

Mathematical Modeling of Epidemics

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Abstract

Each year, millions of people worldwide die from infectious diseases such as measles, malaria, tuberculosis, HIV. While there are many complicating factors, simple mathematical models can provide much insight into the dynamics of disease epidemics and help officials make decisions about public health policy. In this talk, I will discuss two of the classical, and still much used, deterministic epidemiological models for the local spread of a disease. I will then consider a reaction-diffusion model, Fisher's equation, and a new integro-differential equation model for the spread of an epidemic in space.

Outline

- Introduction
- The Simple Epidemic, or SI , Model
- The General Epidemic, or SIR , Model
- Fisher's Equation
- A New Model
- Conclusion

Introduction

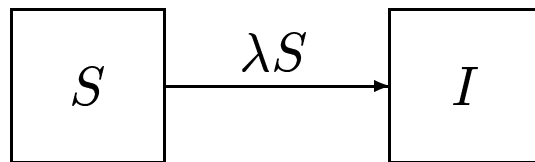
- Epidemics in History
 - Plague in 14th Century Europe killed 25 million
 - Aztecs lost half of 3.5 million to smallpox
 - 20 million people in influenza epidemic of 1919
- Diseases at Present
 - 1 million deaths per year due to malaria
 - 1 million deaths per year due to measles
 - 2 million deaths per year due to tuberculosis
 - 3 million deaths per year due to HIV
 - Billions infected with these diseases

Introduction, Continued

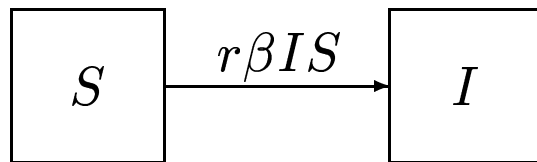
- History of Epidemiology
 - Hippocrates's *On the Epidemics* (circa 400 BC)
 - John Graunt's *Natural and Political Observations made upon the Bills of Mortality* (1662)
 - Louis Pasteur and Robert Koch (middle 1800's)
- History of Mathematical Epidemiology
 - Daniel Bernoulli showed that inoculation against smallpox would improve life expectancy of French (1760)
 - Ross's Simple Epidemic Model (1911)
 - Kermack and McKendrick's General Epidemic Model (1927)

The Simple Epidemic, or SI , Model

- We divide the population into two groups:
 - Susceptible individuals, $S(t)$
 - Infective individuals, $I(t)$



- Assumptions
 - Population size is large and constant, $S(t) + I(t) = N$
 - No birth, death, immigration or emigration
 - No recovery
 - No latency
 - Homogeneous mixing
 - Infection rate is proportional to the number of infectives, i.e. $\lambda = r\beta I$



- A pair of ordinary differential equations describes this model:

$$\frac{dS}{dt} = -r\beta I(t)S(t)$$

$$\frac{dI}{dt} = r\beta I(t)S(t)$$

- But $N = S(t) + I(t)$, so this is equivalent to

$$S(t) = N - I(t)$$

$$\frac{dI}{dt} = r\beta I(t)(N - I(t))$$

The differential equation is known as the **logistic growth equation**, proposed by Verhulst (1845) for population growth.

- We have a nonlinear ODE,

$$\frac{dI}{dt} = r\beta I(t)(N - I(t))$$

This is separable so we divide,

$$\frac{1}{I(t)(N - I(t))} \frac{dI}{dt} = r\beta$$

and integrate,

$$\int_0^t \frac{1}{I(t)(N - I(t))} \frac{dI}{dt} dt = \int_0^t r\beta dt$$

$$\int_{I(0)}^{I(t)} \frac{1}{u(N - u)} du = \int_0^t r\beta dt$$

$$\frac{1}{N} \int_{I(0)}^{I(t)} \frac{1}{u} + \frac{1}{N - u} du = \int_0^t r\beta dt$$

