- Brains change with development, experience, and learning and memory. Understanding the structural and synaptic bases of these changes is a major challenge to investigators.
- The PNS of vertebrates has a somatic division that controls skeletal muscle and an autonomic division that controls effectors associated with internal organs. The autonomic nervous system is divided into sympathetic and parasympathetic divisions, which usually have opposite physiological effects, and the enteric division, which controls gut contraction and other aspects of digestive tract physiology.

Biological Clocks

Animals (and other organisms) possess endogenous physiological timing mechanisms termed **biological clocks** that rhythmically modulate the functioning of cells, tissues, and organs. Biological clocks endow an animal with an intrinsic **temporal organization**, a timed pattern of change in physiology or behavior that is independent from a change in environment (see Chapter 1, pages 14–16, for discussion of temporal frameworks in animal physiology). Biological clocks are typically operations of the nervous system, controlling physiological and behavioral processes via nervous and neuroendocrine output. Characteristically, the physiological state of an animal is endogenously different at different times of day, or in different seasons of the year. One such change is the sleep–wake cycle, discussed in **Box 15.3**.

Biological clocks orchestrate daily and seasonal changes, controlling and integrating the changes in physiological states. **Figure 15.12** shows the daily variation in several physiological functions in a 24-year-old man. These data are from one of the earliest studies designed to test whether humans have endogenous, physiological mechanisms for keeping track of time. The man was placed in living quarters that were entirely isolated from the outside world. He had no clocks in his environment and was unable to distinguish between day and night. Thus he slept, ate, and urinated without any environmental cues. Three dramatic conclusions can be reached by study of these results. First, the man continued to exhibit regular cycles in all the variables studied. Second, he tended to exhibit internal synchronization of his cycles: On any one day, he tended to have the highest rectal temperature and to excrete the most during the block of time when he was principally awake. Finally, however, he did not stay synchronized with the outside world: Relative to clock time in the outside world, his cycles became later and later as the days went by, so that—for example—after 13 days, he elected to be awake after midnight rather than before midnight (outside world time).

Put loosely, the man in Figure 15.12 was able to keep track of time endogenously, but his internal biological clock was not able to stay precisely synchronized with outside time, so that his rhythm was said to be *free-running* (see below). As we will see, these properties are very general among animals.

Organisms have endogenous rhythms

A *rhythm* is a regular, cyclical variation in function. Rhythms that continue in the absence of environmental information about time, such as those of the man in Figure 15.12, are termed **endogenous rhythms**. The first organisms in which endogenous rhythms were demonstrated were certain plants that raise their leaves during some times of day and lower them at others.[3] In 1729, the Frenchman M. de Mairan reported that these plants continue to raise and lower their leaves in approximately a daily rhythm even when they are kept in constant darkness and at constant temperature. That is, their rhythm of leaf movements is intrinsic or endogenous: It continues in more or less a daily pattern *even when the plants are denied environmental sources of information about the time of day*. Experiments of a similar nature have since been performed on many plant and animal systems, and daily

[3] In our discussion of rhythms and biological clocks, we will consistently use the words *day* and *daily* to refer to the 24-hour day, not just to hours of daylight.

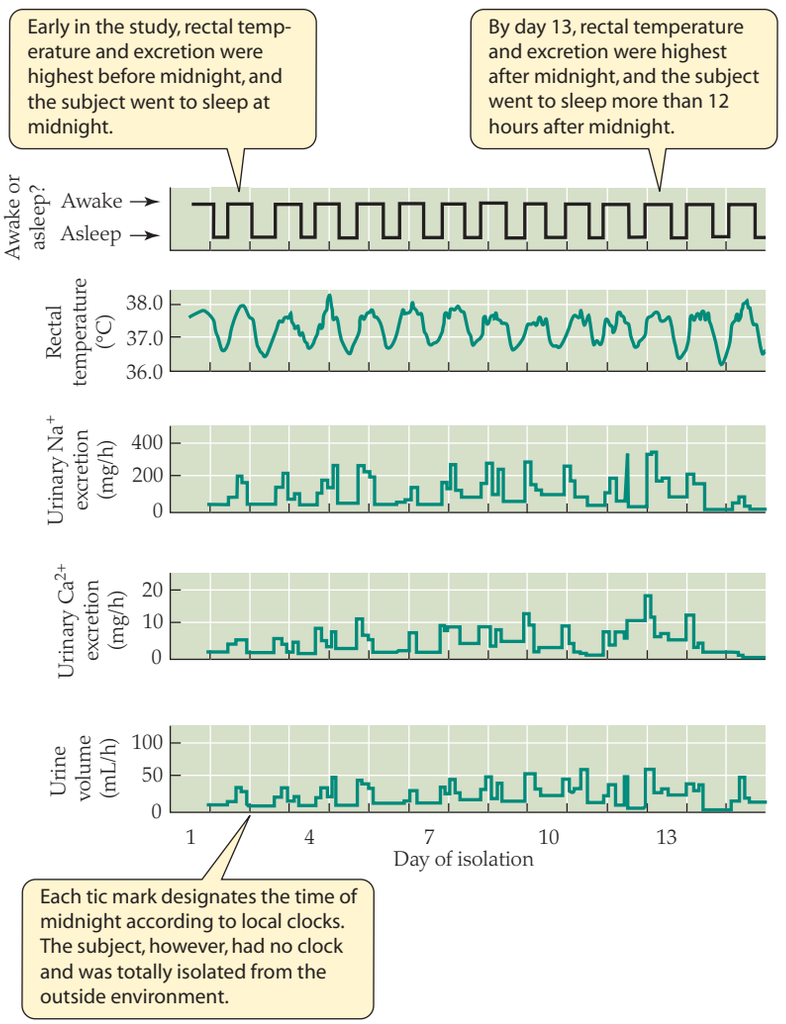


FIGURE 15.12 Daily rhythm of several physiological functions in a human A young man lived by himself in an apartment without clocks, telephones, windows, or other avenues whereby he could know the time of day in the outside world. He could turn the lights on and off, prepare food, go to bed, urinate, and engage in other processes of daily living, but his timing of those activities was based entirely on his endogenous, physiological sense of time. This graph shows his patterns of variation in five remotely monitored functions during his first 15 days of life without knowledge of external time. (After Wever 1979.)

