An essay on mathematical epidemiology, related sciences dealing with essentially non-negative kinetic systems, and on the importance of scientific computing

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Abstract

This mainly expository paper reviews some key concepts in mathematical epidemiology. Our purpose is to make the case that currently this field is focusing too much on simple particular cases, and deemphasizes more complex models, whose challenges would require cooperation with scientific computing experts (as an example, even the SIR model is not yet sufficiently understood). Our paper attempts also to invitate researchers working in the applied "sister sciences" which involve essentially nonnegative kinetic systems (like mathematical epidemiology, virology, chemical reaction networks, population dynamics, etc), to unite their efforts under the banner of "algebraic biology".

Contents

1 The ODE SIR model of Kermack and Mc-Kendrick

The classic ODE Kermack–McKendrick SIR epidemic model divides a population of size N undergoing an epidemic into three classes
$$(S(t), I(t), R(t), t \geq 0)$$
called "susceptibles, infectives and removed". It is assumed that only susceptible individuals can get infected. After having been infectious for some time, an individual recovers and may not become susceptible again. "Viewed from far away", this yields the SIR model with demography [KM27, BCCF19]

$$
\begin{aligned}
S'(t) &= b\,(N - S(t)) - \frac{\beta}{N} S(t) I(t), \\
I'(t) &= I(t) \left(\frac{\beta}{N} S(t) - \gamma - b \right), \\
R'(t) &= \gamma I(t) - b\,R(t), \\
N &= N(t) = S(t) + I(t) + R(t).
\end{aligned}
\tag{1}
$$

Note that:

1. The equation for I factors, and that ensures the existence of a "disease-free equilibrium" (DFE) fixed point. The alternative for $I = 0$ yields the so called "immunity threshold"
$$S = N \frac{\gamma + b}{\beta},$$
which gives rise to a second fixed point called "endemic". Usually, there exists at least one such point, since some attractor must replace the DFE when this becomes unstable (i.e. when elimination of the sickness is impossible).

2. The equality of the rates of birth and death reflects the fact that this is a short term model with constant population N.

1.1 The model for the proportions

$\mathsf{s}(t) = \frac{S(t)}{N}$, $\mathsf{i}(t) = \frac{I(t)}{N}$, $\mathsf{r}(t) = 1 - \mathsf{s}(t) - \mathsf{i}(t)$ is

$$s'(t) = b - b\ s(t) - \beta s(t)\ i(t),$$
$$i'(t) = \beta s(t)\ i(t) - (\gamma + b)\ i(t),$$
$$r'(t) = \gamma\ i(t) - b\ r(t),$$
$$s(0) = s_0, \quad i(0) = i_0, \quad r(0) = r_0,$$

There are four calibration parameters to be determined: (i) β, the transmission rate by which the infectious infect susceptible people; (ii) $1/\gamma$, the average time an infectious individual may infect others; (iii) i_0, the initial number of infected at the detection of the epidemics; (iv) r_0, the initial number of recovered (or s_0, the initial number of susceptibles). The range of variation of the parameter γ is known from the medical literature, so this may also be considered as known. When fitting data, there is also a fifth essential parameter: the proportion of declared infectious cases p.

The SIR model assumes that an individual moves from susceptible to infectious directly when he/she gets infected. This is wrong, and corrected by the SEIR model, but it makes sense to begin calibration by a model with as few parameters as possible.

The points in figure 1 below represent the number of reported cases
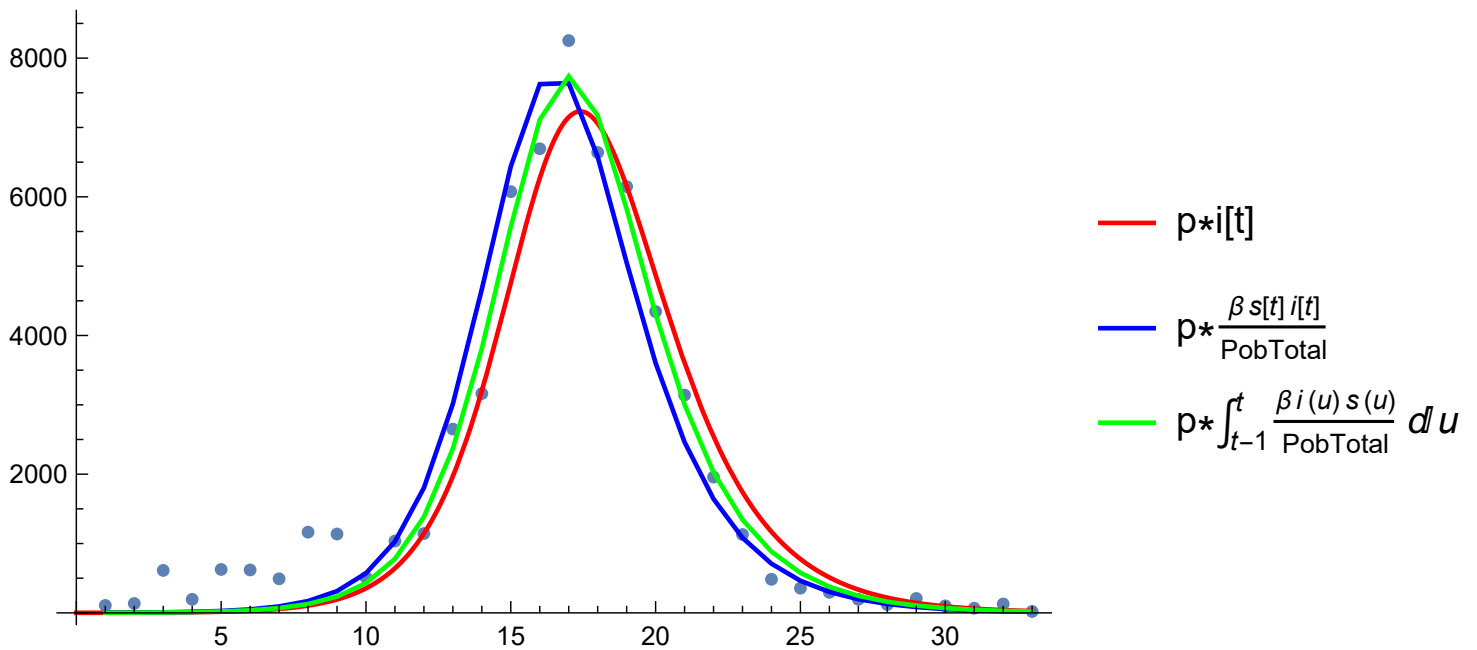
Figure 1: Reported cases of influenza over the total population of the Community of Valencia, Spain, in the season 2016-2017, and their calibration by a SIR model with parameters $\beta = 5.82402, \gamma = 4.08759, s_0 = 3.9624 * 10^6, i_0 = 8.26234, p = 0.0594004$. The last (green) curve representing the integrals of the inflow rate over the preceding week (the inflow increments), is the exact theoretical expression of the newly infected and known data. In the second (blue) curve, each integral is replaced by its approximation by one rectangles. It is very close to the green curve, and they can be made to coincide by using instead Riemann sum approximations via several rectangles for each integral. These approximations are useful in speeding up execution times. Even the first curve (red) of the current infectious is similar enough in shape (at least when $s(t)$ doesn't become too different of the total population), and may be used for calibration, of course, with a modified p. Note that the data may be divided into three periods: until week 10, after week 22, and in between $(5.82402, 4.08759, 3.9624 * 10^6, 8.26234, 0.0594004)$, and the fit is satisfactory only in the middle period. This case study joins thus numerous others which observe that simple epidemic models do not well describe the initial and final segments of epidemic data.

of influenza in the Community of Valencia, Spain, in the flu-season 2016-2017, for 33 weeks. The natural time unit, suggested by the data, is the week.

They are not dissimilar to those analyzed in the foundational paper [KM27], in which Kermack and McKendrick fitted such data via the celebrated ODE SIR compartmental model they introduced (they introduced well as an integro-differential extension).

2 A bird's eye view of mathematical epidemiology

The most fundamental aspect of mathematical epidemiology is the existence of at least two possible "special fixed states". The first, the DFE, it corresponds to the elimination of all compartments involving sickness. Note that the absence of boundary states is

often assumed in chemical reaction network theory, so at this point these two bodies of knowledge are diverging.

A "maximal boundary state" may be found by identifying first a sub-system which factors

$$\boldsymbol{i}' = M\boldsymbol{i},$$

whose components $\boldsymbol{i}$ are called infectious states, and whose indices will be denoted by "infec". Note that specifying "infec" induces a partition of both the coordinates and the equations into infectious (eliminable) components, and the others.

The DFE is easily computed by solving the remaining "non-infectious equations" with $\boldsymbol{i} = 0$. We give now a very elementary script, to emphasize the fact that any ODE model "mod" (like SIR, etc...), is a pair (dyn,X) consisting of a vector field and a list of variables. But, since sometimes only numeric solutions are possible, our fixed point script below has also an optional numerical condition parameter "cn".

```
BdFixedPt[mod_,inf_,cn_:{}]:=Module[{dyn,X},
  dyn=mod[[1]]/.cn;X=mod[[2]];
  Solve[Thread[dyn==0]/.Thread[X[[inf]]->0],X]];
```

2.1 The SAIR/SI²R/SEIR-FA epidemic model, and some Mathematica scripts

Example 1 *The 10 parameters SAIR/SI^{2}R/SEIR-FA epidemic model [VdDW08, RS13, AKK$^+$20, OSS22, AAH22], its next generation matrix, and its basic reproduction number $\mathcal{R}_0$:*
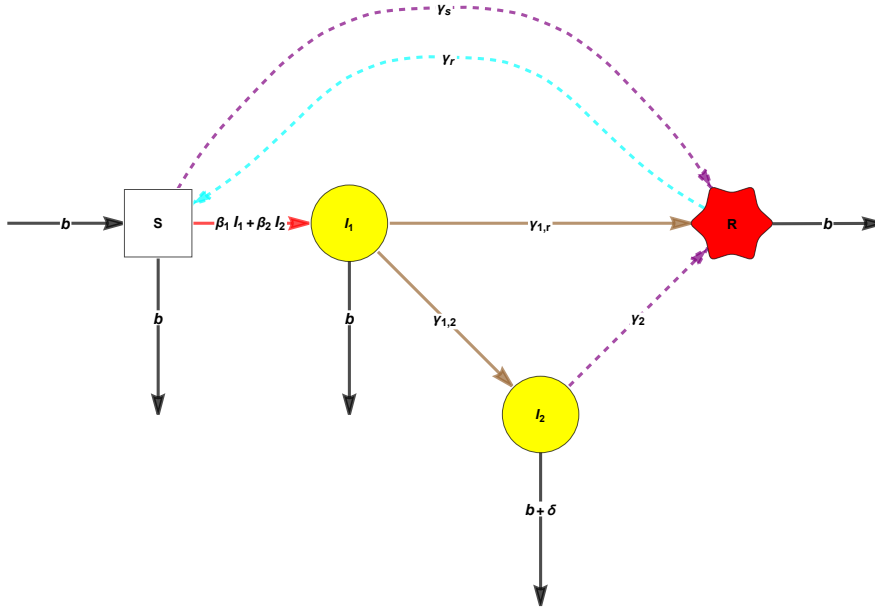
Figure 2: Chart flow of the SI²R model (2). The red edge corresponds to the entrance of susceptibles into the disease classes, the brown edges are the rate of the transition matrix V, and the cyan dashed lines correspond to the rate of loss of immunity. The remaining black lines correspond to the inputs and outputs of the birth and natural death rates, respectively, which are equal in this case.

The proportions of the **long term, varying population model with** $\delta > 0$ defined in Figure 2 satisfy **approximatively** [AABH22, AAH22]:

$$
\begin{cases}
\mathsf{s}'(t) = b - \mathsf{s}(t)\left(\beta_i\,\mathsf{i}(t) + \beta_a\,\mathsf{a}(t) + \gamma_s + b\right) + \gamma_r\,\mathsf{r}(t) \\[2mm]
\begin{pmatrix} \mathsf{e}'(t) \\ \mathsf{i}'(t) \end{pmatrix} = \left[\mathsf{s}(t) \begin{pmatrix} \beta_a & \beta_i \\ 0 & 0 \end{pmatrix} - \begin{pmatrix} \gamma_e + b & 0 \\ -a_i & b + \gamma_i + \delta \end{pmatrix} \right] \begin{pmatrix} \mathsf{a}(t) \\ \mathsf{i}(t) \end{pmatrix} \\[2mm]
\mathsf{r}'(t) = \gamma_s\,\mathsf{s}(t) + a_r\,\mathsf{a}(t) + \gamma\,\mathsf{i}(t) - (\gamma_r + b)\,\mathsf{r}(t)
\end{cases}
\tag{2}
$$

Remark 1 *1. The SAIR model is obtained when* $a_r(\gamma_{1,r}) = 0 = \delta$ *and the classic SEIR model is obtained when furthermore* $\beta_a = 0.$

2. We have written the "infectious" middle equations to empha-size their factorization. Also, for the factor appearing in these equations, we have emphasized a form

$$
F - V.
\tag{3}
$$

This non-unique, not always existing decomposition is used in

the computation of the next generation matrix (NGM)

$$K = F.V^{-1}$$

[DHM90, VdDW02, VdDW08].

