



Link between Truncated Fractals and Coupled Oscillators in Biological Systems

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This article aims at providing a new theoretical insight into the fundamental question of the origin of truncated fractals in biological systems. It is well known that fractal geometry is one of the characteristics of living organisms. However, contrary to mathematical fractals which are self-similar at all scales, the biological fractals are truncated, i.e. their self-similarity extends at most over a few orders of magnitude of separation. We show that nonlinear coupled oscillators, modeling one of the basic features of biological systems, may generate truncated fractals: a truncated fractal pattern for basin boundaries appears in a simple mathematical model of two coupled nonlinear oscillators with weak dissipation. This fractal pattern can be considered as a particular hidden fractal property. At the level of sufficiently fine precision technique the truncated fractality acts as a simple structure, leading to predictability, but at a lower level of precision it is effectively fractal, limiting the predictability of the long-term behavior of biological systems. We point out to the generic nature of our result.

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Introduction

Significant progress has been made in physical and biological sciences due to the discovery of fractal geometry of nature (Mandelbrot, 1982; 1985; Bassingthwaite *et al.*, 1994; Bunde & Havlin, 1995). Fractals are becoming essential components in the modeling and simulation of nature, in particular in life sciences. In biological and medical sciences there is an increasing number of applications of both spatial and temporal fractal structures. Many biological phenomena appear to be fractal, for example the structure of bronchial tree (Shlesinger & West, 1991), heartbeat dynamics (Goldberger *et al.*, 1985; Peng *et al.*, 1996; Ivanov *et al.*, 1999; Makikallio *et al.*, 1999),

protein surfaces (Goetze & Brickman, 1992), chromatin microscopic images of breast epithelial cell nuclei (Einstein *et al.*, 1998), fetal breathing dynamics (Szeto *et al.*, 1992), microbial growth pattern (Obert *et al.*, 1990), reduction law of metabolism (Sernetz *et al.*, 1985), fetal heart rate (Gough, 1993), convoluted surface of mammalian brain (Hofman, 1991), neural networks (Goldberger & West, 1987), urinary collecting tubes (Goldberger & West, 1987), long-range power-law correlation in DNA (Peng *et al.*, 1992; Voss, 1992; Buldyrev *et al.*, 1993), neuronal shape (Caserta *et al.*, 1990), pattern in human retinal vessels (Family *et al.*, 1989), structure of biomembranes (Nonnenmacher, 1989), blood vessel system (Kalda, 1993; Zamir, 1999), etc. In some fractal biological phenomena it is the spatial shape of a biological object itself that exhibits

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obvious fractal features, while in other cases the fractal properties are more hidden and can only be perceived if data are studied as a function of time or of some other variable, or mapped in some particular way (Buldyrev *et al.*, 1995). The latter cases of fractality are referred to as hidden fractal properties.

The reason why nature prefers fractal structures to those generated by classical scaling is that more effective function is achieved, but it may also be related to higher tolerance that fractal structures and processes possess over those of classical structures and processes (West, 1990). It was argued that the fractal geometry may not only be a design principle for living organisms, but may also underlie an evolutionary advantage of biological systems having fractal dimension (West & Deering, 1994).

In all fractals the underlying concept is self-similarity. In mathematical idealization fractals are self-similar at all scales. This is a feature of exact mathematical fractals like, for example, Cantor set or Koch curve (Mandelbrot, 1982; Peitgen *et al.*, 1992). A similar feature appears also for fractal basin boundaries computed for mathematical models of dynamical systems (Grebogi *et al.*, 1983; Grebogi *et al.*, 1987; Ott, 1993), associated with multistability which is a fundamental property of nonlinear systems.

On the other hand, contrary to such mathematical fractals, for any real object in nature fractal properties are observed only over a limited size range. As pointed out by Mandelbrot, naturally fractal objects are statistically self-similar above some lower cutoff ε up to some upper cutoff value Ω (Mandelbrot, 1982). Below, the lower cutoff, the self-similarity of any natural fractal pattern ceases to be valid or changes its character. In theoretical considerations of natural fractals a mathematical fractal set D for which $\varepsilon = 0$ is replaced by a fractal set D_ε which is "like D " on scales above ε . Thus, the dimension of a naturally occurring fractal is associated with self-similarity over some region of space or interval of time. Therefore, such fractals are referred to as truncated fractals.

On the basis of an analysis of 96 reports on fractality of a wide range of natural systems, the narrow range of appropriate scaling properties for declared fractal objects was pointed out,

centered around 1.3 orders of magnitude (Avnir *et al.*, 1997). One of the most extensive fractal systems found in nature comprises the sedimentary rocks, formed from a mixture of organic and inorganic debris deposited in aqueous environment, with the range of length scales extended to over three decades (Radlinski *et al.*, 1999).

In relation to the origin of truncated fractals in nature, we address here a theoretical question: Can truncated fractals be generated in simple mathematical models bearing some features of basic dynamics characterizing biological systems? As a guideline to identify such a simplified mathematical model, we turn to the well-known observation that the key biological systems, such as, for example, cardiac, neural, respiratory, neuromuscular, and hormonal, display intrinsic oscillatory behavior (Othmer, 1980; Glass *et al.*, 1984; Sporns *et al.*, 1987; Glass, 1988; Ermentrout, 1980; Murray, 1993; Han *et al.*, 1995; Barrio *et al.*, 1997; Leloup & Goldbeter, 1999; McLeod *et al.*, 1998; Kaern & Hunding, 1999). Biological oscillators interact with one another and with the environment. Moreover, there are innumerable feedback loops acting on physiological variables. Instigated by this observation, it is tempting to look for a possible origin of truncated biological fractals at the level of a simple mathematical model of coupled oscillators. Thus, we pose the following question: Can a system of coupled oscillators lead to a truncated fractal pattern of some sort? Which particular fractal property should we look at in that case?

It is well known that nonlinear systems can produce fractal basin boundaries that separate basins of different attractors (Grebogi *et al.*, 1983; Mc Donald *et al.*, 1985; Grebogi *et al.*, 1987a; Ott, 1993). Even more complicated examples of riddled and intermingled basins were found for some dynamical systems (Grebogi *et al.*, 1987b; Ott, 1993; Ott *et al.*, 1994). Let us now consider fractal basin boundary as a hidden fractal property in the framework of biological systems. Then we can specify our question in the following way: Can a fractal basin boundary associated with dynamical systems of coupled oscillators, modeling some basic aspects of biological systems, be truncated? If so, we can argue that this result hints at a possible link of truncated fractals and dynamics of coupled oscillators in biological systems.

