Nonlinear Man -
Chaos, Fractal & Homeostatic Interplay in Human Physiology

Nowadays, many physiologists speak about ‘dynamical diseases’ – systemic breakdown in coordination and control. These manifest in disorders of breathing (such as panting, Cheyne-Stokes breathing and Sudden Infant Death Syndrome) and the blood (including a form of leukaemia in which the balance of red and white blood-cells, platelets and lymphocytes is disrupted) and perhaps schizophrenia.

But physiologists have also begun to see chaos as health, allowing organisms to respond to circumstances that vary rapidly and unpredictably.

An interdisciplinary team under the direction of Prof. Ary Goldberger, Professor of Medicine at Harvard Medical School and Director of Cardiography at Beth Israel Hospital, Boston, has been developing the concept of a new kind of chaos-based physiology. This is built on the idea that mathematical tools can help scientists understand global complex systems independent of local detail. This holistic approach was outlined by James Gleick, author of the book ‘Chaos’ (1) "... researchers increasingly recognised the body as a place of motion and oscillation - and they developed methods of listening to its variegated drumbeat. They found rhythms that were invisible on frozen microscope slides or daily blood samples. They studied chaos in respiratory disorders. They explored feedback mechanisms in the context of red and white blood cells. Cancer specialists speculated about periodicity and irregularity in the cycle of cell growth. Psychiatrists explored a multidimensional approach to the prescription of anti-depressant drugs. But surprising findings about one organ dominated the rise of this new physiology, and that was the heart, whose animated rhythms, stable or unstable, healthy or pathological, so precisely measured the difference between life and death."

The two most surprising findings of Prof. Goldberger’s team may be summarised as follows:-

1. Ventricular Fibrillation and related tachycardias causing sudden death are relatively periodic, not chaotic processes.

2. In contrast, the healthy heartbeat shows chaotic dynamics. Sudden death, therefore, may be viewed as a bifurcation out of, not into, chaos.

Researching modern cardiac monitoring and defibrillation devices, one is immediately struck by those statements and by Prof. Goldberger’s findings as documented in ‘Nonlinear Dynamics for Clinicians: Chaos Theory, Fractals and Complexity at the Bedside’ (2) ; "At first it was widely assumed that chaotic time series were produced by pathological systems and that this new non-linear theory would be extremely useful to the clinician as a method of modelling cardiac arrhythmias and in understanding the dynamics of atrial and ventricular fibrillation. However, contrary to earlier theories, the vast weight of current scientific evidence put forward indicates that these erratic arrhythmias are not chaotic." Professor Goldberger proposes "that the most compelling clinical example of cardiac chaos is paradoxically found in the dynamics of normal sinus rhythm".

Although the focus of much recent attention, chaos ‘per se’ is a concept which is often misunderstood. The complex variability that arises from an equation which does not contain any random terms is known as deterministic chaos. The colloquial use of the term chaos to describe unfettered randomness, usually with catastrophic implications, is quite different from this specialised usage.

The extent to which chaos relates to physiological dynamics is a subject of active investigation, and not without controversy. Originally it was considered that chaotic fluctuations were caused by disease such as cardiac electrical activity during arrhythmias, but this has been challenged by the Harvard team and the weight of present evidence is that fibrillations and tachycardias sometimes labelled ‘chaotic’ do not in fact meet the technical criteria for nonlinear chaos. The hypothesis advanced by Professor Goldberger is that the subtle but complex heart rate fluctuations observed during normal sinus rhythm in healthy subjects, even at rest, are due in part to deterministic chaos and that a variety of diseases, such as congestive heart syndromes, may paradoxically involve a decrease in this type of nonlinear variability (Fig.1). Because the mathematical algorithms designed for detecting chaos are not reliably applied to the nonstationary, relatively short and often ‘noisy’ data sets obtained from most clinical and physiological studies, the intriguing question of the role of chaos remains uncertain.

As new generations of detecting devices are devised, such as in the front-line work being carried out in University of Ulster, Jordanstown by NIBEC, it is suggested that the work of Prof. Goldberger’s Harvard team could yield significant clinical benefits.