We code the model as:

```
SEIR =
    Module[{ss, ee, ii, rr, dyn, X, pars},
        ss = b - \[Mu] s - (\[Beta] s i+\[Beta]e s e) +
        ee = (\[Beta] s i+\[Beta]e s e) - e (\[Mu] + ei+
        ii = e ei - i (\[Mu] + \[Gamma]i + \[Delta]);
        rr =br + \[Gamma]s s + er e+ \[Gamma]i i - (\[Ga
        dyn = {ee, ii, rr, ss};
        X = {e, i, r, s};
        pars = Complement[Variables[dyn], X];
        {dyn, X, pars}
    ];
```

The call "NGM[SEIR,{1,2}]" of our "NGM" script:

```
NGM[mod_,inf_]:=Module[{dyn,X,dyni,M,V,li,Fv,F,K},
   dyn=mod[[1]];X=mod[[2]];
   dyni=dyn[[inf]];
   M=Grad[dyni,X[[inf]]];(*the factor in the infectious
   V=-M/.Thread[X->0];(*V is the constant matrix in the
   li= V . X[[inf]] ;(*the part linear X[[inf]] of the g
   Fv=dyni+li;
   F=Grad[Fv,X[[inf]]];
   K=(F . Inverse[V])/.Thread[X[[inf]]->0];
{M,V,F,K}]
```

yields that $K = s \begin{pmatrix} \frac{\beta_i a_i}{(a_i+a_r+\mu)(\delta+\gamma_i+\mu)} + \frac{\beta_e}{a_i+a_r+\mu} & \frac{\beta_i}{\delta+\gamma_i+\mu} \\ 0 & 0 \end{pmatrix}$, and the

Perron-Frobenius eigenvalue of K is

$$\mathcal{R}_0 = \mathsf{s}_{dfe} \frac{\beta_i a_i}{(a_i + a_r + \mu)(\delta + \gamma_i + \mu)} + \frac{\beta_e}{a_i + a_r + \mu}.$$

Remark 2 *On the other hand, the classic Jacobian approach will yield a rather complicated result for the stability of the corresponding 4×4 matrix.*

3 Markovian semi-groups associated to ODE epidemic models, age of infection kernels, and the $\mathcal{R}$ formula for SIR-PH-FA models with one susceptible class and B of rank one

The idea behind the next generation matrix method is that the infectious components may be expressed in function of the others. This is especially easy to state for **SIR-PH-FA models** [AAB$^+$22a], defined by:

$$\boldsymbol{i}'(t) = \boldsymbol{i}(t) \left[\mathsf{s}(t) \, B + A - Diag\left(\boldsymbol{\delta} + b\mathbf{1}\right) \right] := \boldsymbol{i}(t) \boxed{\left(-V + \mathsf{s}(t)B\right)}$$

$$\mathsf{s}'(t) = \left[b - (b + \gamma_s) \, \mathsf{s}(t) \right] - \mathsf{s}(t)\widetilde{i}(t) + \gamma_r \mathsf{r}(t), \;\; \widetilde{i}(t) = \boldsymbol{i}(t)\boldsymbol{\beta}$$

$$\boldsymbol{\beta} = \begin{pmatrix} \boldsymbol{\beta}_1 \\ \vdots \\ \boldsymbol{\beta}_n \end{pmatrix}, \quad \boldsymbol{\beta}_i = (B\mathbf{1})_i = \sum_j B_{i,j}, \, i = 1, ..., n$$

$$\mathsf{r}'(t) = \boldsymbol{i}(t)\boldsymbol{a} + \mathsf{s}(t)\gamma_s - (\gamma_r + b)\mathsf{r}(t), \quad \boldsymbol{a} = (-A)\mathbf{1}. \tag{4}$$

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 $\boldsymbol{i}(t) \in \mathbb{R}^n$ represents the set of individuals in different disease states.

5. $b > 0$ 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 models, and this is indeed the case–see below.

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 $b, \boldsymbol{\delta}$, is also a Markovian sub-generator.

8. B is a $n \times n$ matrix. We will denote by $\boldsymbol{\beta}$ the vector containing the sum of the entries in each row of B, namely, $\boldsymbol{\beta} = B\mathbf{1}$. Its components $\boldsymbol{\beta}_i$ represent the **total force of infection** of the disease class i, and $\mathsf{s}(t)\boldsymbol{i}(t)\boldsymbol{\beta}$ represents the total flux which must leave class s. Finally, each entry $B_{i,j}$, multiplied by s, represents the force of infection from the disease class i onto class j, and our essential assumption below will be that $B_{i,j} = \beta_i \alpha_j$, i.e. that all forces of infection are distributed among the infected classes conforming to the same probability vector $\vec{\alpha} = (\alpha_1, \alpha_2, ..., \alpha_n)$.

[§]Alternatively, $-A$ is a non-singular M-matrix [ABvdD$^+$07], i.e. a real matrix V with $v_{ij} \leq 0, \forall i \neq j$, and having eigenvalues whose real parts are nonnegative [Ple77].

Remark 3 *Note that the factorization of the equation for the diseased compartments $\boldsymbol{i}$ implies a representation of $\boldsymbol{i}$ in terms of s:*

$$\boldsymbol{i}(t) = \boldsymbol{i}(0)e^{-tV+B\int_0^t s(\tau)d\tau} = \boldsymbol{i}(0)e^{\left[-tI_n+BV^{-1}\int_0^t s(\tau)d\tau\right]V}. \quad (5)$$

In this representation intervenes an essential character of our story, the matrix BV^{-1}, which is proportional to the next generation matrix $\mathsf{s}BV^{-1}$. A second representation (10) below will allow us to embed our models in the interesting class of distributed delay/renewal models, in the case when B has rank one.

Proposition 1 *Consider a SIR-PH-FA model (4) with one susceptible class, without $\gamma_r = 0$, so that $r(t)$ does not affect the rest of the system, and with $B = \boldsymbol{\beta}\vec{\alpha}$ of rank one. Let*

$$\widetilde{i}(t) = \boldsymbol{i}(t)\boldsymbol{\beta}$$

denote the total force of infection. Then

1. The solutions of the ODE system (4) satisfy also a "distributed delay SI system" of two scalar equations

$$\begin{cases} \mathsf{s}'(t) = \Lambda - (b + \gamma_s)\,\mathsf{s}(t) - \mathsf{s}(t)\widetilde{i}(t) \\ \widetilde{i}(t) = \boldsymbol{i}(0)e^{-tV}\boldsymbol{\beta} + \int_0^t s(\tau)\widetilde{i}(\tau)a(t-\tau)d\tau, \end{cases} \quad (6)$$

   where

$$a(\tau) = \vec{\alpha}e^{-\tau V}\boldsymbol{\beta}, \quad (7)$$

   with $-V = A - (Diag\,[\boldsymbol{\delta} + \Lambda\mathbf{1}])$ (it may be checked that this fits the formula on page 3 of [BDDG$^+$12] for SEIR when $\Lambda = 0, \delta = 0$). ‡

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

$$\mathcal{R} = \int_0^{\infty} a(\tau)d\tau = \int_0^{\infty} \vec{\alpha}e^{-\tau V}\boldsymbol{\beta}d\tau = \vec{\alpha}\,V^{-1}\,\boldsymbol{\beta}. \quad (8)$$

Proof: 1. The non-homogeneous infectious equations may be transformed into an integral equation by applying the variation

---

$^{\ddagger}a(t)$ is called "age of infection/renewal kernel; see [?, Bra05, BDDG$^+$12, DHB13, CDE18, DGM18, DI22] for expositions of this concept.

of constants formula. The first step is the solution of the homogeneous part. Denoting this by $\Gamma(t)$, it holds that

$$\vec{\Gamma}'(t) = -\vec{\Gamma}(t)V \implies \vec{\Gamma}(t) = \vec{\Gamma}(0)e^{t(-V)}.^{\S} \qquad (9)$$

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

$$\boldsymbol{i}(t) = \boxed{\boldsymbol{i}(0)e^{-tV} + \int_0^t \mathsf{s}(\tau)\boldsymbol{i}(\tau)Be^{-(t-\tau)V}d\tau}. \qquad (10)$$

Now in the rank one case $B = \boldsymbol{\beta}\vec{\alpha}$, and (10) becomes

$$\boldsymbol{i}(t) = \boldsymbol{i}(0)e^{-tV} + \int_0^t \mathsf{s}(\tau)\left[\boldsymbol{i}(\tau)\boldsymbol{\beta}\right]\vec{\alpha}e^{-(t-\tau)V}d\tau. \qquad (11)$$

Finally, multiplying both sides on the right by $\boldsymbol{\beta}$ 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 [ABvdD$^+$07, AAB$^+$22a]. □

Example 2 *The SAIR/SEIR model is an (A, B) Arino-Brauer epidemic models with parameters $\vec{\alpha} = \begin{pmatrix} 1 & 0 \end{pmatrix}, A = \begin{pmatrix} -\gamma_1 & \gamma_{1,2} \\ 0 & -\gamma_2 \end{pmatrix}, \boldsymbol{a} =$*

$(-A)\mathbf{1} = \begin{pmatrix} \gamma_{1,r} \\ \gamma_2 \end{pmatrix}$ and

$\boldsymbol{\beta} = \begin{pmatrix} \beta_1 \\ \beta_2 \end{pmatrix}$, so $B = \begin{pmatrix} \beta_1 & 0 \\ \beta_2 & 0 \end{pmatrix}, \boldsymbol{\delta} = \begin{pmatrix} 0 \\ \delta \end{pmatrix}, V = \begin{pmatrix} \gamma_1 + \Lambda & -\gamma_{1,2} \\ 0 & \gamma_2 + b + \delta \end{pmatrix}$

The Laplace transform of the age of infection kernel is:

$$\widehat{a}(s) = \vec{\alpha}(sI + V)^{-1}\boldsymbol{\beta} = \beta_1\frac{1}{(b + \gamma_1 + s)} + \beta_2\frac{\gamma_{1,2}}{(b + \gamma_2 + \delta + s)(b + \gamma_1}$$
$$(12)$$

and the Arino & al. formula yields $\mathcal{R} = \int_0^\infty a(\tau)d\tau = \frac{\beta_1(b+\gamma_2+\delta)+\gamma_{1,2}\beta_2}{(b+\gamma_2+\delta)(b+\gamma_1)}.$

[‡]This is a first-principles method, whose rich history is described in [?, DHR10]– see also [CDE18, (2.3)], [DGM18, (5.9)].

Remark 4 *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 [WRK05, Fen07, ?, DGM18, ?, ?, ABG20, DI22] for recent contributions and further references. The opposite direction however, i.e. identifying the kernels associated to ODE epidemic models, seems to have been forgotten.*

3.1 The $F - V$ decomposition and the next generation matrix

There are (at least) two flavors of mathematical epidemiology and two corresponding formulas for $\mathcal{R}_0$:

1. One, for ODE/Markovian models, identifies $\mathcal{R}_0$ as the spectral radius of the Perron-Frobenius eigenvalue of the "NGM" FV^{-1}, obtained by splitting the infectious equations as

$$\boldsymbol{i}' = \boldsymbol{i}(F - V),$$

   where F has only nonnegative elements, and $-V$ is a Markovian generating matrix (this result requires that the set "infec" of infectious equations satisfies appropriate conditions – see [DHM90, VdDW02, VdDW08], and guarantees neither existence of "infec", nor its uniqueness).

2. Under the second, "non-Markovian/renewal" approach, $\mathcal{R}_0$ is computed as the integral of an "age of infection kernel" [DHM90].

   The intersection of these two classes, the ODE/Markovian and the non-Markovian/renewal models, is the notable context of "rank one SIR-PH-FA epidemic models" [AAB$^+$22b], which are a particular case of the more general (A, B) Arino-Brauer epidemic modelsintroduced in [AAB$^+$22a]. Alternatively, these are precisely the renewal models with a matrix-exponential kernel. The equivalence

of the two approaches for this class of epidemic models is proved very concisely in [AAB$^+$22b], and it may also be read between the lines of the wider scope papers [DGM18, DI22].

Beyond this class of simple models, mathematical epidemiology is still largely a collection of examples and open problems. Even the simplest 3 compartments SIR process has been fully analyzed only recently in [Nil22a, Nil22b].

4 The $\mathcal{R}_0$ threshold theorem for the stability of the DFE

This pillar result of mathematical epidemiology, already encountered in a particular case in the foundational paper "A contribution to the mathematical theory of epidemics" [KM27], ensures that:

1. The stability region can be expressed via one inequality
$$\mathcal{R}_0 < 1,$$
   where the "basic reproduction number" $\mathcal{R}_0$ has a biological interpretation. More precisely, in the simplest case with one susceptible class only, it is given by
$$\mathcal{R}_0 = \mathsf{s}_{dfe}\mathcal{R},$$
   where $\mathcal{R}$ is the number of secondary infections produced by one infectious individual, and where s_{dfe} is the fraction of susceptibles at the DFE.

   The basic reproduction number was first introduced by Lotka in a particular case, and extended to general epidemiologic models by Diekmann, Heesterbeek and Metz [DHM90].

2. The natural way to compute $\mathcal{R}_0$ requires two steps. First, one applies the "next generation matrix", i.e. computes the spectral radius of a matrix involving the infectious equations **only** (alternatively, the Diekmann kernel may be used). Secondly, one plugs for the non zero coordinates the stationary values obtained by BdFixedPt.

Note that this reduction to the infectious equations may lead to simple symbolic answers, which are not obvious when applying the Jacobian criterion to the whole system.

5 Endemic fixed points. Two examples

Example 3 *The $SI^2R/SAIR/SEIR$-FA model has a unique endemic point, with*

$$\mathsf{s}_e = \frac{\mathsf{s}_{dfe}}{\mathcal{R}_0}, \ \mathsf{e}_e = (\mathcal{R}_0 - 1)A, \ A > 0, \ \mathsf{i}_e = \ \mathsf{e}_e \frac{e_i}{\delta + \gamma_i + \mu}, \ \mathsf{r}_e = \ \mathsf{r}_{dfe} + (\mathcal{R}_0$$

(13)

This point is nonnegative iff $\mathcal{R}_0 \geq 1$, and at equality coincides with the DFE.

(13) may be obtained by a symbolic solve. In general, for harder cases, we may attempt to reduce the system to one scalar polynomial equation. The following script outputs a scalar polynomial in a variable "ind" specified by the user, typically chosen as i:

```
Grobpol[mod_,ind_,cn_:{}]:=Module[{dyn,X,par,elim},
    dyn=mod[[1]];X=mod[[2]];par=mod[[3]];
    elim=Complement[Range[Length[X]],ind];
    Collect[GroebnerBasis[Numerator[Together[dyn]],Join[p
]
```

If the RHS of the infectious equation has not been simplified by i, the polynomial must further be divided by it. Finally, this yields a polynomial of degree 1, and

```
in={1};pol=Grobpol[mode,in];cof = CoefficientList[pol,
po=Sum[cof[[k]] e^{k-2},{k,Length[cof]}];
Solve[po==0,e]//FullSimplify
```

will reveal the complicated formula of A in (13).

