Bifurcation Analyses in a Circadian Oscillator Model of Clock Genes

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Rhythmic phenomena are encountered at all levels of biological organization, with periods ranging from a fraction of a second to a year. Circadian rhythms that occur in nearly all living organisms with a period of about 24 hours play important roles in allowing them to adapt to their periodically varying environment. Among biological rhythms, circadian oscillation possesses the unique characteristic of being continually subjected to periodic forcing. Indeed, although they can occur even in constant darkness, circadian rhythms are naturally driven by light-dark (LD) cycles.

In this study, we investigate the effect of periodic forcing by an LD cycle on limit cycle oscillations produced in a circadian oscillator model of *Drosophila* [1]. The aim of our study is to understand dynamical properties of the *Drosophila* circadian system from a bifurcational point of view. For this purpose, we develop methods for more precise bifurcation analysis. Specifically, we propose a method for calculating bifurcations of periodic oscillations observed in the circadian system driven by the LD cycle with a square wave. The LD cycle generally utilized in laboratory experimental conditions varies periodically like a square wave.

To exemplify the efficacy of our proposed methods, we apply the method for the bifurcation analyses to a circadian model of *Drosophila* that is proposed by Leloup and Goldbeter [1]. Thus, we extend the bifurcation analysis of the autonomous circadian model by Leloup and Goldbeter [1]. Although they have shown that the period of the limit cycle oscillation can be entrained to an LD cycle, it is not clear how the entrainment is affected by changing the period and the light intensity of the LD cycle. Our analysis is also motivated by the following interesting study: Gonze and Goldbeter [2] have shown that when the circadian clock in *Neurospora* is forced by an LD cycle, the generation of various oscillatory phenomena depends on not only the period of the LD cycle and a light-sensitive parameter, corresponding to the light intensity, but also the difference of forms of the LD cycle. Thereby the influence of the waveform of forcing is also investigated; namely the waveform of the periodically varying parameter is altered from that of a square wave to a sinusoidal wave.

We have classified various oscillatory patterns and clarified bifurcation structures related to responses of oscillations observed in the forced system. Furthermore, we found that the influence of the differences in the waveforms on the dynamical behaviors of the *Drosophila* model is opposite to that for the model of *Neurospora*.

References

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[2] Gonze, D., Goldbeter, A., (2000). Entrainment versus chaos in a model for a circadian oscillator driven by light-dark cycles. *J. Stat. Phys.*, **101**, 649-663.