10.2 Dendritic Spines, Synaptic Potency and Neuronal Plasticity (1974), in *Cellular Mechanisms Subserving Changes in Neuronal Activity*, ed. C. D. Woody et al., Brain Information Research Report #3, Los Angeles: University of California

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Dr. Rall discussed a possible role of dendritic spines in neuronal plasticity. Dendritic spines were first reported by Ramón y Cajal in 1888 (*cf.* The Scheibels, 1968). The importance of dendritic spines as sites for synaptic inputs was first noted in 1897 by Berkley (1897). He observed that if a cell was sensitive to all other neighboring cells over its surface there would be chaos, that it was fortunate that the cells were covered with glia, that only the spines stuck out from the glia, and that only the spines would receive inputs, thereby avoiding chaos. In 1952, Chang made the additional observation that, because of their long thin stems, dendritic spines would provide high electrical resistance; this resistance would attenuate the effect of the synapse on the cell (Chang, 1952). He argued that because of this attenuation, a cell could be fired only by a large number of such inputs.

Synaptic inputs to cortical pyramidal cells are mostly by these spines. In 1959 Gray demonstrated synapses on the spines by electronmicroscopy (Gray, 1959). Subsequent studies were made by Colonnier (1968) and others (*cf.* The Scheibels, 1968). Diamond, Gray and colleagues (1970) pointed out that 95% of synaptic input to pyramidal cells is via the spines.

What then is the function of the spines? Presumably they must do something more than simply receive the synaptic input. It cannot be argued that the spines are there to increase receptive surface area since there is considerable surface area that is not occupied by synapses (*cf.* The Scheibels, 1968). With regard to large spine stem resistance, why would attenuation of synaptic potency be desirable? Some have postulated that this large resistance might ensure linear summation of synaptic effects by reducing the coupling between the synapses. One difficulty with this postulate is that extreme amounts of attenuation would be needed to get linear summation. A further possibility is that the dendritic spines could be used to provide a way of changing the relative contributions of different synapses. This could underlie or be a part of neuronal plasticity. This possibility, that spine stem resistance could be used to adjust the relative potency of different synapses on the cell, can be examined biophysically to see if it seems reasonable.

Consider the resistance to electric current flow through a spine stem (Figure 1), from the spine head to its point of attachment on a dendrite. This spine stem resistance is designated R_{SS}. With synaptic membrane

