Networks With Lateral Connectivity. I. Dynamic Properties Mediated by the Balance of Intrinsic Excitation and Inhibition

JING XING AND GEORGE L. GERSTEIN
Department of Neuroscience, University of Pennsylvania, Philadelphia, Pennsylvania 19104

SUMMARY AND CONCLUSIONS

1. We studied the rapid dynamic changes of neuron response properties in the somatosensory cortex by the use of computer simulations. The model consists of three feedforward layers of spiking neurons, corresponding to skin, subcortex, and cortex structures. Measurements and analysis of model activity throughout this work are similar to those used in neurophysiological experiments.

2. The effects of various parameters on response properties of model neurons were investigated. The most important parameters were the lateral excitation and inhibition in the simulated cortical network.

3. The balance between excitation and inhibition is a key factor in determining the stability of the network model. There is a large excitation-inhibition (E-I) parameter region within which the model can stably respond to inputs.

4. The input-output relations and receptive field (RF) sizes of simulated neurons are modifiable by the E-I balance. The shapes of RFS are determined by both feedforward projections and the spatial distribution of lateral connections.

5. We simulated changes in temporal and spatial properties of neurons in response to manipulations that mimic bicuculline methiodide or glutamate application to the cortex. Simulation results agreed well with experimental data, suggesting that cortical transmitter levels play an important role in the dynamic responses of the neural net through their effects on E-I balance.

6. With parameters of the model set to an inhibition-dominant scheme, the model was able to reproduce experimentally observed rapid RF expansions that follow cortical lesion or input denervation. Simulation results also suggested that spontaneous inputs to a sensory system can serve as a source of tonic inhibition in the cortex.

7. We conclude that lateral connections could produce and maintain a cortical network having dynamic properties without the need to invoke synaptic plasticity. Individual neuron properties could be modified by changing the balance of cortical layer excitation and inhibition. In a real brain, this could be achieved either by changing levels of cortical transmitter (γ-aminobutyric acid, for example) or by changing tonic background input to the cortical network.

INTRODUCTION

Traditionally, it has been thought that the nervous system is not capable of change beyond a critical period in development. However, a number of recent reports indicate that cortical representation in mammals remains dynamic throughout life (Jenkins et al. 1990; Wall 1988). Neocortical reorganization in adult mammalian brain has been demonstrated by changes in the response properties of individual neurons and by changes in cortical topographical maps. Such changes can be achieved by either physiological or behavioral manipulations. In the somatosensory cortex, reorganization was found after pathological lesions at various levels of the sensory system, from the skin to the cortex (Clark et al. 1988; Jenkins and Merzenich 1987; Kaas et al. 1983; Merzenich et al. 1983a,b, 1984). Behavioral training of a restricted skin region can also induce changes in both receptive fields (RFs) and cortical maps (Jenkins et al. 1990a; Recanzone et al. 1992a,b). All of these are slow changes that take place over many hours, days, or even months; it is likely that the underlying mechanism is some form of neuronal plasticity such as changes in synaptic strength or axonal sprouting.

In addition, fast changes occur immediately after the manipulations. They are observed within several minutes or hours, and are considered to represent a different dynamic cortical process than the slow changes. Immediate RF expansions have been shown in the affected part of the somatosensory cortex after digital denervation (Kelahan and Doetsch 1984; Rasmussen and Turnbull 1983). Within minutes of denervation or the application of a local anesthetic to a small body area in the adult flying fox, Calford and Tweedale (1991) found that the neurons of the primary somatosensory cortex (SI), which originally represented the small body area, showed greatly enlarged RFs on the adjacent body areas. Moreover, the expanded RFs reverted several minutes after the effects of the anesthesia subsided. Similar RF expansion has been reported in the visual cortex, induced by a local lesion in the cat retina (Gilbert and Wiesel 1992) or by an "artificial scotoma" in the background input pattern (Pettet and Gilbert 1992). The rapid onset and immediate reversibility of the induced RF changes in these experiments suggests that some mechanism other than a synaptic growth process is involved.

Changes in neuronal properties have also been observed after disturbances to cortical neurotransmitters. Cumulative evidence has led to the view that cortical inhibition serves to sharpen or focus afferent activity to a more localized cortical population and thereby to enhance spatial acuity (Costanzo and Gardner 1980; Laskin and Spencer 1979; Sillito 1977; Sillito et al. 1985). Blockade of GABAergic transmission (by bicuculline methiodide [BML]) in somatosensory cortex causes expansion of neuronal RFs and changes in the duration, cortical extent, and latency of the evoked responses (Alloway and Burton 1986; Alloway et al. 1989; Batuev et al. 1982, 1989; Dykes et al. 1984; Hicks and Dykes 1983; London et al. 1989). On the other hand,
cortical injections of glutamate lowered the threshold for neuronal activation and led to an ongoing discharge of cortical neurons without enlarging their RFs (Alloway et al. 1989; Dykes et al. 1984). These experiments strongly suggest an intrinsic mechanism that mediates a dynamic cortical network.

Although the underlying mechanisms are as yet unknown, experiments suggest that cortical dynamic reorganizations are at least partly the result of some intracortical process (Jenkins et al. 1987; Merzenich et al. 1984). For instance, experimental manipulations lead to neuronal activity changes only within a certain limited distance from the manipulation site or its projections. Within such a zone there is apparently some integration of neuronal activities that results in the observed changes. The appropriate substrate may be the relatively long-range horizontal connections that have been extensively reported in a number of sensory cortical areas (Doetsch et al. 1988; Gilbert and Wiesel 1983, 1989; Jones 1986; McDonald and Burkhalter 1993; Rockland et al. 1982; Schwark and Jones 1989). Such lateral connections provide the cortex with the means for communication between neurons over relatively long distances, and facilitate neuronal cooperative activity within a cortical domain. Lateral interactions may also modify the responses of individual cortical neurons to afferent stimuli.

In this paper we address the following questions. How do intracortical lateral connections influence cortical responses? What are the most important factors in such influences? Finally and most importantly, can such lateral connections be the substrate for dynamic changes of cortical response properties both in the long and the short time scales?

Experimental approaches have provided some partial answers to these questions. However, current neurophysiological techniques are limited in their determination of integrative and dynamic processes. Computational modeling and simulations can provide important adjuncts to the experimental data by considering conceptual information processing by the brain, and especially by addressing issues involving the collective and dynamic activity of neurons (Sejnowski et al. 1988). This series of papers utilizes computer simulations closely coupled with relevant experimental data to address the questions posed above.

Two frequently encountered problems in the literature of neuronal net simulations are that 1) to reproduce a specific physiological phenomenon, many constraints on the structure, parameters, and inputs of a model are assumed, sometimes without regard to their physiological basis; and 2) the large number of parameters limits the systematic exploration of the parameter space and therefore obscures the relative importance of the chosen constraints. In other words, the drive toward complexity in models may sometimes be counterproductive. Accordingly, we use a different strategy to explore the possible relationship between cortical dynamic changes and lateral connections. Here, the simulations start from a very simple network model that has few constraints. The basic features of this model are 1) spiking neurons, 2) topographic projections between layers, 3) lateral excitatory and inhibitory connections within the simulated cortical network, and 4) activity-dependent modifications of the connection strengths determined by modified Hebbian rules. Rather than subsequently adding further constraints to reproduce a particular physiological behavior, our simulations are focused on what such a basic model can do. We are able to explore thoroughly the various parameter spaces of the model and thereby hopefully gain insights into processes in the physiological network of the brain.

