

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 pro-

tein 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



## 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

combine reviews of the literature with the presentation of research that was new and exciting at the time of the meeting, although the extent of review is variable from chapter to chapter. Following the sections on ion channels is a section on drug discovery, composed of four chapters describing strategies or experimental models that can be used to find effective antiarrhythmic agents.

The final chapter of the book consists of research recommendations made by a panel of eight leaders in cardiovascular research. Individual clinicians and scientists will have their own lists of directions in which they believe research efforts should be steered, but it is difficult to disagree with the observation made in the final paragraph of this book that the limited amount of effective communication between basic, clinical, and pharmacologic investigators has "impeded an integrated practical understanding of channel dysfunction in disease." The development of effective antiarrhythmic agents will be facilitated by increased collaboration and exchange of insights between clinicians and scientists.

A final consideration not addressed by the authors is that the complexity of the problem will make it difficult to achieve effective antiarrhythmic therapy in the very near future. Therefore it is important to provide stable sources for research support to ensure continuity within this field of research. Present funding realities have placed serious strains on younger investigators and discouraged many talented individuals from pursuing careers in this field. This trend has the potential to seriously inhibit future progress in this clinically important field.

Steve Sorota

Department of Pharmacology,  
Columbia University,  
New York, NY 10032, USA

## Correction

In the Books Received column in the issue of 9 December 1994 (p. 1743) the title of the book *Polyominoes* (2nd ed.; Princeton University Press) was given incorrectly and the name of its author, Solomon Golumb, was omitted. Warren Lushbaugh drew the diagrams in the book.

## Books Received

**AIDS and the Arrows of Pestilence.** Charles F. Clark. Fulcrum, Golden, CO, 1994. xviii, 171 pp., + plates. \$23.95.

**AIDS in Asia and the Pacific.** J. M. Kaldor, Ed. Current Science, London, 1994. vii, 215 pp., illus. \$74.95 or £49.95.

**AIDS Testing.** A Comprehensive Guide to Technical, Medical, Social, Legal, and Management Issues. Gerald Schochetman and J. Richard George, Eds. 2nd ed. Springer-Verlag, New York, 1994. xiv, 411 pp., illus. \$49.

**Algorithmic Learning.** Alan Hutchinson. Clarendon (Oxford University Press), New York, 1994. xxvi, 434 pp., illus. \$90; paper, \$42.50. Graduate Texts in Computer Science.

**Basin Analysis in Petroleum Exploration.** A Case Study from the Békés Basin, Hungary. Paul G. Teleki, Robert E. Mattick, and János Kókai, Eds. Kluwer, Norwell, MA, 1994. xiv, 330 pp., illus. \$145 or £96 or Dfl. 240.

**A Beginner's Guide to Constructing the Universe.** The Mathematical Archetypes of Nature, Art, and Science. Michael S. Schneider. HarperCollins, New York, 1994. xxii, 352 pp., illus. \$30.

**The Biographical Dictionary of Scientists.** Roy Porter, Ed. 2nd ed. Oxford University Press, New York, 1994. ix, 891 pp., illus. \$85.

**Biological Anomalies.** Humans III. William R. Corliss. Sourcebook Project, Glen Arm, MD, 1994. vi, 214 pp., illus. \$19.95.

**Changes in Land Use and Land Cover.** A Global Perspective. William B. Meyer and B. L. Turner II, Eds. Cambridge University Press, New York, 1994. xii, 537 pp., illus., + plates. \$49.95. Office for Interdisciplinary Earth Studies, Global Change Institute, vol. 4. From an Institute, Snowmass Village, CO, 1991.

**Child Psychology.** The Modern Science. Ross Vasta, Marshall M. Haith, and Scott A. Miller. 2nd ed. Wiley, New York, 1994. xvi, 644 pp., illus., + appendices. \$62.95.

**Circumstellar Media in the Late Stages of Stellar Evolution.** R. E. S. Clegg et al., Eds. Cambridge University Press, New York, 1994. xiv, 345 pp., illus. \$59.95. From a conference, Cambridge, UK, July 1993.

**Dynamic Modeling.** Bruce Hannon and Matthias Ruth. Springer-Verlag, New York, 1994. xiv, 248 pp., illus., + diskette (Mac or Windows). \$59.95.

