On the specificity of neurons and visual areas

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Abstract

The dominant view during the past 40 years has been that the visual system analyzes the visual scene by breaking it down into basic attributes such as color, form, motion, depth and texture. Individual, dedicated neurons and specific visual areas were believed to be devoted to the analysis of each of these attributes. Current research has challenged these views by emphasizing that neurons, especially in the cortex, have multifunctional properties and therefore serve as general-purpose analyzers rather than feature detectors. Consequently, it appears that most extrastriate visual areas, rather than each being devoted to the analysis of a specific basic visual attribute, perform several different tasks and thereby engage in more advanced and complex analyses than had been realized.

Keywords: Visual system; Neuron; Visual area; Visual perception

In every field of science time brings about ever changing views. Hypotheses, theories, and sometimes even facts, like living organisms, rise and demise. In the young field of neuroscience we are at the threshold of major changes in our thinking about the workings of the brain that challenge those concepts that have occupied the center stage for the past four decades. Here I will provide a brief overview of the initial ideas about neuronal and areal specificity, how and why they have come under attack today, and what new ideas are about to replace them.

1. The specificity of neurons

In 1906 Santiago Ramon y Cajal traveled to Stockholm to receive the Nobel Prize in Medicine and Physiology he was to share with Camillo Golgi. At the ceremonies Cajal gave a gracious address, the central focus of which was his enunciation of the neuron doctrine. He was followed on the podium by Camillo Golgi who proceeded to attack Cajal viciously while promulgating his own reticular theory. Ironically, these two radically different views of nervous tissue organization, which formed one of the hottest debates of the time, were derived from the same reduced silver-stain method fortuitously discovered by Golgi; looking at such tissue through the microscope Golgi saw a continuous network whereas Cajal perceived individual neurons whose processes were in close apposition to, but not continuous with other neuronal processes [8]. After a protracted battle the neuron doctrine won out and went on to have a major influence on our views of nervous tissue function.

One of the central ideas that has emerged from this effort is the specificity of individual neuronal analysis. This idea had become deeply ingrained in Cajal’s thinking. A specific example comes from his work on the retina and pertains to the inferences he made about the rod and cone pathways. That there are two different kinds of photoreceptors – the rods and the cones – was discovered by Schultze in the 1860s; he conjectured that the rods are for crepuscular vision having observed that they do not exist in the fovea where night vision is poor. Cajal, with excellent anatomical methods at his disposal, wanted to understand the manner in which the rods and cones made their central connections. He reasoned as follows [8]:

“Since the impression received by the rod is different from that taken up by the cone, it is necessary from every point of view that each of these specific impressions
should be conveyed through the retina by a separate channel.”

“When we reason with common sense and lift the war club determined upon vigorous action, nature ultimately hears us. Knowing what I was looking for, I began to explore eagerly... and finally, as the reward of my faith, there deigned to appear most clearly and brilliantly those two types of bipolar cells demanded by theory and guessed by reason... Observe how one variety of bipolar makes a contact...with the body of a certain giant ganglionic neuron... The bipolar cell for the cone... comes into relation with the...medium and small ganglionic cells.”

Here we have what appears to be the first compelling evidence in the visual system for the creation of two parallel pathways, one for the cones and the other for the rods, which Cajal believed to course independently to the central nervous system via separate sets of ganglion cells and perform different analyses. This arrangement is depicted in Fig. 1A. Cajal’s view, as we shall see has recently been effectively challenged.

The neurocentric thought that ascribes highly selective functions to single neurons reached its zenith with the advent of single-cell recordings. Much as the atom had at one time been thought to be the basic unit of matter, the neuron had become the basic functional unit of the brain. Neurons were thought of as feature detectors that extracted specific attributes from the environment [4]. Driven by convictions much like Cajal’s when he conceived of the rod and cone pathways, neuroscientists soon discovered high levels of specificity in many parts of the visual system.

The first recordings from single cells in the visual system were made by the Nobel laureate Halden Keffer Hartline, who arrived at this great achievement by painstakingly dissecting the fibers of the frog optic nerve [20]. His effort yielded immediate payoff by revealing that retinal ganglion cells are of three different types: ON, OFF and ON/OFF, a discovery that became all the more remarkable when it was determined subsequently that the ON and OFF systems are formed not at the level of the photoreceptors, which all hyperpolarize to light and have only graded potentials, but at the level of the bipolar cells, one set of which conserves and the other of which inverts the signals it receives from the photoreceptors [76]. Thus, at the level of the bipolar cells, a dual system is created from a single one. That nature has gone to such complexities suggests that great benefits must be reaped from this arrangement for the analysis of visual information. The initial ideas were that the ON system signals the onset of light and the OFF system the termination of light. As first suggested by Richard Jung, another idea that has gained some degree of acceptance was that the ON system gives rise to the perception of brightness and the OFF system to the perception of darkness [34]. A third consideration was advanced by more physiologically-minded investigators, who suggested that the ON and OFF systems have evolved to provide for the antagonistic center-surround organization of receptive fields in retinal ganglion cells and in the cortex [61].

Further advances and inferences about neuronal function soon followed: the studies of Barlow and of Lettvin and his collaborators identified bug-detector and edge-detector neurons in the frog retina [3,38,46]. In the mammalian cortex the Nobel laureates Hubel and Wiesel discovered neurons that responded selectively to the

![Fig. 1. The basic inferred connections of the rods and cones in the primate retina. (A) Cajal's model according to which the rods and cones connect, via the rod and cone bipolars, to rod and cone ganglion cells yielding thereby separate pathways to the central nervous system. (B) Connections of the rods and cones as determined in recent studies showing that ganglion cells receive convergent input from the rods and the cones; the cone bipolars make direct connections with the ganglion cells while the rod bipolars make their connections via amacrine cells. For a more detailed account of these connections for the ON and OFF channels and for various other classes of retinal ganglion cells see Waessle and Boycott [73] and Schiller [61].](image-url)
orientation, length and width of line segments or to specific directions of motion [27-29]. A hierarchic principle emerged according to which the geniculate input to cortex first forms simple cells, an aggregate of which gives rise to complex cells that in turn, create hypercomplex neurons. Along with this idea came the notion that the visual system first breaks down the visual scene into fine elements, such as the orientation of line segments, spatial frequencies, specific colors, directions of motion and so on, and then somehow combines these attributes to yield a perception of the world [42,43]. This view has led to the idea of the pontifical neuron which, when it fires, signals such highly complex attributes as the faces of specific personages [4].

