Supplementary Methods: Modelling synaptic depression

The justification of the model was described previously (Wang and Manis 2008; Yang and Xu-Friedman 2008), and was based primarily on the model of Dittman *et al.* (2000), which is itself similar to models going back to Liley and North (1953). Briefly, we calculated the relative size of the i^{th} EPSC in a train of stimuli by:

$$EPSC_i = F\, D_i\, S_i \tag{1}$$

where F is the probability of release, D_i is the proportion of release sites that are ready to release on the i^{th} pulse, S_i is the proportion of receptors that are available (i.e. not desensitized). We did not model changes in F, as facilitation does not appear to be present under our conditions.

The number of release-ready sites, D, is reduced by release, such that immediately after a release event, D decreases by FD_i, and then recovers to resting levels at a rate depending on a calcium-dependent process:

$$\frac{dD(t)}{dt} = (1 - D(t))\left(\frac{k_{\max} - k_0}{1 + K_{\mathrm{D}} / CaD(t)} + k_0\right), \tag{2}$$

where k_0 is the resting recovery rate, and $CaD(t)$ is the calcium-bound state of a sensor that drives a rapid recovery process of rate $k_{\max}$. The interaction between the rapid recovery process and the calcium-bound sensor is modelled as a simple affinity given by K_{D}. CaD increments after each EPSC, and decays to resting levels by a simple exponential, given by:

$$CaD_{i+1} = CaD_i e^{-\Delta t / \tau_{\mathrm{D}}} \tag{3}$$

These equations yield an analytical expression for D_{i+1} based on the preceding pulse:

$$D_{i+1} = 1 - (1 - (1 - F)D_i)e^{-k_0 \Delta t}\left(\frac{K_{\mathrm{D}} / CaD_i + 1}{K_{\mathrm{D}} / CaD_i + e^{-\Delta t / \tau_D}}\right)^{-(k_{\max} - k_0)\tau_{\mathrm{D}}} \tag{4}$$

where Δt is the interval between pulses.

Extracellular glutamate in the synaptic cleft drives desensitization according to a simple binding reaction:

$$S = K_S / (K_S + [\text{glutamate}]), \qquad (5)$$

where K_S is the binding affinity of the receptor for extracellular glutamate. After the i^{th} release event, the glutamate concentration increments by the amount just released (FD_i), and then decays exponentially back to resting levels, so that the glutamate concentration at the $(i + 1)^{th}$ pulse is given by:

$$[\text{glutamate}]_{i+1} = ([\text{glutamate}]_i + FD_i)e^{-\Delta t/\tau_S}, \qquad (6)$$

where Δt is the interval between pulses, and τ_S is the rate of glutamate clearance.

The 7 free parameters of the model were fit to recorded PPR and trains data for a given cell using a least-squares approach. Parameters for the high-, middle-, and low-depressing endbulbs are given in Supplementary Table 3.

Supplementary Table 1: Correlations between parameters measured off PPR recovery or train depression curves.

	τ_f	τ_s	A_f	A_s	SS_{100}	SS_{200}	SS_{333}	τ_{100}	τ_{200}	τ_{333}
τ_f	1									
τ_s	-0.016	1								
A_f	-0.52	-0.045	1							
A_s	0.40	-0.48	-0.51	1						
SS_{100}	-0.54	-0.14	0.16	-0.36	1					
SS_{200}	-0.36	0.054	-0.076	-0.17	0.70	1				
SS_{333}	0.12	0.18	-0.52	0.32	0.12	0.50	1			
τ_{100}	-0.65	0.36	0.17	-0.47	0.61	0.67	0.22	1		
τ_{200}	-0.64	0.28	0.15	-0.46	0.70	0.72	0.20	0.95	1	
τ_{333}	-0.53	0.31	0.035	-0.47	0.71	0.69	0.15	0.91	0.95	1

Supplementary Table 2: Principal components analysis. Rows represent the eigenvectors for each principle component X_i.

