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Physiology is Not an Appendage of Anatomy Illustrated with Deterministic Chaos

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PHYSIOLOGY ORGANIZATION

We call ourselves physiologists, but early contributors to the field would not have used the name. Through recorded history curious people have had an interest in both their own and animal bodies. Surface structure was most obvious, but trauma exposed internal structures to which names were attached. Physiology might be considered to have come into existence with the first asking of the question "Here is a structure—what does it do?" With primitive tools that question was applied to gross structures while some of the answers were, to say the least, imaginative. More formal study grew rapidly through the 19th century, and by the beginning of the present century the more scholarly schools of medicine recognized the relevance of Physiology by establishing both courses and chairs in the area. Those early courses taught the then current knowledge which was largely function of organs and organ systems.

At this point a study of medical education by Alexander Flexner lead to advocacy of medical curricula starting with academic education in a few basic disciplines. His influential report was followed by an accreditation program that purged the American medical education system until only about 10% of the medical schools survived. Inappropriate curricula were almost eliminated as well as curricular innovation. Courses offered and even course organization became quite uniform across the nation's schools. Physiology was locked into an organization that fit the then current knowledge of the distinctly different functions of individual organs. As can be seen in the tables of contents in physiology texts of the era (*e.g. Howell's Textbook of Physiology* lst through 14th editions 1905-1940) we find that most chapters were associated with particular giblets such as heart, brain, kidney, digestive tract which along with muscle determined the content of individual chapters.

While in this period research was recognized as essential for good teaching, as time passed there was a growing dichotomy between the research being done by professors and the organization of their teaching. By midcentury basic knowledge had changed but physiology organization had not. Physiological chemistry was now to be found in separate departments called Biochemistry, and most of the reactions being studied were not confined to particular ogans. Joint departments of physiology and pharmacology had largely divided with the absorption of departments of Materia Medica. Purgatives, bichloride of mercury, phenol and tincture of iodine were losing favor while there was a growing interest in drugs that had known effects on specific metabolic processes, processes that often were not restricted to individual organs. In physiology functions like homeostasis were recognized as central to function. The general importance of ion balance to excitable tissues was finally recognized. One deviant even proposed that calcium ion was important. These are but examples of the trend in basic medical sciences to look into the internal working of cells where much common ground was found across different organ systems. Finally, the teaching followed the research trend. Biochemistry was now teaching topics of particular reaction cycles, energy transfers, and physical biochemistry instead of just topics like digestive chemistry and respiratory chemistry. Even in anatomy more time was being devoted to study of cells and tissues and less to visceral organs. The newer physiology books had chapters on cross organ topics such as body fluids, temperature regulation and cellular physiology. The organ based organization of the basic sciences was becoming diluted but was still visible in the textbooks and courses. If the trend continued one might predict that the organ system organization might disappear entirely.

Some changes were occurring in the study of the nervous system that lead to a reversal of this trend. Neuroanatomy had long taught morphology and the Sherringtonian examination of functions dominated neurophysiology. John Fulton, one of Sherrington's students, however, advanced the use of physiological stimulation and recording to trace pathways in the nervous system. With these experimental tools he and his associates were able to identify association between functions and nervous system locations that had not been recognized from the experiments of pathology. This work was advanced in 1938 with the founding of the *Journal of Neurophysiology* by John Fulton. this journal was widely read and functional mapping grew rapidly. Microtomes soon became standard equipment in neurophysiology labs. Neuroanatomy research was also drastically altered. Within a decade oscilloscopes had appeared in most neuroanatomy laboratories. The results of functional tracing of tracts became a major part of both neurophysiology and neuroanatomy courses. An unplanned redundancy exploded in content and soon dominated the separate courses. In those schools where neurophysiology was taught before the Neuroanatomy course, it became necessary for neurophysiologists to devote much of their limited time to introducing anatomical structure, leaving less time to teach about the growing knowledge of neural dynamics. The problems caused by this overlap were widely recognized, but teaching time was still important to departmental status and neither department was willing to give up any of their time or topic.

By mid century one solution was discoveded and put into effect at Western Reserve University. Material related to the nervous system was gathered into a single course called neuroscience. Then the whole basic science curriculum of this school was abruptly reorganized as planned around organ systems instead of by traditional departments. This "unified teaching" innovation spread widely until by 1975 almost all of the North american medical schools had tried some variation of teaching by organ system. In fact, this organization took on an importance it had never before had. The excitement of innovation also generated a new enthusiasm in both teachers and students and many of us developed new perspectives in our areas of interest. At this time some people suggested that physiology as a separate discipline was moribund and would be replaced by elements in this new teaching structure. Supporting this prediction, the Neuroscience Society was founded in 1969 and much of neurophysiology quickly disappeared from the American Physiology Society function. Will the rest of physiology disappear into other organ based fields?

