Computer Modeling and Simulation

Lectures 18 & 19

SARS – An Introduction

- **SARS**, **severe acute respiratory syndrome ,** first case occurred 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).

SARS – An Introduction

- 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.

SARS – Symptoms and Detection

- 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**).
- 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

Modelling SARS

- 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.
- It helps us in modelling Covid-19 and on the basis of this, we can see how easily it spreads and how effective measures can be taken.

Modelling SARS

- 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).

SIR Model – A simpler Model

- Many system models of the spread of disease, including the SARS model, 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.

Rate of change of Recoverds – dR/dt

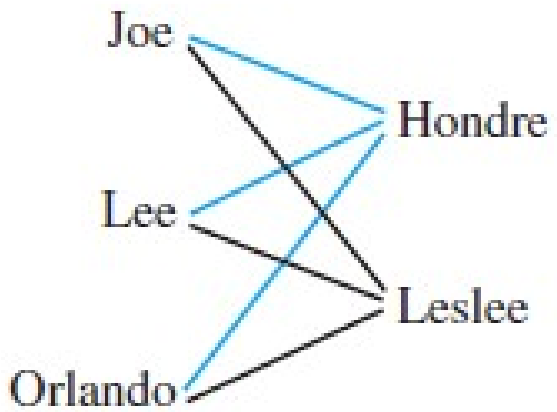
- We assume that after a certain amount of time, an individual with the flu recovers.
- Thus, the rate of change of the number of recovereds is proportional to the number of infecteds.
- The differential equation for the rate of change of the number of recovereds is

$$dR/dt = aI \text{ for recovery rate } a$$

- 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.

Rate of change of Susceptibles – dS/dt

- 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* = {Joe, Lee, Orlando} and the set of infecteds is *I* = {Hondre, Leslee}.
- As the Figure 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.



Possible Contacts between S and I

Rate of change of Susceptibles – dS/dt

- So 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.

Rate of change of Susceptibles – dS/dt

- 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.
- We can find the transmission constant r in an another way.
- 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:

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

$$r = kb/N$$

Transmission Constant

$$r = kb/N$$

- 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:

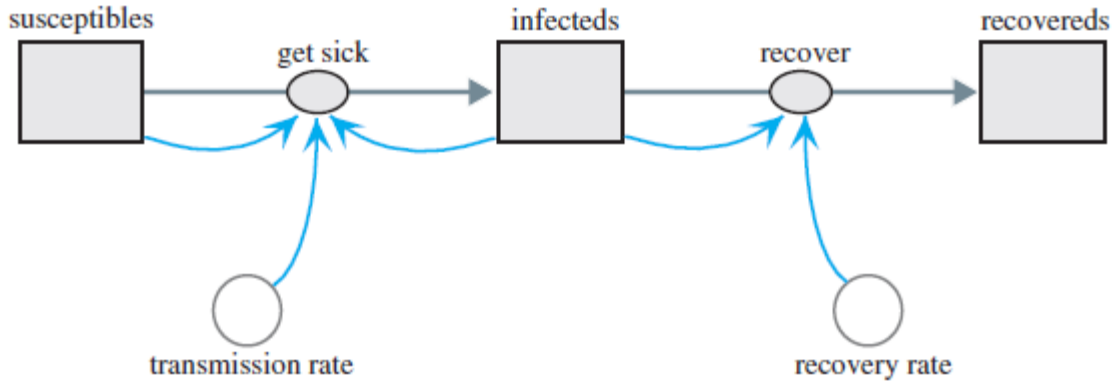
$$\frac{0.80}{3\,\text{weeks}} \times \frac{1\text{week}}{7\,\text{days}} = \frac{0.0381}{\text{day}} = \frac{3.81\%}{\text{day}}$$

Rate of change of Infecteds – dI/dt

- 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:

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

Diagram for the SIR model



SARS Lipsitch 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,
  - **isolation** of those who had SARS to remove them to strictly supervised hospital areas with no contacts other than by healthcare personnel.

SEIR Model

- 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.

