Part I

Introduction

...oh, how much more efficient it would be if students learned to spend more upfront time figuring out what needed to be done before they started trying to do it.

-Lyle Feisel
1.1 Introduction

"I hear, I forget...I see, I remember...I do, I understand."

- Confucius

Engineers and scientists can each study biology. Yet, the ultimate purpose for this study is different for the two groups. Understanding the characteristics and purposes of engineers and bioscientists can explain the approach taken toward the field of biology in this text. Thus, we begin by contrasting these two fields and distinguishing between them.

1.2 Science and Engineering

"Science cannot answer all questions.... It can, however, give some good indications, exclude certain hypotheses. Engaging in the pursuit of science may help us make fewer mistakes. It’s a sort of gamble."

-Francois Jacob

As links between the fields of engineering and biology, biological engineers must appreciate the identities and personalities of both groups. Differences between science and engineering that should be appreciated by both sides fall into three different perspectives to consider: 1) phylogeny, 2) motivation, and 3) methods (Johnson and Phillips, 1995).

1.2.1 Phylogeny

"Fate makes our relatives, choice makes our friends."

-Jacques Delille

The evolution (phylogeny) of technology usually occurs with at least four distinct phases: 1) A random phase where events occur by chance and observation occurs haphazardly. The major outcome of this phase is to make the observers aware of the phenomenon being observed. 2) A descriptive phase where cause and effect relationships are established. The result of this phase is that the observed phenomenon no longer remains random, but can be expected whenever a series of foretold events happens. The phenomenon is still not able to be brought about at will, but its appearance is at least expected. 3) A quantitative phase wherein measurements are refined and dependencies are given numerical values. These values may be deterministic or probabilistic, but during this phase there is a growing knowledge about the intensity of the phenomenon as related to the strength of the precursor variables. 4) A control phase where modeling and predictive equations lead to
knowledge of useful substance amounts, design of systems, and applications to achieve desired ends. The results of this stage are products and processes using the phenomenon. Examples are given in Table 1.2.1.

For some sciences, the early phases began long ago. The science of mechanics, for example, entered its descriptive phase before the time of Aristotle, but the science of electricity was still partially random in the time of Ben Franklin and the science of genetics entered a long descriptive phase in the time of Gregor Mendel.

The first two of these four phases clearly belong to the field of science. Engineering contributes primarily in the control phase by using quantitative information to design useful products. The overlap between science and engineering generally occurs during the quantitative phase. Early attempts at quantification are largely made by scientists, but engineering researchers, usually motivated by the need for design information, can accelerate the quantitative process. Engineering is involved more with the latter stages of technology than with the earlier stages where science dominates.

| Table 1.2.1. The four phases of scientific discipline  
| (Johnson and Davis, 1990) |
| --- | --- | --- | --- |
| Phase | Description | Physical Example | Biological Example |
| Random | Phenomena are encountered haphazardly. | Heavenly bodies are observed to move. | Differences and similarities are noted in animals and plants. |
| Descriptive | Cause and effect relationships are established. | Apparent heavenly movement appears to be related to seasonal changes. | Genetic material is discovered and transgenic organisms are developed. |
| Quantitative | Measurements are refined and dependencies are given numerical values. | Kepler’s laws describe planetary motion | Optimal microbial growth environments are determined. |
| Control | Modeling and predictive equations lead to knowledge of useful substance amounts, design of systems, and applications to achieve desired ends. | Satellites are orbited around the Earth, moon, and other planets. | Transgenic microbial production of biochemicals becomes reality. |
1.2.2 Motivation

Children are born engineers. Everything they see, they want to change.... Grown-up engineering, which is as old as civilization, maintains the youth, vigor, and imagination of a child.

-Henry Petroski

Scientists and engineers can both be highly motivated, but the sources of work-related interests are often different for each group. Neglecting the recent trend toward entrepreneurship in both groups, the major source of motivation and satisfaction for engineers comes in the final products or processes as a result of their efforts. Engineering is largely creative, forming things that never were, and engineers, like artistic painters, become highly motivated by the tangible realization of their ideas and concepts. If, in addition, there are visible groups that can be helped by these realizations, a strong drive and sense of urgency can develop within the engineer.

Biologists, generally more removed from the ultimate applications of their work than are engineers, are often motivated by the subjects of their study. They may feel empathy toward these subjects, and study them because they are interested. This study, of course, leads to more interest, and a strong bond can develop between the observer and the observed. Biologists are thus motivated more by their involvement with their subjects, and engineers by their involvement with the things they produce.

Of course the relatively recent trend towards studying cells and subcellular components has taken a lot of the attachment from the biologist and the object of study. It is hard to feel close to a cell. The idea behind this kind of study may also be to launch a commercial success. Nonetheless, biologists do not usually approach their studies in the same way that engineers do. Biologists may take the results of their research and use them to produce products essentially unchanged from their natural state, while engineers often use the same results to produce products modified more or less from their original forms. Thus, one would expect a biologist who identifies a key enzyme to offer the enzyme for sale. The engineer might take the same enzyme and use it to produce a fuel or a food in a more efficient or effective way.

1.2.3 Methods

If I have ever made any valuable discoveries, it has been owing more to patient attention than to any other talent.

- Isaac Newton

There is a fundamental difference in methods used by scientists and by engineers. Biological scientists often perform experiments to ascertain new facts. Since many of their observations are related to phenomenon description, the pattern of scientific experimental episodes may be determined more by the observed phenomenon than by any regular scientific plan. Such
is often the case while observing various life-forms in their natural habitat: observations about eating only occur when the object of the attention decides to eat. Any attempt to tamper with the behavior of the being would result in criticisms of methods and observations, rendering them practically invalid.

Engineers rarely, if ever, become involved with their experimental objects at the descriptive phase, and hence are often remote from these types of experiments. The impatience of most engineers would not allow them to observe phenomena without trying to tinker with the experiment to see what happens. Engineers are not educated to be distanced, impartial observers; they are educated to become involved, to attempt to predict or control an outcome, and to synthesize fragments that may not naturally fit together.

The advent of biotechnology and genetic manipulation (see Section 8.2.3) has seen a fundamental change in the way scientists approach their objects of study. Scientists working with functional genomics (linking functions to specific genes) are much more likely to tamper with their study subjects. They may attempt to turn off certain genes (see Section 5.3), change genetic sequences (see Section 8.2.3), or manipulate genetic material to observe the results of their trials. In this respect, scientific methods may be considered to be coming closer to engineering methods. The essential difference between the two, however, remains that scientists alter their subjects to discover new scientific knowledge, whereas engineers make their changes to enhance performance of their products.

There is a difference between typical scientific literature and typical engineering literature. Scientific experiments beyond the completely descriptive phase are conducted for specific sets of conditions, with as many variables controlled as possible. To cover an entire scientific field with scientific observations requires a very large number of specific experiments, wherein control over the multitude of variables may be either tightened or relaxed, but many, if not most, combinations of imposed conditions must be tested before a phenomenon is considered to be well-understood.

