The Effects of Intrinsic Noise on Pattern Recognition in a Model Pyramidal Cell

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Abstract

Computer simulation of a CA1 hippocampal pyramidal cell is used to estimate the effects of synaptic and spatio-temporal noise on signal integration. Comparison is made between the pattern recognition ability of the cell in the presence of this noise and that of a computing unit in an artificial neural network model of an heteroassociative memory. The results indicate that the pattern recognition performance of the pyramidal cell is within an order of magnitude of that of the noise-free computing unit. Synaptic noise may be the most serious form of noise from those considered.

1 Introduction

Biological neurons contain many sources of noise that are not generally included in neural network models even when they are designed to mimic the behaviour of a part of the nervous system. This study continues work examining the effects of neurobiological forms of noise on the capacity of associative memory networks. Previously we have determined the impact of partial connectivity and probabilistic synaptic transmission on the capacity of an heteroassociative memory [3, 5]. Here we consider the effects of variance in the magnitude of postsynaptic signals (quantal variance), asynchronous arrival of presynaptic signals and spatio-temporal integration of the postsynaptic signals on the pattern recognition ability of a pyramidal neuron. The overall aim of this work is to obtain more reasonable estimates for the potential memory capacity of parts of the mammalian nervous system, such as the network formed by the axonal projections from pyramidal cells in area CA3 to area CA1 of the hippocampus [10].

2 The Model

A detailed compartmental model of a rat CA1 pyramidal cell [9] has been used to examine sources of noise intrinsic to a biological neuron. Technical details are given in the appendix. In the model, excitatory synapses were distributed randomly throughout the proximal apical dendritic tree, corresponding to Schaffer collaterals from CA3 neurons synapsing in *stratum radiatum*. A pattern of input to the cell consisted of a number of action potentials (APs) arriving synchronously or asynchronously at different synapses. The arrival of an AP at a synapse causes a change in the postsynaptic membrane potential known as an excitatory postsynaptic potential (EPSP). EPSPs travel along the dendrites and multiple EPSPs arriving at overlapping times in the cell body (soma) summate. For most of the results given here the propagation of the EPSPs was passive. In some situations active (voltage-dependent) ion channels generating a persistent sodium current were added to the dendrites to explore their ability to amplify distal EPSPs [6].

This study is concerned with the ability of a pyramidal cell to recognise particular patterns of input. Patterns consisting of 200 APs at separate synapses were used. This level of activity generates a somatic depolarization of around $20mV$ and so should be sufficient to cause the cell to fire its own AP and thus "recognize" the pattern. Fewer active inputs may not cause the cell to fire. Rather than examine the output response of the cell, here I determine how accurately the pyramidal cell can discriminate between different numbers of active synapses on the basis of the peak membrane potential at the soma due to the summed EPSPs (dendritic sum). This indicates how reliably a cell could recognize specific input patterns.

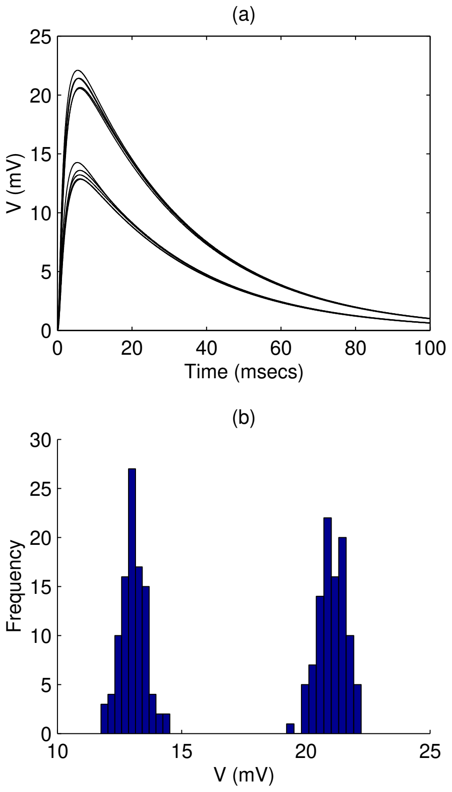

Figure 1: Results from case 1. (a) Five examples of voltage traces from the soma. Upper traces for 200 active synapses, lower traces for 100 synapses. (b) distribution of peak soma voltages for 100 (left) and 200 (right) synapses from 100 trials.

