FREQUENCY-DEPENDENT DISEASE TRANSMISSION AND THE DYNAMICS OF THE *SILENE-USTILAGO* HOST-PATHOGEN SYSTEMPETER H. THRALL,¹ ARJEN BIERE,² AND MARCY K. UYENOYAMA³¹Department of Botany, Box 90339, Duke University, Durham, North Carolina 27708-0339;²Department of Plant Population Biology, Netherlands Institute of Ecology/CTO,P.O. Box 40, 6666 ZG Heteren, The Netherlands; ³Department of Zoology,
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Abstract.—Models incorporating density-dependent disease transmission functions generally provide a good fit for airborne and directly transmitted bacterial or viral diseases. However, the transmission dynamics of sexually transmitted and vector-borne diseases are likely to be frequency- rather than density-dependent, which results in qualitatively different dynamics. Here, we present analyses of a basic epidemiological model in which the transmission process is represented as a function of the population disease frequency. In an extension of the basic model, we consider disease transmission as a probability function that assumes that the chance of becoming infected increases with the number of vector contacts. Stability analyses show that host-pathogen coexistence is possible in vector-transmitted and sexually transmitted disease systems in which transmission is likely to be frequency-dependent; the potential for stable coexistence is greatest for intermediate rates of disease spread and weak density dependence of host growth rate. Extension of the basic frequency-dependent model to allow for multiple contacts among hosts indicates that parameter ranges within which coexistence is predicted are thereby broadened.

In an important series of articles, Anderson and May developed a general theoretical framework for host-parasite systems (see, e.g., Anderson and May 1978, 1979, 1981; May and Anderson 1978, 1979, 1983; Anderson 1981*a*). The essential feature that makes their models suitable for the study of pathogen impact in natural populations is that host population size is represented as a dynamic variable rather than a constant as in earlier studies, including most of the human epidemiology and agricultural literature (see, e.g., Waltman 1974; Bailey 1975; Hethcote 1976). In their models, the likelihood of a healthy individual becoming infected depends on the density of infected individuals in the population; that is, the greater the number of diseased individuals per unit area, the greater the chance that the healthy individual will become diseased. Density-dependent transmission generally offers a good description for airborne and many directly transmitted viral and protozoan diseases (May and Anderson 1979; Anderson and May 1981).

In interactions involving sexually transmitted or vector-borne diseases, the number of host individuals contacted by a disease vector or the number of sexual contacts between individuals will remain relatively constant over a wide range

of population densities. In such cases, disease transmission will be primarily determined by the number of encounters or contacts together with the probability that an encountered individual is infective (Anderson 1981*b*; Getz and Pickering 1983; Diekmann and Kretzschmar 1991; Thrall et al. 1993*a*; Antonovics et al. 1995).

The transmission term in density-dependent formulations can be generalized as some function of $\beta E(Y)$, where β is the probability of transmission given that the disease is encountered, and $E(Y)$ is the expected number of encounters (usually considered to be proportional to the number of infected individuals in the population). The equivalent formulation in a frequency-dependent model can be written as $\beta' C(Y/N)$, where C is the number of vector contacts (or sexual encounters), and Y/N is the frequency of disease in the population. If total population size (N) is constant, then β (from the density-dependent model) can be reparameterized as $\beta = \beta'(C/N)$. If, however, N is a dynamic variable, then the frequency-dependent formulation cannot be recovered by reparameterization. Therefore, models with frequency-dependent disease transmission and variable N are fundamentally different from models with density-dependent transmission and lead to qualitatively different results.

Getz and Pickering (1983) demonstrated that incorporation of frequency-dependent disease transmission eliminated a host density threshold for disease increase and made coexistence between host and pathogen more difficult. Coexistence in frequency-dependent systems requires regulation by some external density-dependent factor (e.g., increased mortality rates due to limited resources at high density) (Getz and Pickering 1983; Thrall et al. 1993*a*). If there is no host recovery and no reproduction by diseased individuals, then coexistence further requires that the degree of density dependence be different in the healthy and diseased classes (Thrall et al. 1993*a*).

For the past several years, we have been working with a naturally occurring host-pathogen system, the anther-smut disease *Ustilago violacea*, which is endemic on host plants in the Caryophyllaceae (Alexander 1987, 1990*a*, 1990*b*; Alexander and Antonovics 1988; Antonovics and Alexander 1993; Thrall et al. 1993*b*). Anther-smut diseases are pollinator transmitted (Baker 1947; Hassan and MacDonald 1971; Lee 1981; Jennersten 1983, 1988; Jennersten et al. 1983) and thus can be considered as examples of plant "venereal diseases"; experimental studies suggest that there is a strong frequency-dependent component to disease transmission (Antonovics and Alexander 1993). Furthermore, the disease caused by *U. violacea* has a number of features in common with animal sexually transmitted diseases. These diseases generally have localized sites of infection and result in sterility, yet have moderate or negligible effects on host survival (Holmes 1983; Felman 1986; A. B. Lockhart, P. H. Thrall, and J. Antonovics, unpublished data).

