

Chapter 1

The mathematical analysis of physiological systems: goals and approaches

Why should anyone bother with mathematical analysis of a physiological system? This is perhaps as much a philosophical question as a scientific one, and the answer at this point will be somewhat philosophical. We can do no better than to draw on the views of the physicist Eugene Wigner (1960) in his classic essay “The Unreasonable Effectiveness of Mathematics in the Natural Sciences,” where he makes the case “that the enormous usefulness of mathematics in the natural sciences is something bordering on the mysterious and that there is no rational explanation for it.” Quite a statement from one of the key physicists of the 20th century, but it serves well to show the awesome power of mathematics in describing physical reality.

Of more practical interest, a mathematical description of a system serves to put our knowledge of that system into a rigorous quantitative form, that is subject to rigorous testing (Robinson 1977). In this sense a mathematical model serves as an embodiment of a hypothesis about how a system is constructed or how it functions. The model forces one to focus thinking and make inexact ideas more precise. You may think that you know how a system works, but creating a model of the system truly puts that understanding to the test.

This book will deal with models of systems and their behaviors in a broad sense: is the system random or deterministic, linear or nonlinear, for example. These are broad areas of categorization, but they are also crucial questions that should be addressed before more finely structured hypotheses are evaluated. A major goal in this work is to identify these properties through the use of appropriate computational tools. Answering

these questions can not only improve one's understanding of the system but also improve the ability to make diagnoses and apply the appropriate therapeutic intervention in case of pathology.

One type of behavior – *chaotic* behavior – will be of particular interest. The concept of chaotic behavior is appealing because it shows that complex behavior can arise from simple models, lending hope that complex physiological behavior might have simple underlying laws.

1.1 The goals of mathematical analysis in physiology

Anyone reading this book probably does not need to be convinced of the value of a mathematical approach to physiological analysis. Nevertheless an outline of our goals – as related to the tools presented in this book – will give a sense of the direction in which we are heading.

We might list as the first and most fundamental goal that of simply understanding how a system works. This goal is pure and laudable, and corresponds with what many investigators consider to be the defining characteristic of a true scholar: learning for the sake of learning. Of course this is not always appreciated by the public nor by those who fund research, but it is important and undoubtedly continues to be a prime impetus for many researchers, whether admitted or not.

On a more practical (and fundable) level, there is the goal of being able to predict the future behavior of a system. Weather prediction is the prototypical example here, and indeed this example holds a prominent place in the history of nonlinear systems analysis. More correctly, we might say that it has a special place in *modern* nonlinear systems analysis – the use of computers and computational tools to analyze systems that are beyond the reach of conventional analytical methods. By this is meant roughly that they do not have closed-form solutions that can be obtained by solving differential equations, but rather their solutions must be found by approximation methods on a computer. We must be careful to make this distinction because, more than a century ago, mathematicians were already making great strides in the analysis of nonlinear systems. The work of Henri Poincaré is most often cited in this regard. It is often said that Poincaré was the last true mathematical

generalist – that is, he was able to grasp and make contributions to all then-extant subfields of mathematics, before specialization became rampant. Some of his most important efforts related to nonlinear systems include work on the fundamentals of topology and celestial mechanics. He was perhaps the first to point out that small uncertainties in the initial conditions can lead to very large uncertainties as a system progresses in time. This is now one of the hallmarks of chaos: sensitive dependence on initial conditions.

He is also, by the way, the author of a set of fine books on the nature of mathematical investigation itself. These books are interesting for the insight they give into the mental processes behind mathematical discoveries. Like watching a great musician or athlete, one might find these works to be either motivational and inspiring, or depressing once the realization sets in that there are people whose abilities are well beyond the upper tail of the normal distribution.

