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Fatal or Harmless: Extreme Bistability Induced by Sterilizing, Sexually Transmitted Pathogens

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Abstract Models of sexually transmitted infections have become a fixture of mathematical epidemiology. A common attribute of all these models is treating reproduction and mating, and hence pathogen transmission, as uncoupled events. This is fine for humans, for example, where only a tiny fraction of sexual intercourses ends up with having a baby. But it can be a deficiency for animals in which mating and giving birth are tightly coupled, and mating thus mediates both reproduction and pathogen transmission. Here, we model dynamics of sterilizing, sexually transmitted infections in such animals, assuming structural consistency between the processes of reproduction and pathogen transmission. We show that highly sterilizing, sexually transmitted pathogens trigger bistability in the host population. In particular, the host population can end up in two extreme alternative states, disease-free persistence and pathogen-driven extinction, depending on its initial state. Given that sterilizing, sexually transmitted infections that affect animals are abundant, our results might implicate an effective pest control tactic that consists of releasing the corresponding pathogens, possibly after genetically enhancing their sterilization power.

Keywords Disease transmission · Mating · Population dynamics · Population management · Sexually transmitted disease

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1 Introduction

Since the short yet seminal article by Getz and Pickering (1983), modelers of infectious disease dynamics have discerned two baseline ways of how to model pathogen transmission. The original model, invariably used until that time and found reasonable for infections triggered by airborne pathogens (Anderson and May 1979), is now known as mass action incidence or density-dependent transmission. The alternative, suggested by Getz and Pickering (1983) and now referred to as standard incidence or frequency-dependent transmission, has since become a norm for modeling vector-borne and sexually transmitted infections (Vynnycky and White 2010). Although many discussions have passed and other transmission models have been suggested and substantiated (McCallum et al. 2001), this dichotomy is still largely used.

However, as revolutionary as this disjunction was, it has affected just the pathogen transmission term and not the other parts of models of infectious disease dynamics. In particular, it has not affected the reproduction part of the models, so that reproduction has standardly been modeled as decoupled from pathogen transmission. That is, the same birth terms (often linear, but also density-dependent) have been used irrespectively of the model of disease transmission (e.g., Busenberg and van den Driessche 1990; Gao and Hethcote 1992; Thrall and Antonovics 1997; O'Keefe and Antonovics 2002; Hilker et al. 2009; Hilker 2010). This is fine for airborne and vector-borne infections, and also for some populations challenging sexually transmitted infections such as humans in which only a tiny fraction of sexual intercourses ends up with having a baby. But it can be a deficiency for sexually transmitted infections in animals in which mating and giving birth are more intertwined, and even tightly coupled, and mating thus mediates both reproduction and pathogen transmission. As an example, consider a system where males guard their mates until they cannot be sneaked by others. In such cases, an appropriate model should let the processes of reproduction and pathogen transmission run on a common basis, which has as yet been not the case.

In this article, we model dynamics of sterilizing, sexually transmitted infections in animals, assuming structural consistency of reproduction and pathogen transmission processes, mediated by mating. Sexually transmitted infections in animals are ubiquitous, both as regards affected host taxa and etiological agents of such infections, and many of these are sterilizing (Lockhart et al. 1996; Knell and Webberley 2004). As one might expect, our model turns out to be structurally different from those commonly used to describe dynamics of sexually transmitted infections. Therefore, there is no surprise that predictions of these two model types can be formidably different. Perhaps most interestingly, highly sterilizing, sexually transmitted pathogens are shown to trigger an extreme form of bistability in the host population—the host population can persist at the disease-free equilibrium or be subject to pathogen-driven extinction, depending on its initial state; endemic equilibria, if they exist, are unstable. We suggest that pathogens triggering this form of bistability might be effective pest control agents, but also discuss limitations our model may have.

2 Models

We develop and analyze a model of infectious disease dynamics that accounts for sterilizing, sexually transmitted pathogens, and that assumes structural consistency

between the processes of reproduction and pathogen transmission, both mediated by mating. To rigorously describe the mechanics of disease transmission, we start with a sex-structured population model, and only then simplify to its asexual version, assuming that males and females share identical life histories (this is arguably one of the most common, and tacit, assumptions used in mathematical ecology and epidemiology).

