Supplementary material for M. Sofonea, S. Alizon, Y. Michalakis, 2015, From within-host interactions to epidemiological competition: a general model for multiple infections, Phil. Trans. R. Soc. B.

Supplementary Text: notations, analytical proofs and computational tools

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## A Notations

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<table>
<thead>
<tr>
<th>notation</th>
<th>∈, /</th>
<th>type</th>
<th>meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\mathbb{N}, \mathbb{Z})</td>
<td>set</td>
<td>of natural numbers, integers</td>
<td></td>
</tr>
<tr>
<td>(\mathbb{Q}, \mathbb{R}, \mathbb{C})</td>
<td>division ring</td>
<td>of rationals, real, complex numbers</td>
<td></td>
</tr>
<tr>
<td>(\in, \notin)</td>
<td>belongs to, does not belong to</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\exists, \notin)</td>
<td>contains, does not contain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\mathcal{M})</td>
<td>set</td>
<td>of matrices (including vectors)</td>
<td></td>
</tr>
<tr>
<td>(\mathcal{A})</td>
<td>set</td>
<td>of applications</td>
<td></td>
</tr>
<tr>
<td>(\mathcal{P})</td>
<td>set</td>
<td>power set</td>
<td></td>
</tr>
<tr>
<td>(.^*)</td>
<td>set</td>
<td>without 0 or the empty set</td>
<td></td>
</tr>
<tr>
<td>([m; p])</td>
<td>set</td>
<td>([m; p] \cap \mathbb{N})</td>
<td></td>
</tr>
<tr>
<td>(\mid)</td>
<td>cardinality</td>
<td>number of elements of a set</td>
<td></td>
</tr>
<tr>
<td>(\setminus)</td>
<td>operator</td>
<td>set-theoretic difference</td>
<td></td>
</tr>
<tr>
<td>(\mathbb{N}_0)</td>
<td>cardinality</td>
<td>of the natural numbers ((\mathbb{N}_0 :=</td>
<td>\mathbb{N}</td>
</tr>
<tr>
<td>(\max_{\mathcal{I}}, \min_{\mathcal{I}})</td>
<td>element</td>
<td>the biggest, the smallest, of a set indexed by (\mathcal{I})</td>
<td></td>
</tr>
</tbody>
</table>

### mathematical objects

<table>
<thead>
<tr>
<th>sets and associated notations</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\mathbb{N}, \mathbb{Z})</td>
</tr>
<tr>
<td>(\mathbb{Q}, \mathbb{R}, \mathbb{C})</td>
</tr>
<tr>
<td>(\in, \notin)</td>
</tr>
<tr>
<td>(\exists, \notin)</td>
</tr>
<tr>
<td>(\mathcal{M})</td>
</tr>
<tr>
<td>(\mathcal{A})</td>
</tr>
<tr>
<td>(\mathcal{P})</td>
</tr>
<tr>
<td>(.^*)</td>
</tr>
<tr>
<td>([m; p])</td>
</tr>
<tr>
<td>(\mid)</td>
</tr>
<tr>
<td>(\setminus)</td>
</tr>
<tr>
<td>(\mathbb{N}_0)</td>
</tr>
<tr>
<td>(\max_{\mathcal{I}}, \min_{\mathcal{I}})</td>
</tr>
</tbody>
</table>

### elementary notations

<table>
<thead>
<tr>
<th>notation</th>
<th>(\mathbb{R})</th>
<th>type</th>
<th>meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a)</td>
<td>scalar</td>
<td>constant</td>
<td></td>
</tr>
<tr>
<td>(A)</td>
<td>(\mathcal{A}(\mathbb{R}))</td>
<td>scalar</td>
<td>time-dependent variable</td>
</tr>
<tr>
<td>(a)</td>
<td>(\mathcal{M}(\mathbb{R}))</td>
<td>matrix</td>
<td></td>
</tr>
<tr>
<td>(\Re)</td>
<td>(\mathcal{R}(\mathbb{C}))</td>
<td>scalar</td>
<td>real part of a complex number</td>
</tr>
<tr>
<td>(\mathbb{I}_{[A]})</td>
<td>({0; 1})</td>
<td>variable</td>
<td>dummy variable of condition (A)</td>
</tr>
<tr>
<td>(\delta_{i,j})</td>
<td>(\mathbb{A}(\mathbb{R}^2, {0; 1}))</td>
<td>number</td>
<td>KRONECKER’s delta, 1 if (i = j), null otherwise</td>
</tr>
<tr>
<td>(0_m)</td>
<td>(\mathcal{M}_{1,m}(\mathbb{R}))</td>
<td>vector</td>
<td>(m)-dimensional null vector, (\begin{pmatrix} 0 &amp; 0 &amp; \cdots &amp; 0 \end{pmatrix}_m)</td>
</tr>
<tr>
<td>(1_m)</td>
<td>(\mathcal{M}_{1,m}(\mathbb{R}))</td>
<td>vector</td>
<td>(m)-dimensional unit vector, (\begin{pmatrix} 1 &amp; 1 &amp; \cdots &amp; 1 \end{pmatrix}_m)</td>
</tr>
<tr>
<td>(\mathbf{e}_i^{(m)})</td>
<td>(\mathcal{M}_{1,m}(\mathbb{R}))</td>
<td>vector</td>
<td>(i)-th vector of the (\mathbb{R}^m) standard basis</td>
</tr>
<tr>
<td>(0_{m,p})</td>
<td>(\mathcal{M}_{m,p}(\mathbb{R}))</td>
<td>matrix</td>
<td>(m \times p) zero matrix</td>
</tr>
<tr>
<td>(I_m)</td>
<td>(\mathcal{M}_{m,m}(\mathbb{R}))</td>
<td>matrix</td>
<td>(m \times m) identity matrix</td>
</tr>
<tr>
<td>(\mathcal{J})</td>
<td>(\mathcal{M}(\mathbb{R}))</td>
<td>matrix</td>
<td>jacobian matrix</td>
</tr>
<tr>
<td>(\text{Sp})</td>
<td>(\mathbb{C})</td>
<td>set</td>
<td>spectrum of a square matrix</td>
</tr>
<tr>
<td>(s)</td>
<td>(\mathbb{R})</td>
<td>set</td>
<td>spectral bound of a square matrix</td>
</tr>
<tr>
<td>(\rho)</td>
<td>(\mathbb{R})</td>
<td>set</td>
<td>spectral radius of a square matrix</td>
</tr>
</tbody>
</table>
### arithmetical operations

<table>
<thead>
<tr>
<th>notation</th>
<th>∈ type</th>
<th>meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ]</td>
<td>floor function</td>
<td></td>
</tr>
<tr>
<td>( \mod_m )</td>
<td>modulo operation, ( m \in \mathbb{Z}, \mod_m(a) = c \iff a \equiv c \pmod{m} )</td>
<td></td>
</tr>
<tr>
<td>( \sum_{i_1, \ldots, i_{k-1}, i_{k+1}, \ldots} )</td>
<td>sum over the ( k )-th index</td>
<td></td>
</tr>
<tr>
<td>( \sum_{i_1, \ldots, i_{k-1}, i_{k+1}, \ldots, i_{\ell-1}, i_{\ell+1}, \ldots} )</td>
<td>marginal arithmetic mean over the ( k )-th and ( \ell )-th indices</td>
<td></td>
</tr>
</tbody>
</table>

### analytical objects

<table>
<thead>
<tr>
<th>notation</th>
<th>∈ type</th>
<th>meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \frac{d}{dt} )</td>
<td>derivative with respect to time</td>
<td></td>
</tr>
<tr>
<td>.</td>
<td>steady-state value of a variable (constant solution of an ODE)</td>
<td></td>
</tr>
<tr>
<td>( \varepsilon \in \mathbb{R} )</td>
<td>quantity negligible, (</td>
<td>\varepsilon</td>
</tr>
<tr>
<td>( C^k )</td>
<td>property for a function to have ( k \in \mathbb{N} ) continuous derivatives</td>
<td></td>
</tr>
</tbody>
</table>

### matrix operations

<table>
<thead>
<tr>
<th>notation</th>
<th>∈ type</th>
<th>meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \odot )</td>
<td>product standard matrix product, scalar product</td>
<td></td>
</tr>
<tr>
<td>( \odot )</td>
<td>HADAMARD product (termwise product), ( (A, B) \in \mathcal{M}<em>{\ell,c}^2 \implies A \odot B = (a</em>{i,j}c_{i,j})_{(i,j)\in[1;\ell]\times[1;c]} )</td>
<td></td>
</tr>
<tr>
<td>( \otimes )</td>
<td>de KRONECKER (outer product), ( A \in \mathcal{M}<em>{\ell,c}, B \in \mathcal{M}</em>{p,q} \implies A \otimes B = (a_{i,j}B)<em>{(i,j)\in[1;\ell]\times[1;c]} \in \mathcal{M}</em>{\ell p,c q} )</td>
<td></td>
</tr>
<tr>
<td>( \mathbf{t} )</td>
<td>operator transpose matrix</td>
<td></td>
</tr>
<tr>
<td>( \text{vec} )</td>
<td>operator vectorized matrix, ( A \in \mathcal{M}<em>{\ell,c} \iff \text{vec}(A) = \left( a</em>{\mod_{c}(i)+1;\left\lceil \frac{i}{c} \right\rceil+1} \right)_{i\in[1;\ell c]} )</td>
<td></td>
</tr>
<tr>
<td>( \text{diag} )</td>
<td>operator diagonalized matrix, ( v \in \mathcal{M}<em>{1,c} \iff \text{diag}(v) = (\delta</em>{i,j}v)_{(i,j)\in[1;c^2]} )</td>
<td></td>
</tr>
<tr>
<td>( \text{det} )</td>
<td>operator square matrix determinant</td>
<td></td>
</tr>
</tbody>
</table>

### dimensions

<table>
<thead>
<tr>
<th>notation</th>
<th>∈ type</th>
<th>meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>( #_p )</td>
<td>parasite load</td>
<td></td>
</tr>
<tr>
<td>( #_h )</td>
<td>host density</td>
<td></td>
</tr>
<tr>
<td>( c )</td>
<td>concentration of public production molecules</td>
<td></td>
</tr>
<tr>
<td>( t )</td>
<td>time</td>
<td></td>
</tr>
</tbody>
</table>

