The Experimental Basis of Modern Biology

J. A. RAMSAY

THE EXPERIMENTAL BASIS OF MODERN BIOLOGY

BY

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PREFACE

Of all the features of this book there is probably none which so openly invites criticism as does the title. A glance through the chapter headings can hardly fail to provoke the comment: is this, then, the sum total of modern biology? is it implied that physiology, ecology, the study of evolution, are worked-out subjects, of no further interest, shouldered aside in the press of new ideas? I confess, lamely, that the title is not a good one, but it is the best I can think of. I might, with stricter attention to accuracy, have called the book 'The Observational and Experimental Basis of Certain Aspects of Modern Biology', or better still '... of Those Aspects of Modern Biology which are Currently Written Up in the Popular Scientific Press'. One can be too pernickety about these things. I do not think that the precise title matters very much; no title could be concise and at the same time convey what I would wish it to convey. But I think it does matter that I should try to explain how the book came to be written and what it hopes to achieve.

Many students, with time and interest to spare, are encouraged to engage in fieldwork to supplement the formal courses given at school and university. But the interests of others lie elsewhere, in the direction of cell biology, and for them a literature exists which presents the results of recent advances in a very appealing way. Such boys find themselves in a situation where on the one hand they learn in school a traditional biology which is still preoccupied with the names of the arteries of the frog, while on the other hand the colourful pages of the *Scientific American* invite them to participate in discovering 'the secret of life'.

I was for many years an examiner for Cambridge college entrance scholarships. It has often been made out that the examinations for college entrance scholarships require a much wider factual knowledge than is specified in the syllabuses and are therefore an important contributory factor in the intensive specialisation at schools, which is so loudly deplored. In view of this it was our policy, in the group of colleges for which I examined, to ensure that the questions we set were fully covered by the syllabuses. Having in mind the large number of hours allotted to the anatomy and physiology of the mammal, I once set a question:

'Describe how a horse converts a meal of oats into work'. I was taken aback, when I came to read the answers, to find that a majority of the candidates, after a few perfunctory remarks about digestion, plunged into the details of anaerobic glycolysis and the Krebs cycle, covering pages with the structural formulae of glyceraldehyde 3-phosphate, *cis*-aconitic acid and what have you. In cases where I was able to follow this up I asked these candidates if they could tell me anything about how the Krebs cycle was discovered, or anything about the methods which were used to investigate these matters. Not a single one of them had any idea. All the elaborate chemical relationships, so painstakingly memorised, had for them no observational basis whatsoever. Since that time I have made a point of putting the same sort of questions to freshmen who have claimed an interest in modern biology. It is always the same story. Everybody knows that the information coded in DNA is passed to RNA in the ribosomes where it acts as a template, etc. But if you ask what evidence there is that DNA has anything to do with inheritance they are at a loss and probably end up by saying that it is present on the chromosomes or something equally inadequate.

I find this all rather disturbing. In the education of scientists we rightly insist that the principles of science rest upon observation and experiment. It is not enough merely to know that there is a mechanical equivalent of heat; we expect our students to know how this equivalence was measured and established. Popular science does not set out to be educative in the true scientific sense; it is written for the information and entertainment of those who want to know what science is about. To be popular it must be easy to read; basic facts, generalisations and working hypotheses, even the latest outrageous speculations, all have to be streamlined into a convincing whole. This is especially true of what is now being written about recent advances in biology. There is much that has been established upon an experimental basis and amply confirmed. There is also a very great deal which is as yet no more than plausible speculation. But from reading some articles it is often hard to know where the one leaves off and the other begins.

What is it that we require of a scientific education that is not provided by a course of popular science? First and foremost we require that it will develop in the student a critical attitude to his subject. We expect the student, as he matures, to appreciate that many of the so-called facts of science are really inferences based upon measurements made with a particular kind of apparatus under specified conditions, that the measurements are liable to error and that the inferences may be compromised by other observations in other fields. As he approaches the frontiers of knowledge he finds the issues are seldom clear cut and the evidence is incomplete and often contradictory; he has to learn to weigh each piece of evidence against the others, and to judge its weight he has to take account of the circumstances under which it was obtained.

