laboratories. The results, as well as those of many other studies, are presented in three chapters organized according to the time and length scales of the motions involved. The chapter on short-time dynamics considers motions during time intervals of less than 100 picoseconds. The treatment of these very fast motions provides the framework for the discussion of activated processes that are intrinsically fast but occur infrequently. Activated dynamics simulations are now being used to study the mechanism of such biologically important processes as electron transfer reactions. The book provides the background required to read the current literature on this subject.

As mentioned in the preface to the book, detailed computer simulations of proteins and nucleic acids involve a fusion of three "high technology" areas: molecular biology, chemical physics, and scientific computing. *Dynamics of Proteins and Nucleic Acids* explains how and why these fields coalesce in the study of biopolymer dynamics and shows how the foundation has been prepared for studies concerned with the interpretation and prediction of biological activity based on the physical properties of these macromolecules. The book serves as a valuable resource for graduate students wishing to enter the field as well as for working scientists in diverse areas of biophysical chemistry who wish to develop an understanding of the macroscopic properties of proteins and nucleic acids by studying their underlying structure and dynamics.

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Neurophysiology

Long-Term Potentiation. From Biophysics to Behavior. PHILIP W. LANDFIELD and SAM A. DEADWYLER, Eds. Liss, New York, 1987. xiv, 548 pp., illus. $140. Neurology and Neurobiology, vol. 35.

In invertebrate animals the inquiry into the physical basis of learning and memory has proceeded from the systematic observation of learned behaviors to the study of nervous-system structures and processes. In mammals the complexity of the central nervous system has hindered straightforward progress. The present volume focuses on an electrophysiologically defined phenomenon, long-term potentiation (LTP), that fulfills many of the criteria expected, a priori, of neural mechanisms of learning and memory and has therefore come under intensive investigation.

The fundamental demonstration of LTP is simple and compelling. A brief train of electrical stimuli delivered to certain fiber bundles in the brain causes a great increase ("potentiation") in the size of subsequent single evoked responses. Most remarkably, the potentiation produced by a stimulus train lasting only a fraction of a second can endure for hours or days depending on the exact experimental conditions.

From its title, one might infer that this book treats a single phenomenon, but this is true only in a general sense. A lot of circumstantial evidence suggests that more than one, perhaps many, superficially similar phenomena are designated "LTP." The subtitle, "From Biophysics to Behavior," should be understood in the same sense in which America is said to extend "from sea to shining sea"; that is, not much sea is included in the territory. Finally, the title does not mention "hippocampus," though nearly all of the work discussed was carried out on this structure for both historical and practical reasons: LTP was discovered in the hippocampus and is produced especially readily there. Structurally, the hippocampus offers a number of technical advantages for studying LTP, and a large base of hippocampal data exists. There is evidence that the hippocampus is involved in behavioral learning. Because of this bias, however, the non-hippocampologist will occasionally find the going a bit rough without a review of the relevant anatomy and physiology handy. Luckily, such reviews are readily available.

The book aims to provide a "highly comprehensive overview of LTP at all major levels of analysis" as well as a detailed discussion of specific research findings and controversies. This ambitious program is undertaken in 15 chapters written by investigators who, for the most part, work on hippocampal LTP. The chapters are a mix of reviews and shorter, more narrowly focused essays. In general, the objectives of the book are well met, and a number of the critical reviews are excellent. Ample coverage is given to the phenomenology of LTP, including stimulus parameters appropriate for its induction: "cooperativity" (there may be a minimal degree of excitation necessary to produce LTP) and "associativity" (coincident inputs from different fiber systems can interact to produce greater LTP than either could produce alone). The major types of analysis applied to LTP to date are thoroughly discussed: anatomical (changes in the size or number of synaptic contacts or in the shape of the dendritic spines on which most synapses are made); biochemical (changes in receptor number, the phosphorylation state of certain proteins, and the role of protein synthesis); and physiological (increases in synaptic potentials, the role of calcium and of the postsynaptic membrane potential in LTP induction). As is pointed out in the last sentence of the book, determining the behavioral relevance of LTP will require much further effort. The evidence available is presented in a balanced way.

The authors seem to have been given a free hand, the better to allow controversial points to surface. This often produces the desired effect, although occasionally at the cost of redundancy on points on which no disagreement is expressed. The most extreme case is the number of not very different renderings of the *N*-methyl-D-aspartate (NMDA) hypothesis. However, the book's open style allows the reader to draw his or her own conclusions. One finds, for instance, general agreement that different forms of LTP exist and that disinhibition enhances the probability of LTP induction. On the other hand, there is no consensus as to whether the important events of LTP occur presynaptically or postsynaptically. Both hypotheses are represented and defended. The phenomena of associativity and cooperativity and the excess potentiation of the action-potential generation all seem to call for a postsynaptic explanation. Measured increases in the release of glutamate, the presumed excitatory neurotransmitter at some synapses undergoing LTP, imply a presynaptic locus.

The NMDA hypothesis provides a modern rationale for an idea put forward in 1949 by D. O. Hebb that memory storage might involve participation of both presynaptic and postsynaptic elements. The emphasis on the state of the postsynaptic element was new. Much recent excitement centers on the NMDA subclass of the excitatory amino acid receptors since it is unique in requiring both the binding of a neurotransmitter to its receptor site and an appropriate level of depolarization for opening of the associated ion channel. Direct support for the NMDA hypothesis in LTP comes from the observation that NMDA antagonists block LTP at certain synapses. Since neurotransmitter release has its provenance in the presynaptic neuron, whereas the membrane potential sensed by the NMDA channel is determined on the postsynaptic side, the NMDA complex seems ideally suited to the requirements of a Hebbian synapse. Even more suitably, calcium, already implicated in the establishment of LTP, is quite permeable in the NMDA channel. Calcium influences are, of course, ubiquitous, and so the number of possibilities for its involvement is rather large. Hence the NMDA hypothesis is compatible with many disparate ideas and helps tie together much of the book, but other

points of view, both competing and complementary, are also presented.

The authors were charged to "speculate freely as a means of generating innovative concepts and new hypotheses." Most of the contributors have plainly taken up the challenge, pointing out gaps in the literature and possibilities for the future. If recent rumors and abstracts are any guide, important new developments in LTP can soon be expected on the biochemical and molecular biological fronts. Years ago it could be said that there were only two answers to any electrophysiological question: voltage clamp and quantal analysis. Neither will provide a satisfying solution to the puzzle of LTP, and a more extensive discussion along the newer lines of investigation might have been interesting.

The book, which includes a commendable number of references to recent work, will do much to put future work in context. Those wishing to get a detailed look at what has been going on in LTP research, as well as laboratory workers interested in taking part, will want to have copies.

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