Supplementary Methods

Detailed experimental procedures

Slice preparation. Horizontal hippocampal slices (350 µm) were prepared from young Wistar rats (postnatal day 13-19) of both sexes after decapitation under deep isoflurane-induced anesthesia, in accordance with British Home Office regulations. Slices were maintained at room temperature in a submerged-style holding chamber with artificial cerebrospinal fluid (ACSF) containing (mM): NaCl 126; KCl 3; NaH₂PO₄ 1.25; MgSO₄ 2; CaCl₂ 2; NaHCO₃ 25; glucose 10; pH 7.2 – 7.4; bubbled with carbogen gas (95% O₂, 5% CO₂) and transferred one by one to the recording chamber.

Recording conditions. Patch-clamp recordings of CA3 pyramidal neurons in hippocampal slices were made under visual guidance by infrared differential interference contrast video microscopy. Patch pipettes were pulled from standard-walled borosilicate tubing. The electrode solution contained (mM): Potassium gluconate 110; Hepes 40; NaCl 4; ATP – Mg 4; GTP 0.3 (pH 7.2 – 7.3; osmolarity 280 – 300 mosmol/l). 1 µM gabazine (SR95531) was added to the extracellular solution in experiments where excitatory postsynaptic potentials (EPSPs) were evoked by extracellular stimulation. Whole-cell current-clamp recordings were made with an Axoclamp-2B amplifier in bridge mode. Capacitance compensation was maximal and bridge balance adjusted (15 – 50 MΩ) during recording. CA3 pyramidal cells were identified by their location, shape and orientation as seen by video microscopy, and by their characteristic responses to step current pulses. All recordings were made at temperatures 29 – 31 °C. Igor Pro software (WaveMetrics, Lake Oswego, OR, USA) was used to generate command signals, and to acquire data online, and subsequently to analyze it.

Recording protocols and dynamic clamp. In order to simulate theta oscillation in the neuron, a sinusoidal inhibitory oscillatory conductance of 1 – 2 nS peak amplitude at 5 Hz (Fig. 3 and 4, Supplementary Fig. 4) or 8 Hz (Supplementary Fig. 3) was injected using dynamic clamp. A positive tonic current was superimposed on the oscillatory input so that the membrane potential was depolarized just enough to reliably evoke one action potential near the positive peak of each cycle of the oscillation. EPSPs were evoked with extracellular stimulation (50 µs, 5 V) using a monopolar stimulation electrode placed in the stratum oriens, within 100 µm from the neuron being recorded from. In order to generate artificial EPSP, dynamic clamp-simulated excitatory postsynaptic conductance (EPSG) of 0.5 – 4.5 nS peak amplitude was injected through the
The shape of EPSG was modeled using an alpha function with time to peak at 3.85 ms. Both EPSPs and EPSGs were elicited at 20 different phases of the oscillatory inhibitory conductance and repeated 10 times for each EPSP (EPSG) phase, and the resulting responses averaged. Dynamic clamp was implemented using ITC-18 A-D board (Instrutech, Port Washington, NY) and custom made macros written in Igor Pro software. The current was calculated as:

\[ I(t) = g(t) \cdot (V_m(t) - E_{rev}) \]

where \( I \) is the current to be injected, \( g \) is the conductance waveform, \( V_m \) is the membrane potential, and \( E_{rev} \) is the reversal potential, which was 0 mV for EPSG and −70 mV for inhibitory conductance.

References