

NEURONAL



THE BIOLOGY OF MIND

'A revolutionary book . . .

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L'Express

JEAN-PIERRE CHANGEUX

NEURONAL MAN

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'an excellent book . . . remarkably clear and easy to read . . . I know of no better book to serve as a guide to neuroscience for the layman.'

Times Higher Education Supplement

Jean-Pierre Changeux is a world-famous neurobiologist. In an era when scientists have become specialists, he is one of the rare few who have not only disregarded interdisciplinary boundaries, but, in fact, bridged them. Published originally in France, where it was a best-seller for months, his *Neuronal Man* is an extraordinarily wide-ranging synthesis of the most up-to-date knowledge we have of the human brain – an account of discoveries as revolutionary as those in atomic physics at the turn of the century or genetics in the fifties. But more than a guided tour of the human brain, the book presents the author's radical and controversial hypothesis: that there is no 'mind' in man, nothing psychic, but rather only neurones, synapses, electricity, and chemistry.

An internationally renowned expert in his field, Jean-Pierre Changeux is professor of neurobiology at the Collège de France and director of the molecular neurobiology laboratory at the Institut Pasteur in Paris.

Neuronal Man (originally published in France as *L'Homme neuronal*) won the Broquette-Gonin Literary Award from the Académie Française in 1983. Professor Changeux lives in Paris.

'Writing with elegance and panache, he assaults dualist notions of a separate mind or spirit, the province of the philosopher and the theologian, like a latter-day knight errant riding through a land of misguided heathens.'

New Scientist

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NEURONAL MAN

The Biology of Mind



by Jean-Pierre Changeux

TRANSLATED BY DR. LAURENCE GAREY

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Preface to the Oxford Edition

Neuronal Man was written in 1982 and has been regularly revised in subsequent printings and also for its English translation. Although the most up-to-date neurobiological data were, of course, taken into account during the initial editing of the work, it was not intended simply to be fashionable and, as such, doomed to becoming rapidly outdated. It represents, rather, an attempt to reflect in depth upon the neurosciences and their implications for mankind, based as much on the history of ideas and the evolution of knowledge as on the most recent discoveries. The examples used to illustrate the arguments put forward in the book were necessarily limited in number and presentation at the outset, but they were chosen with sufficient care to ensure that they still remain valid.

New facts have, of course, emerged to enrich our knowledge. There is room here for no more than a brief résumé of these data, so I will mention just those which are especially remarkable either for their originality or for the results they bring about.

Among the latter, I will refer first, in the chapter on "Animal Spirits," to the fact that, contrary to a frequently held belief, one neurone synthesizes not just one neurotransmitter but in reality several at the same time.¹ This coexistence of several chemical messengers dramatically increases the range of signals available to the nerve cell with which to communicate with its neighbors. Similarly, neurone chemistry has been constantly developing, in particular as a result of the identification of the structure of receptors for various neuronal "messengers" and, more especially, of the ionic channel specific to the sodium ions responsible for the propagation of the nerve impulse.²

For the chapter on "Mental Objects" a huge body of theoretical work, currently growing at an explosive rate, has had to be taken into account. This research draws its inspiration as much from the physics of disordered states of matter, such as the "spin glass"³ as from work on artificial

intelligence and, of course, on the neurobiology of the higher functions of the brain.⁴ The traditionally hierarchical and computational (or digital) views about the functioning of computers have been improved upon or, quite simply, replaced by models where the massive parallelism of the input and the analogical character of the representations predominate. In psychology also functionalist theories—whose purpose is to explain the psyche in terms of (if not to reduce it to) formal operations which are independent of their neuronal substrata—are tending to break the spell of their platonic seduction, and attempts at synthesis between psychology and the neurosciences are appearing more and more fruitful. But it has to be admitted that the code for mental representations, in space and in time, still has to be worked out, and it is there that one of the most important discoveries in the future development of the neurosciences has yet to be made.

