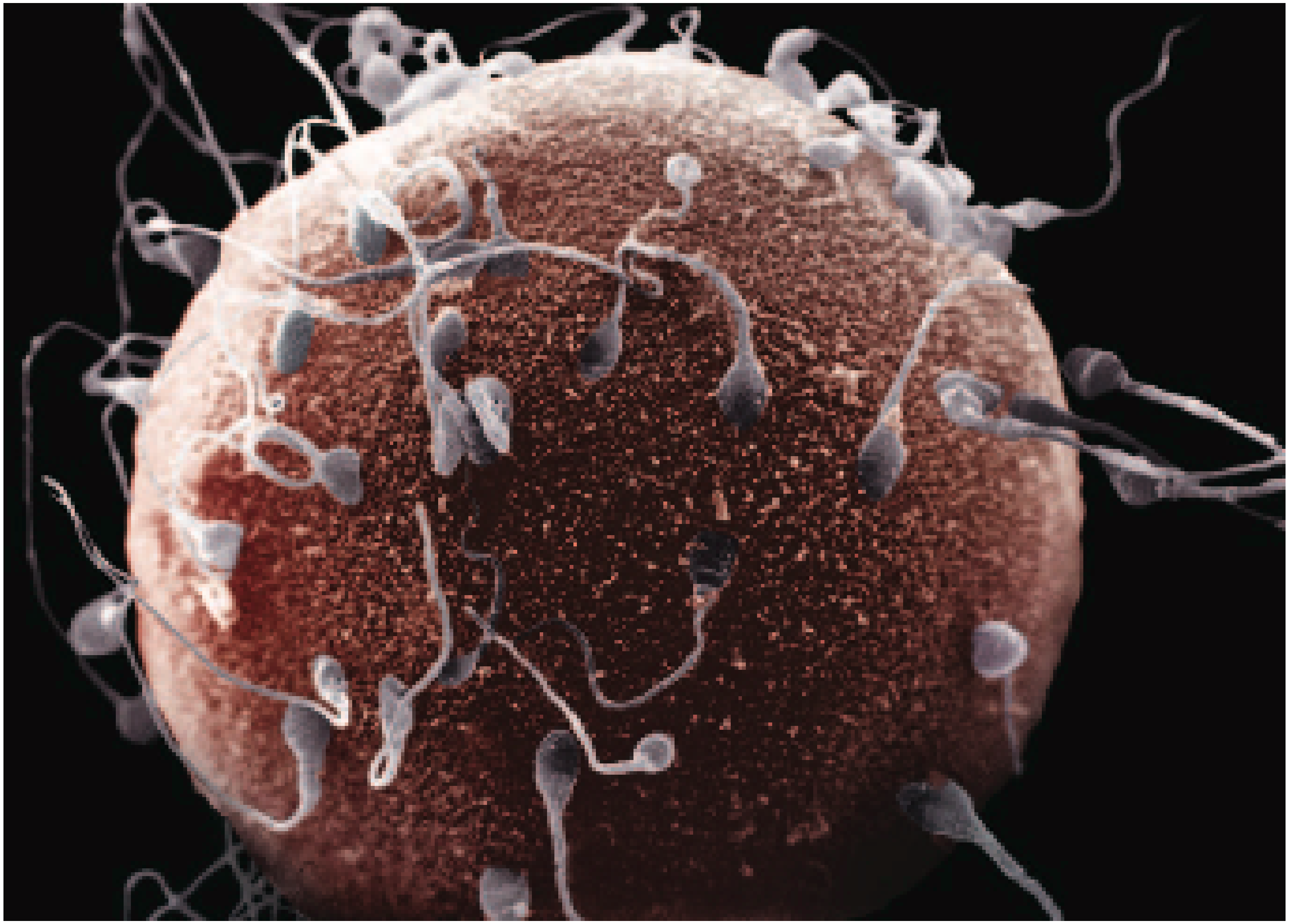
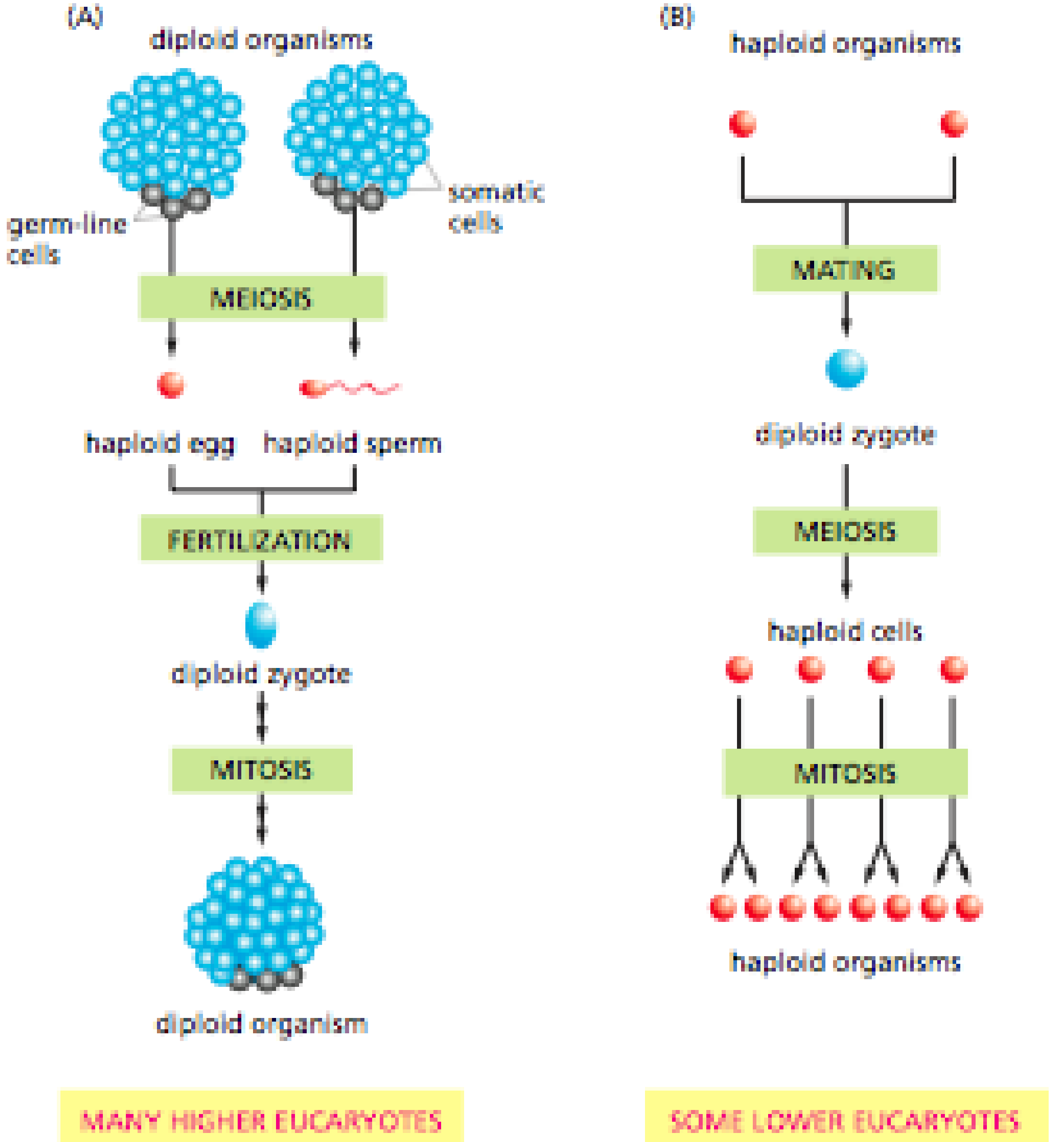



(A)
diploid organisms
germ-line cells
somatic cells
MEIOSIS
haploid egg
haploid sperm
FERTILIZATION
diploid zygote
MITOSIS
diploid organism
MANY HIGHER EUCARYOTES
(B)
haploid organisms
MATING
diploid zygote
MEIOSIS
haploid cells
MITOSIS
haploid organisms
SOME LOWER EUCARYOTES

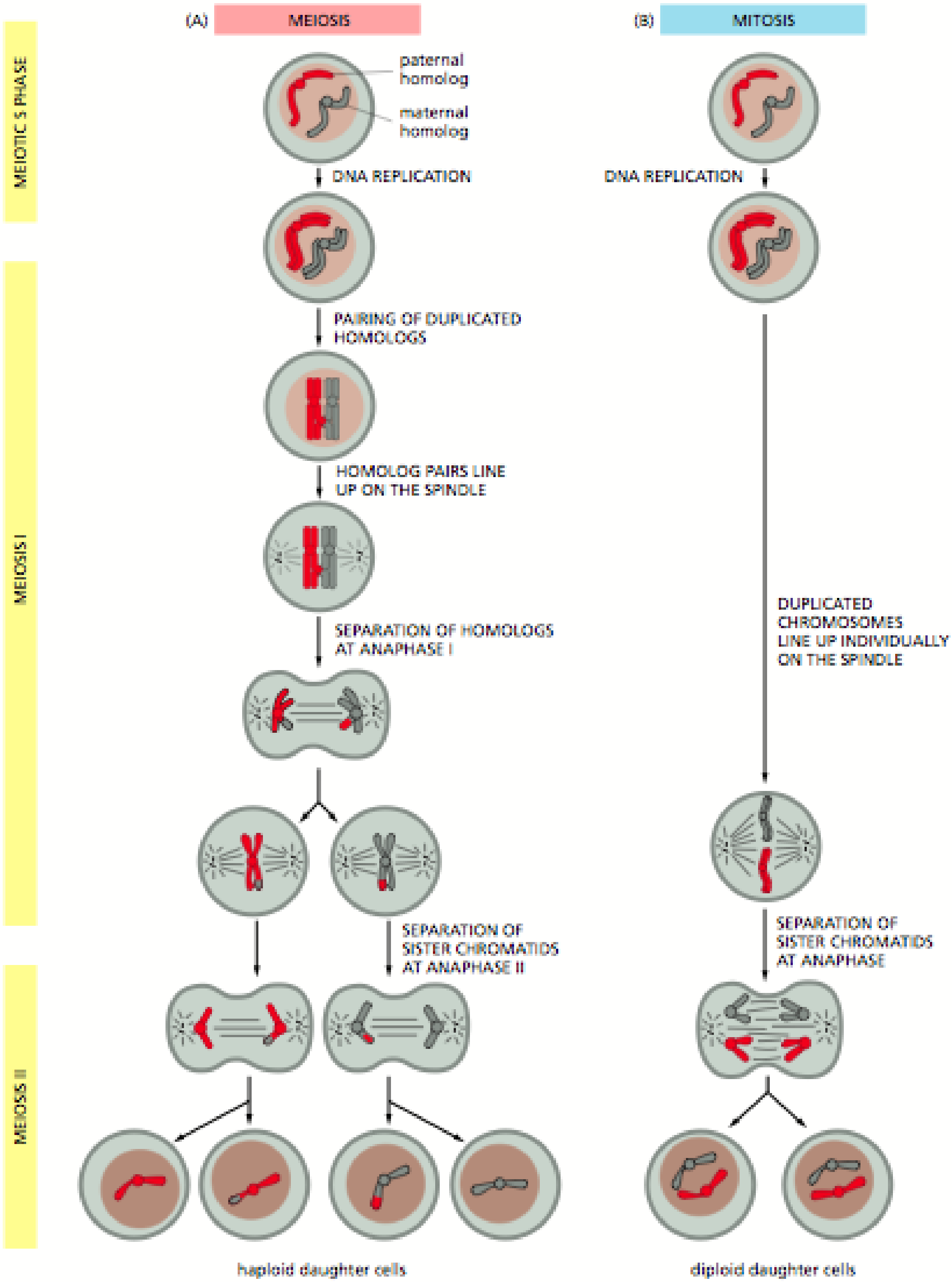


Figure 21–5 Comparison of meiosis and mitotic cell division. For clarity, only one pair of homologous chromosomes (homologs) is shown. (A) In meiosis, after DNA replication, two nuclear (and cell) divisions are required to produce the haploid gametes. The duplicated homologs, each consisting of tightly bound sister chromatids, pair up and are segregated into different daughter cells in meiosis I; the sister chromatids separate only in meiosis II. As indicated by the formation of chromosomes that are partly *red* and partly *gray*, homolog pairing in meiosis leads to genetic recombination (crossing-over) during meiosis I, as discussed later. Each diploid cell that enters meiosis therefore produces four genetically different haploid cells. <AGTG> (B) In mitosis, by contrast, homologs do not pair up, and the sister chromatids separate during the single division. Thus, each diploid cell that divides by mitosis produces two genetically identical diploid daughter cells.

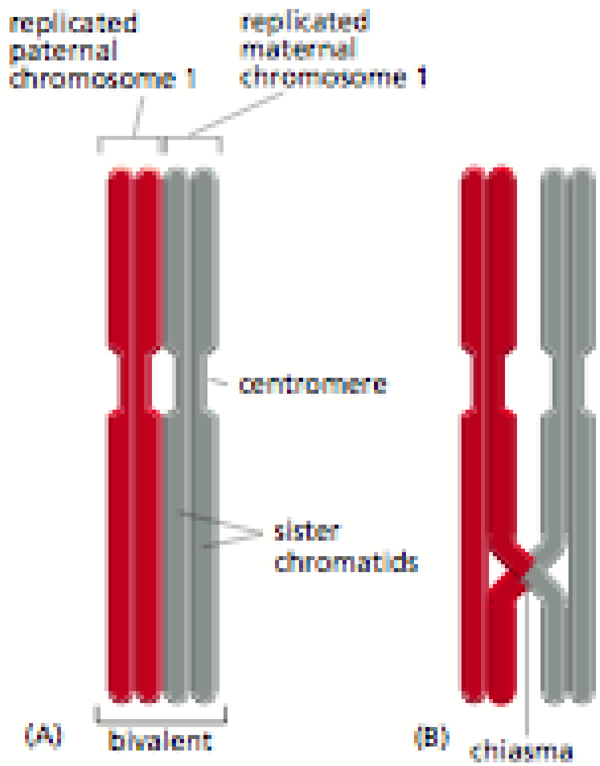
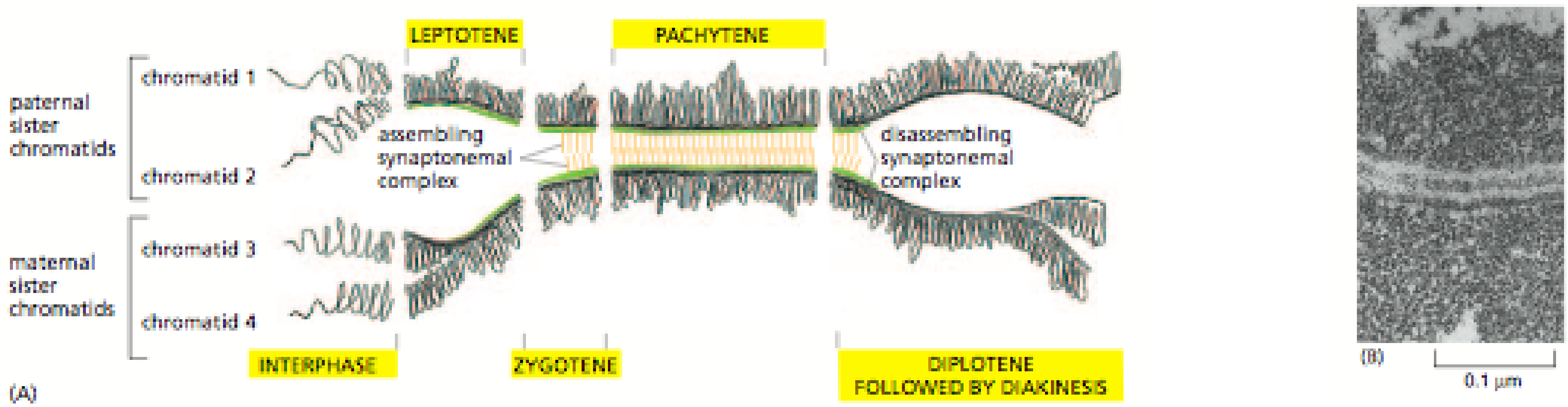


Figure 21–6 Homolog alignment and crossing-over. (A) The structure formed by two closely aligned duplicated homologs is called a *bivalent*. As in mitosis, the sister chromatids in each homolog are tightly connected along their entire lengths, as well as at their centromeres. At this stage, the homologs are usually joined together by a protein complex called the *synaptonemal complex* (not shown; see Figure 21–9). (B) A later-stage bivalent in which a single crossover event has occurred between non-sister chromatids. It is only when the synaptonemal complex disassembles and the paired homologs separate a little at the end of prophase I, as shown, that the crossover is seen microscopically as a thin connection between the homologs called a *chiasma*.



