

On matrix-SIR Arino models with linear birth rate, loss of immunity, disease and vaccination fatalities, and their approximations

Florin Avram^{1*}, Rim Adenane^{2†}, Lasko Basnarkov^{3†}, Gianluca Bianchin^{4*†}, Dan Goreac^{5†} and Andrei Halanay^{6†}

^{1*}Laboratoire de Mathématiques Appliquées, Université de Pau, Pau, 64000, France.

²Department of Mathematics, Ibn-Tofail University, Kenitra, 14000, Morocco.

³Faculty of Computer Science and Engineering, Ss. Cyril and Methodius University in Skopje, Skopje, North Macedonia.

^{4*}Department of Electrical, Computer, and Energy Engineering, University of Colorado Boulder, Boulder, CO 80309, United States.

⁵School of Mathematics and Statistics, Shandong University, 264209, Weihai, China.

⁵LAMA, Univ Gustave Eiffel, UPEM, Univ Paris Est Creteil, CNRS, F-77447, Marne-la-Vallée, France.

⁶Department of mathematics and informatics, Polytechnic University of Bucharest, Bucharest, Romania.

*Corresponding author(s). E-mail(s): florin.avram@univ-pau.fr;
gianluca.bianchin@colorado.edu;

Contributing authors: rim.adenane@uit.ac.ma; lasko.basnarkov@finki.ukim.mk;
dan.goreac@u-pem.fr; andrei.halanay@upb.ro;

†These authors contributed equally to this work.

Abstract

In this work we study the stability properties of the equilibrium points of deterministic epidemic models with nonconstant population size. Models with nonconstant population have been studied in the past only in particular cases, two of which we review and combine. Our main result shows that for simple “matrix epidemic models” introduced in [1], an explicit general formula for the reproduction number \mathcal{R} and the corresponding “weak stability alternative” [2, Thm 1] still holds, under small modifications, for models with nonconstant population size, and even when the model allows for vaccination and loss of immunity. The importance of this result is clear once we note that the models of [1] include a large number of viral and bacterial models of epidemic propagation, including for example the totality of homogeneous COVID-19 models. To better understand the nature of the result, we emphasize that the models proposed in [1] and considered here are extensions of the SIR-PH model [3], which is essentially characterized by a phase-type distribution $(\vec{\alpha}, \mathbf{A})$ that models transitions between the “disease/infectious compartments”. In these cases, the reproduction number \mathcal{R} and a certain Lyapunov function for the disease free equilibrium are explicitly expressible in terms of $(\vec{\alpha}, \mathbf{A})$. Not surprisingly, accounting for varying demography, loss of immunity, and vaccinations lead to several challenges. One of the most important is that a varying population size leads to multiple endemic equilibrium points: this is in contrast with “classic models,” which in general admit unique disease-free and endemic equilibria. As a special case of our analysis, we consider a “first approximation” (FA) of our model, which coincides with the constant-demography model often studied in the literature, and for which more explicit results are available. Furthermore, we propose a second heuristic approximation named “intermediate approximation” (IA). We hope that more light on varying population models with loss of immunity and vaccination, which have been largely avoided until now – see though [4–11] – will emerge in the future.

Keywords: Epidemic models, varying population models, stability, next-generation matrix approach, basic reproduction number, vaccination, loss of immunity, endemic equilibria.

1 Introduction

In this paper, we extend – to epidemic models with varying population size, vaccinations, and loss of immunity – an outstanding formula derived in [1], which expresses the reproduction number of a large class of deterministic epidemic models as a quadratic form with respect to certain input parameters (4.3). We illustrate why this formula is remarkable through a brief historical overview.

Deterministic mathematical epidemiology. Deterministic mathematical models [12–14] have been widely adopted by epidemiologists to model the spread of diseases worldwide, including the Bombay plague in 1905–06 [15], measles, smallpox, chickenpox, mumps, typhoid fever and diphtheria (see for example [16]), and recently COVID-19 (see for example [17–29], to cite just a few representatives of a huge literature). Analytic work in this area appears to have reached the ”dimensionality barrier,” thus remaining limited to models with up to three epidemic states [5, 6].

Stochastic and deterministic models. Stochastic models are the most-natural way to approach epidemic modeling since they inherently capture stochastic mixing within populations [30, 31]. We remark that many deterministic models can be obtained as limiting cases of stochastic models [32, 33]. Notice, however, that although multiple stochastic models may be adequate to model a certain epidemic outbreak, these may yield different deterministic limits – see for example [34], who discusses four stochastic models for a particular study case. The correspondence between stochastic and deterministic models being a delicate point, it implies that well-defined concepts for the first class are more challenging to capture or interpret for the second. To further explain this point and our motivation, next we give an eye-bird’s view of mathematical epidemiology.

The deterministic epidemics literature may be divided roughly into three streams.

1. Models with constant total population size. These models are in general easier to study, often admit a single endemic equilibrium point, and typically obey the “ \mathcal{R}_0 alternative” – see the next class of models. However, since death is an essential factor of epidemics, the assumption of constant population size (clearly an approximation that holds in the short term or for very-large populations) deserves some comment * .
2. Models with constant birth rate. These models include the previous class, and preserve some of its features, such as uniqueness of the endemic fixed point. In general cases, their stability properties can be studied via the next generation matrix approach – see [36] for a recent nice review of several stability results for this class of models. Finally, we notice that these models correspond to limiting cases of stochastic models with emigration.
3. Finally, we arrive to the object of our paper: models with linear birth-rate (corresponding to constant birth-rate per capita in the analog stochastic model), varying total population, and proportionate mixing. This stream of literature precedes the next generation matrix revolution [4, 5], and reveals the possibility of bi-stability when $\mathcal{R}_0 < 1$ (absent from the previous models), even in simple examples ¶ [6]. Despite further remarkable works on particular cases – see, for example, [7–11, 37] (which proposed a direct stability analyses as opposed to the next generation matrix approach used here), the literature on models with varying total population, unlike the two preceding streams, has not yet reached general results.

Despite their importance in describing epidemics evolving over long periods of time or affecting small-size populations, the previous discussion suggests that epidemics model with varying population size and linear birth-rate have not received sufficient attention – even in the simple case of Arino models with linear forces of infection (or bilinear incidence) [1, 3, 38–40] – thus motivating our study. As we will show in this work, these are models to which the next generation matrix approach can be applied, and for which the next generation matrix has rank 1, resulting in an explicit formula for the basic reproduction number \mathcal{R}_0 , provided in [1] for the case of constant population size ¶ .

We remark that Arino [1] calls the class of models considered in this work “simple models” [41]. These models were introduced in Arino’s joint work [1] with several of the founders of mathematical epidemiology: Brauer, van den Driessche, Watmough, and Wu. We took the liberty of renaming this class, since we believe that “simple models” is too generic, while “Arino-Brauer-van den Driessche-Watmough-Wu” is too long. We hope to show here and in further work that for this class \mathcal{R}_0 and other important features continue to have simple formulas in terms of the intervening matrices, and of the vaccination and loss of immunity parameters § .

Related works. We next summarize some works that are related to the model considered in this work.

*One rigorous justification for deterministic constant population epidemiological models comes from slow-fast analysis [35]. This is best understood for models with demography (birth, death), which happen typically on a slower scale than the infectious phenomena. Here there is a natural partition of the compartments into a vector $\vec{i}(t) \in \mathbb{R}_+^n$ of disease/infectious compartments (asymptomatic, infectious hospitalized, etc). These interact (quickly) with the other input classes like the susceptibles and output classes like the recovered and dead.

¶Thus, for an initial number of infectives high, the trajectory may lie in the basin of attraction of a stable endemic point instead of being eradicated. The discrepancy with what is expected from the corresponding stochastic model suggests that in this range the deterministic model is inappropriate

¶Unfortunately, this formula is not known enough, and particular cases of it are being reproved in numerous recent papers. In fact, sometimes several papers reprove the same particular case, due to the confusion caused by the lack of a common notation style; we have a proposition below to remedy that.

§Note also that quadratic models have been found useful in [42] for determining the direction of transcritical bifurcations.

1. The simplest class of “matrix-Arino” epidemics are the “SIR-PH models” [3, 40], in which the infected class is replaced by a vector of disease classes (here denoted by I), there are several output classes (here denoted by R), and there is only one input class (here denoted by S). Note that this particularly simple model has the probabilistic interpretation of a SIR model where the exponential infection time has been replaced by a PH-type $(\vec{\alpha}, A)$ distribution [3].[¶] Note that many of the models recently adopted to model the COVID-19 outbreak belong to this class.
2. Unfortunately, the SIR-PH model precludes important interactions between S and R like loss of immunity and vaccination. We introduce therefore here a class of models, named SIR/V+S, which allows individuals to transfer from the S class to the R class (thus accounting for vaccinations) and from the R class to the S class (thus accounting for loss of immunity).

Contributions. The contribution of this work is twofold. First, we propose a compartmental model for epidemic transmission that accounts for varying population size, vaccinations, and loss of immunity. This model includes three well-studied models as subcases: (i) general varying population epidemic models, (ii) the well-studied “first order” approximations (FA), often adopted in the literature (which is recovered by ignoring certain quadratic terms from the more-general model proposed here), and (iii) a new model, named “intermediate approximations” (IA), introduced here for the first time (obtained by neglect the terms which are quadratic with respect to the disease/infectious compartments).

Second, we characterize the equilibrium points of the proposed model and we study their stability properties. Our analysis builds upon and extends the next generation matrix approach proposed in [36] for models with constant population size. Our results show that the formula for the reproduction number proposed in [1] extends to models with varying population (with small modifications) and that the reproduction number still characterizes the stability of the equilibrium points.

