Entorhinal-CA3 dual-input control of spike timing in the hippocampus

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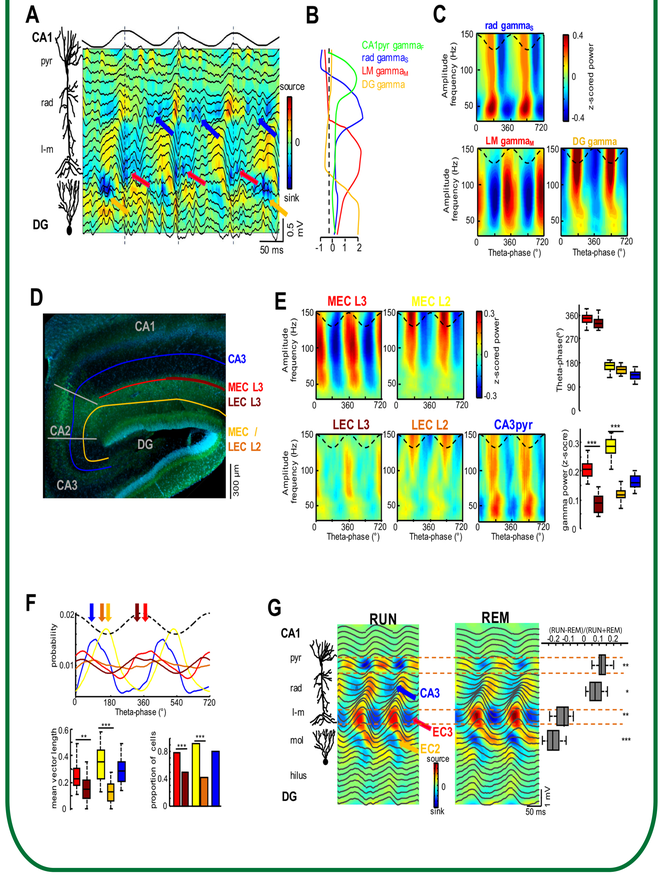
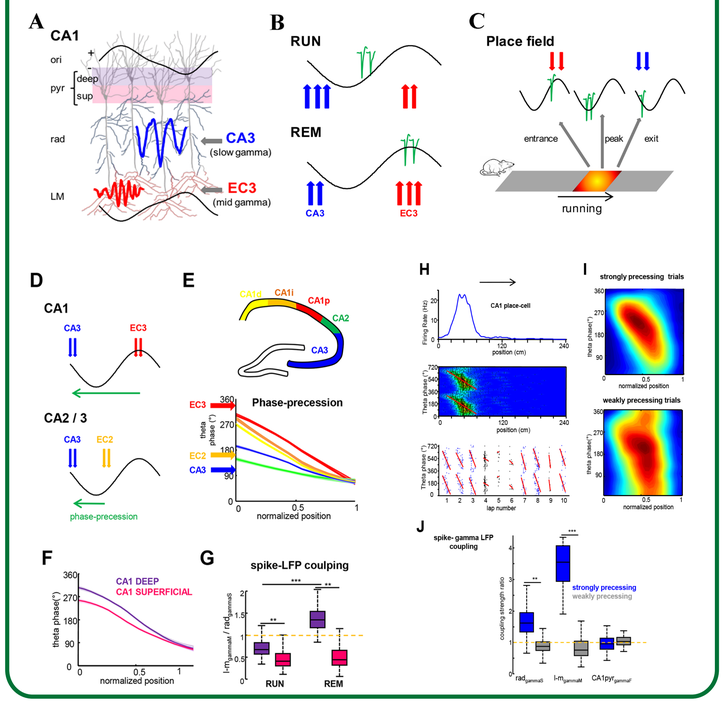
Summary

Theta-gamma phase **coupling** and **spike timing** within theta oscillations are prominent features of the hippocampus and are often related to **navigation and memory**. However, the mechanisms that give rise to these relationships are not well understood. Using high spatial resolution electrophysiology, we investigated the influence of **CA3 and entorhinal inputs** on the timing of CA1 neurons. The theta phase preference and excitatory strength of the afferent CA3 and entorhinal inputs effectively timed the principal neuron activity assisted by the local control of **temporally shifting** perisomatic/ proximal dendritic and distal dendritic **inhibition**. These data support a general mechanism for several physiological phenomena, including laminar profile of theta oscillations, brain state- and task-dependent **theta phase preference of spikes** and spike theta **phase-position correlations of place cells** in different hippocampal subregions and sublayers. Thus, upstream inputs interact with local mechanisms to **determine theta phase timing of hippocampal neurons** to support

