Book Reviews

Neural Plasticity in Learning

Memory and Nerve Cell Connections. Criticism and Contributions from Developmental Neurophysiology. RICHARD MARK. Clarendon (Oxford University Press), New York, 1974. x, 156 pp., illus. $10.95.

"The purpose of this book is to persuade the reader that it is sensible to view the ability of animals to store memories as a marginal extension into adult life of mechanisms that are responsible for the embryological development of the brain." So writes the author, who has himself contributed importantly to our growing awareness of the plasticity of the nervous system that results from experience during late stages of development or regeneration. In this slender volume he captures much of the excitement in the field and argues convincingly that a model of this sort must be seriously considered.

Mark attempts to make his thesis understandable to the layman, first summarizing the basic principles of neurophysiology, then reviewing developmental neurobiology and prior research on memory and learning. The result is not uniformly successful; it is doubtful that one unfamiliar with basic neurophysiology can fully follow his descriptions and reasoning. Similarly, it is impossible in the space he allows to review adequately the vast literature on memory. Nevertheless, he chooses his examples well and puts into clear perspective the systematic deficiencies of most experimental attempts to find the cellular basis of memory. He distinguishes two approaches in memory research, analogous to those of Koch and Ehrlich in the field of bacteriology in the last century. One approach is to look for a stimulus-related change of any kind in a neural circuit suspected of being involved in learning. Although Mark readily acknowledges major recent findings in this area (effects of use on dendritic morphology, conditioned electroencephalogram changes, possibly even learning-specific proteins, to which he gives what some would consider undue credence), he concludes that any observed changes have told us little or nothing about mechanisms of memory and that such changes are unlikely to tell us much without greater simplification of systems tested and a firm theoretical basis for interpretation of results. The second approach, which Mark prefers, is to postulate a mechanism, then devise a way of experimentally interfering with it to see whether the interference has the expected effects on short- and long-term memory. As he recognizes, this approach suffers from the near impossibility of interfering unambiguously with only one possible memory mechanism. On the other hand, it tests a hypothesis. Research in developmental neurobiology has revealed several cases of plasticity in neural circuits that look much like learning. Mark is interested in how this works and in whether a similar mechanism might not be detected as the basis of memory. Knowing what he does about plasticity during development, he proposes a mechanism of learning and a way to interfere with it. The results are most interesting, although it is clear that Mark does not entirely escape the uncertainties of his approach.

A major part of this book deals with several instances in which neural connections or their effectiveness has been shown to be subtly altered by experience during the early part of an animal's postnatal existence. A prime example is the loss of effectiveness of inappropriately used lateral geniculate inputs to the visual cortex, studied brilliantly by Hubel and Wiesel and others. During a short postnatal "critical period" the inputs to visual cortical cells compete for permanent effectiveness. Terminals that are not used regularly in concert with others somehow lose their influence; those that are used regularly and sum with others to drive the postsynaptic cell are reinforced. This selection process is so potent that abnormal visual experience can result in grossly abnormal neural connections.

Mark's own experimental work has dealt mainly with the specificity of motor connections in lower vertebrates. Building on the work of Sperry, he and others have shown that the "homologous response" of Weiss (the normally coordinated movement of amphibian muscles when they have been innervated by what look like inappropriate nerves) is in fact a result of highly specific regrowth of a few motor nerve fibers to the muscles they originally innervated. Not only does this indicate remarkable specificity of cell-cell recognition during regeneration, it also implies that the large number of other nerve fibers entering each muscle do not form permanently functional junctions. Mark's findings suggest that there is suppression of foreign motor nerve endings by the original population of nerve fibers when they regenerate to reestablish connections and that this suppression can, under some circumstances, be reversed. The "displaced" nerves continue to look morphologically normal and to conduct impulses, but they do not drive the muscle. Mark cites possibly similar phenomena in the mammalian central nervous system and suggests that synapse suppression is a normal part of development throughout the nervous system. He sees this as part of an overall pattern of excess proliferation of connections followed by selective functional loss of those that are not reinforced by normal use. Perhaps a large fraction of the morphologically distinguishable synapses in the central nervous system are in fact nonfunctional (but capable of being activated?) in the adult. The secret of learning would lie in the selective suppression or activation of the appropriate synapses. Which synapses are involved, and how they are turned on and off, remain unknown; but Mark is willing to speculate that synaptic efficacy is dependent on a mutual reinforcement process involving informational molecules acting between the presynaptic and postsynaptic cells.

The key to his model is his finding that ouabain, in addition to blocking sodium-potassium pump activity, in approximately the same proportion blocks the uptake of amino acids into synaptosomes and the synthesis of proteins. It also blocks long-term memory in chickens and hastens the decline of short-term memory. Mark proposes that a high level of use in one terminal with increased sodium-potassium pump

activity enhances the uptake of small molecules. These are incorporated into a "marker," probably a protein, that is characteristic of that nerve cell and that, when released, causes the postsynaptic cell in some way to repress transmission from other terminals bearing different markers. What else effect will prove a key to understanding ouabain does, and whether the observed learning, remain to be seen.

