

Multiscale Modeling and Analysis of Circadian Rhythm Generation and Synchronization

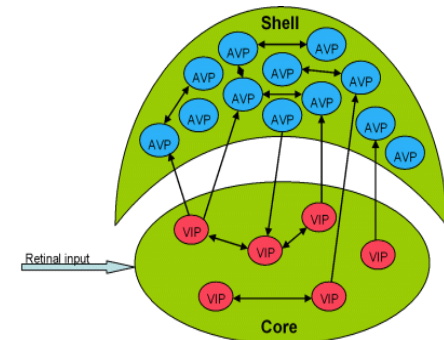
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The objective of this interdisciplinary project is to develop an integrated experimental, modeling, and computational program to decipher the molecular mechanisms responsible for mammalian circadian rhythm generation and synchronization. Our initial computational work involves the construction of a multicellular molecular model that employs the neurotransmitter vasoactive intestinal polypeptide (VIP) as the synchronizing biochemical species. A heterogeneous cell ensemble including both intrinsically rhythmic pacemakers and damped oscillators exhibits experimentally observed behavior such as self-synchronization, entrainment to ambient light-dark cycles, and desynchronization in constant bright light. These simulations suggest that intercellular coupling allows coherent timekeeping with large heterogeneous populations of relatively imprecise pacemaker cells. Our current work is focused on refinement of the multicellular model using neurophysiological data on cellular coupling and population synchronization.

Organization of the Mammalian Circadian Clock



Cell Population Model of the Circadian Rhythm