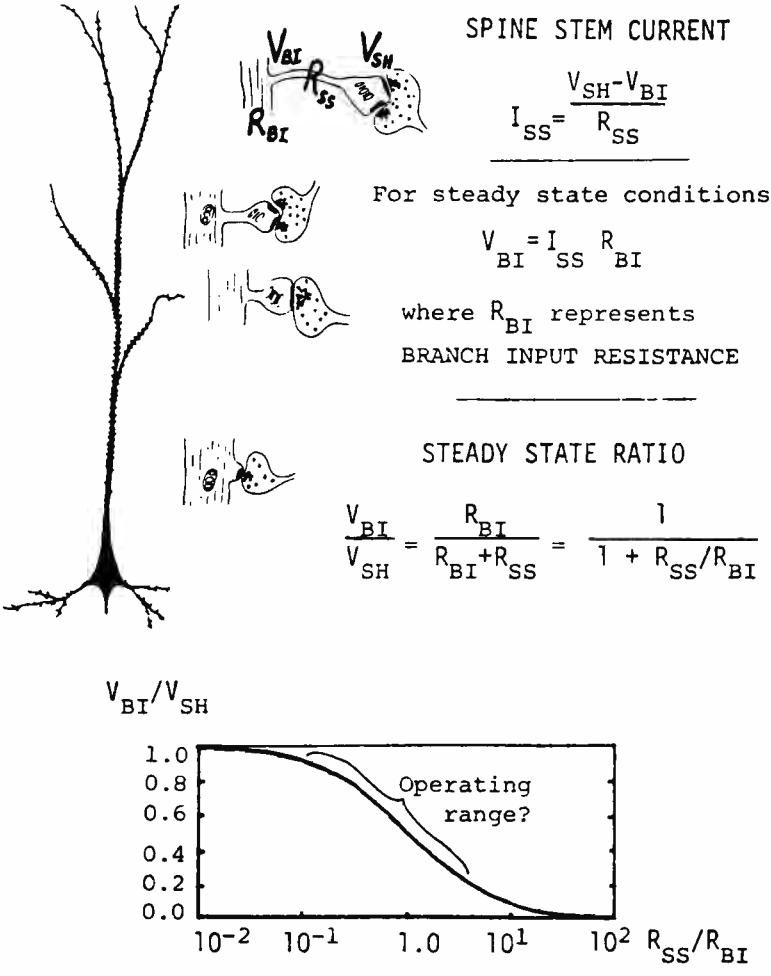


Figure 1
Diagram of the relation of spine stem currents to the resistances and voltages designated in the text.

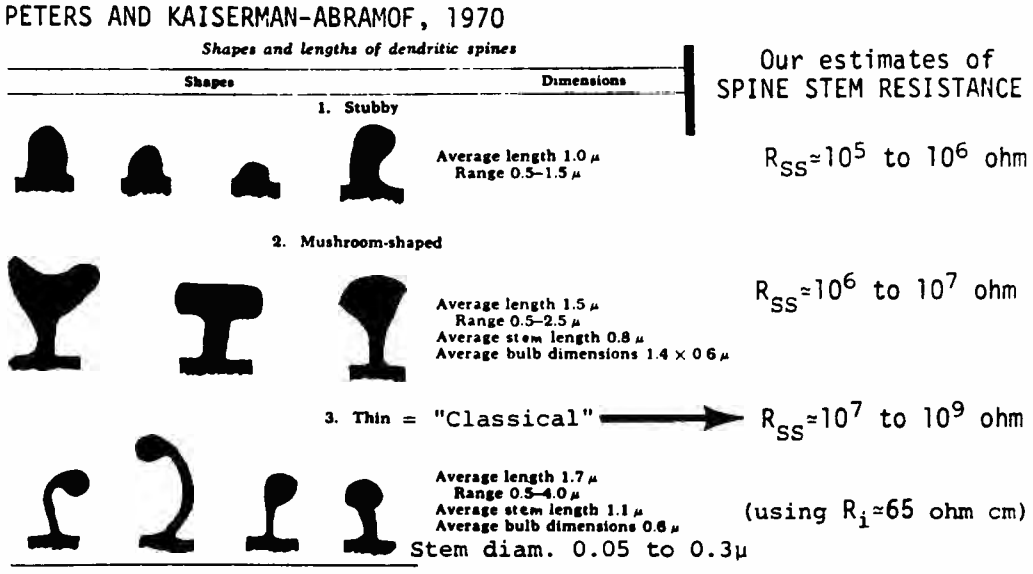


Figure 2
Variations of spine stems and their resistance values. (From Peters and Kaiserman-Abramof, 1970.)

depolarization at the spine head, intracellular current will flow through the spine stem in proportion to the potential difference between the voltage V_{SH} at the spine head and the voltage V_{BI} at the spine base. The potential difference divided by the spine stem resistance gives us the spine stem current I_{SS}, as indicated in Figure 1. For a steady depolarization at the spine head, I_{SS} becomes a steady current which also flows from the spine stem into what is known as the branch input resistance R_{BI} of the cell. This steady current is thus equal to several equivalent ratios:

$$I_{SS} = \frac{V_{BI}}{R_{BI}} = \frac{V_{SH} - V_{BI}}{R_{SS}} = \frac{V_{SH}}{R_{SS} + R_{BI}}$$

From these ratio and from Figure 1, it can be seen that if the spine stem resistance is equal to the branch input resistance, the voltage that is generated out at the synapse would be divided equally between the spine stem resistance and branch input resistance. That is, the voltage V_{BI}, at the branch would be half of that, V_{SH}, which is generated at the spine head. More generally, but still for steady states, the fraction of V_{SH} delivered to the dendrite (*i.e.*, the ratio V_{BI}/V_{SH}) depends upon the resistance ratio, R_{SS}/R_{BI}, as shown in the lower half of Figure 1. The sensitivity (or adjustment) of this relation can be seen to be greatest over the middle range. Can this be used as an operating range for adjusting synaptic potency?