Another distinguished early figure in computational mathematics is John von Neumann, one of the great Hungarian scientists who came to the U.S. early in the 20th century and made major contributions to many fields of mathematical physics, including the calculations behind nuclear weapons and nuclear energy. (This, combined with his ground-breaking work on game theory and his vocal disdain for Soviet communism, made him the model for Dr. Strangelove in the movie of the same name.) von Neumann contributed to the design of the ENIAC, the first electronic digital computer (although the ABC computer by John Atanasoff also has claim to this title), during World War II. In the course of this work, he thought deeply about the logical foundations of computing itself, and co-wrote a key report that described what has come to be known as the “von Neumann machine”: a computer that stores its instructions (software program) internally and makes no hard distinction between stored data and stored instructions, so that the computer itself can operate on its own instructions as easily as it can operate on data (von Neumann 1945). This of course describes virtually every computer that has been made since that time, and has made possible high-level languages and compilers, as just two examples. He was quick to recognize that many intractable problems of mathematical physics could only be solved by recourse to computer approximation methods, and laid out these ideas during the

early years of the electronic computer (von Neumann *et al.* 1995, Goldstine 1980).

But let us return to the case of weather prediction. In the early 1960s, Ed Lorenz at MIT was carrying out a numerical investigation (i.e., computer solution) of a set of three partial differential equations that formed a simple model of atmospheric convection. He had run his simulation and found an interesting result, so he re-entered the same starting values and ran the program again. To his surprise, he found that after a short time, the old and new solutions greatly diverged. What had happened? It turns out that when he re-entered the values, he rounded them off to three rather than six decimal places – a seemingly insignificant change, and one certainly below the precision with which meteorological measurements could be made. In any case, it was expected that such a small change in initial conditions might lead to a slowly-increasing difference between the two computer runs, rather than the large non-proportional change that actually occurred. The recognition that this simple nonlinear system could produce such unexpectedly complex behavior is widely credited as the birth of modern chaos theory.

The trajectories of the system's variables were plotted in a state space (this means of examining system behavior is the central theme of this book). This created a finely detailed structure known as an *attractor* for technical reasons that we will cover in due course. The work was published in a classic paper which is often cited but that likely few have read (Lorenz 1963) – indeed it is the much later references to this finding in more general works on nonlinear dynamics to which most writers refer. The results gave rise to the notion of the “butterfly effect,” whereby a butterfly flapping its wings in one city today can influence the weather thousands of miles away a week from now. The shape of the Lorenz attractor coincides with the butterfly image. There are many reports of this now-legendary event, including one written by Lorenz himself (Gleick 1988, Lorenz 1996).

From the ability to predict the future course of a system's behavior, the related goal of control follows naturally. Once we can predict the future, it is natural to want to try to control that future, in order to guide the system to a preferred state or keep it away from undesired states.

These basic goals of understanding, prediction, and control, are closely related to the practical clinical goals of diagnosis and treatment, which underlie much of the rationale for research into physiological systems. Understanding a system's behavior and how it is altered under pathological conditions is of course a form of diagnosis, and "control" is effectively just another word for "treatment."

Some of the most advanced work on applying nonlinear system analysis to understanding the course of disease is to be found in the area of epidemiology, while much progress in physiological control is in the area of cardiology. We will return to these topics in later chapters.

Significant progress toward the goals described here can be made with the tools that will be presented in this book, and in particular with the state-space approach that is the guiding theme of the work.

Physiology, and the life sciences in general, has come a long way since the time of an anecdote related by the mathematician Ulam (1976, p. 160). Speaking to a group of biologists, his every attempt to posit some general statement about biology was met with a certain contempt and the reproach that there was an exception in such and such special case. "There was a general distrust or at least a hesitation to formulate anything of even a slightly general nature." Things have changed considerably, although the discovery of overriding principles in the life sciences has not occurred to nearly the extent as in physics, for example. While the computational tools presented in this book can provide some common ground in terms of how to approach some near-universal issues in physiology, the greater hope is that the concepts of nonlinear dynamical analysis themselves will help to establish a common way of *thinking* about such systems (Glass 1991).

