Biological rhythms

Types of biological rhythms

- what do we call rhythm in a living organism? – physiological events occurring at approximately regular times
- internally controlled rhythms: breathing, heart beat, gut motility, brain waves, etc.
- externally determined rhythms: singing in certain birds, tulips, etc.
- rhythms controlled by an internal clock that is synchronized to the environment by Zeitgebers (synchronizing factors) – when these are missing: free-running rhythm

External-internal rhythms

Credit: National Library of Medicine

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OBSERVATION BOTANIQUE.

ON sçait que la Sensitive est héliotrope, c'est-à-dire que ses rameaux & ses feüilles se dirigent toûjours vers le côté d'où vient la plus grande lumière, & l'on sçait de plus qu'à cette propriété qui lui est commune avec d'autres Plantes, elle en joint une qui lui est plus particulière, elle est Sensitive à l'égard du Soleil ou du jour, ses feüilles & leurs pédicules se replient & se contractent vers le coucher du Soleil, de la même manière dont cela se fait quand on touche la Plante, ou qu'on l'agite. Mais M. de Mairan a observé qu'il n'est point nécessaire pour ce phénomène qu'elle soit au Soleil ou au grand air, il est seulement un peu moins marqué lorsqu'on la tient toûjours enfermée dans un lieu obscur, elle s'épanoüit encore très-sensiblement pendant le jour, & se replie ou se resserre régulièrement le soir pour toute la nuit. L'expérience a été faite sur la fin de l'Eté, & bien répétée. La Sensitive sent donc le Soleil sans le voir en aucune manière; & cela paroît avoir rapport à cette malheureuse délicatesse d'un grand nombre de Malades, qui s'apperçoivent dans leurs Lits de la différence du jour & de la nuit.

Il seroit curieux d'éprouver si d'autres Plantes, dont les feüilles ou les fleurs s'ouvrent le jour, & se ferment la nuit, conserveroient comme la Sensitive cette propriété dans des lieux obscurs; si on pourroit faire par art, par des fourneaux plus ou moins chauds, un jour & une nuit qu'elles sentissent; si on pourroit renverser par là l'ordre des phénomenes du vrai jour & de la vraye nuit, &c. Mais les occupations ordinaires de M. Mairan ne lui ont pas permis de pousser les expériences jusque-là, & il se contente d'une simple invitation aux Botanistes & aux Physiciens, qui pourront eux-mêmes avoir d'autres choses à suivre. La marche de la véritable Physique, qui est l'Expérimentale, ne peut être que fort lente.

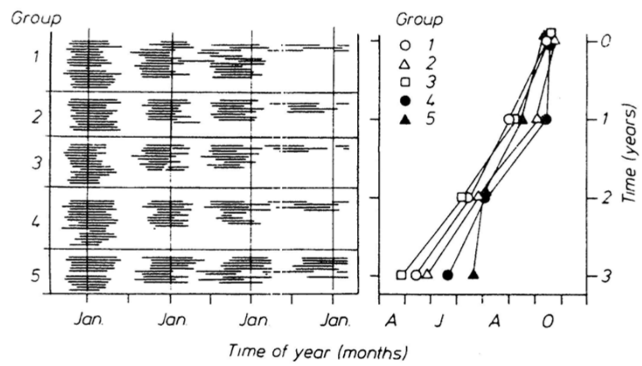
E ij

- De Mairan (1729): leaf movement of mimosa continues in darkness

Rhythms with various periods

- period – determined by the external geophysical variable:
  - tidal: rhythm of high and low tides
    - <u>period:</u> 12.8 h
    - <u>synchronizing factor:</u> pressure, mechanical stimuli
  - daily: rhythm of days and nights
    - <u>period:</u> 24 h
    - <u>synchronizing factor:</u> light, (temperature, activity)
  - lunar: rhythm of moon phases
    - <u>period:</u> 29.5 days
    - <u>synchronizing factor:</u> full moon?
  - annual: rhythm of seasons
    - <u>period:</u> 365 days
    - <u>synchronizing factor: </u>???

