

Supplementary information

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Throughout the supplement we use the notation introduced in the main text to describe (Section II of the main text) and to derive (Appendix of the main text) steady state reduction (SSR). We consider the N-dimensional gLV equations

$$\frac{d}{dt}y_i(t) = y_i(t) \left(\rho_i + \sum_{j=1}^N K_{ij}y_j(t) \right) \quad (\text{S1})$$

and the 2-dimensional gLV equations

$$\begin{aligned} \frac{dx_a}{dt} &= x_a(\mu_a + M_{aa}x_a + M_{ab}x_b) \\ \frac{dx_b}{dt} &= x_b(\mu_b + M_{ba}x_a + M_{bb}x_b), \end{aligned} \quad (\text{S2})$$

with their corresponding microbial dynamics given by $\frac{d\vec{y}}{dt} = \sum_{i=1}^N \frac{dy_i}{dt} \hat{y}_i$ and $\frac{d\vec{x}}{dt} = \frac{dx_a}{dt} \hat{x}_a + \frac{dx_b}{dt} \hat{x}_b$.

IN-PLANE PROJECTION OF HIGH-DIMENSIONAL PHASE SPACE

We consider the correspondence between the 2D plane embedded in N-dimensional space that is spanned by the origin and the unit vectors \hat{x}_a and \hat{x}_b . We can map any point $\vec{x} = (x_a, x_b) \in \mathbb{R}^2$ to a point on the embedded plane $\vec{y} \in \mathbb{R}^N$ with the prescription

$$\vec{y} = x_a \hat{x}_a + x_b \hat{x}_b. \quad (\text{S3})$$

Furthermore, we may project any point in the high-dimensional phase space $\vec{y} \in \mathbb{R}^N$ onto the embedded 2-dimensional plane that corresponds to coordinates $\vec{x} \in \mathbb{R}^2$ under the map

$$\vec{x} = \begin{bmatrix} x_a \\ x_b \end{bmatrix} = \begin{bmatrix} \frac{(\vec{y} \cdot \hat{x}_a) - (\vec{y} \cdot \hat{x}_b)(\hat{x}_a \cdot \hat{x}_b)}{1 - (\hat{x}_a \cdot \hat{x}_b)^2} \\ \frac{(\vec{y} \cdot \hat{x}_b) - (\vec{y} \cdot \hat{x}_a)(\hat{x}_a \cdot \hat{x}_b)}{1 - (\hat{x}_a \cdot \hat{x}_b)^2} \end{bmatrix}. \quad (\text{S4})$$

If $\hat{x}_a \cdot \hat{x}_b = 0$, this projection simplifies considerably to

$$\vec{x} = \begin{bmatrix} x_a \\ x_b \end{bmatrix} = \begin{bmatrix} \vec{y} \cdot \hat{x}_a \\ \vec{y} \cdot \hat{x}_b \end{bmatrix}. \quad (\text{S5})$$

Note that under these mappings, the points $(\|\vec{y}_a\|_2, 0)$ and $(0, \|\vec{y}_b\|_2)$ map to \vec{y}_a and \vec{y}_b , and the points \vec{y}_a and \vec{y}_b map to $(\|\vec{y}_a\|_2, 0)$ and $(0, \|\vec{y}_b\|_2)$, where $\|\cdot\|_2$ is the 2-norm. It is precisely for this reason that we name this model reduction technique *steady state reduction* (SSR).

In Section III of the main text, we introduce scaled variables $\tilde{x}_a = x_a/\|\vec{y}_a\|_2$ and $\tilde{x}_b = x_b/\|\vec{y}_b\|_2$. In this case, the corresponding mappings are

$$\vec{y} = \tilde{x}_a \vec{y}_a + \tilde{x}_b \vec{y}_b \quad (\text{S6})$$

and

$$\vec{\tilde{x}} = \begin{bmatrix} \tilde{x}_a \\ \tilde{x}_b \end{bmatrix} = \begin{bmatrix} \frac{(\vec{y} \cdot \vec{y}_a) \|\vec{y}_b\|^2 - (\vec{y} \cdot \vec{y}_b)(\vec{y}_a \cdot \vec{y}_b)}{\|\vec{y}_a\|^2 \|\vec{y}_b\|^2 - (\vec{y}_a \cdot \vec{y}_b)^2} \\ \frac{(\vec{y} \cdot \vec{y}_b) \|\vec{y}_a\|^2 - (\vec{y} \cdot \vec{y}_a)(\vec{y}_a \cdot \vec{y}_b)}{\|\vec{y}_a\|^2 \|\vec{y}_b\|^2 - (\vec{y}_a \cdot \vec{y}_b)^2} \end{bmatrix}, \quad (\text{S7})$$

and if $\vec{y}_a \cdot \vec{y}_b = 0$ this projection simplifies considerably to

$$\vec{\tilde{x}} = \begin{bmatrix} \tilde{x}_a \\ \tilde{x}_b \end{bmatrix} = \begin{bmatrix} \frac{\vec{y} \cdot \vec{y}_a}{\|\vec{y}_a\|^2} \\ \frac{\vec{y} \cdot \vec{y}_b}{\|\vec{y}_b\|^2} \end{bmatrix}. \quad (\text{S8})$$

Under this mapping, the points $(1, 0)$ and $(0, 1)$ map to \vec{y}_a and \vec{y}_b , and the points \vec{y}_a and \vec{y}_b map to $(1, 0)$ and $(0, 1)$.

Next, we show that SSR preserves (i) steady states and (ii) their stability.

STEADY STATE REDUCTION PRESERVES STEADY STATES

Here we show that SSR preserves steady states, i.e. if \vec{y}_a and \vec{y}_b are steady states of Eq. (S1), then $(\|\vec{y}_a\|_2, 0)$ and $(0, \|\vec{y}_b\|_2)$ are steady states of Eq. (S2).

We show the case regarding \vec{y}_a and $(\|\vec{y}_a\|_2, 0)$; the alternative case is proven identically. Assume \vec{y}_a is a steady state, so that

$$0 = \vec{y}_{ai} \left(\rho_i + \sum_{j=1}^N K_{ij} \vec{y}_{aj} \right), \quad (\text{S9})$$

for $i \in 1, \dots, N$, where \vec{y}_{ai} corresponds to the i th component of \vec{y}_a . Consider the point in

2-dimensional phase space $\vec{x}_a^* \equiv (\|\vec{y}_a\|_2, 0)$, and note that

$$\left. \frac{d}{dt} x_b(t) \right|_{\vec{x}=\vec{x}_a^*} = 0 \quad (\mu_i + M_{ba}\|\vec{y}_a\|_2) = 0. \quad (\text{S10})$$

Then, to show that \vec{x}_a^* is a steady state, we need to show $\left. \frac{dx_a(t)}{dt} \right|_{\vec{x}=\vec{x}_a^*} = 0$. This term is given by

$$\begin{aligned} \left. \frac{d}{dt} x_a(t) \right|_{\vec{x}=\vec{x}_a^*} &= \|\vec{y}_a\|_2 (\mu_a + M_{aa}\|\vec{y}_a\|_2) \\ &= \frac{\|\vec{y}_a\|_2}{\sum_{i=1}^N \vec{y}_{ai}^2} \left[\sum_{i=1}^N \vec{y}_{ai}^2 \left(\rho_i + \sum_{j=1}^N K_{ij} \vec{y}_{aj} \right) \right] \\ &= 0, \end{aligned} \quad (\text{S11})$$

by our assumption in Eq. (S9). Therefore, $(\|\vec{y}_a\|_2, 0)$ is a steady state of Eq. (S2). Therefore, SSR preserves steady states.

STEADY STATE REDUCTION PRESERVES STABILITY

Next we show that SSR preserves stability, i.e. if \vec{y}_a and \vec{y}_b are stable steady states of Eq. (S1), then $(\|\vec{y}_a\|_2, 0)$ and $(0, \|\vec{y}_b\|_2)$ are stable steady states of Eq. (S2). We assume that \vec{y}_a and \vec{y}_b are orthogonal.

We show the case regarding \vec{y}_a and $(\|\vec{y}_a\|_2, 0)$; the alternative case is proven identically. To this end, assume \vec{y}_a is a steady state, so that

$$0 = \vec{y}_{ai}(t) \left(\rho_i + \sum_{j=1}^N K_{ij} \vec{y}_{aj}(t) \right), \quad (\text{S12})$$

for $i \in 1, \dots, N$, and so that the eigenvalues of the Jacobian matrix evaluated at the fixed point \vec{y}_a are all negative. Equivalently, if \vec{y}_a is perturbed, then the perturbed state returns to \vec{y}_a .

To show that $\vec{x}_a^* = (\|\vec{y}_a\|_2, 0)$ is a stable steady state, we must show that the eigenvalues

of the Jacobian evaluated at \vec{x}_a^* are negative. The Jacobian J of Eq. (??) is

$$\begin{aligned} J \Big|_{\vec{x}=\vec{x}_a^*} &= \begin{bmatrix} \mu_a + 2M_{aa}x_a + M_{ab}x_b & M_{ab}x_a \\ M_{ba}x_b & \mu_b + M_{ba}x_a + 2M_{bb}x_b \end{bmatrix} \Big|_{\vec{x}=\vec{x}_a^*} \\ &= \begin{bmatrix} \mu_a + 2M_{aa}\|\vec{y}_a\|_2 & M_{ab}\|\vec{y}_a\|_2 \\ 0 & \mu_b + M_{ba}\|\vec{y}_a\|_2 \end{bmatrix}, \end{aligned} \quad (\text{S13})$$

which has eigenvalues $\mu_a + 2M_{aa}\|\vec{y}_a\|_2$ and $\mu_b + M_{ba}\|\vec{y}_a\|_2$, both of which we will show are negative.

Consider the first eigenvalue $\mu_a + 2M_{aa}\|\vec{y}_a\|_2$. In the previous section, we showed that for a steady state \vec{y}_a , $\mu_a + M_{aa}\|\vec{y}_a\|_2 = 0$. Therefore, we need only show $M_{aa}\|\vec{y}_a\|_2 = -\mu_a < 0$. We find that

$$-\mu_a = -\frac{\sum_{i=1}^N \vec{y}_{ai}^2 \rho_i}{\sum_{i=1}^N \vec{y}_{ai}^2} < 0, \quad (\text{S14})$$

since \vec{y}_{ai}^2 is always non-negative, and since the growth rates ρ_i should be positive for a reasonable gLV model. Therefore, this eigenvalue is negative.

Next, we show that $\mu_b + M_{ba}\|\vec{y}_a\|_2 < 0$. The value of this eigenvalue in terms of the high-dimensional parameters is given by

$$\mu_b + M_{ba}\|\vec{y}_a\|_2 = \frac{\sum_{i=1}^N \vec{y}_{bi}^2 \left[\rho_i + \sum_{j=1}^N K_{ij} \vec{y}_{aj} \right]}{\sum_{i=1}^N \vec{y}_{bi}^2}, \quad (\text{S15})$$

where we have used the simpler version of coefficient M_{ba} since we assume that $\vec{y}_a \cdot \vec{y}_b = 0$. In general, the steady states \vec{y}_a and \vec{y}_b contain both zero and non-zero terms. Let S_a and S_b be the components of steady states \vec{y}_a and \vec{y}_b that are non-zero, respectively, so that $S_\alpha = \{j \mid \vec{y}_{\alpha j} \neq 0, j \in 1, \dots, N\}$ for $\alpha \in a, b$. Then, if we define $S = \overline{S_a} \cap S_b$, where \overline{S} is the complement of S , we find that this eigenvalue reduces to

$$\mu_b + M_{ba}\|\vec{y}_a\|_2 = \frac{1}{\sum_{i=1}^N \vec{y}_{bi}^2} \left[\sum_{i \in S} \vec{y}_{bi}^2 \left(\rho_i + \sum_{j=1}^N K_{ij} \vec{y}_{aj} \right) \right], \quad (\text{S16})$$

Next, consider the elements \vec{y}_{ai} for $i \in \overline{S_a}$. At the fixed point \vec{y}_a , $\vec{y}_{ai} = 0$ for $i \in \overline{S_a}$. These components of this fixed point are also stable, which means that if perturbed by some small positive $\epsilon \ll 1$, that component will return to 0. Consider a vector $\vec{\epsilon}_i \equiv \sum_{j=1}^N \hat{y}_j \epsilon \delta_{ij}$ for

Kronecker delta δ_{ij} . Then, for $i \in \overline{S_a}$,

$$\left. \frac{d}{dt} y_i(t) \right|_{\vec{y}=\vec{y}_a+\vec{\epsilon}_i} = \epsilon \left(\rho_i + \epsilon K_{ii} + \sum_{j=1}^N K_{ij} \vec{y}_{aj} \right) < 0, \quad (\text{S17})$$

and hence

$$\rho_i + \sum_{j=1}^N K_{ij} \vec{y}_{aj} < 0 \quad (\text{S18})$$

for $i \in \overline{S_a}$. Therefore, since $\vec{y}_{bi}^2 \geq 0$, we have shown that

$$\mu_b + M_{ba} \|\vec{y}_a\|_2 = \frac{1}{\sum_{i=1}^N \vec{y}_{bi}^2} \left[\sum_{i \in S} \vec{y}_{bi}^2 \left(\rho_i + \sum_{j=1}^N K_{ij} \vec{y}_{aj} \right) \right] < 0. \quad (\text{S19})$$

We note that this term can never be 0 since S cannot be empty: if S were empty, then $S_a = S_b$, which cannot happen since \vec{y}_a and \vec{y}_b are different, and the presence-absence configuration of each steady state in a gLV model is unique.

Therefore, we have shown that if \vec{y}_a and \vec{y}_b are both stable, and if they are also orthogonal, then the eigenvalues $\mu_a + 2M_{aa} \|\vec{y}_a\|_2$ and $\mu_b + M_{ba} \|\vec{y}_a\|_2$ are both negative, and so the steady state $(\|\vec{y}_a\|_2, 0)$ will be stable as well. Therefore, we have shown that for orthogonal steady states \vec{y}_a and \vec{y}_b , SSR preserves stability.

STEADY STATES OF THE 11D MOUSE MICROBIOME MODEL

In the mouse microbiome model of Stein et al. [2], which takes the form of an 11-dimensional gLV model, there are five steady states that are reachable from the experimentally measured initial conditions. In our previous work [3], we study these steady states in detail by constructing phase diagrams that classify the fate of experimentally measured initial conditions as a function of the amount of antibiotic administered and whether the system was exposed to *C. difficile*.

We focus on two steady states of the Stein 11D model, which are detailed in Table S1. These steady states are both attainable from a *CD-fragile* initial condition: \vec{y}_a is attained if sufficient antibiotics are administered, and \vec{y}_b is attained if no antibiotics are administered. Further, \vec{y}_a is CD-susceptible, whereas \vec{y}_b is CD-resilient— we equate these two properties with our “diseased” and “healthy” steady states of the 2D model.

Steady states:	\vec{y}_a (SS E) (susceptible)	\vec{y}_b (SS C) (resilient)
Barnesiella	0	9.299
undefined genus of Lachnospiraceae	0	0
unclassified Lachnospiraceae	0	12.3085
Other	0.006	3.1627
Blautia	1.2284	0
undefined genus of unclassified Mollicutes	1.1055	0
Akkermansia	0	0
Coprobacillus	0.0352	0
undefined genus of Enterobacteriaceae	1.1694	0
Enterococcus	0	0
Clostridium difficile	0	0
Total microbe count	3.5445	24.7702

TABLE S1. Steady states of the 11D Stein mouse model [2] that are used for steady state reduction. We choose \vec{y}_a to correspond to steady state E and \vec{y}_b to correspond to steady state C, where the steady states C and E are studied in detail in our previous work [3].

