Introduction to the Mathematics of Infectious Diseases

Vrushali A Bokil

Department of Mathematics
Oregon State University, Corvallis, Oregon

2008 REU Program in Mathematics
Oregon State University, August 1, 2008
The Beginnings of Mathematical Epidemiology

1 Bernoulli: 1760
   • Daniel Bernoulli formulated and solved a model for smallpox in 1760
   • Using his model, he evaluated the effectiveness of inoculating of healthy people against the smallpox virus.

2 Hamer: 1906
   • Hamer formulated and analyzed a discrete time model in 1906 to understand the recurrence of measles epidemics.

3 Ross: 1911
   • Ross developed differential equation models for malaria as a host-vector disease in 1911.
   • He won the second Nobel Prize in Medicine

4 Kermack and McKendrick: 1926
   • Extended Ross’s models.
   • Obtained the epidemic threshold results.
We need to develop models that will assist the decision making process by helping to evaluate the consequences of choosing one of the alternative strategies available. Thus, mathematical models of the dynamics of a communicable disease can have a direct bearing on the choice of an immunization program, the optimal allocation of scarce resources, or the best combination of control or eradication techniques.
A mathematical treatment is indispensable if the dynamics of ecosystems are to be analyzed and predicted quantitatively. The method is essentially the same as that used in such fields as classical and quantum mechanics, molecular biology and biophysics... One must not be enamoured of mathematical models; there is no mystique associated with them... physics and mathematics must be considered as tools rather than sources of knowledge, tools that are effective, but nonetheless dangerous if misused.
Why do Mathematical Modeling?

clarification

- The model formulation process clarifies assumptions, variables, and parameters.
- Models provide conceptual results such as thresholds: basic reproduction numbers, contact numbers, and replacement numbers. Thresholds are critical values for quantities such as population size or vector density that must be exceeded in order for an epidemic to occur.

Simulated Experimentation

- Mathematical models and computer simulations are useful experimental tools for building and testing theories, assessing quantitative conjectures, answering specific questions, determining sensitivities to changes in parameter values and estimating key parameters from data.
Why do Mathematical Modeling? (cont)

- **Complex Transmission Interactions**
  - Transmission Interactions in a Population are very complex: It is difficult to comprehend the large scale dynamics of disease spread. Understanding these interaction characteristics can lead to better approaches to decreasing the transmission of diseases.
  - Mathematical models are used in comparing, planning implementing, evaluating, and optimizing various detection, prevention, therapy and control programs.

- **Realistic Experimenting is Impossible**
  - Experiments with Infectious disease spread in human populations are often impossible, Unethical or expensive.
  - Data is sometimes available after the fact from naturally occurring epidemics and is incomplete due to under reporting.
  - Epidemiological modeling can contribute to the design and analysis of epidemiological surveys, suggest crucial data that should be collected, identify trends, make general forecasts, and estimate the uncertainty in forecasts.
Basic Ideas and Assumptions

Deterministic Models

- For a given model structure, chosen (fixed) parameter values, and particular initial conditions, the model produces the same output each time it is simulated.
- This is one way of simulating infectious disease dynamics
- Reasonable if the sizes of the populations are large.

Compartmental Models

- Populations under study are divided into compartments.
- Assumptions are made about the nature and time rate of transfer from one compartment to another.
- Rates of transfer between compartments are expressed mathematically as derivatives with respect to time of the sizes of the compartments.
- Models are systems of differential equations
Crucial Idea!!!
The derivative function represents the rate of change of that function.

Assumptions
- The community size is constant over the duration of the epidemic and is a large number, call it $N$.
- The infection is transmitted primarily by person-to-person contacts (e.g., measles).
- Individuals are homogeneous and mix uniformly.
- Transmission rates, removal rates are constant.
Basic Compartmental Deterministic Models
SIS, SIR, SEIR

**SIS Model**

$$S \rightarrow I \rightarrow S$$

**SIR Model**

$$S \rightarrow I \rightarrow R$$

**SEIR Model**

$$S \rightarrow E \rightarrow I \rightarrow R$$
The choice of which compartments to include in a model depends on the characteristics of the particular disease being modeled and the purpose of the model.
The SIR Epidemic Model

Additional Assumptions
Ignore demography, i.e., births and deaths

The SIR Epidemic Model

Compartmentalization
- **Susceptibles (S)**: Individuals susceptible to the disease
- **Infectious (I)**: Infected Individuals able to transmit the parasite to others
- **Recovered (R)**: Individuals that have recovered, are immune or have died from the disease and do not contribute to the transmission of the disease

Mathematically:

\[ S = S(t), \quad I = I(t), \quad R = R(t) \quad \text{and} \quad N = S(t) + I(t) + R(t) \]
The Basic SIR Epidemic Model: Contact Rates

The SIR Epidemic Model

- Let $s = S/N$, $i = I/N$ and $r = R/N$.
- Let $\beta = \text{Average number of adequate contacts (i.e., contacts sufficient for transmission) of a person per unit time.}$
- $\frac{\beta I}{N} = \beta i = \text{Average number of contacts with infectives per unit time of one susceptible.}$
- $S = \beta N / N_s = \text{Number of new cases per unit time due to the } S = Ns \text{ susceptibles. (Horizontal Incidence)}$
Consider the “cohort” of members who were all infected at one time and let \( u(q) \) denote the number of these who are still infective \( q \) units after having been infected.

