Chapter 16

Maps in Context: Some Analogies Between Visual Cortical and Genetic Maps

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16.1 Introduction

The purpose of this essay is to examine some parallels in the evolutionary and functional significance of replicated maps in the genetic material and the visual cortex. In particular, I would like to explore two related ideas. The first is that the differentiation of replicated maps is an important factor in the development of new functional capacities in evolution. The second is that the properties of maps are influenced by their context. The contextual influences are mediated in genetic systems by various forms of gene regulation. In the visual cortex, contextual influences are expressed by the effects of stimuli located outside the classical receptive fields of individual neurons making up each cortical map. These contextual influences may determine how the organs of the body are assembled by the genes and how percepts

L. M. Vaina (ed.), Matters of Intelligence, 369–393.

and thoughts emerge from the activity of mapped arrays of neurons.

16.2 Multiple maps in the genetic material

The first successful mapping of the genetic material was accomplished by Morgan[1] in 1911 when he deduced that substances controlling certain sex-linked traits, such as eye-color, were located in the X-chromosome in the fruit fly, *Drosophilia.* The presence in the salivary glands of giant chromosomes, 100 times the size of chromosomes in other cells, enormously facilitated gene mapping in fruit flies. The microscopic examination of the salivary gland chromosomes revealed a detailed pattern of transverse bands of different thickness and structure. Bridges[2] noted that these patterns frequently were duplicated in different parts of the chromosomes. He later remarked:

> "In my first report on duplications at the 1918 meeting of the A.A.A.S., I emphasized the point that the main interest in duplications lay in their offering a method for evolutionary increase in lengths of chromosomes with identical genes which could subsequently mutate separately and diversify their effects."[3]

It is ironic that Bridges waited 17 years to publish this revolutionary idea which has become central to the study of the molecular basis of evolution.[4] Lewis [5] and Ohno [6] extended this concept by pointing out that duplicated genes escape the pressures of natural selection operating on the original gene and thereby can accumulate mutations which enable

[1] T. H. Morgan, "An attempt to analyze the constitution of chromosomes on the basis of sex-limited inheritance in drosophilia," *J. Experimental Zoology*, **11**, 365-413, 1911.

[2] C. B. Bridges, "Salivary chromosomes maps," *J. Heredity*, **26**, 60-64, 1935.

[3] *ibid*, page 64.

[4] "Gene duplication is probably the most important mechanism for generating new genes and new biochemical processes that have facilitated the evolution of complex organisms from primitive ones." W.-H. Li, "Evolution of duplicate genes and pseudogenes," in: *Evolution of Genes and Proteins*, Masatoshi Nei and Richard K. Koehn, eds., Sinauer Assoc., Sunderland, Mass., 1983, page 14.

[5] E. B. Lewis, "Pseudoallelism and gene evolution," *Cold Spring Harbor Symposia on Quantitative Biology*, **16**, 159-174, 1951.

[6] S. Ohno, *Evolution by Gene Duplication*, Springer-Verlag, New York, 1970.

the new gene to perform previously non-existent functions, while the old gene continues to perform its original and presumably vital functions. One of the earliest and most elegant examples of the role of gene duplication in evolution was discovered by Ingram,[7] who compared the structure of the oxygen carrying proteins myoglobin, a monomere, and its tetrameric relative, hemoglobin. He deduced that at an early stage in vertebrate evolution, the heme protein inside muscle cells was the same as that in the circulation. The muscle heme protein became myoglobin in the course of evolution; it retained a molecular weight of 17,000 and only one heme group and one peptide chain per molecule. However, the gene producing the circulating heme protein duplicated several times to produce the structure of modern hemoglobin with four homologous peptide chains. Another example is the vast number of closely related immunoglobin genes.[8] Finally, Britten and Kohne [9] developed a technique for determining the abundance of replicated DNA sequences for the entire genomes of higher organisms. They separated the complementary strands of the DNA and sheared them into fragments of about 400 nucleotides in length. Then they measured the time required for the complementary strands to reassociate at different concentrations. They found that much of the DNA reassociated far more rapidly and at lower concentrations than would be expected if there were no redundancy in the DNA sequence, which led to their estimate that more than one-third of the DNA in higher organisms is made up of sequences which are replicated many times. They concluded:

> "The families of repeated sequences range from groups of almost identical copies to groups with sufficient diversity that, after reassociation, only structures of low stability are formed among the members. It seems likely that this situation has arisen from large-scale precise duplication of selected sequences with subsequent divergence caused by mutation and the translo-

[7] V. M. Ingram, *The Hemoglobins in Genetics and Evolution*, Columbia University Press, New York, 1963.

[8] L. Hood, J. H. Campbell and S. C. R. Elgin, "The organization, expression and evolution of antibody genes and other multigene families," *Ann. Review of Genetics*, **9**, 305-353, 1975.

[9] R. J. Britten and D. E. Kohne, "Repeated sequences in DNA," *Science*, **161**, 529-540, 1968.

cation of segments."[10]

They further suggested that each family of repeated sequences arose from relatively sudden events in evolutionary history, which they called "saltatory replications."

16.3 Multiple maps in the visual cortex

In contrast to the linear maps of amino-acid sequences in the base code sequences of the DNA, the representations of the visual field in the visual cortex are two-dimensional. The mapping of the visual cortex began earlier, but has proceeded more slowly than the mapping of the genetic material. In 1881, Munk [11] located the visual cortex in the occipital lobe by making a series of selective lesions in macaque monkeys and observing their post-operative deficits in behavior. After this promising beginning, however, it was not for another generation that the representation of the visual field in the primary visual cortex was established by Inouye[12] and Holmes [13] who related visual field defects to the sites of visual cortex lesions in soldiers who had been injured in the Russo-Japanese and First World Wars respectively. The development of amplifiers and oscilloscopes made possible the electro-physiological study of the responses of the visual cortex beginning in the 1940's. By recording visually evoked potentials, Talbot [14] and Marshall, Talbot and Ades [15] found evidence for several areas beyond the primary visual cortex in cats. The development of microelectrode

[10] *ibid*, page 39.

[11] H. Munk, *Uber die Funktionen der Grosshirnrinde*, A Hirnwald, Berlin, 1881. English translation in G. Von Bonin, *Some Papers on the Cerebral Cortex*, pp. 97-117, Thomas, Springfield, Illinois, 1960.

[12] T. Inouye, *Die Sehstorungen bei Schussverletzungen der Kortialen Sehsphare, nach Beobachtungen an Verwundeten der letzten Japanischen Kriege*, W. Engelmann, Leipzig, 1909.

[13] G. M. Holmes, "Disturbances of vision by cerebral lesions," *Brit. J. Ophthalmology*, **2**, 353, 1918.

[14] S. A. Talbot, "A lateral localization in the cat's visual cortex," *Federation Proc.*, **1**, 84, 1942.