To compare directly the pattern recognition performance of the pyramidal cell with an artificial computing unit, a simulation was run of a simple heteroassociative memory consisting of 8000 input units connected in feedforward fashion to 8 output units [14]. Sixty random binary pattern pairs, each consisting of 200 active input and 4 active output units, were stored in the memory using clipped Hebbian learning to give binary connection weights (0 or 1). On subsequent presentation of an input pattern as a recall cue, each output unit calculated a dendritic sum that was a count of the number of active input units it was connected to by a weight of 1. Given these dendritic sums, an output unit must be able to discriminate between input patterns with which it was associated during storage (*high* patterns) and patterns with which it was not (*low* patterns). *High* patterns produce dendritic sums that are on average higher than the sums due to *low* patterns, and a computing unit can discriminate between a sum of 200 and a sum of 199. A pyramidal cell is unlikely to be able to discriminate sums to the same resolution, due to the corrupting effects of the forms of noise considered here.

3 Results

3.1 Active synapses

The dendritic sums due to either 100 or 200 active synapses in the pyramidal cell dendritic tree were recorded. Activation was by single action potentials (APs) arriving either synchronously (SA) at each synapse, or randomly dispersed over a short ($25msecs$) period (asynchronous arrival, AA). The cell's ability to differentiate between 100 and 200 active synapses was measured by the signal-to-noise ratio (S/N; calculated as the squared mean difference divided by the average variance) between the two dendritic sum distributions collected from 100 trials with different, random spatial distributions of the synapses in the apical dendritic tree on each trial. Eight cases of different combinations of noise were examined as listed in Table 1. Apart from the (a)synchronous arrival of APs, other variations included quantal variance in the peak synaptic conductance (QV; CV=0.66 [2, 13]), scaled conductances (SC) and amplified conductances (AC). Particular cases are explained below.

Case	SA	AA	QV	SC	AC
1	x				
2		x			
3	x		x		
4		x	x		
5	x			x	
6	x				x
7		x	x	x	
8		x	x		x

Table 1: Different combinations of noise.

The results from the initial case (1) are shown in Fig. 1. While the voltage waveforms are very similar in shape, there is variation in the peak amplitude, depending on the spatial distribution of the synapses. This is the result of differing levels of EPSP attenuation and soma arrival times for synapses that are different distances from the cell body.

The S/Ns from the 8 cases are shown in Fig. 2. The difference between S/Ns is mainly due to differences in the variance of each distribution, with the means being largely unchanged. The most remarkable result is the increase in S/N that results from the asynchronous arrival of APs (cases 2 & 4). Randomizing the arrival times over an interval that approximately corresponds to the duration of the summed voltage response results in a reduction in the variance of the peak voltage. Random variation in the peak conductance at each synapse (quantal variance) of the magnitude seen experimentally [2, 13] results in a 60% reduction in the S/N (cases 3, 4, 7 & 8).

