# MODULE 4.3

## Modeling the Spread of SARS—Containing Emerging Disease

### Downloads

The text's website has *SIR* and *SARSRelationships* files, which contain models for the examples of this module, available for download for various system dynamics tools.

### Introduction

Imagine being a college student in New York City and being told not to leave the city. That's what happened in 2003 in Beijing, when thousands of people were ordered to stay home and college students were told to stay in Beijing. Quarantine procedures were instituted for those who were thought to have had "intimate contact" with others who showed signs of a new rapidly spreading respiratory disease. More than 40 had died in the capital, and thousands of people in China were displaying symptoms of this pneumonia. Imagine the feelings of fear and panic that Beijing residents must have had—people in masks, disinfecting their homes, and hoarding of food and other necessities.

This new disease was called **SARS**, **severe acute respiratory syndrome**, with the first case occurring on November 16, 2002, in southern China. Chinese health officials reported the outbreak to the World Health Organization (WHO) on February 11, 2003. By April 2, the total reported cases of SARS were 2000; and by July, the count was over 8400 with more than 800 dead. In response to the initial report, WHO coordinated the investigation into the cause and implemented procedures to control the spread of this disease. The control measures were extremely effective, and the last new case was reported on June 12, 2003 (WHO).

By the third week in March several laboratories worldwide had identified the probable causative agent—*SARS-CoV*, the SARS coronavirus. Coronaviruses represent a large group of +-stranded RNA-containing viruses associated with various

respiratory and gastrointestinal illnesses. Although the human diseases associated with these viruses have been mild previously, this coronavirus is quite different. Like many respiratory pathogens, SARS is spread by close personal contact and perhaps by airborne transmission.

The Centers for Disease Control and Prevention (CDC) in the United States uses clinical epidemiological and laboratory criteria to diagnose SARS. Severe cases exhibit a fever higher than 38 °C and one or more respiratory symptoms—difficulty breathing, cough, or shortness of breath. Additionally, the person must show radiographic evidence (lung infiltrates) of pneumonia, or **respiratory distress syndrome** (**RDS**). RDS is an inflammatory disease of the lung, characterized by a sudden onset of edema and respiratory failure. A few others qualified if they exhibited an unexplained respiratory illness that resulted in death and an autopsy confirmed RDS with no identifiable cause. Epidemiological evidence might include close contact with a known SARS patient or travel to a region with documented transmission within 10 days of onset of symptoms. Today, laboratory tests confirm SARS if they reveal one of the following (CDC):

- Antibody to SARS virus in specimens obtained during acute illness or more than 28 days after onset of illness
- SARS viral RNA detected by RT-PCR
- SARS virus

On July 5, 2003, the World Health Organization declared that SARS had been contained. The outbreak resulted in 812 deaths, but the toll might have been much higher if WHO and other health agencies had not acted so quickly and effectively (WHO). Besides the direct effect on the victims and their families, SARS became a major drag on the economies of China, Taiwan, and Canada. Hong Kong's unemployment rate climbed to an unprecedented 8.3%, and travel warnings for Toronto cost Canada an estimated $30 million per day. One can only imagine the impact of this disease being spread into Africa, where there are poor healthcare systems and the astronomical HIV infection rates generate immunologically compromised populations.

SARS is an interesting disease for modeling, particularly because there is so much epidemiological information. We still have much to learn about SARS, and we still have no available, effective treatment.

## SIR Model

Before developing a model for the spread of SARS, we consider the simpler situation of a disease in a closed environment in which there are no births, deaths, immigration, or emigration. A 1978 *British Medical Journal* article reported on such a situation—influenza at a boys' boarding school. On January 22, only one boy had the flu, which none of the other boys had ever had. By the end of the epidemic on February 4, 512 of the 763 boys in the school had contracted the disease (Murray 1989; NCSLIP).

To model this spread of influenza, we employ the **SIR Model**, which W. O. Kermack and A. G. McKendrick developed in 1927 (Kermack and McKendrick 1927).

Many systems models of the spread of disease, including the SARS model later in this module, are extensions of the SIR Model. The name derives from the following three populations considered:

**Susceptibles** (***S***) have no immunity from the disease.
**Infecteds** (***I***) have the disease and can spread it to others.
**Recovereds** ***(R)*** have recovered from the disease and are immune to further infection.

The model gives the differential equation for the rate of change for each of these populations. We assume that after a certain amount of time, an individual with the flu recovers. Thus, the rate of change of the number of recovereds is proportional to the number of infecteds.

## Quick Review Question 1

With the constant of proportionality being the recovery rate ($a$), give the differential equation for the rate of change of the number of recovereds.

As the answer to Quick Review Question 1 states, the differential equation for the rate of change of the number of recovereds is $dR/dt = aI$ for recovery rate $a$. If the time unit is in days and $d$ is the number of days that someone remains infected, we can consider $a$ to be $1/d$. For example, if a boy is usually sick with the flu for 2 days, then $d = 2$ and $a = 0.5$/day, so that approximately half the infected boys get well in a day.