### modelling objects

<table>
<thead>
<tr>
<th>notation</th>
<th>∈ type</th>
<th>meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>( t \in \mathbb{R}_+ )</td>
<td>time</td>
<td></td>
</tr>
<tr>
<td>( n \in \mathbb{N}^* )</td>
<td>number of parasite genotypes</td>
<td></td>
</tr>
<tr>
<td>( \mathcal{G} = [1; n] )</td>
<td>set of genotypes</td>
<td></td>
</tr>
<tr>
<td>( \mathcal{R} \in \mathbb{R}_+ )</td>
<td>basic reproductive number</td>
<td></td>
</tr>
<tr>
<td>( o )</td>
<td>single infection state (within-host level) or disease-free state (between-host level)</td>
<td></td>
</tr>
<tr>
<td>notation</td>
<td>ε</td>
<td>dimension</td>
</tr>
<tr>
<td>----------</td>
<td>---</td>
<td>-----------</td>
</tr>
<tr>
<td>within-host</td>
<td></td>
<td></td>
</tr>
<tr>
<td>x = (X_k)</td>
<td>(\mathbb{M}<em>{n,1}(\mathbb{R}</em>+))</td>
<td>#p</td>
</tr>
<tr>
<td>g = (G_k)</td>
<td>(\mathbb{M}<em>{n,1}(\mathbb{R}</em>+))</td>
<td>c</td>
</tr>
<tr>
<td>z = (Z_k)</td>
<td>(\mathbb{M}<em>{n,1}(\mathbb{R}</em>+))</td>
<td>c</td>
</tr>
<tr>
<td>U = diag (u_k)</td>
<td>(\mathbb{M}<em>{n}(\mathbb{R}</em>+))</td>
<td>c.#_p^{-1}</td>
</tr>
<tr>
<td>V = diag (v_k)</td>
<td>(\mathbb{M}<em>{n}(\mathbb{R}</em>+))</td>
<td>c.#_p^{-1}</td>
</tr>
<tr>
<td>(\Gamma = (\gamma_{k,i}))</td>
<td>(\mathbb{M}<em>{n}(\mathbb{R}</em>+))</td>
<td>c^{-1}.t^{-1}</td>
</tr>
<tr>
<td>(\Sigma = (\sigma_{k,i}))</td>
<td>(\mathbb{M}<em>{n}(\mathbb{R}</em>-))</td>
<td>c^{-1}.t^{-1}</td>
</tr>
<tr>
<td>H = (\eta_{k,i})</td>
<td>(\mathbb{M}_{n}(\mathbb{R}))</td>
<td>#_p^{-1}.t^{-1}</td>
</tr>
<tr>
<td>(\varrho = (\varrho_{k}))</td>
<td>(\mathbb{M}<em>{n,1}(\mathbb{R}</em>+))</td>
<td>t^{-1}</td>
</tr>
<tr>
<td>(\nu)</td>
<td>(\mathbb{R}_+^n)</td>
<td>t^{-1}</td>
</tr>
<tr>
<td>(P_k)</td>
<td>(\mathbb{R})</td>
<td>t^{-1}</td>
</tr>
<tr>
<td>class handling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\nu (\mathcal{G}))</td>
<td>(\nu (\mathcal{N}))</td>
<td>set</td>
</tr>
<tr>
<td>i</td>
<td>(\nu (\mathcal{G}))</td>
<td>set</td>
</tr>
<tr>
<td>(c)</td>
<td>(A (\nu (\mathcal{G}), {0; 2^n - 1}))</td>
<td>operator</td>
</tr>
<tr>
<td>(c_{i,k})</td>
<td>{0; 1}</td>
<td>coefficient</td>
</tr>
<tr>
<td>c_i</td>
<td>{0; 1}_n</td>
<td>vector</td>
</tr>
<tr>
<td>(i)</td>
<td>{0; 2^n - 1}</td>
<td>label</td>
</tr>
<tr>
<td>(B)</td>
<td>(\varphi (\mathcal{G}))</td>
<td>set</td>
</tr>
<tr>
<td>(E)</td>
<td>(\varphi (\mathcal{G}))</td>
<td>set</td>
</tr>
<tr>
<td>(\phi)</td>
<td>(A (\mathcal{B}^2, \mathcal{B}))</td>
<td>1</td>
</tr>
<tr>
<td>(\varsigma)</td>
<td>(A (\varphi (\mathcal{G}), {0, 1}))</td>
<td>1</td>
</tr>
<tr>
<td>between host</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\beta_{r,d,i})</td>
<td>(\mathbb{R}_+^n)</td>
<td>#_h^{-2}.t^{-1}</td>
</tr>
<tr>
<td>(\beta)</td>
<td>(\mathbb{R}_+^n)</td>
<td>#_h^{-1}.t^{-1}</td>
</tr>
<tr>
<td>(\theta_{d,i})</td>
<td>(\mathbb{R}_+^n)</td>
<td>#_h^{-1}.t^{-1}</td>
</tr>
<tr>
<td>(\theta)</td>
<td>(\mathbb{R}_+^n)</td>
<td>#_h^{-1}.t^{-1}</td>
</tr>
<tr>
<td>(\mu_i)</td>
<td>(\mathbb{R}_+^n)</td>
<td>#_p^{-1}.#_h^{-1}.t^{-1}</td>
</tr>
<tr>
<td>(\mu)</td>
<td>(\mathbb{R}_+^n)</td>
<td>#_p^{-1}.#_h^{-1}.t^{-1}</td>
</tr>
<tr>
<td>(s^o)</td>
<td>(\mathbb{R}_+^n)</td>
<td>#_h</td>
</tr>
<tr>
<td>S</td>
<td>(\mathbb{R}_+^n)</td>
<td>#_h</td>
</tr>
<tr>
<td>(y = (I_{i}))</td>
<td>(\mathbb{M}<em>{n,1}(\mathbb{R}</em>+))</td>
<td>#_h</td>
</tr>
<tr>
<td>X = (x_{i,j})</td>
<td>(\mathbb{M}<em>{n,2n}(\mathbb{R}</em>+))</td>
<td>#p</td>
</tr>
<tr>
<td>(\Psi)</td>
<td>(\mathbb{M}_{2n,2n}(\mathbb{R}))</td>
<td>#_h^{-2}.t^{-1}</td>
</tr>
<tr>
<td>(\Phi)</td>
<td>(\mathbb{M}_{2n,2n}(\mathbb{R}))</td>
<td>#_h^{-2}.t^{-1}</td>
</tr>
<tr>
<td>(\Theta)</td>
<td>(\mathbb{M}_{2n,2n}(\mathbb{R}))</td>
<td>#_h^{-1}.t^{-1}</td>
</tr>
<tr>
<td>(\Xi)</td>
<td>(\mathbb{M}_{2n,2n}(\mathbb{R}))</td>
<td>#_h^{-1}.t^{-1}</td>
</tr>
<tr>
<td>(\Delta)</td>
<td>(\mathbb{M}_{2n,2n}(\mathbb{R}))</td>
<td>#_h^{-1}.t^{-1}</td>
</tr>
</tbody>
</table>


B Within-host dynamics

B.1 Partial genotype combination steady-state

Here we show that there is a unique steady-state parasite load associated to a partial combination of genotypes. Let $i$ be the set of genotypes with non zero parasite loads at steady state (for a given set of initial conditions),

$$i := \{ k \in G : \bar{X}_k \neq 0 \},$$

and $\bar{x}_i$ the steady state parasite load vector associated to $i$. Therefore, the elements of $\bar{x}_i$ the index of which do not belong to $i$ are 0. This gives

$$\forall j \in G \setminus i, \quad \bar{X}_j := 0,$$

$$G_j = 0, \quad \bar{Z}_j = 0,$$

$$0 = \bar{X}_j (M_i \bar{e}_i)_j = 0,$$

where $M := (m_{k,j})_{(k,j) \in G^2}$ is the square matrix of steady-state interactions. In order to solve (2.2) at steady state, it is necessary to extract these tautological rows. If $M_i$ is a sub-matrix and $\varrho_i$ a sub-vector defined as

$$M_i := (m_{k,\ell})_{(k,\ell) \in i^2}, \quad \varrho_i := (\varrho_k)_{k \in i},$$

then the elements of $\bar{x}_i$ are given by

$$\bar{X}_k = \begin{cases} 0, & k \notin i, \\ - (M_i^{-1} \varrho_i)_k, & k \in i. \end{cases} \quad (B.1)$$

Since $M$ is a constant matrix, the elements of $\bar{x}_i$ do not depend on the initial conditions of the within-host system. As a consequence, there is only one steady state parasite load vector for each partial genotype combination.

C Linking the within and between-host levels

C.1 Class labelling

As explained in the main text, labelling the class is a computational requirement to model and simulating parasite dynamics. For $n$ different parasite genotypes, there exist exactly $|\varphi(G)| = 2^n$ different host and inoculum classes. We introduce the following labelling operator:

$$C(i) := \sum_{k=1}^{n} \mathbb{I}_{\{k \in i\}} 2^{k-1},$$

where the set $i \subset G$ is a class and $\mathbb{I}_A$ the indicator function which equals 1 if $A$ is true and 0 otherwise.

The label of the susceptible class, which is uninfected, is then

$$C(\emptyset) = \sum_{k=1}^{n} \mathbb{I}_{\{k \in \emptyset\}} 2^{k-1} = \sum_{k=1}^{n} 0 \times 2^{k-1} = 0.$$
The label of the class which contains all the \( n \) genotypes is

\[
\mathcal{C} (\mathcal{G}) = \mathcal{C} ([1; n]) = \sum_{k=1}^{n} \mathbb{I}_{\{k \in [1;n]\}} 2^{k-1} = \sum_{k=1}^{n} 2^{k-1} = 1 \times \frac{1 - 2^n}{1 - 2} = 2^n - 1.
\]

Since \( \forall i \in \mathcal{G}, \forall k \in \mathcal{G}, I_{\{k \in \mathcal{G}\}} \geq I_{\{k \in i\}} \), all the labels range from 0 to \( 2^{n-1} \) and we use \([0; 2^n - 1]\) to index \( \varphi (\mathcal{G}) \).

\( \mathcal{C} \) is a labelling function if and only it is bijective. To prove so, let us study the following function

\[
f : [0; 2^n - 1] \rightarrow \varphi (\mathcal{G}), \quad i \mapsto f (i) := \left\{ k \in \mathcal{G} : \text{mod}_2 \left\lfloor \frac{i}{2^{k-1}} \right\rfloor = 1 \right\}.
\]

Let us consider an arbitrary label \( i \in [0; 2^n - 1] \). Because \([0; 2^n - 1] \subset \mathbb{N} \), and because any natural number can be written using the binary numeral system, there is a sequence of \( (a_j)_{j \in \mathbb{N}} \in \{0; 1\}^\mathbb{N} \), which is constantly equal to 0 after a certain rank \( N \), and which corresponds to the digits of \( i \) in the binary numeral system (0 or 1), such that \( i = (\ldots 0 \ldots 0a_N a_{N-1} \ldots a_1 a_0) = \sum_{j=0}^{\infty} a_j 2^j \). Then, for any \( k \in \mathcal{G} \), we have

\[
\text{mod}_2 \left\lfloor \frac{i}{2^{k-1}} \right\rfloor := \frac{i}{2^{k-1}} - 2 \left\lfloor \frac{i}{2^{k-1}} \right\rfloor = \frac{\sum_{j=1}^{\infty} a_j 2^{j-1}}{2^{k-1}} - 2 \left\lfloor \frac{\sum_{j=1}^{\infty} a_j 2^{j-1}}{2^k} \right\rfloor
\]

\[
= \left\lfloor \frac{1}{2^k} \sum_{j=1}^{k-1} (a_j 2^j) + \sum_{j=k}^{\infty} (a_j 2^{j-k}) \right\rfloor - 2 \left\lfloor \sum_{j=1}^{k} (a_j 2^{j-k-1}) + \sum_{j=k+1}^{\infty} (a_j 2^{j-k-1}) \right\rfloor,
\]

\[
= \sum_{j=k}^{\infty} (a_j 2^{j-k}) - 2 \sum_{j=k+1}^{\infty} (a_j 2^{j-k-1}),
\]

\[
= a_k,
\]

where \((*)\) is justified by the well-known sum \( \sum_{j=0}^{\infty} \frac{1}{2^j} = 2 \).

Finally, by identifying \( i \) to the label of a class \( i = \mathcal{C} (i) \), we have \( a_k = \mathbb{I}_{\{k \in i\}} \) and \( f (i) = \{ k \in \mathcal{G} : a_k = 1 \} = \{ k \in \mathcal{G} : \mathbb{I}_{\{k \in i\}} = 1 \} = \{ k \in \mathcal{G} : k \in i \} = \{ k \in i \} = i \). So \( f \) is the inverse function of \( \mathcal{C} \). We have proved that \( \mathcal{C} \) is bijective and that its inverse function, which is also bijective, is \( \mathcal{C}^{-1} : i \mapsto \left\{ k \in \mathcal{G} : \text{mod}_2 \left\lfloor \frac{i}{2^{j-1}} \right\rfloor = 1 \right\} \).

Therefore it is possible to know if a genotype belongs to a class directly from the label of the latter. This is done by calculating the following presence coefficient for each couple \((i, k) \in [0; 2^n - 1] \times [1; n]\),

\[
c_{i,k} = \text{mod}_2 \left\lfloor \frac{i}{2^{j-1}} \right\rfloor = \mathbb{I}_{\{k \in \mathcal{C}^{-1}(i)\}},
\]

which is 1 if genotype \( k \) belongs to host class \( i \). As a consequence of this definition, we have
\[ i = \sum_{k \in G} c_{i,k} 2^{k-1}. \]

The presence vector \( c_i := (c_{i,k})_{k \in G} \) is then the vector of the presence coefficients for all genotypes in a given class. The presence vector is useful for calculating class ranks. For a given class with label \( i \), its rank denoted \( n_i \), that is the number of genotypes it contains, is

\[ n_i = c_i \mathbf{1}_n^T, \]

where \( \mathbf{1}_n \) is the unity vector of \( \mathbb{R}_n \).