Circannual rhythm in hibernation



(a)

group 1 – DD, blinded ground squirrels

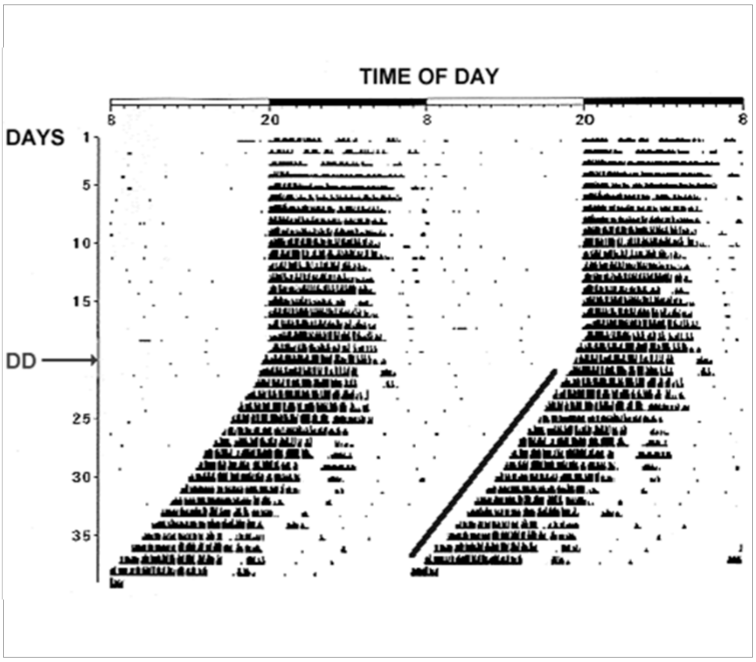
group 2 – LL (500 lux)

group 3 – LL (500 lux), blinded

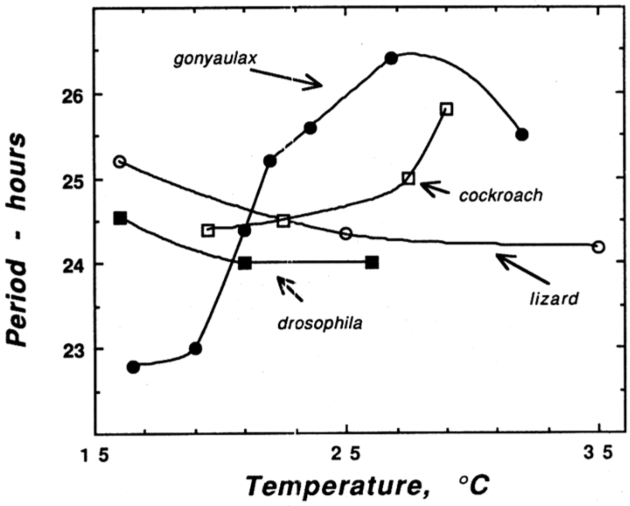
group 4 – LL (20 lux)

group 5 – LD12:12 (200:0 lux)

Circadian rhythm in hamster



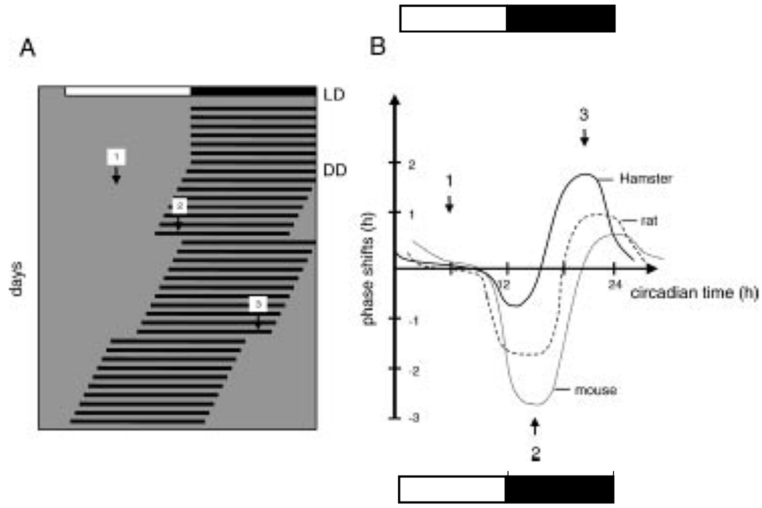
Temperature dependency of circadian rhythms



