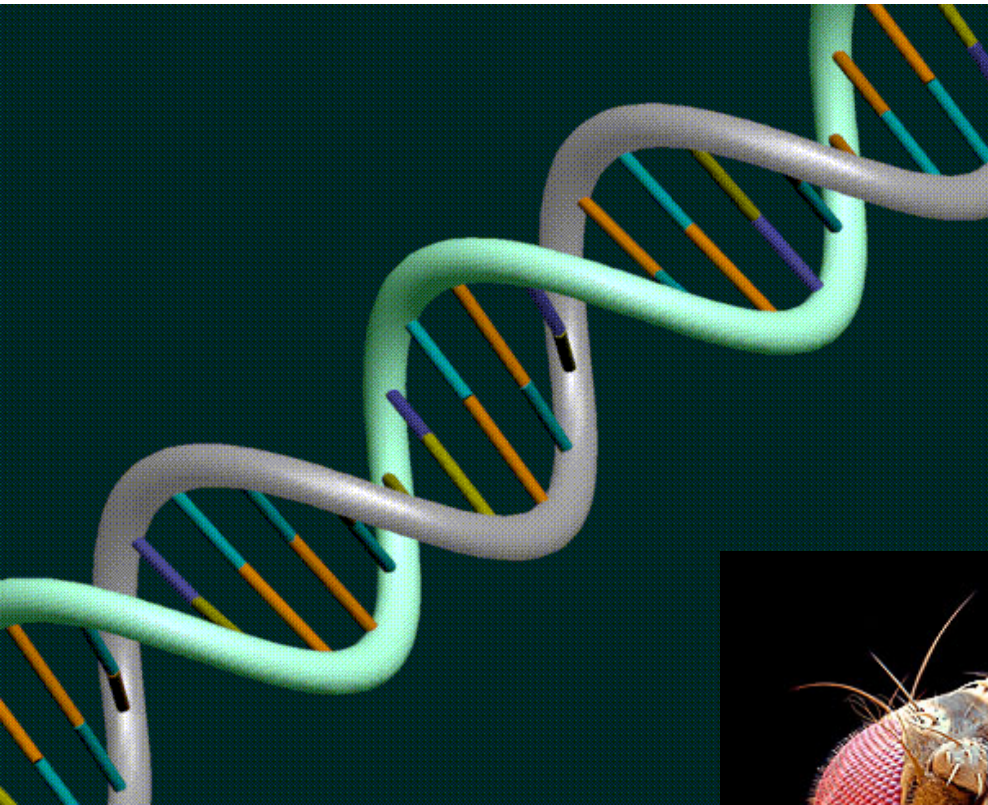


Genes, Brains and Behaviour

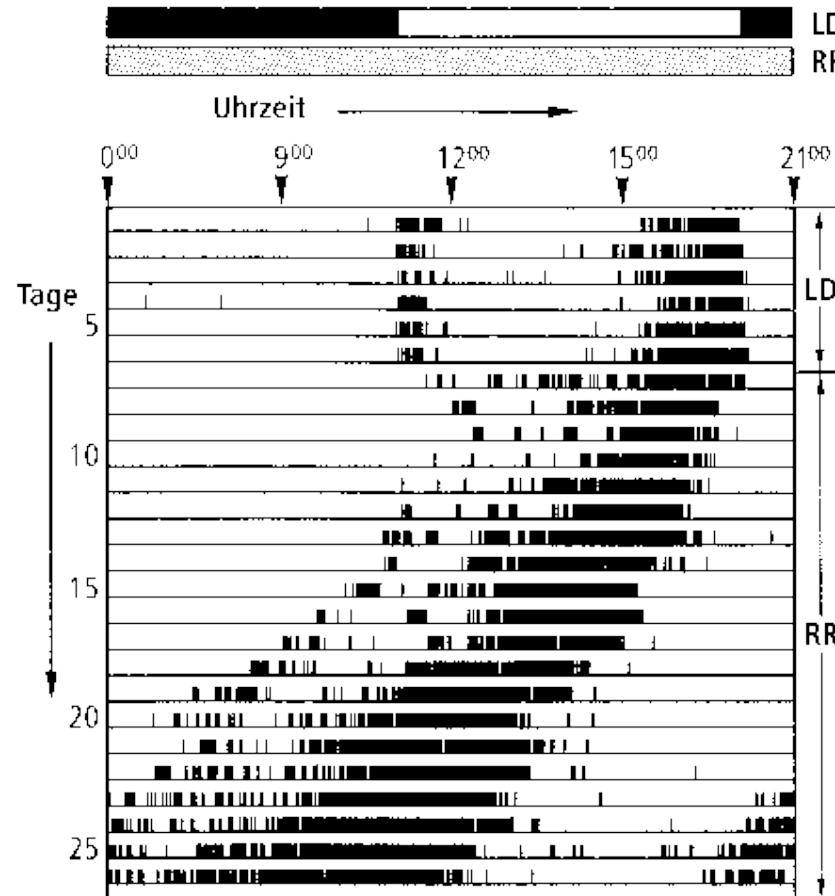
Lecture 6A: Circadian rhythms

Karl-Friedrich Fischbach, Neurogenetics, Freiburg

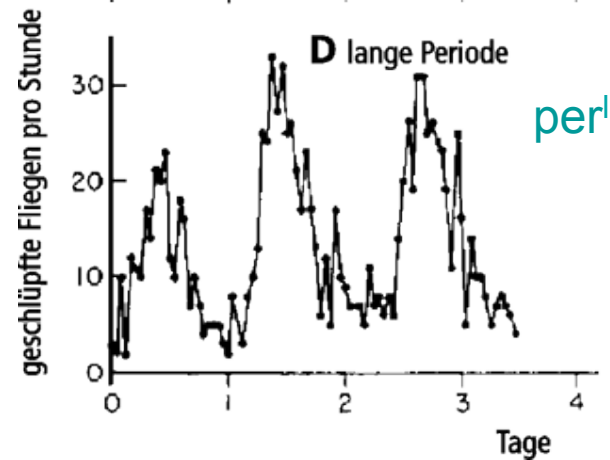
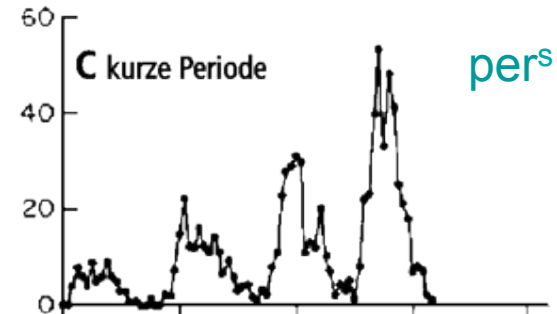
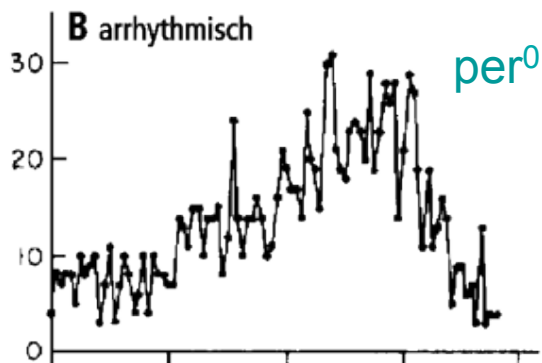
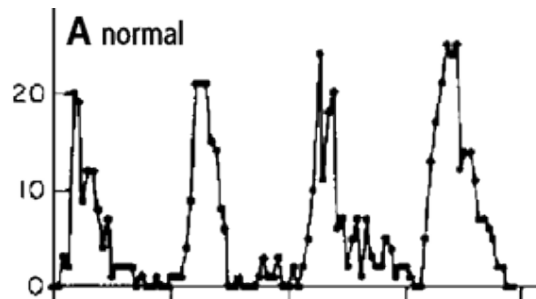


Circadian rhythms

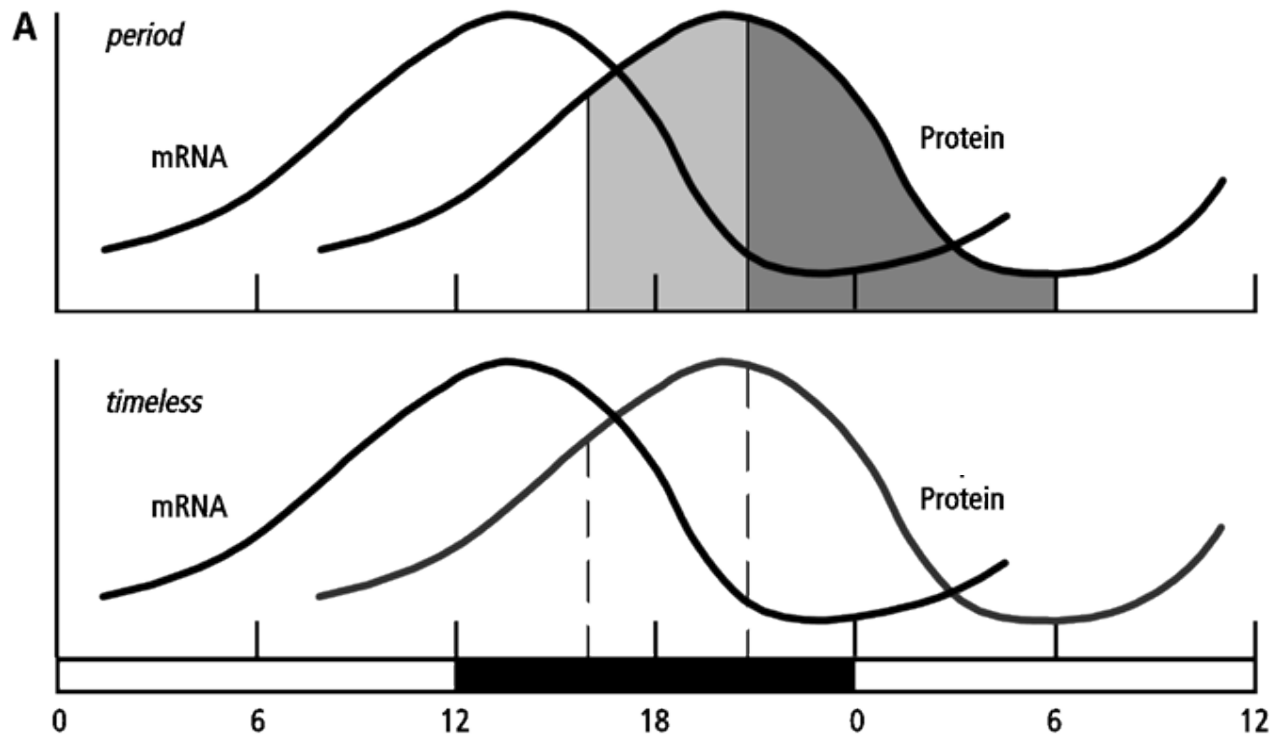
Circadian rhythm continues under constant conditions



