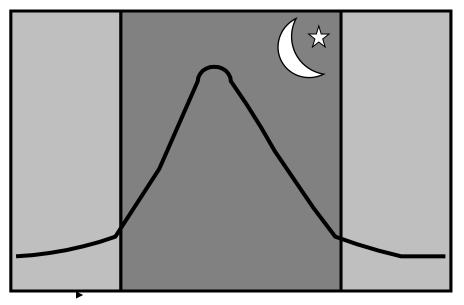
Biological rhythms

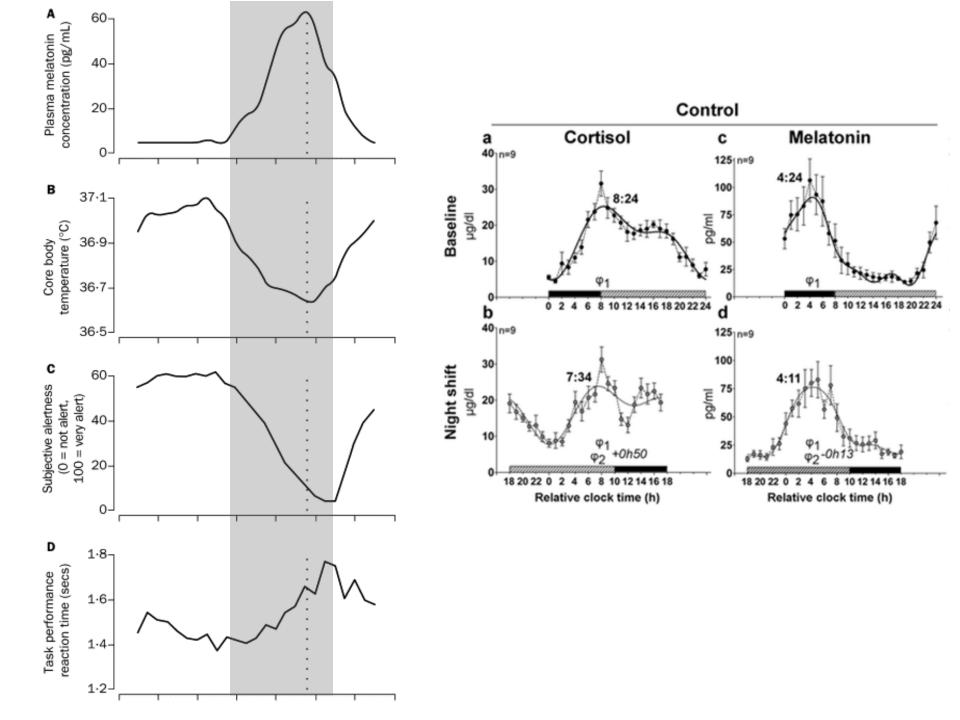


Research Importance

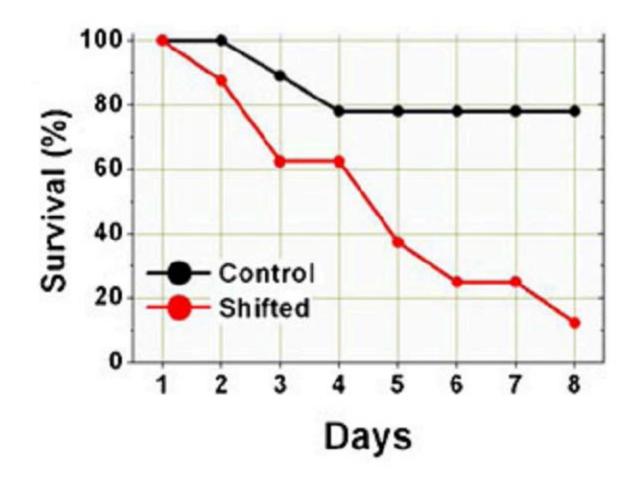
Medical importance: time of treatment, time of symptoms, synchronization of rhythms

Economical importance: accidents, efficiency.

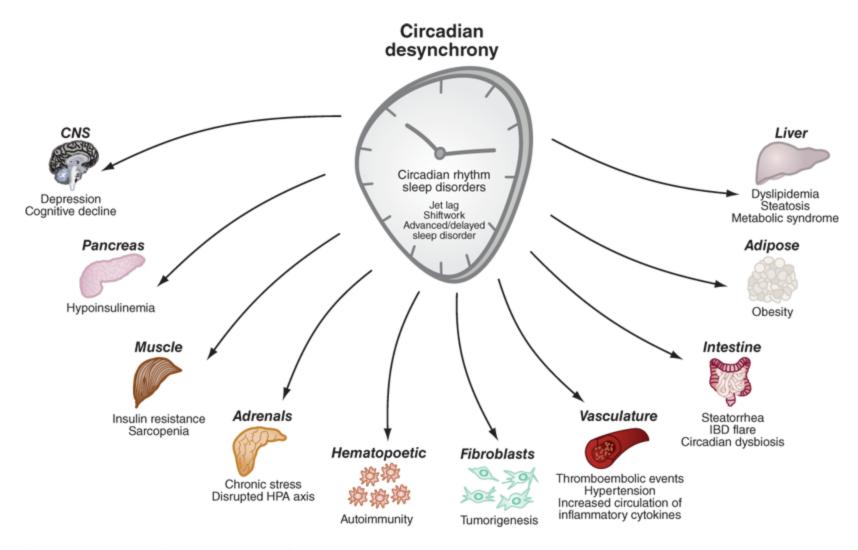
Sleep/wake cycles Locomotor activity Cognitive abilities Reaction time Body temperature Metabolism \square Biological clock Hormone secretion Enzymatic activities Gene expression Is it important?