**Model:** In the SIR model, recovery rate = 1/(number of days infected).

A susceptible boy at the boarding school becomes infected with influenza by having contact with an infected boy. The number of such possible contacts is the product of the sizes of the two populations, $SI$. For example, suppose the set of susceptibles is $S = \{\text{Joe, Lee, Orlando}\}$ and the set of infecteds is $I = \{\text{Hondre, Leslee}\}$. As Figure 4.3.1 illustrates, (3)(2) = 6 possible interactions exist between pairs of boys in different sets. The virus in Hondre can spread through contact to Joe, Lee, and Orlando. Similarly, Joe can become infected with the virus from Hondre or Leslee. With no new students entering the school, the number of susceptibles can only decrease, and the rate of change of the number of boys in this set is directly proportional to the number of possible contacts, $SI$, between susceptibles and infecteds.

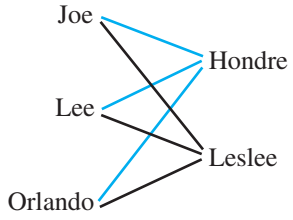


**Figure 4.3.1** Possible contacts between $S$ and $I$

## Quick Review Question 2

**a.** Is the rate of change of $S$ positive, zero, or negative?
**b.** With $r > 0$ being the constant of proportionality, give a differential equation for the rate of change of $S$.

In Module 4.1, "Competition," because of interactions, we modeled competitors' death rates of change using the same proportionality to a product of population sizes. Similarly, in Module 4.2, "Predator-Prey Models," considering contacts between predators and prey, we modeled predator births and prey deaths using the same type of product. Thus, three very different applications employ the same model for rates of change where interaction occurs—the product of a constant and the two interacting population sizes.

**Model:** One model for the rate of change involving the interaction of constituents with sizes $A$ and $B$ is $cAB$, where $c$ is a constant.

As the answers to Quick Review Question 2 reveal, because of the interaction of susceptibles and infecteds in spreading the disease, we employ this model for the rate of change of susceptibles with respect to time: $dS/dt = -rSI$ for positive constant of proportionality $r$. The constant $r$, called the **transmission constant**, reflects the extent and the infectiousness of the disease and the interactions among the students. In the case of the boys' school, we use 0.00218 per day. Thus, 0.00218 = 0.218% of the total number of possible contacts, $SI$, results in the disease being spread from one child to another.

Notice how small the transmission constant (0.00218/day) is in comparison to the recovery rate (0.5/day). Also, recall in interactions for competition and predator-prey, where a rate-of-change model involves a product of populations, the constant of proportionality is small in comparison to constants multiplied by only one population. Breaking down $dS/dt$ another way helps to explain why the constant of proportionality, here $r = 0.00218$ per day, is so small. For a sick child to pass the disease to someone else, the sick boy must come in contact with someone else, that person must be susceptible, and the interaction must result in the spread of the disease. Thus, the rate of change of $S$ with respect to time ($dS/dt$) is minus the product of the mean number of contacts per day an infected has ($k$), the probability such a contact is with a susceptible, the probability that the disease is spread during such a contact ($b$), and the number of infecteds. Moreover, if $N$ is the total population size (here 763) and the group is well mixed, then for an infected, the probability of that contact he has is with a susceptible is $S/N$, and the rate of change of $S$ is as follows:

$$dS/dt = -k(S/N)bI = -(kb/N)SI = -rSI$$

Thus, the transmission constant $r$ is $(kb/N)$. For example, suppose on the average an infected child has 33.3 contacts per day and the probability that a contact results in the spread of the disease is 5% = 0.05. Then, for $N = 763$, the transmission constant is $r = (kb/N) = 0.00218$.

Note that this transmission constant, here 0.00218/day, is not the rate of infection. Suppose a report to the school's principal after all are well states that 80% of the boys had had the flu. The 80% is of the total population of $N = 763$ boys, not of the number of possible interactions, $SI$. Moreover, 80% of the susceptible boys do not become sick in one day. If flu lasted in the school for 3 weeks, as the following shows, on the average 3.81% of the boys get sick in 1 day:

$$\frac{0.80}{3\text{weeks}} \times \frac{1\text{week}}{7\text{days}} = \frac{0.0381}{\text{day}} = \frac{3.81\%}{\text{day}}$$

We must be careful to be consistent in units, such as not mixing days and weeks, and to understand of what we are taking a percentage, such as of $SI$ instead of $S$ or $N$.

Returning to our model, only susceptibles become infected, and infecteds eventually recover. What $I$ gains comes from what $S$ has lost; and what $I$ loses, $R$ acquires. Thus, the differential equation for the rate of change of the number of infecteds is the sum of the negatives of the other two rates of change:

$$dI/dt = -dS/dt - dR/dt$$

## Quick Review Question 3

Give the differential equation for the rate of change of the number of infecteds in terms of $S$, $I$, $R$, the transmission constant ($r$), and the recovery rate ($a$).

