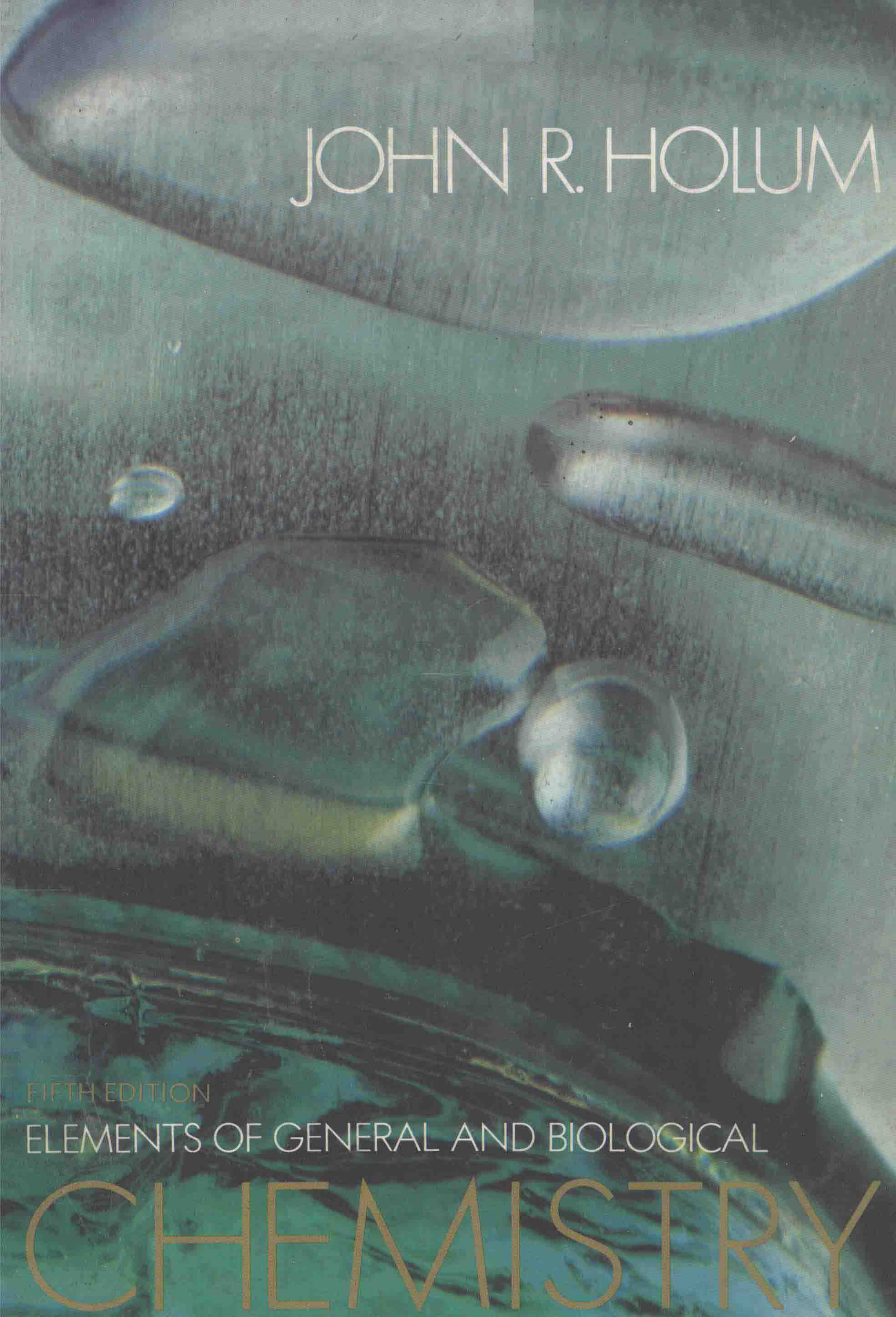

JOHN R. HOLUM

FIFTH EDITION

ELEMENTS OF GENERAL AND BIOLOGICAL CHEMISTRY

Elements of General and Biological Chemistry

AN INTRODUCTION TO THE MOLECULAR BASIS OF LIFE

FIFTH EDITION

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Preface
TO THE FIFTH EDITION

Two recent symposia sponsored by the American Chemical Society dwelt on the subject of chemistry for the allied health sciences. Participants both on the panels and in the audiences spoke of the impact of the ever-increasing sophistication of medicine on professionals in allied health care fields. From the physician to the physical therapist, from the nurse to the health education teacher, the swelling tide of new knowledge and skills makes clear that workers in these fields will never outgrow their need for new learning and continuing education.

