not the rapid one, observed in neutrophils treated with 30 mM NaPr. We assume that membrane fluidization by aliphatic alcohols and NaPr is associated with an impairment of some necessary component of the slow LSR, thus leaving the system with the capability of executing only the chemotaxis-related rapid LSR (*4, 5*). Since membrane fluidization is an integral and inevitable aspect of the NaPr incorporation into the neutrophils, the NaPr-induced LSR should operationally be referred to as the combined effect of fMLP and an aliphatic alcohol (Fig. 1, B and C).

Thus we have shown that the LSR, which correlates with neutrophil chemotaxis, can be specifically induced and suppressed by defined experimental manipulations of the neutrophil cytosolic proton concentration. The comparison of the LSR time course with the kinetics of the concurrently induced cytosolic acidification implies that only the initial decrease in pH is necessary for the intracellular signal. Consequently, we suggest that the perception of a chemoattractant by its specific receptors is translated into an abrupt accumulation of protons at the interface of the plasma membrane and cytoplasm, which can then trigger the chemotactic signal-transduction cascade.

REFERENCES AND NOTES

1. J. I. Gallin, E. K. Gallin, E. Schiffmann, in *Advances in Inflammation Research*, G. Weissmann, B. Samuelsson, R. Paoletti, Eds. (Raven, New York, 1979), pp. 1–123; E. Schiffmann, *Biosci. Rep.* **1**, 89 (1981); R. Snyderman and E. J. Goetzl, *Science* **213**, 830 (1981); R. Snyderman and M. C. Pike, *Annu. Rev. Immunol.* **2**, 257 (1984).
2. E. J. Kawaoka, M. E. Miller, A. T. W. Chenug, *J. Clin. Immunol.* **1**, 41 (1981); G. J. Cianciolo and R. Snyderman, *J. Clin. Invest.* **67**, 60 (1981).
3. C. S. Liao and R. J. Freer, *Biochem. Biophys. Res. Commun.* **93**, 566 (1980); I. Yuli, A. Tomonaga, R. Snyderman, *Proc. Natl. Acad. Sci. U.S.A.* **79**, 5906 (1982).
4. I. Yuli and R. Snyderman, *J. Clin. Invest.* **73**, 1408 (1984); L. A. Sklar, Z. G. Oades, D. A. Finney, *J. Immunol.* **133**, 1483 (1984).
5. I. Yuli and R. Snyderman, *Blood* **64**, 649 (1984).
6. N. H. Valerious, O. H. Stendhal, T. P. Stossel, *Cell* **24**, 195 (1981); J. R. White, P. H. Naccache, R. I. Sha'afi, *Biochem. Biophys. Res. Commun.* **108**, 1144 (1982); M. Fechheimer and S. H. Zigmond, *Cell Motility* **3**, 349 (1983); P. J. Wallace, R. P. Wersto, C. L. Packman, M. A. Lichtman, *J. Cell Biol.* **99**, 1060 (1984).
7. P. D. Lew and P. T. Stossel, *J. Clin. Invest.* **67**, 1 (1981); L. C. McPhail and R. Snyderman, *ibid.* **72**, 192 (1983); L. C. McPhail, C. C. Clayton, R. Snyderman, *J. Biol. Chem.* **259**, 5768 (1984).
8. R. I. Sha'afi *et al.*, *J. Cell Biol.* **102**, 1459 (1986).
9. T. F. P. Molski, P. H. Naccache, M. Volpi, L. M. Wolpert, R. I. Sha'afi, *Biochem. Biophys. Res. Commun.* **94**, 508 (1980). R. Yassin *et al.*, *J. Cell Biol.* **101**, 182 (1985).
10. S. Grinstein and W. Furuya, *Biochem. Biophys. Res. Commun.* **122**, 755 (1984).
11. S. Grinstein, J. D. Joetz, W. Furuya, A. Rothstein, E. W. Gelfand, *Am. J. Physiol.* **247**, C293 (1984); S. Grinstein, B. Elder, W. Furuya, *ibid.* **248**, C379, (1985); S. Grinstein, W. Furuya, W. D. Biggar, *J. Biol. Chem.* **261**, 512 (1986).
12. M. Shinitzky and Y. Barenholtz, *Biochim. Biophys. Acta* **515**, 367 (1978).
13. Y. Shahak, Y. Siderer, M. Avron, in *Photosynthetic Organelles: Structure and Function*, Miyachi *et al.*, Eds. [special issue of *Plant Cell Physiology* (1977), pp. 115–127].
14. L. Simchowitz, *J. Biol. Chem.* **260**, 13237 (1985); *ibid.*, p. 13248; ______ and A. Roos, *J. Gen. Physiol.* **85**, 443 (1985); L. Simchowitz and E. J. Gragoe, *J. Biol. Chem.* **261**, 6492 (1986).