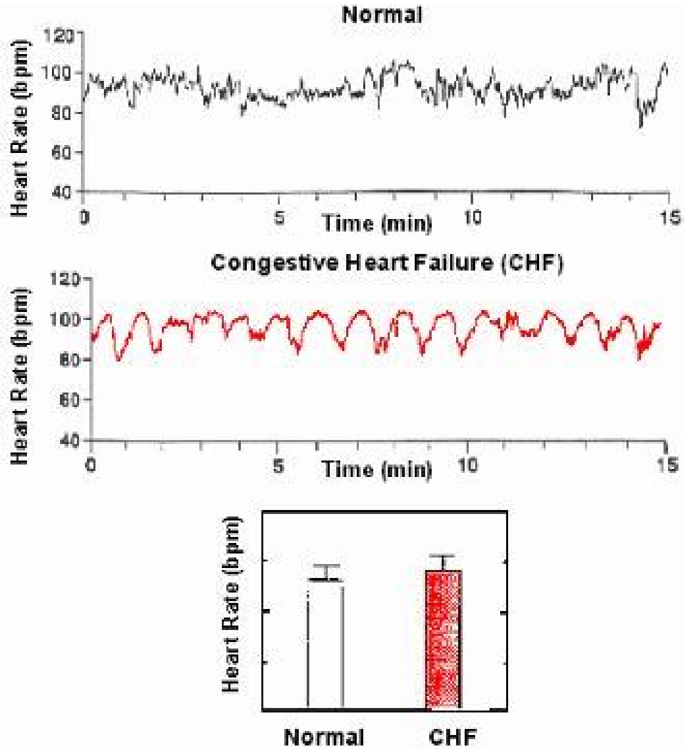

Figure 1 - Heartbeat time series for a healthy subject (top) and one with severe Congestive Heart Failure (centre). Note nearly identical means and variances (bottom) but very different dynamics. Note also the complex, erratic pattern of data from the normal subject compared with slow, periodic oscillation in CHF that correlates with Cheyne Stokes Breathing.

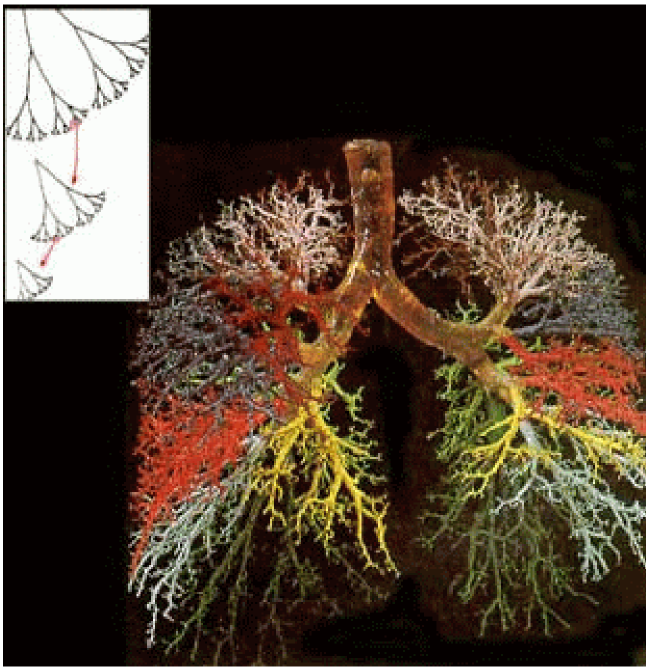

Figure 2(a) - Self-Similar Structure

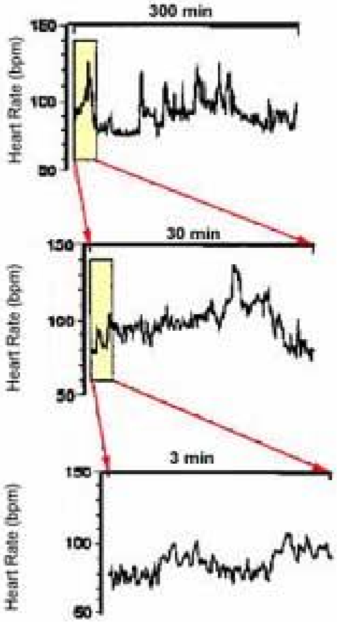

Figure 2(b) - Self-Similar Dynamics

The term fractal is a geometric concept related to, but not synonymous with chaos. While classical geometric forms are smooth and regular with integer dimensions - 1, 2 and 3 for line, surface and volume respectively - fractals are highly irregular and have non-integer, or fractional, dimensions. A fractal line, which has a dimension between 1 and 2, is wrinkly and irregular. Examination of these wrinkles with the low-power lens of a microscope reveals smaller wrinkles on the larger ones, a property referred to as self-similarity. A wide variety of natural shapes share this property, among them branching trees and coral formations, wrinkly coastlines, rugged mountain ranges, clouds, lightning flashes and winding rivers. A depiction of this self-similar property is given in Fig. 2(a). Examples of fractal-like anatomies include the vascular system, the His-Purkinke electrical system in the heart (Fig. 3), the tracheobronchial tree, as well as the folds of the bowel and brain. A surprising discovery in nonlinear dynamics is that these fractal architectures are also exhibited by chaotic processes (when these are depicted as geometrical structures). The self-similar cardiopulmonary structures all serve a common physiological function - rapid and efficient transport over a complex, spatially distributed system. In the case of the ventricular electrical conduction system, the quantity transported is the electrical stimulus regulating the timing of cardiac contraction.

