Spatial rate/phase codes provide landmark-based error correction in a temporal model of theta cells

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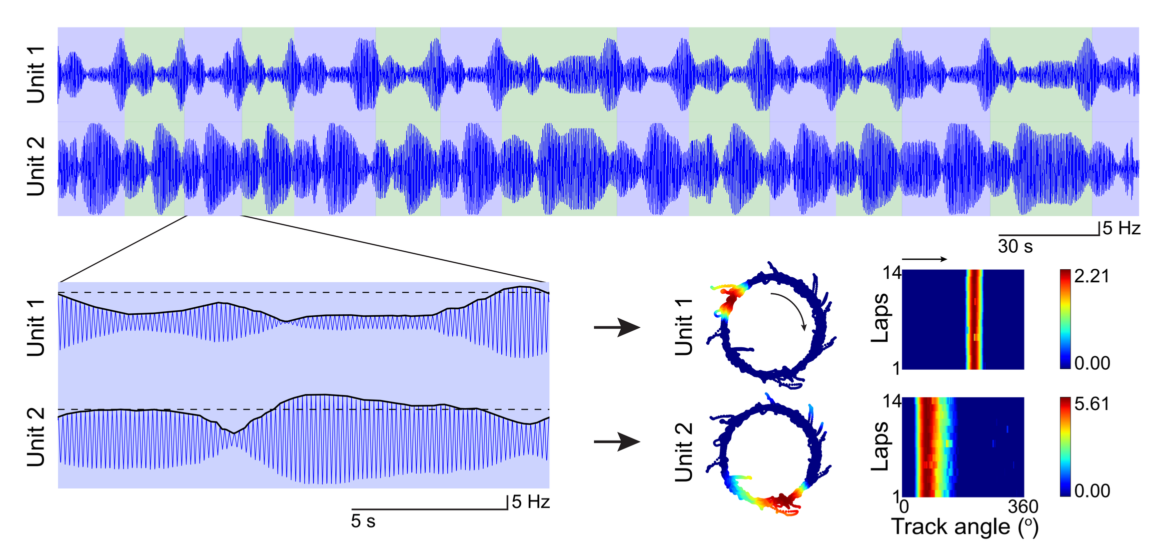
Introduction

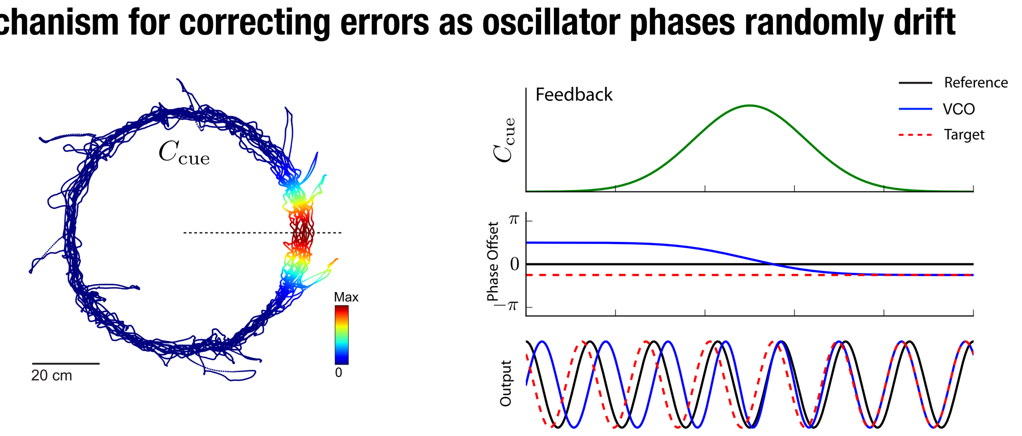
The spatial firing patterns of place cells in hippocampus and grid cells in entorhinal cortex form a spatial representation that is stable during active navigation but also able to encode changes in external landmarks or environmental structure. One class of model that has been investigated as a possible mechanism for generating these spatial patterns relies on temporal synchronization between theta cells, which fire strongly with the septohippocampal theta rhythm (6–10 Hz) and are found throughout the hippocampal formation, that act as velocity-controlled oscillators. However, a critical problem for these models is that the oscillatory interference patterns that they generate become unstable in the presence of phase noise and errors in self-motion signals. Previous studies have proposed hybridizing temporal models with attractor network models or integrating environmental feedback from sensory cues. Preliminary data from subcortical regions in rats suggest that some theta cells exhibit spatially selective firing similar to hippocampal place fields or entorhinal/subicular boundary fields. These cells also demonstrate a consistent phase relationship across space, relative to ongoing hippocampal theta and to other simultaneously recorded cells, that is correlated with the firing rate at a given location. Inspired by this data, we present a novel synchronization model in which place cells or boundary-vector cells provide a stable, landmark-based excitatory input that drives a rate-to-phase mechanism to generate a population of cells that act as location-controlled oscillators. These cells fire preferentially at theta phases that are specific to a given location, determined by the presence of external landmarks.

