Reprinted from Trends in NeuroSciences – *March, 1983* Vol. 6, No. 3, pp. 80 – 83

Computer simulation of neuronal function

Electrical properties of dendritic spines

Since the discovery of dendritic spines by Ramon y Cajal[2], their functional role has remained a matter of speculation. The early hypotheses all consider the establishment of physical contacts with presynaptic terminals as the main function of spines. In a similar spirit, Swindale[20] has proposed in a recent issue of TINS *that spines are primarily a morphological device for connecting axons and dendrites. Ideas of this type, as Swindale points out, do not preclude other functions of spines, nor do they explain why spines should be as plastic as a number of recent studies suggest[6,7,8,19].*

Several other authors have indeed suggested that the functional significance of spines is strictly related to their electrical and biophysical properties. Chang[3] first proposed that the electrical resistance of the spine neck could control the weight of a synapse on the spine. Rall[17] and Rinzel later showed on the basis of a simple model that variations in the spine's neck could effectively change the amplitude of the somatic depolarization due to a synapse on the spine. For this reason, they suggested that memory might be stored in the diameter of the spine's neck. The general idea of spines as a site of neuronal plasticity is the underlying theme of many recent papers, in particular Crick's[4] novel hypothesis of 'twitching spines' and Boycott's[1] account of the effect of a natural state as hibernation on cerebellar spines.

Crucial for these and other suggestions are the electrical properties of spines. Since it is impossible to study directly with electrophysiological techniques the effect of spine parameters (such as the size of the spine neck) on somatic potential a theoretical analysis is called for. The purpose of this paper is to review the main results of a computational study of the electrical properties of dendritic spines following and extending Rall's analysis (Refs 16–18; see also Ref. 9) and then to discuss some implications for the functional roles of spines. We will, in particular, refer to our computer simulations of the 'spiny' pyramidal cell shown in Fig. 1 (Ref. 11).

Theoretical framework

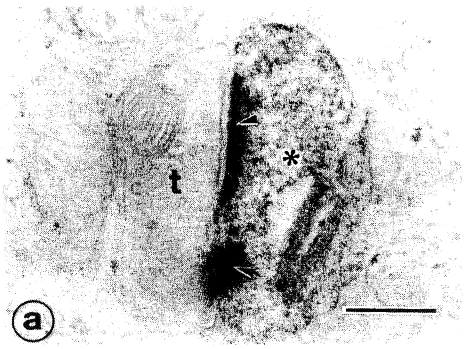
The theoretical framework on which Rall's and our analysis is based on one-dimensional cable theory, as developed by Lord Kelvin for undersea cables and applied to neuronal structures by Hodgkin, Katz and others[13]. The main tool that we have used is a program that computes the electrical properties of any given passive dendritic tree[12]. The branching structure, the lengths and the diameters of the individual branches have been measured from cells like those of Fig. 1. Our algorithm approximates each dendrite in terms of several cylinders, each one with constant diameter. The spines are modeled by a thin and narrow cylindrical spine neck (of length l and diameter d) and a thick and short spine head, as shown in the inset of Fig. 1. The main assumption in this and Rall's analysis is that the membrane is passive.

Linear properties and synaptic inputs

The input resistance of a spine as seen by an imaginary electrode in the spine head, turns out to be well approximated by the sum of the input resistance of the dendritic shaft and the resistance of the spine neck R_N. R_N is the resistance of a cylinder with constant diameter d: it increases linearly with the length l (and the intracellular resistance R_i) while it is inversely proportional to the square of the diameter d. Since spine input resistance values can be much higher than the input resistances on the dendrites (for small spine neck dimensions) current injected into the spine will produce a much larger depolarization than if injected in the dendritic shaft. But what about the effect on the soma? It turns out that it is irrelevant, from the point of view of the soma, whether the current input is in the spine or in the dendrite.

