The Institute of Theoretical Astronomy (as it was first called), founded by Hoyle at Cambridge in 1966, was an instant success. With a rapidly growing number of sabbatical and summer visitors and a vigorous program of international conferences, it became an obligatory mecca for young U.S. astronomers in particular. Many feel that the Institute fostered their best work in the magical six years that followed. Yet Hoyle shows that the Institute was almost stillborn. His account is long on the politics of its birth and life but surprisingly short on its achievements. Nevertheless, it helps explain how he could walk away with some relief when the university's gray men (one described by Lyttleton as "rusted in" to a supposedly rotating position) achieved an underhanded victory in 1972. But even Hoyle's accurate description cannot do justice to puerile academic spite. Years after his successor Martin Rees generously named the Hoyle Building, a resentful opponent continued literally to excise his name—with a razor blade—from posters announcing the location of seminars.

Aptly subtitled "Chapters from a Cosmologist's Life," the book hardly touches some of the contributions, scientific, educational, and cultural, of this extraordinarily creative man. It is particularly ironic that his work on interstellar organic molecules and their implications for the origin of life was downplayed in the year when the amino acid glycine was found at the center of the Milky Way. Many present-day astronomers worldwide could attest to the youthful inspiration his unmentioned classic *Frontiers of Astronomy* provided them. Some stories, however, only Hoyle could have told. One wishes, for example, that he had chosen to describe his co-discovery of a star of first magnitude—the then unknown Royal Academy of Dramatic Arts student Julie Christie—for his "A for Andromeda" sci-fi TV series. It would seem several chapters still remain to be revealed. Nevertheless, all working astronomers and others seeking rich and controversial insights should read this book—for then they will partly know the mind of Hoyle.

John Faulkner
Lick Observatory,
University of California,
Santa Cruz, CA 95064–1077, USA

Vignettes: Instructions for Authors

Avoid digressing into diatribes and areas, especially controversial issues, not central to your research. You may never complete a scientific crusade if you stop to lop off the head of an innocent peasant on the way. . . .

Remember that the review process has a big random element. . . . Be philosophical—remember that sometimes you will be unfairly rejected and at other times undeservedly accepted. Write enough articles so that it averages out! . . .

Carefully read the editor's rejection. It may in fact be a request for resubmission after major changes. The editor doesn't want to appear generous because that would encourage you to resubmit a poorly revised manuscript, and he would feel obligated to accept it. A little humor helps: A politician says "yes" if he means maybe, "maybe" if he means no, and if he says "no" he's not a politician. An editor says "no" if he means maybe, "maybe" if he means yes, and if he says "yes" he's not an editor! . . .

Reviewers may be defensive about a manuscript that provides too large a deviation from received wisdom and perhaps even threatens the reigning paradigm. If you are brilliant enough to come up with such material, it may be wise to publish it in less shocking increments or in a book.

—*Tesfa G. Gebremeddhin* and *Luther G. Tweeten*, in *Research Methods and Communication in the Social Sciences* (Praeger)

Machinery of Learning

Long-Term Potentiation. Vol. 2. MICHEL BAUDRY and JOEL L. DAVIS, Eds. MIT Press, Cambridge, MA, 1994. xiv, 409 pp., illus. $85 or £76.50. A Bradford Book. Based on a meeting, Gif-sur-Yvette, France, 1992.

Leaving aside the major neurological disorders, interest in how we learn and how we remember has arguably drawn more of us to neuroscience than any other subject. Despite the attention these phenomena have received, biological models of memory and learning circuits that have proven mechanistically fruitful are few and therefore precious. These models include reflex sensitization to a noxious stimulus in *Aplysia*, olfactory learning in *Drosophila*, and long-term potentiation (LTP) in mammals. LTP is a long-lasting enhancement of synaptic strength that is produced at certain synapses by high-frequency activation of the afferent nerve. By presenting recent findings addressing two of the three major questions surrounding the phenomenon, the 20 contributions included in this successor to a 1991 book on the subject paint an accurate and interesting picture of our understanding in the early 1990s.

The first question concerns the machinery responsible for the maintained increase in synaptic effectiveness during LTP: does it reside on the pre- or on the postsynaptic side of potentiated synapses, or somehow on both? A derivative question, though not so well developed experimentally in the book, involves the locus of long-term depression (LTD) of synaptic transmission produced by lower-frequency stimulus trains. LTD is suggested to provide a mechanism by which synapses are "reset" and may explain why all of our synapses are not maximally potentiated. Artola's chapter raises the idea that whether a particular synapse undergoes LTP or LTD, or neither, may depend on the postsynaptic calcium concentration reached during repetitive synaptic transmission (LTP requiring more than LTD). Experiments that convincingly demonstrate the need for a transient postsynaptic calcium surge in LTP induction are presented by Manabe, Nicoll, and colleagues. Malinow and coworkers then exhaustively evaluate their quantal analysis of potentiated synapses, which implicates either an increased likelihood of transmitter release or unmasking of postsynaptic receptor clusters.

If release is increased, it follows that retrograde chemical signals that instruct the nerve terminal to release transmitter more reliably must exist. What might these signals be? Nitric oxide (NO) is one of the latest offerings in the menu of retrograde messengers we have been served over the past six years and takes center stage in this debate. The pharmacological arguments of Madison and Schuman supporting a role for NO in the induction of LTP in the hippocampal slice are contested by Barnes and co-workers, however, who have examined LTP in the whole animal. The discrepant

results might be reconciled by work, too recent for this volume, that indicates that the efficacy of NO synthetase inhibitors depends on temperature or developmental stage of the animal. Aside from a convincing postsynaptic role for calcium, the interpretation of virtually every other experiment in the pre- versus post- issue is contested in a balanced fashion in the book. The root of the problem may lie with the myriad ways in which postsynaptic *N*-methyl-D-aspartate (NMDA) receptors can be modulated, as discussed by Malenka, because many if not all the various pharmacological treatments used to probe second-messenger pathways can also affect the activation of NMDA receptor channels and thus influence the very first step in LTP. We are reminded that pharmacological evidence can be unsavory at times, but often it is the best at hand.

