The Evolution of Ideas Concerning the Function of the Neocortex

Vernon Mountcastle

Krieger Mind/Brain Institute and Department of Neuroscience, Johns Hopkins University, Baltimore, Maryland 21218
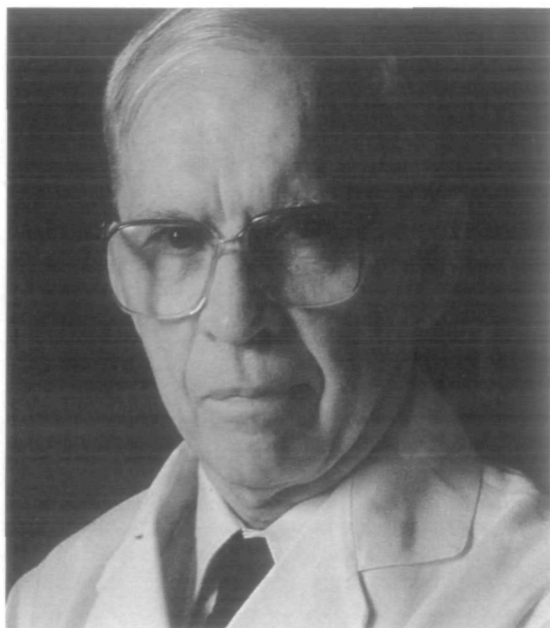
Vernon B. Mountcastle is Professor Emeritus at the Johns Hopkins Medical School and head of the Philip Bard Laboratories of Neurophysiology in the Zangvil Krieger Mind/Brain Institute at that university. His illustrious scientific career has been devoted to the study of the cerebral cortex, and his work has had an enormous impact on the field and on our understanding of the biological basis of higher brain functions. The following article is the text of his History of Neuroscience Lecture, delivered at the 24th annual meeting of the Society for Neuroscience in Miami, Florida, on 14 November 1994. It is a unique perspective on the history of ideas concerning the organization and function of the cerebral cortex from an outstanding scientist who has been at the forefront of this field for over four decades.

I am apprehensive in addressing you on this occasion. I am no historian, and I shall not recite the biographies of great neuroscientists. The real historians have done that already. I wish to discuss ideas that have energized research on the cerebral cortex, and show how some traditional and recent ones are combined in our present concepts. In doing so I shall name no living person, and show no slides.

The Cortical Localization of Function: The Cortical Organ Concept

Gall and Phrenology
It is counterintuitive that the historians of science attribute the general concept of functional localization to Franz Joseph Gall. Indeed, it was the father of phrenology who shortly after the turn of the 19th century generated the idea that the functions controlled by the brain are localized in separate cortical areas—cortical organs. There had, of course, been many discussions of this matter in earlier writings.

However, it was Gall who generalized the idea, and included a wide range of behaviors in his list of functions. In modern terms, Gall correlated the elements of faculty psychology with cortical geography. Gall was opposed to both animal experimentation and the study of humans with brain lesions. Where, then, was he to turn? To the bumps on the head, of course. Phrenology was thus born and prospered, with professional practitioners, academies, symposia, and learned journals. There followed a half-century of head palpations, especially in France, Great Britain, and the United States; and even in Boston, where the skull of Gall's colleague Spurzheim, presumably well palpated, now rests in the Anatomical Museum of the Harvard Medical School.

Flourens and the Experimental Method
Gall met a powerful adversary on the Parisian neurological scene: Pierre Flourens, an intrepid disciple of the experimental method. Alas, virtually all of Flourens's lesion experiments were made in birds, plus a few in small mammals. He declared that functions are not localized in the forebrain, and that all sensory and volitional "faculties" occupied concurrently the same cortical areas. And Flourens carried the day. Gall was virtually driven out of French science. He never made the Academy!

Flourens was wrong. For my present discussion it is trivial that Gall's ideas led to a pseudoscience, for they led also to the era of experimental cerebral localization. Gall was wrong in craniography, wrong in preferring naturalistic observation to the experimental method, wrong to think of a rigid separation of cortical organs; but Gall was right to think of faculties as being differentially related to different areas of the cortex.

Thus, while Flourens won the battle of method, Gall won the war. The idea of functional localization dominated thinking in the neurological sciences from the time of Gall right up to the present day, with, I believe, some detrimental effects.