Although previous theoretical work (Getz and Pickering 1983) suggests that coexistence may be difficult in systems with frequency-dependent disease transmission, natural history observations indicate that host populations can persist even with high endemic levels of anther-smut infection (Baker 1947; Alexander and Antonovics 1988; Jennersten 1988; Antonovics et al. 1994). This raises the question of how such coexistence is maintained. Here we develop simple difference equation models that incorporate the essential features of host-pathogen

systems with frequency-dependent disease transmission, in order to examine the dynamic behavior in detail. Analytical results derived from these models are compared to those from an analogous model with density-dependent transmission.

For any equilibrium state to have relevance for biological systems, it must also be attainable in the sense that all states through which the population passes en route to equilibrium are valid; in the case of models of numerical dynamics, this entails that all population sizes exceed one or the minimum necessary for reproduction (Asmussen and Feldman 1977; see also Roberts 1974; Bernstein 1986). For the models presented below, we therefore numerically iterated the recursions to verify that the equilibria were indeed attainable. While coexistence was possible in these models, only a subset of the predicted equilibrium values could be attained by biologically reasonable trajectories.

THE MODELS

We first describe the basic density-dependent transmission model (Model I) and then discuss two models (Models II, III) that incorporate the essential features of host-pathogen systems with frequency-dependent disease transmission. In all these models, host individuals are classified into one of two categories: uninfected, in which all individuals are susceptible, or infected, in which all individuals are sterile and infective. This structure is consistent with the observation that partially diseased *Silene* individuals are rare and transient in natural populations (plants can have both healthy and diseased stems in the first year of infection) (Alexander and Antonovics 1988). The models also assume that disease transmission, reproduction, and mortality occur simultaneously. Thus, host individuals that are classified as susceptible at time t either die or contribute to reproduction until time $t + 1$, even if they become infected. In the case of *Silene*, there is a considerable lag time between receipt of spores and the appearance of diseased flowers, such that both seeds and pollen are produced during the first year of infection.

Models I and II follow other general epidemiological models (see, e.g., May and Anderson 1979; Anderson and May 1981) in assuming that transmission rate is constant over all frequencies and densities (but see Anderson and May 1991). Model III extends the ideas in Model II by representing transmission rate as a function of the number of contacts by disease vectors, as well as the frequency of infected hosts. For convenience, symbols and parameters used in model equations, together with their definitions, are included in appendix A.

Model I

If disease transmission is density-dependent, the numbers of susceptible (X_{t+1}) and infected (Y_{t+1}) hosts in time period $t + 1$ are determined by

$$X_{t+1} = X_t \left(1 + \frac{b_0}{b_1 N_t + 1} - d - \beta Y_t \right), \quad (1)$$

$$Y_{t+1} = Y_t (1 + \beta X_t - d). \quad (2)$$

In equations (1) and (2), density-dependent factors that act independently of the disease are subsumed by the per capita reproductive rate $b_0/(b_1 N_t + 1)$, which declines hyperbolically as adult population size N_t increases. The parameter b_0 is the maximum host reproductive rate, and b_1 is a constant that determines the strength of density dependence. Density regulation is a function of total population size rather than the number of healthy adults because infected individuals, though sterile, continue to contribute to the population density. Because there is no seed transmission of the disease, all individuals recruited into the population as seedlings are susceptible, whereas infected individuals arise only from (sexual) adults. Moreover, because the seedling stage is very susceptible to density effects (Harper 1977; Shaw 1986, 1987), density dependence is assumed to act on susceptible but not on infected individuals (Thrall et al. 1993a).

Both susceptible and infected hosts have the same constant death rate (d). The model assumes that there is no disease-induced mortality and that infected individuals do not recover. Model validity requires that β and d be sufficiently small in order to ensure that the number of susceptible individuals that die or become infective does not exceed the initial number of susceptible individuals. This requirement entails two conditions on β : First, the population growth of susceptible hosts must be positive, and thus,

$$\beta < \frac{(b_1 N_t + 1)(1 - d) + b_0}{Y_t(b_1 N_t + 1)} \quad (3)$$

(from eq. [1]). Second, the production of newly infected individuals must not exceed the number of susceptible hosts in the previous time interval if

$$\beta < \frac{1}{Y_t} \quad (4)$$

(from eq. [2]). Provided that $b_0 > d$, inequality (4) is always more restrictive than inequality (3).

