

Lectures 24-25, Th., Nov. 9 and Tu., Nov. 14

Reading homework: Chapter 7 of reference 1

1. The Kermack-McKendrick model of infectious diseases. When an infectious disease strikes a closed community, the disease often partitions such a community into three categories: individuals that are yet to be infected ($S(t)$ is often used to describe the number of susceptible people at time t), infected individuals (often assumed to be infectious. We will denote this group at time t by $I(t)$), and those recovered and possess (maybe temporary) immunity to or killed by this disease (we will use $R(t)$ to denote this group of individual at time t).

Throughout the history, mankind has suffered many devastating infectious diseases and continues to be fearful of such diseases. In the 1918-1919 influenza pandemic, over 20 million people perished including more than half a million Americans. What puzzles many people is why these diseases often develop suddenly and why many people can escape from them? The simple Kermack-McKendrick model (1927) provided a plausible answer to this intriguing question. The Kermack-McKendrick model is a SIR model proposed to explain the rapid rise and fall in the number of infected patients observed in epidemics such as the plague (London 1665-1666, Bombay 1906) and cholera (London 1865). It assumes that the population size is fixed (i.e., no births, deaths due to disease, or deaths by natural causes, which obviously are very unrealistic), incubation period of the infectious agent is instantaneous (again very unrealistic), and duration of infectivity is same as length of the disease. It also assumes a completely homogeneous population with no age, spatial, or social structure. In other words, it is a bare bone model with many directions for improvement. The Kermack-McKendrick model consists of a system of three coupled nonlinear ordinary differential equations,

$$S' = -\beta SI, \quad I' = \beta SI - \nu I, \quad R' = \nu I. \quad (1.1)$$

Here β is the infection rate, and ν is the recovery rate. The Kermack-McKendrick model was brought back to life by Anderson and May (1979). More complicated versions of the Kermack-McKendrick model that better reflect the actual biology of a given disease are often used.

The key value governing the time evolution of these equations is the so-called epidemiological threshold,

$$R_0 = \beta S(0)/\nu. \quad (1.2)$$

R_0 is defined as the number of secondary infections caused by a single primary infection. It determines the number of people infected by contact with a single infected person before his death or recovery. This number is also referred in literature as basic reproduction (reproductive) ratio, or basic reproduction (reproductive) number. When $R_0 < 1$, each person who contracts the disease will infect fewer than one person before dying or recovering, so the outbreak will die out ($dI/dt < 0$). When $R_0 > 1$, each person who gets the disease will infect more than one person, so the epidemic will spread ($dI/dt > 0$). R_0 is probably the single most important quantity in epidemiology. Note that the result R_0 is dependent on the expression of dI/dt .

The Kermack-McKendrick model has infinitely many steady state on the disease free SR -plane. They take the form of $E^* = (S^*, 0, R^*)$ with $S^* + R^* = N(0) =$

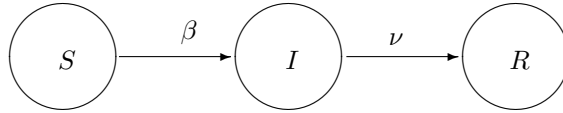


FIG. 1.1. Flow diagram for the Kermack-McKendrick model

$S(0) + I(0) + R(0)$. Observe that once we know S and I , then we can find out R since

$$S + I + R = N(t) \equiv N(0).$$

Hence we can ignore R equation mathematically.

$$S' = -\beta SI, \quad I' = \beta SI - \nu I. \quad (1.3)$$

Clearly the reduced SI -model (1.3) has bounded solution. Since $S(t)$ is strictly decreasing if $I(t) \neq 0$, we see that (1.3) has no nontrivial periodic solutions (you can also apply the Dulac criterion with the Dulac function $1/I$). Hence each solution of (1.3) must approach a disease free steady state $(s^*, 0)$ (dependent on initial condition). Notice that

$$\frac{dI}{dS} = \frac{\beta SI - \nu I}{-\beta SI} = -1 + \frac{\nu}{\beta S}. \quad (1.4)$$

Integrating the above equation yields

$$I = -S + \frac{\nu}{\beta} \ln S + S(0) - \frac{\nu}{\beta} \ln S(0) + I(0). \quad (1.5)$$

Consider the scenario that at the onset of an infectious disease that a given community has a population of $K \gg 1$ and a single infected person (we will think $I(0)$ is almost 0). Then

$$K - \frac{\nu}{\beta} \ln S(0) = S^* - \frac{\nu}{\beta} \ln S^*. \quad (1.6)$$

From this, we obtain that

$$R_0 = \frac{\beta}{\nu} K = \frac{K \ln(S(0)/S^*)}{K - S^*}. \quad (1.7)$$

Observe that the maximum number of infectives at any time is attained when the derivative of I is zero. For the Kermack-McKendrick model (1.1) this happens when $S = \nu/\beta$. Hence the maximum number of infected individuals can be found by substituting S by $\frac{\nu}{\beta}$ in (1.5). That is

$$I_{max} = S(0) + I(0) - \frac{\nu}{\beta} \ln S(0) - \frac{\nu}{\beta} + \frac{\nu}{\beta} \ln \frac{\nu}{\beta}. \quad (1.8)$$

