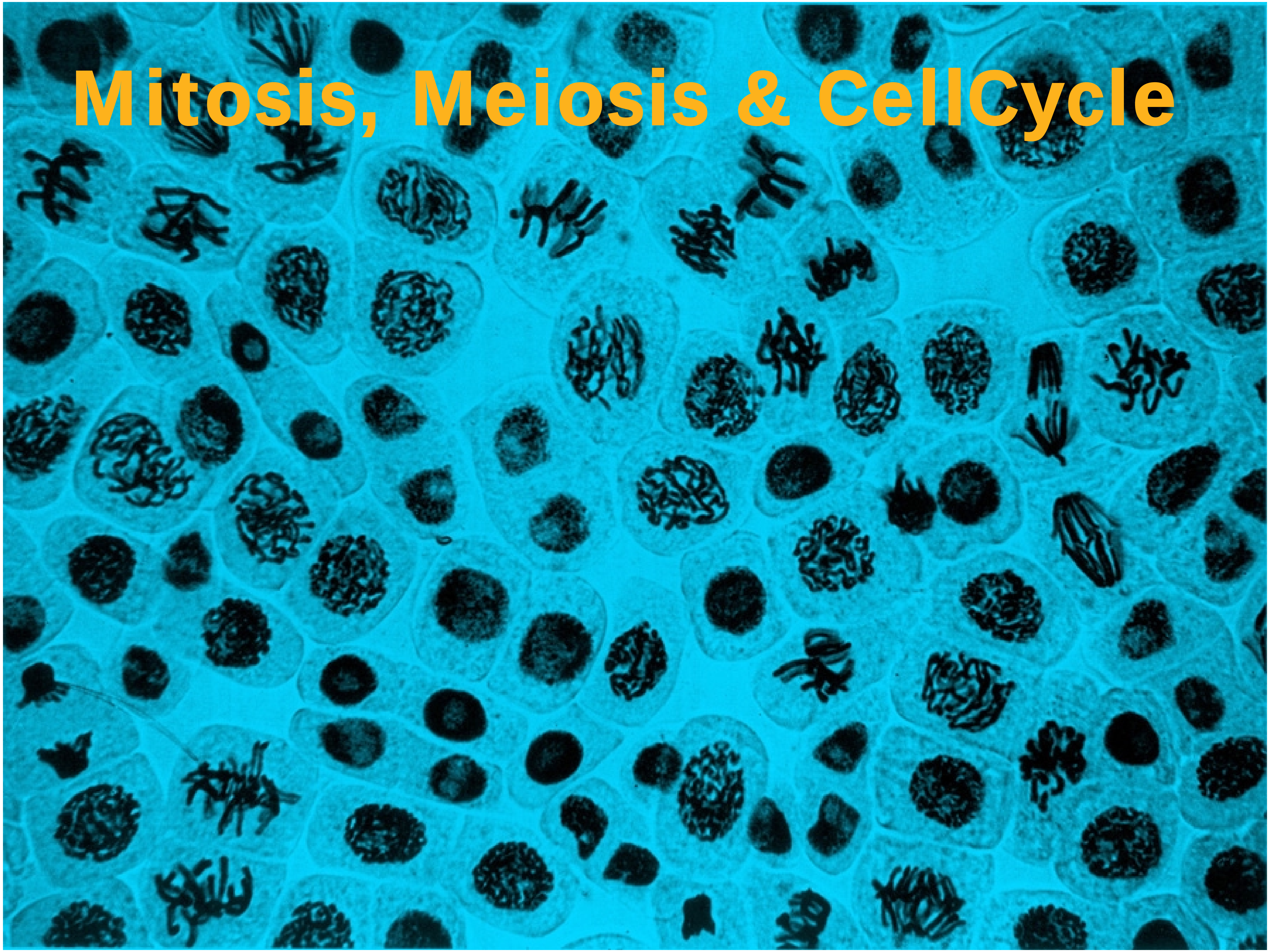
Mitosis, Meiosis & CellCycle



Mitosis / Meiosis

Mitosis:

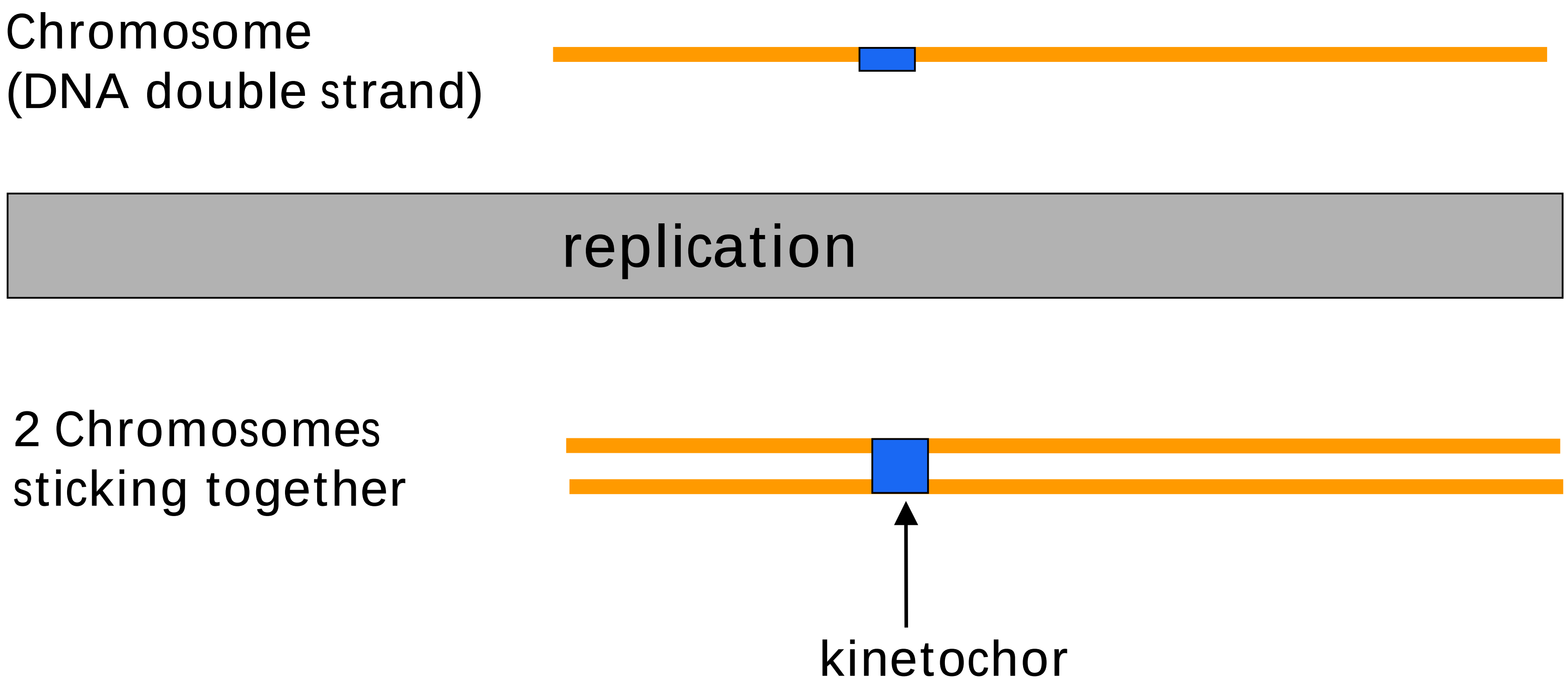
- Segregation of duplicated DNA before celldivision

