

Robustness of circadian clocks to daylight fluctuations: hints from picoeukaryote *Ostreococcus*

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Mathematical modeling is essential to systemic approaches which seek to uncover the design principles behind the regulatory and signaling networks governing cell behavior. Although there is a growing recognition that dynamical effects and timing are important in this context, there are however still few examples where network connectivity is controlled by a purely dynamical mechanism.

The analysis of expression data from two genes of the smallest eukaryotic organism, the microscopic green alga *Ostreococcus tauri*, has allowed us to gain insight into how circadian clocks can be made immune to daylight fluctuations [1]. Circadian clocks, which keep the time of the day in many organisms, rely on daylight sensing to entrain stably to the day/night cycle. However, the daylight intensity perceived can vary significantly from day to day, and these fluctuations could reset the clock erratically.

Very surprisingly, expression profiles from *O. tauri* are accurately reproduced by a simple model of a two-gene feedback loop [1,2]. Even more surprisingly, the model adjusts the data better when it is not coupled to light [1,2]. To explain this paradox, we have shown that if sensitivity to light is confined to specific times where the core circadian oscillator is blind to perturbations, then indeed no signature of an external coupling can be detected in profiles. With this simple and elegant mechanism, the clock is insensitive to light and its fluctuations when it is on time. If the clock becomes out of phase, however, it is subjected to light at a different time of its cycle, and respond to the perturbation so as to be reset to the correct time [1].

Moreover, we have shown that the robustness of a clock to daylight fluctuations can be analyzed in terms of characteristic properties of its phase response curve (PRC), which measures how it reacts to perturbations at different times of the day [3]. Remarkably, PRCs measured in a number of living organisms satisfy the robustness criteria obtained by a wide margin [3].

[1] Q. Thommen et al., "Robustness of circadian clocks to daylight fluctuations: hints from the picoeukaryote *Ostreococcus tauri*", *PLoS Comput Biol* 6, e1000990 (2010).

[2] P.-E. Morant et al., "A robust two-gene oscillator at the core of *Ostreococcus tauri* circadian clock", *Chaos* 20, 045108 (2010).

[3] B. Pfeuty et al., "Robust entrainment of circadian oscillators requires specific phase response curves", *Biophys. J.*, 100, 2557 (2011).