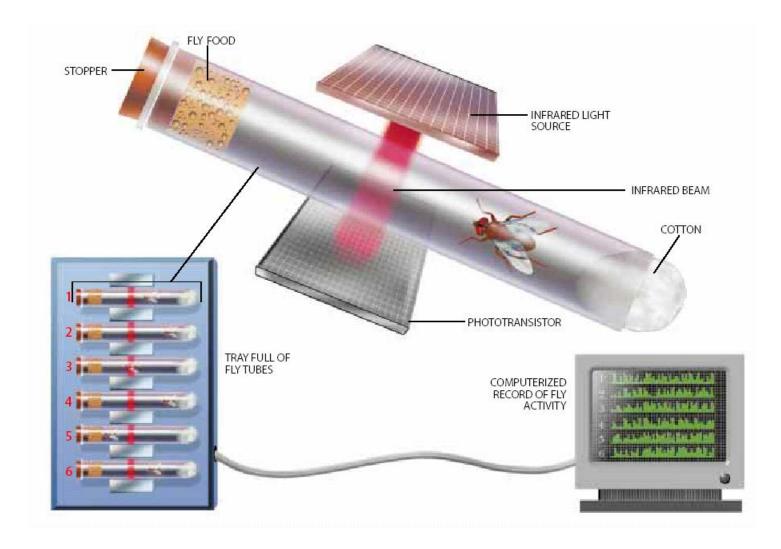
"Shift workers" mice are less resistant to Lipopolysaccharides (LPS)-induced endotoxemic shock



Castanon-Cervantes et al., 2010



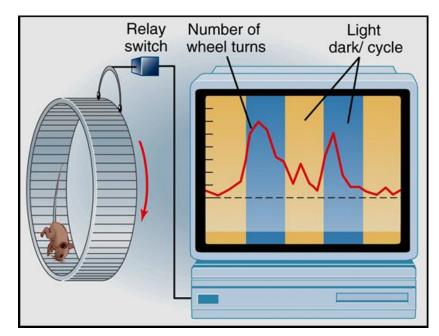
Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition Copyright © McGraw-Hill Education. All rights reserved.

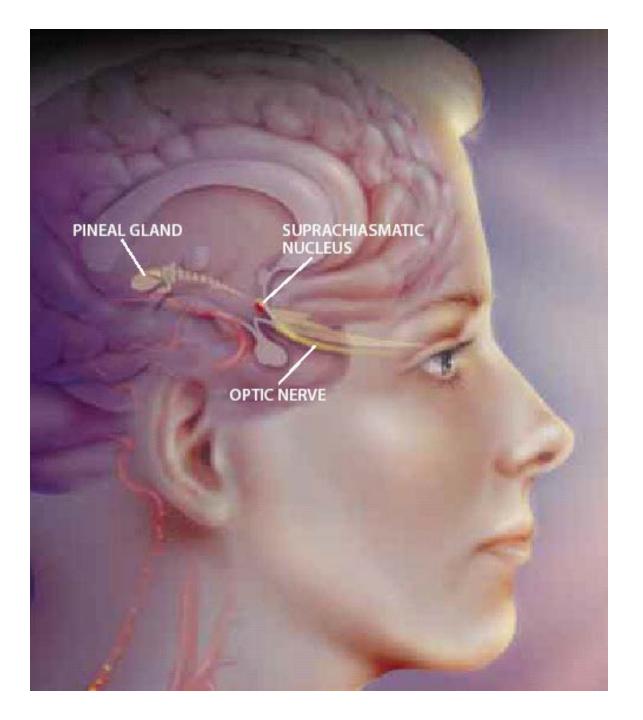


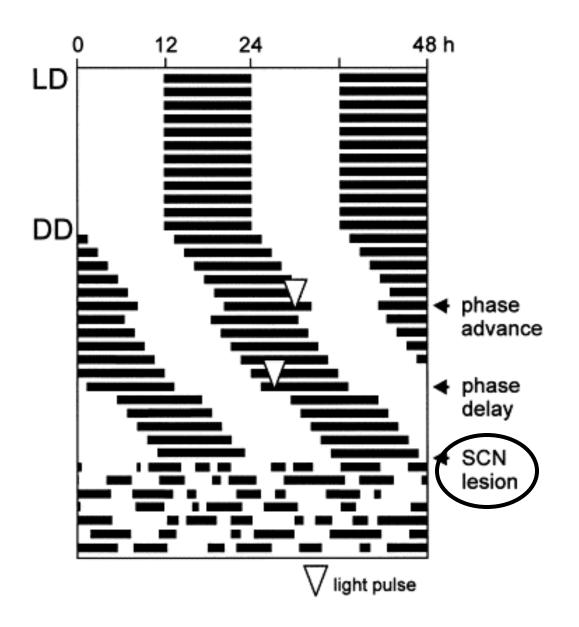
Monitoring circadian rhythms of activity in rodents. Actogram, the secret hand-shake of chronobiologists

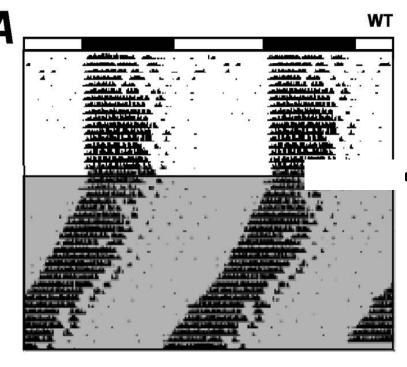
Free running

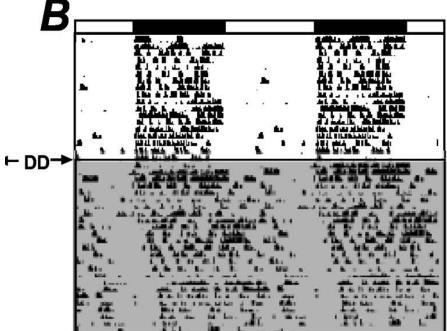
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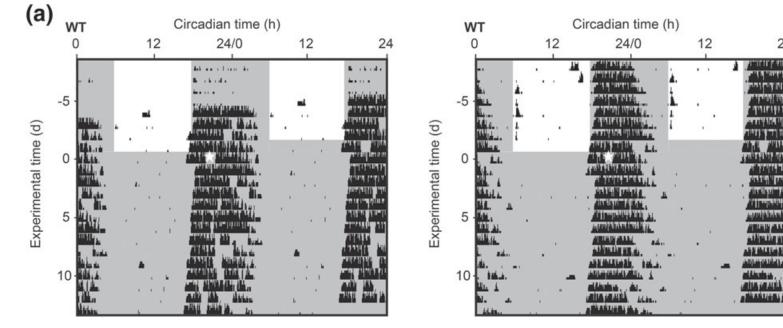