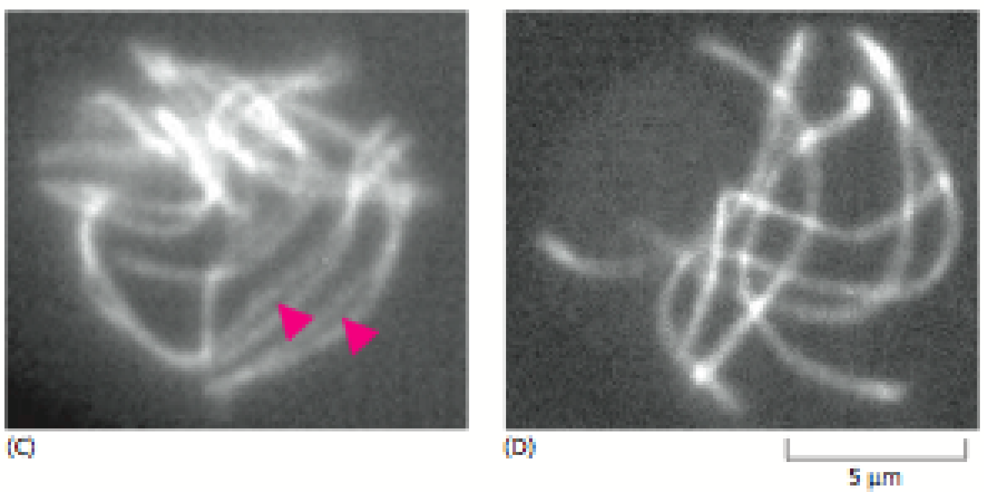


Figure 21–9 Homolog synapsis and desynapsis during the different stages of prophase I. (A) A single bivalent is shown schematically. At leptotene, the two sister chromatids coalesce, and their chromatid loops extend out together from a common axial core. The synaptonemal complex begins to assemble focally in early zygotene. Assembly continues through zygotene and is complete in pachytene. The complex disassembles in diplotene. (B) An electron micrograph of a synaptonemal complex from a meiotic cell at pachytene in a lily flower. (C and D) Immunofluorescence micrographs of prophase I cells of the fungus *Sordaria*. Partially synapsed bivalents at zygotene are shown in (C) and fully synapsed bivalents are shown in (D). *Red arrowheads* in (C) point to regions where synapsis is still incomplete. (B, courtesy of Brian Wells; C and D, from A. Storlazzi et al., *Genes Dev.* 17:2675–2687, 2003. With permission from Cold Spring Harbor Laboratory Press.)

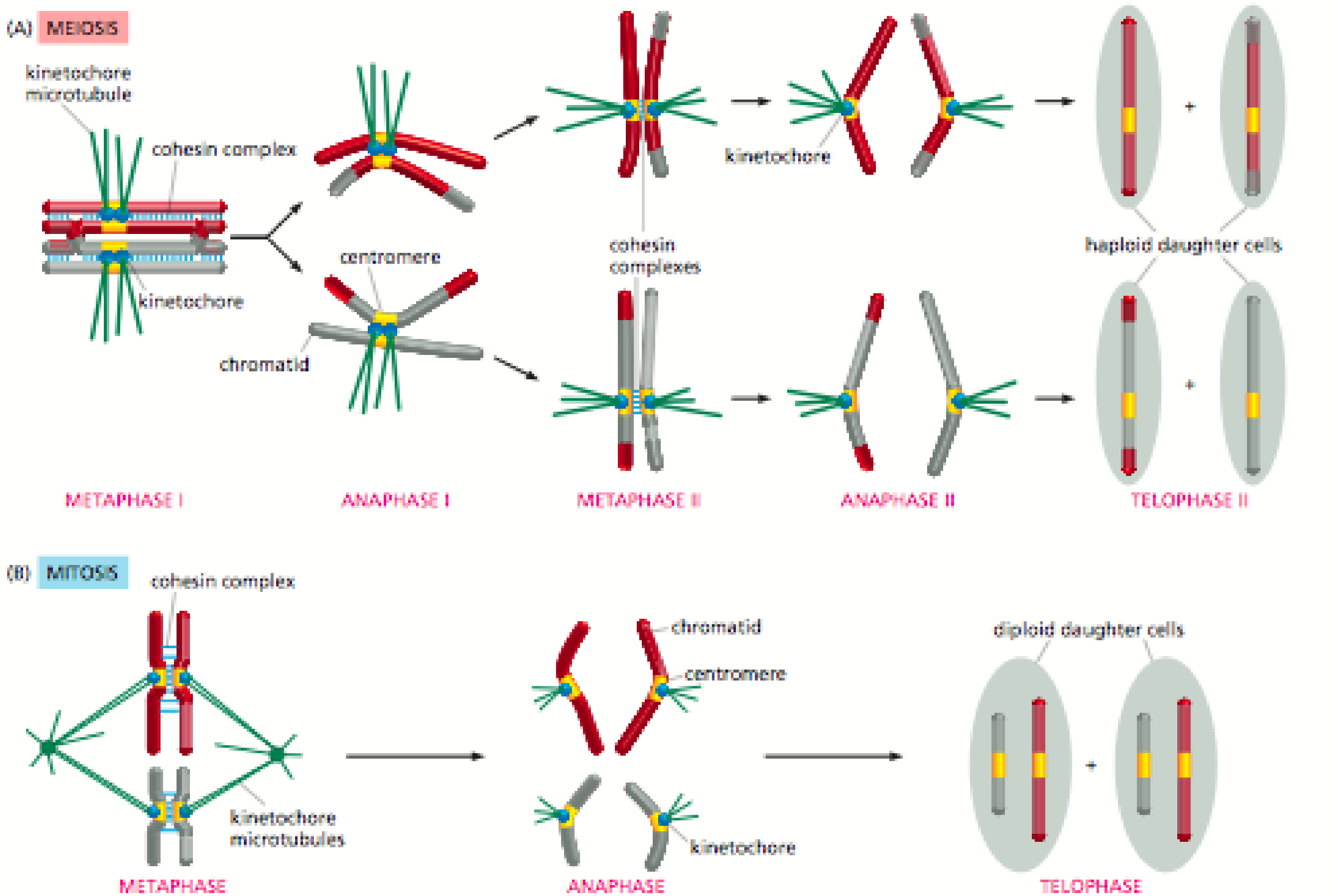


Figure 21–12 Comparison of chromosome behavior in meiosis I, meiosis II, and mitosis. Chromosomes behave similarly in mitosis and meiosis II, but they behave very differently in meiosis I. (A) In meiosis I, the two sister kinetochores are located side-by-side on each homolog at the sister centromeres and attach to microtubules emanating from the same spindle pole. The proteolytic destruction of the cohesin complexes along the sister chromatid arms unglues the arms and resolves the crossovers, allowing the duplicated homologs to separate at anaphase I, while the residual cohesin complexes at the centromeres keep the sisters together. The proteolytic destruction of the residual cohesin complexes at the centromeres allows the sister chromatids to separate at anaphase II. (B) In mitosis, by contrast, the two sister kinetochores attach to microtubules emanating from different spindle poles, and the two sister chromatids come apart at the start of anaphase and segregate into separate daughter cells (discussed in Chapter 17).

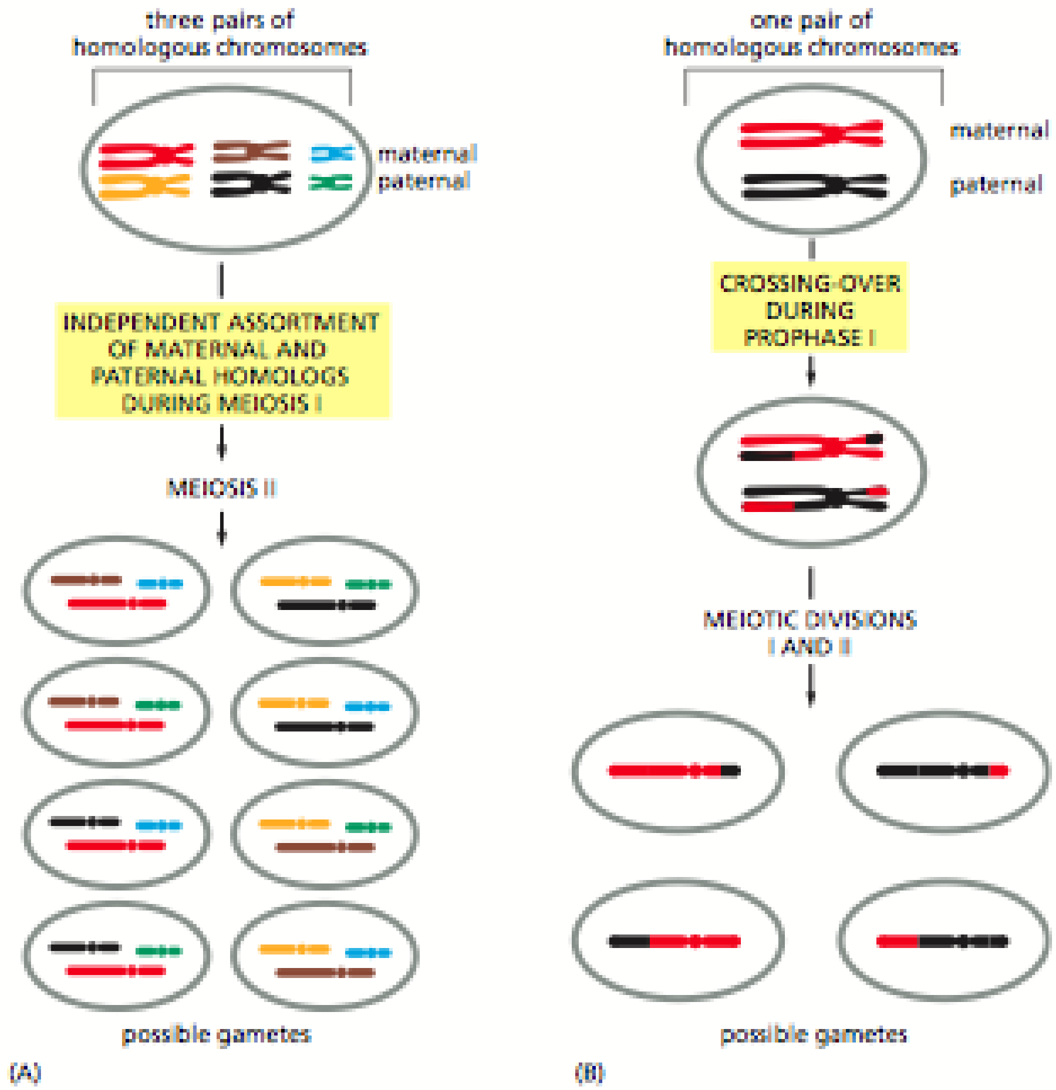


Figure 21–13 Two major contributions to the reassortment of genetic material that occurs in the production of gametes during meiosis. (A) The independent assortment of the maternal and paternal homologs during meiosis produces 2^n different haploid gametes for an organism with n chromosomes. Here $n = 3$, and there are 8 different possible gametes. (B) Crossing-over during prophase I exchanges DNA segments between homologous chromosomes and thereby re-assorts genes on individual chromosomes. Because of the many small differences in DNA sequence that always exist between any two homologs, both mechanisms increase the genetic variability of organisms that reproduce sexually.

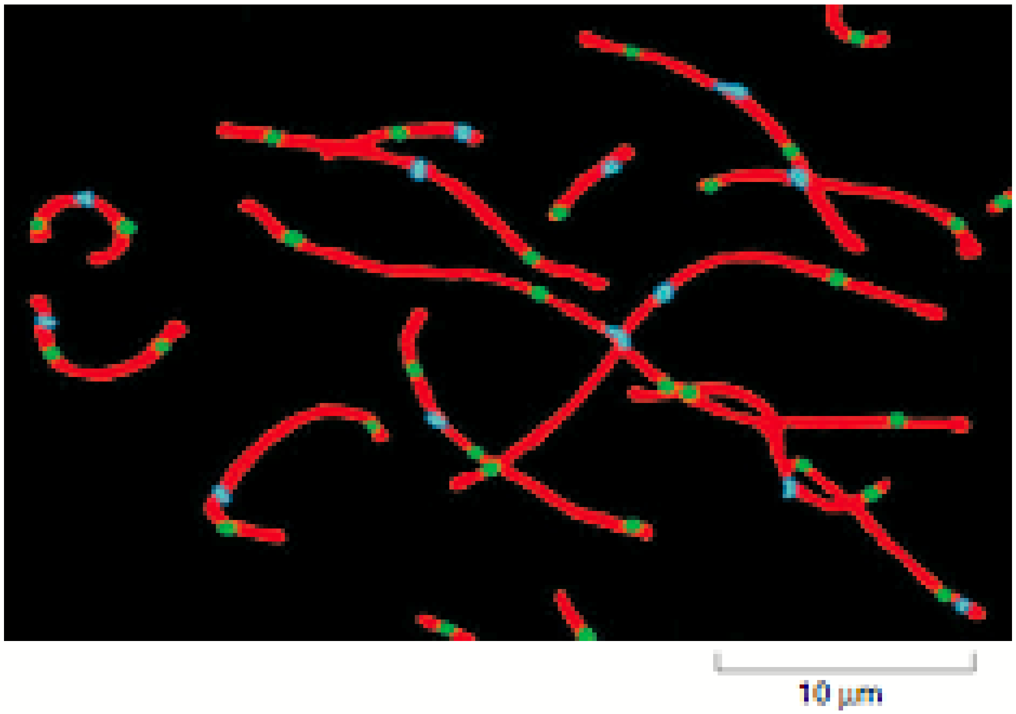


Figure 21–14 Crossovers between homologs in the human testis. In these immunofluorescence micrographs, antibodies have been used to stain the synaptonemal complexes (*red*), the centromeres (*blue*), and the sites of crossing-over (*green*). Note that all of the bivalents have at least 1 crossover and none have more than 3. (Modified from A. Lynn et al., *Science* 296:2222–2225, 2002. With permission from AAAS.)

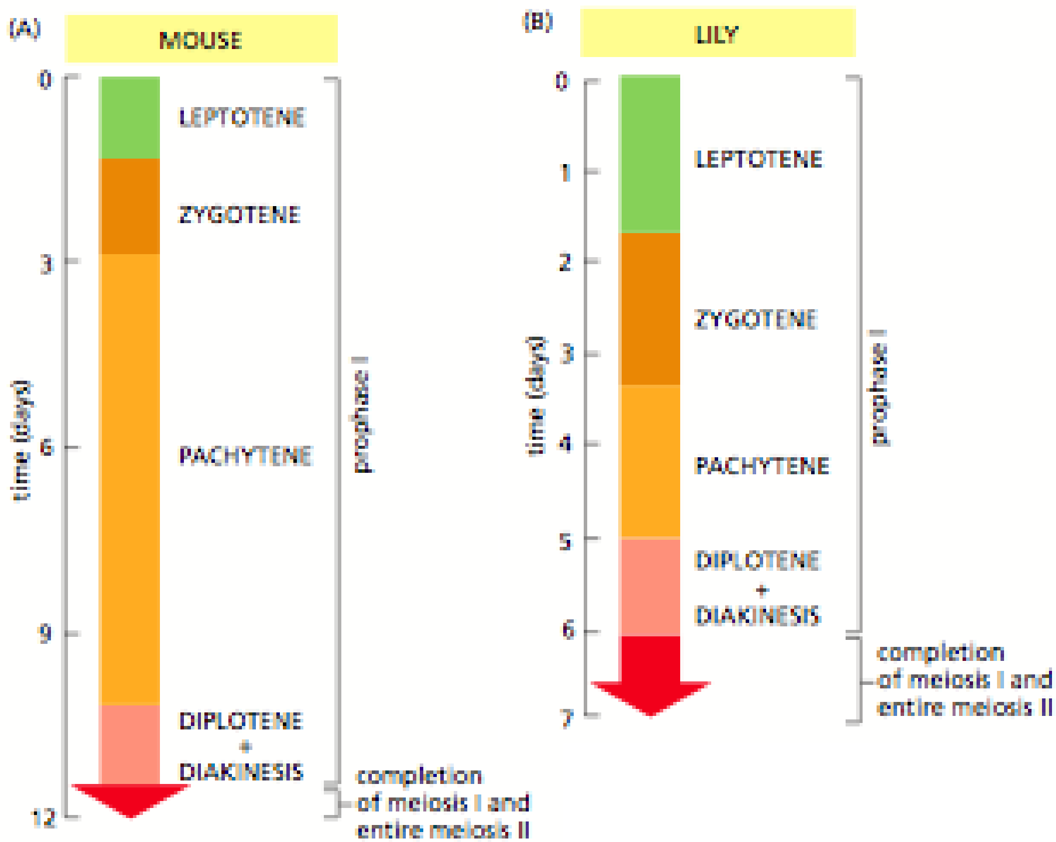


Figure 21–15 Comparison of times required for each of the stages of meiosis. (A) Approximate times for a male mammal (mouse). (B) Approximate times for the male tissue of a plant (lily). Times differ for male and female gametes (sperm and eggs, respectively) of the same species, as well as for the same gametes of different species. Meiosis in a human male, for example, lasts for 24 days, compared with 12 days in the mouse. In human females, it can last 40 years or more, because meiosis I arrests after diplotene. In all species, however, prophase I is always much longer than all the other meiotic stages combined.