Subsequently, many of the discoveries of visual system organization were interpreted with these ideas of neuronal specificity in mind. One of the major findings following on the heels of striate cortex organization was that several parallel pathways, in addition to the rod and cone systems and the ON and OFF channels, originate in the retina [12,60,71]. This was interpreted as further proof that the visual scene is, indeed, broken down into specific sub-elements in the visual system. Among the parallel pathways identified were the cat X, Y and W channels that subsequently acquired several different names as they were found in just about every species that had been subjected to study. In the primate, the putative analogue to the X and Y systems was identified as the midget and the parasol; midget because of the size of the cells, parasol because of the umbrella shaped arbors [75]. Driven by the prevalent view of the times, these two systems were conceived of as extracting different attributes from the visual scene. What exactly these attributes were was not fully agreed upon; according to one view, the midget system, coursing through the parvocellular portions of the lateral geniculate nucleus toward visual cortex, extracts color and the parasol system, coursing through the magnocellular layers of the lateral geniculate nucleus, extracts luminance information. Subsequently new complexities were realized; the midget system was thought to extract both color and form, and the parasol system both motion and stereopsis [42,60]. Thus the idea that the visual scene is broken down into specific basic subunits persisted; what varied was the specific subunits to which the various systems responded.

Just what the basic elements are of visual perception and how many elements there might be remains an unsettled issue to this day. Dominated by philosophical thought and psychological insight, however, it was proclaimed that visual perception is, indeed, broken down into logical subunits; implicit in such thought was the assumption that such subunits should have their counterparts in the brain. The basic elements of visual perception were conceived to be color, form, depth, motion and texture. The assumed neural isomorphism demanded that there be neurons and brain areas that perform these analyses. Even more problematic, if often ignored, was the problem these assumptions created: once broken down into various categories, how does the brain put the image together again? One of my students, Karl Zipser, aptly refers to this as the Humpty Dumpty problem:

Humpty Dumpty sat on a wall, Humpty Dumpty had a great fall; All the King's horses, and all the King's men cannot put Humpty Dumpty together again.

Until recently, then, the prevalent view that has occupied center stage in systems neuroscience is that individual neurons perform dedicated, unique and highly specific analyses of a basic nature.

2. The specificity of brain areas

The specificity of brain tissue has, of course, been debated extensively well before Cajal carved his indelible impressions onto the history pages of biology. Francis Joseph Gall, the father of phrenology, postulated not only that different brain areas perform different jobs, but that qualities in which an individual excels are a product of a greater than average amount of brain tissue devoted to that particular quality which, in turn, is reflected in the protrusions of the skull. He and John Gaspar Spurzheim systematized these qualities and their putative locations in 1809 [15]. Many textbooks to this day are graced by the fanciful picture of the human head with inscriptions designating the 'mental faculties' that were believed to reside in the various brain regions. The fact that scientific thought is strongly driven by the outlook, the values and the politics of the times was clearly reflected in the selection of these qualities: of Spurzheim's 35 areas, 21 were devoted to such propensities and sentiments as amativeness, cautiousness, benevolence, veneration, wonder and ideality. Qualities that in today's world brain scientists – or anyone else for that matter – would allocate only limited space in the brain at best.

While the methods used to derive these brain functions have been much scorned, the idea of areal specificity persisted, soon to be supported by much more respectable efforts. Studying patients with brain injuries Broca and Wernicke identified centers for the processing of language and, after a few false starts, Hermann, Munk and others, established that the primary visual cortex is located in the occipital pole [16]. These findings led, on the one hand, to the elusive task of specifying all brain areas and, on the other, to the denial of specificity for many functions. In the occipital lobe, nearly a hundred years ago, Brodmann histologically differentiated areas 17, 18 and 19, and proposed that each has a distinct visual function [7]. Documented first in the visual cortex
by Talbot and Marshall in 1941 using evoked potentials [73], it was established that in most visual areas the retinal surface – and hence the visual field – is laid out in an orderly fashion. Physiological mapping studies took this discovery several steps further by uncovering many more visual cortical areas, in most of which an orderly representation of the visual field was demonstrated [13].

Fueled in part by the pervasive trend toward neuronal specificity, many brain areas were explored using single-cell recordings that ushered in a new age of phrenology. As more and more brain regions were identified and investigated, in most stunning specificity was documented. That each of these areas has evolved for the purpose of analyzing a specific visual attribute became the most popular and most widely embraced view. In 1970, Hubel and Wiesel published a paper in Nature declaring area 18 (V2) to be the region that is uniquely involved in the analysis of stereoscopic depth perception [31]. Zeki came along shortly thereafter claiming that area V4 is the region devoted to color analysis and area V5 (MT) to the analysis of motion, giving rise thereby to the one-area-one-function hypothesis [80,81]. Among the most celebrated were the neurons recorded in the inferotemporal cortex of the monkey that responded selectively to faces and toilet brushes [17]. Here, at last, seemed to be a region where pontifical cells resided for the perception of complex visual attributes.

The topographic order seen in the visual cortex, coupled with the orderly arrangement of the left and right eye inputs and the orientation selectivity of V1 neurons, led to specific hypotheses about the functional organization, or cytoarchitecture of this area and, subsequently, extrastriate regions. Hubel and Wiesel proposed an elegant model, referred to by some as the ‘ice cube’ model as shown in Fig. 2, according to which the striate cortex is composed of hypercolumns, each of which represents a small region of the visual field within which a full complement of orientations and the left and right eye inputs reside, thus comprising the basic module necessary to perform the local calculations – whatever they might be – for perceptual analysis [33].

