which the line was propagated made a genetic contribution to the next generation. This protocol may have its parallels in Westernized human societies; improvements in nutrition and medicine have permitted reproduction at older ages. High divorce rates are associated with high rates of remarriage and the production of second families relatively late in life. The evolutionary consequences are difficult to predict but could be marked, and may be the best hope for postponement of human aging.

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A Popular Protein

Cytochromes c. Evolutionary, Structural and Physicochemical Aspects. GEOFFREY R. MOORE and GRAHAM W. PETTIGREW. Springer-Verlag, New York, 1990. xvi, 478 pp., illus. $98. Springer Series in Molecular Biology.

This reviewer has often said that it was not difficult to make a living as a scientist studying proteins in general; they are so varied. But making a living out of a single protein required some imagination. As demonstrated in this volume, cytochrome c, a well-behaved small protein having numerous experimental advantages, is an ideal object for such a purpose. Since first observed by David Keilin in 1924 and partially purified some years later, it has attracted a crowd of research workers. Among them are not only those interested in this mitochondrial respiratory-chain electron-transfer heme protein for its own sake but also many who have used it as a model to study phenomena applicable to all proteins. The accumulation of information has become so vast that the mere listing of it in intelligible categories would take more space than is available for this writing. The present volume and its earlier smaller companion by the same authors (*Cytochromes c: Biological Aspects*, Springer-Verlag, 1987) together do a good job of covering this far-flung subject. Experts in various areas will find interpretations they do not agree with or may feel that full justice has not been done to some aspects of the work, particularly of earlier periods. However, such complaints are relatively insignificant compared to the main achievement of these volumes, namely that they give an account, albeit sometimes cursory, of nearly everything that has been achieved with this fascinating biological object.

The present volume deals mostly with the structural aspects of the protein. Starting with the heme prosthetic group itself, it proceeds through amino acid sequences and spatial structure to the numerous variations, natural and artificial, that have been imposed on the primary and tertiary structures. In the process it covers not only the classical mitochondrial cytochrome c but also the other classes of c-type cytochromes. On such a basis one can argue the significance of the numerous studies of the molecular evolution of the protein, possibly the earliest tackled effectively from that point of view, and end up with the major pending problem: that of the protein molecular details of the mechanism of electron transfer to and from cytochrome c. It is somewhat distressing that after all the work, this last item, the *sine qua non* of the protein's existence, remains relatively poorly endowed with hard science, notwithstanding the intellectual foam enrobing the subject.

All in all, Moore and Pettigrew's two volumes provide excellent coverage of cytochrome c at depths that, if not always complete, are better than introductory. They will surely be found, for years to come, on the many desks of the community of scientists fascinated by how individual macromolecules operate so as to be thoroughly integrated with their living world, from molecules to populations of organisms. Students seriously studying proteins, at any level, will have little choice but to master the present volume, for it displays the prime example of how massive a tome of biological information is contained in a single protein and how understanding of this information is limited only by our ability to decipher it.

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Linked Functions

Binding and Linkage. Functional Chemistry of Biological Macromolecules. JEFFRIES WYMAN and STANLEY J. GILL. University Science, Mill Valley, CA, 1990. xvi, 330 pp., illus. $44.50.

It is a truism that any biological function depends on a highly complex set of interrelated chemical reactions. Whether the system is one of control of metabolic pathways, the function of complex enzymes, the regulation of gene expression, the transport of ions across membranes, the transmittal of neuronal signals, or oxygen transport, it consists of a network of interdependent reactions that enhance or hinder each other in complex reciprocal patterns. Such intermeshings have been described by a number of colorful epithets—"switches," "gates," "feedback," "induced fit," "togetherness," and others. This conceptual compartmentalization has left essentially unnoticed the progressive development of a rigorous, ever more insightful thermodynamic approach that could integrate these diverse patterns of coupling within a general phenomenon, that of linked functions, which is the subject of this book.

The idea of linkage in biochemical systems was introduced by Wyman 50 years ago in his analysis of interrelationships in the reactions of hemoglobin. The term "linked function" was coined and defined by Wyman in 1948 to refer to the interdependence of two or more functions on a molecule due to interaction between groups, which frequently involves a change in their position or environment. The equilibrium relations that describe this interdependence were called "linkage relations." The theory was expounded in detail in Wyman's 1964 classical article in *Advances in Protein Chemistry* (vol. 19, p. 223), and a year later it emerged as the basis of the Monod-Wyman-Changeux model of allosteric transitions.

Although the interdependence of interactions in biological systems has been widely recognized by practitioners of the art, few have availed themselves of the powerful arsenal afforded by the Wyman linkage theory for the analysis of these complex systems. This lack of appreciation might be explained in part by the language in which Wyman's papers are written, that of thermodynamics—a language that is, unfortunately, beyond the schooling of most biochemists. The present volume by Wyman and Gill should change this situation. The stated aim of the authors is "to present the allosteric hypothesis about regulation and control of biological systems in simple form." By presenting the theory in terms of clear, easy-to-follow equilibrium relations, with painstaking attention to logical development and detail and numerous illustrations, the authors have eminently succeeded in fulfilling this aim. Throughout, much of the illustrative material is drawn from studies on hemoglobin, to the understanding of which both authors have made major contributions.

