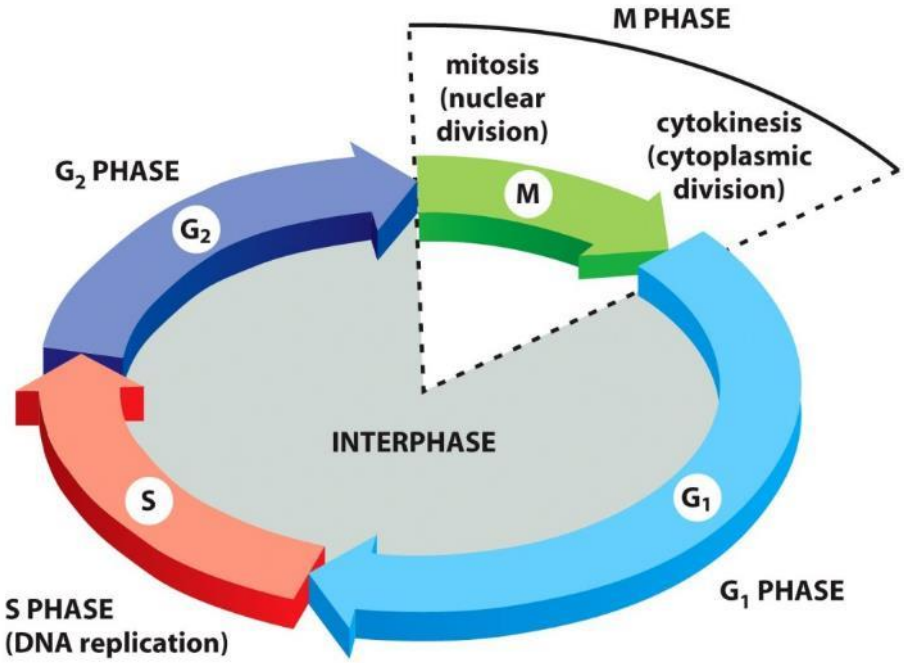
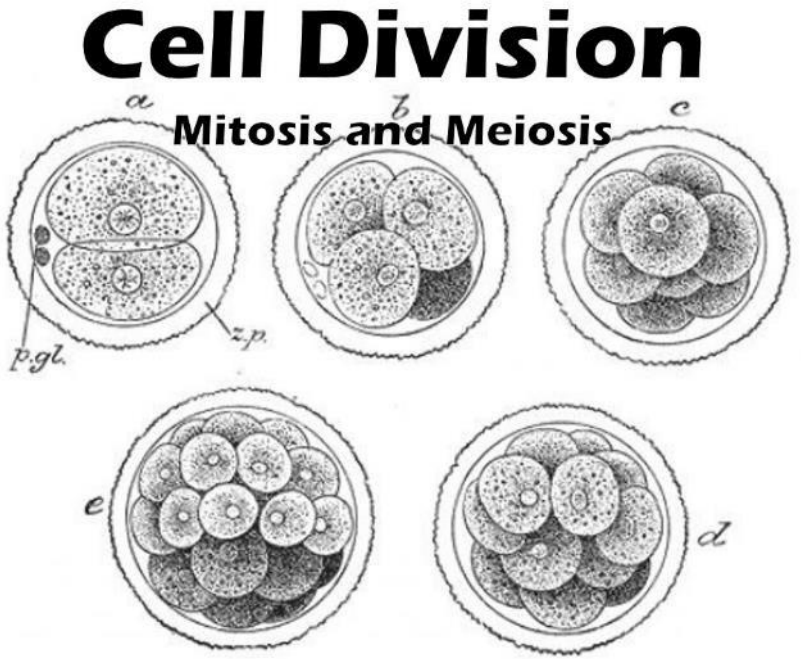
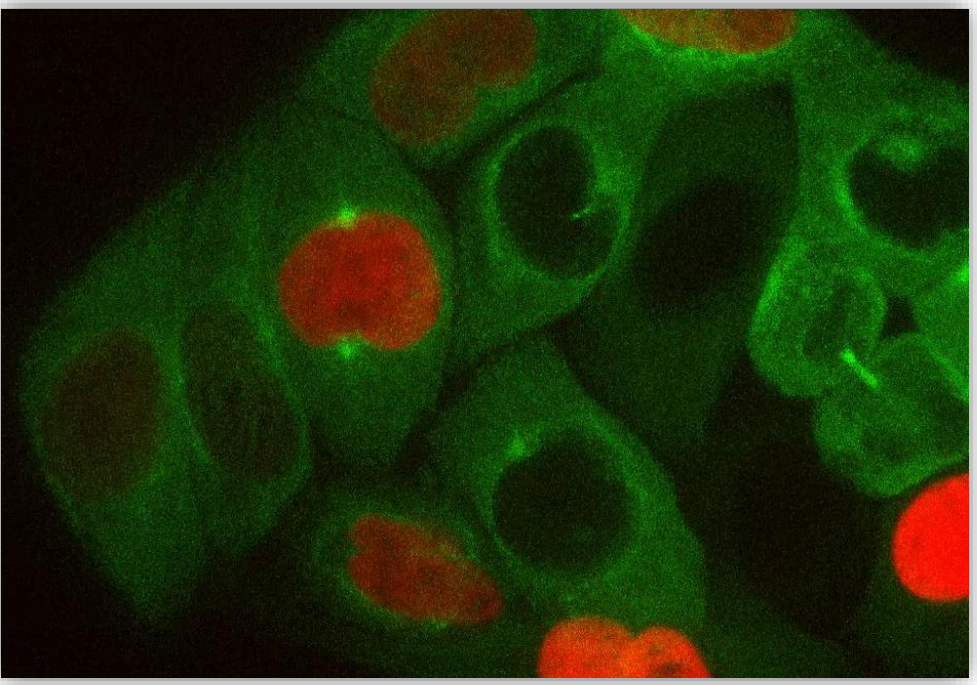
第十二章 细胞周期与细胞分裂

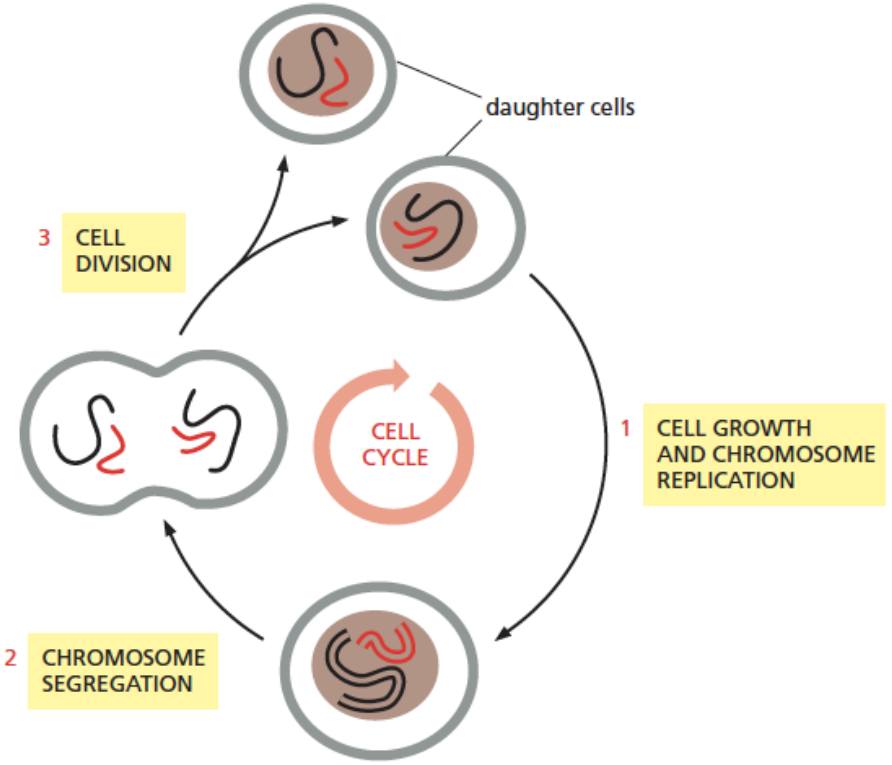




细胞分裂与细胞周期

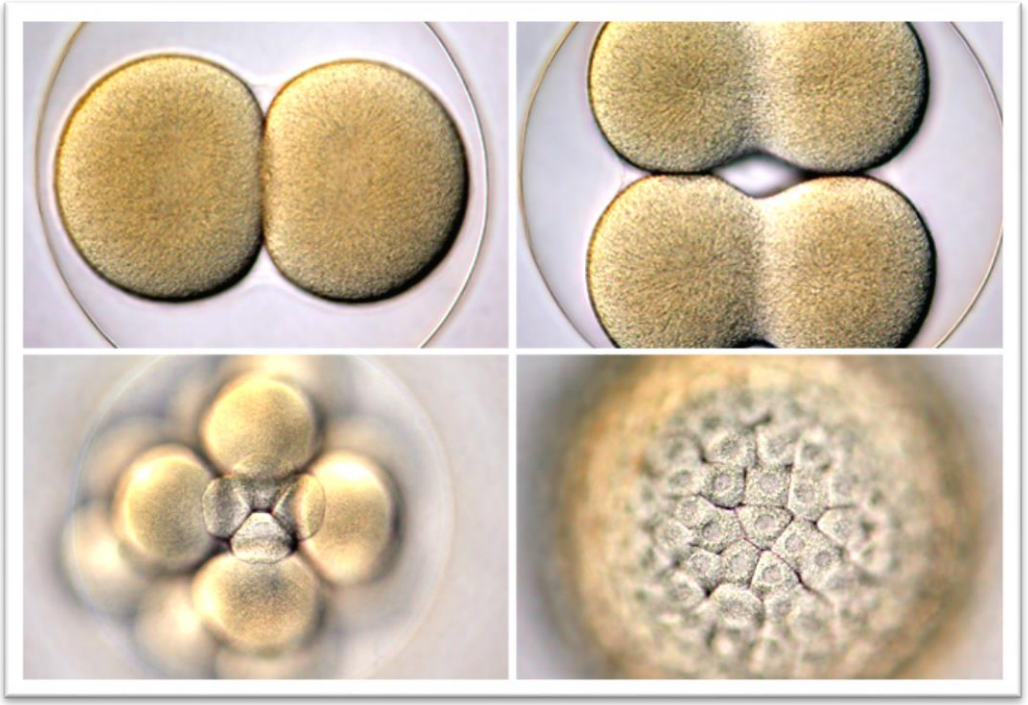
- **细胞分裂 (cell division)：**由原来的一个亲代细胞变为两个子代细胞
- **细胞周期 (cell cycle)：**物质准备和细胞分裂这一相互连续的过程





细胞增殖 cell proliferation

- 通过细胞分裂的方式使细胞的数量增加
- 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



海胆 受精后5小时

细胞增殖 cell proliferation

- 细胞生命活动的重要特征之一
- 单细胞生物：个体数量的增加
- 多细胞生物：由一个单细胞(受精卵)分裂发育而来，细胞增殖是多细胞生物繁殖基础
- 成体生物：弥补代谢过程中的细胞损失

  （衰老死亡、创伤愈合、组织再生等）

  例如：肠上皮细胞，3-5天更新一次

  由肠上皮隐窝中的干细胞增殖、分化、迁移

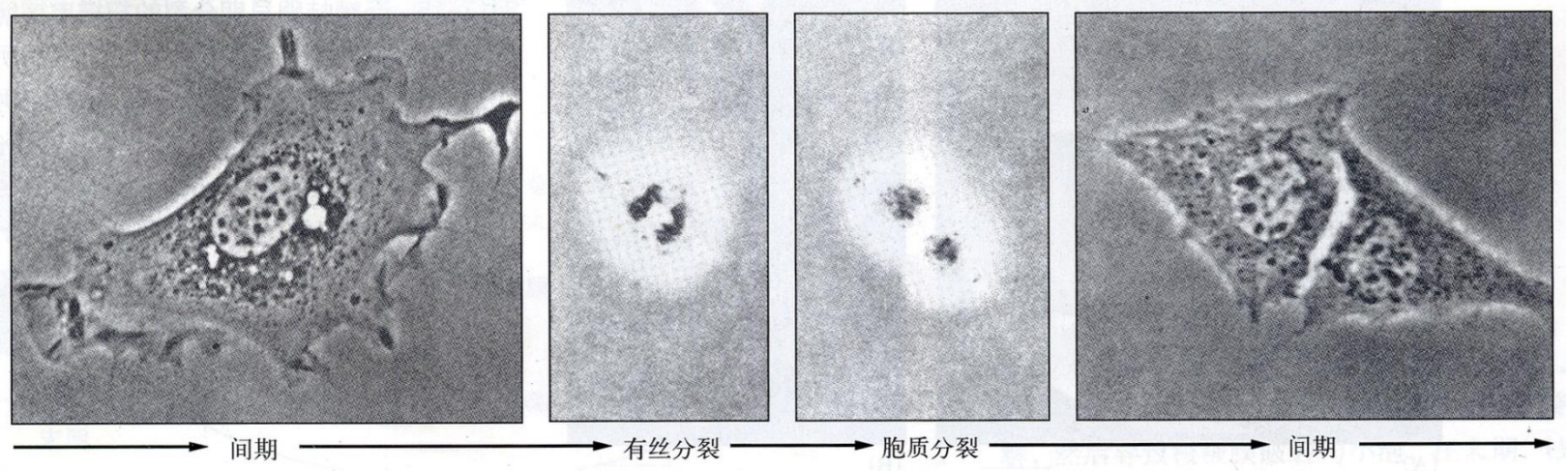
第一节

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

一、细胞周期概述

- 细胞周期：从一次细胞分裂结束开始，经过**物质准备**，直到下一次**细胞分裂**结束为止的过程
- 细胞周期的时期划分
  - 细胞有丝分裂期（mitosis）
  - 分裂间期（interphase）



一、细胞周期概述

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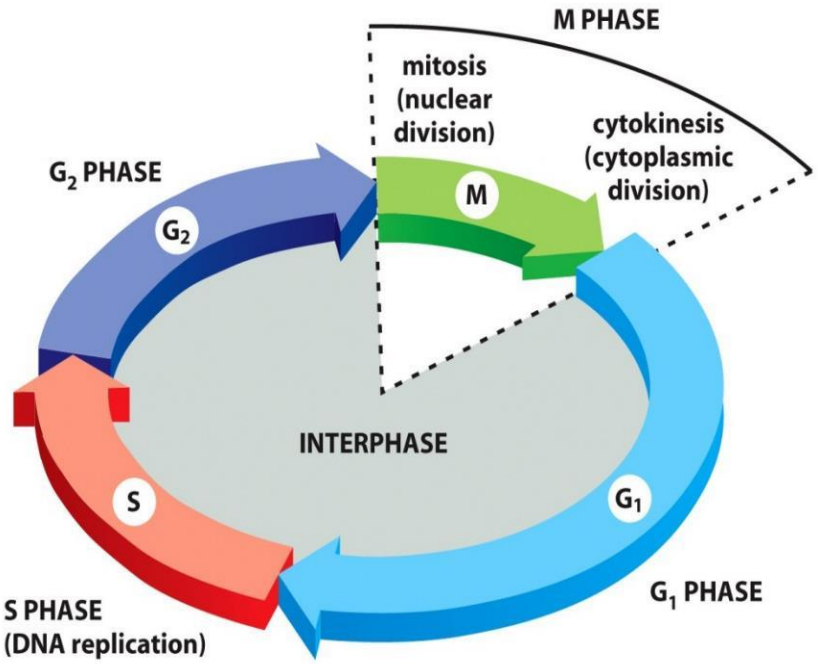


Alma Howard and Stephen Pelc, 1953

^{32}P 标记蚕豆根尖细胞，放射自显影

The discovery of the cell cycle

NATURE|VOL 426 | 18/25 DECEMBER 2003 , 759

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.

Joseph G. Dubrovsky*, Victor B. Ivanov†

** Departamento de Biología Molecular de Plantas, Instituto de Biotecnología, Universidad Nacional Autónoma de México, A. P. 510-3, Cuernavaca Morelos 62250, México*

† 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、细胞周期概述

- **标准的细胞周期 Standard Cell cycle 的四个时相**
- G1期 (gap1)，指从细胞分裂完成到DNA复制之前的间隙时间。
- S期 (synthesis phase)，指DNA复制的时期。
- G2期 (gap2)，指DNA复制完成到细胞分裂开始之前的一段时间。
- M期 (mitosis or division)，细胞分裂开始到结束。

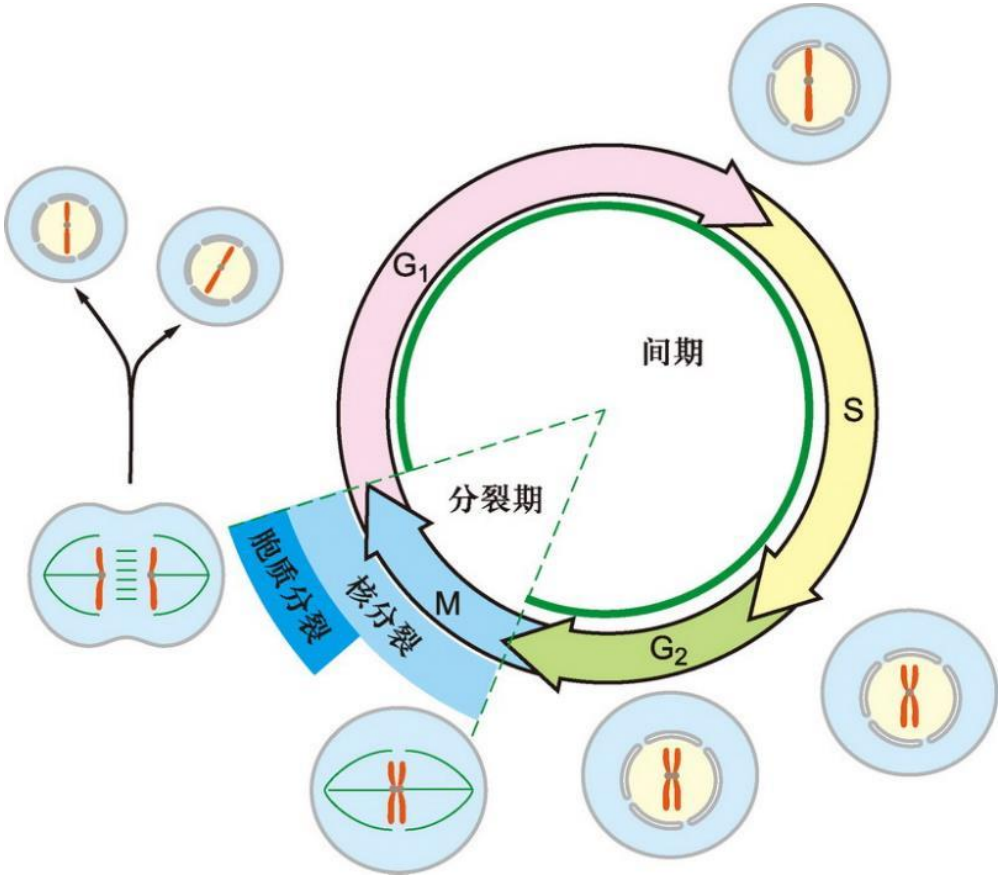


图12-1 标准的细胞周期

一个标准的细胞周期一般包括4 个时相：DNA 合成期（S）、细胞分裂期（M）以及介于二者之间的G1 期和G2 期。细胞周期从G1期开始，经S 期和G2 期，到M 期结束

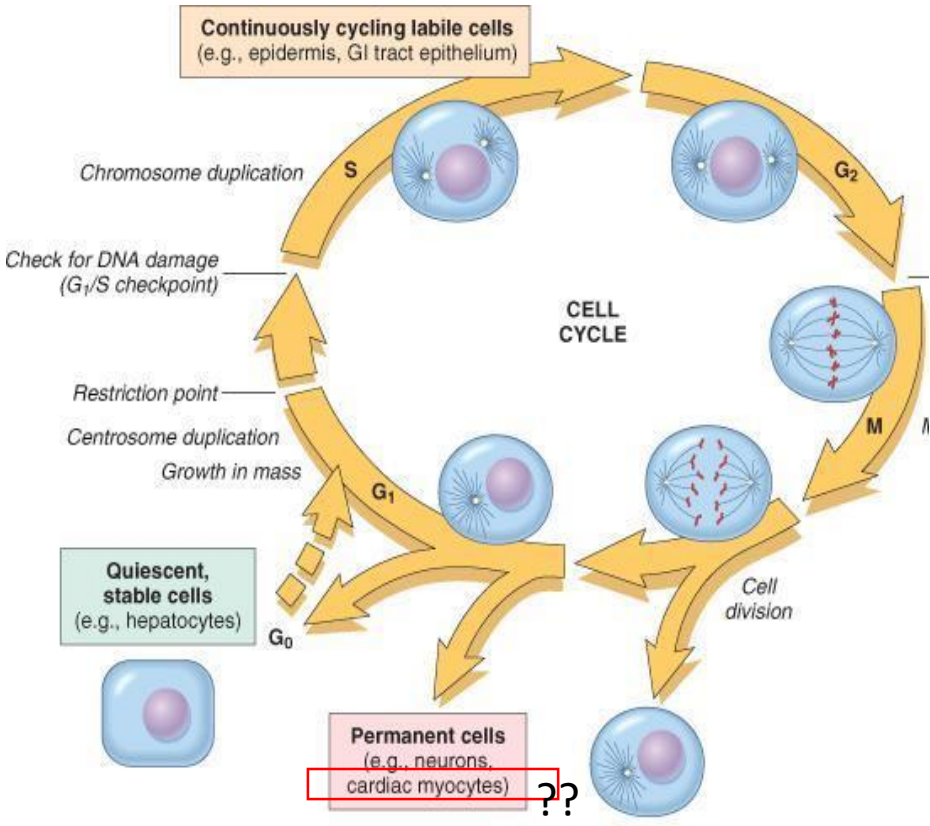
一、细胞周期概述

- 不同的细胞种类其细胞周期时间长短差别很大
- S+G_2+M 的时间变化较小，细胞周期时间长短主要差别在**G_1期**

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

不同细胞的增殖状态

- 周期中细胞(cycling cell): 连续分裂的细胞，即在细胞周期中连续运转的细胞。例如：上皮细胞
- 静止期细胞(quiescent cell)或G_0期细胞: **暂时脱离**细胞周期，不进行增殖，但在适当刺激下可重新进入细胞周期的细胞。例如：成纤维细胞
- 终末分化细胞 (terminally differentiated cell): 高度特化，不可逆地脱离细胞周期，丧失分裂能力，但仍保持生理机能活动的细胞。例如：横纹肌细胞、神经细胞、红细胞



Article | Published: 22 April 2020

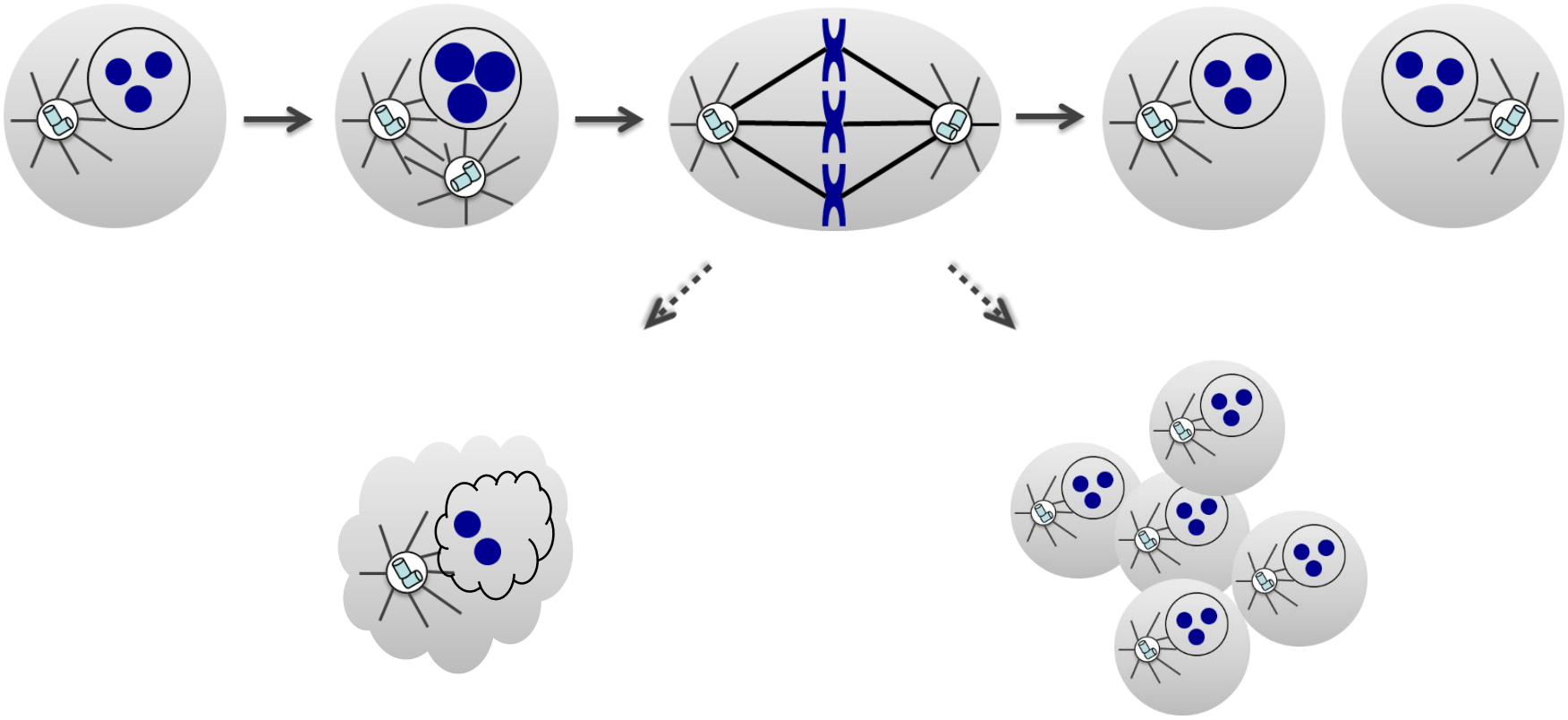
A calcineurin–Hoxb13 axis regulates growth mode of mammalian cardiomyocytes

