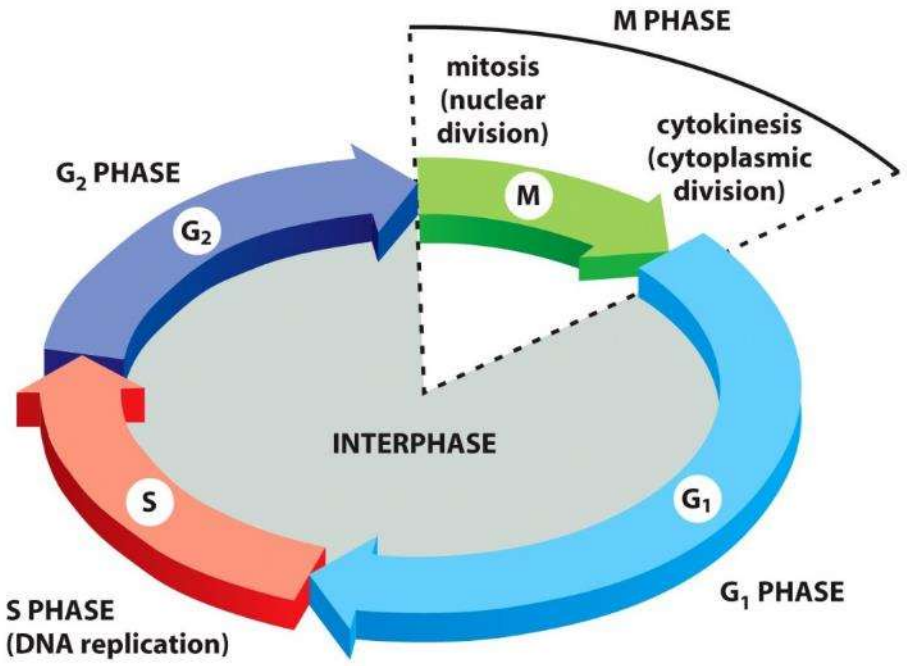
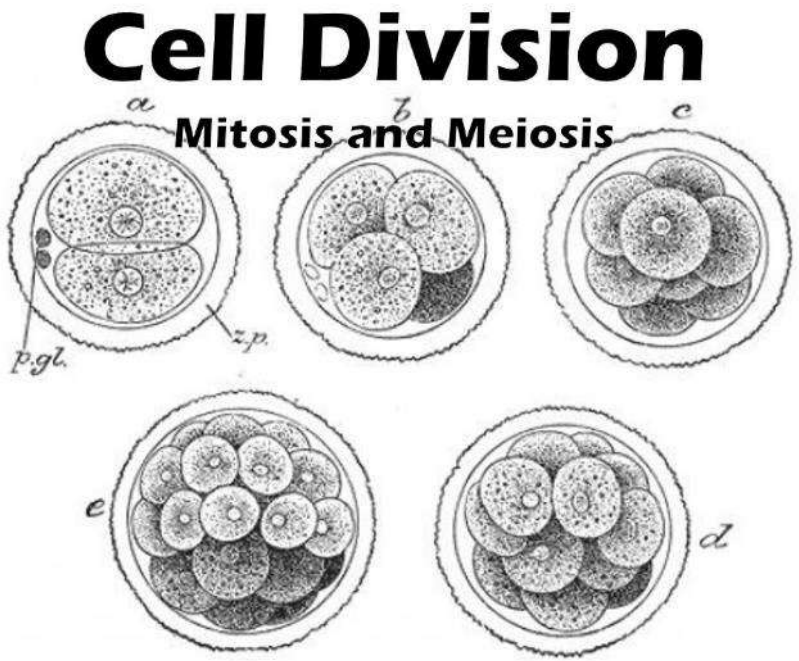
丁明孝 王喜忠 张传茂 陈建国 主编

细胞生物学（第5版）

第十二章 细胞周期与细胞分裂





细胞学说

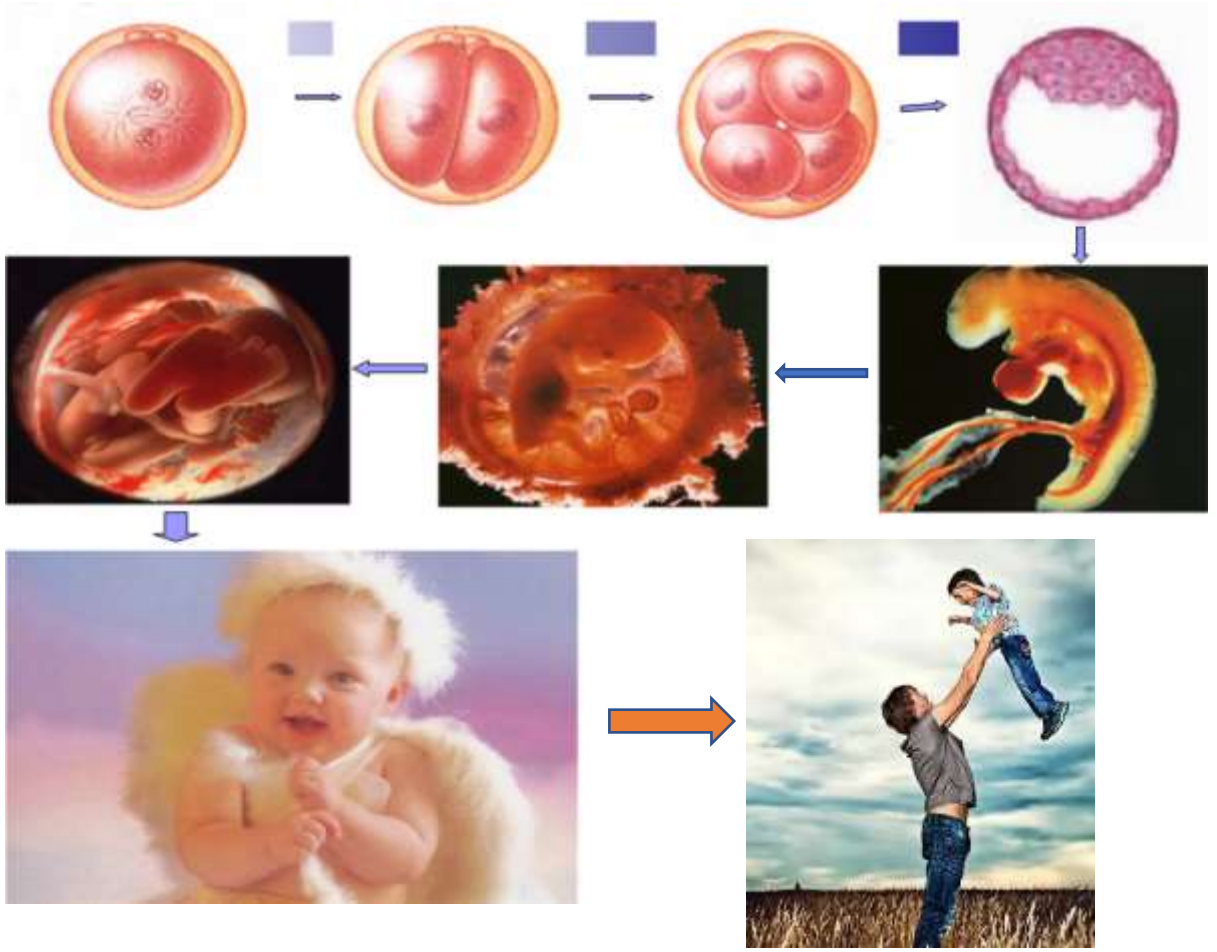
Where a cell arises, there must be a previous cell, just as animals can only arise from animals and plants from plants.

---Rudolf Virchow

德国科学家 魏尔肖

细胞分裂增殖的意义

一、细胞增殖是生物繁育与生长发育的基础



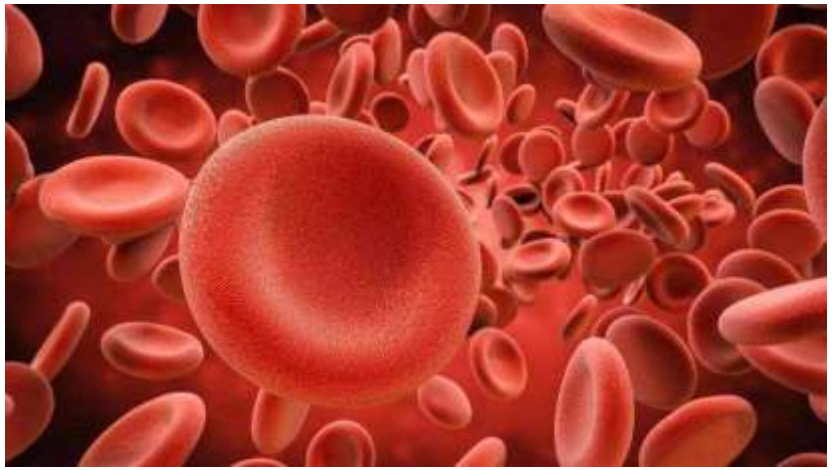
细胞分裂增殖的意义

一、细胞增殖是生物繁育与生长发育的基础

二、细胞增殖可以更新或者弥补代谢过程中衰老或者死亡的细胞

Red blood cell

120 days, 10^{11}/day



细胞周期关注的焦点

一、细胞如何忠实地复制其遗传物质

二、复制后的染色体如何精确分配给其子细胞

三、细胞生长过程与细胞分裂过程如何协调配合

细胞周期4 个时相的发现

correspondence

Celebrating 50 years of the cell cycle

To round off a year of scientific commemoration, let's raise a glass to Howard and Pelc.

Sir — This year the world has celebrated the 50th anniversary of the discovery of DNA's structure (see, for example, *Nature* **421**, 395–453; 2003). Meanwhile, however, another important scientific anniversary is in danger of slipping past unmarked.

Also in 1953, Alma Howard and Stephen Pelc published their work on cell proliferation in bean (*Vicia faba* L.) roots[1]. They grew plants with a ^{32}P isotope label and showed that it was incorporated into DNA in the nucleus only during interphase, and that it took 12 hours from the end of division until the beginning of the isotope uptake into new DNA. By analysing heterogeneous populations of meristematic cells, Howard and Pelc deduced that DNA synthesis takes about six hours, and that cells enter prophase of the next mitosis only eight hours after DNA synthesis is completed.

Howard and Pelc were the first to ascribe a timeframe to cellular life and they proposed the existence of four periods in the cell cycle: a period of cell division, the pre-S-phase (called G1), the S-phase (a period of DNA synthesis) and period G2, or the pre-mitotic period. The concept of the cell cycle was born.

Since then, cell-cycle studies have flourished. It is unfortunate, therefore, that this discovery is now almost forgotten (though not totally: see www.nature.com/celldivision/milestones/full/milestone03.html). The view of the cell cycle formed a basis for determining time parameters of the cell cycle (by labelling mitoses and other methods) and for the biochemical and molecular events that take place at each stage of the life of the cell between divisions in various groups of organisms.

As we know, the concept was later developed and the checkpoints in cell-cycle regulation and universal control mechanisms were determined by using genetics and molecular biology[2].

All these recent achievements stemmed from Howard and Pelc's study — which calls for another 50-year anniversary celebration to be held by the international scientific community.

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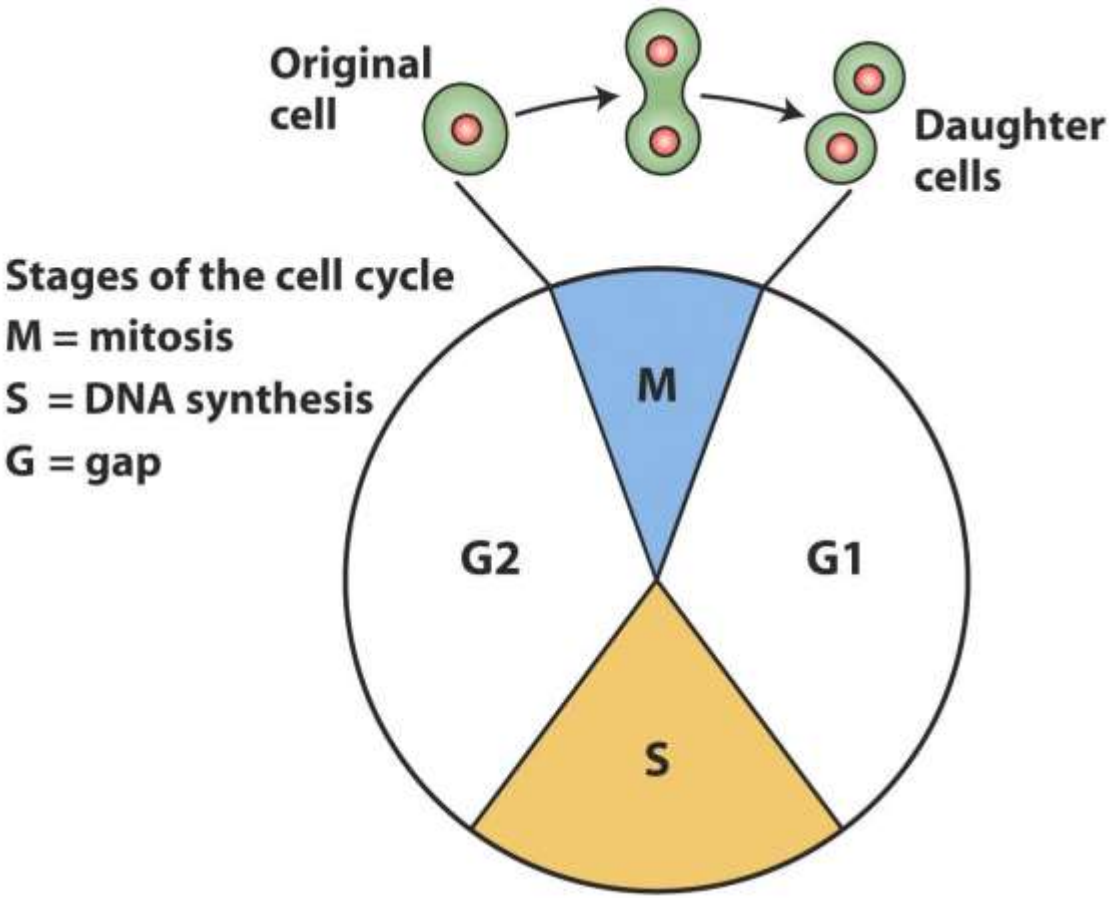
†Timiryazev Institute of Plant Physiology, Russian Academy of Sciences, Botanicheskaya 35, Moscow 127276, Russia

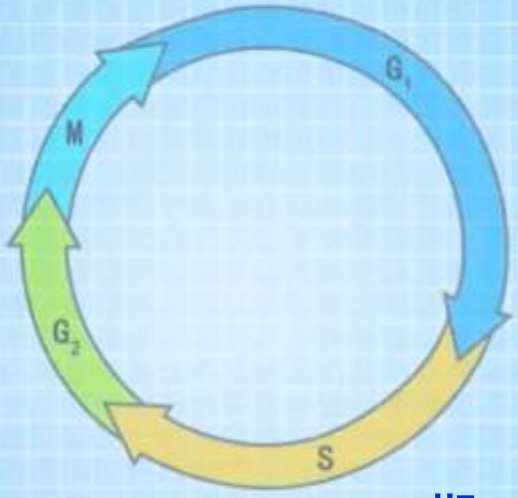
1. Howard, A. & Pelc, S. *Heredity* **6** (suppl.), 261–273 (1953).
2. Nurse, P. *Nature* **344**, 503–508 (1990).

一. 细胞周期 (Cell Cycle)概述



二. 细胞周期中各不同时相及其主要事件

M期：细胞分裂



G1期：合成细胞生长所需的蛋白质、糖类、脂质等

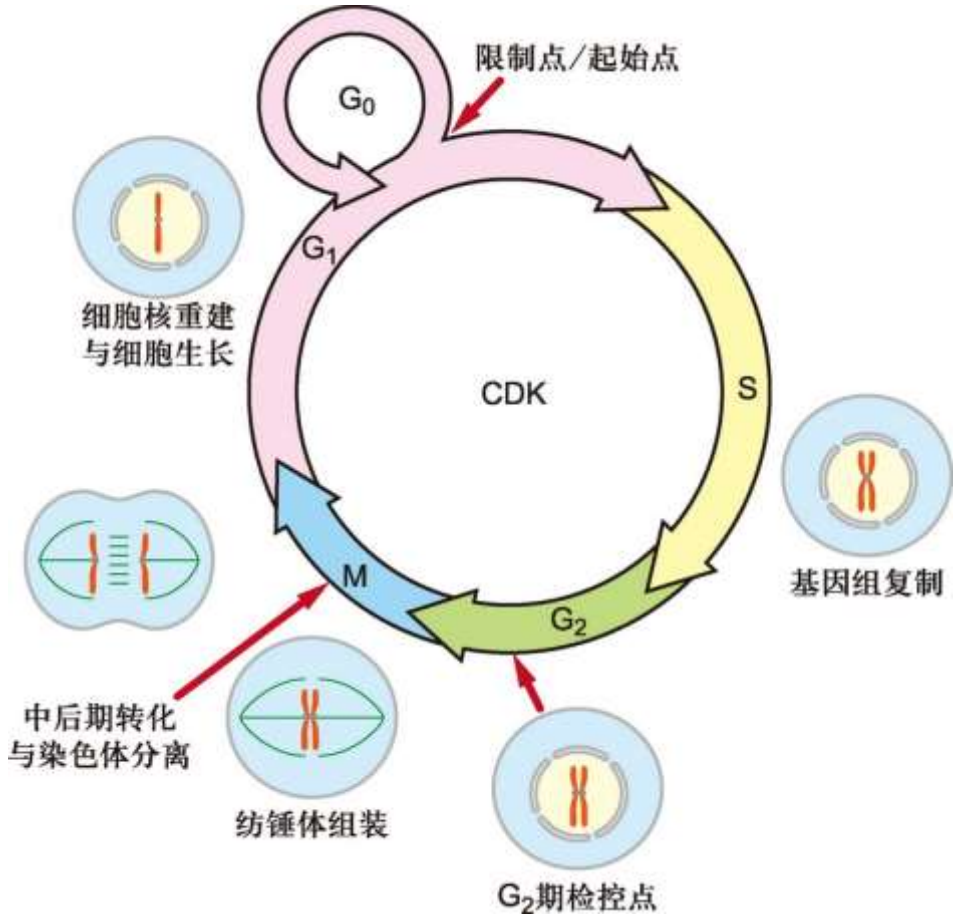
G2期：检查DNA 是否完成复制，细胞是否已生长到合适大小，环境因素是否利于细胞分裂等

S期：DNA复制

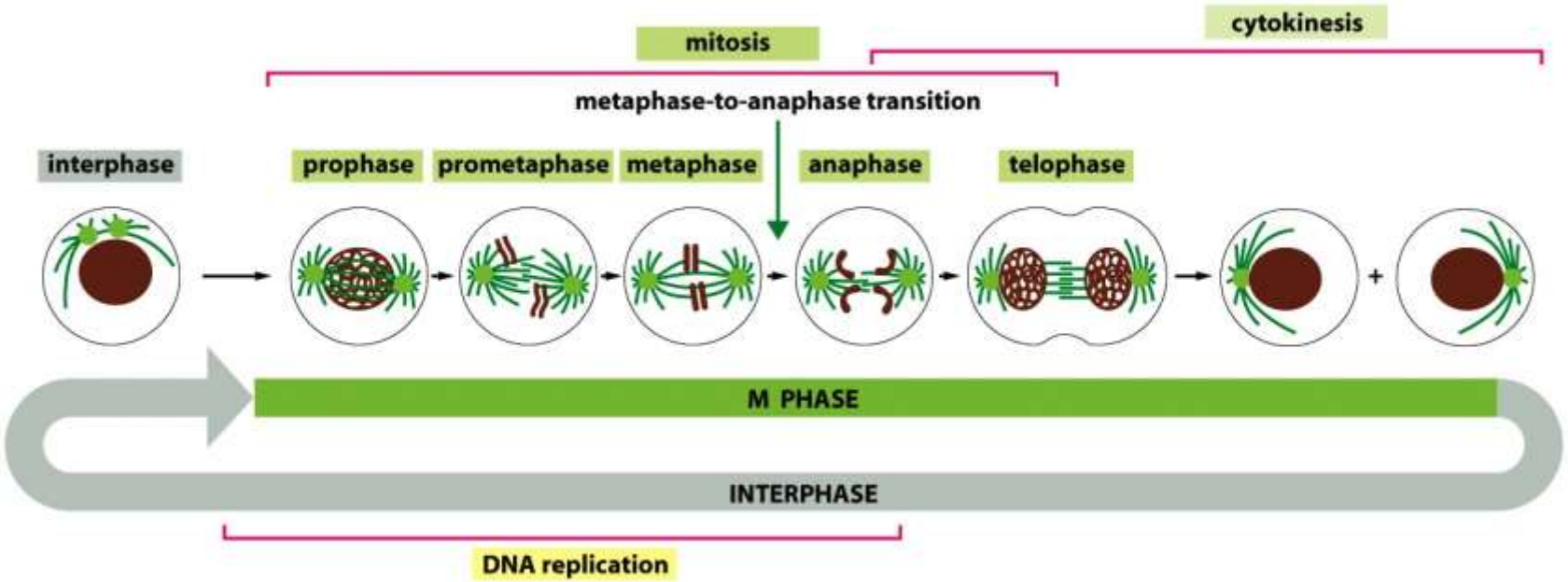
细胞周期

二. 细胞周期中各不同时相及其主要事件

- **G1期：**合成细胞生长所需的蛋白质、糖类、脂质等
- **S期：**DNA复制
- **G2期：**检查DNA 是否完成复制，细胞是否已生长到合适大小，环境因素是否利于细胞分裂等
- **M期：**细胞分裂



细胞周期的差异



Cell Type	Cell-Cycle Times
Early frog embryo cells	30 minutes
Yeast cells	1.5–3 hours
Intestinal epithelial cells	~12 hours
Mammalian fibroblasts in culture	~20 hours
Human liver cells	~1 year

细胞周期的差异

Why so different?