There are very few, if any, surprises appearing in scientific papers of this sort, and these papers have scientific value by extending the realm of the known by additional increments. The differences between scientific papers, cited and uncited, related to a particular field are often few, and they all form a congealing mass that establishes scientific truth by the weight of consistency of experimental results.

Science, therefore, is inductive. Scientific facts accumulate until an overall unifying concept emerges as irrefutable. The conceptual framework is induced, in science, from the many facts that precede it (Figure 1.2.1).
Figure 1.2.1. Science (above) is largely inductive, with many accumulated experimental facts contributing to an overall general theory. Engineering (below) is usually deductive, with theory presented first, and predicted facts derived from the theory.
Sushi Science and Hamburger Science
(excerpted from Motokawa, 1989)

I had always regarded science as universal and believed there are no
differences in science at all between countries. But I was wrong. People
with different cultures think in different ways, and therefore their science
also may well be different. Let me explain:

A visitor to the United States from Japan tried several seafoods.
Most of them were deep, deep-fried denatured protein once called fish; a
blackened red fish: it was nothing but charcoal. The conclusion he drew was
that the cuisine of the West is overcooked. Japanese dishes seem to have no
art of cooking at all. Although sashimi and sushi use uncooked fish meat,
they are one of the most difficult dishes to prepare among Japanese cuisines.
A lot of skills are hidden behind the no-cook. This is really an art, and
definitely a different kind of art than that found in Western cooking.

Similar differences are found also in science. Western science is
hypothesis oriented. A hypothesis is a personal interpretation using words
about how a universal rule works in a particular matter of interest. The
hypothesis should be big: the final rule should be one, and therefore the
biggest and most general hypothesis is the best one. This drives the
hypothesis to become abstract.

Eastern science is fact oriented. It tries to communicate with the
truth not through generality and abstraction as Western science does, but
through specificity and objectivity. A specific fact represents the absolute
truth. Interpretations and hypotheses should be avoided because human
discursive intellects conceal the reality.

When Western people read papers written by Japanese scientists they
will often have difficulties in understanding what the authors wanted to say,
even if the article is written in English. One obvious cause is poor English;
another cause is the difference in “logic.” Western logic is quite clear: it has
a structure in which each statement is tightly connected and linearly arranged
to reach a conclusion. Japanese logic is not so clear. Westerners may well
find no logic at all. Japanese people talk about something and, without
stating a conclusion, move the discussion to another topic. These two topics
often have no logical connection, although they are related in the mind of
Japanese people. What Japanese are trying to do is to describe one fact from
various points of view. Each view is connected by imagery to others, not by
strict logic such as syllogism.

Every scientist in the West tries to establish his ego. Each scientist
has to put forward his own hypothesis to establish his raison d’être, even if
he knows his hypothesis is not the absolute truth. Scientists have to
advertise their hypotheses and their re-created world in a loud voice to be
The engineering approach is different. Engineers generally try to conceptualize first and fit facts within this established framework. Engineering is thus deductive.

This method suits engineers well, because it tends to reduce all knowledge to a small set of fundamental principles: the conservation of matter and energy, Newton’s laws of motion, the laws of thermodynamics, and Maxwell’s equations are among these. Engineering designs are thus based upon a rather limited set of simple principles, or concepts. Given the choice between one of these fundamental principles and a conflicting fact, the principle is nearly always chosen by engineers.

Such a fundamental methodological difference between scientists and engineers inevitably leads to conflicts. Scientists are often bothered by the engineer’s tendency to simplify, while engineers wonder why scientists can’t see readily apparent connections.

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**Table 1.2.2. Summary of contrasts between science and engineering** (Johnson and Phillips, 1995)

<table>
<thead>
<tr>
<th></th>
<th>Science</th>
<th>Engineering</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phylogeny</strong></td>
<td>Random Phase through Quantitative Phase</td>
<td>Quantitative Phase and Control Phase</td>
</tr>
<tr>
<td><strong>Motivation</strong></td>
<td>Objects of study</td>
<td>Objects of creativity</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>Inductive: large numbers of facts suggest a unifying concept</td>
<td>Deductive: a small set of basic principles leads to specifics</td>
</tr>
<tr>
<td><strong>Literature</strong></td>
<td>Incremental</td>
<td>Conceptual</td>
</tr>
<tr>
<td><strong>Synthesis</strong></td>
<td>Scientists need engineers to show eventual applications</td>
<td>Engineers need scientists to identify basic facts</td>
</tr>
</tbody>
</table>
1.2.4 Synthesis

As simple ideas are observed to exist in several combinations united together, so the mind has a power to consider several of them united together as one idea.

- John Locke

Although science and engineering are separated by dominant domain, methodology, and approach, engineering is complementary to science and science is supplementary to engineering (Table 1.2.2). Engineering represents

Figure 1.2.2. Simplified diagram of the interactions occurring in the technology loop.
the ultimate application of the facts generated by science. And, engineering approaches are having their effects on scientific methods (Figure 1.2.2). Science, on the other hand, not only discovers the basic phenomena that are the subjects of later engineering models, but science also discovers pertinent variables for inclusion in those models.

Relative merits of experimental and conceptual (or model) approaches to a scientific phenomenon are well known. Each approach is so compelling that the ideal means to study the phenomenon is to incorporate both approaches. It is the willingness of scientists over the last 30-40 years to include modeling and conceptualization in their work that has enabled the rapid application of scientific knowledge by (usually) engineers.

Although biological scientists are often capable of generating the information necessary for the design of a new product or process involving a biological system, they don’t often deliver the information in a form suitable to make design trade-off decisions. Biological engineers are in positions to function as key participants in the synthesis of biological science and engineering to produce results useful to humankind.
1.3 Scientific Method

*It takes more than a village to raise a scientist. It takes a village full of scientists.*

-Brian Hayes

The scientific method is fundamental to the inductive process used by scientists in their work. It is the basis for all scientific knowledge understood today. Although the act of discovery (the Random phase described earlier) does not depend on the scientific method, the establishment of the truth and reproducibility of modern scientific observations depends almost entirely on this process. Science has made progress (mostly before the early 1800’s) without the scientific method, but the rigor of scientific truths has been enhanced through the use of this method.

Understanding how science develops information allows the student to appreciate the rigor of this process. The scientific method is a relatively simple set of steps that uses established knowledge as the basis to achieve new knowledge, and that in turn can be used to acquire even newer knowledge, and so on. The scientific method is important to a careful and methodical approach to progress in science.

The basis for the scientific method is this: from previous observations, a hypothesis is formed. An experiment is then planned to test this hypothesis. The test may either be one to substantiate the hypothesis or it may be a test to refute the hypothesis. The latter usually forms the more compelling evidence. Sometimes, for particularly strong proof, especially if the subject of the experiment is controversial, both experiments are conducted (see Hellman (2001) or deKruif (1926) for examples). In the conduct of experiments, new observations are made that lead to additional hypotheses, so the pattern: hypothesis
observe
revise hypothesis
observe
etc.
continues (Figure 1.3.1). Through the scientific method, scientific knowledge is enhanced and understanding becomes refined. In some sense, the final truth about a subject may never be learned, but once the state of knowledge reaches a certain point, a technology of useful things can develop from it.