15. We thank L. Rosario, NIH, for assistance in measuring the intracellular pH and Y. Shahak, Weizmann Institute of Science, for the gift of SF-6847. I.Y. is a recipient of a Sir Charles Clore Fellowship.

20 June 1986; accepted 4 November 1986

Chaotic Bursts in Nonlinear Dynamical Systems

ROBERT L. DEVANEY

Several elementary nonlinear dynamical systems in the complex plane may provide models for abrupt transitions to chaotic dynamics. In particular, the complex trigonometric and exponential functions explode into chaos as a parameter is varied. Numerical evidence is presented that supports the contention that these explosions occur whenever an elementary bifurcation occurs. This numerical evidence, in the form of computer graphics, is an example of the increasing importance of experimentation in mathematics research.

RESEARCH OF MATHEMATICIANS, physicists, and others over the past 20 years has made it clear that many systems of physical, biological, or chemical interest exhibit highly unstable or chaotic behavior. How does a relatively tame or stable system make the transition to complete irregularity or instability? Several different scenarios for the transition to chaos have been put forth. There is the older Landau–Lifshitz approach of successive superposition of frequencies (*1*) and the relatively new approach of Feigenbaum (*2*) via successive period-doublings. Both of these transitions have been shown to be mathematically feasible and have been observed in physical systems (*3*). But both of these transitions are gradual transitions; the systems involved become increasingly irregular in well-defined stages, which eventually accumulate and terminate in complete chaos. These scenarios are therefore good models for systems such as fluid flows, which gradually make the transition from steady state to turbulence, and ecological systems, wherein the populations change slowly over time until a chaotic regime is reached. But they do not serve well as models for systems that become chaotic rapidly. A number of systems in nature exhibit this type of burst or explosion into chaos. For example, combustion often involves rapid transitions between stable and chaotic states. The phenomenon in meteorology called microbursts also exhibits rapid changes of state.

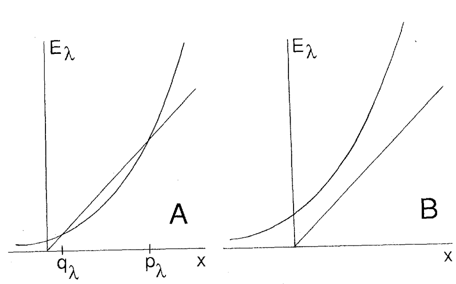

Fig. 1. Graphs of E_λ for real $z = x$. Straight line shows $E_\lambda = x$. (**A**) $\lambda < 1/e$. (**B**) $\lambda > 1/e$.

There are a number of mathematical techniques for studying such abrupt changes in physical systems. For example, the theory of shock waves in partial differential equations is well developed and can be used to construct mathematical models that accurately describe a rapid change of state. Also, catastrophe theory developed by Zeeman (*4*) and others has been applied to a number of systems that undergo such rapid changes. Both of these approaches, however, usually deal with an apparently discontinuous jump in the system between one stable equilibrium and another. These transitions, albeit abrupt, do not in general occur between stable and completely chaotic states.