Example 4 *The SLAIR epidemic model [YB08, AP20, ?] is defined by:*

$$\begin{cases} \mathsf{s}'(t) = \Lambda - \ \mathsf{s}(t)\left(\beta_2 i_2(t) + \beta_3 i_3(t) + \Lambda\right) \\ \left(i_1'(t) \ \ i_2'(t) \ \ i_3'(t)\right) = \left(i_1(t) \ \ i_2(t) \ \ i_3(t)\right) \left[\mathsf{s}(t)\begin{pmatrix} 0 & 0 & 0 \\ \beta_2 & 0 & 0 \\ \beta_3 & 0 & 0 \end{pmatrix} + \begin{pmatrix} -\gamma_1 - \Lambda \\ 0 \\ 0 \end{pmatrix}\right. \\ r'(t) = \gamma_{2,r} i_2(t) + \gamma_3 i_3(t) - \Lambda r(t) \end{cases}$$

$$(14)$$

This is an (A, B) *Arino-Brauer epidemic models with parameters*

$$\vec{\alpha} = \begin{pmatrix} 1 & 0 & 0 \end{pmatrix}, A = \begin{pmatrix} -\gamma_1 & \gamma_{1,2} & \gamma_{1,3} \\ 0 & -\gamma_2 & \gamma_{2,3} \\ 0 & 0 & -\gamma_3 \end{pmatrix}, \boldsymbol{a} = (-A)\mathbf{1} = \begin{pmatrix} 0 \\ \gamma_{2,r} \\ \gamma_3 \end{pmatrix}, \boldsymbol{\beta} = \begin{pmatrix} 0 \\ \beta_2 \\ \beta_3 \end{pmatrix}$$

The Laplace transform of the age of infection kernel is:

$$\widehat{a}(s) = \beta_2 \frac{\gamma_{1,2}}{(b+\gamma_1+s)(b+\gamma_2+s)} + \beta_3 \left(\frac{\gamma_{1,3}}{(b+\gamma_1+s)(b+\gamma_3+s)} + \frac{\gamma_{1,2}\gamma_{2,3}}{(b+\gamma_1+s)(b+\gamma_2+s)}\right.$$

and the Arino & al. formula yields $\mathcal{R} = \dfrac{\beta_3\gamma_{1,2}\gamma_{2,3} + b\beta_2\gamma_{1,2} + \beta_2\gamma_3\gamma_{1,2} + b\beta_3\gamma_{1,3} +}{(b+\gamma_1)(b+\gamma_2)(b+\gamma_3)}$
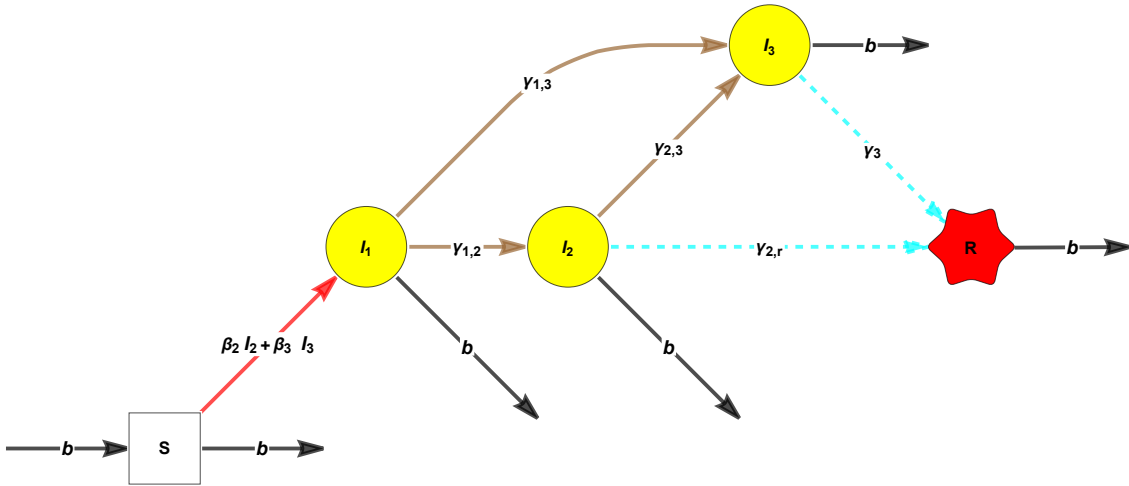

Figure 3: Chart flow of the SLAIR model (14).

6 The universal language of pseudo-linear, essentially non-negative, mass action dynamical systems

6.1 Pseudo-linearity

The sister disciplines of mathematical epidemiology, chemical reaction networks (CRN), ecology, virology, biochemical systems, etc., started all as collections of examples of "pseudo-linear" differential systems **parametrized by two matrices $\mathbf{S}, \mathbf{Y}$**:

$$\dot{\mathbf{x}} = f(\mathbf{x}) = \sum_{k=1}^{n_R} \mathbf{s}_k \mathbf{x}^{\mathbf{y}_k} = \mathbf{S}\mathbf{x}^{\mathbf{Y}}, \quad \mathbf{x}, \mathbf{y}_k, \mathbf{s}_k \in \mathbb{R}_+^{n \times 1}, \quad (15)$$

where $\mathbf{x}^{\mathbf{Y}} \in \mathbb{R}_+^{n_R \times 1}$ is a column vector of monomials, $\mathbf{Y} \in \mathbb{R}^{n \times n_R}$ is the "matrix of source exponents" and $\mathbf{S} \in \mathbb{R}^{n \times n_R}$ is the "stoichiometric matrix of direction vectors" (formed respectively by joining exponents $\mathbf{y}_1, ..., \mathbf{y}_{n_R}$ and directions $\mathbf{s}_1, ..., \mathbf{s}_{n_R}$ as columns). Note that any polynomial dynamical systems can be uniquely written in such form, for some distinct $\mathbf{y}_i$, and non-zero $\mathbf{s}_i$ [CJY22], that $\mathbf{Y}$ is not unique, and that its dimension may be easily increased .

6.2 Essential non-negativity and mass action representation

Kinetic systems must be "essentially non-negative", meaning that they leave invariant the nonnegative orthant.

Remark 5 *An obvious sufficient condition for the essential non-negativity (i.e. the preservation of the nonnegative octant) of a polynomial system $X' = f(X)$ is that each component $f_i(X)$ may be decomposed as*

$$f_i(X) = g_i(X) - x_i h_i(X), \quad (16)$$

where g_i, h_i are polynomials with nonnegative coefficients, i.e. if all negative terms in an equation contain the variable whose rate is given by the equation.

Definition 1 *Terms which do not satisfy (16) are called negative cross-effects.*

Example 5 *The Lorentz system (a famous example of chaotic behavior)*

$$\begin{cases} x' = \sigma(y - x) \\ y' = \rho x - y - xz \\ z' = xy - \beta z \end{cases}$$

does not satisfy (16), due to the $-xz$ term in the y equation.

The following result, sometimes called the "Hungarian lemma" is well-known in the chemical reaction network literature [HT81], [TNP18, Thm 6.27]:

Lemma 1 *A polynomial system admits an essentially non-negative "mass-action" representation iff there are no negative cross-effects, i.e. if (16) holds.*

7 A SIR(S) epidemic model with super-infection, which may have Hopf and Bogdanov-Takens bifurcations

Simple SIR epidemic models do not admit periodic solutions, unless one includes "super-infection" terms, by which we mean interaction terms of order higher than two.

7.1 A varying population eleven parameter SIR(S) model

The varying population SIR-type model introduced here aims at providing a common umbrella for the model of [Nil22a, Nil22b], in which the classes S and R play symmetric roles, and the super-infection model of [AM04, JWX07] (also similar to the "autocatalator" model of chemical reaction network theory [RHMT18, TNP18]), which is known to induce Hopf bifurcations. It is defined by:

$$\begin{cases} S'(t) = b_s N(t) - (b + \gamma_s) S(t) + i_s I(t) + \gamma_r R(t) - \beta_s \frac{I(t)}{N(t)} S(t) \left(1 + \xi \frac{I(t)}{N(t)}\right), \\ I'(t) = I(t) \left[-(b + \delta + \gamma_i) + \beta_s \frac{S(t)}{N(t)} \left(1 + \xi \frac{I(t)}{N(t)}\right) + \beta_r \frac{R(t)}{N(t)} \left(1 + \xi \frac{I(t)}{N(t)}\right) \right], \gamma_i = i_s + i_r, \\ R'(t) = b_r N(t) + \gamma_s S(t) + i_r I(t) - R(t) \left[\beta_r \frac{I(t)}{N(t)} \left(1 + \xi \frac{I(t)}{N(t)}\right) + b + \gamma_r \right], \\ N(t) = S(t) + I(t) + R(t). \end{cases} \tag{17}$$

Remark 6 *1. Adding the derivatives yields*

$$N'(t) = (S(t) + I(t) + R(t))' = (b_s + b_r - b)N(t) - \delta I(t) := (b - b)N(t) - \delta I(t).$$

This epidemic model may be mass-conserving iff $\delta = 0$.

The unfortunately unavoidable term $-\delta I(t)$ reflecting the casualties caused by the epidemic puts in evidence the importance of allowing the total population N to vary.

2. *The model contains "two new infection terms", caused by both the S and R classes, with proportionality constants β_s, β_r. [‡]*

   The particular cases $\beta_s = \beta_r = \beta$, $\beta_s > \beta_r$, and $\beta_s < \beta_r$, correspond respectively to a) indistinguishability between susceptible and recovered, b) to what we hope is true, and c) to a perverse virus, which causes that the re-infections occur at a bigger rate than first infections of the susceptibles.

   In the first case the system simplifies a lot. For example, i is decoupled and satisfies the

   $$\mathsf{i}' = \mathsf{i}\left[(1 - \mathsf{i})(\beta(1 + \xi\,\mathsf{i}) - \delta) - (b + \gamma_i)\right].$$

3. *Both the usual quadratic interactions have been modified by a parameter ξ modeling "super-infection". Under its presence, $[AM04, JWX07]$ have established the possibility of dynamic behaviors richer than for the usual SIR(S) model.*

4. *The susceptibles are renewed via a proportional birth term $bN(t)$. We could have included "immigration" terms, resulting in total birth rates of the form $bN(t) + b_0$, but this creates complications, as explained in the next subsection.*

Remark 7 *Note the eleven parameters are of different kinds:*

1. *easily measurable demography parameters: b_s, b_r, b, δ;*

2. *statistically estimable parameters $\beta_s, \beta_r, i_s, i_r, \gamma_r, \gamma_s$;*

3. *a "qualitative superinfection parameter" ξ; to the best of our knowledge, this parameter has never been estimated statistically.*

We are actually going to study the 10 parameter model (18) obtained by normalizing (17) by the total population, which makes the parameter μ cancel out.

7.2 The ten parameter model for the proportions

The reason we did not allow immigration (or any other non-linearities in the growth term) is that in this way our model (17) simplifies after normalization by $N(t)$. Indeed, in terms of the normalized quantities

$$\mathsf{s} = \frac{S}{N}, \; \mathsf{i} = \frac{I}{N}, \; \mathsf{r} = \frac{R}{N},$$

and $b := b_s + b_r$, we arrive at

$$\begin{cases} \mathsf{s}'(t) & = b_s - \mathsf{s}(t)\left[b + \gamma_s + \beta_s\,\mathsf{i}(t)(1 + \xi\,\mathsf{i}(t))\right] + i_s\,\mathsf{i}(t) + \gamma_r\,\mathsf{r}(t) + \delta\,\mathbf{i(t)\,s(t)} \\ \mathsf{i}'(t) & = \mathsf{i}(t)\left[\left[\beta_s\,\mathsf{s}(t) + \beta_r\,\mathsf{r}(t)\right](1 + \xi\,\mathsf{i}(t)) - (b + \gamma_i + \delta) + \delta\,\mathbf{i(t)}\right] \\ \mathsf{r}'(t) & = b_r + \gamma_s\,\mathsf{s}(t) + i_r\,\mathsf{i}(t) - \mathsf{r}(t)\left[b + \gamma_r + \beta_r\,\mathsf{i}(t)(1 + \xi\,\mathsf{i}(t))\right] + \delta\,\mathbf{i(t)\,r(t)} \end{cases} \tag{18}$$

where one notes that

1. $N(t)$ has disappeared from the model, and the growth rates are now constant (b_s, b_r).

2. The natural death rate b has been replaced by b, and disappears from the model.

3. The initial linear assumption on the growth rate has lead to a double reduction of the dimension due first to the disappearance of N, and then due to the constraint $\mathsf{s} + \mathsf{i} + \mathsf{r} = 1$. The model obtained looks very much like the "classic constant population epidemic models", except that the **epidemic-caused deaths parameter δ appears in three more quadratic terms**, emphasized in the equations, which are usually missing in the literature [§].

The polynomial system (18) does not have negative cross-effects, and is therefore essentially nonnegative and admits a mass-action representation by the "Hungarian lemma" [HT81], [TNP18, Thm 6.27].

Remark 8 *The second equation factors (such equations are called sometimes "Kolmogorov" or "generalized Lotka-Volterra equation" (LV)), but the others don't. This raises an interesting question of extending the theory of LV equations to our set-up, with one-two non LV equations. Note that an epidemiologic model can be quickly put in factored form by shifting the origin to one of the fixed points; however, this way one typically loses the essential non-negativity of LV systems.*

[‡]The parameter β_r describes possibly "perverse viruses" for which recovery from a first infection does not grant total immunity.

