Steven R. Dunbar
Department of Mathematics
203 Avery Hall
University of Nebraska-Lincoln
Lincoln, NE 68588-0130
http://www.math.unl.edu
Voice: 402-472-3731
Fax: 402-472-8466

Topics in Probability Theory and Stochastic Processes Steven R. Dunbar

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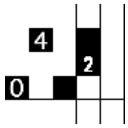
Markov Chain Epidemic Models



Rating

Mathematically Mature: may contain mathematics beyond calculus with proofs.

Section Starter Question

Suppose a single person in a population of S susceptible individuals has a communicable disease. What is a simple probabilistic model of how this person could infect some number of people in a given time interval?

Key Concepts

1. Markov chain **Susceptible-Infected-Removed (SIR) models**. have a population and a disease which infects members of the population for a fixed amount of time, after which we consider them to be removed, in the sense that each one is no longer susceptible and cannot become infected again.

2. The **Greenwood Model** assumes the number of Infectives in generation t is a binomial random variable with parameters S_t and infection success constant p, not depending on the number of Infectives.

3. For the Greenwood model

$$\mathbb{E}\left[S_t \mid S_0 = s_0\right] = (1-p)^t s_0,$$
$$\mathbb{E}\left[I_t \mid S_0 = s_0\right] = p(1-p)^{t-1} s_0.$$

4. The **Reed-Frost model** includes an infective size dependency that the Greenwood model lacks.

5. In comparison to the Greenwood model, the Reed-Frost model gives a higher probability to more new Infectives at generation $t+1$ if there are already a large number Infectives at generation t than if there is only a small population of Infectives. The Reed-Frost model has a positive feedback effect on infectives.

6. Under some common asymptotic assumptions, is, the number of Infectives is the result of a Galton-Watson process or branching process.

Then from the standard theory for branching processes, the epidemic is *subcritical* if $\lambda \leq 1$ and *supercritical* if $\lambda > 1$.

Vocabulary

1. Markov chain **Susceptible-Infected-Removed (SIR) models**. have a population and a disease which infects members of the population for a fixed amount of time, after which we consider them to be removed, in the sense that each one is no longer susceptible and cannot become infected again.

2. The **Greenwood Model** assumes the number of Infectives in generation t is a binomial random variable with parameters S_t and infection success constant p, not depending on the number of Infectives.

3. The **Reed-Frost model** includes an infective size dependency which the Greenwood model lacks.

4. Define the **extinction time τ of an epidemic** to be the generation at which i_t is first zero.

5. The **total damage** of the epidemic is $K = \sum_{j=0}^{\tau} i_j$

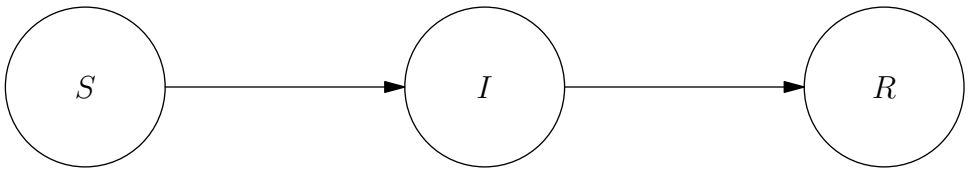


Figure 1: Schematic class diagram for the simple Susceptible-Infective-Removed epidemic model illustrating the classes of the epidemic and the movement from class to class and not the state transitions of the Markov chain.

Mathematical Ideas

Introduction

This section is an introduction to elementary Markov chain **Susceptible-Infected-Removed (SIR) models**. These Markov chains model a population and a disease that infects members of the population for a fixed amount of time, after which we consider them to be removed, in the sense that they are no longer susceptible and cannot become infected again. The removed class includes individuals who are no longer either susceptible either because of recovery and subsequent immunity or because of death. That is, after members of the population have been infected for one time "unit", we will no longer be concerned with them, as they cannot infect anyone else, nor can they become infected again. Therefore only two classes need to be considered, the Susceptibles and the Infectives. Figure 1 shows the movement between the classes.

