A network model with pyramidal cells and GABAergic non-FS cells in the cerebral cortex

Kenji Morita & Kazuyuki Aihara

Department of Complexity Science & Engineering, University of Tokyo, Japan

keywords: GABA, non-FS cells, dendritic inhibition, winner-take-all, neural networks

Abstract

Recent experiments revealed two classes of GABAergic interneurons in the cerebral cortex, fast spiking (FS) cells and non-FS cells. There are increasing evidences that these two classes of GABAergic cells are electrophysiologically, anatomically, and functionally distinct. We propose a neural network model of pyramidal cells and non-FS cells by describing dendritic local inhibition, which is the anatomical hallmark of the non-FS cells. Our model is shown to have several distinctive properties, such as highly specific pattern discrimination and convergence to "I don't know" states, which could not be achieved by the conventional competitive neural networks with FS-mediated somatic inhibitions.

1. Introduction

"What is the function of dendritic trees" has long been one of the most frequently asked questions in systems neuroscience [9,12,20,25]. There are a lot of evidences that the dendritic tree geometries coupled with unique synaptic architectures implement specific computations at the single neuron levels. One of the most classical but interesting ideas is the AND-NOT logical or analog gate postulated by Koch, Poggio, and Torre [11], in which the combination of dendritic morphology coupled with specific synaptic circuits conspires to create a rich class of logical or analog operations based on the nonlinear interactions between AMPA receptor-mediated EPSPs and GABA-A receptor-mediated so-called shunting inhibitions on each dendritic branch.

Although "dendritic gating" as above seems to be conceptually useful, there is an important criticism first pointed out by Mel [15] that in order to perform the specific computation, some genetic mechanisms or activity dependent learning rules have to guide individual synapses to individual branches in the dendritic tree to achieve the precise spatial arrangements. In addition, especially in the case of the cerebral cortex, it has long been almost a consensus that while excitatory synapses are mainly found on distal dendritic trees or spines, GABAergic synapses are located mostly at somata or proximal regions of dendrites [10]. This denies the possibilities that location-specific veto operations are implemented on each dendritic branch independently, while other types of dendritic local operations based on expansive nonlinearities mediated by functional

clustering of glutamergic synapses and voltage-gated NMDA receptor-mediated active conductance have been shown to be plausible [14,15].

Recently, however, several new findings about the synaptic locations in the cerebral cortex were reported. There are a wide variety of GABAergic interneurons in the cerebral cortex. Recent experiments using intracellular dual recordings revealed that these neurons are divided into two classes, fast spiking (FS) cells and non-FS cells including (or maybe dominated by) low threshold spiking (LTS) cells, according to their electrophysiological features. Additionally, and strikingly, this physiological grouping largely accords with the anatomical grouping based on the difference in the locations where they make the synapses on the target pyramidal cells: while FS cells tend to make their synapses at the somata or proximal regions of the dendrites, non-FS cells are apt to target the distal sites of the dendrites [2,3,4,26]. Therefore, localized interaction of the excitatory and inhibitory synaptic inputs on each dendritic branch really occurs, rebirthing the classical dendritic gate concepts at least in some simplified versions. Furthermore, in addition to the physiological and anatomical differences, increasing evidences indicate that these two GABAergic systems are functionally different in many situations [2,3,30], raising the question how their functions are different not only at the single neuron levels but also in the whole networks. In this paper, we propose a firing rate-based neural network model that describes location restricted effects of dendritic inhibitions mediated by non-FS cells. We examine the dynamical properties of the model, showing that this rather simple nonlinearity of single neurons can actually endue the whole network with specific computational capability.

