Modeling the circadian clock:
From molecular mechanism to physiological disorders

Jean-Christophe Leloup and Albert Goldbeter

Faculté des Sciences, Université Libre de Bruxelles,
Campus Plaine, CP 231, B-1050 Brussels, Belgium
http://www.ulb.ac.be/sciences/utc/

Abstract:

Circadian rhythms originate from intertwined feedback processes in genetic regulatory networks. Computational models of increasing complexity have been proposed for the molecular mechanism of these rhythms, which occur spontaneously with a period of the order of 24 h. Models were initially proposed for circadian rhythms in *Drosophila*, and have since been extended to the mammalian circadian clock. The mammalian clock model, based on the intertwined positive and negative regulatory loops involving the *Per*, *Cry*, *Bmal1*, and *Clock* genes, can give rise to sustained circadian oscillations, which correspond to circadian rhythms autonomously generated by suprachiasmatic nuclei and by some peripheral tissues. The model brings to light the possibility of multiple, coupled mechanisms capable of generating oscillations in the genetic regulatory network underlying circadian rhythms. The results pertain not only to the molecular bases of circadian rhythms but also to physiological disorders of the sleep-wake cycle linked to perturbations of the human circadian clock. Among such disorders are the familial advanced sleep phase syndrome, and the non-24 h sleep-wake syndrome associated with a loss of entrainment of the circadian clock by the periodic environment.

References:

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Leloup J-C and Goldbeter A (2008) Modeling the circadian clock : From molecular mechanism to physiological disorders. *BioEssays* **30,** 590-600.