A new level of complexity in the organization of extrastriate cortex was realized when Margaret Wong-Riley discovered the cytochrome oxidase 'puffs' in area V1, an orderly distribution of small, metabolically active ovoid regions of about 25 by 150 μm which were shown to form neat rows centered within each of the ocular dominance columns [26,30,79]. This new finding suggested that another, yet unrealized specialization exists in the striate cortex. In hot pursuit of this curious new discovery, it was soon claimed that the puffs contained cells that were unoriented and color selective [41]. These claims were taken as further proof that the visual scene is, indeed, broken down into the basic attributes of color, form, motion and depth. Specific projections were identified from V1 to other extrastriate areas in support of the specificity of areas for the analysis of color, motion and stereopsis. Revised models followed, one of which is shown in the middle part of Fig. 2, to which one might refer as the radial model.

Further intricacies in the organization of the striate cortex were uncovered when, after arduous and clever efforts, optical recording methods succeeded. Re-examination of striate cortex organization now revealed curious discontinuities or fractures. The stunning pictures generated from this work yielded additional impressions of the spatial layout of striate cortex [5,6]. An example of this is shown in the bottom panel of Fig. 2, entitled the swirl model, which shows the spatial arrangement of orientation selectivities in a patch of cortex; the dark areas designate regions of discontinuity in the layout of orientations.

These relatively modest modifications in the perceived layout of the striate cortex did not question the central
principles of columnar and laminar organization. Anatomical studies disclosed well-defined laminations and established that the inputs from the midget and parafol hemispheres coursing through the lateral geniculate nucleus terminate in separate cortical layers, with the parafol system terminating in layer 4c alpha and the midget system terminating in 4c beta [32].

In one of the most elegant, and at the same time most ambitious schemes, Ungerleider and Mishkin went on to propose that area V1 gives rise to two major information processing streams [74]. According to this hypothesis the so-called dorsal stream receives its input predominantly from the parafol system and courses toward the parietal lobe via areas MT and MST; it was proposed that this pathway plays a central role in the analysis of space, depth and motion. The second, so-called ventral stream, courses toward the temporal lobe via area V4; it was proposed to be involved predominantly in shape and color perception. The basic structures and hypothesized connections of this model are shown in Fig. 3.

Following on the heels of the discovery and the specification of the visual areas in mammals were lesion studies that lent additional support to the one-area-one-function hypothesis. Lesions of area V4 showed deficits in color vision, especially color constancy, and lesions of area MT showed deficits in motion perception [54,78]. Perhaps most dramatic were studies that showed highly selective deficits in humans such as achromatopsia following lesions of regions that putatively included area V4 [23,24,82].

Coupled with the idea of dedicated, specific neuronal analysis, the dominant thought until recently has been that visual areas are highly specific and perform unique visual analyses.

3. Countercurrents to neuronal specificity

Emblematic of events to come that are reshaping our ideas about neuronal specificity today, was the discovery that Cajal's impressions about the connections of the rods and cones were not quite correct. While the rods and cones do, indeed, have their own bipolars, it has now been established that they do not feed into separate pathways coursing toward the central nervous system [61,75]. Instead, in those portions of the retina where rods and cones coexist, ganglion cells receive a convergent input from them and do so via different intraretinal pathways. Consequently, when ganglion cells are driven by the cones, they can contribute to color vision whereas at night, when driven by the rods, they subservie achromatic, crepuscular vision. Thus the same ganglion cell can process two rather different kinds of signals. Also discovered was the fact that both the midget and the parafol retinal ganglion cells receive convergent input from the rods and cones [67,77]. These findings seriously question the idea of labeled lines and highlight the multifunctional properties of neurons even at early stages of visual processing.

Further studies provided additional evidence regarding the multiplicity of messages carried by the ganglion cells. With the discovery of the midget and parafol systems, which were seen as pathways that broke down the visual scene into different components, it has been suggested that the midget system carries wavelength

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**Fig. 3.** Basic hypothesized connections of the midget, parafol and W cells of the retina. The midget cells project to the parietal lobe via the parvocellular layers of the lateral geniculate nucleus, areas V1 (striate cortex), V2 and MT. The parafol cells project to the temporal lobe via the magnocellular layers of the lateral geniculate nucleus, areas V1, V2 and V4. The W cells project to the superior colliculus. For sake of clarity omitted are interconnections among these structures and the projections of the parafol and W cells to other subcortical regions.
information and the parasol system luminance information. This attractive idea, however, was short-lived. Even the earliest single-cell recording studies – the very ones that had shown that the rod and cone input converges on ganglion cells – established that both the midget and the parasol systems are capable of carrying luminance information [77]. Studies in which the visual capacities of animals were examined following selective disruption of either the midget or the parasol systems showed that most basic visual functions, such as brightness, texture, pattern, shape, motion, flicker and depth perception, as well as scotopic and photopic vision, are carried out by both systems [66,67]. The major difference is that the midget system can process information up to higher spatial frequencies, whereas the parasol system can do so up to higher temporal frequencies (see Fig. 7). The exception is differential wavelength analysis, which appears to be done exclusively by the midget system. These findings led to the idea that the midget and parasol systems have evolved not for the purpose of analyzing different basic visual attributes, but to extend the range of vision, with the midget system extending it in the spatial and wavelength domains and the parasol system extending it in the temporal domain [66]. This inference applies also to the rods and cones of the retina whose emergence has resulted in extending the range of vision in the light intensity domain.

