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Temporal foundations of episodic memory

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Abstract

A fundamental question in the development of animal models of episodic memory concerns the role of temporal processes in episodic memory. Gallistel (1990) developed a framework in which animals remember specific features about an event, including the *time of occurrence* of the event and its location in space. Gallistel proposed that timing is based on a series of biological oscillators, spanning a wide range of periods. Accordingly, a snapshot of the phases of multiple oscillators provides a representation of the time of occurrence of the event. I review research on basic timing mechanisms that may support memory for times of occurrence. These studies suggest that animals use biological oscillators to represent time. Next, I describe recently developed animal models of episodic memory that highlight the importance of temporal representations in memory. One line of research suggests that an oscillator representation of time supports episodic memory. A second line of research highlights the flow of events in time in episodic memory. Investigations that integrate time and memory may advance the development of animal models of episodic memory.

Keywords: Episodic memory; animal models of episodic memory; oscillator; pacemaker accumulator; time of occurrence; short interval timing; long interval timing; rat.

Temporal foundations of episodic memory

Our memory of unique events often includes temporal reference points. Language provides a rich range of reference points. Events may be remembered as having occurred at a particular time of day (morning, afternoon, evening, etc.), day of the week (weekend, Friday, yesterday, etc.), part of the year (summer, winter, April, etc.), stage of life (childhood, at university, retirement, etc.), among other descriptions. Although our memory is fallible and plagued by failures of memory and misremembering (Schacter, 2002), a defining feature of episodic memory focuses on our ability to segment an event as having happened at a time in our own past experience (Tulving, 2001). Because our narratives about our memories are deeply embedded in language, as noted above, elements of episodic memory in nonhumans may be fundamentally different than in people. Accordingly, the role of temporal processes in episodic memory in nonhumans has engendered much interest and debate (Clayton et al., 2003; Crystal & Suddendorf, 2019; Suddendorf, 2013; Suddendorf & Corballis, 1997). Moreover, it is difficult to interrogate the subjective experiences of others, and this represents a fundamental barrier to evaluating the similarity of some elements of episodic memory in people and nonhumans. The thesis of this article is that an examination of basic timing mechanisms in animals may provide insight into the range of temporal mechanisms that may support elements of episodic memory in nonhumans. Gallistel (1990) developed a framework in which animals remember specific features about an event, including the *time of occurrence* of the event and its location in space, and Ken Cheng has emphasized the role oscillators play in wide variety of behaviors (Cheng, 2022, 2023). A central feature of Gallistel's proposal for time of occurrence focuses on the use of a series of biological oscillators that span a wide range of

periods. Accordingly, a snapshot of the phases of multiple oscillators provides a representation of the time of occurrence of the event. As noted above, people have a rich calendar-date system for describing their subjective experiences of time. A calendar-date system is a record of the phases of three environmental periodicities, namely day (rotation of the earth), month (rotation of the moon around the earth), and year (rotation of the earth around the sun), and may also include ultradian rhythms (i.e., periodicities with periods less than a day, e.g., (Isomura & Kageyama, 2014)). A major gap in our knowledge concerns the extent to which nonhumans may use biological oscillators as a precursor to a related calendar-date system. Although it is well established that neurobiological oscillators are entrained to environmental periodicities, the central question is whether animals record events and the phases that co-occur with these events.

In this article, I describe evidence that animals such as rats use multiple endogenous oscillators to represent time. This type of evidence is a building block for the development of a model of event representations that relies on the time of occurrence of events. The first part of the article reviews experiments that provide information on basic timing mechanisms that may support memories for time of occurrence. The second part of the article reviews recent experiments that feature temporal aspects of animal models of episodic memory. One line of evidence suggests that rats remember back in time to a specific earlier event which includes information about an oscillator-based time of occurrence of the remembered event (Zhou & Crystal, 2009). A second line of evidence suggests that rats represent the order of multiple unique events in episodic memory and are capable of searching this representation to find targets that occupy a specific temporal location in memory (Panoz-Brown et al., 2018).

Formal Properties of Interval and Circadian Timing

It is well known that animals have a circadian oscillator, but a major gap in our knowledge includes the following questions. Do animals have multiple biological oscillators with periods that depart from 24 hours? Do animals use such biological oscillators to time events? This section summarizes the defining features of oscillatory mechanisms in timing. The next sections review evidence that rats have multiple biological oscillators and use them to make judgments about time.

There is evidence that specialized behaviors occur at periods that range from milliseconds to years; examples include oscillations that drive wingbeats, heartbeats, breathing, locomotion, and feeding (Gerkema, 2002), monthly breeding (Mercier et al., 2011), annual migratory behavior (Vinod Kumar et al., 2010), and 13- and 17-year cicada breeding swarms (Behncke, 2000), among others. Although biological oscillators with periods spanning many orders of magnitude exist (Gerkema, 2002; MacGregor & Lincoln, 2008), a major question is whether their phases are stored in memory as part of the encoding of individual events.

A classic description of the operating characteristics of interval and circadian timing systems was summarized by Gibbon and colleagues (Gibbon et al., 1997). A brief description of the operating characteristics of interval and circadian timing systems is outlined in this section (see Figure 1). According to the classic account, the interval timing system is based on a pacemaker-accumulator mechanism, whereas the circadian system is based on an endogenous-oscillator mechanism. Endogenous means that the oscillator does not require ongoing periodic input to produce continued periodic output. For example, when an animal is exposed to a daily periodic light cycle such as alternation of 12-h of light and 12-h of darkness, activity patterns

107 occur at a species-typical time of day. When the periodic light cycle ends, behavior ‘free runs’
108 with a period that typically departs somewhat from 24 h. Free running behavior after the
109 termination of periodic input provides strong evidence that the timing system is endogenous;
110 this pattern of behavior is important to rule out the hypothesis that the observed behavior is
111 driven by the occurrence of daily environmental changes (e.g., temperature, noise, etc.).
112 Notably, Gibbon et al. (1997) defined the interval timing system as requiring resetting by
113 environmental input. The timing system measures an elapsing interval timed with respect to
114 the occurrence of some stimulus; only a single presentation of the stimulus is necessary and
115 sufficient to reset the interval timing system; this property is referred to as *one-shot reset*.

116 The circadian system functions within a limited range of entrainment. Importantly,
117 presentation of a periodic input entrains the endogenous oscillator only if the periodic input is
118 within a limited range of periods near 24 h. By contrast, the interval timing system has a broad
119 training range covering a few orders of magnitude from seconds to hours.

120 A hallmark of the circadian system is that it adjusts slowly to a phase shift. A phase shift
121 is an abrupt change in the initiation of a periodic process. For example, when we experience jet
122 lag, several days are typically required before activities are synchronized to the new time zone.
123 By contrast, an interval timing system immediately adjusts to a phase shift; a single shift in a
124 cycle produces complete adjustment or complete resetting of the timing processes (i.e., one-
125 shot reset). The phase-response curve describes how variation in this slow adjustment to a
126 phase shift depends on where the synchronizing stimulus falls within the oscillatory cycle (Glass
127 & Winfree, 1984; Johnson, 1990).

Temporal performance based on a circadian oscillator is highly precise as measured by cycle-to-cycle variation. Precision is typically measured relative to the timed interval. For example, the coefficient of variation (CV) is the standard deviation of time estimates divided by the mean of time estimates. The CV of circadian behaviors is approximately 1-5%. By contrast, interval timing is characterized by a lower level of precision (coefficient of variation of 10-35%). Thus, relatively high timing precision is a characteristic of a circadian oscillator. Notably, a consequence of having an endogenous oscillator dedicated to timing a specific value within a limited range appears to be relatively high sensitivity to time this target duration. The variance properties of timing have played a historically important role in understanding interval timing. By contrast, the analysis of variance properties has had relatively less impact in the study of circadian timing. Importantly, the identification of multiple local peaks in sensitivity to time would provide evidence for multiple oscillators. Moreover, a series of multiple oscillators may provide a foundation for representing times of occurrence of unique events, which may support episodic memory.

Oscillator Properties of Interval Timing

The sections that follow describe empirical tests that were designed to evaluate the hypothesis that interval timing is based, at least in part, on oscillatory processes.

Endogenous Oscillations in Short-interval Timing

A critical diagnostic test of a timing mechanism may be assessed by discontinuing periodic input (i.e., extinction) and assessing subsequent anticipatory behavior. As noted above, an essential feature of an oscillator is that periodic output from the oscillator continues after the discontinuation of periodic input. By contrast, a defining feature of a pacemaker-

accumulator system is that elapsed time is measured with respect to the presentation of a stimulus, according to the classic description of this system reviewed above. Thus, output of a pacemaker-accumulator interval timing system is periodic when timing short intervals only when driven by periodic input. Notably, periodic output is expected to cease if periodic input is discontinued. To test pacemaker-accumulator and endogenous-oscillator mechanisms (Crystal & Baramidze, 2007), separate groups of rats were trained with a variety of short intervals (48, 96, and 192 s). The critical manipulation was the suspension of periodic food delivery. Figure 2 shows the pattern of inter-response times from a representative individual rat, and Figure 3 shows group data from a Fourier analysis. As predicted by both mechanisms, periodic delivery of food produced periodic behavior during training (Figure 3, left column). Periodic behavior continued after termination of periodic input (Figure 3, right column), consistent with an endogenous-oscillator, but not a pacemaker-accumulator, mechanism. Because the period in extinction departed somewhat from the period in training, the periodic behavior in extinction appears to be based on entrainment to the discontinued periodic feeding. Thus, short-interval timing is, at least in part, based on a self-sustaining, endogenous oscillator (Crystal & Baramidze, 2007). An early study by Stein (1951; cf. Gallistel, 1990) using sparrows, canaries, and finches (fixed times between 10 and 30 minutes) and a study by Kirkpatrick-Steger and colleagues (1996) using pigeons (fixed intervals between 15 and 60 seconds) suggest that oscillations after the termination of period input occur in birds. In these studies, multiple peaks occurred at periods slightly above the target interval value or at a subset of multiples of the fixed interval.