Markov chain models use discrete time and a discrete state space. The discrete time will be in units of the infectivity period of the disease. Typically this unit time is about 7-8 days for measles, and about 7-9 days for influenza. Call each of these unit time periods a generation, enumerated by the integer variable t. (This is a slight change from the usual notation for discrete time Markov chains using indices i or j for the discrete time. Using t avoids confusion with the number of Infectives.) The infectivity period may either be distinct from, or overlap, the period when the infected person shows symptoms of the disease. The incubation period which is the period between infection and onset of symptoms, and the latent period, the time from infection to infectiousness are different from the infectivity period. Figure 2 illustrates one possible configuration of these disease periods. The states will

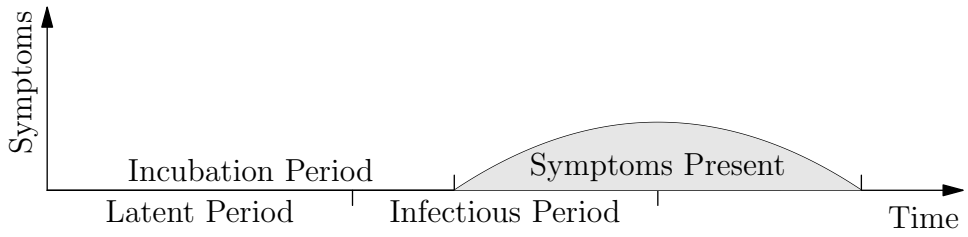


Figure 2: Possible relation of disease stages or periods.

be the number of Susceptibles and Infectives in a homogeneous and well-mixed population. Assume the epidemic takes place over a short enough time interval that the population is a constant value N, that is, assume no births and no emigration or immigration. So it is enough to consider only Susceptibles and Infectives since the number of individuals in the Removed class is determined from the other two.

To keep track of each group, denote the number of Susceptibles at generation t by S_t, and the number of Infectives at generation t by I_t. These random variables may achieve any integer value such that $S_t + I_t$ is in the population range.

A natural first question for any epidemic model is the probability of having I_{t+1} Infectives at generation $t+1$. In asking this question at generation t, assume we know the number of Susceptibles and Infectives at every generation up to t. Since the model is expressed in time units of infectivity periods where individuals move from one class to another, the main focus is on the number of Infectives at generation t, ignoring the past, also keeping track of the Susceptibles. Then the model is a first-order Markov process through the states S_t, I_t with $S_t + I_t \leq N$. If the population is N, the number of states is $N(N+1)/2$ so this is a Markov chain with many states.

Greenwood Model

The **Greenwood Model** assumes the number of Infectives in generation t is a binomial random variable with parameters S_t and infection success constant p, not depending on the number of Infectives

$$\mathbb{P}\left[I_{t+1} = i_{t+1} \mid S_0 = s_0, I_0 = i_0, \ldots, S_t = s_t, I_t = i_t\right] =$$
$$\mathbb{P}\left[I_{t+1} = i_{t+1} \mid S_t = s_t, I_t = i_t\right] = \binom{s_t}{i_{t+1}} p^{i_{t+1}} (1-p)^{s_t - i_t}.$$

The first equality represents the first-order Markov chain assumption. Consider the second equality in further detail. At generation t we have s_t Susceptibles. To find the probability that i_{t+1} members of this group become Infectives, choose i_t of the Susceptibles who will become infected. Similarly p is the probability that a given Susceptible will become infected in one generation. Thus the probability i_{t+1} Susceptibles become Infectives is $p^{i_{t+1}}$. Note that a Susceptible becoming Infective is a "success" (for the disease, not the population) in the binomial random variable sense. Remaining a Susceptible is a failure in the binomial sense. The transition for the Susceptibles is

$$S_{t+1} = S_t - I_{t+1}.$$

Because I_{t+1} is a binomial random variable

$$E[I_{t+1} \mid S_t] = pS_t.$$

This expression gives us the expected number of Infectives at generation $t+1$ given the number of Susceptibles at generation t. Extend this idea to say

$$\mathbb{E}\left[S_{t+1} \mid S_t\right] = \mathbb{E}\left[S_t\right] - \mathbb{E}\left[I_{t+1}\right] = (1-p)S_t.$$

