Biological publication repository

look up

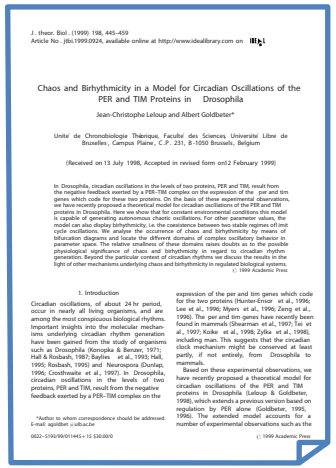
Model database

SED-ML

read

load model

export & store SED-ML



J. theor. Biol. (1999) 198, 445–459
Article No. jtbi.1999.0924, available online at http://www.idealibrary.com on IDEAL

Chaos and Birhythmicity in a Model for Circadian Oscillations of the PER and TIM Proteins in Drosophila

Jean-Christophe Leloup and Albert Goldbeter*

Unité de Chronobiologie Théorique, Faculté des Sciences, Université Libre de Bruxelles, Campus Plaine, C.P. 231, B-1050 Brussels, Belgium

(Received on 13 July 1998, Accepted in revised form on12 February 1999)

In Drosophila, circadian oscillations in the levels of two proteins, PER and TIM, result from the negative feedback exerted by a PER–TIM complex on the expression of the per and tim genes which code for these two proteins. On the basis of these experimental observations, we have recently proposed a theoretical model for circadian oscillations of the PER and TIM proteins in Drosophila. Here we show that for constant environmental conditions this model is capable of generating autonomous chaotic oscillations. For other parameter values, the model can also display birhythmicity, i.e. the coexistence between two stable regimes of limit cycle oscillations. We analyse the occurrence of chaos and birhythmicity by means of bifurcation diagrams and locate the different domains of complex oscillatory behavior in parameter space. The relative smallness of these domains raises doubts as to the possible physiological significance of chaos and birhythmicity in regard to circadian rhythm generation. Beyond the particular context of circadian rhythms we discuss the results in the light of other mechanisms underlying chaos and birhythmicity in regulated biological systems.
© 1999 Academic Press

1. Introduction

Circadian oscillations, of about 24 hr period, occur in nearly all living organisms, and are among the most conspicuous biological rhythms. Important insights into the molecular mechanisms underlying circadian rhythm generation have been gained from the study of organisms such as Drosophila (Konopka & Benzer, 1971; Hall & Rosbash, 1987; Bayliss et al., 1993; Hall, 1995; Rosbash, 1995) and Neurospora (Dunlap, 1996; Crosthwaite et al., 1997). In Drosophila, circadian oscillations in the levels of two proteins, PER and TIM, result from the negative feedback exerted by a PER–TIM complex on the expression of the per and tim genes which code for the two proteins (Hunter-Ensor et al., 1996; Lee et al., 1996; Myers et al., 1996; Zeng et al., 1996). The per and tim genes have recently been found in mammals (Shearman et al., 1997; Tei et al., 1997; Koike et al., 1998; Zylka et al., 1998), including man. This suggests that the circadian clock mechanism might be conserved at least partly, if not entirely, from Drosophila to mammals.

Based on these experimental observations, we have recently proposed a theoretical model for circadian oscillations of the PER and TIM proteins in Drosophila (Leloup & Goldbeter, 1998), which extends a previous version based on regulation by PER alone (Goldbeter, 1995, 1996). The extended model accounts for a number of experimental observations such as the

*Author to whom correspondence should be addressed. E-mail: agoldbet@ulb.ac.be

0022–5193/99/011445 + 15 $30.00/0

© 1999 Academic Press

apply changes

Simulation Tool