ANTAGONISTIC COEVOLUTION BETWEEN HOSTS AND SEXUALLY TRANSMITTED INFECTIONS

Ben Ashby*

*Department of Mathematical Sciences, University of Bath, Bath, BA2 7AY, UK.

benashbyevo@gmail.com

Short title: Host-STI coevolution

Keywords: mate choice, mating strategy, virulence, STI, STD, host-parasite, fluctuating selection, sexual selection, PMSS

Sexually transmitted infections (STIs) are found throughout the plant and animal kingdoms and are predicted to be key drivers of host mate choice. Similarly, changes in host mating patterns will have consequences for STI epidemiology and evolution, and so it is crucial to study hosts and STIs in the context of antagonistic coevolution. However, our understanding of host-STI coevolution is extremely limited, with few theoretical predictions for how STIs are likely to affect the evolution of host mate choice, and vice versa. Here, I present a general model of host-STI coevolution, whereby hosts can evolve a preference for healthy mates and STIs can evolve their degree of virulence. The model differs from previous work in a number of important ways, with: (1) ephemeral sexual contacts as opposed to serial monogamy; (2) both mortality and sterility virulence; (3) recovery from infection; and (4) comparisons between linear and non-linear mate choice functions. I show that coevolutionary cycling and intermediate equilibria still occur in the more general framework, but also that evolutionary branching in host mate choice is possible when mate choice is based on mortality virulence and incurs a relatively small cost. Together these findings generalise and extend our theoretical understanding of host-STI coevolution, providing increased support for parasite-mediated sexual selection as an important driver of host mate choice, and mate choice as a constraint on STI virulence.

INTRODUCTION

Parasite-mediated sexual selection (PMSS) is predicted to lead to the evolution of reproductive strategies that limit the risk of infection from mating (Hamilton and Zuk 1982; Sheldon 1993; Loehle 1997). By preferentially selecting mates, organisms should be able to increase their reproductive success, either because they might choose partners possessing genes which confer resistance to disease (the "good genes" hypothesis; Hamilton and Zuk 1982), or simply because they choose mates that are currently uninfected and hence are a low-risk option (the "transmission avoidance hypothesis"; Loehle 1997). Both hypotheses have been the subject of intense empirical research with varying evidence in support of and against PMSS (Borgia 1986; Borgia and Collis 1989; Clayton 1990, 1991; Hamilton and Poulin 1997; Abbot and Dill 2001; Webberley et al. 2002; Balenger and Zuk 2014; Jones et al. 2015). In some cases females have been found to prefer uninfected males – for example, Clayton (1990) found that female Rock Doves (*Columba livia*) prefer males without lice, suggesting support for PMSS – while in other cases females appear unable to distinguish between infected males – for instance, female milkweed leaf beetles (*Labidomera* clivicollis; Abbot and Dill 2001) and two-spot ladybirds (*Adalia bipunctata*; Webberley et al. 2002), do not avoid males with sexually transmitted mites. In parallel, there has been much theoretical interest in understanding the role of parasites, especially sexually transmitted infections (STIs), in the evolution of host mating strategies, and vice versa (Thrall et al. 1997, 2000; Knell 1999; Boots and Knell 2002; Kokko et al. 2002; Ashby and Gupta 2013; McLeod and Day 2014; Ashby and Boots 2015). STIs are of particular interest as they are inherently tightly linked to host reproduction unlike non-STIs and are more likely to have negative effects on host fecundity (Lockhart et al. 1996). This body of theoretical work has generally predicted that STIs can indeed act as a strong force of selection on host mating strategies. While changes in host mating behaviour arising from PMSS will in turn affect STI evolution, forming a coevolutionary feedback, almost all theoretical studies only consider one-sided adaptation of either the host or the

48 STI. There is therefore a clear need for the further development of theoretical predictions of host-STI
49 coevolution.

50 In what appears to be the only host-STI coevolution model to date, Ashby and Boots (2015) proposed
51 a pair formation model with reciprocal adaptations between host mate choice and sterility virulence
52 (reductions in host fecundity). Crucially, by taking a coevolutionary approach, this study showed that
53 selection against STI virulence due to mate choice was unlikely to lead to a complete loss of mate
54 choice as had been predicted in studies of one-sided adaptation (Knell 1999). By assuming that hosts
55 are able to preferentially choose mates based on visible signs of disease and that more
56 transmissible/virulent STIs are easier to detect, Ashby and Boots (2015) showed that the evolution of
57 mate choice can prevent runaway selection for parasitic castration, leading to either stable levels of
58 choosiness and virulence, or coevolutionary cycling in these traits. Although this study provides
59 several new predictions for PMSS, the model itself is based on a number of restrictive assumptions
60 that limit its generality. For example, hosts were assumed to form serially monogamous pairs with
61 other individuals for an average period of $\frac{1}{2d+u}$, where u is the divorce rate and d is the natural
62 mortality rate, with hosts unable to mate with other members of the population while paired (note
63 parameters changed for consistency). Such pairings can have both positive and negative effects on
64 reproductive success: pairing with an uninfected partner insulates an individual from contracting
65 infection from other members of the population, but pairing with an infected partner will greatly
66 increase the risk of contracting infection and will potentially lower the chance of producing offspring.
67 Thus, the costs of choosing a 'bad' (infected) partner under serially monogamous mating will be
68 greater than when sexual contacts are ephemeral, and so we might expect mate choice to be
69 especially strong under serial monogamy. Furthermore, the model only considered disease effects on
70 host fecundity (sterility virulence) rather than mortality virulence, did not allow for recovery from
71 infection, and used mating functions with potentially strong non-linear effects on the dynamics. The
72 key question, therefore, is do the modelling assumptions made by Ashby and Boots (2015)

qualitatively affect the predicted outcomes? For example, is mate choice only likely to constrain STI virulence and cause coevolutionary cycling when the mating system is serially monogamous or the STI has specific characteristics (e.g. causes sterility, no recovery)? Generalising the theory to capture a much broader range of assumptions and biological effects is crucial to improving our understanding PMSS in the context of host-STI coevolution.

