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Competitive epidemic spreading over networks

Mengbin Ye, *Member, IEEE*, and Brian D.O. Anderson, *Life Fellow, IEEE*

***Abstract*— In this letter, we consider an epidemic model for two competitive viruses spreading over a metapopulation network, termed the 'bivirus model' for convenience. The dynamics are described by a networked continuous-time dynamical system, with each node representing a population and edges representing infection pathways for the viruses. We survey existing results on the bivirus model beginning with the nature of the equilibria, including whether they are isolated, and where they exist within the state space with the corresponding interpretation in the context of epidemics. We identify key convergence results, including the conclusion that for generic system parameters, global convergence occurs for almost all initial conditions. Conditions relating to the stability properties of various equilibria are also presented. In presenting these results, we also recall some of the key tools and theories used to secure them. We conclude by discussing the various open problems, ranging from control and network optimization, to further characterization of equilibria, and finally extensions such as modeling three or more viruses.**

***Index Terms*— infectious disease, multivirus, bivirus, complex networks, Susceptible–Infected–Susceptible, compartmental model**

I. Introduction

MATHEMATICAL models of infectious disease spread have become a central tool for scientists and policy-makers to study and respond to epidemic outbreaks [1], [2]. The recent COVID-19 pandemic has resulted in an explosion in interest in such models across multiple research disciplines, including the systems and control community [2]–[5].

The most popular and well-studied paradigm is that of *compartmental models*: each individual in a population belongs to one of several different *health compartments* that represent the state of the disease for that individual, with transitions between states capturing the disease progression characteristics for the particular disease of interest. Two seminal frameworks are that of Susceptible–Infected–Susceptible (SIS) and Susceptible–Infected–Removed (SIR) [1], [3], [4]. In both, infected individual can transmit the disease to susceptible individuals at a given *infection rate*. Infected individuals can recover from the disease at a given *recovery rate*, and the key difference is that for the SIS framework, there is no temporary or permanent immunity following recovery, i.e. an individual immediately becomes susceptible again. In contrast, the SIR framework posits that permanent immunity is endowed to recovered individuals who are hence removed from the pool of individuals susceptible to the disease.

COVID-19 has resulted in a surge of interest and literature: initial assumptions that permanent immunity was acquired after recovery led to use of SIR and SIR-type models, while recent recognition that immunity may be temporary or wane has led to consideration of SIRS-type models [1], [6]. However, this paper will focus instead on an SIS framework, not only to shed light on other interesting models and results, but to establish the concrete understanding needed as a precursor to more complex SIRS-type competitive virus dynamics.

This paper is concerned with the competitive spread of two infectious diseases (termed virus 1 and virus 2 for convenience – for the purposes of this paper, we can ignore the medical nonequivalence of 'disease' and 'virus'.) over a networked metapopulation in the SIS framework. Each node of the directed network represents a population, and each individual can be infected with virus 1 only, infected with virus 2 only, or susceptible to both viruses – the competitive nature means an individual cannot be infected with both viruses simultaneously. Infection can occur between a susceptible and an infected individual of the same population, or from different populations – the (directed) edges of the network represent infection pathways. The infection pathways for the two viruses can be different (as can the infection rates and recovery rates), meaning the edge sets defining the spread of the two viruses can be different. A standard assumption imposed in the literature is that the spreading network for each virus is strongly connected, which means that there exists a path of edges from every node to every other node.

We term the model as the 'SIS bivirus network model', or 'bivirus model' for short, and it is studied as a continuous-time dynamical system. Used to study two generic competing viruses in [7] and two different strains of gonorrhea in [8], it has since been studied by various communities under different application contexts [9]–[12], and has recently found its way into the systems and control literature [13]–[16], including works by the authors [17], [18]. This paper will aim to survey the known results for the bivirus model, including the state-of-the-art in terms of convergence, equilibria, and stability properties. We then discuss a number of open directions, such as expansion to three or more viruses [14], [15], and control problems, including understanding the use of one virus to render the other extinct [15]. Our paper is focused on the analysis of the dynamical properties of the system, rather than on identification and estimation, and integration of data, which are other key issues for epidemic models in general [2], [5].

The key results can be summarized as answers to a set of

M. Ye is with the Centre for Optimisation and Decision Science, Curtin University, Perth 6102, Australia. (e-mail: mengbin.ye@curtin.edu.au). He is supported by the Western Australian Government through the Premier's Science Fellowship Program.

B.D.O. Anderson is with the School of Engineering, Australian National University, Canberra, Australia (e-mail: brian.anderson@anu.edu.au).

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problems concerning the bivirus dynamical system. Namely,

1) What is the limiting behaviour that is possible? E.g. do trajectories converge to an equilibrium, are there limit cycles, and can chaos occur?
2) What is the nature of the equilibria, including whether they are isolated, and if so, how many equilibria can there be? Importantly, we must consider what the equilibria represent in the modeling context, e.g. whether no virus is present in any population in the network, or one virus is endemic and the other extinct, or both viruses coexist.
3) What are the stability properties of the equilibria, and what are the regions of attraction, global and otherwise, for equilibria or limit cycles?
4) Are there special cases of interest, such as a continuum of equilibria where both viruses coexist, or multiple attractive equilibria representing initial condition-dependent virus propagation outcomes?

The results we cover revolve around identifying model parameter properties or values, which are infection and recovery rates in our situation, that provide answers to the above questions. This includes establishing the notion of generic parameters, and necessary and sufficient conditions, and sufficient conditions. There are key tools that we can draw upon from a range of dynamical systems, and control-theoretic literature, including monotone systems theory [19], linear algebra, Lyapunov theory, and algebraic geometry.

