4 Toward a Unified Theory of Animal Event Timing

Thomas T. Hills

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4.1 INTRODUCTION

At the heart of perception lies an animal's ability to recognize change and to make predictions based on the way change has played itself out in the past. Critical to this behavior is the ability to measure time. Without suggesting that it is the basis of predictive science, the perception of time is a primary ingredient in causal understandings.

Animal event timing refers to the process that an animal undergoes in order to recognize an interval of time. In a very anthropomorphic way, one can ask the question this way: How does an animal know the difference between 2 min and 2 h? Or does it know at all? Absolute time may be an artificial consequence of man-made clocks, but animals do behave on temporally defined schedules, and many of them are observed to solve problems in the wild that require a specific estimate of time. Central place foragers must be able to find their way home, and many of them then communicate information about distance to forage sites after they do so (e.g., Kacelnik, 1984; Seeley, 1995). Prey species adjust vigilance schedules to match predator density (e.g., Arenz and Leger, 1997). Prospective mates choose future partners based on the temporal specificity of mating displays (Kyriacou et al., 1992; Michelsen et al., 1985). Foraging animals move on when the rate of resource intake drops too low (Stephens and Krebs, 1986; Charnov, 1976). In all of these cases, animals must perceive the temporal duration of events.

A unified theory of animal event timing requires that we know two things. First, how do nervous systems perceive and learn key aspects of temporal information? What are the molecular and cellular mechanisms required to build perceptual clocks? And second, why have these clocks come to exist? What evolutionary forces have driven their evolution? The answers to these two questions are generally referred to as the proximate and ultimate definitions of a behavior. However, it is a major assumption of this review that, because molecular mechanisms and evolutionary forces feed back on one another, one cannot fully understand one without the other.

To our advantage, psychophysical studies have already established that some animals do measure short intervals of time. This will provide us with a basis for conceptualizing event timing in a definitive way. The purpose of this review will be to formalize what we know about animal event timing by addressing contributions from psychophysics, molecular genetics, neuroscience, and evolutionary ecology, while hopefully combining that information in a way that furthers our understanding of animal event timing.

I begin by reviewing what is known about animal event timing from psychophysics, establishing that animals can measure time and that time measurement appears to obey specific conserved properties over a wide range of species. I then discuss the molecular mechanisms of circadian clocks, which to date are our most well understood molecular clocks. Circadian mechanisms will help us to understand what the event timer is not and also how an event timer might operate at the cellular level. I then suggest possible mechanisms for event timers that agree with the psychophysical and physiological evidence for where these clocks are and how they operate. Finally, I take a tour of ecologically relevant behaviors where we may hope to find event timers at work in the world. This will further our understanding of the evolution of event timers and also allow us to make predictions about what kind of event timers specific animals are likely to have.

4.2 LESSONS FROM THE PSYCHOPHYSICS OF TIME

The Russian physiologist Ivan Pavlov (1849–1936) recognized the learned perception of time in animals when his salivating dogs began to "wait" to salivate after lengthy durations of the conditioned stimuli (story retold by Roberts, 1998). What was at first an unconditioned response to food had become a finely timed prediction about the arrival of food. Since that time, psychophysics has developed a number of techniques for assaying animal event timing. Before covering some of the more established contributions of psychophysics to animal event timing, I present the three most prevalent assays for measuring time perception in animals, as I will refer to them frequently.

One of the first and most easily used assays of animal event timing is the fixed-interval (FI) schedule. FI schedules present a subject with an operandum (e.g., lever) and reward lever presses after a fixed interval of time. There is no deterrent for lever presses prior to the reinforcement, lending subjects to press the lever at will until food is finally procured. Animals that do not temporally regulate behavior based on experience typically show the break-and-run response, which is characterized by a short pause in procuring the reward followed by a steady response rate until the next reward, as illustrated in Figure 4.1a. An alternative to this behavior is the production of scalloped curves in cumulative response records over time, as shown in Figure 4.1b. The scallop is created by the increase in response rate as the reward time approaches, much like the timed increased in salivation observed by Pavlov (1927).

A more informative variation of the FI schedule is the peak-interval (PI) procedure (e.g., Church et al., 1994; Roberts, 1981). In the PI procedure, animals learn that a response will deliver food after a certain interval has passed following the initiation of a signal. The major difference between the FI schedule and the PI procedure is that in the latter, approximately 50% of the time there is no food reward. Instead, the signal stays on for a set period regardless of how the animal responds. It is during these no-reward trials that responses are recorded. Inevitably, the animal increases its response rate until the approximate time of the reward and then decreases its response until the signal is turned off, as shown in Figure 4.2. Movement of the peak function rate left or right is interpreted as a change in the rate of perceived time by the animal.

The temporal bisection procedure requires the subject to discriminate between two signals, long and short in duration (e.g., by pressing the left or right levers, respectively) (Church and Deluty, 1977; Maricq and Church, 1983). This is another psychophysical method for measuring the lengthening or foreshortening of perceived time. The signal duration at which the subject responds long and short with equal probability is called the point of subjective equality (PSE), with typical results illustrated in Figure 4.3.

While the principles that I report here are not established for all animals, they are well established for vertebrates (i.e., birds, mammals, and fish) (see Paule et al., 1999). I will point out exceptional species in "Species Comparisons" (Section 4.2.6).

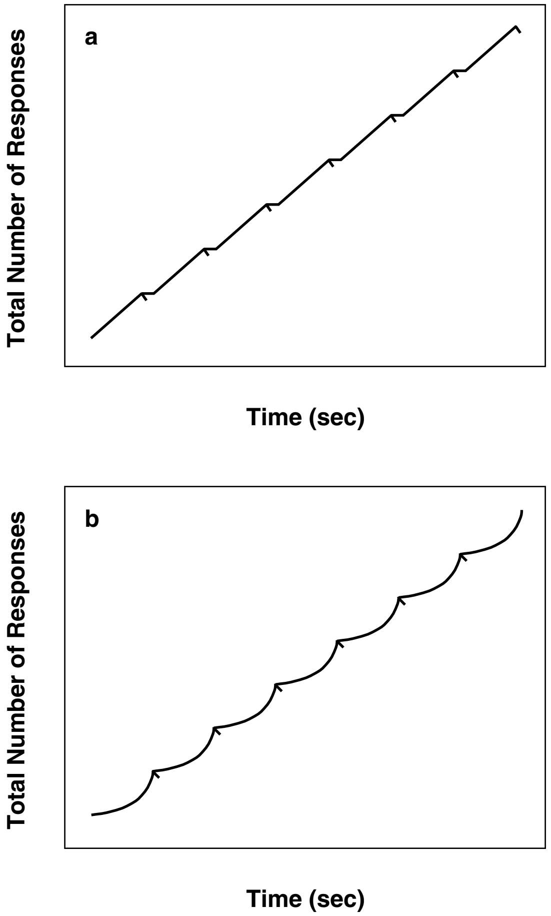

FIGURE 4.1 Typical results from the FI procedure. (a) Break-and-run response. Response rates are constant following a slight delay after the reward (downward slash). (b) Scalloped response. The scalloped curves are the result of increasing response rates near the point of reward. Response rates are not as smooth in real traces, because lever presses lead to discrete jumps in cumulative response number. (Adapted from Ferster, C.B. and Skinner, B.F., *Schedules of Reinforcement*, Appleton-Century-Crofts, New York, 1957.)

The following list of phenomenological characteristics represents a basis for understanding what a mechanistic definition of event timers must ultimately explain. This list will also help us make predictions about how we may expect animals to behave in the wild in response to specific constraints on their perception of temporal events.

4.2.1 TEMPORAL MEMORY IS SCALAR

The ability to discriminate two temporal cues is reduced in a predictable way as the duration of those cues is increased. This property, known as Weber's law, describes

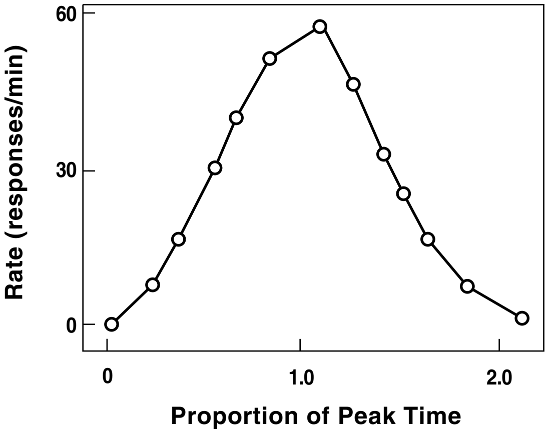

FIGURE 4.2 Typical results from the PI procedure. The animals are trained by rewarding them for the first lever press after a fixed time from the initiation of the signal (e.g., light or tone). Data are recorded on trials without reward. Peak response time is usually near the point of reward. The results here are normalized to the peak time, to show that the relative shape of the curve is conserved for different durations. (Adapted Roberts, S., *J. Exp. Psychol. Anim. Behav. Process.*, 7, 242–268, 1981.)

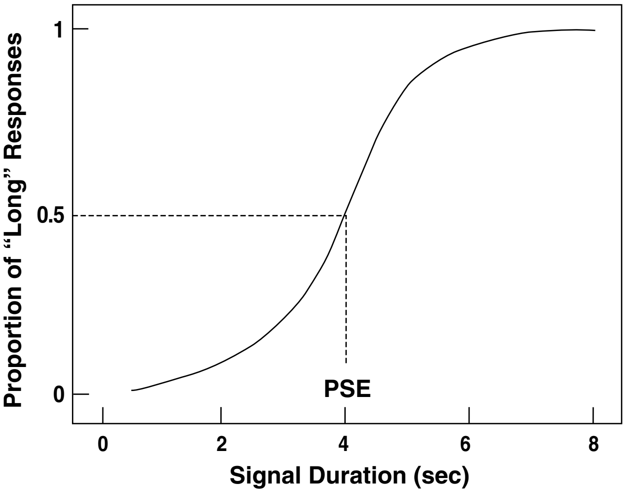

FIGURE 4.3 Typical results from the temporal bisection procedure. Animals are trained by rewarding them for pressing the left or right lever following signals of short or long duration (e.g., 2 and 8 sec), respectively. Probe trials are then conducted in which intermediate times are tested for left or right responses. Animals are not rewarded on probe trials. The PSE is the point at which the animal shows equal proportions of long and short responses. (Adapted from Church, R.M. and Deluty, M.Z., *J. Exp. Psychol. Anim. Behav. Process.*, 3, 216–228, 1977.)

a linear relationship between the duration of a stimulus, I, and the measure of uncertainty associated with that stimulus, ΔI. The relationship

$$\Delta I = kI$$

describes the amount by which a second stimulus must be changed from I in order for the two to be discriminated. It also explains the proportionality between the timed interval and the mean and standard deviations associated with that interval. This relationship breaks down for very short intervals of several seconds (discussed in detail by Cantor, 1981). This relationship also breaks down as timed intervals approach the 24-h phase of the circadian clock (Crystal, 2001).

The results from the PI procedure resemble a Gaussian distribution, as illustrated in Figure 4.2. Longer intervals between the beginning of the signal (e.g., light or sound) and the reward lead to wider distributions (Church et al., 1994; Roberts, 1981). Regardless of the length of the duration, the shape of the curve is conserved, showing that the variance scales with the length of the duration. In the temporal bisection procedure, increasing the time between signals increases the accuracy, and longer duration signals require greater disparity in length in order to achieve the same levels of discrimination (e.g., Bizo and White, 1997; Roberts, 1998).

Weber's law applies in its general form to rats (Church and Gibbon, 1982), pigeons (Cheng and Roberts, 1991), and humans (Wearden, 1991). The ecological consequences of Weber's law are discussed more specifically by Bateson (this volume) and in Section 4.5 of this chapter.

4.2.2 THE CLOCK CAN DISCRIMINATE BASED ON FREQUENCY OF REWARD

Animals can distinguish between the reward reliability of different temporal cues. This insures that animals have the temporal acuity to rate potential rewards based on their frequency. Ecologically, this means that animals can rank foraging sites based on their density of prey.

That rats can associate different cues with different frequencies of reward was shown with the PI procedure. Light was associated with an 80% probability of food, and a tone was associated with a 20% probability of food. Animals responded to the tone at about one quarter of the peak response rate for the light, showing that they can match the memory for two different intervals with the relevant external stimuli (Roberts, 1981). This same behavior has been observed using a different procedure in pigeons (Killeen et al., 1996). In fact, studies of risk-sensitive foraging have established that animals can make the same distinctions in the wild. I will discuss this in more detail in Section 4.5.5.

