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DOES MATHEMATICAL EPIDEMIOLOGY HAVE GENERAL LAWS, BESIDES THE DFE STABILITY THEOREM?

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Abstract. A very large class of ODE epidemic models (2) discussed in this paper enjoys the property of admitting also an integral renewal formulation, with respect to an "age of infection kernel" $a(t)$ which has a matrix exponential form (6). We observe first that a very short proof of this fact is available when there is only one susceptible compartment, and when its associated "new infections" matrix has rank one. In this case, $a(t)$ normalized to have integral 1, is precisely the probabilistic law which governs the time spent in all the "infectious states associated to the susceptible compartment", and the normalization is precisely the basic replacement number. The Laplace transform (LT) of $a(t)$ is a generalization of the basic replacement number, and its structure reflects the laws of the times spent in each infectious state. Subsequently, we state an extension to processes with several susceptible classes. The results outlined reveal that the ODE epidemic models highlighted here have also interesting probabilistic properties.

Keywords: (A, B) Arino-Brauer epidemic models, stability, basic replacement number, basic reproduction number, age of infection kernel, several susceptible compartments, Diekmann matrix kernel, generalized linear chain trick, Erlangization, Coxianization.

AMS classification: 34A34, 34A30, 37N25, 92D30, 92D25.

§1. Introduction

Motivation. The answer to the question in the title is clearly no, since if other laws existed, they would have surely been discovered by now. But, the answer becomes yes if one restricts to models whose "new infections matrix" has rank one [3]. In that case three important laws (or properties) are known already. The first is the "Diekmann law": the existence of a probabilistic renewal kernel – see [11, 3] and references therein. The second is the "Arino & al. law": the representability of the basic replacement number as a bilinear form. This is a consequence of the previous, and may also be proved simply by noting that all the eigenvalues of the next generation matrix except one are 0 [2, 3]. The third general principle, the "generalized linear chain trick" [18, 19], will be included in the full version of this paper (a more descriptive name would be the "phase-type extension of scalar transfer rates"). These results are very important, since they apply to a class of models which includes a very large proportion of the models used in applied studies of Covid-19, influenza, ILI (influenza like illnesses), and other epidemics. In fact, we are not aware of any paper which calibrates epidemic models to real data and does not use models of this type.

While the three results have been known for a while, they are somewhat spread all over the place. Furthermore, the immense majority of the literature seems unaware of them, and

treat instead each particular model as a new exercise. This motivated us to review here the results for the case of one susceptible compartment, and to provide extensions to the case of several susceptible classes; note the formulas (18) and (17), which seem to be new.

A bird's eye view of mathematical epidemiology. Mathematical epidemiology may be said to have started with the celebrated paper "A contribution to the mathematical theory of epidemics" [20] on the 1906 plague epidemic in Bombay, which introduced the SIR (susceptible-infected-recovered) model. [¶] Bacaer shows that better results can be obtained by adding compartments for rats and fleas [5, (7-11)], whose importance had been overlooked in the first study. In this spirit, each of the three fundamental compartments S,I,R, could be replaced by classes of several compartments, specific to each epidemics, to be revealed by further analyses.

The most fundamental aspect of mathematical epidemiology is the existence of at least two possible fixed states: the boundary "disease-free equilibrium" (DFE), corresponding to the elimination of all compartments $\vec{i}$ involving sickness, which may be easily found from the system of non-infectious equations with $\vec{i} = 0$, and the "endemic point" which replaces the DFE when elimination of the sickness is impossible (without intervention, such as quarantine, vaccination, etc...). Note this further induces a partition of all the coordinates and the equations into "infectious" (eliminable), and the others, or "non-infectious". The non-infectious may further be divided into recovered (output compartments) and susceptible (input compartments). The latter are very important; for example, older individuals may be more susceptible than young ones, or viceversa, and therefore differentiating susceptibles into several groups may be crucial.

The most important result of mathematical epidemiology is the "basic reproduction number" $\mathcal{R}_0$ threshold theorem concerning the stability of the DFE, already encountered in [20].

