

# Freerunning and Entrained Circadian Rhythms

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## INTRODUCTION

Circadian rhythms "freerun" in constant conditions like self-sustaining oscillations, and they can be synchronized (entrained) by periodic factors in the environment, the zeitgebers. The period  $\tau$  of the freerunning rhythm depends on the species, on the individual and its physiological state, on environmental conditions, and on the experimental history. Under conditions of entrainment, the rhythm keeps a distinct phase-relationship to the zeitgeber. The record of locomotor activity of a pig-tailed macaque, *Macaca nemestrina*, reproduced in Figure 1, illustrates a few of the major principles. When exposed to a light-dark cycle (LD), the monkey is active during L, with onset of activity occurring shortly before light-on; in constant conditions (LL), the period is shorter than 24 hr and, on the average, somewhat shorter in 0.03 lux than in 0.1 lux; there is day-to-day variability of intervals between the onsets of activity around the mean  $\tau$  that in itself changes slightly over time (especially in 0.03 lux); reentrainment by the zeitgeber after Day 78 is accomplished by a series of delay transients. A more detailed discussion of those phenomena follows below.

## FREERUNNING RHYTHMS

### DEPENDENCE OF FREQUENCY ON EXTERNAL AND INTERNAL FACTORS

**LIGHT.** In most species,  $\tau$  of a freerunning rhythm depends on the intensity of illumination. In many diurnal species,  $\tau$  shortens with an increase in light intensity, and it

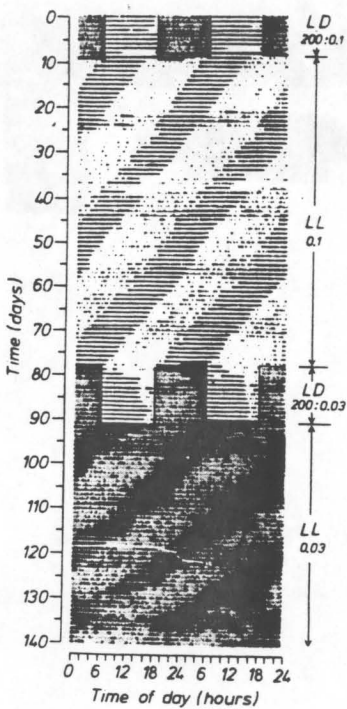


Fig. 1. Circadian rhythm of locomotor activity (black marks) in a pig-tailed macaque, *Macaca nemestrina*, alternatively kept in light-dark cycles (LD) and in conditions of constant dim illumination (LL). Intensity of illumination (in lux) given at the right margin. Original record duplicated once. (From Aschoff, 1979a. Reprinted with permission of Paul Parey Verlag, Berlin.)

lengthens in nocturnal species. In general, this rule is supported by data from fishes, reptiles, and birds. Mammals behave differently in so far as the majority of diurnal species also lengthens  $\tau$  when light intensity increases. Most of the data available from vertebrates are summarized in Figure 2. For arthropods, no consistent rule emerges from the data published so far (cf. Figure 15 in Aschoff, 1979a).

At higher intensities of illumination, locomotor activity often becomes arrhythmic, and other rhythms damp out. The intensity at which this occurs may be quite low, as in some insects (Pittendrigh, 1960); it seems to be higher in diurnal than in nocturnal species, and higher in mammals than in birds (see Figure 2). One has to be careful in interpreting the disappearance of a rhythm as a "stopping" of the circadian pacemaker as opposed to an "uncoupling" of the overt rhythm or a desynchronization among a multiplicity of oscillators.

Circadian periods measured in continuous darkness ( $\tau_{DD}$ ) scatter within a range from 22 hr to more than 26 hr. In mammals,  $\tau_{DD}$  tends to be above 24 hr in diurnal species ( $\bar{\tau}_{DD} = 24.24 \pm 0.52$  hr; 11 species) and below 24 hr in nocturnal species ( $\bar{\tau}_{DD} = 23.85 \pm 0.56$  hr; 26 species); six diurnal avian species have a mean  $\bar{\tau}_{DD}$  of  $24.82 \pm 1.01$  h (Aschoff, 1979a). In arthropods,  $\tau_{DD}$  values below 24 hr prevail. As has been outlined by Pittendrigh and Daan (1976b), the species-specific differences in  $\tau_{DD}$ , together with the species-specific responses of  $\tau$  to light, may reflect parts of a "strategy of entrainment" for diurnal and nocturnal species.

