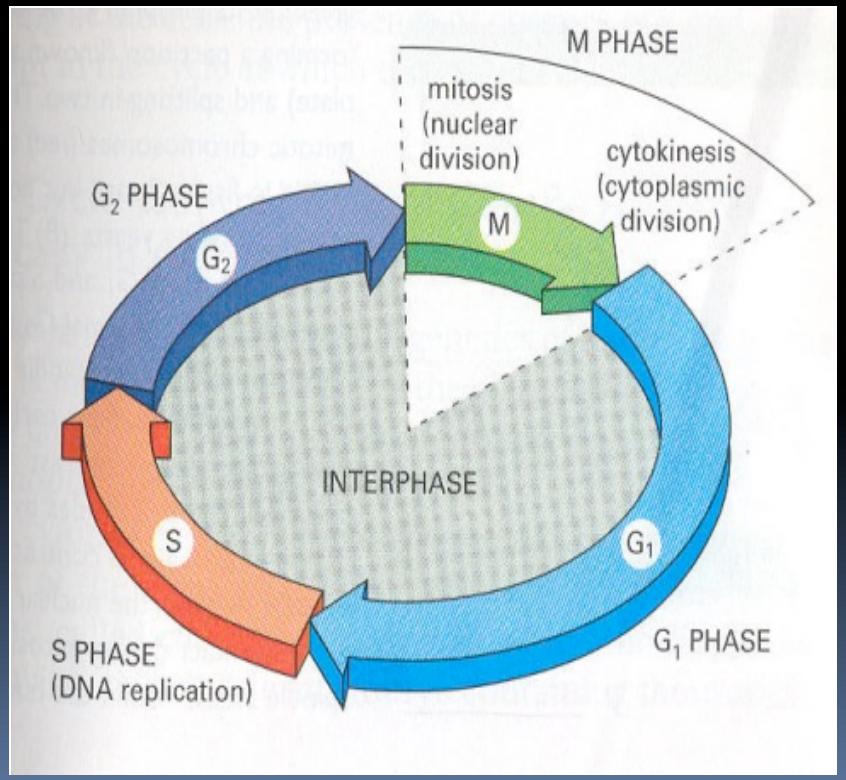
UNIVERSITY of
TERAMO

Biotechnology of Reproduction

MOLECULAR REGULATION OF MEIOSIS

Prof. Luisa Gioia



MPF activity and cellular events in oocyte

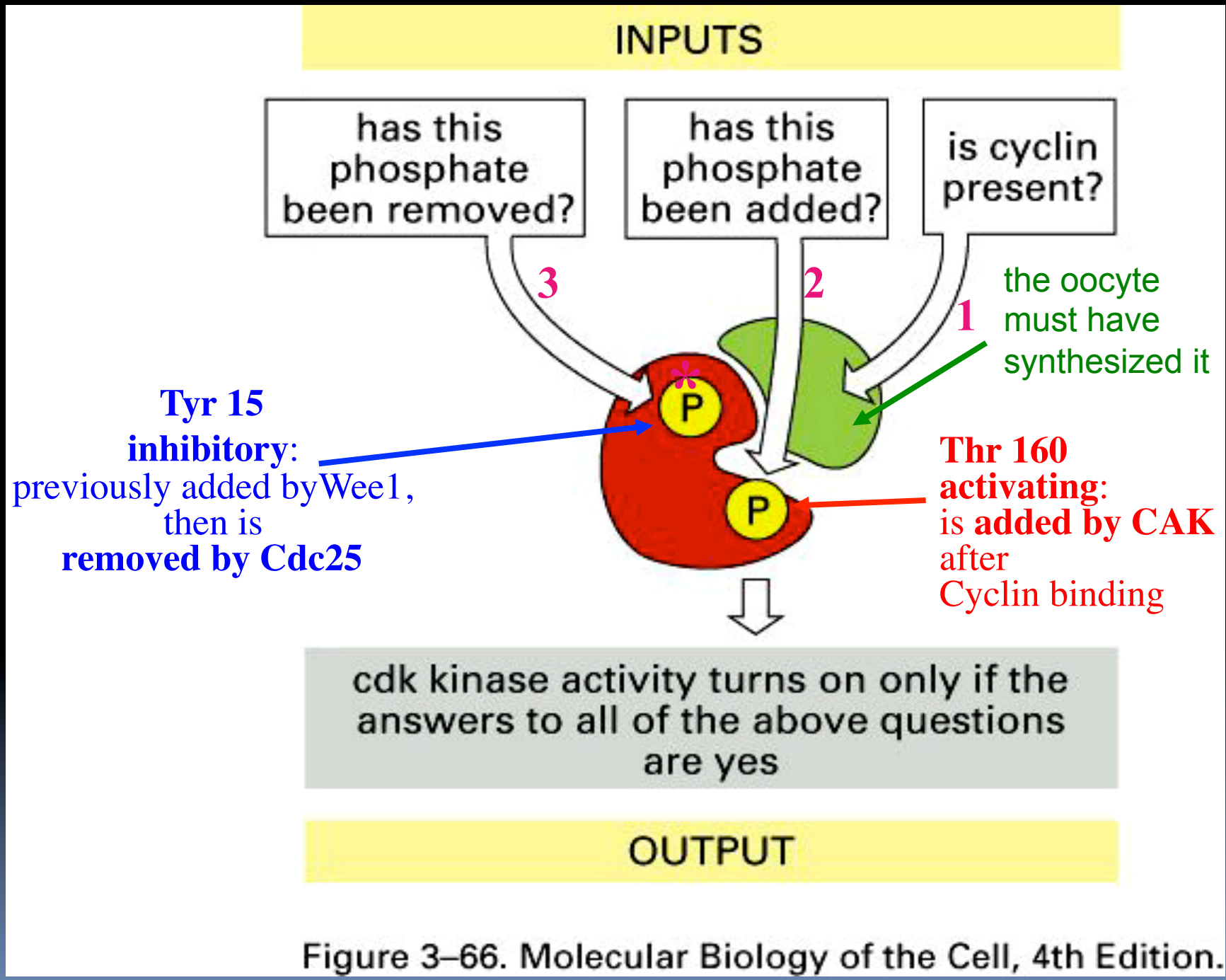
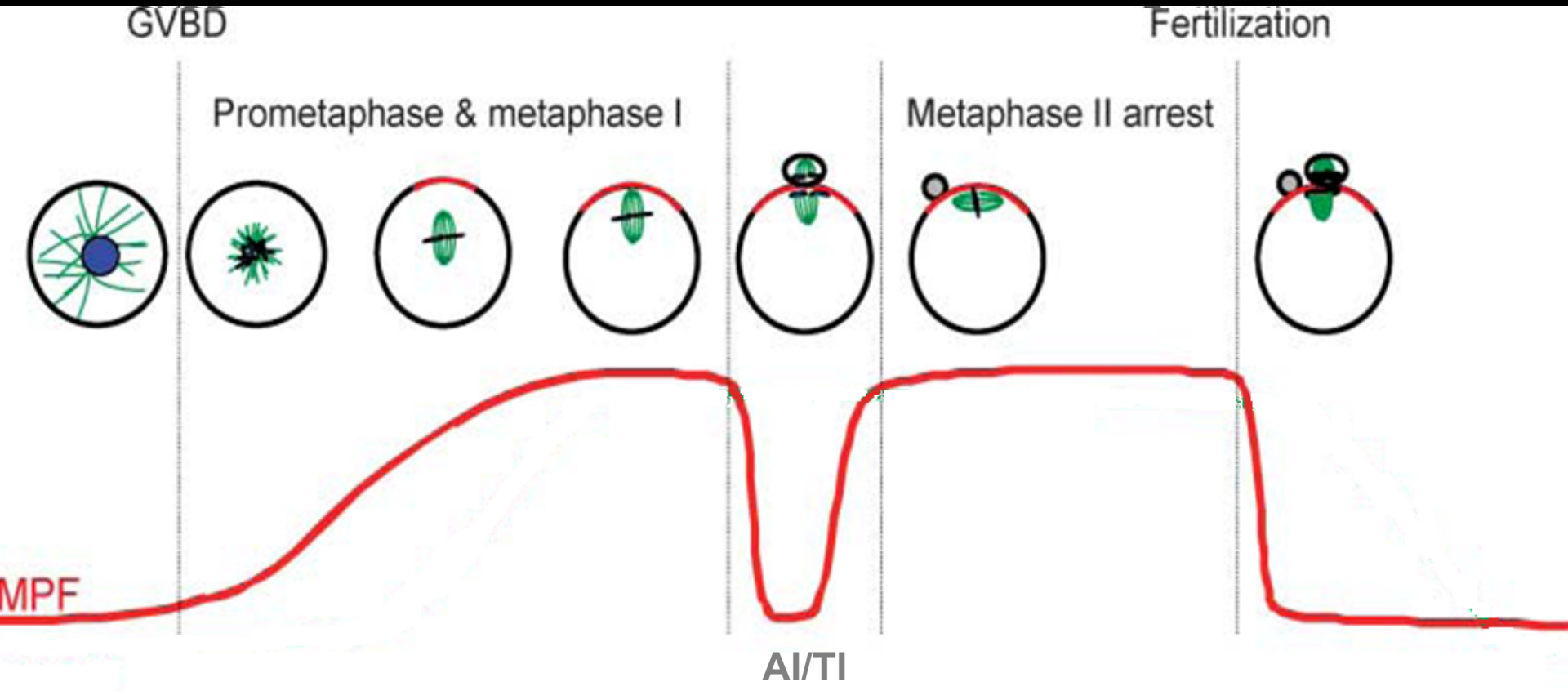


Figure 3–66. Molecular Biology of the Cell, 4th Edition.

