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Nonlinear interactions in a dendritic tree: localization, timing and role in information processing

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Abstract: In a dendritic tree transient synaptic inputs activating ionic conductances with an equilibrium potential near the resting potential can *veto* very effectively other excitatory inputs. Analog operations of this type can be very specific with respect to relative locations of the inputs and their timing. We examine with computer experiments the precise conditions underlying this effect in the case of a δ-like cat retinal ganglion cell. The critical condition required for strong and specific interactions is that the peak inhibitory conductance change must be sufficiently large, i. e. about $5 \cdot 10^{-8} S$ or more, almost independently of other electrical parameters. In this case, a passive dendritic tree may perform hundreds of independent analog operations on its synaptic inputs, without requiring any threshold mechanism.

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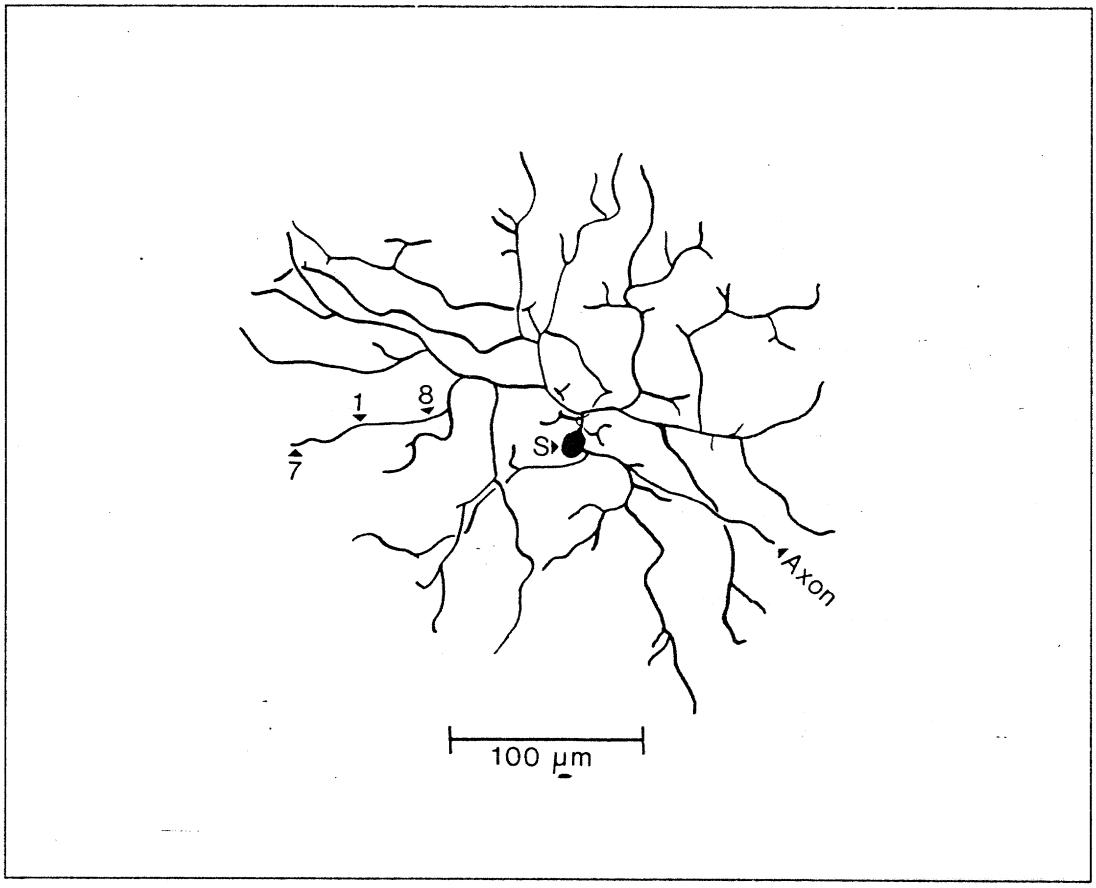

Figure 1. A cat retinal ganglion cell of the δ type (Boycott and Wassle, 1974, Poggio et al., 1981; Koch et al., 1982). In the calculations reported in Figs. 2 and 3, $C_m = 2\mu F cm^{-2}$, $R_m = 2500\Omega cm^2$, $R_i = 70\Omega cm$.