Model II

If, in contrast, disease transmission is frequency-dependent, the numbers of susceptible and infected hosts are determined by

$$X_{t+1} = X_t \left(1 + \frac{b_0}{b_1 N_t + 1} - d - \beta \frac{Y_t}{N_t} \right), \quad (5)$$

$$Y_{t+1} = Y_t \left(1 + \beta \frac{Y_t}{N_t} - d \right). \quad (6)$$

In this case, validity of the model again requires that d and β be small, with now $\beta < N_t/Y_t$ a sufficient condition (from eq. [6]; compare with Model I). The units of β are time^{-1} under Model I and $\text{individual}^{-1} \text{time}^{-1}$ under Model II. All other parameters in equations (5) and (6) are as defined for Model I.

Model III

Here we take into account that vectors are likely to pay multiple visits to each host or that there may be multiple sexual contacts in a venereal disease (see also Antonovics et al. 1995). The probability that a given susceptible individual contracts the disease increases with the number of visits.

We assume that the per-contact probability of becoming infected is equal to $\delta Y_t/N_t$, where Y_t/N_t is the probability of vector-mediated or sexual contact with an infected host, and δ is the probability of successful infection as a result of that contact. Assuming that each host individual receives n contacts per season, the overall probability of becoming infected (P_i) after n contacts is

$$P_i = 1 - \left(1 - \delta \frac{Y_t}{N_t}\right)^n. \quad (7)$$

In the analysis that follows, we approximate equation (7) by ignoring terms of third and higher order in $\delta Y_t/N_t$:

$$P_i \approx \left(\delta n \frac{Y_t}{N_t}\right) - \frac{(n-1)}{2n} \left(\delta n \frac{Y_t}{N_t}\right)^2. \quad (8)$$

This approximation requires that $\delta n Y_t/N_t$ be small, which constrains the relative sizes of δ and n . We require that Θ , defined as δn , be less than unity. Model III is identical to Model II but with $\beta Y_t/N_t$ replaced by P_i from equation (8):

$$X_{t+1} = X_t \left(1 + \frac{b_0}{b_1 N_t + 1} - d - P_i\right), \quad (9)$$

$$Y_{t+1} = Y_t(1 - d) + X_t P_i. \quad (10)$$

In the case of a single contact ($n = 1$), equations (9) and (10) reduce to equations (5) and (6), with Θ/n replacing β . Model III can thus be considered as a generalization of Model II for values of β restricted to less than unity.

MODEL ANALYSIS

Model I

Complete extinction is globally stable if the birth rate lies below the death rate ($b_0 < d$). Otherwise, low transmission rates satisfying

$$\beta < \frac{b_1 d^2}{b_0 - d} \quad (11)$$

ensure that the pathogen cannot increase when rare, and, in the absence of the pathogen, the number of host individuals shows global convergence to

$$X^* = \frac{b_0 - d}{b_1 d}. \quad (12)$$

Both healthy and infected individuals increase when rare if both $b_0 > d$ and the inequality in equation (11) is reversed. In this case the system described by equations (1) and (2) has a single internal equilibrium at

$$X^* = \frac{d}{\beta}, \quad (13)$$

$$Y^* = \frac{F^* \beta - \beta - b_1 d}{b_1 \beta}, \quad (14)$$

where F is a new variable ($F_t = b_1 N_t + 1$) that satisfies the quadratic

$$F^2 \beta - F \beta - b_0 b_1 = 0. \quad (15)$$

Inequality (11) is not a sufficient condition for local stability of the internal equilibrium, which requires sufficiently low transmission rates. Three qualitative behaviors arise depending on the magnitude of β . For low transmission rates ($\beta < \beta_1$), the population returns to the internal equilibrium in a nonoscillatory manner following local perturbations; for intermediate rates ($\beta_1 < \beta < \beta_2$), the approach is oscillatory; and for higher rates ($\beta_2 < \beta$), the equilibrium is unstable. Appendix B describes the analysis and determination of β_1 and β_2 .

Model II

Complete extinction is globally stable if the birth rate lies below either the death rate or the disease transmission rate ($b_0 < \max(d, \beta)$). For $b_0 > d > \beta$, the pathogen cannot increase when rare, and in the absence of the pathogen, the number of host individuals shows global convergence to equation (12) as in Model I.

