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Dynamics of Some Simple Host-Parasite Models with More than Two Genotypes in Each Species [and Discussion]

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Phil. Trans. R. Soc. Lond. B 1988 **319**, 541-555
doi: 10.1098/rstb.1988.0064

Phil. Trans. R. Soc. Lond. B **319**, 541–555 (1988)
Printed in Great Britain

Dynamics of some simple host–parasite models with more than two genotypes in each species

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A two-species genetic model of host–parasite interaction is used to study the dynamical consequences of varying the number of genotypes in each species, and the recombination rate in the host. With two genotypes in each species, the model's behaviour is very simple; there is either a stable interior equilibrium, a stable cycle or a smooth outward spiral toward the boundaries. But with three or more genotypes, complex cycles and apparently chaotic behaviour may arise over wide ranges of parameter values. Increasing the number of genotypes also tends to slow the rate of gene-frequency change. Recombination in the host does not affect the stability of the interior fixed point, but intermediate rates of recombination may give dynamic stability to an otherwise dynamically unstable pattern of cycling. Intermediate rates of recombination also tend to decrease the amplitudes of gene-frequency cycles in the host, which implies that they could promote the accumulation of genetic variation involved in complementary, antagonistic interactions with parasites.

Introduction

The co-evolution of hosts and parasites has traditionally been thought of as a process driven by frequency-dependent selection (see, for example, Haldane 1949; Mode 1958; Person 1966; Clarke 1976). But there is an important difference between the kind of frequency dependence that arises from genotype-specific host–parasite interactions, and the kind that arises from, for example, behavioural interactions among the members of a single species. In behavioural interactions, a genotype's own relative frequency is often imagined to be a direct cause of its own relative fitness, but in host–parasite interactions, the fitnesses of the host genotypes may depend much more on the relative frequencies of the parasite genotypes than on their own frequencies, and the fitnesses of the parasite genotypes may depend mainly on the host genotype frequencies. Under these assumptions, a common host genotype will eventually come to have below-average fitness because the parasite(s) best able to exploit it will have increased in frequency; the host genotype will then decline in frequency, thereby lowering the fitness(es) of the parasite genotype(s) that caused its own decline. The resulting 'virtual' frequency dependence within each species is therefore an indirect (and time-delayed) result of the coupled evolutionary histories of host and parasite.

Certain kinds of frequency-dependent behavioural interaction within a single species can give rise to cyclical or otherwise unstable dynamics (see, for example, Maynard Smith & Brown 1986), but this seems to be the exception rather than the rule. By contrast, almost all models of host–parasite co-evolution show a tendency to cycle (see, for example, Person 1966; Clarke 1976; Eshel & Akin 1983) because the mechanism of frequency-dependence operates with a time delay (see, for example, Hutson & Law 1981; Bell 1982; Bell & Maynard Smith 1987). A stable interior equilibrium may or may not exist depending on the details of the model (and

sometimes on parameter values), but even where such an equilibrium does exist, gene frequencies almost always approach it on oscillating, rather than montonically converging, trajectories (see, for example, Jayakar 1970; Yu 1972; Lewis 1981*a*, *b*; Levin 1983).

The models published so far have explored a wide range of assumptions concerning the biologies of host and parasite (for entries to the literature see Levin (1983); Anderson & May (1982); May & Anderson (1983*a*, *b*); May (1985)) but most have been based on very simple genetic systems consisting of one locus in each species with two alleles, or at most a small fixed number of them. Here I suggest that the dynamics of host–parasite co-evolution are also likely to be affected in significant ways by the structures of the underlying genetic systems. I describe three simple models that differ only with respect to their genetic systems: (1) a model with one locus and two alleles in host and parasite; (2) the generalization of this model to n alleles; (3) a model with two loci and variable recombination in the host. As n increases in the one-locus case, the interior equilibrium becomes stable over a wider range of parameter values, and the dynamics away from the equilibrium become more sluggish but more chaotic. In the two-locus case, recombination has no effect on the stability of the equilibrium, but the amplitudes of the gene-frequency cycles away from equilibrium are usually smallest at recombination rates intermediate between zero and one half, which implies that limited recombination could promote the retention of genetic variation at loci controlling host-resistance phenotypes.

Assumptions common to the three models

All the models described here share the same very simple biology. There is one host species and one parasite species. Generations are discrete and non-overlapping, and the two species reproduce synchronously. Host and parasite individuals encounter each other randomly, at rates proportional to their relative frequencies. Each host genotype is vulnerable to one complementary parasite genotype. If a host encounters its complementary parasite, its fitness is reduced and the parasite's fitness is increased. For the sake of simplicity, these fitness effects are the same for each pair of complementary host and parasite genotypes.

If the frequencies of the host and parasite genotypes are H_i and P_j ($\sum H_i = \sum P_j = 1$), then

$$W_i = 1 - sP_i \quad \text{and} \quad V_j = 1 - t(1 - H_j), \tag{1}$$

where W_i is the fitness of host genotype i, V_j is the fitness of parasite genotype j, s is a constant proportional to the loss of fitness suffered by host genotype i when it is attacked by parasite genotype i (the one to which it is especially vulnerable), and t is a constant proportional to the loss of fitness suffered by parasite genotype j when it attacks a resistant host (i.e. any host genotype other than the one that is especially susceptible to it). Thus the fitnesses within each species are simple linear functions of the genotype frequencies in the other species. Neither species has a direct effect on itself, and there is no explicit density dependence.

The genetic systems of both species are haploid. The parasite always has a single locus (C) with a series of alleles C_j at frequencies P_j. In the first two models the host also has a single locus (A) with alleles A_i at frequencies H_i. In the third model the host has two loci (A and B), each with two alleles, and the loci undergo recombination at a rate r. In this case the host species is assumed to mate randomly, but otherwise the host and parasite species can be thought of either as sexual or as asexual, because each has only a single haploid locus. There is no mutation or migration in the host population, but alleles at the C locus in the parasite mutate

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at random to one of the other available allelic states at a rate m per generation. (Alternatively, the mutation rate can be thought of as the rate at which parasites from distant, genetically uncorrelated populations migrate into the population of interest.)

