Biological Populations with Nonoverlapping Generations: Stable Points, Stable Cycles, and Chaos

Abstract. *Some of the simplest nonlinear difference equations describing the growth of biological populations with nonoverlapping generations can exhibit a remarkable spectrum of dynamical behavior, from stable equilibrium points, to stable cyclic oscillations between 2 population points, to stable cycles with 4, 8, 16, . . . points, through to a chaotic regime in which (depending on the initial population value) cycles of any period, or even totally aperiodic but bounded population fluctuations, can occur. This rich dynamical structure is overlooked in conventional linearized analyses; its existence in such fully deterministic nonlinear difference equations is a fact of considerable mathematical and ecological interest.*

In some biological populations (for example, man), growth is a continuous process and generations overlap; the appropriate mathematical description involves nonlinear differential equations. In other biological situations (for example, in 13-year periodical cicadas), population growth takes place at discrete intervals of time and generations are completely nonoverlapping; the appropriate mathematical description is in terms of nonlinear difference equations. For a single species, the simplest such differential equations, with no time delays, lead to very simple dynamics: a familiar example is the logistic, $dN/dt = rN(1 - N/K)$, with a globally stable equilibrium point at $N = K$ for all $r > 0$.

It is the purpose of this report to point out that many of the corresponding difference equations of population biology have been discussed inadequately, as having either a stable equilibrium point or being unstable, with growing oscillations (*1, 2*). In fact, some of the very simplest nonlinear difference equations even for single species exhibit a spectrum of dynamical behavior which, as the intrinsic growth rate r increases, goes from a stable equilibrium point, to stable cyclic oscillations between 2 population points, to stable cycles with 4 points, then 8 points, and so on, through to a regime which can only be described as chaotic (a term coined by J. A. Yorke). For any given value of r in this chaotic regime there are cycles of period 2, 3, 4, 5, . . . , n, . . . , where n is any positive integer, along with an uncountable number of initial points for which the system does not eventually settle into any finite cycle; whether the system converges on a cycle, and, if so, which cycle, depends on the initial population point (and of course some of the cycles may be attained only from infinitely unlikely initial points). Figure 1 aims to illustrate this range of behavior.

Specifically, consider the simple nonlinear equation

$$N_{t+1} = N_t \exp[r(1 - N_t/K)] \qquad (1)$$

This is considered by some people (*2, 3*) to be the difference equation analog of the logistic differential equation, with r and K the usual growth rate and carrying capacity, respectively. The stability character of this equation, as a function of increasing r, is set out in Table 1 and illustrated by Fig. 1.

Another example is

$$N_{t+1} = N_t[1 + r(1 - N_t/K)] \qquad (2)$$

This quadratic form is probably the simplest nonlinear equation one could write. Although discussed by various people (*4, 5*) as the analog of the logistic differential equation, Eq. 2 is less satisfactory than Eq. 1 by virtue of its unbiological feature that the population can become negative if at any point N_t exceeds $K(1 + r)/r$. Thus, stability properties here refer to stability within some specific neighborhood, whereas in Eq. 1, for example, the stable equilibrium point at $N = K$ is globally stable (for all $N > 0$) for $2 > r > 0$. With this proviso, the stability behavior of Eq. 2 is strikingly similar to that of Eq. 1; see Table 1.

That such single species difference equations should describe populations going from stable equilibrium points to stable cycles as r increases is not surprising, in view of the general engineering precept that excessively long time delays in otherwise stabilizing feedback mechanisms can lead to "instability" or, more precisely, to stable limit cycles (*5*, chapter 4; *6*). What is remarkable, and disturbing, is that the simplest, purely deterministic, single species models give essentially arbitrary dynamical behavior once r is big enough ($r > 2.692$ for Eq. 1, $r > 2.570$ for Eq. 2). Such behavior has previously been noted in a meteorological context (*7*), and doubtless has other applications elsewhere. For population biology in general, and for temperate zone insects in particular, the implication is that even if the natural world were 100 percent predictable, the dynamics of populations with "density dependent" regulation could nonetheless in some circumstances be indistinguishable from chaos, if the intrinsic growth rate r were large enough.