Meiosis:

- Reduction of the diploid chromosome set to the haploid set
- homologue recombination
- only takes place in germ cells of multicell eucaryotes
- production of sperms and eggs
- involves two nuclear divisions rather than one

Before Mitosis or Meiosis:

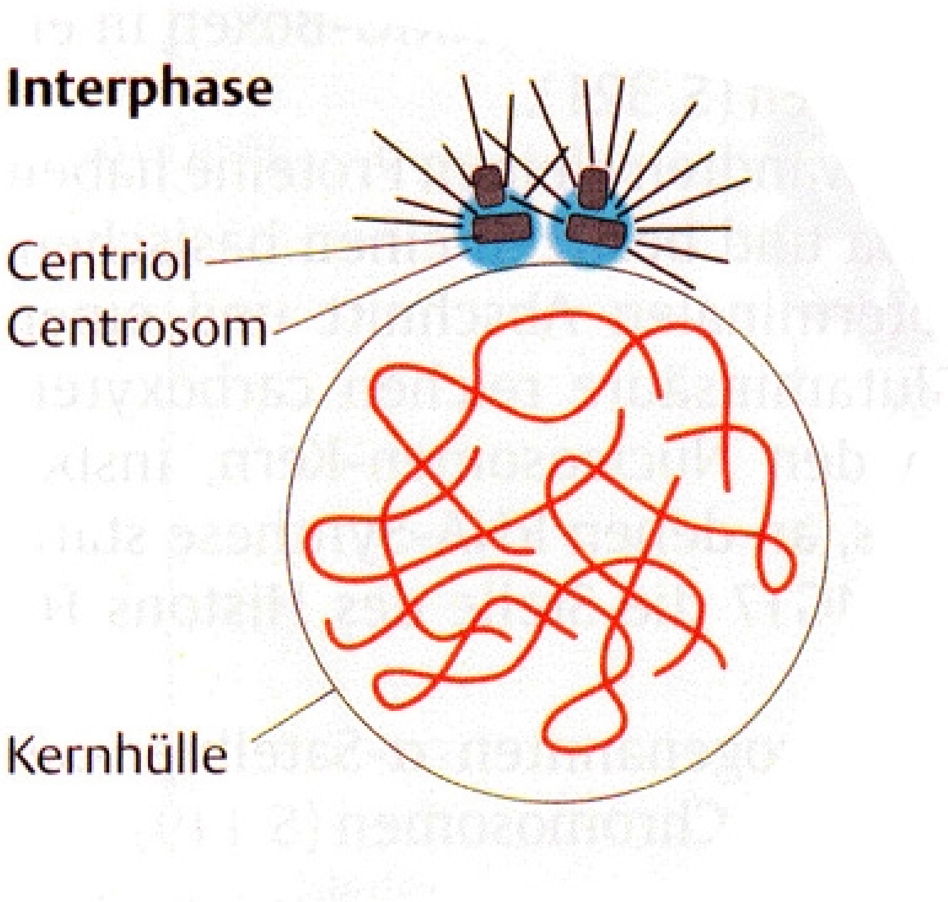
Replication of DNA:



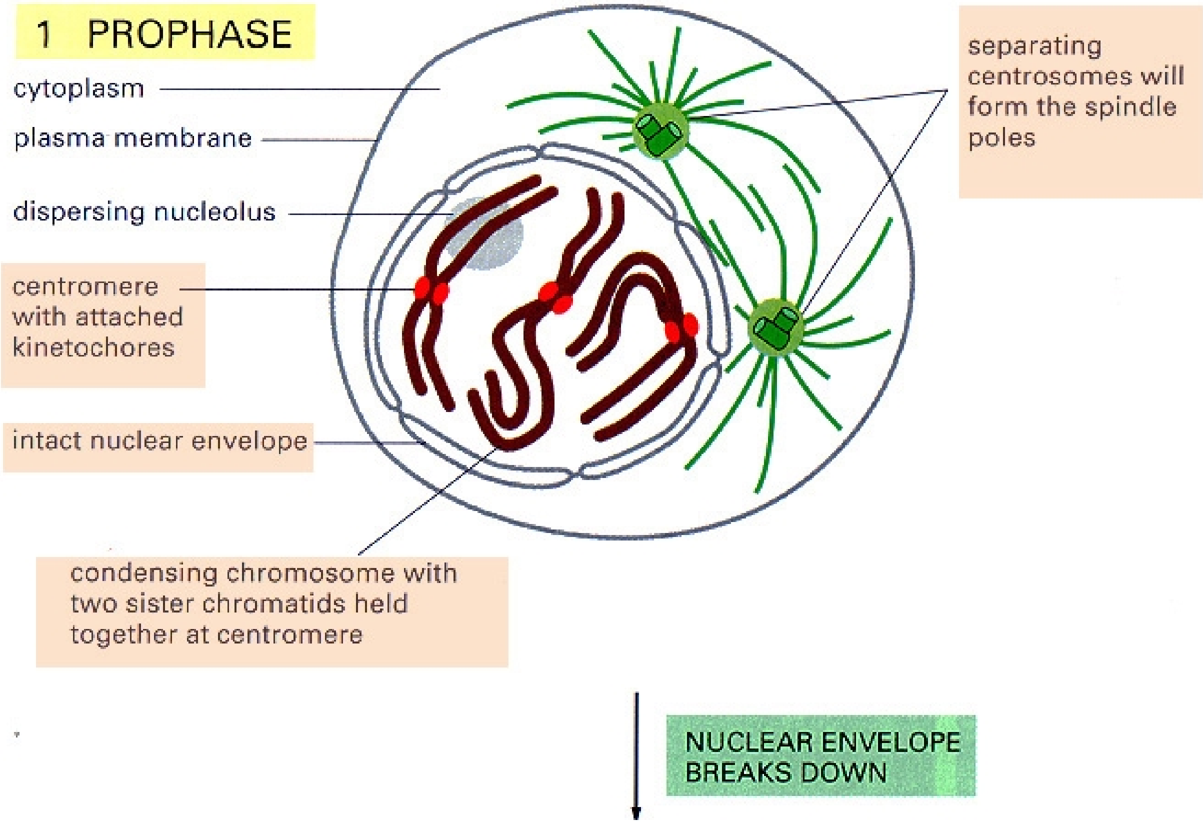
Mitosis

Interphase

- Cell is doing “ general job“
- Chromatin is uncondensed
- Replication takes place during a certain time interval
- Centromer divides into two parts before entering the prophase