Here, I develop and analyse a general framework for host-STI coevolution which relaxes these assumptions, thereby allowing for a broader understanding of the role STIs are likely to play in the evolution of host mating strategies and vice versa. The model allows for ephemeral sexual contacts, mortality and sterility virulence, recovery from infection, and uses both linear and non-linear mating functions. Using evolutionary invasion analysis of the host and STI in isolation, I show how both mortality and sterility virulence are constrained by mate choice and how mate choice is likely to evolve under a variety of conditions. Of particular interest is the discovery of a new outcome, whereby more and less choosy host types may evolve and coexist due to evolutionary branching. I then consider the coevolutionary dynamics of hosts and STIs, showing that coevolutionary cycling is especially common under sterility virulence, with mortality virulence more likely to produce stable states. Together, these results show that while serial monogamy and sterility virulence are likely to increase selection for mate choice, mate choice is likely to evolve due to PMSS under a broad range of conditions.

METHODS

Ashby and Boots (2015) present the following model of host mate choosiness in a well-mixed, serially monogamous and hermaphroditic population (some parameters changed for consistency):

$$\frac{dS}{dt} = b + (d+u)(2[SS] + [SI]) - \frac{p(1-c)^{2g}S}{S+I}(S + f(\beta)^{g}I) - dS \quad (1)$$

$$\frac{dI}{dt} = (d+u)(2[II]+[SI]) - \frac{p(1-c)^{2g} f(\beta)^g I}{S+I}(S + f(\beta)^g I) - dI \quad (2)$$

$$\frac{d[SS]}{dt} = \frac{p(1-c)^{2g} S^2}{2(S+I)} - (2d+u)[SS] \quad (3)$$

$$\frac{d[SI]}{dt} = \frac{p(1-c)^{2g} f_\beta^g SI}{S+I} - (2d+u+\beta)[SI] \quad (4)$$

$$\frac{d[II]}{dt} = \frac{p(1-c)^{2g} f_\beta^{2g} I^2}{2(S+I)} - (2d+u)[II] + \beta[SI] \quad (5)$$

where: S and I are the number of unpaired susceptible and infected individuals, respectively; $[XY]$ is the number of pairs between individuals in classes X and Y; $N = S + I + 2([SS] + [SI] + [II])$ is the total population size; $f(\beta)$ is the fecundity of infected individuals, which is assumed to depend on the transmission rate, β; p is the maximum pairing rate and u is the divorce rate (the rate at which individuals become unpaired); c modifies the probability that a prospective partner is rejected due to an individual being overly cautious, which is assumed to increase with the strength of host mate choosiness, g; $f(\beta)^g$ is the probability of mating with an infected individual; d is the natural death rate; and $b = r(1 - hN)([SS] + f(\beta)[SI] + f(\beta)^2[II])$ is the birth rate, which occurs at a maximum per-pair rate of r and is subject to density-dependent competition given by the parameter h. There is no recovery or additional mortality from disease and mating only occurs between paired individuals.

Here, I generalise this model by: (i) relaxing the assumption of serial monogamy; (ii) allowing recovery from disease at rate γ; (iii) allowing disease-associated mortality at rate $\alpha(\beta)$; and (iv) using generic mating rate functions, $m_S(g)$ and $m_I(g,\beta)$ to describe the probability of mating with a susceptible or infectious individual, respectively. I assume that $m_I(g,\beta)$ can be decomposed according to $m_I(g,\beta) = m_S(g)\tilde{m}_I(g,\beta)$ with $0 \leq \tilde{m}_I(g,\beta) \leq 1$so that $m_S(g) \geq m_I(g,\beta)$. I relax the assumption of serial monogamy by assuming that sexual contacts are ephemeral, which means that p now corresponds to the maximum mating rate per individual and β to the probability of transmission per

sexual contact. Updating the notation accordingly so that $[XY]$ now corresponds to the rate of sexual contact between individuals in classes X and Y, yields:

$$[SS] = \frac{pm_S(g)^2 S^2}{N} \tag{6}$$

$$[SI] = \frac{2pm_S(g)m_I(g,\beta)SI}{N} \tag{7}$$

$$[II] = \frac{pm_I(g,\beta)^2 I^2}{N} \tag{8}$$

giving a total mating rate of

$$M = [SS] + [SI] + [II] = \frac{p(m_S(g)S + m_I(g,\beta)I)^2}{N} \tag{9}$$

and a total birth rate of

$$b(g,\beta) = [SS] + f(\beta)[SI] + f(\beta)^2[II] = \frac{pr(1-hN)(m_S(g)S + f(\beta)m_I(g,\beta)I)^2}{N} \tag{10}$$

Note that M reduces to $M = pN$ in the absence of mate choice and the factor of 2 in the equation for $[SI]$ is required to balance the total mating rate, giving the following generalised model for host mate choosiness in monomorphic populations:

$$\frac{dS}{dt} = b(g,\beta) - \beta[SI] - dS + \gamma I \tag{11}$$

$$\frac{dI}{dt} = \beta[SI] - (d + \alpha(\beta) + \gamma)I \tag{12}$$

In polymorphic populations, the dynamics for hosts with trait g_i and STIs with trait β_j are fully described by the following system of ordinary differential equations:

$$\frac{dS_i}{dt} = b(g_i) - \sum_j \beta_j [S_i I_{\circ j}] - dS_i + \gamma \sum_j I_{ij} \quad (13)$$

$$\frac{dI_{ij}}{dt} = \beta_j [S_i I_{\circ j}] - \left(d + \alpha(\beta_j) + \gamma\right) I_{ij} \quad (14)$$

