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Supplementary Information for

Dynamics in a simple evolutionary-epidemiological model for the evolution of an initial asymptomatic infection stage

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Supporting Information Text

Theorems and Proofs for Results in Main Text

Theorem 1. *Suppose that $\alpha_1[\lambda]$ and $\nu_1[\lambda]$ are such that $\lim_{\lambda\to\infty} \alpha_1'[\lambda] = 0$ and $\lim_{\lambda\to\infty} \nu_1'[\lambda] = 0$. If $\alpha_1'[0] > \frac{\alpha_1[0]-\frac{\alpha_2\delta}{\nu_2+\delta}}{\nu_1[0]+\delta}\nu_1'[0]$, then there either exists at least one positive ESS $\lambda^* > 0$ or $\widehat{S}[\lambda]$ is a strictly decreasing function of λ and the ESS is at $\lambda^* \to \infty$. Conversely, if $\alpha_1'[0] < \frac{\alpha_1[0]-\frac{\alpha_2\delta}{\nu_2+\delta}}{\nu_1[0]+\delta}\nu_1'[0]$, then there either exists at least one unstable evolutionarily singular strategy or alternatively $\widehat{S}[\lambda]$ is a strictly increasing function of λ and the ESS is at $\lambda^* = 0$. If there exists such an unstable strategy, there is bistability with zero latency and (possibly maximal) positive latency.*

Proof. Note that minimizing $\widehat{S}[\lambda]$ is equivalent to maximizing $\mathcal{R}_0[\lambda]$. Differentiating $\mathcal{R}_0[\lambda]$ gives

$$\frac{d\mathcal{R}_0[\lambda]}{d\lambda} = -\frac{1}{(\nu_1[\lambda]+\delta)^2}\nu_1'[\lambda]\left(\alpha_1[\lambda] + \frac{\nu_1[\lambda]\alpha_2}{\nu_2+\delta}\right) + \frac{1}{\nu_1[\lambda]+\delta}\left(\alpha_1'[\lambda] + \frac{\nu_1'[\lambda]\alpha_2}{\nu_2+\delta}\right).$$

At $\lambda^* = 0$, it follows that $\left.\frac{d\mathcal{R}_0[\lambda]}{d\lambda}\right|_{\lambda=0} > 0$ if and only if $\alpha_1'[0] > \frac{\alpha_1[0]-\frac{\alpha_2\delta}{\nu_2+\delta}}{\nu_1[0]+\delta}\nu_1'[0]$. Since $\lim_{\lambda\to\infty}\frac{d\mathcal{R}_0[\lambda]}{d\lambda} = 0$, if $\left.\frac{d\mathcal{R}_0[\lambda]}{d\lambda}\right|_{\lambda=0} > 0$ then there either exists at least one positive local maximum of $\mathcal{R}_0[\lambda]$ that is a positive ESS of latency, or $\mathcal{R}_0[\lambda]$ is a strictly increasing function of λ and the ESS is at $\lambda^* \to \infty$. Conversely, the reversed inequalities establish that if $\alpha_1'[0] < \frac{\alpha_1[0]-\frac{\alpha_2\delta}{\nu_2+\delta}}{\nu_1[0]+\delta}\nu_1'[0]$, then $\mathcal{R}_0[\lambda]$ as a function of λ either has a local minimum or is strictly decreasing. If it is strictly decreasing, then the ESS is at $\lambda^* = 0$. □

Theorem 2. *Suppose that $\lim_{\lambda\to\infty} \alpha_1'[\lambda] = 0$ and $\lim_{\lambda\to\infty} \nu_1'[\lambda] = 0$.*

1. *If $\mathcal{R}_0^{(0)} > \mathcal{R}_0^{(\infty)}$ and $\alpha_1'[0] > \frac{\alpha_1[0]-\frac{\alpha_2\delta}{\nu_2+\delta}}{\nu_1[0]+\delta}\nu_1'[0]$, there exists at least one positive (and finite) ESS $\lambda^* > 0$.*

2. *If $\mathcal{R}_0^{(0)} < \mathcal{R}_0^{(\infty)}$ and $\alpha_1'[0] < \frac{\alpha_1[0]-\frac{\alpha_2\delta}{\nu_2+\delta}}{\nu_1[0]+\delta}\nu_1'[0]$, there exists at least one unstable evolutionarily singular strategy, resulting in bistability of zero and non-zero latency.*

Proof. The proof of this theorem follows almost immediately from the proof of Theorem 1. Noting that the condition $\mathcal{R}_0^{(0)} > \mathcal{R}_0^{(\infty)}$ rules out strictly increasing $\mathcal{R}_0[\lambda]$ as a function of λ, this guarantees the existence of a finite positive ESS if $\alpha_1'[0] > \frac{\alpha_1[0]-\frac{\alpha_2\delta}{\nu_2+\delta}}{\nu_1[0]+\delta}\nu_1'[0]$. Conversely, $\mathcal{R}_0^{(0)} < \mathcal{R}_0^{(\infty)}$ rules out the case of strictly decreasing $\mathcal{R}_0[\lambda]$, establishing the existence of at least one unstable evolutionarily singular strategy if $\alpha_1'[0] < \frac{\alpha_1[0]-\frac{\alpha_2\delta}{\nu_2+\delta}}{\nu_1[0]+\delta}\nu_1'[0]$. □

Theorem 3. *Let $\alpha_{1,0} = \alpha_1[0]$ and $\nu_{1,0} = \nu_1[0]$. First, consider the following key condition*

$$\frac{b_1b_2}{c_1c_2} < \frac{\alpha_{1,0} - \frac{\alpha_2\delta}{\nu_2+\delta}}{\nu_{1,0}+\delta}, \qquad [1]$$

The evolutionary dynamics of latency in our model can be partitioned into multiple cases that are outlined below.

1. *$\frac{\alpha_2}{\nu_2+\delta} \geq \frac{\alpha_{1,\infty}}{\delta}$. If [1] holds, then there exists a unique positive ESS $\lambda^* > 0$. Otherwise, if condition [1] is not met, $\mathcal{R}_0[\lambda]$ is a strictly decreasing function of λ, so $\widehat{S}$ is a strictly increasing function of λ on $(0,\infty)$, and the ESS is at $\lambda^* = 0$.*

2. *$\frac{\alpha_2}{\nu_2+\delta} < \frac{\alpha_{1,\infty}}{\delta}$.*
   - (a) *$c_2 > b_2$. If [1] is satisfied, then there exists a unique positive ESS $\lambda^* > 0$. Otherwise, if [1] does not hold, $\mathcal{R}_0[\lambda]$ is a strictly decreasing function, so $\widehat{S}[\lambda]$ is a strictly increasing function and the ESS is at $\lambda^* = 0$.*
   - (b) *$c_2 < b_2$. If [1] is satisfied, then $\mathcal{R}_0[\lambda]$ is a strictly increasing function, so $\widehat{S}[\lambda]$ is a strictly decreasing function and the evolutionarily stable strategy is at $\lambda^* \to \infty$. Conversely, if $\frac{b_1b_2}{c_1c_2} > \frac{\alpha_{1,0}-\frac{\alpha_2\delta}{\nu_2+\delta}}{\nu_{1,0}+\delta}$, then there exists a unique evolutionarily singular strategy $\lambda^* > 0$ that is the global minimum of $\mathcal{R}_0[\lambda]$ and therefore is the global maximum of $\widehat{S}[\lambda]$. This singular strategy λ^* then implies that the local minima of $\widehat{S}[\lambda]$ (and so the local maxima of $\mathcal{R}_0[\lambda]$) are at the boundaries, i.e. at $\lambda^* = 0$ and $\lambda^* \to \infty$. Thus, there is bistability of zero latency ($\lambda^* = 0$) and maximal latency ($\lambda^* \to \infty$).*