Scientific Facts in Biology

Scientific hypotheses, when dealing with a scale large enough, are also called theories. And theories are tentative explanations for events that await further substantiating evidence. As evidence accumulates to support a theory, it becomes transformed into a “law”, or “principle”. However,
Scientific Facts in Biology cont.

just as there are no absolutely complete works, there are no laws that are completely irrefutable. All laws and scientific principles are derived from empirical data that depend on some arbitrary and relative system of measurements. Likewise, a theory may be as true or may become as well-established as a law, if only enough evidence can be collected to support it.

The dependence on empiricism, however, is the ultimate weakness of all of modern science, because evidential facts can be changed as the technology of measurement advances. As an example of this, consider the measurement of an environmental toxin. Using present methods, we might not be able to detect any toxin, but to call the amount “zero” would be incorrect. Advances in measurement techniques may someday reveal extremely small, but nonetheless measurable amounts of toxin present. The amount present is presumed to be unchanged (although we cannot know this for sure), but the amount may be measurable someday whereas it is not measurable now.

Likewise, all other measurements depend on definition for their correctness. There are international standards for time, length, mass, light intensity, and many other basic units. These are definitions, and if they somehow change, then all dependent measurements change as well. As long as the definitions remain unchanged, there is always something somewhere to compare other measurements to. All measurements, and theories and laws dependent upon these measurements, are indeed relative as well.

It was because he wanted to base a system of logic and philosophy on an absolute basis that Descartes uttered his famous, “I think, therefore I am.” From this statement and other inferences, Descartes was able to construct a non-empirical philosophy. However, the world of real objects and events remains empirical and relativistic.

The formulation of theories as a means to explain related scientific facts contains both elements of absolutism and relativism. The facts themselves are empirical, and thus relative. The theories, however, are often based upon abstract notions about how we can tie those facts together. The theories, then, have an element of absolutism based upon ideals.

It is tempting to believe that a system behaves the way it does because of the way in which we think it should work. We interpret behaviors (in other words, measurements and data, or facts) to mean that the supposed theory is true because there is agreement between the theory and the facts. But theories often go beyond facts by postulating mechanisms of action. Thus, we can believe that a biological system is
Example 1.3.1 Development of the Scientific Method.

Robert Koch (1843-1910) was a German bacteriologist who was the first to actually prove that a disease was caused by a specific microbe. He worked on anthrax, bubonic plague, and sleeping sickness, and established causative agents based on his set of postulates (deKruif, 1926):

1. The suspected agent microorganism is isolated from the victim of the disease, and must be present in every case of the disease.
2. The microbe must be isolated from the victim and cultured in the laboratory.
3. The cultured agent is inoculated into other healthy hosts, where it produces the original disease.
4. The agent is isolated from these animals, cultured in the laboratory, and identified as the same as the suspected microbe.

Koch repeated these procedures, attempting to disprove them, to prove beyond a doubt that this was, indeed, the causative agent.
Remark: This is a powerful procedure. Yoon and his coworkers used it to show that at least some cases of diabetes are caused by a Cocksackie virus that damages the Islets of Langerhans (Maurer, 1979).

Figure 1.3.1. The scientific method diagrammed.

**Example 1.3.2 Statistical Inference**

An experimental relationship suggesting a cause-and-effect should be viewed with utmost suspicion, especially if experimental variables have not or cannot be controlled (Lave and Seskin, 1979). Many epidemiological studies of human disease draw conclusions based on statistical inference. Yet, there are often many covariables that are not always easily recognized. People who are health conscious in some matters are often health conscious in others, so these two effects are difficult to separate. Although epidemiological studies are important to determine long-term effects of various environmental factors on human, animal, and plant health, they never should be confused with controlled experiments constituting the scientific method. One of the most convincing methods in the use of the scientific method is repeatable results, and, especially, results that are repeatable despite attempts to disprove them.
Example 1.3.3 Stem Cell Donations

Stem cells are harvested from neonatal umbilical cord blood, multiplied in a special brew containing disabled skin cells from the potential recipient (these cells supply the needed biochemical mix), and are then injected into the blood stream of the recipient. The cells seem to know where to go to correct existing problems.

Children with metabolic diseases lack critical enzymes to utilize complex sugars in various cells. As the sugars accumulate in vital organs, cells become damaged and die. Children receiving stem cell therapy seem to recover liver, heart, and brain function rapidly. How do you prove that the stem cells are taking the place of native cells?

Solution: Both positive and negative aspects must be shown. Children must improve after receiving the stem cells. This demonstrates that the stem cells are a necessary component of the cure, but it doesn’t prove that these cells are directly responsible. For that, a DNA analysis of the functioning cells is necessary. If the DNA of these cells differs from the DNA of the child, and is the same as the DNA of the donor, then these cells are the ones that have migrated to the site and began to assume their intended function.

The steps that Koch outlined for microbial causes of diseases cannot be followed completely because the life of the recipient child must be protected. It would be unthinkable to somehow remove the stem cells from the child once they were functioning correctly. Nonetheless, by proving that the stem cells are necessary for a cure, and are the cure, the case is logically and scientifically proven.
1.4 Mathematical Modeling

1.4.1 The Value of Models

Building a model is like eating an elephant: it’s hard to know where to begin. As with almost all problems, it is helpful to break a big problem into smaller, more manageable pieces. We do this with model formulation by first creating a qualitative model and then converting this to a quantitative model. Qualitative model formulation, then, is the conversion of an objective statement and a set of hypotheses and assumptions into an informal, conceptual model. This form does not contain explicit equations, but its purpose is to provide enough detail and structure so that a consistent set of equations can be written. The qualitative model does not uniquely determine the equations, but does indicate the minimal mathematical components needed. The purpose of a qualitative model is to provide a conceptual framework for the attainment of the objectives. The framework summarizes the modeler’s current thinking concerning the number and identity of necessary system components (objects) and the relationships among them.

- J. W. Haefner

Just as the scientific method is fundamental to the work of scientific research, mathematical modeling is fundamental to engineering research. A mathematical model may be simple or complex; it may consist of no more than one mathematical equation or may involve hundreds of equations. Its subject may be a comprehensive overview of a total system or it may be the tiniest piece of a microminiature subsystem.

As Grodins (1981) states: [Models]…clarify our thinking about a problem by explicitly identifying and clearly stating every assumption and limitation and…set the stage for a rigorous analysis usually expressed in mathematical language…. They provide a compact, clear, rigorously integrated summary of current conventional wisdom about how some natural system works…. Textbooks in the biological sciences are often swollen with detailed verbal descriptions which do not depart very far from raw experimental observations. Textbooks of physics, on the contrary, are compact because they contain descriptions of models almost exclusively.…. The archival function of models implies that they should also serve a valuable teaching function, as indeed they do in the physical sciences. Dynamic respiratory models, especially in their computerized interactive format, should be very valuable in teaching physiologists, medical students, and physicians the essence of normal and pathological pulmonary physiology.…. Finally, models provide a mechanism for rigorously exploring the observable implications of physiological hypotheses and thus can help to design experiments to test them. Investigators must know what a particular hypothesis commits them to in terms of experimental observations before they can test it. In a complex system with many interacting variables which cannot be experimentally isolated, rigorous modeling may be the only way to obtain
them. Such predictions may sometimes turn out to be unexpected and counterintuitive. If they survive an exhausting recheck of model formulation and computation, this surprising behavior of models is one of their most valuable attributes in hypothesis testing.

