Hippocampal Network Oscillations

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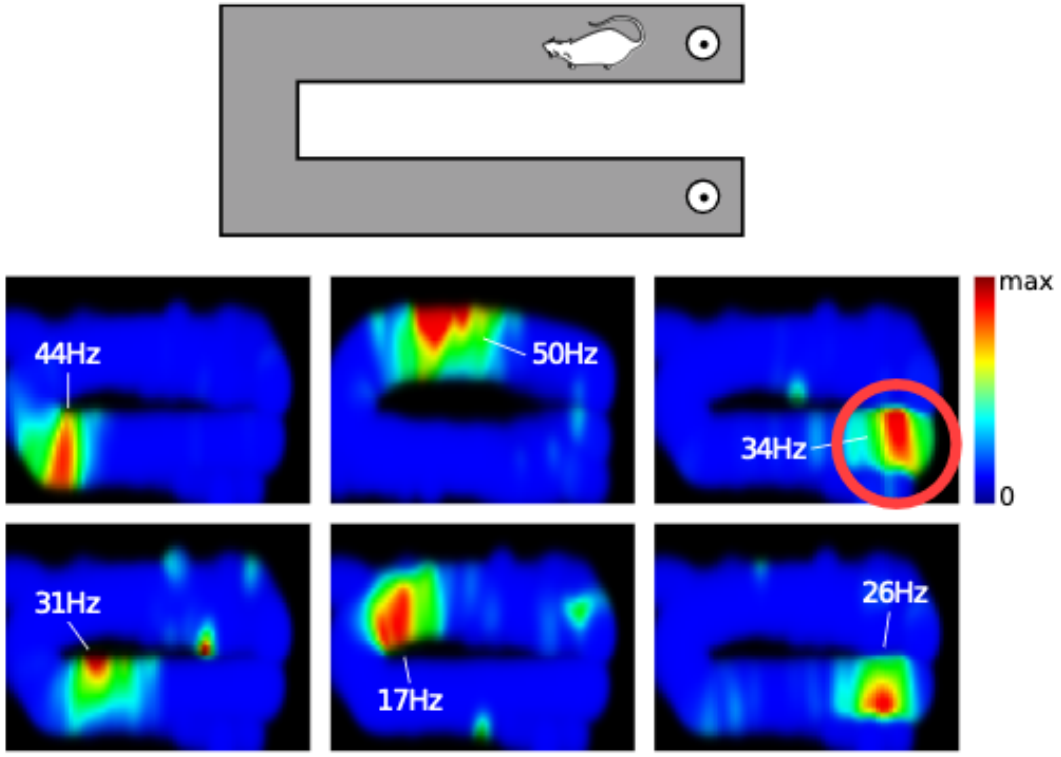
Outline

Place Cells

Place cells discharge in restricted portions of the environment



O'Keefe and Dostrovsky (1971) *Brain Res* 34(1), 171–5. Wilson and McNaughton (1993) *Science* 5124(261)1055–8.

Place Cells

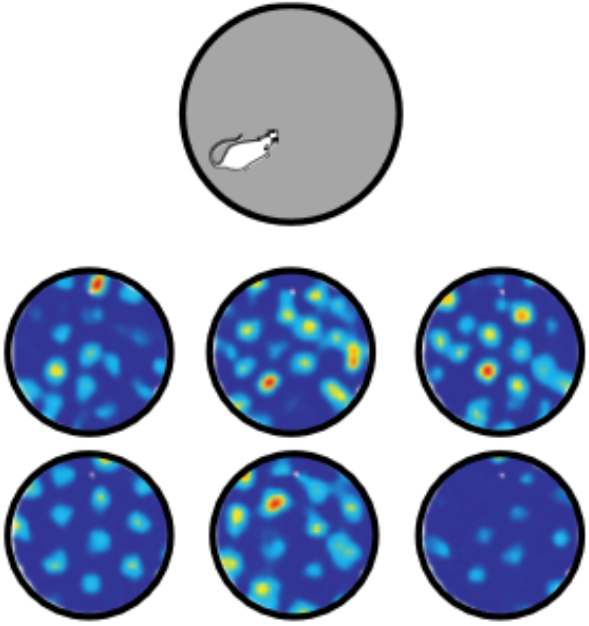
Place cells discharge in restricted portions of the environment

"Cognitive Map"

O'Keefe and Nadel (1978) Clarendon Press, Oxford.

Grid Cells

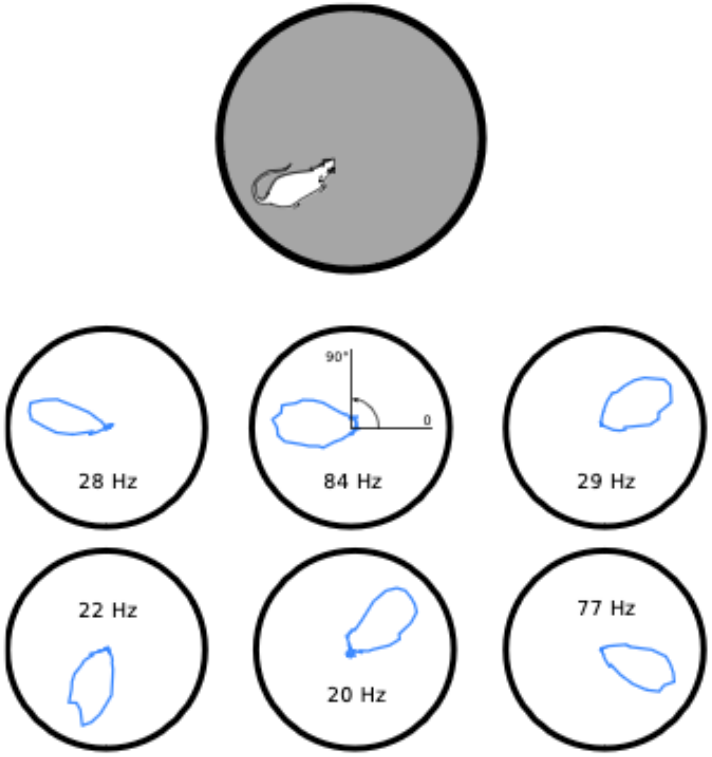
Grid cells discharge at the vertices of a hexagonal grid



Hafting et al. (2005) *Nature* 7052, 801–6.

Head Direction Cells

Head direction cells discharge when the head is oriented in a specific direction



Ranck (1984) *Soc. Neurosci. Abstrcts.* Taube et al. (1990) *J. Neurosci.* 10(2), 420–35.

Head Direction Cells

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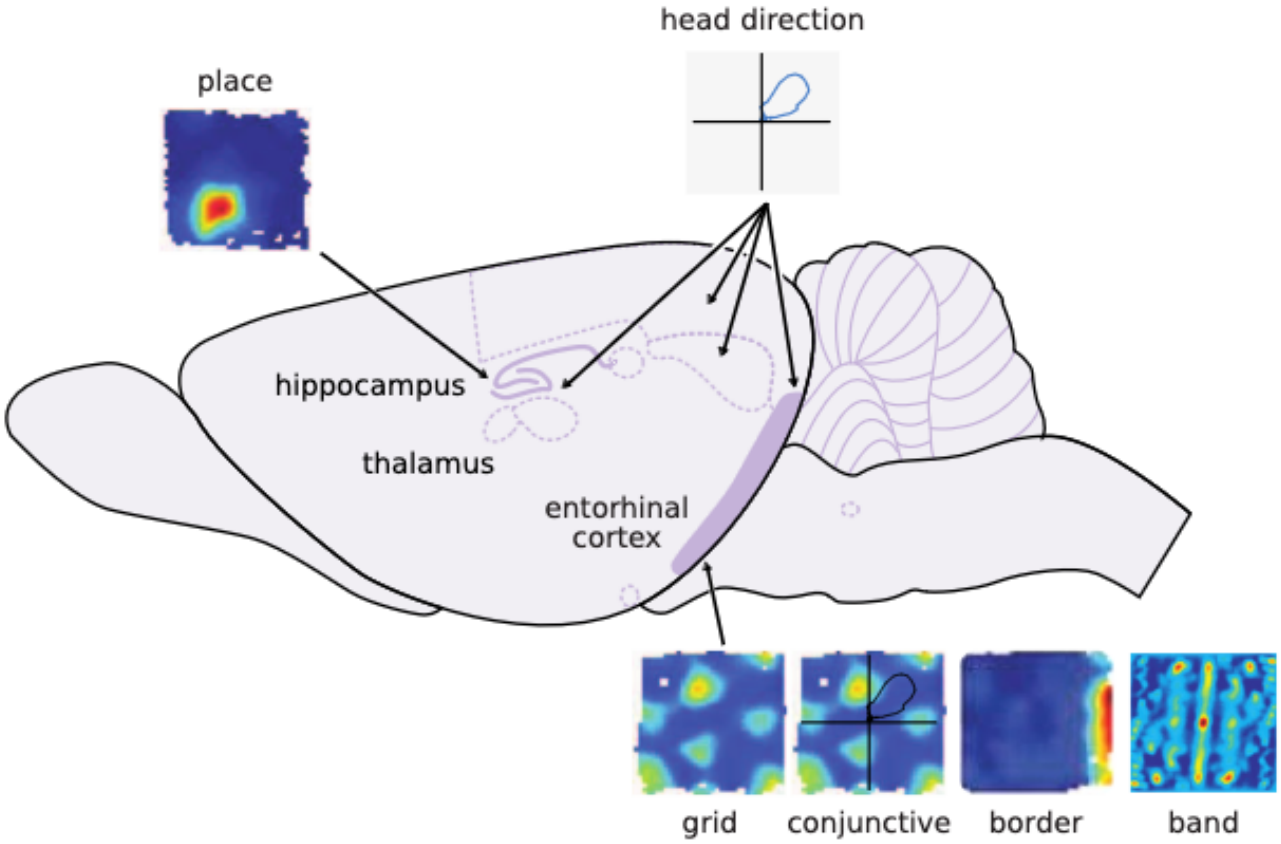
"Neural Compass"

Wiener and Taube (2005) MIT Press.

Anatomical and Functional Coupling

Place, grid and head direction cells are anatomically and functionally coupled



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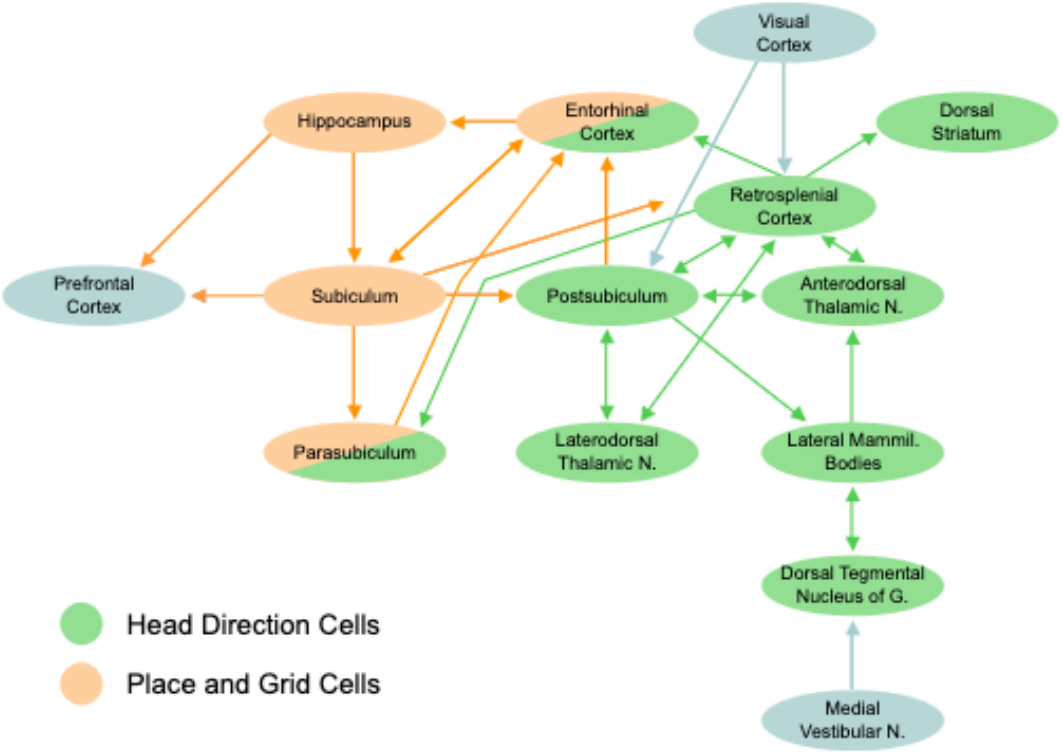
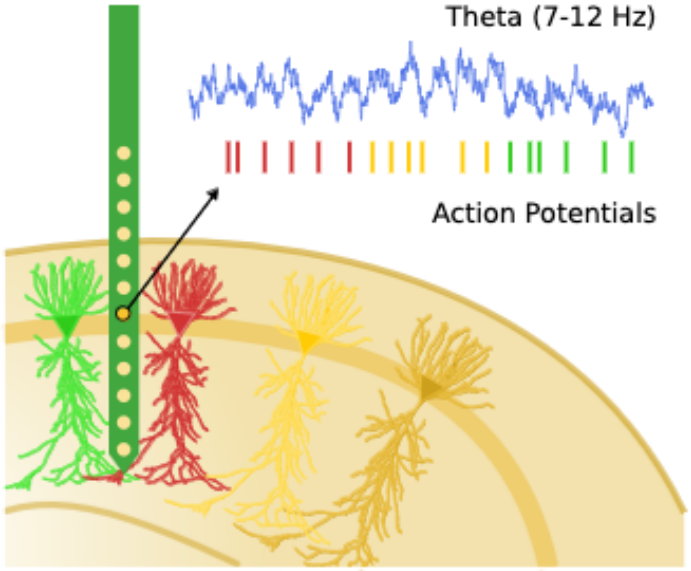


Outline

Theta Rhythm during Exploration

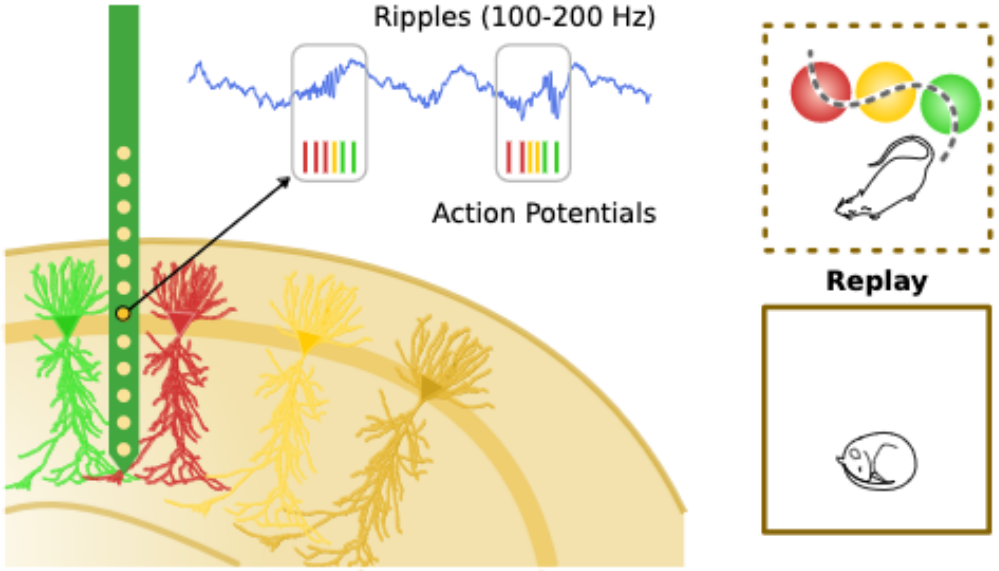
Theta oscillations pace place cell activity during exploration



Place Cells

Ripples during Sleep

Ripples pace reinstatement of place cell activity during sleep

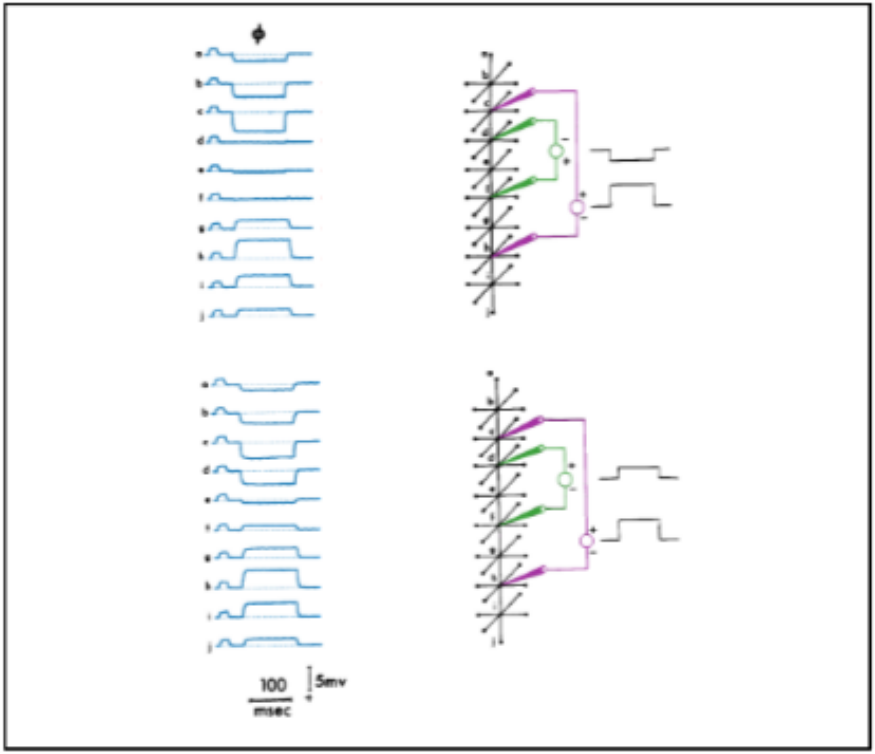


Buzsáki (1989) *Neuroscience* 31(3):551–70, Lee & Wilson (2002) *Neuron* 36(6):1183–94.

Outline

Current Source Density (CSD) Analysis

CSD analysis identifies current sources and sinks



Nicholson and Freeman (1975) *J. Neurophysiol.* 38(2), 356–68.

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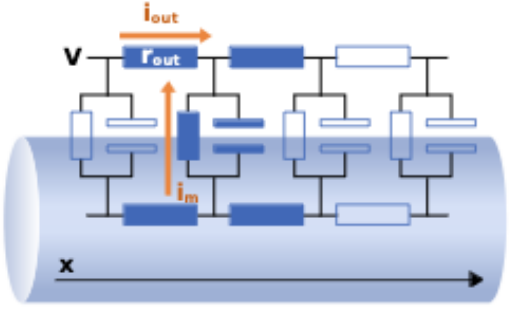

1. $i_m = \frac{\partial i_{out}}{\partial x}$

2. $\frac{\partial V}{\partial x} = -r_{out}.i_{out}$

$$\Rightarrow i_m = \frac{\partial i_{out}}{\partial x} = \frac{\partial}{\partial x}(K.\frac{\partial V}{\partial x}) = K.\frac{\partial}{\partial x}(\frac{\partial V}{\partial x}) = K.\frac{\partial^2 V}{\partial x^2}$$

$$\boxed{i_m = K.\frac{\partial^2 V}{\partial x^2}}$$

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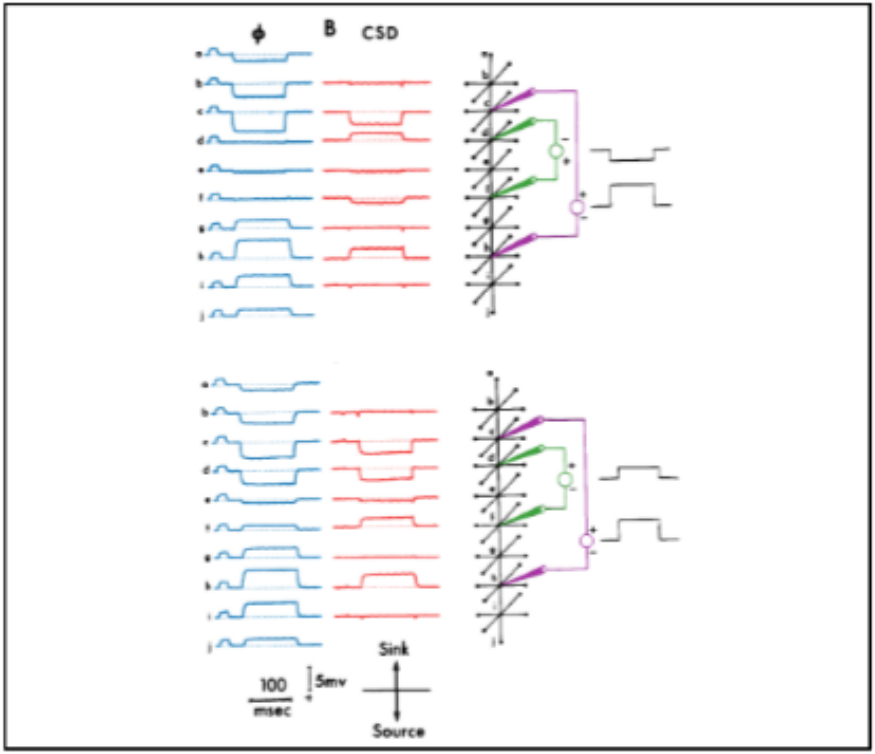

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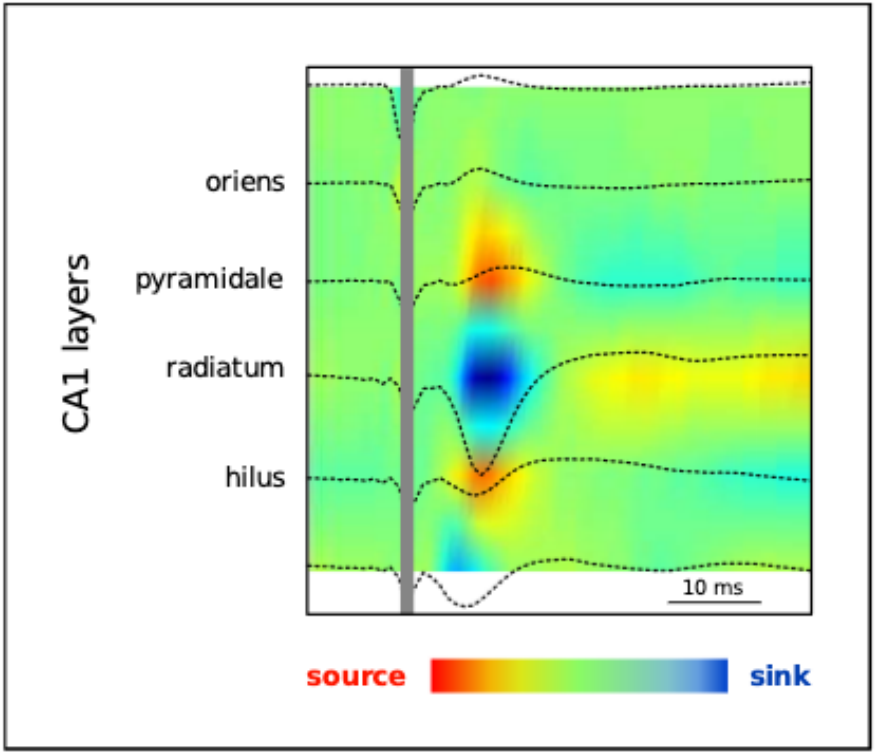


Outline

Behavioral Correlates of Theta

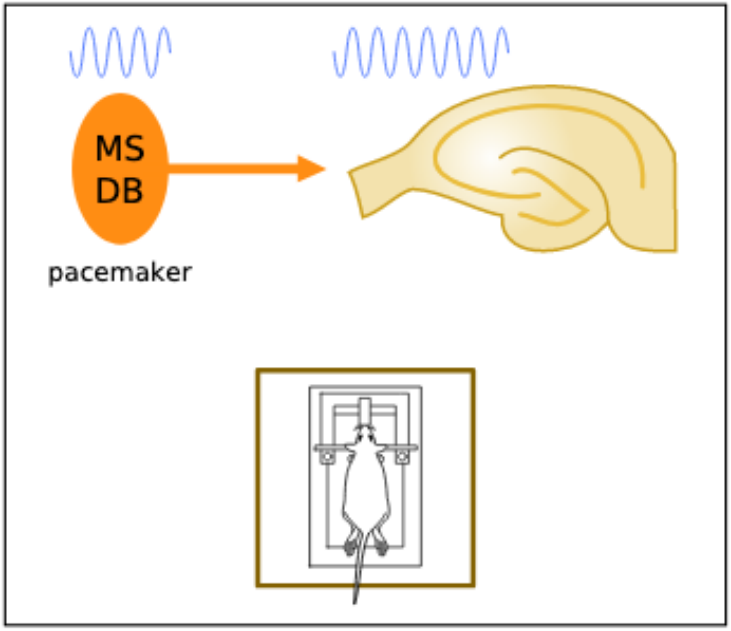
Hippocampal theta has been linked to numerous behavioral correlates

- orienting
- attention
- decision making
- 'voluntary' movement
- navigation
- rapid eye movement (REM) sleep
- ...

Outline

Mechanisms of Theta Rhythmicity

The medial septum – diagonal band of Broca (MSDB) as a pacemaker



Petsche et al. (1962) *Clin. Neurophysiol.* 14, 202–11.