4.2.3 THE CLOCK CAN BE PAUSED

Pigeons and rats trained in the PI procedure will respond to a 10-sec signal blackout in the middle of a trial by moving their peak response rate back by 10 sec (see Buhusi, this volume; Buhusi and Meck, 2002; Buhusi et al., in press; Hopson, this volume; Roberts, 1981, 1998). This is true for a number of different blackout times, with the interesting caveat that longer blackout times can lead to a slower resetting of the clock (de Vaca et al., 1994).

The pausing of the clock suggests higher-order control in the nervous systems of animals capable of event timing. This kind of control is unlikely to be found in more primitive event timers (see Section 4.4 and the discussion of the decay timer) or in timers like the circadian protein oscillations described in Section 4.3.

4.2.4 TEMPERATURE AFFECTS CLOCK SPEED

The first evidence that a temporal sense was not temperature compensated was provided by Hoagland (1935), who made this discovery after subjecting his sick wife to various temporal acuity tests while measuring her temperature. At hotter internal temperatures her counting rate was faster than at lower temperatures. To exclude illness, he did the same for volunteers after short periods in a freezer. His data set exhibits an exquisite linear relationship between the inverse of temperature and the log speed of counting (see Wearden and Penton-Voak, 1995).

In perhaps the only ecological study of direct interval timing and temperature, the parasitoid wasp *Trichogramma dendrolimi* was demonstrated to lay eggs in its insect host based on the duration of its walk across the host's long axis (Schmidt and Pak, 1991). The hosts are eggs of larger insects, which vary greatly in size. This lends itself to an adaptive measure of host size. Too many or too few eggs laid on the host can lead to either starvation or underutilization of resources, providing a clear evolutionary force for optimal host size assessment. The host-crossing can take between 0.5 and 20 sec, depending on the host size, but for identically sized hosts, the speed is increased at higher ambient temperatures. At higher temperatures the wasp also lays its eggs faster. However, the wasp is able to compensate for this temperature adjustment and lays the same number of eggs in identically sized hosts regardless of the ambient temperature. The wasps may have a reduced estimate of elapsed time at lower ambient temperatures to compensate for their reduced speed (Schmidt and Pak, 1991).

In circadian studies of the courtship song of *Drosophila melanogaster*, the timing pattern of the behavior is temperature compensated and directly correlated with the duration of the free-running circadian clock (Iwasaki and Thomas, 1997). Under the assumption that the wasp's internal estimate of time is affected, in the same way that Hoagland's wife was, this is our first evidence that circadian clocks are unrelated to event timing. Circadian clocks are temperature compensated, while event timers are not. I pursue this argument further in Section 4.3.

The linearity of temperature effects is limited. Severe heat stress reduces response rates, and very severe heat stress changes the motivational state of the animal (e.g., they try to escape) (Richelle and Lejeune, 1980). The problem is that temperature changes could be affecting other physiological properties with little effect on the clock. An experiment by Rozin (1965) looked at temperature effect in the goldfish *Carassius auratus*. In FI trials, goldfish at different temperatures showed similar scalloped response curves that were different in absolute, but not relative response rates over the trial interval. This suggests that effects of temperature may be operating downstream of the clock, to modify the absolute rate of behavioral processes.

4.2.5 THE CLOCK RATE CHANGES WITH REINFORCEMENT RATE

Increased rates of reinforcement increase the relative temporal rate such that, in the temporal bisection procedure, the PSE is moved toward the long response. This is supported by several studies that show altered PSEs for different between-trial durations (Bizo and White, 1997; Fetterman and Killeen, 1991; Morgan et al., 1993).

The consequences of reinforcement rate on the subjective perception of time are quite significant. To the extent that this phenomenon is real in the wild, it complicates the possibility of optimal foraging in the sense of Charnov's marginal value theorem (Charnov, 1976). In this and many optimal foraging models, the ability of the animal to measure absolute time is directly responsible for its preference for certain food types and times of patch departure. If animals are incapable of measuring absolute time, then the ability to forage optimally should be predictably changed. The consequences of rate-biased time perception have been worked out in detail for the marginal value theorem (Hills and Adler, 2002). One of the conclusions of this work is that because of the costs associated with running the nervous system, animals have probably evolved to tune their arousal (and therefore temporal accuracy) to meet the requirements of specific environments. So they pay the price of rate-biased optimal foraging to avoid the price of inappropriately tuned perceptual timing.

4.2.6 SPECIES COMPARISONS

Animals show different capacities for learning and different sensory biases (e.g., Bitterman, 1975; Dukas, 1998). The capacity for learning temporal intervals has evolved in vertebrates and is supported in at least one parasitoid wasp. Many vertebrates show scalloped responses (Richelle and Lejeune, 1980). The consensus among fish studies is that some do and some do not (Eskin and Bitterman, 1960; Richelle and Lejeune, 1980; Talton et al., 1999). The African mouthbreeder (*Tilapia macrocephala*) apparently fails to show a scalloped response, whereas goldfish (*Carassius auratus*) appear to have no problem with it (Rozin, 1965). Pigeons can show varying responses under a wide range of different reinforcement regimes (Ferster and Skinner, 1957). Surprisingly (see Section 4.5.2), honeybees (*Apis mellifera*) show break-and-run behavior in pseudonaturalistic environments with delays of 20 or 90 sec (Grossman, 1973).

Are insects in general capable of timing short intervals? It is certainly possible that we have not yet asked the question in the appropriate way. It is equally possible that the genesis of certain brain structures coincident with vertebrate evolution mark a significant dichotomy in the evolutionary history of event timing. The evolution of the vertebrate forebrain facilitates the possibility of a homologous structure with the hippocampus in all vertebrates (Colombo et al., 2001; Portavella et al., 2002). The role of the hippocampus in spatial and temporal learning and memory is widely demonstrated (Jackson et al., 1998; Ono et al., 1995; Thompson, et al., 1982). Given their capacities for spatial learning in navigation, the possibility of an analogous structure in insects should not be ruled out (Dyer, 1998). I address this relationship in more detail in Section 4.4.

4.3 CIRCADIAN AND ULTRADIAN CLOCKS

Little is know of the molecular and cellular mechanisms of event timing. Molecular geneticists have yet to isolate an event timer in animals (see Cevik, this volume). Neuroscientists have the power to isolate function of gross anatomical regions by lesion and transplant, but cell number limits functional understanding of populations of neurons almost completely to neural simulations. Neuroscientists are not readily equipped to investigate genetic and molecular function.

The point of discussing circadian and ultradian clocks is twofold. First, it will allow us to make an important distinction between mechanisms of endogenously controlled time and those of perceived time. Second, it will provide a basic description of a molecular clock as a kind of null model against which we can address future questions.

Animal timing refers to a broad class of behaviors. These include general life history events such as when to stop making sperm and the age of first reproduction. They also include rhythmic behaviors with periods on the order of a year (circannual), longer than a day (infradian), a day (circadian), or shorter than a day (ultradian). The suggestion that animals have evolved to organize their lives in time could refer to any of these levels of behavioral timekeeping. Animal event timing, as I use it here, refers to none of these.

The fundamental mechanisms of animal event timing are sensory based. Event timing requires the ability to perceive and remember the duration of an external event. Rhythmic behaviors and the scheduling of large-scale life events are based on endogenously controlled, often genetically predetermined, timetables. Circadian rhythms are 24 h long not because the animal learns a 24-h period in its lifetime, but because it is genetically predisposed to timing an interval approximating the rotation of the earth. On another planet, or in a lab where light–dark (LD) cycles are manipulated, circadian clocks are far from functional in terms of recording the length of the LD cycle. Daily activity cycles appear to fall into the same category. They are driven in well-defined ways by circadian rhythms. It is rare for an animal to learn when to be most active in the LD cycle (but see Section 4.5.4).

This section is also designed to point out that the clock used to measure event duration is not necessarily the same clock that measures time of day. Experiments designed to expose animal event timers can be confounded by this time-of-day clock. For example, intervals of 24 h do not need to be measured, because they can be posted to the circadian phase. I will provide several lines of evidence in this section that the time-of-day clock is inefficient for measuring intervals different from 24 h and show that it is quite distinct from animal event timers.

4.3.1 CIRCADIAN CLOCK GENE mRNA LEVELS OSCILLATE WITH A CIRCADIAN RHYTHM

Circadian regulation of gene expression is well established in plants (i.e., *Arabidopsis* — Millar et al., 1995), fungi (i.e., *Neurospora* — Dunlap, 1996), insects (i.e., *Drosophila* — Iwasaki and Thomas, 1997), unicellular microorganisms (Lloyd, 1998), and vertebrates (Takahashi, 1995). I will describe in some detail only the *Neurospora* and *Drosophila* system because they are typical and well-studied examples of circadian dynamics. Our understanding of the molecular details governing the circadian clock is growing rapidly (reviewed in Okamura et al., 2002; Stanewsky, 2002) and is beyond the scope of this review, but I hope to describe the basics of the system in enough detail to provide a foundation for thinking about molecular event timers.

The filamentous bread mold, *Neurospora crassa*, exhibits a circadian rhythm in its asexual spore formation (conidiation) (Edmunds, 1988). The *frq* gene encodes a central element in this circadian rhythm. Both the *frq* gene mRNA and its protein product, FRQ, cycle in amount with a period of approximately 24 h (Dunlap, 1996). In a 24-h LD cycle, *frq* mRNA and FRQ levels are at their lowest point near the middle of the dark phase. Slowly rising, they peak approximately 10 to 12 h later, with FRQ levels always lagging behind mRNA levels by about 3 h.

The vinegar fruit fly, *Drosophila melanogaster*, shows oscillations in two of its circadian clock gene transcripts (*per* and *tim*) that are exactly out of phase with its own *frq* (Hardin et al., 1992). Their periods are the same, but when *frq* mRNA is beginning to rise, *per* and *tim* mRNAs are beginning to fall. Like FRQ, PER lags behind its mRNA transcript by several hours (Iwasaki and Thomas, 1997). Interestingly, a recently identified protein in mammals, *mPer1*, sharing high sequence similarity with the *Drosophila* PER protein, oscillates in phase with *frq* (Shigeyoshi et al., 1997), and a mutation in a similar gene in humans is correlated with familial advanced sleep phase syndrome (Toh et al., 2001).

In *Drosophila*, the PER and FRQ proteins are localized to the cytoplasm. In short order, FRQ enters into a binding complex with (at least) itself and PER enters into a 1:1 heterodimeric complex with TIM, as suggested by studies in the yeast two-hybrid system (Dunlap, 1996). These relationships appear to stabilize FRQ and PER in the cytosol. They also appear to be necessary for translocation to the nucleus, where they suppress their own expression (Aronson et al., 1994; Dunlap, 1996). This is the negative feedback mechanism that generates the cyclical rise and fall of protein products, allowing the animal to keep track of time.

In the absence of light (dark–dark (DD)), all of these gene products show free-running periods of about 24 h. The phase of gene expression can also be directly entrained by light, but this response is limited to certain intervals of the cycle. For example, in *Neurospora*, when FRQ levels are low, a pulse of light leads to rapid transcription of the *frq* mRNA, moving the phase of oscillation forward in time (Crosthwaite et al., 1995). Given the swiftness of the response, it is believed that light acts directly on the *frq* promoter (Dunlap, 1996). *mPer1* shows a similar response to light (Shigeyoshi et al., 1997). In *Drosophila*, light has little effect on *per* mRNA but reduces levels of TIM. Constant light breaks down the entire rhythm (Power et al., 1995). Given this evidence, it is not surprising that manipulations by light are unable to change the period of the circadian rhythm, but are able to adjust its phase.

Light is not the only source of entrainment for the circadian clock. Temperature is also a cue (Iwasaki and Thomas, 1997). There is recent evidence that the circadian clock can also be affected by conditioned stimuli (Amir and Stewart, 1996). Some disagreement exists about the extent of this phenomenon. There is evidence that social contacts in humans can synchronize circadian pacemakers (Hastings, 1997), but recent research on blind subjects and manipulated light schedules in sighted subjects supports the necessity of light as an entrainment cue (Czeisler, 1995). Pioneering work by Winfree (1980) led him to predict strong resetting of the circadian clock by light across a wide array of species, and this appears to hold true.

4.3.2 CIRCADIAN CLOCKS ARE TEMPERATURE COMPENSATED

Although there are physiological temperature limits for the maintenance of circadian rhythms, there is no effect of stable temperatures within these limits (Iwasaki and Thomas, 1997). However, temperature changes can elicit rises or falls in gene expression (Edery et al., 1994; Rensing et al., 1995). The mechanism by which this temperature compensation operates has been worked out in detail for *Neurospora*.

