John Byrne, UTH, Professor of Neurobiology and Anatomy; Rice, Adjunct Professor of Electrical and Computer Engineering and Psychology

Computation models of synaptic plasticity and learning and memory

Dr. Byrne has mentored 17 summer undergraduate students during the past 10 years. He has also mentored 22 graduate students and 32 postdoctoral fellows. He is the recipient of the Educator Award from the Association of Neuroscience Departments and Programs (ANDP), the UTH President’s Award for Mentoring Women, and the Hebb Award from the International Neural Network Society.

His laboratory uses a computational approach to study the biochemical and genetic mechanisms underlying synaptic plasticity that contributes to short- and long-term memory. Although a significant body of evidence has accumulated on the mechanisms underlying both the short-term (ST; lasting minutes) and the long-term (LT; lasting days) forms of plasticity, the ways in which the multitude of molecular dynamical processes interact and quantitatively account for the observed cellular behavior is not known.

Project 1) A*nalyze interactions among pre- and post-synaptic processes and investigate the ways in which the component processes contribute to short-term plasticity of sensorimotor synapses.* The specific goals are: 1) Develop a model of short-term plasticity that incorporates both evoked and spontaneous release, postsynaptic modifications (such as receptor desensitization and AMPA receptor insertion), and 3-D Ca2+ reaction-diffusion2) Analyze the contribution of intracellular Ca2+ dynamics and its modulation by serotonin (5-HT) to transmitter release and ST synaptic plasticity; 3) Investigate the relative contributions of various presynaptic processes (e.g., transmitter depletion and vesicle mobilization) to homosynaptic depression (contributing to habituation), facilitation of non-depressed synapses (contributing to sensitization), and facilitation of depressed synapses (contributing to dishabituation); and 4) Examine the contribution of postsynaptic processes, such as receptor desensitization and receptor trafficking, to synaptic depression, post-tetanic potentiation (PTP), and 5-HT-induced short-term facilitation.

Project 2) *Analyze the intracellular biochemical and genetic networks that underlie the induction and consolidation of the long-term synaptic facilitation (LTF) that contributes to long-term memory (LTM).* The specific goals are: 1) Mathematically model and simulate the dynamics of the activation of second-messenger cascades responsible for the induction of LTF; 2) Model and simulate the regulation of CREB1 and CREB2 mRNA and proteins, as well as the ways in which a CREB1 positive feedback loop, a CREB2 negative feedback loop, and second messenger cascades contribute to these dynamics; 3) Expand the model to include additional down-stream signaling cascades and transcription factors; and 4) Use the model to explore optimal training protocols for the induction of LTF. The predictions derived from these models will be tested in experiments as part of other projects in the laboratory. An understanding of the dynamic processes that underlie synaptic plasticity will provide insights into the complex processes underlying memory formation and will be beneficial for the rational design of drugs that can be used to treat disorders that affect memory processes.