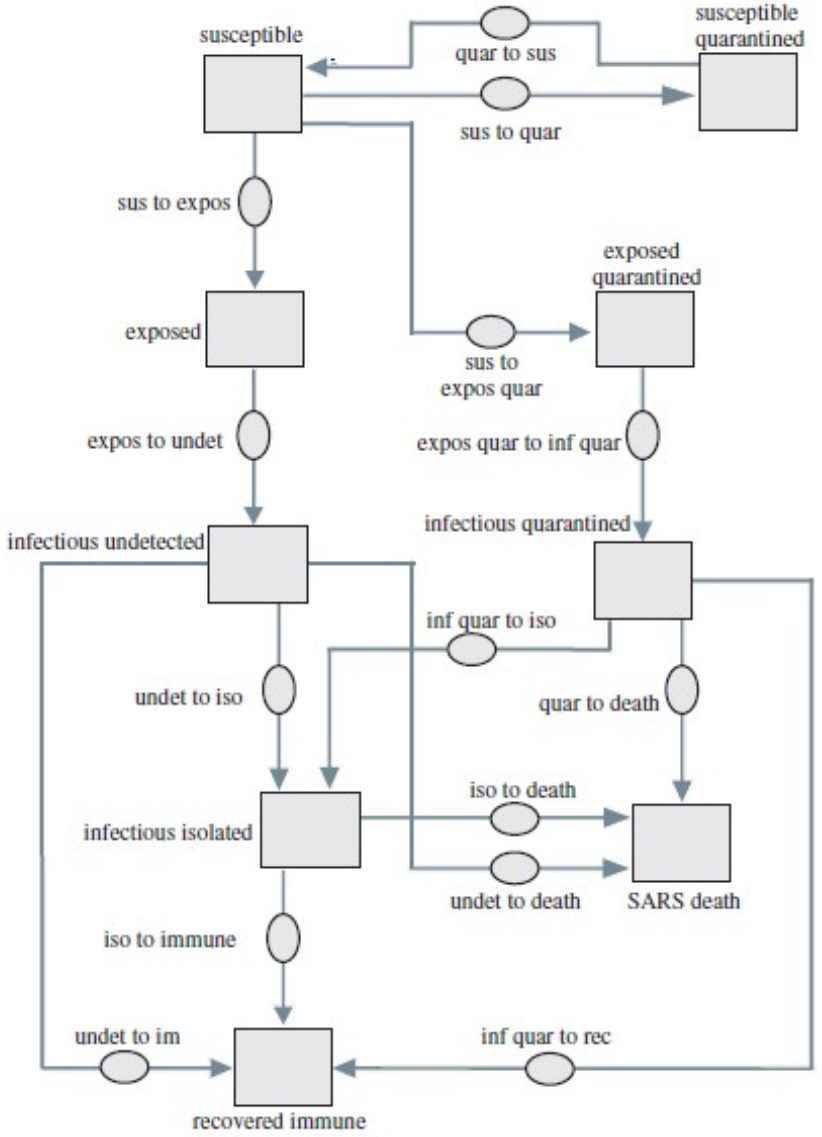
Lipsitch Model for SARS

- The Lipsitch model modifies SEIR to allow for quarantine, isolation, and death.
- The modelers make the following simplifying assumptions:
  - There are no births.
  - The only deaths are because of SARS.
  - The number of contacts of an infected individual with a susceptible person is constant and does not depend on the population density.
  - For susceptible individuals with exposure to the disease, the quarantine proportion (q) is the same for non-infected as for infected people.
  - 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.

Lipsitch Model for SARS

- The populations considered are as follows:
- *susceptible* (*S*) do not have but can catch SARS from infectious individuals.
- *susceptible_quarantined* (*SQ*) do not have SARS, quarantined because of exposure, so cannot catch SARS.
- *exposed* (*E*) have SARS, no symptoms, not yet infectious.
- *exposed_quarantined* (*EQ*) have SARS, no symptoms, not yet infectious, quarantined because of exposure.
- *infectious_undetected* (*IU*) have undetected SARS, infectious.
- *infectious_quarantined* (*IQ*) have SARS, infectious, quarantined, cannot transmit.
- *infectious_isolated* (*ID*) 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* (*IU*) category.
- Those with SARS in other categories are under quarantine or isolation or are not yet infectious.

Initial Diagram for relationships of SARS



Parameters associated with Lipsitch Model

- **b** probability that a contact between person in *infectious_undetected* (*IU*) and someone in *susceptible* (*S*) results in transmission of SARS
- **k** mean number of contacts per day someone from i*nfectious_undetected* (*IU*) has. By assumption, the value does not depend on population density.
- **m** per capita death rate
- $\mathbf{N_0}$ 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* (*IU*) and from *exposed_quarantined* (*EQ*) to *infectious_quarantined* (*IQ*).
  - Thus, 1/*p* is the number of days in the early stages of SARS for a person to be infected but not infectious.

Parameters associated with Lipsitch Model

- **q** fraction per day of individuals in *susceptible* (*S*) who have had exposure to SARS that go into quarantine, either to category *susceptible_quarantined* (*SQ*) or to *exposed_quarantined* (*EQ*)
- **u** fraction per day of those in *susceptible_quarantined* (*SQ*) 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* (*IU*), *infectious_isolated* (*ID*), or *infectious_quarantined* (*IQ*) to category *recovered_immune*.
- **w** fraction per day of those in *infectious_undetected* (*IU*) who are detected and isolated and thus transferred to category *infectious_isolated* (*ID*)

Finding rates of changes of different populations

- Three paths exist for someone to leave *infectious_undetected* (*IU*)
  - to *recovered_immune* at a rate of *v*,
  - to *SARS_death* at a rate of *m*, or
  - to *infectious_isolated* (*ID*) 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 $\mathbf{N_0}$ 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 $\mathbf{(k/N_0)b}$ is the transmission constant.
- As in the SIR model, the product $\mathbf{I_US}$ 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, thefraction ($1 - q$), go into *exposed* (*E*).

Finding rates of changes of different populations

- 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 non-transmission 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 $qk(1 - b)I_US / N_0$.

Reproductive Number

- An important value in evaluating the effectiveness of quarantine and isolation is the **reproductive number *R***,
- Reproductive number is the expected number of secondary infectious cases resulting from an average infectious case once the epidemic is in progress.
- The **basic reproductive number**, 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.

Reproductive Number

- 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 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**, $\boldsymbol{R_0}$, is *kbD*.
- Because the average duration of infectiousness is $1/(v + m + w)$ da, 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

$(kb/(v + m + w))(1-q)$

- The larger *q* is, the smaller R_0 is, and the less severe the impact of the disease is.

Reproductive Number

- 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.
- 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.

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