A possibility that the basin boundaries are truncated fractals was previously investigated for a sinusoidally forced pendulum by introducing an additional exponential factor so that the non-autonomous driving term exponentially decays to zero (Varghese & Thorp, 1988; Dobson & Delchamps, 1994). Moreover, in the case of a single Duffing oscillator it was found that truncated fractal Arnold tongues can be finely intermingled with self-similar fractal Arnold tongues (Paar & Pavin, 1998). In this paper we show that a nonlinear system of coupled oscillators can generate truncated fractal basin boundaries. This can shed new light on the coexistence of coupled oscillators and truncated fractals in biological systems.

Method

In order to show that coupled nonlinear oscillators can generate truncated fractal basin boundaries as a general pattern, we investigate two characteristic cases of coupled oscillators.

The first model is given by a system of harmonic oscillator and nonlinear double-well oscillator coupled by a linear interaction term, with equations of motion

$$\begin{aligned}\ddot{x} + \gamma\dot{x} - x + x^3 + \alpha(x - y) &= 0, \\ \ddot{y} + \gamma\dot{y} + y + \alpha(y - x) &= 0,\end{aligned}\quad (1)$$

where γ and α are the dissipation and coupling strength, respectively. (The linear term $\alpha(y - x)$ in the equations of motion corresponds to a quadratic term in the corresponding Hamiltonian.) The linear coupling between the two oscillators in the equations of motion was previously considered for the nonlinear mass-spring system (Rosenberg, 1966) and in connection with scalar diffusion (Ermentrout *et al.*, 1980).

System (1) has two attractors at positions of local minima of potential energy:

$$(x, y) = (x_{min}, y_{min}), \quad \text{and} \quad (-x_{min}, -y_{min}), \quad (2)$$

where $x_{min} = 1/\sqrt{1 + \alpha}$, $y_{min} = \alpha/\sqrt{(1 + \alpha)^3}$. In the graphical presentation for basin boundaries we denote the initial conditions ending in the attractor $(-x_{min}, -y_{min})$ as black, while the initial conditions ending in the attractor (x_{min}, y_{min}) are left blank. On the other hand, the energeti-

cally inaccessible initial conditions are presented as gray. Initial values (x_0, \dot{x}_0) are taken from a grid of resolution 570×400 , while the initial values (y_0, \dot{y}_0) are kept fixed. For all calculations we take $y_0 = 0$ and \dot{y}_0 is determined from the condition that all initial conditions should lie on a plane defined by the initial energy E_0 :

$$\begin{aligned}\dot{y}_0 &= \sqrt{2} \\ &\sqrt{E_0 - [\frac{1}{2} \dot{x}_0^2 - \frac{1}{2} (x_0^2 - y_0^2) + \frac{1}{4} x_0^4 + \frac{\alpha}{2} (x_0 - y_0)^2]}.\end{aligned}\quad (3)$$

Thus, all coordinates of the initial conditions $(x_0, \dot{x}_0, y_0, \dot{y}_0)$ are fixed by the values x_0, \dot{x}_0 .

The second model investigated in this paper is given by two linearly coupled double-well nonlinear oscillators, with the equations

$$\begin{aligned}\ddot{x} + \gamma\dot{x} - x + x^3 + \alpha(x - y) &= 0, \\ \ddot{y} + \gamma\dot{y} - y + y^3 + \alpha(y - x) &= 0,\end{aligned}\quad (4)$$

where γ and α are again the dissipation and coupling strengths, respectively.

System (4) has four equilibria of the two-dimensional potential energy, which represent attractors:

$$\begin{aligned}(x, y) &= (-1, -1), (-\sqrt{1 - 2\alpha}, \sqrt{1 - 2\alpha}), \\ &(\sqrt{1 - 2\alpha}, -\sqrt{1 - 2\alpha}), \quad \text{and} \quad (1, 1).\end{aligned}\quad (5)$$

They are symbolically denoted as (L, L), (L, R), (R, L) and (R, R), respectively. We investigate the corresponding basins of attraction by computing for each initial condition (x_0, \dot{x}_0) the corresponding attractor at which the trajectory settles. For simplicity, we display each initial condition ending in the attractors (L, L) or (L, R) by a black dot and each initial condition ending in the attractors (R, L) or (R, R) by a white dot.

To fill out the Poincaré section in order to study the basins of attraction, we choose a set of initial conditions consistent with the energy value: the initial values x_0 and \dot{x}_0 are taken again from a grid of a given resolution 570×400 , the value y_0 is fixed at 1 and \dot{y}_0 is determined from

the condition that the system has the same initial energy E_0 for all initial conditions:

$$\dot{y}_0 = \sqrt{2}$$

$$\sqrt{E_0 - \left[\frac{1}{2} \dot{x}_0^2 - \frac{1}{2} (x_0^2 + y_0^2) + \frac{1}{4} (x_0^4 + y_0^4) + \frac{\alpha}{2} (x_0 - y_0)^2 \right]}.$$

(6)

Results

We have computed basin boundaries for the asymmetric system of coupled oscillators (1) and for the coupled two-well system (4).

For system (1) the basins of attraction are calculated for a grid of 570×400 initial conditions (x_0, \dot{x}_0) from the interval $-1.8 < x_0 < 1.8$, $-1.6 < \dot{x}_0 < 1.6$ at several values of initial energy E_0 . These results are displayed in Fig. 1. For low energies the basin boundaries are smooth [Fig. 1(a)]. With increasing energy the structure of basin boundaries becomes more complex [Fig. 1(b)–(e)], but they remain smooth. This is seen from a successively magnified detail of Fig. 1(e) shown in Figs 2(a)–(d). We see that by successive magnifications the structure becomes simpler, so that the last magnification [Fig. 2(d)] shows no more substructure. A further magnification of this figure exhibits a sharp boundary between the basins of attraction. Such a pattern persists over a wide range of parameters γ and α . This is the so-called truncated fractal.

