DENDRITIC EXCITABILITY AND MORPHOLOGY DETERMINE SYNAPTIC EFFICACY

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The photo shows a student of P.G. Kostyuk: Komendantov O.

Introduction

Dendrites play a central role in neuronal information processing. Electrical signals from other neurons are transmitted onto dendrites via synaptic inputs, which are located throughout the dendritic tree. The most important functional characteristic of synaptic inputs is their ability to influence neuronal spiking activity. In real neuronal networks an individual neuron receives many synaptic inputs from numerous other neurons. Under the appropriate circumstance of background activity, even an individual weak synaptic input can be the determining factor for action potential initiation.

The ability of an individual synaptic input to evoke somatic postsynaptic potentials sufficient to trigger or alter the spiking activity is often defined as a syn-

aptic efficacy (SE) (London *et al.*, 2002). SE depends on numerous internal and external factors. Regulation of SE is fundamental for the function of individual neurons and their networks, but the relative and interacting contributions of membrane excitability, background input-output activity, and dendritic morphology have not yet fully understood.

In the present study, we investigated computationally the influence of several factors on the efficacy of individual synapses as well as on the overall synaptic efficacy (OSE) of the dendritic arborization. The investigated factors included the distance of synaptic input from the soma, frequency of the background network activity, neuronal morphology, and expression of voltage-gated channels.

Models and methods

We used multicompartmental models of neurons with different morphologies and variable densities of voltage-gated ionic channels. Both simplified cylindrical dendrites and three-dimensional digital reconstructions of real neuronal morphologies retrieved from a database (http://neuromorpho.org) were used in numerical simulations under the NEURON computational environment. In each of these models, we implemented the same Hodgkin-Huxley (HH) type spike generating mechanism. In a model of CA1 pyramidal neuron with realistic morphology, biophysical properties and channel distribution (Migliore *et al.*, 2005), the basic set of active dendritic properties included sodium (*Na*), potassium delayed rectifier (K_{DR}) and A-type conductances (g_A), as well as the hyperpolarization-activated (h-) conductances (g_h).

Individual excitatory inputs from the same "probe" synapse at varying locations were activated against a realistically massive background of stochastic excitatory and inhibitory bombardment. The resulting somatic output was compared to the recording obtained in exactly identical conditions of background activation, but with no probe input. In each model, the spike frequency of somatic output was matched to the frequency of background excitatory inputs (2, 5, 10, and 20 Hz) by adjusting their synaptic weights. The measure of SE was devised to describe the ability of a single synapse to be the determining factor for triggering an action potential in the postsynaptic neuron. Thus, a synaptic event could "count" if and only if it resulted in a spike that cannot occur in its absence. In addition to the synaptic efficacy of individually identified synapses, we also defined OSE for a given neuron, which meant to capture the average synaptic efficacy of the "typical" synapse for the cell. Also, a measure of weighted path distance (WPD) from the soma to the center of synaptic efficacy was calculated. Thus, while SE and path distance from the soma describe local properties of individual neuronal inputs, OSE and WPD provide a global characterization of the entire dendritic arbor. The general **methods have been described in detail** in our recent paper (Komendantov and Ascoli, 2009).

Synaptic efficacy in model neurons with real morphology

The dependence of SE on the path distance of the probe input from the soma was studied for several cases of real neuronal morphologies including a rat hippocampal granule cell, a mouse spinal motoneuron, a tiger salamander retinal ganglion (RG) cell, and hippocampal CA1 pyramidal neuron. These simulations were all run with different dendritic expressions of voltage-gated conductances, different frequencies of synaptic activity and numbers of active synapses. Thus, we com-

