Multi-Scale Modeling of the Primary Visual Cortex
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Abstract
Using a large-scale computational model, we identify a possible operating state of the primary visual cortex (V1) which results from a rich interplay of a hierarchy of spatial and temporal scales. This state is characterized by (a) high total conductance, (b) strong inhibition, (c) large synaptic fluctuations, and (d) an important role of NMDA conductance in the orientation-specific, long-range interactions. Our model reproduces — and offers possible mechanisms underlying — cortical phenomena including orientation tuning and large-scale spatiotemporal activity patterns in V1.

Keywords: Brain modeling, Large-scale systems.

Introduction
The extraordinary power of the brain is apparent from the vast complexity of its behaviors and the ease with which it performs them. These behaviors are accomplished by a complex system of excitatory and inhibitory neurons of different types, operating with large intrinsic fluctuations, through extensive feedback, and often with competition between many scales in space and time. The behavior of such large-scale neuronal systems is simply not understood; however, today a combination of modern experiments, large-scale scientific computation, and mathematical modeling and analysis, begins to offer us a glimpse into the inner workings of some parts of this fascinatingly complex system.

One of the best-studied parts of the brain is the primary visual cortex (V1). Along the “visual pathway,” it is in V1 where neuronal responses are first simultaneously selective to elementary features of the visual scene, including the orientation of lines and edges, their location, and sharpness. In other words, it is in V1 where the first simple, but nontrivial, neuronal computations take place, eventually giving rise to the visual percept as their results are relayed to the higher visual areas and beyond.

A classical property of V1 is orientation tuning, the selective response of a single neuron to some orientations of a simple visual pattern (e.g., an edge, bar, or grating), but not to other orientations, which was first revealed in microelectrode measurements of spiking activity [1, 2]. Neuronal orientation preference in V1 is organized into mm-scale “orientation hypercolumns” [3] of orientation preference laid out in regular patterns with “spokes” which emanate from “pinwheel centers.”
In contrast, spatial phase preference appears not to have a well-organized distribution across V1 [4].

Recent advances in optical imaging with voltage sensitive dyes have revealed new dynamic information encoded as spatiotemporal patterns of cortical activity beyond that which can be obtained from traditional experimental methods. Two of its striking recent examples are the observed patterns of spontaneous cortical activity [5, 6] and the cortical dynamics corresponding to the Hikosaka line-motion illusion [7, 8]. Such spatiotemporal activity presents an array of intriguing possibilities of functional significance for sensory information processing [9].

Our modeling of neuronal response properties in V1 has revealed a possible distinctive dynamical state or “operating state” of V1, from which it responds to changes in visual stimulation. In this paper, we unify the results obtained from our large-scale, physiologically realistic, yet minimal computational V1 network models [10–12] and identify a single cortical operating state, namely, an intermittent de-suppressed state with fluctuation-controlled criticality. This state dynamically controls various aspects of important model V1 responses. In particular, within this single operating state, our network dynamics have successfully reproduced combined results of real-time optical imaging on spatiotemporal cortical activity patterns [5–7] and of single unit recordings revealing detailed firing-rate information from individual neurons relevant to orientation tuning [13–18]. We have also proposed possible network and synaptic mechanisms underlying these cortical phenomena.

Methods

Our model neuronal networks are composed of single-compartment, conductance-based, integrate-and-fire, point neurons, of which ~75% are excitatory and ~25% inhibitory [10–12]. Incoming spikes from background noise to V1 are modeled as independent Poisson spike trains to each cell. The neurons within V1 are also driven by external stimuli from V1’s primary input layer — the lateral geniculate nucleus (LGN), which is responsible for the organization of both orientation preference and spatial phase preference within V1. The orientation preference is laid out in pinwheel patterns and the preferred spatial phase varies randomly from neuron to neuron.

Every model V1 neuron has local isotropic and non-specific connections sparsely projecting to other nearby V1 neurons. The excitatory and inhibitory connections are mediated by AMPA and GABA\(\alpha\) type receptors, respectively, with respective conductance decay time scales of ~3 ms and ~8 ms [19]. Local monosynaptic inhibition and excitation have length-scales shorter than that of a single orientation hypercolumn ~500 \(\mu\)m. Long-range (~1500 \(\mu\)m) connections terminate at both fast AMPA and slow NMDA (~80 – 200 ms) receptors of both excitatory and inhibitory neurons. These connections are excitatory and
orientation-specific; i.e., only connecting neurons with similar orientation preference [20].

