Visual Cortex: Neurons and Local Circuits

Definition

This essay describes the neuronal elements and the basic circuits they form in the primary visual cortex. The primary visual cortex is a clearly defined area of the neocortex that receives input from the retina relayed by the visual thalamus and contains a complete representation of visual space. It has served as the key example for studies of the circuits and functions of neocortex.

Characteristics

The Structure of Visual Cortex

The visual cortex is one of numerous areas of the neocortex that contribute to high-level perceptual, motor, and cognitive functions. There are about 10^{11} neurons in the Central Nervous System (CNS), of which 10^{10} comprise the neocortex. Over 50% of the non-human primate neocortex is involved in visual processing, compared to about 11% for somatosensory, 8% for motor, and 3% for auditory processing. The visual processing takes place in many different areas of neocortex and they are connected together in a hierarchy. The primary visual cortex, which receives the earliest visual input, comprises less than 10% of the cortex (10^8 neurons in primates, and $10^{(6-7)}$ neurons in rat and cat). The primary visual cortex, also called visual area 1 (V1), striate cortex, or area 17, is the best-studied cortical area and so has been the primary source of knowledge of cortical neurons and circuits. As with the rest of the neocortex, the visual cortex is composed of six distinct layers. Its overall thickness is about 1.5 mm, which is about the average thickness of the neocortex across all mammals despite the wide range of brain size across species. The density of synapses (~10^8 synapses/mm^3) is also remarkably constant across species. On the other hand, the density of neurons varies with cortical region, and histological layer. Sensory cortical areas, such as the visual cortex, have the densest neuronal packing (100,000 neurons/mm^3 in cat visual cortex, for example). On average, neurons receive the same number of synapses as they give, which is about 5,000 synapses. The axons that interlink cortical neurons in their local circuits extend only a few millimeters, but they are highly branched. If joined together, the nerve fibers contained within one cubic millimeter of neocortex would form a 4-km long thread. This is a vivid indication of the extreme degree of connectivity amongst the local cortical neurons.

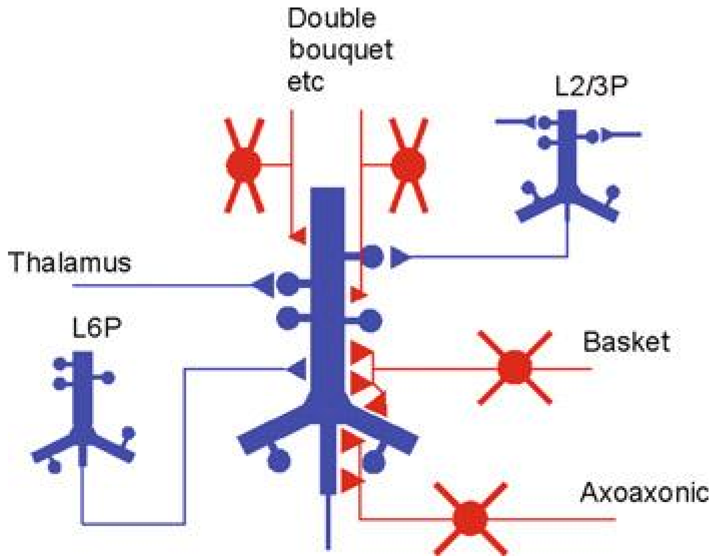
Based on regional histological differences of the cortical layers, the primate neocortex can be divided into about 100 different areas, some of which correspond to functionally distinct areas. The cell densities in these various areas may differ significantly from the averages referred to above, with primary visual cortex. All regions of cortex are composed of the same basic types of neurons, which are found in approximately the same proportions throughout the neocortex.

Synaptic Types

As in many other regions of the brain, the neocortex has two basic functional types of Synapses, excitatory and inhibitory. These functional types correlate with distinct morphological types: asymmetric and symmetric. There is a very useful correlation between the morphology of the synapses, and their function. The asymmetric synapses excite their postsynaptic targets, while the symmetric synapses inhibit their targets. The two types of synapse are named for the presence of electron dense specializations on their postsynaptic membrane, but their neurotransmitter-containing vesicles also have distinctive morphologies. The most obvious distinction is that the electron dense structures lining the pre- and postsynaptic membranes are of equal thickness for inhibitory synapses ("symmetric" synapses), but for excitatory synapses the thicknesses are "asymmetric," being much thicker on the postsynaptic side than the presynaptic. Symmetric synapses also usually have pleomorphic synaptic vesicles, while for asymmetric synapses the vesicles are spherical.

Neuronal Types

There are no universally agreed criteria for classifying cortical neurons, but like synapses they come in two basic types, with many subdivisions (Fig. 1).



