Supplementary Figure 6 A model for rapid, dendrite-wide, sensitization for synaptic potentiation conveyed by local NMDAR and BDNF activity-driven-PSD-95 trafficking to synapses throughout the neuron

(a) A diagram of the proposed positive-feedback pathway driven by NMDAR activity and BDNF. The steps shown in red would greatly facilitate the rapid PSD-95 accumulation at visual synapses observed in vivo after eye-opening: Newly arriving PSD-95 could become associated with TrkB, holding it at synaptic sites where the activity of NMDARs associated with the same or adjacent PSD-95 molecules can cause BDNF/TrkB signaling that would repeat the cycle. The issue of whether PSD-95 is present on ER membranes and how phospho-Akt facilitates PSD-95 delivery to the Golgi remains ambiguous (see text).

(b) Strong local NMDAR stimulation recruits TrkB to synapses, inserts AMPARs into extrasynaptic membrane, and initiates BDNF signaling.

(c) Mature BDNF near the synapse stimulates TrkB. TrkB activates PI3K and Akt resulting in facilitated PSD-95 localization to the Golgi and microtubule based transport along dendrites.

(d) An increased probability (sensitization) of LTP occurs at synapses throughout the dendritic tree as a result of dendrite-wide trafficking of PSD-95 from the Golgi. Synapses with a surplus of PSD-95 can readily bind AMPAR-stargazin complexes at the synapse and consequently strengthen that contact if a young synapse activates NMDARs sufficiently to drive AMPAR-stargazin complexes to the extrasynaptic membrane (see text).