$$\left[\ln(u) - \ln(N - u) \right]_{u=I(0)}^{I(t)} = r\beta N t$$

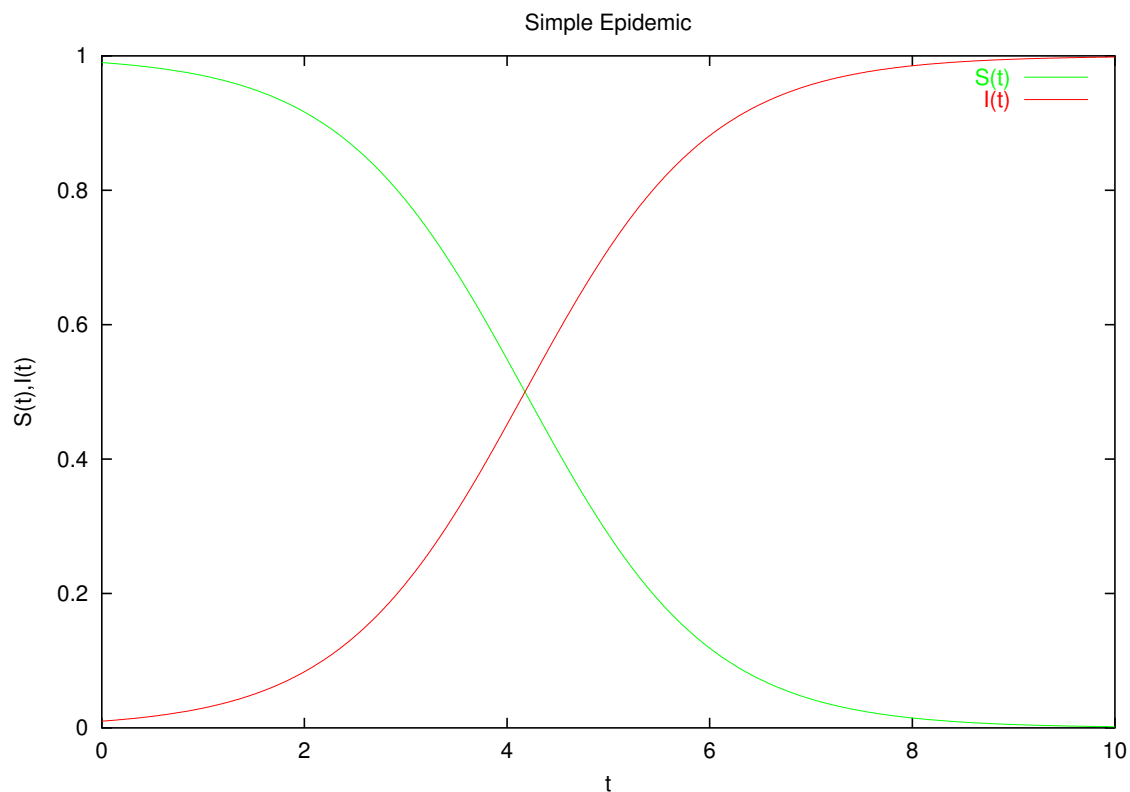
Some algebra gives

$$I(t) = \frac{I(0)N}{I(0) + (N - I(0))e^{-r\beta N t}}$$

- We have the **logistic curve**

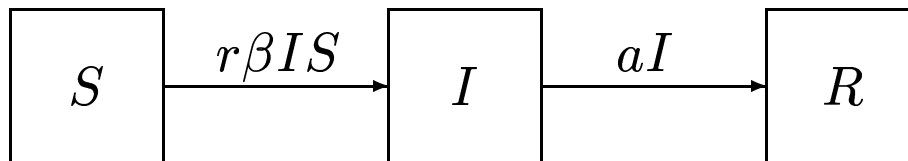
$$I(t) = \frac{I(0)N}{I(0) + (N - I(0))e^{-r\beta Nt}}$$

As $t \rightarrow +\infty$, $I \rightarrow N$, so **everyone becomes infected.**

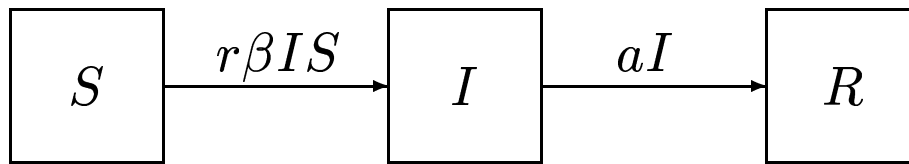


The General Epidemic, or SIR , Model

- We divide the population into three groups:
 - Susceptible individuals, $S(t)$
 - Infective individuals, $I(t)$
 - Recovered individuals, $R(t)$



- Assumptions
 - Population size is large and constant,
 $S(t) + I(t) + R(t) = N$
 - No birth, death, immigration or emigration
 - No latent period
 - Homogeneous mixing
 - Infection rate is proportional to the number of infectives, i.e. $\lambda = r\beta I$
 - Recovery rate is constant