Starfield et al (1990) state that mathematical models are like caricatures: they overly emphasize some aspects at the expense of others to make conspicuous those results due to the emphasized aspects. Thus, models are not always general descriptions of a phenomenon. Indeed, a thorough mathematical description of some scientific phenomenon would be as complicated as the original phenomenon itself, and serve very little purpose. It is often difficult for a scientist to truly believe what value is contained in a model that does not predict all scientific observations related to a particular phenomenon.

### An Engineering Approach to Translational Medicine (excerpted from Liebman, 2005)

In the years since the completion of the Human Genome Project, physician-scientists have applied new energy to translating findings from the laboratory into better treatments for patients. Yet this accelerated, unidirectional transfer of knowledge from the bench to the bedside, a practice that goes by the name of translational medicine, is hitting an obstacle: The generation of data is far outstripping scientists’ ability to convert it into usable knowledge. For example, scientists can now correlate a disease with a specific pattern of gene expression. Such experiments are straightforward and fairly quick when the tools are available, and they provide a massive quantity of data. However, by diverting limited resources of time, money and personnel, mining this wealth of data may actually lead investigators away from grasping the governing laws from which they could build predictive models of the disease.

As clinical investigators, we stand to reap significant benefits on behalf of society by expanding our focus and viewing translational medicine not through the eyes of a scientist, but as an engineer might. Why an engineer? Because an engineer uses the fruits of science to feed the appetite of technology. Unlike scientists, who tend to approach problems from a “bottom-up” perspective by collecting data and seeking patterns, engineers take a “top-down” approach, probing a specific system for clues, taking it apart and considering how each component can be handled in a tailored solution. An engineer is a problem solver.
1.4.2 Types of Models

Imagination is more important than knowledge.  
-Albert Einstein

There are several ways of classifying mathematical models. One way is to split them into theoretical or empirical models. The theoretical model is based on well-established basic principles, such as Ohm’s Law (I = E/R) or Newton’s Second Law (F = ma). Constructing a model from one of these would then involve relating the parameters (I, E, and R) or (F, m, and a) to the target object, and then providing further mathematical descriptions of these parameters in terms specifically related to the object. For instance, electrical resistance (R) can be related to the length, diameter, and resistivity of a
cylindrical object. Theoretical models tend to be idealistic, linear, and relatively simple. They also tend to be relatively easy to solve mathematically for parameters of interest. They often do not reproduce very well details of the object’s responses to input modifications. They are, however, conceptually satisfying and relatively easy to defend.

Empirical models are mathematical descriptions of observations, and they often involve a good deal of fitting curves to data. A large number of mathematical models of biological systems are empirical because the subject matter is often very complex and far removed from the simple application of basic principles. To construct an empirical model, one would begin with a set of numerical observations and attempt to fit the data with a mathematical expression that preserved the essence of the variation of the data without reproducing the unessential (or noise) aspects of data variation. The form of the mathematical expression used to fit the data is usually left up to the person forming the model, and there are many shortcomings of this approach. One particular disadvantage is the lack of confidence that the fitted curve will adequately describe data outside its original range. One should always graph the data and the curve to judge the adequacy of the fit (see Section 4.2).

Because basic principles are ultimately based upon experimental observations, the distinctions between theoretical and empirical models ultimately disappear. It is most common for mathematical models of biological systems to include both theoretical elements (many in the form of Balances, see Section 2.2) and empirical elements mixed together.

Another distinction among mathematical models relates to the centrality of the computer to formation and solution of numerical values. Nearly all modern mathematical models require computers to solve for numerical values of various parameters. In the equation-based models described above, the essence of the model is contained in the equations, and the computer is used only as a convenient means to obtain numerical results. Some models, however, require the computer at the formative stage, and the model is written specifically for computer solution. This type of model, including finite element examples, can be difficult to understand from the basic equations included. Numerical results in graphical form are required in order to understand essential model information.

There are other model classifications, including stochastic vs deterministic models, compartmental models, and others. Whole courses are devoted to the means to construct, obtain results, and properly manage models (Starfield et al, 1990).

1.4.3 Steps in the Modeling Process

Just as there is a prescribed set of steps required for the scientific method, so, too, is there a set of steps recommended for modeling. These are:
1. conceptualize
2. separate model elements
3. capture the essence of each element
4. maintain interface ability
5. mathematically describe each element
6. solve numerically for parameter values (calibration)
7. compare model results against experimental results (validation)
8. revise model

In the conceptualization phase, the modeler decides the objectives of the model (different objectives require different kinds of models), the important properties of the model, and what things are to be included. This is a very important stage, one in which an overview of the model is worked out. The conceptualization phase should not be under-emphasized, or else it is likely that later work will have to be repeated. Material in this text is especially relevant to the conceptualization phase.

Thereafter, the grand scheme of the model is dissected into elements or at least into multi-element modules. It is here that the mathematical details of the model are formulated. Again, only those details important to the objectives of the model will be included. Unnecessary details only add complexity and computational hazards. For instance, a model intended to reproduce the action of the heart during exercise would not include details of the endothelial cells lining the blood vessels. A model concentrating on the development of atherosclerosis would contain these details, but the heart would be omitted entirely. A model designed to look at the interactions among endothelial intracellular constituents would even ignore the blood flowing outside.

The essence of each element means that only the most important and essential means of describing that element should be included, no more and no less (Figure 1.4.1). For instance, the respiratory systems of amphibians, reptiles, birds, and mammals are composed of airways, lung tissue, and the respiratory muscles. Mechanical descriptions of the respiratory system include mass (which has inertia), the elastic tissues (which have nonlinear pressure-volume characteristics), and the geometry of the airways (which determines resistance to flow). These qualities are distributed throughout the respiratory system in some non-uniform fashion. Distributed parameters add a great deal of computational complexity to the model, and are usually unnecessary for most purposes. The essence of the model can usually be captured by describing one inertance value, one resistance value, and one elastance value, and, in addition, these parameters can usually be linearized with no loss of model utility. Some respiratory system models include inertance, resistance, and elastance values for the three elements of airways, lung tissue, and chest wall for each lung. For other models, even this complexity is too great, and one inertance, resistance, and elastance parameter is assigned to the entire respiratory system inclusive of the airways, lung tissue, and chest wall. At normal breathing rates, inertia may usually be neglected, so the essence of the entire respiratory system can be reduced to one resistance value and one elastance value. Depending on the objectives of
this model, this simplification makes a lot of sense and can adequately describe respiratory system function.