Coincidental with this change in teaching, the national funding of research was growing rapidly, and definition of research areas was becoming institutionalized beyond previous experience. With a strong overlap of people involved in planning, the teaching and research developments appreciably influenced each other. Medical basic scientists were increasingly teaching about one organ system and at the same time doing research with important support from an institute identified with that same organ system. Even an individual interested in a function common to many different organs found it expedient to choose a source of funding associated with some particular organ and this choice, in turn, was likely to influence personal teaching assignments. It appeared that basic research and teaching were becoming unified in the same structure that defined the clinical specialties. Then something happened!

Before 1980 schools began to abandon the organ system modules and return to traditional departmental curricula. This reverse trend has deveoloped more in areas other than the nervous system study where two-thirds of the schools still retain neuroscience ourses instead of returning to separate courses of neuroanatomy and a neuro section in physiology. as in any counter revolution the causative factors were many. Certainly some individuals wanted departments to regain controls from the teaching modules. The changing knowledge base, at least in anatomy, biochemistry and pharmacology, also played a part. The new knowledge of structure at the electron microscopic level, the newly identified chemical principles, the drugs designed to alter fundamental cell processes all have more aspects in common across organ systems that those that are restricted to a particular ogan. This changing content is reflected in textbooks that have appeared since the redevelopment of department segmented teaching. Thus, currently both pharmacology and biochemistry texts can be found with no chapters identified with particular organ systems. Presumably anatomy texts with continue to be organized around anatomical divisions, but even there increasing emphasis is being placed on common subcellular principles. The texts are each organized around principles of the individual fields.

Physiology textbooks, including those American texts used in Korea, still retain a significant partitioning along organ system lines in spite of the growth of information about function that crosses organ boundaries. Thus, in research, since 1950 both control system concepts and molecular biology have joined that type of broadly applicable information which was recognized before, but these new topics are still forced into some organ system title for teaching. it appears that major parts of modern physiology are not easily fitted into the way its teaching is organized. in spite of tradition, it seems that it is now time to reexamine the organization we have inherited from historic accident and see if the study of physiology would not be better served by being organized in a new and functionally planned way. Topics should not be eliminated but brought together in functionally instead of spatially related groups.

If done in time, a thoughtful reorganization of teaching and research might avoid the type of politically based changes we see in the history of physiology. One possible, but undesirable alternative is the further fragmentation of our research and teaching by loss of additional functions to new societies and courses organized around those special topics. Even worse, physiology might suffer illogical abandonment of teaching of important information about gross functions following a ċoud d'ėtat' by some frustrated group who rightfully find the organ system structure inappropriate for dealing with their also importat functional interests.

Alternate organization

The question remains, "Which of many alternate organizations could be better?" If we see physiology as just a list of independent facts, then organization is relatively unimportatnt but a dictionary arrangement might be the most convenient. The items in a dictionary need not be related to each other or to a common topic. A dictionary can accommodate any desired topic, but its organizer could as well exclude any topic. On the other hand, if there is some unifying principle then the collection of facts may constitute a subject worthy of both a collective name and survival. The usual defintion of Physiology as the study of and knowlege about function in living systems has always provided such a unifying principle, but long ago that topic grew far too large to be used as a single basis for teaching or research. Subdivision into manageable fractions is the practical necessity that drove the organ system plan and is still inescapable in any new organization that could be practical, yet the basis of that old division is not necessary.

Although Physiology is rooted in several basic disciplines like Anatomy, Chemistry, Physics, Mathematics and Biology, the central theme of function can continue into functional branches that are fed by but not simple extensions of the roots. Sinc function is the central theme of Physiology, the unity of the subject would be better shown by and organization in which all major branches were distinguished by functional classes rather than chemical, anatomical, genetic, mathematical or physical criteria. I see no reason why an organization around functional areas could not provide a logical place for all topics that rightfully fall in the domain of Physiology including both those that now are fitted into organ system classes and those that do not comfortably fit there. In this form the terminal leaves of the organization will commonly overlap with more