Multiple oscillator model of hippocampal-like spatial maps

- Path integration in the phase of velocity-controlled oscillators (VCOs) can produce synchronization patterns in space such as grid or place cells



- However, these spatial patterns are highly susceptible to biological levels of period variance (phase noise) in the oscillators
- Theta phase-code feedback driven by environmental features may be one mechanism for correcting errors as oscillator phases randomly drift

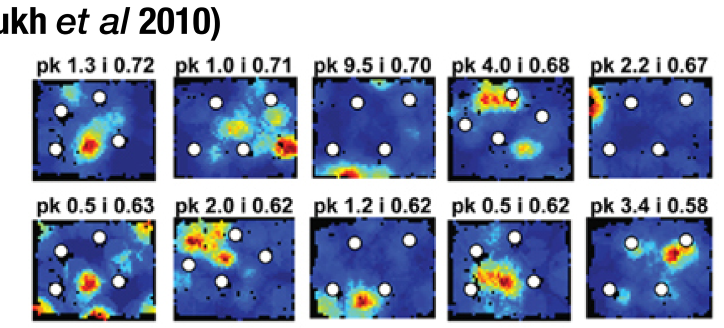


(Adapted from Monaco *et al* 2011)

- Theta-modulated subcortical circuits provide possible pathways for theta phase-specific feedback loops between the hippocampus and the path integration system. Areas mediating this feedback would require theta-bursting neurons that carry a spatially modulated rate code
- The lateral septum receives a major projection from region CA3 of the hippocampus and then projects to other subcortical areas (Luo *et al* 2011) and has been shown to have spatially modulated firing (Takamura *et al* 2006)

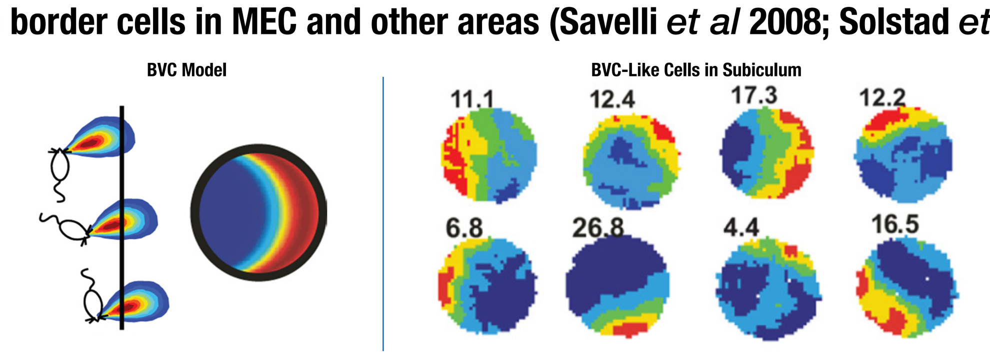
Hypothesis

- Information about landmarks and their location in the environment is encoded by object-related activity in lateral entorhinal cortex (LEC) or landmark-vector cells in hippocampus (Deshmukh & Knierim 2011, 2013; Deshmukh *et al* 2012)
- LEC activity is only weakly theta modulated relative to medial entorhinal cortex (MEC; Deshmukh *et al* 2010)