There are two flavors of mathematical epidemiology and two corresponding formulas for the basic reproduction number:

1. One, for ODE models, identifies $\mathcal{R}_0$, under conditions specified in [23, 24], via a three-steps "next generation matrix" (NGM) procedure:
   (a) computing a "pre-NGM" matrix which involves only the **infectious equations**,
   (b) substituting into it the coordinates of the DFE, which is obtained using only **non-infectious equations**, and
   (c) computing the spectral radius of the resulting NGM matrix.
2. The "non-Markovian/renewal" approach adds one further crucial aspect to mathematical epidemiology: the change in infectivity as function of age of the infection at the time when transmission took place (which was assumed to be exponentially distributed under the previous approach). This factor enters the model via an "age of infection kernel", and the basic reproduction number is computed as the integral of this kernel [14, 13].

The restriction to SIR models with next generation matrix of rank-one renders the connection between the two approaches very elementary and yields powerful explicit formulas – see (18) and (17) below.

[¶] Note that this paper considers the renewal equation formulation, and not just the SIR ODE model.

Contents. Section 2 recalls the definition of SIR-PH models. Section 3 computes the age of infection kernel for these models with one susceptible class, when the "new infections" matrix B is of rank one. Section 4 states an extension to the case of several susceptible compartments. Conclusions and further work are sketched in section 5.

§2. SIR-PH epidemic models

The SIR-PH (phase-type) epidemic models [22] are a particular case of the (A, B) Arino-Brauer epidemic models studied in [4, 3], in which there is only one input class s (and, less importantly, only one output class r). One may think of this class of models as of processes in which the class I has been replaced by a transient Markov chain, the time of transition of which models the law (distribution) of the total infectious period. The modeling of infectious laws more general than the exponential is an old concern in epidemiology– see for example [19] and references therein. Our concern is not only statistical, but also in identifying laws (principles) which hold for large classes of models. Assuming one input class allows decomposing the basic reproduction number $\mathcal{R}_0$, defined as the expected number of secondary cases produced by a **typical** infectious individual during its time of infectiousness– see [17], which serves also as stability threshold of the DFE, as

$$\mathcal{R}_0 = \mathsf{s}_{dfe}\mathcal{R}, \tag{1}$$

where s_{dfe} is the number of susceptibles at the DFE. $\mathcal{R}$ is called basic replacement number (of **one** susceptible individual). These models include a large number of epidemic models, like for example for COVID and ILI (influenza like illnesses). After further ignoring certain quadratic terms for the varying population model [3], we arrive at a **SIR-PH model**, defined by:

$$\begin{aligned}
&\mathsf{s}'(t) = -\mathsf{s}(t)\vec{\mathsf{i}}\,(t)\boldsymbol{\beta} + \Lambda - (\Lambda + \gamma_s)\,\mathsf{s}(t) + \gamma_r \mathsf{r}(t), \quad \boldsymbol{\beta}_i = (B\mathbf{1})_i = \sum_j B_{i,j},\\
&\mathsf{r}'(t) = \vec{\mathsf{i}}\,(t)\boldsymbol{a} + \mathsf{s}(t)\gamma_s - (\gamma_r + \Lambda)\mathsf{r}(t), \quad \boldsymbol{a} = (-A)\mathbf{1}\\
&\vec{\mathsf{i}}\,'(t) = \vec{\mathsf{i}}\,(t)\left[\mathsf{s}(t)\ B + A - Diag\left[\boldsymbol{\delta} + \Lambda\mathbf{1}\right]\right] := \vec{\mathsf{i}}\,(t)\left[\mathsf{s}(t)B - V\right].
\end{aligned} \tag{2}$$

Here,

1. $\mathsf{s}(t) \in \mathbb{R}_+$ represents the set of individuals susceptible to be infected (the beginning state).
2. $\mathsf{r}(t) \in \mathbb{R}_+$ models recovered individuals (the end state).
3. γ_r gives the rate at which recovered individuals lose immunity, and γ_s gives the rate at which individuals are vaccinated (immunized). These two transfers connect directly the beginning and end states (or classes).
4. the row vector $\vec{\mathsf{i}}\,(t) \in \mathbb{R}^n$ represents the set of individuals in different disease states.
5. $\Lambda > 0$ is the per individual death rate, and it equals also the global birth rate (this is due to the fact that this is a model for proportions).