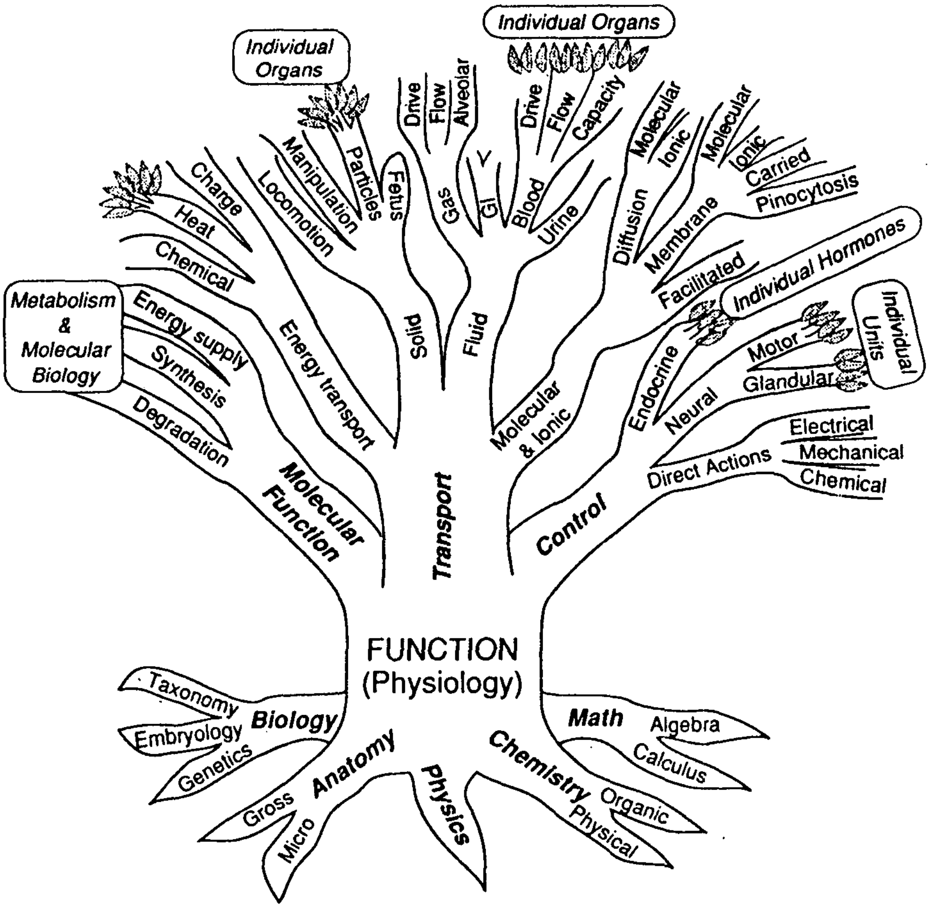

Fig. 1. The organization of physiology around a central trunk of function, rooted in many other disciplines and branching into specialized subdivisions. Chemical functions, transport functions and control and communication functions are relatively unified topics and each has a considerable base in common principles and each is largely separable from the other major branches. More flexibility is to be found in the further branching of this tree.

central topics of other fileds. On the other hand, when the overlap with anatomy is seen to be central to physiology, it would appear that Physiolgy is, in fact, a sub-branch of Anatomy. Further, in that from ther is no place for uniquely Physiological topics except as they derive from inerests of Anatomy.

I shall identify three major branches of physiological function that each encompasses a considerable body of well established and general knowledge while together they seem to span all of Physiology. These are: 1) molecular functions, 2) transport functions and 3) functional controls and communication (Figure 1). Each of these main branches can be subdivided successively into further functional branches before finally reaching the terminal leaflets of individual details. The final leaflets then may represent anatomically separated issues like the circulatory details in a particular organ, biodegradation of a particular molecule in the liver or functional limits of a particular organ controller. Vascular, interstitial and transmembrane transport have more common function and principles than the chemistry, circulation and control of a single organ. Although in Figure 1 a few branches are sketched in all the way to the final leaves only someone who has climbed extensively in a particular part of a tree can identify details of the branching to be found there. The tree illustrated here has a number of problems in its peripheral branches. Thus the multiple transport mechanisms in a nephron are not brought together automatically. However, this type of organizational problem is less common and less severe with function centrally located than with structures in the center where nutrient delivery to heart muscle falls into a different division from nutrient delivery to skeletal muscle.

While investigators need to know the material from the parts of several disciplines surrounding their own area of interest, their field tends to be distinguished by the discipline in which their knowledge spreads farthest along adjacent branches. The trees of knowledge of differing disciplines will each have characteristic branch structure. Thus, to an anatomist the pituitary is next to the hypothalamus, to a physiologist it is related to the adrenal cortex and not far from control in the stretch relfex. While a biochemist describes its relationship to a glycoprotein of the placenta, a psychiatrist should recognize its relationship to sexual behavior as an ophthalmologist should relate it to visual defects and a pediatrician to abnormal growth. A well chosen tree of associations helps to define and distinguish each body of knowledge and to simplify its study. I feel that physiology has not yet clearly identified its natural tree and needs to do so before that tree has too many branches cut away.

Neurophysioloby organization

Many parts of physiology can be organized around function but does this also apply to neurophysiology where the case has been made so often that neuroanatomy and neurophysiology are inseparable? On the other hand, many aspects of nervous system function are either quite similar or identical to functions in other organs and systems. This includes most of the metabolic function of neurons and glia in spite of characteristic quantitative values and a few cases of qualitative specializations. Both the similarties and the differences tend to be lost in the separate courses of neuroscience.