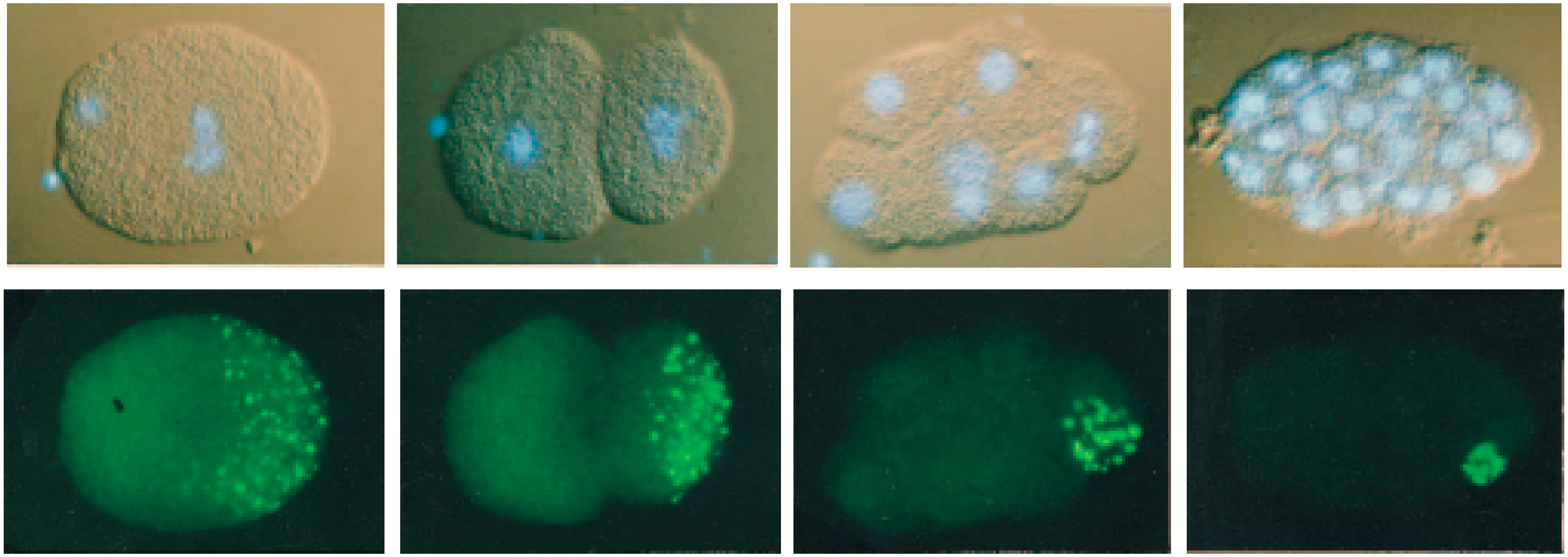


Figure 21–16 Segregation of germ cell determinants in the nematode *C. elegans*. The micrographs in the upper row show the pattern of cell divisions, with the cell nuclei stained *blue*; below, the same cells are stained with an antibody that labels (in *green*) small granules (called *P granules*) that function as germ cell determinants. The P granules are composed of RNA and protein molecules and are distributed randomly throughout the cytoplasm of the unfertilized egg (not shown). As shown in the far left-hand panels, after fertilization, the granules accumulate at one pole of the zygote. The granules are then segregated into one of the two daughter cells at each cell division. The single cell containing the P granules in the embryo shown in the far right-hand panels is the precursor of the germ line. (Courtesy of Susan Strome.)

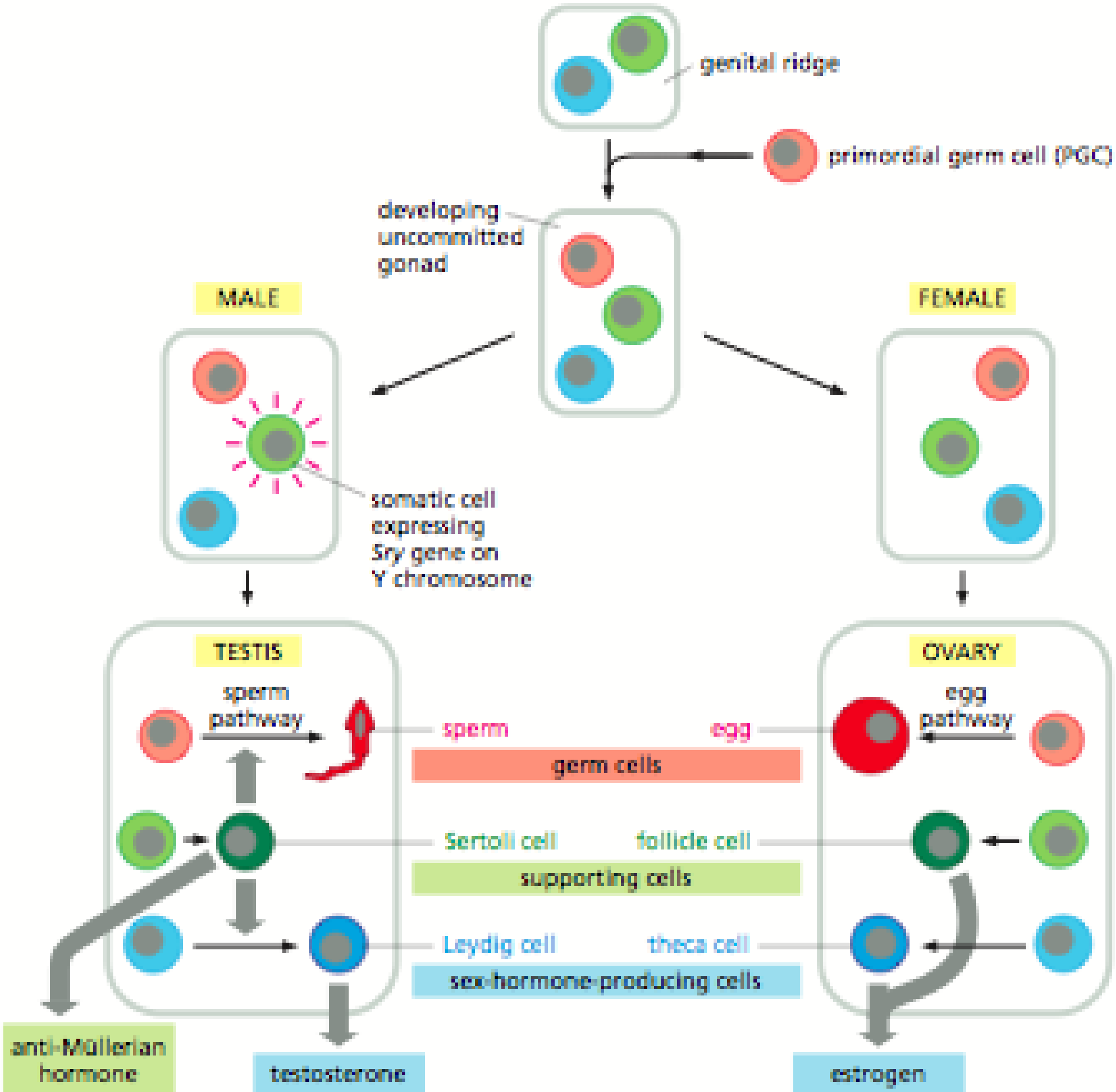


Figure 21–19 Influence of *Sry* on gonad development. The germ-line cells are shaded in *red*, and the somatic cells are shaded in *green* or *blue*. The change from light to darker color indicates that the cell has differentiated. The *Sry* gene acts in a subpopulation of somatic cells in the developing gonad to direct them to differentiate into Sertoli cells instead of follicle cells. The Sertoli cells then prevent the germ-line cells from developing along the egg pathway and help direct them down the sperm pathway of development, beginning at puberty. They also secrete anti-Müllerian hormone, which causes the Müllerian duct to regress, and they help to induce other somatic cells to differentiate into Leydig cells, which secrete testosterone (see Figure 21–29). In the absence of *Sry*, the germ-line cells commit to egg development, and the somatic cells develop into either follicle cells, which support egg development, or theca cells, which produce progesterone; the progesterone is converted to estrogen by the follicle cells. Whereas the testis begins secreting testosterone in the fetus, the ovary does not begin secreting estrogen until puberty.

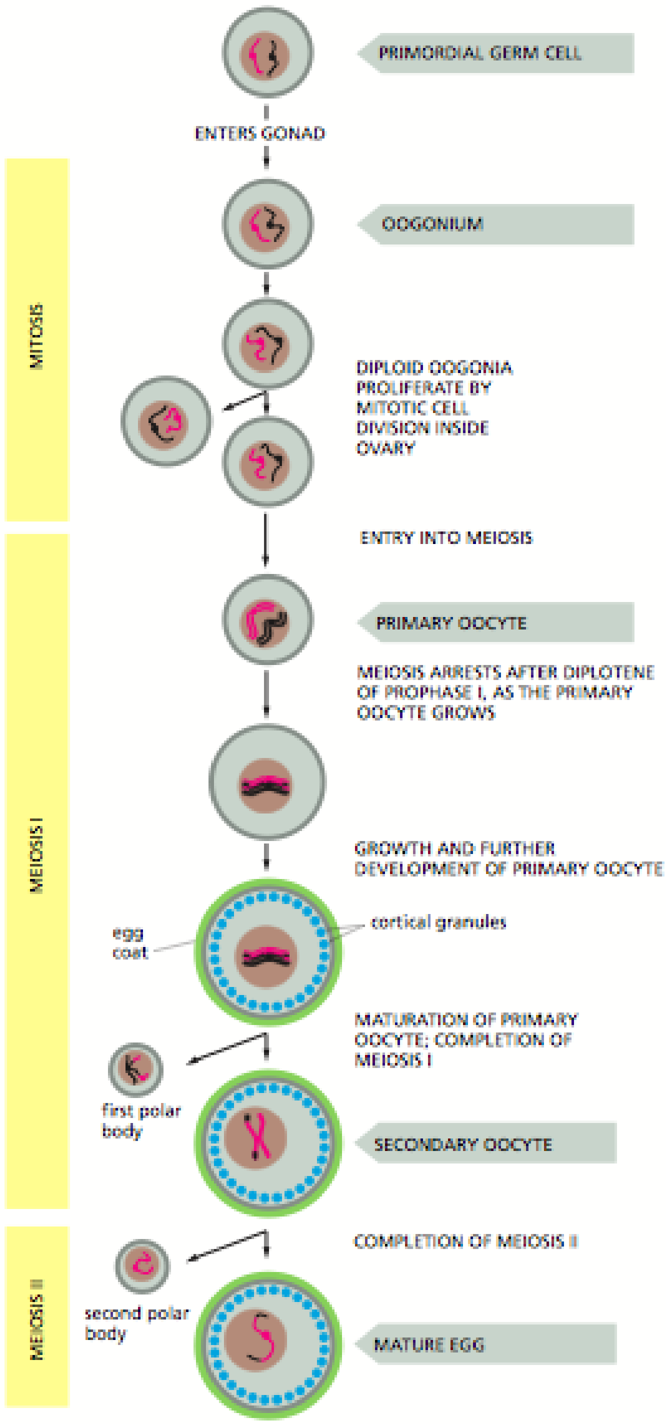


Figure 21–23 The stages of oogenesis. Oogonia develop from primordial germ cells (PGCs) that migrate into the developing gonad early in embryogenesis. For clarity, only one pair of homologous chromosomes is shown. After several mitotic divisions, oogonia begin meiosis and are now called primary oocytes. In mammals, primary oocytes are formed very early (between 3 and 8 months of gestation in the human embryo) and remain arrested after diplotene of prophase I until the female becomes sexually mature. At this point, a small number of primary oocytes periodically mature under the influence of hormones, completing meiosis I to produce secondary oocytes, which eventually undergo meiosis II to produce mature eggs (ova). The stage at which the egg or oocyte is released from the ovary and is fertilized varies from species to species. In most vertebrates, oocyte maturation is arrested at metaphase II, and the secondary oocyte completes meiosis II only after fertilization. All of the polar bodies eventually degenerate. In most animals, the developing oocyte is surrounded by specialized accessory cells that help to isolate and nourish it (not shown).

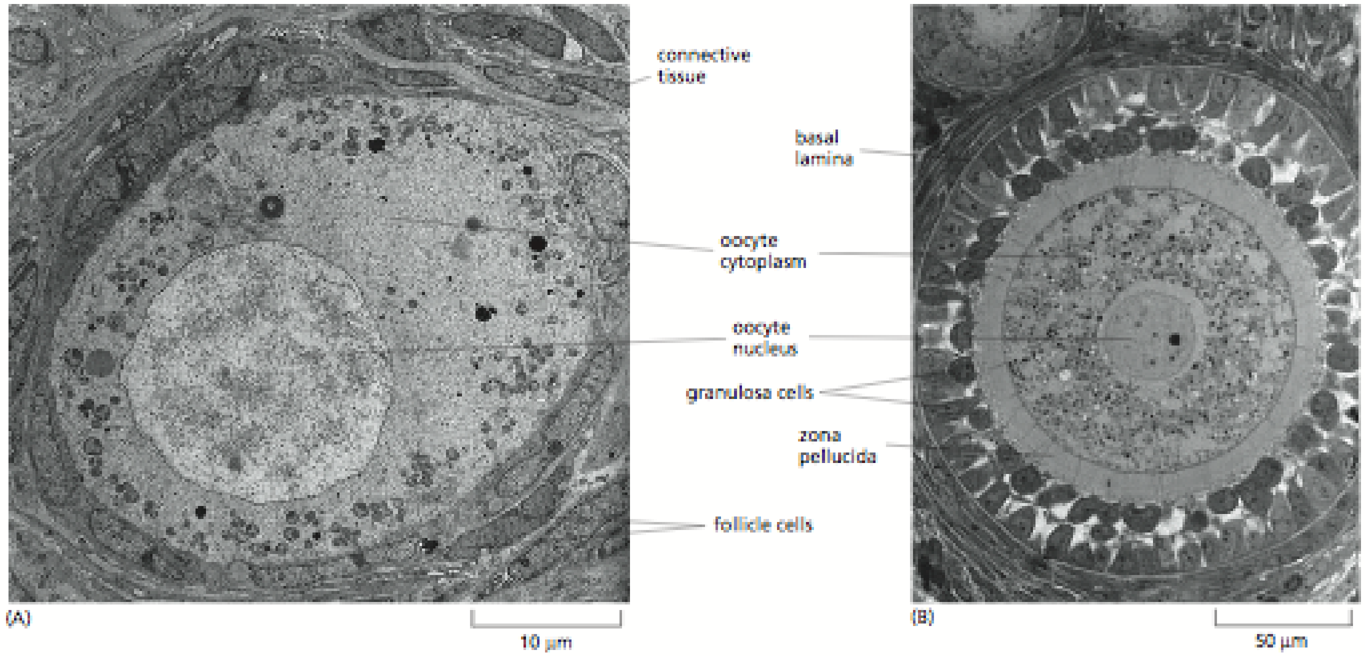


Figure 21–25 Electron micrographs of developing primary oocytes in the rabbit ovary. (A) An early stage of primary oocyte development. Neither a zona pellucida nor cortical granules have developed, and a single layer of flattened follicle cells surrounds the oocyte. (B) A more mature primary oocyte, which is shown at a sixfold lower magnification because it is much larger than the oocyte in (A). This oocyte has acquired a thick zona pellucida and is surrounded by several layers of follicle cells (now called granulosa cells) and a basal lamina, which isolate the oocyte from the other cells in the ovary. The granulosa cells are connected to one another and to the oocyte by gap junctions. (From The Cellular Basis of Mammalian Reproduction [J. Van Blerkom and P. Motta eds.]. Baltimore–Munich: Urban & Schwarzenberg, 1979.)

Most Human Oocytes Die Without Maturing

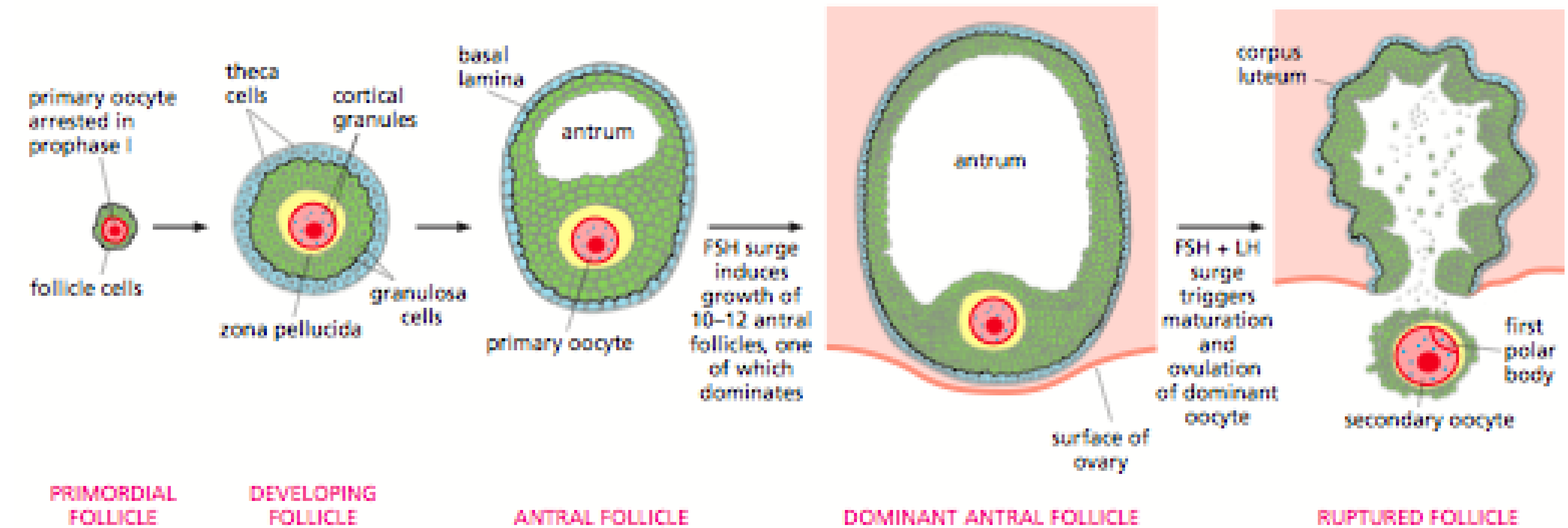


Figure 21–26 The stages in human oocyte development. Note that for most of its development the oocyte is surrounded by granulosa cells *(green)*, which are separated from an outer layer of *theca cells (blue)* by an intervening basal lamina *(black)*. After ovulation, the emptied follicle transforms into an endocrine structure, the *corpus luteum*, which secretes progesterone to help prepare the uterus for pregnancy. If fertilization does not occur, the corpus luteum regresses, and the lining of the uterus is sloughed off during menstruation.

