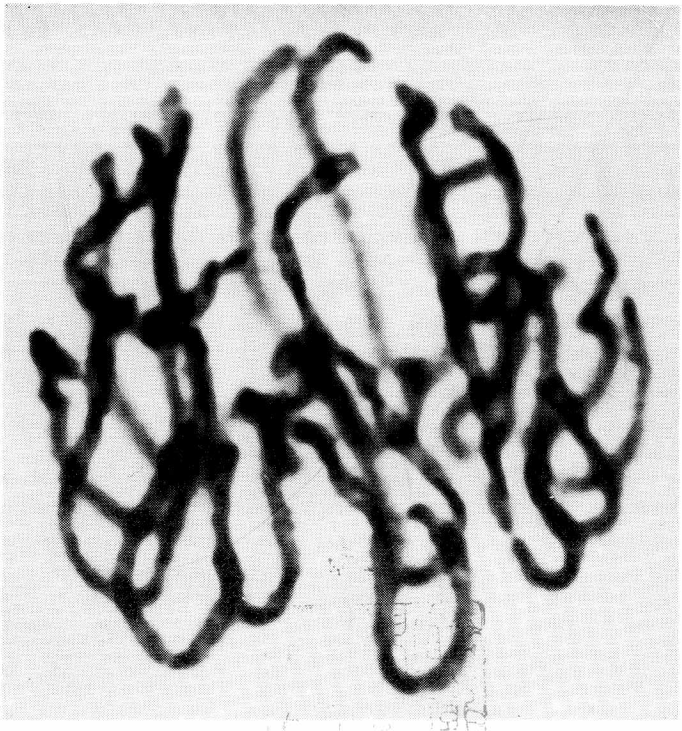

The MOLECULAR BASIS

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OF EVOLUTION

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THE MOLECULAR BASIS
OF
EVOLUTION

TO MY MOTHER

AND

TO THE MEMORY OF

MY FATHER

PREFACE

The writing of this book has been stimulated by the excitement and promise of contemporary protein chemistry and genetics and by the possibilities of integration of these fields toward a greater understanding of the fundamental forces underlying the evolutionary process. It has become, inevitably, a highly personal volume expressing the experimental and philosophical outlook which has resulted from a process of self-education in an unfamiliar area of science. As with many biochemists, pure biology, including genetics, has not been a major exposure in my education, and the process of learning something about these subjects has been both a revelation and a struggle. Various kind, and frequently amused, friends, versed in the complexities of modern genetics, have sifted through these pages, and I hope that most of the misinterpretations and frank mistakes have been eliminated.

It has been highly interesting of late to observe how many scientists, working either in protein chemistry or in genetics, or for that matter in relatively unrelated fields, have arrived at long-range research plans that are similar to my own, down to almost the last detail of experimental planning. This book, therefore, will undoubtedly represent the point of view of numerous other biologically oriented individuals. On the other hand, some of the ideas to be discussed are so new and controversial that for every well-informed reader of this book who, in general, approves them there may be another who considers them nonsense.

The recent advances in the development of techniques for the study of protein structure have made it possible to elucidate the complete amino acid sequences of a number of rather large polypeptides possessing hormonal activity, and nearly complete sequences should soon be available for several with enzymatic activity as well. Concomitantly, there have been developed methods for the analysis of the finer, more subtle, structural aspects of proteins, concerned with folding, intramolecular bonds of various types, and intermolecular interactions. These advances now begin to enable us to discern the vague outlines of macromolecules, in the three-dimensional sense, and to ascribe their physical behavior and biological activity to specific covalent and noncovalent structural features.

We like to believe that Nature has been extremely wise and efficient in the design of the chemical compounds, however large and complicated, which make up the structure and machinery of living things. Thus, although chemical differences are found among the representatives of a given protein as isolated from a variety of species, we tend to suppose that such variations, rather than being fortuitous and unimportant irrelevancies, are part of a complicated and highly integrated set of variations in all the functionally and structurally important elements of the cell, the summation of which accounts for the unique morphology and phenotypic character of the individual organism.