By induction

$$\mathbb{E}\left[S_t \mid S_0 = s_0\right] = (1-p)^t s_0,$$
$$\mathbb{E}\left[I_t \mid S_0 = s_0\right] = p(1-p)^{t-1} s_0.$$

Reed-Frost Model

The Reed–Frost model is an SIR mathematical model of epidemics created in the 1920s by Lowell Reed and Wade Hampton Frost at Johns Hopkins University. Originally presented in a talk by Frost in 1928 and used in courses at Hopkins for two decades, the mathematical formulation was not published until the 1950s.

The Greenwood model has a fixed probability of infection, independent of the number of Infectives at the current generation step. The **Reed-Frost model** includes an infective size dependency which the Greenwood model lacks. The Reed–Frost model is based on the following assumptions:

1. The infection is spread directly from Infectives to Susceptibles by a certain type of contact (termed "adequate contact") and in no other way.

2. Any Susceptible in the group, after such contact with an Infective in a given generation, will develop the infection and will be infectious to others only within the following generation period; in subsequent generation periods, the individual is wholly and permanently immune and moves to the Removed class.

3. Each individual has a fixed probability p of coming into adequate contact with any other specified individual in the group within one time interval, and this probability is the same for every member of the group.

4. The individuals are wholly segregated from others outside the group. (It is a closed population with no births, immigration or emigration.)

5. These conditions stay constant during the epidemic.

Set the following initial parameters:

- size of the population N,
- number of individuals already immune, typically 0,
- number of Infective cases, usually set at 1,
- probability p of adequate contact.

If p is the probability of a given Susceptible *making adequate contact* with 1 specific Infective, then $q = 1 - p$ is the probability of *avoiding* contact with that infective. Make the (vastly simplifying and probably unjustified) assumption that all interactions of the Susceptible with all Infectives are independent events. Then q^{i_t} is the probability the given Susceptible at generation t avoids adequate contact at generation t from *all* Infectives in the population at that generation and remains Susceptible at generation $t+1$.

This is a failure for the epidemic in the binomial random variable sense. The probability of a Susceptible being infected is then $(1 - q^{i_t})$, a success for the epidemic. Then as a binomial random variable, the probability of the number of Infectives in the next generation is

$$\mathbb{P}\left[I_{t+1} = i_{t+1} \mid S_t = s_t, I_t = i_t\right] = \binom{s_t}{i_{t+1}} \left(1 - (1 - q^{i_t})\right)^{i_{t+1}} \left(q^{i_t}\right)^{s_t - i_t}$$

and $S_{t+1} = S_t - I_{t+1}$. In comparison to the Greenwood model, the Reed-Frost model gives a higher probability to more new Infectives at generation $t + 1$ if there are already a large number Infectives at generation t than if there is only a small population of Infectives. The Reed-Frost model has a positive feedback effect on infectives.

A success for the epidemic is a failure for the Susceptibles and a failure for the epidemic is a success for the Susceptibles. Then an alternative expression for the Reed-Frost model is

$$\mathbb{P}\left[S_{t+1} = s_{t+1} \mid S_t = s_t, I_t = i_t\right] = \binom{s_t}{i_{t+1}} \left(q^{i_t}\right)^{i_{t+1}} \left(1 - q^{i_t}\right)^{s_t - i_t}$$

and $S_{t+1} = S_t - S_{t+1}$.