If a fraction \( \alpha \) of these leave the infective class in unit time, then

\[
u' = -\alpha u
\]

whose solution is

\[
u(q) = u(0)e^{-\alpha q}
\]

The fraction of infectives remaining infective \( q \) time units after having become infective is \( e^{-\alpha q} \)

The length of the infective period is distributed exponentially with mean

\[
\int_{0}^{\infty} e^{-\alpha q} dq = 1/\alpha
\]
The Basic SIR Epidemic Model: Waiting Times

The SIR Epidemic Model

The deterministic SIR epidemic model for this process is

\[
\begin{align*}
\frac{dS}{dt} &= -\beta I \frac{S}{N} \\
\frac{dI}{dt} &= \beta I \frac{S}{N} - \alpha I \\
\frac{dR}{dt} &= \alpha I
\end{align*}
\]

The parameters of the model are

- \( \beta = \) the transmission rate (effective contact rate)
- \( \alpha = \) the recovery or removal rate
Let $s = S/N$, $i = I/N$ and $r = R/N$. Dividing the equations for $S$, $I$ and $R$ by $N$ we get the deterministic SIR epidemic model for this process in the form

$$\frac{ds}{dt} = -\beta si$$
$$\frac{di}{dt} = \beta si - \alpha i$$
$$\frac{dr}{dt} = \alpha i$$
An average infective makes contact sufficient to transmit infection with $\beta$ others in unit time.

A fraction $\alpha$ of infectives leave the infective class in unit time.

There is no entry or departure from the population except possibly through death from the disease.
Example 1

- Initial values are: \( i(0) = 0.001, \ s(0) = 0.999, \ r(t) = 0, \)
- Parameter values are: \( \beta = 0.3, \ \alpha = 0.1. \)

Model predicts that there is an epidemic.
Parameter values are: $\beta = 0.3$, $\alpha = 0.1$.

The contact number $R_0 = \frac{\beta}{\alpha} = 3$
Example 2

- Initial values are: $i(0) = 0.001$, $s(0) = 0.999$, $r(t) = 0$.
- Parameter values are: $\beta = 0.3/4$, $\alpha = 0.1$.

Model predicts that the disease dies out.
Parameter values are: $\beta = 0.3/4, \alpha = 0.1$.

The contact number $R_0 = \frac{\beta}{\alpha} = 0.75$.
SIR Epidemic Model:
Two Types of Outcomes

We have seen two types of outcomes

\[ R_0 = 3 \]

Infectives in SIR Model

\[ R_0 = 0.75 \]

Infectives in SIR Model

What values of parameters determine the behavior of the model?
What do Real Curves Look Like?

**Vaccination Status Unknown**
- Black

**Vaccinated**
- White

**Unvaccinated**
- Light Blue

Date:

1999

1999-30

2000

Number:

0 - 300

Apr 11

May 2

Jun 13

Jul 4

Jul 25

Aug 15

Sep 5

Sep 26

Oct 17

Nov 7

Nov 28

Dec 19

Jan 9

Jan 30
Conditions for an Epidemic

Equation for Infecteds

\[
\frac{di}{dt} = \beta si - \alpha i = (\frac{\beta s}{\alpha} - 1)\alpha i
\]

Initially \( s(0) \approx 1 \)

An epidemic occurs if the number of infecteds increases initially

\[
\frac{di}{dt} > 0 \implies \frac{\beta}{\alpha} > 1
\]

The disease dies out if the number of infecteds decreases initially

\[
\frac{di}{dt} < 0 \implies \frac{\beta}{\alpha} < 1
\]

Example 1: \( \frac{\beta}{\alpha} = 3 > 1 \)  
Example 2: \( \frac{\beta}{\alpha} = 0.75 < 1 \)

The number \( \frac{\beta}{\alpha} = R_0 \), is called The Basic Reproduction Number
The Basic Reproduction Number

For the Basic SIR Model

\[ R_0 = \frac{\beta}{\alpha} = \beta \times \frac{1}{\alpha} \]

= (average # of adequate contacts of a person/unit time)
× (mean waiting time in the infectious compartment)

Definition of \( R_0 \)
The mean number of secondary infections generated by a single infected in a completely susceptible population

Conditions for an Epidemic
- If \( R_0 > 1 \) an epidemic occurs in the absence of intervention.
- If \( R_0 < 1 \) the disease dies out.
### Preventing Epidemics

If $R_0 > 1$ an epidemic is prevented when $R_0 s(0) < 1$. Thus, if the initial susceptible fraction has been reduced to less than $1/R_0$, for example by immunization, then an epidemic can be prevented.