MPF activity during meiosis

MPF is activated at GVBD and its activity increases reaching a plateau at the end of MI

MPF is rapidly reactivated to enter the second meiotic division and its activity remains **high during the MII arrest**



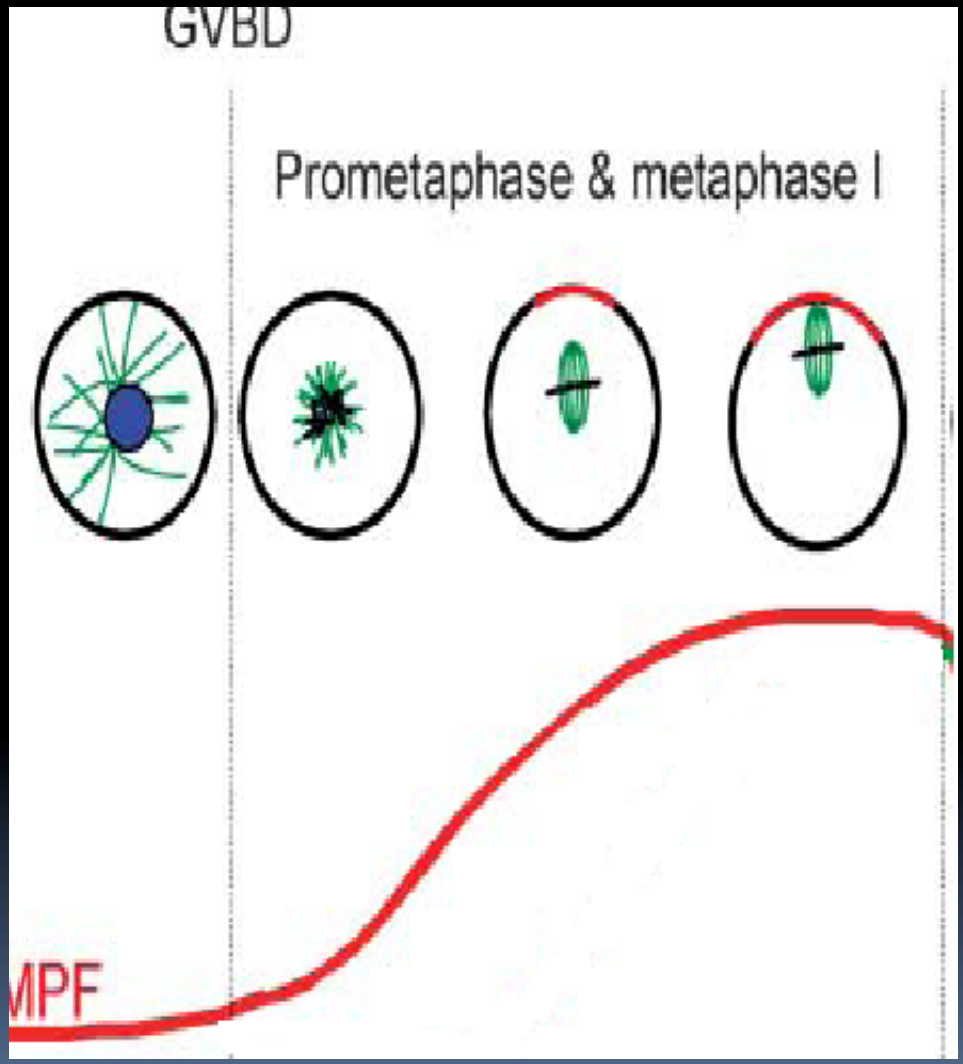
A transient **decline in MPF activity** takes place during the transition between meiosis I and meiosis II

Reproduction (2005)

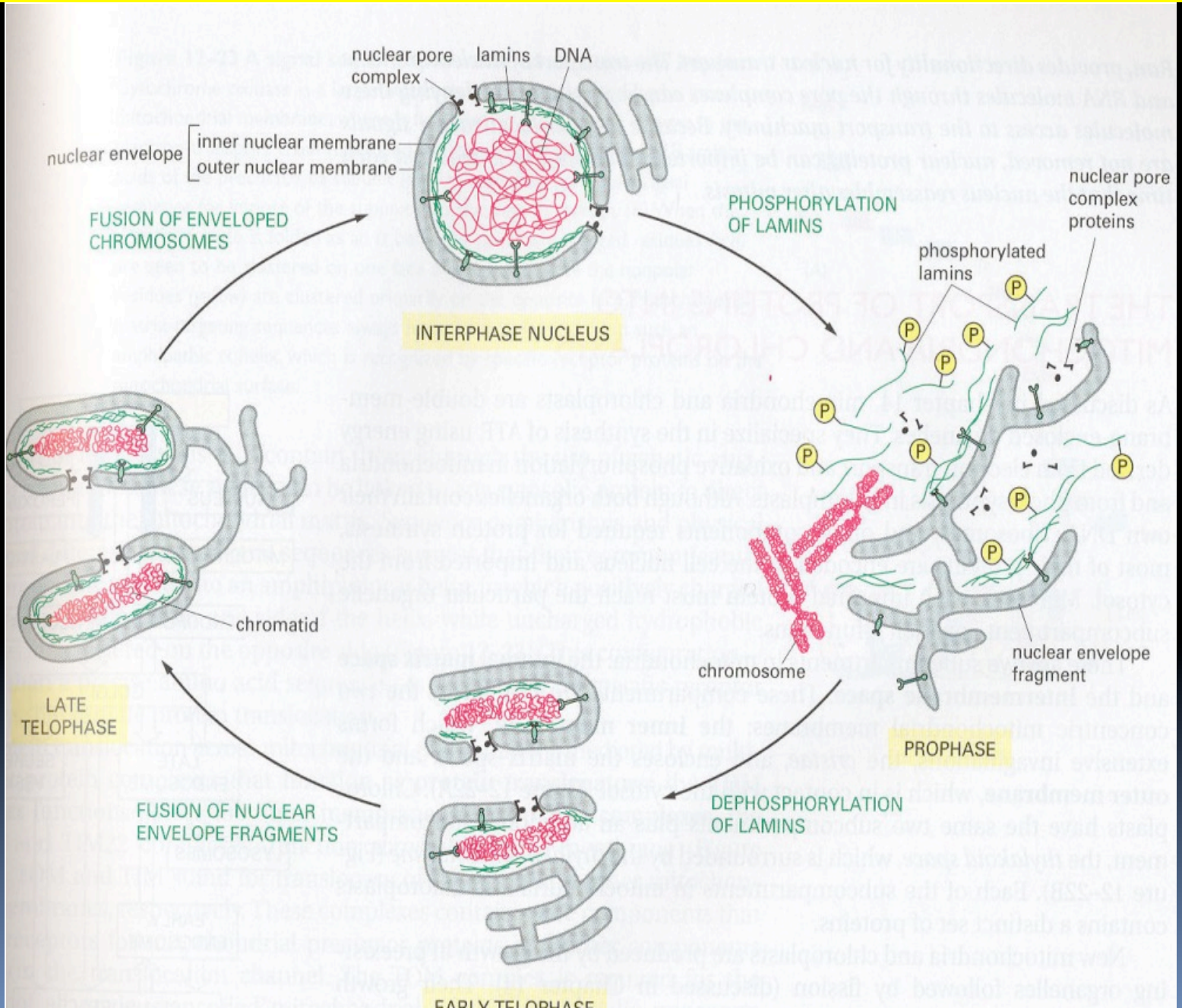
MPF activity

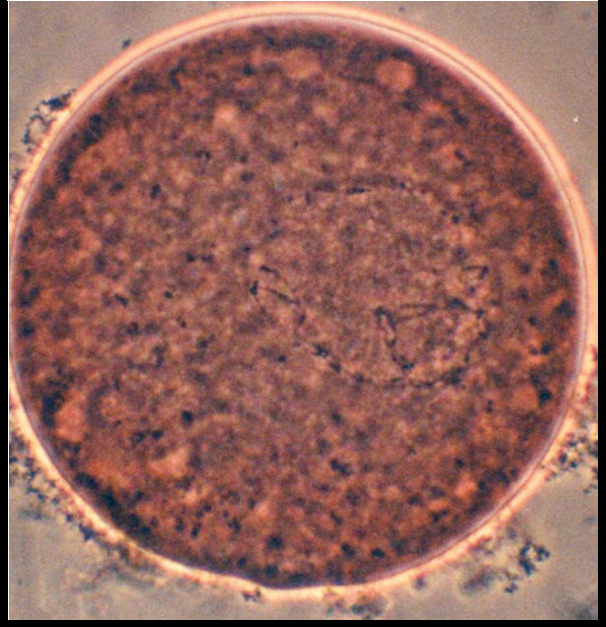
MPF activation triggers:

- GVBD
- chromosomes condensation
- Spindle assembly
- Chromosomes alignment on spindle equatorial plane

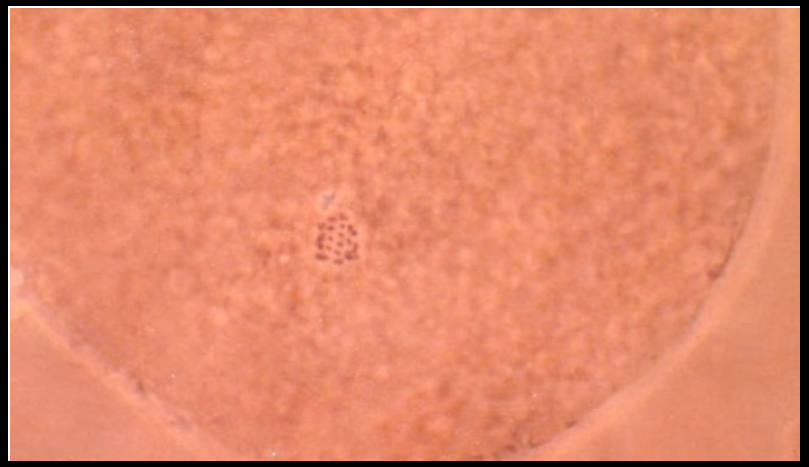


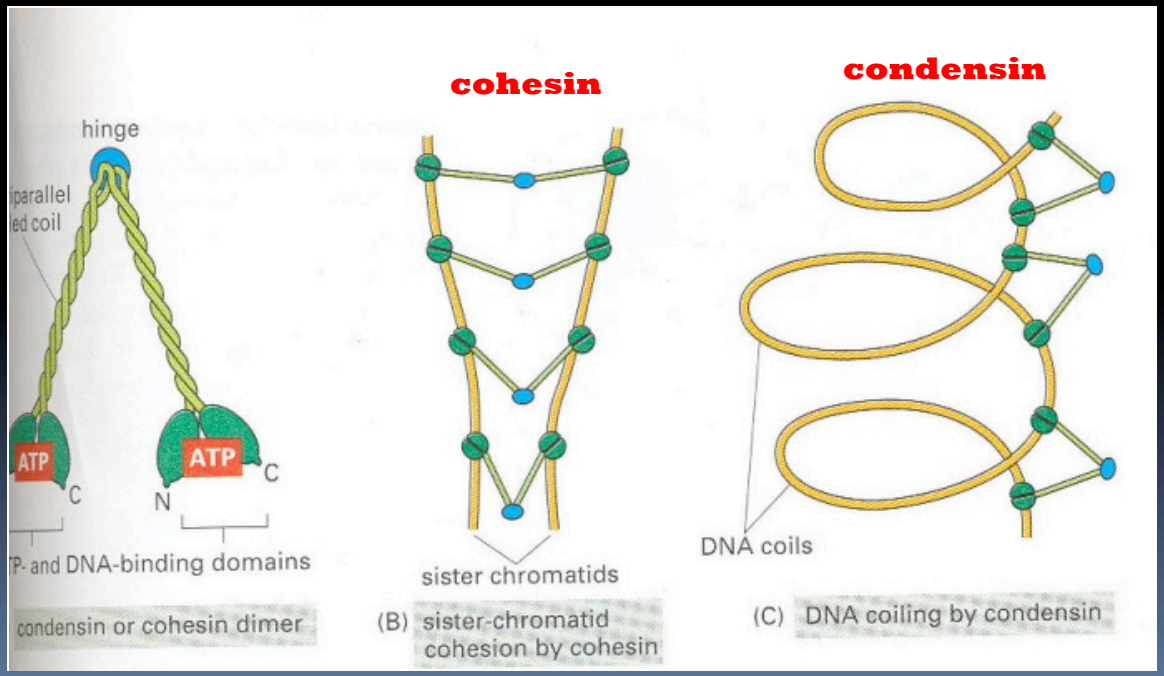
Nuclear membrane breakdown



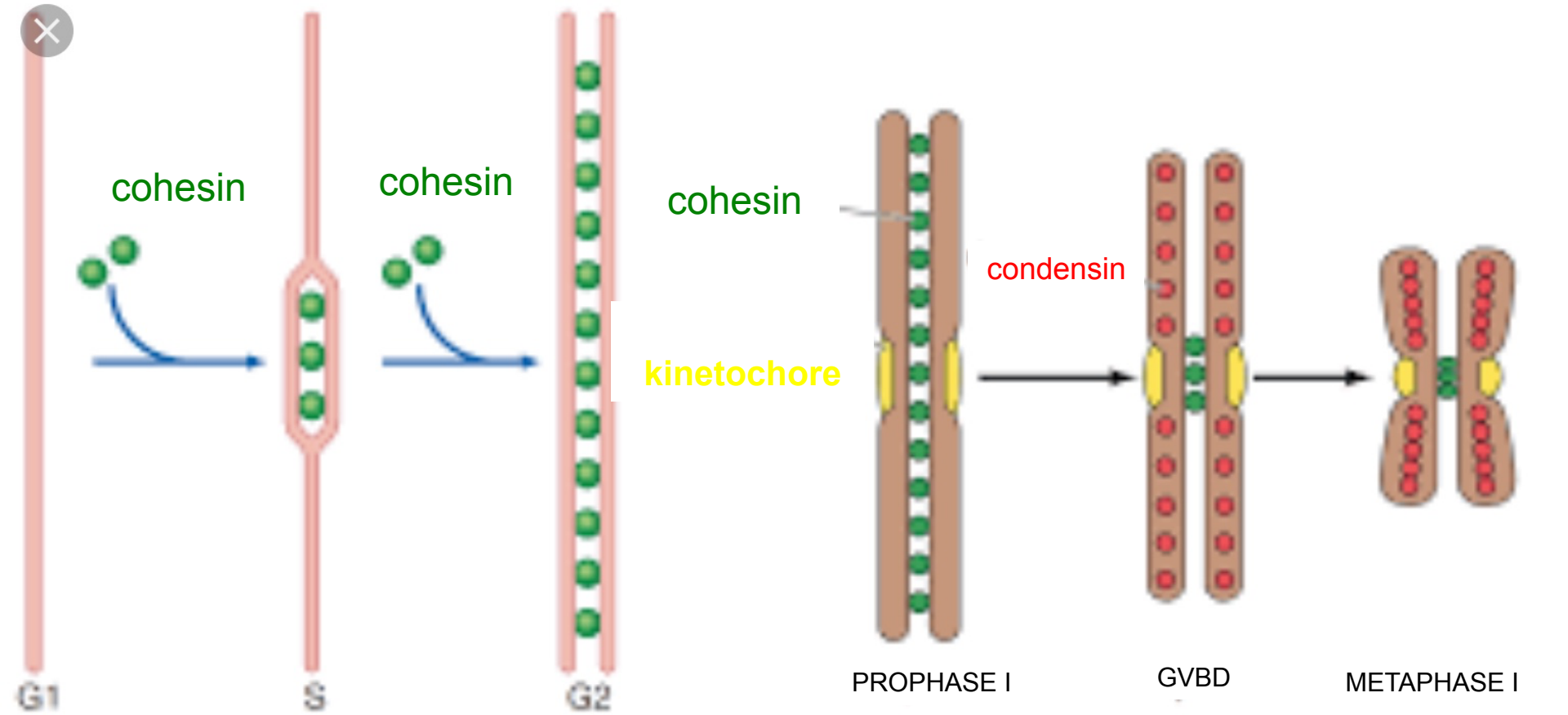


Chromosome condensation

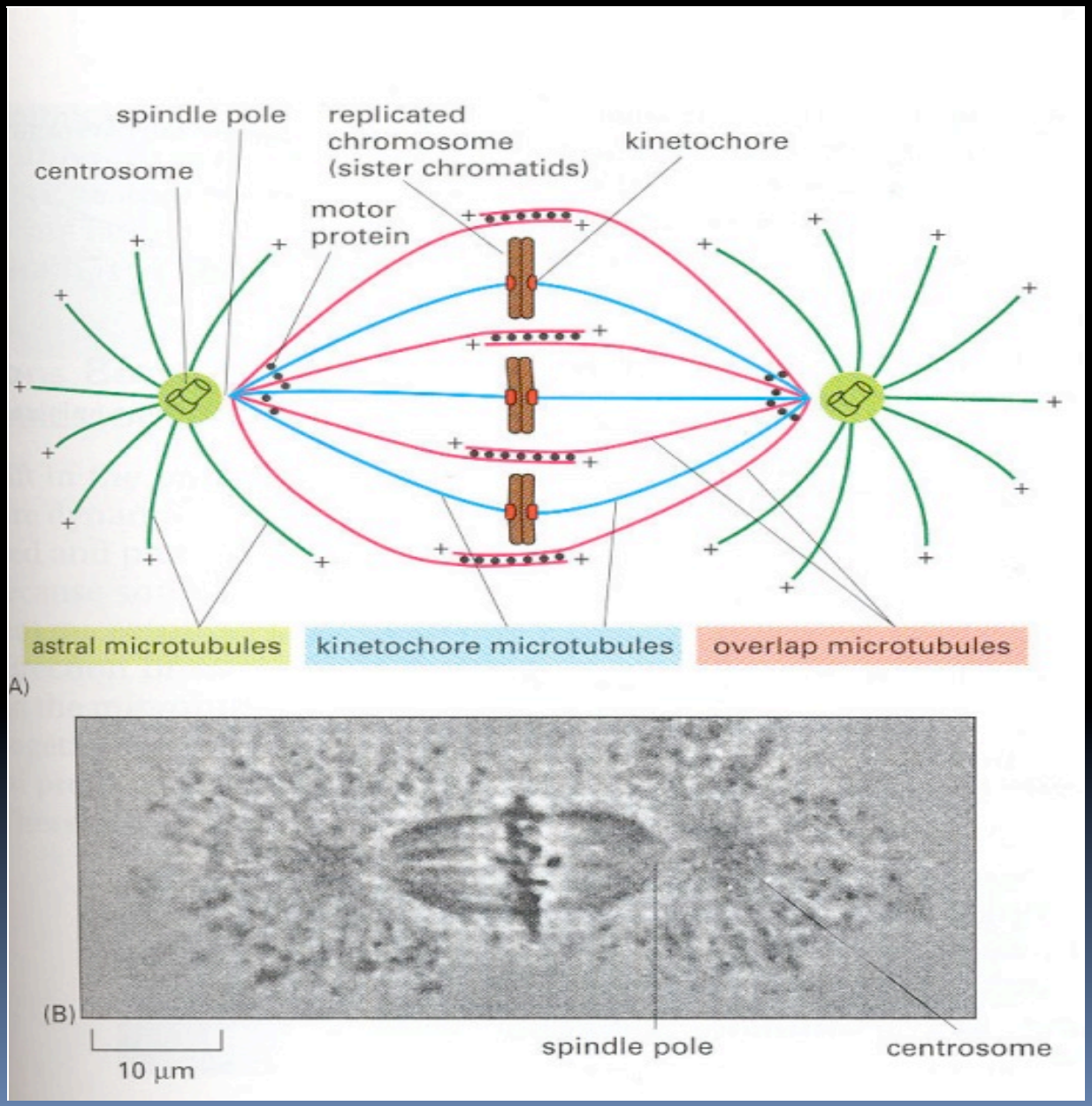




Proteins involved in chromatin/chromosome condensation

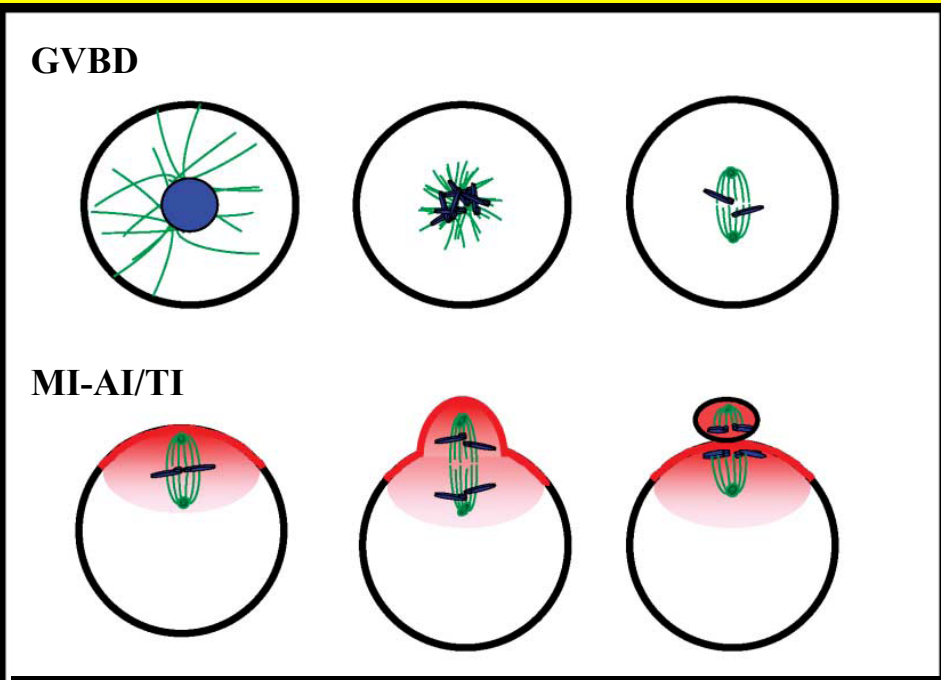


Spindle assembly
Alignment of chromosomes on spindle equatorial plane



Oocytes lack CENTROSOMES and the microtubules (MT) are polymerized at discretes sites in the cytoplasm called **MTOCs** (microtubule organizing centers)

Just after GVBD **MTOCs are preferentially activated** and/or recruited in the vicinity of the chromosomes and MT are preferentially stabilized in this area.