My goal in this report is to suggest some simple mathematical models that do exhibit this type of transition. These models have the advantage of being simple—they are all iterated mappings of the plane—and effectively computable—they involve only complex sines, cosines, or exponentials. In each case, it can be proved rigorously that the systems undergo a burst into complete irregularity as a parameter is varied. Admittedly, these dynamical systems are approximate models of real physical systems, but it is my feeling that the bursts illustrated with these simple models hold the key to understanding similar phenomena in more complicated settings. These sudden chaotic bursts have

Department of Mathematics, Boston University, Boston, MA 02215.

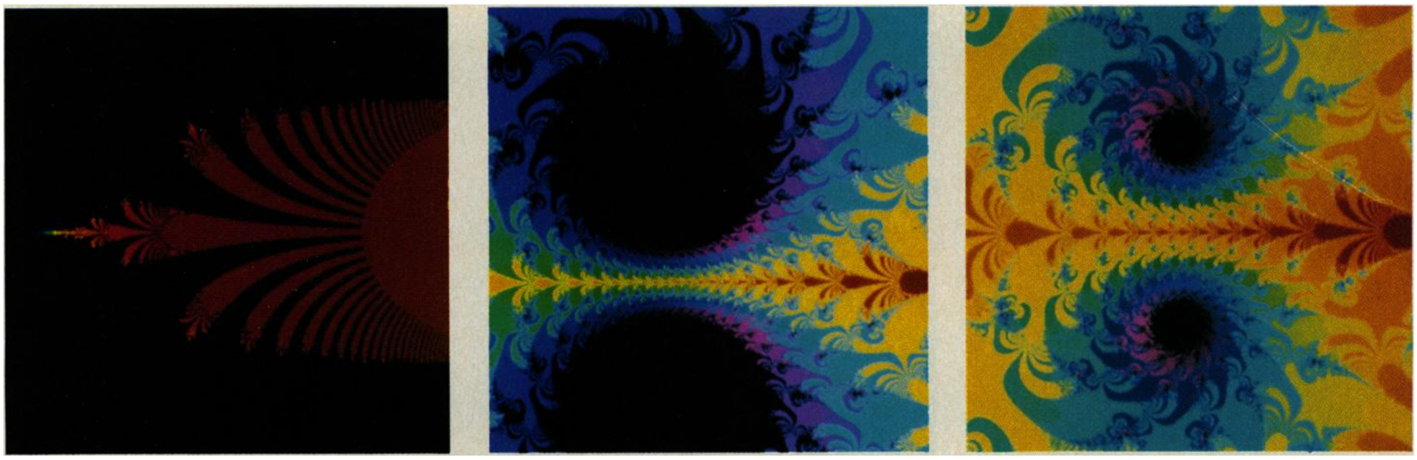

Fig. 2. (**Left**) Julia set for the mapping $E_\lambda = \lambda \exp(z)$ where $\lambda \leq 1/e$ and $N = 50$; (**center**) $\lambda \geq 1/e$ and $N = 50$; (**right**) $\lambda \geq 1/e$ and $N = 200$. Note the explosion into color as λ increases past $1/e$, indicating the burst into chaos.

also been noted in the quasi-periodic route to chaos (*5*) and in studies of intermittency (*6*).

It is known that iterated mappings of low-dimensional spaces provide good models for physical systems. For example, the logistic equation

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

has often been used as a model in ecology (*7*) to predict population growth where the parameter k adjusts various biological constants. This model leads to the iteration of the quadratic function

$$f(x) = kx(1 - x)$$

on the interval $0 \leq x \leq 1$. Similarly, other systems governed by differential equations may be reduced by a variety of mathematical techniques to a simple iteration scheme.

