Epidemic models and the dynamics of infectious diseases

Marco Mazzotti - ETH Zurich - MMM FS 2020 - March 22^{th}, 2020

Mathematical models for epidemics have been proposed in the scientific literature since historical times. A very useful and stimulating overview of models of different levels of complexity is provided in the excellent book by James D. Murray, *Mathematical Biology*, Springer-Verlag Berlin Heidelberg 1989. In these lecture notes part of the text is taken *verbatim* from Chapter 19 of that book (these parts are reported in italic). The simplest models consist of systems of ODEs hence they belong to the types of problems dealt with in the class on *Modeling and Mathematical Methods in Process and Chemical Engineering* at ETH Zurich.

Simple epidemic models - SIR

Let us address the situation where a small group of infected individuals are introduced into a large population of individuals, who have never contracted the virus carried by the infectives. The key question is whether the infection spreads and how, i.e. following which dynamic evolution. We will use the classical SIR model, introduced by Kermack and McKendrick in 1927.

Model equations

By assuming a homogeneous pool of individuals, i.e. no spatial distribution, the population is divided in three classes, namely the susceptibles, S, who can still catch the disease; the infectives, I, who have the disease and can transmit it; and the removed class, R, *namely those who have either had the disease, or are recovered, immune or isolated until recovery*, or

dead. The number of individuals in each class is obviously a function of time, T, and evolves according to the following simple model: susceptibles become infectives through contact with infectives (which act like a catalyst in a chemical reaction), whereas infectives are removed at a rate that is intrinsic to the disease under consideration. By considering *the various classes as uniformly mixed, that is every pair of individuals has equal probability of coming into contact with one another*, the following system of three non-linear ODEs is obtained (time derivatives are indicated by a dot):

$$\dot{S} = -rSI \tag{1}$$

$$\dot{I} = rSI - aI \tag{2}$$

$$\dot{R} = aI \tag{3}$$

with $S(0) = S_0$, $I(0) = I_0$, and $R(0) = 0$ at $T = 0$. As a consequence of the assumption of constant population size, the following constraint holds:

$$S(T) + I(T) + R(T) = S_0 + I_0 \tag{4}$$

Because of the model structure and of the constraint, Eqs (1) and (2) yield a 2D system of nonlinear ODEs that can be solved independently of Eq. (3).

Dimensionless equations

The four parameters in the model above, namely the positive rate constants r and a, and the initial state given by S_0 and I_0, can conveniently be reduced to two (effectively to one from an epidemic dynamics point of view, as we will see) by rewriting the equations in dimensionless form. For educational purposes, we do it in steps. First, three dimensionless variables are defined through arbitrary reference values, namely $x = S/S_r$, $y = I/I_r$, and $t = T/T_r$. Eqs (1) and (2) can be cast as (derivatives with respect to the dimensionless time are again indicated with a dot):

$$\dot{x} = -rT_rI_rxy \tag{5}$$

$$\dot{y} = rT_rS_rxy - aT_ry \tag{6}$$

If I_r is assigned the same value as S_r, then choosing T_r so as $rT_rS_r = 1$ and defining $q = aT_r$ reduces the equations above to the one-parameter system:

$$\dot{x} = -xy \tag{7}$$

$$\dot{y} = xy - qy \tag{8}$$

where the physically meaningful values of x and y are those in the first quadrant of the (x, y) plane. The initial conditions reduce, upon setting $S_r = S_0$, to $x(0) = 1$ and $y(0) = y_0$, with $y_0 = I_0/S_0$. The latter parameter is obviously important, but also obviously very much smaller than 1, because we are interested in situations where an epidemic develops from a very small number of infected individuals, I_0, introduced in a much larger population, S_0. As a consequence of these choices and definitions, we have that $T_r = 1/(rS_0)$ and $q = a/(rS_0)$. The reciprocal of the latter is known as R_0 in epidemiology, i.e. $R_0 = 1/q = rS_0/a$; this is the basic reproduction number of *the infection, that is, the number of secondary infections produced by one primary infection in a wholly susceptible population.*

