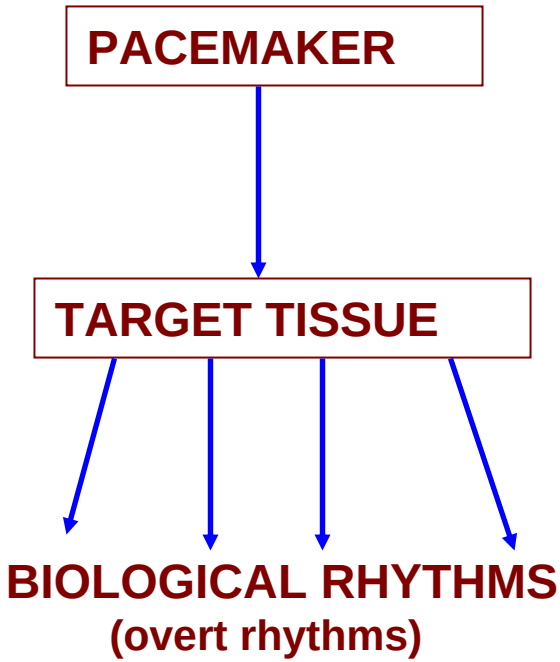
Chronobiology	Study of biological timekeeping
Biological rhythm	Cyclical, repeated variation in a biological function
Ultradian	High frequency – repeats many times in a day
Infradian	Repeats at intervals much longer than 24 hours
Circadian	Approximately a day (24 hours)
Circatidal	Approximately every 12.4 hours (with the tide)
Circalunar	Approximately once a month
Circannual	Approximately once a year
Endogenous	Internally generated rhythm
Free-running	Not synchronized to external signals
Pacemaker	A structure that generates a rhythm
Target tissue	Tissue whose function is regulated by the pacemaker
Overt rhythm	A visible, measurable rhythm
Nocturnal	Active at night
Diurnal	Active during the day
LL	Constant light
DD	Constant darkness
LD 12:12	12 hours of light; 12 hours of dark

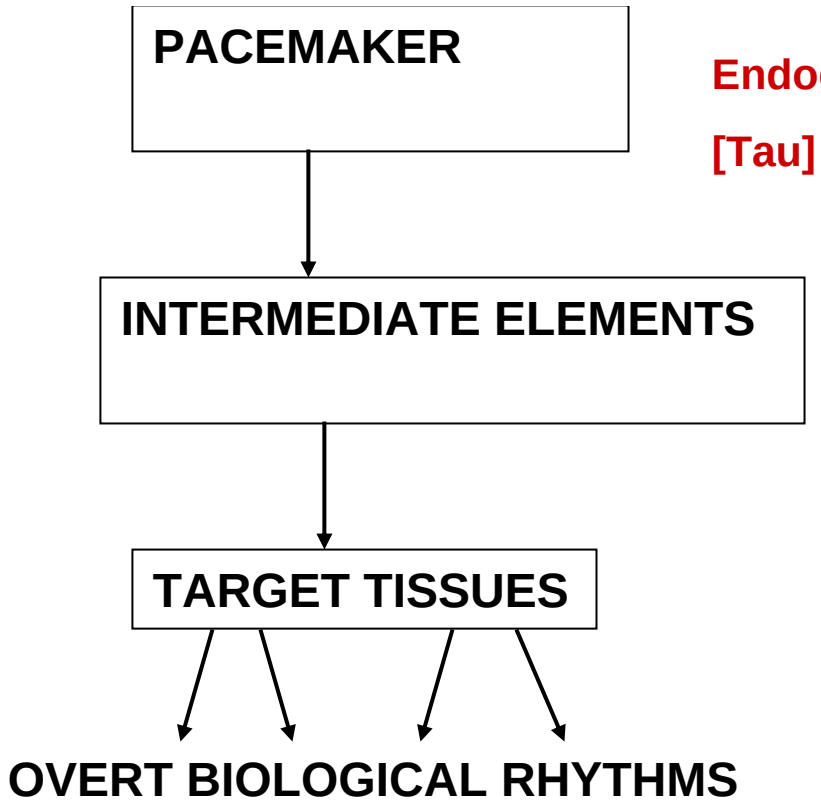
How do we measure endogenous circadian rhythms?

How do we interpret circadian rhythm records?

What are the properties of endogenous circadian rhythms?

How are free-running circadian rhythms entrained or synchronized to environmental rhythms?


PACEMAKER
TARGET TISSUE
BIOLOGICAL RHYTHMS
(overt rhythms)



Endogenous, free-running rhythm

[Tau]

Measuring endogenous circadian rhythms

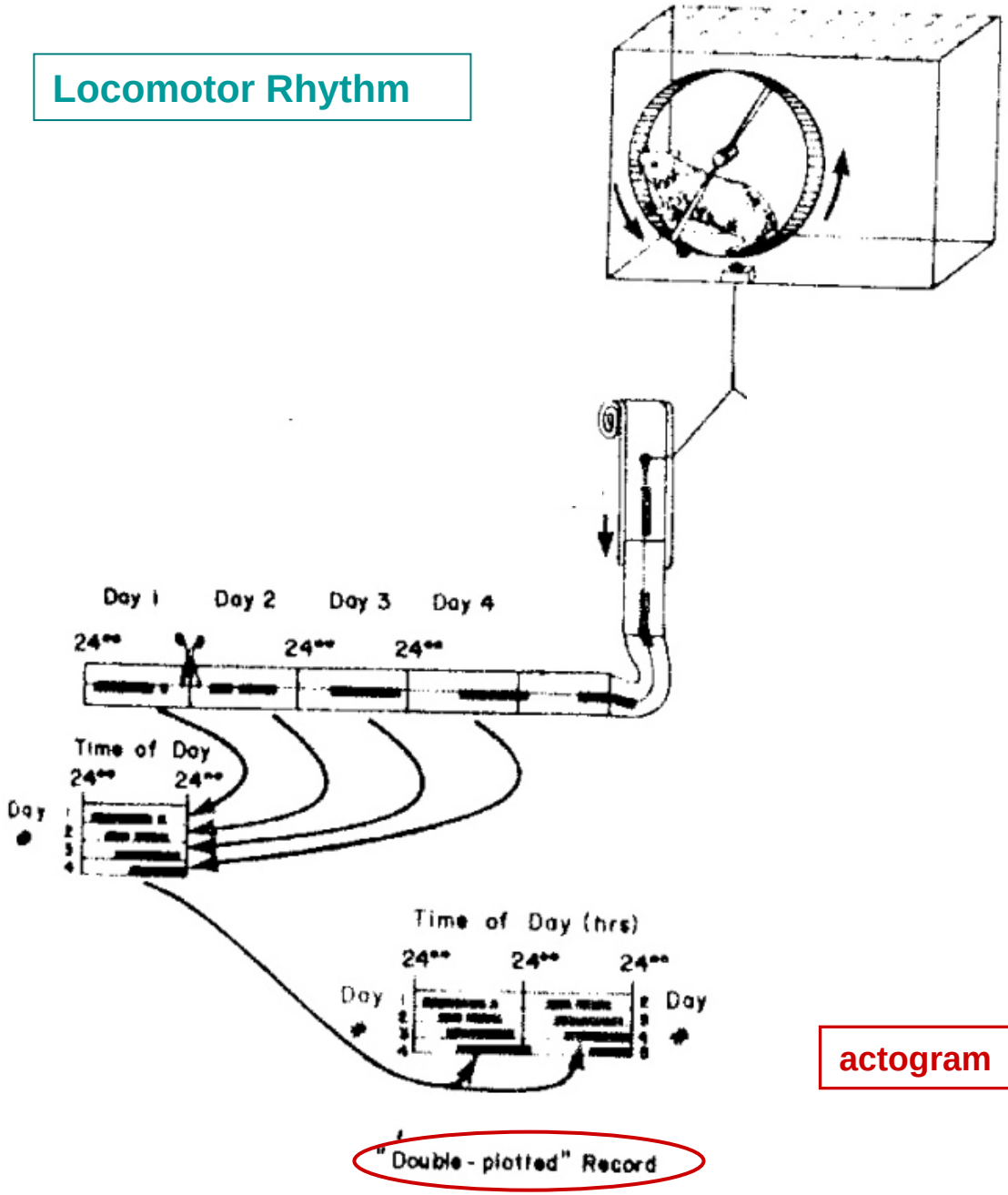
- goals in selecting a circadian rhythm to measure
- least invasive rhythms to study

✓ temperature

✓ activity (locomotor rhythm; sleep/wake cycle)

- Measure in constant conditions
  - Temperature
  - Lighting (LL; DD)
  - Soundproof
  - Humidity
  - Food and water ad libitum
  - Housekeeping at irregular intervals