STEADY STATE REDUCTION IN SCALED VARIABLES

We consider scaled variables $z_a = x_a/\|\vec{y}_a\|_2$ and $z_b = x_b/\|\vec{y}_b\|_2$, so that the in-plane microbial dynamics

$$\frac{d\vec{x}}{dt} = \frac{dx_a}{dt}\hat{x}_a + \frac{dx_b}{dt}\hat{x}_b \quad (\text{S20})$$

may be equivalently described by

$$\frac{d\vec{x}}{dt} = \frac{dz_a}{dt}\vec{y}_a + \frac{dz_b}{dt}\vec{y}_b, \quad (\text{S21})$$

where we can write the change in z_a and z_b in terms of the parameters of Eq. (S2) as

$$\begin{aligned} \frac{dz_a}{dt} &= z_a(\mu_a + M_{aa}\|\vec{y}_a\|_2 z_a + M_{ab}\|\vec{y}_b\|_2 z_b) \\ \frac{dz_b}{dt} &= z_b(\mu_b + M_{ba}\|\vec{y}_a\|_2 z_a + M_{bb}\|\vec{y}_b\|_2 z_b). \end{aligned} \quad (\text{S22})$$

ANALYTIC MANIFOLD DISCOVERY FOR THE MIXED STEADY STATE

We consider a system with two stable homogeneous fixed points and a positive mixed hyperbolic fixed point (x_a^*, x_b^*) , as described in the main text. The stable and unstable

eigenvectors of the mixed steady state (x_a^*, x_b^*) are tangent to the stable and unstable manifolds at that point [1]. We denote these manifolds as $h^{s/u}(x_a)$, and consider their Taylor expansion about the mixed steady state

$$\begin{aligned} h^{s/u}(x_a) &= c_0 + c_1^{s/u}(x_a - x_a^*) + \frac{c_2^{s/u}}{2!}(x_a - x_a^*)^2 + \frac{c_3^{s/u}}{3!}(x_a - x_a^*)^3 + \dots \\ &= \sum_{n=0}^{\infty} \frac{c_n^{s/u}}{n!}(x_a - x_a^*)^n. \end{aligned} \quad (\text{S23})$$

Naturally, $c_0 = x_b^*$ for both manifolds. The other coefficients have two possible values that correspond to either the stable or the unstable manifold. Since these manifolds are invariant under the flow generated by the dynamical system, they must obey [1]

$$\frac{dh^{s/u}(x_a)}{dx_a} = \frac{dx_b}{dt} \bigg/ \frac{dx_a}{dt}. \quad (\text{S24})$$

We consider trajectories along these manifolds so that $x_b = h^{s/u}(x_a)$. Then, substituting in terms and rearranging this equation we find that

$$\begin{aligned} x_a(c_1^{s/u} + c_2^{s/u}(x_a - x_a^*) + \dots)(\mu_a + M_{aa}x_a + M_{ab}(x_b^* + c_1^{s/u}(x_a - x_a^*) + \dots)) \\ = (x_b^* + c_1^{s/u}(x_a - x_a^*) + \dots)(\mu_b + M_{ba}x_a + M_{bb}(x_b^* + c_1^{s/u}(x_a - x_a^*) + \dots)). \end{aligned} \quad (\text{S25})$$

We make the substitution $y = (x_a - x_a^*)$ to simplify the equations to

$$\begin{aligned} (y + x_a^*)(c_1^{s/u} + c_2^{s/u}y + \dots)(\mu_a + M_{aa}(y + x_a^*) + M_{ab}(x_b^* + c_1^{s/u}y + \dots)) \\ = (x_b^* + c_1^{s/u}y + \dots)(\mu_b + M_{ba}(y + x_a^*) + M_{bb}(x_b^* + c_1^{s/u}y + \dots)), \end{aligned} \quad (\text{S26})$$

from which point powers of y may be equated, allowing for the determination of coefficients in the Taylor series. Since (x_a^*, x_b^*) is a steady state of Eq. (S2), this reduces to

$$\begin{aligned} y(y + x_a^*)(c_1^{s/u} + c_2^{s/u}y + \dots)(M_{aa} + M_{ab}(c_1^{s/u} + c_2^{s/u}y + \dots)) \\ = y(x_b^* + c_1^{s/u}y + \dots)(M_{ba} + M_{bb}(c_1^{s/u} + c_2^{s/u}y + \dots)). \end{aligned} \quad (\text{S27})$$

The constant terms (order y^0) are trivially satisfied. The linear terms (order y^1) must

satisfy

$$M_{ab}x_a^*(c_1^{s/u})^2 + (M_{aa}x_a^* - M_{bb}x_b^*)c_1^{s/u} - M_{ba}x_b^* = 0, \quad (\text{S28})$$

and from the resulting quadratic equation we obtain two sets of coefficients $c_1^{s/u}$ corresponding to two manifolds. In the remaining calculation, we omit the s/u superscript. To determine higher-order coefficients we consider the full explicit form of Eq. (S94), which reads

$$\begin{aligned} & \left(\sum_{n=0}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \left(\mu_b + M_{ba}x_a^* + M_{ba}(x_a - x_a^*) + M_{bb} \left(\sum_{n=0}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \right) \\ &= \left(\sum_{n=0}^{\infty} \frac{c_{n+1}}{n!} (x - x_a^*)^{n+1} \right) \left(\mu_a + M_{aa}x_a^* + M_{aa}(x_a - x_a^*) + M_{ab} \left(\sum_{n=0}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \right) \\ &+ x_a^* \left(\sum_{n=0}^{\infty} \frac{c_{n+1}}{n!} (x - x_a^*)^n \right) \left(\mu_a + M_{aa}x_a^* + M_{aa}(x_a - x_a^*) + M_{ab} \left(\sum_{n=0}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \right). \end{aligned} \quad (\text{S29})$$

As noted before, $c_0 = x_b^*$. Then, since $\mu_a + M_{aa}x_a^* + M_{ab}x_b^* = \mu_b + M_{ba}x_a^* + M_{bb}x_b^* = 0$, we may simplify this expression to

$$\begin{aligned} & \left(\sum_{n=0}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \left(M_{ba}(x_a - x_a^*) + M_{bb} \left(\sum_{n=1}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \right) \\ &= \left(\sum_{n=0}^{\infty} \frac{c_{n+1}}{n!} (x - x_a^*)^n \right) ((x - x_a^*) + x_a^*) \left(M_{aa}(x_a - x_a^*) + M_{ab} \left(\sum_{n=1}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \right). \end{aligned} \quad (\text{S30})$$

From here it is plain to see that the $(x_a - x_a^*)^0$ vanishes, and that the $(x_a - x_a^*)^1$ term leads to Eq. (S98). We next consider an arbitrary term of order $(x_a - x_a^*)^m$, given by

$$\begin{aligned} & (M_{ba} + M_{bb} c_1) \frac{c_{m-1}}{(m-1)!} + M_{bb} \sum_{\ell=2}^m \frac{c_{\ell} c_{m-\ell}}{\ell! (m-\ell)!} \\ &= (M_{aa} + M_{ab} c_1) \frac{c_{m-1}}{(m-2)!} + M_{ab} \sum_{\ell=2}^{m-1} \frac{c_{\ell} c_{m-\ell}}{\ell! (m-\ell-1)!} \\ &+ x_a^* (M_{aa} + M_{ab} c_1) \frac{c_m}{(m-1)!} + x_a^* M_{ab} \sum_{\ell=2}^m \frac{c_{\ell} c_{m-\ell+1}}{\ell! (m-\ell)!}. \end{aligned} \quad (\text{S31})$$

We simplify this term for the edge case $m = 2$ to find

$$(M_{ba} + M_{bb} c_1)c_1 + \frac{1}{2}M_{bb}c_0c_2 = (M_{aa} + M_{ab} c_1)c_1 + x_a^*(M_{aa} + M_{ab} c_1)c_2 + \frac{1}{2}x_a^*M_{ab}c_1c_2, \quad (\text{S32})$$

which can be rearranged to show

$$\frac{c_2}{2}(2x_a^*M_{aa} + 3x_a^*M_{ab}c_1 - M_{bb}x_b^*) = c_1(M_{ba} + M_{bb}c_1 - M_{aa} - M_{ab}c_1). \quad (\text{S33})$$

Finally we solve Eq. (S101) for $m > 2$ to find the leading coefficient c_m as a function of the previous coefficients $c_{m-1}, c_{m-2}, \dots, c_0$ to find

$$\begin{aligned} & \frac{c_m}{m!} (mx_a^*M_{aa} + (m+1)x_a^*M_{ab}c_1 - M_{bb}x_b^*) \\ &= \frac{c_{m-1}}{(m-1)!} (M_{ba} + M_{bb}c_1 - (m-1)(M_{aa} + M_{ab}c_1)) \\ &+ \sum_{\ell=2}^{m-1} \left[\frac{c_\ell}{\ell! (m-\ell)!} (M_{bb}c_{m-\ell} - (m-\ell)M_{ab}c_{m-\ell} - x_a^*M_{ab}c_{m-\ell+1}) \right], \end{aligned} \quad (\text{S34})$$

and from this equation we can solve for c_m . Therefore, we can compute the Taylor expansion for the unstable or stable manifolds of the mixed fixed point to arbitrary order.

NONDIMENSIONALIZATION

We begin with the generalized Lotka-Volterra equations in two-dimensions,

$$\begin{aligned} \frac{dx_a}{dt} &= x_a(\mu_a + M_{aa}x_a + M_{ab}x_b) \\ \frac{dx_b}{dt} &= x_b(\mu_b + M_{ba}x_a + M_{bb}x_b). \end{aligned} \quad (\text{S35})$$

To nondimensionalize, let $\tilde{x}_a = \alpha x_a$, $\tilde{x}_b = \beta x_b$, and $T = \tau t$, with nondimensionalization parameters $\tau = \mu_a$, $\alpha = -M_{aa}/\mu_a$, and $\beta = -M_{bb}/\mu_a$. Then, the equations become

$$\begin{aligned} \frac{d\tilde{x}_a}{dT} &= \tilde{x}_a(1 - \tilde{x}_a - \tilde{M}_{ab}\tilde{x}_b) \\ \frac{d\tilde{x}_b}{dT} &= \tilde{x}_b(\tilde{\mu}_b - \tilde{M}_{ba}\tilde{x}_a - \tilde{x}_b), \end{aligned} \quad (\text{S36})$$

where $\tilde{M}_{ab} = M_{ab}/M_{bb}$, $\tilde{\mu}_b = \mu_b/\mu_a$, and $\tilde{M}_{ba} = M_{ba}/M_{aa}$. For convenience, we overwrite our notation so that $\tilde{x}_a \rightarrow x_a$, $\tilde{x}_b \rightarrow x_b$, $T \rightarrow t$, $\tilde{\mu}_b \rightarrow \mu_b$, $\tilde{M}_{ab} \rightarrow M_{ab}$, and $\tilde{M}_{ba} \rightarrow M_{ba}$, so

$$\begin{aligned}\frac{dx_a}{dt} &= x_a(1 - x_a - M_{ab}x_b) \\ \frac{dx_b}{dt} &= x_b(\mu_b - M_{ba}x_a - x_b).\end{aligned}\tag{S37}$$

Therefore, we can study the behavior of this system by considering different parameter sets (M_{ab} , M_{ba} , and μ_b). In the main text, we assume $\mu_b = 1$, but we relax this assumption here in the supplement.

HOMOGENEOUS STEADY STATES

The two homogeneous steady states are $(1, 0)$ and $(0, \mu_b)$. Their eigenvalues are $\lambda_{10} = -1$, $\mu_b - M_{ba}$ and $\lambda_{01} = -\mu_b$, $1 - M_{ab}\mu_b$, respectively. We assume $\mu_b > 0$ to ensure nonnegative steady states. Therefore, for this system to capture the dynamics we are interested in—the switching behavior between healthy and diseased stable steady states—we must have $M_{ba} > \mu_b$ and $M_{ab}\mu_b > 1$.

MIXED STEADY STATE

The solution of Eq. (S37) for the mixed steady state (x_a^*, x_b^*) is

$$\left(\frac{1 - M_{ab}\mu_b}{1 - M_{ab}M_{ba}}, \frac{\mu_b - M_{ba}}{1 - M_{ab}M_{ba}} \right).\tag{S38}$$

Due to the constraint that the homogeneous steady states are stable, we must have $M_{ab}M_{ba} > 1$. To provide bounds on x_a^* and x_b^* , we manipulate the inequalities that result from the stability of the homogeneous steady states. For x_a^* we have

$$\begin{aligned}1 < M_{ab}\mu_b < M_{ab}M_{ba} &\implies 0 > 1 - M_{ab}\mu_b > 1 - M_{ab}M_{ba} \\ &\implies 0 < x_a^* < 1,\end{aligned}\tag{S39}$$

and for x_b^* we have

$$\begin{aligned} 0 > \mu_b - M_{ba} > \frac{1}{M_{ab}} - M_{ba} &\implies 0 < \frac{\mu_b - M_{ba}}{1 - M_{ab}M_{ba}} < \frac{1}{M_{ab}} < \mu_b \\ &\implies 0 < x_b^* < \mu_b. \end{aligned} \quad (\text{S40})$$

Therefore, each component of the mixed steady state is bounded below by 0 and above by the value of its homogeneous steady state.

To check the stability of the mixed steady state, we evaluate the eigenvalues of the Jacobian of Eq. (S37) evaluated at the steady state. If $\mu_b = 1$ then the eigenvalues are

$$\lambda_{\pm} = \frac{(M_{ab} - 1)(M_{ba} - 1)}{M_{ab}M_{ba} - 1}, \quad -1, \quad (\text{S41})$$

but in order for the homogeneous steady states to be stable we must also have $\lambda_+ > 0$, so this fixed point is semistable. For $\mu_b \neq 1$, we have

$$\begin{aligned} \lambda_{\pm} = \frac{1}{2(M_{ab}M_{ba} - 1)} &\left[1 - M_{ab}\mu_b + \mu_b - M_{ba} \right. \\ &\left. \pm \sqrt{(1 - M_{ba}\mu_b + \mu_b - M_{ba})^2 + 4(M_{ab}M_{ba} - 1)(M_{ab}\mu_b - 1)(M_{ba} - \mu_b)} \right] \end{aligned} \quad (\text{S42})$$

The fact that the homogeneous steady states are stable requires $1 - M_{ab}\mu_b + \mu_b - M_{ba} < 0$, and the positivity of the mixed steady state requires $(M_{ab}M_{ba} - 1)(M_{ab}\mu_b - 1)(M_{ba} - \mu_b) > 0$ and $M_{ab}M_{ba} - 1 > 0$. Therefore, one of the eigenvalues will be positive and the other negative for the systems we are considering.

SPLIT LYAPUNOV FUNCTION

The split Lyapunov function for Eq. (S37) as a function of the two microbial populations x_a and x_b is given by

$$V(x_a, x_b) = M_{ba}x_a^2/2 + M_{ab}x_b^2/2 - M_{ba}x_a - M_{ab}\mu_b x_b + M_{ab}M_{ba}x_a x_b. \quad (\text{S43})$$

To verify this equation satisfies the properties of Lyapunov functions, we first demonstrate that the only minima of $V(x_a, x_b)$ correspond to the two stable fixed points of Eq. (S35). Recall that in our system the two stable steady states are at $(1, 0)$ and $(0, \mu_b)$. To find the

minima we consider when $\frac{d}{dx_a}V(x_a, x_b) = 0$ and when $\frac{d}{dx_b}V(x_a, x_b) = 0$. These derivatives are given by

$$\begin{aligned}\frac{d}{dx_a}V(x_a, x_b) &= M_{ba}x_a - M_{ba} + M_{ab}M_{ba}x_b \quad \text{and} \\ \frac{d}{dx_b}V(x_a, x_b) &= M_{ab}x_b - M_{ab}\mu_b + M_{ab}M_{ba}x_a.\end{aligned}\tag{S44}$$

For the state $(1, 0)$, $\frac{d}{dx_a}V(x_a, x_b) = 0$ but $\frac{d}{dx_b}V(x_a, x_b) > 0$. Since the microbe counts are nonnegative and therefore bounded, $(1, 0)$ constitutes a minima. Likewise, the state $(0, \mu_b)$ is a minima. The mixed steady state given in Eq. (S88) also satisfies both $\frac{d}{dx_a}V(x_a, x_b) = 0$ and $\frac{d}{dx_b}V(x_a, x_b) = 0$, but due to topological constraints cannot also be a minima.