In the last few years, a number of studies have shown that various biologically active molecules may be subjected to considerable degradation without loss of functional competency. It becomes necessary, therefore, to consider that the "macromoleculariness" of proteins and other large molecules may, in many cases, be concerned not only with a specific biological property but with other, more subtle, phenomena of cellular activity and engineering not yet apparent, such as adsorption to surfaces or substrates. We must, perhaps, expect a multiplicity of variables in the "natural selection" of variants in molecules, all of which may, together, determine the biological suitability of a particular molecular species.

An understanding of the underlying principles governing the species specific variations in molecular structure and of the effect of such variations on species characteristics must involve a clarification of the process of translating information present in the genetic material of the cell into the chemical language of enzymes, regulators, and the like. Such considerations are only now becoming possible as the result of the dramatic strides taken in the last few years in genetic theory and methodology, and a portion of the discussion in the following pages will have to do with the experimental background of the analysis of genetic fine structure and with the possible significance of such analysis to the question of protein biosynthesis.

It is abundantly clear that the metabolic organization of all living cells, whether plant or animal, shows a remarkable uniformity. Even a cursory examination of the literature of comparative biochemistry and physiology indicates that such biochemical functions as glycolysis, proteolysis, and fatty acid degradation, as well as more integrated processes such as electromotor activity and active transport through membranes, are ubiquitous in nature. Discounting the likelihood of completely parallel evolution in the plant and animal kingdoms, and in their major branches, we are led to conclude that, long before significant specialization, there existed in the waters of the earth various primeval forms of life which were endowed with representatives of most of, if not all, the important biological processes characterizing living things as we know them today. Although it is unlikely that we shall ever have more than opinions regarding the origin of life, it does seem possible to approach, experimentally, the nature of the *speciation* which began when such primeval cells had become established. This approach must involve a backward extrapolation of the information we can obtain on the chemical and genetic factors in organisms chosen from our modern environment.

Before examining for the reader the aspects of the mechanism of evolution that have been particularly illuminated by recent advances in biology and chemistry, it has been necessary to outline, in a broad sort of way, some of the basic fundamentals of evolution and the specific sciences, particularly genetics, that have contributed so essentially to its understanding. In the opening chapter, therefore, I have collected and rephrased some gleanings from the massive literature of morphological evolution to serve as a background for what follows. In several subsequent chapters is presented further preparatory material dealing with classical and contemporary genetics and with the basic facts of protein structure. Finally, after some discussion of the rapidly expanding body of knowledge relating structure to function in biological systems, I have considered a few aspects of natural selection in evolution which suggest themselves as a result of contemporary research, as well as some experimental approaches at the molecular level.

This book was written for pleasure, with the desire for self-enlightenment as the major stimulus. Since I cannot help but feel that everyone in science must be interested in the evolutionary process as the central theme of biology, I have listed a number of the original articles and books which contributed to the subject matter of this book.

I am greatly indebted to many of my friends and colleagues, including Dr. W. F. Harrington, Dr. Daniel Steinberg, Dr. W. R. Carroll, Dr. E. D. Korn, and Dr. W. D. Dreyer, who have read and helped improve various chapters of this book. I should also like to express my gratefulness to Dr. Bruce Ames for his patient help in connection with some of the discussions of genetic subjects. My special thanks are due Professor John T. Edsall of Harvard University and Dr. Michael Sela of the Weizmann Institute of Science, Rehovoth, Israel, who have read the entire manuscript and whose suggestions have been invaluable in the avoidance of error and in the improvement of style and organization. Finally, I should like to thank my wife, Florence Anfinsen, for the cheerful and understanding support she gave to a frequently rather morose husband.