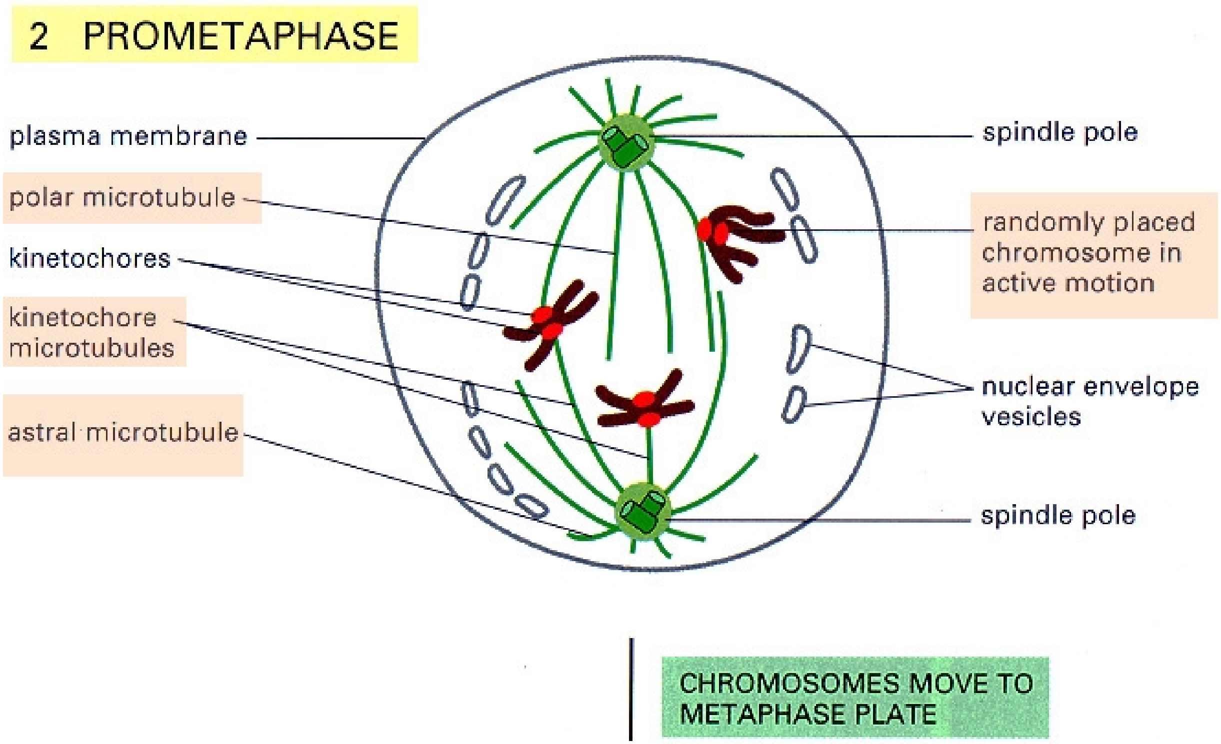
Mitosis



1 PROPHASE

As viewed in the microscope, the transition from the G_2 phase to the M phase of the cell cycle is not a sharply defined event. The chromatin, which is diffuse in interphase, slowly condenses into well-defined chromosomes. Each chromosome has duplicated during the preceding S phase and consists of two sister *chromatids;* each of these contains a specific DNA sequence known as a *centromere,* which is required for proper segregation. Toward the end of prophase, the cytoplasmic microtubules that are part of the interphase cytoskeleton disassemble and the main component of the mitotic apparatus, the *mitotic spindle,* begins to form. This is a bipolar structure composed of microtubules and associated proteins. The spindle initially assembles outside the nucleus between separating centrosomes.

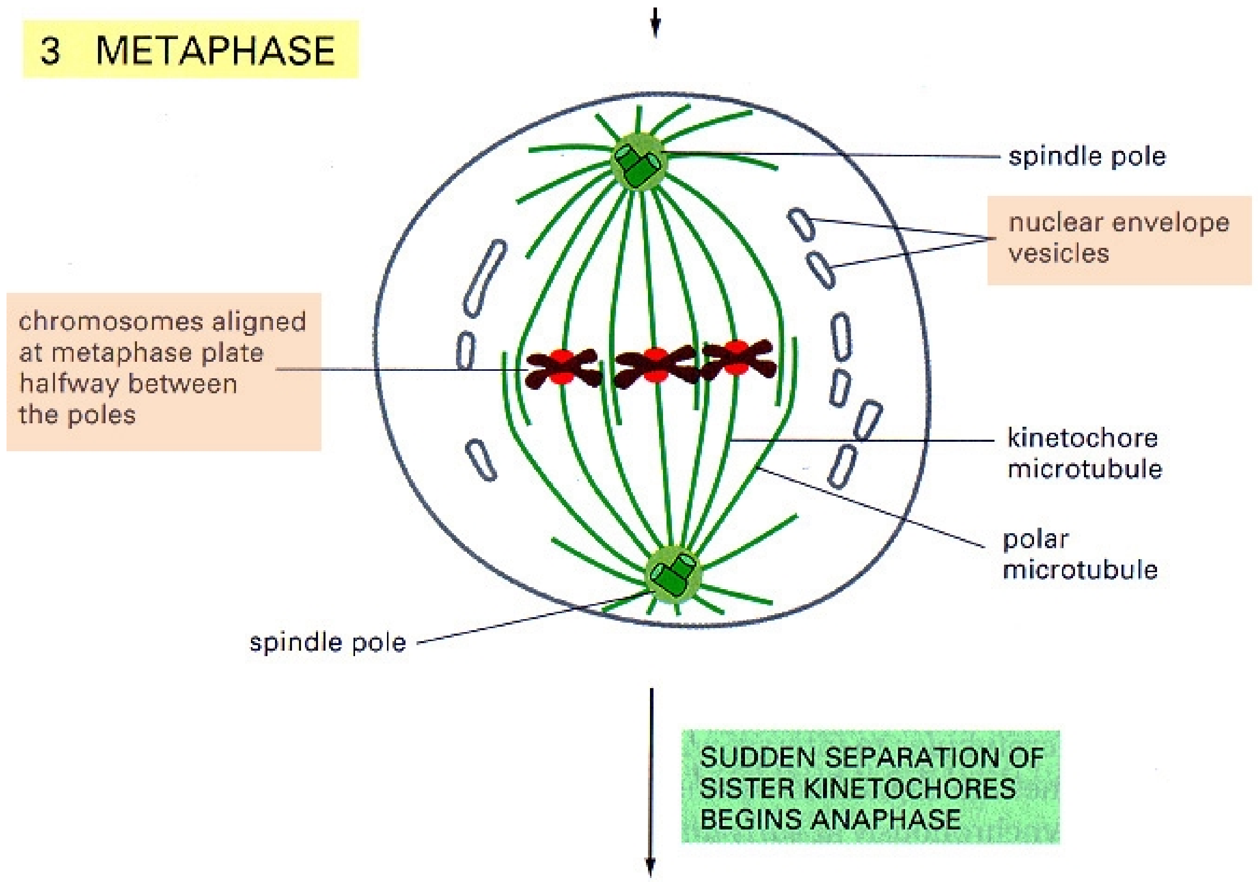
Mitosis



2 PROMETAPHASE

Prometaphase starts abruptly with disruption of the nuclear envelope, which breaks into membrane vesicles that are indistiguishable from bits of endoplasmic reticulum. These vesicles remain visible around the spindle during mitosis. The spindle microtubules, which have been lying outside the nucleus, can now enter the nuclear region. Specialized protein complexes called *kinetochores* mature on each centromere and attach to some of the spindle microtubules, which are then called *kinetochore microtubules*. The remaining microtubules in the spindle are called *polar microtubules,* while those outside the spindle are called *astral microtubules*. The kinetochore microtubules exert tension on the chromosomes, which are thereby thrown into agitated motion.

