Numerical modelling of disease propagation

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2020, Yang and Wang proposed the following compartmental model[1]:

$$
\begin{aligned}
\frac{dS}{dt} &= \Lambda - \beta_E SE - \beta_I SI - \beta_V SV - \mu S \\
\frac{dE}{dt} &= \beta_E SE + \beta_I SI + \beta_V SV - (\alpha + \mu)E \\
\frac{dI}{dt} &= \alpha E - (w + \gamma + \mu)I \\
\frac{dR}{dt} &= \gamma I - \mu R \\
\frac{dV}{dt} &= \xi_1 E + \xi_2 I - \sigma V
\end{aligned}
\tag{1}
$$

Parameters

Λ	Population influx	ξ_1	Rate of the exposed individuals contributing the virus to the environment
μ	Natural death rate	ξ_2	Rate of the infected individuals contributing the virus to the environment
w	Disease induced death rate	σ	Rate of (natural and artificial) removal of the virus from the environment
$1/\alpha$	Mean incubation period		
γ	Recovery rate		
β_I	Transmission rate by infected individual		
β_E	Transmission rate by exposed individual		
β_V	Transmission rate by the environmental reservoir		

- Reasons for the new compartment

Assumptions

We have made the following assumptions:

1.A1 There is always an infected but non-infectious phase.

1.A2 Vaccination is imperfect w.r.t infectious individuals and the environment, but in general for the vaccinated subpopulation to become infected at a lower rate.

1.A3 The imperfection of the vaccine is the same against infected people and the environment.

1.A4 Only susceptibles can get vaccinated.

1.A5 A recovered or vaccinated person can lose immunity.

Our proposed model:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \beta_I SI - \beta_V SV + \Psi C + \delta R - (\chi + \mu)S \\
\frac{dE}{dt} &= \beta_I SI + \beta_V SV + \rho\beta_I CI + \rho\beta_V CV - (\alpha + \mu)E \\
\frac{dI}{dt} &= \alpha E - (\gamma + \omega + \mu)I \\
\frac{dR}{dt} &= \gamma I - (\mu + \delta)R \\
\frac{dC}{dt} &= \chi S - \rho\beta_I CI - \rho\beta_V CV - (\Psi + \mu)C \\
\frac{dV}{dt} &= \xi I - \sigma V
\end{aligned} \tag{2}$$

New Parameters

$1/\delta$	Mean-time spent in the recovered class
$1 - \rho$	Vaccine effectiveness
χ	Vaccination rate of the susceptible class
Ψ	Rate of the vaccination loss
ξ	Rate of the exposed individuals contributing the virus to the environment

The *basic reproduction number* $\mathcal{R}_0$

- Number of secondary infections produced by an infected individual in a fully susceptible population (threshold parameter for invasion of a disease organism into the population)
- Next generation approach[2]:

$$\begin{aligned} x_i' &= \mathcal{F}_i(x,y) - \mathcal{V}_i(x,y) \quad i = 1,2,3 \\ y_j' &= g_j(x,y) \quad j = 1,2,3, \end{aligned} \tag{3}$$

where $(x_1, x_2, x_3) = (E, I, V)$, $(y_1, y_2) = (S, R, C)$

$$\mathcal{F} = \begin{pmatrix} \beta_E SI + \beta_V SV + \rho\beta_I SI + \rho\beta_V SV \\ 0 \\ 0 \end{pmatrix} \quad \mathcal{V} = \begin{pmatrix} (\alpha + \mu)E \\ -\alpha E + (\gamma + \omega + \mu)I \\ -\xi I + \sigma V \end{pmatrix}$$

$\mathcal{R}_0$

- $F = \mathbf{J}\mathcal{F}(X_0)$
- $V = \mathbf{J}\mathcal{V}(X_0)$
- *Next generation matrix* is defined as $K = FV^{-1}$, and its spectral radius is $\mathcal{R}_0$

$$\rho(K) = \mathcal{R}_0 = \frac{\alpha\beta_I S_0}{(\alpha+\mu)(\gamma+\omega+\mu)} + \frac{\alpha\rho\beta_I C_0}{(\alpha+\mu)(\gamma+\omega+\mu)} + \frac{\beta_V S_0 \xi\alpha}{(\alpha+\mu)(\gamma+\omega+\mu)\sigma} + \frac{\rho\beta_V C_0\xi\alpha}{(\alpha+\mu)(\gamma+\omega+\mu)\sigma} = \mathcal{R}_0^1 + \mathcal{R}_0^2 + \mathcal{R}_0^3 + \mathcal{R}_0^4$$