Although this book is so compact that most of its arguments can be made only sketchily, it remains a valuable volume. It critically reviews the many diverse and often conflicting theories of learning. More important, it draws together many strands of evidence that the formation and regeneration of neural connections are highly specific and that, during maturation, these connections can be "enduringly modified" by experience. Mark's specific model may prove to be an overenthusiastic interpretation of findings that are still inadequately established or understood. Nevertheless, it is not a rash extrapolation to suggest that once the mechanisms involved in developmental plasticity are understood one can look for similar mechanisms of adult learning and memory.

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Outermost Components of Cells

Surface Carbohydrates of the Eukaryotic Cell. G. M. W. COOK and R. W. STODDART. Academic Press, New York, 1973. xiv, 346 pp., illus. $19.50.

It has been recognized for about a century that the plasma membrane acts as a permeability barrier. Historically, in the study of membranes, we have started with a presumed knowledge of the function and then proceeded in identifying the molecular structure. This sequence appears to have been reversed for the outer component of the membrane, the cell surface carbohydrates. At present one might call them structures in search of function. We have learned much about their localization and even their molecular composition without understanding why nearly all cells are covered with such material. Our knowledge about these carbohydrates developed, as if incidentally, from investigations apparently having little in common. Laboratories working on such diverse topics as plant lectins, blood group substances, cell-cell interaction, and cancer cells found that they all were studying interactions of cell surface carbohydrates. This book attempts to bring much of this diversified information to bear on that general topic. Its goals, as stated by the authors, are "to cover the basic tenets upon which the subject is founded . . . to draw attention to . . . points of growth for the future [and] to provide a comprehensive view of present knowledge of carbohydrates in cell surfaces."

The first chapter summarizes the structure of plasma membranes. The authors present a comprehensive and well-thought-out review of the steps that led to our present concepts of membrane structure. Naturally, as happens in any fast-moving field, there are some new concepts and ideas that are not included, but they can be easily found in more recent review articles such as that by S. J. Singer (*Annu. Rev. Biochem.* **43**, 805 [1974]).

The next chapter reviews the principal lines of evidence for the presence of carbohydrates on the surface of animal cells. Electrokinetic and microscopic studies are discussed in detail, as well as the evidence obtained by the use of lectins. The following two chapters, constituting a large portion of the text, are devoted to the structural characterization of glycolipids and glycoproteins of animal cell surfaces, fungal cell walls, and the carbohydrates of plant cells. Methods for the study of complex carbohydrates are discussed. Examples of glycopeptides from a variety of tissues are given. It might have been helpful, at least to a beginner in the field, to include some generalizations that can be drawn about the frequency and localization of carbohydrates within polysaccharide chains, the types of linkages between polysaccharide chains and peptides, and the behavior of the chains on hydrolysis. This kind of information was given by R. C. Hughes in a more recent review of the subject (*Prog. Biophys. Mol. Biol.* **26**, 191 [1973]). The problem of microheterogeneity also should have been discussed at this point. The large number of references, however, will allow the beginner to bring himself up to date on these subjects.

The mechanism by which the cell synthesizes a glycoprotein and incorporates it into membranes is a controversial subject. The authors present a well-rounded review of this topic with some critical evaluation, a difficult task because of the insufficiency of knowledge and experimentation in this area.

The final chapter of the book deals with the question, What is the biological role that these materials play in the cell membrane? While the authors restrict themselves to the evidence pertaining to the membrane alone, the question could be asked about the function of carbohydrates attached to proteins in general. One might then obtain additional clues from the work of investigators such as Ashwell and DeVries, which is not discussed in this book. The major topics included in this chapter are cell recognition, intercellular adhesion, the role of glycoproteins in cell growth regulation in animals, and the plasticity, permeability, and hydration of plant cell walls.

This book is welcome as a much-needed treatise on a current topic. It is well balanced and is enjoyable reading and deserves a warm recommendation.

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Surface Analysis

Characterization of Solid Surfaces. PHILIP F. KANE and GRAYDON B. LARRABEE, Eds. Plenum, New York, 1974. xviii, 670 pp., illus. $32.50.

The study of solid state surfaces is one of the most rapidly developing areas of physical science. In the past 10 years a multitude of techniques have become available that can be used to study the structure and composition and the physical chemistry of solid surfaces on a monolayer atomic scale. These techniques have found applications in research on catalysis, adhesion, and lubrication, as well as in the development of integrated circuitry and other solid state devices of high surface-to-volume ratio. As a result, our knowledge in solid state surface science is increasing explosively, and this area promises to be the birthplace of many new technologies.

This book is a timely contribution to the field. There are 23 chapters, each of which concentrates on either a new research technique or a whole field of surface analysis. The first seven chapters discuss techniques of physical structural characterization, including light and scanning electron microscopy and the x-ray diffraction methods that are useful in surface analysis. In later chapters,