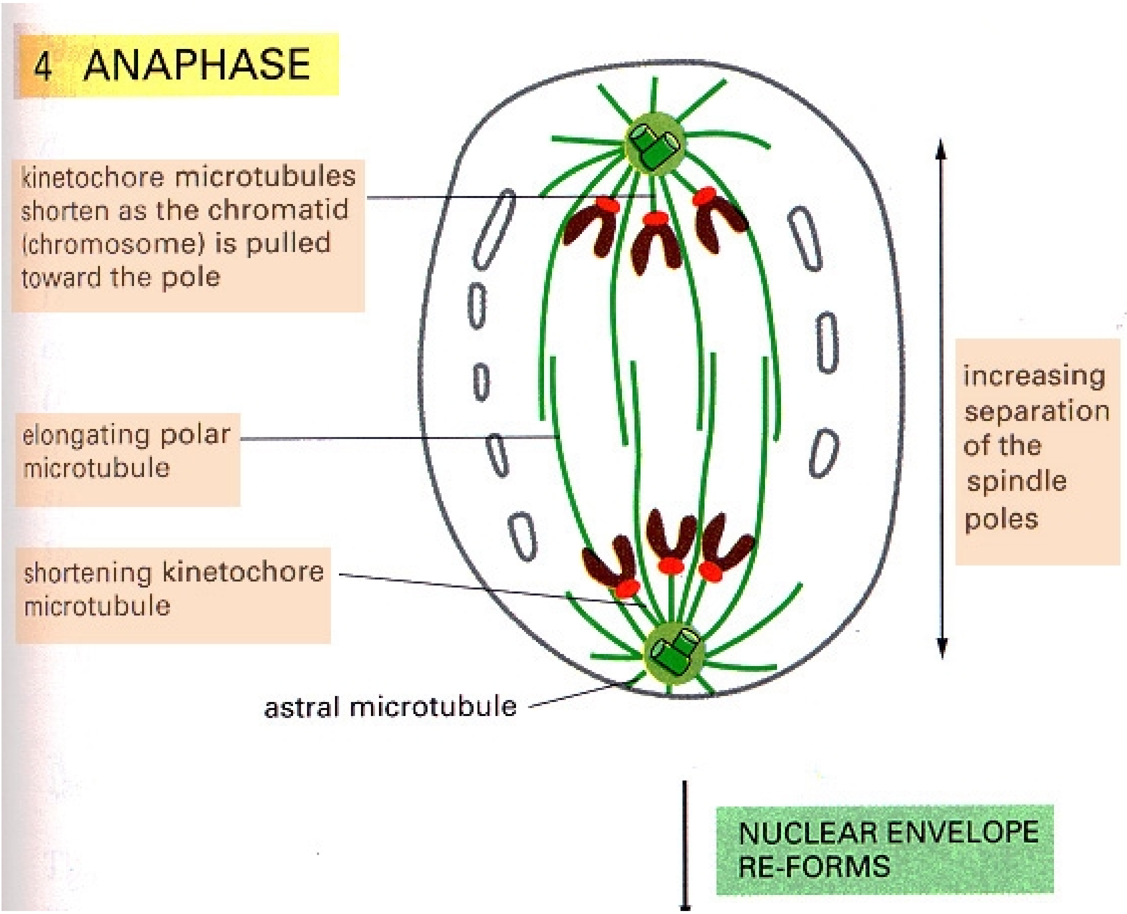
Mitosis



3 METAPHASE

The kinetochore microtubules eventually align the chromosomes in one plane halfway between the spindle poles. Each chromosome is held in tension at this *metaphase plate* by the paired kinetochores and their associated microtubules, which are attached to opposite poles of the spindle.

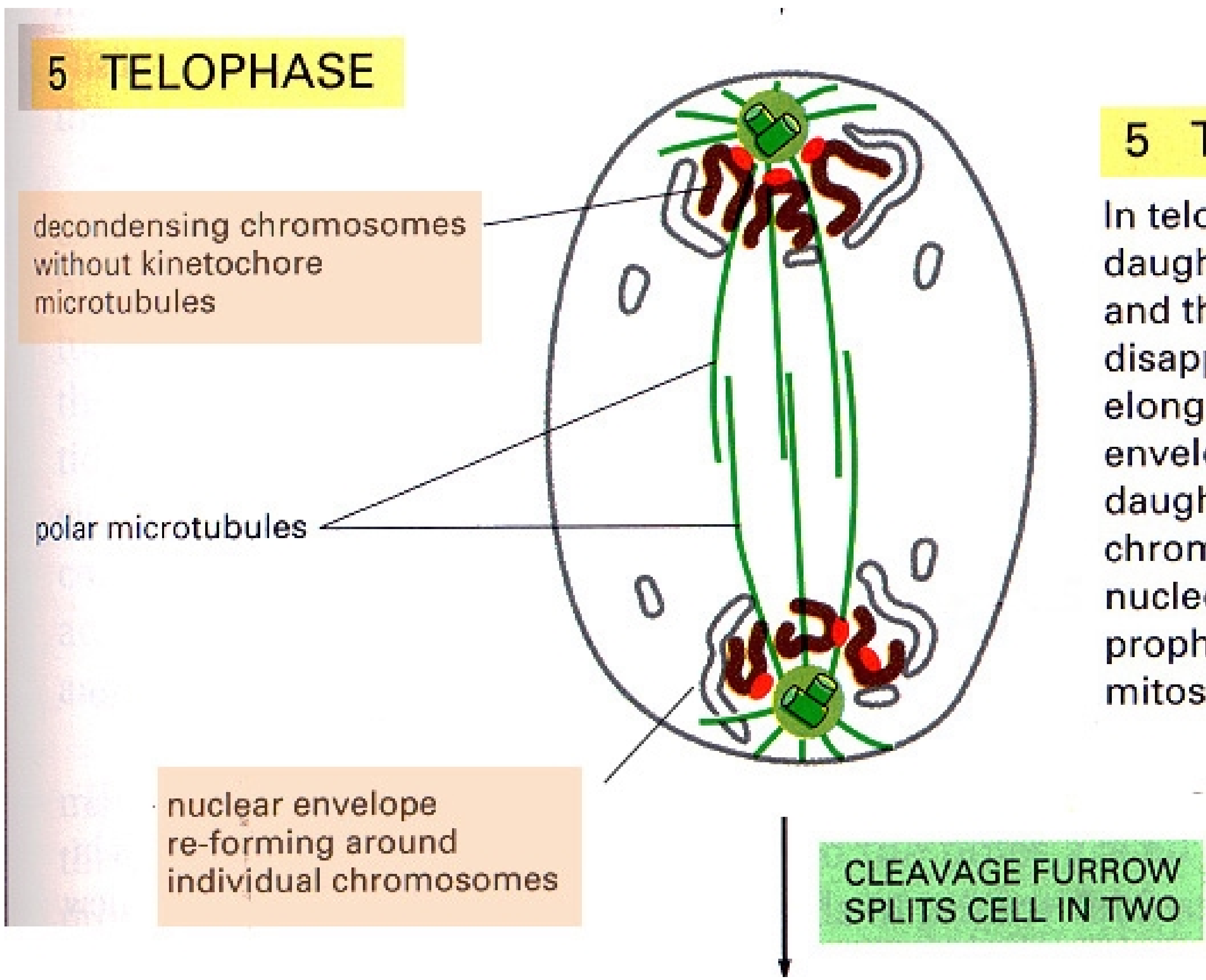
Mitosis



4 ANAPHASE

Triggered by a specific signal, anaphase begins abruptly as the paired kinetochores on each chromosome separate, allowing each chromatid (now called a chromosome) to be pulled slowly toward the spindle pole it faces. All of the newly separated chromosomes move at the same speed, typically about 1 µm per minute. Two catagories of movement can be distinguished. During *anaphase A,* kinetochore microtubules shorten as the chromosomes approach the poles. During *anaphase B,* the polar microtubules elongate and the two poles of the spindle move farther apart. Anaphase typically lasts only a few minutes.