1.2 Outline of dynamic systems

By *dynamic system* we mean one that can be defined by a set of variables whose values change with time. (Variables, not parameters – see below.) The variables that thus describe the course of the system's behavior as a function of time are known as *state variables*, because collectively they describe the *state* of the system at any given time. This

powerful concept leads us to the *state space*, where the values of the state variables trace out trajectories over time. An example of a dynamic system is the regulation of car speed while driving. Clearly an automatic speed-control system fits the description of a dynamic system, but the interactive “human-in-the-loop” type of manual control is a dynamic system as well. Some of the state variables in this case might be instantaneous speed and foot pressure on the accelerator pedal. These are related in a direct but potentially complicated manner. A simple model might consider speed to be proportional to pedal pressure, while a more realistic model might make this a nonlinear function and include time delays resulting from engine dynamics and neural lag. Even more detailed models could include engine dynamics explicitly, as well as air pressure against the front of the car. Knowing which variables are important to include in the model is one of the keys to successful modeling, and this is in many cases more an art than a science. Indeed the realization that some previously ignored quantity actually is an important state variable is one way to gauge progress in modeling.

We have described some of the state variables of this model. The interactions between the state variables are the essence of the model. Often these interactions are described in terms of differential equations (or difference equations if time is in discrete units rather than continuous). If you know these equations, you have tremendous knowledge about the system. If you do not know these equations, your knowledge is limited, and you typically will have to study and describe the system in terms of the variables that you can measure. This is where the material in this book will be most useful. The ability to proceed from these measurements and analyses on the variables, to the equations, is very difficult in general. We will have occasion to touch on this topic, for which no standard approaches yet exist, in Chapter 14.

The model above describes the mostly mechanical aspect of maintaining a given speed, once you have decided on what speed you want. The model can be expanded to include this decision process, now including such state variables as road conditions, expected time of arrival, confidence in the integrity of the vehicles, and so on. This is a legitimate model, but now the variables become harder to quantify and

come under the domain of psychology rather than the physiology of sensorimotor control.

A more purely physiological example is the control of cardiac inter-beat intervals (heart rate). Here the important state variables are probably too numerous to list, and include the concentrations of several chemicals in the blood, metabolic rate, mental state, body temperature, and many others. Fortunately, some of these variable are more important than others, especially if the domain of the model is restricted – for example, if it is desired to know the effect of one type of drug or of a specific electrical intervention (external pacing). Such a practical restriction, and the tight coupling between many of the variables, means that significant progress can be made by considering some manageable subset of the entire set of state variables.

With some cleverness, it is possible to describe as dynamic systems many behaviors that at first glance do not appear suited to this approach. Strogatz (1988) gives a playful example of the fateful lovers Romeo and Juliet. One state variable describes Romeo's feelings (love/hate) toward Juliet, and another state variable describes the feelings in the other direction. Based on the strengths of these feelings and the nature of their interactions, various interesting dynamic behaviors can be produced. It is an amusing exercise to consider what other state variables might be involved in this system. (An accessible exposition of this example can also be found in the excellent textbook by the same author (Strogatz 1994).)

As you might imagine, defining the state variables and measuring their values is of crucial importance in modeling and analyzing these systems. In many cases – indeed in most cases that we will consider – it is in fact *not* possible to identify and measure all of these variables. We will study some powerful techniques that will allow us to investigate such systems mathematically even under these restrictive conditions, as long as at least one variable can be measured on the system over time.

In describing and analyzing systems, it is important to distinguish between *variables* and *parameters*. A parameter is a constant – a term in the equations that is fixed, as opposed to the variables, which change as a function of time to reflect the dynamics of the system. This issue is closely related to that of statistical stationarity, which loosely speaking

means that the statistics of a process do not change with time. If you consider something to be a parameter and in fact it varies over the course of the investigation, then the system has become nonstationary, and you should consider treating the parameter as a state variable.

Probably the best approach to this issue is first to decide on the dynamics that you want to study and model. If a quantity expresses these dynamics – if it changes with time in a manner that reflects these dynamics – then it is a state variable. If that quantity is fixed with respect to the dynamics in question, then it is a parameter. Clearly, what is a parameter and what is a variable depend on what is to be modeled or what behavior is to be analyzed.