Figure 4.3.2 presents a diagram for the SIR model with *susceptibles*, *infecteds*, and *recovereds* replacing the symbols $S$, $I$, and $R$, respectively, and with *transmission_constant* and *recovery_rate* representing the constants of proportionality $r$ and $a$, respectively. Some of the corresponding equations and constants for a particular simulation appear in Equation Set 4.3.1.

## Equation Set 4.3.1

With basic unit of time of 1 day, some equations and constants for SIR model in Figure 4.3.2

*susceptibles*(0) = 762
*transmission_constant* = 0.00218

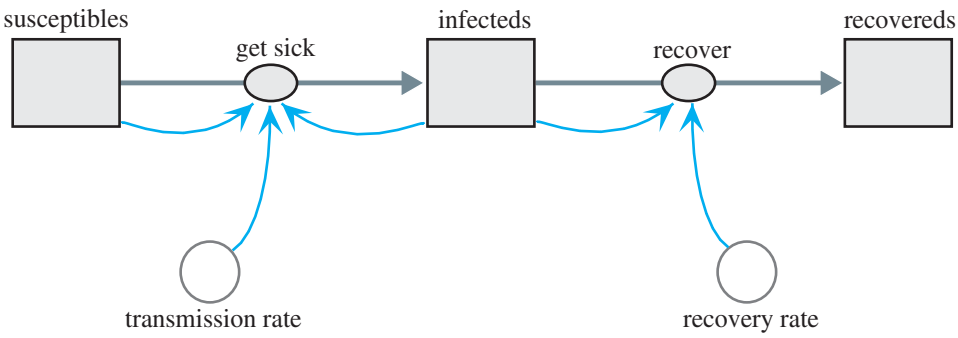


**Figure 4.3.2** Diagram for the SIR model

*get_sick* = *transmission_constant* * *susceptibles* * *infecteds*
*infecteds*(0) = 1
*recovery_rate* = 0.5
*recover* = *recovery_rate* * *infecteds*
*recovereds*(0) = 0

The graphs of the three populations that result from running the simulation are in Figure 4.3.3. The number of *susceptibles* decreases slowly at first before experiencing a rapid decline and subsequent leveling. In contrast, the number of *recovereds*, which is initially 0, has a graph that appears similar to the logistic curve. When the number of *susceptibles* decreases sharply, the *infecteds* increase to their maximum. Afterwards, as the number of *infecteds* decreases, the number of *recovereds* rises. Although not mimicking the final numbers exactly, this model does capture the trend of the data along with the epidemic increase and decrease and the progress towards a steady state.

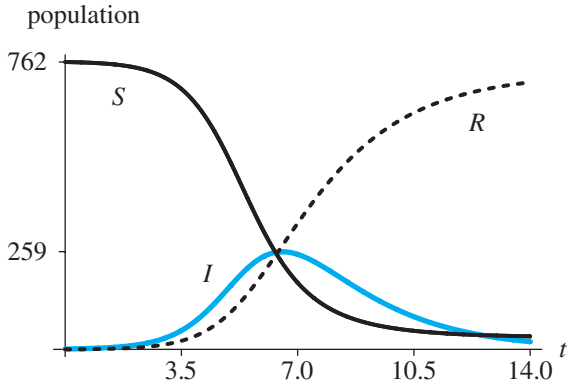


**Figure 4.3.3** Graphs of *susceptibles* (*S*), *infecteds* (*I*), and *recovereds* (*R*) versus time (*t*) in days

## Quick Review Question 4

Answer the following questions referring to Figure 4.3.3.

**a.** On what day was the number of cases the largest?
**b.** On what day were most of the boys sick or recovered?
**c.** On what day were most of the boys recovered?

## SARS Model

Marc Lipsitch in collaboration with others developed a model for the spread of **severe acute respiratory syndrome** (**SARS**) and used the model to make predictions on the impact of public health efforts to reduce disease transmission (Lipsitch et al. 2003). Such efforts included **quarantine** of exposed individuals to separate them

from the susceptible population, perhaps by confinement to their homes, and **isolation** of those who had SARS to remove them to strictly supervised hospital areas with no contacts other than by healthcare personnel. The Lipsitch model is an extension of the SEIR model, which is a refinement of the SIR model. Besides the populations considered by SIR, the **SEIR Model** (**susceptible-exposeds-infecteds-recovereds**) has an intermediate **exposed** (***E***) population of individuals who have the disease but are not yet infectious. The Lipsitch model modifies SEIR to allow for quarantine, isolation, and death. The modelers make the following simplifying assumptions:

1. There are no births.
2. The only deaths are because of SARS.
3. The number of contacts of an infected individual with a susceptible person is constant and does not depend on the population density.
4. For susceptible individuals with exposure to the disease, the quarantine proportion ($q$) is the same for non-infected as for infected people.
5. Quarantine and isolation are completely effective. Someone in quarantine or isolation cannot spread disease or, in the case of a susceptible, cannot catch the disease.