Figure 1.4.1. The essence of an element is obtained by throwing out all descriptive qualities not necessary to the purpose of the model. Too often, students cannot tell for sure the difference between essential and nonessential qualities. Nonessential qualities may be essential in other contexts.

It is important, when adding mathematical details, to remember that model elements must be put back together to constitute the entire model as visualized. Thus, the input and output variables of each element must be satisfied by surrounding elements (Figure 1.4.2). Thus, if predator population is a required computed input parameter for one element of a model, it must be computed as an output parameter of another element.

Calibration and validation are important steps in model development. Calibration is the process of fitting a model to a certain set of data by adjusting numerical values of parameters so the best fit is obtained. The experimental data against which the model is calibrated are substituted for model input and output data, and the model is run backwards or forwards in
order to obtain the best numerical values for model variables. That means two things:

1. model calibration is limited by the quality of the experimental data
2. the model will probably fit calibration data the best of any data that it can be tested against.

Thus, model results plotted for the calibration data set usually are very impressive, but mean little.

![Diagram](image)

Figure 1.4.2. Each element of a model must interface with other elements, and pass information between them. The input parameters of each element must be satisfied by the output parameters of interfaced elements. All elements need not interface with all the others.

That’s where validation comes in. *Validation* is the process of trying the model on an independent set of input data and seeing how well the model output data match the actual set. If the match is good, then the model is validated, at least somewhat. The more independent experimental data sets
are that result in good matches between model output and experimental data, the more valid the model becomes. So, there are degrees of validation.

There are other steps that may be taken in modeling. Sensitivity analyses show how much model outputs change for incremental changes of model parameters. A model is said to be robust if it can accept many changes in values for a wide range of input conditions. All these steps are further explained in other courses and texts on modeling.

1.4.4 Models and Empirical Observations

Although we humans often judge ideas on their plausibility, plausibility is not a rigorous test of the validity of scientific ideas. -Pat Shipman

Although modeling is a fundamental tool of engineers, empirical observations are still necessary to assure that the models are based in reality. Both models and empirical observations are necessary for modern technological advance (Table 1.4.1). Models by themselves only allow deductions and are only compact descriptions of what is already known. Empirical observations allow for the inductive discovery of new knowledge, but do not organize known facts in useful form. Thus, as long as there is new knowledge to be discovered, we will need real-world observations; as long as we require that engineers design new products and processes, we will need mathematical models.

<table>
<thead>
<tr>
<th>Models</th>
<th>Experiments</th>
</tr>
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<tbody>
<tr>
<td>Lead to predictions of experimental events</td>
<td>Guide development of models</td>
</tr>
<tr>
<td>Show what experiments need to be conducted and what parameters require measurement</td>
<td>Calibrate models</td>
</tr>
<tr>
<td>Form a framework into which to form experimental results</td>
<td>Validate models</td>
</tr>
<tr>
<td>Make some experiments unnecessary, either because: 1. all information is known to predict outcomes or 2. some things can be shown to be impossible</td>
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Example 1.4.1 Mathematical Model of an Infectious Disease (Marchuk, 1983).

Disease is caused when certain types of antigens (e.g., bacteria, viruses, etc.) overcome immune responses in an organism (see Section 6.20). The interaction between antigens and immune responses can be modeled at different levels, from macroscopic to intracellular genetic. The type of result the modeler seeks will often determine the type of model that is constructed, and this dictates which properties are included and which are ignored. For example, these models have been formulated:

1. equations to describe the change in the number of circulating antibodies as a function of the number of specific plasma cells (Hege and Cole, 1966).
2. probabilistic models of the interaction of antigens with immunocompetent B cells (Jilek, 1971).
3. model describing antigen-antibody relations as predators and prey (Bell, 1974).
4. bilinear system theory interpretation of immune response as a heterogeneous immunocyte population varying with time and affinity (Bruni et al, 1975).

In each of these cases, the models developed would have different appearances resulting from different starting points. Various computer-based models might also extend the range of models for disease development.

Example 1.4.2 Localized Estrogen Delivery Affects Neural Plasticity

Male song birds have better developed neural song centers in their brains than do females. The more imbalance there is between song delivery by males and females, the more difference there is in their brains. This difference begins to appear during adolescence, when males begin to sing, and is apparently influenced by local estradiol levels. The estradiol (one of the estrogen hormones) is apparently formed in the brain from circulating testosterone produced in the testes outside the brain, but the estradiol is not produced in the song centers where it is needed to influence neuronal structures. Instead, the estradiol is stored in presynaptic boutons that connect to neurons in the song centers.

The amount of stored estradiol varies by a certain amount, the amount released during an action potential can vary, and the fate of the estradiol in the postsynaptic cleft is not completely certain. In addition, the effect of estradiol that manages to reach the target neuron is also variable. To model this problem requires four probabilities: 1) the probable amount stored ($p_1$), 2) the probable percentage of stored estradiol that is actually released ($p_2$), 3) the probability that released estradiol reaches the target neuron ($p_3$), and 4) the
probable effect that a certain concentration of estradiol will have on the target neuron \( (p_4) \). The overall probability of a certain neural outcome is the product of the individual probabilities:

\[
p_{\text{tot}} = p_1 p_2 p_3 p_4
\]
as long as each probability is independent of the others. If there is a dependence of one or more of the probabilities on prior probabilistic events, or if nonlinearities occur so that probabilities are not constant, but vary in some definable way, then the calculation of the overall probability of an outcome is much more complicated.

Each of these probabilities \( p_1 \) through \( p_4 \) has some variability. Just as with flipping a coin, we would not expect the first few trials to yield the same fraction of specific outcomes as would a large number of trials. So, to model the effects of estradiol on target cells requires looking at the outcomes of a given number of trials and noting the results.

In order to do this, we must use a random number generator with the same probability of an occurrence as we expect would happen with the estradiol. In addition, the random number generator should have the same variability (called variance) as the biological process. And, we need to have four random number generators acting simultaneously.

These random number generators could be coin flips or die tosses, but it would be hard to adjust the probabilities and variances to the exact values needed. Instead, computer random number generators are usually used.

The outcome of the model is not known ahead of time. Instead, the model is run as many times as we are interested in, and the number of successes (perhaps a certain level of target neuronal response) is noted. Then, the model is run again, and again, and again, each time for the number of trials of interest. Over time, an overall average success rate may emerge, and that will be considered the model result. Notice that the model does not give a definite answer (nondeterminate) and the results must be obtained numerically. These are characteristics of stochastic (probabilistic) models.

Example 1.4.3 A Grass-Deer Ecosystem

Model the carbon flow in an ecosystem defined as grass and some deer that eat the grass.

Solution:

The qualitative solution is based upon this conceptual framework (Haefner, 1996):

1. Grass will be assumed to have a constant rate of growth. Growth is defined as the mass of carbon newly fixed in grass plants per unit mass of carbon already present in the plants. Total amount of carbon fixed is therefore related to the total amount of carbon present.
2. The only loss to the quantity of carbon present in the grass population is by deer consumption.