Timing Long Intervals

A central hypothesis about an oscillator is that it functions to provide improved sensitivity to time intervals near the oscillator's period. To test this hypothesis, a series of experiments investigating meal anticipation was undertaken to identify a local peak in sensitivity to time 24 hr (Crystal, 2001a, 2006a, 2010, 2015). To examine anticipation of long intervals, food was restricted to 3-h meals, which rats earned by breaking a photo beam in a food trough. Notably, the rats inspected the food trough before meals start, thereby documenting temporal anticipation in each inter-meal interval condition. Figure 4 shows anticipation functions for inter-meal intervals in the circadian range (22 to 26 h) and well outside this range (14 and 34 h) from groups of rats that each received a single inter-meal interval. Response rates increased later into the inter-meal interval for intervals near the circadian range than for intervals outside this range (Crystal, 2001a). The response distributions were used to estimate sensitivity to time; a relatively small spread in the distribution correspond to relatively high sensitivity to time. As shown in Figure 5, inter-meal intervals in the circadian range have spreads that are smaller (i.e., lower variability) compared to intervals outside this range. Notably, the data in Figure 5 document a local maximum in sensitivity to time near 24 h, consistent with the hypothesis that a function of a circadian oscillator is improved sensitivity to time (Crystal, 2001a, 2010).

Endogenous Oscillations in Long-interval Timing

The examples of timing non-circadian long intervals in Figures 4 and 5 indicate that rats time intervals outside the circadian range (Crystal, 2001a, 2015), but these data do not identify the mechanism. These data could be based on an endogenous oscillator mechanism or a

pacemaker-accumulator mechanism reset by meals. By contrast, the examples above document endogenous oscillations in timing short intervals (1-3 min) by demonstrating that behavior continued after the termination of periodic input. The same approach is used in this section to document endogenous oscillations in long-interval timing (Crystal, 2006a).

Rats earned food by interrupting a photo beam in the food trough during 3-h meals using a 16-h inter-meal interval (Crystal, 2006a). After approximately a month of experience with the inter-meal interval, the meals were discontinued. Figure 6 (top panel) shows that response rate increased as a function of time prior to the meals, documenting that the rats timed 16 h, consistent with both oscillator and pacemaker-accumulator mechanisms. When two successive meals were skipped, the rats anticipated the arrival of two successive 16-h intervals (Figure 6 middle and bottom panels), consistent with the use of an endogenous oscillator. Importantly, response rate was substantially higher during the 3-hr omitted meal relative to the earlier 13 h for both first and second nonfood cycles. If timing was based on a pacemaker-accumulator reset by meals, then the rats would be expected to time the first meal, but would not time the second, skipped meal. A pacemaker-accumulator does not predict an increase in response rate prior to the second skipped meal because elapsed time since the last meal is unusually long at this point.

A periodogram analysis was used to assess the periodic trend; a periodogram analysis involves wrapping a response rate function around different proposed periods to identify the period that best fits the observed data. A reliable periodic trend was observed for each rat, and the mean period in extinction (20.4 ± 0.9 h, mean $\pm$ SEM) was substantially different from 16 and 24 h (Crystal, 2006a). These data suggest that the natural period of the oscillator that drove

behavior was 20.4 h, which is distinct from the circadian oscillator. According to this hypothesis, two oscillatory systems are dissociated by their different periods. However, the data are also consistent with the hypothesis that the circadian oscillator's free-running period is modified by the periodic input to which it was exposed. According to both hypotheses, long interval timing is based on a self-sustaining, endogenous oscillator, but the hypotheses differ in specifying the characteristic period of the oscillator(s). In either case, long-interval timing is based on a self-sustaining, endogenous oscillator mechanism.

Variance Properties in Circadian and Short-interval Timing

As mentioned above, the study of variance properties has played an important role in the development of theories of short-interval timing. Because the data summarized in Figure 5 suggest that a function of the well-established circadian oscillator is the relative improvement in sensitivity to time at approximately 24 h, other putative oscillators may be identified by documenting other local maxima in sensitivity to time. Moreover, the observation that short-interval timing in the range of 1-3 min exhibits endogenous, self-sustaining patterns of behavior after the termination of periodic input reinforces the expectation that short-interval timing may be based on an endogenous oscillatory mechanism.

To search for local peaks in sensitivity to time in the short-interval range, a series of experiments were conducted using many, closely spaced target intervals (Crystal, 1999, 2001b; Crystal et al., 1997). Figure 7 shows sensitivity to time plotted as a function of stimulus duration. Sensitivity to time short intervals is characterized by multiple local peaks (Crystal, 1999, 2001b). Each peak in sensitivity to time may identify the period of a short-period oscillator. The approach involved presenting a short or long stimulus followed by the insertion

of two response levers. Left or right lever presses were designated as correct after short or long stimuli. Accuracy was maintained at approximately 75% correct by adjusting the duration of the long stimulus after blocks of trials. Sensitivity to time was approximately constant for short durations from 0.1 to 34 s. However, local maxima in sensitivity to time were observed at approximately 0.3, 1.2, 12, and 24 s (Crystal, 2006b, 2010, 2012).

Figure 8 shows multiple local maxima in sensitivity to time across several orders of magnitude using data from the experiments described above (Crystal, 1999, 2001b, 2012). The data on the right and left sides of Figure 8 come from Figures 5 and 7, respectively. Figure 8 suggests that multiple local peaks in sensitivity to time are observed in timing across several orders of magnitude.

Summary

The sections above provide evidence that rats use biological oscillators when making temporal judgments. The periods of the putative oscillators range from milliseconds to seconds, minutes, hours, and a day. The existence of multiple oscillators may provide a foundation for memory representations of the time of occurrence of an event (Gallistel, 1990). Gallistel proposed that time of occurrence is the primary representation, and intervals are represented by subtracting times of occurrence. Further experiments may explore the quantitative features of endogenous oscillations to evaluate evidence for subtraction of times of occurrence and empirical properties by which behavioral oscillations may dampen over extended periods of extinction.

Animal Models of Episodic Memory

I have argued that the *central hypothesis* of an animal model of episodic memory is that, at the moment of the memory assessment, the animal remembers back in time to a specific earlier event or episode (Crystal, 2013, 2016, 2018, 2021a, 2021b, 2022). When Tulving (Tulving, 1972, 1983) coined the term episodic memory, he proposed that the content of the memory consists of the spatial and temporal characteristics of an event. This definition of episodic memory is tractable for investigations in nonhumans because it focuses on the content of episodic memory, rather than focusing on the subjective experiences that are thought to accompany episodic memory in people. Beginning with Clayton and Dickinson (1998), a number of investigators have sought to develop evidence that animals remember what, where, and when an event occurred. In some initial research, the effort to establish the temporal component was challenging (Bird et al., 2003; Hampton et al., 2005; Roberts & Roberts, 2002); but see (Babb & Crystal, 2005, 2006a, 2006b; Naqshbandi et al., 2007; Roberts et al., 2008). Here, I focus on evidence that the time of occurrence (when) is represented in memory. Our approach begins with the strategies outlined in the first section of this article by noting that a defining feature of a representation of the time of occurrence using an oscillator is that oscillators are endogenous and self-sustaining. By contrast, judgments of elapsed intervals are defined by one-shot reset. Notably, judgments of an elapsed interval (i.e., how-long-ago an event occurred) represents a special problem for animal models of episodic memory (Crystal, 2021a; Roberts et al., 2008; Zhou & Crystal, 2009). Presentation of an event gives rise to a memory trace whose strength evolves as a function of time. Recently presented events may be distinguished from earlier events by direct comparison of the strength of such memory traces

(i.e., judgments of the relative familiarity of events). Judgments of relative familiarity (Henson et al., 1999; Hofer et al., 2007; Schmitter-Edgecombe & Anderson, 2007) –or equivalently judgments of how-long-ago an event occurred– represent a major type of non-episodic memory solution to putative memories of what-where-when.

What-when-when: Evidence of Episodic Memory

Roberts et al (2008) showed that if rats are permitted to choose between the use of a how-long-ago cue and a when cue, the rats use the how-long-ago cue. Therefore, we sought to ask if rats can use a when cue in a situation in which using how-long-ago cues are uninformative in a what-where-when preparation (Zhou & Crystal, 2009). In our approach, rats received a daily session in a radial maze which consisted of a study phase (access to four randomly selected arms) followed by a test phase (access to all eight arms). On some days, the session occurred in the morning, and, on other days, it occurred in the afternoon (Figure 9A). Chocolate was available at a randomly selected location during the initial study phase, and it replenished in the subsequent test phase depending on the *time of day* at which the earlier event had occurred. For some animals, chocolate replenished in the morning, whereas for other animals chocolate replenished in the afternoon. Chow-flavored food was available at the other locations, but chow never replenished. Critically, the retention interval between study and test was a constant delay of a couple of minutes. Therefore, the delay between encoding and memory assessment (i.e., the relative familiarity of the study event or equivalently a how-long-ago cue) did not provide any information to decode replenishment or nonreplenishment. By contrast, the time of day at which the session occurred provided a reliable cue for predicting replenishment and nonreplenishment. If rats use episodic memory to remember what, where,

and when, then they should revisit the chocolate location at a higher rate in replenishment than in nonreplenishment conditions. By contrast, if rats rely only on the relative familiarity of an aspect of the study phase (e.g., being placed in the maze, running down runways, encountering chocolate, etc.), then rats should revisit the chocolate locations at equivalent rates in replenishment and nonreplenishment conditions. Our approach was to make familiarity uninformative for solving the memory problem. In our initial experiment, the rats revisited the chocolate location at a higher rate in the replenishment condition than in the nonreplenishment condition (Figure 10A) while avoiding revisits to chow locations. These data suggest that rats remember what, where, and when (i.e., the time of day at which the event occurred) without using judgments of relative familiarity, consistent with the hypothesis that rats use episodic memory to remember what, where, and when.