2. The model

We propose a neural network model which corresponds to relatively small regions of the cerebral cortex, possibly cortical columns [27], including excitatory pyramidal cells and inhibitory GABAergic interneurons of such types as LTS or other non-FS cells that make synapses onto the distal dendrites of the target pyramidal cells (Fig. 1). We consider four types of connections: 1) excitatory feed-forward connections from input sources such as thalamus, other subcortical regions, or other parts of the cortex to the pyramidal cells, perhaps via excitatory interneurons, 2) excitatory connections from the pyramidal cells' axonal collaterals to the non-FS cell that is activated by the pooled activities of all the pyramidal cells, 3) inhibitory connections from the pooled non-FS cell to each dendritic branch of every pyramidal cell, and 4) excitatory connections from the pyramidal cells' axonal collaterals to each dendritic branch of themselves. As to 1), we assume that all the synapses from the same input source converge to single dendritic branches of individual pyramidal cells, because it has been shown that synaptic input from different input sources is preferentially mapped on to specific regions of the dendritic tree [21]. Connections 2) and 3) constitute the dendritic lateral inhibitions between the pyramidal cells via the pooled non-FS cell,

whereas connections 4) form self-excitations. All the strengths of these connections except for 1) are assumed to be uniform. The firing rate dynamics of n pyramidal cells and a pooled non-FS cell can be described by the threshold linear differential equations as follows (Fig. 1):

$$\frac{dx_j}{dt} = \frac{1}{\tau_p}\left(-x_j + \sum_{i=1}^{m}\left[w_{ji}I_i + \alpha x_j - \beta y\right]^+ \right) \quad \text{for} \quad j = 1,\cdots,n \tag{1}$$

$$\frac{dy}{dt} = \frac{1}{\tau_{nFS}}\left(-y + \gamma\sum_{j=1}^{n} x_j \right) \tag{2}$$

where $[z]^+ = \max\{z,0\}$ denotes rectification, m: the number of the input sources, I_i: the intensity of the i-th component of the input sources (defining the m-dimensional input vector as $\mathbf{I} \equiv (I_1 \cdots I_m)$), x_j: the firing rate of the j-th pyramidal cell, y: the firing rate of the pooled non-FS cell, $w_{ji}(\geq 0)$: the weight of excitation from the i-th input to the j-th pyramidal cell, $\alpha(\geq 0)$: the weight of excitation from every pyramidal cell to each dendritic branch of itself (self-excitation), $\beta(\geq 0)$: the weight of inhibition from the pooled non-FS cell to each dendritic branch of every pyramidal cell, $\gamma(\geq 0)$: the weight of excitation from every pyramidal cell to the pooled non-FS cell, and τ_p and τ_{nFS}: the time constants of the dynamics of the pyramidal cells and the non-FS cell, respectively.

Rectification not after but before summation over the dendritic trees in the equation (1) represents the restricted effects of dendritic inhibition to the same branch they are added to: inhibitions added to one arbor of the dendrites are considered to shunt EPSPs or prevent dendritic spike generation and propagation on the same arbor, but have little effect on EPSPs on the other arbors [13,16,24]. This point is the only difference of our model from conventional lateral inhibition network models [1,5,8,31], which can now be considered as the models of the interaction between pyramidal cells and FS cells that mediate somatic inhibition.

3. Simulation results

We now examine the general dynamical properties of the model for various inputs. To do so, we assume a random feed-forward weight matrix $W = (w_{ji})$, each component of which is a random value taken from the uniform distribution on [0 1] and then normalized so as to satisfy $\sum_{i=1}^{m} w_{ji} = 1$ for $^{\forall} j(=1,\cdots,n)$. In this case, if the input vector $\mathbf{I} = (I_1 \cdots I_m)$ is parallel to one of the feed-forward connections of a certain pyramidal cell, that is, one (e.g. the k-th) of the row vectors of $W = (w_{ji})$, $\mathbf{w}_k = (w_{k1} \cdots w_{km})$, then the total feed-forward synaptic excitation of the very k-th pyramidal cell is expected to be the largest among all the pyramidal cells, because W is a random matrix and then $\mathbf{I}$ should not have any correlation with all the afferents (row vectors of W) except for $\mathbf{w}_k$. In this sense, we refer this input vector $\mathbf{I}$ parallel to $\mathbf{w}_k$ as the input pattern *corresponding to* the k-th pyramidal cell. In these fashions, each pyramidal cell has its own corresponding input pattern in the m-dimensional input space, and the whole network *stores* n input patterns in the feed-forward

connectivity.