Proof. First, let $k = \frac{\alpha_2}{\nu_2+\delta}$ and $P = (1+\lambda)^{-c_2}$. Note also that $\frac{d\mathcal{R}_0[\lambda]}{d\lambda} = 0$ if and only if $\frac{d\mathcal{R}_0[P]}{dP} = 0$. Furthermore, $\frac{d\mathcal{R}_0}{d\lambda} = \frac{d\mathcal{R}_0}{dP}\frac{dP}{d\lambda} = -\frac{d\mathcal{R}_0}{dP}c_2(1+\lambda)^{-c_2-1}$, and so the signs of $\frac{d\mathcal{R}_0}{dP}$ and $\frac{d\mathcal{R}_0}{d\lambda}$ are opposite. Thus, taking the first derivative of $\mathcal{R}_0[P]$ with respect to P gives

$$\frac{d\mathcal{R}_0[P]}{dP} = \frac{\frac{b_2}{c_2}b_1P^{\frac{b_2}{c_2}-1} + kc_1}{\delta + c_1P + \nu_{1,\infty}} - c_1\frac{b_1P^{\frac{b_2}{c_2}} + \alpha_{1,\infty} + kc_1P + k\nu_{1,\infty}}{(\delta + c_1P + \nu_{1,\infty})^2}.$$

Setting $\frac{d\mathcal{R}_0[P]}{dP} = 0$ gives

$$0 = -c_1b_1P^{\frac{b_2}{c_2}} - \alpha_{1,\infty}c_1 + \delta\frac{b_1b_2}{c_2}P^{\frac{b_2}{c_2}-1} + \delta kc_1 + \frac{c_1b_1b_2}{c_2}P^{\frac{b_2}{c_2}} + \nu_{1,\infty}\frac{b_1b_2}{c_2}P^{\frac{b_2}{c_2}-1}$$

Multiplying both sides by $\frac{c_2}{b_1b_2}P^{-\frac{b_2}{c_2}}$, replacing $P = (1+\lambda)^{-c_2}$, gives

$$0 = A_0 + A_1(\lambda+1)^{c_2} + A_2(\lambda+1)^{b_2} = f[\lambda],$$

where

$$\begin{aligned} A_0 &= c_1 - \tfrac{c_1c_2}{b_2}, \\ A_1 &= (\nu_{1,\infty} + \delta), \\ A_2 &= \tfrac{c_1c_2}{b_1b_2}(k\delta - \alpha_{1,\infty}) = \tfrac{c_1c_2\delta}{b_1b_2}\left(k - \tfrac{\alpha_{1,\infty}}{\delta}\right). \end{aligned}$$

Case 1: $k \geq \frac{\alpha_{1,\infty}}{\delta}$**.** We first consider the case that $A_2 \geq 0$. Then, $f[\lambda]$ is a strictly increasing function from $A_0 + A_1 + A_2$ to ∞. Therefore, if $f[0] < 0$, then $f[\lambda]$ crosses the λ–axis exactly once and there exists a unique positive root λ^* to $f[\lambda] = 0$, otherwise if $f[0] > 0$ then $f[\lambda] = 0$ has no positive real roots. If the unique positive root exists, $f[\lambda] < 0$ for $\lambda < \lambda^*$ and $f[\lambda] > 0$ for $\lambda > \lambda^*$.

Furthermore, noting that $\frac{d\mathcal{R}_0[\lambda]}{d\lambda} = -K[\lambda]f[\lambda]$, where $K[\lambda] > 0$ for all λ, it follows that if $f[0] < 0$ then $\left.\frac{d\mathcal{R}_0[\lambda]}{d\lambda}\right|_{\lambda=0} > 0$ and λ^* is the unique maximum of $\mathcal{R}_0[\lambda]$ ($f[0] < 0 < f[\infty]$), and so the unique minimum of $\widehat{S}[\lambda]$, and the evolutionarily stable strategy (ESS) is λ^*. Otherwise , if $f[0] > 0$, then $\left.\frac{d\mathcal{R}_0[\lambda]}{d\lambda}\right|_{\lambda=0} < 0$ and $\mathcal{R}_0[\lambda]$ is a strictly decreasing function of λ. In this case, the maximum of $\mathcal{R}_0[\lambda]$ is at $\lambda^* = 0$ and thus the ESS is $\lambda^* = 0$. If $f[0] = 0$, then $\left.\frac{d\mathcal{R}_0[\lambda]}{d\lambda}\right|_{\lambda=0} = 0$, and $f[\lambda]$ strictly increasing implies that $\lambda^* = 0$ is the only ESS. Therefore, there is a unique ESS $\lambda^* > 0$ if and only if $f[0] = A_1 + A_2 + A_3 < 0$. Rearranging $A_1 + A_2 + A_3 < 0$ gives [1].

Case 2: $k < \frac{\alpha_{1,\infty}}{\delta}$**.** Suppose $A_2 < 0$, so that $k < \frac{\alpha_{1,\infty}}{\delta}$. We now consider the following subcases.

Subcase 2a: $c_2 > b_2$. Suppose first that $c_2 > b_2$. Then, rearranging $f[\lambda]$ gives

$$A_1(\lambda+1)^{c_2} = -A_0 - A_2(\lambda+1)^{b_2},$$

where $-A_0 > 0$, $A_1 > 0$, and $-A_2 > 0$. Multiplying both sides by $(\lambda+1)^{-b_2}$ gives

$$A_1(\lambda+1)^{c_2-b_2} = -A_0(\lambda+1)^{-b_2} - A_2.$$

Denoting $g_1[\lambda] = A_1(\lambda+1)^{c_2-b_2}$ and $g_2[\lambda] = -A_0(\lambda+1)^{-b_2} - A_2$, it is clear that g_1 is a strictly increasing function from A_1 to ∞, and that g_2 is a strictly decreasing function from $-A_0 - A_2$ to $-A_2$. Thus, if $g_1[0] < g_2[0]$, then these curves will intersect exactly once. Such an intersection is a root of $f[\lambda] = 0$, and thus an evolutionarily singular strategy. Otherwise, if $g_1[0] > g_2[0]$, then g_1 and g_2 do not intersect and $f[\lambda] = 0$ has no positive real root. If $g_1[0] = g_2[0]$, then $\lambda^* = 0$ is the only intersection of $g_1[\lambda]$ and $g_2[\lambda]$, and the only root of $f[\lambda]$. Here, $g_1[0] < g_2[0]$ means that $A_1 < -A_0 - A_2$ and so that $A_0 + A_1 + A_2 < 0$. Therefore, in this subcase, $\frac{d\mathcal{R}_0[\lambda]}{d\lambda} = 0$ has a unique positive root λ^* if and only if $A_0 + A_1 + A_2 < 0$. Since $f[\lambda] < 0$ for $\lambda < \lambda^*$ and $f[\lambda] > 0$ for $\lambda > \lambda^*$ in this case as well, λ^* maximizes $\mathcal{R}_0[\lambda]$. As in **Case 1**, this condition also implies that $\lambda^* > 0$ is the ESS if $A_0 + A_1 + A_2 < 0$. Otherwise, also as in **Case 1**, $\lambda^* = 0$ is the ESS.

