Controlling pyramidal cell activity by bistable gamma-frequency oscillations in a network of hippocampal interneurons

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Inhibitory neuronal networks are involved in several aspects of controlling the overall activity of the central nervous system. However, the functional role they play is often ambiguous. GABAergic interneuron-to-pyramidal cell synapses were shown to regulate the back-propagation of action potentials [1], the emergence of calcium spikes [5] and to set membrane excitability of pyramidal cells. Collective oscillations of interneurons are also believed to underlie the generation of distinct hippocampal rhythms, i.e. the gamma ($40-100$ Hz) oscillations [8] and high-frequency ripples (200 Hz) [2]. The above studies either discuss the impact of interneurons' activity on their target neurons (interneuron-to-pyramidal cell connections) or the patterns generated by an interneuron network. Combining the interneuron-network generated behavior with the different ways of affecting target pyramidal cells is a way to unravel how the activity of interneurons is related to the information processing capabilities of the hippocampus. In this study we investigate the different time-scale synchronizing properties of an interneuron network and its effect on their target pyramidal cells will also be explored: conditions necessary for preventing back-propagating action potentials will be assessed.

An interneuron network with two distinct dynamical states is shown. The network show two modes of activity: a stable in-phase locked synchronization and a meta-stable anti-phase synchronization. Previous studies have shown that this interneuron network was able to produce synchronized gamma-frequency oscillation [7] and that the level of synchrony can be periodically changed in theta frequency in an autonomous manner [6]. Here, in an extended model the behavior of a perisomatically innervated pyramidal cell is investigated. It is shown that in-phase synchronized firing of the interneuron-network gate the firing of target pyramidal cell in gamma frequency. During the anti-phase synchronized state the dispersed inhibition results in the full suppression of back-propagation action potentials in the dendritic tree of the pyramidal cell.

First, simulating a two-neuron network stability properties of the coupled oscillator model are assessed. It is shown that the simulated conductance based CA3 interneuron

model has a stable limit cycle corresponding to a higher frequency in-phase locked synchronization, and a meta-stable limit cycle corresponding to a lower frequency anti-phase locked oscillation. Single current pulses delivered to one (or both) of the interneurons was shown to result in the switch between the two states. The weaker stability of the anti-phase oscillation is also expressed in that lower level perturbations (smaller current pulses) are sufficient to switch the system to the other state. Input heterogeneity, i.e. input timing difference, plays a crucial role in network behavior. At a critical level of heterogeneity the anti-phase synchronised state loses its stability. This condition prevents the system from settling in the meta-stable state and perturbations cause only temporal breakdowns of in-phase synchrony. The length of these transient non-synchronous states can be controlled by the level of heterogeneity. Simulating the effect of bistability on a large network it is shown that although the anti-phase locked oscillation is instable (due to the higher level of inherent heterogeneity), it affects the synchronizing properties of the network: the same transients exist in the large network as the one showed using only two cells. This temporarily vanishing synchrony defines a time window where the output of the network is time dispersed thus causing a stronger inhibition on target neurons.

The effect of the intermittent dispersed inhibition is investigated by extending the model with a multicompartmental pyramidal cell, which is driven by the output of the network. Provided that a sufficiently large number of interneurons converge on a single pyramidal cell [3], anti-phase oscillating interneurons cause a time-dispersed inhibition, while in-phase locked oscillations cause periodic gating of action-potential generation. Our investigations show that gamma-frequency gating of pyramidal cells provide sufficient condition for the synchronization of pyramidal cells. Back propagating action potentials into the dendrites of pyramidal cells play a central role in long term potentiation of afferent synapses [4]. As efficiency of back propagation is determined by mechanisms controlled by the perisomatic inhibition, using the interneuron-network dynamics, we investigated the conditions necessary for action-potential back propagation. Depending on the occurrence of the intermittent asynchronous periods it was possible to control the prevention of action potential back-propagation. This way we propose that an interneuron network is able to determine whether only information transfer/processing occurs at pyramidal cells or plasticity at the distal dendrites is also possible.

References

[1] Gy. Buzsáki, M. Penttonen, Z. Nádasdy, and A. Bragin. Pattern and inhibition-dependent invasion of pyramidal cell dendrites by fast spikes in the hippocampus in vivo. *Proc Natl Acad Sci U S A*, 93:9921–5, 1996.

[2] J. Csicsvári, H. Hirase, A. Czurkó, A. Mamiya, and Gy. Buzsáki. Fast network oscillations in the hippocampal CA1 region of t he behaving rat. *J Neurosci*, 19:RC20 1–4, 1999.

[3] T. F. Freund and Gy. Buzsáki. Interneurons of the hippocampus. *Hippocampus*, 6:347–470, 1996.

[4] J. C. Magee and D. Johnston. A synaptically controlled, associative signal for hebbian plasticity in hippocampal neurons. *Science*, 275:209–213, 1997.

[5] R. Miles, K. Tóth, A. I. Gulyás, N. Hájos, and T. F. Freund. Differences between somatic and dentritic inhibition in the hippocampus. *Neuron*, 16:815–823, 1996.

[6] G. Orbán, T. Kiss, M. Lengyel, and P. Érdi. Hippocampal rhythm generation: Gamma-related theta-frequency resonance in CA3 interneurons. *Biol. Cybern.*, 84:123–132, 2001.

[7] X. J. Wang and Gy. Buzsáki. Gamma oscillation by synaptic inhibition in a hippocampal interneuronal network model. *J. Neurosci.*, 6:6402–6413, 1996.

[8] M. A. Whittington, R. D. Traub, and J. G. R. Jefferys. Synchronized oscillations in interneuron networks driven by metabotropic glutamate receptor activation. *Nature*, 373:612–615, 1995.