The Heroic Age of Clinical Neurology
I turn to the golden age of clinical neurology, in which the cortical organ concept dominated ideas about cortical function. Indeed, the methods available allowed little else. In this period study of humans and animals with brain lesions, electrical stimulation of the cerebral cortex, and the development of cytoarchitecture all reinforced—in fact, reified—the cortical organ concept. Neurology's golden age began in the English-speaking world with Hughlings Jackson and those who followed him, paralleled in continental Europe by Broca, Charcot, Wernicke, Henschen, von Monakow, and many others.

The ideas of Spencer and Jackson, and Sherrington were rooted in an idiosyncratic interpretation of Darwinian evolutionary theory as applied to the nervous system, that is, that the brain develops in phylogeny by the successive addition of more cephalad parts, each new addition elaborating more complex behavior, and regulating more caudal and primitive

parts, and the presumably more primitive behaviors they control.

These ideas were applied especially to the cerebral cortex vis-à-vis inferior structures, and between what were regarded as phylogenetically older and newer regions of the cerebral cortex, for example, in Jackson's idea of lower-middle-higher levels of cortical control of movement, and in his theory of dissolution after lesion or disease of the cerebral cortex. In the midst of this, it is worth remembering Spencer's famous aphorism: "A function to each organ, and each organ to its function, is the law of all organization." Gall's shade must have danced with delight on hearing this, and in fact Spencer revealed in his autobiography that he was a devoted adherent of phrenology from childhood until middle age—until the advent of Darwinism.

Thus, the local organ concept was wedded to that of the hierarchy: neocortex on top, everything else in order below, and segregated and hierarchically arranged levels of organs within the neocortex itself.

These ideas were generated by scholars who thought deeply about their problems, and who took into account every shred of evidence available to them. If they arrived at conclusions we now regard as only partly true, or in others clearly wrong, decry them not! They were burdened, as we all are, by their own *Zeitgeist*, and limited by the experimental methods available.

The Discovery of the Electrical Excitability of the Cortex
The discovery of the electrical excitability of the cerebral cortex by Fritsch and Hitzig burst on the neurological world in 1870. It was quickly confirmed by Ferrier and others; it further entrenched the local organ concept, for now there were two: Broca's area for language, and the precentral gyrus for movement! The method is of great value in neurosurgery and in certain types of experiments but it is an anatomical method, a crude one by today's anatomical standards. I know of no general concepts concerning cortical function that derive from it.

Sherrington and the Encephalization of the Reflex Arc
A neurophysiology of the cerebral cortex scarcely existed during the period 1860-1880, when the cerebral organ concept became entrenched. The methods available—cortical lesions and electrical stimulation—were always adjunctive to the study of humans with brain lesions. However, neurophysiology exploded in a related field, in the hands of a man of formidable intellect and experimental skills, Sir Charles Sherrington. By the turn of the century Sherrington had unraveled the reflex organization of the spinal cord, established the concept of reciprocal innervation, and proven that inhibition is an active central process. He was a published poet and, what is more, had composed some of the most obtuse sentences ever written in English.

Dare anyone criticize a saint? Well, I shall, for the institutionalization of sensorimotor physiology as the reigning paradigm for brain function dominated thinking about the cerebral cortex. It led to the erroneous idea that cortical function might be understood in terms of the successive superimposition of complex reflex loops engaging the cortex from below and reflecting action back to efferent structures. This led to an intellectual plateau from which we have just now finally emerged.

I like to think that if Sherrington were here he would agree. Surely he would be fascinated by present knowledge of the dynamic actions in the nervous system, and, I think, eager to study in his own spectacularly creative way what he called the enchanted loom.

The Age of Cytoarchitecture
The development of cytoarchitecture greatly reinforced the cortical organ concept. It is based on the variations in cell types and packing densities in different cortical layers, which allows parcellation of the cortex into areas, sometimes precisely, often vaguely. The field is studded with the names of great neuroanatomists, from Meynert to the Vogts, Brodmann, and von Economo, right up to equally important figures on the present scene.