The biology of the development of the nervous system presented in the chapters on “The Power of the Genes” and “Epigenesis” has developed spectacularly over recent years, in particular through the identification of genes that we have called “communication genes.” They have been regrouped into two distinct categories: one family encodes for surface proteins, such as CAM (cell adhesion molecules), which intervene in the adhesion between embryonic cells from the very first stages of development (but also in later stages) and during the formation of the nervous system;⁵ a second family code for regulatory proteins, which act at the level of chromosome genes in the same way as the “repressor” defined in the regulation of the synthesis of β -galactosidase in the *E. coli* bacillus. Initially identified in the *Drosophila* (fruit fly),⁶ certain of these genes determine the segmentation of the body (for example, their mutation causes the loss of one segment in two); others, known as homeotic, define the identity of each segment (for example, their change transforms a cephalic segment with an antenna into a thoracic segment with a leg). These genes have been found in vertebrates and, in particular, in mammals.⁷ They can manifest themselves several times in the course of development, and the product of some of them appears, selectively, in the embryonic nervous system. The central nervous system of mammals, the spinal cord and, of course, the encephalon display a repeated segment structure. It is tempting to see in this the result of the action of segmentation genes and/or of homeotic genes which might have manifested themselves very early, at the neural disc stage, even before the formation of the groove and its closing into the neural tube. From there we

might go on to speculate that the extremely rapid expansion of the frontal lobe—which, in the course of the evolution of primates, leads to man (see the chapter on “Anthropogenesis”)—may not simply be the result of the prolonged actions of some of these genes. In the near future molecular biology will doubtless provide the answer to a question which has concerned humanity for thousands of years.

The deliberately physicalist philosophy of *Neuronal Man* and the extension of the Darwinian model to the development of the neurone network, as well as to the genesis of mental objects, has sometimes provoked strong reactions which are not all of a scientific nature. The reader should bear in mind that the author of this book has neither claimed to describe exhaustively the functioning of the human brain nor wished to impose a totalitarian view of the human sciences; he desires merely to offer subjects for consideration to a wider public than that of the specialists and, especially, to establish an interface, which is still far from adequate, between the life sciences and the human sciences.

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Preface

Neuronal Man was born in 1979 as a result of a discussion with Jacques-Alain Miller and his colleagues on the review *Ornicar?* (which has since become *L'Âne*). This lively dialogue between psychoanalysts and neurobiologists demonstrated, against all expectations, that the protagonists could talk to each other and even come to an agreement. It is often forgotten that Sigmund Freud was a neurologist, for since his *Project for a Scientific Psychology* of 1895, the multiple avatars of psychoanalysis have cut off its real biological basis.¹ Could this renewed dialogue with the “hard” sciences be the sign of an evolution, a return to basic sources—perhaps even a new departure?

There was another positive aspect to this meeting: it allowed us to judge the distance we must travel before such exchanges can become constructive and a synthesis finally emerge. Perhaps the time has come to rewrite Freud's *Project* and to lay the foundation for a modern biology of the mind.² That is certainly not the pretension of this book; its scope is more limited—to inform and if possible interest readers in the neurosciences. In the last twenty years, our knowledge in this field has undergone an expansion matched only by the growth of physics at the beginning of the century and molecular biology in the 1950s. The impact of the discovery of the synapse and its functions is comparable to that of the atom or DNA. A new world is emerging, and the time seems ripe to open this field of knowledge to a wider public than the specialists and, if possible, to share the researchers' enthusiasm. Since the *Ornicar?* discussion, I have felt the need to bring together recent data relating to developments in the neurosciences. There was no question of presenting an exhaustive picture of contemporary research on the nervous system. A choice had to be made, and I will certainly be accused of partiality in this choice. I admit it. Several years of teaching at the Collège de France have convinced me that a fruitful exchange with one's audience can be established only on the basis of

a few simple but solid ideas. I hope that my partiality will be interpreted as a concern for educating.

The human sciences are in vogue. Much has been said and written about psychology, linguistics, and sociology, but the brain itself has been to a large extent excluded.³ This is not purely by chance. No, the stakes are too high for that. Yet this deliberate neglect is relatively recent. Might it be a question of prudence? Perhaps it is feared that attempts to give a biological explanation of the psyche or mental activity will fall into the trap of simplistic reductionism. Perhaps it would be better to uproot the human sciences from their biological subsoil. Surprisingly, disciplines that began with a physicalist viewpoint, like psychoanalysis, have begun to defend an almost complete autonomy of psychic phenomena, accentuating the traditional split between mind and body.

