Chapter 1

The Biological and Computational Bases of Vision

Hilary W. Thompson*

1.1. Introduction to the Eye

The human visual system, from photoreceptors to higher-order processing of signals in the brain, is a remarkable example of the power of evolutionary processes acting over vast periods to develop a finely tuned system capable of complex recognition, recall, and execution of highly accurate tasks in space and time. In terms of genetics, physiology, and structure, the evolutionary pathway to higher vertebrate vision can be traced.¹ In fact, it has been hypothesized that the development of a complex visual system preceded and provided the evolutionary substrate for the evolution of brain expansion that made possible higher cognitive functions in primates.² Vertebrate vision is one of the most profound and illuminating examples illustrating the operation of evolutionary principles.³

From using chipped stones to the technology of spacecraft and global computer networks, humans have relied on the exceptional powers of vision to survive, prosper in, predict, and, to some degree, control and reshape an often-challenging environment. The primacy of vision in the human experience is evidenced in our language: to “see” also means to understand, as does “to have the eyes opened.” Such definitions occur, not only in the English language, but also in the metaphors and figures of the speech of other languages as well. Humans are visual animals, and the loss of sight

*LSU Eye Center, LSUHSC School of Public Health, Department of Ophthalmology, New Orleans, LA.

is a profound tragedy, which presents challenges to both the individual and society. Compassionate concern about devising applications to save and restore vision has driven biomedical vision researchers as much as the desire to understand the pure science of how something as complicated and wonderful as our vision can work. The computational scientist has also taken lessons from what we know of biological vision systems to base the development of algorithms for detecting three-dimensional (3D) features of the external world as detected by a two-dimensional (2D) array of detectors, whether they are solid-state photocells or biological cellular transducers of light energy. The understanding of biological vision from the viewpoints of these diverse themes has been one of the great intellectual adventures of our species. Vision research has resulted in a number of Nobel prizes in the medicine and physiology category, as well as significant therapies for sustaining our vision and novel algorithms for machine vision.

This chapter will introduce the functional anatomy, sensory physiology, and neuronal information processing involved in human vision. It is our hope that this introduction will provide a background of fundamental insights and resources about biological vision to computer scientists who are interested in computer vision and computational image analysis. A number of important advances in thinking and methods in computational image analysis relate to our understanding of biological visual systems. Many more advances in computer vision methods are possible if we can understand and learn from the highly optimized image processing in biological visual systems.

1.2. The Anatomy of the Human Visual System

As we gaze into our own eyes in a mirror or into the eyes of another human being, we are aware of particular characteristic features. The clear curve of the cornea, set into the white of the conjunctiva, the wrinkled surface of the colored iris behind the clear cornea, the protective lids, and their eyelashes sweeping over the globe in periodic blinks. Handling a human eye removed from its bony orbit (something few of us, except for vision scientists, pathologists, and anatomists ever do), its toughness, and the feel of the globe as pliable but rigid due to fluid contained in its tough outer covering is very striking. The color of the iris and the size of the clear

cornea dominate its appearance when the eye is in place; removed, the cornea and the iris behind it, with the opening (pupil) behind it, seem, in the isolated human eye, much too small for the size of the globe. Straggling off the rear, slightly off to one side (the nasal or side closest to the nose) is the tough sheath surrounding the optic nerve, the eye's output line to the rest of the brain and carrier of the complex visual processing the cellular circuits of the retina achieves. The optic nerve also conducts the nutritive lines, arteries, and veins, which supply the metabolic demands of the eye. Not visible from the outside of the globe (unless using optics to look through the cornea and lens) is the retina, where photoreception and the initial stages of visual processing occur.

Another notable aspect of the outside of the isolated human eye is the ocular muscles, which have attachment points on the tough outer white of the eye (sclera). Their number and orientation are responsible for the coordinated motion of the globes in the bony eye-sockets of the skull. Ocular movements are coordinated in the central nervous system (CNS) and interact with visual stimuli using intricate feedback from visual pathways.

These most evident and outward features of the human eye all play important roles in vision, including the processing of information and control of light required for image formation and binocular vision. The possibility of binocular vision in an animal is evident in the placement of the eyes in the front of a somewhat frontally flattened face, so that part of the fields of light detection of the two eyes can overlap. The connections and crossing-over of the retinal output cells to the next area of processing in the brain (see below) are another important aspect of binocular vision. Let us consider in more detail the layers of the mammalian eye. These layers include the retina where the photoreceptor cells reside, as well as other layers responsible for mechanical and nutritive supports. Within the retinal layer are neurons, which are part of the initial information-processing system to extract visual information even before neuron signals leave the globe of the eye via the optic nerve.

The tough outer "white" of the eye is a connective tissue layer known as the sclera. The intraocular pressure makes the sclera rigid enough to keep the optical length of the eye constant and support the movement of the eye under muscular control. The sclera's cellular makeup and protein molecule configuration change to form the cornea, the clarity of which equals that of

inorganic glasses or crystals. This clarity of the cornea is due to a different size range, spacing, and orientation of the protein molecules (collagen) that make up the cornea as compared to the sclera. Corneal clarity is maintained by metabolic work of cell layers on the backside of the cornea (the corneal endothelial cell layer) and the outer surface (the corneal epithelium). These cell layers use cellular energy to maintain the ionic (and, hence, water) content of corneal tissue; this work prevents corneal swelling, maintains the spacing of collagen molecules and, thereby, keeps the tissue transparent. The corneal epithelium is densely innervated with nerve endings. This density of nerve endings is evident to us humans when “something is in my eye!” i.e. when debris gets onto the corneal surface. The refractive properties of the cornea account for a great percentage of the optical properties of the eye, far more than the lens. The importance of the cornea as a refractive tissue, bending light to help form an image on the photoreceptor layer of the retina, makes modern refractive surgery possible. Such surgery uses knife cuts and lasers to reshape the cornea to alter and correct its optical properties.

The middle of the layers of the eye, besides the retina and the outer sclera, are the several structures called the uveal tract. The choroid is a part of the uveal tract and is the capillary supply of the retina. This capillary system arises and returns from the blood vessels evident on the retinal surface and supplies the highly metabolically active neural tissue of the retina. In human eyes, the cells of the choroid layer contain a light-absorbing pigment, melanin. Placement of a pigment layer under the active regions of the photon receptor areas of the eye enhances visual acuity by absorbing stray photons that would reflect back on the photoreceptors, confounding spatial resolution. We often note that, when caught in the headlights of our cars at night, the eyes of cats, dogs, deer, and many other animals (in particular those with nocturnal habits) shine brightly. The eyes of these animals with eye shine have less melanin in the choroid than the human eye, but also have a reflective layer that enhances low-light vision by bouncing stray photons back to the photoreceptors, rather than sharpening visual acuity by absorbing them. This reflection produces low-light sensitivity at the cost of spatial resolution, and provides the eye shine that we see when light hits the eyes of these animals in the dark.

The ciliary body at the front of the eye is muscle tissue around the lens of the eye. This muscle is capable of changing tension on the lens to

change lens shape and thereby adjust the focus of the image on the retina in near and distance vision (accommodation). Part of the ciliary body, the ciliary process, produces the aqueous humor, the fluid that fills the anterior chamber of the eye (area in front of iris and lens and behind the cornea). This constant fluid production maintains the fluid pressure and the rigidity of the eye, but fluid leakage balances production. This fluid leakage occurs at specialized meshwork structures at the limbus (the juncture of the cornea, the iris, and the white of the eye). Blockage of this drainage system increases the pressure in the eye (intraocular pressure) and can cause tunnel vision and eventual complete blindness by restricting blood flow and damaging the optic nerve in the diseased glaucoma. The iris is the wrinkly colored portion of the eye that we see through the cornea. The iris has muscle layers that control pupil dilation or contraction under feedback from the CNS. Pupil size adapts to light levels and, like the diaphragm of a camera, changes diameter according to light levels impinging on the eye. Between the lens and the retina is most of the fluid volume of the eye, the vitreous humor. The vitreous is not a simple fluid filling a chamber but a gel with complex protein structure that aids in the protection of the retina. It contains phagocytic cells that can remove cellular debris that might affect retinal image formation. The lessening of the ability of these phagocytic cells to remove all debris results in floaters in the vision, which are the shadows of debris projected on the retina. Both the visual accommodation and the power of phagocytic cells of the vitreous to scavenge debris decline as we humans age. As a result, we may wear bifocals and more often notice floaters in our vision should we be as fortunate as to age.

The inner sensory receptor and initial information-processing area known as the retina contains the photoreceptors (rods and cones). In addition, several other types of retinal nerve cells called interneurons form part of an initial information-processing circuit between the photoreceptor input and the retinal ganglion cells, which provide the retina's output to the brain. Interneurons are neurons that interpose between primary sensory receptor cells and nervous system outputs such as motor neurons; in the CNS, the term interneuron denotes neurons that act locally in CNS nuclei, as opposed to those that send out axons to form tracts connecting to other CNS areas. The retinal ganglion cells have axons that form the optic nerve and carry output to the next stage of the visual system. We will focus on the role of

the retina in the visual system in the section below on retinal information processing. The complexity of the neuronal circuits in the retina is unique for a peripheral sense organ. This complex retinal circuitry arises during the embryonic development of the eye, during which the retina forms from an out pocketing of the growing brain.