[§]except for its tiny so-called "time varying population" part

Remark 9 *Note that*

1. *When $\delta = \beta_r = \gamma_r = \gamma_s = i_s = \xi = 0$, (18) reduce to the SIR model with demography [Het00], and when also $b = 0$, it becomes the classic SIR model [KM27] parameterized by β_s, γ.*

2. *when $\beta_r = \gamma_s = i_s = \delta = 0$, (18) reduces to a fixed population (FP) model paramaterized by the five parameters $b, \beta_s, \gamma, \gamma_r, \xi$, which was studied in [JWX07]. These authors assume $\mu \neq b$, having thus six parameters; this is an easy, but we believe unnecessary generalization, from an epidemiologic point of view.*

3. *when $\beta_r = \gamma_s = i_s = \delta = \gamma_r = 0$, (18) the four parameter model paramaterized by b, β, ξ, γ is the fixed population (FP) version of [AM04, Exa 1];*

4. *By taking $\gamma_r = \gamma_s = 0$ and replacing ξ i(t) by $f($ i(t)$, \xi)$, we arrive at the functional parameter model studied in [AM04], under assumptions [AM04, (A1-A3)].*

Remark 10 *The fact that* s $+$ i $+$ r $= 1$ *implies that our system has many equivalent representations. An interesting form was proposed by F. Nill [Nil22a], in which the two "new infection producing classes"* s *and* r *intervene symmetrically. Replacing in (18) b_s by $b_s($ s(t)$+$ i(t)$+$ r(t)$)$ in the first equation, b_r by $b_r($ s(t)$+$ i(t)$+$ r(t)$)$ in the third equation, and $\delta($ i(t)$-1)$ by $-\delta($ s(t)$+$ r(t)$)$ in the second, we arrive to:*

$$
\begin{cases}
\mathsf{s}'(t) &= (i_s + b_s)\,\mathsf{i}(t) + (\gamma_r + b_s)\,\mathsf{r}(t) - \mathsf{s}(t)\left[b_r + \gamma_s + \beta_s\,\mathsf{i}(t)(1 + \xi\,\mathsf{i}(t))\right] + \delta\,\mathsf{i(t)}\,\mathsf{s(t)} \\
\mathsf{i}'(t) &= \mathsf{i}(t)\Big[\left[\beta_s\,\mathsf{s}(t) + \beta_r\,\mathsf{r}(t)\right](1 + \xi\,\mathsf{i}(t)) - (b + \gamma_i)\,{\color{blue}-\delta(\,\mathsf{s}(t) +\,\mathsf{r}(t))}\Big] \\
\mathsf{r}'(t) &= (\gamma_s + b_r)\,\mathsf{s}(t) + (i_r + b_r)\,\mathsf{i}(t) - \mathsf{r}(t)\left[b_s + \gamma_r + \beta_r\,\mathsf{i}(t)(1 + \xi\,\mathsf{i}(t))\right] + \delta\,\mathsf{i(t)}\,\mathsf{r(t)}.
\end{cases}
$$

Putting now

$$
\widetilde{i_s} = i_s + b_s, \widetilde{i_r} = i_r + b_r, d_r = \gamma_r + b_s, d_s = \gamma_s + b_r, d_i = \gamma_i + b,
$$

we arrive to:

$$
\begin{cases}
\mathsf{s}'(t) &= -d_s\,\mathsf{s}(t) + \widetilde{i_s}\,\mathsf{i}(t) + d_r\,\mathsf{r}(t) - \mathsf{s}(t)\left[\beta_s\,\mathsf{i}(t)(1 + \xi\,\mathsf{i}(t))\right] + \delta\,\mathsf{i}(t)\,\mathsf{s}(t) \\
\mathsf{r}'(t) &= d_s\,\mathsf{s}(t) + \widetilde{i_r}\,\mathsf{i}(t) - \mathsf{r}(t)\left[d_r + \beta_r\,\mathsf{i}(t)(1 + \xi\,\mathsf{i}(t))\right] + \delta\,\mathsf{i}(t)\,\mathsf{r}(t) \\
\mathsf{i}'(t) &= \mathsf{i}(t)\Big[-d_i + \left[\beta_s\,\mathsf{s}(t) + \beta_r\,\mathsf{r}(t)\right](1 + \xi\,\mathsf{i}(t)){\color{blue}-\delta(\,\mathsf{s}(t) +\,\mathsf{r}(t))}\Big].
\end{cases}
\tag{19}
$$

Remark 11 *When $\xi = 0$, [Nil22a] observed that the resulting dynamical system*

$$
\begin{cases}
\mathsf{s}'(t) &= -d_s\,\mathsf{s}(t) + \widetilde{i_s}\,\mathsf{i}(t) + d_r\,\mathsf{r}(t) - \mathsf{s}(t)\,\mathsf{i}(t)\,(\beta_s - \delta) \\
\mathsf{r}'(t) &= d_s\,\mathsf{s}(t) + \widetilde{i_r}\,\mathsf{i}(t) - d_r\,\mathsf{r}(t) - \mathsf{r}(t)\,(\beta_r - \delta) \\
\mathsf{i}'(t) &= \mathsf{i}(t)\Big[-d_i + \left[(\beta_s - \delta)\,\mathsf{s}(t) + (\beta_r - \delta)\,\mathsf{r}(t)\right]\Big].
\end{cases}
\tag{20}
$$

depends on δ, β_s, β_r only via the differences $\widetilde{\beta_s} = \beta_s - \delta$ and $\widetilde{\beta_r} = \beta_r - \delta$. {\color{red}*Hence the parameter δ may be dropped, at the price of considering also models with negative infection rates $\widetilde{\beta_s}, \widetilde{\beta_r}$. In this way, one joins the traditional literature where δ is ignored, which turns out quite convenient, since this assumption leads typically to further simplifications.*}
§

7.3 First steps in the analysis of the SIR(S) model (18): boundary analysis (the DFE and its local stability), and a scalar equation for the endemic points

We studied our model with Mathematica, using a slightly more general version of (18), with $b \neq b$, and with δ split into two parts, δ and δ_q. This is necessary in order to include both the model of [Nil22a], and also previous results of [AM04, JWX07], which assume $\delta_q = 0, b \neq b$. The resulting system is:

$$
\begin{cases}
\mathsf{i}'(t) = \mathsf{i}(t)\Big[\left[\beta_s\,\mathsf{s}(t) + \beta_r\,\mathsf{r}(t)\right](1 + \xi\,\mathsf{i}(t)) - (\mu + i_s + i_r + \delta) + \delta_q\,\mathsf{i}(t)\Big] \\
\mathsf{r}'(t) = b_r + \gamma_s\,\mathsf{s}(t) + i_r\,\mathsf{i}(t) - \mathsf{r}(t)\left[\mu + \gamma_r + \beta_r\,\mathsf{i}(t)(1 + \xi\,\mathsf{i}(t))\right] + \delta_q\,\mathsf{i}(t)\,\mathsf{r}(t) \\
\mathsf{s}'(t) = b_s + i_s\,\mathsf{i}(t) + \gamma_r\,\mathsf{r}(t) - \mathsf{s}(t)\left[\mu + \gamma_s + \beta_s\,\mathsf{i}(t)(1 + \xi\,\mathsf{i}(t))\right] + \delta_q\,\mathsf{i}(t)\,\mathsf{s}(t)
\end{cases}
\tag{21}
$$

and its code is:

---

§When $\delta < \min[\beta_s, \beta_r]$, we may say that [Nil22a] reduces formally the varying population SIR to a classic constant population model; but, that paper investigates also what happens when δ crosses the thresholds β_s and β_r.

```
SIRG=Module[{ss,ii,rr,dyn,X,inf,pars},
ss=bs -s (\[Mu]+\[Gamma]s) +is i +\[Gamma]r  r-\[Beta]s s i (1+\[Xi] i)
  + \[Delta]q i s ;
ii=  i  (\[Beta]s s (1+\[Xi] i) + \[Beta]r r (1+\[Xi] i)-(\[Mu] +\[Delta] +ir+is)
  + \[Delta]q i) ;
rr= br+  \[Gamma]s s+ ir  i  -\[Beta]r r i(1+\[Xi] i)-(\[Mu]+\[Gamma]r) r
  + \[Delta]q i r;
dyn={ii,rr,ss};
X={i,r,s};pars=Complement[Variables[dyn],X];{dyn,X,pars}] ;
```

1. The traditional first step for analyzing an epidemic model is computing the hopefully unique boundary point. Plugging $i = 0$ in the last two fixed point equations, or typing "DFE[SIRG,1]" in Mathematica yields a unique disease free equilibrium :
$$\begin{cases} s_{dfe} = \frac{b_r\gamma_r+b_s(\mu+\gamma_r)}{\mu(\mu+\gamma_r+\gamma_s)} \\ r_{dfe} = \frac{b_r(\mu+\gamma_s)+b_s\gamma_s}{\mu(\mu+\gamma_r+\gamma_s)}. \end{cases} \tag{22}$$

2. The Jacobian is obtained as the first output "jac=JTDP[mode][[1]]" of a utility which provides also the trace, determinant, and characteristic polynomial. At the DFE it has a block structure

$$\begin{pmatrix} \frac{b_r\beta_r(\mu+\gamma_s)+b_s\beta_s(\mu+\gamma_r)+b_r\gamma_r\beta_s+b_s\beta_r\gamma_s}{\mu(\mu+\gamma_r+\gamma_s)} - (\delta + i_r + i_s + \mu) & 0 & 0 \\ \frac{-b_r(\mu+\gamma_s)(\beta_r-\delta_q)+b_s\gamma_s(\delta_q-\beta_r)+\mu i_r(\mu+\gamma_r+\gamma_s)}{\mu(\mu+\gamma_r+\gamma_s)} & -\mu - \gamma_r & \gamma_s \\ \frac{-b_s(\mu+\gamma_r)(\beta_s-\delta_q)+b_r\gamma_r(\delta_q-\beta_s)+\mu i_s(\mu+\gamma_r+\gamma_s)}{\mu(\mu+\gamma_r+\gamma_s)} & \gamma_r & -\mu - \gamma_s \end{pmatrix}$$

and its eigenvalues are explicit

$$\begin{cases} \beta s_{dfe}+\beta_r r_{dfe} - (\mu + i_s + i_r + \delta) := (\delta + i_r + i_s + \mu)(\mathcal{R}_0 - 1) \\ -\mu \\ -\mu - \gamma_r - \gamma_s, \end{cases}$$

where $\mathcal{R}_0 := \frac{\beta_s s_{dfe}+\beta_r r_{dfe}}{\delta+i_r+i_s+\mu}$.

3. The computation of the endemic points may be started by eliminating s, r from the non-infectious equations substituting them in the equation $i'/i = 0$, and taking the numerator of the fraction obtained. This yields a fifth order equation for i, whose free coefficient is $det_{DFE} \propto (\mathcal{R}_0 - 1)$, and may be obtained by typing

   (a) In the case $\delta_q = \beta_r = 0$, studied in [JWX07], this polynomial is quadratic.

   (b) In the case $\xi = 0$, studied in [AABH22], this polynomial is of degree 3. However, using the observation of [Nil22a] that one may assume $\delta = 0$ (at the price of allowing for negative β_s, β_r), we end up again with degree 2.

So in both cases, endemic point candidates maybe found by identifying positive solutions of a quadratic polynomial $p(i) = Ai^2 + Bi + C = 0$.

8 Particular case: the SIR(S) model

By plugging $i = 0$ into (19) at the equilibrium and using $s + i + r = 1$, the system admits a unique boundary fixed point $DFE = (s_{dfe}, 0, r_{dfe})$ such that

$$\begin{cases} s_{dfe} := \frac{b_s+\gamma_r}{b_r+b_s+\gamma_r+\gamma_s} \in [0,1], \\ r_{dfe} := \frac{b_r+\gamma_s}{b_r+b_s+\gamma_r+\gamma_s} \in [0,1]. \end{cases}$$

At the DFE, the Jacobian is given by

$$J(DFE) = \begin{pmatrix} -d_s & b_s + i_s + s_{dfe}(\delta - \beta_s) & d_r \\ 0 & r_{dfe}(\beta_r - \delta) + s_{dfe}(\beta_s - \delta) - d_i - \delta & 0 \\ d_s & b_r + i_r + r(\delta - \beta_r) & -d_r \end{pmatrix}.$$

Its eigenvalues are explicit

$$\{0, -d_r - d_s, \beta_s s_{dfe} - \beta_r r_{dfe} - d_i - \delta := (d_i + \delta)(\mathcal{R}_0 - 1)\},$$

where $\mathcal{R}_0 := \frac{\beta_s s_{dfe} + \beta_r r_{dfe}}{d_i + \delta} = \frac{d_s \beta_r + d_r \beta_s}{(d_r + d_s)(b + \delta + \gamma_i)}$ is the basic reproduction number first introduced by Lotka and extended for more general epidemiologic models by Diekmann, Heesterbeek and Metz [DHM90]. Thus, the DFE is stable if $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$. Note that this recovers the result of [Nil22a].

Remark 12 *One may also derive this via the next generation matrix approach [VdDW02, VdDW08].*

When $i \neq 0$, the computation of the endemic points may be started by eliminating s, r. By solving the equation $i'/i = 0$ in (19) with respect to r and by substituting into the first equation yields

$$s = \frac{d_i d_r + \widetilde{ii}_s \left(-\delta + i\xi\beta_r + \beta_r \right)}{\left(-\delta + i\xi\beta_s + \beta_s \right)\left(d_r + i\left(-\delta + i\xi\beta_r + \beta_r \right) \right) + d_s \left(-\delta + i\xi\beta_r + \beta_r \right)}. \tag{23}$$

The third order characteristic polynomial with respect to i is $Ai^3 + Bi^2 + Ci + D = 0$ with

$$\begin{cases} A := \xi^2 \beta_r \beta_s > 0, \\ B := \xi \left(2\beta_r \beta_s - \delta \left(\beta_r + \beta_s \right) \right), \\ C := \delta^2 + \beta_r \left(\xi d_s - \delta + \beta_s \right) + \xi d_r \beta_s - \delta \beta_s, \\ D := d_s \beta_r + d_r \beta_s - \delta \left(d_r + d_s \right) = (\delta + d_i)(\mathcal{R}_0 - 1) + d_i(d_s + d_r), \end{cases}$$

note that $D > 0$ iff $\mathcal{R}_0 > 1$.