The greatest variation occurs in the duration of G_1

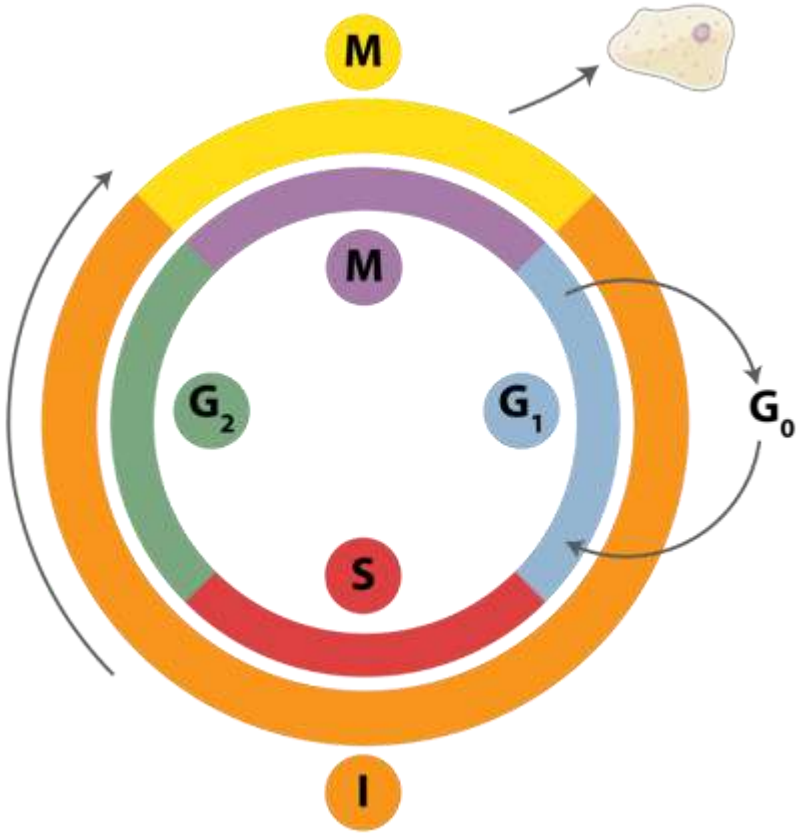
小鼠食管上皮细胞 T=115h G1=103h

十二指肠上皮细胞 T=15h G1=6h

细胞社会中的3 类细胞群体

- **周期中细胞**（cycling cell）

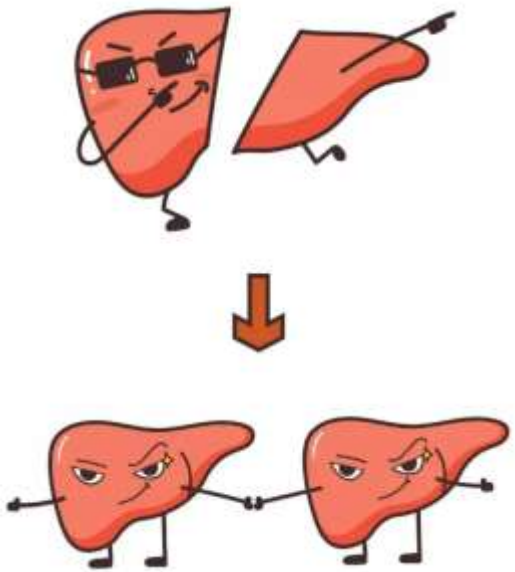
----细胞周期持续运转、增殖，以增加细胞数量



细胞社会中的3 类细胞群体

- **周期中细胞**（cycling cell）
- **G_0 期细胞**（**静止期细胞，**quiescent cell）

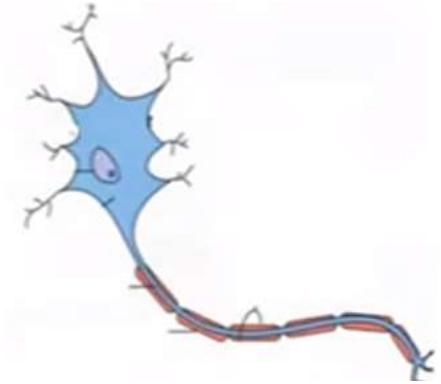
----暂时脱离细胞周期、停止分裂而执行特定生物学功能，若受到刺激，重新进入细胞周期

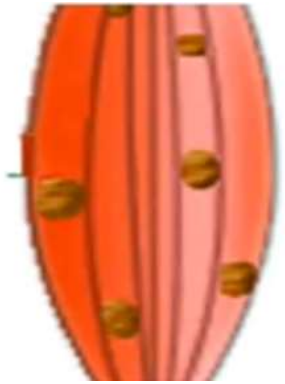


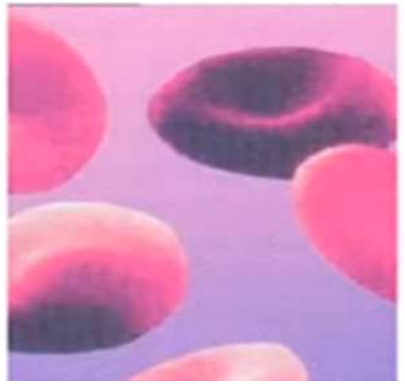
细胞社会中的3 类细胞群体

- **周期中细胞**（cycling cell）
- **G_0 期细胞（静止期细胞，**quiescent cell）
- **终末分化细胞**（terminally differentiated cell）

----**分化程度很高，终身不再分裂**

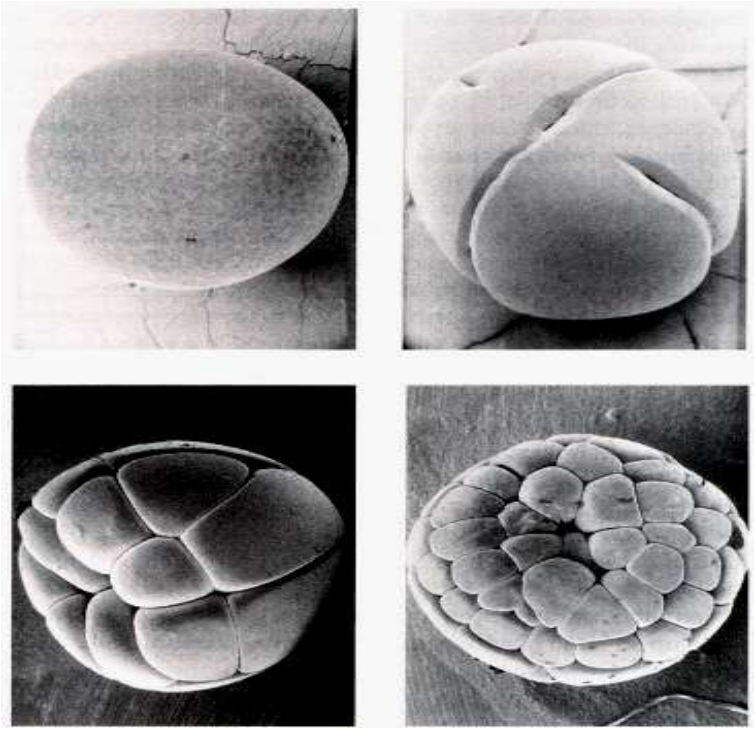






特殊的细胞周期——早期胚胎细胞

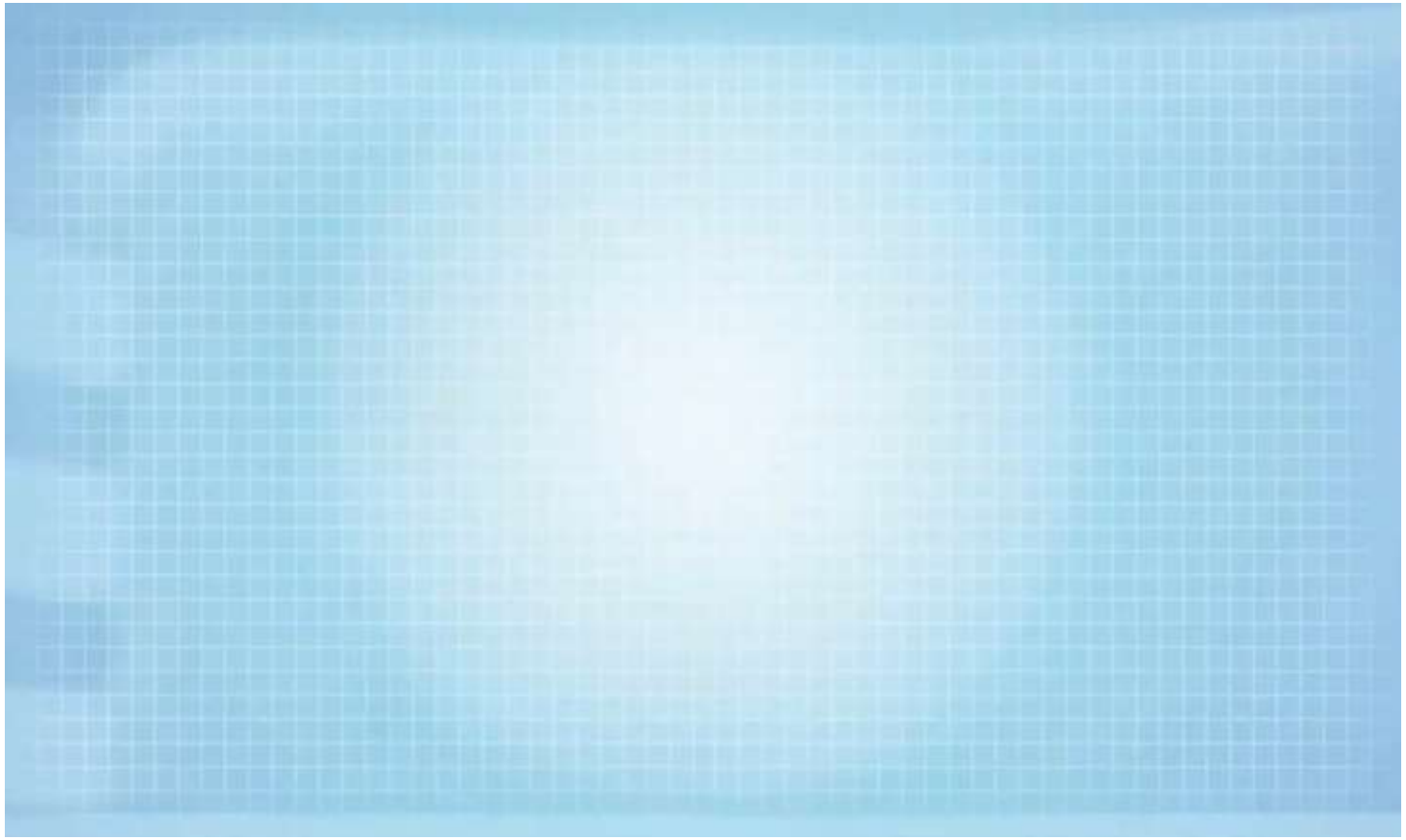
- 受精卵迅速卵裂，卵裂球数量增加，但其总体积并不增加；
- G1 期和 G2 期非常短



三、细胞周期同步化

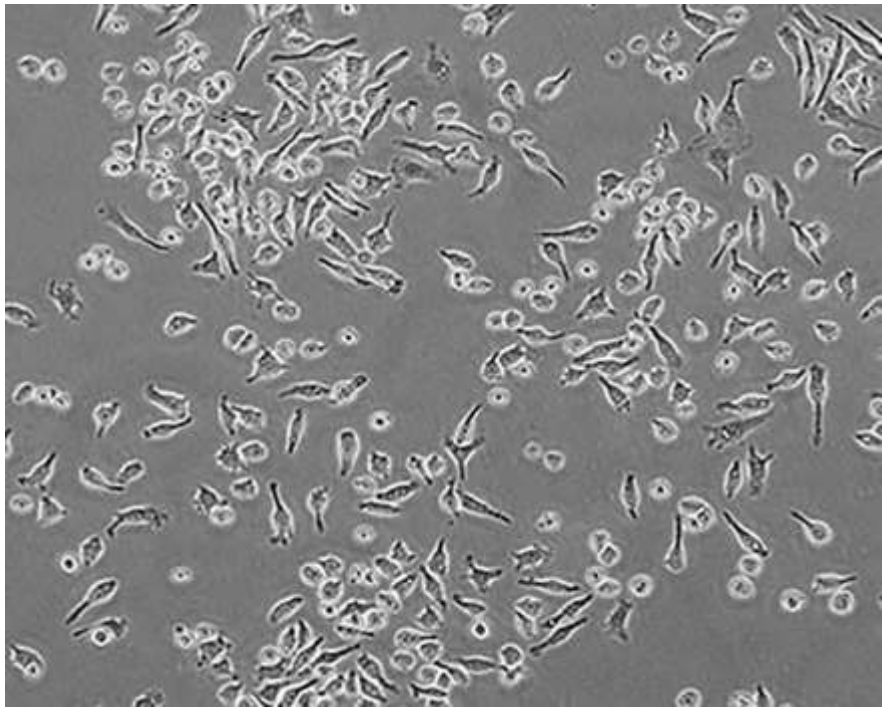
- **天然同步化(natural synchronization)**

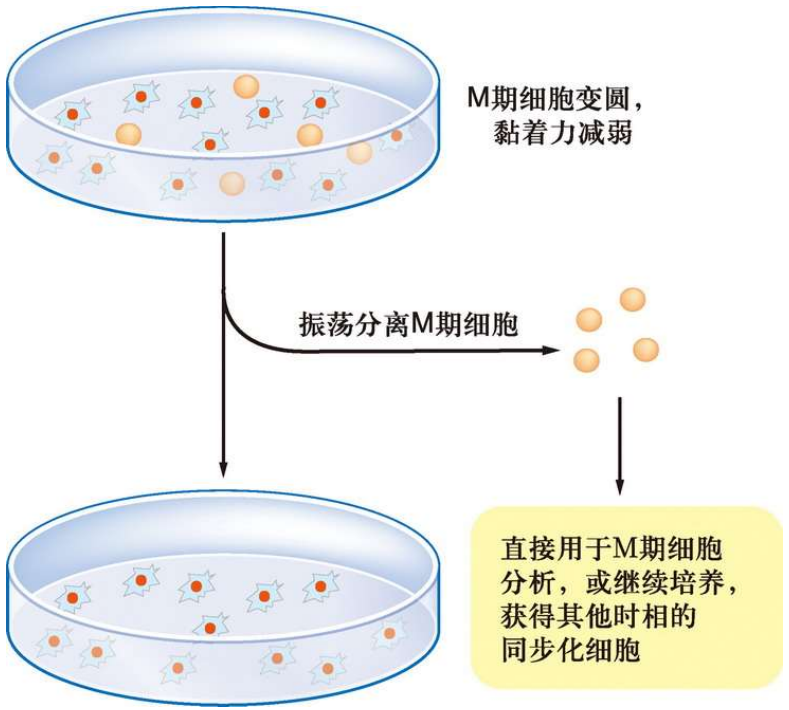
Early embryo in most invertebrates and a few vertebrates



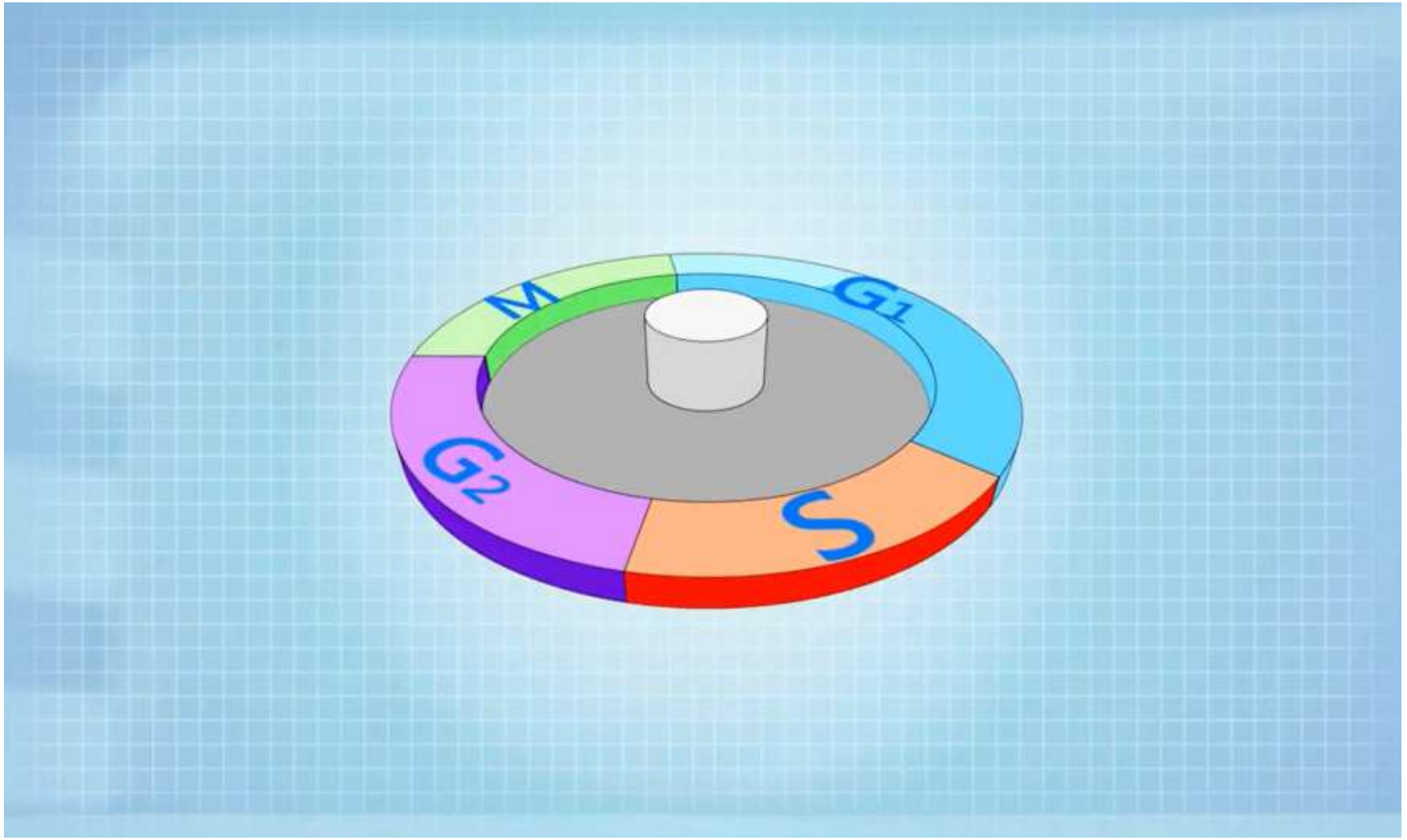
三、细胞周期同步化

- **人工同步化(artificial synchronization)**
  - 选择同步化(Selected synchronization)
  - 诱导同步化(Induced synchronization)





- 诱导同步化（Induced synchronization）



诱导同步化

- DNA 合成阻断法
- 分裂中期阻断法

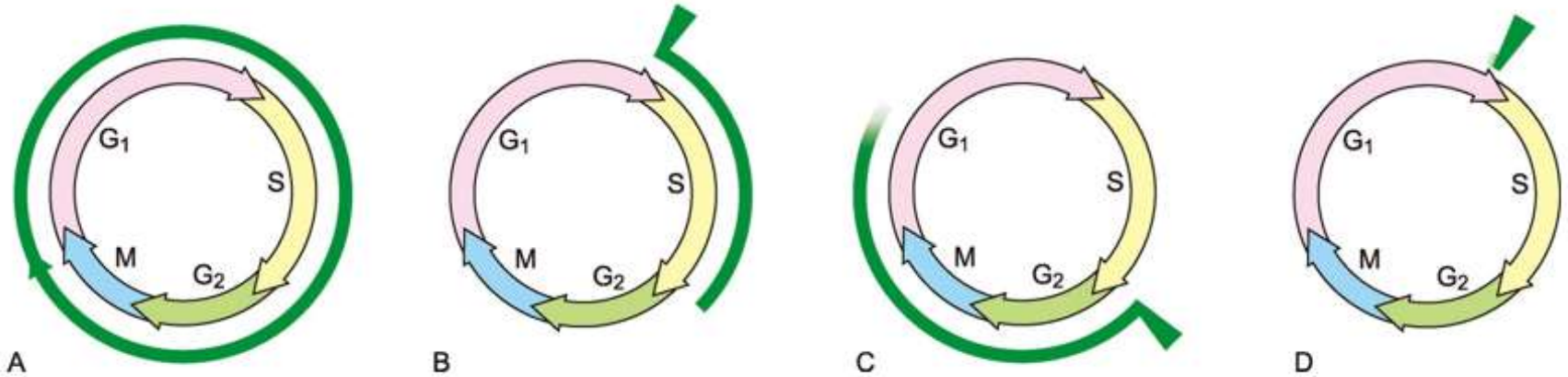
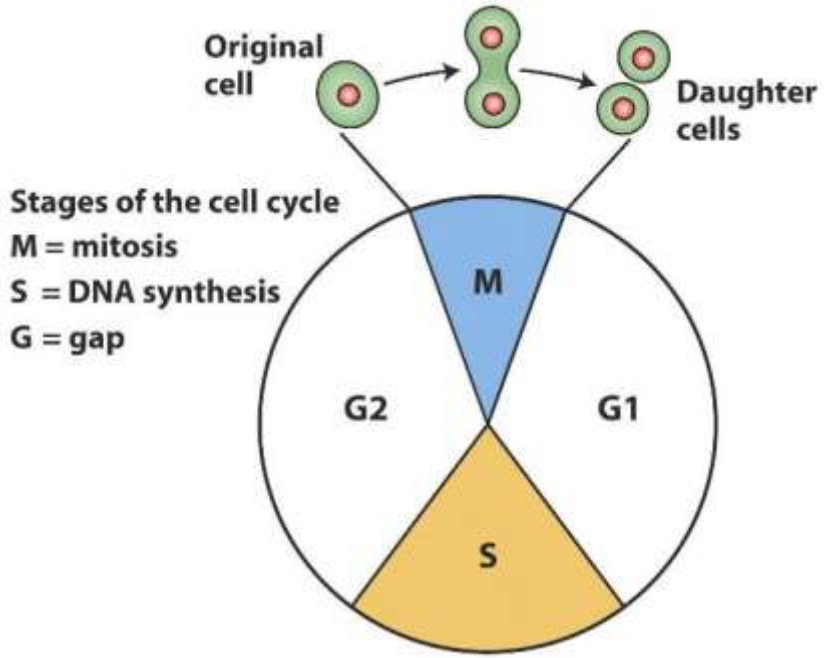


图12-4 应用过量的TdR 阻断法进行细胞周期同步化

A. 处于对数生长期的细胞。B. 第一次加入TdR，所有处于S 期的细胞立即被抑制，其他细胞运行到G1/S 期交界处被抑制。C. 将TdR 洗脱，解除抑制，被抑制的细胞沿细胞周期运行。D. 在解除抑制的细胞到达G1 期终点前，第二次加入TdR 并继续培养，所有的细胞被抑制在G1/S 期交界处