Thereafter, light class indices (such as \( i \)) refer to labelled classes and bold class indices (such as \( i \)) refer to the associated set-theoretic classes. Class-related functions can indifferently be applied to both forms owing to the bijectivity of \( C \).

### C.2 Within-host jacobian matrix

We need to calculate the within-host jacobian matrix \( J_w \) in order to determine the stability of the steady states. \( J_w \) is the \( 3n \times 3n \) matrix given by the following general formula

\[
J_w := \left( \frac{\partial}{\partial W_j} \left( \frac{dW_k}{dt} \right) \right)_{(k,j) \in [1:3n]^2}
\]

where \( W_k = \begin{cases} X_k, & k \in [1;n], \\ G_{k-n}, & k \in [n+1;2n], \\ Z_{k-2n}, & k \in [2n+1;3n], \end{cases} \)

which can be split into nine \( n \times n \) submatrices as follows

\[
J_w = \begin{pmatrix} J_{X,X} & J_{X,G} & J_{X,Z} \\ J_{G,X} & J_{G,G} & J_{G,Z} \\ J_{Z,X} & J_{Z,G} & J_{Z,Z} \end{pmatrix}.
\]

Let us calculate \( \frac{\partial}{\partial X_j} \left( \frac{dX_k}{dt} \right) \),

\[
\frac{\partial}{\partial X_j} \left( \frac{dX_k}{dt} \right) = \frac{\partial}{\partial X_j} \left( \left( \gamma_k + \sum_{\ell \in \mathcal{G}} \sigma_{k,\ell} X_\ell + \sum_{\ell \in \mathcal{G}} \eta_{k,\ell} X_\ell \right) X_k \right),
\]

if \( j \neq k \),

\[
= \eta_{k,j} X_k,
\]

if \( j = k \),

\[
= \gamma_k + \sum_{\ell \in \mathcal{G}} \sigma_{k,\ell} X_\ell + \sum_{\ell \in \mathcal{G}} \eta_{k,\ell} X_\ell + \eta_{k,k} X_k,
\]

so

\[
J_{X,X} = \text{diag} \left( \mathbf{1}_n \mathbf{g} - \mathbf{1}_n \mathbf{z} + \mathbf{H} \mathbf{x} \right) + \mathbf{H} \odot \left( \mathbf{x} \mathbf{1}_n \right).
\]

Let us calculate \( \frac{\partial}{\partial G_j} \left( \frac{dX_k}{dt} \right) \),

\[
\frac{\partial}{\partial G_j} \left( \frac{dX_k}{dt} \right) = \frac{\partial}{\partial G_j} \left( \left( \gamma_k + \sum_{\ell \in \mathcal{G}} \sigma_{k,\ell} X_\ell + \sum_{\ell \in \mathcal{G}} \eta_{k,\ell} X_\ell \right) X_k \right),
\]

\[
= \gamma_{k,j} X_k,
\]
\[
\mathbf{J}_{X,G} = \mathbf{\Gamma} \odot (\mathbf{x}_1) .
\]

Let us calculate \( \frac{\partial}{\partial Z_j} \left( \frac{dX_k}{dt} \right) \),

\[
\frac{\partial}{\partial Z_j} \left( \frac{dX_k}{dt} \right) = \frac{\partial}{\partial Z_j} \left( \left( \varrho_k + \sum_{\ell \in G} \gamma_{k,\ell} G_{\ell} - \sum_{\ell \in G} \sigma_{k,\ell} Z_{\ell} + \sum_{\ell \in \mathbb{G}} \eta_{k,\ell} X_{\ell} \right) X_k \right),
\]

if \( j \neq k \),

\[
= -\sigma_{k,j} X_k,
\]

if \( j = k \),

\[
= 0 \quad \text{(because } \sigma_{k,k} = 0),
\]

so

\[
\mathbf{J}_{X,Z} = -\Sigma \odot (\mathbf{x}_1) .
\]

Let us calculate \( \frac{\partial}{\partial X_j} \left( \frac{dG_k}{dt} \right) \),

\[
\frac{\partial}{\partial X_j} \left( \frac{dG_k}{dt} \right) = \frac{\partial}{\partial X_j} \left( v (u_k X_k - G_k) \right),
\]

if \( j \neq k \),

\[
= 0,
\]

if \( j = k \),

\[
= vu_j,
\]

so

\[
\mathbf{J}_{G,X} = v \mathbf{U}.
\]

Let us calculate \( \frac{\partial}{\partial Z_j} \left( \frac{dG_k}{dt} \right) \),

\[
\frac{\partial}{\partial Z_j} \left( \frac{dG_k}{dt} \right) = \frac{\partial}{\partial Z_j} \left( v (u_k X_k - G_k) \right),
\]

\[
= 0,
\]

so

\[
\mathbf{J}_{G,Z} = 0_{n,n}.
\]

Let us calculate \( \frac{\partial}{\partial G_j} \left( \frac{dG_k}{dt} \right) \),

\[
\frac{\partial}{\partial G_j} \left( \frac{dG_k}{dt} \right) = \frac{\partial}{\partial G_j} \left( v (u_k X_k - G_k) \right),
\]

if \( j \neq k \),

\[
= 0,
\]

if \( j = k \),

\[
= -v,
\]

so

\[
\mathbf{J}_{G,G} = -v \mathbf{I}_n.
\]

Let us calculate \( \frac{\partial}{\partial X_j} \left( \frac{dZ_0}{dt} \right) \),
\[
\frac{\partial}{\partial X_j} \left( \frac{dZ_k}{dt} \right) = \frac{\partial}{\partial X_j} \left( v (v_k X_k - Z_k) \right),
\]
if \( j \neq k \),
\[
= 0,
\]
if \( j = k \),
\[
= vv_k,
\]
so
\[
J_{Z,X} = vV.
\]

Let us calculate \( \frac{\partial}{\partial Z_j} \left( \frac{dZ_k}{dt} \right) \),
\[
\frac{\partial}{\partial Z_j} \left( \frac{dZ_k}{dt} \right) = \frac{\partial}{\partial Z_j} \left( v (v_k X_k - Z_k) \right),
\]
if \( j \neq k \),
\[
= 0,
\]
if \( j = k \),
\[
= -v,
\]
so
\[
J_{Z,Z} = -vI_n.
\]

Let us calculate \( \frac{\partial}{\partial G_j} \left( \frac{dZ_k}{dt} \right) \),
\[
\frac{\partial}{\partial G_j} \left( \frac{dZ_k}{dt} \right) = \frac{\partial}{\partial G_j} \left( v (v_k X_k - Z_k) \right),
\]
\[
= 0,
\]
so
\[
J_{Z,G} = 0_{n,n}.
\]

\( J_w \) can then be written as the following bloc matrix:
\[
J_w (x, g, z) = \begin{pmatrix}
\text{diag} (g + \Gamma g - \Sigma z + Hx) + H \odot (x.1_n) & \Gamma \odot (x.1_n) & -\Sigma \odot (x.1_n) \\
vU & -vI_n & 0_{n,n} \\
vV & 0_{n,n} & -vI_n
\end{pmatrix}.
\]

Finally, in a steady state \((\bar{x}, \bar{g}, \bar{z})\) with non zero values of \( \bar{x} \), it follows from (2.6) that
\[
J_w (\bar{x}, \bar{g}, \bar{z}) = \begin{pmatrix}
H \odot (\bar{x}.1_n) & \Gamma \odot (\bar{x}.1_n) & -\Sigma \odot (\bar{x}.1_n) \\
vU & -vI_n & 0_{n,n} \\
vV & 0_{n,n} & -vI_n
\end{pmatrix}.
\]

### C.3 Susceptible state instability

In an uninfected host, \( x = g = z = 0^T_n \). Therefore the within susceptible host jacobian matrix is
\[ \mathbf{J}_w^\circ = \begin{pmatrix} \text{diag} (\varrho) & 0_{n,n} & 0_{n,n} \\ vU & -vI_n & 0_{n,n} \\ vV & 0_{n,n} & -vI_n \end{pmatrix}, \]

which is a real-valued upper triangular matrix. Its eigenvalues are straightforward \( \text{Sp} (\mathbf{J}_w^\circ) = \{ \varrho_1, \ldots, \varrho_n, -v \} \).

Since we assume that any considered genotype grows when alone within a host, \( i.e. \varrho_k > 0 \), the susceptible state is unstable for any \( n \in \mathbb{N}^* \).

### C.4 Single infection state stability

Assuming \( \varrho > 0 \) makes the susceptible state unstable. Assuming \( \eta + \gamma u < 0 \) makes the single infection steady state positive. The stability of the latter still needs to be proved. The jacobian matrix within singly infected host is the following \( 3 \times 3 \) matrix

\[ \mathbf{J}_w (X, G, Z) = \begin{pmatrix} \varrho + \gamma G + 2\eta X & \gamma X & 0 \\ \nu u & -v & 0 \\ \nu v & 0 & -v \end{pmatrix}, \]

where the indices are not shown for the sake of simplicity. Note that \( \sigma \) does not appear, for we assume that no genotype is affected by the spite it produces.

At steady state, we have \( \varrho + \gamma \hat{G} + 2\eta \hat{X} = \varrho - \gamma u \left( \frac{\varrho}{\eta + \gamma u} \right) - 2\eta \left( \frac{\varrho}{\eta + \gamma u} \right) = \frac{-\varrho \nu}{\eta + \gamma u} \), so

\[ \mathbf{J}_w (x_k^0 (1, u_k, v_k)) = \begin{pmatrix} \frac{-\varrho \nu}{\eta + \gamma u} & \frac{-\varrho \nu}{\eta + \gamma u} & 0 \\ \nu u & -v & 0 \\ \nu v & 0 & -v \end{pmatrix}, \]

the eigenvalues of which ares the roots of the following determinant

\[
| \mathbf{J}_w (x_k^0 (1, u_k, v_k)) - \lambda I_3 | = \begin{vmatrix} \frac{-\varrho \nu}{\eta + \gamma u} & -\varrho \nu & 0 \\ \nu u & -v & 0 \\ \nu v & 0 & -v \end{vmatrix}, \]

\[
= - (v + \lambda)^2 \left( \frac{\varrho \nu}{\eta + \gamma u} + \lambda \right) - (v + \lambda) \frac{\varrho \gamma}{\eta + \gamma u} \nu u, \]

\[
= - (v + \lambda) \left( (v + \lambda) \left( \frac{\varrho \nu}{\eta + \gamma u} + \lambda \right) + \frac{\nu \varrho \gamma u}{\eta + \gamma u} \right), \]

\[
= - (v + \lambda) \left( \lambda^2 + \left( v + \frac{\varrho \nu}{\eta + \gamma u} \right) \lambda + \varrho v \right). \]

A first obvious eigenvalue is \( \lambda_0 = -v < 0 \). The remaining two are the roots of the following polynomial

\[
\lambda^2 + \left( v + \frac{\varrho \nu}{\eta + \gamma u} \right) \lambda + \varrho v = 0, \]

the discriminant of which is
As explained in the main text, labelling the class is a computational requirement to model and simulating parasite dynamics. The set of biological classes $\mathcal{B}$ is formally defined as

$$
\mathcal{B} := \{ i \in \varphi(\mathcal{G})^* : \forall k \in i, \mathbf{x}_i > 0 \wedge \max (|\Re (\text{Sp} (\mathbf{J}_w (\mathbf{I}_n, \mathbf{U}, \mathbf{V} \cdot \mathbf{x}_i))))) < 0 \} \cup \{ \emptyset \},
$$

where $\mathbf{J}_w$ is here the $3|\mathbf{i}| \times 3|\mathbf{i}|$ jacobian matrix obtained by removing the lines and columns related to genotypes absent from $i$ and max $(|\Re (\text{Sp} (\mathbf{J}_w (\mathbf{I}_n, \mathbf{U}, \mathbf{V} \cdot \mathbf{x}_i)))))$ refers to the greatest real part among its eigenvalues.

