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Does a dendritic democracy need a ruler?☆

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Abstract

In hippocampal CA1 cells, distance-dependent synaptic scaling (Nat. Neurosci. 3 (2000) 895, J. Neurosci. 21 (2001) 9151) helps maintain a "dendritic democracy" (Curr. Biol. 11 (2001) R10) where distal and proximal synapses on average contribute equally to the cell's firing. A "dendritic ruler", for example a concentration gradient, might be necessary for synaptic scaling. Alternatively, synapses could "self-regulate" by gauging their distance from the soma using properties of backpropagating spikes. We show in a model CA1 cell (Neuron 37 (2003) 977) that the delay between a synchronous burst of simulated Schaffer collateral input and the arrival of backpropagating spikes at synapses predict the synapse's location and amplitude at the soma well, though the amplitude of the spikes do not. This suggests that a dendritic ruler is not required to scale synapses.

Keywords: Synaptic plasticity; CA1; Backpropagating action potentials

1. Introduction

Large dendritic trees have a tendency to attenuate signals from distal synapses more than from proximal synapses. However, in hippocampal CA1 pyramidal cells at rest, the average EPSP amplitude of synapses measured at the soma (their *effective amplitude*) is independent of their location on the dendritic tree [7]. This phenomenon has been termed *dendritic democracy* [5]. Experiments show that distance-dependent scaling, where the average efficacy of synapses increases with distance from the soma [7,2],

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helps to normalise EPSPs measured at the soma. Active conductances on dendrites also play a role by reducing the attenuation suffered by inputs, but they do not completely eliminate the attenuation.

In this paper we examine how a dendritic democracy might be established. We assume that in a dendritic democracy, the effective amplitude of a synapse depends only on the correlations in the pre- and postsynaptic input it experiences. Inputs from each synapse suffers differing amounts of attenuation according to its distance from the soma, and the cell morphology and conductance distribution. It follows that in order to make the effective amplitude of the synapse depend only on pre- and postsynaptic activity, the plasticity machinery at a synapse has to "know" the attenuation factor corresponding to that location on the dendritic tree. The two ways by which this could happen are: (1) a *dendritic ruler*, where each synapse can read off its distance from the soma using a *static* marker, such as a molecular concentration gradient; or (2) *synaptic self-regulation*, where each synapse adjusts its strength in response to *transient* local electrical and chemical signals.

In this paper we will address the question of whether a dendritic democracy needs a ruler by investigating whether one manifestation of synaptic self-regulation is a feasible alternative. We hypothesise that backpropagating action potentials (BPAPs) following a somatic spike provide the information necessary to the plasticity machinery at the synapse. It is known that the amplitude of BPAPs decays with distance in the apical dendritic trunk, and that the delay in arrival of BPAPs is greater further from the soma [11].

The amplitude (and duration) of BPAPs could determine the amount of calcium influx through NMDA receptors and thereby influence the plasticity rule. The obvious problem with using the delay between initiation of a BPAP in the soma and its arrival at the synapse is that the synapse only knows the BPAP arrival time. However, if synapses over the dendritic tree are activated synchronously, the delay between the initiation of the local EPSP and the arrival of the BPAP will depend on the synapse's distance from the soma. This information could be used by a spike-timing-dependent plasticity (STDSP) [3] learning rule to alter the strength of synapses according to their distance from the soma. Although input to CA1 cells is not synchronous during gamma oscillations [4], the input is modulated by the gamma frequency, and may be more synchronous for inputs that cause the postsynaptic cell to fire.

The decay and amplitude of BPAPs have been measured experimentally in the apical dendritic trunks, but not in the oblique branches, where most of the Schaffer collateral synapses are located [8]. We use a model CA1 cell to investigate whether the amplitude or delay BPAPs are reliable predictors of distance or effective amplitude in the branches as well as in the trunk.

2. Method

We use a model CA1 cell [10] implemented in NEURON [6] available from the ModelDB database (http://senselab.med.yale.edu/senselab/modeldb) that includes calcium buffering and the following currents: I_{Na}, I_{Kdr}, I_A, I_h, I_{CaT}, I_{CaR}, I_{CaL}, I_{AHP} and

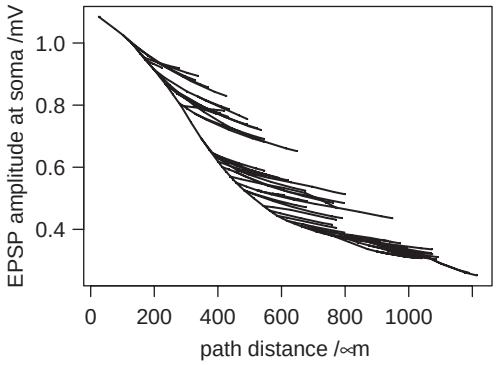

Fig. 1. EPSP amplitude at the soma versus path distance of synapse from soma.