I will consider only iterated mappings of the complex plane **C**, such as $E_\lambda(z) = \lambda \exp(z)$ or $S_\lambda(z) = \lambda \sin(z)$. Here λ should be interpreted as a complex parameter $\lambda = \lambda_{re} + i\lambda_{im}$ where λ_{re} and λ_{im} are the real and imaginary parts, respectively, of λ, and $i = \sqrt{-1}$. Similarly, the state variable z is complex: $z = x + iy$, where x and y are real numbers. Iteration of complex functions has a long and interesting history in mathematics, going back to the early 20th century to the pioneering work of Fatou (*8*) and Julia (*9*). Although many of the basic theoretical developments are due to these men, they did not have high-speed computers and computer graphics to display the spectacular results of this iteration process. This was one of the contributions of Mandelbrot (*10*), who recognized that simple quadratic mappings of the complex plane have chaotic regions that are often fractal in nature. These are the Julia sets of complex maps, which I will describe below. The Mandelbrot set, a compilation of all of the possible chaotic behaviors of these quadratic maps, is, in its own right, an interesting object of study (*10*).

Consider the problem of iterating a complex function F. That is, for a given initial complex number z_0, we compute successively

$$\begin{aligned} z_1 &= F(z_0) \\ z_2 &= F(z_1) = F(F(z_0)) = F^2(z_0) \\ z_3 &= F(z_2) = F^3(z_0) \\ &\vdots \\ z_n &= F^n(z_0). \end{aligned}$$

Note that F^n means the n-fold iteration of F, not F raised to the nth power. The set of points $\{z_0, z_1, z_2, \ldots\}$ is called the orbit of the initial point z_0. The basic goal of dynamical systems theory is to understand the ultimate fate of all orbits of a given system. The question is what happens to $F^n(z_0)$ as n tends to infinity. There are many possible fates in a given system.

For example, an orbit may behave relatively tamely by simply tending to a fixed point, as illustrated by the simple mapping $F(z) = z^2$. If z_0 is a complex number with absolute value less than one, then a simple computation shows that successive squarings yield an orbit that tends to 0 in the limit. That is, all complex numbers inside the circle of radius one tend to 0 under iteration of $F(z) = z^2$. This is stable behavior: all sufficiently nearby initial choices of z_0 lead to the same fate for the orbit.

As another example, consider the exponential function $E_\lambda(z) = \lambda \exp z$ with $\lambda > 0$. For real values of z, Fig. 1 shows that the graph of E_λ assumes two different forms depending upon whether $\lambda > 1/e$ or $\lambda < 1/e$, where $e \approx 2.7128 \ldots$ satisfies $\ln e = 1$. In Fig. 1A, E_λ has two fixed points, q_λ and p_λ, defined by the conditions $E_\lambda(q_\lambda) = q_\lambda$ and $E_\lambda(p_\lambda) = p_\lambda$. All points in the interval $-\infty < x < p_\lambda$ lead to orbits that tend to q_λ as n tends to infinity. On the other hand, in the interval $p_\lambda < x < \infty$, all points have orbits that tend to infinity under iteration. For values of $\lambda > 1/e$ (Fig. 1B), all points have orbits that tend to infinity. This may be easily checked with a calculator by iterating $\lambda \exp(x)$ for various choices of initial x. The rigorous proof is also easy (*11*). It follows that the dynamical system E_λ has two vastly difficult behaviors on the real line depending upon whether $\lambda > 1/e$ or $\lambda < 1/e$. This is an example of a burst into chaos when viewed as a dynamical system in the complex plane.

There are a number of different definitions of chaos in the literature (*12*). We will adopt the following definition: a completely chaotic system must exhibit unpredictability, indecomposability, and recurrence. Precise definitions of chaos are in (*13*); I list the following somewhat imprecise definitions which are peculiar to the special maps considered in this report. An iterated mapping is unpredictable if it exhibits sensitive dependence on initial conditions: given any initial state z_0, there is a nearby state w_0 whose orbit diverges from z_0. That is, the distance between z_n and w_n must eventually be large. Any numerical computation of the orbit of z_0 may be suspect: a small initial error, perhaps because of roundoff, may yield a completely different orbit, thus rendering numerical study inaccurate.

The dynamical system is indecomposable if there is an orbit that eventually enters any preassigned region in the plane, no matter how small. Thus, this orbit comes arbitrarily close to any point whatsoever in **C**, and we cannot separate the given system into two separate subsystems.