Organization. This paper is organized as follows. In Section 2 we present some preliminary background on epidemic models: the basic reproduction number and the next generation matrix method. In Section 3 we introduce matrix Arino models with demography, vaccination and loss of immunity. Section 4 gives stability results for the SIR-PH model – see Propositions 1, 2, 3. Section 5 concludes the paper.

2 Preliminaries

2.1 What is a deterministic epidemic model?

To put in perspective our work, we would like to start by a definition of deterministic epidemic models, lifted from [44].

Definition 1 A deterministic epidemic model is a dynamical system with two types of variables $\vec{x}(t) := (\vec{i}(t), \vec{z}(t)) \in \mathbb{R}_+^N$, where

1. $\vec{i}(t)$ model the number (or density) in different compartments of infected individuals (i.e. latent, infectious, hospitalized, etc) which should ideally disappear eventually if the epidemic ever ends;
2. $\vec{z}(t)$ model numbers (or densities) in compartments of individuals who are not infected (i.e. susceptibles, immunes, recovered individuals, etc).

The system must admit an equilibrium called disease free equilibrium (DFE), and hence a “quasi-triangular” linearization the form

$$\begin{aligned} \vec{i}'(t) &= \vec{i}(t)A_{i,i}(\vec{x}(t)), \vec{x}(t) \in \mathcal{D} \subset \mathbb{R}_+^N \\ \vec{z}'(t) &= \vec{i}(t)A_{z,i}(\vec{x}(t)) + (\vec{z}(t) - \vec{z}_{dfe})A_{z,z}(\vec{x}(t)), \end{aligned} \quad (2.1)$$

where \mathcal{D} is some forward-invariant subset, where “quasi-triangular” refers to the fact that the functions $A_{i,i}, A_{z,i}, A_{z,z}$ depend on all the variables $\vec{x}(t)$, and where N is the dimension of $\vec{x}(t)$. \square

As shown in [44], any epidemic model admitting an equilibrium point $(\vec{0}, \vec{z}_{dfe})$ admits the representation (2.1), under suitable smoothness assumptions. In what follows, we will call the point $x_{dfe} = (\vec{0}, \vec{z}_{dfe})$ a disease free equilibrium (DFE).

Remark 1 Note that the essential feature of (2.1) is the “factorization of the disease equations”. \square

[¶]One may similarly replace the exponential latency time in class E of SEIR by a PH-type [43], and similarly for all the infectious classes, but this is finally unnecessary, since all the infectious classes may be grouped together in one group, whose phase-type will be determined by those of the components (via Kronecker product operations). It suffices therefore to let $(\vec{\alpha}, A)$ denote the phase-type of all the interactions between the disease classes.

2.2 The basic reproduction number \mathcal{R}_0

The basic reproduction number or “net reproduction rate” \mathcal{R}_0 is a pillar concept in demography, population dynamics, branching processes and mathematical epidemiology – see the introduction of the book [45]. One of the central objectives of these fields is to study the stability of DFE, i.e. the conditions which ensure eradicating the sickness (or a part of the population in population dynamics). It was discovered in simple models, that this amounts to verifying that a famous threshold parameter called basic reproduction number is less than 1.

1. The notation \mathcal{R}_0 was first introduced by the father of mathematical demography Lotka [46, 47]. In epidemiology, the basic reproduction number models the expected number of secondary cases which one infected case would produce in a homogeneous, completely susceptible stochastic population, in the next generation. As well known in the simplest setup of branching process, having this parameter smaller than 1 makes extinction sure. The relation to epidemiology is that an epidemics is well approximated by a branching process at its inception, a fact which goes back to Bartlett and Kendall.
 2. With more infectious classes, one deals at inception with multi-class branching processes, and stability holds when the Perron-Frobenius eigenvalue of the “**next generation matrix**” (NGM) of means is smaller than 1.
 3. For deterministic epidemic models, it seems at first that the basic reproduction number \mathcal{R}_0 is lost, since the generations disappear in this setup – but see [45, Ch. 3], who recalls a method to introduce generations which goes back to Lotka, and which is reminiscent of the iterative Lotka-Volterra approach of solving integro-differential equations. At the end of the tunnel, a unified method for defining \mathcal{R}_0 emerged only much later, via the “next generation matrix” approach [2, 48–51]. The final result is that local stability of the disease free equilibrium holds iff the spectral radius of a certain matrix called “next generation matrix”, which depends only on a set of “infectious compartments” \vec{i} (which we aim to reduce to 0), is less than one. This approach works provided that certain assumptions listed below hold [§].
- (C1) The foremost assumption is that the disease-free equilibrium $(\vec{0}, \vec{z}_{dfe})$ is *unique and locally asymptotically stable within the disease-free space* $\vec{i} = 0$, meaning that all solutions of

$$\vec{z}'(t) = (\vec{z}(t) - \vec{z}_{dfe})A_{z,z}(\vec{0}, \vec{z}(t)), \quad \vec{z}(0) = \vec{z}_0$$

must approach the point z_{dfe} when $t \rightarrow \infty$.

- (C2) Other conditions are related to an “admissible splitting” as a difference of two parts \mathcal{F}, \mathcal{V} , called respectively “new infections”, and “transitions”

Definition 2 A splitting

$$\vec{i}'(t) = \mathcal{F}(\vec{i}(t), \vec{z}(t)) - \mathcal{V}(\vec{i}(t), \vec{z}(t))$$

will be called admissible if \mathcal{F}, \mathcal{V} satisfy the following conditions [2, 52]:

$$\begin{cases} \mathcal{F}(\vec{0}, \vec{z}(t)) = \mathcal{V}(\vec{0}, \vec{z}(t)) = 0, \\ \mathcal{F}(\vec{i}(t), \vec{z}(t)) \geq 0, \quad \forall(\vec{i}(t), \vec{z}(t)), \\ \mathcal{V}_j(\vec{i}(t), \vec{z}(t)) \leq 0, \quad \text{when } \vec{i}_j = 0, \\ \sum_{j=1}^n \mathcal{V}_j(\vec{i}(t), \vec{z}(t)) \geq 0, \forall(\vec{i}(t), \vec{z}(t)), \end{cases} \quad (2.2)$$

where the subscript j refers the j 'th component. □

Remark 2 The splitting of the infectious equations has its origins in epidemiology. Mathematically, it is related to the “splitting of Metzler matrices” – see for example [53]. Note however that the splitting conditions may be satisfied for several or for no subset of compartments (see for example the SEIT model, discussed in [2], [12, Ch 5]). Unfortunately, for deterministic epidemic models, there is no clear-cut definition of \mathcal{R}_0 [13, 54, 55]. [‡] □

- (C3) We turn now to the last conditions, which concern the linearization of the infectious equations around the DFE. Putting $L = A_{i,i}(\vec{0}, \vec{z}_{dfe})$, and letting f denote the perturbation from the linearization, we may write:

$$\begin{aligned} \vec{i}'(t) &= \vec{i}(t)L - f(\vec{i}(t), \vec{z}(t)) = \vec{i}(t)(F - V) - f(\vec{i}(t), \vec{z}(t)), \\ F &:= \left[\frac{\partial \mathcal{F}}{\partial \vec{i}} \right]_{x_{dfe}} \quad V = \left[\frac{\partial \mathcal{V}}{\partial \vec{i}} \right]_{x_{dfe}}, \quad L = F - V. \end{aligned} \quad (2.3)$$

[§] And so \mathcal{R}_0 is undefined when these assumptions are not satisfied.

[‡] A possible explanation is that several stochastic epidemiological models may correspond in the limit to the same deterministic model.

The “transmission and transition” linearization matrices F, V must satisfy that $F \geq 0$ componentwise and V is a non-singular M-matrix, which ensures that $V^{-1} \geq 0$.[‡]

Under conditions (C1)-(C3), the next generation matrix method gives an explicit expression for the basic reproduction number, given by $\mathcal{R}_0 := \lambda_{PF}(FV^{-1})$.

The basic reproduction number is a threshold parameter in the following sense [2, Thm 1]:

- 1(a) When $\mathcal{R}_0 < 1$, the DFE is locally asymptotically stable;
- 1(b) when $\mathcal{R}_0 > 1$, the DFE is unstable;
- 2 The DFE is globally asymptotically stable when $\mathcal{R}_0 \leq 1$, provided the “perturbation from linearity” $f = i(F - V) - \mathcal{F} + \mathcal{V}$ is non-negative [2, Thm 2].[¶]

In what follows, we will call the alternative 1(a)-1(b) the “weak \mathcal{R}_0 alternative”. In contrast, the result 2 has been called the “strong \mathcal{R}_0 alternative” in [52, 56].

3 Matrix SIRS epidemics with demography, loss of immunity, vaccination and one susceptible class (SIRS epidemics with phase-type “disease time”)

While the elusive \mathcal{R}_0 can be defined as the spectral radius of a certain matrix, provided that the next generation matrix assumptions apply, it is often possible and considerably more convenient to employ models where \mathcal{R}_0 may be explicitly expressed in terms of the matrices that define the model [1, 39, 57, 58].

The idea behind these models is to further divide the noninfected compartments into S(usceptible)/input classes, defined by producing “new non-linear infections”, and output R classes (like D, D_e in our example), which are fully determined by the rest, and may therefore be omitted from the dynamics. Furthermore, it is convenient to restrict to epidemic models with linear force of infection, since it is known that non-linear forces of infection may lead to very complex dynamics [59–62], which are not always easy to interpret epidemiologically. This is in contrast with the Arino models already studied where one may typically establish the absence of periodic solutions (closed orbits, homoclinic loops and oriented phase polygons) [10, 11].