where $[S_i I_{\circ j}] = \frac{2pm_I(g_i,\beta_j)S_i}{N} \sum_k m_S(g_k) I_{kj}$ is the total mating rate between susceptible hosts with trait g_i and all hosts infected by STIs with trait β_j, and the birth rate for each host type is:

$$b(g_i) = \frac{pr(1-hN)}{N} ([S_i S_\circ]_b + [S_i I_{\circ\circ}]_b + [S_\circ I_{i\circ}]_b + [I_{i\circ} I_{\circ\circ}]_b) \quad (15)$$

where:

$$[S_i S_\circ]_b = m_S(g_i) S_i \sum_k m_S(g_k) S_k \quad (16)$$

$$[S_i I_{\circ\circ}]_b = S_i \sum_j \left(f(\beta_j) m_I(g_i, \beta_j) \sum_k m_S(g_k) I_{kj} \right) \quad (17)$$

$$[S_\circ I_{i\circ}]_b = m_S(g_i) \sum_j \left(f(\beta_j) I_{ij} \sum_k m_I(g_k, \beta_j) S_k \right) \quad (18)$$

$$[I_{i\circ} I_{\circ\circ}]_b = \sum_j \left(f(\beta_j) I_{ij} \sum_l \left(f(\beta_l) m_I(g_i, \beta_l) \sum_k m_I(g_k, \beta_j) I_{kl} \right) \right) \quad (19)$$

I use evolutionary invasion analysis to determine the long-term trait dynamics in each population (Geritz et al. 1998). This assumes that mutations have very small phenotypic effects and are sufficiently rare so that the system has reached a stable state before a new mutant emerges. I solve the dynamics numerically as the system is intractable to other methods of stability analysis. I relax the assumptions of the evolutionary invasion analysis in coevolutionary simulations by having a finite number of host and STI types and mutations before the system has reached a stable state.

RESULTS

ECOLOGICAL DYNAMICS

The disease-free equilibrium $(S, I) = (S^*, 0)$ occurs at:

$$S^* = \frac{1}{h}\left(1 - \frac{d}{m_S(g)pr}\right) \tag{20}$$

and is viable provided $m_S(g)pr > d$ (i.e. the birth rate is higher than the death rate). A newly introduced STI will spread in a monomorphic, susceptible population when the basic reproductive ratio, $R_0(g, \beta)$ is greater than 1, where:

$$R_0(g, \beta) = \frac{2pm_S(g)m_I(g, \beta)\beta}{d + \alpha(\beta) + \gamma} \tag{21}$$

Numerical analysis of the parameter space revealed that when $R_0(g, \beta) > 1$ the system usually tends to a stable endemic equilibrium (~49% of sampled parameter combinations) or the STI drives the host population extinct (~49% of sampled parameter combinations). In rare cases (~1% of parameters), the system may exhibit sustained oscillations (Fig. 1, S1). A stable endemic equilibrium was generally more likely for lower natural and disease-associated mortality, baseline pairing rates, transmission probabilities, sterility virulence, stronger mate choice, and higher baseline reproduction rates and recovery rates (Fig. S1).

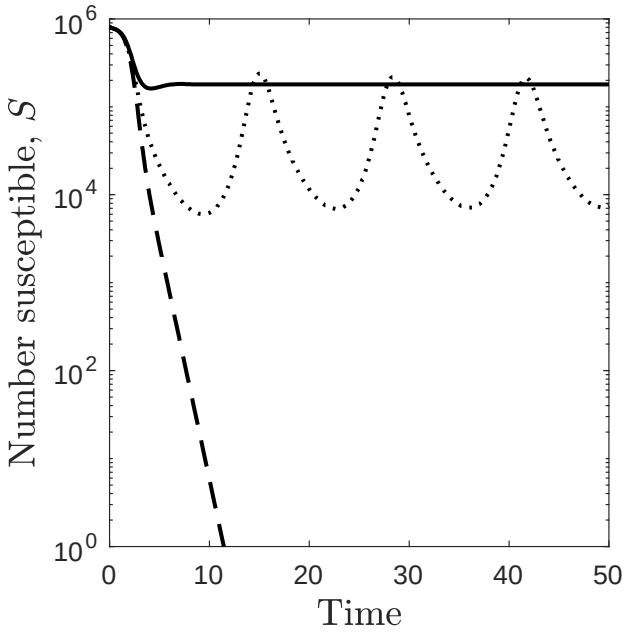

Figure 1 – Ecological dynamics of the generalised mate choice model. When the disease-free host and the STI are both viable, then the STI may: (i) tend to an endemic equilibrium (solid, $f = 1$); (ii) drive both populations extinct (dashed, $f = 0$); or (iii) cycle with the host (dotted, $f = 0.4$). Numerical analysis indicates that cycling is much rarer than the other two outcomes (Fig. S1). Parameters: $d = 1$; $h = 10^{-6}$; $m_S(g) = 0.9$; $m_I(g, \beta) = 0.35$; $p = 7.5$; $r = 0.8$; $\alpha = 0.3$; $\beta = 0.8$; $\gamma = 0.3$.

PARASITE EVOLUTION

The invasion fitness of a rare mutant strain of the STI (subscript m) in a population at equilibrium (superscript *) is:

$$w_P(g, \beta_m) = \frac{1}{I_m}\frac{dI_m}{dt}$$

$$= \frac{2pm_S(g)m_I(g, \beta_m)\beta_m S^*}{N^*} - (d + \alpha(\beta_m) + \gamma) \qquad (22)$$

The mutant STI can only invade when $w_P(g, \beta_m) > 0$, which requires

$$R_{EFF}(g,\beta_m) = R_0(g,\beta_m)\left(\frac{S^*}{N^*}\right) > 1 \quad (23)$$

where $R_{EFF}(\beta_m)$ is the effective reproductive ratio. Since STI fitness can be written in this form, we know that parasite evolution maximises R_0 (Lion and Metz 2018). The STI will therefore evolve in the direction of $\frac{\partial R_0}{\partial \beta}$ until β is maximised at 1, one or both populations are driven extinct, or a singular strategy, β^*, is reached at $\left.\frac{\partial R_0}{\partial \beta}\right|_{\beta=\beta^*} = 0$, which requires:

$$\left.\frac{\partial m_I}{\partial \beta}\right|_{\beta=\beta^*} = m_I(g,\beta^*)\left(\frac{1}{d+\alpha(\beta^*)+\gamma}\left.\frac{d\alpha}{d\beta}\right|_{\beta=\beta^*} - \frac{1}{\beta^*}\right) \quad (24)$$