Randomly oriented growing MT are then progressively organized into a bipolar array around the chromosomes



At the end of the first meiotic division, the bipolar spindle migrates toward the oocyte cortex and during MII arrest is anchored under the oolemma

Microtubules during oocyte meiotic maturation

In mice and more generally in mammalian oocytes, chromosomes act as a ‘territory landmark’ to organize both microtubules and actin microfilaments within the large cytoplasm.

This spatial control is essential to achieve the two ASYMMETRIC MEIOTIC DIVISIONS that lead to the formation of a functional gamete.

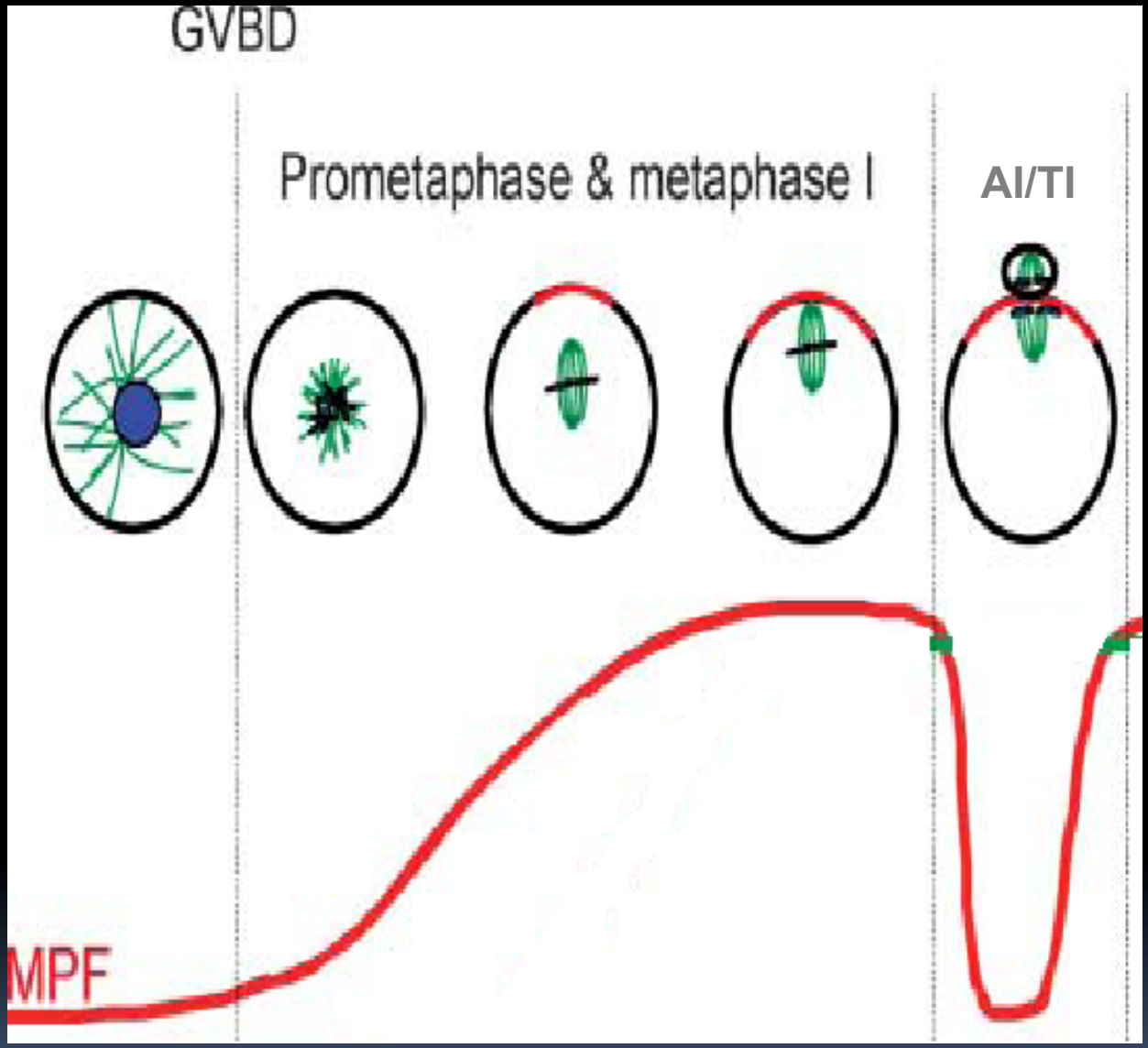
Defects in the cytoskeleton organization during meiosis can first lead to **chromosome segregation errors** with dramatic consequences

