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THE EXCITATORY POST SYNAPTIC POTENTIAL AND THE DENDRITE SPACE CONSTANT INFLUENCES IN THE BEHAVIOUR OF SYSTEM OF NEURONS.

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ABSTRACT

There is a large number of physiological proprieties that influence the behavior of systems of neurons. Each selected group of proprieties used to build a particular neuronal network generates a specific pattern. One computational package, called ***NeuronalSYS***, is used to study the influence of two of these parameters, the post-synaptic excitatory potential and the membrane space constant, in the behavior of systems of neurons. The chosen system is the primary visual cortex of the macaque monkey, which has sufficient data available in the literature. The results show that the system chooses naturally values to these parameters that situate the network in the critical region. In this region it responds properly to small and large stimulus.

INTRODUCTION

The physiological parameters that influence the behavior of neuronal networks are situated in several levels of complexity. Some important phenomena are in the molecular level, where are studied the action of neurotransmitters, such as glutamate and adrenaline, and the action of the main ions, K, Na and Ca, responsible for the membrane potential. On the cellular level is situated the study of the neurons and the cells from de glia. Some of the interesting properties are the velocity of the signal in dendrite and axonal arbors, the space constant of the membrane, the characteristics of the gates, and the summation in the central part of the cell, amongst others. The most important level when simulating neuron systems is the systemic level. In such level the researcher is interested in the way the neurons connect to form a network and how they behave as a group. In this case, some proprieties are the position of the synapses, the characteristics of the receptive fields, etc.

The proposition of a neuron modeling that can integrate a computational package demands the choice of the parameters considered more important for the chosen objectives. The Laboratory of Computational Neuroengineering of the Federal University of Santa Catarina, Brazil, is developing a computational package for the study of neuron systems, for which was determined a set of parameters considered important.

Amongst these parameters are, the speed of the signal in dendrite and axonal arbors, the time involved in the transmission of signal in the synapses, the firing threshold in the axon hillock, the post-synaptic excitatory potential, the attenuation factor of the signal in the dendrites, the refractory period, the number and position of the synapses, the receptive field of the neurons and the characteristics of the synapse distribution in dendrite and axon arbors. The computational package received the name of ***NeuronalSYS*** (ANDREAZZA, 2007).

NeuronalSYS is a computational package with a physiologically plausible neuronal network, developed to simulate a cortical area that includes the synaptic buttons existent in up to $3x10^6$ μm^2 of a mammal's cortex. Its first application was to simulate the primary visual cortex of the macaque monkey. The macaque monkey is one of the most studied, besides that there are a set of information in the literature that allow the gathering of all data necessary for the construction of the network (CALLAWAY, 1998; ADORJÁN et al., 1999; DOW, 2002; HEYDT and PETERHANS, 1989; PETERHANS and HEYDT, 1989; GRÜNERT and MARTIN, 1991; LACHICA et al., 1992; PRZYBYSZEWSKI et al., 2000; NICOLELIS et al., 2003).

To reproduce the nervous system it is necessary first to study its neurophysiologic characteristics. The inspiration in natural system can be a path to the development of systems able to detect, locate, recognize and understand objects and scenes (COLOMBE, 2003).

In this work the influence of some of the properties included in the program are studied. The properties studied are, the post-synaptic excitatory potential, PSP, and the membrane space constant, λ.

NeuronalSYS, A PHYSILOGICALLY PLASIBLE NEURONAL NETWORK

NeuronalSYS was developed at Federal University of Santa Catarina, Brazil, and it is able of building physiologically plausible neuronal networks. Among the physiological characteristics that the software takes into account are the real number of neurons and its synapses in some particular subsystem of neurons, with all synapse–soma distance. Each neuron connects with many others through thousands of synaptic buttons. In this way, a neuron network can also be seen as a synapse group. This is because a fundamental characteristic to the description of the network's dynamic is the spike frequency of each neuron. The only way to describe this frequency is taking into account the position of each synapse, and the moment that each one is stimulated. Each synapse however, has its own characteristics, which control the sign passage and can influence nearby synapses. To consider these characteristics rises significantly the complexity of the problem since it demands description of the phenomena that happens in different levels of complexity. For this reason, the network integrate to the ***NeuronalSYS*** simplifies the molecular and cellular's phenomena, even considering the position of each synapses.

