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Non-linear Transmission Rates and the Dynamics of Infectious Disease

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This study considers how non-linearities in the transmission of microparasitic infections affect the population dynamics of host-parasite systems in which the disease is potentially lethal to the host. Non-linearities can either lead to a locally stable or unstable host-parasite equilibrium point, depending on the respective contributions of healthy and infected hosts to the functional form of the transmission rate. Analysis of the non-linear transmission model results in a revealing pair of local stability criteria. Specifically, stability requires sufficient total levels of intrinsic growth of the host population and total levels of density-dependent transmission. The most stable systems occur when increases in the density of healthy hosts result in increases in transmission efficiency, and increases in the number of infected hosts result in small decreases in transmission efficiency. These appear to be very reasonable relationships for directly transmitted microparasites.

Introduction

A central assumption of many compartmental models of the dynamics of infectious disease is that parasite transmission rate is directly proportional to the densities of the susceptible and infected host populations (e.g. Anderson & May, 1979, 1981; Holt & Pickering, 1985; Hochberg & Holt, 1990). This "random" or "homogeneous" mixing rule applies to host-parasite systems in a manner analogous to random search in prey-predator and host-parasitoid models (for review, see Hassell, 1978). The homogeneous mixing assumption is most appropriate in situations where (1) transmission occurs through direct contact between susceptible and infected hosts, (2) both healthy and diseased hosts are highly mobile and do not discriminate among one another, (3) changes in the density of parasitized hosts do not alter the incidence of infection (i.e. number of new infections initiated per infected host) and (4) changes in the density of healthy hosts do not alter the per capita vulnerability, or risk, to infection. Even when these constraints are not strictly met, the random mixing assumption is generally regarded as a good first approximation of actual parasite transmission rates in nature (e.g. Anderson, 1980; Anderson & May, 1979, 1981).

Nevertheless, there are a number of biological mechanisms which may result in non-linearities in the transmission rates of parasites. For instance, the transmission

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of parasites by intermediate hosts, such as biting arthropods, may give rise to inverse relationships between the population size of healthy hosts and transmission rate (Aron & May, 1982). Under such circumstances increasing the density of susceptible hosts with respect to infected ones results in a dilution effect. On the other hand, transmission rate may rise with host density, but at a less than linear rate. This may happen when the parasite produces relatively short-lived transmission stages which have to reach a certain concentration to cause infections, or when increasing host density results in impediment of the transmission of the disease. For example, infections of insects caused by viruses almost invariably require that more than a single viron be consumed by the host (Burges, 1981). Finally, increases in the vulnerability of healthy hosts to infection may be brought on by nutritional stress, commonly associated with increased competition at high host densities (Steinhaus, 1958; Martignoni & Schmid, 1961; Schultz & Baldwin, 1982; but see Woods & Elkinton, 1987).

Several theoretical studies have explored the implications of non-linearities in transmission rate for host-parasite interactions (e.g. Bailey, 1975; Anderson, 1979*a*, 1980; Post *et al.*, 1983; Liu *et al.*, 1987 and references therein). For instance, Anderson (1979*a*) described how the biology of host-parasite associations could determine the functional form of the transmission rate. He showed, in particular, that a transmission saturation term resulting from, say, the production of short-lived external infectious stages, could transform an otherwise stable interaction into one which exhibits limit cycles. Liu *et al.* (1987) demonstrated that in cases where the host could exhibit lasting immunity to infection (i.e. for transient infections of vertebrate hosts) that non-linear incidence rates of infection could greatly expand the breadth of dynamics caused by the disease. What is to be concluded from these studies is that the biology of parasite transmission can have a profound impact on the dynamic landscape of host-parasite systems.

The purpose of the present work is to consider how transmission biology, as reflected by the relationship between host density and transmission efficiency, may affect the dynamics of a potentially lethal infectious disease. The study is divided into two parts. First, the basic homogeneous transmission model which is employed widely in studies of host-parasite systems is reviewed (Anderson & May, 1979, 1981). In agreement with the analyses of Anderson & May, regulation of the host population can only occur if the net per capita rate of increase of the infected host population is negative in value, and infected hosts can either recover from the disease and/or give birth to healthy offspring. Second, the basic transmission rate term is modified to incorporate situations in which transmission efficiency is not constant, but an independent function of susceptible and infected host densities. It is shown that local equilibrium point stability, and hence the regulation of the host population by the parasite, depends on the contributions of both healthy and diseased host populations to the efficiency of parasite transmission. Examples of the types of systems corresponding to qualitatively different forms of the transmission function are most readily found for systems exhibiting monotonic or slightly oscillatory dynamics.

Constant Transmission Efficiency

Here, the basic model of infectious disease developed by Anderson & May (1979, 1981; May & Anderson, 1979) is briefly reviewed. I will employ this model framework in developing the non-linear transmission model of the next section. The generality of the structure of the Anderson & May model makes it particularly suitable for preliminary explorations of microparasitic (e.g. viruses, bacteria, fungi, and protozoa) infections of invertebrate hosts. A variety of modifications have been made to the model's structure so as to accommodate more realistic representations of features akin to host-parasite systems in nature (e.g. Anderson & May, 1981). The framework of the Anderson & May microparasite model has served as a basis for numerous studies of infectious disease in multiple species systems (e.g. Levin & Pimentel, 1981; Holt & Pickering, 1985; Anderson & May, 1986; Hochberg & Holt, 1990).

MODEL DEVELOPMENT

The system is compartmental in nature, consisting of healthy invertebrate hosts of density S (hereafter referred to as "susceptibles"), and hosts infected with a potentially lethal microparasite of density I ("infecteds"). Actual numbers of parasites per host are not explicitly modelled (see models of macroparasites, e.g. Anderson, 1979*a*, *b*).