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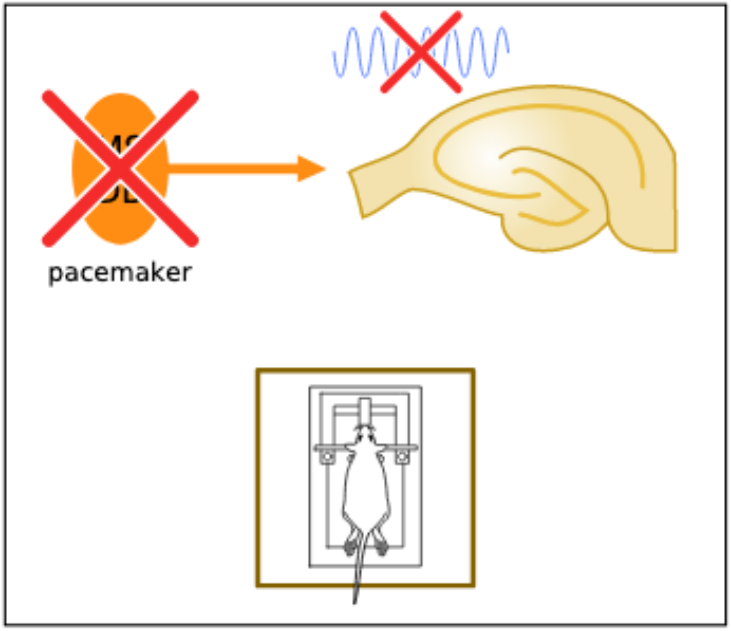
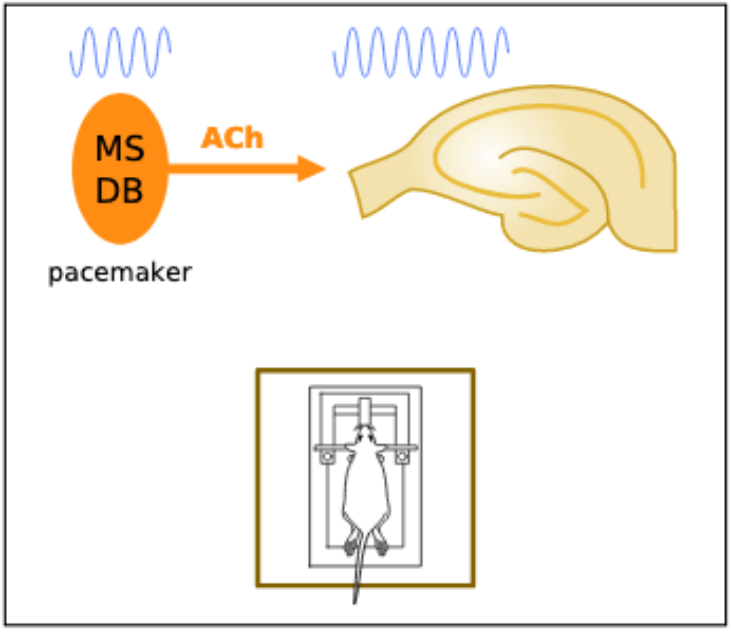


Petsche et al. (1962) *Clin. Neurophysiol.* 14, 202–11.

Mechanisms of Theta Rhythmicity

Two kinds of theta: atropine-sensitive vs atropine-resistant



Kramis et al. (1975) *Exp. Neurol.* 49, 58–85.

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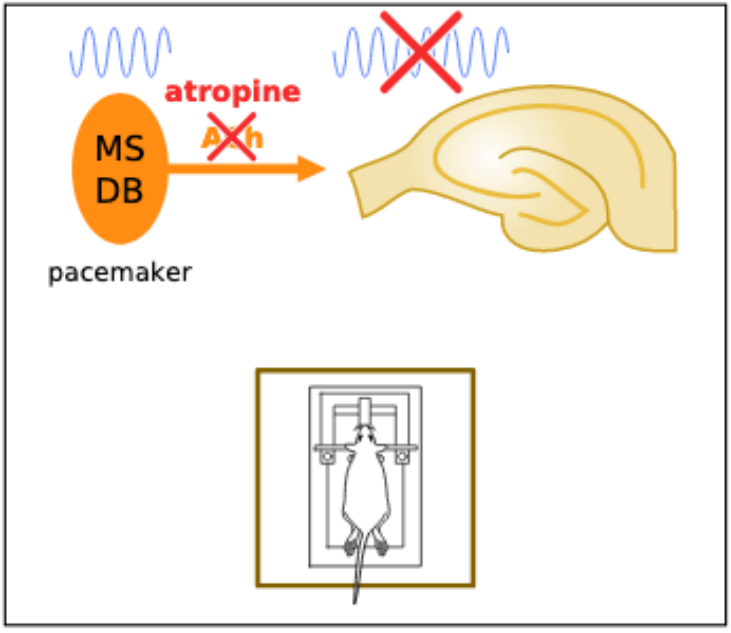

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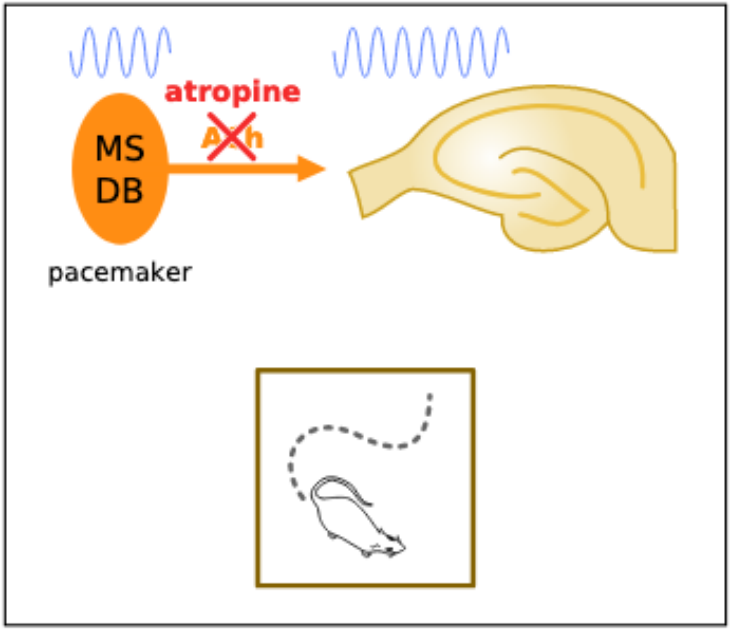
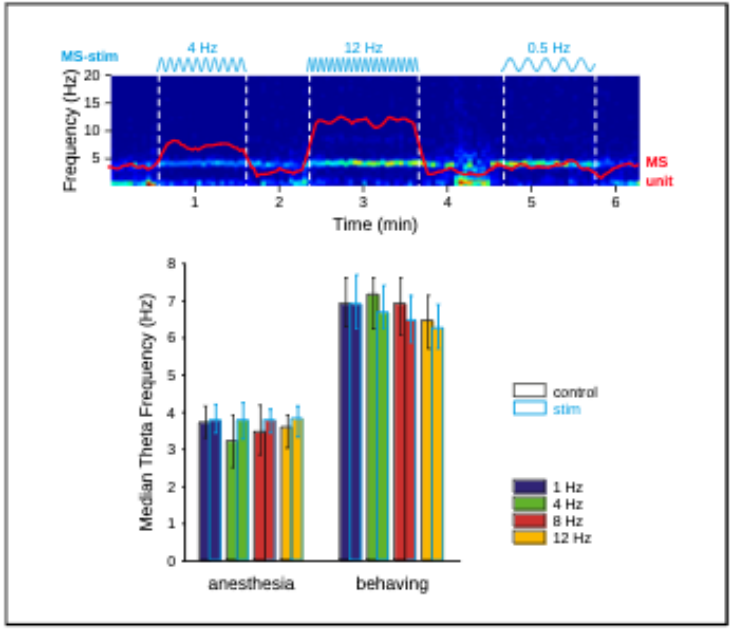


Kramis et al. (1975) *Exp. Neurol.* 49, 58–85.

Mechanisms of Theta Rhythmicity

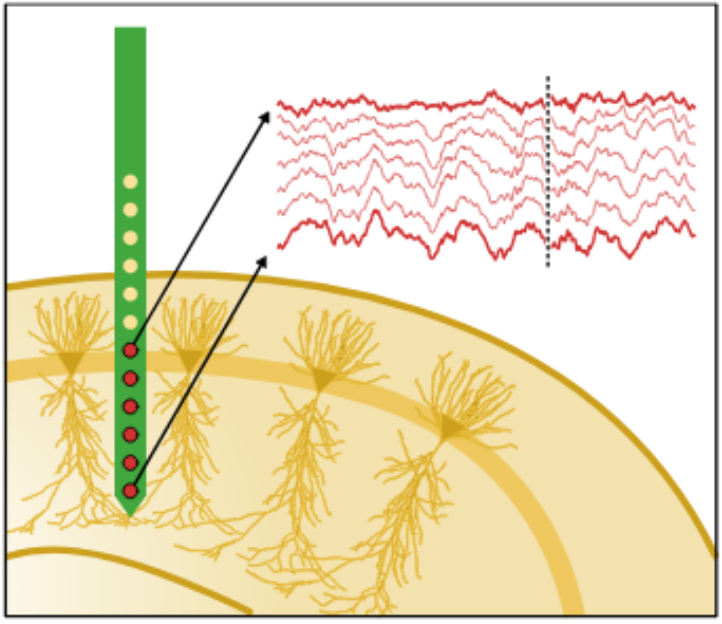
Optogenetic stimulation of septal ACh neurons does not entrain hippocampal theta



Vandecasteele et al. (2014) *PNAS* 111, 13535–40.

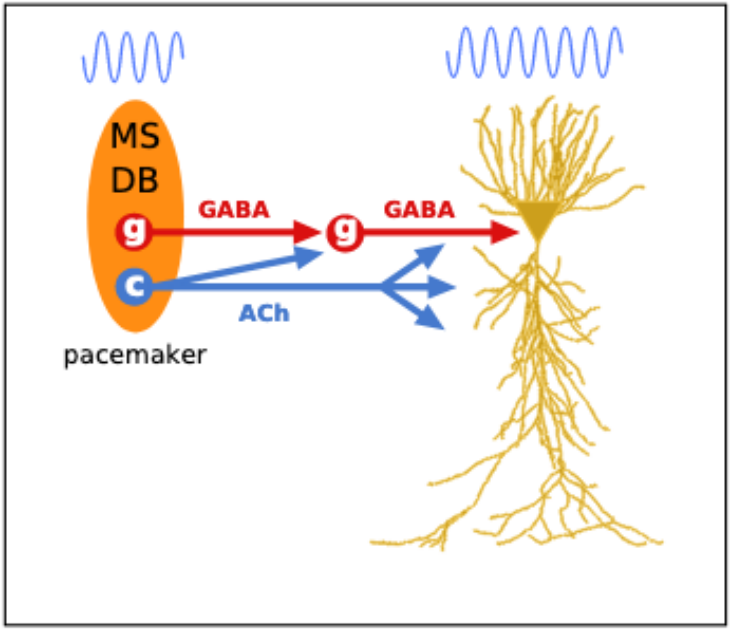
Mechanisms of Theta Rhythmicity

Theta amplitude increases and phase shifts from *oriens* to *lacunosum moleculare*



Mechanisms of Theta Rhythmicity

Entorhinal layer III inputs target *lacunosum moleculare*



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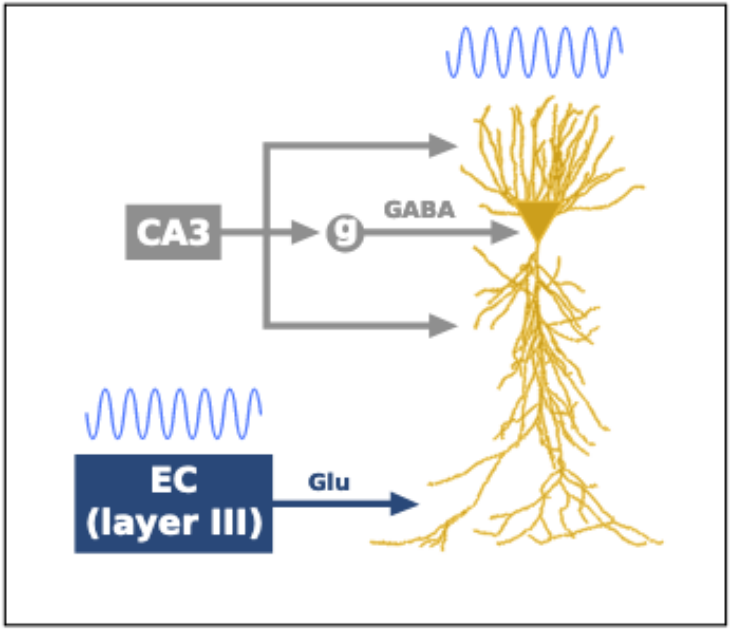
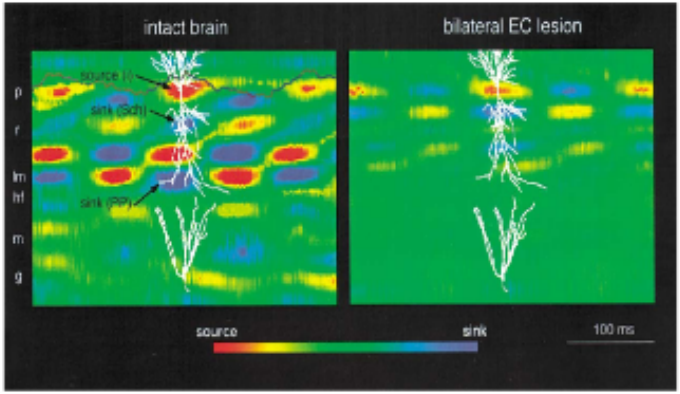


Mechanisms of Theta Rhythmicity

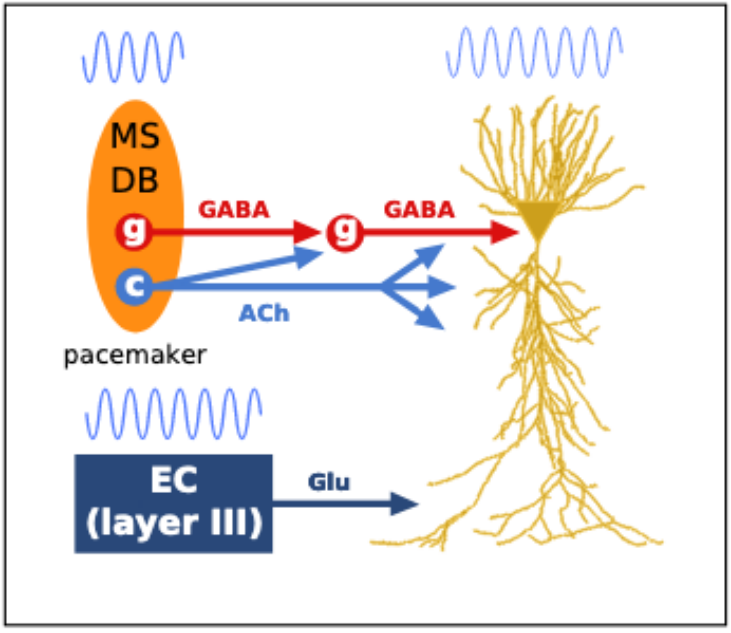
Lesion of the entorhinal cortex suppresses the current dipole in *lacunosum moleculare*



Kamondi et al. (1998) *Hippocampus* 8(3), 244–61.

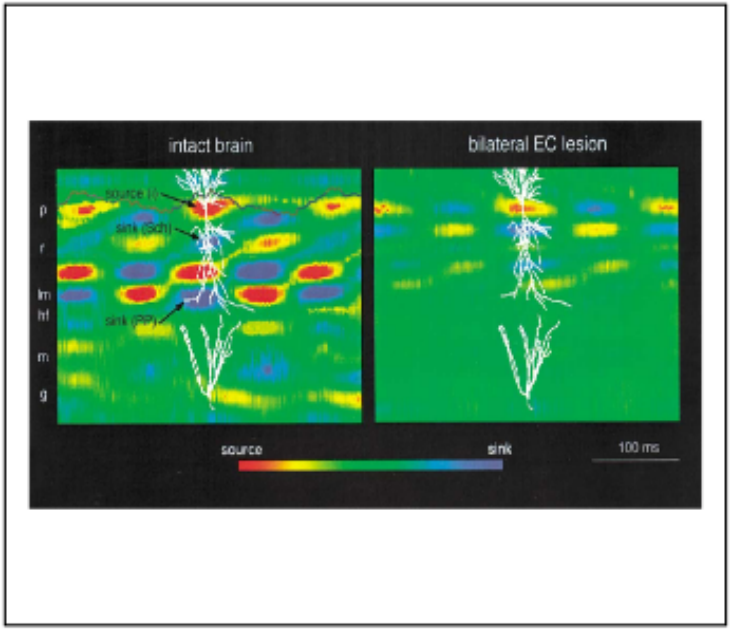
Mechanisms of Theta Rhythmicity

The 'classical' model



Mechanisms of Theta Rhythmicity

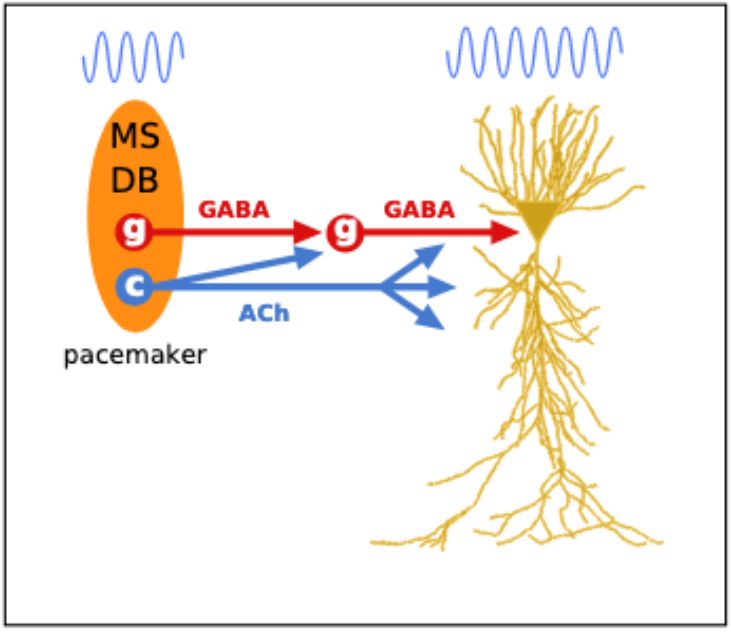
Lesion of the entorhinal cortex spares the current dipole in *pyramidale-radiatum*



Kamondi et al. (1998) *Hippocampus* 8(3), 244–61.

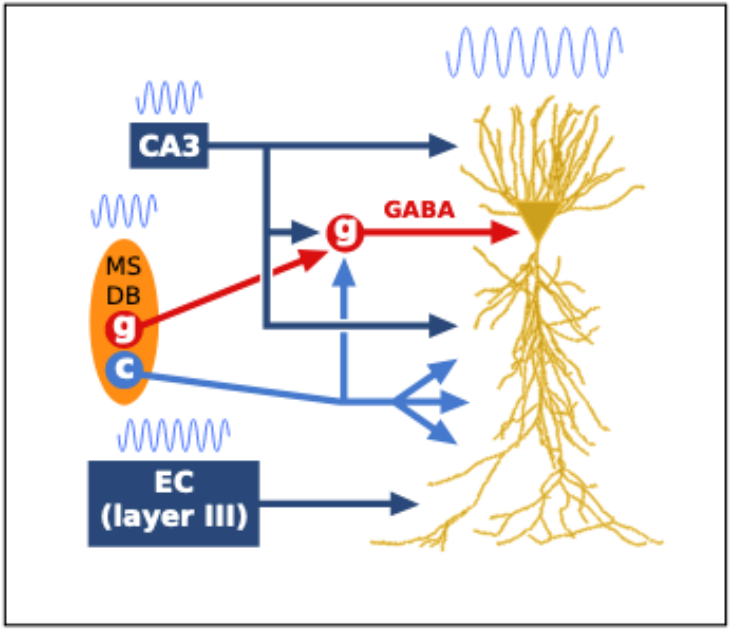
Mechanisms of Theta Rhythmicity

The active contribution of GABA is unclear, ACh targets all layers



Mechanisms of Theta Rhythmicity

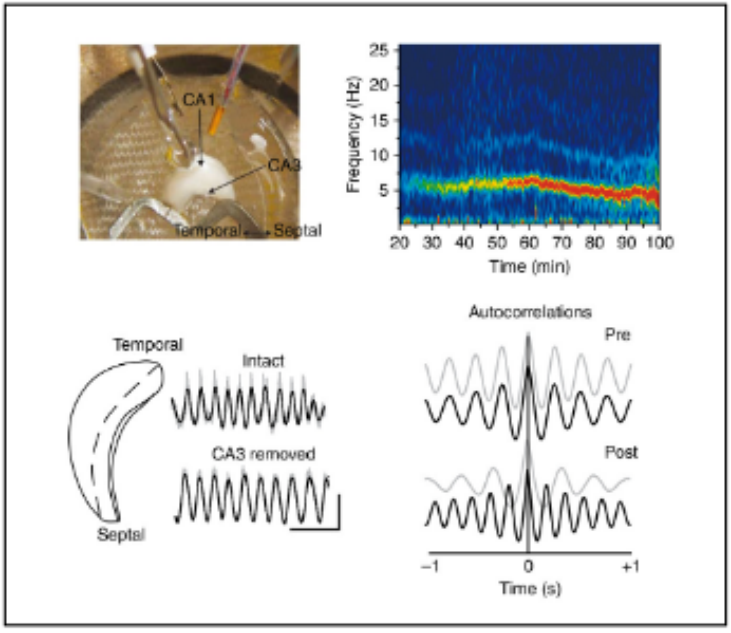
CA3 may be an intrahippocampal theta oscillator



Buzsáki (2002) *Neuron* 33(3), 325–40.

Mechanisms of Theta Rhythmicity

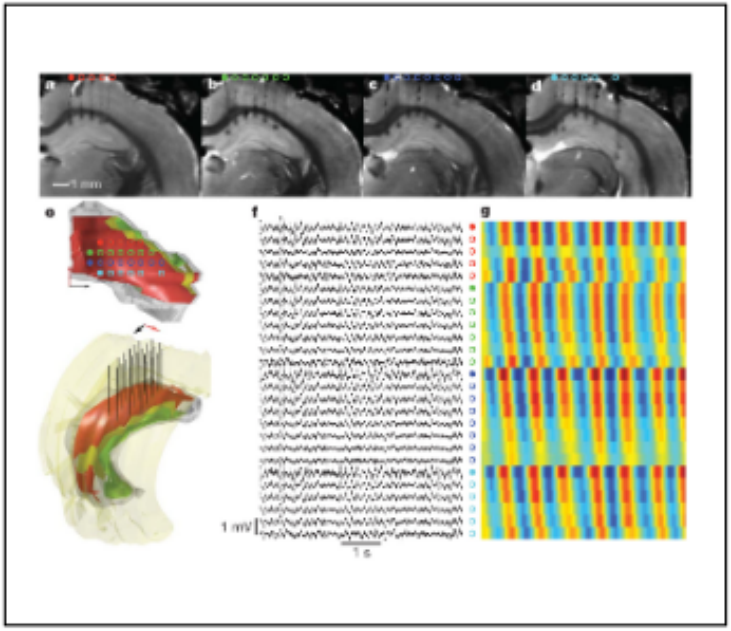
CA1 can generate theta oscillations in isolation



Goutagny et al. (2009) *Nature Neurosci.* 12(12), 1491–3.

Mechanisms of Theta Rhythmicity

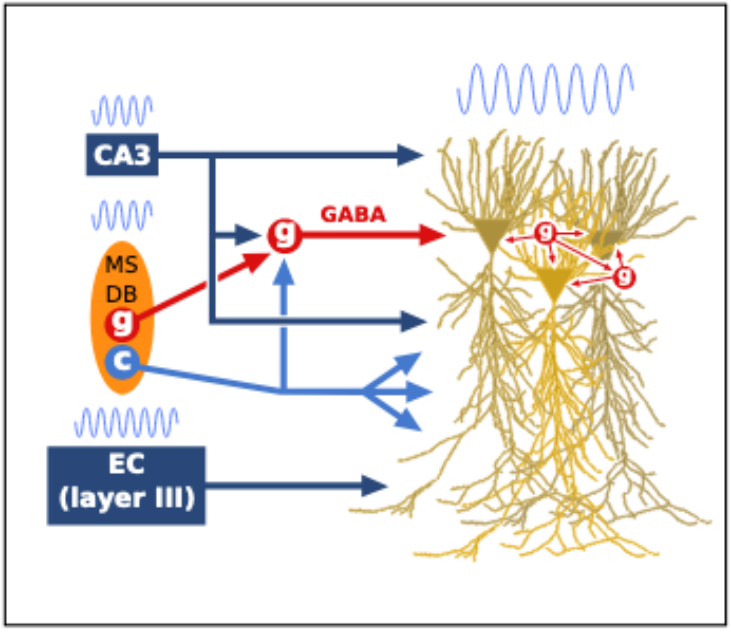
Theta oscillations are travelling waves



Lubenov et al. (2009) *Nature* 459(7246), 534–9.