- In humans, it is estimated that **15–20% of oocytes display chromosome abnormalities linked to segregation errors** (Pellestor et al. 2005)

- Moreover, **at least 5% of all pregnancies are aneuploid as a result of such errors in oocytes**, that strongly correlate to increased maternal age (Hassold & Hunt 2001)

MPF activity

Transition MI ➔AI: Cyclin B degradation **causes MPF inactivity**



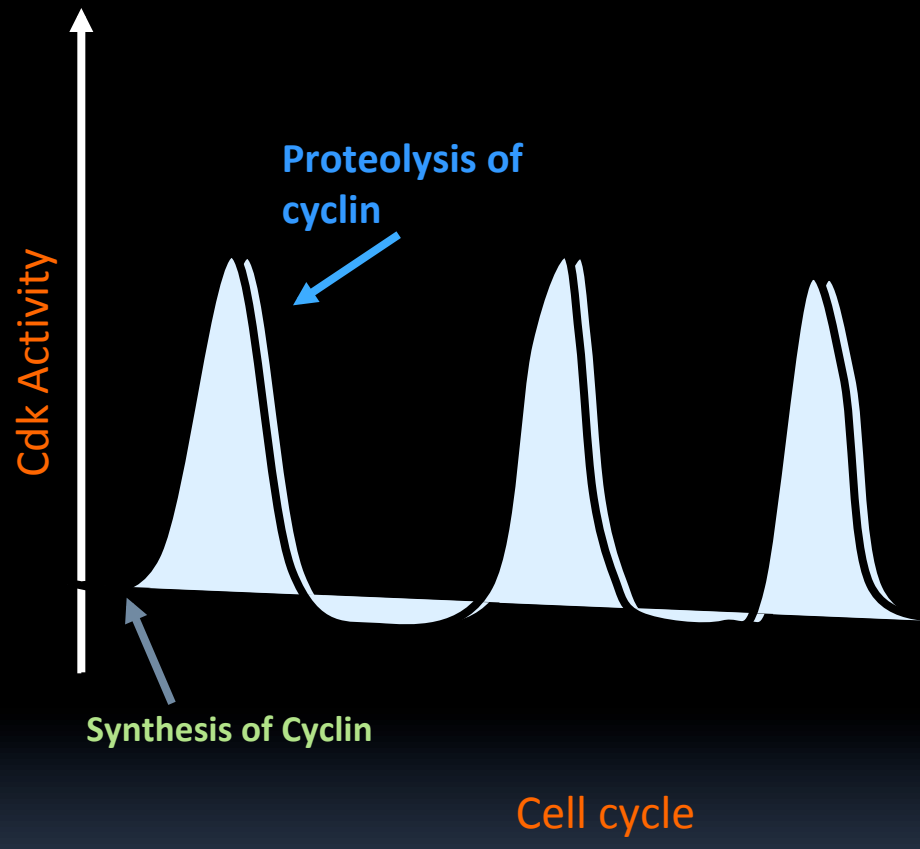
- **Homologous chromosomes separation**
- **PB1 extrusion**
- **Exit from first meiotic division**

decrease of MPF activity during MI/MII transition

Anaphase-Telophase

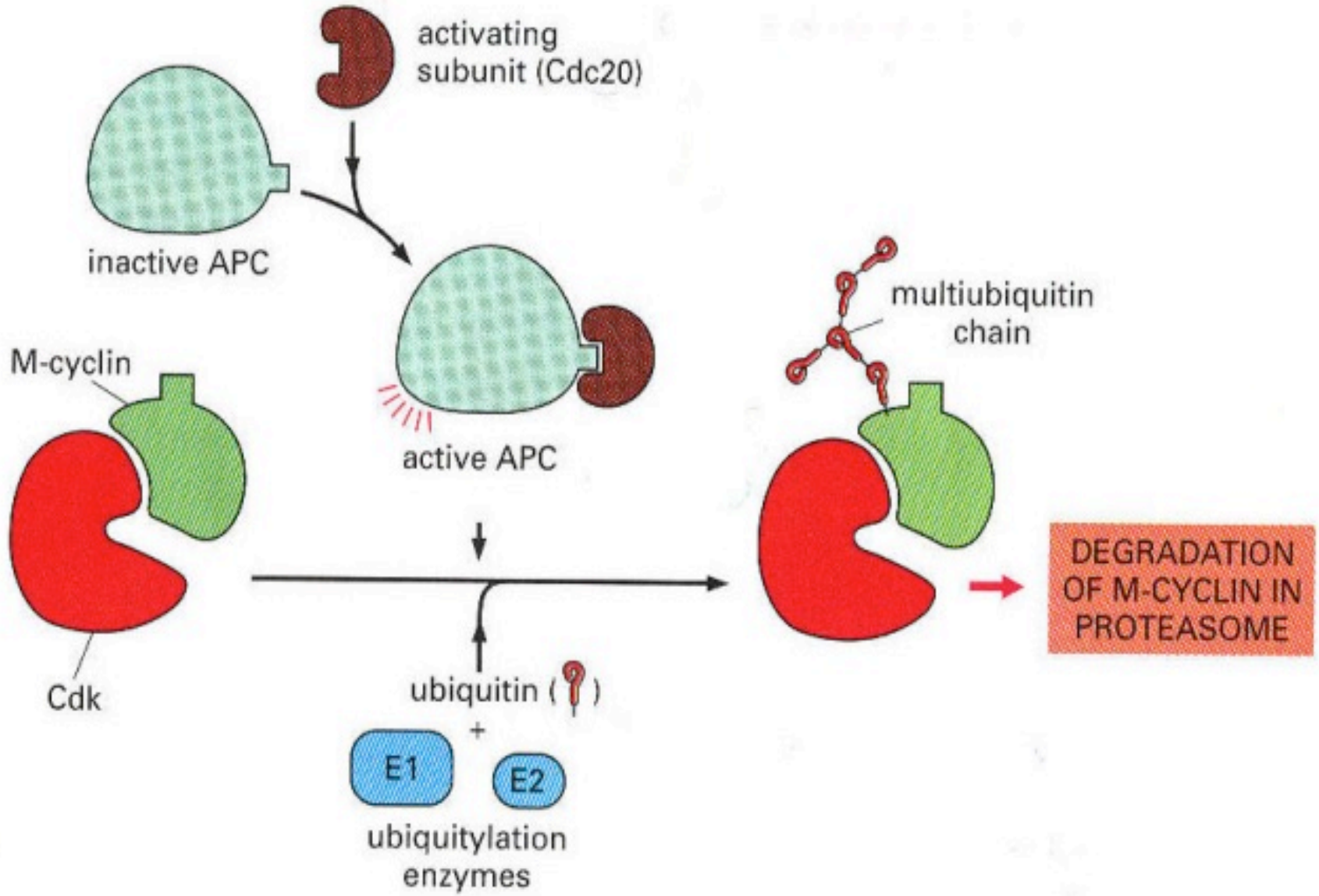
APC activation

MPF activity is turned off during MI/MII transition because **Cyclin B is degradated by APC** (also termed APC/C)*



