Suggested Exercises and Projects

Exercises

1. A survey of Yale University freshmen in 1982 about an influenza outbreak reported that 91.1% were susceptible to influenza at the beginning of the year and 51.4% were susceptible at the end of the year. Assume that the mean infective period is approximately 3 days.

   (a) Estimate the basic reproduction number and decide whether there was an epidemic.
   (b) What fraction of Yale students in Exercise (a) would have had to be immunized to prevent an epidemic?
   (c) What was the maximum number of Yale students in Exercises (a) and (b) suffering from influenza at any time?

2. A disease is introduced by two visitors into a town with 1,200 inhabitants. An average infective is in contact with 0.4 inhabitant per day. The average duration of the infective period is 6 days, and recovered infectives are immune against reinfection. How many inhabitants would have to be immunized to avoid an epidemic?

3. A disease begins to spread in a population of 800. The infective period has an average duration of 14 days and an average infective is in contact with 0.1 person per day. What is the basic reproduction number? To what level must the average rate of contact be reduced so that the disease will die out?

4. An epidemic of a communicable disease that does not cause death but from which infectives do not recover may be modeled by the pair of differential equations

$$S' = -\beta SI, \quad I' = \beta SI.$$

Show that in a population of fixed size K such a disease will eventually spread to the entire population.

5. If a fraction λ of the population susceptible to a disease that provides immunity against reinfection moves out of the region of an epidemic, the situation may be modeled by a system

$$S' = -\beta SI - \lambda S, \quad I' = \beta SI - \alpha I.$$

Show that both S and I approach zero as $t \to \infty$.

6. Compare the qualitative behaviors of the models

$$S' = -\beta SI, \quad I' = \beta SI - \alpha I,$$

and

$$S' = -\beta SI, \quad E' = \beta SI - \kappa E, \quad I' = \kappa E - \alpha I,$$

with

$$\beta = 1/3,000, \quad \alpha = 1/6, \quad \kappa = 1/2, \quad S(0) = 999, \quad I(0) = 1.$$

These models represent an SIR epidemic model and an $SEIR$ epidemic model respectively with a mean infective period of 6 days and a mean exposed period of 2 days. Do numerical simulations to decide whether the exposed period noticeably affects the behavior of the model.

7. To the models in the previous exercise add a constant birth rate of 100/7 births per year and a constant death rate of 1/70 per year. Compare the behaviors of these models with each other and with the models of the previous exercise.

8. Consider the usual SEIR model

$$\begin{aligned} S' &= \Pi - \mu S - \beta SI, \\ E' &= \beta SI - (\mu + \kappa)E, \\ I' &= \kappa E - (\mu + \alpha)I, \\ R' &= \alpha I - \mu R, \end{aligned}$$

where individuals progress from compartment E to I at a rate κ and develop immunity at a rate α, natural mortality claims individuals at a rate μ, and there is a constant recruitment, Π, of susceptible individuals. The basic reproduction number $\mathcal{R}_0$ is calculated as $\mathcal{R}_0 = \frac{\kappa\beta\Pi/\mu}{(\mu+\kappa)(\mu+\alpha)}$, where $S_0 = \Pi/\mu$.

(a) Interpret the above formula for the basic reproduction number.
(b) Verify that the disease-free equilibrium is (locally asymptotically) stable for $\mathcal{R}_0 < 1$ and unstable for $\mathcal{R}_0 > 1$.

(c) Include disease induced death in the above model and compute the basic reproduction number.

9. Consider a model for a disease that confers only temporary immunity after recovery, so that recovered individuals lose their immunity at a per capita rate of c (per time unit). Formulate a model to describe such a disease and analyze its qualitative behavior. Is there a threshold condition for this SIRS model?

10. European fox rabies is estimated to have a transmission coefficient β of 80 km^2 years/fox and an average infective period of 5 days. There is a critical carrying capacity K_c measured in foxes per km^2, such that in regions with fox density less than K_c rabies tends to die out while in regions with fox density greater than K_c rabies tends to persist. Estimate K_c. [Remark: It has been suggested in Great Britain that hunting to reduce the density of foxes below the critical carrying capacity would be a way to control the spread of rabies.]