Both healthy and infected individuals increase when rare if

$$d < \beta < b_0, \quad (16)$$

and the system described by equations (5) and (6) has a single internal equilibrium at

$$X^* = \frac{d(b_0 - \beta)}{b_1 \beta^2}, \quad (17)$$

$$Y^* = \frac{(\beta - d)(b_0 - \beta)}{b_1 \beta^2}. \quad (18)$$

Inequality (16) is not a sufficient condition for local stability of the internal equilibrium (see app. C). The population approaches the equilibrium in a non-oscillatory fashion if

$$\beta < \frac{5b_0 d}{4b_0 + d}. \quad (19)$$

If equation (19) is violated, the population oscillates about the equilibrium following local perturbation, but it returns provided that

FIG. 1.—Equilibrium population size (solid line) and equilibrium disease frequency (broken line) as a function of (A) disease transmission coefficient, β (Model II), and (B) infection rate, θ (Model III, range A), for fixed values of $d = 0.2$, $b_0 = 1.5$, and $b_1 = 0.0083$. The lower graph shows results for two values of n , the number of vector contacts. Vertical dashed lines ($T_1 - T_2$) represent thresholds for changes in dynamic behavior of the system near the internal equilibrium. If β (or θ) is smaller than T_1 (the host death rate, d), the pathogen cannot invade and the host reaches its carrying capacity. Values of β or $\theta > T_4$ (maximum host reproductive rate b_0) lead to extinction of both host and pathogen. For β or $\theta < T_2$, convergence to the internal equilibrium is nonoscillatory; for β or $\theta > T_2$ convergence is oscillatory. Limit cycles occur in the region $T_3 < \beta < T_4$ (Model II). This region is absent in Model III.

$$\beta < 1 + d. \quad (20)$$

If inequality (20) is violated (which requires $\beta > 1$), then stable limit cycles occur. It is easy to see from equation (20) that the effect of increasing d is to increase the range of β values over which a stable equilibrium is possible. Within this region, increasing β leads to increases in the equilibrium disease frequency, with corresponding decreases in total population size (fig. 1A).

Model III

Complete extinction is globally stable for low host reproductive rates satisfying

$$b_0 < \max \left[d, \theta \left(1 - \theta \frac{n-1}{2n} \right) \right]. \quad (21)$$

If the inequality in equation (21) is reversed, then for low infectivity ($d > \Theta$), the pathogen is uniformly purged from the population and the host population increases to its carrying capacity, which is identical to the uninfected carrying capacity for Model II (see eq. [12]). This behavior is qualitatively similar to that exhibited by Model II.

A single internal equilibrium exists for two sets of parameter ranges:

$$b_0 > \theta > d,$$

and for $n > 1$,

$$\theta > b_0 > \theta \left(1 - \theta \frac{n-1}{2n} \right)$$

with

$$b_0 \left(1 - \frac{2n(\theta - b_0)}{\theta^2(n-1)} \right) > d. \quad (22)$$

We refer to these ranges as A and B, respectively. The internal equilibrium is always locally stable (see app. D). The condition for real eigenvalues involves a sixth-degree polynomial in δ ; numerical evaluation of equations (9) and (10) indicates a single threshold in Θ , with oscillatory convergence to the internal equilibrium occurring for Θ near the upper end of range A and nonoscillatory convergence for Θ near the lower end of range A. This behavior is consistent with that observed in Models I and II, in which high β values resulted in oscillations. Figure 1B shows that increasing Θ leads to increases in the equilibrium disease frequency and a decrease in equilibrium population size as in Model II. The equilibrium disease frequency decreases if the number of visits required to achieve a given infection rate increases (compare with fig. 1A).

Two major qualitative differences distinguish this model from Model II, which assumes frequency-dependent transmission but with $n = 1$. First, there is no possibility of limit cycle behavior in Model III (this would also be true for Model II if values of β were restricted to the range (0, 1)). Second, range B requires that $n > 1$ and corresponds to a new equilibrium class that has no analogue in Model II.

Figures 2 and 3 show how the nature of the approach to equilibrium depends on Θ and d for fixed values of n and b_0 . Figure 2 plots the minimum value of Θ that generates oscillatory convergence within range A. In Model II, high β values also result in oscillations (see fig. 1A). Figure 2 also indicates that it is the size of Θ relative to d that determines the nature of the convergence, with n by itself

FIG. 2.—Threshold values for the infection rate, Θ , as a function of the host death rate, d , obtained from Model III, range A ($b_0 > \Theta > d$) for three values of the number of vector contacts: *solid circles*, $n = 2$; *open circles*, $n = 5$; *solid squares*, $n = 100$. Values of Θ greater than threshold values (*plotted lines*) result in oscillatory convergence to equilibrium (shaded area shown for $n = 100$). For Θ less than threshold values, convergence is nonoscillatory. Note that n has little effect on the outcome even in this example, which assumes large maximum host reproductive rate ($b_0 = 10$).

FIG. 3.—Threshold values for the infection rate, Θ , as a function of host death rate, d , obtained from Model III, range B for four values of the number of vector contacts: *solid circles*, $n = 2$; *open circles*, $n = 5$; *solid squares*, $n = 10$; *open squares*, $n = 100$. Values of Θ smaller than threshold values result in oscillatory convergence to equilibrium (shaded area shown for $n = 2$). For Θ greater than threshold values, convergence is nonoscillatory. Families of curves are shown for different maximum host growth rates: A, $b_0 = 0.05$; B, $b_0 = 0.4$; C, $b_0 = 0.6$; D, $b_0 = 0.95$.

having little effect, even for unrealistically high growth rates ($b_0 = 10$; for smaller values of b_0 , n has even less effect). In particular, the threshold for oscillatory behavior determined from Model II ($n = 1$) very closely approximates the threshold for Model III irrespective of n .