Below, we study the equilibrium points and the dynamical behavior of such models, restricting to the case of **one susceptible class**. Our goal is to understand the effects of demography, vaccination and loss of immunity, which are missing in the original paper [1].

Definition 3 A matrix “SIRS epidemic” of type $(1, n, p)$, with demography parameters (Λ, μ) (scalars), loss of immunity column vector γ_r and vaccination row vector $\tilde{\gamma}_s$, is characterized by a set of parameters (A, B, W, ν, ν_r) , where ν, ν_r (in boldface) denote column vectors of extra death rates, and A, B, W denote respectively matrices of dimensions $n \times n$, $n \times n$ and $n \times p$, respectively. This model contains one susceptible class S , a p -dimensional vector of removed states \vec{R} (healthy, dead, vaccinated, etc), and a n -dimensional vector of “disease” states \vec{I} (which may contain latent/exposed, infective, asymptomatic, etc). The dynamics are:

$$\begin{aligned}
 S'(t) &= \Lambda N - \frac{S(t)}{N} \vec{I}(t) \mathbf{b} - (\tilde{\gamma}_s + \mu) S(t) + \vec{R}(t) \gamma_r, & \mathbf{b} &= B \mathbf{1}, \\
 \vec{I}'(t) &= \vec{I}(t) \left(\frac{S(t)}{N} B + A - \text{Diag}(\nu + \mu \mathbf{1}) \right), & & \\
 \vec{R}'(t) &= \vec{I}(t) W + \tilde{\gamma}_s S(t) - \vec{R}(t) (\text{Diag}(\gamma_r + \nu_r + \mu \mathbf{1})), \\
 N'(t) &= \mathbf{S}'(t) + \vec{I}'(t) \mathbf{1} + \vec{R}'(t) \mathbf{1} = (\Lambda - \mu) N - \vec{I}(t) \nu - \vec{R}(t) \nu_r, \\
 D'(t) &= \mu(S(t) + \vec{I}(t) \mathbf{1} + \vec{R}(t) \mathbf{1}), \\
 D_e'(t) &= \vec{I}(t) \nu + \vec{R}(t) \nu_r.
 \end{aligned} \tag{3.1}$$

In short, we will refer to the above model to as matrix SIR/V+S model. □

Here,

1. $\vec{I}(t) \in \mathbb{R}^n$ is a row vector whose components model a set of disease states (or classes).
2. $\vec{R}(t) \in \mathbb{R}^p$ is a row vector whose components model a set of recovered states (or classes), each accounting for individuals who recovered from the infection. In what follows, we will focus on the case of one recovered class.

[‡]The assumption (B) implies that $L = F - V$ is a “stability (non-singular) M-matrix”, which is necessary for the non-negativity and boundedness of the solutions [36, Thm. 1-3].

[¶]Note that the [56] strong \mathcal{R}_0 alternative was only established for a general n-stage-progression, which is a particular case of the model we study below, in which A is an “Erlang” upper diagonal matrix. It is natural to expect that the result continues to hold for other non-singular Metzler matrices

3. B is a $n \times n$ matrix, where each entry $B_{i,j}$ represents the force of infection of the disease class i onto class j . We will denote by \mathbf{b} the vector containing the sum of the entries in each row of B , namely, $\mathbf{b} = B\mathbf{1}$.
4. A is a $n \times n$ Markovian sub-generator matrix (i.e., a Markovian generator matrix for which the sum of at least one row is strictly negative), where each off-diagonal entry $A_{i,j}$, $i \neq j$, satisfies $A_{i,j} \geq 0$ and describes the rate of transition from disease class i to disease class j ; while each diagonal entry $A_{i,i}$ satisfies $A_{i,i} \leq 0$ and describes the rate at which individuals in the disease class i leave towards non-infectious compartments. Alternatively, $-A$ is a non-singular M-matrix [1, 3].[§]
5. $\boldsymbol{\nu} \in \mathbb{R}^n$, $\boldsymbol{\nu}_r \in \mathbb{R}^p$ are column vectors describing the death rates in the disease and recovered compartments caused by the epidemic (and possibly vaccinations), respectively.
6. $\boldsymbol{\gamma}_r$ is a vector describing the rates at which individuals lose immunity (i.e. transition from recovered states to the susceptible state).
7. $\vec{\gamma}_s$ is a vector describing the rates at which individuals are vaccinated (immunized).
8. W is a $n \times p$ matrix whose entries model the rates at which individuals in the disease states transfer to recovered or dead states. In what follows, we assume that the $n \times (n+p)$ matrix $\tilde{A} = (A \ W)$ satisfies $\tilde{A}\mathbf{1} = 0$ (namely, the sum of the entries in each row is equal to 0), which implies mass conservation.

Remark 3 We have not found any work in the literature on models with linear birth-rate, at this level of generality. As mentioned in the introduction, the immense majority of the literature is dedicated to models that may be formally obtained from (3.1) by letting $N = 1$ (the idea being that N is approximately constant, either since it is huge, or since it is observed only over a short period of time). We will call this formally obtained model “classic/pedagogical” where we added the last qualifier to emphasize that it is unrelated to the model we study. This is in contrast with the FA and IA approximations introduced later, which do approximate the scaled version of (3.1) introduced below. \square

- Remark 4* 1. Note that when $p = 1$, then $W = \mathbf{a} := (-A)\mathbf{1}$ is a vector with a well-known probabilistic interpretation in the theory of phase-type distributions: it is the column vector which completes a matrix with negative row sums to a matrix with zero row sums.
2. A particular but revealing case is that when $p = 1$ and matrix B has rank 1, necessarily hence of the form $B = \mathbf{b}\vec{\alpha}$, where $\vec{\alpha} \in \mathbb{R}^n$ is a **probability row vector** whose components α_j represent the fractions of susceptibles entering into the disease compartment j , when infection occurs. We will call this SIR-PH, following Riano [3], who emphasized its probabilistic interpretation – see also [43], and see [64] for an early appearance of such models. \square

Remark 5 Note in the general model the factorization of the equation for the diseased compartments, which turns out to be an essential feature of the model.

Note also that our model includes important epidemiological parameters, such as $\boldsymbol{\nu}$ (describing the death rate when individuals are in the infectious compartments) and $\boldsymbol{\gamma}_r$ (describing the rates at which recovered individuals lose immunity), which are often omitted in simpler models. In what follows, our purpose is precisely to study the emerging behaviors due to the presence of these parameters with respect to the simple Arino model. \square

It is convenient to reformulate (3.1) in terms of the fractions normalized by the total population

$$\mathbf{s} = \frac{S}{N}, \quad \vec{i} = \frac{1}{N}\vec{I}, \quad \vec{r} = \frac{1}{N}\vec{R}N = \mathbf{s} + \vec{i}\mathbf{1} + \vec{r}\mathbf{1}. \quad (3.2)$$

The reader may check that the following equations hold for the scaled variables:

$$\begin{cases} \mathbf{s}'(t) = \Lambda - (\Lambda + \gamma_s) \mathbf{s}(t) + \vec{r}(t)\boldsymbol{\gamma}_r - \mathbf{s}(t) \vec{i}(t) (\mathbf{b} - \boldsymbol{\nu}) + \mathbf{s}(t) \vec{r}(t)\boldsymbol{\nu}_r \\ \vec{i}'(t) = \vec{i}(t) \left(\mathbf{s}(t) B + \left(\vec{i}(t)\boldsymbol{\nu} + \vec{r}(t)\boldsymbol{\nu}_r \right) I_n + A - \text{Diag}[\boldsymbol{\nu} + \Lambda] \right) \\ \vec{r}'(t) = \mathbf{s}(t)\vec{\gamma}_s + \vec{i}(t)W - \vec{r}(t) \left(\text{Diag}[\boldsymbol{\gamma}_r + \boldsymbol{\nu}_r + \Lambda] - \left(\vec{i}(t)\boldsymbol{\nu} + \vec{r}(t)\boldsymbol{\nu}_r \right) I_p \right) \\ \mathbf{s}(t) + \vec{i}(t)\mathbf{1} + \vec{r}(t)\mathbf{1} = 1 \end{cases}, \quad (3.3)$$

where we let $\gamma_s := \vec{\gamma}_s\mathbf{1}$. Moreover, by letting $\mathbf{n} := \mathbf{s} + \vec{i}\mathbf{1} + \vec{r}\mathbf{1}$, we have

$$\mathbf{n}'(t) = (\Lambda - \vec{i}(t)\boldsymbol{\nu})(1 - \mathbf{n}(t)) = 0.$$

Hence, the above equation guarantees that if $\mathbf{s}(t_0) + \mathbf{i}(t_0) + \mathbf{r}(t_0) = 1$ for some $t_0 \in \mathbb{R}_{\geq 0}$, then $\mathbf{s}(t) + \mathbf{i}(t) + \mathbf{r}(t) = 1$ for all $t \geq t_0$. Accordingly, in what follows we will always assume that $\mathbf{n}(t_0) = 1$, which guarantees that $\mathbf{n}(t) = 1, \forall t$.

[§]An M-matrix is a real matrix V with $v_{ij} \leq 0, \forall i \neq j$, and having eigenvalues whose real parts are nonnegative [63].

The following definition puts in a common framework the dynamics for the scaled process and two interesting approximations.

