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**Point sur / Concise review**

# Is there chaos in the brain? I. Concepts of nonlinear dynamics and methods of investigation

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**Abstract** – In the light of results obtained during the last two decades in a number of laboratories, it appears that some of the tools of nonlinear dynamics, first developed and improved for the physical sciences and engineering, are well-suited for studies of biological phenomena. In particular it has become clear that the different regimes of activities undergone by nerve cells, neural assemblies and behavioural patterns, the linkage between them, and their modifications over time, cannot be fully understood in the context of even integrative physiology, without using these new techniques. This report, which is the first of two related papers, is aimed at introducing the non expert to the fundamental aspects of nonlinear dynamics, the most spectacular aspect of which is chaos theory. After a general history and definition of chaos the principles of analysis of time series in phase space and the general properties of chaotic trajectories will be described as will be the classical measures which allow a process to be classified as chaotic in ideal systems and models. We will then proceed to show how these methods need to be adapted for handling experimental time series; the dangers and pitfalls faced when dealing with non stationary and often noisy data will be stressed, and specific criteria for suspecting determinism in neuronal cells and/or assemblies will be described. We will finally address two fundamental questions, namely i) whether and how can one distinguish, deterministic patterns from stochastic ones, and, ii) what is the advantage of chaos over randomness: we will explain why and how the former can be controlled whereas, notoriously, the latter cannot be tamed. In the second paper of the series, results obtained at the level of single cells and their membrane conductances in real neuronal networks and in the study of higher brain functions, will be critically reviewed. It will be shown that the tools of nonlinear dynamics can be irreplaceable for revealing hidden mechanisms subserving, for example, neuronal synchronization and periodic oscillations. The benefits for the brain of adopting chaotic regimes with their wide range of potential behaviours and their aptitude to quickly react to changing conditions will also be considered. © 2001 Académie des sciences/Éditions scientifiques et médicales Elsevier SAS

**nonlinear dynamics / determinism / unpredictability / phase space / entropy / randomness / control**

## 1. Introduction

Many biologists, including neuroscientists, believe that living systems such as the brain, can be understood by application of a reductionist approach. There are strong grounds for this conviction: reductionism has been tremendously successful in recent decades in all fields of science particularly for dissecting various parts of physical or biological systems, including at the molecular level. But despite the identification of ionic channels and the char

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acterization of their responses to voltage, a phenomenon like, for instance, the action potential only makes sense in terms of an 'integrated' point of view, thus the need of Hodgkin–Huxley model to understand its generation. Indeed, complex systems can give rise to collective behaviours, which are not simply the sum of their individual components and involve huge conglomerations of related units constantly interacting with their environment: the way in which this happens is still a mystery. Understanding the emergence of ordered behaviour of spatio-temporal patterns and adaptive functions appears to require additional, and more global, concepts and tools.

A somewhat related and commonly accepted viewpoint is that the strength of science lies in its ability to trace causal relations and so to predict future events. The goal of scientific endeavor would be to attain long-term predictability and this is perhaps "the founding myth of classical science" [1]. This credo is rooted in Newtonian physics: once the laws of gravity were known, it became possible to anticipate accurately eclipses thousand years in advance. Otherwise stated, the Laplacian dogma according to which randomness is only a measure of our "ignorance of the different causes involved in the production of events...." [2] dominates the implicit philosophy of today's neuroscience. Conflicting with this view is the evidence that, for example, some basic mechanisms of the transmission of information between neurons appear to be largely governed by chance (references in [3, 4]).

For a long time it was thought that the fate of a deterministic system is predictable and these designations were two names for the same thing. This equivalence arose from a mathematical truth: deterministic systems are specified by differential equations that make no reference to chance and follow a unique trajectory. Poincaré was the first to show the limits of this faith: with a few words he became the forerunner of a complete epistemological revolution "... it may happen that small differences in the initial conditions produce very great ones in the final phenomena. A small error in the former will produce an enormous error in the latter. Prediction becomes impossible, and we have the fortuitous phenomenon." [5].

Systems behaving in this manner are now called 'chaotic'. They are essentially nonlinear meaning that initial errors in measurements do not remain constant, rather they grow and decay nonlinearly (in this case exponentially) with time. Since prediction becomes impossible, these systems can at first glance appear to be stochastic but this randomness is only apparent because the origin of their irregularities is different: they are intrinsic, rather than due to external influences. Thus, as stated by Vidal, chaos theory "is the challenge to the meaning and to the scope of the ideas of determinism and chance, as we are accustomed to practice them today" and a revision of our definitions is now imperative [6].

The relevance of these considerations to brain functions and neurosciences may not at first be clear. To take an example, a train of action potentials was simulated (*figure 1A*), using a system of differential equations. First

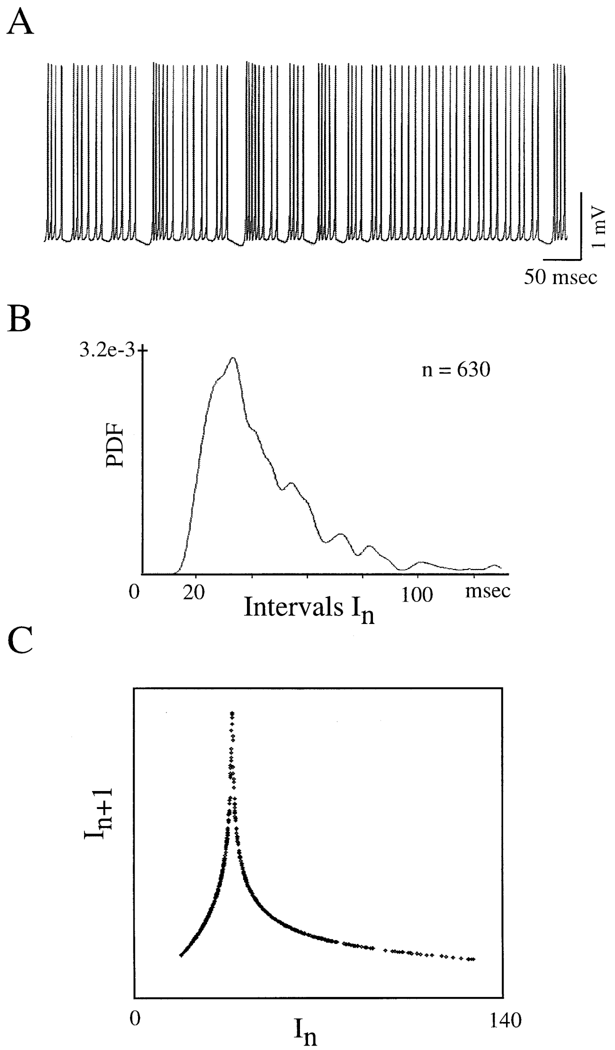


**Figure 1**. Noise versus ordered time series. (A) Computer generated train of action potentials produced by the Hindmarsh and Rose model (1984). At first sight this sequence looks random. (B) Probability density function of time intervals between spikes with an almost exponential decay suggesting independence between the successive spikes. (C) Each interval $I_n$ (axis) is plotted against the next one $I_{n+1}$ (ordinates), indicating a strict relationship between them. This pattern reveals that the sequence in (A) is produced by a deterministic process (Faure and Korn, unpublished).

described by Hindmarsh and Rose [7] this pattern would be interpreted as random on the basis of classical statistical methods analysing interval distributions suggesting exponential probability densities (*figure 1B*); however, a different representation of the interspike intervals (*figure 1C*) reveals a well ordered underlying generating mechanism. More generally, observation of exponential probability density functions is not sufficient to identify a process as conforming to a Poisson distribution [8] and the same remark applies to other forms of distributions.

The essentials of the discovery of chaos can be traced back to the turn of the last century in the mathematical work of three French mathematicians (see [9]). Hadamard and Duhem were interested in the movement of a ball on a negatively curved surface and on the failure to predict its trajectory due to the lack of knowledge of its initial condition. Poincaré tried to solve the so-called three body problem. He found that even though the movement of three celestial bodies is governed by the laws of motion and is therefore deterministic, their behaviour, influenced by gravity, could be so complex as to defy complete understanding. The nonlinearity is brought about in this case by the inverse law of gravitational attraction.

Present part I of this series of reviews describes chaos and the main methods and theoretical concepts now available for studying nonlinear time series with a focus on the most relevant to biological data. In part II (in preparation), we will show that despite the failure of earlier attempts to demonstrate chaos in the brain convincingly, data are now available which are compatible with the notion that nonlinear dynamics is common in the central nervous system.

This leads to the question: then what? We will show that such studies can bring new insights into brain functions, and furthermore that nonlinear dynamics may allow neural networks to be controlled, using very small perturbations, for therapeutic purposes.

## 2. Introduction to chaos theory

### 2.1. What is chaos?

Contrary to its common usage, the mathematical sense of the word chaos does not mean disorder or confusion. It designates a specific class of dynamical behaviour. In the past two types of dynamics were considered, growth or decay towards a fixed point and periodic oscillations. Chaotic behaviour is more complex and it was first observed in abstract mathematical models. Despite its 'banality' [6] it was not discovered until the advent of modern digital computing: nonlinear differential equations for which there are no analytical solutions and, as importantly, no easy way to draw comprehensive pictures of their trajectories, could then be solved.

Among many investigators, pioneers that paved the way of modern theory of chaos were the meteorologist E. Lorenz [10] who modeled atmospheric convection in terms of three differential equations and described their extreme sensitivity to the starting values used for their calculations, and the ethologist R. May [11, 12] who showed that even simple systems (in this case interacting populations) could display very "complicated and disordered" behaviour. Others were D. Ruelle and F. Takens [13, 14] who related the still mysterious turbulence of fluids to chaos and were the first to use the name 'strange attractors'. Soon thereafter M. Feigenbaum [15] revealed patterns in chaotic behaviour by showing how the quadratic map switches from one state to another via period doubling (see definition in section 2.3). The term 'chaos' had been already introduced by T.-Y. Li and J. Yorke [16] during their analysis of the same map (these concepts are further described below).

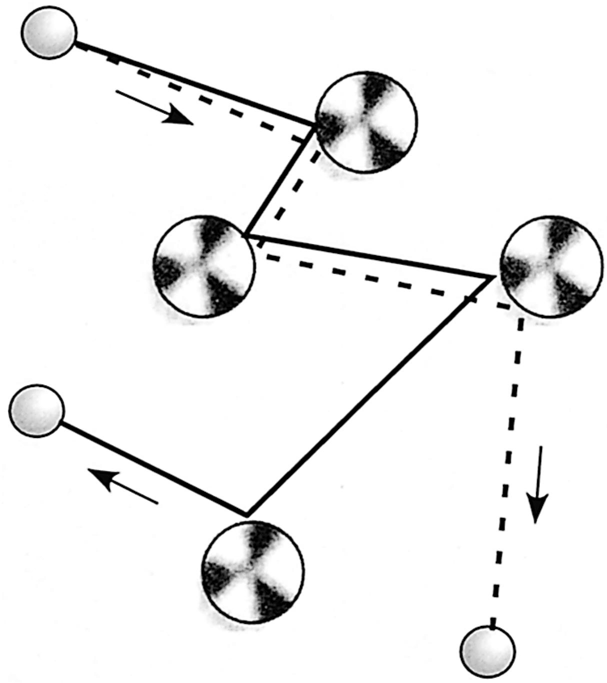

**Figure 2**. Sensitivity to initial conditions. Two initially close trajectories of a billiard ball (thick and dashed lines, respectively) quickly diverge, although they hit the same convex obstacles along their way (see also *figure 1*of [9]).

