Principles of Metabolic Control in Mammalian Systems

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Preface

In this work we present the basic principles of metabolic control which we hope will serve as a foundation for the vast array of factual matter which the biochemist and the physician engaged in metabolic research must accumulate. Accordingly, we attempt to set forth these principles, along with sufficient explanation, so that the reader may apply them to the ever-expanding literature of biochemistry. If we are successful, this will provide a theoretical approach which can be applied to any given set of metabolic reactions.

It is impossible to enumerate each and every biochemical reaction and pathway since such a work would be too unwieldy for efficient use. Rather, we hope our presentation of the principles of metabolic control will be sufficiently basic to be of lasting usefulness no matter how detailed biochemistry may become. We would like to be able to condense biochemistry into a theoretical biology that will not only allow for the general treatment of any given reaction but will enable predictions to be made as to the existence of necessary pathways and the consequences of altered control. Such is not possible today, but this may be accomplished in the future. We believe it is now possible to institute the beginnings of such a theoretical biology.

We hope this book will fulfill the varied needs of the graduate student, physician, and biochemist, as well as selected undergraduates and medical students who wish to augment their understanding of the principles that underlie metabolic regulation. There is a tendency to become so enmeshed in the accumulation of factual knowledge that a firm grasp of the concept and nature of metabolic interrelationships and control mechanisms suffers; we think that our approach may act as a corrective. Perhaps, after the beginning student is introduced to the structural details of carbohydrates, lipids, proteins, enzymes, and nucleic acids, the next logical presentation should be the principles of metabolic control and the means by which the supramolecular entities of life are constructed and maintained.

Obviously, a book such as this cannot hope to give examples of all types of control phenomena, but it can serve as a starting point for the newcomer to biochemistry as well as for individuals engaged in closely related areas who may have hitherto felt somewhat chary about opening up the Pandora's box of metabolic control. Any discussion of regulation must, of necessity, depend on arbitrary and somewhat artificial categories, but an attempt at discrete redundancy has been made in order to present an integrated picture. In this way, one can follow in logical fashion the various principles of metabolic control or, if desired, may read only that selection which is appropriate to his needs.

We have limited our viewpoint to the control principles of mammalian systems although many of the mechanisms have been derived from nonmammalian systems. It appears that many metabolic control systems may be shared by both mammalian and nonmammalian organisms, although certain specific details may vary. Thus, it may be most useful to consider control of metabolic reactions in microorganisms, recognizing that these controls may apply only partially to mammalian organisms. It is assumed that a majority of metabolic control principles are biologically universal and therefore can be derived at any level of biological complexity and can be applied to all organisms. Certain metabolic controls that are present in mammals are lacking in unicellular organisms so that knowledge of these principles must be derived directly from the study of mammalian organisms.

In general, the principles of metabolic control that will be covered will be those principles which govern intracellular reactions and not ordinarily those that deal with intercellular regulation or physiological mechanisms. It is assumed that physiological mechanisms result from intracellular functioning and thus are derivative phenomena. The borderline between intra- and extracellular events is not sharp. There exist areas where one merges into the other. Yet, we would like to make the distinction between intra- and extracellular events and thus have made certain arbitrary choices for our conveniences.

We take the responsibility for our selection and organization of topics. If we have omitted important principles or included those of lesser importance, the fault is ours.

With an endeavor which embraces so many interlocking areas of biochemistry, it is essential for the editors to turn to someone who can organize references and proofread text and reference lists, as well as expedite the thousand little aspects of the compilation process. We have been fortunate to have the services of Louise Pepe who gave so unselfishly of her free time to serve these and many other functions. Our thanks to her and to Steven Weiss, who, in the last frantic stages of manuscript preparation, have done so much in so little time. Addition-

ally, we have been fortunate to have available a cadre of dedicated secretaries, including Clara Polaski and Marie L. Carlson, who have been with us since work on the book began, as well as Ronnie Payton, Linda Braxton, Edith Mayes, Dee Daly, Marie Marcacci, and Sheri Silberg, who worked enthusiastically toward the completion of this book. A large portion of the artwork has been contributed by Nancy Cohn, who graciously met every deadline, no matter how imminent. Stephen Updegrove, Andrew Eisen, Bonnie Yost, and Steven Weiss read several chapters and made suggestions which we feel have improved the comprehensibility of the book.

Two of us (RMC and PDM) wish to thank Dr. Stanton Segal for generously providing the intellectual environment conducive to accomplishing this undertaking.

The editors at Plenum have been understanding and encouraging, but it is our spouses who have shown us a measure of forbearance and support which even we sometimes doubted we deserved. We hope this book merits their confidence in us.

Robert H. Herman
Robert M. Cohn
Pamela D. McNamara

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