The retinal photoreceptors are essentially at the bottom of the several layers of nerve cells of the retina. This location makes the human (primate) retina essentially “inverted,” in the sense that the photons detected by the visual system travel through the output neurons (retinal ganglion cells) that form the optic nerve first, then through several layers of interneurons to finally reach the photoreceptors, the tips of which are just above the pigment epithelial layer of the choroid. The eyes of higher cephalopods (octopus and squids) represent a parallel evolution with the human eye, with many of the cellular features similar, except not “inverted.” The photoreceptors of the cephalopod eye are on the outermost layer, and, therefore, the phototransduction apparatus receives the light first without it having to travel through multiple cellular layers prior to hitting the receptors as in our eyes. It is apparent that vision has arisen independently in various forms multiple times in evolution.¹ In the light of this parallel evolution in visual systems, the “inversion” in the human retina may, in addition to enhancing the sharpening of spatial information by photon absorption, also allow enhanced nutrient supply and support for turnover and restoration of photopigment molecules of photoreceptors by the cells of the retinal pigmented epithelium.

The retinal photoreceptors are of two general classes, rods and cones. These photoreceptors are the specialized sensory receptor cells where the transformation of the energy of photons into neuron signals takes place. This process is sensory transduction. In different sensory systems, the process of sensory transduction shows intricate molecular mechanisms specific for each sensory modality: vision, taste, and smell (the chemical senses), touch and hearing (the mechanoreceptive senses). We will discuss some details of visual transduction in Sec. 1.5 of this chapter. Nerve cells meet and communicate at specialized structures called synapses (Sec. 1.4 of this chapter). A number of synapses are involved in the circuitry of the retina; first, many of the rods and cones synapse onto bipolar cells directly, a neuron in the retina, which connects between photoreceptors and retinal ganglion cells,

forming the most direct information pathway in the retina. Two layers of interneurons modulate the circuitry of this direct pathway in the retina. One layer is composed of the horizontal cells that synapse on photoreceptors at the pre-synaptic elements of their synapses on bipolar cells; this level contains additional synaptic complexity of the retinal circuitry and there are the amacrine cells, which interpose into the bipolar/retinal ganglion cell synapses. Finally, there are the interplexiform cells, which carry modulatory information from the amacrine cells back to the photoreceptor synaptic regions. All of these synapses and cell types are important in retinal function, and we will discuss this function in the section on retinal information processing (Sec. 1.6).

The retinal ganglion cells, as the output elements of the retina and its complex information processing, form the optic nerve. The 2D topology of the retina and the spatial orientation of the image projected on it by the optical system of the eye (cornea and lens, modulated by pupil size) are maintained in the optic nerve and its first synapse with the CNS, and in a number of subsequent higher CNS visual information-processing areas (Note: a “synapse” is a point of communication between two neurons, discussed in detail in Sec. 1.4). In addition, considerable specialization of the outputs of the retinal photoreceptors are also maintained, since there is luminance level, color, fine detail, motion, and shape information, all of which must be routed to specific processing mechanisms further “upstream” in the brain. There is spatial concentration of cones in a central area of the retina where we have the sharpest visual acuity as well as the best color vision. This area is called the fovea (Latin for “pit”), and it is recognizable when we look into the eye and see the surface of the retina. The retina is part of the CNS, and visualization of it is the only part of the CNS that is viewable directly in a noninvasive manner. This noninvasive viewing is via a hand-held instrument called an ophthalmoscope, which medical students and other clinical professionals learn to use when studying ophthalmology and physical examination. It allows a trained observer to look directly into the eye and see the retina, which often can reveal significant pathologic features that may be indicative of systemic diseases such as diabetes or high blood pressure, as well as ocular diseases. The fovea appears as a yellowish spot on the retina where there is a notable absence of larger blood vessels. The paucity of blood vessels goes along with the role of the fovea in our most

acute and color-sensitive central vision. There are densely packed cones at the fovea, with rods absent from the most central part of the fovea.

Another obvious landmark on the retina is the optic nerve head. The blood vessels that spread out over the retina originate at this point, since they enter the eye through the center of the optic nerve, which forms up at the optic nerve head. Since the optic nerve joins with the retina at this point, there are no photoreceptors in the region, and it forms a blind spot in our vision. This blind spot can be explored by closing one eye and fixating the gaze on an “X” on a white piece of paper. A pencil moved away from the point the eye is fixated on disappears at the blind spot. We do not see the blind spot in our ordinary binocular vision due to “filling in” by the higher processing accomplished in the visual system.

There is a remarkable “crossover” of the retinal areas as the retinal ganglion cells project to the next level of the visual system. This crossing-over is important in information processing for color and fine detail, as well as for binocular vision. The crossover occurs at a structure called the optic chiasm in the optic nerve before it synapses with the CNS. About 60% of the retinal ganglion cells from the left eye cross over to the right side of the brain with the remaining 40% continuing onto the left side of the brain. A reciprocal crossover occurs with the retinal ganglion cells from the right eye crossing-over to the left and right side of the brain. The axons of the retinal ganglion cells, after crossing the optic chiasm, become part of the optic tract. Once they are part of the optic tract, they are no longer referred to as the optic nerve. Here, the temporal segments of the left eye retina and the nasal segment of the right eye retina enter the left optic tract, and the nasal segment of the left eye retina and the temporal segment of the right eye retina enter the right optic tract. The functional importance of this crossing-over is to establish a comparative signal for binocular vision and stereoscopic perceptions of depth.

In addition, it is interesting to realize that the optical properties of the cornea and lens result in an inversion of the environmental image, so topographic information from the environment is inverted and projected to the CNS, upside-down with respect to the visualized world. The maintenance of this upside-down representation of topography in the retinal ganglion cell projections throughout the visual system in the CNS is called retinotopic organization. Maps of the retina that maintain the spatial information of the

image falling on the retina occur at multiple levels and in several places within a level in the CNS. The existence of these maps was confirmed by electrophysiological experimentation, as well as studies of the visual defects suffered by humans with focal lesions or damage of specific brain regions.

The first synapse of the retinal ganglion cells in the CNS, after crossing-over from the optic nerve to form the optic tract, is in the thalamus, a relay structure for sensory and motor information to the higher cortical centers. The structure where the retinal ganglion cells make their first synapse in the brain is the lateral geniculate nucleus. Geniculate relates in word origins to the word “genuflect” and indicates the knee-like bend of the structure. Note also that the word “nucleus” in this context refers to an area of the CNS where one area of the brain synapses with another. It may also contain the cell bodies of the neurons involved in the brain region. The term is not to be confused with the neuron’s (or any cell’s) “nucleus,” which is a sub-cellular organelle that contains the cell’s DNA and parts of the gene expression apparatus. Tracts or bundles of myelinated axons connect brain nuclei. These tracts act as communication pathways between processing centers in the brain.

There are three other sites of projection of retinal ganglion cells to areas in the brain in addition to the main visual processing areas. One is the projection to an area known as the pretectum, which projects to the Edinger-Westphal nucleus. This nucleus connects to the oculomotor nerve that controls the constrictor muscle in the iris. Information on light intensity falling on the retina allows this nucleus to control pupil constriction with increases of light into the eye. Another brain area that receives non-visual retinal output is the suprachiasmatic nucleus of the hypothalamus. This area receives output from those retinal ganglion cell axons that control day–night cycles or circadian rhythms. Via this connection, specialized retinal ganglion cells, which have their own photoreceptive pigments and do not need connection to rods or cones, drive rhythmic behavior in response to light–dark cycles.^{4,5} Finally, there is the structure known as the superior colliculus that uses retinal input to control the movements of the head and eye. This chapter will discuss in detail only the function of the visual processing areas, not the aspects of the motor-eye control brain regions to which retinal ganglion cells project.

The main visual pathway in the CNS goes from the synapses of the lateral geniculate nucleus to the visual cortex of the occipital lobe. Areas of the brain are named for the bones of the skull that cover them; in this case, the occipital bone at the back of the head encases the visual cortex of the occipital lobe. Visual cortex is also known as the striate cortex for the banded striate appearance of its histology. The lateral geniculate nucleus neurons send their axons to the visual cortex via structures called the optic radiations. These connections go via two separate courses of the optic radiation, which travel within the internal capsule. The connections, which represent the inferior retina, take a pathway called Myer's loop, which go on an extravagant turn under the temporal lobes and end up in the superior visual cortex. The other bundles of axons from the lateral geniculate nucleus representing the superior retina take a more direct route under the parietal lobe of the brain to the inferior part of the visual cortex. Once again, the retinotopic organization of the retinal ganglion cells maintains its inverted spatial topography in these higher order projections of neurons in the visual system.

Beyond the striate or visual cortex, extrastriate visual processing areas lie in the occipital, parietal, and temporal lobes. Each of these areas again contains a retinotopically organized map of the visual field. In all of these areas, responses may be specialized to a particular aspect of the visual scene, such as color, fine spatial resolution, motion, and the direction and velocity of motion. While research on these extrastriate cortical visual processing areas is ongoing, more than 30 such areas have been discovered to date.^{6,7} All these many parts of the visual processing areas of the brain, with their functions of processing separate (simultaneous) aspects of the visual scene act as a parallel processing system. Adding to the potential complexity of processing is that each of the visual areas mentioned receive not only input from the previous layer of processing, but also synaptic connections from other brain areas. These represent feedback not only from other visual areas, but also from brain regions involved in nonvisual sensory processing, sensory integration, memory, and cognition.