Ngoc Uyen Nhi Nguyen, Diana C. Canseco, [...] Hesham A. Sadek

Nature **582**, 271–276 (2020) | Cite this article

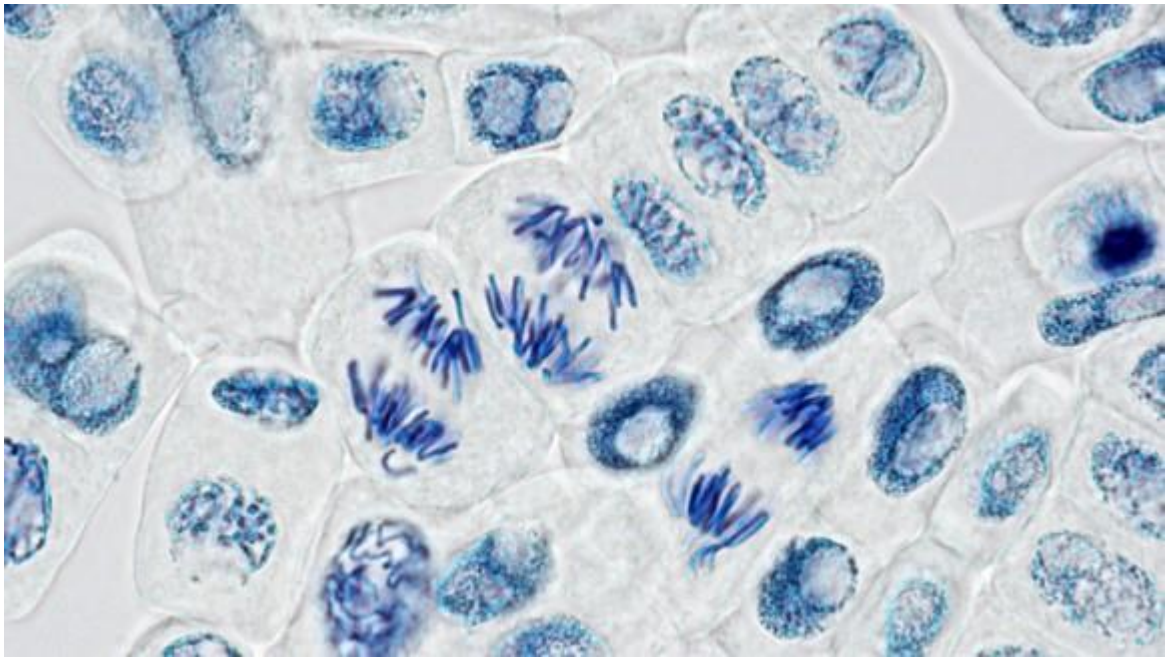
16k Accesses | **25** Citations | **255** Altmetric | Metrics

一、细胞周期概述



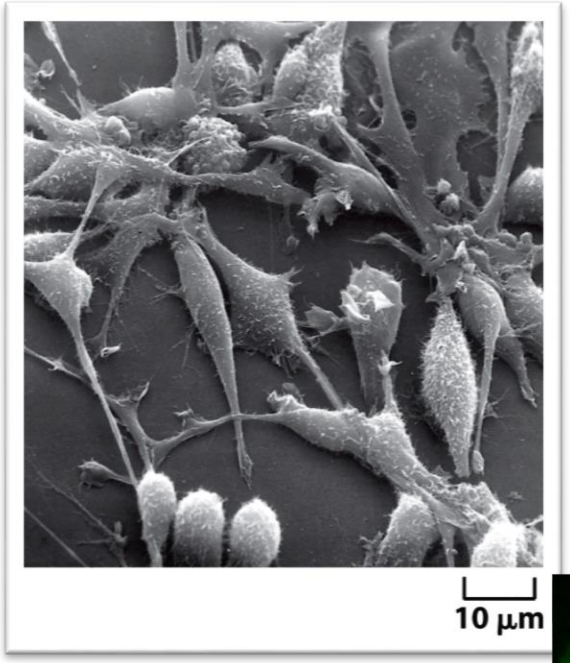
细胞周期中的关键问题

- 细胞周期中3个根本问题
  - 分裂前遗传物质DNA 精确的复制
  - 完整复制DNA 如何准确分配到两个子细胞
  - 物质准备与细胞分裂是如何调控的

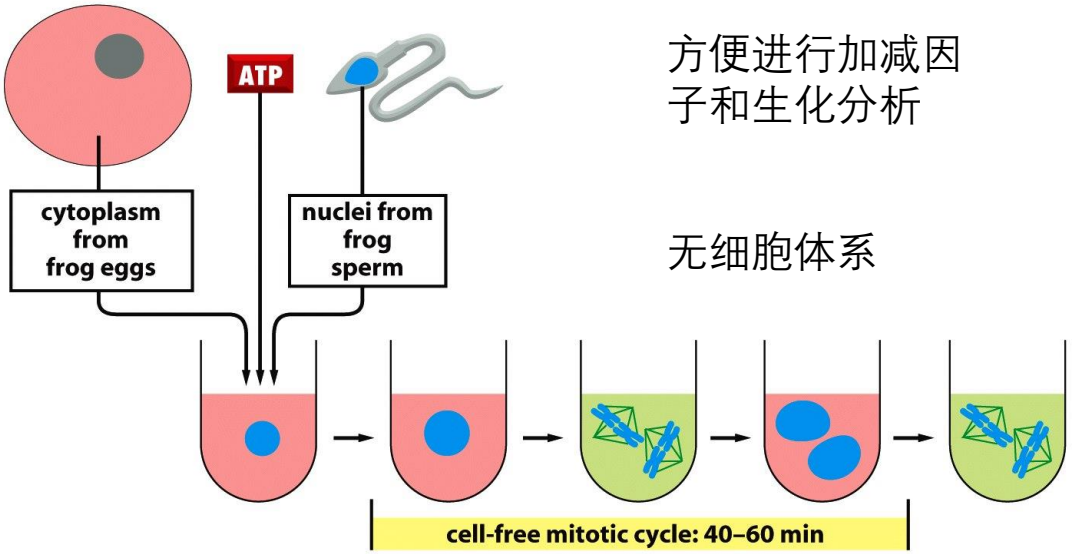


Milestones in Cell Division (nature.com)

细胞周期的研究体系

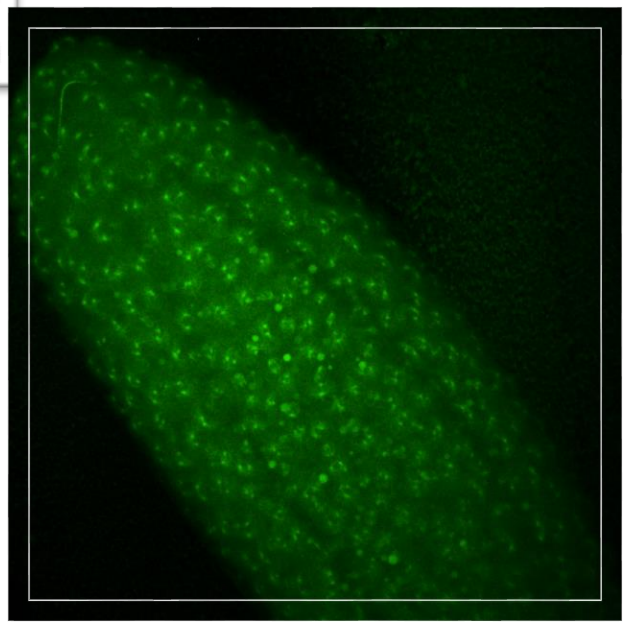


扫描电镜观察的
大鼠成纤维细胞



方便进行加减因
子和生化分析

无细胞体系

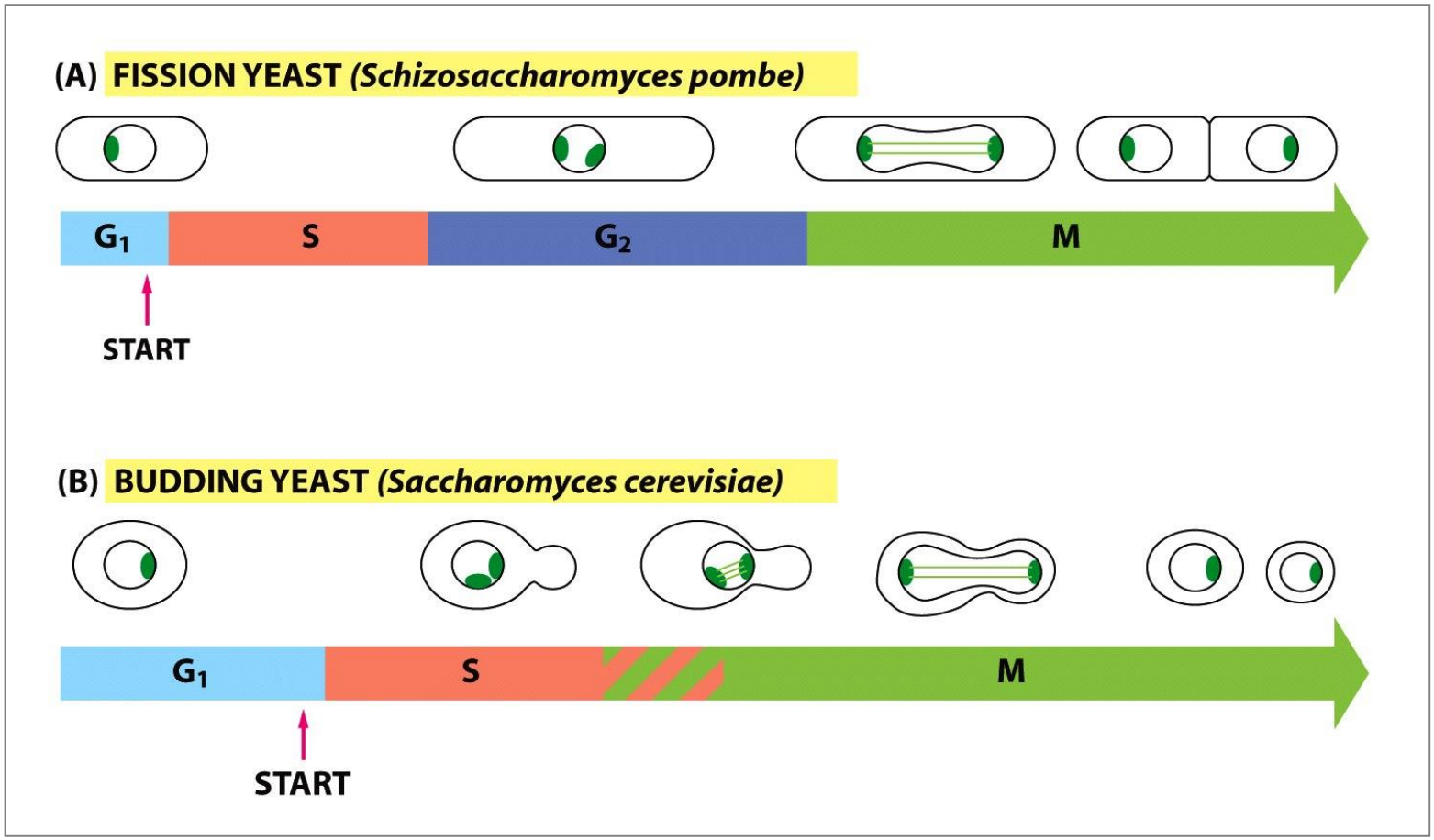


果蝇胚胎早期发育
快速多轮细胞分裂

Gentle centrifugation is used to break open a large batch of frog eggs and separate the cytoplasm from other cell components. The undiluted cytoplasm is collected, and sperm nuclei are added to it, together with ATP. The sperm nuclei decondense and then go through repeated cycles of DNA replication and mitosis, indicating that the cell-cycle control system is operating in this cell-free cytoplasmic extract.

细胞周期的研究体系

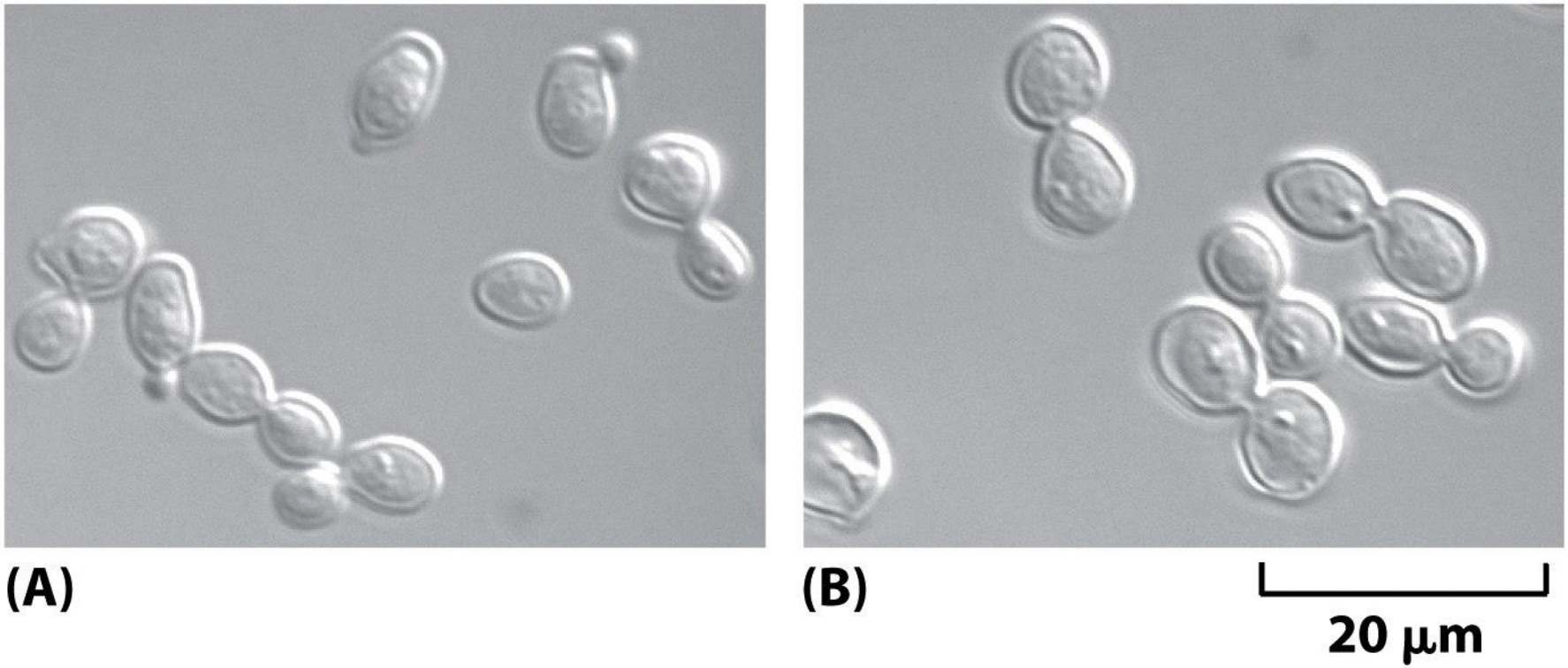
- 酵母模式生物



- 细胞周期短（90min）
- 存在许多突变体
- 温度敏感型突变株

细胞周期的研究方法

- 细胞周期异常的突变体

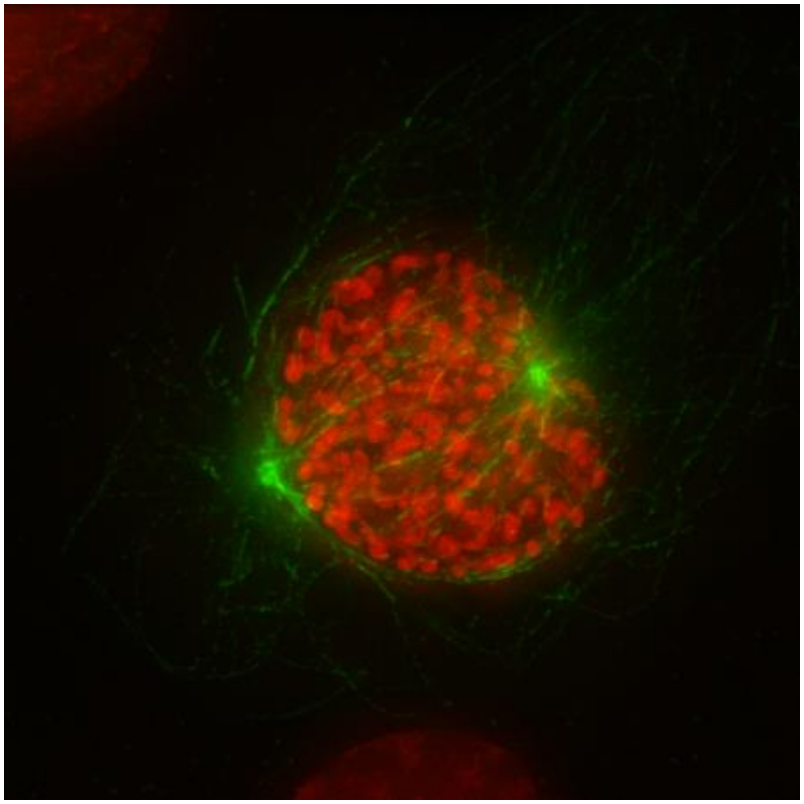


(A) In a normal population of proliferating yeast cells, buds vary in size according to the cell-cycle stage. (B) In a *cdc15* mutant grown at the restrictive temperature, cells complete anaphase but cannot complete the exit from mitosis and cytokinesis. As a result, they arrest uniformly with large buds, which are characteristic of **late M phase**.

细胞周期的研究方法

- 显微镜观察: DIC，荧光显微镜，电子显微镜

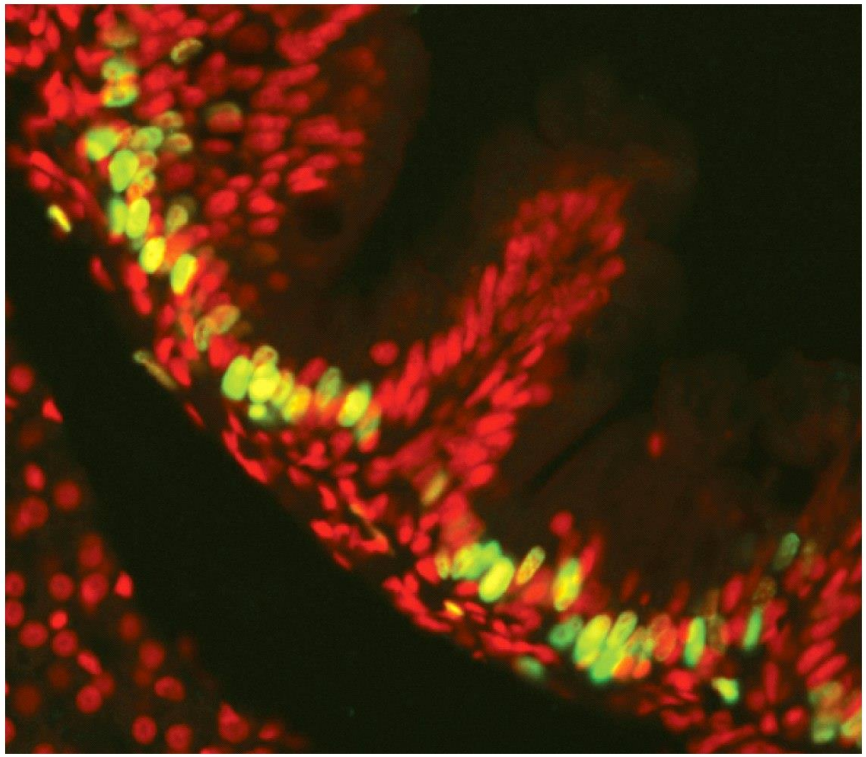
微分干涉显微镜 DIC



荧光显微镜

细胞周期的研究方法

- 免疫荧光染色



斑马鱼肠道上皮细胞

bromodeoxyuridine (BrdU)

5-溴-2-脱氧尿苷

胸腺嘧啶衍生物

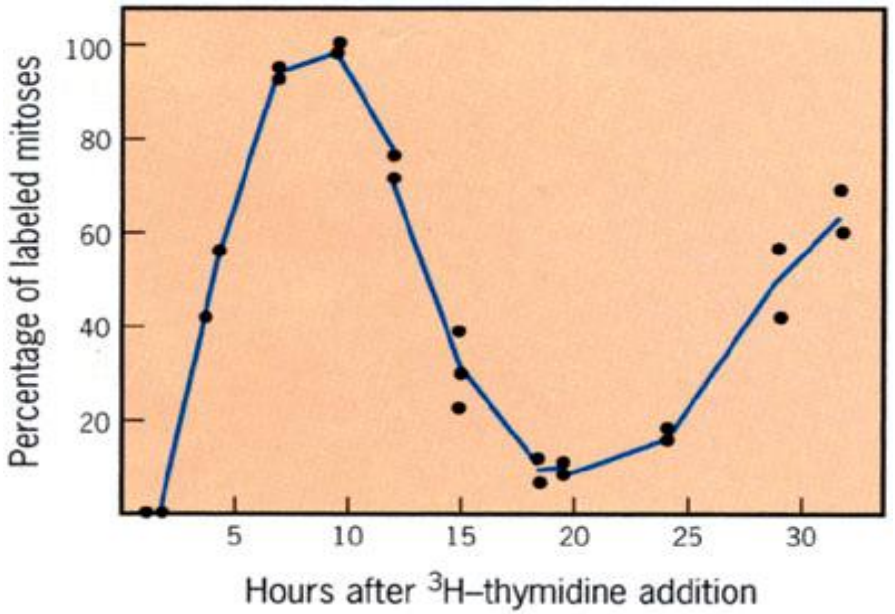
标记S期细胞（绿色）

anti-BrdU 抗体

Figure 17–7 Labeling S-phase cells. An immunofluorescence micrograph of BrdU-labeled epithelial cells of the zebrafish gut. The fish was exposed to BrdU, after which the tissue was fixed and prepared for labeling with fluorescent anti-BrdU antibodies *(green)*. All the cells are stained with a *red* fluorescent dye. (Courtesy of Cécile Crosnier.)

细胞周期的研究方法

- 标记有丝分裂百分率法（percentage labeled mitosis，PLM）
  - 对测定细胞进行脉冲标记、定时取材、利用放射自显影技术显示标记细胞，通过统计标记有丝分裂细胞百分数的办法来测定细胞周期
  - 放射标记物为^{3}H或者^{14}C标记的TdR



细胞周期的研究方法

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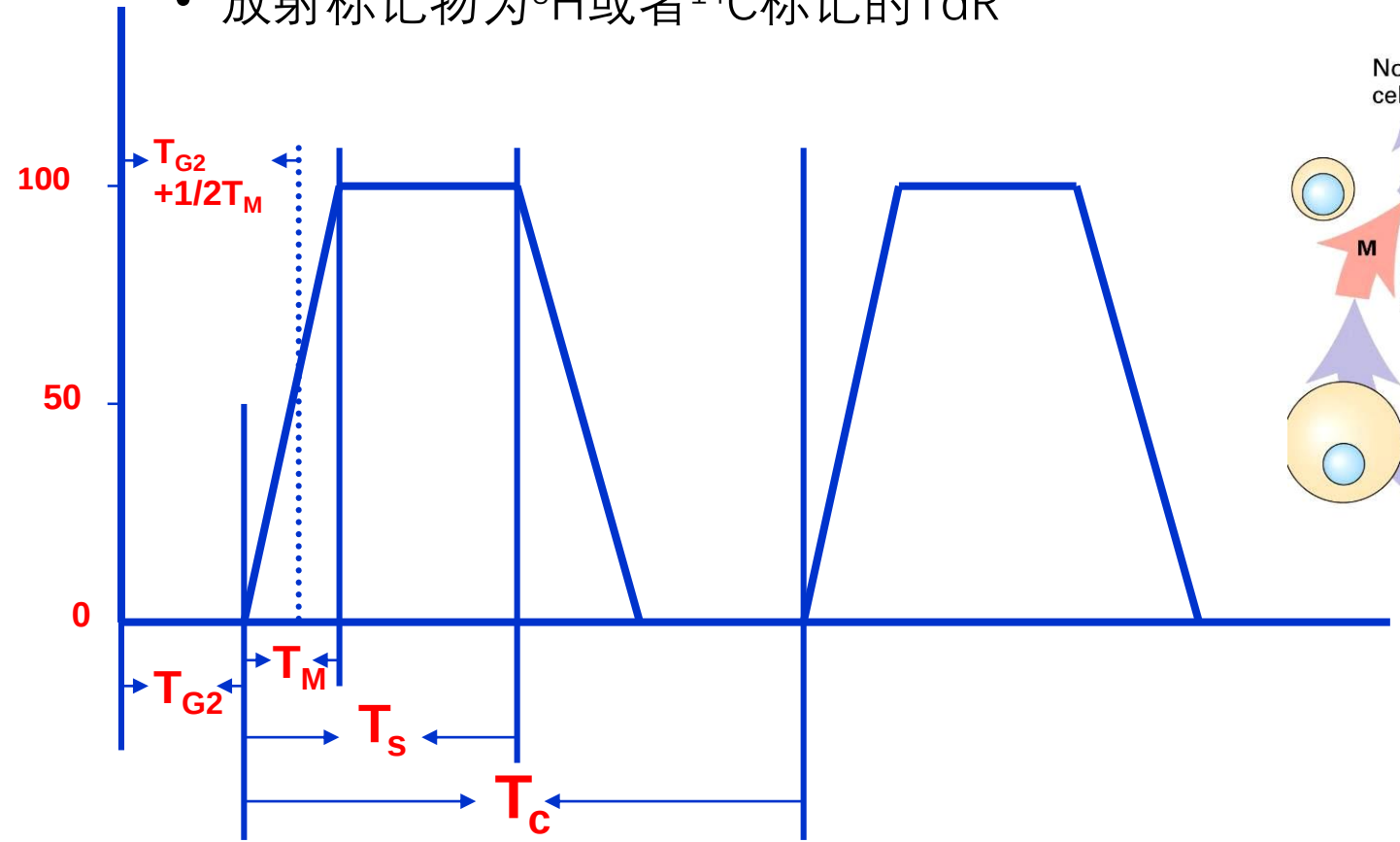
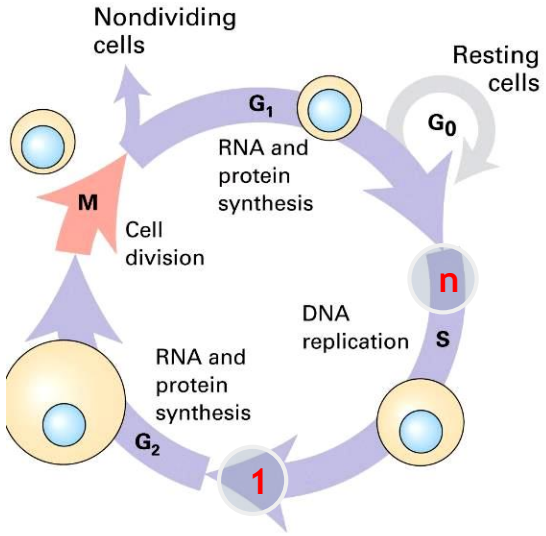
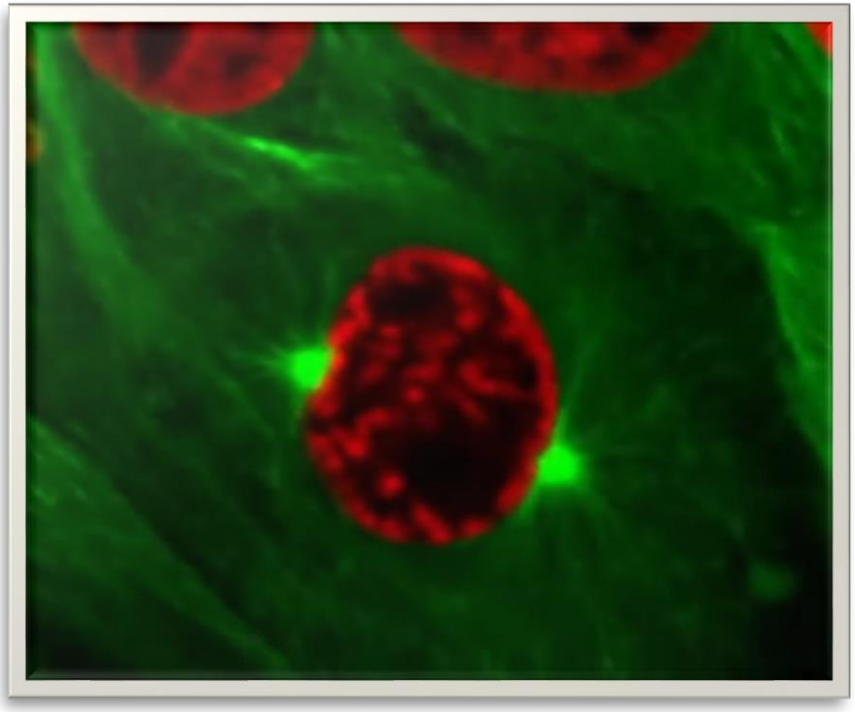