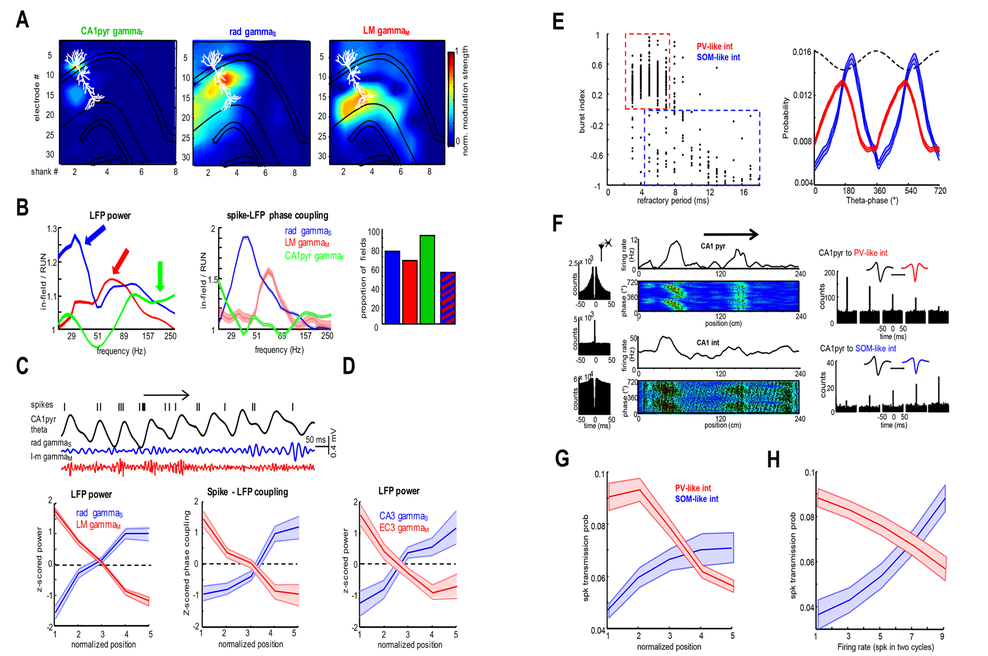
Theta-gamma inputs to hippocampal subregions



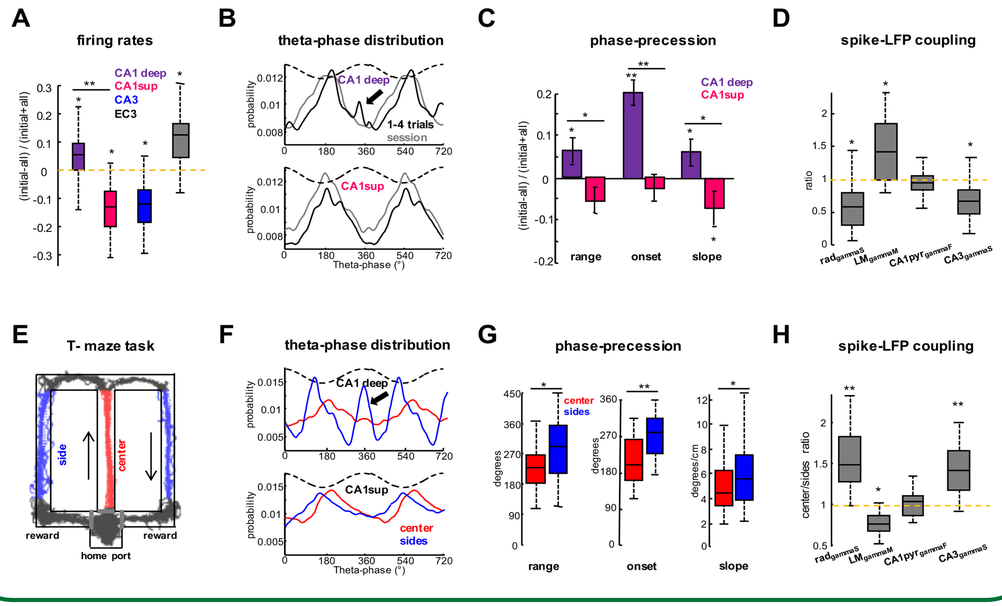
Dual gamma-input model of phase-precession



Intra-place field dynamics of layer-speciic gamma inputs and inhibition



Behavioral modulation of gamma inputs and phase-precession



Conclusions

- **Entorhinal and CA3 gamma inputs** to the hippocampus have different frequency and theta phase preference. Their cooperation or competition **control spike timing** of hippocampal neurons.

- **Phase precession** is under dual entorhinal and CA3 control. The phase range and strengh of phase-position correlation of place cell spikes is **affected by** the theta phase preference and depth of modulation of **upstream drivers**.

- At the **entrance of the place field EC3 input** control the firing of CA1 place cells at the theta peak. Along field transversal EC3 input control decreased and is supplemented by an **increasing CA3 drive**. This gamma input competition is aligned with a **swicthing somatic to distal dendritic feedback inhibition**.

- During **REM sleep and initial exploration** of a familiar enviroment **EC3 input** control CA1 spike timing. During **memory recall** CA1 spike timing and phase precession is mainly under the control of **CA3 input**.

For reading the full story check **Fernandez-Ruiz et al., Neuron, 93: 1213:1226, 2017**.

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