Mathematical Modeling of Circadian Rhythms in
Drosophila melanogaster

Christian I. Hong

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John J. Tyson, Chair

Kenneth B. Hannsgen

David L. Popham

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(Abstract)

 Circadian rhythms are periodic physiological cycles that recur about every 24 hours, by means of which organisms integrate their physiology and behavior to the daily cycle of light and temperature imposed by the rotation of the earth. *Circadian* derives from the Latin word *circa* "about" and *dies* "day". Circadian rhythms have three noteworthy properties. They are endogenous, that is, they persist in the absence of external cues (in an environment of constant light intensity, temperature, etc.). Secondly, they are temperature compensated, that is, the nearly 24 hour period of the endogenous oscillator is remarkably independent of ambient temperature. Finally, they are phase shifted by light. The circadian rhythm can be either advanced or delayed by applying a pulse of light in constant darkness. Consequently, the circadian rhythm will synchronize to a periodic light-dark cycle, provided the period of the driving stimulus is not too far from the period of the endogenous rhythm.

 A window on the molecular mechanism of 24-hour rhythms was opened by the identification of circadian rhythm mutants and their cognate genes in *Drosophila*, *Neurospora*, and now in other organisms. Since Konopka and Benzer first discovered the *period* mutant in *Drosophila* in 1971 (Konopka and Benzer, 1971), there have been remarkable developments. Currently, the consensus opinion of molecular geneticists is that the 24-hour period arises from a negative feedback loop controlling the transcription of clock genes. However, a better understanding of this mechanism requires an approach that integrates both mathematical and molecular biology. From the recent discoveries in molecular biology and through a mathematical approach, we propose that the mechanism of circadian rhythm is based upon the combination of both negative and positive feedback.

Dedication

I would like to dedicate this thesis to my parents, Yun Cho Hong and Jung Sook Hong, for their love and support. I love you mom and dad.

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