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Input/Output Relationship in CA3 Pyramidal Cells: Yr 2 Progress Report

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Giorgio Ascoli
George Mason University

German Barrionuevo
University of Pittsburgh

David Jaffe
University of Texas, San Antonio

This project aims at characterizing the synaptically-driven activity of CA3 pyramidal cells (CA3pcs) in the rat hippocampus. Progress in this second year related to the basic biophysical characterization of CA3pcs (passive and active properties) and their elementary excitatory synaptic inputs. The firing patterns of CA3pcs were studied by whole-cell recording in response to varying amplitudes of somatic current injection. Minimal-threshold current injection triggered either a single early- or late-onset spike (i.e. occurring in the first or second half of the current step). In response to stronger current amplitudes, early- and late-onset cells displayed either rapidly accommodating or reverse accommodating spike trains, respectively. There was no correlation of firing pattern to resting potential, passive properties, or action potential waveform. Burst firing was only observed in a minority of the cells and could not be elicited by perforated patch-recordings, disinhibited conditions, high extracellular K^+, or a Poisson-distribution of noisy input. Because the distal dendrites of CA3pcs are not amenable to intracellular electrical recording, we used high-speed fluorescence Ca^{2+} imaging to study spike backpropagation and the subsequent activation of voltage-gated Ca^{2+} channels. Both in response to single spikes and trains of action potentials, the largest increases in Ca^{2+} was observed ~100 μm from the soma, suggesting that spikes failed to propagate fully into more distal dendrites. Furthermore, the voltage-dependence and kinetics of somatic hyperpolarization-activated currents (I_h) were quantified by standard voltage-clamp. Membrane responses to varying amplitudes of hyperpolarizing current steps were recorded by current clamp, and a simultaneous fit was obtained for multiple cells. In all cases, distribution of all passive (R_m, C_m, R_a) and active (I_h density and relative proportion of fast/slow components) properties were set as uniform and free parameters, based on the same Boltzmann function and average experimental kinetic values, but unconstraining somatic current injection values. Finally, we measured and statistically analyzed the basic characteristics of unitary signals from each of the main synaptic inputs to CA3pcs. Excitatory postsynaptic potentials (EPSPs) and currents (EPSCs) were evoked in the disinhibited slice by minimal extracellular stimulation of the perforant pathway, mossy fibers, and recurrent collaterals, separating the AMPA and NMDA components with D-APV and CNQX, respectively. At somatic failure rates of 0.3-0.5, binomial analysis indicates that the proportion of unitary responses is fairly independent of the number of individual presynaptic sites within a range compatible with known hippocampal stereology. This calculated “unitary yield” was used to identify the elementary postsynaptic signals rank ordered by amplitude. Resulting somatic voltage

and current traces were analytically fitted and quantified in terms of time-to-peak, half-height width, and peak value, capturing both the intra- and inter-cellular variability for each of the excitatory pathways.

Project (or PI) Website

http://krasnow.gmu.edu/L-Neuron

Publications

1. Migliore M., Ferrante M., Ascoli GA (2005) Signal propagation in oblique dendrites of CA1 pyramidal cells. J. Neurophys., 94:4145-4155.

2. Ascoli GA (2006) Mobilizing the base of neuroscience data: the case of neuronal morphologies. Nature Rev. Neurosci., 7:318-324.

3. Li X, Ascoli GA (2006) Computational simulation of the input-output relationship in hippocampal pyramidal cells. J. Comput. Neurosci., In Press.

4. Krichmar JL, Velasquez D, Ascoli GA (Submitted) Effects of β-catenin on dendritic morphology and simulated firing patterns in cultured hippocampal neurons.