Definition 4 Let $\Phi_s, \Phi_i, \Phi_r \in \{0, 1\}$ and let

$$\begin{aligned} \mathbf{s}'(t) &= \Lambda - (\Lambda + \gamma_s) \mathbf{s}(t) + \bar{\mathbf{r}}(t)\gamma_r - \mathbf{s}(t)\bar{\mathbf{i}}(t)\mathbf{b} + \Phi_s \mathbf{s}(t)(\mathbf{s}(t)\bar{\mathbf{i}}(t)\boldsymbol{\nu} + \mathbf{s}(t)\bar{\mathbf{r}}(t)\boldsymbol{\nu}_r), \\ \bar{\mathbf{i}}'(t) &= \bar{\mathbf{i}}(t)\left(\mathbf{s}(t)B + A - \text{Diag}[\boldsymbol{\nu} + \Lambda\mathbf{1}]\right) + \Phi_i \bar{\mathbf{i}}(t)\left(\bar{\mathbf{i}}(t)\boldsymbol{\nu} + \bar{\mathbf{r}}(t)\boldsymbol{\nu}_r I_n\right), \\ \bar{\mathbf{r}}'(t) &= \mathbf{s}(t)\bar{\gamma}_s + \bar{\mathbf{i}}(t)W - \bar{\mathbf{r}}(t)\text{Diag}[\gamma_r + \boldsymbol{\nu}_r + \Lambda\mathbf{1}] + \Phi_r \bar{\mathbf{r}}(t)(\bar{\mathbf{i}}(t)\boldsymbol{\nu} + \bar{\mathbf{r}}(t)\boldsymbol{\nu}_r)I_p, \\ \mathbf{s}(t) + \bar{\mathbf{i}}(t)\mathbf{1} + \bar{\mathbf{r}}(t)\mathbf{1} &= 1. \end{aligned} \quad (3.4)$$

1. The model (3.4) with $\Phi_s = \Phi_i = \Phi_r = 1$ will be called scaled model (SM).
2. The model (3.4) with $\Phi_s = \Phi_i = \Phi_r = 0$ will be called first approximation (FA).
3. The model (3.4) with $\Phi_s = \Phi_r = 1$ and $\Phi_i = 0$ will be called intermediate approximation (IA). □

Fig. 1 compares the qualitative behavior and equilibrium points of the (s, i) coordinates of the three variants of a SIR-type example of (3.1) model (discussed in detail in [65]).

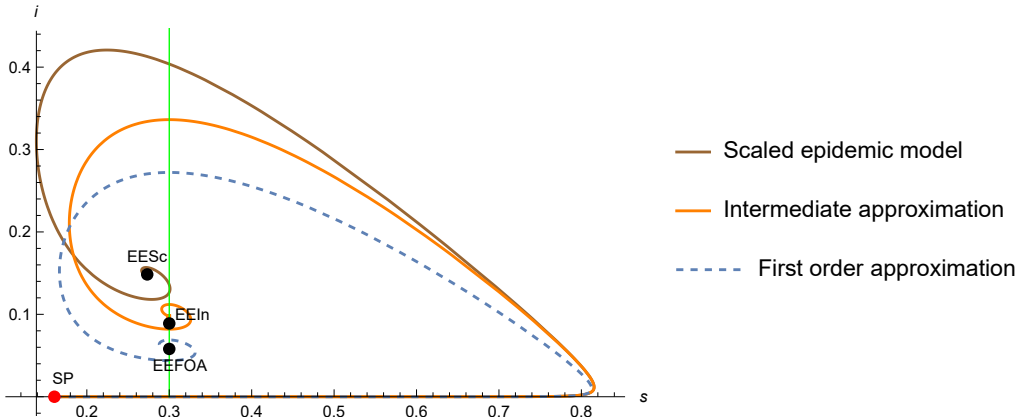


Fig. 1: Parametric (s, i) plots of the scaled epidemic and its FA and intermediate approximations for a SIR-type model with one infectious class, starting from a starting point SP with $i_0 = 10^{-6}$, with $\mathcal{R}_0 = 3.21, \beta = 5, \gamma = 1/2, \Lambda = \mu = 1/10, \gamma_r = 1/6, \gamma_s = .01, \nu_i = .9, \nu_r = 0$. $EESc, EEIn, EEFOA$ are the stable endemic points of the scaled model, intermediate model, and the FA model, respectively. The green vertical line denotes the immunity threshold $1/\mathcal{R} = s_{EEFOA} = s_{EEIn}$. Note that the epidemic will spend at first a long time (since births and deaths have slow rates as compared to the disease) in the vicinity of the manifold $\bar{\mathbf{i}}(t) = 0$, where the three processes are indistinguishable, before turning towards the endemic equilibrium point(s).

Example 1 The classic SEIRS model is a particular case of SIR-PH-FA model (see also next remark) obtained when

$$\bar{\alpha} = (1, 0), A = \begin{pmatrix} -\gamma_e & \gamma_e \\ 0 & -\gamma \end{pmatrix}, W = \mathbf{a} = \begin{pmatrix} 0 \\ \gamma \end{pmatrix}, \mathbf{b} = \begin{pmatrix} 0 \\ \beta \end{pmatrix}, \text{ so } B = \begin{pmatrix} 0 & 0 \\ 0 & \beta \end{pmatrix}, \boldsymbol{\nu} = \begin{pmatrix} 0 \\ \nu \end{pmatrix};$$

this yields:

$$\begin{cases} \mathbf{s}'(t) = \Lambda - \mathbf{s}(t)(\beta \mathbf{i}(t) + \gamma_s + \Lambda) + \gamma_r \mathbf{r}(t) \\ \begin{pmatrix} \mathbf{e}'(t) \\ \mathbf{i}'(t) \end{pmatrix} = \begin{pmatrix} -(\gamma_e + \Lambda) & \beta \mathbf{s}(t) \\ \gamma_e & -(\gamma + \Lambda + \nu) \end{pmatrix} \begin{pmatrix} \mathbf{e}(t) \\ \mathbf{i}(t) \end{pmatrix} \\ \mathbf{r}'(t) = \gamma_s \mathbf{s}(t) + \gamma \mathbf{i}(t) - \mathbf{r}(t)(\gamma_r + \Lambda + \nu_r) \end{cases} \quad (3.5)$$

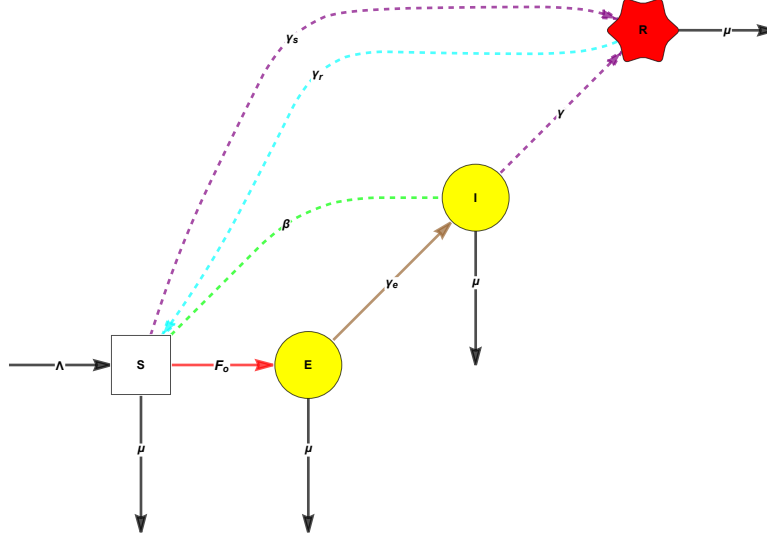


Fig. 2: Chart flow of the SEIRS model. The forces of infection is $F_o = \beta i$. The red edge corresponds to the entrance of susceptibles into the disease classes, the dashed green edges correspond to contacts between diseased to susceptibles, the brown edge is the rate of the transition matrix V , and the cyan dashed line corresponds to the rate of loss of immunity. The remaining black lines correspond to the inputs and outputs of the birth and natural death rates, respectively.

Remark 6 From now on we will write the dynamical systems with the vector state variables pre-multiplying the model matrices. The reason is that we want $\vec{\alpha}$ in the SIR-PH fundamental case to be a row vector, as in the theory of phase-type distributions, which turns out to be convenient in applications. \square

Remark 7 We point out now that the scaled matrix SIR/V+S model belongs to a class of models introduced, for different motivations, in [53]. Indeed, after dropping the first equation

$$\mathbf{s}'(t) = \Lambda - \mathbf{s}(t) \vec{\mathbf{i}}(t) \mathbf{b} - (\Lambda + \gamma_s) \mathbf{s}(t) + \vec{\mathbf{r}}(t) \gamma_r + \left(\vec{\mathbf{i}}(t) \boldsymbol{\nu} + \vec{\mathbf{r}}(t) \boldsymbol{\nu}_r \right) \mathbf{s}(t)$$

and rewriting the rest as:

$$\begin{pmatrix} \vec{\mathbf{i}}'(t) & \vec{\mathbf{r}}'(t) \end{pmatrix} = \begin{pmatrix} 0 & \mathbf{s}(t) \gamma_r \end{pmatrix} + \begin{pmatrix} \vec{\mathbf{i}}(t) & \vec{\mathbf{r}}(t) \end{pmatrix} \left[\begin{pmatrix} \mathbf{s}(t) \mathbf{B} + \mathbf{A} - (\Lambda + \nu) I_n & \mathbf{W} \\ \mathbf{0} & -\text{Diag}(\gamma_r) + \Lambda I_p \end{pmatrix} - \text{Diag}(\boldsymbol{\nu}_x) \right] \\ + \vec{\mathbf{x}} \text{Diag}(\boldsymbol{\nu}_x) \text{Diag}(\vec{\mathbf{x}}),$$

where $\vec{\mathbf{x}} = (\vec{\mathbf{i}}, \vec{\mathbf{r}})$, $\boldsymbol{\nu}_x = (\boldsymbol{\nu}, \boldsymbol{\nu}_r)$, we recognize a particular case of [53, (2.1)]. Finally, we note that the **FA** is obtained by dropping the row of the last matrices. \square