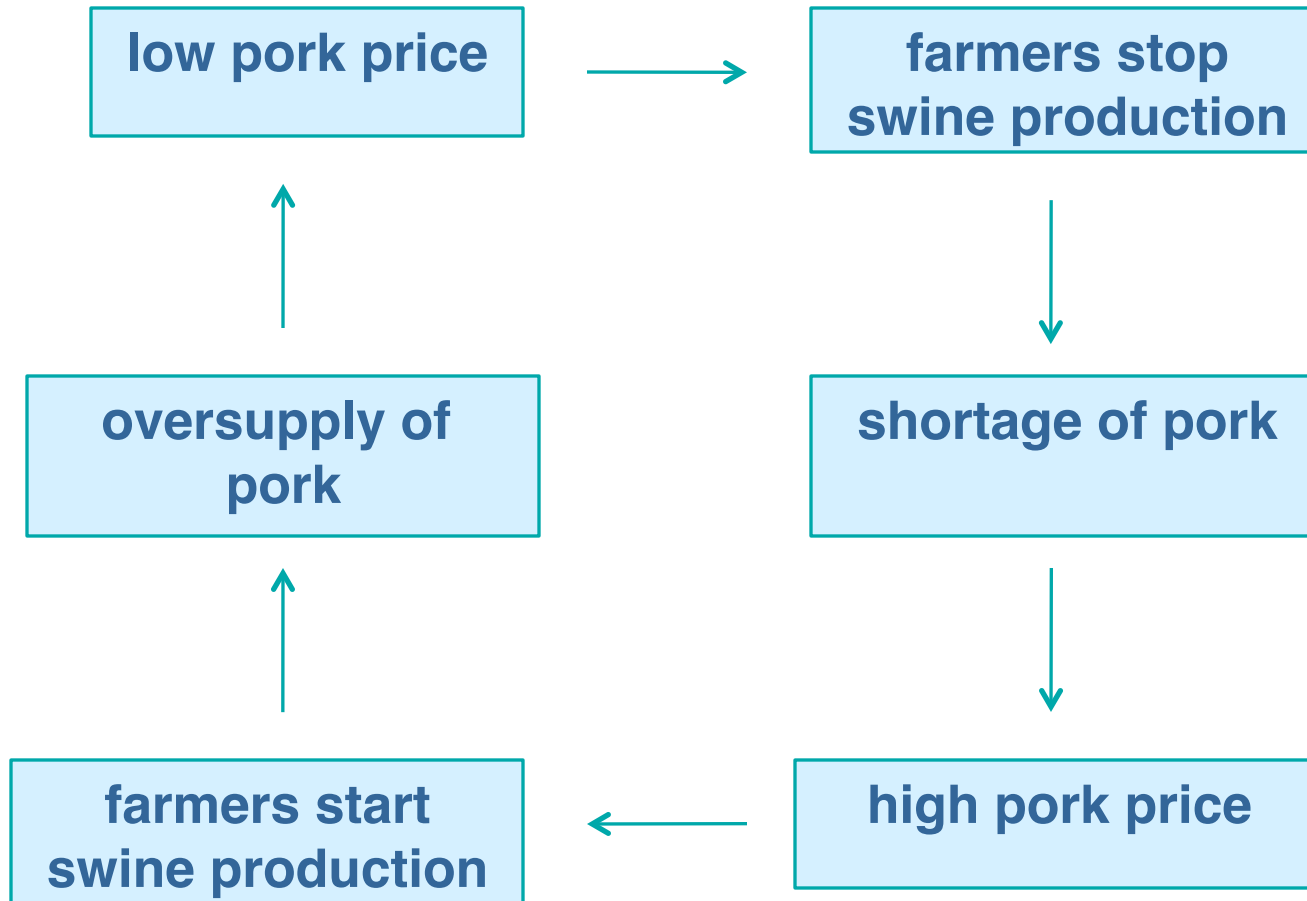
Isolation of *Drosophila* mutants with altered eclosion rhythm



