Introduction to Contagious Disease Transmission and Dynamics

P8406, Spring Semester, 2016

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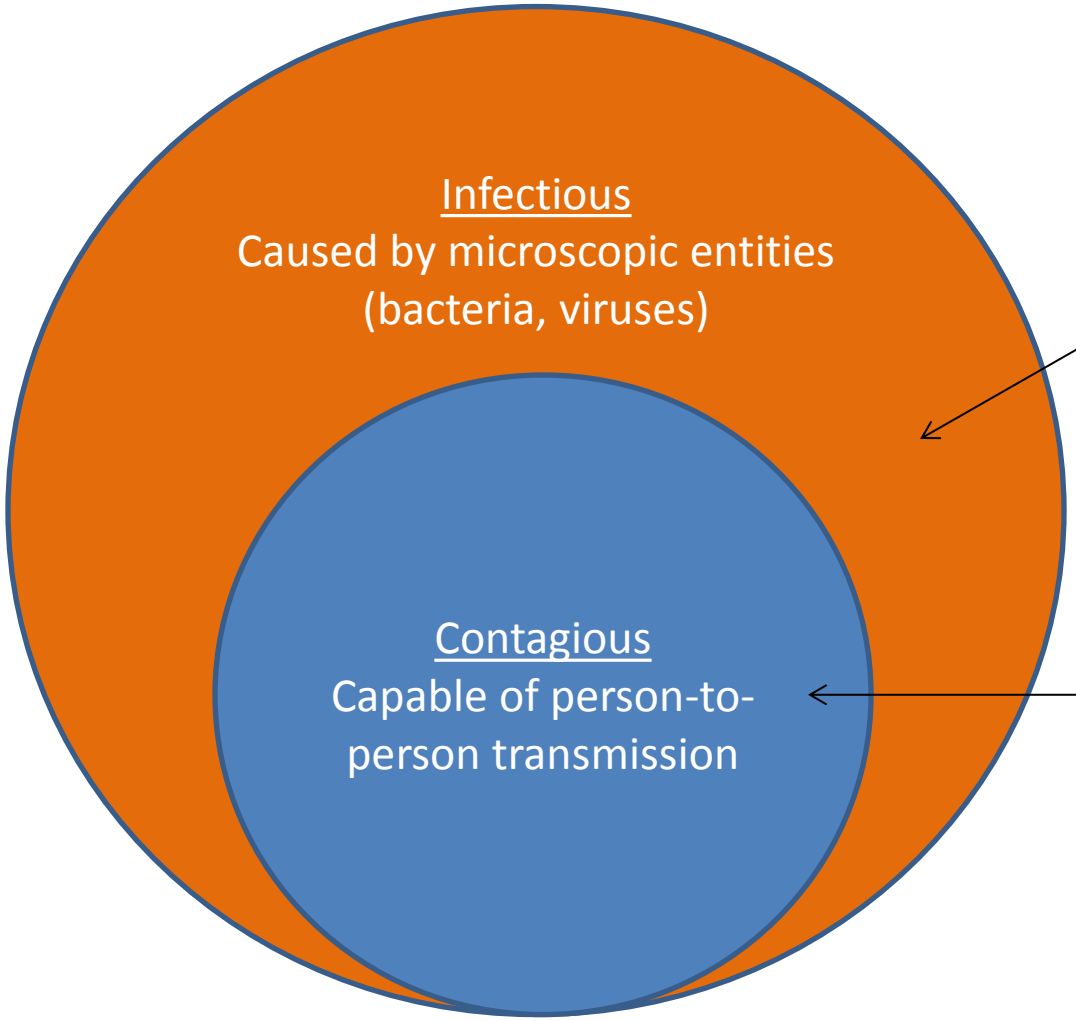
Objectives

- **Part 1: Theory**
  - What's so special about contagious disease?
  - The basic (R_o) and time-specific (R_t) Reproductive Numbers
  - Modeling how contagious disease moves through populations
    - Introduction to compartmental modeling
    - SIS and SIR models
    - Open vs. closed populations
    - The concept of "steady state"
  - Impact of control strategies and "herd immunity" on transmission dynamics
  - The "Epidemic Threshold"
  - Limitations of deterministic (compartmental) models
- **Part 2: Fun and Games!**
  - Playing around with a compartmental model

Some terminology



- Lyme Disease
- Anthrax
- Gangrene
- Shingles*

- HIV
- Flu
- Common Cold
- Measles
- Ebola

Why are contagious diseases different?