Finally, a dynamical system exhibits recurrence if, given an initial condition z_0, there is another initial condition w_0 that is arbitrarily close to z_0 and that is periodic. Periodicity means that there is an iteration n for which $F^n(w_0) = w_0$. Consequently, $w_{n+1} = w_1$,

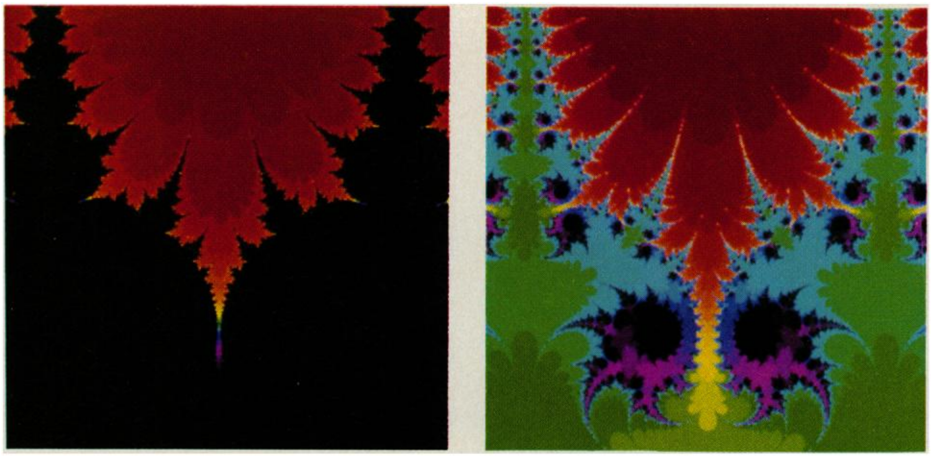

Fig. 3. Julia sets of the function $C_\lambda(z) = i\lambda \cos z$. (**Left**) λ is approximately 0.67; (**right**) λ is slightly larger.

$w_{n+2} = w_2$, and so forth, and the orbit of w_0 is a cycle or periodic orbit. Periodic orbits are usually regarded as among the most important motions in a dynamical system, so our assumption is that they abound.

A dynamical system in **C** is completely chaotic if it exhibits all three of the above properties. This definition is intended to mirror the properties of physical systems that exhibit turbulence.

Spurred on by the computer graphics of Mandelbrot (*10, 14*), a number of mathematicians such as Sullivan, Keen, and Goldberg have given effectively computable criteria for a dynamical system to be completely chaotic (*15, 16*). For example, in the case of systems such as $\lambda \exp(z)$ or $\lambda \sin(z)$, all we need to do is follow the critical orbits of the system. For the exponential mapping, this is the orbit of 0 (the omitted value), and for the sine mapping, these are the orbits of the critical points $\pm\pi/2$ (where the maxima and minima occur on the real line). The critical orbits are defined to be the orbits of the critical and asymptotic values, where critical values are simply the images of the critical points. Note that the sine mapping has infinitely many critical points but only two critical values and no asymptotic values, so checking the above criteria is straightforward. One consequence of Sullivan's recent "no wandering domains" theorem (*15*) is that if all critical orbits of these maps tend to infinity, then the dynamical system is completely chaotic on the whole plane. In the example $E_\lambda(z) = \lambda \exp(z)$, where $\lambda > 1/e$, it is easy to check that 0 indeed tends to infinity, so E_λ is completely chaotic in the whole plane when $\lambda > 1/e$.

Now let us contrast this with the case $0 < \lambda < 1/e$. Consider the vertical line $x = 1$ in the complex plane. By Euler's formula

$$e^{x+iy} = e^x e^{iy} = e^x(\cos y + i \sin y)$$

this vertical line is mapped to the circle Γ of radius $\lambda e^1 < 1$. Moreover, each point in the plane to the left of this vertical line is mapped inside the circle Γ. Thus, the whole left half plane (real part of $z \leq 1$) is contracted inside itself and, in fact, inside Γ. Now apply E_λ again: Γ is contracted further inside itself. Continuing in this fashion, we see that E_λ cannot be chaotic in this half-plane; for example, there cannot be any cycles or periodic points outside of Γ. Indeed, one may check that the only cycle to the left of $x = 1$ is the fixed point q_λ discussed above.