11. Consider a disease spread by carriers who transmit the disease without exhibiting symptoms themselves. Let $C(t)$ be the number of carriers and suppose that carriers are identified and isolated from contact with others at a constant per capita rate α, so that $C' = -\alpha C$. The rate at which susceptibles become infected is proportional to the number of carriers and to the number of susceptibles, so that $S' = -\beta SC$. Let C_0 and S_0 be the number of carriers and susceptibles, respectively, at time $t = 0$.

    (a) Determine the number of carriers at time t from the first equation.
    (b) Substitute the solution to part (a) into the second equation and determine the number of susceptibles at time t.
    (c) Find $\lim_{t\to\infty} S(t)$, the number of members of the population who escape the disease.

12. In this exercise, the expected duration of an epidemic is calculated for different values of the population size N and the basic reproduction number $\mathcal{R}_0$ in the CTMC SIS epidemic model.

    (a) Let the population size $N = 25$, contact rate $\beta = 1$, and birth and recovery rates $b = 1/4 = \gamma$, so that $\mathcal{R}_0 = 2$ in the CTMC SIS epidemic model. Calculate the expected duration $\tau_k = E(T_k)$, $k = 1, \ldots, N$, i.e., $\tau = -D^{-1}\mathbf{1}$, where $\tau = (\tau_1, \ldots, \tau_N)^T$. Then sketch a graph of τ_k for $k = 1, \ldots, N$. Maple, MATLAB or other software may be useful in solving the linear system.
    (b) Use the mean τ computed in part (a) to find the second moment $\tau_k^2 = E(T_k^2)$, $k = 1, \ldots, N$ ($\tau^2 = -D^{-1}\tau$). Then compute the variance in the time to extinction, $\sigma_k^2 = \tau_k^2 - (\tau_k)^2$.

(c) Let $b = 1/2 = \gamma$ so that $\mathcal{R}_0 = \beta$. Calculate the expected duration $\tau_k = E(T_k)$ for different values of the contact rate β and the population size N. Suppose time units are expressed in terms of days. Give the value of τ_N in terms of months or years (whatever unit is appropriate). What happens to τ_N as β increases? as N increases?

13. In this exercise, the approximate quasistationary distribution for the infected population is computed for the CTMC SIS epidemic model and compared to the equilibrium solution of the deterministic model. Assume the approximate quasistationary distribution satisfies

$$p^1_{i+1} = \frac{b(i)}{d(i+1)} p^1_i,$$

where $\sum_{i=1}^{N} p^1_i = 1$, $b(i) = \beta i(N-i)/N$, and $d(i) = (b+\gamma)i$.

(a) Let the population size $N = 50$, contact rate $\beta = 1$, and birth and recovery rates $b = 1/4 = \gamma$. First find the equilibrium solution for I in the deterministic SIS epidemic model. Then find the approximate quasistationary distribution, p^1. Graph p^1 and compute its mean value. How does the mean value compare to the equilibrium solution?

(b) Let $b = 1/2 = \gamma$ so that $\mathcal{R}_0 = \beta$. Choose different values for N and β. For each choice of N and β compute the equilibrium solution for I in the determinstic SIS epidemic model and the approximate quasistationary distribution for the CTMC SIS epidemic model. How do the equilibrium solutions and the mean of the quasistationary distributions compare for different values of N and β?

14. In this exercise, sample paths for the Itô SDE SIS epidemic model are computed and compared to the equilibrium solution of the deterministic model.

(a) Write a computer program for the Itô SDE SIS epidemic model using Euler's method with $\Delta t = 0.01$, population size $N = 100$, contact rate $\beta = 2$, birth and recovery rates $b = 1/2 = \gamma$, and initial number of infected individuals $I(0) = 1$. Graph three sample paths of the Itô SDE for $t \in [0, 20]$. Then graph three sample paths for the same parameter values but for $I(0) = 5$.