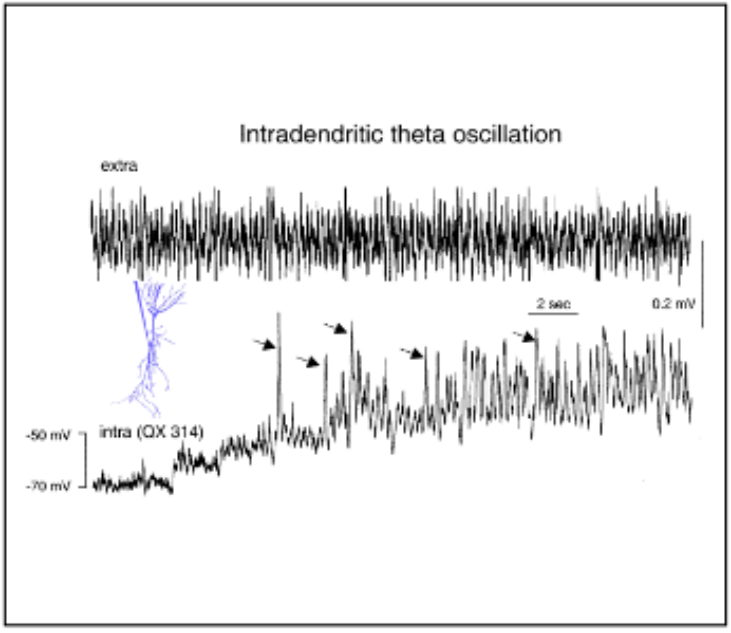
Mechanisms of Theta Rhythmicity

CA1 network properties contribute to theta oscillations



Mechanisms of Theta Rhythmicity

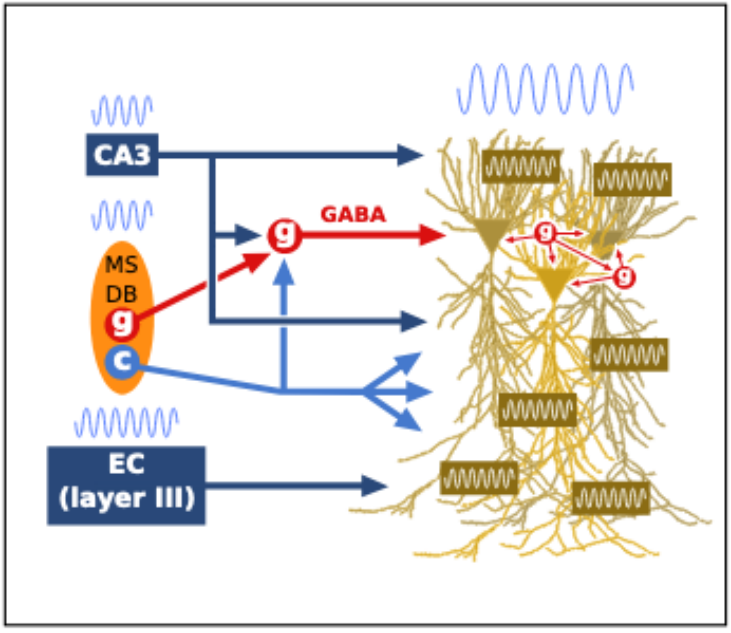
CA1 pyramidal cell dendrites can sustain subthreshold theta oscillations



Kamondi et al. (1998) *Hippocampus* 8(3), 244–61.

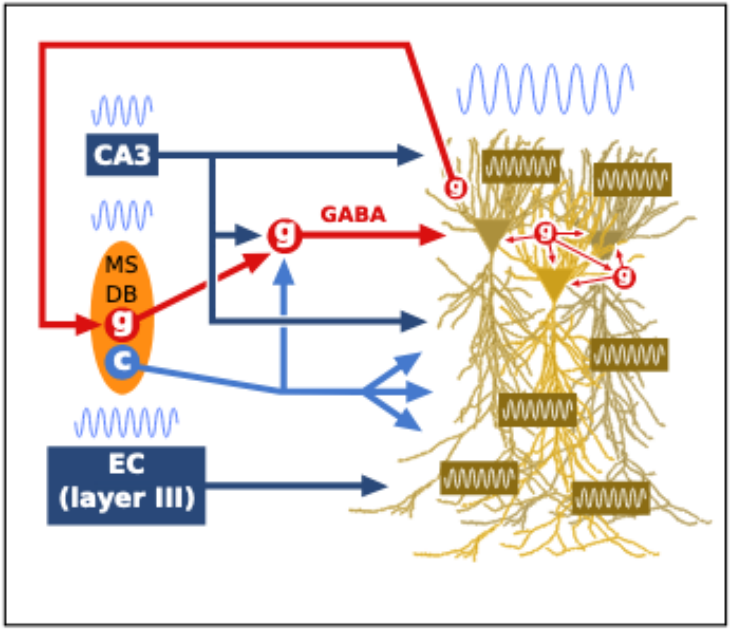
Mechanisms of Theta Rhythmicity

Intrinsic cellular mechanisms contribute to theta oscillations



Mechanisms of Theta Rhythmicity

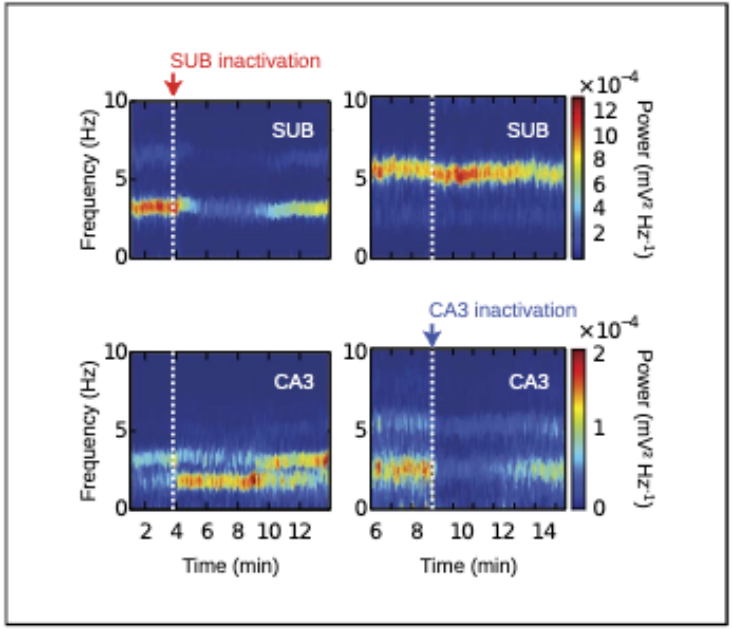
Hippocampo-septal cells provide reciprocal connections to the MSDB



Freund and Buzsáki (1996) *Hippocampus* 6(4), 347–470.

Mechanisms of Theta Rhythmicity

Backward theta propagation within the hippocampus

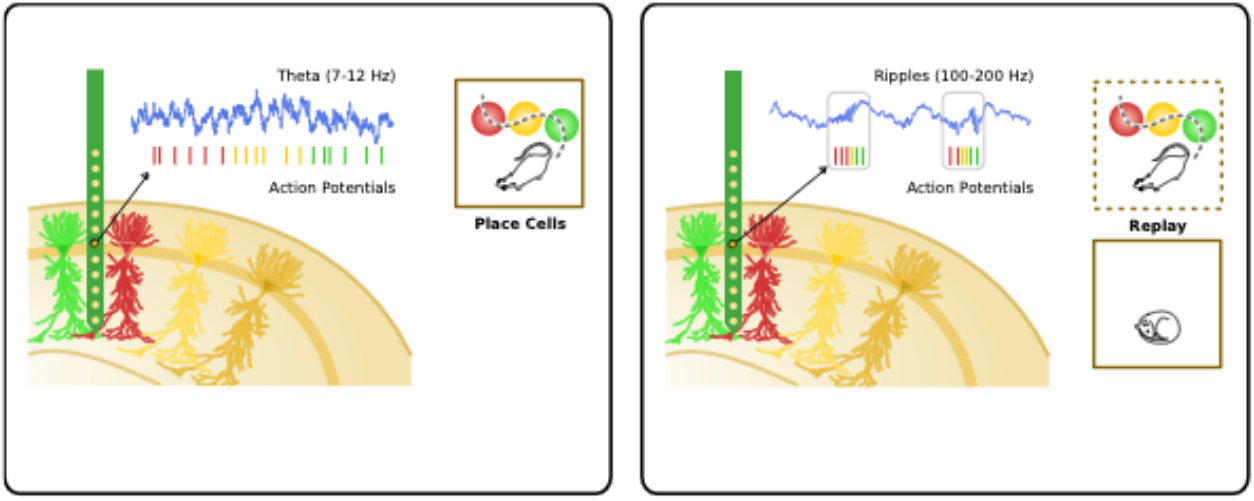


Jackson et al. (2014) *Nature Neurosci.* 17(10), 1362–70.

Outline

Theta Sequences

Spatial trajectories are represented at the theta time scale



Encoding

Consolidation

Theta Sequences

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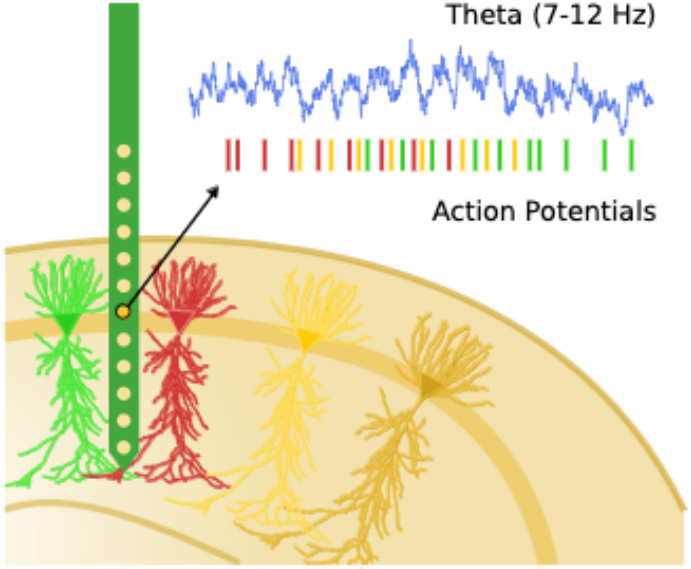

Place Cells

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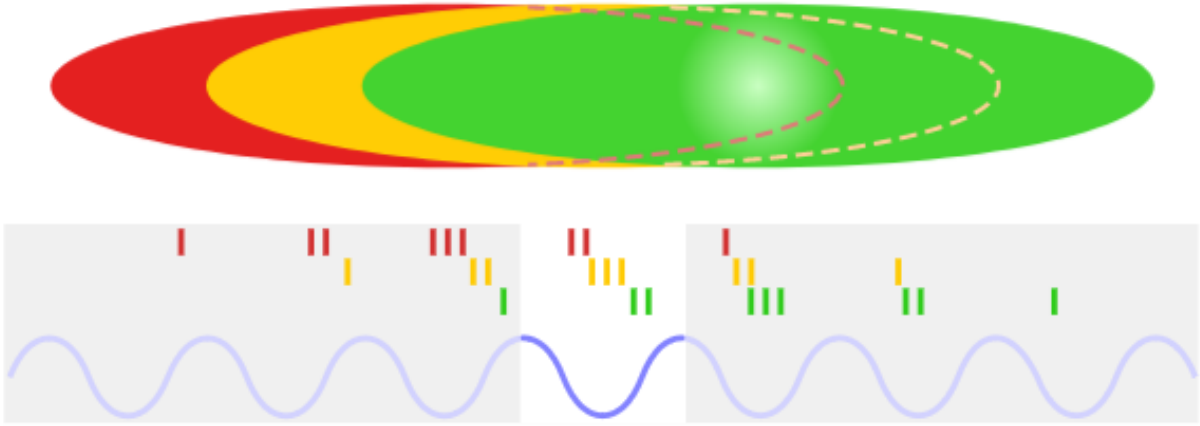

One Sequence per Cycle

Theta Sequences

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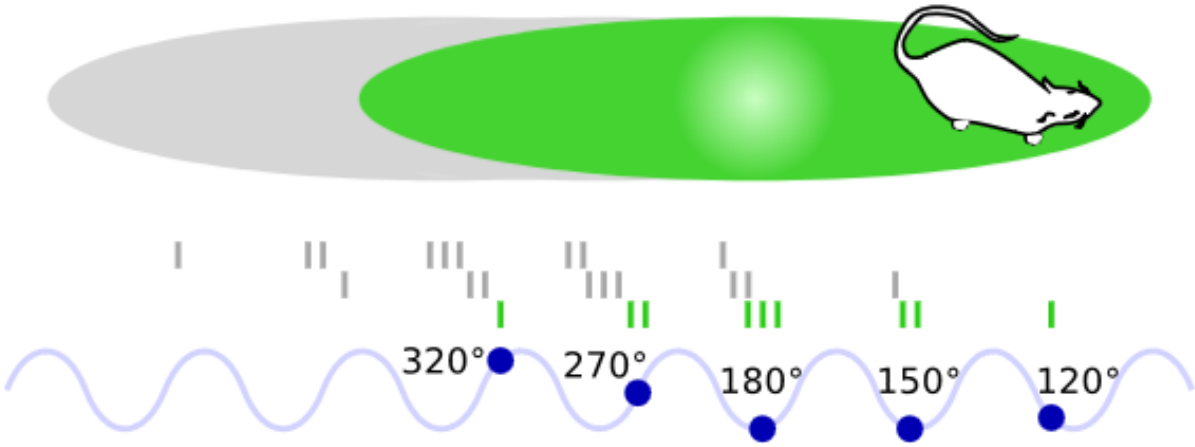

O'Keefe & Recce (1993) *Hippocampus* 3(3):317–30.

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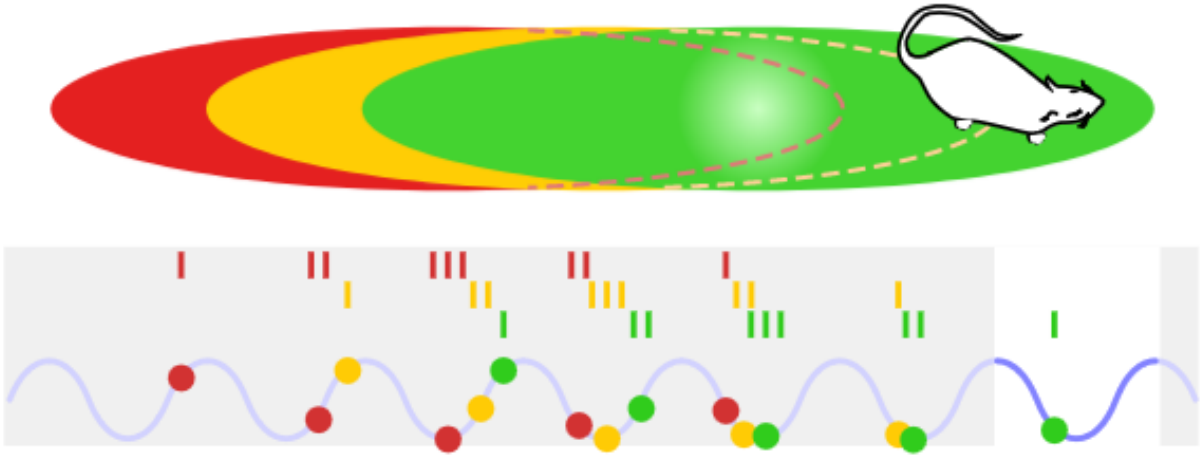

Skaggs et al. (1996) *Hippocampus* 6(2):149–72, Dragoi & Buzsáki (2006) *Neuron* 50(1):145–57.

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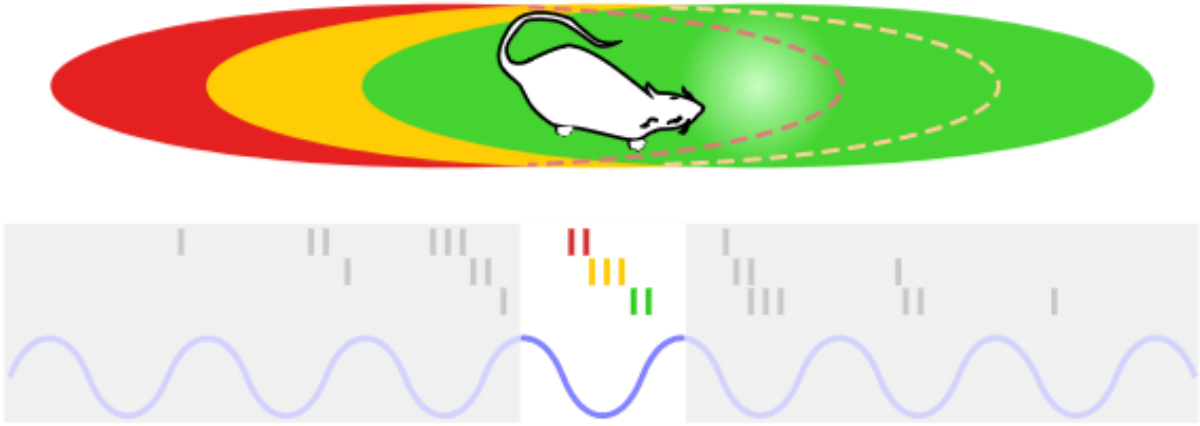

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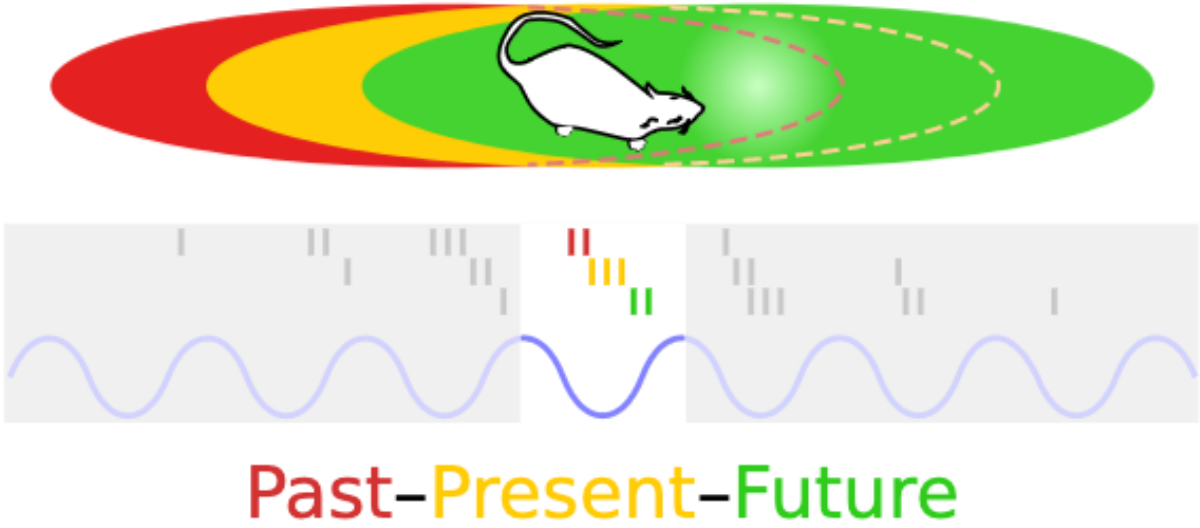

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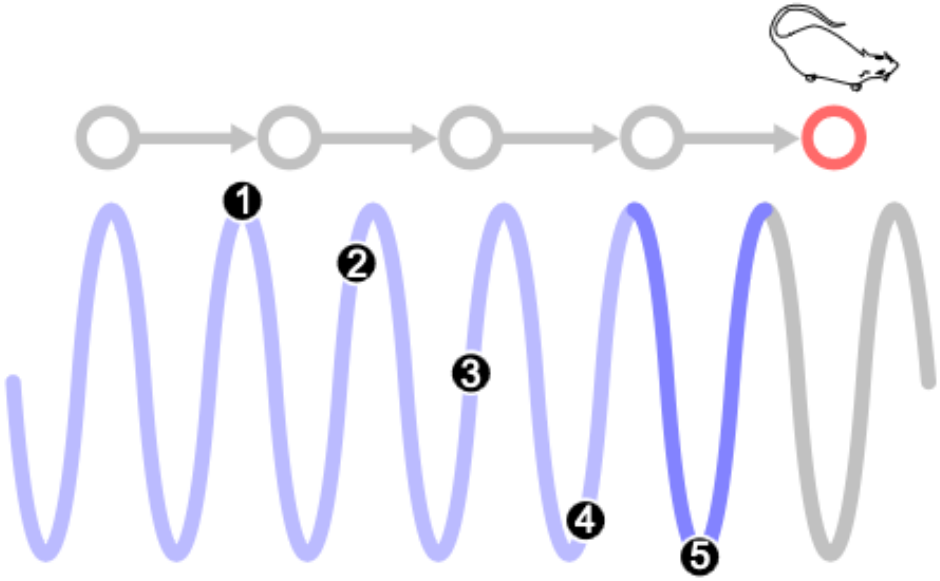
Outline

Model I. Detuned Oscillators

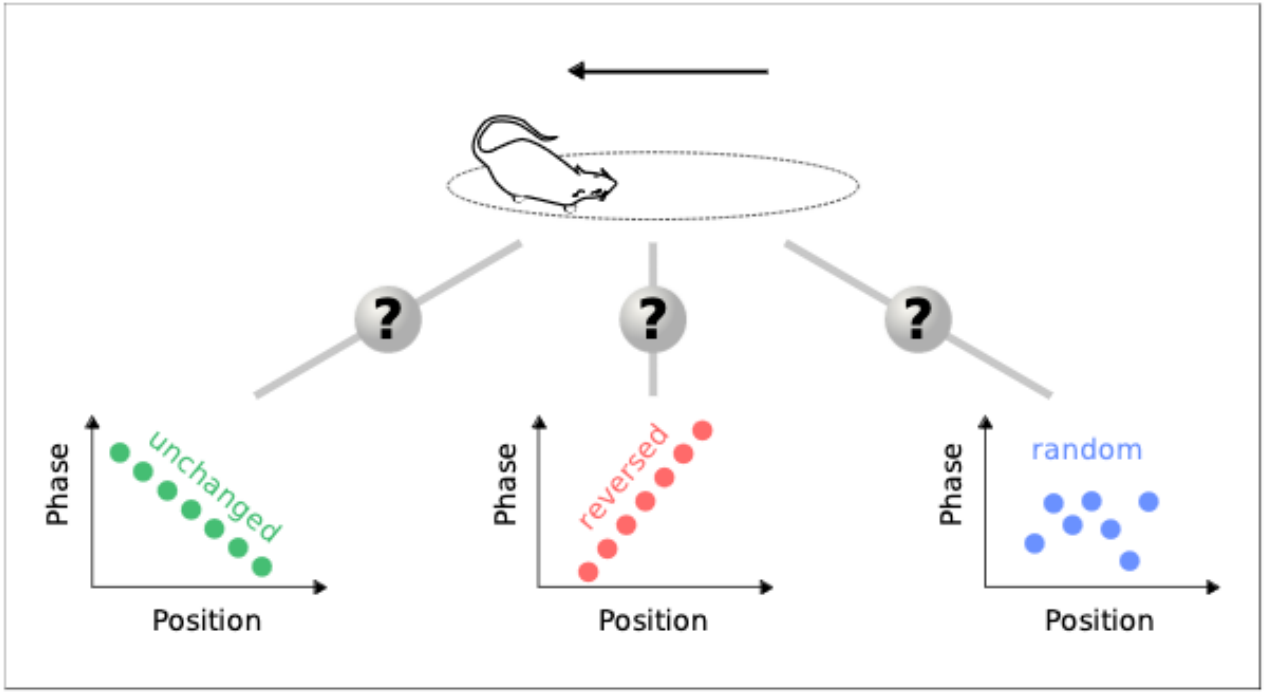
Interactions between two detuned oscillators



Outline

Backward Movement: Rationale

Is the relation between phase and position modified during backward movement?



Cei et al. (2014) *Nature Neurosci.* 5(17), 719–24.