- A system of three ordinary differential equations describes this model:

$$\frac{dS}{dt} = -r\beta I(t)S(t)$$

$$\frac{dI}{dt} = r\beta I(t)S(t) - aI(t)$$

$$\frac{dR}{dt} = aI(t)$$

or, equivalently,

$$\frac{dS}{dt} = -r\beta I(t)S(t)$$

$$\frac{dI}{dt} = r\beta I(t)S(t) - aI(t)$$

$$R(t) = N - S(t) - I(t)$$

- We have the nonlinear system

$$\frac{dS}{dt} = -r\beta I(t)S(t) \qquad \frac{dI}{dt} = r\beta I(t)S(t) - aI(t)$$

Divide to get

$$\frac{dI}{dS} = \frac{a - r\beta S}{r\beta S} = \frac{a}{r\beta S} - 1$$

which is separable and gives a **conserved quantity**

$$S(t) + I(t) - \frac{a}{r\beta} \ln S(t) = S(0) + I(0) - \frac{a}{r\beta} \ln S(0)$$

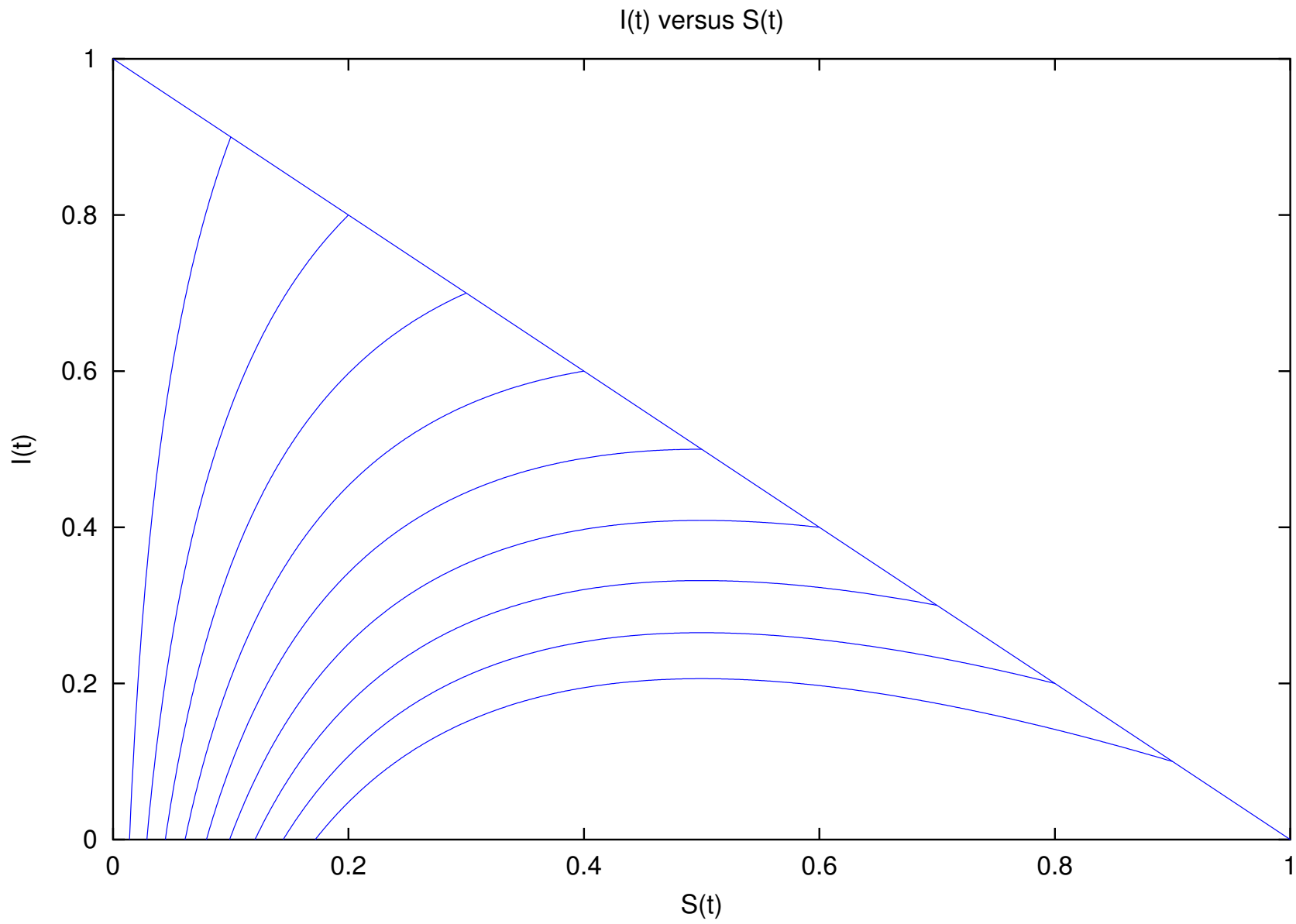
- Similarly,

$$\frac{dS}{dt} = -r\beta I(t)S(t) \qquad \frac{dR}{dt} = aI(t)$$

gives

$$\frac{dS}{dR} = -\frac{r\beta}{a} S(t) \quad \Rightarrow \quad S(t) = S(0)e^{-\frac{r\beta}{a}(R(t)-R(0))} \\ \geq S(0)e^{-\frac{r\beta}{a}N} > 0$$

Not everyone gets infected.



- How many new infectives are caused by a single infective introduced into a population consisting entirely of susceptibles?

In this case the second ODE at the time the infected is introduced is

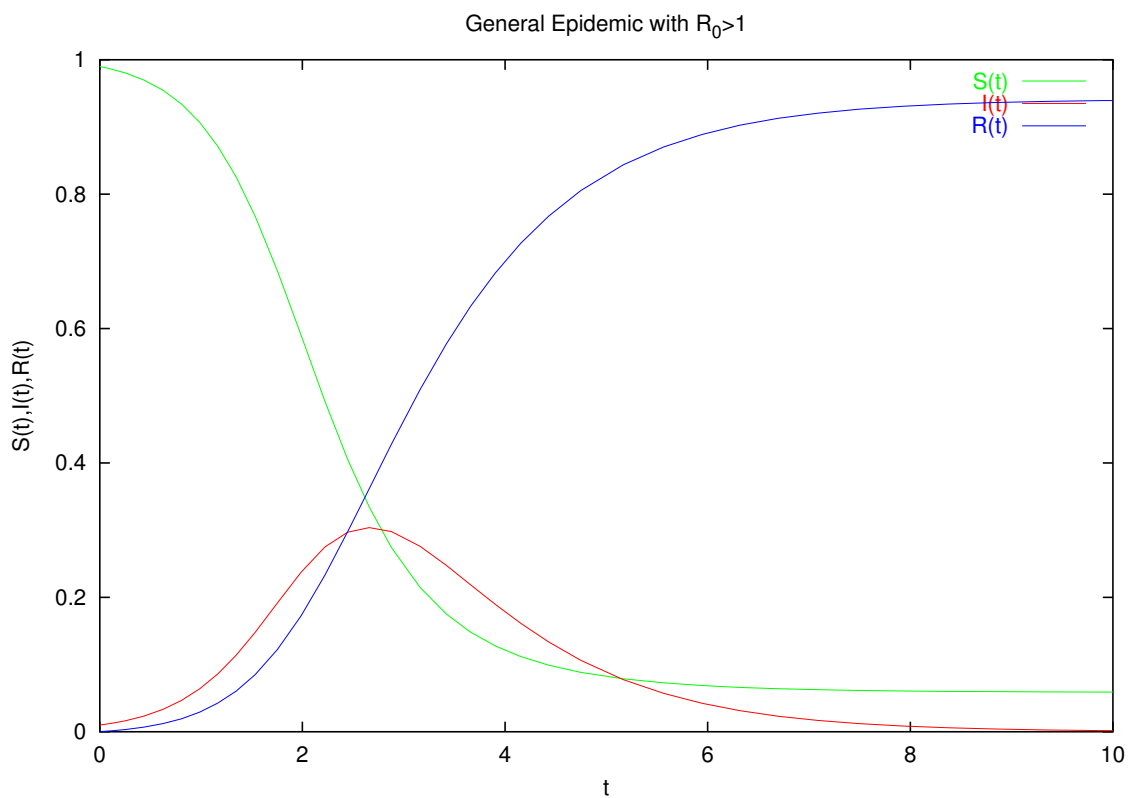
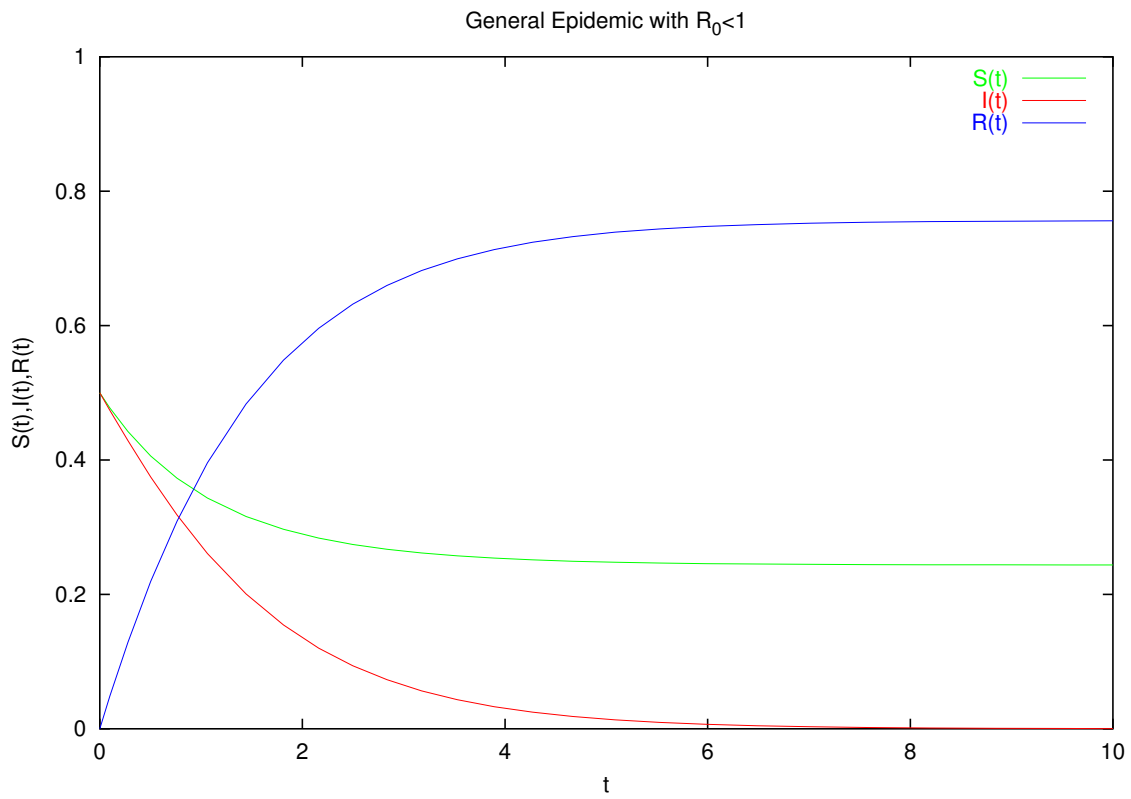
$$\frac{dI}{dt} \approx (r\beta N - a)I(t).$$