Consider now a host belonging to class $\mathbf{r} \in \mathcal{B}$ the parasite loads of which have reached the biologically meaningful within-host steady state $\mathbf{x}_\mathbf{r}$, that is to say positive and stable. Let us further assume that this host is infected by a class $\mathbf{p}$ inoculum. We call $(x^{(r,p)}, g^{(r,p)}, z^{(r,p)}) (t)$ the dynamical system that corresponds to this infection event, defined by its initial condition $(x^{(r,p)}, g^{(r,p)}, z^{(r,p)}) (0) := (\mathbf{x}_\mathbf{r} + \varepsilon \| \mathbf{x}_\mathbf{r} \| \mathbf{c}_\mathbf{p}, \mathbf{g}_\mathbf{r}, \mathbf{z}_\mathbf{r})$, where $0 < \varepsilon \ll 1$ is the inoculation factor.

Given this modelling of infection events, the output class is found through the infection operator defined as

$$
\phi(\mathbf{r}, \mathbf{p}) := \begin{cases}
\min_{i \in B} \left\| \lim_{t \to \infty} x^{(r,p)} (t) - \mathbf{x}_i \right\|, & \left\| \lim_{t \to \infty} x^{(r,p)} (t) \right\| < \infty, \\
0, & \text{otherwise.}
\end{cases}
$$

This definition of $\phi$ holds only if $x^{(r,p)}$ has a finite limit when $t \to \infty$. If the limit is infinite, then $\phi$ is 0 because of our definition of the ultrainfection pattern (see below). If there is no finite nor infinite limit (this occurs when the attractor is not a fixed point), then $\phi$ must be adapted depending on the behaviour of the system, the use of the model and additional assumptions. As alternative definitions of $\phi$, one can think of fixing a finite time for within-host dynamics, that is

$$
0 < T < \infty, \phi(\mathbf{r}, \mathbf{p}) := \min_{i \in B} \left\| \sup_{t \in [0, T]} x^{(r,p)} (t) \right\|, \min_{i \in B} \left\| \lim_{t \to T} x^{(r,p)} (t) - \mathbf{x}_i \right\|,
$$

C.5 Biological, epidemiological classes and infection, stability operators

As explained in the main text, labelling the class is a computational requirement to model and simulating parasite dynamics. The set of biological classes $\mathcal{B}$ is formally defined as

$$
\Delta = \left( v + \frac{\eta}{\eta + \gamma u} \right)^2 - 4\rho v, \\
= v^2 - \frac{2\rho v (2\gamma u + \eta)}{\eta + \gamma u} + \left( \frac{\eta}{\eta + \gamma u} \right)^2, \\
= \left( v - \frac{\eta}{\eta + \gamma u} \right)^2 - 4\rho v \gamma u \frac{\eta + \gamma u}{\eta + \gamma u}.
$$

Owing to the previous assumptions, $\Delta > 0$, and the eigenvalues are the following real real numbers

$$
\lambda_{1,2} = -\frac{1}{2} \left( v + \frac{\eta}{\eta + \gamma u} \pm \sqrt{\left( v + \frac{\eta}{\eta + \gamma u} \right)^2 - 4\rho v} \right) < 0.
$$

These eigenvalues are both negative, implying the single infection steady state stable.
or averaging over a period or an long amount of time, as in
\[
0 < T < \infty, \phi(r, p) := \min_{i \in B} \left\{ \sup_{t \leq [0, 2T]} x(r,p)(t) < \infty \right\} \frac{1}{T} \int_{T}^{2T} x(r,p)(t) \, dt - \bar{x}_i.
\]

Finally, in case of chaos, one should pay attention to the inoculation factor which can greatly influence the output. In the next subsection (C.6) we give a sufficient condition for \( \lim_{t \to \infty} x(r,p)(t) \) to always be a steady-state \( \bar{x}_i \) with \( i \in B \), so the first definition of \( \phi \) holds.

Ultrainfection happens when the growth of at least one genotype is not bounded. Recall that ultrainfection relies on three assumptions:

1. time scale separation between the two levels of dynamics, that is to say at within-host level all hosts of a given class have the same class show the same parasite loads and these are at steady-state,
2. host mortality rate is an increasing non bounded function of total parasite load,
3. constant population size.

Then the set of epidemiological class \( \mathcal{E} \) is defined as
\[
\mathcal{E} := \left\{ i \in B : \exists (r, d) \in B^2, \exists p \subset d, \phi(r, p) = i \right\} \cup \{\emptyset\}.
\]

The stability operator \( \varsigma \), used thereafter in the labelled form of between-host rates, is simply defined as
\[
\forall i \in [0; 2^n - 1], \varsigma(i) := \mathbb{I}_{(c-1)(i) \in \mathcal{E}}.
\]

### C.6 A sufficient condition for global asymptotic stability

In this subsection we use a Lyapunov function [57] to derive a sufficient condition for within-host steady states to be globally asymptotically stable so that non fixed point attractors are avoided. The derivation is inspired from previous works on generalized competitive Lotka-Volterra systems such as [58, 59].

The set of biological infected classes
\[
\mathcal{B}^* := \left\{ i \in \varphi(\mathcal{G})^* : \forall k \in i, \bar{x}_i > 0, \max (\Re (\text{Sp} (J_w (I_n, U, V, \bar{x}_i)))) < 0 \right\}
\]
is characterized by its feasibility, that is the positivity of the steady state parasite loads, and by its local asymptotic stability, provided by the negativity of the real part of all eigenvalues of the jacobian matrix evaluated at the steady state [57]. A steady state is said to be locally asymptotically stable (LAS) if there is a neighbourhood of the steady state where any trajectory starting from it will converge infinitely close to the steady state as time goes to infinity. However, this neighbourhood may be very limited and its boundary difficult to estimate. Thus, local asymptotic stability does not guarantee that any feasible trajectory will get infinitely close to the steady state. The trajectory may be trapped in other attractors that are not a fixed point but a finite set of points, a limit cycle or even strange attractors. The only way to make sure that any trajectory that starts with positive initial conditions will not be trapped by other attractors than steady states is to make these steady states globally asymptotically stable (GAS) [57].
Let us consider \( i \in B^* \) a biological class and assume that that the steady state \( \bar{w}_i = \left( \bar{x}_i, \bar{g}_i, \bar{z}_i \right) \), with \( \bar{x}_{i,k} > 0, \forall k \in i \), is LAS in \((\mathbb{R}^+)^{3n}\). Even though this last condition is more restrictive than \( \bar{w}_i \) being LAS in \((\mathbb{R}^+)^{3|i|}\) (it is straightforward that \( \bar{w}_i \) LAS in \((\mathbb{R}^+)^{3|i|} \implies \bar{w}_i \) LAS in \((\mathbb{R}^+)^{3|i|}\), we use it for the sake of simplicity. Indeed, since \( n \) and \( i \) are arbitrary, the following result can be applied to any nonempty subset of \( G \) without any loss of generality.

First of all, we note that \((\mathbb{R}^+)^{3n}\) is a positively invariant set, that is any trajectory starting in \((\mathbb{R}^+)^{3n}\) remains in \((\mathbb{R}^+)^{3n}\) [57]. This can be intuitively shown as follows. The time derivative in (2.1) and (2.2) are respectively linear and bilinear, and therefore continuous; therefore \( X_k(t) \) cannot become negative without taking the value 0 beforehand. But since \( X_k \) is a common factor in (2.2), it will remain 0 from then on. Similarly, \( G_k(t) \) cannot become negative without taking the value 0 beforehand. Due to the previous argument, it then follows that \( \frac{d}{dt} G_k(t) = u_k X_k \geq 0 \) and the same applies to \( Z_k(t) \). This allows us to define a Lyapunov function on \((\mathbb{R}^+)^{3n}\) (see below).

Let \( w = \left( \begin{array}{c} x \\ g \\ z \end{array} \right) \) be the variable vector and \( \Omega_i \) be the following subset of \((\mathbb{R}^+)^{3n}\):

\[
\Omega_i := \left\{ w \in (\mathbb{R}^+)^{3n} : \forall k \in i, X_k > 0 \right\}.
\]

The usual way of proving that a steady state is GAS on a given set is to prove the existence of a Lyapunov function that satisfies certain definiteness properties on the set [57]. Here, \( \bar{w}_i \) is globally asymptotically stable on \( \Omega_i \) if there is a \( C^1 \) function \( V_i : (\mathbb{R}^+)^{3n} \to \mathbb{R} \) such that

1. \( V_i(\bar{w}_i) = 0 \),
2. \( \forall w \in \Omega_i \setminus \{ \bar{w}_i \}, V_i(w) > 0 \),
3. \( \frac{d}{dt} V_i(\bar{w}_i) = 0 \),
4. \( \forall w \in \Omega_i \setminus \{ \bar{w}_i \}, \frac{d}{dt} V_i(w) < 0 \).

We now present a sufficient condition on within-host parameters for this function to exist.

We now consider the function \( V_i \) defined as

\[
V_i(w) := \sum_{k \in i} q_{k} x_{k} - \bar{x}_{i,k} x_{k} - \bar{x}_{i,k} \log \left( \frac{x_{k}}{\bar{x}_{i,k}} \right) + \sum_{k \in \varnothing} q_{k} x_{k} + \frac{1}{2} \sum_{k \in G} g_{k} (G_{k} - \bar{g}_{i,k})^{2} + \sum_{k \in \varnothing} q_{k} x_{k} (Z_{k} - \bar{x}_{i,k})^{2},
\]

where \( \forall k \in G, (q_{k}, \bar{x}_{k}, \bar{g}_{k}, \bar{x}_{k}) \in (\mathbb{R}^+)^{3} \), and \( \forall k \notin i, \bar{g}_{i,k} = \bar{x}_{i,k} = \bar{x}_{i,k} = 0 \) by definition.

\( V_i \) is \( C^1 \) on \( \Omega \) because it is a sum of elementary single variable functions which are \( C^1 \) on \( \mathbb{R}^+ \) except the logarithm that applies to \( X_k, k \in i \) and is \( C^1 \) on \( \mathbb{R}^+ \).

The first sum of \( V_i \) in (C.1) involves terms of the form \( f(x) := x - a - a \log x - \log a \), with \( a > 0 \). Given that the first derivative of \( f \) is \( f'(x) = 1 - \frac{a}{x} \) and its second derivative is \( f''(x) = \frac{a}{x^2} > 0 \), it follows that the \( \arg \min (f) = a \) and \( \min (f) = 0 \). Thus, and since \( V_i \) is a separable function in each component of \( w \) and \( q_{k}, q_{k}, \bar{g}_{k}, \bar{g}_{k} \) and \( v \) are positive constants, it is straightforward that

\[
\begin{align*}
\forall w \in \Omega \setminus \{ \bar{w}_i \}, V_i(w) & > 0, \\
V_i(\bar{w}_i) & = 0.
\end{align*}
\]
Properties 1 and 2 of the Lyapunov function are satisfied.

Let us now calculate the time derivative of $V_i$ with the help of the following notation of the malthusian growth rate $P_k(w)$ that satisfies

$$\frac{d}{dt} X_k = P_k(w) X_k,$$

hence

$$P_k(w) := \varrho_k + \sum_{\ell \in \mathcal{G}} \gamma_{k,\ell} G_\ell - \sigma_{k,\ell} Z_\ell + \eta_{k,\ell} X_\ell,$$

so the time derivative of $V_i$ is

$$\frac{d}{dt} V_i(w) = \sum_{k \in i} q_{k,i} \left( P_k(w) X_k - \bar{x}_{i,k} \right) + \sum_{k \in \mathcal{G}} q_{k,i} P_k(w) X_k$$

$$+ \sum_{k \in G} q_{k,i} (u_k X_k - G_k) (G_k - \bar{g}_{i,k}) + q_{k,i} (v_k X_k - Z_k) (Z_k - \bar{z}_{i,k}) .$$

Given that $\forall k \notin i, \bar{x}_{i,k} = 0$, it follows that

$$\frac{d}{dt} V_i(w) = \sum_{k \in G} q_{k,i} P_k(w) (X_k - \bar{x}_{i,k}) + q_{k,i} (u_k X_k - G_k) (G_k - \bar{g}_{i,k}) + q_{k,i} (v_k X_k - Z_k) (Z_k - \bar{z}_{i,k}) .$$

It is straightforward that $\frac{d}{dt} V_i(\bar{w}_i) = 0$, that is property 3 is satisfied. The following calculations are then made to find a sufficient condition for property 4.

