Online Supporting Appendices

for *A slow-fast dynamic decomposition links neutral and non-neutral coexistence in interacting multi-strain pathogens*, by Erida Gjini and Sten Madec

Equations in the main text are referred to by their numbers in the main text, whereas equations in the Appendix are preceded by their appendix section indicators (A.1, B.1, etc).

A The g_k functions in system (9)

In the system (9), using the fact that $\alpha_{VV} + \alpha_{NN} = 0$, the functions g_k are given explicitly by :

$$\begin{aligned} g_0(I, I_1, J, J_1) = &- I_1 I(\alpha_{NV} + \alpha_{VN}) \\ &- I_1 J(\alpha_{VV} - \alpha_{NN} + \alpha_{NV} - \alpha_{VN}) \\ &- J_1 I(\alpha_{VV} - \alpha_{NN} - \alpha_{NV} + \alpha_{VN}) \\ &+ J_1 J(\alpha_{NV} + \alpha_{VN}) \end{aligned}$$

$$\begin{aligned} g_1(I, I_1, J, J_1) = &+ I_1 I(\alpha_{NV} - \alpha_{VN}) \\ &+ I_1 J(\alpha_{NV} + \alpha_{VN}) \\ &- J_1 I(\alpha_{NV} + \alpha_{VN}) \\ &- J_1 J(\alpha_{NV} - \alpha_{VN}) \end{aligned}$$

$$\begin{aligned} g_2(I, I_1, J, J_1) = &+ I_1 I(\alpha_{NN} - \alpha_{VV} + \alpha_{NV} - \alpha_{VN}) \\ &+ I_1 J(\alpha_{VN} + \alpha_{NV}) \\ &- J_1 I(\alpha_{VN} + \alpha_{NV}) \\ &- J_1 J(\alpha_{VV} - \alpha_{NN} + \alpha_{NV} - \alpha_{VN}) \end{aligned}$$

$$\begin{aligned} g_3(I, I_1, J, J_1) = &- I_1 I(\alpha_{NV} + \alpha_{VN}) \\ &+ I_1 J(\alpha_{NV} - \alpha_{VN}) \\ &- J_1 I(\alpha_{NV} - \alpha_{VN}) \\ &- J_1 J(\alpha_{VN} + \alpha_{NV}) \end{aligned}$$

B Fast dynamics: the Neutral system

Taking $\varepsilon = 0$ in the system (11), we obtain the system describing the *fast* dynamics

$$\begin{cases} \frac{d}{dt}x &= -(m + \beta k I^*)x + \frac{\beta}{4} f_0(y, z) \\ \frac{d}{dt}y &= -\mu y \\ \frac{d}{dt}z &= 0 \end{cases} \tag{B.1}$$

It is clear that any solution x, y, z tends to $\Phi(z) = (x^*(z), 0, z)$ where $z = z(0)$ and $x^*(z) = \frac{\beta f_0(0,z)}{4(m+\beta k I^*)}$. Remark that, returning to the original variables, the system (B.1) describes the dynamics of the system (10) for $\varepsilon = 0$. This system matches exactly the neutral dynamics: that is the system (3) with $k_{VV} = k_{NN} = k_{NV} = k_{VN} = k$ (Eq. (6)). More precisely, if $\varepsilon = 0$ in (10), it is clear that when $R_0 > 1$,

$$(S(t), I(t), I_1(t)) \underset{t \to +\infty}{\longrightarrow} (S^*, I^*, I_1^*)$$

Moreover, from $y \to 0$ in (B.1) we deduce $J \to I_1^* z$ which implies

$$I_V(t) = \frac{1}{2}(I_1(t) + J_1(t)) \underset{t \to +\infty}{\longrightarrow} \frac{1}{2} I_1^*(1 + z)$$

and

$$I_N(t) = \frac{1}{2}(I_1(t) - J_1(t)) \underset{t\to+\infty}{\longrightarrow} \frac{1}{2} I_1^*(1-z).$$

Besides, we have $J(t) \to I^* z$, so from the last equation of (10), we get

$$I_{VN}(t) \to \frac{k\beta I_1^* I^*}{2m}(1-z^2).$$

Finally, since $I_{VV} = I_2(t) + J(t) - J_1(t) - I_{VN}(t)$, we obtain

$$I_{VV}(t) \underset{t\to+\infty}{\longrightarrow} \frac{I_2^*}{2}(1+z) - \frac{k\beta I_1^* I^*}{2m}(1-z^2)$$

and similarly

$$I_{NN}(t) \underset{t\to+\infty}{\longrightarrow} \frac{I_2^*}{2}(1-z) - \frac{k\beta I_1^* I^*}{2m}(1-z^2).$$

C Slow dynamics: the Non-neutral system

If $0 < \varepsilon \ll 1$, the parameter z is not free, but varies deterministically very slowly. Thus, what remains to compute are the slow dynamics of z. To do so, we define the slow time-scale $\tau = \varepsilon t$. Plugging this in (11), we obtain

$$\begin{cases} \varepsilon \frac{d}{d\tau} x & = -(m + \beta k I^*)x + \frac{\beta}{4} f_0(y,z) + O(\varepsilon) \\ \varepsilon \frac{d}{d\tau} y & = -\mu y + O(\varepsilon) \\ \frac{d}{d\tau} z & = f_2(x,y,z) + O(\varepsilon) \end{cases} \tag{C.1}$$