In general, $m_I(g,\beta)$ and $\alpha(\beta)$ will be decreasing and increasing functions of β, respectively (or constant). In the absence of mate choice $(m_I(g,\beta) = 1)$, a *continuously stable strategy* (CSS) can only exist when $\alpha(\beta)$ is concave up (i.e. mortality virulence accelerates with the transmission rate). In the presence of mate choice, however, a CSS can exist under a broader set of conditions, such as concave down mortality-transmission trade-offs and with sterility-transmission trade-offs. This is clear from the equation for $R_0(g,\beta)$ (equation 21), which features the product of $m_I(g,\beta)$ and β (i.e. the product of decreasing and increasing functions of β) (Fig. 2A).

To illustrate the above, suppose first that sterility virulence is constant $\left(\frac{df}{d\beta} = 0\right)$ and mortality virulence is a linear function of the transmission probability such that $\alpha(\beta) = \kappa\beta$. When there is no mate choice the STI will evolve to maximise β. If, however, we set the mate choosiness function to be a function of mortality virulence such that $m_I(g,\beta) = 1 - g\alpha(\beta)$ for $g\alpha(\beta) < 1$ and 0 otherwise, then a singular strategy exists at

$$\beta^* = \frac{\sqrt{g(d+\gamma)(g(d+\gamma)+1)} - g(d+\gamma)}{g\kappa} \quad (25)$$

194 (Fig. 2B) which is always evolutionarily stable since:

195 $$\left.\frac{\partial^2 R_0}{\partial \beta^2}\right|_{\beta=\beta^*} = -\frac{4gp\kappa m_S(g)}{\sqrt{g(d+\gamma)(g(d+\gamma)+1)}} < 0 \qquad (26)$$

196 Now suppose instead that mortality virulence is constant $\left(\frac{d\alpha}{d\beta} = 0\right)$ and sterility virulence is a function

197 of the transmission probability such that $f(\beta) = 1 - \eta\beta$ where $0 < \eta \leq 1$ controls the strength of

198 the relationship. If we assume that host mate choosiness is a linear function of sterility virulence such

199 that $m_I(g, \beta) = 1 - g\big(1 - f(\beta)\big)$, then the singular strategy occurs at $\beta^* = \frac{1}{2g\eta}$ (Fig. 2B), which

200 again is always evolutionarily stable since:

201 $$\left.\frac{\partial^2 R_0}{\partial \beta^2}\right|_{\beta=\beta^*} = -\frac{4\eta p m_S(g)\sqrt{3g}}{d+\gamma} < 0 \qquad (27)$$

202 In summary, mate choice can constrain the evolution of mortality or sterility virulence in an STI to

203 intermediate stable strategy even when hosts do not form serially monogamous pair bonds.

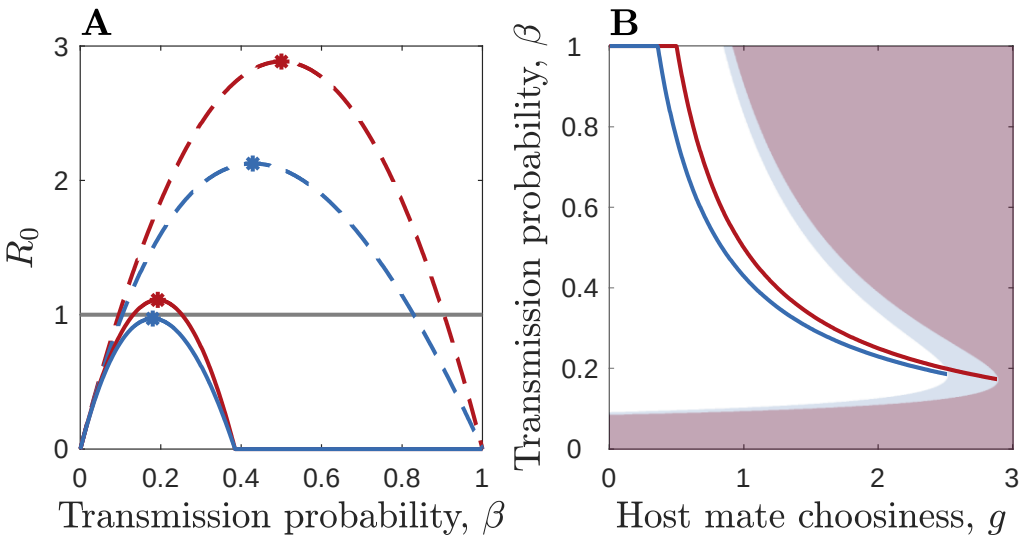

Figure 2 – STI evolution in response to host mate choice for sterility (red) and mortality (blue) virulence. (A) Basic reproductive ratio for weaker (dashed; $g = 1$) and stronger (solid; $g = 2.6$) mate choice. The horizontal line indicates the extinction threshold for the STI. (B) Curves show the continuously stable strategies (CSSs) for a given level of mate choice. The corresponding shaded regions show where the STI is unviable. Mate choice and virulence functions as described in the text. Remaining parameters as described in Fig. 1, except: $m_S(g) = 1$, $\eta = 1$, $\kappa = 1$, and $\alpha = 0$ in the case of sterility virulence.