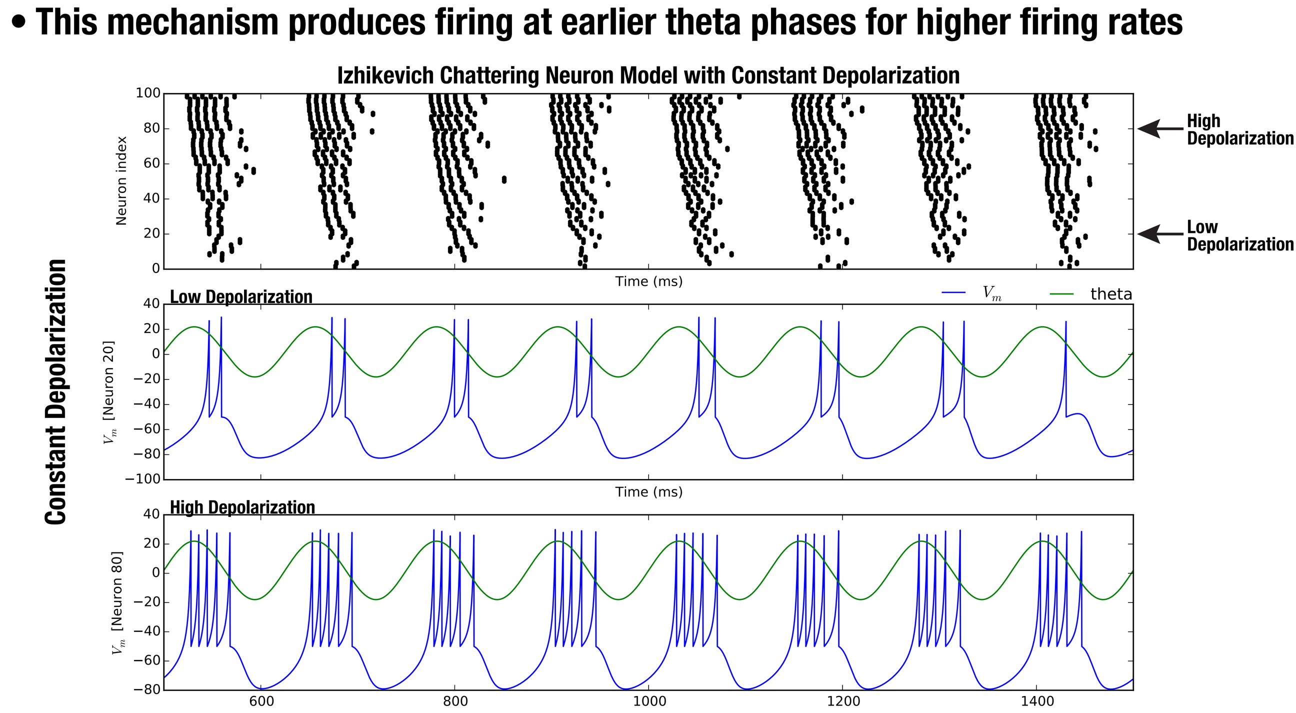
(Adapted from Deshmukh & Knierim, 2011)

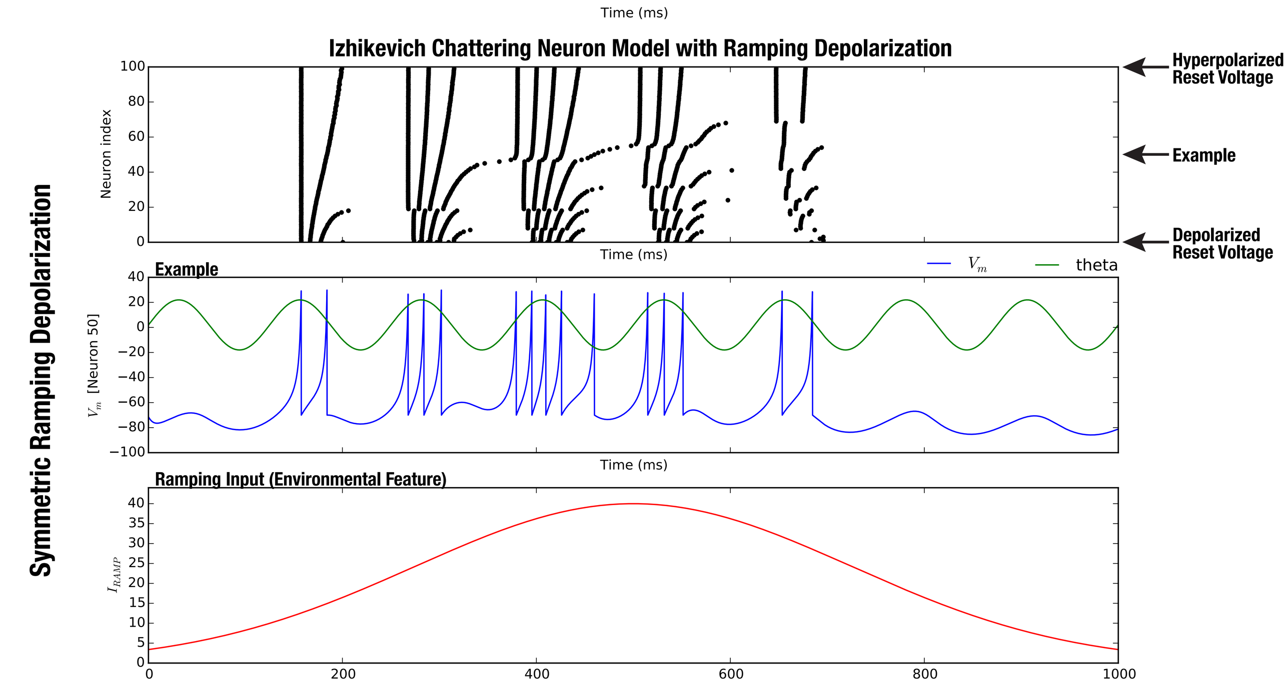
- Hartley *et al* (2000) proposed a model of boundary-vector cells as inputs to hippocampal place cells to explain place field dependence on environmental geometry
- BVC-like cells were subsequently discovered in subiculum (Lever *et al* 2009), along with border cells in MEC and other areas (Savelli *et al* 2008; Solstad *et al* 2008)