Within range B, the nature of convergence to the internal equilibrium again depends on whether Θ exceeds a single threshold. In contrast to range A, low values of Θ satisfying range B lead to oscillatory convergence to the internal equilibrium. Figure 3 plots the threshold value of Θ below which oscillatory convergence occurs. The value of Θ must exceed b_0 for the existence of this parameter range (see eq. [22]). For values of Θ close to b_0 (bottom of range for Θ plotted in fig. 3), convergence to equilibrium is oscillatory for nearly all values of d and n . Oscillatory convergence occurs under a smaller range of parameter values as Θ departs from b_0 . Unlike range A, the number of contacts (n) has a marked effect in this case, with larger numbers of contacts broadening the parameter ranges within which oscillations occur.

In summary, the extension of Model II to incorporate multiple contacts with disease vectors ($n > 1$) permits the existence of an internal equilibrium for high transmission rates ($\Theta > b_0$, range B in eq. [22]) as well as low transmission rates ($b_0 > \Theta$, range A in eq. [22]). While this internal equilibrium is always locally stable, convergence is oscillatory for transmission rates close to the maximal rate of increase of the host (Θ near b_0) and nonoscillatory for transmission rates above or below this value.

The qualitative behavior observed for Model III agrees generally with that reported for previous models incorporating frequency-dependent disease transmission and density-dependent host growth (Getz and Pickering 1983; Alexander and Antonovics 1988; Thrall et al. 1993a). Although these earlier analyses did not investigate whether limit cycle behavior can occur, all models, including ours, indicate three possible stable states: disease-free host populations, host-pathogen coexistence, or extinction of both host and pathogen. In our Model II, these dynamic states arise under low, intermediate, and high rates of transmission, respectively (see fig. 1A).

Attainability of Equilibria

The analyses described above indicate that stable coexistence of hosts and pathogens can be maintained under broad ranges of parameter values. However, numerical iteration of the recursions show that only a subset of these values guarantees internal equilibria that are attainable (*sensu* Asmussen and Feldman 1977), which means that host and pathogen population sizes pass through only biologically valid values ($X_t, Y_t > 1$) en route to equilibrium. Figure 4A illustrates that the attainable fraction of possible internal equilibria is particularly small in Model I, which assumes density-dependent disease transmission. Attainable dynamics in the density-dependent disease transmission model (Model I) are almost entirely restricted to damped oscillations. In the frequency-dependent transmission models (Models II, III), this fraction is increased, with even greater expansion occurring under Model III, which allows multiple visits of the disease vector (compare fig. 4B and C).

FIG. 4.—Parameter values guaranteeing validity (*hatched area*) and attainability (*double-hatched area*) of internal equilibria ($d = 0.2$, $b_0 = 1.5$) in (A) Model I, (B) Model II, and (C) Model III. Note differences in scale in A and B. For Model III, attainability is indicated for two different values of the number of vector contacts: $n = 100$ (*double-hatched*) and $n = 50$ (*densely double-hatched*).

The numerical analyses also show that stable limit cycles cannot be attained for biologically realistic population sizes in either Model I or Model II and are feasible (X^* , $Y^* \geq 1$) only in the frequency-dependent case (Model II); parameter values leading to oscillatory behavior often result in loss of the pathogen or, in some cases, population extinction. Persistent oscillatory behavior also does not occur in Model III, but in this case the approximation requires that we restrict θ to be less than unity (recall that limit cycle behavior only occurs in Model II for $\beta > 1$).

DISCUSSION

The theoretical models for host-pathogen population dynamics developed by May and Anderson (see, e.g., Anderson and May 1978, 1979, 1981; May and Anderson 1983) have provided valuable insight into the ways in which both ecological and genetic factors can affect the spread of disease in susceptible host populations. Models incorporating density-dependent disease transmission have proven to be most useful for understanding the dynamics of systems in which pathogens are passively transmitted, for example, airborne or directly transmitted by viral or protozoan infections (Anderson and May 1981). For example, Jaffee et al. (1992) found that populations of nematodes and pathogenic soil fungi exhibited dynamics consistent with density-dependent disease transmission. However, the biology of sexually transmitted or vector-borne diseases suggests that transmission rates are likely to be more influenced by the proportion than the absolute number or density of infected individuals in the population (May and Anderson 1979; Anderson 1981*b*; Getz and Pickering 1983; Alexander and Antonovics 1988; Alexander 1990*a*; Anderson and May 1991).