mRNA and protein of *period* and *timeless* oscillate

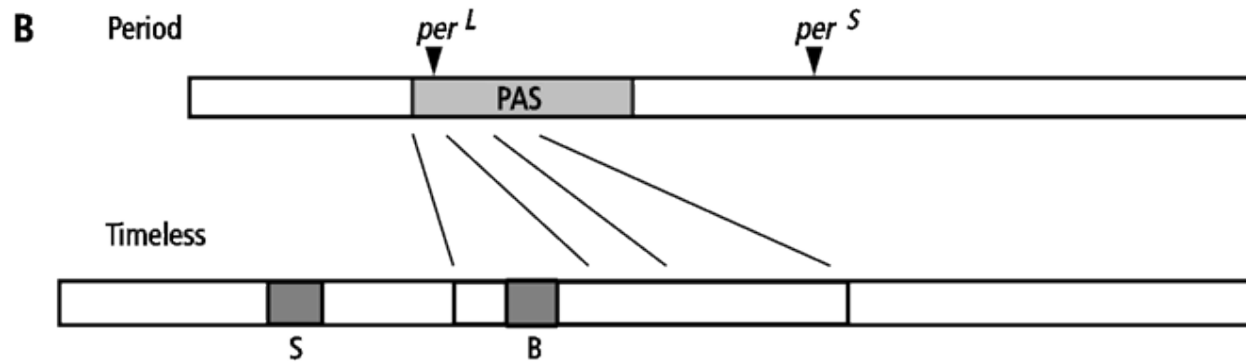


The pork cycle

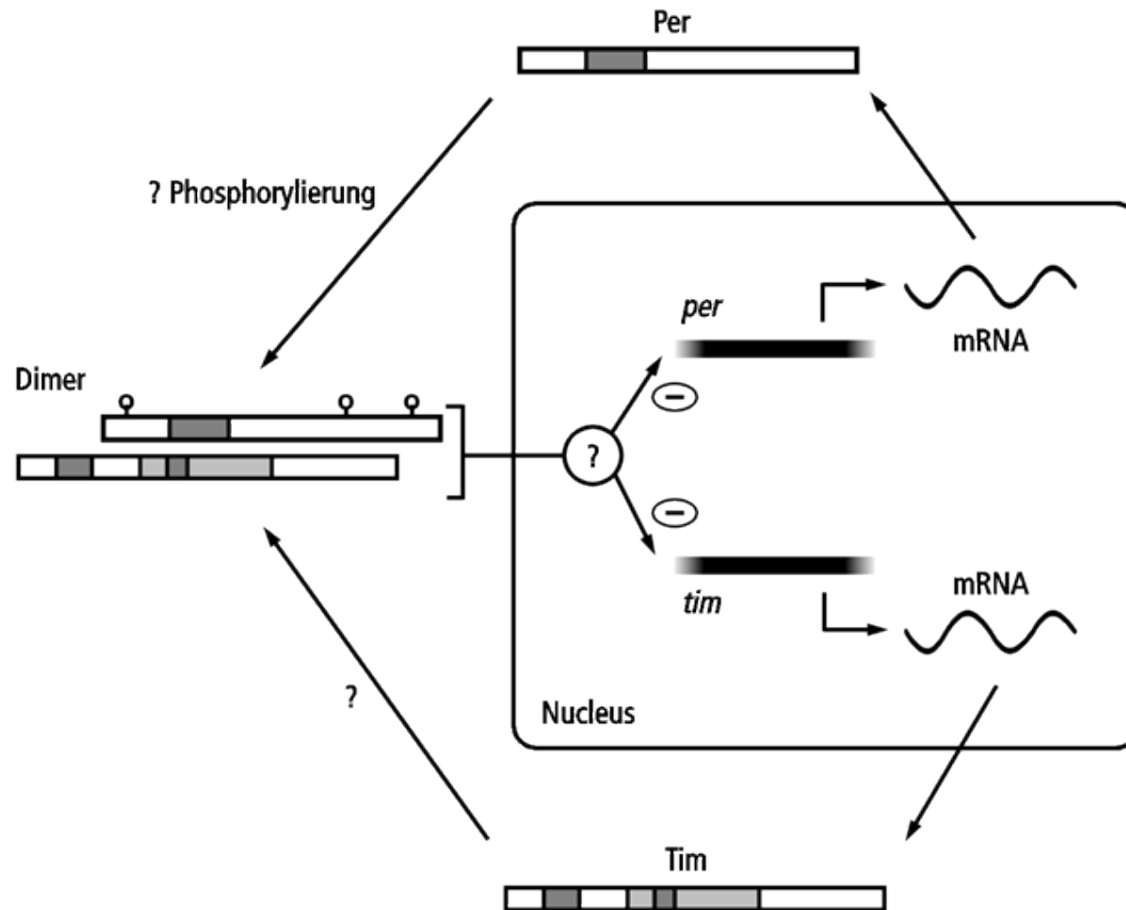


In general systems with feed back tend to oscillate

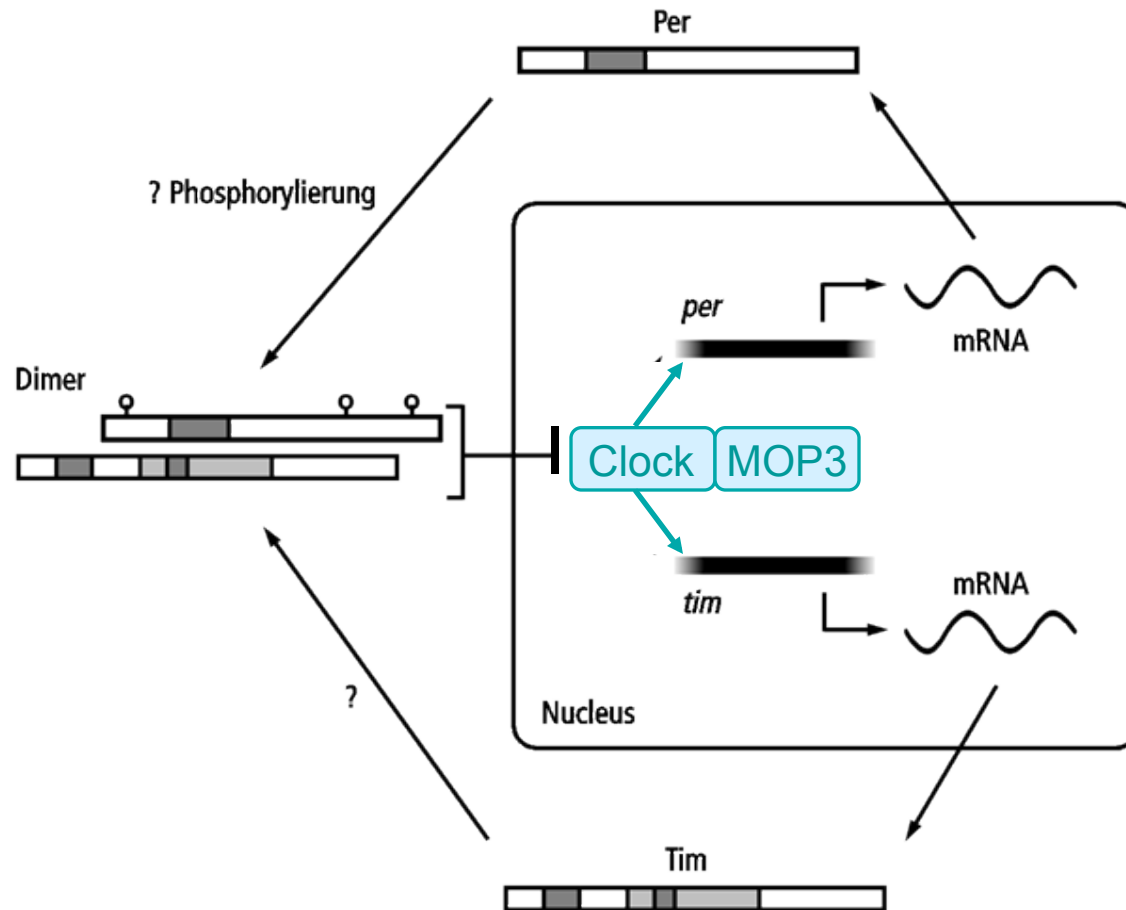