Light effects

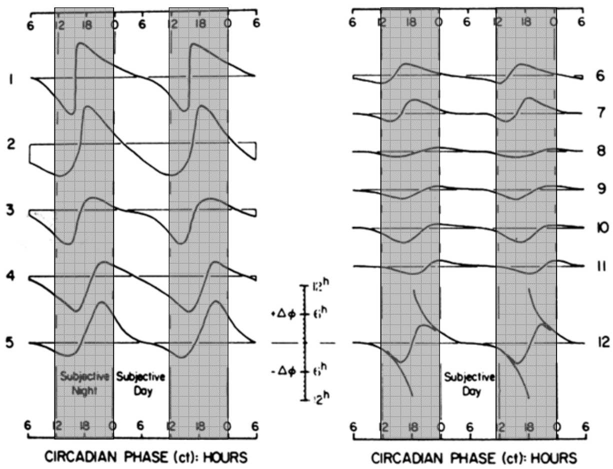
- circadian period (T) of diurnal and nocturnal animals change in opposite direction in constant light (LL) :
  - Aschoff's rule:
    diurnal animal: T decreases with light intensity
    nocturnal animal: T increases with light intensity
  - circadian rule:
    diurnal animal: wake/sleep ratio increases with light intensity
    nocturnal animal: wake/sleep ratio decreases with light intensity
- the strong physiological effect of light is also shown by persistent oestrus
- short light impulses can change the phase of circadian rhythms

Phase-response curve I. (PRC)



Hannibal, Cell & Tissue Res. 309:73,2002

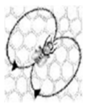
Phase-response curve II. (PRC)



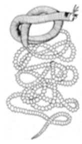
1-Sarcophaga
2-Coleus
3-Periplaneta
4-Euglena
5-Gonyaulax
6-Anopheles
7-Mesocricetus
8-Peromyscus
9-Peromyscus
10-Mus
11-Chiroptera
12-Drosophila

Uses of the biological clock

- prediction of environmental events – burrowing animals, intertidal zone
- navigation based on celestial objects



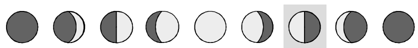
- „waggle dance" – orientation based on the position of the Sun
- measuring the length of days – photoperiodism



- timing of reproduction – Palolo worm
- „gating" – timing of events occurring once in a lifetime – hatching of Drosophila

Palolo (mbalolo) feast

Jan. Febr. March April May June July Aug. Sept. Oct. Nov. Dec.



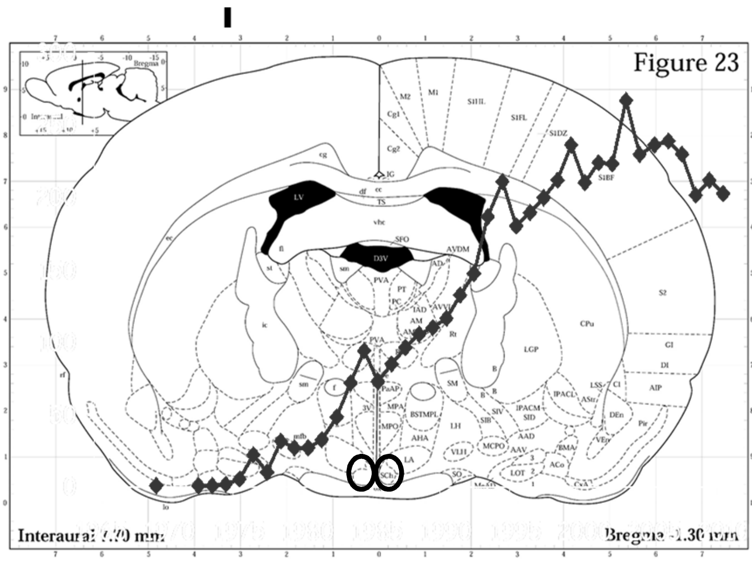
I. II. **III.** IV.