Define the **extinction time τ of an epidemic** to be the generation at which i_t is first zero. This is an absorbing state for the Markov Chain. Note that if the number of Susceptibles becomes 0 in a generation t, then $i_{t+1} = 0$. Of more interest is the probability $S_\tau > 0$ and $I_\tau = 0$. Consider an epidemic for which the Infectives have progressed to extinction $i_1, i_2, \ldots, i_{\tau-1}, i_\tau = 0$. Note that $i_{\tau-1} > 0$. Thus

$$\begin{aligned}\mathbb{P}\left[I_1 = i_1, \ldots, I_k = i_k, I_{k+1} = 0 \mid S_0 = n, I_0 = m\right] = \\ \mathbb{P}\left[I_1 = i_1 \mid S_0 = n, I_0 = m\right] \times \mathbb{P}\left[I_2 = i_2 \mid S_1 = n - i_1, I_1 = i_1\right] \times \cdots \times \\ \mathbb{P}\left[I_\tau = 0 \mid S_{\tau-1} = s_{\tau-1}, I_{\tau-1} = i_{\tau-1}\right].\end{aligned}$$

In this specific epidemic, the **total damage** of the epidemic is $K = \sum_{j=0}^{\tau} I_j$. As K is the sum of I_i's, we can treat it as a random variable. Thus consider:

$$\mathbb{P}\left[K = k \mid S_0 = n, I_0 = m\right] = \sum_{\vec{i}:||\vec{i}=k} \mathbb{P}\left[I_1 = i_1, \ldots, I_\tau = 0 \mid S_0 = n, I_0 = m\right].$$

Some common asymptotics apply here. Let $m = i_0 = o(n)$ and suppose $q = \mathrm{e}^{-\lambda/n}$ so $p = 1 - q = O(n^{-1})$ and the expected number of adequate

contacts q^{it} is approximately constant. At the beginning of the epidemic, using the first formulation of the Reed-Frost model

$$\begin{aligned}\mathbb{P}\left[I_{t+1}\right] &= \text{Bin}(S_t, 1 - \mathrm{e}^{-\lambda I_t/n}) \\ &\approx \text{Bin}(n, \lambda I_t/n) \\ &\approx \text{Poisson}(\lambda I_t)\end{aligned}$$

This means I_{t+1} is the sum of I_t independent Poisson random variables with parameter λ. That is, the number of Infectives is the result of a Galton-Watson process or branching process. Then from the standard theory for branching processes, the epidemic is *subcritical* if $\lambda \leq 1$ and *supercritical* if $\lambda > 1$. That is, the trajectories of this process either die out or explode in an exponential way, at least at the beginning of the epidemic while the asymptotic assumptions hold. This points to more general stochastic process models of epidemics as branching processes. Although the epidemic models are Markov chains, the tools of branching processes are more applicable and yield more detailed results.

Limitations

Both of these models assume a homogeneous population, i.e. everyone is equally likely to get sick assuming the same exposure. Also the Reed-Frost model assumes that the population mixes perfectly, that is, every Susceptible interacts with every Infective and thus has an equally likely chance to get sick from each one. Both models assume independence in these interactions. These assumptions apply best to a moderately-sized (reasonably) closed situations such as a dormitory, a nursing home under quarantine, a cruise ship, a factory, or perhaps a small town.

For large populations such as a city or an entire country, the assumptions of homogeneous population and perfect mixing don't apply. Also for large populations, direct calculation of the binomial coefficients at each stage is inconvenient, and so using continuum limits is appropriate, leading to differential equation epidemic models. However, one advantage of the stochastic process models is the possibility of obtaining a distribution for the extinction times. This is a more realistic property than the asymptotic extinction time given by a deterministic model.

More detailed models have multiple health and infection classes instead of just Infectives. More detailed models may also cross these with factors

influencing mixing, such as age, social class, or geographical location. The mathematical modeling of epidemics has a huge literature, the references below are a starting point.

Section Ending Answer

One particularly simple model is that the infective transmits the disease to a fixed number of susceptibles, this is not probabilistic. A probabilistic model is that the infective transmits to each susceptible with probability p, leading to the binomial probability distribution of the Greenwood model. A third possibility is that the number of infected is a Poisson random variable with parameter λ. This would be appropriate if the population is large and the transmission rate is constant across various size groups of susceptibles.

