Circadian Clocks as Information Processing Devices

Connie Phong[1], Justin Chew[2], and Michael J. Rust[1]

Short Abstract — **We analyze the ability of two-gene networks to track the time of day in the presence of external noise in illumination, as observed in radiometry data. We find that when noise levels are high, a driven limit cycle optimally transmits information about the true time of day. However, when there are large fluctuations in the internal parameters of the network, a stable spiral (damped oscillator) is preferred. This optimality principle may explain why some organisms have self-sustaining circadian rhythms and others do not.**

Keywords — **Circadian clocks, dynamical systems, information theory**

I. Introduction

CIRCADIAN clocks are biological systems that generate near-24 hour rhythms in behavior and gene expression, presumably in anticipation of the daily changes in the environment due to the Earth's rotation. Classically, a true circadian clock is one that continues to generate self-sustaining rhythms in the absence of any external driving force—i.e. a limit cycle oscillator. Indeed, organisms from bacteria to humans exhibit free-running rhythms that persist robustly for weeks without external cues [1].

A long-standing question in circadian biology is therefore: what is the benefit of a free-running oscillator as compared to a damped oscillator or excitable circuit that could be achievable using simpler machinery? Intuitively, the sun rises and sets every day, so a system that requires external input to oscillate might therefore be adequate. Proposed solutions to this puzzle have included the possibility that an organism might be isolated from solar cues for long periods of time, or that the damped oscillator and stable oscillator strategies are in fact evolutionarily neutral. The question is made empirically acute by the existence of organisms that do not, in fact, have circadian clocks. A clear example is found in the cyanobacteria, where the three-gene *kaiABC* system generates highly robust rhythms in the model organism *S. elongatus* [3], but the two-gene *kaiBC* variant found in the *Prochlorococcus* clade does not [4].

Acknowledgements: This work was funded by a Burroughs-Wellcome Career Award at the Scientific Interface

[1]Department of Molecular Genetics and Cell Biology, Institute for Genomics and Systems Biology, University of Chicago, Chicago, IL USA. E-mail: mrust@uchicago.edu

[2]Medical Scientist Training Program, University of Chicago, Chicago, IL USA.

II. Results

Here, we consider the general case of a two dimensional dynamical system (e.g. two gene network) that is coupled to the external environment. We assume that the goal of the dynamical system is to correctly represent the true time of day. Further, the deterministic periodic signal coming from changing solar illumination is contaminated with $1/f$-like noise due to changing cloud cover and weather [5]. Thus we seek to optimize mutual information (a measure of phase locking) between the output of the dynamical system and the true time of day over the parameters of the dynamical system.

We find that when the noise strength is relatively low, the circuit performs well as long as there is a slow negative feedback process in the network. However, when noise strength increases, circuits with positive feedback loops track the environment more closely—in the language of systems engineering, these systems are bandpass filters with a resonance in their transfer function near $(24\ \text{h})^{-1}$. With increasing positive feedback strength, the circuit goes through a Hopf bifurcation and becomes a limit cycle oscillator. When the fixed point of the system becomes unstable, it can no longer be considered a bandpass filter, but has a superior capacity to track the environment in the presence of noise. Mutual information between the system output and the true time of day increases as the amplitude of the limit cycle increases past the bifurcation. However, there is a trade-off: performance degrades sharply at high amplitudes if the oscillator period is not precisely tuned.

III. Conclusion

This analysis suggests a rationale for the existence of circadian clocks based on an information theoretic optimality principle: limit cycles are superior to damped oscillators at phase locking in the presence of environmental noise. However, when the cellular circuitry is highly variable, as may be the case with the low copy numbers of molecules in *Prochlorococcus* sp., damped oscillators can outperform limit cycles.

References

[1] Winfree AT (2000) *The Geometry of Biological Time*. Springer-Verlag, New York.
[2] Enright JT (1970) *Annu. Rev. Ecol. Syst.* **1**, 221.
[3] Nakajima M, *et al*. (2005) *Science* **308,** 414.
[4] Holtzendorff J, *et al.* (2008) *J. Biol. Rhythm.* **23**, 187.
[5] Gu L, *et al.* (2001) *Agr. Forest. Meteorol.* **106**, 117.