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Bethesda, Maryland
May 1959

GROUND RULES FOR THE READER

A prospectus of this book was circulated to a number of experts by the publisher before the actual job of writing was begun. The opinions received have been very helpful in establishing what I hope is the proper slant. One opinion, in particular, expressed a point of view so similar to my own that I have asked its author, Dr. William Stein, of the Rockefeller Institute for Medical Research, for permission to reproduce it here.

It has always seemed to me, and I may be wrong in this, that when an expert communicates with the relatively non-expert, he has a responsibility to stay pretty close to the facts. An expert can speculate to other experts without scruple. They have the equipment to meet him on his own grounds, evaluate the evidence and accept or reject the speculation as they choose. The non-expert has no such basis for evaluation. He has to accept relatively uncritically what the expert tells him, and hypothesis and fact soon become confused in his mind. A plausible speculation—and the speculations of the true expert are always plausible—can soon masquerade successfully as gospel. In the present state of our ignorance, I would regard this as unfortunate. It would seem to me that a book such as this one should aim to stimulate thought and experiment among practicing scientists, and should not lull the uninitiated into thinking that we understand more than we do.

We shall deal, in this book, with many contemporary hypotheses, some of which are far from general acceptance. Consequently, I would like to emphasize two points of caution to the reader. First, simple examples have purposely been chosen to illustrate the presentation of subjects which in fact are sometimes complicated by exceptions and inconsistencies. Second, it will be apparent that the author, like anyone else, has occasionally taken sides.

CONTENTS

chapter 1

THE TIME SCALE AND SOME EVOLUTIONARY PRINCIPLES

To most of us, paleontology is the name of a sort of genteel outdoor science concerned with the collection and gross description of old bones and hardened mud blocks containing preserved animal tracks. To the paleontologist and, for that matter, to any novice who has had the good fortune to pass through what might be called the "Darwin-to-Simpson reading stage," no definition could be further from the truth. Just as history, to the historian, is alive and a part of the continuing pageant of human experience, so is the study of the life of the past a living science to its devotees.

The study of fossils cannot tell us a great deal about the natural forces that shape the evolutionary process, but it does furnish us with guidelines for the consideration of information derived from other sciences. As G. S. Carter[1] has put it, "The part of paleontology in the study of evolutionary theory resembles that of natural selection in the process of evolution; it serves to remove the inefficient but cannot itself initiate." It is clear that we can, and should, present only the most superficial survey of the fossil record and its interpre-