We examine the firing rate responses of cells when the input corresponding to a certain (e.g. the 11-th) pyramidal cell with various amount (μ) of random noise on it:

$$\mathbf{I} = \frac{\mathbf{w}_{11} + \mu\xi}{\frac{1}{m}\sum_{i=1}^{m}(w_{11i} + \mu\xi_i)}$$, where $\xi = (\xi_1 \cdots \xi_m)$ represents random noise satisfying $\sum_{i=1}^{m}\xi_i = 1$,

is added (Fig. 2). When noise is absent (Fig. 2 top row: $\mu = 0$) or not so much (Fig. 2 $\mu = 0.25 \sim 0.5$), only the corresponding pyramidal cell, that is the 11-th cell here, becomes highly active while other pyramidal cells' firing rates remain to be quite low values. Thus, in these cases the network can *discriminate* the input pattern that are *stored* in the feed-forward connectivity by the response in which the corresponding pyramidal cell becomes the only winner. These behaviors will dramatically change, however, as the amount of noise increases (Fig. 2 $\mu = 1 \sim 4$). With the intermediate level of noise, the corresponding cell still becomes more active than all the others, but, the more the noise is, the smaller the 11-th cell's steady firing rate becomes. And ultimately, when the input is completely random that is not correlated with any pyramidal cells' afferent connections (Fig. 2 "random"), all the pyramidal cells have little activity and there is no winner. In other words, the network can tell us that presented input does not match any of the stored patterns by keeping the activities of all the pyramidal cells at quite low levels.

The behaviors of this model when the noise is small are similar to those of the conventional lateral inhibition networks [1, 5, 8, 31], which generally act as maximum input selectors. However, cell's responses to heavily noise-distorted or unknown inputs are quite different from the conventional ones: while the conventional lateral inhibition networks always converges to winner-take-all states in which a single neuron or a group of neurons [31] necessarily become active even when a random input is presented, our model could converges to another states, which are characterized by quite low (but nonzero) activities of all the neurons and thus namely "I don't know" states, when the input is an unknown random pattern. Actually, in our model, cell's responses to random inputs are still lower than those to their corresponding inputs even when the intensity of the former are five times as large as the latter (data not shown) . The performance of the model in a input pattern discrimination is summarized in the Fig. 2 (bottom histogram).

Why do these "I don't know" sates exist? It is easy to see that different from the conventional lateral inhibition networks, perfect winner-take-all states in which all cells except for one are completely inactivated are no longer steady states in our model. Intuitively, every pyramidal cell cannot be completely inhibited because inhibition is added not onto the soma but onto each dendritic branch, and thus EPSP on such a branch that receives extremely strong excitation will not be completely

shunted. In this way, there is no complete losers, and this in turn ensures small but nonzero activity of the GABAergic non-FS cell, resulting in realization of "I don't know" states. It is remained to be proved, however, whether these "I don't know" states are indeed asymptotically stable steady states of the dynamical system mathematically or not. This stability problem may be better understood by reducing the dimension of the system to two, potential winners and losers, using the mean-field like approximation and then performing phase plain analyses [17]. Nonetheless, even without satisfying mathematical stability criteria, those states are lasting stably for a long time compared with the time constants of the neural units of the model (equation (1) & (2)), enough to have a biological meaning.

Next, we examine how the network behaves when the superposition of the two input patterns each of which corresponds to one of the two different pyramidal cells, e.g. the 1-st cell and the 2-nd cell (Fig. 3). It is observed when noise is absent or not so much (four trials of $\mu = 0.2$ are shown in the Fig. 3 left column) that initially both corresponding pyramidal cells, the 1-st and the 2-nd (solid lines in the Fig. 3 left column), are co-activated and reach the higher firing rates than others (below the dashed line) for a while, and then either the 1-st or the 2-nd cell becomes to be inactivated whereas the other becomes a final winner. Although the time when either of these two cells shifts to inactivation is varying from trial to trial depending on the weight matrix and the initial conditions, both of these corresponding cells almost always continue to be highly active for sufficiently long times compared with the time constants of the neural units of the model (Fig. 3 left column). Therefore, these networks can distinguish, or *represent* transiently, the superposition of the two input patterns that are stored in their feed-forward connectivity (summarized in the Fig. 3 right column). Similar behaviors are observed with three superposed input patterns (data not shown), and it is expected that these networks could distinguish the superposition of the small number, relative to the number of the pyramidal cells, of the stored patterns.