So if $r\beta N - a > 0$ then $I(t)$ increases.

Define, the **basic reproductive number**,

$$R_0 = \frac{r\beta N}{a}$$

and so if $R_0 > 1$ then $I(t)$ increases and we have an **epidemic**.



Fisher's Equation

- Let $S(t, x)$ and $I(t, x)$ be the **density** of susceptibles and infectives
- Assumptions
 - Population density is constant, $S(t, x) + I(t, x) = N$
 - No birth or death
 - No recovery or latent period
 - Only local infection
 - Infection rate is proportional to the number of infectives, i.e. $\lambda = r\beta I$
 - Individuals disperse by a diffusion process, with diffusion constant D
- The pair of partial differential equations describes the model

$$\begin{aligned}\frac{\partial S}{\partial t} &= -r\beta I(t, x)S(t, x) + D\frac{\partial^2 S}{\partial x^2} \\ \frac{\partial I}{\partial t} &= r\beta I(t, x)S(t, x) + D\frac{\partial^2 I}{\partial x^2}\end{aligned}$$

- Or, equivalently,

$$S(t, x) = N - I(x, t)$$

$$\frac{\partial I}{\partial t} = r\beta I(t, x)(N - I(t, x)) + D\frac{\partial^2 I}{\partial x^2}$$

The PDE is known as **Fisher's Equation**. It was introduced by Fisher (1937) for the spread of a gene in a population.