细胞周期 cell cycle 细胞分裂 cell division

- **细胞增殖(cell proliferation)：**细胞生命活动的重要特征之一
- **细胞分裂(cell division)：**细胞增殖最直观的表现
- **细胞周期(cell cycle)：**细胞增殖过程



http://barleyworld.org/sites/default/files/figure-03-23.jpg

三、细胞周期同步化

- **天然同步化(natural synchronization)**
  - Early embryo in most invertebrates and a few vertebrates
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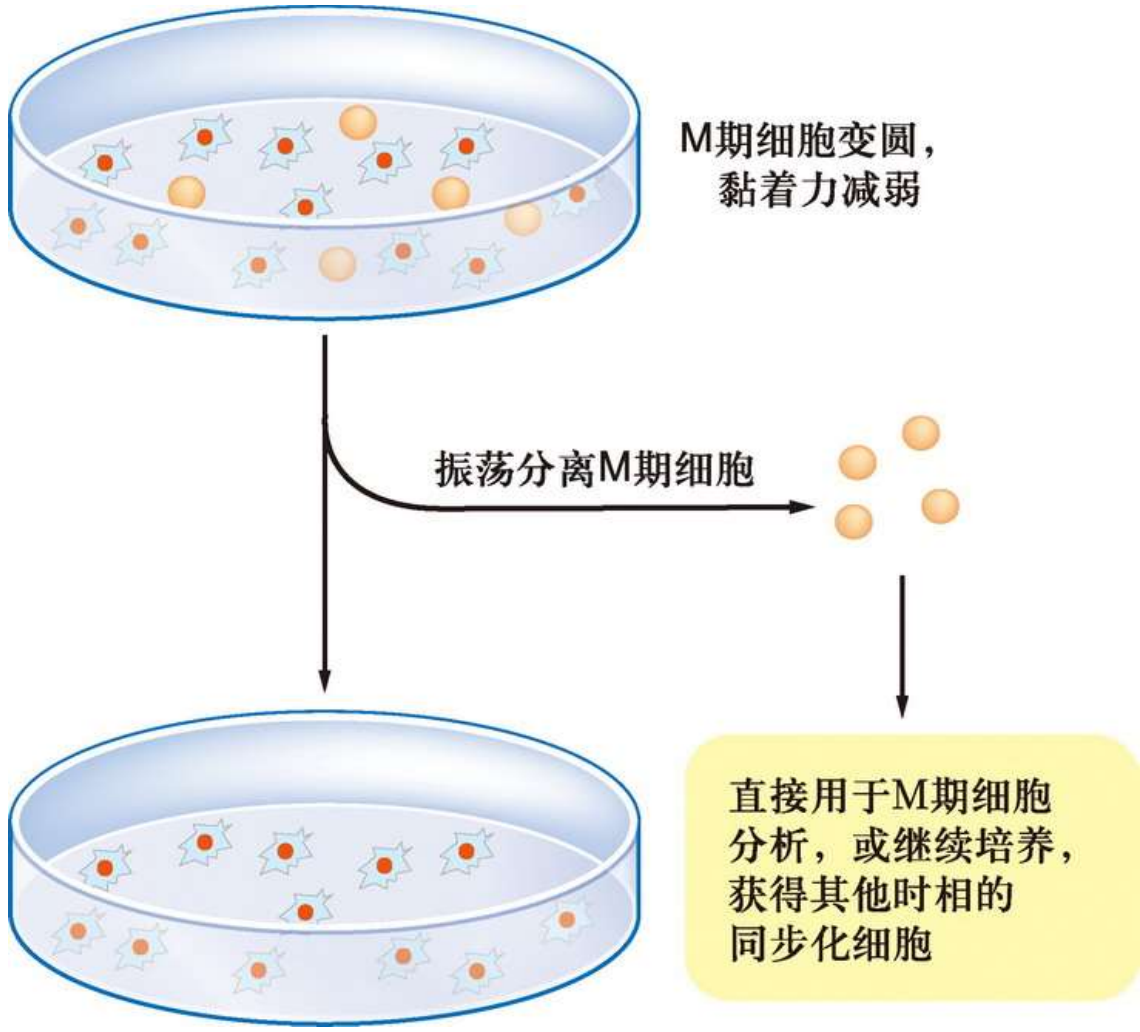


图12-3 从培养细胞中收集M 期细胞的同步化方法

诱导同步化

- DNA 合成双阻断法
- 分裂中期阻断法（秋水仙碱、nocodazole)

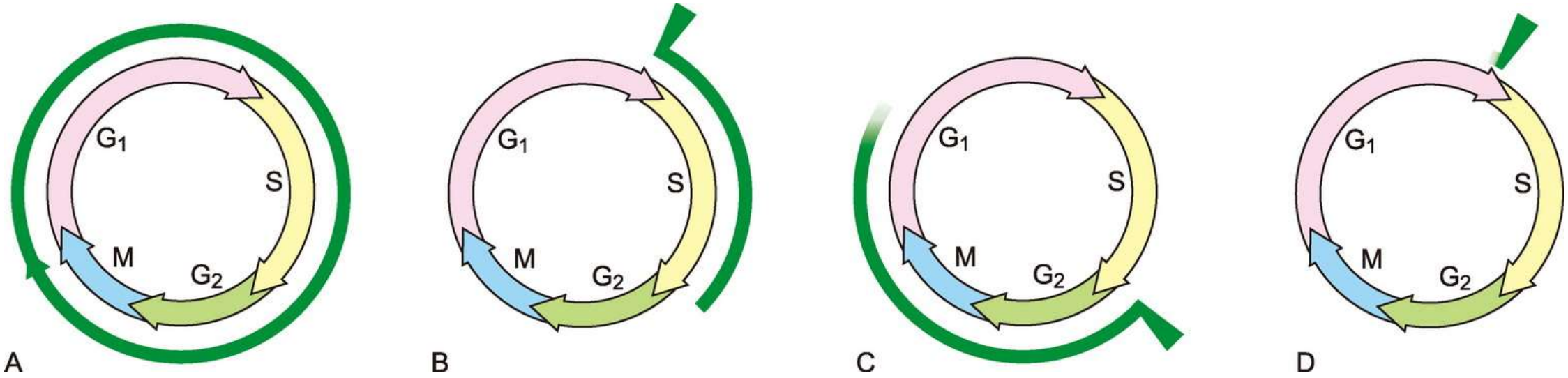
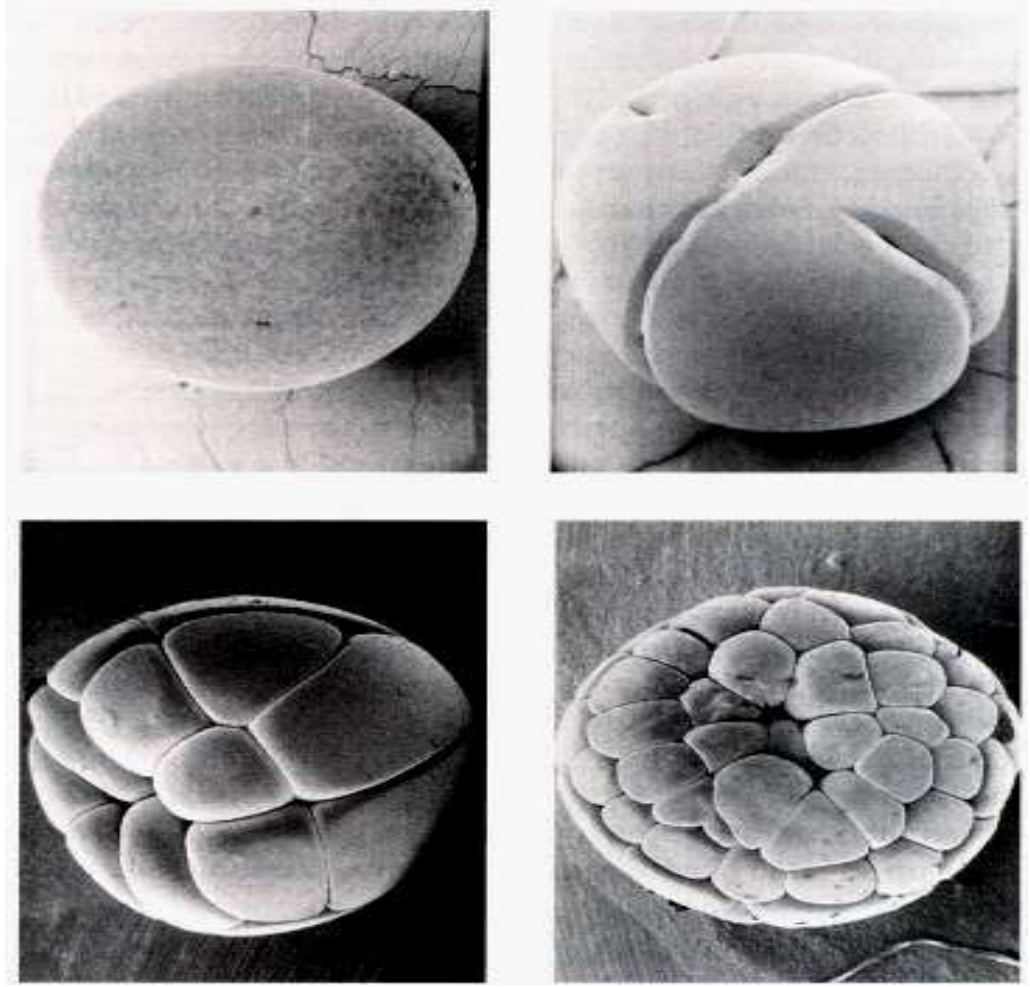


图12-4 应用过量的TdR 双阻断法进行细胞周期同步化

A. 处于对数生长期的细胞。B. 第一次加入TdR，所有处于S 期的细胞立即被抑制，其他细胞运行到G1/S 期交界处被抑制。C. 将TdR 洗脱，解除抑制，被抑制的细胞沿细胞周期运行。D. 在解除抑制的细胞到达G1 期终点前，第二次加入TdR 并继续培养，所有的细胞被抑制在G1/S 期交界处

四、特殊的细胞周期——早期胚胎细胞

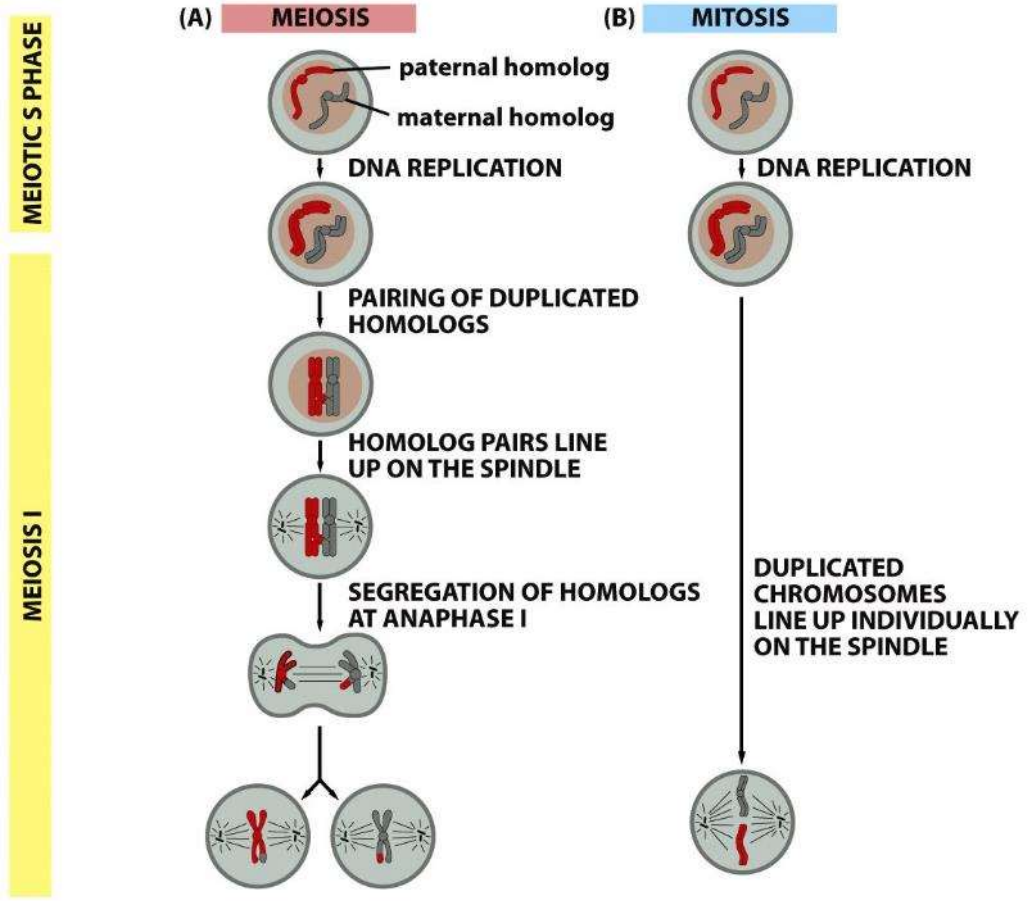
- 受精卵迅速卵裂，卵裂球数量增加，但其总体积并不增加；No cell growth during cell cycle
- **G_1 期和 G_2 期非常短**
- Have little or no need to synthesize components other than DNA during cell division



第二节

细胞分裂

- 有丝分裂
- 减数分裂



一、有丝分裂 Mitosis

- 细胞周期的M 期时相包括**核分裂**与**胞质分裂**两个相互联系的过程
- 细胞**有丝分裂(mitosis)即指核分裂(nuclear division)**
- **有丝分裂过程人为地划分为前期、前中期、中期、后期和末期**
- **胞质分裂（cytokinesis）**相对独立，一般开始于细胞有丝分裂后期，完成于细胞有丝分裂末期
- 通过核分裂与胞质分裂，使已经复制好的染色体DNA 平均分配到2 个子细胞中

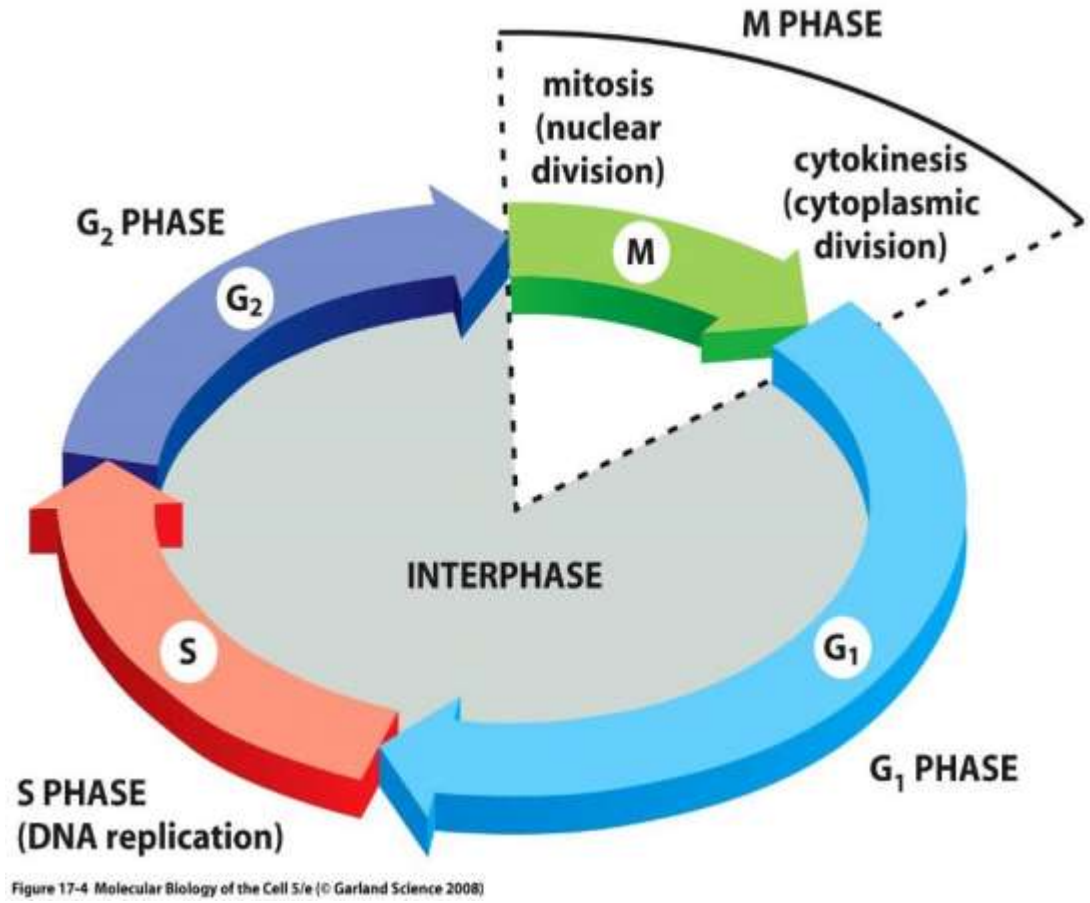
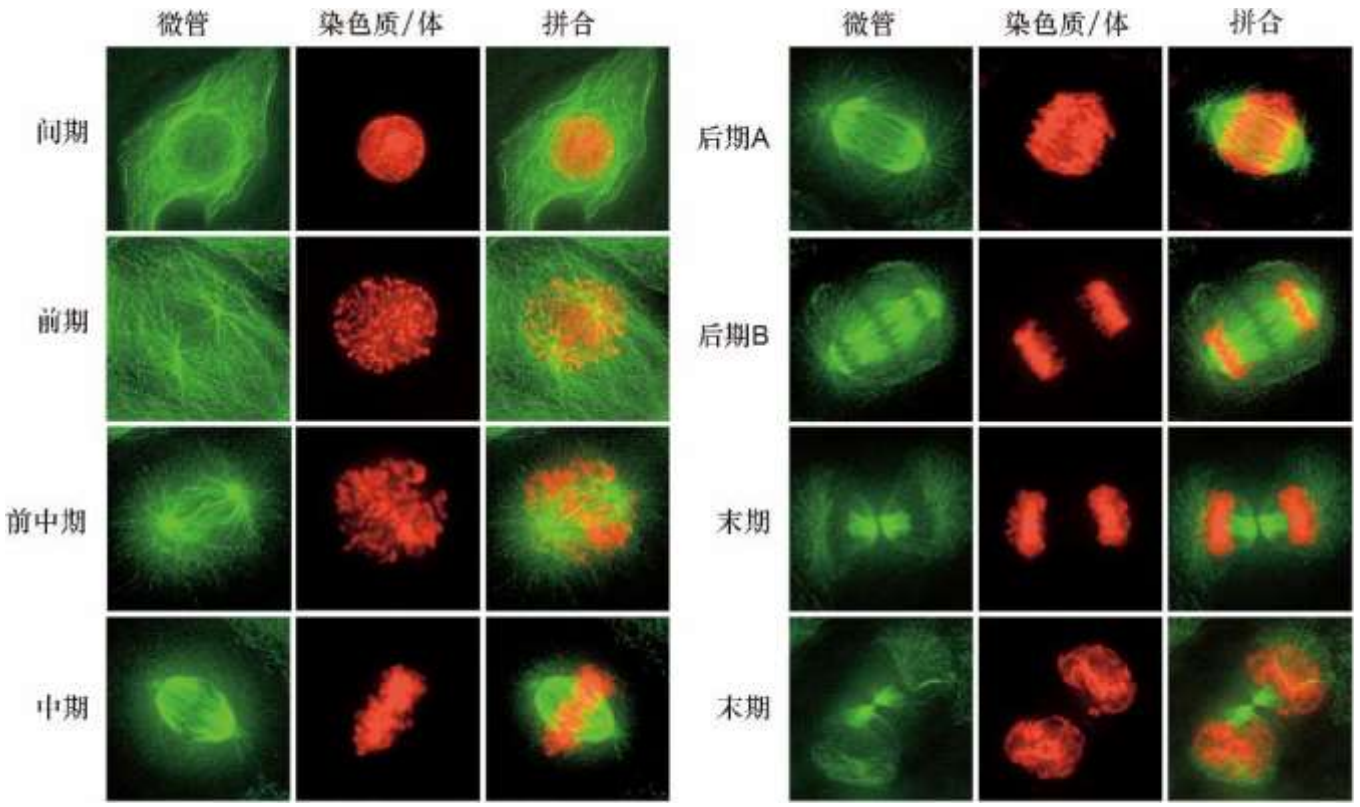


Figure 17-4 Molecular Biology of the Cell 5/e (© Garland Science 2008)

一、有丝分裂 Mitosis



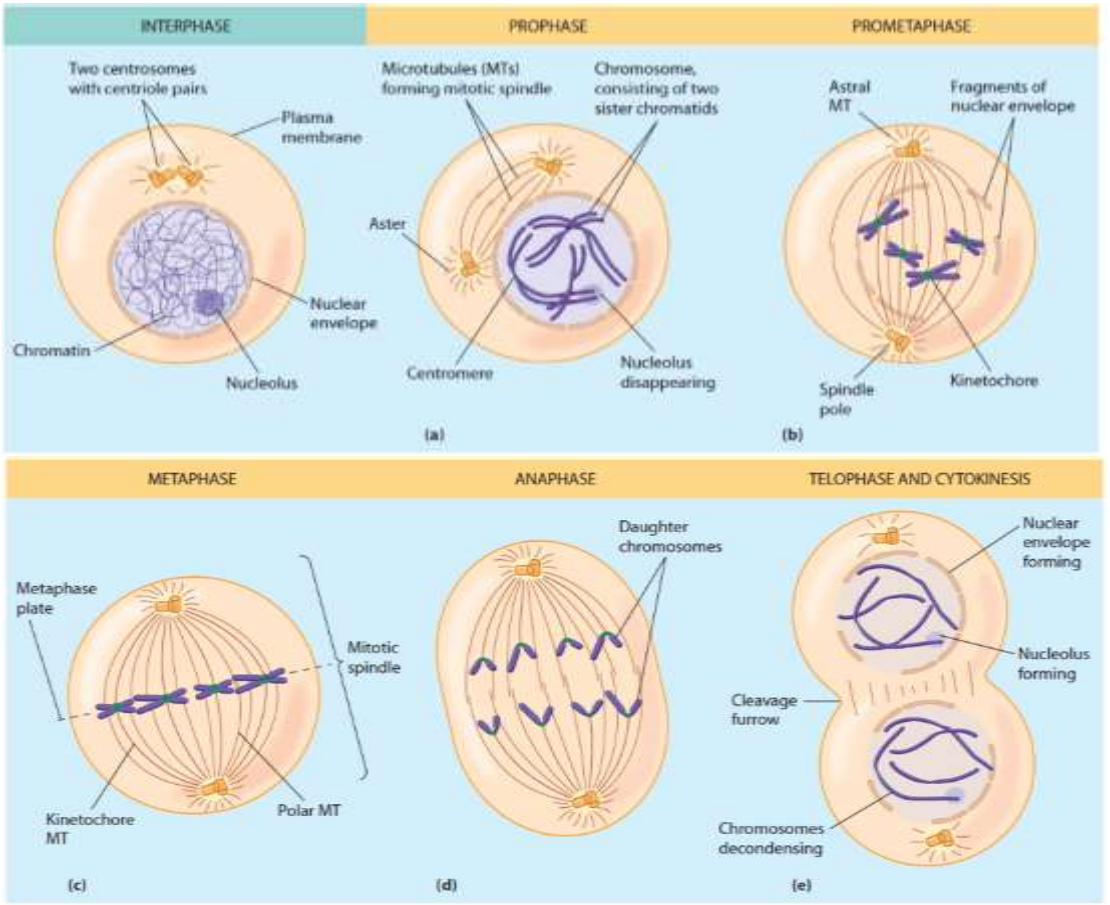
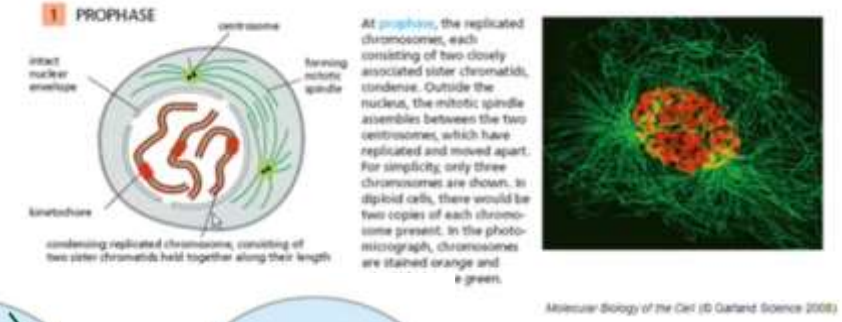