Subcase 2b: $b_2 > c_2$. We now consider the other subcase, namely that $b_2 > c_2$. This condition implies that $A_0 > 0$ and $A_2 < 0$, so rewriting $f[\lambda]$ and multiplying both sides by $(\lambda+1)^{-c_2}$ gives

$$A_0(\lambda+1)^{-c_2} + A_1 = -A_2(\lambda+1)^{b_2-c_2},$$

with $A_0 > 0$, $A_1 > 0$, and $-A_2 > 0$. Denoting $h_1[\lambda] = A_0(\lambda+1)^{-c_2} + A_1$ and $h_2[\lambda] = -A_2(\lambda+1)^{b_2-c_2}$, it is clear that h_1 is a strictly decreasing function of λ from $A_0 + A_1$ to A_1 and that h_2 is a strictly increasing function from $-A_2$ to ∞. Thus, if $h_2[0] < h_1[0]$, then h_1 and h_2 intersect exactly once at $\lambda^* > 0$; otherwise these curves do not cross for positive λ.

Thus, if it exists, $\lambda^* > 0$ is the unique positive root of $f[\lambda] = 0$ and thus the unique positive root of $\frac{d\mathcal{R}_0[\lambda]}{d\lambda} = 0$. Therefore, $\lambda^* > 0$ is a critical point of $\mathcal{R}_0[\lambda]$ if $-A_2 < A_0 + A_1$, which is equivalent to the condition that $A_0 + A_1 + A_2 > 0$. But, as $\left.\frac{d\mathcal{R}_0[\lambda]}{d\lambda}\right|_{\lambda=0} = -K[0](A_0 + A_1 + A_2)$, it follows that if $A_0 + A_1 + A_2 > 0$ then $\left.\frac{d\mathcal{R}_0[\lambda]}{d\lambda}\right|_{\lambda=0} < 0$ and λ^* is a local minimum of $\mathcal{R}_0[\lambda]$, and thus an unstable evolutionarily singular strategy (note that $f[\lambda] > 0$ for $\lambda < \lambda^*$ and $f[\lambda] < 0$ for $\lambda > \lambda^*$). Therefore, the two local maxima of $\mathcal{R}_0[\lambda]$ are at the boundaries, *i.e.* $\lambda^* = 0$ and at $\lambda^* \to \infty$. Thus, in this subcase, *i.e.* $A_1 + A_2 + A_3 > 0$, strategies with zero latency ($\lambda^* = 0$) and with maximal latency ($\lambda^* \to \infty$) are bistable. Rearranging $A_1 + A_2 + A_3 > 0$ results in $\frac{b_1 b_2}{c_1 c_2} > \frac{\alpha_{1,0} - \frac{\alpha_2 \delta}{\nu_2 + \delta}}{\nu_{1,0} + \delta}$. If $A_0 + A_1 + A_2 < 0$, then $\frac{d\mathcal{R}_0[\lambda]}{d\lambda} = 0$ has no roots, and since $\left.\frac{d\mathcal{R}_0[\lambda]}{d\lambda}\right|_{\lambda=0} > 0$ in this case, $\mathcal{R}_0[\lambda]$ is strictly increasing. If $h_1[0] = h_2[0]$, then $\lambda = 0$ is the only intersection of $h_1[\lambda]$ and $h_2[\lambda]$. Since $h_2[\lambda] > h_1[\lambda]$ for $\lambda > 0$, then $\mathcal{R}_0[\lambda]$ is also strictly increasing for $\lambda > 0$ and $S[\lambda]$ is strictly decreasing for $\lambda > 0$. Thus, the evolutionarily stable strategy if $A_0 + A_1 + A_2 \le 0$ is at $\lambda^* \to \infty$.

Equivalent analyses hold when P is replaced with $P = e^{-\lambda c_2}$, *i.e.*, in the case of exponential trade-offs, since $e^{\lambda x}$ is strictly increasing for $\lambda \in [0, \infty)$ if $x > 0$ and strictly decreasing for $\lambda \in [0, \infty)$ if $x < 0$. Thus, the same results hold for trade-offs formulated as exponentials, and an equivalent argument holds for trade-offs as $\alpha_1[\lambda] = b_1(F[\lambda])^{-b_2} + \alpha_{1,\infty}$ and $\nu_1[\lambda] = c_1(F[\lambda])^{-b_2} + \nu_{1,\infty}$ for any function $F[\lambda]$ with $F'[\lambda] > 0$, $F[0] = 1$ and $F[\infty] = \infty$. ◻

Remark 1. *This remark illustrates a different derivation for the condition that* $\widehat{S}'[0] > 0$. *Letting* $A[\lambda] = \alpha_1[\lambda] - k\delta$ *and* $B[\lambda] = \nu_1[\lambda] + \delta$ *and noting that* $\alpha_1'[0] = -b_1 b_2$ *and* $\nu_1'[0] = -c_1 c_2$, *the condition* $\frac{b_1 b_2}{c_1 c_2} > \frac{\alpha_{1,0} - k\delta}{\nu_{1,0} + \delta}$ *becomes* $\frac{A'[0]}{B'[0]} > \frac{A[0]}{B[0]}$. *Rearranging this gives* $B[0]A'[0] - A[0]B'[0] < 0$ *since* $B'[0] < 0$. *Since* $B > 0$, *it follows that* $\frac{B[0]A'[0] - A[0]B'[0]}{B[0]^2} < 0$. *By the quotient rule and noting that* $\frac{A}{B} = \mathcal{R}_0 - k$, $\frac{b_1 b_2}{c_1 c_2} - \frac{\alpha_{1,0} - k\delta}{\nu_{1,0} + \delta} > 0$ *if and only if* $\widehat{S}[\lambda]$ *is increasing at* $\lambda = 0$ *(i.e.,* $\mathcal{R}_0[\lambda]$ *is decreasing at* $\lambda = 0$*).*

Theorem 4. *In our model, all evolutionarily stable strategies are locally stable.*

Proof. First, suppose that the ESS is at $\lambda^* = 0$. Then, by Theorem 3, $\left.\frac{d\mathcal{R}_0[\lambda]}{d\lambda}\right|_{\lambda=0} \le 0$, and $\mathcal{R}_0[\lambda]$ is strictly decreasing in the neighborhood. Thus, if $x < y$ then $\mathcal{R}_0[x] > \mathcal{R}_0[y]$, *i.e.*, mutants progressively closer to 0 are able to invade and the fully symptomatic ESS is eventually reached, *i.e.*, this ESS is a continuously stable strategy. When a positive ESS (or one at infinity) exists as proved in Theorem 3, by a similar argument it can invade any strategy in its neighborhood and so is a continuously stable strategy (CSS). ◻