When two regions of dendritic membrane in close electrical proximity experience simultaneous conductance changes - induced by synaptic inputs - the resulting postsynaptic potential at the soma is not the linear sum of the potentials generated by each synapse alone. The existence of such nonlinear interactions in a passive dendritic tree has been long recognized, both theoretically and experimentally (see Rinzel and Rall 1974; Redman 1976; Barrett and Crill, 1974). Recently it has been proposed that this may represent an important mechanism for implementing elementary information processing operations locally in a passive dendritic tree (Poggio and Torre, 1978,1981). In particular, Torre and Poggio (1978,1981) have suggested that direction selectivity of some retinal ganglion cells is due to the nonlinear interaction on the dendritic membrane of the cell of an excitatory conductance change and of an inhibitory input with an equilibrium potential near the resting potential (shunting inhibition). We have analyzed the interaction of a transient inhibitory conductance input of the shunting type with an excitatory input, on the basis of cable theory, for various types of cat retinal ganglion cells. In this note we report, in particular, our analysis for the δ cell shown in Fig.1, whose quantitative morphology was obtained from histological material of Boycott and Wassle (1974). We wish to show that inputs of the shunting type can "veto" in a nonlinear way the depolarising effect on the soma of an excitatory input.

This nonlinear interaction can be

(a) strong

(b) specific with respect to the relative position of excitation and inhibition

(c) tuned to their (relative) timing.

Properties (a) to (c) depend on the electrical parameters and on the morphology of the cell. By far the most critical condition is the size of the conductance changes involved. For our cells properties (a) to (c) are certainly valid if the peak conductance change is in the order of $5 \cdot 10^{-8} S$ or larger, for a wide range of values of the other electrical parameters. Among the various types of cat retinal ganglion cells (α, β, γ and δ according to Boycott's and Waessle's classification (1974)) this inhibition is maximal for γ and δ cells, while it is relatively weaker for the α and β cells (Koch et al. 1982). The branching structure, the length and the diameters of each dendritic segment were determined from histological material of Boycott and Waessle, as described in detail (Poggio et al., 1981; Koch et al., 1982). The dendritic tree was approximated in terms of short segments, each being equivalent to a cylinder. An algorithm (modified from Butz and Cowan (1974)) was implemented in a program to compute from these data (for a range of values of the electrical parameters, (C_m, R_m, R_i)) the linear electrical properties of the cell. The main assumption is that the membrane is passive (and that linear cable theory holds). The program computes the complex transfer resistances $\tilde{K}_{ij}(\omega)$ for any two locations i, j in the dendritic tree. If a current I_j is injected at location j the resulting voltage at location i is given by

$$V_i(t) = I_j(t) * K_{ij}(t) \tag{1}$$

where $*$ indicates convolution and $K_{ij}(t)$ is the inverse Fourier transform of $\tilde{K}_{ij}(\omega)$. The set of $\tilde{K}_{ij}(\omega)$ for various locations i, j characterizes completely the (linear) electrical properties of a branched passive cable. We made use of two general properties of the $\tilde{K}_{ij}(\omega)$ for dendritic trees (cf. Koch et al. 1982):

symmetry, i.e.

$$\tilde{K}_{ij}(\omega) = \tilde{K}_{ji}(\omega) \tag{2}$$

separability, i.e.,

$$\tilde{K}_{ij}(\omega) = \frac{\tilde{K}_{il}(\omega)\tilde{K}_{lj}(\omega)}{\tilde{K}_{ll}(\omega)} \tag{3}$$

if l is on the "direct path" from i to j.

Let us consider the case of an excitatory synapse modulating the conductance g_e to an ionic species with equilibrium potential $E_e > V_{rest}$ in location e and an inhibitory synapse modulating the conductance g_i to an ionic species with equilibrium potential $E_i = V_{rest} = 0$ in location i (for evidence of shunting inhibition in ganglion cells see Baylor and Fettiplace 1979). For transient conductance inputs the system of Volterra integral equations giving the resulting somatic potential is