The typical geometry of the neurons allows the transference of information in the SNC to be convergent and divergent. Therefore, inputs of many neurons converge on a single neuron. On the other hand, the ramification of its axons can innervate many other neurons (Figure 1).

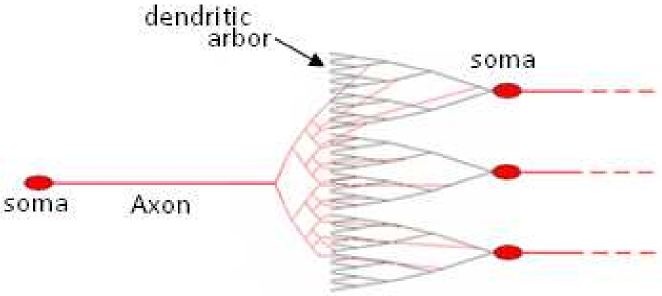


Figure 1: Each neuron of one cortex layer as a receptive field in other layers, that can includes 30-80 neurons. In the innerved neuron, the synapses can be localized in any of the dendrite branches and any distance of the soma.

The ***NeuronalSYS*** has tolls that allow the user to adjust the neuronal network to his specific problem. The user determines the total number of neurons and the number of synapses that each one makes with the neurons of other layers. Between the physiological proprieties that can be manipulated there are the value of the post-synaptic excitatory potential, PSP, the refractory period, RP, the membrane space constant in the dendrites, λ., and the threshold potential for generation of an action potential in the soma. In this work the program is used to verify the influence of the post-synaptic excitatory potential and the membrane space constant. Both parameters combined determine the value of the signal that gets the soma and control the frequency of neuron's spike. It is also possible to determine the pattern of the network for some particular stimulus, with application of temporal and local variations

As a result, it is possible to observe the frequency of the individual spikes of each neuron and the temporal summation of the spikes for each layer of the cortex. The program also does the summation of the PAs that leaves V1, what is consider the final answer of the network. Usually, in the physiological conditions, the network shows a wave pattern, that goes away from the stimulated location. Under the time point of view, the network also shows a wave pattern in the outlet of V1.

POST-SYNAPTIC EXCITATORY POTENTIAL, PSP

The value of the post-synaptic excitatory potential, PSP, depends of the kind of neuron involved and of the local characteristics of each synapse. Among these characteristics is the kind of gate that controls the passage of the signal. The voltage dependent gates can depend on Ca^{2+}, Na^{+} or K^{+}. Many studies show that the neocortical dendrites can sustain action potential depending of any one of these gates. In a general way the PSP vary between 0.4 – 4.0 mV (AMIT, 1989; PERETTO, 1992; JOHNSTON et al., 1996; WILLIAMS e STUART, 2002; KANDEL, 2003). Besides that, as shown in some of the papers, the density of gates varies in the dendrite trees. This density is bigger at distal region (MARTINA et al., 2000). The propagation velocity of the signal and the value of the PSP vary in the same way.

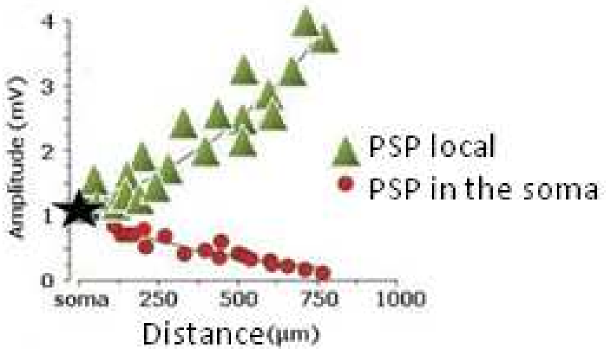


Figure 2 – Dependence of the value of PSP in the cellular soma with the position of the activated synapses. The points that are situated in the same vertical indicate the values of PSP in the synapse (▲) and in the soma (●). The PSP are bigger in the distal region in function of the increasing of the density of the voltage dependent gates. Adapted from WILLIAMS and STUART (2002).