6. A is a $n \times n$ Markovian sub-generator matrix which describes transfers between the disease classes. Recall that a Markovian sub-generator matrix for which each off-diagonal entry $A_{i,j}$, $i \neq j$, satisfies $A_{i,j} \geq 0$, and such that the row-sums are non-positive, with at least one inequality being strict. [§]

   The fact a Markovian sub-generator appears in our "disease equations" suggests that certain probabilistic concepts intervene in our deterministic model, and this is indeed the case–see below. Note also that typical epidemic models satisfy $A_{i,j}A_{j,i} = 0$, $i \neq j$, and so this matrix may be arranged to be triangular.

7. $\boldsymbol{\delta} \in \mathbb{R}_+{}^n$ is a column vectors giving the death rates caused by the epidemic in the disease compartments. The matrix $-V$, which combines A and the birth and death rates $\Lambda, \boldsymbol{\delta}$, is also a Markovian sub-generator.

8. B is a $n \times n$ matrix (called sometimes "new infections" matrix). Each entry $B_{i,j}$, multiplied by s, represents the force of infection from the disease class i onto class j. We will denote by $\boldsymbol{\beta}$ the vector containing the sum of the entries in each row of B, namely, $\boldsymbol{\beta} = B\mathbf{1}$. Thus, $\mathsf{s}\boldsymbol{\beta}_i$ represents the **total force of infection** from the disease class i. Finally, $\mathsf{s}(t)\vec{\mathsf{i}}(t)\boldsymbol{\beta}$ represents the total flux which must leave class s.

   The matrices B and $-V$, intervene in the formulas related to the next generation matrix approach.

Remark 1. 1. Note the factorization of the equation for the diseased compartments $\vec{\mathsf{i}}$, which ensures the existence of a fixed point where these compartments vanish, and implies a representation of $\vec{\mathsf{i}}$ in terms of s:

$$\vec{\mathsf{i}}(t) = \vec{\mathsf{i}}(0)e^{-tV+B\int_0^t s(\tau)d\tau} = \vec{\mathsf{i}}(0)e^{\left[-tId+BV^{-1}\int_0^t s(\tau)d\tau\right]V}. \tag{3}$$

   In this representation intervenes an essential character of our story, the matrix BV^{-1}, which is proportional to the next generation matrix $\mathsf{s}_{dfe}BV^{-1}$.

2. When $B = \boldsymbol{\beta}\vec{\alpha}$, we are in the interesting case when B has rank one. Epidemiologically, this means that each component of the vector of fluxes of infection $\mathsf{s}\boldsymbol{\beta}$ is distributed in the same way to the infection classes, following the same probability vector $\vec{\alpha}$. A typical case is $\vec{\alpha} = (1, 0, 0, ...)$, meaning that all the infected start in the same first class, called latent.

   In this case, it is known by the Arino-Brauer formula [2] generalized in [3] that

$$\mathcal{R}_0 = \lambda_{PF}(\mathsf{s}_{dfe}BV^{-1}) = \mathsf{s}_{dfe}\vec{\alpha}V^{-1}\boldsymbol{\beta}, \tag{4}$$

   where λ_{PF} denotes the Perron-Frobenius eigenvalue (positive eigenvalue of maximum modulus). Note the proof is very simple. The eigenvector must be $v = \boldsymbol{\beta}$, and plugging $\boldsymbol{\beta}$ in $\mathsf{s}_{dfe}\boldsymbol{\beta}\vec{\alpha}V^{-1}v = \mathcal{R}_0 v$ yields the result.

3. Following [3], we have chosen to call the models studied here SIR-PH-FA (adding FA for first approximation), to differentiate them from their version with varying population.

[§] Alternatively, $-A$ is a non-singular M-matrix [2], i.e. a real matrix V with $v_{ij} \leq 0, \forall i \neq j$, and having eigenvalues whose real parts are nonnegative [21].

§3. Associated Markovian semi-groups, age of infection kernels, and an $\mathcal{R}$ formula for SIR-PH-FA models with one susceptible class and B of rank one

We show here that when B has rank one, SIR-PH-FA models have an associated explicit age of infection kernel, which allows in particular obtaining $\mathcal{R}$ via an integral. We may say that rank one SIR-PH-FA epidemic models lie in the intersection of the ODE/Markovian and the non-Markovian/renewal models. Alternatively, they are precisely the renewal models with a matrix-exponential kernel. The equivalence of the two approaches in this simple context is proved concisely below; it may also be read between the lines of the wider scope papers [11, 15].