(Adapted from Lever *et al* 2009)

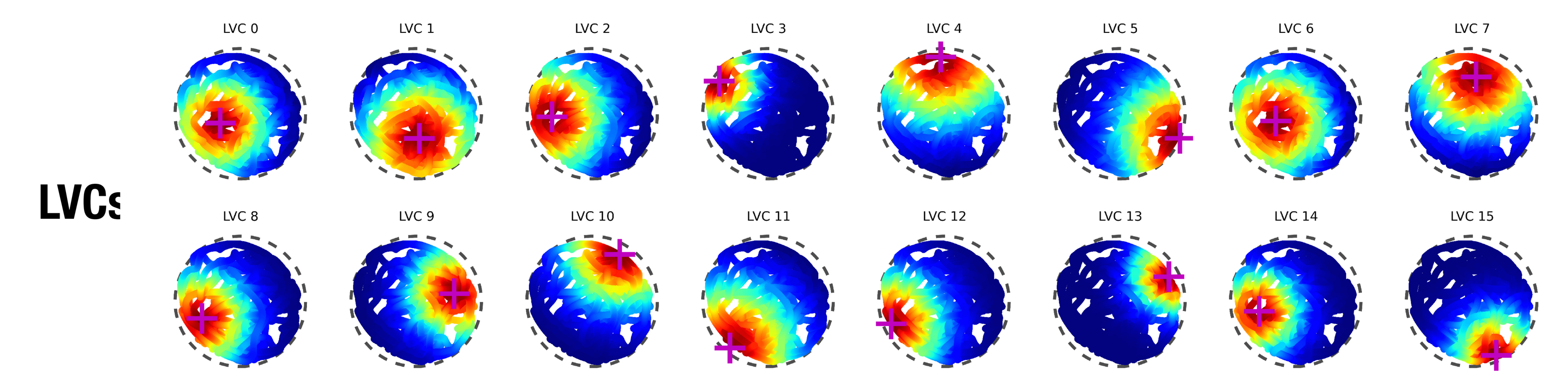
- Converting a rate code (summations over representations of environmental features like boundaries and landmarks) to a temporal code (phase-specific firing needed to entrain oscillatory interference models) can be achieved robustly in bursting neurons by combining depolarization with an ongoing theta oscillation
- This conversion was shown in CA1 place cells by Mehta, Lee, & Wilson (2002)
- This mechanism produces firing at earlier theta phases for higher firing rates