This account is the Western version, but it is far from being complete. Fairness prompts other names to be added to the above, those of Russian scientists who exploited Poincaré's legacy long before others. Their school laid the foundations of the modern theory of dynamical systems and of 'nonlinear mechanics', the most publicized aspect of which is chaos. A detailed description of their efforts and successes, for example those in the fields of nonlinear physics and vibrations, of self maintained oscillations, of bifurcation theory, and of the relations between statistical mechanics and dynamical systems can be found in [17]. The author describes the contributions of A. Kolmogorov, Y.G. Sinai and their collaborators in the characterization of chaos and of its relations with probabilistic laws and information theory.

There is no simple powerful and comprehensive theory of chaotic phenomena, but rather a cluster of theoretical models, mathematical tools and experimental techniques. According to Kellert [18], chaos theory is "the qualitative study of unstable aperiodic behaviour in deterministic dynamical systems". Rapp [19], who also acknowledges the lack of a general definition of chaotic systems considers, however, that they share three essential properties. First, they are dramatically sensitive to initial conditions, as shown in *figure 2*. Second, they can display a highly disordered behaviour; and third, despite this last feature, they are deterministic, that is they obey some laws that completely describe their motion. A more complete description, although in large parts similar, has been given by Kaplan and Glass [20] who define chaos as "aperiodic

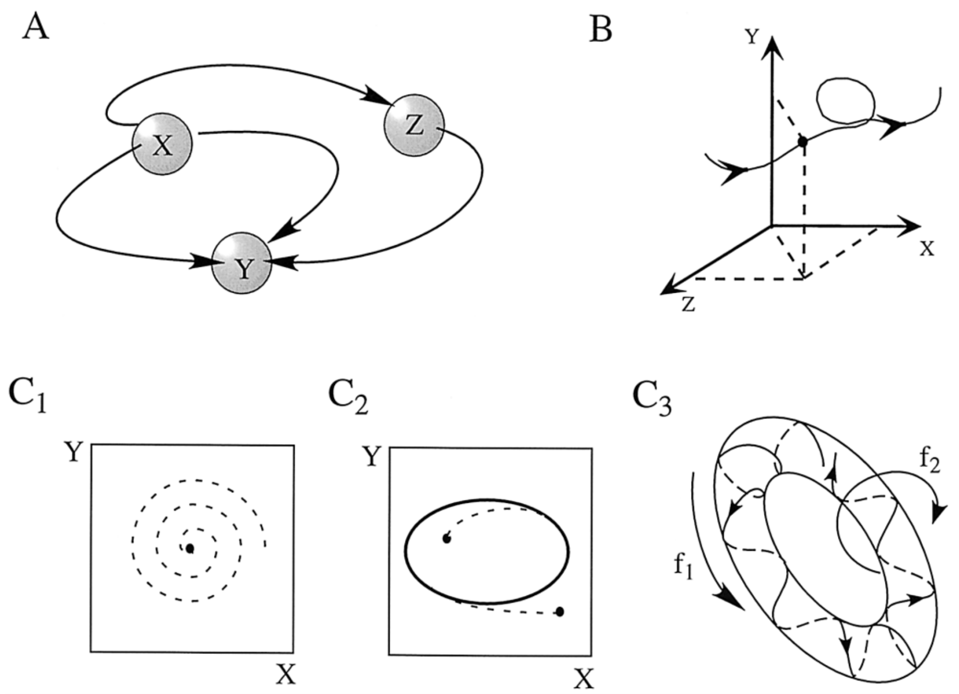


**Figure 3**. Several predictable attractors in their phase spaces. (A) Dynamical system with three interconnected variables. (B) Representation of the trajectory of the system shown in A, in a three dimensional phase space defined by the variables *x, y* and *z*. (C1-C3) Two dimensional phase spaces. (C1) The simplest attractor is a fixed point; after a few oscillations (dashed lines) a pendulum subjected to friction always settles in the same position of rest, indicated by a dot. (C2) A limit cycle that describes stable oscillations forms a close loop in the state space. The same state is reached whatever the departure point of the trajectory. (C3) Quasi periodic behaviour resulting from the motion of two systems that oscillate at frequency $f_1$ and $f_2$, respectively, and conforming to a torus.

bounded dynamics in a deterministic system with sensitive dependance on initial conditions". The additional word aperiodic reinforces the point that the same state is never repeated twice.

More generally, chaos theory is a specialized application of dynamical system theory. Nonlinear terms in the equations of these systems can involve algebraic or other more complicated functions and variables and these terms may have a physical counterpart, such as forces of inertia that damp oscillations of a pendulum, viscosity of a fluid, nonlinear electronic circuits or the limits of growth of biological populations, to name a few. Since this nonlinearity renders a closed-form of the equations impossible, investigations of chaotic phenomena seek qualitative rather than quantitative accounts of the behaviour of nonlinear differentiable dynamical systems. They do not try to find a formula that will make exact numerical predictions of a future state from the present state. Instead, they use other techniques to "provide some idea about the long-term behaviour of the solutions" [21].

Constructing a 'state space' is commonly the first and obligatory step for characterizing the behaviour of systems and their variations in time. This approach began with the work of Poincaré. Current research in this field goes by the name 'dynamical systems theory', and it typically asks such questions as what characteristics will all the solutions of this system ultimately exhibit? We will first give the general principles of this theory as they have been developed from studies of mathematical objects (models) before considering in detail how they apply to biological data.

### 2.2. Phase space, strange attractors and Poincaré sections

The phase space (a synonymous term is state space) is a mathematical and abstract construct, with orthogonal coordinate directions representing each of the variables needed to specify the instantaneous state of a system such as velocity and position (*figure 3A*). Plotting the numerical values of all the variables at a given time provides a description of the state of the system at that time. Its dynamics, or evolution, is indicated by tracing a path, or trajectory, in that same space (*figure 3B*). A remarkable feature of the phase space is its ability to represent a complex behaviour in a geometric and therefore comprehensible form.

A classical example, and the simplest, is that of the pendulum. Its motion is determined by two variables, position and velocity. In this case the phase space is a plane, and the state is a point whose coordinates are these variables at a given time, *t*. As the pendulum swings back and forth the state moves along a path, or orbit. If the pendulum moves with friction (as does a dissipative system), it is damped and finally comes to a halt. That is, it approaches a fixed point, that attracts the closest orbits (*figure 3C1*). This point is an attractor (the term attractor refers to a geometrical configuration in a phase space to which all nearby trajectories tend to converge over time).

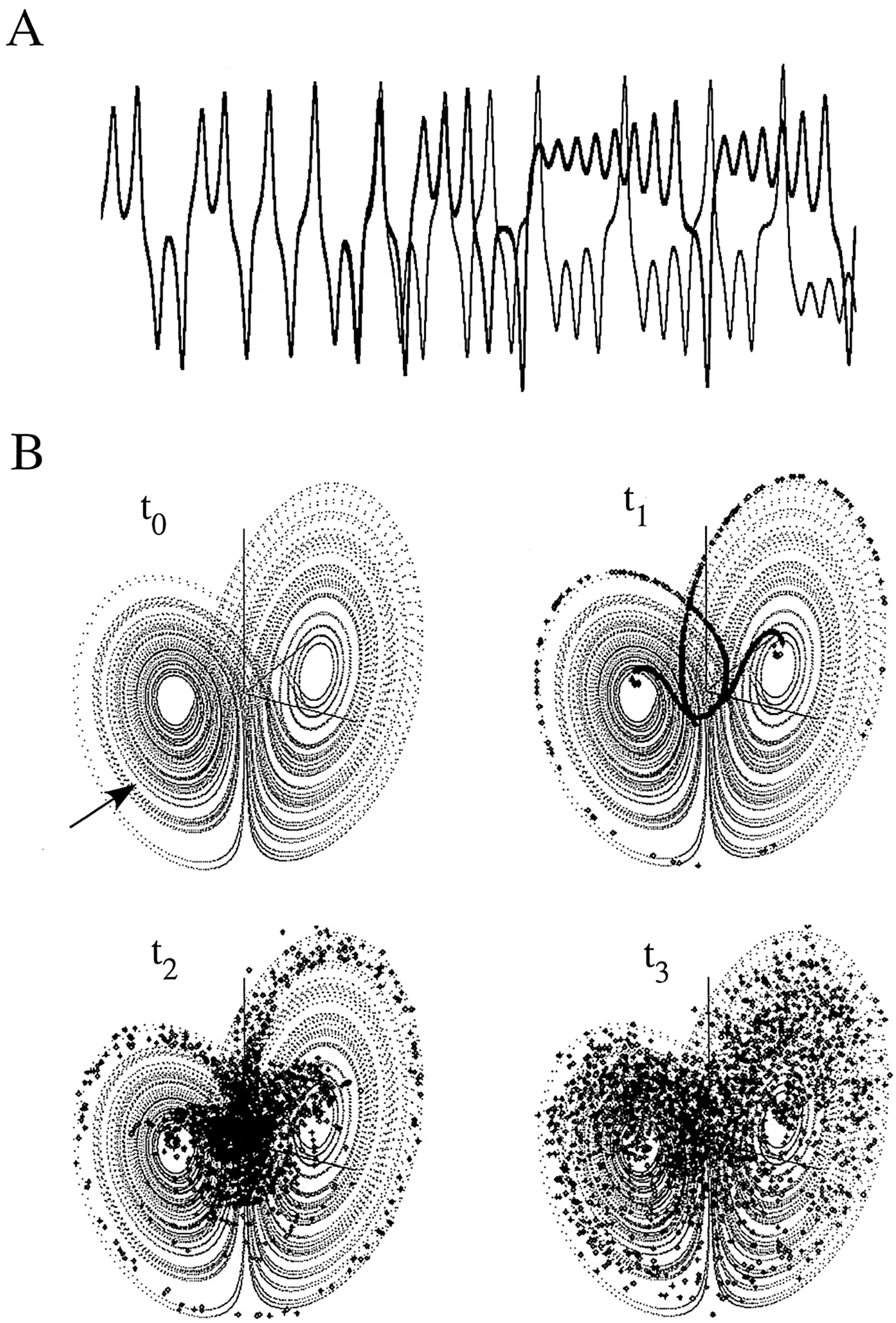


**Figure 4**. Lack of long-term predictability of the Lorentz attractor. (A) The two curves (thick and thin lines) start at initial locations that differ by only 0.0001. Note their random appearance and rapid divergence. (B) Effects of inaccuracy of measurements: 10 000 trajectories start in the same region (arrow, to the left). At the indicated time, they can be found anywhere on the attractor (thin dotted lines) and in regions progressively more distant from each other. Prediction quickly becomes impossible.

In absence of friction, or if the latter is compensated by a weight or another force, the pendulum behaves like a clock that repeats the same motion continuously. This type of motion corresponds to a cycle, or periodic orbit, and the corresponding attractor is called a limit cycle (*figure 3C2*). Many biological systems, for instance the heart and numerous neuronal cells, behave as such oscillators.

Another and a more complicated type of attractor is the two dimensional torus which resembles the surface of a tire. It describes the motion of two independent oscillators with frequencies that are not related by integers (*figure 3C3*). In some conditions the motion of such a system is said to be quasi periodic because it never repeats exactly itself. Rhythms that can be considered as quasi periodic are found, for example in cardiac arrhythmias, because pacemakers which are no longer coupled to each other independently maintain their own rhythm [20].