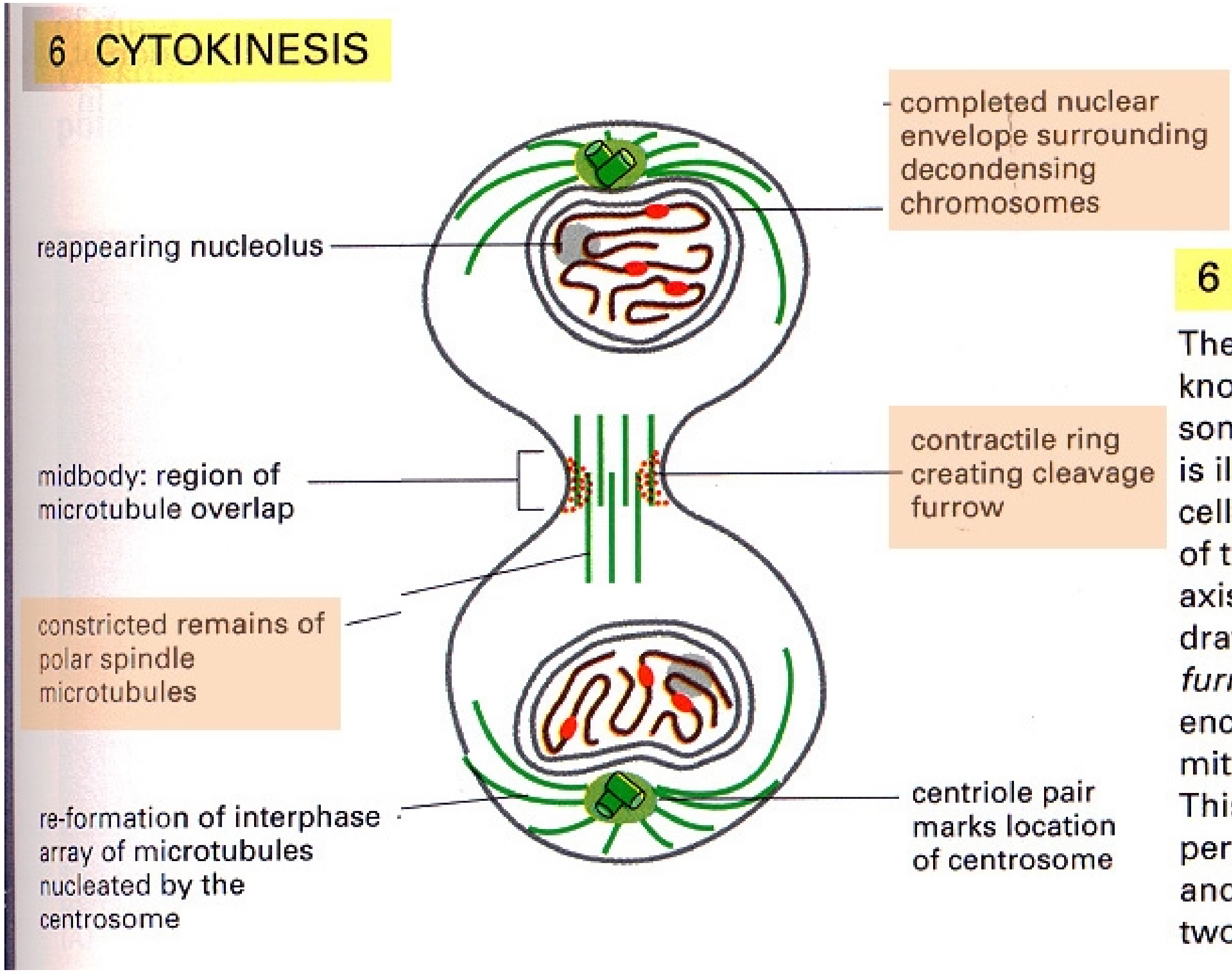
Mitosis



5 TELOPHASE

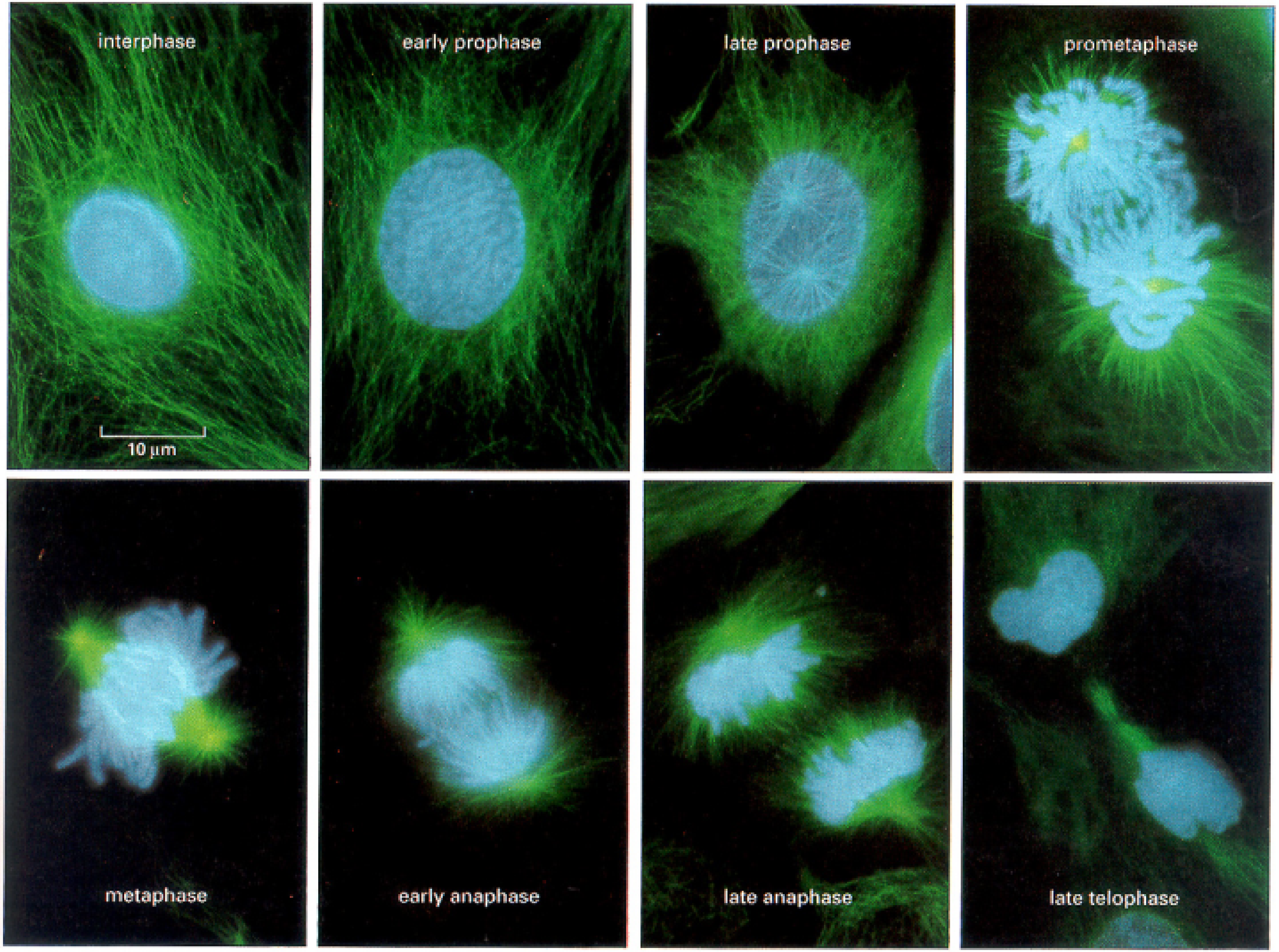
In telophase (*telos*, end) the separated daughter chromosomes arrive at the poles and the kinetochore microtubules disappear. The polar microtubules elongate still more, and a new nuclear envelope re-forms around each group of daughter chromosomes. The condensed chromatin expands once more, the nucleoli—which had disappeared at prophase—begin to reappear, and mitosis is at an end.