As an example, in the case of heart rate, if it is desired to study the effect of a specific short-term physical activity, then other things should be kept constant so that they can be considered as fixed parameters – the subject should not eat during the experiment and it should take place quickly enough so that circadian fluctuations do not have a significant effect. On the other hand, if it is desired to investigate the impact of time of day on the effects of exercise, then time of day becomes a state variable. Time scales such as these constitute one major factor in distinguishing between parameters and state variables.

1.3 Types of dynamic systems – random, deterministic, linear, nonlinear

We can now begin to get to the heart of the matter, by describing and classifying dynamic systems. A very broad categorization, which is nonetheless quite useful for our purposes, considers *randomness* and *linearity*.

While intuitively the notion of randomness is clear to most of us, a rigorous definition is tricky. A *deterministic* system is the opposite of a random system. With a deterministic system, given perfect knowledge of the initial conditions and the system dynamics, the future behavior for all time can be determined. The French mathematician Laplace was a great believer in the concept of determinism as a ruling force in the universe, and made the claim that if given the present positions of all objects and

the forces acting on them, their entire future course of motion could be completely and unambiguously determined. He was a true proponent of the power of Newtonian mechanics. Most systems studied by engineers are treated as deterministic, with noise considered as a separate nuisance random process.

The great value of a deterministic system is that, given sufficient knowledge about the dynamics and the values of the state variables at a given time (the state of the system at that time), the future course of the system can be predicted with some degree of accuracy. A random system, on the other hand, is ruled to some extent by chance. Given complete information on the dynamics and initial state, it is not possible to predict precisely the future course of the system (although it may be possible to determine the statistics of the future course – that is, the likelihood of the system being in particular states at particular times). One aspect of the rise of interest in nonlinear systems analysis is the recognition that very complicated behavior – that which is apparently random – can arise from a relatively simple deterministic system. This is another hallmark of chaos, discussed below.

Although noise in the real world is ubiquitous and is the bane of most every experimenter, obtaining true randomness in numerical simulations and computations is much more elusive. This issue arises in the methods covered in this book because it is often necessary to generate random numbers, or to shuffle data into random order, as part of a test for randomness. In the 1950s, the need for such numbers was sufficient that a book was published just for the purpose of providing random numbers (RAND 1955). Of course, computer random number generators (RNG) are available today; these are based on deterministic equations and rely on the fact that they have a very long period – that is, the values they produce will typically repeat, but only after an extremely large quantity of numbers has been generated. In addition, the RNG must be initialized with a “seed” value, and if the seed is not changed the same sequence of “random” numbers will be generated. This can be useful when debugging a program, but for general use some means of randomizing the seed should be used, such as creating it from manipulations on the date and time at the instant that the program is run. A useful source of truly random numbers, which seems to be as random as it gets, is

radioactive decay. There are web sites from which one can obtain random numbers based on times of emission of radioactive particles, and such numbers have passed many tests of randomness (see Appendix).

An extension of the points raised above is that no finite system is truly random. Understanding this point is crucial to properly applying the computational methods in this book. A basic concern in many situations is whether a system is random or deterministic. In fact, given a finite data set, a deterministic system can always be constructed that will generate that particular data – the system may have as many parameters or state variables as the data set, but it will reproduce that data set. This of course is a completely uninteresting type of model, and in general we require that a model be able to reproduce a data set while being as simple as possible. This might be a ridiculous example, but the point is subtle, especially in cases where there is a mix of deterministic and random properties.

Let us now move on to linear versus nonlinear systems. A linear system is defined by two properties: scaling and superposition. Scaling means that, if a given input produces a given output, then doubling the size of the input will double the size of the output, and so on for any arbitrary scaling of the input:

$$u(t) \rightarrow y(t) \Rightarrow au(t) \rightarrow ay(t)$$

Superposition means that, if one input produces a given output, and a different input produces another output, providing the sum of these two inputs to the system will produce as output the sum of the two individual outputs:

$$\left. \begin{array}{l} u_1(t) \rightarrow y_1(t) \\ u_2(t) \rightarrow y_2(t) \end{array} \right\} \Rightarrow [u_1(t) + u_2(t)] \rightarrow [y_1(t) + y_2(t)]$$