Transport in the nervous system also has its similarities and differences from that in other organ systems. The circulatory transport has much in common with other circulation but its operation within a rigid chamber is an interesting and clinically important specialization that might be better taught than today, is easily lost between not being included with the cardiovascular system and not being neuronal function. Material transport between capillary and neurons also falls into one of these cracks both in teaching and research. This transport has had so little attention that it is hard to say whether its importance demands more study. On the other had, membrane transport has not been overlooked in study of the nervous system. There the loss has been to the rest of physiology. The electrical effects of ionic transport across membranes has been established in neurophysiology for at least half a century but did not contribute to understanding related effects in the kidney and gut until recently. this loss of decades in information transfer probably can be related to organ system barriers as shown by a public statement by a well known GI physiologist who said, "No one else can make any sense to what neurophysiologists do." Perhaps the 1991 Nobel prize in physiology and medicine will speed up the communication of new information about channels in membranes from where they are studied in neurons to those who study cell function in other organs.

The control and communication branch of biological function is dominated by neurophysiological studies even though the endocrine system is probably of comparable importance to these functions. By attaching muscle to the nervous system organization motor control is not isolated from neuroscience but still cardiovascular, respiratory, gastrointestinal systems have been severed from their controllers. Only by establishing the new field of neuroendocrinology has it been possible to retrieve the extensive overlaps between those separate organ systems. This combination still looks like another controller separated from its target. We may need alot more hyphenated names to hold together the future studies of nervous system functions.

Clearly much of neuroscience deals with function and could be returned to physiology even though these, like all other functions, can not exist without a physical substrate. An appreciably larger teaching block deals with spatial relationships and is clearly in the domain of anatomy. We are still left with the problem of how to deal with localization of function. When I examine this part of neuroscience I see no way that localization can be separated from a rather extensive study of the structure even though that structure is defined by function. We can hardly talk about a pathway in the abstract without relating it to the structures that bounds it. Likewise, a nucleus is not usually an isolated station in one functional path but has multiple contributing input paths and sends its outputs to multiple recipients. As recognized by the founders of neuroscience, it is clear that localization of neural function needs to be studied in the context of a relatively complete anatomical foundation. A division on the other side seems not to have been considered. Studies of localization are actually largely anatomical and only call on the identification of a particular function. Thus topics like signal dynamics, signal encoding, and logic functions are usually not considered as part of localization. Localization of neural function could be dealt with while making minimal reference to the functional details, a division that has been accepted by anatomists for nearly half a century. In those schools where physiology has reasserted a claim to study of the function in the nervous system, that claim can better be implemented without doing violence to overall teaching and research goals if the topic of neural function is ceded to anatomy. In that case structure no longer provides a basis for organization, the remainder to nervous system function can be organized in a logical manner even after localizations are extracted as illustrated by the following table to contents of a soon to be published book.

The Nervous System:
Its function and its interaction with the world

INTRODUCTION
TRANSMISSION PHENOMENA
INFORMATION INPUTS
RECEPTOR SELECTIVITY
ACCESSORY STRUCTURES TO SENSORY RECEPTORS
CONVERGENCE
EFFECTOR ACTIONS
FROM RECEPTION TO PERCEPTION
INFORMATION STORAGE
NEUROELECTRIC PHENOMENA
GENERATION OF MEMBRANE POTENTIALS
ALTERATION OF MEMBRANE POTENTIAL
CHEMICAL EFFECTORS
MECHANICAL EFFECTORS
TEMPORAL MODIFICATION
NEURAL NETWORK OPERATIONS
COMBINED NEURAL OPERATION

While it is still illogical to package neurophysiology separately from the rest of physiology this book meets requirements for current separation while illustrating the fact that even the neuro parts of function need not be organized on topics such as spinal cord, medulla, pons, cerebellum, etc. Properly the chapters of this book should be distributed within a more general organization of physiological functions.

You see here that there are no chapters defined by an anatomical location while each is related to a function. This means that the information about transduction in the retina is brought together with related information about transduction in the ear and skin receptors but is separated from the operationally quite different functions of the optics of the eye and mechanics of the ear. Perception of visual space is brought together with both tactile and auditory perception of space. Likewise it becomes quite natural in this organization to relate the similar membrane functions that occur in receptors, nerve fibers and synaptic junctions. In place of emphasis on location of function there is more space devoted to how the nervous system deals with information that changes over time. This unfamiliar organization has a place for all of the function usually covered in anatomically based neurophysiology and in addition has a logical place for inclusion of functions that are not localized.

DETERMINISTIC CHAOS

I shall illustrate neural function that is not localized by the relatively new area of neurophysiological research related to a topic called "Deterministic Chaos." I choose this particular topic for two reasons: 1) Most who have heard of it have not yet taken the time to understand it; 2) Some of its implications are of general importance to almost all areas of physiological research. In neurophysiology functions this topic falls under the heading of Network Operation, but it has implications to any biological system that continues to operate, producing future conditions that are, in part, dependent on its current conditions.