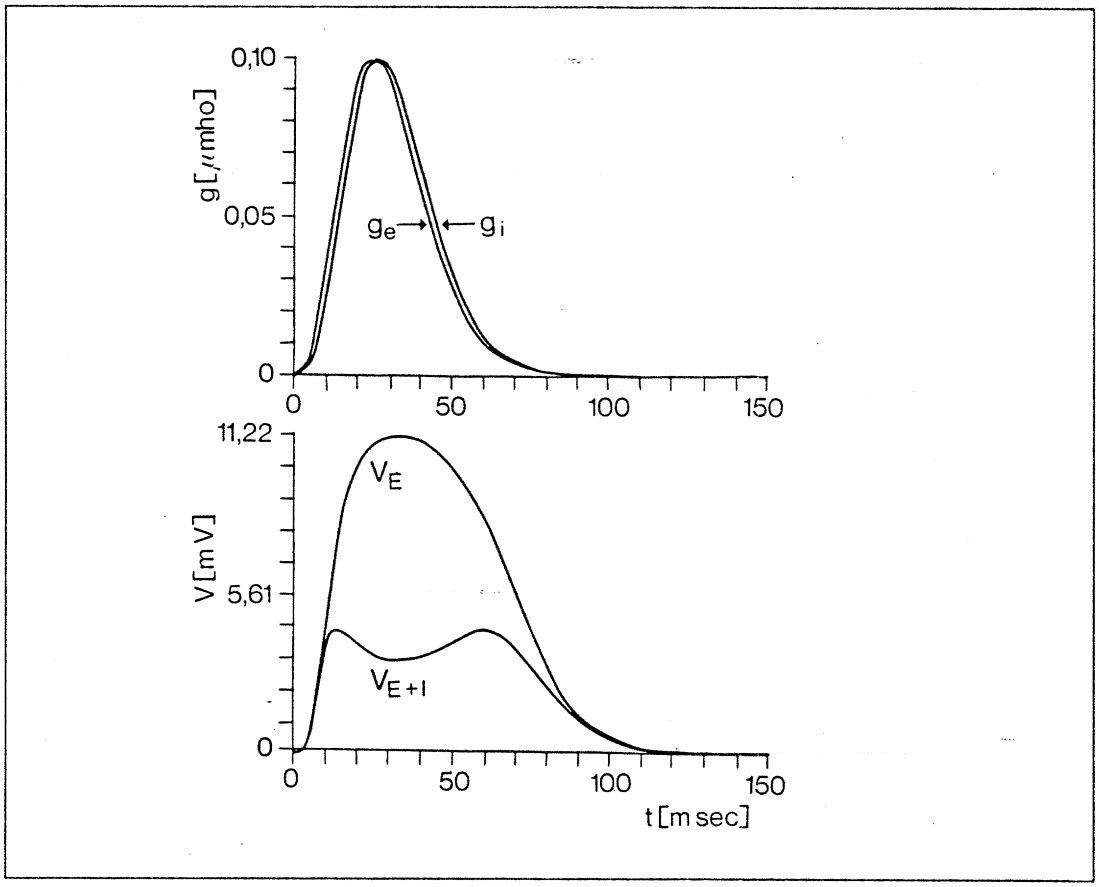

Figure 2. The depolarization in the soma of the delta cell of Fig. 1 for an excitatory input g_e at location 1 and an inhibitory input g_i at location 8. Both inputs have the time course $g(t) = t^4 e^{\frac{-t}{t_{peak}}}$ and are shown in fig. 2a. Location and timing of inhibition are optimal (i.e. the inhibition is delayed by $1.5msec$ see Fig. 3). The excitatory battery is $E_e = 80mV$ and the inhibitory battery is $E_i = 0mV$ (relative to the resting potential). For both inputs, time to peak is $t_p = 25msec$, $g_{max} = 10^{-7}S$. Fig. 2b shows the corresponding somatic depolarization in the absence (V_E) and in the presence (V_{E+I}) of inhibition. The maximum of V in Fig. 2b is for $t = 31msec$. Since $g(t)$ peaks at $t = 25$ msec, the traveling time from location 1 to the soma is about 6 msec, which equals the phase-time-lag of the transfer function $K_{is}(\omega)$ for $\omega = 0$. Inhibition alone is "invisible" (because $E_i = 0$); its effect appears only when *simultaneous* excitation takes place, as expected for a nonlinear interaction.

$$V_s(t) = g_e(t)[E_e - V_e(t)] * K_{es}(t) - (g_i(t)V_i(t)) * K_{is}(t)$$

$$V_e(t) = g_e(t)[E_e - V_e(t)] * K_{ee}(t) - (g_i(t)V_i(t)) * K_{ie}(t)$$

$$V_i(t) = g_e(t)[E_e - V_e(t)] * K_{ei}(t) - (g_i(t)V_i(t)) * K_{ii}(t) \qquad (4)$$

This system of equations was integrated numerically for given inputs g_e and g_i using the K_{ij} functions calculated by our program for the specific cell. Figure 2 shows the somatic potential V_s for various inputs g_e and g_i.