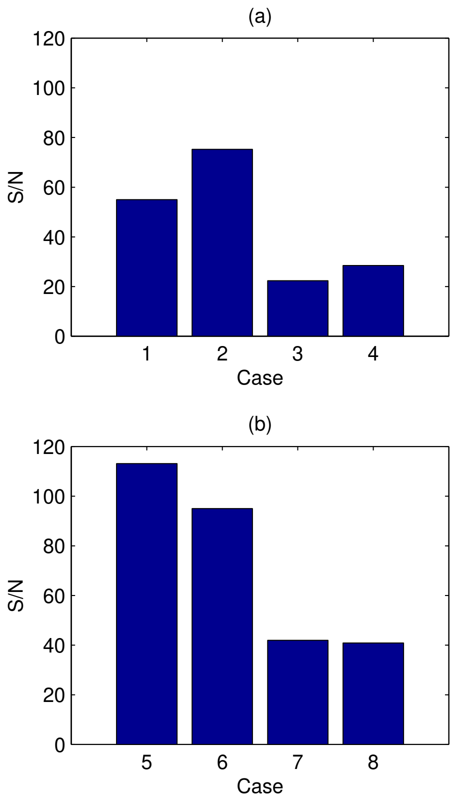

Figure 2: Signal-to-noise ratios between the peak voltage distributions from 100 and 200 synapses, for the 8 different cases.

Experimental data [11, 12] reveals less correlation between peak current (EPSC) amplitudes at the soma and synaptic location than is to be expected if all synapses are equally strong and EPSCs propagate passively to the cell body. Two scenarios that reduce amplitude variation were tested (1) peak synaptic conductances were scaled with distance so that all synapses produced the same peak current in the soma [11] (2) EPSPs were amplified by voltage-activated, persistent sodium channels distributed throughout the dendritic tree [1, 6]. The results for cases 5 to 8 show the benefits of this invariance, with little difference between the two methods of achieving it. The S/N is nearly doubled compared to the corresponding passive cases (1 to 4).

3.2 Pattern recognition

The pattern recognition capability of the pyramidal cell was further tested by examining it's ability to distinguish between *high* and *low* patterns stored in the heteroassociative net. Firstly, the 60 stored input patterns were presented in turn to the network model and the resulting dendritic sum of each output unit was recorded. The distribution of sums over the 60 patterns for the first unit is shown in Fig. 3(a). Note that *high* patterns always produce a sum of 200, while the *low* sums exhibit variability around a mean of about 100. The S/N between the *high* and *low* pattern sums for each output unit was calculated.

For each output unit in turn, the pattern of connection weights in the net was used to set 8000 synaptic connections onto the model pyramidal cell. The 60 input patterns were then presented to the cell. Dendritic sums in the form of peak soma voltage were recorded for each pattern and the S/N between *high* and *low* pattern sums was again calculated. The dendritic sums from the cell corresponding to the first unit are shown in Fig. 3(b). Now there is variability in both the *high* and *low* sums. The mean S/N of the cell compared to the S/N of the output unit was calculated across the 8 output units. The results for the 8 different cell model cases is shown in Fig. 4.

In this more realistic situation, the cell has a S/N that is about 40% of an output unit when only noise from spatio-temporal integration is included (cases 1,2,5 & 6).

This reduces to around 30% when quantal variance is included (cases 3,4,7 & 8). The performance differences between the cases are much less here than when comparing 100 with 200 active synapses. In this situation, *low* patterns activate different numbers of synapses. This variability dominates the spread of *low* sums, so that the noise in the cell does not greatly increase the variance of the *low* sums compared to a network unit.

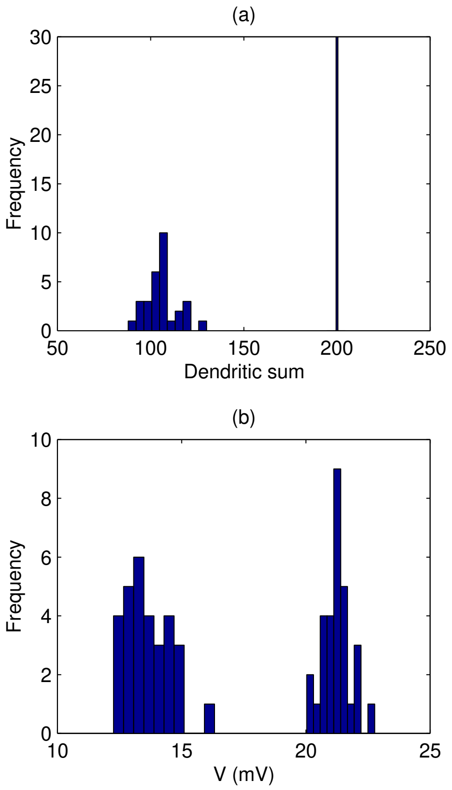

Figure 3: Dendritic sums from 30 *low* and 30 *high* patterns in (a) a network unit (b) the pyramidal cell.