[15] W. H. Marshall, S. A. Talbot and H. W. Ades, "Cortical response of the anesthetized cat to gross photic and electrical afferent stimulation," *J. Neurophysiology*, **6**, 1-15, 1943.

recording [16] from single neurons enabled Hubel and Wisel[17] to conduct their landmark study of the functional organization of two higher cortical visual areas in cats. Inspired by their work, Jon Kaas and I began in 1968 to map the representations of the visual field in the non-primary or extra-striate visual cortex in primates. These regions were presumed to perform higher functions in the analysis of visual information, since the anatomical connectional studies by Polyak [18] indicated that the visual input was mainly funneled through the primary or striate visual cortex. We chose to map the visual cortex in owl monkeys because they possessed a relatively smooth cerebral cortex unencumbered by the deep fissures found in most species of simian primates. We found a virtual embarrassment of riches in the visual cortex of the owl monkey, for instead of there being three or four maps of the visual field as we expected, we soon found evidence for about 10 visual areas which comprised the posterior third of the cortex. (See Figures 16.1 and 16.2.) At the time we were blissfully ignorant of the developments in modern genetics described in the first section, but we were aware of the idea advanced many years earlier by the paleontologist Gregory [19] that a common mechanism of evolution appears to be the replication of body parts due to a genetic mutation in a single generation followed in subsequent generations by the gradual divergence of structure and functions of the replicated parts.[20] We suggested this mechanism as an alternative to the view that topographically organized sensory representations gradually differentiated from "unorganized" cortex, or that individual topographically organized areas gradually differentiated into additional topographical representations.

The evidence for multiple maps in cerebral cortex has cascaded. Working at the same time, and for a period in the late 1960's at the same place

[16]D. H. Hubel, "Tungsten microelectrode for recording from single units," *Science*, **125**, 549-550, 1957.

[17]D. H. Hubel and T. N. Wiesel, "Receptive fields and functional architecture in two non-striate visual areas (18 and 19) of the cat," *J. Neurophysiology*, **28**, 229-289, 1965.

[18]S. Polyak, *The Main Afferent Fiber Systems of the Cerebral Cortex in Primates*, University of California Press, Berkeley, 1932.

[19]W. K. Gregory, "Reduplication in evolution," *Quarterly Rev. of Biology*, **10**, 272-290, 1935.

[20]J. M. Allman and J. K. Kaas, "A representation of the visual field in the caudal third of the middle temporal gyrus of the owl monkey (*Aotus trivirgatus*)", *Brain Res.*, **31**, 85-105, 1971.

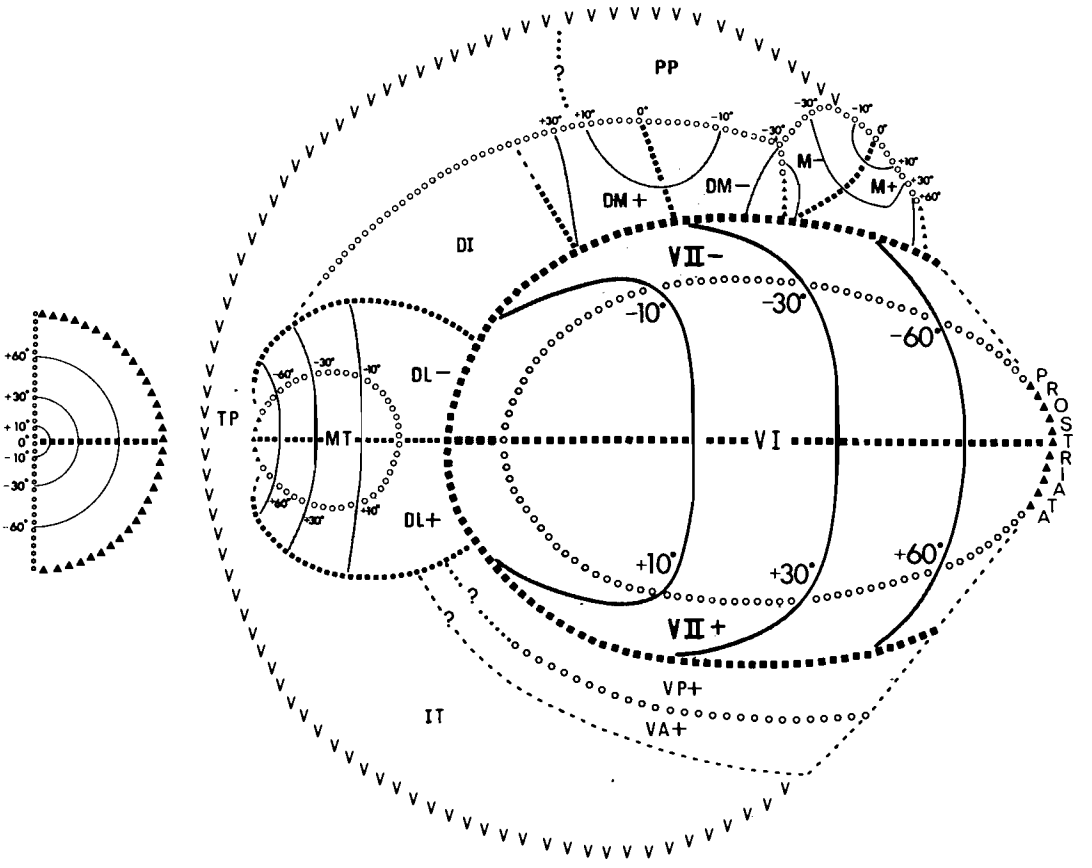

Figure 16.1: See Legends, Section 16.7.

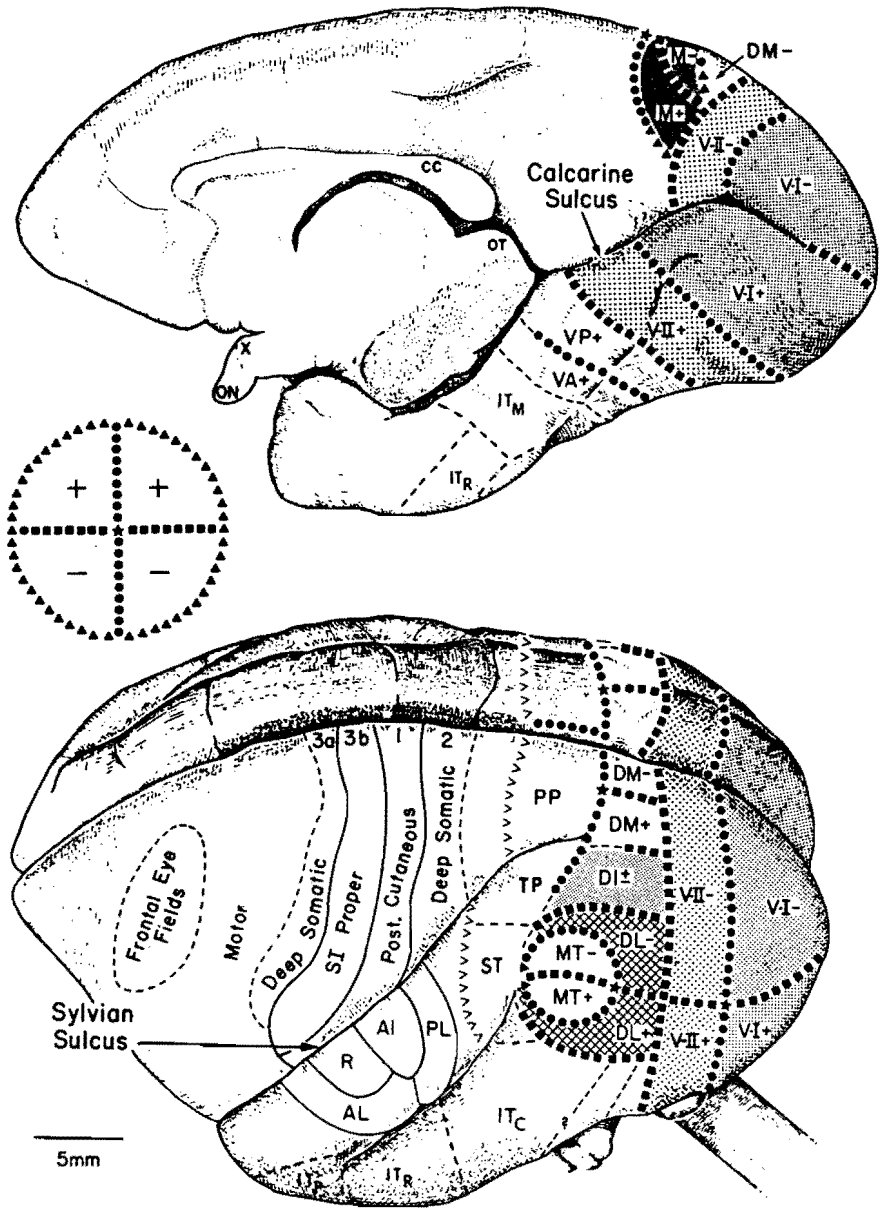

Figure 16.2: See Legends, Section 16.7

(the University of Wisconsin), Zeki[21] uncovered evidence for a number of cortical visual areas in macaque monkeys. Spatz and Tigges,[22] Gross and colleagues,[23] Desimone and Ungerleider,[24] and Maunsell and Van Essen[25] have also made major discoveries in the simian extrastriate cortex.