Early ideas about the functions of the ON and OFF systems that originate in the retina have also given way to different views, largely brought about, as is so often the case, by technical advances. One of these was the use of a newly created artificial neurotransmitter analogue, 2-amino-4-phosphonobutyrate (APB), which was shown to render inoperative the ON bipolar cells without significantly affecting the OFF bipolars [61,70]. This made it possible to examine the consequences of reversibly blocking the ON system on the activity of single cells in various parts of the visual system and also to determine how this procedure affects visual perception [59,61]. These studies established that after ON channel block with APB, OFF cells for the most part retain their center surround organization and cortical cells retain their direction and orientation specificities. It appears, therefore, that the ON and OFF channels did not evolve to create center/surround organization or other receptive field attributes such as orientation and direction specificity in the cortex. Studies in which APB was used to block the ON channel in animals trained to perform on a variety of visual tasks, showed that the prime deficit lay in the ability to detect visual stimuli made visible by virtue of light increment, but not by light decrement. These and related findings suggest, therefore, that the reason the ON and OFF channels have evolved might have been to optimize information transfer by having excitatory processes for both increments and decrements in illumination. The rapidity with which events in the visual world need to be processed in the animal kingdom is at a premium. A fish in the ocean, in order to survive, must be able to respond with minimum delay both to a bird looming dark against the sky as it swoops down and a predatory fish that rises from the dark depths illuminated from above; the OFF systems provides the best signal for the approaching bird and the ON system for the fish.

Surprisingly, visual acuity using high-contrast stimuli is little affected by blocking the ON channel with APB as a result of which half of the bipolar cells in the retina are rendered inoperative. This finding is less baffling now because refined anatomical studies have established that in the central retina of the primate, each cone gives rise to at least two midget bipolar cells and two sets of retinal ganglion cells whose dendritic processes arborize in different sublamina in the inner plexiform layer. In the retina and also in the lateral geniculate nucleus the ON and OFF channels in the midget and parasol systems remain separate [53,61,75]. However, in the striate cortex many cells receive convergent input from all of these systems indicating once again, the consequent multifunctional properties of neurons.

Attesting to the complexity of the visual system is the fact that in the retina there is a class of ganglion cells that falls into the grab-bag category of W-cells which receive a convergent input from ON and OFF bipolar cells, thereby forming cells of the sort already noted by Hartline: the ON/OFF ganglion cells. The W-cells as well as the parasol cells project to several visual nuclei in the primate that include the thalamus, the pretectum and the superior colliculus [22,45,60,66,71]. The midget ganglion cells, however, send their axons only to the lateral geniculate nucleus.

It is noteworthy that the ON/OFF organization seen in the retina has its counterpart in the temperature receptors of the somatosensory system, one set of which is excited by increases and the other by decreases in temperature; both are thereby signalled to the central nervous system by an excitatory process.

Since retinal ganglion cells and LGN cells are capable of carrying numerous messages, it should come as no surprise that cells in the striate cortex, rather than extracting a single feature from the visual scene, have greatly expanded multifunctional properties. Striate cortex cells by virtue of extensive interconnections, transform the thalamic input in a variety of ways. While it is well known that cells in the striate cortex show selectivity for orientation, direction, spatial frequency, wavelength, and depth, often overlooked is the fact that many or all of these properties are commonly found in a single cell. Thus many single cells, rather than being selective for a single specific feature of the visual scene, such as orientation of line segments or direction of motion or a specific color, respond to many different features. That cortical
cells have such multipurpose properties has already been shown in early papers by Hubel and Wiesel [27,29]. It is evident, then, that a given cell will respond to motion when present in the visual scene and will, in addition, respond to line segments of certain orientation in the absence of motion, to small stimuli that contain little information about orientation, to a range of colors when the cones are active and to achromatic stimuli under dark adapted conditions; in addition, the cell's response may be modulated by stereoscopic depth and spatial frequency. These cells, therefore, can convey information about many different aspects of the visual scene: They are multifunctional.

While it was recognized early on that in the striate cortex there is convergent input to single cells from the ON and OFF channels and from the two eyes, it has been assumed that such convergence does not take place for the midget and parasol systems. Instead, these systems were believed to remain separate in the striate cortex and beyond as is depicted in Fig. 3. This issue was examined in a series of studies in which either the parasol or the midget system were selectively blocked at the level of the lateral geniculate nucleus while recording from single neurons in the striate cortex [45]. The results established that while some cells are, indeed, driven selectively by the midget or the parasol systems, there are numerous cells which receive a convergent input from these two systems. Fig. 4 depicts this state of affairs to highlight the multiprocess processing properties of individual striate cortex cells.

Early alternatives to the cortical feature detector idea, which resulted from the discovery of spatial frequency selectivity in the striate cortex, were models in which cells acted as spatial and temporal filters. Rather than extracting specific features, neurons were thought to form classes within each of which cells responded optically to different portions of a continuum such as spatial frequency [10]. This was an idea akin to the way Young and Helmholtz thought about the processing of wavelength information.

The neuronal specificity inferred by the feature detector model gives rise to another major problem: it would require an inordinately large number of neurons in the brain to cope with the incredible richness and variety present in the visual scene, numbers which it fortunately does not possess. Such high specificity would also mean that most neurons would be silent most of the time, a rather uneconomical state of affairs. Yet economy in living organisms is of a premium. The more you can do with less the better. Size, weight and metabolic requirements must be kept to a minimum. To accomplish this, sensory analysis has to be optimized using every possible trick. An example of how the nervous system goes about economizing can be seen in the processing of wavelength information. While we can perceive hundreds of colors, there are only three photoreceptors. Contrary to 'common sense,' for the three photoreceptors to do a good job in recording the color image they need to be broadly rather than narrowly tuned; as a result, typically all three photoreceptors are activated by most stimuli but the ratio of their activity differs even for small differences in the wavelength composition of objects. To facilitate this process further and to increase sensitivity, the output of the photoreceptors is combined in an 'opponent fashion' forming just two major systems in the midget retinal ganglion cells, the red/green and blue/yellow [37]. How these signals are combined in the visual cortex to give rise to the hundreds of colors we are capable of discerning is only marginally known. Unlikely it would seem, however, that each color experience would be a product of singular neuronal activity.

