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A Simplified Method Assessing the Synchronization Properties of the Body Clock with Internal and External Rhythms

The circadian clock or the biological clock adjusts to periodic signals originating internally and externally from the body. Examining the entrainment attributes of the circadian clock involves measuring phase responses to various stimuli at numerous intervals, a time-consuming and expensive process. A team of researchers from the University of Tsukuba has put forward a methodology that simplifies this process. By employing mathematical modeling and a single measurement of desynchronized cells, they have proposed a new approach for evaluating the entrainment properties of the clock.

Tsukuba, Japan— Numerous organisms are equipped with circadian clocks (internal body clocks) that help them adapt to daily environmental changes in light and temperature. For synchronizing the clock phase (timing) with these environmental rhythms, the circadian clock alters its phase in response to synchronizing stimuli such as light and temperature. This is known as a phase response. It is important to note that the magnitude of this response varies, depending on the phase of the stimulus received. These diverse phase responses are collectively represented in a single graph called the phase response curve (PRC), which illuminates the relationship between the circadian clock and the internal and external synchronizing stimuli. However, traditional methods of obtaining a PRC require multiple measurements of the phase response to stimuli at different times of day, a process that is both time-consuming and expensive.

In this study, we adapted a previously developed PRC estimation method, originally used in the context of the plant circadian clock, for use in the mammalian clock. This innovative method involves measuring the phase response to stimuli in a desynchronized state (also known as a singularity response, SR), where each cell's timing varies. This allows for the evaluation of the circadian clock's response characteristics to diverse stimuli. We demonstrated that SR can be observed in mouse- and rat-cultured cells and that the PRC for temperature and chemical stimuli can be assessed from a single measurement. Additionally, measurements using tissue cultures derived from mice showed that the phase response to identical synchronizing stimuli varies depending on the tissue involved. These results are expected to be applied for developing therapeutic drugs for jet lag and circadian rhythm disorders.

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