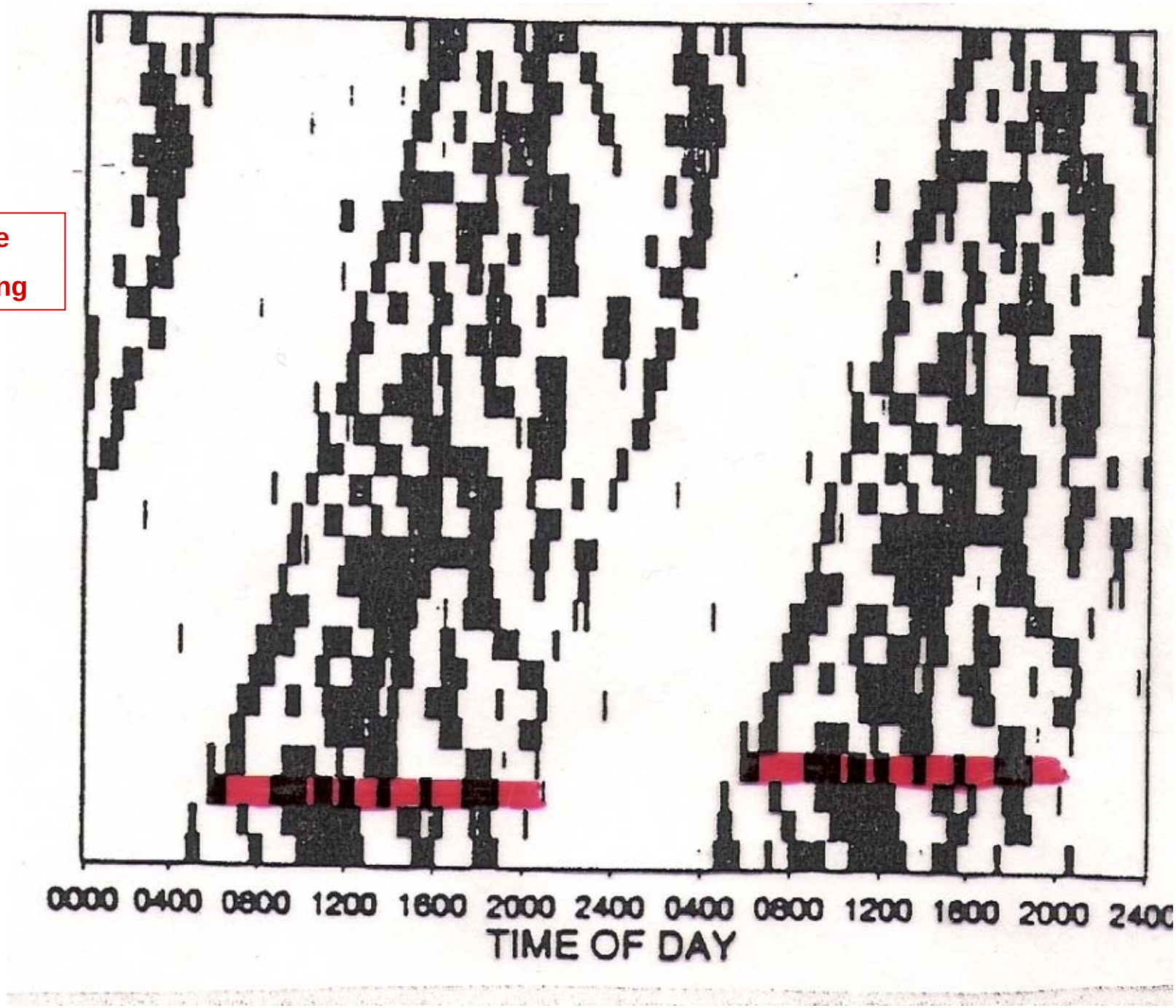
Locomotor Rhythm

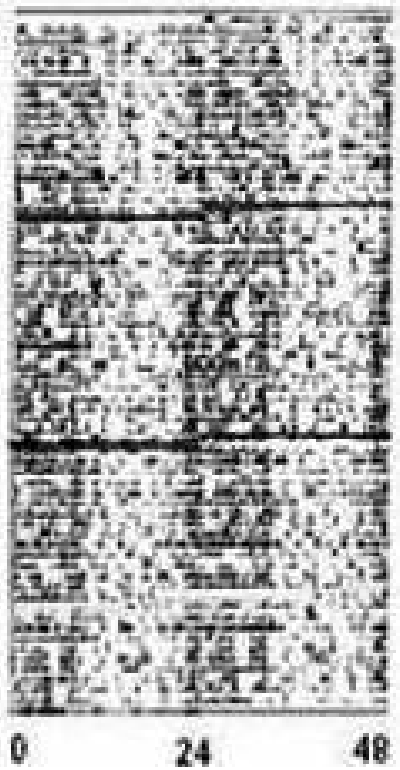


actogram

Active

Resting




0
24
48

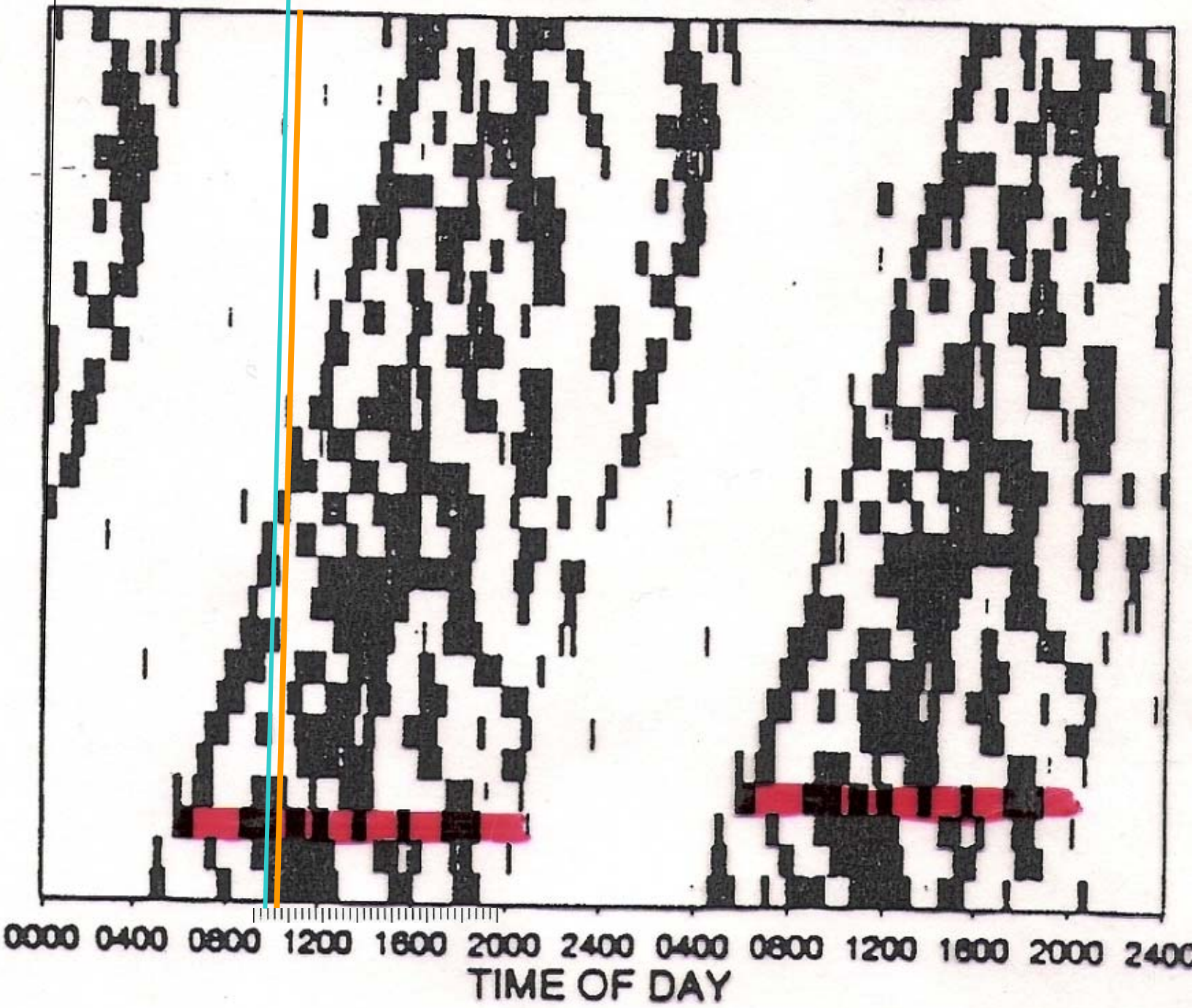
What is the circadian period of this locomotor rhythm?