Similarly, basins of attraction are calculated for system (4). Again, results obtained for a grid of 570×400 initial conditions (x_0, \dot{x}_0) from the interval $-1.8 < x_0 < 1.8$, $-1.6 < \dot{x}_0 < 1.6$ are displayed in Fig. 3 at several values of initial energy E_0 . For low energies the basin boundaries are smooth [Fig. 3(a)]. With increasing energy the structure of basin boundaries becomes more complex. For $E_0 = 0.5$ the basin boundary has the form of a truncated fractal [Fig. 3(c)], as seen from a successively magnified detail of the basin boundary shown in Figs 4(a)–(c). In the last figure we see that self-similarity of the fractal basin boundary stops.

With a further increase of values of one or both model parameters the pattern of basin boundaries changes. Keeping dissipation weak and increasing the coupling strength we obtain

the coexistence of two successive patterns: at some scale the fractal pattern apparently stops, as in the present case. However, with a further magnification an additional finer fractal pattern is obtained which is with truncation at a lower scale than in the previous case.

Discussion

Investigations of basins of attraction reveal some information on dynamics of the system. At small initial energies, as in Fig. 1(a), there is a fast relaxation and therefore a small number of stretching and folding. However, with increase of initial energy the extent of stretching and folding increases and the boundary becomes more complex showing a pattern of a truncated fractal [Fig. 1(e)].

Quite generally, inclusion of dissipation into an autonomous system leads to an irreversible loss of energy and the total energy decreases until the system finally settles in one of the equilibrium states which are at positions of local minima of potential energy. One should note an essential difference between a dissipative system with external forcing and an autonomous system with dissipation. In a system with external forcing energy is brought into the system, while simultaneously dissipation causes a loss of energy and thus an interplay between external force and dissipation takes place. Therefore, it is energetically allowed for the system to return to its initial state. On the other hand, in an autonomous system dissipation leads to a permanent loss of energy and the energy of the system gradually decreases. Therefore, the autonomous system with dissipation cannot return to its initial state. Thus, for systems (1) and (4) every motion is of transient character and a typical trajectory wanders for some time in phase space and finally settles at one of the attractors (2) and (5), respectively.

If the dissipation is excluded ($\gamma = 0$), according to the KAM scenario with increase of energy chaos can appear (Ott, 1993). The appearance of chaos is associated with stretching and folding of the phase space. It is clear that the introduction of dissipation is associated with changes in the system, but it will not completely change its character. Due to the presence of dissipation in the system, periodic orbits cannot exist and therefore

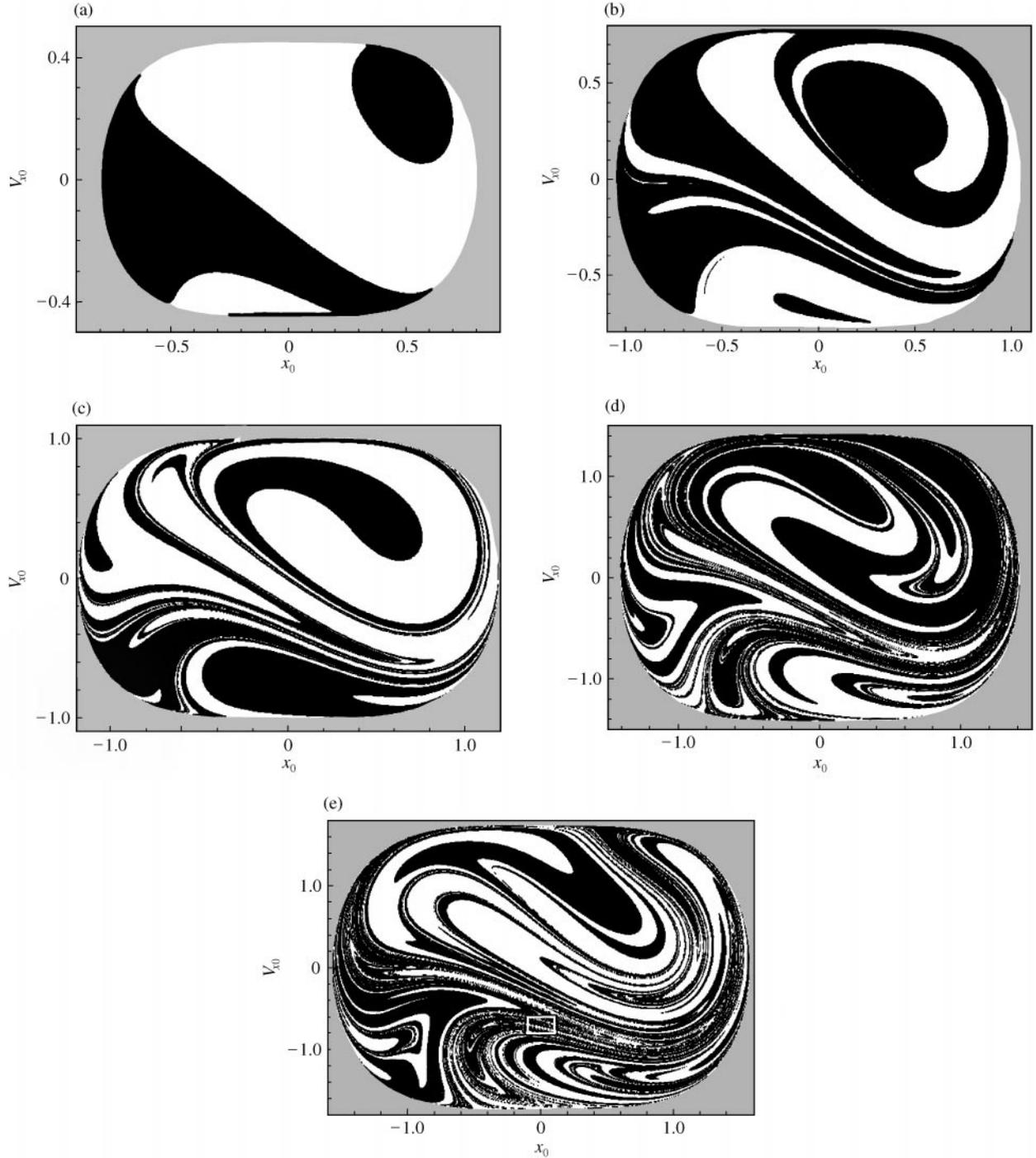


FIG. 1. Basins of attraction for the nonlinear system (1) with dissipation $\gamma = 0.1$ and coupling strength $\alpha = 1$ at energies: (a) $E_0 = 0.1$, (b) $E_0 = 0.3$, (c) $E_0 = 0.5$, (d) $E_0 = 1$, and (e) $E_0 = 1.5$. A 570×400 grid of initial conditions is used in the calculations.