Susceptibles reproduce and die at per capita rates of a and b, respectively. The parasite is transmitted directly at rate β when an uninfected host comes into contact with an infected host (which is assumed to transmit the parasite immediately after infection). The term for overall transmission rate, βIS (with β the constant transmission efficiency), assumes that the healthy and diseased subpopulations of the host mix homogeneously and that there are no long-lived external stages of the parasite which can cause infections. Once infected, a host may either give birth to susceptible offspring at a per capita rate of a_1, vertically transmit the parasite to its offspring at a per capita rate of a_2, recover to the susceptible state at a per capita rate of γ, or die from natural or disease-induced causes at per capita rates of b and α, respectively. The total per capita rate of reproduction of infected individuals is thus a_1+a_2, even though some of these offspring do not become infected with their parent's disease.

A number of realistic refinements could be made to this basic set of interactions, including the production of long-lived stages of the parasite (Anderson & May, 1981; Hochberg, 1989) and the effects of parasitism on intraspecific competition for limiting resources (Anderson, 1979*a*, 1980; Anderson & May, 1981; Hochberg, unpublished ms). The system is schematically presented in Fig. 1.

The differential equations for the densities of susceptible and infected hosts are

$$\frac{dS}{dt}=(a-b)S+(\gamma+a_1)I-\beta IS \tag{1a}$$

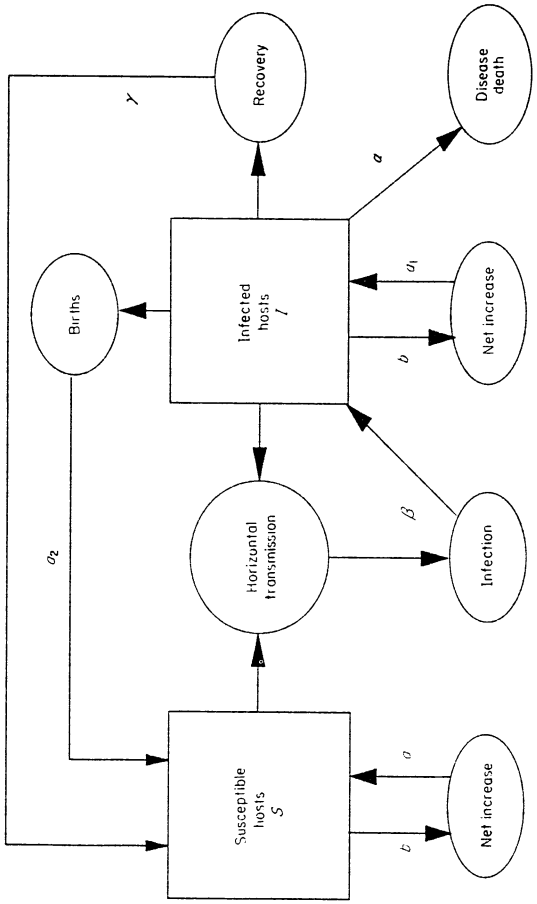


FIG. 1. Schematic flow diagram of host-parasite system (1a and b). See text for details.

$$\frac{dI}{dt} = \beta IS - (b + \alpha + \gamma - a_2)I, \tag{1b}$$

which can be further simplified by letting $r = a - b$, $e = \gamma + a_1$ and $d = b + \alpha - a_2 + \gamma$. Here, r is the familiar intrinsic rate of increase of the susceptible host, e is a measure of the contribution of parasitized individuals to the healthy subpopulation (i.e. feedback), and d represents the net rate of loss of parasitized individuals. Parameter d is a complex mixture of notions involving parasite reproductive strategy and pathogenicity, and host resistance to infection.

Substituting these simplified parameters into eqn (1a and b) gives

$$\frac{dS}{dt} = rS + eI - \beta IS \tag{1c}$$

$$\frac{dI}{dt} = \beta IS - dI. \tag{1d}$$

Note that although seven parameters are required to describe the mechanistic details of the system, four compound parameters encapsulate its dynamics.

THE EQUILIBRIUM AND POPULATION DYNAMICS

Equations (1c and d) have two equilibrium points, a trivial one at densities ($S' = 0$, $I' = 0$), and an unique positive equilibrium given by,

$$S' = \frac{d}{\beta} \tag{2a}$$

$$I' = \frac{rd}{\beta(d - e)}. \tag{2b}$$

Further, the prevalence of infection at equilibrium, Y', is given by

$$Y' = \frac{r}{r + d - e}. \tag{2c}$$

As shown in previous studies (e.g. Anderson & May, 1981; Holt & Pickering, 1985), the equilibrium exists and is locally stable if and only if $r > 0$, $\beta > 0$ and

$$d > e > 0. \tag{3}$$

Thus, stability requires that the intrinsic rate of increase of parasitized hosts be negative (i.e. $e - d < 0$; the death rate of infected individuals exceeds their own birth rate), and that parasitized individuals contribute to the growth of the susceptible subpopulation (i.e. $e > 0$) by their recovery or births. Population trajectories converge fastest, and without oscillations, to the equilibrium point for $e \to d$. Note when this limit is exceeded ($d < e$), the parasite no longer regulates its host. If $e \to 0$ the model leads to neutrally stable dynamics. The two possible dynamical behaviours leading to a positive equilibrium are illustrated elsewhere [Hochberg & Holt, 1990: Fig. 2(a) and (b)].

Thus, we can expect stable persistence of host and parasite to occur when infected hosts can recover from infection (or produce health progeny) and when the parasite is of intermediate levels of virulence to infected hosts (e.g. Anderson, 1979*b*; Anderson & May, 1981). A possible example of such an interaction is the palm rhinoceros beetle, *Oryctes rhinoceros*, and its baculovirus. Adults infected with the virus have a shortened expected life-span, but can reproduce at low levels (Zelazny, 1973). The populations of the host and pathogen show very constant levels over time (Zelazny & Lolong, 1988).

Density-dependent Transmission Efficiency

The basic model [eqn (1c and d)] assumes that the transmission efficiency, β, is constant. Here cases are considered in which transmission efficiency varies with susceptible and/or infected density. Examples of transmission biologies which could give rise to various non-linearities are briefly described where appropriate.

