

# Methods in Enzymology

Volume XXXVIII  
HORMONE ACTION  
Part C  
Cyclic Nucleotides

*Methods in Enzymology*

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*Hormone Action*

*Part C*

*Cyclic Nucleotides*

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## Preface

The compilation of a volume on nucleoside 3',5'-cyclic monophosphates and the separation of it from other volumes dealing with nucleotide-related methodologies may seem to some like arbitrary categorization. However, the close association that these cyclic nucleotides have had with the field of basic endocrinology and hormone action and the technical problems that are peculiar to their study seemed to the editors to justify the construction of this volume and its inclusion in the series of volumes on hormones.

The study of cyclic nucleotide metabolism and action and their alteration by hormones and other factors has met with formidable technical problems from its initiation. The field grew very slowly for almost a decade after Rall and Sutherland discovered cyclic AMP in biological material in the late 1950s. During the last five years, however, cyclic nucleotide-related literature has grown at an exponential rate, in part because of the development of newer and improved methodology and in part because investigators in more and more branches of biology are finding cyclic nucleotides to be of interest.

This volume contains a broad selection of techniques that should be useful to those interested in studying the cyclic nucleotide content of intact cells and the biosynthesis, degradation, and action of cyclic nucleotides in cell-free systems. Techniques for purifying and assaying a single enzyme or nucleotide will be described in more than one article. This is largely by editorial design, not to compile a complete collection of methods, but to offer the investigator a choice of useful techniques. All of them will be reliable when properly used, but none of them will be, for all laboratories, either easier or more reliable to use than any of the others. In some cases (as, for example, with adenylate cyclase from mammalian sources) lability or lack of extensive purification of an enzyme has contributed to technical problems that differ from tissue to tissue. In other cases (as, for example, with cyclic nucleotide phosphodiesterase) certain properties of an enzyme will be found to be distinctly different from tissue to tissue or among multiple forms of the enzyme from a single tissue.

Omissions have inevitably occurred—some because potential authors were overcommitted, some because of editorial oversight, some because of the timing of new developments relative to the publication deadline. Some apparent omissions have been covered in previous volumes of "Methods in Enzymology."

We thank Drs. S. P. Colowick and N. O. Kaplan who originated the



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idea for and encouraged the compilation of this volume. We thank the staff of Academic Press for their help and advice. We especially thank the contributing authors for their patience and full cooperation and for carrying out the research that made this volume possible.

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# METHODS IN ENZYMOLOGY

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- II. Preparation and Assay of Enzymes
- III. Preparation and Assay of Substrates
- IV. Special Techniques for the Enzymologist
- V. Preparation and Assay of Enzymes
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**Earl W. Sutherland, Jr.**  
**(1915-1974)**

This volume is dedicated to the memory of Earl W. Sutherland, Jr., M.D. Seldom has an individual been so closely identified with the development of a field of investigation as has Dr. Sutherland with the field of cyclic nucleotides and their relation to basic endocrinology. His pioneering work on mechanisms of hormone action was appropriately recognized when he was awarded the Nobel Prize for Physiology or Medicine in 1971. His untimely death in March of 1974 left a void in the scientific community.

Dr. Sutherland's work was driven by his intense curiosity and respect for truth. He had a remarkable instinct for asking the right question and for selecting the most straightforward of several possible approaches to its answer. Young associates were often in awe of his ability to see in data trends that were not yet apparent to others, and they frequently attached more significance to Dr. Sutherland's intuition—so often did it lead to a correct solution—than to someone else's carefully calculated arguments.

He was a creative thinker who valued an original idea, but who only critically and cautiously accepted data to support his ideas. Perhaps the lesson he tried hardest to teach his junior colleagues was, as he put it: "Never fall in love with your hypothesis." He stressed the point that an emotional investment in a concept and in its defense not only weakens objectivity but also lessens the chance to take advantage of serendipity, a factor he did not underrate in scientific discovery.

At various times, scientists from several disciplines and from no less than twelve nations worked in his laboratories. To them, he was an inspirational colleague and mentor and a generous friend. To biological scientists at large, Dr. Sutherland was a leader. His work led to insights into fundamental regulatory mechanisms that are now being explored not just by endocrinologists, physiologists, and pharmacologists, but by investigators in virtually every branch of medicine and biology.

JOEL G. HARDMAN

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