Given these assumptions and definitions, it is easy to write down the recurrence equations for the genotype frequencies in each species in generation $T+1$, as functions of s, t and m (and r if necessary), and the genotype frequencies in generation T. If there are n genotypes in host and parasite, then there are $2(n-1)$ equations in all, because the n genotype frequencies in each species must sum to unity. Owing to the model's symmetry, there is always an interior fixed point at which each of the n host and parasite genotypes is present at a frequency of $1/n$. The behaviour of the system in the neighbourhood of this fixed point can be inferred from a straightforward analysis of the linearized recurrence equations, and the behaviour away from equilibrium can be easily examined, for particular sets of parameter values, by numerical iteration of the complete system of equations. This done below for each of the three models.

Two alleles at one locus

The linearized recurrence equations are

$$\begin{bmatrix} 1 & -b \\ c & d \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ y_1 \end{bmatrix} = \begin{bmatrix} x_1' \\ y_1' \end{bmatrix}, \tag{2}$$

where $b = s/(2-s)$, $c = t(1-2m)/(2-t)$, $d = 1-2m$, x_1 and y_1 are the current (generation $-T$) deviations of the host and parasite genotype frequencies from their equilibrium values of one half, and x_1' and y_1' are the deviations in generation $T+1$. The eigenvalues of the coefficient matrix are the solutions of the characteristic equation

$$(\lambda-1)(\lambda-d)+bc = 0 \tag{3}$$

which are

$$\lambda = \tfrac{1}{2}\{(1+d) \pm [(1+d)^2-4(bc-d)]^{\frac{1}{2}}\}. \tag{4}$$

If $m = 0$, then $d = 1$, and the eigenvalues have a real part equal to unity and conjugate imaginary parts whose size depends on the selection parameters s and t; the modulus (absolute magnitude) of the eigenvalues is therefore greater than unity, so the fixed point is unstable and a population will depart from its neighbourhood on an oscillating trajectory. As m is increased from zero (holding s and t constant), the real and imaginary parts of the eigenvalues all become absolutely smaller, and eventually the modulus of the eigenvalues becomes equal to unity. This critical mutation rate is

$$m^* = \tfrac{1}{4}st/(2-s-t+st). \tag{5}$$

For example, if $s = 0.1$ and $t = 0.3$, then $m^* = 0.0046$. Mutation rates larger than this give eigenvalues of modulus less than unity, indicating local stability of the equilibrium. Finally, for very large values of m (relative to the selection parameters), the imaginary parts vanish and the eigenvalues become entirely real, indicating rapid monotonic convergence to the interior equilibrium.

Examples of the full dynamics are shown in figure 1. If there is no mutation, then the system spirals outward, moving ever closer to the boundaries of the H_1-P_1 phase plane (figure 1*a*). (The corner equilibria are unstable and there are no boundary equilibria, if s and t are greater than zero.) Mutation rates greater than zero but less than m^* give rise to stable orbits away from the boundaries, and these orbits are approached from any initial conditions (figure 1*b*).

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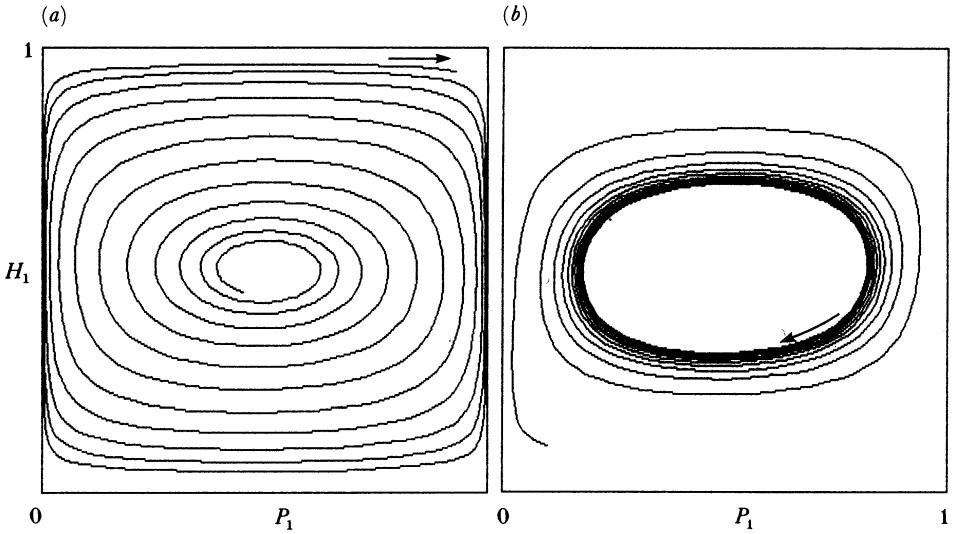

FIGURE 1. Dynamics of the one-locus, two-allele model. These phase diagrams show the frequencies of allele A_1 in the host (H_1, on the vertical axis), against the frequencies of allele C_1 in the parasite (P_1, on the horizontal axis). In both of the cases illustrated here, $s = 0.1$ and $t = 0.3$, and the trajectories are 1000 generations long. (*a*) With no mutation ($m = 0$), the system spirals outward toward the boundaries. (*b*) With a moderate mutation rate ($m = 0.003$) less than that required to stabilize the central fixed point ($m^* = 0.0046$), the system rapidly converges from any initial gene frequencies to a stably attracting orbit well away from the boundaries.