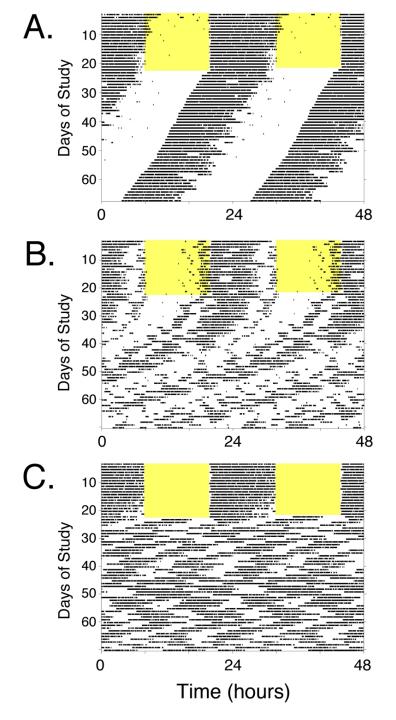




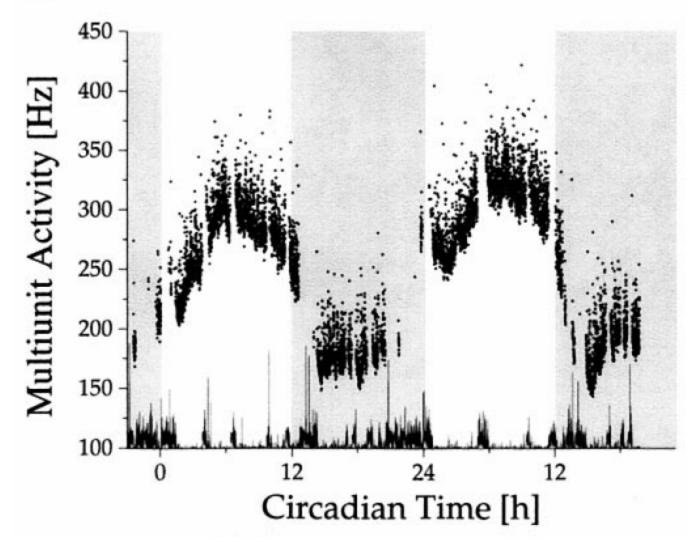
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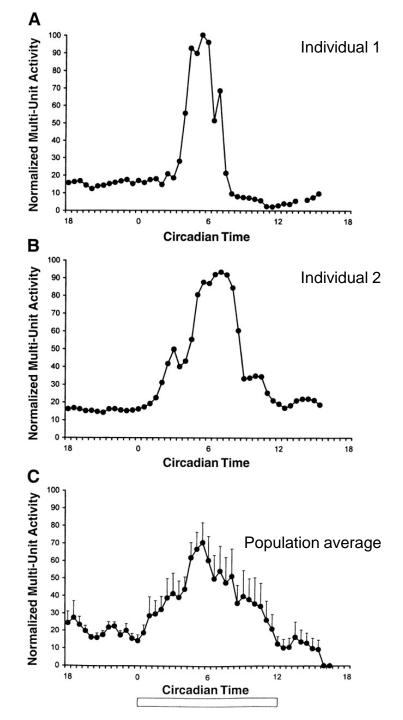