The core part of any sex-structured population model is the mating function, or a model of the rate at which males and females mate. Let $\mathcal{M}(N_M, N_F)$ be a generic mating function, with N_M and N_F denoting male and female density, respectively. With this function, the common two-sex modeling framework is as follows (Hadeler et al. 1988; Lindström and Kokko 1998; Bessa-Gomes et al. 2004; Rankin and Kokko 2007):

$$\begin{aligned} \frac{dN_F}{dt} &= \gamma_F w b \mathcal{M}(N_M, N_F) - \big(\mu_F + d(N_M + N_F)\big) N_F \\ \frac{dN_M}{dt} &= \gamma_M w b \mathcal{M}(N_M, N_F) - \big(\mu_M + d(N_M + N_F)\big) N_M \end{aligned} \tag{1}$$

In this model, b is the density of newborns per female reproductive event, γ_F and γ_M are the proportions of females and males, respectively, among offspring ($\gamma_M + \gamma_F = 1$), w is the fraction of matings that result in reproduction, μ_F and μ_M are the background mortality rates of females and males, respectively, when the population is rare, and d is the strength of density dependence in the background mortality rate, equally affecting both sexes. The reproduction rate $w\mathcal{M}(N_M, N_F)$ is thus modeled as proportional to the mating rate. We adopt this proportionality assumption here, while discussing its potential deficiencies for modeling dynamics of sexually transmitted infection in the concluding section. One may thus view our model as an endpoint of a continuum of potential mating-reproduction relationships that occur in nature, where the other endpoint is formed by the conventional population models in which mating and reproduction are decoupled.

Introducing an infectious disease and assuming homogeneous mixing,

$$\mathcal{M}(N_M, N_F) \frac{X}{N_M} \frac{Y}{N_F} \tag{2}$$

is the rate at which susceptible males ($X = S_M$) or infected males ($X = I_M$) meet and mate with susceptible females ($Y = S_F$) or infected females ($Y = I_F$). Assuming no recovery from the disease and no vertical transmission, and denoting by σ_M and σ_F the probabilities that an infected male and female, respectively, do not become sterilized once infected, our sex-structured model of sterilizing, sexually transmitted pathogens is as follows:

$$
\begin{aligned}
\frac{dS_F}{dt} &= \gamma_F w b \mathcal{M}(N_M, N_F) \frac{(S_M + \sigma_M I_M)}{N_M} \frac{(S_F + \sigma_F I_F)}{N_F} \\
&\quad - \xi_M \mathcal{M}(N_M, N_F) \frac{I_M}{N_M} \frac{S_F}{N_F} - (\mu_F + dN) S_F \\
\frac{dS_M}{dt} &= \gamma_M w b \mathcal{M}(N_M, N_F) \frac{(S_M + \sigma_M I_M)}{N_M} \frac{(S_F + \sigma_F I_F)}{N_F} \\
&\quad - \xi_F \mathcal{M}(N_M, N_F) \frac{S_M}{N_M} \frac{I_F}{N_F} - (\mu_M + dN) S_M \\
\frac{dI_F}{dt} &= \xi_M \mathcal{M}(N_M, N_F) \frac{I_M}{N_M} \frac{S_F}{N_F} - (\mu_F + dN) I_F - \alpha_F I_F \\
\frac{dI_M}{dt} &= \xi_F \mathcal{M}(N_M, N_F) \frac{S_M}{N_M} \frac{I_F}{N_F} - (\mu_M + dN) I_M - \alpha_M I_M
\end{aligned}
\tag{3}
$$

In addition to the symbols introduced in the model (1), $N = N_M + N_F = S_M + I_M + S_F + I_F$ is the total population density, ξ_M and ξ_F are the probabilities of disease transmission upon mating between a susceptible female and an infected male and a susceptible male and an infected female, respectively, and α_F and α_M are the disease-induced mortality rates in females and males, respectively.

Having composed a sex-structured model in which mating drives both reproduction and pathogen transmission, we now assume a 1:1 sex ratio at birth and sex-independent process rates, that is, $\gamma_F = \gamma_M = 0.5$, $\mu_F = \mu_M = \mu$, $\xi_F = \xi_M = \xi$, $\sigma_F = \sigma_M = \sigma$, and $\alpha_F = \alpha_M = \alpha$, and reduce the sex-structured model to its asexual version. Since then $S_F = S_M = S/2$ where $S = S_F + S_M$, and $I_F = I_M = I/2$ where $I = I_F + I_M$, by adding equations for S_F and S_M, and for I_F and I_M, the model (3) reduces to the model

$$
\begin{aligned}
\frac{dS}{dt} &= wb\mathcal{M}\left(\frac{N}{2}, \frac{N}{2}\right) \frac{(S + \sigma I)^2}{N^2} - 2\xi \mathcal{M}\left(\frac{N}{2}, \frac{N}{2}\right) \frac{SI}{N^2} - (\mu + dN) S \\
\frac{dI}{dt} &= 2\xi \mathcal{M}\left(\frac{N}{2}, \frac{N}{2}\right) \frac{SI}{N^2} - (\mu + dN) I - \alpha I
\end{aligned}
\tag{4}
$$

