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Hassan M Fathallah-Shaykh* (hfathall@uab.edu), 1020 Faculty Research Tower, 1530 3rd Avenue S, Birmingham, AL 35294, and **Jerry L Bona** (bona@math.uic.edu). *Model of The Drosophila Circadian Clock: Loop Regulation and Transcriptional Integration.*

Circadian clocks influence key features of daily living including the timing of sleep, awakening and feeding. Eukaryotic circadian clocks include interconnected positive and negative feedback loops. The CLOCK-CYCLE dimer (CLK-CYC) and its homolog, CLK-BMAL1, are key transcriptional activators of central components of the Drosophila and mammalian circadian networks, respectively. In Drosophila, negative loops include period-timeless and vrille; positive loops include par domain protein 1. Clockwork Orange (CWO) is a recently discovered negative transcription factor with unusual effects on period, timeless, vrille, and par domain protein 1. To understand the actions of this protein, we introduced a new system of ordinary differential equations to model regulatory networks. The model is faithful in the sense that it replicates biological observations. CWO loop-actions elevate CLK-CYC; the transcription of direct targets responds by integrating opposing signals from CWO and CLK-CYC. Loop regulation and integration of opposite transcriptional signals appear to be central mechanisms as they also explain paradoxical effects of period gain-of-function and null mutations. (Received September 16, 2009)