3. Deer compete with one another for grass, so that each deer receives less carbon as the number of deer increases.

4. Deer excrete or respire a fixed proportion of their existing carbon as either atmospheric carbon or solid/liquid waste.

None of these stipulations is detailed enough to allow a complete set of mathematical equations, but this is the framework that provides structure to the model to be formulated. From these four conditions, equations can be developed either based on first principles or on empirical evidence. Stating these conditions in this way breaks the overall concept of the model into smaller pieces that can then be worked on one at a time, being sure that the developed equations fit together as a package and that they exclude unnecessary detail.
1.5 Biological Engineering

The emerging discipline-based biological engineering has the potential of using biological materials and living processes in designing systems that are more in harmony with nature. —Brahm Verma

Engineering is a profession. In other words, it is an occupation that involves a liberal education and mental rather than manual labor. Biological engineering is a discipline within the engineering profession. A discipline is characterized by a distinct body of knowledge and commonly-accepted methods. The body of knowledge for biological engineering includes fundamentals of engineering practice, including:

- analysis,
- computation, and
- design

skills, along with a working knowledge of the science of biology, including:

- methods,
- principles, and
- properties

applicable to utilization. Biological engineering methods include:

- systems approach
- modeling techniques
- black-box viewpoint

A systems approach means a broad, conceptual consideration of all the possible influences and characterizations affecting a biological system, whether that system is the interior of a cell, a group of tissues in an organism, or the entire Earthly biome. Modeling techniques capture the essentials of the biological system pertinent to the goals of the model, and deal with biological principles and simplifications. Models usually reduce the biological system to mathematical form, although mechanical, electrical, chemical, or thermal models are also possible. The black-box viewpoint is used to replace complex biological elements with output/input relationships, thus avoiding unnecessary complications in forming the model.

In addition to this knowledge and these approaches is an enthusiastic passion that biological engineers exhibit toward biology in general, and a wonderment at the interconnectedness and sense of apparent order present in the biological world. It is both the complexity and the apparent simplicity of life that inspires biological engineers to work with biological systems on an intimate basis. Passion and creativity are essential attributes of successful engineers, and living systems elicit these attributes in biological engineers.
Engineering disciplines can be classified into two categories: applications-based, and science-based. Applications-based engineering disciplines serve particular economic sectors such as petroleum, mining, military, medicine, or agriculture. Science-based engineering disciplines are much broader, more fundamental, and are based upon particular sciences. The foundational engineering disciplines were all based on some portion of physics: electricity, mechanics, and heat. Chemical engineering added the science of chemistry to engineering. Biological engineering adds biology, although it retains the interest also in physics and chemistry.

The above definitions and descriptions can be very abstruse for many people. Certain descriptors have been used to explain biological engineering, and one or more of these can help to understand what biological engineering is. They are not a definition, but are included here for elucidation:

- Familiar with both engineering and biology.
- Not identified with any particular application.
- Act as bridges between engineering and biology.
- Doesn’t just work with biology. Has a substantial knowledge of, and continuing interest in, the field of biology.
- Should be to the science of biology as chemical engineers are to chemistry, electrical engineers are to electricity, and mechanical engineers are to mechanics.
- Broad, fundamental, integrative, and unspecialized.

and my particular favorite,

- A specialist in technical diversity.

In Table 1.5.1 are found desired attributes of an engineer given by Boeing aircraft company (McMasters and Cummings, 2004). There are no attributes that can be specifically identified as being associated with biological engineering, nor are they identifiable as related to aerospace engineering. Nevertheless, this Table provides a good checklist for the qualities that any engineer, including those primarily dealing with biological systems, should, ideally, possess. Qualities in this Table also remind us that engineering is part science and part art.

The Boeing list of engineering attributes illustrates that engineering integrates many skills with knowledge from many different sources. Biological engineering is even more multidisciplinary than most engineering disciplines because of the broad range of potential applications. Thus, you will find in this book a range of topics not normally found in any engineering or biology text. Nonetheless, the biological engineer should appreciate the many internal and external influences shaping any engineering design involving living things.
### Table 1.5.1 Boeing’s “Desired Attributes of an Engineer” (Boeing, 2004)

- A good understanding of engineering science fundamentals
  - Mathematics
  - Physical and life sciences
  - Information technology (far more than “computer literacy”)
- A good understanding of design and manufacturing processes (i.e., understands engineering)
- A multi-disciplinary, systems perspective
- A basic understanding of the context in which engineering is practiced
  - Economics (including business practice)
  - History
  - The environment
  - Customer and societal needs
- Good communication skills
  - Written
  - Oral
  - Graphic
  - Listening
- High ethical standards
- An ability to think both critically and creatively – independently and cooperatively
- Flexibility – the ability and self-confidence to adapt to rapid or major change
- Curiosity and a desire to learn for life
- A profound understanding of the importance of teamwork
- DIVERSITY – wanted and needed!

### 1.6 Expectations for Biological Engineers
...one definition of engineering might be that it is the avoidance of failure....The engineer ensures that...failures do not occur by analyzing the design on paper, and the objective of the analysis is to calculate the intensity of forces in the structure and compare them with limiting values that define failure....The nature of engineering design is such that emerging fields such as bioengineering...can be expected to follow similar paths as have the older and more traditional fields, in that design errors will be made, failures will occur, and designs will evolve in response to real and perceived failures. We can only hope that when those failures occur, loss of human life will not be the result.

Henry Petroski (2001)

We have seen how engineering involvement with biology is largely at the technological stage where products and processes are produced to provide useful products to fill some predetermined need. Others besides engineers may also operate at this technological stage. For them, the study of biology must involve consideration of the many complexities that living systems have to offer. However, many scientific details of living systems are not necessary to create the products and processes required. Instead, those who use living systems as part of their creative domain must rely upon principles and generalizations, those things that reduce the field of choices from an infinite whole to a limited set. For instance, a certain pollutant could be removed from the environment using any living entity, or a chemical approach, or a physical approach. Knowing that bacteria may use the pollutant as an energy source would open the possibility that bacteria could form part of the solution to the problem. Knowing that bacteria often need moisture, oxygen, and other nutrients as well as an energy source can give a quick idea about how a pollutant-removal solution can be constructed. Although these generalizations are rather simple, they are powerful enough to limit the range of possibilities rather quickly.

Thus, we might expect from engineers who deal with biological systems three things:

1. The knowledge of biological principles and generalizations that can lead to useful products and processes.
2. The ability to transfer information known about familiar living systems to those unfamiliar.
3. The ability to avoid or mitigate unintended consequences of dealing with any living system.

To the third expectation, we add that living systems are not passive: they move, they change, and they influence their surroundings. Thus, they cannot be used blindly without expecting other changes to happen. Anticipating these other changes can distinguish those who are experts in biological engineering from all others. Whether the process involves installing an
artificial heart into a sick human patient or introducing a new law to limit harvesting of a wild food species, there will be other unrelated and perhaps unseen consequences.

