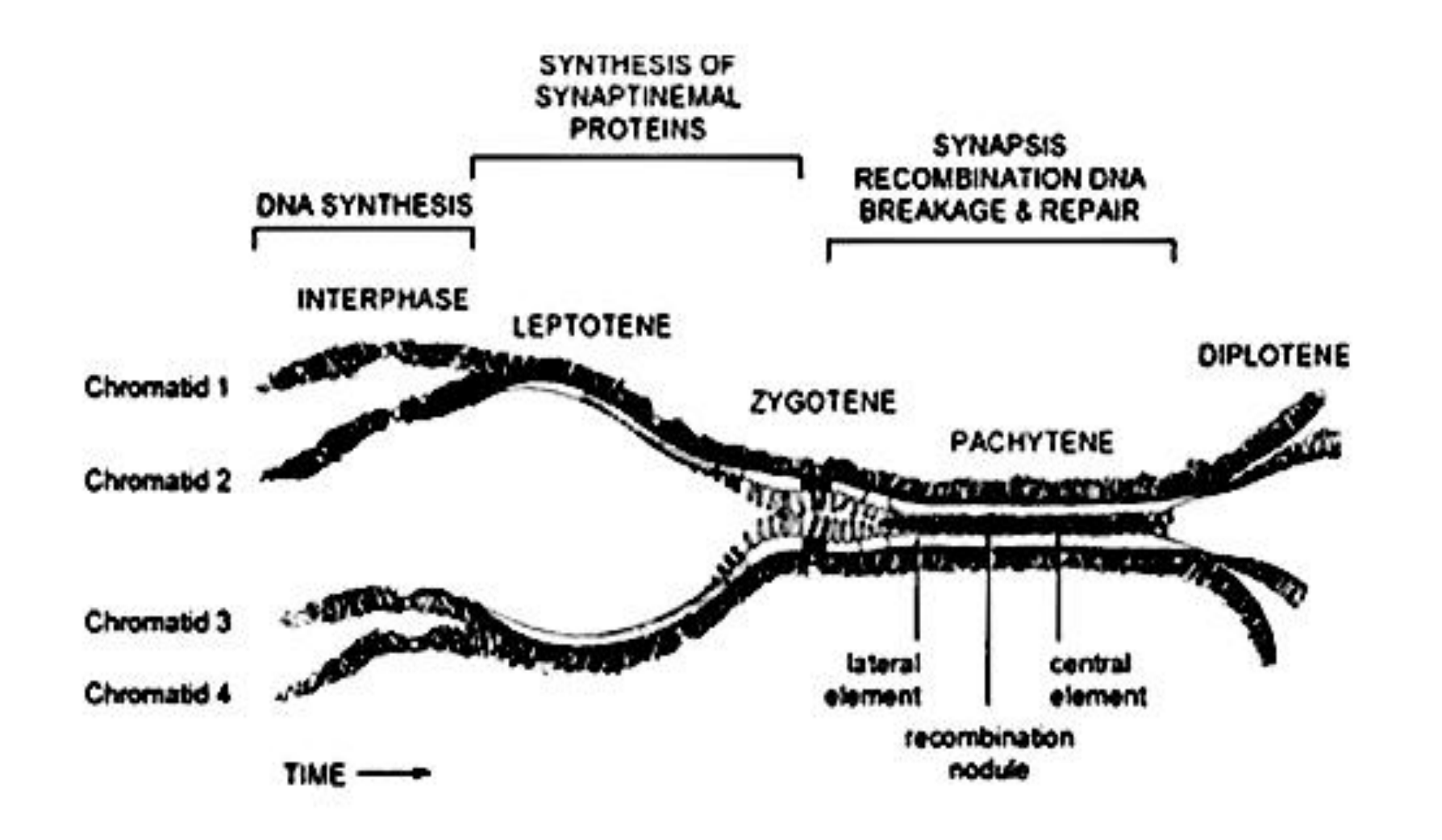
Chromosomes detach from the disrupting nuclear envelope, shorten, and increase in thickness.

The synaptonemal complex disassembles but a short piece remains in the chiasma region.