Fixed points, limit cycles and tori were the only known (and predictable on a long-term) attractors until Lorenz [10] discovered a new system that displays completely different dynamics. In his attempts to forecast the weather, he developed a simple model to describe the interrelations of temperature variation and convector motion. The model involves only three differential equations:

$$\begin{cases} dx/dt = -\sigma x + \sigma y \\ dy/dt = -xz + rx - y \\ dz/dt = xy - bz \end{cases} \quad (1)$$

where σ, $r$, and $b$ are parameters that characterize the properties of a fluid and of the thermal and geometric configuration of the system. The variable $x$ is related to the fluid's flow, $y$ is proportional to the temperature difference between the upward and downward moving parts of a convection roll, and $z$ describes the nonlinearity in temperature difference along the roll. The numerical solution of these equations with parameter values $\sigma = 10$, $r = 28$, and $b = 8/3$ leads to an attractor which can be visualized in a three-dimensional space with coordinates ($x$, $y$, $z$) since the system has three degrees of freedom. Because of its complexity, this geometric pattern, which looks like a butterfly, is the most popular 'strange attractor' (*figure 4*). Numerous sets of equations leading to strange attractors, also shown to be chaotic, have now been described in the literature (Rossler, Hénon, Ikeda attractors, etc). In all cases, the systems are deterministic: the corresponding trajectories are confined to a region of the phase space with a specific shape. Their trajectory rotates about one or two unstable fixed points (as defined below) and eventually escapes to orbit another unstable fixed point which is not an attractor. This process is repeated indefinitely, but the orbits of the trajectory never intersect each other.

The solutions of the above model illustrate the main features of chaos. In a simple time series, it looks random (*figure 4A*). The trajectories rapidly diverge even when they have close starting points. In the 3D phase space, they mimic both the aperiodicity and sensitive dependence on initial conditions (*figure 4B*). In a purely linear system, any exponential growth would cause the system to head off to infinity (to explode), but the nonlinearity folds the growth back. Conversely the exponential decay in a linear system would lead to a steady-state behaviour: the trajectories would converge to a single point. But given that in nonlinear systems there can be exponential growth in some directions, the effect of the exponential decay in other directions is to force the trajectories into a restricted region of the phase space. So nearby trajectories tend to separate from one another all the while being kept on the attractor.

Analysing pictures of strange attractors and their complicated paths can prove a complicated matter. Fortunately, three dimensional phase spaces may be simplified using a Poincaré section or return map, which is obtained by taking a simple slice of the attractor (*figure 5*), thus resulting in a return map. Reducing the phase space dimension in this manner corresponds to sampling the system every time the trajectory hits the plane of the section. This procedure, which simplifies the flow without altering its essential properties, is particularly useful for the studies of biological data, especially of time series obtained during studies of the nervous system (see below). It is also valuable for dealing with high dimensional systems (i.e. more than about 5).

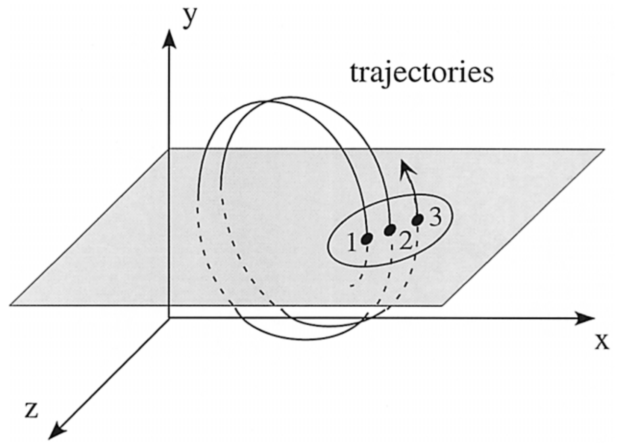


**Figure 5**. Poincaré section. The section of a three dimensional phase space is a two dimensional surface (which is placed here in the $x$, $z$ plane). Crossing points 1, 2, 3 are recorded every time the trajectory hits this section, resulting in a "strobscopic" portrait of the attractor.

### 2.3. From order to chaos: period doubling

Physical systems (as well as modeled data) can undergo transitions between various dynamics as some of their basic parameters are varied. In general a small change in a parameter results in a slight modification of the observed dynamics, except for priviledged values which produce qualitative alterations in the behaviour. For example, consider a creek in which water flows around a large rock, and a device to measure velocity. If the flow is steady, the velocity is constant, thus a fixed point in the state space. As the speed of water increases, modulations of water around the rock cause the formation of swirls, with an increase, and then a decrease in the velocity of each swirl. The behaviour changes from constant to periodic, having a limit cycle in the same phase space. If speed is further increased the motion of water may become quasi periodic, and ultimately random turbulences take the form of chaos (see [9]). Such dramatic matic changes of behaviour are called bifurcations and in a phase space, they occur at what are referred to as bifurcation points that serve as landmarks when studying a dynamical system.

The best studied model of bifurcations is that of the logistic equation which is a first order difference equation that takes the simple form

$$x_{n+1} = kx_n(1 - x_n) \quad (2)$$

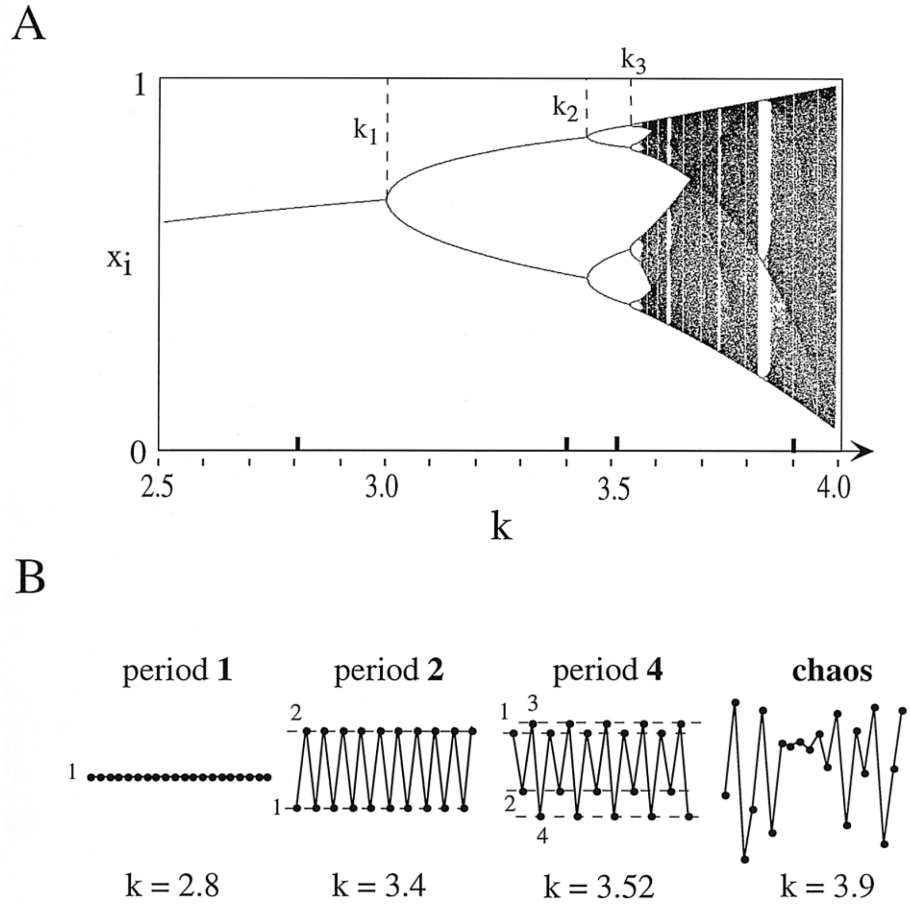


**Figure 6**. The logistic map. (A) Computer generated diagram of the behaviour of the logistic function $x_{n+1} = kx_n(1 - x_n)$, with its branching tree (three bifurcation points labelled $k_1$, $k_2$ and $k_3$ are indicated by vertical dotted lines). Chaos, with dots apparently dispersed at random, occurs at the right hand side of the bifurcation point $k = 3.569...$ (arrow). Magnifying the map in this region would reveal further chaotic vertical stripes, and close-up images would look like duplicates of the whole diagram. (B) Examples of different asymptotic regimes obtained for the indicated values of $k$ (thick bars in A, see text for explanations).

where $k$ is a control parameter. For example consider the specific case where $k = 0.2$ and $x_0 = 3$. Then equation (2) yields $x_1 = 0.2(0.3)(1 - 0.3) = 0.63$. Using this value of $x_1$, $x_2$ can be computed in the same way, by a process called iteration, and so on.

The logistic 'map' (*figure 6A*) was used by May in his famous investigations of the fluctuations of 'populations', which breed and later die off en masse (nonoverlapping generations). The size of a generation is bound by environmental conditions (including food supply and living space), fertility, and interactions with other species. A number between 0 and 1 indicates this size, which is measured as the actual number of individuals in the species: 0 represents total extinction and 1 is the largest possible number in a generation. The term $k$ determines the fate of a population of say, insects: the higher $k$ is, the more rapidly a small population grows or a large one becomes extinct. For low values of $k$, the initial population settles down to a stable size that will reproduce itself each year. As $k$ increases the first unstable fixed point appears. The successive values of $x$ oscillate in a two-year cycle: a large number of individuals produces a smaller population, which in turn reproduces the original large number of individuals the following year. For increasing values of $k$ a cycle repeats every 4 years, 8 years, then every 16, 32, and so on, in what is called a 'period-doubling cascade', culminating into a behaviour that becomes finally chaotic, i.e. apparently indistinguishable visually from a random process: at this stage "wild fluctuations very effectively mask the simplicity of the underlying rule" [22].

Another way to explain the graph of *figure 6* is as follows. In a finite difference equation such as a quadratic, and once an initial condition $x_0$ is chosen, the subsequent values of $x$ can be computed, i.e. $x_1$ and from thereon $x_2$, $x_3$, ..., by iteration. This process can be graphical or numerical [23, 8]. Successive steps, show for example [20] (*figure 6B*), that:

– for $3.000 < k < 3.4495$, there is a stable cycle of period 2;

– for $3.4495 < k < 3.5441$, there is a stable cycle of period 4;

– for $3.5441 < k < 3.5644$, there is a stable cycle of period 8, etc...

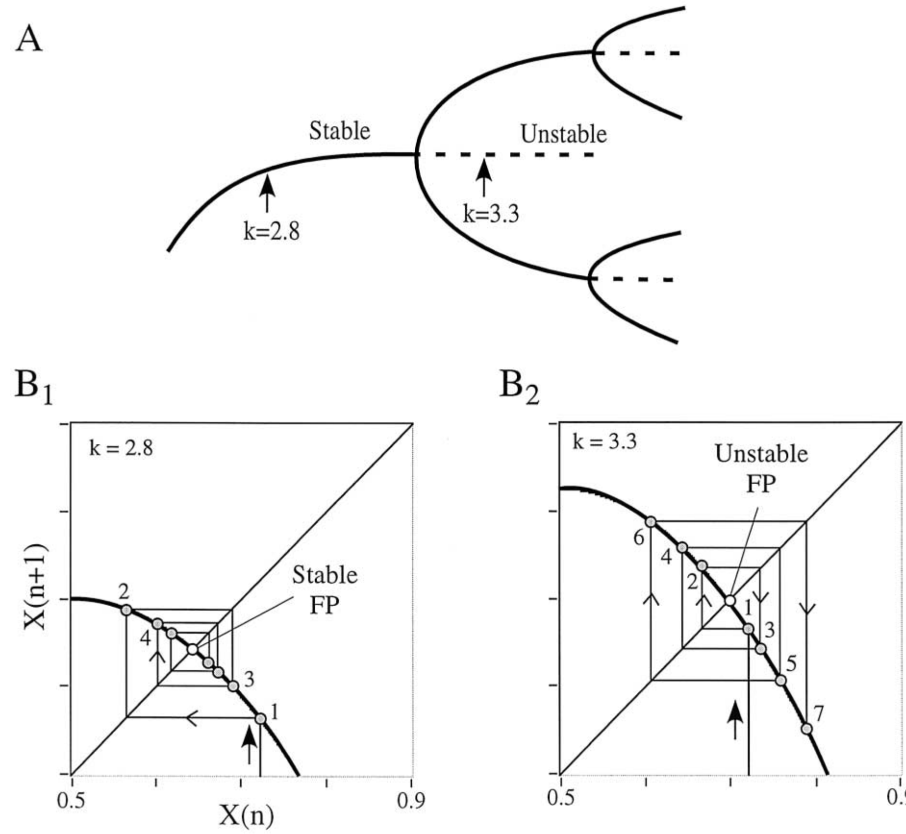


**Figure 7**. The road to chaos. (A) Illustration of the period doubling scenario showing that stable fixed points (solid lines), although they continue to exist, become unstable (dashed line) when iterations are pushed away from bifurcation points. (B1-B2) Graphical iterations at indicated values of the control parameter *k* (arrows in A). (B1) Representation of the logistic function $x_{n+1} = 2.8x_n(1 - x_n)$ (thick line) and of the corresponding fixed point (empty circle) at the intersection with the diagonal of the return map. Successive iterates converge toward this stable fixed point. (B2) Same representation as in B1 with $k = 3.3$; the fixed point is now unstable and iterates diverge away from it. (Note that B1 and B2 have same starting points).

