

Numerical modelling of disease propagation

Math Project I.

Szemenyei Adrián László
Neptun: ZFXRFU

Supervisor: Dr. Faragó István



ELTE

EÖTVÖS LORÁND
TUDOMÁNYEGYETEM

2021. December

The dynamics of infectious diseases show a wide diversity of patterns. By constructing epidemiological models (with the help of mathematics) we can understand the dynamics and their qualitative characteristics of different infectious diseases. Unfortunately, we live in times when the need for this knowledge is undisputed (Malaria, COVID-19, etc.).

Epidemiological models can be categorized by their mathematical structures: deterministic or stochastic. In deterministic models one of the most used are the compartmental models, where the dynamics of different compartments are modeled by ordinary differential equations. Different compartments make it possible to 'heterogenize' the population by its relationship to the disease, age, space, vaccination or lack thereof, etc.

In 2020, Yang and Wang proposed the following model to investigate the epidemic period of COVID-19 in Wuhan from January 23, 2020 to February 10, 2020[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
μ	Natural death rate
w	Disease induced death rate
$1/\alpha$	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
ξ_1	Rate of the exposed individuals contributing the virus to the environment
ξ_2	Rate of the infected individuals contributing the virus to the environment
σ	Rate of (natural and artificial) removal of the virus from the environment

where S , E , I , R are the number of susceptible, exposed (infectious but not yet symptomatic), infected (infectious and symptomatic) and recovered, respectively. All the parameters are non-negative.

From system (1) it is easy to see that the core of the model is the usual SEIR model with variables (S,E,I,R) and the main changes are the mass-action incidence $\beta_V SV$ in the compartment S and E and the new compartment V with its own dynamics, namely, for larger $E(t)$ and $I(t)$ the derivative of V is larger at time t , while if V is increasing, then its derivative is decreasing by factor σ . The reasoning to include the environmental reservoir as a possible transmission route was that when officials took samples from the areas of the Huanan Seafood Market it come back positive. Also, some studies suggest that the virus can survive on different surfaces such as metal, glass, and plastic for up to 9 days. By fitting the outbreak data to the proposed model, they found that the environmental reservoir had a significant contribution to the overall infection risk.

The disease-free equilibrium (DFE) can be obtained by setting all the derivatives of (1) and E, I, V equal to zero (i.e., no infections in the population): $\mathcal{E}_0 = (S_0, E_0, I_0, R_0, V_0) = (\frac{\Lambda}{\mu}, 0, 0, 0, 0)$. While the endemic equilibrium(s) (EE) $\mathcal{E} = (\hat{S}, \hat{E}, \hat{I}, \hat{R}, \hat{V})$ can be found by setting all the derivatives 0 in system (1) and solving the system of equations. We can get the endemic equilibrium for the **usual SEIR** model by setting $\beta_V = 0$. The EE is larger in variables E, I, R , while smaller in S for the system (1) than for the usual (S,E,I,R) model.

The *basic reproduction number* \mathcal{R}_0 for a disease is the number of secondary infections produced by an infected individual in a completely susceptible population (threshold parameter for invasion of a disease organism into the population)[2]. We can compute \mathcal{R}_0 for a compartmental ODE system by the next generation approach, which is the following[2].

The infection components for model (1) are E, I, V . Rewriting the model as:

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

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

$$\mathcal{F} = \begin{pmatrix} \beta_E SE + \beta_I SI + \beta_V SV \\ 0 \\ 0 \end{pmatrix}, \quad \mathcal{V} = \begin{pmatrix} (\alpha + \mu)E \\ -\alpha E + (w + \gamma + \mu)I \\ -\xi_1 E - \xi_2 I + \sigma V \end{pmatrix}$$

where $\mathcal{F}_i(x, y)$ represents the rate of new infection in compartment i , while $\mathcal{V}_i(x, y)$ incorporates the remaining transitional terms. The Jacobi matrices of the subsystems \mathcal{F} and \mathcal{V} at the disease-free equilibrium $(0, y_0) = (E_0, I_0, V_0, S_0, R_0) = (0, 0, 0, \frac{\Lambda}{\mu}, 0)$ are $F = \mathbf{J}\mathcal{F}(X_0)$ and $V = \mathbf{J}\mathcal{V}(X_0)$.

Linearizing system (2) at the DFE gives $x' = (F - V)x$ where the infected compartments x are decoupled from the remaining equations, because for every pair (i, j) :

$$\frac{\partial \mathcal{F}_i(0, y_0)}{\partial y_j} = \frac{\partial \mathcal{V}_i(0, y_0)}{\partial y_j} = 0.$$

The next generation matrix is defined as:

$$K = FV^{-1} = \begin{pmatrix} \frac{\beta_E S_0}{\alpha + \mu} + \frac{\beta_I S_0 \alpha}{(\alpha + \mu)(w + \gamma + \mu)} + \frac{\beta_V S_0 (\alpha \xi_2 + (w + \gamma + \mu) \xi_1)}{(\alpha + \mu)(w + \gamma + \mu) \sigma} & \frac{\beta_I S_0}{w + \gamma + \mu} + \frac{\beta_V S_0 \xi_2}{(w + \gamma + \mu) \sigma} & \frac{\beta_V S_0}{\sigma} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad (3)$$

which is an upper triangular matrix, so its spectral radius is

$$\begin{aligned} \rho(K) &= \mathcal{R}_0 = \frac{\beta_E S_0}{\alpha + \mu} + \frac{\beta_I S_0 \alpha}{(\alpha + \mu)(w + \gamma + \mu)} + \frac{\beta_V S_0 (\alpha \xi_2 + (w + \gamma + \mu) \xi_1)}{(\alpha + \mu)(w + \gamma + \mu) \sigma} \\ &=: \mathcal{R}_1 + \mathcal{R}_2 + \mathcal{R}_3 \end{aligned} \quad (4)$$