Synaptic inputs, however, consist of transient conductance changes to specific ions and the resulting current is not proportional to the conductance change. Synaptic inputs effectively open 'holes' in the membrane for ions with a reversal potential E. Since spines can have a very high input resistance, even a small flux of positive ions may immediately drive the potential in the spine towards the equilibrium potential, thereby limiting the amount of inflowing current during synaptic activation and therefore the change in voltage at the soma. The neck resistance effectively 'chokes' back the flow of ions resulting from a synaptic conductance change. This non-linear saturation effect depends directly on the neck's resistance, which in turn depends on the neck diameter and length. The size of the effect depends on the relative size of the input resistance and conductance change and, to a lesser degree, on the electrical properties of the whole dendritic tree.

Actin *is* present in dendritic spines



*Do dendritic spines twitch? Francis Crick asked this question last year (*TINS, *Vol. 5, pp. 44–46), when he suggested that contractile proteins in the spine would allow it to change shape rapidly during neuronal activity, thus modifying the effectiveness of its synapses. In a recent paper in PNAS (Vol. 79 (1982) 7590–7594) Andrew Matus and colleagues have shown that actin is indeed present in dendritic spines.*

The electron micrograph shown above is of a rat cortex slice stained with antibody against fish muscle actin. A single synapse occupies the centre of the field. Its presynaptic terminal is identified (t) and shows no detectable immunoperoxidase reaction product. In contrast, the postsynaptic element of the synapse (identified by an asterisk) is distinctly stained with the highest intensity being in the postsynaptic density (arrowheads). Matus and his colleagues compared staining intensity inside dendritic spines and in smooth muscle cells around brain blood vessels and found that they were similar. They concluded that actin is present in dendritic spines at high concentrations. They also identified an unknown factor; the apparent lack of staining in glia and other parts of nerve cells could be because of lower actin levels in these places or because the actin is masked by actin-binding proteins. Certainly studies of axoplasmic flow show that there is actin in axons. Just which of these explanations is the right one remains to be seen. Meanwhile one thing is clear, actin is present in substantial amounts in dendritic spines. Reproduced with permission.