(A stable cycle of period 2, 4, 8, ... is a cycle that alternates between 2, 4, 8, ... values of *x*).

The emergence on the map of a new stable cycle coincides with the transformation of the previous cycle into an unstable one (for example cycle 2 in *figure 7A*). This process is illustrated in *figure 7B1-B2* which shows how two different values of the control parameter *k* modify the local dynamics of the period 1 stable fixed point into a period 1 but unstable, fixed point. As *k* increases, this process is repeated until the chaotic state, which is made of an infinite number of unstable cycles, is reached.

The period-doubling bifurcations that characterize logistic maps obey various beautiful scaling relations. The values of the parameter *k* that which each successive bifurcation appears grow closer and closer together (*figure 6A*, vertical dotted lines). That is, successive bifurcation points are always found at a given value of *k* and chaos appears for $k = 3.569...$. Furthermore, if the value at which a cycle occurs is *x* then the ratio $(k_x - k_{x-1})/k_{x+1}$ is $\delta = 4.669...$ This is Feigenbaum's magic universal constant [15].

### 2.4. Other roads to chaos

Among the other roads to chaos two deserve special notice. One is via quasiperiodicity, when a torus becomes a strange attractor. The other route is that of 'intermittency' which means that a periodic signal is interrupted by random bursts occurring unpredictably but with increasing frequency as a parameter is modified. Several types of intermittencies has been observed in models, and the type depends on whether the system switches back and forth from periodic to chaotic or quasiperiodic behaviour [24]; for theoretical considerations see also [6]. In return (or Poincaré) maps the beginning of intermittencies has been reported at 'tangent bifurcations' of graphical iterations (not shown). Although we have not studied them extensively, we have detected similar sequences between the intervals of action potentials recorded from bursting interneurons presynaptic to the Mauthner cells of teleosts.

A wide variety of self organized systems called 'complex', and best described by a power law [25], have a noisy behaviour. The noise level increases as the power spectrum frequency decreases with a 1/*f* frequency depen dence. Although such complex systems are beyond the scope of this review, it is worth noting that intermittency may be one of the mechanisms underlying the 1/*f* noise found in natural systems [24, 26].

### 2.5. Quantification of chaos

Several methods and measures are available to recognize and characterize chaotic systems. Despite the sensitivity of these systems to initial conditions and the rapid divergence of their trajectories in the phase space, some of these measures are 'invariant', meaning that their results do not depend on the trajectory's starting point on the attractor, nor do they depend on the units used to define the phase space coordinates. These invariants are based on the assumption that strange attractors fulfill the conditions satisfying the 'ergodic' hypothesis which posits that trajectories spend comparable amounts of time visiting the same regions near the attractor [27]. Three major invariants will now be considered.

#### *2.5.1. The Lyapunov exponent*

It is a measure of exponential divergence of nearby trajectories or, otherwise stated, of the difference between a given trajectory and the path it would have followed in the absence of perturbation (*figure 8A*). Assuming two points $x_1$ and $x_2$ initially separated from each other by a small distance $\delta_0$, and at time $t$ by distance $\delta_t$, then the Lyapunov exponent, $\lambda$, is determined by the relation

$$\delta_{x(t)} = \delta_{x(0)}\, e^{\lambda t} \qquad (3)$$

where $\lambda$ is positive if the motion is chaotic and equal to zero if the two trajectories are separated by a constant amount as for example if they are periodic.

#### *2.5.2. Entropy*

A chaotic system can be considered as a source of information in the following sense. It makes prediction uncertain due to the sensitive dependence on initial conditions. Any imprecision in our knowledge of the state is magnified as time goes by. A measurement made at a later time provides additional information about the initial state.

Entropy is a thermodynamic quantity describing the amount of disorder in a system [28], and it provides an important approach to time series analysis which can be regarded as a source of information [29]. From a microscopic point of view, the second law of thermodynamics tells us that a system tends to evolve toward the set of conditions that has the largest number of accessible states compatible with the macroscopic conditions [24]. In a phase space, the entropy of a system can then be written

$$H = -\sum_{i=1}^{N} p_i \log p_i \qquad (4)$$

where $p_i$ is the probability that the system is in state *i*. In practice one has to divide the region containing the attractor in *N* cells and calculate the relative frequency (or probability *p*) with which the system visits each cell (*figure 8B*).

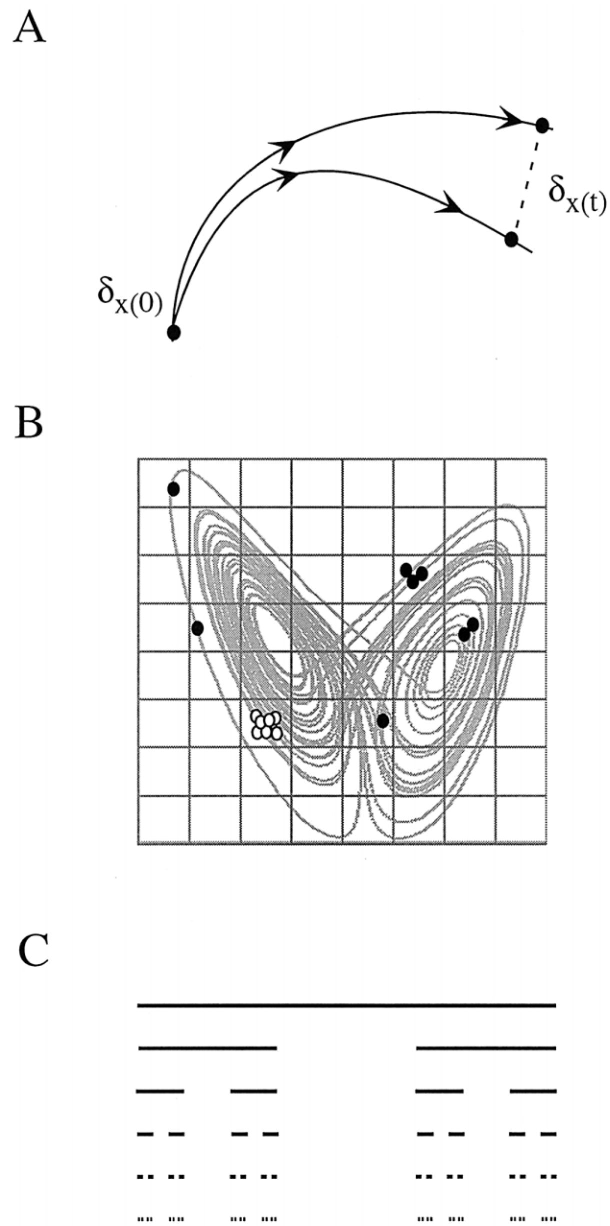


**Figure 8**. Principles underlying the main measures of chaotic invariants. (A) Lyapunov exponents. A small difference $\delta_x(0)$ in the initial point *x* of a trajectory results in a change $\delta_x(t)$ which is an exponential function $\delta_x(0)e^{\lambda t}$ (see equation 4) where $\lambda$ is the Lyapunov exponent. (B) Entropy. The phase space is divided into N cells and the location of all the points that were initially grouped in one cell (empty circles) is determined at a given time, *t* (thick dots). (C) Fractal dimension. A Cantor Set is constructed by removing at each successive step the central third of the remaining lines. At the stage *m*, there are $2^M$ segments of length $(1/3)^M$ each.

In dynamics, an important form of this measure is the Kolmogorov–Sinai entropy (*K*) which describes the rate of change of the entropy as the system evolves (for details see [29]). $K_n$ takes into account the entire evolution of the initial system after $n$ time units rather than concentrating on a few trajectories, such that

$$K_n = \frac{1}{\tau}(H_{n+1} - H_n) \quad (5)$$

where $\tau$ is the time unit.

If the system is periodic, $K_n$ equals zero whereas it increases without interruption, or it increases to a constant value, depending whether the system is stochastic or chaotic (see *figure 12C*).

*2.5.3. Dimension*

The two above described invariants focus on the dynamics (evolution in time) of trajectories in the phase space. In contrast, dimension emphasizes the geometric features of attractors.

Since Descartes, the dimension of a space has been thought of in terms of the number of coordinates needed to locate a point in that space. Describing the location of a point on a line requires one number, on a plane two numbers, and in our familiar 3-dimensional surroundings it requires three numbers. A modern perspective generalizes the idea of dimension in terms of scaling laws. For example, the amount of space enclosed by a circle given by the familiar formula $\pi r^2$. Its numerical value depends on the units with which $r$ is measured. A circle of radius 1 m encloses area $\pi$ when measured in metres, $10^4\pi$ when measured in centimetres, and area $10^{12}\pi$ when measured in microns. In the expressions $\pi r^2$, the dimension can be read off as the exponent on $r$ or as the slope of a log–log plot of the area versus the length scale.

Defining dimension in such manner provides a way to specify a new class of geometrical object called fractal, the dimension of which is non integer.

A simple self-similar shape is the Cantor set (*figure 8C*). It is constructed in successive steps, starting with a line segment of length 1. This length can be covered by a 'box' of side $\epsilon$. For the first stage of construction, one deletes the middle third of that segment. This leaves two segments, each of length 1/3. For the second stage, the middle third of each of those segments is deleted, resulting in four segments, each of length 1/9. Increasing the depth of recursion, and for the $M$th step, one removes the middle third of each of the remaining segments to produce $2^M$ segments, each of length $(1/3)^M$. Continuing as $M \to \infty$, the size $\epsilon$ of each enclosing box $\to 0$.

One can then calculate the box-counting dimension of this set keeping in mind that as $M \to \infty$, there remains only a series of points. Then if $N(\epsilon)$ is the number of boxes of length $\epsilon$ which covers entirely the set (or the attractor), the fractal dimension that cannot be integer, becomes:

$$D = \lim_{\epsilon \to 0} \frac{\log\left(\frac{1}{N(\epsilon)}\right)}{\log(\epsilon)} \quad (6)$$

Strange attractors are fractal objects and their geometry is invariant against changes in scale, or size. They are copies of themselves [30, 26].