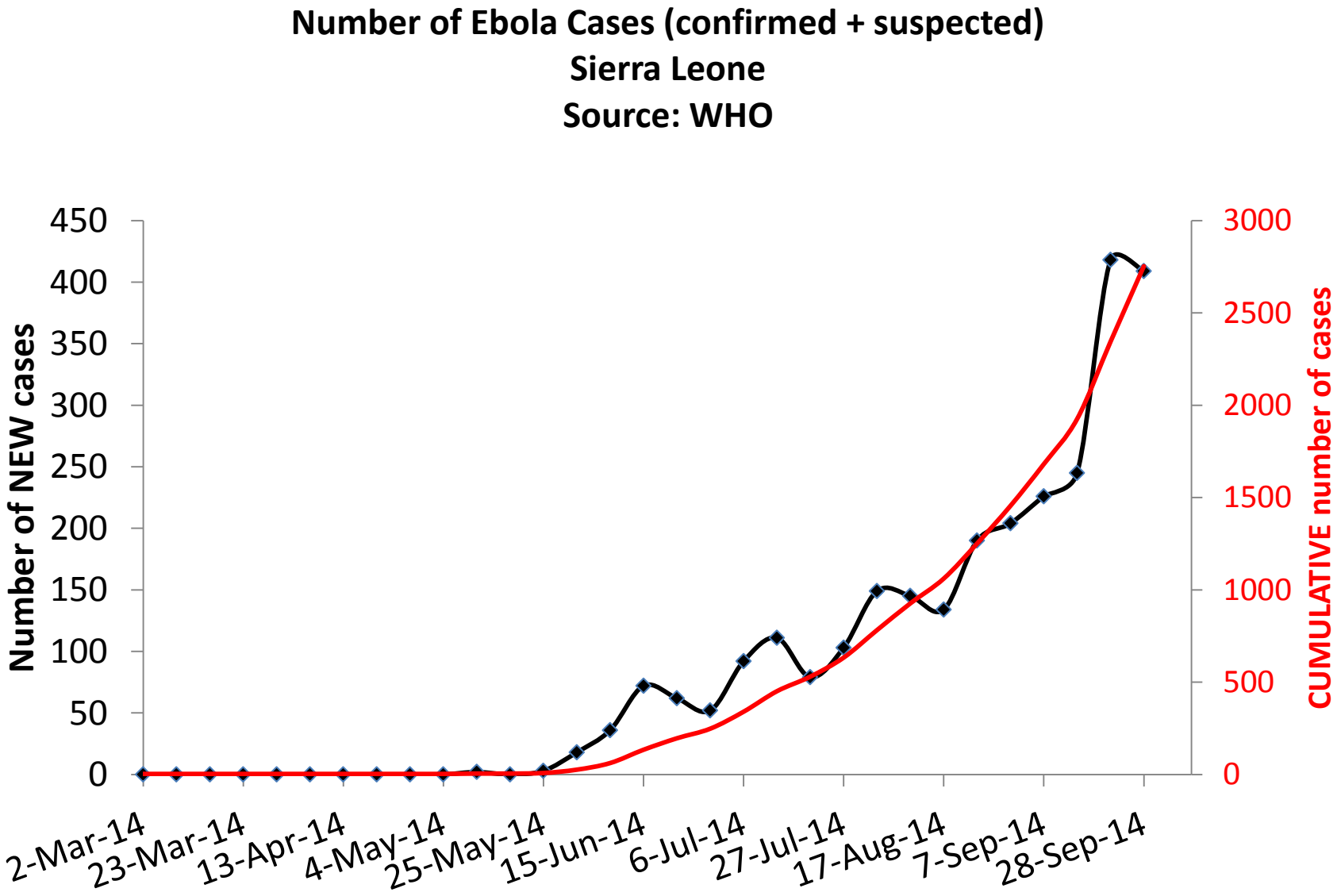
- **Basic English version**
  - they are contagious

- **Math Nerd version**
  - The transmission of infectious diseases creates a **dependence between outcomes** of individuals
  - This violates the assumption of independence of outcomes key to our non-infectious statistical models

Transmission dependence requires different modeling

- For many public health questions involving contagious disease, we already know the necessary cause of the disease
- Instead, we'd like to **model (and predict)** how this contagious disease moves through the population
- Risk factor epidemiology is focused on identifying causes of disease
- Transmission modeling has a different focus

Why do we care about predicting disease transmission?



http://apps.who.int/gho/data/node.ebola-sitrep.other-affected?lang=en

Why do we care about predicting disease transmission?