Figure 2 shows how PSP changes in function of the distance between the synapses and the soma. Considering the membrane constant chosen for this work, $\lambda = 250\ \mu m$, the value of the PSP is between 1.00 and 1.65 mV, with a average of approximately 1.30 mV. On the other hand, the value of the PSP in the soma's arrival is situated, for the same region, between 0.65 and 1.00 mV, with an average around 0.82 mV. This means that, for the studied neurons, the attenuation is approximated 0.37%, what coincides with the value used to the definition of membrane constant, λ.

For one stimulus from the retina, the signal goes though the optical nerve and arrives in the LGN. From there the signal gets out in an intermittent way, controlled by the refractory period of the neurons. The neuronal structure used reproduces the pathway of object recognition of the macaque monkey. In this pathway, the signal of the LGN is leaded to the IVCβ layer, which distributes it to the VI and II/III layers. The figure 3 shows the ways followed by the signal to pass though the V1.

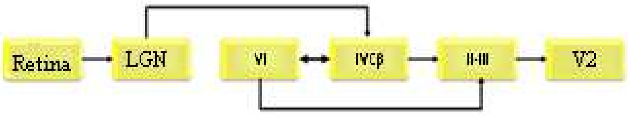


Figure 3 – Pathway of shape recognition in the primary visual cortex of the macaque monkey.

The feedback produced by the layer VI, that returns the expanded signal to the IVCβ layer, produces in each one of the layers a wave behavior. It makes the signal during the time of the refractory period to always returns to each layer, but getting away in circles of the stimulated area. The wave pattern can be seen ether by the gradually distance of the signal, from the stimulus point, or by its own frequency of return. In the first case the signal behaves as waves in a lake, getting gradually away from the point of impact.

In this work the wave behavior is registered in the outlet of V1 and it is shown in figure 4. The figure shows the pattern for several values of PSP. These values, in mV, are shown in the superior right corner of each one of the graphics. It is observed that, for PSP ≤ 1.2 mV, the signal dies before the time of 1500 µs. This time corresponds to the duration of the refractory period used in this work. This means that, for these values of PSP, the signal extinguish before the wave passes though the entire simulated region. Other aspect of the summation of the PAs for these values of PSP is that the total amplitude reduces. This contradicts recent experimental data, which show that the summation of PAs produced remains proximately constant. The network with the shown behavior for PSP ≤ 1.2 mV is called subcritical. A subcritical network does not answer properly to the average and smaller stimulus. These signals extinguish before the information is processed.

For PSP ≥ 1.5 mV, the graphics also show the disappearance of the signal before the time of 1500 µs. Now, the reasons of that are different. In these cases the signal pass through the entire simulated region, but in a higher velocity and the number of PAs does not stays constant. Networks with these characteristics are called supercritical. A supercritical network is the one that reacts excessively to large and medium stimulus, in a way to lose the capacity of recognize them and answer them properly.