Higher cortical centers not solely involved in visual processing may accumulate some of the results of these parallel visual system processes. In turn, decisions as to the nature of the visual content are made, so that the output of parallel processes must be associated somewhere in the brain. This

occurrence in visual processing in the CNS is called the “binding” problem; it concerns how and where (if there is a “where”) these separate parallel processes are bound together or combined into the complete impression (illusion?) of continuous visual information of a real outer world which the visual system provides our consciousness. It is interesting to note that, while it is beyond the scope of our present discussion, the same binding problem extends to the notion of a continuous self-consciousness that must involve parallel processes in many brain regions. Where does the final executive function that we recognize as our consciousness and the sense of personal continuity reside? Is it localized? Alternatively, is it a distributed emergent property of a complex of parallel processes? This deficiency in our understanding of these higher aspects of visual processing demonstrates that there is considerable knowledge to gain in biological vision research.

1.3. Neurons

A brief review of such an enormous area of current research as visual science must make demands on the reader. All the background required for full understanding, including chemistry and cellular biology cannot be provided in a single chapter. Basic texts on neuroscience provide in-depth treatment of these topics.⁸ However, the basic properties of the neuron and signaling in neurons are essential to understand biological vision. Therefore, my goal is to provide a sound basic understanding of neuronal function, as it relates to neuronal signaling processes in vertebrate vision.

The neuron is the basic cell type of the nervous system of all animals. The idea that the neuron is the functional building block of nervous systems, and that signaling within and among neurons is dynamically polarized, indicating that a neuron and its connections to other neurons are a unidirectional communication pathway, is called the “neuron doctrine.” While the neuron doctrine is giving way to a molecular-level understanding of neural function,⁹ it is still a useful simplifying idea in gaining a basic concept of neuron physiology and structure.

There are other cells in the nervous system, glial cells, which outnumber neurons. Glial cells are concerned with provision of physical support, insulation, and metabolic support to neurons, including the absorption of neurotransmitters and buffering ions important in neuronal function. In the

course of describing neural signal transmission, we will briefly discuss the insulating function of specialized glial cells in speeding neural conduction, but not the other functions of glia. It is the case, however, that due to the support and other functions of glia, nervous tissues such as the brain are not composed only of neurons.

A generalized neuron has four regions: a cell body (which contains the neuron nucleus and controls protein synthesis and other aspects of neuronal metabolism), dendrites (the input to the cell), the axon (a usually long signal conducting part), and presynaptic terminals (the connection to the next neuron or output element such as a muscle, in the neuronal circuit). While many specialized neurons vary considerably from this basic pattern of the generalized neuron, it does reflect a useful concept for understanding neuronal function. In neural signaling electrical current is conducted not by electrons *per se*, as in electrical circuits, but rather by atoms or molecules that carry net positive or negative charges in solution, usually in ionic form. Of course, these charges on ions in solution are due to the excess or deficient numbers of atomic or molecular electrons, but in neural function, we are not dealing with mobile electrons being current carriers as they are in metallic conductors. The common salts that form univalent cations (ions with a single unit positive charge), sodium (Na^+) and potassium (K^+), the divalent cation (an ion with a double unit positive charge), calcium (Ca^{++}), the univalent anion (negatively charged ion), chloride (Cl^-), and negative charges on amino acids and proteins, compose the charge carriers that provide the ionic basis of neural signaling.

The fundamentals of the ionic theory of nervous conduction were originally experimentally tested in invertebrates,¹⁰ but research revealed that the basics of neuronal signaling work in a similar manner across the animal kingdom. When a fine recording electrode penetrates their cell membrane, neurons show a charge difference across that membrane, called the resting or membrane potential of around -65 millivolts (mV). This resting potential ranges over -40 to -80 mV in a variety of neurons. The standard convention is to declare the inside of the cell negative compared with the outside of the cell. The unequal distribution of charge across the neuron membrane is the driving force for all types of neuronal signals. Neuronal signals driven by this unequal transmembrane charge are of several distinct types. The diversity of neuron cellular architecture, the different types of

neuronal circuits and the variety of interconnections among nerve cells, makes for an exceptionally large degree of variety and plasticity in neuron circuits.

Neuronal signaling involves shifts in the negative resting membrane potential to a transient positivity. This shift to the positive is due to an influx of positively charged ions, where the direction of current flow is the direction of the movement of positive charges. Increased negative potential is due to an influx of negatively charged ions (or an efflux of positive charges), increasing membrane polarization over the resting potential. The movement of ions across the neuron membrane occurs through membrane channels. These channels are protein molecules that span the lipid bilayers of the cell membrane, providing a conducting channel between the inside and outside of the cell. The properties of these membrane channels allow the selective control of ionic conductance and thereby the regulation of the ionic currents responsible for neuronal signals. Transmembrane channels are important in axonal signaling in neurons, signaling at synapses, and in the process of transduction. Transduction is the transfer of energy in a quantitative manner between environmental stimuli such as photons and ionic currents in sensory neurons. The transduction process is discussed in a Sec. 1.5 of this chapter.

Let us consider the signaling processes in sequence that go on in the parts of the idealized neuron and present the ionic basis of these signals. Neuronal signals are of two basic types: local currents, which decay over short distances of the neuronal membrane, and actively propagated potentials, which are called action potentials. These two kinds of signals are dependent on the distribution of membrane channels with different properties in the different parts of our basic neuron. The different signal types once again increase the possibilities for neuronal plasticity. Neurons can transition between enormous numbers of possible states that represent different signaling conditions and thus have great variation in input–output transfer functions. Furthermore, there are different types of signaling appropriate for local integration of multiple inputs and for unchanged propagation without signal drop across long lengths of neuron axon segments.

Potentials arising in the dendrites are initiated by a synaptic connection from another nerve cell or by some transduction process, which represents the transformation of environmental energy (photons in the case of vision)

to a receptor potential. This input potential arises by the disruption of the resting membrane potential of the neuron in the dendritic or input region. The membrane potential is disturbed by an influx of positive ions into the cell causing a current flow and a disruption of the membrane potential from its negative resting value. This influx of positive charge carried by ions is via membrane pores (or channels) that are specific to ionic species. This selectivity is due to channel pore size and charges that exist on the inside of the protein channels, and the resistance of ionic species to the removal of their shell of water molecules that accompanies them in solution. This shell of hydration represents an energy barrier because the water molecules must be stripped away if the ion is to enter the channel. Forces larger than this energy barrier must drive ions into the channel stripping off this shell of hydration. These forces are the electrical and concentration gradients that are present across a neuron's cell membrane. Such considerations also guarantee the directionality of ionic current flow in membrane channels, and their selectivity for particular types of ions (i.e. ions of a given size, charge polarity, and magnitude).

Once the resting membrane potential is perturbed, made more positive (depolarizing) or more negative (hyperpolarizing), then if there is no active process that causes the membrane potential disturbance to be propagated to other parts of the membrane, the local potential decays as a charged capacitor would, with an exponentially decreasing time and distance function of charge reduction.¹¹ Hyperpolarizing and depolarizing potentials may occur together and allow time and spatial integration of inputs at the input segment of neurons. This integration occurs with a predictable algebraic summation. The integration of depolarizing and hyperpolarizing inputs occurs at an action potential initialization zone in neurons. Neurons of the brain may receive thousands of synaptic inputs, both excitatory and inhibitory, indicating the complex integration of inputs that may occur within one neuron, and in networks of interconnected neurons. Decrementing, not actively propagated potentials, are called local or graded potentials.

Signals are conducted down the lengths of axons without decrement by action potentials. The action potential initialization zone is downstream from the dendritic input segment of the idealized neuron. It is in this region, which is rich in voltage-controlled Na^+ membrane channels, that the integrated inputs to the neuron at the dendritic arborization have their potential

impact on neuronal signaling. The result of an adequate (or threshold) level of depolarization at the initialization zone results in the generation of a new type of signal in the neuron, the action potential. Action potentials are transmitted over the long axon segments of neurons without any decline in amplitude or change in duration. This transmission without change in amplitude and duration occurs because the action potential is generated in a fall-forward active manner that occurs anew in each patch of neuron membrane. The fall forward process of excitation and action potential generation spreads from segment-to-segment along the axon in one direction. Generation of the potential depends on the membrane containing an adequate number and type of voltage gated ion channels.^{12,13} Voltage-gated ion channels allow ionic currents to flow selectively in a particular direction across the neuron membrane as the membrane potential changes. The action potential has a characteristic time course of measurable current changes over time. An initial rising phase (rising means the depolarization of the negative membrane potential, i.e. movement to a more positive potential value) is mediated by a voltage-controlled Na^+ channel that allows an influx of Na^+ ions from the higher concentration outside the neuron membrane to the inside. This voltage-gated Na^+ channel is activated by a depolarizing current at the action potential initialization zone of a neuron. Once initialized, the rapid rise of the action potential depolarizes the voltage-gated Na^+ channels in the next patch of membrane. At the same time, the action potential in the initial segment of the neurons axon has undergone deactivation due to another aspect of the ion channel structure, one that physically closes conduction when a certain potential is reached. This closing of conduction explains why the action potential travel is in one direction; the patch of membrane in which it has just arisen is refractory due to the duration of inactivation, and backwards spread is inhibited.