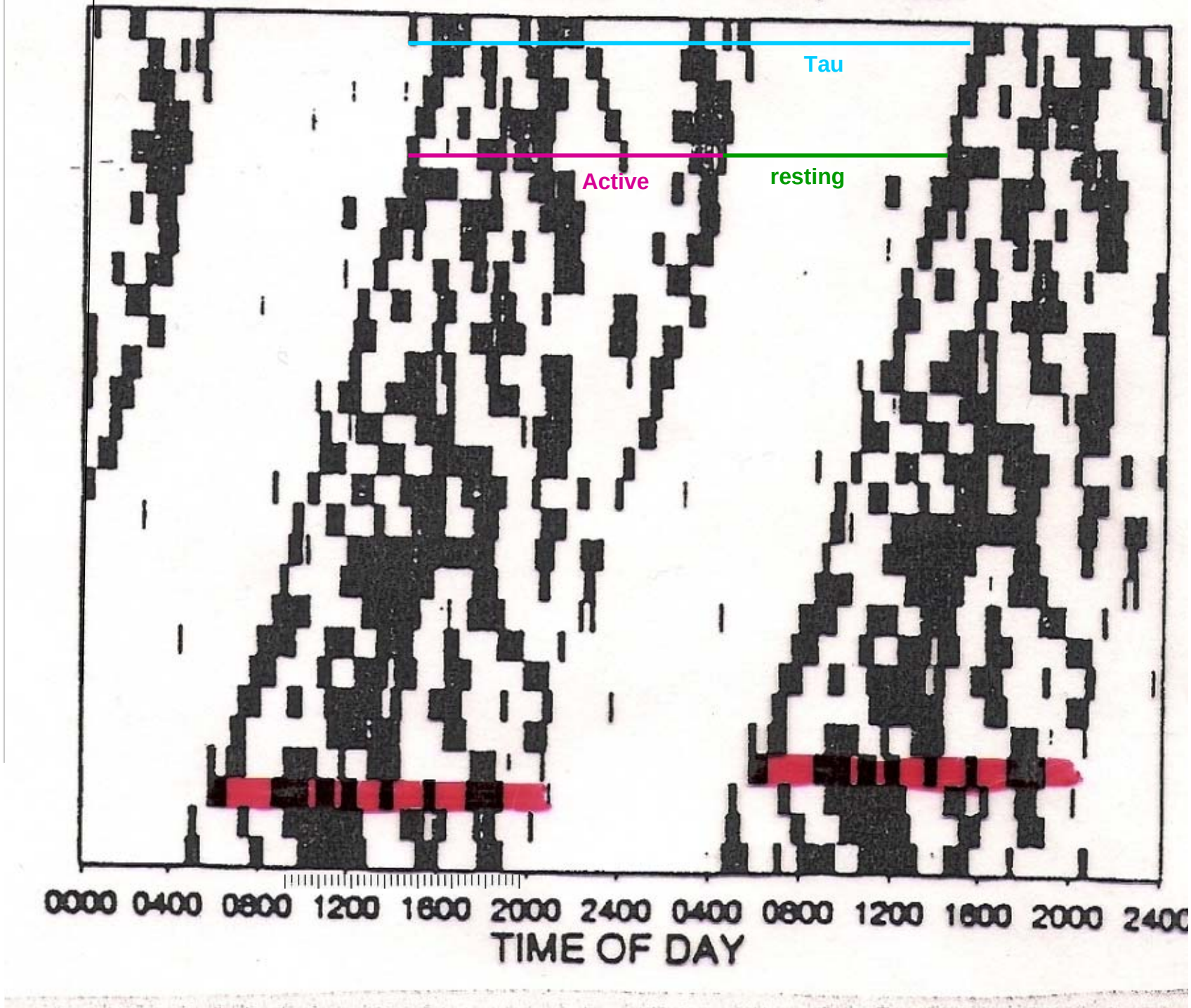
Is this circadian rhythm synchronized to environmental time?

Does the animal run the same number of hours each day?

Observe the *pattern* of activity

How many days has this rhythm been recorded?


0000 0400 0800 1200 1600 2000 2400 0400 0800 1200 1600 2000 2400
TIME OF DAY


Tau
Active
resting
0000 0400 0800 1200 1600 2000 2400 0400 0800 1200 1600 2000 2400
TIME OF DAY

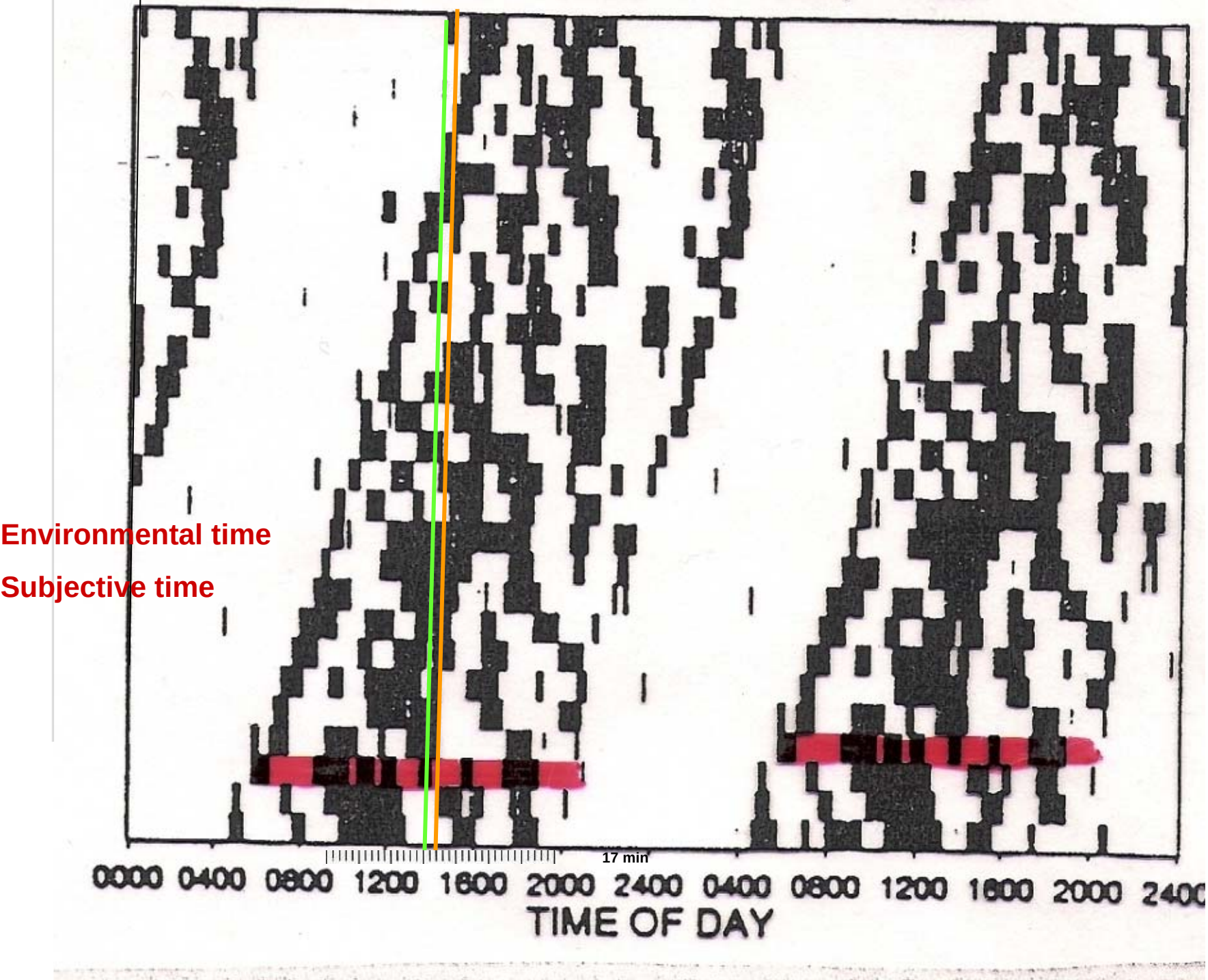
What is the circadian period of this locomotor rhythm? (pick a few points)

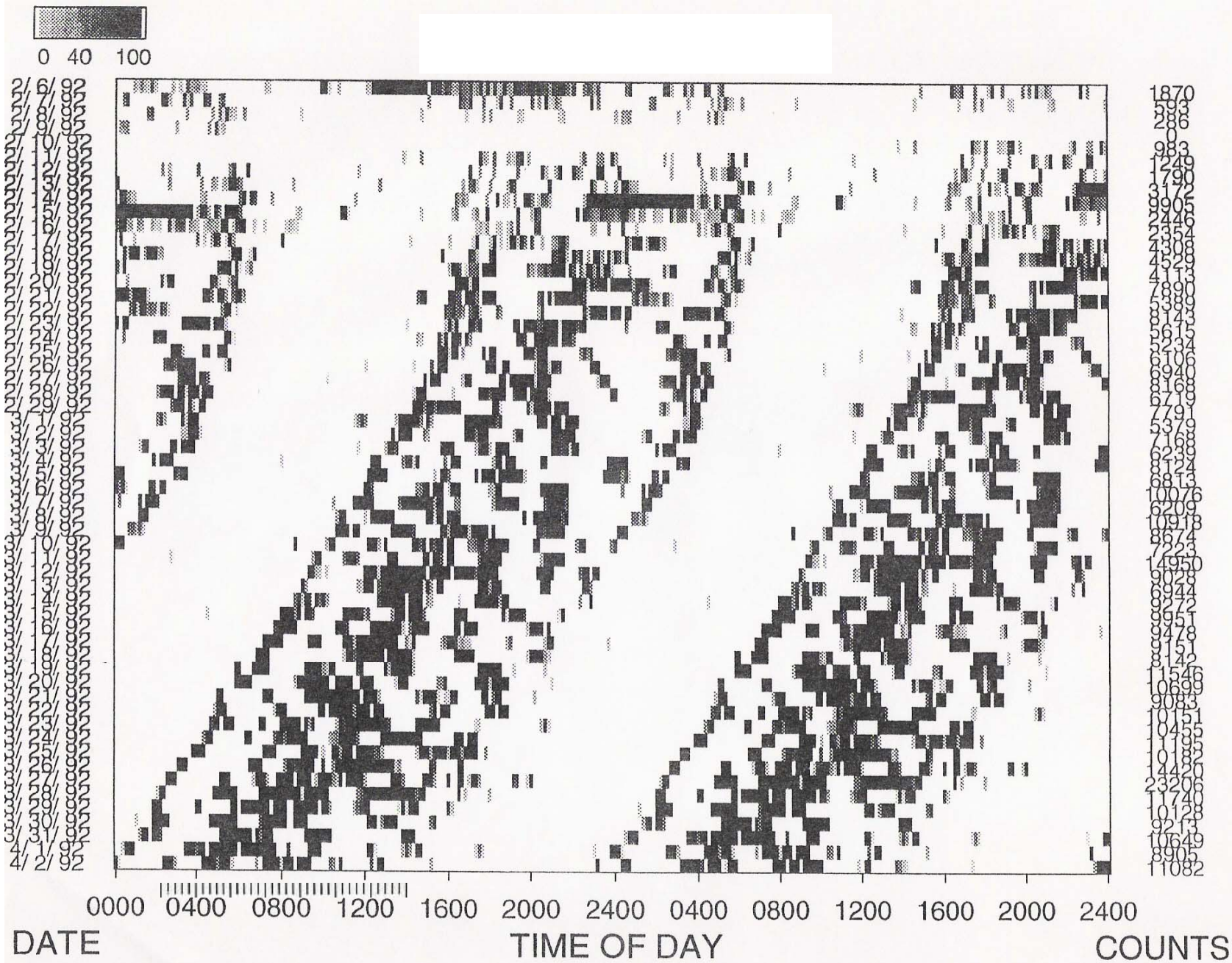
Is this circadian rhythm synchronized to environmental time?

