Structural and biophysical mechanisms underlying dynamic sensitivity of primary sensory interneurons in the cricket cercal sensory system.

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Abstract: (100 words)
Realistic, biophysically-based compartmental models were constructed of several primary sensory interneurons in the cricket cercal sensory system. A dynamic atlas of the afferent input to these cells was used to set spatio-temporal parameters for the simulated stimulus-dependent synaptic inputs. We examined the roles of dendritic morphology, passive membrane properties, and active conductances on the frequency tuning of the neurons. The sensitivity of narrow-band low pass interneurons could be explained entirely by the electrotonic structure of the dendritic arbors and the dynamic sensitivity of the SIZ. The dynamic characteristics of interneurons with higher frequency sensitivity required models with voltage-dependent dendritic conductances.

Summary (954 words)

INTRODUCTION**:** The response properties of a neuron to complex patterns of synaptic inputs are controlled by a combination of factors including: 1) the electroanatomy of the cell, 2) it's biophysical properties and 3) the distribution and activation pattern of synaptic inputs. We have used a combination of electrophysiological experiments and compartmental modeling techniques to 1) calculate detailed, quantitative predictions of a variety of ensemble afferent activity patterns elicited by air current stimuli, 2) use the predicted ensemble response patterns to define dynamic simulated synaptic input patterns onto the dendrites of compartmental interneuron models, and 3) to examine the roles of dendritic morphology, passive membrane properties, and active conductances on the frequency tuning of the neurons.

Primary sensory interneurons in the cercal system are sensitive to the direction and dynamics of air currents (9). The interneurons receive excitatory input from an ensemble of sensory receptor afferents which form a neural map of air current direction in the central nervous system. Interneurons extract and encode information about stimulus direction based on the shape and position of their dendrites within the afferent map. Three independent factors could contribute to the frequency sensitivity of each interneuron: a) its inherent frequency filtering properties, b) the position of its dendrites within the afferent map, and/or c) its selective connectivity with subclasses of afferents having similar directional sensitivities but *different* frequency and adaptation characteristics.

METHODS: Anatomical reconstructions and physiological data were used to create biophysically-based compartmental models of 3 identified sensory interneurons. Values for R_i and C_m were set to experimentally established values. R_m was initially assumed to be uniform throughout the cell, and was set to yield the measured steady-state input resistance and complex input impedance at the equivalent electrode recording point in real neurons. Next, parameter domains for voltage-dependent dendritic and axonal conductances were determined using a variety of validation criteria. Active parameters were set using modified Hodgkin-Huxley descriptions of voltage dependent channels, by matching dynamic model responses to equivalent responses recorded physiological experiments (8). Various types of current injection paradigms were used and, subsequently, simulated, including steps, sine waves and band-passed white noise. Finally, active parameters were refined further to match a variety of statistical and information-theoretic measures. The measures include the coherence between the simulated response and either simulated air-current stimuli or direct current injection.

Dynamic patterns of activity in the ensemble of sensory afferents in response to bi-directional air current stimuli were generated using the following method: Physiological measurements obtained from the different sensory neuron classes (7) were used to carry out a Wiener kernel analysis for each neuron class. The kernels for each afferent type were used to predict their response pattern, as a function of time, to several simulated air current stimulus waveforms. The predicted spiking activity patterns of all of the sensory neurons in the ensemble were combined with the corresponding anatomical data yielding a dynamic spatio-temporal pattern of activity within the ensemble of sensory neurons (2, and Jacobs and Crook in prep).

Previous studies of the dynamics of the mechanoreceptors demonstrated that there are phase lags between the movements of the hairs of different lengths when sinusoidal wind stimuli are applied (5). During a maintained sinusoidal stimulus, the shortest hairs have the smallest phase to the stimulus, followed by progressively larger phases in the medium and longest hairs. We compared our model predictions of afferent activity to these experimental studies, and verified that our model predicted the observed phase relationships with considerable accuracy, for sinusoidal stimuli over the entire observed range of frequencies.

A probabilistic representation of the 3D location and density distribution of membrane surface area of the ensemble of primary afferents was used to estimate the distribution of synaptic inputs to each of the interneuron models (3). In previous work, the mean and variances of the distribution of membrane surface area within each sample of a particular class of sensory neurons was calculated (3). The distributions for each sensory neuron class were combined into a mean density distribution that represents the 3D location and density distribution of membrane surface area. For the modeling studies described here, this mean probability density distribution was used as the anatomical substrate for the prediction of afferent activity patterns. The magnitude of the density distribution at any given point corresponds to our best statistical estimate of the local density of varicosity surface area from that afferent at that point and represents a first-order estimate of the probability with which any dendrite from a post-synaptic target interneuron might encounter a synaptic output site from that particular class of sensory afferent.

Synaptic inputs were assigned to each compartment of the model neurons based on their spatial location with respect to the mean density function (3, 4, 6). Since the density function is non-uniform, the inputs to each compartment were scaled according to the amplitude of the density function at that location. The amplitude and time course of the synaptic inputs were modeled as conductance changes, determined by the predicted activity patterns described above.

RESULTS: For interneurons with narrow-band low pass frequency tuning, the tuning can be explained entirely by the electrotonic structure of the dendritic arbors and the dynamic sensitivity of the spike initiation zone. The passive membrane structure functions as a low-pass filter for synaptic inputs, and the ionic channels that create action potentials function as a band-pass filter for current input waveforms. We also used models to study the mechanisms that could contribute to frequency selectivity in interneurons with broader tuning and higher frequency preferences. Simulations and theoretical studies suggest that the tuning in these cells can be partially explained by dendritic structures that are more electrotonically compact. In some cases, active dendrites are required with ionic channels that resonate in the desired frequency range.

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