The populations considered are as follows:

*susceptible* ($S$) do not have but can catch SARS from infectious individuals.
*susceptible_quarantined* ($S_Q$) do not have SARS, quarantined because of exposure, so cannot catch SARS.
*exposed* ($E$) have SARS, no symptoms, not yet infectious.
*exposed_quarantined* ($E_Q$) have SARS, no symptoms, not yet infectious, quarantined because of exposure.
*infectious_undetected* ($I_U$) have undetected SARS, infectious.
*infectious_quarantined* ($I_Q$) have SARS, infectious, quarantined, cannot transmit.
*infectious_isolated* ($I_D$) have SARS, infectious, isolated, cannot transmit.
*SARS_death* ($D$) are dead due to SARS.
*recovered_immune* have recovered from SARS, immune to further infection.

Because we are assuming that quarantine is completely effective, only someone in the *susceptible* ($S$) category can catch SARS, and transmission to a susceptible can occur only through exposure to an individual in the *infectious_undetected* ($I_U$) category. Those with SARS in other categories are under quarantine or isolation or are not yet infectious.

## Quick Review Question 5

After completing this question and before continuing in the text, we suggest that you make a diagram with stocks (box variables) and flows only to represent possible transitions between categories. For each of the following, give the possible category(ies):

**a.** Flows out of $S$ into what categories?
**b.** Flows into $S$ from what categories?
**c.** Flows into $D$ from what categories?

Without inclusion of converters and connectors, Figure 4.3.4 displays a diagram with the stocks that represent these populations along with the flows between them. As illustrated, a susceptible individual who has had contact with someone having SARS and has moved from the *susceptible* group can be quarantined with or without the disease (to *exposed_quarantined* or *susceptible_quarantined*, respectively) or can be infected and not quarantined (to *exposed*). A susceptible, quarantined person who does not have SARS (in *susceptible_quarantined*) eventually is released from quarantine (to *susceptible*). An exposed but not yet infectious individual who does have SARS, whether quarantined or not (in *exposed_quarantined* or *exposed*, respectively), eventually becomes infectious (to *infectious_quarantined* or *infectious_undetected*, respectively). Regardless of quarantine status, an infectious individual can recover (to *recovered_immune*), go into isolation after discovery (to *infectious_isolated*), or die (to *SARS_death*). Isolated patients who are sick with SARS can recover or die.

## Quick Review Question 6

Using this model, indicate if each of the following situations is possible or not:

**a.** A susceptible person dies of SARS.
**b.** A person who has undetected SARS in the early stages recovers without ever becoming infectious.
**c.** Someone in quarantine diagnosed with SARS recovers without going into isolation.
**d.** Someone who has recovered from SARS becomes infected with the disease again.
**e.** Someone is transferred from isolation to quarantine.

The model employs the following parameters:

- $b$ probability that a contact between person in *infectious_undetected* ($I_U$) and someone in *susceptible* ($S$) results in transmission of SARS
- $k$ mean number of contacts per day someone from *infectious_undetected* ($I_U$) has. By assumption, the value does not depend on population density.
- $m$ per capita death rate
- $N_0$ initial number of people in the population
- $p$ fraction per day of exposed people who become infectious; this fraction applies to the transitions from *exposed* ($E$) to *infectious_undetected* ($I_U$) and from *exposed_quarantined* ($E_Q$) to *infectious_quarantined* ($I_Q$). Thus, $1/p$ is the number of days in the early stages of SARS for a person to be infected but not infectious.
- $q$ fraction per day of individuals in *susceptible* ($S$) who have had exposure to SARS that go into quarantine, either to category *susceptible_quarantined* ($S_Q$) or to *exposed_quarantined* ($E_Q$)
- $u$ fraction per day of those in *susceptible_quarantined* ($S_Q$) who are allowed to leave quarantine, returning to the *susceptible* ($S$) category; thus, $1/u$ is the number of days for a susceptible person to be in quarantine.
- $v$ per capita recovery rate; this rate is the same for the transition from category *infectious_undetected* ($I_U$), *infectious_isolated* ($I_D$), or *infectious_quarantined* ($I_Q$) to category *recovered_immune*.