Does the animal run the same number of hours each day?

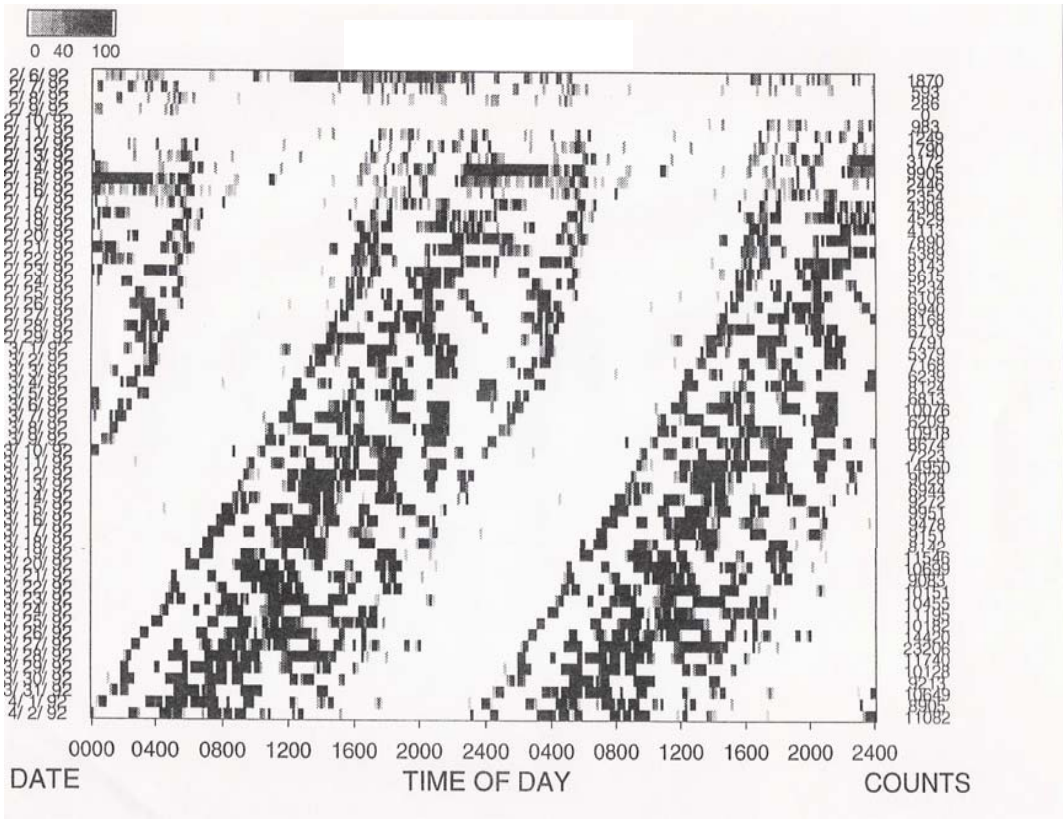
Observe the *pattern* of activity

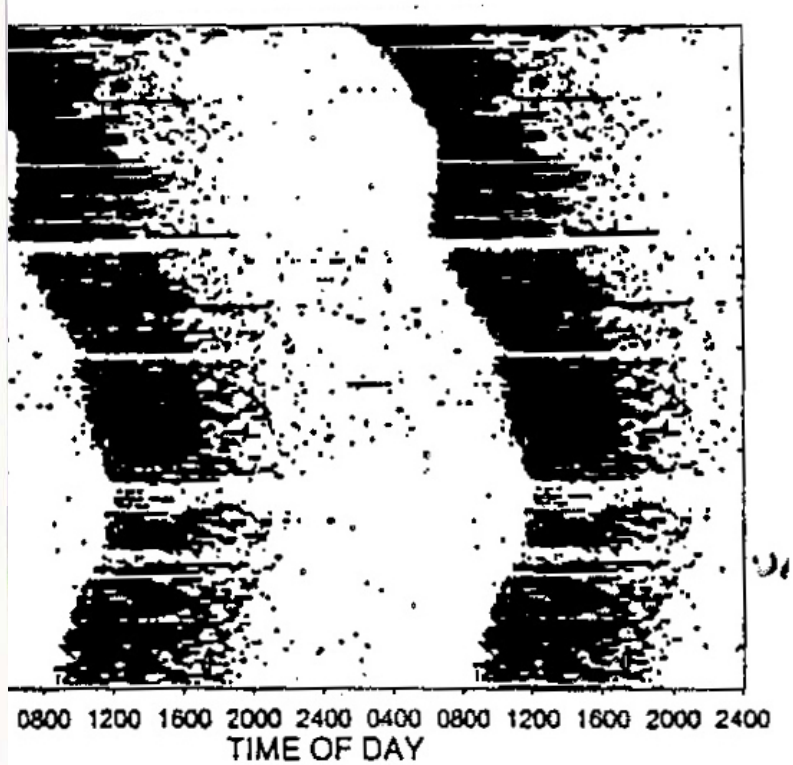
How many days has this rhythm been recorded?


Environmental time
Subjective time
17 min
0000 0400 0800 1200 1600 2000 2400 0400 0800 1200 1600 2000 2400
TIME OF DAY


0 40 100
2/ 6/ 92
4/ 2/ 92
1870
0000 0400 0800 1200 1600 2000 2400 0400 0800 1200 1600 2000 2400
DATE
TIME OF DAY
COUNTS

Period **Pattern** **Intensity**





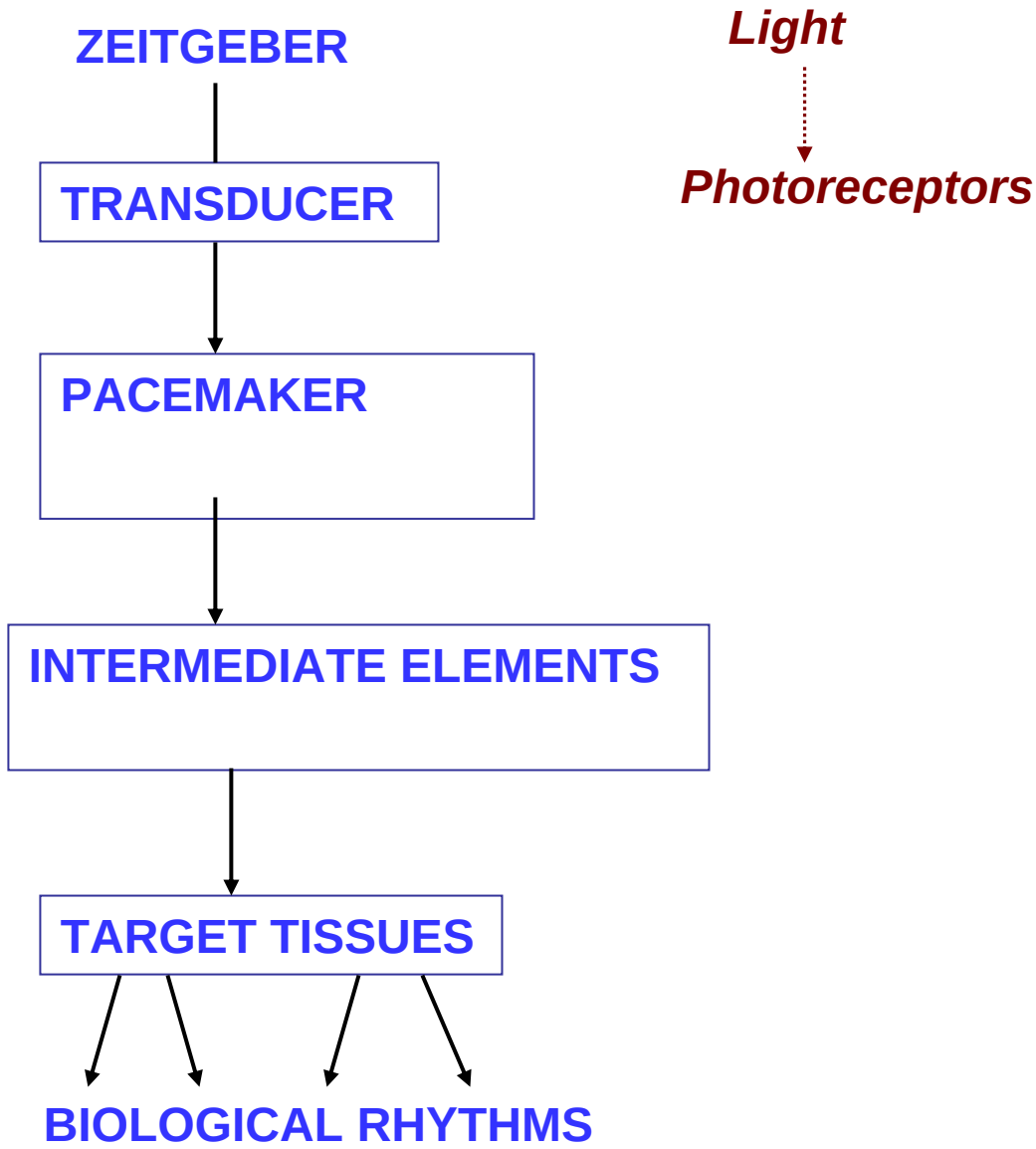
How do we measure endogenous circadian rhythms?