What sort of value should be ascribed to the spine stem resistance? Figure 2 shows us why one must consider more than just one case. Peters and Kaiserman-Abramof (1970) classified the dendritic spines according to their various morphologies: stubby, thin, etc., and it can be seen that there is considerable variety in the dimensions and morphology (Figure 2).

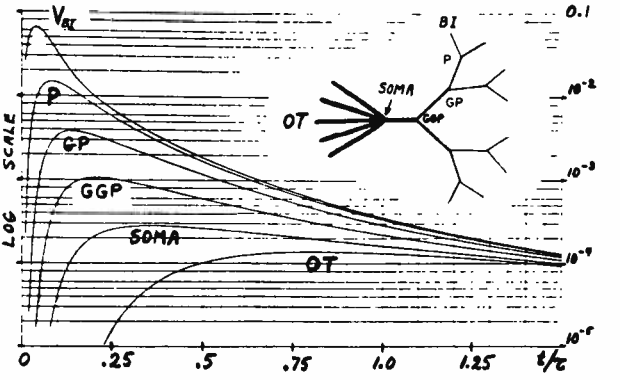
Spine stem resistances can be estimated for these morphological types. Using the specific resistivity noted in Figure 2, we estimated the following ranges of values: for the stubby spines about 0.1 to 1 megohm, for the very thin spines about 10 to 1000 megohms, and for the mushroom shaped spines still other values. Jones and Powell (Jones and Powell, 1969; *cf.* Peters and Kaiserman-Abramof, 1970) noted that long thin spines are more frequent at distal dendritic locations. Near the cell body and the base of the apical dendrite they find more stubby spines. It seems strange that the long thin spine (which would be expected to cause more attenuation) is usually found at distal dendritic locations (which also cause attenuation). This seems paradoxical. Why should the synapse be doubly handicapped by such double attenuation?

Looking at the relationship of the spine stem resistance to the input resistance may provide a clue to this paradox. There seems to be an impedance matching involved here. If one takes seriously the hypothesis that the spines may be involved in adjusting the relative potency of synapses, then the lower half of Figure 1 provides a possible resolution of this apparent paradox. This graph indicates that as long as the spine stem resistance is no more than one per cent of the input resistance, the spine stem poses no disadvantage to synaptic effectiveness. Also, if the spine stem were used to adjust synaptic potency, one might expect the ratio R_{SS}/R_{BI} to lie in the range from 0.1 to 10, which could be regarded as an optimal operating range for such adjustment.

In order to estimate R_{SS}/R_{BI}, we must have estimates of branch input resistance as well as spine stem resistance. A theoretical method of estimating branch input resistance has recently been published in collaboration with John Rinzel (Rall and Rinzel, 1973). This paper provides full details of assumptions and methods, and many examples are tabulated in Table I (*cf.* Rall and Rinzel, 1973). There, the branch input resistance, R_{BI}, is expressed relative to the more familiar neuron (at the soma) input resistance, R_N, for many different amounts of branching and lengths of branches. For a distal branch of a pyramidal cell, one might have $R_{BI}/R_N \simeq 100$, and for a typical value of 10 megohms for R_N, this would imply 10^3 megohms for R_{BI}.