Rhythms of firing rate in the SCN, measurements in the intact animal

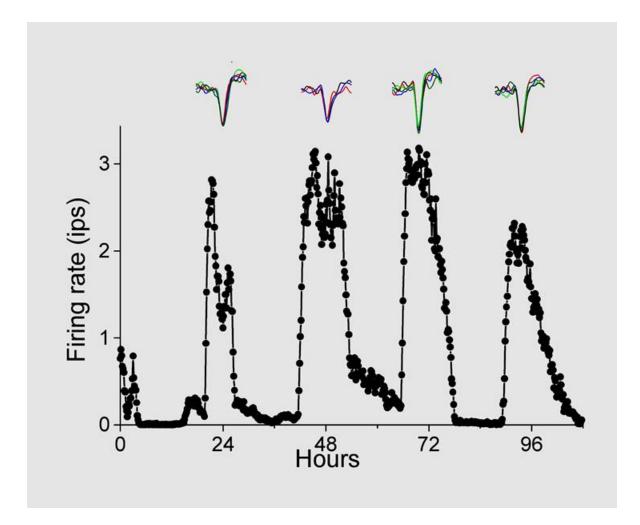


Rhythms of firing rate in the SCN, measurements in tissue culture

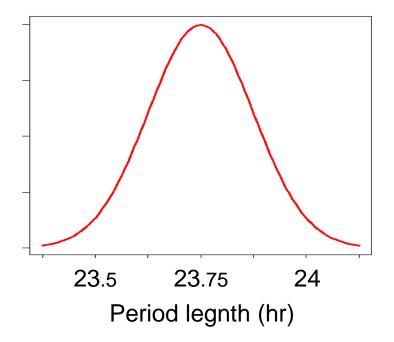


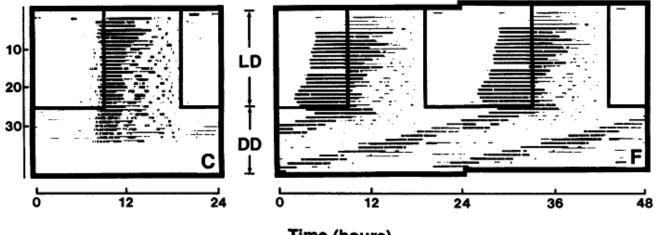
Mrugala et al., 2000

Rhythms of firing rate in the SCN, measurements in SCN cell culture

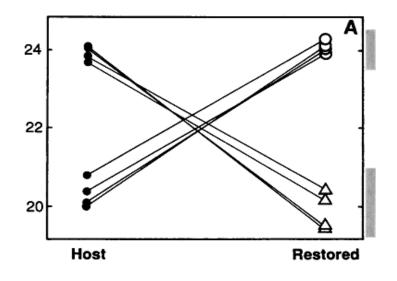




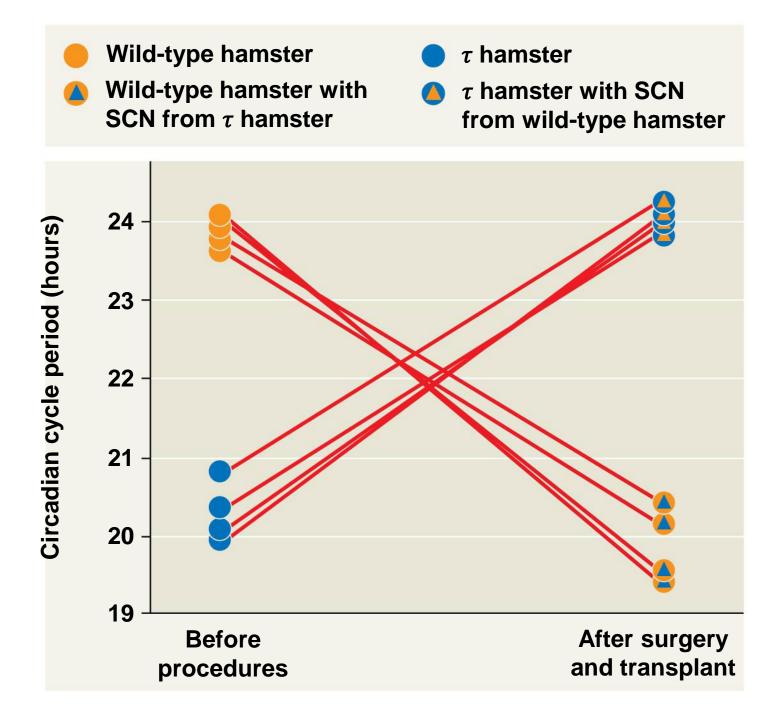




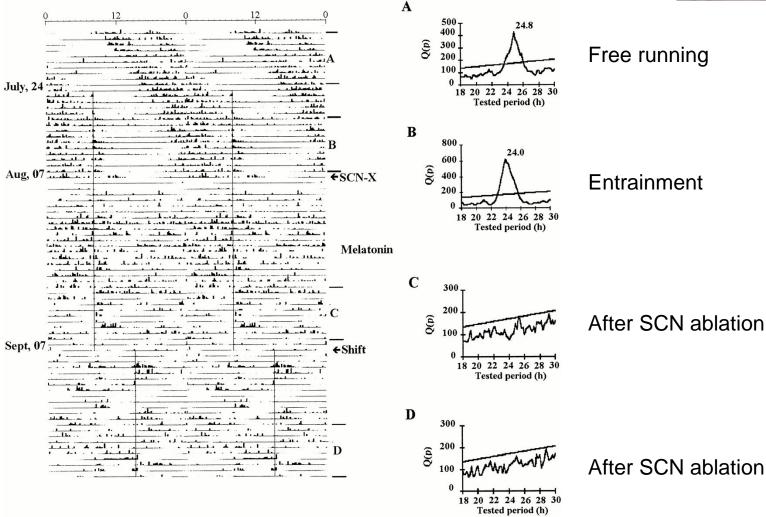
Time (hours)



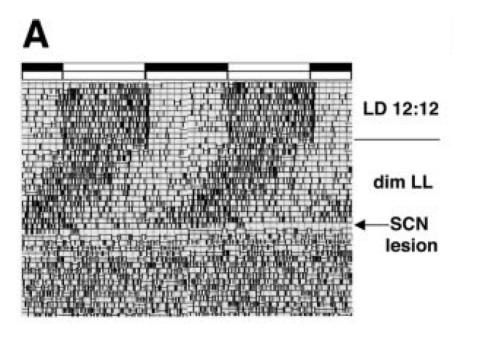
Ralph et al., 1990







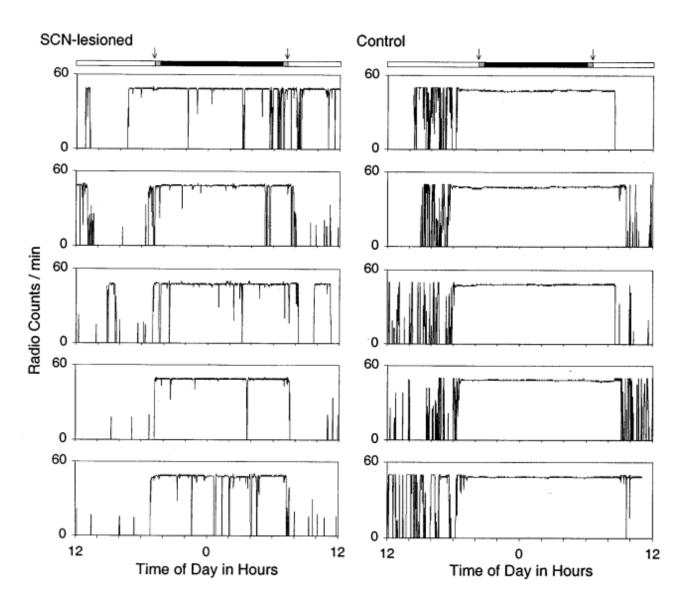




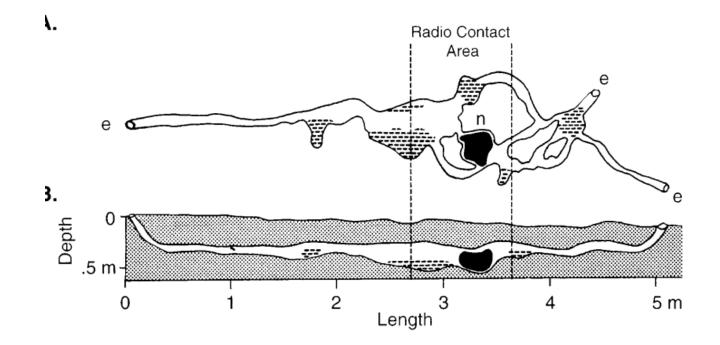
What are the evidence that the SCN is the central pacemaker in mammals?