*w* fraction per day of those in *infectious_undetected* ($I_U$) who are detected and isolated and thus transferred to category *infectious_isolated* ($I_D$)

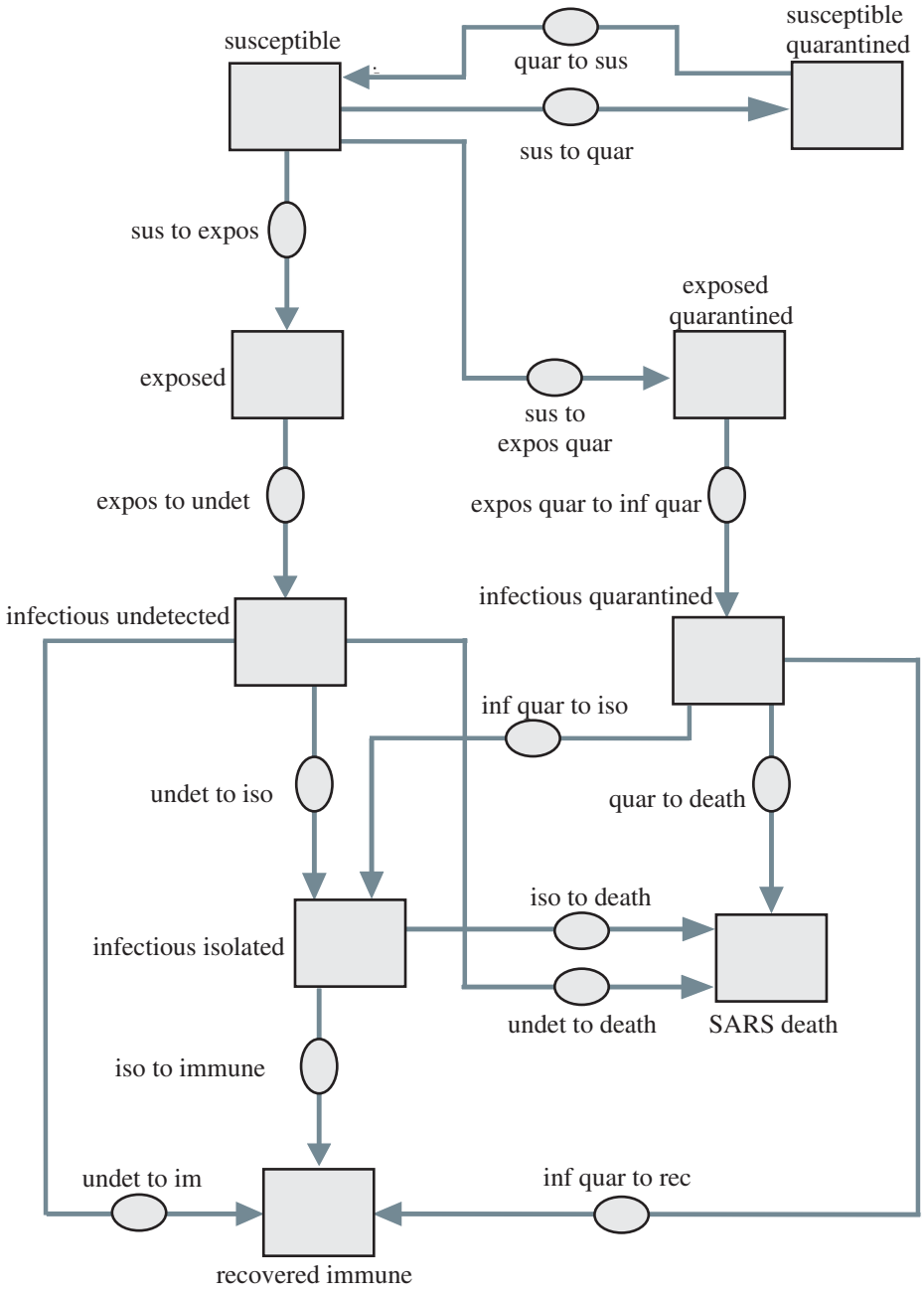


**Figure 4.3.4** Initial diagram of relationships for SARS

## Quick Review Question 7

**a.** Suppose it takes an average of 5 days for someone who has SARS but is not infectious to progress to the infectious stage. Give the value of $p$ along with its units.
**b.** Give the formula for the rate of change of exposed individuals who are not quarantined to move into the phase of being infectious and undetected, from $E$ to $I_U$.
**c.** Give the formula for the rate of change of exposed individuals who are quarantined to move into the phase of being infectious and quarantined, from $E_Q$ to $I_Q$.
**d.** Suppose 10% of the people who have been in quarantine but who do not have SARS are allowed to leave quarantine each day. Give $u$ and the average number of days for a susceptible person to be in quarantine.
**e.** Suppose the duration of quarantine is 16 days. If someone has not developed symptoms of SARS during that time period, he or she may leave quarantine. Give the corresponding parameter and its value.
**f.** Give the formula for the rate of change of susceptible, quarantined individuals leaving quarantine, from $S_Q$ to $S$.

As illustrated in Figure 4.3.4, three paths exist for someone to leave *infectious_undetected* ($I_U$)—to *recovered_immune* at a rate of $v$, to *SARS_death* at a rate of $m$, or to *infectious_isolated* ($I_D$) at a rate of $w$. Thus, the total rate of change to leave *infectious_undetected* ($I_U$) is $(v + m + w)$/day. For example, if $v = 0.04$, $m = 0.0975$, and $w = 0.0625$, $v + m + w = 0.2$/day. In this case, $1/(v + m + w) = 5$ day is the average duration of infectiousness.

