From time to phase: temporal delay drives theta phase precession in the hippocampus

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Behaviour occurs on timescales of seconds, minutes or even longer. Behavioural time is represented within the ongoing activity of neuronal networks in a purely neuronal way, such as the firing of action potentials [1]. Neuronal circuits make use of timescales that range from microseconds to milliseconds. How behavioural time is mapped into the activity of cortical networks remains uncertain. An example which associates behaviour with neuronal firing and temporal compression is phase precession. Phase precession is a phenomenon demonstrated when place cells increase their firing rate when the animal is located in the receptive field that each neuron represents [2]. In essence, the phase of the theta rhythm and the exact timing of an action potential contain information about change in location.

Theta precession occurs in many brain regions including CA3, the dentate gyrus, the subiculum and the ventral striatum. In this study, I examine phase precession in the CA1 region of hippocampus. The exact mechanism supporting phase precession in CA1 is still being debated; various analyses involve NMDA-dependent plasticity, intrinsic properties of the pyramidal cells and dendritic excitation, compression of temporal sequences within individual theta cycles, slow GABAergic modulation influencing the learning and recall of sequence information or involve the enactment of two separate oscillations and the intracellular dynamics of place cells.

Here, I provide a possible explanation of the mechanism responsible for generating phase precession by further developing results published by myself and colleagues [3]; using a detailed biophysical compartmental model of the CA1 pyramidal neuron, I examined the signal interference effects of layer-specific synaptic inputs namely, entorhinal cortex inputs targeting interneurons and distal CA1 dendrites in stratum lacunosum moleculare (SLM) and CA3 originated inputs targeting interneurons and proximal dendrites in the stratum radiatum (SR), on the firing frequency and the firing pattern of the neuron. Findings of this study showed that the CA1 model neuron's firing pattern ranges from suppression to baseline responses depending on the spatial but mostly on the temporal characteristics of the incoming signals; the temporal delay between EC and CA3 activated inputs may act as a mechanism for alternating between excitability states; short delays (0-100 ms) are associated with dendritic calcium spikes and strong somatic excitation in form of bursts while long delays (>160 ms) is associated with strong inhibitory potentials leading to reduced or abolishment of firing. Furthermore, the onset time of the first spike of the burst event, the time-to-first-spike (ttfs) variable is positively correlated with the temporal delay applied between the two inputs and contains information about the delay between EC activation and the CA1 response, when the latter also contains Shaffer Collaterals input information.

Taken together these findings, suppression of the CA1 firing occurs when the temporal offset ranges between 160-300 ms. Maximum firing frequency occurs for short delays (0-100 ms) whereas consistent decline of excitation as the temporal offset increases, is observed for intermediate delays (100-160 ms). I suggest that the temporal offset has a mapping onto the regime of phases: short delays and early ttfs correspond to 200°-270° degrees of the theta cycle whereas intermediate delays and advanced ttfs may correspond to higher theta phases (360°). When cell inhibition dominates excitation during early theta phases (0°-90°)6 the model neuron's inhibition dominates excitation for long temporal offsets.

Based on the upon findings, I describe the components for explaining phase precession and its traits: a) the time delay, or temporal offset, separating the activation of two major synaptic pathways that act selectively upon subcellular dendritic compartments of the neuron; b) the microcircuit in which the CA1 pyramidal neuron is embedded in and, c) the subcellular, slow inhibition induced by the layer specific interneurons. I suggest that the temporal offset has a mapping onto the regime of phases mediated by the time-to-first-spike parameter and that, phase precession and phase shift may be associated with inhibition of return, dwell time and visual attention deployment that change repeatedly in accordance with the eye saccadic movements taking place during navigation.

References

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