BOX 15.3 SLEEP David S. Garbe

Why animals sleep continues to be one of the most elusive and mysterious questions in biology. Sleep, nonetheless, is found widely among animals—from relatively simple phyla such as worms (e.g., *Caenorhabditis elegans*) to higher-order groups such as humans—suggesting that sleep is a required, evolutionarily conserved behavior. Yet from certain perspectives, sleep could be considered disadvantageous to an organism's overall survival and fitness because while animals are sleeping, they are not immediately able to eat, mate, or protect themselves from predation. Still we as humans sleep for approximately one-third of our entire lives. Most scientists conclude that there must be an overriding benefit of sleep that compensates for the lack of interaction with the surrounding environment. In fact, sleep is crucial for survival. Long-term sleep deprivation is lethal to rodents and fruit flies (*Drosophila melanogaster*). Moreover, disturbances in sleep and its regulation are associated with several chronic human disease states, including insulin resistance and diabetes, fatal familial insomnia, shift-work disorder, certain neurodegenerative diseases, and major depressive disorder. **Box Extension 15.3** discusses functions of sleep and mechanisms of its regulation.

Rhesus macaque (*Macaca mulatta*)

rhythms in many types of function in many types of organisms have been shown to persist in constant laboratory environments.

The **period** of a rhythm is the amount of time between a particular part of the rhythm in one cycle (one day) and that same part in the next cycle. Typically the period is measured as the time between the start of one day's episode of activity and the start of the next day's. For example, in the case of Mairan's plants, the period could be measured as the time between the start of leaf raising on one day and the start of leaf raising on the next.

An endogenous rhythm that has a period of about a day is termed a **circadian rhythm** (*circa*, "about"; *dies*, "a day"). Not all daily rhythms prove to be endogenous when tested. Only those that are endogenous—that can persist in the absence of environmental information about the time of day—are properly termed circadian. Circadian rhythms appear to occur in all eukaryotes and some prokaryotes. Thus a capacity for endogenous rhythmicity is believed to be an ancient feature of life. **Table 15.3** lists some examples of the known endogenous circadian rhythms.

Under normal conditions in a state of nature, circadian rhythms are tightly coupled to environmental cues such as a daily light–dark cycle. **Figure 15.13*a*** shows the locomotor activity and metabolic rate of a chaffinch (*Fringilla* sp.) initially kept on a normal light–dark cycle. In diurnal species such as a chaffinch, locomotor activity, metabolic rate, and many other physiological variables increase during the day, usually starting near dawn. Two rhythms are said to be **in phase** if they occur synchronously. Thus, for a chaffinch exposed to a normal light–dark cycle, as you can see from Figure 15.13*a*, both locomotor activity and metabolic rate are in phase with the light–dark cycle.

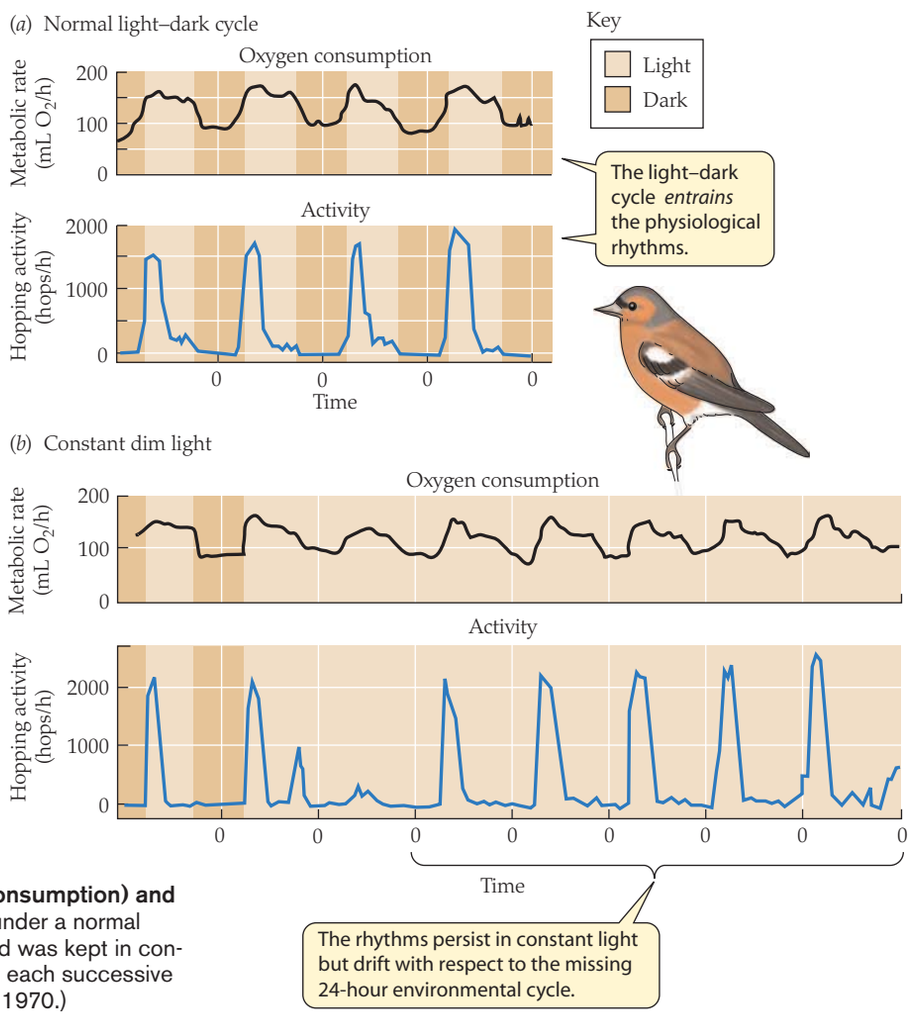


FIGURE 15.13 Circadian rhythm of metabolic rate (O_2 consumption) and motor activity for a chaffinch (*a*) The bird was initially kept under a normal light–dark cycle, which entrained the rhythm. (*b*) Later the bird was kept in constant light. Note that the free-running rhythm started earlier in each successive 24-h period. Zero on the *x* axis denotes midnight. (After Pohl 1970.)