there is neither chaos nor homoclinic orbit. However, one can expect that at the beginning the mapping

$$(x, \dot{x}, y, \dot{y})(t_0) \rightarrow (x, \dot{x}, y, \dot{y})(t_0 + \Delta t)$$

will not cause pronounced effects if γ and Δt are small enough, i.e. the modifications of stretching and folding of the phase space will not be sizeable. The energy in the dissipative systems (1) and (4) decreases with time. Thus, a dissipative system

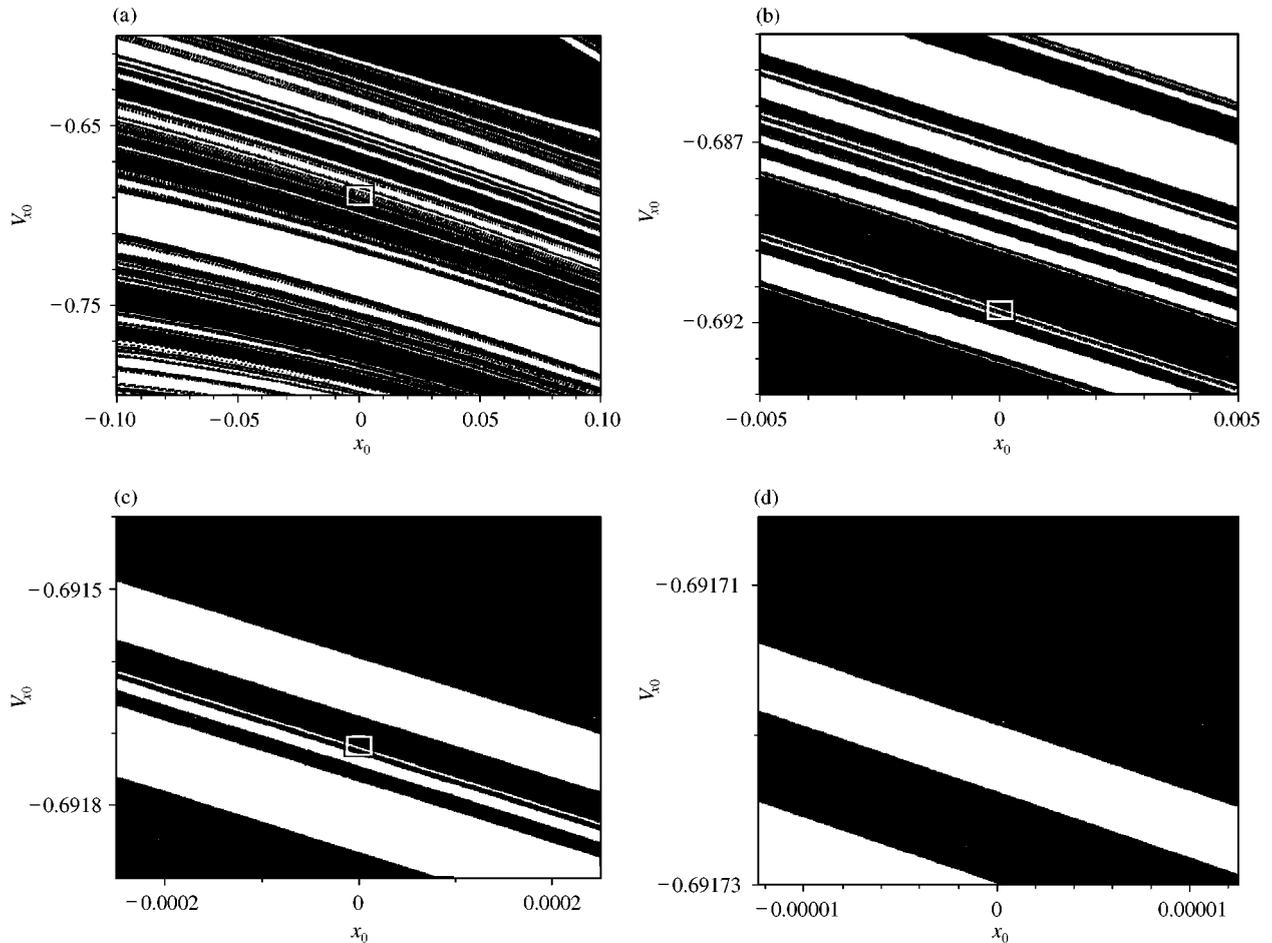


FIG. 2. Blowups of a detail from Fig. 1(e). Four successively expanded views are shown in (a)–(d).

at a later time is similar to the corresponding conservative system, but having smaller energy than its initial value. Due to the absence of chaos for small energies in conservative systems, one can expect the absence of stretching and folding of the phase space at a later time. Therefore, we expect a finite number of stretchings and foldings of the phase space and this number will increase with increasing initial energy E_0 and decreasing dissipation strength γ .

For $\gamma = 0$, $\alpha = 0$ system (4) is dissolved into two independent autonomous nonlinear oscillators, which are integrable (Sagdeev *et al.*, 1992; Ott, 1993). Each double-well oscillator has two stable equilibrium points at the positions -1 and 1 and the point of unstable equilibrium at the position 0 . By coupling these two oscillators in the absence of dissipation, i.e. taking $\alpha \neq 0$, $\gamma = 0$, the Hamiltonian chaos is generated. Chaos is observed in computed results already for

$\alpha \leq 0.01$, and increases with increasing α . Chaotic regions appear first in the region around the point of unstable equilibrium at $x = 0$. This behavior is in qualitative accordance with previous investigations of two nonlinear oscillators with quartic coupling (Sagdeev *et al.*, 1992). Constructing the stable and unstable manifolds we find the homoclinic orbit responsible for the onset of chaos.

