Modeling Cricadian Rhythms

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Motivation

Modelling human circadian rhythm is a topic of great interest in biology and medicine as it is the biological mechanism that governs the periodical processes of the body, such as sleep-wake cycles and body temperature. In academic literature, circadian rhythm is almost exclusively modelled by ODEs, making this topic highly suitable for this ODE course.

Aside from its academic importance, the topic of circadian rhythms is of great personal relevance to the authors as the heavy workload of the program and personal commitments often lead to sleep loss. However, there exist many different mathematical models and would be helpful to have some method of comparing them.

As such, this project will create computational models of the human circadian rhythm using ODEs, investigate the effects of various degrees of sleep loss, and compare the accuracies of different models, by either plotting them against existing data, or comparing them qualitatively to established values.

Objectives

Objective	**Completion Date**
Read ≥ 8 papers and summarize mathematical models (2 papers per group member)	Oct 15, 2025
Investigate database of existing code repositories	Oct 25, 2025
Modify repo to include Kronauer and amplitude–phase models; add forcing term to simulate mistimed light exposure	Nov 5, 2025
Simulate disruption and evaluate models: 1. Compute phase re-entrainment time 2. Measure amplitude suppression/recovery under two conditions: constant darkness vs. light–dark cycles 3. Derive recovery ratio to quantify relative recovery	Nov 25, 2025
Compare results, deduce most suitable model, submit code and final report	Dec 1, 2025

Mathematical Background

Kronauer's model [1] is a well-established model of circadian systems, including sleep-wake cycles. It models the circadian rhythm as a Van der Pol oscillator:

$$\dot{x} = \left(\frac{\pi}{12}\right)\left[x_c + \mu\left(x - \frac{4}{3}x^3\right)\right] \tag{1}$$

$$\dot{x}_c = -\left(\frac{\pi}{12}\right)\left(\frac{24}{\tau_x}\right)^2 x_c \tag{2}$$

Here, x is the primary circadian oscillator indicating the position along the circadian cycle (i.e. wakefulness, body temperature, etc). x_c is the auxiliary variable maintaining stability in the system. τ_x is the intrinsic period; ε is the stiffness ≈ 0.13. Light enters the system as the perceived brightness B.

$$B = (1 - mx_c)I^p \tag{3}$$

Where m = 13, C = 0.018, and r is the arithmetic average of all oscillator's values. [2]

$$\frac{dx}{dt} = \frac{\pi}{12}(x_c + B) \tag{3}$$

$$\frac{dx_c}{dt} = \frac{\pi}{12}\left[\mu\left(x_c - \frac{4x^3}{3}\right) - x\left(\frac{24}{0.99669\tau_x}\right)^2\right] \tag{4}$$

$$\frac{dx}{dt} = \frac{\pi}{12}\left[\mu\left(x_c - \frac{4x^3}{3}\right) + x\left(\frac{24}{0.99669\tau_x}\right) + kB\right] \tag{5}$$

An adaptation to that model is presented by Jewett et al, and later Forger et. al [3], which attempts to model it more accurately.

Expected Outcomes

We expect simulations to demonstrate that different circadian ODE models predict distinct recovery timelines after disruption.

Primary outcome: Re-entrainment time. [4] Each model predicts different days for circadian phase to return to baseline. The improved models should predict slower recovery in darkness and faster recovery under light–dark cycles, while Kronauer's model may predict unrealistically fast or uniform recovery.

Secondary outcome: Amplitude suppression and phase recovery plausibility. Disruptive light exposure is expected to suppress circadian amplitude. Experiments show slow recovery in darkness and faster recovery under light–dark cycles. [5] We will test if each model reproduces this difference.

To quantify this, we define the **Recovery Ratio**:

$$RR = \frac{\text{days to 90\% recovery in darkness}}{\text{days under LD cycles}}.$$

A ratio > 1 indicates biologically plausible dynamics.

References

[1] Kronauer, R.E. (1990). A quantitative model for the effects of light on the amplitude and phase of the deep circadian pacemaker, based on human data. *Sleep*, 90, 306–309.

[2] Achermann, P., & Kunz, H. (1999). Modeling Circadian Rhythm Generation in the Suprachiasmatic Nucleus with Locally Coupled Self-Sustained Oscillators: Phase Shifts and Phase Response Curves. *Journal of Biological Rhythms*, 14(6), 460–468. https://doi.org/10.1177/074873099129001028

[3] Forger, D.B., Jewett, M.E., & Kronauer, R.E. (1999). A Simpler Model of the Human Circadian Pacemaker. *Journal of Biological Rhythms*, 14(6), 533–538. https://doi.org/10.1177/074873099129000867

[4] Goel N, Basner M, Rao H, Dinges DF. Circadian rhythms, sleep deprivation, and human performance. Prog Mol Biol Transl Sci. 2013;119:155-90. doi:10.1016/B978-0-12-396971-2.00007-5.PMID:23899598;PMCID:PMC3963479.

[5] Olmo, M.d., Grabe, S., Herzel, H. (2022). Mathematical Modeling in Circadian Rhythmicity. In: Solanas, G., Welz, P.S. (eds) Circadian Regulation. Methods in Molecular Biology, vol 2482. Humana, New York, NY. https://doi.org/10.1007/978-1-0716-2249-0_4