The name chaos in this context is not yet two decades old and application of its ideas to neurophysiology is even newer but its foundations can be traced back more than a century. The French mathematician, Poincaré, recognized that nonlinear differential equations could define very complex and unpredictable dynamic operation but with the exception of a few Russian theoretical mathematicians, working around mid century, very little attention was paid to his insights. It was still a surprise when an investigation of weather prediction operating on a digital computer, was found to be extremely sensitive to initial conditions. Investigators with related interests increased slowly through the 1970s until a best selling book, "Chaos," by a newspaper reporter, Gleick, caused interest to explode, Since, several groups in physiology and especially in neurophysiology started to look into application of these ideas to biology. Whether or not, as some claim, this concept is one of the three greatest contributions to science in the 20th century (along with relativity and statistical mechanics) study of biological function is a major area of relevance.

While most of us do not find the mathematical approach the easiest and most natural way to understand a biological function, this has been the way the subject of chaos has come to us. On the other hand, within familiar biological ideas it is possible to gain an insight into what it is all about without mathematical manipulations. We have been looking at biological feedback under one name or another since the mid 19th century; yet, within feedback characteristics are a major part of what looks strange when introduced as chaos. By extracting a fraction of the chapter on nerve network operations and pointing out already familiar details there under feedback, you will see that chaos is not an entirely new and strange topic to biologists but is mostly a reorganization of the familiar. Only a simple step further moves into understanding of chaos principles. The new emphasis, however, does reveal problems with some old and basic assumptions and demands attention to some functional topics that we have preferred to ignore.

CHAOS RELATED FRAGMENTS OF NEURAL NETWORK FUNCTIONS

...	
...	
Feedback	(ubiquitous)
...	
Negative	
...	
...	
Oscillation	(Emergent responses) (Phase plane graphs)
damped	(Information loss)
expanding	(Sensitive dependence) (Information generation)
limit cycle	(Nonlinear basis) (sustained oscillation)
chaotic change	(inherits from oscillate +) (deterministic) (>2nd order/intermittent) (complex/bounded) (unpredictable/not random)

The future of most systems is at least, in part, dependent on current conditions of the system but the feedback case is one in which the dependence is easy to manipulate. Further feedback is found widely in the nervous system and in most other biological systems so it is at least somewhat familiar to most of us. It is well known that under some circumstances a negative feedback system can exhibit oscillation that is not found in any of the parts but emerges from the operation of the whole. In a similar way chaos can emerge from the operation of quite simple systems in which the future depends on the past.

Many simple feedback systems will show brief and damped oscillation after an initial disturbance just as does a simple pendulum (Fig. 2a). In such a system, in spite of different initial conditions the oscillation still converges on the same final conditions. This relationship is conveniently illustrated on a so called phase plane graph (Fig. 2b) in which a magnitude is shown on the abscissa and the rate of change of that magnitude on the ordinate. As the magnitude changes over time the instantaneous point moves in a trajectories. Different starting conditions may be quite distinct with converging trajectories that remain distinct for some time but the courses eventually converge on, and are said to be "attracted" to, the same final point, losing all information about particular starting conditions. These damped oscillations occur when the signal fed back in one cycle is not enough to drive the next cycle to as large a response.

The feedback system, but not the pendulum, can easily be adjusted so that the signal feedback is more than enough to produce an increased size of the next cycle. In this case each cycle will be larger than the previous cycle and an expanding oscillation results (Fig. 3). With indistinguishably different inital conditions for different trials the expanding trajectories will move apart making clear distinctions between starting conditions that were not recognizable initially. Thus by the formal definition of information, new information is being generated in a completely deterministic system just as the damped oscillation lost information. This unpredictability or sensitive dependence on initial conditions is also a characteristic of chaotic systems but its basis is most obvious in the simple feedback case.

Between the expanding oscillator and the damped oscillator there should be an adjustment that gives sustained oscillation of constant amplitude. Since this calls for a perfect adjustment of feedback to what is called a gain of one it does not seem likely that a practical system will meet the requirement. However, the introduction of a non-linearity does make constant oscillation practical. For small amplitudes the system is adjusted to give expanding oscilla-