The second major question addressed is the following: does LTP as studied in reduced preparations actually participate in the behavioral processes that we call learning or memory? One message that comes through very clear in this section is that long-lasting changes in synaptic strength are not limited to the hippocampus but are encountered in nearly every layered structure one examines from the cerebellum to olfactory and neocortices, in keeping with the expectation that memory storage areas are distributed throughout the brain. A particularly thoughtful set of studies of the roles of LTP in olfactory learning is presented by Otto and Eichenbaum and by Roman and co-workers, from which it appears that processing of odors by olfactory circuits may be supplanting hippocampus-dependent spatial learning as a paradigm for uncovering the role of LTP in memory consolidation.

Synthesis that attempts to go beyond recounting of published work is perhaps best achieved toward the end of the book, where computational models of modifiable computer algorithms are injected into the fray. The going is predictably rough, but the effort is stimulating and promising of things to come. As Sarvey puts it, "The hope for modeling is that eventually [experimental results] will stop driving models and models begin driving experimental searches for novel mechanisms."

What is missing? The level of analysis achieved by this book is primarily cellular rather than molecular. Memory research is converging on a few simple molecular mechanisms that appear to be cropping up in several of the most widely used models. From fruit flies to sea hares to the longer-lasting forms of hippocampal LTP, genetic cascades triggered by a rise in cyclic adenosine monophosphate seem to mediate forms of synaptic plasticity that require protein synthesis, and these persistent forms of plasticity are probably responsible for memories lasting more than an hour or so. The investigation of these genetic pathways by gene knock-out or substitution is now a major theme in memory research in several species and should provide grist for a third volume.

Raymond Dingledine
Department of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322, USA

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Cardiac Problems

Ion Channels in the Cardiovascular System. Function and Dysfunction. PETER M. SPOONER, ARTHUR M. BROWN, WILLIAM A. CATTERALL, GREGORY J. KACZOROWSKI, and HAROLD C. STRAUSS, Eds. Futura, Armonk, NY, 1993. xxx, 580 pp., illus. $85.

Decades of basic and clinical research have advanced the treatment and prevention of cardiovascular disease. Between 1981 and 1991 age-adjusted death rates for cardiovascular disease fell by 25%. Despite this progress, cardiovascular disease is still the leading cause of death in the United States for both men and women, accounting for more than 900,000 deaths, or more than 40 percent of all deaths, in 1990. No price can be placed on lives lost; however, the estimated cost to this nation of cardiovascular disease in terms of health care costs and lost productivity is projected to be $128 billion in 1994. (These figures were all provided by the American Heart Association.) The only hope for reducing this premature loss of lives and the financial burden on our country is through cardiovascular research.

The pumping activity of the heart is triggered and synchronized by precise control of the initiation, termination, and conduction of electrical impulses. The heart exhibits electrical activity because there are ion channels in the membrane that selectively allow sodium, potassium, calcium, or chloride ions to flow down their respective electrochemical gradients. These channels open and close in complex manners. The opening and closing can depend on voltage, time, intracellular metabolites or messengers, and extracellular neurotransmitters or hormones. Regional variation in the complement of ion channels and the number of electrical connections between cells is important for normal impulse initiation and conduction. Cardiac arrhythmias can result when the normal regulation of ion channels is altered by disease or when structural abnormalities are present in the heart. When arrhythmias are severe, the heart cannot contract in a coordinated fashion and loses its ability to pump blood effectively. More than 300,000 deaths annually are due to sudden cardiac arrest, which is generally presumed to be due to arrhythmias.

The editors of *Ion Channels in the Cardiovascular System* called on nearly a hundred clinicians and basic scientists to review the state of knowledge regarding cardiac electrical activity, ion channel function, channel regulation, and drug development. The book draws heavily on work presented at a meeting held in September 1992. This was a time of both apprehension and great expectations for individuals interested in ion channels and cardiovascular disease. The results of the Cardiac Arrhythmia Suppression Trial (CAST) were the cause of the apprehension. This multicenter controlled clinical trial indicated that when a carefully selected group of patients who were at increased risk for sudden cardiac death were treated with encainide, flecainide, moricizine, or a placebo more patients died in each of the treatment groups than in the placebo group. The increase in mortality occurred despite the demonstrated ability of the drugs to suppress one type of arrhythmia (ventricular premature depolarizations) in these patients. This study caused clinicians, drug companies, and basic scientists to rethink their strategies for controlling cardiac arrhythmias.

The great expectations were based on two factors. First, rapid progress was being made in the understanding of ion channel structure, function, and expression. Many of these advances were made possible by the cloning and expression of voltage-gated ion channels. Second, new antiarrhythmic agents, with mechanisms of action that differed from the drugs used for the CAST study, were continuing to be developed. These new agents were primarily agents that prolong the action potential duration and the effective refractory period (Vaughan Williams class III), usually by blocking potassium currents that assist in the termination of a cardiac action potential.

The book begins with a section on ion channels and cardiac disease. The first chapter in this section is a discussion of CAST and its implications. Subsequent chapters in the first section present clear reviews of the epidemiology of, markers for, and mechanisms of sudden cardiac death. The middle four parts of the book describe various aspects of cardiac ion channels including their relation to cardiovascular function, channel modulation and autonomic control, channel structure and function, and molecular pharmacology. These five sections include 19 of the 28 chapters in the book. In general the chapters in them