4. Discussion

We discuss here the possibility that our simplified network model is related to the real neocortical neuronal networks. At first, consider the problem that though our model includes only non-FS type of GABAergic cells, actually there coexist both types, non-FS and FS, of GABAergic cells in the cerebral cortex. It goes without saying that generally models including both types of GABAergic cells should be constructed. Nevertheless, in some cases the network model with only the non-FS cells, as those proposed above, may have direct biological meanings, which are: 1) FS cells and non-FS cells may be included in different circuitries at least in some parts of the neocortex. In the rat visual cortex, axons of non-FS cells have been found to be mainly distributed vertically to upper layers while those of FS cells primarily confined to layer V, suggesting that non-FS cells mainly mediate intracolumnar inhibition, whereas FS cells primarily mediate intralaminar inhibition [29] (see also refs.

of [29]). If so, our model could be thought as a feasible model of the cortical column, 2) FS cells and non-FS cells may be differentially regulated by some neural modulators. It has been found that both acetylcholine [29] and dopamine [6] modulate the FS mediated somatic inhibition and the non-FS mediated dendritic one to the opposite directions, depressing the former but promoting the latter, suggesting that those neurotransmitters switch the two modes of inhibition and that under certain conditions either FS or non-FS plays a dominant role.

Next, consider the problem that though our model includes only GABAergic interneurons, actually there exist more excitatory glutamatergic interneurons than GABAergic ones in the cerebral cortex [10]. In fact, it is possible to say that our model does include some types of excitatory interneurons *implicitly* in the feed-forward excitatory connections and in the description of self-excitation, because those connections can be regarded as reduced representation of the relaying excitatory interneurons. However, it seems to be an important next step to analyze the model including recurrent excitatory connections explicitly.

Third, consider the problem that there exist wealth of direct interactions between GABAergic interneurons, which are not included in our model that assume the pooled non-FS cells representing the population of those cells. In addition to chemical synapses, it was found that FS cells and non-FS cells densely make electrical couplings with only the same cell-type as themselves [7]. Although the biological meaning of these couplings is still elusive, it was proposed that they would be one of the underlying mechanisms of spike synchronization [18]. These cooperative effects of couplings on neuronal spiking activities are, though not necessarily inconsistent with, but beyond the scope of our firing rate-based model, and so more detailed models using spiking neuron models should be constructed.

Dendrite inhibition was originally implemented by Spratling as a discrete-time neural network model [22, 23], in which they have shown that appropriate strengths, of both feed-forward excitatory and dendritic inhibitory connections, for a certain types of pattern recognition could be self-organized by assuming some Hebbian learning rules. Although we do not concern learning and plasticity in this paper, it may be expected that the weights of the feed-forward connections of our model could also be self-organized by similar Hebbian rules as those proposed by Spratling. On the other hand, there are no clear evidences about Hebbian learning at GABAergic synapses, while rather anti-Hebbian plasticity has been reported in some cases [28]. We assumed uniform strengths on GABAergic synapses in our model, which we consider do not violate biological plausibility.

As we have shown, the neural network model of the pyramidal cells and GABAergic non-FS cells including dendritic local inhibitions can implement a certain types of computations different from the conventional competitive neural networks with somatic inhibitions. Fine discrimination of stored patterns achieved by our model might be used in the human or the animal's brain to represent things that have critical meanings for them, such as human faces or animals' body odors. In addition, convergence to "I don't know" states observed in our model may act as one of the network-level adaptation mechanisms to keep the total firing rate at a low level. From computational neuroscience's point of view, it has been proposed that single cortical pyramidal neurons with branched dendrites include two stages of the nonlinear thresholding functions, one on each dendritic branch and the other on somata, and thus themselves could be regarded as two-layer artificial "neural networks" [19]. It seems likely that various types of specific computations emerge from the networks composed of such extremely nonlinear components. Highly specific pattern discrimination and the appearance of "I don't know" states in our dendritic inhibition networks may be one example of such nonlinear computations.