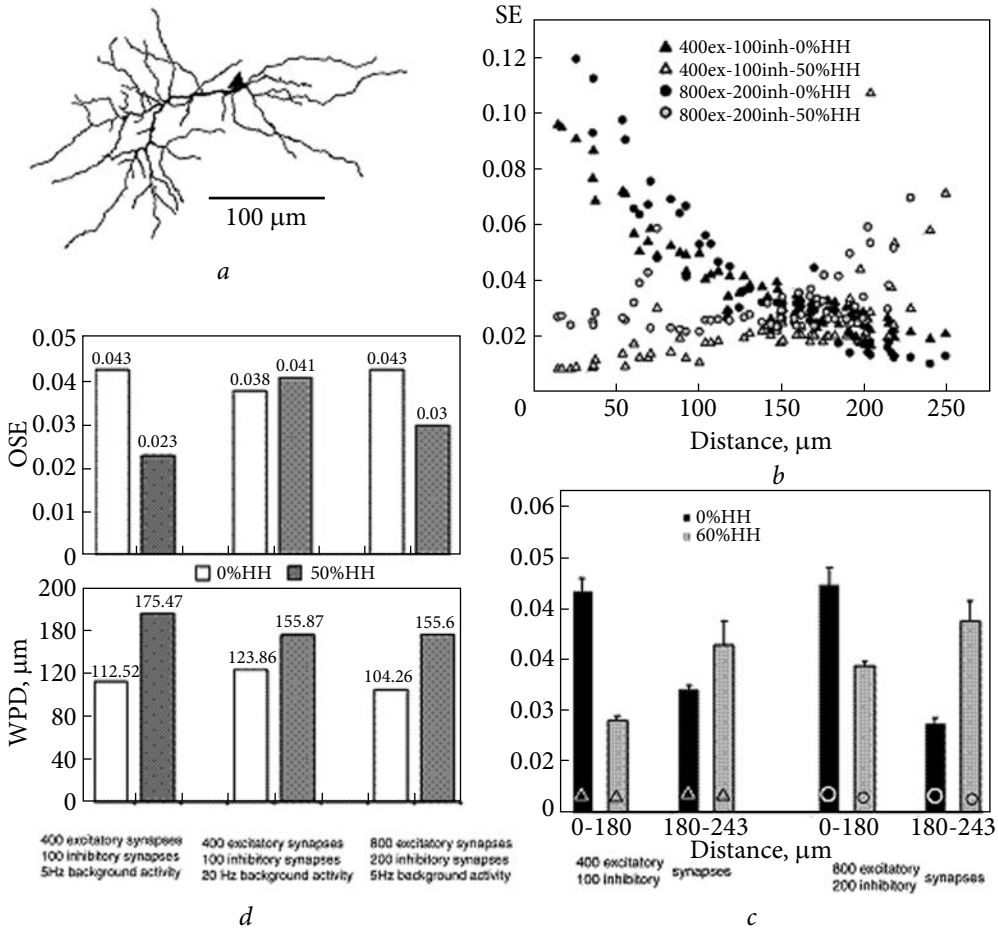

Fig. 1. Synaptic efficacy in the model RG cell under different conditions: *a* — graphical representation of dendritic morphology; *b* — SE measured at varying distances from the soma and with two levels of dendritic excitability. Background activity (5 Hz) was provided by two different sets of synapses; *c* — statistical summary (mean ± standard error) of SE for synapses located within the denoted distance ranges; *d* — OSE and WPD between the center of synaptic efficacy and the soma with different number of synaptic inputs under different frequencies of background activity (modified from Komendantov and Ascoli, 2009)

puted SE in the RG cell model realistic morphology (Fig. 1, *a*) under two different conditions, corresponding to the standard set of active synapses (400 excitatory and 100 inhibitory) and to twice those numbers, respectively.

In both conditions, SE decreases with distance from the soma in the passive dendrite case (0% HH) and increases in the partially active dendrite case (50% HH) (Fig. 1, *b*). With both the standard and doubled number of synapses, expression of active channels decreases SE proximally and increases it distally compared to the passive case. Such an increase in SE of distal inputs compared with that of proximal locations correlates with dramatic increase in the input resistance and generation of dendritic spikes. Doubling the number of synapses makes these tendencies more prominent in the passive case and distally, and less prominent in the active case and proximally (Fig. 1, *c*). Computing the OSE and WPD for both the standard and doubled number of synapses at 5 Hz of background activity demonstrated the same tendencies with expression of active channels (Fig. 1, *d*) shown also in other models with real morphologies. In particular, 50%HH dendritic expression reduced OSE and increased WPD relative to the passive case. Additionally, our simulations suggest the possibility that SE could essentially become independent of the distance from the soma with low levels of dendritic excitability. In a model RG cell this condition was met between 5% and 10% of somatic expression of the voltage-gated channels (Komendantov and Ascoli, 2009). In this intermediate range of voltage-gated channel expression, OSE did not decrease. The impact of other channels (particularly A-type channels and h-channels) on SE changes with the distance from the soma was studied in a realistic model of hippocampal CA1 pyramidal cell (Migliore et al., 2005). While h-channels reduced SE in all dendrites, A-type channels most significantly reduced SE in distal branches of the apical tree (Komendantov and Ascoli, 2009). In these neurons, A-type channels and h-channels are important contributors to passive dendritic properties, reduction of dendritic excitability, and voltage attenuation (Golding et al., 2005).

Conclusions

Our studies suggest that SE may be controlled by expression or regulation of voltage-gated channels in a manner that is variable with the frequency of background activity. Specifically, the models predict that the influence of voltage-gated channel expressions on the SE of individual inputs as well as on the overall SE of dendritic trees is more prominent at a lower background activity. Our general results, which show increased SE in distal active dendrites compared to proximal and/or passive ones, are robust with respect to variations in morphological structure. Interestingly, however, the specific patterns of SE vary among morphological classes even when the same simple biophysical model is maintained unaltered. In neurons with simpler dendritic trees, such as hippocampal granule cells, the ef-

fect is less prominent than in neurons with more complex arbors, such as spinal motoneurons and RG cells. These differences suggest possible variations in the rules of synaptic plasticity and integration for different parts of the dendritic arborization. In particular, the model of CA1 pyramidal cell with realistic distributions of dendritic conductances demonstrated important roles of h-current and A-type K^+ current in controlling the SE of single inputs and overall synaptic efficacy in basal and apical dendrites.

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