Hippocampal Ripples as Inhibitory Transients

Introduction

Sleep is known to be important for memory consolidation, and memories are thought to be stored in the hippocampus during, the sleep. Recently, memory replay – repeatable sequences of potential cell firing – has been demonstrated during sleep, and associated with characteristic brain oscillations, giving rise to the hypothesis that these may form the critical neural substrate of memory consolidation. However, the role of oscillations in memory replay has remained unknown. In the present study, we develop a model of ripple generation to explore active state generation, however specific interactions between ripples and slow oscillation remain unknown. In the present study, we develop a model of ripple generation to explore interaction between cortico-slow oscillations and hippocampal ripples during sleep.

Ripples have many shapes, but only one duration

Ripples are identified by large amplitude excursion of the band-passed LFP. Frequencies are quantified as the inverse of the average peak-to-peak time within a ripple. Ripple inter-arrival times are approximately exponential, with rate ~1.77Hz. Ripples are identified by large amplitude excursion of the band-passed LFP. Frequencies are quantified as the inverse of the average peak-to-peak time within a ripple. Ripple inter-arrival times are approximately exponential, with rate ~1.77Hz. The distribution of ripple durations shows high kurtosis around a mean of ~60ms.

Computational Model of CA1

Adaptive Exponential Integrate-and-Fire model neurons
- Intrinsically, each neuron receives independent Ornstein-Uhlenbeck noise and a membrane DC current
- Fixed synaptic time scales
- All-to-all connectivity, with very fast and weak Pyr-to-Pyr synapses
- Networks: 600 Pyr cells, 600 Int cells
- Input from CA3 localized in time, with different magnitudes for Pyramidal cells and Interneurons

Ripple Oscillation Mechanism
- Synchronous input organizes initial network firing
- Common input evokes initial network firing
- Intrinsically, noise promotes de-synchronization
- Synaptic currents
- Propane: synaptic if enough synaptic inputs are aligned
- Propylene: de-synchronization if enough neurons are synchronous

Model Predictions
- Ripple duration independent of duration of ripple-triggered depolarization events in CA3
- Phase of CA1 Pyr cells recorded in a ripple is modulated by both excitatory drive from CA3 and inhibitory currents within CA3
- Frequency rate in vs vs Pyr Cells has competing effects on Pyr Cell recruitment
- Ripple frequency is not strongly modulated by r

Conclusions
- In vivo ripples have broad frequency distribution and very stereotyped duration
- We design a model of CA1 ripple generation in which synchronization of inhibitory neurons is due to common input from CA3. In the model:
  - Activity of inhibitory interneurons regulates the windows of opportunity for pyramidal cells to spike
  - Ripple frequency and duration depend on CA3 architecture
  - Phase-dispersion induced by noise constraints the duration of a ripple event
  - Sequential activation of pyramidal cells is directly derived from CA3 input.
  - Hence, CA3 optimizes CA1 output for downstream transmission.
  - In a preliminary, open-loop configuration, ripple input biases cortical UP states during slow oscillations

References

Malerba, Paola; Krichman, Giri P; Fellous, Jean-Marc; Bazhenov, Maxim; Buzsaki, Gabor. Hippocampal Ripples as Inhibitory Transients. Neuron, 2014; 82(3): 461-476.

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With every ripple, CA1 produces a stereotyped “package” of information to project downstream. Within this package, Pyramidal cells spiking is organized by selectivity of CA3 input more than local inhibitory mechanisms. If only Interneuron receives CA3 input, oscillations show a much reduced amplitude. If only Pyramidal cells receive CA3 input, both population-firing probabilities decay in time. The high frequency event quickly (<30ms) defaults to a gamma frequency oscillation. The high frequency event quickly (<30ms) defaults to a gamma frequency oscillation. Ripple frequency is not strongly modulated by r.

Pyr Cell Adaptation at 100% CA1 Input to 50% of Int CA3 Input to Pyr Cells within a Sequence

Ripple Input to Cortex during Slow-Wave Sleep affects Timing of Up-Down state transitions

Previously developed Theta-Theta Control model of Slow-wave sleep
- Cortic: 200 Pyr, 50 Int. Theta/4: 50 TC, 50 IC.
- CA1 Pyr to Cortic Pyr.
- Following a Ripple event, Cortical Pyr Cells are more likely to spike
- Framework where sequential cell activation during ripples can be mimicked by Cortical Int neurons.

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