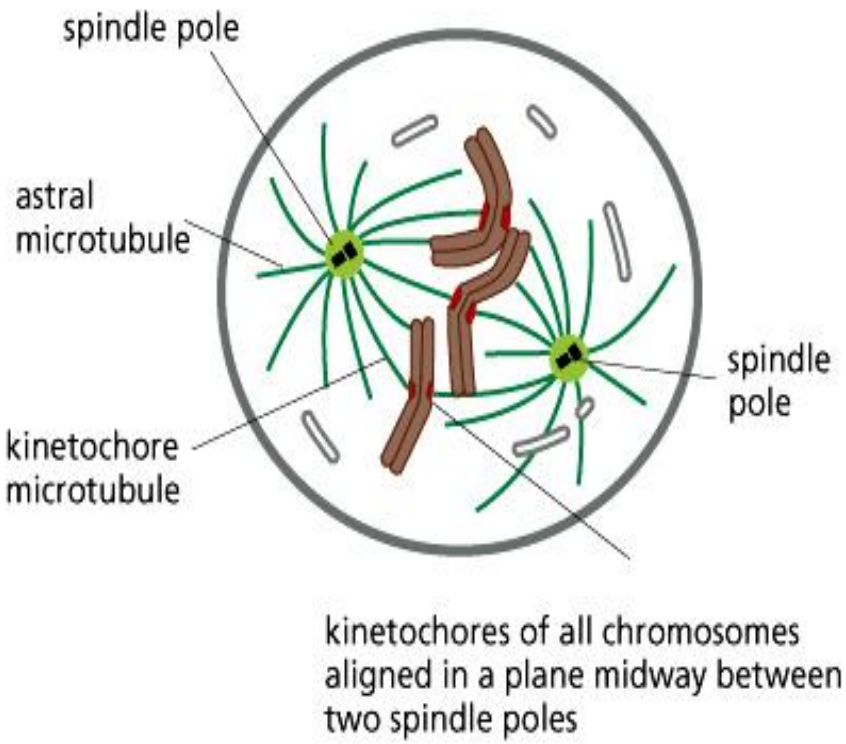
A microtubule spindle begins to develop.

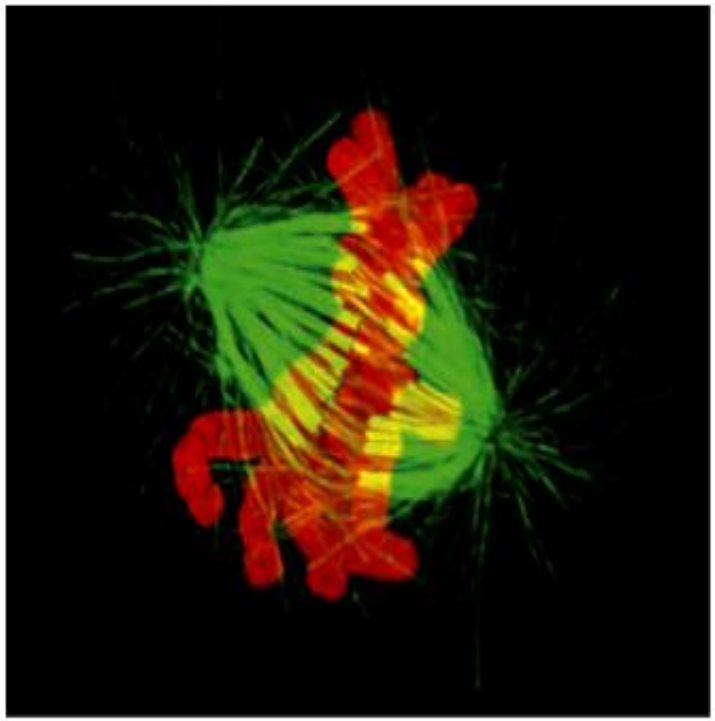
Immunofluorescence microscopy using an antibody to detect SCP3 (green) in a diplotene spermatocyte.

Association of chromosomes at different stages of prophase I.