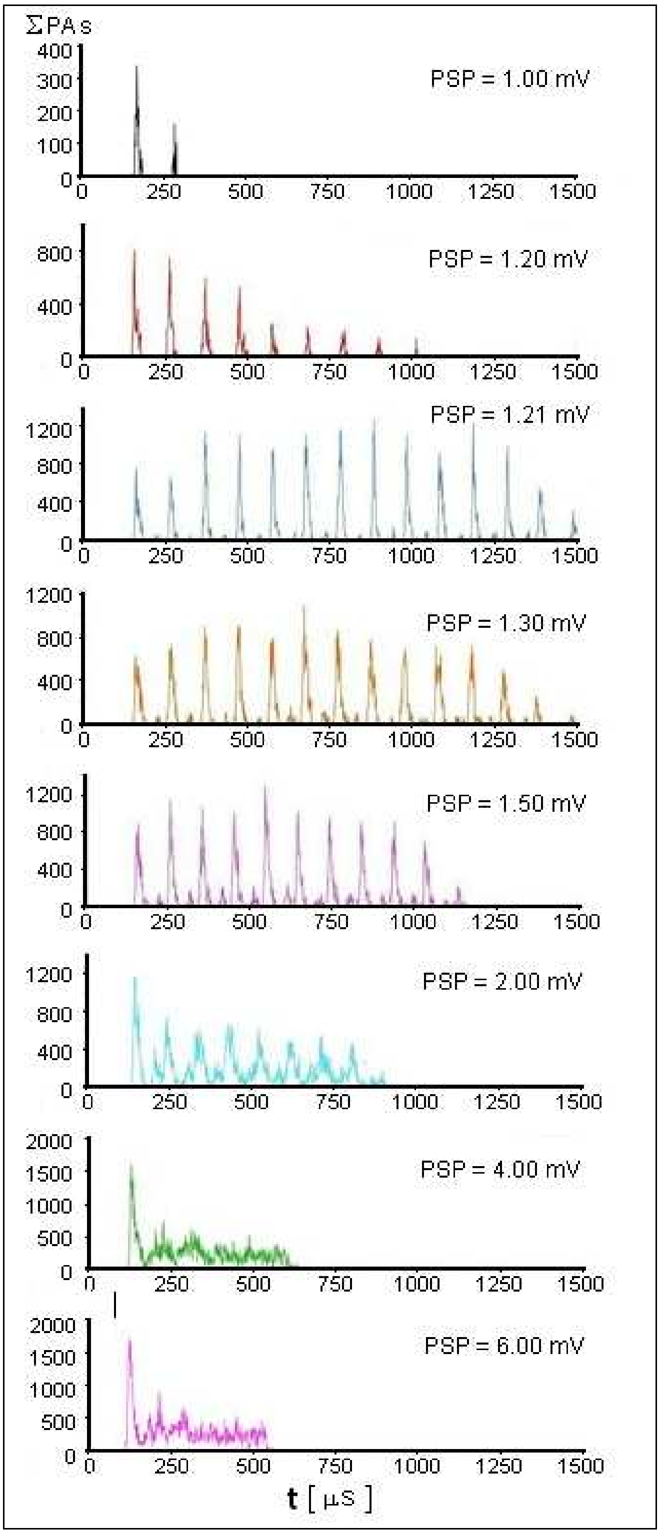


Figure 4 – Summation of PAs at V1 outlet for several values of PSP. The abscissas are in µs and correspond to the number of computational iterations. The signal only goes through the entire simulated region for $\text{PSP} \geq 1.21$ mV. To inferior values, the waves die before to go through the entire region.

The intermediated region shown in the figure 4, for PSP values of 1.21 and 1.30 mV is called critical region. This is particular true for PSP = 1.21 mV, here called **critical point**. This value separates the subcritical region which the signal dies, of the critical region which the signal gets to leave V1 and the number of PAs remains almost constant. In the case of PSP = 1.30 mV the signal goes through the simulated region but the number of PAs gets significant reduction.

For PSP = 1.21 mV, the summation of PAs reproduces the behavior of a sine wave, or sinusoid, with proprieties presented in table 1.

Table 1: Proprieties of the sine wave function that describes the summation of PAs for PSP = 1.21 mV.