How do we interpret circadian rhythm records?

- **pattern of activity**
- **intensity of activity**
- **period of rhythm**

What are the properties of endogenous circadian rhythms?

- **Self-sustained**
- **Approximately but not exactly 24h**
- **Can be synchronized by external time cues**
  - *** Zeitgeber [zeit = time; geber = giver]**


ZEITGEBER
TRANSDUCER
PACEMAKER
INTERMEDIATE ELEMENTS
TARGET TISSUES
BIOLOGICAL RHYTHMS
Light
Photoreceptors

Entrainment – **synchronization to an environmental signal**

Zeitgeber

- **Light**
- **Restricted access to food**
- **Exercise**
- **Social cues**

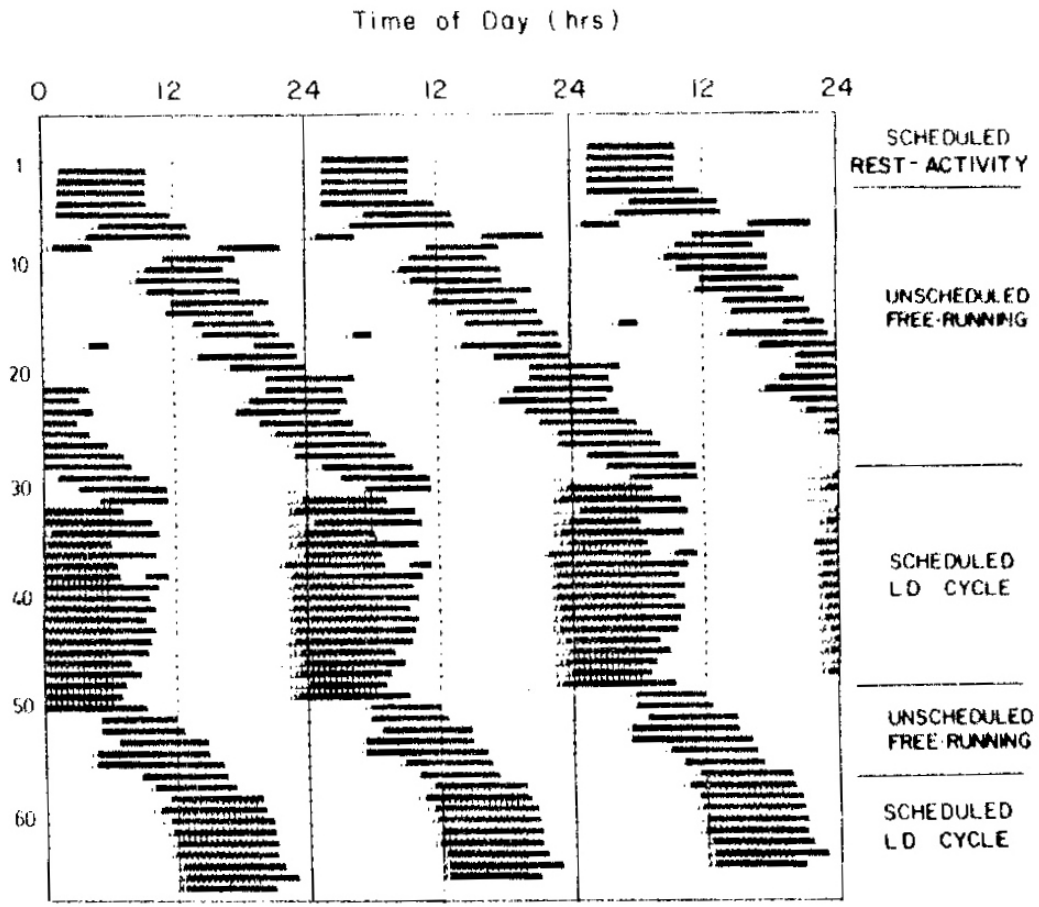


Fig. 2.18 Triple-plotted sleep–wake cycle of a human subject exposed to a strict light–dark cycle. Horizontal black bars = time asleep. On days 1–5 the subject was entrained to normal day–night cues, including scheduled rest–activity, light–dark, and mealtimes. On days 6–31 the subject was allowed to self-select times of sleep, meals, and lighting, and showed a

HOW DO WE KNOW THE CLOCK OR RHYTHM IS ENTRAINED?

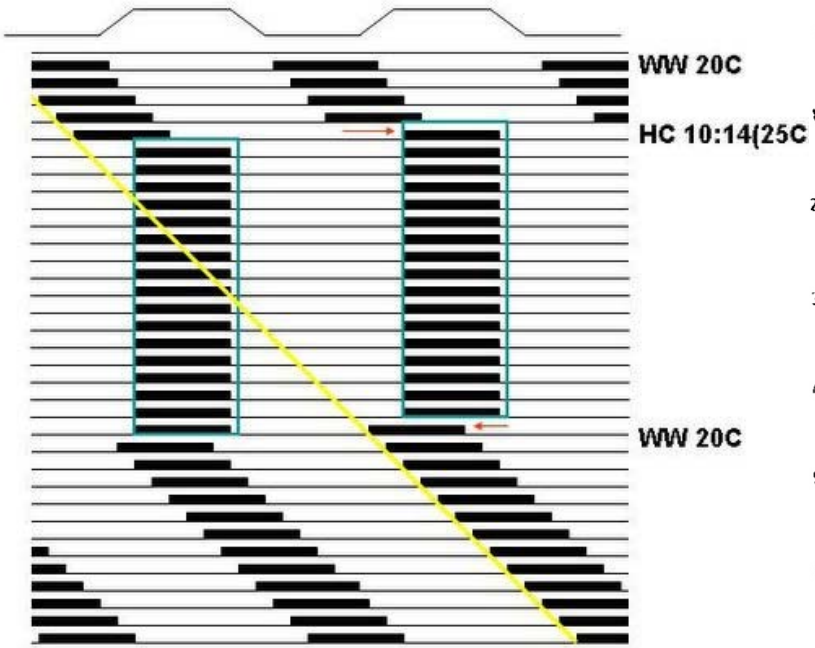
When a rhythm is entrained to a Zeitgeber

1. **The period of the rhythm is locked into the period of the Zeitgeber. The overt rhythm will begin a new cycle every time it is exposed to the Zeitgeber.**

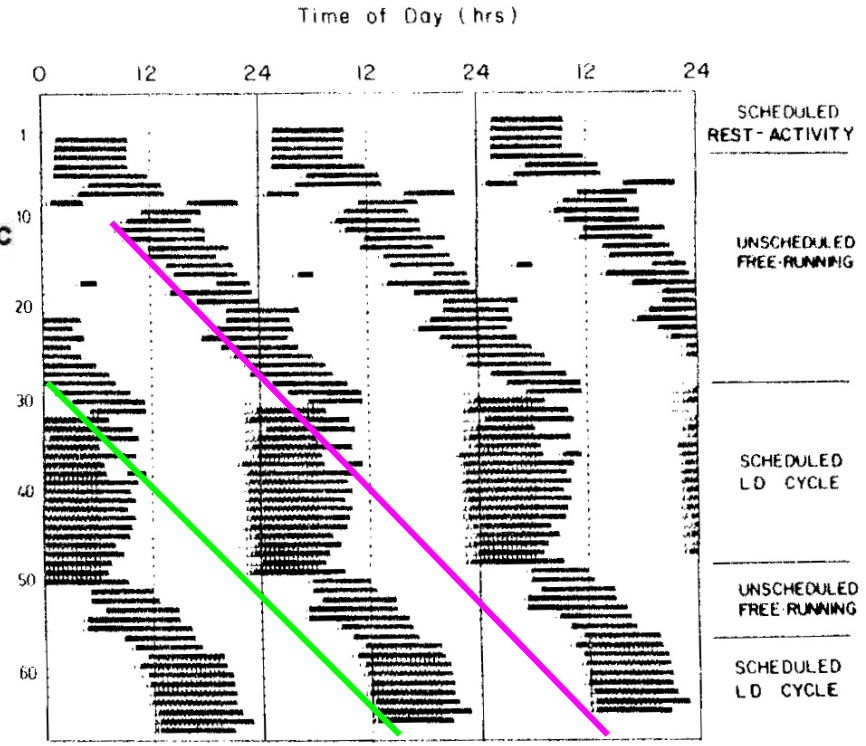
2. **When the Zeitgeber signal is removed, the free running period will resume from entrained phase not as a projection of the previous free-running rhythm.**

If the animal begins running from the previous free running phase we say that the environmental signal was only hiding or covering up or *masking* the internal clock rhythm.