Our models include simple and complex cells, distinguished by the amount of LGN drive they receive, with the simple cells receiving more drive. Our model reproduces the classical behavior of their spatial summation properties: simple cells responses are linear, and complex cell responses are nonlinear [12].

Our model neurons (with simulations containing up to \( \sim 10^6 \) neurons) are uniformly distributed over a cortical area (modeled up to 25 mm\(^2\)). Simple and complex cells are distributed randomly in space. At the cortical scales examined in our model, retinotopic effects can be neglected. Our networks are effective or “lumped” models of V1 since we do not include the detailed laminar structure of V1 in our modeling.

**Fluctuation-controlled criticality**

Our extensive simulations have revealed an operating state of our model cortex, namely, a state near a “fluctuation-controlled criticality” [12]. We first illustrate it for a highly idealized, statistically-uniformly, sparsely connected network model. In this model, one half of the neurons — “simple cells” — receive feedforward drive in the form of uniform Poisson spike trains with identical rates and spike strengths, while the other half — “complex cells” — only receive strong intracortical excitation. The inhibitory cells provide strong intracortical inhibition to other cells in the network.

![Figure 1: Bifurcation diagram near the “fluctuation-controlled criticality” in an idealized network.](https://www.pnas.org)
can be controlled by connectivity sparsity). As we vary $N$ — and thus the variance of synaptic conductances — the gain curve exhibits a transition to bistability and hysteresis. At the critical point where bistability first occurs, the gain in the response curve is the most rapid. In addition to network sparseness, this criticality can also be controlled by the NMDA/AMPA ratio in excitatory conductances. We operate our model V1 networks just below this critical point in order to obtain steep gain on the one hand, and sufficiently high intrinsic fluctuations on the other so that the network avoids the un-physiological, bistability-induced instability.

**Orientation tuning via a local model**

To investigate neuronal orientation tuning in V1, we model a 1 mm$^2$ local patch, incorporating only short-range cortico-cortical connections and covering 4 orientation hypercolumns that contain $\sim 10^4$ model neurons [12]. We constrain it to function in an operating state just below the “fluctuation-controlled criticality.” This state is characterized by high total conductance with strong cortico-cortical inhibition, as well as large synaptic conductance and membrane potential fluctuations achieved through sparsity in network connectivity. The average neuronal membrane potentials in the network remain well below the spiking threshold, thus the spiking is caused by strong, sparsity-induced synaptic fluctuations in the network. The model network gives rise to a continuum of simple and complex cells, as characterized by the modulation ratio $F_1/F_0$ of the cell’s cycle-averaged firing rate, which is the ratio between its first Fourier component and its mean at preferred stimulus orientation. For the population of our V1 neurons, this ratio has a bimodal distribution, while the corresponding $F_1/F_0$ of the intracellular voltages has a unimodal distribution, in agreement with experimental results of [13, 14].

![Figure 2: (a) Circular variance (CV) histograms for excitatory simple (top) and complex (bottom) cells. (b) CV at medium versus low contrasts. (c) Dependence of CV on the distance from a pinwheel center: EC and ES are excitatory complex and simple cells, respectively. [Reproduced with permission from ref. 14, www.pnas.org, (Copyright 2007, National Academy of Sciences, USA).]](image-url)
A quantitative measure of orientation selectivity for drifting grating stimuli is given by the circular variance (CV) [12]. It lies between 0 and 1, and is near 0 for well-tuned and near 1 for poorly-tuned neurons. Figure 2a shows the CV distributions of the simple and complex excitatory cells in our model. Both types of cells are well-tuned, their distributions are broad, and the simple cells appear to be moderately better tuned than the complex cells. Figure 2b demonstrates the approximate contrast invariance of orientation selectivity of our model neurons. Figure 2c shows that orientation selectivity for the firing rates is almost independent of the neuron’s location within the orientation column. The neuronal conductances in our model are tuned more broadly in cells near the pinwheel centers than in iso-orientation domains. All these results are in good agreement with experimental observations in [15–18]. As pointed out in [12], sparsity-induced “near-criticality” plays a crucial role in producing physiologically realistic orientation tuning dynamics of our V1 model.