Similar considerations apply to other sensory attributes, such as stereoscopic depth perception. At one time it had been assumed that there is a separate complement of neurons for each disparity in each hypercolumn that represents a tiny segment of the visual field. Such an arrangement would require an inordinate number of neurons. Instead, it appears now that stereopsis follows principles similar to those of color; only a few distinct disparities are coded [55,56]. The gamut of stereoscopic depths the organism is capable of perceiving is the product of computational processes that are derived from the relative activity of the different neuronal groups. Thus it appears that there is no specific neuron for each depth, just as there is no specific neuron for each color.

Another prevalent view that has recently come under scrutiny is the idea that striate cortical neurons have very small receptive fields whose analysis is consequently confined to very small regions of the visual field. Presaged by work on the retina showing surprisingly extensive lateral interactions [49], current work has
shown that in the striate cortex the responses of neurons can be dramatically influenced by events relatively distant from their receptive fields. Furthermore, such influence can be quite general in nature. Thus it has been shown that the responses of single cells can be modulated by a variety of stimulus conditions: borders that are made visible by texture differences, by luminance, depth, motion and color, can all influence a single cell. An example of this from the work of Zipser et al. [83] appears in Fig. 5. The data shown in this figure establish, first of all, that the presence of a border quite distant from the classical receptive field of the cell notably affects its response. Secondly, it shows that this effect occurs in the cell irrespective of the means by which the border is made visible; borders created by differences in texture composition, depth, motion and luminance all modify the response of a given neuron. The response modification is most evident during the latter portions of the discharge implicating possible feed-back systems to give rise to the effect. Thus it appears that many cells in the striate cortex, instead of being dedicated, have rather general properties that allow them to process several kinds of visual information.

Given these considerations, one might ask why earlier work has placed so much emphasis on the dedicated, feature detection properties of single cells in the visual system. The answer lies, in part, in the limitations of single-cell recordings from which the majority of the inferences have been derived. Most cells can be studied for only brief periods of time before they disappear from the tip of the microelectrode; during this brief period, their responses can be examined for only a rather limited set of stimulus conditions and the stability of the response over time cannot be assessed at all. These techniques are akin to showing a Martian a photograph of a deciduous tree taken in the winter. Based on such a picture the Martian would be most unlikely to gain the idea of leaves, of growth, of damage to the branches due to storms, and of the wide variety of species. Thus when it comes to single-cell physiology, we are much like Martians; we are limited to brief glimpses of a limited sample of neurons. And the sample is limited indeed. During a typical vertical electrode penetration through the two millimeters of cortical gray matter, investigators are lucky to isolate 4 or 5 cells out of the more than 100 that the electrode encounters in its path. Since much of the work has been carried out on paralyzed animals, it is difficult to imagine that the crucial role of the multifarious inputs that include feedback from higher cortical centers, would operate normally. In the case of the analysis of visual stimuli, it must also be recognized that the retinal images of even small objects, will drive thousands of cells, the response of each of which may be only be subtly modified and would be difficult to detect when studied singly.

When Alan Turing conceived of the computer, his ideas were modeled on how he thought the brain worked; the brain, he believed, was a general purpose instrument [25]. Now that computers have reached high levels of sophistication and have become part of everyday life, it is not uncommon to reverse this thought process and use computers as metaphors for the brain. The major input device to the early general purpose computers, however, was a dedicated keyboard not unlike the classic Underwood on which any key, when punched, produced a specific, invariant letter on the paper. By contrast, today's computers have been given keyboards with conditional properties; what the outcome is of pressing any given key depends on the program that is running and on what other keys have concurrently been activated. The situation is similar, but of course far more complicated and elaborate, even at early stages, in the visual system. Already the responses of retinal ganglion cells and certainly of striate cortex cells, is determined not only by the specific stimulus that appears in the center of the cell's receptive field, but, as just shown, on what other stimuli appear in the surrounding parts of the visual field and on what the state is of the system.

According to these new views, then, most neurons in the visual system are not dedicated to the analysis of a singular, highly specific basic feature of the visual scene. Instead, they have multipurpose properties and can integrate information over a considerable area; each neuron has the capacity to perform quite a number of different, if specific tasks. Thus rather than constituting dedicated systems, neurons, especially in the cortex, have
multipurpose properties and engage in parallel, integrated processing. It appears, therefore, that much as the atom is no longer regarded as the basic unit of matter, the neuron is no longer to be regarded as the basic information processing element of nervous tissue.

If specific sensations and perceptions are not signalled by the activity of dedicated sets of neurons, how else could this be accomplished? How can multipurpose neurons yield the necessary specificity? Several hypotheses have been advanced, according to most of which coding involves populations of neurons that produce different spatio-temporal signals for different percepts [48]. A straightforward, basic scheme exemplifying such ideas appears in Fig. 6 in which all connections are excitatory. Each horizontal trace depicts the activity of a different neuron, with the vertical lines representing action potentials generated during a short time period, say 500 milliseconds. In the first area, area V, circumscribed by the dotted rectangle, say the striate cortex, the activity of nine hypothetical neurons is shown whose receptive fields cover three adjacent locations, A, B and C. At each location the three neurons shown have different direction specificities, 1, 2 and 3. The cells respond to both stationary, flickering stimuli and to motion. In the upper display in Fig. 6 (FLICKER) responses elicited by a stationary flickering stimulus are depicted: all the cells whose receptive fields are stimulated by this stimulus discharge to each flash (cells B1, B2 and B3); the other cells remain silent since the stimulus is not within their receptive fields. In the lower display (MOTION) the responses elicited in these same cells are shown to a moving stimulus: only those cells selective to the particular direction of motion extant are activated (cells A2, B2 and C2).

Next it may be assumed that these cells make a variety of connections with other areas in the visual system, say areas MT and V4. In one case the information in this hypothetical scheme is pooled for space but not for direction (area X); in the other information is pooled for direction but not for space (area Y). As can be seen, cells in both of these areas continue to respond both the flashing and the moving stimuli but do so very differently. Even if the outputs of stages X and Y are combined (at area Z), the temporal patterning of activity is distinct thereby providing the opportunity to yield different sensations for flicker and for motion.