Perturbation of the hippocampal-entorhinal system

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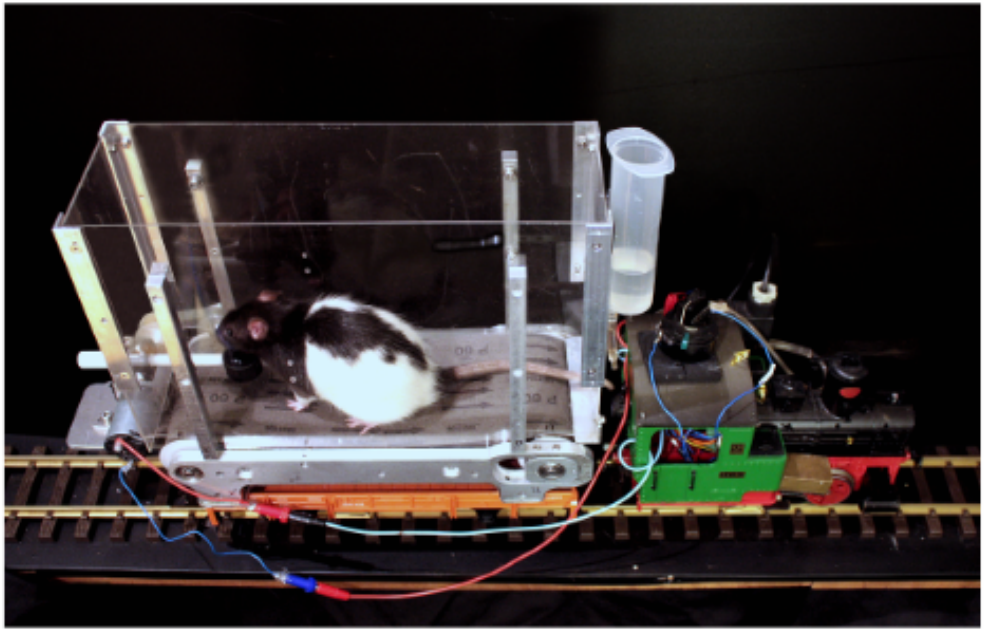

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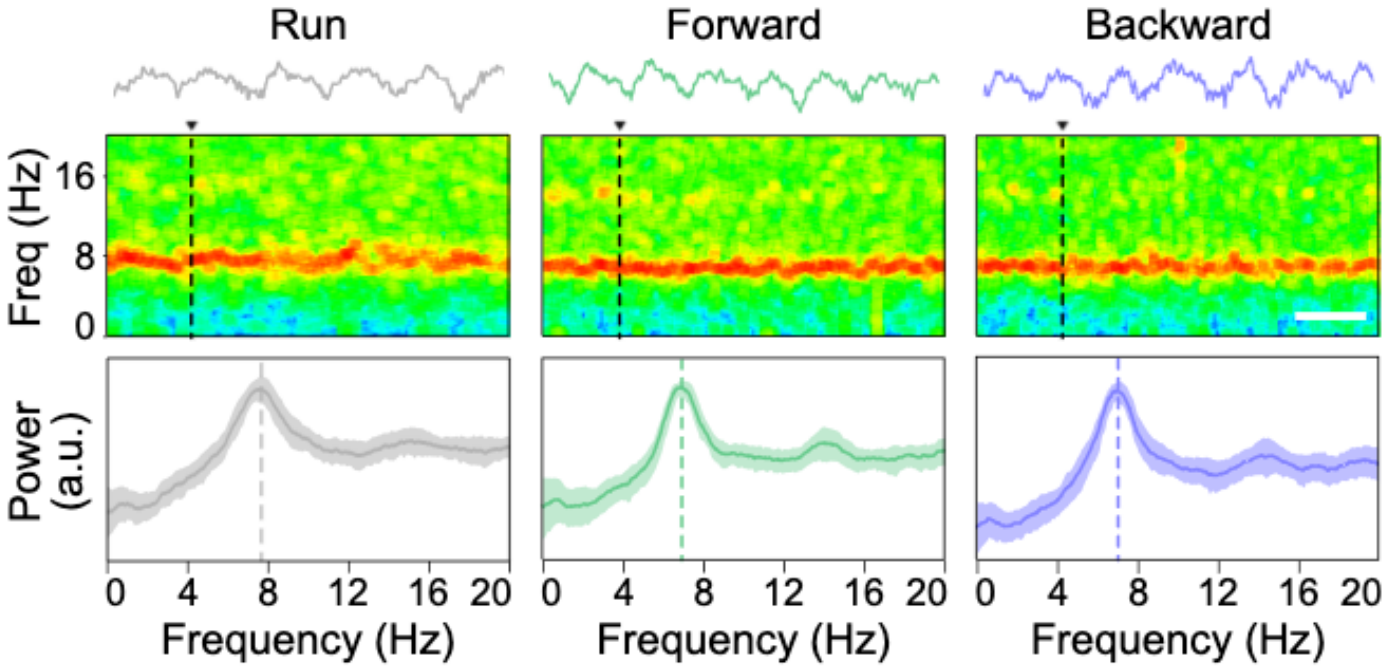
Theta is Maintained on the Train

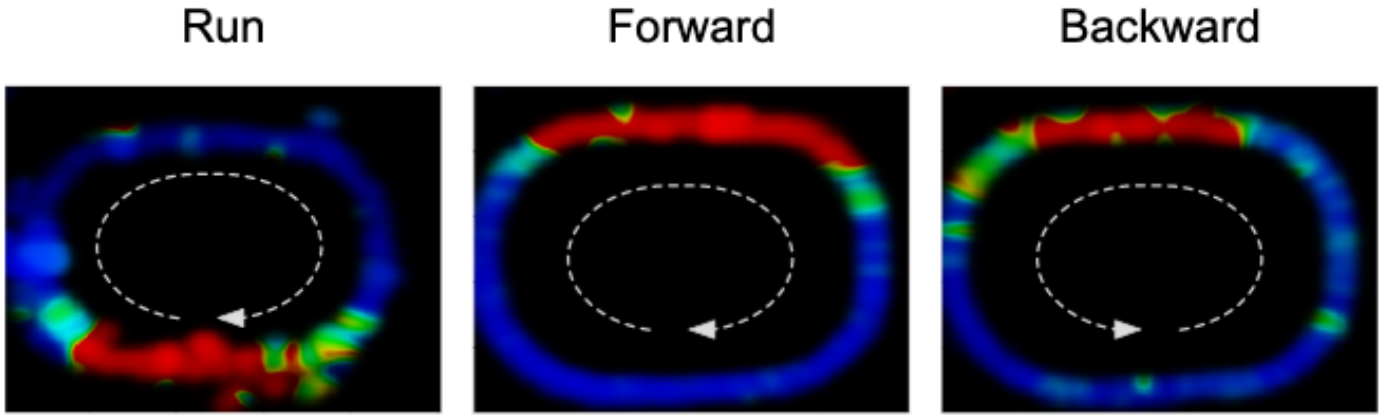
Theta frequency and power do not change with movement direction



Cei et al. (2014) *Nature Neurosci.* 5(17), 719–24.

Firing Fields do not Undergo Random Remapping

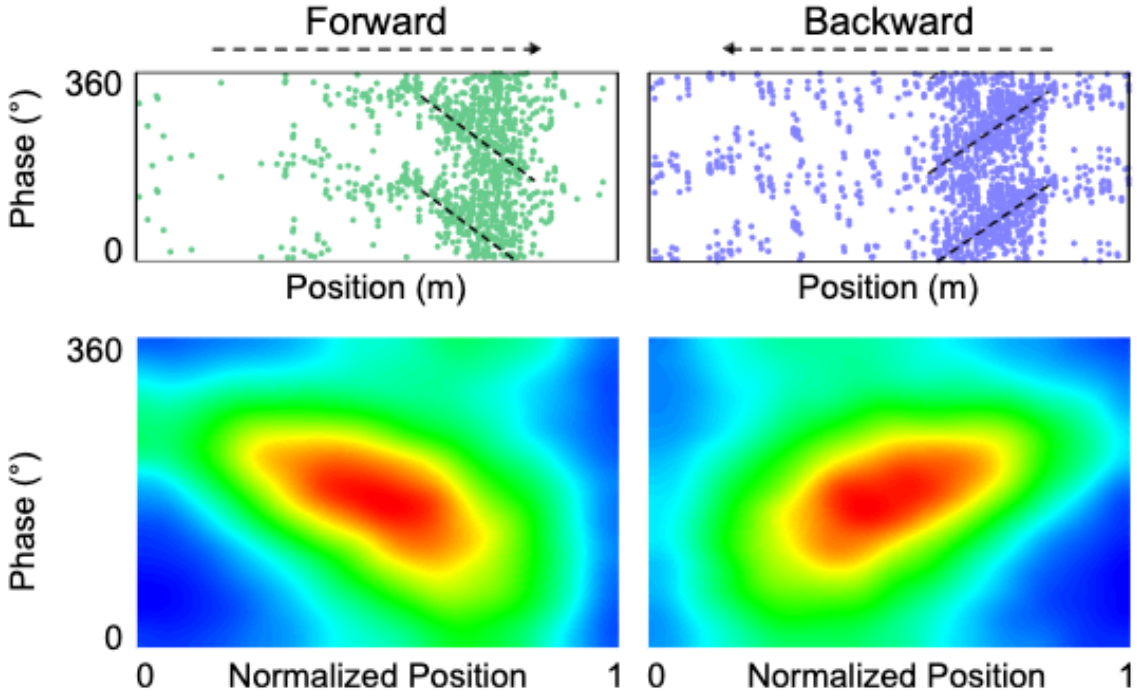
Testing for random remapping during forward vs backward movement



Cei et al. (2014) *Nature Neurosci.* 5(17), 719–24.

Reversed Phase Precession Slopes

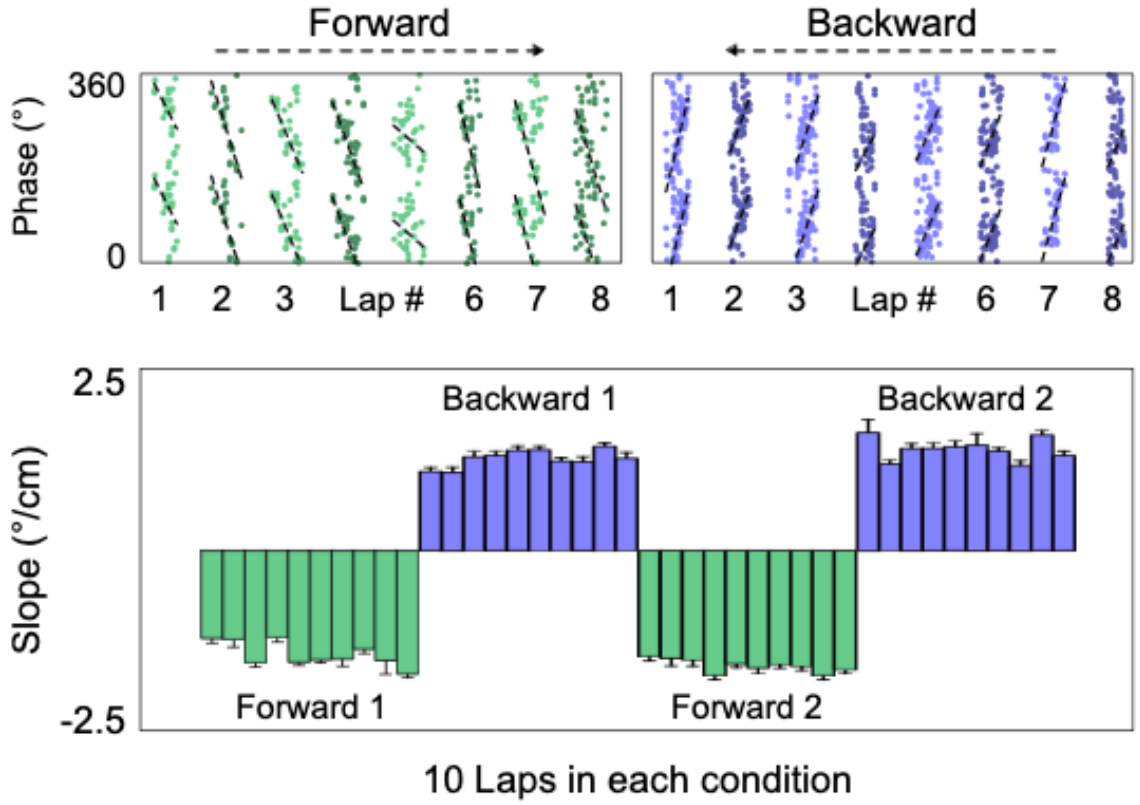
Phase decreases as the animal moves through the fields



Cei et al. (2014) *Nature Neurosci.* 5(17), 719–24.

Slopes do not Progressively Change with Experience

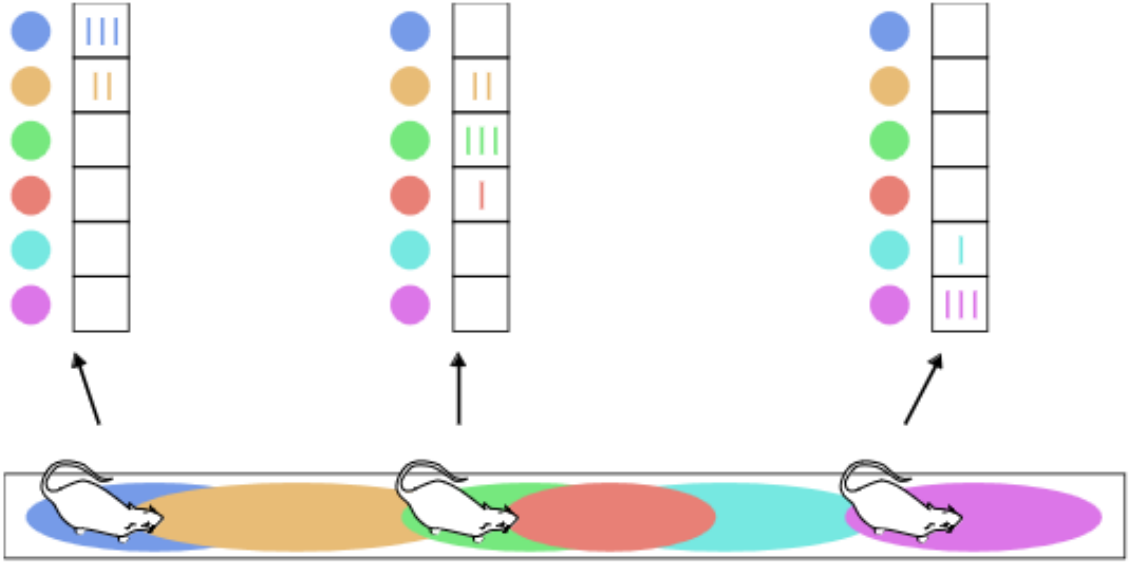
Slopes abruptly change between forward and backward movement



Cei et al. (2014) *Nature Neurosci.* 5(17), 719–24.

Reversed Theta Sequences

Bayesian reconstruction of ongoing trajectory at theta time scale



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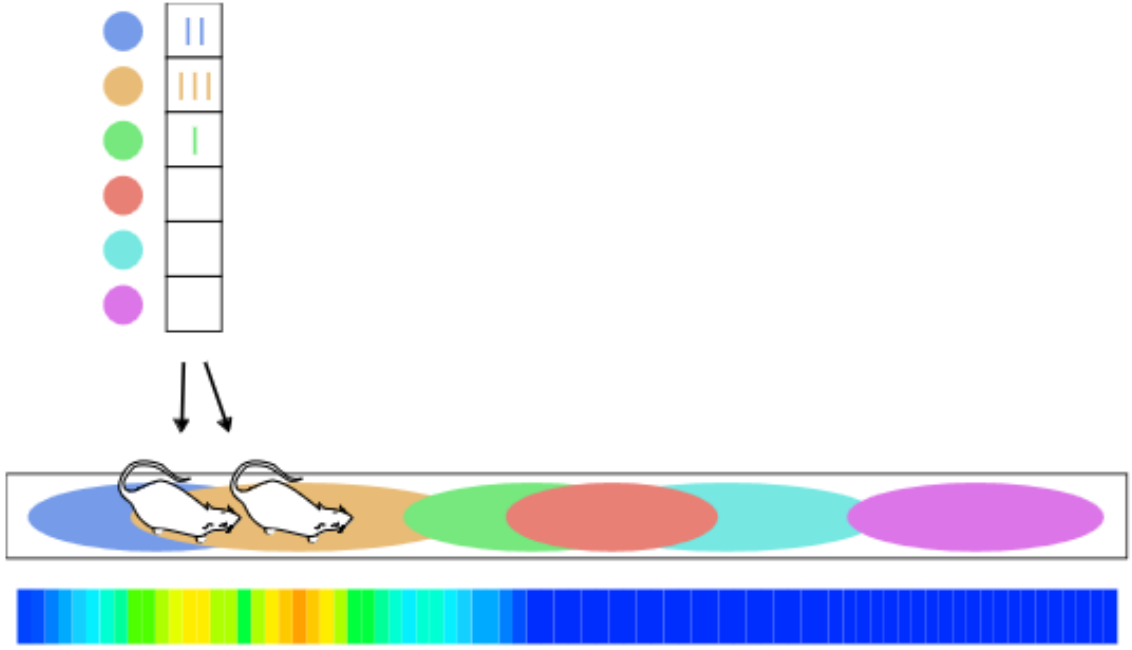

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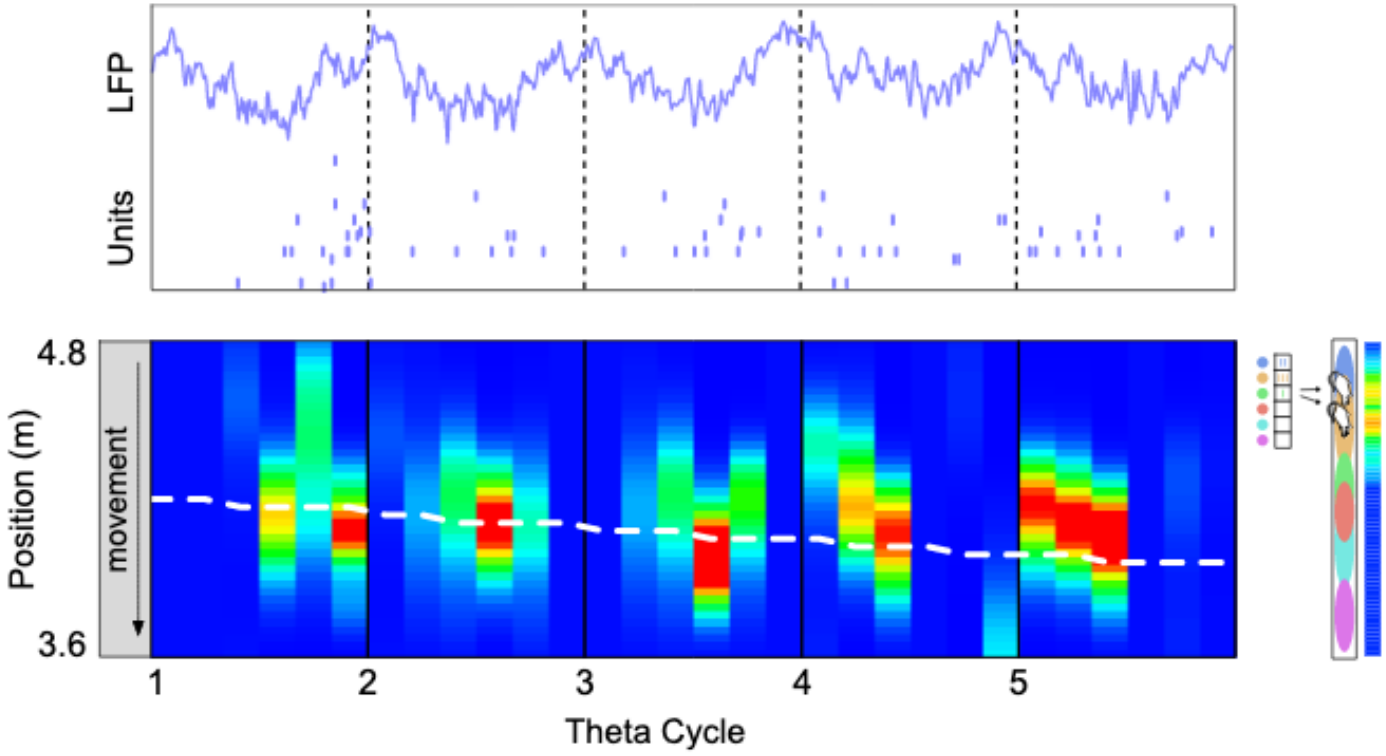

Cei et al. (2014) *Nature Neurosci.* 5(17), 719–24.

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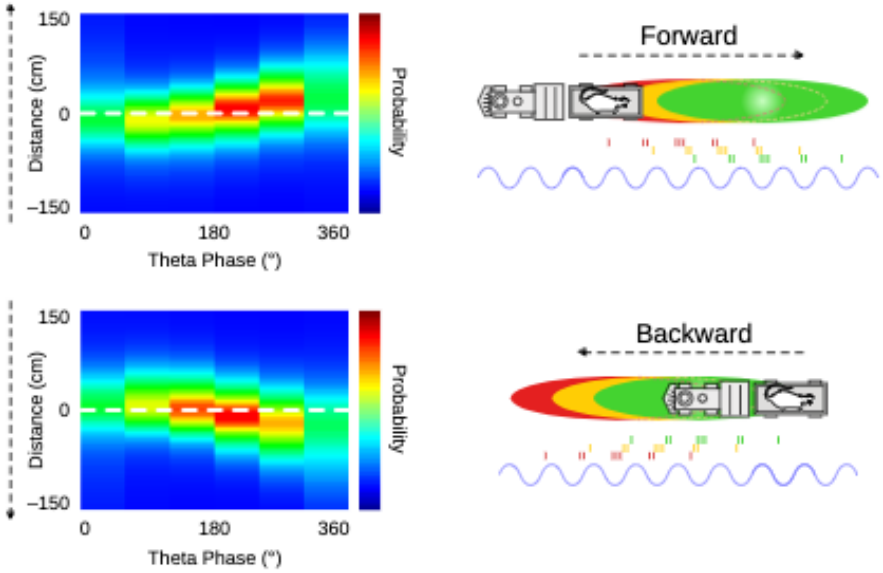
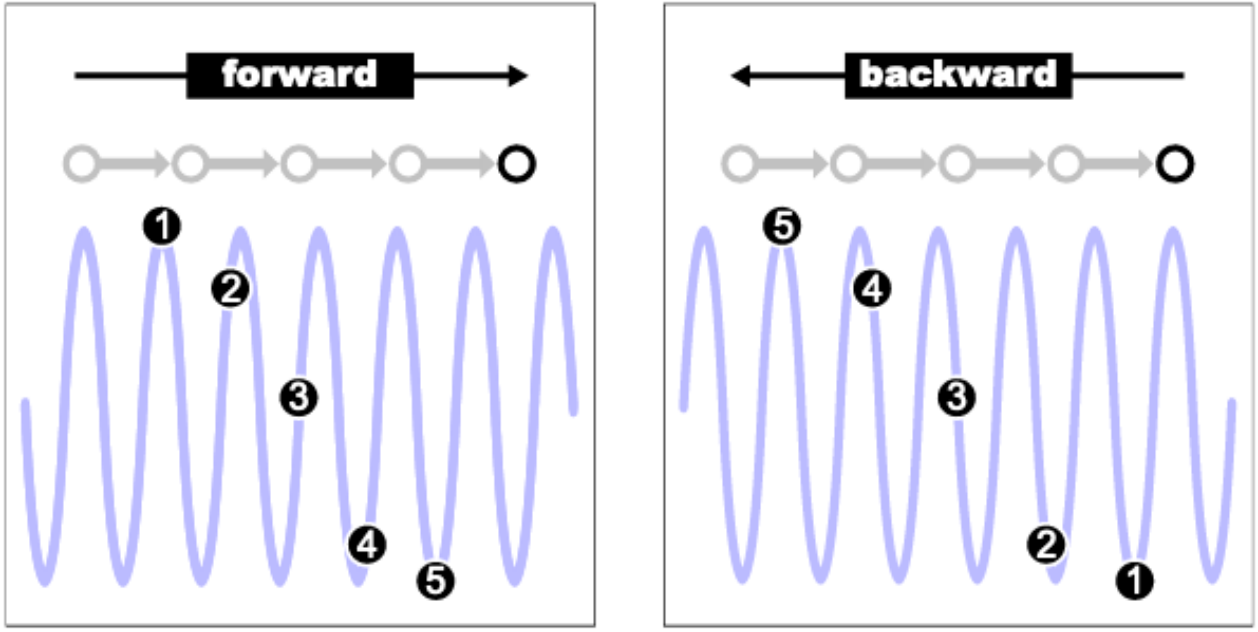


Cei et al. (2014) *Nature Neurosci.* 5(17), 719–24.

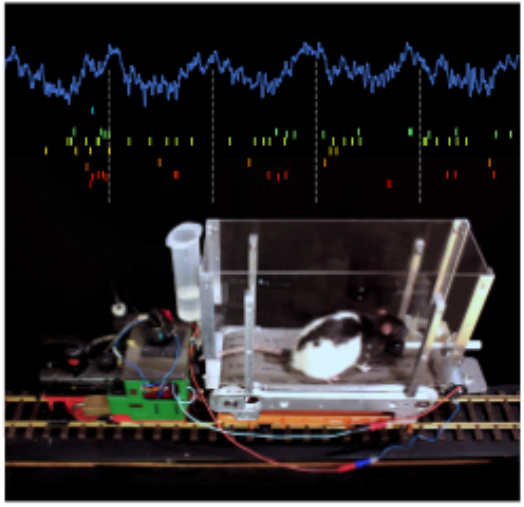
Theoretical Predictions

Network connectivity: unchanged phase precession slopes



Cei et al. (2014) *Nature Neurosci.* 5(17), 719–24.

Conclusion



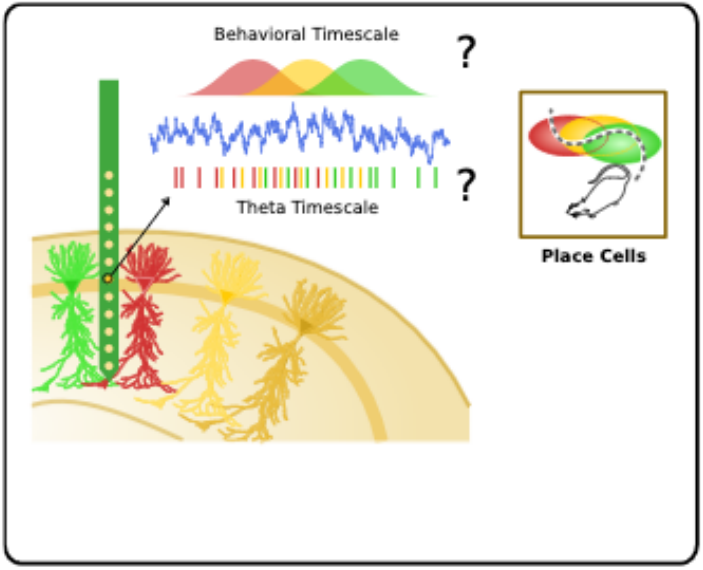
Hippocampal cell assemblies can **coordinate their timing at a very fine timescale**, and are not controlled by locomotor signals. Head direction cells cannot account for sequence direction. These results **challenge most computational models**.

- Maurer et al. (2014) *J Neurosci*

Outline

Theta Sequences for Memory Encoding

Are theta sequences necessary for sleep replay?



