UNDERLYING MEDICINE

Chaos—predicting the unpredictable

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Prediction is difficult, especially of the future.
NEILS BOHR

This short article describes some of the features and history of chaos theory, with emphasis on its implications for predictability in general, and some thoughts on how these ideas might have an impact on medicine. In particular, it is suggested that inability to predict who will contract which diseases, or who will respond to which treatments, may be intrinsic, rather than simply due to incomplete knowledge of the particular patient. It follows that we patients should not expect too much of our doctors!

When I am sick and consult my doctor, what I want to hear might go as follows: "Take these tablets three times a day for a week; you'll feel better after two days, and will be ready for work after four." I am expecting a great deal: not only to be cured, but to have the course of my cure predicted.

Yet prediction is not trivial or easy. In fact chaos, the mainspring of this article, has shown us that predictability is the exception rather. than the rule, even for what seem like simple physical systems. A human being is immeasurably more complex than any demonstrably chaotic system—the question can be turned around: How can anything be predicted about a person?

There is nonetheless a strong social pressure for answers to such questions as, Who will get cancer—or a heart attack? and, How long before a HIV positive subject develops AIDS?. At the risk of presumption, I will suggest analogies and lines of reasoning which imply that such questions make sense but can never be answered. The best that can be done, for an individual as well as a population, is to assess probabilities.

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Determinism and its downfall

The tremendous success and power of Newton's mechanics—especially in predicting planetary orbits—led to the ultimate statement of determinism, paraphrased from Laplace in the eighteenth century:

The cover

The image on the cover (by David Ellis of Why Not Associates, London) relates the abstract elements of chaos theory to the concrete practice of medicine. Most people associate the patterns of fractal geometry with chaos theory: the pills are arranged in a fractal pattern, repeated in exactly the same shape but smaller sizes, spiralling to infinity. The mathematical element is more directly conveyed by the numbers, which are taken from a non-linear progression. Non-linearity is fundamental to chaos, but it can also give stability and hence individuality and continuity, which are represented in the human context by the skeleton. The article fleshes out the background and applications of chaos theory.

"Given accurate positions and velocities for all the particles in the universe, and sufficient calculational power, it would be possible to determine the entire course of history." Leaving aside implications for free will, the statement is an impeccable mathematical consequence of Newtonian mechanics, but it contains two (related) fatal flaws. The hidden assumption is that the calculational power required increases only in rough proportion to the number of particles and the time forward for which prediction is sought. In fact, the increase is exponential, with the consequence that to predict the weather for even just a few years would require that the entire universe be fabricated into a single giant computer. The flaws, then, lie in the innocent words "accurate" and "sufficient." Joseph, in predicting 14 years of Egyptian weather, was either lucky or divinely inspired.

The Laplace hypothesis, therefore, seems to require that small causes have small effects: that a small inaccuracy in the starting data should lead to only a small error in prediction. This property is exactly true only for linear systems, for which—by definition—effect is proportional to cause. "Two heads are better than one" adopts a similar hypothesis but has proved drastically false in many spheres, notably the "two Davids" of British politics in the 1980s. Real systems are almost always non-linear, and small causes can produce huge effects: "For want of a nail the shoe was lost, for want of a shoe the horse was lost, for want of a horse the King was lost" encapsulates the matter rather well. Physics and mathematics have traditionally concentrated on linear systems, for the very good reason that they are predictable and mathematically tractable. The world, however, is non-linear.
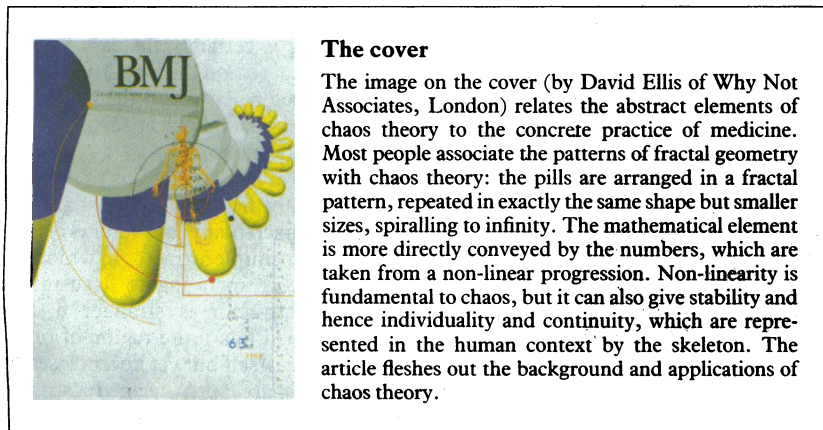
I won't define non-linearity more precisely, beyond one further contrast with linearity. The operation of a linear system is wholly determined by its initial state and its environment, whereas the behaviour of a non-linear system depends upon its own state: it "looks at itself." In the field of economics, Adam Smith's free market ideas were based on a linearity assumption: that there are enough enterprises in the market that no single one could distort the market by its actions. Today, of course, stock markets operate largely on the basis of "second guessing" the behaviour of the market itself, which is a highly non-linear situation. In such cases small, even undetectable, causes can lead to huge effects, such as in the big stock market crash of 1987.

