

strates that have been studied biochemically, whereas substrates whose function is well understood, like ion channels, exist in such small amounts that their biochemistry can only be inferred from indirect experiments.

The main strength of the book lies in the critical approach it takes. Experimental results are usually presented with evaluations of both the experimental designs and the interpretations. One of the most useful parts of the book deals with possible pitfalls and artifacts in studies involving protein phosphorylation. It evaluates the kinds of experiments that are needed to demonstrate unambiguously that phosphorylation regulates the function of a protein. In this regard, the book is an excellent guide to experimental design as well as an introduction to the field and would be suitable for graduate students and seasoned investigators alike. There are abundant references to work published through 1983.

The authors' philosophy is highly evident throughout the book and is best illustrated by their development of the idea that phosphoproteins can provide valuable insights into neuronal function, not only by virtue of their regulatory roles but also by virtue of their cell biology. One of the valuable side benefits of studying protein phosphorylation is that a number of phosphoproteins have been identified that have very characteristic cellular or subcellular distributions. This permits the use of these proteins to trace neuronal pathways. Phosphoproteins have an advantage over plain neuronal antigens for this purpose because one can simultaneously study their distribution and their state of phosphorylation in response to neurotransmitters in order to make inferences about the chemistry of the impinging circuits. One can also make inferences about the kinds of receptors present on certain presynaptic nerve terminals by examining the phosphorylation of phosphoproteins localized to presynaptic terminals. Results arrived at by the use of these techniques, however, are quite preliminary.

Despite these rather impressive strong points, the book has a number of weaknesses. It is repetitive. Several stories are repeated in varying degrees of detail. The repetition is partly the result of trying to make each chapter self-sufficient, but it is also annoyingly frequent within chapters.

Although the book touches on most of the important areas of research in this field, the emphasis, naturally, is on work that was started in Greengard's lab. At several points, however, the authors

spend too much time on their own work and neglect other interesting questions. For example, in the 100-page chapter on substrate proteins, a total of 40 pages is devoted to synapsin-I, a protein associated with synaptic vesicles, and DARPP-32, a phosphoprotein associated with dopaminergic neurons, but only passing notice is given to rhodopsin, phospholamban, and myosin. Although it is possible that these proteins are not considered by the authors to be bona fide neuronal proteins, their phosphorylation has interesting implications for nervous system function. The authors speculate extensively about the possible functions of synapsin-I and DARPP-32 but, in several cases, cite the maxim "correlation does not prove causality" in criticizing the hypotheses of others.

The main thesis of the book is that protein phosphorylation is a final common pathway of "paramount importance" in animal cells (p. vii, 1, 301, 334). There is no question that protein phosphorylation is an important regulatory process, but the data just do not support the assertion that it is the *most* important one. If one uses the stringent criteria advocated by the authors in the book, phosphorylation has been shown to play a physiological role in the regulation of the activity of only a very few proteins. For example, of all the substrate proteins discussed in chapter 4, tyrosine hydroxylase and tryptophan hydroxylase are the only ones for which there is even incomplete evidence of physiological regulation by phosphorylation. I agree with the authors' conviction that phosphorylation regulates the function of these proteins, but one must not fail to distinguish between conviction and fact.

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## **Molecular Biophysics**

**Ionic Channels of Excitable Membranes.**  
BERTIL HILLE. Sinauer, Sunderland, Mass.,  
1984. xiv, 427 pp., illus. \$32.50.

Ion channels are becoming universal in their importance in cell biology. Long studied in excitable membranes, channels have recently been studied in secretory cells, red blood cells, lymphocytes, and plant cell protoplasts, to name a few systems. They have been found in all cell types where they have been looked for. Channels have traditionally been the ter-

ritory of membrane biophysicists, who have used electrical measurements of membrane currents to make inferences about the functional and structural properties of the underlying channel molecules. Recently, however, biochemical techniques have been brought to bear on these channels, and the most well-studied of them, the acetylcholine-activated channel and the voltage-gated sodium channel, have been cloned and sequenced. The future will bring a valuable confluence of these molecular techniques with the biophysical study of engineered structural mutants of ion channels. Bertil Hille's book on ion channels therefore appears at a particularly opportune time.

It is hard to imagine an author more qualified and capable than Hille to write a monograph on this subject. He has been responsible for much of the current conceptual framework of ion channel biophysics, and he is a lucid writer whose review articles have long been basic references for students in the field. In the book Hille provides a masterly explanation of the biophysical concepts that are necessary for making structural inferences about the channel molecules from measurements of the properties of the ionic currents that flow through them. He successfully reviews classic work, important physical theory, and new methodologies.

The book is divided into two parts. The first reviews the properties of the most well-known channel types—voltage-dependent sodium, potassium, and calcium channels and the chemically activated channels. It offers an excellent review of the classic axonal voltage clamp experiments and a summary of the current understanding of the properties of these channels. Unfortunately, as with most reviews, this section will probably date quickly. Already there is much important newer work, such as that on the effects of calcium channel agonists and the amino acid sequence of the sodium channel.

The second part of the book deals with the principles and mechanisms of channel function. The relevant physical theories of ions in solution and of diffusion through pores are discussed along with the fundamental concepts of ionic selectivity and gating. This section is more general, using specific channel types to illustrate the concepts and experimental results. It is clearly written and brings together topics that are spread out through the literature. A familiarity with these chapters would be excellent preparation for reading the biophysical literature on ion channels.

The book is well organized for use both as a textbook and as a reference. It is not necessary to read the chapters in sequence. There are many cross-references between the two parts of the book, and I found it valuable to skip back and forth between the earlier chapters on particular channel species and the later ones on mechanisms. Each chapter ends with a recapitulation of its major points. Many tables are provided, and the bibliography and index are extensive.