Our attention to this subject was drawn by formulas on [7, pg. 3] for the "distributed delay/renewal/age of infection kernels" for particular cases of the SIR and SEIR models. These authors assign as an exercise to extend their formulas to other models; it turned out later that determining which models to extend to was part of the exercise. Six years later the exercise was first solved by Champredon-Dushoff-Earn [10] for Erlang-Seir models. We provide below a further extension to the case of SIR-PH-FA models with B of rank one – see also [11, Thm. 2.2], [15] for related results.

Proposition 1. *Let $\widetilde{i}(t) = \vec{\mathsf{i}}\,(t)\boldsymbol{\beta}$ denote the total force of infection of a SIR-PH-FA model* (2) *with one susceptible class, without loss of immunity, i.e. $\gamma_r = 0$ (so that $\mathsf{r}(t)$ does not affect the rest of the system), and with $B = \boldsymbol{\beta}\vec{\alpha}$ of rank one. Then*

1. *The solutions of the ODE system* (2) *satisfy also an integro-differential "SI system" of two scalar equations*

$$\begin{cases} \mathsf{s}'(t) = \Lambda - (\Lambda + \gamma_s)\,\mathsf{s}(t) - \mathsf{s}(t)\widetilde{i}(t) \\ \widetilde{i}(t) = \vec{\mathsf{i}}\,(0)e^{-tV}\boldsymbol{\beta} + \int_0^t s(\tau)\widetilde{i}(\tau)a(t-\tau)d\tau, \end{cases} \tag{5}$$

   where

$$a(\tau) = \vec{\alpha}e^{-\tau V}\boldsymbol{\beta}, \tag{6}$$

   with $-V = A - (Diag\,[\boldsymbol{\delta} + \Lambda\mathbf{1}])$ (it may be checked that this fits the formula on page 3 of [7] for SEIR when $\Lambda = 0, \delta = 0$). [‡]

2. *The basic replacement number $\mathcal{R}$ has an integral representation*

$$\mathcal{R} = \int_0^\infty a(\tau)d\tau = \int_0^\infty \vec{\alpha}e^{-\tau V}\boldsymbol{\beta}d\tau = \vec{\alpha}\,V^{-1}\,\boldsymbol{\beta}. \tag{7}$$

Proof: 1. The non-homogeneous infectious equations may be transformed into an integral equation by applying the variation of constants formula. The first step is the solution of the homogeneous part. Denoting this by $\Gamma(t)$, it holds that

$$\vec{\Gamma}'(t) = -\vec{\Gamma}(t)V \Longrightarrow \vec{\Gamma}(t) = \vec{\Gamma}(0)e^{t(-V)}. \tag{8}$$

[‡] $a(t)$ is called "age of infection/renewal kernel; see [16, 6, 7, 12, 10, 11, 15] for expositions of this concept.

The variation of constants formula implies then that $\vec{\mathsf{i}}(t)$ satisfies the integral equation:

$$\vec{\mathsf{i}}(t) = \vec{\mathsf{i}}(0)e^{-tV} + \int_0^t \mathsf{s}(\tau)\vec{\mathsf{i}}(\tau)Be^{-(t-\tau)V}d\tau. \tag{9}$$

Now in the rank one case $B = \boldsymbol{\beta}\vec{\alpha}$, and (9) becomes

$$\vec{\mathsf{i}}(t) = \vec{\mathsf{i}}(0)e^{-tV} + \int_0^t \mathsf{s}(\tau)\vec{\mathsf{i}}(\tau)\boldsymbol{\beta}\vec{\alpha}e^{-(t-\tau)V}d\tau. \tag{10}$$

Finally, multiplying both sides on the right by $\boldsymbol{\beta}$ and recalling that $\widetilde{i}(t) = \vec{\mathsf{i}}(t)\boldsymbol{\beta}$ yields the result.

2. By the "survival method" [‡] , $\mathcal{R}$ may be obtained by integrating $\Gamma(t)$ with $\Gamma(0) = \vec{\alpha}$. A direct proof is also possible by noting that all eigenvalues of the next generation matrix except one are 0 [2, 3]. □

Remark 2. When $\vec{\Gamma}(0)$ is a probability vector, (8) has the interesting probabilistic interpretation of the survival probabilities in the various components of the semigroup generated by the Metzler/Markovian sub-generator matrix $-V$ (which inherits this property from the phase-type generator A). Practically, $\vec{\Gamma}(t)$ will give the expected fractions of individuals who are still in each compartment at time t.