9 Particular case: a three dimensional generalization with $\gamma_s \geq 0, \delta \geq 0$ of the model of [JWX07]

By assuming $\beta_r = i_s = 0, \beta_s = \beta$ in (21), and $\delta_q = 0$ (i.e. by ignoring the quadratic terms which appeared via the normalization), we arrive at a dynamical system with eight parameters $\{b, \beta, \gamma, \gamma_r, \mu, \xi, \gamma_s, \delta\}$, which contains two parameters $\gamma_s \geq 0, \delta \geq 0$ more than [JWX07]. Putting $d_1 = i_r + \delta + \mu, d_s = \gamma_r + \mu, d_r = \gamma_r + \mu$, the number of parameters is reduced to 7:

$$\begin{cases} \mathsf{i}'(t) = \mathsf{i}(t) \left(\beta \, \mathsf{s}(t)(1 + \xi \, \mathsf{i}(t)) - d_i \right), \\ \mathsf{s}'(t) = b - \beta \, \mathsf{s}(t) \, \mathsf{i}(t)(1 + \xi \, \mathsf{i}(t)) + \gamma_r \, \mathsf{r}(t) - d_s \, \mathsf{s}(t), \\ \mathsf{r}'(t) = \gamma \, \mathsf{i}(t) + \gamma_s \, \mathsf{s}(t) - d_r \, \mathsf{r}(t). \end{cases} \tag{24}$$

Remark 13 *The first generalization $\gamma_s \geq 0$ is minor, it only increases the time of execution of certain quantities. Including an extra-death rate δ is more substantial, since assuming $\delta = 0$ makes [JWX07]'s problem essentially two-dimensional, while (24) isn't. We note here that a huge proportion of the related mathematical epidemiology literature contains models which are essentially two-dimensional, due to assumptions like $\delta = 0$, or $\gamma_r = 0$, which are not fully justified from the epidemiological point of view.*

9.1 Further calculations for the generalized [JWX07] model

1. As noted already, the system (24) has at most two endemic points, whose i coordinate satisfies a second order equation

$$\begin{cases} Ai^2 + Bi + C = 0 \\ A = \beta\xi \left(\gamma\mu + (\delta + \mu)d_r \right) > 0 \\ B = \beta \left(d_r(\delta + \mu - b\xi) + \gamma\mu \right) \\ C = d_i\mu(d_r + \gamma_s)\left(1 - \mathcal{R}_0 \right) = -det_{DFE}. \end{cases} \tag{25}$$

This checks with [JWX07, (2.2)] when $\gamma_s = \delta = 0$.

2. The discriminant $\Delta = B^2 - 4AC$ satisfies

$$\frac{\Delta}{\beta} = \beta \left(d_r(b\xi + \delta + \mu) + \gamma\mu \right)^2 - 4\mu\xi d_i \left(\gamma\mu + (\delta + \mu)d_r \right) \left(d_r + \gamma_s \right) \tag{26}$$

and is positive iff [¶]

$$\beta > \beta_d = \frac{4\mu\xi d_i \left(d_r + \gamma_s \right) \left(\gamma\mu + (\delta + \mu)d_r \right)}{\left(d_r(b\xi + \delta + \mu) + \gamma\mu \right)^2}. \tag{27}$$

[¶]the result checks with [JWX07, pg. 484-485], after some substitutions like $\xi - > Ap$, etc

3. The equation $i'/i = 0$ yields $s = \frac{d_i}{\beta(i\xi+1)} > 0$. Furthermore, $r = \frac{\gamma i + \gamma_s s}{\mu + \gamma_r}$. Thus, a positive i yields always an endemic point.

We will order the two possible endemic points E_1, E_2 by their i coordinates, given by $i_1 = \frac{-B - \sqrt{\Delta}}{2A}$ and $i_2 = \frac{-B + \sqrt{\Delta}}{2A}$.

Remark 14 *Note that when $C = 0 \Leftrightarrow \mathcal{R}_0 = 1$ we have $i_1 = 0, i_2 = -\frac{B}{A}$, which implies a transition in the number of endemic points when crossing this boundary.*

A major part of [JWX07] is dedicated to bifurcation diagrams which demonstrate the presence of Hopf and Bogdanov-Takens bifurcations. We will review briefly these concepts in the next section.

10 Brief review of saddle-node, Poincaré-Andronov-Hopf and Bogdanov-Takens bifurcations

Let $x'(t) := F(x, \mu), x \in \mathbb{R}^n, \mu \in \mathbb{R}^k$ denote an autonomous dynamical system, and let $\widetilde{F}(x, \mu)$ denote its version extended by eventual conservation constraints (in mathematical epidemiology, it holds often that x represent proportions, and therefore the constraint that their sum is 1 must be added to the system). Note that in practical works k is typically 1 or 2.

Finding fixed points and bifurcations for polynomial systems reduces essentially to solving systems of polynomial equalities and inequalities; see Gaterman [GES05] and Craciun-Dickenstein-Shiu-Sturmfels [CDSS09] for foundational papers exploring this point of view, in the context of chemical reaction networks.

Let us start with the simplest bifurcation example.

Definition 2 *A saddle-node or transcritical bifurcation is a pair (x_*, μ_*) characterized by*

$$\begin{cases} f(x_*, \mu_*) = 0 \\ Det(J(x_*, \mu_*)) = 0 \\ \frac{dDet(J(x,\mu))}{d\mu}\Big|_{\mu=\mu_*} \neq 0 \ (transversality) \end{cases}$$

where $J(x, \mu)$ is the Jacobian, and by further "Routh Hurwitz" (RH) inequality constraints on the coefficients of its characteristic polynomial, to be specified below (to include more significant contributions to this problem, they should be called RHLCSCJ inequality constraints).

At saddle-node bifurcation pairs, a change of stability occurs when μ traverses μ_*, for the fixed point which equals x_* when μ equals μ_*. The determinant of the Jacobian is called "determining function".

10.1 Review of the determining function and the RH inequality constraints for Hopf bifurcations

The Poincaré-Andronov-Hopf bifurcation (named often just Hopf bifurcation) – see for example [GGK97]–concerns the appearance, when μ changes, of a cycle. For that to occur, a pair of complex conjugate eigenvalues of the Jacobian must cross the imaginary axis.

There are several equivalent ways to formulate the existence of a Hopf bifurcation as an algebraic system of equalities and inequalities – see [GMS97] for a survey.

1. A modern approach exploits symmetry of the eigenvalues and resultants [GMS97, GF04].

2. An extensively used classic approach involves only the Hurwitz determinants (which are functions of the coefficients of the characteristic polynomial of the Jacobian):

Proposition 2 *[Liu94] Let $x'(t) := F(x, \mu), x \in \mathbb{R}^n, b \in \mathbb{R}$ denote an autonomous system for which the following holds at x_*, μ_*):*

$$\begin{cases} \exists x \ \left(F(x, \mu) = 0, \ H_{n-1} = 0, \frac{dH_{n-1}}{d\mu} \neq 0, \right. \\ \left. H_{n-2} > 0, ..., H_1 > 0, Sign[Det[J(x, \mu)]] = (-1)^n \right). \end{cases}$$ (28)

where H_i is the ith Hurwitz determinant formed from the coefficients of the characteristic polynomial.

Then, this system has a simple Hopf bifurcation at (x_*, μ_*).

Remark 15 *(a) Note that, like in the famous Routh-Hurwitz stability criterion (see for example [DK09, Thm 4]), the main heroes are the Hurwitz determinants. Importantly, the largest one intervenes via an equality, and is called also determining function.*

(b) Practically, one finds a solution of the two equalities in the first line, and checks then whether the remaining inequality conditions (which are the same as for saddle-node bifurcations) are satisfied.

(c) In the case $n = 2$, the determining Hurwitz determinant reduces to $H_1 = -Tr[J(x, \mu)]$, and in the case $n = 3$ it reduces to $H_2 = Tr(J(x, \mu))M_2(J(x, \mu)) - Det(J(x, \mu))$, where $M_2(J(x, \mu))$ denotes the sum of the second order principal leading minors of $J(x, \mu)$ (see for example [Liu93]).

Remark 16 *The fact that the $(n-1)$-st Hurwitz determinant must be 0 for the characteristic polynomial to have a pair of pure imaginary eigenvalues is a consequence of Orlando's formula [Gan59, GMS97, DK09]. When $n = 3$ for example, this result becomes:*

Lemma 2 *A cubic polynomial $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3$ with real coefficients has a pair of pure imaginary roots if and only if $a_2 > 0$ and $a_3 = a_1 a_2$. When it has pure imaginary roots, these are given by $\pm i\sqrt{a_2}$, the real root is given by $-a_1$, and $a_1 a_3 > 0$.*

see [Tia11, Lem. 3.10] for an elementary proof.

3. Instead of using the Hurwitz determinants of lower orders, one may also mix them with direct inequalities on the coefficients of the characteristic polynomial – see for example [Dau21].

10.2   Review of Bogdanov-Takens bifurcations

A Bogdanov-Takens (BT) bifurcation [Bog75, Kuz98] may occur at an equilibrium pair in a **two-parameter** family of autonomous ODE's when this pair has a **zero eigenvalue** of the Jacobian matrix of (algebraic) multiplicity two.

We are looking therefore for a solution of the equations

$$\exists x_* \text{ such that } \begin{cases} f(x_*) = 0 \\ Det(J(x_*)) = 0 \\ Disc[P_\lambda(J(x_*))] = 0, \end{cases} \tag{29}$$

where Disc denotes the discriminant of the determinant.

Alternatively, instead of the discriminant, one may also use the highest degree Hurwitz determinant $H_{n-1}(J(x)) = 0$ as determining function [KKLN93], which renders clearly the fact that a Bogdanov-Takens bifurcation is the intersection of a branch of Hopf bifurcations, and of a branch of saddle-node bifurcations.

Example 6 *When $n = 2$, the determining functions are*

$$\exists x_* \text{ such that } \begin{cases} f(x_*) = 0 \\ Tr(J(x_*)) = 0 \\ Det(J(x_*)) = 0, \end{cases} \tag{30}$$

[LZ17a, Section 4], [GK22, Theorem 6], [WR04, pg. 783], [LZ17b, Theorem 0.11].

Example 7 *When $n = 3$, the determining functions are*

$$\exists x_* \text{ such that } \begin{cases} f(x_*) = 0 \\ H_2(X_*) \\ Det(J(x_*)) = 0, \end{cases} \tag{31}$$

[Dau21].

For BT bifurcations in mathematical epidemiology, the system (31) should be enlarged to

$$\begin{cases} Det(J(E_i)) = 0, H_{n-1}(J(E_i)) = 0, E_i \geq 0, i = 1, 2, ..., \\ \Delta = 0 \\ \mathcal{R}_0 = 1 \end{cases}, \tag{32}$$

where

1. Det, H_n denote the determinant and traces,

2. $E_i, i \geq 1$ are the fixed **interior** (equilibrium) points, and

3. Δ is the "**discriminant of the fixed points system**", which splits the parameter space in regions with different numbers of fixed points.

   Remark 17 *The fundamental concept of discriminant of a system seems to have first been introduced only recently [GKZ94, Est13], and is not yet implemented in Mathematica. But, one may circumvent this difficulty by reducing the system to a scalar equation in one variable, and using its discriminant.*

4. Note that with respect to (31), we have added the equation $\mathcal{R}_0 = 1$, where $\mathcal{R}_0$ is the famous "basic reproduction number", introduced in examples by Lotka [Lot39] and formalized as the spectral radius of a certain operator by Diekmann, Heesterbeek, and Metz [DHM90]. Now the expression $\mathcal{R}_0 - 1$, which determines the stability of the DFE, appears naturally as a factor of $detG$, but it seems worth singling it out as well.

10.3 Some new symbolic objects for computing bifurcations

Symbolic stability and bifurcation analysis are very time consuming, since they require identifying varieties like traces, determinants and Hurwitz determinants, evaluated at all the fixed points. It is plausible however that the equation satisfied by the union over the fixed points (i.e. the product of all the respective equations), ends up simpler symbolically.

We turn now to the main heroes of this subsection, some symbolic objects which we have introduced, and were not able to find in the previous literature.

Definition 3 *The determinant, trace, and Hurwitz determinant of an algebraic system with respect to a subset of its solutions A is defined by the expressions*

$$\begin{cases} detE = \prod_{i \in A} Det(J(E_i)) \\ trE = \prod_{i \in A} Tr(J(E_i)) \\ H_{n,E} = \prod_{i \in A} H_n(E_i). \end{cases} \tag{33}$$

Remark 18 *1. Two choices of A are of special interest: one, involving the product of the traces over all the fixed points, is useful for general dynamical systems. Another one, involving only the product over the interior points, is the one we used mostly, since eliminating the DFE from the study is advantageous computationally, and anyway the DFE is easy to study separately.*

2. The varieties corresponding to $detE, trE, H_{n,E}$, etc, are the union of the varieties for each branch. Due to the Vieta relations between the roots, they are expected to be considerably simpler than the individual expressions for the various branches.

3. Interestingly, these quantities seem related up to proportionality to the results obtained via the GroebnerBasis elimination commands

$$\begin{cases} detG = GroebnerBasis[Numerator[Together[[\{dyn[[1]], dyn[[2]], Det(X)\}]], par, X] \\ trG = GroebnerBasis[Numerator[Together[[\{dyn[[1]], dyn[[2]], Tr(X)\}]], par, X] \end{cases} . \tag{34}$$

4. The proportionality might be caused by spurious implementation factors. It may be interesting to clarify the relation between $detE, trE$ and the corresponding Mathematica objects $detG, trG$.

Remark 19 *1. The computation of candidates for the Bogdanov-Takens bifurcations for all the fixed points in two dimensions may be achieved via the single command*

$$Reduce[\{trG == 0, detG == 0, cp\}], \tag{35}$$

where cp are positivity and other eventual constraints on the variables and parameters.

2. In our experience, the easiest way to study a kinetic model which is reducible to two dimensions is by checking whether (35) ends up in "reasonable time" (say, less than a Mathematica all-night run). We will call a model for which this happens easy.

3. *In more dimensions, it is enough a priori to replace the trace in (35) by the maximal dimension Hurwitz determinant. However, as well-known, as the dimension and number of parameters increase, these problems become very hard to resolve symbolically.*

Unfortunately, we seldom find information on execution times in the current mathematical epidemiology literature. Furthermore, we found no mention in the extensive part of the literature we analyzed of notebooks, or any offers to provide them. The literature seems to give the impression that the important part of scientific computing is doing computations by hand, as opposed to appealing to appropriate software.

10.4 The Bogdanov-Takens candidates for the [JWX07] example, computed via via "Groebner elimination" of determinants, traces and Hurwitz determinants

To illustrate the convenience of using real algebraic geometry tools in a **simple case**, we review here the bifurcations problem of [JWX07], which is reducible to two dimensions.