细胞周期的研究方法

- 缩时摄像技术 (Time-lapse photography)：可以准确得到分裂间期、分裂期和总的细胞周期时间



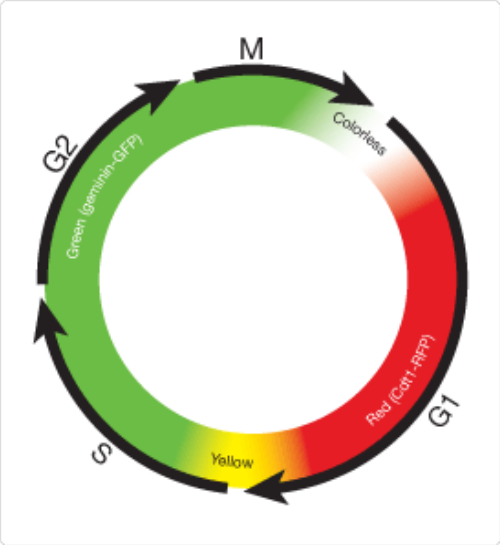
绿色：微管

红色：染色体

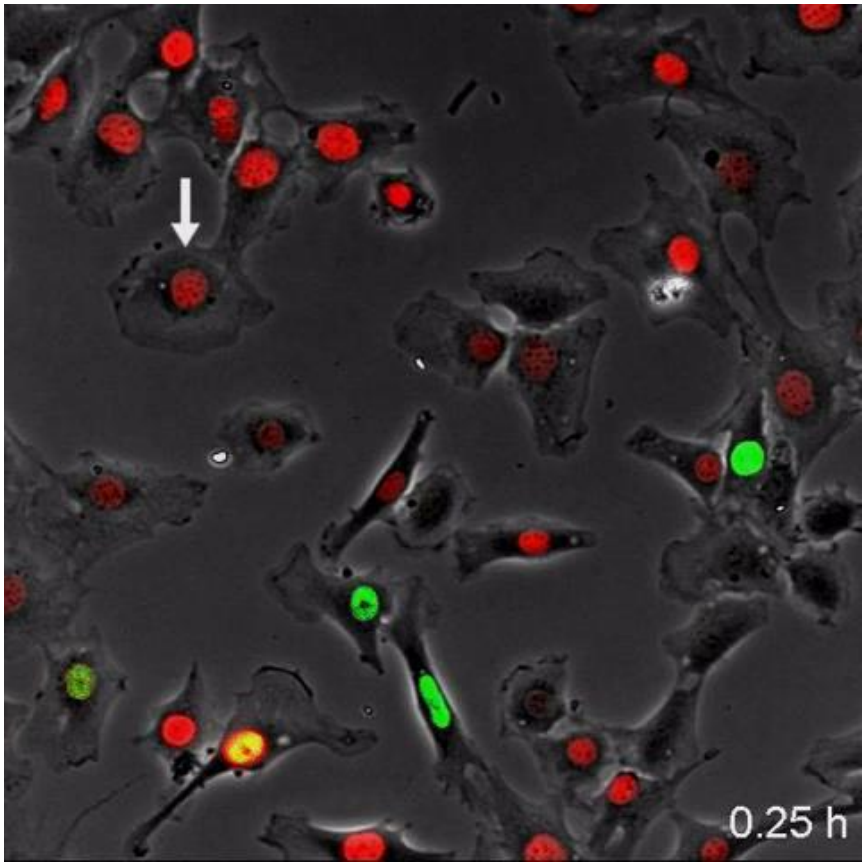
细胞周期的研究方法

- FUCCI细胞周期传感器（fluorescent ubiquitination–based cell-cycle indicator）

  红色-黄色-到绿色的动态颜色变化代表了细胞周期进程



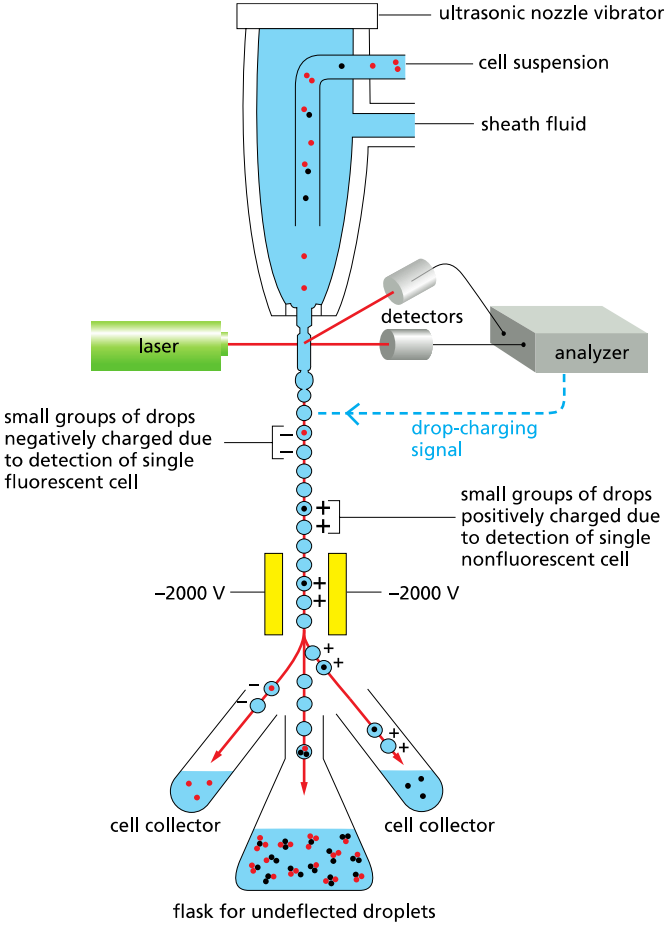
G1期，geminin被降解；RFP标记的cdt1在细胞核内呈现红色荧光。
S、G2和M期，cdt1被降解，GFP标记的geminin保留，从而使细胞核呈绿色荧光。
G1/S转换时，cdt1水平下降且geminin水平增高，细胞核发出黄色荧光。

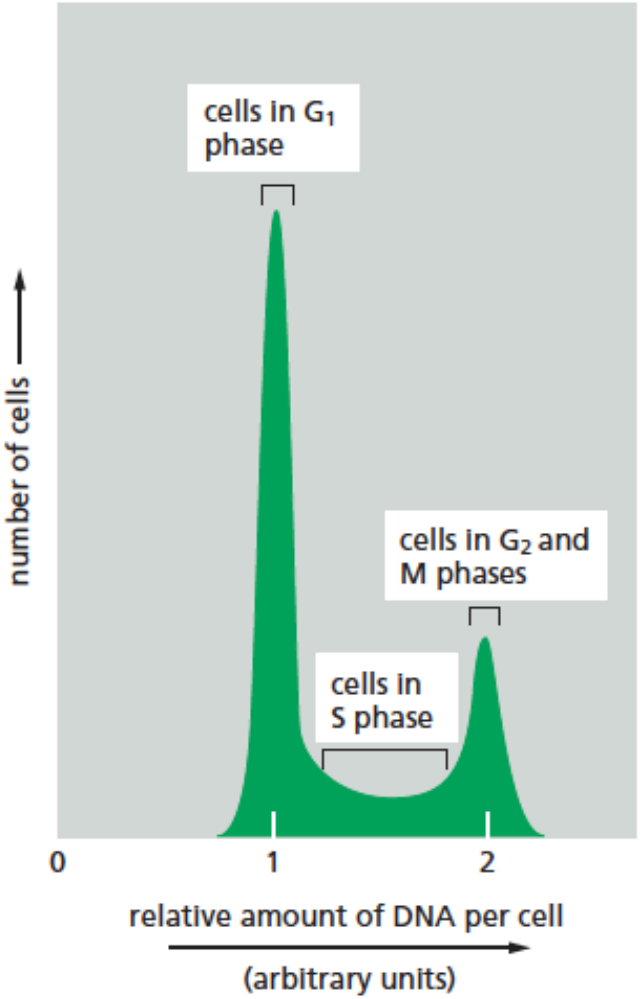


GFP-geminin　RFP-cdt1

细胞周期的研究方法

- 流式细胞仪测定法（Fluorescence-activated cell sorting，FACS）
- 检查DNA含量





G_1期为1

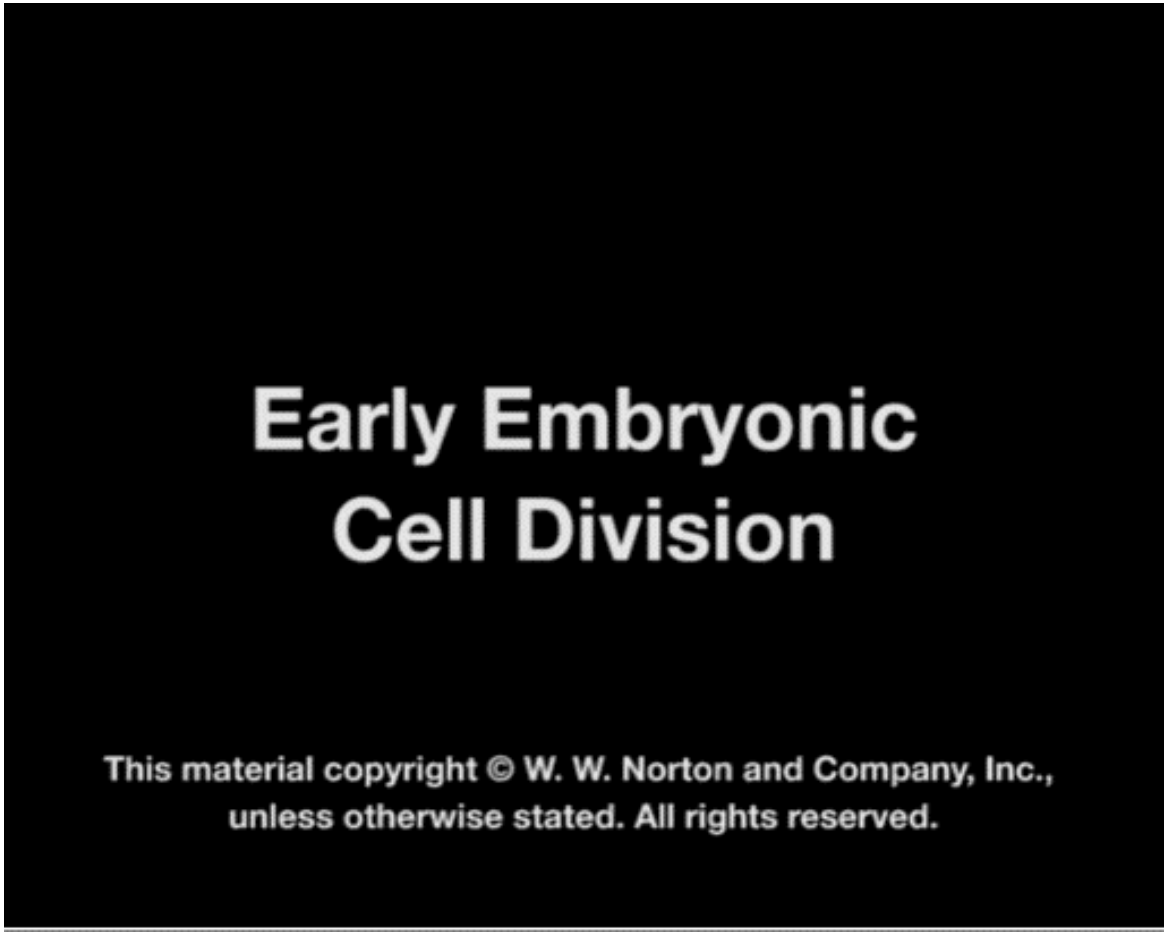
G_2和M期为2

S期介于1和2之间

The cells analyzed here were stained with a dye that becomes fluorescent when it binds to DNA, so that the amount of fluorescence is directly proportional to the amount of DNA in each

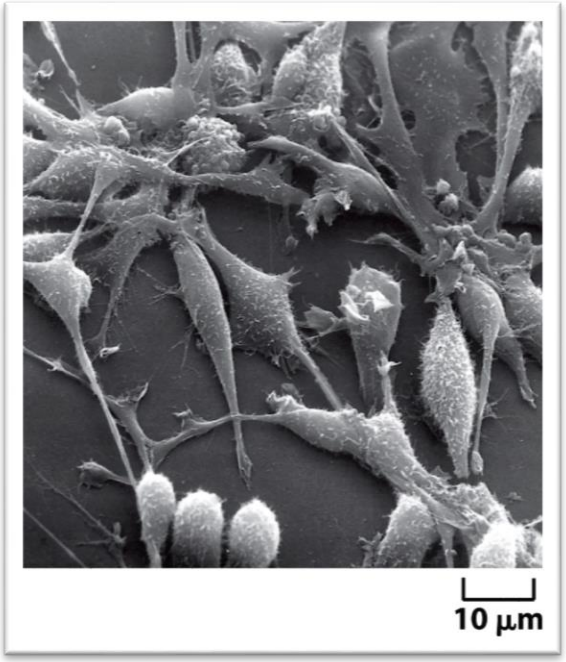
细胞周期同步化

- 让整个细胞群体处于细胞周期的同一个时相
- 天然同步化



细胞周期同步化

- 让整个细胞群体处于细胞周期的同一个时相
- 天然同步化
- 人工选择同步化
  - 有丝分裂选择法和细胞沉降分离法



扫描电镜观察的大鼠成纤维细胞

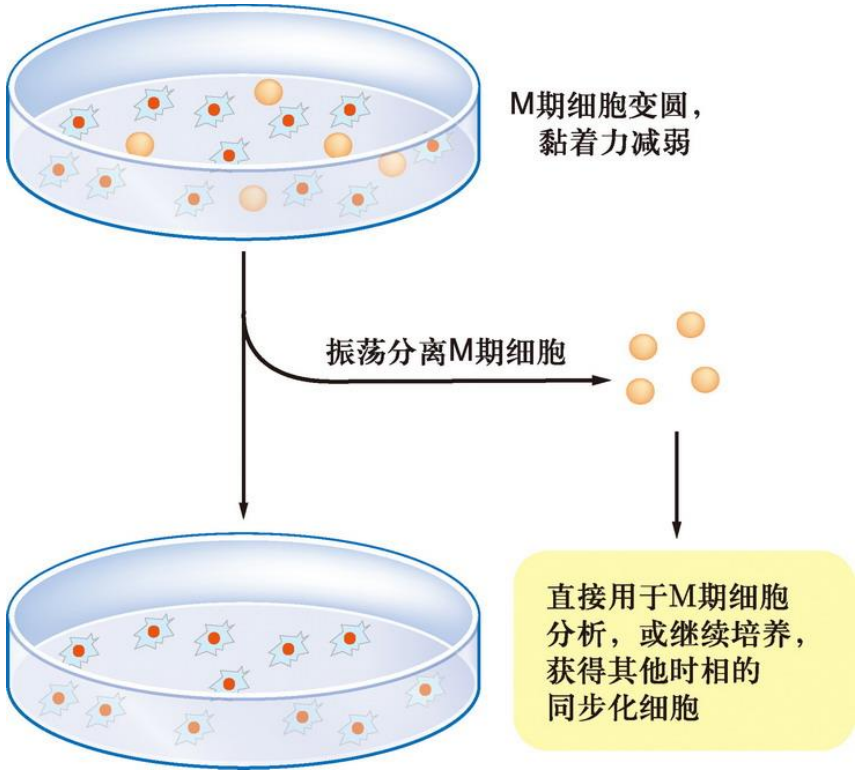


图12-3 从培养细胞中收集M 期细胞的同步化方法

细胞周期同步化

- 让整个细胞群体处于细胞周期的同一个时相
- 天然同步化
- 人工选择同步化
- 人工诱导同步化
  - DNA合成阻断法：同步化程度高，低毒或无毒，广泛采用
  - 分裂中期阻断法

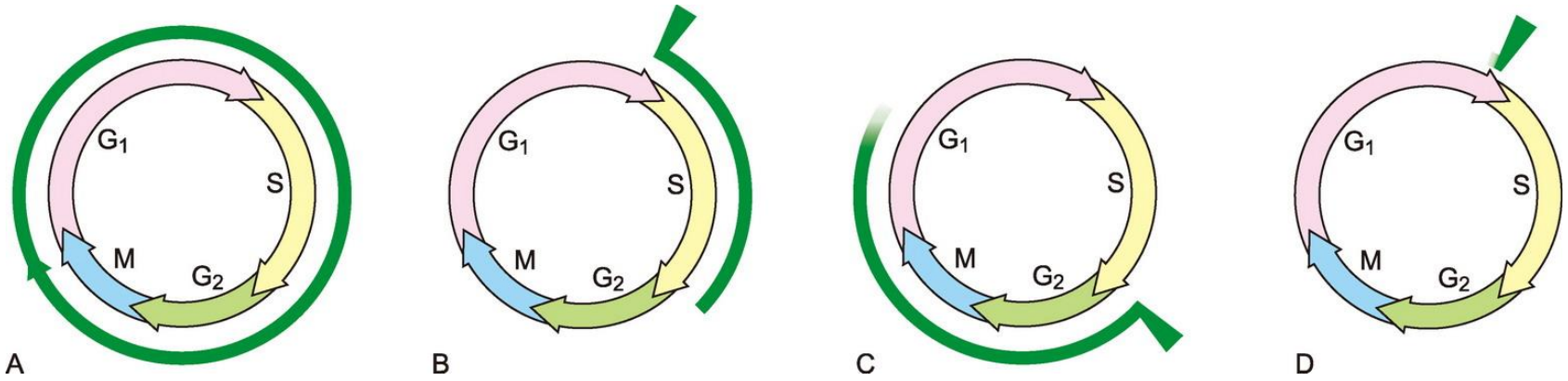
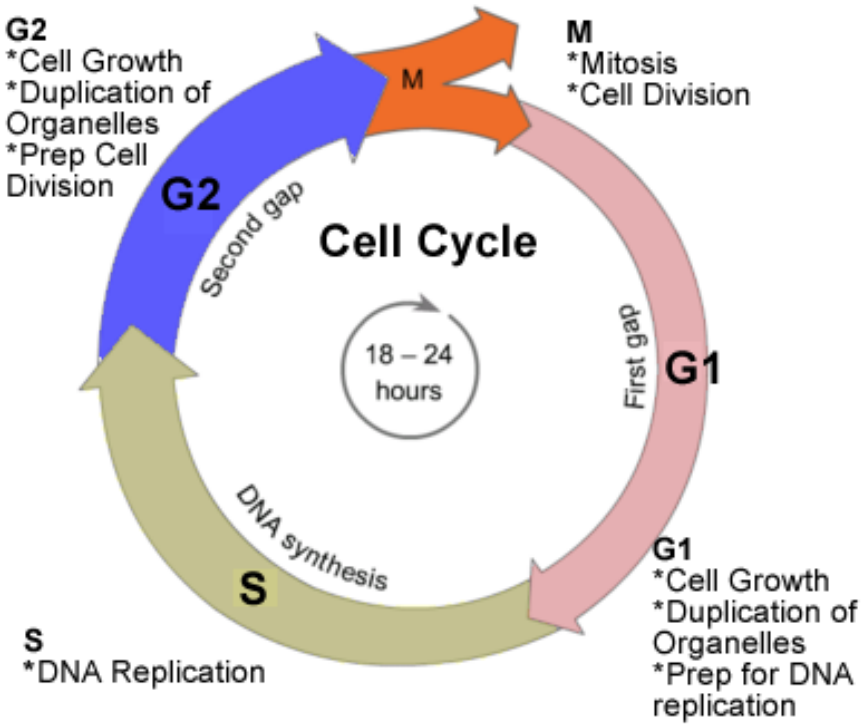


图12-4 应用过量的TdR 阻断法进行细胞周期同步化

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

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：**按照半保留复制的方式**合成DNA**，合成新的组蛋白
- **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**



两个重要事件

DNA复制

细胞分裂

检验点 check point

- 检验点是作用于细胞周期转换时序的调控信号通路
  - G_1/S检验点：G_1期晚期，在酵母中称起始点(start)，在哺乳动物中称限制点 (restriction point, R点)
  - S期检验点
  - G_2/M检验点
  - 中-后期检验点

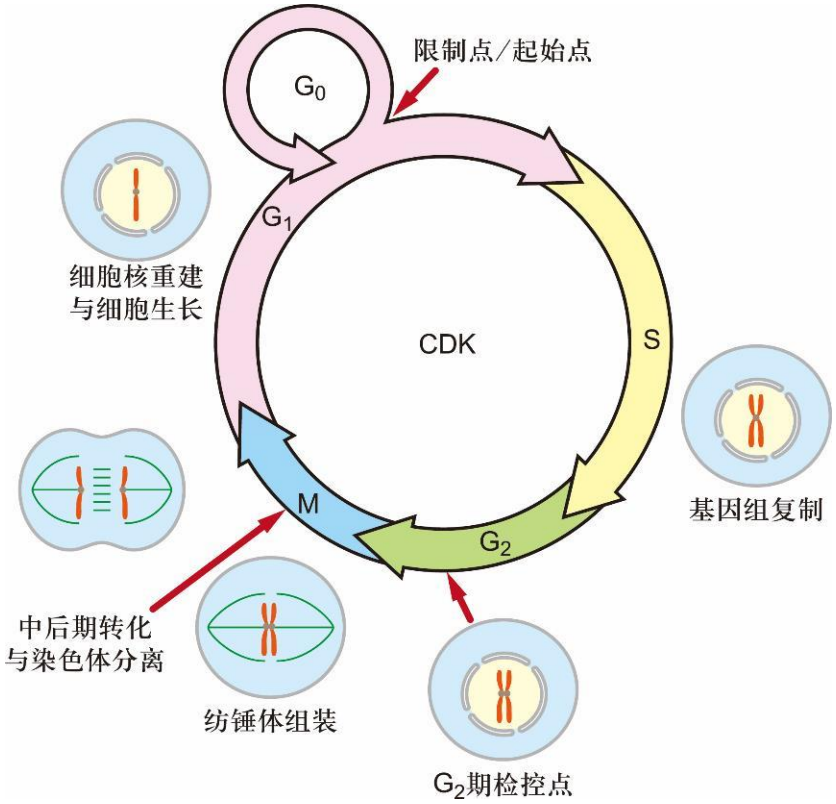


图12-2 细胞周期检验点及其主要事件

“引擎”与“刹车” engine and brake

- 周期蛋白依赖性激酶复合物 (cyclin-dependent kinase complex, CDK)
- 蛋白磷酸水解酶

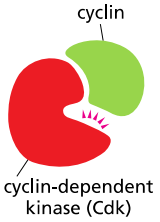
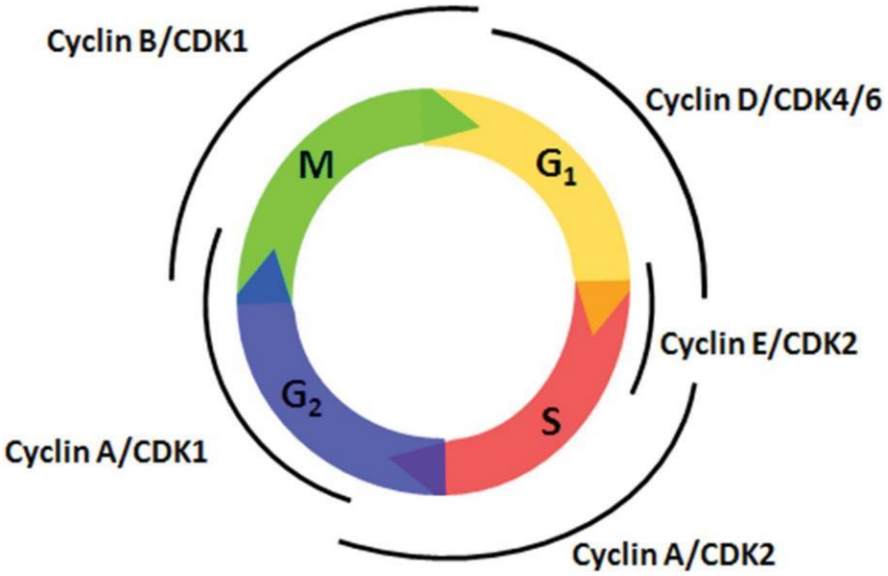
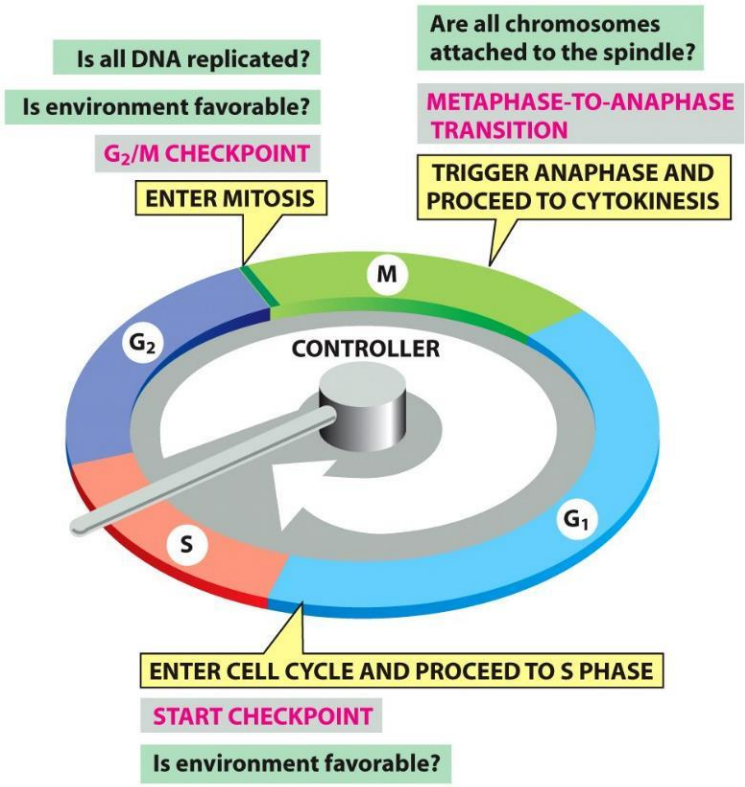


Figure 17–10 **Two key components of the cell-cycle control system.** When cyclin forms a complex with Cdk, the protein kinase is activated to trigger specific cell-cycle events. Without cyclin, Cdk is inactive.