The Vogts identified more than 200 areas in the human cortex, and they sought to assign functions to areas: one function, one area. Gall triumphed again! The maps of Brodmann for monkey and man gained wide acceptance and, although defective in some ways, have remained anatomical landmarks for cortical research right up to the present moment. The cortical organ concept gained support from the discovery that each cytoarchitecturally defined area receives a projection from a specific thalamic nucleus, and in some cases these areas are congruent with cortical maps determined electrophysiologically.

I shall turn shortly to new discoveries that I believe have broken the cerebral organ paradigm. But first, some intervening developments.

The Electrical Activity of the Brain
One can imagine the excitement in the neurological world when Berger's descriptions of the electroencephalogram appeared in 1929 through 1931. Here at last was a method for studying the active brain in waking, behaving subjects. Berger combined two simple methods: voltage amplification and permanent recording. The history of this discovery shows the importance of adequate methods in brain research.

Berger's first publication is separated by 55 years from the discovery of the electrical activity of the brain by Caton in 1874, demonstrated by him in Liverpool in 1875, in London and Washington in 1877, and published in the *British Medical Journal* in that same year. He recorded with a string galvanometer; movements of the string were amplified by projection upon a distant wall of a light beam reflected from a mirror on the string. One had to see to believe.

It is remarkable that there is no evidence from their writings that the leading British neuroscientists of the day even knew of this discovery, or, if they knew of it, believed it. If Caton had only had a Grass machine!

Caton was not alone. Virtually identical discoveries were made independently in Poland by Beck, published in 1890; by Danilewski in Russia with a paper in 1890, but claiming discovery in 1876; and by von Fleisch in Vienna in 1883, who deposited this information in a sealed letter not opened and published until 1890. He recorded the visual evoked potential, I think for the first time ever. A discovery of this magnitude, deposited for seven years in a sealed letter? Well, perhaps better a sealed letter than a nationally televised news conference. After all, he might have been wrong!

The Age of Electroencephalography
Berger's observations were quickly confirmed by Adrian. Methods were rapidly improved and investigations exploded. Prominent among them was a search for correlations between EEG patterns and behavioral states—including psychotic states. One result is the modern triumph in studies of sleep and wakefulness. Next was an effort to discover whether previously defined cerebral organs generated organ-unique patterns of electrical activity. Some regional variations were discovered, but no area-specific patterns.

Something important followed: the sophisticated clinical discipline of electroencephalography. Next was a study of event-related potentials and their correlation with behavioral

performances measured objectively, then the study of induced rhythms in the brain, and, in the present decade, a renewed interest in the nature of slow wave events. These latter are aimed at solving questions that bear directly upon our evolving concepts of neocortical function: whether slow waves are epiphenomena, the algebraic summation of local synaptic current flows through the impedance of brain tissue; or, are they active agents harmonizing levels of excitability in large populations of neurons; or, are they active agents binding together populations of neurons simultaneously active in perceptual operations. These and similar questions are major themes in ongoing programs of research.

The Era of Cortical Mapping

It was Wade Marshall who first saw the value of the evoked potential method for study of cortical geography. The method depends upon the fact that a sensory stimulus evokes synchronous volleys of impulses in primary afferents that after transmission evoke slow wave responses in sensory cortical areas. The early publications of Marshall, Gerard, and Saul and of Bartley and Bishop, both in 1933, were quickly followed by others.

The development of the field of cortical mapping with this method is largely due to the lifelong efforts of Clinton Woolsey and his many students and colleagues. They created and led the era of mapping from the mid-1930s on, an era that extends right to the present time. The results obtained are invaluable. They provide definitions of the primary sensory areas of the neocortex that serve as guides to experiments on the cerebral cortex.

The first era of evoked potential mapping was followed by a second, but now with microelectrode recording as the mapping tool. This produced a series of landmark discoveries about the cerebral cortex. Among them are the following:

(1) That regions of uniform cytoarchitecture may contain more than one map, and that these several maps may have different functional specializations: a death blow to the cytoarchitectural—cerebral organ match.

(2) That sensory areas previously thought to contain but a single map of a sensory sheet may contain several: there are four in the postcentral gyrus of the macaque monkey.

(3) That cortical maps are mutable; that is, their size, exact position, and internal details can be changed, by changing afferent inputs to sensory areas, or output targets for motor areas.

