



## Nonlinear Dynamics of Biological Rhythms

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**Abstract**—Oscillations arise in genetic and metabolic networks as a result of various modes of cellular regulation. In view of the large number of variables involved and of the complexity of feedback processes that generate oscillations, mathematical models and numerical simulations are needed to fully grasp the nonlinear dynamics of biological rhythms. Models are also necessary to comprehend the transition from simple to complex oscillatory behaviour. To illustrate how mathematical modeling contributes to clarify the dynamical bases of biological oscillations, the presentation will focus on circadian rhythms. These autonomous rhythms, with have a period close to 24h, are conspicuous by their ubiquity and by the key role they play in allowing organisms to adapt to their periodically changing environment. Mathematical models closely related to experimental observations will be considered for circadian clocks. Models of increasing complexity predict the occurrence of sustained circadian oscillations corresponding to the evolution toward a limit cycle. Chaos can occur in the model either in autonomous conditions, or as a result of periodic forcing by light-dark cycles. Stochastic simulations show how circadian oscillations are affected by molecular noise. Extending the model to circadian rhythms in mammals permits an investigation of the dynamical bases of physiological disorders of the sleep-wake cycle in humans. Finally, the analysis of a model for the mammalian cell cycle shows how the latter can be entrained by the circadian clock.

### References

- [1] Gérard C, Goldbeter A. 2009. Temporal self-organization of the cyclin/Cdk network driving the mammalian cell cycle. *Proc. Natl. Acad. Sci. USA* 106, 21643-21648.
- [2] Goldbeter, A. 2002. Computational approaches to cellular rhythms. *Nature* 420, 238-245.
- [3] Gonze, D., Halloy, J. and Goldbeter, A. 2002. Robustness of circadian rhythms with respect to molecular noise. *Proc. Natl Acad. Sci. USA* 99, 673-678.
- [4] Gonze, D., Halloy, J. and Goldbeter, A. 2002. Stochastic versus deterministic models for circadian rhythms. *J. Biol. Physics* 28, 637-653.
- [5] Leloup J.C.. and Goldbeter, A. 2003. Toward a detailed computational model for the mammalian circadian clock. *Proc. Natl Acad. Sci. USA* 100, 7051-7056.
- [6] Leloup, J.-C. and Goldbeter, A. 2008. Modeling the circadian clock : From molecular mechanism to physiological disorders. *BioEssays* 30, 590-600.