- We look for **traveling waves**.

Let $I(x, t) = \tilde{I}(z)$ with $z = x - ct$. Then the PDE becomes an ODE,

$$-c\frac{d\tilde{I}}{dz} = r\beta\tilde{I}(z)(N - \tilde{I}(z)) + D\frac{d^2\tilde{I}}{dz^2}$$

- This has two equilibria, $\tilde{I} = 0$ and $\tilde{I} = N$.

Linearizing about $\tilde{I} = 0$ gives the **linear** ODE

$$D\frac{d^2\tilde{I}}{dz^2} + c\frac{d\tilde{I}}{dz} + r\beta N\tilde{I}(z) = 0$$

which has a solution of the form $\tilde{I}(z) = Ae^{\alpha z}$.

- Thus, we have the characteristic equation

$$D\alpha^2 + c\alpha + r\beta N = 0$$

and so

$$\alpha = \frac{-c \pm \sqrt{c^2 - 4Dr\beta N}}{2D}$$

- If $c^2 - 4Dr\beta N < 0$, then $\alpha = u \pm iv$ and

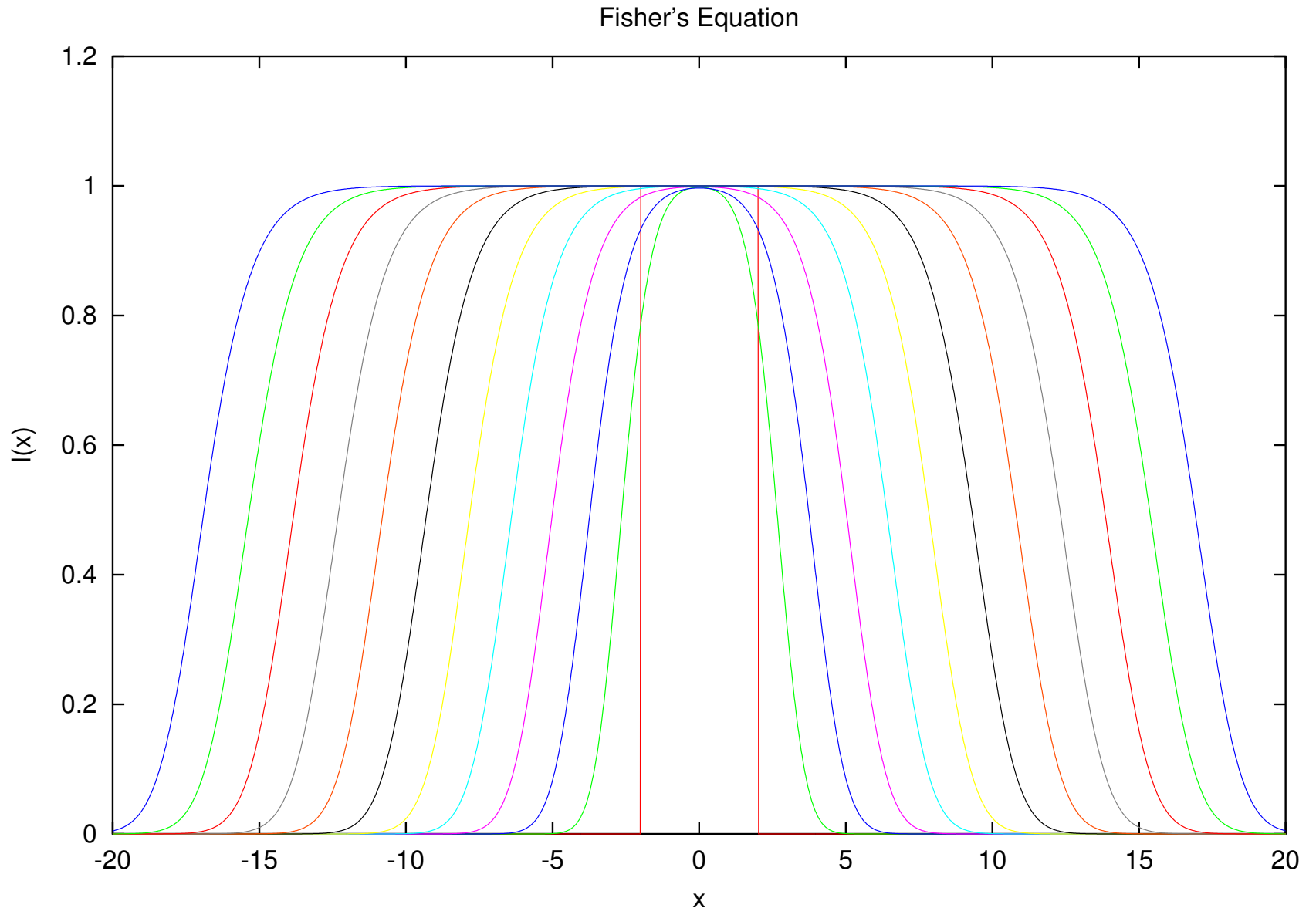
$$\tilde{I}(z) = e^{uz}(A_1 \sin(vz) + A_2 \cos(vz))$$