**Spatiotemporal activity: spontaneous patterns and line-motion illusion**

**Spontaneous patterns of cortical activity:** Experiments on anaesthetized cats, described in [5, 6], show that spontaneous cortical activity of single V1 neurons forms intriguing coherent patterns, persisting over ~ 80 ms on the spatial scales of several millimeters, appearing in regions of similar orientation preference over many orientation hypercolumns. To investigate the network mechanisms underlying these patterns, we incorporated both isotropic and lateral long-range cortico-cortical connections — the latter being orientation-specific and containing both fast AMPA and slow NMDA components — in our large scale (~ 10^6 neurons) network model of V1, and examined their dynamical consequences [10].

To quantify our numerical observations, we follow [5, 6] and consider the “preferred cortical state of a neuron,” defined as the average of the voltage snapshots taken over the network at the firing times of this neuron while the network is driven by a strong stimulus at this neuron’s preferred orientation. In addition, for the same neuron, we consider the “spike-triggered spontaneous activity pattern,” which is the analogous voltage snapshot average taken in the network without an external stimulus.

Our study reveals the mechanism underlying the spontaneous cortical activity patterns, which is characterized by an “intermittent de-suppressed (IDS) state”. This IDS operating state is an intermittent cycle: after the decay of cortical inhibition, neurons in an iso-orientation domain become correlated in subthreshold activity, so a spontaneous firing of a single excitatory neuron will recruit many other neurons to fire within a few milliseconds. This recruitment
causes de-suppression in the network and rapidly spreads to neurons in other iso-orientation domains of like preference via the long-range connections by significantly elevating the highly correlated NMDA conductances and voltages in these domains within ~ 1 mm. As a result, the induced spatial patterns of the voltage closely resemble the orientation preference map and the “preferred cortical state.” The excitatory recruitment events trigger strong inhibition mediated by local connections, which suppresses any further recruitment. The pattern then slowly drifts or decays on the NMDA conductance decay scale, which is ~ 80 ms, and the inhibition decays with it, hence, giving rise to a possible initiation of another cycle of this kind. These cycles persist intermittently through the evolution of the model V1 dynamics. The NMDA component present in the long-range corticocortical connections is crucial for ensuring the correct spatiotemporal scales of the activity patterns.

Figure 3: (a) Orientation hypercolumns, with preferred neuronal orientation denoted by the color. Small white dots: pinwheel centers. Black/white annulus inner/outer radius: length-scale of local inhibitory/excitatory couplings. Large ellipse: extent of long-range connections. Rhombuses: orientation domains coupled by the long-range connections to the neurons in the orientation domain in the middle of the ellipse. (b,c) Two instantaneous spontaneous activity patterns. The two ovals in (b) represent regions in which membrane potentials can be highly correlated in time. [Reproduced with permission from ref. 12, www.pnas.org, (Copyright 2007, National Academy of Sciences, USA).]

In Fig. 3a, we display the neuronal orientation preference as conferred on the V1 neurons by their afferent LGN input to which we compare two instantaneous patterns of spontaneous cortical activity within our IDS operating state (Fig. 3b,c). In Fig. 3b, the regions of high activity cover iso-orientation domains belonging to predominantly one preferred angle, while those in Fig. 3c belong to two angles, and are thus largely separate, with an occasional small penetration into each-other's territory. Spatially-separated iso-orientation regions tend to become activated simultaneously and persist for ~ 80 ms before switching to neighboring orientations, in agreement with experimental observation [5, 6].
At the IDS operating state, our model cortex reproduces the experimental observation [5, 6] that the measures of the preferred cortical state and the spike-triggered spontaneous activity pattern strongly resemble one another, as seen in Fig. 4a,b. Both of them have a strong correlation with the neuronal orientation preference map from Fig. 3a.

To measure the predominant time scale of the patterns, we compute the “similarity index” $\rho$, defined as the instantaneous spatial correlation between a neuron’s “preferred cortical state” and the membrane potential of the neurons in the network. Its time evolution is presented in Fig. 4c, and its time trace at $\theta = -60$ deg in Fig. 4d. Both indicate the typical pattern duration to be $\sim 80$ ms, which is also visible from the temporal auto-correlation functions shown in Fig. 4e,f. The network operates in a state of high total conductance with strong inhibition. The membrane potential $V$, the effective reversal potential $V_S$, and the NMDA conductances are all highly correlated, as can be seen from Fig. 4g,h,i. The voltages largely stay well below the firing threshold. A near synchronization of neuronal membrane potentials within $\sim 1$ mm (see Fig. 4i) occurs even when the neurons are not spiking, and is caused by the common synaptic inputs from long-
range connections. These dynamical properties of the membrane potential evolution in our network are consistent with experiment observations [5,6]

Importantly, the IDS state not only captures the spontaneous dynamics, but also generates physiologically observed spatiotemporal responses under external stimuli. We comment that other operating states (such as the state of marginal mode [21]) cannot produce spontaneous cortical activity patterns with correct spatial and temporal scales as observed experimentally. In particular, spontaneous cortical activity arising in a marginal state often produces an overly excitatory dynamics, leading to run-away instability, if an external stimulation is applied.