Next we will demonstrate that all trajectories flow down the Lyapunov landscape by showing $\dot{V}(x_a, x_b) < 0$. First, note that

$$\begin{aligned}\nabla V(x_a, x_b) &= \hat{x}_a(M_{ba}x_a - M_{ba}\mu_a + M_{ab}M_{ba}x_b) + \hat{x}_b(M_{ab}x_b - M_{ab}\mu_b + M_{ab}M_{ba}x_a) \\ &= \hat{x}_aM_{ba}(x_a - \mu_a + M_{ab}x_b) + \hat{x}_bM_{ab}(x_b - \mu_b + M_{ba}x_a) \\ &= -\frac{\dot{x}_a}{x_a}\hat{x}_aM_{ba} - \frac{\dot{x}_b}{x_b}\hat{x}_bM_{ab}\end{aligned}\tag{S45}$$

Then, we find

$$\begin{aligned}\dot{V}(x_a, x_b) &= \nabla V \cdot (\dot{x}_a\hat{x}_a + \dot{x}_b\hat{x}_b) \\ &= -\frac{\dot{x}_a^2}{x_a}M_{ba} - \frac{\dot{x}_b^2}{x_b}M_{ab} \leq 0\end{aligned}\tag{S46}$$

in our parameter regime. Therefore, $V(x_a, x_b)$ is a split Lyapunov function for Eq. (S37).

To further pursue the physical correspondence between the split Lyapunov function and a potential energy function, we note that the Lyapunov function leads to force-like relations for the microbial trajectories $\frac{dx_a}{dt} = -(\nabla V)_a x_a / M_{ba}$ and $\frac{dx_b}{dt} = -(\nabla V)_b x_b / M_{ab}$, where $(\cdot)_i$ indicates index i .

EIGENVECTORS OF THE SEMISTABLE FIXED POINT

The eigenvectors of the semistable fixed point, which we denote \vec{u} (unstable eigenvector) and \vec{v} (stable eigenvector), are found by computing the eigenvectors of the Jacobian of

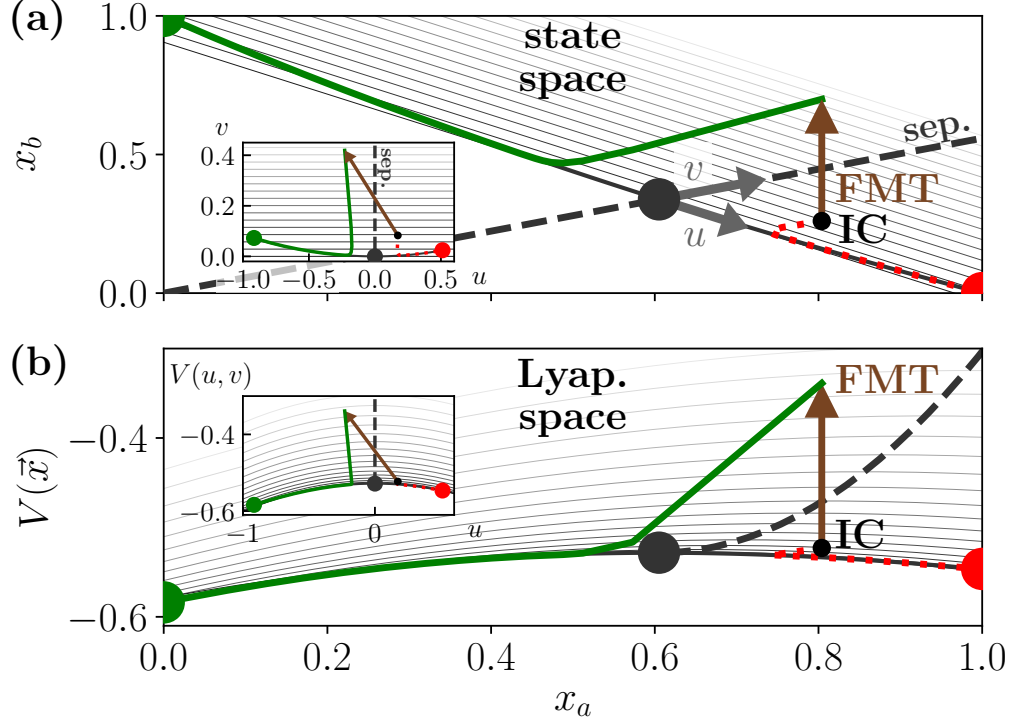


FIG. S1. The influence of FMT on microbial trajectories in (a) state space and (b) Lyapunov space. A disease-prone IC is converted into a health-prone state with FMT administration, shown in the original coordinates (x_a, x_b) (main frames) and in transformed coordinates (u, v) (insets), where u and v are the eigenvectors of the semistable fixed point (x_a^*, x_b^*) . (b) Conversion from a disease- to a health-prone state requires overcoming a “potential energy” barrier characterized by the split Lyapunov function V . To visualize this energy landscape we plot the Lyapunov functions along level cuts parallel to u (shown in (a)), then superimpose the Lyapunov functions along the trajectories in (a).

Eq. (S37) evaluated at the semistable fixed point (x_a^*, x_b^*) given in Eq. (S88). Under the previously mentioned assumptions $M_{ab} > 1$ and $M_{ba} > 1$, we solve for these eigenvectors to find

$$\vec{u} = \left\{ \frac{1}{2M_{ba}} \left[\frac{x_a^*}{x_b^*} - 1 - \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab} M_{ba}} \right] \right\} \hat{x}_a + \hat{x}_b \quad (\text{S47})$$

and

$$\vec{v} = \left\{ \frac{1}{2M_{ba}} \left[\frac{x_a^*}{x_b^*} - 1 + \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab} M_{ba}} \right] \right\} \hat{x}_a + \hat{x}_b. \quad (\text{S48})$$

Under the simplification $\mu_b = 1$, these eigenvectors become

$$\vec{u} = \begin{bmatrix} -\frac{M_{ab}}{M_{ba}} \\ 1 \end{bmatrix} \quad \text{and} \quad \vec{v} = \begin{bmatrix} \frac{M_{ab}-1}{M_{ba}-1} \\ 1 \end{bmatrix}. \quad (\text{S49})$$

Note that all of these eigenvectors should be properly normalized, so that $\hat{u} = \frac{\vec{u}}{\|\vec{u}\|}$ and $\hat{v} = \frac{\vec{v}}{\|\vec{v}\|}$.

CHANGE OF COORDINATES TO THE EIGENVECTORS OF THE SEMISTABLE FIXED POINT

We can represent each point (x_a, x_b) as a point (u, v) in the (\hat{u}, \hat{v}) basis so that

$$\begin{aligned} x_a &= x_a^* + u \hat{u}_a + v \hat{v}_a \\ x_b &= x_b^* + u \hat{u}_b + v \hat{v}_b, \end{aligned} \tag{S50}$$

where $(\cdot)_i$ corresponds to the \hat{x}_i direction. Then we can solve for u and v in terms of x_a and x_b to find

$$\begin{aligned} u(x_a, x_b) &= \frac{\hat{v}_a(x_b^* - x_b) + \hat{v}_b(x_a - x_a^*)}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \\ v(x_a, x_b) &= \frac{\hat{u}_a(x_b - x_b^*) + \hat{u}_b(x_a^* - x_a)}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a}. \end{aligned} \tag{S51}$$

From here, we can solve for $\dot{u} = \dot{u}(x_a, x_b) = \dot{u}(x_a(u, v), x_b(u, v))$ and for $\dot{v} = \dot{v}(x_a(u, v), x_b(u, v))$.

In particular, we find

$$\begin{aligned} \dot{u}(u, v) &= \frac{\hat{v}_b \dot{x}_a(u, v) - \hat{v}_a \dot{x}_b(u, v)}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \quad \text{and} \\ \dot{v}(u, v) &= \frac{-\hat{u}_b \dot{x}_a(u, v) + \hat{u}_a \dot{x}_b(u, v)}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a}, \end{aligned} \tag{S52}$$

where

$$\begin{aligned} \dot{x}_a(u, v) &= (x_a^* + u \hat{u}_a + v \hat{v}_a)(1 - (x_a^* + u \hat{u}_a + v \hat{v}_a) - M_{ab}(x_b^* + u \hat{u}_b + v \hat{v}_b)) \\ &= -(x_a^* + u \hat{u}_a + v \hat{v}_a)(u(\hat{u}_a + M_{ab}\hat{u}_b) + v(\hat{v}_a + M_{ab}\hat{v}_b)) \\ \dot{x}_b(u, v) &= (x_b^* + u \hat{u}_b + v \hat{v}_b)(\mu_b - M_{ba}(x_a^* + u \hat{u}_a + v \hat{v}_a) - (x_b^* + u \hat{u}_b + v \hat{v}_b)) \\ &= -(x_b^* + u \hat{u}_b + v \hat{v}_b)(u(M_{ba}\hat{u}_a + \hat{u}_b) + v(M_{ba}\hat{v}_a + \hat{v}_b)), \end{aligned} \tag{S53}$$

where the simplification $(1 - x_a^* - M_{ab}x_b^*) = (\mu_b - M_{ba}x_a^* - x_b) = 0$ occurred because (x_a^*, x_b^*) is a steady state of Eq. (S37). Expanding these derivatives in powers of u and v we find

$$\begin{aligned}
\dot{x}_a(u, v) &= u[x_a^*(-\hat{u}_a - M_{ab}\hat{u}_b)] + v[x_a^*(-\hat{v}_a - M_{ab}\hat{v}_b)] \\
&\quad + uv[\hat{u}_a(-\hat{v}_a - M_{ab}\hat{v}_b) + \hat{v}_a(-\hat{u}_a - M_{ab}\hat{u}_b)] \\
&\quad + u^2(-\hat{u}_a^2 - M_{ab}\hat{u}_a\hat{u}_b) + v^2(-\hat{v}_a^2 - M_{ab}\hat{v}_a\hat{v}_b) \\
\dot{x}_b(u, v) &= u[x_b^*(-M_{ba}\hat{u}_a - \hat{u}_b)] + v[x_b^*(-M_{ba}\hat{v}_a - \hat{v}_b)] \\
&\quad + uv[\hat{u}_b(-M_{ba}\hat{v}_a - \hat{v}_b) + \hat{v}_b(-M_{ba}\hat{u}_a - \hat{u}_b)] \\
&\quad + u^2(-M_{ba}\hat{u}_a\hat{u}_b - \hat{u}_b^2) + v^2(-M_{ba}\hat{v}_a\hat{v}_b - \hat{v}_b^2).
\end{aligned} \tag{S54}$$

Therefore, we can write \dot{u} and \dot{v} in powers of u and v , so that

$$\begin{aligned}
\dot{u} &= A_{10}u + A_{01}v + A_{20}u^2 + A_{11}uv + A_{02}v^2 \\
\dot{v} &= B_{10}u + B_{01}v + B_{20}u^2 + B_{11}uv + B_{02}v^2.
\end{aligned} \tag{S55}$$

In the following text, we show that $A_{01} = B_{10} = 0$ and that the values of A_{10} and B_{01} correspond to the eigenvalues of the semistable fixed point. Then, we show that for $\mu_b = 1$, $A_{02} = B_{11} = 0$, but for $\mu_b \neq 1$, these coefficients are not 0. Finally, we provide analytic forms for the remaining coefficients A_{11} , A_{20} , B_{02} , and B_{20} .

First, we consider the A_{01} term which is given by

$$\begin{aligned}
A_{01} &= \frac{1}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} [\hat{v}_b(x_a^*(-\hat{v}_a - M_{ab}\hat{v}_b)) - \hat{v}_a(x_b^*(-M_{ba}\hat{v}_a - \hat{v}_b))] \\
&= \frac{1}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} [\hat{v}_a^2(M_{ba}x_b^*) + \hat{v}_a\hat{v}_b(x_b^* - x_a^*) + \hat{v}_b^2(-M_{ab}x_a^*)].
\end{aligned} \tag{S56}$$

We replace the unit eigenvectors by their unnormalized counterparts defined in Eq. (S109)

and (S110), setting $\hat{v}_i = \frac{\vec{v}_i}{\|\vec{v}\|}$ for $i \in a, b$. Since $\vec{v}_b = 1$, this yields

$$\begin{aligned}
A_{01} &= \frac{1/\|\vec{v}\|^2}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\vec{v}_a^2 (M_{ba} x_b^*) + \vec{v}_a \vec{v}_b (x_b^* - x_a^*) + \vec{v}_b^2 (-M_{ab} x_a^*)] \\
&= \frac{1/\|\vec{v}\|^2}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} M_{ba} x_b^* \left[\vec{v}_a^2 + \vec{v}_a \left(\frac{1 - x_a^*/x_b^*}{M_{ba}} \right) - \frac{M_{ab} x_a^*}{M_{ba} x_b^*} \right] \\
&= \frac{M_{ba} x_b^*/\|\vec{v}\|^2}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \left[\left(\vec{v}_a + \frac{1 - x_a^*/x_b^*}{2M_{ba}} \right)^2 - \left(\frac{1 - x_a^*/x_b^*}{2M_{ba}} \right)^2 - \frac{M_{ab} x_a^*}{M_{ba} x_b^*} \right] \\
&= \frac{M_{ba} x_b^*/\|\vec{v}\|^2}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \left[\frac{1}{4M_{ba}^2} \left(\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab} M_{ba} \right) - \left(\frac{1 - x_a^*/x_b^*}{2M_{ba}} \right)^2 - \frac{M_{ab} x_a^*}{M_{ba} x_b^*} \right] \\
&= 0.
\end{aligned} \tag{S57}$$

Thus $A_{01} = 0$. In the same way, $B_{10} = 0$ as well. Next, we consider the A_{10} term, given by

$$\begin{aligned}
A_{10} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{v}_b (x_a^* (-\hat{u}_a - M_{ab} \hat{u}_b)) - \hat{v}_a (x_b^* (-M_{ba} \hat{u}_a - \hat{u}_b))] \\
&= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_a \hat{v}_a (M_{ba} x_b^*) - \hat{u}_a \hat{v}_b (x_a^*) + \hat{u}_b \hat{v}_a (x_b^*) - \hat{u}_b \hat{v}_b (M_{ab} x_a^*)].
\end{aligned} \tag{S58}$$

As before, we replace \hat{u} and \hat{v} by their unnormalized counterparts in both the numerator and denominator (the norms of which cancel) to see

$$\begin{aligned}
A_{10} &= \frac{1}{\vec{u}_a \vec{v}_b - \vec{u}_b \vec{v}_a} [\vec{u}_a \vec{v}_a (M_{ba} x_b^*) - \vec{u}_a \vec{v}_b (x_a^*) + \vec{u}_b \vec{v}_a (x_b^*) - \vec{u}_b \vec{v}_b (M_{ab} x_a^*)] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} [\vec{u}_a \vec{v}_a (M_{ba} x_b^*) - \vec{u}_a (x_a^*) + \vec{v}_a (x_b^*) - (M_{ab} x_a^*)] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} \left[\frac{x_b^*}{4M_{ba}} \left(\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 - \left(\frac{x_a^*}{x_b^*} - 1 \right)^2 - 4 \frac{x_a^*}{x_b^*} M_{ab} M_{ba} \right) \right. \\
&\quad \left. - \vec{u}_a (x_a^*) + \vec{v}_a (x_b^*) - (M_{ab} x_a^*) \right] \\
&= \frac{-\vec{u}_a x_a^* + \vec{v}_a x_b^* - 2M_{ab} x_a^*}{\vec{u}_a - \vec{v}_a}
\end{aligned} \tag{S59}$$

For the case $\mu_b = 1$, this coefficient simplifies to become

$$\begin{aligned}
A_{10} &= \frac{1}{-\frac{M_{ab}}{M_{ba}} - \frac{M_{ab}-1}{M_{ba}-1}} \frac{1}{1 - M_{ab}M_{ba}} \left(\frac{M_{ab}}{M_{ba}} (1 - M_{ab}) + \frac{M_{ab}-1}{M_{ba}-1} (1 - M_{ba}) - 2M_{ab}(1 - M_{ab}) \right) \\
&= \frac{1}{1 - M_{ab}M_{ba}} \left(\frac{1}{M_{ba}} \right) \left(\frac{M_{ba}(M_{ba}-1)}{M_{ab} - 2M_{ab}M_{ba} + M_{ba}} \right) \\
&\quad \times (M_{ab} - 2M_{ab}M_{ba} + M_{ba} - M_{ab}(M_{ab} - 2M_{ab}M_{ba} + M_{ba})) \\
&= \frac{(M_{ab}-1)(M_{ba}-1)}{M_{ab}M_{ba}-1}.
\end{aligned} \tag{S60}$$