Living organisms are certainly non-linear in the above senses. Indeed, Darwinian selection is intrinsically non-linear, since the breeding success of a species is affected by the actions of the species itself. The same is true of ecosystems: it is the non-linearity of predator-prey competition which led population dynamics to be one of the pathbreakers in the study of chaos.[1]

Non-linearity is necessary for, and is fundamental to, chaos, but it can also endow stability. Non-linear systems can seek out and maintain essentially the same

optimum state in response to a wide variety of external conditions: it is precisely this feature that gives us individuality and continuity.

Chaos

Chaos, in the modern technical sense, is used to denote a form of time evolution in which the difference between two states that are initially closely similar grows exponentially with time. This type of behaviour was suspected by Poincaré around 1900 for Newtonian dynamics, but he did not have available the computational power that has fuelled chaos studies in recent decades. The discovery of chaos is often ascribed to Lorenz, who was interested in weather forecasting by computer.[2]

Basically, weather is caused by a traffic problem in the earth's heat balance. Solar energy is primarily absorbed at the surface, heating it up. In equilibrium, that heat has to be dumped into cold space. The warm air, because it is below the cool air, tends to rise, but self evidently all of it can't do so at the same time; hence the traffic problem. For convection to occur, the air rising in one location must sink back in another. Rising air means low pressure and rain, sinking air means high pressure and fine weather, so the resolution of the traffic problem is at the heart of the problem of weather prediction. Lorenz's computer was primitive by today's standards, and so he sought to simulate the weather with an absurdly simplified model, assuming among other things a flat earth, but one that had what seemed to be the essential ingredients: amplitudes for convective circulation and for vertical and horizontal temperature variation. At any one time the values of these three quantities can be represented by a single point in a three dimensional space: as time evolves that point traces out a trajectory or orbit.

Lorenz's model is deterministic—that is, the orbit is unique, in the sense that there is only one orbit passing through a given point of the space (phase space) in which the orbit lies. Is it also predictable, in the sense that nearby orbits stay close to each other? The answer, as Lorenz found from watching the output chart from his computer,[23] is an emphatic "No." Starting the computer with similar, but slightly different, initial data led to orbits that stayed close to each other for a while but eventually always diverged in a manner that turned out to be exponential. Figure 1 shows a phase space orbit with this property, actually for an electronic oscillator. It consists of two lobes joined by a kind of

neck; for the Lorenz model the lobes are somewhat flatter, but that is of no importance here.

One lobe can, in simple terms, be regarded as corresponding to anticyclonic weather and the other to a depression. The exponential divergence means that two orbits starting close to each other sooner rather than later end up in different lobes, corresponding to quite different weather. Real weather forecasting necessarily involves errors and uncertainties in the initial data (that is, current weather over a large area, Laplace notwithstanding). Thus the starting position must be considered not a point but a box (error box) in the phase space. Exponential divergence then means that that box gets stretched in at least one direction as time develops,[3] until eventually it is smeared across both lobes, at which point weather forecasting has become guesswork.