I_m. All synaptic conductances are described by dual exponential function with rise time constant $\tau_1 = 0.1$ ms and fall time constant $\tau_2 = 10$ ms. Each synaptic reversal potential is $E_s = 0$ mV.

We first measure the effective amplitude of synapses at all positions on the apical dendritic tree by finding the maximum membrane potential deflection at the soma in response to synapses with maximum conductance of 0.872 nS. We then simulate the Schaffer collateral input by distributing 1000 excitatory synapses over the stratum radiatum part of the apical dendritic tree in line with the experimentally observed distribution over the thick proximal, thick medial and thick distal parts of the trunk and the thin branches [8]. All maximum conductances are 0.03 nS (ensuring just one spike in response) and inputs are synchronous. We record the membrane potential at each synapse and derive the corresponding BPAP amplitude and delay between synaptic input and the peak of the BPAP.

3. Results

Fig. 1 shows the EPSP amplitude at the soma versus the path distance of the synapse from the soma. It can be seen that the amplitude of the EPSPs is attenuated more by the dendritic trunks than by the oblique branches. This is due to the sealed-end boundary conditions making it harder for current to leak out from the oblique branches than from the rest of the dendritic tree, which has a higher load.

Fig. 2a shows the BPAP amplitude decays in the apical dendritic trunk, in line with experimental evidence, but increases once the BPAP is propagating through a branch. It also shows that BPAP amplitude is not a good predictor of soma–synapse path distance. For example, a BPAP with an amplitude of 70 mV only localises the path distance of the synapse from the soma to within 300 and 800 μm. Fig. 2b shows that BPAP amplitude does not predict effective amplitude well either. Here a 70 mV BPAP localises the effective amplitude to be between 0.4 and 0.9 mV.

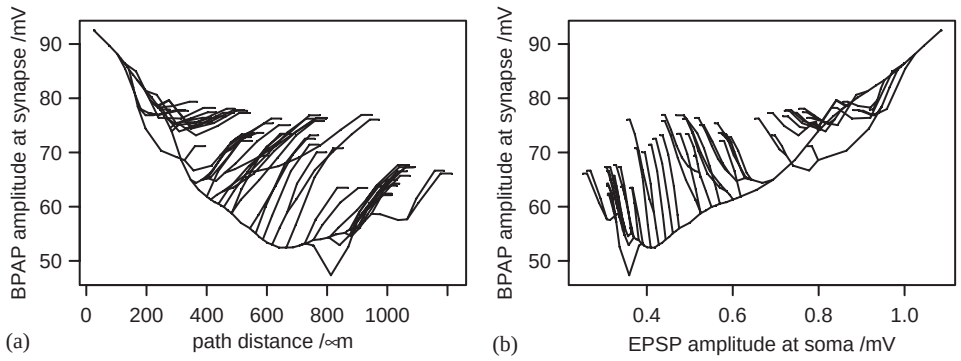

Fig. 2. Amplitude of single BPAP versus (a) path distance of synapse from soma and versus (b) effective amplitude.

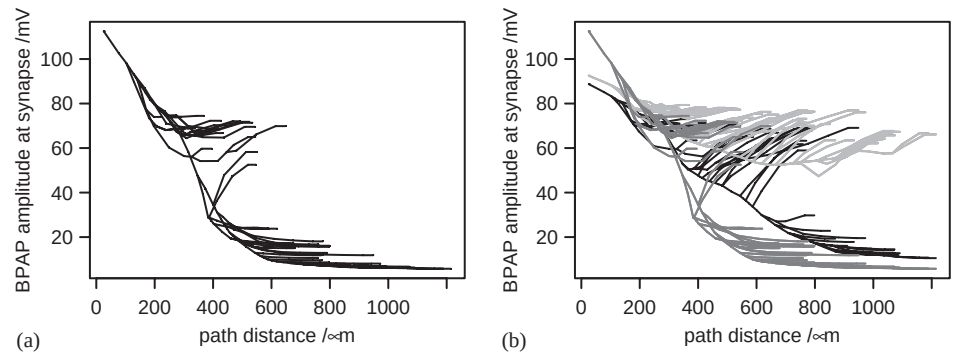

Fig. 3. BPAP amplitude versus distance. (a) BPAPs induced by somatic current injection. (b) Dendritically activated BPAP with slowed A-type potassium inactivation (black) with somatic injection BPAP (dark grey) and dendritically activated BPAP with normal A-type inactivation (light grey).