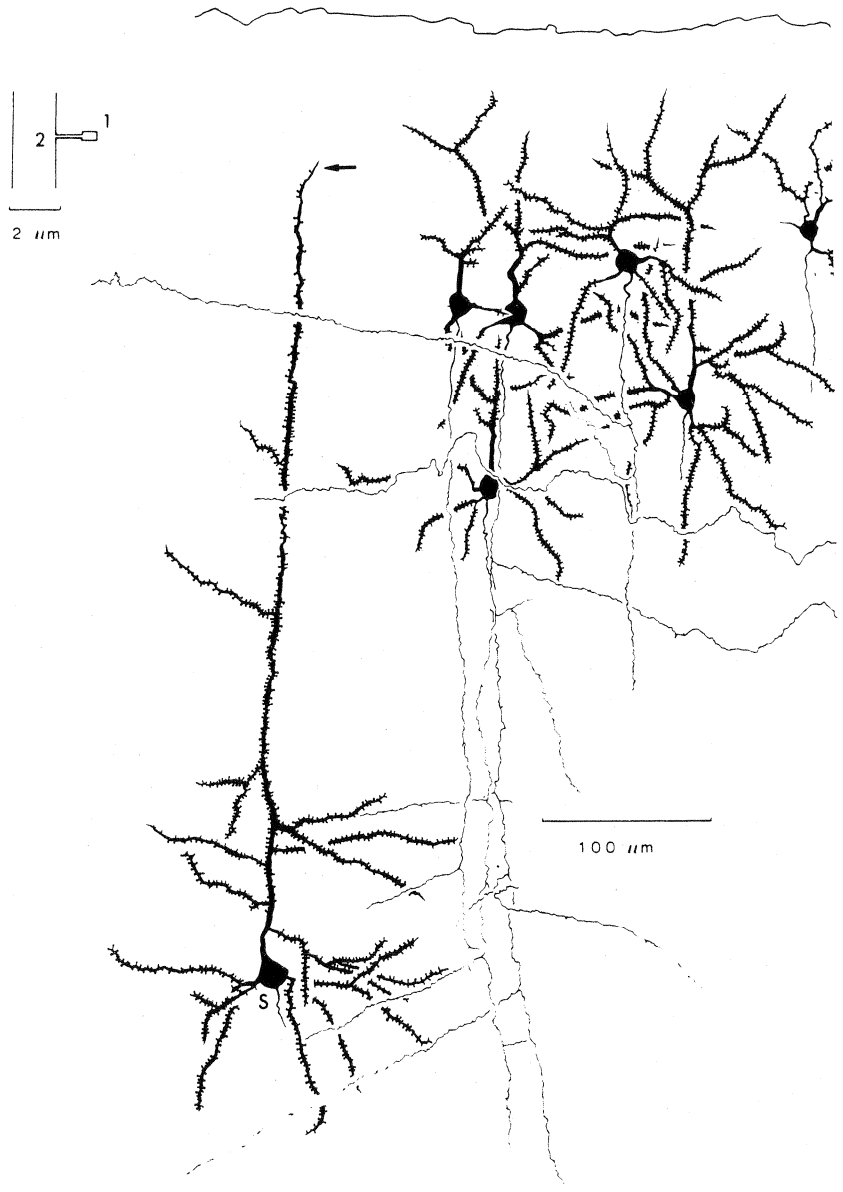


Fig. 1. *The pyramidal cell from the sensorimotor cortex of an adult mouse (on the left) used for our computer simulations. The arrow shows the distal spine whose properties are computed in Fig. 2. With our parameters (R_m = 4 000 Ωcm²; R_i = 70 Ωcm; C_m = 2 μF cm⁻²) the electrotonic distance of this spine to the soma is 1.19 space constants. The inset show our model of the spine.*

If synaptic change in conductance is small (i.e. much smaller than the input conductance of the spine), then the depolarization does not depend on the spine. In this linear range ('small' synaptic inputs, i.e. 'large' neck diameters), spines do not have any special electrical effect. Alternatively, for 'large' inputs, the potential inside the spine saturates to the ions' reversal potential and the potential in the soma is now independent of synaptic strength and depends mainly on the spine neck and dendritic shaft resistance. In the intermediate range, i.e. when the input conductance is of the same order as synaptically induced changes in conductance, the somatic potential depends both on the attenuation and on the amount of saturation in the spine. Effectively, this represents a gain control mechanism set by the neck's diameter.

The question at this point is what actually happens in a realistic dendritic tree with physiological values of neuronal parameters. Fig. 2(a) shows the effect a synapse on a distal spine of our pyramidal cell has on the somatic potential as a function of the neck's diameter or length for small, medium and large conductance changes. The actual size of the conductance change at a synapse on a cortical dendritic spine is an open question, though a value between 10^{-8} and 10^{-7} S is not unreasonable. For the sake of comparison, recall that a single ACh quantum at the neuromuscular junction induces a conductance change around 6×10^{-8} S (with a total duration of about 1 ms). Fig. 2(a) shows that for conductance values of this size relatively small changes of the spine dimensions in the cell of Fig. 1 can significantly change the effectiveness of a synapse. Because of the large number of spines on most spiny cells, the overall effect of these small changes in the spine shape could easily be quite significant.

Very fast transient inputs show non-linear saturation

It may be argued that this picture may change dramatically when transient conductance inputs are considered since input resistances of dendrites decrease rapidly with faster inputs. After all, the release of a single quantum of transmitter usually induces a very fast change of conductance. Spines, however, have very little impedance attenuation at high frequencies, since their total membrane capacitance is very small. Their structure may indeed optimize the conflicting needs of a high input impedance for transients with a correspondingly small current loss. Thus a significant saturation effect can take place even for short transient inputs [see Fig. 2(b)]. The dendritic shaft itself would provide a much smaller saturation or choking effect: the difference increases with transience of the input.

Should spines have inhibitory input?

The previous discussion is restricted to single excitatory inputs on a spine – by far the most frequent case. Isolated inhibitory inputs are not expected on a spine (if inhibition has an equilibrium potential close to the resting potential, a possibly common situation in the cortex), since it can be proved[12] that for maximum effectiveness, shunting inhibition must be located on the direct path between excitation and soma. For inhibition to effectively veto excitation, the best design would be to locate excitatory inputs distally, possibly on spines, and inhibitory inputs proximal to the soma directly on the dendritic shaft. This arrangement is indeed common in the cortex[15].

