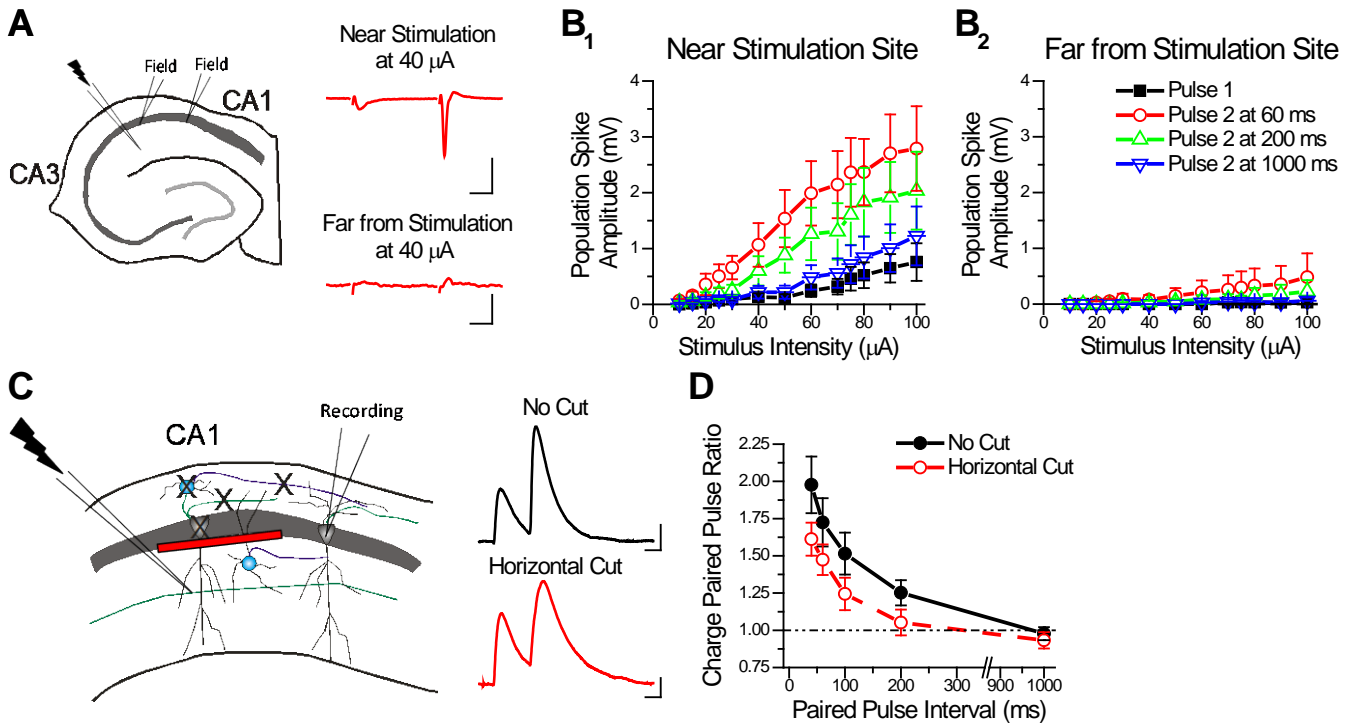


Supporting Information:

Figure S1: Feedback inhibition can be recruited during paired-pulse, but is not responsible for the facilitating capabilities of disynaptic inhibition.



A, Schematic of the dual field recording performed in CA1 *s. pyramidale*. Example traces of the paired-pulse (60 ms) extracellular population spikes at sites near (within 75 μm) and far (300 to 400 μm away) from the stimulation in *s. radiatum*. Scale Bars: 15 ms, 0.5 mV (top), 0.25 mV (bottom).

