The quantification of navigation independent neuronal phase precession

Connor Braun

Introduction. For the last thirty years, hippocampal place cells have been consistently observed to exhibit phase precession with respect to theta-range (8-12 Hz) local field potential oscillations. That is, as an organism traverses a place field, a corresponding place cell bursts progressively earlier on each subsequent theta cycle. In accordance with the temporal coding hypothesis, phase precession has been implicated as a putative mechanism for encoding sequence structure of events into memory, suggesting that it could be a more general neurocomputational phenomenon and not strictly limited to spatial behaviors. To date, phase precession has been observed primarily during such spatial behaviors as traversing linear tracks or open fields, but there is very limited evidence to suggest that pyramidal cells of the CA1 exhibit phase precession during specific non-spatial behaviors including REM sleep and stationary head wheel running. As such, it is unknown to what extent phase precession dynamics might be a more general coding strategy independent of navigation.

Hypothesis. If hippocampal theta phase precession is a general mechanism for temporal encoding, then it will not only be identifiable, but quantifiable independent of navigational behaviors.

Objectives. The problem is that conventional methods of identifying phase precession rely on *a priori* knowledge of neural tuning so that spike timing with respect to local theta oscillations can be fit to some function of behavior. This curtails our ability to investigate the generality of phase precession, since neuron-behavior tuning is typically not knowable beforehand. For this reason, we first seek to develop a behavior-agnostic algorithm for quantification of hippocampal theta phase precession. Next, we will construct a computational model of neuronal phase precession which will allow us to simulate data *in silico* independent of any notion of concurrent behavior. We can then proceed to characterize the biologically-relevant conditions under which our metric returns type I or type II error. Finally, our quantification will be used to seek phase precession dynamics in hippocampal single-unit recordings from animals undergoing REM sleep or other non-navigational behaviors.

Methodology. The quantification algorithm will rely on theoretical underpinnings from discrete dynamical systems. Our initial neuron modeling strategy will be to numerically integrate a stochastic leaky integrate-and-fire model with a subthreshold spike frequency adaptation term using the Advanced Research Computing cluster at the University of Calgary. This model will be made to precess in phase with respect to an idealized (sinusoidal) theta rhythm by a dual linear oscillator input. Furthermore, the complete model will have parameters controlling biologically relevant dynamic phenomena, such as noise characteristics, excitability, spike frequency adaptation and phase precession characteristics. This will allow us to define biologically relevant conditions under which our quantification algorithm is type I or type II erroneous. The complete quantification algorithm will then serve as a dependent variable to seek and quantify phase precession in single-unit recordings (alongside concurrent extracellular local field potential recordings) taken from neurons in the hippocampal formation. Organism behavior at the time of these recordings will be the independent variable; categorically either navigational or non-navigational. These data will be obtained from the Collaborative Research in Computational Neuroscience database. Single-unit place cell recordings from entorhinal cortex, CA1 and CA3 taken from animals undergoing REM sleep will also be contributed by David Dupret lab, University of Oxford — a close collaborator of the Nicola lab.

Significance. We expect to successfully develop a behavior independent quantification and identify navigation independent phase precession in the hippocampus, liberating it as a primarily navigational phenomenon. In doing so, this project will potentially yield valuable insight not only into how living systems form memories at the level of neural dynamics, but also into principles of neural coding at large.