A variety of mating functions has been proposed, most of which originating in the demographic literature where they are commonly referred to as marriage functions (Iannelli et al. 2005). Of these, almost all demographic and ecological two-sex models assume mating functions that are degree-one homogeneous: $\mathcal{M}(\alpha x, \alpha y) = \alpha \mathcal{M}(x, y)$ for any positive x, y, and α (Caswell and Weeks 1986; Hadeler et al. 1988; Castillo-Chavez and Huang 1995; Lindström and Kokko 1998; Iannelli et al. 2005; Rankin and Kokko 2007; Miller and Inouye 2011). Loosely speaking, doubling population density so that the sex ratio is preserved, the mating rate should also double. Despite this property being widely accepted, it is at the same time quite controversial. While scale invariant and "naturally generalizing" the linear reproduction rate commonly used in many asexual models (Iannelli et al. 2005), the degree-one homogeneous mating functions keep the per female mating rate constant if the sex ratio is constant, whatever low male and female densities are. This latter feature is at least in

some cases questionable, such as when population members challenge a mate-finding Allee effect, that is, an enhanced difficulty in finding mates in low-density populations (Courchamp et al. 2008; Gascoigne et al. 2009). As most ecological papers on two-sex modeling do, also we here assume a degree-one homogeneous mating function, while commenting on the use of an Allee-effect-driven mating function in the discussion. With a degree-one homogeneous mating function, the model (4) becomes

$$\begin{aligned}\frac{dS}{dt} &= \frac{wb}{2}\,\mathcal{M}(1,1)\,\frac{(S+\sigma I)^2}{N} - \xi\,\mathcal{M}(1,1)\,\frac{SI}{N} - (\mu + dN)\,S \\ \frac{dI}{dt} &= \xi\,\mathcal{M}(1,1)\,\frac{SI}{N} - (\mu + dN)I - \alpha I\end{aligned} \tag{5}$$

Finally, denoting $\beta = wb\mathcal{M}(1,1)/2$ and $\lambda = \xi\,\mathcal{M}(1,1)$, we get the model

$$\begin{aligned}\frac{dS}{dt} &= \beta\frac{(S+\sigma I)^2}{N} - (\mu + dN)\,S - \lambda\frac{SI}{N} \\ \frac{dI}{dt} &= \lambda\frac{SI}{N} - (\mu + dN)I - \alpha I\end{aligned} \tag{6}$$

It is the model (6) that we are going to study in what follows. Although it is unlikely that males and females would be identical in their response to pathogens, virtually all published models of host-parasite dynamics are asexual. The purpose of our reduction of the sex-structured model (3) to the asexual model (6) is to compare our results to those of the conventional models. The value of the sex-structured model is thus here primarily to correctly derive an asexual model. We can see in the model (6) that assuming a degree-one homogeneous mating function actually implies a standard incidence model of pathogen transmission (frequency-dependent transmission). We also note that $\sigma = 0$ means that all infected individuals get sterilized, while $\sigma > 0$ corresponds to an imperfect sterilization.

In the absence of infection, the model (6) reduces to

$$\frac{dN}{dt} = \beta N - (\mu + dN)\,N \tag{7}$$

This is a model for logistic population growth: as soon as $\beta > \mu$ (reproduction exceeds mortality), the population attains a carrying capacity $N^* = \frac{\beta-\mu}{d}$; if $\beta < \mu$ it goes extinct. Naturally, we focus on the case in which the population is able to persist without infection, so we assume $\beta > \mu$ from here on. All statements about existence and stability of model equilibria are thus made with respect to this constraint.

The basic reproduction number for the infection described by the model (6), if the population is at its carrying capacity, is

$$R_0 = \frac{\lambda}{\mu + dN^* + \alpha} = \frac{\lambda}{\beta + \alpha} \tag{8}$$

It thus equals the average number of adequate contacts, λ, of an infected individual during its mean infectious period, $1/(\mu + dN^* + \alpha)$, when the population is at the disease-free equilibrium, N^*.

3 Results

Due to singularity of the right-hand sides of the model (6) at $S = I = 0$, we study its behavior in terms of the total population density $N = S + I$ and the proportion of susceptible individuals $s = S/N$. The transformed model is as follows:

$$\begin{aligned} \frac{dN}{dt} &= N\left[\beta\big(s+\sigma(1-s)\big)^2 - (\mu + dN) - \alpha(1-s)\right] \\ \frac{ds}{dt} &= (1-s)\left[\beta\big(s+\sigma(1-s)\big)^2 - \lambda s + \alpha s\right] \end{aligned} \tag{9}$$

To simplify the analysis, we denote by $G(s)$ the quadratic function in the equation for s. Hence,

$$\frac{ds}{dt} = (1-s)G(s)$$

Any feasible equilibrium for the proportion of susceptible individuals, s, lies in the interval $(0, 1)$. Since $G(0) = \beta\sigma^2 > 0$ we have three cases to analyze:

1. $G(1) < 0$. This is equivalent to $R_0 > 1$ and implies the existence and uniqueness of one endemic equilibrium s_e in the interval $(0, 1)$. Since $G(s) > 0$ for $s < s_e$ and $G(s) < 0$ for $s > s_e$ it follows that s_e is globally stable.