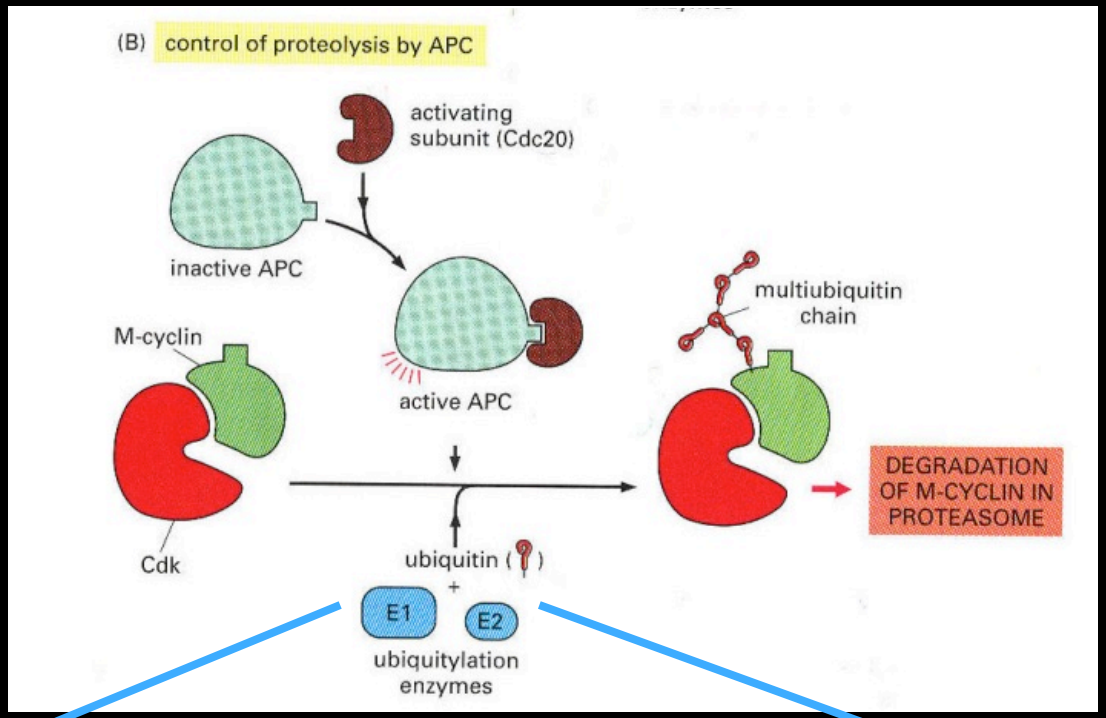
*APC/C=Anaphase Promoting Complex/Cyclosome

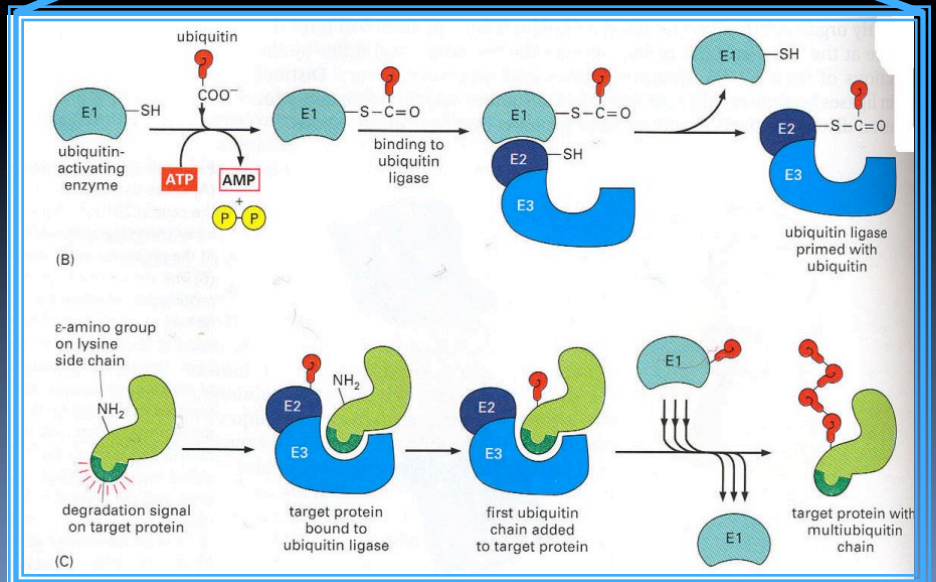
Proteolysis of cyclin by APC through proteasomes



Proteolysis of cyclin by APC through proteasomes

*__APC/C__ polyubiquitinates key proteins, such as cyclin B, targeting them for proteolysis by proteasomes