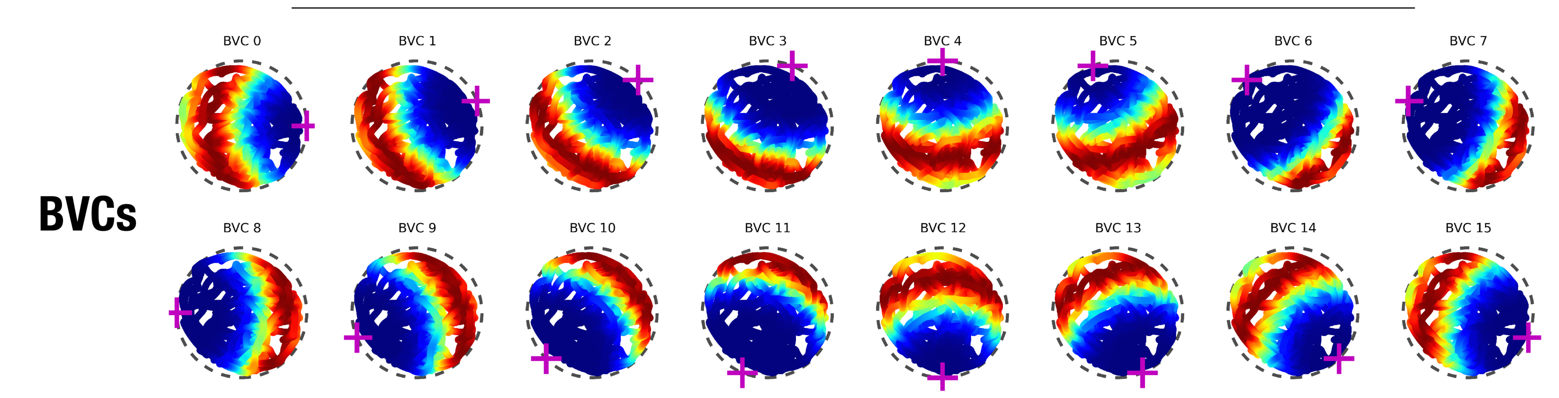


Model of location-controlled oscillators

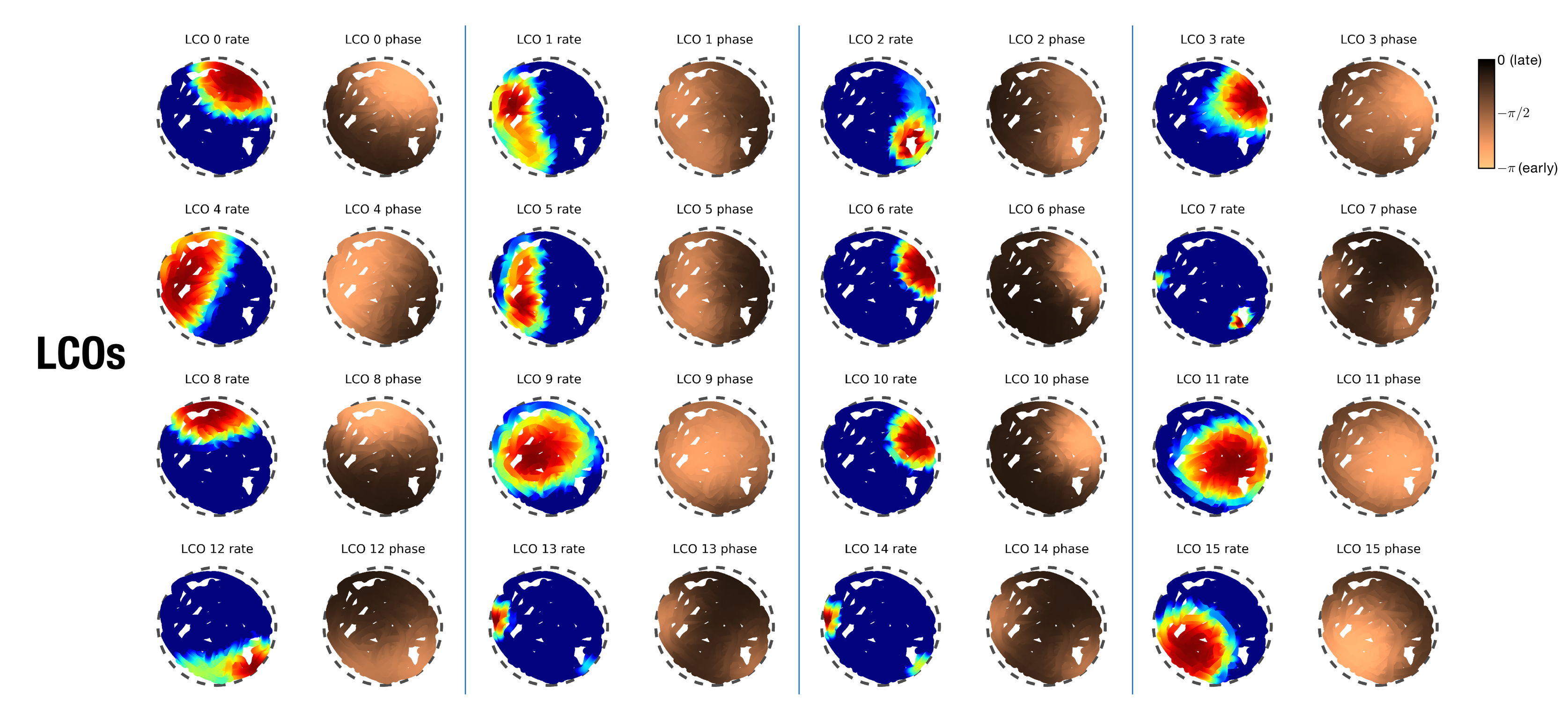
Location-controlled oscillators (LCOs) receive input from landmark-vector cells (LVCs) and boundary-vector cells (BVCs) and project to velocity-controlled oscillators (VCOs) as in previous phase interference models.