Mitosis



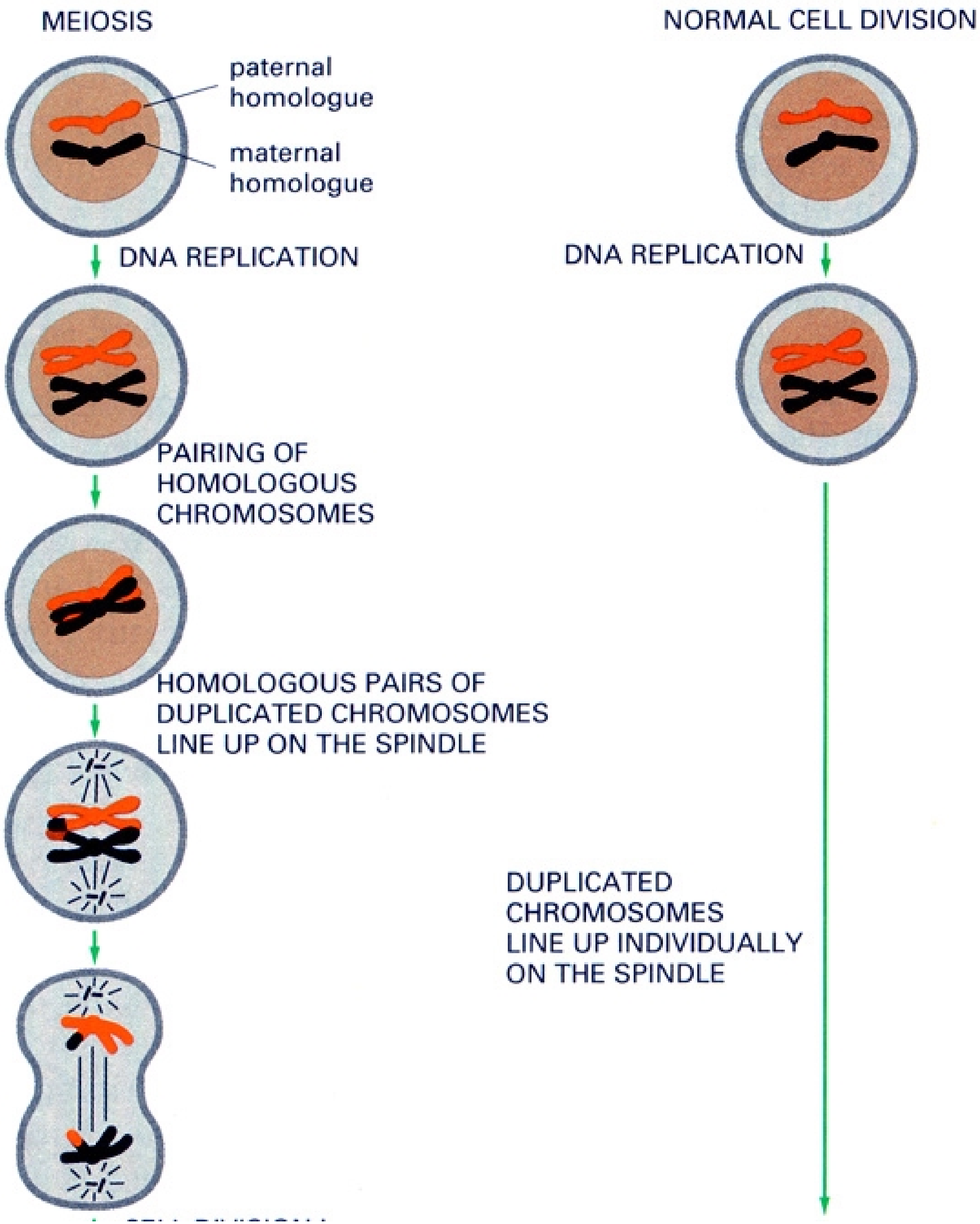
6 CYTOKINESIS

The cytoplasm divides by a process known as *cleavage*, which usually starts sometime during anaphase. The process is illustrated here as it occurs in animal cells. The membrane around the middle of the cell, perpendicular to the spindle axis and between the daughter nuclei, is drawn inward to form a *cleavage furrow*, which gradually deepens until it encounters the narrow remains of the mitotic spindle between the two nuclei. This thin bridge, or *midbody*, may persist for some time before it narrows and finally breaks at each end, leaving two separate daughter cells.


interphase
10 μm
early prophase
late prophase
prometaphase
metaphase
early anaphase
late anaphase
late telophase