第二节

细胞分裂

- 有丝分裂
- 减数分裂

一、有丝分裂 Mitosis

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)
- 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

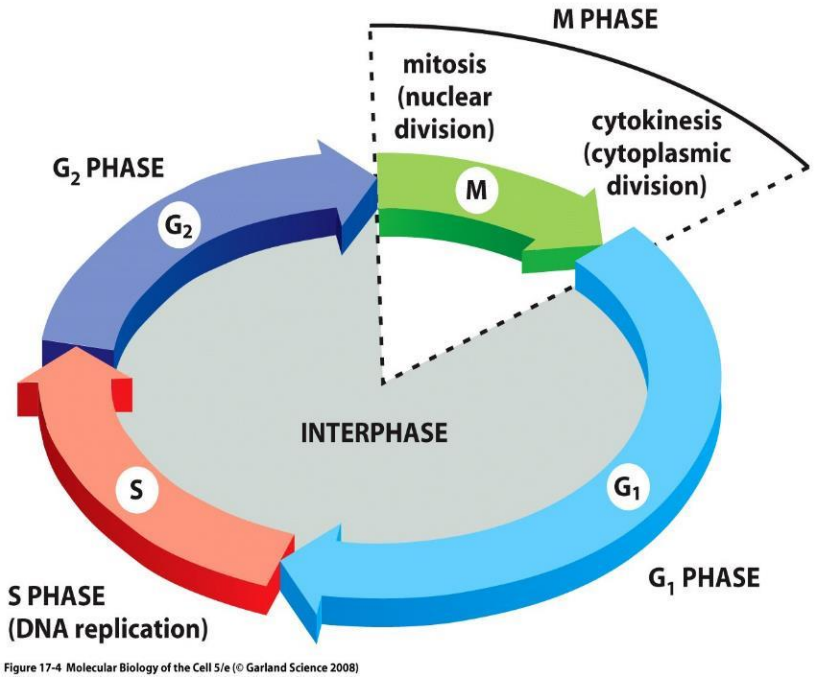


Figure 17-4 Molecular Biology of the Cell 5/e (© Garland Science 2008)

一、有丝分裂 Mitosis

- 有丝分裂过程人为地划分为前期 Prophase 、前中期 Prometaphase 、中期 Metaphase 、后期 Anaphase和末期 Telophase

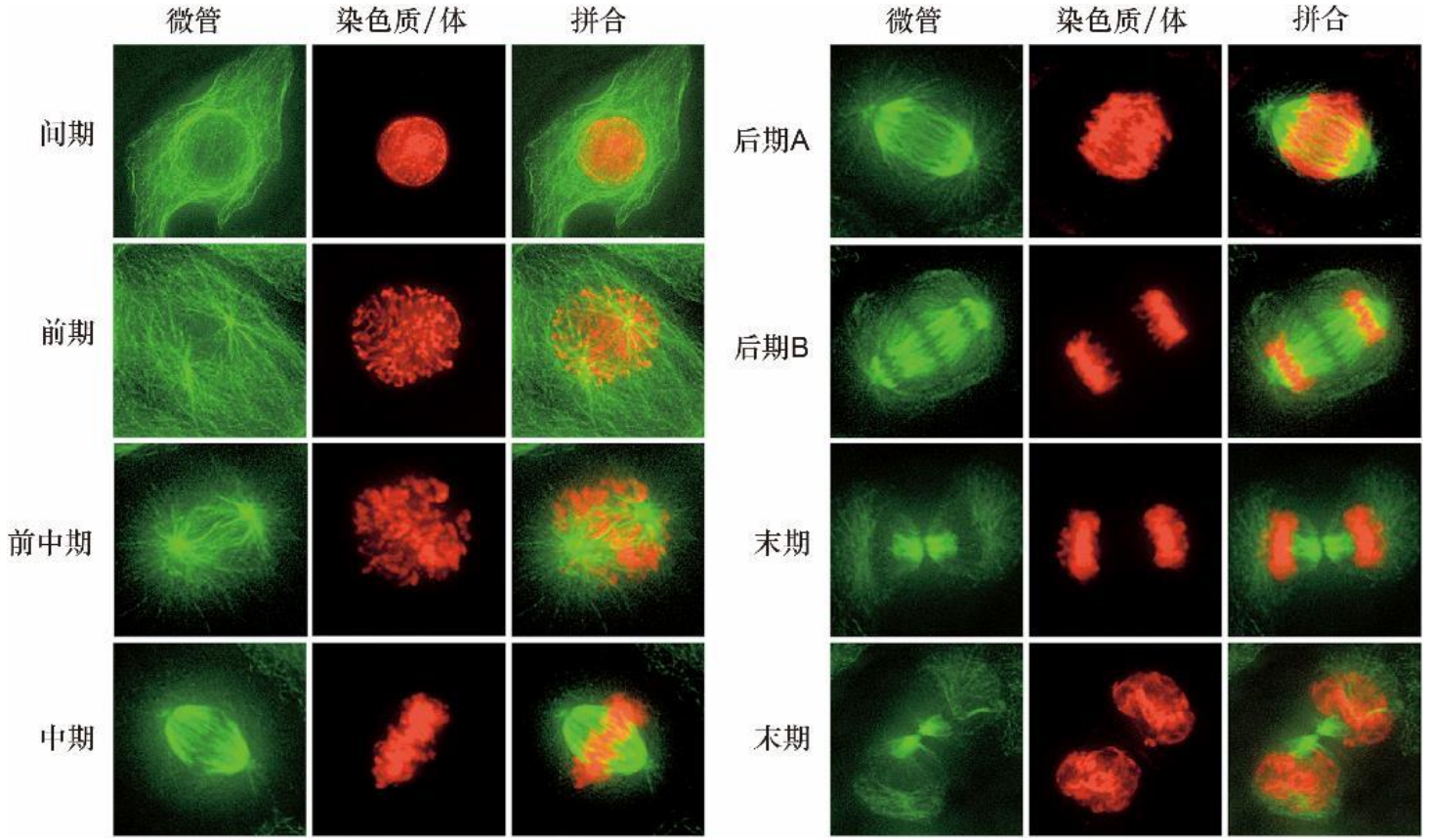
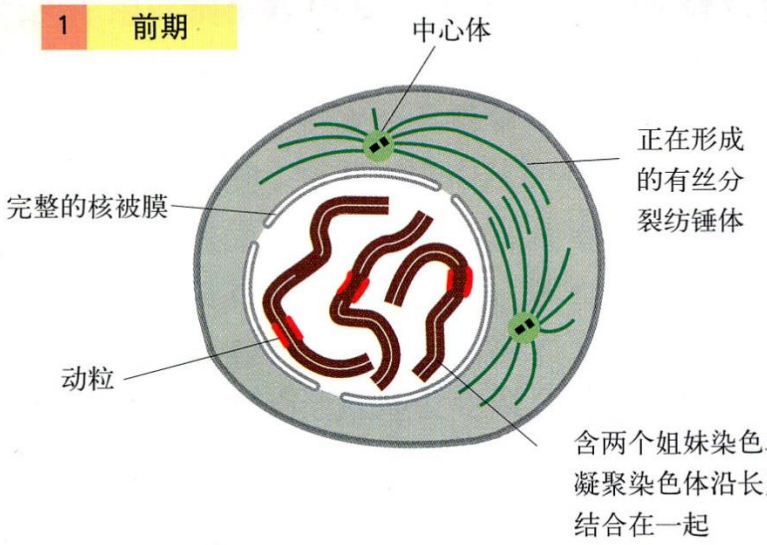


图12-9 高等动物细胞有丝分裂过程

1. 前期 prophase

- 染色体凝缩、细胞分裂极的确立和纺锤体的装配



在前期，每一复制好的染色体包含两个紧密相连的姐妹染色单体，它开始凝聚，核外有丝分裂纺锤体在两个复制后分开的中心体间组装。

时间 =0min

1. 前期——染色体凝缩 (chromatin condensation)

- 由间期细长、弥漫样分布的线性染色质，经过进一步螺旋化、折叠和包装(packing)等过程，逐渐变短变粗，形成光镜下可辨的早期染色体结构。

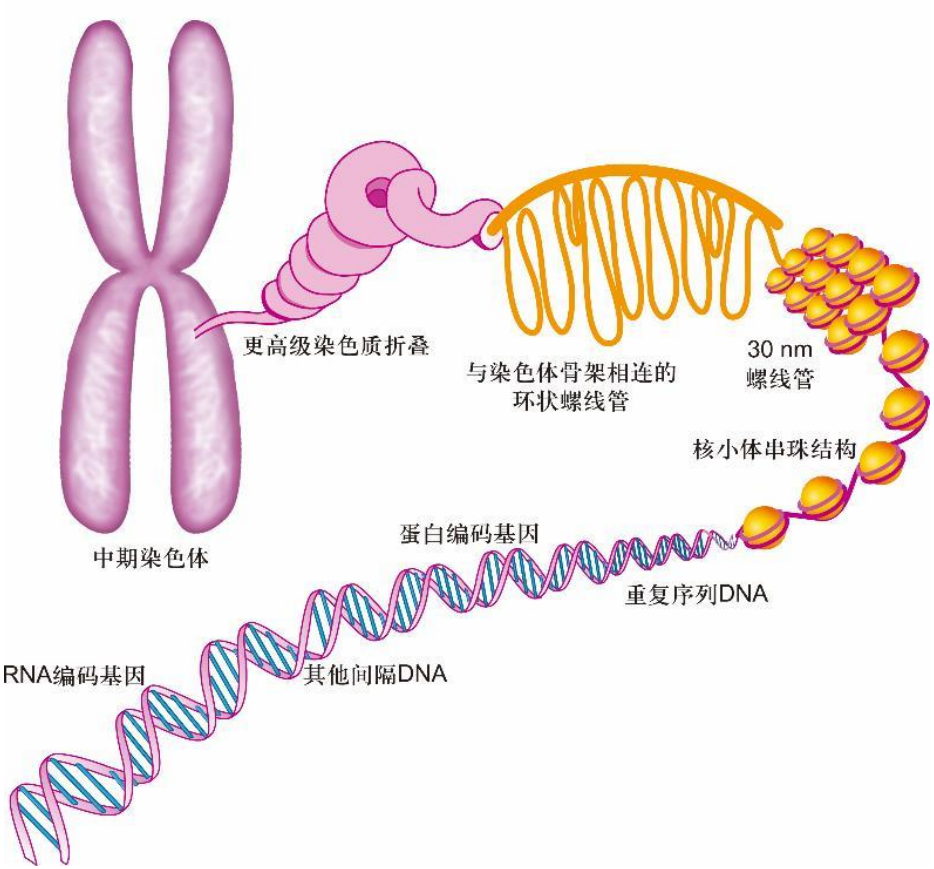


Figure 17–21 The mitotic chromosome. Scanning electron micrograph of a human mitotic chromosome, consisting of two sister chromatids joined along their length. The constricted regions are the centromeres. (Courtesy of Terry D. Allen.)

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
    - 两个SMC蛋白异二聚体和两个或多个非SMC蛋白亚基
    - ATP酶活性: 类ATP结合盒 （ATP binding cassette, ABC）
  - 黏连蛋白 (cohesin) 介导姐妹染色单体的黏着

    凝缩蛋白 (condensin) 介导染色体的凝缩

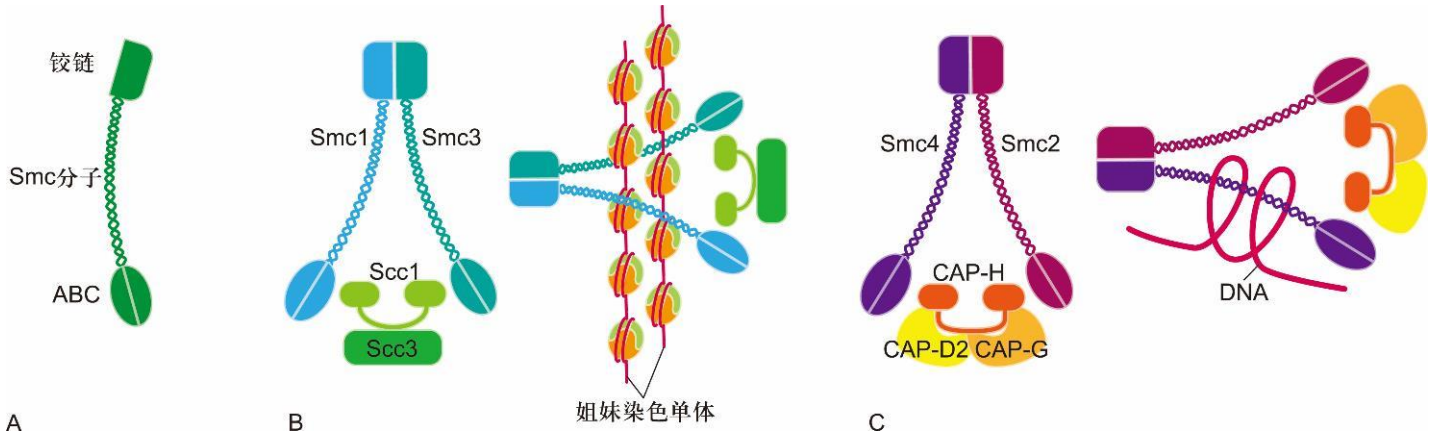


图12-10 Smc 蛋白（A）及其黏连蛋白（Smc 1/3）（B）、凝缩蛋白（Smc2/4）（C）异二聚体的作用

1. 前期——染色体凝缩 (chromatin condensation)

- 黏连蛋白 (cohesin) 介导姐妹染色单体的黏着

  凝缩蛋白 (condensin) 介导染色体的凝缩

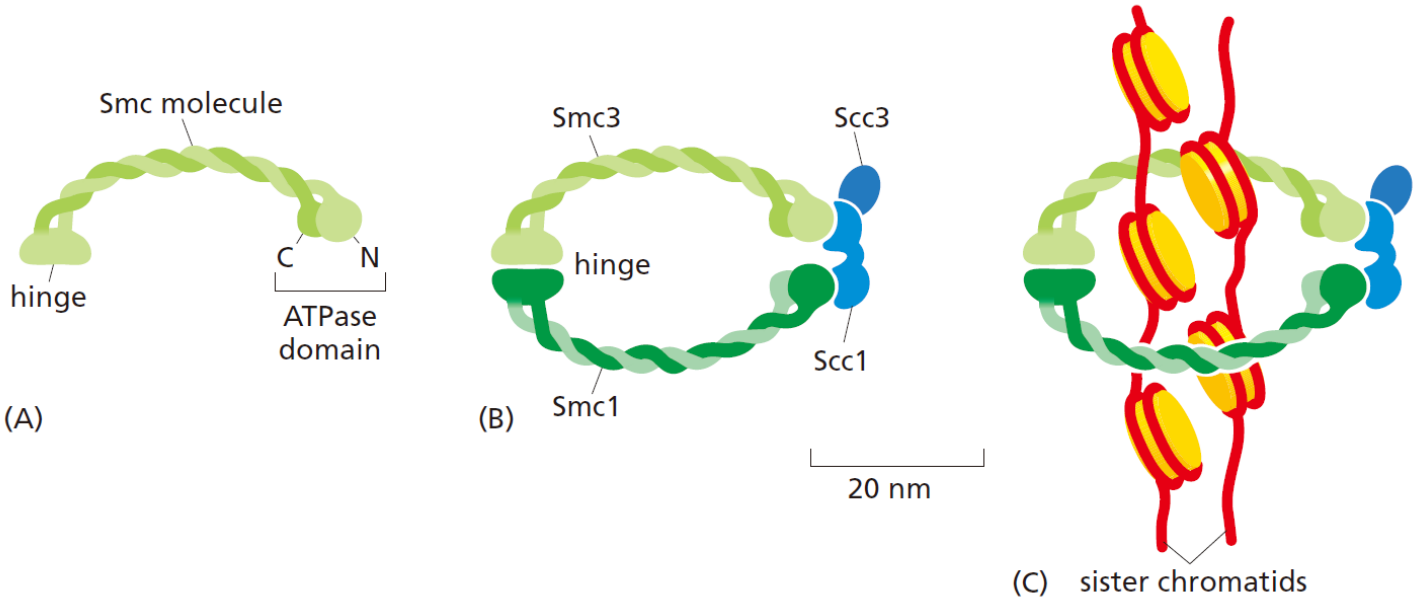


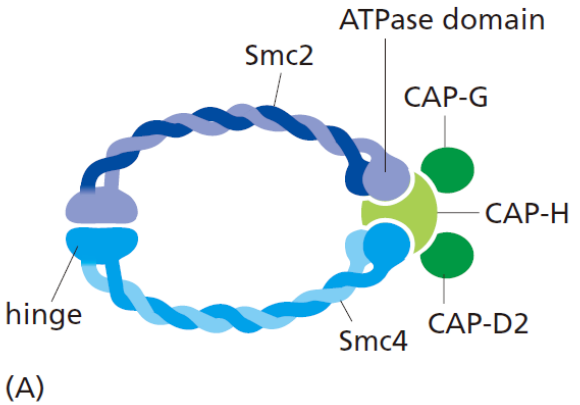
Figure 17–19 Cohesin. Cohesin is a protein complex with four subunits. (A) Two subunits, Smc1 and Smc3, are coiled-coil proteins with an ATPase domain at one end; (B) two additional subunits, Scc1 and Scc3, connect the ATPase head domains, forming a ring structure that may encircle the sister chromatids as shown in (C). The ATPase domains are required for cohesin loading on the DNA.

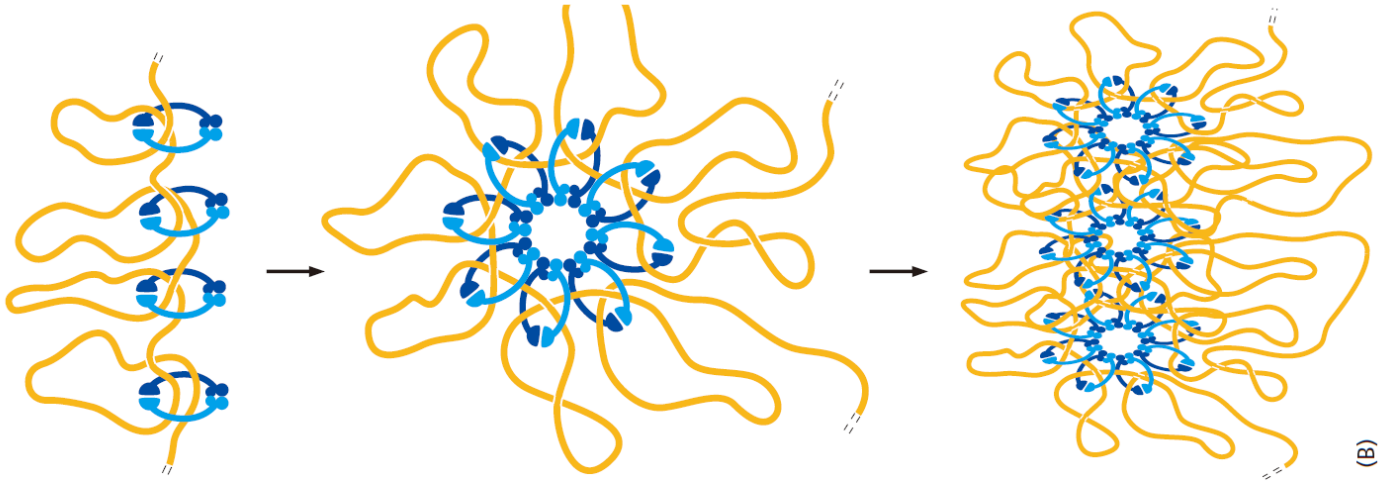
1. 前期——染色体凝缩 (chromatin condensation)

- 黏连蛋白 (cohesin) 介导姐妹染色单体的黏着

  凝缩蛋白 (condensin) 介导染色体的凝缩

Figure 17–22 Condensin. (A) Condensin is a five-subunit protein complex that resembles cohesin (see Figure 17–19). The ATPase head domains of its two major subunits, Smc2 and Smc4, are held together by three additional subunits. (B) It is not clear how condensin catalyzes the restructuring and compaction of chromosome DNA, but it may form a ring structure that encircles loops of DNA within each sister chromatid.

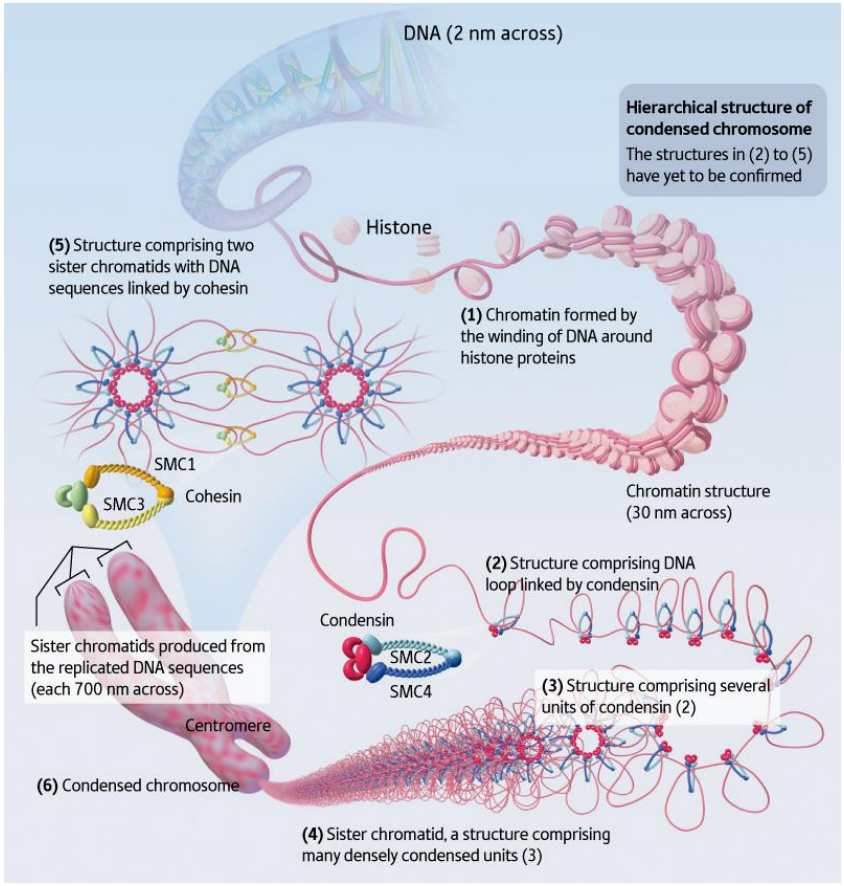




1. 前期——染色体凝缩 (chromatin condensation)

- 黏连蛋白 (cohesin) 介导姐妹染色单体的黏着

  凝缩蛋白 (condensin) 介导染色体的凝缩



1. 前期——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
  - 中心体含有**一对彼此垂直的桶状中心粒**
  - 微管起源于中心粒外周物质区域（PCM）
  - γ- 微管蛋白在中心体周质中形成的环状结构可诱导微管的成核与组装

S期中心体复制

半保留复制

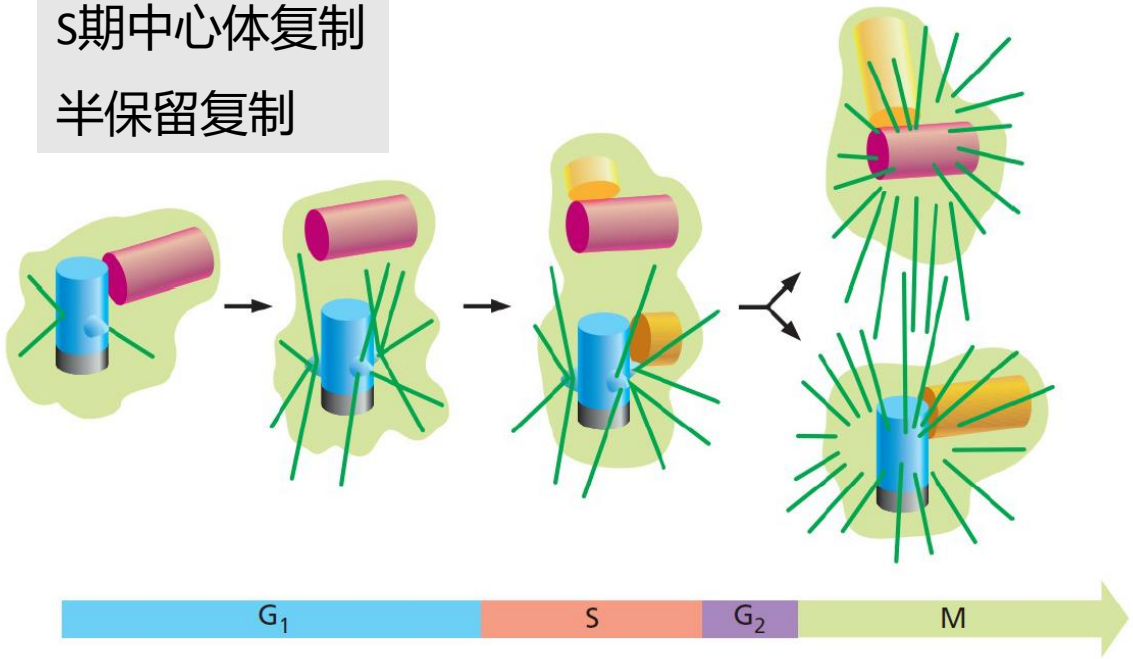


Figure 17–26 Centriole replication. The centrosome consists of a centriole pair and associated pericentriolar matrix *(green).* At a certain point in G_1, the two centrioles of the pair separate by a few micrometers. During S phase, a daughter centriole begins to grow near the base of each mother centriole and at a right angle to it. The elongation of the daughter centriole is usually completed in G_2. The two centriole pairs remain close together in a single centrosomal complex until the beginning of M phase, when the complex splits in two and the two daughter centrosomes begin to separate. Each centrosome now nucleates its own radial array of microtubules (called an aster), mainly from the mother centriole.