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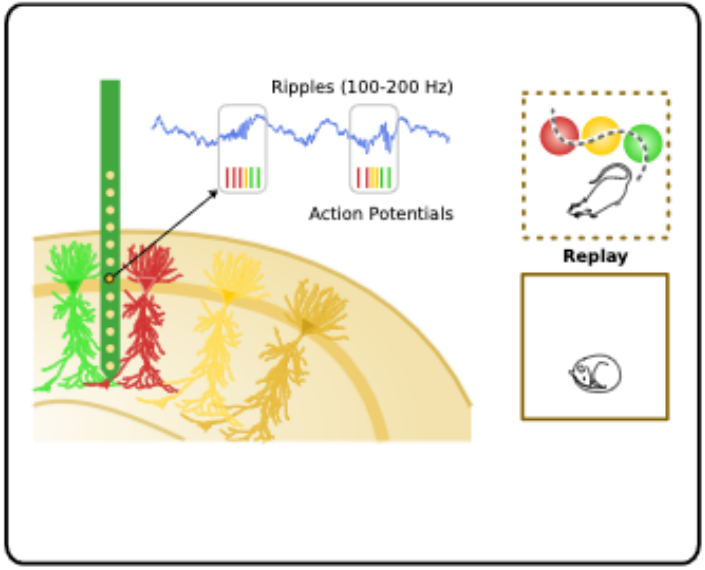

Consolidation

Bittner et al. (2017) *Science* 357(6355):1033–6, Skaggs et al. (1996) *Hippocampus* 6(2):149–72

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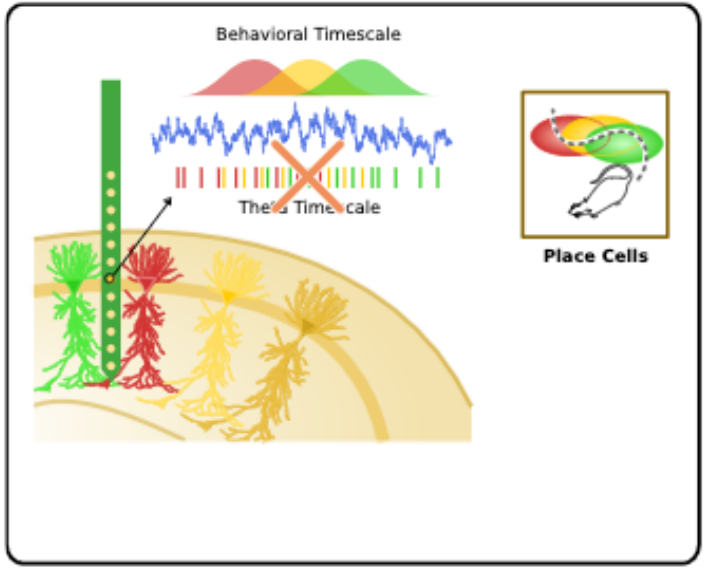

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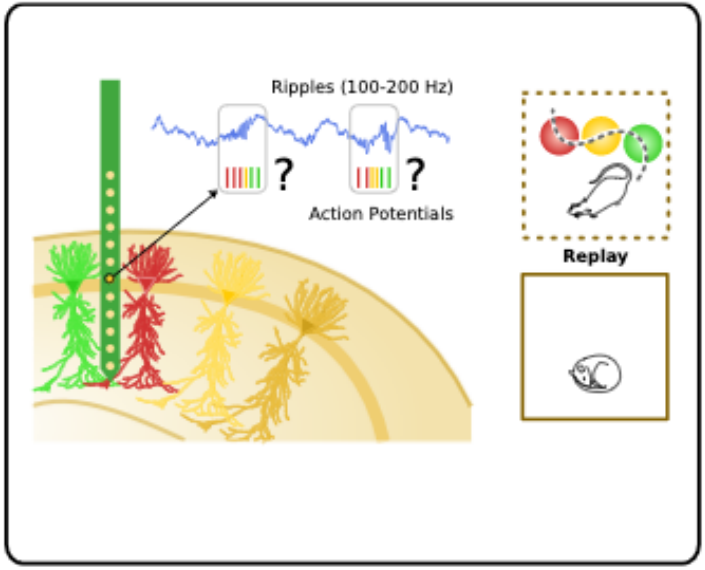

Consolidation

Drieu, Todorova and Zugaro (2018) *Science* 362(6415):675–679

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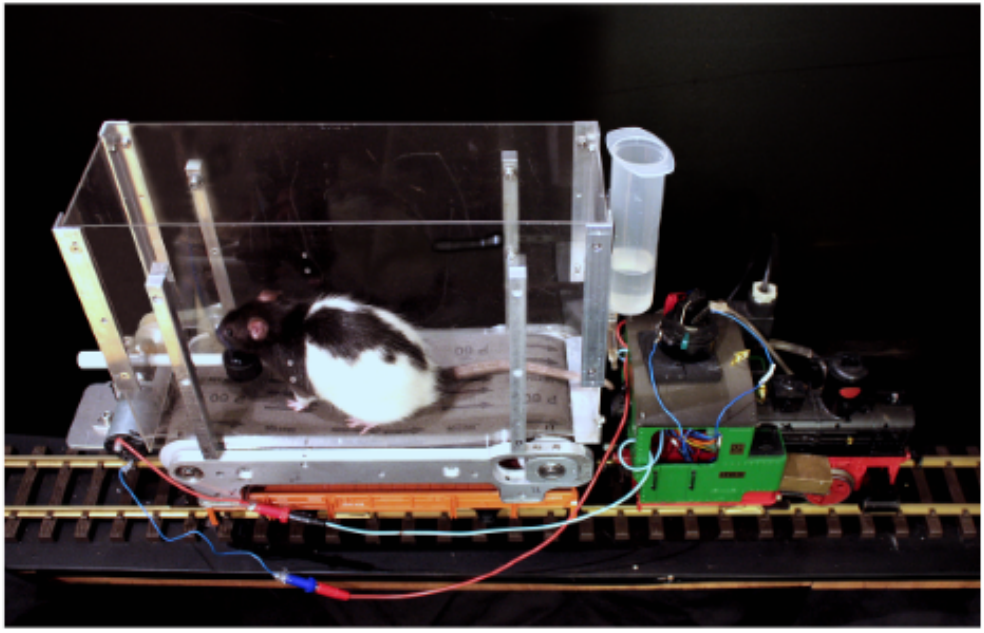

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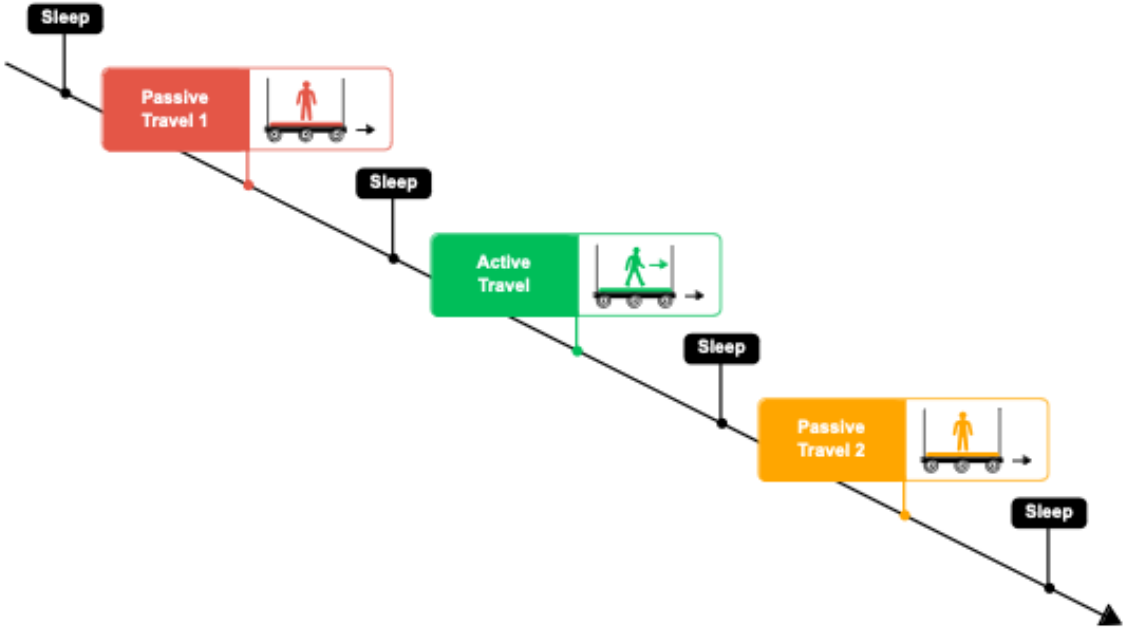

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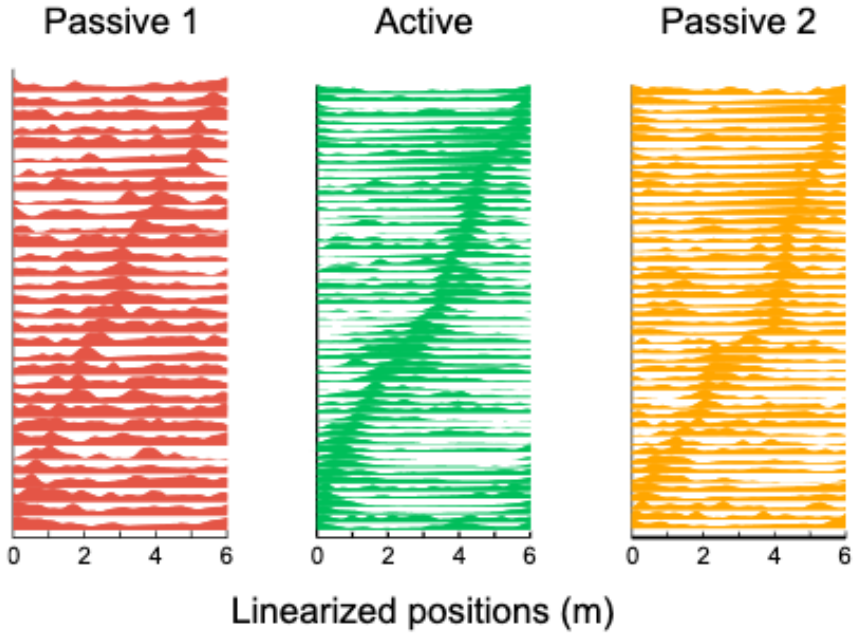

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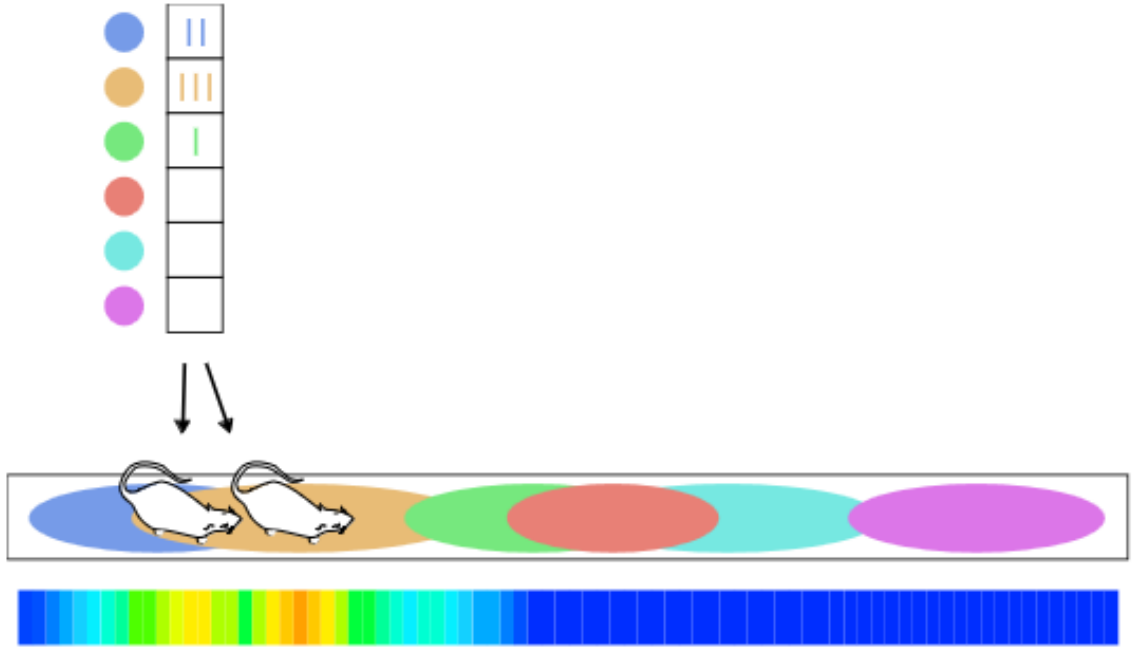

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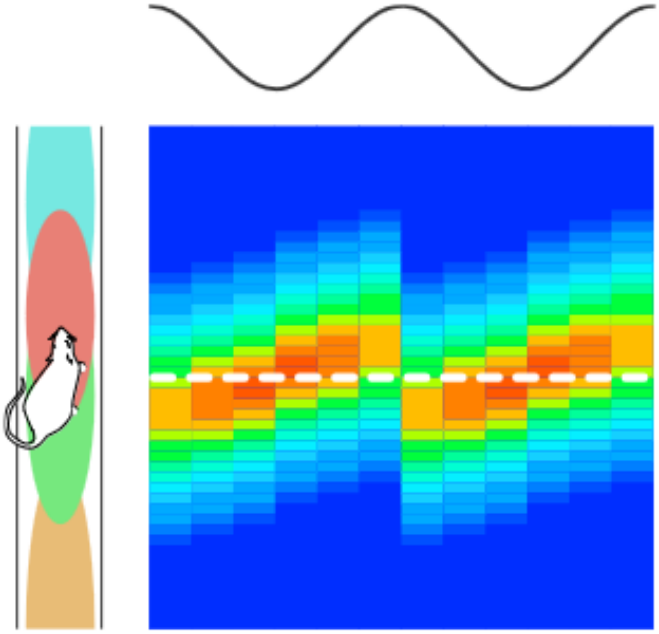

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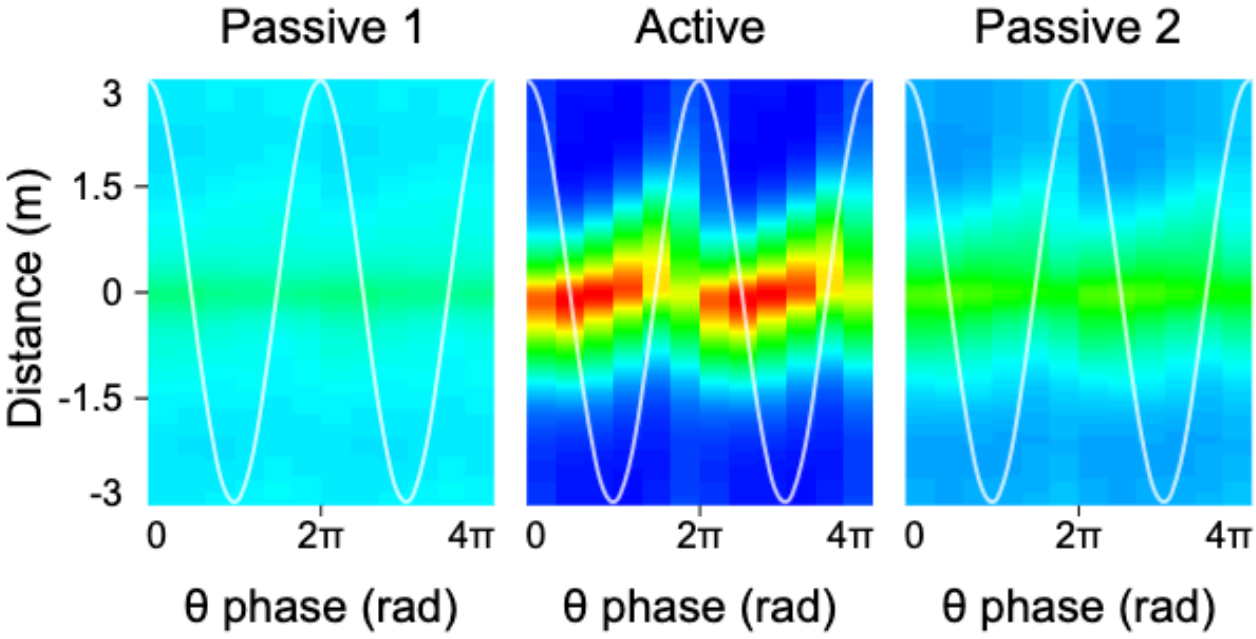

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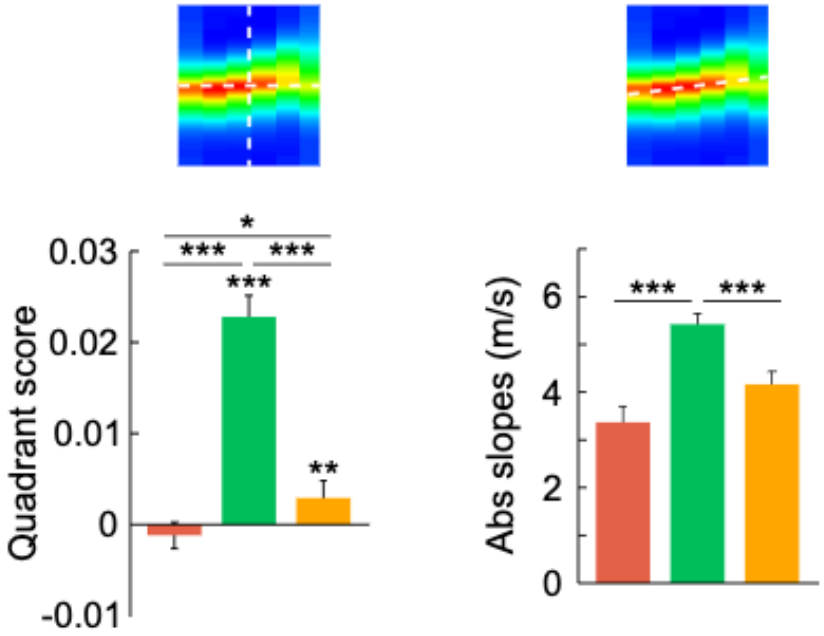

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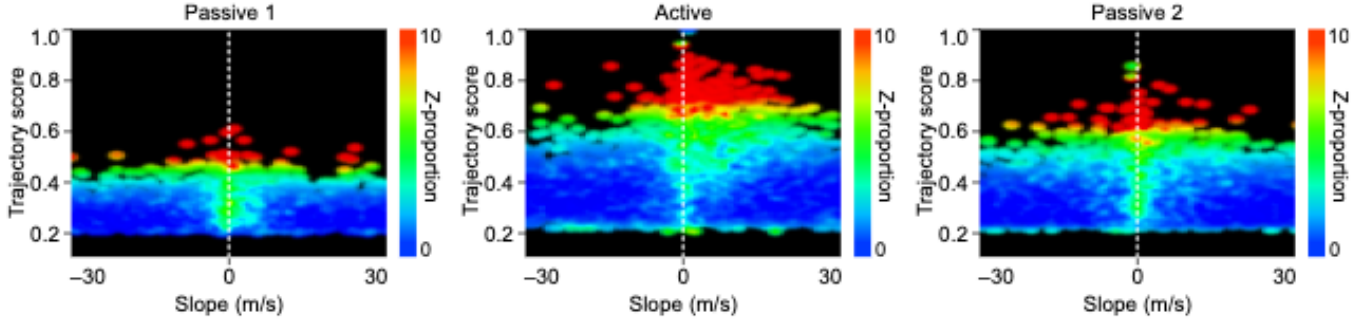

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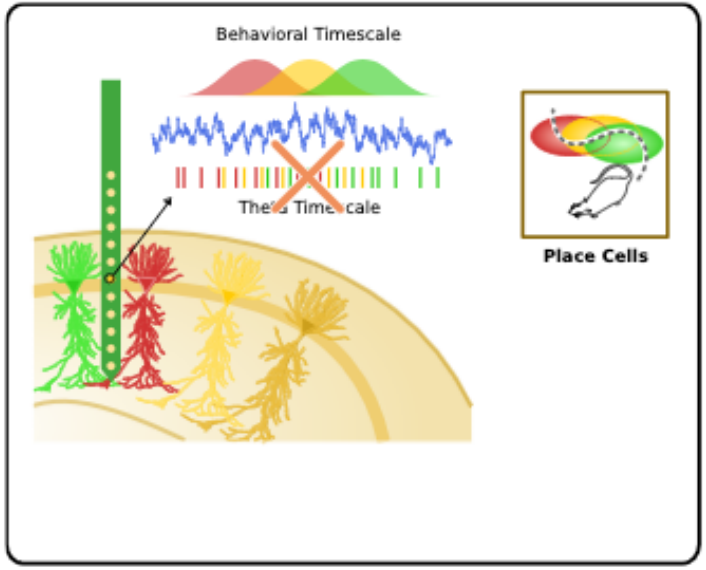
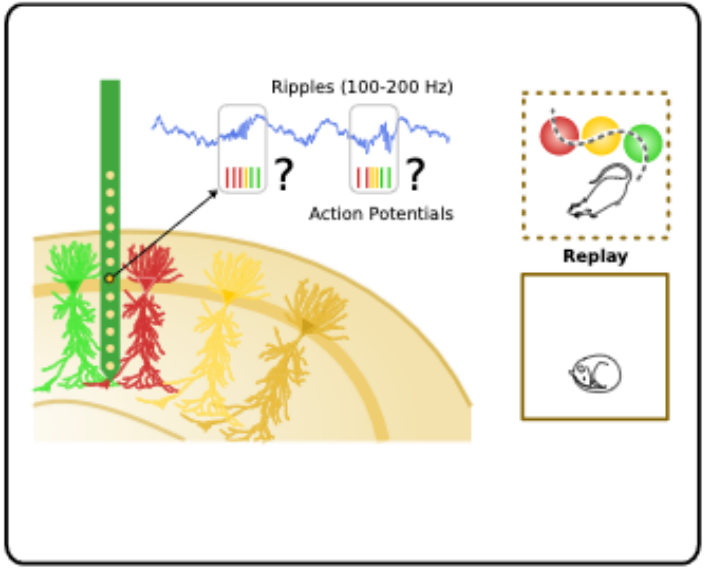


Encoding



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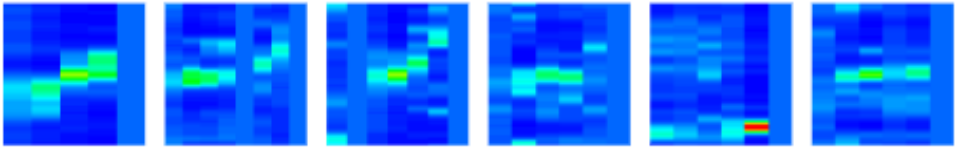
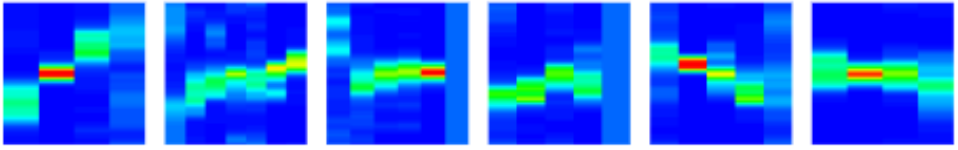
Are theta sequences necessary for sleep replay?