- SCN lesion led to loss of rhythms
- SCN neurons have an intrinsic clock
- Stimulation of SCN neurons synchronized rhythms
- An implanted SCN dictates the rhythm

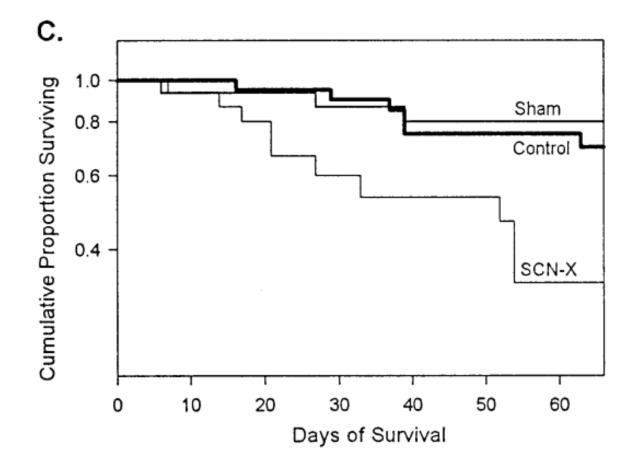
How important is the SCN? A wild experiment

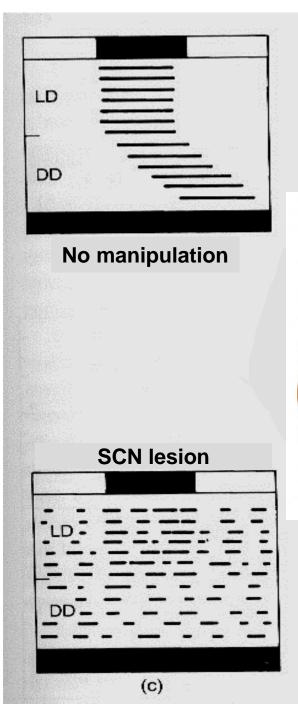


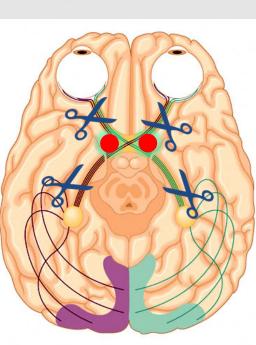


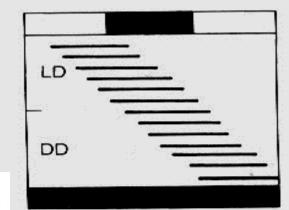


SCN-lesioned animals did not survive well



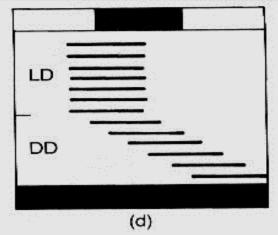


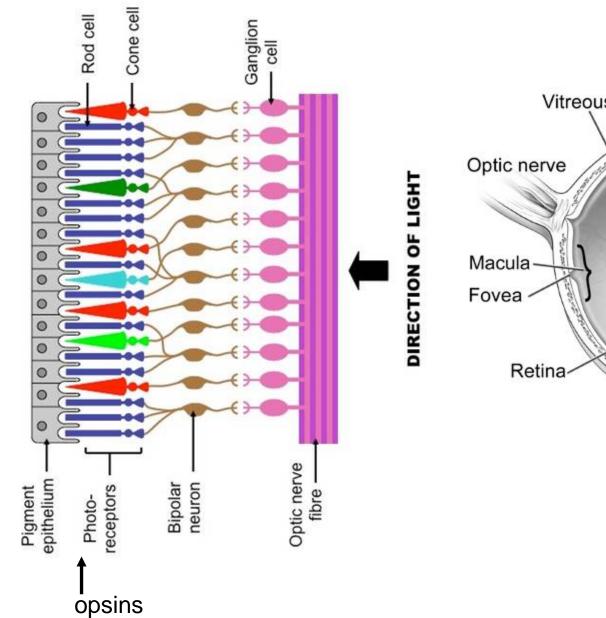


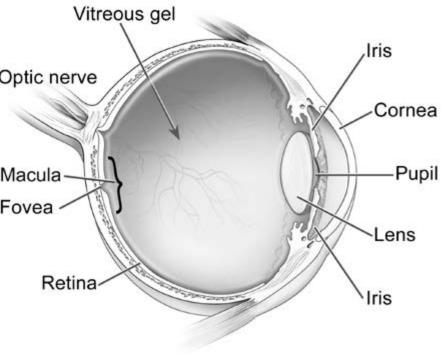


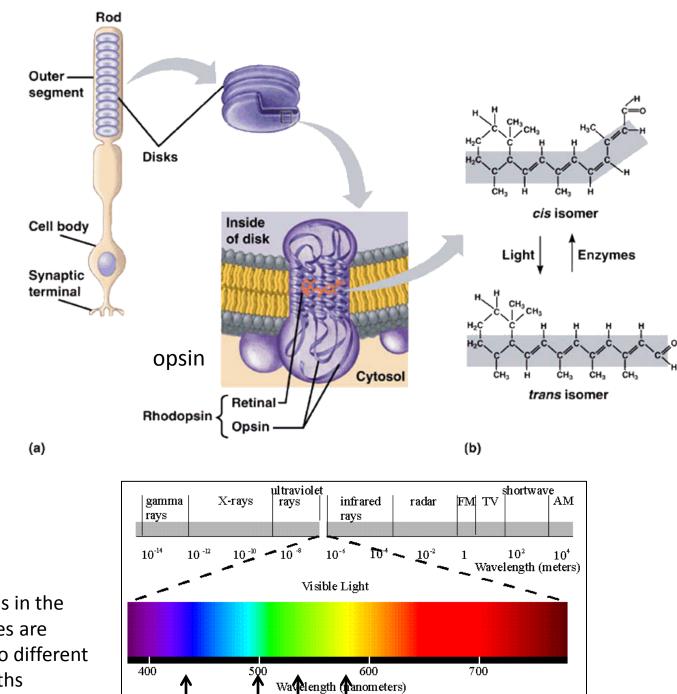
Pre-chiasmatic dissection of the optic nerve