Within the first 100 codons of the *frq* gene there are three methionine codons (AUG) at codons 1, 11, and 100 (Liu et al., 1997). Codon 11 is not used to initiate the sequence under normal conditions, but codons 1 and 100 are. Thus, in wild-type *Neurospora* there are two FRQ proteins, $\text{FRQ}^{100\text{-}989}$ and $\text{FRQ}^{1\text{-}989}$, and either of them alone is sufficient for circadian rhythms. At low temperatures, $\text{FRQ}^{100\text{-}989}$ is preferentially transcribed. At high temperatures, $\text{FRQ}^{1\text{-}989}$ is preferentially transcribed. The ratio between the absolute levels of the two gene products is thus controlled by temperature. Removal of either form disturbs the ability of the clock to compensate for physiological temperature extremes (Liu et al., 1997).

It is possible that other mechanisms operate to compensate for temperature. Both *per* and *frq* encode an internally repetitive array of Thr-Gly codons. In *D. melanogaster* this region is polymorphic in length (Kyriacou et al., 1992). Work done by Rosato et al. (1996) shows a significant latitudinal cline in this repeat sequence ranging from Europe to North Africa. These sequences are directly related with the ability of the flies to maintain a compensated circadian rhythm at different temperatures (Sawyer et al., 1997). Furthermore, deleting the Thr-Gly region produces flies that have temperature-sensitive circadian periods (Kyriacou et al., 1992).

4.3.3 CIRCADIAN AND ULTRADIAN RHYTHMS ARE CONNECTED, BUT NOT WITH EVENT TIMING

Ultradian behaviors appear to oscillate in circadian time. They consist of such behaviors as the defecation cycle in *Caenorhabditis elegans* (Iwasaki et al., 1995) and wheel-running behavior in mice (Antoch et al., 1997). The relationship between circadian and ultradian behaviors is best understood in *D. melanogaster.* In a screen looking for mutants of the pupal–adult eclosion phenotype, Konopka and Benzer (1971) identified three mutants of the per gene: per^{s} showed a 19-h cycle, per^{L1} showed a 29-h cycle, and per^{01} appeared to be arrhythmic. per^{s} and per^{L1} mutations are due to single amino acid substitutions. per^{01} encodes a stop codon at the 460th residue (Yu et al., 1987). The amazing thing about these mutants is that their ultradian behaviors, like activity and courtship song cycles, are proportional to their circadian behaviors (Kyriacou et al., 1992). Where wild-type male flies have 60-sec courtship song cycles, *per*^{s} flies have 40-sec cycles, *per*^{L1} flies have 80-sec cycles, and *per*^{01} flies show little evidence of cycling at all.

D. melanogaster females show a preference for 55-sec songs, and *D. simulans* females prefer 35-sec songs. It is a reasonable assumption then that the various *per* mutations would show changes in female preference for male song duration. In fact, just the opposite is true (Kyriacou et al., 1992). *D. melanogaster* females, regardless of their *per* genotype, prefer 55-sec songs. To the extent that flies are not able to use other cues, this provides a fundamental difference between ultradian transmitter and receiver mechanisms. It also suggests that the event timer in *Drosophila* is not driven by an underlying circadian oscillation. This may be one of the more telling observations about circadian and event timing, explaining the peculiar inability of bees to discriminate short intervals despite their mastery of circadian time.

The *Zeitgedachtnis* (time sense) of honeybees is widely reported (Saunders, 1971; Seeley, 1995; Wilson, 1971). Bees can relocate almost anything provided it is presented at 24-h intervals (Saunders, 1971; Moore et al., 1989). As well, "marathon" dancers who return to the hive dance floor to dance for hours following a fruitful foraging trip compensate for the sun's motion as the day passes (Wilson, 1971). However, in FI trials, honeybees show no evidence that they can learn anything about a 2-min interval (Richelle and Lejeune, 1980).

Despite this evidence for a distinction between perceived time and circadian time, the relationship between ultradian and circadian behaviors is a profound one. The Syrian hamster *tau* mutant has a circadian rhythm that is shortened by 4 h from the wild type. Wild-type females have approximately 30-min periods of cortisol and luteinizing hormone fluctuations that are slightly shortened in the *tau* mutant (Loudon et al., 1994). The recently cloned circadian *Clock* gene in the mouse was isolated in a massive screen for mutants that exhibited altered wheel-running activity rhythms in constant darkness (King et al., 1997a, 1997b). Close inspection of King et al.'s (1997a) wheel-running data shows that the wheel-running activity cycle is very cyclical in its ultradian oscillations.

The pineal gland's circadian rhythm and direct control of numerous hormonally controlled behaviors is further evidence for this relationship between circadian and ultradian time. At the receiving end of the suprachiasmatic nucleus (see Section 4.3.4), the pineal gland is located at the posterior dorsal aspect of the diencephalon. The rhythmic release of melatonin is its most obvious circadian feature, as melatonin is directly responsible for transmitting the circadian LD signal to the rest of the organism (Menaker, 1997). Among other things, melatonin is known to affect human thermoregulation. Given the definitive relationship between body temperature and sleep (Wever, 1992), the pineal gland has a clear role in the sleep–wake cycle. In an experiment reported by Lavie (1992), eight young male adults experienced 20-min "days" for 48 h in a sleep–wake cycle of 7 and 13 min. In this experiment subjects were instructed to attempt to fall asleep and to resist sleep for 7 and 13 min, respectively, every 20 min. The results show a well-defined sleep–wake cycle at 24 h, despite the best efforts of the subjects to overcome this interval.

Studies of interval timing also reveal a circadian influence on attention and memory. Meck (1991) tested rats for their ability to discriminate 2- and 8-sec durations (temporal bisection procedure) over the course of the day. There was no effect of circadian phase on the clock rate — the PSE did not change. However, the overall sensitivity to time (measured by the variability of the response) was highest during the dark phase and lowest during the light phase. This relationship has also been demonstrated for honeybee arrival times, with more accuracy in the morning than later in the day (Moore et al., 1989). If there is a clear relationship between circadian clocks and event timing, this is likely to be it: circadian phase influences the accuracy of event timers. As an example, experiments on human isolation in Antarctica, submarines, and underground are typically difficult to interpret because subjects often lose their abilities to concentrate; it is as if the circadian mechanisms controlling attention are somehow lost (Harrison et al., 1989).

Unfortunately, the majority of psychophysical literature fails to mention the time of day at which experiments were performed or any salient features of the LD cycle. Ecological studies on animal behavior are seldom better, the unspoken assumption being that the behavior, once initiated, is stereotypical. Variance is regarded as "noise" in the form of genetic variance or sensitivity of the animal to subtle environmental factors. However, given Meck's (1991) results, it may be predictable circadian oscillations in the animal's sensitivity or general attention that is responsible for the behavioral variance. If multiple animals are observed over a given day, then time-of-day effect must be considered in the analysis.

A second issue with respect to the importance of recording LD cycles is that animals that are not reared in 24-h LD oscillations may not exhibit circadian rhythms (Richelle and Lejeune, 1980). For example, if the LD cycle at a particular geographical location or in a particular lab is highly unpredictable, then the activity rhythms observed in animals reared there may be quite arrhythmic or may be based on other cues, such as temperature or resource availability. These may lead to uncontrolled or unpredictable behavioral results that are not replicable under other LD cycles.

Finally, animals that exhibit circadian rhythms may be biased toward remembering 24-h event times. Honeybees are exceptionally good at following the daily peaks in pollen and nectar production by visiting only certain species of flowers at certain times of day (Saunders, 1971; Seeley, 1995). However, bees are unable to learn to return at non-24-h periods. Kestrels (*Falco tinnunculus*) and starlings (*Sturnus vulgaris*) have also been observed to follow food abundance in time, and both can be trained to return to a feeder at specific times of the day (Bell, 1991). Food-anticipatory activity rhythms have also been observed for rats fed at 24-h intervals (Rosenwasser, 1984). Rats show a clear inclination for remembering feeding times set at 24-h intervals over much shorter (3 to 14 h) or longer (34 h) times, as shown by Crystal (2001). Given the nature of temporal memory, which I discuss further in "How Event Timers Might Work" (Section 4.4), it is probably also the case that there is an annual memory bias, as animals may be able to remember more clearly their seasonal context simultaneously with important events.

More work needs to be done to verify the distinction between circadian rhythms and event timers (see Crystal, this volume). Molecular examinations of mechanisms involved in event timing require a phenotype for the isolation and cloning of relevant genes. A designer behavior would be useful in this respect. Tim Tully (DeZazzo and Tully, 1995) has made superb use of electrical stimulus to dissect memory formation in *Drosophila*. To determine if flies are capable of learning temporal durations, experimenters could train flies in a periodic shocking regime. For example, every 60 sec the experimenter runs a current through the cage. If flies have event timers, they may learn to associate flight at specific temporal intervals with the absence of shock. Reward paradigms might also be useful, in which flies are rewarded with food at consistent intervals. Once the phenotype is established, various *per* mutants could be assayed for defects in event timing (see Cevik, this volume). These mutants could then be assayed for more ecologically relevant behaviors associated with fitness. *C. elegans* might also be a useful subject for molecular study of event timers, as their nervous system and genome are amenable to neural and genetic investigation.

4.3.4 CIRCADIAN CLOCKS AND EVENT TIMERS ARE LOCALIZED TO DIFFERENT AREAS OF THE NERVOUS SYSTEM

The observation of circadian rhythms in unicellular organisms and the expression of circadian genes in many peripheral tissues in mammals suggest the possibility that all cells contain circadian rhythms (Balsalobre, 2002). While it is difficult to discount this possibility, expression patterns of circadian genes and brain lesion and transplant studies support specific localization of circadian clocks and event timers.

It is fairly well established in vertebrates that there is one circadian pacemaker: the suprachiasmatic nucleus (SCN) (Ralph and Hurd, 1995). The SCN is located over the optic chiasm rostral to the supraoptic nucleus. Cross-genotype transplants of SCN for Syrian hamster *tau* mutants have unambiguously defined the SCN as the major control mechanism of the mammalian circadian period (Ralph et al., 1990). The SCN, when moved from one hamster to another, is sufficient to alter the circadian rhythm. The SCN also shows strong expression of the *mPer1* and *Clock* genes, which are rapidly induced there by exposure to light (Hastings, 1997; Shigeyoshi et al., 1997).

SCN neurons in hypothalamic slices are observed to fire rhythmically at around 8 to 10 Hz during the day and 2 to 4 Hz at night (Hastings, 1997; Wagner et al., 1997). Isolated SCN neurons show a spontaneous rate of firing at near the same rates as in slices (Hastings, 1997). They also show a higher-order rhythm in frequency over the circadian day. The SCN reaches most of its targets via thalamus- and hypothalamus- (e.g., the pineal gland) mediated hormonal control (Hastings, 1997).

SCN function in natural environments is still poorly understood. In the laboratory, rodents rendered arrhythmic by SCN lesions live normal life spans (DeCoursey and Krulas, 1997). Besides circadian arrhythmia, the hibernation cycle is also affected by SCN lesions. SCN-lesioned female squirrels (*Spermophilus lateralis*) were observed to hibernate for almost 2 years in a laboratory setting (Ruby et al., 1996). Psychophysical experiments on event timing in SCN-lesioned animals show that, despite their inability to maintain daily rhythms, they can accurately time short intervals (Mistleberger, 1993).

An ambitious study of SCN-lesioned chipmunks returned these animals to the wild after surgery. Unfortunately, after 3000 h of fieldwork over slightly more than 2 years, there was essentially no observed effect of the SCN removal (DeCoursey and Krulas, 1998). The SCN-lesioned chipmunks did show evidence of brief arrhythmia and nighttime restlessness in the wild, but the activity cycles were largely the same for all chipmunks studied. There was also no significant effect on survivability, reproduction, or winter torpor duration.

While there is no direct relationship between the SCN and event timers, event timing does have a direct relationship with the hippocampus. The hippocampus has played a starring role in mammalian learning and memory since the lesioning of the human subject H.M.'s medial temporal lobes in the 1950s. After the surgery, H.M. was completely unable to form new declarative memories (Churchland and Sejnowski, 1994). Declarative memories are akin to semantic memory in the sense that the memory is based on the learning of semantic statement. Procedural memory, for which H.M. showed only minor deficit, is based on a kind of implicit function learning. For example, H.M. was perfectly capable of learning a motor skill, but he would be unlikely to remember that he had learned it.

