

Supplementary Methods

Model simulation

The model consists of one postsynaptic neuron and 100 presynaptic inputs, 50 to proximal and 50 to distal dendrites.

Stimulus. The input to the model circuit is a temporally random (white noise) signal, $s(t)$, that is used to represent sensory stimuli (Supplementary Fig. 6a).

Presynaptic spike trains. The firing probability of the i th presynaptic neuron, $p_i(t)$, was computed from the convolution of its impulse response function $k_i(t)$ (Fig. 5a) and the stimulus $s(t)$, subtracted by threshold T_{pre} and rectified:

$$p_i(t) = \beta_{pre} \max\left[\int_0^{\infty} s(t-t')k_i(t')dt' - T_{pre}, 0\right] \quad (1)$$

Where $k_i(t) = \begin{cases} \frac{t}{\tau_i^2} e^{-t/\tau_i} - \frac{t}{(5\tau_i)^2} e^{-t/(5\tau_i)} & \text{if } t \geq 0 \\ 0 & \text{if } t < 0 \end{cases}$, which is a temporally

biphasic impulse response function that is typical for visual cortical neurons. Among both the distal and proximal presynaptic neurons, τ_i was evenly distributed between 1.5 and 75 ms. T_{pre} was a positive number, set somewhat arbitrarily to be

$\max\left[\int_0^{\infty} s(t-t')k_i(t')dt'\right]/2$. β_{pre} was adjusted so that the mean firing rate of each

presynaptic neuron was 10 spikes/s, which is comparable to the mean firing rate of cortical neurons recorded in vivo in response to visual stimuli (Yao et al., *PNAS* **101**:

5081, 2004). The spike train of the i th neuron was generated with a rate-modulated Poisson process based on $p_i(t)$. Example presynaptic spike trains are shown in Supplementary Fig. 6a.

Postsynaptic spike train. For the postsynaptic cell, the synaptic input to each dendritic compartment (distal or proximal) is computed as:

$$V(t) = \sum_{j=1}^{50} w_j \sum_{i=1}^{N_j} F(t - \tau_{ij}) \quad (2)$$

Where w_j is the synaptic weight of the j th presynaptic neuron, and τ_{ij} is the timing of the i th spike of the j th neuron, N_j is the number of spikes in the j th neuron, and $F(t)$

denotes the temporal waveform of EPSP: $F(t) = \begin{cases} c^2 t e^{-ct} & \text{if } t \geq 0 \\ 0 & \text{if } t < 0 \end{cases}$, $c = 0.5 \text{ ms}^{-1}$

(following Chance et al., *J. Neurosci.* **18**: 4785, 1998). The postsynaptic firing probability $P(t)$ was computed by summing the inputs to both the distal and proximal dendrites:

$$P(t) = \beta_{post} \max[V_{dist}(t) + V_{prox}(t) - T_{post}, 0] \quad (3)$$

Where T_{post} was set at the mean excitatory input received by the postsynaptic neuron given the initial synaptic weights, which was used to approximate the effect of inhibitory inputs that are balanced with excitatory inputs. β_{post} was set at 10 spike/s, resulting in a mean postsynaptic firing rate of 5-10 spikes/s. A segment of postsynaptic spike train is shown in Supplementary Fig. 6a.

Spike-timing-dependent synaptic modification. The effect of each pre-/postsynaptic spike pair on synaptic modification was computed as:

$$\frac{\Delta w}{w} = \begin{cases} A_+ e^{-|\Delta t|/\tau_+} & \text{if } \Delta t \geq 0 \\ A_- e^{-|\Delta t|/\tau_-} & \text{if } \Delta t < 0 \end{cases} \quad (4)$$

Where $\Delta w/w$ is the percentage change in synaptic weight, Δt is the pre/post spike interval. For proximal dendrite, $\tau_+ = 15.9$ ms, $\tau_- = 19.3$ ms, $A_+ = 0.013$, and $A_- = -0.008$; for distal dendrite, $\tau_+ = 12.5$ ms, $\tau_- = 103.4$ ms, $A_+ = 0.006$, and $A_- = -0.005$, which were obtained from exponential fit of the experimental data (Fig. 1d), with A_{\pm} divided by 60 (number of spike pairs in experiment). All connection weights were initialized to 0.5 plus a small random number, and they were constrained to between 0 and 1 (see Fig. 5b).