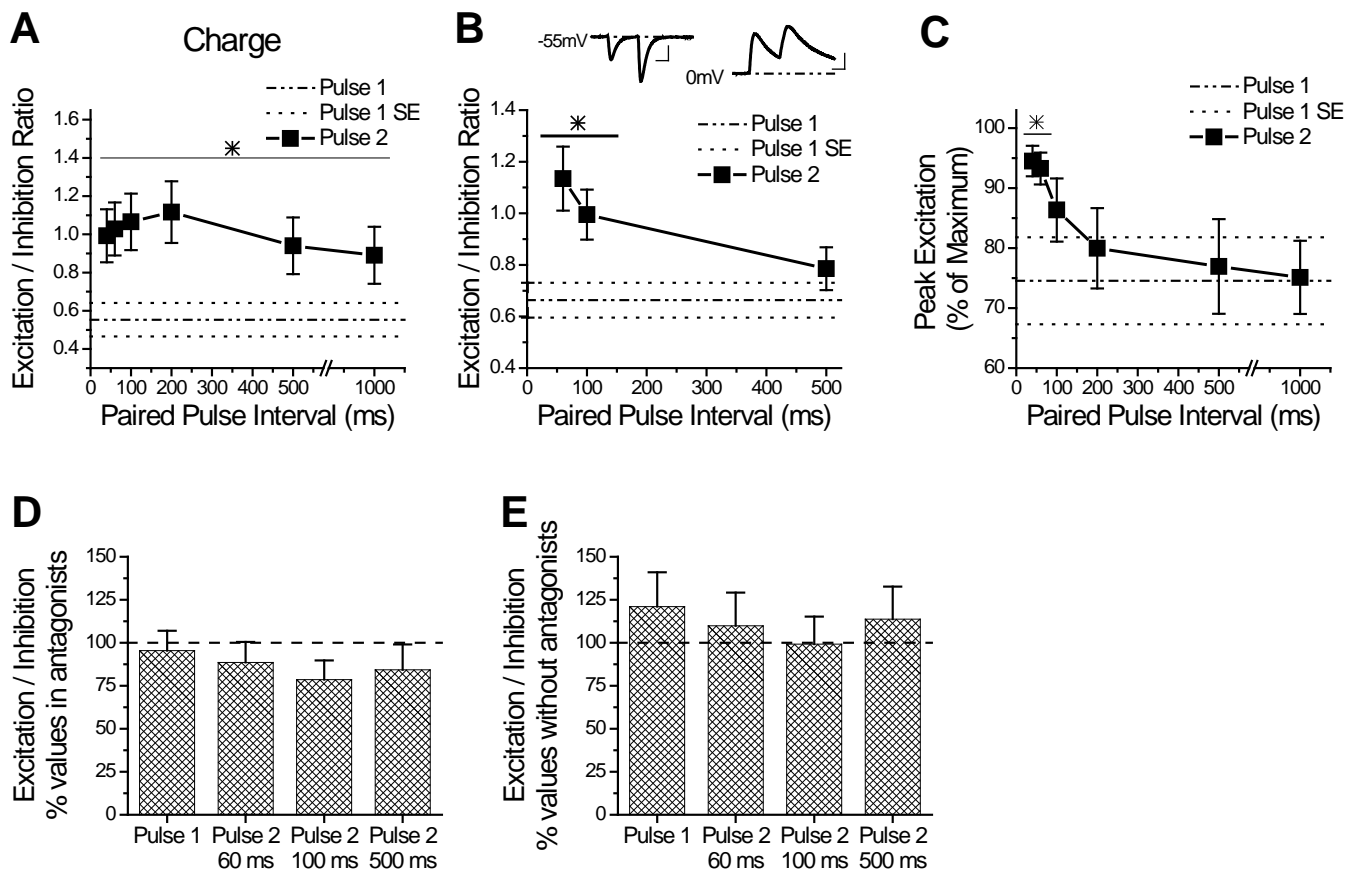
B, Group results for the population spike amplitude plotted against stimulation intensity for a single pulse and various paired-pulse intervals ($n=8$). **B₁** shows that near the site of stimulation large population spikes are generated with greater stimulation intensities, especially for short paired-pulse intervals. However, for the recording site far from the stimulating electrode, a slight increase in the population spike amplitude was only seen on the second pulse when paired-pulse facilitation is the highest (60 ms) and the stimulation was very strong ($> 80 \mu\text{A}$) (**B₂**).

C, Schematic of the recording conditions after applying a horizontal cut below *s. pyramidale* (red rectangle). Interneurons are represented as circles and the pyramidal neurons are shown as triangles. The 'Xs' indicate cells and axons that are unresponsive to Schaffer collateral stimulation in the presence of the horizontal cut.

Example traces of paired-pulse disynaptic IPSCs obtained from slices without and with the horizontal cut. Scale Bars: 25 ms, 50 pA (top), 25 pA (bottom)

D, Group results for paired-pulse ratio of disynaptic inhibition based on the charge plotted against the paired-pulse interval from slices without and with the horizontal cut (n= 18, 13). The horizontal cut shows a trend for a reduction in the paired-pulse facilitation, although the differences were not statistically significant ($p>0.5$).

Figure S2: E/I ratio is enhanced in response to paired-pulse stimulation and does not involve NMDARs.



A, Group results for the E/I ratio determined from the charge transfer of the compound PSC (n=14). The line over the data points indicates the values that are significantly different from pulse 1.

B, Group results for the E/I ratio calculated from the peaks of excitation and inhibition, each measured at the holding potential with the maximum driving force (excitation at -55 mV, the reversal potential of GABA; inhibition at 0 mV, the reversal potential of glutamate) (n=6). The line over the data points indicates the values that are significantly different from pulse 1. Insets: Left, example trace of an excitatory 50 ms paired-pulse response at holding potential of -55 mV. Right, example trace of an inhibitory 50 ms paired-pulse response at holding potential of 0 mV. Scale Bars: 20 ms, 100 pA.

C, Group results for the amount of excitation transmitted during the compound PSC (n=6). The peak of the excitatory component of the compound is a percent of the peak of the excitatory trace with inhibition blocked (maximum EPSC). The line over the data indicates the values that are significantly different from pulse 1.

D, Group results for the E/I ratio measured without antagonists as a percentage of the responses with antagonists present, based on the peaks of the components (50 μ M D-APV, 1 μ M AM 251, and 10 μ M CGP 55845) (n=5).

E, Group results for the E/I ratio measured with only NMDA receptors blocked (50 μ M D-APV), as a function of the responses in no antagonists, based on the peaks of the components (n=4).