In this paper, with the use of such a model, the influence of lateral interactions, especially the balance between excitation and inhibition, on the properties of simulated cortical neurons is examined without invoking plasticity. We examine the fast dynamic changes of neuronal response properties in the simulations. The effect of plasticity on network behaviors and long-term reorganization is addressed in the two companion papers. Portions of these results have been presented in abstracts (Xing and Gerstein 1992, 1993).

METHODS

Overview of the model

The model (shown in Fig. 1) is a three-layered neural network, corresponding to input, subcortex (thalamus), and cortex. Having a thalamic layer allows us to investigate the effect of subcortical-cortical projections. This is especially important in the two companion reports (Xing and Gerstein 1996a,b), in which plasticity within the cortex and in the subcortical-cortical pathway are examined separately. There are both excitatory and inhibitory lateral connections among neurons of the cortical layer, but feedback between layers is not considered. The total number of neurons and connections used in the model varies with different tests. To simplify the computations, the number of nodes in each of the three layers is the same, typically 32 × 32.

Connections

The connections of a neuron are expressed in terms of its outward synapses. A "neuronal ring" represents all neurons at a given
radius from the central neuron. The connection density in a given ring is defined as the fraction of neurons that are targeted, and varies between 0 (no connection) and 1 (full connections). A density function is defined as the set of connection densities for each surrounding neuronal ring as a function of the radial distance of that ring. The density function of thalamic projections determines the spatial distribution in the cortical layer of the thalamocortical synapses from a simulated thalamic neuron. The density functions of lateral excitation or lateral inhibition determine the spatial distributions of excitatory or inhibitory lateral connections from a simulated cortical neuron. Given a connection density within a particular ring, the individual connections to the neurons within the ring are chosen randomly.

To decrease the number of variables, the synaptic weight functions are kept constant with respect to spatial distance, i.e., the strengths of all the synapses from a neuron are taken as equal. Therefore the spatial distribution of lateral interaction is determined entirely by the density functions. With such an arrangement, instead of using the synaptic strength of an individual connection we may use the total synaptic strength of a neuron. This value reflects the “impact” of a particular neuron on the network. The sum of all outward excitative synaptic strengths of a cortical neuron will be represented by “E,” and the sum of the corresponding inhibitory synaptic strengths will be represented by “I”; these quantities are global constants in any single realization of the network model. For each type of interaction, the average value of individual synaptic strengths is the total E or I strength of a neuron divided by the total number of corresponding connections from it. In the model, the synaptic strength actually assigned to an individual connection is randomly chosen within ±50% of the average value. This arrangement is just a computational simplification.

A common problem in all simulations of interconnected networks is the “edge effect,” i.e., the cutoff of connections along the edges of the network. In this model, the edge effect is avoided by considering each layer of the model as “cylindrical” in two dimensions, i.e., the connections beyond an edge will project to the corresponding locations on the opposite side of the square network.

Structure of the model

INPUT LAYER (SKIN). The input layer consists of arrays of “receptors.” Because the mechanical properties of skin receptors are beyond the scope of this report, we simply represent stimulations to the network by a pattern on the receptors of the “input sheet.” In effect, this simply means injecting stimulus current into the corresponding model neurons of the thalamic layer. The projection from the input sheet to the thalamic layer is 1 → 3 × 3 in register.

THALAMIC LAYER. Neurons in the thalamic layer receive projected excitation from the input layer and in turn pass input stimuli to the cortical layer through divergent projections. In the model, all thalamocortical synapses are excitatory. The density function of thalamocortical projection decays monotonically with radial distance. The spatial range of this projection is a variable that will be tested. Two density functions have been used in this work: 1) a narrow projection in which each thalamic neuron projects to 3 × 3 cortical neurons and 2) a broad projection in which each thalamic neuron projects to 121 randomly chosen neurons within a 15 × 15 neuron area of the cortical network. Unless otherwise specified, the primary thalamocortical density function used in this paper will be the broad projection.

CORTICAL LAYER. There are both excitatory and inhibitory neurons in the array of the simulated cortical network. Each node contains both an “E neuron” and an “I neuron” arranged so that they fire simultaneously. In other words, we assume a 1:1 E-I projection. The connection strength is adjusted so that a spike in the excitatory presynaptic neuron always causes a spike in the associated inhibitory postsynaptic neuron. (This is simply a way to have available both excitatory and inhibitory output from each node for interaction among the nodes. A physiologically more realistic method would be to use inhibitory interneurons; our simplification greatly reduces the computational cost without loss of information.) In a real cortex, excitatory neurons and inhibitory interneurons do not fire at the same time. This inaccuracy in our arrangements is compensated for by randomizing the latency and rise time of inhibitory postsynaptic potentials (IPSPs) in the model.

The model contains extensive lateral connections among cortical neurons. These connections are determined by the I-E spatial density function and E-E spatial density function. (Note: The model does not have explicit E-I connections or I-I connections. Activity of the E and I neurons at any given node is identical, which is equivalent to E-I and I-I connections.) The two spatial density functions that we use are important variables because one of our main purposes is to explore the functional consequences of lateral connections.

Our typical arrangement of connections is adjacent excitation and distant inhibition, as plotted in the spatial density functions of Fig. 2. For the excitatory density function, each cortical layer neuron forms excitatory synapses with 24 others within its three surrounding rings; the connection density first increases and then decreases with distance. Recent experimental results provide evidence for this kind of arrangement (Thomson and Deuchars 1994).

Model neuron

Rather than the commonly used input-output rate function for each neural element, this model utilizes spiking model neurons that produce relatively realistic ongoing input-output dynamics similar to experimental records. The activity of each neuron in the net was simulated using a variation of program PTNRN10 (MacGregor 1987) with both an added absolute refractory period and added spontaneous activity. The neuron is modeled as a point, neglecting the propagation of membrane current along axons and dendrites. Incoming action potentials activate excitatory or inhibi-
tory synapses; these create transient changes in the postsynaptic membrane conductance and the corresponding excitatory postsynaptic potentials (EPSPs) or IPSPs. Changes in the membrane potential depend on total conductance and are smoothed by a time constant. If the membrane potential rises above a threshold, the neuron emits an action potential, followed by a transient increase in the membrane’s potassium conductance. Threshold itself has a time constant, and is briefly raised immediately after the action potential to mimic refractory effects. Action potentials propagate to other neurons and there in turn create excitatory or inhibitory effects. The memory of neurons is determined by the time constants of the postsynaptic conductance changes, the membrane, and the afterdischarge potassium conductance—all short-term effects.

The behavior of a single neuron thus can be described with four state variables that include transmembrane potential ($U$), threshold ($TH$), potassium conductance ($G_k$), and a spike variable ($S$). The evolution of a neuron’s state is described by the following coupled differential equations

$$SCN = [SC \times R_m + (G_e + G_i) \times (UE - U) + G_i \times (UI - U)] \times \frac{G_e + G_i}{G_e + G_i + G_k}$$

$$\frac{dU}{dt} = \frac{-U + [SCN + G_e \times (UK - U)]}{TMEM}$$

$$\frac{dTH}{dt} = \frac{-(TH - TTH) + C \times U}{TTH}$$

$$S = \begin{cases} 0 & \text{if } U < TH \\ 1 & \text{if } U \geq TH \end{cases}$$

$$\frac{dG_k}{dt} = \frac{-G_k + B \times S}{TGK}$$

Here $SCN$ is the potential change produced by the total input current to a neuron. $SC$ is the injected current, $R_m$ is the neuron’s input resistance, which is a constant in the model, taken as $100 \times 10^6 \Omega$.

and $G_e$, $G_i$, and $G_k$ are dimensionless values related to conductances, where $G_i = G_e \times R_m$, $G_e = G_e \times R_m$, and $G_k = G_k \times R_m$.