SPERM

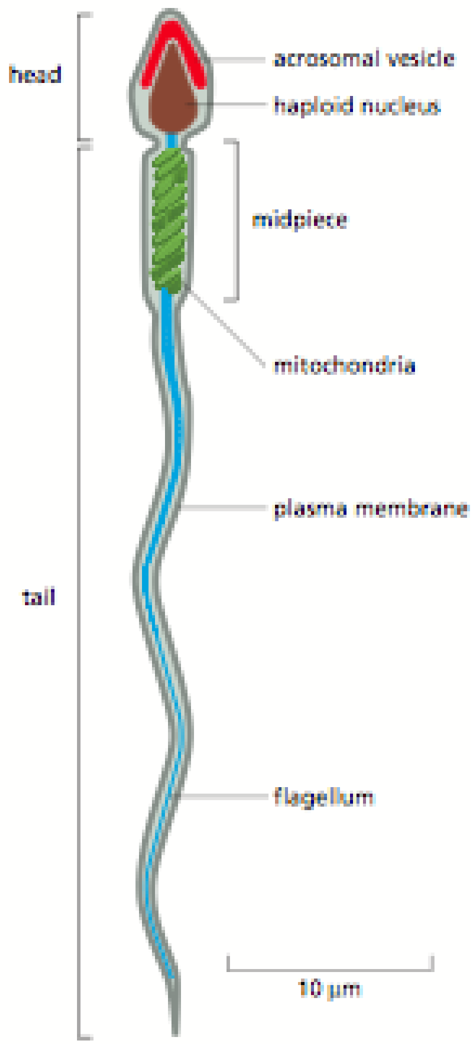


Figure 21–27 A human sperm. It is shown in longitudinal section.

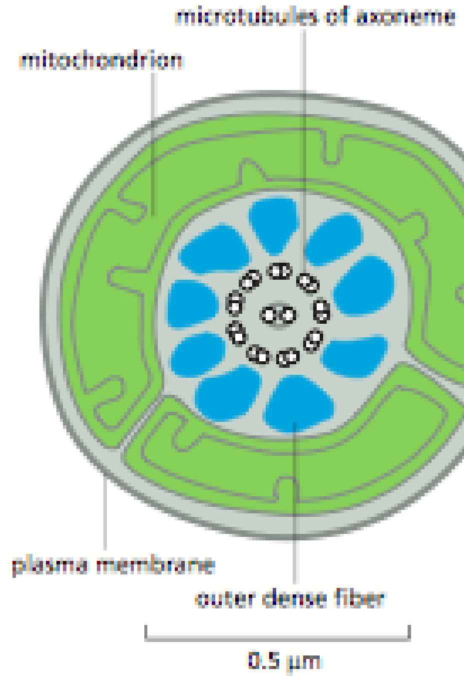


Figure 21–28 Drawing of the midpiece of a mammalian sperm as seen in cross section in an electron microscope. The core of the flagellum is composed of an axoneme surrounded by nine dense fibers. The axoneme consists of two singlet microtubules surrounded by nine microtubule doublets. The mitochondria (shown in *green*) are well placed for providing the ATP required for flagellar movement; they are distributed in an unusual spiral arrangement around the axoneme (see Figure 21–27).

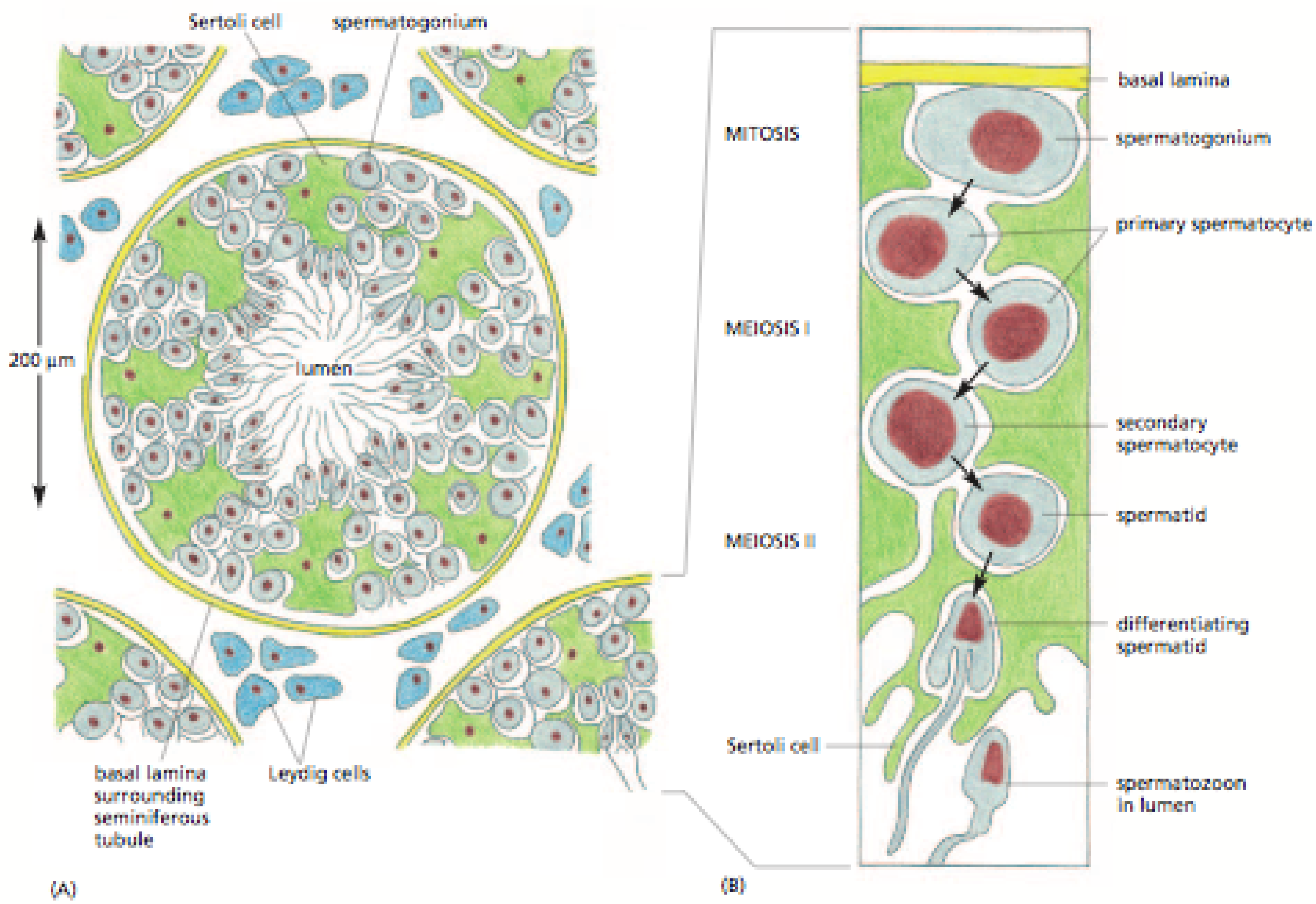


Figure 21–29 Highly simplified drawings of a cross section of a seminiferous tubule in a mammalian testis. (A) All of the stages of spermatogenesis shown take place while the developing germ-line cells are in intimate association with Sertoli cells. Sertoli cells direct sexual differentiation along a male pathway. They are large cells, extending from the basal lamina to the lumen of the seminiferous tubule; they are required for the survival of the spermatogonia and are analogous to follicle cells in the ovary (see Figure 21–19). Spermatogenesis also depends on testosterone secreted by Leydig cells, located between the seminiferous tubules. (B) Spermatogonia divide by mitosis at the periphery of the seminiferous tubule. Some of these cells enter meiosis I to become primary spermatocytes; they then complete meiosis I to become secondary spermatocytes. The secondary spermatocytes then complete meiosis II to become spermatids, which differentiate into spermatozoa (sperm) and are released into the lumen of the tubule (see Figure 21–30). In man, it takes a spermatogonium about 24 days from the onset of meiosis to emergence as a spermatid and another 5 weeks for the spermatid to develop into a sperm.

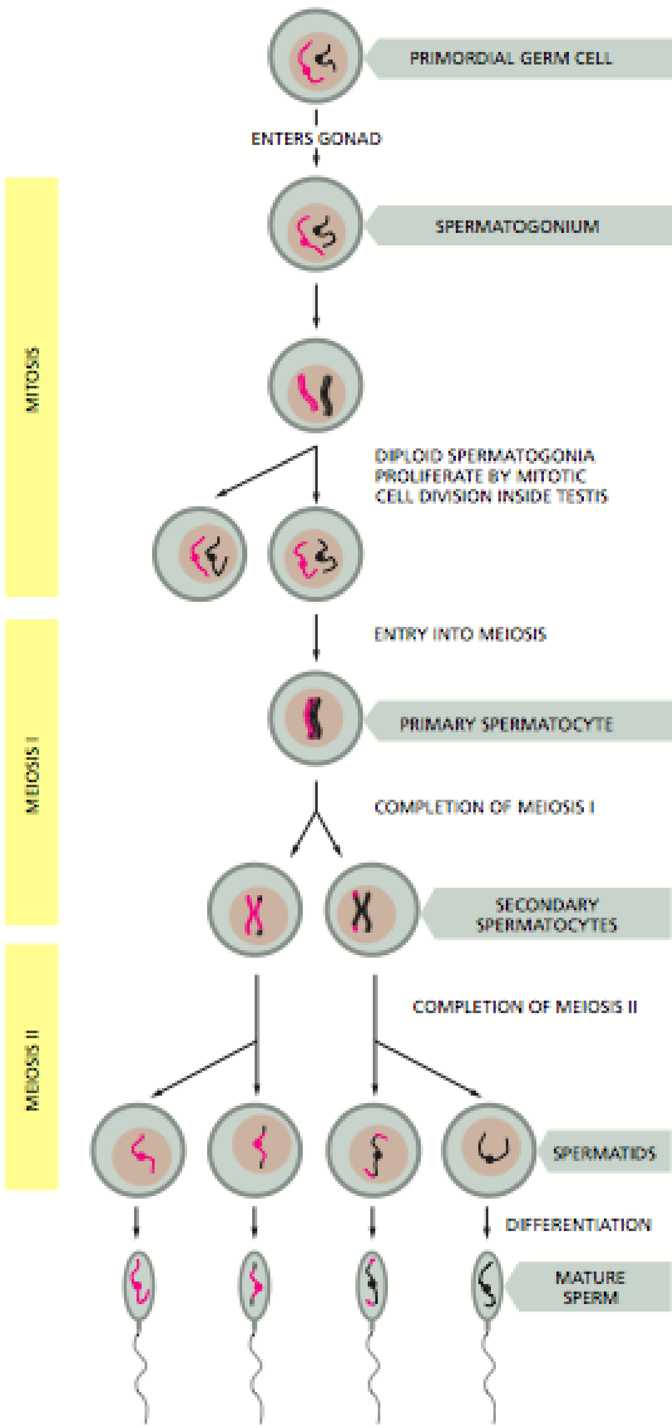


Figure 21–30 The stages of spermatogenesis. Spermatogonia develop from primordial germ cells (PGCs) that migrate into the developing gonad early in embryogenesis. When the animal becomes sexually mature, the spermatogonia begin to proliferate rapidly by mitosis. Some retain the capacity to divide indefinitely (as stem-cell spermatogonia). Others (maturing spermatogonia) undergo a limited number of mitotic division cycles before beginning meiosis to become spermatocytes, which eventually become haploid spermatids and then sperm. Spermatogenesis differs from oogenesis (see Figure 21–23) in several ways. (1) New cells enter meiosis continually from the time of puberty. (2) Each cell that begins meiosis gives rise to four mature gametes rather than one. (3) Mature sperm form by an elaborate process of cell differentiation that begins after meiosis is complete. (4) About twice as many cell divisions occur in the production of a sperm as in the production of an egg; in a mouse, for example, it is estimated that on average about 56 divisions occur from zygote to mature sperm, and about 27 divisions occur from zygote to mature egg.

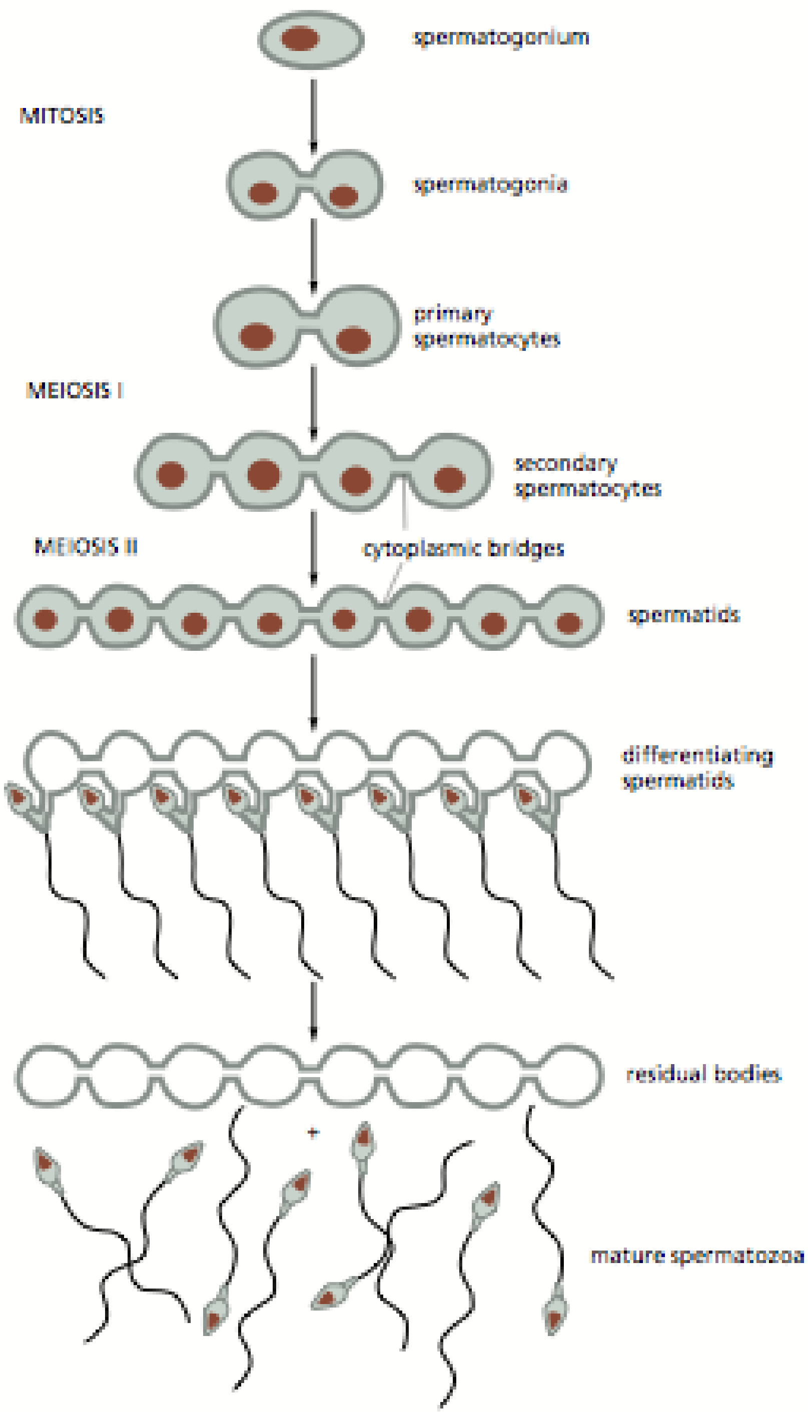


Figure 21–31 Cytoplasmic bridges in developing sperm cells and their precursors. The progeny of a single maturing spermatogonium remain connected to one another by cytoplasmic bridges throughout their differentiation into mature sperm. For the sake of simplicity, only two connected maturing spermatogonia are shown entering meiosis, eventually to form eight connected haploid spermatids. In fact, the number of connected cells that go through meiosis and differentiate synchronously is very much larger than shown here. Note that in the process of differentiating, most of the spermatid cytoplasm is discarded as *residual bodies*, which are phagocytosed by Sertoli cells.

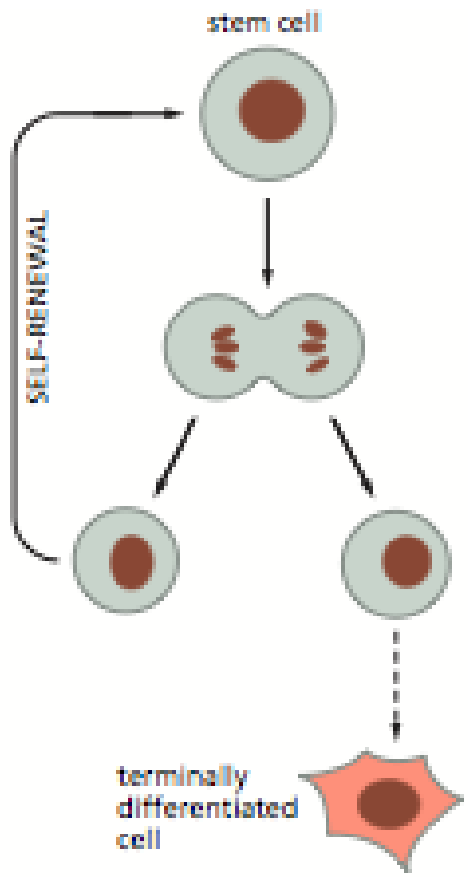


Figure 23–5 The definition of a stem cell. Each daughter produced when a stem cell divides can either remain a stem cell or go on to become terminally differentiated. In many cases, the daughter that opts for terminal differentiation undergoes additional cell divisions before terminal differentiation is completed.