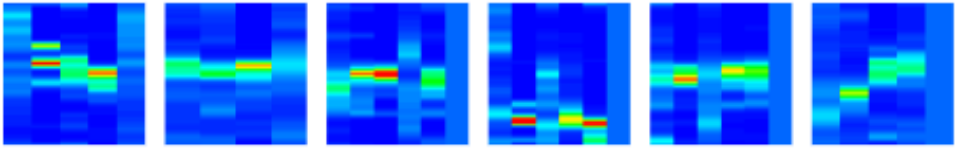
Sleep after Passive 1



Sleep after Active



Sleep after Passive 2



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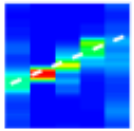

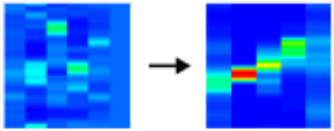

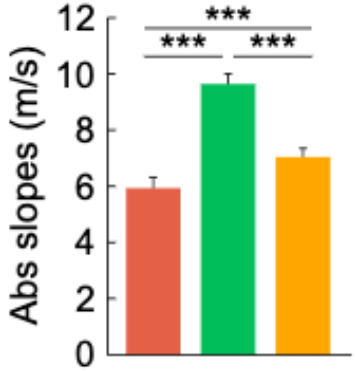

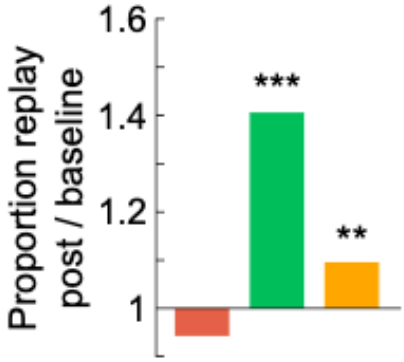

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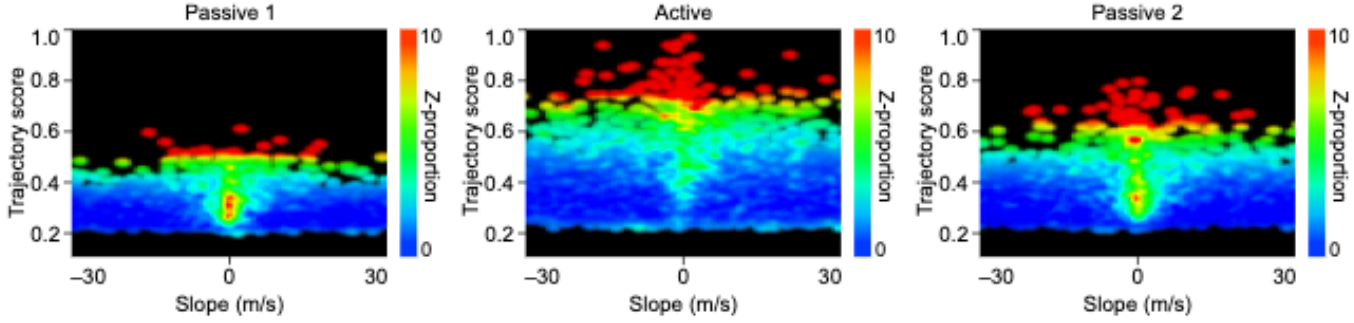

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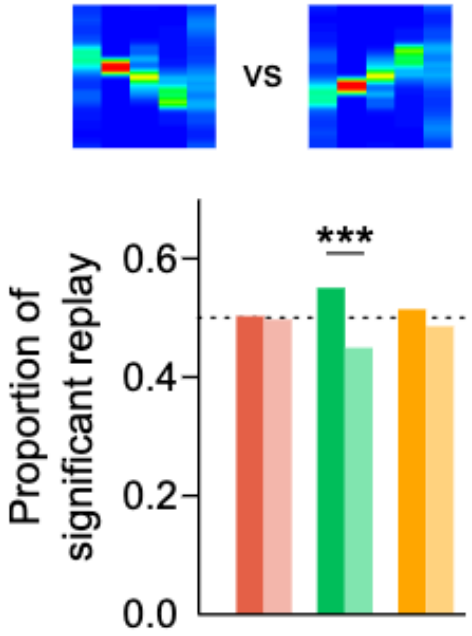

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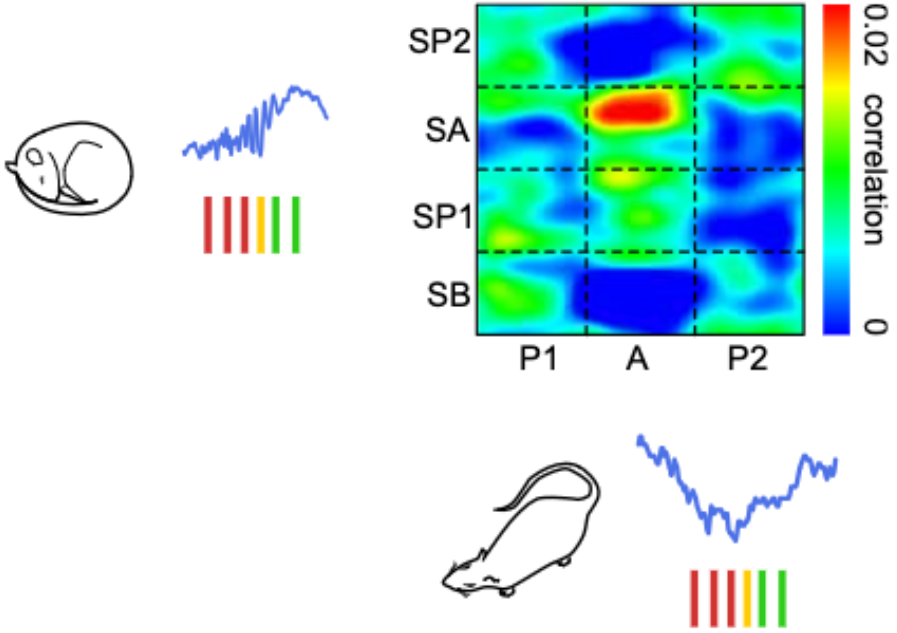
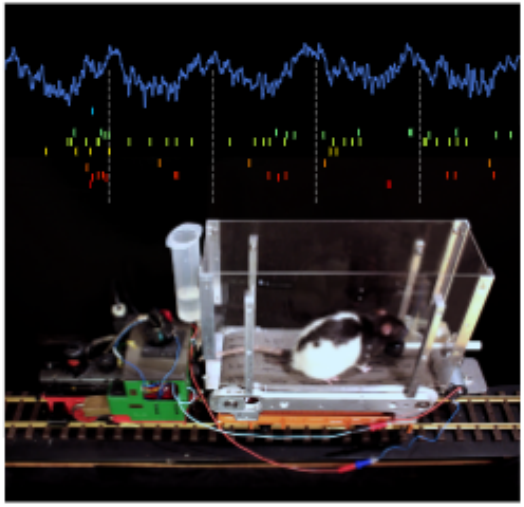


Drieu, Todorova and Zugaro (2018) *Science* 362(6415):675–679

Conclusion



Theta sequences during exploration are required for subsequent replay during slow wave sleep.

Outline

Behavioral Correlates of Sharp Wave - Ripples

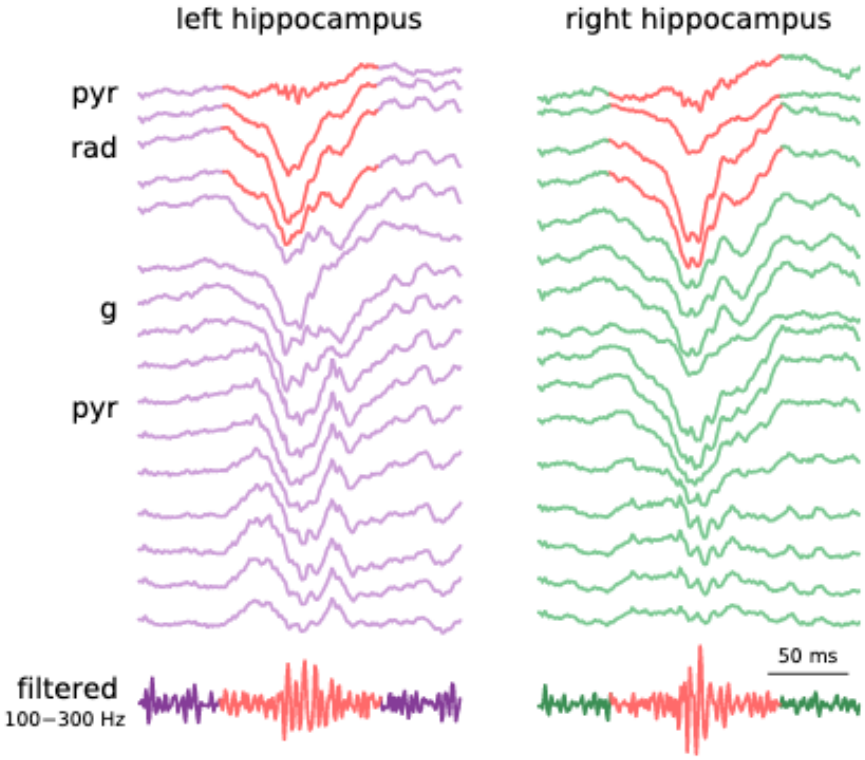
Several behavioral correlates have been linked to SPW-Rs activity in the hippocampus

- slow-wave sleep
- quiet rest
- consumatory behaviors
- grooming
- . . .

Outline

Mechanisms of SPW-Rs

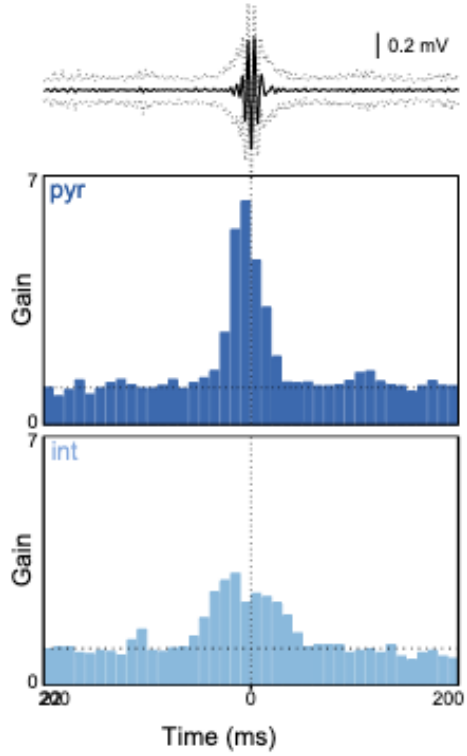
Field potentials display large amplitude irregular activity during slow-wave sleep



Buzsáki et al. (1992) *Science* 5059(256), 1025–7.

Mechanisms of SPW-Rs

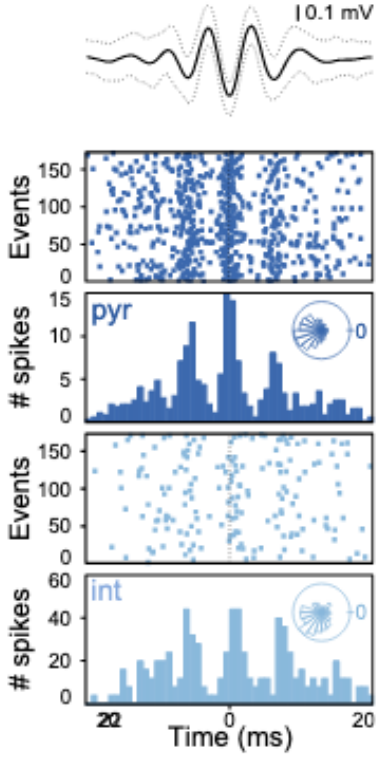
Pyramidal cells and interneurons are strongly activated during SPW-Rs



Girardeau et al. (2009) *Nature Neurosci.* 12(10), 1222–3.

Mechanisms of SPW-Rs

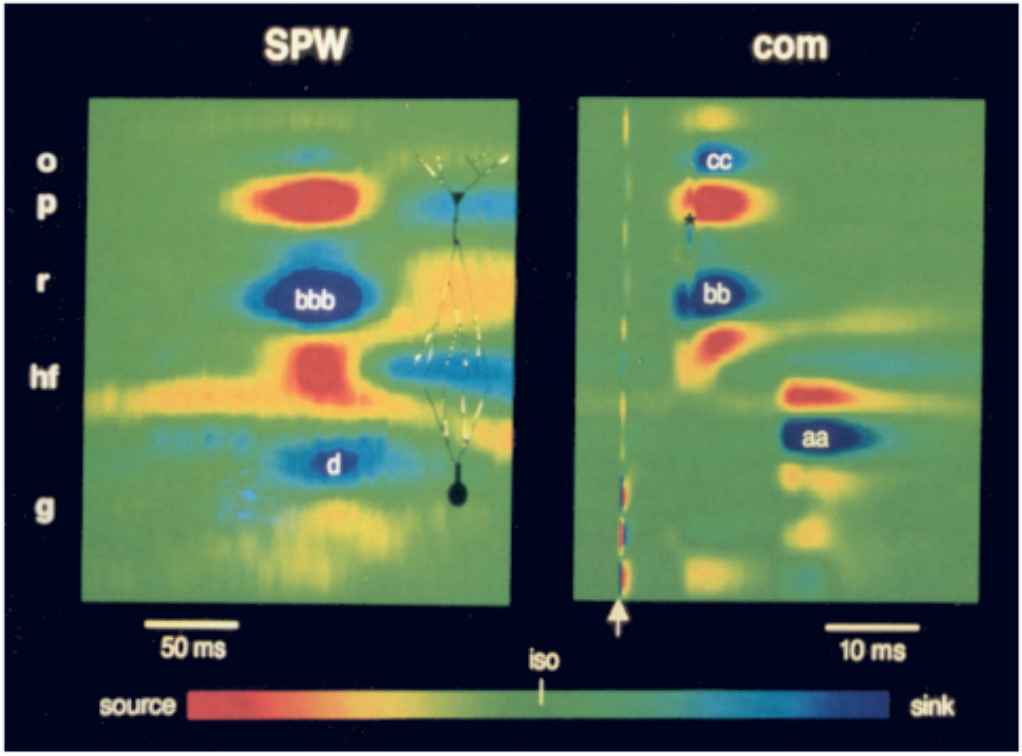
Pyramidal cells and interneurons are phase locked to SPW-Rs



Girardeau et al. (2009) *Nature Neurosci.* 12(10), 1222–3.

Mechanisms of SPW-Rs

Ripples result from strong population depolarisation and fast rhythmic inhibition



Ylinen et al. (1995) *J. Neurosci.* 15(1), 30–46.

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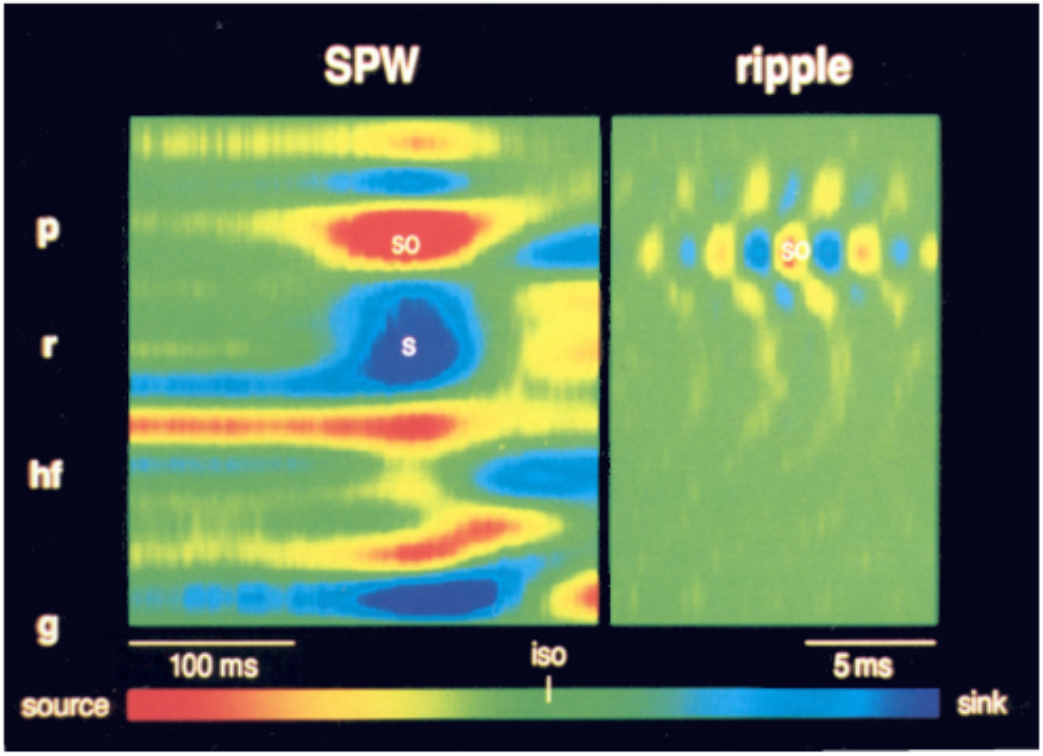
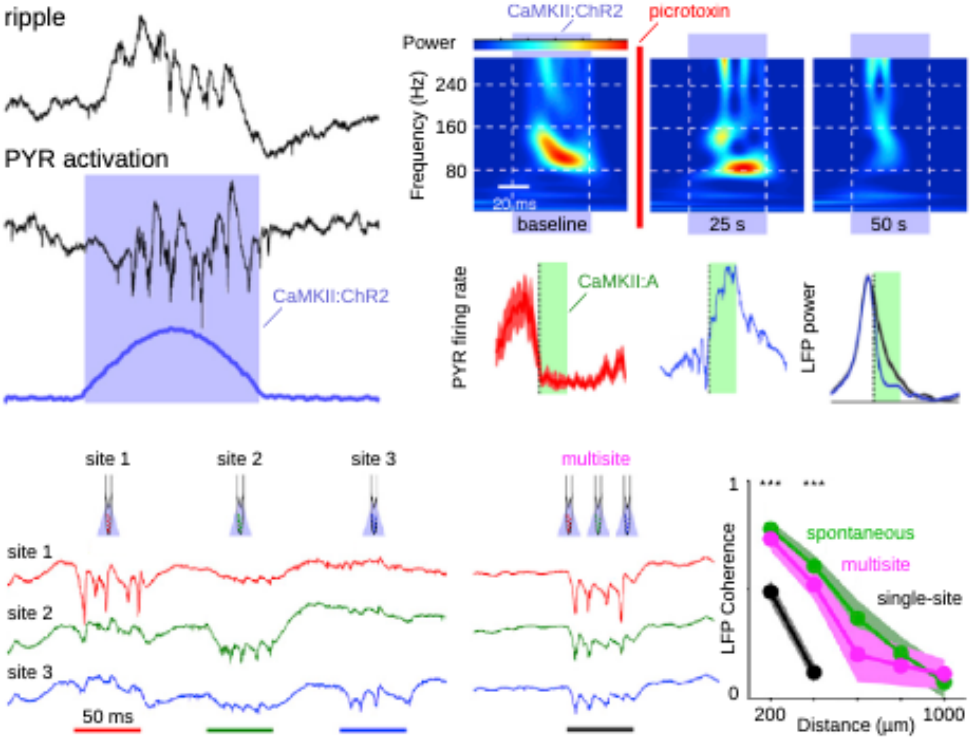


Ylinen et al. (1995) *J. Neurosci.* 15(1), 30–46.

Mechanisms of SPW-Rs

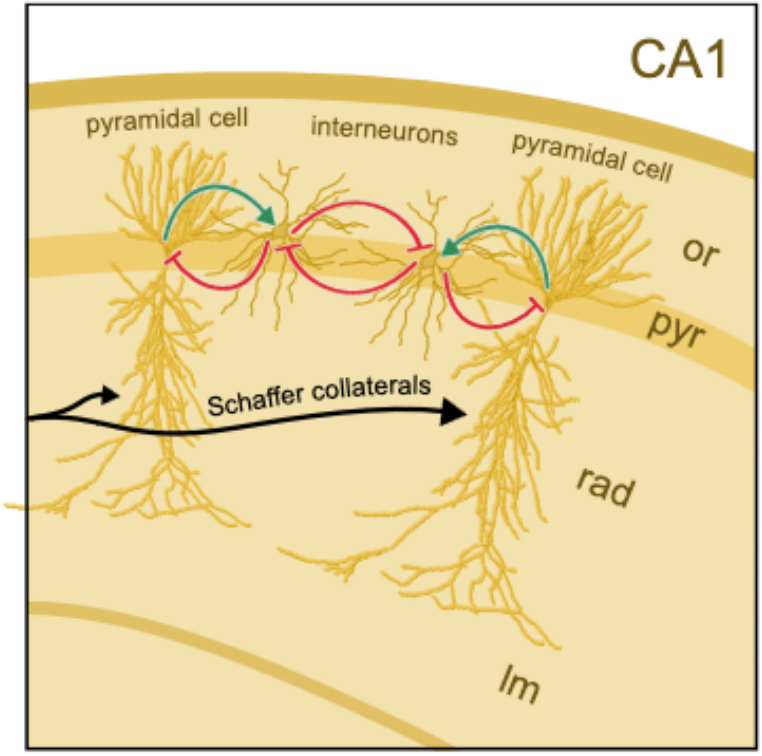
Interneuron spiking mediates the coordination of local oscillators



Stark et al. (2014) *Neuron* 83(2), 467–480.

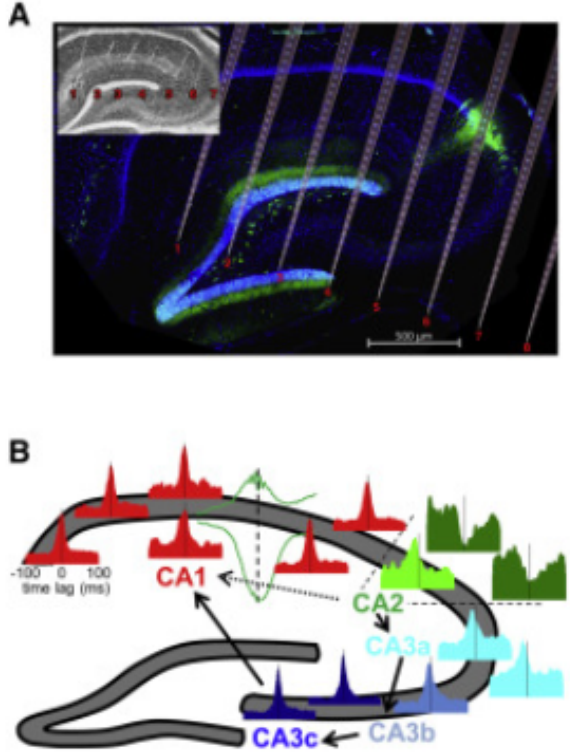
Mechanisms of SPW-Rs

Pyramidal cells and interneurons mediate hippocampal ripples



Mechanisms of SPW-Rs

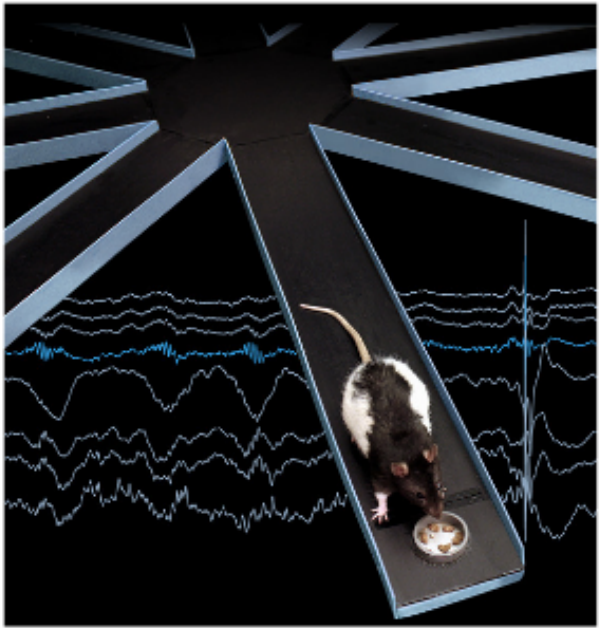
CA2 pyramidal cells are ripple initiators



Oliva et al. (2016) *Neuron* 91(6), 1342–55.

Outline

Conclusion

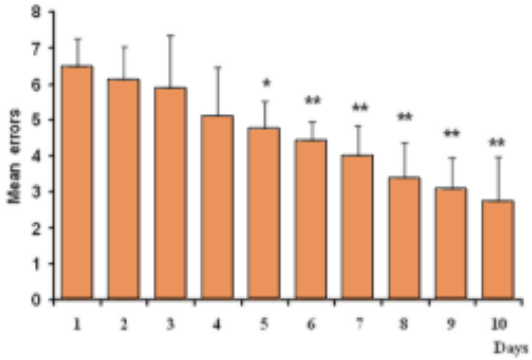


Hippocampal ripples and associated neuronal reactivation play a **prominent role** in memory consolidation.

- Ego-Stengel et al. (2010) *Hippocampus*

More on Sequence Replay and Memory Consolidation

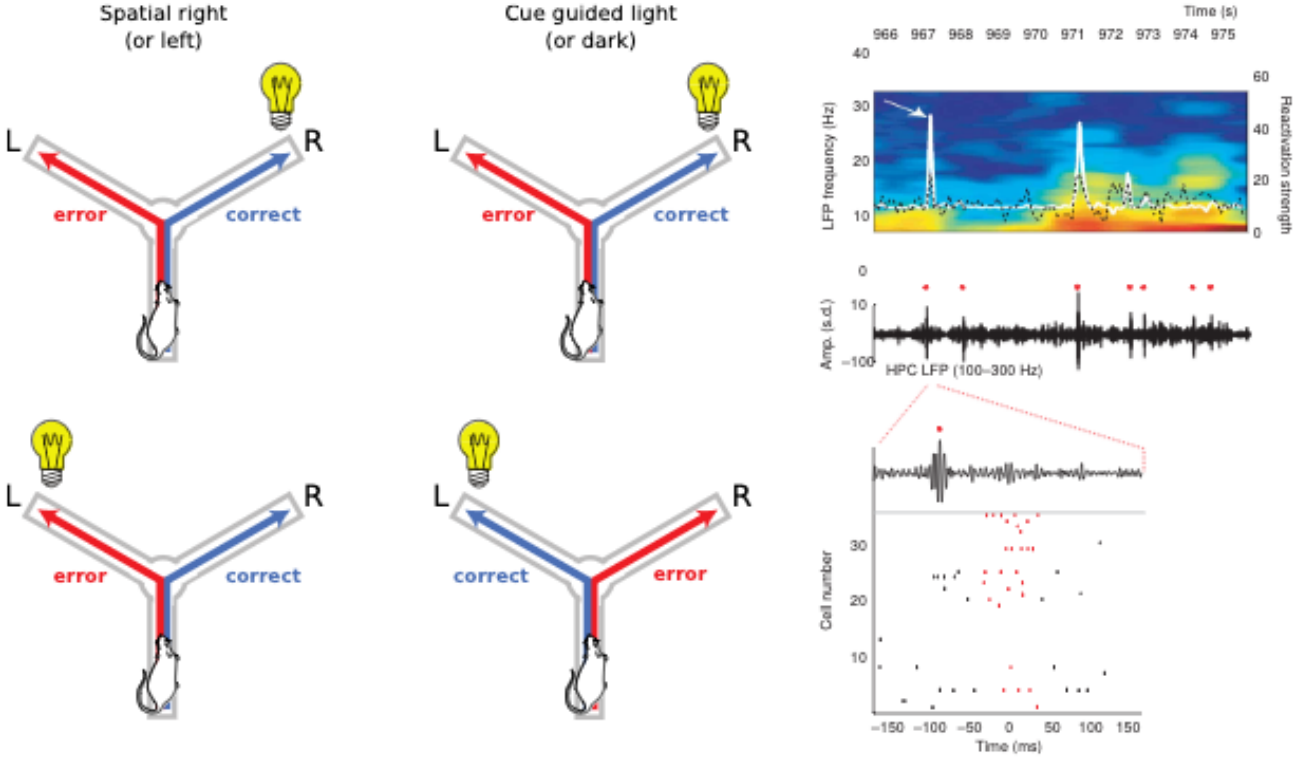
SPW-Rs density increases upon learning



Ramadan et al. (2009) *PLoS One* 4(8), e6697.