The voltage-gated Na^+ channels open in large numbers when the membrane potential in the action potential initialization zone reaches a threshold level. During this rising phase of the action potential, the membrane potential is driven toward the Na^+ equilibrium potential. This potential level is that to which Na^+ will force membrane voltage when Na^+ conductance controls the membrane potential.¹⁴ This potential, known as the equilibrium potential for Na^+ , can be compared to a current from a battery, where the battery is the potential difference due to the unequal distribution of Na^+ across the

neuron membrane. As the voltage-gated Na^+ ion channel becomes inactivated, another channel, the voltage-gated K^+ channel, opens and takes the control of the membrane potential, pushing it in turn back downwards toward the equilibrium potential of K^+ . The K^+ voltage-controlled channel in turn is inactivated, and a slight undershoot at the end of the action potential occurs due to a brief voltage-controlled opening of Cl^- ion channels. The result is a return to the membrane resting potential. All of these events have electrical analogies, the initial unequal concentrations of ions across the resting membrane act like batteries with potential levels and polarities specific to the distribution of the particular ions in the resting membrane potential. The lipid bilayer and proteins of the neuron membrane act as a capacitor, storing the charges, and act as resistors reducing the ability of charge to cross the membrane. All of these ionic membrane events lead to an equivalent circuit that physically or computationally can be used to model neuron membranes and neuron signaling.

The speed of axonal conduction via action potentials is important in motor evocation of escape mechanisms when sensory inputs signal danger. In invertebrates, the greater speed of axonal conduction is accomplished by increasing axon diameter, resulting in “giant axons” that are involved in sensory to motor system connections. Increases of axonal conduction speed in vertebrates are accomplished in another manner, insulation. Insulation of axons is via specialized glial cell types that wind around axons forming a multilayer myelin sheath. This sheath is interrupted by “nodes” or areas in the myelin sheath that expose the neuron membrane. In these nodal regions, the concentration of voltage-gated Na^+ channels is very high, and the action potential is speeded up by “saltatory” or jumping conduction, where rather than separately activating each patch of membrane along the axon, only the nodes need to generate action potentials, which in turn jump to the next node.¹⁵

1.4. Synapses

Synapses are the points at which individual neurons communicate with other neurons to provide the inputs and outputs for neurons. The communication between neurons in neuronal circuits is through the actions of synapses, and synaptic actions have a great deal of flexibility to modulate information

flow between neurons. At the synapse, the signal transfer functions of connections between neurons are altered in a way that shapes information transmission in the nervous system. Synapses and changes in synaptic efficacy are an important part of the mechanisms by which memories and other information are encoded and stored in the CNS. The plasticity that synapses impart to neuronal circuits allows learning, conditioned responses, and makes them important targets for drug development for neurological and mental diseases.

Synapses are characterized by distinctive anatomical and cellular structures that reflect the capacity of the neurons for manifold variations in communication and control, integration, and local processing of information. They are of two basic types, electrical and chemical; with electrical synapses providing direct coupling of neurons and chemical synapses acting over a synaptic cleft, a space that chemical neurotransmitters diffuse over to act on post-synaptic neurons. Synapses utilize the main ionic current-control mechanisms described for signaling within neurons. These include voltage-controlled ion channels that respond to and integrate incoming signals and establish outgoing signals, and initial differential ion concentrations inside and outside the membrane, resulting in a resting potential, and resting channels that allow ions to move down an electrical and concentration gradient to maintain and reestablish the resting potential. In addition, chemical synapses have novel mechanisms that allow the amplification and control of the time duration of neuronal signaling, as well as enhance the number of possible neuron response types and response flexibility.

Electrical synapses are connections between nerve cells that represent a physical connectivity of the cytoplasm within one neuron to the neuron with which it electrically synapses. The function of electrical synapses was first described in crayfish.¹⁶ The connections of the neuronal membranes are made with adhesion structures called gap junctions. Channels made of proteins called connexins¹⁷ form these gap junctions. Connexins form a partial channel on each side of the membrane and have subunits that match up to form the neuron-to-neuron channel. Connexin subunits can rotate with respect to each other, and can close off the connection, which may limit damage after trauma to the neurons.

Chemical synapses operate over a measurable gap between neurons. Depolarization of a synaptic ending in a chemical synapse initiates release

of membrane contained vesicles containing a neurotransmitter substance. The vesicles release their contents by fusing with the presynaptic membrane, and the neurotransmitter substance diffuses across the small gap between the pre- and postsynaptic cells, binds to postsynaptic receptors, which in turn affect a neuronal signal in the postsynaptic neuron by acting to induce ionic currents and causing postsynaptic potentials. Neurotransmitter substances are mostly small molecules such as the amino acids L-glutamate, arginine, or glycine, but include other molecules such as gamma aminobutyric acid (GABA), or acetylcholine. Peptides can be neurotransmitters as well, including such substances as vasoactive intestinal peptide, or calcitonin gene-related peptide and many others.¹⁸ Peptide neurotransmitters differ from small molecule neurotransmitters in their metabolism, actions and release mechanisms. Inhibitory synapses in the CNS often involve GABA or glycine. These inhibitory actions depend on receptor channels in which the binding of the neurotransmitter molecules directly causes a change in the channel conductance, conducting Cl^- ions into the cell, which depolarize the postsynaptic cell, making it less likely to fire an action potential. Excitatory synapses involve glutamate-gated ion channels that conduct Na^+ and K^+ ions. An influx of positively charged ions depolarizes the membrane and makes generation (firing) of an action potential more likely. There are synapses in the retinal neural circuits that represent exceptions to GABA and glycine as inhibition-related neurotransmitters. In fact, it is not the transmitter *per se* that is inhibitory or excitatory, but rather the kinds of channels, which the binding of the neurotransmitter activates on the postsynaptic membrane. In addition, other modulatory substances that are in the extracellular milieu of the synaptic regions, but which are not neurotransmitters released from presynaptic endings, are present in the nervous system. Receptors for these substances were discovered by the study of the action of neurotoxic substances and named for them, and the molecules that bind these modulatory sites on synapses discovered later. For example, synapses that use glutamate as a neurotransmitter are all excitatory but fall into several classes based on these other molecules. Thus, we can classify glutamate receptors as those that directly gate ion channels and those that invoke a second messenger system to activate ion channels indirectly. The direct acting glutamate receptors are classified as AMPA, kainite, and NMDA types (alpha amino-3-hydroxy-5-methylisoxazole-4-propionic acid, kainite, and

N-methyl-D-aspartate). These molecules are the toxic agents that allowed discovery of these synaptic subtypes.⁸

There is increasing knowledge from ongoing research on the properties of inhibitory and excitatory synapses, the drugs that affect them and the diseases that may involve alterations in the function of synaptic physiology. The present review will not address any further detail on the pharmacology or pathology of synaptic function.

The pre- and postsynaptic elements of communicating nerve cells can be of vastly different sizes. This size difference allows for further complexity of integration of neuronal signals in situations where a number of small presynaptic elements contact a much larger postsynaptic neuron. Inhibitory and excitatory synaptic inputs undergo spatial and temporal integrations, giving rise to enormous numbers of possible states for the neuron-to-neuron communication effected by synapses.

1.5. Vision — Sensory Transduction

All the information we have concerning the state of the world outside our bodies, as well as the position of our bodies in space, and the forces acting on and within our body, are due to the activity of neurons in sensory systems. Thus, all of the wonder of the world we experience, light, sound, touch, taste, and smell, all arise through neuronal processes that begin with the transduction of environmental energy into neuronal signaling, and subsequent processing of the signals from primary sensory neurons in other neuronal circuits. Survival dictates that these representations of the outside world be largely accurate. Food, threats, shelter, and other members of our and other species must all be located accurately in the visual space for us to interact with them successfully.

In the case of vision, photon energy is transduced into neuronal activity in a quantitative manner that informs the nervous system about the luminance, spectral differences, orientation, and motion of light energy that impinges on the photoreceptors of the retina. A long pathway of discovery in neuroscience led to our current detailed molecular level understanding of the beginning of the process of seeing: the mechanism of transduction of the energy of photons into neural signals.

Rods are elongate cells that are comprised of an outer segment connected to an inner segment by a thin ciliary process, subsequently attached to the cell body and synaptic outputs by a narrow waist. Cones are similar in structure with differences in shape (hence, the names rod and cone), and in the details of the organization of the membrane and photoreceptor protein apparatus. In broad detail, cones and rods are similar, and we will describe the events of phototransduction in the rod where transduction was first explored. Rod outer segments are filled with photoreceptor discs, organelles that concentrate and manage the photoreceptive pigment and protein and the associated signaling pathways.

In the dark, rods are depolarized.¹⁹ This depolarization is the opposite of the physiology of excitation in most sensory neurons, where a stimulus leads to the generation of an action potential and subsequent output at the synaptic or output end of the idealized neuron. Thus, sound vibrations excite hair cells in hearing; chemical binding excites chemical receptors in the smell and taste systems, all producing depolarization and action potentials. However, by this common standard, dark seems like excitation to rods and light an inhibitory input. Light hyperpolarizes rods and cones; in the dark, the receptor is depolarized. The reason for this apparent reversibility of the sense of sensory signaling in vertebrate photoreceptors remains unexplained.

The sequence of events that set phototransduction in motion causes the reduction of cyclic guanine monophosphate (cGMP) when a photon is absorbed by a form of vitamin A (retinol) associated with the protein opsin. This visual pigment called rhodopsin is in the photoreceptor discs. The retinol part of the photopigment absorbs the photon and the photon's energy causes the transmission of a conformational change in the retinal molecule to the associated protein molecule or opsin. In turn, the altered conformation allows the new conformation of the opsin molecule to activate a series of signaling proteins that reduce the concentration of cGMP in the outer segment, closing the cGMP-gated channels and reducing the inward Na^+ , Ca^{++} current.²⁰ The K^+ channels are thus able to overcome the influx and drive the membrane potential toward hyperpolarization.