Definition 4 *In two dimensions, the candidates for Hopf bifurcations equations are the points $B_1, B_2, ...$ where the "branches of the trace", (i.e. the traces) at the endemic points $E_1, E_2, ...$, become 0.*

In our case, these points, which feature as the main heroes of the one dimensional bifurcation diagrams with respect to β, and also in the two-parameter bifurcation diagrams (see Figures 4, 6, 9), will be specified by critical values $\beta_1, \beta_2, ...$

The set of Bogdanov-Takens candidates for the model of [JWX07], slightly generalized by assuming $\gamma_s > 0$, is found by Mathematica in a tenth of a second, yielding

$$\begin{cases} \beta = \beta_d \\ \gamma_s < \gamma \\ \xi > \frac{(\gamma+\mu+\gamma_r)(\mu+\gamma_r+\gamma_s)}{2(\gamma+\mu)(\gamma-\gamma_s)} \\ b = \frac{\mu\left(\frac{2(\gamma+\mu)(\gamma-\gamma_s)}{\mu+\gamma_r+\gamma_s} - \frac{\gamma+\mu+\gamma_r}{\xi}\right)}{\mu+\gamma_r}. \end{cases} \tag{36}$$

This confirms and generalizes the corresponding conditions (S2,S1,S3) of the section 4 of [JWX07] (note that the original results of [JWX07] were derived via quite complicated computations, without the use of symbolic software). [§] (36) is obtained via the following code:

```
jacJ = Grad[dynJ,X];
trJ  = Tr[jacJ];
detJ = Det[jacJ];
pars=Complement[Variables[dynJ],X];
model={dynJ,X,pars};

Print[" detG is ", detG = GBH[model, detJ][[1]] // FullSimplify]
Print[" trG is", trG = GBH[model, trJ][[1]] // FullSimplify]
eq   = Join[Thread[{trG, detG} == 0], Thread[pars > 0]];
re   = Reduce[eq] // FullSimplify
```

where "GBH" computes the variables eliminated version of a scalar characteristic via:

```
GBH[mod_,scal_,cn_ : {}] :=
    GroebnerBasis[Numerator[Together[[Join[ mod[[1]], \{ sc\}]]],
    mod[[3]],  mod[[2]]]
```

with $mod = \{dyn, var, par\}$.

Using the inequalities induced by the equalities (32), one obtains a division of the parameter space into regions with different properties. After providing a "cut" where all but two parameters are specified, one may display in two dimensions a "bifurcation diagram" providing the regions, and the edges and corners between, which are "candidates" for Hopf and Bogdanov-Takens bifurcations – see Figure 4.

Here is a two-parameter bifurcation diagram for the problem of [JWX07], which summarizes well what we achieve via bifurcation analysis, and was achieved as sketched above.

[§] [JWX07] dedicates considerable effort to simplifying the necessary condition $trG = 0$ for Hopf bifurcations (see [JWX07, Thm 3.1]). Their result is very hard to check, due to many changes of variables.
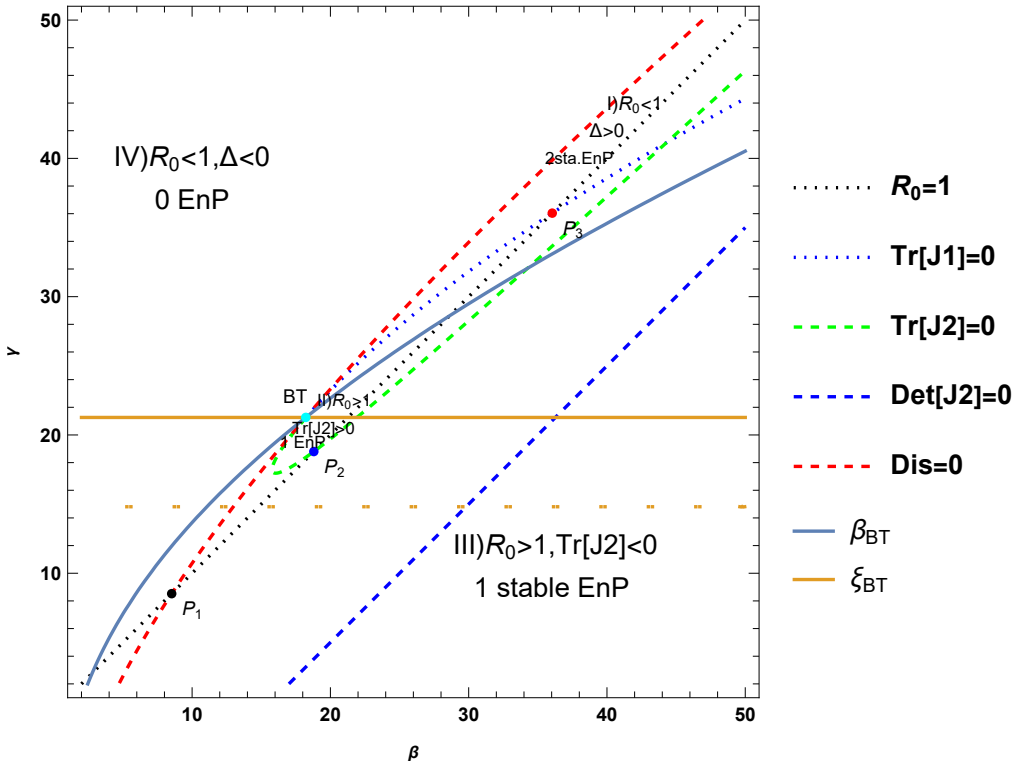
Figure 4: Bifurcation map in the (β, γ) plane for the [JWX07] model. The intersection of the curves $Dis = 0$ and $Tr[J2] = 0$ occurs at two Bogdanov-Takens point $BT = (18.2203, 21.269)$, at which the eigenvalues of $J2$ are $(0, 0)$. The point P_1 is at the intersection of the curves $Dis = 0$ and $R_0 = 1$, the point P_2 is at the intersection of the curves $Tr[J2] = 0$ and $R_0 = 1$, and the point P_3 is at the intersection of the curves $Tr[J1] = 0$ and $R_0 = 1$.

10.5 Computing saddle-node, Poincaré-Andronov-Hopf, and Bogdanov-Takens bifurcations by optimization

It is quite rare that systems with several determining functions d_i may be solved symbolically. It is natural therefore to replace the equalities by the optimization problem of minimizing

$$\min \sum_{i=1}^{I} d_i^2(x, \mu), \tag{37}$$

where $I = 2$ for BT bifurcations.

More precisely, the optimization problem for saddle-node bifurcations [OMYS17] is:

$$\begin{cases} \min f_{det}^2(x, \mu) \\ \widetilde{F}(x, \mu) = 0 \\ x \geq 0, b \geq 0 \\ \text{"RH stability inequality constraints"} \\ \text{rank constraint on the Jacobian?} \end{cases} \tag{38}$$

We conjecture that in the presence of several determining functions d_i, the appropriate generalization is simply replacing the objective by (37).

To motivate this, we recall that

1. The stability of autonomous continuous dynamical systems may be characterized by any of several equivalent Routh-Hurwitz-Lienard-Chipart-Schur-Cohn-Jury inequalities (RH/RHLCSCJ) [AJ73, WP18, Dau21].

2. Codimension one bifurcations are determined by systems involving the same inequalities, except that one, called determining function, turns into an equality constraint $f_{det}(x, \mu) = 0$. The determining function is specific to each type of bifurcation; for example, for saddle-node and Poincaré-Andronov-Hopf bifurcations, they are the determinant and the higher order Hurwitz determinant, respectively. [§]

_____

[§]In fact, $f_{det}(x, \mu)$ must satisfy also a transversality condition which we have not included in the optimization formulation, since this can be ignored at first and easily checked a posteriori for all "candidate bifurcation points" (x, μ). Similarly, the inequality constraints on the coefficients of the characteristic polynomial may be included in the optimization problem from the beginning, or just checked a posteriori.

This is just a reflection of the fact that at a Hopf or saddle-node pair, a steady state loses or gains stability as (x, μ) moves through (x_*, μ_*), and therefore in a subset of any neighborhood of the pair, some form of the RH stability conditions must hold. All these criteria involve a mix of direct inequality constraints on the coefficients of the characteristic polynomial, and of inequality constraints on Hurwitz determinants. There is still debate on the most convenient form to mix these, but maybe the main point, not always clarified in the literature is that except for the determining function, this mix may be chosen to be the same for saddle-node and Hopf bifurcations.

11 Bifurcation diagrams for the system (24)

11.1 One dimensional bifurcation diagram in the case $\beta_0 < \beta_2$

We exemplify this case using the SIR model of [AM04] (**??**).
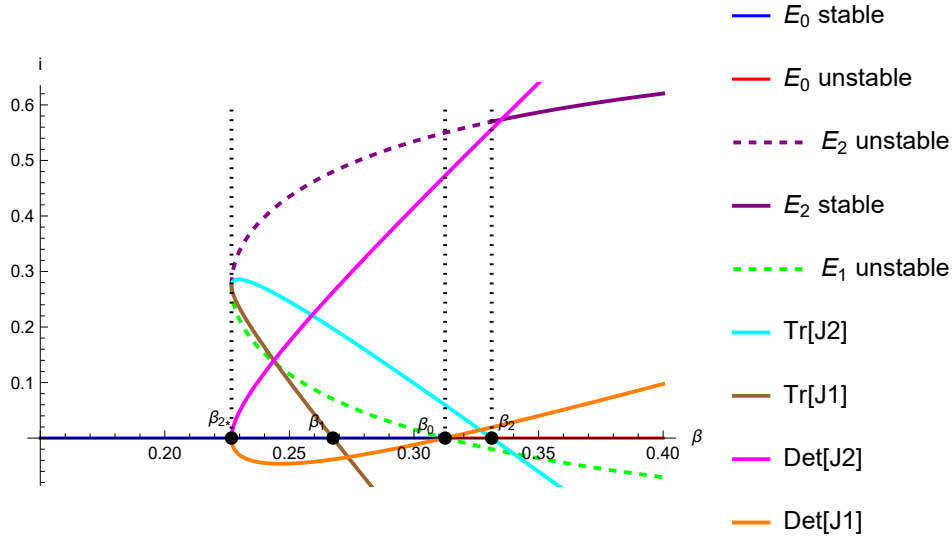
Figure 5: Bifurcation diagram with respect to β when $b = 1, \gamma = 1, \xi = 4, d = 1/4$ in (**??**). In between $\beta_d = 0.226757$ and $\beta_0 = 0.3125$ there exist three fixed points, with E_0 stable and E_1, E_2 unstable. After β_0 E_1 exits the domain, E_0 becomes unstable. E_2 becomes stable after $\beta_2 = 0.331182$. In between β_0, β_2 there is no fixed stable point, and there exists at least one stable cycle –see Figure 7. At β_2 and $\beta_1 = 0.267457$ the respective traces change sign.
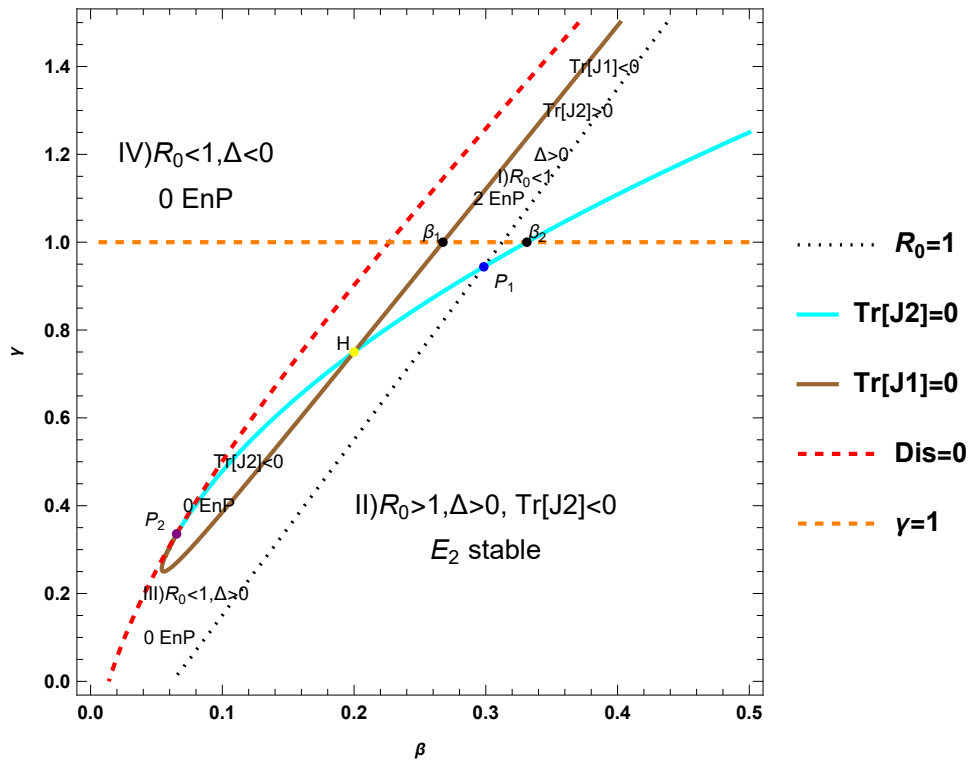
11.1.1 Bifurcation diagram of co-dimension two

Figure 6: Bifurcation diagram of co-dimension two for the system (??) with $b = 1, \xi = 4, d = 1/4$. The blue curve $Tr[J_2] = 0$ contains Hopf candidates (for example, at $P_1 = (0.298484, 0.943937)$, $H = (0.2, 0.75)$, $\beta_2 = (0.331182, 1)$, the eigenvalues of the Jacobian at E_2 are respectively $\pm 0.541022 Im$, $\pm 0.701516\ Im$ and $\pm 0.745862\ Im$). The point $P_2 = (0.0652696, 0.335786)$, the intersection of the curve $Tr[J2] = 0$ with $Dis = 0 = det[J2]$ is a Bogdanov-Takens candidate, with eigenvalues at $E_2 = E_1$ are $(0,0)$.