The detailed analysis substantiating these remarks, and deriving Table 1, will be set out in the technical literature. A very brief outline is as follows:
(i) For the general nonlinear difference equation

$$N_{t+1} = f(N_t) \qquad (3)$$

the locally stable equilibrium point or points can be found by the conventional techniques of linearized stability analysis. For Eq. 1, a fully nonlinear analysis can be given by observing that $V_t = (N_t - K)^2$ is a Lyapunov function, with the properties $V_t \geq 0$ and $\Delta V_t \equiv V_{t+1} - V_t \leq 0$ for all $N_t > 0$, for $2 > r > 0$: this ensures that the equilibrium point is globally stable. (ii) Next, the possible occurrence of cycles with period 2 may be studied for the equation

$$N_{t+2} = f[f(N_t)] \qquad (4)$$

For Eqs. 1 and 2 this has a unique nontrivial equilibrium solution, $N^* = K$, for $r < 2$, corresponding to the above stable point; as r increases above 2 this solution of Eq. 4 becomes unstable, and (as

Table 1. Dynamics of a population described by the difference equations 1 or 2.

Dynamical behavior	Value of the growth rate, r	
	Equation 1	Equation 2
Stable equilibrium point	$2 > r > 0$*	$2 > r > 0$
Stable cycles of period 2^n		
2-point cycle	$2.526 > r > 2.000$†	$2.449 > r > 2.000$
4-point cycle	$2.656 > r > 2.526$‡	$2.544 > r > 2.449$
8-point cycle	$2.685 > r > 2.656$	$2.564 > r > 2.544$
16, 32, 64, . . .	$2.692 > r > 2.685$	$2.570 > r > 2.564$
Chaotic behavior. (Cycles of arbitrary period, or aperiodic behavior, depending on initial condition.)	$r > 2.692$§	$r > 2.570$

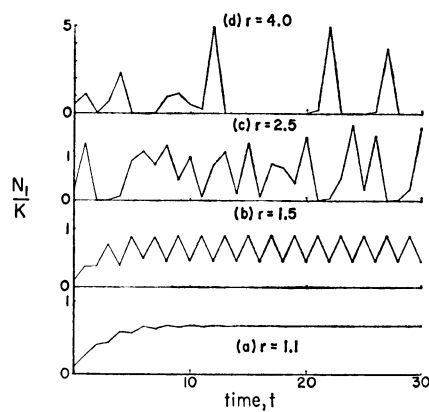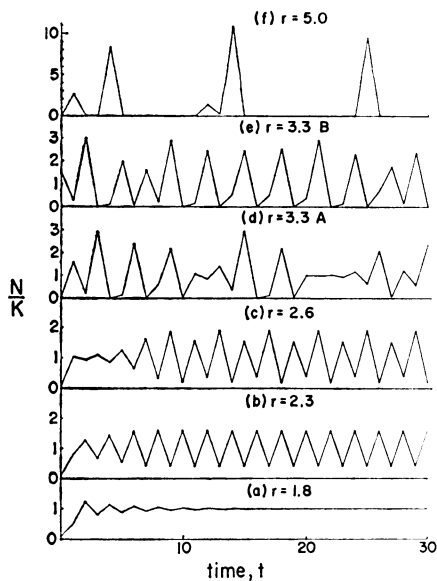* See Fig. 1a.   † See Fig. 1b.   ‡ See Fig. 1c.   § See Fig. 1, d, e, and f.