Anderson and May (1980, 1981) described stable limit cycles and chaotic dynamics in host-parasite models with density-dependent disease transmission. They suggested that dynamic behavior of this sort is most likely to occur when infective stages are long-lived and pathogenicity is high. In our Models I and II, stability analyses indicate that high transmission rates combined with no disease-induced mortality lead to limit cycles but no chaos, and such dynamics do not appear to be a property that emerges readily from our models. In Model III, in which the expected number of successful infections per individual is constrained to fall below unity ($\Theta < 1$), persistent oscillations cannot occur. We note that the differences in our results from those of May and Anderson may be entirely due to the use of a discrete framework here, whereas their models are continuous in nature. Continuous models are certainly appropriate in the case of diseases that operate on short time scales (as do the diseases they discuss), but other cases may be better described by discrete models (e.g., anther-smuts, in which discrete time intervals are the rule).

Moreover, numerical evaluations of our models show that for all parameter combinations examined, limit cycles are not attainable for biologically meaningful population sizes. Numerical iterations of our models further showed that only a small subset of equilibria involving stable coexistence of host and pathogen is attainable. The results for Model I in particular (density-dependent disease transmission; fig. 4A) indicate that the fraction of feasible equilibria that are attainable is extremely limited. As a consequence, the range of biologically meaningful dynamic behaviors exhibited by these models is rather more restricted than local stability analyses would indicate.

We concur with the statement made by Asmussen and Feldman (1977) that it is necessary to examine the overall behavior of a given model to determine its actual relevance for biological systems. Although examination of model equilibria for attainability has been rare in the literature, attainability is likely to be a matter

of general concern for ecology and population biology, especially in evaluating models of antagonistic interactions between species (e.g., host-pathogen, predator-prey, competition) for which oscillatory dynamics are often predicted by local stability or isocline analyses.

Under the assumption that transmission rates are constant, susceptible hosts will contract the disease with a fixed probability for a given level of exposure. However, transmission rates may well vary over the growing season or with changes in disease frequency. For example, in vector-mediated diseases, disease vectors are likely to pay multiple visits to hosts. While it is reasonable to assume that the chance of contracting the disease will increase monotonically with the number of visits, with increasing disease frequency, a higher proportion of these visits will result in spore deposition on already-infected individuals. Thus, the number of new infections as the number of visits increase will increase at a slower rate at higher disease incidence (see Heesterbeek and Metz 1993).

At high disease frequencies, Models I and II can predict the production of more individuals in the next time interval that are infected than were present as healthy individuals in the previous time interval for high transmission rates. Biologically, this situation corresponds to extinction rather than the limit cycle behavior indicated by stability analyses. This problem arises in both Model I and Model II, in which model validity requires that external restrictions be placed on the allowable range of values for β (see The Models). Because the transmission parameter β was not derived from any consideration of the biology of host-pathogen interactions, there are no natural constraints. This is not the case for the transmission term derived in Model III, in which the constraint on Θ arises only in the context of the approximation (eq. [8]) used to analyze the model.

Model III incorporates a generalized functional form for the infection probability per unit time (see eq. [7]). For one vector contact per time unit ($n = 1$), the infection probability (P) reduced to a linear function of disease incidence as in Model II (fig. 5). For greater numbers of contacts ($n > 1$), the probability of transmission increases nonlinearly with disease incidence (fig. 5). Unlike the parameter β in many previous models, δ has a clear interpretation as the probability of successful infection once there has been contact with a diseased individual or vector; it is thus a true probability taking on nonnegative values less than or equal to unity.

Clearly, the dynamic outcomes of epidemiological models will depend critically on assumptions about the transmission process. Future development of theory should include exploration of more realistic models of the transmission dynamics that can accommodate the whole range of infection processes from extreme cases in which disease transmission is purely density-dependent to the more general situation of frequency-dependent transmission. In vector-borne and sexually transmitted diseases, both mating frequencies and vector transmission rates are unlikely to be completely independent of population density. It does not seem unreasonable that at the extremes of population density, there may be qualitative changes in vector behavior such that transmission will shift from frequency to density-dependent or vice versa. Characterization of the transmission process in

FIG. 5.—Transmission probability (P) as a function of disease prevalence (Y/N) for different mean numbers of vector contacts (n). A, Per-contact probability of infection (δ) = 0.1; B, δ = 0.5.

a conceptually unified manner is essential for comparative studies on how the transmission process affects population dynamics and for studies on the evolution of different transmission modes (Antonovics et al. 1995).

It has been argued that frequency-dependent or ratio-dependent models may be generally more useful than mass-action models in reflecting processes that occur in situations in which individual organisms interact actively to produce dynamics observed at the population level (Getz 1984; Arditi and Ginzburg 1989; Berryman 1992; Ginzburg and Akcakaya 1992). For example, in predator-prey systems there is also likely to be a dynamic interaction between a predator population and its prey, such that population growth is a function of both the numbers of prey and the numbers of predators. Such "ratio-dependent" models have much in common with frequency-dependent disease transmission models, in which the prey/resource is the susceptible host, and transmission is a function of the number of encounters per infected host.