More on Sequence Replay and Memory Consolidation

Replay in prefrontal cortex is coordinated with hippocampal SPW-Rs

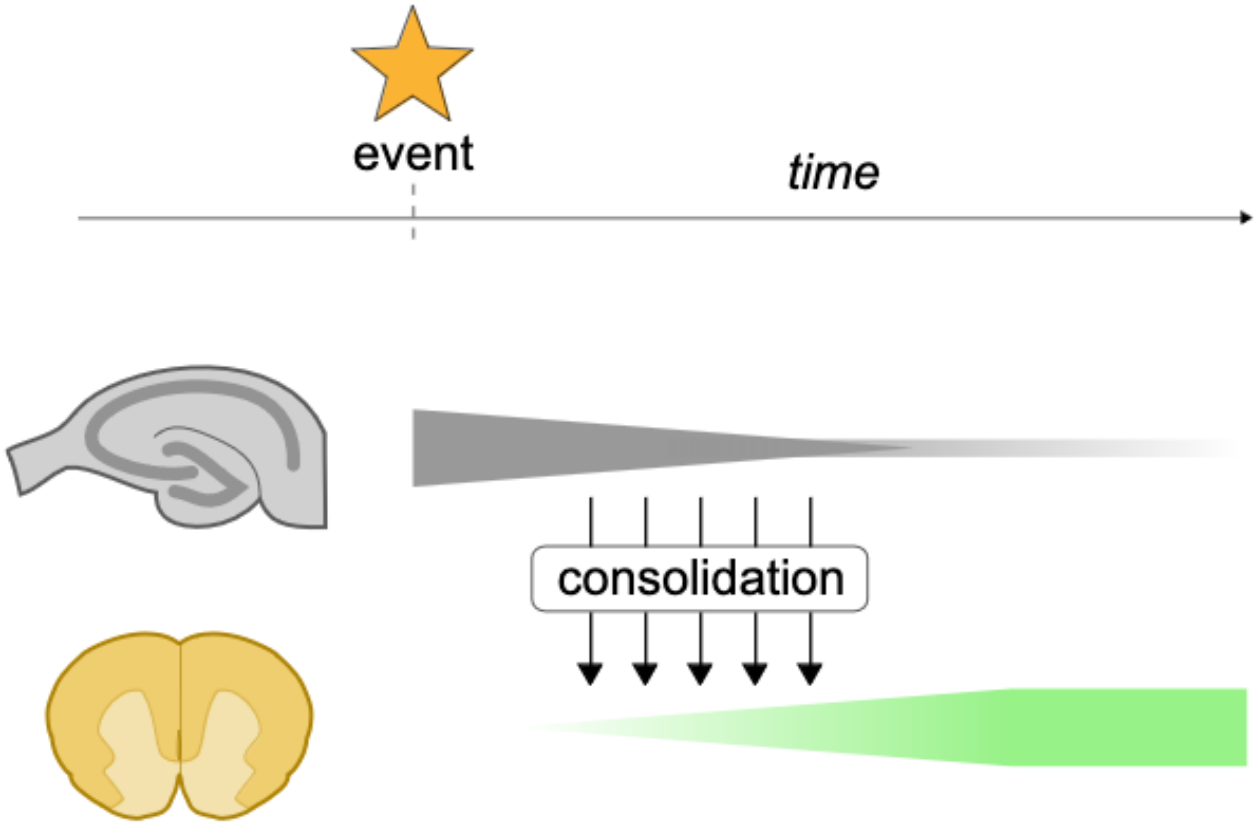


Peyrache et al. (2009) *Nature Neurosci.* 12(7), 919–26.

Outline

The Hippocampo-Cortical Dialogue (2)

Does the cortex actually process hippocampal information for memory consolidation?



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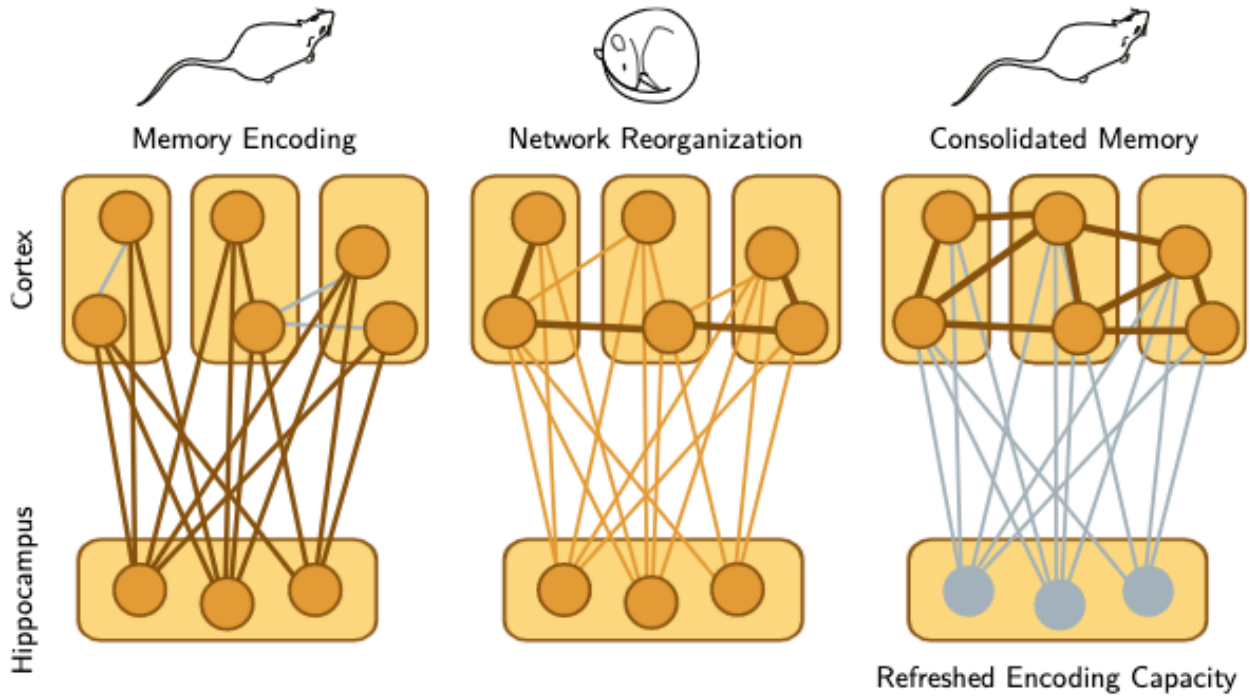
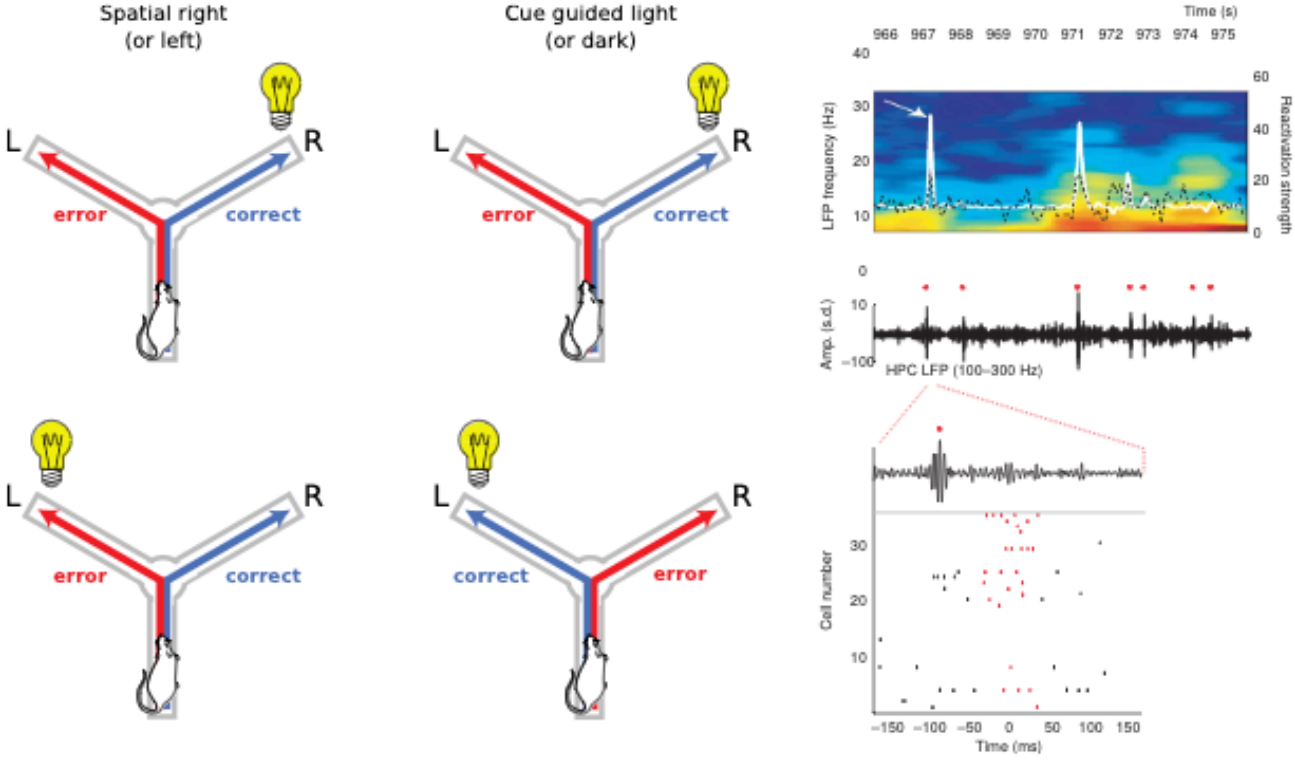


Frankland and Bontempi (2005) *Nat Rev Neurosci* 6(2), 119–30.

Reactivation of Prefrontal Assemblies During Sleep

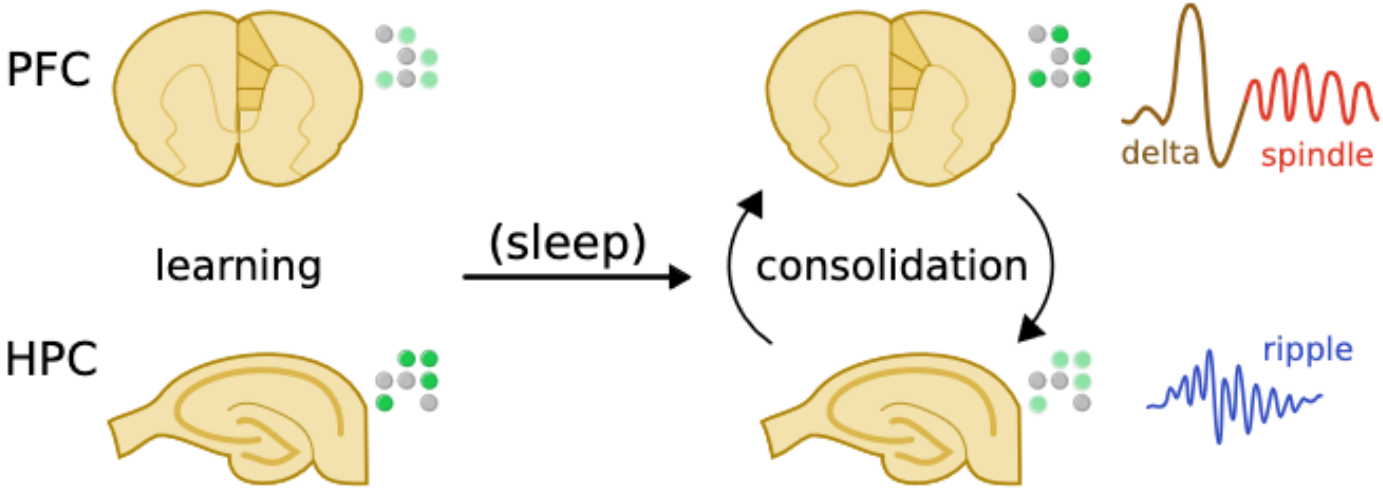
Replay in prefrontal cortex is coordinated with hippocampal SPW-Rs



Peyrache et al. (2009) *Nature Neurosci.* 12(7), 919-26.

Coupled Hippocampo-Cortical Rhythms

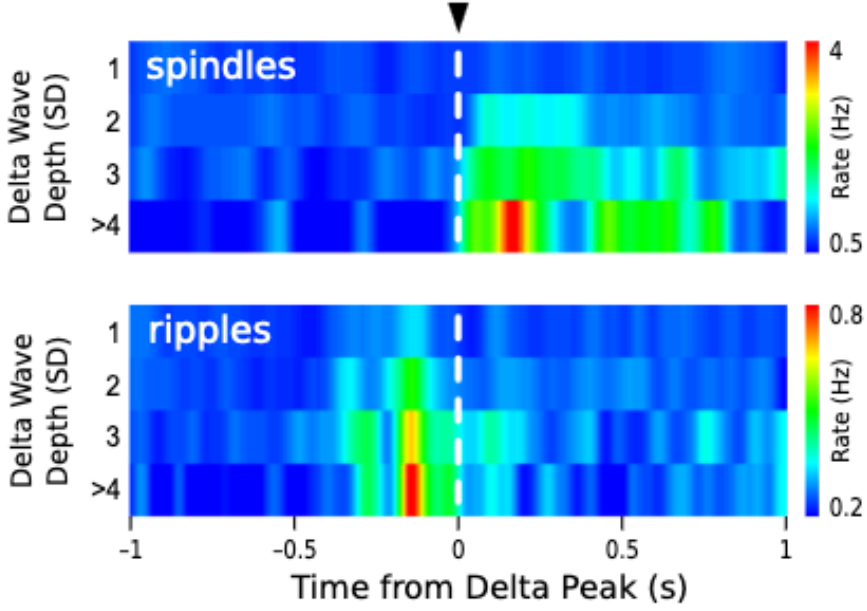
Consolidation is thought to involve a dialogue between these structures during sleep

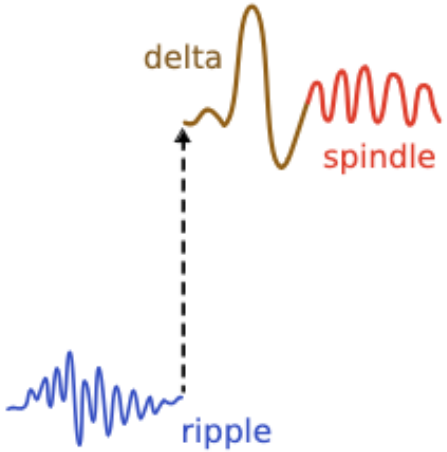


Maingret, Girardeau*, Todorova*, Goutierre and Zugaro (2016) *Nature Neurosci.* 19(7), 959–64.

Coupled Hippocampo-Cortical Rhythms

Ripples are weakly coupled to delta-spindle sequences

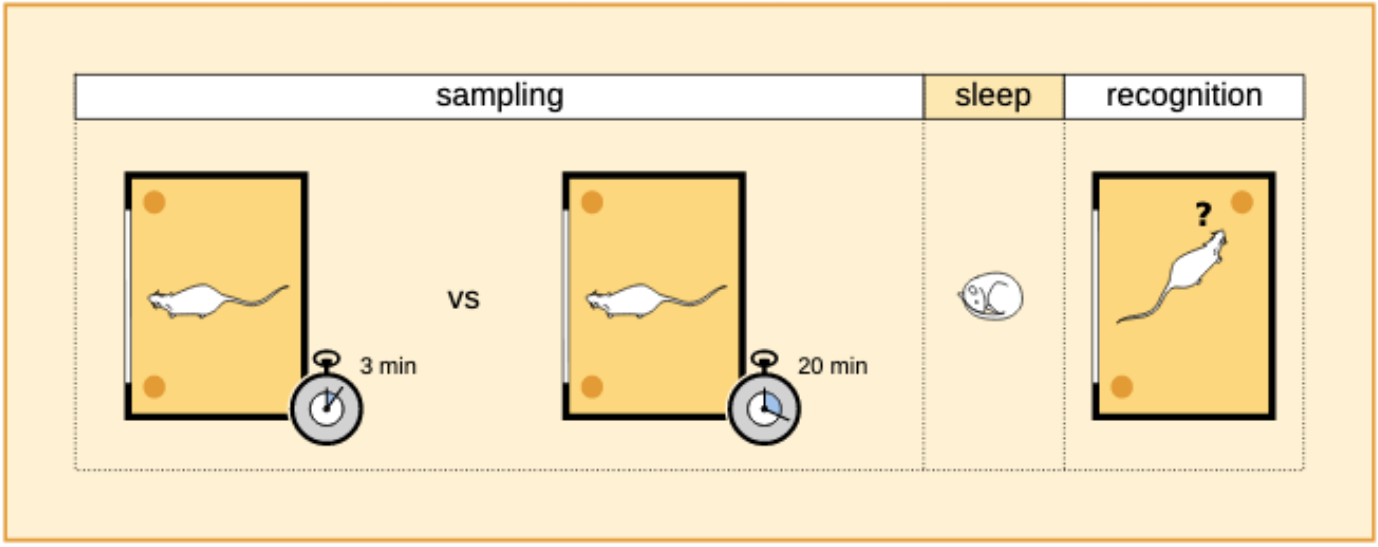




Maingret, Girardeau*, Todorova*, Goutierre and Zugaro (2016) *Nature Neurosci.* 19(7), 959–64.

Endogenous Coupling

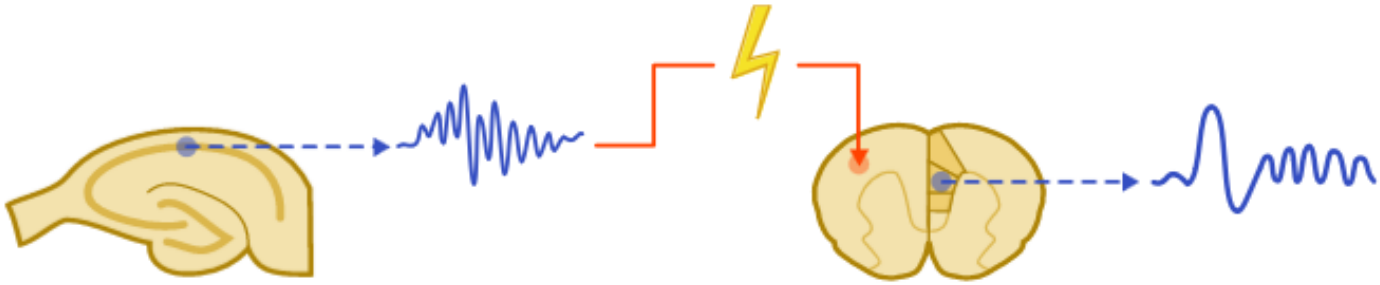
Endogenous hippocampo-cortical coupling increases with consolidation



Maingret, Girardeau*, Todorova*, Goutierre and Zugaro (2016) *Nature Neurosci.* 19(7), 959–64.

Experimental protocol

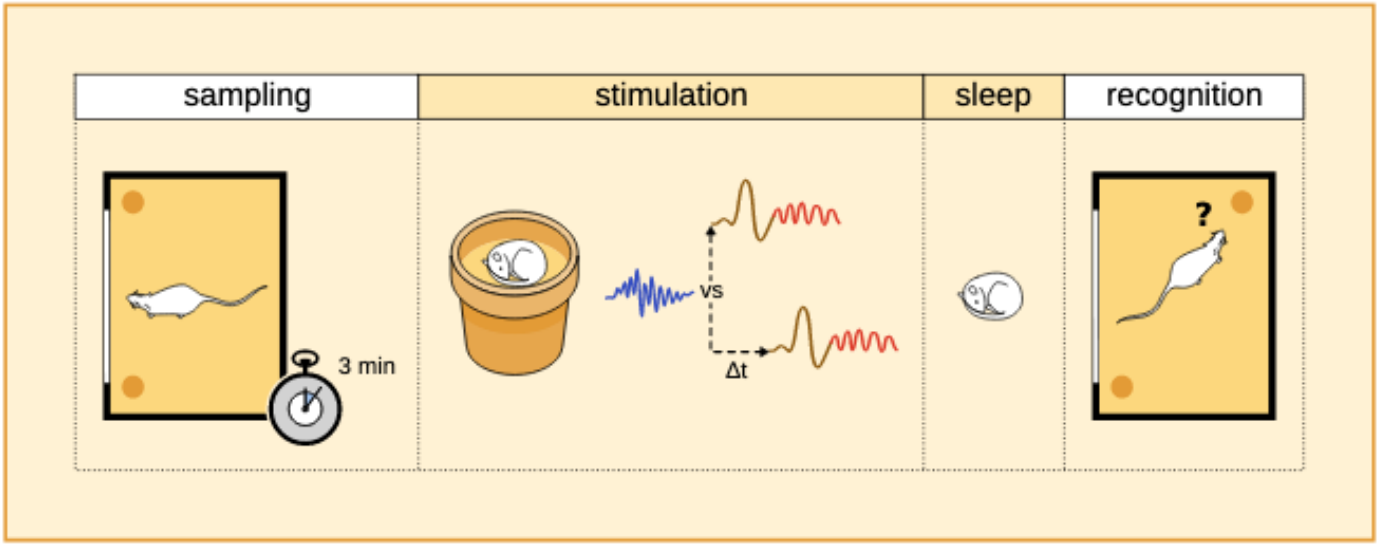
Increasing hippocampo-cortical coupling by timed stimulation



Maingret, Girardeau*, Todorova*, Goutierre and Zugaro (2016) *Nature Neurosci.* 19(7), 959–64.

Spatial reference memory task

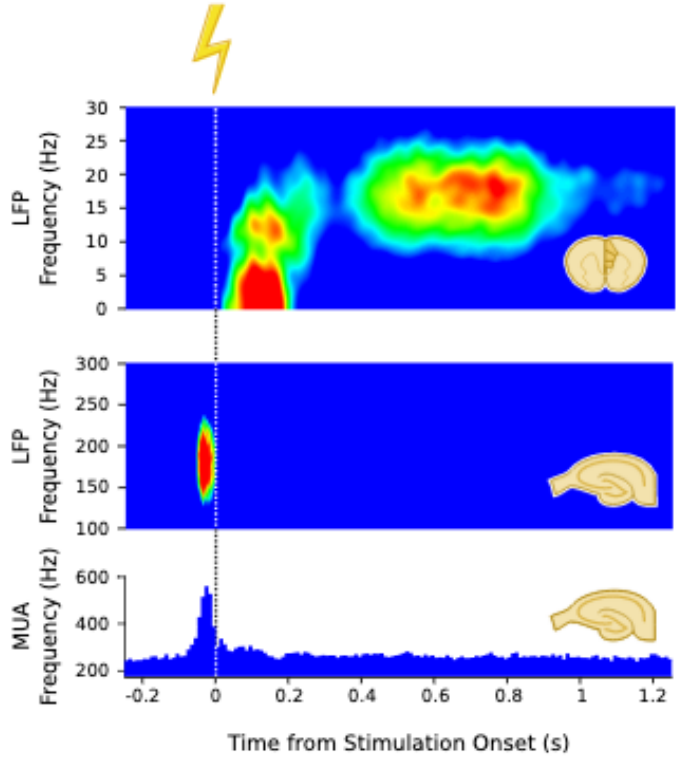
Rats were weakly trained to recognize a spatial configuration of objects



Maingret, Girardeau*, Todorova*, Goutierre and Zugaro (2016) *Nature Neurosci.* 19(7), 959–64.

Increased Hippocampo-Cortical Coupling

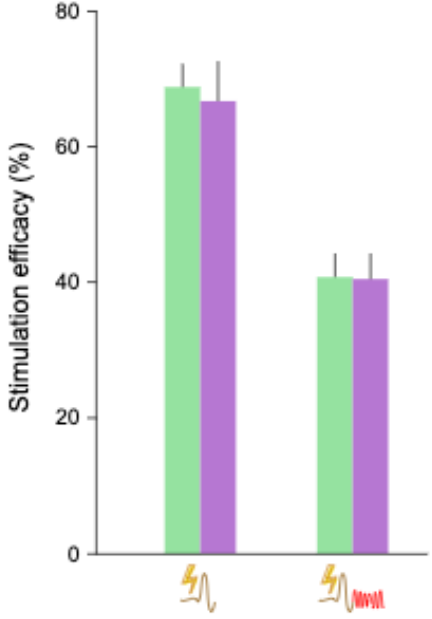
Stimulations trigger delta-spindle sequences correlated with ripples

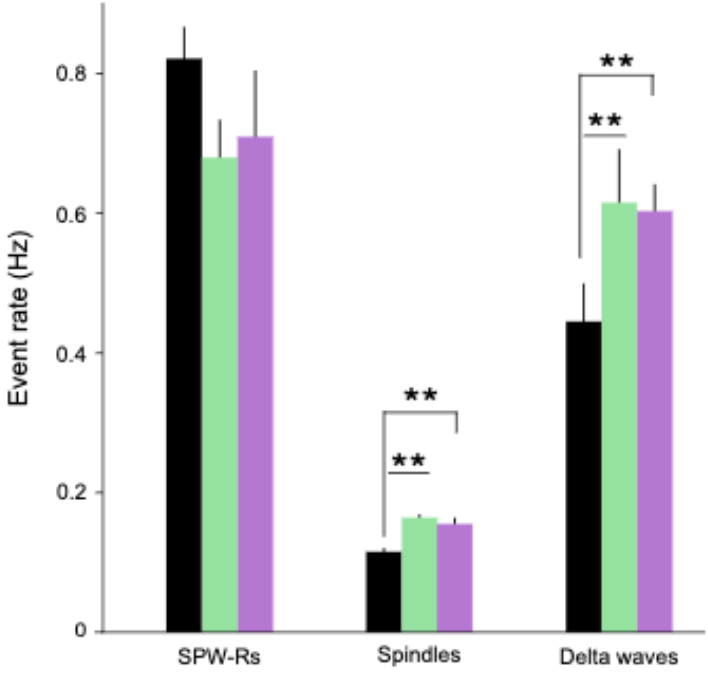


Maingret, Girardeau*, Todorova*, Goutierre and Zugaro (2016) *Nature Neurosci.* 19(7), 959–64.