Propriety		*Value*
Wave length	δ	30.09 µm
Period	T	102 µs
Frequency	f	0.0098 μs^{-1}
Amplitude	$\overline{\sum PA}_{MAX}$	1105.4 mV
Velocity	v	0.295 µm / µs
initial time	t_0	140 µs

Each wave component has its own amplitude or partial amplitude, given thorough the larger summation of PAs that it presents. The average of the partial amplitudes, $\overline{\sum PA}_{MAX}$, is the wave amplitude. The wave's equation is:

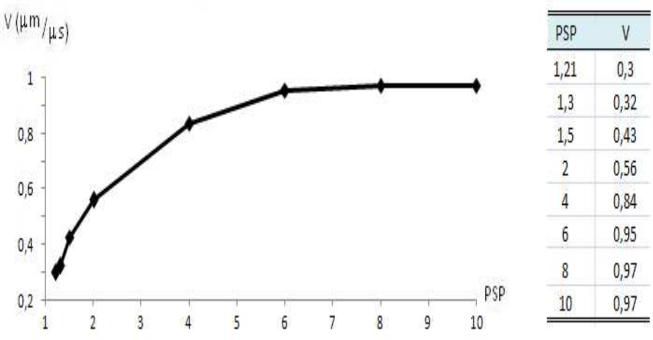
$$PA(x,t) = \overline{\sum PA}_{MAX} . sen\left[2\pi\left(\frac{1}{\delta} + \frac{1}{T}.(t - t_0)\right)\right] \quad (1)$$

In accord with the results presented by WILLIAMS and STUART (2002), for dendrites with dimensions up to 100 µm, the more likely values of PSP are close to 1 mV. The value chosen in this work, PSP = 1.21 mV, is located in the critical point of the network functionality.

The network of neurons is a complex system that works near the phase transitions, or critical region. The criticality is propriety of networks and its concept can be used to analyze the brain transmission of information. A network is subcritical when reduces the signal produced by one stimulus, in a way that little stimulus get extinguish before to be processed. On the other hand, the network is called supercritical when it is saturated by intermediate stimulus, eliminating its specificity and not letting the recognition of the information. (BEGGS and PLENZ, 2004; ABBOTT and ROHRKEMPER, 2006; CHIALVO, 2006; COPELLI and CAMPOS, 2007; COPELLI and KINOUCHI, 2005).

Figure 5 shows the effect of the PSP's value in the wave's velocity. The velocity (v) is the reason between the waves length (δ), it means, the difference in the distance of propagation between the first and the last point to "light" in the outlet of the V1 and the period (T) that takes to this event to happen, it means a complete cycle of movement. The velocity of the wave is calculated by Equation 2.

$$v = \delta . T^{-1} \quad (2)$$



PSP	V
1,21	0,3
1,3	0,32
1,5	0,43
2	0,56
4	0,84
6	0,95
8	0,97
10	0,97

Figure 5 – Dependence of the wave's velocity with the values of PSP. For values superior of 6mV, the velocity of the waves reaches the maximum value. In these conditions it is said that the network is in supercritical conditions. For PSP values inferior than 1.21 mV the signal is interrupt and the network does not processes the information. In other words, the network is in subcritical conditions.

The neurons fire when they accumulate enough PSP and reach the potential threshold, receiving signals with several different time intervals. As shown on figure 5, the propagation speed of the wave increases, until it reaches a maximum. In this way, the waves have a limited speed, which is given only by the characteristics of the network. Since new PSP increases no longer change the speed, and the network is considered in supercritical condition.

It is possible to conclude, in Figure 5, that these conditions have already been reached with PSP close to 4 mV, since from this point significant additions in the value of PSP cause little variation in the wave's velocity.

This is also true for the region between [2.0; 4.0] mV, because the speed of the wave is already in about 60 to 80% of the maximum possible value. Since the signal doesn't travel the network for PSP smaller than 1.21mV, it is concluded that the ideal conditions for the operation of a neuronal network is in the region of $PSP = [1.2\,;2.00]\ mV$, being $PSP = 1.21mV$ the critical point. In other words, the network operates in critical conditions.