Masking



Entrainment



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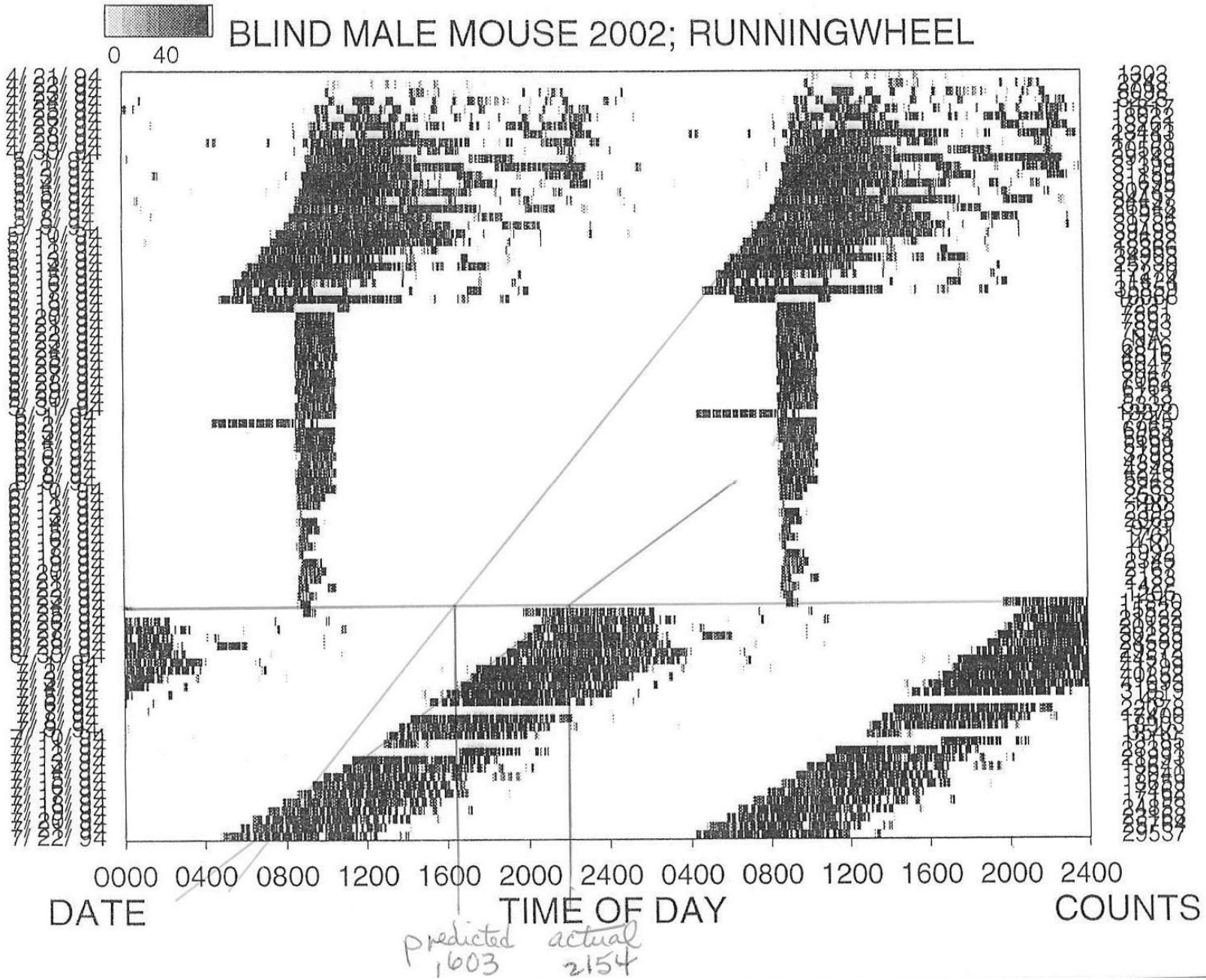
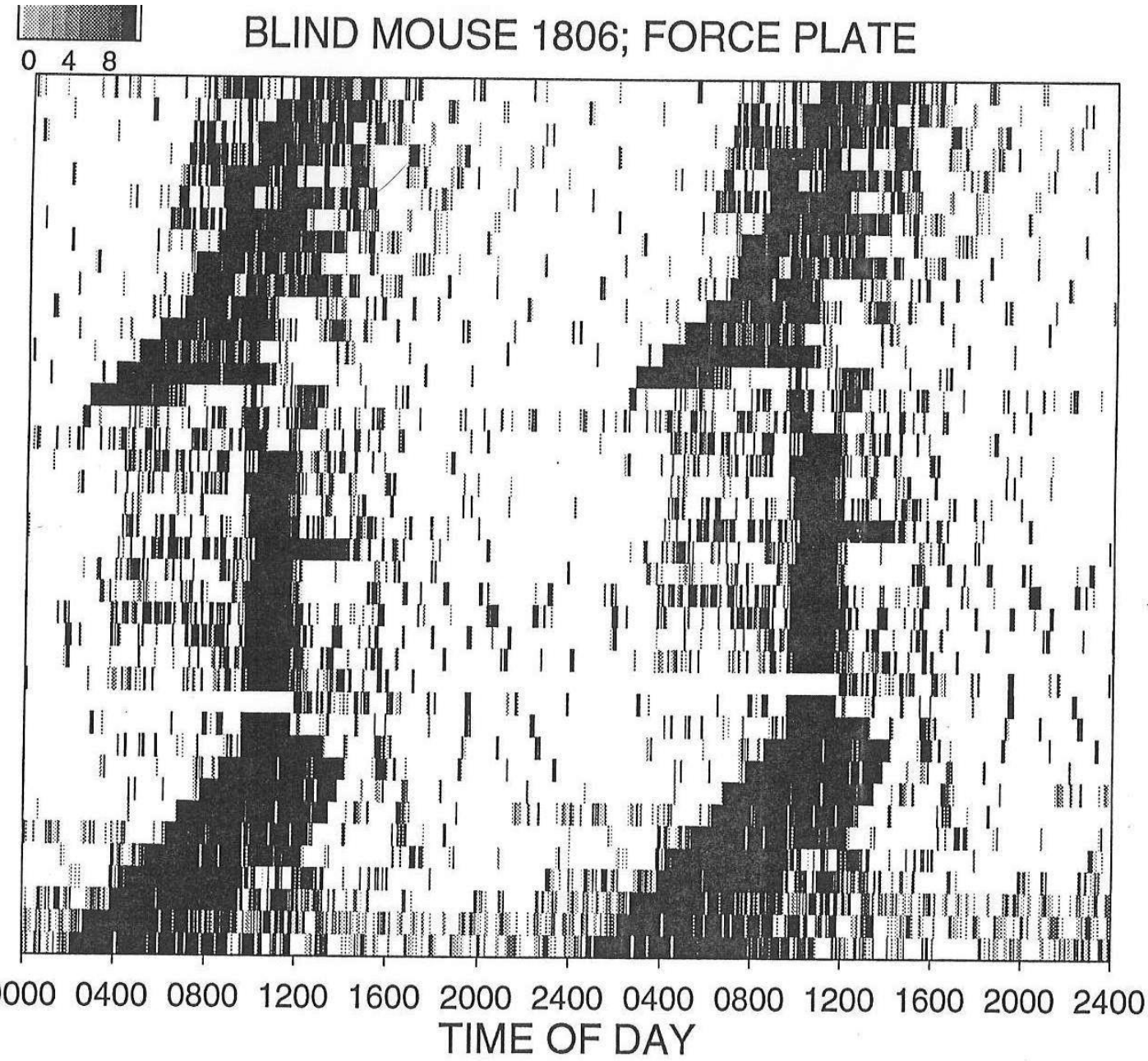

0 40
BLIND MALE MOUSE 2002; RUNNINGWHEEL
0000 0400 0800 1200 1600 2000 2400 0400 0800 1200 1600 2000 2400
DATE
TIME OF DAY
COUNTS
predicted 1603
actual 2154