Thus we see that as λ increases through $\lambda = 1/e$, there is a dramatic change in the set of points on which the dynamical system is chaotic. When $\lambda < 1/e$, there are no such points to the left of $x = 1$, whereas when $\lambda > 1/e$, E_λ is completely chaotic on the entire plane. This is the burst into chaos.

The set of points in the complex plane for which a dynamical system such as $\lambda \exp(z)$ or $\lambda \sin(z)$ is completely chaotic is called the Julia set. This set is often a fractal (*10*) and may assume spectacular geometric shapes. There are a number of different techniques for plotting the Julia sets numerically. A procedure that works for polynomials is described in (*17*) and (*18*). For the transcendental maps that we are considering there is a special and rather simple algorithm due to Hubbard that allows for easy plotting of the Julia set (*18*). It is known that the Julia set of a map such as $\lambda \exp(z)$ or $\lambda \sin(z)$ is the closure of the set of points whose orbit tends to infinity (*17*). That is, any point whose orbit tends to infinity and any limit point of such points lies in the Julia set. Note an apparent contradiction: periodic cycles must occur arbitrarily close to any point in the Julia set according to the definition of recurrence, but so too must points whose orbits tend to infinity. Indeed, bounded and unbounded orbits accumulate at all points of the Julia set, giving further indication of the unpredictability of these systems on the Julia set.

Using Hubbard's algorithm, we may thus plot the outline of the Julia set by iterating a grid of points in the plane a preselected number of times N. If the orbit of the point remains bounded for all N iterations, we assume that the point does not lie in the Julia set and color it black. If, however, the orbit escapes to infinity (that is, becomes too large for the computer), we assume that the point lies in or near the Julia set. To capture the dynamics on the Julia set, we color such a point according to a scheme that assigns the color depending on the number of iterations that have occurred before escape. Points that are colored shades of red escape very quickly. Points are then colored shades of orange, yellow, green, blue, and violet in increasing order, so that violet points escape only after a number of iterations close to N.

I have plotted the results for $\lambda \exp(z)$ in Fig. 2. Note the small chaotic region for $\lambda \leq 1/e$ (left). In this picture, almost the entire plane is black. Black points never lie in

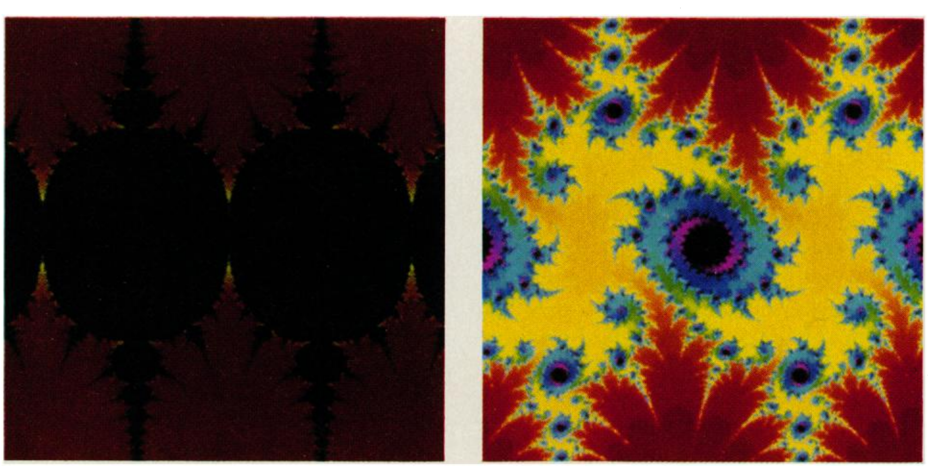

Fig. 4. Julia sets of the function $S_\lambda(z) = (1 + \lambda i) \sin z$. (**Left**) $\lambda = 0$, there is a large basin of attraction (black) consisting of points attracted to 0; (**right**) $\lambda \gtrsim 0$, the basin is destroyed and the entire screen fills with color, suggesting a burst into chaos.

the Julia set; indeed, all of these points are attracted to the fixed point that I have denoted by q_λ. No matter how large N is chosen, a similar picture results. The two different pictures for $\lambda \gtrsim 1/e$ (Fig. 2, center and right) are computed with different values of N and different values of λ. We have set N equal to 50 in Fig. 2 (left and center); choosing N larger will result in the disappearance of the black region as more points have a chance to escape. N was chosen to be 200 in Fig. 2 (right).

