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SOME APPROACHES TO THE MODELLING OF COEVOLUTIONARY INTERACTIONS

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ABSTRACT

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The role of models in the understanding of coevolutionary interactions is explored, ranging from explicit genetic models to purely phenotypic ones. Special attention is devoted to gene-for-gene plant-pest resistance systems, the evolution of avirulence in host-parasite associations, and the evolution of aspect diversity in predator-prey communities.

Explicit genetic models are most appropriate to small ensembles of tightly interacting species in which the genetic basis of change is well understood. The gene-for-gene systems of cereal plants and their fungal pathogens are ideal in this regard. However, most classical models ignore ecological and epidemiological interactions, which are critical to the understanding of phenomena such as the evolution of reduced virulence in parasite-host associations and the stabilization of such associations at intermediate levels. Models which incorporate these elements are discussed in some detail, with special reference to extensions of the work of Levin and Pimentel (1981) on the interaction between the myxoma virus and the Australian rabbit (Oryctolagus cuniculus).

Diffuse coevolution, involving many species, requires yet a different perspective. The work of Levin and Segel (1982) on the evolution of aspect diversity in predator-prey communities is discussed, and the critical issues identified. Extensions to other systems are suggested.

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I. Introduction

Models of evolutionary and coevolutionary processes, just as models in so many branches of science, serve primarily to aid our understanding and to provide a framework within which to couch questions. As Jacob (1977) points out, the process of evolution is more the work of a tinkerer than that of a master craftsman. The influences of the historical record and stochastic events predominate. Hence, whereas explanation is an achievable goal, prediction is often impossible.

There are exceptions: the development of heavy metal tolerance and pesticide resistance are predictable responses to stresses, and even estimates of the time to develop resistance can sometimes be forecast with reasonable accuracy (B. Levin et al. 1982). But these relate to single factor influences. What makes evolutionary prediction so difficult is the coevolutionary context, including both interspecific and frequency-dependent intraspecific effects. Because of the complexity of interactions within ecosystems, the problem of predicting changes is a vexing one even on an ecological time scale. Prediction of evolutionary change is even more refractory. The difficulties are basic and inherent in the nature of large-scale nonlinear systems with complex linkages; their dynamic behavior is typically erratic and highly sensitive to slight parameter changes. Deviations in the behavior of initially similar systems may become magnified as effects are propagated through the network of system interactions and feedbacks; this makes detailed forecasting a virtually impossible chore. On the other hand, the retrospective approach has been a very profitable one in evolutionary theory, and has led to great advances in our understanding.

II. Population genetics and evolutionary theory

Much of the classical theory leading to the modern synthesis of population genetics and evolutionary theory emerged from beginnings in plant and animal breeding, in which selection regimes were generally single factor and were well understood because they were imposed by the breeder. Within the context of artificial selection, remarkable strides were made in bridging the gap between a phenotypic view of evolution and one based on genotypic proportions; but in the study of evolution in natural settings, the problems remain severe (Lewontin 1980). In fact, Mayr (1982; see also discussion in Lewin (1982)) argues that population geneticists present a reductionist view of evolutionary change which is an impediment to understanding.

Important among the contributors to the synthesis of the 1930's were three men--Sewall Wright, Ronald Fisher, and J. B. S. Haldane--who developed the mathematical theory and explored its ramifications. Among the major achievements of the theory were ways to relate population-level properties, such as changes in mean fitness, to events at the individual level. The search for macroscopic parameters and the description of their dynamics were and remain central problems in evolutionary theory. Fisher's Fundamental Theorem of Natural Selection and Wright's Adaptive Surface together tell the story of the population's gradual progress through inferior regimes of mean fitness until some pinnacle of fitness is achieved, albeit perhaps not the highest of pinnacles. This paradigm has undoubtedly been among the most powerful in evolutionary theory, and has contributed to the rise of optimization theory in evolutionary ecology.

But it is a misleading paradigm. The conclusion that populations evolve towards maximization of mean fitness is easily vitiated, and the worst culprit is frequency dependence (see Levin 1978). Indeed, there are other impediments--environmental change, linkage, epistasis, and density dependence. But provided the effects of these complications are not too severe, weakened versions of the Fundamental Theorem can be constructed. In theory that is also the case with frequency dependence; but, where

ecological interactions are involved, frequency-dependent effects must eventually become severe as populations reach the limits of available resources. By definition, a population in near steady state has mean fitness near 1, and evolution cannot improve on that over the long term. An evolving population necessarily is genetically heterogeneous, and one in which the frequencies of genotype are changing. As a consequence of this change, the environmental milieu also shifts. Thus, even in the intraspecific case, the population is coevolving with its environment. This leads to nonlinear feedbacks which confound the simplistic theory. Indeed, theoretical examples involving frequency dependence can be constructed in which mean fitness is minimized rather than maximized at equilibrium.

Theorists delight in the demonstration of such problems, for they show that the mathematical theory is not tautological. The paradox arises because, while Nature selects the most fit within a given environmental context, simultaneously that context changes (coevolves) as a consequence of selection. Gould (1977) points out, "Natural selection is a theory of local adaptation to changing environments. It proposes no perfecting principles, no guarantee of general improvement." Lewontin (1977) succinctly summarizes, "Adaptation, for Darwin, was a process of becoming rather than a state of final optimality."

III. The classical theory applied to interacting populations

Wright set forth a discrete-time framework (summarized in Wright 1955) for describing evolutionary change, one which has influenced the mathematical development ever since. This framework extends naturally to systems of interacting populations and to changing environments, including effects resulting from frequency and density dependence. Mode (1958) pioneered models of coevolving populations in considering the gene-for-gene resistance systems of cereal grasses and their associated pathogens. Subsequently, numerous others have studied similar genetic models (e.g. Jayakar 1970; Yu 1972; Levin and Udovic 1977; Levin 1978). Levin and Udovic (1977) summarize the

complexity of possible relationships when gene frequencies and population densities in only two species are considered (Fig. 1). ← Fig 1 here

In the case of m populations, denoted by $k = 1, \ldots, m$, and each with n_k alleles at a single locus, the equations of change are

$$(p_i^k)' = p_i^k \, w_{i\cdot}^k / \bar{w}^k \; ; \; (N^k)' = N^k \bar{w}^k \; , \qquad (1)$$
$$k = 1, \ldots, m \; ; \; i = 1, \ldots, n_k \, .$$

Here p_i^k and $(p_i^k)'$ denote respectively the frequencies of the i^{th} allele in the k^{th} population in two successive generations, $\bar{w}^k$ is the mean fitness of the k^{th} population, $w_{i\cdot}^k$ is the mean fitness associated with the i^{th} allele in the k^{th} population, and N^k and $(N^k)'$ are the successive population densities of the k^{th} population (Levin and Udovic 1977).

As already suggested, it is in general impossible to use models of this form (or multi-locus extensions) as the basis for prediction of the coevolutionary process. Yet they fulfill an indispensable role in providing a basis for thought, and as aids to the understanding of the influences of evolving populations upon one another (Levin and Udovic 1977, Levin 1978).

Literal interpretation of models of the form (1) is most nearly justified when they deal with interacting species which are tightly coevolved, for example highly specific mutualist or parasite-host systems (see Janzen 1980, Feeny 1982). The best such examples are for the cereal rust gene-for-gene systems already mentioned, in which coevolution is tight and the genetic basis well understood.

Cereal rusts damage their hosts by injecting hyphae to collect nutrients, and forming surface pustules which may contain tens of thousands of uredospores capable of dispersal for thousands of miles and subsequent germination on new host plants (Stakman and Christensen 1946, Hogg et al. 1969, Van der Plank 1975). Damage to the host plants may be severe.

Flor (1955, 1956) studied the genetics of the interaction between flax (Linum usitatissimum) and the rust Melampsoa lini, and his fundamental work has inspired theoretical investigations (e.g. Mode 1958, 1960, 1961; Person 1966; Leonard and Czochor 1978; Lewis 1978, 1981a, b; Fleming 1980, 1982) and empirical studies of other cereal-cereal rust associations.

Flor found that there were 27 genes for resistance (R genes) distributed as multiple alleles at five loci in flax. Only two of the loci are linked (with 26 per cent recombination) (Flor 1955, 1956). Resistance is inherited as a dominant character. Virulence in rust is controlled by a complementary system that identifies in a one-to-one relationship each gene in the host with one in the parasite. Virulence is recessive, and the genes for virulence are located at distinct loci which segregate independently. Because of the "gene-for-gene" duality, resistance will only be operative provided at least one gene for resistance is present in the host and the corresponding gene for avirulence is present in the parasite. That is, the (homozygous) virulent parasite can overcome the corresponding resistance in the host.

Such single gene-for-gene relationships have been found in a great many other parasite-host systems (Person 1966, Pimentel 1982), although their genericness as models for disease resistance has been sharply challenged (Gracen 1982). Their structure makes them the perfect subjects for coevolutionary modelling.

Because parasite generation time is much shorter than that in the host, the potential for parasites to evolve virulence to overcome single resistance factors is great. On the other hand, because the primary method of dealing with pathogenicity on cereals is the continual introduction of resistant varieties, the possibility exists for a highly oscillatory relationship between parasite and host. Such oscillations are common in U.S. agricultural cereal systems.

However, in the Middle East fertile crescent region, the comparable systems are relatively stable, free of epidemics despite favorable environmental conditions which are

paradises of opportunities for plant diseases (Browning 1974, Dinoor 1974). Numerous authors (e.g. Browning 1974, 1980; Pimentel 1982) argue convincingly that this disparity is a consequence of the genetic oversimplification of American agriculture, and that parasite outbreaks will be rare in systems where host populations have been allowed to evolve heterogeneously or where host individuals with differing resistance mechanisms are interplanted. Host interspersion creates a "flypaper" effect, in which resistant hosts trap individuals which have dispersed from nearby vulnerable plants; this concept has been used in the control of plant pathogens on wheat and oats (Jensen 1965, Browning and Frey 1969).

Because of the importance of stability in these systems, models which allow exploration of the conditions under which the parasite-host interactions will stabilize have received considerable study. However, in general these have been closely tied to the gene-for-gene hypothesis and have not considered epidemiological detail or geographical distribution, or aspects such as cross resistance among hosts or host diversity.

Mode (1958) considers a host-parasite model in which there are two resistance genes at a single locus in the host, and two corresponding virulence alleles at independent loci in the pathogen. As with many similar efforts which have built on Mode's approach, the model is formulated entirely in terms of the frequencies of different types within the population, and mass-action assumptions are substituted for a detailed consideration of the host-parasite relationship. Thus the probability that a particular type of host will come into contact with a particular type of pathogen is assumed to be proportional to the frequencies of those types in the population. In later work, Mode (1961) allows for the possibility that some pairings are more likely than others, but according to a fixed preference scheme. Such assumptions, which are more appropriate to predator-prey than to parasite-host interactions, ignore the fact that parasites are non-uniformly distributed over their hosts, especially in microparasitic infections in which the parasite multiplies on the host (Anderson and May 1979, 1982a). The significance of this will be developed later.