It follows that the determinism of the Lorenz model (and by extension of Laplace) is only mathematical: the physical universe is unpredictable, even if deterministic, because of unavoidable uncertainties in our knowledge of initial conditions. This kind of chaotic behaviour has also been identified in systems as diverse as dripping taps, traffic flows, lasers, heartbeats, and stock markets. Chaos is also cumulative, in the sense that when two non-linear systems are coupled together they tend to be more prone to chaos and unpredictability than are their several parts. In short, the universe may be predetermined but there is no conceivable experimental procedure by which we could determine the future and expose free will as an illusion.

It can be shown that all systems are linear close to any static equilibrium, so that chaos is impossible unless or until there is a continuous injection of enough energy to drive the system to a high enough excitation that non-linearity becomes appreciable. Chaos also usually requires some kind of dissipative mechanism, if only because a continuous unbalanced energy input would soon blow the system apart. Thus the weather is driven by solar energy, and viscous losses and radiation to space dissipate that energy. Chaos is endemic in strongly driven, dissipative systems. Organisms such as people are typical of such systems; they are driven by food and oxygen. It is not, therefore, surprising that we are, in whole and in numerous parts, chaotic.[4]

Attractors

Lorenz showed that the weather is intrinsically unpredictable for all practical purposes. But his model still offers us a substantial measure of predictability if only we make a more modest demand. The weather doesn't swing all over the place, with blizzards one day and blistering heat the next. We have a reasonably well defined climate. In the Lorenz model this can be linked with the fact that the orbit remains confined to the region occupied by the two lobes. A massive volcanic eruption, or meteor strike, might kick the weather off the lobe structure, but we would expect it to settle back to it (after a time). This is certainly the case for the Lorenz model, and for that reason the lobe structure in figure 1 is called an attractor. Any orbit that starts off outside the attractor will inevitably be attracted into it by the dynamics; hence the name.

The simplest attractor of all corresponds to the case where all motion eventually dies out and is just a single point in phase space. A "fixed point" attractor is clearly not chaotic, nor is another simple attractor in which the orbit is a closed loop corresponding to a sustained oscillation. A chaotic attractor is strange: it is a continuous curve, confined to a finite region of phase space, which never crosses itself but yet never closes on itself. Chaotic attractors are aptly termed "strange attractors." The geometrical structure of chaotic
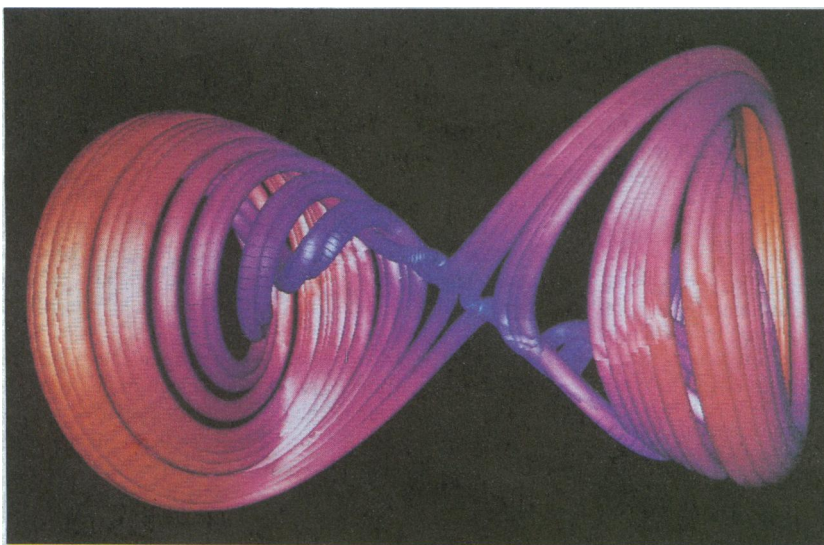