Sources

Details of the Greenwood and Reed-Frost models are adapted from "Criticality in Epidemic Models" by R. Dolgoarshinnykh, [1]. Comments on epidemics as branching processes and more detailed assumptions for epidemics are from "Branching Processes: Their Role in Epidemiology", by C. Jacob, [2]. See also [3] for a survey of mathematical models of infectious diseases. The exercise is adapted from the Ohio Supercomputer Center Summer Institute, Reed-Frost Epidemic Model.

Algorithms, Scripts, Simulations

Algorithm

Epidemic models

Comment Post: Simulation of epidemics with Greenwood and Reed Frost models

1 Set initial Susceptibles, Infectives, probability, time
2 Loop over time
3 Get random binomial variate from number of Susceptibles
4 Update the infectives
5 **return** Plot of Susceptibles, Infectives versus time.

Scripts

R R script for Greenwood model.

```
S0 <- 999
I0 <- 1
p  <- 0.2

T <- 30
S <- numeric(T + 1)
I <- numeric(T + 1)

S[1]  <- S0
I[1]  <- I0
for (t in 2:(T + 1)) {
    I[t]  <- rbinom(1, size=S[t-1], prob=p)
    S[t] <-  S[t - 1] - I[t]
}

plot(1:(T + 1), S, col="blue",
     xlim = c(0, (T + 1)), ylim=c(0, (S0 + I0)),
     main="Greenwood Epidemic Model",
     xlab="Time", ylab="S, I")
points(1:(T + 1), y=I, col="red")
```

R script for Reed-Frost model.

```
S0 <- 9999
I0 <- 1
p  <- 0.00001
```

```
q  <- 1 - p

T <- 25
S <- numeric(T + 1)
I <- numeric(T + 1)

S[1]  <- S0
I[1]  <- I0
for (t in 2:(T + 1)) {
    QT = q^I[t-1]
    I[t]  <- rbinom(1, size=S[t-1], prob=1-QT)
    S[t] <-  S[t - 1] - I[t]
}

plot(1:(T + 1), S, col="blue",
     xlim = c(0, (T + 1)), ylim=c(0, (S0 + I0)),
     main="Reed-Frost Epidemic Model",
     xlab="Time", ylab="S, I")
points(1:(T + 1), y=I, col="red")
```

Problems to Work for Understanding

1: Write a script that simulates a place-based epidemic model. For this modification, assume that all the individuals are standing next to each other on a two-dimensional grid. Let one individual be an infective case. An infective can now probabilistically infect only his immediate neighbors on the grid. In the next time period, those people who got sick now have a chance to infect their neighbors and so on. Display on a two-dimensional grid that shows all the individuals what state they are in (i.e., Susceptible, Infective, or Recovered), with an animation if possible. Run the script many times with different input parameters. How does the pattern of the epidemic flow change with affective contact probability?

Reading Suggestion:

References

[1] Regina Dolgoarshinnykh. Criticality in epidemic models. accessed April 17, 2020.

[2] Christine Jacob. Branching processes: their role in epidemiology. *Int J Environ Res Public Health*, 7(3):1186–1204, March 2010.

[3] Constantinos I. Siettos and Lucia Russo. Mathematical modeling of infectious disease dynamics. *Virulence*, 4(4):295–304, May 2013.

Outside Readings and Links:

1. *Introduction to Probability*, Grinstead and Snell. Chapter 11 - Markov Chains -
   http://tinyurl.com/qw6sa

2. Generalized Markov Models of Infectious Disease Spread

3. Criticality in Epidemic Models

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Steve Dunbar's Home Page, `http://www.math.unl.edu/~sdunbar1`

Email to Steve Dunbar, `sdunbar1 at unl dot edu`

Last modified: Processed from LaTeX source on November 16, 2020