This value is precisely the eigenvalue that corresponds to the unstable eigenvector \vec{u} of the semistable fixed point (x_a^*, x_b^*) . In a similar way, we may calculate B_{01} , which yields

$$\begin{aligned}
B_{01} &= \frac{1}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} [-\hat{u}_b(x_a^*(-\hat{v}_a - M_{ab}\hat{v}_b)) + \hat{u}_a(x_b^*(-M_{ba}\hat{v}_a - \hat{v}_b))] \\
&= \frac{1}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} [-\hat{u}_a\hat{v}_a(M_{ba}x_b^*) - \hat{u}_a\hat{v}_b(x_b^*) + \hat{u}_b\hat{v}_a(x_a^*) + \hat{u}_b\hat{v}_b(M_{ab}x_a^*)] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} [-\vec{u}_a\vec{v}_a(M_{ba}x_b^*) - \vec{u}_a(x_b^*) + \vec{v}_a(x_a^*) + (M_{ab}x_a^*)] \\
&= \frac{-\vec{u}_ax_b^* + \vec{v}_ax_a^* + 2M_{ab}x_a^*}{\vec{u}_a - \vec{v}_a}.
\end{aligned} \tag{S61}$$

For the case $\mu_b = 1$ this term becomes

$$\begin{aligned}
B_{01} &= \frac{1}{-\frac{M_{ab}}{M_{ba}} - \frac{M_{ab}-1}{M_{ba}-1}} \left(\frac{1}{1 - M_{ab}M_{ba}} \right) \left(\frac{M_{ab}}{M_{ba}} (1 - M_{ba}) + \frac{M_{ab}-1}{M_{ba}-1} (1 - M_{ab}) + 2M_{ab}(1 - M_{ab}) \right) \\
&= \frac{1}{1 - M_{ab}M_{ba}} \left(\frac{1}{M_{ba}(M_{ba}-1)} \right) \left(\frac{M_{ba}(M_{ba}-1)}{M_{ab} - 2M_{ab}M_{ba} + M_{ba}} \right) \\
&\quad \times -M_{ab}(1 - M_{ba})^2 - M_{ba}(1 - M_{ab})^2 - 2M_{ab}M_{ba}(1 - M_{ab})(1 - M_{ba}) \\
&= \frac{-M_{ab} + 2M_{ab}M_{ba} - M_{ba} + M_{ab}^2M_{ba} + M_{ab}M_{ba}^2 - 2M_{ab}^2M_{ba}^2}{M_{ab} - 2M_{ab}M_{ba} + M_{ba} - M_{ab}^2M_{ba} - M_{ab}M_{ba}^2 + 2M_{ab}^2M_{ba}^2} \\
&= -1,
\end{aligned} \tag{S62}$$

which is the eigenvalue that corresponds to the stable eigenvector \vec{v} .

Next we solve for A_{02} , and find that

$$\begin{aligned}
A_{02} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{v}_b(-\hat{v}_a^2 - M_{ab} \hat{v}_a \hat{v}_b) - \hat{v}_a(-M_{ba} \hat{v}_a \hat{v}_b - \hat{v}_b^2)] \\
&= \frac{\hat{v}_a \hat{v}_b}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{v}_b(1 - M_{ab}) + \hat{v}_a(M_{ba} - 1)] \\
&= \frac{\hat{v}_a \hat{v}_b}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} (1 - M_{ab} M_{ba})(\hat{v}_b x_a^* - \hat{v}_a x_b^*),
\end{aligned} \tag{S63}$$

which is nonzero in general. However, for the specific case $\mu_b = 1$ we can simplify this expression to find

$$\begin{aligned}
A_{02} &= \frac{\hat{v}_a \hat{v}_b / \|\vec{v}_b\|}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\vec{v}_b(1 - M_{ab}) + \vec{v}_a(M_{ba} - 1)] \\
&= \frac{\hat{v}_a \hat{v}_b / \|\vec{v}_b\|}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \left[1 - M_{ab} + \frac{M_{ab} - 1}{M_{ba} - 1} (M_{ba} - 1) \right] \\
&= 0.
\end{aligned} \tag{S64}$$

Next we consider the B_{11} term, which is given by

$$\begin{aligned}
B_{11} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \{ -\hat{u}_b [\hat{u}_a(-\hat{v}_a - M_{ab} \hat{v}_b) + \hat{v}_a(-\hat{u}_a - M_{ab} \hat{u}_b)] \\
&\quad + \hat{u}_a [\hat{u}_b(-M_{ba} \hat{v}_a - \hat{v}_b) + \hat{v}_b(-M_{ba} \hat{u}_a - \hat{u}_b)] \} \\
&= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_a \hat{u}_b (\hat{v}_a(2 - M_{ba}) + \hat{v}_b(M_{ab} - 2)) + M_{ab} \hat{u}_b^2 \hat{v}_a - M_{ba} \hat{u}_a^2 \hat{v}_b] \\
&= \frac{1/\|\vec{u}\|}{\vec{u}_a - \vec{v}_a} [\vec{u}_a \vec{v}_a (2 - M_{ba}) + \hat{u}_a (M_{ab} - 2) + \vec{v}_a M_{ab} - \vec{u}_a^2 M_{ba}].
\end{aligned} \tag{S65}$$

As was the case for A_{02} , this is nonzero in general. However, for the specific case where $\mu_b = 1$ this simplifies to become

$$\begin{aligned}
B_{11} &= \frac{1/\|\vec{u}\|}{\vec{u}_a - \vec{v}_a} \left[-\frac{M_{ab}(M_{ab} - 1)}{M_{ba}(M_{ba} - 1)} (2 - M_{ba}) - \frac{M_{ab}}{M_{ba}} (M_{ab} - 2) + \frac{M_{ab} - 1}{M_{ba} - 1} M_{ab} - \frac{M_{ab}^2}{M_{ba}^2} M_{ba} \right] \\
&= \frac{1/\|\vec{u}\|}{\vec{u}_a - \vec{v}_a} \left(\frac{M_{ab}}{M_{ba}(M_{ba} - 1)} \right) [-(M_{ab} - 1)(2 - M_{ba}) - (M_{ba} - 1)(M_{ab} - 2) \\
&\quad + (M_{ab} - 1)M_{ba} - M_{ab}(M_{ba} - 1)] \\
&= 0.
\end{aligned} \tag{S66}$$

In a similar way, we find that

$$\begin{aligned}
A_{11} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \{ \hat{v}_b [\hat{u}_a (-\hat{v}_a - M_{ab} \hat{v}_b) + \hat{v}_a (-\hat{u}_a - M_{ab} \hat{u}_b)] \\
&\quad - \hat{v}_a [\hat{u}_b (-M_{ba} \hat{v}_a - \hat{v}_b) + \hat{v}_b (-M_{ba} \hat{u}_a - \hat{u}_b)] \} \\
&= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_b \hat{v}_a^2 (M_{ba}) - \hat{u}_a \hat{v}_b^2 (M_{ab}) + \hat{u}_b \hat{v}_a \hat{v}_b (2 - M_{ab}) - \hat{u}_a \hat{v}_a \hat{v}_b (2 - M_{ba})],
\end{aligned} \tag{S67}$$

that

$$A_{20} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{v}_b (-\hat{u}_a^2 - M_{ab} \hat{u}_a \hat{u}_b) - \hat{v}_a (-M_{ba} \hat{u}_a \hat{u}_b - \hat{u}_b^2)], \tag{S68}$$

that

$$B_{02} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-\hat{u}_b (-\hat{v}_a^2 - M_{ab} \hat{v}_a \hat{v}_b) + \hat{u}_a (-M_{ba} \hat{v}_a \hat{v}_b - \hat{v}_b^2)], \tag{S69}$$

and that

$$\begin{aligned}
B_{20} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-\hat{u}_b (-\hat{u}_a^2 - M_{ab} \hat{u}_a \hat{u}_b) + \hat{u}_a (-M_{ba} \hat{u}_a \hat{u}_b - \hat{u}_b^2)], \\
&= \frac{\hat{u}_a \hat{u}_b}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_a (1 - M_{ba}) + \hat{u}_b (M_{ab} - 1)], \\
&= \frac{\hat{u}_a \hat{u}_b}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} (1 - M_{ab} M_{ba}) (\hat{u}_a x_b^* - \hat{u}_b x_a^*).
\end{aligned} \tag{S70}$$

Therefore, we have analytic forms for every coefficient of the (u, v) transformed gLV equations in Eq. (S117).

SIGNS OF THE GLV COEFFICIENTS IN (u, v) COORDINATES

For the special case $\mu_b = 1$, we will evaluate the sign of each coefficient of Eq. (S117). In the next section we show $A_{10} > 0$ and $B_{01} < 0$. Next, here we show that $A_{11} < 0$. Consider

\hat{u} and \hat{v} as in Eq. (S111). Then

$$\begin{aligned}
A_{11} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_b \hat{v}_a^2 (M_{ba}) - \hat{u}_a \hat{v}_b^2 (M_{ab}) + \hat{u}_b \hat{v}_a \hat{v}_b (2 - M_{ab}) - \hat{u}_a \hat{v}_a \hat{v}_b (2 - M_{ba})] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} [\vec{v}_a^2 (M_{ba}) - \vec{u}_a (M_{ab}) + \vec{v}_a (2 - M_{ab}) - \vec{u}_a \vec{v}_a (2 - M_{ba})] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} [\vec{v}_a (M_{ba} \vec{v}_a + 2 - M_{ab}) - \vec{u}_a (-M_{ba} \vec{v}_a + 2 \vec{v}_a + M_{ab})] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} \left[\frac{\vec{v}_a}{M_{ba} - 1} (M_{ba} (M_{ab} - 1) + 2(M_{ba} - 1) - M_{ab} (M_{ba} - 1)) \right. \\
&\quad \left. - \frac{\vec{u}_a}{M_{ba} - 1} (-M_{ba} (M_{ab} - 1) + 2(M_{ab} - 1) + M_{ab} (M_{ba} - 1)) \right] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} \left[\frac{\vec{v}_a}{M_{ba} - 1} (M_{ba} + M_{ab} - 2) - \frac{\vec{u}_a}{M_{ba} - 1} (M_{ba} + M_{ab} - 2) \right], \tag{S71}
\end{aligned}$$

and since $\vec{u}_a < 0$, $\frac{1}{\vec{u}_a - \vec{v}_a} < 0$, $M_{ab} > 1$, and $M_{ba} > 1$, we must have $A_{11} < 0$. Next, we show $A_{20} < 0$. We find

$$\begin{aligned}
A_{20} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{v}_b (-\hat{u}_a^2 - M_{ab} \hat{u}_a \hat{u}_b) - \hat{v}_a (-M_{ba} \hat{u}_a \hat{u}_b - \hat{u}_b^2)] \\
&= \frac{1}{\hat{u}_a - \hat{v}_a} [-\hat{u}_a (\hat{u}_a + M_{ab} - M_{ba} \hat{v}_a) + \hat{v}_a] \\
&= \frac{1}{\hat{u}_a - \hat{v}_a} \left[-\frac{\hat{u}_a}{M_{ba} (M_{ba} - 1)} (-M_{ab} (M_{ba} - 1) + M_{ab} M_{ba} (M_{ba} - 1) - M_{ba}^2 (M_{ab} - 1)) + \hat{v}_a \right] \\
&= \frac{1}{\hat{u}_a - \hat{v}_a} \left[-\frac{\hat{u}_a}{M_{ba} (M_{ba} - 1)} (M_{ab} + M_{ba}^2) + \hat{v}_a \right] < 0, \tag{S72}
\end{aligned}$$

since $u_a < 0$, $v_a > 0$, $M_{ab} > 1$, and $M_{ba} > 1$. Next, we show $B_{02} < 0$. We find

$$B_{02} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-\hat{u}_b (-\hat{v}_a^2 - M_{ab} \hat{v}_a \hat{v}_b) + \hat{u}_a (-M_{ba} \hat{v}_a \hat{v}_b - \hat{v}_b^2)] > 0 \tag{S73}$$

based on the orientation of \hat{u} and \hat{v} . Finally, we show $B_{20} > 0$. We find

$$B_{20} = \frac{\hat{u}_a \hat{u}_b}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_a (1 - M_{ba}) + \hat{u}_b (M_{ab} - 1)] > 0 \tag{S74}$$

based on the orientation of \hat{u} and \hat{v} . Therefore, for the special case $\mu_b = 1$, we have $A_{10} > 0$, $A_{11} < 0$, $A_{20} < 0$, $B_{01} < 0$, $B_{02} < 0$, and $B_{20} > 0$.

COMPARISON OF SPEEDS OF UNSTABLE AND STABLE MANIFOLDS

Here we will show that the speed of the stable manifold is faster than the unstable manifold, or equivalently, that $|A_{10}| < |B_{01}|$. Recall that

$$B_{01} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-\hat{u}_a \hat{v}_a (M_{ba} x_b^*) - \hat{u}_a \hat{v}_b (x_b^*) + \hat{u}_b \hat{v}_a (x_a^*) + \hat{u}_b \hat{v}_b (M_{ab} x_a^*)] \quad (\text{S75})$$

and that

$$A_{10} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_a \hat{v}_a (M_{ba} x_b^*) - \hat{u}_a \hat{v}_b (x_a^*) + \hat{u}_b \hat{v}_a (x_b^*) - \hat{u}_b \hat{v}_b (M_{ab} x_a^*)]. \quad (\text{S76})$$

We choose an orientation for \hat{u} and \hat{v} as in Eqs. (S109) and (S110) so that $\hat{u} = (-, +)$ and $\hat{v} = (+, +)$. Then, $B_{01} < 0$, and so $|B_{01}| = -B_{01}$. To show that $A_{10} > 0$, we consider the term

$$\begin{aligned} A_{10} &= \frac{-\vec{u}_a x_a^* + \vec{v}_a x_b^* - 2M_{ab} x_a^*}{\vec{u}_a - \vec{v}_a} \\ &= \frac{x_a^*}{\vec{u}_a - \vec{v}_a} \left(-\vec{u}_a + \vec{v}_a \frac{x_b^*}{x_a^*} - 2M_{ab} \right) \\ &= \frac{x_a^*}{\vec{u}_a - \vec{v}_a} \left(\frac{1}{2M_{ba}} \right) \left(2 - \frac{x_a^*}{x_b^*} - \frac{x_b^*}{x_a^*} - 4M_{ab}M_{ba} + \left(1 + \frac{x_b^*}{x_a^*} \right) \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab}M_{ba}} \right). \end{aligned} \quad (\text{S77})$$

Note that $\frac{x_a^*}{2M_{ba}(\vec{u}_a - \vec{v}_a)} < 0$, so to show $A_{10} > 0$ we must show the right term must be negative.