Period and Timeless proteins form dimers



heterodimers of Per and TIM migrate into the nucleus and inhibit the transcription of their genes



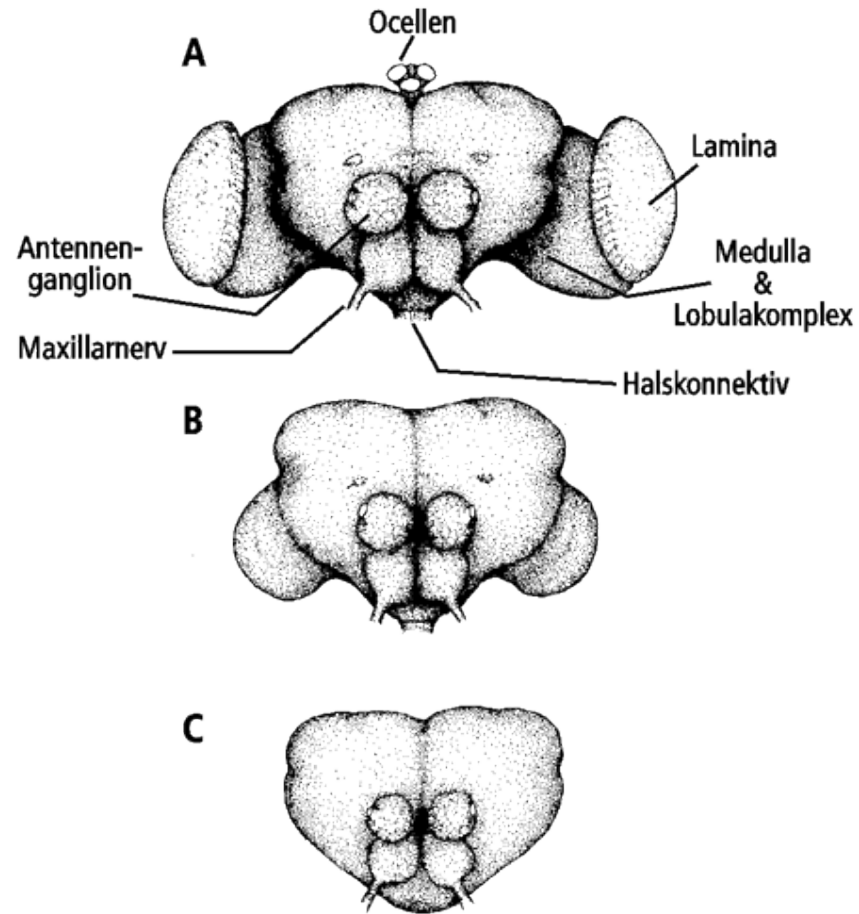
The negative feedback is via the inhibition of the transcription factor „clock“