Since that time, a great deal of attention has been paid to the role of the hippocampus in the formation of spatial memory. In food-storing birds, damage to the hippocampus disrupts memory for storage sites (Krebs et al., 1989). As well, bird species that store food have significantly larger hippocampal formations than those that do not. The operation of the spatial function of the hippocampus appears to work via location-coding neural cells (place fields) (e.g., Mizumori et al., 1996). When the animal returns to a specific spatial location, similar cells in the hippocampus fire. This information appears to be primarily visually coded.

The function of the hippocampus has also been established in the formation of episodic memory, but not necessarily in its retrieval (Fletcher et al., 1997). Episodic memory is typically associated with the ability to recollect past events, as originally introduced by Endel Tulving (1972). It was coined to represent any type of memory that was not strictly lexical (semantic memory), and thus it would represent essentially all temporal forms of learning. Recent evidence using positron emission tomography (PET) finds the retrieval of episodic memory events localized in the right prefrontal cortex, with a limited functional role played by the hippocampus (Fletcher et al., 1997).

Hippocampal lesions are shown to operate in the formation of temporal memory in rats (Meck et al., 1984). Once the memory is formed, however, the hippocampus becomes less important. Effects of hippocampal lesions include a lack of avoidance for previously visited maze sites, the inability to withhold or inhibit previously learned response patterns, and the foreshortening of temporal memories (Kesner, 2002; Meck, 1988; Meck et al., 1984).

4.4 HOW EVENT TIMERS MIGHT WORK

Given the hippocampal evidence, it seems likely that the hippocampus operates as a kind of ticking backdrop upon which episodic events can be hung until they are stored in a longer-term reference memory. Certainly hippocampal patterns are utilized in numerous ways, as previously assigned place fields do fire in new locations over the lifetime of a rat (Mizumori, et al., 1996).

This kind of hippocampal tagging has been modeled in detail for sequential spatial memory using a large-scale simulation of hippocampal function (Wallenstein and Hasselmo, 1997; Wallenstein et al., 1998). Multicompartmental pyramidal cells are shown to have synchronizing behavior over multitrial learning, and this is suggested as a mechanism for sequential learning. The pyramidal cells, which fire chaotically before the learning trial, use this prerandomization to settle into nonpredictable and location-specific patterns of firing. This is reminiscent of the kind of unsupervised self-organization exhibited by Kohonen networks (Haykin, 1994). It is different in that neighboring events in space share similar contextual patterns of hippocampal cell firing. In this way, when a sensory stimulus arises that is unfamiliar, the cells that fire in response to that stimulus partially stimulate the "memory" of familiar neighboring events.

Is it possible that temporal interval discrimination works by a similar mechanism? Coexisting with place fields, we would expect to find an analogous kind of "time field." By necessity, the time field could not operate exactly like the place field. In space, sensory input is constant and animals could run spatial information through the hippocampal filter persistently. This would perpetuate the synchronous cell firing in a way that time fields might be unable to do. For example, in order for a rat to learn the duration between signal and reward, it must have a sense of time. In space, the interval is exogenously applied — the space field moves and the sensory cells respond. In time, the interval must be measured by an internal clock.

What could the clock be if it is not related in some way to the circadian clock? The observation of high-frequency intracortical oscillations by electroencephalograph (EEG) provides a basis for a possible clock hand in vertebrates. It has been suggested before that composite cortical waveforms measured by EEG operate as a pacemaker in duration timing (see Artieda and Pastor, 1996; Pouthas, this volume; Sakata and Onoda, this volume; Treisman et al., 1994). Unfortunately, EEGs measure waveforms produced by populations of cells, and it is often very difficult to isolate particular areas of the brain for specific analyses. Nonetheless, evidence for the EEG pacemaker hypothesis has been provided by work showing interactions between auditory click rates, certain EEG components, and the simultaneous assessment of duration (Treisman et al., 1994).

A more specific neural pacemaker central to the hippocampus is provided by observations of theta and gamma oscillations from *in vivo* recordings of the hippocampus (Wallenstein and Hasselmo, 1997). In the sequential place field model referred to above, theta and gamma oscillations are produced by GABAergic receptor inhibition of recurrent collaterals among pyramidal cells and between pyramidal cells and nonpyramidal neurons. The effective nature of this system is to iterate and check at each time step, such that internal and external signals are integrated with the background hippocampal pattern in a meaningful way. Cells may oscillate at different or longer intervals and become associated with the duration when in specific states, such that a series of population patterns is gradually learned over progressive trials.

Iterate and check, however, may be only half of the story. Animals involved in temporal training tasks often behave in a peculiar but stereotypical way that might be further related to the spatio-temporal integration of the hippocampus. This behavior is characterized by seemingly unrelated activities between the stimulus and the reward. For example, a rat might chew its tail, a monkey might jump around its cage in a repetitive way, and a human might tap her finger or shake her head. It is also observed that animals engaging in these collateral behaviors are more efficient in their response time than animals that do not perform these behaviors (Richelle and Lejeune, 1980). These behaviors could act as a kind of context counting. Assuming the animal is unable to count (or asked not to, in the case of humans), it may, in the process of learning the interval, learn sequential behaviors associated with the particular sequence of population patterns in the hippocampus. This makes perfect sense in terms of the spatio-temporal aspects of hippocampal learning — it provides an efficient way to turn time into space, which can then be sensed continuously over the interval. It also provides a physiological basis for the behavioral theory of timing and multiple-timescale theory. Not only does the animal iterate and check, it reinforces the dynamic pattern of cellular events by engaging in context-specific behavior.

This contextual theory of timing may also explain why humans appear to have different timers for long and short durations — one temperature compensated and one not, respectively (Aschoff, 1998). The explanation may be that for short intervals, animals count either behaviors or some internally registered series, but for longer intervals, especially in humans, they do not keep track of time, but reflect on how much time should have passed given the events that have taken place in the interval. Whereas counting provides instantaneous and a more likely temperature-modulated mechanism for measuring time, reflection is initiated on a more variable schedule and is more a measurement of what the interval looked like after the fact than what it actually felt like while it was happening. That is to say, reflecting is a different kind of event timer than counting.

Evidence for an embedded, context-specific memory is supported by research on temporal memory in humans (Friedman, 1993). An appropriately reflective model for how events are recollected is the theory of reconstructive memory. Reconstruction of remembered events is based on recognition of an event with respect to extant cues during the event interval. Reconstructive memory explains otherwise anomalous characteristics of memory, like primacy (enhanced memory for initial events), scale effects (e.g., more accuracy for time of day than month or year), and facilitative effect of background temporal structure (Friedman, 1993). Subjects may be self-generating temporal structure through collateral behaviors. Reconstructive memory also supports a bias toward memory of events with more endogenous and external cues, as in 24-h and seasonal memories (see Section 4.3.4).

Because most organisms do not have a hippocampus, I would now like to discuss a smaller timer, one that is easily carried by individual cells. It shares some molecular features with that of the circadian clock, but it is linear in its response. It involves the activity of a single protein induced by a specific stimulus, which is then followed by a decay of the protein back to its original state. The protein activity could involve its production (as in circadian rhythms), its mobilization to a specific area of the cell (e.g., ion channels localized to the membrane of a neuron), or a structural change in the protein (e.g., exposing a protein binding domain). The metabolic nature of the decay timer also makes it agreeable with temperature effects on clock speed. These “clocks,” for which I will use the general term decay timers, have been described in the control of countless molecular interactions (e.g., Ishijima and Yanagida, 2001; Takai et al., 2001) and are potentially our most primitive event timers.

An example of an ecological problem that is most feasibly solved by a decay timer is that of local search time in the absence of further resource acquisition. For example, if an animal in the presence of a reinforcing signal (e.g., food or mating pheromone) suddenly finds that the signal is reduced or absent, it must make a decision about how long to continue searching for the reinforcer in its present location before it decides to search elsewhere. This behavioral strategy of looking first locally and then globally is called an area-restricted search and has been observed in a wide variety of organisms (Kareiva and Odell, 1987; White et al., 1984). Underlying this strategy is a clock that keeps track of the time elapsed since the animal last encountered food. A decay timer would be appropriate for this behavior, as it could be reset by food and then directly control turning behavior by modulating proteins that control turning rates.

The run-and-tumble behavior of *Escherichia coli* bacteria follows this description, involving a phosphorylation cascade that begins with membrane proteins that bind to extracellular ligands. In the absence of a stimulating resource, these membrane proteins act through phosphorylation of downstream secondary messenger proteins, which then bind to the flagellar motor components to cause flagellar reversal and tumbly swimming (Stock and Surette, 1996). The phosphorylation schedule of these proteins is on the order of seconds, and the whole system works like clockwork to move the animals up concentration gradients.

While this is an example of a timed endogenous behavior, it is not an example of an interval timer, because the bacteria do not learn the duration of an external signal. If the animal could change the temporal dynamics of its turning in response to different resource environments, this would provide us with an understanding of how external events that are not necessarily timed with an event timer can lead to developmental changes in optimally timed behavior patterns. This developmental retiming of behaviors is likely to be a critical step in the evolution of interval timers. Promising organisms for this kind of study are *Drosophila melanogaster* and the nematode *Caenorhabditis elegans*, which are convenient organisms for molecular and genetic study that also have the wherewithal to search for food when it is no longer around. I do not believe that we are likely to find fully formed interval timers in these animals, but instead the molecular machinery from which interval timers are constructed.

Experiments designed to distinguish between decay timers and time fields, without taking into account the molecular machinery involved, are probably bound to fail. The reason is that the time field model is perfectly capable of acting like a decay timer and, in fact, undoubtedly consists of numerous decay timers that set the context for contiguous spatial and temporal phenomenon (Young and McNaughton, 2000). However, there is a rather deep distinction between these different event timers in the form of the credit-assignment problem as it is established in the psychological literature (Machado, 1997; Staddon and Higa, 1999). The credit-assignment problem is based on the animal's attention to the relevant reward cue. How, for example, does a rat learn that the onset of the red light signals food in 40 sec and that changes in air temperature are unrelated? I believe one of the premises of the decay timer must be that the credit is assigned in the evolutionary history of the animal. Bacteria, bees, and other invertebrates do not learn to assign a particular stimulus to a decay timer. That is given to them for free. On the other hand, the decay timers in the hippocampus are actually used to solve the credit-assignment problem. They do this by maintaining the firing rates of certain pyramidal cells even after the response stimulus is gone. This allows contiguous events in time and space to be contextually associated with neighboring events (Wallenstein et al., 1998). The relevant cues to which any given event timer is sensitive are intimately related to an evolutionary bias for certain environmental cues. Thus, negative results on event timing experiments may be limited to telling us about a very specific environmental stimulus (see "Navigation," Section 4.5.2).

4.5 EVENT TIMERS IN THE NATURAL WORLD

The remainder of this review is devoted to understanding why animals need event timers. One might argue that there is no need; all ecologically relevant behaviors could just as easily be performed without this faculty. I recognize this argument not because it is helpful to understanding the behavior, but because it elucidates a very real constraint on our understanding of animal event timing. In the natural world, it is very difficult to tell by what cues an animal makes its decisions. Until we can isolate the event timer or show that its properties are consistent with behavioral predictions (see Bateson, this volume), any assumptions we make about the behavioral ecology of animals using event timers run the risk of oversight. On the other hand, without understanding the ecological context to which the event timer might be adapted, claims that an animal does or does not have an event timer based on laboratory tests assume a similar risk.

With respect to the argument of clock existence, however, we are at a slight advantage. From the psychophysics, we know the behavior exists. At this point we are merely in the business of knowing why. But how can we know why if we are not sure when the behavior really exists? Pigeons in cages can learn the difference between 2 and 8 sec. Does this mean that an osprey uses time to capture prey? It does not. Does this mean that squirrels make assumptions about how much time they would have to escape given the appearance of a predator in a particular location? It does not mean this either.

The first step toward understanding the adaptive contribution of event timers is to recognize the contribution they would make if they were being used. This will provide us with some sense of the situations that might have facilitated the evolution of event timers. The following tour through event timing in the natural world will focus primarily on the domains of animal behavior that would show a positive fitness relationship in the presence of a cost-free event timer that can associate nonoverlapping events in time. I will discuss the difficulties with assessing event timer cost in "Conclusions" (Section 4.6).

4.5.1 COMMUNICATION

Communication is a distinctly temporal behavior. It requires transmitting signals in sequence and duration such that a receiving organism understands the message. There are cases when the timing of symbolic components is unimportant, for example, when one is merely trying to get another's attention. Here we are interested in the relationship between syntactical elements in time and the way in which that conveys information. More specifically, we are interested in animals that learn how to communicate.

Songbirds acquire songs by listening to other birds (Beecher et al., 1998). The primary reason for this appears to be ecological. For song sparrows, the song repertoire is usually learned after the bird leaves its birthplace and during the first season of territory establishment (Beecher, 1994). In this way, the song sparrow learns the social communication strategies of its neighbors. This is further evidenced by song sparrows showing a preference for the learning of already shared songs (Beecher et al., 1998).