An important extension of the fractal concept was the recognition that it applies not just to irregular geometric or anatomic forms that lack a characteristic single scale of length, but also to complex processes that lack a single scale of time; fractal processes generate irregular fluctuations on multiple time scales. Furthermore, such temporal variability is statistically self-similar.

For example, Fig 2(b) plots the time series of heart rate from a healthy subject on three different scales. All these graphs have an irregular (wrinkly) appearance, reminiscent of a coastline or mountain range. The roughness of these time series, therefore, possesses a self-similar, scale-invariant property. A disease state tends to cause complexity loss and tends towards highly periodic dynamics.

Professor Goldberger suggests that fractal structures in the human body arise from the slow dynamics of embryonic development and evolution and that this evolutionary advantage accounts for their ubiquitous presence in biomedical phenomena (2). Fractal branches (Fig.4) or folds greatly amplify the surface area available for absorption (as in the small intestine), distribution or collection (by blood vessels, bile ducts and bronchial tubes) and information processing (by the nerves). Fractal structures, partly by virtue of their redundancy and irregularity, are robust and resistant to injury. The heart, for example, may continue to pump with little mechanical dysfunction despite extensive damage to the His-Purkinje system, which conducts cardiac electrical impulses.

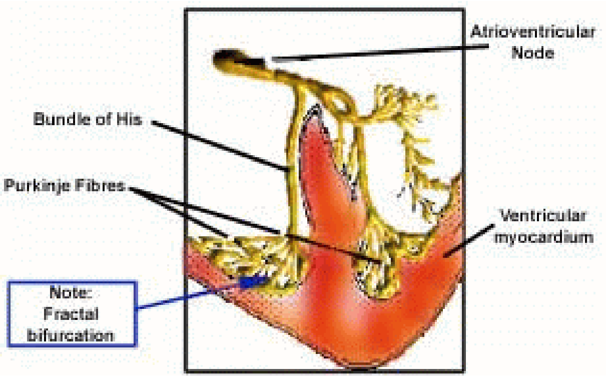

Figure 3 - Fractals Bifurcation in the His-Purkinje Network.

What is the mechanism in this unexpectedly healthy chaos of the normal heartbeat? Professor Goldberger suggests that the answer appears to lie in the chaos of the nervous system, since parasympathetic stimulation decreases the firing rate of the pacemaker cells in the heart's sinus node; sympathetic stimulation has a 'speeding up' effect. The competing influences of these two branches of the nervous system result in a constant tug-of-war on the sinus node. The result of this constant neural buffeting is the type of chaotic heart rate variability that is recorded in healthy subjects, even during resting or sleeping hours.
Figure 4 – Fractal self-similarity occurs in the small intestine right down to the microscopic level.

An analysis was carried out (4) by Peng et al in 1993 on the digitised ECG's of beat-to-beat heart rate fluctuations over long time intervals, up to 24 hours, recorded with an ambulatory monitor. The time series obtained by plotting the sequential beat intervals (Fig. 1) typically reveals a complicated variability. There is a much more complex pattern of fluctuations for a representative healthy adult (a), compared to the pattern of interbeat intervals for a subject (b) with severe heart disease associated with congestive heart failure.

Dr. Peng observed that the long-range power-law correlations present in the healthy heartbeat imply that the underlying control mechanisms actually drive the system away from a single steady state. Therefore, "... the classical theory of homeostasis, according to which stable physiological processes seek to maintain 'constancy' and its more recently proposed modifications under the rubric of 'homeodynamics' need to be revised and extended to account explicitly for this far from equilibrium behaviour."

The principle of homeostasis in heart rate fluctuations was developed by Dr. Cannon of Harvard Medical School in the 1920's, and was generally accepted for more than half a century later. This states that physiological systems normally operate to reduce variability and to maintain a constancy of internal function. According to this theory, any physiological variable, including heart rate, should return to its 'normal' steady state after it has been perturbed. The principle of homeostasis suggests that variations of the heart rate are merely transient responses to a fluctuating environment. Chaos theory is not completely incompatible with the classical concept of homeostasis, but there are several fundamental differences between these approaches to the understanding of physiological variability. These are summarised in Table 1 (5).

Homeostasis	Chaos
System will settle down to a steady state (constancy) if unperturbed.	System does not settle down to constant state.
Fluctuations result from external influences.	Fluctuations arise from internal feedback and do not require external perturbation.
Destabilising factors such as disease or ageing are anticipated to decrease order (increase chaos).	Destabilising factors such as disease or ageing usually decrease the degree of complex variability (reduce chaos).