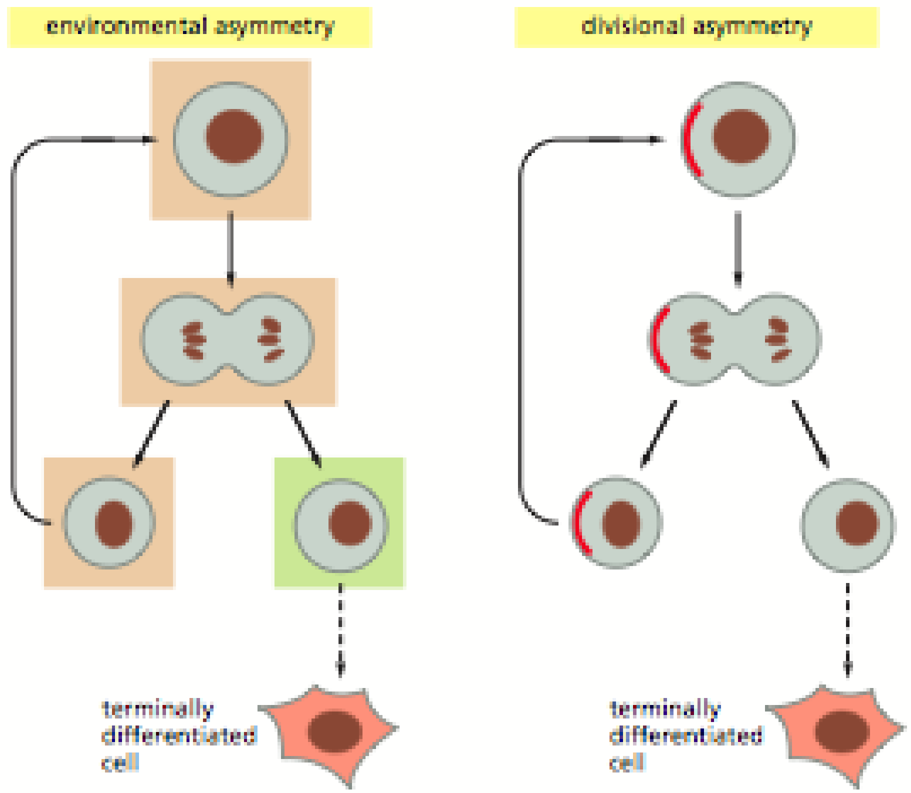


Figure 23–6 Two ways for a stem cell to produce daughters with different fates. In the strategy based on environmental asymmetry, the daughters of the stem cell are initially similar and are directed into different pathways according to the environmental influences that act on them after they are born. The environment is shown as *colored shading* around the cell. With this strategy, the number of stem cells can be increased or reduced to fit the niche available for them. In the strategy based on divisional asymmetry, the stem cell has an internal asymmetry and divides in such a way that its two daughters are already endowed with different determinants at the time of their birth. In some cases, the choice between the alternative fates may be made at random for each daughter, but with a defined probability, like a coin-toss, reflecting the intrinsic randomness or "noise" in all genetic control systems (discussed in Chapter 7).

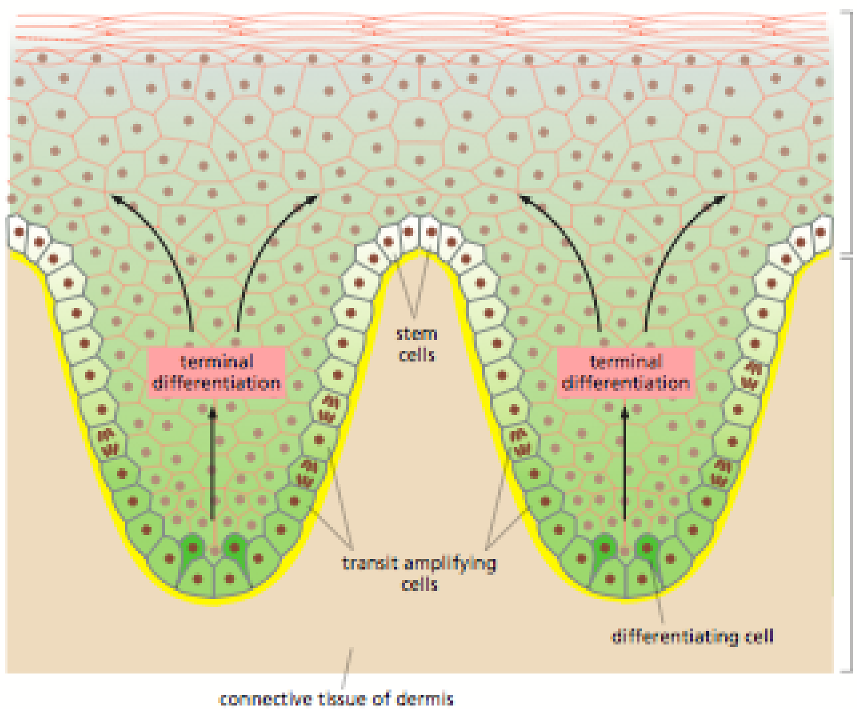


Figure 23–7 The distribution of stem cells in human epidermis, and the pattern of epidermal cell production. The diagram is based on specimens in which the location of the stem cells was identified by staining for β1 integrin, and that of the differentiating cells by staining for keratin-10, a marker of keratinocyte differentiation; dividing cells were identified by labeling with BrdU, a thymidine analog that is incorporated into cells in S phase of the cell division cycle. The stem cells seem to be clustered near the tips of the dermal papillae. They divide infrequently, giving rise (through a sideways movement) to transit amplifying cells, which occupy the intervening regions. The transit amplifying cells divide frequently, but for a limited number of division cycles, at the end of which they begin to differentiate and slip out of the basal layer. The precise distribution of stem cells and transit amplifying cells varies from one region of epidermis to another. (Adapted from S. Lowell et al., *Curr. Biol.* 10:491–500, 2000. With permission from Elsevier.)

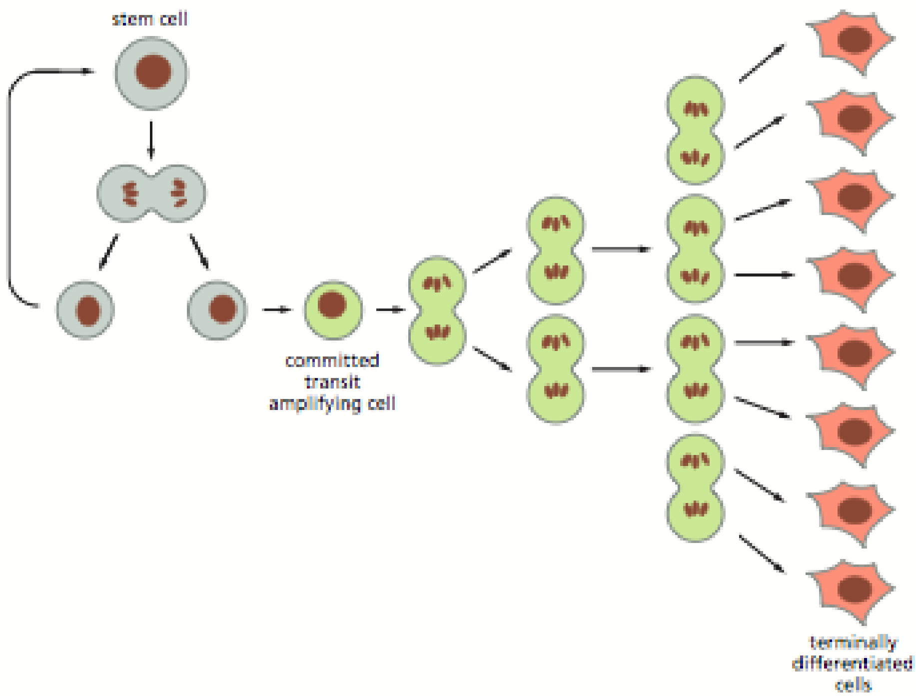


Figure 23–8 Transit amplifying cells. Stem cells in many tissues divide only rarely but give rise to transit amplifying cells—daughters committed to differentiation that go through a limited series of more rapid divisions before completing the process. In the example shown here, each stem cell division gives rise in this way to eight terminally differentiated progeny.

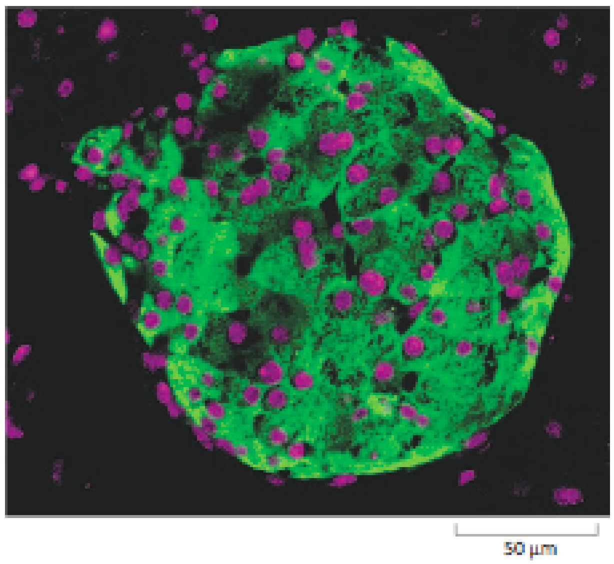


Figure 23–29 An islet of Langerhans in the pancreas. The insulin-secreting cells (β cells) are stained *green* by immunofluorescence. Cell nuclei are stained *purple* with a DNA dye. The surrounding pancreatic exocrine cells (secreting digestive enzymes and bicarbonate via ducts into the gut) are unstained, except for their nuclei. Within the islet, close to its surface, there are also small numbers of cells (unstained) secreting hormones such as glucagon. The insulin-secreting cells replace themselves by simple duplication, without need of specialized stem cells. (Adapted from a photograph courtesy of Yuval Dor. © 2004 Yuval Dor, The Hebrew University, Jerusalem.)

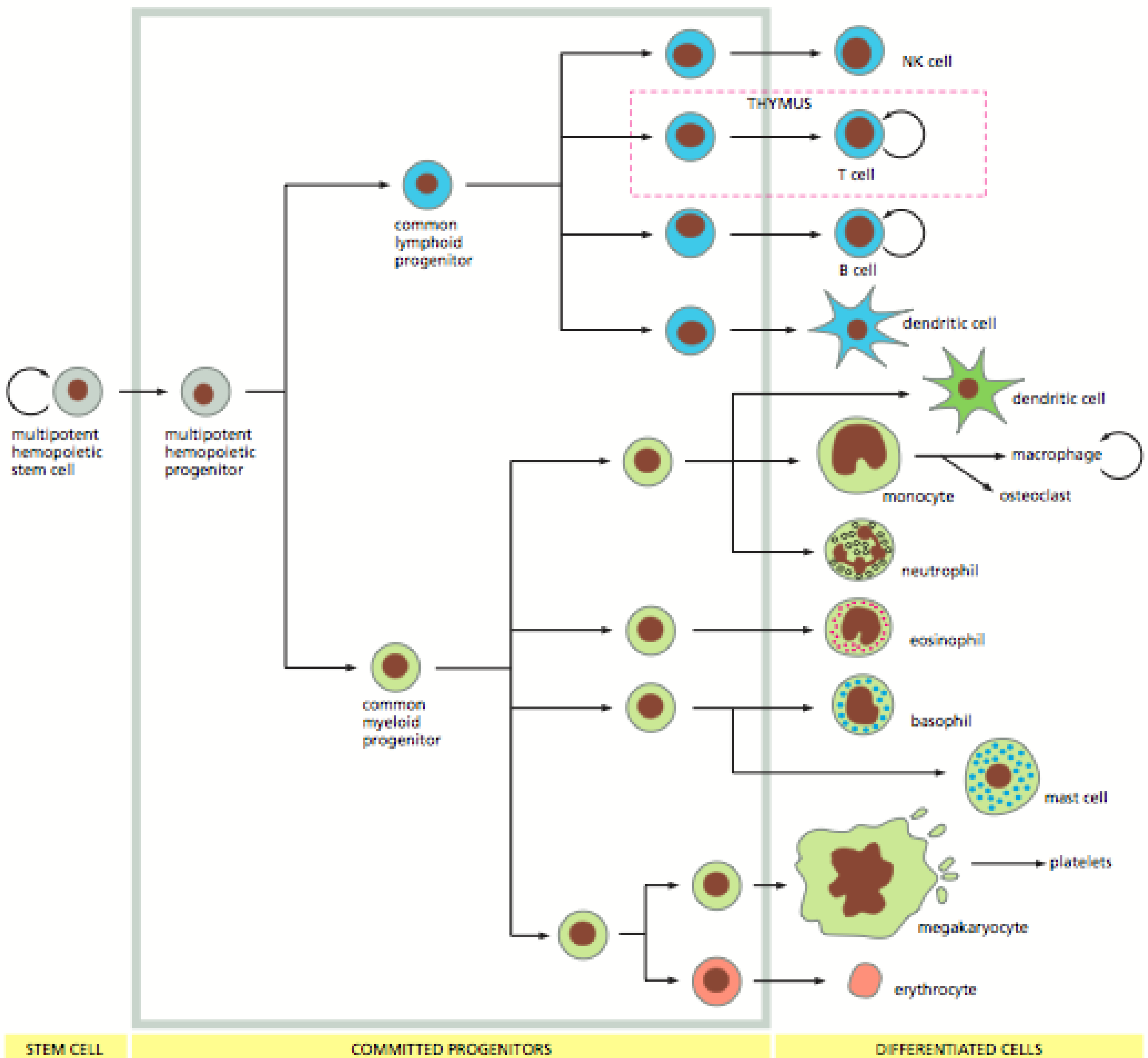


Figure 23–42 A tentative scheme of hemopoiesis. The multipotent stem cell normally divides infrequently to generate either more multipotent stem cells, which are self-renewing, or committed progenitor cells, which are limited in the number of times that they can divide before differentiating to form mature blood cells. As they go through their divisions, the progenitors become progressively more specialized in the range of cell types that they can give rise to, as indicated by the branching of the cell-lineage diagram in the region enclosed in the *gray* box. Many of the details of this part of the lineage diagram are still controversial, however. In adult mammals, all of the cells shown develop mainly in the bone marrow—except for T lymphocytes, which develop in the thymus, and macrophages and osteoclasts, which develop from blood monocytes. Some dendritic cells may also derive from monocytes.

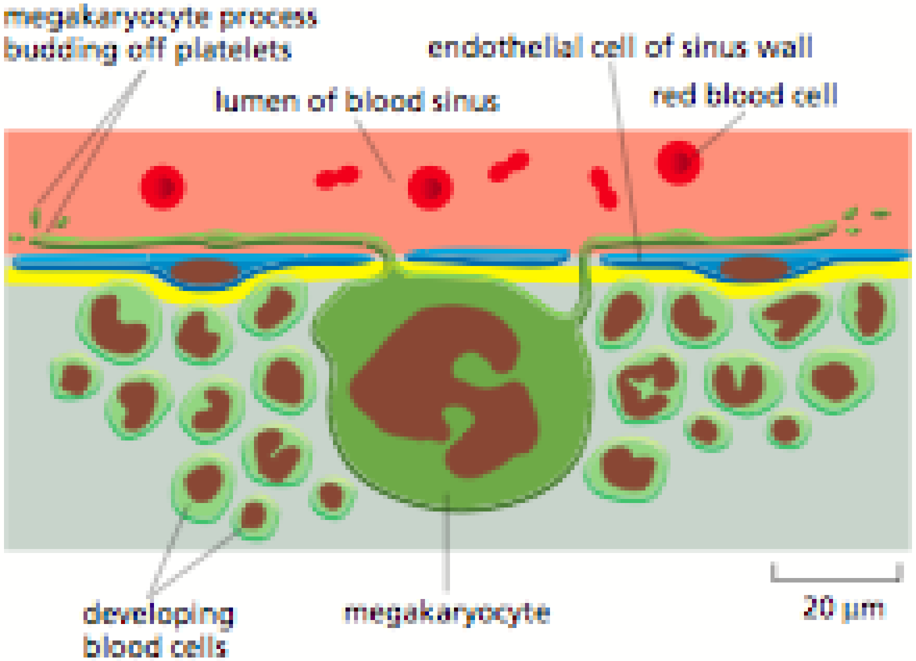


Figure 23–40 A megakaryocyte among other cells in the bone marrow. Its enormous size results from its having a highly polyploid nucleus. One megakaryocyte produces about 10,000 platelets, which split off from long processes that extend through holes in the walls of an adjacent blood sinus.

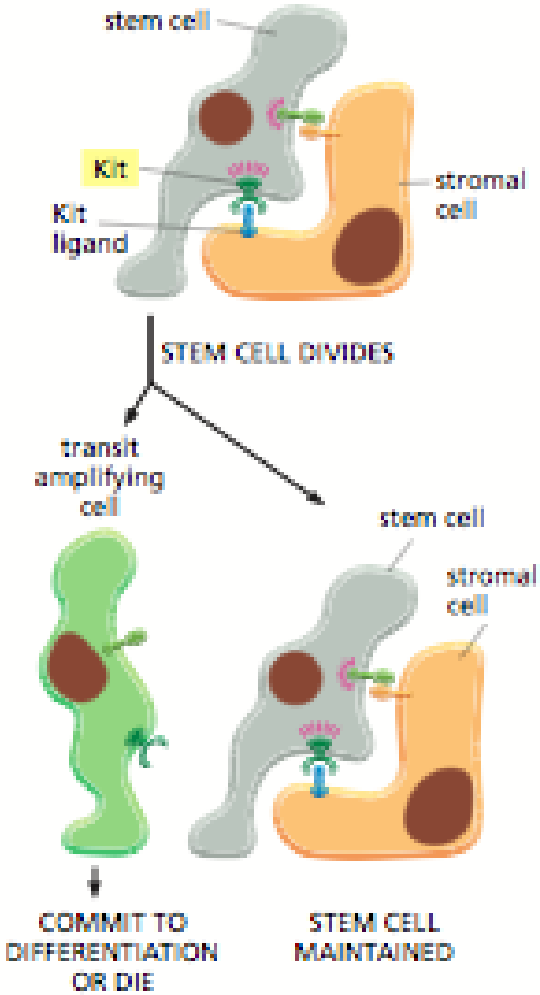


Figure 23–43 Dependence of hemopoietic stem cells on contact with stromal cells. The contact-dependent interaction between Kit and its ligand is one of several signaling mechanisms thought to be involved in hemopoietic stem-cell maintenance. The real system is certainly more complex; the dependence of hemopoietic cells on contact with stromal cells cannot be absolute, since small numbers of the functional stem cells can be found free in the circulation.

