teins, are "best able to explain aging . . . and . . . should receive the highest priority for future investigations." This controversial viewpoint is defended on the grounds that collagen represents 25 to 30 percent of total body protein and has an exceedingly low turnover rate. Progressive cross-linking might inhibit tissue flexibility and capillary-to-tissue cell mobility. Furthermore, cross-linking could satisfy a proposed requirement, often mentioned in this volume, that a true aging process affecting the intact mammal must begin or accelerate after maturity.

This latter proposition is also used to discriminate against the notion that intrinsic cellular aging processes exist. Studies indicating decreased rates of protein synthesis or decline in rates of DNA synthesis and cell proliferation and studies measuring rates of cell loss with animal age are judged to be of less gerontological significance because the major changes occur during growth and prior to maturation. One could challenge this central argument, however, since there is as yet no reason to exclude the possibility that age-associated functional decline may result from a continuation of the progressive drop in rates of protein synthesis and cell proliferation observed between birth and maturity. This general hypothesis dates back to the work of Minot in 1908, and its acceptance underlies many of the studies Kohn cites. His argument that there is no substantial supportive evidence is rendered less effective when one considers that the same objection might be directed against cross-linking theories. Thus, for example, although cross-linking of collagen molecules is well established, evidence that this impairs permeability and function is equivocal or contradictory.

Several other hypotheses and model systems are also judged to be of lesser significance, at least with regard to aging of the whole animal. For example, the limited survival of human diploid cells in culture, proposed as a model for studies on intrinsic cellular aging, is considered to be more relevant to questions of growth cessation and neoplasia. This conviction apparently is based on the fact that intermitotic cell types in vivo exhibit declining growth rates mainly in correlation with animal growth. Much less change is observed following maturity. Furthermore, at the time of publication no relationship between potential survival of cells in vitro and age of adult donor had been established. The former point, however, need not be considered an effective argument against the model for reasons outlined in the paragraph above. Concerning the latter point, the recent works of Goldstein and of Martin have shown a definite relationship between postnatal donor age and survival of human fibroblasts in culture. Kohn regards as improbable hypotheses that implicate somatic mutations, the immune system, or cell damage due to free radicals as major factors effecting aging in the animal. This conclusion is also based, at least in part, on arguments against involvement of inherent cellular change in the aging syndrome.

Both novices and more experienced investigators in the field of gerontology may gain perspective through examination of this volume. The controversial issues discussed and the stand taken by its author should stimulate both thought and experimentation.

ROBERT J. HAY
Department of Biological Sciences, Wright State University, Dayton, Ohio

Drug Action

Essentials of Molecular Pharmacology. Background for Drug Design. ANDREJUS KOROLKOVAS. Wiley-Interscience, New York, 1970. xviii, 340 pp., illus. $16.50.

The major purpose of this monograph is to illustrate fundamental principles of drug actions at the molecular level, as far as they can be explained in terms of modern chemistry and biochemistry. To this end, the first half of the text develops logically from consideration of the physicochemical properties of small molecules, through the pharmacological effects of specific moieties, to an analysis of drug-receptor interactions. This development is handled with reasonable balance between chemistry and its relationship to drug action by the use of frequent and, on the whole, clear examples.

By way of illustration, the steric, electronic, and obstructive effects of halogenation are documented effectively by reference to changes in the pharmacological activity of many drugs including steroids, thyroid hormones, antimetabolites, and central nervous system depressants. Similarly, stereochemical considerations are presented with clarity and relative simplicity. I admire, particularly, the facility of the author in summarizing results obtained by sundry advanced chemical and physical techniques to illustrate the relationship between electronic distribution and configuration and also the concept of preferred conformation in terms of neurotransmitter agents. Drug-receptor interactions are introduced from the standpoint of the types of bonding possible between small drug molecules and macromolecules. Since numerous examples are given, I was a little surprised to find no mention of the interaction between inert-gas anesthetics and myoglobin or hemoglobin, perhaps the best-documented example of a drug-macromolecule interaction based on Van der Waals forces.

If this section of the text has a limitation it resides in a tendency to "show you the cookies but to take the plate away before you can accept one." For example, although the author acknowledges the usefulness of mathematical derivations based on polarizability (Hansch) and molar attraction constants (Ostrenga), these models are treated cursorily and exceptions are not discussed.

The second half of the monograph includes a lengthy discussion of receptor topography and more succinct appraisals of theories and mechanisms of drug action. The first topic is handled well, and quite recent interpretations of the nature of receptors for drugs from analgetics to steroids are covered. A brief and useful review of membrane excitability and autonomic pharmacology precedes discussion of cholinergic and adrenergic receptors.

In this reasonably short monograph, chemistry is favored over biology, but this is not a serious limitation since descriptive pharmacological information is readily available in other texts. There is little mention of the attempted isolation and characterization of receptors, presumably because the first real success in this area has occurred so recently. The book is well illustrated and referenced and is easy to read if one is not "chemophobic." It is quite different from previous monographs on molecular pharmacology, which, in my opinion, either have been simplistic or have suffered from an inordinate preoccupation with receptor theory. It is recommended to anyone with an interest in the *precise* nature of drug action.

ANTHONY TREVOR
Department of Pharmacology, University of California School of Medicine, San Francisco