Interaction of Sub-threshold Oscillations with Synaptic Input in the Cortex.
Klaus M. Stiefel1, Jean-Marc Fellous1 and Terry Sejnowski1,2
1. CNL, The Salk Institute Biological Studies, La Jolla, CA, USA
2. Department of Biology, U.C.S.D, La Jolla, CA, USA

Introduction:

Neurons communicate amongst each other via synaptic transmission. Postsynaptic potentials in the cortex in vivo encounter membrane potentials that are strongly fluctuating due to massive synaptic input from other sources (Destexhe et al., 2003) and/or intrinsic membrane properties (Klink & Alonso, 1990). We investigated the interaction of inhibitory postsynaptic potentials (IPSPs) with intrinsic subthreshold oscillations, emphasizing the effect IPSPs have on the phase of these oscillations.

Experimental Methods:

We recorded with the patch-clamp technique from layer III/HI pyramidal neurons and interneurons in the slices of the mouse (P28 to P15) visual and prefrontal cortex. We then evoked subthreshold oscillations in these cells by injecting long (2 to 6 sec) positive current pulses to depolarize the cell to around firing threshold. An initial zero to six spikes were followed by episodes of subthreshold oscillations. Traces with additional spikes interrupting these oscillations were discarded. During the oscillations we either evoked an IPSP by monopolar extra-cellular stimulation or injected a short (20 to 60msec) hyperpolarizing current pulse, mimicking an IPSP. During the majority of experiments excitatory synaptic transmission was blocked by DNQX (20μM) and APV (50μM).

Data Analysis:

To determine the phase of the oscillations as a function of time we first band-pass filtered the voltage signal (Fig.1A), subtracted from it a fit to the IPSP or the voltage response to the current pulse (Fig.1B), and then plotted it against its Hilbert transformation (Fig.1C). The cumulative angle (θ) in this plot represents the cumulative phase of the oscillation and was plotted as a function of time (Fig.1D). To determine the phase progression of the voltage signal containing the IPSP or i-pulse we averaged the phase during the 300msec before and after the pulse and subtracted them (θm). We plotted θm as a function of a number of properties of the oscillation, such as voltage average and fluctuation, power in the 1 to 5Hz and 5 to 15Hz bands as well as θ at the onset of the IPSP or i-pulse.

In addition we averaged all individual plots of θm vs. time and θm vs. time of every cell (temporally aligned at the beginning of the IPSP/i-pulse). We extrapolated a linear fit to the 500msec before the IPSP/i-pulse of both averages to see how long it takes either of them to cross that extrapolation (and thus return to baseline).

Results:

1. Phase deflections can persist for extended time spans. In 2 out of 6 experiments conducted with IPSPs, the average phase shift persisted until the end of the sweep (avg. 1156 msec). In the remaining 4 experiments, the phase intersected with the extrapolation of the linear fit to the 500 msec before the pulse on average after 887 msec. The experiments in which the IPSP was substituted with a negative current pulse, mirrored the results of the experiments with IPSPs. In 3 out of 5 cells phase averaged, did not intersect with the extrapolation (in the remaining two cells the pulse failed to cause a phase shift).

2. Voltage deflections persist for much shorter time spans. In contrast, the voltage average intersected with the extrapolation in all but one case, on average 212 msec after the onset of the IPSP (Fig.2). In the experiments with i-pulses, the voltage average intersected with the extrapolation in all cases, on average 446 msec after the onset of the pulse (Fig.2).

3. Dependence of phase shift on parameters of the oscillation and dependence of the shape of the IPSP on the phase. The phase shift was negatively correlated with the standard deviation of the voltage during the oscillations and the power of the oscillations in the 1Hz to 5Hz and 5 to 15Hz bands (Fig.3). The shape of the IPSP waveform was uncorrelated to the phase shift (Fig.4) but showed a dependence on the phase at which the IPSP occurred (Fig.5). We fit the IPSP with a sum of two β-functions (β1(t)=t/β1^2 + 1 and β2(t)=t/β2^2 + 1). The parameters β1 and β2 thus correspond to the amplitude, β1 and β2 to the time constants of the IPSP.

Conclusions:

Changes in the phase of subthreshold oscillations can persist much longer than voltage deflections causing them. Neurons with a rich repertoire of intrinsic properties can store information in them for extended time spans.

References:


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