These properties make linear systems mathematically tractable, and a vast body of work has been devoted to the analysis of linear systems of many kinds. Even so, it should be recognized that, in the real world, there is no such thing as a true linear system. Scaling implies that a system will respond in proportion to the size of the input, but clearly this cannot happen for arbitrarily large inputs. Eventually, an input can be applied that is so large that the system cannot respond in a linear fashion

– the system may saturate or even fail, and in general will produce a distorted output. Thus all physical (and physiological) systems are inherently nonlinear. Nonetheless, there is often a large range of inputs (amplitudes, frequencies, waveforms) for which the system will respond in a linear fashion, or close to it. The trick in carrying out a linear analysis is to know these limits and to restrict the inputs to this range.

In all cases – whether it be an assessment of randomness versus determinism or of linearity versus nonlinearity – one can see that any categorization must take into account the domain over which the analysis is to take place. One must never lose sight of this fact, either during the investigation itself or in its later interpretation.

1.4 Types of dynamic behaviors – random, fixed point, periodic, quasi-periodic, chaotic

Having discussed some ways to categorize *systems*, we now turn our attention to categorizing different system *behaviors*.

Random behavior is, as one might expect, unpredictable. But as mentioned above, once a given data set (typically a time series) has been obtained from a system, the data are no longer random but fixed. Thus the question of randomness in a data series is a relative one, and the methods in this book are designed to give insight into potential mixtures of determinism and randomness. Since noise is present in all physical measurements, determining if randomness is inherent in the system dynamics or in the measurement process is not always straightforward.

Among deterministic behaviors, a *fixed point* is the simplest. It is just what its name implies: a point or state of the system (set of variables) that, once attained, is not departed. A fixed point is sometimes a degenerate state of little interest – a pendulum with a frictional bearing, for example, will have oscillations that slowly decay until the pendulum comes to rest at the fixed point of hanging straight down (zero position, zero velocity), never to move from this state unless externally perturbed. There are more interesting fixed points. One simple nonlinear system is the *logistic equation*:

$$x(n+1) = \mu x(n)[1 - x(n)].$$

This equation is a simplified model of, among other things, the population of an organism from generation to generation, in the face of limited resources. The population at generation n is given by $x(n)$, and the equation shows that the population will grow from one generation to the next until it becomes too large for the available resources (at $x(n)=0.5$), and then it will decrease, until it again is small relative to the resources, and this behavior will alternate (though not always in an orderly way) between these two modes. A fixed point for this system occurs when the population $x(n)$ does not change from one generation to the next: $x(n+1)=x(n)$. The solution to this is easily found: $x^*=1-(1/\mu)$, where the asterisk indicates that it is a fixed point. The dynamics of this extremely simple nonlinear system are fascinating, and some of the original work in bringing this to the attention of the general science community was done by R May (1976).

The next most complicated type of system behavior is *periodicity*. Mathematically, periodicity with period T is expressed as:

$$x(t + T) = x(t).$$

This means that the behavior repeats itself after time T , and then repeats again and again. The classic example of periodic behavior is *simple harmonic motion*, often represented by a theoretical undamped pendulum, which will swing forever if not perturbed.

Nonlinear systems can exhibit a form of periodic motion termed a *limit cycle*, which is an *isolated periodic trajectory* of the state (Strogatz 1994). It can be stable, in which case nearby states are attracted to it, or unstable, so that nearby states are repelled. Various nonlinear oscillators have limit cycles as attractors (Andronov *et al.* 1987). Simple harmonic motion from a linear system, for example from a spring-mass or pendulum, does not produce a limit cycle, since nearby points in state space belong to oscillations of different amplitudes and are neither attracted to nor repelled from the limit cycle: the periodic orbit in this case is not isolated.

A modification of periodic behavior is *quasi-periodicity*, which is a combination of periodic behaviors that have incommensurate periods – that is, their periods cannot be expressed as a ratio of integers. An example is two sine waves, with periods of 1 and $\sqrt{2}$:

$$\sin(t) + \sin(t/\sqrt{2}).$$

This signal is not periodic because, each time the first sine returns to its starting value of zero, the second sine takes on a different value, and the two sines never “match up” because nt and $nt/\sqrt{2}$ (where n is the number of cycles of the first sine) will never be equal to each other for any integer value of n .

