planetary mass. As an effective and key player in the scientific planning of a highly complex and demanding mission, Miner has continued to contribute to the accomplishments of Voyager through this authoritative amalgamation of the more noteworthy scientific, technical, and human elements that have characterized this great adventure.

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A Paradox for Biology

Evolutionary Biology of Aging. MICHAEL R. ROSE. Oxford University Press, New York, 1991. xiv, 221 pp., illus. $35.

The existence of aging presents something of a paradox for evolutionary biologists. If natural selection favors high reproductive success and high survival to the next opportunity to reproduce, then why do both traits show such widespread decline in old age? Why cannot organisms continue to achieve late in life biological feats of which they were capable in youth? These are the questions Michael Rose sets out to answer. "Why" questions in general can be answered at varying levels of proximity. Building on Dobzhansky's famous dictum that "nothing in biology makes sense except in the light of evolution," Rose's thesis is that to understand aging we must understand its evolution. Only then do its taxonomic distribution and its genetic and physiological mechanisms become intelligible. Gerontologists may require some persuading of this point of view, but Rose is the advocate to do it.

An evolutionary account of aging would be unnecessary if the process were inevitable; it could be that organisms are simply incapable of overcoming the effects of damage, wear, and tear they encounter. However, there is variation in the extent to which damage is combated. The life forms of today are the progeny of a line of descent unbroken for at least a billion years; germ lines do not die out.

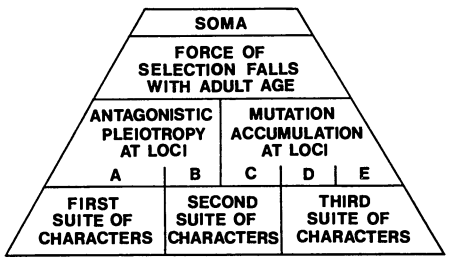
In evolutionary terms, what matters is the frequency at which a gene is represented in future generations. A compelling evolutionary reason for the occurrence of aging is the declining intensity of natural selection on mutant genes with effects late in the normal life-span. New mutations occur at a low rate during the copying of genes, and most lower either survival or reproductive success. Rose makes a compelling case that many are also age-specific; their effects are not equally apparent at all times of life, Huntington's chorea being an unwelcome human instance. Late-acting mutations of this kind are more difficult for natural selection to eliminate because by the time their effects are expressed many of their original carriers will already have died of something else, at a rate no different from that in non-carriers of the mutation. These mutations will therefore reach a higher frequency in the population than ones with an equivalent effect earlier in the life-span, and they will lead to a drop in fertility and survival later in life.

In addition, many mutations may affect survival and fertility at more than one age. For instance, a mutation leading to high rates of reproduction in young adults may do so by diverting resources away from repair or growth of the parent, and may thereby cause lower fertility or survival later in life. The evolutionary fate of such mutations will depend upon the magnitude of their early and late effects, and in general natural selection will act more intensely on the early positive effect than on the late negative one, so that aging will evolve as a side-effect of earlier benefits. A verbal account cannot do justice to the demographic and population genetic work that has led to these conclusions. Rose gives a fascinating historical account of the contributions of the major players on this field: Weismann, Medawar, Hamilton, and Charlesworth.

Theoretical population genetics is sometimes (wrongly) viewed as an arcane abstraction even by workers in nearby disciplines. One beauty of the evolutionary theory of aging is its testability; it stands or falls on the pattern of age-specificity of genetic effects on survival and fertility, and these are open to empirical investigation. Rose himself is a leader in this field, his work on genetics of aging in *Drosophila* having become a classic demonstration both of age-specific gene effects on survival and fertility and of genes with opposing effects on fitness at different ages. He produces an excellent review of the current state of knowledge on this point, not only for the classic animal models for work on aging, "the" nematode, fruit fly, and mouse, but also for lesser-known breeds including plants.

An evolutionary view of aging has some not altogether welcome messages for gerontologists and geriatricians. One is that the human progeroid syndromes, which give the appearance of greatly accelerated senescence, may be poor models for normal aging. They are caused by defects in single genes and are present at frequencies so low that they can be explained as the product of the balance between the input of the new mutations that cause the diseases and their subsequent elimination through premature death and impaired fertility of their carriers. The mechanisms of gene action in progeroid syndromes are not known, but what is clear is that they involve single mutations of drastic negative effect on both survival and fertility at all ages. In contrast, normal aging is expected to be the consequence of the activities of many genes, whose effects on survival and fertility are expected to be age-specific and even of variable sign. In addition, Rose makes a convincing case that there are few generalizations to be made about the cellular and molecular causes of aging. There are therefore unlikely to be any magic bullets for geriatricians; any mechanism involved in producing continuing survival and fertility is likely to fall victim, and the benefits from any single environmental or genetic intervention will therefore be limited.

It is possible to postpone aging in fruit flies, by artificial selection on genes of small effect, as Rose himself has demonstrated. The lines in which aging has been postponed were produced by breeding from adults when they were old; only those individuals still alive and fertile at the age at-



"Hierarchy of causation of aging. At the top of the pyramid is the ultimate determinant of whether or not an organism senesces: the possession of a soma distinct from its germ line. This gives rise to a fall in the force of selection with adult age, in all cases where survivorship is concerned and in most cases where fecundity is concerned. There are then two subsidiary population-genetic mechanisms for the evolution of aging: antagonistic pleiotropy and mutation accumulation. Specific suites of characters may be subject to either or both of these mechanisms. In any case, multiple suites of interconnected physiological mechanisms are expected to determine the pattern of aging in any one species, with even greater diversity among species." [From *Evolutionary Biology of Aging*]

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,