Mode (1958) utilizes a continuous time (weak selection) analogue of the equations of Wright (see Kimura 1958, Crow and Kimura 1965), and obtains by standard methods the conditions for stability of polymorphic equilibria. Of course, in the absence of costs to resistance or of constraints (e.g. due to segregation) on its evolution, a host population should evolve towards maximal resistance. Similarly, in the absence of costs and constraints, maximal parasitic virulence should evolve.

But there are costs, some metabolic and others ecological or epidemiological. For example, as resistance at a particular locus declines, parasites which are virulent at that locus are likely to be at a competitive disadvantage. This general feature has been incorporated into most models, including Mode's original work involving many strains of parasites which differ in their loci of virulence (Mode 1960, 1961). The prototypical model is that introduced by Mode (1960), in which both populations are effectively asexual. As Mode (1960, 1961) discovered, such models never lead to a stable equilibrium unless some form of intraspecific frequency dependence is assumed.

The classical formulation (ã la Mode) has been explored recently by numerous authors. Leonard (1977) develops a mathematical model which is a slight variant. But as is pointed out by Sedcole (1978), Leonard's model is still unable to support a stable equilibrium. Computer simulations by Leonard and Czochor (1978) suggest the existence of a stable equilibrium. But as Fleming (1980) discusses, this stabilization is due to a transformation of the cereal model from a parallel or simultaneous form to a serial or sequential one (which Leonard and Czochor (1980) argue is biologically more appropriate); this introduces an artificial stabilizing frequency dependence (Levin 1972, Lewis 1981a).

All of these models are based on the assumption that fitnesses within each species depend only on the characteristics of the other. Host fitnesses may depend on relative parasite levels, but not on the level of resistance in the host population; parasite fitnesses are determined entirely by the host. The continuous time description of the evolution of a single gene-for-gene system is then

$$\frac{dR}{dt} = R(1 - R)F_R(V)$$
$$\frac{dV}{dt} = V(1 - V)F_V(R) \qquad (2)$$

(Fleming 1982). Here $\underline{R}$ is the frequency of the resistant gene in the host, and $\underline{V}$ is the frequency of virulence in the parasite. $\underline{F_R}(\underline{V})$ and $\underline{F_V}(\underline{R})$ are functions of $\underline{V}$ and $\underline{R}$ respectively which are often taken to be linear, but that is not essential. The system (2) can never support a stable polymorphic equilibrium; any such equilibrium will be neutrally stable. The orbits of (2) are the solutions to

$$\frac{F_R(V)}{V(1 - V)}\,dV = \frac{F_V(R)}{R(1 - R)}\,dR \qquad (3)$$

and thus have the first integral

$$\int \frac{F_R(V)}{V(1 - V)}\,dV - \int \frac{F_V(R)}{R(1 - R)}\,dR = \text{constant}. \qquad (4)$$

As with the Lotka-Volterra equations, there exist a family of curves (defined by (4)), among which the system can be arbitrarily shifted by perturbations. There is no homeostatic response towards any particular path, no tendency to return to an initial curve after displacement. In general, under reasonable assumptions, these curves will be closed orbits about a neutrally stable equilibrium point (see Fleming 1982).

If diploid genetics are introduced, it is possible to stabilize such parasite-host interactions by some form of heterozygote non-intermediacy. Mode (1958), in a paper which curiously is not cited in Mode (1960, 1961), considers a diallelic-digenic model of a host-pathogen system. There are three host genotypes--$\underline{R}_1\underline{R}_1$, $\underline{R}_1\underline{R}_2$, $\underline{R}_2\underline{R}_2$--where $\underline{R}_1$ and $\underline{R}_2$ are distinct alleles for resistance. Pathogenic virulence with respect to $\underline{R}_1$ and $\underline{R}_2$ is assumed to be controlled at a pair of unlinked loci, although Mode discusses briefly the possible effects of linkage. Mode finds that a stable equilibrium, polymorphic at every

locus, can be maintained in this model provided a number of conditions apply, the most critical of which is that a parasite which is heterozygous at a particular locus, when associated with a homozygous host with the corresponding resistance, is at a competitive disadvantage relative to the avirulent homozygote. This assumption means that there is a cost associated with carrying a single recessive gene for virulence. It is further assumed that, on a host homozygous for a given type of resistance, a parasite homozygous for virulence at both loci is at a disadvantage relative to an individual carrying only the necessary virulence. No data are presented to support these assumptions, and in fact they seem contrary to the evidence (Sidhu 1975). The stable equilibrium in Mode's model involves marginal underdominance in the parasite, and marginal overdominance (cf. Wallace 1968) in the host.

Fleming (1982) considers a model describing the interaction between an asexual host and an outcrossing parasite, in which the dominance of avirulence is incomplete. He shows that a stable polymorphic equilibrium is possible if the penetration of dominance is greater on susceptible than on resistant hosts. Fleming points out that the resultant stable equilibrium also requires marginal overdominance for the host.

Other attempts to incorporate diploid genetics have treated the parasite as asexual, but the host as a diploid self-fertilizing form. Lewis (1981a, b) develops the general framework, built on the structure and notation (1) developed by Wright (1955; see Levin and Udovic 1977, Levin 1978). Related mathematical studies may be found in Jayakar (1970), Levin (1972), Yu (1972), and Clarke (1976).

Following Lewis' treatment, consider the interaction between a panmictic diallelic diploid host and a diallelic haploid pathogen. Let $\underline{A}$, $\underline{a}$ be the host alleles, with frequencies $\underline{p}$, $1 - \underline{p}$; and let $\underline{B}$, $\underline{b}$ be the pathogen alleles, with frequencies $\underline{q}$, $1 - \underline{q}$. In the simplest (symmetric) case, the mean fitnesses of the two pathogen types are given by

$$v_B = p^2\alpha + 2p(1-p)\beta + (1-p)^2\gamma \qquad (5)$$

and

$$v_b = p^2\gamma + 2p(1-p)\beta + (1-p)^2\alpha \ , \qquad (6)$$

in which α, β, and γ are the fitnesses of the pathogens respectively on the host genotypes $\underline{AA}$, $\underline{Aa}$, $\underline{aa}$.

Correspondingly, the host fitnesses in the presence of a given pathogenic infection are taken to be the complements of the associated pathogenic virulences; thus, for example, $1 - \alpha$ is the fitness of $\underline{AA}$ when associated with pathogen $\underline{B}$. $\underline{x}$ is the probability that a given host will be attacked, and uninfected hosts are equally fit. The overall fitnesses of the three host genotypes are then given by

$$\begin{aligned} w_{AA} &= 1 - x + x[q(1-\alpha) + (1-q)(1-\gamma)] = 1 - x[q\alpha + (1-q)\gamma] \\ w_{Aa} &= 1 - x + x[q(1-\beta) + (1-q)(1-\beta)] = 1 - x[\beta] \\ w_{aa} &= 1 - x + x[q(1-\gamma) + (1-q)(1-\alpha)] = 1 - x[q\gamma + (1-q)\alpha] \ . \end{aligned} \qquad (7)$$

This model generalizes those of Jayakar (1970) and Yu (1972). However, it is not consistent with those gene-for-gene systems in which resistance is dominant.

Following standard procedure (see Levin 1978) one obtains the equations of change of gene frequency. Letting primed variables denote frequencies in a successor generation, we obtain

$$p' = p\frac{pw_{AA} + (1-p)w_{Aa}}{p(pw_{AA} + (1-p)w_{Aa}) + (1-p)(pw_{Aa} + (1-p)w_{aa})} = p\frac{w_{A\cdot}}{pw_{A\cdot} + (1-p)w_{a\cdot}} \qquad (8)$$

$$q' = q\frac{v_{B\cdot}}{qv_{B\cdot} + (1-q)v_{b\cdot}} \qquad (9)$$

(8) - (9) is a special case of (1), with densities ignored.

As Lewis shows, and as symmetry dictates, the polymorphic equilibrium of this system occurs at $\underline{p} = \underline{q} = 0.5$. Stability is analyzed by standard linearization methods, and

shown to be tied to the necessary and sufficient condition

$$\beta^2 < \alpha\gamma - \frac{(\alpha - \gamma)^2}{4} = \left(\frac{\alpha + \gamma}{2}\right)^2 - \frac{(\alpha - \gamma)^2}{2} . \qquad (10)$$

Lewis (1981a) acknowledges the validity of Levin and Udovic's (1977) conclusion that in such coevolutionary situations host heterozygote superiority or inferiority is a necessary condition for a polymorphic equilibrium, but argues that it is not clearly interpretable on the individual level. In fact, this claim is a bit misleading. The symmetry of the problem assures that the heterozygote cannot be strictly intermediate at equilibrium; thus the condition is a trivial one. However, something stronger can be said: once again, marginal overdominance is essential. The condition for host heterozygote advantage at equilibrium is

$$\beta < (\alpha + \gamma)/2 , \qquad (11)$$

which clearly is a necessary condition for (10) to be satisfied, and hence a necessary condition for stability. Condition (11) is easily interpretable at the individual level. Note that the stricter condition $\beta < \min(\alpha , \gamma)$, which states that the heterozygote is most fit at every pathogen frequency, is neither necessary nor sufficient for the existence of a stable equilibrium.

Lewis notes further that if α and γ are too different, no stable equilibrium is possible, citing the case when one of these vanishes. In fact, it may be easily seen from (10) that the relevant necessary condition is that the right-hand side be positive, which will be the case provided the ratio of the larger to the smaller of α and γ not exceed $3 + 2\sqrt{2}$. If this condition is satisfied, then there are β's satisfying (10); otherwise, there are not. If the ratio is less than 5, $\beta < \min(\alpha , \gamma)$ is a sufficient condition for stability; but in the thin region (of α/γ or γ/α) between 5 and $3 + 2\sqrt{2} \sim 5.8$, heterozygote

superiority at all levels still fails to insure the existence of a stable polymorphic equilibrium.

Heterozygote non-intermediacy is in general a necessary condition for the existence of a polymorphic equilibrium in such systems (Levin and Udovic 1977), although there are degenerate examples in which this condition is not strictly satisfied. For example, in the extreme case that the heterozygote fitness is always the geometric mean of the two homozygote fitnesses, the system (6) - (7) reduces to a doubly haploid model of the type discussed earlier (Nagylaki 1977, Lewis 1981b), and creates a rather special situation whereby polymorphic equilibria are feasible with all three fitnesses equal. But as we saw earlier, such models are not inherently stable in character.