From (2.3) and (B.1), we have that $\forall k \in i, P_k(\bar{w}_i) = 0$, which gives

$$\theta_k = -\sum_{\ell \in \mathcal{G}} \gamma_{k,\ell} \bar{g}_{i,\ell} + \sigma_{k,\ell} \bar{z}_{i,\ell} - \eta_{k,\ell} \bar{x}_{i,\ell},$$

thus $\forall k \in i$,

$$P_k(w) = \sum_{\ell \in \mathcal{G}} \gamma_{k,\ell} (G_\ell - \bar{g}_{i,\ell}) - \sigma_{k,\ell} (Z_\ell - \bar{z}_{i,\ell}) + \eta_{k,\ell} (X_\ell - \bar{x}_{i,\ell}).$$

Note now that $\forall k \notin i$, the following equality holds

$$P_k(w) = \sum_{\ell \in \mathcal{G}} \gamma_{k,\ell} (G_\ell - \bar{g}_{i,\ell}) - \sigma_{k,\ell} (Z_\ell - \bar{z}_{i,\ell}) + \eta_{k,\ell} (X_\ell - \bar{x}_{i,\ell}) + \varrho_k + \sum_{\ell \in \mathcal{G}} \gamma_{k,\ell} \bar{g}_{i,\ell} - \sigma_{k,\ell} \bar{z}_{i,\ell} + \eta_{k,\ell} \bar{x}_{i,\ell} .$$

Moreover, note that $\forall k \in \mathcal{G}, u_k X_k - G_k$ can be written as

$$u_k X_k - G_k = u_k X_k - u_k \bar{x}_{i,k} + u_k \bar{x}_{i,k} - G_k,$$
$$= u_k (X_k - \bar{x}_{i,k}) - (G_k - \bar{g}_{i,k}) ,$$
and the same holds for $v_k X_k - Z_k$

$$v_k X_k - Z_k = v_k (X_k - \bar{z}_{i,k}) - (Z_k - \bar{z}_{i,k}).$$

Therefore, the time derivative of $V_i$ can be written as

$$\frac{d}{dt} V_i (w) = \sum_{k \in G} \left( \sum_{\ell \in G} q_{k,\ell} (X_k - \bar{x}_{i,k}) (G_\ell - \bar{g}_{i,\ell}) - \sigma_{k,\ell} (Z_\ell - \bar{z}_{i,k}) + \eta_{k,\ell} (X_\ell - \bar{x}_{i,k}) (X_k - \bar{x}_{i,k}) \right)$$

$$+ \sum_{k \in G} q_{k,k} u_k (X_k - \bar{x}_{i,k}) (G_k - \bar{g}_{i,k}) - q_{g,k} (G_k - \bar{g}_{i,k})^2$$

$$+ q_{k,k} v_k (X_k - \bar{x}_{i,k}) (Z_k - \bar{z}_{i,k}) - q_{z,k} (Z_k - \bar{z}_{i,k})^2$$

$$+ \sum_{k \in G} q_{k,k} P_k (\bar{w}_i) X_k.$$

Then, because $\bar{w}_i$ is assumed to be LAS, we can apply the following theorem by Takeuchi [59],

$$\forall N \in \mathbb{N}^*, \quad \mathbf{f} : \mathbb{R}^N \to \mathbb{R}^N \text{ is } C^1, \quad \Rightarrow \mathbf{f} (\bar{w}) \in (\mathbb{R}_-)^N.$$ 

Hence, $\sum_{k \in G} q_{k,k} P_k (\bar{w}_i) X_k \leq 0$ so we have

$$\frac{d}{dt} V_i (w) \leq \sum_{k \in G} \left( q_{k,k} u_k (X_k - \bar{x}_{i,k}) (G_k - \bar{g}_{i,k}) - q_{g,k} (G_k - \bar{g}_{i,k})^2 \right)$$

$$+ q_{k,k} v_k (X_k - \bar{x}_{i,k}) (Z_k - \bar{z}_{i,k}) - q_{z,k} (Z_k - \bar{z}_{i,k})^2$$

$$+ \sum_{\ell \in G} q_{k,\ell} \gamma_{k,\ell} (X_\ell - \bar{x}_{i,\ell}) (X_k - \bar{x}_{i,k})$$

$$+ q_{k,k} \eta_{k,\ell} (X_\ell - \bar{x}_{i,\ell}) (X_k - \bar{x}_{i,k})). \quad (C.2)$$

If we use now generalized variable notations $W_k$ and $\bar{w}_{i,k}$ such that

$$\forall k \in \mathcal{G}, \quad \begin{cases} W_k := \mathbb{I}_{\{k \in [1; n]\}} X_k + \mathbb{I}_{\{k \in [n+1; 2n]\}} G_k + \mathbb{I}_{\{k \in [2n+1; 3n]\}} Z_k, \\
\bar{w}_{i,k} := \mathbb{I}_{\{k \in [1; n]\}} \bar{x}_{i,k} + \mathbb{I}_{\{k \in [n+1; 2n]\}} \bar{g}_{i,k} + \mathbb{I}_{\{k \in [2n+1; 3n]\}} \bar{z}_{i,k}, \end{cases}$$

where $\mathcal{G} := [1; 3n]$. Similarly, we define

$$\forall k \in \mathcal{G}, q_k := \mathbb{I}_{\{k \in [1; n]\}} q_{k,k} + \mathbb{I}_{\{k \in [n+1; 2n]\}} q_{g,k} + \mathbb{I}_{\{k \in [2n+1; 3n]\}} q_{z,k}.$$ 

Using these notations, we can now see that

$$\frac{d}{dt} V_i (w) \leq \sum_{(k,\ell) \in \mathcal{G}^2} q_{k,\ell} a_{k,\ell} (W_k - \bar{w}_{i,k}) (W_\ell - \bar{w}_{i,\ell}) = \frac{1}{2} (w - \bar{w}_i)^T (Q A + A^T Q) (w - \bar{w}_i), \quad (C.3)$$

where $Q = \text{diag} (q_k)_{k \in \mathcal{G}}$ and $A := (a_{k,\ell})_{(k,\ell) \in \mathcal{G}^2}$. By comparing (C.2) and (C.3), it follows that $A$ is the following matrix of within-host parameters.
\[ A = \begin{pmatrix} H & \Gamma & -\Sigma \\ U & -I_n & 0_{n,n} \\ V & 0_{n,n} & -I_n \end{pmatrix}. \] \hspace{1cm} (C.4)

From (C.3), it follows that property 4 is satisfied if and only if there exists a positive diagonal matrix \( Q \in \mathbb{R}_{3n,3n}^+ \) such that \( QA + A^TQ \) is negative definite.

We finally use a theorem from Berman & Plemmons \([60]\) that states for all \( N \in \mathbb{N}^* \), \( A = (a_{i,j})_{i,j} \in [1;N]^2 \in \mathbb{R}_{N,N}^N \) diagonal: \( QA + A^TQ \) is negative definite.

The premise of this theorem is called strict row diagonal dominance. Then, a sufficient condition for property 4 to be satisfied is the following by setting \( d = 1_n \) for instance,

\[
\forall k \in \mathcal{G}, a_{k,k} < - \sum_{\ell \in \mathcal{G} \setminus \{k\}} |a_{k,\ell}| < 0,
\]

that is to say, by (C.4),

\[
\forall k \in \mathcal{G}, \begin{cases} 
\eta_{k,k} < - \sum_{\ell \in \mathcal{G} \setminus \{k\}} |\eta_{k,\ell}| - \sum_{\ell \in \mathcal{G}} |\gamma_{k,\ell} + \sigma_{k,\ell}| < 0, \\
0 < u_k < 1, \\
0 < v_k < 1.
\end{cases}
\] \hspace{1cm} (C.5)

We have thus proved that if \( \bar{w}_i \) is a LAS steady state in \( (\mathbb{R}_+)^{3n} \) and the within-host parameters satisfy (C.5), then \( \bar{w}_i \) is GAS in \( \Omega_i \), that is \( \bar{w}(0) \in \Omega_i \Rightarrow \lim_{t \to \infty} \bar{w}(t) = \bar{w}_i \).

### D Between host level

#### D.1 Transmission rates properties

Hereafter we provide a proof of the two transmission rate properties which are (4.4), the overall transmission rate is constant whatever the host class, and (4.5), which gives the transmission rate of a given genotype from a given host class. For the sake of simplicity, the proof is provided for an abstract finite set instead of a set of parasite genotypes.

Let \( \Omega \) be a finite set such that

\[
\Omega = \left\{ \omega_1, \omega_2, \ldots, \omega_{|\Omega|} \right\}, |\Omega| < \aleph_0.
\]

We define an arbitrary measure \( \mu \) on \( \Omega \) as follows

1. \( \mu \in \mathcal{A}(\Omega, [0; 1]) \),
2. \( \mu(\emptyset) = 0 \),
3. \( \mu(\Omega) = 1 \),
4. \( \forall \omega \in \Omega, 0 < \mu(\{\omega\}) < 1 \),

5. \( \forall P \in \wp(\Omega), \mu(P) = \sum_{\omega \in P} \mu(\{\omega\}) \).

One can see \( \mu \) as an elementary probability associated to \( \Omega \). As a consequence of points 3. and 5. of this definition, we have

\[
\sum_{\omega \in \Omega} \mu(\{\omega\}) = \mu(\Omega) = 1.
\]

(D.1)

Next, we introduce the operator \( F_{\cdot,\cdot} \) that is a function of a couple of disjoint subsets of \( \Omega \),

\[
\forall (P, Q) \in \wp(\Omega)^2 : P \cap Q = \emptyset, F_{P,Q} := \prod_{\omega \in P} \mu(\{\omega\}) \prod_{\omega \in Q} (1 - \mu(\{\omega\}))
\]

This operator is the product over all the measures of each element of its first subset argument and the complementary measures of each element of its second subset argument. It has the following properties

6. \( \forall \alpha \in \Omega, F_{\{\alpha\},\emptyset} = \mu(\{\alpha\}) \),

7. \( \forall \alpha \in \Omega, F_{\emptyset,\{\alpha\}} = 1 - \mu(\{\alpha\}) \),

8. \( \forall \alpha \in \Omega, F_{\{\alpha\},\emptyset} + F_{\emptyset,\{\alpha\}} = 1 \),

9. \( \forall (P, Q, R, S) \in \wp(\Omega)^4 \) mutually disjoint, \( F_{P,Q}F_{R,S} = F_{P\cup R, Q \cup S} \),

10. \( \forall \alpha \in \Omega, \forall (P, Q) \in \wp(\Omega \setminus \{\alpha\})^2 : P \cap Q = \emptyset, F_{P,Q} = F_{P\cup\{\alpha\},Q} + F_{P,Q\cup\{\alpha\}} \).

Let us prove them all.

The proof of property 6. is the following

\[
\forall \alpha \in \Omega, F_{\{\alpha\},\emptyset} \quad := \quad \prod_{\omega \in \{\alpha\}} \mu(\{\omega\}) \prod_{\omega \in \emptyset} (1 - \mu(\{\omega\}))
\]
\[
= \mu(\{\alpha\}) \times 1,
\]
\[
= \mu(\{\alpha\})
\]

since the empty product is the neutral element of multiplication, that is one, such for \( \forall x \in \mathbb{R}^*, x^0 = 1 \).