Continuing education cannot be pursued without something to continue. It starts with the first courses, the formal, basic studies. These courses will not serve the long-term needs either of students or society if they do not deal as carefully with the basics as time and the entering levels of the students allow. The first encounter with chemistry by students in the allied health care fields must above all else supply a basic vocabulary of terms and principles that will last a lifetime even as they become modified by new discoveries. For some time I have served as the chairperson of a joint committee of hospital nursing administrators and nurses that oversees the standards of continuing education for nurses in the metropolitan area of Minneapolis and St. Paul. I have seen how the planners of seminars, institutes, workshops, and minicourses depend from time to time on topics and terms from chemistry. The text in chemistry for those in the allied health professions must therefore not only "cover" a variety of subjects, it must also define basic terms unambiguously and use them with consistent care. In preparing this new edition I have regarded that task as primary.

Not all possible topics and terms are equally important or relevant to these students. To guide myself in selecting topics and arranging them, I have continued to use the theme, the molecular basis of life. Over the years I have found it to work especially well in encouraging and motivating students who may at first be dubious about the importance of chemistry to their careers. They need no persuasion that life has a physiological and anatomical basis. At first they are skeptical about the molecular basis, but that doubt soon disappears in all but the least serious. In an article entitled "Providing Relevance in Chemistry for Nursing Students" (*Journal of Chemical Education,* September 1976, page 581), Professor Theodore H. D. Jones of the University of San Francisco wrote of the challenge in teaching introductory chemistry to nurses. He quickly brings home the need for chemistry by organizing his course around the kinds of clinical data most frequently consulted by a nurse. A clinical laboratory report on a patient's blood chemistry makes the point more dramatically than any number of words by the professor. Borrowing with permission Professor Jones' idea, I have given a new slant to the first chapter of this edition. Although I have not pursued it as tightly as Professor Jones does, most of the clinical entries of importance emerge one by one in succeeding chapters.

The principal changes made in moving from the previous edition to this one are as follows. Old Chapter 8 ("Nonmetallic Elements of the Biosphere") has been dropped. A little of its material has been put in other chapters where health problems caused by the environmental pollutants seemed best to fit. Old Chapter 12 ("Carbonyl Compounds") has been split into two chapters, one called "Aldehydes and Ketones" (Chapter 11) and another called "Carboxylic Acids and Derivatives" (Chapter 12). I found the old, combined chapter too long, and I am sure others did too. Chapter 2 ("The Nature of Matter: The Atomic Theory") has been redone to lay a better foundation for modern atomic theory. Our indebtedness to the Bohr theory is explained, but it is less prominently used than in earlier editions. Old Chapter 4 ("Moles, States of Matter, Chemical Energy") was completely rewritten and retitled "Chemical Reactions. Kinetic Theory." I have concluded, after years of struggle, that when time is short the best way to teach the mole concept is to start with definitions rather than work one's way up to definitions. At least it has worked for me recently. The unit called "Kinetic Theory" in the fourth chapter of this edition begins with a discussion of metabolism, heat, and the problem of managing the body's heat budget. Changes in state such as from liquid water to water vapor are important in that effort, and that provides the transition to the states of matter and their observable properties. With the properties of gases the emphasis is on the concept of pressure and partial pressure and their units. Other gas laws are surveyed, leading to a brief description of the model of an ideal gas and how it helps explain gas properties. I know of no single topic in chemistry that has acquired in recent times such importance to future nurses as the chemistry of respiration. This topic needs to be carefully developed, and we start that in Chapter 4. It continues in Chapter 6 with the properties of acids, bases, and salts in general and the carbonate system in particular. Buffers, so important in respiration, are explained in Chapter 7.