In the absence of stabilizing forces, host-parasite systems will have a tendency to oscillate; consequently, one may observe sustained oscillations of limit-cycle or more complicated type, or system collapse. The existence of "invariant circles"--discrete analogues of limit cycles--may be studied by way of appropriate versions of the Hopf bifurcation theorem (Guckenheimer et al. 1977) for β close to the threshold suggested by (10). For β larger, it is likely that not only periodic, but aperiodic and chaotic patterns will emerge (see also Anderson and May 1982a). These may be asymptotically stable, unlike those in the system (2). Study of sustained nonlinear behavior of the solutions to host-parasite equations in the unstable case has been largely restricted to numerical simulation (Yu 1972, Leonard and Czochor 1978, Fleming 1980, Lewis 1981a).

More general models of host-parasite interactions will lead to stabilization of polymorphic equilibria without heterozygote overdominance. These consider both intra-specific and interspecific frequency and density dependence. There are a wide variety of possible influences on stability, represented by the many feedback loops shown in Figure 1. Following Wright (1955), Levin and Udovic (1977) derive the general set of equations (12) , which are a special case of (1):

$$p_i' = p_i w_{i\cdot}/\bar{w}\ ,\quad q_j' = q_j v_{j\cdot}/\bar{v}\ ,$$
$$N' = N\bar{w}\ ,\quad M' = M\bar{v}\ . \qquad (12)$$

Here, $\underline{p}_i$, $\underline{q}_j$, $\underline{N}$, $\underline{M}$ denote respectively the gene frequencies and population densities in the two populations. The subscripts distinguish alleles, and hence any number may be treated. The system (8) - (9) is easily seen to be a special case of (12).

System (12) allows consideration of ecological interactions that are more general than host-parasite, and Levin and Udovic (1977) explore the interplay between the "genetical" conditions for stability and the "ecological" ones. Special cases include Levin's (1972) study of stability in host-parasite or prey-predator genetic feedback systems, in which host (prey) genetics interact with parasite (predator) densities, and Gillespie's complementary work (Gillespie 1975), in which intraspecific frequency dependence in host evolution emerges from consideration of parasite numbers. These are discussed in more detail in the next section, as are more general epidemiological models.

Other mechanisms may also serve to stabilize host-parasite systems: environmental patchiness (Karlin and McGregor 1972, Clarke 1976), multi-locus effects, inbreeding (see for example Mode 1961), and alternative hosts (Lewis 1981b, Fleming 1982). Some aspects of these also relate to epidemiology, but will not be treated further in this paper.

IV. Host-parasite models incorporating epidemiological considerations.

Anderson and May (1982a) provide a useful categorization of host-parasite models. These include the "explicitly genetic" models of the preceding section; ones which posit some frequency dependence in host genetics; those which "let conventional epidemiological assumptions . . . dictate the form of the frequency dependent fitnesses"; and those which focus more on the epidemiology and suppress the genetic details. These represent a spectrum, not a set of discrete choices, and one must let the problem at hand dictate the particular form.

It is nearly dogma in the parasitological literature that host-parasite systems will evolve towards commensalism (Mode 1958, Burnet and White 1972, Hoeprich 1977, Alexander 1981, Anderson and May 1982b, B. Levin et al. 1982). As Anderson and May (1982a) summarize, most textbooks simply take as obvious that parasitic species which destroy their hosts cannot long survive, and will be replaced in time by less and less virulent strains in inexorable progress towards commensalism. But the situation is much more complicated.

Evolution in parasite populations represents an interplay between conflicting factors: within an individual host, the race is to the swift and evolution will favor those with the highest rates of reproduction, which is likely to mean those with higher virulence. But the parasite population is a shifting mosaic of demes associated with individual hosts, and the capacity for profligate growth dooms one's host to a shorter life expectancy and reduces the contribution to the larger (mega-) population. Depending on the balance between these factors, some evolution towards attenuation might be expected among parasites, but this attenuation may be checked far short of commensalism (Levin and Pimentel 1981, Anderson and May 1982a, Bremermann and Pickering 1982). These points are most clearly manifest for monoclonal infections, but remain valid even when secondary infections and polyclonality are possible (Levin and Pimentel 1981, Bremermann and Pickering 1982). However, theoretical arguments suggest that in polyclonal situations, where the genetic relatedness of individuals associated with a particular host is lessened, parasite evolution towards attenuation should be less effective than if monoclonality obtained. This further suggests that there will be less parasitic evolution towards avirulence in macroparasitic organisms such as helminths, and increased pressure for the development of resistance among their hosts.

One might expect evolutionary pressures in the host to present a less equivocal picture (Person 1959). In general, there will be no advantage to the host to be susceptible to the ravages of the parasite, and there should be a continual, if slow, evolution of

increased resistance. However, as we infer from examples in which the removal of selective pressures results in a loss of resistance, there may be costs associated with the resistance. As suggested earlier, when such costs exist there will be selection against resistance at low disease levels. Thus, as in the case of parasitic virulence, one should expect protected polymorphisms for intermediate levels of resistance. Of course, there will also be cases where resistance becomes fixed and the parasite is virtually eliminated. As long as polymorphism in both species exists, the inherent oscillatory character of the host-parasite system encourages occasional localized outbreaks and even system-wide fluctuations. As already mentioned, such oscillations may be stable and sustained, unlike those observed for the system (2).

Motivated by Haldane's insights (Haldane 1948), Pimentel (1961, 1968) and Levin (1972) explicitly incorporate cost into a model of the interaction between host (prey) genetics and parasite (predator) density. As discussed in the previous section, Levin (1972) shows that a balanced polymorphism for resistance may result, at levels which will regulate parasite density; but this stabilization requires marginal overdominance. On the other hand, by incorporating epidemiological considerations, Gillespie (1975) was able to obtain stabilization at intermediate levels of resistance in a haploid host, or in a diploid host in which resistance is dominant (as in the gene-for-gene systems) or recessive. Gillespie's work has been extended by Kemper (1982), Longini (1982), and Anderson and May (1982c, d) to include wider classes of disease (see review in Anderson and May 1982a).

Parasitic evolution towards attenuation is of a different sort, and relies on interdemic selection. Because of the integral nature of the association between host and parasite, and the fact that in monoclonal infections the host is in essence a parasite deme, these systems represent the best of all possible candidates for interdemic selection to be important. This is, of course, the basis for the conventional wisdom in parasitology that parasite-host systems should evolve reduced virulence. But the fact that there should be a tendency towards some attenuation does not imply that the end result will be

commensalism. Available data (e.g. Fenner and Myers 1978) and theory (Levin and Pimentel 1981, Anderson and May 1982a, Bremermann and Pickering 1982) suggest that stable intermediate levels of resistance are to be expected (see review in B. Levin et al. 1982). For example, the smallpox virus seems to have achieved virulence stasis long ago, and has not undergone substantial change in a millenium and a half (Fenner, pers. comm.).

It is has often been pointed out (Lewontin 1970, Levin and Pimentel 1981, B. Levin et al. 1982) that landmark studies by Fenner and his colleagues (Fenner and Marshall 1957, Fenner 1965, Fenner and Ratcliffe 1965, Fenner and Myers 1978; see also Saunders 1980) of the interaction between the European rabbit (Oryctolagus cuniculus) introduced into Australia and the myxoma virus introduced to control it present perhaps the best documented evidence for the evolution of reduced virulence in host-parasite systems. Similar studies on myxomatosis in Oryctolagus in Britain and France are reported in Ross (1982), and discussed by Anderson and May (1982a). ← Fig 2 here

In the Australian system, Oryctolagus was at outbreak levels by 1880. The myxoma virus, which lives in the South American tropical rabbit Sylvilagus brasiliensis without producing any generalized disease, was introduced in 1950 as a control mechanism, and Oryctolagus showed a 99.8% case mortality. This led to a near elimination of the rabbit population (Fig. 2). Evolution in the virus towards reduced virulence was rapid, and was subsequently reinforced by evolution of resistance in the rabbit. This led to an overall reduction in observed mortality (Fig. 3). Whereas the viral population in 1950-51 was composed almost totally of grade I virulence individuals, by 1963-64 grades I and II were virtually eliminated and the average individual was about a IIIB (see Table 1). Similar trends were observed in Great Britain and France (Anderson and May 1982a, Ross 1982) after introduction of myxoma in 1952. It is not yet known whether these represent stable equilibria or whether there will be a continuing trend towards avirulence. ← Fig 3, Table 1 here

Inspired by Fenner's work, Levin and Pimentel (1981) analyze evolution of avirulence in parasites by means of a model based on the system described in Figure 4. The

fundamental nature of the model is that hosts are divided into a number of categories based on which parasites they harbor; only two strains are considered, but in principle any number could be. The model ignores parasite densities on a host, and considers only whether the host has been infected with a particular strain. This is an obvious oversimplification, but does not affect the main conclusions. Nonetheless, given the relation of mortality to parasite load (Anderson and May 1981) and the influence on transmission characteristics, it would be of interest to examine the effects of parasite densities.

Based on Figure 4, one obtains immediately the system

$$\begin{aligned}
\frac{dS}{dt} &= r(S + I_1 + I_2) - bS - \beta_1 S I_1 - \beta_2 S I_2 \\
\frac{dI_1}{dt} &= \beta_1 S I_1 - (b + \alpha_1) I_1 + (\sigma_1 \beta_1 - \sigma_2 \beta_2) I_1 I_2 \\
\frac{dI_2}{dt} &= \beta_2 S I_2 - (b + \alpha_2) I_2 + (\sigma_2 \beta_2 - \sigma_1 \beta_1) I_1 I_2
\end{aligned} \tag{13}$$

in which $\underline{S}$ is the number of susceptible rabbits, $\underline{I}_1$ is the number of rabbits infected with parasite 1, and $\underline{I}_2$ is the number of rabbits infected with parasite 2. All hosts have the same birth rate $\underline{r}$, and newborns are uninfected. $\underline{b}$ is the death rate of susceptible individuals, and $\underline{b} + \alpha_{\underline{i}}$ is the death rate of those housing parasite $\underline{i}$. $\beta_{\underline{i}}$ is the transmissibility of strain $\underline{i}$, and $\sigma_{\underline{i}}$ measures the susceptibility to invasion by strain $\underline{i}$ of individuals infected with the competitor strain. Here invasion implies competitive displacement of the resident parasite. For simplicity, the mixed stage $\underline{I}_3$ is ignored. This assumption will be relaxed later (system (20)), but consideration of the intermediate stage does not affect qualitatively the results. I shall also later relax the assumptions that the birth rates for all hosts are identical, and will allow for recovery from infection.