   Treating now the equation for N as an asymptotically autonomous equation, its limiting equation is

   $$\frac{dN}{dt} = N(\lambda s_e - \mu - \alpha - dN)$$

   where we used the fact that $G(s_e) = 0$ implies $\beta(s_e + \sigma(1 - s_e))^2 = (\lambda - \alpha)s_e$. This is a logistic equation in N and the limit of $N(t)$ depends on the sign of

   $$s_e - \frac{\mu+\alpha}{\lambda}$$

   If $s_e < \frac{\mu+\alpha}{\lambda}$ then $N(t) \to 0$ and the host population goes extinct. Otherwise, if $s_e > \frac{\mu+\alpha}{\lambda}$ then the host population approaches the endemic equilibrium (N_e, s_e) where

   $$N_e = \frac{\lambda s_e - \mu - \alpha}{d}$$

   Notice that $\frac{\mu+\alpha}{\lambda} < 1$ due to $R_0 > 1$ and our general assumption $\beta > \mu$. Therefore,

   $$s_e < \frac{\mu+\alpha}{\lambda} \quad \text{is equivalent to} \quad G\left(\frac{\mu+\alpha}{\lambda}\right) < 0$$

   which is

   $$\beta\left[(1-\sigma)\frac{\mu+\alpha}{\lambda} + \sigma\right]^2 - (\lambda - \alpha)\frac{\mu+\alpha}{\lambda} < 0$$

Denoting by $h(\sigma)$ the left-hand side of this inequality, we notice that

$$h'(\sigma) = 2\beta\left[\frac{\mu+\alpha}{\lambda} + \sigma\left(1 - \frac{\mu+\alpha}{\lambda}\right)\right]\left(1 - \frac{\mu+\alpha}{\lambda}\right)$$

which is positive under the conditions of this case. So, $h(\sigma)$ is increasing. On the other hand

$$h(0) = \left(\frac{\mu+\alpha}{\lambda}\right)\left[\frac{\beta(\mu+\alpha)}{\lambda} - (\lambda - \alpha)\right] < 0$$

This means that, with enough sterility ($\sigma \to 0$), the host population always goes extinct.

2. $G(1) > 0$ (equivalent to $R_0 < 1$) and $G(s)$ has no roots in $(0, 1)$. In this case, 1 is the only feasible equilibrium for s which is globally stable. This corresponds to a disease-free equilibrium and

$$\lim_{t\to\infty} N(t) = \frac{\beta - \mu}{d}$$

3. $G(1) > 0$ (equivalent to $R_0 < 1$) and $G(s)$ has two roots in the interval $(0, 1)$. Denoting by $s_{\min}$ the s-coordinate of the vertex of $G(s)$, this case is possible if $G'(0) < 0$, $G'(1) > 0$, and $G(s_{\min}) < 0$ where

$$s_{\min} = \frac{\lambda - \alpha - 2\beta\sigma(1-\sigma)}{2\beta(1-\sigma)^2}$$

All these conditions, together with $R_0 < 1$ are equivalent to

$$\lambda - \alpha < \beta, \qquad 2\beta\sigma(1-\sigma) < \lambda - \alpha$$
$$2\beta(1-\sigma) > \lambda - \alpha, \qquad 4\beta\sigma(1-\sigma) < \lambda - \alpha$$

Eliminating redundancies, these conditions are equivalent to

$$4\beta\sigma(1-\sigma) < \lambda - \alpha < \beta \quad \text{and} \quad \sigma < \frac{1}{2}$$

Under these conditions, we have two endemic equilibria $0 < s_e^1 < s_e^2 < 1$. It is clear from the sign of $G(s)$ that s_e^1 and 1 are locally stable points and s_e^2 is unstable. Therefore, if $s(0) > s_e^2$ then $s(t) \to 1$ leading to a disease-free equilibrium, and if $s(0) < s_e^2$ then $s(t) \to s_e^1$ which leads again to either a stable endemic state or host extinction depending on the sign of

$$\lambda s_e^1 - \mu - \alpha$$

This means that we have host extinction if either

$$s_{\min} < \frac{\mu+\alpha}{\lambda}$$

Table 1 Stability analysis of the model (9) with $\sigma = 0$ (full sterilization) $s_e = (\lambda - \alpha)/\beta$, $N_e = [\lambda(\lambda - \alpha)/\beta - (\alpha + \mu)]/d$