## 3. Detecting chaos in experimental data

The preceding section examined 'ideal' dynamical phenomena produced by computer models and defined by known mathematical equations. These models generate pure low dimensional chaos which is, however, only found rarely in the natural world. Furthermore when dealing with natural phenomena, a 'reverse' approach is required: the dynamics need to be determined starting from a sequence of measurements and, whenever possible, the type of appropriate equations have to be identified to model the system. Most often this proves to be a very difficult task.

The nonlinear methods described above are generally of limited help when dealing with experimental time series due to the lack of stationarity of the recorded signals, meaning that all the parameters of a system, particularly of a biological one, rarely remain with a constant mean and variance during the measurement period. This creates an inherent conflict between this non stationarity and the need for prolonged and stable periods of observation for reaching reliable and unambiguous conclusions.

A second problem is that in contrast to computer outputs, pure determinism and low dimensional chaos (which can be modeled with a small number of variables, i.e. < 4–5) are unlikely in real world systems. Natural systems interact with their surroundings so that there is generally a mixture of fluctuations (or noise): those produced by the environment, those by the systems themselves and those by the recording techniques. Thus special and sophisticated procedures are needed to distinguish, if possible, between nonlinear deterministic or linear stochastic (or Gaussian) behaviour [31] (see also section 4).

Despite initial expectations, most statistical measures may not be adequate for signal processing in the context of nonlinear dynamics. For example broad band power spectra with superimposed peaks have often been associated with chaotic dynamics. This conclusion is often premature because similar power spectra can also be produced by noisy signals [8, 20].

Nevertheless, given that the dynamical properties of a system are defined in phase spaces, it is also helpful when analysing experimental data to start investigations by constructing a phase description of the phenomenon under study.

### 3.1. Reconstruction of the phase plane and embedding

Since a time series consists of repeated measurements of a single variable, the problem is to establish multidimensional phase spaces without knowing in advance the number of degrees of freedom that need to be represented, i.e. the number of variables of the system. This difficulty can be bypassed because even for a phenomenon that comprises several dimensions, the time series involving a single variable can be sufficient to determine its full dynamics [14, 32]. The procedure used in practice differs according to whether one is dealing with a continuous or with a discrete time series.

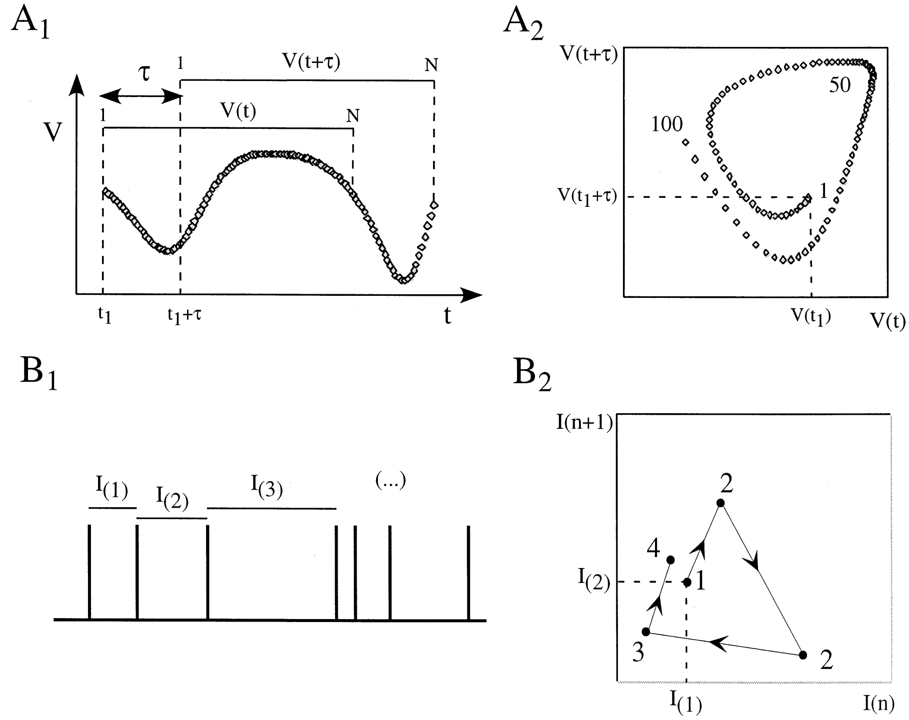


**Figure 9**. Reconstruction of phase spaces with the delay method. (A1-A2) Case of a continuous signal, as for example the recording of membrane potential, *V*. (A1) The time series is subdivided into two sequences of measurements of the same length N (here equal to 100 points). Their starting point is shifted by the time lag τ. (A2) The trajectory in a two dimensional phase space is obtained by plotting, for each point of the time series, $V_t$ against $V_{t+\tau}$. (B1-B2) In the case of a discrete signal, such as time intervals between action potentials in a spike train (B1), the same procedure is applied to time intervals $I_1, I_2 \ldots I_N$ (B2).

In the case of a continuous signal the experimentally recorded time series is split into successive segments using the method of delays (*figure 9A1-A2*). Successive segments can then be used to obtain a multidimensional embedding space in which the reconstructed dynamics are geometrically similar to the original ones.

Briefly, the measured time series is divided at equal time intervals *h* into sequences of measurements $V_0, V_1, V_2, \ldots$ and a three dimensional space can be reconstructed by plotting $(V_t, V_{t-\tau}, V_{t-2\tau})$.

Similarly, to embed the time series in an m-dimensional space, one plots

$$V = (V_t, V_{t+\tau}, V_{t+2\tau}, \ldots, V_{t+(m-1)\tau}) \quad (7)$$

where *m* is the embedding dimension and τ the embedding lag. Mathematical definitions and optimal conditions for finding appropriate embedding dimensions and time lags can be found in numerous reports (for example see [29]).

If the signal is discontinuous (spike trains are typical examples of such discrete time series – see [33]) it is possible to display the relationship between successive events or time intervals ($I_n$ versus $I_{n+1}$) with the help of a return plot (*figure 9B1-B2*). The resulting scatter plots, also named first return plots or Poincaré maps (given their analogies with the Poincaré sections described above) are fundamental for studies of biological data, particularly of nerve cell dynamics.

### 3.2. Characterization of chaos

When dealing with natural systems, it is often problematic to assess chaotic dynamics: in particular, discriminating between such systems and noisy data can be difficult. Consequently many claims for chaos in biology are subject to skepticism [34]. For example the Lyapunov exponent, which is positive in a chaotic time series, may also be positive for some forms of periodic oscillations or in time series contaminated with noise [35].

Consequently, numerous methods have been proposed to quantify naturally occurring data. All of them are based on the calculation of the proximity of points of nearby trajectories lying in a given sphere or volume of radius ϵ, and of their divergence with time (*figure 10*).

These measurements can be made in phase spaces or in so-called recurrence plots specifically designed to locate recurring patterns and to reveal dynamic behaviours possibly hidden in non-stationary biological signals [27, 36].

#### *3.2.1. Recurrence plots*

Recurrence plots are so called because they depict how the reconstructed trajectory recurs, or repeats itself. They distinguish patterns of activity with respect to the organization of the plots along diagonal lines. Thus they provide a useful framework for visualizing the time evolution of a system and for discerning subtle changes or drifts in dynamics [36] as, for example in the case of spontaneously occurring synaptic signals in central neurons [37].

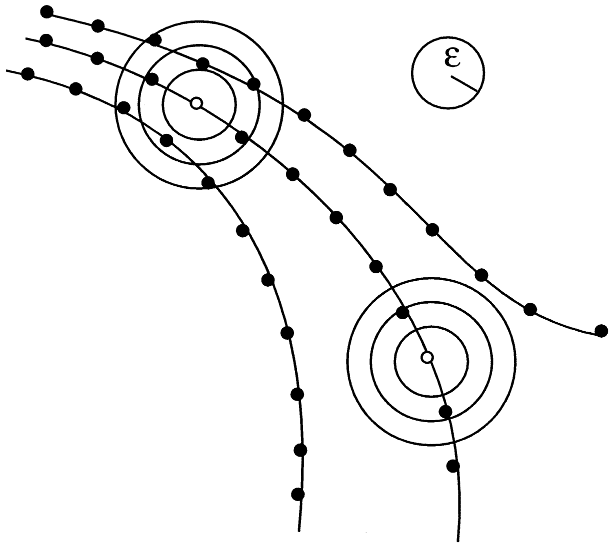


**Figure 10**. Computation of invariants in a dynamical flow. Since the trajectories of a deterministic system can visit, at different times, the same regions of the phase space, most of the invariants reflect the density of nearby (recurrent) points and their divergence. This density and its changes are assessed using spheres of a varying radius $\epsilon$, centered on a point of reference (open circles).

Let $X(i)$ be the $i$th point on an orbit describing the system in a d-dimensional space (*figure 11A*). Recurrence plots are then $N * N$ arrays in which a dot is placed at $(i, j)$ whenever $X(i)$ is close to $X(j)$, i.e. within resolution $\epsilon$. Given a voltage value $V(i)$ at time $i\Delta t$, the d-dimensional signal $X(i)$ can be obtained using the time delay method $X(i) = (V_i, V_{i+\tau}, ..., V_{i+(m-1)\tau})$, where $m$ and $\tau$ are the embedding dimension and lag, respectively. Each matrix contains $N^2$ locations, where $N$ is the number of vectors $X(i)$. A dot is plotted at each point $(i, j)$ whenever $X(i)$ and $X(j)$ are located within a given radius, $\epsilon$ (*figure 11B*).

*Figure 11 (C1-C3)* illustrates the resulting plots and exemplifies the typical visual aspect of the most commonly encountered classical dynamics.

*3.2.2. Specific measures*

Several quantification methods based on the analysis of the diagonal segments of recurrence plots have been described [38, 39]. They are aimed at assessing the degree of 'determinism' of the studied system, the term determinism meaning the extent to which future events are causally specified by past events [20].

These measures include:

– The correlation integral, $C(\epsilon)$ which takes into account the fact that the total number of dots in the plot tells us how many times the trajectory came within distance $\epsilon$ of a previous value. Then,

$$C(\epsilon) = \frac{\text{number of times } |X_i - X_j| \leq \epsilon}{N(N-1)} \quad (8)$$

– The percentage of determinism, *%det.*, indicates the percentage of points included in diagonal segments of a defined minimal length (*figure 12A*).

Faure and Korn [40] have shown that the lengths of the diagonal line segments are expomentially distributed (*figure 12B*). The slope of this distribution, μ, is easily computed and it provides a robust estimate of the Kolmogorov–Sinai entropy (see also [41]).

These calculations are called 'coarse grained' because they involve only one resolution of $\epsilon$ and $\epsilon$ that remains the same for every embedding dimension. Therefore they are mostly used to compare the evolution of various time series, as will be further detailed below. Conversely, invariants such as entropy (*figure 12C*) or fractal dimension, which identify more specifically the nature of the dynamics (i.e. periodic, chaotic, or random), are estimated at mathematical limits, as $m \to \infty$ and $\epsilon \to 0$. Such measures require several successive embedding procedures, with decreasing values of $\epsilon$.

In particular, the behaviour of the correlation integral $C(\epsilon)$ can be calculated as $\epsilon$ becomes progressively smaller. This technique was introduced by Grassberger and Procaccia [42] and it gives access to the correlation dimension, which has been, until recently, one of the most fundamental quantities used both to i) analyse chaotic time series and ii) look for attractors of chaotic systems since there is a close relationship between the correlation integral and the fractal dimension [42].

Specifically, for a given embedding dimension, and as $\epsilon$ gets smaller,

$$C_m(\epsilon) = \epsilon^{v} \quad (9)$$

where υ, the correlation dimension, gives a good estimate of the fractal dimension of the attractor, which can be written as,

$$\lim_{m \to \infty} v = D \quad (10)$$

The various steps of this procedure are illustrated in *figure 13*.