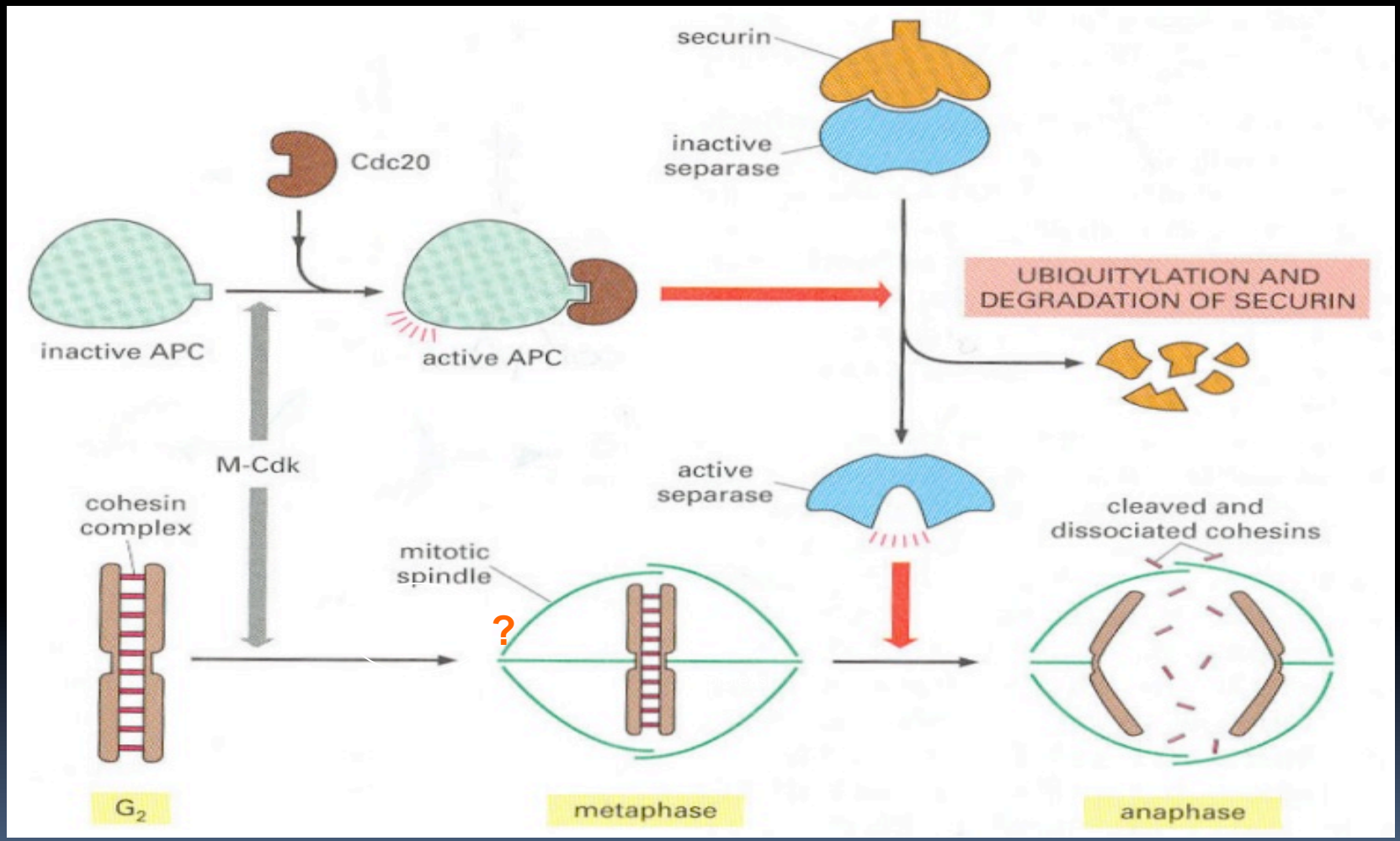




proteasomes

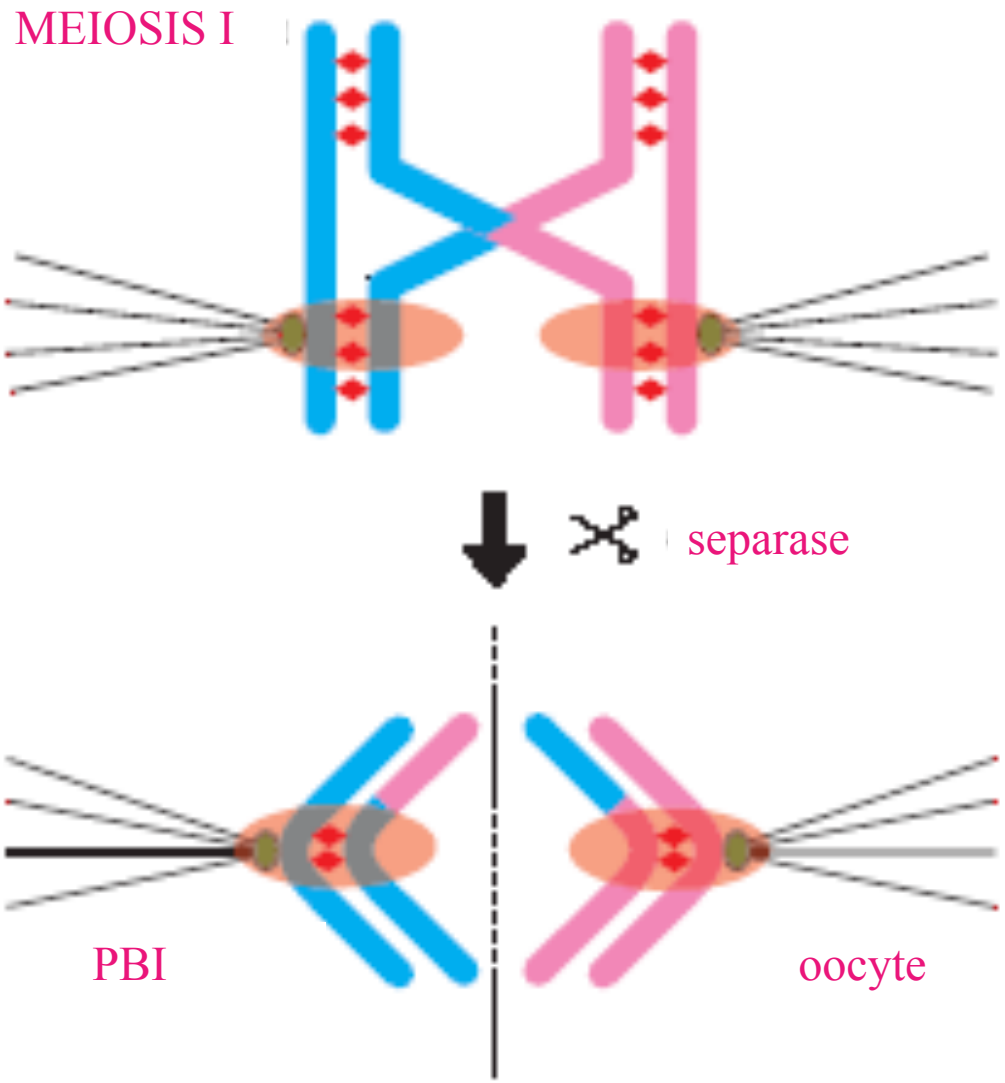
Activation of anaphase-promoting complex (APC)

The same molecular complex (APC) is involved at **AI and AII**, even if some differences exist in the mechanisms



Proteolisis is a crucial process to complete M phase, necessary to accomplish PB extrusion at Anaphase/ Telophase

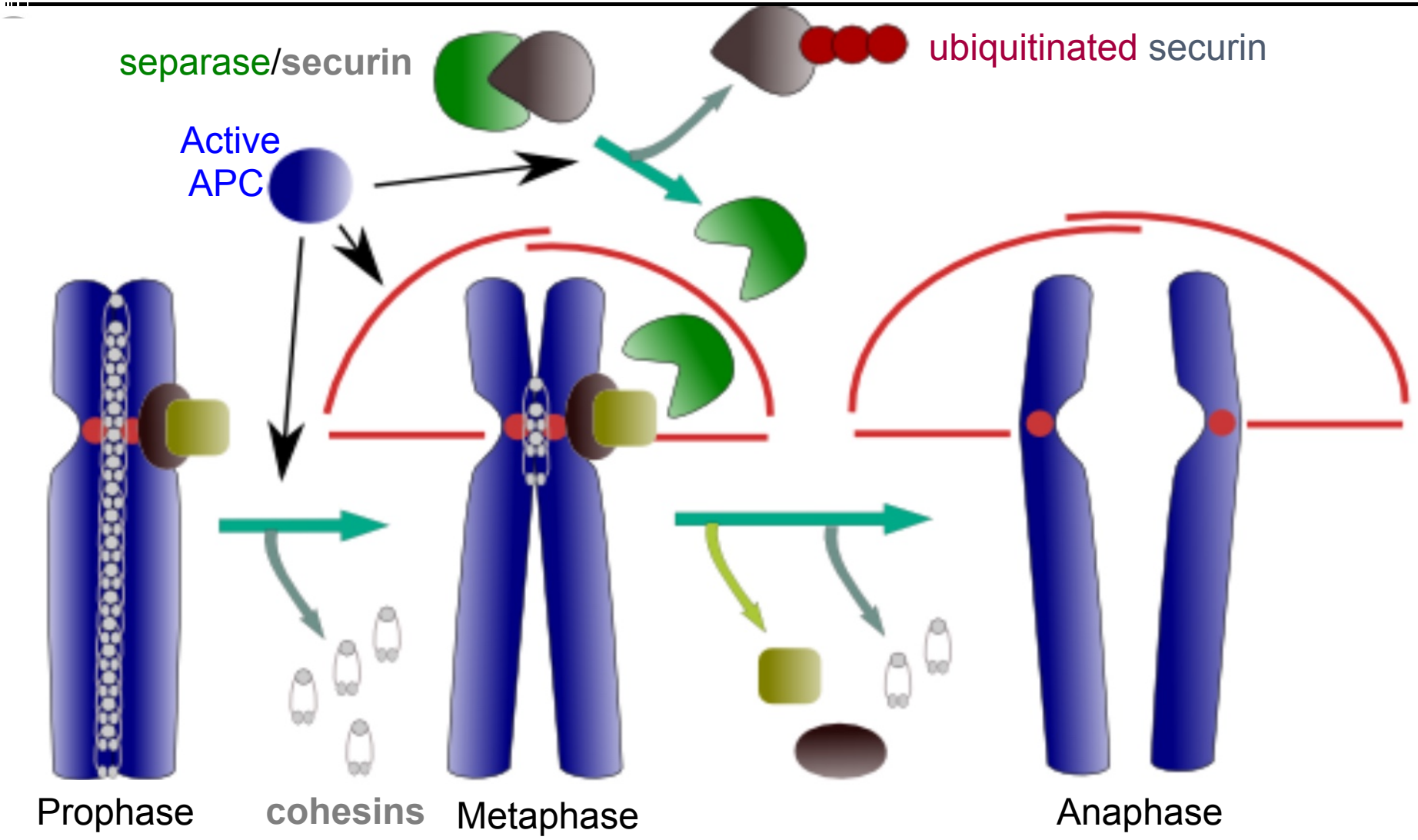
Activation of anaphase-promoting complex (APC) at Anaphase-Telophase transition



degradation of securin and separase activation

- Anaphase I: homologous chromosomes are separated

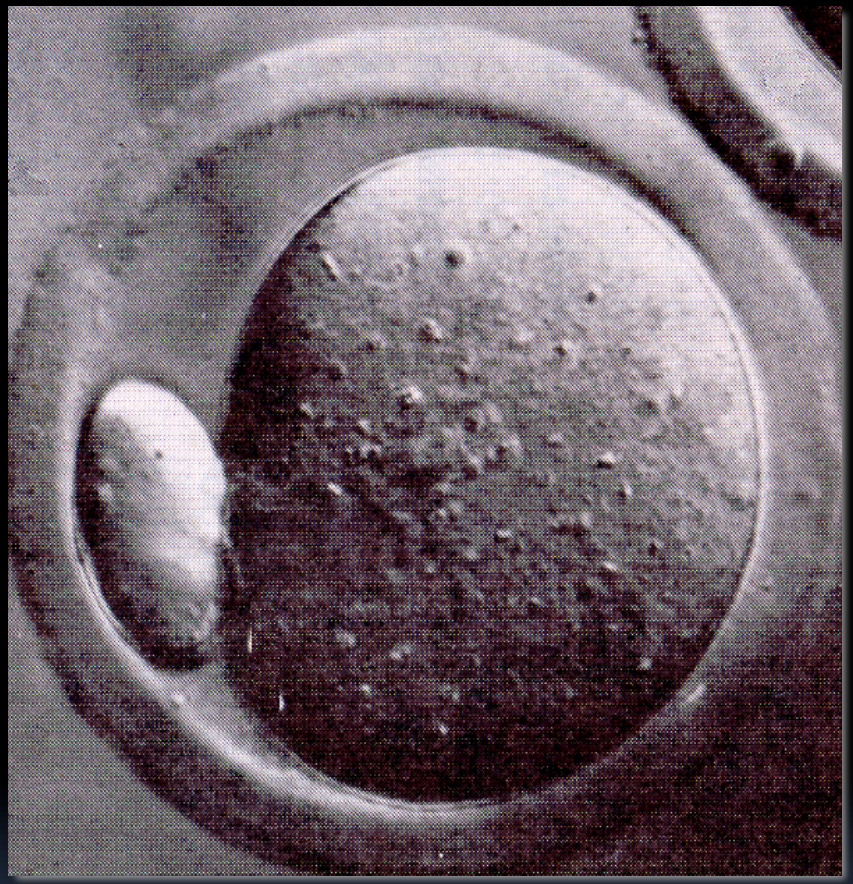
Degradation of securin due to APC activity causes separase activation which is responsible of cohesin degradation