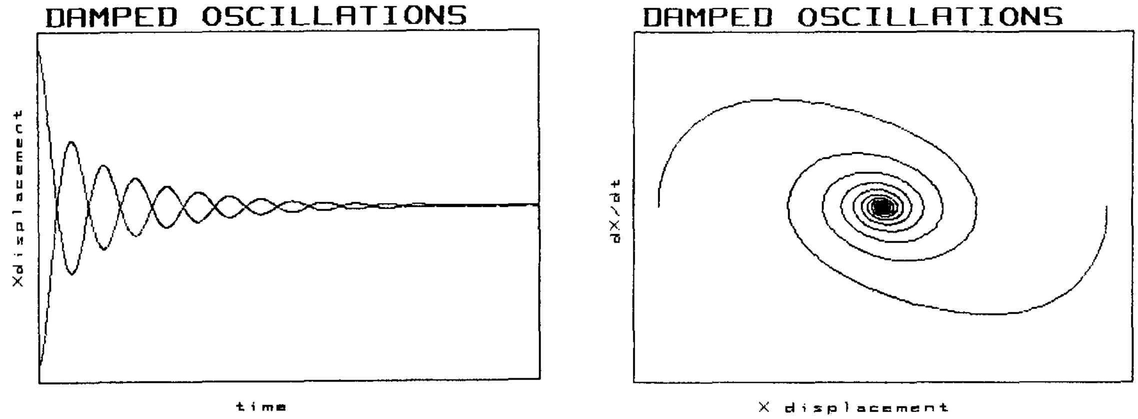

Fig. 2. *Two different damped oscillations drawn superimposed on each of two types of graph. a) Time graph showing the two oscillations to start with opposite deviations from the neutral condition. b) The same two oscillations plotted on the phase plane (displacement vs rate of change of displacement). Since a positive rate of change is associated with increasing positive displacement and a negative rate with a decrease, time always progresses in a clockwise direction on this plane. The direction of progression of the trajectory defined by a second order differential equation is unambiguously defined for all points on this plane even though the equation may be non-linear. The clearly separated trajectories near their start, coverage on a point attractor in this damped oscillation and in the process loose information about the differences in their starting conditions.*

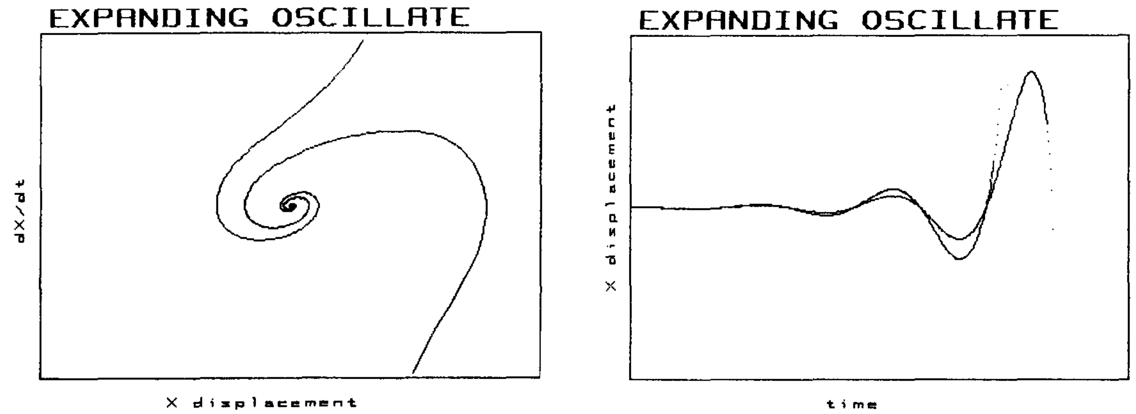

Fig. 3. *Two expanding oscillations of a feedback system. a) both plotted on the same phase plane; b) both plotted on a time graph. The solid lines show the same part of the oscillation in both a and b graphs. On the time graph a few additional points taken at equal increments of time are shown beyond the point where the trajectory exceeded the velocity bounds on the phase plane. These two oscillations start at indistinguishably different conditions but as they progressed the trajectories diverge, providing information about their different starting condition that was not discernable at the beginning. Thus, this response to completely deterministic rules actually generates new information as it runs.*

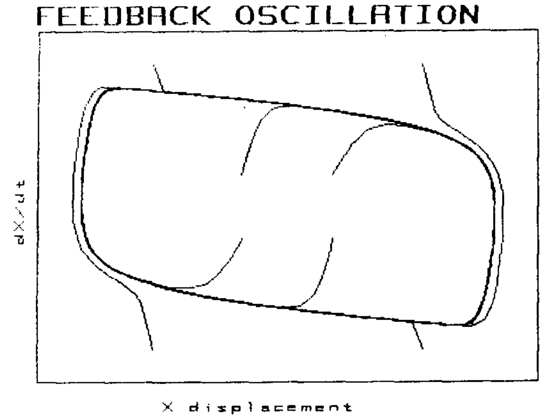

Fig. 4. Phase plane graph of 8 oscillations starting with different conditions in the same feedback oscillator. Each of these oscillations converge on the same limiting oscillation, a "limit cycle". Half of the oscillations start within the limit cycle and expand to it while the other four start outside of the limit cycle and are damped until reaching the same cyclic response, which from any start then continues to repeat indefinitely.

tion and for large amplitude oscillations a damped oscillation will result. Together these result in a system where from any starting condition the trajectory will be attacted to a limit in the form of a cycle with constant amplitude ("limit circle") (Fig. 4). The system then has automatically found the amplitude at which the ideal gain of one exists. Thus in this simple feedback, as in chaotic systems, a non-linearity has introduced bounds for the sustained variation but in this simple case those bounds restrict the trajectory to repeating a constant oscillation shown as a single orbit.