$G_e$ is the total inhibitory synaptic conductance that the neuron receives from other neurons, $G_i$ is the total received excitatory synaptic conductance, and $G_k$ is the conductance used to mimic the spontaneous activity of the neuron. In the model, $G_i$ and $G_k$ are computed through the temporal and spatial summations of inhibitory and excitatory synaptic strengths, and are therefore time-dependent variables. $G_k$ is dependent on bandwidth and variance, and is created randomly. These parameters were adjusted to produce weak spontaneous activity, typically 1–3 spikes/s.

$UK$ is the equilibrium potential of the potassium conductance, typically assumed to be 10 mV below the resting membrane potential. $UE$ and $UI$ are excitatory and inhibitory synaptic equilibrium potentials, taken as 70 mV and −10 mV relative to the resting membrane potential, respectively. $TMEM$, $TTH$, and $TGK$ are time constants for the decay of $U$, $TH$, and $G_k$. $B$ is the amount by which the potassium conductance increases when the neuron fires an action potential. $B$ and $TGK$ determine the “refractoriness” of the neuron. $C$ and $TTH$ are parameters that describe the increase in the threshold that is used to simulate accommodation of the neuron. $C$ represents the amount of threshold increase associated with a given value of membrane potential, and it varies between 0 and 1.0. Phasic responses can be elicited with large values of $C$. $TTH$ denotes the time constant of this increase in threshold. All variables are updated with a time step of 1 ms. Figure 3 shows an example of the membrane potential from a model neuron in response to a strong stimulus of input current.

Individual EPSPs and IPSPs that result from the change in synaptic conductance exhibit latencies and short rise times, followed by a long period of decay. The time course can be described by the following functions

$$g_e = g_0 \times 1 \times \exp(-UT_e)/T_e$$

$$g_i = g_i0 \times 1 \times \exp(-UT_i)/T_i$$

where $g_e$ and $g_i$ are the excitatory and inhibitory synaptic conductances produced by a spike. The summation of $g_e$ is $G_e$, and the summation of $g_i$ is $G_i$. The variables, $g_0$ and $g_i0$, are the synaptic strengths assigned to individual excitatory and inhibitory connections, and $T_e$ and $T_i$ represent the decay time constants of EPSP and IPSP, respectively. $T_e = 20 \text{ ms}$ and $T_i = 8 \text{ ms}$ are implicitly used in our simulations. Figure 4 shows the time courses of a typical EPSP and IPSP at these parameters. Later simulations show that no significant performance changes were observed for the time constants in the range of 5–50 ms. There is a tradeoff between the total synaptic strengths and the time constants of EPSPs and IPSPs. The latencies of the IPSPs were made 3–10 ms longer than those of EPSPs on the average, to mimic the fact that IPSPs are usually delivered through interneurons. The neuron membrane uses inhibitory input essentially in a multiplicative manner, i.e., mimicking a conductive shunt.

**FIG. 4.** Time courses of excitatory postsynaptic potential (EPSP) and inhibitory postsynaptic potential (IPSP). Time constants of the model EPSP (—) and IPSP (---) are 8 and 20 ms, respectively. The magnitudes of the model EPSP and IPSP are normalized to ±1.0 for this figure.
**TABLE 1. Parameter ranges and units of the model**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Range</th>
<th>Typical Values</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>20–70</td>
<td>30</td>
<td>dimensionless</td>
</tr>
<tr>
<td>TGK</td>
<td>0.5–10.0</td>
<td>5.0</td>
<td>ms</td>
</tr>
<tr>
<td>Te</td>
<td>2–20</td>
<td>8</td>
<td>ms</td>
</tr>
<tr>
<td>Ti</td>
<td>5–50</td>
<td>20</td>
<td>ms</td>
</tr>
<tr>
<td>C</td>
<td>0–1</td>
<td>0.65</td>
<td>dimensionless</td>
</tr>
<tr>
<td>TTH</td>
<td>20–50</td>
<td>30</td>
<td>ms</td>
</tr>
</tbody>
</table>

**Summary of parameters**

**VARIABLE PARAMETERS.** The influence of these parameters on the model performance are to be tested. The initial default values are chosen from the middle of each parameter’s dynamic range. For example, results are robust from $I = 2$ to $I = 20$, and we choose $I = 10$ as the default value of inhibition.

**FIXED PARAMETERS.** Some parameters have minor quantitative effects on the performance of the model, but do not affect the intrinsic characteristics or the significance of the results in these papers. Therefore these parameters were fixed in an appropriate range (shown in Table 1) instead of being used as variables. The fixed parameters include potassium sensitivity ($B$), time constant of the conductance of potassium (TGK), time constant of the excitatory conductance ($T_e$) and inhibitory conductance ($T_i$), rate of accommodation ($C$), and time constant of the action potential threshold (TTH).

**Measurements**

A typical stimulus used to measure the output of the network is a “dot” test stimulus. An example is a pulse current with a duration of 5 ms applied to an array of $3 \times 3$ input receptors. Neurophysiological experiments typically measure the RFs of neurons. In the simulations, the two-dimensional (2-D) RF of a neuron is measured by the following procedure. The number of spikes from a neuron is counted while a dot test stimulus stimulates the best-responding neuron. The RF of a neuron is defined as the input region within which the test stimulus induces 0.7–1 spike in the best-responding neuron. The RF of a neuron is defined as the input region within which the test stimulus induces >0.3 spikes per stimulus. The size of an RF is defined as its area (number of input receptors).

**RESULTS**

We first study the parameter dependence and stability of the model, and then examine the ability of the model to replicate experimental observations of cortical dynamic changes.

**Parameter dependence and stability**

Response properties of simulated cortical neurons were tested across changes in 1) parameters of the input stimuli, 2) parameters of the single neuron model, and 3) parameters of the connections. Of all these, the most important parameters for changing the response properties were lateral excitation and inhibition. Therefore we concentrated on the effects of lateral connections on performance of the model.

**STABILITY OF THE MODEL.** Instability is a common problem in network modeling. In a network with neurons exciting each other, mutual excitation can result in positive feedback, which can cause oscillatory activity and lead to unstable responses. For this reason, the stability of the cortical network in this model was examined first.

By stability, we mean that within some reasonable input operating range there are finite outputs for finite inputs. Thus examples of “unstable” states of our neuronal network model are as follows: 1) neurons in the network fire maximally irrespective of inputs, and 2) neurons in the network do not respond to inputs. Stability in this sense can be evaluated by the cross correlation between input and output signals. (These signals could, for example, be defined as the summed activity to and in the whole net.) A high, narrow peak in such a cross correlogram reflects a very stable response of the system. To describe this more quantitatively, we define a “signal-noise ratio” (SNR) in terms of an input-output cross correlation: $\text{SNR} = (\text{area in the peak region above the average level})/ (\text{area in the peak region below the average level})$. According to this definition, input-output cross correlograms with a prominent peak correspond to large SNRs.