Rosenquist, Palmer and Tusa[26] have mapped in cats an extensive array of visual areas, many of which have probably arisen independently in evolution from those in primates.

There is fossil evidence that visual cortex underwent rapid expansion in the early primates. (See Figure 16.3.) The primitive mammals that were the common ancestors of the living eutherian mammals had poorly developed visual systems, and depended instead on olfaction, touch and hearing.[27] However, primates, which emerged as a very successful group rather suddenly at the beginning of the Eocene, 55 million years ago, possessed large frontally directed eyes and a greatly expanded visual cortex.[28] This suggests that the large array of extrastriate visual areas in primates, like some of the families of repeated DNA sequences, may have arisen during

[21]S. M. Zeki, "Functional specialization in the visual cortex of rhesus monkey," *Nature*, **274**, 423-428, 1978. References 22 through 26 list some of the major publications on the topographic organization of the cortical visual areas.

[22]W. B. Spatz and J. Tigges, "Experimental-anatomical studies on the 'Middle Temporal Visual Area (MT)' in primates. I. Efferent corticocortical connections in the marmoset (*Callithrix jacchus*)", *J. Comparative Neurology*, **146**, 451-463, 1972.

[23]C. Gross, C. Bruce, R. Desimone, J. Fleming and R. Gattass, "Cortical visual areas of the temporal lobe," in: *Multiple Cortical Visual Areas*, pp. 187-216, C. N. Woolsey, ed., Humana Press, Clifton, New Jersey, 1981.

[24]R. Desimone and L. Ungerleider, "Multiple visual areas in the caudal superior temporal sulcus of the macaque," *J. Comparative Neurology*, in press.

[25]J. H. R. Maunsell and D. C. Van Essen, "The connections of the middle temporal visual area (MT) and their relationship to a cortical hierarchy in the macaque monkey," *J. Neuroscience*, **3**, 2563-2586, 1983.

[26]R. J. Tusa, L. A. Palmer and A. C. Rosenquist, "Multiple cortical visual areas: visual field topography in the cat," in: *Multiple Cortical Visual Areas*, pp. 1-31, C. N. Woolsey, ed., Humana Press, Englewood Cliffs, New Jersey, 1981.

[27]M. Cartmill, "Rethinking primate origins," *Science*, **184**, 436-443, 1974.

[28]L. B. Radinsky, "The oldest primate endocast," *American J. Physical Anthropology*, **27**, 385-388, 1967. L. B. Radinsky, *The Fossil Record of Primate Brain Evolution*, American Museum, New York, 1979. J. M. Allman, "The evolution of the visual system in the early primates," in: *Progress of Psychobiology and Physiological Psychology*, James Sprague and Alan Epstein, eds., **7**, 1-53, Academic, New York, 1977.

relatively short periods of time in saltatory replications. [29]

16.4 Maps and functions

One of the central ideas of modern genetics is that a particular gene contains the instructions to make a particular protein that has a specific function. One example is the system of genes for photoreceptor proteins. Recently, Nathans *et al*[30] have mapped the DNA sequences of the genes for the rod and cone receptor proteins in man. It appears on the basis of sequence homologies that the genes that produce the rod and cone receptor proteins are replicas of an ancient gene for a receptor protein.[31] The genes for the red and green receptor proteins are located adjacent to each other on the X chromosome and have a 96% sequence homology.[32] Many individuals have up to three slightly different versions of the gene for the green receptor protein. It is not clear how these multiple green receptor genes contribute to perception, but this result does point to a seeming redundancy in the genetic organization of the visual system, which raises comparable questions about the functional meaning of multiple cortical visual areas.

The notion that a cortical visual area performs a specific and probably unique perceptual or information processing function has been the implicit

[29] "The first primates of modern aspect" appeared rather suddenly and in considerable abundance at the beginning of the Eocene (Elwyn Simons, *Primate Evolution*, MacMillan, New York, 1972). The ancestry of these Eocene primates is obscure. Most of the very early primates, the plesiadapiformes, from the Cretaceous and Paleocene, appear to be too specialized in their dentition and other features of their anatomy to have been ancestral to later primates (F. S. Szalay and E. Delson, *Evolutionary History of the Primates*, Academic, 1979). The brain case is small relative to skull size in the plesiadapiformes, unlike the later primates.

[30] J. Nathans, D. Thomas and D. Hogness, "Molecular genetics of human color vision: the genes encoding blue, green and red pigments," *Science*, **232**, 193-202, 1986.

[31] The receptor protein encoded by this ancient gene may not have been photoreceptive in function, but had some other, perhaps more ubiquitous, receptor function.

[32] The comparative study of the photoreceptor genes could contribute much to our understanding evolutionary development of perceptual capacities. One approach would be to study the system of the photoreceptor genes in New World Monkeys, which vary considerably in their capacities to discriminate colors. (G. Jacobs, *Comparative Color Vision*, Academic, New York, 1980.) It would also be very useful to determine how the central mechanisms for color perception relate to organization of photoreceptor proteins in New World Monkeys.