Few changes were made in the chapters on organic chemistry other than the splitting of old Chapter 12 described above. Material on organic chemicals in smog has been deleted. (The problems of carbon monoxide and ozone, however, are mentioned.) More is said about food additives than before.

The chapters on biochemistry begin with Chapter 13, "Carbohydrates," which opens with an overview of biochemistry, a suggestion of one professor that we survey at this place where we are about to go. Chapter 14 ("Lipids") now includes new material on biological membranes. Chapter 16, which contains a study of enzymes, now deals with the subject of isoenzymes because we now explain how electrophoresis is used in diagnosis. Clinical laboratories separate the isoenzymes of lactic dehydrogenase (LDH) in serum and tell if a patient had a heart attack or not, and how severe it was. The reverse side of the blood chemistry report sheet given in Figure 1 of the first chapter in the book is now shown. The use of glucose oxidase and peroxidase in test papers (e.g., Clinistix®) is explained in this chapter, too.

Chapter 17 emphasizes the chemistry of respiration. A number of applications to clinical situations are made, and the students see how data on pH, pCO_2, pO_2 and $[HCO_3^-]$ help in diagnosis and treatment. Anyone who might deal with emergency room cases eventually must learn these topics.

Chapter 18 has been rewritten partly to clarify the important point that glycolysis is not limited to anaerobic conditions. I continue to organize biochemical energetics in the order in which its segments "start up"—the need for ATP makes the respiratory chain go to work, which pulls the citric acid cycle into action, which draws on sources of acetyl coenzyme A, including glycolysis. Some people would prefer the reverse order, but I have stayed with what is more comfortable to me and what appears to be more comfortable to a number of others. Either order makes sense and the decision comes down to personal preference.

The discovery that perhaps most people suffering from adult-onset diabetes have nearly normal serum levels of insulin has kept the pot on the causes of diabetes stewing. I have tried to bring that topic up to date in this new edition.

The last chapter has been reduced in its coverage of all the ways of describing radiations. The curie, rad, rem, and half-life are retained. An entirely new entry is a discussion of radioimmunoassay, one of the most dramatic advances in diagnosis in recent years. Its development won for Rosalyn Yalow a share in the 1977 Nobel Prize in Medicine and Physiology.

Another feature new to this new edition is the inclusion of drill exercises within most chapters. Answers for all these are given at the end of the book.

As some readers may know, a longer version of this text is available called *Fundamentals of General, Organic and Biological Chemistry* (John Wiley, 1978). The major difference between the two texts is that the longer version has more chemistry and more applications to health care. This fifth edition would be the preferred text for a one-term course or a two-term course in which entering students have had no high school preparation in chemistry and in which there is not time for greater coverage.

Supplementary Material for Students and Teachers

What To Do for the Accompanying Laboratory. The laboratory manual, *Experiments in General, Organic and Biological Chemistry,* is available in its fifth edition together with a separate booklet that gives recipes for solutions, answers to questions, chemicals to purchase, and lists for each experiment. The longer version of this text also has a laboratory manual, and because it has several additional experiments, many of a quantitative nature, some who use the fifth edition of this book may wish to use the laboratory manual for the longer version. The title is *Experiments for Fundamentals of General, Organic and Biological Chemistry,* 1978, by John R. Holum and Ruth Denison (John Wiley).

Student Study Guide. This softcover book has been prepared to accompany the fifth edition. It includes many units of special help, particularly in solving mathematical problems. Each chapter has detailed learning objectives, and sample examinations with answers. Each chapter also has a glossary in which the terms appearing in boldface in the text are defined. The overall emphasis in the *Study Guide* is the mastery of topics and terms. The answers to about half of the end-of-chapter questions of the text appear in the *Study Guide*, many with notes and explanations.

Slide Masters for Overhead or Slide Projectors. Teachers who adopt this fifth edition may obtain from the publisher[1] without charge a set of $8\frac{1}{2} \times 11$ inch, black-and-white line drawings that duplicate a large number of the figures in this book, with particular attention given to the more complicated figures in the biochemistry chapters. These may be used to prepare slides.

Teachers' Manual. Teachers adopting the fifth edition of either the text or laboratory maual may obtain the *Teachers' Manual*. It includes the usual services.