MODEL DEVELOPMENT

The model developed here considers a closed system (i.e. no immigration or emigration) in which non-linearities in the transmission process are assumed to be the average of the various contributing mechanisms over the whole of the subpopulations of susceptibles and infecteds. Though undoubtedly important, more mechanistic representations of the various heterogeneity generating processes are not explored in this study (e.g. Anderson Gordon, 1982; Post *et al.*, 1983; Chesson & Murdoch, 1986).

The basic transmission rate is extended and generalized by considering departures from the bilinear transmission rate βIS, in terms of two new constants, p and q, and a rescaled transmission coefficient $\hat{\beta}$, such that the transmission efficiency is given by $\beta = \hat{\beta}S^pI^q$. Constants p and q can be interpreted to represent how the densities of susceptible and infected hosts may affect (independently of one another) the per capita transmission efficiency of the parasite. In real biological systems, these constants are probably not much different from zero, and it is difficult to readily imagine situations in which their absolute values would be greater than unity. Similar transmission functions have been considered in host-parasite models incorporating immunity to infection (Liu *et al.*, 1987 and references therein).

The modified transmission term takes the form

$$\hat{\beta}[S^pI^q]IS. \tag{4}$$

Although not mechanistic in form, this function is probably a reasonable first approximation of some more general transmission processes (Liu *et al.*, 1987).

As illustrated in Fig. 2, departures from constant transmission efficiency manifest themselves in terms of no relationship, or a linear or non-linear relationship between density and the partial derivative of the transmission rate with respect to density. The shape of this relationship is determined uniquely by the values of the coefficients p and q. The contribution of p to the overall transmission rate will hereafter be

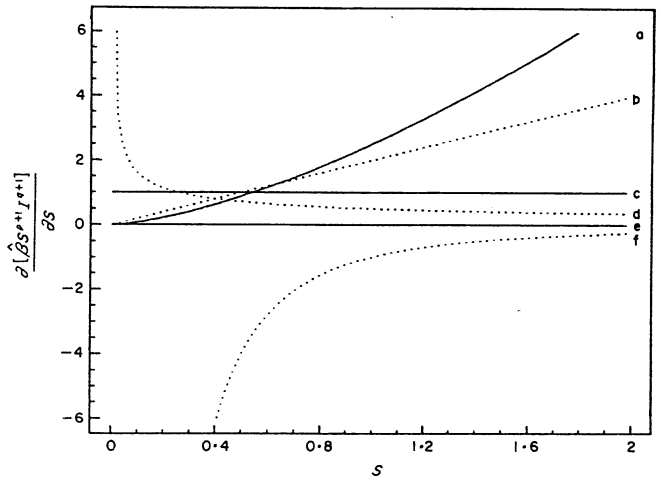


FIG. 2. Effects of transmission response and the population density of healthy hosts on the partial derivative of the transmission rate with respect to the density of healthy hosts. $\hat{\beta}$ and the density of infecteds, I, are both scaling factors and are set to unity. Type of transmission: a. $p=2$ (accelerating response); b. $p=1$ (accelerating response); c. $p=0$ (constant response); d. $p=0{\cdot}5$ (decelerating response); e. $p=-1$ (density-independent transmission); f. $p=-1.5$ (negative response).

referred to as the "susceptible response", whereas the influence of q will be called the "infected response". The "total response" is simply $p+q$.

Three types of transmission responses are distinguished below. The first two fall into the general category of positive responses to density (abbreviated "PR"), whereas the third is a negative relationship between density and transmission rate ("NR"). These and other responses are summarized in Table 1.

TABLE 1

Summary of the types of transmission responses of susceptible and infected hosts as defined in this study

Response type†	Abbreviation‡	Susceptible response	Infected response
Accelerating	AR	$p>0$	$q>0$
Constant	—	$p=0$	$q=0$
Decelerating	DR	$-1<p<0$	$-1<q<0$
Positive	PR	$p>-1$	$q>-1$
Density-independent	—	$p=-1$	$q=-1$
Negative	NR	$p<-1$	$q<-1$

† Effect of one subpopulation (i.e. susceptibles or infecteds) on the non-linearity of the transmission rate. The total response is the effect of both sub-populations on the non-linearity of the transmission rate (i.e. $p+q$).

‡ Not all responses are abbreviated in the text.

Accelerating response ($p>0$ *and/or* $q>0$), *or "AR"*

In this case, transmission efficiency increases as a function of host density, and the partial derivative of the transmission rate with respect to susceptible density increases in either a greater than linear (i.e. $p>1$) or less than linear (i.e. $0<p<1$) fashion as a function of density (Fig. 2). At the lower limit $p=0$ we regain the random mixing case for susceptibles. (Note that these same considerations apply for infecteds via parameter q.) In real systems, values of p or q greater than zero could result, for example, from stress involved in crowding (e.g. Steinhaus, 1958), giving rise to density related increases in susceptibility to infection.

Decelerating response ($-1<p<0$ *and/or* $-1<q<0$), *or "DR"*

When $-1<p<0$, this is in some ways analogous to Type II functional responses commonly observed for arthropod hosts exhibiting discrete, non-overlapping generations (Holling, 1965; Hassell, 1978). Transmission rate still increases as a function of density, but its partial derivative (i.e. transmission efficiency) decreases with density (Fig. 2). At low densities the response resembles the random mixing case, whereas at high densities it approaches transmission rates which are independent of density. Decelerating responses could arise if the efficiency of transmission were to decrease with host density due to, for example, the spatial segregation of susceptible and infected hosts, such that only segments of the two host classes mixed homogeneously.

Negative response ($p<-1$ *and/or* $q<-1$) *or "NR"*

Here, the partial derivative of transmission rate is always negative, but it increases as a function of density to a plateau of zero with increases in density (i.e. to density independence, Fig. 2). It is difficult to readily envision cases where marginal increases in either susceptible or infected density result in decreases in transmission rates. One possibility is for some vector-borne diseases, where transmission rate may be inversely proportional to the density of the host population (Aron & May, 1982). Nevertheless, it seems reasonable to assume that other processes, such as preferences for infected hosts (Kingsolver, 1987) or those described for AR, could limit or counteract the negative response, resulting in a net response which is decelerating or accelerating.