This method is however liable to misinterpretations and criticism [43], for example when used to clarify the temporal structure of experimental data.

## 4. Is chaos the most critical issue?

In addition to stimulating the curiosity of both scientists and the public by extending greatly the domains of nature that could be subjected to deterministic analysis, the discovery of chaos theory raised considerable expectations in neuroscience as in many other scientific disciplines. The hopes were, and still are for a large part, that understanding the sources of seemingly randomness of complex brain functions and behaviour, and unraveling their underlying (and simpler) neuronal mechanisms, had become attainable objectives. But in practice things did not turn out to be that easy, primarily for technical reasons: the signature of chaos, i.e. invariance of something observable, is far from being robust to noise and to small sample sizes. Further

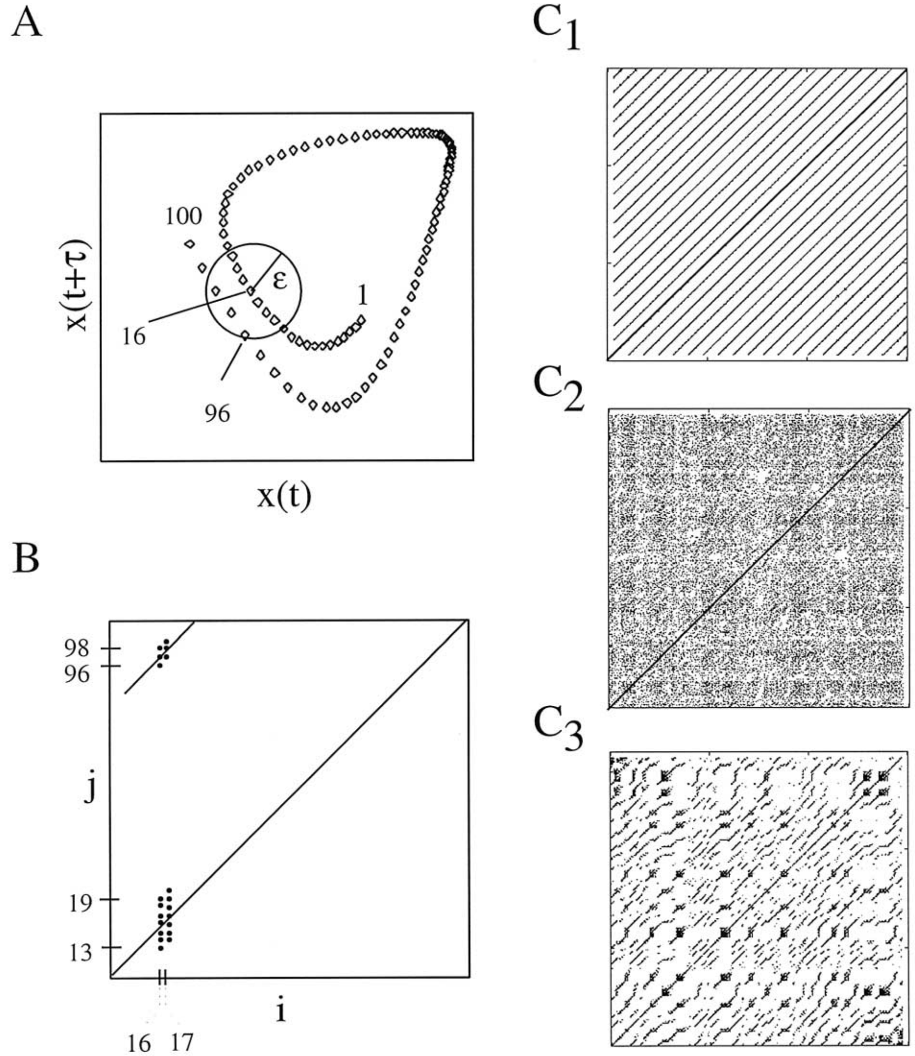


**Figure 11**. Visualization of dynamics with recurrence plots. (A-B) Construction of a recurrence plot. Points *j* located within a distance ε of points *i* in the phase space shown in (A) are ranked in the ordinate of a matrix (B) in which points *i* are ordered, in sequence, in the horizontal coordinate. (C1-C3) Appearance of typical reconstructed trajectories. (C1) Periodic signal, with parallel stripes at 45°, separated by a constant distance in both directions. (C2) Random signal with dots filling the space and lacking a specific pattern. (C3) For a chaotic time series, there are clusters of dots interrupted by interspersed short periodic stripes.

more, assessment of 'true' chaos requires sophisticated and painstaking quantification procedures, the results of which are generally far less rigorous and therefore less convincing with biological data than those obtained with mathematical models or stable physical systems. As a consequence, the least ambiguous criterion for assessing chaos in the nervous system is, most often, the identification of a bifurcation scenario. As will be shown later (in part II of this series, in preparation) several groups have presented unambiguous bifurcations at the cellular level with the analysis of experimentally observed spike trains complemented by computational studies (see for example [44–46]). Results with a Hindmarsh and Rose model obtained during an extensive study of central inhibitory interneurons recorded by ourselves in the brain of a fish [47] are shown in *figure 14* which illustrates bifurcations of spike train discharges induced by progressively decreasing currents 'injected' into mimicked cells.

Neurobiologists have become gradually more interested in practical issues such as the comparisons of dynamics of neuronal assemblies, and therefore of time series, in various experimental or physiological conditions. With these new, and perhaps less ambitious expectations, measures of nonlinearity centered on the studies of coarse grained quantities, which can be defined on intermediates length scales [31, 46] have been designed and often adapted to specific experimental material and objectives.

#### 4.1. Methods related to invariants

Finite length scale versions of invariants such as the correlation dimension, Lyapunov exponent and Kolmogorov entropy (obtained with a given ε) and the embedding dimension (*m*) are useful for comparative purposes. For example the correlation integral obtained at a single resolution ε and with a single embedding can already be used to quantify the distribution of all points in the phase space.

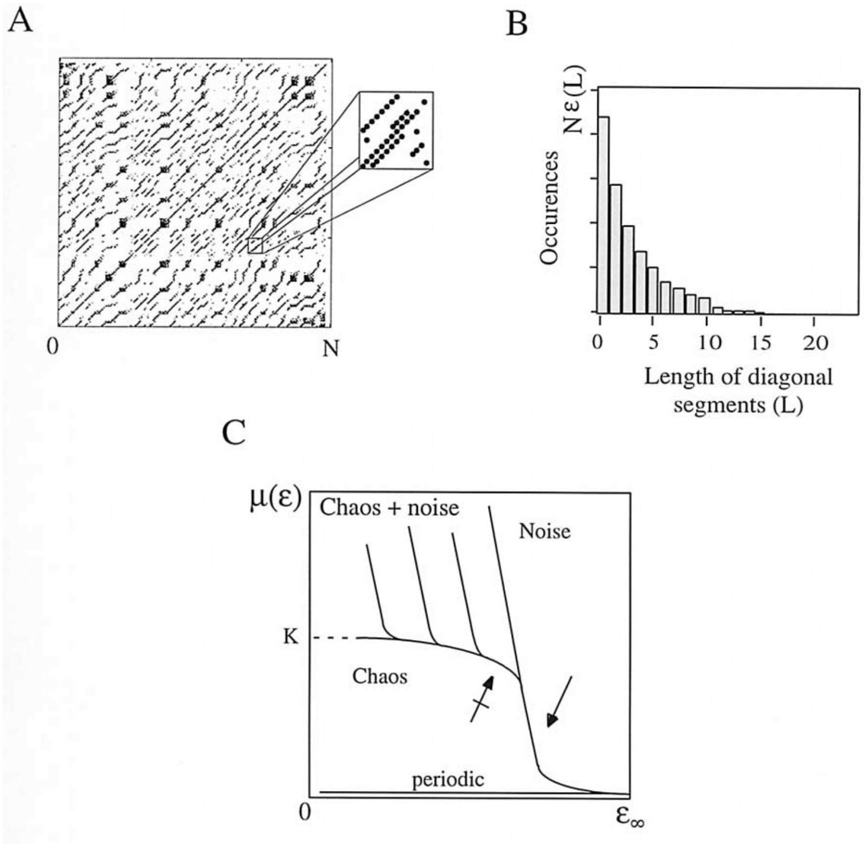


**Figure 12**. Quantification of determinism on recurrence plots. (A) Plot obtained from a chaotic time series (*N* points) embedded in a two-dimensional phase space. (Inset) Enlargement of the boxed area, with diagonal line segments of various length, *L*. (B) (Left) Histogram of the number $N\epsilon(L)$ of line segments of length *L*, as they can be counted in the recurrence plot shown in (A). (C) Expected variations of μ versus ϵ for chaotic data without and with added noise, and for stochastic time series; for the latter the computed plot of μ(ϵ) is curved (arrow). Note that as the noise level increases the flat component of μ(ϵ), which indicates chaos, is interrupted by an upward swing. Therefore, for a given level of noise $\epsilon_{div}$, the convergence of μ towards the Kolmogorov-Sinai entropy (*K*), can be only inferred by extrapolating the computed curve starting at the second inflection (crossed arrow) (modified from [40]).

The main idea behind this approach is that such a distribution is more closely clustered in a dynamical system than in a random one. The one percent radius, which is the value of (ϵ) such that the correlation integral is equal to 0.01 % [48], or the maximum likelihood estimators [49] are examples of such measures. Similarly, families of statistics which measure the rate of variation of information in time series have been developed. These are for example, the so-called approximate entropy [50], the generalized redundancy information [51] or the coarse grained entropy rates [52].

### 4.2. Predictability

Since chaotic trajectories are generated by deterministic equations, it should be possible to predict the evolution of their dynamics, at least in a proximate future. The basic notion is that determinism will cause identical present states to evolve similarly in the future (this is the method of 'analogues' of Lorenz [53]). Therefore, in order to make predictions from a given point, one has, again, simply to form a neighbourhood with a fixed radius ϵ or a constant number of points. The prediction is then provided by the average of the coordinates, in the phase space, of all the points belonging to this neighbourhood. This average can be calculated with the help of various linear or nonlinear fitting functions (see [31, 54] for reviews).

For instance, Sugihara and May [55] split the time series into two parts. The first part is used to determine the local properties of the trajectory. These properties then serve as a template to predict the evolution of points in the second part and to examine the degree of correlation between the predicted and observed results. An average error between predicted and observed values can also be employed [56].

Nonlinear forecasting has been successfully achieved in the nervous system to demonstrate determinism in spike trains [57, 58] but with averages rather than individual predictions. Yet, individual predictions are also possible as documented by *figure 15* which was obtained during the already mentioned study of the mode of firing of inhibitory interneurons in the teleost hindbrain (Faure and Korn, in preparation).