But that means for some z , $\tilde{I}(z) < 0$.

- We require $c^2 - 4Dr\beta N \geq 0$, which implies

$$|c| \geq c_{\min} = 2\sqrt{Dr\beta N}$$

- For many initial conditions, the solutions of the *PDE* tend to the traveling wave with minimum wave speed.



A New Model

- Same idea as Fisher's Equation, except with general dispersal
- Assumptions
 - Population density is constant, $S(t, x) + I(t, x) = N$
 - No birth or death
 - No recovery or latent period
 - Only local infection
 - Infection rate is proportional to the number of infectives, i.e. $\lambda = r\beta I$
 - Individuals leave at rate D
 - Proportion of individuals leaving y and going to x is $k(x, y)$
- The pair of integro-differential equations describes the model

$$\frac{\partial S}{\partial t} = -r\beta I(x, t)S(x, t) - DS(x, t) + D \int_{\Omega} k(x, y)S(y, t)dy$$

$$\frac{\partial I}{\partial t} = r\beta I(x, t)S(x, t) - DI(x, t) + D \int_{\Omega} k(x, y)I(y, t)dy$$

- Equivalently,

$$\begin{aligned}
 S(x, t) &= N - I(x, t) \\
 \frac{\partial I}{\partial t} &= r\beta I(x, t)(N - I(x, t)) - DI(x, t) \\
 &\quad + D \int_{\Omega} k(x, y) I(y, t) dy
 \end{aligned}$$

- We assume $k(x, y) = k(x - y)$ and $\Omega = \mathbb{R}$
- We look for **traveling waves**. $I(x, t) = \tilde{I}(z)$ with $z = x - ct$ gives

$$-c \frac{d\tilde{I}}{dz} = r\beta \tilde{I}(z)(N - \tilde{I}(z)) - D\tilde{I}(z) + D \int_{\mathbb{R}} k(z - y) \tilde{I}(y) dy$$

- This has two steady-state solutions, $\tilde{I}(z) = 0$ and $\tilde{I}(z) = N$. Linearizing about $\tilde{I}(z) = 0$ gives the **linear** integro-differential equation

$$-c \frac{d\tilde{I}}{dz} = r\beta N \tilde{I}(z) - D\tilde{I}(z) + D \int_{\mathbb{R}} k(z - y) \tilde{I}(y) dy$$

which has a solution of the form $\tilde{I}(z) = Ae^{-\theta z}$.