**Eating on the Wild Side.** The Pharmacologic, Ecologic, and Social Implications of Using Noncultigens. Nina L. Etkin, Ed. University of Arizona Press, Tucson, 1994. x, 305 pp., illus. \$37.50.

**Economic Aspects of Water Management in the Prehispanic New World.** Vernon L. Scarborough and Barry L. Isaac, Eds. JAI, Greenwich, CT, 1994. xii, 471 pp., illus. \$73.25. Research in Economic Anthropology, supplement 7, 1993.

**Entitlement and the Affective Bond.** Justice in Close Relationships. Melvin J. Lerner and Gerold Mikula. Plenum, New York, 1994. xvi, 358 pp. \$49.50.

**Environment and Mental Health.** Stephen M. Williams. Wiley, New York, 1994. xii, 184 pp., illus. \$54.95.

**Glial Cells in the Central Nervous System and Their Reaction to Injury.** Amico Bignami and Doris Dahl. Landes, Georgetown, TX, 1994 (distributor, CRC Press, Boca Raton, FL). x, 109 pp., illus. \$89.95.

**Going Native.** Biodiversity in Our Own Backyards. Janet Marinelli, Ed. Brooklyn Botanic Garden, Brooklyn, NY, 1994. 112 pp., illus. Paper, \$6.95. Handbook no. 140.

**Handbook of Phytoalexin Metabolism and Action.** M. Daniel and R. P. Purkayastha, Eds. Dekker, New York, 1994. xii, 615 pp., illus. \$195.

**Human Stress and the Environment.** Health Aspects. J. Rose, Ed. Gordon and Breach, Langhorne, PA, 1994 (U.S. distributor, International Publishers Distributor, Brooklyn, NY) xii, 228 pp., illus. \$147 or £96 or ECU 123. Environmental Topics, vol. 5.

**Imagining the Universe.** A Visual Journey. Edward Packard. Perigee, New York, NY, 1994. vi, 154 pp., illus. Paper, \$15.

**Industrial Metabolism.** Restructuring for Sustainable Development. Robert A. Ayres and Udo E. Simonis, Eds. United Nations University Press, Tokyo, 1994 (U.S. distributor, Unipub, Lanham, MD). xiv, 376 pp. illus. Paper, \$35.

**Liver Gene Expression.** François Tronche and Moshe Yaniv. Landes, Georgetown, TX, 1994 (distributor, CRC Press, Boca Raton, FL). xvi, 350 pp., illus. \$89.95.

**Low-Capacity Cryogenic Refrigeration.** G. Walker and E. R. Bingham. Clarendon (Oxford University Press), New York, 1994. xvi, 302 pp., illus. \$68. Monographs on Cryogenics, 9.

**Low-Fat Meats.** Design Strategies and Human Implications. Harold D. Hafs and Robert G. Zimbelman, Eds. Academic Press, San Diego, CA, 1994. xvi, 330 pp., illus. \$85.

**Measurement, Regression, and Calibration.** Philip J. Brown. Clarendon (Oxford University Press),

New York, 1994. x, 201 pp., illus. \$45. Oxford Statistical Science Series, 12.

**Mechanisms of Lymphocyte Activation and Immune Regulation V.** Molecular Basis of Signal Transduction. Sudhir Gupta et al., Eds. Plenum, New York, 1994. x, 264 pp., illus. \$85. Advances in Experimental Medicine and Biology, vol. 365. From a conference, Newport Beach, CA, Feb. 1994.

**Modules and Rings.** John Dauns. Cambridge University Press, New York, 1994. xviii, 442 pp. \$69.95.

**Nature as Landscape.** Dwelling and Understanding. Kraft E. von Maltzahn. McGill-Queen's University Press, Montreal, 1994. x, 149 pp., illus. \$34.95.

**The Nature of Nature.** New Essays from America's Finest Writers on Nature. William H. Shore, Ed. Harcourt Brace, New York, 1994. xiv, 299 pp., illus. \$24.95.

**Numerical Methods and Scientific Computing.** Using Software Libraries for Problem Solving. Norbert Köckler. Clarendon (Oxford University Press), New York, 1994. xviii, 328 pp., illus. \$49.95.