Increased Hippocampo-Cortical Coupling

Stimulation was highly effective

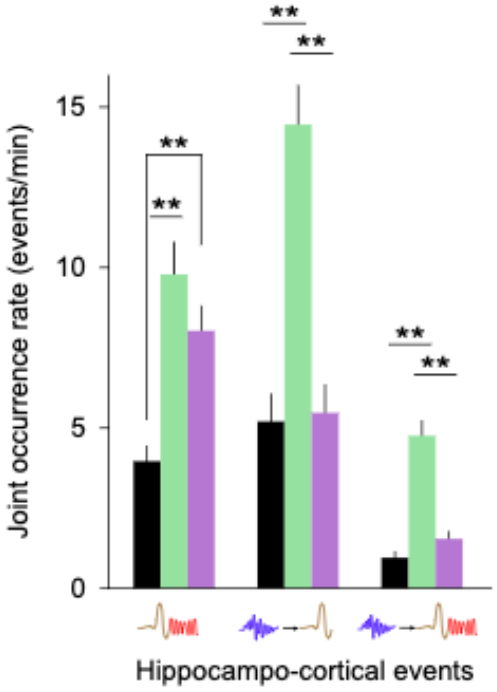


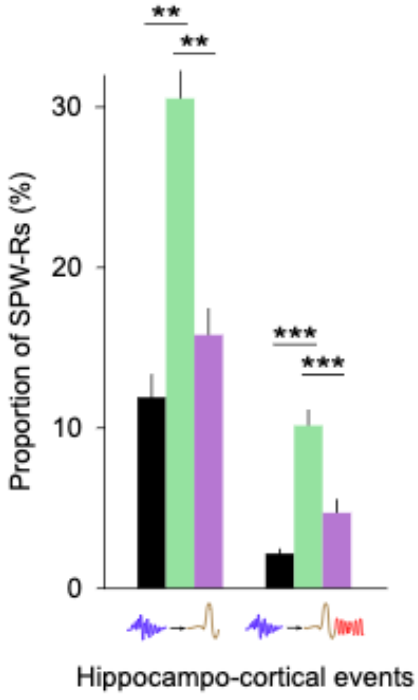


Maingret, Girardeau*, Todorova*, Goutierre and Zugaro (2016) *Nature Neurosci.* 19(7), 959–64.

Increased Hippocampo-Cortical Coupling

Stimulation increases coupling of hippocampal and cortical rhythms

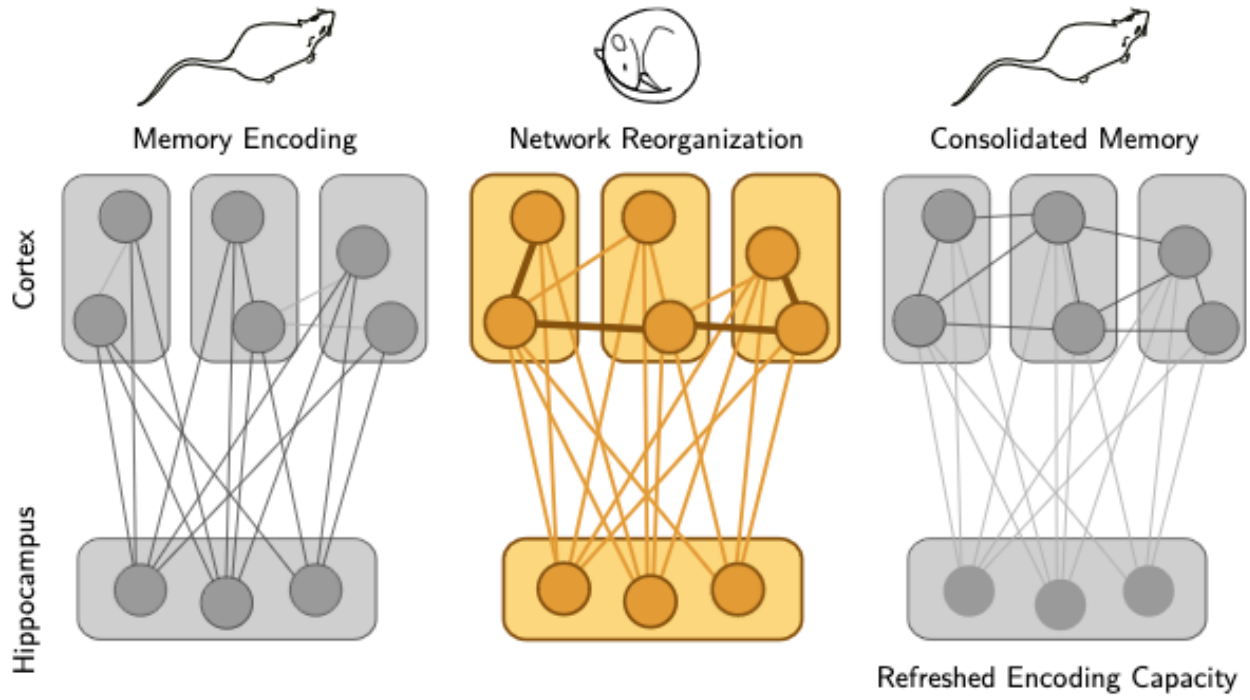




Maingret, Girardeau*, Todorova*, Goutierre and Zugaro (2016) *Nature Neurosci.* 19(7), 959–64.

Reorganization of mPFC Networks During Sleep

Activity profiles of selected mPFC neurons reorganize following induced delta waves



Frankland and Bontempi (2005) *Nat Rev Neurosci* 6(2), 119–30.

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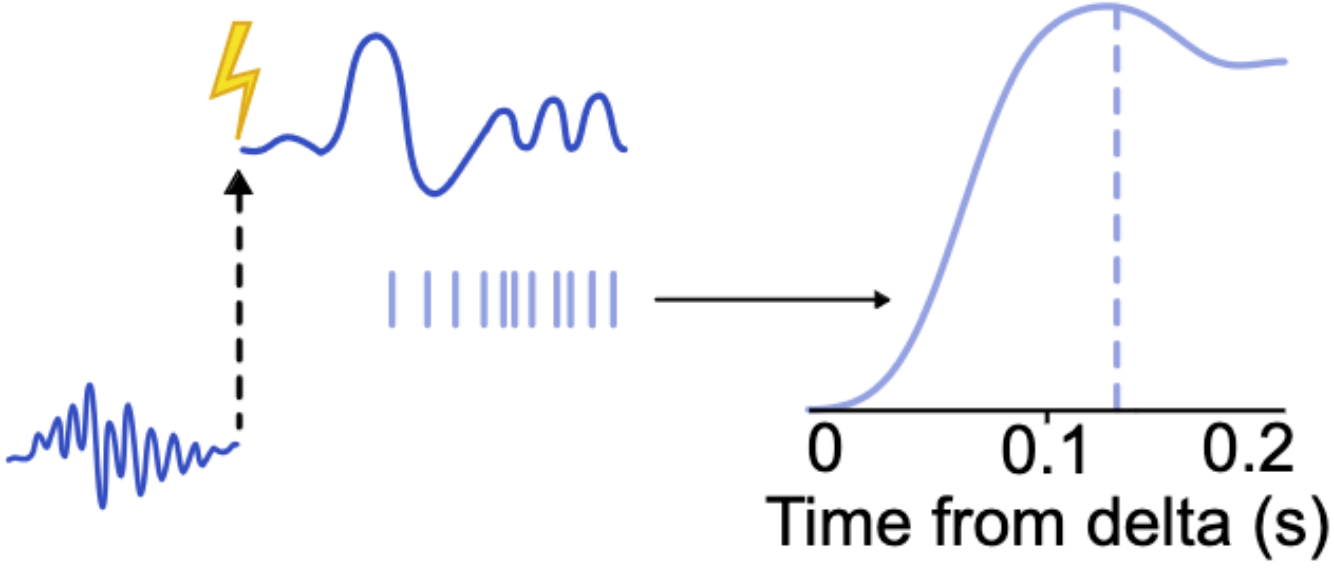

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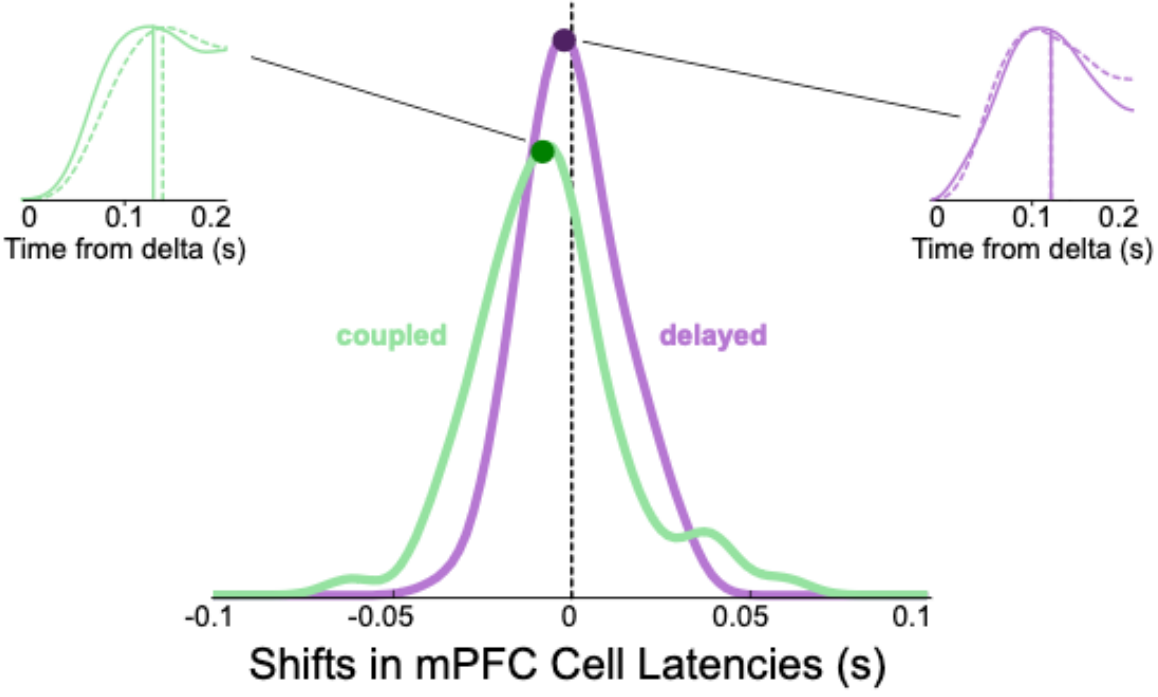

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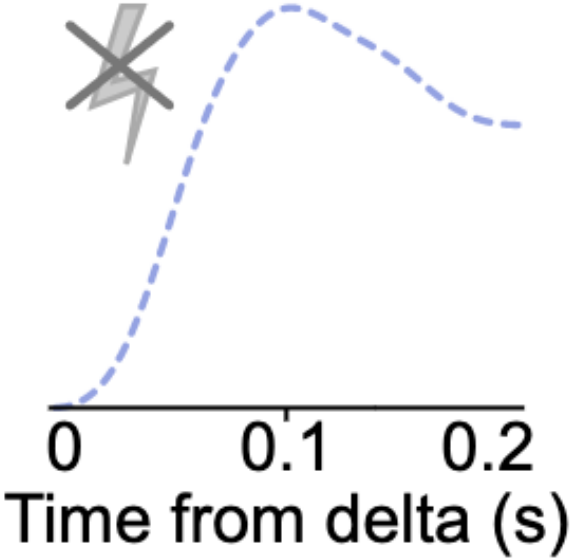

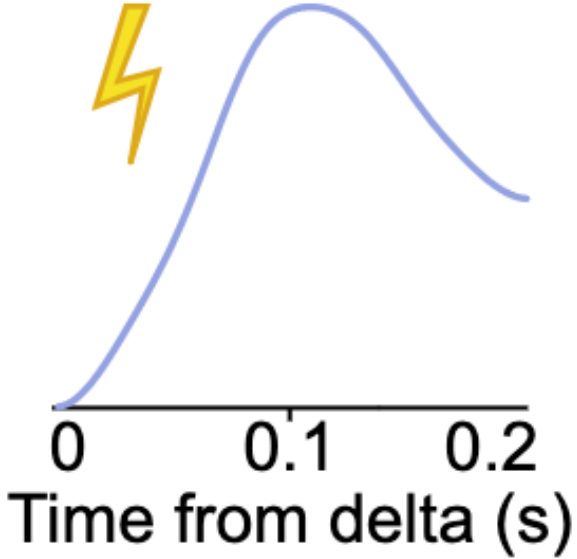

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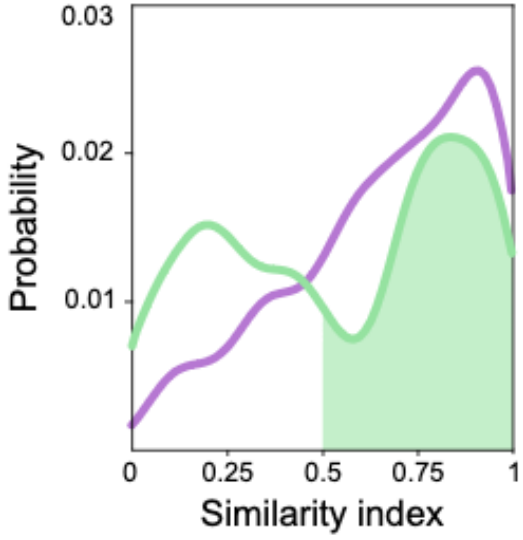

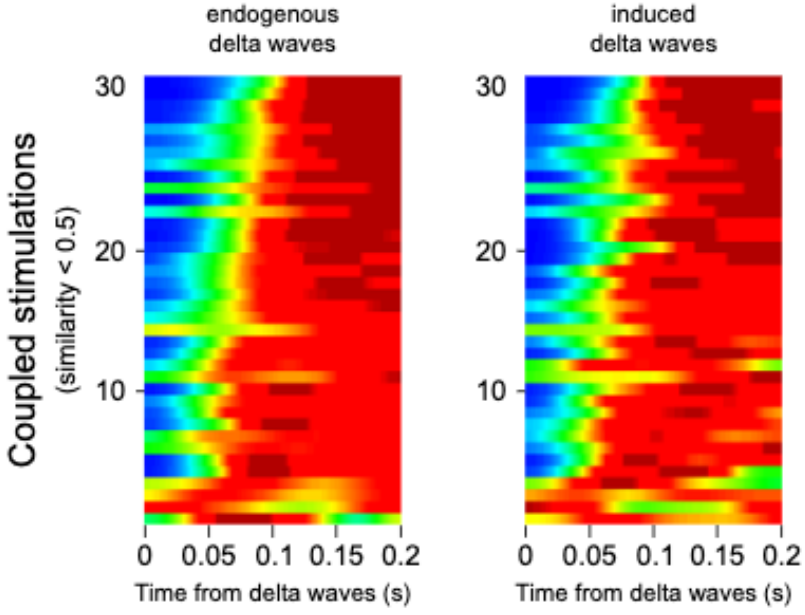

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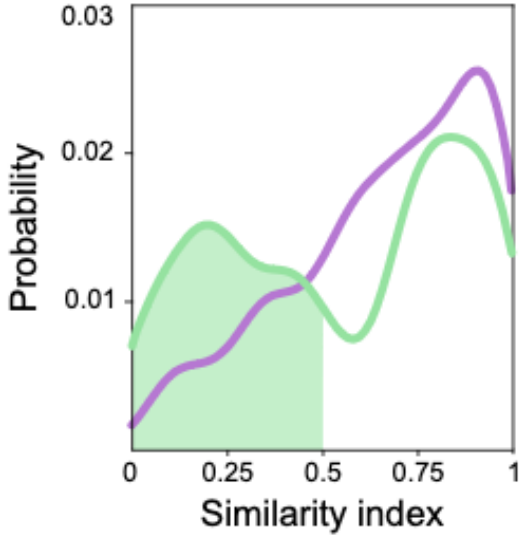
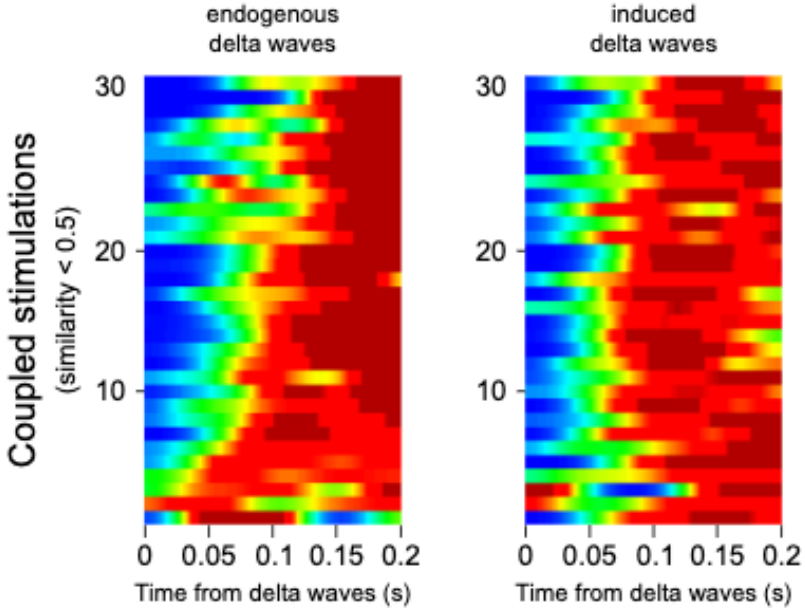
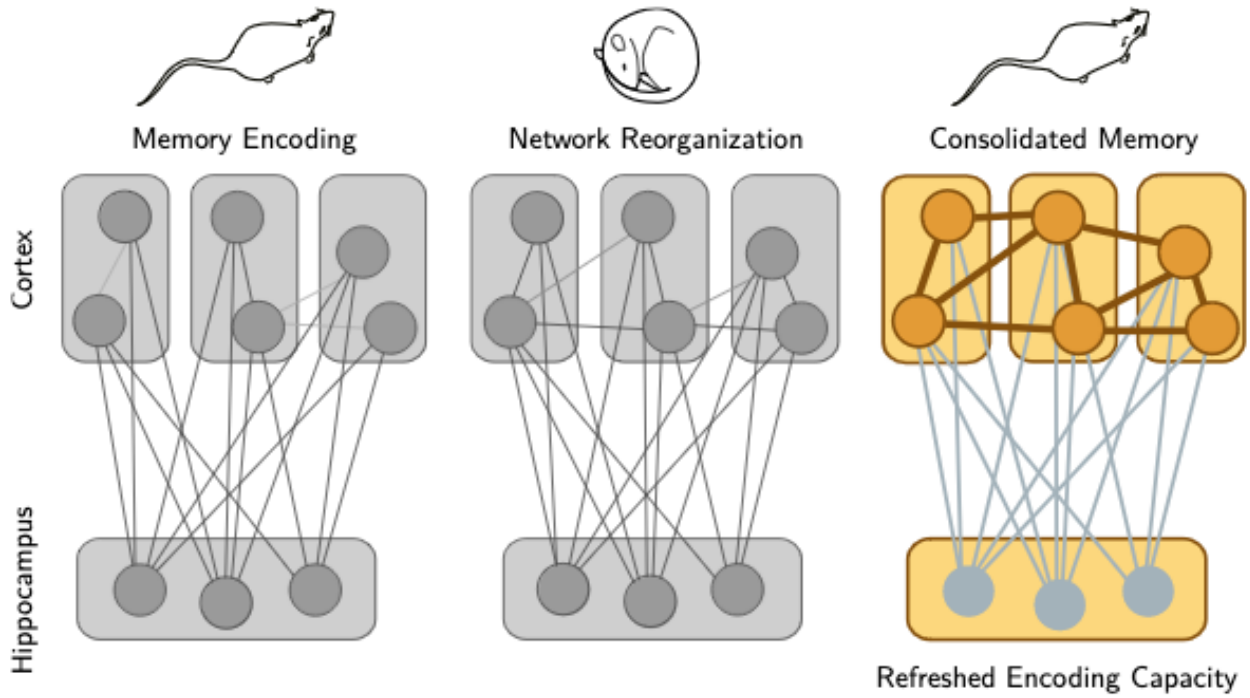




Increased mPFC Task Responsivity

Task responsivity increases in mPFC neurons parallel memory consolidation



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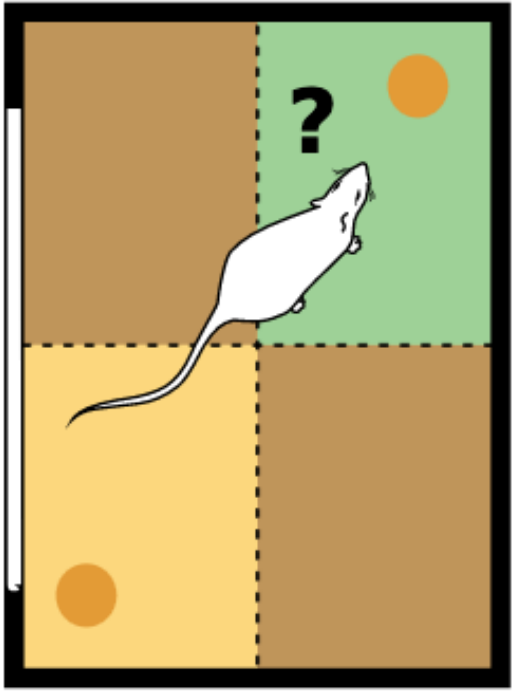

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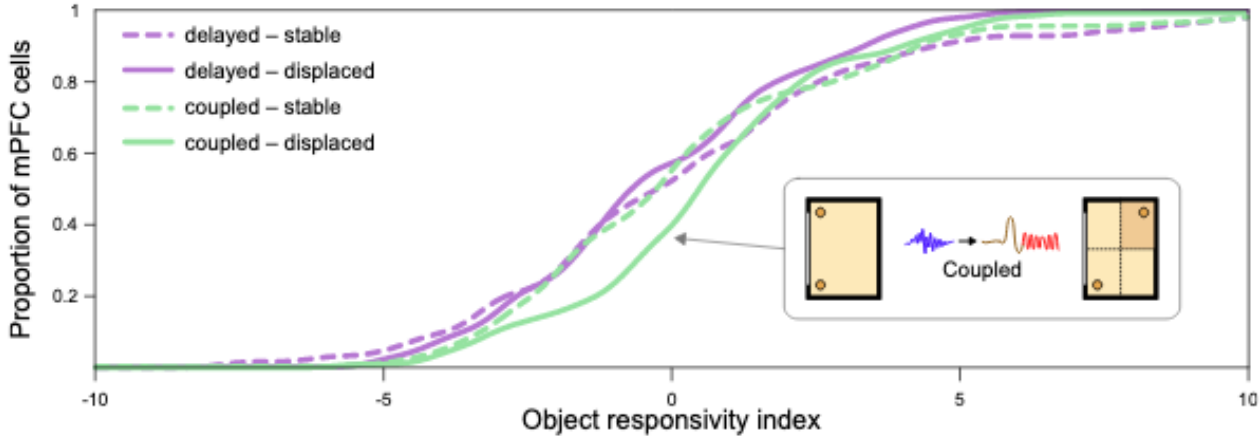
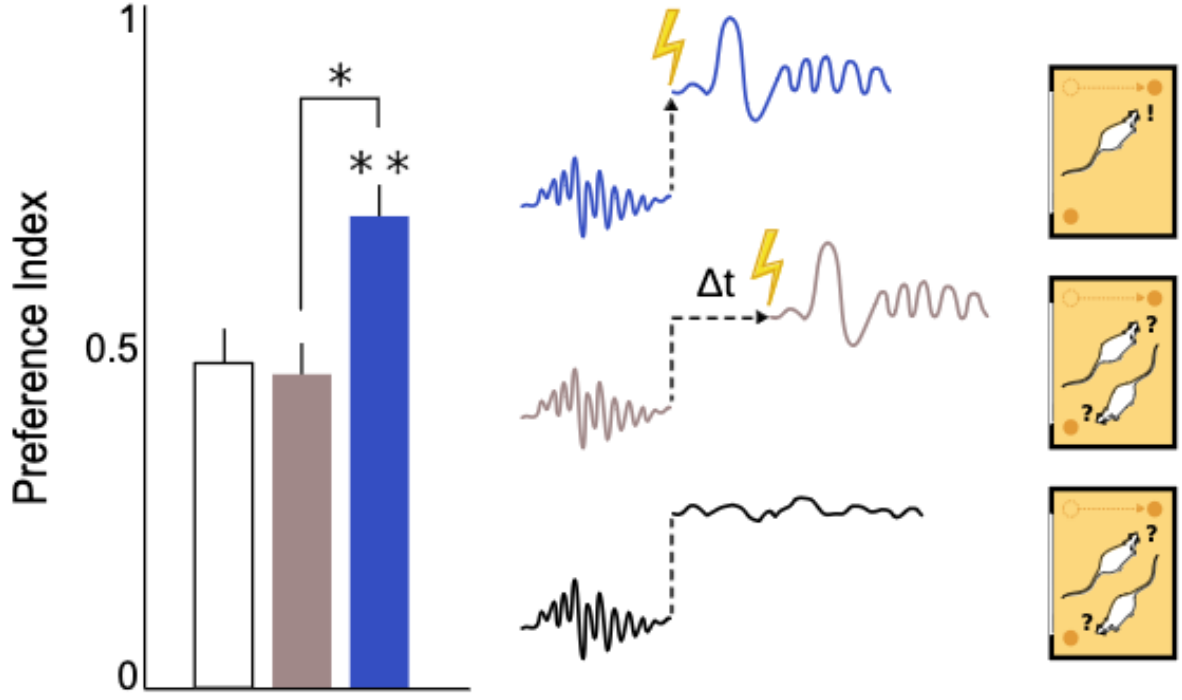


Behavioral Results

Increasing the hippocampo-cortical dialogue boosts consolidation



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Conclusion

Our results provide the first direct evidence of a **causal role for a hippocampo-cortical dialogue in memory consolidation**.

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