9:00 12:00 15:00 18:00 21:00 **24:00** 3:00 6:00

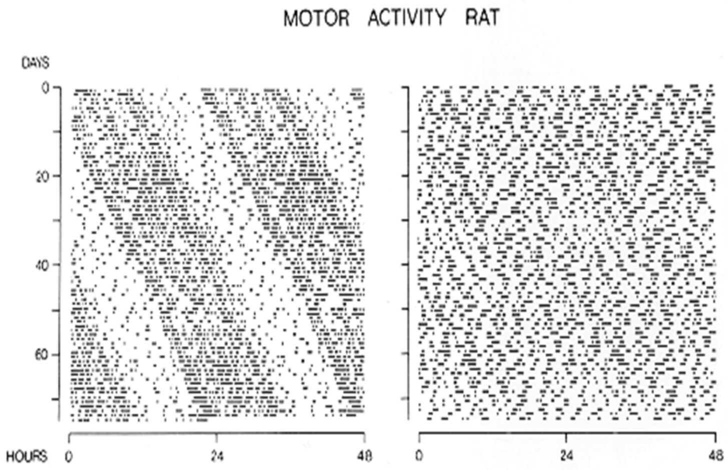
Master clock of daily rhythms

- daily rhythms can be examined the most easily and probably they are the most important
- master clock was sought along the optic pathway lesioning various neuron groups
- two teams, independently, but simultaneously located the master clock:
  - Stephan and Zucker, 1972
  - Moore and Eichler, 1972
- it is the tiny, paired nucleus in the anterior hypothalamus, above the crossing of the optic tract: the nucleus suprachiasmaticus (SCN)
- in non-mammalian species, clock is also associated with the optic pathway

Publications on the SCN



Effect of SCN ablation in rats



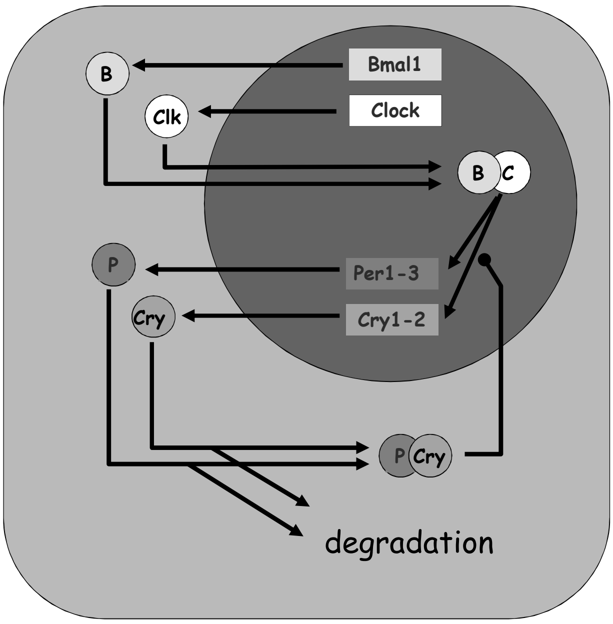
Basic questions about the master clock

1. How does it generate the rhythm?

Discovery of clock genes

- 1985 – Martin Ralph – tau-mutant hamster
- short period in continuous dark (DD), Mendelian inheritance (20/22/24)
- breakthrough in 1994 using forward genetics – Vitaterna (PhD student)
- Clock mutant among the first 42 mice – abnormally long period, ceases in DD
- the mutation caused loss of a glu-rich region characteristic for bHLH type transcription factors
- conclusion: CLOCK is a transcription factor
- CLOCK also contains a PAS (Per-Arnt-Sim) domain – ability to form dimers with similar proteins

Clock mechanism (mammals)