The fact that birds can learn frequency and durational components of a song implies a usefulness for event timing (see MacDonald and Meck, this volume). If one bird intends to mimic the call of another, then it must be able to record that call in memory. Functionally, the mechanism that records the call is an event timer; it learns the sequence and duration of notes that constitute the local song. Whether this ability can be generalized to record the times of nonsyntactic events remains to be established.

Linguistic studies in humans recognize a temporal component, but a clear understanding of exactly how that component is manifested is far from understood (Port et al., 1995). Some models of language acquisition are distinctly similar to contemporary models of hippocampal function in their use of recurrent networks (Port et al., 1995; Wallenstein et al., 1998). There is also evidence that perceived time is shorter for familiar auditory signals than it is for unfamiliar signals, suggesting that perceived time is not absolute for auditory signals but is influenced by the content of the perceived signal (Kowal, 1984). The main difficulty with results from linguistic studies, as it is for essentially all studies on communication, is that it is extremely difficult to separate the meaning from the message.

Insect communication is understood to carry information in its gross rhythms. There is evidence that insects distinguish likely mates by the gaps between signals, the interpulse interval (Kyriacou et al., 1992; Michelsen et al., 1985). In the case of *Drosophila* the interpulse interval appears to be under genetic control with a well-defined relationship with circadian rhythms (see Section 4.3.3).

What about the receiver? Moths are useful for studying auditory transduction because they have a relatively simple ear, with one or two receptor cells attached to an accessible tympanum. In moths, specific cells can operate as frequency filters (Michelsen et al., 1985), tuned to specific sensory stimuli. Pattern-sensitive neurons have also been observed in the pyloric network of lobster (Hooper, 1998). The presence of such neurons in *D. melanogaster* would explain stable female preferences despite differences in the circadian schedule. In this way, invertebrates may bypass the need for the higher cortical functioning that goes along with vertebrate event timers.

4.5.2 NAVIGATION

Animal navigation involves a gamut of sensory acuities to various environmental signals. As a consequence, there are countless ways to avoid noncircadian clocks:

birds, insects, and fish use celestial and magnetic compasses; honeybees use polarized light; wasps have memory for landmarks; salmon can find their breeding grounds by smell; and amphipod crustaceans use the slope of the ground (Daan, 1981; Dyer, 1998; Gould, 1998). In fact, the only evidence for an event timer in navigation is that some animals appear to know how far they have gone.

This is best exemplified by the waggle dance of honeybees. Remarkably, honeybees returning to the nest can inform other workers of the exact whereabouts of a forage site. The waggle dance transmits direction by establishing an angular relationship between the sun and the forage site in the form of a linear waggle movement at the same angle from the vertical axis of the hive. The distance to the site is transmitted by the distance of the linear waggle. The worker increases her waggle distance by about 75 msec per 100 m of foraging distance (Seeley, 1995). A decay timer would be useful in transmitting this signal, but a kind of event timer would be required for measuring the initial distance and for other bees receiving the signal at the hive. Time based on metabolic costs is probably far more prevalent than time based on the observation of events. The energy expenditure in flight could be used as the assay of flight duration. Bees may leave the hive or return to it with tuned energy stores so as to accomplish this. That another bee watches or follows the dance and then knows the distance to the forage site implies a more complicated mechanism.

The behavior of honeybees in the wild makes the FI data for honeybees particularly cumbersome (Grossman, 1973). It suggests that despite Grossman's effort to simulate a naturalistic environment in order to measure honeybee event timing, he may have been asking the question in the wrong way. There is no evidence that honeybees are confronted with anything that replenishes itself at 1-min intervals in the wild (Seeley, 1995). A honeybee may return to the hive to communicate the exact location of a new nectar source and still be unable to learn that a flower takes 20 sec to replenish its nectar stores. This entire behavior pattern appears to follow the logic of the specificity of decay timers. In general, if one expects to find event timers in insects, then one needs to accept the possibility that these event timers are very phylogenetically derived and highly specified.

The role of chemotaxis or navigation by thermal gradients is typically overlooked in the standard navigation literature. Gradient navigation requires either spatially or temporally separated samples of the environment. Which of these to choose depends critically on the size of the organism. For *Escherichia coli*, and similarly sized animals, the primary difficulty lies in the signal-to-noise ratio introduced by Brownian motion (Berg, 1983). Temporally spaced samples are of limited utility if animals are unable to find their way back to previous positions. It is for this reason that as size decreases, spatial mechanisms become more informative (Dusenberry, 1998). While there is support of spatially distributed processing at the opposite ends of *E. coli* (Grebe and Stock, 1998; Dusenberry, 1998), there is also evidence that they weight temporal experiences over time (Segall et al., 1983) (also see Section 4.4).

4.5.3 REPRODUCTION

Reproduction involves a highly defined series of behaviors. To locate a mate, an animal must know where and when to look. I was unable to find any evidence that animals learn the temporal aspects of this behavior. In most cases, the timing of mating behaviors appears to be a possible form of sympatric speciation. For example, the temporal staggering of male mating flights in East African army ants and the nocturnal activity patterns of moths maintains a temporal separation between species in reproductive timing (Daan, 1981).

There is a relationship between event timing and circadian rhythms in the time-sharing behavior of parent doves (*Streptopelia risioria*) (Gibbon et al., 1984; Silver and Bittman, 1984). The female spends up to 18 h on the nest each day and is relieved by the male during one 6-h interval. If the male is prevented from starting his sit bout at the appropriate time, the female will return after 6 h regardless of the duration of the male's effort. The male, however, will dispute the rightful sitter with her until his 6 h are finished. Given that it is unknown whether the male learns the appropriate sitting interval, it is almost impossible to conclude that the dove has a generalized event timer. The male dove might simply have a genetically timed 6-h alarm clock in his brain that is started by sitting on the nest.

How might this alarm clock work? Presumably, in a way very similar to that of the operation of light on the circadian clock. In the case of the male dove, sitting on the nest causes a pulse of gene expression in the hypothetical "sit" gene. The SIT proteins degrade over time until they reach a minimum threshold level, at which point the dove gets up. This is, of course, the decay timer.

4.5.4 PREDATOR AVOIDANCE

Animals attempting to avoid predators can do so in a number of ways. They can wait for them to arrive and then try to escape. They can time their activity out of phase with predator foraging. Or they can attempt to satiate predators with fellow members of the species. All of these behaviors could gain from event timers.

There are several methods of escape in the sense that I use it above. An animal might run for cover, or it might trick the predator into thinking it is not a prey item. In either case, learning the principles of predator vigilance can increase foraging efficiency. In some cases, the presence of predators actually enhances foraging efficiency (Holtcamp et al., 1997).

For an animal foraging in the open, attention to predators is necessary for survival. But how much time should an animal devote to vigilance? Animals that economize predator vigilance strike an optimal relationship between eating and being eaten (Dukas, 1998). Potential environmental factors are the nearest possible escape and the proximity of possible predators. In the latter case, there is evidence that adult ground squirrels with obstructed views of their surroundings are more vigilant than those with clear views (Arenz and Leger, 1997). Juveniles were undeterred, suggesting the behavior is learned.

A useful trick against predators is feigning death. Vigilance is helpful here, but of equal importance is knowing how long one should stay "dead." Anxious resurrection will indubitably lead to real mortality. But staying dead until a predator unbeguiled by death arrives is an equally poor outcome. Domestic chicks perform the death-feigning behavior instinctively. The time spent inanimate is associated with the circadian phase (Richelle and Lejeune, 1980), suggesting a control mechanism possibly analogous to that found in the courtship behavior of fruit flies.

Predator avoidance can also take the form of knowing when predators are active and choosing to be active at other times. This is exemplified by the behavior of baby alligators (*Alligator* spp.), which, when heavily preyed upon by African fish eagles (*Haliatus vocifer*), move from diurnal to nocturnal activity rhythms (Curio, 1976). This suggests a phenotypic plasticity in the way behaviors are linked to circadian clocks, reminiscent of honeybees learning the daily cycles of nectar production.

By far, one of the most popular forms of predator avoidance is feeding them your neighbors. This form of predator avoidance also leads to some of the longest-known temporal periods for behavioral synchronization. Plants do this in the form of masting, which is a form of synchronized seed production that can occur over periods of many years (Silvertown, 1980). Periodical cicadas (*Magicicada* spp.) are one of the more artful exemplars of this phenomenon (Lloyd and Dybas, 1966). Having the longest-known life cycles of any insect (barring some queen ants), they emerge from the ground to mate, lay eggs, and die within weeks of one another every 13 or 17 years, depending on the species. The behavior is hypothesized to be a predator-satiating mechanism above ground and a predator avoidance mechanism below ground (Lloyd and Dybas, 1966).

The predator-satiating mechanism works on the premise that predators are limited in their maximal intake rate of prey. This can be due to simple satiation or to prey handling times. For example, when guillemot fledglings (*Uria lomvia*) jump from their breeding cliffs, the probability of death is significantly enhanced if the bird jumps alone (Daan, 1981). The usual strategy is to jump with everyone else, so that the fledglings are shielded from the predatory glaucous gulls (*Larus hyperboreus*) by other members of their cohort. If the glaucous gulls did not have a maximal intake rate, they would eat everyone as soon as they were exposed.

4.5.5 FORAGING

Animals acquire resources in countless ways. Temporal perception is useful in many of them. For example, speciation mechanisms are undoubtedly related to competitive exclusion in competition for resources. This provides a force for sympatric speciation via resource partitioning in time. In this case, animals forage at different times of day but still eat the same foods, as is observed in several species of tern, lizards, crustaceans, and gastropods (Schoener, 1970, 1974). This reduces competition while simultaneously economizing resource acquisition in a kind of temporal ideal free distribution (for a description of the ideal free distribution in space, see Milinski and Parker, 1991). Whether these behaviors are learned remains to be established.

An area that seems most promising for the discovery of event timers in the wild is in the empirical testing of optimal foraging theory. A basic assumption of optimal foraging theory is that animals recognize something about resource distribution (the psychophysical evidence for this was discussed in Section 4.2.2). This recognition can be more or less behaviorally plastic, depending on the cognitive faculties of the animal. If resource distribution is relatively stable over time, a species may evolve a patch departure schedule that is based on generations of trial and error without regard for the present environmental conditions. At the other extreme, animals with event timers could measure the rate of food intake at different patches or with different foods and compare them to optimize foraging schedules in the future. Animals could also measure the time between patches and incorporate this information into the overall strategy. This updating of foraging behavior based on prior information is commonly referred to as Bayesian foraging (Getty and Krebs, 1985; Killeen et al., 1996). This is in direct contrast to the assumptions of the marginal value theorem, which assumes that animals know resource distribution, transit, and handling times even before they begin foraging (Charnov, 1976; Valone and Brown, 1989). While the marginal value theorem provides a useful null model against which to compare animal behaviors, it does not require an event timer per se, as animals may evolve to forage at optimal schedules. However, when resource distributions change over the lifetime of the animal, an event timer will be required for animals to appropriately update their Bayesian expectations. The study of Bayesian foraging behavior in organisms amenable to molecular and genetic study would provide another promising inlet into the mechanisms involved in sensing and integrating information about temporal intervals into future behavior patterns.

Bayesian foraging behavior is also likely to be ubiquitous. Many animals require patch assessment before they can make optimal foraging decisions (Valone and Brown, 1989). Constraints on forager memory and resource changes over time force the reinvestigation of patches (Belisle and Cresswell, 1997). Animals use recent information about temporal aspects of resource distribution to make decisions about patch departure. Among central place foragers, there is a positive correlation between distance traveled to the foraging site and the patch residence time (see Bateson, this volume; Kacelnik, 1984).

Studies of risk-sensitive foraging show the ability of animals to detect the variance of resource acquisition even when the mean is unchanged (Real and Caraco, 1986). For example, honeybees prefer stable rewards to unstable rewards, regardless of the mean. This requires an event timer. The adaptive explanation for stable vs. unstable preferences is described by Bateson (this volume).

The data on animal preferences do not entirely corroborate the theory of risk-sensitive foraging (Bateson and Kacelnik, 1998; Ha et al., 1990; Stephens, 1980). Explanations for this are based on cognitive constraints related to time perception and memory. Animals may discount time in different ways, depending on past experience or genetic predisposition, or they may average rate intake over different intervals. Animals also have certain constraints on their abilities to discriminate event times, as typified by Weber's law (Bateson and Kacelnik, 1998; described in Section 4.2.1). I suggested earlier that animals may suffer from distorted perceptions of time based on intake rate. The consequences for rate-biased time perception have been described by Hills and Adler (2002).