By assumption, $k$ is the number of contacts an undetected infectious person has, regardless of population density. Thus, with $N_0$ being the initial population size, $k/N_0$ is the fraction per day of such contacts. Because $b$ is the probability of transmitting the disease, the product $(k/N_0)b$ is the transmission constant. As in the SIR model, the product $I_US$ gives the total number of possible interactions. Thus, $(k/N_0)b\,I_US = kbI_US/N_0$ is the number of new cases of SARS each day. Of these new cases, a fraction ($q$) go into category *exposed_quarantined* ($E_Q$), while the remainder, the fraction $(1 - q)$, go into *exposed* ($E$).

## Quick Review Question 8

**a.** Suppose $k = 10$ contacts/day, and $N_0 = 10{,}000{,}000$ people. Give the percentage of contacts per day.
**b.** Suppose 6% of contacts between an infectious and a susceptible person result in transmission of the disease. Give the corresponding parameter, its value, and units.
**c.** Using your answers to Parts a and b, what percentage of all possible contacts results in transmission of SARS each day?
**d.** If the sizes of *infectious_undetected* ($I_U$) and *susceptible* ($S$) are 5000 and 9,000,000, respectively, give the total number of possible contacts.

**e.** Using your answers to Parts c and d, give the number of contacts per day that result in transmission of SARS.
**f.** Suppose $q = 0.1 = 10\%$ of the individuals who have had contact with an infectious person go into quarantine. Give the number of those from Part e who go into *exposed_quarantined* ($E_Q$).
**g.** Give the formula for the rate of change from *susceptible* ($S$) to *exposed_quarantined* ($E_Q$).
**h.** Assuming $q = 0.1$, give the number of those from Part e who go into *exposed* ($E$).
**i.** Give the formula for the rate of change from *susceptible* ($S$) to *exposed* ($E$).

For those transferring from *susceptible* ($S$) to *susceptible_quarantined* ($S_Q$), although they have been exposed to an infectious person, the disease was not transmitted to them. The fraction of total possible contacts, $I_US$, is $(k/N_0)$, and the probability of nontransmittal is $(1 - b)$. Thus, the total number of nontransmission contacts is $(k/N_0)(1 - b)I_US = k(1 - b)I_US/N_0$. However, only a fraction ($q$) of those go into quarantine. Thus, the rate of change of those going from *susceptible* ($S$) to *susceptible_quarantined* ($S_Q$) is $qk(1 - b)I_US/N_0$.

### Quick Review Question 9

Using the values from Quick Review Question 8, determine the rate of change of those going from *susceptible* ($S$) to *susceptible_quarantined* ($S_Q$).

## Reproductive Number

Several exercises deal with the differential equations for this SARS model, and a project completes the model. In this model, an important value in evaluating the effectiveness of quarantine and isolation is the **reproductive number** $\boldsymbol{R}$, which is the expected number of secondary infectious cases resulting from an average infectious case once the epidemic is in progress. The **basic reproductive number**, $\boldsymbol{R_0}$, is the initial reproductive number with one infectious individual and all others being susceptible. For example, if at the start of a disease in an area the infectious individual transmits SARS to a mean of three other people who eventually become infectious, then the basic reproductive number is $R_0 = 3$. Such a number results in the alarming prospect of exponential growth of the disease. On the average, one person transmits infectiousness to three other people, who each cause three other people to become infectious, and so forth. In such a situation, at stage $n$ of transmission, $3^n$ new people would eventually become infectious. For example, at stage $n = 13$, $3^{13}$, or more than 1.5 million, new people, would get sick. Because of such exponential growth, it very important that $R$ be less than 1. With $R < 1$, there is no epidemic. For $R > 1$, there is an epidemic. The larger the reproductive number, the more virulent the epidemic.

For this SARS model, on the average, an undetected infectious person has $k$ contacts per day. At the beginning of the disease with all individuals except one being

**Definitions** The **reproductive number *R*** is the expected number of secondary infectious cases resulting from an average infectious case once the disease has started to spread. The **basic reproductive number $R_0$** is the expected number of secondary infectious cases resulting from one infectious individual in a completely susceptible population.

susceptible, each such contact can result in the disease spreading. Thus, with a probability $b$ of transmission, approximately $kb$ secondary cases of SARS per day derive from the first infections individual. Thus, for mean disease duration of $D$ days, the **basic reproductive number**, $R_0$, is $kbD$. Because the average duration of infectiousness is $1/(v + m + w)$ da (see explanation after Quick Review Question 7), without quarantine being a factor, one infectious person eventually gives rise to $R_0 = kb/(v + m + w)$ secondary infectious cases of SARS. However, when a fraction, $q$, go into quarantine so that a fraction $(1 - q)$ do not, the reproductive number is $R_0 = \frac{kb}{v+m+w}(1-q)$. The larger $q$ is, the smaller $R_0$ is, and the less severe the impact of the disease is.