Remark 3. We may relate (10) to the age of infection equation of the distributed delay/renewal model, by noting that it holds that

$$\vec{\mathsf{i}}(t) = \int_{-\infty}^t s(\tau)\widetilde{i}(\tau)a(t-\tau)d\tau, \tag{11}$$

provided that $\widetilde{i}(\tau)$ on the interval $(-\infty, 0]$ is $\frac{k}{s_0}\delta_0(\tau)$, where $\delta_0(\tau)$ denotes the generalized Dirac function, and that $\vec{\mathsf{i}}(0) = k\vec{\alpha}$. This second equation is related to [10, (2.7b),(2.8),(2.9)] and [7, (1)]. [§] Equations like (11), called DD (distributed delay) equations appear already in the founding paper [20], which is quite natural. Indeed, if it were known that infections arise precisely τ_0 units of time after a contact, then the second equation of the SI model would involve the Dirac kernel $a(\tau) = \delta_{\tau_0}(\tau)$. But, since the value of τ_0 is never known, it is natural to replace the Dirac kernel by a continuous one.

Remark 4.

1. The fact that DD systems can be approximated by ODE systems, by approximating the delay distribution via one of Erlang, and more generally, of matrix-exponential type, has long been exploited in the epidemic literature, under the name of "linear chain trick" (which has roots in the Erlangization of queueing theory)– see for example [26, 25, 11, 8, 18, 1, 15] for recent contributions and further references. The opposite direction however, i.e. the solution of the exercise in [7] of identifying the kernels associated to ODE models, seems not to have been resolved in this generality, prior to our paper.

[‡] This is a first-principles method, whose rich history is described in [16, 13]– see also [10, (2.3)], [11, (5.9)].

[§] In fact, these authors work with the related *incidence flux* between the s and $\vec{\mathsf{i}}$ variables $Incid := s\,\vec{i}\,\mathbf{b}$, denoted by $i(t)$ in [10], and by $F(t)$ in [7].

2. Finally, for DD models, normalizing the kernel by its integral $\mathcal{R}_0$ yields the density of the "intrinsic generating interval" for the age of infection [9, 10, 15]: $g(t) = \frac{a(t)}{\mathcal{R}_0} = \frac{\vec{\alpha} e^{-\tau V} \boldsymbol{\beta}}{\mathcal{R}_0}$ –see [10, (2.6)].

§4. Extension to several susceptible compartments and time-dependent inputs

We show here that SIR-PH epidemic models with two or more susceptible compartments may also satisfy renewal type integro differential equations.

Consider the ODE model with two susceptible classes, defined by:

$$\begin{aligned}
\vec{\mathsf{i}}'(t) &= \vec{\mathsf{i}}(t)\left[\mathsf{s}_1(t)\, B_1 + \mathsf{s}_2(t)\, B_2 + A - Diag\left(\Lambda(t)\mathbf{1} + \boldsymbol{\delta}\right)\right] := \vec{\mathsf{i}}(t)\, \widetilde{B}(t) - \vec{\mathsf{i}}(t)V,\\
\mathsf{s}_1'(t) &= \Lambda_1(t) + \gamma_{r,1}\mathsf{r}(t) - \mathsf{s}_1(t)\left[\vec{\mathsf{i}}(t)\boldsymbol{\beta}_1 + \Lambda(t) + \gamma_s\right],\ \ \boldsymbol{\beta}_1 = B_1\mathbf{1},\\
\mathsf{s}_2'(t) &= \Lambda_2(t) + \gamma_{r,2}\mathsf{r}(t) - \mathsf{s}_2(t)\left[\vec{\mathsf{i}}(t)\boldsymbol{\beta}_2 + \Lambda(t) + \gamma_s\right],\ \ \boldsymbol{\beta}_2 = B_2\mathbf{1},\\
\mathsf{r}'(t) &= \vec{\mathsf{i}}(t)\boldsymbol{a} + (\mathsf{s}_1(t) + \mathsf{s}_2(t))\gamma_s - (\gamma_r + \Lambda(t))\mathsf{r}(t),\ \ \boldsymbol{a} = (-A)\mathbf{1},
\end{aligned} \tag{12}$$