Technological advances have made unintended consequences almost inevitable. Like a phantom in a bag that pops out in every direction that isn’t held, secondary effects that are masked by primary effects assume much more importance when the primary effects are conquered (Tenner, 1996). Chronic illnesses such as cancer, silicosis, and cumulative trauma disorder probably were not recognized as important because acute illnesses such as typhoid, plague, and pneumonia killed so many. After anesthetics allowed painless surgery, the number of surgical procedures skyrocketed and the total amount of pain experienced by the total human population is higher because of it.

This message is discouraging, because it implies that unintended consequences can never be avoided. As the more acute problems affecting humans and their environment are tackled and cured, problems that had seemed inconsequential can suddenly become limiting. Nevertheless, the experienced biological engineer should be more able than others to anticipate the likely consequences of her technological fixes and to be prepared to deal with them.

It is the intention, then, that the approach toward the life sciences taken in this text should support the three expectations given above.

Example 1.6.1 Environmental Conditions and Human Disease

There is a direct link between environmental conditions and human diseases. Diseases such as hantavirus in the southwestern USA, cholera in South Asia, dengue fever in Vietnam, and malaria in Peru all seem to be related to the periodic warming of the tropical waters of the southern Pacific Ocean, called El Niño. During El Niño years, Peru’s mountainous valleys are warmer and rainier; this promotes the reproduction and growth of sand flies called *lutzomyia*, which prefer meals of human blood. While sucking, they transmit *Bartonellosis* bacteria that enter the red blood cells of its victims and destroy them. Between 40 and 60% of its victims die; the rest develop a rash and bleeding warts. Knowing this environmental connection to human disease can make prevention and control easier by concentrating resources to the times of most peril (Roylance, 2002).

This is just one example among many of the link between the environmental portion of the biosphere and individual organisms. This is one reason why the connections among biological components need to be known: understanding these connections can point to key steps where cycles can be disrupted and disease outbreaks controlled.

Example 1.6.2 Sickle Cell Anemia
Sickle cell anemia is a disease caused by a gene that makes defective hemoglobin. The defective hemoglobin molecules form long, sticky polymers that cause the red blood cells to be sickle-shaped rather than round. These abnormal cells clog the blood passageways and starve vital organs of oxygen. Gene therapy has been suggested to cure this disease; placing the desired gene in the shell of a neutralized virus vector could introduce the gene into the patient’s cells. However, this technology is mostly hit-or-miss, and may be dangerous to the people receiving the cure. Suggest alternative means to treat the disease.

Solution: Several possible treatments present themselves. On an organismal scale, altering the blood or breathing hyperbaric oxygen so that the blood can carry more oxygen than normal might be a possibility. Or, perhaps a substance could be added to the blood to make the sickle cells less likely to clump. Blood transfusions with healthy blood certainly could help.

Another possibility exists. There is a gene present in all fetuses that makes a protein to draw oxygen from the mother’s blood into its own. This is fetal hemoglobin, and it has a higher affinity for oxygen than does adult hemoglobin. This gene never causes sickling, but the gene is turned off at birth. If the environmental switch that turns off the gene can be reversed, then the sickle cell patient may be cured of the disease.

Remark: When attempting to solve a problem involving living things, there are usually many possibilities for a solution. The biological engineer must know enough about all aspects of biology to be able to enumerate as many possibilities as she or he can. Then the best choice can be made.
1.7 About Predictions

You may wish to become a physician and save people one at a time or to become a biomedical engineer and save them a thousand at a time.

-Raj Tonnosh

Modern biology is headed more and more toward being predictable. That is, as new knowledge is gained and integrated into those things already known, patterns emerge that make possible the foretelling of future facts. When the degree of sophistication of this process reaches a sufficient level, then vaticinatory models can be formulated, and further experimental observation becomes redundant rather than exploratory.

![Figure 1.7.1](image)

Figure 1.7.1. Biological predictions lead to the establishment of new knowledge, whereas engineering prediction leads to a successful application of existing knowledge. Designs requiring new knowledge are never attempted.
Hypotheses have always been important in biology, as in the rest of science. The scientific method is based upon the cycle of hypothesis – test – hypothesis – test, and hypotheses made, whether proved true or false, indicate a state of knowledge somewhat above complete ignorance.

It is against this background that we wish to distinguish between predictions made in the exercise of the scientific method and those made by technologists in the applications of or with biological systems (Figure 1.7.1).

Figure 1.7.2. The more data points are known, the better is the prediction of the location of the next data point. If the prediction involves deduction rather than induction, then the prediction can be made very precisely.

Successful predictions depend very strongly on the amount of knowledge we already possess. Take the case of prediction of the location of the next data point in a time series. If we have no knowledge whatsoever, there is nothing we can base our prediction on. With one known data point,
the next is probably located somewhere in the same vicinity, but we have no idea about the direction locating the second data point from the first (Figure 1.7.2). With two data points, the number of likely directions is reduced somewhat. With many data points, we can often make a pretty good prediction of the location of the next data point (even if the data points are randomly scattered). Thus, we can conclude that the more knowledge we have of biology, the better able we can be to utilize biological systems for some useful purpose. A better prediction means a more confident design is possible.

Better yet, if the next data point is located within the confines of a data set, then the prediction of the next data point can be made with very high assurance of correctness. This illustrates the difference between induction (or extrapolation) and deduction (interpolation). Engineers who use already-existing knowledge to predict the behavior of biological systems can do so with a high degree of certainty, especially if they know how biological systems normally react and how they react in the extreme.

Biologists would say that “scientific theories are built by testing their predictions of new findings, not simply by explaining existing knowledge” (Beckwith, 2001). Technologists including biological engineers might use the word “prediction” a little differently; prediction to them would be most useful if it could lead to a successful biological application. In other words, prediction is a term that describes the summarization of all that is known about a subject in order that it be usefully applied. Predict, therefore, is what one does when one designs a new product or process using old knowledge in a new way.

This book has the intentional purpose of interpreting biology in a manner most useful to biological engineers and others who engage in activities at the control stage of technology (see Section 1.2.1). Thus, the predictions made in this text may seem to be obvious and mundane. However, they are not intended to expand the state of knowledge, but to consolidate what is already known. If this approach disappoints the biological scientist, at least it will guide the engineer toward a successful design career.

Engineers need to know about typical responses, some idea about the range of responses, and important exceptions. These pieces of information are not normally referred to as “predictions”. However, in order to demonstrate the utility of the information presented in each subsequent section, predictions, both sublime and ridiculous, have been included at the ends.

Example 1.7.1 Predictions About Water Temperature Control Downstream from Dams Across Spawning Rivers.

The Rogue River in southwest Oregon has been widely known for its runs of Pacific salmon and steelhead trout. Following severe flooding, however, three large dams were constructed to control the river’s outflow. These dams cut off the upstream waters from migrating salmon. To mitigate the loss of spawning waters, thousands of adult migrants are collected each
year below the dam and brought to a hatchery to reproduce. Juvenile fish raised in the hatchery are released downstream from the dam later in the year.

In the lake behind the dam is a $20 million free-standing, 256 foot tall tower with water-intake ports at four widely-spaced elevations. It had been predicted that water temperature downstream from the dam could be controlled by drawing water from different levels, and that, by controlling water temperature, growth of the fish would be enhanced.

