Research in Biology & Medicine - Ingle

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Principles of Research in Biology and Medicine

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TO

DAVID, ANN AND JANE

Preface

THE PREPARATION of this book has been an exercise in self-expression about those problems which I find entertaining and consider to be commonly neglected in scientific education. Important gaps remain between what I have said and all that should be said to students who are preparing for or are beginning research in macrobiology and medicine; they are the audience to whom the book is directed. Most of the discussion of principles is elementary, but some difficult and controversial concepts are included here and there to challenge the reader to further inquiry. Principles of research are taught best in the laboratory, but many individuals live, work and die without achieving from laboratory experience alone an appreciation of how difficult it is to establish a fact.

Some of the information and a few of the concepts presented in this book will not be found elsewhere, but it is not a complete treatise and should serve as an introduction to principles or as a supplement to the study of a more extensive text. The investigator should be a student of the philosophy and the principles of research throughout his life. It is especially important to know statistical methods, which are of increasing importance in the design of experiments as well as in the interpretation of data. Statistical methods are not described in this book, although there is frequent reference to them. Self-teaching of statistics is seldom adequate.

With the aid of Lewis Carroll and the immortal Alice, I have emphasized the foibles of the scientist and the difficulties to be recognized in the laboratory and the restrictions to be placed upon ideas. Knowledge of pitfalls is important, but this alone will not guide the student to success. I wish that I could say more on the positive side to aid the student who will search this and other books in vain to learn how to deal with other than cut-and-dried problems. Although there are general principles of experimental design and interpretation of data that can be taught, there are no cook-book plans which permit the skilled but unimaginative technician to deal successfully with the unknown. The scientist must be adaptive and creative. Experience and varying amounts of individualized guidance are required to feed the growth of these qualities. It is no more possible to teach a scientist how to make a great discovery than it is possible to teach a poet how to write a great poem, an artist to paint a great picture, or a composer to write a great symphony. Creative men, including the intuitive researcher and the great diagnostician, are usually unable to verbalize the secrets of their artistry.

There is risk that a review of the limitations of mind and emphasis upon the problems of inquiry and requirements for proof will dismay some students. Attention to the contemporary history of science should reassure those who have the basic qualities needed to do well in research. In my lifetime science has changed the physical face of civilization. The pock-marked faces, bowed legs and pendulous goiters seen frequently when I was a boy have almost disappeared. Once typhoid and diphtheria were likely to visit any home, and either disease carried greater risk than a sentence of death by the average court today. Now many infectious diseases can be prevented or treated effectively. Science does get results. Surely, at some future time clever minds will bring circulatory diseases, cancer and mental diseases under control. And if the life sciences learn how to eliminate the physical diseases of man, there remains the challenge to deal with crime, greed and hate and to help people everywhere use the new tools and opportunities. There is still time for students who have not yet entered science to be pioneers.

A number of my colleagues have read parts or all of this book in manuscript and have offered invaluable suggestions. I have imposed to the greatest extent upon the following: Elizabeth Munger, Maurice S. Goldstein, Leonard J. Savage, Maurice E.

Krahl, Ira G. Wool, Phillip E. Gertler, Estelle R. Ramey, Nicolas Rashevsky, Donald W. Fiske, John R. Platt, Guy Williams-Ashman, Irving B. Fritz, Clifford S. Patlak and Donald Mainland. The weaknesses of the book did not escape the attention of those who read it in manuscript, and failure to meet some of the criticisms represents my own foibles. For example, several readers have objected to the listing of the assumptions of science in Chapter 1 and to the listing of common fallacies in Chapter 5 without detailed discussion of each. In searching the literature on principles of research, I found only incomplete lists of basic assumptions and of fallacies, none matching another. It became personally important to me to prepare more extensive lists than can be found elsewhere. Some points in each list are self-evident. Others could not be analyzed by me without adding confusion. I have attempted to discuss some concepts in other sections of the book. Also, on the basis of a sample of opinions about the manuscript, it seems probable that some readers will not enjoy my use of either Father Brown or Alice. To them I apologize for yielding to the appeal that whimsey and fantasy have for me.

The preparation of this little book has been an exercise in learning as well as in self-expression. I hope to have the privilege of continuing to learn from constructive criticisms offered by readers.

Prologue

ALL METHODS of inquiry employ logic and seek insight, the success of which is determined by information, perspective, and powers of cerebration. Some of the world's favorite investigators have existed only in fantasy—heroes of detective fiction. There is Hercule Poirot, he of the enormous mustache, who accepts a challenge to "the little grey cells" with the comment: "It makes one furiously to think." And there are the stories of G. K. Chesterton. Chesterton was a master of paradox, none more striking than the person of his detective hero, Father Brown. Chesterton once described Father Brown at a distance as a round dot which grew larger as it approached but did not change in shape. Above is a sketch of Father Brown, who does not resemble any other great detective of fact or fiction, but whose deductive powers qualify him to sit by the side of the great Holmes himself.