Additional Preliminaries

For simplicity, the model we present in the main text does not consider death due to disease. Here, we show why our analyses also hold when we consider a model that does include death due to disease. As with the SIIRS model presented in the main text, the model formulated below is equivalent to special cases of existing epidemiological models: see, for example, the models presented by Melesse and Gumel (1) and Saad-Roy and colleagues (2). Since the total population can now vary, we denote by S, I_1, and I_2 the number of individuals that are susceptible, infectious in the first stage, and infectious in the second stage, respectively. We denote by δ the demographic death rate, and by α_1 and α_2 the transmission rates from stages 1 and 2, respectively. We also denote by ν_1 the progression rate from stage 1 to stage 2, and by ν_2 the death rate due to disease. Lastly, the number of new individuals per unit time is denoted by Λ. The model is thus

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \alpha_1 I_1 S - \alpha_2 I_2 S - \delta S, \\
\frac{dI_1}{dt} &= \alpha_1 I_1 S + \alpha_2 I_2 S - \nu_1 I_1 - \delta I_1, \\
\frac{dI_2}{dt} &= \nu_1 I_1 - \nu_2 I_2 - \delta I_2.
\end{aligned}$$

Using the next-generation matrix method (3, 4), the basic reproduction number for this model is

$$\mathcal{R}_0 = \frac{\alpha_1 \frac{\Lambda}{\delta}}{\nu_1 + \delta} + \frac{\nu_1}{\nu_1 + \delta} \frac{\alpha_2 \frac{\Lambda}{\delta}}{\nu_2 + \delta}.$$

Solving the S, I_1, and I_2 equations for equilibria yields a disease-free equilibrium, along with an endemic equilibrium with $\widehat{S} = \frac{\frac{\Lambda}{\delta}}{\mathcal{R}_0}$ if $\mathcal{R}_0 > 1$. The equations governing this model are equivalent to the decoupled equations in Theorem 7 of Saad-Roy and coauthors (2) with $\eta \to \infty$, $\tau_1 = 0$, and $\tau_2 = 0$. Thus, the global stability of the endemic equilibrium when $\mathcal{R}_0 > 1$ that was established by Saad-Roy *et al.* (2) therefore applies here also. Furthermore, Theorems 1–4 presented in *SI Appendix* hold under this model as well, since evolutionarily stable strategies are such that $\widehat{S}$ is minimized.

SI Results

Transitions with trade-offs as sums of logistic-like functions. As briefly mentioned in the main text, it is also possible that the trade-offs take more complicated shapes, such as logistic-like functions, *i.e.*,

$$\alpha_1[\lambda] = \sum_{i=1}^{n} \frac{b_{1,i}}{1+e^{-b_{2,i}(b_{3,i}-\lambda)}} + \alpha_{1,\infty},$$
$$\nu_1[\lambda] = \sum_{i=1}^{n} \frac{c_{1,i}}{1+e^{-c_{2,i}(c_{3,i}-\lambda)}} + \nu_{1,\infty}.$$

With these logistic-like trade-off formulations for $n = 1$, we also numerically characterized certain transitions in evolutionary dynamics as functions of key parameters (Figs. S7, S8). Note that these are only possible evolutionary dynamics and we have not proven any behavior analytically with these logistic-like trade-offs. We find that changes in $b_{2,1}$, the parameter governing the speed of decay (as a function of latency) of the stage 1 transmission rate, can lead to transitions in behavior (Fig. S7). For example, if this parameter is small enough (and smaller than the equivalent parameter $c_{2,1}$ for the stage 1 progression rate), then there can exist bistable strategies at zero latency and at an interior strategy. As $b_{2,1}$ increases, $\widehat{S}[\lambda]$ becomes strictly decreasing (and so the ESS is at maximal latency). Eventually, two interior singular strategies emerge again: however the boundary local minimum is now at infinite latency. Thus, in this regime, the system exhibits bistability with maximal latency and an interior strategy at some finite latency (Fig. S7). We also numerically investigated the effect of the 'threshold' parameter $b_{3,1}$, *i.e.*, the latency value where the logistic-like function changes concavity (Fig. S8). If $b_{2,1} = c_{2,1}$, then we find at most a single evolutionarily singular strategy. This strategy is unstable for small enough $b_{3,1}$ and then becomes stable as $b_{3,1}$ increases through $c_{3,1}$ (Fig. S8A). If $b_{2,1} > c_{2,1}$, then there is a single unstable evolutionarily singular strategy initially for small enough values of $b_{3,1}$, followed by two interior strategies as $b_{3,1}$ becomes larger, one stable and one unstable (Fig. S8B). A reciprocal effect is seen if $b_{2,1} > c_{2,1}$, with a single interior ESS present for large enough $b_{3,1}$ (Fig. S8C). As $b_{3,1}$ decreases, an unstable evolutionarily singular strategy emerges in addition to the interior ESS (Fig. S8C).

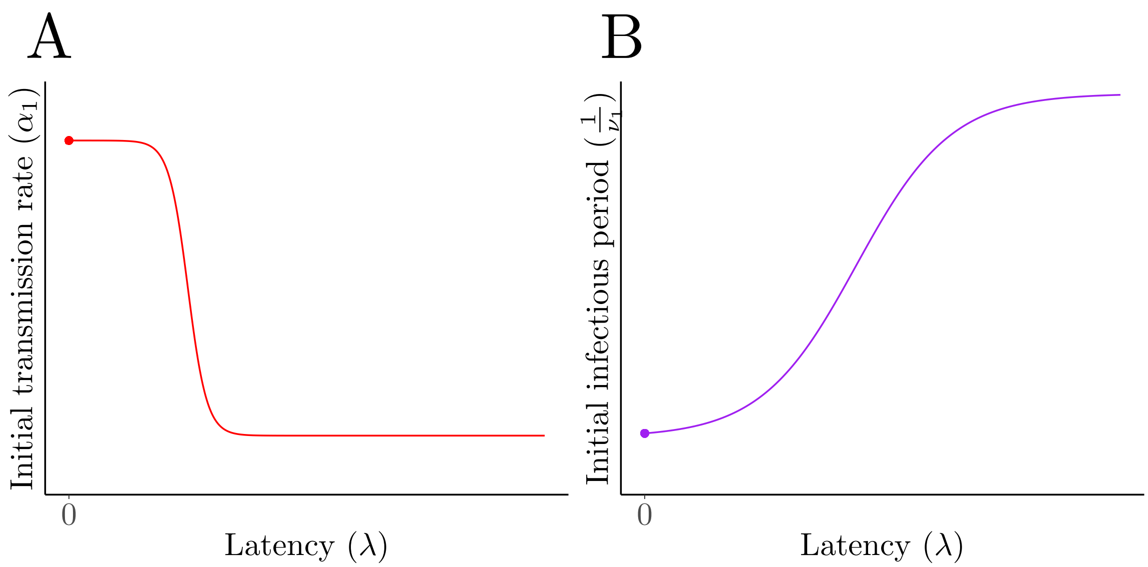

Fig. S1. Schematics of threshold-like trade-offs. Here, we model the transmission and progression rates in the first stage as (*A*) $\alpha_1[\lambda] = \frac{b_{1,1}}{1+e^{-b_{2,1}(b_{3,1}-\lambda)}} + \alpha_{1,\infty}$ and (*B*) $\nu_1[\lambda] = \frac{c_{1,1}}{1+e^{-c_{2,1}(c_{3,1}-\lambda)}} + \nu_{1,\infty}$, respectively.

