only one of them will contain the mutation; the polymorphism will then be uninformative. (In the case of autosomal defects — where the mutation is not on the sex chromosomes — the position is further complicated by the possibility that the father may also carry the polymorphism in a normal gene; but this problem does not arise in X-linked diseases such as haemophilia because a boy inherits only one X chromosome, from his mother.)

Polymorphisms are most easily detected by bacterial enzymes (restriction enzymes) that cut DNA at specific sequences. A variation in the target sequence will prevent the enzyme from cutting at that point, and change the sizes of the fragments into which the gene is cut by the enzyme. Gitschier *et al.* experimented with 37 restriction enzymes, and found only one polymorphism in the 90,000 base pairs of the factor VIII gene that they searched¹. This is, as they point out, remarkably low compared with, for example, globin genes. The polymorphism that they did find is revealed by the restriction enzyme *BclI*, and has two alleles, present at roughly 70 and 30 per cent in the population. This makes it reasonably informative: five of eight tested carriers were heterozygous.

Much more informative, however, is the polymorphism recently reported by Oberle *et al.*⁵. It lies outside the factor VIII gene itself but is in the DNA that flanks the gene and so is usually inherited with it. Termed St14, the site has 10 polymorphic variants.

The disadvantage of this marker, as with any linked marker, is that genetic recombination can occasionally separate the marker from the gene giving a false result in a screening test. Nevertheless, St14 and *BclI* combined with another linked marker, DX13, provide a powerful genetic screening tool in those families where the necessary pedigree data are available.

Even with routine screening, given the high rate of *de novo* mutation and the existence of a normal carrier state, haemophilia A is not going to disappear from human populations. There is much talk of using genetically manipulated bone marrow to correct genetic defects where, as in haemophilia, the site of action of the gene is the plasma. This would entail the introduction of a normal factor VIII gene into the patient's own bone-marrow cells, which do not normally express the gene. At this stage, such therapy could not be justified in the face of unknown risks, for a disease treatable by more conventional, albeit imperfect, means. Nor is it clear whether the problem of antibody production against factor VIII could be avoided, for instance by very early bone-marrow therapy. In all likelihood, we shall see. □

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2. Wood, W.I. *et al.* *Nature* **312**, 326 (1984).
3. Gitschier, J. *et al.* *Nature* **312**, 330 (1984).
4. Gitschier, J. *et al.* *Nature* (in the press).
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Mathematics

Feigenbaum's fixed function

from Ian Stewart

FOR several years there has been a flurry of activity on the topic of 'deterministic chaos' whereby quite simple systems, described by equations having no explicit random terms, nevertheless exhibit behaviour that seems to be stochastic. Using ideas from renormalization group theory (originally invented to handle problems in quantum field theory), Mitchell Feigenbaum of Cornell University was led to conjecture some very specific 'universal' properties of such systems. Feigenbaum's conjecture was proved in full rigour by M. Campanino, H. Epstein and D. Ruelle (*Commun. math. Phys.* **79**, 261; 1981 and *Topology* **21**, 125; 1982) and by Oscar Lanford (*Bull. Am. math. Soc.* **6**; 1982). Both proofs made heavy use of complicated (though exact) numerical estimates, which required computer assistance. Remarkably, Lanford — who works at the Institut des Hautes Etudes Scientifiques in Bures-sur-Yvette — has now improved the proof so that only a calculator is required.

Feigenbaum's conjecture arose from a numerical study of the behaviour of the nonlinear recurrence equation $x_{n+1} = kx_n(1-x_n)$, as the constant k increases from 0 to 4. An initially stable fixed point bifurcates into a pair of points of period 2, which in turn split into periods 4, 8, 16, ... and so on. By the time k reaches a value around 3.7, an infinite number of these bifurcations has occurred; this is called a period-doubling cascade. Such cascades are of interest in a variety of applications, notably fluid turbulence. Feigenbaum was interested in the rate at which successive steps in the cascade developed. Let k_n be the value of k at which the n th period-doubling occurs. The ratio of gaps between consecutive bifurcation points is $\delta_n = (k_{n+1} - k_n)/(k_{n+2} - k_{n+1})$; as n tends to infinity the value of δ approaches 4.6692016... That is, the successive bifurcation points accumulate according to a geometric progression at a rate measured by δ . On repeating the calculation for other nonlinear recurrence equations, Feigenbaum discovered that the values of δ were identical. This coincidence has important implications for experimental confirmation of mathematical models based on nonlinear recurrence equations (discrete dynamical systems), because by observing the values of k at which the first five or six period-doublings occur, one may obtain an experimental estimate for δ , to be compared with a very precise theoretical prediction.

Further investigation suggested a reason for the 'universality' of δ . If $f(x) = kx(1-x)$ is the function being iterated in the recurrence equation, then it turns out that the second iterate $f^2(x) = f(f(x))$ has almost the same shape of graph as f , pro-

vided the axes of the graph are similarly positioned and scaled, and provided attention is confined to a suitable range of values of x . The clue to the universality lies in finding a function g for which this scaling process is exact. In other words, g must satisfy the Feigenbaum-Cvitanovic functional equation

$$g(x) = -g(g(-ax))/a$$

for a positive constant a (representing the required scale factor). The difficulty is to show that such a function g exists.

To do so, one starts with a function that satisfies this equation to a very high degree of approximation and uses it to construct a sequence of functions, by a process of renormalization, that converges to the desired solution. Abstractly one thinks of the desired g as living in a space X of functions: the renormalization operator T transforms any function h in X into a new function Th . The operator T is chosen so that the Feigenbaum-Cvitanovic equation boils down to the requirement that g be a fixed point (or fixed function) of T . Standard theorems, concerning fixed points of operators on function spaces, then finish the proof.

The difficulty is to obtain a sufficiently close initial estimate. It is here that the computer comes in. Although in the normal run of things the numbers held in a computer are subject to rounding error, it is possible to keep track of the largest size such errors can be, and hence keep exact estimates of the degree of accuracy of the calculations. In the present case, the initial choice of function h is somewhat complicated and so, therefore, are these estimates.

Lanford has succeeded in simplifying the procedure to the point at which the estimates may be performed using a hand-held calculator (here a Hewlett-Packard HP-15C, accurate to nine decimal places). The proof remains delicate, but is much simpler than its predecessors. Note, however, that to apply g to period-doubling, some additional properties must be established, which can still only be obtained using Lanford's computer-assisted proof.

The essence of the problem seems to be that the Feigenbaum fixed function g cannot be related in any very direct way to more standard functions, such as polynomials, for which methods of calculation can easily be found. Functional equations themselves have been something of a mathematical backwater. The prospect of applying them to nonlinear dynamics now makes it important to develop new and better techniques to handle their solutions. In such a way may new mathematics be born from a good physical problem. □

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