What actually happened was that water temperature could not be controlled as well as was expected. Summertime release of thermally sub-optimal water slowed the growth of juvenile salmon; release of warm water in the summer accelerated upstream migration of adult spring Chinook salmon and overwhelmed the hatchery; sudden changes in the rate of water release activated downstream migration of juvenile fish. Peak releases in the spring and summer caused downstream migrating juveniles to crowd downstream areas where temperatures were too high, and juveniles emigrated prematurely to the sea where their survival chances were greatly reduced.

The predictions that technological remedies could compensate for the presence of the dams were far off target. In this case these predictions served as hypotheses in costly time-consuming experiments and were found to be wrong (Larson, 2002).
1.8 About This Book

One of the gravest charges ever made against science is that biology has now put it into our power to corrupt both the body and the mind of man.

-Peter Medawar

The engineering design process begins with a concept and continues to completion using various tools of engineering, such as mathematics, physics, engineering sciences, computers, and models. Some have suggested that a book on biology for engineers ought to be chock full of equations, quantitative models, and numbers. That approach has not been taken here because the very beginning of an engineering solution, the art of engineering, is the concept, or the vision of what the solution should do and how it should do it. In order to produce an engineering design involving living things, one must be familiar first with how living things work. Then, and only then, should an engineer investigate the question of “how much?”.

No one reading this book will become an expert in biology. Additional texts and courses will be necessary for that. And, even the experts must read constantly in order to stay abreast of the many new developments that are happening these days. This book is intended to give perspective – to give an appreciation for the entire interface between technology and the life sciences.

Biological systems are not exempt from the laws of physics, chemistry, and other sciences. Therefore, the next section deals with scientific principles relevant to biology. It would be extremely presumptive to expect that all relevant principles are included, and no such claim is made. However, an attempt was made to identify and explain those principles that form the basis for biological responses appearing later in the text.

Following the scientific synopsis is a section dealing with biological responses. A “black-box” approach has been used; impose a set of conditions on the black-box, and a certain response is expected. When the opportunity presents itself, some additional mechanistic explanation has sometimes been given, but it is the input-output responses that are of primary concern here.

Scaling of biological responses and attributes is important to be able to make quantitative predictions, especially when few data are available. The section on scaling is the most mathematical of all in this book, but although somewhat inconsistent with the general nature of this text, is included because a thorough presentation of scaling relationships is hard to find elsewhere.

Finally, the last section of the book, short as it is, provides a classification of different types of applications related to biological systems. It is in this section that the engineer or technologist can see the broad relevance of this predictive approach to biology.

This material may be either a review or a preview for students. As a review, it can help to tie together many loose ends from many other courses; it can add perspective. As a preview, it can help to show why later courses are necessary; it can add perspective. There is no ideal placement of this text in a
curriculum. It can be helpful both at the beginning and at the end, and the student may wish to use it that way; read it first for motivation for studying all those other topics, and read it last to see why you had studied them.

Given the above, there is no ideal background for this text. To understand everything included, a host of other courses would have been required. However, if this text is to be used as an introduction to biology, then the student should not be expected to learn all details included herein. The student should try to read for perspective and to form general concepts, realizing that further study is necessary to fill in the details.

Lastly, the amount of mathematics included in this text has been minimized in order that the conceptual nature of the material not be lost. This is not to say that math isn’t important to the application of biology, because it is. However, in these times that emphasize multimedia learning there are few opportunities to exercise the conceptual mind. It is at the concept level that this material is targeted.
QUESTIONS
Chapter 1

1.2.1. Give at least two biological examples of the stages of technology.

1.2.2. What do we mean by the “control phase” of technology? What does this phase mean for biological engineers?

1.2.3. Describe what you think engineering is.

1.2.4. Are biologists who manipulate genes really “genetic engineers”?

1.2.5. What are the differences between inductive and deductive fields of study?

1.2.6. How would you go about explaining an idea to a scientist? What if the listener were an engineer?

1.2.7. Make a list of engineering contributions that have enabled scientific progress.

1.2.8. Give an example where an understanding gap is likely to exist between a scientist working in that area and an engineer who also wishes to work in that same area. How could you, as a biological engineer, help each to understand the other?

1.3.1. Why is the scientific method so powerful? Can any kind of science proceed without using the scientific method?

1.3.2. Why is Koch’s method of proving a connection between a microbe and a disease so powerful? Are there other possible causes of the disease if microbes identified by his procedure pass all tests?

1.3.3. Name some diseases whose cause would not be able to be identified through Koch’s method.

1.3.4. If you are told that a certain drug is effective against a disease, what kind of evidence should you look for in order to be convinced?

1.3.5. State a principle of science. Trace its evolution from isolated facts through theory to its present form.

1.3.6. Ohm’s law (I = E/R) was originally published with an additive constant term (I = E/R + C). Ohm spent the rest of his life trying to amend his original mistake. If you were George Simon Ohm, how would you go about doing this?
1.3.7 Give an example where some physical or biological phenomenon is explained with a human motivation. How could you go about proving or disproving the explanation of the event?

1.4.1 Give an example of a model that includes both theoretical and empirical elements. How can one be distinguished from the other? When is it necessary to use empirical models? When is it desirable to base models on theory?

1.4.2 Someone tells you that they have an equation that nearly perfectly fits the data, and so that equation is the best description of the phenomenon. You inquire, and find out that parameter values for the equation were obtained from the data set for which the fit is nearly perfect. Why should you be suspicious about the value of the equation? What could you do to determine how good the equation is?

1.4.3 How can a mathematical model help an experimentalist? How can experimental facts be used to guide model development?

1.5.1 Give your own additional descriptions for biological engineering.

1.5.2 What part of engineering is science and what part is art?

1.5.3 What is meant by a “specialist in technical diversity”? Why a “specialist”?

1.6.1 Give an example where unintended consequences resulted from some attempt to fix a problem.

1.6.2 Should there be other expectations of biological engineers? If so, what and why?

1.6.3 If the gene controlling the protein to draw oxygen from the mother’s blood were able to be turned on to cure sickle cell anemia, what unintended consequences would you suspect would happen?

1.7.1 What number am I thinking of? If the number is somewhere between 1 and 10, what is the number? If the number is odd, and between 1 and 10, what is the number? If the number is evenly divisible by the integers 3 and 9, is odd, and is between 1 and 10, what is the number? What does this game have to do with engineering predictions?

1.7.2 Why can it be said that an engineer must be able to predict the future? How does prediction relate to design?
1.7.3 List five biological attributes that can be predicted and five that cannot. Justify each.

1.7.4 Give an example of an inductive argument and an example of a deductive argument.

1.8.1 Give an example of a product of engineering design and the original concept that led to the final product.

1.8.2 What expectations do you have for this book? What do you hope to learn?

1.8.3 Look through the Table of Contents. Are there topics that particularly interest you?

1.8.4 Contrast the knowledge that you already possess about biology with the contents of this book. Does this look to you like a biology book?