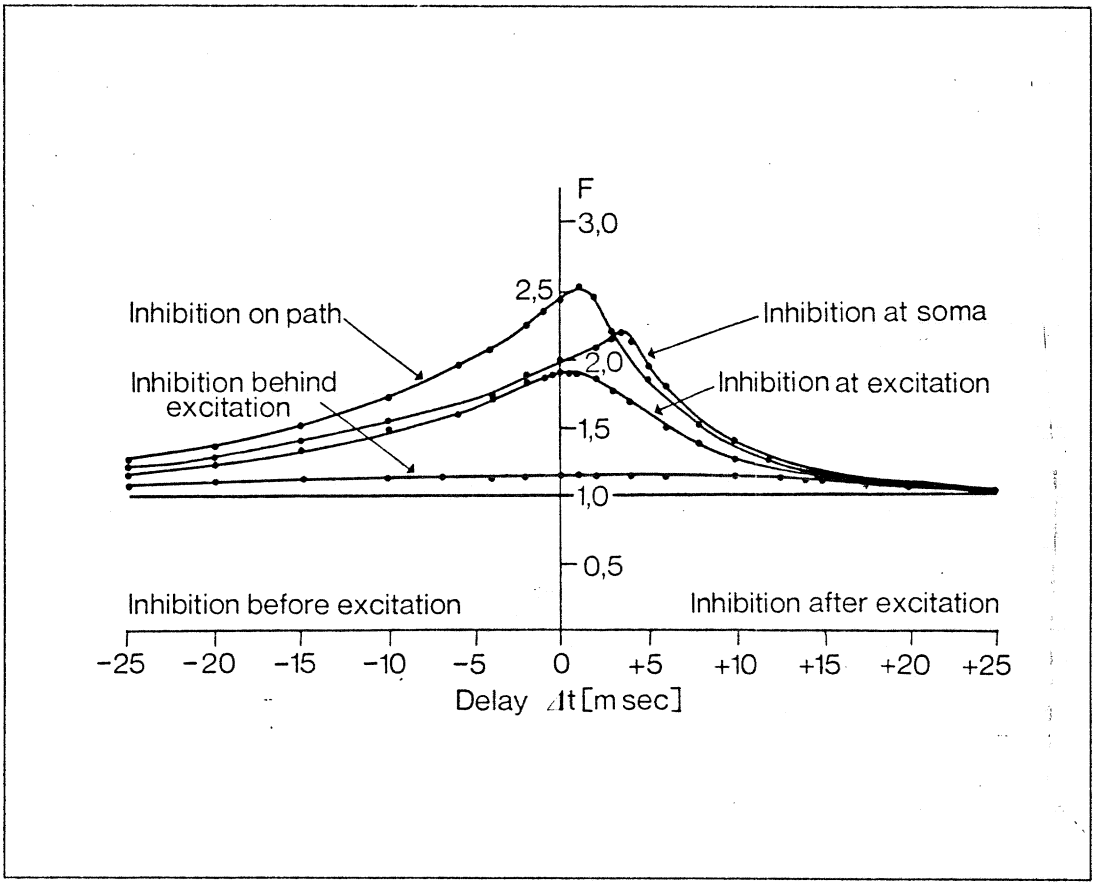

Figure 3. F factor (ratio of the maximum of the somatic depolarisation without inhibition to the somatic depolarisation with inhibition) for various locations of excitation and (shunting) inhibition in the cell of Fig. 1 as a function of relative timing. The conductance inputs are as in Fig. 2, but with various delays between them. Notice that the optimal timing for $e = i$ is not for $\Delta t = 0$ (Segev,pers. comm.; Poggio and Torre, 1981); the deviation is, however, very small. In these calculations, we have assumed $C_m = 2\mu Fcm^{-2}$, $R_i = 70\Omega cm$, $R_m = 2500\Omega cm^2$. The excitation is always at location 1, while inhibition can be behind excitation (7), coincident with excitation, on 'the direct path' (8)or at the soma (S). The basic results hold over a wide range of parameters: in particular R_m can be increased by several order of magnitudes without a significant change in the "direct path" property, which depends critically on branching geometry and effective intracellular resistance.