The order of experiences also appears to play a role in event timing. A kind of first impression among animals, called side bias, sometimes confounds psychophysical results (Ha et al., 1990). Side bias generally refers to some unknown force controlling the animal's behavior. Experimenters typically make an effort to remove these animals from the analyses. Nonetheless, every animal may experience this kind of bias with variable time reinforcement schedules. Large initial rewards could lead to particularly strong cognitive bias. A series of large rewards might also instill a memory of a rare event that keeps the animal coming back. Exactly how the temporal sequence of events establishes memory biases is still an open question.

Another temporal factor in foraging is the effect of time horizons (Krebs and Kacelnik, 1984). Time horizons affect the behaviors of animals that are able to anticipate the ends of foraging bouts. Late in the day an animal may choose to continue foraging in a poor patch because it does not have enough time to get to a better one. A mechanism to avoid this problem involves organizing a series of patches in time and visiting them so as to maximize resource gain over the duration.

Traplining fits the criteria of serial patch arrangement. It is a behavior seen in bats and a number of birds and frugivorous primates. It involves following a prespecified path during the daily foraging bout (Bell, 1991). Time horizons undoubtedly affect traplining schedules, but once scheduled, traplining provides a short-term answer to the time horizon problem. A similar behavior pattern is cropping. Cropping involves visiting locations at intervals that allow for resource replenishment. Cody (1971) observed various species of finches cropping seeds in the Mohave Desert at the base of a mountain range. These birds moved their foraging sites to different distances from the mountain each day, scheduling revisitation rates to match replenishment rates. Insect-eating shore birds also appear to crop along the shore. Consistent with these observations, lab experiments on cache recovery in scrub jays (*Aphelocoma coerulescens*) show that they can learn and recall what, where, and when information about stored food items for up to 5 days (Clayton and Dickinson, 1998). In some manifestations of cropping, an event timer could help an animal know when to return to a foraging site.

4.5.6 PREY PURSUIT AND CAPTURE

For an American osprey (*Pandion haliaetus*) to intercept a fish in shallow water, it must perfectly time its descent and penetration of the water to match the location of its prey. Individual osprey have been observed catching many different kinds of fish, and this suggests that osprey learn to anticipate the position of their prey by observing something about individual fish (Bent, 1961). Numerous predators intercept moving prey (Curio, 1976), whether it is wolves (*Canis lupus*) taking down moose (*Alces alces*) in the Yukon or golden eagles (*Aquila chrysaetos*) catching rabbits (*Lepus* spp.) in the plains. The behavior seems to be a general one. But does it require an event timer?

For insects, the answer is probably no. At least in tiger beetles, the method of pursuit and capture is to constantly move where the prey is, with rapid halts to reorient its direction toward the location of the prey (Gilbert, 1997). An alternative strategy is that the insect measures the velocity of its prey and moves to where the prey will be. Evidence of the latter does not exist.

Do osprey pursue like tiger beetles? It is too early to tell. Computer imaging of predator and prey paths, like those done for the tiger beetle (Gilbert, 1997), is not yet used for larger animals. In the case of fish pursuit by birds, even simple video analysis is constrained by simultaneous water and air analyses. Still, this is likely to be the most informative method for determining the nature of larger predator pursuit and the mechanisms involved.

Another case where predator pursuit may involve timing is in group foraging efforts. Members of a concerted predatory effort must understand their duties in relation to other members. For example, observations of predatory groups breaking up to surround prey on scales at which they are not visible to one another requires an estimation of other group members in space and time (Curio, 1976). Similarly, knowing when to take over in the pursuit of prey in serial efforts necessitates an understanding of when to act. Knowing the traits of other individuals in the group, recognizing fatigue or opportunity, being at the right place at the right time — all of these things require clocks plus ample cognitive space for allocating memories and learned predatory skills. Interestingly, evolution has had no trouble solving similar problems under more predictable settings; honeybees appear to perform essentially the same feats of temporal economy within the hive (Moore et al., 1998).

4.5.7 GENERALIZED LEARNING

The role of the hippocampus is well established in associative learning assays of the conditioned stimulus–unconditioned stimulus (CS-US) type (Ono et al., 1995; Thompson et al., 1982). Typically in CS-US trials an animal is trained to associate a neutral CS (e.g., an odor) with a previously meaningful US (e.g., pain or reward). The archetypical example is that of Pavlov and his bell-stimulated salivating dog. The paradigm takes advantage of the fact that the animal has some unconditioned response (UR) to the US, so that the experimenter can verify association of the CS by omitting the US while still observing the UR.

As one might expect, there is a clear relationship between the timing of various components of the CS-US and the ability of the animal to learn the association. For example, there is an optimal time of CS length that maximizes learning rate (Cooper, 1991). This is reminiscent of the credit-assignment problem and suggests that the duration of environmental signals may affect attention for those signals when they are subsequently paired with relevant stimuli.

At the level of the synapse, long-term potentiation (LTP) in the hippocampus is a form of learning based on the modulation of synaptic gain between the presynaptic and postsynaptic cell (Churchland and Sejnowski, 1994). N-methyl-D-aspartate (NMDA)–type glutamate receptors are required for LTP, and their voltage-gated properties necessitate that the postsynaptic cell fire for a certain temporal duration while the presynaptic cell fires in order for the NMDA receptors to be activated. NMDA activation operates on gene transcription (Bading et al., 1993), and this may be a mechanism for the modulation of long-term synaptic gain. Several phases exist for hippocampal LTP, and these have been compared to the various phases exhibited in vertebrate memory (DeZazzo and Tully, 1995). A recent finding suggests that this mechanism may also operate in a retrograde fashion by weakening synapses when the presynaptic cell fires after the postsynaptic cell action potential (Markram et al., 1997). This mechanism is not an event timer in the usual sense; it is more akin to a coincidence detector. But it does exhibit the flavor of event timers, and it possibly explains the contiguity of the CS-US sequence (see Matell and Meck, 2000; Matell et al., this volume).

The hippocampus appears to be required in order to get beyond coincidence-limited association. In trace conditioning assays, in which a puff of air follows a brief tone, the hippocampus is required for association of nonoverlapping stimuli (Thompson et al., 1982). Hippocampal lesions only allow learning when the CS and US are overlapping in time.

Hippocampal-type event timers offer substantial associative powers in the development of tool use and causal recollection. A Japanese macaque (*Macaca fuscata*) washing a potato must somehow learn to associate the improved potato with the action that preceded it. A more common example of this kind of temporally gapped causal association is the learned food avoidance response exhibited in a large number of vertebrates. If an animal becomes sick from eating a toxic food, it may learn to avoid that food in the future. There is a temporal relationship here because delay of adverse consequences inevitably limits the association of the food with its effects (Stephens and Krebs, 1986).

4.6 CONCLUSIONS

Time is easily one of the more slippery subjects in four dimensions. Our linear and subjective experience of it makes it rather difficult to define. Understanding how other organisms experience it is even more problematic. Although when one stops to take it all in, a considerable amount is actually known about how animals perceive time. Molecular geneticists and neurobiologists are in fact making numerous inroads into the mechanisms controlling event timing. Ecologists as well are refining their ideas to incorporate evidence from psychophysical studies of timing and time perception (see Bateson, this volume; Bateson and Kacelnik, 1998; Hills and Adler, 2002).

A hopeful contribution of this review is the distinction between circadian time and event timing. Circadian timers are temperature compensated, while event timers are most likely not. Circadian timers do not appear useful for recording event intervals that deviate from the 24-h LD cycle, whereas event timer accuracy appears to be a function of the linear increment in duration (Weber's law). Vertebrate circadian and event timers also seem to be isolated to different areas of the nervous system, but this remains to be corroborated in invertebrates. Circadian time also affects the variance in event timer responses, but not the duration. These distinctions provide us with a basis for understanding the relationship between the two mechanisms and for understanding why, in an adaptive sense, an animal is biased toward certain environmental stimuli and patterns of behavior that follow geophysical rhythms.

I have also presented possible mechanisms for event timers that are in agreement with the available evidence from psychophysics and neurophysiology. Time fields are an analogous structure to space fields and may operate by the same mechanism. Molecular decay timers are presented as an explanation for essentially all timed events (as the hippocampus contains decay timers, potentially in the form of ion channel conformation changes). The difference between decay timers and time fields may simply be in the number of cells used and the allocation of receptors to specific sensory cues. This difference may also explain failures to show evidence for event timers in invertebrates, as a consequence of sensory bias.

The problem with event timers is one that is shared by much of the literature on the adaptive value of cognitive mechanisms. We do not yet understand the costs of nervous tissue (Aiello, 1997). Costs associated with changes or new development of nervous tissue are still far from quantified. Genetic perturbations may be bringing us closer to this, but the distributed nature of nervous tissue will presumably confound our efforts for some time. In the SCN example, a portion of the brain was removed with no observable effect over a 2-year span. This suggests that a trait of nervous systems in general may be their plasticity. The costs and adaptive value of phenotypic plasticity, even though animal event timing is one of them, are still very much in the dark. Why not perceive everything, record perfect memories of it all, and be able to tell me to the minute (without looking at a clock) how long you have been reading this?

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REFERENCES

Aiello, L.C., Brains and guts in human evolution: the expensive tissue hypothesis, *Braz. J. Genet*., 20, 141–148, 1997.

Amir, S. and Stewart, J., Resetting of the circadian clock by a conditioned stimulus, *Nature*, 379, 542–545, 1996.

Antoch, M.P., Song, E.-J., Chang, A.-M., Vitaterna, M.H., Zhao, Y., Wilsbacher, L.D., Sangoram, A.M., King, D.P., Pinto, L.H., and Takahashi, J.S., Functional identification of the mouse circadian Clock gene by transgenic BAC rescue, *Cell,* 89, 655–667, 1997.

Arenz, C.L. and Leger D.W., The antipredator vigilance of adult and juvenile thirteen-lined ground squirrels (*Sciuridae: Spermophilus tridecemlineatus*): visual obstruction and simulated hawk attacks, *Ethology*, 103, 945–953, 1997.

Aronson, B., Johnson, K., Loros, J.J., and Dunlap, J.C., Negative feedback defining a circadian clock: autoregulation in the clock gene frequency, *Science*, 263, 1578–1584, 1994.

Artieda, J. and Pastor, M.A., *Neurophysiological Mechanisms of Temporal Perception*, Elsevier, Amsterdam, 1996.

Aschoff, J., Human perception of short and long time intervals: its correlation with body temperature and the duration of wake time, *J. Biol. Rhythms*, 13, 437–442, 1998.

Bading, H., Ginty, D.D., and Greenberg, M.E., Regulation of gene expression in hippocampal neurons by distinct calcium signaling pathways, *Science*, 260, 181–186, 1993.

Balsalobre, A., Clock genes in mammalian peripheal tissues, *Cell Tissue Res*., 309, 193–199, 2002.

Bateson, M. and Kacelnik, A., Risk-sensitive foraging: decision making in variable environments, in *Cognitive Ecology*, Dukas, R., Ed., University of Chicago Press, Chicago, 1998, pp. 297–342.

Beecher, M.D., Correlation of song learning and territory establishment strategies in the song sparrow, *Proc. Natl. Acad. Sci. U.S.A.*, 91, 1450–1454, 1994.

Beecher, M.D., Campbell, S.E., and Nordby, J.C., The cognitive ecology of song communication and song learning in the song sparrow, in *Cognitive Ecology*, Dukas, R., Ed., University of Chicago Press, Chicago, 1998, pp. 175–199.

Belisle, C. and Cresswell, J., The effects of a limited memory capacity on foraging behavior, *Theor. Popul. Biol.*, 52, 78–90, 1997.

Bell, W.J., *Search Behavior: The Behavioral Ecology of Finding Resources*, Chapman & Hall, New York, 1991.

Bent, A.C., *Life Histories of North American Birds of Prey*, Dover, New York, 1961.

Berg, H.C., *Random Walks in Biology*, Princeton University Press, Princeton, NJ, 1983.

Bitterman, M.E., Comparative analysis of learning, *Science*, 188, 699–708, 1975.

Bizo, L.A. and White, K.G., Timing with controlled reinforcer density: implications for models of timing, *J. Exp. Psychol. Anim. Behav. Process.*, 2, 44–55, 1997.

Buhusi, C.V. and Meck, W.H., Differential effects of methamphetamine and haloperidol on the control of an internal clock, *Behav. Neurosci.*, 116, 291–297, 2002.