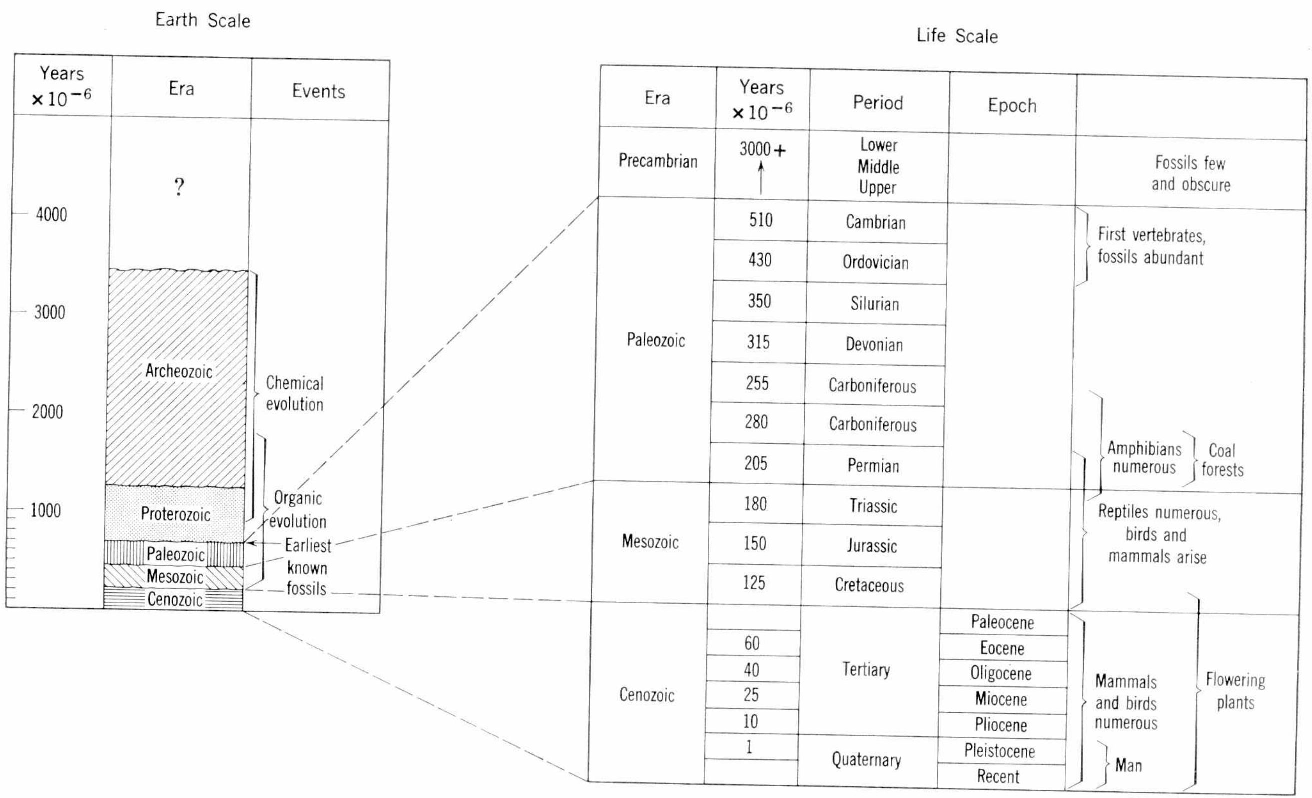

Figure 1. Time scales for the earth and for life on the earth.

tation in the present volume. For our purposes here we need only arrive at some general appreciation of the arbitrary divisions of geological time and outline the phylogenetic relationships that exist between the various living and extinct forms of life.

Measurements of the extent of decay of long-lived radioactive elements in the rock strata of the earth's crust enable us to make reasonable estimates of the ages of various strata. Utilizing such data as check points, but relying mostly on time estimates arrived at by classical geological methods, the paleontologist can arrange the fossilized remnants of life in a consecutive order with reasonable accuracy. He can also, in many cases, make certain deductions concerning the relation of specific upheavals and rearrangements of the earth's surface to the changing patterns in the nature and distribution of life as it was in the past.

For the purposes of those interested in the earth sciences, time may be expressed perfectly well on a linear scale, as shown on the left of Figure 1. Such a scale serves to emphasize the relatively small fraction of global time during which life has existed on the earth. The biologist is, however, more naturally preoccupied with "protoplasmic" time and must magnify the portion of the time scale that has to do with living things. The right half of Figure 1 is more useful to the biologist and lists some of the landmarks in evolution, assigned to their proper paleontological time period.

The earliest fossils that occur in any abundance may be assigned to the Cambrian and Ordovician periods and include a large proportion of the basic types of aquatic animals and the possible beginnings of the vertebrates. The record for the Pre-Cambrian period is extremely sparse and is represented mostly by the relatively primitive plants, the algae. At the end of the Pre-Cambrian, most of the invertebrate phyla were relatively well differentiated, although the absence in most instances of structural elements that could survive as fossils makes the reconstruction of their phylogenetic tree somewhat controversial. One scheme is presented in Figure 2. This arrangement of the phyla, which includes the higher vertebrate forms for comparison is, according to its author, L. H. Hyman, not to be taken literally but is only suggestive. It is based on an arrangement of animals in order of structural complexity, without separation of the allied phyla. The bacteria, yeasts, etc., are not shown, for they branched off at some early point in time when the momentous biological accident occurred which led to the establishment of plant and animal kingdoms.