Next, we present the notations. Following this, Section II introduces the bivirus network model, and we then survey key results in Section III. The paper is concluded with a discussion on open problems in Section IV.

A. Notation

The n-column vector of all ones and zeros are given by $\mathbf{1}_n$ and $\mathbf{0}_n$, respectively. The $n \times n$ identity and $n \times m$ zero matrices are given by I_n and $\mathbf{0}_{n\times m}$, respectively. For a vector a and matrix A, we denote the i^{th} entry of a and $(i,j)^{th}$ entry of A as a_i and a_{ij}, respectively. For any two vectors $a, b \in \mathbb{R}^n$, we write $a \geq b$, $a > b$ and $a \gg b$ if for all $i \in \{1, 2, \ldots, n\}$, there holds respectively $a_i \geq b_i$, $a_i \geq b_i$ with $a_j > b_j$ for some j, and $a_i > b_i$. The same notation is used for real matrices $A, B \in \mathbb{R}^{n\times m}$ when the particular property is satisfied by $\mathrm{vec}(A)$ and $\mathrm{vec}(B)$. For scalars $a, b \in \mathbb{R}$, $a > b$ and $a \gg b$ are equivalent. For a real square matrix M with spectrum $\sigma(M)$, we use $\rho(M) = \max\{|\lambda| \ : \ \lambda \in \sigma(M)\}$ and $s(M) = \max\{\mathrm{Re}(\lambda) \ : \ \lambda \in \sigma(M)\}$ to denote respectively the spectral radius of M and spectral abscissa of M, viz. the largest real part among the eigenvalues of M. A matrix M is said to be *Hurwitz* if $s(M) < 0$.

II. Model for multivirus spreading dynamics

Understanding a model for multivirus spreading rests on a prior understanding of single virus spreading. For survey material on such problems, with much contextual content, see [3]–[5]. Here, we provide only a concise summary. Our work focuses on the Susceptible-Infected-Susceptible framework, which implies that no (temporary or permanent) immunity is gained by an individual after recovery from infection.

A. Single virus model

1) Modeling in a single population: Consider a single population of constant size, and suppose that individuals can transition between two compartments, viz. infected and susceptible (see Fig. 1a and consider only the green and orange compartments). We let $x(t)$ denote the fraction of the population infected with a virus at time t. The deterministic SIS model describes the transition between the compartments by positing that infections increase due to direct interaction between members of the infected fraction $x(t)$ and the susceptible fraction $1 - x(t)$, while infected members recover from the disease over time [3]. The dynamics are:

$$\dot{x} = -dx + b(1 - x)x. \tag{1}$$

Here $d > 0$ is the recovery rate parameter and $b > 0$ is the infection rate parameter. It is easy to see that with $x(0) \in [0, 1]$, there results $x(t) \in [0, 1]\, \forall t$. Moreover, $x = 0$ and, if the infection rate is greater than the recovery rate, $x = 1 - d/b$ are the only equilibria in $[0, 1]$, and they are termed 'healthy' and 'endemic' respectively. A more detailed analysis shows that 0 is exponentially stable if $d/b > 1$, asymptotically but not exponentially stable if $b = d$, and unstable if $d/b < 1$. Further, convergence always occurs to an equilibrium.

Since populations involve an integer count, the real value of x must be rational, and Eq. (1) can at best be an approximation. Sophisticated Markov chain models exist, whose mean field approximation as $n \to \infty$ is given by Eq. (1), see Refs. [3]–[5] for more details and original references.

2) Modeling a metapopulation: Next one can consider a single virus in a set of $n > 1$ populations, constituting a *metapopulation*, with infection pathways between populations potentially constrained by a network structure (see Fig. 1b). A key underlying assumption is that we assume intra-population homogeneity but allow for inter-population heterogeneity with respect to the disease. I.e., individuals within a population have the same recovery rate, and disease transmission between individuals depends only on the population they are in. Such an assumption is quite general, allowing a population to contain individuals distinguished by e.g. location, gender, or age[1].

In addition to the infection-recovery dynamics of the single population model, the disease may be transmitted to susceptible members of population i by infected members of population j (with $j = i$ permitted), thereby increasing the fraction x_i of infected individuals. This arrangement can be described by a simple generalization of Eq. (1), and is

$$\dot{x}_i = -d_i x_i + (1 - x_i) \sum_{j=1}^{n} b_{ij} x_j \quad i = 1, 2, \ldots, n \tag{2}$$

with all $0 < d_i < \infty$, while $0 \leq b_{ij} < \infty$. With $D = \mathrm{diag}(d_i)$, $B = (b_{ij})$ and $X = \mathrm{diag}(x_i)$, we can write

$$\dot{x} = -Dx + (I_n - X)Bx \tag{3}$$

It is useful to associate B with a network (graph) $\mathcal{G}$ with each node corresponding to a population, and an edge from

[1]The pioneering Ref. [20] considered the disease gonorrhea. In a simple $n = 2$ example, the two populations may represent males and females.

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node j to node i if and only if $b_{ij} > 0$. Almost all works assume B is irreducible, which is equivalent to G being strongly connected [21, p. 418]. If the strong connectivity condition fails, the metapopulation can be broken into two (or more) components, each component being a strongly connected subnetwork, with only unidirectional transmission from one component to the other. By interpreting unidirectional transmission (if any) as a time-varying input into a given component, each component can be analyzed separately using notions of Input-to-State stability, see Ref. [22] for details.