Buhusi, C.V., Sasaki, A., and Meck, W.H., Temporal integration as a function of signal/gap intensity in rats (*Rattus norvegicus*) and pigeons (*Columba livia*), *J. Comp. Psychol.*, in press.

Cantor, M.B., Information theory: a solution to two big problems in the analysis of behavior, in *Advances in the Analysis of Behavior*, Vol. 2, *Predictability, Contiguity and Contingency*, Harzem, P. and Zeiler, M., Eds., Wiley, New York, 1981, pp. 286–320.

Charnov, E.L., Optimal foraging, the marginal value theorem, *Theor. Popul. Biol.*, 9, 129–136, 1976.

Cheng, K. and Roberts, W.A., Three psychophysical principles of timing in pigeons, *Learn. Motiv.*, 22, 112–128, 1991.

Church, R.M. and Deluty, M.Z., The bisection of temporal intervals, *J. Exp. Psychol. Anim. Behav. Process.*, 3, 216–228, 1977.

Church, R.M. and Gibbon, J., Temporal generalization, *J. Exp. Psychol. Anim. Behav. Process.*, 8, 165–186, 1982.

Church, R.M., Meck, W.H., and Gibbon, J., Application of scalar timing theory to individual trials, *J. Exp. Psychol. Anim. Behav. Process.*, 20, 135–155, 1994.

Churchland, P.S. and Sejnowski, T.J., *The Computational Brain*, MIT Press, Cambridge, MA, 1994.

Clayton, N.S. and Dickinson, A., Episodic-like memory during cache recovery by scrub jays, *Nature*, 395, 272–274, 1998.

Cody, M.L., Finch flocks in the Mohave Desert, *Theor. Popul. Biol.*, 2, 142–148, 1971.

Colombo, M., Broadbent, N.J., Taylor, C.S., and Frost, N., The role of the avian hippocampus in orientation in space and time, *Brain Res.*, 919, 292–301, 2001.

Cooper, L.D., Temporal factors in classical conditioning, *Learn. Motiv.*, 22, 129–152, 1991.

Crosthwaite, S.K., Loros, J.J., and Dunlap, J.C., Light-induced resetting of a circadian clock is mediated by a rapid increase in frequency transcript, *Cell*, 81, 1003–1012, 1995.

Crystal, J.D., Circadian time perception, *J. Exp. Psychol. Anim. Behav. Process.*, 27, 68–78, 2001.

Curio, E., *The Ethology of Predation*, Springer-Verlag, Berlin, 1976.

Czeisler, C.A., The effect of light on the human circadian pacemaker, in *Circadian Clocks and Their Adjustment*, Chadwick, D.J. and Ackrill, K., Eds., John Wiley & Sons, New York, 1995, pp. 254–290.

Daan, S., Adaptive daily strategies in behavior, in *Biological Rhythms*, Aschoff, J., Ed., Plenum Press, New York, 1981, pp. 275–298.

de Vaca, S.C., Brown, B.L., and Hemmes, N.S., Internal clock and memory processes in animal timing, *J. Exp. Psychol. Anim. Behav. Process*., 7, 59–69, 1994.

Decoursey, P.J. and Krulas, J.R., Behavior of SCN-lesioned chipmunks in natural habitat: a pilot study, *J. Biol. Rhythms*, 13, 229–244, 1997.

DeZazzo, J. and Tully, T., Dissection of memory formation: from behavioral pharmacology to molecular genetics, *Trends Neurosci*., 18, 212–218, 1995.

Dukas, R., Constraints on information processing and their effects on behavior, in *Cognitive Ecology*, Dukas, R., Ed., University of Chicago Press, Chicago, 1998, pp. 89–128.

Dunlap, J.C., Genetic and molecular analysis of circadian rhythms, *Ann. Rev. Genet*., 30, 579–601, 1996.

Dusenberry, D.B., Spatial sensing of stimulus gradients can be superior to temporal sensing for free-swimming bacteria, *Biophys. J*., 74, 2272–2277, 1998.

Dyer, F., Cognitive ecology of navigation, in *Cognitive Ecology*, Dukas R., Ed., University of Chicago Press, Chicago, 1998, pp. 201–260.

Edery, I., Rutila, J., and Rasbash, M., Phase shifting of the circadian clock by induction of the *Drosophila* period protein, *Science*, 263, 237–240, 1994.

Edmunds, L.N., *Cellular and Molecular Bases of Biological Clocks*, Springer-Verlag, New York, 1988.

Eskin, R.M. and Bitterman, M.E., Fixed-interval and fixed ratio performance in the fish as a function of prefeeding, *Am. J. Psychol*., 73, 417–423, 1960.

Ferster, C.B. and Skinner, B.F., *Schedules of Reinforcement*, Appleton-Century-Crofts, New York, 1957.

Fetterman, J.G. and Killeen, P.R., Adjusting the pacemaker, *Learn. Motiv.*, 22, 226–252, 1991.

Fletcher, P.C., Frith, C.D., and Rugg, M.D., The functional neuroanatomy of episodic memory, *Trends Neurosci*., 20, 213–218, 1997.

Friedman, W.J., Memory for the time of past events, *Psychol. Bull*., 113, 44–66, 1993.

Getty, T. and Krebs, J.R., Lagging partial preferences for cryptic prey: a signal detection analysis of great tit foraging, *Am. Naturalist*, 125, 39–60, 1985.

Gibbon, J., Morrell, M., and Silver, R., Two kinds of timing in circadian incubation rhythm of ring doves, *Am. J. Physiol*., 247, R1083–R1087, 1984.

Gilbert, C., Visual control of cursorial prey pursuit by tiger beetles (*Cicindelida*e), *J. Comp. Physiol. Sensory Neural Behav. Physiol*., 181, 217–230, 1997.

Gould, J.L., Sensory bases of navigation, *Curr. Biol*., 8, R731–R738, 1998.

Grebe, T.W. and Stock, J., Bacterial chemotaxis: the five sensors of bacterium, *Curr. Biol*., 8, R154–R157, 1998.

Grossman, K.E., Continuous, fixed-ratio and fixed interval reinforcement in honey bees, *J. Exp. Anal. Behav*., 20, 105–109, 1973.

Ha, J.C., Lehner, P.N., and Farley, S.D., Risk-prone foraging behavior in captive grey jays, Perisoreus canadensis, *Anim. Behav*., 39, 91–96, 1990.

Hardin, P.E., Hall, J.C., and Rasbash, M., Circadian oscillations in period gene mRNA levels are transcriptionally regulated, *Proc. Natl. Acad. Sci. U.S.A*., 89, 11711–11715, 1992.

Harrison, A.A., Clearwater, Y.A., and McKay, C.P., The human experience in Antarctica: applications to life in space, *Behav. Sci*., 34, 253–271, 1989.

Hastings, M.H., Central clocking, *Trends Neurosci*., 20, 459–464, 1997.

Haykin, S., *Neural Networks*, Macmillan College Publishing Company, New York, 1994.

Hills, T.T. and Adler, F.R., Time's crooked arrow: rate-biased time perception and optimal foraging theory, *Anim. Behav*., 64, 589–597, 2002.

Hoagland, H., *Pacemakers in Relation to Aspects of Behavior*, Macmillan, New York, 1935.

Holtcamp, W.N., Grant, W.E., and Vinson, S.B., Patch use under predation hazard: effect of the red imported fire ant on deer mouse foraging behavior, *Ecology*, 78, 308–317, 1997.

Hooper, S.L., Transduction of temporal patterns by single neurons, *Nat. Neurosci*., 1, 720–726, 1998.

Ishijima, A. and Yanagida, T., Single molecule nanobioscience, *Trends Biochem. Sci*., 26, 438–444, 2001.

Iwasaki, K., Liu, D.W., and Thomas J.H., Genes that control a temperature-compensated ultradian clock in *Caenorhabditis elegans*, *Proc. Natl. Acad. Sci. U.S.A*., 92, 10317–10321, 1995.

Iwasaki, K. and Thomas, J.H., Genetics in rhythm, *Trends Genet*., 13, 111–115, 1997.

Jackson, P.A., Kesner, R.P., and Amann, K., Memory for duration: role of hippocampus and medial prefrontal cortex, *Neurobiol. Learn. Mem*., 70, 328–348, 1998.

Kacelnik, A., Central place foraging in starlings (*Sturnus vulgaris*): I. Patch residence time, *J. Anim. Ecol*., 53, 283–299, 1984.

Kareiva, P. and Odell, G., Swarms of predators exhibit "preytaxis" if individual predators use area-restricted search, *Am. Naturalist*, 130, 233–270, 1987.

Kesner, R.P., Neural mediation of memory for time: role of the hippocampus and medial prefrontal cortex, in *Animal Cognition and Sequential Behavior: Behavioral, Biological, and Computational Perspectives*, Fountain, S.B., Bunsey, M.D., Danks, J.H., and McBeath, M.K., Eds., Kluwer Academic, Boston, 2002, pp. 175–200.

Killeen, P.R., Palombo, G., Gottlob, L.R., and Beam, J., Bayesian analysis of foraging by pigeons (*Columba livia*), *J. Exp. Psychol. Anim. Behav. Process*., 22, 480–496, 1996.

King, D.P., Zhao, Y., Sangoram, A.M., Wilsbacher, L.D., Tanaka, M., Aantoch, M.P., Steeves, T.D.L., Vitaterna, M.H., Kornhauser, J.M., Lowrey, P.L., Turek, F.W., and Takahashi, J.S., Functional identification of the mouse circadian Clock gene by transgenic BAC rescue, *Cell*, 89, 655–667, 1997a.

King, D.P., Zhao, Y., Sangoram, A.M., Wilsbacher, L.D., Tanaka, M., Aantoch, M.P., Steeves, T.D.L., Vitaterna, M.H., Kornhauser, J.M., Lowrey, P.L., Turek, F.W., and Takahashi, J.S., Positional cloning of the mouse circadian Clock gene, *Cell*, 89, 641–653, 1997b.

Konopka, R.J. and Benzer, S., Clock mutants of *Drosophila melanogaster*, *Proc. Natl. Acad. Sci. U.S.A*., 68, 2112–2116, 1971.

Kowal, K., Familiar melodies seem shorter, not longer, when played backwards, *Ann. N.Y. Acad. Sci*., 423, 610–611, 1984.

Krebs, J.R. and Kacelnik, A., Time horizons of foraging animals, *Ann. N.Y. Acad. Sci*., 423, 278–291, 1984.

Krebs, J.R., Sherry, D.F., Healy, S.D., Perry, V.H., and Vaccarino, A.L., Hippocampal specialization of food-storing birds, *Proc. Natl. Acad. Sci. U.S.A*., 89, 1388–1392, 1989.

Kyriacou, C.P., Greenacre, M.L., Ritchie, M.G., Peixoto, A.A., Shiels, G., and Hall, J.C., Genetic and molecular analysis of ultradian rhythms in Drosophila, in *Ultradian Rhythms in Life Processes*, Lloyd, D. and Rossi, R.L., Eds., Springer-Verlag, New York, 1992, pp. 89–105.

Lavie, P., Ultradian cycles in sleep propensity; or, Kleitman's BRAC revisited, in *Ultradian Rhythms in Life Processes*, Lloyd, D. and Rossi, R.L., Eds., Springer-Verlag, New York, 1992, pp. 284–302.

Liu, Y., Garceau, N.Y., Loros, J.J., and Dunlap, J.C., Thermally regulated translational control of FRQ mediates aspects of temperature responses in the Neurospora circadian clock, *Cell*, 89, 477–486, 1997.

Lloyd, M. and Dybas, H.S., The periodical cicada problem: I. Population ecology, *Evolution*, 20, 133–149, 1966.

Lloyd, D., Circadian and ultradian clock-controlled rhythms in unicellular microorganisms, *Advances in Microbiol Physiology,* 39, 291–338, 1998.

Loudon, A.S.I., Wayne, N.L., Krieg, R., Iranmanesh, A., Veldhuis, J.D., and Menaker, M., Ultradian endocrine rhythms are altered by a circadian mutation in the Syrian hamster, *Endocrinology*, 135, 712–718, 1994.

Machado, A., Learning the temporal dynamics of behavior, *Psychol. Rev.*, 104, 241–265, 1997.

Maricq, A.V. and Church, R.M., The differential effects of haloperidol and methamphetamine on time estimation in the rat, *Psychopharmacology*, 79, 10–15, 1983.

Markram, H., Lubke, J., Frotscher, M., and Sakmann, B., Regulation of synaptic efficacy by coincidence of postsynaptic aps and epsps, *Science*, 275, 213–215, 1997.

Matell, M.S. and Meck, W.H., Neuropsychological mechanisms of interval timing behaviour, *Bioessays*, 22, 94–103, 2000.