Using now $\nabla \vec{\mathbf{i}}(t) \boldsymbol{\nu} \vec{\mathbf{i}}(t) = \boldsymbol{\nu} \vec{\mathbf{i}}(t) + \vec{\mathbf{i}}(t) \boldsymbol{\nu} I_n$, and putting $x = \vec{\mathbf{i}} \boldsymbol{\nu} + \vec{\mathbf{r}} \boldsymbol{\nu}_r$, we find that the transpose of the Jacobian matrix of the scaled model (3.3) is given by

$$J = \begin{pmatrix} x - \vec{\mathbf{i}} \mathbf{b} - (\Lambda + \gamma_s) & \vec{\mathbf{i}} \mathbf{B} & \vec{\gamma}_s \\ \mathbf{s}(\boldsymbol{\nu} - \mathbf{b}) & \mathbf{s} \mathbf{B} + \mathbf{A} - \text{Diag}(\boldsymbol{\nu} + \Lambda \mathbf{1}) + \boldsymbol{\nu} \vec{\mathbf{i}} + (\vec{\mathbf{i}} \boldsymbol{\nu} + \vec{\mathbf{r}} \boldsymbol{\nu}_r) I_n & \mathbf{W} + \boldsymbol{\nu} \vec{\mathbf{r}} \\ \gamma_r + \mathbf{s} \boldsymbol{\nu}_r & \boldsymbol{\nu}_r \vec{\mathbf{i}} & \boldsymbol{\nu}_r \vec{\mathbf{r}} - \text{Diag}[\gamma_r + \boldsymbol{\nu}_r + \Lambda] + (\vec{\mathbf{i}} \boldsymbol{\nu} + \vec{\mathbf{r}} \boldsymbol{\nu}_r) I_p \end{pmatrix}.$$

At the disease-free equilibrium $(s_{dfe}, \vec{\mathbf{0}}, \vec{\mathbf{r}}_{dfe})$, we have

$$J_{dfe} = \begin{pmatrix} -(\Lambda + \gamma_s) + \vec{\mathbf{r}}_{dfe} \boldsymbol{\nu}_r & 0 & \vec{\gamma}_s \\ s_{dfe}(\boldsymbol{\nu} - \mathbf{b}) & s_{dfe} \mathbf{B} + \mathbf{A} - \text{Diag}(\boldsymbol{\nu} + \Lambda \mathbf{1}) + \vec{\mathbf{r}}_{dfe} \boldsymbol{\nu}_r I_n & \mathbf{W} + \boldsymbol{\nu} \vec{\mathbf{r}}_{dfe} \\ \gamma_r + s_{dfe} \boldsymbol{\nu}_r & 0 & \boldsymbol{\nu}_r \vec{\mathbf{r}}_{dfe} - \text{Diag}[\gamma_r + \boldsymbol{\nu}_r + \Lambda] + (\vec{\mathbf{r}}_{dfe} \boldsymbol{\nu}_r) I_p \end{pmatrix}.$$

Remark 8 a) This is (up to a transpose) a generalization of the Jacobian of the scalar SIR/V+S model, with the middle element replaced by a $n \times n$ matrix.

b) Note the structure of the second column, which is equivalent to the factorization property, and implies Proposition 1, below. \square

4 Stability results for the SIR-PH model

We consider here the particular case with a single recovered class, called SIR-PH model, where $W = \mathbf{a} = (-A)\mathbf{1}$. Notice that, in this case, we have a reduced set of parameters $(\Lambda = \mu, \bar{\alpha}, A, \mathbf{b}, \nu, \nu_r, \gamma_s, \gamma_r)$.

4.1 The basic reproduction number for SIR-PH, via the next generation matrix method [49, 50]

We follow up here on a remark preceding [1, Thm 2.1], and show in the following proposition that their simplified formula for the basic reproduction number still holds when loss of immunity and vaccination are allowed, provided that $p = 1$ and $B = \mathbf{b}\bar{\alpha}$ has rank one.

Proposition 1 *Consider a SIR-PH model (i.e. a single recovered class), with parameters $(\Lambda = \mu, \bar{\alpha}, A, \mathbf{b}, \nu, \nu_r, \gamma_s, \gamma_r)$, and matrix of recovery rates $W = \mathbf{a} = (-A)\mathbf{1}$.*

1. (a) When $\nu_r = 0$, the unique DFE is $(\frac{\Lambda + \gamma_r}{\Lambda + \gamma_r + \gamma_s}, 0, \frac{\gamma_s}{\Lambda + \gamma_r + \gamma_s})$.
- (b) When $\nu_r > 0$, exclude the case $\Lambda = \gamma_r = 0$. Then, there exists a unique DFE $(s_{dfc}, 0, 1 - s_{dfc}) \in \mathcal{D}$, where s_{dfc} satisfies the second order equation $\mathbf{s}[\nu_r \mathbf{s} + \Lambda + \gamma_r + \gamma_s - \nu_r] - (\Lambda + \gamma_r) = 0$ and is given by

$$s_{dfc} = \frac{\sqrt{4\nu_r(\Lambda + \gamma_r) + (\Lambda + \gamma_r + \gamma_s - \nu_r)^2} - (\Lambda + \gamma_r + \gamma_s - \nu_r)}{2\nu_r}. \quad (4.1)$$

2. The weak \mathcal{R}_0 alternative holds for the threshold parameter

$$\mathcal{R}_0 = \lambda_{PF}(FV^{-1}), \quad (4.2)$$

where F, V are defined in (4.9), and λ_{PF} denotes the (dominant) Perron-Frobenius eigenvalue.

3. For rank one, $B := \mathbf{b}\bar{\alpha}$ and $\nu_r = 0$, we further have

$$(a) \quad \mathcal{R}_0 = s_{dfc} \mathcal{R}, \text{ where } \mathcal{R} = \bar{\alpha} V^{-1} \mathbf{b}. \quad (4.3)$$

- (b) If $\mathcal{R}_0 \leq 1$, and if the perturbation from linearity defined in (2.3) is nonnegative, then the scalar combination

$$Y = \bar{\mathbf{i}} V^{-1} \mathbf{b} \quad (4.4)$$

is a Lyapunov function for the DFE.

Proof: 1. The disease free system (with $\mathbf{i} = 0$, $\mathbf{r} = 1 - \mathbf{s}$) reduces to

$$\mathbf{s}'(t) = \Lambda - (\gamma_s + \Lambda) \mathbf{s}(t) + (\gamma_r + \nu_r \mathbf{s}(t))(1 - \mathbf{s}(t)). \quad (4.5)$$

For the fixed points we must, depending on ν_r , solve either a quadratic, or a linear equation

$$\begin{cases} \Lambda + \gamma_r - \mathbf{s}[\nu_r \mathbf{s} + \Lambda + \gamma_r + \gamma_s - \nu_r] = 0 & \nu_r > 0 \\ \mathbf{s}[\Lambda + \gamma_r + \gamma_s] - (\Lambda + \gamma_r) = 0 & \nu_r = 0 \end{cases}.$$

One root

$$s_{dfc} = \begin{cases} \frac{\Lambda + \gamma_r}{\Lambda + \gamma_r + \gamma_s} & \nu_r = 0 \\ \frac{\sqrt{\Delta_{dfc}} - (\Lambda + \gamma_r + \gamma_s - \nu_r)}{2\nu_r}, & \Delta_{dfc} = 4\nu_r(\Lambda + \gamma_r) + (\Lambda + \gamma_r + \gamma_s - \nu_r)^2 & \nu_r > 0 \end{cases} \quad (4.6)$$

is always in $[0, 1]$ and will be denoted by s_{dfc} .

Remark 9 s_{dfc} is continuous in ν_r , since for ν_r small, $s_{dfc} \approx \frac{\Lambda + \gamma_r + \gamma_s - \nu_r + \frac{2\nu_r(\Lambda + \gamma_r)}{\Lambda + \gamma_r + \gamma_s - \nu_r} - (\Lambda + \gamma_r + \gamma_s - \nu_r)}{2\nu_r} \rightarrow \frac{\Lambda + \gamma_r}{\Lambda + \gamma_r + \gamma_s}$ (this approximation may be made rigorous by applying the rule of l'Hospital). \square

The other root in the quadratic case $\nu_r > 0$

$$\frac{\nu_r - (\Lambda + \gamma_r + \gamma_s) - \sqrt{4\nu_r(\Lambda + \gamma_r) + (\Lambda + \gamma_r + \gamma_s - \nu_r)^2}}{2\nu_r} \quad (4.7)$$

is strictly negative, unless

$$\begin{cases} \Lambda + \gamma_r = 0 \\ \nu_r \geq \gamma_s + \Lambda + \gamma_r \end{cases} \Leftrightarrow \begin{cases} \Lambda = \gamma_r = 0 \\ \nu_r \geq \gamma_s \end{cases}, \quad (4.8)$$

in which case it yields a second DFE point with $\mathbf{s} = 0 = \mathbf{i}$, which we exclude (in order to be able to apply the next generation matrix method).

2. It is enough to show here that the conditions of [2, Thm 2] hold, with respect to the infectious set $\vec{\mathbf{i}}$, and a certain splitting.

The DFE and its local stability for the disease-free system have already been checked in the SIR/V+S example.