Condition	$\alpha > \lambda$	$\lambda - \beta < \alpha < \lambda$	$\alpha < \lambda - \beta$
R_0	<1	<1	>1
Equilibrium			
$(0, 0)$	Unstable	Locally stable	Locally stable
$(0, 1)$	Unstable	Unstable	Unstable
$(0, s_e)$	–	Unstable	–
(N_e, s_e)	–	May or may not exist, unstable if it exists	–
$((\beta - \mu)/d, 1)$	Locally stable	Locally stable	Unstable
Outcome	Infection cannot invade	Infection cannot invade but triggers bistability	Disease-induced extinction

or

$$s_{\min} > \frac{\mu + \alpha}{\lambda} \quad \text{and} \quad G\left(\frac{\mu + \alpha}{\lambda}\right) < 0$$

Notice that, with full sterilization ($\sigma = 0$), $s_{\min} > (\mu + \alpha)/\lambda$ implies $G((\mu + \alpha)/\lambda) < 0$, and hence one of these two conditions must be true. Also, the existence conditions are all equivalent to $\lambda > \alpha$. This means we will always have bistability between the disease-free equilibrium and host extinction with σ low enough. Otherwise, we have bistability between the disease-free equilibrium and the endemic state given by

$$N_e^1 = \frac{\lambda s_e^1 - \mu - \alpha}{d}$$

These results are summarized in Table 1 in the case of full sterilization ($\sigma = 0$). They correspond to infections not able to invade the population (high virulence, $\alpha > \lambda$), infections that always induce population extinction (low virulence, $\alpha < \lambda - \beta$), and infections that can cause any of these endpoints to be attained, depending on the initial state of the population; this latter situation occurs when

$$\lambda - \beta < \alpha < \lambda \tag{10}$$

(intermediate virulence). The most interesting of these situations is the one leading to bistability: the endemic equilibrium at which both the population and the pathogen coexist, if it exists, cannot be attained (is unstable), and the infection is either not able to invade the population or otherwise causes the population to go extinct (Fig. 1). Note that any of these two extreme outcomes is eventually fatal for the pathogen. Sample dynamics of the model (9) leading to disease-free persistence versus population extinction are given in Fig. 2.

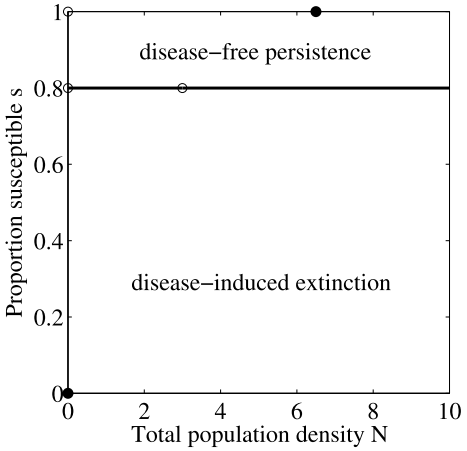
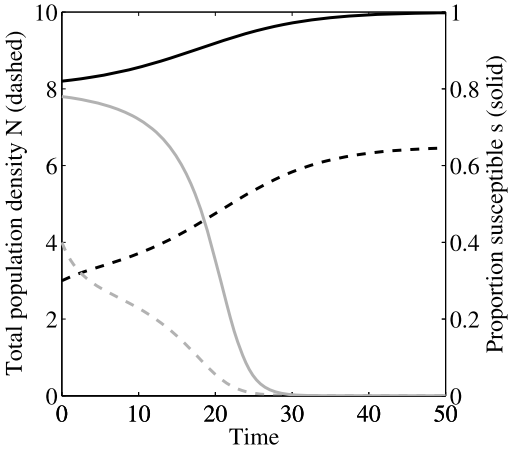


Fig. 1 Phase space of the model (9) with $\sigma = 0$ (full sterilization) in case the bistability scenario occurs, i.e., $\lambda - \beta < \alpha < \lambda$. Parameter values: $\beta = 0.75$, $\alpha = 0.4$, $\lambda = 1$, $\mu = 0.1$, $d = 0.1$. The circles mark stable (*full*) and unstable (*open*) model equilibria. A line parallel to the total population density axis delimits the region of disease-free population persistence (infection cannot invade) from that of population extinction (disease-induced extinction), and is the stable manifold of the unstable endemic equilibrium (N_e, s_e). If (N_e, s_e) does not exist, e.g., for $\lambda = 0.41$, the *horizontal line* is formed by the stable manifold of the extinction equilibrium $(0, s_e)$

Fig. 2 Temporal dynamics of the model (9) with $\sigma = 0$ (full sterilization) in case the bistability scenario occurs, i.e. $\lambda - \beta < \alpha < \lambda$. Parameter values: $\beta = 0.75$, $\alpha = 0.4$, $\lambda = 1$, $\mu = 0.1$, $d = 0.1$. Initial conditions leading to population extinction: $N(0) = 4$, $s(0) = 0.78$ (*gray lines*), and to disease-free population persistence: $N(0) = 3$, $s(0) = 0.82$ (*black lines*)



In terms of R_0, the condition (10) yields

$$0 < \frac{\alpha}{\beta + \alpha} < R_0 < 1 \tag{11}$$

So, the infection can extirpate the population even if $R_0 < 1$, if the initial disease prevalence is sufficiently high.