Fig. 1 (left). (a to f) Spectrum of dynamical behavior of the population density, N_t/K, as a function of time, t, as described by the difference Eq. 1 for various values of r. Specifically: (a) $r = 1.8$, stable equilibrium point; (b) $r = 2.3$, stable 2-point cycle; (c) $r = 2.6$, stable 4-point cycle; (d to f) in the chaotic regime, where the detailed character of the solution depends on the initial population value, with (d) $r = 3.3$ ($N_0/K = 0.075$), (e) $r = 3.3$ ($N_0/K = 1.5$), (f) $r = 5.0$ ($N_0/K = 0.02$). Fig. 2 (right). Stability character of the difference equation model of two-species competition, Eq. 5. Specifically, the figure is for $r_1 = r$, $r_2 = 2r$, $K_1 = K_2 = K$, $\alpha_{11} = \alpha_{22} = 1$, $\alpha_{12} = \alpha_{21} = \alpha$: under these conditions the criterion for a stable point, Eq. 7, reduces to the requirements $\alpha < 1$ (as for the analogous Lotka-Volterra differential equation), together with $[3 - (1 + 8\alpha^2)^{\frac{1}{2}}]/[2(1 - \alpha)] > r > 0$. The first population, expressed as N_1/K, is shown as a function of time for $\alpha = 0.5$ and several values of r: (a) $r = 1.1$; (b) $r = 1.5$; (c) $r = 2.5$; (d) $r = 4.0$.

illustrated by Fig. 1b) bifurcates into a pair of points, between which the population alternates in a 2-point cycle which is stable provided $2 < r < 2.526$ for Eq. 1, and $2 < r < 2.449$ for Eq. 2. Beyond this, the 2-point cycle in turn becomes unstable and each of the points bifurcates into 2 further points, giving a stable 4-point cycle (for example, Fig. 1c), and so on. (iii) As r continues to increase, there is a limit to this process whereby cycles of period 2^n become unstable and bifurcate into stable cycles of period 2^{n+1}. This limiting value of r, r_c say, may be calculated [either by brute force, or by analytic methods developed in (8)], and is as set out in the final line in Table 1. For $r > r_c$, there ensues a regime of chaos, in which there exist an uncountable number of initial points N_0 for which the system does not eventually settle into any cycle (that is, is not "asymptotically periodic"). (iv) In particular, at yet larger values of r ($r > 3.102$ for Eq. 1, and $r > 2.828$ for Eq. 2), Eqs. 1 and 2 may be shown to have cycles with period 3; that is, solutions such that $N_{t+3} = N_t \neq N_{t+1} \neq N_{t+2}$. But Li and Yorke (9) have recently proved an elegant and abstract mathematical theorem, which states that if the general difference equation, Eq. 3, has a 3-point cycle, it necessarily follows that for the same parameter

values there are cycles of period n, where n is any positive integer, and furthermore there exist an uncountable number of initial points for which the system is not even asymptotically periodic. Li and Yorke's general theorem for cycles of period 3 may be extended (8) to show that equations of the generic form of 1 and 2 will enter a regime of chaos, with an uncountable number of cycles of integral period along with an uncountable number of aperiodic solutions, beyond the limiting value r_c defined above.

The dynamical behavior of Eqs. 1 and 2 in this chaotic regime, $r > r_c$, is illustrated in Fig. 1, d, e, and f. Figure 1, d and e, are for the same value of r, and differ only in their initial population value. Note that either of these figures, if looked at only over particular short time intervals, could convey the impression of being locked into a 3-point cycle; around this value of r there is a tendency to be "captured" into almost-periodic 3-point cycles, in between episodes of apparently chaotic behavior. A detailed understanding of these properties remains an interesting mathematical problem, related to that of determining what fraction of the totality of initial points converge to a 3-point cycle, what fraction to a 5-point cycle, and so on, ending with a determination of the fraction of initial points

which lead to aperiodic behavior. For relatively large values of r beyond r_c (for example, Fig. 1f) the population variations become more severe, although the mean population value may be shown to remain around K; as r becomes larger, this mean value is increasingly constituted of a few fairly large population values, together with long sequences of very low population values.

The above discussion is restricted to single species systems obeying difference equations. However, similar considerations are likely to apply, a fortiori, to multispecies situations.