图12-9 高等动物细胞有丝分裂过程

1. 前期（Prophase)——细胞分裂极的确立和纺锤体装配

- 动物细胞分裂极确立与中心体复制、分离和有星纺锤体的装配密切相关
- 高等植物细胞装配无星纺锤体，分裂极确立机制尚不清楚
- 中心体半保留复制



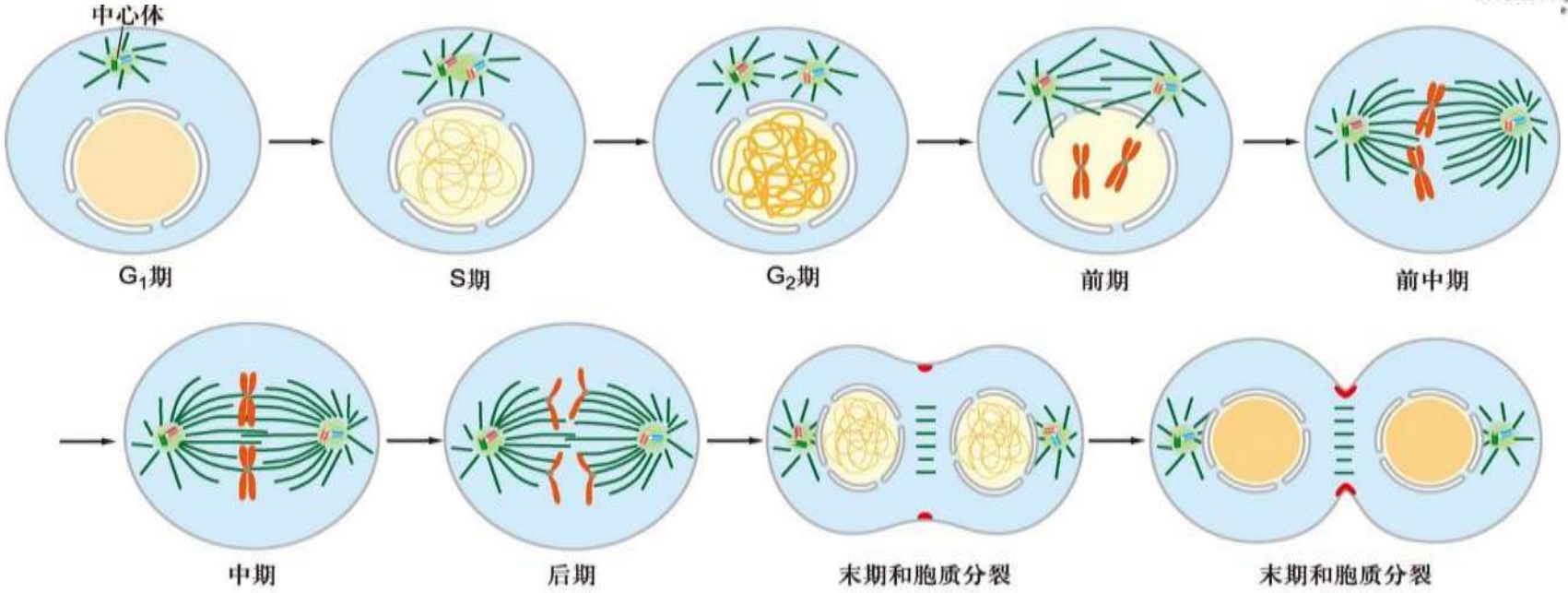


图12-11 动物细胞中心体的复制与细胞周期的关系

在每个细胞周期中，中心体进行一次半保留复制。在有丝分裂末期，每个子代细胞继承一个中心体，而在下次有丝分裂开始之前，它又包含2 个中心体

1. 前期——染色体凝缩（chromatin condensation）

- 姐妹染色单体间彼此黏着和凝缩是基因组准确分离的先决条件
  - **Smc** (structural maintenance of chromosome) 蛋白复合物
  - **Cohesin** (黏连蛋白)和**Condensin** (凝缩蛋白)

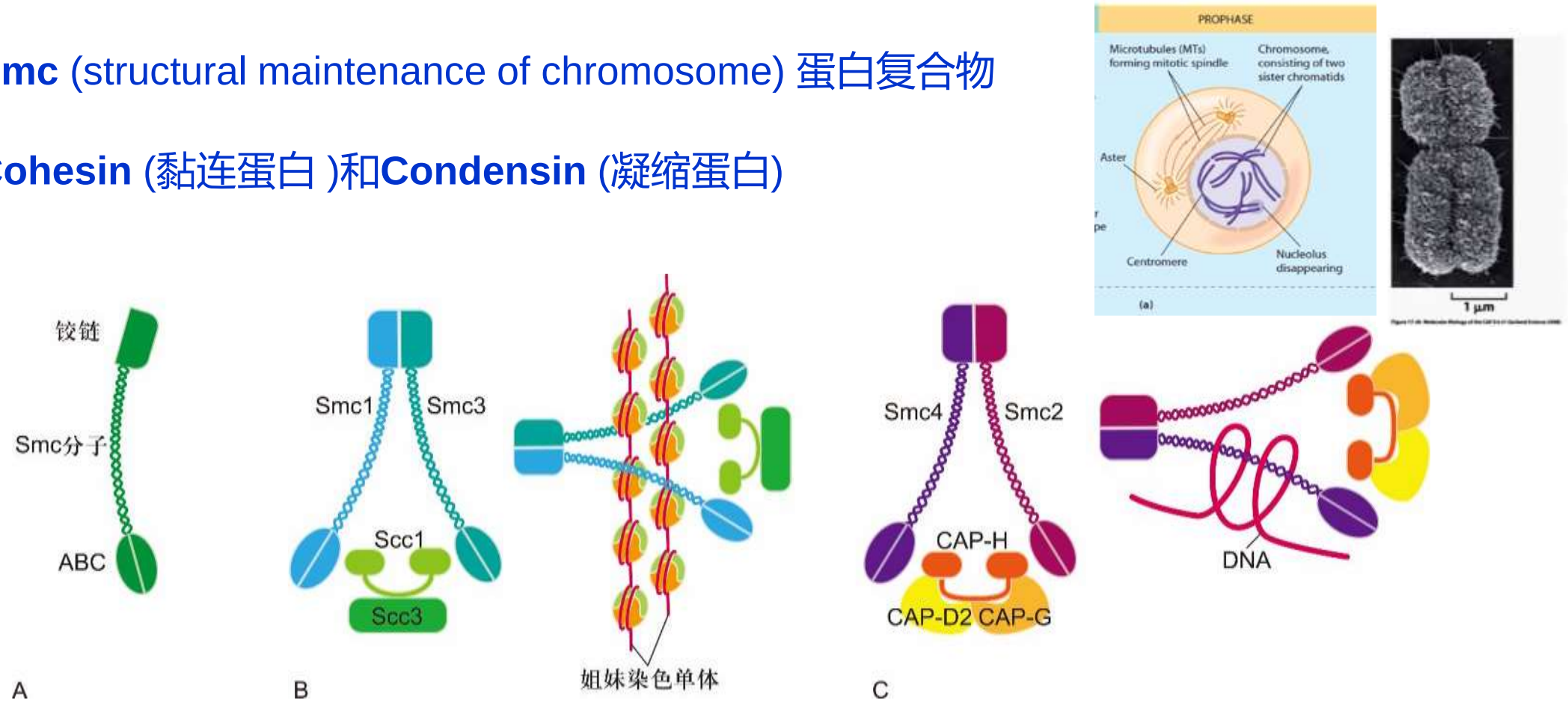


图12-10 Smc 蛋白（A）及其黏连蛋白（Smc 1/3）（B）、凝缩蛋白（Smc2/4）（C）异二聚体的作用

中心体复制与细胞周期的关系

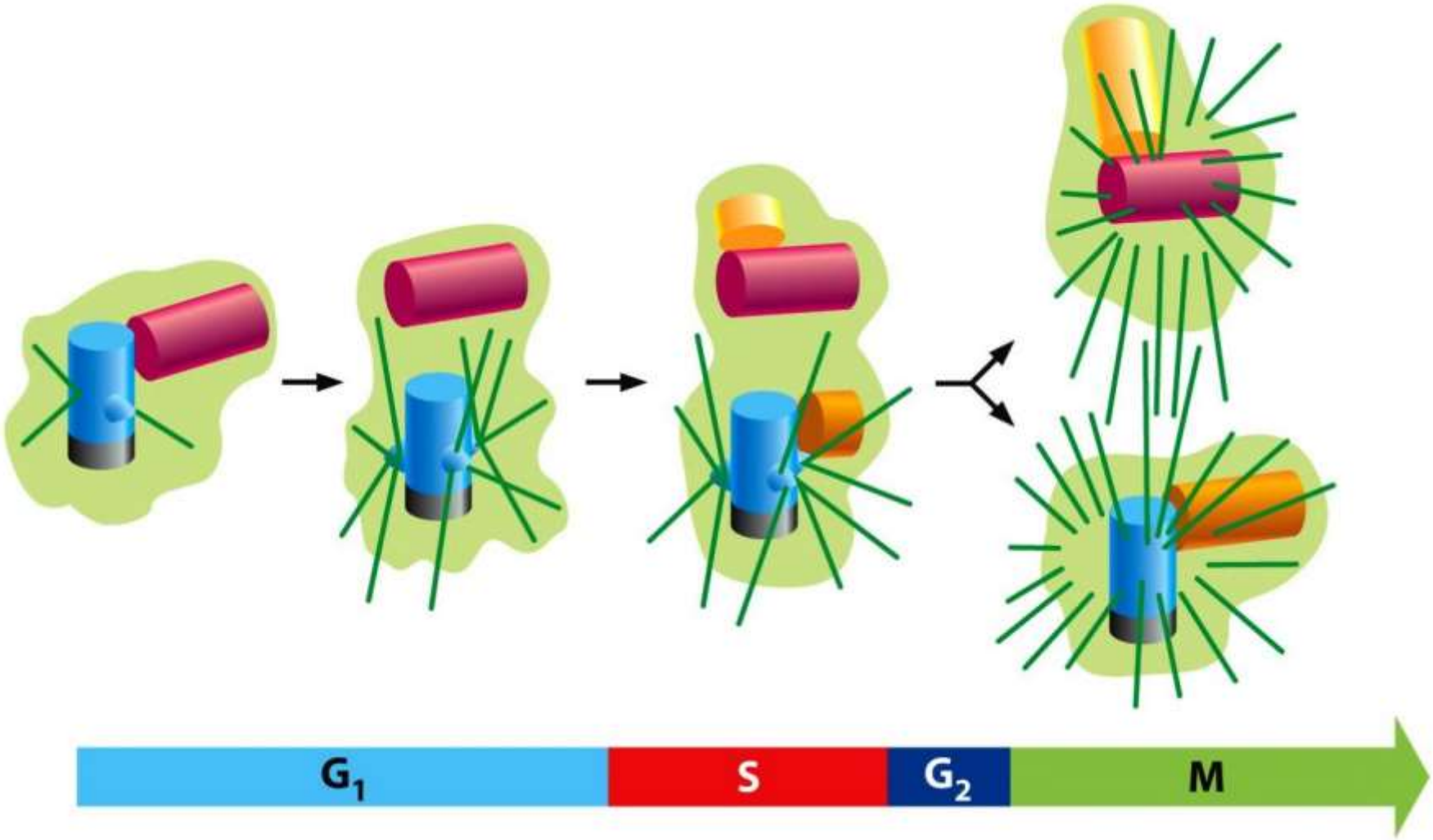
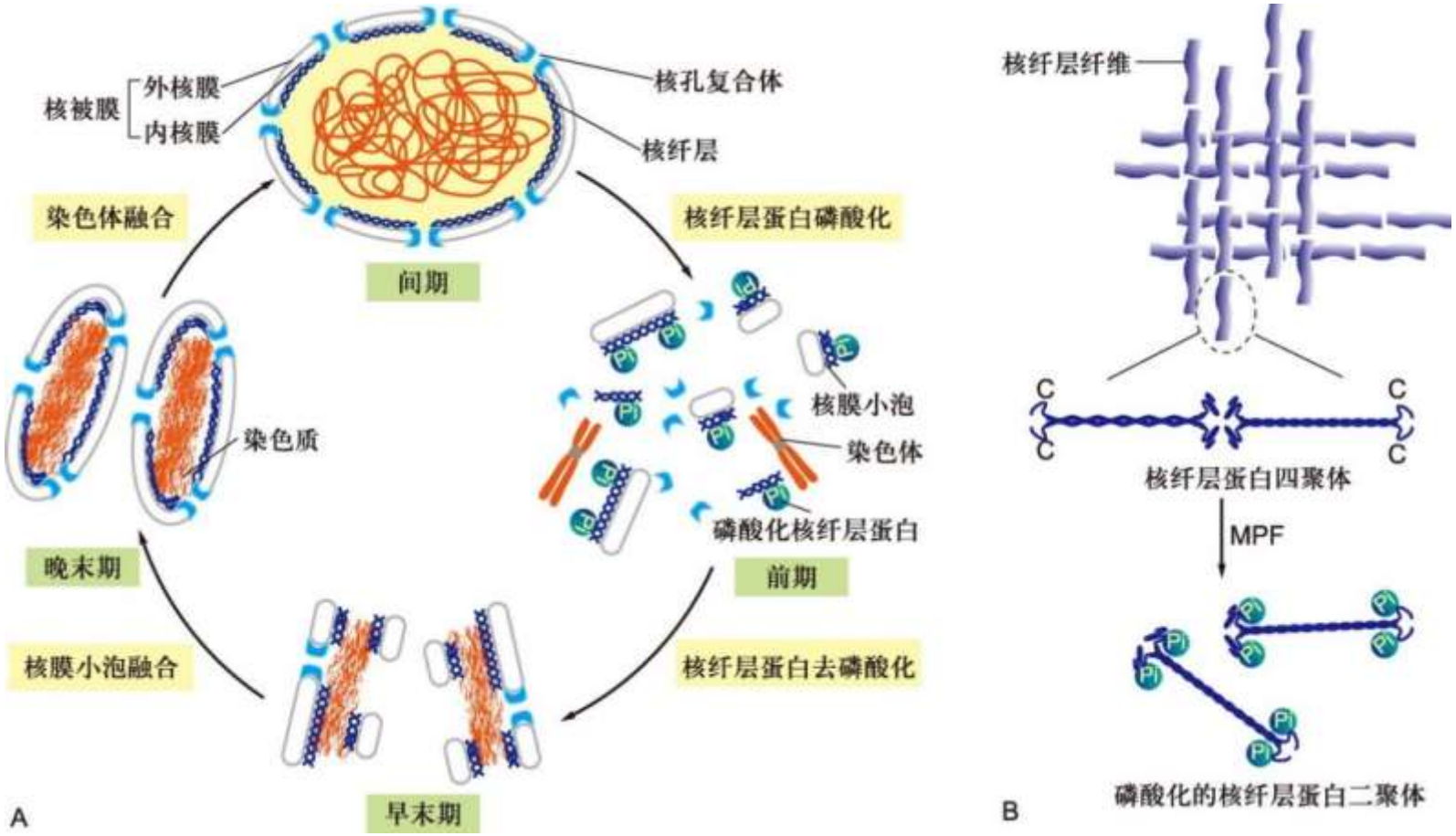


Figure 17-31 *Molecular Biology of the Cell* (© Garland Science 2008)

2. 前中期——核膜崩解

- 核纤层蛋白的磷酸化与去磷酸化



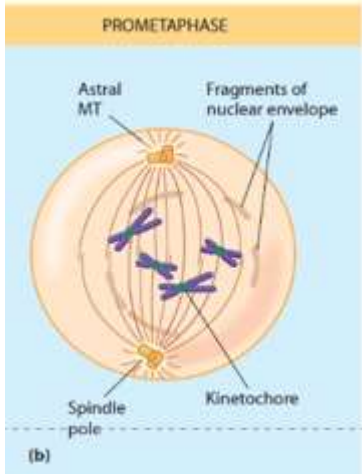


图12-12 细胞分裂过程中核被膜和核纤层的动态变化

A. 核被膜在细胞有丝分裂中有规律地解体与重建。 B. 核纤层解聚

2. 前中期——完成纺锤体装配，形成有丝分裂器(mitotic apparatus)

- 动物细胞有丝分裂器
  - 由星体微管、 染色体动粒微管和极间微管及其结合蛋白构成**有星纺锤体**
- 植物细胞不含中心体，但能形成**无星纺锤体**介导植物细胞的核分裂

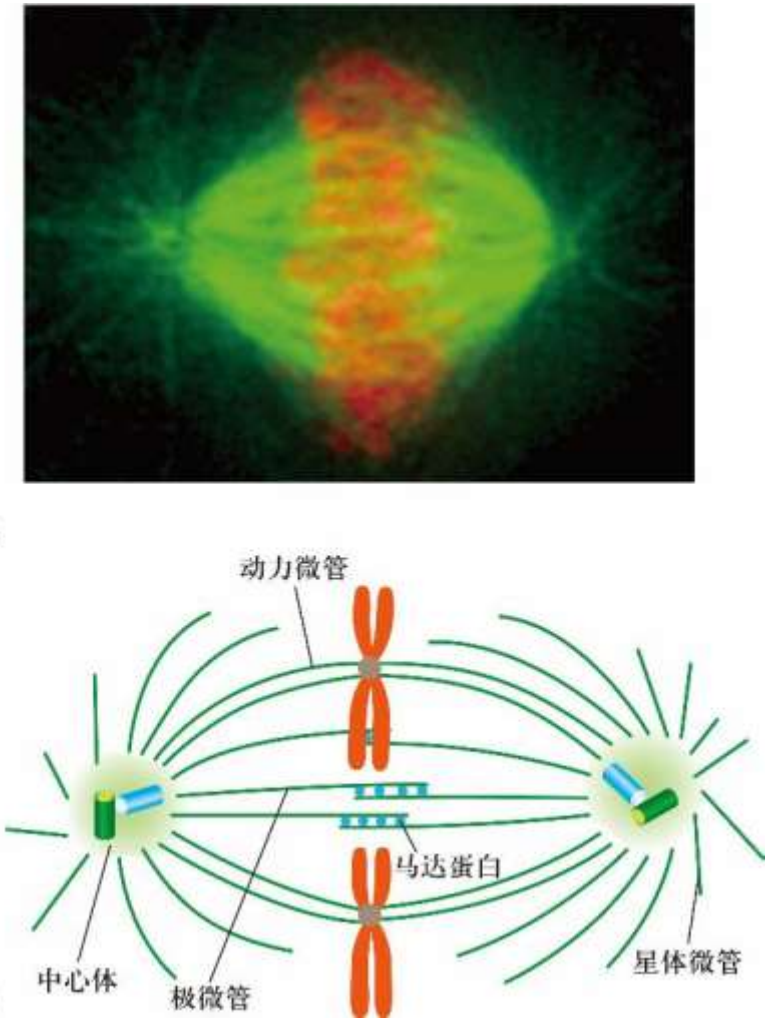


图12-13 高等动物细胞纺锤体结构

A. DNA 荧光染料染色（红色）和抗微管蛋白抗体免疫荧光染色（绿色）。B. 染色体和纺锤体结构模式图

2. 前中期——纺锤体组装过程

- 微管在中心体周围组装
- 中心体的分离
  - **驱动蛋白相关蛋白**
  - **细胞质动力蛋白**
  - **中心体列队**

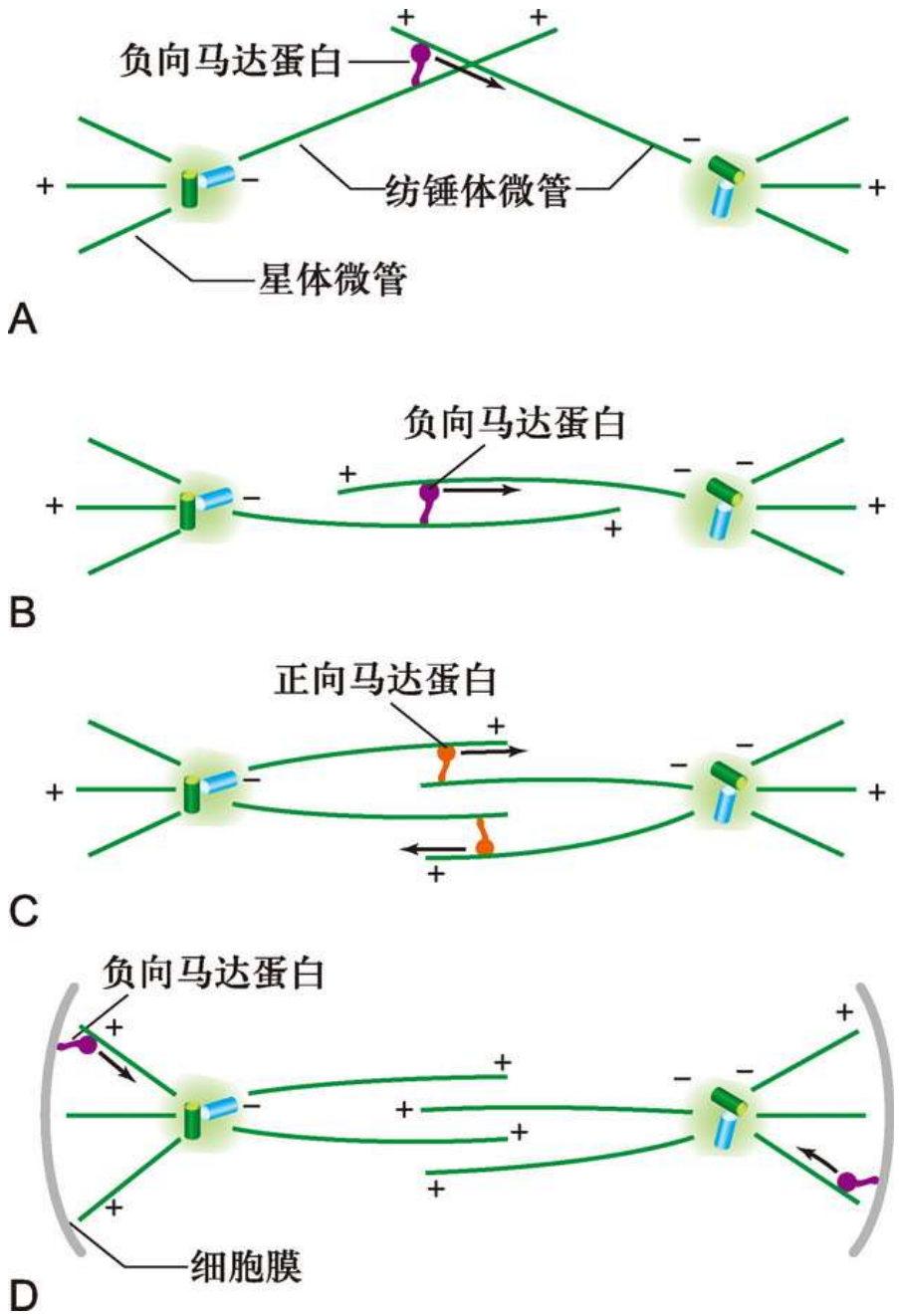
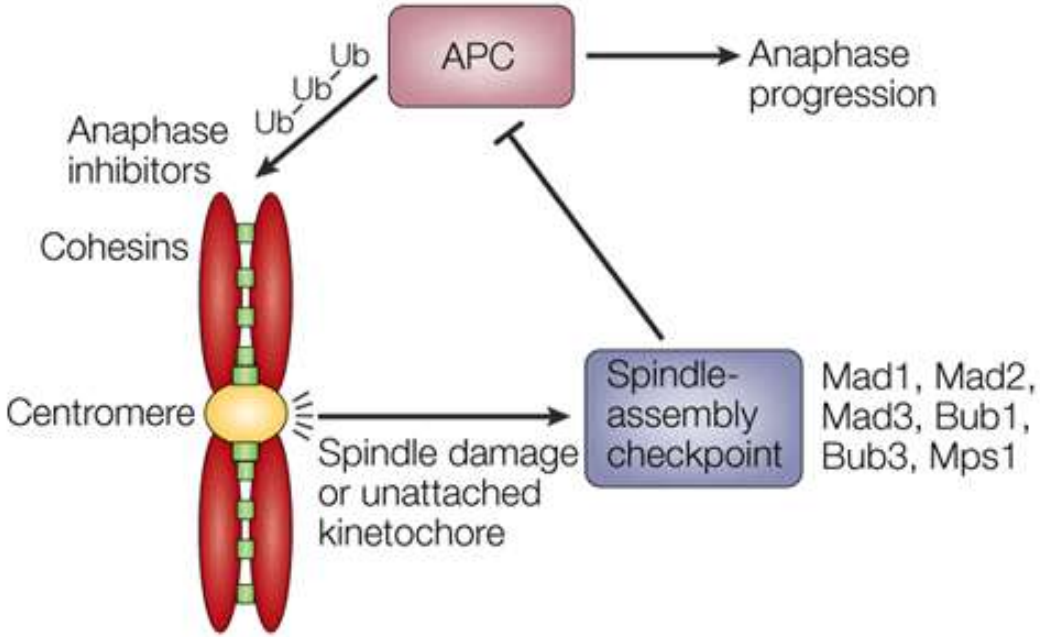