**Peptide Synthesis Protocols.** Michael W. Pennington and Ben M. Dunn, Eds. Humana, Totowa, NJ, 1994. xii, 321 pp., illus. Spiralbound, \$64.50. Methods in Molecular Biology, 35.

**Pharmaceutical and Biomedical Applications of Liquid Chromatography.** C. M. Riley, W. J. Lough, and I. W. Wainer, Eds. Pergamon (Elsevier Science), Tarrytown, NY, 1994. x, 379 pp., illus. \$136 or £85.

**Physics and Our View of the World.** Jan Hilgevoord, Ed. Cambridge University Press, New York, 1994. x, 304 pp., illus. \$49.95; paper, \$22.95. From a symposium, 1992.

**Regional Silviculture of the United States.** John W. Barrett. 3rd ed. Wiley, New York, 1994. xii, 643 pp., illus. \$79.95.

**Regulation of Atmospheric CO<sub>2</sub> and O<sub>2</sub> by Photosynthetic Carbon Metabolism.** N. E. Tolbert and Jack Preiss, Eds. Oxford University Press, New York, 1994. x, 272 pp., illus., \$75.

**Reproduction and Development of Marine Invertebrates.** W. Herbert Wilson, Jr., Stephen A. Stricker, and George L. Shinn, Eds. Johns Hopkins University Press, Baltimore, MD, 1994. x, 325 pp., illus. \$75. From a symposium, Seattle, June 1992.

**The Scientific Revolution.** A Historiographical Inquiry. H. Floris Cohen. University of Chicago Press, Chicago, 1994. xviii, 662 pp. \$75; paper, \$26.95.

**Stellar Evolution.** Amos Harpaz. Peters, Wellesley, MA, 1994. x, 261 pp., illus. \$39.95.

**Stress-Induced Gene Expression in Plants.** Amarjit Singh Basra, Ed. Harwood, Langhorne, PA, 1994 (distributor, International Publishers Distributor, Brooklyn, NY). xiv, 287 pp., illus. \$125 or £81 or ECU 104.

**Structures in the Stream.** Water, Science, and the Rise of the U.S. Army Corps of Engineers. Todd Shallat. University of Texas Press, Austin, 1994. xii, 276 pp., illus. \$34.95.

**Subgroup Lattices of Groups.** Roland Schmidt. De Gruyter, Hawthorne, NY, 1994. xvi, 572 pp. \$148.95 or DM 248. De Gruyter Expositions in Mathematics, 14.

**Those of Little Note.** Gender, Race, and Class in Historical Archaeology. Elizabeth M. Scott, Ed. University of Arizona Press, Tucson, 1994. xvi, 217 pp., illus. \$45.

**Tropical Ecosystems.** A Synthesis of Tropical Ecology and Conservation. Mundanthra Balakrishnan, Reidar Borgström, and Stein W. Bie, Eds. International Science, Lebanon, NH, 1994. x, 441 pp., illus. \$69.

**Tyrosine Kinases and Neoplastic Transformation.** Stuart Kellie. Landes, Georgetown, TX, 1994 (distributor, CRC Press, Boca Raton, FL). iv, 100 pp., illus. \$89.95.

**The Vortex State.** Nicole Bontemps et al., Eds. Kluwer, Norwell, MA, 1994. x, 328 pp., illus. \$156 or £104 or Dfl. 260. From an institute, Cargèse, Corsica, France. NATO ASI series C, vol. 438.

**Voyage to the Great Attractor.** Exploring Intergalactic Space. Alan Dressler. Knopf, New York, 1994. xii, 356 pp. illus. \$25.

**Wavelets, Images, and Surface Fitting.** Pierre-Jean Laurent et al., Eds. Peters, Wellesley, MA, 1994. xvi, 528 pp., illus. \$69.95. From a conference, Chamonix-Mont-Blanc, France, June 1993.

**Wild Dogs.** The Wolves, Coyotes, and Foxes of North America. Erwin A. Bauer. Photographs by Erwin and Peggy Bauer. Chronicle, San Francisco, 1994. 120 pp., illus. \$27.50; paper, \$16.95 or £C21.95.