sider some aspects of national culture, as well as to profit from a somewhat different perspective.

Typically French is a high regard for the intellect. True to form, Limoges deals with the growth of an idea, natural selection. He not only exploits the rich supply of Darwin's marginalia and notes preserved at Cambridge, but also considers the works that Darwin used while he was developing his theory. It is especially pleasing to have information about Darwin's indebtedness to the French literature, particularly to Milne-Edwards and de Candolle. Perhaps the most important contribution is the demonstration that ecological ideas were crucial to the discovery of natural selection. This aspect of Darwin's work has been dealt with by earlier students of his work, but never in such detail or depth. Hence Limoges's book focuses upon a crucial point, and is most welcome.

Equally French is a deep concern for language. The positive benefit of literary excellence is sometimes offset by an excessive placing of style before content. Rhetoric is confused with logic, and words become more important than concepts. Such excesses would seem to have affected Limoges's analysis, so that his interpretation, although basically correct, sometimes deals with matters that others would consider epiphenomenal.

Limoges's thesis that Darwin's biogeographical thinking played an important role as his ideas developed can scarcely be denied. Yet precisely what biogeography contributed to the theory is open to question. Much of Darwin's concern for such matters is perhaps better explained as an effort to refute the idea of special creation than as a search for an evolutionary mechanism. Furthermore, the ecological aspect of Darwin's work becomes a procrustean bed, to which documents are fitted in a rather questionable manner. Historians now seem to be reaching a consensus in agreeing that Darwin did not become an evolutionist until after he had returned from his voyage on the *Beagle*. Limoges accepts this view, but perhaps goes too far. Time and again, he invokes purely negative evidence to show that Darwin had no evolutionary interests during the voyage. But he fails to mention the positive evidence that clearly demonstrates an early interest in "centers of creation" and in temporal changes in faunas.

The fallacy of negative evidence is again apparent in Limoges's criticism of the notion that the study of artificial selection helped Darwin to discover natural selection. He rightly observes that Darwin's consuming interest in artificial selection was a late development. However, we need not infer that it had no significance, merely because the term "selection" does not occur in Darwin's earlier notebooks. The perniciousness of such negative evidence is apparent when we find Darwin using the term "picking" in his second notebook on the transmutation of species. The concept is there, even though the word is absent.

Like so many historians, Limoges finds it necessary to explain away the influence of Malthus. At first sight this seems odd, for the main thrust of Limoges's argument is to show that Darwin developed a new conception of the natural economy. That a work on political economy might provide some crucial insight is therefore only to be expected. Limoges maintains that Darwin owed Malthus only an impression of the intensity of the struggle for existence. It seems to me that Malthus led Darwin to see who was struggling with whom and for what: the struggle involves a reproductive competition between members of the same species. This insight, the fundamental event in the Darwinian revolution, has been quite generally overlooked. Perhaps the resistance to natural selection, in France as elsewhere, derives from an insufficient appreciation of how much such a change in outlook implies. As Ernst Mayr has pointed out, Darwin's insight not only demolished the old conception of the natural economy, it refuted the whole system of metaphysics from which that conception derived. But older ways of thinking tend to linger on, particularly when fundamental to educational practices and religious beliefs.

MICHAEL T. GHISELIN
Department of Zoology,
University of California, Berkeley

Laboratory Pharmacology

Importance of Fundamental Principles in Drug Evaluation. Proceedings of an American Pharmaceutical Association symposium, May 1968. DAVID H. TEDESCHI and RALPH E. TEDESCHI, Eds. Raven, New York, 1968. xvi, 496 pp., illus. $18.95.

These proceedings are concerned with the *laboratory* evaluation of drugs. They review and discuss the assets and liabilities of most of the methods that have appeared in the last several years and that are changing the scope and increasing the potential of pharmacological research. Investigations of drug metabolism, drug interactions, drug receptors, behavioral effects of drugs, pharmacokinetics, and pharmacodynamics are all represented. The value of studies of inter- and intraspecies variation in drug responses is stressed in clear, honest, and sometimes humorous language (Ahlquist). Newer discoveries in catecholamine synthesis and metabolism, dose-dependent kinetics, disposition of drugs as a function of drug action, morphologic and biochemical factors contributing to the differences in responses between organs, and observations on drug elimination by the lungs, all fundamentally important in modern-day drug evaluation, are well reviewed and referenced. The value of multidisciplinary approaches to drug evaluation is clearly demonstrated in chapters by Giarman and Beyer.

The professor of pharmacology or medicine could not hope to find more convenient and concisely written analyses of the merits and shortcomings of in vivo and in vitro assays in selected studies or better reasoning and examples to show his students why both are needed to solve most problems. The student will be particularly gratified by the spectrum of coverage; most chapters cover the subjects from their ideals and philosophy to the mathematics necessary to begin analogous experiments. The book will probably be most valuable as a reference text to be consulted for help in experimental design and in assessing the scientific merit of technical presentations. It will also be useful to the student interested in the new currents in pharmacologic research, who with its help will be able, for example, to assess the advantages and shortcomings of methods using isolated organs or parts of organs, administration of drugs directly into parts of the central nervous system, and electrophysiologic techniques, and to appreciate the complexity of approach in the new and exciting studies of drug interactions.

