BIOLOGICAL RHYTHMS

A biological rhythm is one or more biological events or functions that reoccur in time in a repeated order and with a repeated interval between occurrences.

The periodic (cyclic) phenomena in living organisms and their adaptation to solar- and lunar-related rhythms are known as biological rhythms. The science that describes timing in biological clocks and their associated rhythms is called Chronobiology.

Biological rhythms are the ways that organisms adapt and live with the environmental rhythms around them, such as the spin of the earth, the movement of the earth around the sun, and movement of the moon around the earth. Often generated by "biological clocks" (the term for the internal physiological systems that track the environmental rhythms), biological rhythms allow an organism to harmonize successfully with its environment. Although biological rhythms have not been studied in every living thing, they have been found in every organism in which experiments were performed. Accordingly, scientists believe biological rhythms are ubiquitous.

Generally, there are two types of biological rhythms, exogenous and endogenous. Exogenous biological rhythms are driven directly by the environment or another external influence. Another term for this type of biological rhythm is a direct effect. An example of an exogenous biological rhythm is the hopping of sparrows on a perch when a light is turned on. Such rhythms are said to have a geophysical counterpart; in this case, the presence of light.

In contrast, endogenous biological rhythms are driven by internal biological clocks and are maintained even when environmental cues are removed. Some examples of endogenous biological rhythms are the wake-sleep cycle and the daily body temperature cycles. Sometimes it is difficult to determine whether the activity of an animal is due to a direct effect or that of an endogenous biological clock, because the two types of rhythms can mask each other.

True biological clocks have four important characteristics. First, the clock is endogenous, meaning it gives the organism an innate ability to maintain periods of a particular length between biological functions. Experiments in space, with animals completely isolated from earthbound geophysical input, have supported the innate nature of the clocks. Second, the clock is temperature independent very unusual situation in biology but an essential characteristic to avoid biological rhythms being governed by the weather. Third, biological clocks have the ability to be reset in order to maintain a relationship with environmental cues. Finally, biological clocks are an internal continuous monitor of the passage of time, allowing the organism to keep track of duration biologically.
Chronobiology, the study of biological rhythms, categorizes rhythms by the length of the cycle. The most studied type of biological rhythm are circadian rhythms, which fluctuate on a daily basis. Alertness, body temperature, and the circulating concentrations of growth hormone, cortisol, and postassium are all examples of physiological functions that run on a circadian basis. Infradian cycles last about a month or longer. Menstruation in the human adult female is an example of an infradian biological rhythm. Circannual cycles last about a year; over-winter hibernation as a common example. The shortest cycles are ultradian, where the cycles are less than 24 hours. Heart rate and breathing are two examples of ultradian biological rhythms.

**Function**

The function of biological clocks and the resulting biological rhythms involves two factors: the capacity of the biological clock to freerun (operate without external indications), and the ability of timing signals, known as Zeitgeber (German for "time-giver"), to synchronize the cycles to the environmental signals. Some common Zeitgebers include light, temperature, and social cues such as clocks, sound, or physical contact. A biological clock is said to be freerunning when these external cues are removed. Based on multi-day isolation experiments, the average freerun period for circadian rhythms in humans is 25 hours. Thus, if isolated from outside input, people tend to go to sleep one hour later each day, quickly becoming out of sync with the rest of the 24-hour-based human world.

Entrainment is the process of aligning a biological rhythm with an environmental stimulus. There are limits to the time periods that biological rhythms can be entrained. For circadian rhythms in most animals, 18 hours is the shortest period tolerated, with an upper limit of about 28-30 hours. If Zeitgebers are provided for shorter or longer intervals, the organism reverts back to freerunning. A good example of entrainment is the acquisition of the 24-hour wake-sleep schedule by human infants after birth. Newborn circadian rhythms freerun, significantly disrupting the sleeping patterns of their parents. However, as they mature and become responsive to Zeitgebers such as light and dark, infants gradually adopt the 24-hour schedule of adults.

**Physiology of Biological Clocks**

The physiological location of biological clocks has been studied in a number of animal systems, including humans. In most vertebrates other than mammal for example sparrows, the primary biological clock has been located in the pineal gland. This gland is located at the base of the brain and is responsible for the production of melatonin, a hormone produced in high levels at night and low levels during the day.