In the vicinity of the interior fixed point, the orbital period can be estimated from the angle defined by the real axis and either of the eigenvalues, when the latter are viewed as vectors anchored at the origin of the complex plane. (Algebraically, the eigenvalues can be expressed in polar form, $\lambda = re^{i\theta}$.) The orbital period τ is then inversely related to the angle θ, as

$$\tau = 2\pi/\theta. \tag{6}$$

For small values of m, s and t, θ is approximately equal to the imaginary part of the eigenvalues (4), which gives roughly $\theta \approx \frac{1}{2}(st)^{\frac{1}{2}}$, or

$$\tau \approx 4\pi/(st)^{\frac{1}{2}}. \tag{7}$$

Even when s and t are large, as in the examples shown in figure 1, this approximation is fairly good ($\tau \approx 73$ generations), and it gives roughly the correct period even for trajectories that are well away from the interior equilibrium, as long as they are not very close to a boundary.

n ALLELES AT ONE LOCUS

If there are n possible alleles at each of the single loci in host and parasite, then the linearized recurrence equations can be arranged in block-diagonal form as

$$\begin{bmatrix} 1 & -b & & & \\ c & d & & & \\ & & 1 & -b & \\ & & c & d & \\ & & & & \cdots \\ & & & & \cdots \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ y_1 \\ x_2 \\ y_2 \\ \cdot\,\cdot \\ \cdot\,\cdot \end{bmatrix} = \begin{bmatrix} x_1' \\ y_1' \\ x_2' \\ y_2' \\ \cdot\,\cdot \\ \cdot\,\cdot \end{bmatrix}, \tag{8}$$

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where $b = s/(n-s)$, $c = t(1-nm)/[n-(n-1)t]$, and $d = 1-nm/(n-1)$. When $n = 2$, equation (8) reduces to equation (2). The characteristic equation is of degree $2(n-1)$, but owing to the block-diagonal form of the matrix, it can be factored into a product of quadratics:

$$[(\lambda-1)(\lambda-d)+bc]^{n-1} = 0. \tag{9}$$

Equation (9) is satisfied whenever any of its $n-1$ quadratic factors is equal to zero, so the eigenvalues are again the roots of simple quadratic equations; each pair of eigenvalues is repeated $n-1$ times. In the more general case where the selection parameters s and t are different for each pair of complementary host and parasite genotypes, the coefficient matrix takes the same block-diagonal form and the characteristic equation factors into a product of $n-1$ quadratics. But in this case each quadratic differs from the others and must be solved separately, so that a different pair of eigenvalues is associated with each complementary pair of genotypes. In the yet more general case of arbitrary fitness effects for every pair of host and parasite genotypes (involving n^2 pairs of selection parameters s_{ij} and t_{ij}), the matrix is not reducible to block-diagonal form and the characteristic equation cannot in general be solved in closed form. The block-diagonal form of the matrix arises from the biological assumption that each genotype in one species sees the genotypes of the other species as falling into two groups: the one complementary genotype, and $n-1$ 'others'; encounters with any of the latter have the same effect on fitness.

For the symmetrical case being considered here, the critical stabilizing mutation or migration rate is

$$m^* = (n-1)\,st/\{n(n^2-ns-n(n-1)\,t+2(n-1)\,st]\}, \tag{10}$$

which for small selection parameters and moderately large n gives approximately

$$m^* \approx st/n^2. \tag{11}$$

Thus as the number of alleles increases from few to several to many, there is a sharp reduction in the amount of mutation or migration needed to stabilize the interior fixed point.

The period of the orbit near the fixed point increases approximately linearly with the number of alleles. The generalized form of the approximation given as (7) in the two-allele case is

$$\tau \approx 2\pi n/(st)^{\frac{1}{2}}. \tag{12}$$

The modulus of the eigenvalues is proportional to the rate at which the system tends to move radially away from the fixed point. This rate of outward movement is easily shown to scale as $1/n^2$ per generation, and therefore as $1/n$ per complete cycle about the fixed point. Thus in two different senses (orbital speed and rate of outward movement), increasing the number of alleles would appear to slow the dynamics of this model, even in cases where the rate of mutation is not sufficient to stablize the interior fixed point.

These inferences about the quantitative effects of increasing the number of alleles were confirmed by iterating the full recurrence equations for particular sets of parameters and initial conditions. The numerical experiments also revealed a striking qualitative difference between the dynamics of the two-allele case and the dynamics of all cases involving three or more alleles. Irregular, apparently 'chaotic' orbits easily arise with three or more alleles, but never with only two, under the simple biological assumptions of this model (figure 2). Complex behaviour

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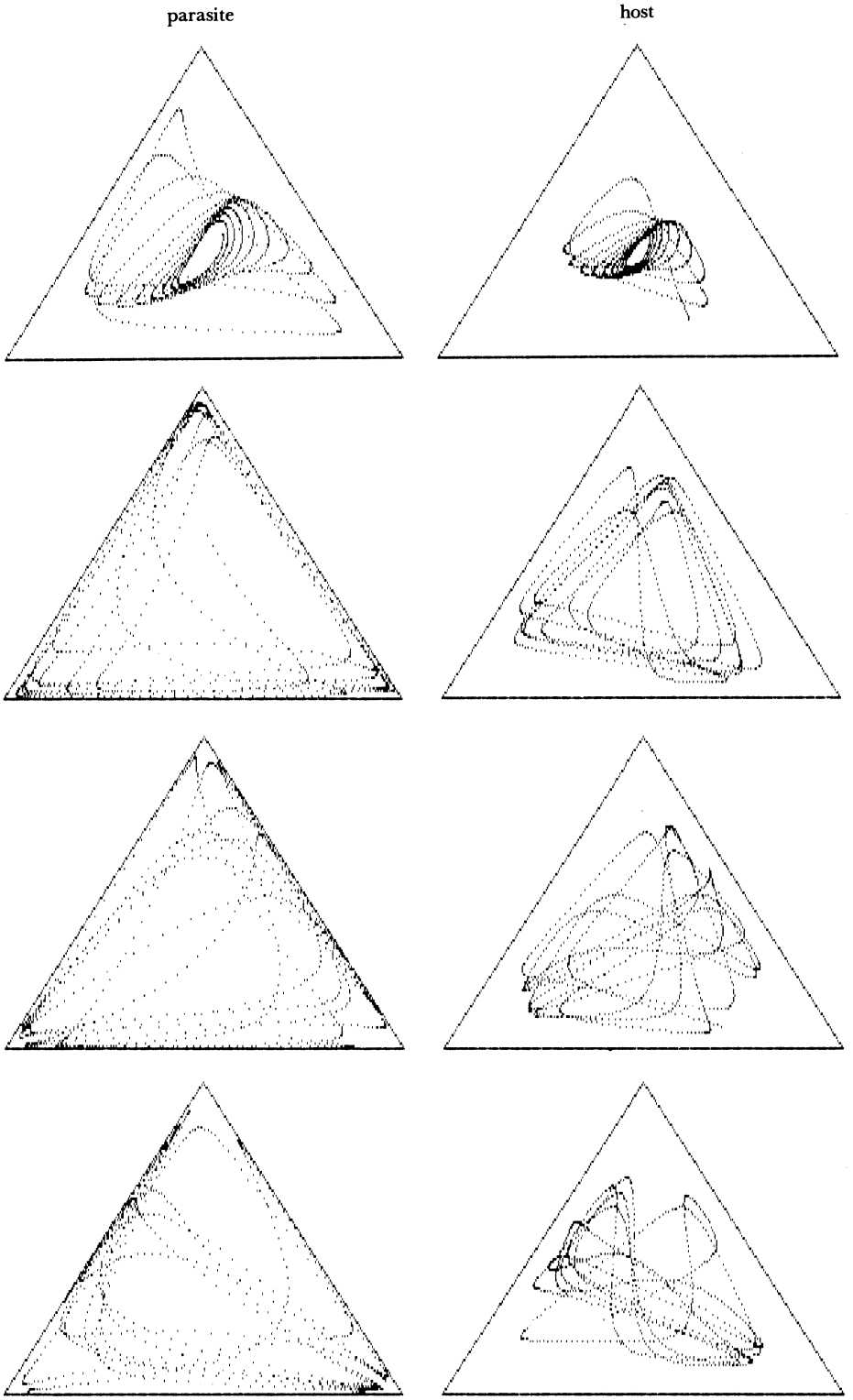