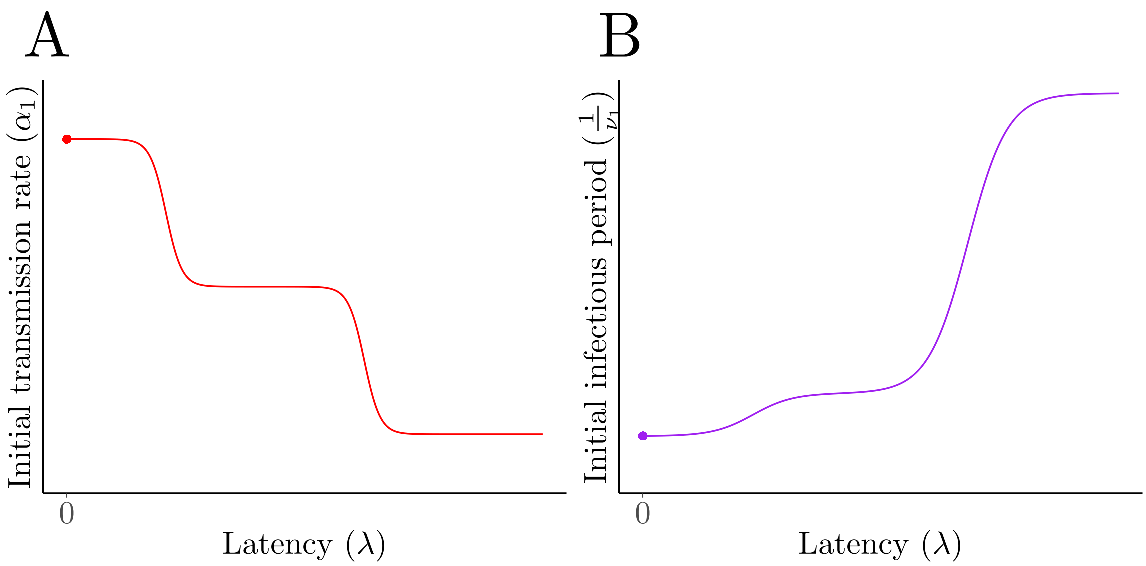

Fig. S2. Logistic-like trade-offs as in Fig. S1, but with two thresholds instead of one. (*A*) For the disease parameters of the first stage, the transmission rate is modelled as $\alpha_1[\lambda] = \frac{b_{1,1}}{1+e^{-b_{2,1}(b_{3,1}-\lambda)}} + \frac{b_{1,2}}{1+e^{-b_{2,2}(b_{3,2}-\lambda)}} + \alpha_{1,\infty}$ and (*B*) the first to second stage progression rate takes the form of $\nu_1[\lambda] = \frac{c_{1,1}}{1+e^{-c_{2,1}(c_{3,1}-\lambda)}} + \frac{c_{1,2}}{1+e^{-c_{2,2}(c_{3,2}-\lambda)}} + \nu_{1,\infty}$.

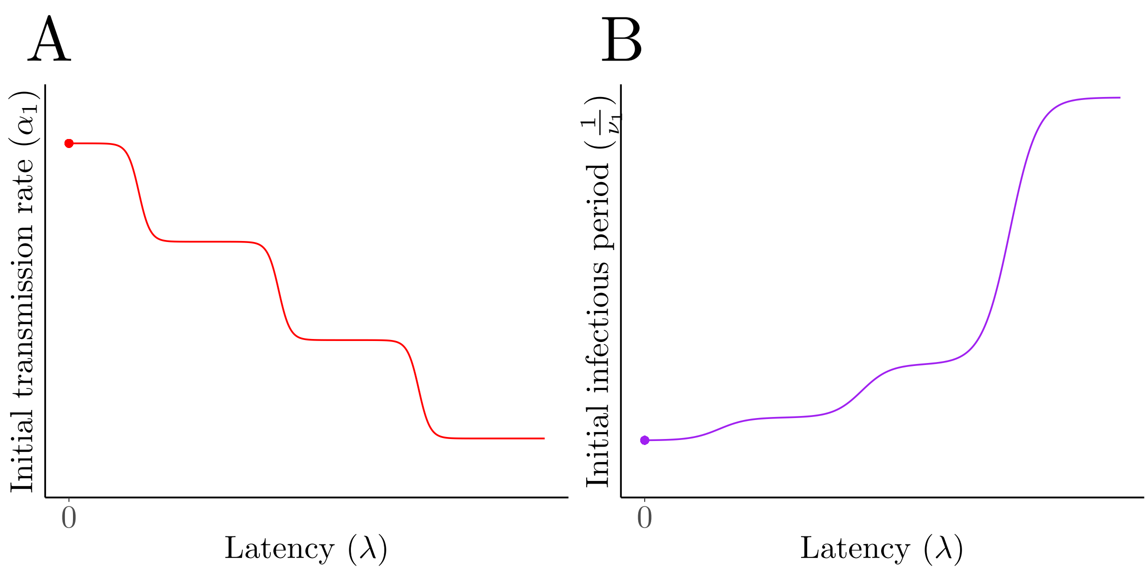

Fig. S3. Trade-off formulations as the sums of three logistic-like functions, as compared to one (Fig. S1) and two (Fig. S2). (*A*) The transmission rate in the first stage takes the form $\alpha_1[\lambda] = \frac{b_{1,1}}{1+e^{-b_{2,1}(b_{3,1}-\lambda)}} + \frac{b_{1,2}}{1+e^{-b_{2,2}(b_{2,3}-\lambda)}} + \frac{b_{1,3}}{1+e^{-b_{2,3}(b_{3,3}-\lambda)}} + \alpha_{1,\infty}$ and (*B*) the rate of progression from the first to the second stage is modelled as $\nu_1[\lambda] = \frac{c_{1,1}}{1+e^{-c_{2,1}(c_{3,1}-\lambda)}} + \frac{c_{1,2}}{1+e^{-c_{2,2}(c_{3,2}-\lambda)}} + \frac{c_{1,3}}{1+e^{-c_{2,3}(c_{3,3}-\lambda)}} + \nu_{1,\infty}$.

