Transmitter co-release from single axons may enable robust and efficient computation of uncertainty during decision-making

Decision-making under uncertainty is a key topic in cognitive sciences. Recent brain research has revealed dopamine neurons to be pivotal for the genesis, and internal broadcast, of signals that reflect learned expectations regarding rewards. At the NSF-supported Center of Excellence for Learning in Education, Science, and Technology (CELEST; PI: Stephen Grossberg), computational neuroscientists Daniel Bullock (Boston University) and Can Tan (Harvard University) are constructing an adaptive neural-circuit model to enable simulations of how dopamine cells learn to signal both reward predictions and the uncertainties in those predictions. For their October 2008 report in *J. Neuroscience*, they performed parametric simulations to assess the robustness of their proposed novel basis by which the brain may compute uncertainty, which is maximal when “the odds are even”, e.g., when the learned conditional probability of a reward, given a cue, is .5. Specifically, uncertainty can be defined as the product p(1-p), which is an inverted-U-shaped function of the conditional probability, p. The Figure below shows that the adaptive neural model computes a good approximation to this function under a wide range of neural-circuit parameters. The proposed computation is also highly efficient and illuminates a previously mysterious neural feature: co-release of an excitatory neuropeptide (substance P, SP) and the inhibitory transmitter GABA. Although the model integrates a wide range of disparate observations, its most novel feature is the role for GABA/SP co-release in genesis of dopaminergic uncertainty responses. The hypothesized mechanism links two conspicuous brain features that are pivotal in neurodegenerative disease: loss of SP-releasing neurons underlies Huntington’s disease, whereas loss of dopamine neurons underlies Parkinson’s disease.

Right: Simulations of sustained uncertainty responses in model dopamine neurons. The ordinate shows sustained dopamine cell response ($D_{sust}$) as a function of the learned conditional probability of reward (shown as the value of $x$, on the abscissa) given a predictive cue. The three curves show that the computed inverted-U is robust, i.e., relatively insensitive to variability in neural parameters.