





Supplementary Figure 1. Synaptic pattern developed by cell 36 at the end of Simulation 1. This simulation is described in the text and in Figures 2, 3, and 6. (A) Each plot corresponds to one of the 100 grid inputs. The grey line denotes the rat's foraging trajectory over the whole 15-min session (identical across all plots). The green dots denote the locations of the input spikes. The red dots denote the locations of the spikes generated by the output cell (identical across all plots). Grid cells are ordered (from high to low) based on the final strength of the synaptic weight onto the place cell. Inputs that finished the simulation with high weights were those in which one vertex overlapped the place field of the output cell. The remaining inputs, for which the place field typically occurred between vertices, were depressed. (B) The histogram represents the final distribution of synaptic weights ranging from 0 to the saturation limit  $(0.1 \ \mu S)$ .







Supplementary Figure 2. Synaptic pattern developed by cell 92 at the end of Simulation 1. (See Supplementary Fig. 1 for legend). These are the same cell and simulation as in Fig. 2.







Supplementary Figure 3. Synaptic pattern developed by cell 99 at the end of Simulation 1. (See Supplementary Fig. 1 for legend).

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Supplementary Figure 4. Firing rate maps of all the 'place cells' simulated in Simulation 1. The cells are ordered based on the original numbering of the output cells in the simulation. Spatial information scores (Skaggs et al., 1996) were calculated from the rate maps and were compared with the scores of place field maps produced by random shuffling of the spike train with the position data for each cell (a standard statistical analysis for place-field data). In all cases, the information score for the original rate map was greater than the scores produced by 100 random shuffles. It is possible that this result could be obtained if a cell fired a single burst of spikes at one location. However, the place-field definition criterion of > 0.033 Hz firing rate meant that the cell had to fire a minimum of 30 spikes in the 15-min session to meet criterion as a place field. In fact, in Simulation 1, 497/500 cells produced at least 50 spikes, and 484/500 cells produced at least 100 spikes. Visual inspection of the session data showed that all cells fired at multiple time points in the session. Thus, the significant p values for spatial information for all 500 cells show that all output cells in this simulation provided a reliable spatial signal that was not an artifact of one or two random bursts of activity.

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Supplementary Figure 5. Firing rate maps of all the "place cells" simulated as in Simulation 1 (see Suppl. Fig. 4) but with a different range of input grid spacing (70-93 cm instead of Simulation 1's 30-53 cm). The resulting fields are larger, with fewer subfields, and with more irregular shape than those in Suppl. Fig. 4. We also ran a simulation with an intermediate range of grid spacing (50-73 cm). As expected, the resulting place fields were intermediate in size and shape (data not shown).



Supplementary Figure 6. Physiological alternatives to heterosynaptic depression. (A) Example of input grid cell with (right) and without (left) intervertex background activity. (B) Comparison

of rate maps of cells across different simulations. Rate maps in the first column were obtained from the simulation without synaptic plasticity. Rate maps in the second column were generated by the simulation with synaptic plasticity with heterosynaptic depression. Rate maps in the third to sixth columns were obtained from simulations with synaptic plasticity in which heterosynaptic depression was excluded, with increasing time constants ( $\tau$ ) used for the calculation of the presynaptic firing rate in the synaptic rule. The top and bottom rows of each pair show results for simulations in the absence or presence, respectively, of intervertex background activity in the grid inputs. Slower integration of presynaptic spikes compensates greatly for the lack of heterosynaptic depression, whereas the presence of intervertex grid background activity has a weaker contribution.

Results for Supplementary Figure 6. Recent experimental results at perforant path synapses suggest that presynaptic activity that is not directly controlled in *in vivo* experiments could disguise homosynaptic depression as heterosynaptic (Abraham et al., 2007). That is, the lowrate, spontaneous activity that typically occurs *in vivo* might provide a background level of activity of presynaptic cells that allows depression of these low-rate synapses using homosynaptic mechanisms (Abraham et al., 2007). A nonzero level of baseline activity in grid cells would cause the cells to fire at a low rate when the animal occupied a location in between the vertices of the grid. A longer time constant in the calculation of the momentary presynaptic firing rate would also provide a trace of presynaptic activity as the animal exits a vertex and enters an intervertex region. To test the interaction of these two possible mechanisms, we ran simulations in which the rule lacking heterosynaptic depression was used, with different time scales for the presynaptic firing rate decay, with or without spontaneous activity of grid cells in the intervertex spaces. For these simulations, we increased the value of  $\theta_d$  compared to the other simulation of heterosynaptic depression in the main text (Fig. 2D and 2E). The threshold  $\theta_d$  used in those simulations (0.05 Hz) was very low because it was important to demonstrate that even a minimal relaxation of the heterosynaptic property caused the failure of robust place-field formation in the model. Here we are in a logically opposite position, since we would like to test if the putative mechanisms can compensate for the lack of heterosynaptic depression, and so a higher threshold ( $\theta_d = 0.3 \text{ Hz}$ ) was chosen. This value approaches the rate of stimulation at which it becomes possible to induce homosynaptic depression in in vitro protocols (Steele and Mauk, 1999; Dudek and Bear, 1992; Mulkey and Malenka, 1992). The value of  $\theta_p$  was the same as in Simulation 3 described in the main text ( $\theta_p = 5$  Hz, see Fig. 2 and Table 1), in which the lack of heterosynaptic depression had its most dramatic effect. We tried time constants for the ongoing calculation of the presynaptic firing rate in the range 100–1000 ms. When included, intervertex activity was implemented by keeping the firing-rate of the grid cell above 0.5 Hz at every location in the environment (Supplementary Fig. 6A). Column 1 of Supplementary Figure 6B shows the rate map for each example cell produced with no plasticity; column 2 shows the rate map produced by Eq. (2) (i.e., including heterosynaptic plasticity); and columns 3-6 show the rate maps produced without heterosynaptic plasticity ( $\theta_d = 0.3$  Hz) at 4 different time constants. For each cell, the first row of these 4 columns shows the rate maps produced with no spontaneous activity in between vertices and the second row shows the rate maps produced with an intervertex spontaneous activity of 0.5 Hz. Increasing the time constant of the presynaptic firing-rate decay improved the quality of place cells, moving from no spatial specificity due to the widespread runaway potentiation discussed in the previous section ( $\tau = 100$  ms) to a behavior that is comparable to the use of the intact rule of Eq. (2) ( $\tau = 500-1000$  ms). The addition of intervertex spontaneous activity was less effective. However, intervertex activity did provide a

positive contribution in combination with longer time constants, as relatively shorter time constants with intervertex activity performed comparably to longer ones without intervertex activity.

Supplementary Reference List

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