1. 前期——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
  - 中心体含有**一对彼此垂直的桶状中心粒**
  - 微管起源于中心粒外周物质区域（PCM）
  - γ- 微管蛋白在中心体周质中形成的环状结构可诱导微管的成核与组装

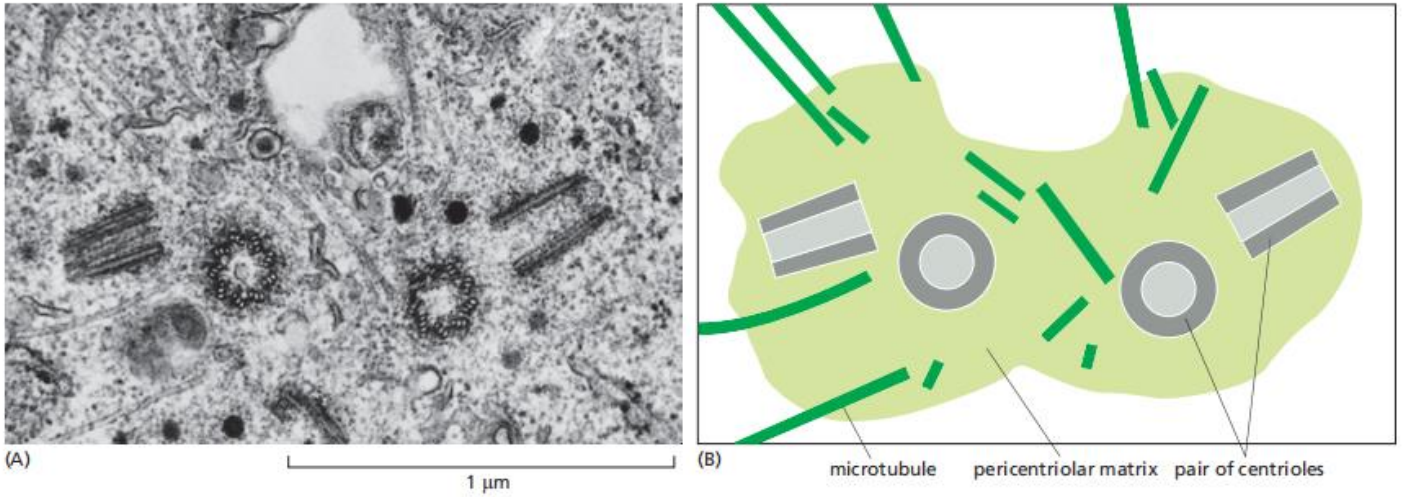


Figure 17–24 The centrosome. (A) Electron micrograph of an S-phase mammalian cell in culture, showing a duplicated centrosome. Each centrosome contains a pair of centrioles; although the centrioles have duplicated, they remain together in a single complex, as shown in the drawing of the micrograph in (B). One centriole of each centriole pair has been cut in cross section, while the other is cut in longitudinal section, indicating that the two members of each pair are aligned at right angles to each other. The two halves of the replicated centrosome, each consisting of a centriole pair surrounded by pericentriolar matrix, will split and migrate apart to initiate the formation of the two poles of the mitotic spindle when the cell enters M phase. (A, from M. McGill, D.P. Highfield, T.M. Monahan, and B.R. Brinkley, *J. Ultrastruct. Res.* 57:43–53, 1976. With permission from Academic Press.)

1. 前期——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

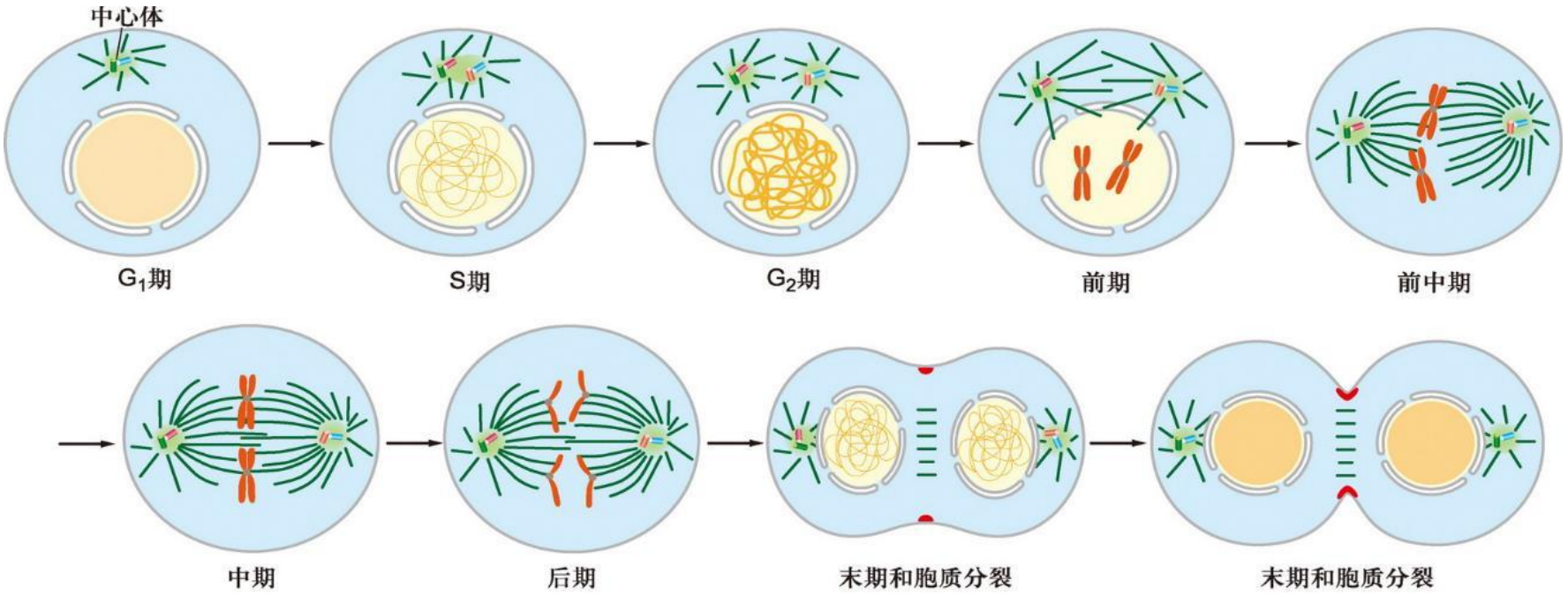
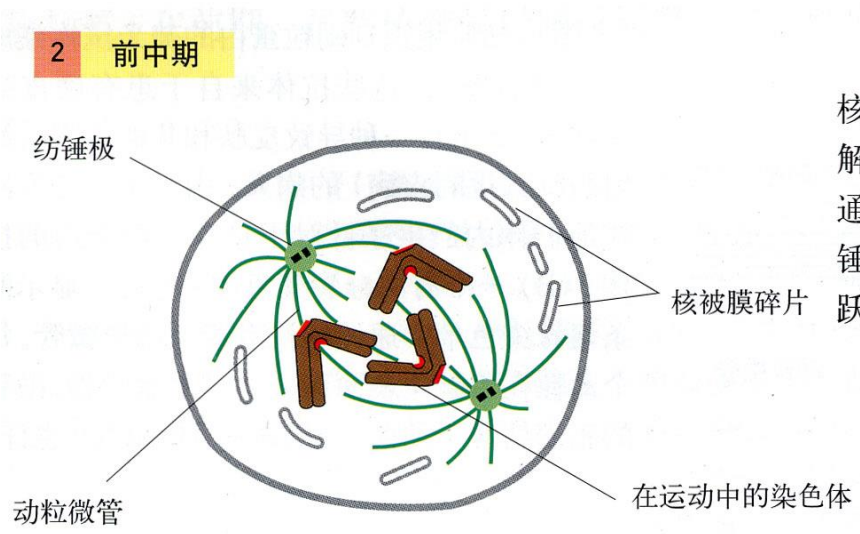


图12-11 动物细胞中心体的复制与细胞周期的关系

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

2. 前中期 prometaphase

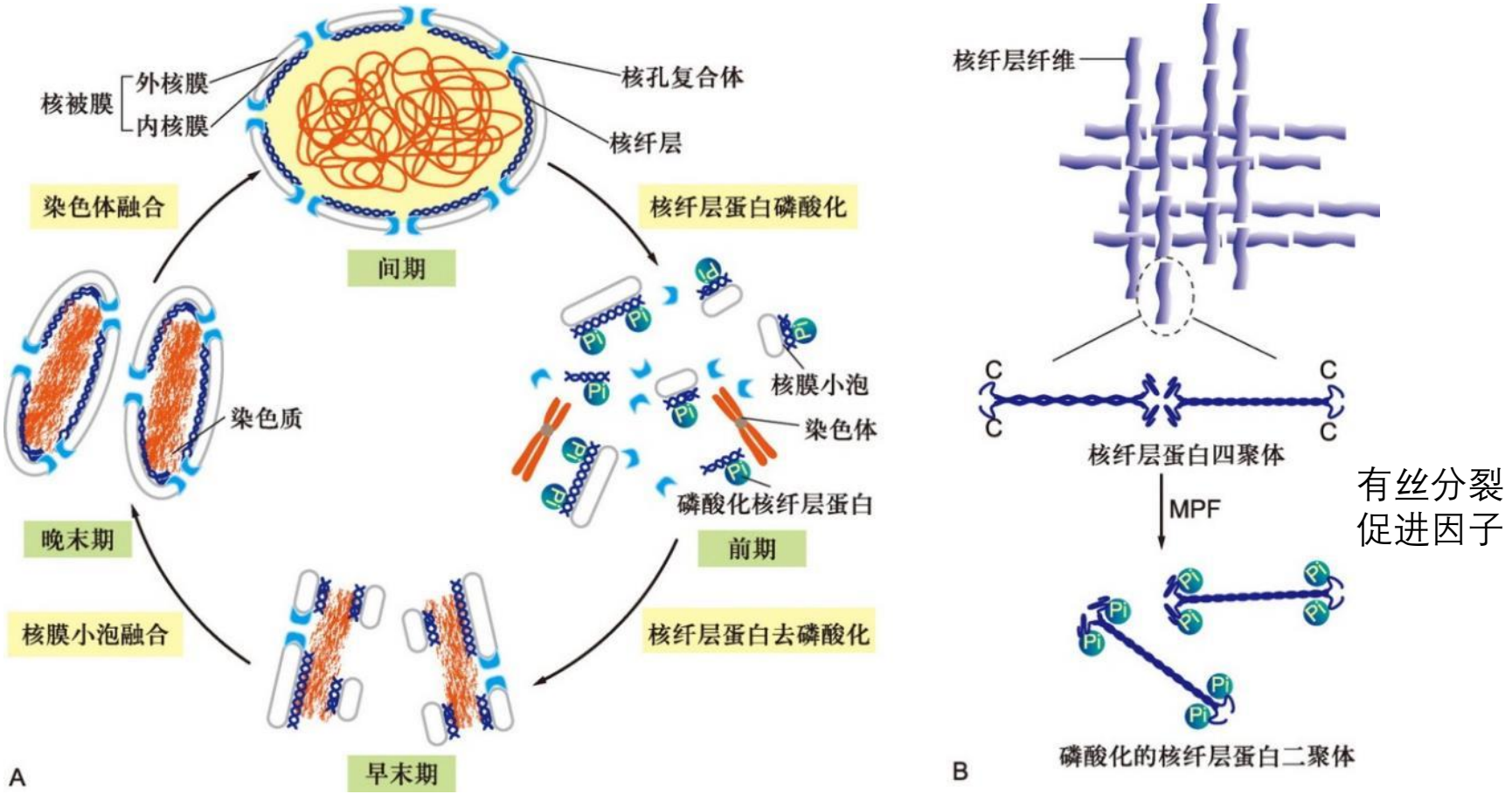
- 核膜崩解、完成纺锤体装配、染色体整列



前中期开始于核被膜的突然崩解。现在染色体能通过动粒附着于纺锤体微管并进行活跃运动。

2. 前中期——核膜崩解

- 核纤层蛋白的磷酸化与去磷酸化



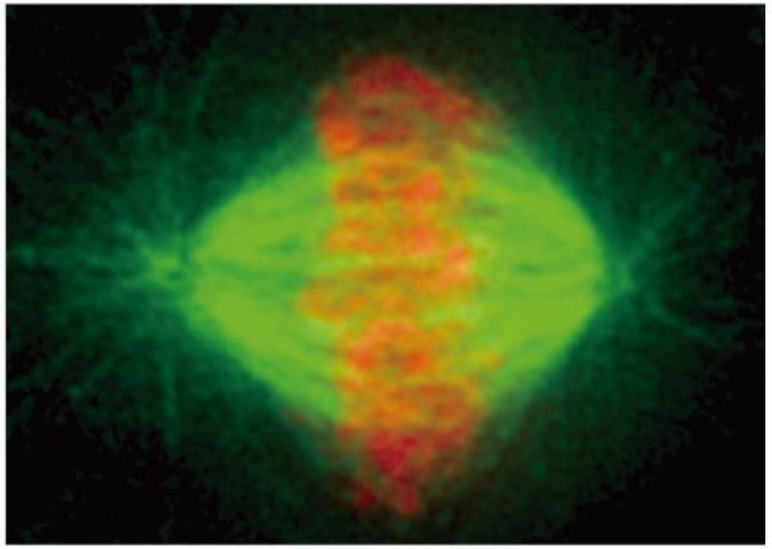
有丝分裂促进因子

图12-12 细胞分裂过程中核被膜和核纤层的动态变化

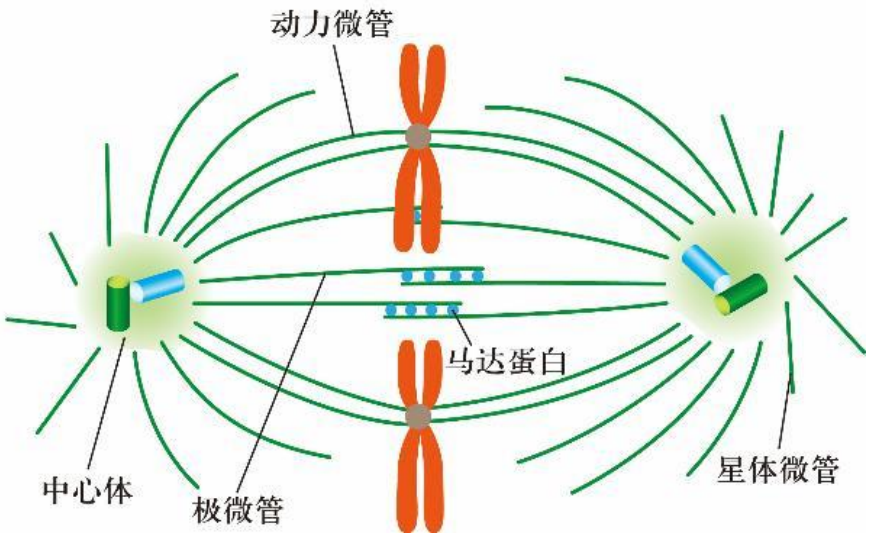
A. 核被膜在细胞有丝分裂中有规律地解体与重建。 B. 核纤层解聚

2. 前中期——完成纺锤体装配

- 形成动物细胞有丝分裂器（Mitotic apparatus）
  - 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



A



B

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

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 KRP
  - 细胞质动力蛋白

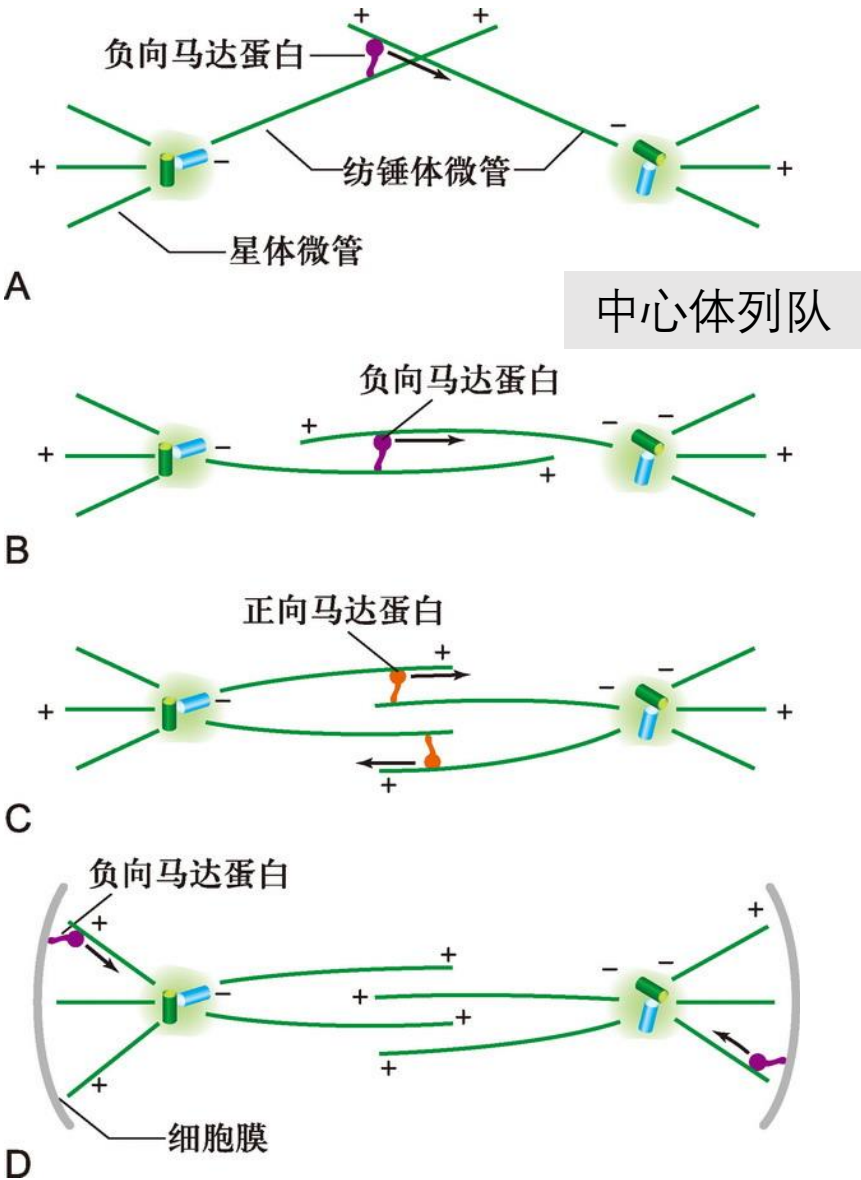


图12-14 纺锤体组装过程

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

纺锤体组装过程

- 马达蛋白对纺锤体组装至关重要

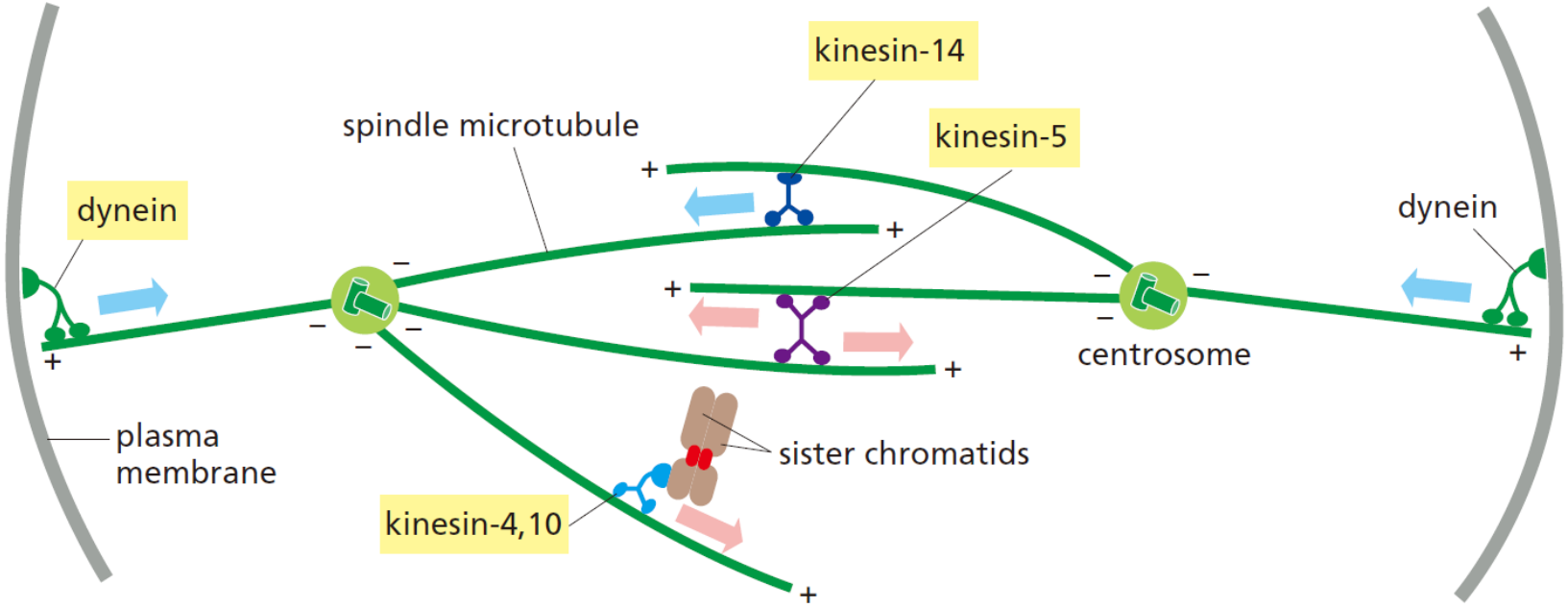
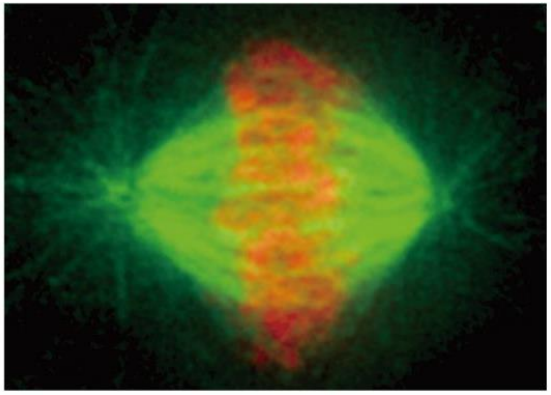
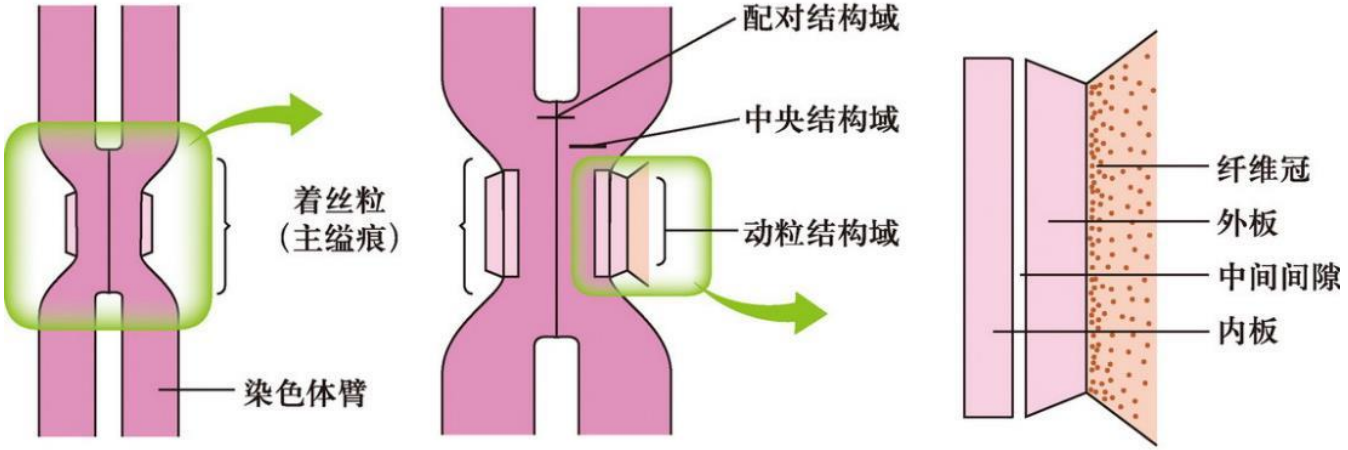


Figure 17–25 Major motor proteins of the spindle. Four major classes of microtubule-dependent motor proteins *(yellow boxes)* contribute to spindle assembly and function (see text). The colored arrows indicate the direction of motor protein movement along a microtubule—*blue* toward the minus end and *red* toward the plus end.