图12-14 纺锤体组装过程

A. 中心体分离，负向运动马达蛋白与来自姐妹中心体的纺锤体微管结合。B. 借助马达蛋白向微管负极运动，将纺锤体微管牵拉在一起，形成早期纺锤体。C. 正向运动马达蛋白在纺锤体微管之间搭桥，借助正向运动，将纺锤体拉长。D. 负向运动的马达蛋白在细胞膜和星体微管之间搭桥，借助负向运动，将中心体进一步拉近两极的细胞膜，纺锤体进一步被拉长

2. 前中期——染色体整列

- 染色体整列
  - 染色体向赤道面运动的过程
- Mad 和Bub 蛋白



Nature Reviews Molecular Cell Biology 2, 678-687 (September 2001)

Nature Reviews | Molecular Cell Biology

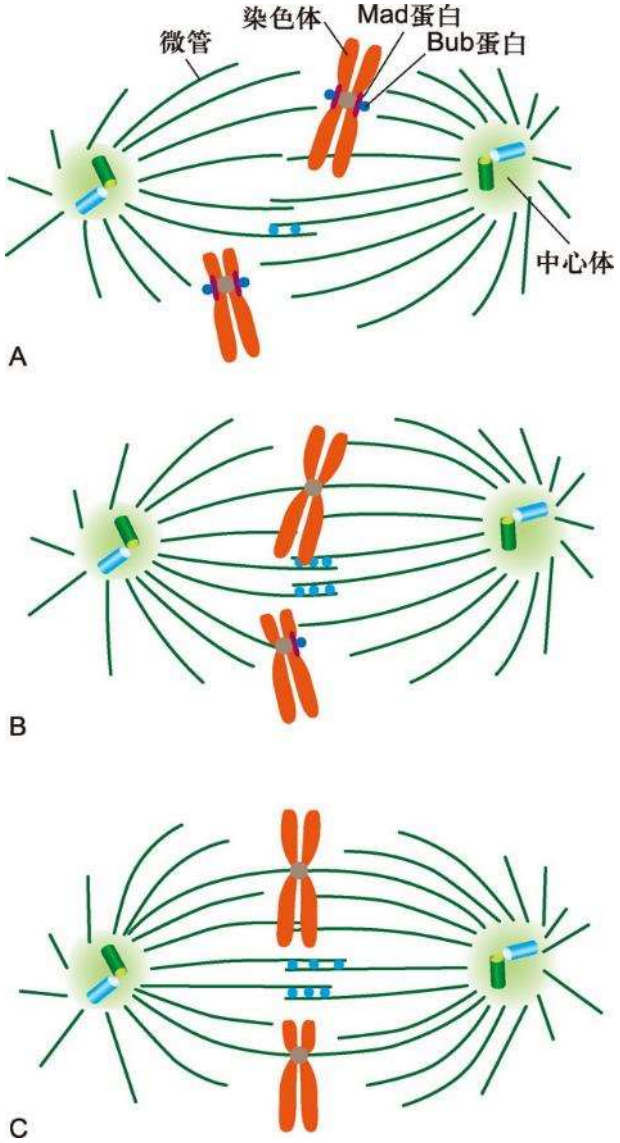


图12-16 染色体整列

A. 细胞分裂前期和前中期，Mad 和Bub 蛋白在染色体的动粒上聚集。B. 微管与动粒联结后，Mad 和Bub 蛋白消失，某些染色体滞后，未与微管联结的动粒依然含有Mad 和Bub 蛋白。C. 所有染色体的动粒均与微管联结，Mad 和Bub 蛋白消失，染色体列队到赤道板

3. 中期（metaphase）

- 染色体整列完成，所有染色体排列到赤道面上，纺锤体结构呈现典型纺锤样
- **牵拉（pull）假说**
- **外推（push）假说**

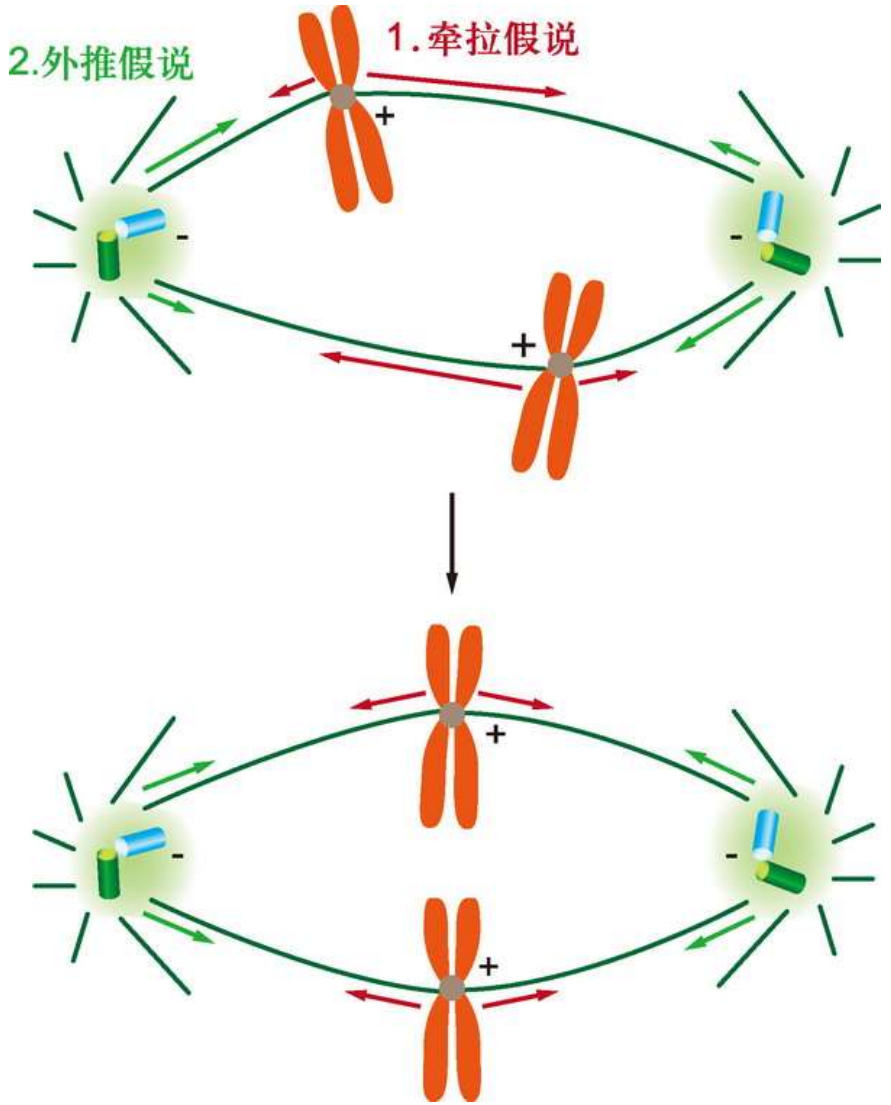
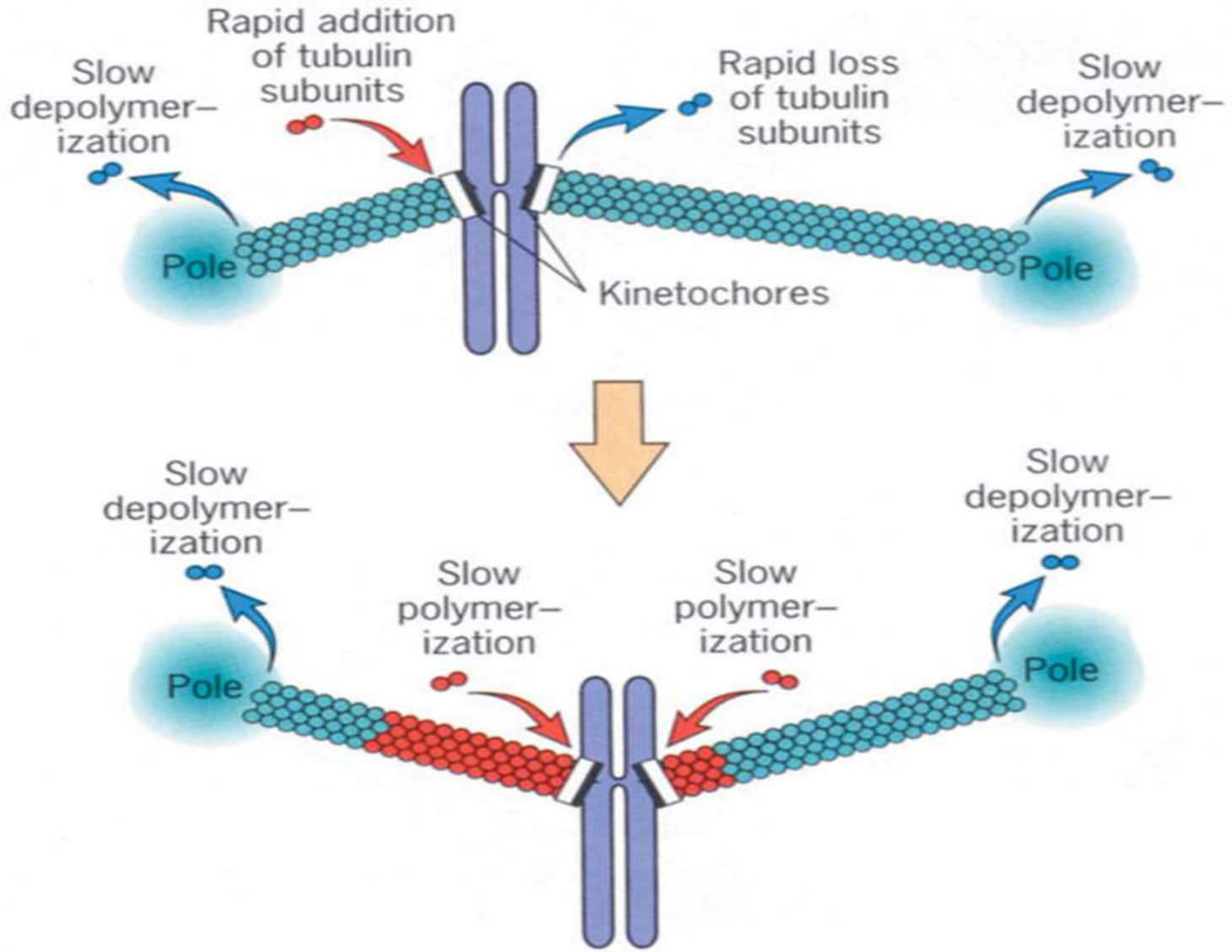


图12-17 解释染色体在赤道面整列的两种假说

Metaphase


Rapid addition of tubulin subunits
Slow depolymer–ization
Rapid loss of tubulin subunits
Slow depolymer–ization
Pole
Kinetochores
Pole
Slow depolymer–ization
Slow depolymer–ization
Slow polymer–ization
Slow polymer–ization
Pole
Pole

4. 后期（anaphase）

- 姐妹染色单体分离向两极运动
  - 依靠纺锤体微管的作用
- Anaphase A
  - 动粒微管变短，牵动染色体向两极运动
- Anaphase B
  - 极性微管长度增加，两极之间的距离逐渐拉长

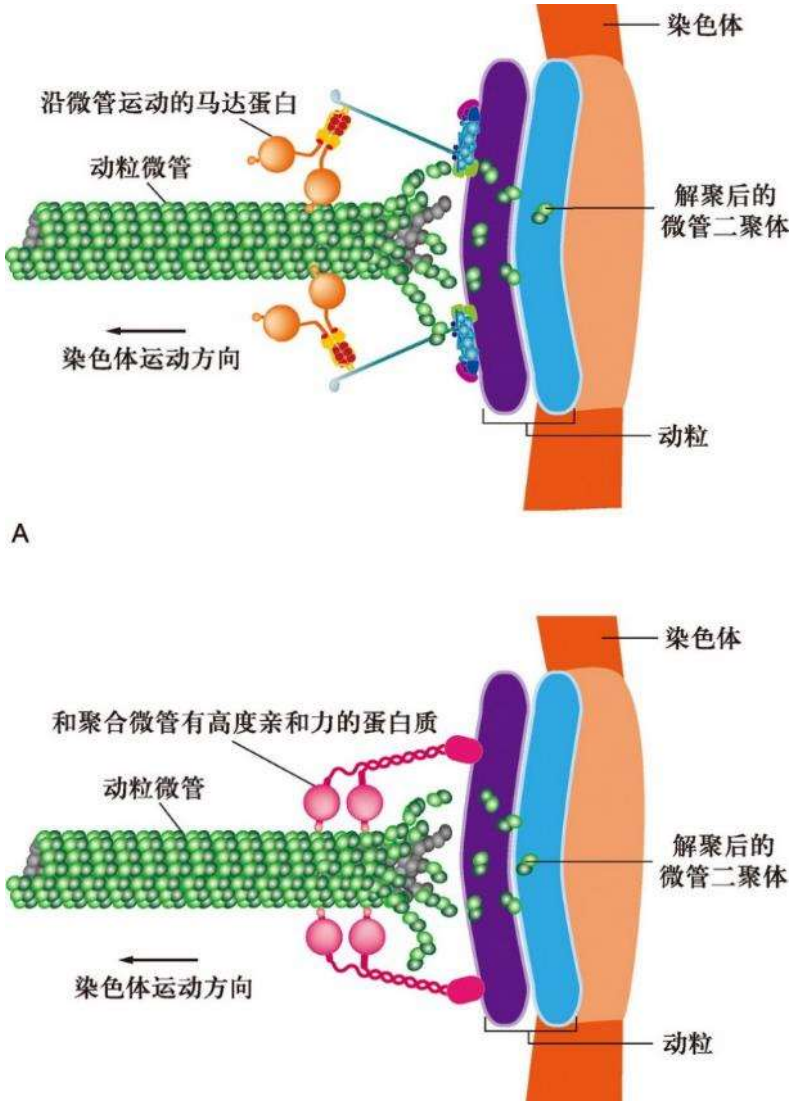


图12-18 细胞有丝分裂后期由ATP 驱动的马达蛋白沿微管向极部运动使染色体分开

A. ATP- 驱动的染色体运动促使微管解聚。B. 微管解聚促使染色体运动

4. 后期（anaphase）

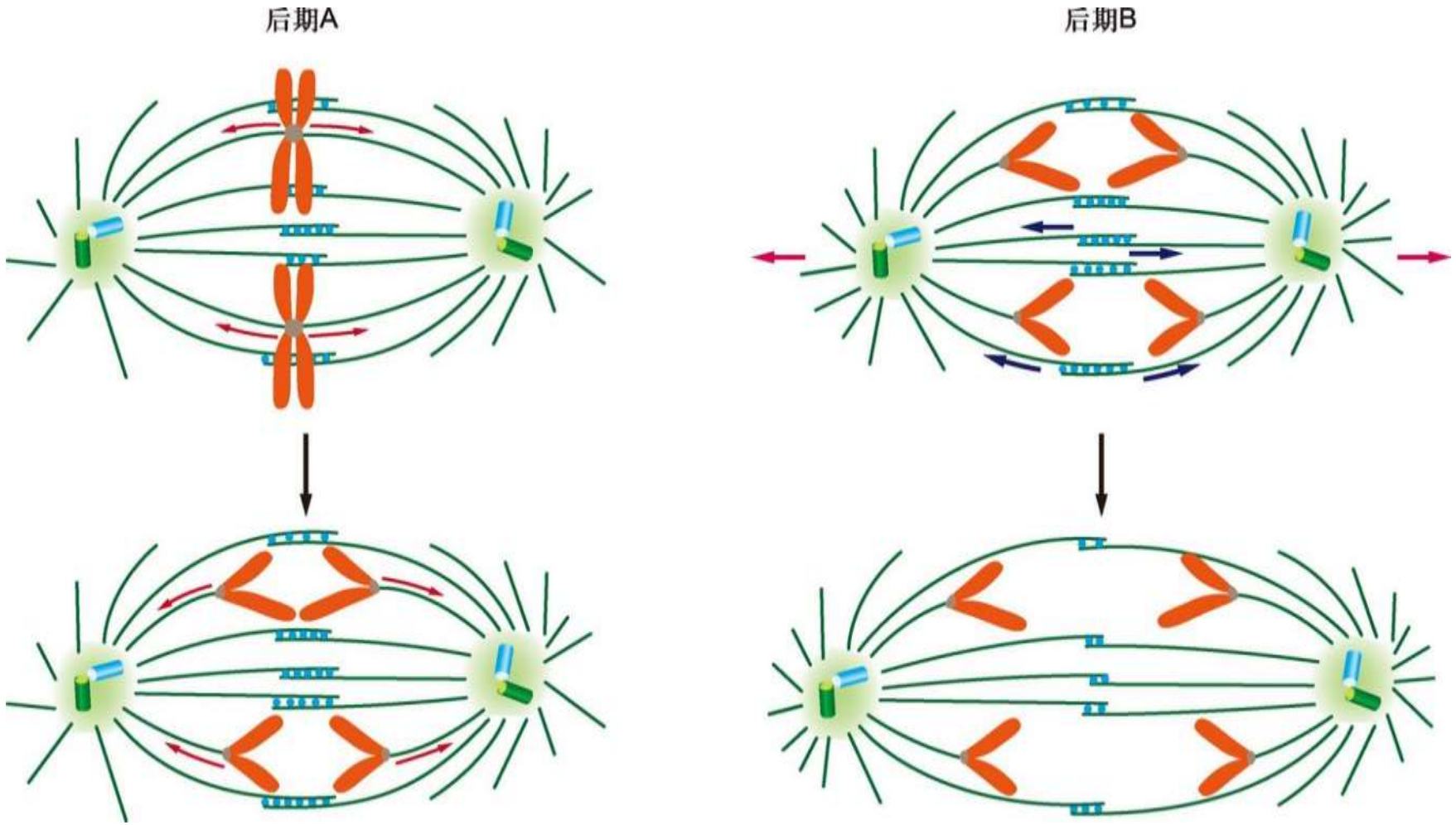
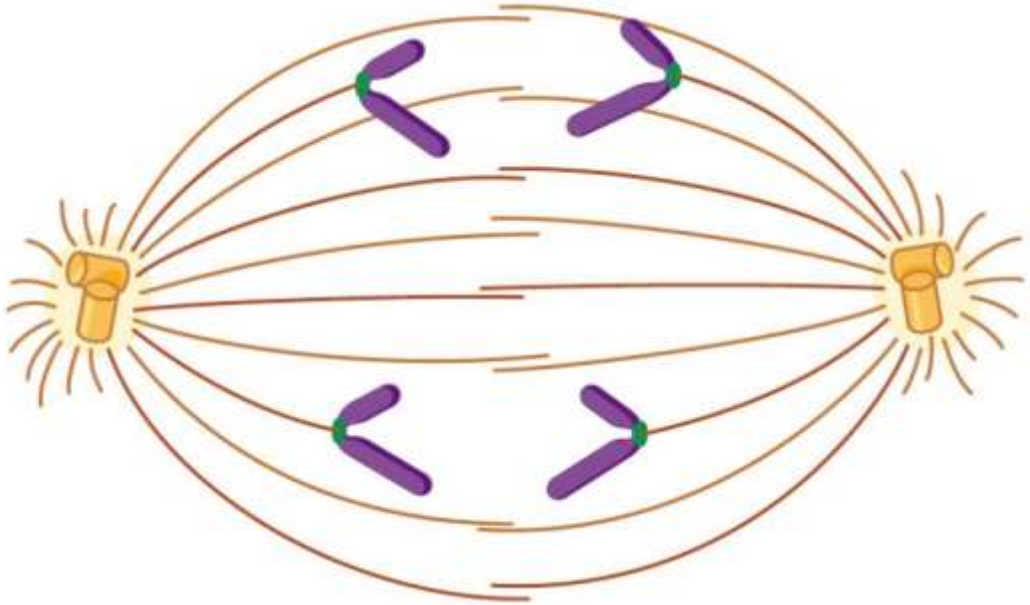


图12-19 细胞分裂后期A和后期B产生染色体向极部运动的示意图

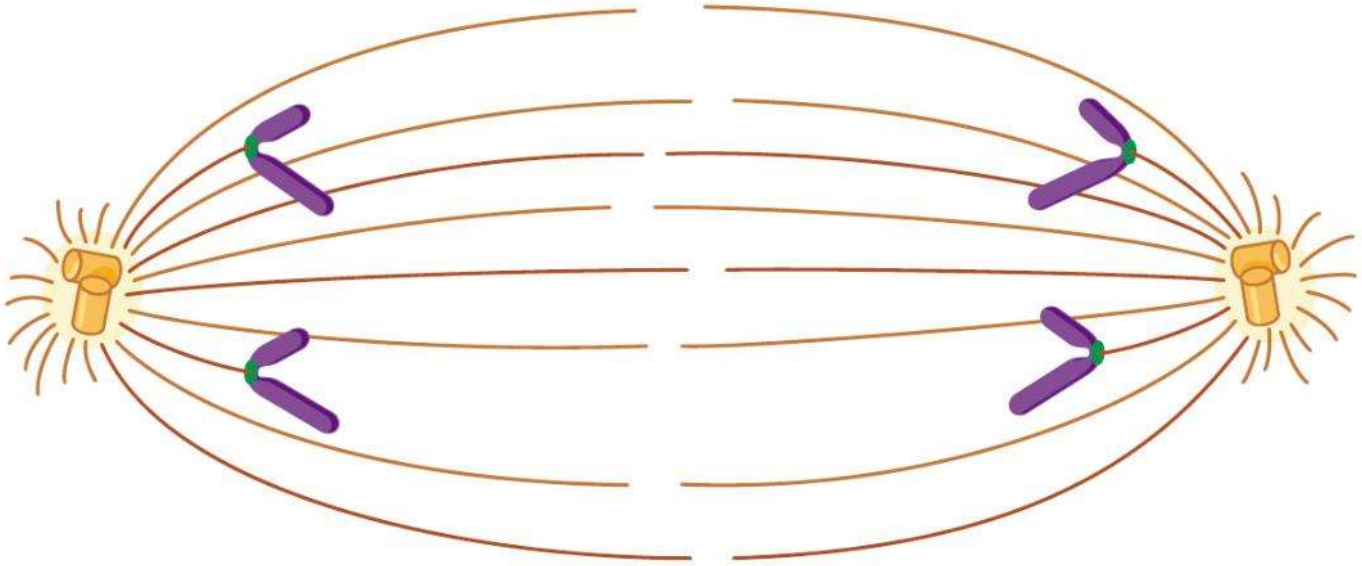
后期A：动粒微管在两端解聚缩短，致使姐妹染色单体向两极运动。后期B：通过星体微管牵拉和极微管重叠区滑动，使纺锤体两极和染色体进一步分开

