Adventures in synaptic integration in neocortical pyramidal neurons

On the path to understanding the diverse computing functions of the neocortex, it will be essential to develop good models of individual neurons, and to understand how individual cells contribute to circuit-level computations. Focusing on the principal cell type of the cerebral cortex -- the pyramidal neuron (PN) -- the central question in this work is how the vast number of "modulatory" inputs to PNs alter PN responses to their classical "driver" inputs; Using detailed compartmental modeling studies combined with electrophysiologiccal recordings of layer 5 PNs in brain slices (with with Jackie Schiller's group at Technion), we recently found that the relative locations of synaptic contacts along the proximal-distal axis of PN basal dendrites has a profound effect on the way synaptic inputs are combined in the presence of synaptically activated NMDA currents. In particular, we found that both excitatory (E) and inhibitory (I) inputs terminating distally on basal dendrites act primarily (and oppositely) on local response thresholds (i.e. left vs. right shift the dendrite's input-output curve. On the other hand, E and I nputs terminating proximally primarily influence dendritic response gain in opposite directions. This novel biophysical mechanism suggest that cortico-cortical pathways that modulate PN responses may achieve their specific functional effects -- threshold shifting vs. gain boosting or combinations thereof -- in part through selective targeting of their synapses to perisomatic vs. distal sites of the basal dendritic arbor. The implications for cortical information processing of this type of location-based modulatory action will be discussed.