For the **usual SEIR** model the infection components are E and I with DFE $(0, y_0) = (E_0, I_0, S_0, R_0) = (0, 0, \frac{A}{\mu}, 0)$ and the next generation matrix and its spectral radius is the same as (3) and (4) with $\beta_V = 0$. So, the basic reproduction number differs in one term between the two models. \mathcal{R}_1 and \mathcal{R}_2 can be interpreted as the human-human transmissions while \mathcal{R}_3 is the human-environment transmission. To be precise, in both cases \mathcal{R}_0 is the $K_{1,1}$ entry, what can be interpreted as the expected number of secondary infections produced in compartment E by an infected individual originally in compartment E[2]:

- \mathcal{R}_1 is the secondary infections from an exposed individual, because the incidence of the exposed is $\beta_E S_0 E$, so one exposed individual causes $\beta_E S_0$ number of secondary infections in a totally susceptible population S_0 per unit time. The exposed individual spends $1/(\alpha + \mu)$ time in the exposed compartment.
- \mathcal{R}_2 is the number of the secondary infections of the initially exposed individual in his/her infectious stage because the ratio $\frac{\alpha}{\alpha + \mu}$ is the fraction of individuals that progress from E to I and one infectious individual causes $\frac{\beta_I S_0}{w + \gamma + \mu}$ secondary infections in his/her infectious stage.
- After rewriting \mathcal{R}_3 as $\frac{\beta_V S_0 \xi_1}{(\alpha + \mu) \sigma} + \frac{\beta_V S_0 \alpha \xi_2}{(\alpha + \mu)(w + \gamma + \mu) \sigma}$ we can see that it is the secondary infections by the environment from the initially exposed individual. The first term is the fraction of initially exposed individuals that progress to V through E ($\frac{\xi_1}{\alpha + \mu}$) causing $\frac{\beta_V S_0}{\sigma}$ number of new infections in $\frac{1}{\sigma}$ time. The second term is the fraction of initially exposed individuals that progress to V through I ($\frac{\alpha}{\alpha + \mu} \frac{\xi_2}{w + \gamma + \mu}$) causing $\frac{\beta_V S_0}{\sigma}$ number of new infections in $\frac{1}{\sigma}$ time. By setting $\beta_V = 0$ this transmission route disappears.

From (4) we can see that \mathcal{R}_3 is a (convex) decreasing function of the virus removal rate from the environment μ , while \mathcal{R}_3 is an increasing function of ξ_1 and ξ_2 ('transmission rates' from exposed to the environment and from infected to the environment, respectively). Because $\lim_{\sigma \rightarrow 0} \mathcal{R}_0(\sigma) = \infty$ and $\lim_{\sigma \rightarrow \infty} \mathcal{R}_0(\sigma) = \mathcal{R}_{0u} = \mathcal{R}_1 + \mathcal{R}_2$ we can see that σ can have a major effect on the dynamic of the epidemic. Because σ is interpreted as the (natural and artificial) removal rate of the virus from the environment, we can think about it as a control parameter.

Yang and Wang proved that the system (1) exhibits forward bifurcation[1]: if $\mathcal{R}_0 < 1$ then the only stable point is the DFE, while for $\mathcal{R}_0 > 1$ the DFE is unstable and the EE is globally asymptotically stable (for non-negative initial values). Their proof is valid for the 'core' SEIR system too (**usual SEIR** system).

Because our system (1) is a biological system, we would expect that the solutions are biologically reliable. One aspect of this is that the region $\Omega = \mathbb{R}_+^5$ is positively invariant (i.e., the solutions with initial conditions in Ω stays in Ω for all $t > 0$). This can be proved by checking the sign of the derivatives at the boundary points. If the trajectories are reflected back when they reach the boundary of Ω , then no solutions with initial conditions in Ω can leave Ω . With this, the positive invariance of system (1) and for the **usual SEIR** model can be easily checked.

Discussion, future directions

Our main goal for Math Project I. was (for me) to get familiar with the different aspects and techniques of epidemiological modelling. For this, my main sources were [3] and [4]. I used these techniques to model (1) from [1], mainly to compare it with the **usual SEIR** model, where the idea that infectious people can transmit the disease to the environmental reservoir, from where susceptible people can get infected was not incorporated into the model. For future directions, it would be interesting to check other models with the additional dynamics of the environmental reservoir. For example for Lagrangian and Eulerian movement models, where the total population occupies n regions with the possibility of movement from one region to another and all of the n regions has their own disease dynamics. Also, we want to further study the parameters $\beta_b, xi_1, xi_2, \sigma$ from the aspect of control. Also, we are interested in the numerical modeling aspect of these models (i.e. which properties of the model are inherited after discretization). The discretization of the different continuous epidemiological models are inevitable if we want to solve them numerically. For example, one property that the continuous model (1) holds is the positive invariance, while it can be shown that for the discretized version for (1) by the explicit Euler discretization does not inherit this property for all discretization-step (proof not shown). Another property is the stability of the disease-free and endemic equilibriums for different discretization steps.

References

- [1] C. Yang and J. Wang, “A mathematical model for the novel coronavirus epidemic in wuhan, china,” *Mathematical biosciences and engineering: MBE*, vol. 17, no. 3, p. 2708, 2020.
- [2] P. Van den Driessche and J. Watmough, “Further notes on the basic reproduction number,” in *Mathematical epidemiology*, Springer, 2008, pp. 159–178.
- [3] V. Capasso, *Mathematical structures of epidemic systems*. Springer, 1993, vol. 88.
- [4] M. Martcheva, *An introduction to mathematical epidemiology*. Springer, 2015, vol. 61.