Finally, we come to the behavior that motivated this entire field: *chaos*. For a long time – decades if not centuries – the behaviors listed above were recognized as the only ones possible from a dynamic system. Then came Poincaré, and Lorenz and his weather prediction, and nothing has been quite the same since. There are three defining features of chaos:

1. behavior that appears complicated or even random,
2. sensitive dependence on initial conditions,
3. determinism.

The important point is that chaos arises from a deterministic system, yet is so complex in appearance that it might be mistaken for randomness. It is easy to see the importance of this, for once it is recognized that a potentially simple deterministic system can produce complex behavior, a wide array of complex-appearing behaviors come under investigation with a new view toward identifying the underlying system as being deterministic. If the underlying system is deterministic, then it follows rules, and this opens a whole realm of possibilities for understanding and controlling the system.

We are careful in this discussion to distinguish between types of *systems* and types of *behaviors*. There is overlap, of course, as a random system can be expected to produce random behavior. But there is not in all cases a one-to-one correspondence between the two groups, as for example a nonlinear system can produce any of a variety of behaviors such as chaos and fixed points, depending on the system parameters and initial conditions.

1.5 Follow the “noise”

In 1932 Karl Jansky, a communications engineer at Bell Labs (which has since become part of Lucent Technologies) was given the task of

finding the source of radio static (noise) in transatlantic telephone circuits (which were carried over shortwave radio at that time, in addition to undersea cable). He determined that, although thunderstorms created much of the noise, there was another source, which varied throughout the day but was not precisely synchronized with the sun. He eventually determined that the source was the Milky Way galaxy, the variation being due to the fact that Earth is not at the center of the galaxy. This finding that stars and other astronomical objects emitted radio waves was the start of the entire field of radio astronomy.

Years later, in 1965, Arno Penzias and Robert Wilson, also at Bell Labs, made a similar discovery. They were looking for the source of noise in some microwave measurements, and they noted a constant low-level signal, without directionality or temporal variation. Little did they know at the time, this turned out to be the “cosmic background radiation” – a remnant of the big bang and convincing evidence for the big bang theory. For this they won a Nobel Prize in 1978.

The point to these stories is this: follow the noise. In these cases, noise turned out indeed to be noise, but the source of the noise turned out to be most interesting and unexpected. In the research that forms the basis of chaos theory, it is often the exploration of variability and apparent noise – random-appearing signals from physical and physiological systems – that has been the starting point for progress.

1.6 Chaos and physiology

Probably the greatest appeal of chaos for physiology is the simple observation that so much physiological activity is highly variable, appearing random or noisy. A chaotic system can appear this way as well, but there is an underlying deterministic structure. The possibility of bringing systematic order to such highly variable phenomena holds great allure and fascination. The ability to use a set of standard analytical and computational tools to do this only makes the appeal stronger.

Associated with this on the mathematical physics side is the growing realization that even simple nonlinear deterministic systems can exhibit chaotic behavior, and in fact chaos may turn out to be more the rule than

the exception in these systems. For example, it has been demonstrated that there are chaotic solutions to cellular membrane equations (Chay 1985, Chay & Rinzel 1985), which has spurred interest in finding experimental demonstrations.

Two main forces drive the interest in chaotic descriptions of human movement control. First, apparently random behavior can arise from non-random systems. Second, variable (random-appearing) behavior can have a functional role (Riley & Turvey 2002). Related to this is the realization – not exactly new but growing – that random noise can have a complex structure of its own, as for example Brownian motion and fractional Brownian motion (Teich & Lowen 2005). There may be optimal levels of random noise and deterministic chaotic dynamics that use the best features of both in tailoring overall system performance.