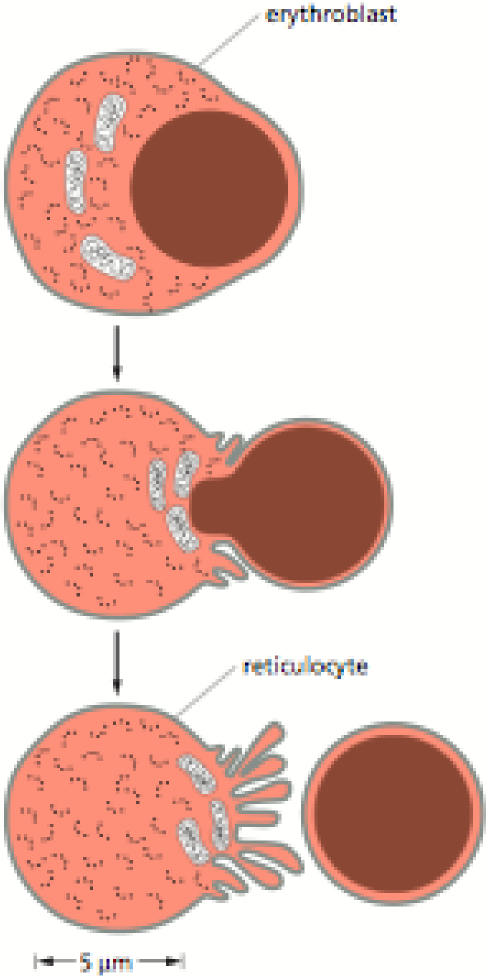


Figure 23–44 A developing red blood cell (erythroblast). The cell is shown extruding its nucleus to become an immature erythrocyte (a reticulocyte), which then leaves the bone marrow and passes into the bloodstream. The reticulocyte will lose its mitochondria and ribosomes within a day or two to become a mature erythrocyte. Erythrocyte clones develop in the bone marrow on the surface of a macrophage, which phagocytoses and digests the nuclei discarded by the erythroblasts.

Table 23–2 Some Colony-stimulating Factors (CSFs) That Influence Blood Cell Formation

FACTOR	TARGET CELLS	PRODUCING CELLS	RECEPTORS
Erythropoietin	CFC-E	kidney cells	cytokine family
Interleukin 3 (IL3)	multipotent stem cell, most progenitor cells, many terminally differentiated cells	T lymphocytes, epidermal cells	cytokine family
Granulocyte/macrophage CSF (GMCSF)	GM progenitor cells	T lymphocytes, endothelial cells, fibroblasts	cytokine family
Granulocyte CSF (GCSF)	GM progenitor cells and neutrophils	macrophages, fibroblasts	cytokine family
Macrophage CSF (MCSF)	GM progenitor cells and macrophages	fibroblasts, macrophages, endothelial cells	receptor tyrosine kinase family
Kit ligand	hemopoietic stem cells	stromal cells in bone marrow and many other cells	receptor tyrosine kinase family

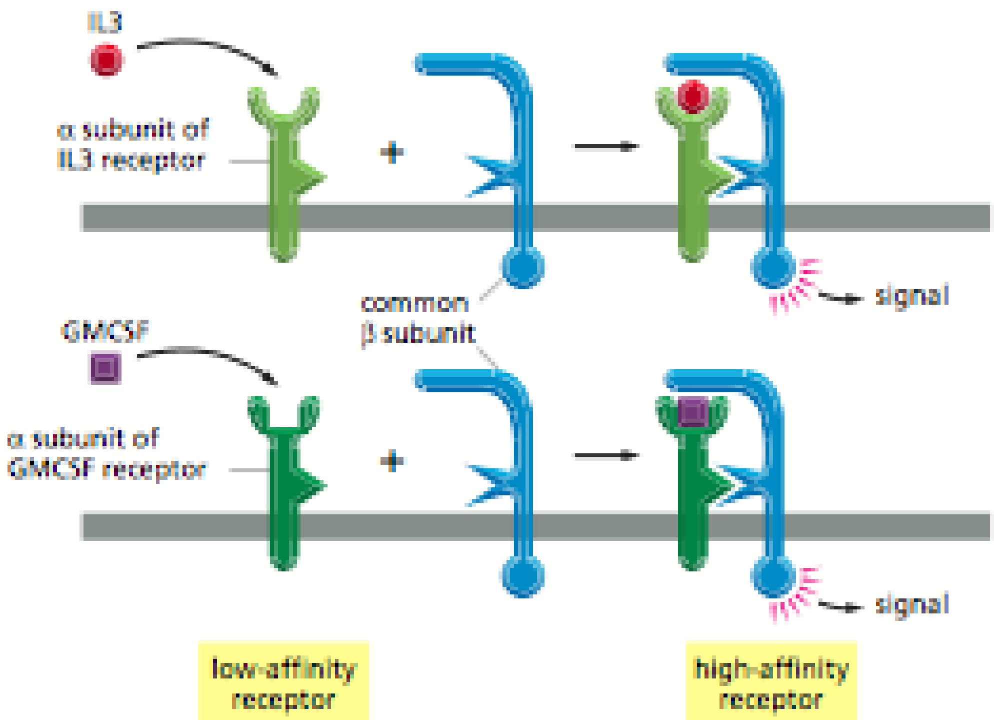


Figure 23–45 Sharing of subunits among CSF receptors. Human IL3 receptors and GMCSF receptors have different α subunits and a common β subunit. Their ligands are thought to bind to the free α subunit with low affinity, and this triggers the assembly of the heterodimer that binds the ligand with high affinity.

The Behavior of a Hemopoietic Cell Depends Partly on Chance

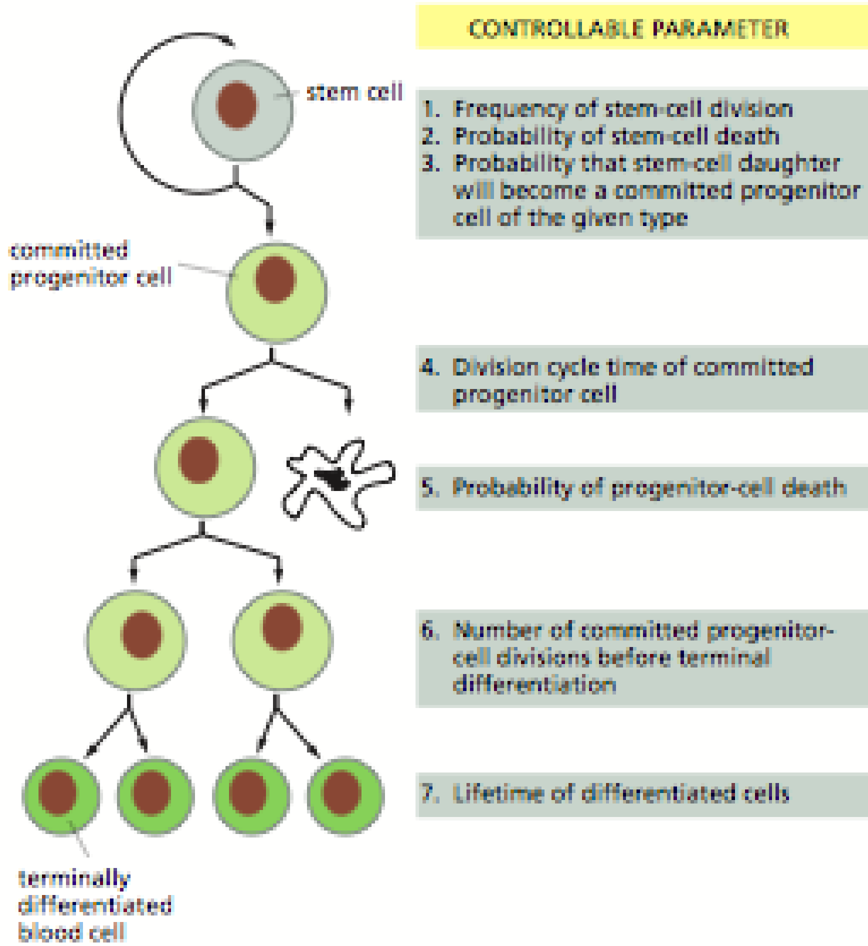


Figure 23–46 Some of the parameters through which the production of blood cells of a specific type might be regulated. Studies in culture suggest that colony-stimulating factors (CSFs) can affect all of these aspects of hemopoiesis.

Fibroblasts Change Their Character in Response to Chemical Signals

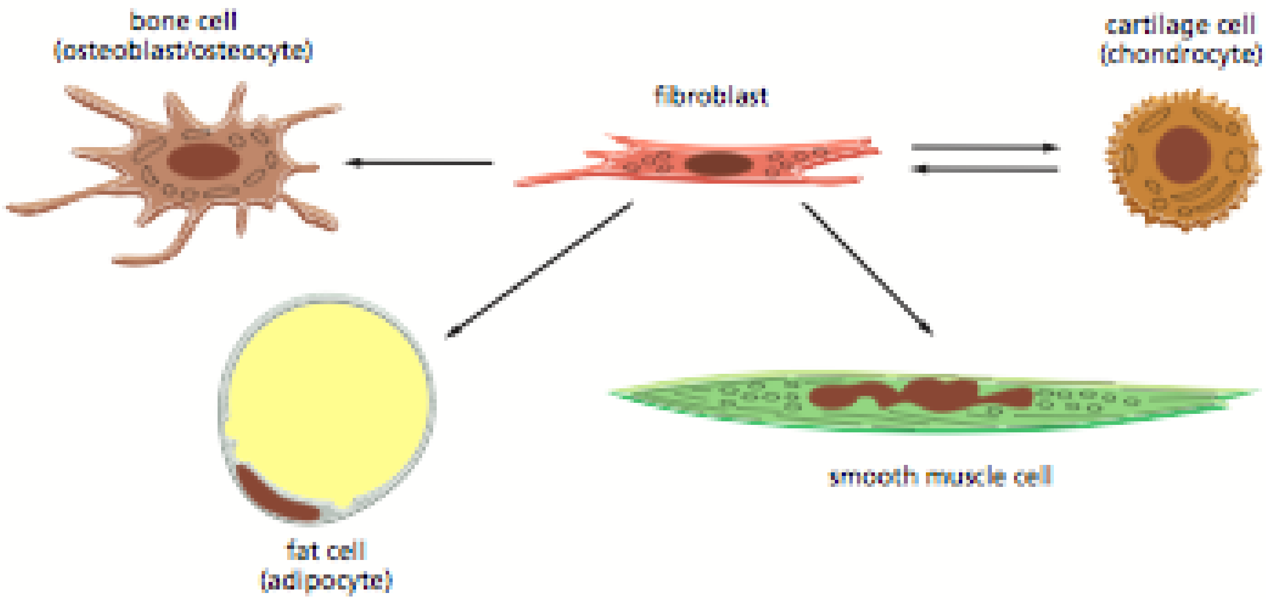


Figure 23–52 The family of connective-tissue cells. *Arrows* show the interconversions that are thought to occur within the family. For simplicity, the fibroblast is shown as a single cell type, but it is uncertain how many types of fibroblasts exist in fact and whether the differentiation potential of different types is restricted in different ways.

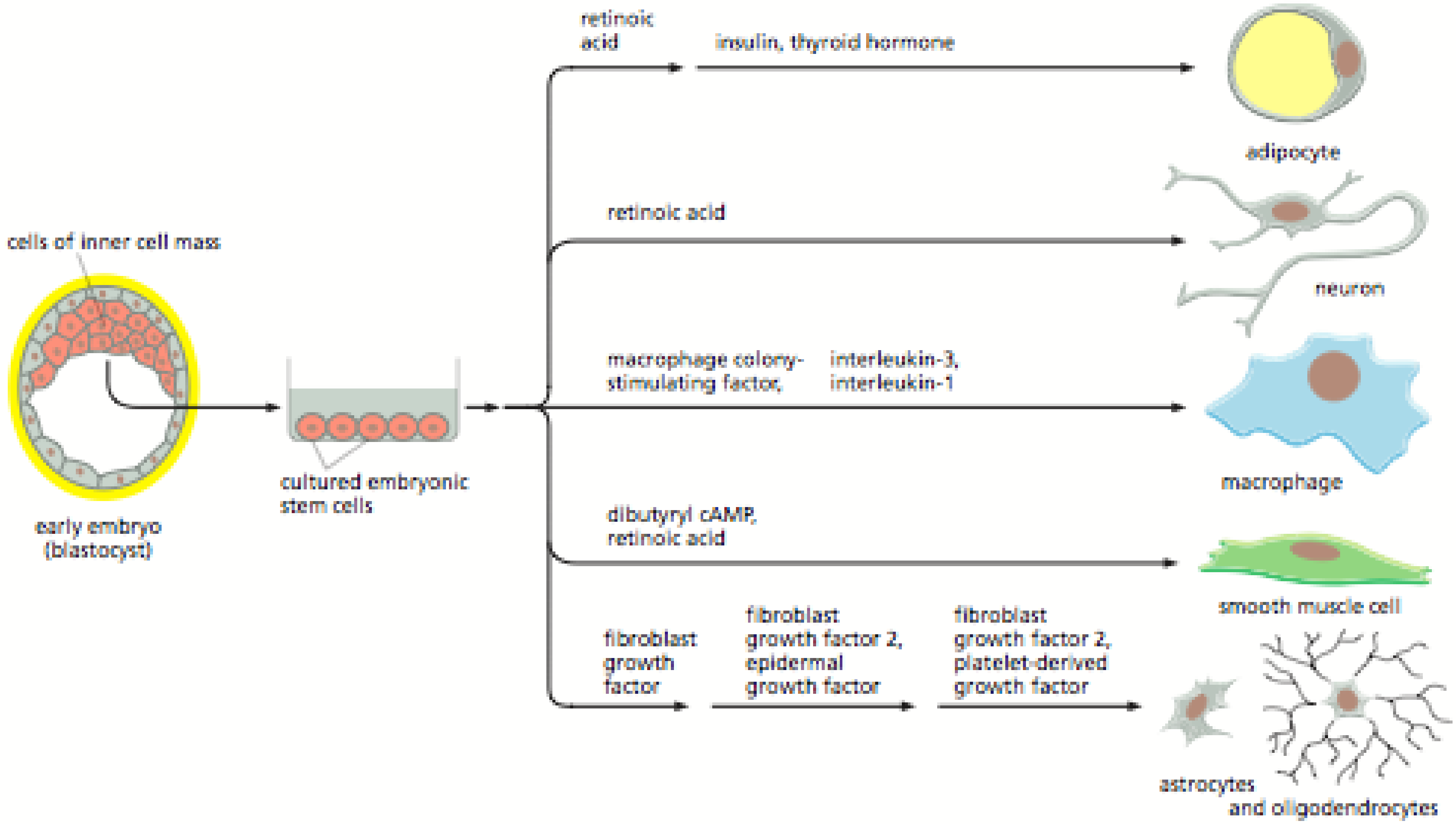


Figure 23–68 Production of differentiated cells from mouse ES cells in culture. ES cells derived from an early mouse embryo can be cultured indefinitely as a monolayer, or allowed to form aggregates called embryoid bodies, in which the cells begin to specialize. Cells from embryoid bodies, cultured in media with different factors added, can then be driven to differentiate in various ways. (Based on E. Fuchs and J.A. Segre, *Cell* 100:143–155, 2000. With permission from Elsevier.)