The book brings together much information and many ideas and is therefore

particularly useful for novices to the field or for neurobiologists, molecular biologists, and cell biologists who are interested in ion channels. It will also be a valuable reference for working channel biophysicists. Hille's scholarship and authority contribute much to the quality of the book, and it should become a long-lived standard work in this increasingly fast-moving field.

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## The Emergence of *Homo sapiens*

**The Origins of Modern Humans.** A World Survey of the Fossil Evidence. FRED H. SMITH and FRANK SPENCER, Eds. Liss, New York, 1984. xxii, 590 pp., illus. \$70.

In the main, two fundamental question sets confront paleoanthropologists: When, where, and how did our lineage diverge from the apes? and When, where, and how did *Homo sapiens* emerge as a distinct species? The early evolution of the Hominidae has received wide attention and generous funding from American and other institutions and private donors over the past quarter century. The result has been a flood of fossils, solid geochronological dates for major sites, clarification of some issues, and acrimonious debate over others. Per contra, much of the fossil record pertaining to the origin (or origins) of *Homo sapiens* was collected before 1960 and is blighted by poor data on provenience and inadequate contextual information. Numerous specimens (Zhou Kou Dian, Le Moustier, Combe Capelle, Podbada, Brno, Dolní Věstonice, Mladeč, Šipka, Předmostí) were lost during World War II and through other mishaps.

Still there has been notable progress in the form of new discoveries and the application of modern field and laboratory methods for their interpretation. Smith and Spencer have admirably assembled the old, the new, and the borrowed in this blue-jacketed volume. It is a major resource for students of human evolution. The meat of the work is in six chapters that are surveys of evidence from gross geographical regions: western Europe (Stringer *et al.*), central Europe (Smith), western Asia and the U.S.S.R. (Trinkaus), sub-Saharan Africa (Right-

mire), Africa (Bräuer), and China, Indonesia, and Australia (Wolpoff *et al.*). In addition, Howell provides an excellent introduction giving an overview of major issues and his opinions about them and Spencer pens yet another history of the Neandertal debate. Three chapters (Freyer, Brace *et al.*, and Owen) that deal with aftermath and deployment rather than with origins fit less neatly with the rest.

Most of the authors deal with questions of when and where *Homo sapiens* evolved but pass over the important question of how (vis-à-vis natural selection) the transition was achieved. It is generally conceded that the answer lies in the archeological record.

Africa, the homeland of *Australopithecus* and *Homo erectus*, is very much in the running as the place where *Homo sapiens* emerged. Anatomically modern (a.m.) human bits have been recovered from Middle Stone Age deposits at Klasies River Mouth, South Africa. The youngest Middle Stone Age deposits at Klasies are reliably dated to about 60,000 years ago, and the human cranial fragments are probably close to 100,000 years old. More complete but less certainly dated remains from Border Cave also attest to the existence of anatomically modern human populations during the South African Middle Stone Age. They have the closest morphological affinities with modern southern African peoples. Coastal inhabitants exploited marine resources in addition to continuing the clever hunting traditions of their Acheulian predecessors (Rightmire).

Eastern and northern Africa also have yielded tantalizing evidence for the early appearance of a.m. *Homo sapiens*. Bräuer includes the cranium designated

Omo 1 from the Kibish Formation, Ethiopia; the fragmentary crania from Kanjera, Kenya; teeth from Middle Stone Age horizons in the Mumba Rock Shelter, Tanzania; perhaps the Singa calvaria from the Sudan; and the Témara occipitoparietal fragment from Morocco in early a.m. *Homo sapiens*. But the dates for these specimens are less secure than those of Klasies.

Africa has been a relatively rich source for specimens of archaic *Homo sapiens* that bridge the gap between Early Pleistocene *Homo erectus* and a.m. *Homo sapiens*. Notable among them are the Saldanha calvaria (South Africa); the Broken Hill (Kabwe) cranium (Zambia); the Ndutu and Laetoli 18 crania (Tanzania); the Kapthurin mandible (Kenya); the Bodo and Omo 2 crania (Ethiopia); the Haua Fteah mandibles (Libya); and the Jebel Ighoud cranial remains (Morocco). Many problems remain for those who would arrange the widely scattered African specimens into a phylogenetic sequence and link them to the archaic and a.m. *Homo sapiens* of other continents. Bräuer's model (p. 394) is a provocative starter, but one also must respect Rightmire's conservatism in these matters.

Western Asia (herein encompassing Iraq, Israel, and the U.S.S.R.) and central Europe also may have been important centers for the origin of a.m. *Homo sapiens*. Smith argues the case for continuity between Neandertals and a.m. *Homo sapiens* in central Europe more insistently than Trinkaus does for western Asia albeit on the basis of more fragmentary material.

Trinkaus bravely discusses at length the nature of the adaptive shift from archaic (Neandertal) to a.m. *Homo sapiens* in addition to surveying his chunk of the fossil record. He sorts the early human remains from western Asia into four samples. The oldest, exemplified by the unique Zuttiyeh cranium, resembles European early Neandertals. The Shanidar (Iraq) and most of the Russian specimens and the Mousterian specimens from Amud, Kebara, and Tabūn in Israel are like the classic European Neandertals. Early a.m. *Homo sapiens* are best represented by numerous specimens from Skhūl and Qafzeh, and later a.m. *Homo sapiens* are exemplified by skeletons from Aurignacian horizons at Kebara. A good case can be argued that a transition from Neandertal to a.m. *Homo sapiens* occurred locally in the Middle East, but wobbly dates preclude a verdict beyond reasonable doubt.

The pattern of human evolution in western Europe during the Upper Pleis-