Another way of looking at the phyla is shown in Figure 3, taken

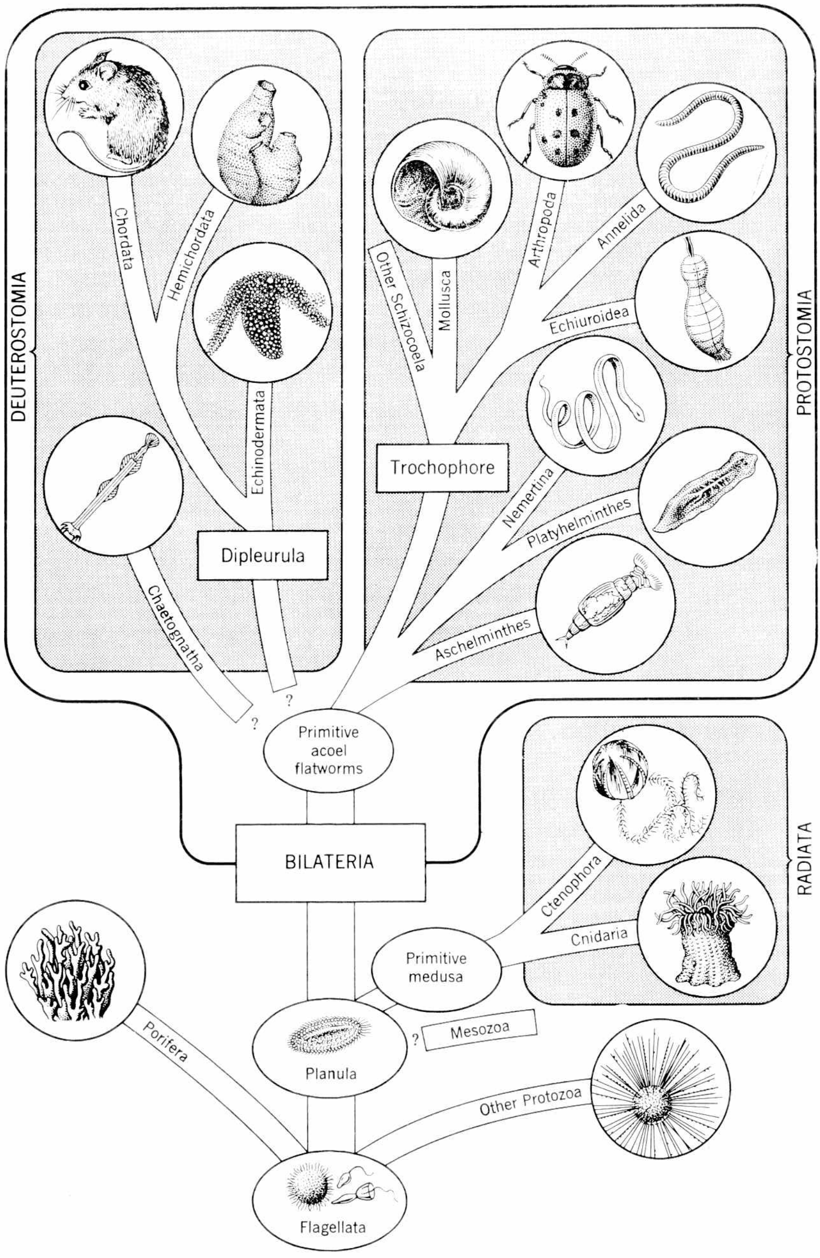

Figure 2. Relationships of the phyla of the animal kingdom. The arrangement here is based on the scheme given by L. H. Hyman in *The Invertebrates*, volume 1, McGraw-Hill Book Company, p. 38, 1940.