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The continuing support of my wife Mary and my children, Liz, Ann and Kathryn, has been indispensible to these efforts. I have thanked them in many ways, and saying thanks in print is an added privilege.

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My typist, Mrs. Doris Berg, is a wizard at following looping arrows and making neat, clean copies from copy that would baffle most typists. My thanks for her diligent, careful, patient, and cheerful work.

Dr. Gary Hemphill, head of the Clinical Laboratories of Metropolitan Medical Center in Minneapolis, gave me generously of his time and expertise as I learned about radioimmunoassay and about trends in the use of enzymes in medical diagnosis. Dr. Arlin Gyberg of our Chemistry Department also helped me in these areas. I thank them both.

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A modern day guru once said that if you do not plan where you are going you are certain to wind up somewhere. Whether we consider a life in general or a course in particular, it is better to have goals and methods than not. In science, what disciplines our goals and methods, what keeps us from forever wandering in a haze, are measurements. With them, the haze may still persist longer than we like, but without them the haze is eternal.

Contents

chapter 1

Goals, Methods, and Measurements

The helping hand meets here a need that is urgent, yet simple. In more complicated crises of physical need, helping hands must be guided by skill and knowledge obtained by practice and study. Sometimes that knowledge is chemical, because the need wells up from the molecular basis of life, the overarching theme of this book. (Sylvia Johnson/Woodfin Camp.)

1.1 Caring for People

People yet alive remember the days when a pinprick could mean death. In the desperate anguish of that prospect a chemist once fed a red dye to his fevered daughter knowing that some infections are caused by bacteria, that bacteria absorb dyes, and that the dye did kill bacteria in mice. It worked. The fever disappeared overnight, and with that drama the sulfa drugs broke into human medicine.

Not too many decades ago a broken leg could mean an amputation, and without the benefit of anesthesia. Common childhood diseases brought families together at bedsides to watch helplessly as the crisis mounted, the temperature rose and then, if the fight had been successful, finally broke. The appearance of a single case of polio in a community meant instant cancellation of social events and the closure of swimming beaches. Children were kept at home as someone in this family or that died or was permanently crippled. A trip to the dentist meant fearsome encounters with slow speed drills, whining sounds, and the knuckle-whitening fear of sudden, skull-piercing pain. It wasn't that people didn't care. Their knowledge and skills had not yet reached today's level, but people cared deeply.

Caring for people and about people has been a powerful motive in the history of the health sciences. Some who cared were particularly curious about how we are put together, how we catch disease, how we are affected by various injuries, and how we get well. Building on the discoveries and inventions of those studies, other people have found great personal satisfaction in delivering the fruits of new knowledge to people in pain. No doubt you have been moved to participate in that work at least partly because you want to share in that satisfaction. It is a high calling, and society rightly sets high standards of excellence for those to whom it entrusts its health needs. The physician, nurse, medical technologist, histotechnologist, dietician, inhalation therapist, physical therapist, health education teacher—the list is much longer—all are now expected to operate at a higher level of sophistication than was possible when you were born. Moreover, advances in health care and in disease prevention will continue, and specialists who begin their education today will never end it. You will never outgrow your need for new learning. Society expects you to accept that, and you expect it from those who bring medical services to you and your loved ones.

The basic scientific vocabulary and the fundamental scientific principles needed for that continuing education are largely acquired during the courses you take at the entrance of your career. One of the important purposès of this book is to supply you with the terms and principles from chemistry that you will need not only for other courses but also for a lifetime of professional growth. We shall organize that study around one of the great insights into the human condition—all of life has a molecular basis.

1.2 The Molecular Basis of Life

Centuries before anyone believed in atoms and molecules, people could not help but notice that many different kinds of animals drank at the same water holes, breathed the same atmosphere, ate the same kinds of food, and delighted in the same salt licks. Ancient farmers knew that the droppings of animals could nourish the lives of plants. Animals could eat plants and grow. Some animals could eat weaker animals and grow. At some deep level of existence living things can exchange parts. The curious who looked at nature carefully found an astonishing unity to it all. In this course we shall go deep into the cell to its molecular level to learn of that unity and to see how that knowledge can make great differences in retaining health, preventing illness, and curing injury and disease. The selection and organization of every topic in this book have been made with the general theme in mind—the molecular basis of life.

