Supporting information for Shouval *et al.* (2002) *Proc. Natl. Acad. Sci. USA*, 10.1073/pnas.152343099

Simulation Details and Methods

Model of NMDA Receptor. The calcium current through the NMDA receptor, given glutamate binding at time $t = 0$, is assumed to have the form:

$$I_{NMDA}(t_i) = P_0 G_{NMDA}[I_f \theta(t_i) e^{-t_i/\tau_f} + I_s \theta(t_i) e^{-t_i/\tau_s}] B(V)(V - V_r),$$

where I_f and I_s are the relative magnitude of the slow and fast component of the NMDA receptor current. We assume throughout that $I_f + I_s = 1$. The θ function is zero if its argument is smaller than zero and one if its argument is larger than zero. The peak NMDA receptor conductance is assumed to be $G_{NMDA} = -1/500$ [μM/(ms∗mV)], unless otherwise stated. In Fig. 10 of supporting information, this is changed to $G_{NMDA} = -1/1350$ [μM/(ms∗mV)]. The parameter P_0 denotes the fraction of NMDARs that move from the closed to open state after each presynaptic action potential. This accounts for the saturation of NMDAR currents. We have chosen the values $P_0 = 0.5$. The voltage dependence of the current is assumed to have the form $B(V)(V - V_r)$. In Eq. **4** of the paper, we use the notation: $H(V) = B(V)(V - V_r)$. The term $(V - V_r)$ expresses the driving force, given V_r, the reversal potential for calcium, which we have taken to be $V_r = 130$ mV. We have used this simple form, although it is not precise for calcium channels (1) because of its simplicity. The effect of the magnesium block is expressed by B, which has the form (2):

$$B(V) = \frac{1}{1 + \exp(-0.062V)\ ([Mg]/3.57)}.$$

We have assumed throughout this paper that the magnesium concentration is $[Mg] = 1$. To calculate calcium concentration we used the following equation:

$$\frac{d[Ca(t)]}{dt} = I_{NMDA}(t) - (1/\tau_{Ca})[Ca(t)],$$

where $[Ca(t)]$ is the calcium concentration at the spine at time t and τ_{Ca} is the decay time constant of calcium in the spine. Throughout these simulation we assumed that $\tau_{Ca} = 50$ ms.

Functional Form of Ω. The Ω function we have used throughout this paper (Fig. 1*a*) has the form:

$\Omega = 0.25 + sig(Ca - \alpha_2, \beta_2) - 0.25 sig(Ca - \alpha_1, \beta_1)$, where $sig(x, \beta) = \exp(\beta x)/(1 + \exp(\beta x))$.

We have used $\alpha_1 = 0.35$, $\alpha_2 = 0.55$ and $\beta_1 = 80$, $\beta_2 = 80$ throughout most of the paper. In Fig. 10, $\alpha_2 = 0.45$. A different choice of an Ω function which has similar properties would not alter the qualitative results obtained.

Functional Form of η. The calcium-dependent learning rate, η**,** is inversely related to the learning time constant, $\eta = 1/\tau$. The functional form of τ we have chosen (Fig. 1*b*) is $\tau = \frac{P_1}{P_2 + (Ca)^{P_3}} + P_4$. We used throughout the parameters $P_1 = 0.1$ sec, $P_2 = P_1/10^{-4}$, $P_3 = 3$ and $P_4 = 1$ sec. Different details of the functional form as well as different parameters would not significantly alter the results as long as the time constant during LTD is longer than during LTP. In addition, we set these parameters so that when $[Ca] \approx 0$, $\tau \approx 3$ h (3, 4). Implicitly throughout this paper, we assume that resting calcium levels are zero. This implies that we are measuring calcium with respect to its resting value, which are believed to be 50–100 nM.

Functional Form of BPAP. The BPAP is assumed to have the form:

$BPAP(t) = 100 * ((I_f^{bs} \exp(-t/\tau_f^{bs}) + I_s^{bs} \exp(-t/\tau_s^{bs}))$, where the 100 is the maximal value in mV that the BPAP will depolarize the cell to above resting potential, and $I_s^{bs} = 1 - I_f^{bs}$ are the relative magnitudes of the fast and slow components of the back spike, respectively. In all simulations except in Figs. 2*A* and 4*A*, we have used the same set of parameters: $\tau_f^{bs} = 3\ ms$, $\tau_s^{bs} = 25\ ms$, and $I_f^{bs} = 0.75$. In Fig. 4*A* we used $\tau_s^{bs} = 15\ ms$ and $\tau_s^{bs} = 50\ ms$. We

have also assumed different values in some of the supporting information figures as described in the figure captions. Throughout the paper, we assume a 2-ms delay in the arrival time of the BPAP to the spine.

Postsynaptic Activity. We assume that the resting membrane potential is –65 mV, slightly lower than found in most hippocampal cells and slightly above the value for most cells in neocortex.

We have assumed that forms of depolarization add linearly. These include the BPAP and EPSPs generated by binding glutamate to the AMPA receptors; we did not take into account the contribution NMDAR currents to the depolarization.

The EPSPs were all assumed to have the form:

$$EPSP\ (t) = \frac{s}{norm} * \sum_i \ (\exp(\ -(t - t_i)/\tau_1^{ep}) - \exp(\ -(t - t_i)/\tau_2^{ep}))\ ,$$

where t_i are the times of presynaptic spikes, and the time constants are $\tau_1^{ep} = 50\ ms,\ \tau_2^{ep} = 5\ ms$. The parameter s reflects the different spatial summation under different types of stimulation protocols. For stimulation from a single presynaptic neuron (Figs. 2, 3*a* and *c*, 5*a* and *c*) we assumed s = 1 mV, for extracellular stimulation (Figs. 3*B* and 5*B*) we assume s = 10 mV. The parameter *norm* is chosen so that the max potential of each single EPSP is s. This implies, that given the extracellular stimulation that induces plasticity in such cases, the peak of the local integrated EPSP is s. To account for temporal integration we simply added the single EPSPs linearly.

For simulation of pairing experiments (Figs. 3*A* and 5*A*), we assumed that the postsynaptic voltage is clamped throughout the cell at the specified values.

When simulating plasticity induced by presynaptic stimulation in the presence of postsynaptic spikes, we used a statistical model to determine the times of the postsynaptic

spikes. We estimated the voltage at the cell body by using an equation similar to the one that determined the local EPSP above only we used the parameter *sc* instead of the parameter *s*. To produce Figs. 3*B* and 5*B* we used *sc* = 20 mV. If the voltage exceeded the resting potential by more than 15 mV we allowed postsynaptic spikes, that were chosen randomly from a binomial (nearly Poisson) distribution with a mean firing rate proportional to the postsynaptic potential. This neural model is essentially the SRM_0 model (5).

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