Table 1 - Homeostasis vs. Chaos as defined with reference to Physiology (5).

Chaotic systems generate variable behaviour even in the absence of external stimuli, whereas homeostatic systems should settle down to a constant steady state in the absence of perturbation. Therefore, the type of nonlinear mathematical modelling required to simulate chaotic systems is quite different from the linear equations that suffice for systems with one steady state. Furthermore, homeostatic systems might be expected to become more variable as they are destabilised.

Chaos theory predicts just the opposite - namely, that factors such as disease and ageing may decrease the dimensionality or degree of chaos. On the other hand, chaotic systems are not random and, like homeostatic systems, the range of chaotic fluctuations is constrained. Chaotic systems may also be perturbed by external stimuli that further complicate their dynamic patterns.

Evidence for the existence of chaos in the central nervous system is also supported by the dimensional analysis of EEG waveforms of healthy individuals which shows a broad type of spectrum and a phase space attractor that is very unlike a limit cycle. Furthermore, chaos in neuroendocrine function is suggested by time series analysis of serum hormone levels in healthy subjects (2). Such plots do not display the regularity expected by a classical homeostatic system.

A revealing group of graphs (Fig. 5) summarises the findings of Professors Goldberger’s Harvard team using the above described tools of dimensional analysis in describing the heart rate dynamics of healthy subjects and different pathological conditions. (5)

Figure 5 - Heart rate dynamics: left column is a healthy subject, middle column a patient with oscillatory sinus rhythm, right column a patient with overall loss of sinus variability. (5)

Analysis of the phase-space representations of normal sinus rhythm in healthy subjects (left side column) shows complex variability with a broad spectrum of frequencies and consistency with a strange (chaotic) attractor. Patients with heart disease may show altered dynamics, sometimes with oscillatory sinus rhythm heart rate dynamics (middle column). The spectrum in this case shows a sharp peak, and phase space plot shows a more periodic attractor, with trajectories rotating about a central hub. The right column, for a patient with overall loss of sinus variability, has a flat pattern time series, the spectrum shows an overall loss of power and the phase space plot is more reminiscent of a fixed-point attractor.

The periodic patterns in diseases and the apparently chaotic behaviour in health do not imply that all pathologies are associated with increased regularity. In some cardiac arrhythmias the pulse rate is so erratic that the individual may complain of ‘palpitations’.

Some of these events actually represent oscillations that seem irregular but when carefully analysed are actually periodic. In other arrhythmias the heartbeat is in fact unpredictably erratic. None of those irregular pathologies, however, has been shown to represent nonlinear chaos - although the pulse may feel quite ‘chaotic’ in the colloquial sense.

Professor Goldberger (2), summarised the way forward as follows:-

* Broad spectra of time series appear to be markers of physiological information, not ‘noise’ as might appear from a casual glance.
* Deterministic chaos, contrary to its vernacular connotation, is not a completely random state. Instead, chaos gives rise to fractal structures and complex variability that bring an elegant and essential order to physiological self-organisation.
* In regard to novel therapeutic interventions, certain mathematical or physical systems with complex dynamics can be controlled by properly timed external stimuli, i.e. chaotic dynamics can be made more regular (chaos control) and periodic ones can be made chaotic (chaos anti-control).
* Nonlinear dynamics can yield practical bedside physiological monitoring. A number of indices derived from chaos theory have shown promise in forecasting subjects at high risk of electrophysiological instability, including

1. automated detection of the onset and departure of pathological low frequency (<0.10 Hz) heart rate oscillations’
2. detection of a breakdown in fractal scaling
3. quantification of differences or changes in the nonlinear complexity or dimension of a physiological time series.

* Findings for nonlinear dynamics have challenged conventional mechanisms of pathological control based on classical homeostasis, which presumes that healthy systems seek to attain a constant steady state. In contrast, nonlinear systems with fractal dynamics, such as the neuroautonomic mechanisms regulating heartbeat variability, behave as if they were driven far from equilibrium under normal conditions. This kind of complex variability, rather than a regular homeostatic steady state, appears to define the free-running function of many physiological systems.
* It is important to analyse continuously sampled variations in physiological output and not to rely only on averaged values or measures of variance. Dynamical analysis demonstrates that physiological time series plots often conceal vital information and certain fluctuations often called ‘noise’ may represent important signals. Messages contained in apparent ‘noise’ of electronic nonlinear amplifier circuitry is an interesting analogue of this behaviour pattern.

Nonlinear investigation of physiological systems is still in its infancy. Physiology in fact may prove to be one of the richest laboratories for the study of fractals, chaos and nonlinear dynamics in general. Its mathematics could soon become the most powerful tool for quantitatively describing the apparently nonhomeostatic variability of normal medical dynamics and the changes that accompany a variety of diseases.

References

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