Parasite 2 is the virulent strain, and hence $\alpha_2 > \alpha_1$. In Levin and Pimentel (1981), it is assumed that $\beta_1 = \beta_2$ and $\sigma_1 = 0$. However, as observed by Anderson and May (1982a), the model and its conclusions apply equally when $\sigma_1 \neq 0$. Then, assuming $\underline{r} > \underline{b}$,

the system (13) with $\beta_1 = \beta_2$ supports a locally stable polymorphism provided the relativized life expectancy of the virulent-infected host, $\underline{r}/(\underline{b} + \alpha_2)$, is sufficiently short, and that of the avirulent-infected host, $\underline{r}/(\underline{b} + \alpha_1)$, is sufficiently long. Specifically, the conditions are

$$\frac{r}{b + \alpha_2} < 1 - \frac{(\sigma_2 - \sigma_1)(r - b)}{\alpha_2 - \alpha_1} < \frac{r}{b + \alpha_1} \quad . \tag{14}$$

If the first inequality in (14) is violated, the virulent strain will eliminate the avirulent; if the second is violated, avirulence will win. But if (14) is satisfied, intermediate levels of virulence will result, at the levels

$$\bar{S} = r/\theta \ , \ \bar{I}_1 = \frac{b + \alpha_2 - \beta\bar{S}}{\beta(\sigma_2 - \sigma_1)} \ , \ \bar{I}_2 = \frac{\beta\bar{S} - (b + \alpha_1)}{\beta(\sigma_2 - \sigma_1)} \ , \tag{15}$$

where

$$\theta = \beta(1 - (\sigma_2 - \sigma_1)(r - b)/(\alpha_2 - \alpha_1)) \, . \tag{16}$$

These conditions are simply translation of the results obtained by Levin and Pimentel (1981). Coexistence of strains here depends on the invasion of avirulent-infected hosts by virulent viruses. If the right inequality in (14) is violated, a new steady state is attained at host densities too low to allow the virulent strain to survive in the population.

It is important to note that selection for intermediate levels of virulence does not depend on coexistence between strains. The discussion so far simply indicates that under some conditions a less virulent strain will displace a virulent one; under others the reverse will be true; and under others there will be coexistence. A generalization of the results given here would demonstrate that when many strains are placed in competition, the outcome may be coexistence, competitive dominance by a single intermediate type, or selection for an extreme type.

More generally, assume $\beta_1 \leq \beta_2$ (the transmissibility of the virulent strain is at least equal to that of the avirulent strain). Then, provided $\sigma_1\beta_1 < \sigma_2\beta_2$, the polymorphic equilibrium (15) generalizes to

$$\bar{S} = r/\theta^* , \quad \bar{I}_1 = \frac{b + \alpha_2 - \beta_2\bar{S}}{\beta_2\sigma_2 - \beta_1\sigma_1} , \quad \bar{I}_2 = \frac{\beta_1\bar{S} - (b + \alpha_1)}{\beta_2\sigma_2 - \beta_1\sigma_1} , \tag{17}$$

where

$$\theta^* = \frac{\alpha_2\beta_1 - \alpha_1\beta_2}{\alpha_2 - \alpha_1} + \frac{(\sigma_1 - 1)\beta_1 - (\sigma_2 - 1)\beta_2}{\alpha_2 - \alpha_1}(r - b) . \tag{18}$$

As before, the local stability condition is that (17) be feasible; i.e.

$$\beta_2 \frac{r}{b + \alpha_2} < \theta^* < \beta_1 \frac{r}{b + \alpha_1} , \tag{19}$$

which reduces to (14) if $\beta_1 = \beta_2$.

In interpreting (19), it should first be noted that $\beta\, r/(b + \alpha)$ is a measure of the transmission rate of a strain, the product of its transmissibility times the relativized expected lifetime of its host. θ^* measures the relative strengths of intra-demic selection and inter-demic selection, where a deme is the total parasite colony associated with a particular host.

For many diseases, secondary infections may be uncommon, especially if the course of the disease is swift. Nonetheless, we expect some susceptibility, including cases where the host has fought off the primary infection. σ is a measure of the relative susceptibility of an already infected host; normally it will be between 0 and 1 because $\sigma\beta$ measures not the rate of invasion by a secondary infection, but the rate at which a secondary infection becomes the dominant one. For such considerations, the model (13) is an oversimplification, and it is best to consider explicitly the intermediate stage I_3 (both infections present) and the appropriate rates of recovery.

The equations of interest then become

$$\begin{aligned}
\frac{dS}{dt} &= (r_o S + r_1 I_1 + r_2 I_2 + r_3 I_3) - bS - \beta_1 S I_1 - \beta_2 S I_2 + v_1 I_1 + v_2 I_2 \\
\frac{dI_1}{dt} &= \beta_1 S I_1 - (b + \alpha_1) I_1 - v_1 I_1 + w_2 I_3 - \gamma_2 \beta_2 I_1 I_2 \\
\frac{dI_2}{dt} &= \beta_2 S I_2 - (b + \alpha_2) I_2 - v_2 I_2 + w_1 I_3 - \gamma_1 \beta_1 I_1 I_2 \\
\frac{dI_3}{dt} &= (\gamma_1 \beta_1 + \gamma_2 \beta_2) I_1 I_2 - (w_1 + w_2) I_3 - (b + \alpha_3) I_3 .
\end{aligned} \tag{20}$$

Here, (13) has been generalized in several ways. First, infected hosts are allowed to have a different reproductive rate from uninfected, the deviation being dependent on the nature of the infection. Second, v_i is the rate at which hosts infected with strain i alone recover, and w_i is the rate at which those infected with both strains lose strain i. Third, $b + \alpha_3$ is the death rate of doubly infected hosts. Finally, $\gamma_i\beta_i$ is the rate at which hosts infected with strain $j \neq i$ acquire a secondary infection by i. γ_i is not identical with σ_i in (13), since it measures only the rate of acquisition of the secondary infection, not the rate of displacement. Thus $\gamma_i \geq \sigma_i$.

If $w_1 + w_2 >> (b + \alpha_3)$--that is, if the rate of intra-host competitive exclusion is fast relative to the death rate of doubly infected hosts--and if the dynamics of I_3 are taken to be fast, then a pseudo-steady-state assumption allows the approximation

$$I_3 \cong (\gamma_1\beta_1 + \gamma_2\beta_2) I_1 I_2 / (w_1 + w_2) \tag{21}$$

to be made in (20). This reduces the equation for dI_1/dt, for example, to

$$\frac{dI_1}{dt} = \beta_1 S I_1 - (b + \alpha_1 + v_1) I_1 + (\sigma_1\beta_1 - \sigma_2\beta_2) I_1 I_2 , \tag{22}$$

where

$$\sigma_1 = \gamma_1 \frac{w_2}{w_1 + w_2} \text{ and } \sigma_2 = \gamma_2 \frac{w_1}{w_1 + w_2} . \tag{23}$$

Thus the relationship between σ_i and γ_i is made clearer.

More generally, if the pseudo-steady-state approximation is not made, the system (20) may still possess a stable polymorphic equilibrium. The conditions are complicated (Levin 1983), and are not given in detail here. However, most important is that for a stable polymorphic equilibrium to exist, necessarily the transmission rates satisfy a condition

$$\beta_2 r_o/(b + \alpha_2 + v_2) < \theta^{**} < \beta_1 r_o/(b + \alpha_1 + v_1) , \tag{24}$$

where θ^{**} is a generalization of (18), and further

$$\gamma_1 \beta_1 w_2 > \gamma_2 \beta_2 (w_1 + b + \alpha_3) \tag{25}$$

(which replaces the earlier condition $\sigma_2 \beta_2 > \sigma_1 \beta_1$).

If secondary infections are ignored, but recovery is permitted, (20) reduces to

$$\begin{aligned} \frac{dS}{dt} &= (r_o S + r_1 I_1 + r_2 I_2) - bS - \beta_1 S I_1 - \beta_2 S I_2 + v_1 I_1 + v_2 I_2 \\ \frac{dI_1}{dt} &= \beta_1 S I_1 - (b + \alpha_1 + v_1) I_1 \\ \frac{dI_2}{dt} &= \beta_2 S I_2 - (b + \alpha_2 + v_2) I_2 . \end{aligned} \tag{26}$$

Then, as Anderson and May (1982a, c) and Bremermann (1980, Bremermann and Pickering 1982) discuss for the case $\underline{r}_0 = \underline{r}_1 = \underline{r}_2$, coexistence is not possible; the winning strain is that which maximizes the ratio $\beta/(\underline{b} + \alpha + \underline{v})$, subject to whatever constraints exist. Note that this is equivalent to maximizing the intrinsic reproductive rate

$$R_o = \frac{\beta}{b + \alpha + v} N \tag{27}$$

of the parasite (Dietz 1975) for a given population density $\underline{N}$ of hosts. Thus it defines an evolutionarily stable strategy (Maynard Smith 1976, 1977).

Anderson and May (1982a) derive a functional relationship between α and $\underline{v}$ and maximize $\underline{R}_o$ (for $\underline{N}$ fixed); $\underline{b}$ is determined from data, and β is taken to be a constant. A similar technique was suggested independently by Bremermann and Pickering (1982). Using data taken from Fenner and Ratcliffe (1965) to determine the parameters and the functional relationships, Anderson and May (1982a) determine a theoretical optimal type, which is remarkably close (but not identical) to the modal strain which emerged in the Australian system; similar conclusions apply to the European data. Of course, as stated earlier, it is not yet certain whether either the Australian or European system has stabilized.

In conclusion, models which take into account the details of the epidemiological distribution of populations can demonstrate behavior not possible in the more classical host-parasite models. In this section I have discussed some of the most primitive of such models, but these are sufficient to provide insights into the evolution of avirulence in host-parasite associations. Because in natural populations parasite burdens are highly heterogeneous in their distributions, it would be worthwhile to examine extended models which incorporate more detail regarding population distributions.

Epidemiological considerations allow one to recognize that populations have a demic structure, with restricted flow between demes; it is well recognized that such structure is important for selection to favor group-oriented behavior (D. Wilson 1977, Wade 1978). Demic structure is simply a special case of geographical structure, which is also known to be important in any evolutionary analysis (Malécot 1948, Wright 1949, Kimura and Weiss 1964, Maruyama 1971, Karlin and McGregor 1972, Nagylaki 1978) as well as in ecological considerations (Levin 1974, 1976, 1981). Many traits, for example allelopathy, are locally specific in their nature, and their spread is determined by the geographical structure of

the environment. In an elegant recent paper (Chao and B. Levin 1981), it is shown that E. coli that produce an anti-competitor toxin (colicin) may be favored by selection when rare, but only in a structured habitat, a soft agar matrix. This is because the costs of producing the toxin reduce the intrinsic rate of increase of the colicinogenic bacteria, which places them at a competitive disadvantage in liquid cultures which are well-mixed. In agar, clones form inhibition zones around themselves, and these permit their spread.