Next, we used a phase shift of light onset in the colony room (Pizzo & Crystal, 2004, 2006) to determine whether the rats used time of day (i.e., circadian phase, morning vs. afternoon) or an interval cue (i.e., how-long-ago since light onset) to revisit the chocolate location. Under conditions in which predictions for circadian time of day and a how-long-ago cue were dissociated, we observed revisits to the chocolate location based upon circadian time of day. In Figure 10A the rats could have timed the interval between light onset in the colony and the daily session and used this cue to adjust revisit rates. As illustrated in Figure 9A, light onset occurred at 6 am in the initial experiment. Because morning sessions occurred 1 hr after light onset and afternoon sessions occurred 7 hr after light onset, an alternative explanation for the chocolate-revisit data shown in Figure 10A is that rats used these intervals to guide revisits to the chocolate location. In the next experiment, using the same rats, we put predictions of

circadian time-of-day and how-long-ago hypotheses in conflict by shifting the light onset by 6 hr (to 12 am). The study phase occurred at 7 am in this experiment, which was 7 hr after 12 am, as shown in Figure 9B. A circadian oscillator is not affected by a single manipulation of light onset whereas an interval would be affected in this case (one-shot reset) (Buhusi & Meck, 2005; Gibbon et al., 1997; Takahashi et al., 2001). According to the time-of-day hypothesis, if rats used circadian time of day, then they should revisit chocolate at the same rate that usually occurs in a *morning* session. Alternatively, according to the interval hypothesis, if the rats timed 7 hours from light onset, then they should revisit chocolate at the same rate that usually occurs in an *afternoon* session.

Rats adjusted revisit rates based upon the circadian time of day at which the session occurred rather than using the interval between light onset and the session. Figure 10B shows data from this experiment relative to baseline data from the initial experiment according to interval and time-of-day hypotheses (i.e., the baseline data come from Figure 10A). Observed revisit rates were substantially different from the baseline for the interval hypothesis, suggesting that the rats did not time the interval between light onset and study-test sessions. The observed data were not substantially different from the time-of-day hypothesis, consistent with the hypothesis that the rats adjusted their revisit rates to chocolate based on the time of day at which sessions occurred.

In summary, because light onset is necessarily more recent (hence, more familiar) in the morning than in the afternoon, we sought to rule out this last remaining familiarity-based solution to the memory problem (Figure 9B). Thus, we showed that the rats used a circadian representation of time (Figure 10B), rather than timing an interval from light onset in the

colony to the occurrence of the session (Zhou & Crystal, 2009). We ruled out timing the interval between light onset and the feeding opportunities by shifting light onset to an earlier time that put interval and time-of-day predictions in conflict. Presumably, the estimate of time of day comes from an endogenous circadian oscillator. A characteristic feature of such a system is that adjustment to phase shifts of the light cycle is gradual (Johnson, 1990; Takahashi et al., 2001); thus, the representation of time of day would be unaffected by a single manipulation of light onset. The rats did not use the interval between light onset and the session, which suggests that they used time of day.

The experiments reviewed above provide evidence that rats remember what-where-when based on the time of occurrence of an event. However, episodic memory is memory of an *earlier encoded event*. Therefore, to establish that the rats are using episodic memory, it is necessary to show that the rats remembered the time at which the *study event* occurred (*study time* hypothesis) rather than using information about the time of day at which the *memory assessment* occurred (*test time* hypothesis) (cf. Babb & Crystal, 2006a). Because the study and test phases occurred at a constant time of day (e.g., 7 am and 1 pm in morning and afternoon sessions, respectively), according to the test time hypothesis, rats may have learned to search for chocolate replenishment in the morning test phase but not to do so in the afternoon test phase); merely being reactive at one time of testing is not consistent with episodic memory because it does not involve remembering back to an earlier study event (Babb & Crystal, 2006a). By contrast, according to the study time hypothesis, the rats are remembering back in time to the study phase, and they retrieve information about the time of day at which the study event occurred (in addition to information about location and flavor). Study time and test time

were difficult to distinguish in the earlier experiments because the rats had been trained with a short retention interval. Therefore, we dissociated study time and test time hypotheses by transferring the rats to a much longer retention interval (7 hours; Figure 9C), using the same rats (Zhou & Crystal, 2009). Now an early session occurred at the typical study-phase time (7 am) but the test phase occurred at a novel time of day (2 pm); similarly, a late session occurred at the typical study-phase time (1 pm) but the test phase occurred at a novel time of day (8 pm). Initially, the rats received a single early session and a single late session (counterbalance across animals for order of presentation). Notably, the study time occurred at the usual time of day for study phases as in earlier training conditions. However, the test time occurred at novel times of day for test phases (i.e., literally the animals had never been in the room or maze at these novel times). According to the study time hypothesis, the rats should revisit the chocolate location in the replenishment condition at a higher rate than in the nonreplenishment condition. According to the test time hypothesis, performance should be disrupted (equal rates of revisiting in replenishment and nonreplenishment conditions) in the transfer test because test phases occurred at times of day about which they have no information regarding replenishment. The rats revisited the chocolate location at a higher rate in replenishment than nonreplenishment conditions (Figure 10C-D), consistent with the study time hypothesis and episodic memory of the study episode (Zhou & Crystal, 2009). These data were collected using a single early session and a single late session so that all data were obtained before the rats had an opportunity to learn about the consequence of visits at the novel times of day.

We used a 7-hour retention interval so that the study-test sequences from early and late sessions overlapped in time (7 am to 2 pm in early sessions, and 1 pm to 8 pm in late

sessions; Figure 9C); notably, the *late* study phase (1 pm) occurred at an *earlier* time than the *early* test phase (2 pm). Therefore, in an additional experiment after extended training with early and late sessions (Figure 10D), we provided a second dissociation of study time and test time hypotheses (Zhou & Crystal, 2009). In this experiment, we began with a study phase at the time of the *late* session (1 pm) and a test phase that occurred at the time of a typical *early* session (2 pm; Figure 9D). Revisit rates to the chocolate location in the test phase could be based on the study time or the test time. The study time hypothesis predicts that the rats will revisit the chocolate location at the rate typical for a study phase (treating the session like a *late* session because the study phase occurred at the late study time). The test time hypothesis predicts that the rats will revisit the chocolate location at the rate typical for the test time (treating the session like an *early* session). We found that rats relied on the study time (Figure 10E), consistent with episodic memory of the study episode.

In other experiments, we ruled out a number of alternative hypotheses. For example, we showed that rats did not fail to encode the chocolate location on nonreplenishment sessions (Zhou & Crystal, 2011). Overall, these experiments provide compelling evidence that rats use episodic memory to remember what, where, and when the study event occurred (Crystal, 2021a).

Replay of Episodic Memories

In the section above, the experiments focused on testing the central hypothesis that rats remember back in time to a specific earlier event. The experiments showed that rats remember what, where, and when an event occurred. Notably, at the moment of the memory assessment, the rats remembered the time of occurrence of the earlier study event, in addition

to what happened and where the event occurred. Non-episodic memory solutions to the memory problem were ruled out by showing that the rats did not use judgments of how long ago the event occurred, or equivalently timing intervals, judging relative familiarity of earlier events, or memory trace strength. Although this demonstration focuses on what-where-when memory, episodic memory may include memory for other unique events, which may be investigated using other approaches (Crystal, 2021a). For example, we have shown that rats remember items (odors) and the contexts (e.g., arenas) in which the items occurred (Panoz-Brown et al., 2016). This work established that rats remember *many* episodic memories – at least 30 item-in-context events using episodic memory. Because rats remember many episodic memories, it is possible to explore the hypothesis that rats are capable of searching episodic memory to find items that occupied a particular temporal position in a stream of unique events. In this section, I develop the case that rats remember the sequential order of episodic memories, an ability that would enable a rat to replay its episodic memories. We propose that rats represent multiple items in episodic memory and engage in memory replay, a process by which the rat searches its representational space in episodic memory to find items at particular points in the sequence (Panoz-Brown et al., 2018). A key aspect of episodic memories in people involves the replay of the flow of past events in sequential order (Dede et al., 2016; Eichenbaum, 2000; Eichenbaum et al., 2007; Kurth-Nelson et al., 2016; Staresina et al., 2013; Tulving, 2002). Our approach was to develop a behavioral approach that gave rats opportunities to report, via their behavior, about a stream of events in sequential order using episodic memory.

Rats were presented with a list of trial-unique odors presented in a distinctive memory encoding context (a distinctive arena). The odors presented in the list were selected from a large pool of odors in the lab (Figure 11A). An important feature of the list was that the items and the length of the list were randomly determined for each new list. The length ranged from 5 to 12 items, and the actual length was randomly selected on each trial. Consequently, the rat could not predict the length of the list until the list ended. To signal to the rat that the list had ended, the rat was placed into one of two distinctive memory assessment contexts. In a memory assessment context, two items from the list were presented and the rat had the opportunity to choose an item. The correct item was rewarded. In one context, the second to the last item from the list was the correct choice. In the other context, the fourth from the last item was the correct choice. The incorrect choice (foil) was randomly selected from elsewhere in the list. Because the list length was randomly selected for each list, it was *impossible* for the rat to identify the correct choices *before* the list ended. Therefore, when an odor was encoded in a list, the identity of the memory assessment choices were unknown, and it was not yet known that the current item would subsequently be the correct or incorrect choice in the later memory assessment. Throughout the experiments, the locations of odors in arenas were randomly selected and thus provided no information about the correct choice. Our approach was to ask what a rat capable of episodic replay can do via its behavior. If the rat could replay the sequence of episodic memories, it would select the correct item in second- and fourth-last contexts. Over a number of experiments (Panoz-Brown et al., 2018), we documented high accuracy with rats choosing the second last item in the second-last memory assessment context and the fourth last item in the fourth-last memory assessment context (Figure 11C).