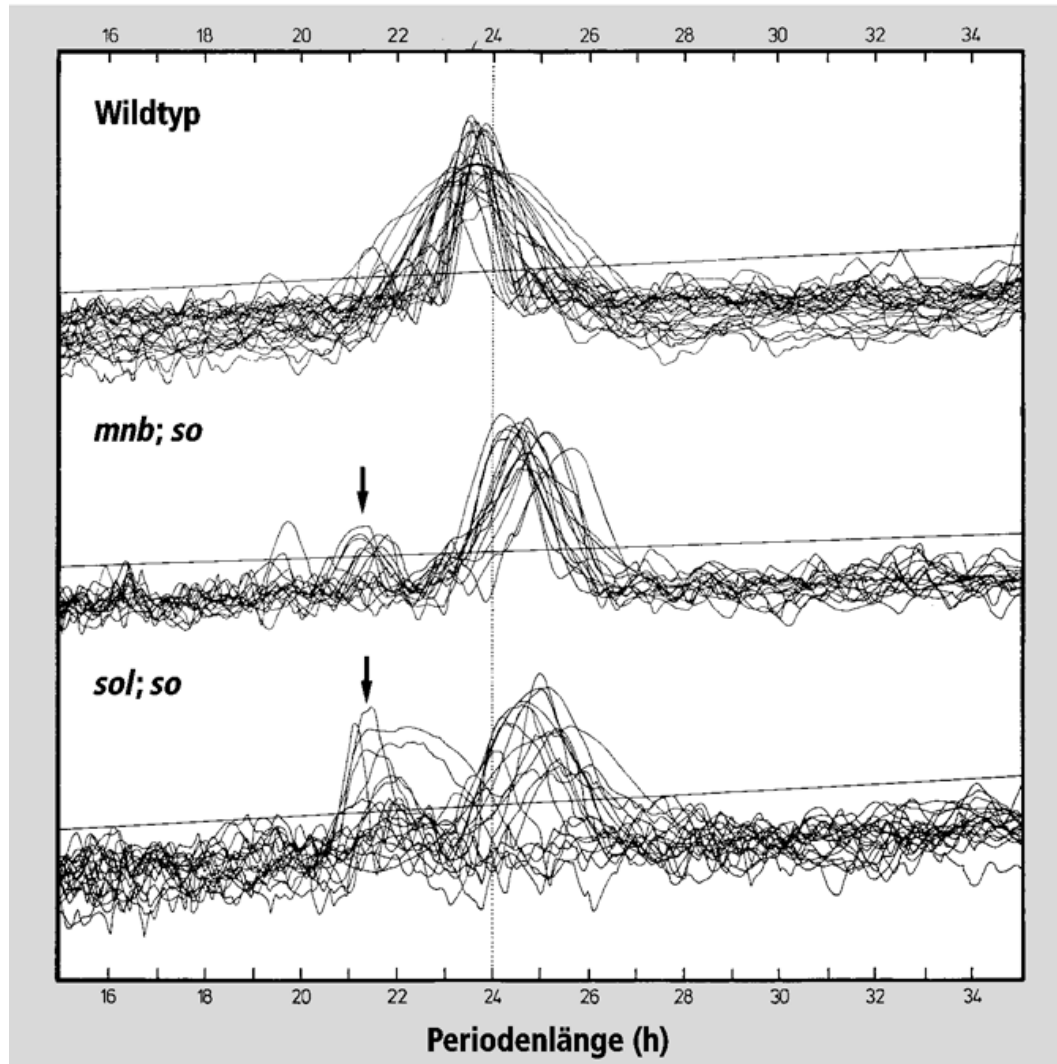
How is circadian behaviour coupled to such a cellular clock?

Where is the clock localized in the nervous system?