A “population test stimulus” consisting of repeating cycles of activity and quiescence is used to examine the stability of the network. At each time step within the duration of an activity period, a different set of receptors is randomly chosen to be stimulated. For the chosen duration, this provides a uniform but randomly located “rain” of stimulation across the input layer, and thereby allows investigation of the model’s global temporal properties. The output of the model is the population activity, measured as the total number of spikes for all of the neurons in the cortical layer versus time. The SNR is calculated from the cross correlation between these input and output population activities, and provides an estimate of the network stability.

In the examples shown in Fig. 5A, the total simulation time is 1,000 ms. To show cortical responses at different stimulus rates, the frequency of the input pulse is 20 Hz for the first 500 ms and 10 Hz for the second 500 ms (Fig. 5A, top). Three examples of cortical population activities are shown in Fig. 5A at different E-I parameters.

The population response without lateral interactions ($E = 0$ and $I = 0$) consists of regular response peaks phase-locked to the input pulses and some weak spontaneous spikes. The other two examples of cortical population responses were obtained with $I = 10.0$, but with differing levels of excitation. With $E = 1.0$, although the amplitudes of the response peaks are not as regular as those without lateral interactions (where $E = 0$ and $I = 0$), the response peaks are still phase-locked to the input pulses. Random spontaneous activity occurs between the response peaks. When the excitation was increased to $E = 4.0$, shown in Fig. 5A, bottom, the network responses became unstable: the neurons fire according to their own spontaneous synchronization, irrespective of the input stimulus.
The corresponding cross correlograms of input-output activities are shown in Fig. 5B for each of the levels of excitation and inhibition. The SNR in the absence of lateral interaction is 4.5. Weak excitation results in sharp peaks (E = 0 or E = 1); the SNR for E = 1.0 and I = 10.0 is 3.8. Strong excitation reduces the correlation peak; the SNR for E = 4.0 is only 0.32.

To define a stable parameter region of the network, a systematic calculation of SNRs was performed across the E and I parameters, where E varied from 0.0 to 2.0 and I varied from 0.0 to 20.0. Within this E-I parameter region, the SNRs varied from nearly 0 to 4.5, as shown in Fig. 5C. The smooth SNR function is shown digitized into four levels: 0–0.5, 0.5–1.0, 1.0–2.0, and 2.0–4.5. The gray level and size of each square in Fig. 5C are proportional to the digitized value of the SNR at the corresponding E-I value. The largest squares represent the highest SNRs (2.0–4.5). The smallest squares represent the SNRs <0.5; they occur at regions of low inhibition and high excitation, and represent unstable states of the network. A large region of E-I parameters provides the network with relatively high SNRs and therefore with adequate stability.

SNRs were also calculated from the correlation of the input signal and the output spike trains of single neurons, and were significantly lower than the SNRs of population activities. The maximum SNRs are ~1.0. Thus a direct comparison cannot be made between the absolute values of the SNRs in Fig. 5C with experimental measurements on single neurons. Nevertheless, Fig. 5C demonstrates a stable E-I parameter region of the model. In all simulations, the values of E and I were kept within the stable parameter region.

**INPUT-OUTPUT RELATIONSHIP FOR A SINGLE NEURON.** The input-output function of a neuron in the cortical network was measured by the number of spikes per stimulus versus an input current strength of the 3 × 3 dot stimulus. First, the location where the stimulus caused the neuron to respond maximally was determined. Then, with stimuli presented at this location, the number of spikes evoked by each stimulus pulse was determined as a function of the input current. The final input-output function was based on the average of five trials. Similar procedures were followed with several E and I variations.

Figure 6 shows a set of input output functions at different E and I values. Without lateral interactions (i.e., E = 0 and I = 0), the input-output function rises monotonically and saturates at ~1.2 spikes per stimulus. The input current strength of 0.02 nA can evoke ~0.7 spikes per stimulus; this value is used as the typical input strength for the dot test stimulus throughout the simulations. When E = 1.0 and I = 10.0 (the typical E-I values), the rising phase of the input-output function is slower and saturation is only ~0.8 spikes per stimulus. The output for the typical input strength 0.02 nA is ~0.5–0.6 spikes per stimulus.

An increase in the level of inhibition lowers the amplitude of the input-output functions and increases the minimum
adjacent neurons, “scattered” RFs are formed, with “holes”

that remain even when the RF maps are averaged over repeated measurement trials (shown in the middle and top sets of RF maps). Such scattered RFs are more apparent when the inhibition is strong (shown in the top set of RF maps). In contrast, with a more distant distribution of inhibition, response profiles of neurons are Gaussian-like and RFs are topologically continuous, similar to experimental observations (bottom set of RF maps). Thus we used distant inhibition (as shown Fig. 2) in simulations of this series of papers. Recent experimental evidence favors this kind of arrangement (Thomson and Deuchars 1994).

RF sizes change with the balance of E-I. RFs were measured with E varied between 0 and 2.0 and I varied between 0 and 20.0. As expected, RF sizes increase with higher E levels and lower I levels. Figure 8A shows RFs of a typical neuron at several sets of E-I values. With strong inhibition and weak excitation, the RFs are relatively small and localized. When excitation is very strong (E > 2.0), or the excitation is moderate while the inhibition is very low (I < 0.2), the response of the neuron loses its spatial specificity; the neuron fires for all locations of input stimuli and the measured RFs spread to the entire input layer. Except for these two extreme cases, the RFs and the neuron’s responsiveness varied smoothly with E and I.

Statistical results for the changes in RF size of neurons with E-I variations are shown in Fig. 8B. The RFs of the 20 × 20 neurons in the center of the cortical layer were measured with E varied between 0.0 and 2.0 and I varied between 0.7 and 70.0. We define the RF size ratio as the RF size of a neuron at a given E-I value divided by the RF size measured without lateral interactions. Figure 8B illustrates the average RF size ratios for the 20 × 20 neurons at various E-I values.

The E-I values in Fig. 8B cover the main parameter region in which the network has stable responses (except for I = 0.2; see Fig. 5C). Within this region, the average RF size ratios vary from 0.16 (E = 0 and I = 20) to 1.27 (E = 2 and I = 1), an eightfold change. The majority of the ratios are <1.0 (Fig. 8B). In other words, within the E-I parameter region for stable responses, the network does not allow neurons to have their potential RFs fully expressed. A large portion of a neuron’s input projection is suppressed by lateral inhibition. For the typical E-I values used in these simulations (E = 1.0 and I = 10.0), the RF size ratio is 0.28; thus less than one third of the RF area that would have resulted from afferent thalamus-cortex projections is expressed. These neurons have the potential to expand their RFs with appropriate manipulations of the lateral influences.

The above simulation and analysis were also performed with the narrow thalamocortical projection (each thalamic neuron projects to 3 × 3 cortical neurons). Although the absolute values of RF sizes and the mean responsiveness were smaller than the values obtained with the broad projection, similar results were obtained with respect to the E-I balance. In the narrow projection, the spatial range of lateral connections is quite extensive compared with its thalamocortical projection range. Therefore the effect of lateral excitation and inhibition is even more dominant in the determination of the final RF size.

**FIG. 6.** Input output relation of a model neuron in the network. The input-output relation is measured as the averaged maximum spike numbers of a neuron per stimulus against the current strength of that input stimulus. A set of such functions at various E-I values (as indicated in the figure) are illustrated. Note that the scale of the response along the vertical axis changes beyond 2.0.
Inhibition

Correlation density

Excitation

Spatial distance (rings)

**FIG. 7.** Receptive fields (RFs) are affected by the spatial distributions of excitation and inhibition. Two-dimensional (2-D) RF maps of a typical neuron are shown at various combinations of inhibitory and excitatory density functions, as indicated on the left and bottom.

