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,