V. Diffuse coevolution

Although the general formulation (1) is unrestricted in dimension, the models so far considered deal principally with tight coevolution between a pair of closely associated species. But many problems of interest involve diffuse coevolution involving many species. For example, immune systems represent a generalized response of vertebrates to a suite of possible hostile agents, and it would be fruitless to try to study such responses in models of the form of the previous chapters. Similar remarks apply to the evolution of chemical defenses in plants, which are to a large extent also a generalized response to diverse enemies (Feeny 1975, 1982; Janzen 1980). Clarke (1975, 1976) has focused attention on the influence of natural enemies in the maintenance of diversity, and others have addressed more specifically the importance of natural enemies to the evolution of sex as a diversifying mechanism (Jaenike 1978, Hamilton 1980, 1982). To consider such questions, which deal with the coevolution of many factors on a virtual continuum of responses, requires a new point of view.

The problem of the evolution of a diversity of anti-enemy defense mechanisms is a restriction of the more general problem of the evolution of aspect diversity (Rand 1967, Ricklefs and O'Rourke 1975, Endler 1978, Levin and Segel 1982), with the notion of aspect interpreted broadly. To approach this problem, Lee Segel and I (Levin and Segel 1982) have proposed a quite different framework which builds on models of the evolution of quantitative characters, such as those discussed by Slatkin (1970) and others (Bossert

1963, Kimura 1965), coupled with descriptions of ecological dynamics. Related models have been utilized by Roughgarden (1972) and Rocklin and Oster (1976) in studying the evolution of competition. The approach is introduced briefly in this section; for the details, the reader is referred to Levin and Segel (1982). As discussed more generally earlier, such models are not intended to be used for literal prediction, but rather to help in understanding the evolutionary patterns which have emerged, to aid in framing questions, and to identify those key parameters which seem to control the dynamic responses.

The approach is illustrated most easily for predator-prey interactions, for they permit a mass-action formulation. As discussed in the previous section, for parasite-host interactions it is important to revise classical approaches to consider epidemiology, and that represents an important future extension of the work discussed here. Another extension is concerned with plant-pollinator associations, in which many of the same questions are at issue (Schemske, this volume): What accounts for diversity? What determines the specificity of associations? That is, under what conditions will the community evolve towards generalized associations, as opposed to rather specific (predator-prey, parasite-host, pollinator-plant) assemblages? Timm's discussion (this volume) of conditions in parasite-host communities which favor resource tracking versus Farenholz's rule highlights this dichotomy.

In the model presented here, the generation time of the predators is considered to be longer than that of the prey, so that coevolution among the various prey species is taking place on the same time scale as that of the ecological responses of the prey. Evolution in the predators is not treated, although it would be a straightforward extension of the model to incorporate it.

It has often been suggested (Cain and Sheppard 1950, 1954; Rand 1967; Clarke 1969; Ricklefs and O'Rourke 1975) that apostatic selection, in which predators preferentially form a labile search image for more common prey, is an important mechanism in

determining the diversity of aspects (color, wing or shell patterns, defensive characteristics, etc.) in prey. Although the significance of apostasis in maintaining aspect diversity is debatable, predation in general is of obvious importance (Endler 1978). Models can help us to assess the relative importance of the various mechanisms.

The model summarized here assumes that prey aspect may be arrayed along a single gradient, scored by z. This single-dimensional illustration is chosen for ease of presentation, and represents no fundamental restriction. Prey aspect is assumed to be genetically determined; predator search image for a particular aspect shifts in inverse relation to the numbers of available prey of that aspect. Prey may mate more readily with similar types (assortative mating) or preferred types (sexual selection). The prey are assumed to be distributed along the aspect gradient z according to the density function $v(z, t)$, which changes over evolutionary time. Similarly, predator search image is distributed at time t according to a density function $e(z, t)$, which shifts as predators shift search images.

We have proposed using this scheme to examine both intraspecific evolution, as for example the diversification of spot patterns in guppies (Poecilia reticulata Peters) discussed by Endler (1978), and interspecific coevolution in high diversity communities, as for example the proliferation of wing patterns among moths (Ricklefs and O'Rourke 1975). Ecologically, we believe that the mechanisms are the same. Of course, there are fundamental differences in the genetic constraints which must be imposed at the intraspecific versus the interspecific level, especially regarding hybridization and outcrossing. But the extremes of random mating and complete reproductive isolation simply represent the poles of a spectrum of possibilities observed in Nature, and the biological species concept is based on a separation of this spectrum. The art of model building at any level of description requires the suppression of much detail at lower levels, and the summary of this detail in a few macroscopic parameters. Thus, to a first approximation we suggest that mating structure can be represented by the assortativity of

the mating function, with the interspecific case corresponding to total or near-total positive assortativity.

Rare prey are relatively favored by predator apostasis, but to what degree? If predator search image is broad, then prey with aspects close to target prey benefit less than otherwise from the predator's attention to other aspects. Similarly, but more subtly, positive assortative mating which extends to nearby types can result in the depression of their growth rates and serve as a strong influence in population subdivision and the formation of reproductive isolation.

What are the relative importances of the competing tendencies to subdivision and diversification? When will uniform distributions result, in which all types are equally represented? When will peaks occur (precursors to population subdivision and possibly speciation), in which a restricted number of types are numerically dominant, and in which predator-prey associations will become relatively specialized (with predators locked in ecological time to the prey's genetically fixed aspects)? What determines the diversity of types and their relative similarities? When can more general patterns of diversity result, such as the persistent fluctuations analogous to those observed in many parasite-host assemblages?

Predator switching is governed by the transitions shown in Figure 5. The possibilities exist both for switching to prey of a different aspect within the evolutionary group being considered, and for switching to a different class of prey altogether. The latter, described by the function m, is allowed to depend not only on the local density of prey $v(z, t)$, but more generally on some weighted average of prey densities $V(z, t)$ representing the predator's recent experiences and range of selectivities. m is related inversely to V. ← Figs here

Similarly, predator density is measured by a function $e(z, t)$. Predators shift among the available aspects according to a switching function s (which bears an inverse relationship to v or to some weighted average of v), and a redistribution "kernel" $\Psi(z, n)$

(which is the distribution of probabilities that a predator switching from aspect z will select aspect η as its new search image). Most typically, but not necessarily, $\Psi(z, \eta)$ is a unimodal function with peak at z. The function $n(z, t)$ includes new recruits plus the reentry of predators from alternative prey (outside the evolving group being considered). More generally, n could be allowed to depend upon predator diversity in some way, although on the time scale of interest we expect such dependency to be weak--recall that predator search image is assumed to have no genetic component. θ defines the weight function implicit in V. Thus, summarizing the exchanges shown in Figure 5, we obtain the equation

$$\frac{\partial e}{\partial t} = -em(V_1) + n(e, v) - s(V_2)e + \int \Psi(z, \eta)s(V_2)ed\eta \ , \qquad (28)$$

where s has been allowed to depend on the weighted average V_2 rather than simply on v, and V_1 is the weighted average defined by θ.

Prey evolution is governed by a model similar to that discussed by Slatkin (1970) for polygenic characters, supplemented by a predator per capita consumption rate $f(v)$. The approach of Slatkin is modified to include a continuous time description, most appropriate if selection is weak, and to allow for density- and frequency-dependent influences. The relative availability of desirable mates for prey of a particular aspect z is measured by the weighted average.

$$W(\eta, t) = \int \alpha(\eta, \xi)v(\xi, t)\, d\xi \ , \qquad (29)$$

in which $\alpha(\eta, \xi)$ defines a selection index. The per capita number of offspring per female, r, depends on W and perhaps on η. Finally, the function $\phi(\eta, \xi; z)$ is the redistribution kernel, describing the probability distribution for the offspring of a mating between an η-female and a ξ-male. These definitions lead to the equation

$$\frac{\partial v}{\partial t} = -f(v)e + \int\int v(\eta, t)v(\xi, t)\alpha(\eta, \xi)\frac{r(\eta, W(\eta, t))}{W(\eta, t)}\phi(\eta, \xi; z)\, d\xi d\eta \qquad (30)$$

for the rate of change of the victim aspect distribution with time.

The behavior of the system (28) - (30), under particular assumptions, is discussed in Levin and Segel (1982). All forms of patterns of diversity alluded to earlier are observed: uniform distributions, multimodal distributions representing population subdivision, and oscillatory distributions. These, and their descriptive parameters, are related to such critical variables as the switching rates and sensitivities of the predators, predation pressure, selectivity of mating, and the characteristics of the offspring distribution of a given mating. Some analytical results are possible; other conclusions can emerge only from numerical treatment.

The significance of the example presented is not in the detailed conclusions which may be drawn from it, but as a framework fundamentally different from the ones appropriate for the study of tight coevolution. The model just described may be extended to other situations, e.g. plant-pollinator assemblages. The point is that when one is concerned with general patterns at the community level--degree of specialization, diversity, etc.--the most appropriate models are ones which emerge from knowledge of the population genetic basis of inheritance, but which do not retain superfluous genetic detail. Of course, deciding what is superfluous is not always easy, and must be determined by the intuitions and arrogance of the investigator.

VI. Summary

Coevolution presents a fascinating class of evolutionary problems, and introduces difficulties which extend those of frequency-dependent responses in classical evolutionary theory. Coevolution implies nonlinear feedback among interacting species, and such nonlinearities substantially complicate any attempt to understand evolutionary change.

The classical approach, based on explicit description of gene frequency change, is most appropriate to small ensembles of tightly interacting species in which the genetic basis of change is well understood. The gene-for-gene resistance systems of cereal plants

and their associated pests provide the ideal systems for such modelling, and the relevant literature is briefly reviewed. Models of quantitative inheritance are not discussed in this context, but are appropriate for tight coevolution when the genetic basis is polygenic.

More generally, because of the tight relationship between parasite and host, the parasite-host interaction is an ideal one in which to study pairwise coevolution (Day 1974). One of the most enticing consequences of the association is the evolution of reduced virulence in parasites in order to preserve their hosts (Fenner 1965, Lewontin 1970). However, to study such evolution requires an approach which deviates from the classical mold, and explicitly incorporates epidemiological considerations (Levin and Pimentel 1981, Anderson and May 1982a, Bremermann and Pickering 1982). Such models are discussed in section IV, and hold tremendous potential for the examination of the evolution of host-parasite systems. Anderson and May (1979, 1981; May and Anderson 1979), by their introduction of host-parasite dynamics into classical parasitology and epidemiology, have already had a major influence on the development of those fields (Anderson and May 1982b), and all of the work discussed in section IV builds on their approach. Thus, it is all of recent vintage and preliminary. Extensions will certainly broaden our understanding of the dynamics of these systems.

Finally, it is argued that diffuse coevolution (sensu Janzen 1980, Feeny 1982) requires yet a different perspective, particularly when attention is focused on system-level integrative parameters such as diversity or degree of specialization. An approach due to Levin and Segel (1982), but building on previous work of others on quantitative inheritance, is outlined and some specifics discussed. This too represents a new paradigm, one which is likely to be a productive source of insights into diffuse coevolution.