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Figure legends

Figure 1.

Schematic diagrams of the neuronal networks of the pyramidal cells and the GABAergic non-FS cells.

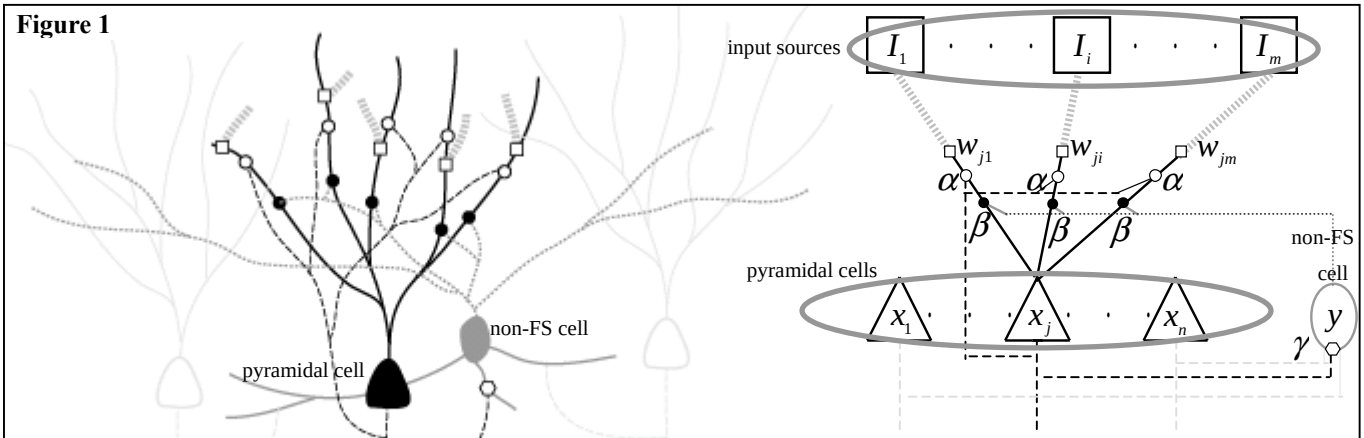
Figure 2.

Responses of the dendritic inhibition network model to the stored patterns with various noise levels ($\mu = 0 \sim 4$) or to a random pattern. (Left column) 10×10 images indicating those input patterns permutated in ascending order at the case of $\mu = 0$ (shadings signify the magnitude) for purpose of comparison. (Middle and right columns) Horizontal axis: index of neurons (20 pyramidal cells and 1 non-FS cell in the right most). Vertical axis: steady state firing rates. Examples of single simulation trials in which the pattern corresponding to *the 11-th* pyramidal cell (*i.e.* parallel to $\mathbf{w}_{11}$) with various amounts (μ) of noise is presented (middle column), and overpaintings of 50 trials (right column). (Bottom histogram) Discrimination abilities (vertical axis, % : fraction of 1000 trials) of the model for a stored pattern with various noise levels (horizontal axis) or for a random pattern (the right most). Black: success ($x_{11} \geq 4$ and $^{\forall} j (\neq 11), x_j < 4$), Dark gray: "I don't know" ($^{\forall} j, x_j < 4$), Light gray: misrecognition (other cases, and only a little fraction). The parameter values and conditions: $m = 100$, $n = 20$, $\alpha = 1/100$, $\beta = 1/150$, $\gamma = 1/20$, and $\tau_p = \tau_{nFS} = 1$; W and $\mathbf{I}$ are reset for each trial; the initial values of x_j are distributed uniformly on [0 0.02] and $y(t = 0) = 0.02$.

Figure 3.