(b) Graph the mean of 1,000 sample paths for the two different sets of parameter values in part (a). How do your results for the mean compare with the equilibrium solution of the deterministic model?

Projects

These suggested projects are taken in part from the recent book "A Course in Mathematical Biology: Quantitative Modeling with Mathematical and Computational Methods" by Gerda de Vries, Thomas Hillen, Mark Lewis, Johannes Müller, and Birgit Schönfisch, Mathematical Modeling and Computation 12, SIAM, Philadelphia (2006).

1 Cholera

The cholera virus, *Vibric cholerae*, is present in brackish water through algae blossom and through human faeces. Not every infection leads to sickness. Only 10–20% of infected individuals suffer from severe symptoms. Many do not show symptoms at all but their faeces are infectious. Cholera is a serious disease since the progress of symptoms can be very fast if not treated.

Large outbreaks are usually related to contaminated water. There are four major control mechanisms, which are recommended by the WHO: hygienic disposal of human faeces, adequate supply of safe drinking water, good food hygiene and cooking, washing hands after defecation and before meals. More information about this disease, control mechanisms and vaccination can be found at the WHO Web sites (www.who.int).

Develop a model for an outbreak of cholera:

1. Model the epidemic first without any control mechanism.
2. Extend your model to include the above control mechanisms and estimate which is most effective.

2 Ebola

The Ebola virus erupts occasionally in Africa. Ebola causes hemorrhaging and death in humans after about 10 days, and people in contact with infectives can be infected. Quarantine (isolation) of patients is an effective control procedure for Ebola. Develop a model for the spread of Ebola that includes quarantine of a fraction of the patients.

3 Gonorrhea

Gonorrhea is a sexually transmitted disease caused by a gonococcus bacteria. Assume that it is spread from women to men and from men to women.

Recovery from gonorrhea does not confer immunity. Formulate a model for gonorrhea with heterosexual transmission. How would you change your model to include consistent condom use by a fraction of the population?

4 HIV/AIDS

The human immunodeficiency virus (HIV), which is the etiological agent for acquired immunodeficiency syndrome (AIDS), emerged in 1981 and has become an important sexually-transmitted disease throughout the world. The two main components of transmission are needle sharing among injecting drug users, and prostitution.

1. In the absence of intervention methods or changes in social behavior, what is the expected size of the HIV epidemic, either as peak, final size or endemic level?
2. Some locations offer free needle exchange, so that injecting drug users can get clean needles. What effect would a needle-exchange program have on your model?

5 HIV in Cuba

In the article "A non-linear model for a sexually transmitted disease with contact tracing" by H. De Arazoza and R. Lounes in the IMA Journal of Mathematical Medicine and Biology, 19 (2002), pp. 221–234, we find the following data about HIV-positives, AIDS outbreak and death cases caused by AIDS from 1986 until 1997 in Cuba.

Year	HIV-cases	AIDS-cases	Death through AIDS
1986	99	5	2
1987	75	11	4
1988	93	14	6
1989	121	13	5
1990	140	28	23
1991	183	37	17
1992	175	71	32
1993	102	82	59
1994	122	102	62
1995	124	116	80
1996	234	99	92
1997	364	121	99
1998	362	150	98
1999	493	176	122
2000	545	251	142

Design a model which describes the epidemic spread of HIV after 1997 in Cuba and fit the above data. Which are the relevant parameters of your model? Try to introduce control mechanisms to lower the number of AIDS cases. Compare your control mechanism with the data of the given time period.

6 Human Papalonoma Virus

According to the Health Canada Web site (www.hc-sc.gc.ca), "HPV is likely one of the most common sexually transmitted infections (STIs) in Canada". Several types of HPV are know to circulate in the population. Some types lead to genital warts, while others lead to cancers. The virus is often asymptomatic and can switch between active and inactive states. Develop a model for HPV transmission. Include vaccination in you model, and use your model to estimate the fraction of the population that would need to be effectively vaccinated to control the disease.