FIGURE 2. Dynamics of the one-locus model with $n = 3$. With three or more alleles, phase diagrams of the kind shown in figure 1 give only partial representations of the state of the population. Where $n = 3$, trilineal diagrams can be used to show complete but separate gene-frequency trajectories for each species; the frequency of an allele is represented by its distance perpendicular to one of the faces of an equilateral triangle. Here the upper pair of diagrams illustrate the first 1000 generations of a run that begins at a point near the interior fixed point (all alleles at a frequency of $\frac{1}{3}$). The second pair of diagrams show the next 1000 generations of the same run, and so on for a total of 4000 generations. To give a feeling for the speed of movement, gene frequencies are represented as individual points plotted every generation. As in figure 1, the selection parameters are $s = 0.1$ and $t = 0.3$, but the mutation rate is an order of magnitude smaller than in figure 1*b* ($m = 0.0003$). Although the parasite population comes to spend much of its time near the boundaries, it continues to pass regularly through the interior of its gene-frequency space, and it continues to keep the host population away from the boundaries of its gene-frequency space. Several different orbital 'motifs' or modes of oscillation periodically reappear. One of these motifs can be seen in two different orientations (qualitative phase relations among genotypes) in the third and fourth pairs of diagrams (main axes perpendicular to the upper right-hand faces of the diagrams, in the third pair, and perpendicular to the upper left-hand faces in the fourth). No motif ever seems to be repeated in exactly the same way, at these parameter values, and there are continual shifts among the different motifs, and among the three different orientations.

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can arise in two-allele models where the mode of interaction between hosts and parasites is more complicated than the simple 'mass action' of the present model (see, for example, Auslander *et al.* 1978; May & Anderson 1983*b*), but the present results imply that complex behaviour should in general become more likely, the more degrees of freedom there are in the genetic systems of host and parasite. Similar conclusions emerge from studies of multi-species competition models (see, for example, Gilpin 1975; May & Leonard 1975).

Two alleles at each of two loci

Recombination changes the frequencies of genotypes in a way that is, in some respects, analogous to mutation. Given that mutation is one force (among others) that tends to stabilize the interior equilibrium in simple models of host–parasite co-evolution, it seems natural to ask whether recombination might have a similar effect. In the third and final model to be considered here, four host genotypes are determined by two loci (A and B), each with two alleles (A_1 and A_2; B_1 and B_2). The frequency of allele A_1 is h_1, the frequency of B_1 is h_2, and the frequencies of the four host genotypes are:

Genotype	Frequency
$A_1 B_1$	$H_1 = h_1 h_2 + D,$
$A_1 B_2$	$H_2 = h_1(1-h_2) - D,$
$A_2 B_1$	$H_3 = (1-h_1) h_2 - D,$
$A_2 B_2$	$H_4 = (1-h_1)(1-h_2) + D.$

(13)

Here D is the coefficient of linkage disequilibrium (also called the coefficient of gametic phase disequilibrium), which measures the degree of non-random association between alleles at different loci. It can be defined in terms of the genotype frequencies as:

$$D = H_1 H_4 - H_2 H_3. \tag{14}$$

(If the numeric value '1' is associated with alleles A_1 and B_1, and '0' is associated with A_2 and B_2, then D is equal to the covariance of these allelic values within genotypes.)

As in the previous models, the parasite species has a single locus. Here its four genotypes (C_1 through C_4, at frequencies P_1 through P_4) are complementary to the four host genotypes, in the order implied by the use of subscripts in the list of genotype frequencies above (13). Thus if r is set equal to zero, this model reduces to the previous one-locus model with $n = 4$.

If r is greater than zero, then mating and recombination alter the genotype frequencies according to the relations

$$H'_1 = H_1 - rD, \quad H'_2 = H_2 + rD, \quad H'_3 = H_3 + rD, \quad H'_4 = H_4 - rD. \tag{15}$$

Thus when D is not equal to zero, recombination will reduce its magnitude in the offspring (before selection) to a fraction $(1-r)$ of its value in the parents (after selection). The largest meaningful value of r is 0.5, which corresponds to free recombination (i.e. loci on different chromosomes).

In finite populations, linkage disequilibrium is created by sampling error, even in the absence of selection, and even between loci on different chromosomes (Hill & Robertson 1968). But the populations being modelled here are effectively infinite in size, so any linkage disequilibrium that arises must be created by selection.