Paralleling the single population case, one finds that if $\mathbf{1}_n \geq x(0) \geq \mathbf{0}_n$, the same inequalities apply with $x(t)$ replacing $x(0)$ for all $t \geq 0$ [23]. We define the reproduction number[2] of the metapopulation as $\mathcal{R} \triangleq \rho(D^{-1}B)$, and if $\mathcal{R} < 1$, then the healthy equilibrium $\mathbf{0}_n$ is globally exponentially stable, while if $\mathcal{R} = 1$, convergence still occurs (globally) to $\mathbf{0}_n$ but it is not exponential. If however $\mathcal{R} > 1$, then from all initial states except the healthy state, convergence occurs to a unique nonzero endemic equilibrium, call it $\bar{x}$, with $\mathbf{1}_n \gg \bar{x} \gg \mathbf{0}_n$. For general n, D and B, no explicit expression for $\bar{x}$ is available (though computation is possible, either through simulation of the differential equations or recursive solution of the equilibrium equation). The proofs of convergence can be sophisticated, using as noted in [3] Lyapunov theory and positive systems theory.

It is perhaps remarkable that a nonlinear n-dimensional differential equation gives rise to such comparatively simple behavior, at least in the region of interest. As will be seen, there is a great contrast with the bivirus case.

B. Bivirus model

Bivirus models capture the situation where two viruses may be active, and most attention has been given to the *competitive* case, where each member of a population may be healthy, or infected with virus 1, or infected with virus 2, but never infected with both. See Fig. 1a. Work on metapopulations with two active viruses goes back some decades, see e.g. [8].

Going straight to a metapopulation scenario, let x_i^1, x_i^2 denote the fractions of population i infected with viruses 1 and 2 respectively, so that $1 - x_i^1 - x_i^2$ denotes the healthy fraction, which is 'susceptible' to infection by an individual belonging to the fraction x_j^1 or x_j^2 for any $j \in \{1, 2, \dots\}$. Building on the single virus model, that for the bivirus model involves adjusting the healthy fraction in the relevant equations appropriately, yields

$$\dot{x}_i^1 = -d_i^1 x_i^1 + (1 - x_i^1 - x_i^2) \sum_{j=1}^{n} b_{ij}^1 x_j^1, \tag{4a}$$

$$\dot{x}_i^2 = -d_i^2 x_i^2 + (1 - x_i^1 - x_i^2) \sum_{j=1}^{n} b_{ij}^2 x_j^1. \tag{4b}$$

[2]In epidemiology, the basic reproduction number $\mathcal{R}_0$ of a disease is the number of secondary infectious contacts a single infected individual is expected to generate in an entirely susceptible population. An epidemic outbreak is predicted to occur if $\mathcal{R}_0 > 1$. This concept maps conveniently to the relation between $\mathcal{R}$ and the limiting state of Eq. (3).

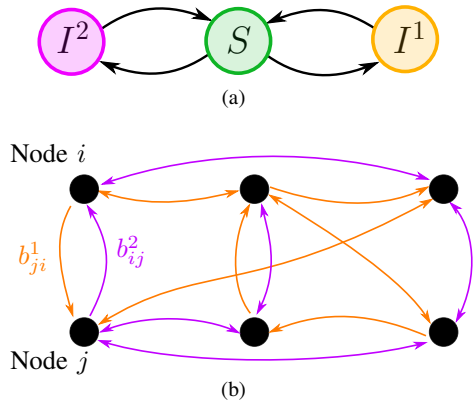

Fig. 1: Schematic of (a) the compartmental transitions and (b) metapopulation network. (a) Each individual exists in one of three health compartments: Susceptible (S), infected with virus 1 (I, orange), or infected with virus 2, (I, purple). Arrows represent possible transition paths between compartments. (b) Each black node represents a single population. The (directed) edge sets of the two viruses do not need to match, so that virus 1 (orange edges) can spread between a particular node pair, but virus 2 (purple edges) cannot, and vice versa.

With $x^k, k = 1, 2$ an n-dimensional vector of the x_i^k's, the more compact form is given by

$$\begin{aligned} \dot{x}^1 &= -D^1 x^1 + (I_n - X^1 - X^2) B^1 x^1 \\ \dot{x}^2 &= -D^2 x^2 + (I_n - X^1 - X^2) B^2 x^2, \end{aligned} \tag{5}$$

with obvious definition of D^k, B^k and $X^k = \mathrm{diag}(x_i^k)$, $k = 1, 2$. We impose the following standing assumption.

Assumption 1: For $k = 1, 2$, the matrices D^k are diagonal with positive diagonal entries, and the matrices B^k are nonnegative and irreducible.

Similar to the single virus case, we can thus consider two strongly connected directed networks associated with irreducible B^1 and B^2, capturing the infection pathways of virus 1 and virus 2 within and between the populations, see Fig. 1b. While the node set is the same (since we consider the n populations), the edge sets and their weights certainly are not necessarily the same. Indeed, it would be almost counter-intuitive to assume that two different viruses have the same edge set (transmission pathways) *and* the same edge weights (transmission intensity/strength).

1) The single population case: Models such as the above can of course be constructed for a single population, rather than a metapopulation. In that case there are just two scalar equations for fractions x^1 and x^2, and it is possible to perform an analysis rather like that for single virus systems. See Ref. [9] for a treatment. For generic values of the parameters, and if the healthy equilibrium is not attractive, a phenomenon termed *winner-takes-all* or *survival-of-the-fittest* is encountered, meaning that from any nonzero initial condition, one ends at an equilibrium state in which one virus is completely suppressed by the other. The 'winning' virus is that with the larger reproduction ratio (which is b^i/d^i for virus i).

Remark 1 (Stochastic vs. deterministic models): Although we consider deterministic metapopulation models, real-

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world epidemic processes are in fact stochastic [1], [3]. We touched on stochastic single virus models below Eq. (1), and connections between Eq. (5) and Markov chain models, including accuracy of approximation, are explored in Ref. [13]. Deterministic models are easier to analyze (computationally and theoretically), and may be suitable for modeling long term dynamics (convergence to equilibria, recurrent outbreaks, etc.). Meanwhile, stochastic models may better capture probabilistic events which may play important roles in the initial epidemic outbreak and transient dynamics, e.g. superspreader events [1], [6].