Visual Cortex: Neurons and Local Circuits. Figure 1 Schematic of excitatory and inhibitory cortical neurons and their synaptic targets. In the center is a pyramidal cell (blue) with typical club-like spines, which form excitatory synapses with thalamic axons arising from the dorsal lateral geniculate nucleus (dLGN) and other pyramidal cells of layers 2/3 (L2/3P). The layer 6 pyramidal cells (L6P) form excitatory synapses. The pyramidal cell shown to be inhibited by axo-axonic or "chandelier" cells, by basket cells and by double-bouquets cells, each of which forms synapses on different parts of the pyramidal cell, including the initial segment of the pyramidal cell's axon.

These two classes have physiological correlates: the spiny neurons of neocortex are excitatory, while the smooth neurons are inhibitory. The "spiny" cells are so-named, because their dendrites bear thousand of club-like protrusions called " Spine", which are a few microns in length. The smooth neurons are so-named, because they lack dendritic spines. Different types of spiny neurons are classified according to their shape of their dendritic tree and the layer in which their cell body is located, while the smooth neurons are classified, not on the basis of dendritic morphology, but on the basis of their axonal morphology. Spiny neurons have about 10^3-10^4 spines per neuron. Spines are the major location where synapses are formed and each spine receives only one excitatory synapse. In addition to the excitatory synapse, about 8% of spines receive also an inhibitory synapse. Why some cells have spines and others do not, is not known. The role of the spine itself remains mysterious. One possibility is that spines offer some electrical advantage in controlling the effect of the spine synapse on the input to the post-synaptic neuron. Another possibility is that spines provide a local chemical environment that is isolated from the trunk dendrite and able to support specific metabolically mediated long-term changes in synaptic efficacy. Yet another is that the spines provide a motile "leash" that enables the postsynaptic neuron to select actively amongst the possible presynaptic input synapses in the vicinity of the spine.

Spiny Neurons

Spiny neurons can be broadly subdivided into two groups: the spiny stellate cells, named for their radially symmetrical dendrites that give them a star-like appearance, and the pyramidal cells, which are characterized by one apical dendrite, which is much thicker than the basal dendrites (4-8 μm diameter, compared to 1-1.5 μm for the basal dendrites) and extends upward to the surface of the cortex. In the primary sensory areas such as the primary visual cortex, spiny stellate cells are the main cell type in layer 4, which is the major target layer of input from the thalamus. The axons of spiny stellate cells project horizontally within layer 4 and upward into the more superficial layers. Only rarely do they project out of their own cortical area. However, in the remaining layers the spiny neurons are represented exclusively by the pyramidal cells, which comprise 70-80% of all cortical neurons.

Pyramidal cells each have about 8 basal dendrites, dispersed radially about the soma and one apical dendrite, which gives rise to oblique branch dendrites close to the soma. Although the apical dendrite is a very prominent feature, it contributes only about 10% of the total dendritic length of the pyramidal cell. The overall length of basal dendrites, measured from soma to their tips, is 150-200 μm. The length of the apical dendrite depends on the cortical depth of the soma. Some layer 5 (L5) pyramidal cells have apical dendrites of over 1.0 mm. The pyramidal cells found in the superficial layers of cortex (layers 2 and 3) have apical dendrites that ramify in the top of layer 2 and in layer 1. The local arborization of their axon is either in the superficial layers, or in layer 5 and 6.

In general the axons of the deep pyramidal cells arborize in the superficial layers or in the deep layers, only rarely in both. Many have axons that project out of the cortical area. The pyramidal cells of layer 5 can also be divided into two classes on the basis of the morphology of their dendrites. One class has thick apical dendrites that branch in top layer 2 and layer 1, and the others have thin apical dendrites that end in the superficial layers without further branching. Layer 5 is the only layer of visual cortex that projects to nuclei involved in motor control. A major target of the layer 5 cells is the superior colliculus, which is part of the system that drives saccadic eye movements. The apical dendrites of L6 pyramidal neurons ramify in layer 4, and the single thin apical trunk ends in the superficial layers. Their axons mainly in layer 4, but unusually, the majority of synapses made by layer 6 pyramidal cells are with dendritic shafts of other spiny neurons, not with their spines. Many layer 6 pyramidal cells also project back to the dorsal Lateral Geniculate Nucleus (dLGN).

Spiny neurons make most of their synapses onto the spines and shafts of other spiny cells. 85% of the contacts are onto spines, and 14% onto shafts. Less than 50% of the postsynaptic shafts are GABA-ergic. 1% of the synapses are made with the cell bodies of GABA-ergic neurons. Overall, 80-90% of pyramidal cell synapses are made onto spiny cells, which are usually other pyramidal cells, and the remainder are made with smooth cells. Each pyramidal neuron usually forms only 1-5 synapses with a single target cell.