THE EQUILIBRIUM

When transmission term (4) is substituted for βIS in eqn (1c and d) a single positive equilibrium (S^*, I^*),

$$S^* = \left[\frac{d}{\hat{\beta}}\left\{\frac{r}{d-e}\right\}^{-q}\right]^{1/(p+q+1)} \tag{5a}$$

$$I^* = \left[\frac{d}{\hat{\beta}}\left\{\frac{r}{d-e}\right\}^{p+1}\right]^{1/(p+q+1)} \tag{5b}$$

results if $d>e$ and the other rate parameters (with the exception of p and q) are positive. Note that $e>0$ is no longer a strict requirement for point stability (see below). This means that non-linearities in transmission rates can stabilize an otherwise unstable (or stable but oscillatory) system in which the parasite is invariably lethal.

With respect to the existence of a non-trivial equilibrium point, except for the special case that the sum of responses is density-independent (i.e. $p+q=-1$ and no feasible equilibrium exists), the conditions for a positive equilibrium are identical to the case of bilinear transmission [see conditions in (3)]. Moreover, it can easily be shown that, like for the case of bilinear transmission reviewed in the previous section, the equilibrium prevalence of infection $[I^*/(S^*+I^*)]$ is independent of the parameters which govern the transmission process (i.e. $\hat{\beta}$, p, q). In other words, introducing constant non-linearities in the transmission response has no influence on the proportion of the host population which harbours the infection at equilibrium.

As illustrated in Fig. 3 the relationship between transmission response and resultant equilibrium values of susceptible and infected hosts is more or less constant, with the exception of a discontinuity corresponding to the sum of the parameters governing density dependence approaching the value -1 (i.e. $p+q\approx-1$). Here, as the total response due to both susceptibles and infecteds becomes density-independent, the equilibrium levels of one or both tend towards either infinity or zero (corresponding to the discontinuity at $p+q=-1$). The former course $[(S^*, I^*)\rightarrow(\infty,\infty)]$ occurs if the terms in the square brackets of (5 a and b) are greater than unity, whereas the equilibrium approaches zero if these terms are less than unity (Fig. 3). This phenomenon is similar to functional responses in host–parasitoid models, where host densitities explode as the parasitoid functional response becomes independent of parasitoid density (e.g. $k\rightarrow 0$ for the negative binomial model; May, 1978; Hassell, 1978). The model presented here reveals that it is the *total* transmission response which determines this discontinuity, and not simply the contributions of either species in isolation. This result is supported by other studies showing how the inclusion of additional density-dependent mortality factors (such as other species) can change the conditions yielding local equilibrium point stability (e.g. May & Hassell, 1981; Hochberg *et al.*, 1990; Hochberg & Lawton, 1990).

As the total transmission response departs from density independence, the effects of marginal increases in either p or q on equilibrium levels will depend in complex ways upon the values of all parameters. Inspection of (5a and b) reveals that marginal changes in parameters p or q will have large impacts on equilibrium densities, as the terms $d/\hat{\beta}$ (an inverse measure of transmission efficiency over the lifespan of the infected host) and $r/(d-e)$ (the ratio of intrinsic rates of increase between susceptibles and infecteds) deviate substantially from unity. For example, if $r/(d-e)$ is much greater than unity, marginal increases in the infected response, q, will result in large decreases in the equilibrium density of susceptibles. In contrast, if $r/(d-e)\ll 1$ then increasing q will result in correspondingly large increases in susceptible density. It is important to note that the actual value of q (about which the marginal change occurs), as well as the values of p and $d/\hat{\beta}$, also influence the magnitude of the equilibrium change.

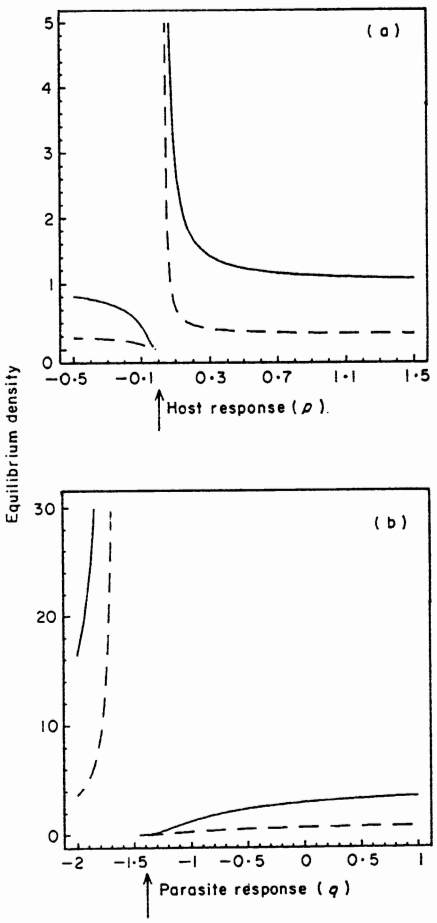


FIG. 3. Effect of transmission response on the equilibrium levels of susceptible and infected hosts. (a) Susceptible response (p). (b) Infected response (q). Solid lines refer to the equilibrium density of susceptible hosts and broken lines to hosts infected with the parasite. Arrows refer to response level where equilibrium is infeasible. Parameter values (except when otherwise varied): $r=0{\cdot}2$, $e=0{\cdot}1$, $d=1$, $\hat{\beta}=0{\cdot}2$, $p=0{\cdot}5$, and $q=-1$.