Because familiarity cues are pervasive, we developed a technique to dissociate familiarity and episodic memory solutions to the memory problem (Figure 11B). According to the episodic memory replay hypothesis, rats represent multiple items in episodic memory and engage in memory replay, a process by which the rat searches its representational space in episodic memory to find information. Alternatively, we outlined a non-episodic memory solution. As described above, when an item is presented, it gives rise to a memory trace whose probability of retrieval declines over time. Therefore, it is possible that the rats had learned to match the strength of memory traces in each memory assessment context (i.e., judgments of relative familiarity). Accordingly, they could have learned to successfully choose the second last (relatively large trace) and the fourth last (smaller trace) items in the appropriate context. The foils would be avoided because they have memory traces strengths above or below the levels of second and fourth last items, depending on its position in the list. In summary, the non-episodic strategy involves picking the item that matches the typical memory strength for the current context while avoiding values above and below the typical level. Critically, using such a solution, the rat would choose the correct item but would not need to replay episodic memories. To dissociate familiarity and episodic memory, we doubled the time between list items (Figure 11B), which impacts memory trace strength of items without impacting the sequential order of items. Importantly, in the memory assessment, the foil (i.e., the incorrect choice) was selected so that it had the typical memory strength of a correct item. For example, the foil in the second last memory assessment was an attractive choice because it occurred in the list at the delay typical of a second last item; thus, an animal that is relying on familiarity will choose the wrong item yielding accuracy that is below chance. In contrast, an animal that

uses episodic memory replay will choose the second last item correctly (yielding above chance accuracy) despite the unusually long delay since this particular second last item appeared in the list. Similarly, in the fourth last context, the foil was an attractive choice because it occurred in the list at the delay typical of a fourth last item. In both dissociation tests, we observed above chance accuracy (Figure 11C), which rules out judgments of familiarity (or equivalently memory trace strengths, the age of memories, and timing intervals from each event to the memory assessment) and supports the hypothesis that rats replay episodic memory. In other experiments, we showed that episodic replay is intact after at least a 1-hour retention interval and survives interference provided by memory of other odors (Figure 11C); these data are consistent with the hypothesis that episodic memory is a part of long-term memory and rule out the use of working memory. Finally, we used DREADDs (Designer Receptor Exclusively Activated by Designer Drug) to document that temporary inhibition of neurons in the hippocampus impaired replay of episodic memories while sparing measures of hippocampal-independent memory (new-old recognition memory and an associative discrimination; Figure 11D) (Panoz-Brown et al., 2018).

Temporal Foundations of Episodic Memory

Gallistel (1990) proposed that animals compute and store quantities that represent aspects of the animal's environment. Accordingly, when an event occurs, the animal stores a record of the event (i.e., its features or qualities), its location in space, and the time of occurrence of the event in a fixed temporal framework. By storing times of occurrence, it is possible to compute temporal intervals between events (Gallistel, 1990). Gallistel's framework provides a model for memory of what, where, and when an event occurred, which is a classic

definition of episodic memory (Tulving, 1983). The studies focused on timing in rats reviewed above provide evidence in support of the type of calendar date system proposed by Gallistel. Searching event records that are linked to their times of occurrence may represent a fundamental aspect of episodic memory. For example, in Zhou and Crystal's (2009) studies reviewed above, we showed that, at the moment of a memory assessment, the rat remembered back in time to earlier study event, including when in time, where, and what occurred. In Panoz-Brown and colleagues' (2018) studies reviewed above, we showed that rats are capable of searching a stream of events in episodic memory. I propose that the times of occurrence of the events is an essential feature for replaying episodic memory, which may provide a mechanism for mental time travel.

Conclusions

People can describe when earlier events occurred using calendar-date-time systems, i.e., a representational system that retains the time of occurrence of earlier events (Gallistel, 1990). Our data suggest that, at the moment of memory assessment, rats remember back in time to when a specific event occurred in time. Moreover, these experiments provide insight into the type of temporal representational systems (Langille & Gallistel, 2020) that may be used in animal models of episodic memory, namely a timing system that retains the time of occurrence of earlier events. Investigations that integrate time and memory may advance the development of animal models of episodic memory.

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Figure Captions

Figure 1. Classic definitions of oscillator and pacemaker-accumulator mechanisms. An oscillator is endogenous and self-sustaining, whereas a pacemaker-accumulator requires reset by a stimulus. Consequently, an oscillator does not require ongoing periodic input to produce continued periodic output, whereas an interval timing system is reset by the single presentation of an environmental input. Adapted with permission from Gibbon, J., Fairhurst, S., and Goldberg, B. (1997). Cooperation, conflict and compromise between circadian and interval clocks in pigeons. In C. M. Bradshaw & E. Szabadi (Eds.), *Time and behaviour: Psychological and neurobehavioural analyses* (pp. 329-384). Elsevier.

Figure 2. The pattern of inter-response times continues after termination of periodic feeding. Short-interval timing is characterized by many small inter-response times punctuated by longer inter-response times. The relatively long inter-response times continued after termination of periodic food delivery. Inter-response time (times of responses $R_{n+1} - R_n$) is plotted as a function of response time for a representative rat exposed to training with food delivered on a fixed interval 96-s schedule. During testing, food did not occur (i.e., extinction). Extinction began at a randomly selected time in the session. The dependent measure was the time of occurrence of photo beam interruptions in the food trough. Reproduced from Crystal JD and Baramidze GT (2007) Endogenous oscillations in short-interval timing. *Behavioural Processes* **74**: 152-158. © 2007, with permission from Elsevier.

Figure 3. Endogenous oscillations in short-interval timing continue after the termination of periodic input. Short time Fourier transforms (averaged across rats) are shown for training (left panels) and testing (right panels) conditions using fixed interval 48-, 96-, and 192-s food delivery in training. The 3-dimensional images show frequency (period = $1/\text{frequency}$) on the vertical axis as a function of time within the session on the horizontal axis; the color scheme represents the amount of power from the Fourier analysis. Concentrations of high power occur at a frequency of approximately 0.02, 0.01, and .0005 which correspond to periods of approximately 50, 100, and 200 s in top, middle, and bottom panels, respectively. Adapted from Crystal JD and Baramidze GT (2007) Endogenous oscillations in short-interval timing. *Behavioural Processes* **74**: 152-158. © 2007, with permission from Elsevier.

Figure 4. Superior sensitivity to time in circadian meal delivery. Response rate (photo beam breaks in the food trough) increased later into the interval for inter-meal intervals in the circadian range (unfilled red symbols) relative to intervals outside this range (filled blue symbols); dashed lines indicate the width of the response rate functions. Anticipatory responses increase immediately prior to the meal for all inter-meal intervals except 34 h. Each 45-mg food pellet was contingent on a photo beam break after a variable interval during 3-hr meals. Inter-meal intervals were tested in separate groups of rats ($n = 3-5$ per group). The end of the meal corresponds to 1 on the x-axis. The experiment was conducted in constant darkness. Adapted from (Crystal, 2001a). Reproduced from Crystal JD (2006b) Time, place, and content. *Comparative Cognition & Behavior Reviews* **1**: 53-76 with permission.

Figure 5. Local peak in sensitivity to time in circadian meal delivery. Intervals near the circadian range (red symbols) are characterized by higher sensitivity than intervals outside this range (blue symbols). Variability in anticipating a meal was measured as the width of the response distribution prior to the meal at 70% of the maximum rate, expressed as a percentage of the interval ($N = 29$). The interval is the time between light offset and meal onset in a 12-12 light-dark cycle (leftmost two circles) or the inter-meal interval in constant darkness (all other data). The percentage width was smaller (superior sensitivity to time) in the circadian range than outside this range. The width/interval did not differ within the circadian or noncircadian ranges. The same conclusions were reached when the width was measured as 25%, 50%, and 75% of the maximum rate. The data are plotted in reversed-order on the y-axis so that local maxima in the data correspond to high sensitivity, which facilitates comparison with other measures of sensitivity (e.g., Figure 7). Mean $SEM = 2.4$. Adapted from (Crystal, 2001a). Reproduced from Crystal JD (2006b) Time, place, and content. *Comparative Cognition & Behavior Reviews* 1: 53-76 with permission.

Figure 6. Endogenous oscillations in long-interval timing continue after the termination of periodic input. Response rate increased as a function of time within the 16-hr inter-meal interval cycle during the first and second nonfood cycle. Response rate (frequency of responses expressed as a proportion of the maximum frequency within the cycle) is plotted as a function of time within the cycle. The cycle included meals (solid rectangle) during training (top panel). The meals were omitted (dashed rectangles) in the first (middle panel) and second (bottom panel) nonfood cycles. Reproduced from Crystal JD (2006a) Long-interval timing is based on a

self sustaining endogenous oscillator. *Behavioural Processes* **72**: 149-160, © 2006, with permission from Elsevier.

Figure 7. Timing is characterized by local peaks in sensitivity to time. Sensitivity to time is characterized by local maxima at 12 and 24 s (left panel), 12 s (middle panel), and 0.3 and 1.2 s (right panel). Green symbols: average across rats. Red symbols: a running median was performed on each rat's data and the smoothed data were averaged across rats to identify the most representative local maxima in sensitivity. Left panel: Rats discriminated short and long noise durations with the long duration adjusted to maintain accuracy at approximately 75% correct. Short durations were tested in ascending order with a step size of 1 s ($n = 5$) and 2 s ($n = 5$). Sensitivity was similar across step sizes, departed from zero, and was nonrandom. Mean $SEM = 0.03$. Middle panel: Methods are the same as described in left panel, except short durations were tested in random order ($n = 7$) or with each rat receiving a single interval condition ($n = 13$); results from these conditions did not differ. Sensitivity departed from zero and was nonrandom. Mean $SEM = 0.02$. Right panel: Methods are the same as described in left panel, except intervals were defined by gaps between 50-ms noise pulses and short durations were tested in descending order with a step size of 0.1 s ($n = 6$). Sensitivity departed from zero and was nonrandom. Mean $SEM = 0.04$. Sensitivity was measured using d' from signal detection theory. $d' = z[p(\text{short response} \mid \text{short stimulus})] - z[p(\text{short response} \mid \text{long stimulus})]$. Relative sensitivity is $d' - \text{mean } d'$. Adapted from (Crystal, 1999, 2001b). Reproduced from Crystal JD (2006b) Time, place, and content. *Comparative Cognition & Behavior Reviews* **1**: 53-76 with permission.