**Line-motion illusion:** The Hikosaka line-motion illusion stimulus consists of a small stationary square flashed on a display for ~ 50 ms, followed by an adjacent stationary bar [8], creating the illusion that the bar continuously grows out of the square. Optical imaging experiments using voltage sensitive dye reveal that this stimulus creates an activity pattern in V1 that closely resembles the pattern created by a small moving square [7]. This close resemblance is likely linked to the pre-attentive perception of illusory motion.

![Figure 5: Cortical activity corresponding to the (a) flashed and (d) moving square, and (h) Hikosaka stimuli. (b,e,i) Signal measured in the experiments. [Reproduced with permission from ref. 7, (Copyright 2004, Macmillan Publishers Ltd.).] (c,f,j) Effective reversal potentials in our model. (g,k) NMDA conductances in our model. [Reproduced with permission from ref. 13, www.pnas.org, (Copyright 2007, National Academy of Sciences, USA).]
We simulated the V1 activity patterns associated with this illusion using our model cortex operating in the IDS state [11]. We calibrated the strength of our model LGN by comparing the V1 activity of our model cortex and the experimental signal obtained for a flashed square, as displayed in Fig. 5a,b,c. In Fig. 5d–k, we next present the cortical activity patterns evoked by the moving square and the Hikosaka stimulus. The spatiotemporal profiles of the effective reversal potential are in good agreement with the experimental signal. In the IDS state, the NMDA conductance is strongly correlated with the membrane potential in our model, as seen in Fig. 5 f,g and j,k. The moving square produces a rightward growing area of activity that fills out its path (Fig 5e,f,g). The Hikosaka stimulus (square followed by a bar) produces a rightward growing area of activity, which starts growing near the area of activity evoked by the square (Fig 5i,j,k). The dynamics of the two activity patterns — both in the model and real V1 — are remarkably similar, and this similarity may be associated with the illusory motion perception.

Our computations reveal the network mechanism underlying the spatiotemporal activity associated with the line-motion illusion. The LGN input modulation due to the square causes recruitment in the immediate cortical area corresponding to the square. The neuronal spiking due to this recruitment causes the increase of the NMDA conductance in neurons that can be reached from the recruited area by the long-range connections in the IDS state. This increase persists for about ~80 ms after the initial LGN input modulation has subsided. Due to the correlation between the membrane potentials and NMDA conductances in the IDS state, the membrane potentials of these neurons are also elevated, but stay below the firing threshold because long-range connections are not strong enough to cause spiking by themselves. When the LGN input modulation due to the bar arrives, spiking initiates in this already “primed” cortical area near the trace of the square, due to the already elevated activity there. This firing sends additional activity, via the long-range NMDA connections, into the region affected by the bar, which causes a wave of activity growing along the V1 area corresponding to the bar away from the V1 area corresponding to the square.

The crucial ingredients of the underlying network mechanism are the spatiotemporal input profile sculpted by the model LGN, the facilitative effect of the long-range NMDA cortico-cortical conductances that is induced by the (square) cue, and the strong correlation between the neuronal NMDA conductances and membrane potentials which exist at the IDS operating state.

Discussion
Through modeling V1 dynamics as revealed by intracellular and extracellular measurements of orientation tuning dynamics [13–18] and optical imaging of large-scale spatiotemporal cortical patterns using voltage sensitive dyes [5–7],
our study suggests a possible operating state of V1 characterized by high total conductance with strong inhibition, large synaptic fluctuations, and the important role played by the NMDA conductance in long-range, orientation-specific interactions [10–12]. All of these ingredients appear essential for the stable operation of the model cortex and its ability to quantitatively and qualitatively reproduce a host of dynamical phenomena exhibited by the real cortex. The network mechanisms as revealed in the IDS state with fluctuation-controlled criticality in our model V1 dynamics, in turn, may offer suggestions for the physiological underpinnings of the neuronal dynamics in the real V1.

References