The Two Types of Movement Involved in Chromosome Separation During Anaphase



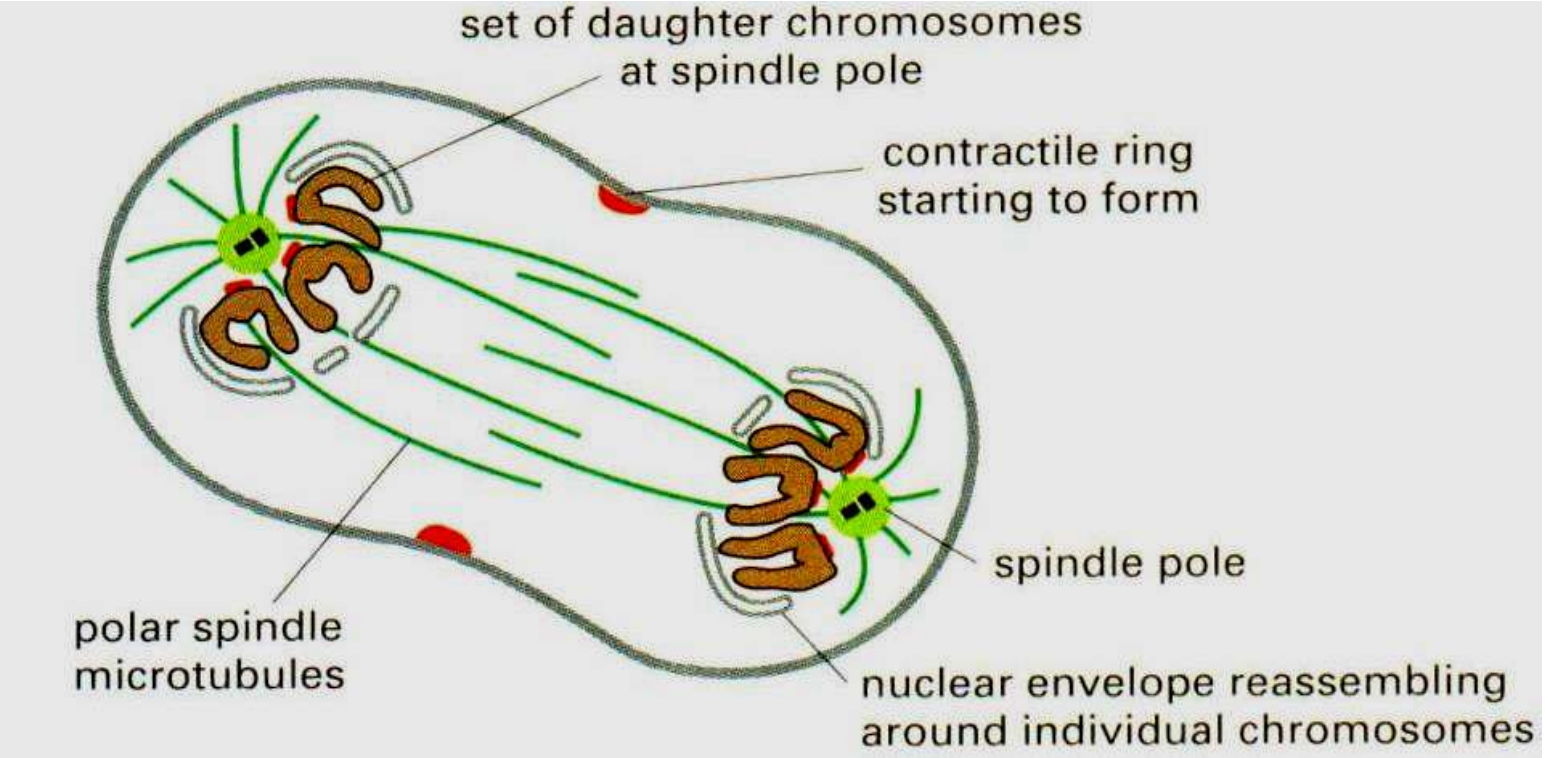
Anaphase A (chromosome-to-pole movement)

Anaphase B (pole-pole separation)



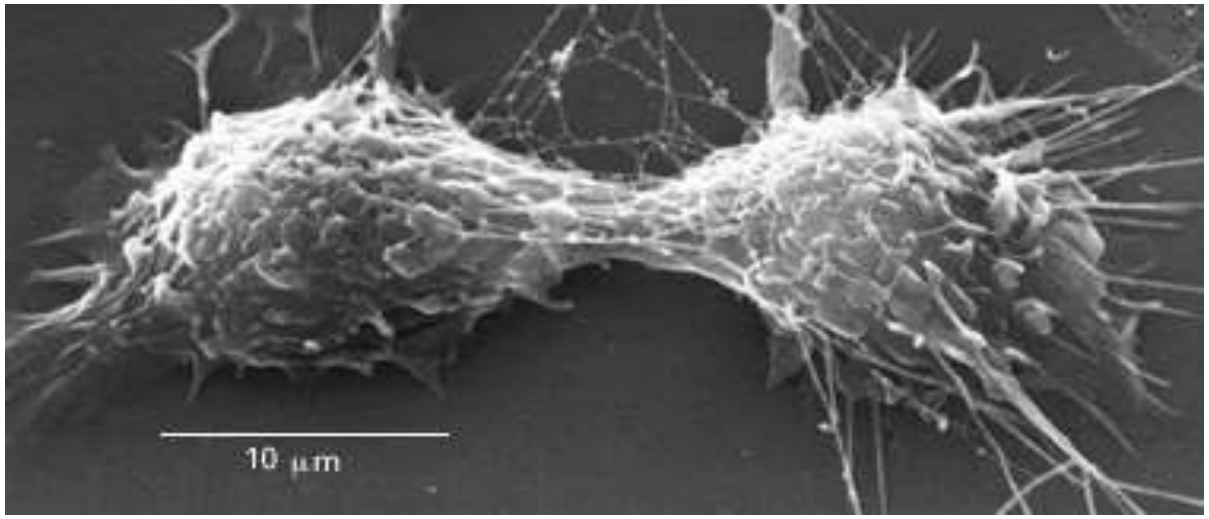
5. 末期（telophase）

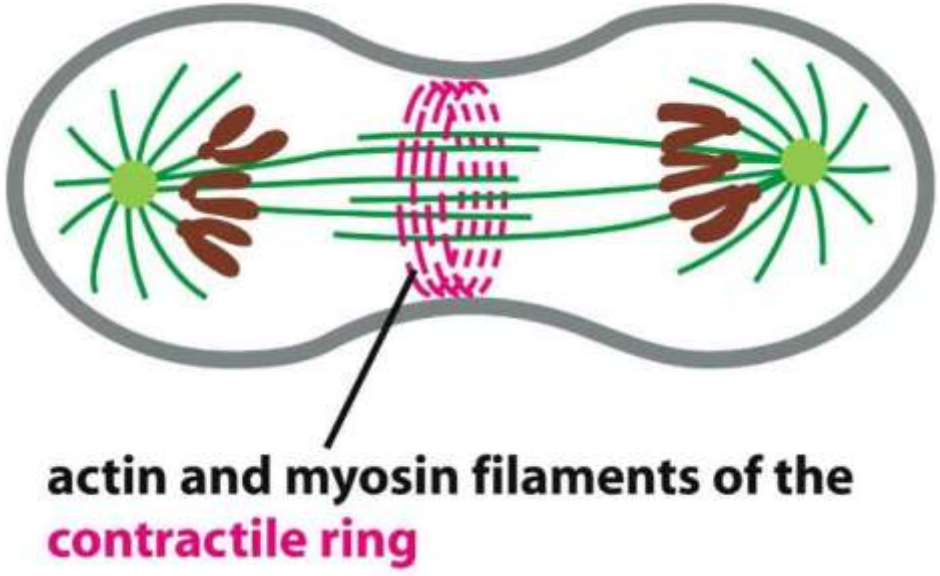
- 动粒微管消失，极微管继续加长
- 染色单体去浓缩
- 核纤层与核膜重新组装



6. 胞质分裂 Cytokinisis (Cytoplasm division)

- **Furrow** 分裂沟
- **Midbody** 中体
- **Contractile ring** 收缩环





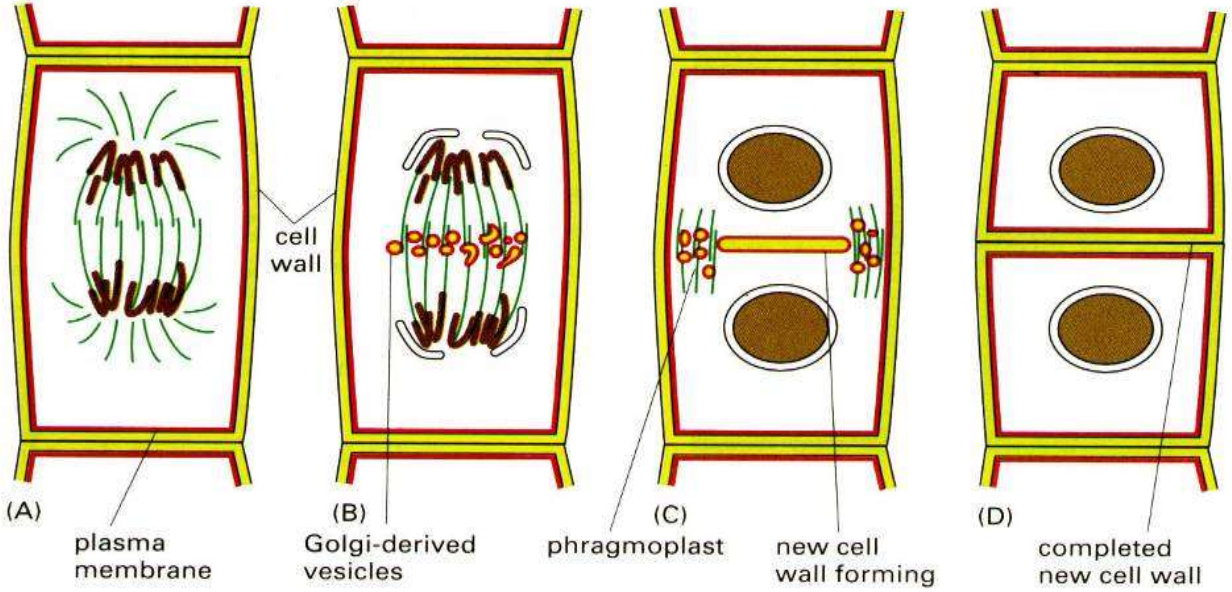
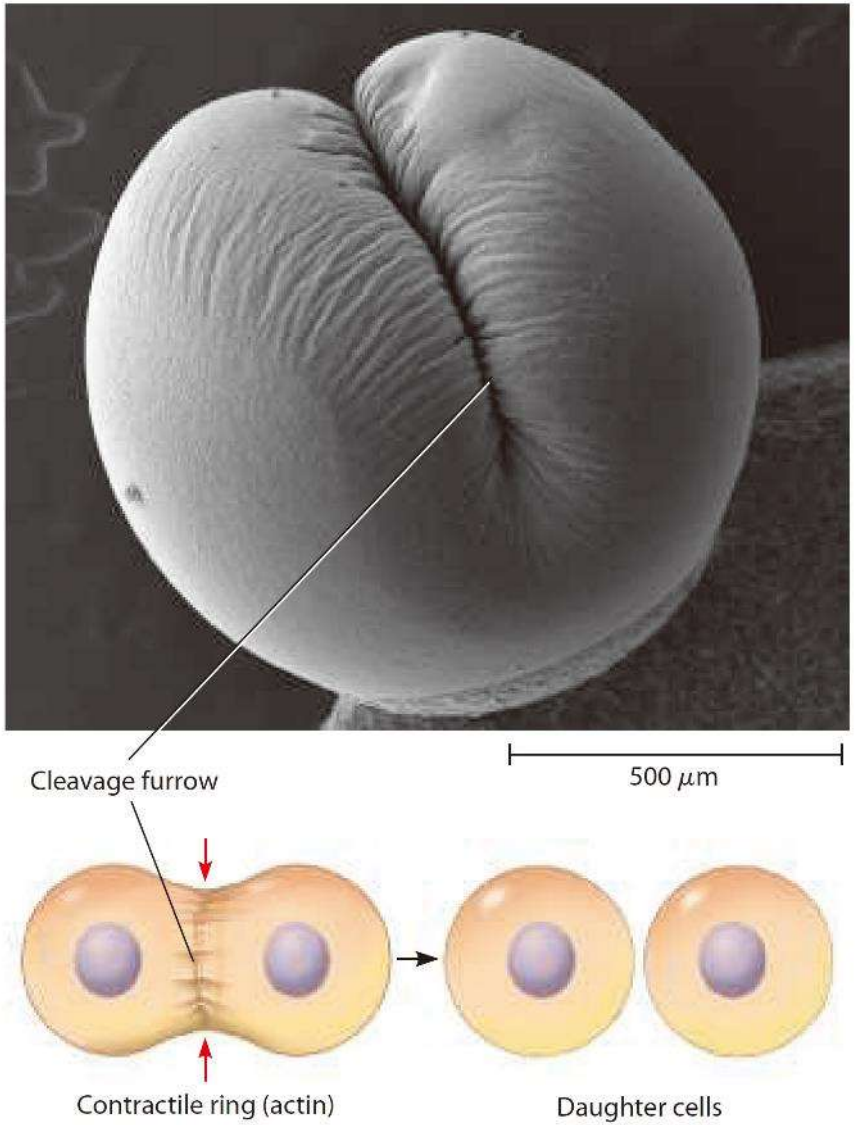


Figure 17-49a *Molecular Biology of the Cell* (© Garland Science 2008)

Cytokinesis in an Animal Cell



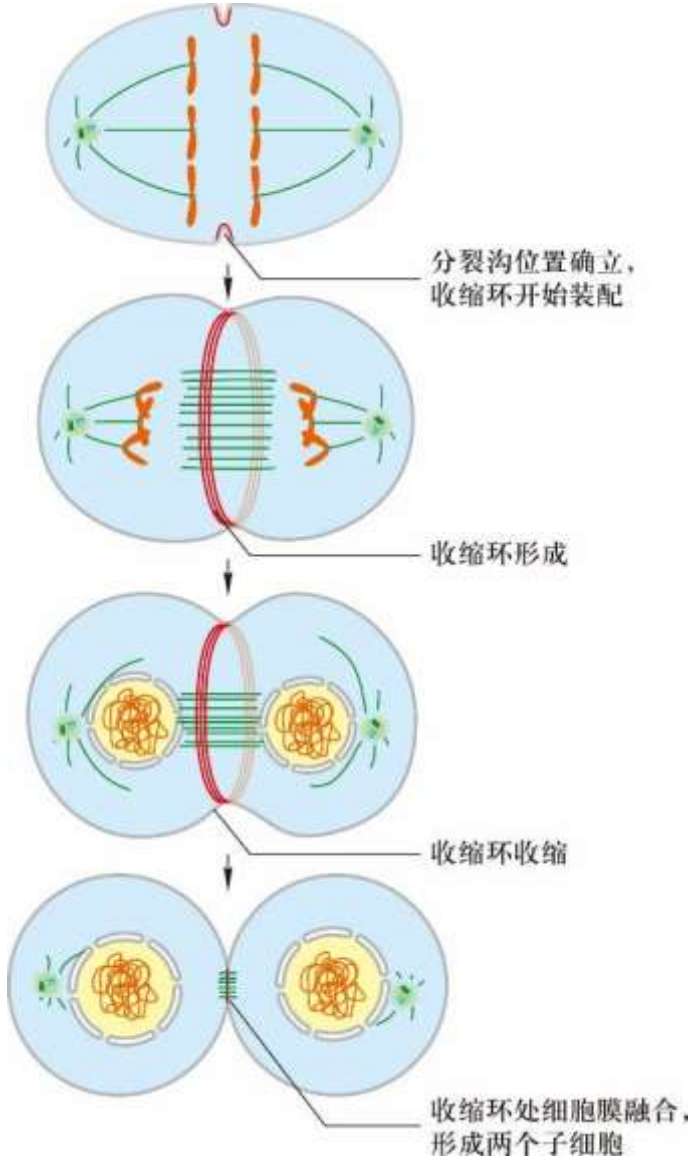


图13-21 动物细胞胞质分裂示意图

中央纺锤体和星体微管作用于细胞皮层并诱导分裂沟形成

- 胞质分裂4 个步骤
  - 分裂沟位置的确立；肌动蛋白聚集和收缩环形成；收缩环收缩；收缩环处细胞融合并形成两个子细胞
- 中央纺锤体和星体微管共同决定了分裂沟形成的位置，星体微管参与了分裂沟的形成

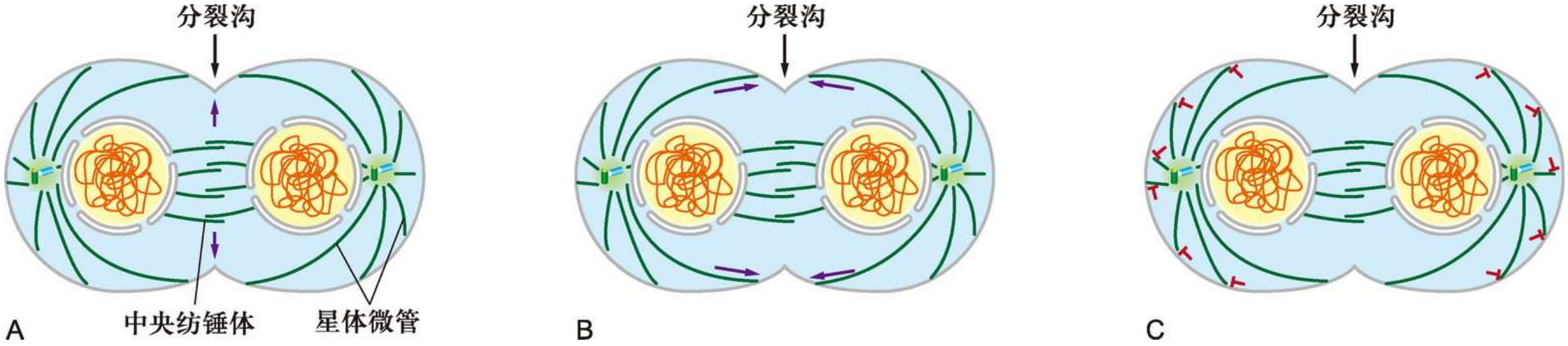
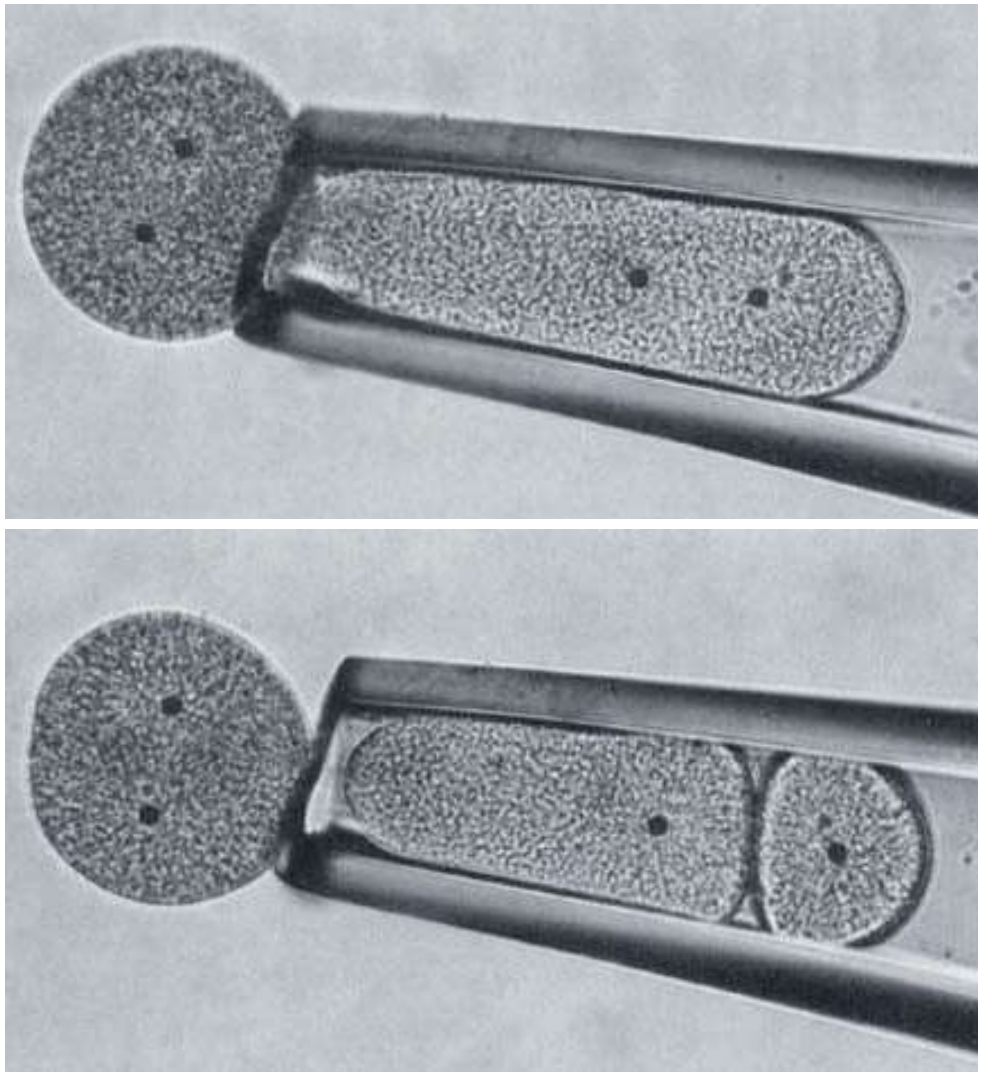