Figure 8. Multiple local maxima in sensitivity to time are observed in the discrimination of time across 7 orders of magnitude. The existence of a local maximum near a circadian oscillator (peak on right side; purple squares) and other local maxima in the short-interval range (peaks on left side; blue, red and green circles) are consistent with the hypothesis that timing is mediated by multiple oscillators. Left side: Rats discriminated short and long durations, with the long duration adjusted to maintain accuracy at 75% correct. Short durations were tested in sequential order (blue and red circles; $N = 26$) or independent order (green circles; $N = 20$). Circles represent relative sensitivity using d' from signal detection theory and are plotted using the y-axis on the left side of the figure. Right side: Rats received food in 3-hr meals with fixed inter-meal intervals by breaking a photo beam inside the food trough. The rate of photo beam interruption increased before the meal. Squares represent sensitivity, which was measured as the width of the anticipatory function at 70% of the maximum rate prior to the meal, expressed as a percentage of the interval ($N = 29$). The interval is the time between light offset and meal onset in a 12-12 light-dark cycle (leftmost two squares) or the inter-meal interval in constant darkness (all other squares). Squares are plotted with respect to the reversed-order y-axis on the right side of the figure. Y-axes use different scales, and the x-axis uses a log scale. Adapted from (Crystal, 1999, 2001a, 2001b). Reproduced from Crystal JD (2006b) Time, place, and content. *Comparative Cognition & Behavior Reviews* 1: 53-76 with permission.

Figure 9. What-Where-When Episodic Memory in the Rat: Experimental Design. Schematic representation of experimental design of Zhou and Crystal's (2009) study. **A.** Design of

793 Experiment 1. First helpings (study phase; encoding) and second helpings (test phase; memory
794 assessment) of food was presented either in the morning or afternoon, which was randomly
795 selected for each session and counterbalanced across rats. Study and test phases show an
796 example of the accessible arms, which were randomly selected for each rat in each session.
797 Chocolate or chow flavored pellets were available at the distal end of four arms in the study
798 phase (randomly selected). After a 2-min retention interval, the test phase provided chow-
799 flavored pellets at locations that were previously blocked by closed doors. The figure shows
800 chocolate replenished in the test phase conducted in the morning (7 am) but not in the
801 afternoon (1 pm), which occurred for a randomly selected half of the rats; these contingencies
802 were reversed for the other rats (not shown). One session was conducted per day with morning
803 or afternoon sessions randomly selected. **B.** Phase-shift design of Experiment 2. Performance in
804 Experiment 1 could have been based on the time of day of sessions (morning vs. afternoon) or
805 based on a judgment of how long ago light onset in the colony occurred (short vs. long delay;
806 i.e., familiarity of light onset). Light onset occurred at midnight on a single occasion in
807 Experiment 2, which was 6 hr earlier than in Experiment 1, and the session occurred in the
808 morning in Experiment 2. The horizontal lines highlight the similarity of the 7-hr gap between
809 light onset and sessions in probe (solid; Experiment 2) and training (dashed; Experiment 1)
810 conditions. This design puts the predictions for time-of-day and familiarity cues in conflict;
811 performance typical of the morning baseline is expected based on time of day whereas
812 afternoon performance is expected based on familiarity. **C.** Transfer-test design of Experiment
813 3. Study phases occurred at the same time of day as in Experiment 1. Test phases occurred at
814 novel times of day (7 hr later than usual). Thus, early and late sessions had study times (but not

test times) that corresponded to those in Experiment 1. The initial two sessions in Experiment 3 were one replenishment and one nonreplenishment condition, counterbalanced across rats for order of presentation. An early or late session was randomly selected on subsequent days. More revisits to the chocolate location are expected in replenishment compared to nonreplenishment conditions if the rats remembered the time of day at which the study episode occurred. Alternatively, revisit rates are expected to be equal in early and late sessions if the rats used the current time of day when the test phase occurred. Study and test phases were as in Experiment 1, except that they were separated by 7-hr delays (shown by horizontal brackets). **D.** Conflict-test design of Experiment 4. The study phase occurred at 1 pm and was followed by a test phase at 2 pm. These times correspond, respectively, to the time of day at which a late-session study phase and early-session test phase occurred in Experiment 3, which put predictions for time of day at study and time of day at test in conflict. If rats remembered the time of day at which the study episode occurred, they would be expected to behave as in its late-session, test-phase baseline. Alternatively, if the rats used the current time of day at test, they would be expected to behave as in its early-session, test-phase baseline. **A-D.** Reproduced with permission from Zhou, W., & Crystal, J. D. (2009). Evidence for remembering when events occurred in a rodent model of episodic memory. *Proceedings of the National Academy of Sciences of the United States of America*, 106, 9525-9529. © 2009 National Academy of Sciences, U.S.A.

Figure 10. What-Where-When Episodic Memory in the Rat: Data. Data from Zhou and Crystal's (2009) study. **A.** Rats preferentially revisited the chocolate location when it was about to

837 replenish in Experiment 1 (see experimental design in Figure 9A). The probability of a revisit to
838 the chocolate location in the first four choices of a test phase is plotted for replenishment and
839 nonreplenishment conditions. **B.** Rats used time of day, rather than information about temporal
840 remoteness, to adjust revisit rates in Experiment 2 (see Figure 9B). The figure shows the
841 difference between observed and baseline revisit rates. For the bar labeled interval, the
842 baseline is the probability of revisiting chocolate in the afternoon. The significant elevation
843 above baseline shown in the figure documents that the rats did not use familiarity or an interval
844 timing mechanism. For the bar labeled time of day, the baseline is the probability of revisiting
845 chocolate in the morning. The absence of a significant elevation above baseline is consistent
846 with the use of time of day. The horizontal line corresponds to the baseline rate of revisiting the
847 chocolate location in Experiment 1. Positive difference scores correspond to evidence against
848 the hypothesis shown on the horizontal axis. **C.** and **D.** Rats preferentially revisited the
849 replenishing chocolate location when the study, but not the test, time of day was familiar in
850 Experiment 3 (see Figure 9C). The probability of a revisit to the chocolate location in a test
851 phase is shown for first replenishment and first nonreplenishment sessions (**C**; initial) and for
852 subsequent sessions (**D**; terminal). **E.** Rats remembered the time of day at which the study
853 episode occurred in Experiment 4 (see Figure 9D). Rats treated the novel study-test sequence
854 as a late-session test phase, documenting memory of the time of day at study rather than
855 discriminating time of day at test. The figure shows the difference between observed and
856 baseline revisit rates. For the bar labeled test time, the baseline was the probability of revisiting
857 chocolate in the test phase of the early session in Experiment 3. The significant elevation above
858 baseline documents that the rats did not use the time of day at test to adjust revisit rates. For

the bar labeled study time, the baseline was the probability of revisiting chocolate in the test phase of the late session in Experiment 3. The absence of a significant elevation above baseline is consistent with memory of the time of day at study. The horizontal line corresponds to the baseline revisit rate to the chocolate location from Experiment 3 (terminal). Positive difference scores correspond to evidence against the hypothesis indicated on the horizontal axis. **A-E**. Error bars represent 1 SEM. **A**, **C**, and **D**. The probability expected by chance is 0.41. Repl = replenishment condition. Non-repl = nonreplenishment condition. **A**. * $P < 0.001$ difference between conditions. **B**. * $P < 0.05$ different from baseline. **C** and **D**. * $P < 0.05$ and ** $P < 0.0001$ difference between conditions. **E**. * $P < 0.001$ different from baseline. Reproduced with permission from Zhou, W., & Crystal, J. D. (2009). Evidence for remembering when events occurred in a rodent model of episodic memory. *Proceedings of the National Academy of Sciences of the United States of America*, 106, 9525-9529. ©2009 National Academy of Sciences, U.S.A.

Figure 11. Replay of Episodic Memory in the Rat. Rats replay a stream of multiple episodic memories. **A**. A list of odors (, , , etc.) is presented in a distinctive context (). When the list ends, the rat is moved to one of two different contexts (, ; randomly selected). In one context (), the second from the last item from the list is the correct choice (depicted by "v"); the foil is another item from the list. In the other context (), the fourth from the last item is correct. The correct item is not known until the list ends because the list length is randomly selected on each trial. Trial-unique odors are randomly selected from a large pool of odors. **B**. The presentation of an item gives rise to a memory trace

whose probability of retrieval decreases with the passage of time (delays depicted by arrows at top of **A** and **B**). Thus, the correct choice in **A** could be based on judgments of relative familiarity (memory trace strength) of second and fourth last items (the time between second last item and memory assessment is shorter than between fourth last item and memory assessment). Familiarity and sequential information are dissociated in **B** by doubling the amount of time between list items. The foils in **B** were selected to pit the "correct" familiarity item vs. the "correct" sequential item. **C**. Rats chose the correct sequential item when familiarity and sequential information were dissociated (Exp 2, depicted in **B**). Similarly high accuracy was observed in training (Exp 1, depicted in **A**) and other conditions (Exp 3: long retention interval (60 min); replay was intact when other items were remembered after list encoding (Exp 4A: foils from list; Exp 4B: foils from intervening task). **D**. Temporary inhibition of hippocampal neurons using the chemogenetic technique DREADDs (Designer Receptor Exclusively Activated by Designer Drug) impaired replay of episodic memories while sparing measures of hippocampal-independent memory (new-old recognition memory and an associative discrimination). **A-D**. Our approach provides an animal model of episodic memory replay, a process by which the rat searches its representations in episodic memory in sequential order to find information. Error bars represent 1 SEM. Adapted from and reproduced with permission from Panoz-Brown, D., Iyer, V., Carey, L.M., Sluka, C.M., Rajic, G., Kestenman, J., Gentry, M., Brotheridge, S., Somekh, I., Corbin, H.E., Tucker, K.G., Almeida, B., Hex, S.B., Garcia, K.D., Hohmann, A.G., & Crystal, J.D. (2018). Replay of episodic memories in the rat. *Current Biology*, 28(10), 1628-1634.e1627. ©2018