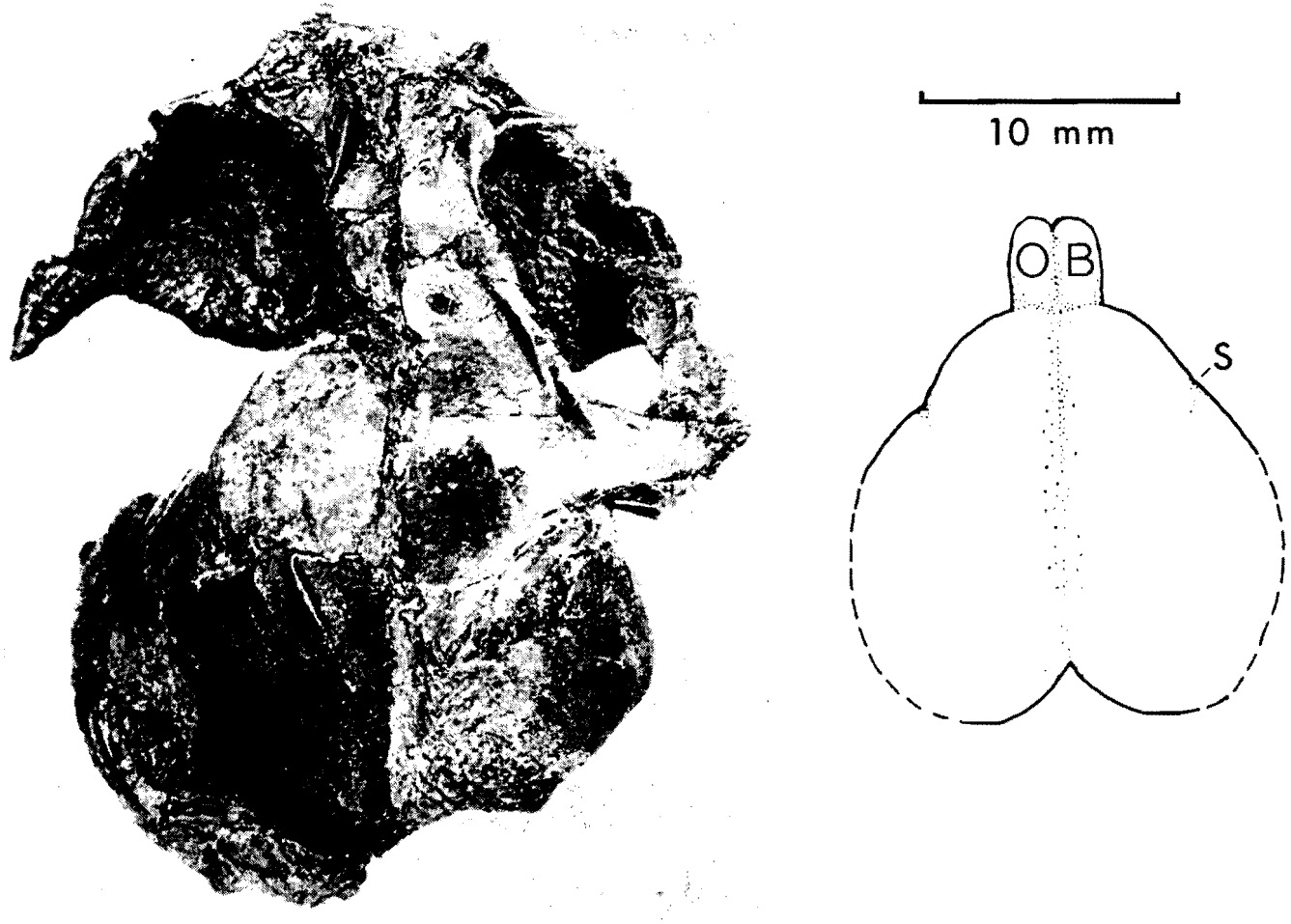

Figure 16.3: See Legends, Section 16.7.

or explicit hypothesis of most of the research conducted in the extrastriate areas. However, perhaps the best evidence for this hypothesis comes not from the visual cortex itself but from the dorsal lateral geniculate nucleus, which receives input from the retina and relays to the visual cortex. In a number of mammalian orders, including primates and carnivores that possess well developed visual systems with a fair degree of binocular vision, the dorsal lateral geniculate nucleus is divided into a series of laminae receiving input from the ipsilateral or contralateral eye.[33] The laminae are stacked in registers so that the same point in the visual field is represented in a line approximately perpendicular to the laminae. Most carnivores have two major laminae. Laminae A receives input from the contralateral hemiretina; laminae A1 receives input from the ipsilateral hemiretina. However, these laminae are duplicated in minks and ferrets,[34] and the response properties of the cells in these laminae are segregated so that one set of the duplicated laminae have neurons with ON-center receptive fields while the other half have OFF-center receptive fields.[35] The ON and the OFF center cells are mingled together in the unduplicated laminae in other carnivores. This segregation of ON and OFF laminae is also present in the dorsal lateral geniculate nucleus in tree shrews[36] and to a less complete extent in macaque monkeys.[37] There is evidence in the mink that ON-OFF segregation is maintained at the next level of visual processing in layer 4 of primary visual cortex.[38]

In monkeys, there exist strong quantitative distinctions between the two major sets of laminae in the dorsal lateral geniculate nucleus that re-

[33] J. H. Kaas, R. W. Guillery and J. M. Allman, "Some principles of organization in the dorsal lateral geniculate nucleus," *Brain, Behavior and Evolution*, **6**, 253-299, 1972.

[34] K. J. Sanderson, "Lamination of the dorsal lateral geniculate nucleus in carnivores of the weasel (*Mustilidae*), raccoon (*Procyonidae*) and Fox (*Canidae*) families," *J. Comparative Neurology*, **153**, 239-266, 1974.

[35] S. LeVay and S. K. McConnell, "ON and OFF layers in the lateral geniculate nucleus of the mink," *Nature*, **300**, 350-351, 1982; M. P. Stryker and K. R. Zahs, "ON and OFF sublaminae in the lateral geniculate nucleus of the ferret," *J. Neuroscience*, **3**, 1943-1951, 1983.

[36] J. Conway and P. Schiller, "Laminar organization of the lateral geniculate body and the striate cortex in the tree shrew (*Tupaia glis*)," *J. Neuroscience*, **4**, 171-197, 1984.

[37] P. Schiller and J. Malpeli, "Functional specificity of lateral geniculate nucleus laminae of the rhesus monkey," *J. Neurophysiology*, **41**, 788-797, 1978.

[38] S. K. McConnell and S. LeVay, "Segregation of ON- and OFF-center afferents in mink visual cortex," *Proc. National Academy of Science*, **81**, 1590-1593, 1984.

lay input to the primary visual cortex. The magnocellular laminae contain large cells that are fast conducting and receive fast input from the retina; the parvocellular laminae contain smaller cells that are slower conducting and receive slower input from the retina.[39] The neurons of the magnocellular laminae are much more sensitive to low contrast stimuli and have larger receptive fields.[40] The magnocellular laminae contain proportionally smaller representations of the central visual field than do the parvocellular laminae.[41] The neurons in the parvocellular laminae of macaque monkeys are rich in opponent-color mechanisms.[42]

The magnocellular laminae project to layer 4Cα of primary visual cortex (V-I),[43] then to the adjacent layer 4B[44], then to the middle temporal visual area (MT).[45] The neurons in layer 4B of V-I[46] and in MT[47] are usually

[39]S. M. Sherman, J. R. Wilson, J. H. Kaas and S. V. Webb, "X- and Y-cells in the dorsal lateral geniculate nucleus of the owl monkey (*Aotus trivirgatus*)," *Science*, **192**, 475-477, 1976; B. Dreher, Y. Fukada and R. W. Rodieck, "Identification, classification and anatomical segregation of cells with X-like and Y-like properties in the lateral geniculate nucleus of old-world primates," *J. Physiology*, **258**, 433-452, 1976; P. Schiller and J. Malpeli, *opus cit.*, 1978.

[40]E. Kaplan and R. M. Shapley, "X and Y cells in the lateral geniculate nucleus of macaque monkeys," *J. Physiology*, **330**, 125-143, 1982; A. M. Derrington and P. Lennie, "Spatial and temporal contrast sensitivites of neurons in lateral geniculate nucleus of macaque," *J. Physiology*, **357**, 219-240, 1984.

[41]M. Connolly and D. Van Essen, "The representation of the visual field in the parvocellular and magnocellular laminae of the lateral geniculate nucleus in the macaque monkey," *J. Comparative Neurology*, **226**, 544-564, 1984.

[42]T. N. Wiesel and D. H. Hubel, "Spatial and chromatic interactions in the lateral geniculate body of the rhesus monkey," *J. Neurophysiology*, **29**, 1115-1156, 1966.

[43]D. H. Hubel and T. N. Wiesel, "Laminar and columnar distribution of geniculo-cortical fibers in the macaque monkey," *J. Comparative Neurology*, **146**, 421-450, 1972.