Throughout history, research on the nervous system has run into bitter ideological obstacles and visceral fears, on the right as well as the left. Any research that directly or indirectly challenges the immaterial nature of the soul threatens faith and risks being burned at the stake. There is also an understandable fear of the social impact of biological discoveries that, if abused, could become weapons of oppression. It might be wiser to cut the deep bonds that link the social to the cerebral. Rather than meet the problem head on, why not hide away this dangerous organ and “decerebrate” the social order?

Finally, the best writings in the human sciences generally deal with problems that touch one personally, like political involvement, sex life, or the education of children. The quest for the “internal” mechanisms underlying these concerns appears much less interesting. In the short term, this search will not lead to a code of good conduct, nor disclose the secret of happiness, nor permit us to predict the future (unless the knowledge so acquired stimulates a deeper reflection on human nature and the world around us).

Seen from another planet, human behavior would seem rather surprising. We are one of the rare species that kills our kind deliberately. Even worse, sometimes we condemn an individual murder while rewarding those responsible for collective homicide and the inventors of terrible war machines. This absurd madness has pursued man throughout history, from the invention of the Stone Age ax to the perfecting of thermonuclear bombs. It has resisted all religions and all philosophies, even the most magnanimous. As emphasized by Arthur Koestler,

it is hard-wired into the organization of the human brain. But man also decorated the Sistine Chapel, composed the *Rite of Spring*, discovered the atom. "What is this chimera called man? What novelty, what monstrosity, what chaos, what contradiction, what prodigy!"⁴ What can be in the head of this *Homo* who shamelessly attributes to himself the epithet *sapiens*?

This book would never have seen the light of day without the initiative and the diligence of Odile Jacob, who followed its publication so competently and attentively. The work benefited from scientific contacts, conferences, and discussions made possible by the Neuroscience Research Program, directed initially by Francis O. Schmitt in Boston and more recently by Gerald Edelman and Vernon Mountcastle in New York. Seven years of teaching in the Collège de France in front of an ever-critical audience eager for knowledge have helped my research and documentation as well as influenced my choice of examples and, of course, my synthesizing reflections.

Finally, my thanks are due to P. Benoit, C. Bertheleu, S. Carcassonne, H. Condamine, J. Costentin, H. Hecaen, and A. Klarsfeld for their critical reading of the manuscript and constructive comments and also to J. Cartaud, M. Donskoff, M. Fardeau, J. Gaillard, C. Sotelo, A. Trautmann, and S. Tsuji for providing valuable information. The illustrations owe much to the careful and painstaking photography of P. Lemoine.

Neuronal Man

Acetylcholine: one of the first neurotransmitters discovered; its effect at the neuromuscular junction is blocked by curare.

Adenosine triphosphate (ATP): small molecule produced by cell metabolism and used in storing and transferring energy.

Agnosia: a defect in the recognition of sensory stimuli that is not due to a change in the body's basic sensory mechanisms or to a lowered state of attention.

Allosteric protein: regulatory protein (enzyme, gene repressor, or pharmacological receptor) carrying at least two distinct categories of binding sites, which interact, indirectly, via discrete conformational transitions of the protein molecule.

Amino acids: organic compounds containing amino and carboxyl groups that form the essential structure of proteins and are also active as neurotransmitters. Some examples are glutamic acid, aspartic acid, and gamma-aminobutyric acid (GABA).

Aphasia: a defect in the production and/or comprehension of written and/or spoken language due to a brain lesion (see Figure 40).

Aplysia: the sea slug, a mollusk of the gastropod class whose very simple nervous system has been the subject of important studies at the cellular level (see Figure 26).

Axon: a single fiber growing out of a neuron, along which impulses travel from the cell body to the axon terminal. It is the output channel of the nerve cell and terminates in branches, at the end of which synapses form (see Figure 8).

Basal ganglia: a large group of neurons in the floor of the forebrain (see Figure 13).

Brainstem: an important part of the brain from the medulla to the midbrain.

Catecholamines: a family of chemical substances with a catechol nucleus to which an amine group is attached. Several of them act as neurotransmitters—for example, noradrenaline and dopamine (see Figures 11 and 44).