No single approach holds all of the answers for the examination of coevolutionary processes. Classical population genetics has not often addressed itself to ecological interactions, whereas ecologists have fallen back too comfortably on adaptationism and optimalogy without adequate recognition of the inherent contradictions in that approach

(Lewontin 1977, Levin 1981). More recent applications of game theory and the development of the concept of evolutionarily stable strategies (Maynard Smith 1976, 1977) are advances; but they still retain a number of difficulties, including especially the fact that they are equilibrial in nature. Even when equilibrial approaches are justified, they sometimes provide little information about processes. In this paper, I have emphasized the importance of dynamic models, ranging from detailed genetic ones to ones couched entirely in phenotypic terms. All of these approaches contribute to our understanding of evolution.

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REFERENCES

Alexander, M. 1981. Why microbial predators and parasites do not eliminate their prey and hosts. Annual Review of Microbiology 35: 113-133.

Anderson, R. M. and R. M. May. 1979. Population biology of infectious diseases: Part I. Nature 280: 361-367.

Anderson, R. M. and R. M. May. 1981. The population dynamics of microparasites and their invertebrate hosts. Philosophical Transactions of the Royal Society of London, Series B 291: 451-524.

Anderson, R. M. and R. M. May. 1982a. Coevolution of hosts and parasites. Parasitology. To appear.

Anderson, R. M. and R. M. May (editors). 1982b. Population Biology of Infectious Diseases. Dahlem Konferenzen. Springer-Verlag, Heidelberg. To appear.

Anderson, R. M. and R. M. May. 1982c. Frequency and density dependent effects in the coevolution of hosts and parasites. Manuscript.

Anderson, R. M. and R. M. May. 1982d. Directly transmitted infectious diseases: control by vaccination. Science 215: 1053-1060.

Bossert, W. H. 1963. Simulation of character displacement. Unpublished Doctoral Dissertation, Harvard University, Cambridge, Massachusetts.

Bremermann, H. J. 1980. Sex and polymorphism as strategies in host-pathogen interactions. Journal of Theoretical Biology 87: 671-702.

Bremermann, H. J. and J. Pickering. 1982. A game theoretical model of parasite virulence. Submitted.

Browning, J. A. 1974. Relevance of knowledge about natural ecosystems to development of pest management programs for ecosystems. Proceedings of the American Phytopathological Society 1: 191-199.

Browning, J. A. 1980. Genetic protective mechanisms of plant-pathogen interactions: their coevolution and use in breeding for resistance. Pages 52-75 in M. K. Harris (editor), Biology and Breeding for Resistance to Arthropods and Pathogens in Agricultural Plants. Texas A & M Press, College Station, Texas.

Browning, J. A. and K. J. Frey. 1969. Multiline cultivars as a means of disease control. Annual Review of Phytopathology 7: 355-382.

Burnet, M. and D. O. White. 1972. Natural History of Infectious Disease. Cambridge University Press, Cambridge,.

Cain, A. J. and P. M. Sheppard. 1950. Selection in the polymorphic land snail Cepaea nemoralis. Heredity 4: 275-294.

Cain, A. J. and P. M. Sheppard. 1954. Natural selection in Cepaea. Genetics 39: 89-116.

Chao, L. and B. R. Levin. 1981. Structured habitats and the evolution of anticompetitor toxins in bacteria. Proceedings of the National Academy of Sciences USA 78: 6324-6328.

Clarke, B. C. 1969. The evidence for apostatic selection. Heredity 24: 347-352.

Clarke, B. C. 1975. The causes of biological diversity. Scientific American 233(2): 50-60.

Clarke, B. C. 1976. The ecological genetics of host-parasite relationships. Pages 87-103 in A. E. R. Taylor and R. Muller (editors), Genetic Aspects of Host-Parasite Relationships. Blackwell, Oxford.

Crow, J. F. and M. Kimura. 1965. Evolution in sexual and asexual populations. American Naturalist 103: 89-91.

Day, P. R. 1974. Genetics of Host-Parasite Interactions. W. H. Freeman, San Francisco.

Dietz, K. 1975. Transmission and control of arbovirus diseases. Pages 104-121 in D. Ludwig and K. L. Cooke (editors), Epidemiology. Society of Industrial and Applied Mathematics, Philadelphia.

Dinoor, A. 1974. The role of the alternate host in amplifying the pathogenic variability of oat crown rust. Research Reports on Science and Agriculture, Hebrew University of Jerusalem 1: 734-735.

Endler, J. A. 1978. A predator's view of animal color patterns. Evolutionary Biology 11: 319-364.

Feeny, P. 1975. Biochemical coevolution between plants and their insect herbivores. Pages 3-19 in L. E. Gilbert and P. H. Raven (editors), Coevolution of Animals and Plants. University of Texas Press, Austin and London.

Feeny, P. 1982. Coevolution of plants and insects. Chapter 11 in T. R. Odhiambo (editor), Current Themes in Tropical Sciences, 2: Natural Products for Innovative Pest Management. Pergamon Press, Oxford.

Fenner, F. 1965. Myxoma virus and Oryctolagus cuniculus: two colonizing species. Pages 485-501 in H. G. Baker and G. L. Stebbins (editors), The Genetics of Colonizing Species. Academic Press, New York.

Fenner, F. and I. D. Marshall. 1957. A comparison of the virulence for European rabbits (Oryctolagus cuniculus) of strains of myxoma virus recovered in the field in Australia, Europe and America. Journal of Hygiene 55: 149-191.

Fenner, F. and K. Myers. 1978. Myxoma virus and myxomatosis in retrospect: the first quarter century of a new disease. Pages 539-570 in E. Kurstak and K. Maramorosch (editors), Viruses and Environment. Third International Conference on Comparative Virology, Mont Gabriel, Quebec.

Fenner, F. and F. N. Ratcliffe. 1965. Myxomatosis. Cambridge University Press, Cambridge.

Fleming, R. 1980. Selection pressures and plant pathogens: robustness of the model. Phytopathology 70: 175-178. (Errata 1981, 71: 268)

Fleming, R. 1982. Stability properties of simple gene-for-gene relationships. To appear.

Flor, H. H. 1955. Host-parasite interaction in flax rust--its genetics and other implications. Phytopathology 45: 680-685.

Flor, H. H. 1956. The complementary genic systems in flax and flax rust. Advances in Genetics 29-54. Academic Press, New York.

Gillespie, J. N. 1975. Natural selection for resistance to epidemics. Ecology 56: 493-495.

Gould, S. J. 1977. Ever Since Darwin. Norton, New York.

Gracen, V. 1982. Role of genetics in etiological phytopathology. Annual Review of Phytopathology 20: 219-233.

Guckenheimer, J., G. Oster, and A. Ipaktchi. 1977. Dynamics of density-dependent population models. Theoretical Population Biology 4: 101-147.

Haldane, J. B. S. 1948. The theory of a cline. Journal of Genetics 48: 277-284.

Hamilton, W. D. 1980. Sex versus non-sex versus parasite. Oikos 35: 282-290. Reprinted in R. W. Hiorns and D. Cooke (editors), The Mathematical Theory of the Dynamics of Biological Populations II, pages 139-155. Academic Press, London.

Hamilton, W. D. 1982. Pathogens as causes of genetic diversity in their host populations. In R. M. Anderson and R. M. May (editors), Population Biology of Infectious Diseases. Dahlem Konferenzen. Springer-Verlag, Heidelberg. To appear.

Hoeprich, P. D. 1977. Pages 34-45 in P. D. Hoeprich (editor), Infectious Diseases. Harper and Row, New York.

Hogg, W. H., C. E. Hounam, A. K. Mallik, and J. C. Zadocs. 1969. Meteorological factors affecting the epidemiology of wheat rusts. Technical Note #99, World Meteorological Organization, Geneva.

Jacob, F. 1977. Evolution and tinkering. Science 196: 1161-1166.

Jaenike, J. 1978. An hypothesis to account for the maintenance of sex within populations. Evolutionary Theory 3: 191-194.

Janzen, D. H. 1980. When is it coevolution? Evolution 34: 611-612.

Jayakar, S. D. 1970. A mathematical model for interaction of frequencies in a parasite and its host. Theoretical Population Biology 1: 140-164.

Jensen, N. F. 1965. Multiline superiority in cereals. Crop Science 5: 566-568.

Karlin, S. and J. L. McGregor. 1972. Polymorphisms for genetic and ecological systems with weak coupling. Theoretical Population Biology 3: 210-238.

Kemper, J. T. 1982. The evolutionary effect of endemic infectious disease: continuous models for an invariant pathogen. Journal of Mathematical Biology. To appear.

Kimura, M. 1958. On the change of population fitness by natural selection. Heredity 12: 145-167.

Kimura, M. 1965. A stochastic model concerning the maintenance of genetic variability in quantitative characters. Proceedings of the National Academy of Sciences USA 54: 731-736.

Kimura, M. and G. H. Weiss. 1964. The stepping stone model of population structure and the decrease in genetic correlation with distance. Genetics 49: 561-576.

Leonard, K. J. 1977. Selection pressures and plant pathogens. Annals of the New York Academy of Sciences 281: 207-222.

Leonard, K. J. and R. J. Czochor. 1978. In response to "Selection pressures and plant pathogens: stability of equilibria." Phytopathology 68: 971-973.

Leonard, K. J. and R. J. Czochor. 1980. Theory of genetic interactions among populations of plants and their pathogens. Annual Review of Phytopathology 18: 237-258.

Levin, B. R., A. C. Allison, H. J. Bremermann, L. L. Cavalli-Sforza, B. C. Clarke, R. Frentzel-Beyme, W. D. Hamilton, S. A. Levin, R. M. May, and H. R. Thieme. 1982. Evolution in host-parasite systems. In R. M. Anderson and R. M. May (editors), Population Biology of Infectious Diseases. Dahlem Konferenzen. Springer-Verlag, Heidelberg. To appear.

Levin, S. A. 1972. A mathematical analysis of the genetic feedback mechanism. American Naturalist 106: 145-164. (Erratum 1973, 104: 320)

Levin, S. A. 1974. Dispersion and population interactions. American Naturalist 108: 207-228.

Levin, S. A. 1976. Population dynamic models in heterogeneous environments. Annual Review of Ecology and Systematics 7: 287-310.

Levin, S. A. 1978. On the evolution of ecological parameters. Pages 3-26 in P. F. Brussard (editor), Ecological Genetics: The Interface. Springer-Verlag, Heidelberg.

Levin, S. A. 1981. Mechanisms for the generation and maintenance of diversity in ecological communities. Pages 173-194 in R. W. Hiorns and D. Cooke (editors), The Mathematical Theory of the Dynamics of Biological Populations II. Oxford Symposium on the Dynamics of Populations. Academic Press, London.

Levin, S. A. 1983. Coevolution. In H. Freedman (editor), Population Biology. To appear.

