1993. 261:50–58). It would have been beneficial to examine the features of both the actin and myosin structures and the model for their interaction (Rayment et al. *Science*. 1993. 261:58–65) in the same textbook.

Given that an economical style has been employed, there are sections where the reader might want more information than is provided. In discussing the ability of vanadate to stabilize a myosin nucleotide complex, the only reference I found was to vanadate photo-cleavage paper, with no references to papers that establish the biochemical effects of vanadate on myosin (e.g., Goodno and Taylor. 1981. *Proc. Natl. Acad. Sci. USA*). 79:21–25) or the mechanical effects of vanadate in muscle fibers (e.g., Dantzig and Goldman. 1985. *Biophys. J.* 86:305–327).

Of considerable utility is the manner in which the rudimentary principles of many of the physical techniques used to study muscle are explained. X-ray diffraction, electron spin resonance, the use of caged nucleotides, and in vitro motility are clearly outlined so that the nonspecialist can get more out of papers from the literature.

For a small book covering a large field, the use of jargon seems to have been kept to a minimum. In most cases, each new term is accompanied by a clear definition. As in the first edition, there is specific reference material at the end of each chapter, annotated to include a thumbnail sketch of what the reader will find in each paper. A general reference section is found at the end of the book along with a very useful appendices containing general physiological data on muscle fibers and the sizes and proposed functions of the major muscle proteins.

The second edition includes two new chapters. "Mechanochemical coupling" (Chapter 7) was a subsection of the chapter on the "Molecular Basis of Contraction" (Chapter 6, volume 1) in the first edition. The expansion of this section of the book provides a more fitting discussion of a principle focus of modern muscle research. A completely new and completely warranted chapter in the second edition is the chapter on in vitro motility assays (Chapter 9). This technique has emerged as a major tool for the study of actin-myosin interactions during the past decade. Variations of the technique have provided important evidence for the minimum size of the myosin motor domain and the influence of actin polarity on the direction of myosin movement. In vitro motility is also providing crucial information relating to the quantitation of the magnitude of the force and the step-size of a myosin molecule per ATP hydrolyzed.

The final chapter of both the first and second volumes is on "Problems and prospects." It was gratifying to note that there has been progress made on a couple of the major problems listed in the first edition. Crystal structures of G-actin and the myosin head are leading to more precise molecular models for the interaction of these proteins in muscular contraction. Molecular biological techniques are beginning to unravel some of the mysteries of muscle development and muscle abnormalities. However, as Bagshaw has clearly surmised, the advances of the past decade have more sharply defined the questions that take us into the next. Is the coupling between the ATPase of myosin and force production tight or weak? What are the conformational changes that allow for the conversion of chemical energy into mechanical work?

This book is perhaps the first reference source that should be handed to a beginning student in a muscle laboratory. By using examples from the original literature, Bagshaw leads the student away from classical textbook descriptions of rigid oar-like crossbridge interactions towards more up-to-date models that are in tune with the dynamic properties of the myosin crossbridge. The current edition of "Muscle Contraction" has brought the field up-to-date again, and when the answers to Dr. Bagshaw's current questions are available, the next edition will provide a clear distillation of the advances in the study of muscle contraction.

Malignant Hyperthermia: A Genetic Membrane Disease by S. T. Ohnishi and T. Ohnishi

CRC Press, Boca Raton, FL, 1994. 331 pages. $129.95 cloth

Reviewed by Charles F. Louis and James R. Mickelson, Department of Veterinary Biology, University of Minnesota

Malignant Hyperthermia: A Genetic Membrane Disease, a volume in the CRC series "Membrane-Linked Diseases," provides an account of this interesting inherited skeletal muscle syndrome of humans and pigs. Malignant hyperthermia is characterized by a rapid elevation in body temperature and muscle rigidity after exposure to halogenated volatile anesthetics. Unless promptly treated with the skeletal muscle relaxant dantrolene, death quickly follows. In one respect, this volume is a timely review of this subject because the molecular basis for this disease in the pig has been defined and research into the more heterogeneous syndrome in humans is generating great interest. Studies by a number of groups, including one of the editors (S. T. Ohnishi), initially identified an abnormality in some aspect of the process of sarcoplasmic reticulum Ca^{2+} release in the muscle of malignant hyperthermia susceptible pigs. This has ultimately led to the definition of a mutation in the sarcoplasmic reticulum Ca^{2+} release channel as being highly linked to malignant hyperthermia in pigs as well as a number of human families.

This book is divided into five major sections and starts with a poignant set of vignettes from malignant hyperthermia-susceptible families. The hard work and enthusiasm of such people led in 1981 to the establishment of

the Malignant Hyperthermia Association of the United States. This organization has done much to help malignant hyperthermia families through newsletters, a hotline, a registry of patients and, most important, the development of a standardized diagnostic test protocol. Subsequent sections describe the history of malignant hyperthermia, our current understanding of the syndrome, the clinical diagnosis procedures and, finally, the molecular genetics of this syndrome.