[44]J. Lund, "Organization of neurons in the visual cortex Area 17 of the monkey (*Macaca mulatta*)," *J. Comparative. Neurol.*, **147**, 455-496, 1973.

[45]W. B. Spatz, "Topographically organized reciprocal connections between areas 17 and MT (visual area of superior temporal sulcus) in the marmoset (*Callithrix jacchus*)," *Exp. Brain Res.*, **27**, 559-572, 1977.

[46]B. Dow, "Functional classes of cells and their laminar distribution in monkey visual cortex," *J. Neurophysiology*, **37**, 927-946, 1974; M. Livingstone and D. H. Hubel, "Anatomy and physiology of a color system in the primate visual cortex," *J. Neuroscience*, **4**, 309-356, 1984; J. A. Movshon and W. T. Newsome, "Functional characteristics of striate cortical neurons projecting to MT in the macaque," *Soc. Neurosci. Abstr.*, **10**, 933, 1984.

[47]S. Zeki, "Functional organization of a visual area in the posterior bank of the superior

highly sensitive to the direction of stimulus motion. Recently, Movshon and collaborators[48] have found that some MT neurons respond to the apparent direction of motion of complex grating patterns, whereas V-I neurons respond to the actual direction of motion of the components of the stimulus, which can be quite different from the apparent direction of motion of the whole pattern. Thus the properties of MT neurons more nearly match perception and constitute a significant elaboration of function beyond that found in V-I.

The parvocellular laminae project to layer 4Cβ in V-I,[49] then to layers two and three in V-I,[50] then to sectors the second visual area (V-II),[51] then to the dorsolateral visual area (DL),[52] then to inferotemporal cortex. This

temporal sulcus of the rhesus monkey," *J. Physiology*, **236**, 549-573, 1974; J. F. Baker, S. E. Petersen, W. T. Newsome and J. Allman, "Response properties in four extrastriate visual areas of the owl monkey (*Aotus trivirgatus*): a quantitative comparison of the medial, dorsomedial, dorsolateral and middle temporal areas," *J. Neurophysiology*, **45**, 397-416, 1981; J. H. R. Maunsell and D. Van Essen, "Functional properties of neurons in middle temporal visual areas (MT) of macaque monkey. I. Selectivity for stimulus direction, velocity and orientation," *J. Neurophysiology*, **49**, 1127-1167, 1983; T. D. Albright, "Direction and orientation selectivity of neurons in visual area MT of the macaque," *J. Neurophysiology*, **52**, 1106-1130, 1984.

[48] J. A. Movshon, E. H. Adelson, M. S. Gizzi and W. T. Newsome, "The analysis of moving visual patterns," in: *Pattern recognition mechanisms*, C. Chagas, R. Gattass and C. Gross, eds., 117-151, Springer, New York, 1985; J. A. Movshon and W. T. Newsome, "Functional characteristics of striate cortical neurons projection to MT in the macaque," *Soc. Neurosci. Abstr.*, **10**, 933, 1984.

[49] D. H. Hubel and T. N. Wiesel, "Laminar and columnar distribution of geniculo-cortical fibers in the macaque monkey," *J. Comparative Neurology*, **146**, 421-450, 1972.

[50] J. Lund and R. Boothe, "Interlaminar connections and pyramidal neurons organization in the visual cortex, area 17, of the macaque monkey," *J. Comparative Neurology*, **159**, 305-334, 1975.

[51] W. B. Spatz, J. Tigges and M. Tigges, "Subcortical projections, cortical associations and some intrinsic interlaminar connections of the striate cortex in the squirrel monkey (*Saimiri*)," *J. Comparative Neurology*, **140**, 155-173, 1970; M. Livingston and D. Hubel, "Anatomy and physiology of a color system in the primate visual cortex," *J. Neuroscience*, **4**, 309-356, 1984.

[52] R. E. Weller and J. H. Kaas, "Cortical projections of the dorsolateral visual area in owl monkeys: the prestriate relay to inferior temporal cortex," *J. Comparative Neurology*, **234**, 35-59, 1985. Area DL in New World Monkeys and prosimians probably corresponds to part or all of the "V4 complex" in macaque monkeys. The V4 complex also receives input from V-II. See S. Shipp and S. Zeki, "Segregation of pathways leading from area V2 to areas V4 and V5 of macaque monkey visual cortex," *Nature*, **315**, 322-325, 1985; E. DeYoe and

system appears to be devoted to the analysis of form and in some species to color. DL neurons are highly selective to the size and shape of visual stimuli irrespective of their exact position within their receptive fields.[53] Desimone and collaborators[54] have found striking evidence for shape selectivity for neurons in inferotemporal cortex. Inferotemporal cortex is also strongly implicated in the ability to learn to discriminate visual shapes.[55]

Recently, evidence has emerged that there is a duplication of the map within V-I in primates.[56] Stains for the activity of the mitochondrial enzyme, cytochrome oxidase, have revealed a regular, repeating pattern that is unique to primates.[57] Livingstone and Hubel[58] have found that the neurons in the cytochrome oxidase rich "blobs" lack orientation selectivity, are rich in opponent-color mechanisms, and project to "thin stripes" of high cytochrome oxidase activity in V-II. By contrast, they found that the neurons in the "interblobs" in V-I are orientation selective and project to stripes of low cytochrome oxidase activity in V-II. The thin stripes and the interstripes project to the fourth visual area (V4).[59] There are also "thick stripes" of high cytochrome oxidase activity in V-II that project to MT.[60] Thus, there are maps within maps in the first and second visual areas of pri-

D. Van Essèn, "Segregation of efferent connections and receptive field properties in visual area V2 of the macaque," *Nature*, **317**, 58-61, 1985. The V4 complex in turn projects to infero-temporal cortex. See R. Desimone, J. Fleming and C. G. Gross, "Prestriate afferents to inferior temporal cortex: an HRP study," *Brain Res.*, **184**, 41-55, 1980.

[53]S. E. Petersen, J. F. Baker and J. M. Allman, "Dimensional selectivity of neurons in the dorsolateral visual area of the owl monkey," *Brain Res.*, **197**, 507-511, 1980.

[54]R. Desimone, T. Albright, C. G. Gross and C. Bruce, "Stimulus selective properties of inferior temporal neurons in the macaque," *J. Neuroscience*, **4**, 2051-2062, 1984.

[55]C. G. Gross, "Inferotemporal cortex and vision," *Prog. in Physiological Psychology*, **5**, 77-115, 1973.

[56]I am indebted to Richard Andersen for suggesting this point of view to me.

[57]M. Wong-Riley first described the cytochrome-oxidase rich structure in primate visual cortex; they have been studied extensively in a large number of primate species by J. C. Horton in "Cytochrome oxidase patches: a new cytoarchitectonic feature of the monkey visual cortex," *Phil. Trans. Roy. Soc. Lond.*, **304**, 199-253, 1984.

[58]M. Livingstone and D. Hubel, "Anatomy and physiology of a color system in the primate visual cortex," *J. Neurosci.*, **4**, 309-356, 1984.

[59]E. A. DeYoe and D. Van Essen, "Segregation of efferent connections and receptive field properties in visual area V2 of the macaque," *Nature*, **317**, 58-61, 1985; S. Shipp and S. Zeki, "Segregation of pathways leading from area V2 to areas V4 and V5 of macaque monkeys visual cortex," *Nature*, **315**, 322-325, 1985.

[60]*ibid.*

mate visual cortex, which may represent a gradual differentiation of maps and related functions within a visual area.

