Dynamics of ripple oscillations in recurrent interneuron networks on micro- and mesoscopic level

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Hippocampal ripple oscillations have long been implicated in important cognitive functions such as memory consolidation or planning [1][2]. The underlying mechanisms however are still under debate. One hypothesis is that inhibitory interneurons, such as PV^+ basket cells, act as the primary pacemaker that entrains the excitatory pyramidal-cell population to also oscillate in the ripple band (140-220 Hz). Modeling studies have shown that a network of recurrently coupled interneurons can indeed produce oscillations in the ripple band when driven with sufficiently strong, excitatory input [3].

In particular, a recent study by Donoso et al. [4] identified three distinct dynamical regimes of such an inhibitory network driven by excitatory Poisson input: (i) an asynchronous irregular regime in response to low stimulation with single units firing sparsely and irregularly and no significant oscillation in the network; (ii) a sparsely synchronized regime for intermediate stimulation with a clear network oscillation in the ripple band, but only a fraction of the neurons participating in each cycle; (iii) a fully synchronized regime where network frequency and unit frequencies coincide. In the sparsely synchronized regime the network frequency depends mainly on the short synaptic time scales [3], whereas in the fully synchronized regime the input level is the main determinant of network frequency.

Interestingly, the same model could also reproduce intra-ripple frequency accommodation (IFA) – an additional feature of ripple dynamics: In response to a transient, sharp-wave-like stimulation the instantaneous frequency is highest in the first half of the ripple and then monotonically decays towards the end of the event. Donoso et al. reasoned that IFA is caused by a transition of the network from the sparsely to the fully synchronized regime and a subsequent hysteresis effect, which keeps the network frequency sensitive to the input level on the downstroke of excitation [4]. Yet, the exact dynamics of the interplay between this hysteresis phenomenon and the time course of excitation still remain unclear.

In an effort to gain a deeper understanding of ripple dynamics and the prerequisites for the occurrence of IFA, we compare models on different scales of abstraction. In a first approach, we replicate the results of Donoso et al. in a microscopic simulation of a recurrent interneuronal network (using the spiking network simulator “Brian” [5]). We then simulate the same network on a mesoscopic scale using a population density approach [6], where mean-field assumptions are made but microscopic fluctuations and spike-history effects are approximately retained by introducing correction terms.

In the subsequent comparison of network dynamics we find that on the mesoscopic scale the sparsely synchronized regime seems to vanish and the occurrence of IFA becomes less reliable. This might be due to the model-intrinsic uniformity of the stochastic input across neurons. To test this we investigate possible extensions of the mesoscopic approach to incorporate or at least mimic variability of the input across neurons. Apart from model features like input variability and connectivity we also look at the time course of excitation as a possible influence on IFA. We hope that a thorough theoretical understanding of the dynamical differences observed in micro-, meso- and potentially macroscopic models of ripple oscillations will allow us to construct a reduced model reflecting the core mechanism of ripple generation in interneuron networks and IFA in particular. Apart from neuroscientific insights this might also open up interesting, new theoretical questions on network dynamics and modeling across scales in general.

References

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