A simple measure of the effectiveness of shunting inhibition is the ratio (F) between the maximum of somatic depolarization in the absence of inhibition and in the presence of the inhibitory input. Equations (4) can be solved analytically for steady state inputs. In this case, it can be shown, using the properties above that

$$F = \frac{g_e K_{es}}{1 + g_e K_{ee}} \quad \frac{1 + g_e K_{ee} + g_i K_{ii} + g_e g_i K^*}{g_e K_{es} + g_e g_i K^+} \tag{5}$$

with $K^* = K_{ee}K_{ii} - K_{ie}K_{ie}$ and $K^+ = K_{es}K_{ii} - K_{ie}K_{is}$.

(The K_{ij} represent the DC values of the transfer impedances; that is $\tilde{K}_{ij}(0)$).

This formula shows that F can take quite high values, even for g_i significantly smaller than g_e, quite differently from the lumped circuit case (see Koch et al, 1982). Figs. 2 and 3 (for the delta cell)

show that sufficienly large inhibition is highly effective in vetoing excitation also for transient inputs, provided location and timing are optimal. For steady state inputs it is possible to prove rigorously (from eq. 5) that the most effective location for inhibition is always on the direct path from the location of the excitatory synapse to the soma (optimal location on the path depends on the values of g_e and g_i, approaching e for small g_e, g_i and s for large g_e). For $g_i > 5 \cdot 10^{-8}S$, F is quite large, for "on path" inhibition over a wide range of R_m (between $500\Omega cm^2$ and $1M\Omega cm^2$). F increases for increasing R_m but not very much (at most by a factor 3 for R_m increasing 3 orders of magnitude). Over the same R_m range the "on path" effect maintains a good specificity. The situation changes for conductance peak values below $5 \cdot 10^{-8}S$.

Two cases must be then distinguished: (a) R_m is low: then F is between 1 and 2 (foi $R_m = 500\Omega cm^2$, $g_e = 10^{-9}S$ and $g_i = 10^{-8}SF = 1.6$ under optimal conditions). (b) R_m is larger: then the F values are also larger (for $R_m = 20000\Omega cm^2$ and the above conductance values $F = 2.9$) but the "on the path" effect is weak. The effect of inhibition depends in this case mainly on the distance from excitation (especially for small values of g_e); for very large values of R_m (around $1M\Omega$) inhibitory inputs at any location throughout the dendritic tree have very similar effect. Notice that for "large" values of R_m the soma usually becomes the optimal location for inhibition. F values and the "on path" specificity are more sensitive to changes in R_i, increasing with intracellular resistance. The physiological range of R_i is however quite restricted (between 50 and $100\Omega cm$). Thus one can envisage that a neuron can work in two different modes of operation, depending on the strenght of the synaptic inputs. For small conductance inputs their interaction is mainly a function of the distance between the synapses involved, while for larger inputs the interaction is more specific, showing a strong "on path" effect. Fig. 2b shows an example of the strength and specificity of shunting inhibition for the transient inputs shown in Fig. 2a. For these conductance changes inhibition on the direct path is strong whereas inhibition behind excitation or on a side branch a few microns further away is almost completely ineffective. Fig 3 shows how the timing of the excitatory vs. the inhibitory input influences the effectiveness of the interaction. The width of the tuning curves of Fig. 3 reflects the time course of the input conductance changes (shown in Fig. 2) and the cable properties. The optimal delay is essentially due to the propagation time from excitation to the location of inhibition (the effective propagation time for "long" transients is given by the phase-time-lag of $\tilde{K}_{ij}(\omega)|_{\omega=o}$, i.e., by

$$\frac{d}{d\omega}[atan \quad \frac{\mathbf{Im}\tilde{K}_{ij}(\omega)}{\mathbf{Re}\tilde{K}_{ij}(\omega)}]_{\omega=0}$$

(see Koch and Poggio, in preparation). For $t_{peak} = 25msec$, inhibition "on the path" can effectively veto excitation if it occurs within $10msec$ of the onset of the excitatory input. Similar effects can be obtained by a longer lasting inhibition (instead of delayed inhibition). We investigated the effect of changing t_{peak} of the inhibitory input for a fixed delay between excitation and inhibition. Reducing t_{peak} for inhibition below the fixed value for excitation reduces drastically F. Thus, inhibition in order to be effective must last at least as long as excitation, but does not need to last much longer (depending on location).When the locations of excitation and inhibition coincide, maximal effectiveness of inhibition is reached for a t_{peak} as long as the excitatory t_{peak}. Inhibition in the soma needs to last roughly twice as long as excitation, in order to be maximally effective.