Oscillator

Pacemaker Accumulator

Timing Properties

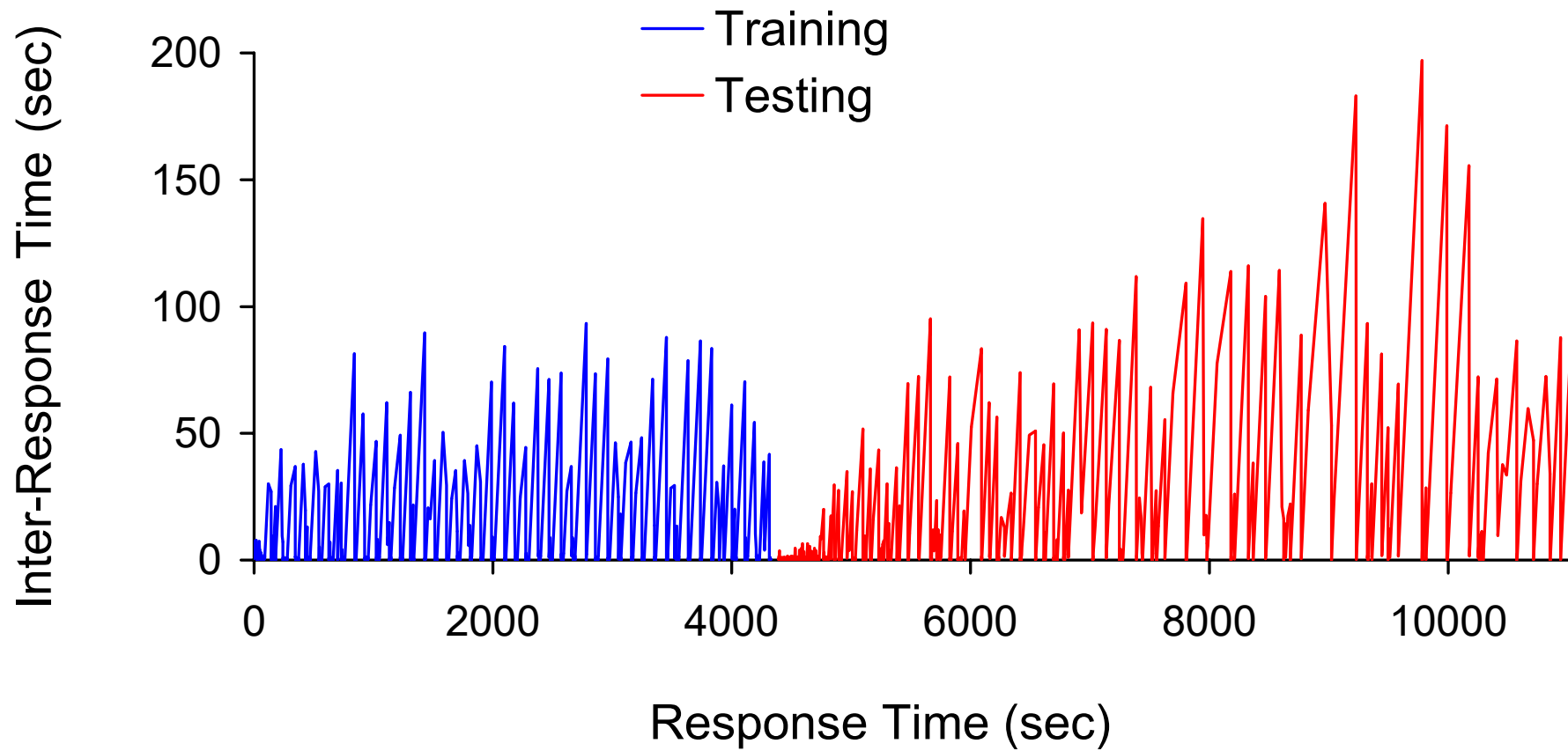
- Endogenous oscillation
 - Free run
- Entrainment range
 - Limited
- Phase shift adjustment
 - Slow, several cycles usually required

- Requires reset
 - One shot
- Training range
 - Broad
- Phase shift immediate
 - Arbitrary onset phase

Variance Properties

- High level of precision
 - $CV = 1-5\%$
- Relationship to entrainment period (?)

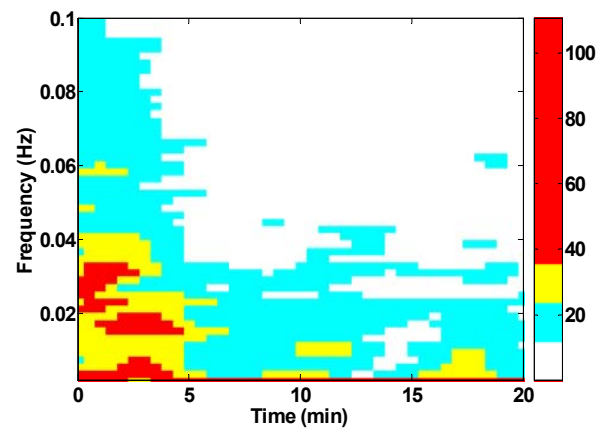
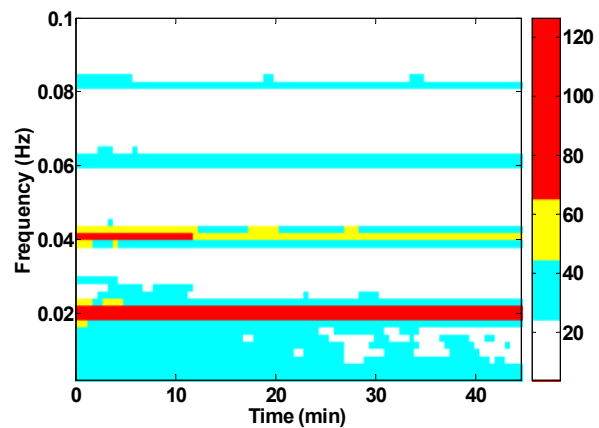
- Low level of precision
 - $CV = 10-35\%$
- Scalar property



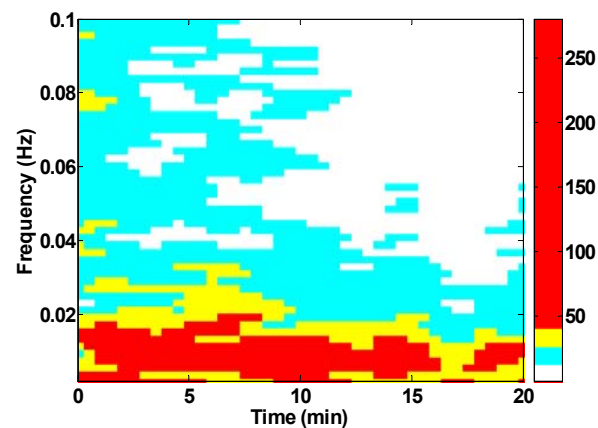
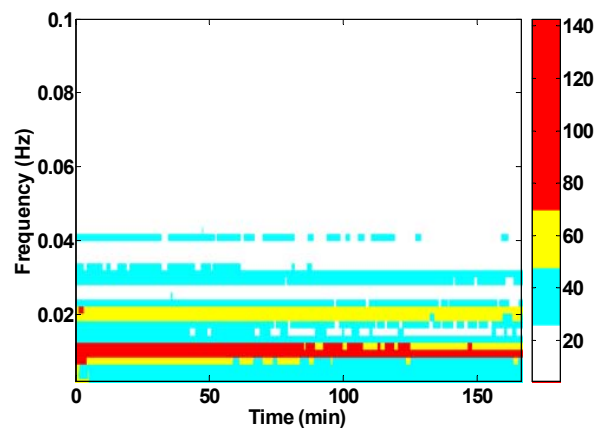
Training