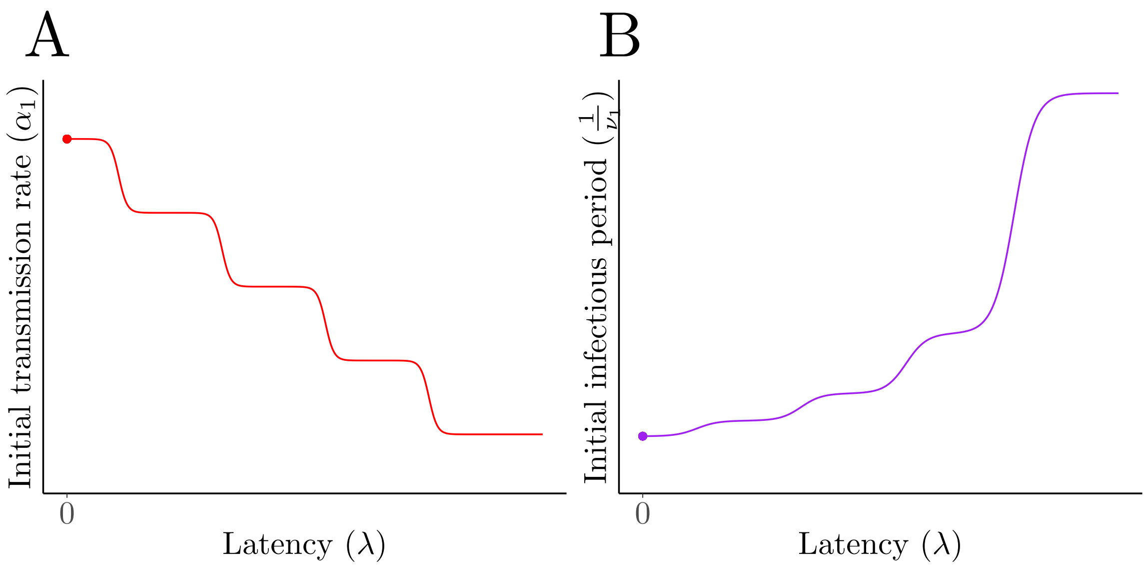

Fig. S4. Illustrative schematics for trade-offs with four thresholds, instead of 1 to 3 (Figs. S1 to S3, respectively). (*A*) The transmission rate during the first stage is modelled as $\alpha_1[\lambda] = \frac{b_{1,1}}{1+e^{-b_{2,1}(b_{3,1}-\lambda)}} + \frac{b_{1,2}}{1+e^{-b_{2,2}(b_{2,3}-\lambda)}} + \frac{b_{1,3}}{1+e^{-b_{2,3}(b_{3,3}-\lambda)}} + \frac{b_{1,4}}{1+e^{-b_{2,4}(b_{3,4}-\lambda)}} + \alpha_{1,\infty}$. (*B*) The progression rate from the first to the second stage is formulated as $\nu_1[\lambda] = \frac{c_{1,1}}{1+e^{-c_{2,1}(c_{3,1}-\lambda)}} + \frac{c_{1,2}}{1+e^{-c_{2,2}(c_{3,2}-\lambda)}} + \frac{c_{1,3}}{1+e^{-c_{2,3}(c_{3,3}-\lambda)}} + \frac{c_{1,4}}{1+e^{-c_{2,4}(c_{3,4}-\lambda)}} + \nu_{1,\infty}$.

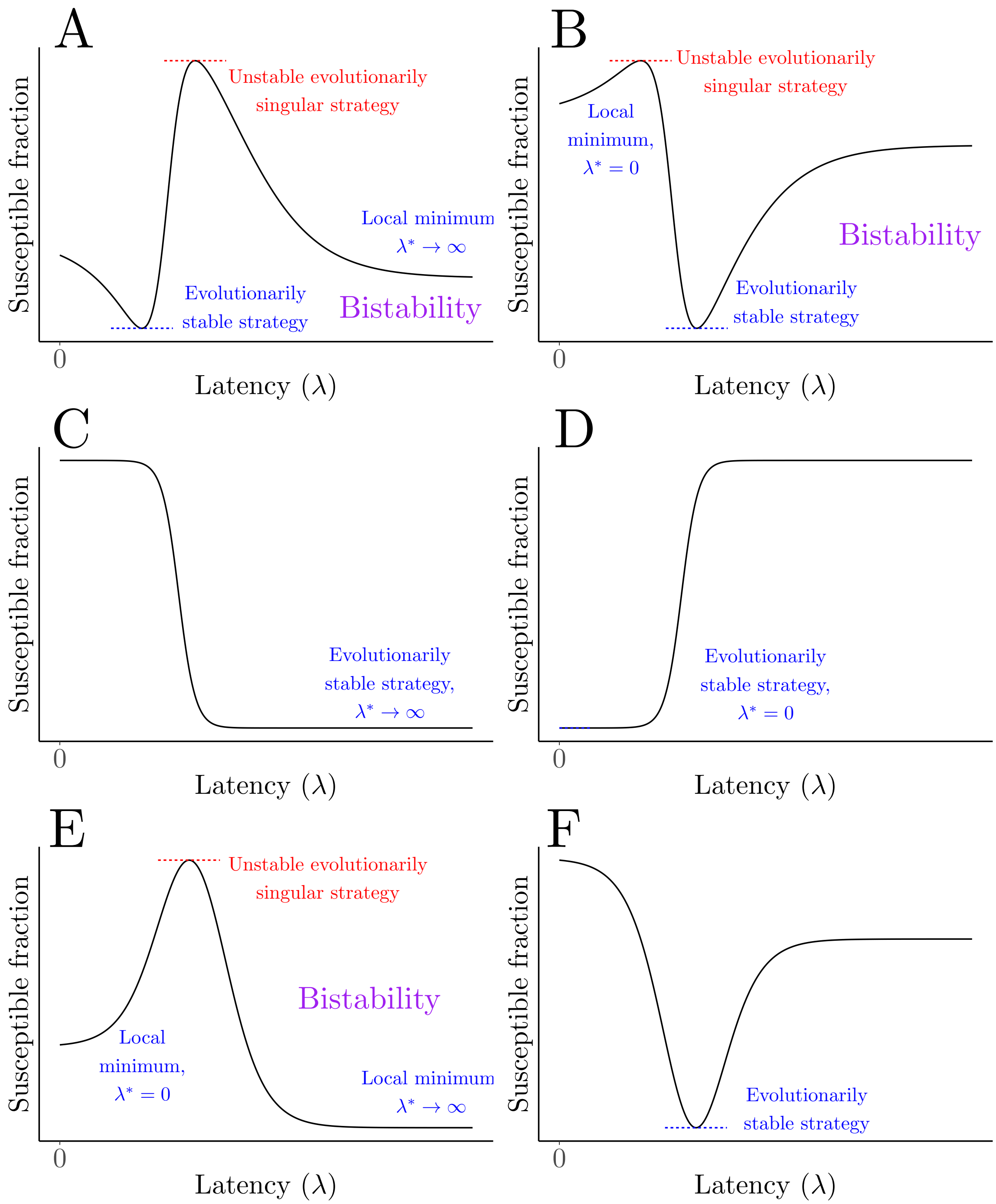

Fig. S5. Schematics of possible evolutionary dynamics of latency with logistic-like trade-offs. (*A*) Two interior evolutionarily singular strategies, one which is stable and thus an ESS and one which is unstable. The boundary at infinite latency is also stable, giving rise to bistability. The bistable strategies are infinite latency and some positive latency. This cannot occur under power-law or exponential thresholds. (*B*) Another case of bistability between an extremum and an interior strategy, with the extremum strategy at zero latency, *i.e.*, fully symptomatic. (*C*) The susceptible fraction is a strictly decreasing function, and so the ESS is at maximal latency. (*D*) The susceptible fraction is a strictly increasing function, and so the ESS is at zero latency. (*E*) A single interior unstable evolutionarily singular strategy, which leads to bistability. (*F*) A single interior ESS that minimizes the susceptible fraction at equilibrium.