Similarly, the proof of property 7. is

\[
\forall \alpha \in \Omega, F_{\emptyset,\{\alpha\}} \quad := \quad \prod_{\omega \in \emptyset} \mu(\{\omega\}) \prod_{\omega \in \{\alpha\}} (1 - \mu(\{\omega\}))
\]
\[
= 1 \times (1 - \mu(\{\alpha\}))
\]
\[
= 1 - \mu(\{\alpha\})
\]

The proof of property 8. is straightforward from the previous two

\[
\forall \alpha \in \Omega, F_{\{\alpha\},\emptyset} + F_{\emptyset,\{\alpha\}} \quad = \quad 6. \text{ and 7.}
\]
\[
= \mu(\{\alpha\}) + (1 - \mu(\{\alpha\}))
\]
\[
= 1.
\]
To prove property 9., let $\mathcal{P}, \mathcal{Q}, \mathcal{R}, \mathcal{S}$ a family of four mutually disjoint subsets of $\Omega$, then

$$F_{\mathcal{P}, \mathcal{Q}, \mathcal{R}, \mathcal{S}} := \left( \prod_{\omega \in \mathcal{P}} \mu(\{\omega\}) \prod_{\omega \in \mathcal{Q}} (1 - \mu(\{\omega\})) \right) \left( \prod_{\omega \in \mathcal{R}} \mu(\{\omega\}) \prod_{\omega \in \mathcal{S}} (1 - \mu(\{\omega\})) \right),$$

$$= \left( \prod_{\omega \in \mathcal{P} \cup \mathcal{R}} \mu(\{\omega\}) \prod_{\omega \in \mathcal{Q} \cup \mathcal{S}} (1 - \mu(\{\omega\})) \right),$$

$$=: F_{\mathcal{P} \cup \mathcal{R}, \mathcal{Q} \cup \mathcal{S}}.$$ 

Finally, to prove property 10., let $\alpha$ be an element of $\Omega$ and $\mathcal{P}, \mathcal{Q}$ two disjoint susbets of $\Omega \setminus \{\alpha\}$, that is none of them contains $\alpha$. Using properties 8. and 9. we have

$$F_{\mathcal{P}, \mathcal{Q}} \overset{8}{=} \left( F_{\{\alpha\}, \emptyset} + F_{\emptyset, \{\alpha\}} \right) F_{\mathcal{P}, \mathcal{Q}},$$

$$= F_{\{\alpha\}, \emptyset} F_{\mathcal{P}, \mathcal{Q}} + F_{\emptyset, \{\alpha\}} F_{\mathcal{P}, \mathcal{Q}},$$

$$\overset{9}{=} F_{\mathcal{P} \cup \{\alpha\}, \mathcal{Q}} + F_{\mathcal{P}, \mathcal{Q} \cup \{\alpha\}}.$$ 

Let us now do the following calculation starting from $F_{\{\omega_1\}, \emptyset}$ and using $|\Omega| - 1$ times property 8,

$$F_{\{\omega_1\}, \emptyset} \overset{8}{=} F_{\{\omega_1\}, \emptyset} \left( F_{\{\omega_2\}, \emptyset} + F_{\emptyset, \{\omega_2\}} \right) \left( F_{\{\omega_3\}, \emptyset} + F_{\emptyset, \{\omega_3\}} \right) \cdots \left( F_{\{\omega_{\Omega-1}\}, \emptyset} + F_{\emptyset, \{\omega_{\Omega-1}\}} \right),$$

$$= F_{\{\omega_1\}, \emptyset} \left( \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\omega_1\})} \prod_{\omega \in (\Omega \setminus \{\omega_1\}) \setminus \mathcal{P}} F_{\omega, \emptyset} \prod_{\omega \in (\Omega \setminus \{\omega_1\}) \setminus \mathcal{P}} F_{\emptyset, \omega} \right),$$

$$\overset{9}{=} F_{\{\omega_1\}, \emptyset} \left( \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\omega_1\})} F_{\mathcal{P}, \emptyset} \cdot F_{\emptyset, (\Omega \setminus \{\omega_1\}) \setminus \mathcal{P}} \right),$$

$$\overset{9}{=} F_{\{\omega_1\}, \emptyset} \left( \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\omega_1\})} F_{\mathcal{P}, (\Omega \setminus \{\omega_1\}) \setminus \mathcal{P}} \right),$$

by noticing that each term of the expansion contains either $F_{\{\omega_k\}, \emptyset}$ or $F_{\emptyset, \{\omega_k\}}$, for a given $\omega$ of $\Omega \setminus \{\omega_1\}$. Each term of the expansion is then a unique partition $(\mathcal{P}, (\Omega \setminus \{\omega_1\}) \setminus \mathcal{P})$ of $\Omega \setminus \{\omega_1\}$, whence the sum index.

Including $F_{\{\omega_1\}, \emptyset}$ in the sum, we have

$$F_{\{\omega_1\}, \emptyset} = \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\omega_1\})} F_{\{\omega_1\}, \emptyset} F_{\mathcal{P}, (\Omega \setminus \{\omega_1\}) \setminus \mathcal{P}},$$

$$\overset{9}{=} \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\omega_1\})} F_{\mathcal{P}, \emptyset} \cdot F_{\emptyset, (\Omega \setminus \{\omega_1\}) \setminus \mathcal{P}},$$

$$= \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\omega_1\})} F_{\mathcal{P}, \emptyset} \cdot F_{\emptyset, \Omega \setminus \mathcal{P}}.$$ 

The same calculation can be done for each $\omega$ of $\Omega$. The following equality holds
∀ω ∈ Ω, F_{\{\omega\}} = \sum_{\mathcal{P} \in \mathcal{P}(\Omega) \ni \omega} |\mathcal{P}| F_{\mathcal{P}, \Omega \setminus \mathcal{P}}. \quad (D.2)

Let us now do the following calculation

\begin{align*}
1 \overset{\text{(D.1)}}{=} & \sum_{\omega \in \Omega} \mu(\{\omega\}), \\
6. \overset{\text{=} \text{(D.2)}}{=} & \sum_{\omega \in \Omega} F_{\{\omega\}}, \\
= & \sum_{\omega \in \Omega} \sum_{\mathcal{P} \in \mathcal{P}(\Omega) \ni \omega} |\mathcal{P}| F_{\mathcal{P}, \Omega \setminus \mathcal{P}}, \\
= & \sum_{\mathcal{P} \in \mathcal{P}(\Omega)} \sum_{\omega \in \mathcal{P}} F_{\mathcal{P}, \Omega \setminus \mathcal{P}}, \\
= & \sum_{\mathcal{P} \in \mathcal{P}(\Omega)} \sum_{\omega \in \mathcal{P}} F_{\mathcal{P}, \Omega \setminus \mathcal{P}}, \\
= & \sum_{\mathcal{P} \in \mathcal{P}(\Omega)} |\mathcal{P}|.
\end{align*}

Thus we proved that

\sum_{\mathcal{P} \in \mathcal{P}(\Omega)} |\mathcal{P}| F_{\mathcal{P}, \Omega \setminus \mathcal{P}} = 1. \quad (D.3)

Let us now reversely apply the previous argument to the sum \( \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} |\mathcal{P}| F_{\mathcal{P}, (\Omega \setminus \{\alpha\}) \setminus \mathcal{P}}, \forall \alpha \in \Omega \) (note that \( \Omega \) is replaced by \( \Omega \setminus \{\alpha\} \)). We have

\begin{align*}
\sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} |\mathcal{P}| F_{\mathcal{P}, (\Omega \setminus \{\alpha\}) \setminus \mathcal{P}} &= \sum_{\omega \in \Omega \setminus \{\alpha\}} \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} F_{\mathcal{P}, (\Omega \setminus \{\alpha\}) \setminus \mathcal{P}} ,
\overset{\text{(D.2)}}{=} & \sum_{\omega \in \Omega \setminus \{\alpha\}} F_{\{\omega\}}, \\
6. \overset{\text{=} \text{(})}{=} & \sum_{\omega \in \Omega \setminus \{\alpha\}} \mu(\{\omega\}), \\
= & \sum_{\omega \in \Omega} \mu(\{\omega\}) - \mu(\{\alpha\}), \\
\overset{\text{(D.1)}}{=} & 1 - \mu(\{\alpha\}). \quad (D.4)
\end{align*}

It is then straightforward that
\[
\sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} |\mathcal{P}| F_{\mathcal{P},\Omega \setminus \{\alpha\}} = \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} |\mathcal{P}| F_{\emptyset,\{\alpha\}} F_{\mathcal{P},(\Omega \setminus \{\alpha\}) \setminus \{\alpha\}} \\
= F_{\emptyset,\Omega} \left( \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} |\mathcal{P}| F_{\mathcal{P},(\Omega \setminus \{\alpha\})\setminus \{\alpha\}} \right), \\
7. \text{ and } (D.4) \quad (1 - \mu(\{\alpha\}))(1 - \mu(\{\alpha\}))
\]

that is

\[
\forall \alpha \in \Omega, \quad \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} |\mathcal{P}| F_{\mathcal{P},\Omega \setminus \{\alpha\}} = (1 - \mu(\{\alpha\}))^2.
\]

Finally, we have \(\forall \alpha \in \Omega,\)

\[
\sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} |\mathcal{P}| F_{\mathcal{P},\Omega \setminus \{\alpha\}} = \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} |\mathcal{P}| \left( F_{\mathcal{P},\Omega \setminus \{\alpha\}} - F_{\mathcal{P} \setminus \{\alpha\}, (\Omega \setminus \{\alpha\}) \cup \{\alpha\}} \right), \\
= \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} |\mathcal{P}| F_{\mathcal{P},\Omega \setminus \{\alpha\}} - \sum_{\mathcal{P} \in \mathcal{P}(\Omega \setminus \{\alpha\})} |\mathcal{P}| F_{\mathcal{P} \setminus \{\alpha\}, (\Omega \setminus \{\alpha\}) \cup \{\alpha\}}, \\
= \sum_{\mathcal{P} \in \mathcal{P}(\Omega) \setminus \{\alpha\}} |\mathcal{P}| F_{\mathcal{P},\Omega} - \sum_{\mathcal{P} \in \mathcal{P}(\Omega)} |\mathcal{P}| F_{\mathcal{P} \setminus \{\alpha\}}, (\Omega \setminus \{\alpha\}) \cup \{\alpha\},
\]

(D.3) and (D.5) \quad \quad 1 - (1 - \mu(\{\alpha\}))^2, \\
= 1 - 1 + 2\mu(\{\alpha\}) - \mu(\{\alpha\})^2, \\
= \mu(\{\alpha\}) (2 - \mu(\{\alpha\})).
\]

Now, by identifying \(\Omega\) to host class \(d\), \(\omega_k\) to genotypes, \(\mu(\{\omega_k\})\) to genotypes frequencies \(\sum_{\ell \in d} x_{d,\ell}\), it is straightforward that (D.3) implies (4.4) and (D.6) implies (4.5).