BPAPs induced by somatic current injection decrease in amplitude in both the trunk and branches (Fig. 3a) in marked contrast to synaptically induced BPAPs. Potassium A-type channel inactivation due to synaptic input can boost BPAP amplitude [9]. To test whether this mechanism was responsible for the increasing BPAP amplitude in the branches we raised the minimum A-type inactivation time constant from 2 to 2000 ms. This caused synaptically induced BPAPs to attenuate significantly more than in the control synaptic-induction case but less that the somatic current injection case (Fig. 3b), showing that inactivation of potassium A-type channels by the dendritic EPSPs partly accounts for the increase of the amplitude in the branches.

In contrast to BPAP amplitude, BPAP delay is a reasonably good predictor of soma–synapse distance (Fig. 4a) and a better predictor of effective amplitude (Fig. 4b), although the range of the delays is small, being under 2 ms. Fig. 4b shows that propagation in the branches is faster than in the apical dendritic trunk. This leads to a worse

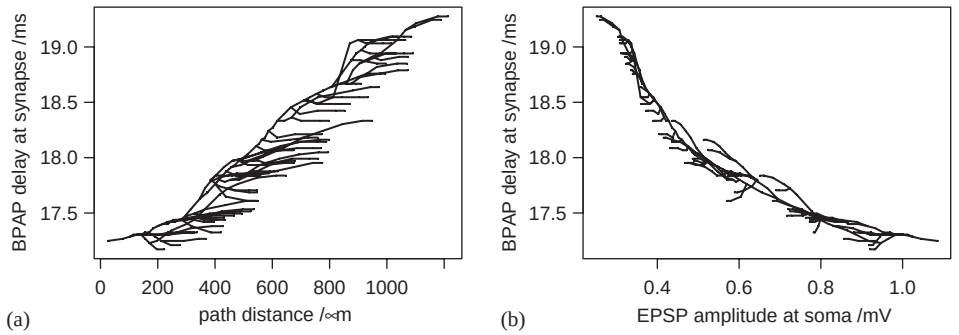

Fig. 4. Delay of single BPAP versus (a) path distance of synapse from soma and (b) effective amplitude of synapse.

correlation with distance than if the speed had been uniform. However, the increased speed in the branches leads to better correlation with effective amplitude than would have been obtained with uniform propagation speed. The reason for the increased propagation speed in branches could be related to end-effects similar to those accounting for the dependence of the effective amplitude on distance.

4. Discussion

In summary, these results show that the amplitude of BPAPs induced by synchronous activation of Schaffer collateral synapses correlates with synaptic distance and effective amplitude but is not a good predictor of them. However, the delay of the BPAP peak from the onset of synaptic activity predicts them well. Thus BPAP delays after a burst of synaptic input could provide the information required to maintain a dendritic democracy, negating the need for a dendritic ruler.

The delays between synaptic input and BPAP arrival are within the potentiation part of an experimentally measured STDSP curve [3]. However, the difference in delay between proximal and distal synapses is small (under 2 ms), which would make it hard for the STDSP to distinguish proximal and distal inputs in a noisy environment. Nevertheless, averaging inputs over long periods of time might be able to reduce the noise sufficiently to create a scaled distribution of synaptic strength. One other caveat is that the typical dual-exponential form of STDSP [3] would tend to lead to proximal synapses being potentiated more than distal ones, so it is not clear that the same mechanism is responsible for scaling. On the other hand, a number of other forms of STDSP have been observed [1], and a rule with positive slope within the range of delays we observe could potentiate distal synapses more than proximal ones.

A critical aspect of the model is the behaviour of BPAPs in the apical oblique branches. The BPAP behaviour is determined by morphology, and passive and active conductances in the branches. No experimental data constrains these parameters directly in the model we use. Other choices of parameters might still allow the model to fit the

validation data [10] but could modify our results critically. Other factors that might influence our results are the inclusion of NMDA synapses, synapses that are already scaled, and inhibitory inputs.

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