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The surprising complexity of signal processing in clock neurons

Neurons within the suprachiasmatic nucleus (SCN) of the hypothalamus act as the central daily pacemakers in mammals. Within these neurons, a molecular circadian clock is closely coupled to the neurons electrical activity to process timekeeping signals from the external world, and to determine the signals the neurons will send to the rest of the body. This is one of many emerging examples of how neuronal firing influences, and is influenced by, intracellular biochemical systems.

For as long as these neurons had been studied, they had been assumed to encode the time of day indicated by their internal molecular clock by the rate at which they fire action potentials. Here, I will present analysis of mathematical models that suggests much more complex coding, largely based on a balance between calcium and sodium dynamics. Bifurcation analysis of a mathematical model we have developed of neurons which control daily timekeeping in mammals suggested a variety of electrical states, including depolarized low amplitude membrane oscillations and depolarization block. These states were confirmed experimentally by colleagues. Further simulations suggest that rest membrane potential may be more important than spike rate for signaling in clock neurons. This suggests a new modeling paradigm when considering signaling from membrane to DNA and back.