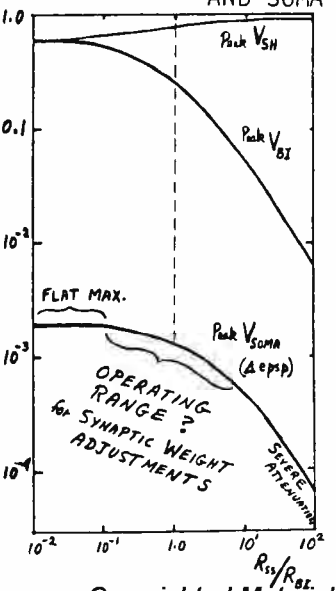
Also, when computations were generalized from simple steady state considerations to transient synaptic potentials, such as those illustrated in Figure 3 (top), Rall and Rinzel found that when the transient peak

VOLTAGE TRANSIENTS AT DIFFERENT LOCATIONS
FOR BRIEF INJECTION OF CURRENT AT ONE BRANCH



Attenuation of Peak Ampl.		(Compare Steady State)
P	1/4.6	(1/2.3)
GP	1/17	(1/5.3)
GGP	1/62	(1/12)
SOMA	1/232	(1/24)

SYNAPTIC INPUT TO SPINE,
EFFECT OF SPINE STEM RESISTANCE (R_{SS}/R_{BI})
UPON PEAK TRANSIENT VOLTAGES AT
SPINE HEAD (V_{SH}),
INPUT BRANCH (V_{BI}),
AND SOMA (V_{SOMA}).



R_{SS}/R_{BI}	Peak V_{SOMA}
10^{-2}	~.002
10^{-1}	~.002
1.0	~.0013
10^{1}	~.0004
10^{2}	$<10^{-4}$

(.002)(75mV)=0.15mV

amplitudes were plotted against R_{SS}/R_{BI} as in Figure 3 (bottom), the results (note log amplitude scale) were qualitatively similar to the steady state results of Figure 1. The attenuation from peak V_{SH} to peak V_{SOMA} is 500 or more, but that still can imply an EPSP amplitude of about 0.15 mV at the soma. It is important to notice the "flat maximum" at the soma for R_{SS}/R_{BI}, from 0.01 to 0.1; this means that adjusting the spine stem resistance to values smaller than one tenth of the branch input resistance would gain nothing in synaptic potency.

These results for the peak at the soma have been replotted in Figure 4. Peak V at the soma is plotted relative to its maximum value for that particular dendritic location, and this is plotted on an arithmetric scale (in contrast with the log scale of Figure 3). This also shows the flat maximum for R_{SS}/R_{BI} from 0.01 to 0.1, and the presumed optimal range, from 0.1 to 2 or 3, for adjusting the potency at the soma for the synapse on a spine at that particular dendritic location.

If we think in term of evolution, and conjecture that there is survival value in keeping the relative potency of many synapses adjustable, then one might expect to find that actual R_{SS}/R_{BI} values lie in this "optimal operating range". The lower half of Figure 4 summarizes the results of our order of magnitude estimates for the spine stem types most commonly found at three locations: distal dendritic, mid-dendritic, and somatic or proximal dendritic. The overall range of 10^7 to 10^9 ohms for R_{SS} of thin spines is separated into 10^8 to 10^9 ohms for the longer-thinner ones most frequent at distal locations, and 10^7 to 10^8 ohms for those most frequent at mid-dendritic locations. Using these estimates, together with the branch input resistance estimates noted earlier for a pyramidal cell, we see that the ratio R_{SS}/R_{BI} does seem to lie in this expected range for both the distal and mid-dendritic locations, whereas the stubby spines at proximal locations would seem to lie in the flat maximum region of maximum potency without flexibility.

It should be emphasized that this agreement with prediction is based upon rough order of magnitude calculations. It is not presented as a proof that our conjecture is correct, but rather as an approximate biophysical test that suggests plausibility and indicates that this possibility cannot yet be ruled out. The design principle involved here is to sacrifice maximum power in order to gain flexibility and control. Adjustability of potency means either increase or decrease relative to other synapses. Thus we think of delicate adjustments of the relative weights (potency) of many different synapses to any given neuron. We think of these changes as

Figure 3
Summary of the effects of brief EPSP time courses based on computations by Rinzel and Rall. (unpublished)