Smooth Neurons

The smooth neurons comprise between 15-20% of cortical neurons. They are called "smooth" merely to indicate that they have very few, if any, spines. The smooth neurons have varicose, multipolar dendrites and are rather irregular in appearance. Smooth cells contain GABA and they make symmetrical synapses with their targets. Not all the symmetrical synapses of the cortex are made by synaptic boutons that contain GABA. Immunocytochemical studies have shown that some symmetrical synapses are formed by boutons that contain Acetylcholine, Noradrenalin, dopamine, Serotonin, or neuroactive peptides. However, the vast majority (99%) of symmetrical synapses are formed by GABA-ergic synaptic boutons. The symmetrical synapses account for 16% of all synapses in the primary visual cortex.

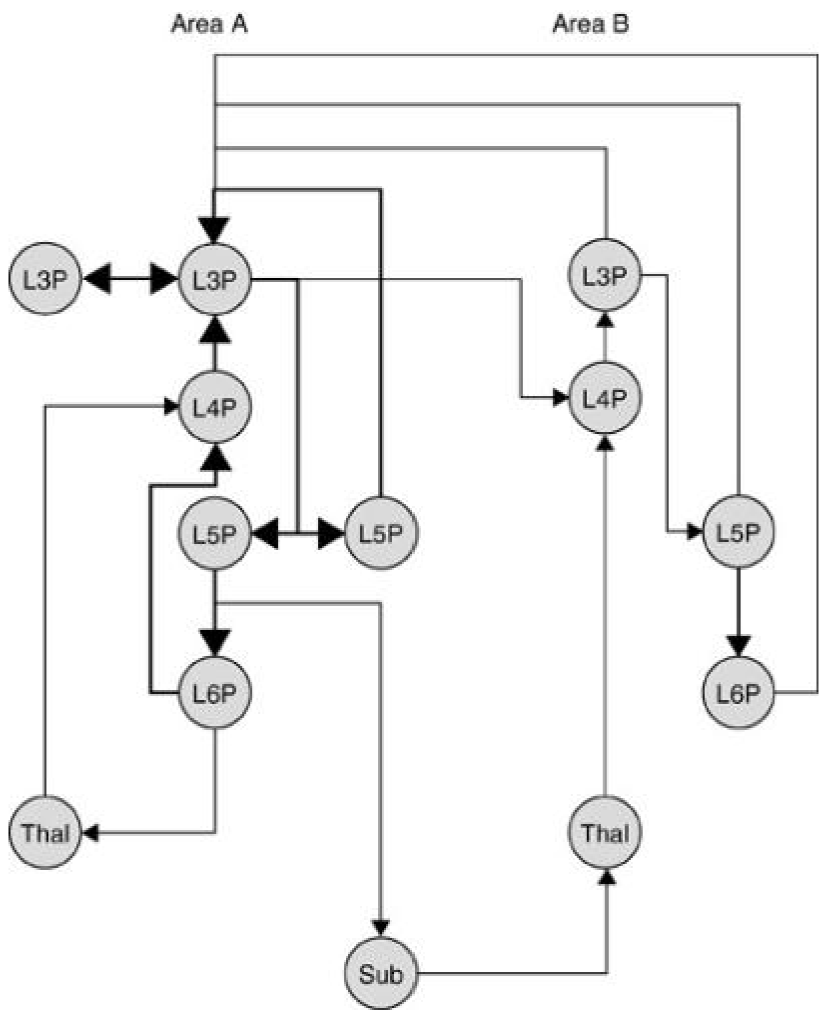
Although smooth neurons only constitute a minority of cortical neurons, they seem to have more variety in their morphological appearance. The total number of different varieties is not certain, but each layer seems to possess its characteristic types. Layer 1, which is sparsely populated with neurons, contains only GABA-ergic neurons, which include the large horizontal Cajal-Retzius cell, which contain the protein "reelin," which is important for the control of neuronal migration. Many other types are found in all the other layers and include basket cells, chandelier cells (or "axo-axonic" cells), double-bouquet cells, neurogliaform cells and Martinotti cells. The exact proportions and connectivity of each cell type is not known. Each GABA-ergic neuron contains one of three different Ca^{2+}-binding proteins. The basket cells and chandelier cells contain a Ca^{2+}-binding protein called parvalbumin, while the double-bouquet cells contain calretinin, or calbindin. The parvalbumin-containing neurons form synapses on the proximal portions of their target neurons (cell body, axon initial segment, and proximal dendrites), while the calbindin- and calretinin-containing neurons form synapses on the distal parts of the dendritic tree of their targets. Experimentally, the basket cells are encountered most frequently, so most is known about them. Their axons ramify within the layer of its cell body. The superficial and deep basket cell axons may extend 1-1.5 mm, but the clutch cell axonal arborization is restricted to only about 0.3-0.5 mm. Each basket cell contacts about 300 target cells, making roughly ten synapses with each target. Each pyramidal cell receives input from about 10-30 basket cells.