In the case of vanishing dissipation basin boundaries can coincide with stable manifolds of unstable periodic orbits. This is not the case for dissipative systems because in this case there are no periodic orbits. However, the corresponding conservative systems (i.e. systems (1) and (4) with $\gamma = 0$) have periodic orbits. For example, the phase space of system (1) without dissipation at the energy $E_0 = 1.5$ is almost completely chaotic. The pronounced unstable periodic orbit of period 1, together with its stable manifold, is shown

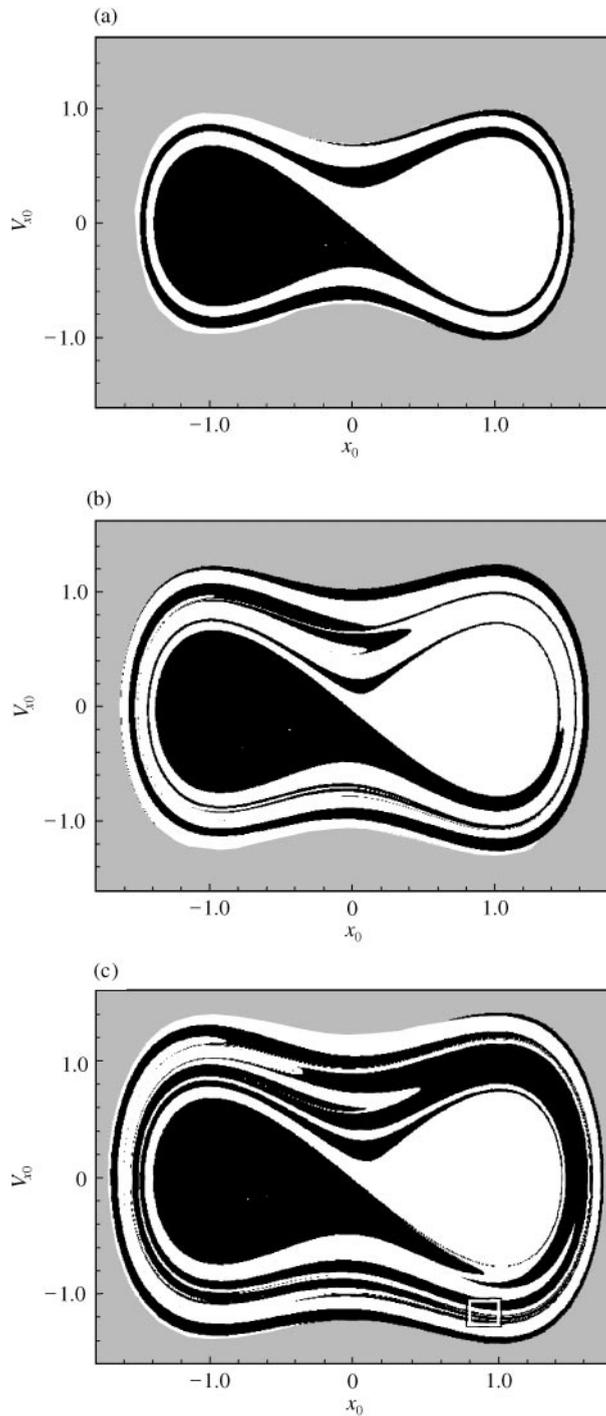


FIG. 3. Basins of attraction for the nonlinear system of two coupled double-well oscillators (4) with dissipation $\gamma = 0.04$ and coupling strength $\alpha = 0.02$ at three different energies: (a) $E_0 = 0$, (b) $E_0 = 0.3$, (c) $E_0 = 0.5$. A 570×400 grid of initial conditions is used in the calculations.

in Fig. 5. Comparison of Figs 1(e) and 5 shows that the basin boundaries from Fig. 1(e) to a large extent coincide with the manifolds from Fig. 5.

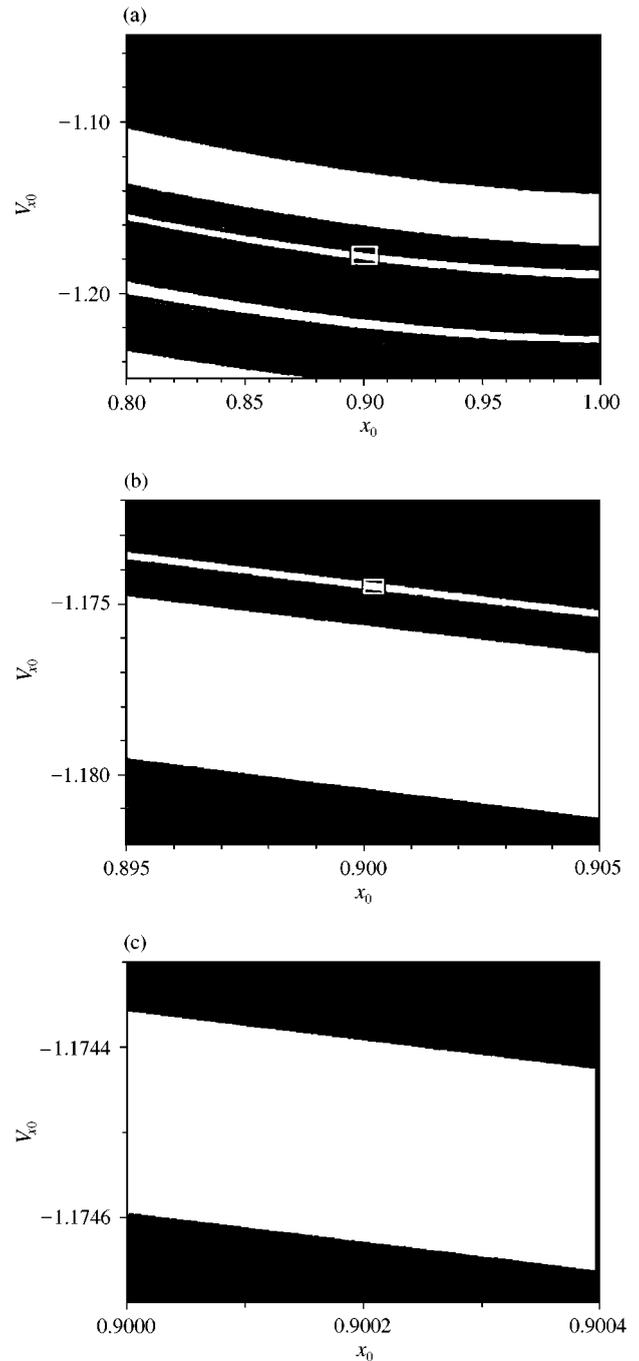


FIG. 4. Blowups of a detail from Fig. 3(c). Three successively expanded views are shown in (a)–(c).