In mammals, additional cells responsible for biological clock functions were located in the hypothalamus, in two clusters of nerve cells called the suprachiasmatic nuclei (SCN). Light receptors in the retina are connected by nerves to the SCN. The SCN and the mammalian pineal gland are linked, by both nervous connections and by the presence of melatonin receptors on SCN cells. Thus, light is detected by the eye, which
passes this information on to the SCN, which in turn passes the information on to the pineal gland, controlling melatonin production.

The exact function of melatonin in mammals is not completely understood. Scientists believe this hormone is likely involved in many aspects of biology, including the wake-sleep cycle, body temperature control, and (particularly with mammals that have seasonal mating) sexual maturity and reproduction.

**Genetic Control of Biological Clocks**

The molecular basis for the control of circadian rhythms has been studied extensively in the fruit fly insect model, where the first genetic mutants that affected circadian rhythms were discovered. Because homologs to the fruit fly genes (genes which have a similar structure, and therefore likely have a similar function) have been discovered in mammals, including mice and humans, scientists strongly suspect that similar control mechanisms have been conserved in mammals.

In fruit flies, five genes are believed responsible for the baseline oscillation of the circadian rhythms: period (per), timeless (tim), clock (clk), cycle (cyc), and double-time (dbt). The protein products of these genes work together to produce a negative feedback loop that allows the concentration of the period and timeless proteins to build in concentration slowly over the 12-hour day. Both clock and cycle are positive transcription elements. These proteins work together to result in the production of the period and timeless proteins.

When the period protein is produced, the double-time protein modifies it, marking it with a phosphate molecule for quick destruction by the cell if not paired with the timeless protein. Thus, the period protein will be degraded until the concentration of timeless protein is high enough so that period and timeless dimers form. The destruction resulting from the phosphate modification delays the formation of the dimers, stretching out the process over the 12-hour evening.

Eventually, dimers of period and timeless are present in high enough concentrations to interact with clock and cycle proteins to turn off production of both period and timeless proteins, closing the feedback loop. At dawn, the highly light-sensitive timeless protein is degraded, leaving the phosphorylated period protein unpaired and vulnerable to degradation as well. In this way, light resets the feedback loop to start again, making it the Zeitgeber for this biological clock.

In early 2001, studies of the molecular basis of biological rhythms were extended to humans, with the report of the first known human gene homologous to the fruit fly genes. The gene is called hPer2 and is homologous to the period gene. A mutation in this gene is present in a Utah family and results in an advanced sleep phase syndrome. The mutation maps to the location where the period gene is marked with a phosphate, suggesting that the mutant protein would be not be phosphorylated. The details of the mutation fit the proposed function of the protein and the problems seen by those having
the mutation. Lack of phosphorylation would cause the mutant protein to be degraded more slowly, speeding up the circadian rhythms of the person having the mutation.

Role in Human Health

The exact role of biological rhythms and biological clocks in human health is not fully understood. However, it is clear that humans are subject to biological clocks in a number of physiological areas, most notably hormone secretion and wake-sleep cycles. A well-functioning biological clock is important for falling asleep and getting enough of the various stages of normal sleep. This affects, in turn, alertness, job performance, interpersonal relationships, and day-to-day safety issues. Well-functioning circadian rhythms may also play a role in psychological health, particularly for persons living in areas with decreased light in the winter months.

Common Diseases and Disorders

The most common human disorders related to biological rhythms are due to disassociations of the endogenous biological clock and the external environmental cue. These displacements are called phase shifts and occur with rapid travel across time zones and shift work. The resulting disorientation produces the symptoms known as jet lag: sleep disturbances, fatigue, indigestion, and nausea. When occurring in the workplace these symptoms can have serious consequences. The Exxon Valdez, Chernobyl, and Challenger shuttle disasters all occurred on the night shift. Research is ongoing to develop methods of using melatonin and bright light exposure to help compensate.

The role of biological rhythms in seasonal affective disorder (SAD), a form of depression with symptoms more severe in the winter months, is much less clear. Studies have been unable to find other evidence of circadian disorder in persons diagnosed with SAD. However, treatment with light therapy does bring significant improvement in the majority of patients.