Owing to the interconversion of host genotypes by recombination, the linearized recurrence equations no longer take a simple block-diagonal form:

$$\begin{bmatrix} 1 & -b & a & -ab & a & -ab \\ c & d & & & & \\ & & 1-a & b(a-1) & -a & ab \\ & & c & d & & \cdot \\ & & -a & ab & 1-a & b(a-1) \\ & & & & c & d \end{bmatrix} \cdot \begin{bmatrix} x_1 \\ y_1 \\ x_2 \\ y_2 \\ x_3 \\ y_3 \end{bmatrix} = \begin{bmatrix} x_1' \\ y_1' \\ x_2' \\ y_2' \\ x_3' \\ y_3' \end{bmatrix}. \tag{16}$$

Here $a = r/2$, $b = s/(4-s)$, $c = t(1-4m)/(4-3t)$, $d = 1-4m/3$, and the x_i, y_i, x_i', and y_i' are the deviations of the host and parasite genotype frequencies from their interior equilibrium values of 1/4. When $r = 0$, then $a = 0$, and the matrix reduces to block-diagonal form. But even when $r > 0$, the characteristic equation still factors into a product of three quadratics:

$$[(\lambda-1)(\lambda-d)+bc]^2[\lambda^2+\lambda(r-d-1)+(1-r)(bc+d)] = 0 \tag{17}$$

Two of the factors are identical to those for the equivalent one-locus model with $n = 4$; these two are functions of s, t and m only, not of r. The third factor is a function of all four parameters, and yields a distinct pair of eigenvalues whenever r is different from zero. Thus two identical pairs of eigenvalues are not associated with recombination, and one distinct pair is associated with recombination.

The stability of the interior fixed point is determined by the modulus of the largest eigenvalue(s). It follows that recombination will not stablize an interior equilibrium that would be unstable in the absence of recombination, because only when $r > 0$ does the pair of eigenvalues associated with recombination become different from the two pairs that are unaffected by recombination; if the latter had modulus greater than unity for $r = 0$, then they would still have modulus greater than unity for $r > 0$, and so the fixed point would remain unstable. In principle, recombination could destabilize an otherwise stable equilibrium (by giving rise to eigenvalues of modulus greater than unity), but it can be shown that for meaningful parameter values, the modulus of the eigenvalues associated with recombination is always less than or equal to that of the eigenvalues not associated with recombination. Thus at least under the simple assumptions of this model, recombination has no effect on the stability of the interior equilibrium. In this respect it appears not to play a role analogous to that of mutation, which does affect the stability of the equilibrium.

None the less, for parameter values giving an unstable interior equilibrium (and hence persistent cycling), recombination has very important quantitative and qualitative effects on the actual dynamics of gene-frequency change. These are illustrated in figures 3–5 for $s = 0.1$, $t = 0.3$, and a range of values of m and r. An enormous, almost bewildering variety of dynamical patterns is uncovered by systematically varying these four parameters. This variety is only partly revealed by the limited number of examples illustrated here, but some interesting and possibly general patterns do seem to emerge from these numerical experiments.

The most surprising result is that intermediate rates of recombination tend to give the smallest, smoothest, most regular orbits, whereas very low and very high rates of recombination tend to give more complicated, irregular orbits in which there is greater fluctuation of gene frequencies, genotype frequencies, and linkage disequilibria.

In particular, at sufficiently high mutation rates there is a critical value of r above which the

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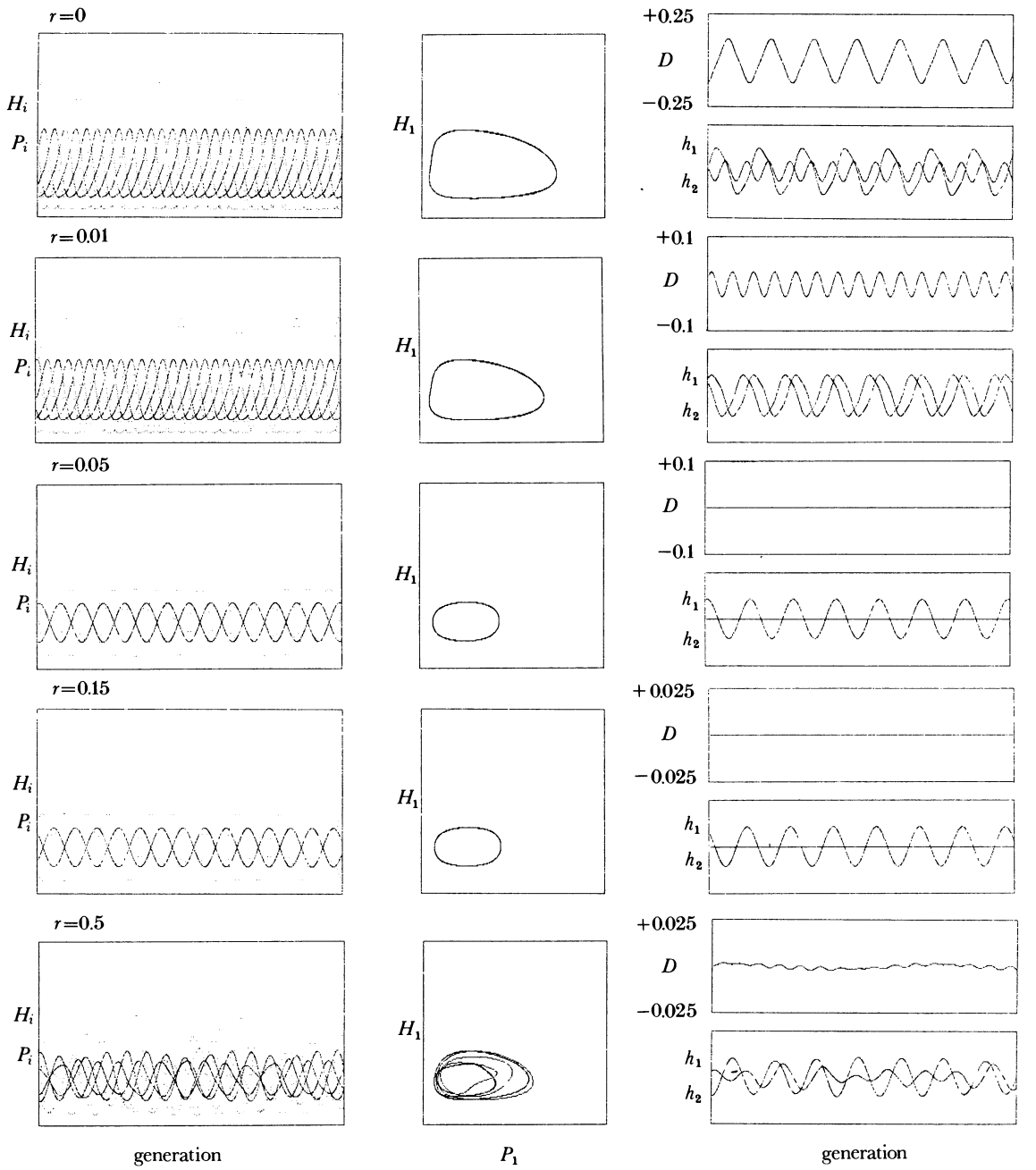