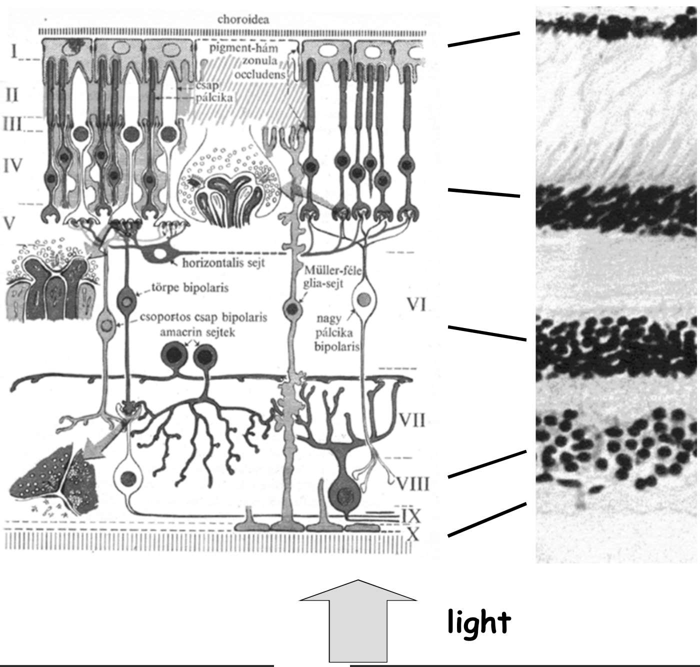


Basic questions about the master clock

1. How does it generate the rhythm?

2. How is the rhythm adjusted to the external cycles?

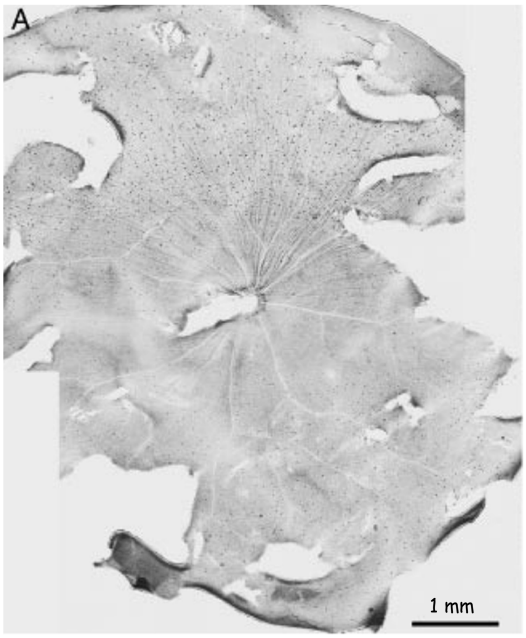
Layers of the retina



Szentágothai, Medicina, 1971, Fig.8-60

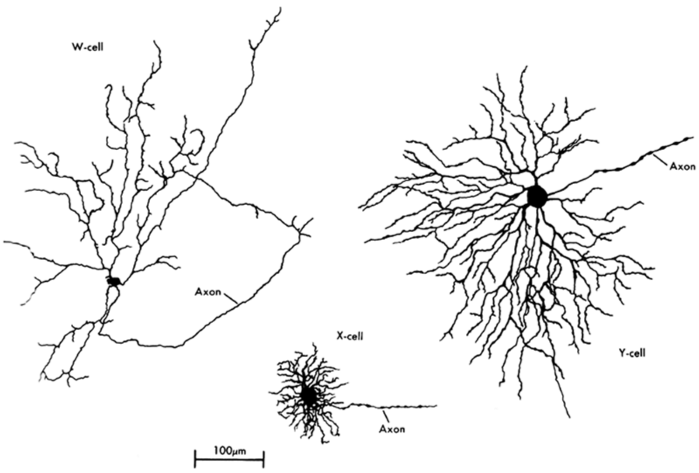
Berne and Levy, Mosby Year Book Inc, 1993, Fig. 9-6

Photosensitive ganglion cells



Hannibal, J., Cell Tissue Res., 309:73, 2002

Ganglion cells of the retina



Berne and Levy, Mosby Year Book Inc, 1993, Fig. 9-16

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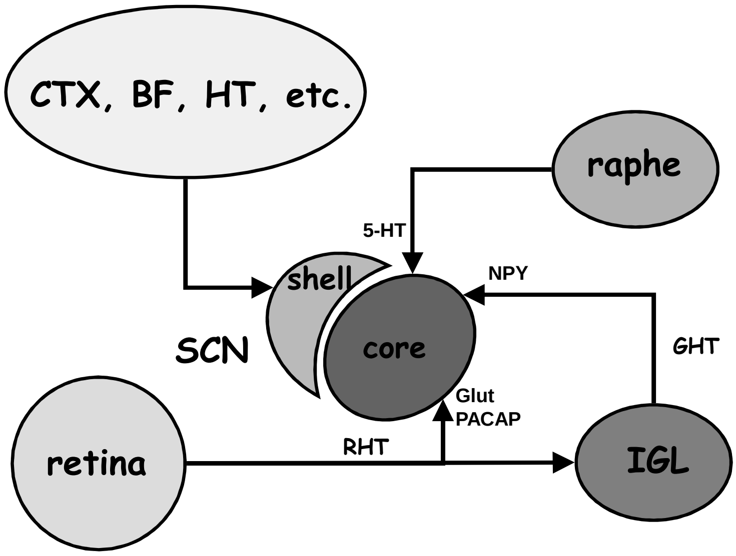
Inputs to the SCN