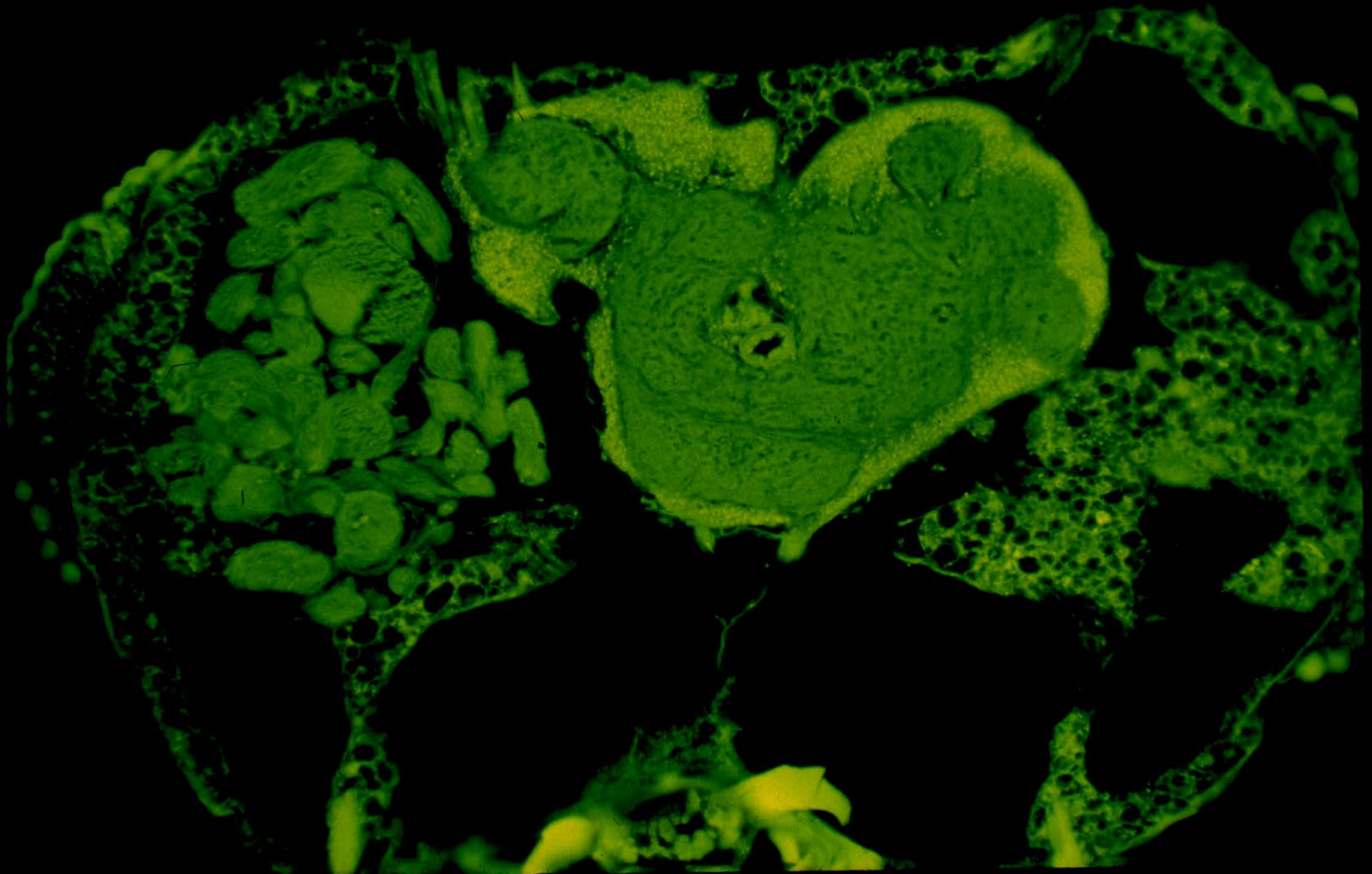
mutants of the optic lobe of *Drosophila*