7 Influenza

The recent rapid spread of avian influenza and the potential for the emergence of a pandemic strain of the virus are concerns of governments worldwide. Current influenza vaccines will most likely provide little protection against a shift in the virus, and the main control methods are antiviral treatments, quarantine and isolation.

1. Assuming a significant shift does occur, what is the expected size of an outbreak?
2. Would quarantine and isolation be as effective with influenza as they were with SARS?
3. How many doses of antivirals would be needed to control an epidemic in the Greater Toronto area?

8 Malaria

Now that mosquitoes are resistant to DDT, malaria has reemerged in many areas and is spreading into new regions as temperature changes occur. Malaria spreads from infected mosquitoes (the vector) to humans (the host) by biting, and susceptible mosquitoes can be infected when they bite an infected human. Humans can recover from malaria, but infected mosquitoes remain infected for their lifetime.

1. In the absence of intervention methods or change in social behavior, what is the expected size of the malaria burden, either as peak, final size or endemic level?
2. How effective could bednets be at reducing the cost of malaria?

9 Measles

Measles is no longer endemic in Canada, although small, isolated outbreaks can still occur among unvaccinated groups. Worldwide, an estimated 30 million infections occur each year with over 500,000 deaths in 2003 (www.hc-sc.gc.ca). Develop a model for measles transmission in Canada and estimate the fraction of the population that must remain vaccinated to maintain Canada's "herd immunity". Extend your model to a two patch model, with one patch vaccinated and one unvaccinated. How does travel between the two patches influence the dynamics in the vaccinated patch?

10 Poliomyelitis (Polio)

Polio is spread by a wild enteric coxackie virus and can cause paralysis in some people. The polio vaccine virus interferes with binding of the wild virus by filling the attachment site. Thus the vaccine virus interferes with the wild virus in the sense that a person cannot have both. Recovery from a polio infection gives immunity.

Most cases of polio are asymptomatic, but a small fraction of cases result in paralysis. In the 1950s in the United States, there were about 60,000 paralytic polio cases per year. In 1955 Jonas Salk developed an injectable polio vaccine from an inactivated polio virus. This vaccine provides protection for the person, but the person can still harbor live viruses in their intestines and can pass them to others. In 1961 Albert Sabin developed an oral polio vaccine from weakened strains of the polio virus. This vaccine provokes a powerful immune response, so the person cannot harbor the "wild-type" polio viruses, but a very small fraction (about one in 2 million) of those receiving the oral vaccine develop paralytic polio. The Salk vaccine interrupted polio transmission and the Sabin vaccine eliminated polio epidemics in the United States, so there have been no indigenous cases of naturally-occurring polio since 1979. In order to eliminate the few cases of vaccine-related paralytic polio each year, the United States now recommends the Salk injectable vaccine for the first four polio vaccinations, even though it is more expensive. In the Americas, the last case of paralytic polio caused by the wild virus was in Peru in 1991. In 1988 WHO set a goal of global polio eradication by the year 2000. Most countries are using the live-attenuated Sabin vaccine,

because it is inexpensive (8 cents per dose) and can be easily administered into a mouth by an untrained volunteer. The WHO strategy includes routine vaccination, National Immunization Days (during which many people in a country or region are vaccinated in order to interrupt transmission), mopping-up vaccinations, and surveillance for acute flaccid paralysis. Polio has disappeared from many countries in the past 10 years, so that by 1999 it is concentrated in the Eastern Mediterranean region, South Asia, West Africa and Central Africa. It is likely that polio will be eradicated worldwide soon. WHO estimates that eradicating polio will save about $1.5 billion each year in immunization, treatment, and rehabilitation around the globe.

Formulate a model for polio with the wild and vaccine virus competing for the attachment site. How would your model be changed if the vaccine virus were transmissible?