The curve of \(\beta_{d,k}\) as a function of \(x_{d,k}\) is given in Figure 4.
The plateau corresponds to the overall transmission rate $\beta$, and is the limit of genotype $k$ transmission rate when its frequency goes to 1, that is

$$\lim_{x_{d,k} \to \infty} \beta_{d,k} = \lim_{x_{d,k} \to \infty} \beta \frac{x_{d,k}}{\sum_{\ell \in d} x_{d,\ell}} \left(2 - \frac{x_{d,k}}{\sum_{\ell \in d} x_{d,\ell}}\right),$$

$$= \beta \lim_{x_{d,k} \to \infty} \frac{1}{1 + \sum_{\ell \in d \setminus \{k\}} \frac{x_{d,\ell}}{x_{d,k}}} \left(2 - \frac{x_{d,k}}{x_{d,k} \left(1 + \sum_{\ell \in d \setminus \{k\}} \frac{x_{d,\ell}}{x_{d,k}}\right)}\right),$$

$$= \beta.$$

However, the transmission rate of genotype $k$ reaches half of the overall transmission rate relatively quickly. Indeed, if we denote $x_{d,0.5}$ the parasite load that satisfies the following equation

$$\beta \frac{x_{d,0.5}}{\sum_{\ell \in d} x_{d,\ell}} \left(2 - \frac{x_{d,0.5}}{\sum_{\ell \in d} x_{d,\ell}}\right) = \frac{\beta}{2},$$

we have

$$\left(\frac{x_{d,0.5}}{\sum_{\ell \in d} x_{d,\ell}}\right)^2 - 2 \frac{x_{d,0.5}}{\sum_{\ell \in d} x_{d,\ell}} + \frac{1}{2} = 0.$$  

The discriminant of this polynomial is $\Delta = 2$ so its only root lying in $[0; 1]$ is

$$\frac{x_{d,0.5}}{\sum_{\ell \in d} x_{d,\ell}} = \frac{+2 - \sqrt{2}}{2} = 1 - \frac{\sqrt{2}}{2} \approx 29\%.$$

Figure 4: Transmission rate of genotype $k$ from hosts $d$ as a function of the parasite load of genotype $k$ (the parasite loads of the other genotypes being fixed), for $|d| \geq 2$. 
If we denote by $\bar{x}_{d,0}$ the average parasite load of the $|d| - 1$ other genotypes in $d$, the half overall transmission parasite load $x_{d,0.5}$ is

$$x_{d,0.5} = \left(1 - \frac{\sqrt{2}}{2}\right) (x_{d,0.5} + (|d| - 1) \bar{x}_{d,0}),$$

$$= \frac{1 - \sqrt{2}}{\frac{2}{2}} (|d| - 1) \bar{x}_{d,0},$$

$$= \left(\sqrt{2} - 1\right) (|d| - 1) \bar{x}_{d,0},$$

where $\sqrt{2} - 1 \approx 41\%$. A numerical application shows that $x_{d,0.5}$ is smaller than $\bar{x}_{d,0}$ only in bi- and tri-infected hosts.

The main result of this calculation is that whatever the rank of the coinfected host class (provided that $|d| \geq 2$), a given genotype is involved in at least half of the transmissions if its frequency is higher than about 29% (reminding us that the sum of the parasite transmission rates can be greater than the overall transmission rate because of shared inoculas).

D.2 Labelled forms of between-host equations

Based on the labelling previously defined, we present here the labelled alternative forms of the equations and rates written in the set-theoretic form in the main text. We also detail the master equation matrices, for readers interested in computing the model. Thereafter $\delta_{a,b}$ refers to the Kronecker’s delta, which is 1 if $a = b$ and 0 otherwise.

D.2.1 Between-host ODEs

The labelled form of the between-host ODEs is the following

$$\frac{dI_i}{dt} = \sum_{r=0}^{2^n-2} \sum_{d=0}^{2^n-1} \beta_{r,d,i} I_r I_d + \sum_{d=0}^{2^n-1} \theta_{d,i} I_d - \left(\sum_{d=0}^{2^n-1} \sum_{\ell=0}^{2^n-1} \beta_{i,d,\ell} I_d + \sum_{\ell=0}^{2^n-1} \theta_{i,\ell} + \mu_i\right) I_i,$$

$$\frac{dS}{dt} = \sum_{d=0}^{2^n-1} \mu_d I_d + \sum_{r=0}^{2^n-1} \sum_{d=0}^{2^n-1} \beta_{r,d,0} I_r I_d + \sum_{d=0}^{2^n-1} \theta_{d,0} I_d - \sum_{d=0}^{2^n-1} \sum_{\ell=0}^{2^n-1} \beta_{0,d,\ell} I_d S.$$  

D.2.2 Infection rates

The labelled form of the infection rates is the following

$$\beta_{r,d,i} := \beta \varsigma(r) \varsigma(d) \varsigma(i) \left(1 - \delta_{r,i}\right) \sum_{p=0}^{2^n-1} \left(\min_{k \in [1,|d|]} \left(\delta_{c_{d,k},c_{d,k}+c_{p,k}-c_{d,k},c_{p,k}}\right) \delta_{i,\phi(r,p)} n_p \right) \prod_{k=1}^{n} \frac{\left(2 \delta_{c_{p,k},1} - 1\right) x_{d,k} + \left(1 - \delta_{c_{p,k},1}\right) \sum_{\ell=1}^{n} x_{d,\ell}}{\sum_{\ell=1}^{n} x_{d,\ell}},$$

where

1. $\beta$ is the constant transmission factor,
2. $\varsigma(r) \varsigma(d) \varsigma(i)$ cancels out if one of the three involved classes is not epidemiological,
3. \((1 - \delta_{r,i})\) cancels out if the infection event is trivial (the receiver class is already the output),

4. \(\sum_{p=0}^{n-1}\) is the sum over all inocula,

5. \(\min_{k \in [1,n]} \left( \delta_{c_{d,k},c_{d,k}+c_{p,k} - c_{d,k}c_{p,k}} \right)\) cancels out whenever a genotype belongs to \(p\) but not to \(d\) (ensuring that inoculum \(p\) can be produced by donor host \(d\)),

6. \(\delta_{i,\phi}(r,p)\) cancels out whenever host class \(r\) does not turn into host class \(i\) when infected by inoculum class \(p\),

7. \(n_p\) is the rank of the inoculum class,

8. \(\prod_{k=1}^{n_p}\) is the product over all genotypes (nested in the inocula),

9. \(\sum_{k=1}^{n_p} (2\delta_{p,k,1} - 1)(1 - \delta_{d,i})\) cancels out whenever host class \(d\) does not turn into host class \(i\) when losing genotype \(k\).

D.2.3 Recovery rates

The labelled form of the recovery rates is the following

\[
\theta_{d,i} := \theta \varsigma (d) (1 - \delta_{d,i}) \sum_{k=1}^{n_p} \delta_{i,\phi(0,c_{d,k}(d-2^k-1))},
\]

where

1. \(\theta\) is the constant recovery factor,

2. \(\varsigma (d)\) cancels out if the recovering class is not epidemiologically meaningful,

3. \((1 - \delta_{r,i})\) cancels out if the recovery event is trivial (the recovering class is already the output),

4. \(\sum_{k=1}^{n_p}\) is the sum over all genotypes,

5. \(\delta_{i,\phi(0,c_{d,k}(d-2^k-1))}\) cancels out whenever host class \(d\) does not turn into host class \(i\) when losing genotype \(k\).

D.2.4 Death rate

The labelled form of the death rates is the following

\[
\mu_i := \mu \sum_{k=1}^{n_p} x_{d,k}.
\]

D.2.5 Master equation matrices

Recall that the master equation of between-host dynamics is:

\[
\frac{d}{dt} \mathbf{y} = \Phi. (\mathbf{y} \otimes \mathbf{y}) - (\Phi. \mathbf{y}) \otimes \mathbf{y} + (\Xi - \Theta - \Delta). \mathbf{y}.
\]
The expression of each matrix are the following:

\[
\Phi := \left( \beta_{i,j,\ell} \right)_{(i,j) \in [0;2^{n-1}] \times [0;2^{n-1}], (\ell,J) \in [0;2^{n-1}]^2}, \\
\tau (j) := \left\lfloor \frac{j}{2^n} \right\rfloor, \quad \vartheta (j) := \text{mod}_{2^n} (j), \\
\Psi := \left( \sum_{\ell=0}^{2^n-1} \beta_{i,j,\ell} \right)_{(i,j) \in [0;2^{n-1}]^2}, \\
\Xi := (\theta_{i,j})_{(i,j) \in [0;2^{n-1}]^2}, \\
\Theta := \left( \delta_{i,j} \sum_{\ell=0}^{2^n-1} \theta_{i,\ell} \right)_{(i,j) \in [0;2^{n-1}]^2}, \\
\Delta := ((\delta_{i,j} (1 - \delta_{i,0}) - \delta_{i,0}) \mu_j)_{(i,j) \in [0;2^{n-1}]^2}.
\]

Note that the \( \Phi \) matrix has a nested structure (donor host classes are nested into receiver host classes) that requires arithmetical calculation on indices, whence the \( \tau \) and \( \vartheta \) functions.

### E Basic reproduction numbers calculation

#### E.1 Next-generation basic reproduction number

The next-generation basic reproduction number, \( R_0^1 \), is derived from the susceptible steady state instability. First, we need to calculate the between infected hosts jacobian matrix, denoted by \( J_b \), the elements of which are found through the following partial derivative

\[
\frac{\partial}{\partial I_j} \left( \frac{dI_i}{dt} \right) = \sum_{(r,d) \in (E \setminus \{i\}) \times E^*} \beta_{r,d,i} \frac{\partial I_r}{\partial I_j} I_d + \sum_{d \in E^*} \theta_{d,i} \frac{dI_d}{\partial I_j} - \frac{\partial}{\partial I_j} \left( \sum_{(d,\ell) \in E^* \times (E \setminus \{i\})} \beta_{i,d,\ell} I_d + \sum_{\ell \in E \setminus \{i\}} \theta_{i,\ell} + \mu_i \right) I_i,
\]

where we used the fact that \( \beta_{j,j,i} = 0 \) since self class infection does not turn into another host class.

If \( i \neq j \), we have

\[
\frac{\partial}{\partial I_j} \left( \frac{dI_i}{dt} \right) = \sum_{r \in E \setminus \{i\}} \beta_{r,j,i} I_r + \sum_{d \in E^*} \beta_{j,d,i} I_d + \theta_{i,j} - I_i \sum_{\ell \in (E \setminus \{i\})} \beta_{i,j,\ell},
\]

and if \( i = j \),

\[
\frac{\partial}{\partial I_i} \left( \frac{dI_i}{dt} \right) = \sum_{r \in E \setminus \{i\}} \beta_{r,i,i} I_r + \sum_{d \in E^*} \beta_{i,d,i} I_d + \theta_{i,i} \sum_{\ell \in (E \setminus \{i\})} \beta_{i,i,\ell} - \left( \sum_{(d,\ell) \in E^* \times (E \setminus \{i\})} \beta_{i,d,\ell} I_d + \sum_{\ell \in E \setminus \{i\}} \theta_{i,\ell} + \mu_i \right),
\]

where we used the fact that \( \beta_{i,i,\ell} = 0 \) (see above), and \( \beta_{i,d,i} = 0 \) and \( \theta_{i,i} = 0 \) both because these events do not correspond to a flow between compartments.

In a fully susceptible host population, that is to say when \( \forall i \in E^*, I_i = 0 \) and \( I_0 = S = s^0 \), the expression are simplified as
and the between infected hosts jacobian matrix evaluated at susceptible steady state can be written as

\[
J_b \left( \mathbf{0}_{|\mathcal{E}^s|} \right) = \left( \beta_{\emptyset, j, i} s^0 + \left( 1 - \mathbb{1}_{\{i=j\}} \right) \theta_{j, i} - \mathbb{1}_{\{i=j\}} \left( \theta_{i, \bullet} + \mu_i \right) \right)_{(i, j) \in \mathcal{E}^{s^2}},
\]

where \( \bullet \) stands for the sum over the given index. Note that at this point there is still no need to order the classes (the diagonal holds whatever the order).

The next-generation theorem, as given in [41], is the following equivalence

\[
\forall \left( \mathbf{F}, \mathbf{V} \right) \in \mathfrak{M} (\mathbb{R}) \times GL_n (\mathbb{R}), \quad \left\{ \begin{array}{l}
\mathbf{J} = \mathbf{F} - \mathbf{V}, \\
\mathbf{F} \succeq 0, \\
\mathbf{V}^{-1} \succeq 0,
\end{array} \right. \quad \iff \quad \left( \begin{array}{l}
s (\mathbf{J}) \preceq 0 \iff \rho (\mathbf{F} \cdot \mathbf{V}^{-1}) \preceq 1,
\end{array} \right)
\]

where the spectral bound is defined as \( s (\mathbf{M}) := \max \{ \Re (\lambda_i), \lambda_i \in \text{Sp} (\mathbf{M}) \} \) and the spectral radius as \( \rho (\mathbf{M}) := \max \{|\lambda_i|, \lambda_i \in \text{Sp} (\mathbf{M})\} \).