- This gives the characteristic equation

$$\theta c = r\beta N - D + DM(\theta)$$

where

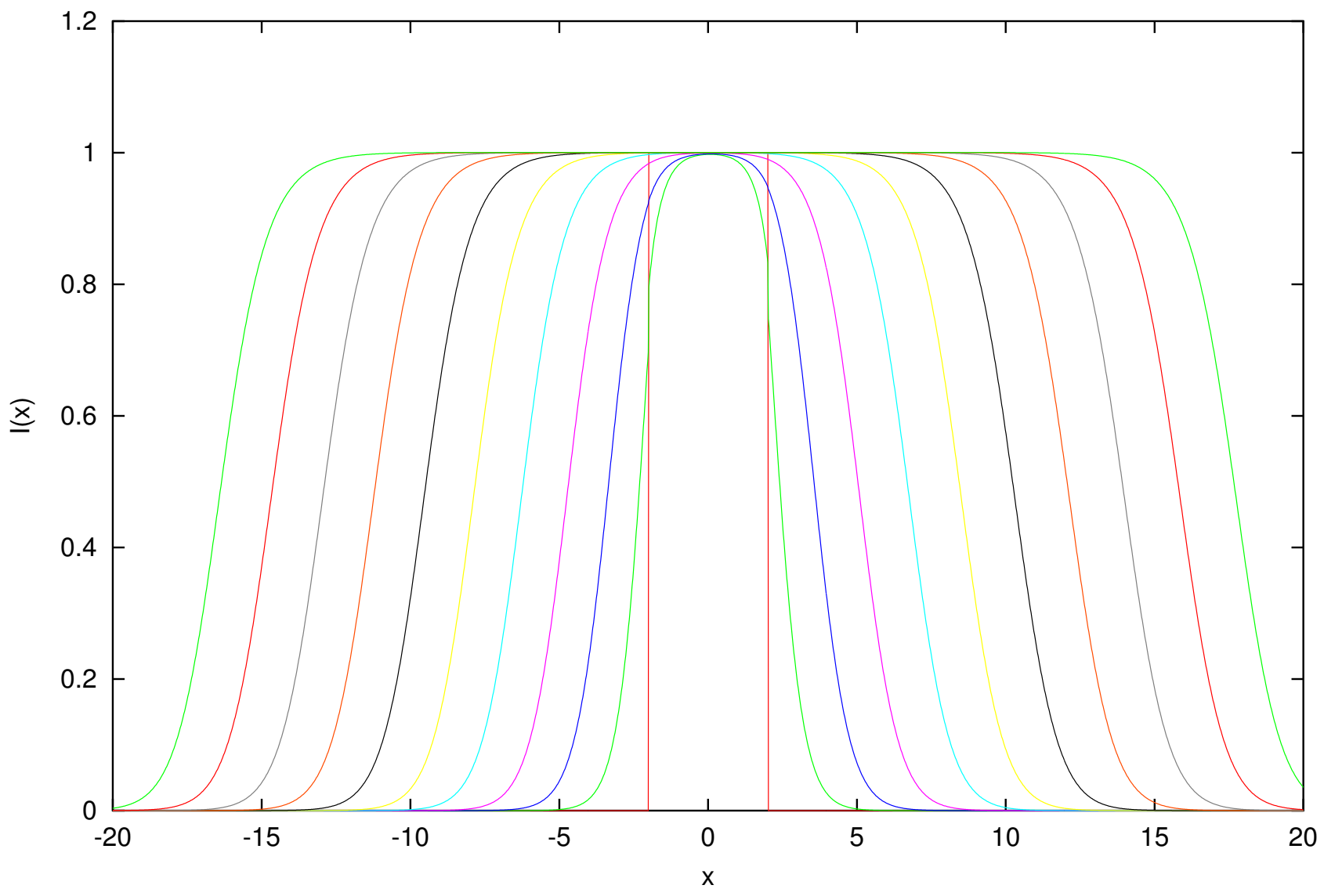
$$M(\theta) = \int_{\mathbb{R}} k(u)e^{\theta u} du$$

- We look for non-oscillatory wave fronts, which gives the minimum wave speed parametrically,

$$\begin{aligned}c_{\min} &= DM'(\theta) \\ r\beta N &= D [1 - M(\theta) + \theta M'(\theta)]\end{aligned}$$

- For many initial conditions, solutions of the full IDE tend to the traveling wave with minimum wave speed.

Integro-Differential Equation



Conclusion

- **Infectious diseases** are a major health problem throughout the world
- **Mathematical modeling** can help to better understand the spread of infectious diseases and to test control strategies
- The simple mathematical tools presented here are the basis for much of mathematical epidemiology
- For greater accuracy for small populations we must use **stochastic models**
- **Diffusion** is a very limited framework for **dispersal** and can be replaced by a more general dispersal

References

- R.M. Anderson and R.M. May. *Infectious Diseases of Humans: Dynamics and Control*. Oxford University Press, Oxford, UK, 1991.
- N.T.J. Bailey. *The Mathematical Theory of Infectious Diseases*. Hafner, New York, 2nd Edition, 1975.
- R.B. Banks. *Growth and Diffusion Phenomena*. Springer-Verlag, New York, 1994.
- D.J. Daley and J. Gani. *Epidemic Modelling: An Introduction*. Cambridge University Press, Cambridge, UK, 1999.
- S.A. Levin, T.G. Hallam and L.J. Gross, Eds. *Applied Mathematical Ecology*. Springer-Verlag, New York, 1989.
- J.D. Murray, *Mathematical Biology*. Springer-Verlag, New York, 2nd Edition, 1993.