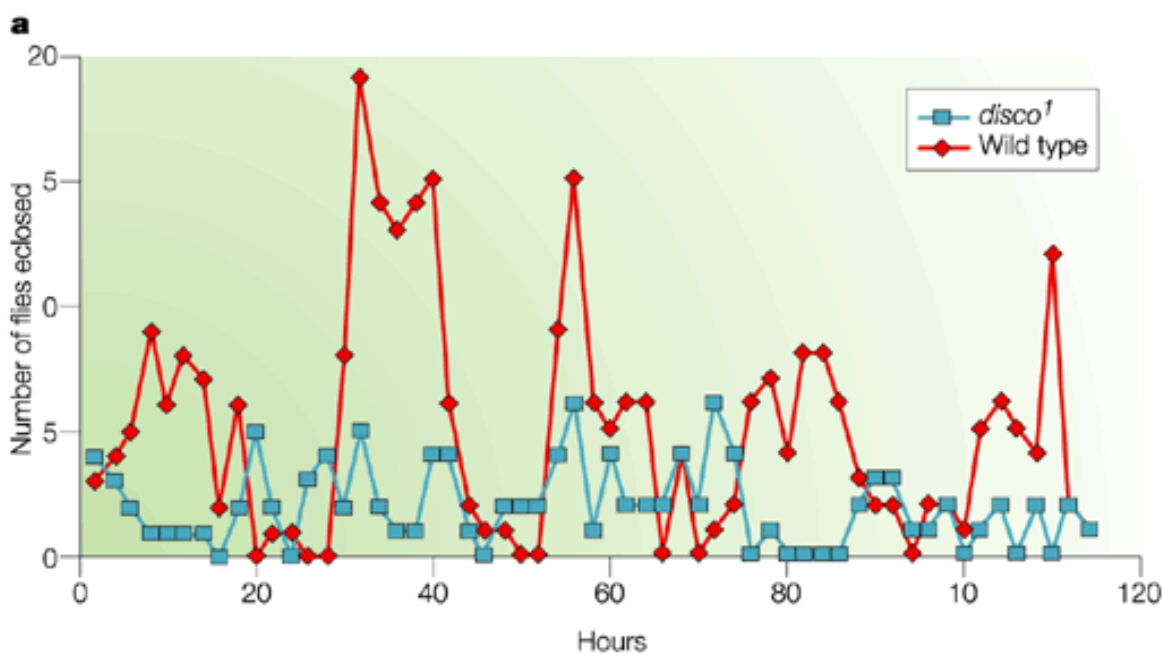


period length of optic lobe mutants of *Drosophila*



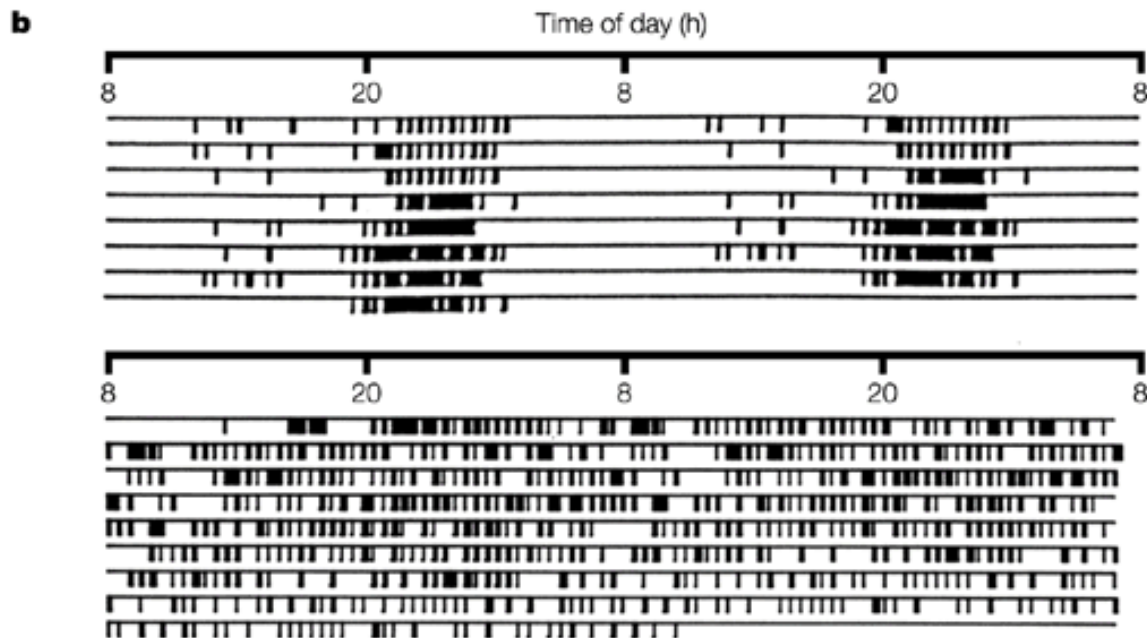
Brain phenotype of the *disconnected* (*disco*) mutant