2. 前中期——染色体整列(chromosome alignment)

- 染色体整列: 染色体向赤道面运动的过程
- 由纺锤体极体发出的微管捕捉染色体动粒， 形成染色体动粒微管，这是染色体整列的必要前提
- 着丝粒－动粒复合体
  - 着丝粒DNA 主要由α 卫星DNA 构成
  - 动粒为一个圆盘状结构，分 内、中、外三层
  - 着丝粒动粒蛋白质





2. 前中期——染色体整列(chromosome alignment)

- 着丝粒－动粒复合体

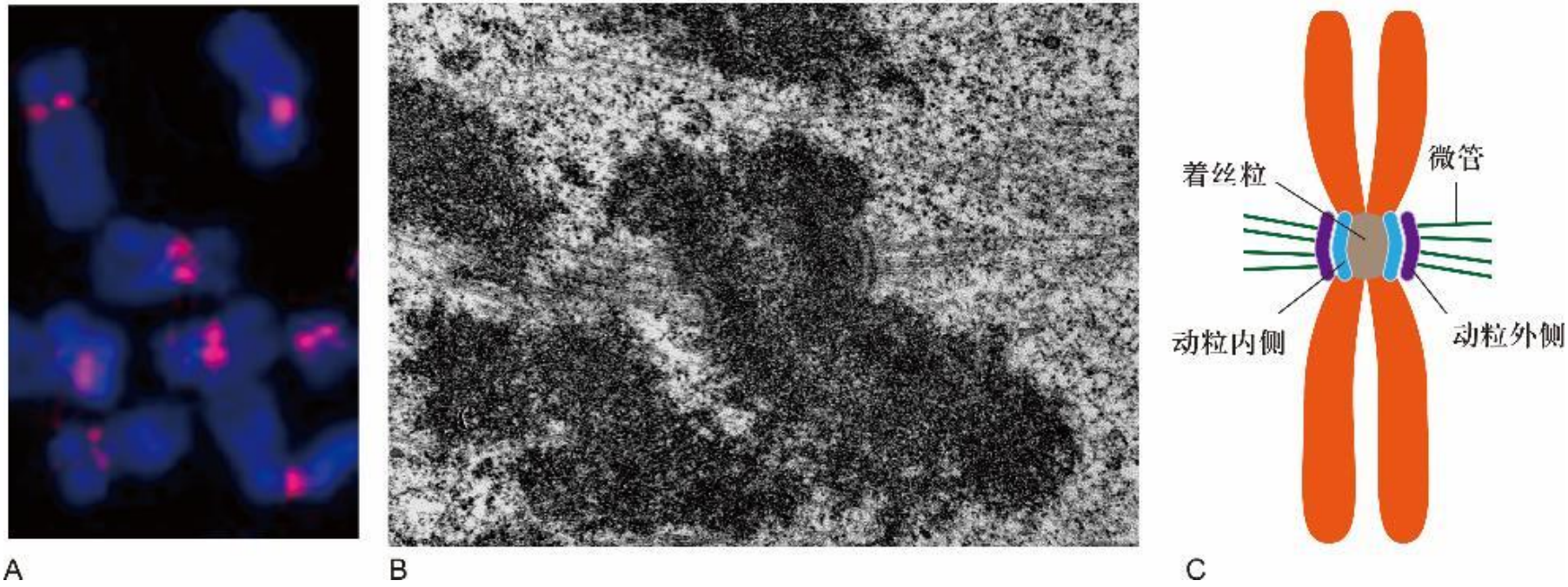


图12-15 应用免疫荧光技术和电镜技术显示动粒位置和结构

A. DNA（蓝色）和动粒蛋白HEC1（红色）双重荧光染料染色。B. 透射电镜技术显示染色单体上的动粒结构及其与动粒微管的连接。 C. 动粒结构及动粒- 微管相互连接示意图

2. 前中期——染色体整列(chromosome alignment)

- 着丝粒 – 动粒复合体

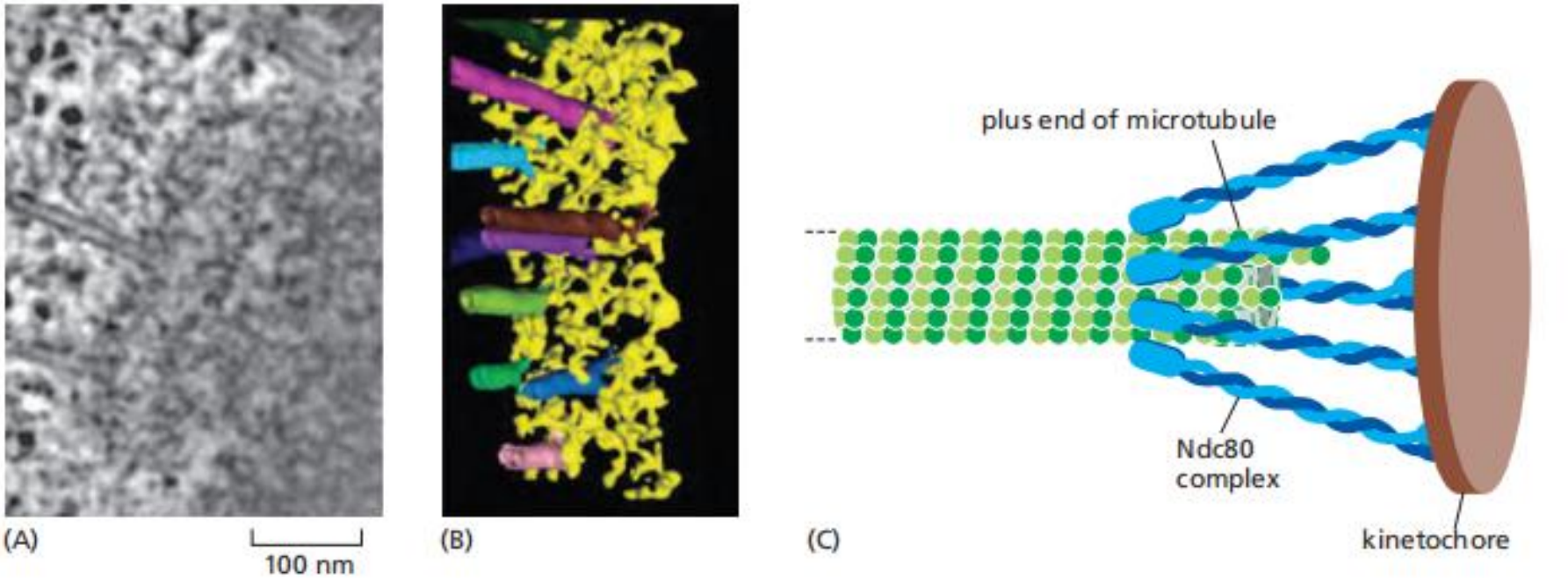


Figure 17–31 **Microtubule attachment sites in the kinetochore.** (A) In this electron micrograph of a mammalian kinetochore, the chromosome is on the right, and the plus ends of multiple microtubules are embedded in the outer kinetochore on the left. (B) Electron tomography (discussed in Chapter 9) was used to construct a low-resolution three-dimensional image of the outer kinetochore in (A). Several microtubules (in multiple colors) are embedded in **fibrous material of the kinetochore**, which is thought to be composed of the Ndc80 complex and other proteins. (C) Each microtubule is attached to the kinetochore by interactions with multiple copies of the Ndc80 complex (blue). This complex binds to the sides of the microtubule near its plus end, allowing polymerization and depolymerization to occur while the microtubule remains attached to the kinetochore.(A and B, from Y. Dong et al., Nature Cell Biol. 9:516–522, 2007.）

2. 前中期——染色体整列(chromosome alignment)

- 着丝粒 – 动粒复合体

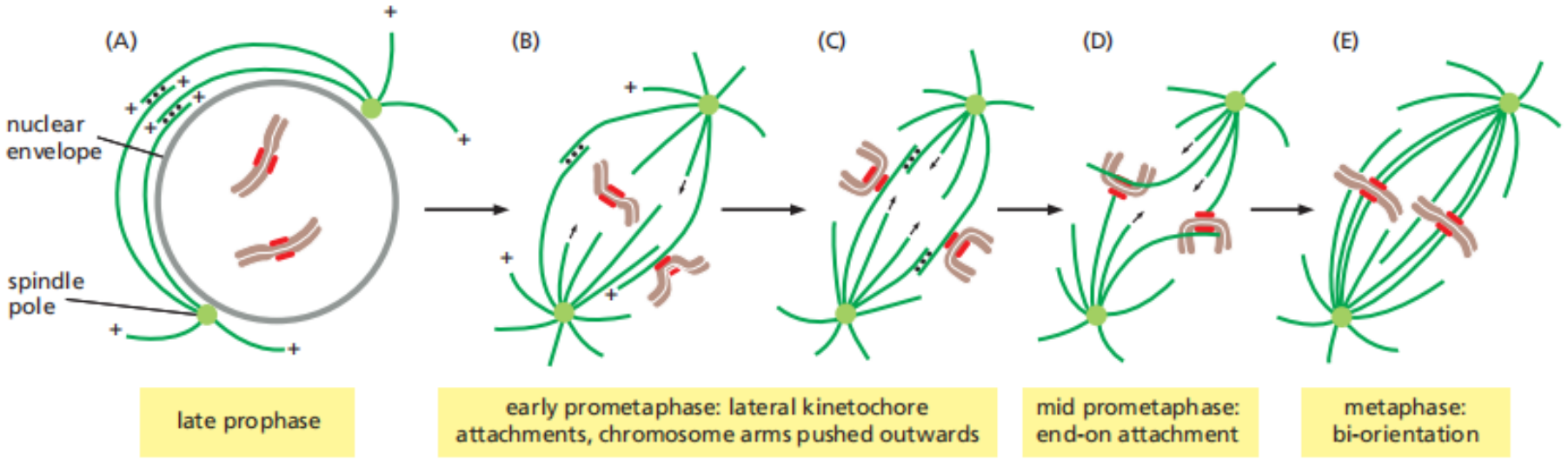


Figure 17-32 Chromosome attachment to the mitotic spindle in animal cells. (A) In late prophase of most animal cells, the mitotic spindle poles have moved to opposite sides of the nuclear envelope, with an array of overlapping microtubules between them. (B) Following nuclear envelope breakdown, the sister-chromatid pairs are exposed to the large number of dynamic plus ends of microtubules radiating from the spindle poles. In most cases, the kinetochores are first attached to the sides of these microtubules, while at the same time the arms of the chromosomes are pushed outward from the spindle interior, preventing the arms from blocking microtubule access to the kinetochores. (C) Eventually, the laterally-attached sister chromatids are arranged in a ring around the outside of the spindle. Most of the microtubules are concentrated in this ring, so that the spindle is relatively hollow inside. (D) Dynamic microtubule plus ends eventually encounter the kinetochores in an end-on orientation and are captured and stabilized. (E) Stable end-on attachment to both poles results in *bi-orientation*. Additional microtubules are attached to the kinetochore, resulting in a *kinetochore fiber* containing 10–40 microtubules.

2. 前中期——染色体整列(chromosome alignment)

- Mad 和Bub 蛋白使动粒敏化，促使微管与动粒接触
- 染色体被纺锤体微管捕获，二者消失

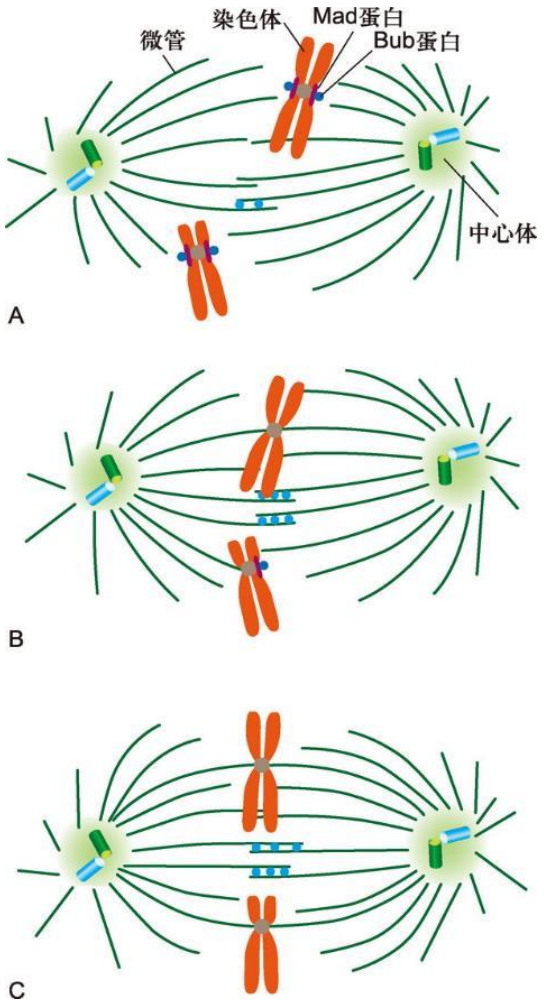


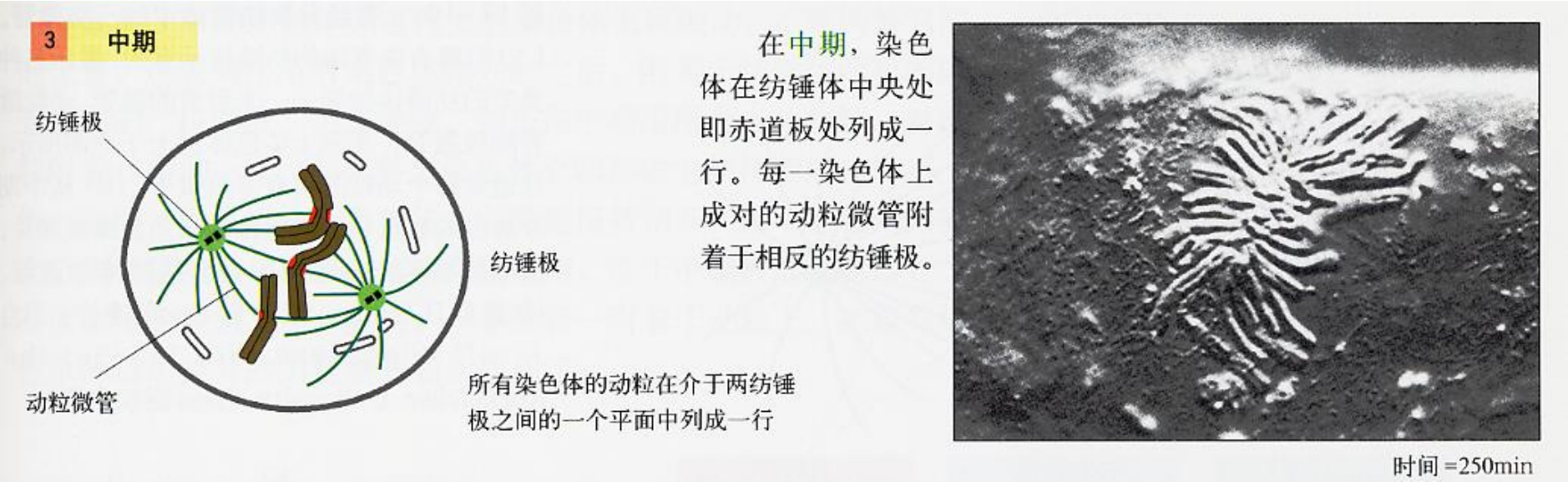
图12-16 染色体整列

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

Mitotic Spindles in a Fly Embryo

3. 中期（metaphase）

- 染色体整列完成并且所有染色体排列到赤道面上



3. 中期（metaphase）

- 染色体排列到赤道面上的 牵拉(pull) 和外推(push) 假说
- 染色体整列后： 两侧的动粒微管长度相等，作用力均衡

动粒微管牵拉

星体对染色体的外推力

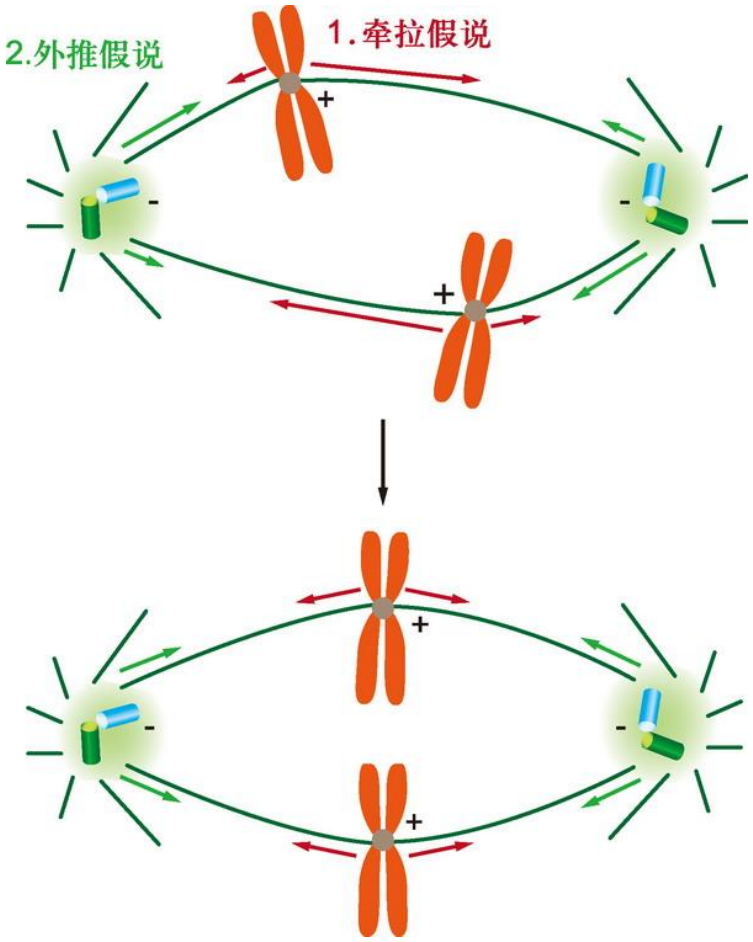
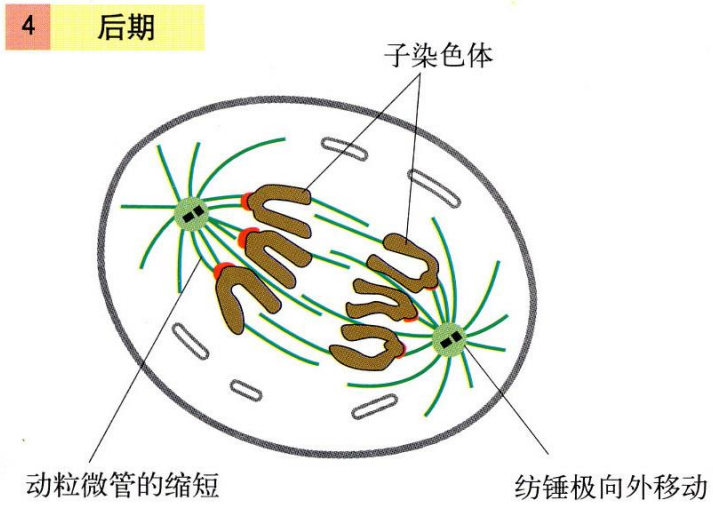


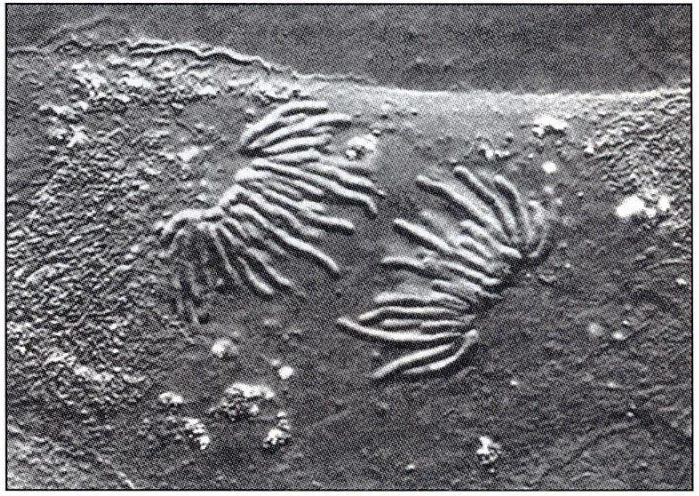
图12-17 解释染色体在赤道面整列的两种假说

4. 后期（anaphase）

- 中期整列的染色体其两条姐妹染色单体分离，分别向两极运动



在后期，配对的染色单体同时分离形成两套子染色体，每一套染色体被缓慢拉向它所面对的纺锤极。动粒微管逐渐变短且纺锤极也互相分离，两者都对染色体的分离作出贡献。



4. 后期（anaphase）

- 中期整列的染色体其两条姐妹染色单体分离，分别向两极运动

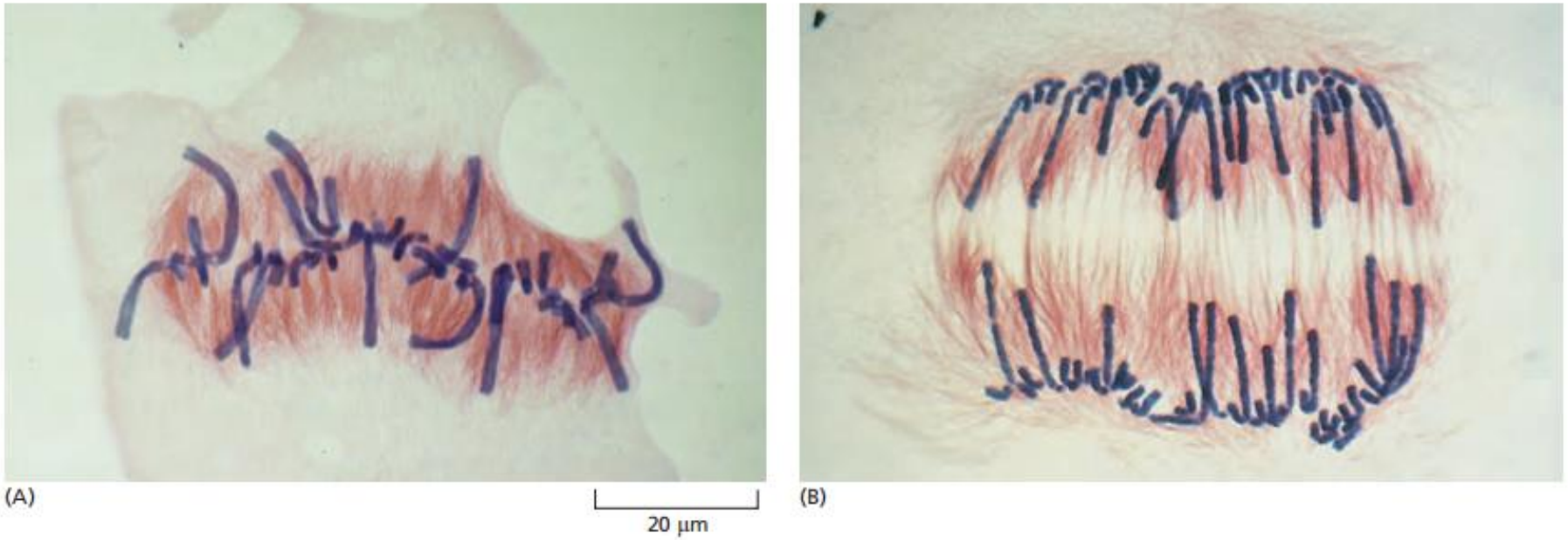


Figure 17–37 Sister-chromatid separation at anaphase. In the transition from metaphase (A) to anaphase (B), sister chromatids suddenly and synchronously separate and move toward opposite poles of the mitotic spindle—as shown in these light micrographs of *Haemanthus* (lily) endosperm cells that were stained with gold-labeled antibodies against tubulin. (Courtesy of Andrew Bajer.)