Remark 2 (Bivirus applications): The bivirus model was first presented in [8] to consider gonorrhea (virus 1) and a strain of drug-resistant gonorrhea (virus 2), and Eq. (5) has clear applications for studying two viruses (either different strains or entirely different pathogens) which cannot simultaneously occupy a host. Such a phenomenon is sometimes termed "viral interference", whereby the infection of a host by one virus prevents host infection by a second virus, and has been observed with rhinovirus and influenza [24], and between different influenza lineages [25]. Other works have considered the bivirus SIS models in more abstract contexts, such as competing internet rumours or products [9], and virus (virus 1) and vaccine (virus 2) dynamics [11].

III. Key results for the bivirus model

This section deals with the model Eq. (5) under Assumption 1. We discuss a number of properties, noting in each case the technical issues involved in obtaining the particular result, and discussing their importance from an epidemiological or dynamical systems perspective.

A. Invariance property

Obviously, one never expects the fractions of a population infected with either virus to be negative or for the two combined fractions to exceed one. This invariance property, as reported in [13, Lemma 8] and [17, Lemma 3.2], is formally captured as follows.

Lemma 1: If the initial conditions for Eq. (5) satisfy $\mathbf{0}_n \leq x^k(0) \leq \mathbf{1}_n$ (or $\mathbf{0}_n < x^k(0) < \mathbf{1}_n$) for $k = 1, 2$ and $x^1(0) + x^2(0) \leq \mathbf{1}_n$, then for all finite $t > 0$, there holds $\mathbf{0}_n \leq x^k(t) \leq \mathbf{1}_n$ (or $\mathbf{0}_n \ll x^k(t) \ll \mathbf{1}_n$) for $k = 1, 2$ and $x^1(t)+x^2(t) \leq \mathbf{1}_n$ (or $x^1(t) + x^2(t) \ll \mathbf{1}_n$).

For future reference, we shall define Ξ to be the set

$$\Xi = \{(x^1, x^2) \,|\, \mathbf{0}_n \leq x^k \leq \mathbf{1}_n \text{ for } k = 1, 2 \cap x^1 + x^2 \leq \mathbf{1}_n\},$$

and Ξ° to be its interior.

The result, showing that Ξ is an invariant set, can be obtained by a fairly standard argument encountered for positive or compartmental systems. In the light of this result, no attention is given to studying the model outside Ξ. There are also two invariant sets within Ξ: for $k = 1$ or 2, if $x^k(0) = 0$, then the system equation evidently yields $x^k(t) = 0 \forall t$. Logically, if one virus is not initially present, it is never present, and the system is effectively a single virus system. Lemma 1 also ensures that $x^k(t)$ retain their physical interpretations for all $t \geq 0$, i.e., the model is well-defined.

B. Are equilibria isolated?

Observe that $(\bar{x}^1, \bar{x}^2)$ is an equilibrium of Eq. (5) if:

$$\begin{aligned} -D^1\bar{x}^1 + (I_n - \bar{X}^1 - \bar{X}^2)B^1\bar{x}^1 &= \mathbf{0}_n, \\ -D^2\bar{x}^2 + (I_n - \bar{X}^1 - \bar{X}^2)B^2\bar{x}^2 &= \mathbf{0}_n, \end{aligned} \tag{6}$$

where $\bar{X}^k = \text{diag}(\bar{x}_i^k)$ for $k = 1, 2$. There are $2n$ scalar equations and $2n$ scalar unknowns. Unsurprisingly, for generic values of D^k, B^k, i.e. for all values obeying the sign constraints in Assumption 1 and avoiding certain algebraic sets defined by equalities in the entries of the matrices, the number of equilibria can be shown to be finite. A formal proof based on algebraic geometry can be found in Ref. [17].

Remark 3 (Importance of the genericity assumption): The qualification that the matrices D^k, B^k are generic is important. Several works have identified that a connected set containing an infinite number of equilibria can exist in Ξ° for special choices of D^k, B^k: [17] provides a general result dealing with such special choices, extending the earlier work of Ref. [9], [13]. In all cases, the set forms a segment of a straight line. It is an open question whether there are other nongeneric sets of parameter matrices which yield equilibrium sets with other geometric shapes. One can appreciate that for policymakers and public health planners, knowing a priori that one should expect isolated equilibria allows for more straightforward planning (which may be based on simulations), because the alternative is to have a continuum of equilibria.

C. Where are the equilibria?

The equilibria of the bivirus system can be split into three types, as we now describe.

1) The healthy equilibrium: There is self-evidently always the healthy equilibrium, with $(\bar{x}^1 = \mathbf{0}_n, \bar{x}^2 = \mathbf{0}_n)$.

2) Boundary equilibria: There can also be zero, one or two *boundary* equilibria. Define $\mathcal{R}^i = \rho((D^i)^{-1}B^i)$ as the reproduction number of virus i, for $i = 1, 2$. If one starts a trajectory with $x^2(0) = \mathbf{0}_n$, then as earlier argued, $x^2(t)$ is identically zero, and the system behaves as a single virus system. Accordingly, if and only if $\mathcal{R}^1 > 1$, there will be an equilibrium of the form $(\bar{x}^1 \gg \mathbf{0}_n, \bar{x}^2 = \mathbf{0}_n)$, where $\bar{x}^1$ is the unique endemic equilibrium of the single virus system defined by D^1, B^1. Likewise, if and only if $\mathcal{R}^2 = \rho(D^{-2}B^2) > 1$, there will be an equilibrium of the form $(\bar{x}^1 = \mathbf{0}_n, \bar{x}^2)$, where $\bar{x}^2$ is the unique endemic equilibrium of the single virus system defined by D^2, B^2.