TABLE 15.3 Some processes that show circadian rhythmicity in animals and other eukaryotes

Locomotor activity in many vertebrates and invertebrates
Sleep–wake cycles in many animals
Metabolic rate in many animals
Variations of body temperature (including torpor) in birds and mammals
Urine output and drinking in mammals
Adrenocortical hormone secretion and epidermal mitosis in mammals
Integumentary color change in fish and crabs
Oviposition, mating, and emergence of adults from pupae in insects
Female pheromone release and male pheromone sensitivity in insects
Mating in *Paramecium*
Bioluminescence and photosynthetic capacity in dinoflagellate algae

To test whether a daily rhythm is an endogenous circadian rhythm, an experimenter must remove the environmental timing information. In the case of the chaffinch, this means removing the light–dark cycle. When a chaffinch is exposed to constant, dim light (Figure 15.13*b*), both its locomotor rhythm and rhythm of oxygen consumption persist—demonstrating that they are endogenous rhythms—but the rhythms fail to remain synchronized with the time dawn would have come each day. Instead, under these conditions, the period of each rhythm is a little shorter than a day—about 23 hours (h)—meaning that with each passing 24-h day, activity starts earlier and earlier relative to the time dawn would have come. When environmental cues are absent, the biological rhythm that persists is said to **free-run** or to be a **free-running rhythm**. Like the chaffinch and like the man in Figure 15.12, most organisms have rhythms with free-running periods that are circadian—close to but not exactly equal to 24 h.

The difference between a free-running rhythm and one that is synchronized to environmental cues is easier to see if the records of activity on successive days are stacked one below the last, to make a chart called an *actogram*. Figure 15.14 shows the activity rhythms of two nocturnal flying squirrels (*Glaucomys volans*) for 23 consecutive days stacked in this way: One squirrel was studied in a normal light–dark cycle and the other squirrel was studied in constant darkness. The light–dark cycle (when present) synchronizes the activity rhythm of a flying squirrel, bringing it into phase, so that the onsets of activity periods are lined up at the same time each day, as seen in Figure 15.14*a*. However, when a squirrel is placed in constant darkness and has no environmental information about the time of day, the squirrel's endogenous rhythm of activity persists, but because the period of the endogenous circadian rhythm is not precisely 24 h, the free-running rhythm drifts in its timing (see Figure 15.14*b*). Specifically, in this case the period of the free-running rhythm is *more* than 24 h, and therefore the activity interval drifts to occur later and later each day.

The process by which a biological rhythm is brought into phase with an environmental rhythm is called **entrainment**. During this process, the biological rhythm is said to become *entrained* by environmental cues, as illustrated in Figure 15.14*a*. An environmental cue that is capable of entraining (setting the phase) of a biological rhythm is called a **phasing factor** or **zeitgeber** (a term adopted from German and meaning "time-giver"). In nature, the onset of darkness each night cues the activity of nocturnal flying squirrels—not so much directly as indirectly—by resetting the biological clock that generates the circadian rhythm (see below). The squirrels do not wait in total ignorance each day to see when darkness will arrive. Rather, they have an endogenous sense of the time of day, and the onset of darkness simply serves as a cue that maintains a *precise* 24-h rhythm in a system that, in itself, would maintain an *approximate* 24-h rhythm.

Several types of environmental stimuli serve as phasing factors for circadian rhythms. Daily cycles of light intensity entrain the great majority of rhythms. In addition, rhythms can be entrained by cycles of temperature, sound, food availability, social interaction, or other parameters.

Biological clocks generate endogenous rhythms

A *biological clock* is a physiological mechanism that times an endogenous rhythm. This statement does not explain the mechanism by which the clock works; it merely presents the logical necessity of the existence of such a mechanism. Most (but not all) biological clocks are located in the animal's nervous system, as might be expected for their control functions. In examples such as those discussed above, when we speak of entraining a circadian rhythm to a light–dark cycle, it is really the biological clock that is entrained. The endogenous rhythm is the output of the clock. In essence, the clock controls effectors that allow investigators to see what the clock is doing.

Often a biological clock is localized in a discrete region of the nervous system. For example, the biological clock controlling circadian rhythms in vertebrates is located in the suprachiasmatic nucleus of the brain (discussed later in this chapter). In insects and molluscs, the eyes—or structures closely associated with the eyes—often act as the principal circadian control centers or pacemakers. If the optic lobes of the brain are transplanted from one cockroach to another, for example, the recipient takes on the rhythms of the donor!

Control by biological clocks has adaptive advantages

The major adaptive advantage of biological clocks is that they are predictive: They enable an animal to anticipate and prepare for regular environmental changes. Biological clocks exert *feed-forward control* over effectors, in contrast to homeostatic feedback control (see Box 10.2). Feed-forward control, by definition, initiates changes in physiological systems, rather than correcting for changes after they happen. An animal that is strictly dependent on external cues must wait until the cues appear to trigger or stimulate a response. An animal with an internal clock, however, can anticipate when a physiological or behavioral action will be necessary and can initiate it unbidden.

