Mathematical and Experimental Modeling of Physical and Biological Processes

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Chapter 1

Introduction

1.1 Modeling: Philosophical Remarks

We begin this chapter with a brief discussion of certain philosophical notions that are important in the modeling of physical and biological systems. Modeling in our view is simply a means for providing a conceptual framework in which real systems may be investigated. The modeling process itself is (or should be) most often an iterative process: one can distinguish in it a number of rather separate steps which usually must be repeated. One begins with the real system under investigation and pursues the following sequence of steps:

(i) empirical observations, experiments, and data collection;

(ii) formalization of properties, relationships and mechanisms which result in a *biological or physical model* (e.g., stoichiometric relations detailing pathways, mechanisms, biochemical reactions, etc., in a metabolic pathway model; stress-strain, pressure-force relationships in mechanics and fluids);

(iii) abstraction or mathematization resulting in a *mathematical model* (e.g., algebraic and/or differential equations with constraints and initial and/or boundary conditions);

(iv) model analysis (which can consist of simulation studies, analytical and qualitative analysis including stability analysis, and use of mathematical techniques such as perturbation studies);

(v) interpretation and comparison (with the real system) of the conclusions, predictions and conjectures obtained from step (iv);

(vi) changes in “understanding” of mechanisms, etc., in the real system.

As one completes step (vi), one is led naturally to reformulate the physical or biological model by returning to either step (i) (if new experiments are indicated) or step (ii). In either case one then proceeds through the steps again, seeking to improve the findings of the previous transit through the sequence.

Steps (i), (ii), (iii) belong to what one might term the *formulation* stage of the modeling process, while step (iv) is the *solution* stage of the modeling process, and steps (v) and (vi) constitute the *interpretation* stage. In practice, however, it is often (unfortunately) the case that investigators do not make a clear distinction in the steps outlined here. This can lead to confusion and, in some cases, incorrect conclusions and gross misunderstanding of the real system.

Let us turn next to the reasons frequently given for modeling. Perhaps the one most often offered is *simplification*: the use of models makes possible the investigation of very complex systems in a systematic manner. A second rationale is *ease in manipulation*: investigations involving separation of subunits and hypothesis testing may often be facilitated through use of simulations in place of experimentation. The suggestive features in modeling can also help in *formulation of hypotheses* and in the *design of critical experiments*. The modeling process also requires *preciseness* in investigation in that one must move from a general, verbal explanation of phenomena to a specific, quantitative one.

But a rationale perhaps more fundamental than any of these is that modeling leads to an *organization* of inquiry in that it tends to polarize one’s thinking and aid in posing basic questions concerning what one does and does not know for certain about the real system. Whatever the reasons that have been advanced to justify modeling attempts, it is sufficient perhaps to note that the primary goal must be *enlightenment*, that is, *to gain a better understanding of the real system*, and the success or lack thereof of any modeling attempt must be appraised with this in mind.

One must recognize the various *levels* of modeling in any attempt to compare or assess the validity of several models for a phenomenon. For example, consider the phenomena involved in the transmission of a nerve impulse along an axon: this process is likely to be described by the mathematician or biophysicist in terms of partial differential equations, wave phenomena, or transmission line analogies, whereas a neurophysiologist might speak in terms of local circuit analogies and changes in conductances. The cell physiologist might describe the phenomena in the context of transport properties of membranes and ion flow, while the molecular biochemist could insist that the real story lay in the theory of molecular binding.

A second example involves the physical motion (vibration) of a structure such as a plate or beam. Again the mathematician might describe this in terms of a partial differential equation whereas the mechanical engineer might use a modal analysis (in terms of natural frequencies of oscillation) based on internal stress-strain relationships.

In each of the examples above the different modeling approaches move to an increasingly more micro level. Each approach involves an attempt to explain a phenomenon that is not understood at one level by description at a more micro level (in general) where understanding is more complete. This attempt to explain "unknowns" in terms of more basic "knowns" is clearly the foundation of most modeling investigations. Indeed, in addition to noting that nerve impulse phenomena are described in terms of membrane conductances, permeabilities, ion flow, etc., one might observe that blood circulation is studied in the context of elementary hydrostatics and fluid dynamics while metabolic processes are usually investigated via use of the language of elementary chemical kinetics and thermodynamics.

The choice of the level (micro vs. macro) at which one models depends very much upon the training and background of the investigator. Furthermore, the perception of whether a model is a "good" one or not is also greatly influenced by this factor, and it is therefore not surprising that all of the approaches to the nerve impulse phenomena mentioned above (or indeed those for modeling any physical or biological phenomena) can be subjected to valid criticisms in any attempt to evaluate them.

Before discussing the criteria one might use in evaluating modeling investigations, let us list some of the common difficulties and limitations often encountered in the modeling of systems:

(a) Availability and accuracy of data;

(b) Analysis of the mathematical model;

(c) Use of local representations that are invalid for the overall system;

(d) Assumptions that the "model" is the real system;

(e) Obsession with the solution stage;

(f) Communication in interdisciplinary efforts.