BLIND MOUSE 1806; FORCE PLATE
0 4 8
0000 0400 0800 1200 1600 2000 2400 0400 0800 1200 1600 2000 2400
TIME OF DAY

Criteria for a Zeitgeber

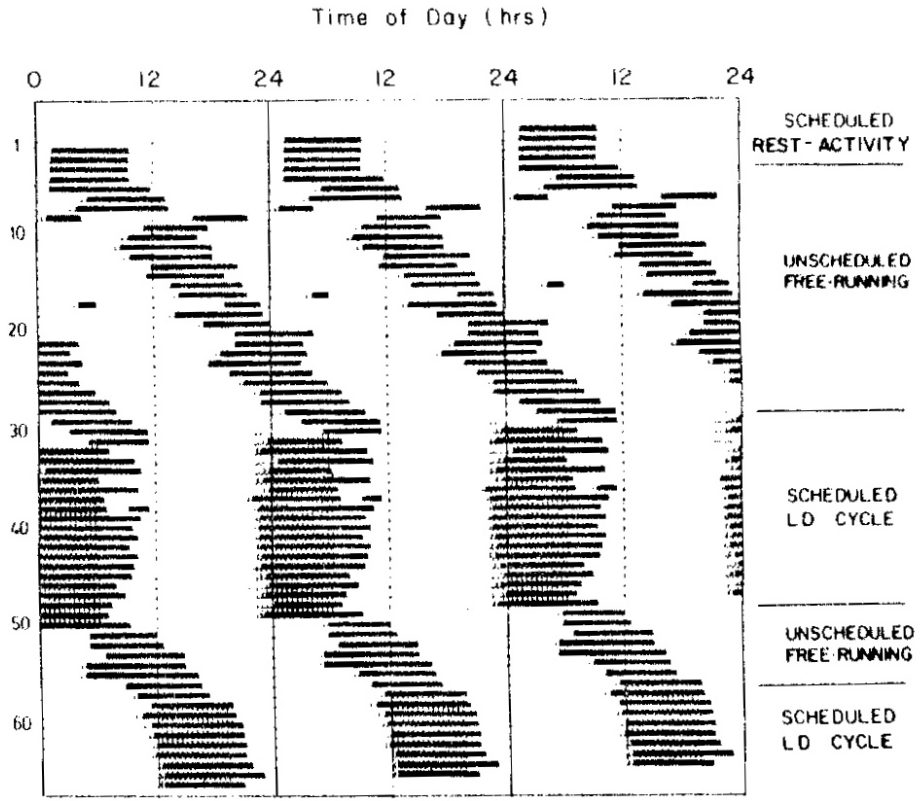
To demonstrate that an an environmental variable acts as a time cue to the circadian system, one must show that the following criteria are met:

1. Monitored circadian rhythm must be free-running with an independent period before the time cue is imposed on the animal and must resume free running after the time cue is removed.

2. Once the animal is exposed to the environmental cycle, the period of the circadian rhythm must adjust so as to equal the period of the zeitgeber.

3. A stable and reproducible relationship must emerge and be maintained between the timing of the observed rhythm and the timing of the Zeitgeber;

4. When the Zeitgeber is removed, the rhythm must start to free-run from a phase determined by the environmental cycle and not by the rhythm prior to entrainment.



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How are free-running circadian rhythms entrained or synchronized to environmental rhythms?