**TEMPERATURE.** A near independence of  $\tau$  from ambient temperature was first clearly demonstrated for the rhythm of emergence in *Drosophila pseudoobscura* by Pittendrigh (1954). However, most of the lower organisms, plants, and poikilothermic animals studied later on show a slight dependence of  $\tau$  on temperature, with  $Q_{10}$  values either above or

below 1.0 (see the review article of Sweeney and Hastings, 1960). More recently, similar dependencies have been described for birds and mammals. A survey of all data available suggests that with an increase in ambient temperature,  $\tau$  shortens in most diurnal and lengthens in nocturnal species (see Figure 23 in Aschoff, 1979a). The dependence of  $\tau$  on temperature is less than that on light intensity and certainly far below any dependence that could be expected from metabolic effects of temperature. Models to explain this unique feature of circadian systems are usually based on mechanisms of compensation (e.g., Brinkman, 1971). The phenomenon of temperature compensation has been discussed by Pittendrigh and Calderola (1973) as a special case of the general homeostatic conservation of frequency of circadian oscillations.

**VARIOUS EXPERIMENTAL CONDITIONS.** If in a continuously illuminated cage a dark nestbox is provided where the animal can hide,  $\tau$  differs from that measured in the empty cage (Saint Paul, 1973). The reason is that by alternating between shelter and cage, the animal itself produces an LD cycle that influences  $\tau$  via the response curve (see Chapter 5 of the circadian system. Similar effects can be observed when the animal is allowed to turn lights on and off by itself. Usually, such self-selected LD cycles result in lengthening of  $\tau$  as shown for birds, monkeys, and man (for references, see Aschoff, 1979a). Other observations suggest that  $\tau$  of an activity rhythm is longer if measured in animals with access to a running wheel, as compared with those whose activity is recorded in spring-suspended cages, and that animals living together in a group may have rhythms with a shorter  $\tau$  than animals kept singly (see Figures 11 and 12 in Aschoff, 1979a).

**INTERNAL FACTORS.** There is increasing evidence that hormones influence freerunning rhythms. In mice, castration results in a lengthening of  $\tau$ , and testosterone replacement is a shortening (Daan, Damassa, Pittendrigh, and Smith, 1975). Similarly,  $\tau$  gets shorter in female hamsters after implantation of estradiol (Morin, Fitzgerald, and Zucker, 1977), and in the house sparrow, *Passer domesticus*, after implantation of melatonin (Turek,

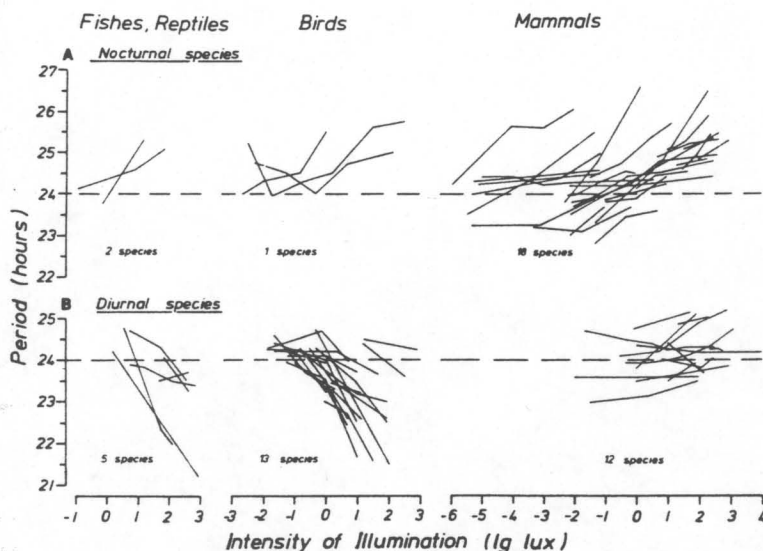


Fig. 2. Dependence of circadian period on intensity of illumination in constant light. (For species and reference sources, see Aschoff, 1979a.)