Post-chiasmatic dissection of the optic nerve









Four opsins in the human eyes are sensitive to different wave lengths

Genetic ablation of both rods and cones using diphtheria toxin did not affect light-induced phase shifts

"The eye contains additional photoreceptors that regulate the circadian clock." Freedman et al, 1999

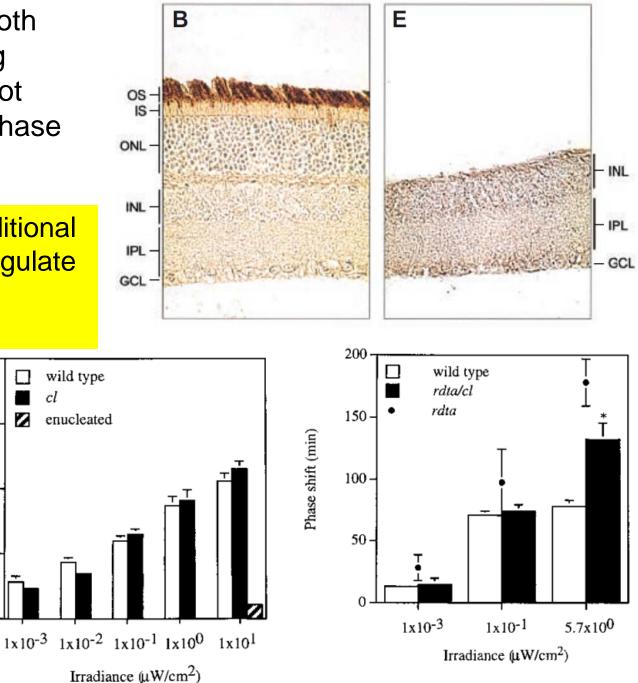
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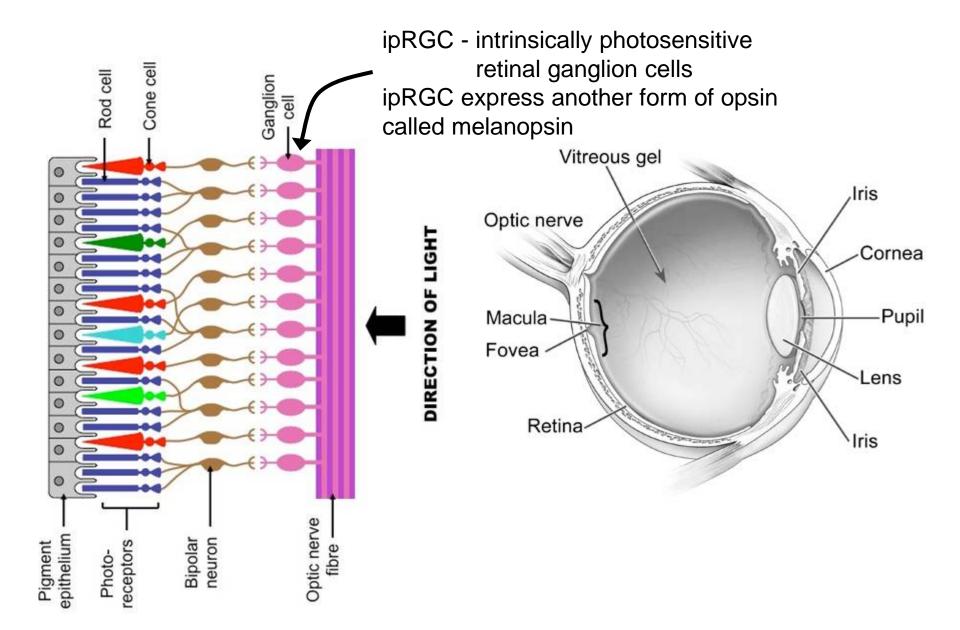
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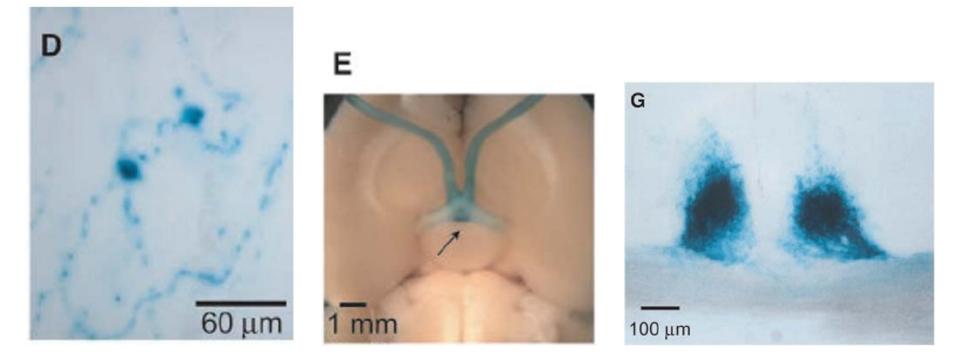
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Phase shift (min)