Using simple feedback we have now introduced the phase plane as a presentation form and reviewed several characteristics that are also factors in chaotic behavior. Feedback in a nonlinear system can produce bounded and sustained oscillation. Feedback under other conditions can generate new information. We have also used the terms trajectory, attractor, bounded operation and a sensitive dependence that are often encountered in discussion of chaotic behavior. Only minor additions to these already familiar terms and relationships are needed to produce and explain chaotic behavior.

Some of the systems that produce chaotic activity differ from the simple feedback systems that have been discussed by only one of two small details. While the feedback systems discussed were all describable by second order differential equations, many chaos-producing systems differ in that they require higher than second order description. In other chaos-generating systems the equations are not an intrinsically higher order but they operate in a discontinuous manner. The role of discontinuous function will be used as an example since the nervous system is made discontinuous by its pulsatile signaling. It is also important to recognize that even models of continuous systems will involve discrete time operation if calculated on a digital computer and may in this way show spurious chaos in their behavior.

The complexity introduced by discrete time operation is easily described in intuitive terms but is representative of the principles that might be treated as a mathematical problem in nonlinear dynamics. For an oscillatory feedback system to produce repeated identical limit cycles it is necessary that the starting condition for one cycle be identical to the starting condition of the previous cycle. In the phase plane representation this identity involves the same combination of magnitude and rate of change of that magnitude at the beginning of each cycle. A sampled case requires that the sampling point starting each cycle also is the same. thus, the number of sample per cycle must be an exact integer for successive cycles to be identical.

The discrete nature of a sampled operation can introduce complexity into the oscillation of a feedback system. Information that drives the future trajectory is acquired in a sample, but that discrete information is all that is available to determine the path until the next sample is taken. If the system is nonlinear in such a way that the orbit is bounded, a deviation from the ideal trajectory, sensed in one sample will lead

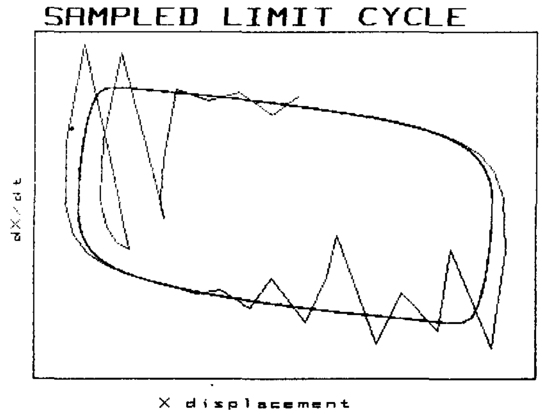

Fig. 5. Two different operations of the same set of feedback rules that produce continuing fluctuation of the variable. One operation was calculated in what was essentially a continuous manner and generated a limit cycle (same as Fig. 4). The other calculation of the dynamic response of the same equation was calculated intermittently, completing one orbit between the 44th and 45th sample. (On comparison with nerve impulse encoding of physiological signals this is a relatively high sampling rate.) This response initially followed the limit cycle but then then deviated and overcorrected from successive points giving a complex response. In the left half of this graph can be seen instances in which the overshoot of the calculated point crosses zero velocity resulting in a short cycle mode of operation.

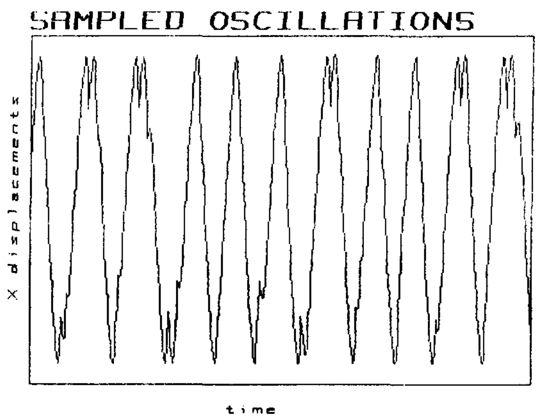

Fig. 6. Time graph of ouppput from sampled operation of the same feedback equation as used for Fig. 5 but extended to cover the first 500 sample points. Those orbits ranged in length from 40 to 60 uniformly spaced sample points. The temporal result of short duration orbits can be seen superimposed on several of long duration orbits.

to an adjustment back toward the ideal. Without continuous information about the progress of the correction, the adjustment projected until the next sample is likely to be in error. The sample driven trajectory can repeatedly cross the ideal trajectory, following a complex path over time (Fig. 5). Here, we see complex behavior arising in a simple system because of the effect of discrete time operation A longer sample of the same behavior produces the time graph of Fig. 6.