I seem to be getting myself into the absurd position of saying that all popular science is pernicious and that you can only approach modern biology by reading the original papers. To discourage the reading of popular science would be unthinkable. Modern biology is wildly exciting and lively young minds are just not going to be told that they must work steadily through traditional biology and put off modern biology to their third year at university. And they are quite right. There is nothing about modern biology which makes it unsuitable for discussion at an elementary level and nothing about its presentation as popular science which cannot be made wholesome with a pinch of salt. But we cannot inculcate a proper scientific attitude of mind merely by flitting from one bright idea to the next. There must be some discipline —some recourse to the original observations and how they were made, some discussion of the arguments, some appraisal of the interpretation.

What I have set out to do in this book is to examine some of the recent advances in biology and to test the strength of the evidence upon which our present conceptions rest. It has also been my aim to provide something of a bridge between school science and popular science. I have assumed that the book is to be read by students who already have a basic knowledge of physics, chemistry and biology, such as is required for the British General Certificate of Education, Scholarship Level, and similar examinations elsewhere. I have not presumed knowledge of any principles not included in the 'S' level syllabus and, where it is necessary to go further in describing modern research methods, as in discussing the resolution of microscopes, oxidation-reduction potentials and other topics, I have tried to introduce these as extensions of the syllabus. If the student has already encountered the diffraction of light by a grating it should be possible, without having to write at excessive length, to convey to him the manner in which the same principles apply in X-ray diffraction, the nature of the information so obtained and how this information can be combined with information from other sources in working out the structure of things like DNA. In pursuit of this policy my problem has been to tell the truth and nothing but the truth but not the whole truth—and at the same time to avoid statements which are dangerously misleading.†

I must also make it clear that I have not tried to write a textbook of cell biology. I have not tried to give a balanced treatment of what should be included in this field, but instead I have chosen certain parts of the field, those which seemed best to lend themselves to my purposes, for discussion at greater length than could be attempted in a balanced textbook. In making this selection I have been guided by my own estimate of the educative content of the subject matter and the possibility of keeping the treatment at an elementary level; for example, I decided not to include nerve and muscle because it did not seem that they could be usefully discussed except at a biophysical level which was more difficult than I thought desirable. I also decided to keep the details of organic chemistry out of the text as far as possible, and to refer to compounds by name, providing their structural formulae in an appendix.

Being myself no more than an elementary student of the subjects with which this book is concerned, I have had perforce to seek the help of various friends and colleagues who can speak with authority. The book has been read in whole or in part by Dr J. W. L. Beament, Dr M. J. P. Canny, Dr R. R. A. Coombs, Dr A. V. Grimstone, Dr B. S. Hartley, Dr R. Hill, Dr J. C. Kendrew, Dr D. G. I. Kingston, Dr K. E. Machin, Dr E. A. C. MacRobbie, Dr J. A. Pateman, Dr L. E. R. Picken, Dr G. Salt and Dr A. O. W. Stretton, to whom my gratitude is due. With their kind help many glaring errors were removed from earlier drafts. I also solicited and received from them many suggestions as to approach and treatment. Most of these suggestions I was only too willing to accept, but there were some issues on which I was resolved to persist in the line I had chosen to follow. I have to say this so as to make it clear that those whose generous help I have just acknowledged do not necessarily endorse everything I have written.

J. A. R.

Queens' College, Cambridge
May, 1963

† The following quotations are examples of what I would describe as dangerously misleading:

'The second law states that there are two forms of energy: "free", or useful, energy; and entropy, or useless or degraded energy.'

'Fibers of these macromolecules can be prepared and an X-ray picture of them can be obtained in a manner based on principles similar to those used to obtain an X-ray picture of the human hand.'

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CONTENTS

PART III. INHERITANCE

INTRODUCTION

1

ORGANISMS AND CELLS

We recognise that living matter differs from non-living matter in its capacity for growth and reproduction. A crystal can grow, but only by adding to itself more of the ready-made units of which its structure is built up. The growth of living matter differs significantly from the growth of crystals in that living matter grows by taking into itself materials of one kind and fashioning them into another kind which it then adds to its organised structure. There is yet another distinction. Given suitable conditions there is no theoretical limit to the size to which a crystal can grow; but living matter grows only to a size which is characteristic of the type of organism to which it belongs, after which the organism reproduces itself and thereby growth results in an increase in the number of organisms. The idea of an organism is bound up with this characteristic natural discontinuity of living matter, which exists not as an indefinite continuum but as lumps of various sizes and shapes, belonging to recognisable categories, such as those which in higher organisms we call species.

