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Modeling circadian clocks as coupled damped oscillators

Circadian rhythms represent one of the more conspicuous examples of biological rhythms. Manifested at the physiological, behavioral, and cellular levels, these 24-hour rhythms originate at the molecular level, through a complex gene regulatory network. In mammals, the circadian pacemaker is located in the suprachiasmatic nuclei of the hypothalamus (SCN). We have developed deterministic models using non-linear ordinary differential equations that account for the occurrence of autonomous circadian oscillations in single cells, for their entrainment by light-dark cycles, and for their phase shifting by light pulses. The model can be used to unravel the links between molecular alterations (e.g. mutations in clock genes) and clock-related physiological pathologies (such as sleep phase disorders). We have investigated the coupling between the SCN cells and proposed a synchronization mechanism based on neurotransmitter release. Numerical analysis of the model predicts that (1) efficient synchronization is achieved when the average neurotransmitter concentration dampens individual oscillators and (2) phases of individual cells are governed by their intrinsic periods. These results illustrate the possible interplay between the single-cell oscillator and the inter-cellular coupling mechanisms.