Testing

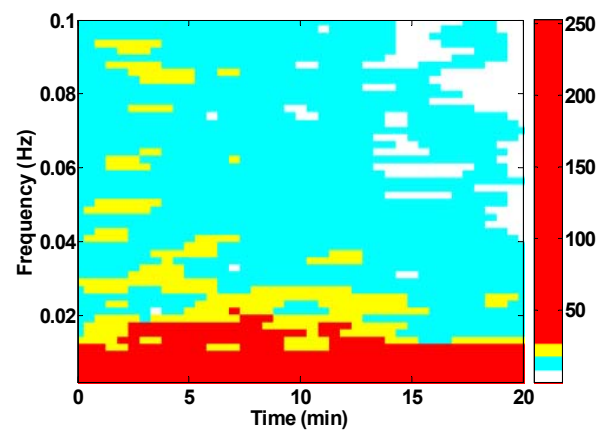
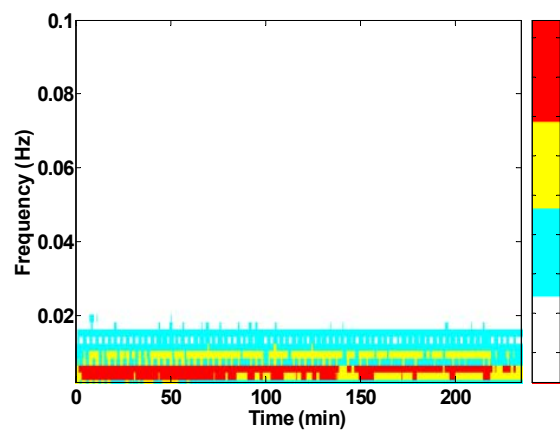
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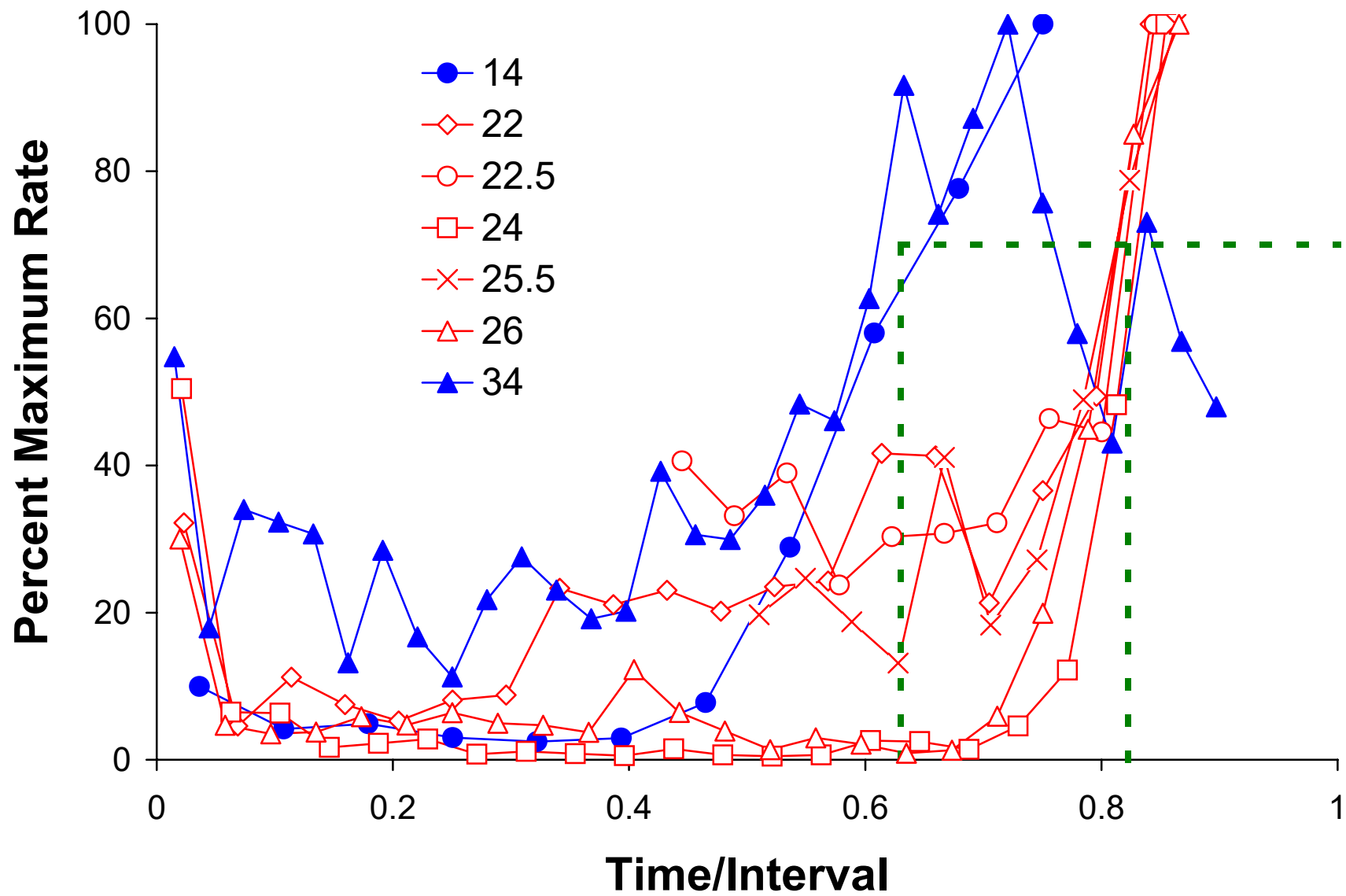


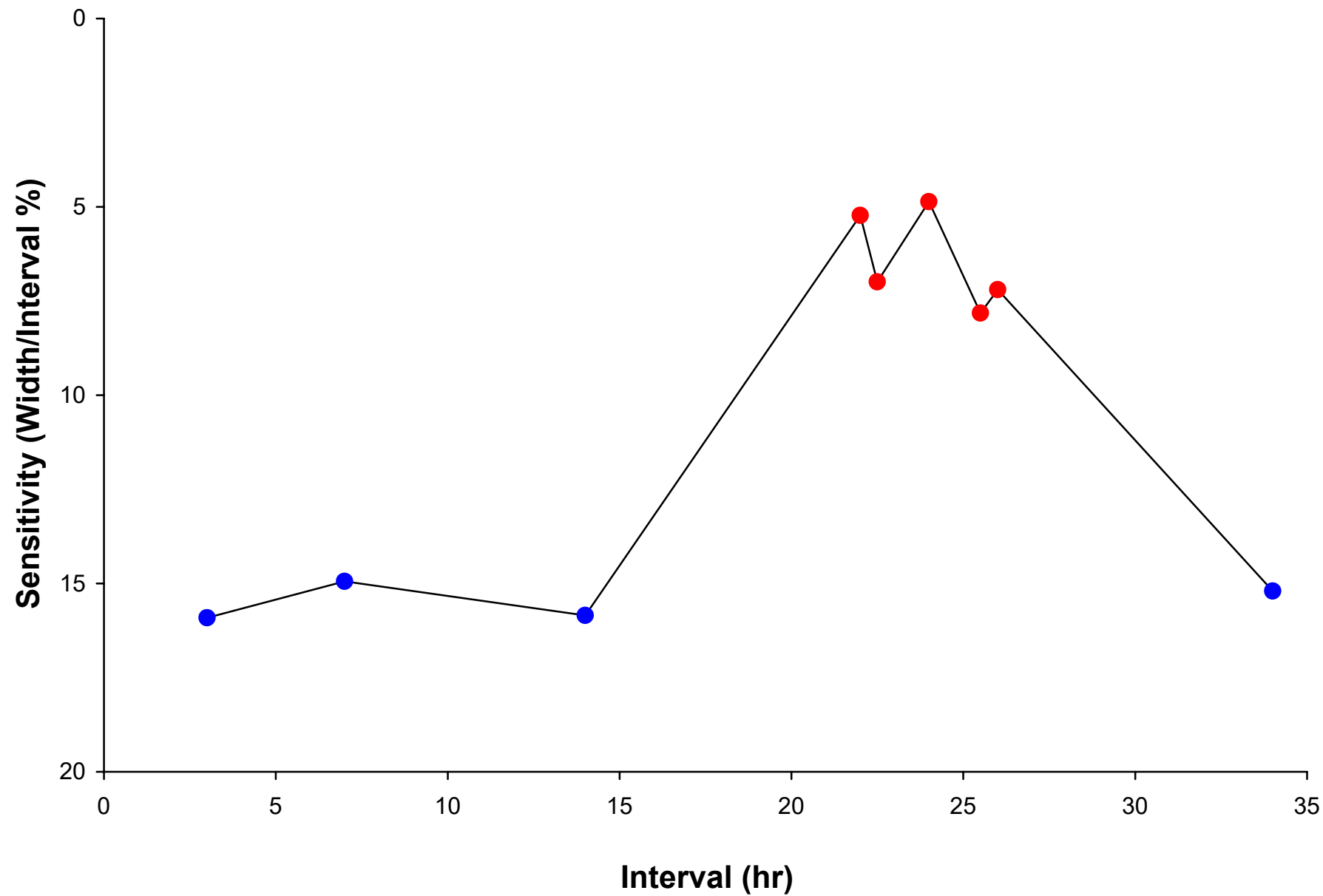
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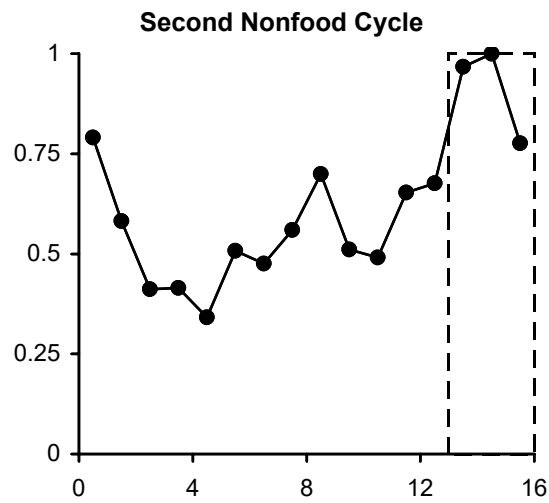
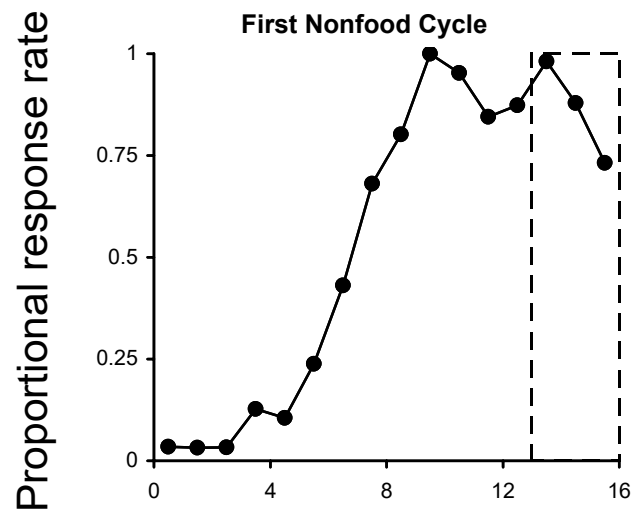
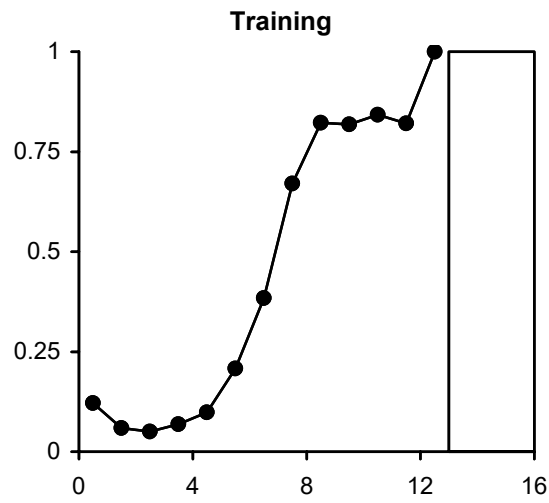