On the other hand, the pairing on one spine of two inputs of different types offers the possibility of synthesizing local circuits performing different operations. For instance, the combination on one spine of an excitatory and a (shunting) inhibitory input would represent an almost ideal module for performing a selective AND-NOT-like operation effectively decoupled from other such subunits. All the available data indicate that probable inhibitory inputs (Gray Type 2) on spines, when present, are never alone but always accompanied by an excitatory synapse (Gray Type 1)[10,15]. Spines with both excitatory and inhibitory inputs are not very common but still represent 5% to 20% of the total number of cortical spines. What is especially remarkable is

that the vetoing effect of inhibition is very sharply dependent on relative timing of inhibition and excitation. Whereas inhibition on the dendritic shaft can effectively veto more distal excitation within a temporal window of the order of the membrane time constant, inhibition on a spine is stronger and more selective, being effective only in a window of ± 120 μs (for inputs with time-to-peak = 0.25 ms). Thus, an inhibitory and an excitatory input on a spine could implement a discrimination circuit of the AND-NOT type with a time resolution around the 100 μs range[5,11].

The main properties of spines

In summary, the electrical properties most characteristic for spines are:

1. Depending on the size of the conductance inputs a spine may have no special role at all (small synaptic inputs), perform a simple gain control mechanism on the inputs (medium synaptic inputs), or totally saturate to a level independent of the input (large synaptic inputs). In the middle range, the effect of the spine is to map a possible wide range of input amplitudes on to a restricted range of output depolarizations.
2. The saturation property is valid not only for slow, but also for very fast conductance changes. The local voltage increase is much higher than for the same input on the dendritic shaft [see Fig. 2(b)].
3. Except for very small conductance changes, the effectiveness of a synaptic input on a spine in terms of somatic depolarization depends on the dimension of the spine's neck more than on any other parameter.
4. There is an optimal neck's dimension for which relatively small variations of the neck are most effective in controlling the weight of the excitatory spine synapse [see Fig. 2(a)]. For reasonable parameter values, this optimal value is consistent with anatomical data[11,14].
5. Isolated inhibitory synapses on a spine cannot have any interesting electrical properties and are not expected to occur (they do not). Conjunction of shunting inhibition with excitation on a spine can implement a veto operation which is highly specific, both in space and time.

All these properties depend on the assumed parameter values, most critically on the size of the synaptic conductance change at the spine. In particular, if the peak value of the conductance change were much smaller than 10^{-8} S, a spine would behave almost linearly, other parameters being equal, and would have no useful electrical function. It must be emphasized that these conclusions rest on the assumption of passive or non-regenerative membrane properties. The situation could change if the dendrites or