(4) That this adult plasticity exists in the cortices of a large number of species and is now regarded as a uniform characteristic of mammalian brains. And, in this manner differences in homologous areas in conspecifics are attributed in part to different life experiences.

(5) That the most likely mechanism of this plasticity is a change in synaptic efficiency of fringe synapses present but ineffective before alterations. However, the possibility that delayed changes may be due to new growth cannot be dismissed.

The New Connectivity and Distributed Systems

Discoveries of the last three decades concerning connectivity have shown that the cortex consists of widely distributed systems, linked to external channels through cortical entry areas with some degree of hierarchy. The relevant sets of facts are these:

First, a large number of hitherto unknown cortical areas have been identified, often by their functional specializations discovered in electrophysiological experiments. At last count 72 areas have been identified in the macaque cortex.

Second, the distributed connectivity in the neocortex is so great as to make a new qualitative fact about the brain. In the

macaque, for example, 758 connections link those 72 areas—only 15% of the theoretical total, so undoubtedly more to come. And this does not take into account transcallosal or thalamic connections. The to-and-fro connections between cortical areas—there are 311 reciprocal pairs, 622 of the 758 connections—are often not equivalent in their source-sink relations. The meaning of this for function remains uncertain.

Similarly unnerving is the discovery that the heavily interconnected areas of the parietal and frontal lobes engage convergently upon 15 cortical targets in common, in some cases by laminar interleaving of their terminals in common columnar targets, in others by isolated projections to adjacent pairs of columns.

Last, the cortical areas involved are organized in a columnar manner, which I shall shortly discuss.

Definition of a Distributed System and Its Properties

A distributed system is a collection of processing units that are spatially separate and communicate by exchanging messages. A system is distributed if the message transmission delay is a significant fraction of the time between single events in a single processing unit.

So far so good, but the definition infers the presence of a real-time clock. The discovery of such a clock in the cerebral cortex would be a megaevent.

Some further properties of distributed systems are these:

(1) They are not hierarchical, although some subsystems may have hierarchical properties.

(2) Signal flow through such a system may follow any of a number of different paths.

(3) Action may be initiated at any of a number of nodal loci within a distributed system.

(4) Local lesions within such a system may degrade but not eliminate its function completely.

(5) Recovery of function after a lesion is a dynamic reorganization, and does not necessarily depend upon a modified connectivity.

(6) Distributed systems are re-entrant systems, and their nodes are open to both externally induced and internally generated signals.

Intuitive understanding of such a system is difficult. Topological analysis helps greatly, creating images of the areas of the cortex as if floating in two-dimensional space, each area located in terms of its connections to other areas, not its physical location in the brain. These are images of the brain in cyberspace, and very beautiful.

The distributed nature of higher cortical functions has been confirmed in studies in which human subjects emit a set of behavioral events as images of their brain activities are obtained, frequently by measuring changes in blood flow. The areas of increased flow frequently include major nodal, or funnel areas, but always a number of others distributed in sometimes unpredictable places, so that the findings can only rarely be correlated directly with classical notions derived from studies of humans with brain lesions. Here as in earlier studies the concept of functional localization is giving way to that of functional specialization. What is badly needed for further advance in this field, I believe, is a definition of the relations between changes in blood flow and the underlying causative neuronal activity. This has always, of course, been one of the handicaps in electroencephalographic studies, as it is now for those using magnetoencephalography.

Single Neurons and Neural Networks: Four Conceptual Changes

I turn now to the era of single cortical neurons and neural networks, a revolution that has progressed in a sort of punctuated equilibrium. Four of the major changes are these:

(1) From the idea of the cerebral cortex as a tissue, to the view that it is composed of neurons linked in neural networks by the connections between them.

(2) The transition from the Gallian idea of functional localization to functional specialization. This is not a play on words, not a semantic difference, but fundamentally different concept.

(3) The definition of the modular organization of the cortex, and its meaning for local and distributed dynamic operations in the cortex.

(4) The fracture of the schema of cytoarchitecture, for areas of uniform cytoarchitecture have been shown to contain sometimes several regions that differ in functional specialization; the prestriate regions of homotypical cortex serve as a major example.