- LVCs carry a firing-rate code and and are not theta-modulated in this model, though biological landmark-vector cells or other carriers may be weakly theta-modulated
- They represent general input tied to a fixed location (plus sign) relative to some landmark or cue
- The LVC output may theoretically represent an average over a set of place cells

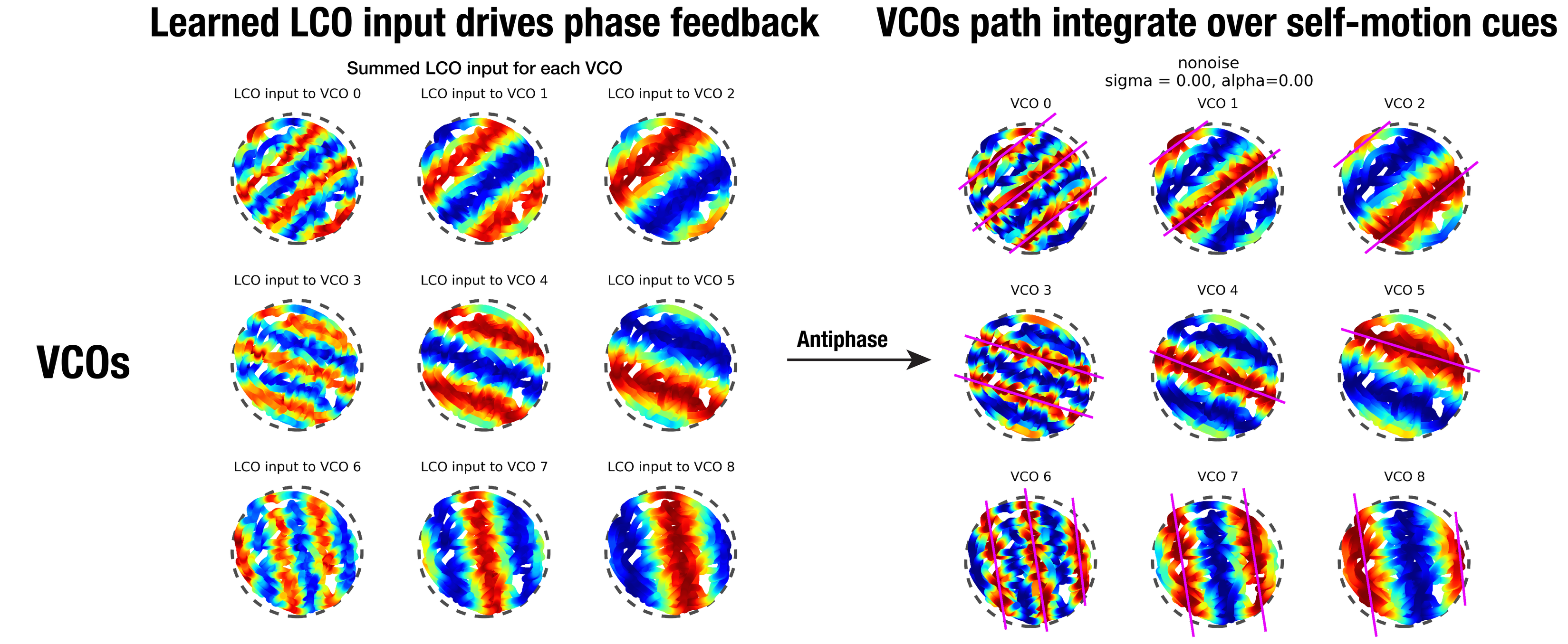


- Boundary-vector representations are computed as a skewed Gaussian profile that peaks at a preferred radial distance from the arena boundary in the preferred direction