- Can be interpreted as the expected number of secondary infections produced in compartment E by an infected individual originally in compartment E

invariance, positivity

$$\Omega = \left\{ S, E, I, R, C, V \in \mathbb{R}^{+} : S + E + I + R + C \le \frac{\Lambda}{\mu}; V \le \frac{\xi}{\omega}\frac{\Lambda}{\mu} \right\} \subset \mathbb{R}^6$$

Definition (Positivity of ODE/IVP)

We say that the ODE/IVP is positive if whenever $\mathbb{R}^n \ni u_0 \ge 0$, then $u(t) \ge 0, \ \forall t \ge 0$ (where the relation is considered componentwisely).

Theorem (The proposed epidemic model positive)

The proposed system is positive in the sense of (1).

Theorem (Ω is positively invariant)

The proposed system is positively invariant on Ω.

Equilibria

The disease free equilibrium (DFE):

$$\mathcal{E}_0 := (S_0, E_0, I_0, R_0, C_0, V_0) = \left(\frac{\Lambda(\Psi + \mu)}{\mu(\Psi + \chi + \mu)}, 0, 0, 0, \frac{\Lambda\chi}{\mu(\Psi + \chi + \mu)}, 0 \right)$$

For the endemic equilibrium when $\rho \neq 1$, we get a quadratic function for I, where the signs of the coefficients are not fixed (coefficients not shown). When $\rho = 0$, the function reduces to a linear function.

Stability of DFE

Theorem (Stability of the DFE)

If $\mathcal{R}_0 < 1$, then the DFE $\mathcal{E}_0$ for the proposed system is locally asymptotically stable, while for $\mathcal{R}_0 > 1$ it is unstable.

Proof follows from [2].

Endemic equilibria

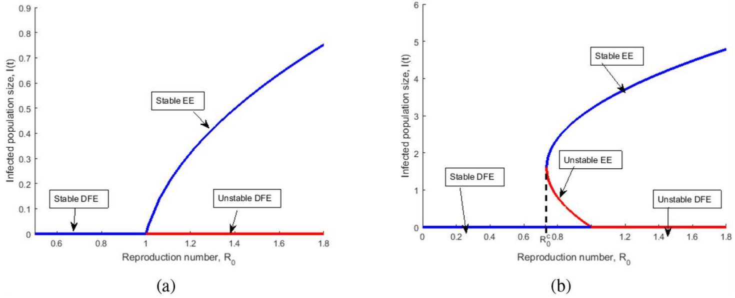


Figure: Forward (left figure) and backward (right figure) bifurcation. Figure from [3]

- sign of $\left.\frac{d\,I(\mathcal{R}_0)}{d\,\mathcal{R}_0}\right|_{\mathcal{R}_0=1}$

Theorem (Condition on backward bifurcation)

(From [4]): Consider the system of ODEs with parameter ϕ*:*

$$\frac{dx}{dt} = f(x;\phi), \ \ f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n, \ \ f \in C^2(\mathbb{R}^n x \mathbb{R}),$$

where 0 is an equilibrium for the system for all ϕ*. Assume that*

- A1 *Denote* $\mathcal{A} := D_x f(0,0) = (\frac{\partial f_i}{\partial x_j}(0,0))$*. Assume that zero is a simple eigenvalue of* $\mathcal{A}$*, and all the other eigenvalues have negative real part.*
- A2 *The matrix* $\mathcal{A}$ *for the eigenvalue* 0 *has a non-negative right eigenvector* w *and left eigenvector* v*.*

Let

$$a : = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0)$$

$$b : = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0,0)$$

Theorem

Then the local dynamics of the system is fully determined by the signs of a and b, specifically:

i. $a > 0$, $b > 0$. *When* $\phi < 0$ *with* $|\phi| \ll 1$, 0 *is locally asymptotically stable, and there exists a positive unstable equilibrium; when* $0 < \phi 1$, 0 *is unstable and there exists a negative and locally asymptotically stable equilibrium;*

ii . $a < 0$, $b > 0$. *When* ϕ *changes from negative to positive,* 0 *changes its stability from stable to unstable. Correspondingly, a negative unstable equilibrium becomes positive and locally asymptotically stable.*

iii. *...*

iv. *...*

$$\mathbb{R}^n = \mathcal{E}^c \oplus \mathcal{E}^s;\ W^c = \{c(t)w + h(c,\phi) : v \cdot h(c,\phi) = 0, |c| \le c_0, c(0) = 0\},$$

where $c(t) \in \mathcal{E}^c$ and $h(c,\phi) \in \mathcal{E}^s$.