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Basic questions about the master clock

1. How does it generate the rhythm?

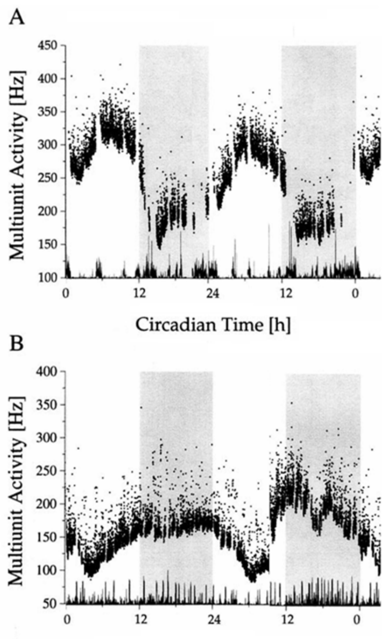
2. How is the rhythm adjusted to the external cycles?

3. How does the clock regulate the biological rhythms of the body?

SCN activity in vivo

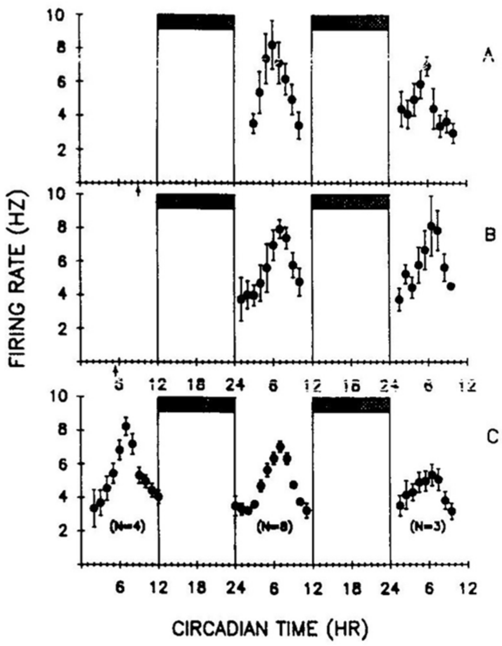
SCN

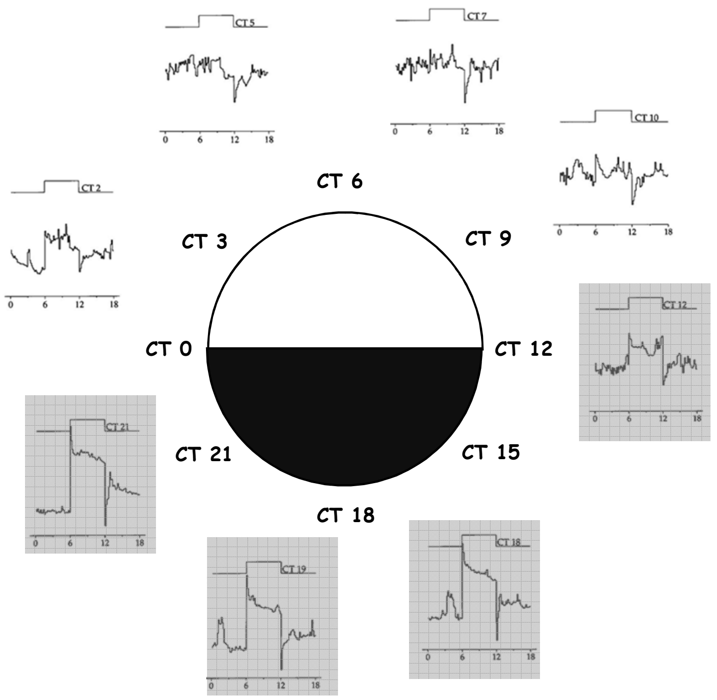
HT



Meijer, J.H., Watanabe, K., Schaap, J., Albus, H., **Détári, L.**., J. Neurosci. 18(1998):9078