This book is written on two levels. Starting with the most elementary binding equilibrium and assuming little previous knowledge on the part of the reader, the authors gradually develop their subject until it encompasses highly complex phenomena. The book opens with an introductory chapter that presents in descriptive terms the concepts of binding curves, binding capacity,

and linkage. The whole is amply illustrated with pertinent binding curves and corresponding three-dimensional structures. In the structure-function analysis, the examples are drawn from systems as varied as respiratory proteins, electron-binding proteins, allosteric enzymes, and nucleic acid–binding processes. This is followed by two chapters in which the general principles of binding equilibria are described. Starting with a simple single-site binding, the authors develop the various types of plots (Scatchard, double-reciprocal, Hill) and the binding isotherm. This analysis is then extended to increasingly complex systems—two independent sites, cooperative binding, allosteric effects. The concepts of the binding partition function and binding polynomial are introduced. The binding polynomial is then developed for various cases of binding interactions. The significance of the Adair constants and the analysis of cooperativity by Hill plots are explained for various cases of linkage. It is shown how electron binding can be treated by the same relations.

The middle of the book includes a discussion of allosteric systems that should be particularly appreciated by biochemists dealing with controlled reactions. This discussion is built upon a historical account of the development of the concept of allosterism since early in this century. The Monod-Wyman-Changeux model and the induced-fit Koshland model, itself a conceptual development of Pauling's early "interaction bonds" model, are seen to be special cases of the parent allosteric model based on Wyman's recognition 40 years ago that the essence of these controlled systems resides in the shifting of preexisting equilibria by the addition of ligands at binding sites. The fifth chapter of the book is devoted to a generalization of the term "binding" to include changes in amounts of heat or volume associated with a reaction, with applications to scanning calorimetry and isothermal titration calorimetry, and effects of pressure on macromolecular reactions. Two chapters are devoted to the complex topics of ligand-controlled aggregation, linkage between ligand binding and macromolecular phases, solubility, the triple point, and phase equilibria. The book closes with a chapter on the thermodynamics of macromolecules.

Binding and Linkage not only admirably meets its stated goal, it goes far beyond that. The authors have brought together the fruits of many years of insightful reflection on a central problem in biochemistry with the experience of many years of teaching this subject to first-year graduate students. The result is a short volume that both presents the basics of binding and cooperativity and develops in depth the powerful arsenal that the linkage concept makes available to experimental biochemists in dissecting interrelations that exist in biological systems. As such, the book can serve as an excellent textbook for the teaching of binding on the elementary level. It is also a must on the desk of any bioscientist dealing with coupled, controlled, interrelated reactions, that is, with linkages. The publication of this work must be regarded as a major event, and the book will surely find a place among the classics of the scientific literature.

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The Phylogenetic Perspective

Phylogeny, Ecology, and Behavior. A Research Program in Comparative Biology. DANIEL R. BROOKS AND DEBORAH A. MCLENNAN. University of Chicago Press, Chicago, IL, 1991. xii, 434 pp., illus. $45; paper, $21.

From the human appendix to life's common genetic code (not to mention the panda's thumb), history's indelible mark is ubiquitous. Nonetheless, consideration of historical influences in ecological and ethological studies steadily diminished from the neo-Darwinian synthesis of the 1940s until very recently. Implicit in ahistorical analyses is the assumption that traits are infinitely plastic and molded to their current environment by the omnipotent and omnipresent power of natural selection. Because this assumption in many cases is of dubious validity, recent methods have attempted to incorporate historical information into studies of adaptation and diversity.

Stemming from these advances, *Phylogeny, Ecology, and Behavior* is the first book devoted exclusively to the use of phylogenetic methods in studies of organismal functions, interactions, and evolution. In an ambitious volume jam-packed with case studies (111 cladograms of real taxa, with 200 more hypothetical examples!), Brooks and McLennan endeavor to demonstrate that the phylogenetic perspective can enlighten our understanding of topics as diverse as biogeography, host-parasite coevolution, speciation, and community ecology. Their method, phylogenetic systematics (in other words, cladistics), has two components. First, phylogenetic relationships are inferred on the basis of the presence of shared derived characters. The favored hypothesis is that tree ("cladogram") which requires the fewest evolutionary changes in character states. Second, evolutionary changes in biological parameters of interest (such as body size, geographic range, or host plant) are mapped onto this tree in such a way that the number of evolutionary changes required is minimized ("character optimization").

For example, to investigate whether aggressive behavior and ritualized behavior have evolved independently among stickleback fishes, one would first derive a phylogenetic hypothesis and then determine where on the tree each trait evolved. Indeed, in this example, Tinbergen's hypothesis that the two types of behavior have evolved in synchrony is confirmed. The versatility of the cladistic method allows it to be applied in a similar manner to a wide range of questions. To investigate whether the geographic distribution of a particular group of taxa has resulted from geological processes (such as continental drift), one can compare a cladogram of the organisms to a geologically based "area cladogram." Congruence of the cladograms would suggest that the geological splitting of areas has been associated with the evolutionary splitting of taxa. Similarly, the cladograms of hosts and parasites can be compared to test for congruence in their patterns of speciation.

The authors break new ground in their application of the cladistic approach to community ecology, emphasizing that history's mark can be discerned even in studies of contemporary processes such as the role of interspecific interactions in structuring communities: "Much of the confounding data compiled by evolutionary ecologists is due to the inability to distinguish effects stemming from historical background and those stemming from proximal dynamics." Nonetheless, to use phylogenies to test mechanistic hypotheses requires that different processes lead to predictably different outcomes. Unfortunately, as is evident in their discussion of speciation, extrapolating from the phylogenetic pattern to the underlying process is not as straightforward as the authors suggest.

Brooks and McLennan argue that by considering the geographic ranges of species in the context of their phylogenetic relationships, one can determine how a particular