HOST EVOLUTION

The initial dynamics of a rare mutant host (subscript m) in a resident population at equilibrium are given by:

$$\frac{dS_m}{dt} = b(g_m, \beta) - \beta[S_m I^*] - dS_m + \gamma I_m \tag{28}$$

$$\frac{dI_m}{dt} = \beta[S_m I^*] - (d + \alpha(\beta) + \gamma) I_m \tag{29}$$

with

$$b(g_m,\beta) = \frac{p}{N^*}\left(r(1-hN^*)(m_S(g_m)S^* + f(\beta)m_I(g_m,\beta)I^*)(m_S(g)S_m + f(\beta)m_I(g,\beta)I_m)\right) \quad (30)$$

Using the next-generation method (see *Supporting Information;* Hurford et al. 2010), it can be shown that host fitness is sign-equivalent to

$$w_H(g_m,\beta) = \frac{prm_S^g(1-hN^*)\left(2pf_\beta m_I^{g,\beta} m_I^{g_m,\beta}\beta I^* + \Gamma_\beta N^*\right)\left(m_S^{g_m}S^* + f_\beta m_I^{g_m,\beta}I^*\right)}{N^*\left(2p\beta m_S^g m_I^{g_m,\beta}I^*(\Gamma_\beta - \gamma) + d\Gamma_\beta N^*\right)} - 1 \quad (31)$$

where $\Gamma_\beta = d + \alpha(\beta) + \gamma$, $f_\beta = f(\beta)$, $m_S^g = m_S(g)$ and $m_I^{g,\beta} = m_I(g,\beta)$ for the sake of brevity. The host will evolve in the direction of $\frac{\partial w_H}{\partial g}$ until g is minimised at 0, one or both populations are driven extinct, or a singular strategy, g^*, is reached at $\left.\frac{\partial w_H}{\partial g}\right|_{g=g^*} = 0$.

Suppose initially that there are no costs of mate choice $(m_S(g) = 1)$ and that mate choice of infected individuals is a linear function of virulence, $v(\beta)$, such that $m_I(g,\beta) = 1 - gv(\beta)$, with $v(\beta) = 1 - f(\beta)$ for sterility virulence and $v(\beta) = \min(1,\alpha(\beta))$ for mortality virulence. In this scenario there may be one or two singular strategies. The singular strategy at $g_1^* = (2p\beta - d - \alpha(\beta) - \gamma)/2p\beta v(\beta)$ always exists, and corresponds to the point where the host drives the STI extinct. The second singular strategy (g_2^*), if it exists, is a repeller with $0 < g_2^* < g_1^*$. Hence if there are two singular strategies the outcome depends on the initial conditions, with $g < g_2^*$ causing selection against mate choice, and $g > g_2^*$ leading to STI extinction due to mate choice (Fig. 3).

Mate choice is likely to evolve for intermediate transmission probabilities when virulence is fixed (Fig. 3A-B). When the probability of transmission is small, the STI is unable to spread even in the absence of mate choice $(R_0(0,\beta) < 1)$. When the probability of transmission is close to 1, there may be selection against weak mate choice caused by the evolutionary repeller. This is because disease

prevalence is high and so most attempted matings are with infected individuals, meaning that even weak mate choice dramatically reduces the mating rate for invading mutants compared to the resident population. If, however, there is already a sufficient level of mate choice in the resident population (i.e. the initial conditions are above the repeller), disease prevalence is low enough to allow runaway selection for mate choice, eventually driving the disease extinct. This pattern is similar regardless of whether virulence has fixed effects on mortality or sterility (Fig. 3A-B). When sterility or mortality virulence is linked to the transmission probability, the dynamics are more complex (Fig. 3C-D). Notably, the threshold for driving the STI extinct is lower at high transmission probabilities because virulence (and hence the effects of mate choice) are also stronger. An evolutionary repeller may exist, but it now occurs for intermediate values of β.

The system is intractable to classical analysis when there are costs associated with mate choice (i.e. $m_S(g) < 1$ for $g > 0$), and so one must find the evolutionary dynamics using numerical analysis. While many of the results are qualitatively similar to the no-cost scenario, there are some notable exceptions. In particular, if the host evolves mate choice then it no longer drives the STI extinct, and is instead likely to reach a *continuously stable strategy* with the STI endemic in the population. When virulence is linked to the transmission probability, the host only evolves mate choice *de novo* at sufficiently high values of β (Fig. 3C-D). Additionally, when there is a mortality virulence-transmission trade-off, there is a very small region of parameter space at intermediate values of β that can yield evolutionary branching, with stable coexistence between two host types: one which exhibits moderate mate choice and the other which does not discriminate against infected mates.