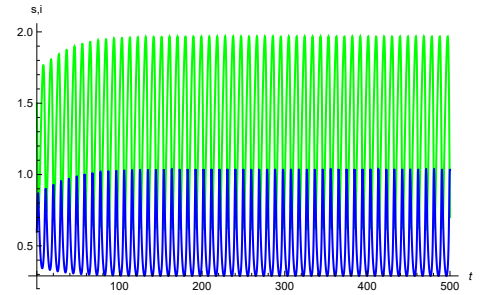## 11.1.2 Time and phase plots at $(\beta = 0.32 \in (\beta_0, \beta_2), \gamma = 1)$

In the following figures, we provide time and phase plots at the point $(\beta = 0.32 \in (\beta_0, \beta_2), \gamma = 1)$:
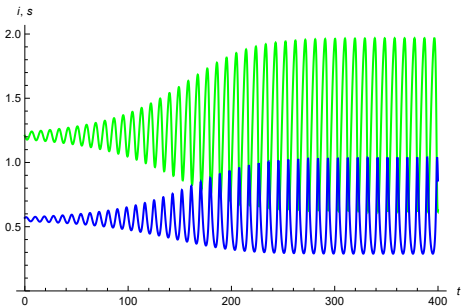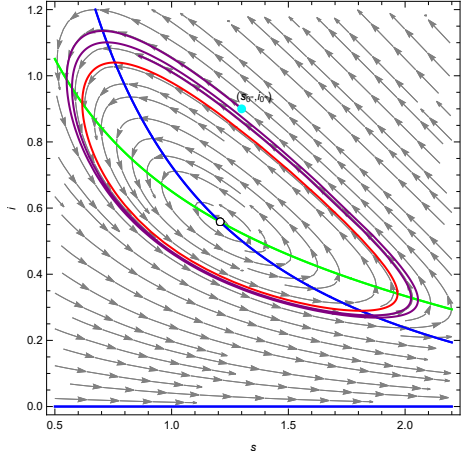
(a) Plot of the dynamics in time with $t_f = 400$ and $(s_0'', i_0'') = (1.3, 0.9)$, indicating the existence of a limit cycle surrounding $E_2 = (1.208, 0.5584)$.
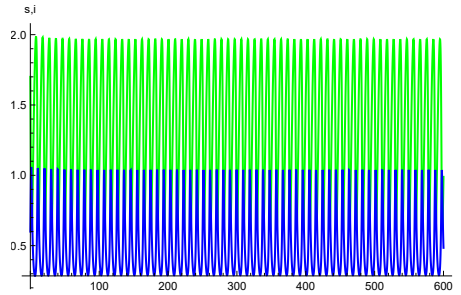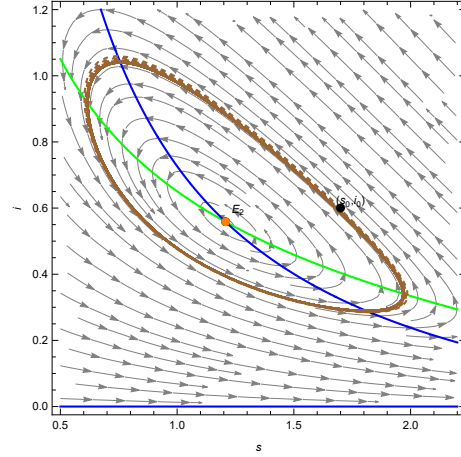
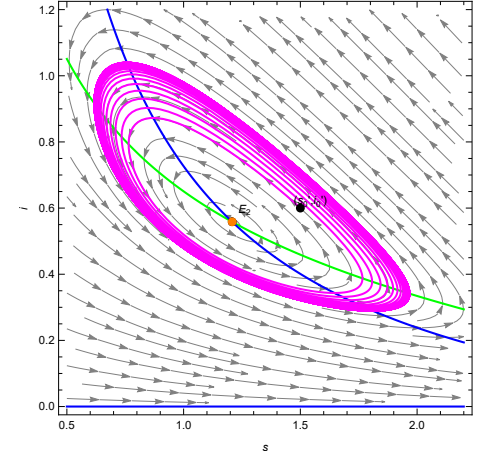(b) Time plot of (s, i) with $t_f = 600$ and $(s_0, i_0) = (1.7, 0.6)$.

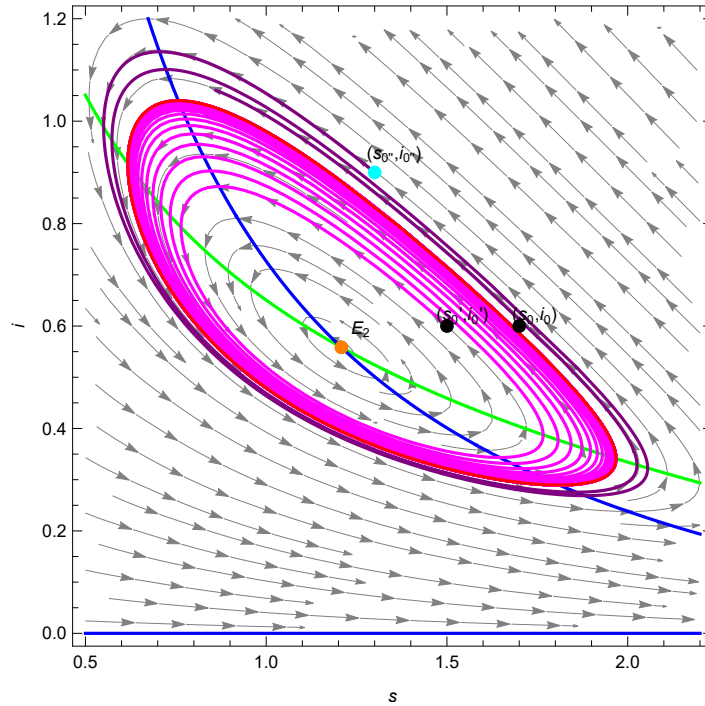(c) Time plot of (s, i) with $t_f = 500$ and $(s_0', i_0') = (1.5, 0.6)$.

(d) Phase plot corresponding to the time plot 7a, including a trajectory in violet starting outside the cycle.

(e) Phase plot corresponding to the time plot 7b, including a trajectory starting very close to the cycle.

(f) Phase plot corresponding to the time plot 7c, including a trajectory starting inside the cycle.

(g) (s, i) phase plot. The fixed point E_2 is unstable with eigenvalues $0.01782 \pm 0.711 Im$. The Floquet exponents of the cycle are $(-1.0331 \times 10^{-7}, -0.0367982)$. The point $E_0 = (4, 0)$ is a saddle point with eigenvalues $(-0.25, 0.030)$ (and the fixed point E_1 is outside the domain).

Figure 7: Time and phase plots at the point $(0.32, 1)$, with $\beta \in (\beta_0, \beta_2)$ –see also figure (5).
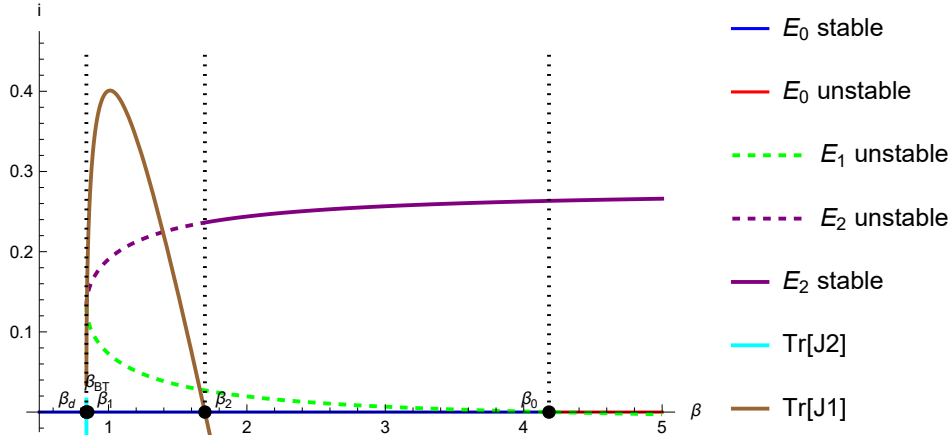
11.2 The case $\beta_0 > \beta_2$

Figure 8: Bifurcation diagram when β varies and $b = 1, \gamma = 21/8, \gamma_s = 5/32, \xi = 64, \gamma_r = 1/64, \delta = 0$ in (24) with $\beta_d = 0.840316, \beta_{BT} = 0.85$. At $\beta_1 = 0.840474$ and $\beta_2 = 1.69662$, the respective traces change sign. At β_{BT}, the eigenvalues of the Jacobian at E_2 are $(0.399276 \pm 0.870892 Im)$. Between β_2 and $\beta_0 = 4.18269$, the fixed points E_0 and E_2 coexist and are stable. The eigenvalues of J_2 at $\beta_1 \in (\beta_d, \beta_2)$ are $(0.879784, 0.120216)$, and between β_1 and β_2, by taking $\beta = 0.9$, the eigenvalues of J_2 are $(0.168899 \pm 1.6339 Im)$. At β_2, the point E_2 becomes stable with eigenvalues $(-2.1183 \pm 3.8813 Im)$, and remains stable between (β_2, β_0), since the eigenvalues of J_2 after β_2, at $\beta = 2$, are $(-2.9316 \pm 4.1104 Im)$, and E_2 remains stable after β_0 since the eigenvalues of J_2 after β_0, at $\beta = 5$ for example, are $(-16.7533, -4.97068)$.
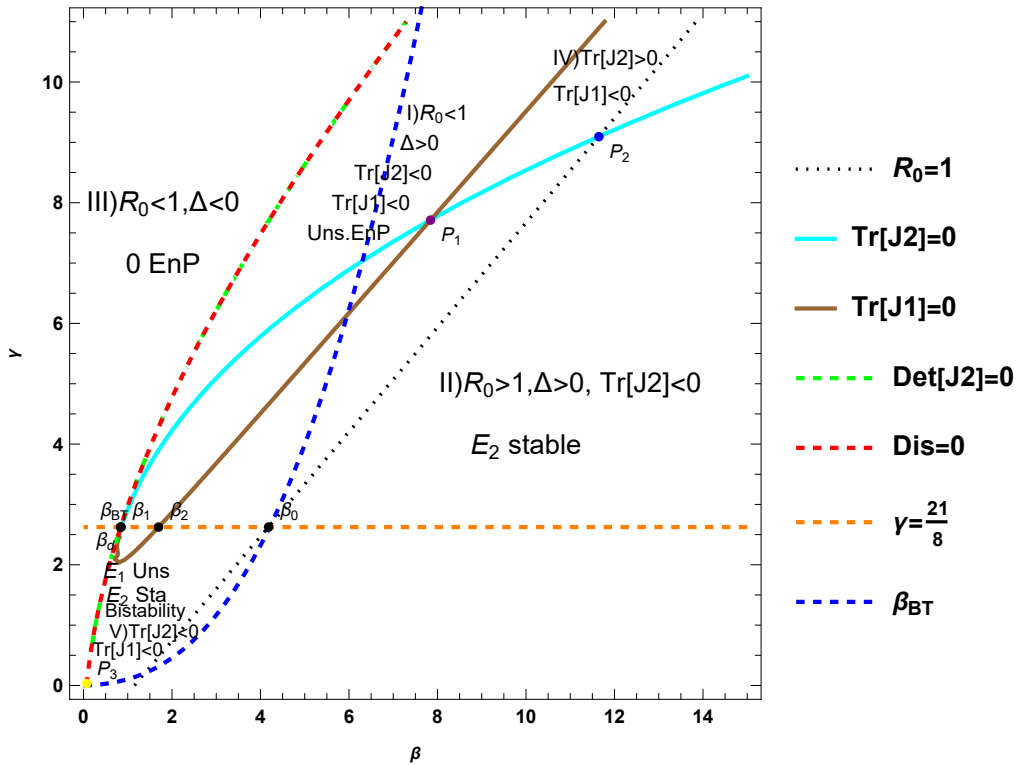
11.2.1 Bifurcation diagram of co-dimension two

Figure 9: Bifurcation diagram of co-dimension two for the system (24) with $b = 1, \gamma_s = 5/32, \xi = 64, \gamma_r = 1/64, \delta = 0$. The point $P_3 = (0.826821, 2.59409)$ denotes the intesection between $Tr[J2] = 0$ and $\beta = \beta_{BT}$, at this point, it has been checked using Mathematica that $Tr[J2] = Tr[J1] = \Delta = 0$, and the eigenvalues corresponding to E_2 at this point are $(1, 0)$. The intersection points of the curves $Tr[J2] = 0$ with $Tr[J1] = 0$ and $R_0 = 1$ are, respectively, $P_1 = (7.84298, 7.71203)$ and $P_2 = (11.6475, 9.09449)$.

Remark 20 *In the general case of [JWX07], when $\gamma_s > 0$, we could verify with the help of Mathematica, that there is no Bogdanov-Takens point, since the eigenvalues of the Jacobian are not zero.*

11.2.2 Time and phase plots corresponding to Figure 9

- **At** $\beta_1 \in (\beta_d, \beta_2)$

  At this, $Tr[J2] = 0$, and the DFE $E_0 = (0.8666, 0, 0)$ is stable. The interior points $E_2 = (0.451329, 0.133692)$ and $E_1 = (0.463879, 0.129653)$ are unstable, with eigenvalues $(0.879784, 0.120216)$ and $(1.14004, -0.089969)$, respectively.

(a) Plot of the dynamics in time indicates convergence towards $E_0 = (0.8666, 0)$.