Cajal and the Study of Single Cortical Neurons

The modern era began with Ramon y Cajal and the neuron theory, a heritage of neuroscience so often recounted I shall not repeat it here. Cajal used Golgi's method to describe the morphologies of different cortical types, their local and some of their distant connections, and brought knowledge of synaptic structure to the limit of the light microscope.

Then, Cajal-type research programs fell dormant for decades, to be renewed only after midcentury. Since then his methods and general approach have been combined with electron microscopy, immunohistochemistry, tracing by intracellular injection, synaptic biochemistry, cellular physiology, and the powerful tools of molecular biology to produce a glittering array of knowledge of the morphology and connections of cortical neurons, and their synaptic mechanisms, transmitters, receptors, second messenger systems, mechanisms for plastic change, and, I think not far off, a flow diagram of intrinsic cortical circuits. And already a covey of theories and models of the operations of local neuronal networks in the cortex.

The Method of Single Neuron Analysis

Studies of single cortical neurons by microelectrode recording began in 1952–1953 almost simultaneously in half a dozen laboratories. Studies of this sort had been made in the late 1940s in the hippocampus, in the brainstem nuclei of the auditory system, and in the thalamic nuclei of the somesthetic system.

The field expanded rapidly, attended by great optimism, for it appeared that many new principles of brain function were about to be revealed. *Not quite!* Nevertheless, the rate of discovery was high, though not quite as high as we expected. It included the following, among many:

(1) That the receptive field is a defining property of cortical sensory neurons; that one could plot the range of sound frequencies, the zone in visual space, or the area on the skin within which adequate stimuli would excite the cell under study. Receptive field data were used to construct some images of cortical operations, at least in the static mode. The doctrine of the receptive field is still an active but perhaps no longer a leading concept in sensory research.

(2) The discovery that some stimuli inhibited cortical cells, and that the inhibitory receptive field is frequently disposed in the surround pattern in reference to the excitatory field.

(3) The discovery of modality specificity, for example, in the somatic afferent system, where the stimulus selectivity so clear for large-sized primary afferent fibers innervating the skin is preserved through the lemniscal system to the somesthetic cortex. A similar specificity was discovered in visual and auditory systems.

(4) The discovery of feature detection, or triggering: that many neurons of sensory areas are selectively responsive to features of the sensory stimuli that are not signaled by any single set of primary afferent fibers, for example, orientation and directional selectivity in the striate cortex.

Trigger sensitivities appear to be matched with certain features of the sensory stimuli to achieve in an economical way a complete representation, and the further elaboration of trigger properties in regions of cortex beyond primary sensory areas strongly supports the functional specialization idea.

(5) It then became possible to use these properties of the receptive field and trigger features to define the functional organization of the cortex.

However, there was a major handicap, for it was only with considerable strain that explanations could be made of the sensory-perceptual capacities of primates in terms of the properties of cortical neurons studied in anesthetized animals, in which only the static and not the dynamic properties of cortical neurons could be studied. The direct comparison became possible with a new method, to which I shall shortly turn. First, I wish to describe one of the results obtained in anesthetized animals concerning the organization of the cerebral cortex.

The Columnar Organization of the Cerebral Cortex

That was the discovery of the columnar mode of organization of the neocortex. The basic unit of the mature cortex is the minicolumn, which contains 80–100 neurons and includes all major neuronal types. It extends vertically across the cellular laminae II–VI, and its neurons are heavily interconnected in the vertical dimension. The minicolumn is produced by the generative action of a local group of progenitor cells in the germinal epithelium, via the intervening ontogenetic unit of the cortical plate of the developing neocortex.

Several hundred minicolumns are bound together in the horizontal dimension to form the functional columns of the mature cortex, linked both by internal connections and by the patchy, spatially intermittent pattern of ingrowth of thalamocortical and corticocortical afferents. Columnar identity is also dynamically maintained by pericolumnar inhibition.

Cortical columns vary from 300 to 600 μm in dimension, a size invariant among mammalian cortices that vary in surface area by 3 orders of magnitude. Cortical expansion in evolution is achieved largely by increases in surface area, and thus by increases in the number, not the size, of constituent columns.