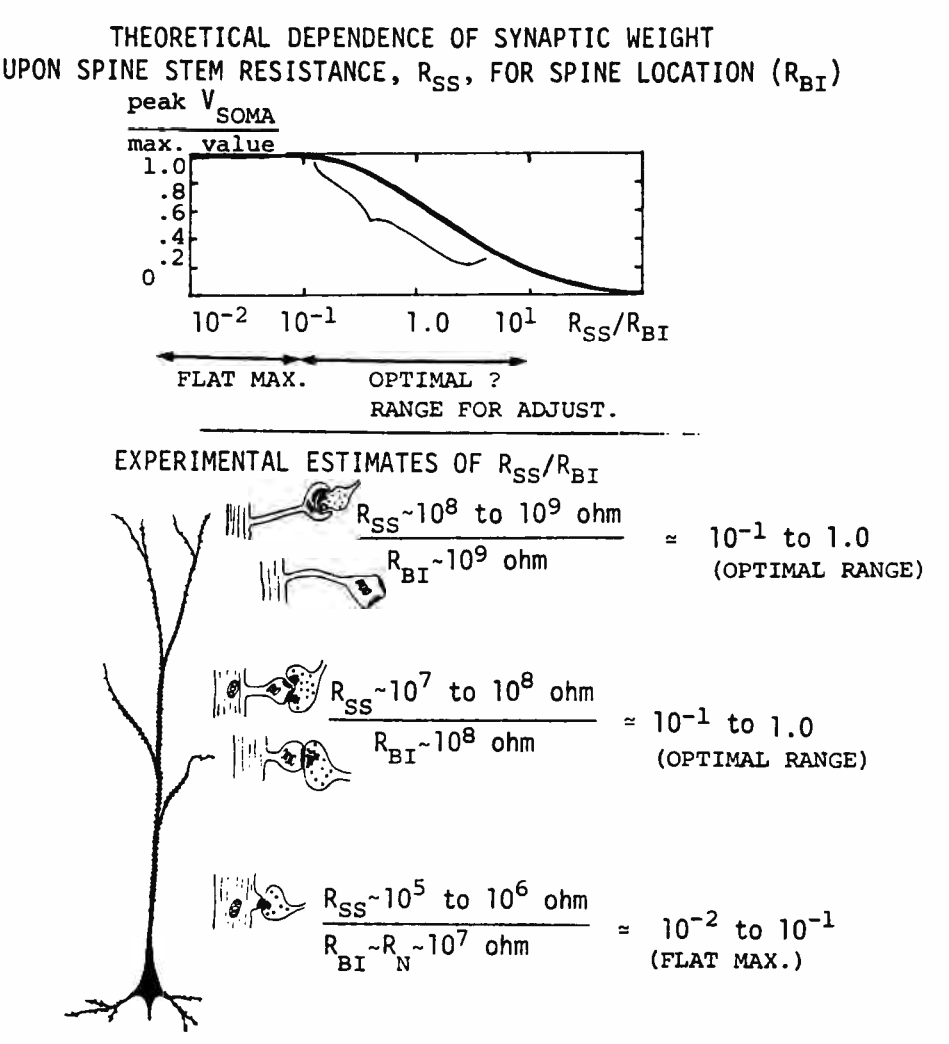


Figure 4
Summary of conclusions.

responsible for changes in dynamic patterns of activity in assemblies of neurons organized with convergent and divergent connective overlaps.

We do not pretend to have explained how the spine stem changes would be controlled. Also, we emphasize that other possible ways of adjusting synaptic potent should not be dismissed. Some other possibilities are: (a) the synaptic contact area could be increased or decreased, (b) the amount of chemical transmitter released could change, (c) the duration of synaptic action could be changed, (d) the caliber of the dendritic branch or its entire dendritic tree could change R_{BI}. It is noteworthy that a change in the duration would be especially valuable if the depolarization at the spine head is essentially maximal. A change in a dendritic branch or dendritic tree has some interesting properties regarding synaptic specificity (Rall, 1962) which may relate to some of Dr. Woody's earlier remarks concerning specificity. If just one spine is changed, there is only a change in the weight of that particular synapse. If the weight of the dendritic tree is changed, there is a change in the weight of *all* the synapses that end on that tree, but this is still more specific than changing the threshold of the entire neuron. One could conceive of various conditioning or plasticity situations in which either or any of the above could be most advantageous.

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