If there should hold $\mathcal{R}^1 \leq 1$ for the bivirus system, one can argue formally, see [13], or heuristically, see [17], that the presence of virus 2 simply 'speeds up' the decay to zero of $x^1(t)$ as $t \to \infty$, which is the behavior that would occur in the absence of virus 2. When that occurs, the behavior of virus 2, as indicated by $x^2(t)$, follows what would occur in the single virus case, as predicted by the value of $\mathcal{R}^2$. An important consequence follows. *If either or both of the reproduction numbers $\mathcal{R}^i$ do not exceed 1, behavior of the bivirus system is essentially nothing more than the behavior of two single virus systems. Only if $\mathcal{R}^k > 1, k = 1, 2$ can we anticipate some*

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kind of behavior specific to the bivirus context, i.e. not just mimicking the single virus case.

3) Coexistence equilibria: Some bivirus-specific behavior is instanced by the third type of equilibria, which are termed *coexistence* equilibria. These are equilibria $(\bar{x}^1, \bar{x}^2)$ in which neither $\bar{x}^k$ is zero, with mild restrictions on their location.

Lemma 2: ([17, Lemma 3.1]). Any coexistence equilibrium has $\bar{x}^1 \gg \mathbf{0}_n, \bar{x}^2 \gg \mathbf{0}_n$ and $\bar{x}^1 + \bar{x}^2 \ll \mathbf{1}_n$. If $(\bar{x}^1, \bar{x}^2)$ and $(\bar{x}^1, \tilde{x}^2)$ are two coexistence equilibria, then $\bar{x}^2 = \tilde{x}^2$.

At a coexistence equilibrium, each node has a fraction of individuals in each health compartment, and there cannot exist two coexistence equilibria in which the equilibrium vector is the same for one virus and different for the other. The properties of a coexistence equilibrium $(\bar{x}^1, \bar{x}^2)$ are tied directly to the irreducibility of $B^k, k = 1, 2$ (or equivalently the strong connectedness of the associated graphs). Details on the arguments are found in the proof of [17, Lemma 3.1].

The existence of the boundary equilibria is directly tied to the values of $\mathcal{R}^i, i = 1, 2$, while their location is secured from existing results for Eq. (2). Significantly less can be said concerning coexistence equilibria, and characterization of their existence and associated properties remain important open questions, especially on directed networks. Obviously, if $\mathcal{R}^k \leq 1$ for either $k = 1, 2$, then based on the prior arguments dealing with boundary equilibria, there cannot exist a coexistence equilibrium. However, if $\mathcal{R}^k > 1$ for $k = 1, 2$, a key open challenge is in fact to establish how many (if any) coexistence equilibria exist as a function of the parameter matrices $D^k, B^k, k = 1, 2$. There are obvious public health management reasons for understanding the conditions for coexistence, as this informs health practitioners whether one requires medicine, health infrastructure, and trained personnel to deal with just one or both viruses in the long term.

So far, for $n = 1$, Ref. [9] establishes that there are never isolated coexistence equilibria, but rather for nongeneric parameter values there exists a continuum of coexistence equilibria; see Remark 3. The case of $n = 2$ was studied in [17, Section 3.2]– there can either be one or zero coexistence equilibrium (though this is by no means obvious)– and $n = 3$ with a special tree network topology was considered in [8]. For arbitrary $n \geq 3$, the findings in [12] were substantially extended in [26] (but for the highly restrictive case of undirected networks with homogeneous infection rates). For general directed networks, limited results are available [13], [15], [17]. Sufficient conditions on D^k, B^k for there to be *no* coexistence equilibria are given implicitly in [11], and explicitly in [15], [17].

It would be natural at this point to consider the stability of equilibria. It is however opportune to first address a number of properties of trajectories, before we investigate further their associated limits and equilibria generally.

D. Key properties of general trajectories and their limits

Having characterized the three distinct types of equilibria and some of their characteristics, we now state a general result, due to [17, Theorem 3.6] on the limiting points of trajectories. We comment on its implications, before discussing the key arguments used to secure this conclusion, arguments which form the foundation of additional results reported in the sequel.

Theorem 1: Suppose Eq. (5) has generic parameter matrices $D^i, B^i, i = 1, 2$, and hence there are a finite number of equilibria. Then, for all initial conditions $(x^1(0), x^2(0)) \in \Xi$, except possibly for a set of measure zero, the system Eq. (5) will converge to an equilibrium. This set of measure zero (if it exists) consists of nonattractive limit cycles and points on trajectories that converge to them.

This result establishes that chaos is not possible for the bivirus system in Eq. (5), and if a limit cycle exists, it is nonattractive. A nonattractive limit cycle is like a nonattractive equilibrium point. There may exist initial conditions for which the trajectories will approach the limit cycle as $t \to \infty$, but no point on the limit cycle has an open neighborhood such that all trajectories entering that neighborhood approach the limit cycle. As elaborated upon in [17] through arguments concerning basins of attraction, in addition to the convergence statement in Theorem 1, we further know that for all initial conditions except possible a set of measure zero, convergence occurs to a *stable* equilibrium. This is due to the fact that an unstable equilibrium may have associated with it a stable manifold of dimension less than $2n$, defined by trajectories which converge to it. Ruling out periodic behaviour for the bivirus model is important from an epidemiological context, as other epidemic model dynamics can in fact yield stable and attractive limit cycles, i.e., recurrent epidemic outbreaks [1].