Let us first consider the size of organisms. Fig. 1.1 sets out the size range of organisms with a few physical points of reference at the lower end of the scale. The range is in fact so very great that we have to use a logarithmic scale to display it. The largest known animal, the blue whale, is about 30 metres long, while one of the smallest known organisms, the poliomyelitis virus, is about 300 Å† in diameter. The blue whale is about one thousand million times—9 orders of magnitude—longer than the virus, and organisms of all sizes lie between these two extremes.

We may next ask ourselves whether we can point to any factors which may set upper and lower limits to the possible size of an organism. It seems likely that the upper limit is set by the strengths of the materials of which organisms are made. For bodies of the same shape the area is proportional to the square of the length and the weight is proportional to the cube of the length. If we scale up a horse by a factor of 2 in length we scale up its weight by a factor of 8 and we scale up the area

† $1\ \mu = 10^{-3}$ mm, $1\ m\mu = 10^{-3}\ \mu$, 1 Å $= 10^{-4}\ \mu$.

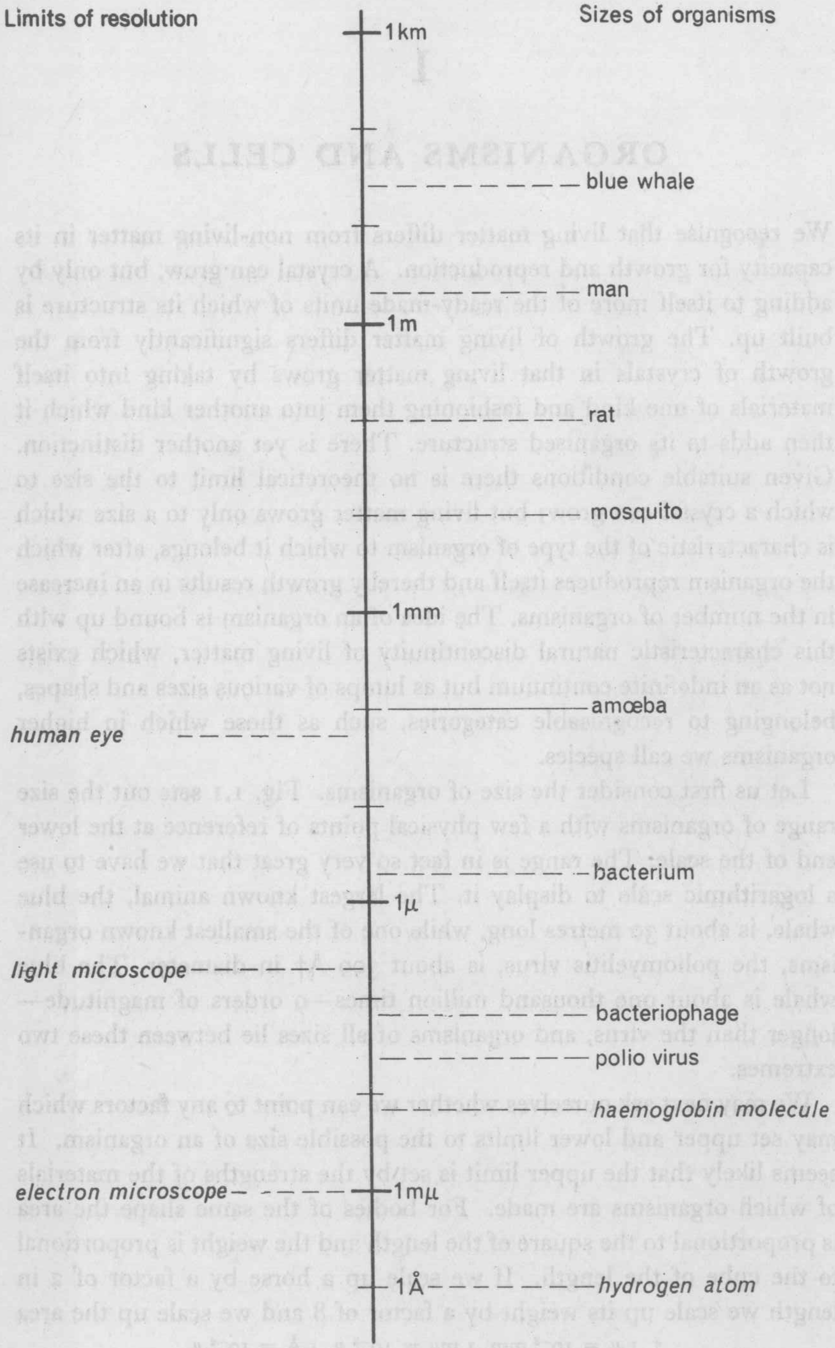

Fig. 1.1. To illustrate the size range of organisms.