In our case, the following matrices satisfy the assumptions of the next-generation theorem,

\[
\mathbf{F} := \left( \beta_{\emptyset, j, i} s^0 + \left( 1 - \mathbb{1}_{\{i=j\}} \right) \theta_{j, i} \right)_{(i, j) \in \mathcal{E}^{s^2}},
\]

\[
\mathbf{V} := \left( \mathbb{1}_{\{i=j\}} \left( \theta_{i, \bullet} + \mu_i \right) \right)_{(i, j) \in \mathcal{E}^{s^2}}.
\]

\( \mathbf{V} \) is diagonal, so its inverse is directly

\[
\mathbf{V}^{-1} = \left( \frac{\delta_{i, j}}{\theta_{i, \bullet} + \mu_i} \right)_{(i, j) \in \mathcal{E}^{s^2}},
\]

and the product of \( \mathbf{F} \) with \( \mathbf{V}^{-1} \) is

\[
\mathbf{F} \cdot \mathbf{V}^{-1} = \left( \frac{\beta_{\emptyset, j, i} s^0}{\theta_{j, \bullet} + \mu_j} \right)_{(i, j) \in \mathcal{E}^{s^2}}.
\]

A straightforward calculation of the spectrum of \( \mathbf{F} \cdot \mathbf{V}^{-1} \) requires to order the classes. To do so we use the labelling previously defined and replace bold indices by light indices with no loss of information. In this case, \( \beta_{\emptyset, j, i} \) becomes \( \beta_{0, j, i} \) with \((i, j) \in \{0; 2^n - 1\}^2 \). Therefore we have \( \beta_{0, j, i} = 0 \) for all \( j < i \).

Indeed, if a susceptible is infected by a donor \( j \), the resulting class \( i \) can only contain genotypes that donor \( j \) already has. Using the presence coefficients, we have

\[
\forall k \in \mathcal{G}, c_{i, k} \leq c_{j, k},
\]

\[
c_{i, k} 2^{k-1} \leq c_{j, k} 2^{k-1},
\]

then by summing over all \( k \), it follows that \( i < j \), from the presence coefficient property (see C.1).

The inequality \( i < j \) is a necessary condition for the event ‘turning a susceptible into a host \( i \)
through infection by $j'$ to occur. As a consequence, such an event does not occur if $j > i$, leading to $\beta_{0,j,i} = 0$ in this case. Thus, $F_jV^{-1}$ is a triangular matrix the eigenvalues of which are its diagonal terms

$$\text{Sp} = \left\{ \frac{\beta_{0,i,i} s^0}{\theta_{i,\bullet} + \mu_i} \right\}_{i \in \mathcal{E}^*}.$$  

Following the next-generation theorem, the basic reproduction number according to this method is then

$$R_0 = \max_{i \in \mathcal{E}^*} \left( \frac{\beta_{0,i,i} s^0}{\theta_{i,\bullet} + \mu_i} \right).$$

Explicitation of the infection, recovery and death rates finally gives

$$\frac{\beta_{0,i,i} s^0}{\theta_{i,\bullet} + \mu_i} = \beta s^0 (|i| \theta + \mu x_{i,\bullet})^{-1} \sum_{p \in \varphi(i)} \prod_{p \neq (\theta, p)} x_{i,k} \prod_{k \in c_{d,p}} \left( 1 - \frac{x_{i,k}}{x_{i,\bullet}} \right).$$

### E.2 Endemic basic reproduction number

An epidemic reaches an endemic state if and only if the sum of the infected host densities is positive at steady state. Such a condition is an alternative definition of the basic reproduction number, which we note $R_0$. Let us call $J$ the sum of the infected host densities, $J := \sum_{i \in \mathcal{E}^*} I_i$. The time derivative of $J$ is then

$$\frac{dJ}{dt} = \sum_{i \in \mathcal{E}^*} \frac{dI_i}{dt} = S \sum_{i \in \mathcal{E}^*} \sum_{d \in \mathcal{E}^*} \left( \sum_{\partial \varphi(d)} \beta_{0,d,i} \mu_d - \sum_{\partial \varphi(d)} \beta_{i,\partial \varphi(d)} \mu_d \mu_i - \sum_{\partial \varphi(d)} \beta_{i,\partial \varphi(d)} \mu_i \right),$$

$$= J \left( S \sum_{i \in \mathcal{E}^*} \sum_{d \in \mathcal{E}^*} \beta_{0,d,i} \mu_d - \sum_{i \in \mathcal{E}^*} \sum_{d \in \mathcal{E}^*} \beta_{i,\partial \varphi(d)} \mu_i \mu_d - \sum_{i \in \mathcal{E}^*} \sum_{d \in \mathcal{E}^*} \beta_{i,\partial \varphi(d)} \mu_i \mu_d \right).$$

We used here both the fact that the derivative is linear and that the only flows that come or leave the infected compartment $J$ as a whole are the ones related to the susceptibles, that is infection of the susceptibles, ultrainfection, recovery to the susceptibles and deaths. The last expression is written such that infection, recovery and death rates can be seen as weighted by the frequency of the associated hosts (for a given index). Using the marginal arithmetic mean notation, as in $\overline{y_{i,j}} := \sum_i y_{i,j} f_i$, we get at steady state

$$J \left( S \sum_{i \in \mathcal{E}^*} \beta_{0,i,i} - \sum_{i \in \mathcal{E}^*} I_i \beta_{0,i,\partial} - \beta_{0,\partial, \partial} \right) = 0. \quad (E.1)$$

Because infection flows are quadratic, another sum can be performed for the infection-related terms. While the second sum in (E.1) is straightforward, it is worth pointing out that in the first one, sums over the third index of $\beta_{a,b,c}$ do not need to be weighted since the overall infection flow does not depend on the density of the outcoming class of the infections (the total infection flow is given by the formula $\sum_{a,b} \beta_{a,b,c} I_a I_b$) but only on their number, which is $|\mathcal{E}^*|$. Assuming that $J \neq 0$, we have
\[ |E^*| \beta \, \hat{S} - \beta \, \hat{J} - \theta - \mu = 0. \]

Then, by using the fact that the population size is constant, that is \( \hat{S} + \hat{J} = s^0 \), it follows that

\[ \hat{J} = \frac{|E^*| \beta \, s^0 - \theta - \mu}{|E^*| \beta + \beta \, \theta}, \tag{E.2} \]

and this steady-state density is positive if and only if the following quantity, which defines \( R_{0}^{II} \), is greater than one,

\[ R_{0}^{II} = \frac{|E^*| \beta \, s^0}{\theta + \mu}. \]

Note that the three marginal arithmetic means involved in the latter formula depend on the densities of infected hosts at steady-state so they cannot be calculated directly from the parameters.

### E.3 Epidemiological feedback sensitivity

In order to see that the basic reproduction numbers can capture the epidemiological feedback, we arbitrarily decide to derive them twice with respect to the constant transmission factor \( \beta \), as if it were a variable. If the second derivative is 0, the basic reproduction number responds linearly to a change in epidemiological parameters, and hence cannot capture epidemiological feedbacks.

The next-generation basic reproduction number gives

\[
\frac{\partial R_{0}^{I}}{\partial \beta} = s^0 \max_{i \in E^*} \left( |i| \theta + \mu x_i, \right)^{-1} \sum_{p \in \varphi(i)} \left| \prod_{\phi(p) = i} \frac{u_{i,k}}{x_i} \prod_{k \in d \setminus p} \left( 1 - \frac{x_{i,k}}{x_i} \right) \right),
\]

then

\[
\frac{\partial^2 R_{0}^{I}}{\partial \beta^2} = 0.
\]

\( R_{0}^{I} \) cannot capture epidemiological feedbacks in any case.

The endemic basic reproduction number gives

\[
\frac{\partial R_{0}^{II}}{\partial \beta} = |E^*| \, s^0 \left( \frac{1}{\beta \, \theta + \mu} \frac{\partial \beta \, \beta \, \theta}{\partial \beta} + \beta \, \theta \frac{\partial}{\partial \beta} \left( \frac{1}{\beta \, \theta + \mu} \right) \right).
\]

Under the assumption of \( \frac{\partial R_{0}^{II}}{\partial \beta} = 0 \), we have

\[
\frac{\partial R_{0}^{II}}{\partial \beta} = |E^*| \, s^0 \frac{\beta \, \beta \, \theta}{\beta \, \theta + \mu},
\]

and
\( \partial^2 R_{II}^0 \frac{\partial^2}{\partial \beta^2} = \frac{|E^*| s^o}{\beta \cdot \beta + \mu^*} \left( \frac{\partial}{\partial \beta} \left( \frac{\beta \cdot \beta}{\beta^2} \right) \right), \)

\[ \Rightarrow \] \[ = 0. \]

The contraposition of this result is

\( \frac{\partial^2 R_{II}^0}{\partial \beta^2} \neq 0 \Rightarrow \frac{\partial I_i}{\partial \beta} \neq 0. \)

In other words, if we observe a non-zero second derivative of \( R_{II}^0 \) with respect to \( \beta \) in certain cases, \( R_{II}^0 \) does capture the epidemiological feedback.

**E.4 Basic reproduction numbers for \( n = 1 \)**

Let us consider only one parasite genotype (\( n = 1 \)), arbitrary denoted \( 1 \). Because of assumption (3.2), \( \{1\} \) is an epidemiological host class, carrying \( x_{\{1\},1} > 0 \) units of parasite load.

The between-host dynamics are at their simplest form because there are only two compartments, \( S \) and \( I_{\{1\}} \). The ODE the latter satisfies is sufficient to characterize these dynamics because of the constant population size assumption \( S + I_{\{1\}} = s^o \). We have

\[ \frac{dI_{\{1\}}}{dt} = \beta_{\{1\},1} S I_{\{1\}} - \theta_{\{1\},1} I_{\{1\}} - \mu_{\{1\}} I_{\{1\}}, \]

and, by explicitating infection, recovery and death rates, we get

\[ \frac{dI_{\{1\}}}{dt} = \beta S I_{\{1\}} - \theta I_{\{1\}} - \mu x_{\{1\},1} I_{\{1\}}, \]

\[ = \left( \beta \left( s^o - I_{\{1\}} \right) - \theta - \mu x_{\{1\},1} \right) I_{\{1\}}. \] (E.3)

The Jacobian matrix of the system is reduced to a single quantity, which is

\[ \frac{\partial}{\partial I_{\{1\}}} \left( \frac{dI_{\{1\}}}{dt} \right) = -2\beta I_{\{1\}} + \beta s^o - \theta - \mu x_{\{1\},1}. \]

The next-generation basic reproduction number \( R_{0}^1 \) is defined from the condition that this quantity evaluated at the disease-free equilibrium, that is \( I_{\{1\}}(0) = 0 \), is positive (unstable equilibrium), whence

\[ \frac{\partial}{\partial I_{\{1\}}} \left( \frac{dI_{\{1\}}}{dt} \right)(0) > 0 \iff R_{0}^1 > 1, R_{0}^1 = \frac{\beta s^o}{\theta + \mu x_{\{1\},1}}. \]

On the contrary, the endemic basic reproduction number involves the endemic steady-state value of \( I_{\{1\}} \). At the endemic steady-state, \( \frac{dI_{\{1\}}}{dt} = 0 \) and \( \hat{I}_{\{1\}} \neq 0 \), (E.3) then gives
\[
\beta \left( s^o - \bar{I}_{\{1\}} \right) - \theta - \mu x_{\{1\},1} = 0,
\]
\[
\bar{I}_{\{1\}} = s^o - \frac{\theta + \mu x_{\{1\},1}}{\beta},
\]

and the endemic basic reproduction number is defined from the condition that this quantity is positive, whence

\[
\bar{I}_{\{1\}} > 0 \iff \mathcal{R}_{II} > 1, \mathcal{R}_{II} = \frac{\beta s^o}{\theta + \mu x_{\{1\},1}}.
\]

We have proved that for \( n = 1 \) the two methods lead to the same basic reproduction number,

\[
\mathcal{R}_0 = \mathcal{R}_{II}.
\]
F Additionnal bibliography