4 Discussion

Various forms of noise interfere with a neuron's ability to calculate the weighted sum of its inputs, compared to a computing unit in an artificial neural network. The accuracy with which a hippocampal CA1 pyramidal cell can add up its inputs has been examined by use of computer simulation. Quantal variance, asynchronous signal arrival and spatio-temporal integration ensure that the weighted input sum seen at the cell body for a particular number of active synaptic inputs varies from trial to trial and with the spatial distribution of the synaptic connections in the dendritic tree.

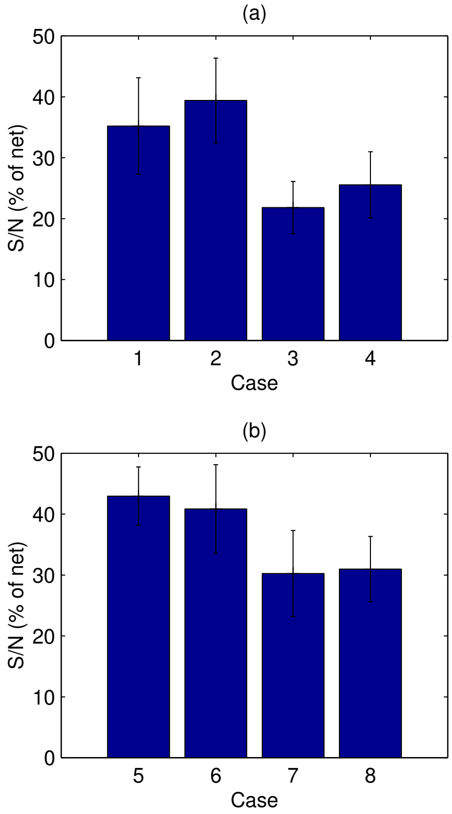

Figure 4: S/N between dendritic sum distributions from high and low patterns for the 8 different pyramidal cell cases as a percentage of the S/N in the heteroassociative net. Error bars are the standard deviation across the 8 output units.

The results indicate that the major source of noise may be quantal variance, given current estimates of its magnitude [2, 13]. Asynchronous signal arrival may actually act to linearize and improve the accuracy of the dendritic sum, provided the signals are dispersed over a suitably short period of time. The $25 msec$ period used here has a physiological basis in that the signals from presynaptic CA3 cells are often in the form of bursts of action potentials of about that duration, with probabilistic transmission ensuring that maybe only a single EPSP results from the burst [7]. The model uses a realistic, but possibly worst-case scenario for spatio-temporal integration in that the membrane potential is set at a relatively low value that includes the effects of low frequency background excitatory and inhibitory inputs. Using $R_m = 100k\Omega cm^2$ (near the top of the physiologically measured range [8]) doubles the S/N ratio when no other forms of noise are present.

In a simple pattern recognition task based on an heteroassociative memory model, a pyramidal cell including all these forms of noise may have a S/N that is still 25% of that achieved by a noise-free network computing unit. Earlier work showed a one to two order of magnitude reduction in the S/N with a model neocortical pyramidal cell, when the input signals were in the form of trains of action potentials of a fixed mean frequency [4]. Pyramidal neurons may be better tuned to respond to patterns of roughly synchronous single action potentials, rather than to trains of action potentials.