Transgenic mice expressing x-gal under the control of the melanopsin gene

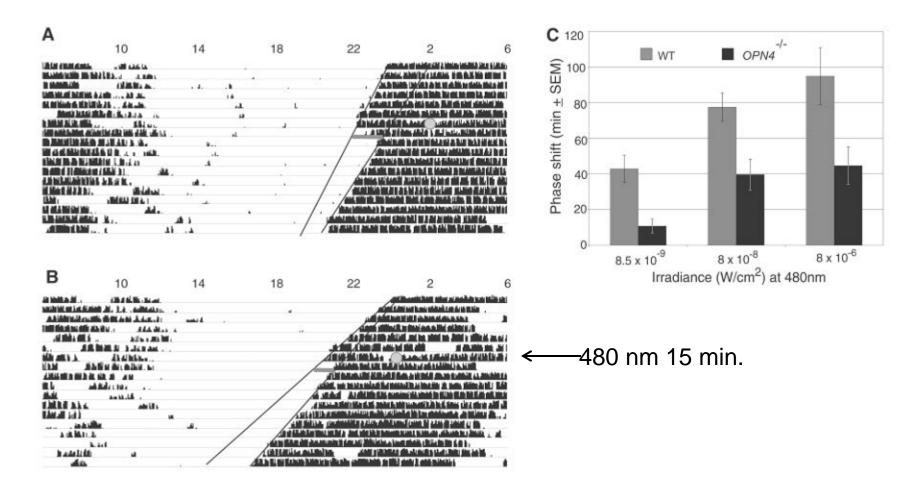


Hattar et al, 2002

Knock out of the melanopsin gene

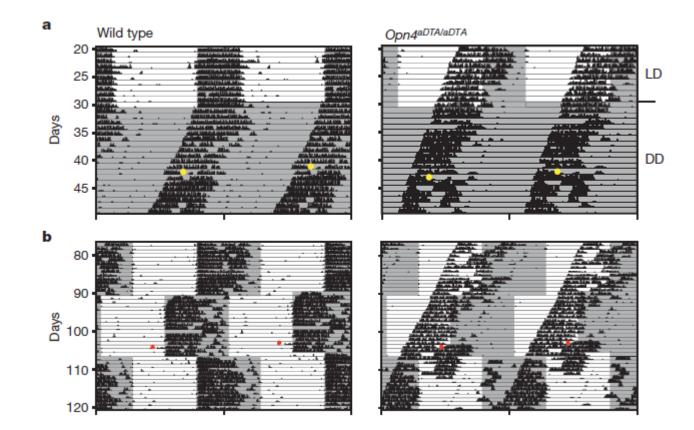
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Knock out of the melanopsin gene

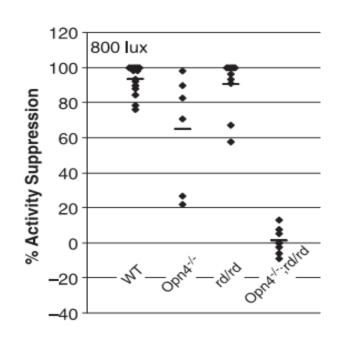


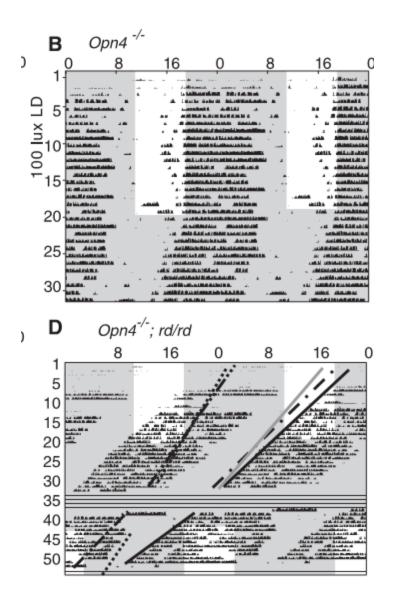
Panda et al, 2002

Ablation of the ipRGCs

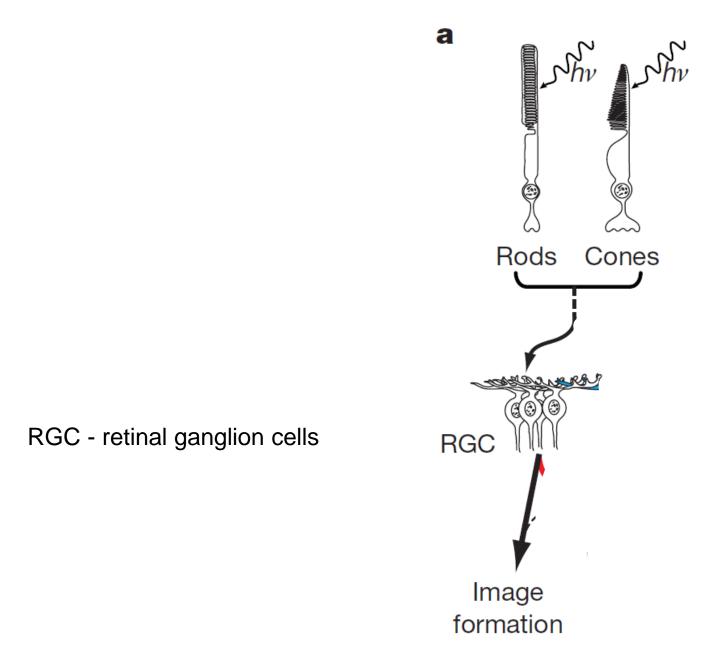


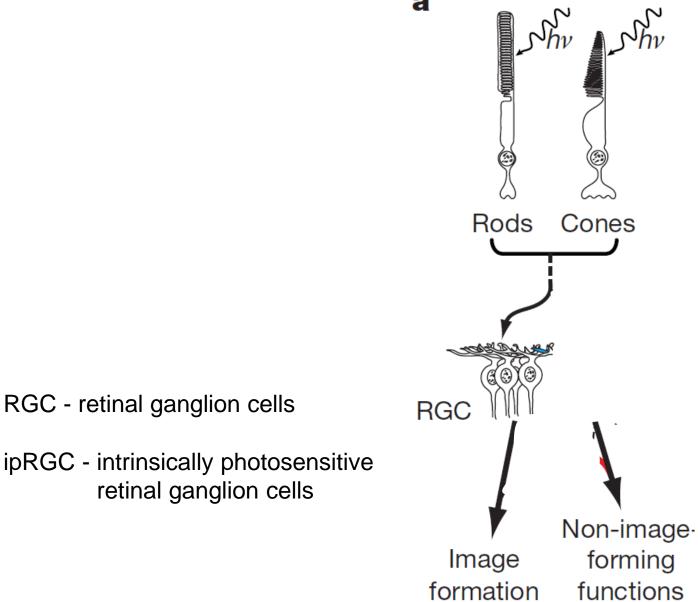
Guler et al, 2008





Panda et al, 2003





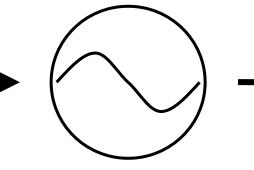
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Organization of the mammalian clock system