There exists a good deal of evidence to support the notion that different visual field maps perform different functions in the visual system; however there is also evidence that they share many visual response properties in common.[61] Molecular biology provides precedents for other possible functions of duplicated structure that may have some relevance to our efforts to determine the functions of cortical maps. The tetrameric hemoglobin molecule is more efficient in binding and releasing oxygen than the monomeric myoglobin molecule, and thus, the function of the four homologous chains of hemoglobin is to act cooperatively in this process, rather than for each chain to have a separate and distinct function.[62] The functions of the members of the vast family of immunoglobins are highly overlapping.[63] These examples from molecular biology of cooperativity and highly overlapping function of replicated structures provide some precedence for similar distributions of function within the multiple cortical visual areas.

16.5 Differentiation of replicated structures

Modern genetics has provided some insights as to how replicated structures differentiate in development. As Lewis[64] has put it:

> "The segmentation pattern of the fly provides a model system for studying how genes control development... Flies almost certainly evolved from insects with four wings instead of two, and insects are believed to have come from arthropod forms with many legs instead of six. During the evolution of the fly, two major groups of genes must have evolved: leg-suppressing

[61] J. F. Baker, S. E. Petersen, W. T. Newsome and J. M. Allman, *opus cit.*, 1981.

[62] V. M. Ingram, *The Hemoglobins in Genetics and Evolution*, Columbia University Press, New York, 1963.

[63] L. Hood, J. H. Campbell and S. C. R. Elgin, "The organization, expression and evolution of antibody genes and other multigene families," *Ann. Rev. Genetics*, **9**, 305-353, 1975.

[64] E. B. Lewis, "A gene complex controlling segmentation in *Drosophilia*," *Nature*, **276**, 565-570, 1978.

genes which removed legs from abdominal segments of millipede-like ancestors followed by haltere-promoting genes which suppressed the second pair of wings of four-winged ancestors."

In fruit flies, series of genes have been discovered that govern the formation of segments and their differentiation. These genes regulate the action of other genes that cause each segment to differentiate. Lewis[65] has proposed that these regulatory genes were the product of a series of gene duplications, and indeed the genes that control the differentiation of the posterior thoracic and abdominal segments are located in an orderly series on the third chromosome that corresponds to the order of differentiation of the segments.[66] An analogous and possibly even homologous set of genes has been discovered that governs the differentiation of the segments that constitute the anterior thorax and head.[67] Each of these genes contains an 180 base pair sequence of DNA, called the "homeobox" that shows a high degree of correspondence. The homeobox is also found in a large number of other organisms including frogs, mice and humans.[68] The "homeobox" encodes for a 60 amino acid long "homeo domain" that is rich in the basic amino acids, lysine and arginine, which would enable the homeo domain to bind to DNA.[69] The homeo domain apparently has been strongly conserved in evolution, possibly to perform the function of binding the regulatory gene product to regulation sites in the DNA. Each regulatory gene may have been the result of ancient gene replications, but only the correspondence in this highly conserved portion is still easily identifiable.[70] Some of these regulatory genes for the fruit fly have been cloned. The *in situ* hybridization of the cloned DNA is located primarily in the nervous system, where presumably the genes regulate the differentiation of the neural circuitry for each

[65]E. B. Lewis, "Pseudoallelism and gene evolution," *Cold Spring Harbor Symposia in Quantitative Biology*, **16**, 159-174, 1951.

[66]E. B. Lewis, *opus cit.*, 1978.

[67]W. J. Gehring, "The molecular basis of development," *Scientific American*, October, 1985, pp. 153-162.

[68]*ibid.*

[69]A. Laughton and M. P. Scott, "Sequence of a *Drosophilia* segmentation gene: protein structure homology with DNA-binding proteins," *Nature*, **310**, 25-31, 1984.

[70]Alternatively, these highly conserved sequences could be the product of convergent evolution.

segment.[71] In mammals, an analogous set of genes could regulate the segmentation of the cerebral cortex into distinct areas, and the differentiation the neural circuitry in each area.

16.6 The influence of context

Gene expression is the integrated product of a host of influences arising from the action of regulatory genes, circulating hormones and many other factors that comprise the context. Similarly, the visual responses of neurons within a visuotopic map in a cortical area are likely to be the product of a broad array of contextual influences. However, it has typically been assumed that neurons at any particular locus within a map are not influenced by visual stimuli presented outside their receptive fields. Further, it has been widely assumed that perceptual functions that require the integration of inputs over large portions of the visual field must be either collective properties of arrays of neurons representing the visual field, or features of those neurons at the highest processing levels in the visual system, such as the cells in inferotemporal or posterior parietal cortex that typically possess very large receptive fields and do not appear to be organized in visuotopic maps.[72] These assumptions have been based on the results of the many studies in which receptive fields were mapped with conventional stimuli, presented one at a time, against a featureless background. This has been termed the *classical receptive field* or CRF.[73] However, unlike the neurophysiologist's tangent screen, the natural visual scene is rich in features, and there is a growing body of evidence that in many visual neurons, stimuli presented outside the CRF strongly and selectively influence neural responses to stimuli presented within the CRF. For example, Miezin, McGuiness and I[74] found that the direction and velocity of stimuli presented outside the

[71] M. P. Scott, "Homeotic gene transcripts in the neural tissue of insects," *Trends in Neurosciences*, **7**, 221-223, 1984.

[72] J. Allman, F. Miezin and E. McGuinness, "Stimulus specific responses from beyond the classical receptive field: neurophysiological mechanisms for local-global comparisons in visual neurons," *Ann. Rev. Neurosci.*, **8**, 407-430, 1985.

[73] *ibid.*

[74] *ibid.*; J. Allman, F. Miezin and E. McGuinness, "Direction and velocity specific responses from beyond the classical receptive field in cortical visual area MT," *Perception*, **4**, 105-126, 1985.

CRF for MT neurons strongly and selectively influenced the responses of the stimuli presented simultaneously within the CRF. (See Figure 16.4.) By selectively masking off various regions of the visual field outside the CRF, we mapped the total receptive field (TRF) for these neurons, which turned out to be 50 to 100 times the area of the CRF's or virtually the whole visual field in some cases. About 90% of MT neurons possess these large surrounds, which can only be detected by measuring the influence of stimuli presented there on the responses to stimuli presented within the CRF. We also have found similar, but less extensive, surround effects beyond the CRF for neurons in V-I and V-II. Similar effects have been reported in the optic tectum in pigeons[75] and in visual cortex in cats.[76] Recent recordings from neurons in the V4 complex in macaque monkeys have revealed broad surround regions tuned for orientation, spatial frequency and color.[77] The TRF's provide mechanisms that may serve as the basis for many functions in vision, such as the perceptual constancies, figure-ground discrimination, and depth perception through motion.

As mentioned above, some MT neurons lack the surround. We have recorded adjacent neurons that had the same CRF and direction preference, one neuron *with* and one neuron *without* an antagonistic surround. By comparing the responses of these two neurons, it would be possible for a higher order neuron to infer whether a particular movement had been a local movement restricted to a small part of the visual field or part of a larger pattern of movement in the same direction, which might have been due to movement by the animal itself. Such computations could contribute to the organism's solution of the "stability of the visual world problem" through visual input alone, as has been suggested by Gibson[78] and Koenderink.[79]

[75] J. I. Nelson and B. Frost, "Orientation selective inhibition from beyond the classic visual receptive field," *Brain Res.*, **139**, 359-365, 1978; P. L. Scilley, S. C. P. Wong, "Moving background patterns reveal double-opponency of directionally specific pigeon tectal neurons," *Exp. Brain Res.*, **43**, 173-185, 1981.