The setting of the story, "The Pursuit of Mr. Blue," was a little resort town on the coast of England. Here Mr. Muggleton, a private detective, was presently sad, for a client had been murdered despite the fact that Mr. Muggleton had been engaged to prevent the anticipated crime. The client was a wealthy man whom Mr. Muggleton had never seen but from whom he had received a letter stating that a cousin, a ne'er-do-well scoundrel, had threatened his life. Mr. Muggleton was instructed to meet his client in a small circular pavilion at the end of a pier, over the water. The detective entered the little building at the appointed time and was promptly locked in.

There was one small, round window in the pavilion. Mr. Muggleton saw a distinguished-looking, well-dressed man circle the building, then there appeared an unshaven, sinister figure wearing a coarse woolen scarf, and the two became pursued and pursuer. Three times the desperately running figures passed the helpless observer at the little window. Then there was a shot and a splash, and all was quiet until the pavilion was opened. Mr. Muggleton gave the alarm and a description of the man with the scarf, who was nowhere to be found. It was judged that he could not have passed the gates of the pier without being seen and he could not have escaped by the sea, for the waves were high. The search widened without success. Since the details were such as to make escape seem impossible, the mystery was described to Father Brown. It was deduced by Father Brown that the cause-and-effect relationships were not as judged by Mr. Muggleton. The unshaven man with the scarf was not the murderer; it was he who had fled unsuccessfully for his life. The better-dressed murderer, who had been sought only as a corpse, had made good his escape. This hypothesis was confirmed when the body of the victim was washed up out of the sea.

At this point we will leave Father Brown, Mr. Muggleton, the corpse and the murderer, who was hung, and turn to the field of science and inductive reasoning, where also cause-and-effect relationships can be confused by limited perspective.

The story " The Pursuit of Mr. Blue" is from the following book: Chesterton, G. K.: The Scandal of Father Brown, New York, Dodd, Mead & Co., 1943.

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Nature and Nature's laws lay hid in night.
God said: "Let Newton be" and all was light.
—POPE

It did not last. The Devil, shouting "Ho!
Let Einstein be," restored the status quo.
—SQUIRE

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Introduction

THIS INTRODUCTORY CHAPTER presents in outline form some definitions of the aims and the methods of science and a list of the basic assumptions of science which have guided research in biology and medicine. There is no fixed number of aims, methods and assumptions of science. Simple definitions of the sort which follow are likely to lose some of the information associated with the concepts which they represent. There is reason to debate these and other generalizations and to reflect upon the more than occasional inadequacy of words as symbols of information about science. Some of the basic assumptions of science will be discussed in greater detail in subsequent chapters.

THE GENERAL AIMS OF SCIENCE

1. To understand natural phenomena.
2. To predict and control.
3. Enjoyment of inquiry.

THE METHODS OF SCIENCE

1. **Observation.** The accumulation of information by the scientific method requires repeated observation by one observer and independent confirmation by others.

2. **Experimentation.** The experimental method distinguishes science from all other forms of inquiry, although it shares with

them trial, error and chance success. This method has not been applied successfully to all problems of science. It is especially difficult to study the causes of past events which are unlike events that can be made to occur in the present.

A. Dissection and Analysis. By surgical, chemical and physical methods, the experimenter may seek to reduce the whole to its parts and to study the behavior and the properties of the parts in isolated systems. When man deals with living things, he finds a physical barrier to information at the body surface, the cell wall, the mitochondrial membrane, the endoplasmic reticulum, the Palade granules, the nuclear surface, etc. In order to study the functional units at each lower level of organization, it is necessary to destroy structures and to alter the environment within which the unit functions.

B. Synthesis.

(a) The synthesis of a chemical system is a final step in the proof of the identity of a system or a substance isolated from natural sources.

(b) In recognition of the fact that the whole is the reality and that its separation into parts may create artifacts which do not exist naturally in nature, the experimenter may study a system at several levels of disorganization and, when possible, test upon the whole system concepts based upon isolated bits of information about its parts. Synthesis is not a mere summation but must be based upon knowledge of organization.

C. The Controlled Experiment. The method is to change systematically certain conditions of the experiment and to note changes in results while all other conditions are kept constant or randomized. The objective is to ascertain the effect of the independent variable.