FIG 1—A strange attractor reconstructed from experimental data from a non-linear electronic oscillator which flips chaotically between two states much as the weather does in Lorenz's model. The colour indicates the speed on a trajectory: thus the blue region corresponds to the slow motion near the saddle which separates the two lobes. (Courtesy T Mullin)

attractors somewhat resembles that of millefeuille pastry, which is made by repeatedly rolling out (stretching) and folding dough. Consider the effect of this stretching and folding on two particles of the mix (say salmonella bacteria from the eggs), which are originally very close together. It can be shown that their separation distance doubles at each stage, and increases exponentially with time. This is very close to the basis for the unpredictability of chaotic motion: if there was only one bacterium it would be impossible to predict which item of hors d'oeuvre it would contaminate.

These remarks on the geometry of chaotic attractors suggest that they may be fractals.[5] Fractals are a class of objects with the property of having structure—often the same structure—on many measurement scales. For example, branching systems such as trees or blood vessels often seem self similar in the sense that the form of the structure looks much the same at many different magnifications. Another example is a coastline: look at a map showing only the outline of an island and it is impossible to tell whether it is an islet in a loch or a continent—apart from familiarity with the latter, of course. To measure the length of the coastline of, say, Ireland, one could get out some maps and some measurement device—with the result that the larger the scale of the map, the longer would be the coastline's measure. Self similarity and "odd" behaviour of lengths of coastlines are linked through being characteristic of objects whose dimension, instead of the simple one, two, three of lines, surfaces, and solids can have values like 1·23, which is the sort of value found for natural coastlines. Abstraction and generalisation of these observations led to the development of fractal geometry, which is a rich and beautiful branch of mathematics that deals with objects of non-integer dimension. Chaotic attractors have been proved to be fractal in some cases and conjectured to be so in many more. Though very different in essence, chaos and fractals seem to be closely linked in practice.

The Mandelbrot set is a rightly famous example of a fractal structure, named for a pioneer of fractal geometry.[6] This set, often said to be the most complex —and beautiful—object known to man is generated by a trivially simple rule: take a number, square it, and add the number you first thought of; repeat ad infinitum. For most starting numbers the process diverges to infinity, but for some the successive answers remain always bounded—these form the Mandelbrot set. The interest and beauty of the Mandelbrot set lies in the amazing complexity of its boundary, which cannot be predicted or defined, only explored and admired. (One technicality: this beauty flowers only when complex numbers, represented as points of a plane, are allowed.) The infinite complexity of the boundary of the Mandelbrot set represents an extreme sensitivity to initial conditions—the starting number—highly reminiscent of chaotic dynamics but actually more closely related to the infinitely structured basin boundaries discussed below.

In the physiological sphere, one would suppose the human heart to have an oscillatory attractor. In fact there are indications that the healthy heartbeat is actually slightly irregular, indeed chaotic. Be that as it may, it must also have a fixed point attractor (cardiac arrest) into which it can be "kicked" from the normal state by an electrical or other shock. With luck or skill, or both, it can sometimes be kicked back again: resuscitation. These remarks illustrate a general and important feature of non-linear systems: they can possess more than one attractor, so that their actual state depends on their history as well as their environment, which again is impossible in linear systems. That a kick is needed to induce switching is in the nature of an attractor: it attracts any nearby trajectories. In the
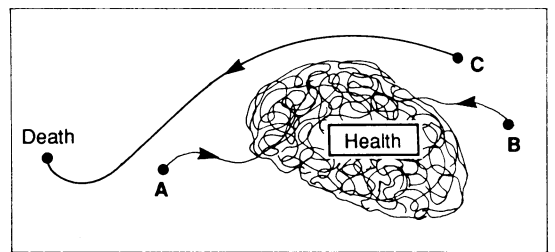

FIG 2—Schema of "health" and "death" as two coexistent attractors. Unhealthy states A and B recover along the trajectories shown, but C is fatal

case of the climate, there is reason to suspect that an ice age type of climate coexists with our present more or less equable climate, and thus that a big enough volcanic eruption might trigger an ice age.