Light input

Oscillator



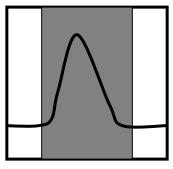


SCN

Feeding Activity Social interaction

ipRGC

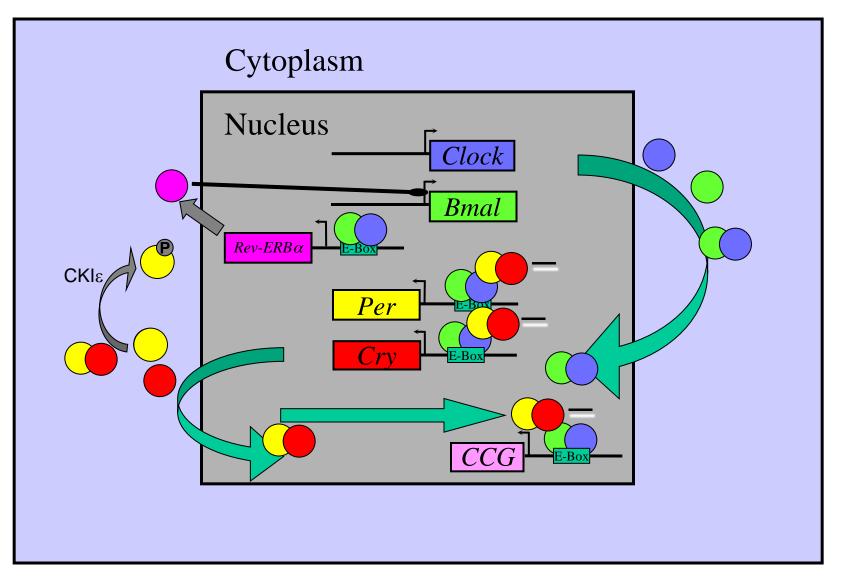
Independent Light-entrained **Output rhythm**



Circadian rhythms

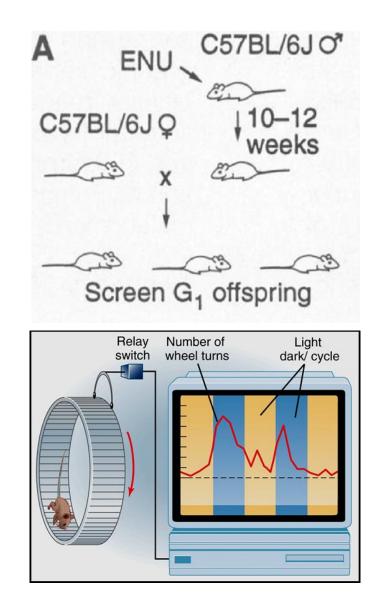
Sleep/wake cycles Locomotor activity Cognitive abilities Reaction time Body temperature Metabolism Hormone secretion Enzymatic activities Gene expression

Molecular oscillator based on a transcription feedback loops

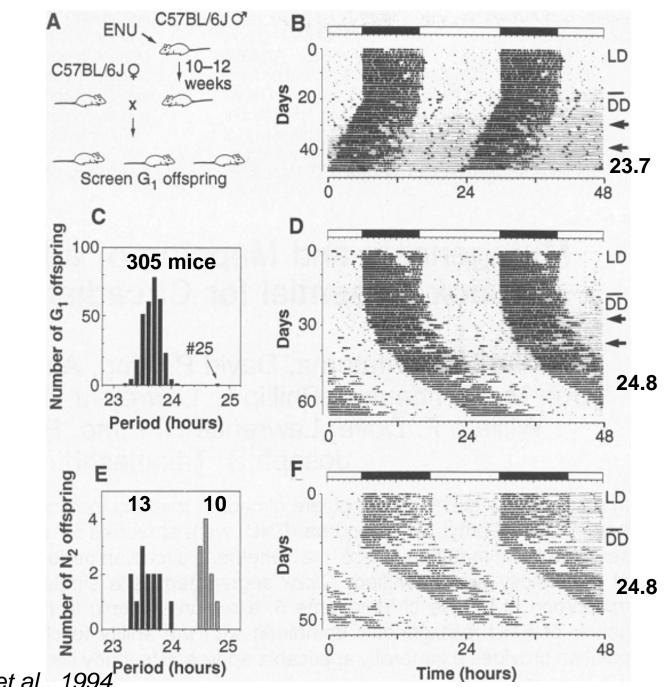


Discovering *clock*

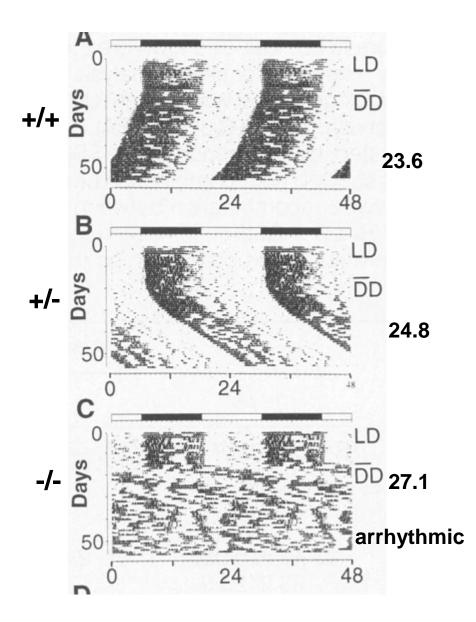
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Vitaterna et al., 1994



Vitaterna et al., 1994



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