While the models presented here are simplistic and general in their assumptions, such models can provide a useful starting point for studying the dynamics of host-pathogen systems. The models described above have been evaluated

(Thrall and Jarosz 1994a, 1994b) using long-term experimental populations of the anther-smut *Ustilago violacea* and its associated host, *Silene alba*. The results showed that observed dynamics were qualitatively similar to model predictions and that dynamics were best described by a nonlinear frequency-dependent transmission function. While the results of the empirical studies suggest that the current models have some basis in reality, such models need to be extended to consider a wider range of host-pathogen systems, including both animal and human sexually transmitted diseases, and to examine other features likely to be important, including host recovery, immunity, and vertical transmission.

Variation in transmission rates due to genetic variation in the levels of resistance in hosts and virulence in pathogens can also have important consequences for both the numerical and genetic dynamics (May and Anderson 1983; Antonovics 1994). These situations may give rise to quite different dynamics; for example, under the assumption that costs of resistance are borne by males only, stable limit cycles are possible (Antonovics 1994).

Recently, there has been a surge of interest in the dynamics of the transmission process itself (see, e.g., Diekmann and Kretzschmar 1991; Blower and McLean 1991; Heesterbeek and Metz 1993; Antonovics et al. 1995). The transmission dynamics of sexually transmitted or vector-transmitted host-pathogen systems will depend on the behavior of sexual partners in the former and on both host and vectors in the latter (Antonovics et al. 1995). Characterizing the functional form of the transmission process and how it depends on behavioral changes in component organisms is of obvious importance for the population dynamics of host-pathogen systems.

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APPENDIX A

DEFINITIONS OF MODEL PARAMETERS AND SYMBOLS

SYMBOLS USED IN MODELS I–III

X_t	Numbers of healthy (susceptible) hosts at time t
Y_t	Numbers of infected hosts at time t
N_t	Total population size at time t ($= X_t + Y_t$)
b_0	Maximum per capita production of offspring
b_1	Constant determining the strength of density-dependent effects on juvenile survival
d	Disease-independent host death rate
β	Disease transmission parameter

ADDITIONAL SYMBOLS USED IN MODEL III

- δ Per-contact probability of infection
 n Number of vector-mediated or sexual contacts
 P_i Overall probability of infection given n contacts
 Θ δn (equivalent to β in the case of a single contact)

APPENDIX B

MODEL I

We rewrite equations (1) and (2) in terms of N (total population size):

$$N_{t+1} = N_t \left(1 + \frac{X_t b_0}{N_t (b_1 N_t + 1)} - d \right). \quad (\text{B1})$$

Total population size declines uniformly ($N_{t+1} < N_t$) if $d > b_0$, which indicates that $d > b_0$ is sufficient for extinction from all starting conditions.

Positivity of the internal equilibrium (from eqq. [13] and [14]) requires that

$$F^* > \frac{\beta + b_1 d}{\beta}, \quad (\text{B2})$$

where F^* is the positive root of equation (15). Condition (B2) entails that the equilibrium described by equations (13) and (14) exists only if the inequality in equation (11) is reversed.

REAL EIGENVALUES

The slope of the characteristic equation ($C(\lambda)$) evaluated at $\lambda = 0$ for the internal equilibrium is

$$C'(0) = b_0 b_1 d - 2b_0 b_1 - 2F\beta, \quad (\text{B3})$$

which is always negative. Thus, if the roots of $C(\lambda)$ are real, the eigenvalue that is largest in absolute value is positive. Similarly, the slope of $C(\lambda)$ evaluated at $\lambda = 1$,

$$C'(1) = \frac{b_0 b_1 d}{F^2 \beta}, \quad (\text{B4})$$

is always positive. The value of $C(\lambda)$ at $\lambda = 1$ is a linear decreasing function in F :

$$C(1) = 2b_0 b_1 + \beta + b_1 d - F(\beta + 2b_1 d). \quad (\text{B5})$$

Using equation (15), we find that $C(1)$ is positive for values of β violating inequality (11). Thus, the leading eigenvalues of $C(\lambda)$ lie in $(0, 1)$ and the internal equilibrium is stable for real roots.