In the case of imperfect sterilization ($\sigma > 0$), the equilibria s_e^i $(i = 1, 2)$ become 0 and s_e given in Table 1 in the limiting case $\sigma \to 0$. For σ sufficiently close to zero,

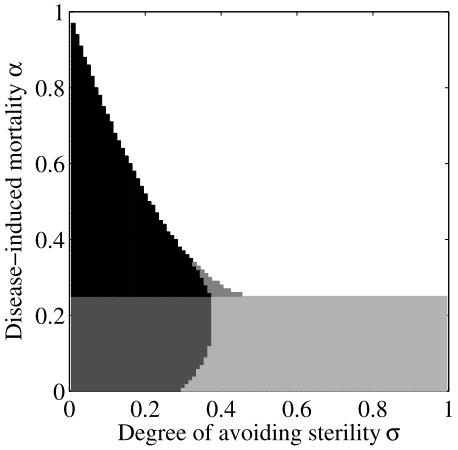


Fig. 3 Extreme bistability still occurs for the model (9) provided that the degree of sterilization is sufficiently large (degree of avoiding sterility σ is sufficiently small). Parameter values: $\beta = 0.75$, $\lambda = 1$, $\mu = 0.1$, $d = 0.1$. The parameter space is split into five regions: (i) where only the disease-free equilibrium is locally stable (*white*), (ii) where only an extinction equilibrium is locally stable (*dark gray*), (iii) where both the disease-free equilibrium and an extinction equilibrium are locally stable (*black*), (iv) where the disease-free equilibrium and an endemic equilibrium of the infection are locally stable (*middle gray*), and (v) where only an endemic equilibrium of the infection is locally stable (*light gray*)

we thus expect the smaller of s_e^i's to also be close to zero. An example confirming this result is presented in (Fig. 3).

Hence, the extreme bistability observed for $\sigma = 0$ occurs also in the case of an imperfect sterilization (Fig. 3). Interestingly, for some intermediate values of σ we also observe bistability of the disease-free population state and the state of host-pathogen coexistence (an endemic equilibrium; Fig. 3).

4 Discussion

Conventional models of sexually transmitted infections consider reproduction and pathogen transmission as uncoupled processes. Whereas the pathogen transmission term adopts one of a number of suggested forms (McCallum et al. 2001), the reproduction term is commonly modeled as linear in population density (e.g., Busenberg and van den Driessche 1990; Thrall and Antonovics 1997), rarely with density dependence included (e.g., Gao and Hethcote 1992; O'Keefe and Antonovics 2002; Hilker et al. 2009; Hilker 2010). Whether developed by analogy with models of other disease types or from first principles, this is fine in some situations but most likely inadequate in others; see the Introduction for more on this issue. Here, we developed and analyzed a model of dynamics of sterilizing, sexually transmitted infections, which considered structural consistency between the processes of reproduction and pathogen transmission, mediated by mating.

Coupling of the processes of reproduction and pathogen transmission significantly impacts infection dynamics. Whereas a conventional model of the interaction we consider in this article (i.e., the model (6) with the reproduction term $\beta(S + \sigma I)^2/N$

replaced by $\beta(S + \sigma I)$) predicts that a system state is always globally stable, be it the disease-free state of the host population, host-pathogen coexistence, or disease-induced host extinction (Pugliese 1990), our model predicts occurrence of an extreme bistability regime, in which the host population either attains the disease-free state or goes extinct due to pathogen, depending on the initial proportion of susceptible individuals: whereas low proportions imply population extinction, high proportions allow the population to persist at the disease-free state. This extreme bistability regime is triggered by highly sterilizing pathogens; it tends to wane with decreasing sterilization power of the infection. Endemic equilibria are in this case either unstable or do not exist. Our results tend to be quite robust, since we prove them for any mating function from a broad class of commonly used, degree-one homogeneous mating functions.

Why does the extreme bistability regime occur? The tight coupling of the processes of reproduction and pathogen transmission causes the reproduction rate in the model (6) to depend not only on the population density of reproductive individuals (as is the case in conventional models), but also on the proportion of these individuals. As the degree of sterilization increases, more and more matings are lost to those individuals that cannot reproduce (i.e., are not fertile). Moreover, as the proportion of susceptible individuals decreases, the proportion of sterilized individuals increases, the proportion of matings that result in birth decreases and eventually the population goes extinct.