Additional scaling or amplification mechanisms to decrease the effect of synaptic distance from the cell body only increased the S/N by 5%, calling into question the need for such mechanisms. This contrasts with the major improvement in associative memory recall performance seen with a similar model involving CA1 pyramidal cells [1]. The relative improvement achieved by reducing distance effects may depend on the initial performance. The input signals in [1] were trains of action potentials, which resulted in poor performance, as in our earlier work [4]. In this situation it seems that reducing distance effects is more valuable.

A crude comparison between the effects of the forms of noise considered here and other sources of noise, namely partial connectivity and probabilistic synaptic transmission, can be made by considering the variance in dendritic sums with a mean value of 200, when the different forms of noise are present individually. Connectivity levels in the cortex are on the order of a few percent. Suppose the CA1 cell receives connections from only 5% of the CA3 cells. If each input pattern is represented by 4000 active CA3 cells, the mean *high* pattern dendritic sum at the CA1 cell will be 200 active synapses with a standard deviation of 14. To consider only the effects of probabilistic transmission when the input signals are single action potentials, suppose the CA1 cell is connected to all of the CA3 cells that belong to input patterns with which it is associated. Given the probability that a presynaptic action potential causes an EPSP is only 0.2 and the input pattern consists of 1000 active cells, the mean *high* pattern sum is again 200, but with a standard deviation of 13. If the probability of transmission is 0.8 and patterns contain 250 cells, the standard deviation reduces to 6. In units of numbers of active synapses (rather than peak voltage), the standard deviation of *high* pattern sums for the forms of noise considered in this paper is of the order of 6 to 7. Thus partial connectivity and probabilistic transmission are potentially much greater sources of noise and so may significantly shape the pattern recognition capabilities of a pyramidal cell.

Future work will seek to quantify the effect on associative memory capacity of all the forms of neurobiological noise mentioned in this paper. The current results suggest that the memory performance of parts of the mammalian brain such as the hippocampus may be within an order of magnitude of artificial neural network models.

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A Pyramidal Cell Details

Cell: rat CA1 pyramid as per Fig.2 of [9].

Compartments: 890

Passive properties: $R_m = 30k\Omega cm^2$, $C_m = 1\mu F/cm^2$, $R_i = 200\Omega cm$ [8].

Synapse: excitatory, AMPA type with synaptic current

$$I_s = g_s(V - E_s)$$

where V is the local membrane potential, $E_s = 0mV$ is the synaptic reversal potential and g_s is the synaptic conductance given by

$$g_s = \bar{g}_s \frac{\tau_1 \tau_2}{\tau_1 - \tau_2}(e^{-t/\tau_1} - e^{-t/\tau_2})$$

where $\tau_1 = 0.2msec$, $\tau_2 = 2msec$ and $\bar{g}_s = 6nS$ gives a peak conductance of about $1nS$ [2, 8] (provides peak somatic depolarization of $\approx 20mV$ with 200 active synapses).

Scaling: conductance, $\bar{g}_s$ scaled to give constant peak current in the soma via empirical equation

$$\bar{g}_s = g_0 e^{0.0046x}$$

where x is the soma-synapse distance (μm) and $g_0 = 1.8nS$ is the maximum conductance at the soma (value gives peak somatic depolarization of $\approx 20mV$ with 200 synapses).

Amplification: EPSPs amplified by a persistent sodium current uniformly distributed throughout the dendritic tree

$$I_p = g_p m(V - E_{Na})$$

where $E_{Na} = 65mV$ and activation, m is controlled by standard first-order dynamics with [6]

$$\alpha_m = \frac{-1.74 * (V - 11)}{(exp(-(V - 11)/12.94) - 1)}$$

$$\beta_m = \frac{0.06 * (V - 5.9)}{(exp((V - 5.9)/4.47) - 1)}$$

$$\tau_m = 1/(\alpha_m + \beta_m)$$

$$m_\infty = 1/(1 + exp(-(V + 49)/5))$$

Setting $g_p = 0.01mS/cm^2$ and $\bar{g}_s = 5.3nS$ provides EPSP amplification with a peak somatic depolarization of $\approx 20mV$ with 200 synapses.

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