FIGURE 3. Dynamics of the two-locus model for $m = 10^{-3}$. Each row of panels illustrates the behaviour of the model at a different rate of recombination. Here, and in figures 4 and 5, the selection parameters are as in figure 1. In each row, the left-hand panel shows the genotype frequencies as functions of time, for generations 50000 to 51000 (i.e. for 1000 generations, long after the initial transients have died out). The four host genotypes are plotted every generation, so they appear as dark lines. The parasite genotypes are plotted every fifth generation, so they appear as a faint cloud of points that indicates the envelope within which the parasite genotype frequencies oscillate. The central panel is a phase diagram of the kind shown in figure 1; here the (unstable) fixed point is at genotype frequencies of $\frac{1}{4}$. The upper panel on the right shows the coefficient of linkage disequilibrium, D, as a function of time. Note that the scaling of its vertical axis differs for different rates of recombination. The lower panel on the right shows the gene frequencies at the A and B loci in the host, again as a function of time. All gene- and genotype-frequency axes represent the full range of possible frequencies, from 0 to 1, and all four panels in each group represent the same 1000 generations, taken from the same run. The first two cases ($r = 0$ and $r = 0.01$) are very similar at the genotype-frequency level, but they have qualitatively different patterns of linkage disequilibria and gene-frequency oscillation. The third and fourth cases ($r = 0.05$ and $r = 0.15$) are identical, as discussed in the text.

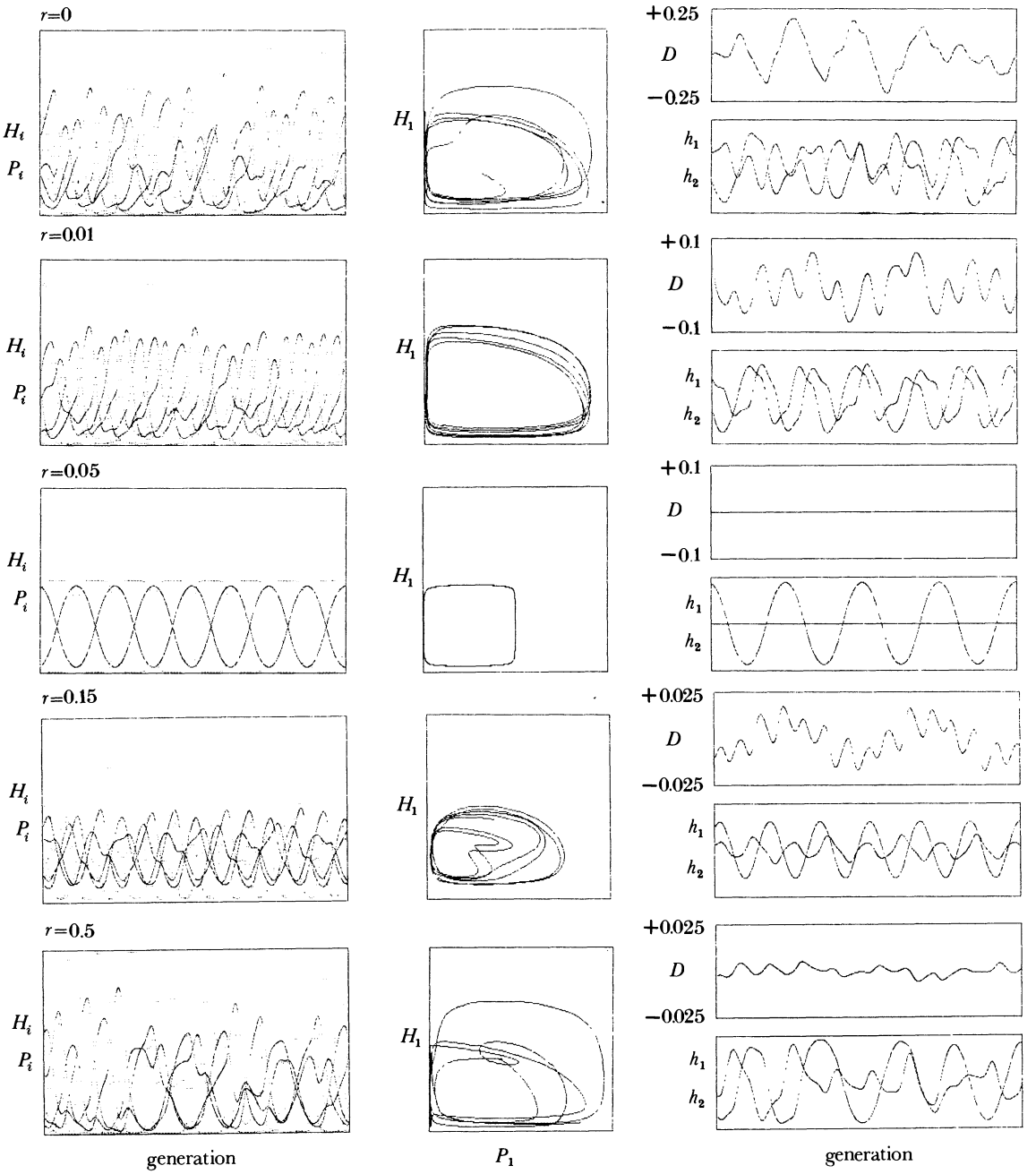

FIGURE 4. Dynamics of the two-locus model with $m = 10^{-5}$. As the mutation rate is lowered, orbits tend to become more complex, and the '$D = 0$' cycle becomes restricted to a narrower range of recombination rates.

host population suddenly switches into a very symmetrical pattern in which pairs of genotypes cycle in unison. At one locus (A or B, depending on initial conditions) there is no gene-frequency change, whereas at the other there is a cycle of moderate amplitude, and there is no linkage disequilibrium (see figure 3, for $r = 0.05$ and $r = 0.15$). This pattern persists unchanged through a range of increasing values of r, and then gradually breaks up into a more complex pattern involving gene-frequency changes at both loci, irregular genotype-frequency changes, and alternating linkage disequilibria.