Meck, W.H., Hippocampal function is required for feedback control of an internal clock's criterion, *Behav. Neurosci*., 102, 54–60, 1988.

Meck, W.H., Modality-specific circadian rhythmicities influence mechanisms of attention and memory for interval timing, *Learn. Motiv.*, 22, 153–179, 1991.

Meck, W.H., Church, R.M., and Olton, D.S., Hippocampus, time, and memory, *Behav. Neurosci*., 98, 3–22, 1984.

Menaker, M., Commentary: what does melatonin do and how does it do it? *J. Biol. Rhythms*, 12, 532–534, 1997.

Michelsen, A., Larsen, O.N., and Sulrykke, A., Auditory processing of temporal cues in insect songs: frequency domain or time domain? in *Time Resolution in Auditory Systems*, Michelsen, A., Ed., Springer-Verlag, New York, 1985, pp. 3–27.

Milinski, M. and Parker, G.A., Competition for resources, in *Behavioral Ecology*, 3rd ed., Krebs, J.R. and Davies, N.B., Eds., Blackwell Scientific, Oxford, 1991, pp. 137–168.

Millar, A.J., Straume, M., Chory, J., Chua, N., and Kay, S.A., The regulation of circadian period by phototransduction pathways in Arabidopsis, *Science*, 267, 1163–1166, 1995.

Mistleberger, R.E., Circadian food-anticipatory activity: formal models and physiological mechanisms, *Neurosci. Biobehav. Rev.*, 18, 171–195, 1993.

Mizumori, S.J.Y., LaVoie, A.M., and Kalyani, A., Redistribution of spatial representation in the hippocampus of aged rats performing a spatial memory task, *Behav. Neurosci*., 110, 1006–1016, 1996.

Moore, D., Angel, J.E., Cheeseman, I.M., Fahrbach, S.I., and Robinson, G.E., Timekeeping in the honeybee colony: integration of circadian rhythms and division of labor, *Behav. Ecol. Sociobiol*., 43, 147–160, 1998.

Moore, D., Siegfried, D., Wilson, R., and Rankin, M.A., The influence of time of day on the foraging behavior of the honeybee, *Apis mellifera*, *J. Biol. Rhythms*, 4, 305–325, 1989.

Morgan, L., Killeen, P.R., and Fetterman, J.G., Changing rates of reinforcement perturbs the flow of time, *Behav. Process*., 30, 259–272, 1993.

Okamura, H., Yamaguchi, S., and Yagita, K., Molecular machinery of the circadian clock in mammals, *Cell Tissue Res*., 309, 47–56, 2002.

Ono, T., Nishijo, H., Eifuku, S., Kobayashi, T., and Tamura, R., Conjunctive multiple stimuli-encoding in the hippocampal formation of rats and monkeys, in *Brain Processes and Memory*, Ishikawa, K., McGaugh, J.L., and Sakata, H., Eds., Elsevier, Amsterdam, 1995, pp. 187–201.

Paule, M.G., Meck, W.H., McMillan, D.E., Bateson, M., Popke, E.J., Chelonis, J.J., and Hinton, S.C., The use of timing behaviors in animals and humans to detect drug and/or toxicant effects, *Neurotoxicol. Teratol*., 21, 491–502, 1999.

Pavlov, I.P., *Conditioned Reflexes,* Oxford University Press, Oxford, 1927.

Port, R.F., Cummins, F., and McAuley, J.D., Naive time, temporal patterns, and human audition, in *Mind as Motion*, Port, R.F. and van Gelder, T., Eds., MIT Press, Cambridge, MA, 1995, pp. 339–372.

Portavella, M., Vargas, J.P., Torres, B., and Salas, C., The effects of telencephalic pallial lesions on spatial, temporal, and emotional learning in goldfish, *Brain Res. Bull.*, 57, 397–399, 2002.

Power, J.M., Ringo, J.M., and Dowse, H.B., The effects of period mutations and light on the activity rhythms of *Drosophila melanogaster*, *J. Biol. Rhythms*, 10, 267–280, 1995.

Ralph, M.R., Foster, R.G., Davis, F.C., and Menaker, M., Transplanted suprachiasmatic nucleus determines circadian period, *Science*, 247, 975–978, 1990.

Ralph, M.R. and Hurd, M.W., Circadian pacemakers in vertebrates, in *Circadian Clocks and Their Adjustment*, Chadwick, D.J. and Ackrill, K., Eds., John Wiley & Sons, New York, 1995, pp. 67–81.

Real, L. and Caraco, T., Risk and foraging in stochastic environments, *Ann. Rev. Ecol. Syst.*, 17, 371–390, 1986.

Rensing, L., Kallies, A., Gebauer, G., and Mohsenzadeh, S., The effects of temperature change on the circadian clock of neurospora, in *Circadian Clocks and Their Adjustment*, Chadwick, D.J. and Ackrill, K., Eds., John Wiley & Sons, New York, 1995, pp. 26–41.

Richelle, M. and Lejeune, H., *Time in Animal Behavior*, Pergamon Press, Oxford, 1980.

Roberts, S., Isolation of an internal clock, *J. Exp. Psychol. Anim. Behav. Process.*, 7, 242–268, 1981.

Roberts, S., The mental representation of time: uncovering a biological clock, in *Methods, Models, and Conceptual Issues: An Invitation to Cognitive Science*, Vol. 4, Scarborough, D. and Sternberg, S., Eds., MIT Press, Cambridge, MA, 1998, pp. 53–106.

Rosato, E., Peixoto, A.A., Gallippi, A., Kyriacou, C.P., and Costa, R., Mutational mechanisms, phylogeny, and evolution of a repetitive region within a clock gene of *Drosophila melanogaster*, *J. Mol. Evol.*, 42, 392–408, 1996.

Rosenwasser, A.M., Rats remember the circadian phase of feeding, *Ann. N.Y. Acad. Sci.*, 423, 634–635, 1984.

Rozin, P., Temperature independence of an arbitrary temporal discrimination in the goldfish, *Science*, 149, 561–564, 1965.

Ruby, N.F., Dark, J., Heller, H.C., and Zucker, I., Albation of suprachiasmatic nucleus alters timing of hibernation in ground squirrels, *Proc. Natl. Acad. Sci. U.S.A.*, 93, 9864–9868, 1996.

Saunders, D.S., *Insect Clocks*, Pergamon Press, Oxford, 1971.

Sawyer, L.A., Hennessy, M.J., Peixoto, A.A., Rosato, E., Parkinson, H., Costa, R., and Kyriacou, P.C., Natural variation in a Drosophila clock gene and temperature compensation, *Science*, 278, 2117–2120, 1997.

Schmidt, J.M. and Pak, G.A., The effect of temperature on progeny allocation and short interval timing in a parasitoid wasp, *Physiol. Entomol.*, 16, 345–353, 1991.

Schoener, T.W., Nonsynchronous spatial overlap of lizards in patchy habitats, *Ecology*, 51, 408–418, 1970.

Schoener, T.W., Resource partitioning in ecological communities, *Science*, 185, 127–185, 1974.

Seeley, T.D., *The Wisdom of the Hive: The Social Physiology of Honey Bee Colonies*, Harvard University Press, Cambridge, MA, 1995.

Segall, J.E., Block, S.M., and Berg, H.C., Temporal comparisons in bacterial chemotaxis, *Proc. Natl. Acad. Sci. U.S.A.*, 83, 8987–8991, 1983.

Shigeyoshi, Y., Taguchi, K., Yamamoto, S., Takekida, S., Yan, L., Tei, H., Moriya, T., Shibata, S., Loros, J.J., Dunlap, J.C., and Okamura, H., Light-induced resetting of a mammalian circadian clock is associated with rapid induction of the mper1 transcript, *Cell*, 91, 1043–1053, 1997.

Silver, R. and Bittman, E.L., Time sharing by parent doves, *Ann. N.Y. Acad. Sci.*, 423, 488–514, 1984.

Silvertown, J.W., The evolutionary ecology of mast seeding in trees, *Biol. J. Linnean Soc.*, 14, 235–250, 1980.

Staddon, J.E.R. and Higa, J.J., Time and memory: towards a pacemaker-free theory of interval timing, *J. Exp. Anal. Behav.*, 71, 215–251, 1999.

Stanewsky, R., Clock mechanisms in *Drosophila*, *Cell Tissue Res.*, 309, 11–26, 2002.

Stephens, D.W., The logic of risk-sensitive foraging preferences, *Anim. Behav.*, 29, 628–629, 1980.

Stephens, D.W. and Krebs, J.R., *Foraging Theory*, Princeton University Press, Princeton, NJ, 1986.

Stock, J.B. and Surette, M.G., Chemotaxis, in *Escherichia coli and Salmonella: Cellular and Molecular Biology*, Neidhardt, F.C., Ed., ASM Press, Washington, D.C., 1996, pp. 1103–1129.

Takahashi, J.S., Molecular neurobiology and genetics of circadian rhythms in mammals, *Ann. Rev. Neurosci.*, 18, 531–553, 1995.

Takai, Y., Sasaki, T., and Matozaki, T., Small GTP-binding proteins, *Physiol. Rev.*, 81, 153–208, 2001.

Talton, L.E., Higa, J.J., and Staddon, J.E.R., Interval schedule performance in the goldfish *Carassius auratus*, *Behav. Process.*, 45, 193–206, 1999.

Thompson, R.F., Berger, T.W., Berry, S.D., Clark, G.A., Kettner, R.N., LaVond, D.G., Mauk, M.D., McCormick, D.A., Solomon, P.R., and Weisz, D.J., Neuronal substrates of learning and memory: hippocampus and other structures, in *Conditioning: Representation of Involved Neural Functions*, Woody, C.D., Ed., Plenum Press, New York, 1982, pp. 1103–1129.

Toh, K.L., Jones, C.R., He, Y., Eide, E.J., Hinz, W.A., Virshup, D.M., Ptacek, L.J., and Fu, Y.H., An hPer2 phosphorylation site mutation in familial advanced sleep phase syndrome, *Science*, 9, 1040–1043, 2001.

Treisman, M., Cook, N., Naish, P.L.N., and MacCrone, J.K., The internal clock: electroencephalographic evidence for oscillatory processes underlying time perception, *Q. J. Exp. Psychol.*, 47, 241–289, 1994.

Tulving, E., Episodic and semantic memory, in *Organization of Memory*, Tulving, E. and Donaldson, W., Eds., Academic Press, New York, 1972, pp. 381–403.

Valone, T.J. and Brown, J.S., Measuring patch assessment abilities of desert granivores, *Ecology*, 70, 1800–1810, 1989.

Wagner, S., Castel, M., Gainer, H., and Yarom, Y., GABA in the mammalian suprachiasmatic nucleus and its role in diurnal rhythms, *Nature*, 387, 598–603, 1997.

Wallenstein, G.V., Eichenbaum, H., and Hasselmo, M.E., The hippocampus as an associator of discontiguous events, *Trends Neurosci.*, 21, 317–323, 1998.

Wallenstein, G.V. and Hasselmo, M.E., Gabaergic modulation of hippocampal population activity: sequence learning, place field development, and the phase precession effect, *J. Neurophysiol.*, 78, 393–408, 1997.

Wearden, J.H., Do humans possess an internal clock with scalar properties? *Learn. Motiv.*, 22, 59–83, 1991.

Wearden, J.H. and Penton-Voak, I.S., Feeling the heat: body temperature and the rate of subjective time, revisited, *Q. J. Exp. Psychol. B*, 48, 129–141, 1995.

Wever, R.A., The sleep-wake threshold in human circadian rhythms as a determinant of ultradian rhythms, in *Ultradian Rhythms in Life Processes*, Lloyd, D. and Rossi, R.L., Eds., Springer-Verlag, New York, 1992, pp. 307–322.

White, J., Tobin, T.R., and Bell, W.J., Local search in the housefly *Musca domestica* after feeding on sucrose, *J. Insect Physiol.*, 30, 477–487, 1984.

Wilson, E.O., *The Insect Societies*, The Belknap Press, Cambridge, UK, 1971.

Winfree, A.T., *The Geometry of Biological Time*, Springer-Verlag, New York, 1980.

Young, B. and McNaughton, N., Common firing patterns of hippocampal cells in a differential reinforcement of low rates of response schedule, *J. Neurosci.*, 20, 7043–7051, 2000.

Yu, Q., Jacquir, A.C., Citri, Y., and Colot, H.M., Molecular mapping of point mutations in the period gene that stop or speed up biological clocks in *Drosophila melanogaster*, *Proc. Natl. Acad. Sci. U.S.A.*, 84, 784–788, 1987.