The book does have its deficiencies. There is little organized discussion of the principles of drug evaluation in man, and, as may have been surmised, no effort is made to present the difficulties of the evaluation of drugs as they affect disease (after all the *raison d'être* of pharmacology). Clearly the book may help the clinically oriented pharmacologist to understand, simulate, or try to

emulate the molecular, biochemical, or biophysical pharmacologist, but the psychologist and ecologist (mentioned in the foreword) have not had an equal opportunity to make their colleagues aware of the principles with which they are concerned. In addition, the editors could have filled a most useful function if they had provided summaries of the principles they intended to relate in those chapters that deal primarily with methods but whose titles connote a more sweeping purpose. Finally, the publishers could have helped the student for whom this book presumably was intended by producing the book in a form that would have permitted a lower price.

KENNETH L. MELMON
Division of Clinical Pharmacology,
San Francisco Medical Center,
University of California, San Francisco

Biological Stereochemistry

Molecular Asymmetry in Biology. RONALD BENTLEY. Academic Press, New York, 1969–70. 2 vols. Vol. 1, xii, 324 pp., illus., $14; vol. 2, xvi, 568 pp., illus., $27.50. Molecular Biology Series.

Don't be misled by the title of the book. The subject is stereochemistry—the either/or world of *cis/trans, R/S, threo/erythro, chiral/achiral,* and *syn/anti.* The subject has its roots in the historical contributions of Van't Hoff, Pasteur, and Ogston. The books do not deal with macromolecules or to any great extent with the shape of molecules as a whole.

Volume 1 gives a rather complete and readable presentation of the principles of stereochemistry—the symmetry operations that define configurational isomers as distinguishable and determine whether identical substituents of a carbon atom are distinguishable.

The currently used (contending) nomenclatures are carefully detailed. This is perhaps one of the more important contributions of this volume, since translation of the current research literature from symbols and words into stereochemical reality is at stake. Especially important for biochemists are the ideas and terms used to define the asymmetry that only derives from isotopic substitution, prochirality. A large section of this volume is given to the preparation of optically active molecules by synthetic and resolution methods and to an enumeration of examples in which stereoisomers are known to have different biochemical properties.

The major goal of volume 2 is to provide a review of the facts and logic used in solving problems of the stereochemistry of the main classes of metabolites and of the stereochemical course of the enzyme reactions concerned with them. No reference has been left unturned in making the coverage as complete as possible. In general, the problems of stereochemistry for the biochemist have not been concerned so much with the determination of structures, although this still engages the natural products chemist; these problems were mainly solved by chemists before 1950, with notable exceptions such as natural isocitrate. Instead the concern has been to depict the steric course of reactions in which reactants or products or both have structures that are ambiguous with respect to the groups involved in the reaction. Thus, what could be more cryptic than the addition of acetyl CoA to oxalacetate to produce citrate? The challenge of such questions has been met with increasing sureness over the past 20 years, and progress toward completeness is so accelerated as to make this volume noticeably behind the times despite the best efforts of the author. Thus such important subjects as the stereochemistry of reactions concerned with the $-CH_2$ groups of glycine, pyridoxamine-P, and phosphoenol pyruvate or of proton replacement on $-CH_3$ groups already call for a supplementary volume. After this, the future lies in the mechanistic interpretation of this wealth of stereochemical detail when considered with other data.

The author has claimed that the discussion of reaction mechanisms is beyond the scope of the volume. In this he is at one with the vast majority of stereochemists who have preferred the either/or world to the mortal vulnerability of the curved arrow. Nor does the author tie these matters together in their biological frame—since the key to the choice between alternative courses in the stereochemistry of prochiral centers must lie in the natural evolution of enzyme mechanisms. However, the volume is not sterile of mechanistic content, since Bentley occasionally reviews a paper that puts its stereochemical conclusions in these terms. Unfortunately, the marriage of the two is often somewhat strained, as in the section on lactate racemase, where, since there is no stereochemistry to talk about, we get unabridged speculations on a number of unlikely mechanisms; and in the discussion of sugar isomerase, speculation on a role of lysine in ring opening is misinterpreted as evidence against a *cis*-enediol intermediate in the enolization. A greater regard for mechanism would have changed the context of many of the discussions—thus, for example, dioldehydrase would have been put in with the cobamide enzymes rather than the hydratases, and aldolases would have been taken up with citrate synthase.

The subjects covered include most of the classes of enzymes: dehydrogenases, condensation and elimination reactions, and the reactions of intermediary metabolism. There are also extensive reviews of the stereochemical course of reactions involving the isoprenoids, steroids, and alkaloids. Lengthy side trips into the analysis of substrate specificities of alcohol dehydrogenases, glutamine synthase, and chymotrypsin seem tangential to the main goals of the volume, but they provide instructive examples of a genre. On the whole the effort comes off well, and many students and workers will find it a welcome directory and guide to the literature through most of 1968.

IRWIN A. ROSE
Institute for Cancer Research,
Philadelphia, Pennsylvania

Botanical Relationships

Principles and Methods of Plant Biosystematics. OTTO T. SOLBRIG. Macmillan, New York, 1970. xiv, 226 pp., illus. $9.95. Macmillan Biology Series.

The employment of experimental methods to improve our understanding of biological relationships within and between species of plants and to their environment was begun about 50 years ago. Studies by workers in different countries have contributed substantially to this still relatively new and expanding field, now often referred to as biosystematics. Solbrig's book is a pioneer effort to bring together basic principles and techniques that have evolved from such studies in the form of a textbook suitable for undergraduates.

This attractive volume consists of 12 relatively short chapters. Part 1, The Process of Speciation and the Forces that Control It, consists of seven chapters. In the introductory chapter biosystematics is defined as "the application of genetics (and cytogenetics), statistics, and chemistry to the solution