disco – mutants do not show any rhythmicity

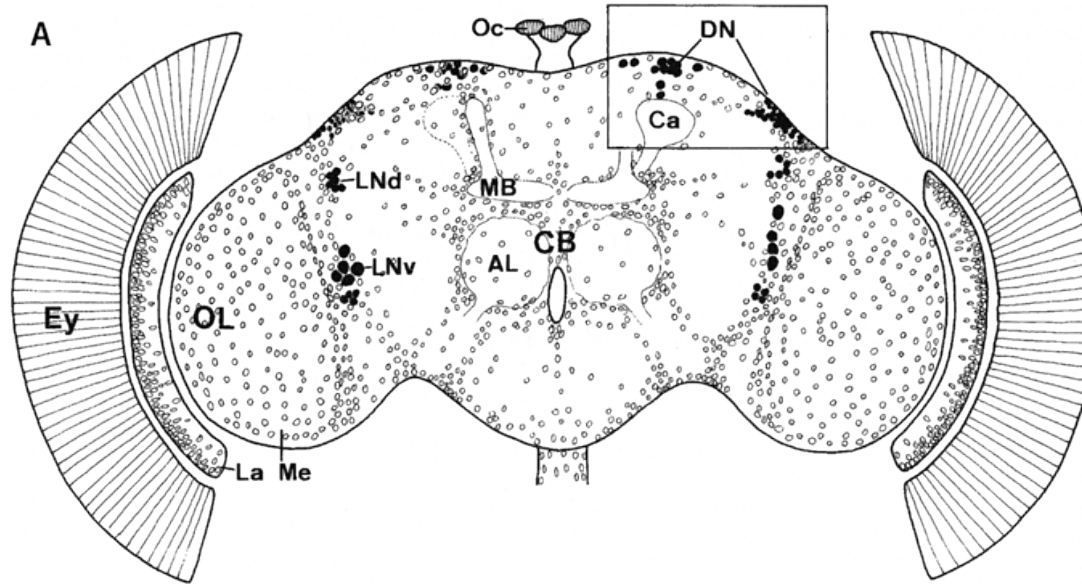
a) emergence from the pupal case



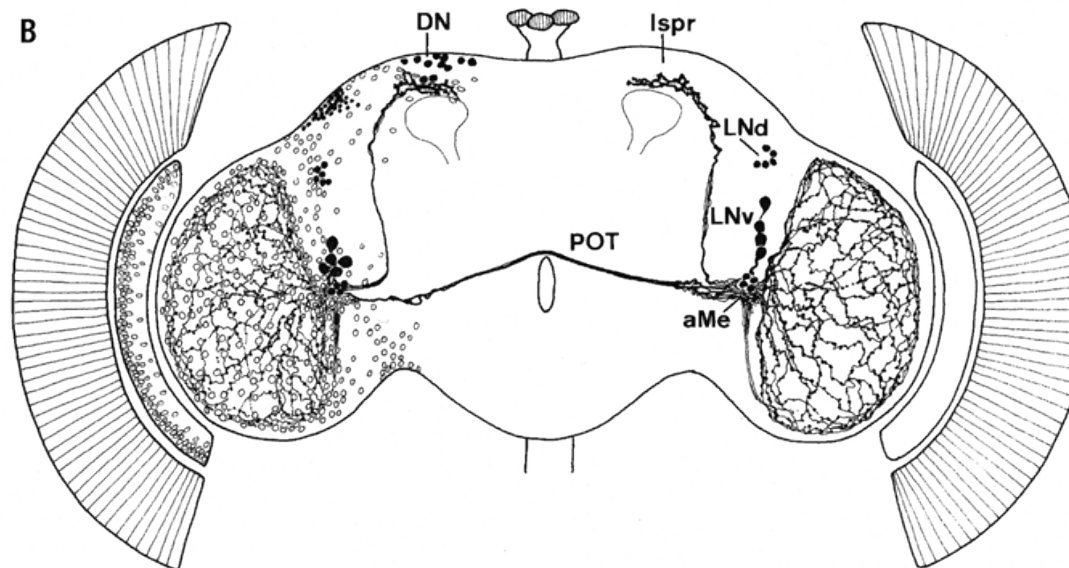
b) running activity

PER and PDH expressing neurons (both missing in *disco mutants*) are identical

PER



PDH



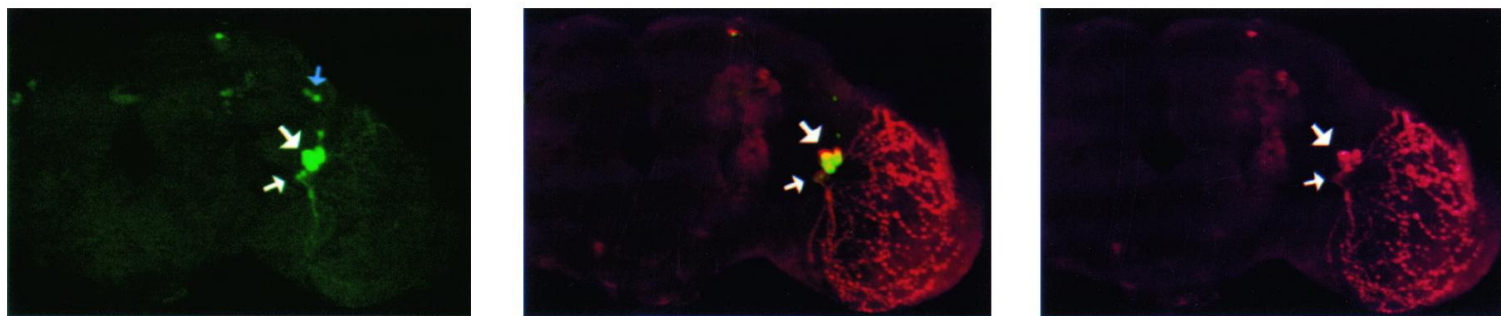
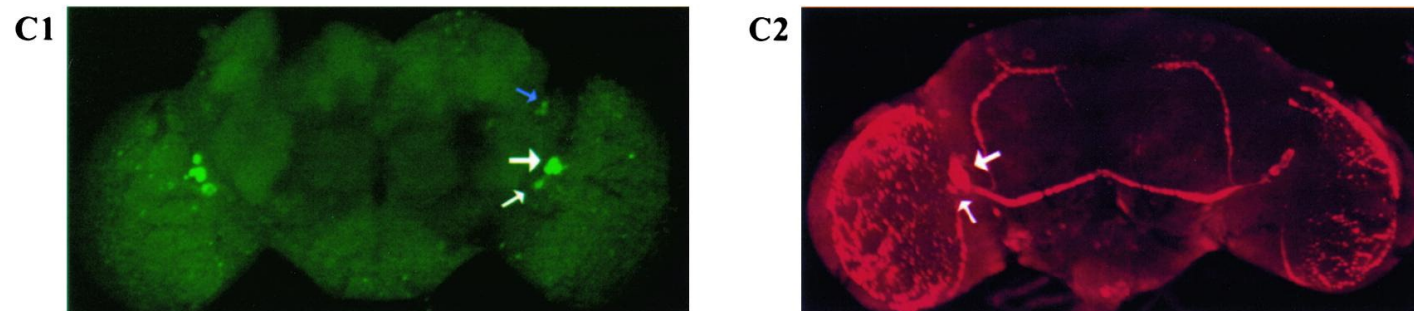
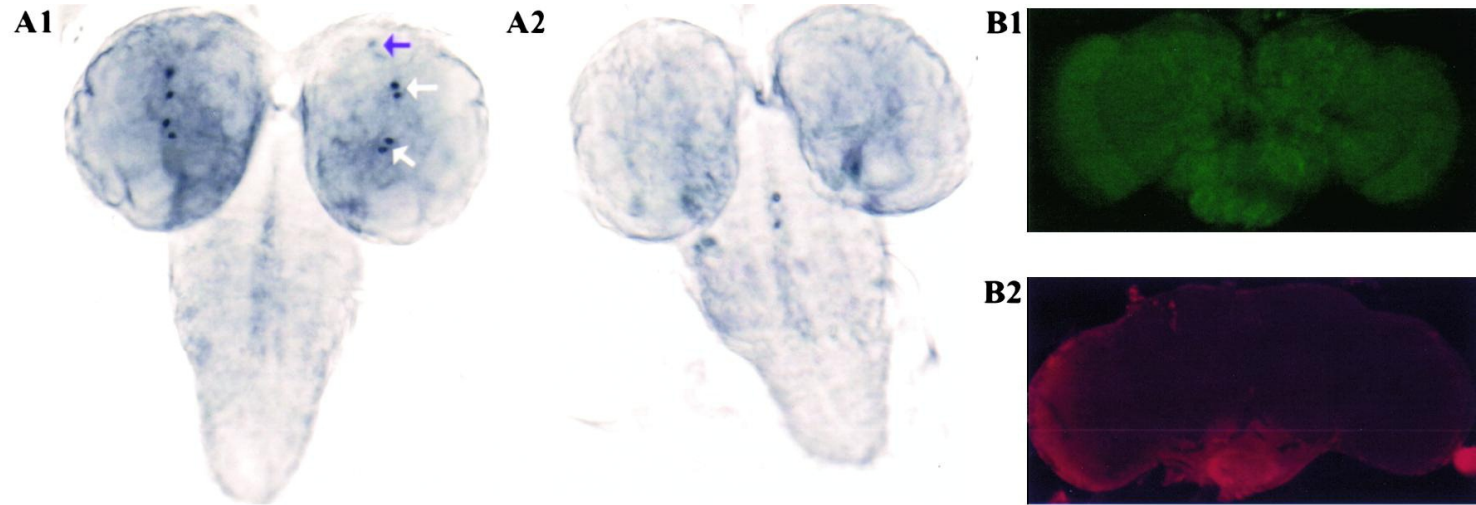
How is the circadian clock synchronized with the day-light cycle?

Eyes do not seem to be required.

In insects **Cryptochrome**, a blue light receptor, does the job.



Cryptochrome and Pigment Dispensing Factor Expression Colocalize



D1

D2

D3

Differential regulation of mammalian *Period* genes and circadian rhythmicity by cryptochromes 1 and 2

Martha Hotz Vitaterna^{*†}, Christopher P. Selby^{†‡}, Takeshi Todo^{†§}, Hitoshi Niwa[¶], Carol Thompson[‡], Ethan M. Fruechte^{*}, Kenichi Hitomi[§], Randy J. Thresher[‡], Tomoko Ishikawa[§], Junichi Miyazaki[¶], Joseph S. Takahashi^{*¶}, and Aziz Sancar^{***}

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Communicated by Johann Delsenhofer, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, August 26, 1999 (received for review July 23, 1999)