The key to establishing this result is by analysis of the linearization of Eq. (5) about a general point $(x^1, x^2) \in \Xi$, viz. the Jacobian of Eq. (5), which we denote by $J(x^1, x^2)$. Defining $P = \mathrm{diag}(I_n, -I_n)$, one can compute that

$$PJ(x^1, x^2)P = \begin{bmatrix} Z_1(x^1, x^2) & \tilde{B}^1(x^1) \\ \tilde{B}^2(x^2) & Z_2(x^1, x^2) \end{bmatrix}, \qquad (7)$$

where $\tilde{B}^k(x^k) \triangleq \mathrm{diag}\,(B^k x^k)$, i.e. $\tilde{B}^k(x^k)$ is diagonal with i-th diagonal entry $\sum_j b^k_{ij} x^k_j$, and $Z_k(x^1, x^2) = -D^k - \tilde{B}^k(x^k) + (I_n - X^1 - X^2)B^k$ for $k = 1, 2$.

With all off-diagonal entries of $PJ(x^1, x^2)P$ nonnegative, we call such a matrix a *Metzler* matrix. This matrix is also irreducible for all $(x^1, x^2) \in \Xi^\circ$. These properties can be used to establish that Eq. (5) is a *monotone dynamical system* [17], and more specifically a *cooperative system* in the literature terminology. The results of Theorem 1 are established by drawing on the comprehensive literature on monotone systems.

A key property of cooperative monotone systems is a trajectory ordering property, which can be summarized as follows. Consider two initial conditions $(x^1_A(0), x^2_A(0)$ and $(x^1_B(0), x^2_B(0))$ in Ξ°, satisfying the inequality conditions

$$x^1_A(0) > x^1_B(0)\,, \quad x^2_A(0) < x^2_B(0). \qquad (8)$$

Then for all $t > 0$, the inequality conditions propagate, i.e.

$$x^1_A(t) \gg x^1_B(t)\,, \quad x^2_A(t) \ll x^2_B(t). \qquad (9)$$

Below, we present a number of results established by exploiting monotone systems theory, along with traditional tools such as Lyapunov theory.

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E. Stability of equilibria

At this point in the development, we can explain some of the simpler aspects of the stability of equilibria, noting that the equilibria are finite in number and isolated. The stability properties can usually be examined by looking at the stability properties of the system linearized about the equilibrium.

Equivalently, with $(\bar{x}^1, \bar{x}^2)$ an equilibrium, the eigenvalues of the associated Jacobian matrix, $J(\bar{x}^1, \bar{x}^2)$ usually determine the stability or otherwise of the equilibrium. This matrix is similar to the corresponding specialization of Eq. (7). Since this latter matrix is an irreducible Metzler (off-diagonal entries nonnegative) matrix, by a simple variant on the Perron-Frobenius theorem [21, p. 534], $s(J(\bar{x}^1, \bar{x}^2))$ is a simple eigenvalue, and there are no other eigenvalues with the same abscissa – see [17] for a concise summary. Assuming $s(J(\bar{x}^1, \bar{x}^2)) \neq 0$, its sign then determines the stability properties of the equilibrium.

1) Healthy equilibrium stability properties: It is straightforward to study the healthy equilibrium and boundary equilibrium. The relevance of Jacobian use is clearly set out in Ref. [13] – this reference and [14] also explore use of Lyapunov functions to study equilibria. Indeed, [14] goes further to consider time-varying $B^k(t)$, sometimes attributable to mutating/time-varying infection pathways.

The Jacobian associated with the healthy equilibrium is:

$$J(\mathbf{0}_n, \mathbf{0}_n) = \begin{bmatrix} -D^1 + B^1 & 0_{n\times n} \\ 0_{n\times n} & -D^2 + B^2 \end{bmatrix}.$$

The condition $\mathcal{R}^k = \rho((D^k)^{-1}B^k) < 1$ is equivalent to $s(-D^k + B^k) < 0$. Thus, $(\mathbf{0}_n, \mathbf{0}_n)$ is stable, i.e. the associated Jacobian is Hurwitz, if and only if $\mathcal{R}^k < 1,\ k = 1, 2$, as discussed to above. Convergence to the healthy equilibrium thus requires taming and controlling *both viruses separately*.

2) Boundary equilibria stability properties: Now consider the stability of the boundary equilibria. As explained already, distinctive behavior for the bivirus problem (as compared with a single virus problem) can only arise when $\mathcal{R}^k > 1,\ k = 1, 2$. Under this condition, and supposing that $\bar{x}^1$ is the single virus equilibrium, $J(\bar{x}^1, \mathbf{0}_n)$ is immediately obtained as

$$\begin{bmatrix} -D^1 + (I_n - \bar{X}^1)B^1 - \tilde{B}^1(\bar{x}^1) & -\tilde{B}^1(\bar{x}^1) \\ 0_{n\times n} & -D^2 + (I_n - \bar{X}^1)B^2] \end{bmatrix}$$

The upper diagonal block matrix is Hurwitz, see [17], [23]. Thus, the stability of $(\bar{x}^1, \mathbf{0}_n)$ is determined by the eigenvalues of $[-D^2 + (I_n - \bar{X}^1)B^2]$, which are functions of D^k, B^k for both $k = 1, 2$ (with $\bar{X}^1$ an implicit function of D^1, B^1). In other words, the survival or extinction of virus j around its boundary equilibrium depends nontrivially on the dynamics of virus i. Depending on the precise values of D^k, B^k for $k = 1, 2$, examples exist in fact where both boundary equilibria are locally exponentially stable [8], [17], [18], both are unstable [8], [12], [15], [17], and one locally exponentially stable and the other unstable [11], [12], [15], [17]. Indeed, several of the aforementioned works secure *sufficient* conditions for any desired stability configuration of the two boundary equilibria.