EFFECTS OF PARAMETER EVOLUTION ON HOST ABUNDANCE

The precise relationship between marginal increases in parameters p and q and equilibrium densities is found simply by taking the partial derivative of density with respect to the parameter under scrutiny. Omitting the intervening algebraic steps, the effects of the evolution (i.e. marginal change) of the parameter p on equilibrium densities are given by

$$\frac{\partial S^*}{\partial p} = S^* \tau_p \tag{6a}$$

$$\frac{\partial I^*}{\partial p} = I^* \tau_p. \tag{6b}$$

where, for notational convenience, τ_p is defined by

$$\tau_p = \frac{-\ln[d/\hat{\beta}] + q \ln[r/(d-e)]}{(1+p+q)^2}. \tag{6c}$$

Marginal changes in the susceptible response affect the magnitude of the change in equilibrium densities through the equilibrium density itself (S^* or I^*), as well as through a less recognizable term, τ_p, which incorporates all of the system parameters. The numerator of τ_p affects *both* the magnitude and sign resulting from the increment in p. The condition for marginal increases in p to result in increases in equilibrium density is simply $\tau_p > 0$ and can be restated as (after some algebraic manipulation)

$$\frac{d}{\hat{\beta}}\left[\frac{r}{(d-e)}\right]^{-q} < 1. \tag{6d}$$

This is identical to the term within the square brackets for the equilibrium level of susceptibles [i.e. eqn (5a)]. The relative magnitude of change in the equilibrium densities of susceptibles and infecteds is simply proportional to their actual densities, or

$$\frac{\partial S^*}{\partial p} \Big/ \frac{\partial I^*}{\partial p} = S^*/I^*. \tag{6e}$$

Similarly, the effects of the evolution of q on equilibrium densities are given by

$$\partial S^*/\partial q = S^* \tau_q \tag{7a}$$

$$\partial I^*/\partial q = I^* \tau_q. \tag{7b}$$

where τ_q is defined by

$$\tau_q = \frac{-\ln[d/\hat{\beta}] - (1+p)\ln[r/(d-e)]}{(1+p+q)^2} \tag{7c}$$

Equation parts (7a-c) are almost identical in form to eqn (6a-c), with the exception that the term $1+p$ has replaced $-q$ in the numerator of the term τ. Therefore, the important difference in the evolution of non-linearities arising from healthy and infected hosts occurs in the term controlling the sign of the change in equilibrium

density. Specifically, marginal increments in q will result in increases in susceptible and infected densities if

$$\frac{d}{\hat{\beta}}\left[\frac{r}{(d-e)}\right]^{p+1}<1. \tag{7d}$$

Quick inspection of (6c and d) and (7c and d) reveals that increments in p and q will always have opposing influences on the sign of the partial derivatives (and therefore on whether densities increase or decrease with changes in the shape of the form of the transmission response); on the other hand, their influences on the magnitude of change is not immediately apparent from eqns (6a-c) and (7a-c).

As shown in Table 2, the effects of the other system parameters, r, e, $\hat{\beta}$ and d, on equilibrium densities depend upon the values of the transmission response parameters p and q. For example, when the total transmission response is positive (i.e. $p+q>-1$) marginal increases in r or e result in increases in the densities of susceptibles if $q<0$, and in infecteds if $p>-1$. If either of these latter two inequalities are reversed, then the corresponding effects on equilibrium density are also reversed. If both are reversed, then the effect on equilibrium densities remains the same as for the first case. In contrast to the effects of r and e, marginal increases in transmission efficiency ($\hat{\beta}$) are always met by decreases in equilibrium densities of both healthy and infected hosts if $p+q>-1$. Finally, the effects of changes in the pathogenicity of the parasite (as measured by d) are more complicated than for the other parameters (Table 2). For instance, if the total interaction is NR (i.e. $p+q<-1$), then increases in pathogenicity result in higher densities of susceptibles if the infected response is also NR (i.e. $q<-1$), whereas lower densities result if the relationship is DR (i.e. $-1<q<0$).

In summary, these properties highlight the complex interrelationships between parameter evolution and equilibrium densities.

TABLE 2

Effect of marginal increases in parameter values on the equilibrium levels of the susceptible host (see footnotes for effects on the infected host)

	Condition			
	$p+q>-1$		$p+q<-1$	
Parameter	$q<0$†[a]	$q>0$†[b]	$q<0$†[a]	$q>0$†[b]
r	↑	↓	↓	↑
e	↑	↓	↓	↑
$\hat{\beta}$	↓	↓	↑	↓
d	$q<-1$ ↓†[c]	↑	$q<-1$ ↑†[c]	↑
	$q>-1$ ↑†[d]		$q>-1$ ↓†[d]	

† Condition giving same effect on equilibrium of infected hosts is: a. $p>-1$, b. $p<-1$, c. $p>0$, d. $p<0$.

EQUILIBRIUM POINT STABILITY AND POPULATION DYNAMICS

Given that the host and parasite persist in the system, we can now ask whether the non-trivial equilibrium point is stable, and if so, what sort of dynamics do the healthy and infected sub-populations exhibit.

A straightforward local stability analysis (May, 1974) results in the conditions

$$q+p>-1 \tag{8a}$$

and

$$q<r\left[\frac{e+pd}{d(d-e)}\right] \tag{8b}$$

for the point equilibrium to be stable to small perturbations [illustrated in the $S-I$ phase plane in Fig. 4(a)]. The first inequality is, in part, a consequence of the discontinuity of the equilibrium point at $p+q=-1$. It says that there must be a minimum level of total positive density dependence in the transmission term for the parasite to regulate the host. In addition, whereas inequality (8a) is determined only by the transmission response constants, the validity of (8b) is decided by a combination of transmission response and density independent growth and death rates. Finally, note that the transmission constant, $\hat{\beta}$, does not enter into stability considerations. This is consistent with the model presented in the first section, with other differential equation models of host-parasite systems (Anderson & May, 1981), and with difference equation models of host-parasitoid interactions (Hassell, 1978).

Inequalities (8a) and (8b) can be combined into a multiple statement for the local stability of the equilibrium point (5a and b)

$$-(1+p)<q<r\left[\frac{e+pd}{d(d-e)}\right]. \tag{9}$$

Numerical simulations of the model suggest that when both inequalities of (9) hold the equilibrium is also globally stable. It is important to stress that for more realistic transmission functions or larger species assemblages the stability results presented here would only be true for small perturbations from the equilibrium populations (Takehashi, 1964).