When the experimenter cannot manipulate the variables, he may, as in astronomy, take advantage of naturally occurring changes to make appropriate time-sampling measurements. Some of the most elegant experiments of science and some of the most highly developed forms of inference are based on this procedure.

3. **Reasoning.** The development and the communication of ideas are important processes of science and are basic to its progress. Science cannot be equated to measurement, although many contemporary scientists behave as though it can. For example, the editorial policies of many scientific journals support the publication of data and exclude the communication of ideas.

A. Logic. Inductive reasoning is a principal method of science, but deductive reasoning may be of use chiefly when there is a well-developed body of theory to work from; historically, deductive reason has been of occasional use even when the body of information was small. The science of mathematics is a highly developed application of logic. The use of statistical arithmetic permits both logical analysis of data into factors and synthesis into more comprehensive concepts.

B. Intuitive Reasoning. Only a few ideas which represent creative thinking are derived by the conscious application of the processes of logic. Logic is more often applied in the proof of the idea after it has been formed. The individual is usually unable to verbalize the steps by which the concept developed. The idea may appear suddenly, and the individual may report that he has no conscious recall of its genesis. It is possible that the neurologic basis of intuitive reasoning is similar to or identical with that of logical reasoning, i.e., in each case the brain may function somewhat as an electronic calculator having built-in logic. But from the standpoint of either the behaviorist or the introspectionist, intuitive reasoning is a different phenomenon from the conscious application of logic. In this area of creativity, basic to the sciences as well as the arts, control is largely lacking.

FUNCTIONS OF LABORATORY AND STATISTICAL METHODS

1. To acquire information.

2. To define the restrictions which are imposed upon ideas (hypotheses). The idea or hypothesis is basic to all progress in

science, although most hypotheses are invalid. The application of the principles of research and the scientific method serve to test the validity of ideas.

3. To permit guarded extrapolations from experimental or observational data. Generalization is the essence of science.

BASIC ASSUMPTIONS OF SCIENCE

1. **Self-evident Assumptions.** Certain propositions and axioms are not independently testable but are regarded by the scientist as self-evident and necessary for the acceptance of the experimental method as a form of inquiry. These and all other assumptions have been questioned at one time or another in the history of philosophical thought.

A. Own Continued Personal Existence.

B. All knowledge is subjective. The more specific assumption that *all information comes through the senses* must be qualified by noting inborn behavior (instincts) relating to physiologic needs and drives; insight into relationships not yet experienced but based upon elements of information acquired by experience; and, the possibility of extrasensory perception as claimed by some scientists.

> It is the mind that sees; the outward eyes
> Present the object, but the mind descries. —

C. Reality of the External World. The external world exists independently of the observer.

D. The universe is orderly. All events take place in accordance with natural laws. Some degree of uncertainty, however slight, remains in all phenomena, and natural laws are presently regarded as statistical.

E. The human mind is capable of comprehending natural laws. Statements of natural laws represent agreement by observers on summaries of information about the order of the universe. Since natural laws are not perfectly known, they are subject to revision in accord with new information.

2. **Tenable Assumptions.** There is a second order of assump-

tions, based in part upon experience with the universe, which are useful in science although they are not self-evident or given *a priori*. These assumptions concern the structure of natural laws and are subjects of some debate.

A. UNIFORMITY OF NATURE. If conditions are the same, the results will be the same. Since each event and pattern of conditions is probably unique, it is assumed that if conditions are similar the results will be similar.

B. CONTIGUITY OF NATURE. All phenomena are related by certain basic properties and natural laws. A closely related assumption is that of *spatiotemporal contiguity;* causal connection between two events requires that they be contiguous or that they be connected by contiguous events. This concept is meaningful when applied in the man-sized world. The physicist must qualify the concept when he deals with quantum mechanics.

C. PRINCIPLE OF CAUSALITY. Each individual event and condition has necessary antecedent and concomitant events and conditions. The concept that an event cannot occur without a cause is known as *the principle of sufficient reason*. This principle is not regarded as necessary by all philosophers and scientists. The view held in this book is that causality is a useful assumption for scientists in the fields of biology and medicine.

D. MEASURABILITY OF THE EXTERNAL WORLD. There are true values of the quantities measured, although the observed values are approximations. The student may be interested in studying this assumption in relation to the principle of operationalism, which holds that a concept can be defined only in terms of the set of operations assigned to assess it.

E. THE HEISENBERG UNCERTAINTY PRINCIPLE. It is not possible to measure the position and the velocity of a particle accurately at the same time; whichever one of them we try to measure, the process effects the other, and indeterminacy remains in both. This principle represents a theoretical barrier to complete knowledge, not merely a practical limitation.