In the rest of this lecture, we consider a slightly more general version of the above Kermack-McKendrick model by assuming there is a loss of the temporary immunity in the removed class. We assume that the rate for the loss of immunity is γ . We arrive at the following model

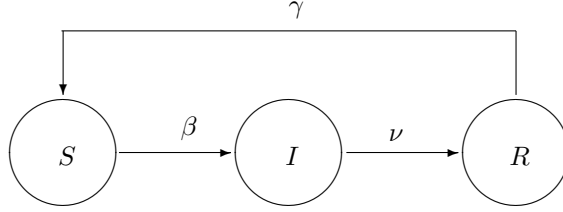


FIG. 1.2. Flow diagram for the modified Kermack-McKendrick model with loss of immunity

$$S' = -\beta SI + \gamma R, \quad I' = \beta SI - \nu I, \quad R' = \nu I - \gamma R. \quad (1.9)$$

This model also possesses the property that the total population N is constant, hence it can be reduced to the following two dimensional system

$$S' = -\beta SI + \gamma(N - S - I), \quad I' = \beta SI - \nu I. \quad (1.10)$$

Local stability analysis was beautifully documented in the text. It is show there that if an endemic equilibrium $E^* = (S^*, i^*), I^* > 0$ exist, then it is locally asymptotically stable. With the Dulac function $1/(SI)$, we can show that (1.10) has no nontrivial periodic solution. Hence we conclude that E^* is globally stable when exists.

Notice that E^* exists if and only if $S^* = \frac{\nu}{\beta} < N(0)$. Therefore the textbook (on page 246, boxed material) claims that in order to have an epidemics, the total population must be larger than a threshold size of $\frac{\nu}{\beta}$. This is a very misleading statement. **Why?** A simple answer is that a more realistic transmission function shall be $\alpha SI/N$ instead of βSI , where α is the maximum contact rate for a infected individual in a unit of time. In other words, $\beta = \alpha/N$. With this understanding of β , we see that $S^* = \frac{\nu}{\beta} < N(0)$ becomes $\frac{\nu}{\alpha} < 1$, which has nothing to do with $N(0)$. A take home message: while constant total population reduces the more plausible proportion function infection rate $\alpha S/N$ to the linear function infection rate βS , it also introduces additional possibility for misinterpretation of mathematical findings.

An infectious disease, almost by definition, will in general have a basic reproduction ratio (number) R_0 larger than 1 in the concerned community. In order to prevent the outbreak of an epidemic in a relatively closed population, it is necessary to reduce the disease's basic reproduction ratio (number) R_0 to a value below one. This can be done in several ways, including forced and self-imposed quarantine, fast detection and treatment, and whole (or almost whole) population immunization. Immunization has the effect of transferring members of the population from the susceptible class to the removed class and thus effectively reducing $S(0)$. If a fraction p of the population is successfully immunized the effect is to replace $S(0)$ by $S(0)(1 - p)$, and thus to reduce the basic reproduction number to $\beta S(0)(1 - p)/\nu = (1 - p)R_0$. To ensure that $(1 - p)R_0 < 1$, we need to have

$$p > 1 - \frac{\nu}{\beta S(0)} = 1 - \frac{1}{R_0}.$$

This relation is associated to the idea of **herd immunity**. Herd immunity describes an type of immunity that occurs when the vaccination of the majority of the population (or herd) provides protection to un-vaccinated individuals.

Vaccination acts as a sort of “firebreak” in the spread of the disease, slowing or preventing further transmission of the disease to others. Although no vaccine offers

100% protection, the spread of disease from person to person is much higher in those who remain unvaccinated. Virologists have found that when a certain percentage of a population is vaccinated, the spread of the disease is effectively stopped. This critical percentage depends on the disease and the vaccine, but 90% is not uncommon. For example, the approximate value of p for measles is 92 and whooping is 94, while for chicken is 90 in US.

Example 1. (This solves exercises 1-3 in reference 1, page 287) A survey of Yale students [Evans (1982), reported by Hethcote(1989)] reported that 91.1 percent were susceptible to influenza at the beginning of the year and 51.4 percent were susceptible at the end of the year.

1) Estimate the value β/ν and basic reproductive number R_0 and decide whether there was an epidemic.

Solution: For simplicity, we can assume that there are $K = 1000$ students in Yale in that period. We have $S(0) = 911$ and $S^* = 514$. Hence

$$\frac{\beta}{\nu} = \frac{\ln(S(0)/S^*)}{K - S^*} = 0.001484.$$

Hence

$$R_0 = S(0)\frac{\beta}{\nu} = 1.35 > 1.$$

Therefore, there is an epidemic.

2) What fraction of Yale students would have had to be immunized to prevent an epidemic?

Solution: The fraction $p = 1 - 1/R_0 = 0.26$.

3) What was the maximum number of Yale students suffering from influenza at any time?

Solution: $I_{max} = S(0) + I(0) - \frac{\nu}{\beta} \ln S(0) - \frac{\nu}{\beta} - \frac{\nu}{\beta} \ln \frac{\nu}{\beta} = 33.92$, or about 3.4%.