Some of the ramifications of this intriguing set of conditions are illustrated in Figs 4 and 5. We see that local stability of the equilibrium point requires, for a given response on the part of susceptibles, low to intermediate levels of infected response (Fig. 5).

If we specify the values of parameters r, d, e, and p, then we can deduce the boundaries of q which will result in a stable equilibrium point. In particular, beyond a minimum value of p given by

$$p>-\frac{re+d(d-e)}{rd+d(d-e)}, \tag{10}$$

the boundaries of infected response permitting a stable point, increase as the susceptible PR increases (Fig. 5); below this minimum value, a stable point is not possible. Increases in reproduction on the part of susceptible (r) and infected hosts

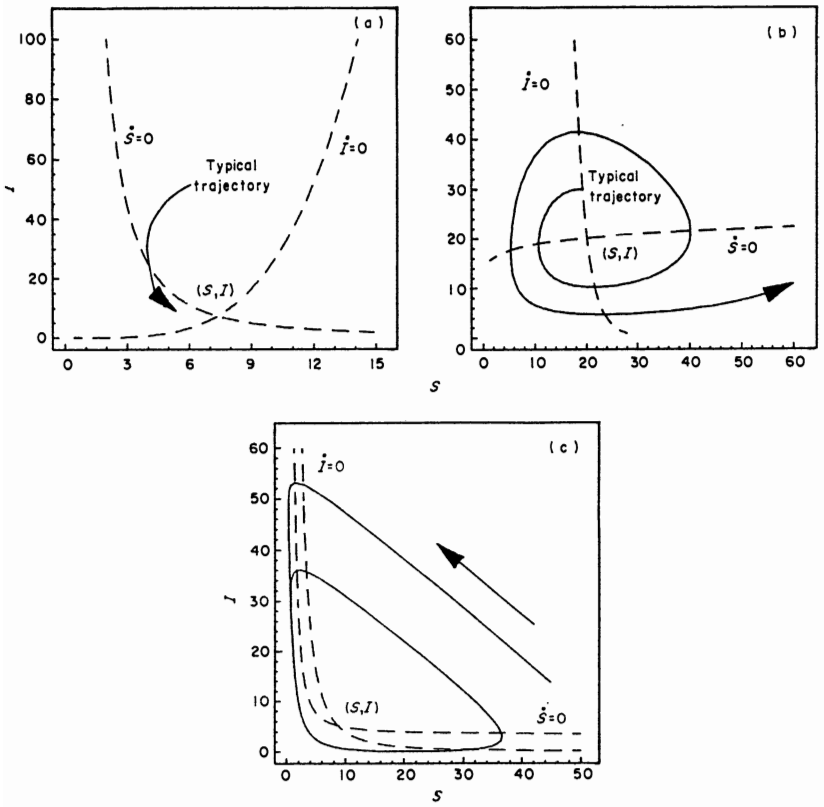
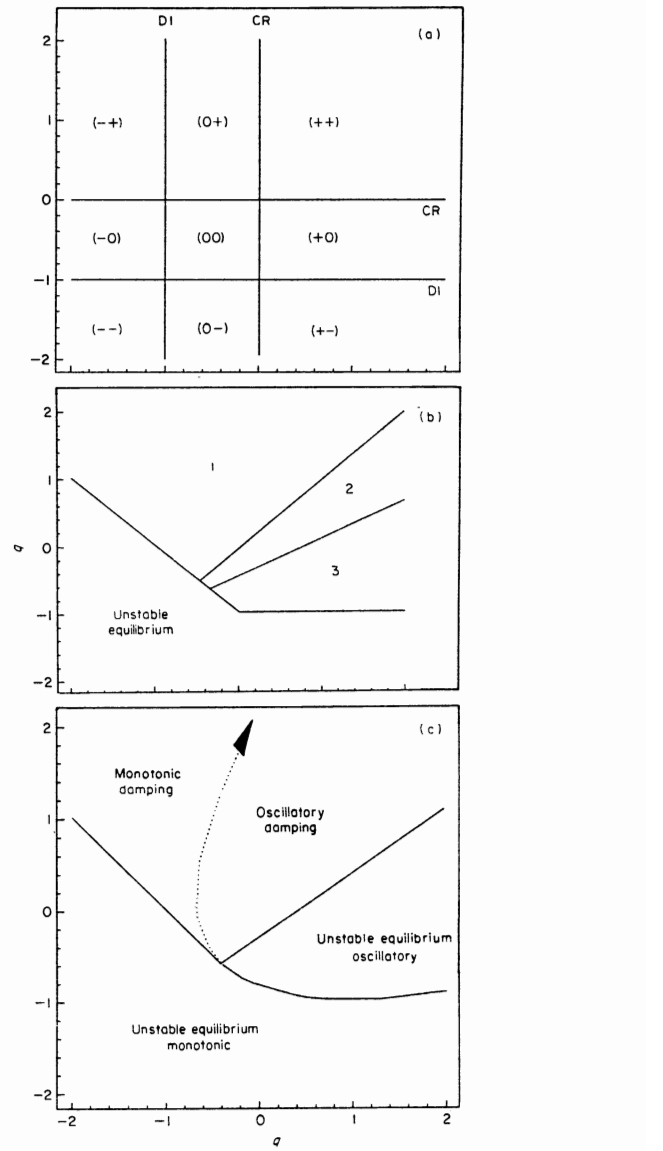


FIG. 4. Some examples of phase planes for the host-parasite system with non-linear transmission rates. (a) Locally stable equilibrium, $p=1$ and $q=-0{\cdot}5$. (b) Unstable equilibrium leading to expanding oscillations, $p=-0{\cdot}1$ and $q=0{\cdot}1$. (c) Limit cycle, $p=0$, $q=0{\cdot}5$, $e=0{\cdot}5$ and $r=0{\cdot}3$. Equilibrium is indicated by (S^*, I^*). $\dot{S}=0$ and $\dot{I}=0$ are the isoclines of zero population growth for susceptible and infected hosts, respectively. Parameters unless otherwise specified: $r=1$, $e=0$, $\hat{\beta}=0{\cdot}05$, and $d=1$.