We provide now a splitting for the infectious equations:

$$\vec{\mathbf{i}}'(t) = \vec{\mathbf{i}}(t) \left[\mathbf{s}(t)B + \vec{\mathbf{i}}(t)\boldsymbol{\nu}I_n + \nu_r r(t)I_n \right] - \vec{\mathbf{i}}(t) [\text{Diag}(\boldsymbol{\nu} + \Lambda\mathbf{1}) - A] := \mathcal{F}(\mathbf{s}, \vec{\mathbf{i}}) - \mathcal{V}(\vec{\mathbf{i}})$$

(where $r = 1 - \mathbf{s} - \vec{\mathbf{i}}\mathbf{1}$). The corresponding gradients at the DFE $\vec{\mathbf{i}} = 0$ are

$$\begin{cases} F = \left[\frac{\partial \mathcal{F}(X^{(DFE)})}{\partial \vec{\mathbf{i}}} \right] = \mathbf{s}B + \nu_r r I_n, \\ V = \left[\frac{\partial \mathcal{V}(X^{(DFE)})}{\partial \vec{\mathbf{i}}} \right] = \text{Diag}(\boldsymbol{\nu} + \Lambda\mathbf{1}) - A. \end{cases} \quad (4.9)$$

We note that F has non-negative elements, and that V is a M-matrix, and therefore V^{-1} exists and has non-negative elements, $\forall \Lambda, \boldsymbol{\nu}$. We may check that the conditions (2.2) are satisfied.

For example, the last non-negativity condition in (2.2)

$$\vec{\mathbf{i}}(t) [\text{Diag}(\boldsymbol{\nu} + \Lambda\mathbf{1}) - A] \mathbf{1} \geq 0, \forall \vec{\mathbf{i}} \in \mathcal{D}, \quad (4.10)$$

is a consequence of $-A$ being a M-matrix, which implies $-A\mathbf{1} \geq 0$, componentwise.

3.a) Now if $n = 1$, or if $B = \mathbf{b}\vec{\alpha}$ has rank 1, and $\nu_r = 0$, the matrix F in (4.9) is the product of a column vector and a row vector, the dimension of its image is one, and the same holds for BV^{-1} . Equivalently, $\text{rank}(BV^{-1}) = 1$. The "rank-nullity theorem" $\text{rank}(BV^{-1}) + \text{nullity}(BV^{-1}) = n$ [66] implies that $(n - 1)$ of the eigenvalues of BV^{-1} are zero, and the Perron-Frobenius eigenvalue is the remaining one. This latter one must be equal to the trace of $BV^{-1} = \mathbf{b}\vec{\alpha}V^{-1}$ which may be checked to equal $\vec{\alpha}V^{-1}\mathbf{b}$. Finally, the linearity $\mathcal{R}_0 = s_{dfe} \mathcal{R}$ is obvious.

3.b) is a particular case of [52], since the Perron-Frobenius eigenvector in our rank-one case may be taken as \mathbf{b} . ■

4.2 The classic/pedagogical SIRS-FA model

In this section, we give more explicit results for the disease free equilibrium and the endemic equilibrium of the following model, referred to as SIRS-FA,

$$\begin{cases} \mathbf{s}'(t) = \Lambda - (\mu + \gamma_s) \mathbf{s}(t) + \vec{r}(t)\boldsymbol{\gamma}_r - \mathbf{s}(t) \vec{\mathbf{i}}(t)\mathbf{b} \\ \vec{\mathbf{i}}'(t) = \vec{\mathbf{i}}(t) (\mathbf{s}(t) \mathbf{b}\vec{\alpha} - V) \\ \vec{r}'(t) = \mathbf{s}(t)\vec{\gamma}_s + \vec{\mathbf{i}}(t)W - \vec{r}(t) (\text{Diag}[\boldsymbol{\gamma}_r + \boldsymbol{\nu}_r + \mu\mathbf{1}]) \\ \mathbf{s}(t) + \vec{\mathbf{i}}(t)\mathbf{1} + \vec{r}(t)\mathbf{1} = 1 \end{cases}, \quad (4.11)$$

Proposition 2 1. *The pedagogical $(\Lambda, \mu, A, \vec{\gamma}_s, \boldsymbol{\gamma}_r)$ SIRS system (4.11) has a unique disease-free equilibrium (DFE) fixed point*

$$(s_{dfe}, \vec{0}, \vec{r}_{dfe}), \quad s_{dfe} = \frac{\Lambda}{\mu + \gamma_s - \vec{\gamma}_s (\text{Diag}(\boldsymbol{\gamma}_r + \boldsymbol{\nu}_r + \mu\mathbf{1}))^{-1} \boldsymbol{\gamma}_r}, \quad \vec{r}_{dfe} = s_{dfe} \vec{\gamma}_s \text{Diag}(\boldsymbol{\gamma}_r + \boldsymbol{\nu}_r + \mu\mathbf{1})^{-1}.$$

In the SIR-PH case, the DFE simplifies to § :

$$(s_{dfe}, \vec{0}, r_{dfe}) = \left(\frac{\Lambda(\mu + \gamma_r + \nu_r)}{\mu\gamma_r + (\mu + \nu_r)(\mu + \gamma_s)}, \vec{0}, s_{dfe}\gamma_s \right). \quad (4.12)$$

§ This formula has appeared already in many particular cases –see for example [67, (19-20)]

2. If $\mathcal{R}_0 > 1$, then the pedagogical system (4.11) has a unique second fixed point within its forward-invariant set, which is locally asymptotically stable. This endemic fixed point is such that $1/s_{ee}$ is an eigenvalue of the matrix BV^{-1} .

In the SIR-PH case it must satisfy

$$1/s_{ee} = \frac{1}{\mathcal{R}} = \bar{\alpha} V^{-1} \mathbf{b}.$$

The disease components \vec{i}_{ee} satisfy:

$$\vec{i}_{ee} \left(\frac{1}{\mathcal{R}} B + A - \text{Diag}(\boldsymbol{\nu} + \mu \mathbf{1}) \right) := \vec{i}_{ee} M = 0 \quad (4.13)$$

(\vec{i}_{ee} is a Perron-Frobenius eigenvector of the matrix M related to the next generation matrix).

3. The normalization of \vec{i}_{ee} is given by (4.18) below. When $\mu = \Lambda$, this becomes:

$$\vec{i} \left(\mathbf{b} - \mathcal{R} \mathbf{a} \frac{\gamma_r}{\gamma_r + \nu_r + \Lambda} \right) = \Lambda \mathcal{R} - \Lambda + \gamma_s \left(\frac{\gamma_r}{\Lambda + \gamma_r + \nu_r} - 1 \right). \quad (4.14)$$

4. The disease-free equilibrium is locally asymptotically stable if $\mathcal{R}_0 < 1$ and is unstable if $\mathcal{R}_0 > 1$.
 5. When $\nu_r = 0$, the critical vaccination defined by solving $\mathcal{R}_0 = 1$ with respect to γ_s is given by

$$\gamma_s^* := (\Lambda + \gamma_r) (\bar{\alpha} V^{-1} \mathbf{b} - 1) = (\Lambda + \gamma_r) (\mathcal{R} - 1). \quad (4.15)$$

We show in Fig. 3 a stream plot of the SIRS-FA model that illustrates the above properties.

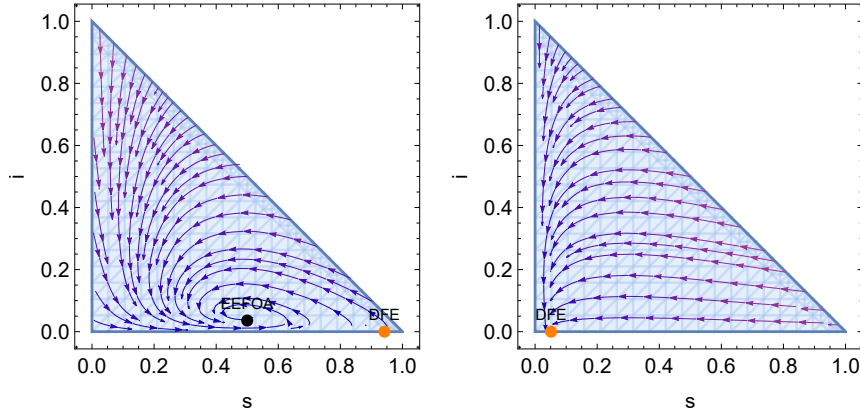


Fig. 3: Stream plots of (s, i) for an example of SIRS-FA model with one infectious class [65], when $\gamma_s \in \{1/100, 3\}$ is smaller and bigger, respectively, than the critical vaccination $\gamma_s^* = 0.239087$ defined in (4.15).

Proof: The proof starts by examining the two cases which arise from factoring the disease equations. More precisely, we will search separately in the **disease free set** $\mathcal{I} := \{\vec{i} = \vec{0}\}$ and in its complement \mathcal{I}^c . Then:

1. either $\vec{i} \in \mathcal{I}$ and solving

$$\begin{cases} \Lambda = (\mu + \gamma_s) s - \vec{r} \gamma_r \\ \vec{0} = s \vec{\gamma}_s - \vec{r} \text{Diag}(\gamma_r + \boldsymbol{\nu}_r + \mu \mathbf{1}) \end{cases} = (s \ \vec{r}) \begin{pmatrix} \mu + \gamma_s & \vec{\gamma}_s \\ -\gamma_r & -\text{Diag}(\gamma_r + \boldsymbol{\nu}_r + \mu \mathbf{1}) \end{pmatrix}$$

for s, \vec{r} yields the unique DFE (it may be shown by induction that the determinant is negative). Or,

2. the determinant of the resulting homogeneous linear system for $\vec{i} \neq \vec{0}$ must be 0, which implies that $s = s_{ee}$ satisfies

$$\det[s_{ee} B + A - \text{Diag}(\boldsymbol{\nu} + \mu \mathbf{1})] = 0. \quad (4.16)$$

Note now that $V = \text{Diag}(\boldsymbol{\nu} + \mu \mathbf{1}) - A$ is an invertible matrix. Using $\det(UU') = \det(U)\det(U')$, (4.16) may be written as

$$\det[(s_{ee} B - V) V^{-1}] = 0 \Leftrightarrow \det[s_{ee} B V^{-1} - \mathbf{I}] = 0$$

Dividing then by s_{ee} yields the characteristic polynomial of a matrix

$$\det \left[BV^{-1} - \frac{1}{s_{ee}} \mathbf{I} \right] = 0. \quad (4.17)$$

In the SIR-PH case, noting that the rank one matrix BV^{-1} has $(n-1)$ eigenvalues equal to zero, we conclude that the inverse of the susceptible fraction $1/s_{ee}$ of an endemic state must equal the Perron-Frobenius eigenvalue \mathcal{R} . Note that $s_{ee} < 1$ follows from our assumption on \mathcal{R} . The other coordinates are determined starting with \vec{i} , which must be proportional to a Perron-Frobenius nonnegative eigenvector.