Category: the smallest possible grouping of cells of the same morphology and biochemical type (see Figure 15).

Cellular crystal: an ensemble of nerve cells of the same category organized in a regular pattern, such as the Purkinje cells of the cerebellum (see Figures 21 and 22).

Cerebellum: an outgrowth of the hindbrain that is specialized for motor coordination; it contains only a small number of neuron categories, including Purkinje and granule cells (see Figures 3, 13, and 21).

Cerebral cortex: the layer of gray matter forming the outer shell of the cerebral hemispheres; it is highly developed in mammals, particularly the *neocortex* (see Figures 3, 13, 14, 15, and 16).

Chromosome: a rodlike body in the cell nucleus containing DNA and visible by microscopy during cell division (see Figure 73).

Clone: an individual (or cell) derived from a single individual (or cell) by asexual reproduction (see Figure 58).

Corpus callosum: the large fiber bundle connecting the cerebral hemispheres (see Figures 3 and 5).

Cortical areas: distinct zones of the cortex characterized by their cellular architecture and function (see Brodmann's maps in Figure 6). Classically, one distinguishes the primary *sensory* areas, responsible for receiving input from the sensory organs; the *motor* areas, dealing with motor commands; and the remaining *association* areas.

Cyclic AMP: a small cyclic molecule derived from ATP and used as an internal signaling mechanism in the cell.

Dendrites: multiple, branched outgrowths of a neuron that receive numerous synaptic contacts from axon terminals, thus collecting signals and transmitting them to the cell body (see Figure 8).

Deoxyribonucleic acid (DNA): the molecular basis of heredity, made up of linear chains of nucleotides, themselves formed of an organic base, a sugar (deoxyribose), and phosphate. Usually two complementary DNA chains form a double helix.

Dopamine: a catecholamine neurotransmitter that is implicated in one theory of schizophrenia (see Figure 44).

Enkephalin: a peptide neurotransmitter that acts like morphine. There are two types: leu-enkephalin and met-enkephalin (see Figure 36).

Gamma-aminobutyric acid (GABA): an amino acid that acts as an inhibitory neurotransmitter.

Gene: a segment of the chromosome composed of DNA and with a defined function. Structural genes code for proteins, while regulatory genes govern the activity of structural genes (see Chapter 6).

Genome: all the genetic material (DNA) of a cell.

Genotype: the genetic constitution of an individual.

Graph: a mathematical expression providing a rigorous description of the geometry of a network.

Hippocampus: a cortical structure in the medial part of the mammalian temporal lobe; it results from the infolding of an "old" cortical area found in reptiles and primitive mammals. It does not have the typical six layers of the neocortex (see Figures 14 and 37).

Homoeotic: describes genes whose mutation (in invertebrates) causes the replacement of one organ by another; for example, in the *ophthalmoptera* mutation a wing appears in the place of an eye.

Hypothalamus: a cluster of neurons in the forebrain beneath the thalamus. Despite its small size, it plays an important role in "vital" functions, including feeding, drinking, sexual behavior, sleep, temperature regulation, emotion, and hormone balance (see Figure 13 and Chapter 4).

Ion: an atom or molecule carrying an electrical charge, such as sodium (Na^+) or chloride (Cl^-) ions.

Ion channel: the pore through which ions cross the cell membrane. There are several categories, defined by their ion specificity and their electrical sensitivity. The propagation of a nerve impulse involves sodium-selective channels (see Figure 30).

Isogenic: describes individuals with the same genotype, like identical twins (see Figure 58).

Lateral geniculate nucleus: thalamic nucleus relaying the visual pathways (see Figure 50).

Limbic system: a group of primitive structures important for the control of emotional behavior, including the hippocampus, parts of the thalamus and hypothalamus, and related nuclei of the septum and amygdala (see Figure 37).

Locus coeruleus: nucleus in the central part of the brainstem whose neurons contain noradrenaline (see Figure 11).

Mauthner cell: a giant neuron; only two are situated in the medulla of fish. It is involved in the flight reflex (see Figure 34).

Membrane: a continuous lipid and protein film delimiting and enveloping all cells, including nerve cells. Among its constituent molecules, there are molecule channels, enzyme pumps, and neurotransmitter receptors.