**Simulations of experiments on cortical dynamic changes**

We simulated a number of typical experimental manipulations such as BMI injection or digit denervation. The neurons in the cortical network responded with rapid and dynamic changes.

**EXPERIMENTS WITH MANIPULATIONS OF NEUROTTRANSMITTER.**

In a large body of experiments, researchers have reported immediate RF changes after cortical inhibition was blocked by an injection of BMI, a \(\gamma\)-aminobutyric acid (GABA) antagonist (Alloway et al. 1989; Batuev et al. 1989; Dykes et al. 1984; London et al. 1989). In these experiments, an increase in RF sizes and in the firing levels of neurons was observed. We simulated such experiments by uniformly decreasing the global inhibition in the network. To understand the functional roles of inhibition, two additional simulations were performed for comparison: 1) an increase in excitation and 2) a decrease in the firing threshold of cortical neurons. Both these simulations act as a mimic of glutamate injection; this has been used for comparison with BMI experiments. The parameters chosen for the control conditions include \(I = 10.0, E = 1.0,\) and action potential threshold \((TH0) = 10.0.\) The typical variations of these parameters for the three manipulations are \(I = 1.0\) (decreased inhibition), \(E = 2.0\) (increased excitation), and \(TH0 = 5.0\) (reduced threshold). For each simulation, the spatial and temporal response properties of neurons were determined.

**Responsiveness and spontaneous activity.** With the use of the dot test stimulus, three properties of neurons in the cortical layer were measured: RF size, responsiveness (defined as the total number of spikes evoked during the RF measurement), and spontaneous activity level (defined as the total number of spontaneous spikes within the same time period as the RF measurement). The results presented below are the average of five measurement trials from 15 \(\times\) 15 neurons.

When inhibition is decreased from 10.0 to 1.0, the RF area is enlarged \(~2.7\)-fold. The responsiveness is \(~4\) times stronger than in the control condition, whereas the spontaneous activity remains about the same. These changes are in accord with experiments in which BMI was injected into primary somatosensory cortex (Alloway and Burton 1986; Alloway et al. 1989).

When excitation was increased from \(E = 1.0\) to \(E = 2.0,\) the average RF area was increased by \(~40\)%. A further increase in the level of excitation leads to a larger increase in the RF size, but the overall network response becomes unstable. To make parallel comparisons, because inhibition had been decreased 10-fold (from \(I = 10.0\) to \(I = 1.0\) ), the RF profile was calculated when excitation was increased 10-fold (from \(E = 0.2\) to \(E = 2.0\) ). The RF area is enlarged \(~70\)% for this increase in excitation, a small change compared with that produced by a 10-fold decrease in inhibition. The overall responsiveness increases \(~50\)%.

On the other hand, the peak response in the center of the RF increases dramatically because of the strong mutual excitation among adjacent neurons. The spontaneous activity is essentially unchanged.

A decrease in the spiking threshold of cortical neurons
(\(THO = 5.0\)) caused an increase in firing rate. Both the response to the test stimulus and the spontaneous activity increased by an approximately equal amount. Thus the input region within which evoked responses were significantly above spontaneous activity was approximately constant. This is in accordance with experimental observations (Alloway et al. 1989; Dykes et al. 1984).

The matrix in Fig. 9 illustrates the above descriptions for responsiveness of the neurons (top), RF size (middle), and spontaneous activity (bottom) in conditions of 1) decrease in inhibition (left), 2) increase in excitation (middle), and 3) decrease in neuron firing threshold (right). A decrease in inhibition resulted in a significant RF expansion and an increase in the responsiveness of cortical layer neurons, whereas the spontaneous level was essentially unaffected. An increase in excitation caused a slight RF expansion, and also slightly raised the level of spontaneous activity. Only when excitation was increased to the extent of synchronizing the spontaneous activity (i.e., the unstable states of the network) was there a large increase in spontaneous activity. A decrease in the neuronal firing threshold resulted in an overall increase in neuron excitability; both the responsiveness to the input stimuli and the spontaneous activity decreased, and the RF size did not change appreciably.

Cortical representation of inputs. One proposal for the functional role of cortical inhibition is that it limits the number of cortical neurons activated by a stimulus and confines these to a relatively small region (Dykes et al. 1984). We measured the cortical "point image" of the model with different parameters. We define point image as the area of activated neurons by a small local stimulus presented on the input layer. A 3 × 3 dot stimulus is presented five times at a 100-ms interval to the center of the input layer. For each of the central 20 × 20 neurons in the cortical network, the number of evoked spikes is measured; results are shown in the maps of Fig. 10, A–D. Within each panel, a small square represents a neuron, with the gray level proportional to its response. Figure 10A shows responses under control conditions, with \(E = 1.0\) and \(I = 10.0\). In total, -20 neurons are activated. We then vary parameters: inhibition is decreased to \(I = 1.0\) (Fig. 10B), excitation is increased to \(E = 2.0\) (Fig. 10C), and the neuronal firing threshold is decreased from 10.0 to 5.0 (Fig. 10D).

When inhibition is decreased to 1.0 (Fig. 10B), the num-

---

**Fig. 8.** RFs are affected by the E-I balance. A: 2-D RF maps of a typical neuron at various values of E-I balance. Excitation and inhibition used are indicated at the bottom and left, respectively. B: average RF size ratios at various E-I values as indicated. The ratio is defined as the RF size of a neuron measured at the given E-I parameters divided by the RF size of the same neuron measured without lateral interactions.

**Fig. 9.** Responsive and spontaneous activities with parameter variations. Averaged responses (top), RF sizes (middle), and spontaneous activities (bottom) are demonstrated for 3 parameter manipulations: decreasing inhibition (left), increasing excitation (middle), and decreasing the neuron firing threshold (right).
RAPID CHANGES OF RECEPTIVE FIELDS 193

FIG. 10. Changes in cortical representations with parameter variations. The responses of 20 × 20 neurons to a 3 × 3 dot stimulus are demonstrated. (Note that we are here showing activity of many individual neurons rather than the RF of a single neuron) A: responses at the control condition: E = 1.0, I = 10.0, and action potential threshold (TH0) = 10.0. B: decreasing inhibition to 1.0. C: increasing E to 2.0. D: Decreasing TH0 to 5.0.

The number of activated neurons increases, with ~100 neurons participating in the representation of the 3 × 3 tested receptors. Compared with the control condition, such an abundance of responsive neurons is a very inefficient way of coding. This inefficiency provides support for the functional role of inhibition as a localizer of activity.

With the excitation doubled, the activated area (Fig. 10C) remains approximately the same as in the control condition (17 neurons in this example). However, in contrast to the control condition, the pattern of cortical representation is concentrated to a small set of highly active neurons. Spontaneous firing is increased in the active neurons but not in the neurons surrounding the responsive region. Further examination revealed that the surrounding neurons are under strong inhibition caused by the firing of the neurons in the center of the active zone.

With the decrease of firing threshold, the number of neurons that responded to the test stimulus did not increase (Fig. 10D). However, there was an increase in spontaneous activity of many neurons. Thus the SNR of such a system may be very low.