Levin, S. A. and D. Pimentel. 1981. Selection of intermediate rates of increase in parasite-host systems. American Naturalist 117: 308-315.

Levin, S. A. and L. A. Segel. 1982. Models of the influence of predation on aspect diversity in prey populations. Journal of Mathematical Biology. In press.

Levin, S. A. and J. D. Udovic. 1977. A mathematical model of coevolutionary populations. American Naturalist 111: 657-675.

Lewin, R. 1982. Biology is not postage stamp collecting. Science 216: 718-720.

Lewis, J. W. 1978. Maintenance of genetic polymorphism for two species in a host pathogen relationship. Masters Thesis, Iowa State University, Ames.

Lewis, J. W. 1981a. On the coevolution of pathogen and host: I, General theory of discrete time coevolution. Journal of Theoretical Biology 93: 927-951.

Lewis, J. W. 1981b. On the coevolution of pathogen and host: II, Selfing hosts and haploid pathogens. Journal of Theoretical Biology 93: 953-985.

Lewontin, R. C. 1970. The units of selection. Annual Review of Ecology and Systematics 1: 1-18.

Lewontin, R. C. 1977. Adaptation. In Enciclopedia Einaudi Turin 1: 198-214.

Lewontin, R. C. 1980. Models of natural selection. In C. Barigozzi (editor), Vito Volterra Symposium on Mathematical Models in Biology. Lecture Notes in Biomathematics 38. Springer-Verlag, Heidelberg.

Longini, I. M., Jr. 1982. Models of epidemics and endemicity in genetically variable host populations. Manuscript.

Malécot, G. 1948. Les Mathématiques de l'Hérédité. Masson et Cie, Paris. (English translation, 1969, W. H. Freeman, San Francisco)

Maruyama, T. 1971. The rate of decrease of heterozygosity in a population occupying a circular or a linear habitat. Genetics 67: 437-454.

May, R. M. and R. M. Anderson. 1979. Population biology of infectious diseases: II. Nature 280: 455-461.

Maynard Smith, J. 1976. Evolution and the theory of games. American Scientist 64: 41-45.

Maynard Smith, J. 1977. Evolution and the theory of games. In W. Matthews (editor), Mathematics in the Life Sciences. Lecture Notes in Biomathematics. Springer-Verlag, Berlin-New York.

Mayr, E. 1982. The Growth of Biological Thought. Diversity, Evolution, and Inheritance. Harvard University Press, Cambridge, Massachusetts.

Mode, C. J. 1958. A mathematical model for the coevolution of obligate parasites and their hosts. Evolution 12: 158-165.

Mode, C. J. 1960. A model of a host-pathogen system with particular reference to the rusts of cereals. Pages 84-96 in Biometrical Genetics. Pergamon Press, New York.

Mode, C. J. 1961. A generalized model of a host-pathogen system. Biometrics 17: 386-404.

Myers, K., I. D. Marshall, and F. Fenner. 1954. Studies in epidemiology of infectious myxomatosis of rabbits. III. Observations on two succeeding epizootics in Australian wild rabbits on the Riverine Plain of south-eastern Australia 1951-1953. Journal of Hygiene 52(3): 337-360.

Nagylaki, T. 1977. Selection in one- and two-locus systems. Lecture Notes in Biomathematics. Springer-Verlag, Heidelberg.

Nagylaki, T. 1978. The geographical structure of populations. Pages 588-623 in S. A. Levin (editor), Studies in Mathematical Biology II: Populations and Communities. Mathematical Association of America, Washington, D.C.

Person, C. 1959. Gene-for-gene relationships in host-parasite systems. Canadian Journal of Botany 37: 1101-1130.

Person, C. 1966. Genetic polymorphism in parasitic systems. Nature 212: 266-267.

Pimentel, D. 1961. Animal population regulation by the genetic feedback mechanism. American Naturalist 95: 65-79.

Pimentel, D. 1968. Population regulation and genetic feedback. Science 159: 1432-1437.

Pimentel, D. 1982. Genetic diversity and stability in parasite-host systems. Manuscript.

Rand, A. S. 1967. Predator-prey interactions and the evolution of aspect diversity. Atas do Simposio Sobra a Biota Amazonica 5 (Zoologia): 73-83.

Ricklefs, R. and K. O'Rourke. 1975. Aspect diversity in moths: a temperate-tropical comparison. Evolution 29: 313-324.

Rocklin, S. M. and G. F. Oster. 1976. Competition between phenotypes. Journal of Mathematical Biology 3: 225-261.

Ross, J. 1982. Myxomatosis: the natural evolution of the disease. In Animal Disease in Relation to Animal Conservation. Symposium of the Zoological Society of London. In press

Roughgarden, J. 1972. Evolution of niche width. American Naturalist 106: 683-718.

Saunders, I. W. 1980. A model of myxomatosis. Mathematical Biosciences 48: 1-16.

Sedcole, J. R. 1978. Selection pressures and plant pathogens: stability of equilibria. Phytopathology 68: 967-970.

Sidhu, G. S. 1975. Gene-for-gene relationships in plant parasitic systems. Scientific Progress, Oxford 62: 467-483.

Slatkin, M. 1970. Selection and polygenic characters. Proceedings of the National Academy of Sciences USA 66: 87-93.

Stakman, E. C. and C. M. Christensen. 1946. Aerobiology in relation to plant disease. Botanical Review 12(4): 205-253.

Van der Plank, J. E. 1975. Principles of Plant Infection. Academic Press, New York.

Wade, M. J. 1978. A critical review of the models of group selection. Quarterly Review of Biology 53: 101-114.

Wallace, B. 1968. Topics in Population Genetics. W. W. Norton, New York.

Wilson, D. S. 1977. Structured demes and the evolution of group-advantageous traits. American Naturalist 111: 157-185.

Wright, S. 1949. Adaptation and selection. Pages 365-389 in G. L. Jepson, G. G. Simpson, and E. Mayr (editors), Genetics, Paleontology, and Evolution. Princeton University Press, Princeton.

Wright, S. 1955. Classification of the factors of evolution. Cold Spring Harbor Symposia on Quantitative Biology 20: 16-24.

Yu, P. 1972. Some host-parasite genetic interaction models. Theoretical Population Biology 3: 347-357.

FIGURE LEGENDS

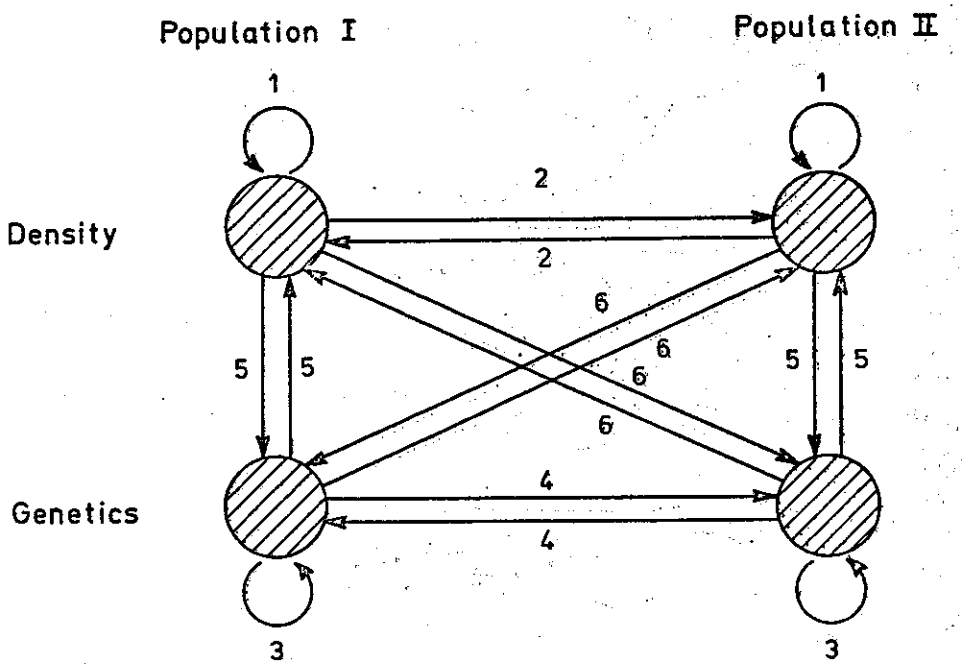
Fig. 1 -- Schematic diagram of types of interactions among densities and genetic systems of interacting populations (from Levin and Udovic 1977). Numbers differentiate different types of interactions.

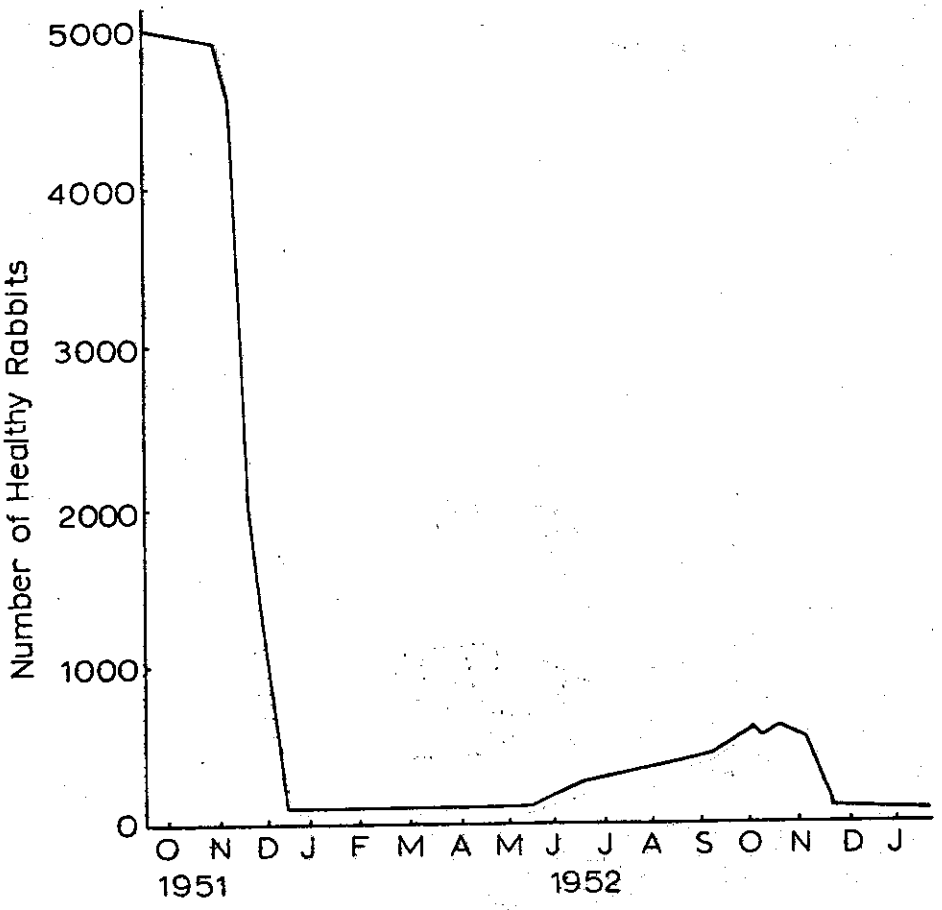
Fig. 2 -- Number of healthy rabbits per standardized transect counts at Lake Urana region immediately after the introduction of the myxoma virus into the host rabbit population (after Myers et al. 1954, Levin and Pimentel 1981).