Conrad (1986) provides a list of some of the possible functional roles for chaos. One is the deliberate generation of diverse behavior, for a number of reasons including the facilitation of exploratory behavior. Another role might be the generation of unpredictable defensive behavior (butterfly motion is given as an example). A third possibility is that it is a metabolically efficient way to generate “noise” or variability, and so prevent the entrainment of different neural structures, so as to maintain flexibility and adaptability.

These ideas all touch on the notion of the “attractor hypothesis” as an appealing paradigm for the rapid and flexible storage and processing of neural information, with advantages such as the avoidance of local minima and systematic exploration. (Similar arguments have been applied to genetic variation and population dynamics: Emlen *et al.* 1998.) The term “attractor” will be defined, with many examples, in Chapter 4. For now, we can think of an attractor as a geometric pattern generated by some measured physiological signal, such as a closed loop generated by plotting velocity versus position during periodic behavior. A more complex example is the higher-dimensional pattern formed by appropriate manipulations of electroencephalogram (EEG) signals. An attractor is an appealing depiction because it represents a type of stable definable behavior that is, if generated by a chaotic system, very flexible and easily altered. Chaotic systems can lead to very interesting attractors.

A paradigmatic though simple study of rhythmic limb movement demonstrates one of the characteristics of studies in this field (Mitra *et al.* 1997). Is the resulting pattern, for example in a graph of velocity versus position, due to an essentially simple periodic oscillation with additive noise, or to an inherently more complicated set of dynamics that are not adequately captured in a simple two-dimensional plot? While the question is still open, and indeed continues to drive much research, it is fruitful to consider the interactions and combinations of variability and determinism (Riley & Turvey 2002), in particular with the view that “more variable does not mean more random.” Indeed variation from trial to trial or moment to moment may provide more information than the more time-invariant aspects of a behavior. (Chapter 16 has more on this.)

Another example involves recordings from olfactory bulb EEG (Skarda & Freeman 1987). The authors claim that multiple simultaneous attractors encode different odors, which allows for rapid access to stored odors without the danger of entrainment into local minima. There is rapid convergence of ongoing chaotic activity to an attractor upon inhalation, yet the ability to acquire new odors/attractors. The attractors are not “fixed points” but dynamic entities reflecting continuing neural firing patterns and flexibility even in the case when an odor has been identified. Although the work is based on some simple chaotic measures which might be called into debate in light of subsequent advances, the “chaos paradigm” still resonates with appealing possibilities for the description of brain function. It might be considered a next step in brain modeling, after the digital computer paradigm and the connectionist (neural network) paradigm.

One counterintuitive finding along these lines relates to the “complexity” of cardiovascular dynamics in aging populations (Kaplan *et al.* 1991). At this point we, like the authors of the cited study, use the term “complexity” in a rather loose manner to mean “more noise-like” and “less regular.” This study found that complexity decreased with aging. In other words, there is such a thing as “healthy variability.” A decrease in this variability can indicate a decrease in health. Based on this and similar results the interpretation came about that variability can endow a system with flexibility and hence the ability to respond and adapt to environmental stressors. (Whether this variability is random or

chaotic is a key question which will be addressed in various places in this text.)

Clearly these are largely philosophical issues. They serve to demonstrate some of the great appeal of “chaos theory” in physiological modeling. Our aims in this book are somewhat more mundane. Although we will touch upon larger interpretations when appropriate, and attempt to provide background and historical perspective at times, the main thrust will be on the correct understanding, implementation, and interpretation of computational tools that can help to visualize and quantify nonlinear dynamics in physiological systems. An additional application that has been little explored to date is the use of these computational tools to test and validate mathematical models (Shelhamer & Azar 1997).

One of the hopes of the recent application of nonlinear dynamical methods to physiology is that they can provide a general mathematical framework that has been missing from this traditionally rather qualitative field (Glass 1991). In the main section of this book we will see some tools that can be used to explore noise-like signals, determine if they are truly random or have a deterministic component, and allow us to draw some conclusions about the underlying system. In the rush to apply these methods, there have undoubtedly been many cases in which the apparent ease of the computational procedures has outpaced the users’ understanding of the underlying mathematics (May 2004); it is with some hope of preventing further damage along these lines that this book was written.

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