$$\frac{d\,c(t)}{dt} = \frac{a}{2}(c(t))^2 + b\phi c(t)$$

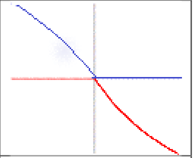
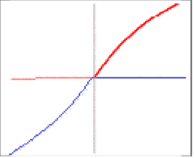
a and b	stability of 0	stability and sign of x^*	diagram
$a > 0, b > 0$	$\phi < 0$, S $\phi > 0$, U	$\phi < 0, x^* > 0$, U $\phi > 0, x^* < 0$, S	
$a < 0, b > 0$	$\phi < 0$, S $\phi > 0$, U	$\phi < 0, x^* < 0$, U $\phi > 0, x^* > 0$, S	

Figure: Case i. and ii.In the bifurcation diagrams, the vertical axis represents equilibrium points x^*, and the horizontal axis is the parameter ϕ. Figure from [4]

We will use the above theorem for the DFE $\mathcal{E}_0$, with the parameter $\phi := \Lambda$. Λ^* is the critical value obtained from $\mathcal{R}_0 = 1$:

$$\Lambda^* = \frac{\sigma\mu(\alpha+\mu)(\gamma+\omega+\mu)(\Psi+\chi+\mu)}{\alpha(\Psi+\mu+\rho\chi)(\sigma\beta_I+\xi\beta_V)}$$

The matrix of the linearized system of the proposed model at $(\mathcal{E}_0, \Lambda^*)$ is $\mathcal{A}$ such that the assumptions holds.

Theorem

The proposed system exhibits forward bifurcation at $\mathcal{R}_0 = 1$ if

$$\frac{\delta\gamma}{(\delta+\mu)} > \frac{(\alpha+\mu)(\gamma+\mu+\omega)(\mu+\Psi+\rho(\chi+2\mu))}{\alpha(\mu+\Psi+\chi\rho)}$$

, otherwise it exhibits backward bifurcation at $\mathcal{R}_0 = 1$.

Numerical methods

In general, numerical k-step methods with fixed step size for autonomous ODEs generate a discrete map:

$$\Phi_{f,\Delta t} : (u_{n-1}, \dots, u_{n-k}) \mapsto u_n$$

where $u_1, u_2, \dots, u_{k_1}$ initial values are given and u_n approximates $u(t_n) = u(hn)$, where Δt is the fixed step-size.

In the 1980's it was noticed that numerical ODE solvers can be considered as dynamical systems and since then their qualitative properties have been studied in detail.

Now on, for the simplicity we will suppose that we have an autonomous IVP.

Regularity of (linear) numerical metods

- $\mathcal{F} := \{u \in \mathbb{R}^n : f(u) = 0\}$
- $\mathcal{F}^*_{\Delta t} := \{u^* \in \mathbb{R}^n : \Phi_{f,\Delta t}(u^*, \dots, u^*) = u^*\}$

Q: $\mathcal{F} \stackrel{?}{=} \mathcal{F}^*_{\Delta t}$

LMM: $\mathcal{F} = \mathcal{F}^*_{\Delta t}$

RK: $\mathcal{F} \subset \mathcal{F}^*_{\Delta t}$ but $\mathcal{F}^*_{\Delta t} \nsubseteq \mathcal{F}$ for arbitrary f.

RK methods such that $\mathcal{F} = \mathcal{F}^*_{\Delta t}$ are called regular.

From [5]: The explicit-Euler method is the only explicit regular RK method, while for implicit methods we have the following barrier:

Theorem

The order p of a regular s stage RK method satisfies

$$p \le s + 2 \quad \textit{if s is even}$$
$$p \le s + 1 \quad \textit{if s is odd}$$

One can also talk about spurious 2-cycles.

Positivity preservation

Similarly for the continuous, one can define positivity for numerical methods.

Definition

Let there be given a numerical method, a set of functions $\mathcal{F} \subset \mathcal{P}$ and a real number $0 < H \leq \infty$. We call the method positive on $\mathcal{F}$ with threshold H if the numerical approximation (**??**) are non-negative whenever $f \in \mathcal{F}$, $u_0 \in \mathbb{R}_+^n$ with step size $0 < \Delta t \leq H$. If $H = \infty$, then we call the method unconditionally positive, otherwise conditionally positive.