### How large Will the Outbreak be?

We can calculate this from the equations.
The SIR Endemic Model

Additional Assumptions
Include demography, i.e., births and deaths

The SIR Endemic Model

- Births
- Transmission
- Recovery
- Deaths
The Basic SIR Deterministic Endemic Model

- An infection is endemic in a community when transmission persists.
- It requires replenishment of susceptibles.
- This happens by births, so we add births and deaths.
- We are now working on longer time scales.

Let $s = S/N$, $i = I/N$ and $r = R/N$. The SIR endemic model is

\[
\frac{ds}{dt} = \lambda - \lambda s - \beta si
\]

\[
\frac{di}{dt} = \beta si - \alpha i - \lambda i
\]

\[
\frac{dr}{dt} = \alpha i - \lambda r
\]

The parameters of the model are

- $\beta =$ the transmission rate (effective contact rate)
- $\alpha =$ the recovery or removal rate
- $\lambda =$ birth, death rate
SIR Endemic Model: Phase Portrait, Disease-Free Equilibrium

- Parameter values are: $\lambda = 1/60$, $\beta = 1.05$, $\alpha = 1/3$.
- The contact number $R_0 = \frac{\beta}{\alpha + \lambda} = 0.5$
Parameter values are: $\lambda = \frac{1}{60}$, $\beta = 1.05$, $\alpha = \frac{1}{3}$.

The contact number $R_0 = \frac{\beta}{\alpha + \lambda} = 3$
Endemic Equilibrium

- The solution to the endemic SIR model eventually settles down to a steady state.
- We determine this steady state by solving the equations

\[
\frac{ds}{dt} = 0, \quad \text{and} \quad \frac{di}{dt} = 0
\]

- At equilibrium we have

\[
s_e = \frac{\alpha + \lambda}{\beta} = \frac{1}{R_0} \quad \text{and} \quad i_e = \frac{\lambda(R_0 - 1)}{\beta}
\]
Example

- $N = 1,000,000$, $R_0 = 15$ (e.g., measles)
- $\lambda = 1/(70 \times 365)$ (life expectancy of 70 years)
- $\alpha = 1/7$ (mean infectious period of 1 week)

**Equilibrium Values**

- $s_e = 1/15$, i.e., $1,000,000/15 = 66,667$ susceptibles
- $i_e = [7/(70 \times 365)] \times (1 - 1/15)$, i.e., 256 infecteds

In practice, numbers fluctuate around these values because of random fluctuations and seasonal variations in $\beta$. 
Limitations of Models

- The two classic models presented assume that the total population size remains constant.
- They assume that the population is uniform and homogeneously mixing. Mixing depends on many factors including age.
- Different geographic and social-economic groups have different contact rates.
- These models ignore random effects, which can be very important when $s$ or $i$ are small, e.g., during early stages.
Conclusions

- Different deterministic models can be constructed by choosing different number and types of compartments.
- Analysis based on theory of dynamical systems.
- Modeling clarifies what the underlying assumptions are.
- Model analysis and simulation predictions suggest crucial data that should be gathered.
- Model analysis and simulation suggest control strategies that could be implemented.
- Estimates of $R_0$ for various diseases, although crude ballpark estimates for the vaccination-acquired immunity level in a community required for herd immunity, are useful for comparing diseases.
Present and Future Work: A Model for BYDV

- Undergraduate student: Samuel Potter (U. of Minnesota, Mathematics)
- PhD students: Carrie Manore (Mathematics), Sean Moore (Zoology)
- OSU Faculty: Elizabeth Borer (Zoology), Phil Rossignol (Fisheries and Wildlife) and Vrushali Bokil (Mathematics)
- Outside Faculty: Parviez Hosseini (Princeton, Ecology and Evolutionary Biology)
References and Further Reading I

N. T. J. Bailey.
*The Mathematical Theory of Infectious Diseases.*

A. Okubo.
*Diffusion and Ecological Problems: Mathematical Models.*

Herbert W. Hethcote.
The Mathematics of Infectious Diseases.

Fred Brauer.
Basic Ideas of Mathematical Epidemiology.
Niels G Becker
How does mass immunization affect disease incidence?

Mathematical Modeling of Infectious Diseases: Dynamics and Control, Workshop organized by Institute for Mathematical Sciences (NUS) and Regional Emerging Diseases Intervention (REDI) Centre, Singapore, Oct 2005.