These results, together with many similar bursts, were suggested initially by mathematical experimentation. The idea of experimentation is becoming increasingly important in mathematics as the computer becomes the mathematician's laboratory. Experimentation has led to a number of significant new ideas, particularly in dynamical systems. As further examples of this, the above algorithm may be used with minor adjustments to find bursts in other families of complex entire functions. Figure 3 illustrates a burst in the family $i\lambda \cos(z)$ as λ is changed from ≈ 0.67 (left) to a value slightly larger (right). Figure 4 illustrates a burst in the family $(1 + \lambda i) \sin z$ for $\lambda = 0$ (left) and $\lambda \gtrsim 0$ (right).

Each of these bursts may be rigorously proven to occur. For the cosine family, $C_\lambda(z) = i\lambda \cos z$, the mechanism that produces the burst is analogous to that which occurs in the exponential family: an elementary saddle-node bifurcation occurs at the critical parameter value and allows the critical orbits to slip away to infinity. For the sine family, however, the mechanism is entirely different. The family $\lambda \sin z$ experiences an elementary bifurcation as λ increases through the value 1. This bifurcation is reminiscent of the period-doubling bifurcation as described in (*2, 13*), although it is technically somewhat different. It is known that such a bifurcation does not lead to a burst into chaos; rather, the states both before and after the bifurcation are quite stable. Nevertheless, if a different route in parameter space is chosen through the value $\lambda = 1$, then a burst is possible. Figure 4 (left) depicts the Julia set of $(1 + \lambda i) \sin z$; note the large black basin on either side of 0. For λ small and positive, the Julia set of $(1 + \lambda i) \sin z$ changes dramatically, as shown in Fig. 4 (right). As before, the computer screen fills with color, suggesting the explosion. Indeed, one may prove that there are parameter values arbitrarily close to 1 for which the corresponding Julia set is the whole plane (*19*). In fact, the above results suggest that any elementary bifurcation in complex dynamics (for entire transcendental functions) is accompanied by a direction in parameter space that leads to a similar burst.

REFERENCES AND NOTES

1. L. D. Landau and E. M. Lifshitz, *Fluid Mechanics* (Addison-Wesley, Reading, MA, 1959).
2. M. Feigenbaum, *J. Stat. Phys.* **21**, 669 (1978).
3. P. Collet, J.-P. Eckmann, O. E. Lanford, *Commun. Math. Phys.* **76**, 211 (1980).
4. E. C. Zeeman, *Catastrophe Theory: Selected Papers 1972–1977* (Addison-Wesley, Reading, MA, 1977).
5. R. Meron and I. Procaccia, *Phys. Rev. Lett.* **56**, 1323 (1985).
6. Y. Pomeau and P. Manneville, *Commun. Math. Phys.* **74**, 189 (1980).
7. R. B. May, *Nature (London)* **261**, 459 (1976).
8. P. Fatou, *Acta Math.* **47**, 337 (1926).
9. G. Julia, *J. Math. Pures Appl.* **4**, 47 (1918).
10. B. Mandelbrot, *The Fractal Geometry of Nature* (Freeman, San Francisco, 1982).
11. R. L. Devaney, *Phys. Lett.* **104**, 385 (1984).
12. T. Y. Li and J. Yorke, *Am. Math. Mon.* **82**, 985 (1975).
13. R. L. Devaney, *An Introduction to Chaotic Dynamical Systems* (Benjamin-Cummings, Menlo Park, CA, 1985).
14. H.-O. Peitgen and P. H. Richter, *Frontiers of Chaos* (Mapart, Bremen, West Germany, 1985).
15. D. Sullivan, *Acta Math.* **155**, 243 (1985).
16. L. Keen and L. Goldberg, *Ergodic Theory Dyn. Syst.*, **6**, 183 (1986).
17. P. Blanchard, *Bull. Am. Math. Soc.* **11**, 85 (1984).
18. A. Douady and J. Hubbard, *C. R. Acad. Sci. Ser A.* **294**, 123 (1982).
19. R. L. Devaney, in *Chaotic Dynamics and Fractals*, M. F. Barnsley and S. G. Demko, Eds. (Academic Press, Orlando, 1986), p. 141.