网球花属植物胚乳细胞

4. 后期（anaphase）

- 后期A Anaphase A **(chromosome-to-pole movement)**
  - 动粒微管变短，牵动染色体向两极运动
- 后期B Anaphase B **(pole-pole separation)**
  - 极性微管长度增加，两极之间的距离逐渐拉长

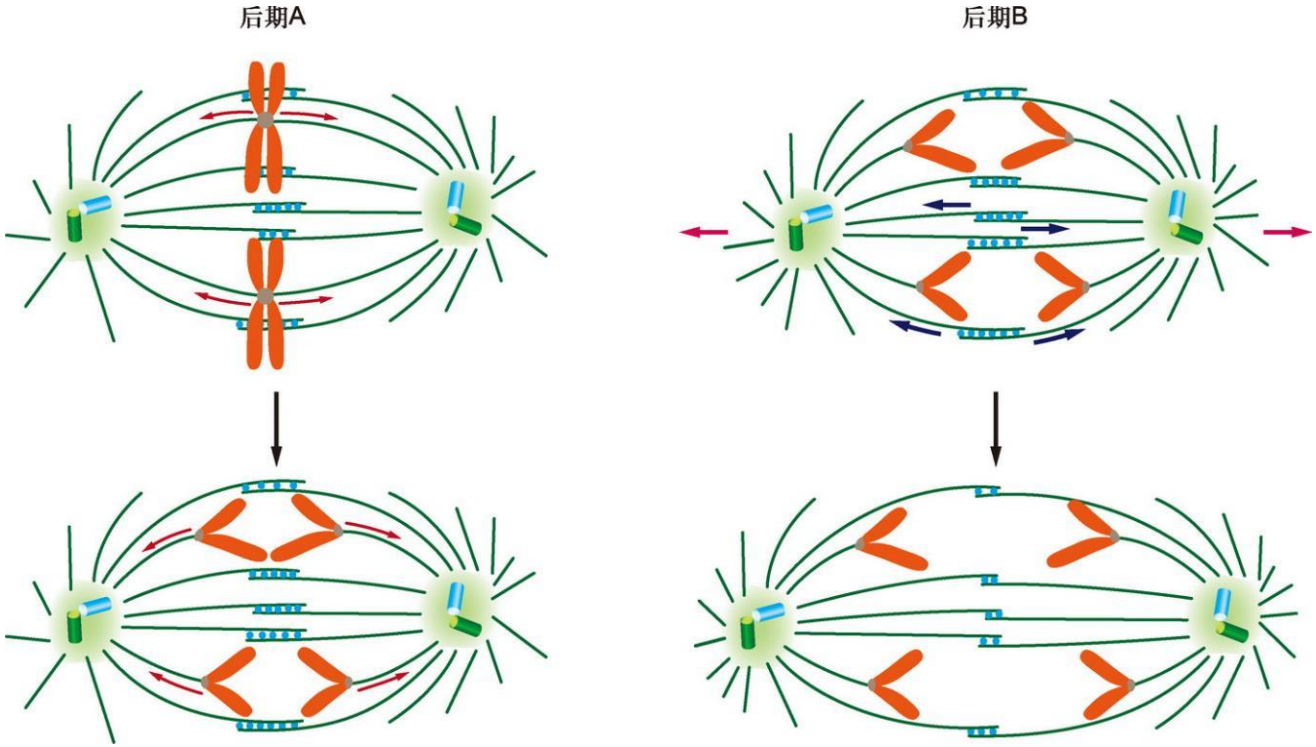


图12-19 细胞分裂后期A和后期B产生染色体向极部运动的示意图

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

4. 后期（anaphase）

- 后期A Anaphase A
  - 动粒微管变短，牵动染色体向两极运动
- 后期B Anaphase B
  - 极性微管长度增加，两极之间的距离逐渐拉长

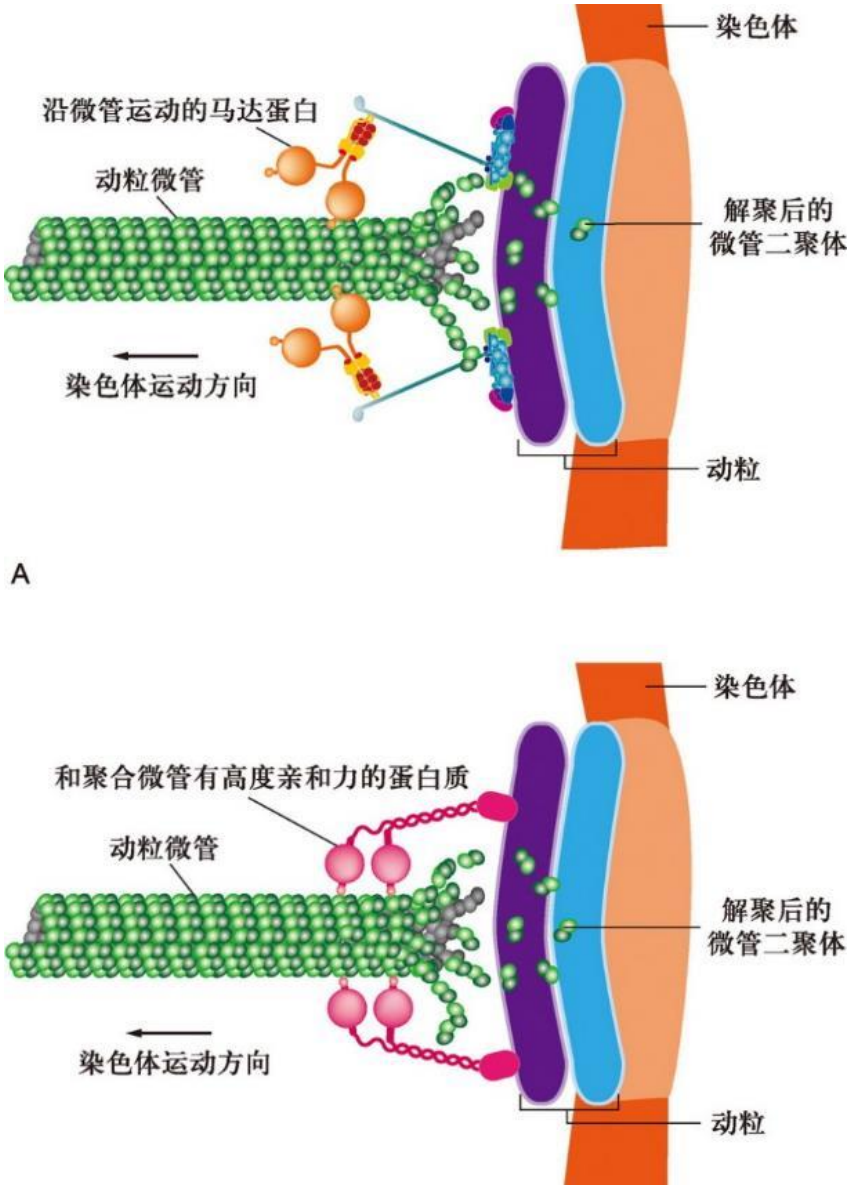


图12-18 细胞有丝分裂后期由ATP 驱动的马达蛋白沿微管向极部运动使染色体分开

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

有丝分裂中后期转换

- 在姐妹染色单体分离过程中，黏连蛋白被分离酶(Separase)降解
- 后期促进复合物 anaphase-promoting complex (APC/C)

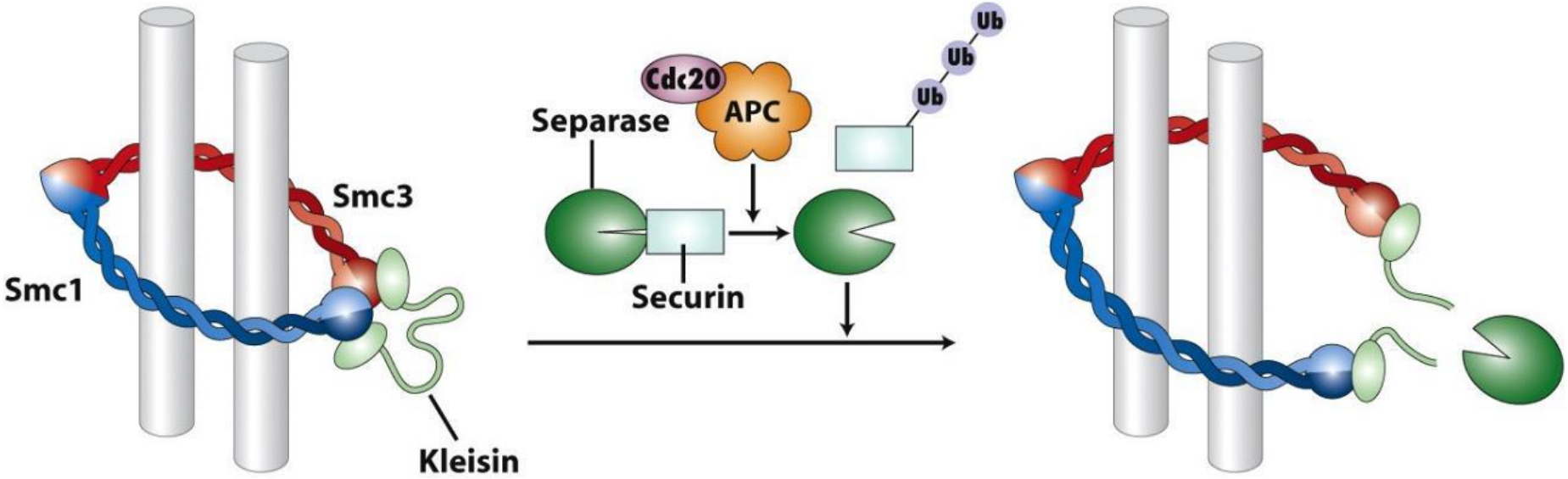
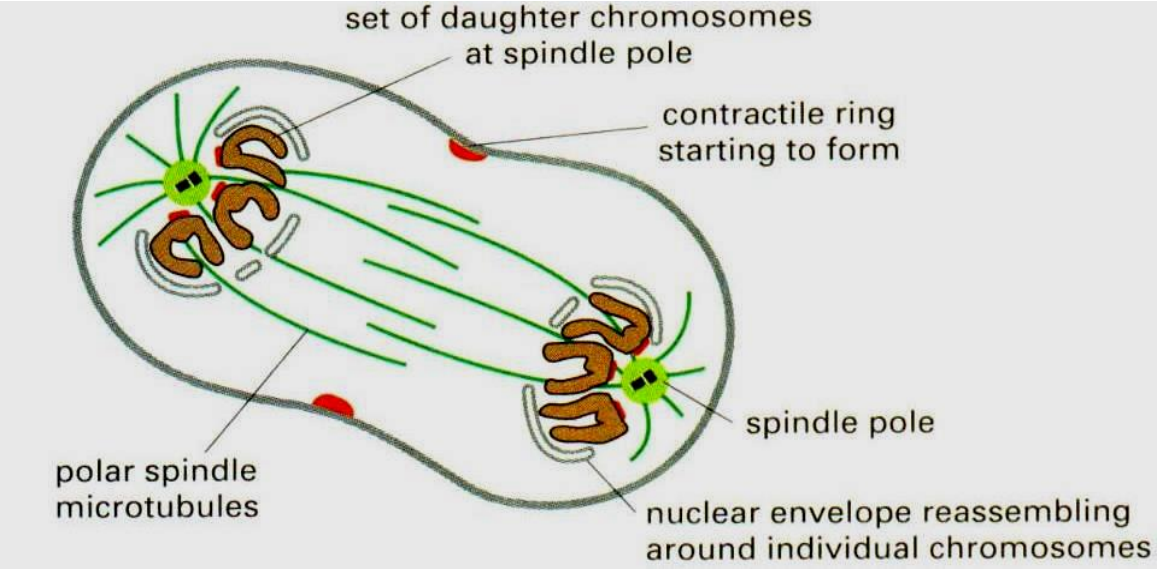


Figure 20-23
Molecular Cell Biology, Sixth Edition

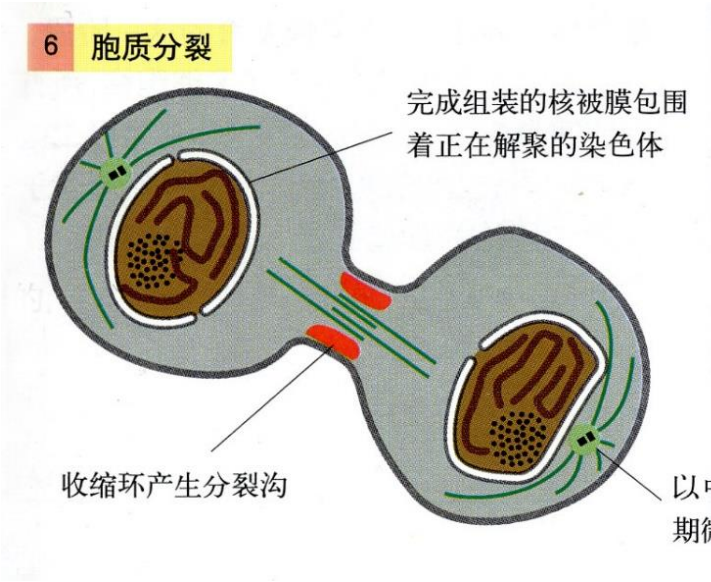
5. 末期（telophase）

- 染色单体分离到达两极
- 染色单体去浓缩
- 动粒微管消失，极微管继续加长
- 核纤层、核膜和核孔复合体重新组装
- 核仁重新组装，rRNA合成功能逐渐恢复

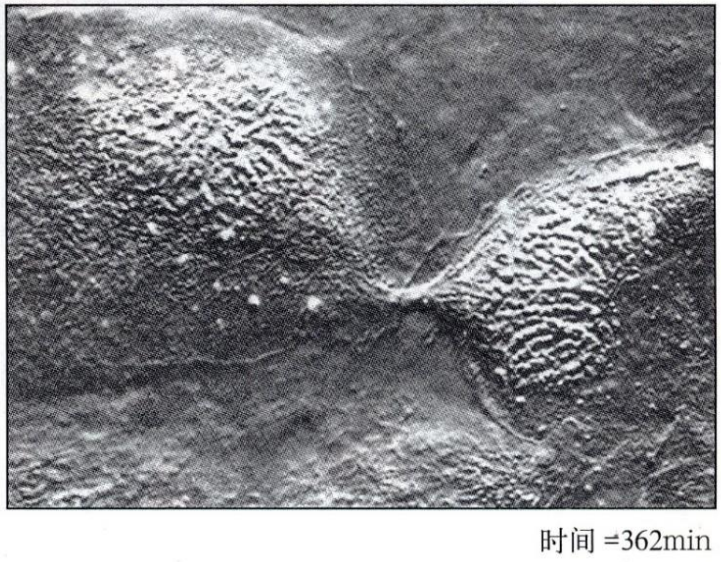


6. 胞质分裂 Cytokinisis (Cytoplasm division)

- 分裂沟位置的确立，收缩环形成、收缩、形成两个子细胞



在一个动物细胞的胞质分裂期间，细胞质被肌动蛋白和肌球蛋白构成的收缩环分为两个，收缩环在细胞内收缩，形成各含一个细胞核的两个子细胞。



6. 胞质分裂 Cytokinisis (Cytoplasm division)

- Furrow 分裂沟: 赤道板周围细胞表面下陷
- Midbody 中体：分裂沟下方，初激动蛋白之外，还有微管、核膜小泡等物质聚集，共同构成一个环形致密层
- Contractile ring 收缩环：大量肌动蛋白和肌球蛋白II组装成反向排列的微丝束，环绕细胞

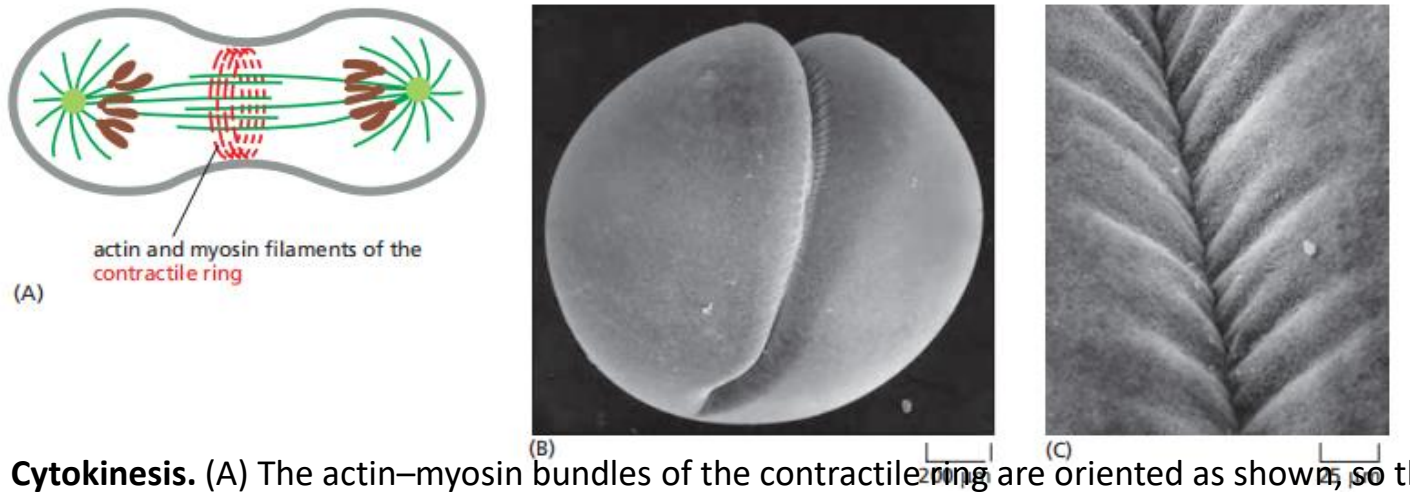


Figure 17–41 **Cytokinesis.** (A) The actin–myosin bundles of the contractile ring are oriented as shown, so that their contraction pulls the membrane inward. (B) In this low-magnification scanning electron micrograph of a cleaving frog egg, the cleavage furrow is especially prominent, as the cell is unusually large. The furrowing of the cell membrane is caused by the activity of the contractile ring underneath it. (C) The surface of a furrow at higher magnification. (B and C, from H.W. Beams and R.G. Kessel, Am. Sci. 64:279–290, 1976. With permission from Sigma Xi.)

6. 胞质分裂 Cytokinisis (Cytoplasm division)

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

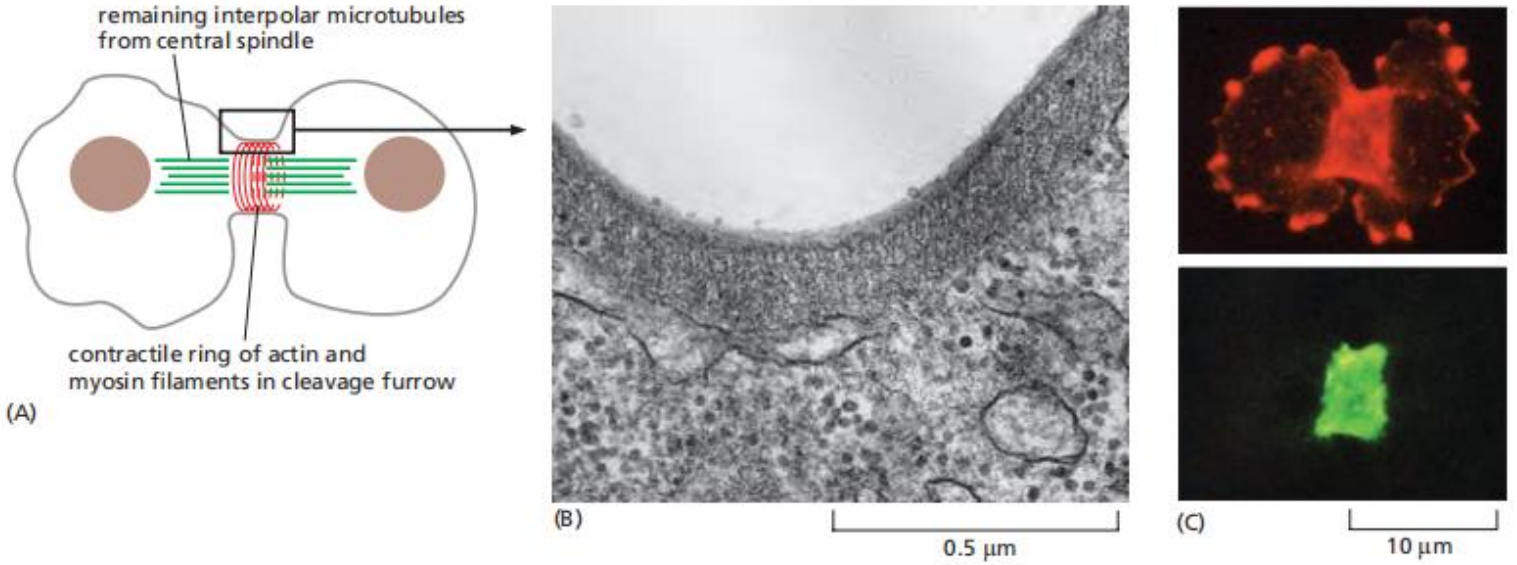


Figure 17–42 **The contractile ring.** (A) A drawing of the cleavage furrow in a dividing cell. (B) An electron micrograph of the ingrowing edge of a cleavage furrow of a dividing animal cell. (C) Fluorescence micrographs of a dividing slime mold amoeba stained for actin (red) and myosin II (green). Whereas all of the visible myosin II has redistributed to the contractile ring, only some of the actin has done so; the rest remains in the cortex of the nascent daughter cells. (B, from H.W. Beams and R.G. Kessel, Am. Sci. 64:279–290, 1976. With permission from Sigma Xi; C, courtesy of Yoshio Fukui.)

6. 胞质分裂 Cytokinisis (Cytoplasm division)

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

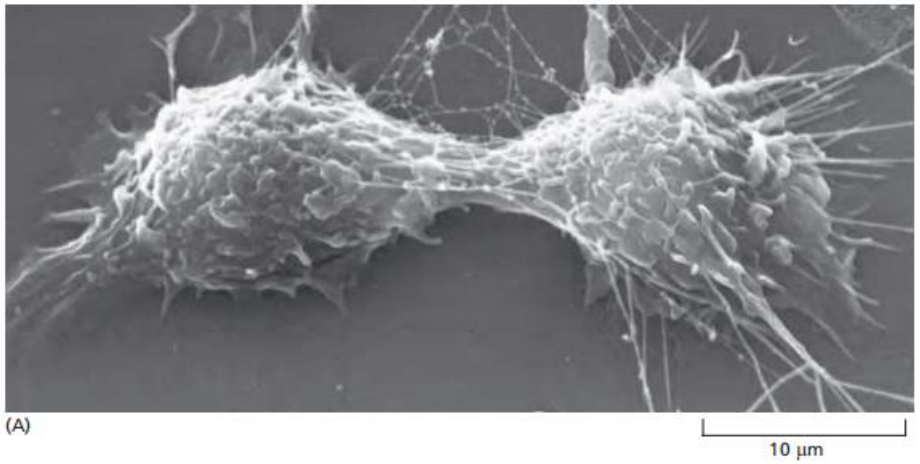


Figure 17–43 The midbody. (A) A scanning electron micrograph of a cultured animal cell dividing; the midbody still joins the two daughter cells. (B) A conventional electron micrograph of the midbody of a dividing animal cell. Cleavage is almost complete, but the daughter cells remain attached by this thin strand of cytoplasm containing the remains of the central spindle. (A, courtesy of Guenter Albrecht-Buehler; B, courtesy of J.M. Mullins.)

6. 胞质分裂 Cytokinisis (Cytoplasm division)

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

1. 分裂沟位置的确立
2. 肌动蛋白聚集和收缩环形成
3. 收缩环收缩
4. 收缩环处细胞融合并形成两个子细胞

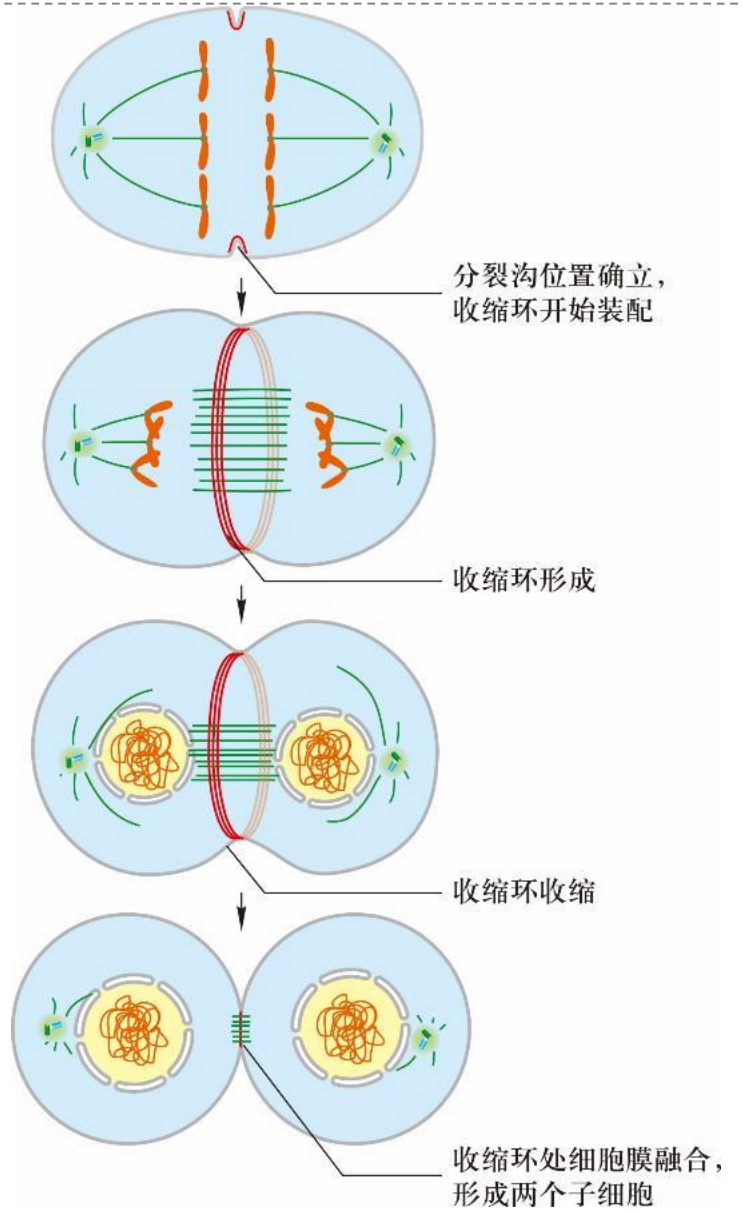


图13-21 动物细胞胞质分裂示意图

6. 胞质分裂 Cytokinisis (Cytoplasm division)

- 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
- 星体微管参与了分裂沟的形成

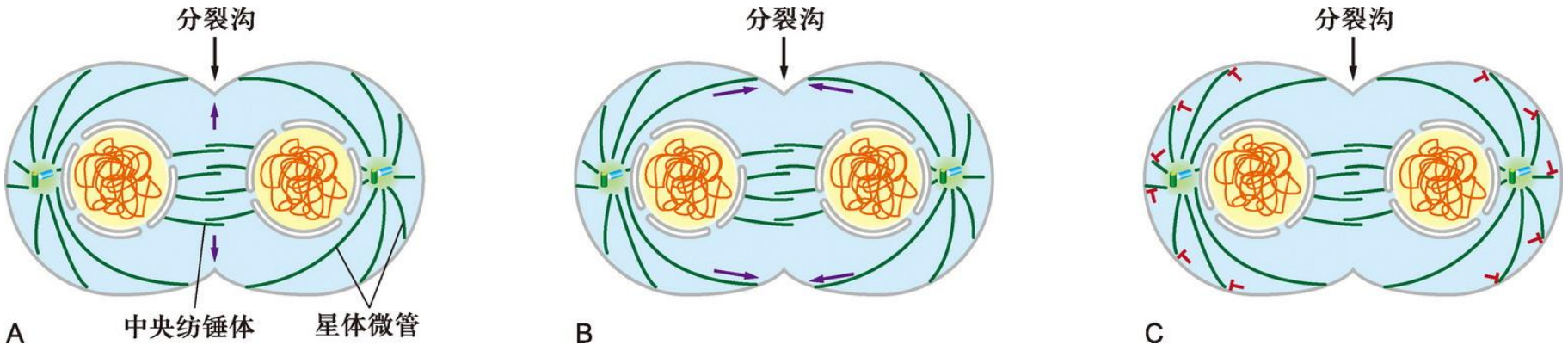
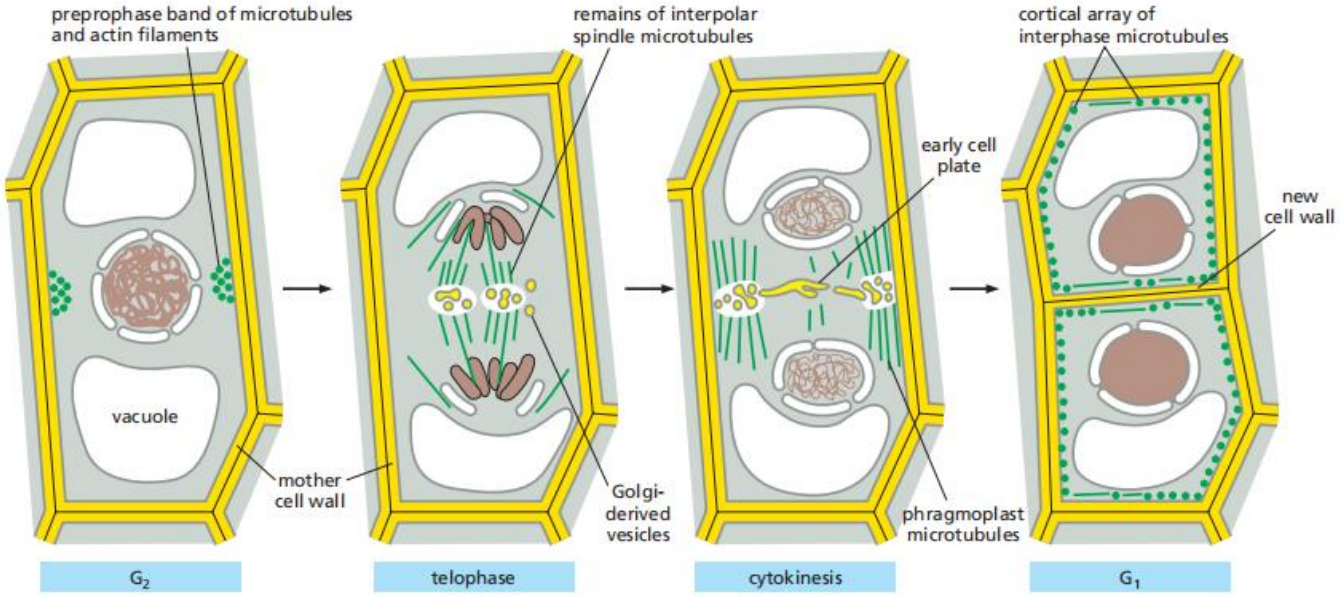