In order to do this we multiply it by its conjugate, which is positive since

$$\begin{aligned} &-2 + \frac{x_a^*}{x_b^*} + \frac{x_b^*}{x_a^*} + 4M_{ab}M_{ba} + \left(1 + \frac{x_b^*}{x_a^*} \right) \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab}M_{ba}} \\ &> 2 + \frac{x_a^*}{x_b^*} + \frac{x_b^*}{x_a^*} + \left(1 + \frac{x_b^*}{x_a^*} \right) \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab}M_{ba}} \\ &= 2 \left(1 + \frac{x_b^*}{x_a^*} \right) \left(1 + \frac{x_a^*}{x_b^*} \right) > 0. \end{aligned} \quad (\text{S78})$$

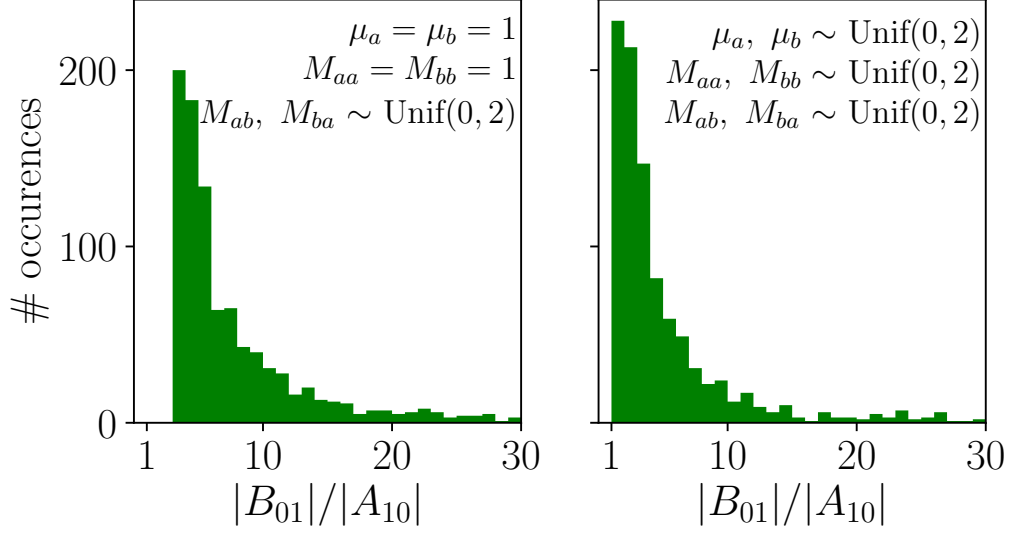


FIG. S2. Comparison of speeds of the fast and slow manifolds over random parameter draws. Parameters were drawn 1000 times from the distributions (a) $\mu_a = \mu_b = M_{aa} = M_{bb} = 1$, $M_{ab} \sim \text{Unif}([0, 2])$, and $M_{ba} \sim \text{Unif}([0, 2])$; and (b) $\mu_i \sim \text{Unif}([0, 2])$ for $i \in a, b$ and $M_{ij} \sim \text{Unif}([0, 2])$ for $i, j \in a, b$.

Then, the sign of A_{10} is determined by the sign of

$$\begin{aligned}
& \left[\left(\frac{x_a^*}{x_b^*} - 1 \right) \left(\frac{x_b^*}{x_a^*} - 1 \right) - 4M_{ab}M_{ba} + \left(1 + \frac{x_b^*}{x_a^*} \right) \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4\frac{x_a^*}{x_b^*}M_{ab}M_{ba}} \right] \\
& \times \left[- \left(\frac{x_a^*}{x_b^*} - 1 \right) \left(\frac{x_b^*}{x_a^*} - 1 \right) + 4M_{ab}M_{ba} + \left(1 + \frac{x_b^*}{x_a^*} \right) \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4\frac{x_a^*}{x_b^*}M_{ab}M_{ba}} \right] \\
& = \left(1 + \frac{x_b^*}{x_a^*} \right)^2 \left[\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4\frac{x_a^*}{x_b^*}M_{ab}M_{ba} \right] - \left(\frac{x_a^*}{x_b^*} - 1 \right)^2 \left(\frac{x_b^*}{x_a^*} - 1 \right)^2 \\
& \quad + 8M_{ab}M_{ba} \left(\frac{x_a^*}{x_b^*} - 1 \right) \left(\frac{x_b^*}{x_a^*} - 1 \right) - 16M_{ab}^2M_{ba}^2 \\
& = \left(\frac{x_a^*}{x_b^*} - \frac{x_b^*}{x_a^*} \right)^2 + \left(1 + \frac{x_b^*}{x_a^*} \right)^2 4\frac{x_a^*}{x_b^*}M_{ab}M_{ba} - \left(2 - \frac{x_a^*}{x_b^*} - \frac{x_b^*}{x_a^*} \right)^2 \\
& \quad + 8M_{ab}M_{ba} \left(2 - \frac{x_a^*}{x_b^*} - \frac{x_b^*}{x_a^*} \right) - 16M_{ab}^2M_{ba}^2 \\
& = 4\frac{x_a^*}{x_b^*}(1 - M_{ab}M_{ba}) + 4\frac{x_b^*}{x_a^*}(1 - M_{ab}M_{ba}) - 8(2M_{ab}M_{ba} - 1)(M_{ab}M_{ba} - 1) \\
& < 0,
\end{aligned}$$

(S79)

where the final inequality is because $1 - M_{ab}M_{ba} < 0$. Therefore, $A_{10} > 0$, and so $|A_{10}| = A_{10}$. Then, using the expressions of B_{01} and A_{10} in Eqs. (S137) and (S138), we can compare the speeds of the manifolds by considering the sign of $|A_{10}| - |B_{01}| = A_{10} + B_{01}$, which is

$$A_{10} + B_{01} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-2\hat{u}_a \hat{v}_b(x_a^*) + 2\hat{u}_b \hat{v}_a(x_b^*)] < 0. \quad (\text{S80})$$

Therefore, $|A_{10}| < |B_{01}|$, and due to this we call the stable manifold “fast” and the unstable manifold “slow.”

Next, we evaluate the ratio of $|B_{01}|/|A_{10}|$ over many sets of randomly chosen parameter values. If we set $\mu_a = \mu_b = M_{aa} = M_{bb} = 1$ and pick $M_{ab} \sim \text{Unif}([0, 2])$ and $M_{ba} \sim \text{Unif}([0, 2])$, we find that $|B_{01}|/|A_{10}|$ has a median of 5.88 with an IQR of [2.70, 9.05]. If we choose $\mu_i \sim \text{Unif}([0, 2])$ for $i \in a, b$ and $M_{ij} \sim \text{Unif}([0, 2])$ for $i, j \in a, b$, we find that $|B_{01}|/|A_{10}|$ has a median of 3.34 with an IQR of [1.20, 5.49]. We plot a histogram of the ratio $|B_{01}|/|A_{10}|$ for parameters drawn from these two parameter distributions in Fig S4.

INITIAL CONDITION OF FIG. 2 SATISFIES SIMPLIFYING ASSUMPTIONS

In the main text, we interpret the rates of increase of the necessary transplant size α and β of the main trajectory of Fig. 2 according to Eq. (3) of the main text, and in doing so claim that the trajectory satisfies certain assumptions. Here, we justify those assumptions.

In (x_a, x_b) coordinates, the post-antibiotic initial condition of the main (colored) trajectory in Fig. 2 is (0.127, 0.034), and in (u, v) coordinates is (0.033, -0.576). For this set of parameters ($\mu_b = 1$, $M_{ab} = 1.167$, and $M_{ba} = 1.093$), we find that the coefficients of the (u, v) -transformed coordinates are $A_{10} = 0.057$, $A_{20} = -0.046$, $A_{11} = -1.360$, $B_{01} = -1.000$, $B_{20} = -1.442$, and $B_{20} = 0.096$.

Therefore, we have $|B_{01}|/|A_{10}| = 17.637$, which indicates a separation of time scales between u and v . We find $B_{20}u_0^2 = 0.0002$ which is small compared to other terms (for example, $B_{01}v_0 = .575$). Under these assumptions, and replacing $B_{20} = -B_{20}$ and $B_{01} = -B_{01}$ so that coefficients are positive, the equation that governs $\frac{dv}{dt}$ simplifies to

$$\frac{dv}{dt} = -B_{01}v - B_{02}v^2, \quad (\text{S81})$$

which is autonomous and has a solution

$$v(t) = \frac{B_{10}v_0}{(B_{10} + B_{20}v_0) e^{B_{10}t} - B_{20}v_0}. \quad (\text{S82})$$

We substitute this solution of $v(t)$ in order to solve for the minimum transplant size s dynamics, given by

$$\frac{ds}{dt} = s \left(A_{10} - A_{20}(\hat{u} \cdot \hat{x}_b)s - A_{11} \frac{B_{10}v_0}{(B_{10} + B_{20}v_0) e^{B_{10}t} - B_{20}v_0} \right). \quad (\text{S83})$$

Since time scales are sufficiently separated, $u(t) \approx u_0$ while microbial trajectories follow the fast manifold. Then, we can solve for the optimal transplant time t_{opt}^* by setting $\frac{ds}{dt} = 0$, from which we find

$$t_{opt}^* = \frac{1}{B_{10}} \ln \left(\frac{1}{B_{10} + B_{20}v_0} \left(\frac{A_{11}B_{10}v_0}{A_{10} - A_{20}u_0} + B_{20}v_0 \right) \right). \quad (\text{S84})$$

Under the assumption $B_{02}v_0^2 \ll B_{01}v_0$, equations Eqs. (S145) and (S146) reduce to the forms given in the main text, Eqs. (3) and (4). The form of t_{opt}^* given in Eq. (S146) is the form used to color the background of Fig. 3 in the main text.

NONDIMENSIONALIZATION

We begin with the generalized Lotka-Volterra equations in two-dimensions,

$$\begin{aligned} \frac{dx_a}{dt} &= x_a(\mu_a - M_{aa}x_a - M_{ab}x_b) \\ \frac{dx_b}{dt} &= x_b(\mu_b - M_{ba}x_a - M_{bb}x_b). \end{aligned} \quad (\text{S85})$$

To nondimensionalize, let $\tilde{x}_a = \alpha x_a$, $\tilde{x}_b = \beta x_b$, and $T = \tau t$, with nondimensionalization parameters $\tau = \mu_a$, $\alpha = M_{aa}/\mu_a$, and $\beta = M_{bb}/\mu_a$. Then, the equations become

$$\begin{aligned} \frac{d\tilde{x}_a}{dT} &= \tilde{x}_a(1 - \tilde{x}_a - \tilde{M}_{ab}\tilde{x}_b) \\ \frac{d\tilde{x}_b}{dT} &= \tilde{x}_b(\tilde{\mu}_b - \tilde{M}_{ba}\tilde{x}_a - \tilde{x}_b), \end{aligned} \quad (\text{S86})$$

where $\tilde{M}_{ab} = M_{ab}/M_{bb}$, $\tilde{\mu}_b = \mu_b/\mu_a$, and $\tilde{M}_{ba} = M_{ba}/M_{aa}$. For convenience, we overwrite our notation so that $\tilde{x}_a \rightarrow x_a$, $\tilde{x}_b \rightarrow x_b$, and $T \rightarrow t$, and so

$$\begin{aligned}\frac{dx_a}{dt} &= x_a(1 - x_a - M_{ab}x_b) \\ \frac{dx_b}{dt} &= x_b(\mu_b - M_{ba}x_a - x_b).\end{aligned}\tag{S87}$$

Therefore, we can study the behavior of this system by considering different parameter sets (M_{ab} , M_{ba} , and μ_b). In the main text, we assume $\mu_b = 1$, but we relax this assumption here in the supplement.

HOMOGENEOUS STEADY STATES

The two homogeneous steady states are $(1, 0)$ and $(0, \mu_b)$. Their eigenvalues are $\lambda_{10} = -1$, $\mu_b - M_{ba}$ and $\lambda_{01} = -\mu_b$, $1 - M_{ab}\mu_b$, respectively. We assume $\mu_b > 0$ to ensure nonnegative steady states. Therefore, for this system to capture the dynamics we are interested in—the switching behavior between healthy and diseased stable steady states—we must have $M_{ba} > \mu_b$ and $M_{ab}\mu_b > 1$.

MIXED STEADY STATE

The solution of Eq. (S37) for the mixed steady state (x_a^*, x_b^*) is

$$\left(\frac{1 - M_{ab}\mu_b}{1 - M_{ab}M_{ba}}, \frac{\mu_b - M_{ba}}{1 - M_{ab}M_{ba}} \right).\tag{S88}$$

Due to the constraint that the homogeneous steady states are stable, we must have $M_{ab}M_{ba} > 1$. To provide bounds on x_a^* and x_b^* , we manipulate the inequalities that result from the stability of the homogeneous steady states. For x_a^* we have

$$\begin{aligned}1 < M_{ab}\mu_b < M_{ab}M_{ba} &\implies 0 > 1 - M_{ab}\mu_b > 1 - M_{ab}M_{ba} \\ &\implies 0 < x_a^* < 1,\end{aligned}\tag{S89}$$

and for x_b^* we have

$$\begin{aligned} 0 > \mu_b - M_{ba} > \frac{1}{M_{ab}} - M_{ba} &\implies 0 < \frac{\mu_b - M_{ba}}{1 - M_{ab}M_{ba}} < \frac{1}{M_{ab}} < \mu_b \\ &\implies 0 < x_b^* < \mu_b. \end{aligned} \quad (\text{S90})$$

Therefore, each component of the mixed steady state is bounded below by 0 and above by the value of its homogeneous steady state.

To check the stability of the mixed steady state, we evaluate the eigenvalues of the Jacobian of Eq. (S37) evaluated at the steady state. If $\mu_b = 1$ then the eigenvalues are

$$\lambda_{\pm} = \frac{(M_{ab} - 1)(M_{ba} - 1)}{M_{ab}M_{ba} - 1}, \quad -1, \quad (\text{S91})$$

but in order for the homogeneous steady states to be stable we must also have $\lambda_+ > 0$, so this fixed point is semistable. For $\mu_b \neq 1$, we have

$$\begin{aligned} \lambda_{\pm} = \frac{1}{2(M_{ab}M_{ba} - 1)} &\left[1 - M_{ab}\mu_b + \mu_b - M_{ba} \right. \\ &\left. \pm \sqrt{(1 - M_{ba}\mu_b + \mu_b - M_{ba})^2 + 4(M_{ab}M_{ba} - 1)(M_{ab}\mu_b - 1)(M_{ba} - \mu_b)} \right] \end{aligned} \quad (\text{S92})$$

The fact that the homogeneous steady states are stable requires $1 - M_{ab}\mu_b + \mu_b - M_{ba} < 0$, and the positivity of the mixed steady state requires $(M_{ab}M_{ba} - 1)(M_{ab}\mu_b - 1)(M_{ba} - \mu_b) > 0$ and $M_{ab}M_{ba} - 1 > 0$. Therefore, one of the eigenvalues will be positive and the other negative for the systems we are considering.