图12-22 中央纺锤体和星体微管作用于细胞皮层并诱导分裂沟形成

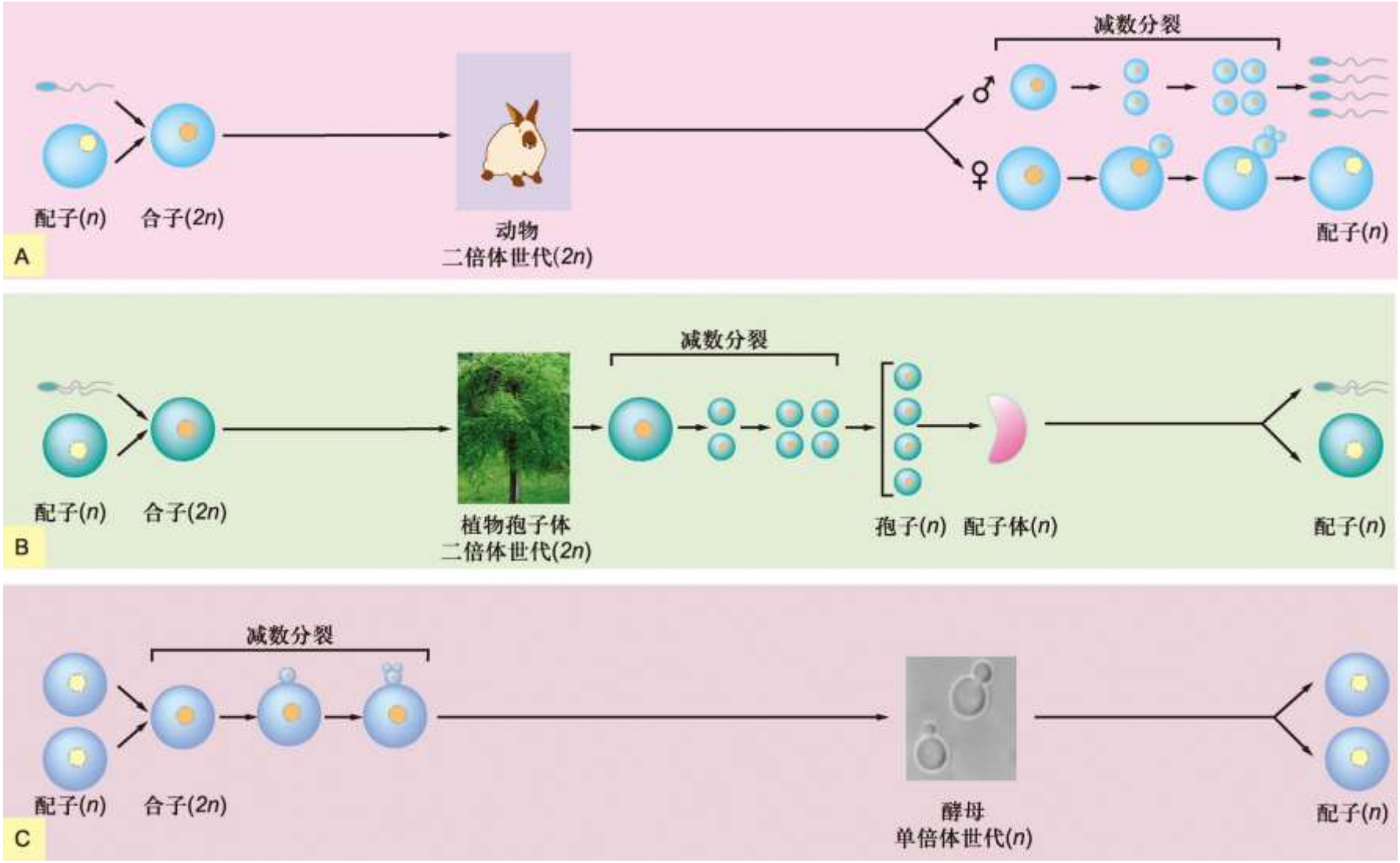
A. 中央纺锤体发出的信号决定分裂沟的定位。B. 接近分裂沟位置的纺锤体微管发出信号，促进分裂沟的形成。C. 远离分裂沟位置的星体微管发出抑制性信号 (T 形箭头)，抑制远离分裂沟端部的细胞皮层收缩，间接促进分裂沟的形成

The site of formation of the cleavage plane



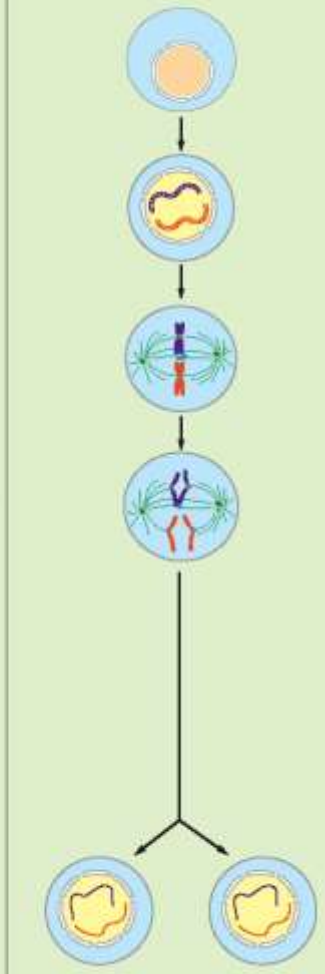
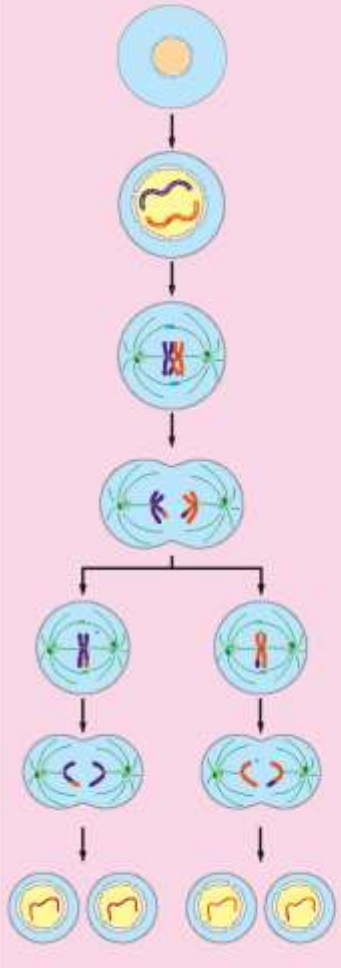
Echinoderm egg

二、减数分裂

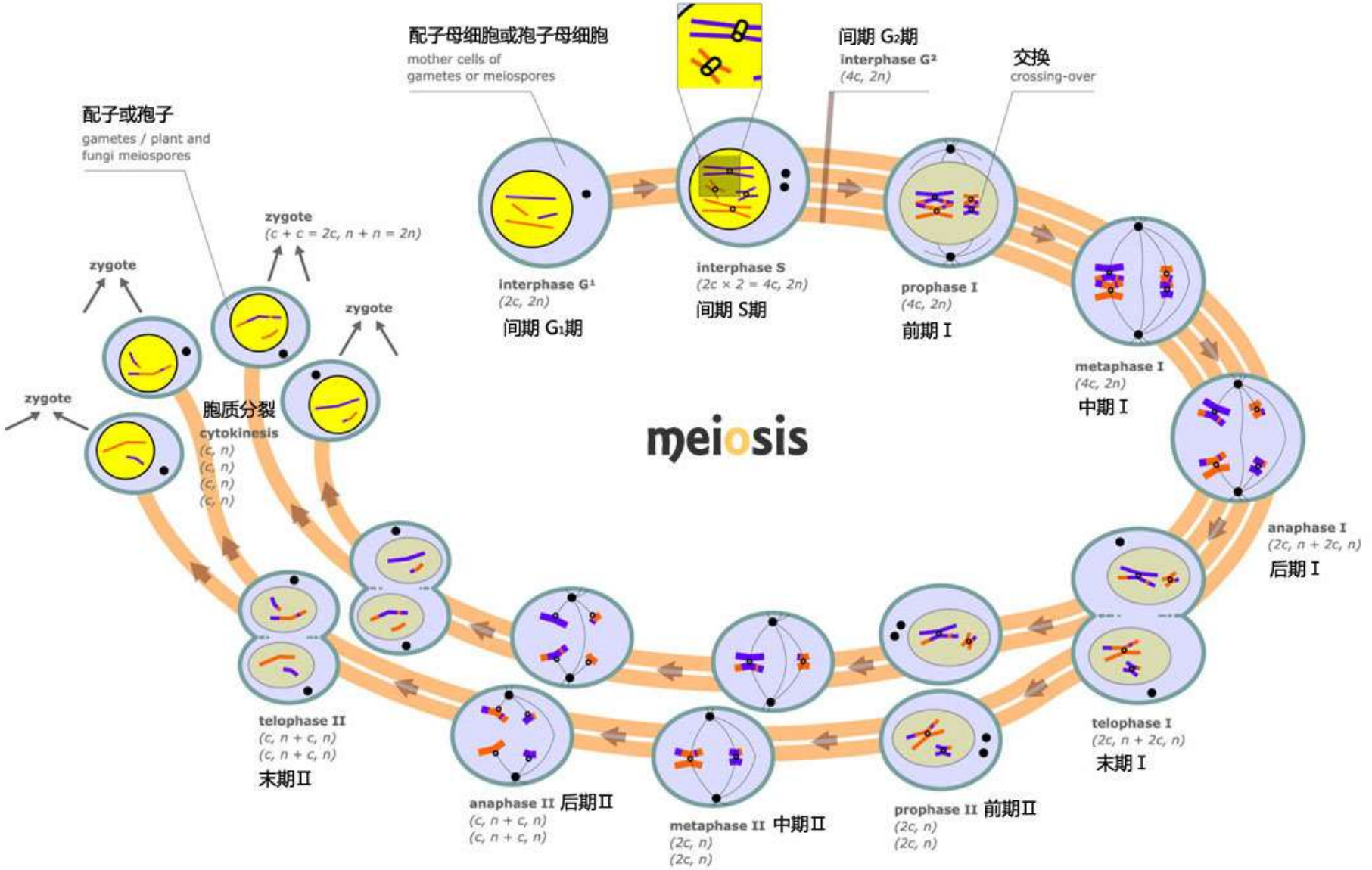

减数分裂
配子(n)
合子(2n)
动物
二倍体世代(2n)
配子(n)
A
减数分裂
配子(n)
合子(2n)
植物孢子体
二倍体世代(2n)
孢子(n)
配子体(n)
配子(n)
B
减数分裂
配子(n)
合子(2n)
酵母
单倍体世代(n)
配子(n)
C

有丝分裂和减数分裂比较

表13-1 有丝分裂与减数分裂比较

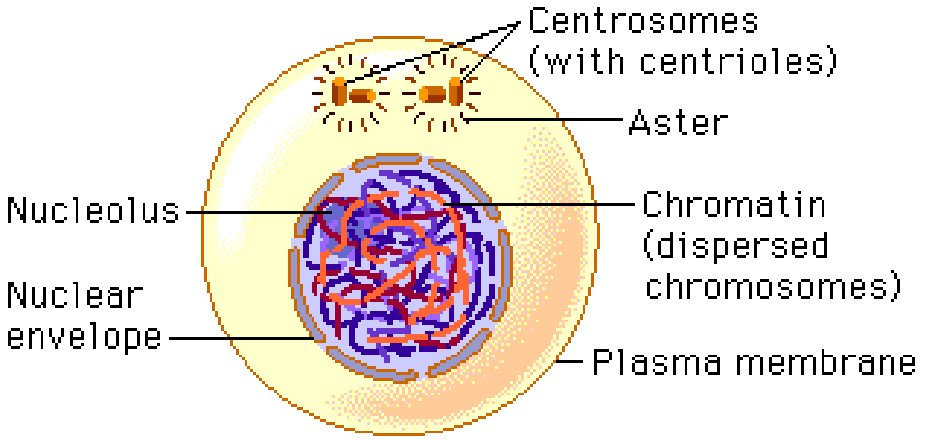
有丝分裂特征	有丝分裂	减数分裂	减数分裂特征
有丝分裂发生在体细胞，在时空上无严格限定			减数分裂只发生在有性生殖的特定时空
在有丝分裂间期，每个体细胞核DNA复制1次，细胞分裂1次			减数分裂前间期DNA复制1次，细胞连续分裂2次
有丝分裂前期一般不发生同源染色体配对，也不发生交换和重组			减数分裂前期Ⅰ发生同源染色体配对(联会)，并伴随发生同源染色体非姐妹染色单体之间交换和重组
有丝分裂中—后期同源染色体姐妹染色单体分离			减数分裂中—后期Ⅰ同源染色体分离，姐妹染色单体不分离
			减数分裂中—后期Ⅱ姐妹染色单体分离
子细胞染色体数目与母细胞染色体数目相同($2n \rightarrow 2n$) 有丝分裂产生2个子细胞，保持遗传稳定			子细胞染色体数目减半($2n \rightarrow n$) 减数分裂产生4个子细胞，增加遗传变异

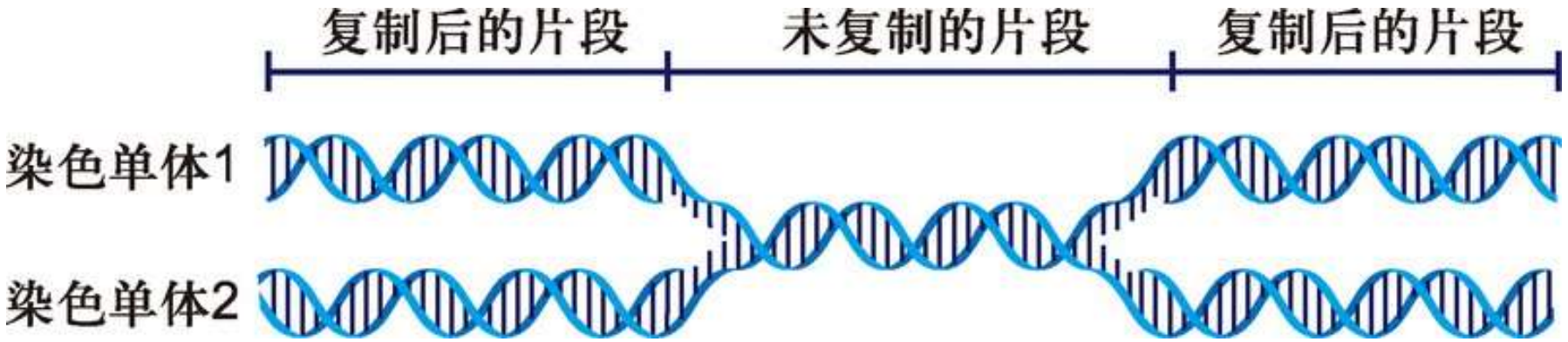
（一）减数分裂过程


配子母细胞或孢子母细胞
mother cells of
gametes or meiospores
间期 G2期
interphase G2
(4c, 2n)
交换
crossing-over
配子或孢子
gametes / plant and
fungi meiospores
zygote
(c + c = 2c, n + n = 2n)
zygote
zygote
zygote
interphase G1
(2c, 2n)
间期 G1期
interphase S
(2c × 2 = 4c, 2n)
间期 S期
prophase I
(4c, 2n)
前期 I
metaphase I
(4c, 2n)
中期 I
anaphase I
(2c, n + 2c, n)
后期 I
telophase I
(2c, n + 2c, n)
末期 I
胞质分裂
cytokinesis
(c, n)
(c, n)
(c, n)
(c, n)
meiosis
telophase II
(c, n + c, n)
(c, n + c, n)
末期II
anaphase II 后期II
(c, n + c, n)
(c, n + c, n)
metaphase II 中期II
(2c, n)
(2c, n)
prophase II 前期II
(2c, n)
(2c, n)

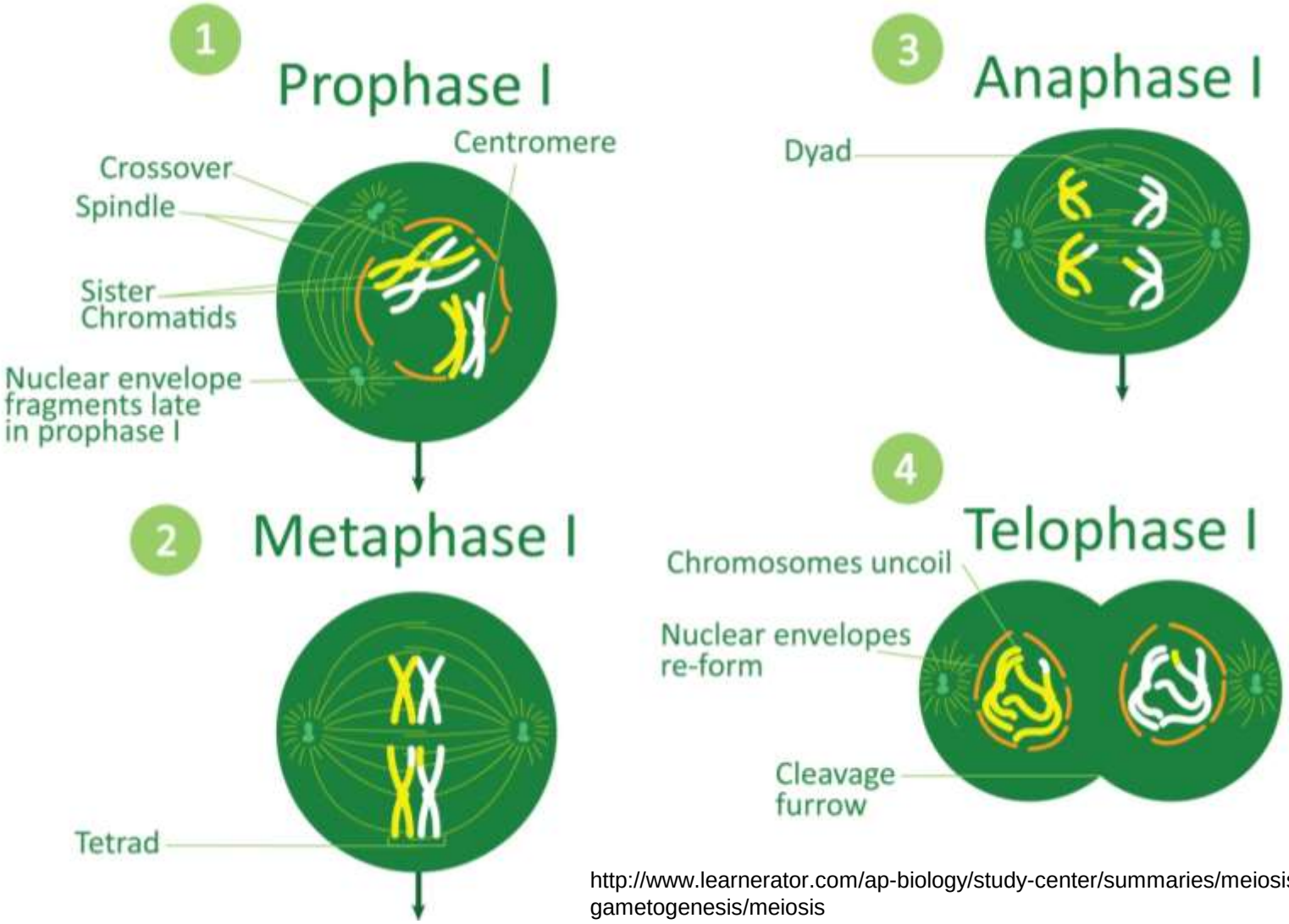
（二）减数分裂前间期

- 细胞核大于其体细胞核；分G1期、S期和G2期
- S 期持续时间较长，但DNA未全部复制完成
- G2 期的长短变化较大





1. 减数分裂 I



http://www.learnerator.com/ap-biology/study-center/summaries/meiosis-&-gametogenesis/meiosis