Coexistent attractors lead to a new kind of unpredictability, which brings us back to the question of medical prognosis. Let us suppose that "health" is an attractor (probably chaotic) which must coexist with "death" (a fixed point attractor) in some multidimensional phase space which we don't need to even try to imagine, but which could be given a schematic representation as in figure 2. "Illness" would then be a state in which the system had got out of the health attractor because of infection, injury, or whatever. What is the prognosis?

Most ill states lead to recovery (even without medical attention). That is a consequence of health being an attractor state, which is in turn an inevitable consequence of evolution: those "fittest" species which prosper have robust healthy states. Thus we could picture ill states A and B in figure 2 as being attracted back to health along the paths indicated. They probably correspond to the kind of illness I referred to at the start of this article, where medical treatment affects mainly the rate, rather than the fact, of recovery. Furthermore, the return to health is by a fairly predictable path, even if the healthy state is itself chaotic.

Some illnesses are fatal, however, as illustrated by point C in figure 2. Treatment is essential in this case, but can we predict whether it will be successful? Can we even predict which ill states are type C, and which are type A or B?

In simpler or model systems with coexistent attractors we can map out the phase space by simply starting off at each point and watching where it ends up. Figure 3 is an example of this procedure. Black points end up on a fixed point, white on a coexistent attractor. There are substantial regions (close to the attractors themselves) of solid colour, corresponding to full predictability. The most striking feature of this figure is that further out the black and white pattern becomes very intricate, and indeed it can be shown that the pattern has a black and white structure on all scales, so that predictability is lost unless there is infinite accuracy of knowledge of the starting point, which is of course impossible. Technically, the white and black regions of figure 3 are termed the basins of attraction of the two attractors, and the division between them— which we can see is extremely convoluted—the basin boundary.

This kind of unpredictability seems to me to relate to questions about whether a seriously ill patient will recover: what is often said to be a fine line between life and death corresponds to the basin boundary. It is indeed a fine line, and also an infinitely convoluted and folded one, such that it is practically impossible to tell on which side one is. If one is in the black region, treatment is essential; but in the white region treatment is likely to do more harm than good. The only sensible course is to take a statistical view, and try to estimate the "greyness" of different regions. But when a doctor
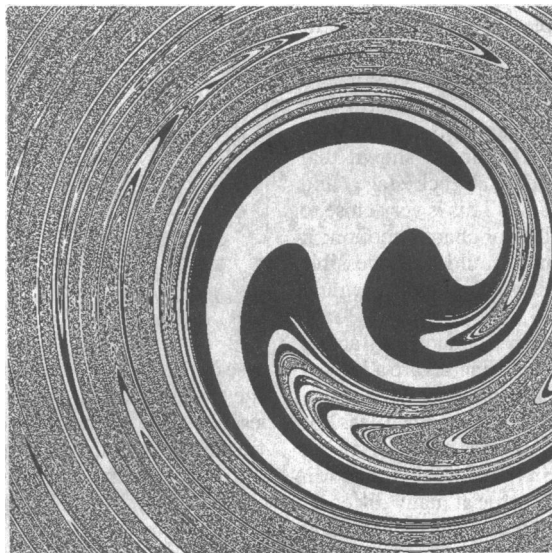
FIG 3—*Example (from non-linear optics) of a complex, probably fractal, boundary between the basins of attraction of two competing attractors. The white region is the set of points attracted to one attractor (a fixed point) while the black region is attracted to the other (an oscillation). The boundary between black and white has complex structure on all scales accessible to a computer*

estimates a 50-50 survival chance for a patient, it is usually, I would guess, with the feeling that more detailed knowledge of the patient would allow a better prediction. What I am saying is that this is true, but that the extra knowledge required increases much faster than the improvement in prediction, so that to all intents and purposes the outlook for individual patients is at best statistically determinable.