ANALYTIC MANIFOLD DISCOVERY FOR THE MIXED STEADY STATE

The stable and unstable eigenvectors of the mixed steady state (x_a^*, x_b^*) are tangent to the stable and unstable manifolds at that point [1]. We denote these manifolds as $h^{s/u}(x_a)$, and consider their Taylor expansion about the mixed steady state

$$\begin{aligned} h^{s/u}(x_a) &= c_0 + c_1^{s/u}(x_a - x_a^*) + \frac{c_2^{s/u}}{2!}(x_a - x_a^*)^2 + \frac{c_3^{s/u}}{3!}(x_a - x_a^*)^3 + \dots \\ &= \sum_{n=0}^{\infty} \frac{c_n^{s/u}}{n!}(x_a - x_a^*)^n. \end{aligned} \quad (\text{S93})$$

Naturally, $c_0 = x_b^*$ for both manifolds. The other coefficients have two possible values that correspond to either the stable or the unstable manifold. Since these manifolds are invariant under the flow generated by the dynamical system [1],

$$\frac{dh^{s/u}(x_a)}{dx_a} = \frac{dx_b}{dt} \bigg/ \frac{dx_a}{dt}. \quad (\text{S94})$$

We consider trajectories along these manifolds so that $x_b = h^{s/u}(x_a)$. Then, substituting in terms and rearranging this equation we find that

$$\begin{aligned} x_a(c_1^{s/u} + c_2^{s/u}(x_a - x_a^*) + \dots)(\mu_a - M_{aa}x_a - M_{ab}(x_b^* + c_1^{s/u}(x_a - x_a^*) + \dots)) \\ = (x_b^* + c_1^{s/u}(x_a - x_a^*) + \dots)(\mu_b - M_{ba}x_a - M_{bb}(x_b^* + c_1^{s/u}(x_a - x_a^*) + \dots)). \end{aligned} \quad (\text{S95})$$

We make the substitution $y = (x_a - x_a^*)$ to simplify the equations to

$$\begin{aligned} (y + x_a^*)(c_1^{s/u} + c_2^{s/u}y + \dots)(\mu_a - M_{aa}(y + x_a^*) - M_{ab}(x_b^* + c_1^{s/u}y + \dots)) \\ = (x_b^* + c_1^{s/u}y + \dots)(\mu_b - M_{ba}(y + x_a^*) - M_{bb}(x_b^* + c_1^{s/u}y + \dots)), \end{aligned} \quad (\text{S96})$$

from which point powers of y may be equated, allowing for the determination of coefficients in the Taylor series. The constant terms (order y^0) satisfy

$$c_1^{s/u}x_a^*(\mu_a - M_{aa}x_a^* - M_{ab}x_b^*) = x_b^*(\mu_b - M_{ba}x_a^* - M_{bb}x_b^*) \quad (\text{S97})$$

trivially, since (x_a^*, x_b^*) is a steady state of Eq. (S35). The linear terms (order y^1) must satisfy

$$M_{ab}x_a^*(c_1^{s/u})^2 + (M_{aa}x_a^* - M_{bb}x_b^*)c_1^{s/u} - M_{ba}x_b^* = 0, \quad (\text{S98})$$

and from the resulting quadratic equation we obtain two sets of coefficients $c_1^{s/u}$ corresponding to two manifolds. In the remaining calculation, we omit the s/u superscript. To determine higher-order coefficients we consider the full explicit form of Eq. (S94), which

reads

$$\begin{aligned}
& \left(\sum_{n=0}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \left(\mu_b - M_{ba}x_a^* - M_{ba}(x_a - x_a^*) - M_{bb} \left(\sum_{n=0}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \right) \\
&= \left(\sum_{n=0}^{\infty} \frac{c_{n+1}}{n!} (x - x_a^*)^{n+1} \right) \left(\mu_a - M_{aa}x_a^* - M_{aa}(x_a - x_a^*) - M_{ab} \left(\sum_{n=0}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \right) \\
&+ x_a^* \left(\sum_{n=0}^{\infty} \frac{c_{n+1}}{n!} (x - x_a^*)^n \right) \left(\mu_a - M_{aa}x_a^* - M_{aa}(x_a - x_a^*) - M_{ab} \left(\sum_{n=0}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \right).
\end{aligned} \tag{S99}$$

As noted before, $c_0 = x_b^*$. Then, since $\mu_a - M_{aa}x_a^* - M_{ab}x_b^* = \mu_b - M_{ba}x_a^* - M_{bb}x_b^* = 0$, we may simplify this expression to

$$\begin{aligned}
& \left(\sum_{n=0}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \left(-M_{ba}(x_a - x_a^*) - M_{bb} \left(\sum_{n=1}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \right) \\
&= \left(\sum_{n=0}^{\infty} \frac{c_{n+1}}{n!} (x - x_a^*)^n \right) ((x - x_a^*) + x_a^*) \left(-M_{aa}(x_a - x_a^*) - M_{ab} \left(\sum_{n=1}^{\infty} \frac{c_n}{n!} (x - x_a^*)^n \right) \right).
\end{aligned} \tag{S100}$$

From here it is plain to see that the $(x_a - x_a^*)^0$ vanishes, and that the $(x_a - x_a^*)^1$ term leads to Eq. (S98). We next consider an arbitrary term of order $(x_a - u)^m$, given by

$$\begin{aligned}
& - (M_{ba} + M_{bb} c_1) \frac{c_{m-1}}{(m-1)!} - M_{bb} \sum_{\ell=2}^m \frac{c_{\ell} c_{m-\ell}}{\ell! (m-\ell)!} \\
&= - (M_{aa} + M_{ab} c_1) \frac{c_{m-1}}{(m-2)!} - M_{ab} \sum_{\ell=2}^{m-1} \frac{c_{\ell} c_{m-\ell}}{\ell! (m-\ell-1)!} \\
&- x_a^* (M_{aa} + M_{ab} c_1) \frac{c_m}{(m-1)!} - x_a^* M_{ab} \sum_{\ell=2}^m \frac{c_{\ell} c_{m-\ell+1}}{\ell! (m-\ell)!}.
\end{aligned} \tag{S101}$$

We simplify this term for the edge case $m = 2$ to find

$$- (M_{ba} + M_{bb} c_1) c_1 - \frac{1}{2} M_{bb} c_0 c_2 = - (M_{aa} + M_{ab} c_1) c_1 - x_a^* (M_{aa} + M_{ab} c_1) c_2 - \frac{1}{2} x_a^* M_{ab} c_2 c_1, \tag{S102}$$

which can be rearranged to show

$$\frac{c_2}{2}(2x_a^*M_{aa} + 3x_a^*M_{ab}c_1 - M_{bb}x_b^*) = c_1(M_{ba} + M_{bb}c_1 - M_{aa} - M_{ab}c_1). \quad (\text{S103})$$

Finally we solve Eq. (S101) for $m > 2$ to find the leading coefficient c_m as a function of the previous coefficients $c_{m-1}, c_{m-2}, \dots, c_0$ to find

$$\begin{aligned} \frac{c_m}{m!} (mx_a^*M_{aa} + (m+1)x_a^*M_{ab}c_1 - M_{bb}x_b^*) \\ = \frac{c_{m-1}}{(m-1)!} (M_{ba} + M_{bb}c_1 - (m-1)(M_{aa} + M_{ab}c_1)) \\ + \sum_{\ell=2}^{m-1} \left[\frac{c_\ell}{\ell! (m-\ell)!} (M_{bb}c_{m-\ell} - (m-\ell)M_{ab}c_{m-\ell} - x_a^*M_{ab}c_{m-\ell+1}) \right], \end{aligned} \quad (\text{S104})$$

and from this equation we can solve for c_m . Therefore, we can compute the Taylor expansion for the unstable or stable manifolds of the mixed fixed point to arbitrary order.

SPLIT LYAPUNOV FUNCTION

The split Lyapunov function for Eq. (S37) as a function of the two microbial populations x_a and x_b is given by

$$V(x_a, x_b) = M_{ba}x_a^2/2 + M_{ab}x_b^2/2 - M_{ba}x_a - M_{ab}\mu_b x_b + M_{ab}M_{ba}x_a x_b. \quad (\text{S105})$$

To verify this equation satisfies the properties of Lyapunov functions, we first demonstrate that the only minima of $V(x_a, x_b)$ correspond to the two stable fixed points of Eq. (S35). Recall that in our system the two stable steady states are at $(1, 0)$ and $(0, \mu_b)$. To find the minima we consider when $\frac{d}{dx_a}V(x_a, x_b) = 0$ and when $\frac{d}{dx_b}V(x_a, x_b) = 0$. These derivatives are given by

$$\begin{aligned} \frac{d}{dx_a}V(x_a, x_b) &= M_{ba}x_a - M_{ba} + M_{ab}M_{ba}x_b \quad \text{and} \\ \frac{d}{dx_b}V(x_a, x_b) &= M_{ab}x_b - M_{ab}\mu_b + M_{ab}M_{ba}x_a. \end{aligned} \quad (\text{S106})$$

For the state $(1, 0)$, $\frac{d}{dx_a}V(x_a, x_b) = 0$ but $\frac{d}{dx_b}V(x_a, x_b) > 0$. Since the microbe counts are nonnegative and therefore bounded, $(1, 0)$ constitutes a minima. Likewise, the state $(0, \mu_b)$

is a minima. The mixed steady state given in Eq. (S88) also satisfies both $\frac{d}{dx_a}V(x_a, x_b) = 0$ and $\frac{d}{dx_b}V(x_a, x_b) = 0$, but due to topological constraints cannot also be a minima.

Next we will demonstrate that all trajectories flow down the Lyapunov landscape by showing $\dot{V}(x_a, x_b) < 0$. First, note that

$$\begin{aligned}\nabla V(x_a, x_b) &= \hat{x}_a(M_{ba}x_a - M_{ba}\mu_a + M_{ab}M_{ba}x_b) + \hat{x}_b(M_{ab}x_b - M_{ab}\mu_b + M_{ab}M_{ba}x_a) \\ &= \hat{x}_a M_{ba}(x_a - \mu_a + M_{ab}x_b) + \hat{x}_b M_{ab}(x_b - \mu_b + M_{ba}x_a) \\ &= -\frac{\dot{x}_a}{x_a} \hat{x}_a M_{ba} - \frac{\dot{x}_b}{x_b} \hat{x}_b M_{ab}\end{aligned}\tag{S107}$$

Then, we find

$$\begin{aligned}\dot{V}(x_a, x_b) &= \nabla V \cdot (\dot{x}_a \hat{x}_a + \dot{x}_b \hat{x}_b) \\ &= -\frac{\dot{x}_a^2}{x_a} M_{ba} - \frac{\dot{x}_b^2}{x_b} M_{ab} \leq 0\end{aligned}\tag{S108}$$

in our parameter regime. Therefore, $V(x_a, x_b)$ is a split Lyapunov function for Eq. (S37).

To further pursue the physical correspondence between the split Lyapunov function and a potential energy function, we note that the Lyapunov function leads to force-like relations for the microbial trajectories $\frac{dx_a}{dt} = -(\nabla V)_a x_a / M_{ba}$ and $\frac{dx_b}{dt} = -(\nabla V)_b x_b / M_{ab}$, where $(\cdot)_i$ indicates index i .

EIGENVECTORS OF THE SEMISTABLE FIXED POINT

The eigenvectors of the semistable fixed point, which we denote \vec{u} (unstable eigenvector) and \vec{v} (stable eigenvector), are found by computing the eigenvectors of the Jacobian of Eq. (S37) evaluated at the semistable fixed point (x_a^*, x_b^*) given in Eq. (S88). Under the previously mentioned assumptions $M_{ab} > 1$ and $M_{ba} > 1$, we solve for these eigenvectors to find

$$\vec{u} = \left\{ \frac{1}{2M_{ba}} \left[\frac{x_a^*}{x_b^*} - 1 - \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab} M_{ba}} \right] \right\} \hat{x}_a + \hat{x}_b \tag{S109}$$

and

$$\vec{v} = \left\{ \frac{1}{2M_{ba}} \left[\frac{x_a^*}{x_b^*} - 1 + \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab} M_{ba}} \right] \right\} \hat{x}_a + \hat{x}_b. \tag{S110}$$

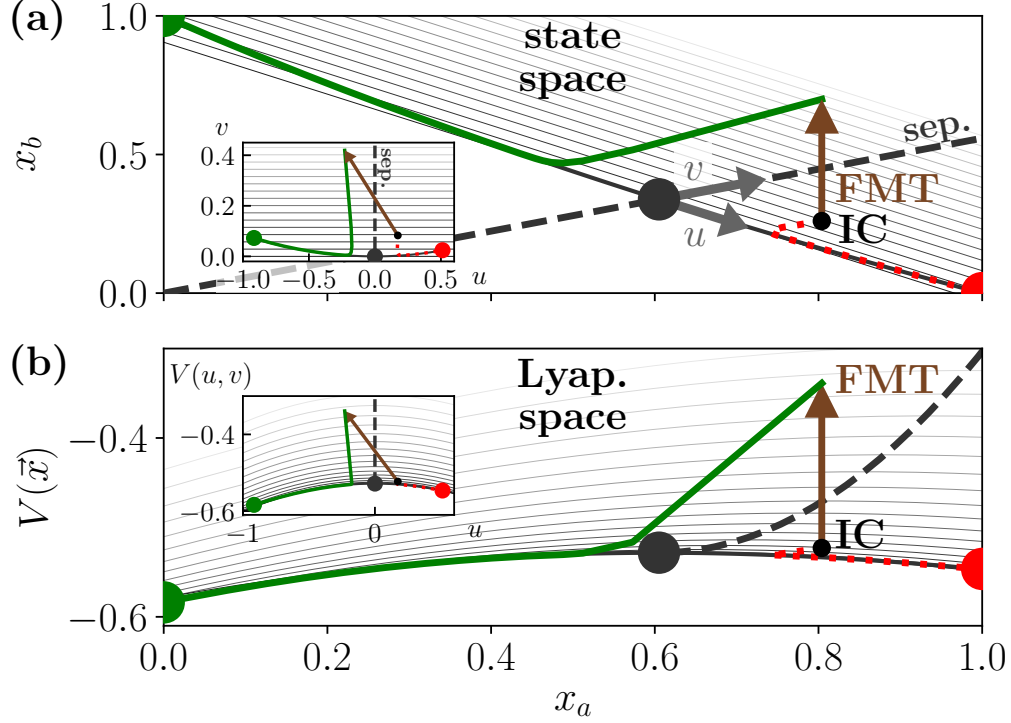


FIG. S3. The influence of FMT on microbial trajectories in (a) state space and (b) Lyapunov space. A disease-prone IC is converted into a health-prone state with FMT administration, shown in the original coordinates (x_a, x_b) (main frames) and in transformed coordinates (u, v) (insets), where u and v are the eigenvectors of the semistable fixed point (x_a^*, x_b^*) . (b) Conversion from a disease- to a health-prone state requires overcoming a “potential energy” barrier characterized by the split Lyapunov function V . To visualize this energy landscape we plot the Lyapunov functions along level cuts parallel to u (shown in (a)), then superimpose the Lyapunov functions along the trajectories in (a).

Under the simplification $\mu_b = 1$, these eigenvectors become

$$\vec{u} = \begin{bmatrix} -\frac{M_{ab}}{M_{ba}} \\ 1 \end{bmatrix} \quad \text{and} \quad \vec{v} = \begin{bmatrix} \frac{M_{ab}-1}{M_{ba}-1} \\ 1 \end{bmatrix}. \quad (\text{S111})$$

Note that all of these eigenvectors should be properly normalized, so that $\hat{u} = \frac{\vec{u}}{\|\vec{u}\|}$ and $\hat{v} = \frac{\vec{v}}{\|\vec{v}\|}$.

CHANGE OF COORDINATES TO THE EIGENVECTORS OF THE SEMISTABLE FIXED POINT

We can represent each point (x_a, x_b) as a point (u, v) in the (\hat{u}, \hat{v}) basis so that

$$\begin{aligned} x_a &= x_a^* + u \hat{u}_a + v \hat{v}_a \\ x_b &= x_b^* + u \hat{u}_b + v \hat{v}_b, \end{aligned} \tag{S112}$$

where $(\cdot)_i$ corresponds to the \hat{x}_i direction. Then we can solve for u and v in terms of x_a and x_b to find

$$\begin{aligned} u(x_a, x_b) &= \frac{\hat{v}_a(x_b^* - x_b) + \hat{v}_b(x_a - x_a^*)}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \\ v(x_a, x_b) &= \frac{\hat{u}_a(x_b - x_b^*) + \hat{u}_b(x_a^* - x_a)}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a}. \end{aligned} \tag{S113}$$

From here, we can solve for $\dot{u} = \dot{u}(x_a, x_b) = \dot{u}(x_a(u, v), x_b(u, v))$ and for $\dot{v} = \dot{v}(x_a(u, v), x_b(u, v))$.