Columnar organization allows for the intermittently recursive mapping, so that a number of variables can be mapped to the two-dimensional surface of the neocortex. Specific connections are maintained among ordered sets of columns in different cortical areas, so that topological relations are maintained in the transit of activity through distributed systems. All the columns of a cortical area are not linked to all the targets engaged by the area. The result is that a given cortical area can be a member of a number of distributed systems.

A cortical column is a complex processing and distributing unit that links a number of inputs to a number of outputs via internal processing chains that overlap but are to a certain degree separate. The cells of origin of different output pathways are segregated by cortical layer, which carries the inference that neuronal processing within different pathways in a column may show certain properties in common, others that differ.

Columns and minicolumns have been identified in all sensory and motor areas, and the general mode of columnar organization has been observed in all areas of the homotypical cortex studied intensively. It has frequently been confirmed in imaging studies, as well.

The Combined Experiment

There is no doubt among those who experienced it that a "sea change" occurred in CNS physiology in the 1960s, and with it changes in concepts of cortical function. It was generated by new techniques and new experimental designs. Three things changed the field.

The first was the realization that experimental psychology and brain physiology are simply different ways of looking at what are generically the same set of problems and that neurophysiological observations could provide answers to psychological questions.

The second was the development of a psychophysics for nonhuman primates, so that it was possible to measure the sensory-perceptual performance of monkeys, and other complex behaviors like directed attention, short-term memory, and so forth.

The third was revolutionary: the development of the combined experiment, in which one observes behavior and relevant neuronal activity simultaneously. The method was first devised—permit me to break my rule—by Herbert Jasper, and developed further by the late Edward Evarts. The aim of the method always was to reconstruct population events, at first in a post hoc manner, but now increasingly by recording from numbers of neurons with many microelectrodes.

Here are a few of the new concepts that emerged:

(1) That all but the simplest signals are embedded in the population patterns of neural activity.

(2) That what we call by the much-mangled word "representations" of objects and events in the world are not passive projections on a screen, but constructions compounded by our sensory-perceptual systems from afferent streams in sensory systems, from the retrieved neural signals of past experience, and by the controlling effect of the modulatory systems of the central core. This allows recognition, categorization, and the discrimination of objects independently of background, movement, location, and so forth.

(3) That many brain functions we commonly regard as "higher" can now be brought under direct experimental observation, and many of these are now under study in humans, by the combination of various methods of imaging in controlled behavioral situations.

(4) The shift from the concept of hierarchy to that of distribution was greatly strengthened by the discovery that the different components of sensory stimuli are processed separately in different cortical areas, each specialized for a particular mode of processing, all linked together in distributed systems. This was further a shift away from the local organ concept.

(5) The discovery that a few primary afferent channels from a sensory surface like the hand can by their permutations evoke complex perceptual experiences like stereognosis, and that equally complex permutations of the evoked neural activity are seen in higher-order areas of homotypical cortex.

Synaptic Transmission in the Neocortex

The knowledge accumulated in the last decade concerning synaptic transmission in the neocortex is so vast it boggles the mind. It is the result of the intensive application of the methods and concepts of molecular neurobiology. I touch here upon only a few of the salient features.

(1) The biophysical properties of cortical neurons vary with neuron type, and the dynamic integration of these properties with synaptic responses determines local network properties.

(2) Dendrites do possess the capacity for electrogenesis, and the single trigger model of synaptic transmission has been modified to take this into account. Spines function as

biochemical segregators, particularly by confining to a restricted postsynaptic region the calcium surge produced by NMDA receptor activation.

(3) Small molecule and polypeptide transmitters at cortical synapses have been identified, together with the relevant postsynaptic receptor molecules. The mechanisms of both direct and second messenger–mediated transmission have been elucidated.

(4) Studies in slice preparations will soon yield a description of dynamic of operations in intrinsic cortical circuits.

(5) The molecular and cellular mechanisms of long-term potentiation and depression, prominent forms of synaptic plasticity, have been shown to be more or less universal properties of neocortical synapses, giving further strength to the idea that the neocortical mechanisms of learning and memory are widely distributed.

Uniformity and Diversity in Local Cortical Operations

How are different cortical areas specialized in their operations? What appear to be quite different operations— or computations, to use the current buzzword—are made in the cortical areas similar in architecture, neuron types, and local circuitry. Thus, their functional specialization might be attributed to differences in afferent input. This idea is supported by the results of thalamocortical redirection experiments.