图12-22 中央纺锤体和星体微管作用于细胞皮层并诱导分裂沟形成

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

植物细胞分裂的特点

- 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
- 植物细胞分裂是在成膜体指导下，以形成细胞板的形式完成胞质分裂



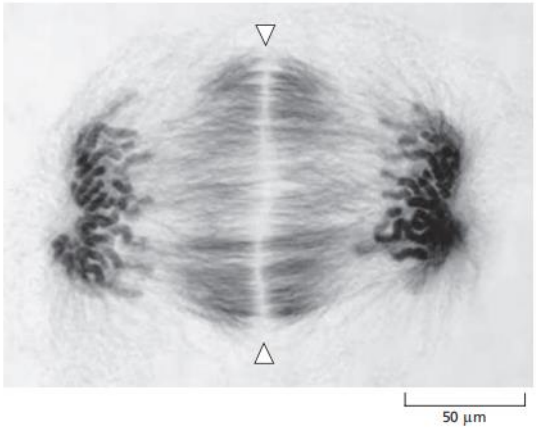
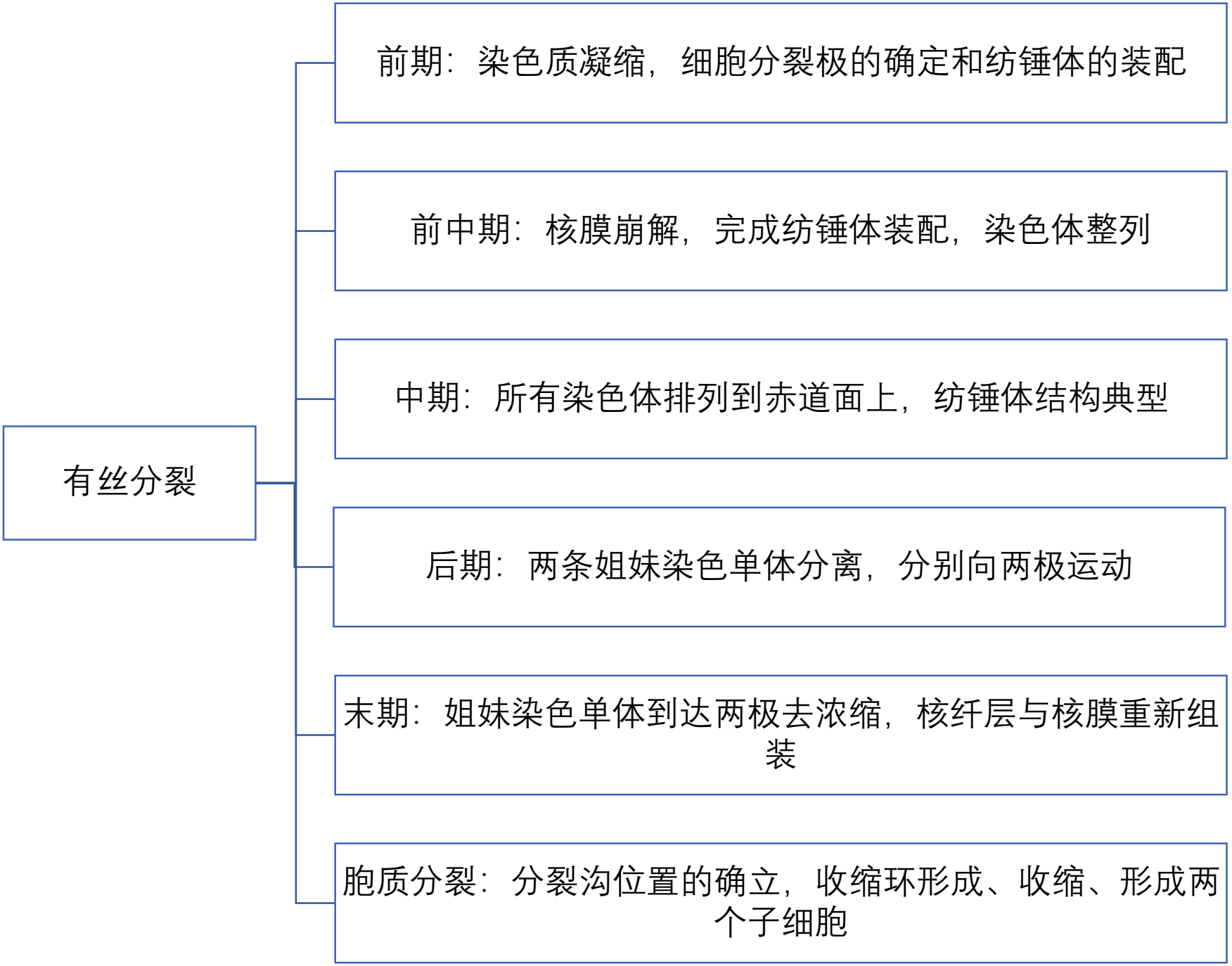
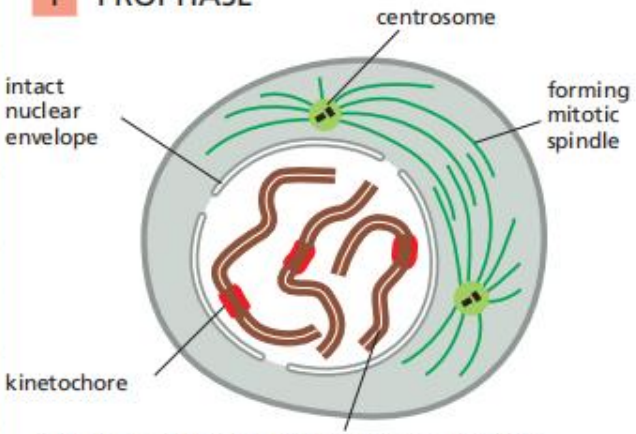


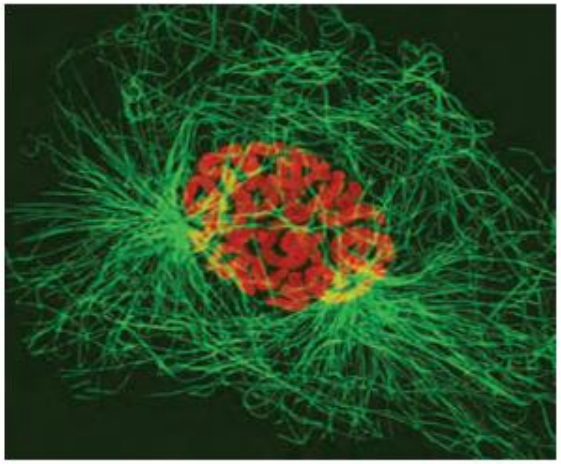
Figure 17–49 **The special features of cytokinesis in a higher-plant cell.** The division plane is established before M phase by a band of microtubules and actin filaments (the preprophase band) at the cell cortex. At the beginning of telophase, after the chromosomes have segregated, a new cell wall starts to assemble inside the cell at the equator of the old spindle. **The interpolar microtubules of the mitotic spindle remaining at telophase form the phragmoplast.** The plus ends of these microtubules no longer overlap but end at the cell equator. Golgi-derived vesicles, filled with cell-wall material, are transported along these microtubules and fuse to form the new cell wall, which grows outward to reach the plasma membrane and original cell wall. The plasma membrane and the membrane surrounding the new cell wall fuse, separating the two daughter cells.


有丝分裂
前期：染色质凝缩，细胞分裂极的确定和纺锤体的装配
前中期：核膜崩解，完成纺锤体装配，染色体整列
中期：所有染色体排列到赤道面上，纺锤体结构典型
后期：两条姐妹染色单体分离，分别向两极运动
末期：姐妹染色单体到达两极去浓缩，核纤层与核膜重新组装
胞质分裂：分裂沟位置的确立，收缩环形成、收缩、形成两个子细胞

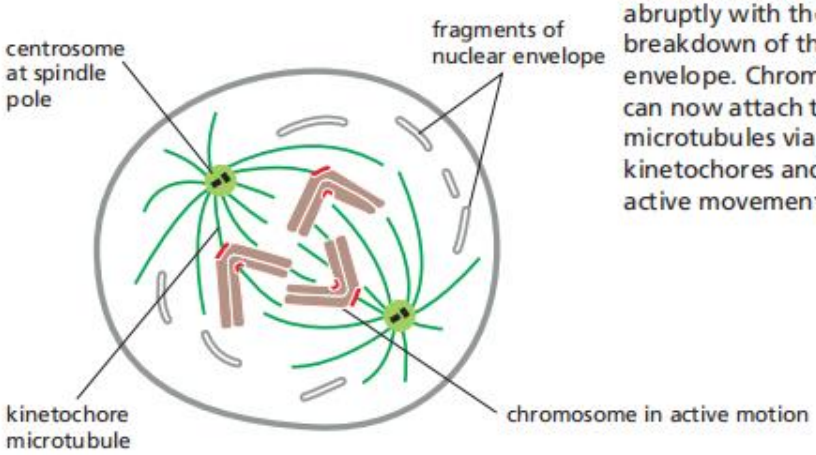
1 PROPHASE



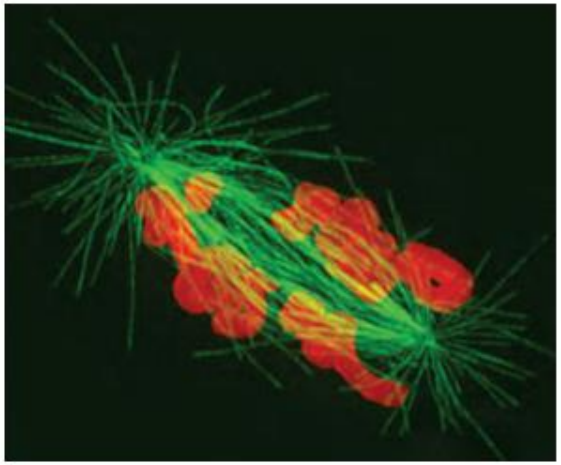
At prophase, the replicated chromosomes, each consisting of two closely associated sister chromatids, condense. Outside the nucleus, the mitotic spindle assembles between the two centrosomes, which have replicated and moved apart. For simplicity, only three chromosomes are shown. In diploid cells, there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



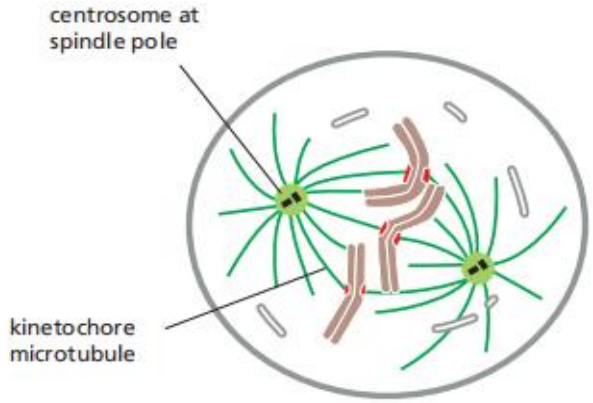
2 PROMETAPHASE



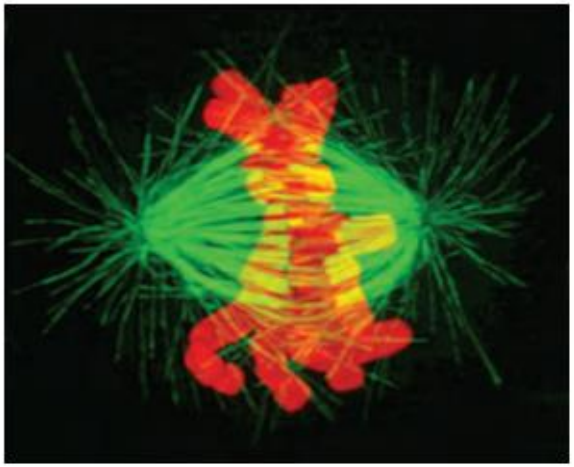
Prometaphase starts abruptly with the breakdown of the nuclear envelope. Chromosomes can now attach to spindle microtubules via their kinetochores and undergo active movement.



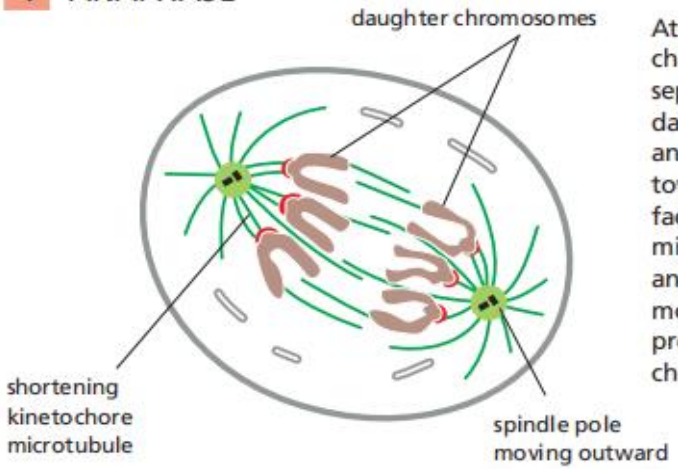
3 METAPHASE



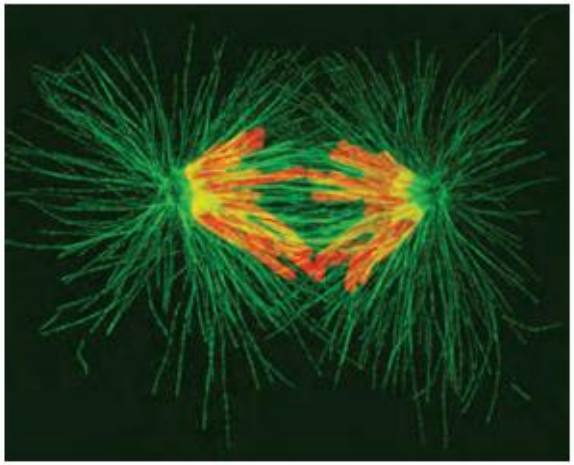
At metaphase, the chromosomes are aligned at the equator of the spindle, midway between the spindle poles. The kinetochore microtubules attach sister chromatids to opposite poles of the spindle.



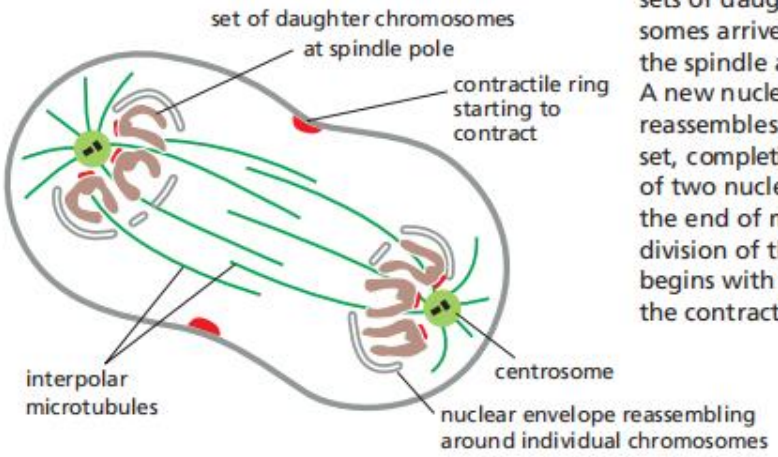
4 ANAPHASE



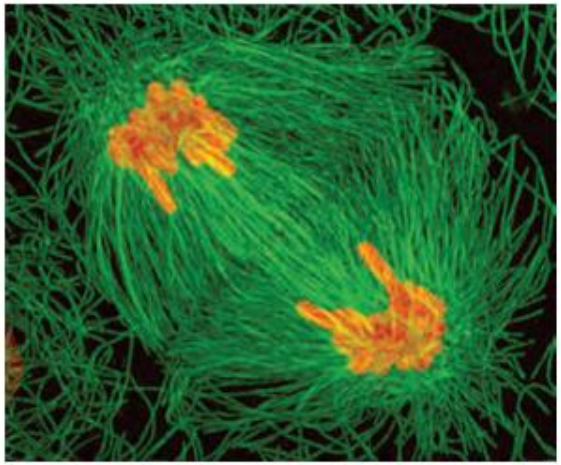
At anaphase, the sister chromatids synchronously separate to form two daughter chromosomes, and each is pulled slowly toward the spindle pole it faces. The kinetochore microtubules get shorter, and the spindle poles also move apart; both processes contribute to chromosome segregation.



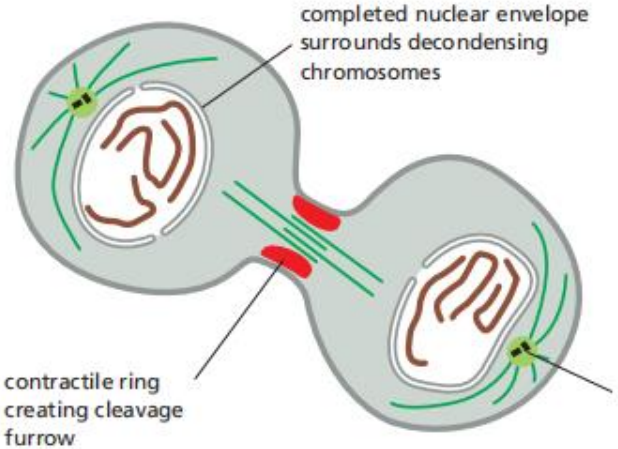
5 TELOPHASE



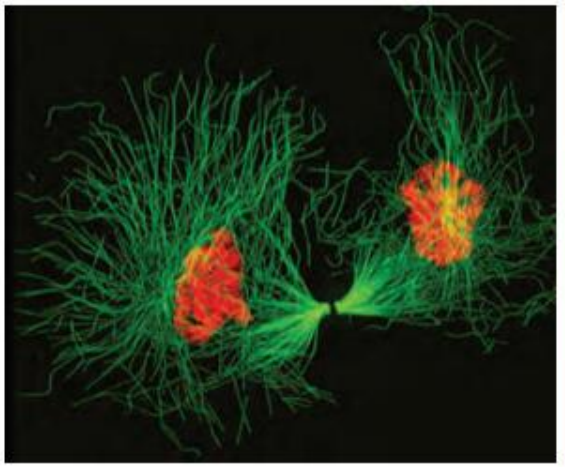
During telophase, the two sets of daughter chromosomes arrive at the poles of the spindle and decondense. A new nuclear envelope reassembles around each set, completing the formation of two nuclei and marking the end of mitosis. The division of the cytoplasm begins with contraction of the contractile ring.



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.



(Micrographs courtesy of Julie Canman and Ted Salmon.)

有丝分裂


Mitosis
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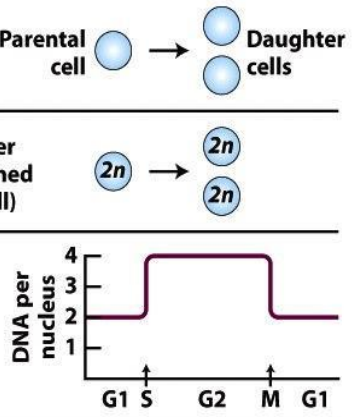
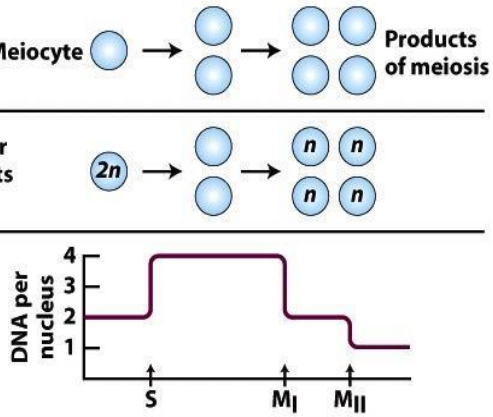
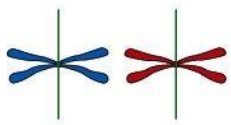
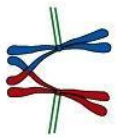
二、减数分裂（meiosis）

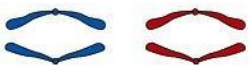
Row	Mitosis	Meiosis
	In somatic cells	In cells in the sexual cycle
1	One cell division, resulting in two daughter cells	Two cell divisions, resulting in four products of meiosis
2	Chromosome number per nucleus maintained (e.g., for a diploid cell)	Chromosome number halved in the products of meiosis
3	One premitotic S phase per cell division	One premeiotic S phase for both cell divisions
4	Normally, no pairing of homologous chromosomes in prophase	Full synapsis of of homologous chromosomes in prophase
5	Normally, norecombination in prophase	At least one recombination between nonsister chromatids
6	Bi-oriented sister kinetochores	Co-orientation of sister kinetochores
7	Loss of cohesion between sister chromatid arms during metaphase	Maintenance of cohesion between sister chromatid arms during metaphase of meioses I
8	Centromeres divide at anaphase	Centromeres do not divide at anaphase I but do at anaphase II
	Conservative process: daughter cells' genotypes identical with parental genotype	Promotes variation among the products of meiosis



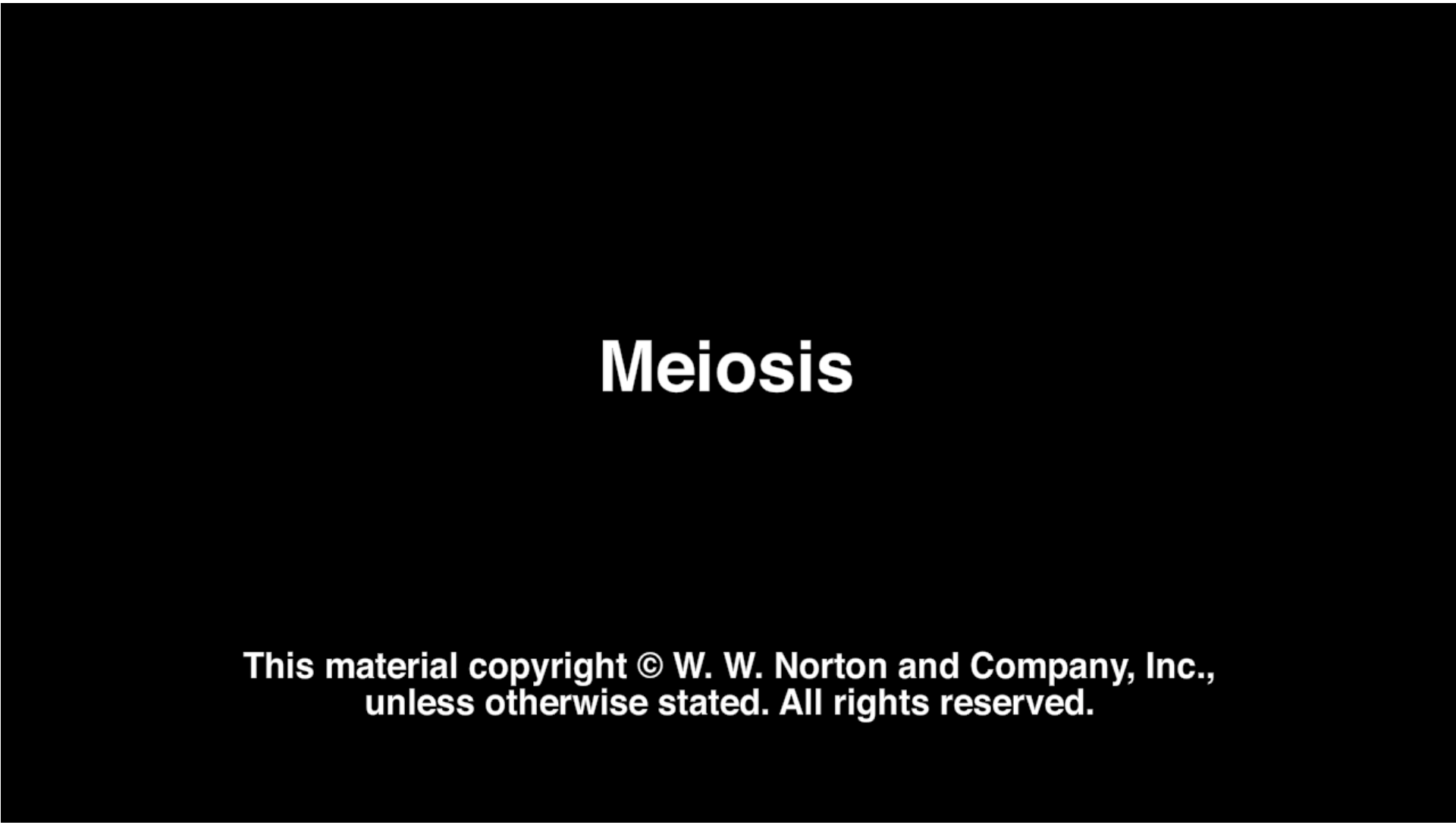








二、减数分裂（meiosis）



二、减数分裂（meiosis）