Circadian clocks permit timing of processes during periods of the 24-h day when environmental cues about time are vague or unreliable. For instance, consider a nocturnal animal that emerges from its nest each evening at dusk, spends the night in feeding and other activities, and retires to its nest each dawn. If it has a circadian clock, it can entrain the clock to the daily environmental cycle defined by dawn and dusk, cues that are obvious and reliable. Then the clock can time the animal's activities accurately throughout the dark of night, when environmental sources of time information are less obvious and less reliable.

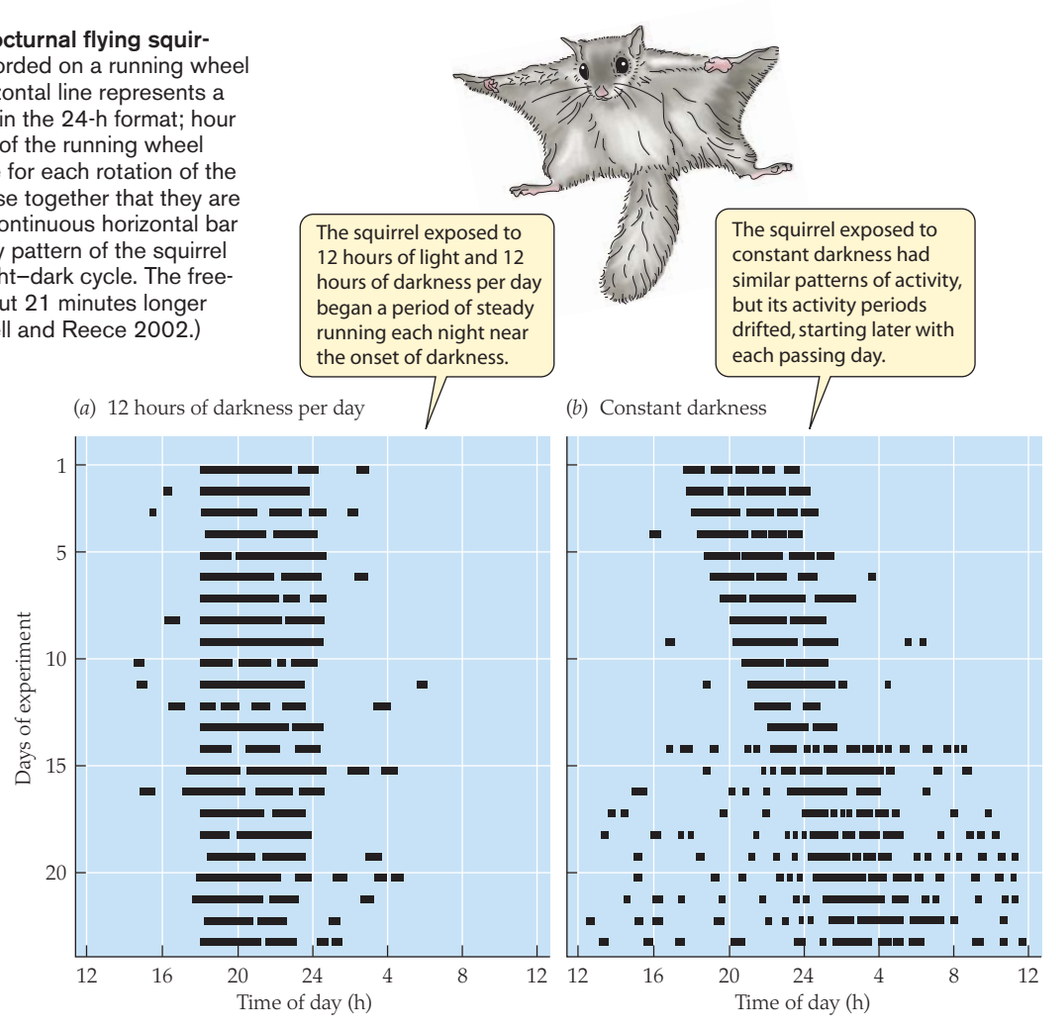


FIGURE 15.14 Activity rhythms of two nocturnal flying squirrels (*Glaucomys volans*) Activity was recorded on a running wheel over a period of 23 days at 20°C. Each horizontal line represents a 24-h day. Times on the *x* axis are expressed in the 24-h format; hour 12 is noon and hour 24 is midnight. Turning of the running wheel activated a pen to record a short vertical line for each rotation of the wheel; these vertical blips are usually so close together that they are fused and give the appearance of a heavy, continuous horizontal bar during periods of steady running. The activity pattern of the squirrel in (*a*) was entrained by the environmental light–dark cycle. The free-running rhythm of the squirrel in (*b*) was about 21 minutes longer than 24 h. (After P. J. DeCoursey in Campbell and Reece 2002.)

Circadian clocks also enable animals to measure changes in **photoperiod**, the number of hours of daylight in a 24-h day. Many animals depend on changes in photoperiod over the course of the year for timing annual events in their life cycles. For example, the long photoperiods of spring may be used as a cue for reproduction or migration.

Finally, circadian clocks enable some animals to use the sun to determine the compass direction, for example in migration. Consider the fact that, if you see the sun on the horizon, you know the direction is west only if you know the time is afternoon. Similarly, certain animals can determine compass directions from the position of the sun, but only if they know the time of day. In these animals, circadian clocks provide the time-of-day information necessary to use the sun as a compass. Homing pigeons orienting relative to the sun, for example, will orient at wrong compass directions if their circadian clocks have been abnormally shifted (see Chapter 18, page 491).