X_i	τ_f	τ_s	A_f	A_s	SS_{100}	SS_{200}	SS_{333}	τ_{100}	τ_{200}	τ_{333}	Eigenvalue	Cum. var.
1	-0.32	0.13	0.11	-0.26	0.36	0.34	0.08	0.43	0.44	0.42	4.9	0.49
2	0.26	0.01	-0.58	0.38	0.04	0.31	0.59	0.05	0.06	0.08	2.1	0.7
3	-0.23	-0.8	0.13	0.35	0.36	0.17	-0.09	-0.09	-0.01	-0.06	1.4	0.84
4	-0.53	0.14	0.39	0.31	-0.37	0	0.47	0.14	0	-0.27	0.57	0.9
5	-0.27	-0.03	-0.38	0.42	-0.28	-0.41	-0.38	0.27	0.23	0.3	0.47	0.94
6	0.53	-0.14	0.42	0.21	-0.46	0.35	-0.17	0.23	0.21	0.16	0.25	0.97
7	0.34	-0.14	0.29	0.04	0.28	-0.68	0.4	0.18	0.16	0.15	0.16	0.99
8	-0.07	-0.54	-0.25	-0.59	-0.45	-0.07	0.23	0.19	0.07	-0.05	0.13	1
9	0.09	0.02	-0.08	0.03	0.18	0.03	-0.13	0.77	-0.47	-0.34	0.046	1
10	0.1	0.05	-0.12	0	0.11	-0.02	-0.13	0.03	0.68	-0.7	0.027	1

Supplementary Table 3. Parameters used for the models in Fig. 4. The model is described in detail in Yang & Xu-Friedman (2008), and the Supplementary Methods.

Parameter	Meaning	low	middle	high
F	probability of release	0.35	0.65	0.9
k_0	baseline recovery rate from depletion	1/s	0.5	0.6
k_{max}	maximal recovery rate from depletion	20/s	27	15
τ_{D}	decay time constant for calcium-dependent recovery	10 ms	10	30
K_{D}	affinity of fast recovery process for calcium sensor	0.1	0.01	0.2
τ_{S}	decay time constant of glutamate clearance	5 ms	5	5
K_{S}	affinity of receptor desensitization for glutamate	1	1	1

Supplementary Table 4. Steady-state conductance amplitudes predicted by the three depression models at three stimulation frequencies. In addition, the rightmost column indicates the postsynaptic threshold measured in current-clamp experiments after a train of 30 pulses normalized to threshold at the beginning (*N* = 4 experiments).

	Depression model			
Frequency (Hz)	high	middle	low	Threshold
333	0.045	0.105	0.138	1.47 ± 0.12
200	0.074	0.170	0.213	1.93 ± 0.23
100	0.14	0.310	0.355	2.38 ± 0.34

Supplementary Table 5. Comparison between sibling and non-sibling inputs onto the same target bushy cell using the Kolmogorov-Smirnov (K-S) test for individual measures. Data are from 10 pairs of siblings compared against the overall distribution of distances (i.e. 190 comparisons). *P* values below 0.05 are highlighted in bold. The main text and Fig. 6 report the plots and P-values for measures grouped together.

Parameter	*P*-value
$EPSC_1$	0.0657752
PPR (Δt in ms)	
3	0.0820644
5	0.212364
10	0.140841
20	0.249175
50	0.179377
100	0.334117
200	0.304269
500	0.334117
1000	0.101354
4000	0.349546
100 Hz trains (pulse #)	
2	**0.0242287**
3	**0.0521546**
4	0.200975
5	**0.0242287**
6	**0.0112116**
7	**0.00592289**
8	**0.0221065**
9	**0.00529738**
10	**0.020144**
11	**0.00820421**
12	**0.0037559**
13	**0.0183318**
14	0.0881462
15	**0.0289917**
16	**0.00205284**
17	**0.0112116**
18	**0.0183318**
19	**0.0265205**
20	**0.00529738**
200 Hz trains (pulse #)	
2	**0.0221065**
3	**0.00592289**
4	**0.0443896**
5	**0.0289917**
6	**0.0316522**
7	**0.0443896**
8	0.140841
9	0.0564202
10	0.275905
11	0.159329
12	0.108498
13	0.249175
14	0.304269
15	0.464839
16	**0.0242287**
17	**0.0481476**
18	0.0564202
19	0.628767
20	0.108498
333 Hz trains (pulse #)	
2	**0.020144**
3	**0.0183318**
4	0.212364
5	0.319018
6	0.189984
7	0.289892
8	0.289892
9	0.159329
10	0.108498
11	0.289892
12	0.51742
13	0.554358
14	0.304269
15	0.482079
16	0.249175
17	0.249175
18	0.200975
19	0.349546
20	0.36528