Opsin acts differently depending on the wavelength of the energy absorbed and creates effects that are specific to particular wavelength ranges of photons. This behavior accounts for the wavelength sensitivity of photoreceptors and is the beginning of the mechanism of color sensitivity. Note,

however, that although the cones may be “tuned” for a specific wavelength range of light, each receptor receives just as many photons as any other receptor, and neuronal circuits that allow comparison of the different classes of cone output must distinguish the spectral sensitivity differences of cones. In the section on retinal processing, we will see how these retinal circuits work and how the information is processed in higher visual areas within the brain.

As to the details of the process of phototransduction, the changes in the opsin protein in turn activate a protein known as transducin (named for its role in the process of sensory transduction). The activated transducin protein in turn activates an enzyme that breaks down cGMP and prevents its activation of cGMP-gated Na^+ , Ca^{++} channels. This complicated sequence has the advantage of enhancing the sensitivity of photon detection by an amplification process. Absorption of a single photon can cause closure of a considerable percentage of the channels in a rod membrane. This closure accounts for early observations that the photon threshold of human vision is at the level of the absorption of single photons in five to seven rods in a dark-adapted eye.²¹ Other mechanisms act as molecular brakes and restore the rhodopsin to its initial state to start the photoreceptor cascade over. After a number of cycles, the photopigment-containing discs of the rods shed from the ends of the rod cell, then are phagocytized (“cell eaten”) by the retinal pigment epithelial cells and degraded. Some components are recycled back to the base of the inner segments and used in the formation of new disc membranes where they add to the stack of discs in the outer segment. Processes are similar in cones, except that cones have membrane folding rather than separate discs; and, as mentioned above, in the cones the proteins in the retinol–opsin complex respond to different wavelengths of light.

1.6. Retinal Processing

The cell types of the retina combine into different circuits that are specific for the detection of different features of the visual scene. Rod and cone photoreceptors are different in shape (hence their names), and differ in their distribution over the human retina. Cones are concentrated in high density at the fovea or focal point of the image on the retina. Rods are absent from

the center of the foveal region where there is the greatest visual acuity and color sensitivity, and where the cones are most densely packed. Rods are concentrated in the extra-foveal peripheral retinal regions, and are present at the furthest periphery of the retina where cones are almost absent. The circuits that the rod and cone photoreceptors make with the other retinal neurons differ as well, not only from rods to different types of cones but over regions of the retina for a particular receptor type as well. Rods are poor at spatial resolution but specialized for sensitivity to low light levels. Cones, due to their high concentration at the fovea, and their low degree of convergence on the other cells in the retinal circuits, have a high spatial resolution that we depend on for our sharpest visual acuity. Subsequent retinal and CNS circuits build on and maintain these differences in rod and cone processing.

Over much of the retina, rods and cones converge on the same retinal ganglion cells. Individual retinal ganglion cells respond to both rods and cone inputs. However, the neuronal circuits that rods and cones are connected to differ significantly, and these differences account for differences in visual acuity, motion detection, and color processing both in retinal processing and in subsequent higher levels of CNS visual processing as well. Rods are maximized as low-level detectors that sacrifice spatial accuracy; cones are organized to have maximum spatial and spectral acuity while sacrificing optimum possible sensitivity. Rods synapse with bipolar cells as do cones, but many rods (15–30) synapse on one bipolar cell. Cones, particularly those in the foveal region, synapse on one bipolar cell, and these cone bipolar cells synapse directly with retinal ganglion cells. Bipolar cells connected to rods also differ in being connected not directly to retinal ganglion cells but rather to a particular type of amacrine cell, which makes both electrical synapses (gap junctions) and chemical synapses with cone bipolar cells as well. In turn, these amacrine cells synapse with retinal ganglion cells. Each rod bipolar cell contacts a number of rods and a number of rod bipolar cells contact each rod amacrine cell before it synapses with a retinal ganglion cell. Single cones, especially in the fovea, contact one bipolar interneuron that in turn synapses on one retinal ganglion cell. This high-degree of convergence makes the rod circuits of the retina designed for optimal light detection, but at the same time poor in spatial resolution due to this same convergence, since the stimulus that activates a rod circuit

could have come from anywhere in a large area covered by a number of photoreceptors. The one-on-one cone to bipolar cell circuits of the cone system maximizes spatial acuity. Cone bipolar cells, while they synapse with a single cone, do not synapse in turn on only one retinal ganglion cell. The convergence on retinal ganglion cells of several different types of cones (with different spectral sensitivities) is what makes possible the detection of color; it is only in comparing the output of different types of cones that makes spectral discrimination (distinguishing colors) possible. The mechanism involves the center-surround mechanisms described in the next paragraph.

The output of the retina is not simple photoreception; much more sophisticated processing is done in the retina. Retinal ganglion cells, in experiments using electrophysiological recordings to determine the responses of these cells to focal light stimuli on a screen, viewed by the retina of an experimental animal demonstrated that there is a center-surround effect of retinal ganglion cell responses to their receptive fields.²² Single cell recordings with fine electrodes can reveal the receptive field of a retinal ganglion cell, which is the area of the visual space; in this case, a screen in front of an experimental animal, within which a light spot or other visual stimulus can activate that retinal ganglion cell. The area of the receptive field is accounted for by the retinal ganglion cell synapsing with a number of rods (or cones), giving it a spatially distributed input pattern. Center-surround effect means that a spot of light on the center of the receptive field evokes more signal (more action potentials occurring together in time in a train or burst), than that same light spot in an area of the cell's receptive field that is away from the center in the surround of the cell's receptive field. Such is the case for an "on-center" retinal ganglion cell. "Off-center" retinal ganglion cells show an opposing pattern; they are suppressed (producing fewer action potentials than their spontaneous background rate) when a spot of light is projected on the center of their receptive field and stimulated (producing more action potentials) when the spot is projected on the periphery of their receptive field. Off-center and on-center retinal ganglion cells are present in about equal numbers in the retina. They involve both rods and cones, and their receptive fields overlap so that several on-center and off-center retinal ganglion cells cover each point in visual space. The function of this coverage at the level of the retina is to detect not the absolute

level of light falling on the retina, but rather differences in illumination over a wide range of levels.²³ The on-center and off-center retinal ganglion cells have the distinct characteristics they possess due to differences in synaptic mechanisms with their input rods and cones, bipolar cells, and amacrine cells.

Color vision is also of the center-surround contrast-detection type at the level of retinal ganglion cells. In color vision, each type of cone is in effect color blind, as it alone cannot distinguish between wavelengths of light. Because the spectral sensitivities of the three receptors overlap, any given wavelength will stimulate all three receptor types to different degrees. Cones fall into three spectral sensitivity ranges, and are named not by color sensitivity but in terms of their wavelength sensitivity optima. There are so-called S cones (for short wavelength); these absorb maximally at 440 nm. M cones or medium wavelength cones absorb maximally at 530 nm. In addition, L cones, long wavelength cones absorb maximally at 560 nm,²⁴ S cones represent about 5–10% of cones, twice as many L cones as M cones; with the ratio of cone types being L:M:S = 10:5:1.²⁵ The center-surround circuitry for cones on the retinal ganglion cells allows the initial discrimination of color in the retina. Note that it is all too easy to say “color” as in color vision, when talking about cones, however, to be technically correct, color sensations are a perception and a naming process that involves higher cortical functions. We should be referring to spectral sensitivity rather than color at this initial level of visual processing.

Trichromatic cones provide one representation of the spectral information in the circuits of the retina. The cone systems: S, M, and L become represented as opposing pairs at the level of retinal ganglion cells: R/G, Bl/Y, and Bk/W. “R” here is for red, or what might be called red-sensitive cones (L) (except for our caveat above about color sensation depending on higher cortical processing), G (green) is for the M cones, Bl (blue) for the S cones. “Y” is for yellow, which is detection of the summation of the M and L cone activity. The Bk/W (black and white) is a center surround comparison of the output of rods and represents the overall “volume” of light, being excited by all wave lengths of light and inhibited by reduced light or vice versa. As is indicated by the above descriptions, these color opponent retinal ganglion cell types, like the rod center-surround retinal

ganglion cells exist as two types, center-on and center-off. Consider what these two types are for the R/G opposing pairs: one with an $R + G -$ center, and $G + R -$ surround and another with $G + R -$ center, $R + G -$ surround. Red spectral range light on the center of the first type is excitatory, and green light inhibitory; green light is excitatory on the surround and red inhibitory on the surround. The other type of R/G color opponent cell is the vice-versa pairing of the first. The BI/Y color opponent cell pairs are arranged in similar manner. In addition to enabling recognition of the spectral character of the light impinging on the retina, the R/G and BI/Y systems provide useful contrast information to distinguish changes in color with illumination level (such as when there is shading of part of a colored surface). They also aid in the distinction these shadings of colors from surfaces that are actually two different colors.²⁶

Other retinal ganglion cell receptive fields do not have the center-surround organization. They have instead an overlap of opposing inputs. The activity of such a retinal ganglion cell might be a function of the relative levels of short, medium, and long wavelength cone responses such as: $S - (L + M)$.

P cells are the name for the above-described color opponent retinal ganglion cells. P cells represent a class of cells sensitive to color contrast, but which have little (comparatively speaking) sensitivity to luminance contrast, higher sensitivity to spatial frequency (the number of dark bars in a variegated pattern falling on the retina), and lower sensitivity to temporal frequency (how fast a visual stimulus is turned on and off). The other major group in this classification of retinal ganglion cells is the M cells. These cells have the opposite characteristics of the P cells; they are not connected only to cones in such a way as to have sensitivity to color contrast, but instead have sensitivity to luminance contrast, lower spatial frequency sensitivity, and higher temporal sensitivity.²⁷ The size of the nuclei and axons are smaller in the P cells and larger in the M cells. All of these differences are maintained and even spatially segregated in the next area of the visual system. The M of M cell stands for magnocellular, with *magno-* as a Latin word root indicating “large”; P in turn stands for parvocellular and *parvo-* is a Latin word root meaning small. These differences are reflected in further segregation of these classes in higher centers of the nervous system.