[76] M. Von Grunau and B. J. Frost, "Double-opponent-process mechanism underlying RF-structure of directionally specific cells of cat lateral suprasylvanian visual area," *Exp. Brain Res.*, **49**, 84-92, 1983.

[77] R. Desimone, S. Schien, J. Moran and L. Ungerleider, "Contour, color and shape analysis beyond the striate cortex," *Vis. Res.*, **25**, 441-452, 1985.

[78] J. J. Gibson, *The Senses Considered as Perceptual Systems*, Houghton Mifflin, Boston, 1966.

[79] J. J. Koenderink, "Space, form and optical deformation," in: *Brain Mechanisms and*

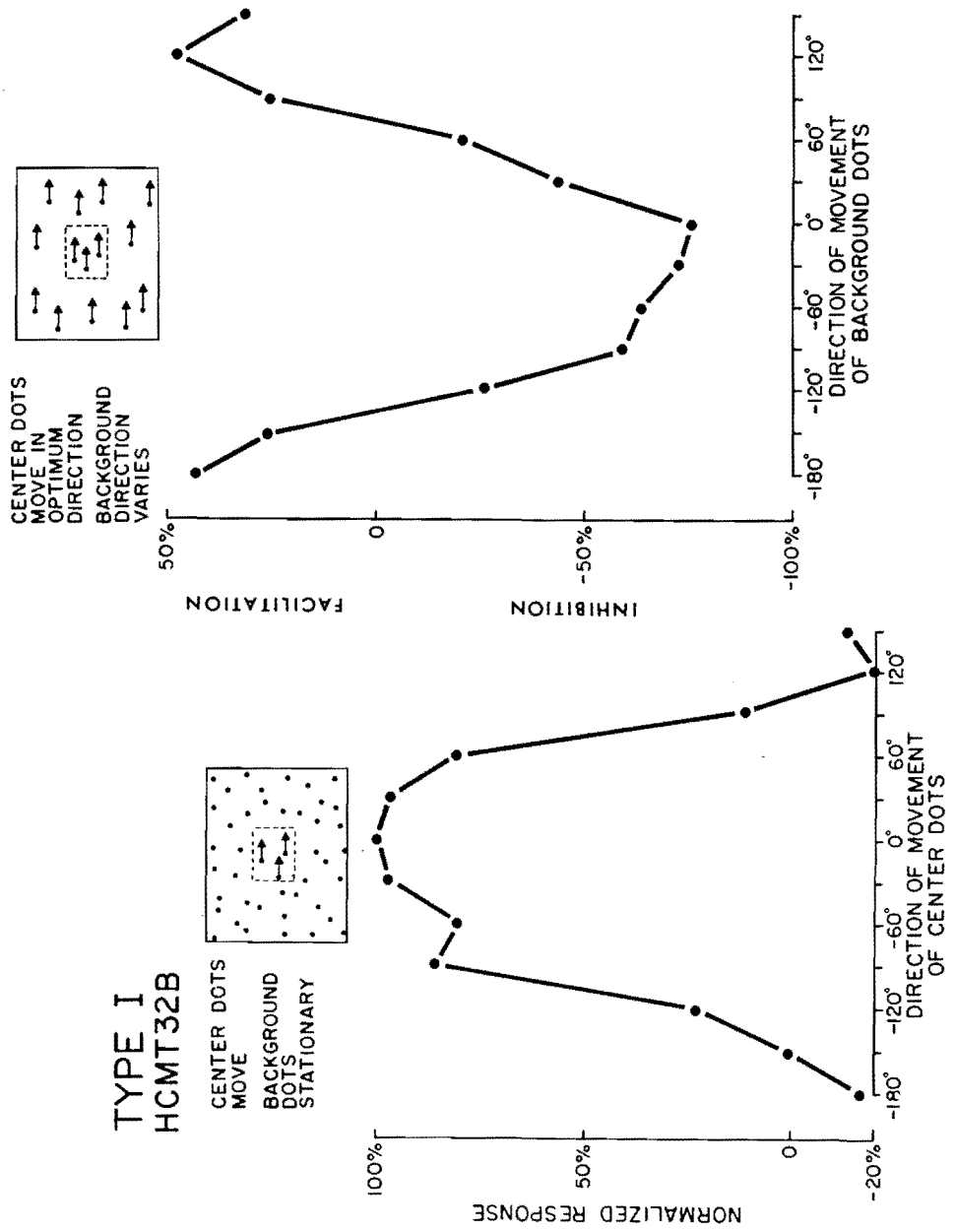

Figure 16.4: See Legends, Section 16.7.

Visual cortex neurons have been demonstrated to have the potential to make other types of inferences on the basis of responses to stimuli presented beyond the CRF. Von der Heydt and collaborators[80] discovered that about one third of the neurons in the second visual area in awake macaque monkeys respond to illusory contours when the real contours evoking the response were located entirely outside the CRF. The perception of illusory contours might be considered as a type of constancy, since the visual system is interpolating a continuous contour from an interrupted contour, which under natural conditions would be produced by a partially occluding surface. The tropical forest environment, in which primates evolved, abounds with occluding foliage and branches, and the ability to reconstruct surfaces that are partially hidden from view would be very adaptive. Similarly, Zeki[81] has recorded neurons in the V4 complex that exhibit color constancy, that is they respond to the apparent color of the stimulus regardless of the spectral content of the stimulus. Again, the ability to make such inferences would have been of great adaptive value to our primate forebearers since it would have enabled them, for example, to identify ripe fruit, suitable to eat, on the basis of their colors under a broad range of different environmental lighting conditions. In each case, the neuron appears to be making *inferences* about what is happening within its CRF on the basis of stimuli occurring elsewhere in the visual field. This process for making inferences on the basis of comparisons between local and more global stimuli may have served as the base upon which other cognitive capacities for logical inference developed in the evolution of other cortical areas.

What is the anatomical basis in fiber connections for the extensive surrounds of visual cortical neurons? The ascending connections closely match the visuotopic organization of the CRF's.[82] Intrinsic connections within each visuotopic map probably contribute to some extent to the surrounds,

Spatial Vision, D. Ingle, D. Lee and M. Jeannerod, eds., Nijhot, The Hague, 1984.

[80]R. Von der Heydt, E. Peterhands and G. Baumgartner, "Illusory contours and cortical neuron responses," *Science*, **224**, 1260-1262, 1984.

[81]S. M. Zeki, "Color coding in the cerebral cortex: the responses of wavelength-selective and color-coded cells in monkey visual cortex to changes in wavelength composition," *Neuroscience*, **9**, 767-781, 1983.

[82]R. E. Weller and J. J. Kaas, "Retinotopic patterns of connections of area 17 with visual areas V-II and MT in macaque monkeys," *J. Comparative Neurology*, **228**, 81-104, 1983.

but the main source of input to the surrounds probably comes from structures higher in the system.[83] Ascending projections terminate in layer 4 of each cortical area, while descending projections terminate in the other layers, particularly in layers 1 and 6.[84] It is particularly interesting that one cortical area, the medial (M), which has a map which emphasizes the more peripheral parts of the visual field, has no ascending outputs according to its laminar connections; it only feeds back upon other cortical areas.[85] Thus, the function of area M and perhaps some of the other extrastriate areas may be largely to provide feedback for the elaboration of surround mechanisms in other areas. They would thus have functions analogous to regulatory genes or controlling elements in genetics.[86]

Recent investigations have also demonstrated important attentional and non-visual inputs to visuotopically mapped cortical areas. For example, Moran and Desimone[87] have found in trained monkeys that the spatial location of focal attention gates visual processing by filtering out irrelevant visual information within the classical receptive fields of neurons in V4 and IT. Maunsell and Haenny[88] have trained monkeys to match the orientation of a visually presented grating with a tactually presented grating and recorded the responses of V4 neurons during this task. Sixty percent of the V4 cells were influenced by the orientation of the tactile grating which was not visible to the monkey; some of these responses were very specific and are likely to have developed as a consequence of the animal's training. It is not clear how these influences are relayed to the visuotopically mapped areas; however, one very interesting set of connections has recently been demonstrated between the amygdala, which is strongly implicated in memory processes,[89] and the visual cortex. The inferotemporal visual cortex

[83] J. Allman, F. Miezin, E. McGuinness," *opus cit.*, 1985.