Temporal response pattern. In experiments with local infusions of BMI, cortical responses last longer, and neurons often fire in bursts (Hicks and Dykes 1983). We examined the temporal response properties in our model by recording the membrane potential and action potentials of stimulated cortical layer neurons (Fig. 11). The protocol consists of a delay of 50 ms, presentation of a 3 × 3 dot stimulus for 20 ms, and continuation of “recording” time until 150 ms (Fig. 11A). The membrane potential of the typical neuron in the control condition (E = 1.0 and I = 10.0) is shown in Fig. 11B. Only one spike is evoked during the 20 ms stimulating period. Figure 11, C–E, shows the membrane potentials of the same neuron after the parameters were varied to I = 1.0, E = 2.0, and TH0 = 5.0. A decrease in inhibition from 10.0 to 1.0 leads to neuronal bursting, followed by a long period of inhibition during which time the membrane potential is, on average, more hyperpolarized than the resting level (Fig. 11C). An increase in excitation caused the neuron to fire more spikes to the test stimulus, as shown in Fig. 11D. When the firing thresholds were decreased to half of the control value, both evoked and spontaneous bursting activity was observed. These results are similar to the experimental observations by Hick and Dykes (1983).

Our simulation results with decreased inhibition and neuron firing threshold are in agreement with the experimental data for both BMI and glutamate injections in the cortex.

FIG. 11. Temporal firing patterns of a neuron and parameter variations. The membrane potentials and spikes of a typical neuron in response to a 3 × 3 dot stimulus presented to the input layer within its RF are demonstrated. The parameter variations are the same as in Fig. 10. A: input stimulus. B: responses in the control condition, E = 1.0, I = 10.0, and TH0 = 10.0. C: decreasing inhibition to 1.0. D: increasing E to 2.0. E: decreasing TH0 to 5.0.
to disturb the balance of lateral excitation and inhibition is to make a local “lesion” in the cortical layer. The simulation is performed in an inhibition-dominant network (\(E = 1.0\) and \(I = 10.0\)) with the initial RFs at only about one thirds of the size they would be without lateral interactions. We inactivated the neurons in the right half of the cortical layer to mimic a cortical lesion. The RFs of intact neurons are measured and compared before and after such a manipulation.

Figure 12, A and B, illustrates four examples of RF maps before and after the simulated lesion, respectively. The dashed line in each map indicates the location in the input layer that corresponds to the lesion boundary in the cortical layer. The RFs of neurons near the boundary expanded severalfold after the lesion (Fig. 12B), frequently into the input region that had previously been mapped to the lesioned part of the cortical layer. This expansion may be viewed as a functional compensation of the cortical network for the lesioned region.

To measure the statistical distribution of the changes, we recorded the RFs of 6 \(\times\) 30 neurons adjacent to the lesioned region. Size changes were calculated using the ratio of the RFs before and after the lesion was made. The histogram of these ratios is plotted in Fig. 13 and shows that the RFs expanded about two- to sixfold with the peak distribution around fourfold. The RF expansion ratio in our simulation depends on various computational choices and details such as the individual neuronal parameters, lateral connectivities, and the measurement used to define the area of an RF. The expansion is particularly dependent on the inhibition to excitation ratio (I:E ratio); the larger the I:E ratio, the larger the observed RF expansion ratio. Thus the magnitudes of the RF expansion ratios presented here should be viewed qualitatively, rather than quantitatively.

Peripheral damage. Immediately after digital amputation, input denervation, or local skin anesthesia, the RFs of neurons in the somatosensory cortex that surround the damaged area increase in size (Calford and Tweedale 1991; Kelahan and Doetsch 1984; Rasmusson and Turnbull 1983). These experiments suggest that there is a tonic input from the skin to primary sensory cortex may operate under the control of an inhibition-dominant scheme, as used in the model.

**DYNAMIC RFs MEDIATED BY LATERAL CONNECTIONS.** In many experiments, researchers have recorded the changes in RF sizes and in cortical representations within several minutes after digital denervation or anesthesia. In these experiments, the RFs of adjacent areas are often enlarged severalfold after the manipulation (Calford and Tweedale 1991; Gilbert and Wiesel 1992; Kelahan and Doetsch 1984; Rasmusson and Turnbull 1983). The relatively fast changes and the immediate reversibility of the RF changes suggest that a mechanism other than synaptic plasticity may be involved. One plausible mechanism involves the cortical excitation and inhibition that is mediated via long-range horizontal connections; these allow the integration of the activities of individual neurons in the cortex. Disturbances in the firing activity of a restricted cortical region would cause disruption in the local balance of cortical excitation and inhibition. This would in turn affect the RF properties of nearby cortical neurons. The local decrease of inhibition to a neuron can cause an enlargement of the RFs and increased responsiveness. We tested this hypothesis by simulating both cortical lesion and input denervation.

**Lesion of a local region in the cortical layer.** A direct way to disturb the balance of lateral excitation and inhibition is to make a local “lesion” in the cortical layer. The simulation is performed in an inhibition-dominant network (\(E = 1.0\) and \(I = 10.0\)) with the initial RFs at only about one thirds of the size they would be without lateral interactions. We inactivated the neurons in the right half of the cortical layer to mimic a cortical lesion. The RFs of intact neurons are measured and compared before and after such a manipulation.

Figure 12, A and B, illustrates four examples of RF maps before and after the simulated lesion, respectively. The dashed line in each map indicates the location in the input layer that corresponds to the lesion boundary in the cortical layer. The RFs of neurons near the boundary expanded severalfold after the lesion (Fig. 12B), frequently into the input region that had previously been mapped to the lesioned part of the cortical layer. This expansion may be viewed as a functional compensation of the cortical network for the lesioned region.

To measure the statistical distribution of the changes, we recorded the RFs of 6 \(\times\) 30 neurons adjacent to the lesioned region. Size changes were calculated using the ratio of the RFs before and after the lesion was made. The histogram of these ratios is plotted in Fig. 13 and shows that the RFs expanded about two- to sixfold with the peak distribution around fourfold. The RF expansion ratio in our simulation depends on various computational choices and details such as the individual neuronal parameters, lateral connectivities, and the measurement used to define the area of an RF. The expansion is particularly dependent on the inhibition to excitation ratio (I:E ratio); the larger the I:E ratio, the larger the observed RF expansion ratio. Thus the magnitudes of the RF expansion ratios presented here should be viewed qualitatively, rather than quantitatively.

Peripheral damage. Immediately after digital amputation, input denervation, or local skin anesthesia, the RFs of neurons in the somatosensory cortex that surround the damaged area increase in size (Calford and Tweedale 1991; Kelahan and Doetsch 1984; Rasmusson and Turnbull 1983). These experiments suggest that there is a tonic input from the skin...
to the cortex, because otherwise the cortex could not differentiate between denervation and a lack of stimulation to a normal skin. With appropriate conditions, such widespread inputs would produce background inhibition in the cortex; RFs of neurons would then expand when such an inhibition is locally removed. Tonic inhibition requires that some neurons be active continuously to maintain inhibitory synaptic bombardment of cortical neurons.

There are several possible ways to provide such tonic inhibition: for example, 1) tonic input may excite some brain system that, in turn, sends “in-register” inhibition to the somatosensory cortex; or 2) with our present model, under the assumption that the network functions in an inhibition-dominant scheme, activities in cortical neurons evoked by a tonic input can spread inhibition over a large cortical region through their lateral connections. So far there has not been any solid experimental evidence for the first mechanism. We explored the case in which background inhibition in the network is provided by a tonic input and lateral connections.

