Robustness of circadian clocks to daylight fluctuations: hints from an unicellular alga

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The development of systemic approaches in biology has put emphasis on identifying genetic modules whose behavior can be modeled accurately so as to gain insight into their structure and function. However most gene circuits in a cell are under control of external signals and thus quantitative agreement between experimental data and a mathematical model is difficult. Circadian biology has been one notable exception: quantitative models of the internal clock that orchestrates biological processes over the 24-hour diurnal cycle have been constructed for a few organisms, from cyanobacteria to plants and mammals.

Here we present first modeling results for the circadian clock of the green unicellular alga Ostreococcus tauri. Two plant-like clock genes have been shown to play a central role in Ostreococcus clock. We find that their expression time profiles can be accurately reproduced by a minimal model of a two-gene transcriptional feedback loop. Remarkably, best adjustment of data recorded under light/dark alternation can be obtained for vanishing coupling between the oscillator and the forcing cycle, suggesting that coupling to light is restricted to specific time intervals and has a limited effect when the circadian oscillator is synchronized to the diurnal cycle. We indeed find that there exist gated coupling schemes which generate oscillations close to those of the uncoupled model and thereby preserve adjustment of model to experimental data.

These coupling schemes are shown to minimize the impact of daylight fluctuations on the core circadian oscillator, a type of perturbation that has been seldom considered when assessing the robustness of circadian entrainment. These robustness properties are interpreted in terms of the structure of the Arnold tongue (i.e. the region of synchronization in the forcing amplitude-frequency plane). Finally, we show how the shape of the phase response curve (PRC) characterizing a light coupling mechanism indicates whether it gives rise to robust entrainment of the circadian clock.