Werner Kalow's personal account of the discovery of malignant hyperthermia reminds us how this syndrome is a rather "recent" discovery, because the first published report of an abnormal response of patients to volatile anesthetics was only made in 1960 by Denborough. It is interesting to learn that a proposal to name malignant hyperthermia "Denborough's myopathy" was rejected as being "undesirable in principle"; this contrasts with earlier times when the clinicians who discovered a disease had it named after them! It was only in 1973 that the first International Symposium on Malignant Hyperthermia was held indicating the slow rate of progress made initially in understanding the underlying cause of this syndrome. This section, dealing with the history of malignant hyperthermia, includes an excellent account by Harrison of the identification of the malignant hyperthermia susceptible pig as well as a report on the infrequently described "hot dog." Harrison provides a highly amusing account of his efforts to develop a herd of these malignant hyperthermia-susceptible pigs—it took him six months to recognize that the two boars chosen for breeding had been castrated shortly after having been weaned! Although the intimate details of Ohnishi's frustrating quest to study malignant hyperthermia are recounted in great detail in this section, the views presented are limited to his own (as indicated by the list of references where 29 of the 34 are from the author's own studies). For example, no mention is given of the several reports indicating that dantrolene is without effect on sarcoplasmic reticulum Ca^{2+} release, that the Ca^{2+} release channel gene is different in skeletal and cardiac muscle, or that others made the seminal discoveries as to the identity of the Ca^{2+} release channel in the sarcoplasmic reticulum membrane.

The description of the major clinical findings in malignant hyperthermia by Gronert provides a useful explanation of this syndrome for both lay persons and the nonclinical researcher. The studies of Lopez and colleagues are well summarized in a chapter that documents what has become the central tenet of malignant hyperthermia; namely, malignant hyperthermia is the result of an abnormal regulation of intracellular Ca^{2+} concentration by skeletal muscle. Long hypothesized, the altered sarcoplasmic Ca^{2+} regulation in malignant hyperthermia-susceptible muscle documented by Lopez provided important data for studies that ultimately led to the identification of the gene responsible for this syndrome. Chapters by Duthie and Caroff, on the role of free radicals and neuroleptic malignant syndrome, point to some of the unresolved questions regarding how drugs (such as antipsychotic agents) or altered levels of a metabolite (Ca^{2+}) can result in a multiplicity of secondary effects.

The section describing the clinical diagnosis of malignant hyperthermia provides details for the clinician of the procedures necessary for the accurate interpretation of the caffeine-halothane contracture test, which is now used as the main method for diagnosing malignant hyperthermia. One of the major drawbacks to this test is that it requires a surgical biopsy of muscle, and other chapters in this section evaluate efforts to develop a noninvasive diagnostic test. Unfortunately, as these authors note, none of these noninvasive tests have proven as accurate as the biopsy test.

The most exciting section, in these reviewers' estimation, is reserved for the end of this volume, where new developments in the molecular genetic diagnosis of malignant hyperthermia are discussed. Unfortunately, with the rapid progress occurring in this area, the chapters by MacLennan and Hogan are now sorely out of date. Furthermore, contributions from European groups with the largest number of malignant hyperthermia-susceptible families were not obtained for this book. The chapter by MacLennan, whose sequencing of the porcine ryanodine receptor allowed him to prove that this candidate gene was indeed responsible for malignant hyperthermia, is actually a summary of data first published in 1991. The chapter by Hogan provides the most help for the clinical audience hoping to understand whether a molecular genetic test will replace the muscle biopsy test any time soon. Although the last chapter in the book, this author provides a nice overview of the strengths and weaknesses of molecular genetic testing for disease diagnosis. The problem for malignant hyperthermia is that this clinical syndrome is now recognized to result from multiple mutations in the ryanodine receptor as well as mutations in other yet unidentified genes. Clearly the altered halothane-caffeine sensitivity of a muscle can result from many different mutations so compounding the problems of developing a molecular genetic test that will diagnose all malignant hyperthermia-susceptible individuals. However, it is interesting to note in a recent report from a large group of European laboratories (*Hum. Mol. Genet.* 1994. 3:471–476) that 10% of all malignant hyperthermia-susceptible patients in the investigators study have a unique ryanodine receptor mutation.

In conclusion, this book suffers somewhat from trying to define who the audience is. Should the researcher interested in malignant hyperthermia rush out to buy this book? Maybe, if one wants an eclectic account of this intriguing syndrome. Otherwise, one could read a number of recent excellent books and reviews on this topic. Alternatively, one could await the shortly to be published update on the definitive review of malignant hyperthermia by Gronert. If this review matches his 1980 masterpiece (*Anesthesiology.* 53:395–423), all other products, including the present volume edited by Ohnishi and Ohnishi, will pale by comparison!