

Proximal-distal interactions in pyramidal neuron basal dendrites

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Neocortical pyramidal neurons exchange a dense plexus of interconnections that both drive and modulate each other's responses, and most of these synapses are formed directly onto basal dendrites (BDs). While it is known that BDs can function as separately-thresholded integrative units (Polsky, Mel, and Schiller 2004), a full description of the "arithmetic" of synaptic integration in these branches is lacking, and their basis, if any, for distinguishing driver from modulatory influences remains unknown (Sherman and Guillery 1998). One hypothesis is that driver and modulatory inputs project to different zones along the proximal-distal axis of BDs, and that the dendrites themselves impose a functional asymmetry on the two categories of inputs. To explore this possibility, we combined computer modeling and experimental studies in brain slices to quantify how synaptic summation depends on the absolute and relative locations of two inputs to a single BD. Consistent with previous findings, we found that two co-localized inputs combine additively followed by a dendritic spike thresholding nonlinearity (Archie and Mel 2000; Schiller et al. 2000; Poirazi, Brannon, and Mel 2003a; Losonczy and Magee 2006). In contrast, owing to the very different cable properties at the proximal and distal ends of a basal dendrite, summation of two spatially-separated inputs was profoundly nonlinear and asymmetric: distal synapses when viewed as modulators were primarily "additive", having a threshold-lowering effect on responses evoked by proximal synapses. In contrast, proximal synapses had a primarily "multiplicative" effect, increasing the gain and asymptote of distally-driven responses. Our findings lead to the prediction that the diverse contextual, attentional, and gain-boosting effects reported in the neocortex may result from non-uniform targeting of otherwise identical driver vs. modulatory synapses along the proximal-distal axis of pyramidal neuron BDs, and that multiplicative modulators specifically target more proximal BD sites.