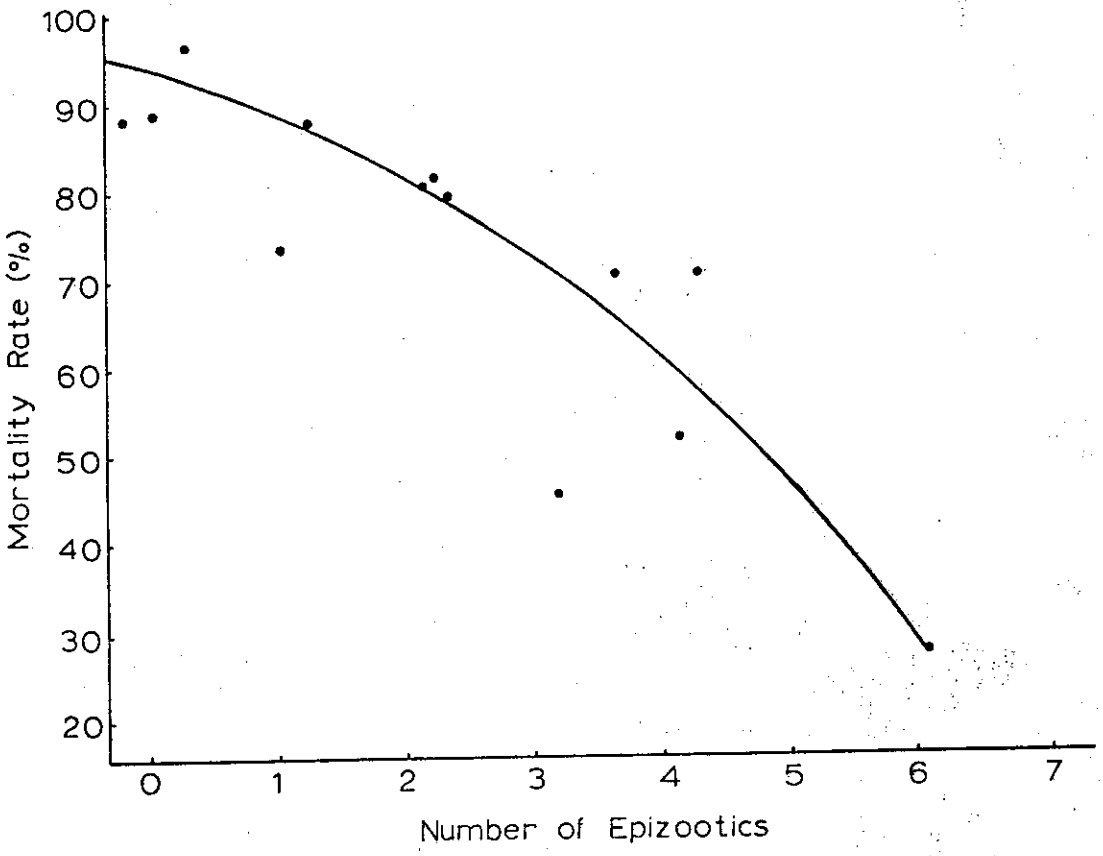
Fig. 3 -- Mortality rates of wild rabbits from Lake Urana region after exposures to several epizootics of myxoma virus, after challenge infection with strain of myxoma virus grade III virulence (after Fenner and Myers 1978, Levin and Pimentel 1981). Abscissa is weighted for immune rates among survivors of each epizootic.

Fig. 4 -- Schematic diagram of transitions and rates in interaction between host and two strains of virulence.

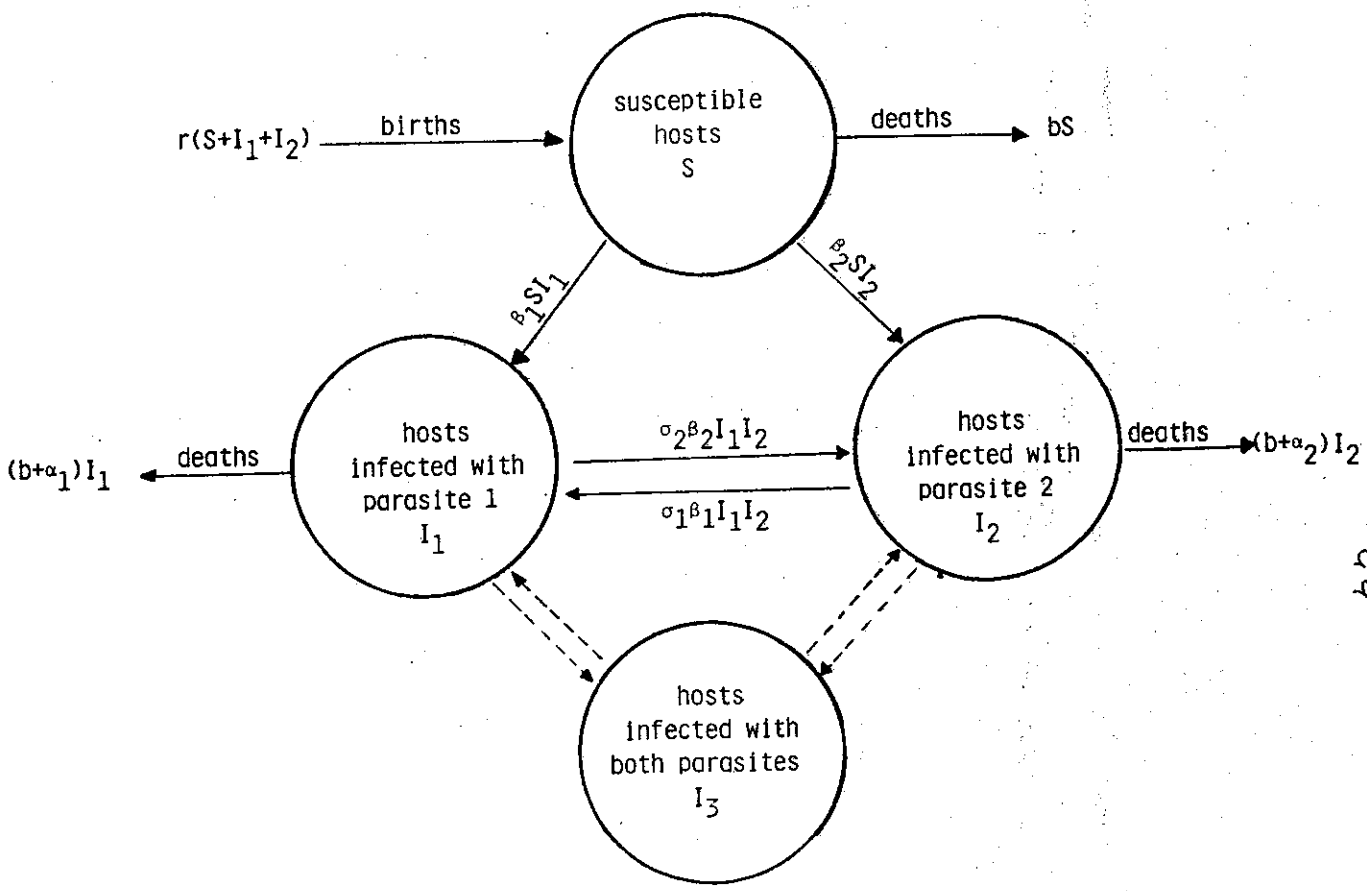
Fig. 5 -- Schematic diagram of (rates of) transitions of predator search image. Symbols explained in text.


Population I
Population II
Density
Genetics
1
2
3
4
5
6


Number of Healthy Rabbits
5000
4000
3000
2000
1000
0
O N D J F M A M J J A S O N D J
1951
1952



MYXOMATOSIS-ORYCTOLAGUS SYSTEM
modified from
LEVIN AND PIMENTEL 1981



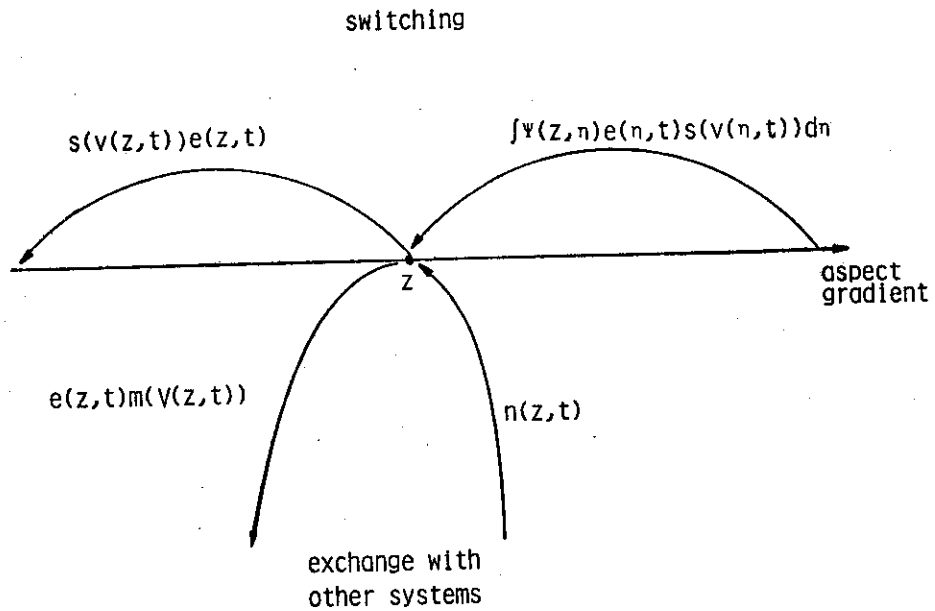


TABLE 1
(Fenner and Myers, 1978)
VIRULENCE OF FIELD MYXOMA VIRUS TYPES IN RABBITS IN AUSTRALIA

Grade of Severity	VIRULENCE TYPE GRADE I	II	IIIA	IIIB	IV	V
Mean survival times of rabbits (days)	<13	14-16	17-22	23-28	29-50	...
Case-mortality rate (%)	>99	95-99	90-95	70-90	50-70	<50
Australia						
1950-1951	100	...	...	...	...	...
1958-1959	0	25	29	27	14	5
1963-1964	0	3	26	33	31	9