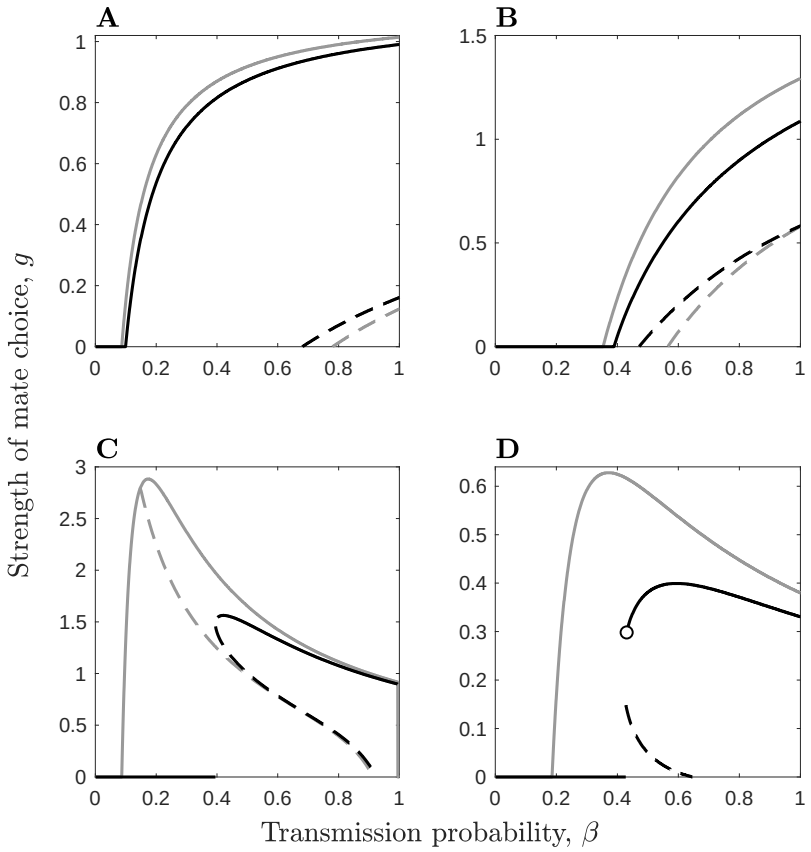

Figure 3 – Evolution of host mate choice, g, in the presence of a non-evolving STI. Solid lines correspond to evolutionary attractors, dashed lines to evolutionary repellers, and circles to branching points, in the presence (black; $\zeta = 0.1$) and absence (grey; $\zeta = 0$) of host costs, with $m_S(g) = 1 - \zeta g$. Mate choice of infected individuals is given by $m_I(g, \beta) = max\left(0, m_S(g)\left(1 - gv(\beta)\right)\right)$, where $v(\beta)$ is the relative virulence of the STI. Only one type of virulence (mortality or sterility) is assumed to occur in each panel with mate choice of infected individuals based on: (A) fixed sterility virulence, $v(\beta) = 1 - f(\beta) = 0.9$; (B) fixed mortality virulence, $v(\beta) = \alpha(\beta)/\kappa = 0.5$; (C) variable sterility virulence, $v(\beta) = 1 - f(\beta) = \eta\beta$; (D) variable mortality virulence, $v(\beta) = \alpha(\beta)/\kappa = \beta$. Remaining parameters as described in Fig. 1, except $r = 20$, $\eta = 1$, and $\kappa = 8$.

COEVOLUTION

Suppose now that the host and STI coevolve. I will focus on if and when the generalised model with ephemeral sexual contacts, recovery, mortality virulence, and generic mate choice functions, is able

to produce two of the key outcomes in Ashby and Boots (2015), namely: (i) *co-continuously stable strategies* (co-CSSs) where STI virulence is constrained by host mate choice; and (ii) coevolutionary cycling, whereby host and STI phenotypes fluctuate through time. These outcomes are of particular interest since they represent fixed and dynamic constraints on STI virulence through host mate choice. I will also examine whether additional outcomes are possible in the model presented herein.

The results of the coevolutionary simulations are summarised in Fig. 4 and 5. First I consider the dynamics when recovery is moderate $(\gamma = 0.3)$. Coevolutionary cycling between host mate choosiness and STI virulence is common for sterility virulence (Fig. 4F) over a wide range of mate choice costs (ζ) (Fig. 4A, B). For sufficiently high costs, however, the system reaches an intermediate co-CSS, hence mate choice constrains the evolution of sterility virulence to a stable level (Fig. 4E). The switch from cycling to a co-CSS occurs for smaller cost values when mate choice is a linear function of virulence (Fig. 4A) rather than a quadratic function (Fig. 4B). Coevolutionary cycling is less common when the STI causes mortality virulence with these dynamics only occurring when mate choice is a non-linear function of virulence (Fig. 4D, I). When the strength of mate choice accelerates with greater virulence, not only can the system produce coevolutionary cycling (intermediate values of ζ) or a co-CSS (high values of ζ), but also evolutionary branching leading to a stable polymorphism between more and less choosy hosts (low values of ζ; Fig. 4D, H). The STI did not branch under any conditions.

Increasing the recovery rate had a stabilising effect on the dynamic, as shown in Fig. 5. Although coevolutionary cycling was still possible for sterility virulence, both the parameter range for generating cycles and the resulting amplitude of any cycles was smaller (Fig. 5A-B). The stabilising effect of greater recovery was especially apparent under mortality virulence with no cycling or branching occurring (Fig. 5C-D), unlike in the case of moderate recovery (Fig. 4C-D).