We suspect that the different smooth cell types and the different distributions of synapses on their target neurons reflect different functions, but this has not yet been established. It is possible, for example, that different types of smooth cells effect either local, or inter-areal operations; or that some mediate different dynamics of inhibition. One celebrated case that begs a linkage between connectivity and function is that of the chandelier (axo-axonic) cell. These cells are located mainly in superficial layers and their axons terminate exclusively on the initial segment of pyramidal cells, mainly in the superficial layers. The initial segment is a thickening at the beginning of the axon that is thought to be the locus of action potential initiation, and is an attractive site for possible inhibitory control. However, the action of such inhibition is unknown.

Inputs to Visual Cortex

Subcortical Inputs

The local circuits in visual cortex receive their input from the dorsal lateral geniculate nucleus (dLGN) of the thalamus, which is the major nucleus for processing retinal information before passing it on to the primary visual cortex. In primates there are about 10^6 neurons in the dLGN that project to the 10^8-10^9 cells of V1. The input ratio of 1:1,000 gives some indication of the active role that the cortical circuitry must play in the interpretation of the input data. Layer 4 is the principal target layer of the dLGN input (Fig. 2), but all other layers also receive an input from the dLGN. The dLGN is divided into eye-specific sublayers and this segregation of left and right eye is maintained in the distribution of dLGN axon terminals in layers 4 and 6, where they form patchy domains of terminals about 0.5 mm wide.



Visual Cortex: Neurons and Local Circuits. Figure 2 Graph showing the dominant interactions between significant excitatory cell types in neocortex, and their sub-cortical and interareal relations. The nodes of the graph are organized approximately spatially; vertical corresponds to the layers of cortex, and horizontal to the lateral extent. Linking arrows show the direction of excitatory transmission. Lines in bold indicate the relations between excitatory neurons in a local patch of neocortex Thin lines indicate excitatory connections to and from subcortical structures and other cortical areas. Each node is labeled for its cell type. For cortical cells the number after "L" refers to the layer in which the cell body is located and P indicates that it is an excitatory neuron (generally of pyramidal morphology). "Thal" denotes the dorsal lateral geniculate nucleus of the thalamus, and "Sub" indicates target structures such as the superior colliculus.

The left and right eye columns are reminiscent of zebra stripes when looked at from above and this pattern is known as " ocular dominance columns."
The dLGN synapses are excitatory (glutamate is the neurotransmitter) and they activate both spiny and smooth cells. However, even in layer 4 the dLGN provides less than 10% of the total number of excitatory synapses. The arbor of a single dLGN terminal forms 1,000-10,000 boutons and each bouton forms on average more than one synapse. However,

any particular cortical cell receives only a few synapses from a single dLGN relay cell, so each relay cell may form synapses with several thousand cortical cells. Thus, the contribution from one relay cell to a particular cortical cell is very small, and provides only a fraction of a percent of its total excitatory synaptic input.

In addition to the dLGN, which provides the major sensory input, about 20 other subcortical structures project to the neocortex. The monoaminergic systems are the best studied of these and include the dopamine-positive fibers arising from the rostral mesencephalon, the noradrenalin fibers originating from the locus coeruleus, and the serotonin fibers that originate from the mesencephalic raphé nuclei. The monoaminergic projections are thought to be facultative in the processes of cortical plasticity. However, the dopaminergic neurons, which are thought to provide an error signal during trial-and-error learning, project mainly to the prefrontal cortex and not to the primary visual cortex.

Outputs from Visual Cortex

Of the 10^{10} cells in cortex, only about $10^{(7\text{-}8)}$ project to extra-cortical targets. This means that over 99% of cortical cells are involved only in intracortical circuits. The inter-areal projections are exclusively axons of spiny cells. The targets of these projections are always both spiny and smooth cells. None of the projections in cortex that have been studied so far terminate exclusively on excitatory or inhibitory targets. However, the ratio of excitatory to inhibitory terminations may vary and so the balance of excitation and inhibition could be an important aspect of each projection.