Mathematical analysis

Eqs (7) and (8) have infinite steady states for $y = 0$, i.e. on the horizontal axis. One can show that these are indifferent equilibrium points (the associated linearized system of ODEs has a zero eigenvalue). The vector field points leftward, since $\dot{x} \leq 0$ always. It points upward for $x > q$ and downward for $x < q$. From an epidemiologic perspective, this implies that for a given value of q, as long as x is larger than q the epidemic spreads, whereas the infection starts to decline as soon as x becomes smaller than the value of q. When $x = q$ the dimensionless number of infected individuals attains its maximum value. It follows that the steady states $(x, 0)$ with $x > q$ are unstable (the second eigenvalue of the linearized system is positive) and approached for $t \to -\infty$, whereas those with $x < q$) are stable (the second eigenvalue of the linearized system is negative) and approached for $t \to +\infty$

The solution trajectories of Eqs (7) and (8) in the (x, y) plane can be calculated by dividing Eqs (7) and (8) term by term, thus obtaining the following differential equation (after separating variables:

$$dy = (q/x - 1)dx \tag{9}$$

to be solved from the generic initial point (x_0, y_0).

The explicit solution is:

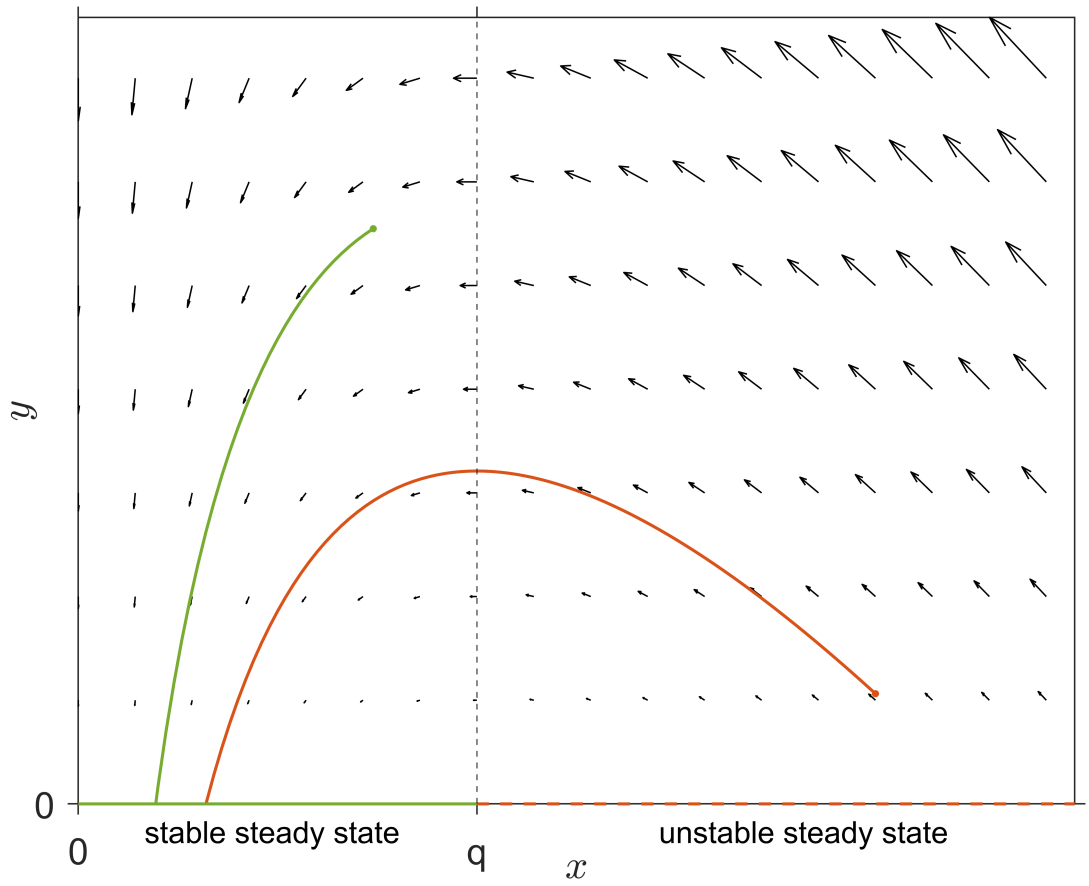
$$y(x) = q \log(x/x_0) - x + x_0 + y_0 \tag{10}$$