One can say that the fractals of truncated type remain as “shadows” of stationary chaos in the conservative system.

In connection with the relevance of the present results for biological systems it should be noted that a nonlinear two-coupled-oscillator model

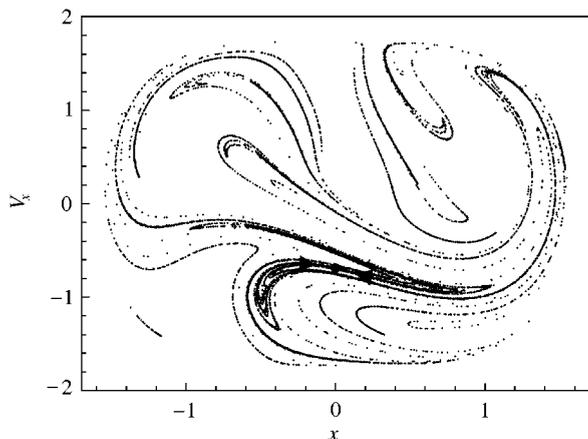


FIG. 5. Stable manifold for system (1) without dissipation ($\gamma = 0$). Diagram displays Poincaré section of the manifold. The surface of section is defined by $y_0 = 0$ at $y_0 > 0$.

was implemented in several recent studies of the dynamics of various biological systems. Let us mention a few examples. A simple theoretical model of two interacting biochemical oscillators was used for description of oscillations in two cyclin-dependent protein kinases activity, involving mutual inhibitions of the two oscillators and the coexistence of various attractors (Romond *et al.*, 1999). Calcium oscillations in leaves of *Desmodium pulvini* were simulated by a physiological model of coupled oscillators (Engelmann & Antkowiak, 1998). Insects that live in the interior of caves show the basic internal temporal organization of coupled oscillators of the coupled moulting and oviposition cycles of *Folsomia candida* (Oda *et al.*, 2000). Dopaminergic neuron was represented as a set of electrically coupled oscillators (Wilson & Callaway, 2000). Mode locking and Arnold tongues were studied for the case of two synaptically coupled neural oscillators (Coomes & Bressloff, 1999). A living coupled oscillator system was constructed by a cell patterning method with a plasmodial slime mold in which parameters of coupling can be systematically controlled (Takamatsu *et al.*, 2000). A model of coupled oscillators was used as a basis for the study of the cultured cells of cardiac pacemakers (Ikeda, 1982). Circadian locomotor rhythm of nocturnal rodents was discussed in terms of regulation by the two coupled oscillators (Honma *et al.*, 1985). The human sleep-wake and body temperature rhythms were assumed to be driven by a pair of coupled oscillators (Strogatz, 1987).

Solutions of coupled oscillators were employed as a model of the central pattern generator generating functional (also locomotional) rhythms (Zielinska, 1996). Photoperiodic induction of diapause in a drosophilid fly *Chymomyza costata* was interpreted with the help of the two-oscillator model of circadian rhythmicity (Kostal *et al.*, 2000). As the simplest model of the sinoatrial node, a two-cell oscillator model was used with cells being electrically coupled by a linear conductance (Cai *et al.*, 1993). A model of two coupled oscillators was used for the study of heartbeat dynamics to describe the interaction between the sinoatrial and the atrioventricular node (Di Bernardo *et al.*, 1998). One can expect that many more examples of coupled biological oscillators will be found to play an important role in biological processes.

Furthermore, as shown in this paper, a simple mechanism of coupled oscillators can lead to the complex coexistence of various modes involving a truncated fractal pattern, as truncated fractal basin boundaries and consequently the fractal boundaries in the parameter space. This fractality may play a role in generating some basic features of biological systems. On the one hand, the appearance of fractality at a certain range of scale can be associated with a higher tolerance in physiological functions which is important for the adaptability of biological systems (West & Deering, 1994). On the other hand, the appearance of truncation in the fractal pattern enables the appearance of a predictable long-term behavior of the system in conjunction with fractality once a certain level of precision in investigating and/or treating a biological system has been achieved. Consequently, a possible erratic nature of the systems behavior due to truncated fractality may disappear once the experimental errors in the measurement and/or treatment of biological system reaches a certain level of precision.

Conclusion

An approach to study a complex situation of coexisting nonlinear oscillators, which characterize dynamics associated with biological systems, is to investigate simplified mathematical models which capture some essential aspects of this mechanism. Here we point out that a model of

coupled nonlinear oscillators with weak dissipation generates a truncated fractal pattern for basin boundaries, and consequently of boundaries in parameter space, which can be considered as a kind of hidden fractal property in the context of biological fractals. We have shown that a truncated fractal pattern of similar type appears both for two coupled double-well oscillators, and for coupled double- and single-well oscillators, giving a hint that this feature is of generic character.

We expect truncated fractals to be more common in biological applications than the idealized case of true fractals. In the case of a rougher precision technique truncated fractals can cause for practical purposes a similar obstruction to estimating the long-term behavior as true fractals, but on the other hand, for a sufficiently fine precision technique the predictability of the long-term behavior of biological systems is not fundamentally limited. This may give a new insight into the problem of truncated fractals in biological systems, which are characterized by a plethora of oscillatory behavior.