To mimic a tonic input, at each time step a randomly located 4% of all input receptors were chosen to be weakly stimulated. Without lateral interactions in the network, such a tonic input would cause cortical neurons to fire 4–5 spikes/s. With the typical E-I parameters (E = 1.0 and I = 10.0), neurons fired ~1–3 spikes/s. RFs of neurons were measured in the presence of the tonic input. A 12 × 32 array of receptors was then inactivated to mimic skin damage and the RFs were remeasured with the tonic input applied only to the “intact” skin.

Changes in RFs after “skin” damage are summarized as follows. Neurons with RFs outside but adjacent to the damage boundary showed an asymmetric increase in RF size after the damage, moving the RF centers away from the damaged skin. Before the skin damage, these neurons receive inhibition from the neurons that will be deafferented. After the damage, the activity of deafferented neurons decreases because of the loss of tonic input from the inactivated skin, so that they exert less lateral inhibition on the neurons to which they project. This in turn reveals portions of RFs that had been suppressed by inhibition. The asymmetric expansion is also partly due to the lack of stimulus responses from the damaged area. Some neurons whose RFs had been within but close to the boundary of the damaged area show new RFs in the undamaged area near the boundary, but with smaller size than before skin inactivation.

The RF expansion is limited by the spatial range of lateral connections and thalamocortical projections. With an inactivated area of 12 × 32 receptors, some neurons whose RFs had been in the center of the damaged area became completely unresponsive, because even the fringes of their potential RF had been deafferented. Thus, in contrast to the RF expansion after cortical layer lesion, damage in the input layer resulted in both increased and decreased RF sizes, depending on the location of the recording sites in the cortical layer.

The above RF changes are similar to results observed immediately after local skin anesthesia or amputation (Calford and Tweedale 1991; Kelahan and Doetsch 1984; Rasmussen and Turnbull 1983). Thus the model can reproduce the RF expansion caused by input damage under the assumption that the cortical network works in a inhibition-dominant lateral interaction scheme. In the model, RF changes were caused by interaction between the release from lateral inhibition and the divergence of thalamocortical projections.

**DISCUSSION**

**Dynamic RFs**

Various experiments have shown that RFs of cortical neurons are capable of changing dynamically throughout life. Some of these changes can occur very rapidly, within several minutes after manipulations. It is also known that on removal of GABA-mediated inhibition in the somatosensory cortex, neuronal responses to stimuli increase and RFs expand (Alloway et al. 1989; Costanzo and Gardner 1980; Dykes et al. 1984; Laskin and Spencer 1979). These observations suggest that somatosensory cortical neurons are normally under a tonic inhibitory influence and that its modulation may account for rapid RF dynamics.

Rapid RF expansions have been observed in both peripheral and central lesion experiments. Immediately after local skin anesthesia or amputation (Calford and Tweedale 1991; Gilbert and Wiesel 1992; Kelahan and Doetsch 1984; Rasmussen and Turnbull 1983), many RFs adjacent to the damaged area expand to several times their original sizes. Moreover, unlike the long-term reorganizations in somatosensory cortex (Clark et al. 1988; Jenkins et al. 1987; Kaas 1983; Merzenich et al. 1983a,b, 1984), the rapid RF expansions are instantaneously reversible on the removal of the (temporary) manipulations.

Similar dynamic changes in RFs also occur in visual cortex. Gilbert and Wiesel (1997) reported that RFs of neurons in striate cortex expanded several minutes after a local retina lesion. Pettet and Gilbert (1992) found that RF expansion could be induced by an artificial scotoma, i.e., conditioning the visual field with a pattern of moving bars while masking out an area covering the original RF of the recorded cell. The observation of similar patterns of dynamic RFs in the two sensory systems suggests that these dynamic changes may share mechanisms based on lateral connectivity and interactions that result in local release of cortical inhibition. Appropriate long-range horizontal connections within primary cortex have been well documented (Doetsch et al. 1988; Gilbert and Wiesel 1983, 1989; Jones et al. 1986; McDonald and Burkhalter 1993; Rockland et al. 1987; Schwark and Jones 1989).

In this report we set up a simple neural network model mimicking the main information pathway of the somatosensory system: input, thalamus, and somatosensory cortex. Excitatory and inhibitory lateral connections were built between model neurons of the cortical layer. We then explored the ability of the model to produce dynamic RFs. It turned out that such a simple model is sufficient to account for all current observations of dynamic RF changes in somatosensory cortex. We have previously demonstrated that a similar model could replicate the RF expansions induced by an artificial scotoma in visual cortex (Xing and Gerstein 1994).

The key element for such results is operation of the network in an inhibition-dominant mode. We found that the
linear. Such properties have indeed been demonstrated on the population response of some motoneurons (Rosenblueth et al. 1986). The output firing rate of such a model neuron allows considerable simplification of the computational processes. Thus, when the network is made to be strongly inhibitory, the network has the ability to expand neural RFs consequent on local reduction of inhibition.

Simulations demonstrate that changes in inhibition could modify RFs to a larger extent than could changes in excitation. Several reasons can account for this difference. 1) Inhibitory connections spread further than excitatory ones so that they can modulate neuron’s responses in a larger spatial region. 2) The decrease of inhibition releases the suppressed thalamic projection region, whereas the increase of excitation mainly increases the responsiveness of neurons. 3) Increase of excitation is largely limited by the network’s instability. In the model, inhibition has a much broader numerical parameter range than has excitation: inhibition can be as high as I = 20 without suppressing network activity, whereas E > 2.0 triggers instability. When inhibition is very weak (I = 0.2, for example), the network becomes unstable at I = 0.5 (Fig. 5C). Thus a network with minimal inhibitory connections would not allow even the range of E changes that we have tested in making RF modifications. To extend the modulation ability of excitation, we would need to design a network that remains stable with strong excitation.

Most results in this report were run with parameters of E = 1.0 and I = 10.0. This parameter choice does not mean that a 10-fold inhibition over excitation is required for the results, because the neurons are used differently by the model (i.e., shunting vs. subtracting). The default values were chosen from the middle of each parameter’s dynamic range; for inhibition the range is very large. Results are robust from I = 2 to I = 20, with some quantitative differences. The effective I-E parameters in a real cortex are unknown. Experimental observations such as unmasking of RFs after BMI injection or input loss suggest that the cortex is under strong tonic inhibition (Calford and Tweedale 1991; Dykes et al. 1984), but no direct numerical information is available. Thus we can only make qualitative comparison between our results and the available experimental data.

Model of single neuron

Much of the extant network modeling literature makes use of neurons described entirely by a sigmoidal relationship between input and output firing rates. Such model neurons allow considerable simplification of the computational process. (Freeman 1968; Reilly and Cooper 1990; Rumelhart et al. 1986). The output firing rate of such a model neuron is determined by a nonlinear function of the sum of all the input rates received instantaneously. The input-output function exhibits saturation for large and small inputs, and has a region for intermediate values that is close to linear. Such properties have indeed been demonstrated on the population response of some motoneurons (Rosenblueth et al. 1949) and in the steady firing of single spinal motoneurons (Kernell 1965a,b). Other types of neuron models appearing in the literature involve many compartments and much physiological and anatomic detail (Koch 1984; Koch et al. 1983; Traub 1982; Traub and Miles 1992; and many others). Such models allow analysis of the signal propagation and interactions within the dendritic tree. However, the computational complexity generally makes such detailed neurons impractical for studies of networks and network properties.