Note that the extreme bistability regime occurs for $R_0 < 1$ (for $R_0 > 1$, a highly sterilizing pathogen triggers only host extinction). It thus corresponds to the situation where the infection is not able to invade the host population when rare, but can make it extinct once its (initial) prevalence is sufficiently high. One might term this situation "antiherd-immunity" or "antivaccination," pointing to the fact that "inoculating" a given proportion of the host population drives it to extinction, and thus prevents or "vaccinates" the environment against its invasion if it corresponds to an invading pest species. Indeed, the type of bistability generated by our model might possibly be exploited to develop an efficient control tactic to eradicate an unwanted pest species. With a pathogen having a sufficient degree of sterilization (and possibly also a sufficient disease-induced mortality rate) at hand, it "suffices" to inoculate a minimum number of individuals and the pathogen does the rest—ensures both pest eradication and its self-destruction. Moreover, if by chance a small amount of the pathogen escapes the focal population, because of $R_0 < 1$ it is unlikely that it will cause much harm before it (quickly) dies out. Due to this, we might achieve the required safety aspects of any pathogen to be used as a potential biocontrol agent.

That said, we need to address two related questions. How can one get a highly sterilizing, sexually transmitted infection, given that both extreme bistability outcomes are deleterious to the pathogen? And what types of populations our model is most appropriate to? Highly sterilizing, sexually transmitted infections indeed appear to exist (Lockhart et al. 1996; Knell and Webberley 2004; Sloan et al. 2008). In addition, both empirical (Sloan et al. 2008) and theoretical (Jaenike 1996; O'Keefe and Antonovics 2002) studies suggest that selection on sterilizing pathogens will favor high to complete sterilization. Assuming for the moment that our model is a correct representation of at least some host populations, a highly sterilizing pathogen

triggering only host extinction ($R_0 > 1$) or the bistability between host extinction and disease-free host persistence ($R_0 < 1$) indeed would not occur naturally. Moreover, application of the adaptive dynamics approach to evolution (Dieckmann 2002) to our model suggested an evolutionary route to complete sterilization provided that the degree of sterilization $1 - \sigma$ and the transmission rate λ were positively related, a pattern suggested in the literature (Jaenike 1996; Sloan et al. 2008). We do not provide any details here, but obviously we have here an example of evolutionary suicide (Parvinen 2005). This implies that our extreme bistability regime can only be a transient state of a pathogen, which can only exist if there is a persistent source population of its "relative." For this relative, the critical value of sterilization power beyond which pathogens cannot persist (about 0.37 in Fig. 3) needs not be reached. Indeed, O'Keefe and Antonovics (2002) found that in spatially structured populations sterilization power evolved to intermediate degrees. A natural possibility of observing a highly sterilizing pathogen triggering the extreme bistability regime then might be due to a pathogen that is endemic in a certain host (e.g., mildly sterilizing), but has a strong sterilizing effect when affecting a different host (Jaenike 1996). An artificial way, tightly related to the above mentioned pest control implications, is then a genetic manipulation of a more benign virus (Hardy et al. 2006). Sterilizing, sexually transmitted pathogens can thus exist that demonstrate the extreme bistability under some conditions, while persisting under other conditions.

Regarding the question of our model's applicability, the only real difference between our model and conventional models of sterilizing, sexually transmitted infections, is consideration of structural consistency between the mechanisms of reproduction and pathogen transmission. Both model types are time-continuous so that both suffer from all known limitations this kind of models (which form the overwhelming majority of all existing epidemiological models) has: they essentially describe populations having overlapping generations with close to continuous reproduction that are relatively large, distributed in a homogeneous environment and able to interact over large distances. The central assumption behind our consistency mechanism is that the reproduction rate is proportional to the mating rate. That is, that the number of reproductive events per time step is proportional to the number of matings per time step. So, in a way, we consider an endpoint of a continuum of potential mating-reproduction relationships that occur in nature; the other endpoint is formed by the conventional models in which mating and reproduction are decoupled. Independent of its applicability, our study may provide insights into what can happen at this endpoint. Quite likely, our assumption is not appropriate in all possible situations. Sexually transmitted infections in humans provide a good example here since the reproduction control is strong and reproduction is not strongly linked to the number of sexual contacts (which are responsible for disease transmission). Still, while our proportionality assumption is mathematically the simplest form we can adopt (and we can liken this, e.g., to linear death rates in many population models or linear divorce rates in many demographic models), we think we can provide some cases from the animal world where it can be acceptable.

Since we are considering a population model, and moreover a time-continuous model, we cannot model any individual mating behavior in any detail. Rather, we are restricted to modeling rates, that is, numbers per time step. Thus, all we can afford is a phenomenological description of a mean output of a mating system, rather

than any description of its details and any corresponding variability in mating success. Our assumption of proportionality can be linked to any mating behavior from at least two perspectives. In both, the meaning of mating rate is the number of matings per unit time, where matings both within and outside couples are counted. First, if $\mathcal{M}(N_M, N_F)$ is the (total) mating rate, then $\mathcal{M}(N_M, N_F)\,dt$ is the number of matings per small time interval dt. Let dt be so small that at most one mating can occur within it. Moreover, let w be the probability of fertilization per mating event. Then $w\mathcal{M}(N_M, N_F)\,dt$ is the number of reproduction events within dt. That is, $w\mathcal{M}(N_M, N_F)$ is the (total) reproduction rate. This perspective seems to be most appropriate if the chance of fertilization per any mating event is roughly constant. This may be the case, e.g., when ovulation in females is triggered by the copulation act, such as in felines (Little 2001).