However, the possibility cannot be dismissed that such areas may differ in their intrinsic, dynamic operations, in which small differences in one or another property might influence output disproportionally. This problem can be addressed directly with the elegant new methods of local circuit analysis, preferably applied in the waking, working, neocortex.

The Mind–Brain Problem

These ideas and the experimental programs they drive have brought neuroscientists abruptly face to face with complex problems long avoided. Foremost among them is the ancient one of brain and mind, or, in updated terms, brain and behavior. It is not a field in which neuroscientists have distinguished themselves, but even after 2000 years of effort, philosophers have not done so well, either!

When I entered neuroscience in 1946 it was soon made clear to me that the mind–brain problem was not suitable for scientific discussion. To speak of it was bad form, and revealed a certain lack of scientific class! Indeed, we had before us then examples of world-class neuroscientists who had unburdened themselves of considerable foolishness on this subject. They were regarded as having gone a bit soft, or in Thomas Wolfe's memorable phrase, as "lost and by the wind grieved."

But the problem remains, and we can no longer ignore or make fun of it. Major research programs aim directly at and achieve some success in understanding the brain mechanisms of those aspects of the inner life of man traditionally thought of as his minding. Among them are perception, intentionality, learning and its remembrance, forgetting, planning, execution. These and others are brought to some level of scientific enquiry. Not that we understand them very well, but they are now in play in the scientific arena.

Now, every neuroscientist is his own amateur philosopher. Each of us upon looking into this disputatious arena forms opinions about this wordy world. It is my own that no form of dualism will do, whether in traditional Cartesian form, whether parallel, or interactionist, or in any other derived format. The idea that a nonmaterial essence exists that interacts with, controls, or is controlled by the brain seems to me to be so unlikely as to be outside the realm of scientific discourse and action. But remember, one can never prove a negative!

Dualism is dead! And what a relief! However, this puts a

heavy responsibility on those dedicated to the study of the function of the brain and how it controls and generates behavior. Indeed, dualism had one saving grace, for it provided a face-saving escape from unsolvable problems. The death of dualism evokes in the neuroscientist a pervasive sense of modesty, for he more than any other understands how difficult these problems are, and how far we are from their solution.

But it also evokes a certain intrepidity, for he observes the steady progress of neuroscience toward solutions by the traditional method of successive approximations toward the truth, even if never reaching that nirvana. And, the death of dualisu.i allows one to view the history of hominid evolution with a certain sense of pride: *We have got here on our own!*

What replaces dualism is of course some form of physicalism, or psychophysical monism. I am much taken with the general thesis of emergent materialism described by Mario Bunge in his monographs of 1980 and 1987. The thesis is founded in neurological facts—here is a philosopher who knows the brain! The properties of a system like the brain are emergent, and are to be understood in terms of its constituent elements and their couplings. System properties are not the simple result of summing identical properties over the elements of a population, but emerge from dynamic interactions between elements of the system.

The monistic thesis is that every mental process is a brain process, but not that every mentalistic sentence is identical to some neurophysiological sentence. Mind and brain are not identical, no more than lung and respiration are identical. Emergent materialism holds that the brain is not a machine, and above all not a computer, but a biosystem. As such it has evolutionary and ontogenetic histories and is endowed with properties and laws peculiar to living things, and a brain has some properties not shared by all biosystems.

Conclusion
I now propose a synthesis of ideas concerning the function of the neocortex. It is of course tentative, complex, not epitomized in a brief phrase, changes constantly in the light of new discovery, and, I myself retain a high degree of skepticism about much of it! I describe it in a series of statements.

(1) It defines the cortex as a multinoded set of nested and widely distributed systems in which hierarchy obtains at levels of entry and exit, much less so in the large in between.

(2) It includes what is useful from nearly two centuries of study of the localization of function in the cortex, but avoids the error of defining function as the reciprocal of the defects produced by lesion. Where nodes are funnels at entrance or exit from a system, lesion will obliterate or seriously degrade a function, but this is weak evidence that the function is executed exclusively within that node or area. Lesions of the fusiform gyri eliminate color vision, but no one proposes that we see color there! Higher-order processes like those of somesthetic or visual perception are embedded in the dynamic neuronal processes within systems in which certain nodes may be of cardinal importance.