Another way to see this is the analysis of the PAs summation. Figure 6 shows the behavior of the PAs summation in the network for several PSP values. For PSP = 1.20 mV, the number of PAs drops quickly and the signal dies before travels the whole simulated region. This extinction of the signal also occurs in the sense of the visual pathway, not quite leaving the V1 in direction of V2. The other values of PSP (1.21 – 1.5 – 2.0 mV) are located in the region of transition between the sub and supercritical conditions. In the three cases the PAs summation remains approximately constant.

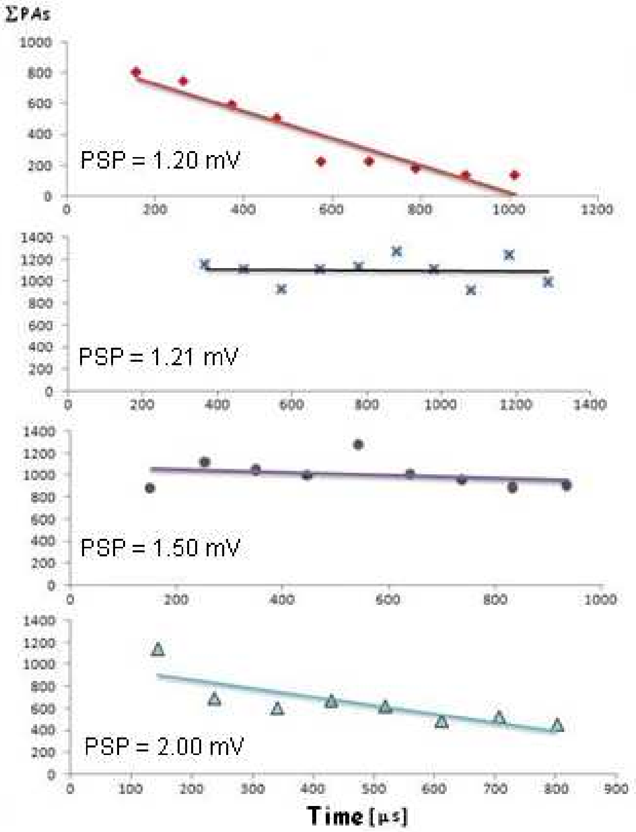


Figure 6 – PSP influence on the network behavior. For PSP=1.2mV the signal doesn't percolate. For PSP=1.21 – 2.00 mV, the signal stays approximately constant during the whole avalanche.

DENDRITIC ATTENUATION FACTOR

The choice of the membrane space constant, λ,, determines the decay in the dendritic arbors. In the ***NeuronalSYS***, the decay is contained in the parameter **attenuation**, which determines the PSP decay between any of the levels in the arbor. Its value can be found by Eq. 3, where Δx = 1 µm is the distance between two nodes, or levels, of the dendritic arbor.

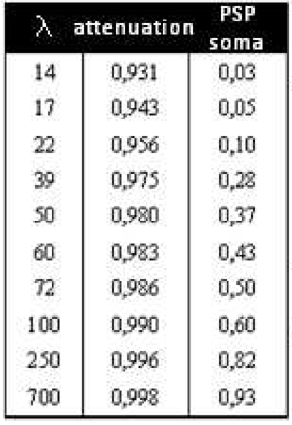
$$attenuation = e^{-\frac{\Delta x}{\lambda}} \qquad (3)$$

Remembering that the dendritic arbor has a radius of 100 µm, and that, for the localization of the synapses, one-dimensional Gaussian distribution was utilized, it's possible to say that the average synapse is situated in the intermediate position, (50 µm). Replacing in Eq. 3 Δx for this distance, it is possible to calculate the average fraction of the signal that reaches the soma for given λ.