Our second perspective is as follows. Let $\mathcal{R}(N_M, N_F)$ denote the (total) reproduction rate, that is, the number of reproduction events per unit time. Moreover, let k be the average number of matings females that mate per unit time have (so not all females, just those that mate). Finally, let $w(k)$ be the probability that a female gets fertilized and reproduces given she had k matings. Then $\mathcal{R}(N_M, N_F) = w(k)\mathcal{M}(N_M, N_F)/k$ since $\mathcal{M}(N_M, N_F)/k$ is the average number of females that mate per unit time. Provided that k is roughly constant, we again have the reproduction rate proportional to the mating rate. This second perspective seems closer to the idea that the more uniformly are matings distributed among females (again not all females, just those that mate), the more linear is expected to be the actual relationship between the reproduction rate and the mating rate. An example of when this may hold is mate guarding behavior where males guard their mates until paternity is ensured (Kokko and Morrell 2005, and references therein) or a harem system in which males again guard their harem against aliens (Shuster and Wade 2003). We can even consider a combination of these two perspectives, such as in birds with extra-pairs copulations, where "the probability of fertilization [thus] may be approximately proportional to the relative number of pair copulations, if inseminations occur less than a few hours apart" (Møller and Birkhead 1992).

To summarize, we tend to think that in many cases the mating system will determine the particular form of the mating rate $\mathcal{M}(N_M, N_F)$, while the chance of fertilization per mating event and/or the distribution of matings over different mating females will affect the link between reproduction and mating rates—we expect this relationship (close to) linear if the per mating chance of fertilization is (close to) constant and/or the distribution of matings over mating females is (close to) uniform.

A few other epidemiological models exist that demonstrate bistability and even tristability (Diekmann and Kretzschmar 1991; Hilker et al. 2009; Hilker 2010). The observed bistability types include bistability between the disease-free equilibrium and an endemic equilibrium (Diekmann and Kretzschmar 1991; Hilker et al. 2009; Hilker 2010), bistability between the disease-free equilibrium and periodic fluctuations around an endemic equilibrium (Diekmann and Kretzschmar 1991; Hilker et al. 2009), and most importantly from our perspective, bistability between the disease-free equilibrium and an equilibrium corresponding to pathogen-driven extinction (Hilker 2010). Unfortunately, this latter type of bistability was not discussed in Hilker (2010) at all, as the author likely found it less interesting relative to the other dynamical regimes his model generated.

Nevertheless, the model we developed and analyzed in our article differs from that of Hilker (2010) in two important aspects. First, contrary to Hilker (2010), we do not assume that the host population challenges a strong Allee effect in the absence of infection. Strong Allee effects refer to the situation where individual fitness declines with population density, and where the per capita population growth rate becomes negative once population density falls below an Allee threshold (Berec et al. 2007; Courchamp et al. 2008). Presence of a strong Allee effect in the host population keeps an extinction equilibrium locally stable also in the presence of infection, and the extreme bistability regime of disease-free population persistence versus disease-induced population extinction observed by Hilker (2010) is thus not triggered by the pathogen itself. Our results imply that the extreme bistability regime exists also without assuming an Allee effect. This is important, since many populations, including those invading nonnative habitats, likely do not possess strong Allee effects. This is not to say that populations with strong Allee effects cannot invade nonnative habitats; they indeed can as is, for example, the case of the gypsy moth *Lymantria dispar* (Tobin et al. 2009). Rather, this is to say that many invading species may not have an Allee effect at all. In fact, strong Allee effects have so far been convincingly demonstrated in several species only (Kramer et al. 2009), some of them invading, while much more species have been found to successfully invade a variety of nonnative habitats. Second, Hilker (2010) likely did not have any specific pathogen type in mind. Here, we considered sterilizing, sexually transmitted pathogens for which we developed our alternative modeling framework, since the sexual transmission route is a necessary prerequisite for our central assumption of consistency between the processes of reproduction and pathogen transmission.

In this article, we modeled dynamics of sterilizing, sexually transmitted infections, suggesting a framework in which the processes of reproduction and pathogen transmission were assumed structurally consistent as mediated by mating. We by no means consider our model as a fundamental new vision, but rather develop and analyze an alternative to conventional models used to describe this specific type of infectious diseases. Even if the insights gained from our study might be of an interest to pest control practitioners, we especially believe that the model we propose in this article will open the way to further explorations of implications of consistency between the processes of reproduction and pathogen transmission mediated by mating, that is, implications of innerpoints of the mating-reproduction relationships continuum.

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