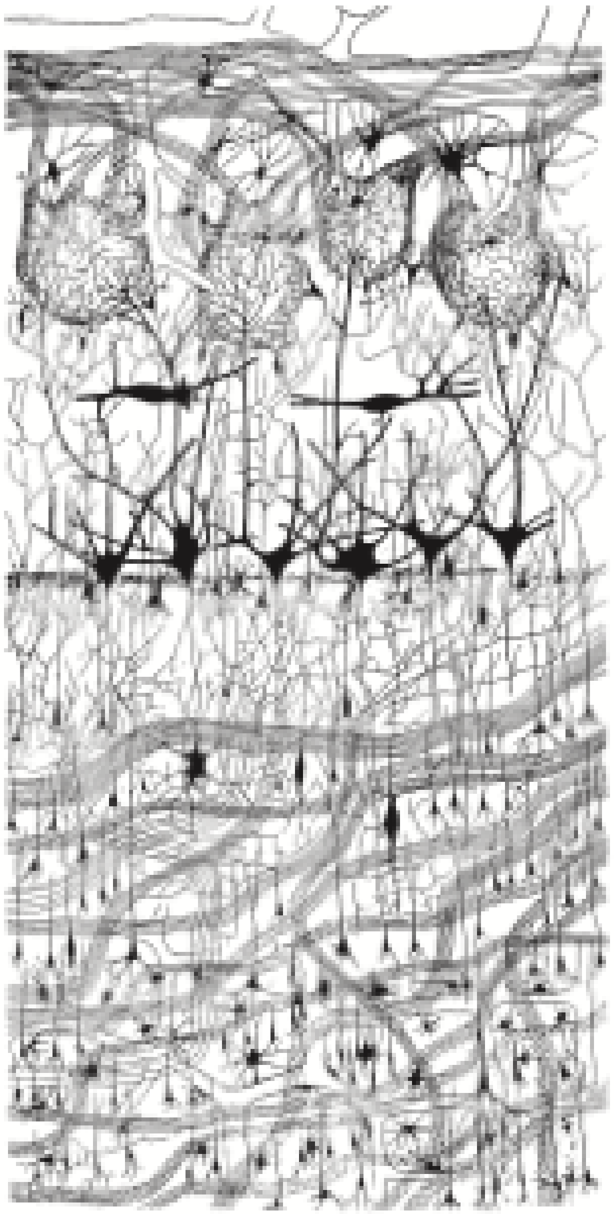
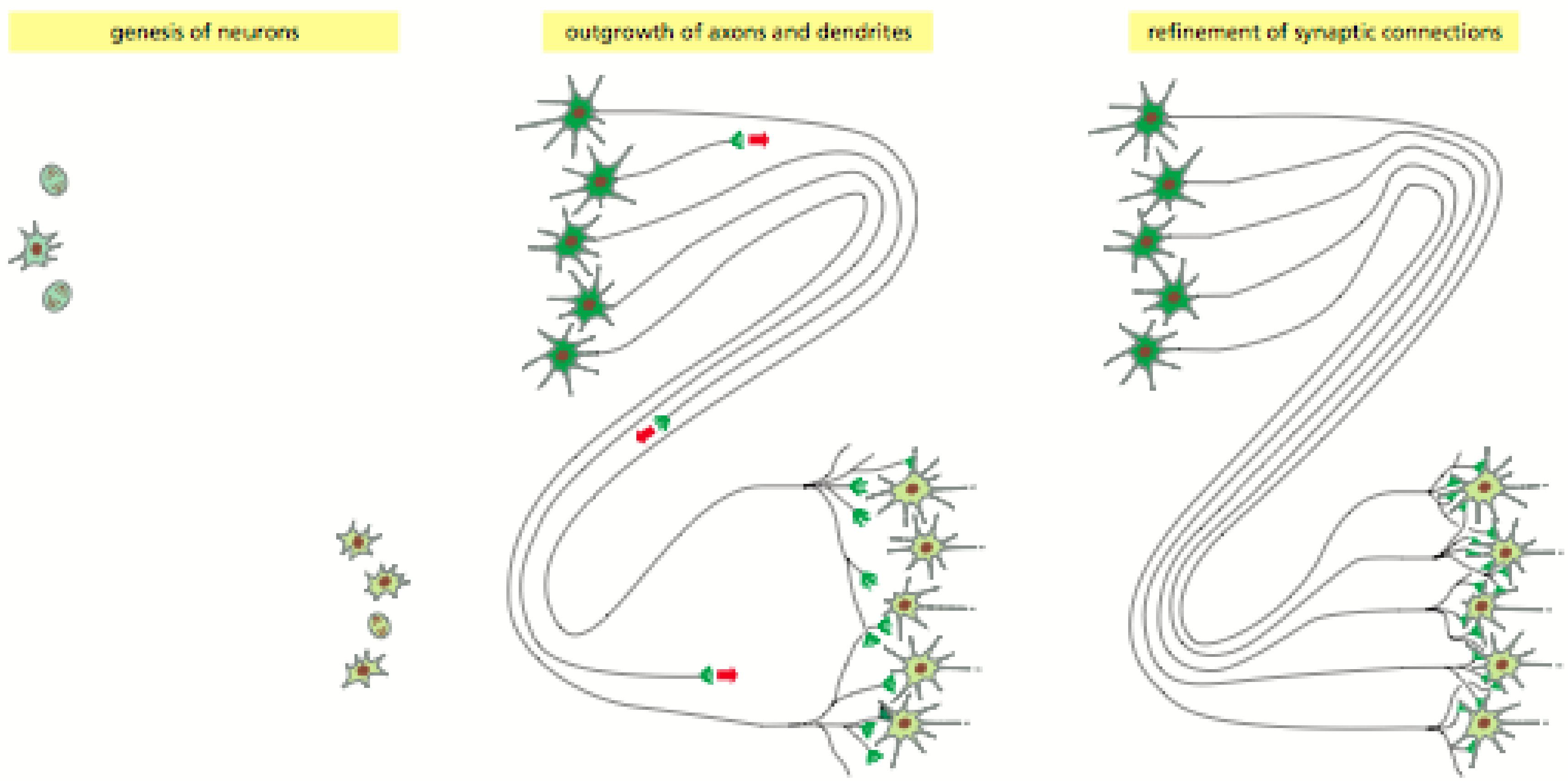


Figure 22–94 The complex organization of nerve cell connections. This drawing depicts a section through a small part of a mammalian brain—the olfactory bulb of a dog, stained by the Golgi technique. The black objects are neurons; the thin lines are axons and dendrites, through which the various sets of neurons are interconnected according to precise rules. (From C. Golgi, *Riv. sper. freniat. Reggio-Emilia* 1:405-425, 1875; reproduced in M. Jacobson, Developmental Neurobiology, 3rd ed. New York: Plenum, 1992.)


genesis of neurons
outgrowth of axons and dendrites
refinement of synaptic connections

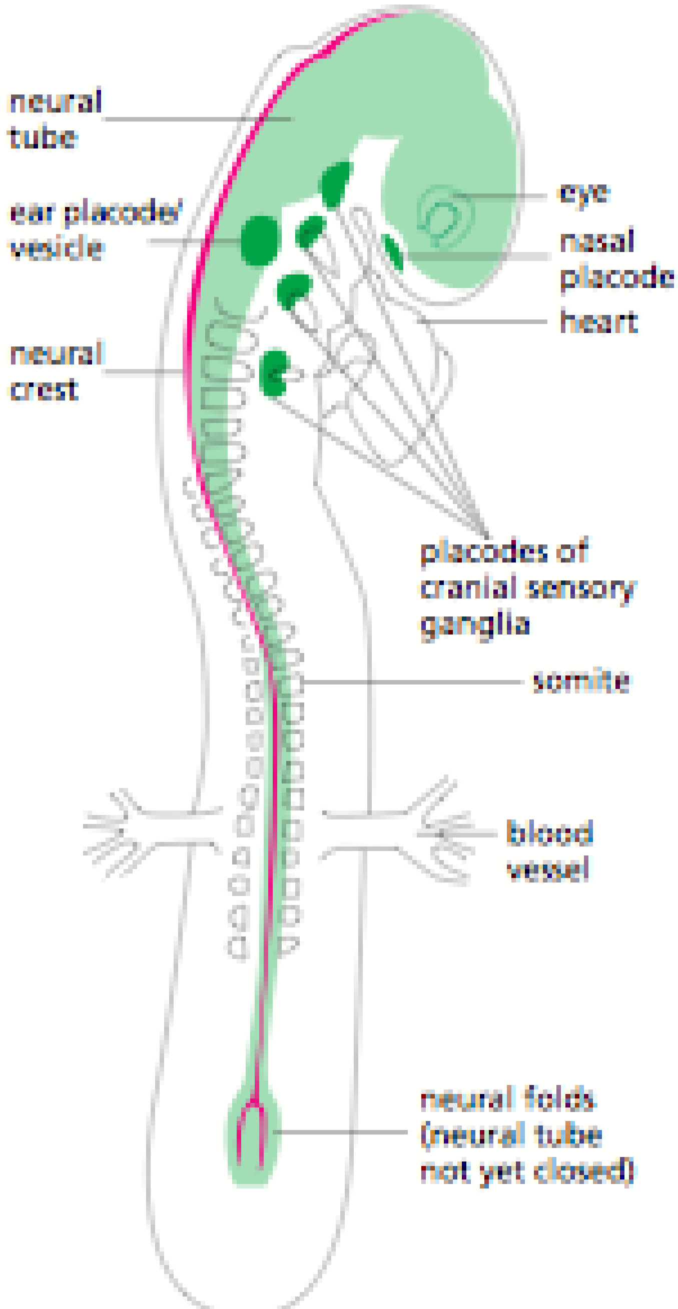


Figure 22–96 Diagram of a 2-day chick embryo, showing the origins of the nervous system. The neural tube *(light green)* has already closed, except at the tail end, and lies internally, beneath the ectoderm, of which it was originally a part (see Figure 22–78). The neural crest *(red)* lies dorsally just beneath the ectoderm, in or above the roof of the neural tube. In addition, thickenings, or placodes *(dark green)*, in the ectoderm of the head give rise to some of the sensory transducer cells and neurons of that region, including those of the ear and the nose. The cells of the retina of the eye, by contrast, originate as part of the neural tube.

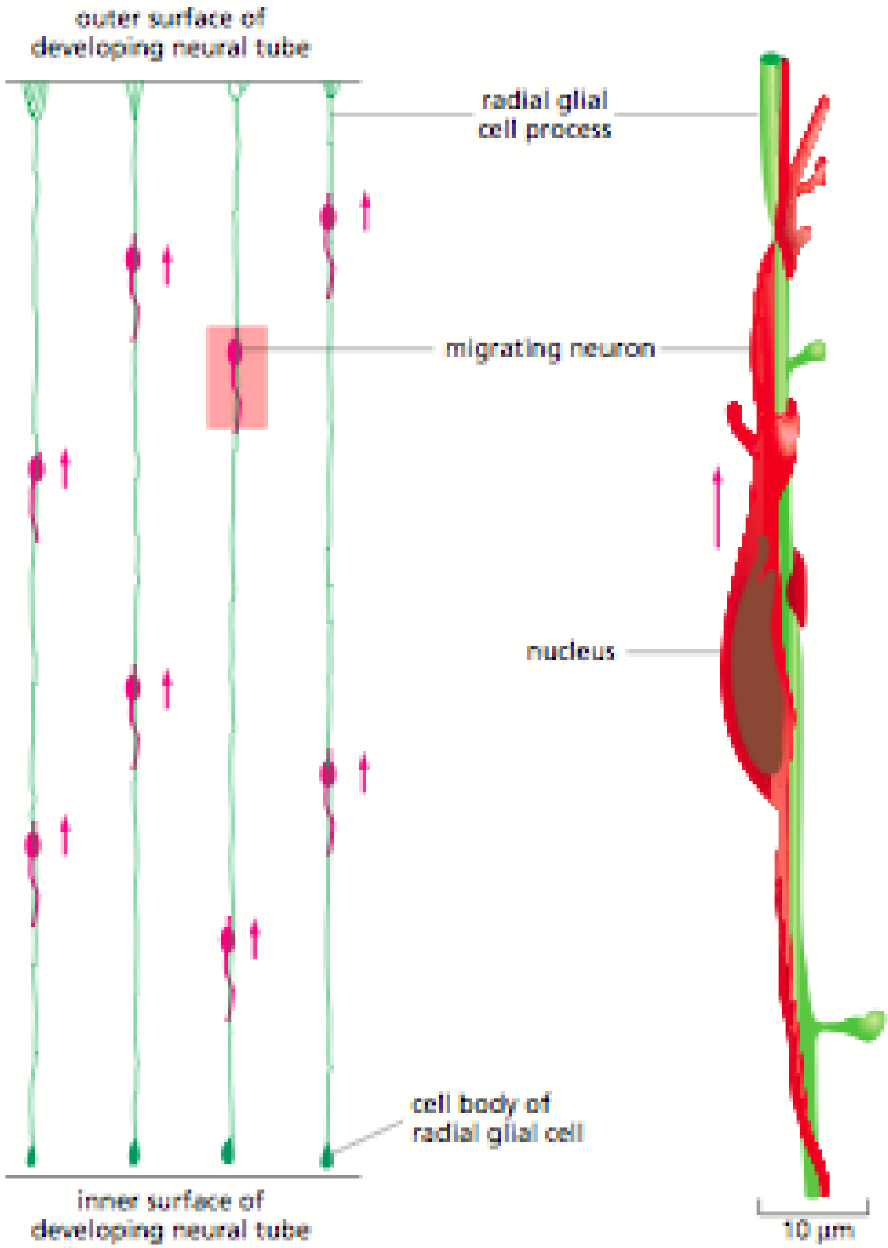


Figure 22–98 Migration of immature neurons. Before sending out axons and dendrites, newborn neurons often migrate from their birthplace and settle in some other location. The diagrams are based on reconstructions from sections of the cerebral cortex of a monkey (part of the neural tube). The neurons go through their final cell division close to the inner, luminal face of the neural tube and then migrate outward by crawling along radial glial cells. Each of these cells extends from the inner to the outer surface of the tube, a distance that may be as much as 2 cm in the cerebral cortex of the developing brain of a primate. The radial glial cells can be considered as persisting cells of the original columnar epithelium of the neural tube that become extraordinarily stretched as the wall of the tube thickens. (After P. Rakic, *J. Comp. Neurol.* 145:61–84, 1972. With permission from John Wiley & Sons, Inc.)

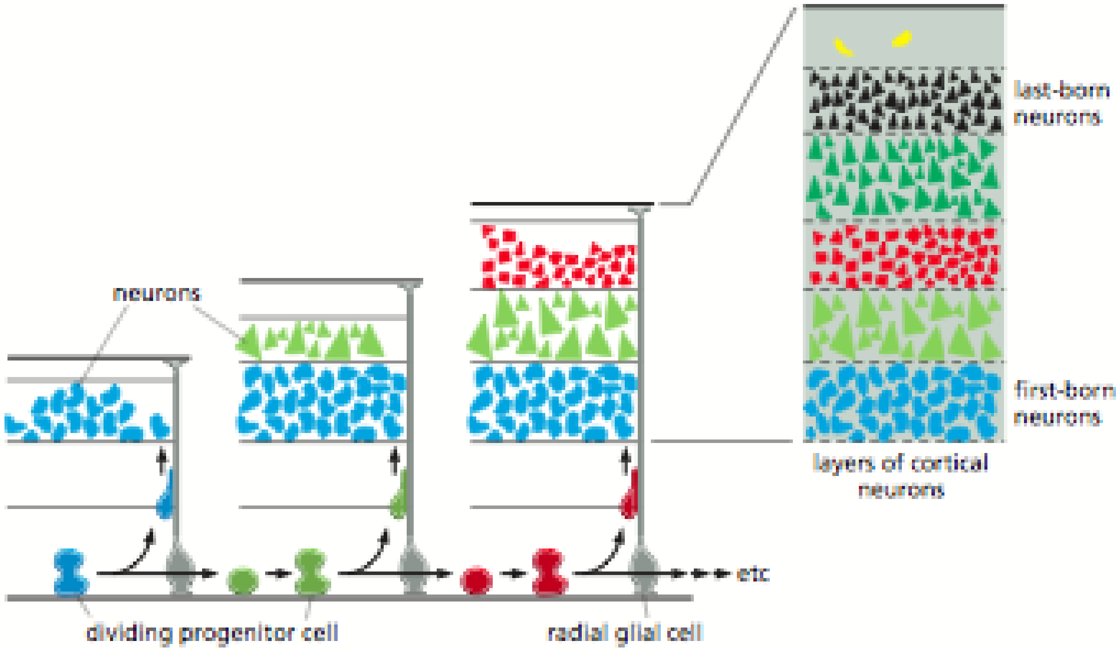


Figure 22–99 Programmed production of different types of neurons at different times from dividing progenitors in the cerebral cortex of the brain of a mammal. Close to one face of the cortical neuroepithelium, progenitor cells divide repeatedly, in stem-cell fashion, to produce neurons. The neurons migrate out toward the opposite face of the epithelium by crawling along the surfaces of radial glial cells, as shown in Figure 22–98. The first-born neurons settle closest to their birthplace, while neurons born later crawl past them to settle farther out. Successive generations of neurons thus occupy different layers in the cortex and have different intrinsic characters according to their birth dates.

Each Axon or Dendrite Extends by Means of a Growth Cone at Its Tip

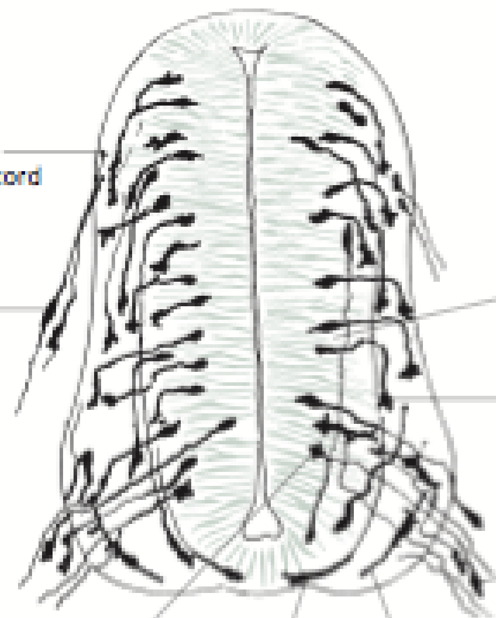


Figure 22–100 Growing axons in the developing spinal cord of a 3-day chick embryo. The drawing shows a cross section stained by the Golgi technique. Most of the neurons, apparently, have as yet only one elongated process—the future axon. An irregularly shaped expansion—a growth cone—is seen at the growing tip of each axon. The growth cones of the motor neurons emerge from the spinal cord (to make their way toward muscles), those of the sensory neurons grow into it from outside (where their cell bodies lie), and those of the interneurons remain inside the spinal cord. Many of the interneurons send their axons down toward the floor plate to cross to the other side of the spinal cord; these axons are called commissural. At this early stage, many of the embryonic spinal-cord cells (in the regions shaded *gray*) are still proliferating and have not yet begun to differentiate as neurons or glial cells. (From S. Ramón y Cajal, Histologie du Système Nerveux de l'Homme et des Vertébrés, 1909–1911. Paris: Maloine; reprinted, Madrid: C.S.I.C., 1972.)