Tightly intertwined with the key open challenge discussed in Section III-C.3 is the need to further our understanding of how D^k, B^k determine the stability properties of the boundary equilibria. A desirable objective is to identify conditions on D^k, B^k which simultaneously establish the stability properties of boundary equilibria, and establish if there exist coexistence equilibria (and how many and stability properties). So far, results are limited to undirected networks (a restrictive assumption) [12], a special $n = 3$ network [8], and two conditions discussed in Section III-E.4 below.

3) Simplifying the parameter set: Consider two different systems, one defined by a generic quadruple $\{D^1, B^1, D^2, B^2\}$ and the second defined by the quadruple $\{I_n, (D^1)^{-1}B^1, I_n, (D^2)^{-1}B^2\}$. It is an immediate conclusion from Eq. (6) that the equilibria associated with the two systems are identical. What is perhaps more surprising is the fact that the *stability properties* of any given equilibrium point are unchanged between the two systems [17]. On the other hand, the basins of attraction of a common stable equilibrium points across the two systems will not necessarily be the same, and hence trajectories originating from the same point across the two systems may not end up at the same equilibrium. The associated analyses primarily rely on the fact that the Jacobian matrix is similar to a Metzler matrix as noted by Eq. (7), and then further drawing on linear algebra results related to a class of matrices know as M-matrices [21, p. 533].

One can find at least two immediate uses of this result. First, for many purposes, especially theoretical analysis concerning stability properties, one can *without loss of generality* assume that $D^1 = D^2 = I_n$. This significantly simplifies any relevant analysis, useful for both theoretical analysis and for practical applications. Second, we can assert that a mere time scaling of the operation of one virus, equivalent to the replacement of $\{D^1, B^1, D^2, B^2\}$ by $\{\epsilon D^1, \epsilon B^1, D^2, B^2\}$ for some $\epsilon > 0$ capturing this time scale separation, gives the same equilibrium points with the same stability properties. This is exploited in Ref. [18] to examine the effects of having one virus evolving significantly faster than the other.

4) Survival-of-the-fittest outcome: Some of the earlier work focused on questions relating to survival-of-the-fittest scenarios, in which the only stable equilibrium is one of the two boundary equilibria. In such a scenario, and from Theorem 1, it immediately follows that for any $(x^1(0), x^2(0)) \in \Xi^\circ$, Eq. (5) will converge to the stable boundary equilibrium, ensuring only one virus survives. A very early analysis was for the case $n = 1$: D^k, B^k become scalars, and taking $D^1 = D^2 = 1$, the virus 2 boundary equilibrium is (globally) asymptotically stable if and only if $B^2 > B^1$ [9]. The most comprehensive extensions to the case of general n are probably to be found in [11], [15], [17] and they are based on matrix generalizations of the scalar inequality condition between B^2 and B^1, identified in Ref. [9]. Assume, without loss of generality that $D^1 = D^2 = I_n$. Under either of the conditions

1) $B^2 > B^1$;
2) The minimum row sum of entries of B^2 exceeds the maximum row sum of entries of B^1,

the boundary equilibrium $(\mathbf{0}_n, \bar{x}^2)$ is the only stable equilibrium of Eq. (5). Note that neither of the two conditions implies the other, and both permit intuitive epidemiological interpretations. The first condition simply relates the topology (edge presence) and transmission strength (edge weight) of

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the two viruses. To interpret the second condition, notice that $\sum_{j=1}^{n} b_{jk}^{i}$ for $k \in \mathcal{V}$ can be viewed as the "incoming infection rate" of virus i at node k. Then, the second condition is satisfied if the smallest total incoming infection rate for virus 2 among all nodes exceeds the largest total incoming infection rate for virus 1 among all nodes. The only other results are for undirected networks [12], [26], and a complex necessary and sufficient condition for survival-of-the-fittest in a special $n = 3$ tree network structure [8]. Whether other generalizations again would give rise to a survival-of-the-fittest outcome is unknown.

5) Testing for a single stable coexistence equilibrium: The second result from [17] drawing on monotone systems properties incorporating both trajectories and equilibria concerns a test for the existence of a single stable coexistence equilibrium, and its computation, at least by simulation. As discussed above, characterizing coexistence equilibria, including location and stability properties, is still an open challenge.

Consider two initial conditions for two trajectories A and B defined by 'corner points' of the region of interest, viz. $x_A(0) = [(1-\epsilon)\mathbf{1}_n, \epsilon\mathbf{1}_n]$ and $x_B(0) = [\epsilon\mathbf{1}_n, (1-\epsilon)\mathbf{1}_n]$ and imagine that $\epsilon > 0$ goes to zero. Let $x_C(0)$ be an arbitrary initial condition in Ξ°. Then evidently, $x_A^1(0) > x_C^1(0) > x_B^1(0)$ and $x_A^2(0) < x_C^2(0) < x_B^2(0)$, and the inequalities propagate with t (see Eq. (8) and Eq. (9)). We need to simulate just two trajectories, beginning at $x_A(0)$ and $x_B(0)$, with convergence assured by Theorem 1 (we simply perturb any initial conditions that yield nonconvergence). Suppose the two trajectories converge to equilibria $\bar{x}_A \in \Xi^\circ$ and $\bar{x}_B \in \Xi^\circ$, respectively. If there is a single stable coexistence equilibrium, then $\bar{x}_A = \bar{x}_B$ and because the x_C trajectory is 'squashed' between the x_A and x_B trajectories, it too must converge to this common equilibrium. Evidently, this will occur if and only if there is a single coexistence equilibrium, and it is globally convergent for initial conditions in Ξ°.