The first item in this list requires no further comment; the second includes both theoretical and computational difficulties in the mathematical treatment of a given set of equations. Although formidable obstacles can still arise, this is a much less critical problem today in modeling than it was, say, in the physical sciences in Newton's time. This is due in large part to great strides that have been made in the last several decades with the advance of modern computing facilities and the concomitant development of rather sophisticated numerical procedures. We remark that (c) is especially prevalent in certain physiological modeling, where systems are not easily manipulated experimentally. *In vitro* data and parameter values (determined via experimentation in non physiological ranges) are often used to model, predict and draw conclusions about *in vivo* situations. While (e) is likely to be a problem for investigators with a mathematical or physics background (in their enthusiasm for finding solutions of their model equations and various generalizations, they tend to forget or ignore the fact that the model is only an approximation and that certain aspects of the physical or biological model on which it is based are very poorly understood). Item (d) can be a problem for both mathematical and physical and/or biological scientists. Even physicists and biologists sometimes have a penchant for disbelieving data that contradicts model simulations and predictions. It can be very tempting to throw out "faulty" data rather than reformulate the basic model. Finally, because most serious physical and biological modeling projects involve an interdisciplinary effort, there is always the possibility of serious lack of communication and cooperation due to differences in vocabulary, goals, and attitudes. Often mathematicians are only looking for a "problem" to which their already highly developed theory and techniques apply; i.e., they are in possession of a "solution" and in search of the "problem" they have solved! On the other hand, physicists and biologists can be too impatient with the mathematicians' desire to hypothesize rather implausible mechanisms and relationships (which can sometimes lead to exciting new perspectives about a phenomenon!)

Finally, we turn to the question of how one appraises a specific modeling attempt. There are a number of criteria that one might use. Among those proposed by various authors are the suggestions that a good model should: fit data accurately; be theoretically consistent with the real system; have parameters with physical meaning which can be measured independently of each other; prove useful in prediction; not so much explain or predict, but organize and economize thinking; pose new empirical questions and help answer them through the iterative process; help us understand the phenomena it represents and think comfortably about them; point to inadequacies in some way of available data. It is clear, though, that for a modeling investigation to be deemed a success, it must have enhanced our overall knowledge and understanding of the phenomena in question. As one of our students (having been attacked by other students for some rather unorthodox and, at the time, unsupported hypothesis about mechanisms) noted in defending his efforts, "We learn little indeed if the models we build never stretch our understanding, but only tell us what we already feel is safely known."

In concluding our philosophical remarks, we remark that one can distinguish between at least two basic types of scientific models: *descriptive* and *conceptual* models. Descriptive models, those designed to explain observed phenomena, will be the focus of our attention here. Conceptual models, models constructed to elucidate delicate and difficult points in some scientific theory, are often used to help resolve apparent paradoxes involving two descriptive models. Conceptual models do not appear widely in the biological literature since in many cases basic descriptive models are still under development.

1.2 The Scope of the Book

For the past several years, the authors have developed a two-semester modeling course sequence based on fundamental physical processes: heat flow, wave propagation, fluid and structural dynamics, structured population dynamics, and electromagnetism. Among the specific topics covered in the course were thermal imaging and detection, dynamics properties (stiffness, damping) of structures such as beams and plates, acoustics and fluid transport, size structured population dynamics, electromagnetic dispersion and optics.

One of the major difficulties (theoretically, computationally, and technologically) in mathematical model development is the process of comparing models to the field data. Typically, mathematical models contain parameters and coefficients that are not directly measurable in experiments. Hence, experiments must be carefully designed in order to provide sufficient data for model parameters and/or coefficients to be determined accurately. In this context, a major innovative component of the course has been the exposure of students to specific laboratory experiments, data collection and analysis. As usual in such modeling courses, the pedagogy involves beginning with first principles in a physical, chemical or biological process and deriving quantitative models (partial differential equations with initial conditions, boundary conditions, etc.) in the context of a specific application, which has come from a "client discipline" - academic, government laboratory, or industrial research group, such as thermal nondestructive damage detection in structures, active noise suppression in acoustic chambers, smart material (piezoceramic sensing and actuation) structures vibration suppression, or optimizing the introduction of mosquitofish into rice fields for the control of mosquitos. The students then use the models (with appropriate computational software - some from MATLAB, some from the routines developed by the instructors specifically for the course) to carry out simulations and analyze experimental data. The students are exposed to experimental design and data collection through laboratory demos in certain experiments and through actual hands-on experience in other experiments.

Our experience with this approach to teaching advanced mathematics with a strong laboratory experience has been, not surprisingly, overwhelmingly positive. It is one thing to hear lectures on natural modes and frequencies (eigenfunctions and eigenvalues) or even to compute them, but quite another to go to the laboratory, *excite* the structure, *see* the modes, and *take* data to verify your theoretical and computational models.

Indeed, in writing this book, which is based on this experimentally oriented modeling course, the authors aim to provide the reader with a fundamental understanding of how mathematics is applied to problems in science and engineering. Our approach will be through several "case studies" problems which arise in industrial and scientific research laboratory applications. For each case study problem the perception on why a model is needed and what goals are to be sought will be discussed. The modeling process begins with the examination of assumptions and their translation into mathematical models. An important component of the book is the designing of appropriate experiments that are used to validate the mathematical model's development. In this regard, both hardware and software tools, which are used to design the experiments, will be described in sufficient details so that the experiments can be duplicated by the interested reader. Several projects, which were developed by the authors in their own teaching of the above mentioned modeling course, will also be included.

The book is aimed at advanced undergraduate and/or first year graduate students. The emphasis of the book is on the application as well as what mathematics can tell us about it. The book should serve both to give the student an appreciation of the use of mathematics and also to spark student interest for deeper study of some of the mathematical and/or applied topics involved.