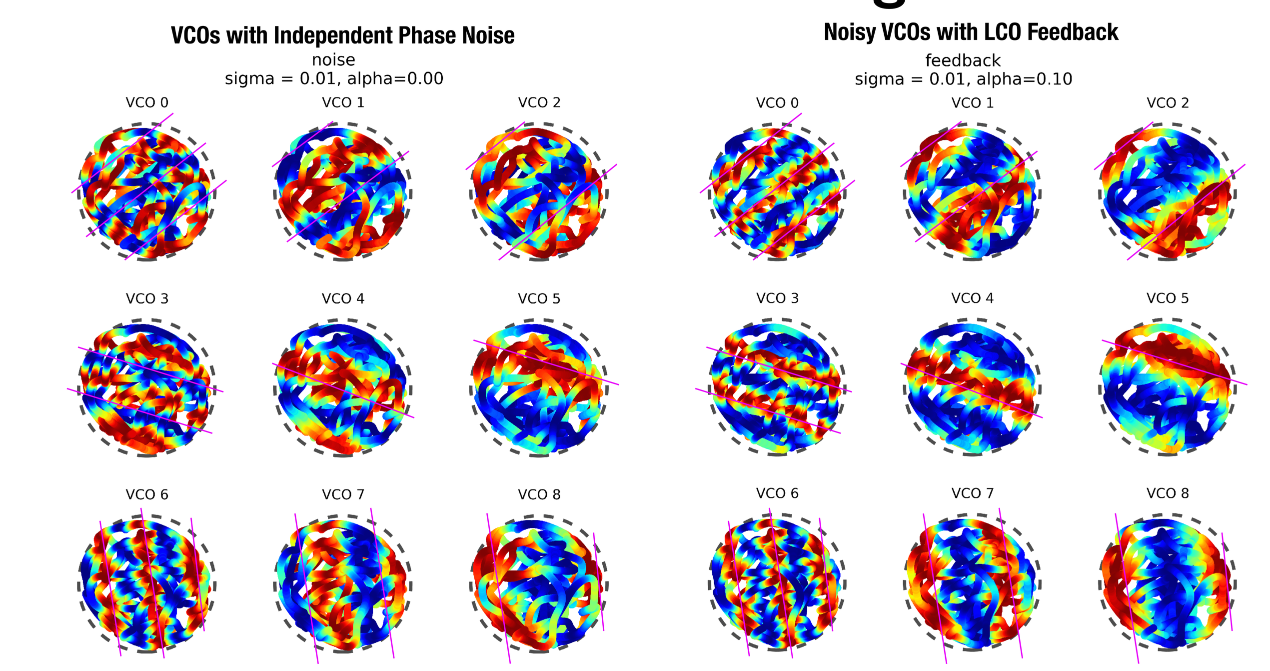


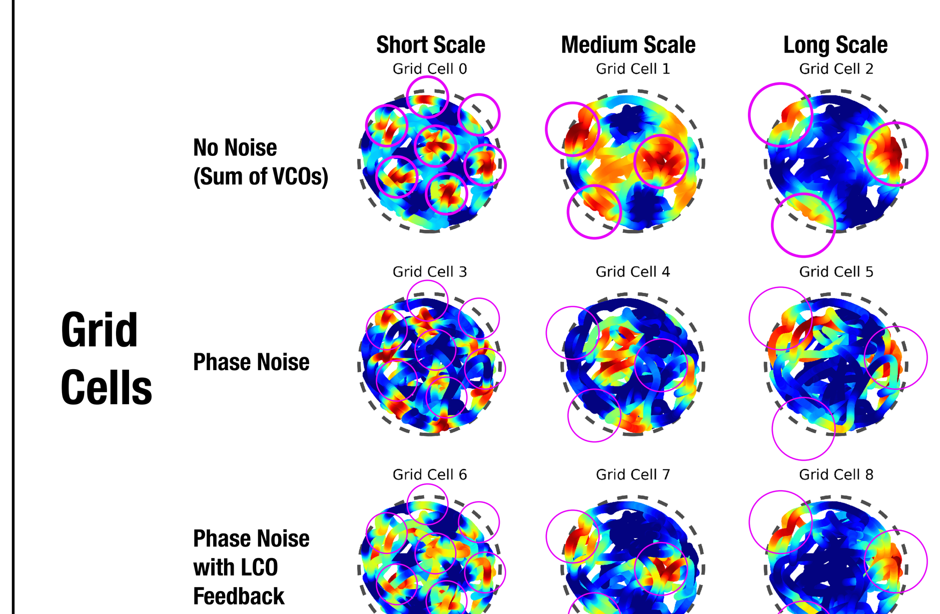
- Theta oscillations and landmark/boundary information (from BVC/LVCs) are integrated within putative "location-controlled oscillators" using a firing-rate nonlinearity that creates a correlation between high firing rates (red, left plots) and early theta phases (copper, right plots)