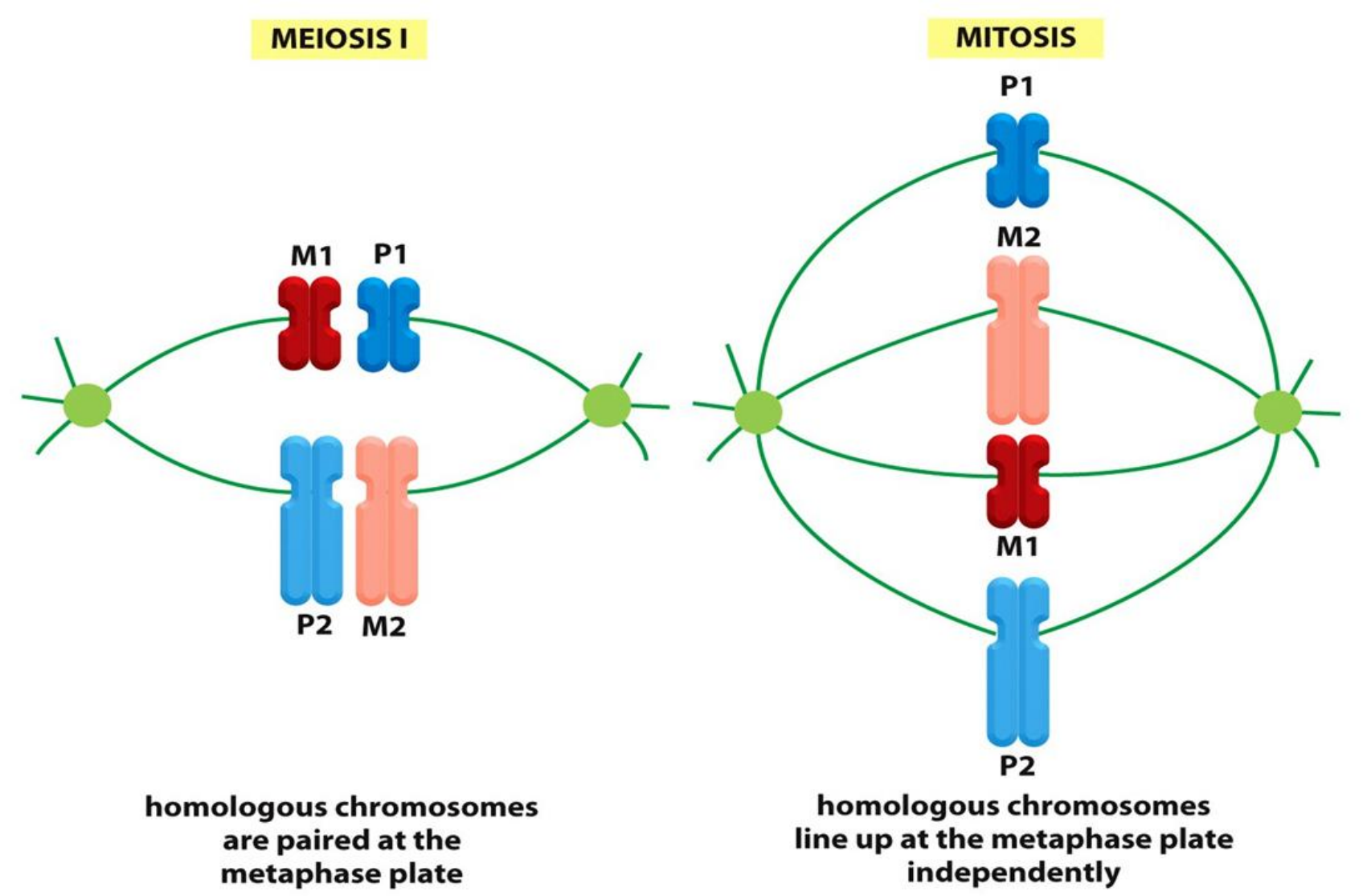
3. Metaphase





- **The chromosomes align at the equator of the spindle**

In meiosis I, homologous chromosome pairs line up



Thank you for your attention!