PB1 extrusion

Both meiotic divisions of the oocyte are asymmetric

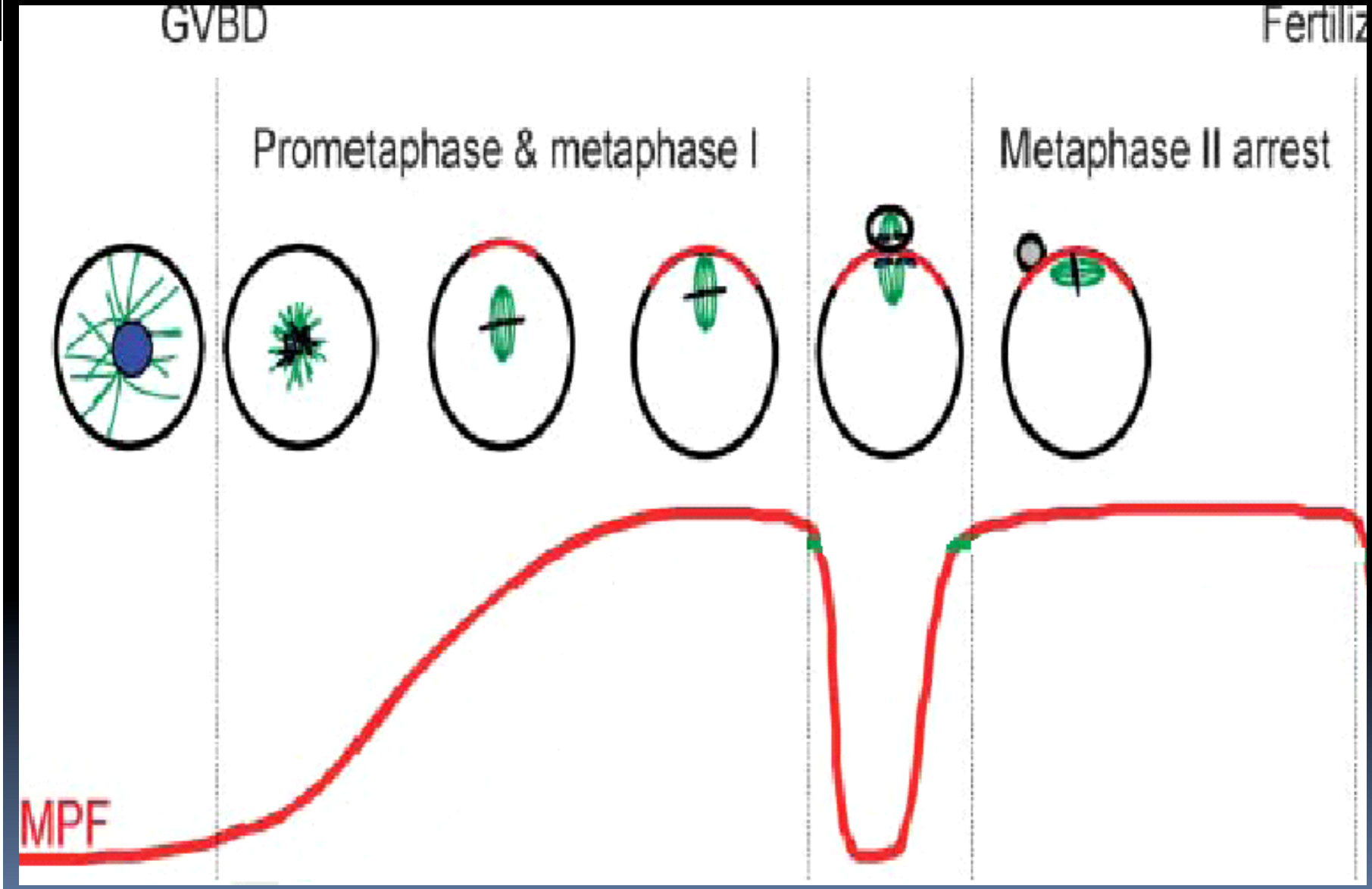
They produce a small cell called the polar body (PB) and the oocyte, which conserves its original size.
Such asymmetry is ensured by the positioning of the spindle in the periphery of the large oocyte.



Cytoskeleton-dependent asymmetry of the meiotic division maintains the maternal stores accumulated during oogenesis in the oocyte (Matzuk et al. 2002)

MPF activity

High MPF acivity during MII arrest



Metafase II

- Syntesis of Cyclin
- **MPF activity must be maintained until fertilization**

↘

The arrest at MII is due to an activity that has been termed ***Cytostatic Factor*** **(CSF)** which maintains arrest through **preventing MPF inactivation**

- Physiologically, CSF-induced arrest at MII is only broken by a Ca^{++} raise at fertilization

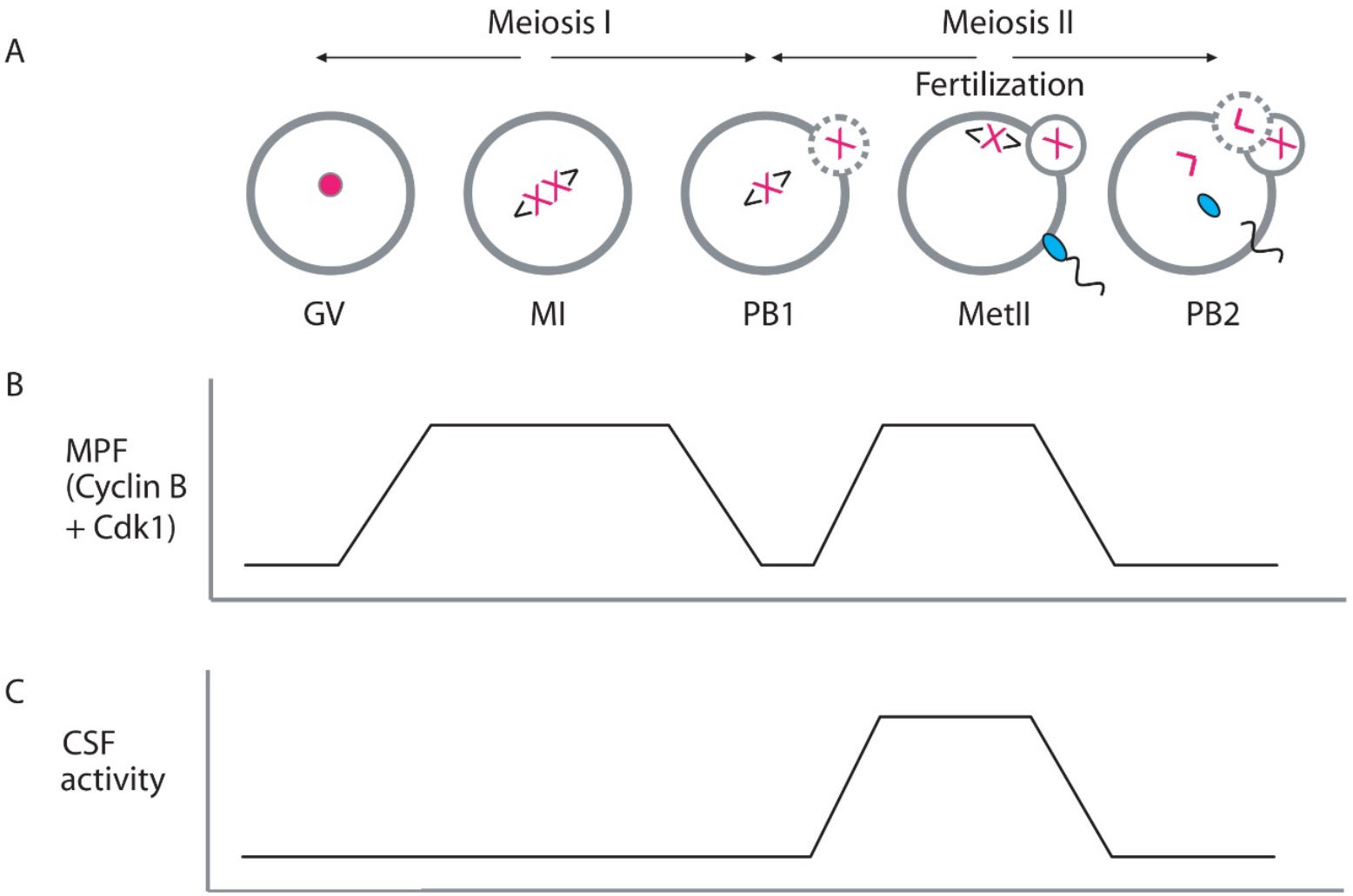


Figure 1
The events of female meiosis. (A) Only one pair of homologous chromosomes is shown. After S-phase two cell divisions are required to produce a haploid gamete. During MI, homologous chromosomes segregate between the egg and the first polar body. On MI completion, eggs arrest their cell cycle at MetII. MetII exit is blocked through CSF activity, until sperm break the arrest. Eggs complete MII and in so doing segregate sister chromatids and extrude a second polar body. (B) MPF activity oscillates in time with entry to, and exit from metaphase. (C) At MetII eggs arrest their cell cycle with high levels of CSF activity.