As one among many possible examples, consider a simple difference equation model for competition between two species

$$N_1(t + 1) = N_1(t)\exp\{r_1[K_1 - \alpha_{11}N_1(t) - \alpha_{12}N_2(t)]/K_1\} \quad (5a)$$

$$N_2(t + 1) = N_2(t)\exp\{r_2[K_2 - \alpha_{21}N_1(t) - \alpha_{22}N_2(t)]/K_2\} \quad (5b)$$

Just as Eq. 1 may be regarded as a difference equation analog of the logistic, Eq. 5 may be regarded as an analog of the familiar Lotka-Volterra differential equation model for two-species competition. As usual, r_i are the growth rates, K_i the carrying capacities, and α_{ij} the competition coefficients. The dynamical properties of such Lotka-Volterra differential equations are straightforward: the two species coexist, with a globally stable equilibrium point, if and only if

$$D > 0 \quad (6)$$

where D is defined as $D = \alpha_{11}\alpha_{22} - \alpha_{12}\alpha_{21}$. Failing this, one or the other species is extinguished. But for the system of difference equations, Eq. 5, the criterion for the existence of a stable two-species equilibrium point is more restrictive, namely

$$A > D > 0 \quad [\text{if } A < 2] \quad (7a)$$
$$A > D > 2A - 4 \quad [\text{if } A > 2] \quad (7b)$$

Here D is as above, and A is defined as $A = (\alpha_{11}K_2/r_2N_2^*) + (\alpha_{22}K_1/r_1N_1^*)$, with N_1^* and N_2^* the equilibrium solutions of Eq. 5. [The methodology for stability analysis of such two-species difference equations is indicated elsewhere (6)]. If the right-hand side of Eq. 7a is violated, one of the species is eliminated, as in the differential equation model, Eq. 6. If any of the other inequalities in Eq. 7 is transgressed, the two species continue to coexist, but there is no longer a stable equilibrium point. Numerical studies reveal a regime of stable cycles, giving way to one

of apparent chaos, as for the single species systems discussed in detail above. The behavior of the system of Eq. 5 in these various regimes is illustrated in Fig. 2.

Equations 1 and 2 are two of the simplest nonlinear (density dependent) difference equations that can be written down. Their rich dynamical structure, and in particular the regime of apparent chaos wherein cycles of essentially arbitrary period are possible, is a fact of considerable mathematical and ecological interest, which deserves to be more widely appreciated. Without an understanding of the range of behavior latent in such deterministic difference equations, one could be hard put to make sense of computer simulations or time-series analyses in these models.

ROBERT M. MAY
*Biology Department, Princeton
University, Princeton, New Jersey 08540*

References and Notes

1. Previous work in this general area of population biology consists largely of remarks on the relation between differential equation models and difference equation models [H. R. Van der Vaart, *Bull. Math. Biophys.* **35**, 195 (1973); R. M. May, *Am. Nat.* **107**, 46 (1972); J. M. Smith, *Models in Ecology* (Cambridge Univ. Press, Cambridge, 1974)] and linearized analyses of Eqs. 1 and 2 showing the equilibrium point to be locally stable only if $2 > r > 0$ [L. M. Cooke (2) for Eq. 1; J. M. Smith, *Models in Ecology*, for Eq. 2].
2. L. M. Cooke, *Nature (Lond.)* **207**, 316 (1965).
3. A. Macfadyen, *Animal Ecology: Aims and Methods* (Pitman, London, ed. 2, 1963).
4. J. M. Smith, *Mathematical Ideas in Biology* (Cambridge Univ. Press, Cambridge, 1968); J. R. Krebs, *Ecology: The Experimental Analysis of Distribution and Abundance* (Harper & Row, New York, 1972).
5. R. M. May, *Stability and Complexity in Model Ecosystems* (Princeton Univ. Press, Princeton, N.J., 1973).
6. ——, M. P. Hassell, G. R. Conway, T. R. E. Southwood, *J. Anim. Ecol.*, in press.
7. E. N. Lorenz, *Tellus* **16**, 1 (1964); *J. Atmos. Sci.* **20**, 448 (1963).
8. R. M. May and G. F. Oster, in preparation.
9. T.-Y. Li and J. A. Yorke, *SIAM (Soc. Ind. Appl. Math.) J. Math. Anal.*, in press.
10. I am indebted to many people, and particularly to J. A. Yorke, for stimulating discussions.