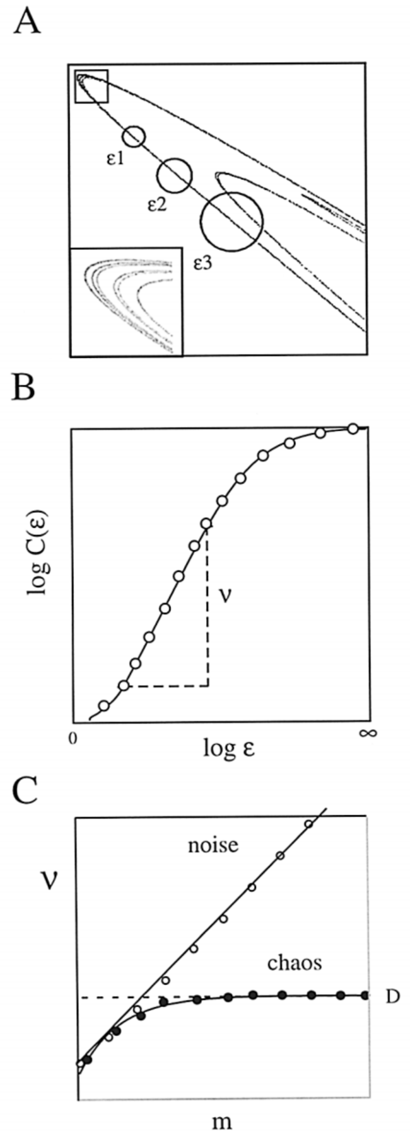


**Figure 13**. Calculation of the correlation dimension. (A) The correlation integral is computed for various resolutions of ε (ε1, ε2, ε3) in the phase space which contains in this example a Henon attractor (the self-similarity of which is illustrated in the inset by the enlargement of the boxed area of the figure). (B) Log-log plot of the correlation integrals (ordinate) as a function of the radius ε. The correlation dimension ν is the slope of the linear part of the plot. (C) Plot of the measured dimension ν (ordinate) as a function of the embedding dimension *m* (abscissa). Note that ν converges to a constant value, or diverges, for chaotic or noisy time series, respectively.

## 4.3. Unstable periodic orbits

An alternative to conventional measures of chaos is to search for geometric figures called unstable periodic orbits (UPOs) in the reconstructed phase space or in return maps. A Poincaré section across an attractor (*figure 16A*) captures an infinite number of UPOs which constitute the skeleton of chaotic systems [59, 60] and deterministic trajectories wander endlessly around them (see also [61]). Before describing UPOs it is essential to remember that periodic intervals are revealed in return maps as intersections with the line of identity $I_n = I_{n+1}$. Chaotic trajectories tend to approach such periodic states but because of their instability they quickly escape them.

Therefore, in return maps (*figure 16B*) each UPO is made by a double sequence of points. The first sequence approaches a given fixed point on the identity line along a 'stable' manifold (which is not necessarily a straight line, see [62]), with ever decreasing separations. It is followed by a second series of points, departing from the same fixed point at ever increasing distances, along an 'unstable' direction and according to well defined and strict mathematical rules [63].

UPOs centered around the identity line $I_n = I_{n+1}$ correspond to period 1 orbits but in dynamical time series there is a hierarchy of orbits with increasing periodicities, i.e. period 2, 3 and so on... orbits. These are pairs of points with reflection symmetry across the diagonal (*figure 16C*), triplets of points with triangular symmetry, and so on... [61]. Periodic orbits have been observed in several neuronal systems including crayfish photoreceptors [63], the hippocampus of vertebrates [61] and, as shown in *figure 16D*, in teleost Mauthner cells [37].

The complex geometry of UPOs corresponds well to the bifurcation scenario represented in *figure 7* which also explains why, in the chaotic state, there is an infinity of such orbits. It is important to recognize that the instability reflected by UPOs could paradoxically become an advantage for the control of chaotic systems by external perturbations (see section 5.2).

## 4.4. Complexity and symbolic analysis

An extreme coarse grained approach called symbolic dynamics consists in encoding the time series as a string of symbols. This procedure results in a severe reduction of available information but it may prove to be useful if the data are contaminated by high noise levels. It can also be used to assess the amount of information carried for example by spike trains.

There are several ways [64, 65] to determine the complexity $C(x)$ of a time series, which is the size of its minimum representation, when expressed in a chosen vocabulary.

For example, consider the case of a binary sequence $x$.

$$x = 101101011010001001$$

The purpose is to reduce the message, according to its regularities, into a sequence constructed with the smallest possible number of symbols. Then, if $a = 01$ is repeated 6 times in the series the message becomes

$$x = 1a1aa1a00a0a$$

This sequence exhibits three sequences of $1a$. If $b = 1a$, thus:

$$x = bbab00a0a$$

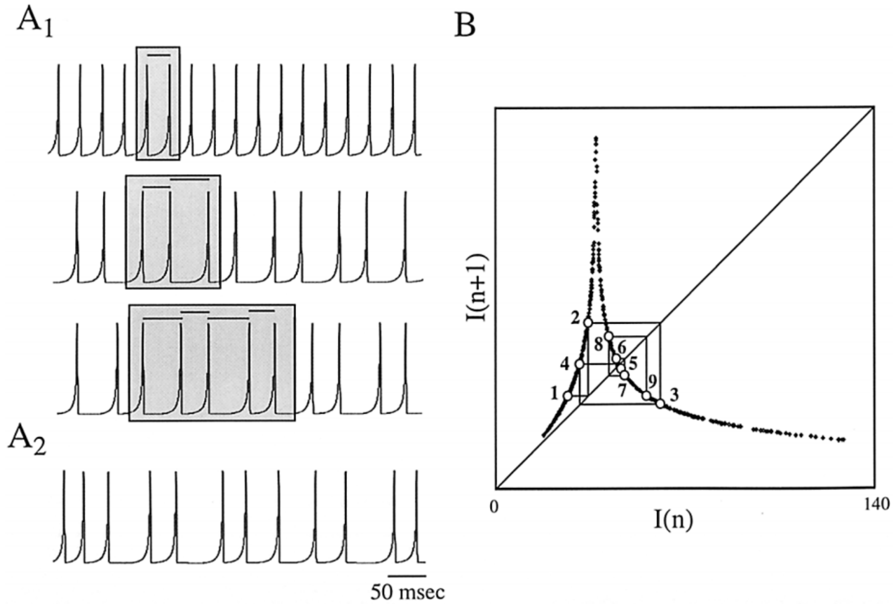


**Figure 14**. Period-doubling scheme as a function of decreasing stimulating current. (A1-A2) Membrane potential of a modeled interneuron firing in a 1, 2 or 4 cycle mode (A1 top to bottom) and in chaotic (A2) modes. (The basic intervals between spikes are indicated above each trace). (B1) Return map of the chaotic regime with successive iterates around a fixed point.

which becomes

$$x = b^2 \; ab0^2 \; a0a = m$$

As explained in details by Rapp [65] it is necessary to assign a quantitative measure to the amount of information encoded in such a measure. Specifically, the size of this representation is determined by applying the following rules. Each symbol in the sequence contributes a value of 1 and exponentials add logarithmically. For example, in the final reduction above, seven symbols appear in *m* and the exponent 2 appears twice. Thus *m* contributes $7 + 2 \log_2 2$ and the symbols *a* and *b* each contribute 2. Then

$$C(x) = \left[7 + 2 \log_2 2 + 2 + 2\right] = 13$$

which is less than 18, the length of the original sequence. The compression can be more dramatic. For a message of a given length the lowest complexity is obtained when there is a single symbol: an estimate of 22 is computed if it is repeated 1000 times (the logic being that *a* appears 1000 times, *b* = *aa* appears 500 times and so on..).

The values of *C*(*x*) are low in periodic systems, intermediate for deterministic behaviour, and high for complete randomness. An important and related measure is the so-called algorithmic complexity which is the length (expressed in bits) of the shortest computer program that can reproduce a sequence. Thus the algorithmic complexity of a periodic time series is small since it needs only to specify the pattern that repeats itself, and an instruction to replicate that pattern. Conversely a time series can be defined as random when its description requires an algorithm that is as long as the sequence itself ([66], see also [67]).

## 5. Testing and controlling dynamical systems

Systems with many degrees of freedom are particularly difficult to study with nonlinear tools even if multiple channels of information (such as multiple recordings) are available. The dynamics of the brain represents an extreme challenge because the number of neurons and synapses in vertebrates is so high, particularly in man, their connections are widespread throughout the nervous system, and they constantly interact with their environment. Thus, and for the reasons described in the introduction to section 3 of this paper, experimental data such as recordings from nerve cells and axons are most often time series that comprise mixtures of nonlinear deterministic and stochastic signals.

### 5.1. Chaos versus chance: Surrogate data testing

The word chaos has been equated to randomness by several authors, including Prigogine and Stengers [1] and Ford [68, 69]. On the other hand Lorentz [30] insists that the current use of the term chaos refers to processes that only 'appear' to proceed according to chance although their behaviour is determined by precise laws. He then includes, in a "more liberal concept of chaos", processes with some randomness, provided that they would exhibit similar behaviour if the randomness could be removed. He goes on to consider the suggestion that chaos is so ubiquitous that all the phenomena described as behaving randomly should be recognized instead as being chaotic "a question that Poincaré asked in his essay on chance". This concern is justified by examples of particular sequences obtained with logistic maps, the high algorith

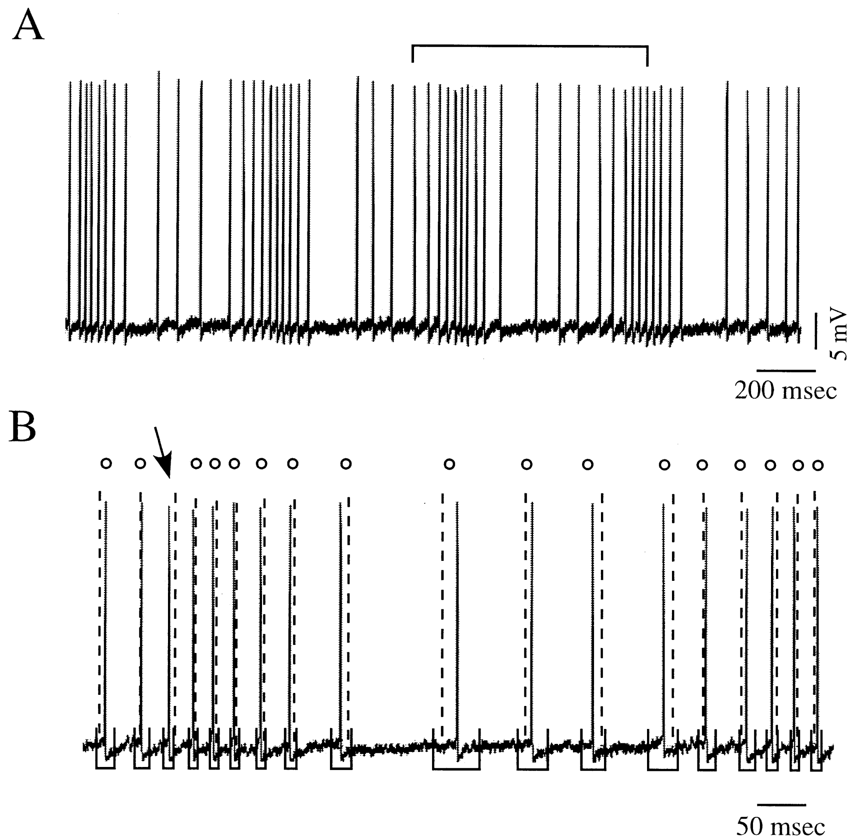


**Figure 15**. Short-term predictability of a neuronal discharge pattern. (A) Continuous spontaneous activity recorded *in vivo* from an identified inhibitory interneuron which was presynaptic to a teleost Mauthner cell. (B) Enlarged and schematized segment indicated in (A) by a bracket, showing the accuracy of predictions obtained with the average of twenty closest neighbors in the phase space constructed with all preceding data points (see text). The observed and predicted spikes are represented by solid and dashed vertical bars, respectively. Successes in forecasting with errors less than 20 % (delineated by brackets below each action potential) are indicated by circles. Note one false prediction, pointed out by an arrow (Faure and Korn, unpublished data).

mic complexity of which makes them equivalent to random sequences [24]. Also, if many weakly coupled degrees of freedom are active, their evolution may often be averaged to quantities that are to a first approximation, Gaussian random variables (see [31, 70]). In the light of our present knowledge two separate issues must be addressed.