**Model:** A model of the basic reproductive number is as follows:

$$R_0 = kbD$$

where $k$ is the mean number of contacts an undetected infectious person has per time unit (such as day), $b$ is the probability of disease transmission, and $D$ is the mean duration of the disease.

## Quick Review Question 10

Evaluate the basic reproduction number, $R_0$, using the values of Quick Review Question 8 and text material: $k = 10$ contacts/da, $b = 0.06$, $v = 0.04$, $m = 0.0975$, $w = 0.0625$, and $q = 0.1$.

Examining $R_0$, the death rate, and other factors, WHO and other health organizations realized that they must act quickly with bold measures involving quarantine and isolation to avoid a major, worldwide epidemic of SARS. Computer simulations with scenario analyses verified the seriousness of the disease. Thanks to aggressive actions, a terrible catastrophe was averted.

## Exercises

**1.** Write the system of differential equations for the SIR model using a transmission constant of 0.0058 and a recovery rate of 0.04.

*In the SARS model, give the differential equation for each rate of change in Exercises 2–10.*

**2.** $dS_Q/dt$ **3.** $dE/dt$ **4.** $dE_Q/dt$ **5.** $dS/dt$ **6.** $dI_U/dt$
**7.** $dI_D/dt$ **8.** $dI_Q/dt$ **9.** $d(recovered\_immune)/dt$ **10.** $dD/dt$

**11. a.** For basic reproductive number of $R_0 = 3$, give the number of new people that will eventually become infectious at stage $n = 10$ of transmission of the disease.
**b.** Give the total number of people who will eventually become infectious.
**c.** Repeat Part a for $n = 15$.
**d.** Repeat Part b for $n = 15$.

## Projects

*For additional projects, see Module 7.11, "Fueling Our Cells—Carbohydrate Metabolism"; Module 7.14, "Control Issues: The Operon Model"; and Module 7.15, "Troubling Signals: Colon Cancer."*

**1.** Adjust the SIR model to allow for vaccination of susceptible boys. Assume that 15% are vaccinated each day, and make a simplifying assumption that immunization begins immediately. Discuss the effect on the duration and intensity of the epidemic. Consider the impact of other vaccination rates.
**2.** Adjust the SIR model to allow for vaccination of susceptible boys. Assume that 15% are vaccinated each day and that immunization begins after 3 days. Discuss the effect on the duration and intensity of the epidemic. Consider the impact of other vaccination rates.
**3.** Adjust the SIR model to allow for vaccination of susceptible boys. Assume that all children are vaccinated 2 days before a boy comes down with the flu and that immunization begins after 4 days. Discuss the effect on the duration and intensity of the epidemic. Consider the impact of other vaccination rates.
**4.** Develop an SEIR model of disease.
**5.** Complete the Lipsitch SARS model introduced in the text. Have the model evaluate $R$. Produce graphs and a table of appropriate populations, including *susceptible*, *recovered_immune*, *SARS_death*, and the total of the five categories of infecteds. Employ the following parameters: $k = 10$/day; $b = 0.06$; $1/p = 5$ days; $v = 0.04$, $m = 0.0975$, and $w = 0.0625$, so that $v + m + w = 0.2$/day and $1/(v + m + w) = 5$ days; $1/u = 10$ days; $N_0 = 10{,}000{,}000$ people. Vary $q$ from 0 upward. Note that in each case, the graph of the number of susceptibles appears logistic and the solution eventually reaches equilibrium. Describe the shapes of the graphs and discuss the results.
**6.** After developing the model of Project 5, with a fixed value of $q$, test other ranges of $k$ from 5 to 20 per day. Discuss the results.
**7.** After developing the model of Project 5, with a fixed value of $q$, test other ranges of $1/(v + m + w)$ from 1 to 5 days.
**8.** Adjust the model of Project 5 so that the simulation is allowed to run for a while before quarantine and isolation measures that reduce $R$ to below 1 are instituted. Discuss the implications on the number of people quarantined and on the health care system of not taking aggressive measures initially.

**9.** Complete the Lipsitch SARS model introduced in the text. Run the simulation for various values of $R_0$. Produce graphs and a table of appropriate populations, including *susceptible*, *recovered_immune*, *SARS_death*, and the total of the five categories of infecteds. Describe the shift of the steady state as $R_0$ becomes larger, and discuss the implications.

**10.** Develop a model of strep throat. Bacterium Group A *Streptococcus* causes strep throat, which occurs most frequently in school-aged children. The bacterium spreads through direct or airborne contact with the mucus from an infected person. Symptoms start from 1 to 5 days after exposure and include fever, sore throat, and tender and swollen neck glands. If untreated, people with strep throat are infectious for 10 to 21 days. Usually, 24 h after antibiotic treatment, those who are ill are no longer contagious. The spread of strep throat can be minimized by infectious people covering their mouths when sneezing or coughing and by washing their hands frequently (IDEHA).