Taking $\varepsilon = 0$ in (C.1) yields

$$\begin{cases} 0 & = -(m + \beta k I_1^*)x + \frac{\beta}{4} f_0(y,z) \\ 0 & = -\mu y \\ \frac{d}{d\tau} z & = f_2(x,y,z) \end{cases} \tag{C.2}$$

The manifold $\Phi(z) = (x^*(z), 0, z)$ is invariant for (C.2). The dynamics of z along this manifold are given by the slow equation

$$\frac{d}{d\tau} z = f_2(x^*(z), 0, z)$$

Replacing f_2 and x^* by their expressions, we obtain:

$$\frac{d}{d\tau} z = C(\Theta - \Gamma z)(1 - z^2), \tag{C.3}$$

where the constant C and the hyper-parameters Θ and Γ are given by:

$$C = \frac{\beta I^* I_1^* I_2^*}{8(I^*)^2 - 4 I_1^* I_2^*},$$

$$\Gamma = \alpha_{VN} + \alpha_{NV}$$

and

$$\Theta = \alpha_{VV} - \alpha_{NN} + \left(1 + 2\frac{I_1^*}{I_2^*}\right)(\alpha_{NV} - \alpha_{VN}).$$

D Details of the mathematical derivations

D.1 Details of the computation of the slow-fast form (11)

The explicit slow-fast form is given by making the following linear change of variables in the system (9):

$$\begin{pmatrix} J(t) \\ J_1(t) \end{pmatrix} = P \begin{pmatrix} y(t) \\ z(t) \end{pmatrix} \text{ where } P = \begin{pmatrix} I_2^* & I^* \\ 2I^* & I_1^* \end{pmatrix}.$$

Thus, we obtain

$$\begin{aligned}\frac{d}{dt}\begin{pmatrix}y\\z\end{pmatrix} &= P^{-1}\frac{d}{dt}\begin{pmatrix}J\\J_1\end{pmatrix}\\ &= P^{-1}AP\begin{pmatrix}y\\z\end{pmatrix} + \frac{\varepsilon}{2}k\beta x P^{-1}\begin{pmatrix}1 & 0\\0 & 0\end{pmatrix}P\begin{pmatrix}y\\z\end{pmatrix}\\ &\quad + \frac{\varepsilon}{4}\beta P^{-1}\begin{pmatrix}g_1^*(I_2^*y + I^*z, I^*y + I_1^*z)\\ g_2^*(I_2^*y + I^*z, I^*y + I_1^*z)\end{pmatrix} + O(\varepsilon^2).\end{aligned}$$

From the very definition of P, we get the following:

$$P^{-1}AP = \begin{pmatrix}-\mu & 0\\0 & 0\end{pmatrix}.$$

Straightforward calculations give:

$$P^{-1}\begin{pmatrix}1 & 0\\0 & 0\end{pmatrix}P = \frac{1}{\det(P)}\begin{pmatrix}I_1^*I_2^* & I^*I_1^*\\ -2I^*I_2^* & -2(I^*)^2\end{pmatrix}$$

$$P^{-1}\begin{pmatrix}g_1^*(I_2^*y + I^*z, I^*y + I_1^*z)\\ g_2^*(I_2^*y + I^*z, I^*y + I_1^*z)\end{pmatrix} = \frac{1}{\det(P)}\begin{pmatrix}\upsilon(y,z)\\ \gamma(y,z)\end{pmatrix},$$

where υ and γ are two polynomials of y and z of degree 2, and may easily be computed using the definitions of the functions g_i^* and of the matrix P. Thus, denoting

$$f_2(x,y,z) = -\frac{k\beta x}{\det(P)}\left[I^*I_2^*y + (I^*)^2 z\right] + \frac{\beta}{4}\gamma(y,z), \tag{D.1}$$

we obtain the system (11).

D.2 Explicit derivation of the slow dynamics equation

Denote $\Delta_1 = \alpha_{VV} - \alpha_{NN}$, $\Delta_2 = \alpha_{NV} - \alpha_{VN}$ and $\Gamma = \alpha_{VN} + \alpha_{NV}$. From $y = 0$, we deduce $J = I^*z$ and $J_1 = I_1^*z$ which provides

$$\gamma(0,z) = \frac{I^*I_1^*I_2^*}{\det(P)}\left((\Delta_2 - \Delta_1) - z^2(\Delta_2 + \Delta_1) - 2\frac{I^*}{I_2^*}\Delta_2(1 - z^2)\right).$$

and

$$x^*(z) = \frac{I_1^*I_2^*}{4kI^*}\left(\gamma(1 - z^2) + 2\Delta_1 z\right).$$

Plugging these two expressions into (D.1) and remarking that $\det(P) < 0$, yields the final expression

$$\begin{aligned}f_2(x^*(z),0,z) &= \frac{\beta I^*I_1^*I_2^*}{4\det(P)}\left(\Gamma z + (\Delta_2 - \Delta_1) - 2\frac{I^*}{I_2^*}\Delta_2\right)(1 - z^2)\\ &= \frac{\beta I^*I_1^*I_2^*}{4|\det(P)|}\left(\Delta_1 + \Delta_2(1 + \frac{I_1^*}{I_2^*}) - \Gamma z\right)(1 - z^2).\end{aligned}$$

Note that $\Delta_1 = \Delta_{self}$ favouring V type dominance in the system, and $\Delta_2 = \Delta_{non-self}$ favouring again type V through strain interactions and altered susceptibilities in mixed co-colonization.