Phase Response Analysis of the Circadian Clock in *Neurospora crassa*

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Introduction

Circadian rhythm plays a vital role in maintaining the daily activities of ~24 hours in many organisms. Malfunction of the circadian clock may be dangerous to an organism, and even life threatening. Disorders associated with circadian malfunction include sleep disorders, jet lag, and even cancer. In this research, mathematical models simulate the circadian clock of the fungus *Neurospora crassa*, specifically focusing on the phase of the clock in response to light. Our results suggest a crucial balance of molecular reactions to light is necessary for optimal phase response. The results from this research may provide new information for treating circadian-related diseases.

**Neurospora Circadian Clock**

The negative feedback loop between frequency (frq) and the transcription factor White Collar Complex (WCC) is the core mechanism of the Neurospora circadian clock that produces robust oscillations. Reactions to light include induced transcription of frq, wc-1, and vvd as well as degradation of WCC.

**Experimental Reactions to light in the Neurospora Circadian Clock**

The plot of the change in phase against the time of an applied pulse is known as a phase response curve (PRC). An experimental PRC of Neurospora in response to light can be found below [1].

**A Basic Circadian Model**

\[
\frac{dW}{dt} = k_6 - k_5 W + k_2 W F_m
\]

\[
\frac{df_{m}}{dt} = k_3 f_{m} + p(t)
\]

**A Complex Circadian Model [4]**

The model on the left [4] produces an incorrect PRC shape with the original parameter set, as seen below.

**References**


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