Superficial pyramidal cells tend to project to other cortical areas, whereas deep pyramidal cells tend to project both to other cortical areas and subcortically (Fig. 2). The extent of the subcortical projections is quite large in some contexts. For example, the projections from the L6 pyramidal cells to the LGN are ten times more numerous than the geniculocortical projections themselves. The purpose of this arrangement is still not known.

Although most pyramidal cells project outside their cortical area, they have extensive collaterals that project within their local area and they make about 80% of their synaptic contacts within a few dendritic diameters (1-2 mm) of their cell body. Thus, the major component of cortical processing seems to be local. Where projections between cortical areas occur, they are usually associated with a reciprocal connection from their target area. Usually the forward projections arise from the pyramidal cells of the superficial layers and terminate in the middle layers of the target area, whereas the backward projections arise in layers 3 and 5 of the target area and terminate outside the middle layers - in layer 1 and 2 and layer 5 and 6 of the target area.

Organization of Neuronal Types in Circuits

There are two features of cortical neurons that simplify the analysis of cortical circuits. One is that the dendritic and axonal projections of the different types of neurons are laminar specific. The second is that the different types of neurons make stereotyped synaptic connections with each other. For example, all spiny cells make 85% of their connections with other spiny cells. When a layer 5 pyramidal cell axon is observed to form most of its synaptic boutons in layer 6, then it is safe to assume that its major connection is to the pyramidal cells of layer 6. By defining the principal layers to which the different spiny cell axons project and assuming that they connect mainly to the neurons located in the target layers, a possible basic circuit of the cortex emerges (Fig. 2).

In this basic circuit, the thalamic input arrives in layer 4. The excitatory cells in layer 4 project to the superficial layers. The superficial pyramidal neurons project to layer 5, which in turn project to layer 6, and the loop is closed by a projection from layer 6 to the input layer 4 (Fig. 2). This circuit infers only the connections of the spiny, excitatory neurons. The spiny neurons as a class provide most of the inter-laminar connections within a cortical area, whereas the axons of smooth neurons principally arborize locally within their layer of origin. The cardinal feature of the circuits of the necortex is that they form rich excitatory and inhibitory connections with each other. These are referred to as "recurrent" circuits.

Overall, the spiny cells provide the basic framework of long distance excitation in both the vertical and lateral dimensions, which is then shaped by local inhibitory neurons. In the visual cortex this sequence of processing was thought to be the mechanism by which the receptive fields are elaborated from simple to complex. The interlaminar connections are also the means whereby common properties are transmitted to a radial "column" of cells. This "columnar" organization of functional properties is the means whereby common functional attributes can be represented by all the neurons in a given patch of cortex. In the visual cortex there are many common properties shared by all the neurons in a radial column that extends from layer 1 to layer 6, including common position in their representation of visual space, orientation of the stimulus, and their eye preference. These local circuits between and within the 6 layers of the visual cortex provide the major processing required to correctly interpret the enormous amount of information relayed from the retina by the dLGN every second. While we understand more about the elements that make up the visual cortex than any other area, we are still some way from understanding the general principles by which visual cortex processes its inputs.

Acknowledgements

This work was supported by EU FP6-2005 IST-1583. ANR-05-NEUR-088(HK); SNF NCCR NEURAL PLASTICITY AND REPAIR (KM).

Reference

- 1. Binzegger T, Douglas R, Martin K (2004) A quantitative map of the circuit of cat primary visual cortex. Journal of Neuroscience, 24:8441-8453
- 2. Douglas RJ, Markram H, Martin KAC (2003) Neocortex in the Synapatic Organization of the Brain, GM shepherd (ed), 499-558, Oxford university Press
- 3. Douglas RJ, Martin KAC (2004) Neuronal circuits of the neocortex. Annual Review of Neuroscience 27:419-451
- 4. Douglas RJ, Martin KAC (2007) Recurrent neuronal circuits in the neocortex. Current Biology 17:R496-R500

Visual Cortex: Neurons and Local Circuits

Rodney J. Douglas	Institute of Neuroinformatics UZH/ETH Winterthurerstrasse, Zurich, Switzerland
Henry Kennedy	INSERM u846, Stem Cell and Brain Research Institute, Department of Integrative Neuroscience, Bron cedex, France
Kevan A. C. Martin	Institute of Neuroinformatics UZH/ETH Winterthurerstrasse, Zurich, Switzerland

DOI:	10.1007/SpringerReference_119894
URL:	http://www.springerreference.com/index/chapterdbid/119894
Part of:	Encyclopedia of Neuroscience
Editors:	Prof. Marc D. Binder, Nobutaka Hirokawa and Prof. Uwe Windhorst
PDF created on:	February, 04, 2012 13:37