Membrane potential: the difference in electrical potential across the cell membrane due to a difference in concentration of ions inside and outside a cell.

Mutation: a spontaneous or induced modification, transmissible by heredity, of the genetic material, the DNA.

Myelin: the lipid substance forming a sheath around certain nerve fibers.

Neocortex: see **Cerebral cortex**.

Neuron: the nerve cell, formed of a cell body (or soma) containing the nucleus, and outgrowths of two types: dendrites, converging toward the cell body, and a single axon leaving it (see Figure 8).

Neurotransmitter: a chemical substance involved in the transmission of the nerve signal at a chemical synapse. There are probably dozens of such transmitters in the brain (see Figure 11).

Noradrenaline (norepinephrine): a catecholamine neurotransmitter with multiple functions in the central and peripheral nervous systems (see Figure 11).

Peptide: a linear chain of amino acids, like a protein, but shorter (up to twenty amino acids). Some examples are enkephalin, substance P, and LHRH.

Phenotype: the cluster of apparent, observable characteristics of an individual resulting from the interaction between the genotype and the environment in which the individual develops.

Planum temporale: a cortical area near the auditory cortex (see Figure 70).

Pleiotropic: describes the capacity of a gene to influence several distinct characteristics in the phenotype; for example, the albino gene affects both skin pigment and the anatomical organization of the visual pathways in the brain (see Figure 50).

Postsynaptic: on the "downstream" surface of a synapse, the part usually formed by a dendrite, a muscle, or a gland (see Figures 9, 17, and 30).

Presynaptic: on the "upstream" side of a synapse, normally formed by an axon terminal (see Figures 9 and 17).

Protein: the fundamental cell component; it is a "macromolecule" formed of linear chains of a large number of amino acids (sometimes more than a thousand). The amino acid sequence is characteristic of each type of protein. Enzymes, receptors, molecule channels, and antibodies are all proteins (see Figure 31).

Pump: an enzyme that uses ATP to actively transport ions and create a concentration gradient across the cell membrane.

Purkinje cell: a neuron characterized by its bushlike dendritic tree; it is the principal cell category in the cerebellar cortex (see Figures 21, 51, and 62).

Pyramidal cell: the main cell category in the cerebral cortex, out of which it sends its axon (see Figure 15).

Receptor: a term for two different receivers: (1) the sensory *cells* of the sense organs (e.g., the rods and cones of the retina) and (2) the *molecules* that recognize specific substances such as neurotransmitters or hormones (e.g., the acetylcholine receptor; see Figure 31).

Repressor: an allosteric protein regulating the expression of structural genes as proteins.

Reticular formation: groups of cell bodies in a bed of nerve fibers in the ventral part of the brain, from the medulla to the thalamus. In fact the groups are discrete; the best known contain catecholamines like noradrenaline or dopamine (see Figures 11 and 44).

Ribonucleic acid (RNA): a linear macromolecule related to DNA and important in transcribing and translating DNA to produce proteins.

Septum: a group of neurons related to the limbic system (see Figure 37).

Serotonin: a neurotransmitter derived from an aromatic amino acid, tryptophan.

Singularity: the distinguishing characteristic of each cell in a given category based on the precise set of connections that it gives and receives.

Soma: the cell body of a neuron, containing the nucleus and cytoplasm, together with mitochondria and other organelles (see Figure 8).

Stellate cell: a cortical neuron whose axon remains within the cortex (see Figure 15).

Substance P: a peptide neurotransmitter involved in the handling of pain messages in the spinal cord.

Superior colliculus: a paired nucleus in the roof of the midbrain responsible for certain visual reflexes.

Synapse: the junction between neurons or between neurons and other cells, such as muscles and glands. At a synapse the membrane of the axon terminal and that of the postsynaptic surface are juxtaposed, but not fused. There exist electrical synapses, where electrical signals are

transmitted directly, and chemical synapses, which use a transmitter to cross the intercellular cleft (see Figures 9 and 17).

Thalamus: a group of nuclei in the forebrain, beneath the cortex. Most pathways entering or leaving the cortex relay in the thalamus, and it receives fibers from the cortex in turn (see Figures 3, 13, and 18).