In the present work we try to strike a balance between the above extremes by using a spiking model neuron (modified from MacGregor 1987) with membrane properties, ionic currents, and postsynaptic conductances, but only a single compartment. Incoming spikes evoke a transient change in membrane conductance that possibly causes spikes during the time that the membrane potential is above threshold. Although calcium effects and activities in the dendritic tree and the axons are not included, this model is a better descriptor of physiological neurons than the sigmoid firing rate function because it does represent at least some of the crucial mechanisms. It offers sufficient computational simplicity that quite large networks can be investigated.

Bedenbaugh (1993) recently demonstrated that a sigmoid neuron has more information loss in the input-output transformation than a MacGregor neuron. This implies that the performance of a neuronal network simulated with sigmoid neurons may be different than a similar network with spiking neurons. In addition, spiking model neurons allow spike train analysis (like cross correlation, etc.) and a comparison with the corresponding analysis of electrophysiological data. In our opinion, using spiking neurons is an appropriate modeling approach to simulations intended to explore possible physiological mechanisms on the network level.

On the other hand, even a spiking model neuron, like the one we use in this work, may be too simple to simulate a given physiological problem. The allowed level of simplicity in the model neuron depends on the specific physiological issue to be investigated. More elaborate model neurons may make the simulation results more reliable and allow more insight into the underlying physiological mechanisms. However, an elaborate and detailed model may be impractical in terms of computation time with a network comprising thousands of neurons. Furthermore, the use of a complicated neuron in a network model results in a large number of parameters whose complex interactions may obscure identification of the most important mechanisms.

In this series of papers, our main interest is focused on the changes of cortical representations and RF properties of individual neurons that are mediated through lateral connections. Thus a spiking neuronal model and lateral excitatory and inhibitory connections are essential minimums. To keep the computational requirements at a level corresponding to our resources, we chose to simulate a network of thousands of relatively simple spiking neurons.

The communications among model neurons are carried out through EPSPs and IPSPs. There is little experimental evidence and much discussion about whether IPSPs act on the membrane in a shunting or a subtracting mode (Douglas et al. 1988; Koch and Poggio 1992). Nelken (1988) demon-
strated analytically that subtracting and multiplicative (shunting) inhibition are identical over a large range of parameters. For our model, we expect that the use of subtracting rather than shunting inhibition, with appropriate adjustment of parameters, would produce qualitatively similar results. However, the numerical parameter range in which inhibition produces dynamic changes would become narrower. It is also likely that the numerical parameter values for network stability would change and their range would become narrower.

**Structure of the model**

The structure of the model is rather simple, with divergent feedforward projections and spread of lateral connections mimicking the basic anatomy of a real sensory nervous system. The model can be viewed as a minimal scaffold for a primary sensory system; additional detail and mechanisms could easily be incorporated.

The projections from thalamic layer to the cortical layer are made exclusively excitatory, as reported experimentally by Penny et al. (1983) and Spreatifico et al. (1983). Feedback from the cortical layer to the lower layers has not been considered in the model. The reasons are as follows. 1) In these papers we are most interested in the changes caused through lateral interactions. 2) The anatomic details and function of descending projections are not clear. The big feedback loop probably has no direct effect on lateral interactions. Note, however, that many of the global aspects of descending control over the lower layers could be variously accomplished by feedbacks within the cortex delivered through lateral connections.

A common problem in building a neural network is how to deal with the edge effects. The usual solutions are truncation, reflection, or cylindrical continuation of the edge connections. It is also possible to create a much larger network than needed, and to study only the central portion that is far from the edges: this is computationally expensive. There is little information about connectivity near anatomic or functional boundaries in real brains. However, the absolute numbers of elements and the edge to middle ratios are far different than in practical models, so that even if the information existed, detailed mimicry might not be useful. Investigation of the edge problem is beyond the scope of this paper; we are mostly interested in the effects of lateral connectivity. We chose to use cylindrical continuation, i.e., a rectangular network that is cylindrical in two dimensions, so that the upper and lower edges are joined, as are the left and right edges. As far as possible, we have limited our observations to the interior regions of the net.

The key connectivity variables that we tested are the spatial distribution rules. Otherwise no special constraints are applied to the “hardware” connections of the model. Every individual connection is chosen randomly; thus individual connections can be removed without influencing overall performance. The model is robust; all parameters show a broad region within which performance is barely affected. The stability analysis demonstrates in particular that there is a large E-I parameter range within which the network responds stably to input. This, then, is a general model that can be used to investigate fundamental and general issues in a simulated primary sensory system.

**Significance of lateral interactions in the cortical network**

When lateral connections exist, the afferent input is no longer the only source determining cortical response properties. These now depend also on inputs through lateral excitation and inhibition. Such modification can change RF sizes, overall responsiveness, and the temporal firing patterns of individual neurons.

At first glance, it seems that a decrease in neuron firing thresholds, an increase in excitation, or a decrease in inhibition would all have a similar effect of increasing cortical response. Our simulations indicate that, although they all can increase the responsiveness of neurons, there are numerous differences in both the spatial and temporal response patterns. A decrease in the firing thresholds of neurons leads to response changes similar to those obtained with glutamate injected into the cortex. An increase in excitation leads to an increase in spontaneous activity of individual neurons together with its synchronization. This substantially increases the noise relative to neuronal responses, and makes the network unstable. Finally, a decrease in inhibition results in changes of neuronal responses similar to those observed experimentally when BMI is used to block inhibition in the cortex. Varying inhibition gives a large dynamic range of RF changes that could not be achieved through adjustment of excitation or thresholds alone. A decrease in inhibition can result in considerable RF expansion while still maintaining the stability of the network.

Even for fixed parameters, response properties of a cortical neuron are not fixed. With the lateral connections, each cortical neuron does not encode a focal input area independently. Instead, lateral connections result in global information integration. In the model a neuron’s response can be modified by activities outside its classic RF. A lesion to a restricted cortical region and denervation of focal input skin leads to RF changes of neurons that are not directly affected by the manipulations. These results suggest that lateral connections can maintain a dynamic cortex without invoking synaptic plasticity.

Simulations throughout this report demonstrate the importance of cortical lateral excitation and inhibition for cooperative effects. Excitation enables neurons to work together and share information, and it is the substrate of neuronal synchronizations (Fig. 5A). Excitation also causes instability of the network and thus has practical upper bounds. On the other hand, inhibition can largely control the instability induced by excitation, while providing the network with dynamic features. The balance between excitation and inhibition decides the states of the cortex as it actively responds to inputs.

In summary, with a simple neural network, we have demonstrated that response properties of individual elements can be greatly affected by lateral connections. From a comparison of simulation results with experimental data, we suggest the following. 1) Cortical lateral connections can maintain a dynamic cortex without the involvement of synaptic plasticity. 2) Cortical networks usually function in the inhibition-
dominant state and are amenable to modulation through a change in the balance between cortical excitation and inhibition. 3) Changes in the excitation-inhibition balance could be achieved either by a change in cortical transmitter levels or by a change in the tonic background input to the cortex.

We thank Prof. Kenneth Miller for helpful discussions and comments on the manuscript, Dr. Amy Harkins for reading and helping edit an earlier version of this manuscript, Z. Pan for computer assistance, and C. Taylor for administrative help.

This work was supported by National Institutes of Health Grants MH-46748 and DC-01749.

Present address and address for reprint requests. J. Xing, Div. of Biology, 216–76, Caltech, Pasadena, CA 91125.

Received 18 July 1994; accepted in final form 23 August 1995.

REFERENCES


RECANZINE, G. H., MERZENICH, M. M., JENKINS, W. M., GRAISKI, K. A., and DISNE, H. R. Topographic reorganization of the hand representation...