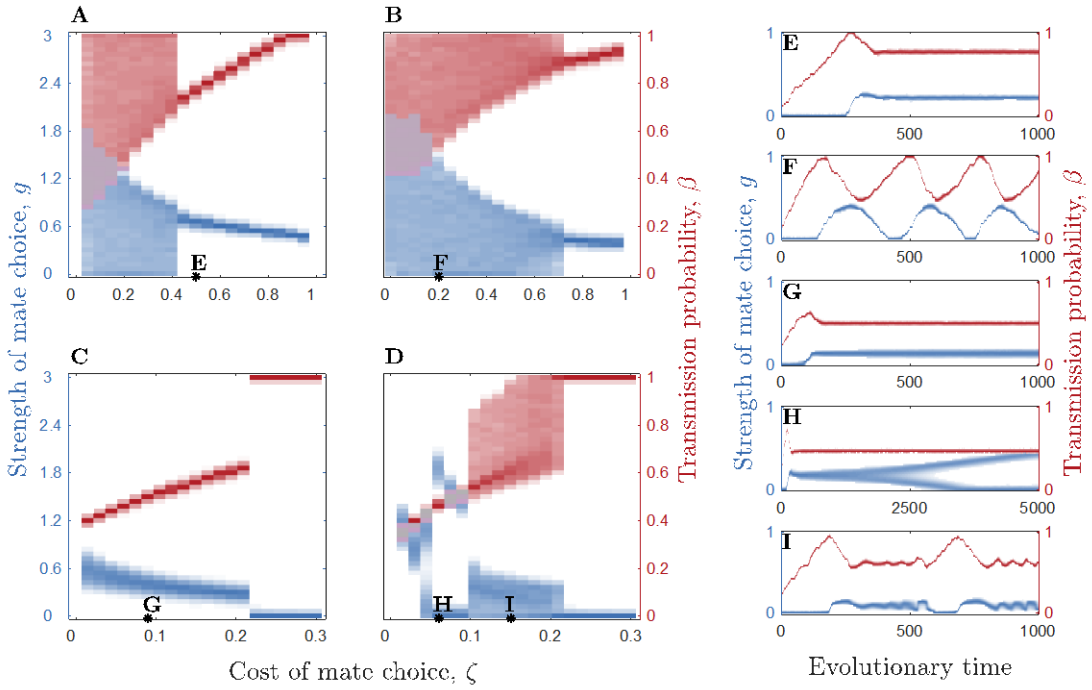

Figure 4 – Coevolution of host mate choice, g, and STI transmission probability, β. (A-D) Mean distribution of host (blue) and STI (red) traits over the final 2,000 time steps of a simulation as the mate choice cost parameter, ζ, varies, with $m_S(g) = \max(0,1-\zeta g)$. The region where host and parasite traits overlap is shaded purple and the stars correspond to the parameters for panels (E)-(I). Wide distributions indicate cycling (e.g. panels F and I), single narrow distributions correspond to co-continuously stable strategies (e.g. panels E and G), and two narrow distributions imply diversification in the host through evolutionary branching (e.g. panel H). Mate choice of infected individuals is given by: (A, C) $m_I(g,\beta) = m_S(g)(1-gv(\beta))$ and (B, D) $m_I(g,\beta) = m_S(g)(1-gv(\beta)^2)$, each with lower bounds of 0, and with: (A, B) sterility virulence, $v(\beta) = 1-f(\beta)$, $f(\beta) = \eta\beta$, $\alpha(\beta) = 0$ and (C, D) mortality virulence, $v(\beta) = \frac{\alpha(\beta)}{\kappa}$, $\alpha(\beta) = \kappa\beta$, $f(\beta) = 1$. Remaining parameters as described in Fig. 1, except $\eta = 1, \kappa = 8, r = 10$.

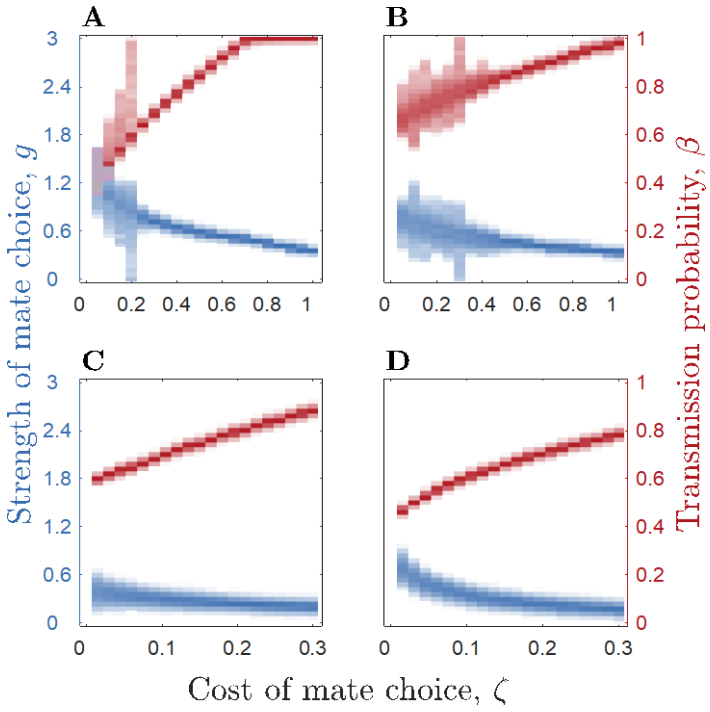

Figure 5 – Coevolution of host mate choice, g, and STI transmission probability, β with increased recovery ($\gamma = 1$). Panels and remaining parameters otherwise as described in Fig. 4.

Discussion

Understanding the role of STIs in the evolution of host mating strategies, and in turn, the effects of mating behaviour on disease evolution are inherently linked, yet to date theoretical models have almost exclusively focussed on one-sided adaptation rather than coevolution (Thrall et al. 1997, 2000; Knell 1999; Boots and Knell 2002; Kokko et al. 2002; Ashby and Gupta 2013; McLeod and Day 2014). The lack of coevolutionary perspectives on host-STI dynamics remains a major gap in the theoretical literature, which is surprising since (1) host coevolution with non-STIs is common in theoretical models (van Baalen 1998; Gandon et al. 2002; Lion and Gandon 2014; Best et al. 2017; Ashby et al. 2019), and (2) coevolution was a key feature in the seminal paper on parasite-mediated sexual selection by Hamilton and Zuk (1982). As an exception, Ashby and Boots (2015) recently proposed a theoretical model of host-STI coevolution, showing that reciprocal adaptations in host mate

choosiness and STI virulence could lead to stable levels of both traits or fluctuating selection. However, the model made a number of restrictive assumptions, such as serially monogamous mating, no recovery from infection, no mortality virulence, and highly non-linear mating functions, each of which could reduce the generality of the predictions. Here, I have derived and analysed a related but more general framework for host-STI coevolution which relaxes these assumptions, showing that the key findings are indeed robust under a wide range of conditions, as well as discovering the potential for evolutionary branching (dimorphism) in host mate choice.

Relaxing the aforementioned modelling assumptions may have conflicting effects on the costs and benefits of mate choice. For example, when sexual contacts are ephemeral rather than serially monogamous, individuals no longer spend a period of time paired (and hence isolated) from the rest of the population, which means that on average hosts will come into contact with a larger number of mates. Under serial monogamy, choosing a 'bad' partner is very costly because of this isolation effect (higher risk of infection due to sustained contact, fewer offspring), but under ephemeral mating the risk of eventually coming into contact with an infected mate will be higher (more rapid partner turnover). Although the mating behaviours are quite different, one can see that mate choice readily evolves in both scenarios.