Meiosis vs. Mitosis

Meiotic division 1

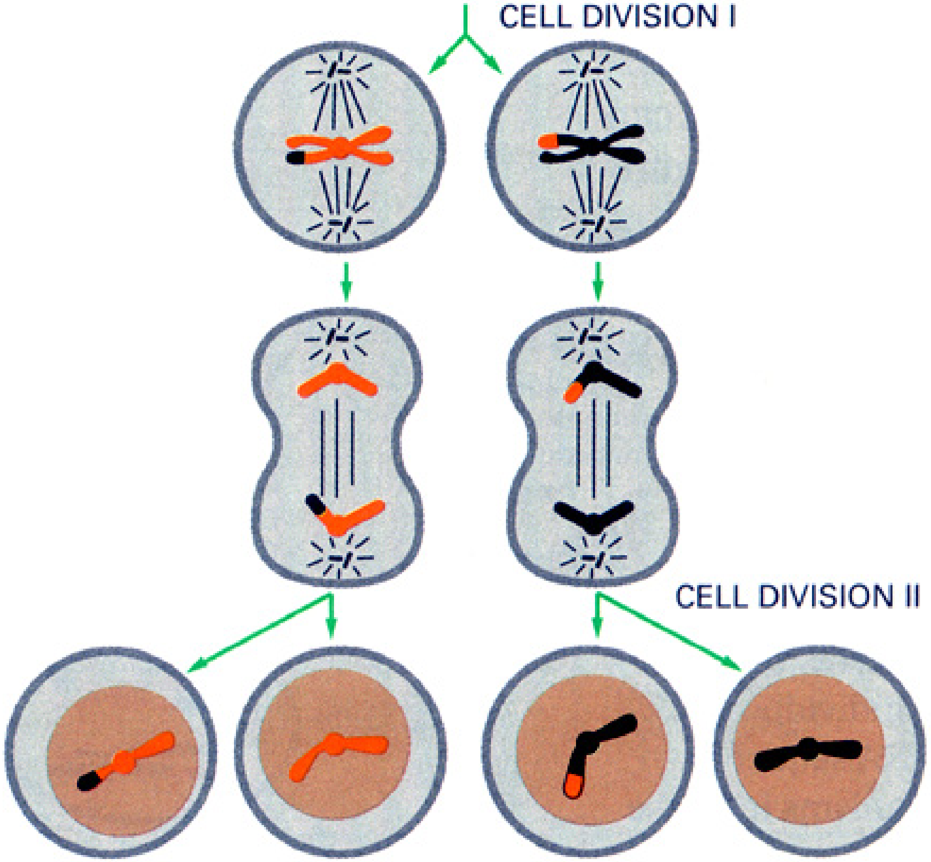


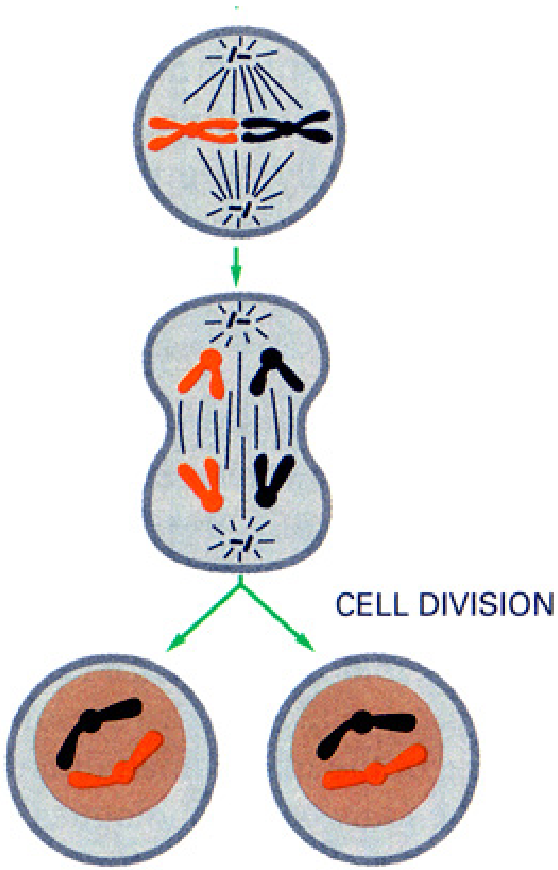
Meiosis vs. Mitosis

Meiotic division 2

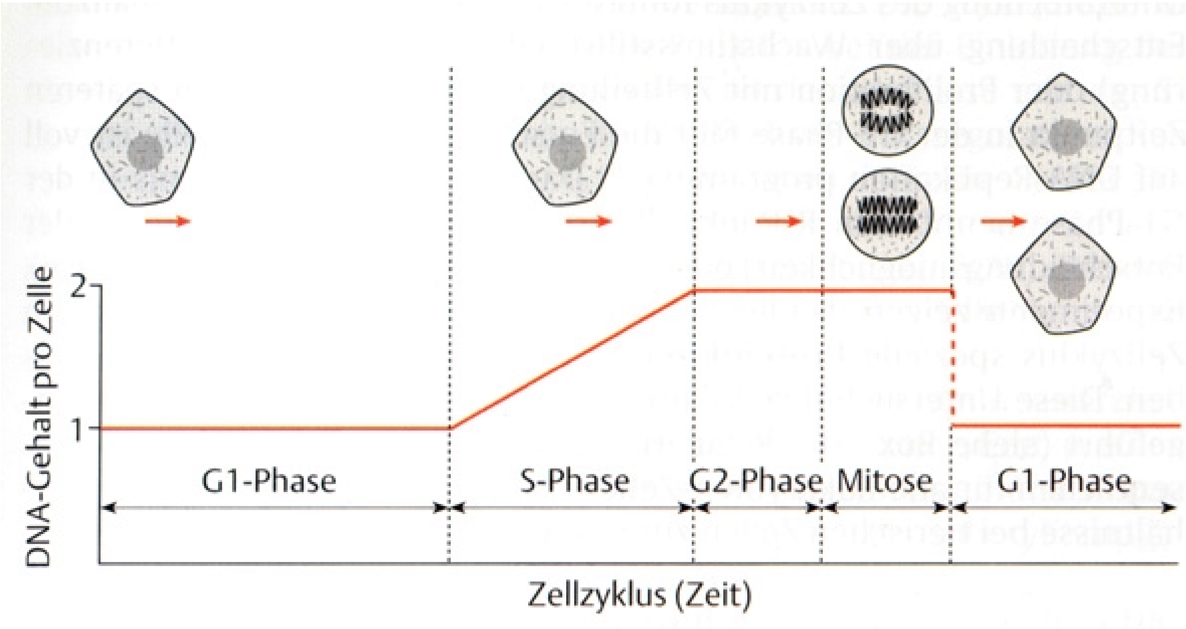
Meiosis

Mitosis





CellCycle in Eucaryotes



Interphase

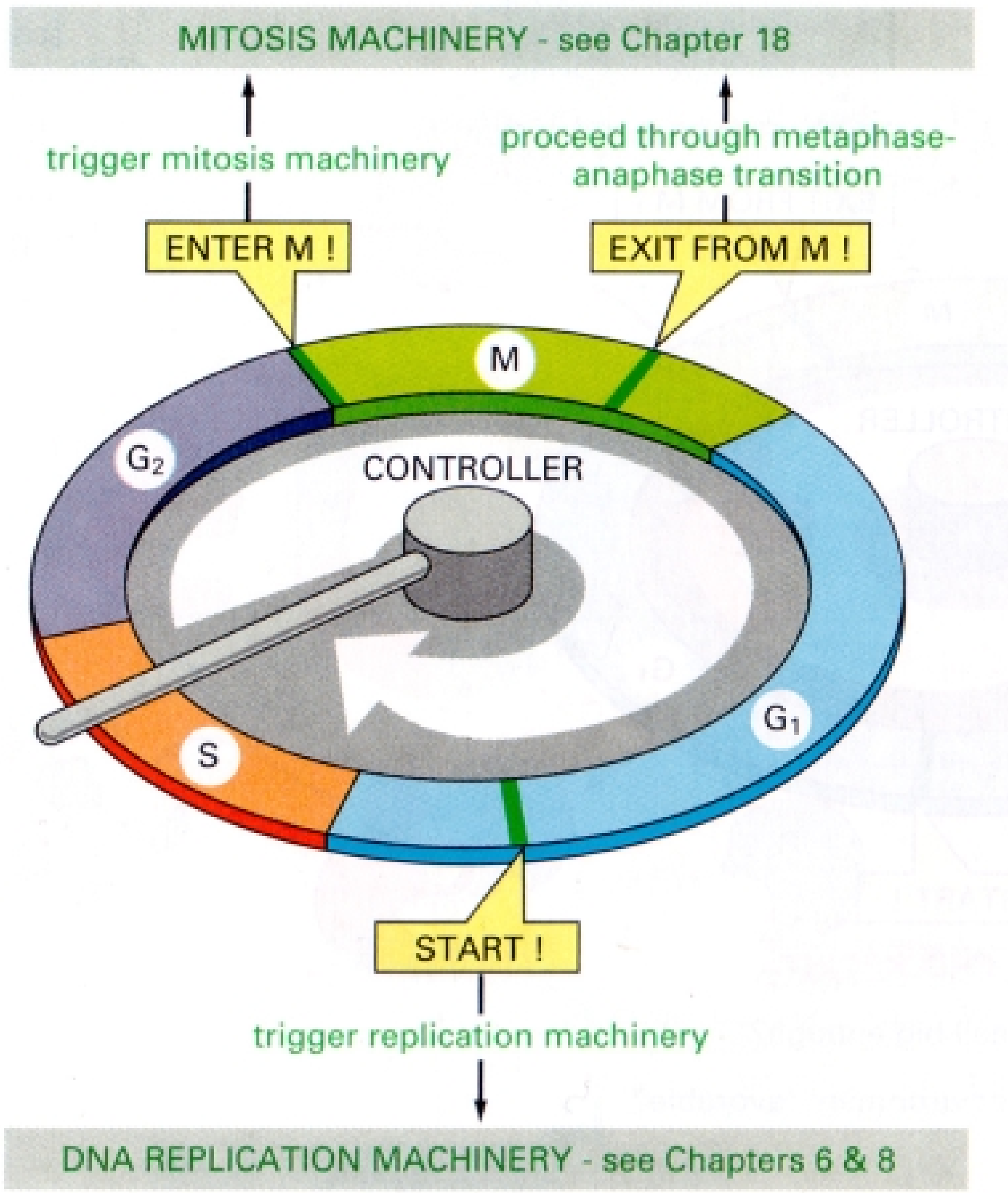
- G1-phase and G2-phase (G = gap) are the phase of cell growth
- S-phase (S = synthesis) is the phase of DNA replication. The DNA content of the cell is increasing during this phase.