**11.** Develop a model of the viral infection mumps. Symptoms include painful and swollen salivary glands, painful swallowing, fever, weakness, fatigue, and a tender, swollen testicle. Infection is spread through breathing of infected saliva droplets. About one-third of those with mumps experience no symptoms. If present, symptoms usually start 2 to 3 weeks after infection. The person is contagious from approximately 1 day before salivary gland swelling occurs and remains contagious for at least another 3 days. As the swelling diminishes, so does the degree of the contagion. Before licensing of the mumps vaccine in 1967, the United States had more than 200,000 cases per year. Since then, the country has had fewer than 1000 cases per year (Mayo Clinic Staff 2012).

**12.** Diphtheria has been virtually eradicated in the United States because of a vaccine, which was introduced in the 1920s. Before that time, the United States had 100 to 200 cases per 100,000 people. The disease is still a problem in developing countries. Two types of diphtheria exist, respiratory and cutaneous. The former is more serious, and death results in about 10% of those cases. The disease is spread through respiratory droplets and from contaminated objects or food. The incubation period for the disease is usually 2 to 5 days. Develop a model for respiratory diphtheria (NCBI).

**13.** Using data and mathematical models implemented in spreadsheets, the Dutch Ministry of Health, Welfare and Sports developed "a national plan to minimize effects of pandemic influenza." Through scenario analysis, scientists examined various intervention options and estimated the number of hospitalizations and deaths. In the base case, in which no intervention was possible, they assumed 30% of the population would become ill with influenza. In the Influenza Vaccination Scenario, they considered two strategies:

1. Vaccinate two risk groups, persons 65 years of age or older ($N = 2.78$ million (M)) and healthcare workers ($N = 0.80$ M)
2. Vaccinate the total population ($N = 15.6$ M)

They assumed the vaccine to be 56% effective in preventing hospitalizations and deaths for the older at-risk group and 80% effective for those younger than 65. Develop a model for the first strategy. With no intervention, assume a hospitalization rate (per 100,000) for influenza and influ-

enza-related illnesses of 125 (per 100,000) for persons 65 years of age or older and a rate (per 100,000) of 50 for the younger age group; and assume death rates (per 100,000) of 56 and15, respectively, for the two age groups. (In the actual study, scientists considered three age groups and a more involved set of input variables; van Genugten et al. 2003)

**14.** Develop a model for the second strategy in Project 13.

**15.** Develop models for the two strategies in Project 13, discuss the results, and make recommendations.

**16.** Adjust a SIR model to have seasonal changes in infectiousness by having a periodic function for a transmission coefficient (see Project 1 in Module 4.2, "Predator-Prey Model"). Discuss the results.

**17.** Repeat Project 16 for a SEIR model.

**18.** Obtain information and data about another infectious disease, where the disease spreads from one individual to another. Model at least one aspect of the spread of the disease, starting with one infected individual in a particular area. Run the model for various scenarios, produce graphs and tables, and discuss the results. The following are some suggested diseases: pinkeye in cattle (see "Introduction" in Module 11.2, "Agents of Interaction: Steering a Dangerous Course"), rotavirus, pertussis, meningitis, bacterial/viral pneumonia, cold (rhinovirus), tuberculosis**,** various STD's, impetigo, herpes (cold sores).

## Answers to Quick Review Questions

**1.** $dR/dt = aI$

**2.** **a.** negative while people are getting sick because the number of susceptibles is decreasing
**b.** $dS/dt = -rSI$

**3.** $dI/dt = rSI - aI$

**4.** **a.** day 7
**b.** day 6
**c.** day 8

**5.** **a.** $E$, $E_Q$, $S_Q$
**b.** $S_Q$
**c.** $I_U$, $I_Q$, $I_D$

**6.** **a.** no
**b.** no
**c.** yes
**d.** no
**e.** no

**7.** **a.** 0.2/day
**b.** $pE$
**c.** $pE_Q$
**d.** 0.1/day, 10 days
**e.** $u$ = 1/16 per day = 0.0625/day
**f.** $u\,S_Q$

**8. a.** $k/N_0 = 10/10{,}000{,}000 = 0.000001 = 0.0001\%$/day
**b.** $b = 0.06$/day
**c.** $(0.000001)(0.06) = 0.00000006 = 0.000006\%$/day
**d.** $(5000)(9{,}000{,}000) = 45{,}000{,}000{,}000$
**e.** $(0.00000006)(45{,}000{,}000{,}000) = 2700$
**f.** $(0.1)(2700) = 270$ people
**g.** $qkbI_US/N_0$
**h.** $(1 - 0.1)(2700) = (0.9)(2700) = 2430$ people; or $2700 - 270 = 2430$ people
**i.** $(1 - q)kbI_US/N_0$

**9.** $qk(1 - b)I_US/N_0 = (0.1)(10)(1 - 0.06)(5000)(9{,}000{,}000)/(10{,}000{,}000) = 4230$ people

**10.** $R_0 = (1 - q)kb/(v + m + w) = (1 - 0.1)(10)(0.06)/(0.04 + 0.0975 + 0.0625) = 2.7$

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