1. 减数分裂 I —— 前期 I（同源染色体配对和基因重组）

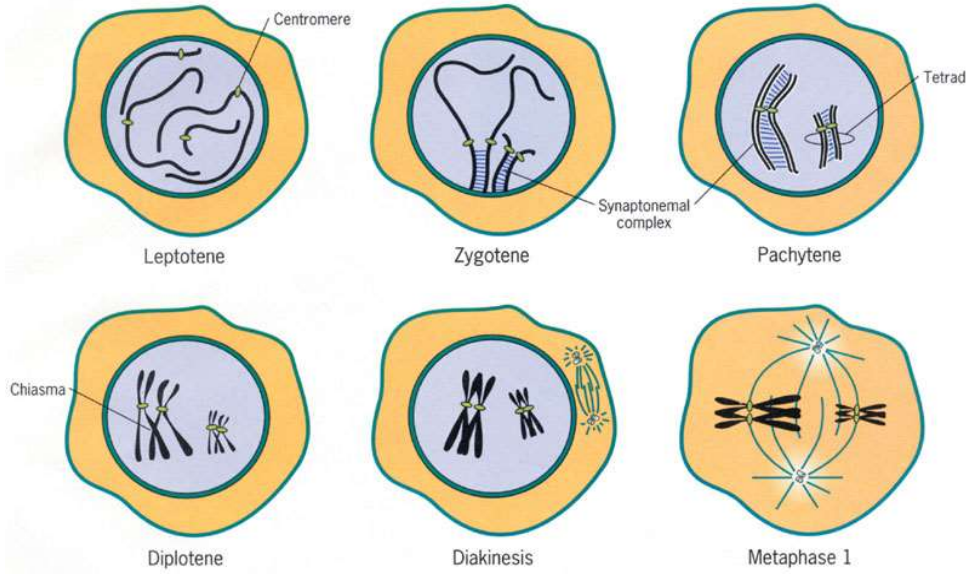
细线期：染色质凝缩；染色粒；接触斑

偶线期：配对（二价体、四分体）；联会复合体；偶线期DNA复制转录（0.3%）

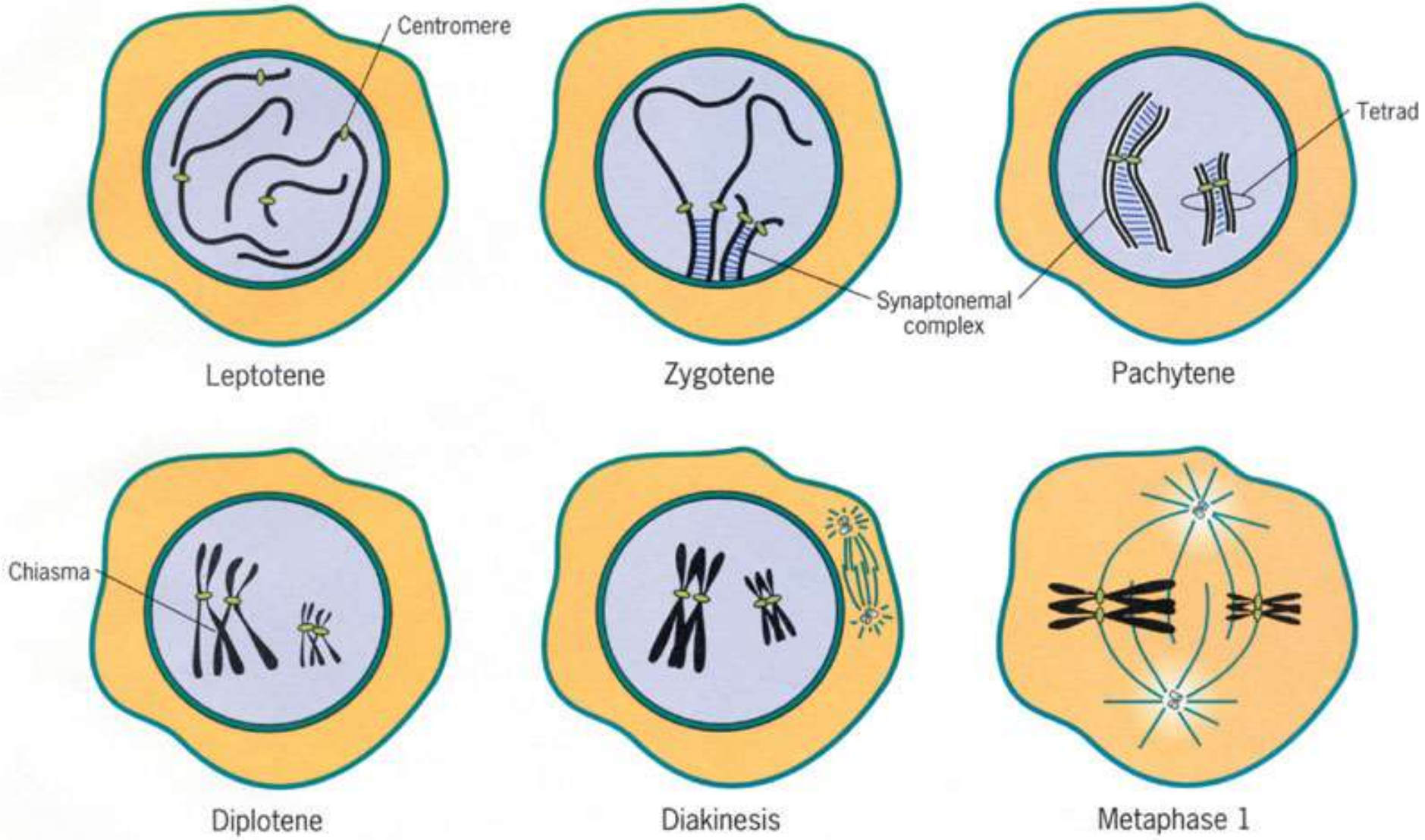
粗线期：重组节；P-DNA复制；专用组蛋白合成；rDNA扩增

双线期：同源染色体分离；交叉；染色质部分去凝集，RNA转录活跃，部分物种形成灯刷染色体

终变期：染色质重新凝集；交叉端化；转录停止，核仁消失

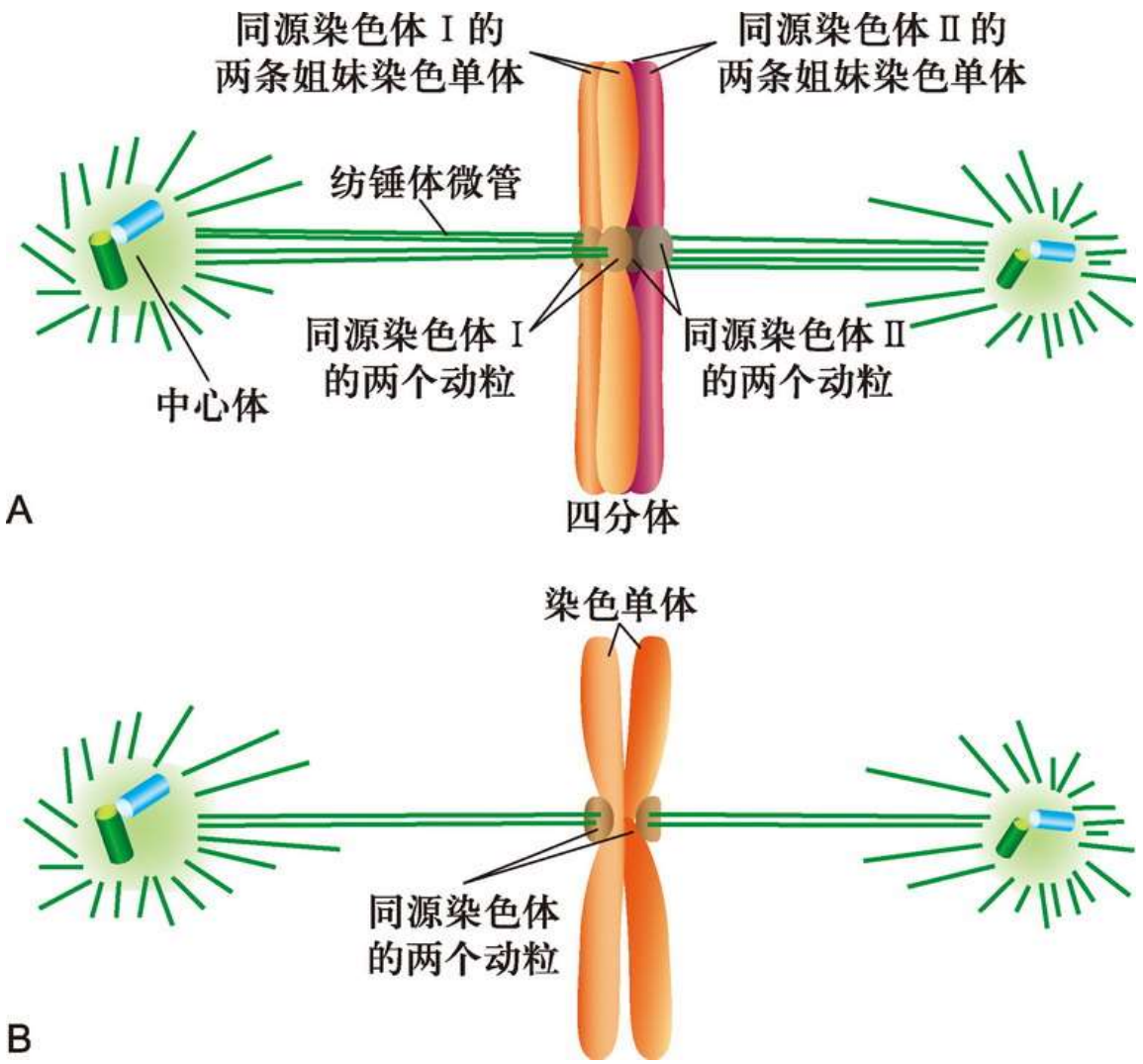


1. 减数分裂 I —— 前期 I


Centromere
Leptotene
Zygotene
Synaptonemal complex
Tetrad
Pachytene
Chiasma
Diplotene
Diakinesis
Metaphase 1

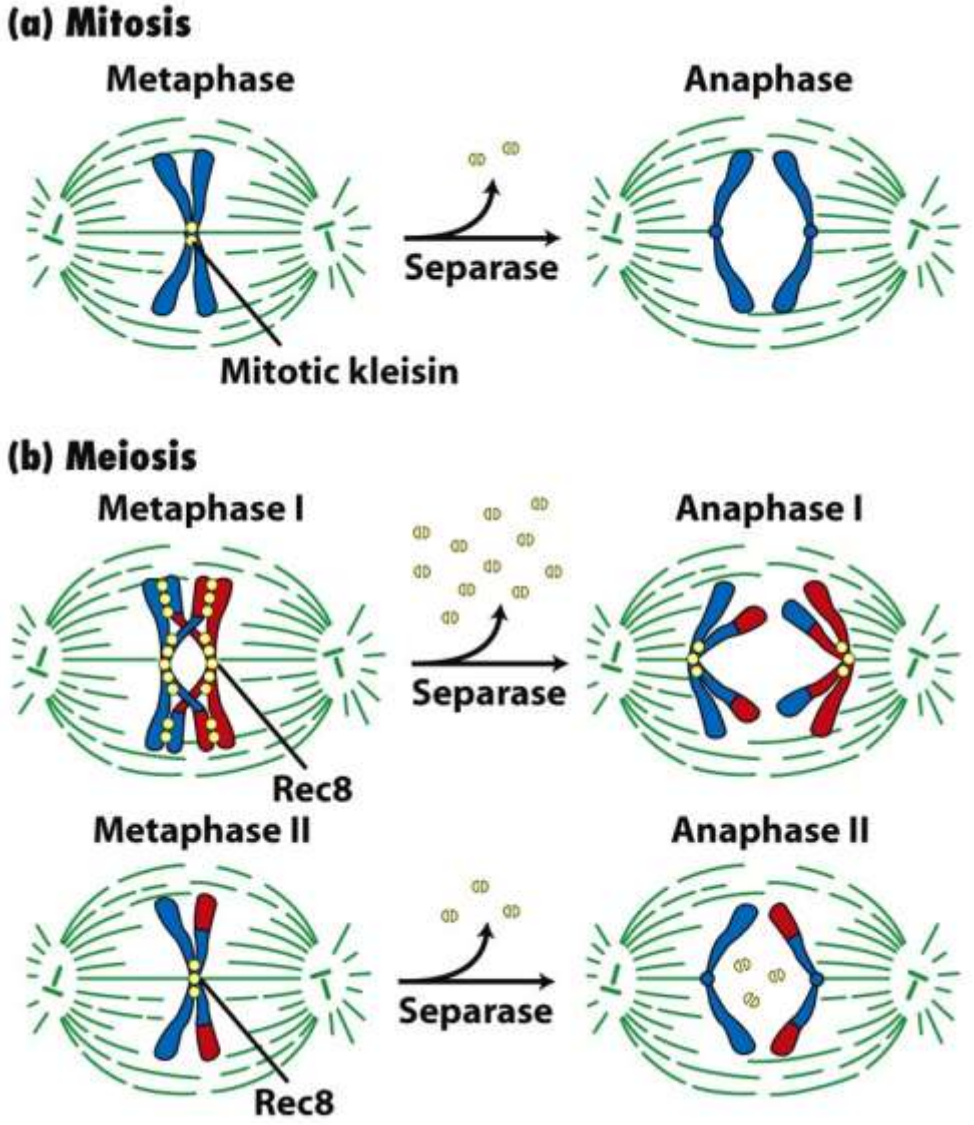
1. 减数分裂 I —— 中期 I

- 核膜破裂
- 纺锤体微管捕获四分体
- 四分体排列到赤道面上

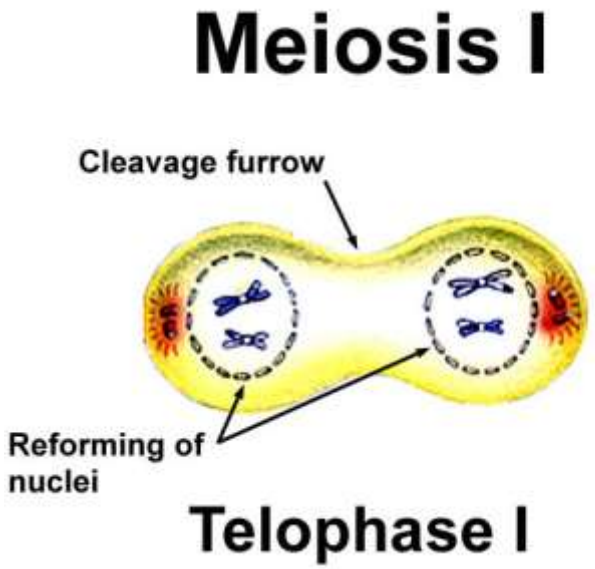


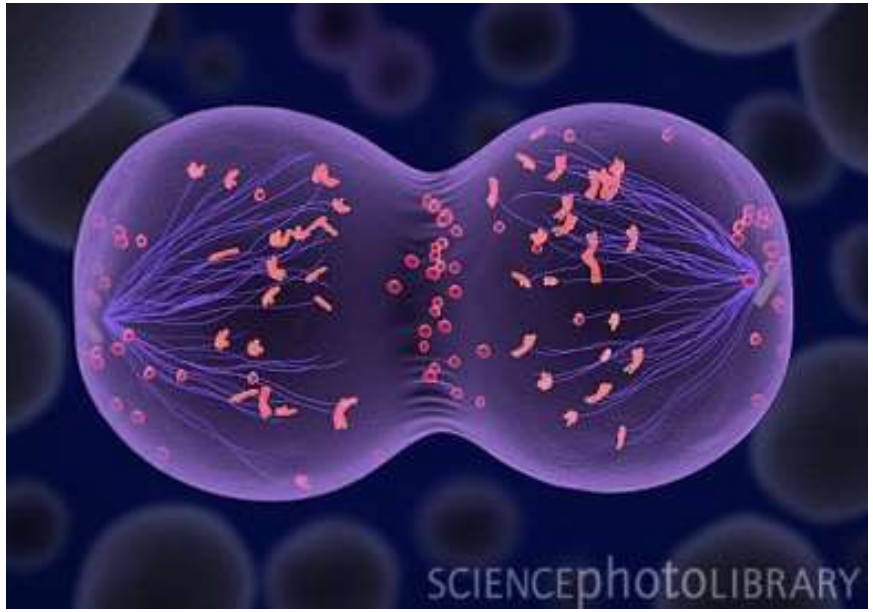
1. 减数分裂 I —— 后期 I

- 同源染色体对分离并向两极移动
- 同源染色体的随机分配、自由组合
- 第一次分裂后染色体数减半

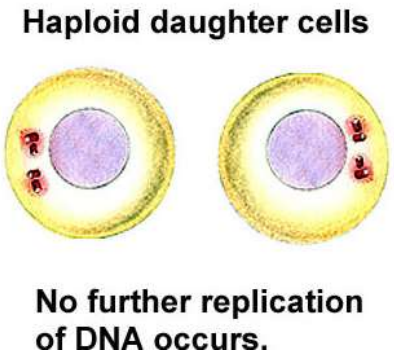


1. 减数分裂 I —— 末期 I、胞质分裂和减数分裂间期





Interkinesis

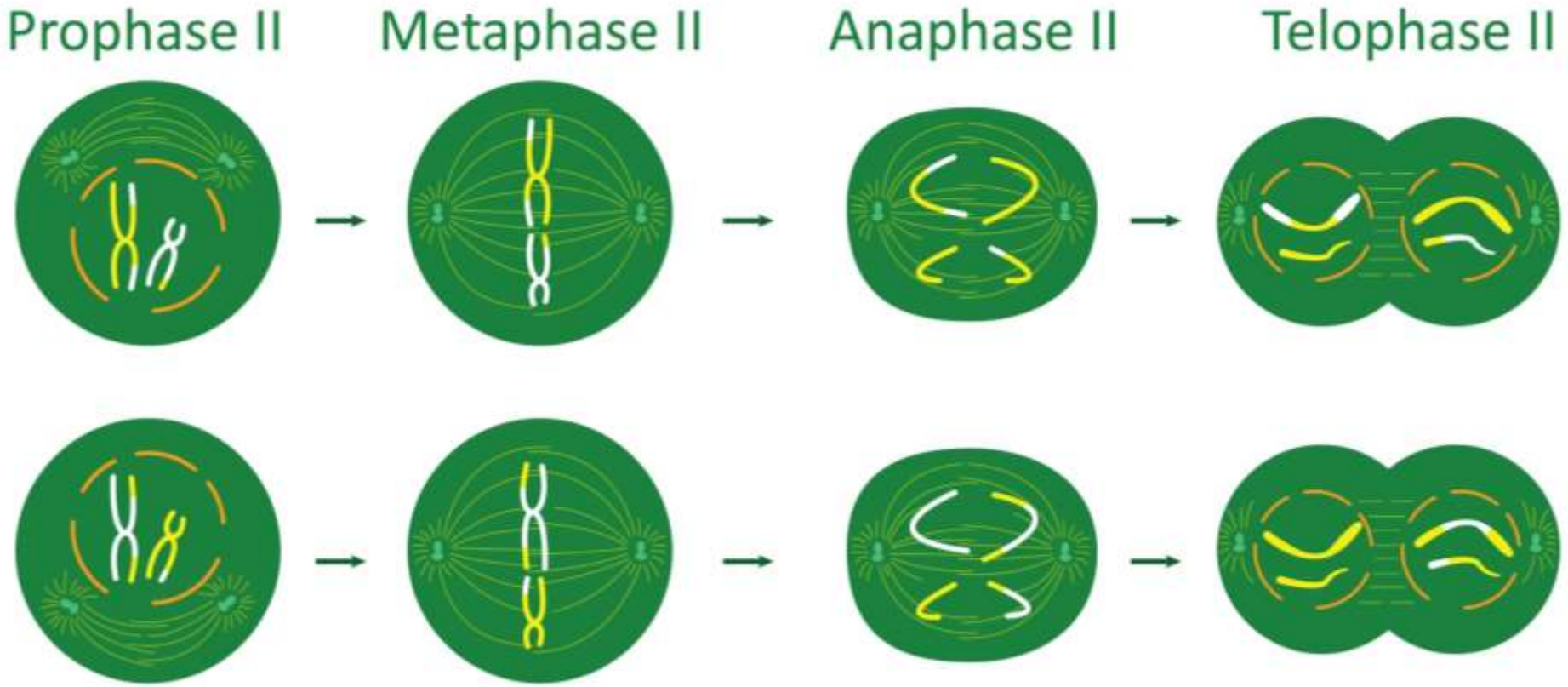


http://www.sciencephoto.com/image/410930/530wm/C0099567-Meiosis,_artwork-SPL.jpg

http://iws.collin.edu/biopage/faculty/mcculloch/1406/outlines/chapter%2012/Ar14-11d.JPG

http://iws.collin.edu/biopage/faculty/mcculloch/1406/outlines/chapter%2012/Ar14-11i.JPG

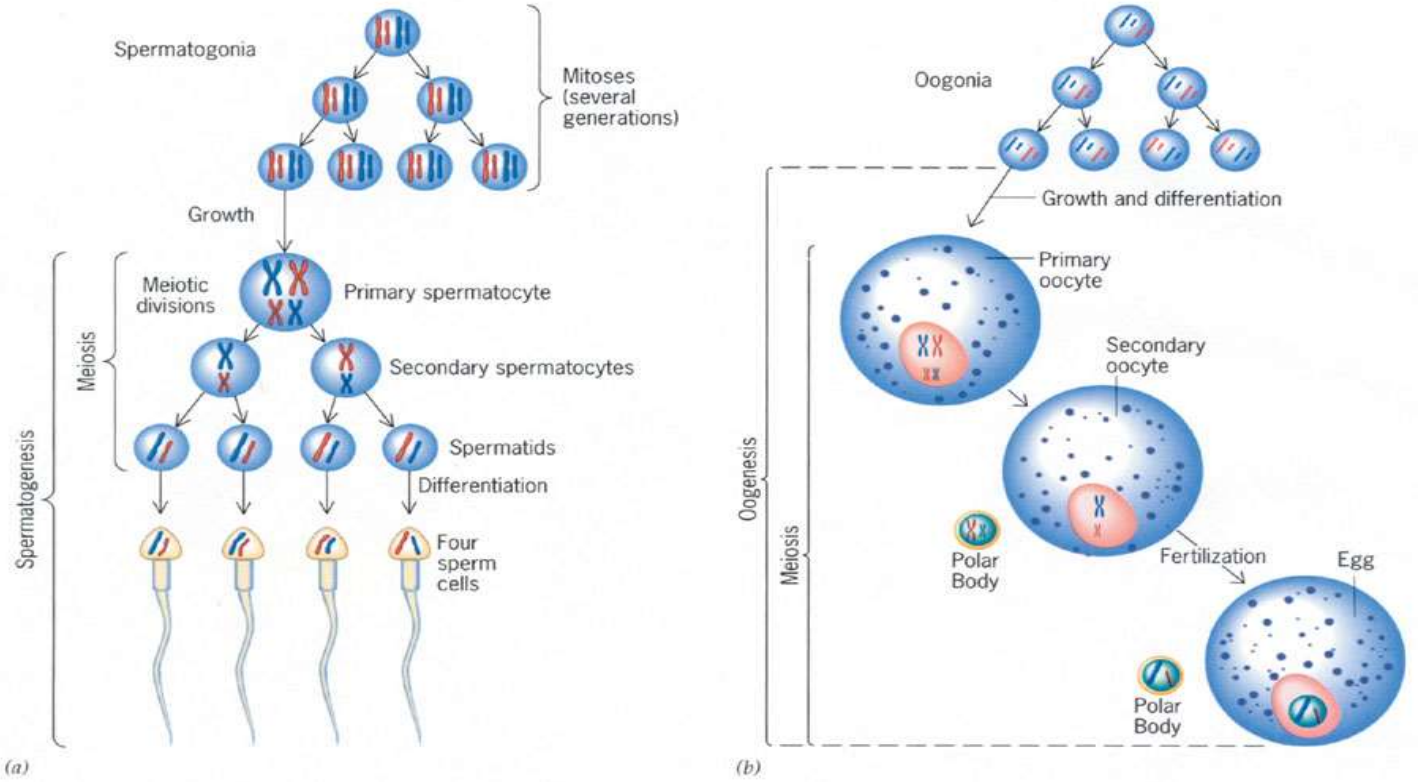
2. 减数分裂 II



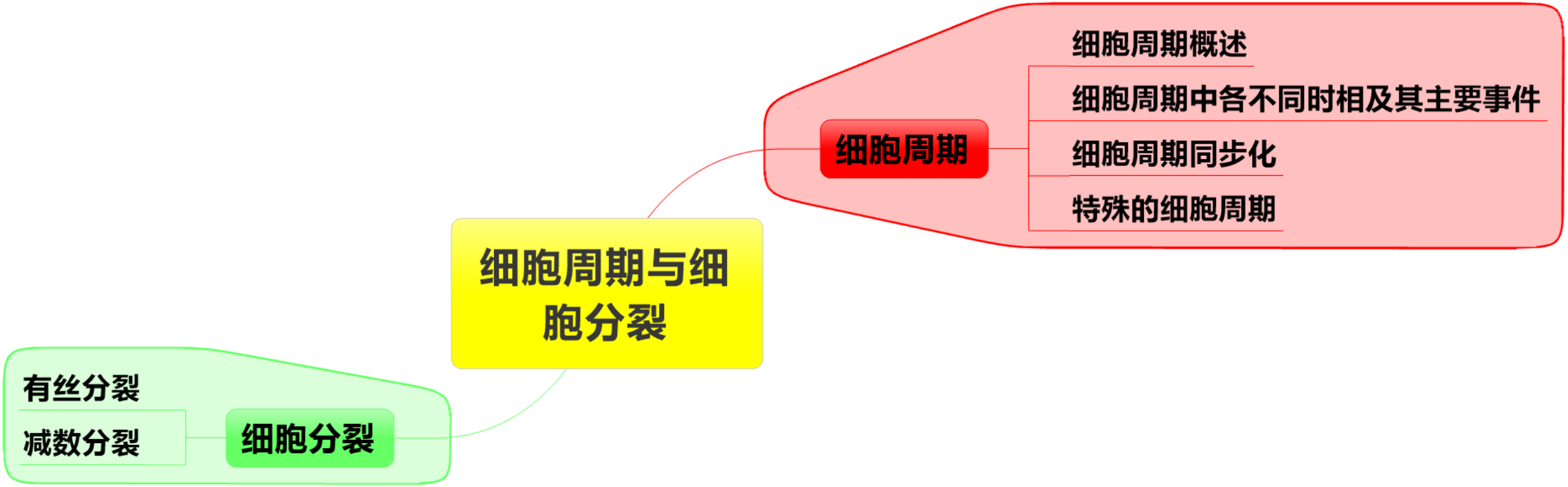
https://www.bilibili.com/video/BV1ix411m7Vf/?spm_id_from=333.337.search-card.all.click&vd_source=c5090343149d17b29be71f6182e43da4

你知道吗？Why?

- 女性卵巢中卵母细胞约从胚胎期第五个月开始进入前期I的双线期，可保持几十年
- 脊椎动物排出的卵减数分裂进程停滞在中期II?



本章内容提要


细胞周期与细胞分裂
细胞周期
细胞周期概述
细胞周期中各不同时相及其主要事件
细胞周期同步化
特殊的细胞周期
细胞分裂
有丝分裂
减数分裂