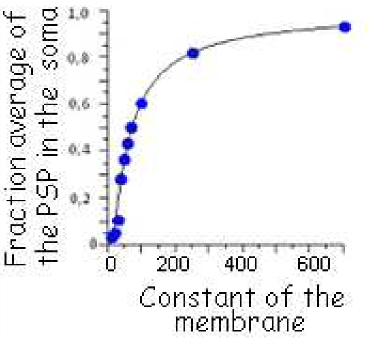
The average PSP fraction that reaches the soma is shown, for several λ, in Table 2. As an example, for λ = 50 µm, the attenuation of the signal between the levels of the network is 0,980, in a way that the signal that reaches the cellular body has 37% of the magnitude of the original signal, in the location of the synaptic stimulus. Therefore λ is an efficiency measure of the signal in the dendrite.

In other words, the higher the λ value, better the signal network transmission will be. The value chosen for the simulations in this work is λ = 250 µm. The correspondent value for the attenuation factor between the levels is attenuation = 0,996. Since in the conception of the ***NeuronalSYS*** the dendritic arbor has a constant length of 100 µm, this corresponds to a total average attenuation, or reduction, of 18%. In this conditions, for PSP = 1.21 mV the network operates in the critical zone. As shown on table 2, from this point on, significant changes in the space constant of the membrane take the minimal variations in the reduction of the signal. As a result, Figure 6B, the number of PAs also has little variation.

Table 2 – Attenuation values in the computer program and average PSP fractions that reach the soma, for several values of the space constant, λ.



λ	attenuation	PSP soma
14	0,931	0,03
17	0,943	0,05
22	0,956	0,10
39	0,975	0,28
50	0,980	0,37
60	0,983	0,43
72	0,986	0,50
100	0,990	0,60
250	0,996	0,82
700	0,998	0,93



The amplitude of the signal in the soma depends on the PSP values and the summation of all the synaptic entrances occurring in different regions of the arbor. For this reason it is important to evaluate the space constant once the value of the signal's amplitude in the soma is directly related to this propriety. Because the attenuation in the dendrite, the post-synaptic excitatory distal events present a relative smaller contribution than the proximal events (MAGEE, 2000).

CONCLUSIONS

The patterns presented by the ***NeuronalSYS*** can be defined as avalanches and waves. Neuronal avalanches are defined as spontaneous activities, in which the neurons fire in synchronism and that have precise time duration. This kind of avalanches has been verified experimentally, normally in cultures with layers of rat's cortex (BEGGS and PLENZ, 2003, 2004; STEWART et al., 2004; VOGELS et al., 2005, ABBOTT and ROHRKEMPER, 2006, TERAMAE and FUKAI, 2007).

For ABBOT and ROHRKEMPER, an avalanche is characterized by an event in which the activity is observed in a certain amount of time and is interrupted by a period of silence.

In this work an avalanche is defined as a set of signals produced by a stimulus. The signal produced by a stimulus travels the network forming waves of activity.

Between the waves, the layers present periods of apparent inactivity, since no PA is being fired by its neurons. The inactivity is apparent because, during these periods, there are signals traveling through both, dendritic and axonal arbors. This wave pattern can be approximated by a sine function.

Analyzing the influence of some of the main functional parameters, like post-synaptic excitatory potential, PSP, and dendritic attenuation factor, is possible verify that the network operates in a very particular region. It's a region of phase transition. Out of it the network stops transmitting the signal or gets saturated. This region is defined as a phase transition region, or region of critical state.

BEGGS and PLENZ (2004) define the critical state as that in which the size distribution of the avalanches follows a power rule. Besides that, each neuron in the network is connected to "n" other neurons. When it fires a PA, each neuron on its receptive field has a "p" probability of, in consequence, firing a PA. If $p < 1/n$, the network activity tends to perish. In the case of $p > 1/n$, the network tends to saturate. In the same reasoning, if $p = 1/n$, the network operates in a phase transition region, or changing behavior zone. In the last case, each neuron has a p = 1 probability of causing PA in at least one neuron of its receptive field. Around this "p" value the network is in a critical zone and is capable of generating and maintaining activity patterns (ABBOTT e ROHRKEMPER, 2006). The analysis of the results shows that, in the conditions used, the network generated by the ***NeuronalSYS*** operates in this region.

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