Endogenous clocks correlate with natural history and compensate for temperature

Free-running circadian rhythms of animals have periods that are longer or shorter than 24 h, as we have seen. For many animals the period is correlated with natural history. Whereas nocturnal animals often have periods of free-running rhythm that are longer than 24 h (and that thus drift later and later each day, as Figure 15.14*b* illustrates), many diurnal animals have periods shorter than 24 h. However, there are many exceptions. Moreover, experimenters have found that the period of an animal's free-running rhythm is also affected by the level of constant illumination under which the rhythm is measured. The way in which light pulses or light–dark cycles entrain a circadian rhythm also differs somewhat for diurnal and for nocturnal animals.

One remarkable feature of the clocks controlling circadian rhythms is that their timing is relatively insensitive to tissue temperature. Although some clocks can be entrained by temperature changes, the free-running period of the clock itself does not speed up or slow down much with changes in cellular temperature. As seen in Chapter 10 (pages 235–236), the rates of most metabolic processes are quite sensitive to body temperature; heart rate, breathing rate, and metabolic rate, for example, are likely to double or triple if the body temperature of an animal is raised by 10°C. In sharp contrast, the frequencies of free-running circadian rhythms typically increase by less than 5% when body temperature is elevated by 10°C.

A biological clock would obviously be of little use if it were highly sensitive to temperature; imagine the chaos if our wristwatches were to double their rate when warmed by 10°C! The low thermal sensitivity of biological clocks is therefore adaptive. Given, however, that the primary timing mechanisms of these clocks operate on a

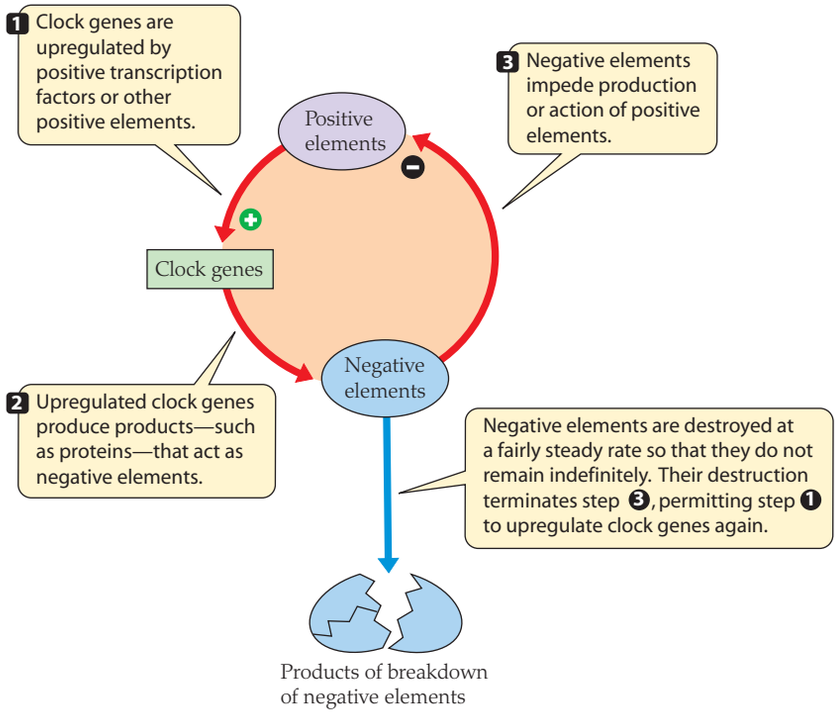
cellular level, how do the clocks manage to be so immune to the thermal effects that so strongly influence most metabolic processes? This is a major unsolved question in circadian physiology.

Clock mechanisms are based on rhythms of gene expression

How biological clocks *work* has remained one of the great mysteries of physiology until recently, when new molecular studies of genetic mutants have provided revolutionary insights. Investigators have identified mutations that modify or disrupt clock function in the fruit fly *Drosophila melanogaster*, hamsters, mice, and other model organisms. For example, a mutation in golden hamsters (*Mesocricetus auratus*) causes the activity rhythm of the animals to exhibit an exceptionally short (20-h) free-running period. By determining the biochemical consequences of such mutations, investigators have identified many of the key components of clock mechanisms.

The timekeeping mechanism in a cell typically depends on a rhythmic alternation between enhanced and inhibited expression of key *clock genes* that are broadly homologous among phyla. As diagrammed in steps ❶ and ❷ in Figure 15.15*a*, enhanced expression of a clock gene (increased transcription and translation) leads to increased levels of the protein coded by the gene. The protein, however, is a negative factor for expression of the gene. That is, as shown in step ❸, the protein eventually suppresses, directly or indirectly, the expression of its own gene; a common action of the protein, for example, is to interfere with the action of transcription factors that promote the gene's expression. Such a mechanism can cycle back and forth between two states of gene expression in much the same way that a pendulum swings between two extremes of position, permitting accurate timekeeping. The details of the timekeeping mechanism vary from one group

(*a*) A universal model of the mechanism of biological timekeeping



(*b*) Some aspects of the timekeeping mechanism in neurons of the mammalian suprachiasmatic nuclei