FI 192

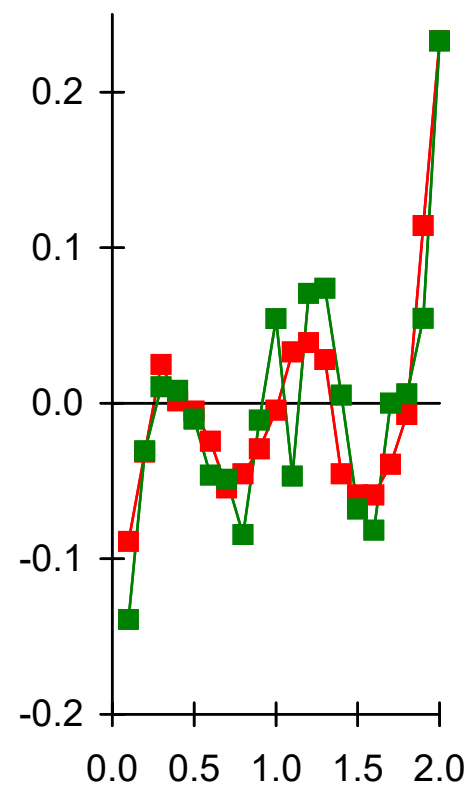
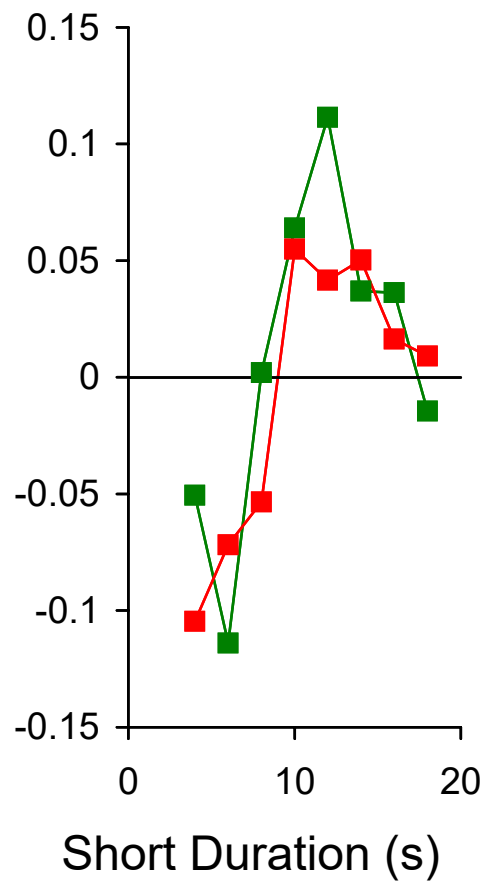
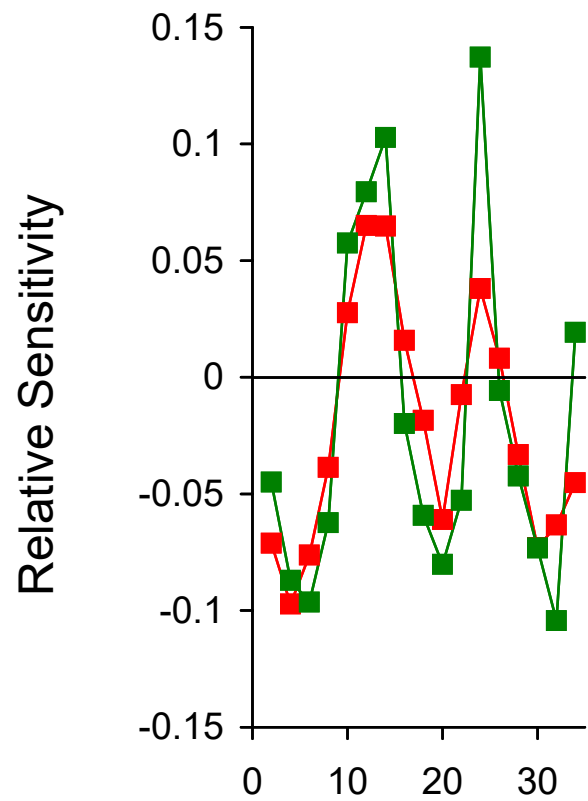


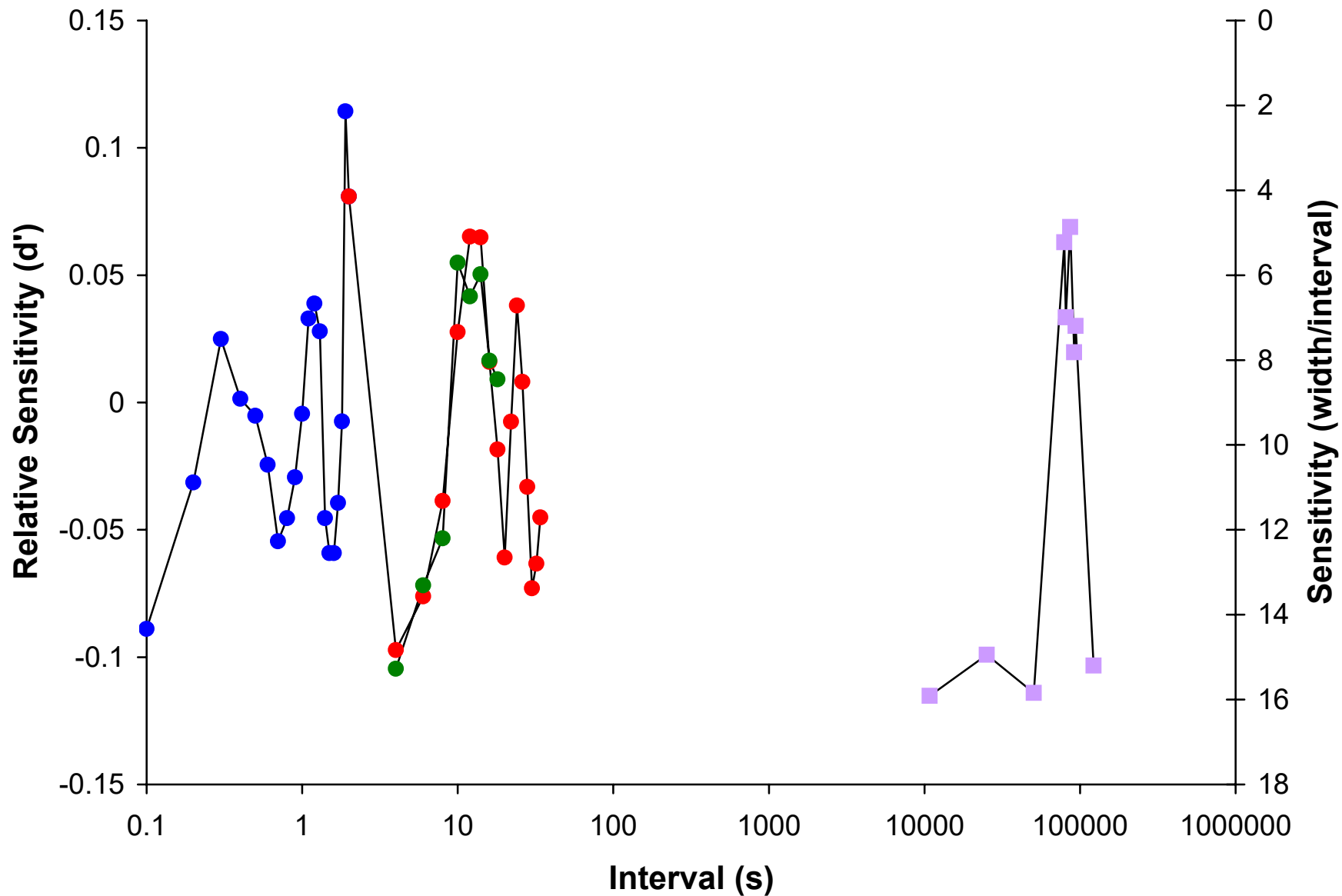




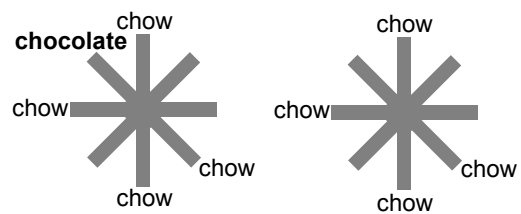
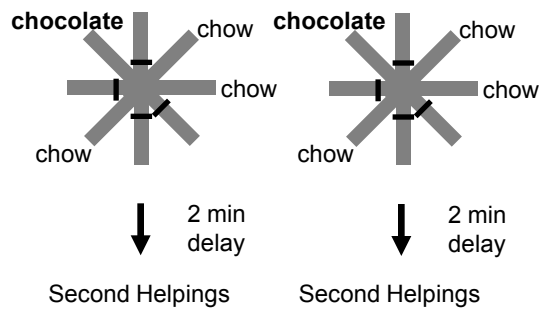
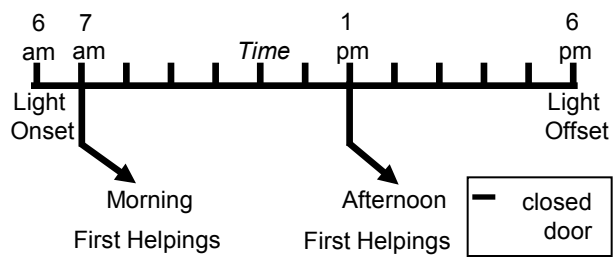


Time within cycle (hr)

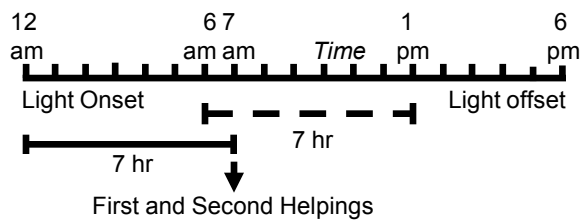




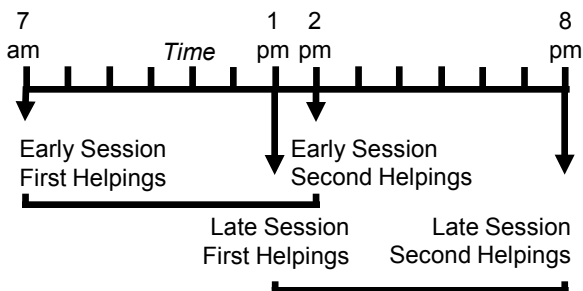
A Experiment 1



B Experiment 2



C Experiment 3



D Experiment 4