Lastly in this context, it must be remarked that the existence and location of attractors is not set in stone but is a function of the environment—though not a linear one. Thus I would reckon that smoking, for example, would pull the health attractor towards the death attractor in figure 2, making most forms of illness more perilous. More generally, at some time for all of us the basin boundary between life and death will, whether through bad life habits or just age, come into contact with our chaotic health attractor, and we will die. My point again relates to predictability: because the basin boundary is so complex, detailed prediction is impossible, especially as to whether we exit via a trajectory marked "cancer," "heart attack," or whatever.

What use is chaos?

I would like to close with some remarks on how chaos and the associated ideas that have motivated this article might be used more positively than as just a better or more enlightening description of the real world.

First of all, chaos has stimulated some important technical developments in the way we can analyse and interpret medical and other time series data. A key concept here is "fractal dimension," which as the name implies was developed for fractals, but the practical application of which has emerged as a byproduct of attempts to prove that certain systems have strange (chaotic, fractal) attractors, by analysing time evolution data. When brain wave data in rats are "reconstructed" the attractor for a healthy rat is computed to have a "dimension" of about 5·9, while that for the same rat in epileptic seizure has a dimension of only 2·5.[7] The

suggestion is that the "dimension" correlates with the flexibility and adaptability of the organism: the larger number implies a chaotic system with a well developed, flexible response to stimuli, whereas the low value associated with the seizure can be regarded as evidence of suppression or malfunction of a number of key elements of the rat's physiology.

A somewhat similar argument can be applied to electrocardiographic data: a healthy heart has a chaotic beat instead of a simple, periodic one because a periodic attractor has a low dimension, indicating a (too) limited responsiveness to external stimuli or crises. Indeed there is evidence that the heartbeat may become very regular immediately before a heart attack. Here, as above, chaos suggests new ways of analysis of data which already offer some evidence of new diagnostic approaches that could lead on to new preventive techniques or treatment strategies.

This somewhat vague association of chaos with adaptability can be and has been fleshed out.[8] I believe that it can also be useful in getting to grips with the detailed operation of natural selection, which still seems unsatisfactorily understood even if the basic genetic mechanisms are. Indeed, on a different tack, genetic variability may provide the same sort of barrier to disease as chaos does to prediction. Spread of a disease might even be regarded as due to an over-predictability of the target organism, much as a static or straight running mouse is easy meat for a cat.

Problems such as the spread of disease involve spatial complexity which adds, literally, new dimensions to the already rich phenomenology of dynamical chaos. This is an essential development if we are to do more than hand wave about life and death in the way I have done, for example, in figure 2. I believe, however, that the insights gained through exploring chaos give us some important clues as to how living organisms can maintain themselves—and indeed how they might have emerged in the first place.

Conclusion

What, finally, do I mean by "predicting the unpredictable" in my title? I suggest two things: firstly, that we can predict that very many important systems will have intrinsically unpredictable behaviour and, secondly, and more positively, we can by taking a broader view retain some predictive power—climate versus weather—as well as gaining useful insight into complexity.

1 May RM. Simple mathematical models with very complicated dynamics. *Nature* 1976;261:459-67.
2 Gleick J. *Chaos: making of a new science.* New York: Viking, 1987.
3 Chaos [videocassette]. InCA Productions. London: Channel 4, 1988.
4 Goldberger AL, Rigney DR, West BJ. Chaos and fractals in human physiology. *Sci Am* 1990 February:35-41.
5 Peitgen HO, Richter PH. *The beauty of fractals.* Berlin: Springer, 1986.
6 Mandelbrot BB. *The fractal geometry of nature.* San Francisco: Freeman, 1982.
7 Freeman WJ. Strange attractors that govern mammalian brain dynamics shown by trajectories of electroencephalographic (EEG) potential. *Transactions on Circuits and Systems* 1988;35:781.
8 Conrad M. What use is chaos? In: Holden AV, ed. *Chaos.* Manchester: Manchester University Press, 1986.