Remark 10 Equivalently, it is easy to check that (4.17) may be reformulated as saying that s_{ee} must satisfy

$$\lambda_{PF}(s_{ee} B (A - \text{Diag}(\boldsymbol{\nu} + \mu \mathbf{1})))^{-1} = 1 \Leftrightarrow \lambda_{PF}(s_{ee} B + A - \text{Diag}(\boldsymbol{\nu} + \mu \mathbf{1})) = 0,$$

where λ_{PF} denotes the Perron-Frobenius eigenvalue. We note that the matrices in the last formulation intervene also in the next generation matrix approach. \square

3. Recall the system

$$\begin{cases} 0 = \Lambda - (\mu + \gamma_s) \mathbf{s} + \vec{r}(t)\gamma_r - \mathbf{s} y \\ 0 = \vec{i} (\mathbf{s} B + A - \text{Diag}(\boldsymbol{\nu} + \mu \mathbf{1})) \\ 0 = \vec{i} W + \mathbf{s} \vec{\gamma}_s - \vec{r} (\text{Diag}(\gamma_r + \nu_r + \mu \mathbf{1})) \end{cases} .$$

Since $s_{ee} = \frac{1}{\mathcal{R}}$, and \vec{i}_{ee} is known up to the proportionality constant $y = \vec{i} \mathbf{b}$, it only remains to solve the last equation in (4.18) below:

$$\begin{cases} \vec{r} = \left[\vec{i} W + \mathbf{s} \vec{\gamma}_s \right] \text{Diag}(\gamma_r + \nu_r + \mu \mathbf{1})^{-1} \\ \vec{i} (\mathbf{s} \mathbf{b} - W \text{Diag}(\gamma_r + \nu_r + \mu \mathbf{1})^{-1} \gamma_r) = \Lambda - (\mu + \gamma_s) \mathbf{s} + \mathbf{s} \vec{\gamma}_s \text{Diag}(\gamma_r + \nu_r + \mu \mathbf{1})^{-1} \gamma_r \end{cases} \quad (4.18)$$

This equation may be solved numerically. When $p = 1 \Rightarrow W := \mathbf{a} = (-A)\mathbf{1}$, the last formula yields

$$\vec{i} \left(\mathbf{b} - \mathcal{R} \mathbf{a} \frac{\gamma_r}{\gamma_r + \nu_r + \mu} \right) = \Lambda \mathcal{R} - \mu + \gamma_s \left(\frac{\gamma_r}{\gamma_r + \nu_r + \mu} - 1 \right) \quad (4.19)$$

In the particular case $\mu = \Lambda$, this yields (4.14).

4. This follows from [52, Theorem 2.1] (it is a consequence of the fact that a linear function proportional to the associated Perron eigenvector is a Lyapunov function when $\mathcal{R}_0 < 1$).
5. The result is immediate by solving $\mathcal{R}_0 = 1$ with respect to γ_s , where \mathcal{R}_0 is defined in (4.3). \blacksquare

4.3 A glimpse of the intermediate approximation model for matrix SIRS

The intermediate approximation associated to (3.3) is

$$\begin{cases} \mathbf{s}'(t) = \Lambda - (\Lambda + \gamma_s) \mathbf{s}(t) + \vec{r}(t)\gamma_r - \mathbf{s}(t) \vec{i}(t) (\mathbf{b} - \boldsymbol{\nu}) + \mathbf{s}(t) \vec{r}(t) \boldsymbol{\nu}_r \\ \vec{i}'(t) = \vec{i}(t) (\mathbf{s}(t) B + A - \text{Diag}[\boldsymbol{\nu}] - \Lambda I_n) \\ \vec{r}'(t) = \mathbf{s}(t) \vec{\gamma}_s + \vec{i}(t) W - \vec{r}(t) (\text{Diag}[\gamma_r + \nu_r] - (\vec{i}(t) \boldsymbol{\nu} + \vec{r}(t) \boldsymbol{\nu}_r - \Lambda) I_p) \end{cases} ; \quad (4.20)$$

when $i = 0$, we have

$$s_{dfe} = \frac{\Lambda + \vec{r}_{dfe} \gamma_r}{\Lambda + \gamma_s - \vec{r}_{dfe} \boldsymbol{\nu}_r}, \quad (4.21)$$

and from the last equation in (4.20), \vec{r}_{dfe} satisfies the following quadratic equation

$$(\Lambda + \gamma_s - \vec{r}_{dfe} \boldsymbol{\nu}_r) \vec{r}_{dfe} (\text{Diag}[\gamma_r + \nu_r] - (\vec{r}_{dfe} \boldsymbol{\nu}_r - \Lambda) I_p) - \vec{r}_{dfe} \gamma_r \vec{\gamma}_s = \Lambda \vec{\gamma}_s$$

Proposition 3 When $\boldsymbol{\nu}_r = 0$, the DFE points of the scaled, the intermediate approximation, and the FA are equal. In the SIR-PH case, they reduce all to $(\frac{\Lambda + \gamma_r}{\Lambda + \gamma_r + \gamma_s}, 0, \frac{\gamma_s}{\Lambda + \gamma_r + \gamma_s})$ (4.6).

Proof: The equations determining the three DFE's coincide. \blacksquare

5 Conclusions and further work

We have provided here a few general results for Arino models with varying population, and one susceptible class only. The following directions seem worthy of further work.

1. The case of two or more susceptible classes.
2. The determination of the largest domain of attraction of the DFE, through which some linear Lyapunov function decreases, might also be approachable via linear programming.

Acknowledgments

We thank N. Bacaer for providing the references [45, 46], and the referees for their reviews and suggestions.

Declarations

Competing interests. The authors declare no affiliation or involvement in any organization or entity with a financial or non-financial interest in the subject matter or materials discussed in this manuscript.

Funding. This work was supported in part by the AB Nexus seed grant from the University of Colorado.

References

- [1] Arino, J., Brauer, F., van den Driessche, P., Watmough, J., Wu, J.: A final size relation for epidemic models. *Mathematical Biosciences & Engineering* **4**(2), 159 (2007)
- [2] Van den Driessche, P., Watmough, J.: Further notes on the basic reproduction number. In: *Mathematical Epidemiology*, pp. 159–178. Springer, Berlin, Heidelberg (2008)
- [3] Riaño, G.: Epidemic models with random infectious period. *medRxiv* (2020)
- [4] Busenberg, S., van den Driessche, P.: Analysis of a disease transmission model in a population with varying size. *Journal of mathematical biology* **28**(3), 257–270 (1990)
- [5] Busenberg, S., van den Driessche, P.: A method for proving the non-existence of limit cycles. *Journal of mathematical analysis and applications* **172**(2), 463–479 (1993)
- [6] Derrick, W., van den Driessche, P.: A disease transmission model in a nonconstant population. *Journal of Mathematical Biology* **31**(5), 495–512 (1993)
- [7] Greenhalgh, D.: Hopf bifurcation in epidemic models with a latent period and nonpermanent immunity. *Mathematical and Computer Modelling* **25**(2), 85–107 (1997)
- [8] Li, M.Y., Graef, J.R., Wang, L., Karsai, J.: Global dynamics of a SEIR model with varying total population size. *Mathematical biosciences* **160**(2), 191–213 (1999)
- [9] Sun, C., Hsieh, Y.-H.: Global analysis of an SEIR model with varying population size and vaccination. *Applied Mathematical Modelling* **34**(10), 2685–2697 (2010)
- [10] Razvan, M.: Multiple equilibria for an SIRS epidemiological system. *arXiv preprint* (2001). arXiv:0101051
- [11] Yang, W., Sun, C., Arino, J.: Global analysis for a general epidemiological model with vaccination and varying population. *Journal of Mathematical Analysis and Applications* **372**(1), 208–223 (2010)
- [12] Martcheva, M.: *An Introduction to Mathematical Epidemiology* vol. 61. Springer, New York, NY (2015)
- [13] Thieme, H.R.: *Mathematics in Population Biology*. Princeton University Press, Princeton, NJ (2018)
- [14] Brauer, F., Castillo-Chavez, C., Feng, Z.: *Mathematical Models in Epidemiology*. Springer, New York, NY (2019)
- [15] Kermack, W.O., McKendrick, A.G.: A contribution to the mathematical theory of epidemics. *Proc. R. Soc. Lond. Series A, Containing papers of a mathematical and physical character* **115**(772), 700–721 (1927)
- [16] Earn, D.J.: A light introduction to modelling recurrent epidemics. In: *Mathematical Epidemiology*, pp. 3–17. Springer, Berlin, Heidelberg (2008)