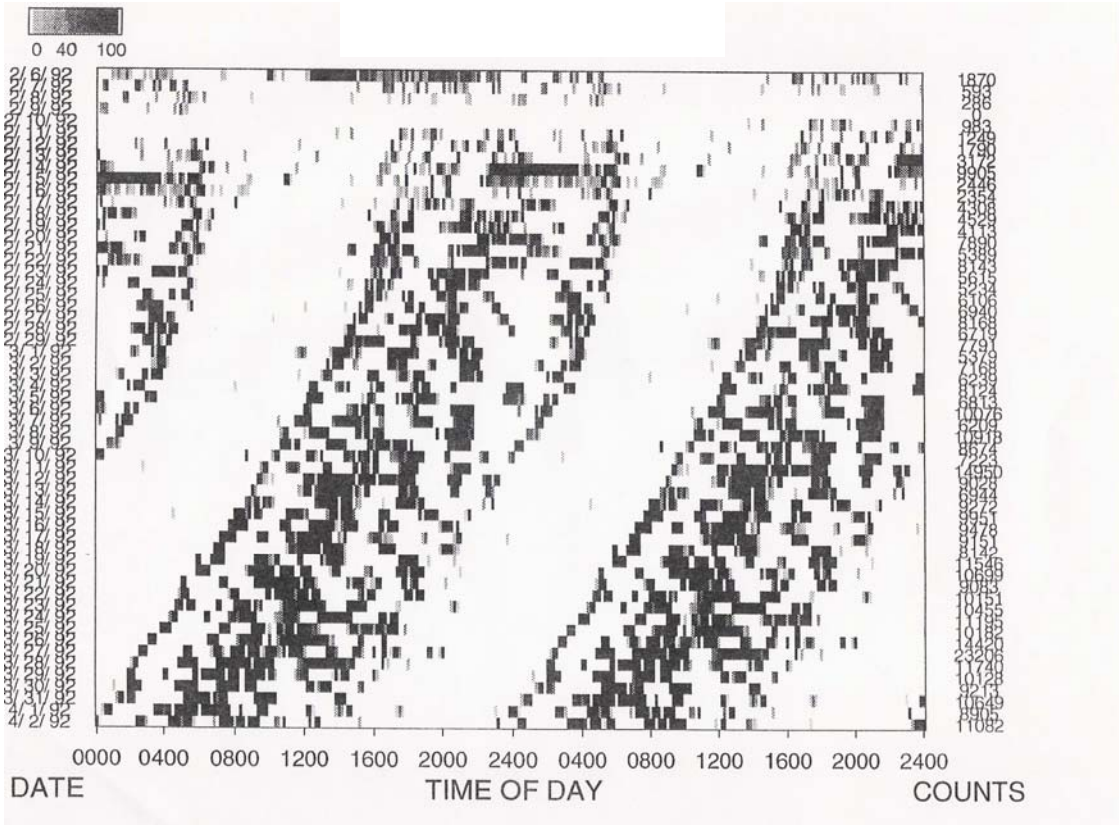
Phase shifts

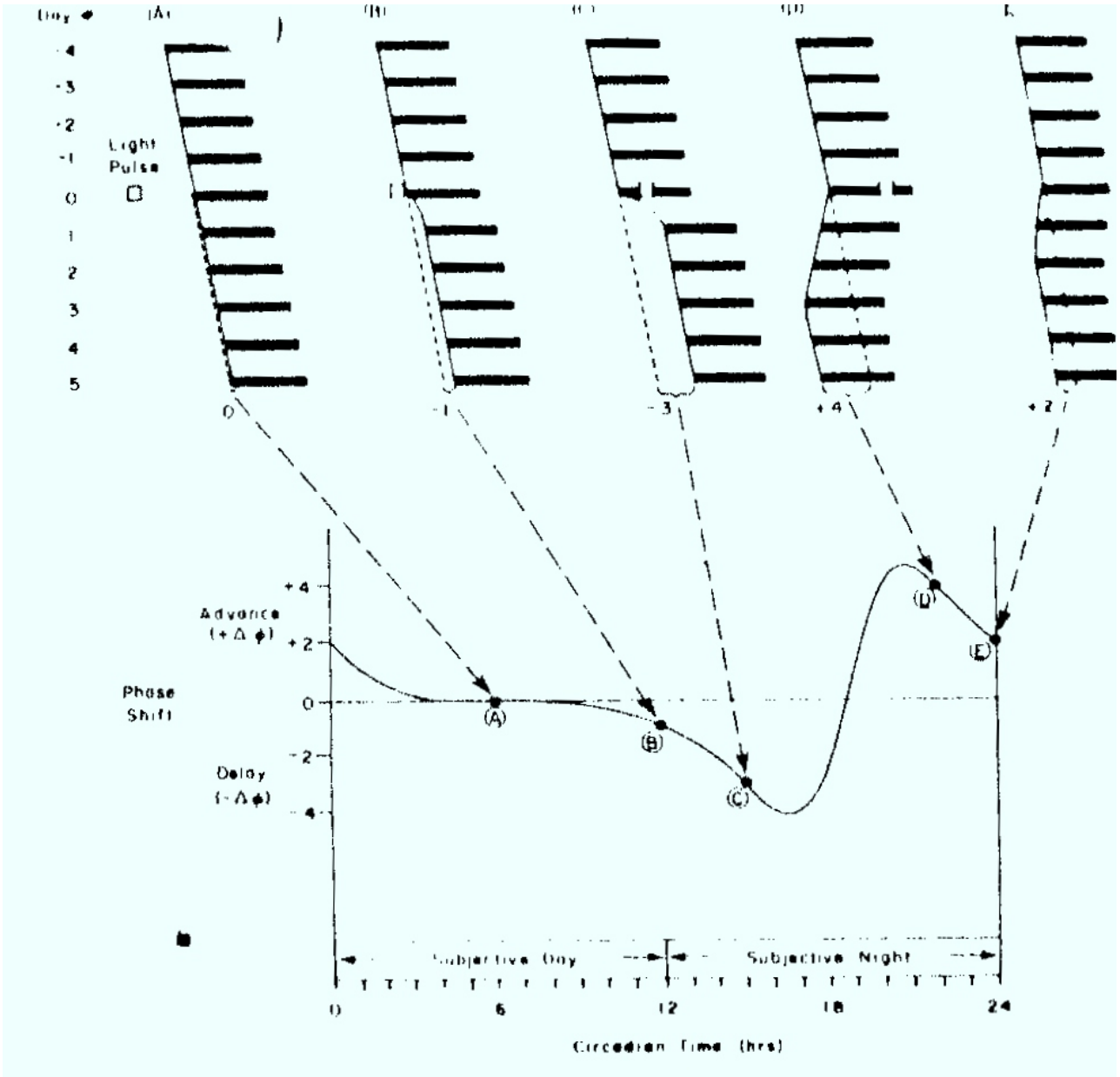
phase advance

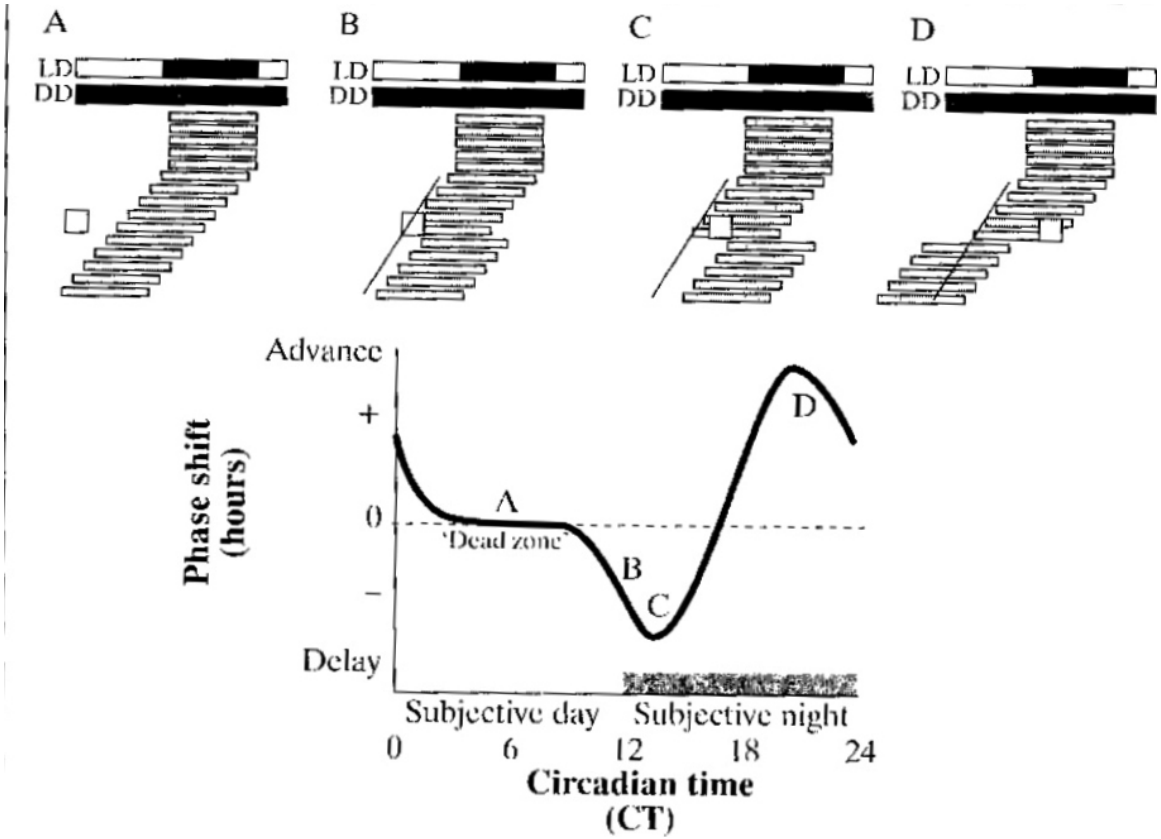
phase delay

Effects of light on free-running rhythm

- Subjective day – no effect
- Early subjective night – phase delay
- Late subjective night – phase advance




Day #
-4
-3
-2
-1
0
1
2
3
4
5
Light Pulse
0
-1
-3
+4
+2
Advance (+Δφ)
Phase Shift
Delay (-Δφ)
+4
+2
0
-2
-4
(A)
(B)
(C)
(D)
(E)
Subjective Day
Subjective Night
0
6
12
18
24
Circadian Time (hrs)



Text Figure 6.1

Range of Entrainment

* **Aschoff, 1978**

Forced desynchrony

Homeostasis = the attempt to maintain a constant internal environment

- body temperature
- blood sugar levels

set point = optimal level

- Exhibits circadian rhythm

Many physiological functions are regulated by a combination of homeostatic and circadian processes

- Optimal body temperature = 37^{o}C
- Set point is lower in AM and higher late afternoon/evening

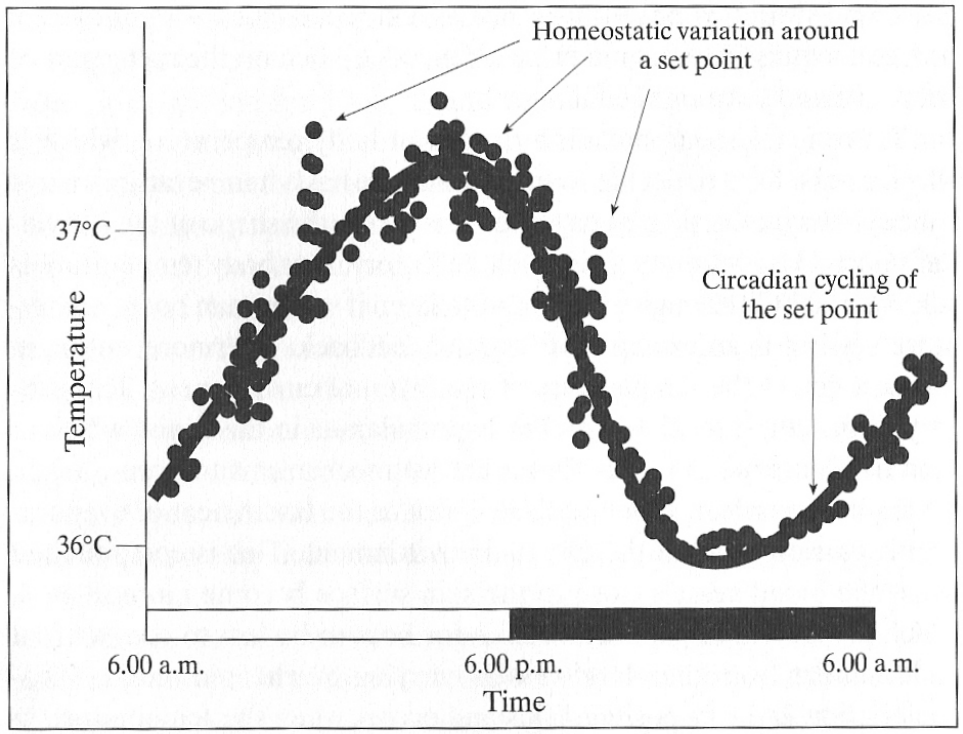


Figure 4.1. Diagram depicting the homeostatic and circadian variation in human body temperature. Body temperature constantly fluctuates at any

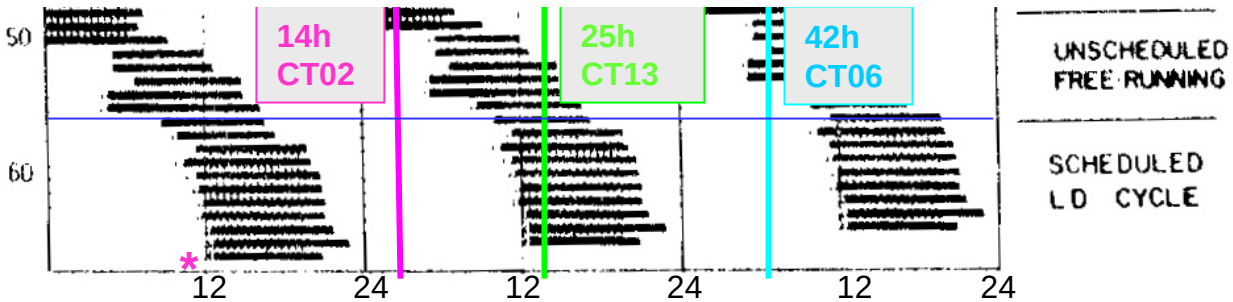
A combined homeostatic/circadian mechanism explains the feeding behavior of rats.

***That the rat becomes hungry is the result of a homeostatic process**

***How hungry the rat becomes is a function of the phase of the circadian feeding cycle.**

Because the sensitivity of control mechanisms varies with a circadian rhythm, animals cannot compensate for long periods of deprivation or for exposure to circadian periods outside of the range of entrainment

FOOD DEPRIVATION



Actogram	**Circadian rhythm record**
Entrained	**Synchronized to an evironmental signal (zeitgeber)**
Period	**Length of one complete cycle of a rhythm**
Phase shift	**Single, persistent displacement of phase due to zeitgeber**
Phase advance	**Phase begins earlier**
Phase delay	**Phase begins later**
Phase response curve	**Graphical plot of relationship between zeitgeber time and phase shift**
Range of entrainment	**Range of periods within which a pacemaker can be entrained by a zeitgeber**
Subjective time	**Pacemaker (internal clock) time**
Zeitgeber	**Environmental signal which can entrain a pacemaker**
Transducer	**Component of a biological system which detects environmental stimuli and converts it into a form that can be used by the organism**