FIG. 5. Locally stable and unstable parameter space for small perturbations from the single positive equilibrium point. (a) The nature of the transmission response due to the healthy host (p) and the infected host (q): DI, density-independent, CT, constant transmission efficiency, +, accelerating; 0, decelerating; −, negative. (b) Stable and unstable domains as functions of p, q, and e. Stable space: 1 ($e=0$); 1+2 ($e=0{\cdot}45$); 1+2+3 ($e=1$). (c) Non-equilibrium behaviour of the populations. Arrow indicates direction along broken line giving the combinations of p and q which lead to the most rapid approaches to the equilibrium ($e=0{\cdot}3$). Limit cycles occur for responses falling in the unstable oscillatory area. Other parameter values: $r=1$, $d=1$, $\hat{\beta}=0{\cdot}05$.



(e), and decreases in parasite pathogenicity (d) always increase the stable equilibrium point parameter space of allowable infected PRs (Fig. 5).

On the other hand, the susceptible response can result in a stable equilibrium if it is either decelerating or accelerating. Although unlikely in real systems (except, perhaps some vectored parasites), a susceptible NR, however, always results in an unstable equilibrium point. Note that for cases where the susceptible response is decelerating, and infected recovery and birth rates are near zero, point stability can only occur for infected DR. The parameter space permitting a stable equilibrium is largest for a pronounced susceptible PR, infected DR ($q \approx -0{\cdot}5$), and large intrinsic rates of increase of both healthy and infected hosts (i.e. r and $|e-d|$) (Fig. 5). Note that whereas susceptible PR is required for the system to persist, the equilibrium may be stable for either infected PR or NR. As the intrinsic rates of increase of susceptibles and infecteds decrease, so too must the response due to the infecteds be less PR in order for them to regulate the subpopulation of susceptible hosts.

When either or both conditions of (9) are violated, then the equilibrium point is unstable. Specifically, if inequality (8a) is violated then both susceptible and infected host populations either grow unbounded or go extinct. If inequality (8b) does not hold, then the populations may either exhibit unstable [Fig. 4(b)] or stable [Fig. 4(c)] limit cycles, or explosion of the susceptibles and extinction of the infecteds, or vice versa, depending on initial densities. A necessary requirement for limit cycles to occur is that (8a) be satisfied and (8b) violated [shaded area of Fig. 5(c)], or for high values of q and intermediate values of p. Thus, as the infected response goes from DR to AR and the susceptible response is approximately constant, the populations will tend to cycle. It could not be determined from numerical simulations if the limit cycles were globally stable or unstable.

Numerical simulations suggest that the fastest approaches to the equilibrium point after a perturbation occur as the susceptible response increases into the AR domain [Fig. 5(a) and (c)]. The relationship between population trajectories and the infected response is more complex. Here, as the susceptible response varies from density independent to random mixing, resilience increases as infected DR decreases [Fig. 5(c)]. Further, as the susceptible response continues to grow and become accelerating, the most resilient interactions occur as the infected response goes from DR to AR. The need for this shift to AR becomes more pronounced as the feedback from infected to susceptible (i.e. e) increases. Since there will undoubtedly be an upper-limit on susceptible AR, it is reasonable to assume that in real systems where susceptible AR is pronounced the most resilient interactions should occur for infecteds exhibiting approximate constant responses (i.e. $q \approx 0$).

Additional modifications to the simple model considered here could give rise to qualitatively different population behaviours. For instance, in cases where infected hosts can recover to an immune state and there exists a population equilibrium of the host in the absence of disease (requiring some sort of density-dependent regulation), Liu *et al.* (1987) showed that transmission function [eqn (4)] can permit a variety of population behaviours, including Hopf bifurcations, saddle-node bifurcations, and homoclinic loop bifurcations.

SPECIAL CASES

Before concluding, some special cases are presented below which highlight how the nature of the transmission response impinges upon the dynamics of infectious disease.

Parasite is functionally similar to a predator ($e = 0$)

Here, all parasitized hosts eventually succumb to the infection (or die of natural causes in the infected state) and the model structure resembles the classic Lotka–Volterra prey–predator equations. This is the case for many viral and bacterial infections of invertebrate hosts, especially insects (e.g. van Beek *et al.*, 1990). If we take the conversion rate from prey to predator to be σ, then the prey–predator equilibrium, S^*_{prey}, I^*_{pred}, is given by

$$S^*_{\text{prey}} = \left[\frac{d}{\beta}\left\{\frac{r}{d}\right\}^{-q}\sigma^{-q-1}\right]^{1/(p+q+1)} \tag{11a}$$

$$I^*_{\text{pred}} = \left[\frac{d}{\beta}\left\{\frac{r}{d}\right\}^{p+1}\sigma^{p}\right]^{1/(p+q+1)}. \tag{11b}$$

The local stability conditions for this interaction are simply

$$-(1+p) < q < \frac{rp}{d}. \tag{12}$$

Thus, a Lotka–Volterra type prey–predator interaction is stable if the total response (i.e. prey + predator) is positive and if the product of the prey response and intrinsic growth rate for the prey item exceeds the product of the predator response and the death rate of the predator. For the special case of a constant response of the prey (i.e. $p = 0$) the point is stable only if the predator is DR. Such a situation could arise, in principle, if predator interference (e.g. aggression) increases as a function of its density (for relevant studies, see Hassell, 1978: table 5.1).

The net intrinsic rate of increase of infecteds is zero ($d \approx e$)

When the parasite is at its limit in ability to regulate the host for the case of bilinear transmission [i.e. condition (3)], the parameter space for a stable equilibrium point is at its maximum (Fig. 5). In other words, when the host has a high recovery rate and/or the parasite is non-pathogenic, the parasite *always* regulates the host if $q > 0$ (i.e. the infected is AR). Such situations could occur for some viruses and microsporidia of insects which can be transmitted either horizontally or vertically and are relatively innocuous to their host (Steinhaus, 1963).