of its hoof by a factor of 4; thus the weight borne per unit area of hoof is scaled up by a factor of 2. But we are not able to scale up the strength of the materials of which the hoof is made. Obviously, if we continue to scale up the length of the horse there will come a time when the hoof is unable to bear the weight applied to it. It is not possible to state in any precise way how these considerations may affect the form of large terrestrial animals, but in view of the susceptibility of horses to injury when galloped on hard surfaces we are at liberty to suppose that Nature is working to fairly narrow margins of safety. Any marked increase in size would almost certainly entail some sacrifice of speed and a modification of the form of the body in the direction of that of the elephant. In the case of the whale, although it is less affected by gravity by being water-borne, one can see that there must be some limit to size here too, imposed by mechanical considerations.

At the lower end of the scale we observe that the size of the smallest organisms approaches the size of protein molecules. We know that the chemical processes which go on in living organisms require enzymes and that all enzymes are proteins. It is therefore easy to appreciate that a small virus can accommodate only a limited number of protein molecules and that on this account the complexity of its metabolic processes may be drastically restricted. Indeed this seems to be the case. Viruses cannot grow and reproduce in isolation but only within the cells of other organisms, and as we shall see later they are only able to grow and reproduce by taking over the metabolic machinery of the host cell and directing its operations to their own ends.

By contrast with the great size range of organisms, the size range of cells is very small. The largest single cell produced in the animal body is the yolk of a bird's egg, say 5 cm in diameter in the case of the ostrich, and the smallest we may take as the spermatozoon, say 5 μ excluding the tail. This represents only 4 orders of magnitude, but this size range is quite unrepresentative of non-reproductive cells. Typical cells from the bodies of plants and animals are all of the same order of magnitude, about 20 μ across.

Cells were so named by Robert Hooke who built the first compound microscope. In 1685 he described how he had cut a thin slice of cork with a sharp pen knife and how, placing it under his microscope, he had observed that it was divided up into minute compartments which he called cells. Little more was heard of cells for about 150 years, no doubt because in those days one had to make one's own microscope and it was not every investigator who had the necessary skill and enthusiasm. By the beginning of the nineteenth century one could have a microscope made by a professional instrument maker, and as these early instruments became available Hooke's observations were soon extended. Cells were seen and described in tissues other than cork, and it was realised that they were not empty but contained a viscid substance to which Purkinje gave the name 'protoplasm'. It was also observed that within each cell there was generally a visibly differentiated body, the nucleus. In retrospect it is clear that in the early years of the nineteenth century the significance of cellular organisation was beginning to impress itself on the minds of a great many microscopists; and in 1839 Schleiden and Schwann, independently, proclaimed the generalisation that the bodies of plants and animals were composed of cells. To this was later added the idea of cell lineage by Virchow in 1858: *omnis cellula e cellula*—cells arise only from pre-existing cells.

In this way there emerged one of the most important generalisations in biological science, particularly important in its implication that all the cells of multicellular organisms are basically the same, however much they may be specialised for different functions. All modern work has confirmed and extended this conception of the essential similarity of the structural and functional endowment of unspecialised cells from multicellular organisms of all types.

Unfortunately, there were those who were not content with these substantial gains, and in their hands the cell theory, or 'Cell Doctrine' as it was sometimes unhappily called, gathered unto itself a certain mystique, and from it there grew the conception of the cell as the unit of life.

There is a certain amusement to be had from contemplation of the difficulties which biologists have got themselves into by their preoccupation with units and definitions, and in the idea of the cell as the unit of life we have an excellent example of man being trapped in a pit of his own digging. Once the cell concept had been raised to this higher level and extended to organisms other than multicellular plants and animals all sorts of awkward questions presented themselves to be answered. What are the essential attributes of a cell—does it have to have a nucleus, for example? If so, bacteria are not cells, yet they would appear to be units of life. What is a unit of life? Many would reply that the organism—the rabbit, the oak-tree, the amoeba—is the unit of life. Yet even so simple a conception as this runs into difficulties.

Among the lower organisms there is a group known as the slime