Mechanisms of ripple generation and sequence repetition in the hippocampus:

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Sleep is known to be important for memory consolidation, and memories are thought to be stored in the hippocampus during wakefulness and “transferred” to cortex during sleep. Recently, memory replay – repeated sequences of pyramidal cell firing – has been demonstrated during sleep. Furthermore, sequence replay is associated with characteristic oscillations, giving rise to the hypothesis that these may form the critical neural substrate of memory consolidation. Tampering with replay can disrupt memory formation and consolidation, and the mechanisms underlying sequence replay are still unknown.

Among hippocampal-specific activity patterns, sharp-wave ripple complexes are brief high-frequency events, during which the firing sequences of previously activated cells are re-played. It is believed that sequence reactivation during ripples contributes to memory formation in awake patterns and to memory consolidation during sleep. Ripples in the pyramidal layer of hippocampal area CA1 are believed to be triggered by an excitatory event in area CA3.

Commonly, during a ripple only a few pyramidal (excitatory) cells are recruited, and spike at the peak of the event, while perisomatic interneurons (a type of inhibitory cells) spike across the duration of the event. The distribution of spike timing with respect to ripple peak is different for different types of interneurons. In hippocampal area CA1, axo-axonic cells tend to spike only at ripple initiation and be suppressed in the later part of a ripple. Since axo-axonic cells are in a crucial position to suppress the spikes of the pyramidal cell they impinge upon, we hypothesize that they can regulate the initiation of cell specific activity replay. In this work, we designed a computational model of ripple generation in hippocampal network. In our model, perisomatic interneurons are organized in brief oscillatory transients by common excitation, and such high-frequency firing mediates high-frequency LFP oscillations in pyramidal neurons. The model incorporates different cell types and emphasizes the role of axo-axonic cells in selecting which pyramidal cells are participating in ripple activity, hence what spiking sequence is replayed during a given ripple event.