These trajectories can easily be plotted for given values of q (possible values are between 0.1 and 10, more likely between 0.3 and 3), and for any value of x_0. It is worth noticing that $y(x)$ is dominated by $\log(x)$ for small values of x, and by $(-x)$ for large values of x. The corresponding Matlab code is for instance:

```
tspan = [0 50];
y0 = [1 0.000001];
[t,y] = ode15s(@sir, tspan, y0);

function dydt = sir(t,y)
q=0.5;
dydt = zeros(2,1);
dydt(1) = -y(1)*y(2);
dydt(2) =(y(1)-q)*y(2);
```

The figure below shows the vector field associated to the system of Eqs (7) and (8) , as well as two trajectories with different initial points. On the horizontal axis stable and unstable steady states are highlighted in green and red, respectively. Note that the $\dot{x} = 0$ nullclines consist of the two axes $y = 0$ and $x = 0$, whilst the $\dot{y} = 0$ nullclines consist of the axis $y = 0$ and of the vertical straight line $x = q$.



Analysis of the epidemic model

Let us now consider the case at hand, namely where we are interested in the spreading of an epidemic and $x_0 = 1$ as to our problem statement. Then Eq. (13) can be written as:

$$y(x) = q\log(x) - x + 1 + y_0 \tag{11}$$

It is easy to see that, as $t \to +\infty$, y approaches 0, and $x \to x_\infty$, which is obtained by solving the following algebraic equation obtained by substituting $y = 0$ in Eq. (11):

$$x_\infty + q\log(x_\infty) = 1 + y_0 \tag{12}$$

The function $y(x)$ reaches its maximum value for $x = q$ (as seen from Eq. (9)) , namely:

$$y_{max} = q\log(q) - q + 1 + y_0 \tag{13}$$

One can easily see (by plotting Eq. (11) for instance) that an epidemic ensues if and only if $q < 1$ (or else if and only if the basic reproduction number, R_0 is larger than 1), because the (dimensionless) number of infectives initially increases. On the contrary an infectious disease does not spread in an epidemic manner if $q > 1$, i.e. if the basic reproduction number, R_0 is smaller than 1.

Let us consider the typical situation where $y_0 \ll 1$, when $q < 1$ as well. The evolution of x and y in time can be approximated in interesting ways. During the early stages of the epidemic, one can then assume that $\dot{x} = 0$ in Eq. (7), and $x \approx 1$. As a consequence, in Eq. (8) $\dot{y} \approx (1 - q)y$ and y exhibits the much debated exponential growth given by $y \approx y_0 \exp((1 - q)t)$. As y increases, x decreases and approaches q, where $y \approx y_{max}$; then in Eq. (7) $\dot{x} \approx -xy_{max}$ and x decays as $x \propto \exp(-y_{max}t)$. Finally, as $x \to x_\infty$, in Eq. (8) $\dot{y} \approx (x_\infty - q)y$ and y exhibits an exponential decay given by $y \propto \exp((x_\infty - q)t)$.

Considering the definition of q, i.e. $q = a/(rS_0)$, one observes that the initial size of the population involved, S_0, is what it is, whereas the rate constant of removal, a, depends on the biological characteristics of the human reaction to the virus, which of course depends on the available therapies. Neither S_0 nor a can be affected by changes in behavior. On the contrary, the value of the rate constant of infection, r, which depends obviously on a number of parameters that are lumped into the parameter r in the simple SIR model, can be reduced through prevention measures, e.g. like those that are recommended in these days by the public health authorities in Switzerland and in other countries affected by the spreading of the new coronavirus.