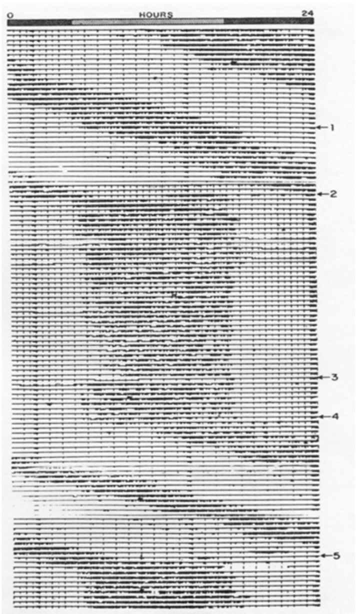
SCN activity in vitro





Meijer, J.H., Watanabe, K., Schaap, J., Albus, H., **Détári, L.**., J. Neurosci. 18(1998):9078

Role of pineal gland in sparrow



blinded sparrow, in LD

1 – removal of feathers from the back

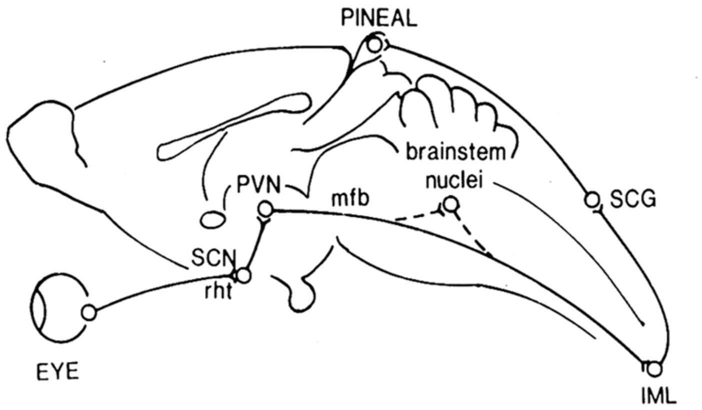
2 - removal of feathers from the head

3 – removal of regrown feathers

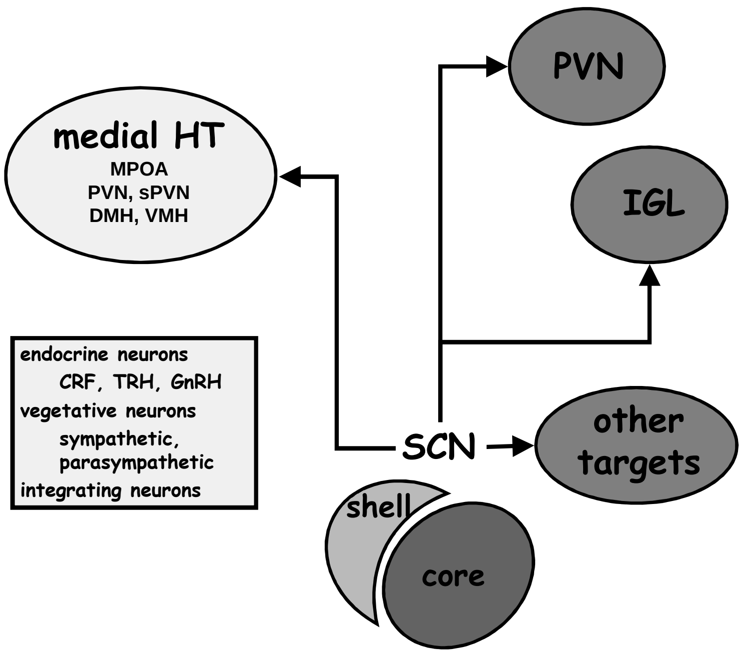
4 – subcutaneous Chinese ink injection

5 – removal of skin and ink

Pineal gland in mammals



Output of the SCN



One clock or several clocks?

- several organs posses the clock mechanism (genetically all)
- explanation for the persistence of rhythms in isolated organs
- the master clock regulates through the hormonal system and through the behavior
- rhythms might get desynchronized:
  - travel through time zones
  - blind people
  - limitation of access to food in time
  - in certain cases constant (no Zeitgebers) environment

Desynchronization in humans