In particular, we find

$$\begin{aligned} \dot{u}(u, v) &= \frac{\hat{v}_b \dot{x}_a(u, v) - \hat{v}_a \dot{x}_b(u, v)}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \quad \text{and} \\ \dot{v}(u, v) &= \frac{-\hat{u}_b \dot{x}_a(u, v) + \hat{u}_a \dot{x}_b(u, v)}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a}, \end{aligned} \tag{S114}$$

where

$$\begin{aligned} \dot{x}_a(u, v) &= (x_a^* + u \hat{u}_a + v \hat{v}_a)(1 - (x_a^* + u \hat{u}_a + v \hat{v}_a) - M_{ab}(x_b^* + u \hat{u}_b + v \hat{v}_b)) \\ &= -(x_a^* + u \hat{u}_a + v \hat{v}_a)(u(\hat{u}_a + M_{ab}\hat{u}_b) + v(\hat{v}_a + M_{ab}\hat{v}_b)) \\ \dot{x}_b(u, v) &= (x_b^* + u \hat{u}_b + v \hat{v}_b)(\mu_b - M_{ba}(x_a^* + u \hat{u}_a + v \hat{v}_a) - (x_b^* + u \hat{u}_b + v \hat{v}_b)) \\ &= -(x_b^* + u \hat{u}_b + v \hat{v}_b)(u(M_{ba}\hat{u}_a + \hat{u}_b) + v(M_{ba}\hat{v}_a + \hat{v}_b)), \end{aligned} \tag{S115}$$

where the simplification $(1 - x_a^* - M_{ab}x_b^*) = (\mu_b - M_{ba}x_a^* - x_b) = 0$ occurred because (x_a^*, x_b^*) is a steady state of Eq. (S37). Expanding these derivatives in powers of u and v we find

$$\begin{aligned}
\dot{x}_a(u, v) &= u[x_a^*(-\hat{u}_a - M_{ab}\hat{u}_b)] + v[x_a^*(-\hat{v}_a - M_{ab}\hat{v}_b)] \\
&\quad + uv[\hat{u}_a(-\hat{v}_a - M_{ab}\hat{v}_b) + \hat{v}_a(-\hat{u}_a - M_{ab}\hat{u}_b)] \\
&\quad + u^2(-\hat{u}_a^2 - M_{ab}\hat{u}_a\hat{u}_b) + v^2(-\hat{v}_a^2 - M_{ab}\hat{v}_a\hat{v}_b) \\
\dot{x}_b(u, v) &= u[x_b^*(-M_{ba}\hat{u}_a - \hat{u}_b)] + v[x_b^*(-M_{ba}\hat{v}_a - \hat{v}_b)] \\
&\quad + uv[\hat{u}_b(-M_{ba}\hat{v}_a - \hat{v}_b) + \hat{v}_b(-M_{ba}\hat{u}_a - \hat{u}_b)] \\
&\quad + u^2(-M_{ba}\hat{u}_a\hat{u}_b - \hat{u}_b^2) + v^2(-M_{ba}\hat{v}_a\hat{v}_b - \hat{v}_b^2).
\end{aligned} \tag{S116}$$

Therefore, we can write \dot{u} and \dot{v} in powers of u and v , so that

$$\begin{aligned}
\dot{u} &= A_{10}u + A_{01}v + A_{20}u^2 + A_{11}uv + A_{02}v^2 \\
\dot{v} &= B_{10}u + B_{01}v + B_{20}u^2 + B_{11}uv + B_{02}v^2.
\end{aligned} \tag{S117}$$

In the following text, we show that $A_{01} = B_{10} = 0$ and that the values of A_{10} and B_{01} correspond to the eigenvalues of the semistable fixed point. Then, we show that for $\mu_b = 1$, $A_{02} = B_{11} = 0$, but for $\mu_b \neq 1$, these coefficients are not 0. Finally, we provide analytic forms for the remaining coefficients A_{11} , A_{20} , B_{02} , and B_{20} .

First, we consider the A_{01} term which is given by

$$\begin{aligned}
A_{01} &= \frac{1}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} [\hat{v}_b(x_a^*(-\hat{v}_a - M_{ab}\hat{v}_b)) - \hat{v}_a(x_b^*(-M_{ba}\hat{v}_a - \hat{v}_b))] \\
&= \frac{1}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} [\hat{v}_a^2(M_{ba}x_b^*) + \hat{v}_a\hat{v}_b(x_b^* - x_a^*) + \hat{v}_b^2(-M_{ab}x_a^*)].
\end{aligned} \tag{S118}$$

We replace the unit eigenvectors by their unnormalized counterparts defined in Eq. (S109)

and (S110), setting $\hat{v}_i = \frac{\vec{v}_i}{\|\vec{v}\|}$ for $i \in a, b$. Since $\vec{v}_b = 1$, this yields

$$\begin{aligned}
A_{01} &= \frac{1/\|\vec{v}\|^2}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} [\vec{v}_a^2(M_{ba}x_b^*) + \vec{v}_a\vec{v}_b(x_b^* - x_a^*) + \vec{v}_b^2(-M_{ab}x_a^*)] \\
&= \frac{1/\|\vec{v}\|^2}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} M_{ba}x_b^* \left[\vec{v}_a^2 + \vec{v}_a \left(\frac{1 - x_a^*/x_b^*}{M_{ba}} \right) - \frac{M_{ab}x_a^*}{M_{ba}x_b^*} \right] \\
&= \frac{M_{ba}x_b^*/\|\vec{v}\|^2}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} \left[\left(\vec{v}_a + \frac{1 - x_a^*/x_b^*}{2M_{ba}} \right)^2 - \left(\frac{1 - x_a^*/x_b^*}{2M_{ba}} \right)^2 - \frac{M_{ab}x_a^*}{M_{ba}x_b^*} \right] \\
&= \frac{M_{ba}x_b^*/\|\vec{v}\|^2}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} \left[\frac{1}{4M_{ba}^2} \left(\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4\frac{x_a^*}{x_b^*}M_{ab}M_{ba} \right) - \left(\frac{1 - x_a^*/x_b^*}{2M_{ba}} \right)^2 - \frac{M_{ab}x_a^*}{M_{ba}x_b^*} \right] \\
&= 0.
\end{aligned} \tag{S119}$$

Thus $A_{01} = 0$. In the same way, $B_{10} = 0$ as well. Next, we consider the A_{10} term, given by

$$\begin{aligned}
A_{10} &= \frac{1}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} [\hat{v}_b(x_a^*(-\hat{u}_a - M_{ab}\hat{u}_b)) - \hat{v}_a(x_b^*(-M_{ba}\hat{u}_a - \hat{u}_b))] \\
&= \frac{1}{\hat{u}_a\hat{v}_b - \hat{u}_b\hat{v}_a} [\hat{u}_a\hat{v}_a(M_{ba}x_b^*) - \hat{u}_a\hat{v}_b(x_a^*) + \hat{u}_b\hat{v}_a(x_b^*) - \hat{u}_b\hat{v}_b(M_{ab}x_a^*)].
\end{aligned} \tag{S120}$$

As before, we replace \hat{u} and \hat{v} by their unnormalized counterparts in both the numerator and denominator (the norms of which cancel) to see

$$\begin{aligned}
A_{10} &= \frac{1}{\vec{u}_a\vec{v}_b - \vec{u}_b\vec{v}_a} [\vec{u}_a\vec{v}_a(M_{ba}x_b^*) - \vec{u}_a\vec{v}_b(x_a^*) + \vec{u}_b\vec{v}_a(x_b^*) - \vec{u}_b\vec{v}_b(M_{ab}x_a^*)] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} [\vec{u}_a\vec{v}_a(M_{ba}x_b^*) - \vec{u}_a(x_a^*) + \vec{v}_a(x_b^*) - (M_{ab}x_a^*)] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} \left[\frac{x_b^*}{4M_{ba}} \left(\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 - \left(\frac{x_a^*}{x_b^*} - 1 \right)^2 - 4\frac{x_a^*}{x_b^*}M_{ab}M_{ba} \right) \right. \\
&\quad \left. - \vec{u}_a(x_a^*) + \vec{v}_a(x_b^*) - (M_{ab}x_a^*) \right] \\
&= \frac{-\vec{u}_ax_a^* + \vec{v}_ax_b^* - 2M_{ab}x_a^*}{\vec{u}_a - \vec{v}_a}
\end{aligned} \tag{S121}$$

For the case $\mu_b = 1$, this coefficient simplifies to become

$$\begin{aligned}
A_{10} &= \frac{1}{-\frac{M_{ab}}{M_{ba}} - \frac{M_{ab}-1}{M_{ba}-1}} \frac{1}{1 - M_{ab}M_{ba}} \left(\frac{M_{ab}}{M_{ba}} (1 - M_{ab}) + \frac{M_{ab}-1}{M_{ba}-1} (1 - M_{ba}) - 2M_{ab}(1 - M_{ab}) \right) \\
&= \frac{1}{1 - M_{ab}M_{ba}} \left(\frac{1}{M_{ba}} \right) \left(\frac{M_{ba}(M_{ba}-1)}{M_{ab} - 2M_{ab}M_{ba} + M_{ba}} \right) \\
&\quad \times (M_{ab} - 2M_{ab}M_{ba} + M_{ba} - M_{ab}(M_{ab} - 2M_{ab}M_{ba} + M_{ba})) \\
&= \frac{(M_{ab}-1)(M_{ba}-1)}{M_{ab}M_{ba}-1}.
\end{aligned} \tag{S122}$$

This value is precisely the eigenvalue that corresponds to the unstable eigenvector \vec{u} of the semistable fixed point (x_a^*, x_b^*) . In a similar way, we may calculate B_{01} , which yields

$$\begin{aligned}
B_{01} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-\hat{u}_b(x_a^*(-\hat{v}_a - M_{ab}\hat{v}_b)) + \hat{u}_a(x_b^*(-M_{ba}\hat{v}_a - \hat{v}_b))] \\
&= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-\hat{u}_a \hat{v}_a(M_{ba}x_b^*) - \hat{u}_a \hat{v}_b(x_b^*) + \hat{u}_b \hat{v}_a(x_a^*) + \hat{u}_b \hat{v}_b(M_{ab}x_a^*)] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} [-\vec{u}_a \vec{v}_a(M_{ba}x_b^*) - \vec{u}_a(x_b^*) + \vec{v}_a(x_a^*) + (M_{ab}x_a^*)] \\
&= \frac{-\vec{u}_a x_b^* + \vec{v}_a x_a^* + 2M_{ab}x_a^*}{\vec{u}_a - \vec{v}_a}.
\end{aligned} \tag{S123}$$

For the case $\mu_b = 1$ this term becomes

$$\begin{aligned}
B_{01} &= \frac{1}{-\frac{M_{ab}}{M_{ba}} - \frac{M_{ab}-1}{M_{ba}-1}} \left(\frac{1}{1 - M_{ab}M_{ba}} \right) \left(\frac{M_{ab}}{M_{ba}} (1 - M_{ba}) + \frac{M_{ab}-1}{M_{ba}-1} (1 - M_{ab}) + 2M_{ab}(1 - M_{ab}) \right) \\
&= \frac{1}{1 - M_{ab}M_{ba}} \left(\frac{1}{M_{ba}(M_{ba}-1)} \right) \left(\frac{M_{ba}(M_{ba}-1)}{M_{ab} - 2M_{ab}M_{ba} + M_{ba}} \right) \\
&\quad \times -M_{ab}(1 - M_{ba})^2 - M_{ba}(1 - M_{ab})^2 - 2M_{ab}M_{ba}(1 - M_{ab})(1 - M_{ba}) \\
&= \frac{-M_{ab} + 2M_{ab}M_{ba} - M_{ba} + M_{ab}^2 M_{ba} + M_{ab}M_{ba}^2 - 2M_{ab}^2 M_{ba}^2}{M_{ab} - 2M_{ab}M_{ba} + M_{ba} - M_{ab}^2 M_{ba} - M_{ab}M_{ba}^2 + 2M_{ab}^2 M_{ba}^2} \\
&= -1,
\end{aligned} \tag{S124}$$

which is the eigenvalue that corresponds to the stable eigenvector \vec{v} .

Next we solve for A_{02} , and find that

$$\begin{aligned}
A_{02} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{v}_b(-\hat{v}_a^2 - M_{ab} \hat{v}_a \hat{v}_b) - \hat{v}_a(-M_{ba} \hat{v}_a \hat{v}_b - \hat{v}_b^2)] \\
&= \frac{\hat{v}_a \hat{v}_b}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{v}_b(1 - M_{ab}) + \hat{v}_a(M_{ba} - 1)] \\
&= \frac{\hat{v}_a \hat{v}_b}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} (1 - M_{ab} M_{ba})(\hat{v}_b x_a^* - \hat{v}_a x_b^*),
\end{aligned} \tag{S125}$$

which is nonzero in general. However, for the specific case $\mu_b = 1$ we can simplify this expression to find

$$\begin{aligned}
A_{02} &= \frac{\hat{v}_a \hat{v}_b / \|\vec{v}_b\|}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\vec{v}_b(1 - M_{ab}) + \vec{v}_a(M_{ba} - 1)] \\
&= \frac{\hat{v}_a \hat{v}_b / \|\vec{v}_b\|}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \left[1 - M_{ab} + \frac{M_{ab} - 1}{M_{ba} - 1} (M_{ba} - 1) \right] \\
&= 0.
\end{aligned} \tag{S126}$$

Next we consider the B_{11} term, which is given by

$$\begin{aligned}
B_{11} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \{ -\hat{u}_b [\hat{u}_a(-\hat{v}_a - M_{ab} \hat{v}_b) + \hat{v}_a(-\hat{u}_a - M_{ab} \hat{u}_b)] \\
&\quad + \hat{u}_a [\hat{u}_b(-M_{ba} \hat{v}_a - \hat{v}_b) + \hat{v}_b(-M_{ba} \hat{u}_a - \hat{u}_b)] \} \\
&= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_a \hat{u}_b (\hat{v}_a(2 - M_{ba}) + \hat{v}_b(M_{ab} - 2)) + M_{ab} \hat{u}_b^2 \hat{v}_a - M_{ba} \hat{u}_a^2 \hat{v}_b] \\
&= \frac{1/\|\vec{u}\|}{\vec{u}_a - \vec{v}_a} [\vec{u}_a \vec{v}_a (2 - M_{ba}) + \hat{u}_a (M_{ab} - 2) + \vec{v}_a M_{ab} - \vec{u}_a^2 M_{ba}].
\end{aligned} \tag{S127}$$

As was the case for A_{02} , this is nonzero in general. However, for the specific case where $\mu_b = 1$ this simplifies to become

$$\begin{aligned}
B_{11} &= \frac{1/\|\vec{u}\|}{\vec{u}_a - \vec{v}_a} \left[-\frac{M_{ab}(M_{ab} - 1)}{M_{ba}(M_{ba} - 1)} (2 - M_{ba}) - \frac{M_{ab}}{M_{ba}} (M_{ab} - 2) + \frac{M_{ab} - 1}{M_{ba} - 1} M_{ab} - \frac{M_{ab}^2}{M_{ba}^2} M_{ba} \right] \\
&= \frac{1/\|\vec{u}\|}{\vec{u}_a - \vec{v}_a} \left(\frac{M_{ab}}{M_{ba}(M_{ba} - 1)} \right) [-(M_{ab} - 1)(2 - M_{ba}) - (M_{ba} - 1)(M_{ab} - 2) \\
&\quad + (M_{ab} - 1)M_{ba} - M_{ab}(M_{ba} - 1)] \\
&= 0.
\end{aligned} \tag{S128}$$

In a similar way, we find that

$$\begin{aligned}
A_{11} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} \{ \hat{v}_b [\hat{u}_a (-\hat{v}_a - M_{ab} \hat{v}_b) + \hat{v}_a (-\hat{u}_a - M_{ab} \hat{u}_b)] \\
&\quad - \hat{v}_a [\hat{u}_b (-M_{ba} \hat{v}_a - \hat{v}_b) + \hat{v}_b (-M_{ba} \hat{u}_a - \hat{u}_b)] \} \\
&= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_b \hat{v}_a^2 (M_{ba}) - \hat{u}_a \hat{v}_b^2 (M_{ab}) + \hat{u}_b \hat{v}_a \hat{v}_b (2 - M_{ab}) - \hat{u}_a \hat{v}_a \hat{v}_b (2 - M_{ba})],
\end{aligned} \tag{S129}$$

that

$$A_{20} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{v}_b (-\hat{u}_a^2 - M_{ab} \hat{u}_a \hat{u}_b) - \hat{v}_a (-M_{ba} \hat{u}_a \hat{u}_b - \hat{u}_b^2)], \tag{S130}$$

that

$$B_{02} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-\hat{u}_b (-\hat{v}_a^2 - M_{ab} \hat{v}_a \hat{v}_b) + \hat{u}_a (-M_{ba} \hat{v}_a \hat{v}_b - \hat{v}_b^2)], \tag{S131}$$

and that

$$\begin{aligned}
B_{20} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-\hat{u}_b (-\hat{u}_a^2 - M_{ab} \hat{u}_a \hat{u}_b) + \hat{u}_a (-M_{ba} \hat{u}_a \hat{u}_b - \hat{u}_b^2)], \\
&= \frac{\hat{u}_a \hat{u}_b}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_a (1 - M_{ba}) + \hat{u}_b (M_{ab} - 1)], \\
&= \frac{\hat{u}_a \hat{u}_b}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} (1 - M_{ab} M_{ba}) (\hat{u}_a x_b^* - \hat{u}_b x_a^*).
\end{aligned} \tag{S132}$$

Therefore, we have analytic forms for every coefficient of the (u, v) transformed gLV equations in Eq. (S117).