11 Severe Acute Respiratory Syndrome (SARS)

Detailed data on the day-to-day probable and suspect cases for 2002–2003 Severe Acute Respiratory Syndrome (SARS) are given at

http://www.hc-sc.gc.ca/pphb-dgspsp/sars-sras/cn-cc/index.html.

Go to this Web site, and see what data were recorded there.

Construct a model that can be used to determine the number of new SARS cases, SARS deaths, and SARS recoveries each day. Initially assume that there is no quarantining of SARS patients, and that there are no measures taken to reduce the likelihood of infection from one individual to another. One key disease control goal was to eradicate the outbreak of SARS through quarantining and preventative measures. Assess the effectiveness of these control measures on the disease dynamics.

12 Smallpox

An outbreak of smallpox in Abakaliki in southeastern Nigeria in 1967 has been reported by Bailey and Thomas. People living there belong to a religious group that is quite isolated and declines vaccination. Overall there were 30 cases of infection in a population of 120 individuals. The time (in days) between newly reported pox-cases is given in the following sequence:

$$13, 7, 2, 3, 0, 0, 1, 4, 5, 3, 2, 0, 2, 0, 5, 3, 1, 4, 0, 1, 1, 1, 2, 0, 1, 5, 0, 5, 5$$

Develop a model which describes these data and analyze the epidemic outbreak.

13 Tuberculosis

Worldwide, tuberculosis (TB) accounts for more deaths than all other diseases combined. The standard treatment for active tuberculosis is to give multiple drugs for at least 6 months. This therapy is effective if the person has drug-sensitive TB. Drug resistant strains of TB emerge when people do not complete the treatment.

1. Formulate a model for TB with drug-sensitive and drug-resistant strains of TB.
2. How would your model be changed to include improved compliance with drug therapy?

14 West Nile Virus

The West Nile virus is a vector born disease that has been found in over 150 bird species in North America. The virus is transmitted from bird to bird by mosquitoes. Bites by infected mosquitoes can also lead to infection in humans and other mammals. Develop a model of West Nile virus transmission between birds, mosquitoes and humans. What factors have the highest influence on the prevalence of the virus in the mosquito population? Currently, the West Nile virus season runs from April through September in Canada. Would you expect the prevalence of the virus in the mosquito population to increase as a result of global warming?

15 Yellow Fever in Senegal 2002

Yellow fever (YF) is a viral hoemorrhagic fever transmitted by infected mosquitoes. Yellow fever is spread into human populations in three stages:

1. *Sylvatic (or jungle).* YF occurs in tropical rain forests where mosquitoes, which feed on infected monkeys, pass the virus to humans who work in the forest.
2. *Intermediate.* YF occurs as infected individuals bring the disease into rural villages, where it is spread by mosquitoes amongst humans (and also monkeys).
3. *Urban.* YF occurs as soon as an infected individual enters urban areas. This can lead to an explosive epidemic in densely inhabited regions. Domestic mosquitoes carry the virus from person to person.

The epidemic can be controlled by vaccination. YF vaccine is safe and effective and provides immunity within 1 week in 95% of those vaccinated.

Below is a data set of YF cases and YF deaths of an outbreak in Senegal in 2002 collected from the internet archives of the World Health Organization (WHO). As soon as the virus was identified a vaccination program was started (Oct 1, 2002). On Oct 11, 2002 the disease was reported in Touba, a city of 800,000 residents. More information can be found on the WHO Web sites (www.who.int).

Report date	Cases (total)	Deaths (total)
Jan 18th	18	0
Oct 4th	12	0
Oct 11th	15	2
Oct 17th	18	2
Oct 24th	41	4
Oct 31st	45	4
Nov 20th	57	10
Nov 28th	60	11

1. Develop a model for the three stages of YF as outlined above.
2. Include a fourth stage that describes vaccination in urban areas.
3. Fit your model to the data.
4. What would have happened without vaccination?
5. Would you expect that the disease dies out, or that it becomes persistent?

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