REFERENCES

- AVNIR, D., BIHAM, O., LIDAR, D. & MALCAI, O. (1997). Is the geometry of nature fractal? *Science* **279**, 39–40.
- BARRIO, R. A., ZHANG, L. & MAINI, P. K. (1997). Hierarchically coupled ultradian oscillators generating robust circadian rhythms. *Bull. Math. Biol.* **59**, 517–532.
- BASSINGTHWAIGHT, J. B., LIEBOVITCH, L. S. & WEST, B. J. (1994). *Fractal Physiology*. New York: Oxford University Press.
- BULDYREV, S. V., GOLDBERGER, A. L., HAVLIN, S., PENG, C.-K., SIMONS, M., SCIORTINA, F. & STANLEY, H. E. (1993). Long range power-law correlation in DNA. *Phys. Rev. Lett.* **71**, 1776–1779.
- BULDYREV, S. V., GOLDBERGER, A. L., HAVLIN, S., PENG, C.-K. & STANLEY, H. E. (1995). In: *Fractals in Science* (Bunde, A. & Havlin, S. eds), pp. 49–87. Berlin: Springer.
- BUNDE, A. & HAVLIN, S. (eds) (1995). *Fractals in Science*. New York: Springer.
- CAI, D., LAI, Y.-C. & WINSLOW, R. L. (1993). Complex dynamics in coupled cardiac pacemaker cells. *Phys. Rev. Lett.* **71**, 2501–2504.
- CASERTA, F., STANLEY, H. E., ELDRED, W. D., DACCORD, G., HAUSMAN, R. E. & NITTMANN, J. (1990). Physical mechanisms underlying neurite outgrowth: a quantitative analysis of neuronal shape. *Phys. Rev. Lett.* **64**, 95–98.
- COOMBES, S. & BRESSLOFF, P. C. (1999). Mode locking and Arnold tongues in integrate-and-fire neural oscillators. *Phys. Rev. E* **60**, 2086–2096.
- DI BERNARDO, D., SIGNORINI, M. G. & CERUTTI, S. (1998). A model of two nonlinear coupled oscillators for the study of heartbeat dynamics. *Int. J. Bifurcation Chaos Appl. Sci. Eng.* **8**, 1975–1985.
- DOBSON, I. & DELCHAMPS, D. F. (1994). Truncated fractal basin boundaries in the pendulum with nonperiodic forcing. *J. Nonlinear Sci.* **4**, 315–328.
- EINSTEIN, A. J., WU, HAI-SHAN & GIL, J. (1998). Self-affinity and lacunarity of chromatin texture in benign and malignant breast epithelial cell nuclei. *Phys. Rev. Lett.* **80**, 397–400.
- ENGELMANN, W. & ANTKOWIAK, B. (1998). Ultradian rhythms in *Desmodium*. *Chronobiol. Int.* **15**, 293–307.
- ERMENTROUT, G. B. (1985). The behavior of rings of coupled oscillators. *J. Math. Biol.* **23**, 55–74.
- ERMENTROUT, R. (1980). In: *Nonlinear Oscillations in Biology and Chemistry* (Othmer, H. G., ed.), pp. 98–114. Berlin: Springer.
- FAMILY, F., MASTERS, B. R. & PLATT, D. E. (1989). Fractal patterns formation in human retinal vessels. *Physica* **D38**, 98–103.
- GLASS, L. (1988). Simple mathematical models for complex dynamics in physiological systems. In: *Directions in Chaos* (Bai-lin, H., ed.), Vol. 2, pp. 90–108. Singapore: World Scientific.
- GLASS, L., GUEVARA, M. R., BELAIR, J. & SHRIER, A. (1984). Global bifurcations of a periodically forced biological oscillator. *Phys. Rev. A* **29**, 1348–1357.
- GOETZE, T. & BRICKMAN, J. (1992). Self-similarity of protein surfaces. *Biophys. J.* **61**, 109–119.
- GOLDBERGER, A. L., BHARGAVA, V., WEST, B. J. & MANDELL, A. J. (1985). On a mechanism of cardiac electrical stability: the fractal hypothesis. *Biophys. J.* **48**, 525–528.
- GOLDBERGER, A. L. & WEST, B. (1987). Fractals in physiology and medicine. *Yale J. Biol. Med.* **60**, 421–435.
- GOUGH, N. A. J. (1993). Fractals, chaos and fetal heart rate. *The Lancet* **339**, 182–183.
- GREBOGI, C., OTT, E. & YORKE, J. A. (1983). Fractal basin boundaries, long-lived chaotic transients, and unstable-unstable pair bifurcation. *Phys. Rev. Lett.* **50**, 935–938.
- GREBOGI, C., OTT, E. & YORKE, J. A. (1987a). Chaos, strange attractors, and fractal basin boundaries in nonlinear dynamics. *Science* **238**, 632–638.
- GREBOGI, C., KOSTELICH, E., OTT, E. & YORKE, J. A. (1987b). Multidimensional intertwined basin boundaries: basin structure of the kicked double rotor. *Physica* **D25**, 347–360.
- HAN, S. K., KURRER, C. & KURAMOTO, Y. (1995). Dephasing and bursting in coupled neural oscillators. *Phys. Rev. Lett.* **75**, 3190–3193.
- HOFMAN, M. A. (1991). The fractal geometry of convoluted brains. *J. Hirnforsch.* **32**, 103–111.
- HONMA, K., HONMA, S. & HIROSHIGE, T. (1985). Response curve, free-running period, and activity time in circadian locomotor rhythm of rats. *Jpn. J. Physiol.* **35**, 643–658.
- IKEDA, N. (1982). Model of bidirectional interaction between myocardial pacemakers based on the phase response curve. *Biol. Cybernetics* **43**, 157–167.
- IVANOV, P. C., AMARAL, L. A. N., GOLDBERGER, A. L., HAVLIN, S., ROSENBLUM, M. G., STRUZIK, Z. R. & STANLEY, H. E. (1999). Multifractality in human heartbeat dynamics. *Nature* **399**, 461–465.
- KAERN, M. & HUNDING, A. (1999). The effect of slow allosteric transitions in a coupled biochemical oscillator model. *J. theor. Biol.* **198**, 269–281.
- KALDA, J. (1993). Fractal model of blood vessel systems. *Fractals* **1**, 191–197.