Recovery from infection is likely to reduce the benefits of mate choice as both disease prevalence and the costs of contracting an infection are lower (since infection is acute rather than chronic), yet recovery did not prevent the evolution of mate choice in the model. Instead, recovery tended to have a stabilising effect on the coevolutionary dynamics (Fig. 4, 5). For simplicity, I assumed that recovery does not lead to immunity from future infection and that the condition of recovered individuals does not differ from those who have yet to experience infection. The former assumption is fairly standard for most STIs, which are less likely than non-STIs to result in lasting immunity (Lockhart et al. 1996), but the latter deserves further investigation. While it is possible for hosts to fully recover from

343 infection, it is also reasonable to suspect that host condition may remain lower for some time
344 following pathogen clearance, in which case these hosts should have lower mating success than
345 individuals who have never been infected. In future, a simple extension of the current model would
346 be to explore the effects of temporary or permanent reductions in host condition following infection,
347 as this will separate the effects of mate choice into components representing transmission avoidance
348 (i.e. avoiding infectious individuals) and partner fertility (i.e. choosing more fertile partners).

349 The third assumption relaxed in the present study was the inclusion of mortality virulence. Ashby and
350 Boots (2015) only allowed for sterility virulence (a reduction in the fecundity of infected hosts), which
351 is reasonable given that STIs often have sterilising effects and tend to cause less mortality than non-
352 STIs (Lockhart et al. 1996). Still, given that many STIs do cause mortality (e.g. Syphilis in humans) the
353 effects of mortality virulence on host-STI coevolution deserve investigation. One might expect the
354 benefits of mate choice to be greater if STIs cause sterility rather than mortality, as (1) individuals may
355 be unable to reproduce at all and (2) disease prevalence is likely to be higher as mortality virulence
356 reduces R_0 by lowering the infectious period (equation 21), which means all else being equal the risk
357 of infection will be lower under mortality virulence. While the impact on one-sided host or STI
358 adaptation under mortality or sterility virulence were broadly the same (Fig. 2-3), there were some
359 notable differences in the coevolutionary dynamics. In particular, coevolutionary cycling was much
360 more common under sterility virulence – likely because reductions in fecundity can cause sudden
361 declines in population size and are generally known to induce oscillatory dynamics (Ashby and Gupta
362 2014) – but under mortality virulence hosts were also able to branch into two coexisting strategies.
363 This suggest that under certain conditions (mortality virulence and low costs of mate choice) choosy
364 hosts may coexist with non-choosy hosts in the same population. This outcome was not previously
365 observed by Ashby and Boots (2015) where the model focussed on sterility virulence.

366 Finally, using mating functions that are highly non-linear is likely to accentuate the costs and benefits
367 of mate choice in certain regions of the parameter space (e.g. low/high virulence), leading to strong
368 selection for or against mating behaviour which may precipitate cycling. Indeed, Ashby and Boots
369 (2015) explored a variety of different mate choice functions as extensions of the primary model,
370 which produced the same range of qualitative outcomes as the exponent functions examined in the
371 main text. Here, I have further generalised the mate choice functions into separate components
372 representing the probability of accepting a healthy mate, $m_S(g)$, and the probability of accepting an
373 infectious mate $m_I(g,\beta)$, with $m_I(g,\beta) \leq m_S(g)$. As expected, moving from linear to non-linear
374 mating functions tends to have a destabilising effect leading to more coevolutionary cycling (Fig. 4-5).

375 By generalising the theory for host-STI coevolution, the present study opens the door to testing
376 predictions in a wider range of systems. To date, many empirical studies have struggled to find
377 evidence that hosts are able to discriminate between individuals with and without STIs (Abbot and Dill
378 2001; Webberley et al. 2002; Nahrung and Allen 2004). At first this seems surprising given that hosts
379 should, in theory, be under strong selection to avoid choosing infected mates. There are a number of
380 possible reasons as to why this may not always be the case. For example, hosts may simply be unable
381 to detect signs of infection due to their own physiological limitations. This is not a particularly
382 satisfying or general explanation, since various species have been found to prefer social or sexual
383 contacts based on visual or olfactory cues relating to infection (Clayton 1990; Willis and Poulin 2000;
384 Moshkin et al. 2012). Instead, it is more likely that hosts may be unable to detect infection due to
385 strong selection on STIs to be inconspicuous, potentially through low virulence. For instance, sexually
386 transmitted mites in ladybirds and the eucalypt beetle appear to have no negative impact on fertility
387 or mortality under non-stress conditions (Webberley and Hurst 2002; Nahrung and Clarke 2007).
388 Another related possibility is that hosts can sometimes discriminate between infected and uninfected
389 individuals, but the costs of mate choice are too high relative to infection. In the model, mate choice
390 only evolves under certain conditions, and may not evolve even when the STI is relatively virulent,

391 conspicuous, or prevalent, if mate choice is intrinsically costly. Thus, any costs associated with mate
392 choice (e.g. fewer mating opportunities) must be weighed against the potential benefits of avoiding
393 infection. Another alternative is that hosts have other, more effective, forms of defence against STIs,
394 such as post-copulatory grooming or urination to remove parasites (Hart et al. 1987; Nunn 2003). This
395 area has received very little theoretical attention and is an intriguing target for future theoretical
396 research on host-STI coevolution.

397 CONCLUSION

398 The lack of coevolutionary theory on host-STI relationships remains a challenge for understanding
399 parasite-mediated sexual selection, but the present study provides new insights into these dynamics.
400 Despite fundamental changes in mating dynamics and disease characteristics, the model explored
401 herein reveals new coevolutionary dynamics and generalises those observed previously (Ashby and
402 Boots 2015). Hence, one can conclude that coevolutionary outcomes such as fluctuating selection
403 (cycling) or stable levels of mate choice and virulence are likely to be broadly applicable with regards
404 to mating patterns, disease effects and mate choice relationships.

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