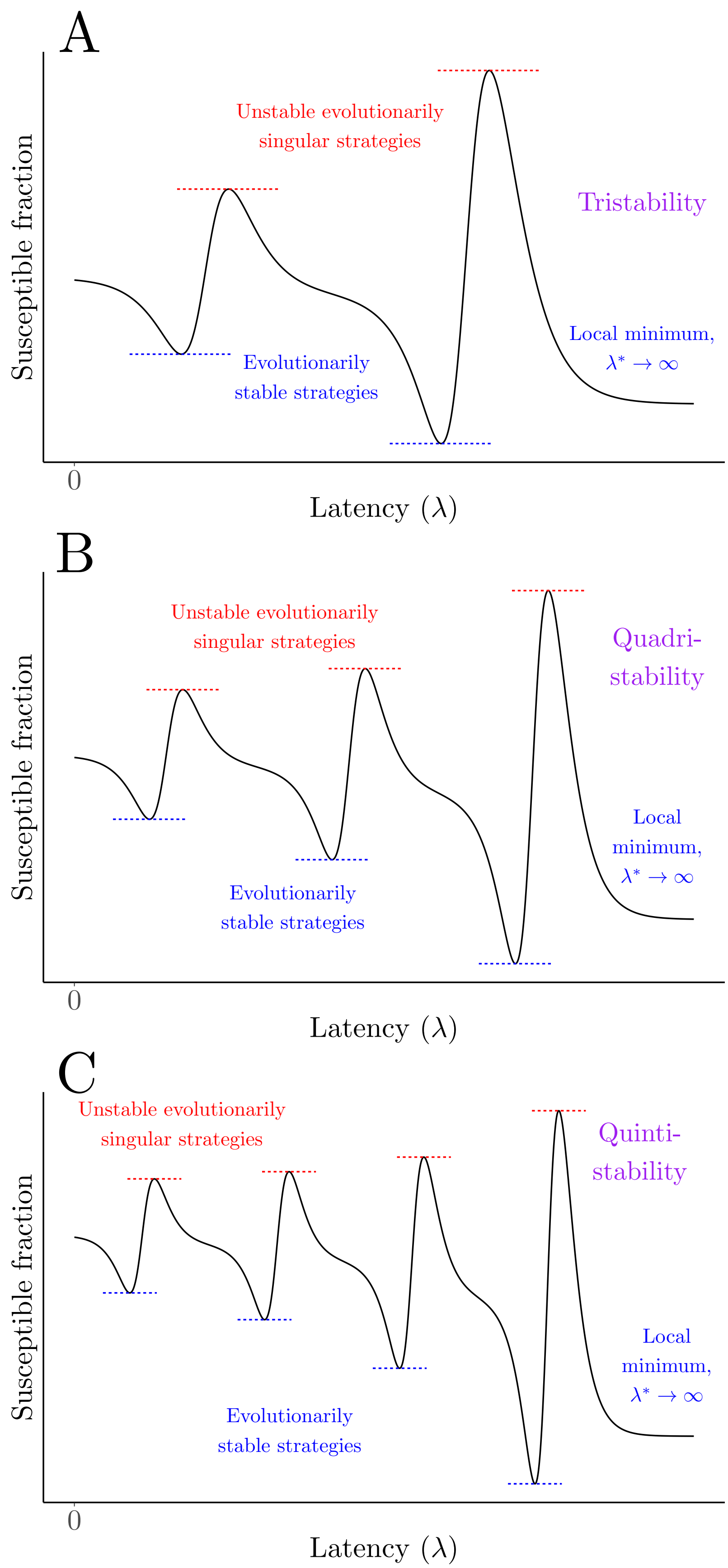

Fig. S6. Schematics of possible complex evolutionary dynamics obtained with more complicated functional forms for the trade-offs. (*A*) Using a logistic-like function with two threshold can give two interior ESSs and one ESS at infinite latency, in addition to two unstable evolutionarily singular strategies. (*B*) With three thresholds, it is possible that two additional interior singular strategies emerge, one stable and one unstable. (*C*) With four thresholds, a further two strategies can again emerge, for a total eight interior evolutionarily singular strategies, four unstable and four stable, in addition to one stable strategy at infinite latency.