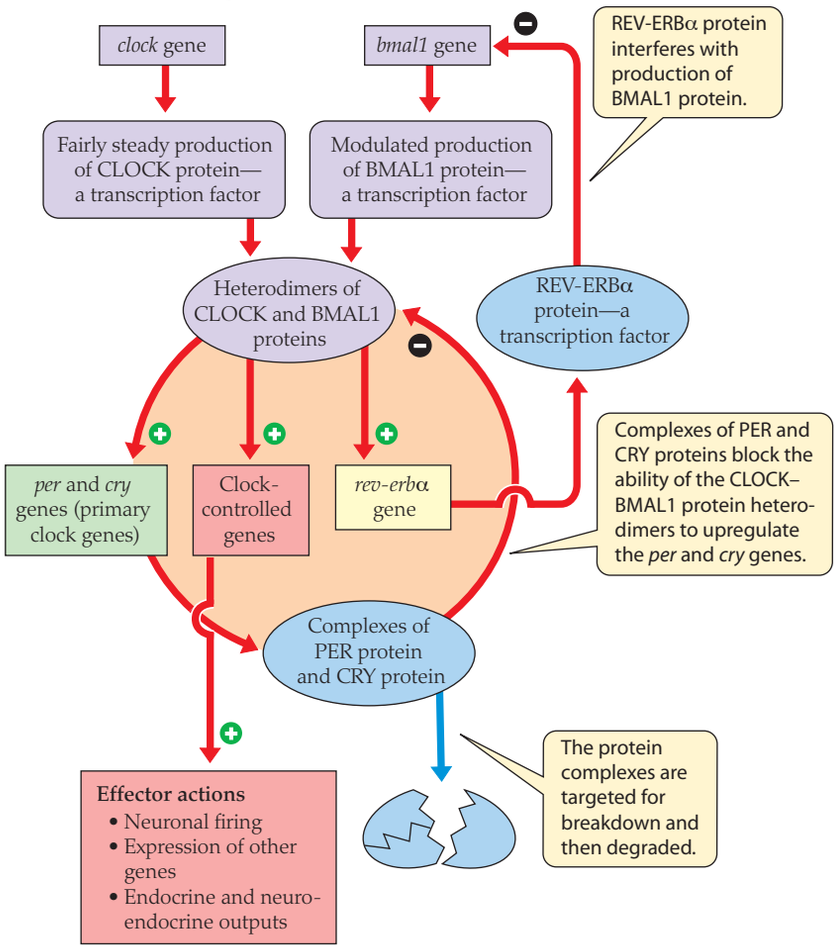


FIGURE 15.15 Cellular mechanisms of circadian timekeeping Circadian timekeeping mechanisms—circadian oscillators—exist within the confines of single cells. They depend on the linked, alternating upregulation and downregulation of *clock genes*, to produce proteins that regulate gene expression. A significant aspect not shown here is that mRNAs must cross from the cell nucleus to the cell cytoplasm to be translated, and the proteins thereby produced must cross from the cytoplasm to the nucleus to regulate genes. The dynamics of nuclear–cytoplasmic exchange are thus important elements of the clock mechanism. Protein phosphorylation (not shown) regulates both the rate of translocation and the rate of destruction of the clock proteins. (*a*) A universal model of a circadian timekeeping mechanism, thought to apply to all organisms. (*b*) Some of the details of the mechanism in neurons of the mammalian suprachiasmatic nuclei. CLOCK and BMAL1 are the primary positive elements, promoting *per* and *cry* genes as well as clock-controlled genes that govern the effector actions of the rhythm. Complexes of PER and CRY proteins are primary negative elements, blocking upregulation of the *per* and *cry* genes and, in a secondary cycle, also blocking upregulation of the *rev-erbα* gene to de-repress the *bmal1* gene (by reducing production of REV-ERBα protein, which itself represses the *bmal1* gene). These primary and secondary cycles are modulated and stabilized by a wide array of other clock-modifying genes, as demonstrated by genome-wide screens. (After Bell-Pedersen et al. 2005.)

of organisms to another and are proving often to be exceedingly complex. **Figure 15.15*b*** shows the core elements of the timekeeping mechanism that exists in neurons of the suprachiasmatic nuclei in mammals. A mechanism of this sort is often called a **circadian oscillator** because timekeeping is achieved by oscillation between two states of gene expression.

The loci of biological clock functions vary among animals

Animals exhibit circadian organization throughout their bodies: Many tissues are capable of acting as circadian clocks. Typically, however, one tissue (or more) acts as a *master clock* that entrains, or imposes its rhythm on, all the other tissues. The entrainment ensures that arrays of tissues and organs ordinarily exhibit synchronous rhythms.

In mammals, the master circadian clock resides in the paired **suprachiasmatic nuclei** of the hypothalamic region of the diencephalon. Each *suprachiasmic nucleus* (SCN) is just dorsal to the optic nerve at the optic chiasm (**Figure 15.16*a***). Neurons in the SCN express a rhythmic circadian activity of clock genes (**Figure 15.16*b***). A stunning experiment demonstrated the primacy of the SCN. Researchers destroyed the paired suprachiasmatic nuclei in a group of genetically normal hamsters. Later they implanted in each hamster paired SCNs taken from a mutant hamster that exhibits an unusual, 20-h free-running activity period. Although the genetically normal hamsters exhibited normal free-running activity rhythms before destruction of their SCNs, they did not show circadian rhythms of activity when they lacked SCNs. **Figure 15.16*c*** illustrates this loss of circadian rhythmicity after SCN destruction. After the hamsters received replacement SCNs, they once again exhibited circadian rhythms, but the free-running period of the rhythms was the unusual, short period characteristic of the mutant donor hamsters.

Individual neurons in the SCN are independently rhythmic when maintained in tissue culture. Communication between neurons in the SCN, as well as between the SCN and the rest of the body, remains inadequately understood; ventral and dorsal SCN neurons differ in neurotransmitters, intrinsic rhythmicity, and connections with other brain areas. Neural connections from the eyes in mammals provide information to the SCN about the daily light–dark cycle in the environment. Interestingly, the light sensors responsible for this entrainment are specialized photosensitive ganglion cells that employ the photopigment *melanopsin*, rather than the (rhodopsin-based) rod and cone photoreceptors of the rest of the visual system.