The scheme shown here is exceedingly simple. The majority of neurons, already in the striate cortex, have more than two specificities; furthermore, the interactions among neurons involve both excitatory and inhibitory circuitry. Increasing complexity by adding just one additional factor, such as color, for example, would necessitate a three dimensional representation in the scheme shown in Fig. 6. Additional capacities in multifunctional cortical cells, such as selectivity for spatial frequency or for stereoscopic depth, would add further dimensions to the scheme, and would yield so many possible interconnections and spatio-temporal response profiles that it would boggle the mind. Yet examination of the connectivity of cells within and between the various visual areas reveals a complexity that far exceeds what is seen most models that have been proposed [13, 44, 48].

4. Countercurrents to areal specificity

Adherents to the specialization of cortical function, spearheaded by Gall and Spurzheim in the beginning of the 19th century, encountered powerful opposition a hundred years later. In 1927, Heinrich Klüevers, in summarizing the visual functions of occipital cortex, concluded that it is impossible to reduce visual perception to simple capacities that are separately localized [35].
A more general argument was made by Henry Head (1926) who said [21]:

“No function is ‘localized’ strictly in any part of the cortex and no form of activity, somatic or physical, is built up into a mosaic of elementary processes which become evident when it is disturbed by a lesion of the brain."

These views received experimental support subsequently from Lashley whose influential lesion studies in rats showed that deficits in learning were a product not of what region of cortex, but of how much of it had been removed [36].

The ensuing anatomical and physiological discoveries during the past 40 years swung the pendulum back, reasserting the specificity of cortical areas. Now, as a result of many recent discoveries, the pendulum is once again on the reverse swing. A series of careful studies revealed that there are more than 30 visual areas in the primate cortex that make more than 300 interconnections [11,13]. Most of the extrastriate areas are not uniformly organized as one might expect; were each devoted to the execution of a single, unique function; instead, each area contains modules within which neurons perform a great variety of analyses. Even the claimed specificity within identified modules has come under fire recently. In the striate cortex, where modules defined by the cytochrome oxidase label had been thought to contain unoriented, color-selective cells and regions outside these areas orientation selective neurons, recent studies have failed to find such clearcut specialization [39,57,72]. In V2, the characteristics of neurons in the various anatomically identified modules have also been shown to exhibit less specialization than past studies had postulated [40].

These and related studies raised questions about the specificity of laminar and columnar organization in the visual cortex which were central to the idea of neuronal and areal specificity in the visual system. In addition to the studies questioning the selective nature of neuronal analysis in the various cortical modules, it was shown that the inputs and outputs of the striate cortex are not quite as specific as had been believed. The inputs from the lateral geniculate nucleus were shown to terminate not only in layers 4c alpha and beta (see Fig. 2), but in many other layers as well. The outputs from the deeper layers of the cortex were shown to project not only to subcortical areas but also to other cortical areas [44]. With the discovery of several other specific analyses by neurons, each assumed to be done within a specific little module, such as the analysis of spatial frequency, depth, direction, and color, just how all of these might be laid out in the cortex became quite a conceptual problem. It was established, furthermore, that simple cells, rather than being confined to layers that lie in close apposition to 4c, reside in most cortical layers. Studies failed to find compelling evidence for columnar or laminar organization for direction selectivity; in fact many simple cells were shown to have subfields with opposing selectivity for light and dark edges [64]. No obvious spatial organization has been demonstrated for spatial frequency and stereopsis in the primate. The segregation of the left and right eye inputs, while exhibiting clearcut columnar organization in layer 4c, turned out to be less obvious in other layers where most cells were shown to be binocularly activated. These new considerations highlight the multifunctional properties of neurons and regions in the striate cortex and suggest that a new, more dynamic model, superseding those shown in Fig. 2, may be just around the corner.

It was also discovered that the inputs to some of the extrastriate areas are not as specific as the one-area-one-function hypothesis would demand. Neurophysiological studies in which the midget or the parasol inputs to cortical cell were reversibly blocked at the level of the lateral geniculate nucleus, revealed that many cells in area V4 receive convergent input from both the midget and parasol systems [14]. Area MT, on the other hand, appears more specialized; it receives a predominant, although not unique, input from cells in V1 and V2 that are driven by parasol cells [47]. In fact, as noted in the previous section, many neurons already in V1 receive convergent input from the midget and parasol systems much like the retinal ganglion cells that receive convergent input from the rods and cones [45]. It has been estimated, in fact, that a single cell in area V4 receives input from several thousand V1 cells; each of these V1 cells is, in turn, influenced by input not only from many LGN cells, but also from lateral and feedback processes, from thousands of other V1 and extrastriate cells [9,58].

Recent studies that have examined the characteristics of single cells in area V4 have shown that this area is not uniquely devoted to the analysis of color [5,63,68]. Many cells process information about shape, depth and even motion. More strikingly, studies carried out in trained, behaving monkeys show that the responses of many of these cells are modulated by such factors as attention and the state of the animal; inputs through modalities other than visual can also have an influence [18,19,52,63]. Thus area V4 appears to have properties that in the past have been attributed to regions called ‘association cortex.’ Even in area MT, which for the most part continues to be perceived as a region devoted to the analysis of motion [1,2], it is clear that most single cells in addition to exhibiting directional preference, are also orientation specific; the cells respond vigorously to stationary stimuli that are flashed on and off or that impinge on the retina in the course of saccadic eye movements, suggesting that they participate in the analysis of the visual scene in the absence of motion information.