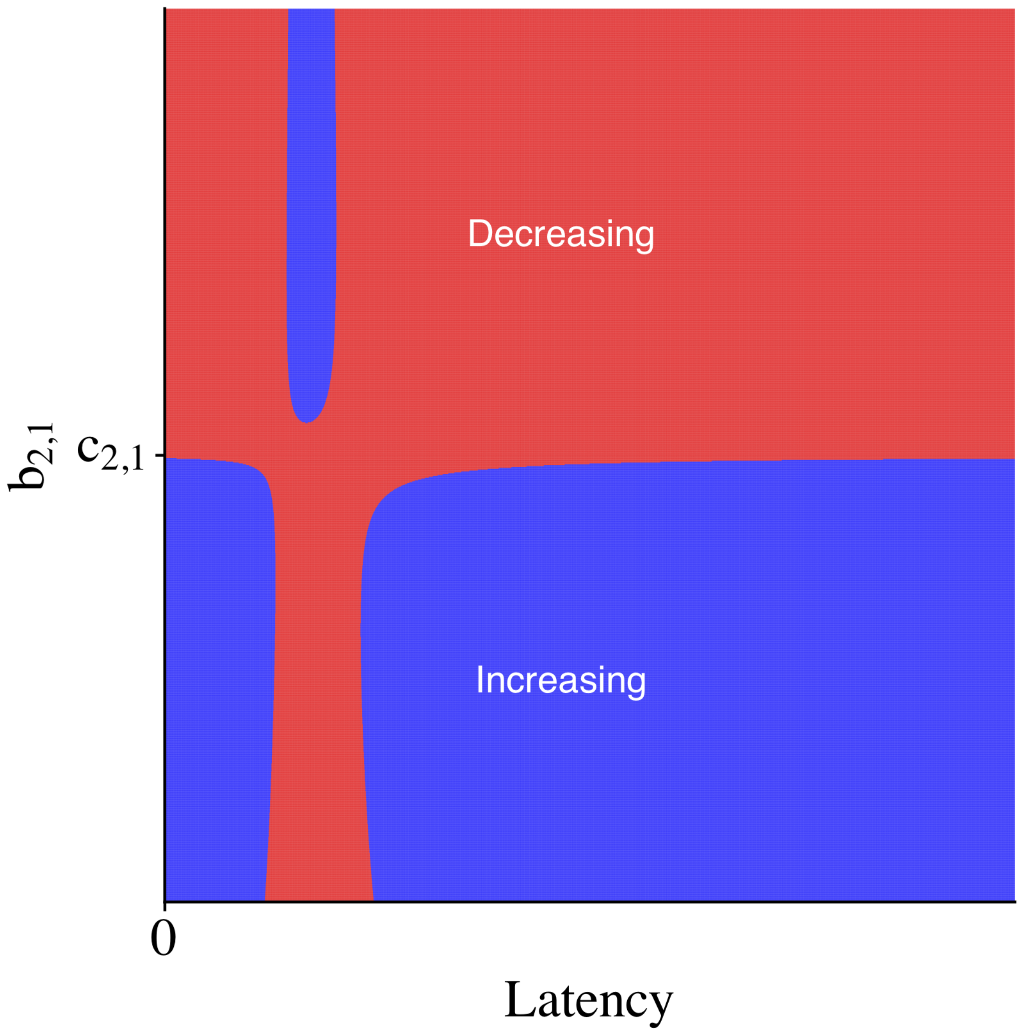

Fig. S7. Schematic of possible evolutionary transitions (sign of $\frac{dS}{d\lambda}$) mediated by changes in $b_{2,1}$ with logistic functional forms. Here, α_1 and ν_1 take the form of $\alpha_1[\lambda] = \frac{b_{1,1}}{1+e^{-b_{2,1}(b_{3,1}-\lambda)}} + \alpha_{1,\infty}$ and $\nu_1[\lambda] = \frac{c_{1,1}}{1+e^{-c_{2,1}(c_{3,1}-\lambda)}} + \nu_{1,\infty}$, and all other parameters apart from $b_{2,1}$ are fixed, with $b_{3,1} = c_{3,1}$. The *blue* and *red* regions are where $\widehat{S}[\lambda]$ is increasing and decreasing, respectively. Since $\frac{dS}{d\lambda}$ is continuous, if a point is at the intersection of a blue and red region, then it is an evolutionarily singular strategy, and classification (stable or unstable) follows by examining the sign change of $\frac{dS}{d\lambda}$. As $b_{2,1}$ increases, the stable states transition from bistability to a unique minimum at zero latency, and then to bistability again. For $b_{2,1}$ values that are slightly less than $c_{2,1}$ and smaller, the bistable states consist of one interior equilibrium and zero latency. For larger $b_{2,1}$ values, the bistable states also consists of one interior equilibrium and one extremum equilibrium, but the extremum equilibrium is at infinite latency.

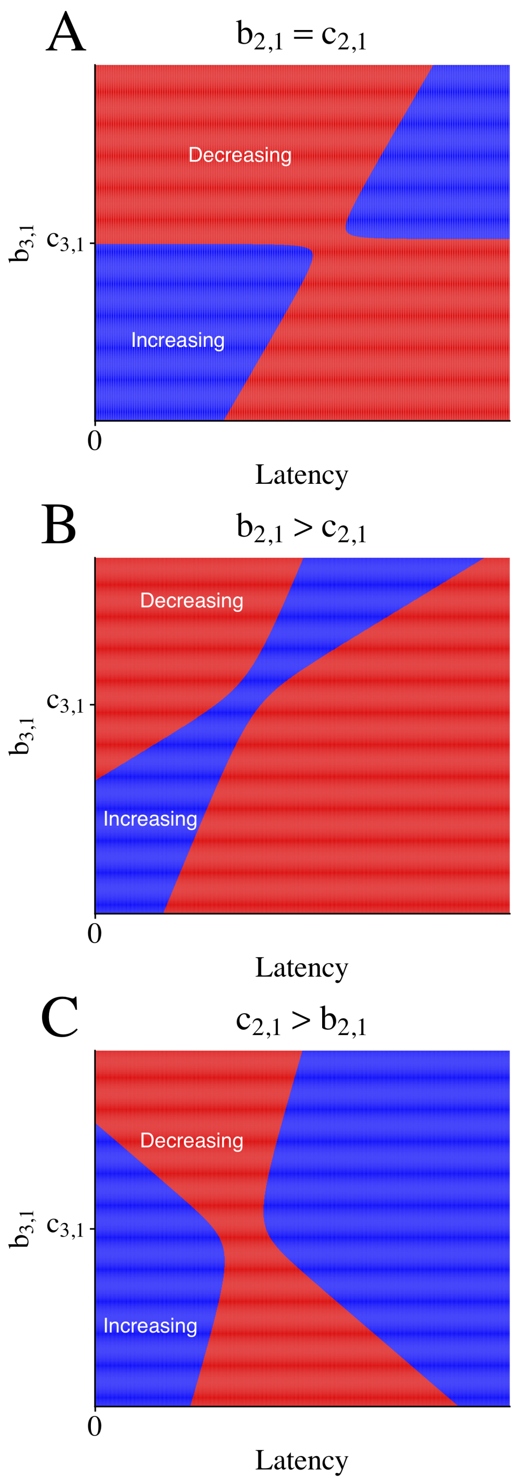

Fig. S8. Schematics of possible changes in evolutionary dynamics due to shifts in the threshold position of the logistic transmission trade-off. The trade-offs are formulated as $\alpha_1[\lambda] = \frac{b_{1,1}}{1+e^{-b_{2,1}(b_{3,1}-\lambda)}} + \alpha_{1,\infty}$ and $\nu_1[\lambda] = \frac{c_{1,1}}{1+e^{-c_{2,1}(c_{3,1}-\lambda)}} + \nu_{1,\infty}$, and only $b_{3,1}$ varies within the depicted regime for the relation between $b_{2,1}$ and $c_{2,1}$ in each panel. The *blue* and *red* regions are as in Figure S7. (*A*) $b_{2,1}$ and $c_{2,1}$ are equal, and there is either at most one interior evolutionarily singular strategy, or $\widehat{S}[\lambda]$ is strictly decreasing. For small enough $b_{3,1}$ values, the interior evolutionarily singular strategy is unstable, and leads to bistability of extrema phenotypes, *i.e.*, zero and infinite latency. For larger $b_{3,1}$ values, the evolutionarily singular strategy is a stable strategy, and thus a unique ESS. *(B)* $b_{2,1}$ and $c_{2,1}$ are chosen so that $b_{2,1} > c_{2,1}$. For small enough $b_{3,1}$ values, there is a single interior evolutionarily singular strategy that is unstable, leading to bistability with zero and infinite latency. For large values of $b_{3,1}$, two interior singular strategies emerge, with one interior stable equilibrium and a stable extremum strategy at maximal latency. (*C*) $b_{2,1}$ and $c_{2,1}$ are now such that $c_{2,1} > b_{2,1}$, and opposing behaviour to (*B*) is observed. Namely, for large enough $b_{3,1}$ values, there is a single interior ESS which is globally stable. For smaller $b_{3,1}$ values, there exist bistable states: one interior equilibria and one extremum strategy, at zero latency.

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