[84] J. H. R. Maunsell and D. C. Van Essen, "The connections of the middle temporal visual area (MT) and their relationship to a cortical hierarchy in the macaque monkey," *J. Neuroscience*, **3**, 2563-2586, 1983.

[85] J. Graham, J. Wall and J. Kaas, "Cortical projections of the medial visual area in the owl monkey, *Aotus trivirgatus*," *Neuroscience Letters*, **15**, 109-114, 1979.

[86] B. McClintock, "Controlling elements and the gene," *Cold Spring Harbor Symposia in Quantitative Biology*, **21**, 197-216, 1956.

[87] J. Moran and R. Desimone, "Selective attention gates visual processing in the extrastriate cortex," *Science*, **229**, 782-784, 1985.

[88] J. H. R. Maunsell, personal communication.

[89] M. Mishkin, "A memory system in the monkey," *Phil. Trans. of the Roy. Soc. B*,

projects upon portions of the amygdala in an ascending fashion; the amygdala nuclei are extensively interconnected, and other parts of the amygdala are reciprocally interconnected with the neuroendocrine centers of the hypothalamus. Recently Amaral and Price[90] have demonstrated that the amygdala projects to the junction between layers 1 and 2 in many of the cortical visual areas in macaque monkeys. This provides an avenue for influences from systems involved in memory and neuroendocrine functions to mediate responses within the visuotopically mapped cortical areas.

The function of the visual system is not merely to create a precise neural analogue of the optic image on the photoreceptors, but beyond this, to reconstruct behaviorally significant features of the visual environment on the basis of imperfect and unconstant information. Neurons in cortical maps appear to make inferences about attributes of the visual world on the basis of local-global comparisons in the visual field, while taking into account the organism's past experience and attentional state.

Finally, I would like to return to the original theme of this essay and make one last comparison between molecular genetics and the neurobiology of visual cortex. Molecular geneticists have discovered a great deal about the organization and action of specific genes, but, apart from some promising leads, they have not yet discovered how even simple organs are put together from the genetic instructions. Similarly, those of us who study the visual cortex have been able to learn a great deal about its anatomical organization and the properties of individual neurons within it, but again, apart from some promising leads, we have not yet discovered how these are put together to form percepts or thoughts. I would like to suggest that the molecular genetics of organ assembly and the neurobiology of perception and cognition will each provide a rich source of analogies to stimulate exploration in the other field.

Acknowledgement: This work was supported by NIH grant EY-03851.

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298, 85-96, 1982.

[90]D. G. Amaral and J. L. Price, "Amygdalo-cortical projections in the monkey (*Macaca fascicularis*)," *J. Comparative Neurology*, **230**, 465-496, 1984.

owl monkey (*Aotus trivirgatus*)," *Brain Res.*, **35**, 89-106, 1971; "The organization of the second visual area (V-II) in the owl monkey: a second order transformation of the visual hemifield," *Brain Res.*, **76**, 247-265, 1974; "A crescent-shaped cortical area surrounding the middle temporal area (MT) in the owl monkey (*Aotus trivirgatus*)," *Brain Res.*, **81**, 199-213, 1974; "The dorsomedial cortical visual area: a third tier area in the occipital lobe of the owl monkey (*Aotus trivirgatus*)," *Brain Res.*, **100**, 473-487, 1975; "Representation of the visual field on the medial wall of the occipital-parietal cortex of the owl monkey (*Aotus trivirgatus*)," *Science*, **191**, 572-575, 1976; W. T. Newsome and J. Allman, "The interhemispheric connections of visual cortex in the owl monkey, *Aotus trivirgatus*, and the bushbaby, *Galago senegalensis*," *J. Comp. Neurol.*, **194**, 209-234, 1980]. The somatosensory areas were mapped by M. Merzenich, J. Kaas, M. Sur and C. S. Lin ["Double representation of the body surface within cytoarchitectonic areas 3b and 1 in the owl monkey (*Aotus trivirgatus*)," *J. Comp. Neurol.*, **181**, 41-74, 1978]. The auditory areas were mapped by T. J. Imig, M. A. Ruggero, L. M. Kitzes, E. Javel and J. Brugge ["Organization of auditory cortex in the owl monkey (*Aotus trivirgatus*)," *J. Comp. Neurol.*, **171**, 111-128, 1977]. The subdivisions of superior temporal and inferotemporal visual cortex are based on the connectional studies of R. Weller [*Subdivisions and connections of inferior temporal cortex in owl monkeys*, Doctoral Dissertation, Vanderbilt University, Nashville, Tennessee].

Figure 16.3: Left: dorsal view of the skull of *Tetonius homunculus*. A.M.N.H. No. 4194. Right: dorsal view of Radinsky's reconstruction of the cranial endocast of *Tetonius*. OB: olfactory bulb. S: sylvian sulcus. Reproduced from L. B. Radinsky, "Oldest primate endocast," *American J. Phys. Anthropology*, **27**, 385-388, 1967. Courtesy of Wistar Press. Note the large expansion of occipital-temporal cortex in *Tetonius*. Many of the areas illustrated in Figure 16.2, including V-I, V-ii; DL, MT, M and IT_C were probably present in the early primates of the Eocene such as *Tetonius* because they are present in modern galagos, whose most recent common ancestor with monkeys would have lived no more recently than the early Eocene. [J. Allman, J. Kaas and R. Lane, "The middle temporal visual area (MT) in the bushbaby, *Galago senegalensis*," *Brain Res.*, **40**, 197-202, 1973; J. Allman, C. B. G. Campbell and E. McGuinness, "The dorsal third tier area in *Galago senegalensis*," *Brain Res.*, **179**, 355-361, 1979; J. Allman

and E. McGuinness, unpublished mapped data for *Galago senegalensis.*]

Figure 16.4: Direction-selective neuron with an antagonistic direction-selective surround recorded from the middle temporal visual area (MT) in the owl monkey. The left graph depicts the response of the cell to 12 directions of movement of an array of random dots within an area coextensive with its CRF. The response is normalized so that 0% is equal to the average level of spontaneous activity sampled for 2-second periods before each presentation. Negative percentages in the left graph indicate inhibition relative to the level of spontaneous activity. In the left graph, the response to the optimum direction is 100%. The right graph depicts the response of the cell to different direction of background movement, while the CRF was simultaneously stimulated by the array of dots moving in the cells preferred direction. The stimulus conditions are depicted schematically above each graph. In the experiment, the dots were 50% dark, 50% light, and the background was much larger relative to the center than is depicted schematically. Reproduced from: J. Allman, F. M. Miezin and E. McGuinness, "Stimulus selective responses from beyond the classical receptive field," *Ann. Rev. Neuro.*, 8, 407-430, 1985. Courtesy of Annual Review, Inc.