Current lesion studies for the most part lend strong support to a more generalist view of information process-
ing in the visual cortex. It can be safely asserted that selective lesions of areas V4 and MT in monkeys fail to ‘knock out’ highly specific basic visual functions [23, 24, 62, 68]. After MT lesions monkeys show deficits in motion and flicker perception, but do so only when the tasks introduced by the experimenter are made quite difficult. A surprising degree of motion processing is retained; furthermore, after MT lesions there is notable recovery with time. V4 lesions result in only mild to moderate deficits on color perception tasks and on pattern perception tasks. More pronounced deficits are evident, however, when tasks are used that necessitate higher-level analyses, such as the recognition of objects that have undergone various transformations (size and perspective changes, partial occlusions, etc.) visual learning, and the selection of objects in the visual scene that are smaller or have less contrast than other objects with which they appear.

It has also been established that paired lesions of areas V4 and MT do not produce deficits that are more than the sum of the deficits produced by the lesions separately. Such paired lesions fail to manifest deficits in brightness perception, stereopsis, and coarse shape perception. These findings are not in consonance with the two-streams hypothesis, according to which one stream passes through V4 and the other through MT, and indicate that additional pathways must be involved in visual information processing that bypass these two areas.

Fig. 7 provides a summary of deficit magnitudes on a broad range of visual capacities following lesions of the parvocellular and magnocellular portions of the lateral

### Deficit magnitude following PLGN, MLGN, V4 and MT lesions

<table>
<thead>
<tr>
<th>VISUAL CAPACITY</th>
<th>PLGN</th>
<th>MLGN</th>
<th>V4</th>
<th>MT</th>
<th>V4+ MT</th>
</tr>
</thead>
<tbody>
<tr>
<td>color vision</td>
<td>severe</td>
<td>none</td>
<td>mild</td>
<td>none</td>
<td>mild</td>
</tr>
<tr>
<td>texture perception</td>
<td>severe</td>
<td>none</td>
<td>mild</td>
<td>none</td>
<td>mild</td>
</tr>
<tr>
<td>pattern perception</td>
<td>severe</td>
<td>none</td>
<td>mild</td>
<td>none</td>
<td>mild</td>
</tr>
<tr>
<td>shape perception</td>
<td>severe</td>
<td>none</td>
<td>mild</td>
<td>none</td>
<td>mild</td>
</tr>
<tr>
<td>brightness perception</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>coarse scotopic vision</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>contrast sensitivity</td>
<td>severe</td>
<td>none</td>
<td>mild</td>
<td>mild</td>
<td>mild</td>
</tr>
<tr>
<td>fine/coarse</td>
<td>mild</td>
<td>none</td>
<td>mild</td>
<td>mild</td>
<td>mild</td>
</tr>
<tr>
<td>stereopsis</td>
<td>severe</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>fine/coarse</td>
<td>pronounced</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>motion perception</td>
<td>none</td>
<td>moderate</td>
<td>none</td>
<td>moderate</td>
<td>moderate</td>
</tr>
<tr>
<td>flicker perception</td>
<td>none</td>
<td>severe</td>
<td>none</td>
<td>pronounced</td>
<td>pronounced</td>
</tr>
<tr>
<td>choice of &quot;less&quot; stimuli</td>
<td>severe</td>
<td>none</td>
<td>severe</td>
<td>none</td>
<td>severe</td>
</tr>
<tr>
<td>visual learning</td>
<td>not tested</td>
<td>not tested</td>
<td>severe</td>
<td>none</td>
<td>severe</td>
</tr>
<tr>
<td>perception of transformed objects</td>
<td>not tested</td>
<td>not tested</td>
<td>pronounced</td>
<td>not tested</td>
<td>not tested</td>
</tr>
</tbody>
</table>

Fig. 7. Summary results of deficit magnitude on visual tests following lesions of the parvocellular and magnocellular portions of the lateral geniculate nucleus, of area V4, and area MT. The choice of ‘less’ stimuli refers to conditions in which monkeys perform on an oddity task in which one stimulus, the target is different from the other stimuli which are all identical; this target stimulus is smaller, has less contrast, or contains dots that move at a slower rate than do the other stimuli in the array. When the situation is reversed so that the target is the ‘greater’ stimulus the deficit seen is minimal in all cases. The perception of transformed objects refers to a condition in which the monkey performs on a match to sample paradigm and he has to make matches to samples that have been transformed in a variety of ways. The transforms include changes in the size of the match stimuli, in occluding them to various degrees and in varying the amount of contour information provided. The other visual tasks listed should be self explanatory. For details see Schiller et al. [66].
geniculate nucleus that selectively block the midget and parasol systems and of areas V4 and MT [62,66].

Clinical studies of patients have been another significant source of support for areal specificity [24,50,63,82]. It has been demonstrated, for example, that some patients with damage to the lingual and fusiform gyri of the occipital lobe have major deficits in color vision (achromatopsia). Although damage to visual cortex in most afflicted patients is not sharply confined, and typically involves both white and gray matter, these reports have been hailed as major support for areal specificity. However, it must be noted that clinical studies suffer from two serious fallacies. The first is a sampling fallacy. Published clinical case studies for the most part report on only interesting cases. Of the thousands of humans that suffer brain damage, only a handful make it into published reports. The plethora of unreported cases are likely to have deficits that are complex, diffuse and uninterpretable; hardly the stuff of a good report. What we have, therefore, is a heavily biased sample in favor of specificity that provides a simple and probably rather incorrect view of brain specialization. The second fallacy lies in the limited number of tests administered to the patient and the choice of these tests, typically based on preconceived notions. As an extreme example, if one hypothesizes that area V4 processes color and then proceeds to administer only tests for color vision, a deficit seen would, by exclusion, seem specific for this capacity. To assert specificity convincingly, a detailed battery of tests assessing many visual capacities is essential. These considerations suggest, therefore, that considerable caution must be exercised in inferring areal specificity from clinical reports.

During the past few years some of the most dramatic results raising questions about neuronal and areal specificity have come from studies examining the plasticity of the nervous system. What these studies revealed is that in many, but not all parts of the brain dramatic reorganization can take place. Several mechanisms have been identified. The rapidity with which some of these changes can occur suggest that dynamic, in-place networks are involved. Longer-term changes involving structural changes have also been documented. Some regions of course are more subject to such reorganization than are others. What is surprising that such changes have been reported to also occur near both the sensory and motor ends [51].

