Supplementary document. Derivation of IRN for autonomous systems

We begin by establishing notation, consistent with [31, 32] for convenience (see table 3 for a summary). Let $x = (x_1, ..., x_n)^T$, with each $x_i \geq 0$, denote the number of individuals in each compartment of a system, and let the infection dynamics of the system be described by $\dot{x} = f(x)$, where f is a vector such that $\dot{x}_i = f_i(x)$. The system's BRN, R_0, can then be defined using next-generation methods [8, 31].

Now suppose that there are k different infections ($k \leq n$), either multiple strains of the same pathogen or infections of different types, and let $A \subseteq \{1, ..., k\}$ be a subset of these infections assumed resident within the population. Any other infections (not in A) which appear are then considered invading infections. This structure provides a context against which to define IRNs.

Just as in deriving a BRN, the first step in next-generation operator methods is epidemiological. To derive an IRN with respect to a set A of resident infections, one begins by reclassifying all resident infections as non-infected. Now one can calculate the invasion reproductive number of all the infections not in A with respect to all the infections in A, that is, the IRN of A_c where A_c denotes the complement of A in $\{1, \ldots, k\}$. This invasion reproductive number will be denoted as $_A\tilde{R}_0$, in order to specify the set of infections assumed resident. The IRN is calculated for the set of infections $j \in A_c$ and so only those classes with such infection(s), including single and co-infected classes, are considered to be infected. The invasion reproductive number is then the expected number of secondary cases that one infected individual with some infection $j \in A_c$ produces in a population where all (and only) infections in A are resident.

The system's compartments are then arranged so that the first m compartments correspond to infected individuals with infections from A_c. Define $\mathbf{E}_A$ to be the set of all A_c-infection free states, that is,

$$\mathbf{E}_A = \{x \geq 0 | x_i = 0, i = 1, ..., m\}. \tag{27}$$

Let $\mathscr{F}_i(x)$ be the rate of new infections in compartment i, $\mathscr{V}_i^+(x)$ be the rate of transfer into compartment i by all other means, and $\mathscr{V}_i^-(x)$ be the rate of transfer out of compartment i. Assume that each function is continuously differentiable at least twice in each variable. Now the model becomes:

$$\dot{x}_i = f_i(x) = \mathscr{F}_i(x) - \mathscr{V}_i(x), i = 1, ..., n, \tag{28}$$

where $\mathscr{V}_i = \mathscr{V}_i^- - \mathscr{V}_i^+$. In addition, these functions need to satisfy the following assumptions:

- (A1) If $x \geq 0$, then $\mathscr{F}_i, \mathscr{V}_i^+, \mathscr{V}_i^- \geq 0$ for $i = 1, ...n$

- (A2) If $x_i = 0$ then $\mathscr{V}_i^- = 0$. If $x \in \mathbf{E}_A$, then $\mathscr{V}_i^- = 0$ for $i = 1, ...m$

- (A3) $\mathscr{F}_i = 0$ if $i > m$

- (A4) If $x \in \mathbf{E}_A$ then $\mathscr{F}_i = 0$ and $\mathscr{V}_i^+ = 0$ for $i = 1, ...m$

- (A5) If $\mathscr{F}_i$ is set to zero, then all eigenvalues of $Df(x_0)$ have negative real parts, for some A-endemic equilibrium, $x_0 \in \mathbf{E}_A$.

For (A3), no new invading infections can happen in those classes that are considered non-infected classes. (A4) states that if the system is at a state free of infections in A_c, then it will stay that way. (A5) states that there is an A-endemic equilibrium which is locally stable in the A_c-free subspace, $\mathbf{E}_A$. This last condition requires, in turn, additional conditions, in general that reproductive numbers for the A-only subsystem be greater than 1, which is an existence criterion for the A-endemic equilibrium. This allows the matrix $Df(x_0)$ to be partitioned using the following lemma.

Lemma 2. *Assume that for the subsystem of system* (28) *beginning with component* $m+1$ *(i.e., excluding all invading infections), all BRNs and IRNs exceed 1. If* $x_0 \in \mathbf{E}_A$ *is an equilibrium free of infections in* A_c *and* $f_i(x)$ *satisfies (A1)–(A5), then the derivatives* $D\mathscr{F}(x_0)$ *and* $D\mathscr{V}(x_0)$ *are partitioned as*

$$D\mathscr{F}(x_0) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}, D\mathscr{V}(x_0) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix}$$

where F *and* V *are the* $m \times m$ *matrices defined by*

$$F = \left[\frac{\partial \mathscr{F}_i}{\partial x_j}(x_0)\right] \qquad V = \left[\frac{\partial \mathscr{V}_i}{\partial x_j}(x_0)\right] \qquad 1 \leq i, j \leq m.$$

Further, F *is non-negative,* V *is a non-singular* M*-matrix and all eigenvalues of* J_4 *have positive real part.*

The proof is similar to [31]. The difference here in the Lemma is that it requires that all A-only reproductive numbers exceed 1 in the hypothesis. This is important in order to distinguish between a disease-free equilibrium and an A_c-free equilibrium. Requiring that $R_0 > 1$, for instance, ensures that the disease-free equilibrium can never be stable.

Now the invasion reproductive number can be calculated. The goal here is to see if the extension of the method for the BRN gives the same threshold behavior for the IRN for some A_c-infection free equilibrium. That is, if all reproductive numbers in the A-only subsystem exceed 1 and $_A\tilde{R}_0 < 1$, then the A_c-infection free equilibrium, x_0, is stable, but if $_A\tilde{R}_0 > 1$ then it is unstable. Recall that the invasion reproductive number is the expected number of secondary cases one infected individual with some infection $j \in A_c$ produces in a population where all (and only) infections in A are resident. This definition can be interpreted by looking at the entries of FV^{-1}. Thus we can mathematically define $_A\tilde{R}_0$ as:

$$_A\tilde{R}_0 = \rho(FV^{-1}) \tag{29}$$

where $\rho(A)$ is the spectral radius of the matrix A. This leads to the following theorem.

Lemma 3. *Consider the disease transmission model given by (28) with $f(x)$ satisfying conditions (A1)–(A5). Assume that all reproductive numbers in the A-only subsystem exceed 1. If x_0 is an A_c-infection free equilibrium of the model, then x_0 is locally asymptotically stable if $_A\tilde{R}_0 < 1$, but unstable if $_A\tilde{R}_0 > 1$, where $_A\tilde{R}_0$ is as defined in (29).*

The proof proceeds in a similar way to [31], the differences being epidemiologically as described above where only those infections from A_c are considered infected.

A	Set of resident pathogens
A_c	Set of invading pathogens
f	Vector of compartmental population growth rates
k	Total number of pathogens cocirculating in the population
m	Number of compartments involving invading (A_c) pathogens
n	Total number of compartments/classes
R_0	Overall BRN for the entire system
R_i	BRN for pathogen i
$_A\tilde{R}_0$	Overall IRN when [all] pathogens in A are resident
$_A\tilde{R}_T$	Time-average RN for periodic system with pathogens in A resident
$_A\tilde{R}_i$	IRN of pathogen $i \in A_c$ when [all] pathogens in A are resident
$\tilde{R}_i$	IRN of pathogen i in a two-pathogen system where the other pathogen is assumed resident
x	State vector of all compartments/classes
$x_i(t)$	Number of individuals in compartment i at time t

Table 3: Notation