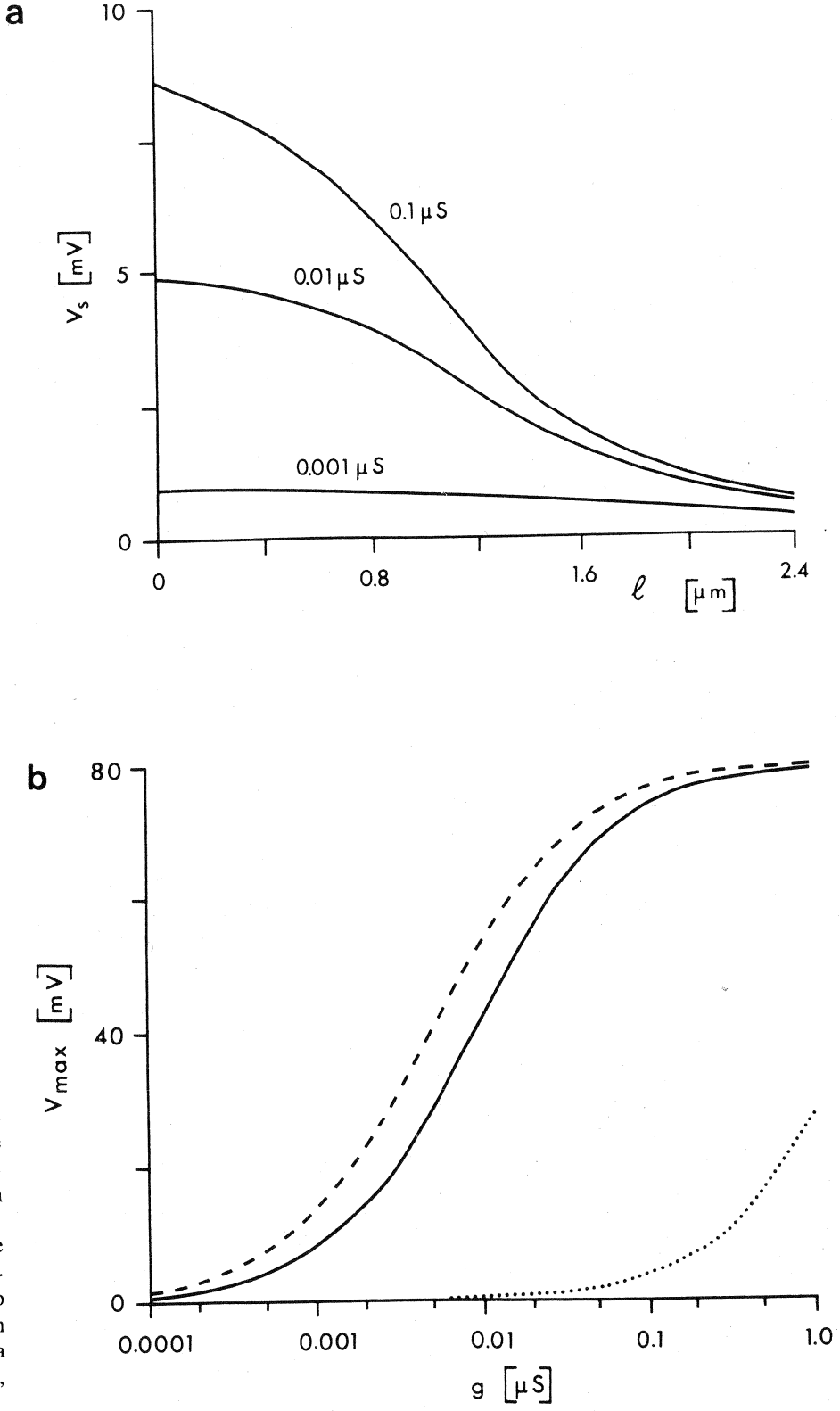


Fig. 2 (a). *The somatic voltage corresponding to different neck dimensions for small, medium and large DC conductance inputs. Transient inputs (time to peak 0.25 ms and total duration 0.9 ms) yield very similar curves for peak conductance values equal to the DC values shown here, except that they are scaled down by about a factor of 10. The assumed reversal potential is 80 mV. The spine neck dimensions were changed in such a way as to leave the total neck surface area constant and equal to 0.1 μm^2. Optimal plasticity (for g = 10^{-7} S) imply a proximal spine neck length of about 0.59 μm (neck diameter 0.17 μm) while distal spines should be about 50% longer. Plausible changes in neck length (from 1.0 to 1.6 μm) could alter the 'weight' of the synapses by a factor of 2.*

(b). *The maximum of the depolarization at the synapse, for a fast transient conductance input of peak amplitude g (time-to-peak = 0.25 ms and total duration = 0.9 ms) at the distal spine of Fig. 1 (solid line; at location 1 in inset of Fig. 1) or at the dendritic shaft just below the spine (dotted line; at location 2). The dashed line shows that a DC conductance change yields essentially the same depolarization in the spine as the transient input; the membrane time constant is 8 ms.*

even the spine itself would be capable of producing spikes.