Timespan of the cellcycle phases in fast proliferating cells:

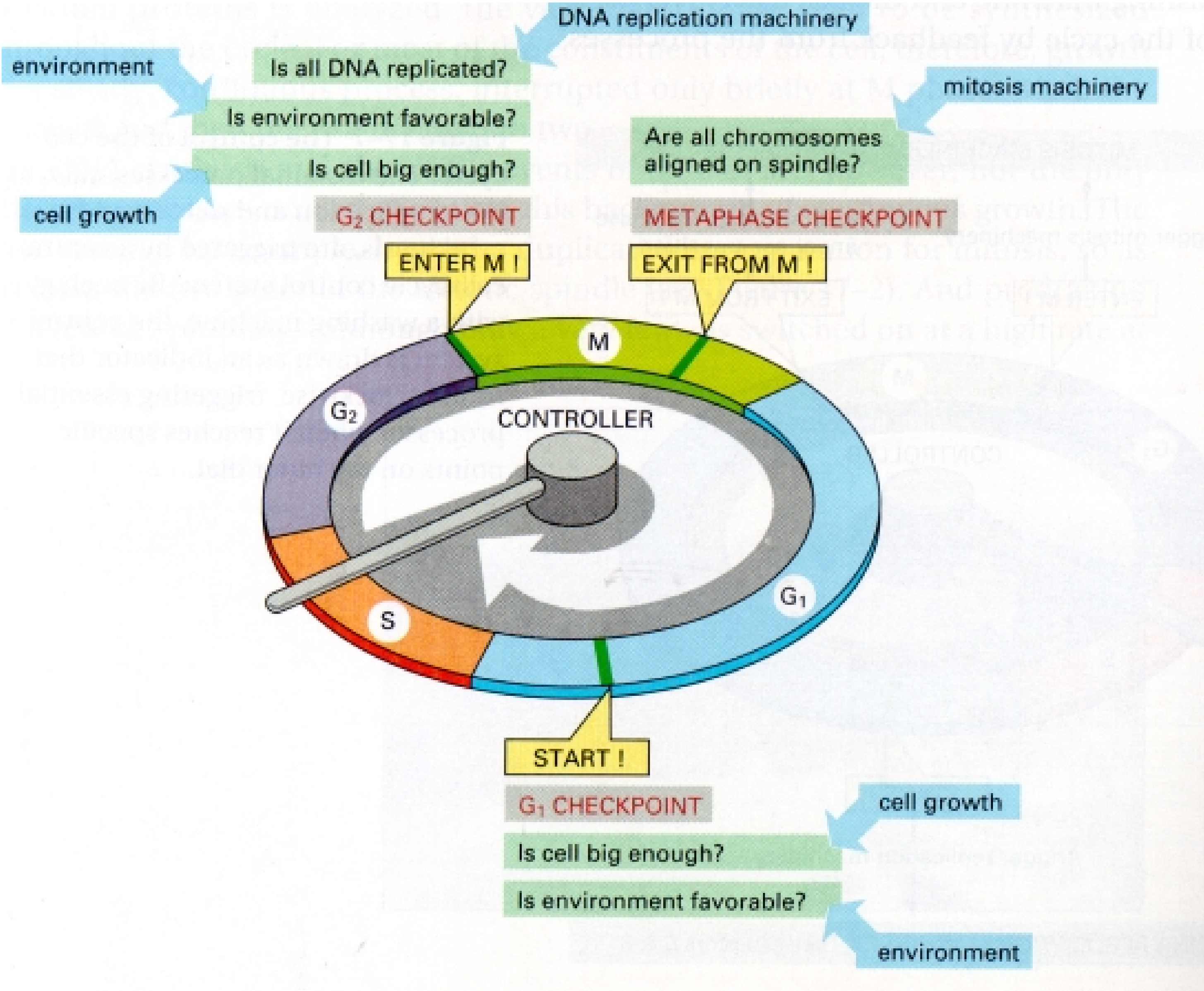
- G1: 2 - 20 h may also last for “ever”
- S: 6 - 10 h
- G2: 2 - 4 h
- M (Mitosis): 3 - 4 h

Control of cellcycle

Essential processes such as DNA replication and mitosis are triggered by central cell-cycle control system. By analogy with a washing machine, the control system is drawn as an indicator that rotates clockwise, triggering essential processes when it reaches specific points on the outer dial.



Checkpoints of cellcycle control



Cyclin dependent kinases

- Mammalian cells have at least 5 Cdk
- Cdk are enzymes
- The Cdk are activated one after another by regulatory Cyclines, this drives the cell cycle.
- by the washing machine analogy, Cdk are the indicator and the Cyclines are the motor, driving the indicator.

Activation of Cdk

inner clockwork of cell
(washing machine indicator)

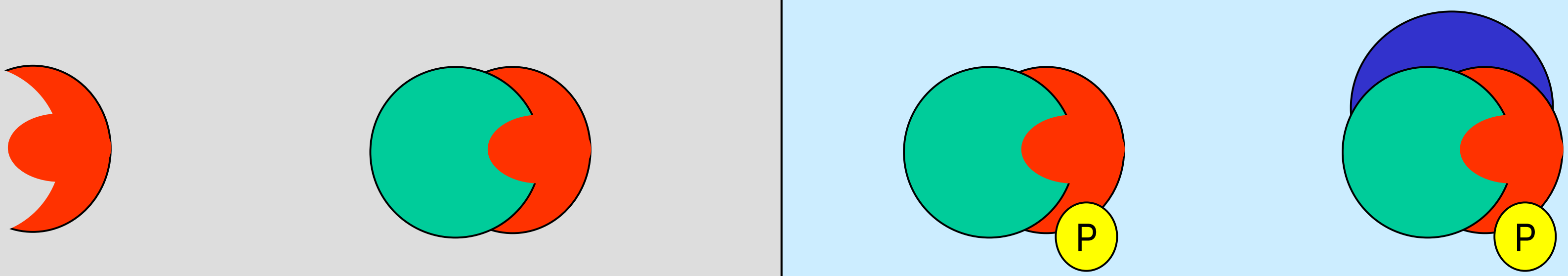
Cdk

Cycline
binds to
Cdk

regulation of cellcycle
(checkpoints)

Cdk has to
be phos-
phorylated
to be active

Cdk
inhibitors
inactivate
the Cdk



inactive

inactive

active

inactive

Cellcycle Regulation

- Cyclines are built periodically during cellcycle
- Every cycline activates special Cdk

<u>Cdk Inhibitors (CKI):</u>

- DNA damage -> p21 is built, p21 binds all G1- active Cdk and stops cellcycle.
- Growth factor (TGF-b) leads to an increase of p27, p27 binds Cyclin E/Cdk2 and prevents the cell from entering the S-phase