First, is randomness a special case of chaos? For dynamical systems, the answer turns on the concept of dimension which, is i) the number of distinct dynamical variables in the equation, or ii) the minimum number of dimensions necessary to depict the behaviour of empiric data in a phase space. Within this restricted domain, a random process has an infinite number of dimensions and can be considered as being the limiting case of a finite chaotic system.

Second, how can one distinguish between chaotic and random signals? A major difficulty in the analysis of natural and biological systems is the question: is the randomness observed in a time series only apparent (and the consequence of true nonlinear determinism with structural instability), or is it real (and produced by random inputs and/or statistical fluctuations in the parameters)? As we have seen (section 3.1) there are methods such as embedding to determine the number of active degrees of freedom but these methods can fail. A more sophisticated way to address this problem is to test the significance of the measures (entropy, dimension,...) by redoing calculations with 'surrogate' data [71]. For this, data consistent with a null hypothesis, called surrogate data, are created [71, 19] by randomly reordering the original time series, but keeping some of their original statistical properties (such as the mean, variance, or the Fourier spectrum). Also, a null hypothesis is established against which the data will be tested (the main idea being to reject this hypothesis). The null hypothesis can be that the original signal is indistinguishable i) from a random variable (algorithm zero or random shuffle surrogates), ii) from a linearly filtered random variable (algorithm one, or random phase and Fourier transform surrogates), and iii) from a linearly filtered random variable that has been transformed by a static monotone nonlinearity (algorithm two or Gaussian scale surrogates). The level of significance that can be accepted for rejecting the null hypothesis must also be specified.

A measure $M$ is then applied to the original time series giving the result $M_{Orig}$. The same measure is applied to the surrogate data sets. Let $<M_{surr}>$ denote the average value of

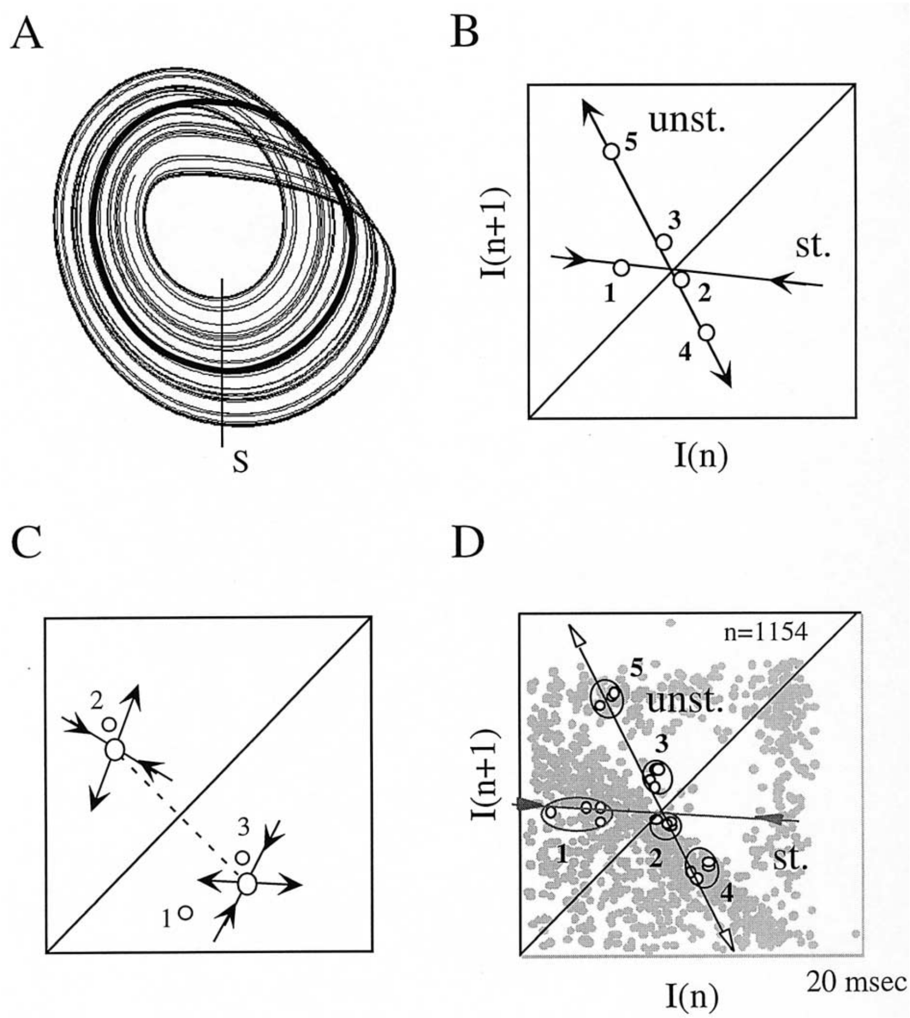


**Figure 16**. Unstable periodic orbits. (A) Poincaré section (S) across a Rössler attractor with a schematic presentation of an unstable period-1 orbit (thick line). (B) Unstable period-1 orbit visualized on the Poincaré section, with successive points that converge into, and diverge from, the unstable fixed point labeled 2, along a stable (st) and unstable (unst) manifold, respectively (the sequence of events is as numbered). (C) Schematic representation of a period-2 orbit with a sequence of three points that alternate across the identity line. (D) Return map obtained from an actual series of 1 154 successive synaptic events (shaded points) recorded intracellularly from a teleost Mauthner cell. Note that five unstable periodic orbits were detected in this time series (modified from [47]).

M obtained with surrogates. If $\langle M_{surr} \rangle$ is significantly different from $M_{Orig}$, then the null hypothesis can be rejected.

Like all statistical procedures the method of surrogate data can be misapplied. In particular false positive rejections of the null hypothesis are not uncommon [72–74]. Also, it is possible that the null hypothesis is not rejected because the signal was generated by a finite dimensional system that was large enough to make the time series indistinguishable from noise, at least for the specific case of the applied measure.

Precautions for interpreting the different surrogates and their possible limitations are considered in Schreiber and Schmitz [75].

### 5.2. Stabilizing chaos

A major advantage of chaotic systems over stochastic processes is that their extreme sensitivity can be used to direct them rapidly towards a desired state using minimal perturbations. Viewed in this context the unpredictable behaviour of chaotic systems becomes an advantage rather than an undesirable 'noisy' disturbance. The basic idea is that a chaotic system explores a large region of a state space. This region contains many unstable fixed points (or unstable periodic orbits). Using a weak control signal, it is possible to force the system to follow closely any one of these numerous orbits and to obtain, thereby, large beneficial changes in the long-term behaviour at least as long as the control is maintained. Thus one can select a given behaviour from an infinite variety of behaviours and, if necessary, switch at will between them.

This type of adaptive control was first proposed, on a theoretical basis, by Mackey and Glass [76] who sought to demonstrate, with bifurcation schemes, that there is a large class of functional disturbances (respiratory and hematopoietic ones were used as examples) that can be

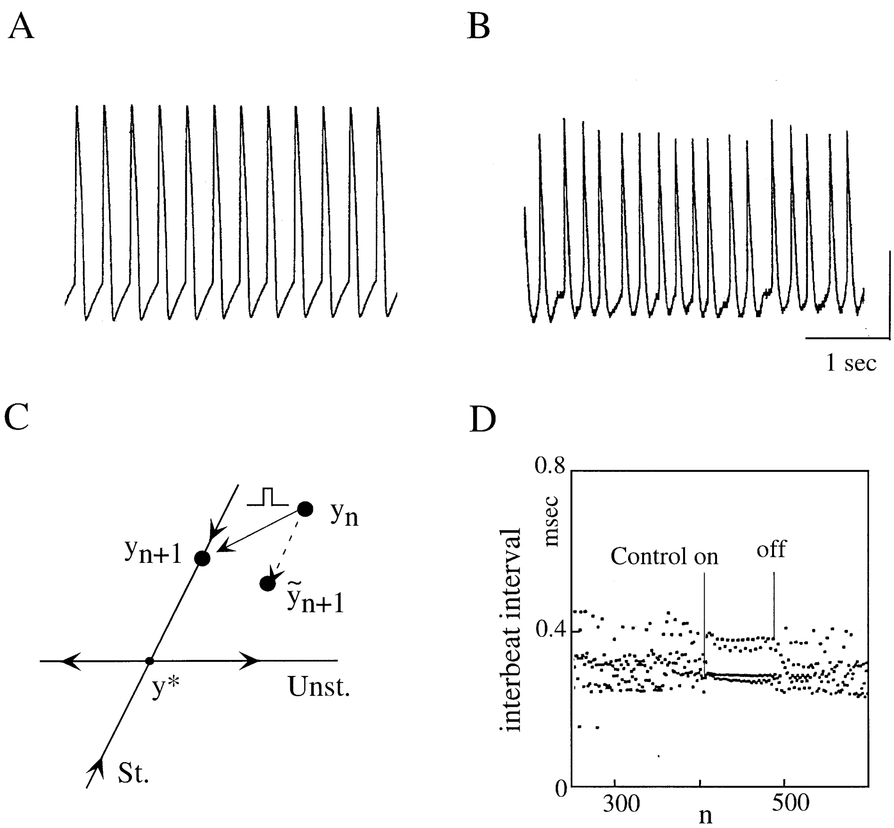


**Figure 17**. Strategy for controlling chaos. (A-B) Recordings of rabbit cardiac action potentials in a control situation (regular intervals, in A) and in presence of ouabain, leading to an aperiodic pattern (compatible with chaos) in (B). (C) Principle of the control using an unstable periodic orbit with its stable (St.) and unstable (Unst.) manifolds, and with a fixed point $y^*$. A point $y_n$ in the attractor close to the unstable fixed point which, next, would move to $\tilde{y}_{n+1}$ (dashed arrow) is forced to lie on the stable manifold at $y_{n+1}$ by an electrical stimulus (Ω). (Modified form Garfinkel et al., 1992). (D) Plot of interbeat intervals (ordinates) versus beat number (abscissa) during the aperiodic arrhythmia and its control obtained by delivering electrical stimuli that stabilize chaos on an unstable period-3 orbit.

characterized by the abnormal operation of simple control parameters and that these parameters can be tuned for therapeutic purposes.

Since key parameters that govern behaviour in most natural phenomena are unknown, a method first described by Ott, Grebogi and Yorke (OGY, [77]) has been adopted for most theoretical speculation and in many laboratories. This method is model-independent and does not require prior knowledge of the system's dynamics. For this approach the system's behaviour itself is used to 'learn' from data how to identify and select a given unstable periodic orbit and what kind of perturbation is necessary to stabilize the system on that orbit. *Figure 17* illustrates how this strategy can help to reestablish a regularly oscillating output in an arrhythmic, ouabain-treated rabbit heart.

The OGY approach has been used successfully to control simple magnetic systems, lasers and nonlinear optics, chemical reactions, electronic circuits, jumps in convective fluids and thermodynamics (ref in [78–81]).

It is also important to note that the OGY technique has been extended to high dimensional attractors [82]. Other methods for controlling chaos are described in Bocaletti et al. [83].

To date, a successful control of biological determinist dynamics has only been reported in the isolated heart of the rabbit [84] and in epileptic hippocampal slices of the rat [85]. These results are however of potential importance: it has been proposed that abnormalities of physiological rhythms, ranging from differing periodicities to irregular 'noise-like' phenomena, define a group of 'dynamical diseases' of the heart, of blood cells, of respiration, of locomotion and motor coordination [86]. Whether such is the case remains an exciting challenge for future work.

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