- Patankar-Runge-Kutta methods

SSP LMM methods

Suppose that for the given f the explicit-Euler method is conditionally positive for step sizes Δt_{FE}, i.e.

$$0 \le u + \Delta t f(u), \ \ \forall\, u \in \mathbb{R}^n_+, \ \forall \Delta t \le \Delta t_{FE}$$

Then for an explicit LMM:

$$\sum_{j=0}^{k} \alpha_j u_{n-j} = \sum_{j=1}^{k} \beta_j f(u_{n-j})$$

$$u_n = \sum_{j=1}^{k} -\alpha_j \left(u_{n-j} + c_j \Delta t f(u_{n-j}) \right)$$

where $c_j := \dfrac{-\beta_j}{\alpha_j}$. The positivity holds for arbitrary starting values if $\alpha_j \le 0, \ \beta_j \ge 0$ and $c_j \Delta t \le \Delta t_{FE}$, $j = 1, \ldots, k$ i.e.

$$\Delta t \le \mathcal{C} \Delta t_{FE}, \ \ \mathcal{C} := min_{j=1,\ldots,k} \frac{\alpha_j}{-\beta_j}$$

The method-dependent constant $\mathcal{C}$ is called the SSP-coefficient.

Strong Stability Preserving methods

- Generally used for the semi-discretized system of nonlinear partial differential equations.
- They are based on the preservation of the monotonicity property for some semi-norm $||u_{n+1}|| \leq ||u_n||$.
- e.g. $||v|| := TV(v) := \sum_{j=2}^{n} |v_j - v_{j-1}|$. (Total Variation)
- SSP Runge-Kutta methods can be defined similarly
- Theory is developed to get unique representation (and the "true" SSP coefficient)

Back to our proposed epidemic model

Theorem (Suff. cond. for the positivity of system discretized by the EEM)

The explicit-Euler discretization of the system (2) is conditionally positive with step-size

$$H = min\left(\frac{1}{\alpha+\mu}, \frac{1}{\sigma}, \frac{1}{\mu+\delta}, \frac{1}{\gamma+\omega+\mu}, \frac{1}{\chi+\mu+\frac{\Lambda}{\mu}(\beta_I+\beta_V\frac{\xi}{\sigma})}, \frac{1}{\Psi+\mu+\rho\frac{\Lambda}{\mu}(\beta_I+\beta_V\frac{\xi}{\sigma})}\right)$$

Numerical simulations

- Classical RK4 method ($\mathcal{C} = 4$)
- SSPM42 Optimal explicit 4 step second order LMM method ($\mathcal{C} = \frac{2}{3}$)

$$u_{n+1} = \frac{8}{9}\left(u_n + \frac{3}{2}\Delta t f(u_n)\right) + \frac{1}{9}u_{n-3}$$

- All parameters fixed (except Λ) in a non-systematic way.
- Multiple initial values from Ω (unif. distributed/near the boundaries). Multiple step-sizes.
- Methods lost their positivity when losing their stability.
- We also have not seen stable spurious equilibria (which changes continuously for the different step sizes).

Future Directions

- Numerical simulation in a more-systematic way
- Discrepancy between theory and simulation

→ Subclass of positive functions, possibly dissipative systems.

→ Higueras: systems for which EEM maximal time step (for positivity-preservation) is nonzero for $-f$, RK4 is conditionally positive[6].

References I

[1]–Yang, Chayu, and Jin Wang. "A mathematical model for the novel coronavirus epidemic in Wuhan, China." Mathematical biosciences and engineering: MBE 17.3 (2020): 2708.
[2]–Van den Driessche, P., and James Watmough. "Further notes on the basic reproduction number." Mathematical epidemiology. Springer, Berlin, Heidelberg, 2008. 159-178.
[3]–Juga, M. L., F. Nyabadza, and F. Chirove. "An Ebola virus disease model with fear and environmental transmission dynamics." Infectious Disease Modelling 6 (2021): 545.
[4]–Castillo-Chavez, Carlos, and Baojun Song. "Dynamical models of tuberculosis and their applications." Mathematical Biosciences Engineering 1.2 (2004): 361.
[5]–Hairer, Ernst, Arieh Iserles, and Jesus Maria Sanz-Serna. "Equilibria of Runge-Kutta methods." Numerische Mathematik 58.1 (1990): 243-254.

References II

[6]–Sanz, Inmaculada Higueras. "Positivity properties for the classical fourth order Runge-Kutta method." Monografías de la Real Academia de Ciencias Exactas, Físicas, Químicas y Naturales de Zaragoza 33 (2010): 125-139.