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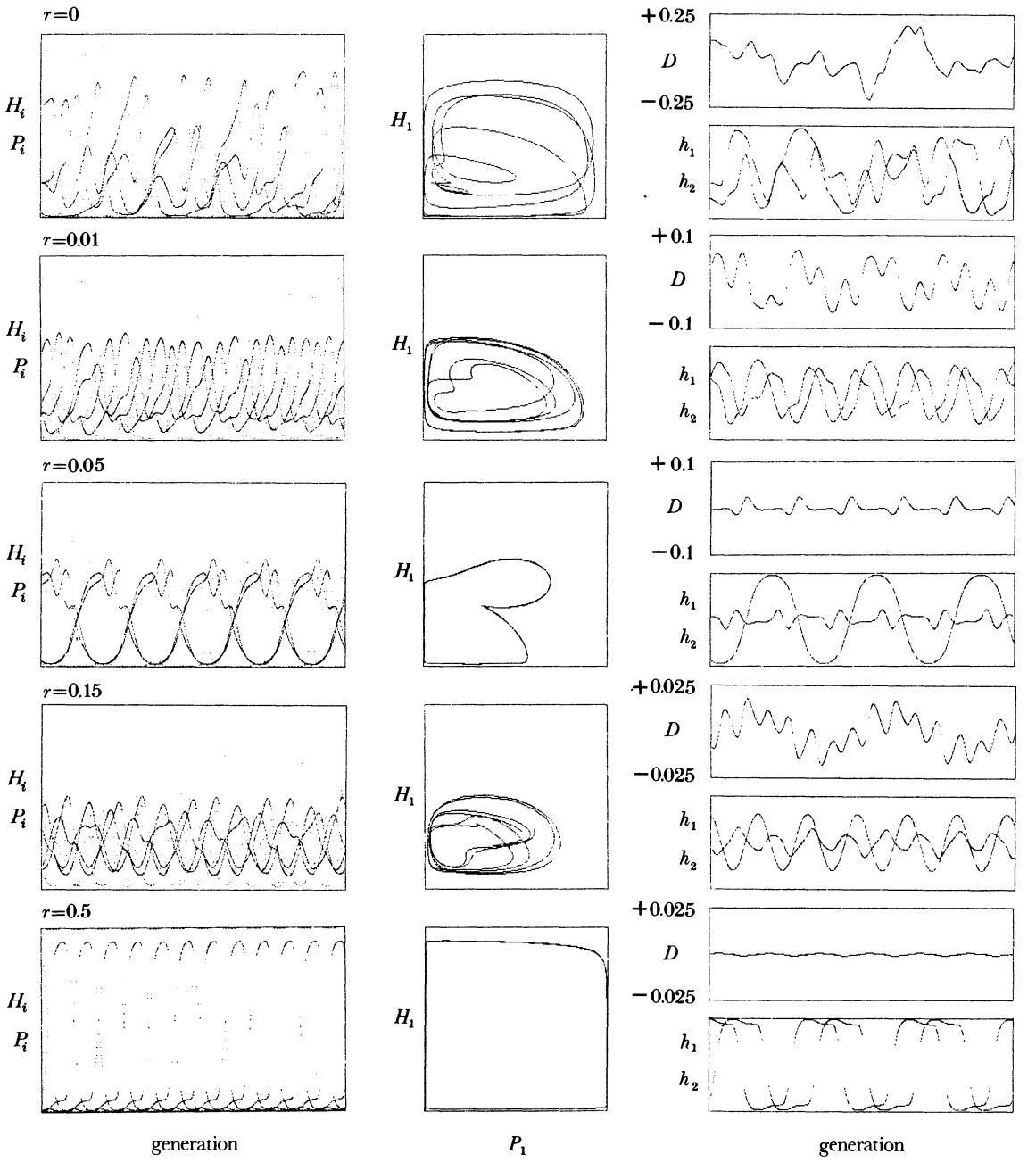

FIGURE 5. Dynamics of the two-locus model with $m = 10^{-7}$. At these selection parameters ($s = 0.1$, $t = 0.3$) and mutation rate, the '$D = 0$' cycle does not appear at any rate of recombination, but a 'folded' version of the cycle does appear in the vicinity of $r = 0.05$. The genetic variation of the host is protected best near $r = 0.15$, where the orbit is fairly complex. A simple orbit appears under free recombination ($r = 0.5$; compare with figures 3 and 4), but it involves the most extreme gene- and genotype-frequency excursions seen in any of the cases illustrated.

The '$D = 0$' cycle is dynamically possible at any recombination rate, including zero (because there is never any linkage disequilibrium). But apparently it is dynamically stable only over a limited but sometimes fairly wide range of intermediate rates of recombination, depending on the values of the other parameters.

As the mutation rate is lowered, gene and genotype frequencies tend to undergo larger and

larger excursions toward the boundaries. But even at the very low mutation rate of 10^{-7} (figure 5), intermediate rates of recombination can be very effective in keeping the gene frequencies of the host well away from fixation. (Compare $r = 0.15$ to $r = 0.05$ and $r = 0.5$.)

Discussion

The models described here are intended to focus attention on the possible dynamical consequences of variations in the genetic systems controlling phenotypes through which hosts and parasites interact. The specific biological assumptions embodied in the models are extremely simple, and thus fairly unrealistic. But to the extent that antagonistic complementarity is a feature of real host–parasite relations, the models seem to imply that the dynamics of host–parasite co-evolution may depend in significant ways on elementary parameters such as the number of available allelic states, and rates of recombination between functionally related loci.

Like most recent genetic models of host–parasite co-evolution, the ones discussed here are motivated by, and based loosely on, the classical gene-for-gene model first applied by Flor (1956) to the interaction of domesticated flax and some of its fungal pathogens, and extended since then to a number of other (mainly agricultural) plant–pathogen systems. Barrett (1983, 1985) argues that the genetics of these systems are usually much more complex than the classical model would suggest, and that in addition, the genetics of many domesticated systems may actually be simpler than those of their wild ancestors. The two-locus model described here makes only a small departure from the usual gene-for-gene formalism, yet its behaviour is in some respects qualitatively different from that of an equivalent one-locus gene-for-gene model (i.e. the same model with $r = 0$).