With an exactly integer number of samples and also an exact return to the same combination of magnitude and rate of change, it is possible for a sampled feedback to produce complex but periodic activity. If, instead of an integer number of samples in one orbit of the phase plane, there is a rational number of samples it would be possible, instead, for an exact repetition to occur after several orbits. However, it is more likely that a change determination fo sampling rate will produce an irrational number of samples per cycle with the result that sampling alone will never exactly repeat. With nonlinearity that holds the sample points within bounds and an irrational number of samples per orbit we have the basis for a deterministic but chaotic response. Periods of expanding trajectory would give it unpredictability in detail while the bounds imposed by nonlinearity would make the long term range of variation predictable. The periods of extrapolation from each discrete sample point introduces complexity into the trajectory (Fig. 7). The sample point distribution is complex, and superimposed on a quasi periodic fluctuation that is unpredictable in detail but

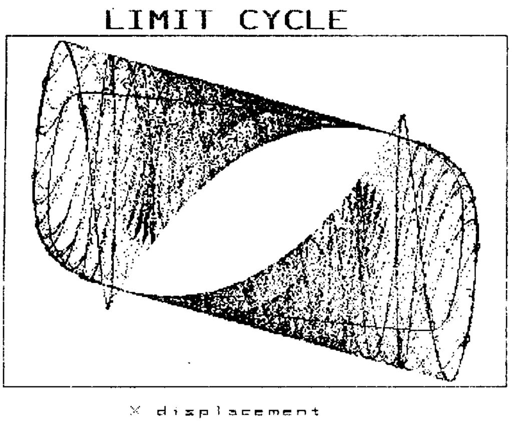

Fig. 7. Phase plane graph of same limit cycle and superimposed the location of the first 50,000 sample pints in an extended calculation of the same equation. This Poincaré style graph shows that the discretely calculated points have a complex but certainly not random distribution. In the middle of the graph lies a region with no points. The other points fall in a sharply bounded region, within there is found a fine grained pattern. Although due to the finite number set of the computer used this calculation would eventually return to a previously calculated point within the fires 50,000 points no repetition occurred. Thus this simple but non-linear feedback oscillator produces a response with many of the characteristics of chaotic behavior while obeying rules that are simpler than found even in a two neuron feedback path.

bounded and far from random.

What can we learn from this kind of function that has importance to study of physiology? Clearly complex behavior can be generated by a simple system while it is obeying rules exactly. It is important to distinguish between deterministic complexity and random variation since statistical treatment is only appropriate for the random variation. In fact, in deterministic complexity a single measurement of some value may be exactly correct as one possible case while the result of a statistical treatment of a large number of measurement of that value may lead to an indication of a central value that is prohibited by the rules of the system. In such a case statistical treatment is not only theoretically improper but can be seriously misleading.

Nonlinear dynamic complexity does not always look the same. Under some circumstances it may produce widely changing values with no recognizable pattern within its bounds. In other cases, it may only produce small deviations around a quite uniform pattern of oscillation or even around a stationary condition. In some cases it may orbit within rather simple defined bounds but in other cases the trajectory may have more than one possible mode, (as in Figs, 5-7) jumping unpredictably from one mode to another. The dynamic things we study in biology or even the stationary values we attempt to identify over time can not be proven to be free of this type of complexity. In fact, our very selection of subjects for study that are simple enough that we have some hope of understanding them increases the probability of finding this type of complexity instead random deviation from a central value. We may have been overly critical of studies done before statistics were established.

The subject of nonlinear dynamics is of importance to all studies of physiology and can not be packaged within one organ system. I expect that in the next few years many of us will find problems with our established and statistically based theories. On the other hand, the narrow subject of dynamic chaos may be seen as only a small part of the subject. For example, the nervous system usually deals with transient responses to inputs while the strict definition of chaos deals only with internally generated activity during stationary input conditions. This is a limitation in the mathematical theory that has developed around chaos and may require new theoretical developments for the treatment of transient dynamics. In any case deterministic complexity is probably present in most of the simple systems we study and should be a seriously considered alternative to random variability. On the other side, I must warn you that a digital study can mislead you. If you attempt to test your hypothesis with a digital computer model of some biological system, it is possible that you will observe some complex behavior that is not even characteristic of your model but is generated in the process of digital simulation.

CONCLUSIONS

Whether or not you share my interest in personally learning more about the effect of nonlinear dynamics in biological function, I hope I have convinced you that the study of a variety of functional topics can be badly fractured by being studied in an organ system organization. I offer a first draft suggestion of a functional organization that might simplify teaching and help to communicate the unifying principles of Physiology. Perhaps we should return to Aristotle's separation of biological science into function and form. My purpose will be accomplished if you individually are now more aware of parts of your teaching, meeting organization and research activities that would be better served by functionally based combination. Any change is not easy. Thus, a complete shift of teaching would leave you with no suitable textbook. On the other hand, we must recognize that a reorganization by physiologists' default and by outside forces would not be easy for us either.

We can individually or as committee members make changes. I can tell you that I am interested in biological processing of information instead of saying I am involved in Neurophysiology. A meeting sessions or teaching lecture on counter current exchange that included all different locations might be more efficient than a session on all aspects of kidney function.

I shall look forward to hearing about your related ideas and experiments. When making our plans it may be worthwhile to note that chaos is more orderly than is random.