1.7. Visual Processing in the Brain

The processing of visual information at higher levels of the brain continues when the optic tracts, containing retinal ganglion cell axons from both eyes reach the first brain area where they synapse. This process is (as described in the anatomy of the human visual system section above) the lateral geniculate nucleus. The majority ($\sim 90\%$) of the retinal ganglion cells from the optic tract synapse in the lateral geniculate nucleus. The retinotopic organization of the retinal ganglion cells is maintained in the lateral geniculate nucleus; however, an important segregation of retinal ganglion cells occurs here prior to visual information passing onto higher visual centers. Retinal ganglion cells are recognizable as distinct by the size of the cell nucleus and axon diameters. These size distinctions reflect the type of connections that the retinal ganglion cell received in the retinal circuits. The M-type retinal ganglion cells segregate to the lateral geniculate nucleus area known as the magnocellular layer; while the P-type retinal ganglion cells are specific to a lateral geniculate region known as the parvocellular layer. The separate action of these layers of the lateral geniculate nucleus was discovered in lesion studies²⁸ in which visual testing of color sensitivity and spatial and temporal frequency testings were conducted before and after the destruction of the layers in animal (primate) models. These and other experiments demonstrate that P cells are important for color vision and vision with high spatial resolution and low temporal resolution. M cells have the contrasting properties having no color sensitivity, low spatial sensitivity, and high temporal resolution.

In terms of receptive fields and retinal information processing, lateral geniculate nucleus cells have a similar physiology to that described for the retinal ganglion cells, having center-surround antagonistic organization and specialization for color and acuity or sensitivity to light levels and temporal sensitivity. The lateral geniculate nucleus is a six-layered structure with the magnocellular inputs synapsing in the ventral two layers (ventral in this case indicates “toward the bottom of the skull”) and the parvocellular pathways projecting to the dorsal-most (top of skull) four layers of the lateral geniculate nucleus. This separation of different retinal ganglion cell types was not evident in the organization of the retina; although the separation into magno- and parvocellular pathways each separately maintain

the topographic organization of the retina. It has been proposed^{6,29} that the parvo- and magnocellular pathways in the lateral geniculate nucleus and visual cortex represent separate parallel processing channels for motion and depth perception (magno-) and color and shape in formation (parvo-).

The responses to light stimuli of the lateral geniculate nucleus neurons resemble those of the retinal ganglion cells with a center-surround organization, but the lateral geniculate nucleus neurons have larger receptive fields and a stronger opposing effect of the surround. The layers of the lateral geniculate nucleus receive input from one or the other eye alone, alternating between the two eyes. Cells that receive input from both eyes first appear in the primary visual cortex to which the lateral geniculate neurons project. The spatial organization or topography of the retinal cells is maintained in the lateral geniculate nucleus. If retinal ganglion cells are close on the retina, they project to adjacent regions of the lateral geniculate nucleus layers.

The function of the cells of the striate cortex to which the lateral geniculate nucleus neurons project via the optic radiations was examined by single neuron electrophysiological recording techniques.³⁰ It was discovered that there are distinct types of responses that characterize classes of visual cortex cells. The so-called “simple” cells had receptive fields with both excitatory and inhibitory regions, so that the response of simple cells to bars of light or moving edges or bars of light could be predicted from the cell’s responses in all its receptive field areas. Subclasses of these simple cells were seen as edge detectors, others (with elongate receptive fields) were seen as line or bar detectors. The behavior of these cortical cells was related to the behavior of several grouped center-surround units from the lateral geniculate nucleus.

A more frequent type of cell in the striate cortex is the complex cell (~75%). These were initially hard to identify, since, unlike retinal ganglion cells, they do not respond to stationary small spots of light, but are highly responsive to moving lines or edges in their receptive fields that move in a preferred direction. The receptive fields of complex cells are larger than those of simple cells. The activity of complex cells was explainable by response integration from many simple cells. Logically, this connection explains why they can act as edge detectors sensitive to a particular direction of movement.

A third class of striate cortex cells is hypercomplex cells, which had more complex receptive fields than complex cells. While they are sensitive

to the lines and edges of light in their visual fields, they are inhibited when a line extends beyond their receptive fields. Thus, the hypercomplex cells seemed to be candidates for line or edge “end” detectors. More recently, other research has suggested that end detection is a continuous rather than an all or none phenomena and that it is due to lateral inhibition from surrounding striate cortical cells.³¹ The end stopping property could work by convergence of excitatory and inhibitory complex cell inputs.³²

In terms of color processing the striate cortex has “double opponent cells.”³³ Double opponent cells of the visual cortex consist of center-surround-organized cells of four classes: those with an $R + G -$ center, an $R - G +$ surround, a $Bl + Y -$ center, a $Bl - Y +$ surround, an $R - G +$ center, an $R + G -$ surround, a $Bl + Y -$ center, a $Y + Bl -$ surround, and achromatic center-surround cells, with a $Bk - W +$ center, $Bk + W -$ surround (and vice versa). These cells provide the basis for simultaneous color contrast effects and receive input from the color-sensitive parvocellular regions of the lateral geniculate nucleus.

The organization of cells of these various orientations and type in the striate cortex were studied by electrophysiological and metabolic techniques (neuron uptake of radioactive nonmetabolizable sugar) that labeled active neurons in large brain areas.³⁴ The rescaling to greater numbers of cells of the primary retinotopic map from fewer cells of the lateral geniculate nucleus to the cortical visual areas is cortical magnification. Cortical magnification is the name for the observed effect of the central retinal areas spread over a larger brain area (hence enlarged) and distorted relative to peripheral retinal areas. This phenomenon has its primary source in the greater packing density of receptors in the foveal region of the retina compared to the periphery. The cortical magnification can be seen in published images of striate cortex.³⁴ The so-called “ocular dominance” columns or slabs are observed in striate cortex.³⁵ These are interleaved maps from the two eyes (hence “ocular dominance”) organized in columnar fashion down the structure of the striate cortex. However, in recent work,³⁶ the functional importance of the structures such as ocular dominance columns has been questioned, since there appears to be little consistency in their presence or absence in different species with similar or distinct ecological preferences (as nocturnal vs. diurnal) or even within the members of a species. The functional importance of structures such as ocular dominance columns for

visual systems where they are present remains unclear; it is possible that data on similarities between similar species are lacking because they have not been adequately studied, or that the relevant experimental questions have not been asked as of yet.

Considerable evidence on the development of receptive fields and cortical cell types during the growth of animals has been accumulated, beginning with the work of Hubel and Wiesel in the 1960s.^{37,38} I will not describe this work in detail here except to note that if the young animal is visually deprived, visual system cells will have impoverished connections, and the animal will have reduced visual capacities.

Recent research into the physiology of the visual system above the level of the striate cortex has used neuroimaging techniques such as magnetic resonance imaging (MRI), functional MRI (fMRI),³⁹ and tensor diffusion MRI (diffusion MRI).⁴⁰ These methods allow researchers to make a more global assessment of activation of cortical regions and their connectivity, and have been applied to various visual systems including humans.

A variety of methods for assessing the connections and physiology of the higher visual system cortical areas has been extensively applied in a variety of primate species.⁴¹ Methods in such studies include an extensive array of neuroscience techniques for understanding neuronal circuits including single cell electrophysiology of receptive fields and detection characteristics of cortical cells, MRI and fMRI, and histological tract-tracing methods. Understanding the connectivity and the neurophysiology of the cells in higher cortical visual areas has not reached the level of our present understanding of visual area 1. The physiology of visual area 1 provides the understanding that adds the biological vision aspect to the next section on biological vision and computer vision algorithms.

1.8. Biological Vision and Computer Vision Algorithms

Our understanding of the logic of the circuits of the visual system has inspired the development of a number of computational algorithms for various facets of computer vision. Much of this research is not tied to direct knowledge of the processing inherent in the neuronal circuits of the visual system, but rather only based on the knowledge that biological visual systems accomplish a particular task (such as pursuit projection and shooting

targets from the air), and postulating that the task may be accomplished algorithmically. Novel image-analysis algorithms have also been developed from the more direct knowledge of visual system physiology.

There are a number of areas of computational science, some related to our detailed physiological knowledge of the visual system. The related research and results could be a book topic in themselves. Here, I will address two examples, image-analysis methods, such as edge or line detection algorithms derived from biological visual circuits, and machine-learning methods, in particular unsupervised hierarchical Bayesian methods for target matching.

Knowledge of the function of the visual system, in particular knowledge of the primary visual system processing in the retina, lateral geniculate nucleus, and striate cortex, inspired computer scientists to program work-alike algorithms that accomplished basic tasks in image analysis. An example of this line of research was the Marr-Hildreth algorithm.