The two-locus model could profitably be extended in several directions. For example, the parasite could be given a similar two-locus genetic system, and the number of possible alleles at each locus could be made greater than two. It would also be of interest to know whether the dynamically stabilizing effects of intermediate recombination rates are seen in finite-population versions of these models, and in versions with explicit density dependence as well as the pure frequency dependence modelled here.

Many realistic complications could be added to the biologies of host and parasite. For example, host and parasite genotypes are likely to show varying levels of cross-reactivity, rather than the all-or-nothing pattern of interaction assumed here. In addition, no real host–parasite system is an isolated two-species island unto itself, as is also assumed here; parasites may share hosts, and hosts may share parasites. Hamilton (1986) has described a four-species model of population dynamics (two hosts, two parasites), but so far there seems to be almost no work on multi-species host–parasite models with explicit genetics in each of the species.

The random-encounter, mass-action assumption is far from realistic for most kinds of host–parasite systems. May & Anderson (1983*b*) modified some simple single-species models first studied by Hamilton (1980, 1982), by deriving the fitness functions directly from standard epidemiological models. Their results are generally similar to those obtained using Hamilton's simpler, less realistic fitness functions, but it is possible that the dynamics of fully co-evolutionary two-species (or multi-species) models will turn out to be very sensitive to the detailed mechanisms through which hosts encounter and interact with particular parasite genotypes.

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Charlesworth (1976), Hutson & Law (1981), Sasaki & Iwasa (1987), and Bell & Maynard Smith (1987) have shown that intermediate rates of recombination can evolve under regimes of fluctuating selection. These results seem to imply that intermediate rates would evolve in a generalized version of the present two-locus model, because selection fluctuates with periods and intensities that seem at least superficially consistent with the regimes that favoured intermediate rates of recombination in the earlier studies. But the patterns of selection that arise in the present model could differ in subtle but critical ways from ones that would actually favour intermediate values of r. Or it could turn out that although the evolutionarily stable values of r were greater than zero and less than one half, they were nonetheless very far from those that would be most effective in retaining genetic variation.

The models recently described by Bell & Maynard Smith (1987) are fully co-evolutionary. Both host and parasite have two haploid fitness loci and one locus controlling the rate of recombination. With respect to the fitness loci the models are similar in spirit to the two-locus model described here, except that the two patterns of interaction studied by Bell & Maynard Smith are somewhat more complicated than the simple all-or-nothing scheme of complementarity used in the models described here. Under one of these patterns of interaction ('quantitative'), Bell & Maynard Smith find that free recombination is favoured in the parasite, whereas zero recombination is favoured in the host. Under the other pattern ('gene-for-gene), the free-recombination allele increases to similar low frequencies in both the host and the parasite, implying that the evolutionary equilibrium would probably be fixation for alleles causing low rates of recombination. These results clearly demonstrate that different patterns of complementarity may have very different effects on the evolution of rates of recombination.

In summary, the models described here suggest that the dynamics of host–parasite co-evolution may become much more complex, but slower-moving, as the number of interacting genotypes in each species is increased. These effects of increased genotype number have straightforward intuitive explanations. More complicated modes of genotype-frequency change are made possible by an increased number of degrees of freedom in the genetic systems of host and parasite, and the variance of fitness among genotypes tends to be reduced, as the number of genotypes in each species is increased. Recombination in the host does not affect the stability of the interior fixed point, under the simple biological assumptions of these models, but intermediate rates of recombination may give rise to orbits that are simpler, smaller and more symmetrical than those produced by lower or higher rates of recombination, for ranges of the other parameters that lead to persistent cycling. There seems to be no intuitively obvious reason why intermediate rates of recombination should tend to simplify the dynamics away from equilibrium.

I thank W. D. Hamilton, F.R.S., and R. M. May, F.R.S., for helpful advice and discussion.

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Discussion

J. Antonovics (*Department of Botany, Duke University, U.S.A.*). From Dr Seger's simulations showing less extreme dynamics at intermediate recombination rates, would he predict that intermediate recombination rates would be favoured if a modifier gene affecting recombination rate were introduced into the population?

J. Seger. Yes, I think it is very likely that an intermediate rate of recombination would evolve in the host, if a full range of modifier alleles was available. This seems to be implied by the existing work on recombination modification in fluctuating environments, and especially by the very recent results of Bell & Maynard Smith (1987), who have studied a fully co-evolutionary three-locus model that is similar in many ways to this one. But it seems to be an

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open question whether a recombination modifier can be said to have increased in frequency because of its effect on the dynamics of gene and genotype frequency change. At least to some extent, the cause-and-effect relation clearly works the other way around, because an externally imposed fluctuating environment can favour intermediate rates of recombination. In host–parasite models, the pattern of environmental fluctuation arises from the interaction between the two species and therefore depends, in part, on the recombination rate, which evolves in response to the pattern of environmental fluctuation. This feedback between the recombination rate and the genotype-frequency fluctuations that favour its modification could hardly fail to have an effect on the evolutionary equilibrium, but I have no idea how strong the effect will turn out to be.

Sasaki & Iwasa (1987) have suggested that the evolutionarily stable recombination rate in a fluctuating environment will usually be the one that maximizes the population's long-term geometric mean fitness. The geometric mean fitness of the host is indeed maximized at intermediate rates of recombination, and this makes sense to the extent that intermediate recombination rates give rise to relatively restrained dynamics. But the fitness differences caused by varying the r of the host (and thus the dynamics of the system) are small compared with the fitness differences caused by the loss or addition of alleles. For example, the geometric mean fitness of the host varies by about 0.5% (as a function of r) for the parameter values shown in figure 4, with a global maximum near $r = 0.05$ and two or more local maxima at much higher values of r. But if an allele is lost from either the A or the B locus, so that the host has only two distinct genotypes, then its geometric mean fitness drops by more than 2.5%. This suggests that, in a finite population, the recombination rate might be more strongly selected for its effect on the maintenance of genic variation than for its effect on the dynamics as such, given any particular level of variation.

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