1.3 Strategy

Although life has a molecular basis, the molecules of life are sometimes so complex that they numb the mind, at least at first glance. But the score of a Beethoven symphony, to a beginner, does the same thing. A third-grader, viewing the arithmetic homework of a fifth-grader, quietly despairs of the future. Beginners to any field of study, regardless of age, forget (or have yet to learn) that there are common ways of handling problems that seem so complex at the start. We look for relations, common features, and we get the most basic things straight from the beginning—definitions, symbols, scales, and the like.

We shall look at the complicated molecules of life as a mountain climber views a contour map. He does not try to commit it to memory. He uses his knowledge of a few signs and symbols with which any number of such maps can be read and interpreted. Complicated molecules also carry "map signs." Once we recognize them and see them in any complex molecule, we need not memorize the structure of the molecule. Yet we can still understand and possibly make intelligent predictions of the chemical behavior of the substance in this or that setting. These molecular "map signs" (functional groups) are best introduced among simple substances. That is why we have a few chapters that include acids, bases, and organic chemicals before we go too far into the molecular basis of life. The most basic principles in our study concern atomic and molecular structure, and we shall start with these in the next chapter.

1.4 Scientific Method

Think for a moment about the difference between these two questions. "Why do we get sick?" "How do we get sick?" They are different questions, although many ask one but mean the other. The "why?" question has led to little more than lengthy arguments and debates over the meaning of pain and suffering. Those are very important matters, but the arguments fostered very few practical cures except perhaps patience. The "how?" question, "How do we get sick?", asks an unarguably answerable question. The question demands observations and measurements rather than expressions of opinions.

The data gathered by this work attain worldwide acceptance the more they can be reproduced by independent observers conducting repeatable tests and measurements. Not everything that can be observed in nature down through history can be repeated, and science has known its greatest victories when it has realized this limitation. Science cannot answer all questions, but it has enjoyed spectacular success with those that begin with "how. . . ?"

Soon after putting some "how?" questions to nature, the scientist devises a hesitant, tentative answer called an **hypothesis.** A good hypothesis is not necessarily the correct one, although when first thought of it is believed to be quite true. A good hypothesis is one that draws out ideas for testing its worth. The scientist says, "Well, if this is true, then we ought to be able to observe the following in a new experiment." Data from that experiment either strengthen the hypothesis or make it seem less correct. Ideas for new experiments emerge. The hypothesis is revised as needed or rejected, and a new one is tried. This pattern of activity can be seen in so many success stories in science that we have come to call it the **scientific method.**

No cut-and-dried formula describes the scientific method. Intuition, guesses, hunches, and just plain luck have been important elements in the history of science, too. Penicillin, the aniline dyes, vulcanized rubber, and radioactivity were discovered by accident. They could not have been discovered, however, except by people who knew enough to realize the significance of what they were seeing. The story is often told of how Isaac Newton, in noticing an apple fall, suddenly realized that what attracted the apple to the ground must also hold the moon near the earth. Newton discovered universal gravitation, but both Newton and Newton's dog saw the apple fall.