Learned LCO input drives phase feedback / VCOs path integrate over self-motion cues



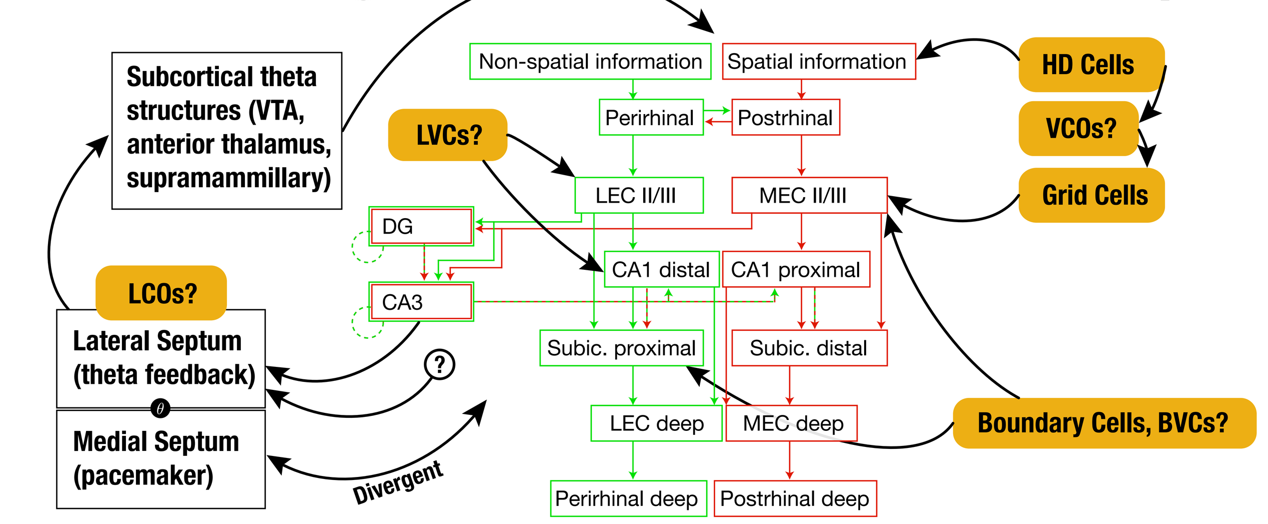
Landmark calibration in grid cells





- (Top left) Small amounts of phase noise perturb the stripe structure of VCO output and cause drift relative to noise-free VCOs (magenta lines)
- (Top right) Phase feedback from LCOs, where LCO input entrains VCOs to early theta phases, preventing differential drifting of the stripe patterns
- (Left) Additively constructed grid cells in the three conditions (rows) across three spatial scales (columns)

Processing streams, feedback loops



(Adapted from Knierim & Lee, 2006)

Conclusion We previously demonstrated a model of synchronization among multiple oscillators that performed path integration along randomized preferred directions (Monaco *et al* 2011). Using that model, we showed that generalized phase-code feedback could correct errors caused by intrinsic variability in the underlying oscillations, but did not characterize any specific mechanism for the feedback pathway. Here, we tested the hypothesis that theta-modulated subcortical areas such as lateral septum could support theta cells with spatial correlations of high firing rate and early theta phase, based on mechanisms established by Mehta *et al* (2002). Putative LCOs fire strongest at early theta phases at a particular location in the environment determined by landmarks and boundaries. By learning an input basis set of antiphase LCOs, we showed that a layer of VCOs produce spatial patterns that remain fixed relative to the environment, and that grid cells constructed from these VCOs withstand drifting due to intrinsic phase noise. Thus landmark-based rate/phase correlations in extrahippocampal areas may provide the sensory feedback required by temporal models of neural representations of space.

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