Because of the strength and specificity of such nonlinear interactions we wish to propose that

they may perform characteristic information processing operations in (passive) dendritic trees. Since inhibition vetoes effectively more distal excitatory inputs only when it is "on the path" to the soma, a variety of local operations can be performed, exploiting the branching geometry of a dendritic tree with a suitable localization of excitatory and inhibitory inputs. Timing of inputs provides an additional important control variable: inhibition "on the path" can veto in an "and-not" fashion an excitatory input only when it takes place within a well defined temporal window.

Our results hold also for the more unusual case of a conductance decreasing inhibitory input (Dudel and Kuffler, 1960; Gerschenfeld and Paupardin-Tritsch, 1974): in this case, an inhibitory input *facilitates* the excitatory effect implementing an analog approximation of an "and" logical operation instead of the "and-not" discussed in this paper.

Simple operations of the "and not" type may underly, for instance, direction selectivity to motion of certain neurons (Torre and Poggio,1978; Poggio et al., 1981; Koch et al., 1982); mechanisms of the "and" type could be used in other motion sensitive cells. We recently proposed (Poggio et al., 1981; Koch et al., 1982) that a δ-like morphology is the substratum of directional selectivity in the cat retina.

In summary, we have shown that shunting inhibition may *veto* or *facilitate* very effectively and specifically excitatory inputs in a δ-like cell, *if* the associated conductance change is large enough.

REFERENCES

Barrett, J.N., Crill, W.E., "Influence of dendritic location and membrane properties on the effectiveness of synapses on cat motoneurones," *J. Physiol.* **239** (1974), 325-345.

Baylor, D.A., Fettiplace, R., "Synaptic drive and impulse generation in ganglion cells of turtle retina," *J. Physiol.* **288** (1979), 107-127.

Boycott, B.B., Wassle, H., "The morphological types of ganglion cells of the domestic cat's retina," *J. Physiol.* **240** (1974), 397-419.

Butz, E.G., Cowan, J.D., "Transient potentials in dendritic systems of arbitrary geometry," *Biophys. J.* **14** (1974), 661-689.

Dudel, J., Kuffler, S.W., "Excitation at the crayfish neuromuscular junction with decreased membrane conductance," *Nature* **187** (1960), 246-247.

Gerschenfeld, H.M., Paupardin-Tritsch, D., "Ionic mechanisms and receptor properties underlying the responses of mulluscan neurones to 5-hydroxytryptamine," *J. Physiol.* **243** (1974), 427-456.

Koch, C., *Nonlinear information processing in dendritic trees of arbitrary geometries,* PhD Thesis, Tubingen, Germany, 1982.

Koch, C., Poggio, T., Torre, V., "Retinal ganglion cells: A functional interpretation of dendritic morphology," *Phil. Trans. Roy. Soc.* **in press.**

Poggio, T.,Koch, C., Torre, V., "Microelectronics in nerve cells: dendritic morphology and information processing," *M.I.T. A.I. memo No. 650* (October 1981).

Poggio, T., Torre, V., *A new approach to synaptic interaction. In: Lecture Notes in Biomathematics 21. Theoretical Approaches to Complex Systems. Proceedings.*, Springer-Verlag, Berlin/Heidelberg/New York; R. Heim & G. Palm, eds., 1978, 89-115.

Poggio, T., Torre, V., *A theory of synaptic interactions. In: Theoretical approaches in neurobiology,* M.I.T. Press, Eds. W.Reichardt and T.Poggio, 1981.

Redman, S.J., *A quantitative approach to integrative function of dendrites. In: International review of Physiology Neurophysiology II,* Vol. 10, Ed. R. Porter. Baltimore: University Park Press, 1976.

Rinzel, J., Rall, W., "Transient response in a dendritic neuron model for current injected at one branch," *Biophys. J.* **14** (1974), 759-790.

Torre, V., Poggio, T., "A synaptic mechanism possibly underlying directional selectivity to motion," *Proc. R. Soc. Lond B.* **202** (1978), 409-416.

Torre, V., Poggio, T., *An application: a synaptic mechanism possibly underlying motion detection. In: Theoretical approaches in neurobiology,* M.I.T. Press, Eds. W.Reichardt and T.Poggio, 1981.