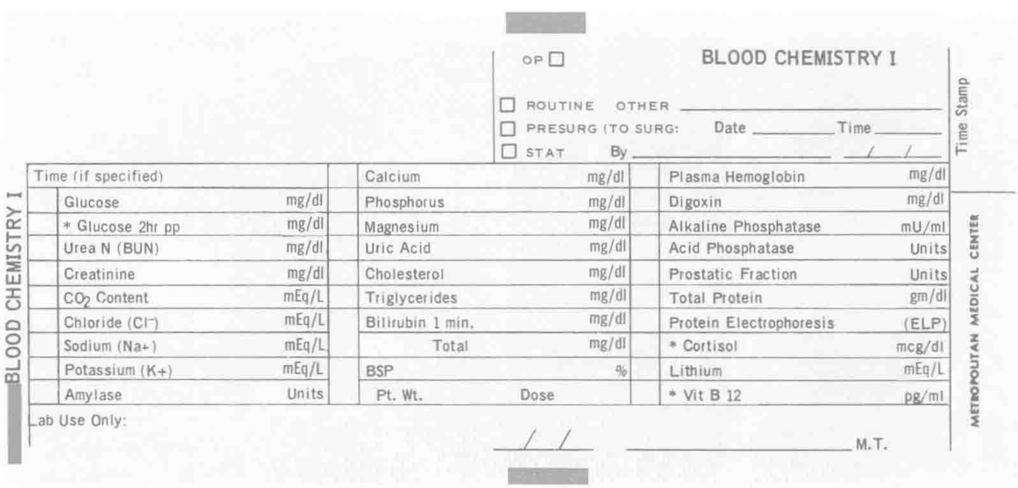
A few hypotheses are on such a grand scale, taking in such a wide variety of observations, and have been so often checked and found valid, that we call them **laws of nature.** Newton's law of universal gravitation is an example; in its terms we understand a common cause for the falling (down, not up) of an apple, the paths of the planets, the trajectory of a bullet, and the changes of the tides. A law of nature is quite simply a universal, repeatable experience, one we have every reason to believe will continue to be true, and one we believe applies not just to our planet but to the entire universe. The statement of a law of nature is simply the description of that experience. In the first law of thermodynamics we say that energy is neither created nor destroyed; the sum total of all energy in the universe is a constant. No one has done all the measurements to verify this law in all possible circumstances on all planets in all solar systems in all galaxies. Yet so invariably has it been observed to be true and so widely applicable is it that it has long been beyond serious argument.

1.5 Measurement

Advances in science depend on human measurement; without it, there is no science. While the five senses are important tools, the most important the scientist has, they are yet quite limited. We can easily tell if an object is hot or cold, but the difference between 98.6 °F and 100 °F is another matter and much depends on it. To measure small differences with great accuracy we need instruments, and once we make that decision we automatically need to agree on how we will give them measuring marks and scales. If scientist "X" doing important research on the circulatory system insists on reporting the rate of circulation of blood in cubic furlongs per fortnight and others insist on units of minims per minute, confusion and error (to say nothing of human irritation) stalk the halls of science. Happily scientists get along with each other better than that, and out of a common, universal need for simple yet clear and concise units for measurement the International System of Units has emerged.

You have to become very familiar with many parts of this system because in your professional future you will repeatedly encounter its standards and units. Figure 1.1 is a reproduction of one side of a typical clinical laboratory report on blood chemistry. Some of the abbreviations on that form are as follows:

mg/dl = milligrams per deciliter
mEq/L = milliequivalents per liter
ng/ml = nanograms per milliliter
gm/dl = grams per deciliter
mcg/dl = micrograms per deciliter
pg/ml = picograms per milliliter



BLOOD CHEMISTRY I

OP ☐

☐ ROUTINE OTHER ____
☐ PRESURG (TO SURG: Date ____ Time ____
☐ STAT By ____ / /

Time Stamp

BLOOD CHEMISTRY I

Time (if specified)		Calcium	mg/dl	Plasma Hemoglobin	mg/dl
Glucose	mg/dl	Phosphorus	mg/dl	Digoxin	mg/dl
* Glucose 2hr pp	mg/dl	Magnesium	mg/dl	Alkaline Phosphatase	mU/ml
Urea N (BUN)	mg/dl	Uric Acid	mg/dl	Acid Phosphatase	Units
Creatinine	mg/dl	Cholesterol	mg/dl	Prostatic Fraction	Units
CO_2 Content	mEq/L	Triglycerides	mg/dl	Total Protein	gm/dl
Chloride (Cl^-)	mEq/L	Bilirubin 1 min.	mg/dl	Protein Electrophoresis	(ELP)
Sodium (Na^+)	mEq/L	Total	mg/dl	* Cortisol	mcg/dl
Potassium (K^+)	mEq/L	BSP	%	Lithium	mEq/L
Amylase	Units	Pt. Wt.	Dose	* Vit B 12	pg/ml

Lab Use Only:

/ / ____ M.T.

METROPOLITAN MEDICAL CENTER

Figure 1.1
A typical clinical report sheet for the results of a number of analyses of human blood components. (Courtesy Clinical Laboratory, Metropolitan Medical Center, Minneapolis, Minnesota)