where we put $\vec{\mathsf{i}} = (i_1, i_2)$, $\widetilde{B}(t) = \sum_i \mathsf{s}_i(t)B_i$, $\Lambda = \Lambda_1 + \Lambda_2$, $\boldsymbol{\delta} = \begin{pmatrix}\delta_1\\ \delta_2\\ \vdots\end{pmatrix}$, $\gamma_r = \gamma_{r,1} + \gamma_{r,2}$. Note that

$$N(t) = \mathsf{s}_1(t) + \mathsf{s}_2(t) + \mathsf{r}(t) + \vec{\mathsf{i}}(t)\mathbf{1} \text{ satisfies } N'(t) = \Lambda(t)(1 - N(t)) - \vec{\mathsf{i}}(t)\boldsymbol{\delta}.$$

Assume further that $B_i = \boldsymbol{\beta}_i\vec{\alpha}_i, i = 1, 2$, put $\widetilde{B}_i(t) = \boldsymbol{\beta}_i(\mathsf{s}_i(t)\vec{\alpha}_i), i = 1, 2$, and put

$$\widetilde{B}(t) = \sum_i \widetilde{B}_i(t) := \vec{\beta}\begin{pmatrix}\mathsf{s}_1(t) & 0\\ 0 & \mathsf{s}_2(t)\end{pmatrix}\vec{\alpha},\ \text{where recall that}\vec{\beta} = \begin{pmatrix}\boldsymbol{\beta}_1 & \boldsymbol{\beta}_2\end{pmatrix}, \vec{\alpha} = \begin{pmatrix}\vec{\alpha}_1\\ \vec{\alpha}_2\end{pmatrix}. \tag{13}$$

The variation of constants formula applied to (12) implies that $\vec{\mathsf{i}}(t)$ satisfies the integral equation:

$$\begin{aligned}
\vec{\mathsf{i}}(t) = \ & \vec{\mathsf{i}}(0)e^{-tV} + \int_0^t \vec{\mathsf{i}}(\tau)\widetilde{B}(\tau)e^{-(t-\tau)V}d\tau = \vec{\mathsf{i}}(0)e^{-tV} + \int_0^t \vec{\mathsf{i}}(t-\tau)\widetilde{B}(t-\tau)e^{-\tau V}d\tau\\
:= \ & \vec{\mathsf{i}}(0)e^{-tV} + \int_0^t \vec{\mathsf{i}}(t-\tau)\widetilde{K}(t,\tau)d\tau, \quad \widetilde{K}(t,\tau) := \widetilde{B}(t-\tau)e^{-\tau V}.
\end{aligned} \tag{14}$$

We will call $\widetilde{K}(t,\tau)$ implicit kernel, to emphasize the fact that it depends still on the unknown $\mathsf{s}_i(t)$.

When $B_i = \boldsymbol{\beta}_i\vec{\alpha}_i, i = 1, 2$, putting $\widetilde{i_i}(t) = \vec{\mathsf{i}}(t)\boldsymbol{\beta}_i, i = 1, 2$ (14) becomes

$$\vec{\mathsf{i}}(t) = \vec{\mathsf{i}}(0)e^{-tV} + \int_0^t \left[\sum_{i=1}^2 \mathsf{s}_i(\tau)\widetilde{i_i}(\tau)\vec{\alpha}_i e^{-(t-\tau)V}\right]d\tau. \tag{15}$$

Multiplying further by $\boldsymbol{\beta}_k, k = 1,2$ and putting $a_{i,j}(t) = \vec{\alpha}_i e^{-tV}\boldsymbol{\beta}_j, i,j = 1,2$, yields a system of two equations for $\widetilde{i_k}(t) = \vec{\mathsf{i}}(t)\boldsymbol{\beta}_k, k = 1,2$:

$$\begin{cases} \widetilde{i_1}(t) = \vec{\mathsf{i}}(0)e^{-tV}\boldsymbol{\beta}_1 + \int_0^t \left[\mathsf{s}_1(\tau)\widetilde{i_1}(\tau)a_{1,1}(t-\tau) + \mathsf{s}_2(\tau)\widetilde{i_2}(\tau)a_{2,1}(t-\tau)\right]d\tau \\ \widetilde{i_2}(t) = \vec{\mathsf{i}}(0)e^{-tV}\boldsymbol{\beta}_2 + \int_0^t \left[\mathsf{s}_1(\tau)\widetilde{i_1}(\tau)a_{1,2}(t-\tau) + \mathsf{s}_2(\tau)\widetilde{i_2}(\tau)a_{2,2}(t-\tau)\right]d\tau \end{cases} \tag{16}$$

