Circadian oscillations in genetic regulatory networks: Mathematical modelling of a key biological rhythm

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Abstract:

In view of the large number of variables involved and of the complexity of cellular feedback processes that can generate oscillations, mathematical models and numerical simulations are needed to fully grasp the molecular mechanisms and functions of biological rhythms. The presentation will focus on circadian rhythms, which occur spontaneously with a period close to 24 h in nearly all living organisms. These rhythms allow the organisms to adapt to their periodically changing environment. In all organisms studied so far circadian rhythms originate from the negative auto-regulation of gene expression. Mathematical models of increasing complexity for the genetic regulatory network producing circadian rhythms in the fly *Drosophila* predict the occurrence of sustained circadian oscillations of the limit cycle type. When incorporating the effect of light, the models account for phase shifting of the rhythm by light pulses and for entrainment by light-dark cycles. The models also provide an explanation for the long-term suppression of circadian rhythms by a single pulse of light. Stochastic simulations permit to test the robustness of circadian oscillations with respect to molecular noise. Extensions of the mathematical models to the mammalian circadian clock allow us to investigate the dynamical bases of physiological disorders related to perturbations of the sleep-wake cycle in humans.

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