Fig. 8 shows some of the modifications that need to be made now in the initial scheme that was presented in Fig. 3. Since the interconnections and areas involved are far too numerous to be readily assimilated, only those pathways and structures are depicted that are most salient to the arguments I have made. Three major pathways are shown to originate in the retina, although several more have been identified. The midget system projects only to the lateral geniculate nucleus, whereas the parasol and W-systems project to several other regions besides the lateral geniculate nucleus of which only the superior colliculus is shown [22,65,66]. Cells projecting from the striate cortex to other regions may be driven by the midget, the parasol, or by both systems. Area MT and the superior colliculus receive inputs predominantly from the parasol system, whereas area V4 receives a mixed input from these two pathways. Little is known about the role of the W pathway in the geniculo-striate system. In addition to inputs from area MT and V4, the parietal and temporal lobes receive inputs from other, not yet clearly identified extrastriate regions. The superior colliculus receives projections from most extrastriate regions as well as from the temporal,

Fig. 8. Modified and expanded schematic of major structures and connections in the visual system as considered in the text.
parietal and frontal (not shown) lobes, which in turn most likely receive inputs from all three systems that originate in the retina. Most of the areas shown make extensive interconnections.

According to current views, then, it appears that each extrastriate visual area, rather than performing a unique, one-function analysis, is engaged, as are most neurons in the visual system, in many different tasks. Visual areas in posterior cortex make profuse interconnections and receive input from many different systems that originate early in the visual pathways. Consequently, they carry out interactive analyses of many different aspects of the visual scene. It is therefore entirely possible that the process of visual analysis does not truly involve the breaking down of the visual scene into basic elements. It appears, therefore, that Humpty (Vision) Dumpty may not have fallen and broken up after all. He is still sitting up there, whole and healthy, wondering just what the process really is that makes him visible.

5. Resolution

Neuroscientists have made remarkable progress during this century. It is a field studded with discoveries and Nobel prizes; we have learned more about the organization and functions of the nervous system during this period than in all of the time preceding it. It is a vital, exciting field. Consequently it is not surprising that it also abounds with controversy. As depicted so far in this paper it may appear that those investigators in the field of neuroscience who study the visual system form two irreconcilable groups, one of which is committed to neuronal and areal specificity and the other to general, multipurpose systems. In reality, most investigators nowadays realize that in the brain both dedicated and general purpose systems exist and that there is a complex interplay between such systems.

One may conjecture that the multifunctionality seen in the nervous system arose out of necessity rather than pure choice for creating the best analyzers. Dedicated systems, after all, tend to perform a better job. Dedicated tools, such as pliers, hammers and screwdrivers do better than the multipurpose tools one can buy, for example, at Sears or Brookstone. We buy multipurpose tools mostly out of necessity, the necessity having often to do with spatial restrictions; one cannot readily carry around a well-equipped tool chest in the glove compartment. A multipurpose tool will fit and will do a passable job. Similar considerations may have arisen for the evolution of the nervous system. Due to space limitations, the number of neurons, which nature had difficulty miniaturizing, needed to be kept to a minimum. Thus to increase computing power, they were turned into more complex, multipurpose devices where possible. That this is not an ideal solution can be seen in the fact that in most species some dedicated systems remain. In the visual system numerous examples can be seen. One of these is the accessory optic system, which begins with a specialized set of ganglion cells in the retina, the displaced cells of Dogiel, that project to the terminal nuclei and from there through the dorsal cap of Kooy of the inferior olive to the cerebellum [69]. The circuit is completed by projections to the vestibular nuclei and from there to the oculomotor complex. This system is dedicated to the stabilization of the eye to the visual scene. Any retinal slip is recognized by the specialized, directionally selective ganglion cells whose signals are converted in the circuit to activate the eye muscles to cancel the retinal slip. This is an effective dedicated system which in the rabbit utilizes only 6 to 7000 ganglion cells out of a population of more than 350,000.

The advantages of maintaining some degree of specialization can also be seen in the geniculostriate system of primates. Whereas in most regions of the retina, presumably for the sake of economy, rods and cones converge on the ganglion cells, thereby giving rise to pathways that can carry different messages under different illumination conditions, this is not the case in the fovea. The fovea is rod free. The main reason for this appears to be the necessity to optimize acuity. By eliminating the rods and reducing the diameter of the cones, high packing density can be realized which thereby provides for the analysis of fine detail. The cortical cells to which the fovea projects, however, comprise a multipurpose system, many cells of which are capable of analyzing several different attributes of the visual scene.

The considerations presented in this paper bring us now to the following conclusions: In the nervous system there are both dedicated and multipurpose systems; multipurpose systems are evident already at early stages of processing.

Neurons become increasingly multifunctional as one ascends from peripheral to central structures in the nervous system; this is an especially notable property of cortical neurons.

Neuronal multifunctionality represents a major evolutionary trend. Thus, rather than creating more and more dedicated systems to meet the ever rising demands organisms had to face over the eons, general purpose systems have evolved that not only are able to perform a number of analyses concurrently, but, instead of being 'hard wired,' are also modifiable by experience.

The process of perceptual analysis in the visual system is not to "break down the visual scene" into basic components. Such analysis is performed interactively by areas and neurons with multipurpose properties.

In the course of evolution, the numerous extrastriate visual areas did not arise for the purpose of analyzing basic visual attributes such as color, motion, pattern and depth. Even relatively primitive systems lacking multiple visual cortical areas, or lacking cortex entirely
for that matter, had to perform such analyses. Nature did not have the freedom to rework everything completely and to thereby relegate basic analyses to newly created structures. Instead, it would seem reasonable to assume that these areas have evolved for entirely different reasons; among these was the need to improve on existing analyses, to meet new contingencies, and to allow for selective modification as the result of experience.

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