We may conclude that proposition 1 extends as follows:

Proposition 2. *Consider a SIR-PH-FA model* (12) *with two susceptible classes with* $B_i = \boldsymbol{\beta}_i\vec{\alpha}_i, i = 1,2$, *with constant input inflows* Λ_1, Λ_2, *and which satisfies the conditions of [23]. Then, it holds that :*

1. *The solutions of* (12) *satisfy also an integro-differential system*

$$\begin{cases} \mathsf{s}_1'(t) = \Lambda_1 + \gamma_{r,1}\mathsf{r}(t) - \mathsf{s}_1(t)\left[\vec{\mathsf{i}}(t)\boldsymbol{\beta}_1 + \Lambda + \gamma_s\right], \ \boldsymbol{\beta}_1 = B_1\mathbf{1}, \\ \mathsf{s}_2'(t) = \Lambda_2 + \gamma_{r,2}\mathsf{r}(t) - \mathsf{s}_2(t)\left[\vec{\mathsf{i}}(t)\boldsymbol{\beta}_2 + \Lambda + \gamma_s\right], \ \boldsymbol{\beta}_2 = B_2\mathbf{1}, \\ \mathsf{r}'(t) = \vec{\mathsf{i}}(t)\boldsymbol{a} + (\mathsf{s}_1(t) + \mathsf{s}_2(t))\gamma_s - (\gamma_r + \Lambda)\mathsf{r}(t), \ \boldsymbol{a} = (-A)\mathbf{1} \\ \widetilde{i}(t) = \vec{\mathsf{i}}(0)e^{-tV}\vec{\beta} + \int_0^t \widetilde{i}(\tau)Diag(\mathsf{s}(\tau))a(t-\tau)d\tau, \end{cases} \tag{17}$$

   where $a(\tau) = \left(\mathsf{s}_i(\tau)a_{i,j}(\tau)\right)_{i,j=1,2}, \mathsf{s}(\tau) = (\mathsf{s}_1(\tau), \mathsf{s}_2(\tau))$.

2. *The DFE satisfies* ($\mathsf{r}_{dfe} = \frac{\gamma_s}{\Lambda+\gamma_r+\gamma_s}, \mathsf{s}^i_{dfe} = \frac{\Lambda+\gamma_s}{\Lambda_i+\gamma_{r,i}\mathsf{r}_{dfe}}, i = 1,2$), *and the basic reproduction number* $\mathcal{R}_0$ *is the Perron-Frobenius eigenvalue of the two by two matrix*

$$\begin{pmatrix} \mathsf{s}^1_{dfe}\vec{\alpha}_1V^{-1}\boldsymbol{\beta}_1 & \mathsf{s}^1_{dfe}\vec{\alpha}_1V^{-1}\boldsymbol{\beta}_2 \\ \mathsf{s}^2_{dfe}\vec{\alpha}_2V^{-1}\boldsymbol{\beta}_1 & \mathsf{s}^2_{dfe}\vec{\alpha}_2V^{-1}\boldsymbol{\beta}_2 \end{pmatrix} = \vec{\alpha}\begin{pmatrix} \mathsf{s}^1_{dfe} & 0 \\ 0 & \mathsf{s}^2_{dfe} \end{pmatrix}V^{-1}\vec{\beta}, \tag{18}$$

   with an obvious generalization to the case of several compartments.

§5. Conclusions and further work

Solving the exercise of [7] revealed that the (A,B) Arino-Brauer epidemic models with B of rank one have the remarkable property of having a natural associated "age of infection kernel" which implies a very simple formula for $\mathcal{R}$. [§] This continues to be true for models with several susceptible classes, and is of considerable interest for epidemic models structured by the age of the individuals.

Another question worth further research is whether an age of infection kernel may be associated to (A,B) Arino-Brauer epidemic models with one susceptible class, but with a matrix B of rank bigger than 1.

[§]Thus, these deterministic models have also one foot in the stochastic world, which reveals itself when all the infectious equations are grouped into one equation.

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