The density of susceptible hosts does not influence transmission efficiency ($p = 0$)

Here, increases in the density of susceptibles are met by linear increments in transmission rate (Fig. 2). Infected hosts alone could affect transmission efficiency in cases where the disease is transmitted via a vector and it is simply the number of bites by the vector which will determine the efficiency of transmission. The effect

is to limit the feasible parameter space for a stable equilibrium point to a small band of values for q (Fig. 5). The size of this band increases in the positive direction along the abscissa with increases in r and e, and decreases in d. The range of q permitting a stable equilibrium point is given by

$$-1 < q < \frac{re}{d(d-e)}, \tag{13}$$

or, the infected response must be PR if the equilibrium is to be stable.

The density of infected hosts does not influence transmission efficiency ($q = 0$)

Here $p > 0$ always results in a stable equilibrium. As the intrinsic rates of increase of susceptibles and infecteds rise, there are corresponding increases in the parameter space yielding a stable equilibrium point for susceptible DR (Fig. 5). Situations such as this could arise for parasites which are transmitted via short-lived external stages (Anderson, 1979*a*).

Density-independent transmission ($p = -1$ *and/or* $q = -1$)

In cases where transmission rate is independent of the density of susceptible hosts, equilibrium point stability is not possible. Essentially, the parasite is vertically transmitted and host mortality due to parasite pathogenicity is insufficient to stabilize the interaction (such an interaction could be stable if intraspecific competition were to occur, Hochberg, unpublished ms). However, transmission rates which are independent of infected density *do* give rise to a stable equilibrium point if the susceptible response is accelerating. [Constant susceptible responses (i.e. $p = 0$) will give rise to neutrally stable cycles.] Therefore, if transmission is independent of infected density (i.e. $q = -1$), $p > 0$ constitutes a necessary and sufficient condition to stabilize the host-parasite interaction. In this case, the transmission term itself resembles density-dependent responses used to model intraspecific competition! I know of no real situations in which this is likely to occur.

Negative response by the healthy host ($p < -1$)

If the transmission (or attack) rate is NR in healthy hosts, then the equilibrium point is always unstable. Here, increasing the number of healthy hosts results in decreases in transmission rate. As previously discussed, NR is probably rare in nature.

Same level of non-linearity in susceptible and infected subpopulations ($q = p$)

Here, the presence of the parasite within the host results in no net difference in how changes in the density of those hosts (i.e. infecteds) contribute to non-linearities in transmission rate. Assuming that the parasite is sufficiently pathogenic, i.e.

$$d > r + e, \tag{14a}$$

the stability criteria become [from (9)]

$$-\tfrac{1}{2} < p < \frac{re}{d(d-e-r)}. \tag{14b}$$

If the pathogenicity condition (14a) is not satisfied, then the direction of the right-hand side inequality is reversed. Note immediately that the conditions for stability given by (14b) are more stringent than those set out in (9). [The parameter space yielding a stable equilibrium point is the 45° line in the p, q plane (Fig. 5).] Interestingly, point stability is only rendered for *intermediate* levels of p if the parasite is sufficiently pathogenic, whereas if (14a) is reversed, stability results only if values of p are sufficiently large.

Discussion

This work demonstrates how departures from a simple bilinear model of parasite transmission can influence the dynamics of infectious disease in cases where the infection can lead to death of the host. Specifically, the parasite is most likely to regulate its host if transmission efficiency increases with susceptible host density, but has a small negative relationship to the density of infected hosts. The former requirement (i.e. $p > 0$) is a valid one for many directly transmitted microparasites of invertebrate hosts, since the density of healthy hosts is probably a good indicator of the amount of nutrient limitation (and hence susceptibility to infection) experienced. Diseased hosts on the other hand are less likely to contribute substantially to this density related susceptibility. The latter requirement (i.e. $-1 < q < 0$) is a reasonable one since the average per capita risk of a healthy host contracting the parasite cannot increase indefinitely with the number of infected hosts. Rather, any variance within the host population in the risk of contact between healthy and diseased hosts will result in a depensatory response.

It is not known whether transmission biologies which lead to oscillatory dynamics (e.g. $p < 0$, or $p > 0$ and $|q| \gg 0$) are more limited in nature. Perhaps the most readily envisaged scenario for $p < 0$ are systems in which the parasite is transmitted via a biting vector. But, mechanistic models of vector transmission show that additional details about vector biology can change the dynamics of the system (e.g. Aron & May, 1982; Kingsolver, 1987; Dobson, 1988). Situations in which $p > 0$ and $q > 0$ could be obtained when increases in the density of both healthy and infected hosts lead to increased susceptibility to the parasite. However, if the competitivity of diseased hosts is to be increased (leading to $q > 0$), the parasite should be relatively non-pathogenic. This non-pathogenicity can result in dampening population fluctuations caused by the transmission relationship [see Fig. 5(c)]. Therefore, it is reasonable to conclude that in real systems, oscillatory dynamics are not likely to be exacerbated by non-linearities in transmission efficiency, but rather stabilized by them.

A well-known result in the dynamics of host-parasite associations is that, in the absence of other regulatory factors, the parasite can only regulate the host if the former is sufficiently pathogenic (Anderson & May, 1979, 1981; May & Anderson, 1979). When non-linearities in transmission rate are explicitly included in the same model framework, this condition of sufficient pathogenicity only assures the existence of a positive equilibrium point. Regulation requires additional conditions be met. Specifically, a locally stable equilibrium point requires (1) sufficient *total* positive

density dependence in the system, contributed by susceptibles and infecteds (i.e. $p+q>-1$) and (2) a sufficiently large combination of density-independent growth and density-dependent transmission (i.e. $[re/d]+rp+(e-d)q>0$). These properties are in agreement with studies showing that regulation (=locally stable equilibrium point) requires a source of density dependence, but that the presence of density dependence does not assure regulation (for review, see Murdoch & Walde, 1988).

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