Responses of the dendritic inhibition network model to the superposition of the two stored patterns corresponding to *the 1-st* and *the 2-nd* pyramidal cells. (Left column) Time courses of firing rates of the corresponding two pyramidal cells (solid lines: the 1-st and the 2-nd) and the maximum of the others at each time points (dashed line). Four trials of $\mu = 0.2$ are shown. Horizontal axis: time. Vertical axis: firing rates. (Right column) Recognition abilities (vertical axis, % : fraction of 100 trials) of the model at various time points (horizontal axis) for four noise levels. Black: success in representing both patterns ($x_1, x_2 \geq 4$ and $^{\forall} j (\neq 1,2), x_j < 4$), Dark gray: represent only one of the two ($\max(x_1, x_2) \geq 4, \min(x_1, x_2) < 4$ and $^{\forall} j (\neq 1,2), x_j < 4$), Light gray: "I don't know" ($^{\forall} j, x_j < 4$).

Figure 1



□: excitatory feed-forward synapses on the dendritic trees of the pyramidal cells (w_{ji})
○: self-excitations of the pyramidal cells (α)
●: dendritic inhibition from the non-FS cell to each dendritic branch of the pyramidal cells (β)
⬡: excitation from the pyramidal cells to the pooled non-FS cell (γ)

Figure 2

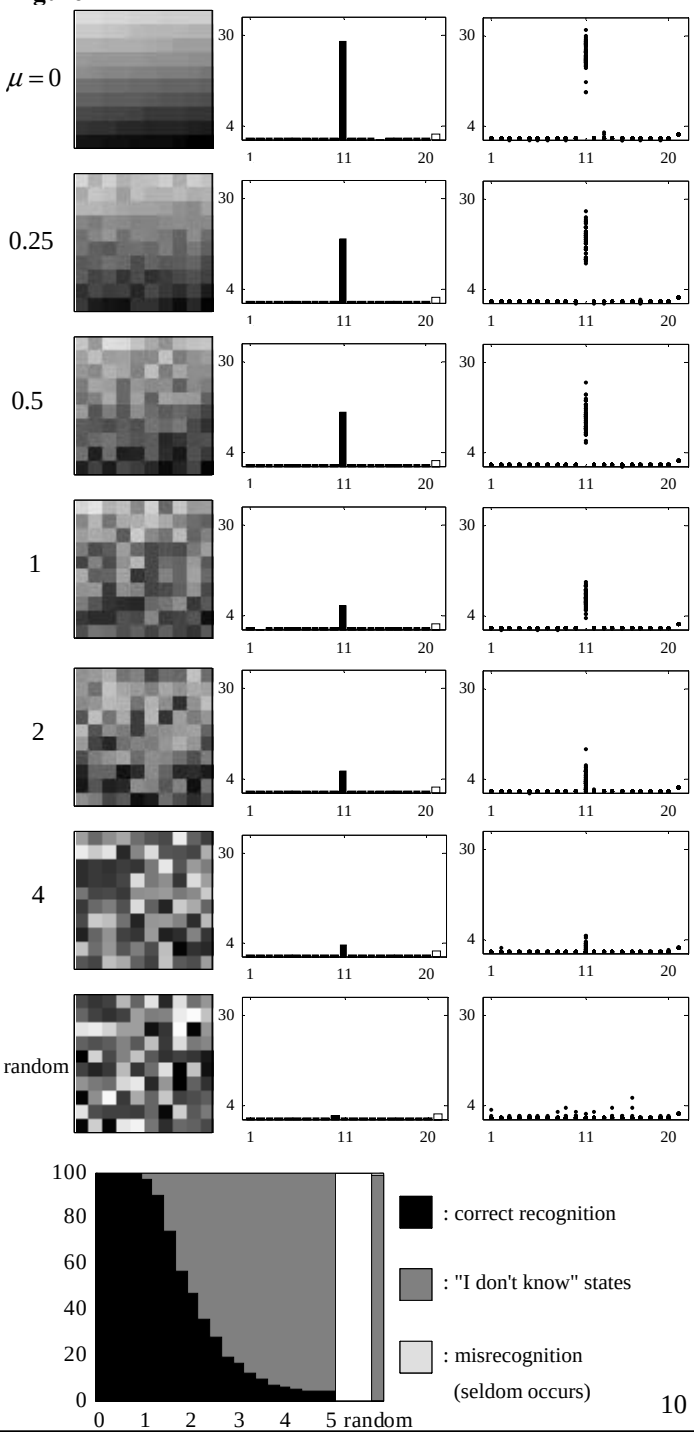


Figure 3