Other than those concerning the STDP windows (based on experimental data), the parameters in the model were chosen to illustrate the effects qualitatively; the predicted differential input selection at distal and proximal dendrites is robust and relatively insensitive to these parameters.

Analysis of model behavior

In addition to numerical simulations, the behavior of the model can also be understood at a more intuitive level. The direction of synaptic modification at each input is determined by both the STDP window and the temporal correlation between the pre- and postsynaptic spike trains; the net effect of a pair of pre/post spike trains can be roughly estimated by examining the cross-correlation of the pre- and postsynaptic spike trains (Song et al., *Nat. Neurosci.* **3**: 919, 2000). Supplementary Figure 6b shows the

cross-correlograms between several presynaptic neurons and the postsynaptic cell. Each cross-correlogram shows the occurrence probability of a spike pair as a function of pre-/postsynaptic inter-spike interval (interval > 0 indicates pre \rightarrow post). For a presynaptic neuron with fast-onset, transient response function, its cross-correlogram with the postsynaptic cell has a peak located clearly on the right side of 0, indicating that most of the presynaptic spikes precede the postsynaptic spikes. For an input with a slow-onset, sustained impulse response function, on the other hand, the peak in the cross-correlogram broadens into the left side, giving rise to more post \rightarrow pre spike pairs (e.g., in Supplementary Fig. 6a, compare the presynaptic spike train with 67.5 ms response time constant with the postsynaptic spike train). Note that the amplitude of the peak in the cross-correlogram is also larger for inputs with more sustained responses. This is due to the biphasic shape of the impulse response function (see Fig. 5a), which is common for sensory neurons.

To understand the relationship between the shape of the cross-correlogram and the direction of synaptic modification, we used the two shaded areas, which were defined based on the STDP window at distal dendrite (Supplemental Fig. 6c), to indicate the areas under each curve that contribute most significantly to LTP and LTD (light shading: LTD, width = 103.4 ms; dark shading: LTP, width = 12.5 ms). The direction of synaptic modification for each input can be roughly predicted by comparing the light and dark shaded areas under each curve. For $\tau = 3$ ms, the dark shaded area is smaller than the light shaded area (due to the small amplitude of the peak in the cross-correlogram), indicating that there are more spike pairs contributing to LTD than to LTP. This is why inputs with very transient responses are weakened (Fig. 5b, after training, distal). For $\tau =$

7.5 ms, the increase in the amplitude of the peak in the cross-correlogram causes a marked increase in the dark shaded area, thus a dominance of LTP over LTD for this input (Fig. 5b). As τ continues to increase, however, the broadening of the peak primarily increases the light shaded area under each curve, causing LTD to dominant for these inputs. This is why inputs with more sustained response properties are weakened. Although at proximal dendrite the LTP window is stronger, it is still narrower than the LTD window. Thus the broadening of the peak in the cross-correlogram eventually causes a dominance of LTD over LTP, weakening the inputs with the most sustained responses (Fig. 5b).

Multiple dendritic compartments

Although in our experiments the STDP window was only measured at two dendritic regions, this property is likely to vary continuously along the apical dendrite. To test whether the input segregation demonstrated in the two-compartment model holds for a more continuous dendritic gradient of the STDP window, we repeated the simulation with a model neuron containing 4 dendritic compartments (Supplementary Fig. 6d). Each dendritic compartment receives the same set of inputs as that described in the two-compartment model, and the postsynaptic neuron integrates the inputs from all four compartments. To implement spike-timing-dependent synaptic modification, we used the experimentally measured STDP parameters for the most proximal ($\tau_+ = 15.9$ ms, $\tau_- = 19.3$ ms, $A_+ = 0.013$, and $A_- = -0.008$) and most distal ($\tau_+ = 12.5$ ms, $\tau_- = 103.4$ ms, $A_+ = 0.006$, and $A_- = -0.005$) compartments. For the two intermediate compartments, we obtained each parameter by linear interpolation of the proximal and distal parameters

(e.g., for the second compartment $\tau_+ = 15.9 + (12.5 - 15.9)/3$ ms; for the third compartment $\tau_+ = 15.9 + (12.5 - 15.9)/3 * 2$ ms). As shown in Supplementary Fig. 6d, the dendritic inhomogeneity of the STDP window led to differential selection of synaptic inputs along the dendrite in a manner similar to that for the two-compartment model.