SIGNS OF THE GLV COEFFICIENTS IN (u, v) COORDINATES

For the special case $\mu_b = 1$, we will evaluate the sign of each coefficient of Eq. (S117). In the next section we show $A_{10} > 0$ and $B_{01} < 0$. Next, here we show that $A_{11} < 0$. Consider

\hat{u} and \hat{v} as in Eq. (S111). Then

$$\begin{aligned}
A_{11} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_b \hat{v}_a^2 (M_{ba}) - \hat{u}_a \hat{v}_b^2 (M_{ab}) + \hat{u}_b \hat{v}_a \hat{v}_b (2 - M_{ab}) - \hat{u}_a \hat{v}_a \hat{v}_b (2 - M_{ba})] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} [\vec{v}_a^2 (M_{ba}) - \vec{u}_a (M_{ab}) + \vec{v}_a (2 - M_{ab}) - \vec{u}_a \vec{v}_a (2 - M_{ba})] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} [\vec{v}_a (M_{ba} \vec{v}_a + 2 - M_{ab}) - \vec{u}_a (-M_{ba} \vec{v}_a + 2 \vec{v}_a + M_{ab})] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} \left[\frac{\vec{v}_a}{M_{ba} - 1} (M_{ba} (M_{ab} - 1) + 2(M_{ba} - 1) - M_{ab} (M_{ba} - 1)) \right. \\
&\quad \left. - \frac{\vec{u}_a}{M_{ba} - 1} (-M_{ba} (M_{ab} - 1) + 2(M_{ab} - 1) + M_{ab} (M_{ba} - 1)) \right] \\
&= \frac{1}{\vec{u}_a - \vec{v}_a} \left[\frac{\vec{v}_a}{M_{ba} - 1} (M_{ba} + M_{ab} - 2) - \frac{\vec{u}_a}{M_{ba} - 1} (M_{ba} + M_{ab} - 2) \right],
\end{aligned} \tag{S133}$$

and since $\vec{u}_a < 0$, $\frac{1}{\vec{u}_a - \vec{v}_a} < 0$, $M_{ab} > 1$, and $M_{ba} > 1$, we must have $A_{11} < 0$. Next, we show $A_{20} < 0$. We find

$$\begin{aligned}
A_{20} &= \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{v}_b (-\hat{u}_a^2 - M_{ab} \hat{u}_a \hat{u}_b) - \hat{v}_a (-M_{ba} \hat{u}_a \hat{u}_b - \hat{u}_b^2)] \\
&= \frac{1}{\hat{u}_a - \hat{v}_a} [-\hat{u}_a (\hat{u}_a + M_{ab} - M_{ba} \hat{v}_a) + \hat{v}_a] \\
&= \frac{1}{\hat{u}_a - \hat{v}_a} \left[-\frac{\hat{u}_a}{M_{ba} (M_{ba} - 1)} (-M_{ab} (M_{ba} - 1) + M_{ab} M_{ba} (M_{ba} - 1) - M_{ba}^2 (M_{ab} - 1)) + \hat{v}_a \right] \\
&= \frac{1}{\hat{u}_a - \hat{v}_a} \left[-\frac{\hat{u}_a}{M_{ba} (M_{ba} - 1)} (M_{ab} + M_{ba}^2) + \hat{v}_a \right] < 0,
\end{aligned} \tag{S134}$$

since $u_a < 0$, $v_a > 0$, $M_{ab} > 1$, and $M_{ba} > 1$. Next, we show $B_{02} < 0$. We find

$$B_{02} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-\hat{u}_b (-\hat{v}_a^2 - M_{ab} \hat{v}_a \hat{v}_b) + \hat{u}_a (-M_{ba} \hat{v}_a \hat{v}_b - \hat{v}_b^2)] > 0 \tag{S135}$$

based on the orientation of \hat{u} and \hat{v} . Finally, we show $B_{20} > 0$. We find

$$B_{20} = \frac{\hat{u}_a \hat{u}_b}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_a (1 - M_{ba}) + \hat{u}_b (M_{ab} - 1)] > 0 \tag{S136}$$

based on the orientation of \hat{u} and \hat{v} . Therefore, for the special case $\mu_b = 1$, we have $A_{10} > 0$, $A_{11} < 0$, $A_{20} < 0$, $B_{01} < 0$, $B_{02} < 0$, and $B_{20} > 0$.

COMPARISON OF SPEEDS OF UNSTABLE AND STABLE MANIFOLDS

Here we will show that the speed of the stable manifold is faster than the unstable manifold, or equivalently, that $|A_{10}| < |B_{01}|$. Recall that

$$B_{01} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-\hat{u}_a \hat{v}_a (M_{ba} x_b^*) - \hat{u}_a \hat{v}_b (x_b^*) + \hat{u}_b \hat{v}_a (x_a^*) + \hat{u}_b \hat{v}_b (M_{ab} x_a^*)] \quad (\text{S137})$$

and that

$$A_{10} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [\hat{u}_a \hat{v}_a (M_{ba} x_b^*) - \hat{u}_a \hat{v}_b (x_a^*) + \hat{u}_b \hat{v}_a (x_b^*) - \hat{u}_b \hat{v}_b (M_{ab} x_a^*)]. \quad (\text{S138})$$

We choose an orientation for \hat{u} and \hat{v} as in Eqs. (S109) and (S110) so that $\hat{u} = (-, +)$ and $\hat{v} = (+, +)$. Then, $B_{01} < 0$, and so $|B_{01}| = -B_{01}$. To show that $A_{10} > 0$, we consider the term

$$\begin{aligned} A_{10} &= \frac{-\vec{u}_a x_a^* + \vec{v}_a x_b^* - 2M_{ab} x_a^*}{\vec{u}_a - \vec{v}_a} \\ &= \frac{x_a^*}{\vec{u}_a - \vec{v}_a} \left(-\vec{u}_a + \vec{v}_a \frac{x_b^*}{x_a^*} - 2M_{ab} \right) \\ &= \frac{x_a^*}{\vec{u}_a - \vec{v}_a} \left(\frac{1}{2M_{ba}} \right) \left(2 - \frac{x_a^*}{x_b^*} - \frac{x_b^*}{x_a^*} - 4M_{ab} M_{ba} + \left(1 + \frac{x_b^*}{x_a^*} \right) \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab} M_{ba}} \right). \end{aligned} \quad (\text{S139})$$

Note that $\frac{x_a^*}{2M_{ba}(\vec{u}_a - \vec{v}_a)} < 0$, so to show $A_{10} > 0$ we must show the right term must be negative.

In order to do this we multiply it by its conjugate, which is positive since

$$\begin{aligned} &-2 + \frac{x_a^*}{x_b^*} + \frac{x_b^*}{x_a^*} + 4M_{ab} M_{ba} + \left(1 + \frac{x_b^*}{x_a^*} \right) \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab} M_{ba}} \\ &> 2 + \frac{x_a^*}{x_b^*} + \frac{x_b^*}{x_a^*} + \left(1 + \frac{x_b^*}{x_a^*} \right) \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4 \frac{x_a^*}{x_b^*} M_{ab} M_{ba}} \\ &= 2 \left(1 + \frac{x_b^*}{x_a^*} \right) \left(1 + \frac{x_a^*}{x_b^*} \right) > 0. \end{aligned} \quad (\text{S140})$$

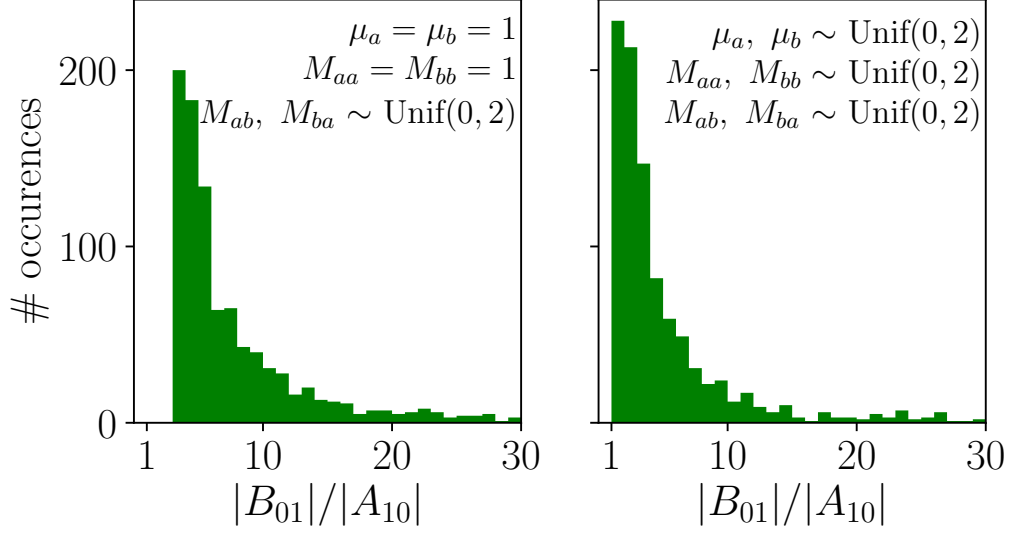


FIG. S4. Comparison of speeds of the fast and slow manifolds over random parameter draws. Parameters were drawn 1000 times from the distributions (a) $\mu_a = \mu_b = M_{aa} = M_{bb} = 1$, $M_{ab} \sim \text{Unif}([0, 2])$, and $M_{ba} \sim \text{Unif}([0, 2])$; and (b) $\mu_i \sim \text{Unif}([0, 2])$ for $i \in a, b$ and $M_{ij} \sim \text{Unif}([0, 2])$ for $i, j \in a, b$.

Then, the sign of A_{10} is determined by the sign of

$$\begin{aligned}
& \left[\left(\frac{x_a^*}{x_b^*} - 1 \right) \left(\frac{x_b^*}{x_a^*} - 1 \right) - 4M_{ab}M_{ba} + \left(1 + \frac{x_b^*}{x_a^*} \right) \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4\frac{x_a^*}{x_b^*}M_{ab}M_{ba}} \right] \\
& \times \left[- \left(\frac{x_a^*}{x_b^*} - 1 \right) \left(\frac{x_b^*}{x_a^*} - 1 \right) + 4M_{ab}M_{ba} + \left(1 + \frac{x_b^*}{x_a^*} \right) \sqrt{\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4\frac{x_a^*}{x_b^*}M_{ab}M_{ba}} \right] \\
& = \left(1 + \frac{x_b^*}{x_a^*} \right)^2 \left[\left(\frac{x_a^*}{x_b^*} - 1 \right)^2 + 4\frac{x_a^*}{x_b^*}M_{ab}M_{ba} \right] - \left(\frac{x_a^*}{x_b^*} - 1 \right)^2 \left(\frac{x_b^*}{x_a^*} - 1 \right)^2 \\
& \quad + 8M_{ab}M_{ba} \left(\frac{x_a^*}{x_b^*} - 1 \right) \left(\frac{x_b^*}{x_a^*} - 1 \right) - 16M_{ab}^2M_{ba}^2 \\
& = \left(\frac{x_a^*}{x_b^*} - \frac{x_b^*}{x_a^*} \right)^2 + \left(1 + \frac{x_b^*}{x_a^*} \right)^2 4\frac{x_a^*}{x_b^*}M_{ab}M_{ba} - \left(2 - \frac{x_a^*}{x_b^*} - \frac{x_b^*}{x_a^*} \right)^2 \\
& \quad + 8M_{ab}M_{ba} \left(2 - \frac{x_a^*}{x_b^*} - \frac{x_b^*}{x_a^*} \right) - 16M_{ab}^2M_{ba}^2 \\
& = 4\frac{x_a^*}{x_b^*}(1 - M_{ab}M_{ba}) + 4\frac{x_b^*}{x_a^*}(1 - M_{ab}M_{ba}) - 8(2M_{ab}M_{ba} - 1)(M_{ab}M_{ba} - 1) \\
& < 0,
\end{aligned}$$

(S141)

where the final inequality is because $1 - M_{ab}M_{ba} < 0$. Therefore, $A_{10} > 0$, and so $|A_{10}| = A_{10}$. Then, using the expressions of B_{01} and A_{10} in Eqs. (S137) and (S138), we can compare the speeds of the manifolds by considering the sign of $|A_{10}| - |B_{01}| = A_{10} + B_{01}$, which is

$$A_{10} + B_{01} = \frac{1}{\hat{u}_a \hat{v}_b - \hat{u}_b \hat{v}_a} [-2\hat{u}_a \hat{v}_b(x_a^*) + 2\hat{u}_b \hat{v}_a(x_b^*)] < 0. \quad (\text{S142})$$

Therefore, $|A_{10}| < |B_{01}|$, and due to this we call the stable manifold “fast” and the unstable manifold “slow.”

Next, we evaluate the ratio of $|B_{01}|/|A_{10}|$ over many sets of randomly chosen parameter values. If we set $\mu_a = \mu_b = M_{aa} = M_{bb} = 1$ and pick $M_{ab} \sim \text{Unif}([0, 2])$ and $M_{ba} \sim \text{Unif}([0, 2])$, we find that $|B_{01}|/|A_{10}|$ has a median of 5.88 with an IQR of [2.70, 9.05]. If we choose $\mu_i \sim \text{Unif}([0, 2])$ for $i \in a, b$ and $M_{ij} \sim \text{Unif}([0, 2])$ for $i, j \in a, b$, we find that $|B_{01}|/|A_{10}|$ has a median of 3.34 with an IQR of [1.20, 5.49]. We plot a histogram of the ratio $|B_{01}|/|A_{10}|$ for parameters drawn from these two parameter distributions in Fig S4.

INITIAL CONDITION OF FIG. 2 SATISFIES SIMPLIFYING ASSUMPTIONS

In the main text, we interpret the rates of increase of the necessary transplant size α and β of the main trajectory of Fig. 2 according to Eq. (3) of the main text, and in doing so claim that the trajectory satisfies certain assumptions. Here, we justify those assumptions.

In (x_a, x_b) coordinates, the post-antibiotic initial condition of the main (colored) trajectory in Fig. 2 is (0.127, 0.034), and in (u, v) coordinates is (0.033, -0.576). For this set of parameters ($\mu_b = 1$, $M_{ab} = 1.167$, and $M_{ba} = 1.093$), we find that the coefficients of the (u, v) -transformed coordinates are $A_{10} = 0.057$, $A_{20} = -0.046$, $A_{11} = -1.360$, $B_{01} = -1.000$, $B_{20} = -1.442$, and $B_{20} = 0.096$.

Therefore, we have $|B_{01}|/|A_{10}| = 17.637$, which indicates a separation of time scales between u and v . We find $B_{20}u_0^2 = 0.0002$ which is small compared to other terms (for example, $B_{01}v_0 = .575$). Under these assumptions, and replacing $B_{20} = -B_{20}$ and $B_{01} = -B_{01}$ so that coefficients are positive, the equation that governs $\frac{dv}{dt}$ simplifies to

$$\frac{dv}{dt} = -B_{01}v - B_{02}v^2, \quad (\text{S143})$$

which is autonomous and has a solution

$$v(t) = \frac{B_{10}v_0}{(B_{10} + B_{20}v_0) e^{B_{10}t} - B_{20}v_0}. \quad (\text{S144})$$

We substitute this solution of $v(t)$ in order to solve for the minimum transplant size s dynamics, given by

$$\frac{ds}{dt} = s \left(A_{10} - A_{20}(\hat{u} \cdot \hat{x}_b)s - A_{11} \frac{B_{10}v_0}{(B_{10} + B_{20}v_0) e^{B_{10}t} - B_{20}v_0} \right). \quad (\text{S145})$$

Since time scales are sufficiently separated, $u(t) \approx u_0$ while microbial trajectories follow the fast manifold. Then, we can solve for the optimal transplant time t_{opt}^* by setting $\frac{ds}{dt} = 0$, from which we find

$$t_{opt}^* = \frac{1}{B_{10}} \ln \left(\frac{1}{B_{10} + B_{20}v_0} \left(\frac{A_{11}B_{10}v_0}{A_{10} - A_{20}u_0} + B_{20}v_0 \right) \right). \quad (\text{S146})$$

Under the assumption $B_{02}v_0^2 \ll B_{01}v_0$, equations Eqs. (S145) and (S146) reduce to the forms given in the main text, Eqs. (3) and (4). The form of t_{opt}^* given in Eq. (S146) is the form used to color the background of Fig. 3 in the main text.

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