20. Research supported in part by the Applied and Computational Mathematics Program at the Defense Advanced Research Projects Agency and the Mathematical Sciences Division of NSF. All of the computations that generated the pictures in this report were carried out on an IBM 3081 computer at Boston University. The pictures were displayed on an AED 512 color graphics terminal. Hard copy was produced with a Matrix Instruments camera. The resolution of each photo is 400 by 400. I acknowledge the assistance of C. Mayberry, S. Smith, and C. Small with the computer graphics.

6 June 1986; accepted 30 October 1986

Forskolin and Phorbol Esters Reduce the Same Potassium Conductance of Mouse Neurons in Culture

DEBRA S. GREGA, MARY ANN WERZ, ROBERT L. MACDONALD*

Second messenger systems may modulate neuronal activity through protein phosphorylation. However, interactions between two major second messenger pathways, the cyclic AMP and phosphatidylinositol systems, are not well understood. The effects of activators of cyclic AMP–dependent protein kinase and protein kinase C on resting membrane properties, action potentials, and currents recorded from mouse dorsal root ganglion neurons and cerebral hemisphere neurons grown in primary dissociated cell culture were investigated. Neither forskolin (FOR) nor phorbol 12,13-dibutyrate (PDBu) altered resting membrane properties but both increased the duration of calcium-dependent action potentials in both central and peripheral neurons. By means of the single-electrode voltage clamp technique, FOR and PDBu were shown to decrease the same voltage-dependent potassium conductance. This suggests that two independent second messenger systems may affect the same potassium conductance.

PHOSPHORYLATION OF INTRACELLULAR proteins may affect a variety of neurobiological control mechanisms (*1*). Second messenger systems such as adenosine 3′,5′-monophosphate (cAMP) and phosphatidylinositol (*2*) are important in regulating protein phosphorylation through protein kinases. Adenylate cyclase catalyzes the conversion of adenosine triphosphate to cAMP, which increases protein kinase A activity (*3*). Phospholipase C hydrolyzes phosphatidylinositol 4,5-bisphosphate to inositol phosphates, which mobilize intracellular calcium, and to diacylglycerol, which activates protein kinase C (*4*). We have investigated the effects of activators of protein kinases A and C on resting membrane properties and action potentials recorded from mouse dorsal root ganglion (DRG) neurons and cerebral hemisphere neurons grown in primary dissociated cell culture. Forskolin (FOR) indirectly activates protein kinase A by activating adenylate cyclase (*5, 6*) whereas phorbol esters, which can substitute for diacylglycerol, directly activate protein kinase C. FOR and the phorbol ester phorbol 12,13-dibutyrate (PDBu) increased the duration of calcium-dependent action potentials in central and peripheral neurons without altering resting membrane properties. Data obtained by means of the single-electrode voltage clamp technique demonstrated that FOR and the PDBu decreased the same voltage-dependent potassium conductance.

Application of PDBu (1 μ*M*) or FOR (10 or 100 μ*M*) prolonged action potentials in a saturable and additive manner for DRG (Fig. 1; A1, A2, and B1) and cerebral hemisphere (*7*) neurons. Prolongation was maximal on the first action potential after application and action potential duration

Department of Neurology, Neuroscience Laboratory Building, 1103 East Huron, University of Michigan, Ann Arbor, MI 48104.

*To whom correspondence should be addressed.