This change in concept is a fundamental not a semantic one, from the cerebral organ concept of functional localization to the present idea of functional specialization in cortical areas.

(3) It includes a sophisticated knowledge of the ontogenesis of the neocortex: the mosaicism of the germinal neuroepithelium; the molecular mechanisms guiding migration; the definition of an ontogenetic unit, the prodrome of the elementary processing columnar units, the minicolumns, many of which are combined to form operating modules in the mature cortex; the interaction of genetically defined and experientially modifying factors in the maturation of the cortex and development of its connectivity; and some idea of how new cortical areas might have arisen in evolution.

(4) It includes increasing knowledge of the operations in intrinsic local circuits of the cortex, of their synaptic operations, transmitter, and receptors; and open to the idea of volume conduction. It seeks to define the degree of operational commonality or difference that may obtain between cortical modules that have a remarkably uniform neuronal content and internal connectivity. The question is, What is the local cortical computation?

(5) It considers once again the questions of whether slow wave events are more than epiphenomenal signs of population actions, or indeed may be active agents, or act as carriers, or may indicate/be processes of oscillation and synchrony between populations in binding, in differentiating figure from ground, in perceiving global scenes.

(6) It attacks with both theory and experiment the problem of population actions, the transitions from impulse to topographic to vector coding, and what for want of knowledge I simply call the populations transfer functions, for example, between sensory representation and the composition of motor actions.

(7) It accepts for experimental test the hypothesis that consciousness is the behavioral sign of the dynamic activity of certain but not all cerebral systems, and regards this hypothesis with no astonishment at all!

(8) It incorporates the facts of synaptic plasticity and modifiability in the cerebral cortex, emphasizes its important role in secondary histogenesis of the cortex, and in learning and memory. However, I add what is frequently disregarded, that the most powerful and obvious plasticity is the regulation and control of dynamic activity in forebrain circuits over short time scales by the afferent modulatory systems of the central core, producing adaptive changes in an otherwise unchanging connectivity. Here is plasticity, "a go-go."

(9) It explores with increasing sophistication models of the action of cerebral systems, particularly models created bottom up, whose initial assumptions are the properties of real neurons, their connections, and their functional properties.

(10) It needs specific theories abut the operations of subsystems within the brain, and it seeks in an open-minded way more global theories of brain function, particularly those in whose context hypotheses can be generated for experimental test, for example, the exact neural mechanisms of an association, or the role of reentrance in cerebral processing for perceptual operations, or the importance of reciprocal couplings between activities in parallel maps.

A distinguished theorist has recently written, "no theory or model of brain function has survived its birth by more than a decade, and most die in infancy." I believe this is due to our ignorance of the local cortical operation.

(11) There is little doubt that the greatest influence in our century upon neuroscience in general, and especially for studies of the cerebral cortex, is the abandonment of the dualistic philosophy. The dominant theme now is that all behaviors, including those we have traditionally regarded as mental, are externally observable and/or internally experienced aspects of brain processes. There is no transition or interface between the two—mental states are brain states. This has freed us to plan and execute studies of the higher functions of the neocortex in a rigorously scientific manner, and it leads to an era in which cognitive theory and neuroscientific theory are synthesized in a general theory of brain function.

Finale
I come down in the end to a central problem. We know that the dynamic processes of things like perception, intentional-

ity, attention, learning, and memory are embedded in the activity in widely distributed systems of the cortex and its subcortical connections. Ideas abound about how these processes in multiply-reentrant systems can be coupled. How does one process monitor another process, and how does the result flow through to conscious experience, to the acquisition of knowledge of the world around us? How do we avoid the obvious trap of the infinite regress, now in terms of processes rather than cells or modules? This sphinx is as enigmatic as ever—the problem for the next century.

Pessimists despair of its solution, ever. Optimists believe that by successive approximations and intermittent recursions we will gradually close on the answer. But the journey will be long and hard.

I wish you exciting journeys.

Notes

Address correspondence to Vernon Mountcastle, Krieger Mind/Brain Institute, Johns Hopkins University, Krieger Hall, Room 347, Charles and 34th Streets, Baltimore, MD 21218.

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