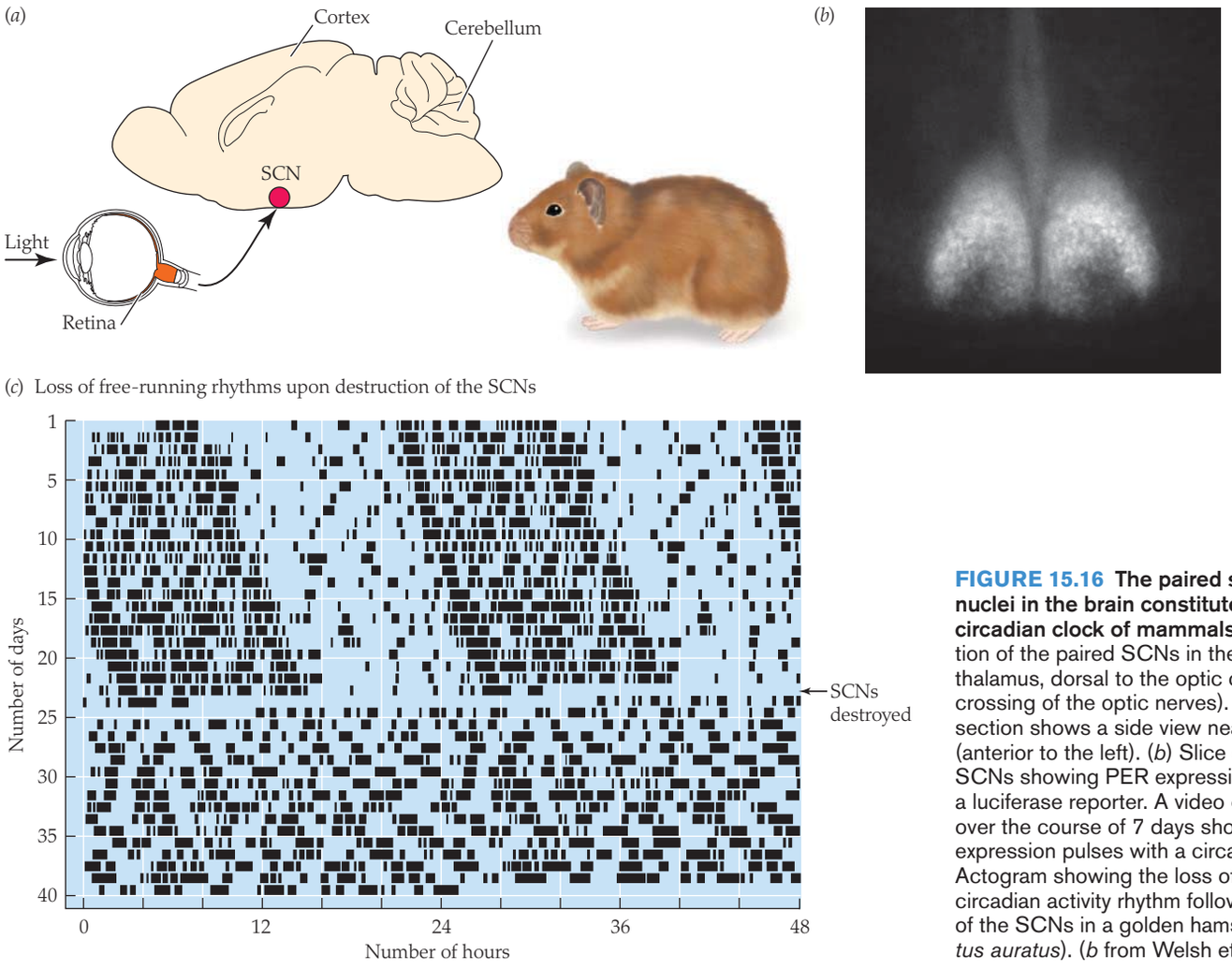


FIGURE 15.16 The paired suprachiasmatic nuclei in the brain constitute the major circadian clock of mammals (*a*) The location of the paired SCNs in the ventral hypothalamus, dorsal to the optic chiasm (the crossing of the optic nerves). The sagittal section shows a side view near the midline (anterior to the left). (*b*) Slice of the paired SCNs showing PER expression visualized with a luciferase reporter. A video of the SCN slice over the course of 7 days shows that PER expression pulses with a circadian rhythm. (*c*) Actogram showing the loss of a free-running circadian activity rhythm following destruction of the SCNs in a golden hamster (*Mesocricetus auratus*). (*b* from Welsh et al. 2010).

The SCN is not the only anatomical location of circadian control in mammals, although it is the principal control center and the best understood. The retinas are also endogenously rhythmic; however, they do not seem to exert substantial direct control over other tissues. Sometimes certain circadian rhythms in addition to the retinal rhythms persist in mammals after SCN inactivation, pointing to additional clocks. For example, liver cells can maintain a circadian rhythm that can be entrained by feeding. Such peripheral clocks are probably controlled (entrained) by the SCN in normal circumstances.

One important output of the SCN clock controls the pineal gland. The **pineal gland** is a small, unpaired gland that forms embryologically as an evagination of the roof of the brain and is found in virtually all vertebrates. Its principal hormonal secretion is **melatonin**, a compound synthesized from the amino acid tryptophan. In mammals, according to current evidence, the pineal gland is not independently rhythmic; it secretes melatonin in a circadian rhythm because of circadian control from the SCN. Pineal melatonin is secreted at night in mammals (both diurnal and nocturnal) and in virtually all other vertebrates. Thus melatonin is sometimes called the *darkness hormone*. Pineal melatonin is also of great importance in controlling many seasonal rhythms, such as reproduction.

The pineal physiology of nonmammalian vertebrates often differs from that of mammals in two important ways. First, the nonmammalian pineal gland may be endogenously rhythmic and thus can act as a primary circadian control center. Second, the pineal gland is often light-sensitive and acts as a "third eye," providing extraocular information on the environmental day–night cycle (light may reach the pineal gland through the skull). Interaction between the SCN and the pineal gland in the control of circadian rhythms in nonmammalian vertebrates is complex, diverse, and not well understood. The retinas in nonmammalian vertebrates are endogenously rhythmic, but as in mammals, the retinas seem not to serve as circadian control centers for the rest of the body.