The motivation for the development of line and edge detection visual system mechanisms developed as computational algorithms came from the work of David Marr.⁴² The kernel of Marr's concepts of visual systems was that the neuronal events in biological vision systems are essentially accomplishing a computation task, and thereby complex systems such as biological vision systems are information-processing systems. Marr proposed a general idea for the construction of theories of information-processing systems, in particular visual systems. He noted three stages of description in understanding complex information-processing systems such as the visual system. These are the computational, algorithmic, and implementation levels. Understanding all of these levels is important for understanding information-processing systems. The computational level is the informational constraints that apply to the mapping of input to output information in an information-processing system. Mathematical methods can be used to model and check the computational level for validity. The algorithmic level is conceptually similar to the role of a computer program in computer science. The algorithmic level is the manner in which the computational level mapping of input to output is accomplished. As with computer code, there are many algorithmic ways a given computational mapping might be realized. The implementation level is the physical hardware (or "bioware" in the case of biological vision systems) by which a given algorithm, which

realizes the computational level mapping, can be physically realized. These levels represent different levels of description and understanding of the same phenomena; understanding at only one of the levels is insufficient for full understanding of any complex information-processing system.

According to Marr's formulation, all three levels are necessary for complete understanding of, and effective theory construction for an information-processing system such as the visual system. In addition, if one level is correctly understood, our understanding of the realization at that level may constrain the possibilities at the other levels. Thus, if we can see how the neuronal circuitry we have discovered in living organisms implies an algorithm, and we realize that algorithm in computer code or verify that its mathematical machinery can produce the observed result given the known input, we have made a considerable step toward validating observations of visual system processing. The hardware implied an algorithm, and the algorithm of the proposed character provides a reasonable semblance of the output of the biological visual system at some level, given the input image. Therefore, we have obtained a suggestive confirmation of our ideas about how neuronal circuits accomplish the tasks we observe them to accomplish. We thus have the potential for double gain here, as we have a way to evaluate ideas about how the nervous system accomplishes its information-processing tasks, and we may discover novel algorithms that can improve machine tasks such as computer vision, independent of our research concerns in biological vision.

The performance of the biological visual system is described (over and above subjective experience and introspection) by an area of psychology called psychophysics. Psychophysics is human sensory physiology by interview, or asking humans to respond verbally or by some task when there are changes in their sensory input that they recognize consciously. Psychophysics thus provides the performance specifications for the system, telling us what the human visual system can perform. Similar methods are used in animal research, except that rather than a verbal response the experiment is arranged so that the animal can respond with a task to which it has been trained. The knowledge we have thus gained of the bioware, or the neuronal circuits that process the system inputs represents the implementation level that the visual system uses, analogous perhaps to the hardware circuitry of a computer. Marr, in attempting to develop a computational theory to accomplish the tasks a given level of the visual system could perform

was attempting to realize the algorithmic level of understanding the visual system. The performance of the algorithms he devised could then be compared to the observed performance (determined by electrophysiology and psychophysics) of the biological visual processor. In turn, in understanding the algorithmic level and improving our algorithms to fit the implementational data better, we can iteratively improve our ideas of how the biological processing occurs.

Computational scientists, in their approaches to the problem of vision, long ago realized that an effective first step in automated visual recognition of objects was the discovery of lines and edges.⁴³ Marr expressed this recognition by postulating that the initial stages of biological visual processing systems develop a “primal sketch.” This primal sketch was the input to subsequent stages that processed and compared it to other information about the visual scene to extract dimensional information in several steps. The primal sketch represented one aspect of the initial information that Marr postulated the neuronal circuitry of the early visual system (striate cortex or visual area 1, often denoted as V1) extracted from the 2D images on the retina. Marr thus set out to devise an algorithm to implement center surround and edge detection similar to that used by striate cortex neurons, in order to discover what sort of image information could be available at this stage of processing, and how useful such information could be in later visual processing. The results of this approach⁴⁴ combined a number of then commonly used methods in computer image analysis for edge detection. Improvements in their algorithm by other workers produced more effective edge detection routines that form the basis of modern methods.^{45,46}

The combination of edge detection methods that were proposed by Marr and Hildreth were combined in a way that not only did a passable job of edge detection, but also matched Marr’s concepts of what the visual system cells of the striate cortex were doing. This notion of neurons in visual area 1 as edge detectors also was in line with the original suggestions Hubel and Wiesel had made for the nature of the visual area 1 cortical cell physiology they had observed.³⁰ The receptive fields of striate cortex cells were revealed by later research to be more complex than the early Hubel and Wiesel research suggested.⁴⁶

However, after Hubel and Wiesel’s 1959 work, there were alternative concepts put forward that proposed a different scheme for the significance of

the striate cortical cell responses. These concepts involved ideas that became quite important in our understanding of image processing in the visual cortex. They involved the idea that the neurons of the cortical visual area 1 are performing transforms on the input from the retina that act as filters for image feature scale and orientation; in other words, the cells perform a basis function fit on the input. This notion of visual system filters has progressed as being conceived of as Fourier transforms^{48,49} to windowed Fourier transforms such as Gabor transforms,^{50,51} to sums of Gaussian functions,⁵² and finally to wavelet transforms.⁵³

If these models are correct, researchers have asked, why were wavelet type basic functions realized in the biological vision systems that have evolved? A compelling answer, suggestive of much further research is that the statistical distributions of values in natural scenes (trees, landscapes, rocks, grass, and so on) dictate that orthogonal (decorrelated) basic functions provide the best fit to the observed statistical properties of natural scenes.⁵⁴ Natural scenes present considerable redundancy and orthogonal wavelet transforms provide an economic means of reducing this redundancy. While we are accustomed to this use of wavelets for image compression, compression is not the point of visual system neural coding. Rather, it has been proposed⁵³ that wavelet transforms realized in neuronal receptive field shapes allow for the reduction of correlations between the responses of different neurons, and thereby allows any one neuron to encode maximal information about the stimulus. Wavelet-based codes would be selected for because their scales could match the localized band-restricted structure the values of the retinal images of natural scenes take on. With decorrelation, the activity of any given cell is relatively independent of the activity of other cells, and inspection of a bank of such neuron activity at the next higher level of neuronal processing would allow the detection and extraction of complex structures characteristic of the statistics of natural scenes in the input signal.

While we are familiar with the attributes and the advantages of wavelets in modern computer image analysis, it is clear that wavelets are an exciting aspect of computer image analysis that has great power to extend our knowledge of the algorithms and implementation of seeing systems further. In computational image analysis, in particular in applications such as automated biomedical image analysis and computer-aided manufacturing,

numerous current successful applications of statistical learning algorithms are applied to make decisions that discriminate conditions that have been segmented from image spaces using wavelet transforms. The work described above suggests that wavelet transforms are an optimization built into biological vision systems. Visual science at present only poorly understands higher levels of cortical function that process output from lower levels of the visual processing system. Output of lower level visual processing is sent to higher cortical levels that in turn feedback to lower visual processing areas. Memory matching and output decisions based on those matching results occur as the observable results of visual perception and human behavior tell us. That is, our visual brain is very good at fast visual processing to respond to visual input, predict, and react to the predicted consequences of what we see. Is it possible that statistical methods used in image analysis and statistical decision processes are realized in biological neural systems for making effective visual discriminations based on visual system feature extraction?

The answer, it has been suggested, is yes. In addition to ideas on computational image analysis being drawn from biological vision systems, decision theory and the design of machine-learning algorithms have also been furthered by research on the visual cortex.^{55,56} This area of research represents the potential for future convergence of our models of biological vision with optimized algorithms for computer vision. At present, it is recognized that primate vision systems accomplish rapid identification of objects in the noisy visual space of natural scenes at speeds and accuracy superior to any current computer vision algorithms.⁵⁷ It has been pointed out that visual processing experiments, which use artificial visual stimuli, may mislead us about visual function, and the complexity of natural images may confound simple edge detectors or other low-level feature extraction methods.⁵⁸

Because of the hierarchical nature of the nervous system, hierarchical Bayesian analysis seems a natural fit to the problem of how higher visual processing areas might categorize the processing results of lower (cortical visual area 1) processing by recalling and matching abstracted properties of visual information held in memory in higher cortical centers. We recognize objects or familiar faces in many different levels of illumination, orientations, distances, and backgrounds, in motion or at rest. A comparison to hierarchical prior distributions of parameters representing different levels

of feature abstraction from visual stimuli stored in higher cortical areas would make accurate classification of lower visual processing information possible, if the computational machinery of hierarchical Bayesian inference were realized in neuronal circuits.⁵⁸ The store of prior distributions of abstracted parameters of visual targets could be learned from experience and stored in relatively compact form in memory.

The possibility of hierarchical Bayesian methods being realized in the function of neuronal circuits has been argued convincingly by several authors.^{55,56,58} Furthermore, the concept of hierarchical processing across levels of the visual system and higher cortical centers suggests a number of testable hypotheses, some of which have been evaluated by fMRI and behavioral experiments.⁵⁷ Overall, the most compelling conclusion of this line of research is that the brain is apparently using algorithms as sophisticated (and perhaps identical to) the most advanced methods used in current image analysis and computational science. A further exciting aspect is that the brain is likely using methods we have yet to learn that are even more intricate and efficient than the best of our current computational methods.⁵⁸

In conclusion, the visual system is the best-studied sensory system. It has incredible facility for rapid recognition of objects in the visual field and evocation of appropriate responses. As our understanding of higher processing in the visual system advances, we have great opportunity for learning and profiting from the methods used by the optimized biological image processors that have resulted from eons of natural selection.

References

1. Horridge, G.A. The evolution of visual processing and the construction of seeing systems. *Proc R Soc Lond Biol Sci* **230**:279–292, 1987.
2. Barton, R.A. Binocularity and brain evolution in primates. *Proc Natl Acad Sci USA* **101**(27):10113–10115, 2004.
3. Steering Committee on Science and Creationism, National Academy of Sciences. *Science and Creationism: A View from the National Academy of Sciences*, Second edition, ISBN: 0-309-53224-8, 48 pages, National Academy Press, Washington, DC, 1999. Free PDF can be downloaded from: <http://www.nap.edu/catalog/6024.html>.
4. Berson, D.M. Strange vision: ganglion cells as circadian photoreceptors. *Trends Neurosci* **26**:314–320, 2003.