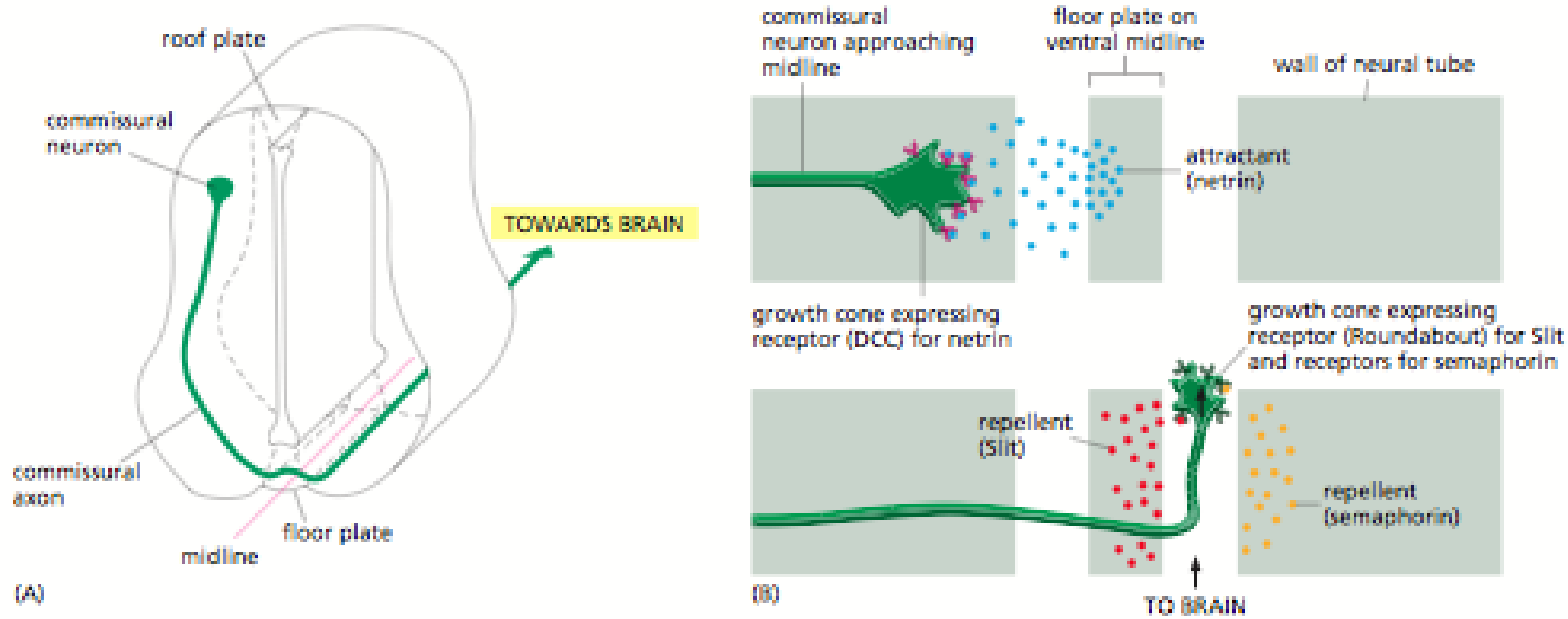
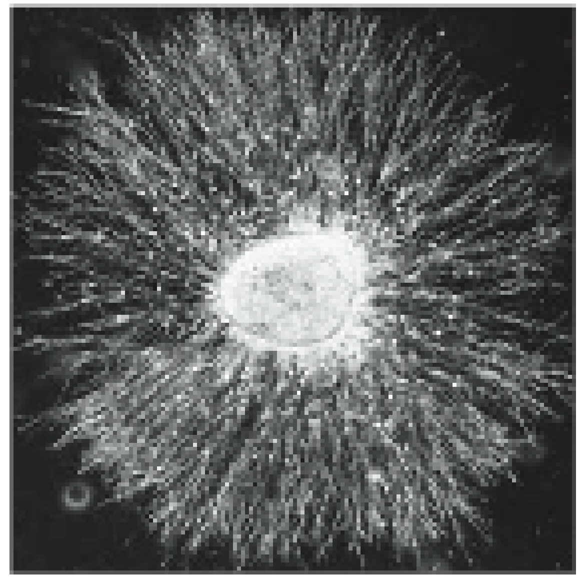


Figure 22–102 The guidance of commissural axons. (A) The pathway taken by commissural axons in the embryonic spinal cord of a vertebrate. (B) The signals that guide them. The growth cones are first attracted to the floor plate by netrin, which is secreted by the floor-plate cells and acts on the receptor DCC in the axonal membrane. As they cross the floor plate, the growth cones upregulate their expression of Roundabout, the receptor for a repellent protein, Slit, that is also secreted by the floor plate. Slit, binding to Roundabout, not only acts as a repellent to keep the cells from re-entering the floor plate, but also blocks responsiveness to the attractant netrin. At the same time, the growth cones switch on expression of receptors for another repellent protein, semaphorin, that is secreted by the cells in the side walls of the neural tube. Trapped between two repellent territories, the growth cones, having crossed the midline, travel in a tight fascicle up toward the brain.

Figure 22–103 NGF effects on neurite outgrowth. Dark-field photomicrographs of a sympathetic ganglion cultured for 48 hours with *(above)* or without *(below)* NGF. Neurites grow out from the sympathetic neurons only if NGF is present in the medium. Each culture also contains Schwann (glial) cells that have migrated out of the ganglion; these are not affected by NGF. Neuronal survival and maintenance of growth cones for neurite extension represent two distinct effects of NGF. The effect on growth cones is local, direct, rapid, and independent of communication with the cell body; when NGF is removed, the deprived growth cones halt their movements within a minute or two. The effect of NGF on cell survival is less immediate and is associated with uptake of NGF by endocytosis and its intracellular transport back to the cell body. (Courtesy of Naomi Kleitman.)



NGF

control

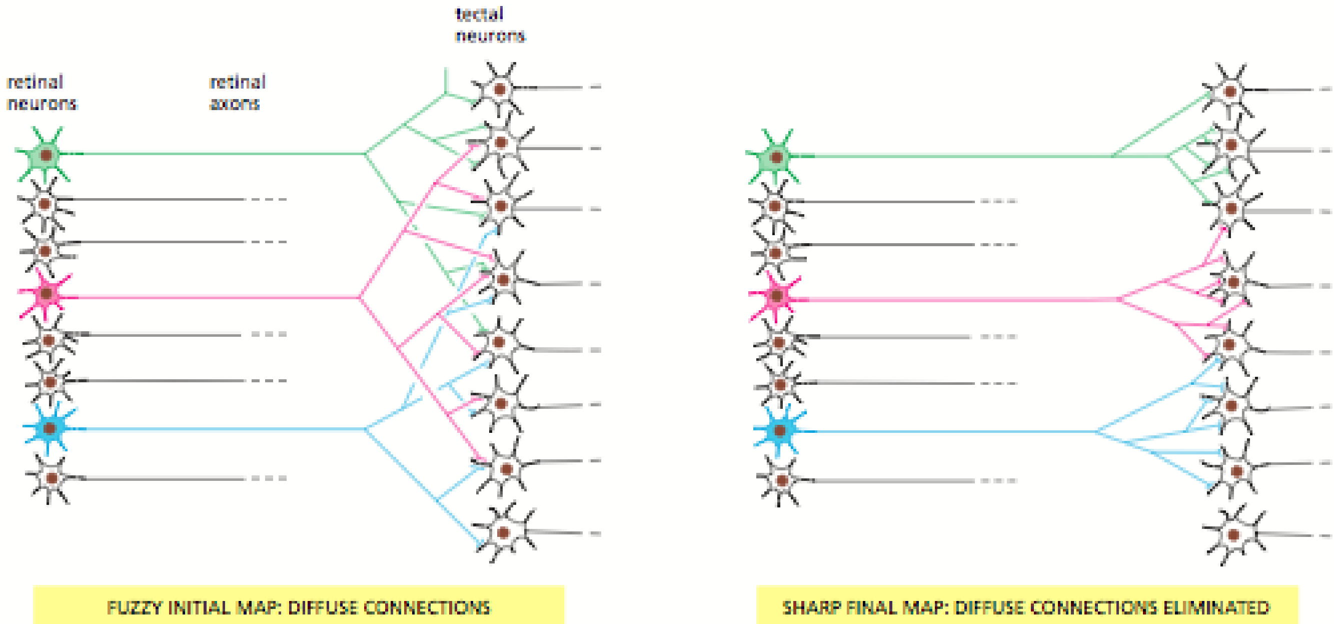


Figure 22–107 Sharpening of the retinotectal map by synapse elimination. At first the map is fuzzy because each retinal axon branches widely to innervate a broad region of tectum overlapping the regions innervated by other retinal axons. The map is then refined by synapse elimination. Where axons from separate parts of the retina synapse on the same tectal cell, competition occurs, eliminating the connections made by one of the axons. But axons from cells that are close neighbors in the retina cooperate, maintaining their synapses on shared tectal cells. Thus each retinal axon ends up innervating a small tectal territory, adjacent to and partly overlapping the territory innervated by axons from neighboring sites in the retina.

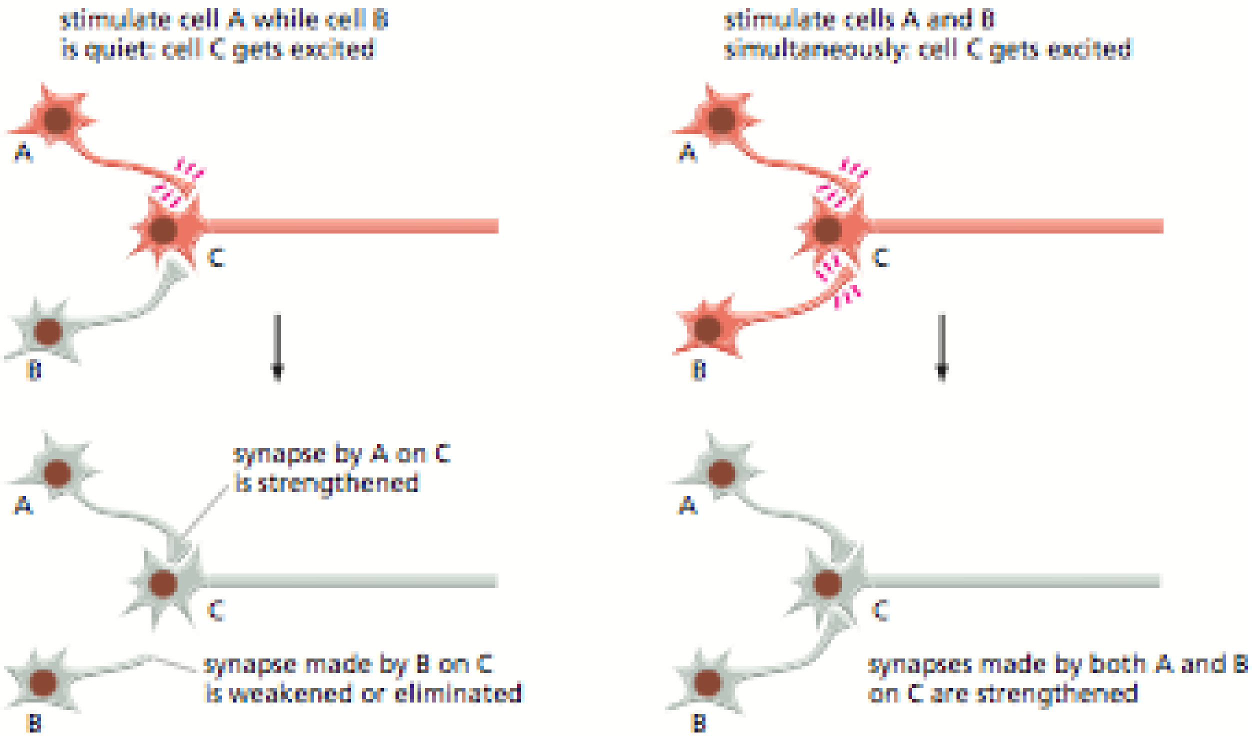


Figure 22–108 Synapse modification and its dependence on electrical activity. Experiments in several systems indicate that synapses are strengthened or weakened by electrical activity according to the rule shown in the diagram. The underlying principle appears to be that each excitation of a target cell tends to weaken any synapse where the presynaptic axon terminal has just been quiet but to strengthen any synapse where the presynaptic axon terminal has just been active. As a result, "neurons that fire together, wire together." A synapse that is repeatedly weakened and rarely strengthened is eventually eliminated altogether.

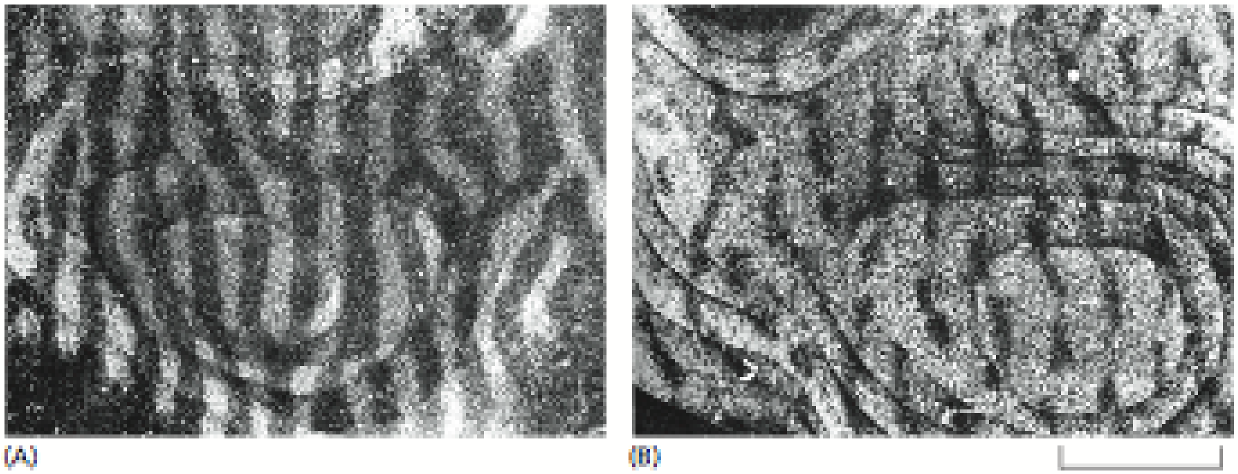


Figure 22–109 Ocular dominance columns in the visual cortex of a monkey's brain, and their sensitivity to visual experience. (A) Normally, stripes of cortical cells driven by the right eye alternate with stripes, of equal width, driven by the left eye. The stripes are revealed here by injecting a radioactive tracer molecule into one eye, allowing time for this tracer to be transported to the visual cortex, and detecting radioactivity there by autoradiography, in sections cut parallel to the cortical surface. (B) If one eye is kept covered during the critical period of development, and thus deprived of visual experience, its stripes shrink and those of the active eye expand. In this way, the deprived eye may lose the power of vision almost entirely. (From D.H. Hubel, T.N. Wiesel and S. Le Vay, *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 278:377–409, 1977. With permission from The Royal Society.)

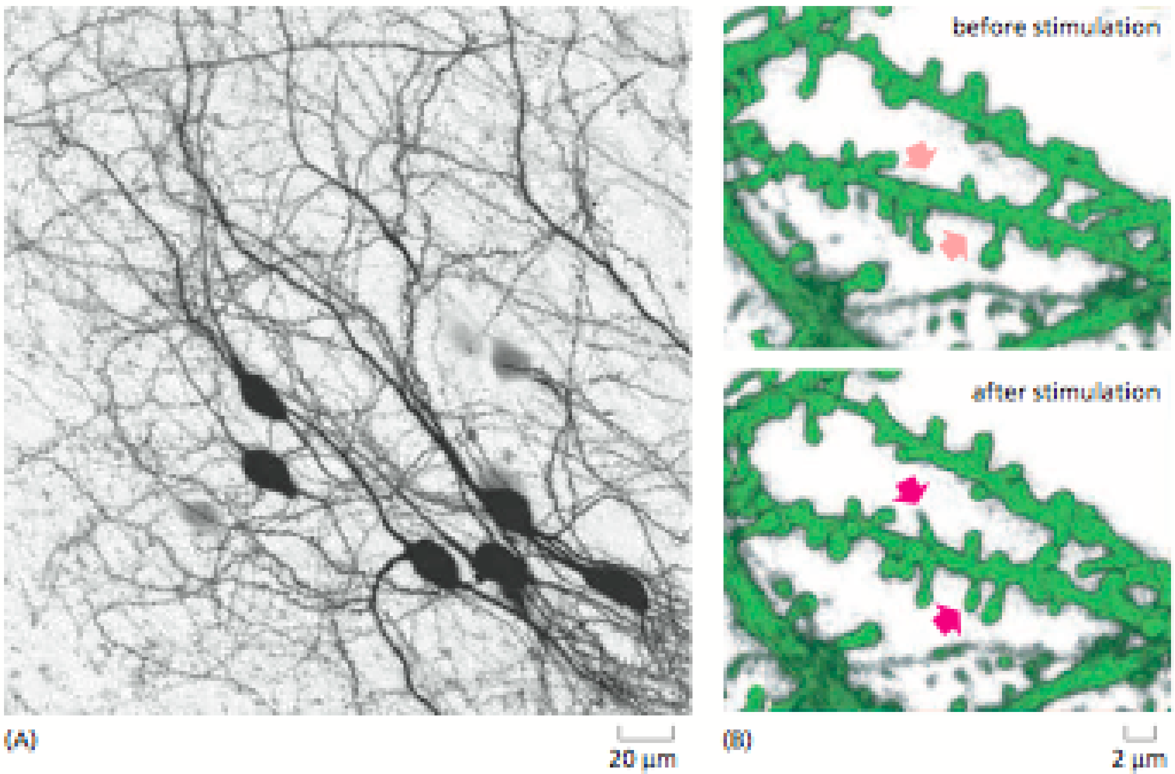


Figure 22–110 Growth of dendritic spines in response to synaptic stimulation. (A) Neurons in a slice of living tissue from the hippocampus of a young mouse. The cells are labeled by expression of Green Fluorescent Protein and observed with a two-photon laser scanning microscope, which allows individual dendrites to be seen at high resolution. The insert shows a processed image of a small part of some of the dendrites. These are covered with tiny dendritic spines, which are the sites of synapses. (B) Repeated intense bursts of synaptic stimulation, triggered by a nearby microelectrode, cause new spines to form within 30 minutes. Low-frequency stimulation has an opposite effect, causing a subset of spines to regress. (From U.V. Nägerl, N. Eberhorn, S.B. Cambridge and T. Bonhoeffer, *Neuron* 44:759–767, 2004. With permission from Elsevier.)