Studies of transcription profiling in various tissues of different animals show that there are daily rhythms of transcription of hundreds of genes (see Chapter 3, page 78–80). In many cases the circadian nature of these daily rhythms has not yet been demonstrated, but it is likely that they result from the output of the circadian clock in the SCN, either directly or via entrainment of other local circadian clocks.

Circannual and circatidal clocks: Some endogenous clocks time annual or tidal rhythms

Daily rhythms have been the most-studied of all biological rhythms, and so we have emphasized them in our discussion of biological clocks. However, animals exhibit rhythmic physiological and behavioral variations that operate on other timescales as well. Annual rhythms of reproduction, migration, fat accumulation, dormancy, and so on are well-known examples. Animals living along the seashore often display rhythms synchronized with the tides, which usually rise and fall every 12.4 h (half a lunar day). For instance, fiddler crabs (*Uca* spp.) that scavenge for food on the sand or mud exposed by low tide become rhythmically more active at each time of low tide.

Some, but not all, annual and tidal rhythms are endogenous: They persist even when animals are placed in a laboratory environment where they are denied environmental information about the time of year or the time of the tidal cycle. Typically the periods of the free-running endogenous rhythms are only *approximately* a year or a tidal cycle in length. Thus the endogenous rhythms are termed **circannual** or **circatidal**.

Under natural conditions, of course, certain environmental parameters vary in phase with the annual or tidal cycle. The endogenous circannual and circatidal rhythms of animals become entrained, so in nature the biological rhythms are kept in phase with the actual seasons and tides. For instance, the annual cycle of photoperiod length (long days in summer, short days in winter) is the phasing factor for certain circannual rhythms; and features of ebbing and flowing tidal water, such as mechanical agitation, serve as phasing factors for some of the circatidal rhythms. It is not clear whether the endogenous timing mechanisms for circannual and circatidal rhythms depend on circadian oscillators. Arguments have been presented on both sides. As yet, the nature of these timing mechanisms remains unresolved.

Interval, or "hourglass," timers can time shorter intervals

In addition to circadian oscillators—which rhythmically cycle—animals appear to possess physiological timing mechanisms that permit timing of *parts* of days by functioning like stopwatches or hourglasses. These noncyclic timers are called **interval timers** or **"hourglass" timers**. Once activated on a given day, they measure the passage of time; but like stopwatches, they are noncyclic and must be restarted to operate again. Male pigeons, for example, seem to use an interval timer to determine how long they incubate eggs in a particular stint; they stay on the eggs for a relatively fixed length of time after they start, regardless of the time of day when they start. Recent research locates the neurophysiological sites of the interval timers of birds and mammals in different parts of the brain than the circadian oscillators.

What about the star-nosed mole with which we started this chapter? Moles live underground; star-nosed moles have reduced vision, and other moles are considered blind. Thus, moles might be good candidates as animals for which circadian rhythms are of little adaptive advantage. Yet there is evidence that moles have circadian activity rhythms, and all moles are seasonal breeders that presumably can measure day length. Mole visual systems, despite substantial losses of other visual pathways, have robust connections from the retina to the SCN, with prominent melanopsin-containing retinal ganglion cells (shown to be the neurons that entrain SCN clock cells to light). Thus even in fossorial moles, it appears that circadian clocks and the ability to reset them persist.

SUMMARY Biological Clocks

- A circadian rhythm has a period of about a day. It is an example of an endogenous rhythm, one that does not require sensory information for timing.
- A circadian rhythm of an animal will drift, or free-run, in constant light or darkness, when there are no sensory timing cues. A light–dark cycle entrains the circadian rhythm to exactly 24 h.

- A biological clock is the physiological basis of an animal's ability to time an endogenous rhythm. Biological clocks exert rhythmically changing control, modulating the outputs of the nervous and endocrine systems to prepare an animal for daily changes and seasonal changes. In mammals, the suprachiasmatic nucleus (SCN) of the brain is the principal biological clock for circadian rhythms.
- Animals may possess other timing mechanisms for shorter rhythmic periods (such as circatidal rhythms) or longer periods (such as circannual rhythms) than those of circadian rhythms.

Study Questions

1. How does the physiological control exerted by the nervous system and endocrine system relate to the concept of homeostasis?
2. Compare and contrast the nervous system organization in arthropods and vertebrates. What are their functional similarities and differences?
3. How, in general, is the vertebrate autonomic nervous system organized? Is it redundant to have separate sympathetic and parasympathetic control of many organs?
4. The sympathetic and parasympathetic divisions of the autonomic nervous system employ the same neurotransmitter (acetylcholine) for preganglionic neurons, but different neurotransmitters for postganglionic neurons (norepinephrine for sympathetic, and acetylcholine for parasympathetic; see Figure 15.10). How would it affect autonomic function if the situation were reversed—that is, if the preganglionic neurotransmitters were different and the postganglionic neurotransmitters were the same?
5. What adaptive advantages might centralization and cephalization offer in the evolution of nervous system organization?
6. Mammals have brains that are more complex than those of fish and amphibians, particularly in terms of expansion of the cerebral cortex. Does this increased complexity make mammals more advanced and fish and amphibians more primitive? Why or why not?
7. The paired suprachiasmatic nuclei (SCNs) usually function as the master circadian clock in mammals. In some circumstances the circadian rhythms of animals may become split, with some effectors following one free-running rhythm and some following another. Give two hypotheses of how such a split might happen—one compatible with an SCN always being a master clock and one not.
8. One of the first genes that was determined to control circadian-clock timing is the *per* gene in *Drosophila*. Mutants of this gene have shorter or longer circadian free-running rhythms, as well as shorter or longer periods of a much faster rhythmic courtship song. What does this observation suggest about the relationship between circadian rhythms and shorter, hourglass-timing rhythms?

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