(b) (s, i) phase plot. The black and red curves illustrate the unstable manifolds corresponding to the unstable fixed points E_1 and E_2, respectively.
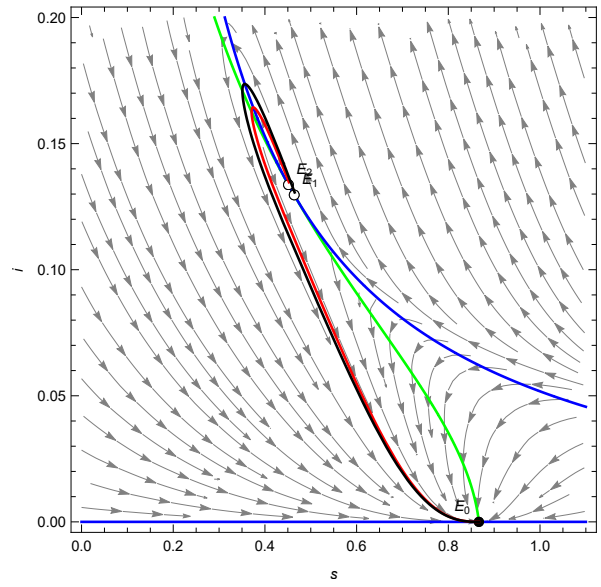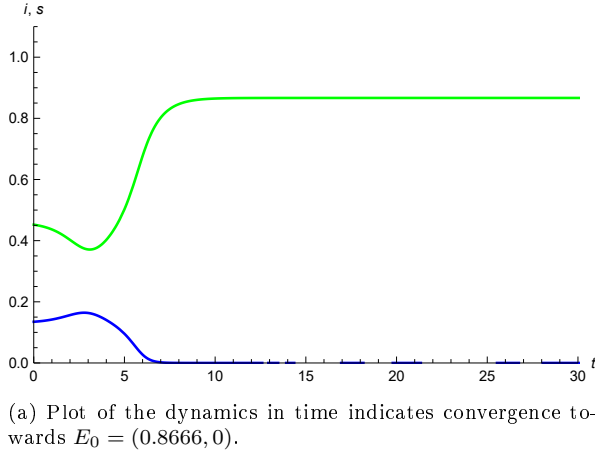
Figure 10: Time and phase plots at $\beta_1 = (0.840474, 21/8) \in (\beta_d = 0.840316, \beta_2 = 1.69662)$ when $\gamma_s > 0$ and $\delta = 0$ (see Figure 9).

- **At β_2**

  Here, $Tr[J1] = 0$, and the fixed point $E_1 = (0.782701, 0.0270277)$ is unstable with eigenvalues $(2.07675, -1.07675)$, and the point $E_2 = (0.132508, 0.236317)$ becomes stable with eigenvalues $(-2.1183 \pm 3.8813Im)$. The disease-free equilibrium $E_0 = (0.8666, 0)$ remains stable with eigenvalues $(-2.15459, -1.17188)$.
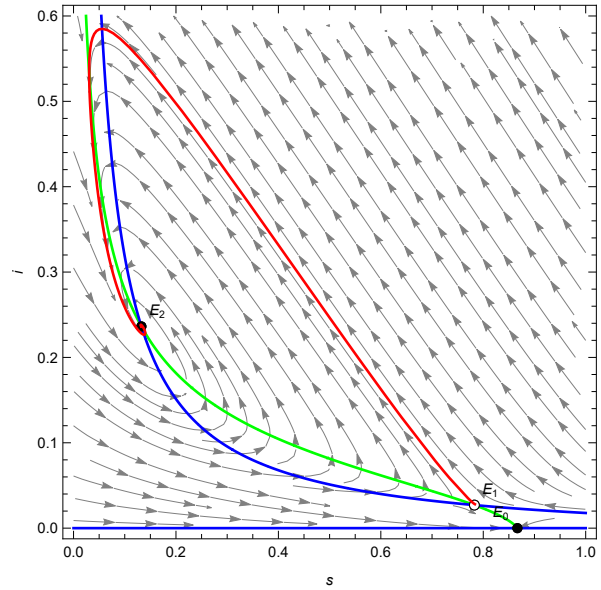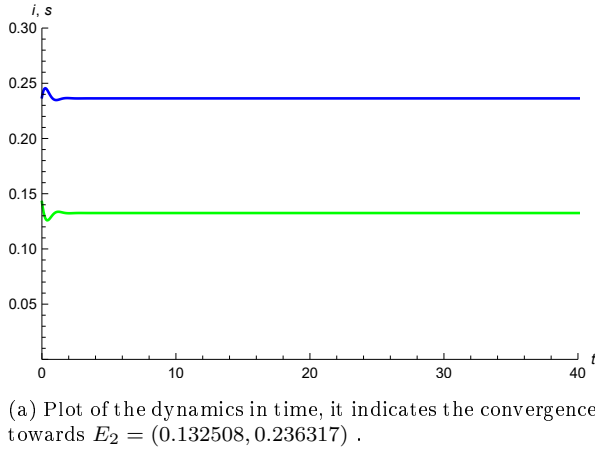

(a) Plot of the dynamics in time, it indicates the convergence towards $E_2 = (0.132508, 0.236317)$.

(b) (s, i) phase plot. The red curve depicts the stable manifold of E_2 which delimits its basin of attraction.

Figure 11: Time and phase plots at $\beta_2 = (1.69662, 21/8)$.

- **At $\beta \in (\beta_2, \beta_0)$**

  After crossing β_2, we obtain a bistability of the points $E_2 = (0.109151, 0.243836)$ and $E_0 = (0.8666, 0)$ whose eigenvalues respectively are $(-2.9316 \pm 4.1104Im)$, and $(-1.89167, -1.17188)$. The remaining point $E_1 = (0.806058, 0.0195094)$ is a saddle with eigenvalues $(1.85355, -1.10028)$.

(a) Plot of the dynamics in time indicates the convergence towards $E_0 = (0.8666, 0)$ and $E_2 = (0.109151, 0.243836)$.

(b) (s, i) phase plot. The black and orange curves illustrate the unstable and stable manifolds, respectively, corresponding to the fixed points E_1 and E_2
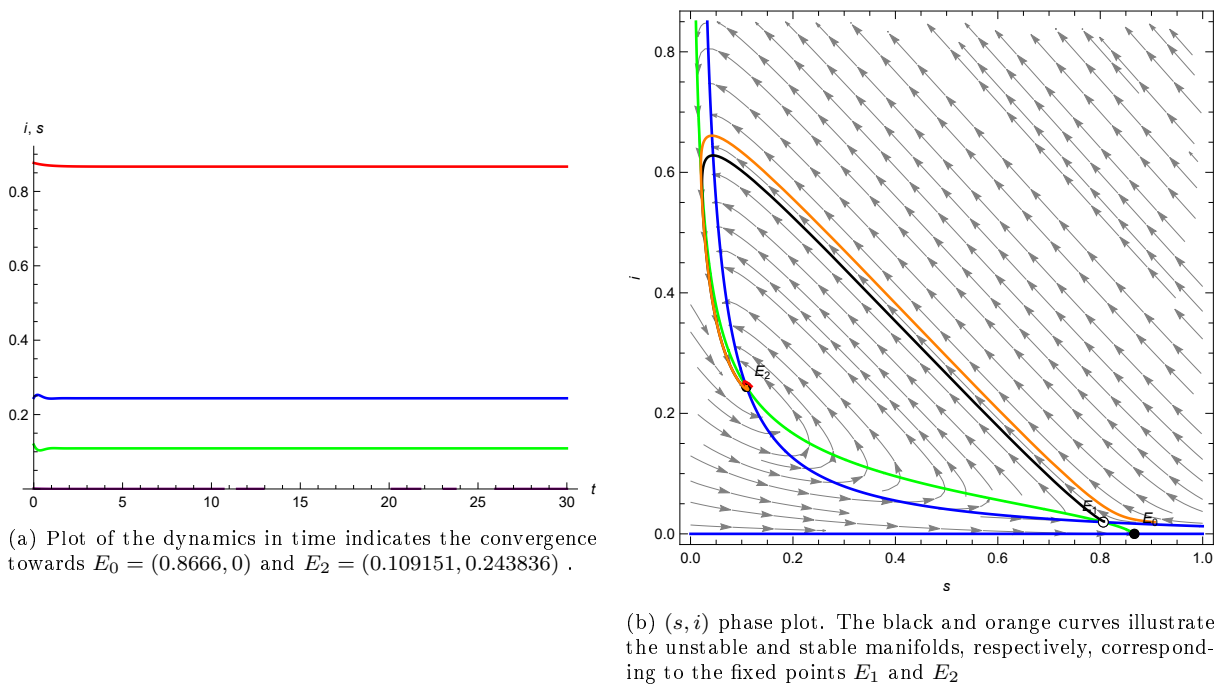
Figure 12: Time and phase plots at $\beta = (2, 21/8) \in (\beta_2 = 1.69662, \beta_0 = 4.18269)$.

11.3 Two parameters bifurcation diagram for the original problem of [JWX07]

In this case, using the numerical values of [JWX07, Fig6], we obtain $b = \mu = 1, \beta = \beta_{BT} = 3.72669, \xi = 8.96984, \gamma_r = 0.445832, \gamma = 3.61458$. Moreover, by cutting the parameter β and solving $Tr[J1] = 0, \Delta = 0$ we get $\beta_1 = 3.72669 = \beta_d$. In the following figure, we illustrate a bifurcation diagram by varying β and γ in the case of [JWX07] where we can see clearly that β_1, β_d and β_{BT} coincide. The eigenvalues of E_1 and E_2 at this point are $(6.7196 \times 10^{-9} \pm 0.000336759)$ and $(-0.000336766, 0.000336752)$, respectively. Furthermore, the determinants corresponding to E_1 and E_2 are $\pm 1.13407 \times 10^{-7}$, and their traces are respectively $\pm 1.34392 \times 10^{-8}$.
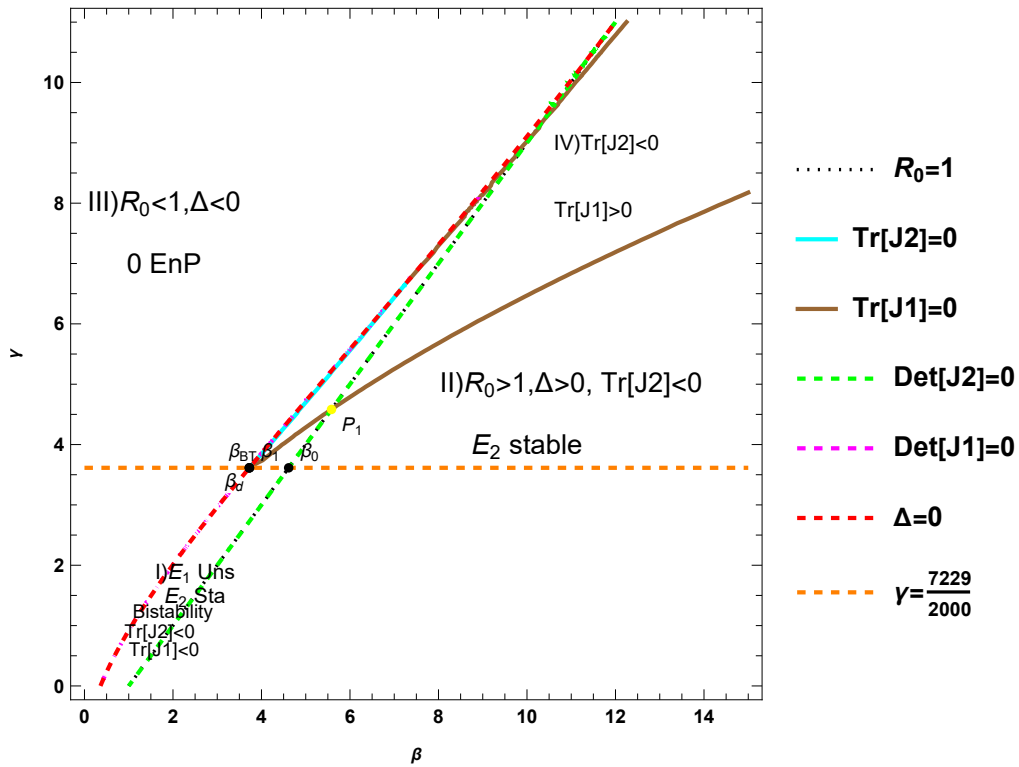

Figure 13: Bifurcation diagram of co-dimension two for the system (24) with $b = \mu = 1, \xi = 8.96984, \gamma_r = 0.445832$. The point $P_1 = (5.58207, 4.58207)$ denotes the intesection between $Tr[J1] = 0$ and $det[J2] = 0$, at this point, it has been checked using Mathematica that the eigenvalues corresponding to E_1 and E_2 are $(-0.817509 \pm 3.32109Im)$ and $(-2.06276, -0.770236)$ respectively.
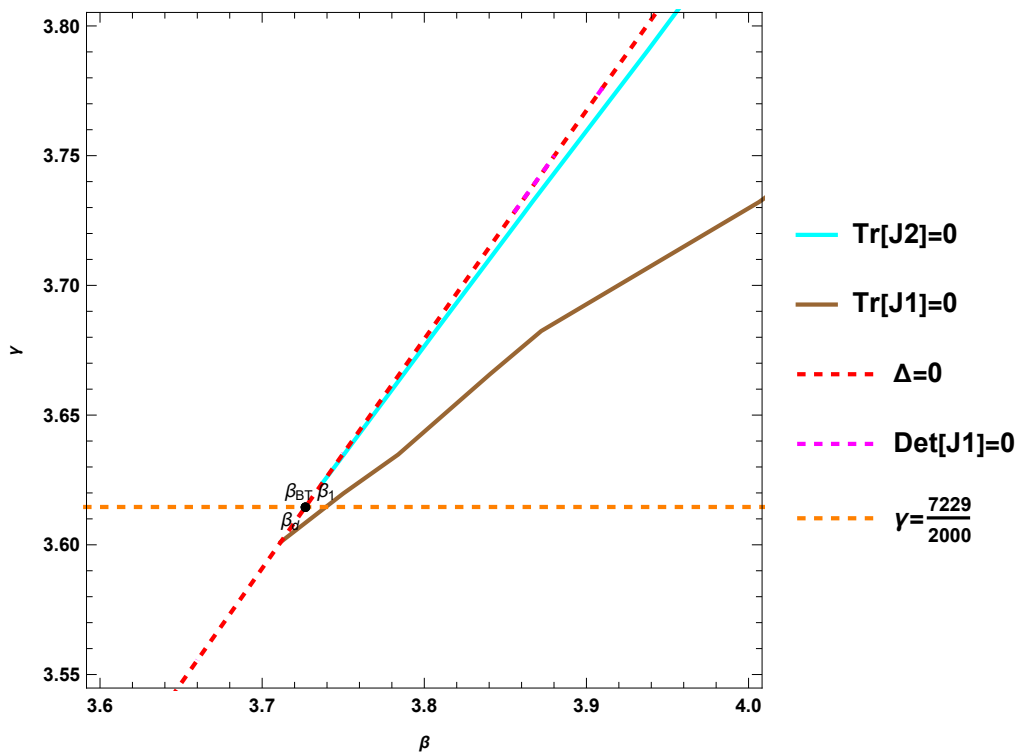
Figure 14: Blow-up of Figure 13 around β_{BT}.

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