5. Hattar, S., Liao, H.W., Takao, M., Berson, D.M., and Yau, K.W. Melanopsin containing retinal ganglion cells: architecture, projections, and intrinsic photosensitivity. *Science* **295**:1065–1070, 2002.
6. DeYoe, E.A. and Van Essen, D.C. Concurrent processing streams in monkey visual cortex. *Trends Neurosci* **11**:219–226, 1988.
7. Van Essen, D.C. and DeYoe, E.A. Concurrent processing in the primate visual cortex. In: Gazzaniga, M.S. (ed.), *The Cognitive Neurosciences*, pp. 383–400, MIT Press, Cambridge, MA, 1995.
8. Kandel, E.R., Schwartz, J.H., and Jessel, T.M. *Principles of Neural Science*. Fourth edition, 1414 pp. McGraw-Hill, New York, NY, 2000.
9. Guillery, R.W. Observations of synaptic structures: origins of the neuron doctrine and its current status. *Phil Trans R Soc B* **360**:1281–1307, 2005.
10. Hodgkin, A.L. and Huxley, A.F. A quantitative description of membrane current and its application to conduction and excitation in nerve. *J Physiol (Lond)* **117**:500–544, 1952.
11. Hodgkin, A.L. and Ruston, W.A.H. The electrical constants of a crustacean nerve fibre. *Proc R Soc Lond Biol Sci* **133**:444–479, 1946.
12. Armstrong, C.M. Voltage-dependent ion channels and their gating. *Physiol Rev* **72**:S5–S13, 1992.
13. Armstrong, C.M. and Hille, B. Voltage-gated ion channels and electrical excitability. *Neuron* **20**:371–380, 1998.
14. Hodgkin, A.L. and Katz, B. The effect of sodium ions on the electrical activity of the giant axon of the squid. *J Physiol (Lond)* **108**:37–77, 1949.
15. Huxley, A.F. and Stampfli, R. Evidence for saltatory conduction in peripheral myelinated nerve fibres. *J Physiol* **108**:315–339, 1949.
16. Furshpan, E.J. and Potter, D.D. Mechanism of nerve-impulse transmission at a crayfish synapse. *Nature* **180**:342–343, 1957.
17. Goodenough, D.A., Goliger, J.A., and Paul, D.L. Connexins, connexons and intracellular communication. *Ann Rev Biochem* **65**:475–502, 1996.
18. Gordon, W.C. and Bazan, N.G. Retina. In: John J. Harding (ed.), *Biochemistry of the Eye*, Chapman and Hall, London, 1997.
19. Schnapf, J.L. and Baylor, D.A. How photoreceptor cells respond to light. *Sci Amer* **256**:40–47, 1987.
20. Stryer, L. Cyclic GMP cascade of vision. *Ann Rev Neurosci* **9**:87–119, 1986.
21. Hecht, S., Shlaer, S., and Pirenne, M.H. Energy at the threshold of vision. *Science* **93**:585–587, 1941.
22. Kuffler, S.W. Discharge patterns and functional organization of mammalian retina. *J Neurophysiol* **16**:37–68, 1953.
23. Schiller, P.H., Sanall, J.H., and Maunsell, J.H.R. Functions of the on and off channels of the visual system. *Nature* **322**:824–825, 1986.
24. Schnapf, J.L., Kraft, T.W., and Baylor, D.A. Spectral sensitivity of human cone receptors. *Nature* **352**:439–441, 1987.
25. De Valois, R.L. and De Valois, K.K. A multi-stage color model. *Vision Res* **33**:1053–1065, 1993.
26. Dacey, D.M. Circuitry for color coding in the primate retina. *Proc Natl Acad Sci USA* **93**:582–588, 1996.

27. Shapley, R. and Perry, V.H. Cat and monkey retinal ganglion cells and their visual functional roles. *Trends Neurosci* **9**:229–235, 1986.
28. Merigan, W.H. and Maunsell, J.H.R. Macaque vision after magnocellular lateral geniculate lesions. *Vis Neurosci* **5**:347–352, 1993.
29. Livingstone, M.S. and Hubel, D.H. Segregation of form, color, movement, and depth: anatomy, physiology, and perception. *Science* **240**:740–749, 1988.
30. Hubel, D.H. and Wiesel, T.N. Receptive fields of single neurons in the cat's striate cortex. *J Physiol (London)* **148**:574–591, 1959.
31. de Angelis, G.D., Ohzawa, I., and Freeman, R.D. Receptive field dynamics in the central visual pathways. *Trends Neurosci* **18**:451–458, 1995.
32. Kuffler, S.W. and Nichols, J.G. *From Neuron to Brain: A Cellular Approach to the Function of the Nervous System*, Sinauer Associates, Sunderland, MA, 1976.
33. Michael, C.R. Color vision mechanisms in monkey striate cortex: dual-opponent cells with concentric receptive fields. *J Neurophysiol* **41**:572–588, 1978.
34. Tootel, R.B.H., Silverman, M.S., Switkes, E., and DeValois, R.L. Deoxyglucose analysis of retinotopic organization of the second visual area in primates. *Science* **220**:737–739, 1982.
35. LeVay, S., Hubel, D.H., and Wiesel, T.N. The pattern of ocular dominance columns in macaque visual cortex revealed by a reduced silver stain. *J Comp Neurol* **159**:559–575, 1975.
36. Horton, J.C. and Adams, D.L. The cortical column: a structure without a function. *Phil Trans Biol Sci* **360**:837–862, 2005.
37. Hubel, D.H. and Wiesel, T.N. Receptive Fields of cells in striate cortex of very young, visually inexperienced kittens. *J Neurophysiol* **26**:994–1002, 1963.
38. Hubel, D.H. and Wiesel, T.N. The period of susceptibility to the physiological effects of unilateral eye closure in kittens. *J Physiol* **206**:419–436, 1970.
39. Shomstein, S. and Behrmann, M. Cortical systems mediating visual attention to both objects and spatial locations. *Proc Natl Acad Sci USA* **103**:11387–11392, 2006.
40. Le Bihan, D., Urayama, S., Aso, T., Hanakawa, T., and Fukuyama, H. Direct and fast detection of neuronal activation in the human brain with diffusion MRI. *Proc Natl Acad Sci USA* **103**:8263–8268, 2006.
41. Gattass, R., Nascimento-Silva, S., Soares, J.G.M., Lima, B., Jansen, A.K., Diogo, A.C.M., Farins, M.F., Marcondes, M., Bothelho, E.P., Mariani, O.S., Azzi, J., and Fiorani, M. Cortical visual areas in monkeys: location, topography, connections, columns, plasticity and cortical dynamics. *Philosophical Transactions of the Royal Society (London)* B 709–731. Online publication 29 April, 2005.
42. Marr, D. *Vision*. Freeman and Co., New York, 1982.
43. Roberts, L.G. Machine perception of three-dimensional solids. In: Tippett, J.T., Berkowitz, D.A., Clapp, L.C., et al. (eds.) *Optical and Electro-optical Information Processing*, MIT Press, Cambridge, MA, 1965.
44. Marr, D. and Hildreth, E.C. Theory of edge detection. *Proc R Soc Lond Biol Sci* **207**:187–217, 1980.
45. Canny, J.F. A computational approach to edge detection. *IEEE Trans Pattern Anal Mach Intell* **8**:769–798, 1986.
46. Deriche, R. Using Canny's criteria to derive an optimum edge detector recursively implemented. *Int J Comput Vis* **2**:167–187, 1987.

47. DeValois, R.L. and DeValois, K.K. *Spatial Vision*, Oxford University Press, New York, 1988.
48. Campbell, F.W. and Robson, J.G. Application of Fourier analysis to the visibility of gratings. *J Physiol* **197**:551–556, 1968.
49. Blakemore, C. and Campbell, F.W. On the existence of neurons in the human visual system selectively sensitivity to the orientation and size of retinal images. *J Physiol* **203**:237–260, 1969.
50. Marcelja, S. Mathematical description of the responses of simple cortical cells. *J Opt Soc Am* **70**:1297–1300, 1980.
51. Jones, J. and Palmer, L. An evaluation of the two-dimensional Gabor filter model of simple receptive in cat striate cortex. *J Neurophysiol* **58**:1233–1258, 1987.
52. Stork, D.G. and Wilson, H.R. Do Gabor functions provide appropriate descriptions of the visual cortical receptive fields? *J Opt Soc Am A* **7**:1362–1373, 1990.
53. Field, D.J. Wavelets, vision and the statistics of natural scenes. *Philosophical Trans R Soc Lond A* **357**:2527–2542, 1999.
54. Field, D.J. What is the goal of sensory coding? *Neural Comput* **6**:559–601, 1994.
55. Lee, T.S. and Mumford, D. Hierarchical Bayesian inference in the visual cortex. *J Opt Soc Am Opt Image Sci Vis* **20**:1434–1448, 2003.
56. Friston, K. A theory of cortical responses. *Philosophical Trans Biolo Sci* **360**:815–836, 2005.
57. Kourtze, Z. and DiCarlo, J.J. Learning and neural plasticity in visual object recognition. *Curr Opin Neurobiol* **16**:152–158, 2006.
58. Friston, K. Hierarchical models in the brain. *PLoS Comput Biol* **4**:1–24, 2008.