3 June 1974

hycanthone is mutagenic (4) and teratogenic (5), and that it induces prophage (6), mitotic crossing-over (7), cytogenic changes (8), and malignant transformations (9); hycanthone is carcinogenic in mice infected with *S. mansoni* (10). As pointed out by Firminger (11), a report (12) which seemingly did not support the last observation was based on such a small number of animals that no significant negative results could have been obtained. Since a number of compounds chemically related to hycanthone exhibit antischistosomal activity, the question arose whether structural alterations can bring about a dissociation of undesirable toxicological properties from chemotherapeutic activity. Data summarized below indicate that this is the case.

A chloroindazole analog (IA-4, structure in Table 1) of hycanthone has the same antischistosomal activity in mice as hycanthone (13), while its acute toxicity and its hepatoxicity are lower (13, 14). Compound IA-4 failed to induce demonstrable malignant transformations in cells infected with Rauscher virus (9). Its mutagenic activity was found to be lower in *Salmonella* (15), bacteriophage T4 (15), and mouse lymphoblasts (16); no mutagenic effects were detected in yeast (17); no cytogenetic effects were detected in rat bone marrow cells (18). Furthermore, in contrast to hycanthone and to a number of chemical carcinogens, IA-4 failed to induce breaks in rat liver DNA (19). Another indazole analog (IA-3) had lower antischistosomal activity; but since there is decreased acute toxicity, the chemotherapeutic index of IA-3 approximately equals that of IA-4 (13).

We found that chloro substitution in position 8 produced a marked decrease in the acute toxicity of the indazole analogs for mice. For example, the median intramuscular lethal dose (LD_{50}) of IA-3 and of IA-4 was more than seven times higher than that of the corresponding deschloro derivatives.

In further studies of the effect of structural modifications on antischistosomal activity and on mutagenicity, *N*-oxides of active thioxanthenones and benzothiopyranoindazoles were prepared. The parent bases were oxidized with *m*-chloroperbenzoic acid in dichloromethane solution, and after chromatography (Al_2O_3) the *N*-oxides so obtained were converted to their water-soluble methanesulfonate salts. *N*-Oxidation at the diethylaminoethyl group consistently resulted in a marked reduction in mutagenicity for *Salmonella*

Hycanthone Analogs: Dissociation of Mutagenic Effects from Antischistosomal Effects

Abstract. *N-Oxidation at the diethylamino group of hycanthone, of lucanthone, and of two chlorobenzothiopyranoindazoles resulted in a marked reduction in mutagenic activity, while antischistosomal activity was retained or even enhanced. Introduction of chlorine into the 8-position of benzothiopyranoindazoles reduced acute toxicity but had no effect on chemotherapeutic potency. These dissociations of biological activities indicate that safer antischistosomal compounds of this class can be developed.*

The geographical distribution and the nature of human schistosomiasis require special care in the selection of chemotherapeutic agents for the treatment of this infection. More than 200 million human subjects are infected with schistosomes and the incidence is on the increase. Even a low frequency of delayed serious complications, produced by mutagenic, teratogenic, and carcinogenic actions of a drug, can involve a large absolute number of individuals. Populations infected with schistosomes are not protected by national drug laws or regulatory agencies. Moreover, in an undetermined number, and possibly the majority, of subjects infected with *Schistosoma hematobium*, overt clinical and pathological manifestations disappear in adulthood (1). This must be taken into account when considering a drug for the mass treatment of children whose life expectancies are longer and whose reproductive potentials are greater than those of adults. As was stated by Rubidge *et al.* (2), "urinary tract bilharziasis is

a relatively mild disease in South Africa and serious sequelae are rare. Hence, therapy must be safe."

It is estimated that during the past 6 years, in Brazil, Africa, and the Middle East, at least 700,000 human subjects infected with *S. hematobium* and *S. mansoni* have been treated with the antischistosomal thioxanthenone derivative hycanthone (the drug is ineffective in infections produced by *S. japonicum* prevalent in mainland China and the Philippines) (3). Reports from a variety of laboratories have indicated that
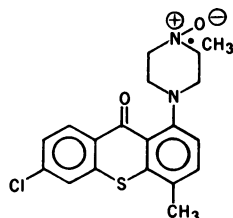

Fig. 1. Mutagenic activity: none detectable (less than 0.1 percent as active as hycanthone). Antischistosomal activity: intramuscular, 0.4; oral, 0.3.