6) Patterns of equilibria: We conclude Section III by commenting briefly on *patterns* of equilibria, rather than individual equilibria. The fact that there is one healthy equilibrium and two boundary equilibria (assuming $\mathcal{R}^k > 1, k = 1, 2$ of course) is an example of a result encompassing a pattern. The literature contains further examples, as we now explain.

Key constraints arise from monotone systems theory; see the key Ref. [19]. Suppose there are two stable equilibria $\bar{x}_A = (\bar{x}_A^1, \bar{x}_A^2)$ and $\bar{x}_B = (\bar{x}_B^1, \bar{x}_B^2)$ (which may be boundary equilibria) obeying the ordering conditions $\bar{x}_A^1 > \bar{x}_B^1$ and $\bar{x}_A^2 < \bar{x}_B^2$. Then there necessarily exists an unstable coexistence equilibrium, call it $\bar{x}_C$, lying 'between' $\bar{x}_A$ and $\bar{x}_B$, in the sense that $\bar{x}_A^1 > \bar{x}_C^1 > \bar{x}_B^1$ and $\bar{x}_A^2 < \bar{x}_C^2 < \bar{x}_B^2$. Conversely, if there exists an unstable coexistence equilibrium, there exist stable equilibria $\bar{x}_A, \bar{x}_B$ (which may be boundary equilibria) satisfying the above ordering conditions.

Evidently, if the two boundary equilibria of a system are known to be stable, there must be an unstable coexistence equilibrium, and such examples appear in [8], [17], [18]. It is also not difficult to conclude from this fact that if there are no coexistence equilibria, precisely one of the two boundary equilibria is a stable equilibrium, and the whole of Ξ° is in its region of attraction, see [17, Corollary 3.16]. These results represent a step along the road to uncovering all the possible ways that equilibra can arise, but are far from providing the last word, which will yield important insight for policymakers planning a response to an epidemic.

IV. Open Problems

We conclude this paper by discussing various open problems and potential directions of future research, focusing first on control problems and then on extensions of the model.

A. The key omission in this paper: control

To date, there has been only limited exploration of control strategies for bivirus models [13]–[15], perhaps because until recently [17], general convergence and equilibria properties have been limited for large-scale networks. We hope this paper serves as a stimulus for further consideration of control for bivirus (and multivirus) models, perhaps along three greatly different approaches. *Pharmaceutical interventions* in some way will seek to modify most commonly the recovery parameters d_i^k, increasing them [13], [14]. *Nonpharmaceutical interventions* will seek to modify the infection parameters (entries of B^k), perhaps based on quarantining or travel and mobility restrictions. *Vaccine interventions* can also be considered, as in [11], by considering virus 1 to represent the true virus and virus 2 to represent the vaccine.

One could use the extensive literature covering a variety of epidemic control approaches to single virus SIS and SIR (network) models for inspiration and starting points [3]–[5]. For example, one could consider network optimization and design (involving both network topology and parameters such as recovery and infection rates) [4]. By considering the vaccine intervention idea, given D^1, B^1, one could ask how to design D^2, B^2 to ensure that virus 2 emerges as the winner of a survival-of-the-fittest scenario. Alternatively, one could consider optimization to reduce peak infection levels or endemic steady states. State feedback strategies used for single virus network models, including adaptive, distributed, or decentralized control, could also be considered [13], [23], [27], [28]. A good theory of approximation might be welcome too, in which populations are aggregated to reduce the integer n.

B. Gaps in knowledge regarding bivirus dynamics

Throughout the paper, several instances of open issues were flagged for the fundamental bivirus model. We highlight several we consider of particular importance. First, we could pursue the application of monotone systems theory and its consequences to the modified bivirus model due to Yang *et al.* [10], anticipating that many results will carry through. Given the success in applying monotone systems theory, we believe that other established results from the dynamical systems literature, such as Morse–Smale systems [29], could also be applied to further our understanding of the bivirus dynamics. It would also be of interest to decide whether a nonattractive limit cycle can exist, and identify further sufficient conditions on D^k, B^k for survival-of-the-fittest outcomes. Coexistence equilibria are still understudied relative to boundary and healthy equilibria, and several directions could

be explored. For instance, one could determine whether a continuum of coexistence equilibria must be an interval of a straight line as in Remark 3, or form another geometric shape. Alternatively, it would be especially interesting to identify scenarios, including conditions on D^k, B^k, where there are *multiple isolated* coexistence equilibria. In recognition of Remark 1, stochastic implementations of the bivirus model could be used to explore existence, and convergence to, boundary and coexistence equilibria while examining robustness by incorporating additional probabilistic features present in real-world epidemic outbreaks.

C. Changes of scenario

Practical applications are not all so limited as to be capable of treatment using the bivirus ideas summarized here. The bivirus model could be varied to accommodate *partial competitiveness* rather than full competitiveness of two viruses [16], [30]. In another direction, the model can be adjusted to accommodate the inclusion of an *intervening medium in the infection channel such as water, or another biological species*, work here having been initiated in Ref. [15]. And in another direction again, consideration of *three or more competitive viruses* can be contemplated, see e.g. [14], [15]. In this connection, we remark that many of results presented are obtained by exploiting the Metzler nature of the matrix in Eq. (7), including the monotone systems property. For three or more viruses, the Jacobian is no longer similar to a Metzler matrix, and so many bivirus conclusions will not straightforwardly extend. It remains an open challenge for three or more viruses to establish general convergence when the reproduction number $\mathcal{R}^k > 1$ for all k viruses, and rule out the possibility of chaos and (attractive) limit cycle behavior occurring. Other gaps identified above concerning bivirus dynamics, such as coexistence equilibria properties, are equally relevant to models dealing with three or more viruses.

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