Functional role of spines

Assuming that spines have the non-linear saturation properties outlined above, we now ask what their function could be (in the case of isolated excitatory synapses). At least six somewhat different possibilities can be envisaged, none excluding the others. (1) Spines may effectively compress the range of each single synapse, showing a high sensitivity to small conductance inputs and keeping the maximum depolarization which could be achieved by a single synapse below a certain predetermined value. (2) This maximum value may be always attained: the synapse would always work in the saturation range and the spine would effectively '*binarize*' the synaptic input. (3) It is possible that – because of the non-linear range compression – inputs on different spines are kept more isolated than they might otherwise be, simply because the spine would reduce their effectiveness. (4) As suggested by Perkel (personal communication), the strong depolarization within the spine may have a number of local effects, such as triggering local action potentials in excitable membranes or opening calcium channels. (5) Fine control of synapse effectiveness via the spine neck diameter (and length) may be used during development to fine-tune the relative importance of the various inputs. (6) In a similar vein, as Rall first suggested, this may also represent a basic mechanism for learning in the nervous system. Several authors have followed this idea[4,6–8,19] and presented experimental evidence that spines can indeed change their shape (for instance following massive stimulation). Crick[4] has recently proposed that the spine's neck diameter may be controlled on a very short time scale by a contractile protein in the spine's cytoplasma. Thus, Rall's and our calculations suggest indeed that learning may result from the change of the shape of spines. It should, however, be clear that this is little more than an attractive possibility. Given the present uncertainty about appropriate parameters, it is possible that conductance changes at a spine are effectively small: in this case spines would not have any specific electrical properties that could play a role in learning.

Reading list

1 Boycott, B. B. (1982) *Trends NeuroSci.* 5, 328–329

2 Cajal, y S. R. (1911) *Histologie du Systeme Nerveaux de l'Homme et des Vertebres*, Vols 1 and 2, A. Maloine, Paris

3 Chang, H. T. (1952) *Cold Spring Harbor Symp. Quant. Biol.* 17, 189–202

4 Crick, F. (1982) *Trends NeuroSci.* 5, 44–46

5 Diamond, J., Gray, E. G. and Yasargil, G. M. (1970) in *Excitatory Synaptic Mechanisms* (Anderson, P. and Jansen, J. K. S., eds), pp. 212–222, Oslo Universitetsforlag

6 Desmond, N. L. and Levy, W. B. (1981) *Anat. Rec.* 199, 68A

7 Fifkova, E., Anderson, C. L., Young, S. J. and van Harreveld, A. (1982) *J. Neurocytol.* 11, 183–210

8 Fifkova, E. and van Harreveld, A. (1977) *J. Neurocytol.* 6, 211–230

9 Jack, J. J. B., Noble, D. and Tsien, R. W. (1975) *Electric Current Flow in Excitable Cells*, Clarendon Press, Oxford

10 Jones, E. G. and Powell, T. P. S. (1969) *J. Cell. Sci.* 5, 509–529

11 Koch, C. (1982) *Ph.D. Thesis*, University of Tübingen

12 Koch, C., Poggio, T. and Torre, V. (1982) *Phil. Trans. R. Soc. London, Ser. B* 298, 227–264

13 Kuffler, S. W. and Nicholls, J. G. (1976) *From Neuron to Brain*, Sinauer Associates, Sunderland Massachusetts

14 Peters, A. and Kaiserman-Abramof, I. R. (1970) *Am. J. Anat.* 127, 321–356

15 Peters, A., Palay, S. L. and Webster, H. de F. (1970) *The Fine Structure of the Nervous System*, W. B. Saunders Company, Philadelphia

16 Rall, W. (1970) in *Excitatory Synaptic Mechanisms* (Anderson, P. and Jansen, J. K. S., eds), pp. 175–187, Oslo Universitetsforlag

17 Rall, W. (1974) in *Cellular Mechanisms in Neuronal Activity* (Woody, C. D., Brown, K. A., Crow, T. J. and Knispel, J. D., eds), Brain Information Service Research Report 3, 13–21

18 Rall, W. (1978) in *Studies in Neurophysiology* (Porter, R., ed.), pp. 203–209, Cambridge University Press

19 Schüz, A. (1981) *J. Hirnforsch.* 22, 113–127

20 Swindale, N. V. (1981) *Trends. NeuroSci.* 4, 240–241

C. KOCH
T. POGGIO

MIT Department of Psychology and Artificial Intelligence Laboratory, Cambridge, MA 02139, U.S.A.