Networks Involving Protein-Protein Interactions
G-Protein Signaling Pathways
Tyrosine Kinase Signaling Pathways

Pullamsetti and Shermully, 2010
JAK-STAT Signaling Pathway

Shuai and Liu, 2003
Multi-Layer Perceptron

Invented in 1957 by Frank Rosenblatt, the “father” of the field of artificial neural networks.
Ultrasensitivity

Higher sensitivity to stimulus with high-order Hill function
Oscillatory Gene Expression

Ultradian and Circadian Oscillations in CORT Secretion

Key Components of the Stress Axis
Model Simulation of CORT Oscillations

Oscillations begin when CRH is sufficiently high, and are terminated when the time delay is too small.
Two-Parameter Diagram for CORT Model

Oscillation Period Depends Greatly on the Time Delay

Experimental Test of Key Model Predictions

Oscillations are produced even though “input” CRH is constant.
From Walker et al., PLoS Biology, 2012

CRH infusion of 0.5 μg/h
CRH: 1.0 μg/h
CRH: 2.5 μg/h
Wheel running activity of a hamster over a period of 10 days.
Nuclei of the Hypothalamus
Circadian Firing Frequency from Dissociated SCN Neurons of a Hamster

Circadian Fluctuations in Period Gene Expression

Circadian Oscillations with the Scheper Model

Free-running period is 24.6 hr. From Scheper et al., J. Neurosci., 19:40, 1999
Entrainment of Scheper Model to Short Pulses of “Light”

Light is simulated by short periodic pulses in which $q_p$ is doubled.

- Stimulus period = 24 hr
- (dashed = free-running)
- Stimulus period = 28 hr
System Diagram of the Goldbeter Model