COMPLEX EIGENVALUES

The value of $C(\lambda)$ has complex roots if

$$F(4b_0\beta + 9b_0b_1d + \beta d) - 8b_0^2b_1 - 4b_0\beta - 6b_0b_1d - \beta d < 0. \quad (\text{B6})$$

Elimination of F in equation (B6) using equation (15) indicates that the condition for complex roots is

$$\beta^2(16b_0^2 - 12b_0d - 4d^2) + \beta(64b_0^3b_1 - 48b_0^2b_1d - 36b_0b_1d^2) - (9b_0b_1d)^2 > 0. \quad (\text{B7})$$

Equation (B7) has one positive root, β_1 . The eigenvalues are real only for values of β less than β_1 .

Stability of the internal equilibrium in the case of complex eigenvalues requires that the zero term of $C(\lambda)$ be less than unity, or equivalently

$$\beta + b_1(1 + 2b_0 + d) - F(b_1 + 2b_1d + \beta) < 0. \quad (\text{B8})$$

Elimination of F permits reduction of the left side of (B8) to

$$\beta^2(b_0 - d) + \beta b_1(4b_0^2 - 4b_0d - d - d^2) - b_0b_1^2(1 + 4d + 4d^2) < 0. \quad (\text{B9})$$

The left side of equation (B9) has one positive root, β_2 , which lies above the minimum value of β required for existence of the internal equilibrium (from eq. [11]). For values of β greater than β_2 , the internal equilibrium is unstable.

APPENDIX C

MODEL II

We rewrite model equations (5) and (6) in terms of N (total population size) and the frequency of susceptible hosts (f_x):

$$N_{t+1} = N_t \left(1 - d + \frac{b_0 f_x}{b_1 N_t + 1} \right), \quad (\text{C1})$$

$$f_{x,t+1} = f_{x,t} \left\{ 1 + \frac{[b_0 - \beta(b_1 N_t + 1)](1 - f_{x,t})}{(b_1 N_t + 1)(1 - d) + b_0 f_{x,t}} \right\}. \quad (\text{C2})$$

From equation (C1) it can be seen that the population size uniformly declines if $d > b_0$. Similarly, equation (C2) shows that the frequency of susceptible hosts declines if $\beta > b_0$. Hence, $b_0 < \max(d, \beta)$ implies extinction of the population. Setting $N_t = X_t$ in equation (6), we find that infected individuals decrease when rare if $d > \beta$. Under equation (16) a single internal equilibrium described by equations (17) and (18) comes into existence.

The value for $C(\lambda)$ has real roots with nonoscillatory convergence to the internal equilibrium if equation (19) holds. If the eigenvalues are complex (eq. [19] is violated), the stability condition reduces to

$$C(0) < 1, \quad (\text{C3})$$

which holds under condition (20).

Under inequality (20), oscillatory convergence to the internal equilibrium occurs. For values violating equation (20), the equilibrium is locally unstable, and trajectories will depart from equilibrium in an oscillatory fashion.

APPENDIX D

MODEL III

From equations (9) and (10), we derive an equilibrium expression in terms of F (see text):

$$F^2 d \theta^2 \frac{(n-1)}{n} - F b_0 \theta \left(\theta - \frac{\theta}{n} - 2 \right) - 2b_0^2 = 0. \quad (\text{D1})$$

Equation (D1) has one positive root, F^* . Positivity of X^* and Y^* requires that F^* lie in $(1, b_0/d)$. A single valid internal equilibrium exists under either of the parameter ranges (A and B) described in equation (22).

REAL EIGENVALUES

The characteristic equation $C(\lambda)$, evaluated at $\lambda = 1$, assumes the value

$$C(1) = \frac{d(F-1)(F^2d\theta - 2Fb_0d + b_0^2)}{F^2b_0}, \quad (D2)$$

and the slopes of the function $C(\lambda)$ at $\lambda = 0$ and $\lambda = 1$ are

$$C'(0) = \frac{F^2d\theta - b_0d - 2Fb_0}{Fb_0} \quad (D3)$$

and

$$C'(1) = \frac{d(F^2\theta - b_0)}{Fb_0}. \quad (D4)$$

Under conditions necessary for the existence of the internal equilibrium ($\Theta > d$ and $F > \max(1, b_0/\Theta)$), $C(1)$ and $C'(1)$ are positive and $C'(0)$ is negative. Hence, whenever $C(\lambda)$ has real roots, trajectories initiated close to the internal equilibrium approach it in a non-oscillatory fashion.

COMPLEX EIGENVALUES

If the roots of $C(\lambda)$ are complex, the condition for local stability is

$$F^3\theta(1-d) + F^2d(2b_0 + \theta) - Fb_0(1 + b_0 + 2d) + b_0^2 > 0. \quad (D5)$$

Under both ranges A and B in equation (22), condition (D5) has three real roots: one negative, one in $(0, \min(1, b_0/\Theta))$, and one between b_0/Θ and 1. Because condition (D5) is positive for F greater than $\max\{1, b_0/\Theta\}$, the range in which F^* lies, we conclude that the internal equilibrium is always locally stable, even if $C(\lambda)$ has complex roots.

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