- [17] Schaback, R.: On COVID-19 modelling. *Jahresbericht der Deutschen Mathematiker-Vereinigung* **122**(3), 167–205 (2020)
- [18] Bacaër, N.: Un modèle mathématique des débuts de l'épidémie de coronavirus en france. *Mathematical Modelling of Natural Phenomena* **15**, 29 (2020)
- [19] Ketcheson, D.I.: Optimal control of an SIR epidemic through finite-time non-pharmaceutical intervention. arXiv preprint arXiv:2004.08848 (2020)
- [20] Charpentier, A., Elie, R., Laurière, M., Tran, V.C.: COVID-19 pandemic control: balancing detection policy and lockdown intervention under ICU sustainability. *Mathematical Modelling of Natural Phenomena* **15**, 57 (2020)
- [21] Djidjou-Demasse, R., Michalakis, Y., Choisy, M., Sofonea, M.T., Alizon, S.: Optimal COVID-19 epidemic control until vaccine deployment. medRxiv (2020)
- [22] Sofonea, M.T., Reyné, B., Elie, B., Djidjou-Demasse, R., Selinger, C., Michalakis, Y., Alizon, S.: Epidemiological monitoring and control perspectives: application of a parsimonious modelling framework to the COVID-19 dynamics in France (2020)
- [23] Alvarez, F.E., Argente, D., Lippi, F.: A simple planning problem for COVID-19 lockdown. Technical report, National Bureau of Economic Research (2020)
- [24] Horstmeyer, L., Kuehn, C., Thurner, S.: Balancing quarantine and self-distancing measures in adaptive epidemic networks. arXiv preprint arXiv:2010.10516 (2020)
- [25] Di Lauro, F., Kiss, I.Z., Miller, J.: Optimal timing of one-shot interventions for epidemic control. medRxiv (2020)
- [26] Franco, E.: A feedback SIR (fSIR) model highlights advantages and limitations of infection-based social distancing. arXiv preprint arXiv:2004.13216 (2020)
- [27] Baker, R.: Reactive social distancing in a SIR model of epidemics such as COVID-19. arXiv preprint arXiv:2003.08285 (2020)
- [28] Caulkins, J., Grass, D., Feichtinger, G., Hartl, R., Kort, P.M., Prskawetz, A., Seidl, A., Wrzaczek, S.: How long should the COVID-19 lockdown continue? *Plos one* **15**(12), 0243413 (2020)
- [29] Caulkins, J.P., Grass, D., Feichtinger, G., Hartl, R.F., Kort, P.M., Prskawetz, A., Seidl, A., Wrzaczek, S.: The optimal lockdown intensity for COVID-19. *Journal of Mathematical Economics* **93**, 102489 (2021)
- [30] Bartlett, M.S.: Deterministic and stochastic models for recurrent epidemics. In: *Contributions to Biology and Problems of Health*, pp. 81–110. University of California Press, Berkeley and Los Angeles (2020)
- [31] Baxendale, P.H., Greenwood, P.E.: Sustained oscillations for density dependent markov processes. *Journal of mathematical biology* **63**(3), 433–457 (2011)
- [32] Kurtz, T.G.: Strong approximation theorems for density dependent markov chains. *Stochastic Processes and their Applications* **6**(3), 223–240 (1978)
- [33] Britton, T., Pardoux, E., Ball, F., Laredo, C., Sirl, D., Tran, V.C.: *Stochastic Epidemic Models with Inference*. Springer, Switzerland (2019)
- [34] Naasell, I.: The influence of immunity loss on persistence and recurrence of endemic infections. *Bulletin of mathematical biology* **75**(11), 2079–2092 (2013)
- [35] Jardón-Kojakhmetov, H., Kuehn, C., Pugliese, A., Sensi, M.: A geometric analysis of the SIR, SIRS and SIRWS epidemiological models. *Nonlinear Analysis: Real World Applications* **58**, 103220 (2021)
- [36] De la Sen, M., Nistal, R., Alonso-Quesada, S., Ibeas, A.: Some formal results on positivity, stability, and endemic steady-state attainability based on linear algebraic tools for a class of epidemic models with eventual incommensurate delays. *Discrete Dynamics in Nature and Society* **2019** (2019)

- [37] Li, J., Ma, Z.: Qualitative analyses of SIS epidemic model with vaccination and varying total population size. *Mathematical and Computer Modelling* **35**(11-12), 1235–1243 (2002)
- [38] Feng, Z., Thieme, H.R.: Endemic models with arbitrarily distributed periods of infection i: fundamental properties of the model. *SIAM Journal on Applied Mathematics* **61**(3), 803–833 (2000)
- [39] Feng, Z.: Final and peak epidemic sizes for SEIR models with quarantine and isolation. *Mathematical Biosciences & Engineering* **4**(4), 675 (2007)
- [40] Avram, F., Adenane, R., Ketcheson, D.: A review of matrix SIR arino epidemic models. *MDPI* **11**(4), 89–104 (2021)
- [41] Arino, J., Portet, S.: A simple model for COVID-19. *Infectious Disease Modelling* **5**, 309–315 (2020)
- [42] Buonomo, B.: A note on the direction of the transcritical bifurcation in epidemic models. *Nonlinear Analysis: Modelling and Control* **20**(1), 38–55 (2015)
- [43] Hurtado, P.J., Kirosingh, A.S.: Generalizations of the ‘linear chain trick’: incorporating more flexible dwell time distributions into mean field ODE models. *Journal of mathematical biology* **79**(5), 1831–1883 (2019)
- [44] Kamgang, J.C., Sallet, G.: Computation of threshold conditions for epidemiological models and global stability of the disease-free equilibrium (DFE). *Mathematical biosciences* **213**(1), 1–12 (2008)
- [45] Bacaër, N.: *Mathématiques et épidémies*. Cassini (2021)
- [46] Lotka, A.J.: *Analyse Démographique Avec Application Particulière À L’espèce humaine*. Hermann, Paris (1939)
- [47] Dietz, K.: The estimation of the basic reproduction number for infectious diseases. *Statistical methods in medical research* **2**(1), 23–41 (1993)
- [48] Diekmann, O., Heesterbeek, J.A.P., Metz, J.A.: On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. *Journal of mathematical biology* **28**(4), 365–382 (1990)
- [49] van den Driessche, P., Watmough, J.: Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical biosciences* **180**(1-2), 29–48 (2002)
- [50] Diekmann, O., Heesterbeek, J., Roberts, M.G.: The construction of next-generation matrices for compartmental epidemic models. *Journal of the Royal Society Interface* **7**(47), 873–885 (2010)
- [51] Perasso, A.: An introduction to the basic reproduction number in mathematical epidemiology. *ESAIM: Proceedings and Surveys* **62**, 123–138 (2018)
- [52] Shuai, Z., van den Driessche, P.: Global stability of infectious disease models using Lyapunov functions. *SIAM Journal on Applied Mathematics* **73**(4), 1513–1532 (2013)
- [53] Fall, A., Iggidr, A., Sallet, G., Tewa, J.-J.: Epidemiological models and Lyapunov functions. *Mathematical Modelling of Natural Phenomena* **2**(1), 62–83 (2007)
- [54] Roberts, M.: The pluses and minuses of R_0 . *Journal of the Royal Society Interface* **4**(16), 949–961 (2007)
- [55] Li, J., Blakeley, D.: The failure of R_0 . *Computational and Mathematical Methods in Medicine* **2011**
- [56] Guo, H., Li, M.Y.: Global dynamics of a staged progression model for infectious diseases. *Mathematical Biosciences & Engineering* **3**(3), 513 (2006)
- [57] Ma, J., Earn, D.J.: Generality of the final size formula for an epidemic of a newly invading infectious disease. *Bulletin of mathematical biology* **68**(3), 679–702 (2006)
- [58] Andreasen, V.: The final size of an epidemic and its relation to the basic reproduction number. *Bulletin of mathematical biology* **73**(10), 2305–2321 (2011)
- [59] Liu, W.-M., Levin, S.A., Iwasa, Y.: Influence of nonlinear incidence rates upon the behavior of SIRS

- epidemiological models. *Journal of mathematical biology* **23**(2), 187–204 (1986)
- [60] Liu, W.-M.-, Hethcote, H.W., Levin, S.A.: Dynamical behavior of epidemiological models with nonlinear incidence rates. *Journal of mathematical biology* **25**(4), 359–380 (1987)
- [61] Georgescu, P., Hsieh, Y.-H.: Global stability for a virus dynamics model with nonlinear incidence of infection and removal. *SIAM Journal on Applied Mathematics* **67**(2), 337–353 (2007)
- [62] Tang, Y., Huang, D., Ruan, S., Zhang, W.: Coexistence of limit cycles and homoclinic loops in a SIRS model with a nonlinear incidence rate. *SIAM Journal on Applied Mathematics* **69**(2), 621–639 (2008)
- [63] Plemmons, R.J.: M-matrix characterizations. I—nonsingular M-matrices. *Linear Algebra and its Applications* **18**(2), 175–188 (1977)
- [64] Hyman, J.M., Li, J., Stanley, E.A.: The differential infectivity and staged progression models for the transmission of hiv. *Mathematical biosciences* **155**(2), 77–109 (1999)
- [65] Avram, F., Adenane, R., Bianchin, G., Goreac, D., Halanay, A.: Stability analysis of a seven parameter sir-type model including loss of immunity, and disease and vaccination fatalities. Preprint (2021)
- [66] Horn, R.A., Johnson, C.R.: *Matrix Analysis*. Cambridge university press, New York, NY (2012)
- [67] De la Sen, M., Ibeas, A.: On an SE(Is)(Ih)AR epidemic model with combined vaccination and antiviral controls for COVID-19 pandemic. *Advances in Difference Equations* **2021**(1), 1–30 (2021)