- KOSTAL, V., NOGUCHI, H., SHIMADA, K. & HAYAKAWA, Y. (2000). Circadian component influences the photoperiodic induction of diapause in a drosophilid fly *Chymomyza costata*. *J. Insect Physiol.* **46**, 887–896.
- LELOUP, J. C. & GOLDBETER, A. (1999). Chaos and biorhythmicity in a model for circadian oscillations of the PER and TIM proteins in drosophila. *J. theor. Biol.* **198**, 445–459.
- MAC LEOD, K., BAECKER, A. & LAURENT, G. (1998). Who reads temporal information contained across synchronized and oscillatory spike trains? *Nature* **395**, 693–698.
- MAKIKALLIO, T. H., HOIBER, S., KOBER, L., TORP-PEDERSEN, C., PENG, C. K., GOLDBERGER, A. L. & HUIKURI, H. V. (1999). Fractal analysis of heart rate dynamics as a predictor of mortality in patients with depressed left ventricular function after acute myocardial infarction. *Am. J. Cardiol.* **83**, 836–839.
- MANDELBROT, B. B. (1982). *The Fractal Geometry of Nature*. San Francisco: Freeman.
- MANDELBROT, B. B. (1985). Self-affine fractals and fractal dimension. *Phys. Scr.* **32**, 257–260.
- MCDONALD, S. W., GREBOGI, C., OTT, E. & YORKE, J. A. (1985). Fractal basin boundaries. *Physica* **D17**, 125–153.
- MURRAY, D. J. (1993). *Mathematical Biology*. Berlin: Springer.
- NONNENMACHER, T. F. (1989). Fractal scaling mechanics in biomembranes. *Eur. Biophys.* **16**, 375–379.
- OBERT, M., PFEIFER, P. & SERNETZ, M. (1990). Microbial growth patterns described by fractal geometry. *J. Bacteriol.* **172**, 1180–1185.
- ODA, G. A., CALDAS, I. L., PIQUEIRA, J. R. C., WATERHOUSE, J. M. & MARQUES, M. D. (2000). Coupled biological oscillators in a cave insect. *J. theor. Biol.* **206**, 515–524.
- OTHMER, H. G. (ed) (1980). *Nonlinear Oscillations in Biology and Chemistry*. Berlin: Springer.
- OTT, E. (1993). *Chaos in Dynamical Systems*. Cambridge: Cambridge University Press.
- OTT, E., ALEXANDER, J., KAN, I., SOMMERER, J. C. & YORKE, J. A. (1994). The transition to chaotic attractors with riddled basins. *Physica* **D76**, 384–410.
- PAAR, V. & PAVIN, N. (1998). Intermingled fractal Arnold tongues. *Phys. Rev.* **E57**, 1544–1549.
- PEITGEN, H. O., JUERGENS, H. & SAUPE, D. (1992). *Chaos and Fractals*. Berlin: Springer.
- PENG, C. K., BULDYREV, S. V., GOLDBERGER, A. L., HAVLIN, S., SCIORTINO, F., SIMONS, M. & STANLEY, H. E. (1992). Long range correlations in nucleotide sequences. *Nature* **356**, 168–170.
- PENG, C.-K., HAVLIN, S., HAUSDORF, J. M., MIETUS, J. E., STANLEY, H. E. & GOLDBERGER, A. L. (1996). Fractal mechanisms and heart rate dynamics: long-range correlations and their breakdown with disease. *J. Electrocardiol.* **28**, 59–65.
- RADLINSKI, A. P., RADLINSKA, E. Z., AGAMALIAN, M., WIGNALL, G. D., LINDNER, P. & RANDL, O. G. (1999). Fractal geometry of rocks. *Phys. Rev. Lett.* **82**, 3078–3081.
- ROMOND, P. C., EUSTICI, M., GONZE, D. & GOLDBETER, A. (1999). Alternating oscillations and chaos in a model of two coupled biochemical oscillators driving successive phases of the cell cycle. *Ann. N.Y. Acad. Sci.* **879**, 180–193.
- ROSENBERG, R. M. (1966). On nonlinear vibrations of systems with many degrees of freedom. *Adv. Appl. Mech.* **9**, 155–241.
- SAGDEEV, R. Z., USIKOV, D. A. & ZASLAVSKY, G. M. (1992). *Nonlinear Physics*. Chur: Harwood Academic Publishers.
- SERNETZ, M., GELLERI, B. & HOFMANN, J. (1985). The organism as bioreactor. Interpretation of the reduction law of metabolism in terms of heterogeneous catalysis and fractal structure. *J. theor. Biol.* **117**, 209–230.
- SHLESINGER, M. F. & WEST, B. J. (1991). Complex fractal dimension of the bronchial tree. *Phys. Rev. Lett.* **67**, 2106–2108.
- SPORNS, O., ROTH, S. & SEELIG, F. F. (1987). Chaotic dynamics of two coupled biochemical oscillators. *Physica* **D26**, 215–224.
- STROGATZ, S. H. (1987). Human sleep and circadian rhythms: a simple model based on two coupled oscillators. *J. Math. Biol.* **25**, 327–347.
- SZETO, H. H., CHENG, P. Y., DECENA, J. A., CHENG, Y., WU, D. & DWYER, G. (1992). Fractal properties of fetal breathing dynamics. *Am. J. Physiol.* **262**, R141–R147.
- TAKAMATSU, A., FUJII, T. & ENDO, I. (2000). Time delay effect in a living coupled oscillator system with the plasmodium of *Physarum polycephalum*. *Phys. Rev. Lett.* **85**, 2026–2029.
- VARGHESE, M. & THORP, J. S. (1988). Truncated-fractal basin boundaries in forced pendulum system. *Phys. Rev. Lett.* **60**, 665–668.
- VOSS, R. (1992). Evolution of long-range fractal correlations and $1/f$ noise in DNA base sequences. *Phys. Rev. Lett.* **68**, 3805–3808.
- WEST, B. J. (1990). Physiology in fractal dimensions: error tolerance. *Ann. Biomed. Eng.* **18**, 135–149.
- WEST, B. J. & DEERING, W. (1994). Fractal physiology for physicists: Levy statistics. *Phys. Rep.* **246**, 1–100.
- WILSON, C. J. & CALLAWAY, J. C. (2000). Coupled oscillator model of the dopaminergic neuron of the substantia nigra. *J. Neurophysiol.* **83**, 3084–3100.
- ZAMIR, M. (1999). On fractal properties of arterial trees. *J. theor. Biol.* **197**, 517–526.
- ZIELINSKA, T. (1996). Coupled oscillators utilized as gait rhythm generators of a two-legged walking machine. *Biol. Cybernetics* **74**, 263–273.