HEALTH

The New York Times

246 COMMEN

Ebola Cases Could Reach 1.4 Million Within Four Months, C.D.C. Estimates

By DENISE GRADY SEPT. 23, 2014

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Supplement / Vol. 63 / No. 3

September 26, 2014

Estimating the Future Number of Cases in the Ebola Epidemic — Liberia and Sierra Leone, 2014–2015

(Figure 2). Extrapolating trends to January 20, 2015, without additional interventions or changes in community behavior (e.g., notable reductions in unsafe burial practices), the model also estimates that Liberia and Sierra Leone will have approximately 550,000 Ebola cases (1.4 million when corrected for underreporting) (Appendix [Figure 2]). The

Why do we care about modeling disease transmission?

1. To identify the scope and magnitude of the problem
2. To predict the trajectory of the epidemic
3. To better understand how interventions can reduce the impact of a given epidemic
   - and to re-assess the epidemic after intervention

Modeling contagious disease transmission, made (relatively) easy

1. Estimate the number of infectives, and the number of susceptibles, at time t_o
2. With the transmission probability, calculate the number of new infectives and susceptibles at time $t_o + dt$
3. Repeat for time $t_o + 2dt$, $t_o + 3dt$, etc.

Differential equations are your friend

- Differential equations model the rate of change of one variable (e.g., infections) over a second variable (e.g., time)
- We model **rates** of flow between susceptible to infectious using differential equations
  - Key question: What is the rate of change from Susceptible to Infectious?

But first, let's make things easier (aka: assumptions!)

- Instead of modeling an individual's probability or rate of infection, let's model the average flow of a population between different **compartments (disease states)**
  - Susceptible (at risk for getting disease)
  - Latent (has infection, not yet infectious)
  - Infectious (can pass on infection to a susceptible)
  - Resistant (immune)

Compartmental Epidemic Models

- Model the rate of flow between different susceptibility and infectiousness states (compartments) over time
- Based on engineering models of flow of liquid into and out of compartments
  - Therefore, population-based instead of individual-based

We model **rates** of flow between compartments

Compartmental Epidemic Models

- Think of each compartment as a water tank with entrances and exits
  - Assume homogeneity within the compartment
  - Create as many compartments as necessary to make this a realistic assumption
- The population flows from one compartment to the next with a rate
- We use infectious disease principles to estimate this rate, run a model, and see what happens

Model #1: the SIS Model

- Assumes all individuals are either susceptible or infectious at a given time
  - Individuals who become infectious have an average duration of infectiousness, after which they return to susceptible
    - no acquired immunity
  - All individuals who are infected instantly become infectious
    - No “latent” individuals

Model #1: the SIS Model

- What governs the rate of flow from Susceptible to Infectious?
  - Per-contact transmission probability (b)
  - Contact rate (number of contacts per time) (c)
  - Number of infectives in the population (I)
  - The proportion of contacts that are with a susceptible (S/N)

$$Susceptible\ to\ Infectious = -bcI\frac{S}{N}$$

Model #1: the SIS Model

- What governs the rate of flow from Infectious to Susceptible?
  - Number of infectives (I)
  - The recovery rate
    - Which equals 1 over the average duration of infectiousness (d)

$$Infectious\ to\ susceptible = I/d$$

Model #1: the SIS Model

- Let's put this into a differential equation
- The rate of change in S over time:

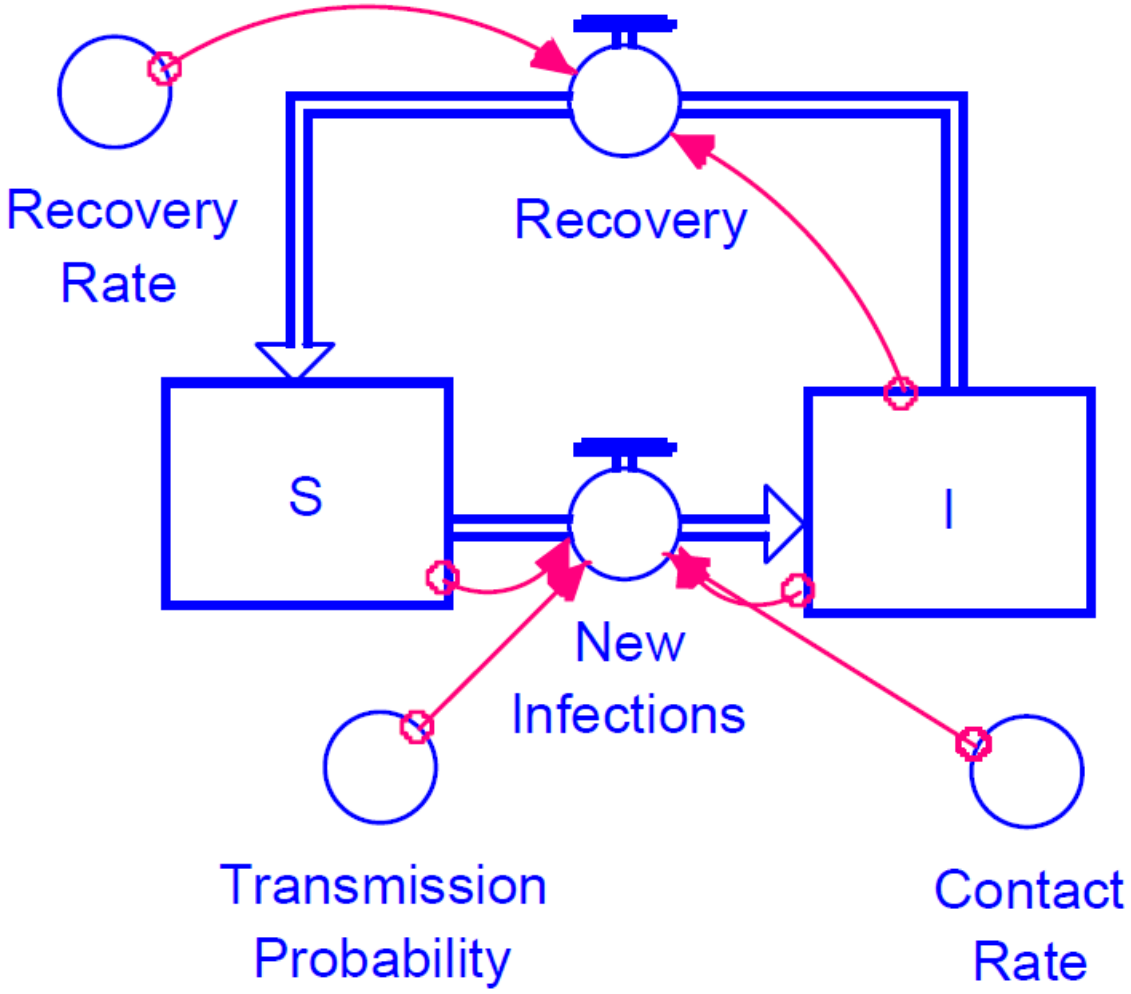
Infectious to Susceptible Susceptible to Infectious

$$\frac{dS}{dT} = \frac{I}{d} - bcI\frac{S}{N}$$

- Similarly, we can write a differential equation for the rate of change in I over time

$$\frac{dI}{dT} = bcI\frac{S}{N} - \frac{I}{d}$$

Model #1: the SIS Model



Transmission probability (b)

- Average "per contact" probability of infection

Contact rate (c)

- Average number of contacts per unit time

Recovery Rate (1/d)

- Rate of transfer from infectious to susceptible
- = 1/ average duration of infectiousness

Where have we seen these before?

The Basic Reproductive Number (R_o)

- Helps us to understand transmission dynamics
- Its components will formulate our models of infectious disease transmission

$$R_o = b*c*d$$

b = transmission probability

c = contact rate

d = duration of infectiousness

$R_o = b*c*d$

b: transmission probability

Average probability that an infected individual will transmit the infection to a susceptible individual during a single contact

c: contact rate

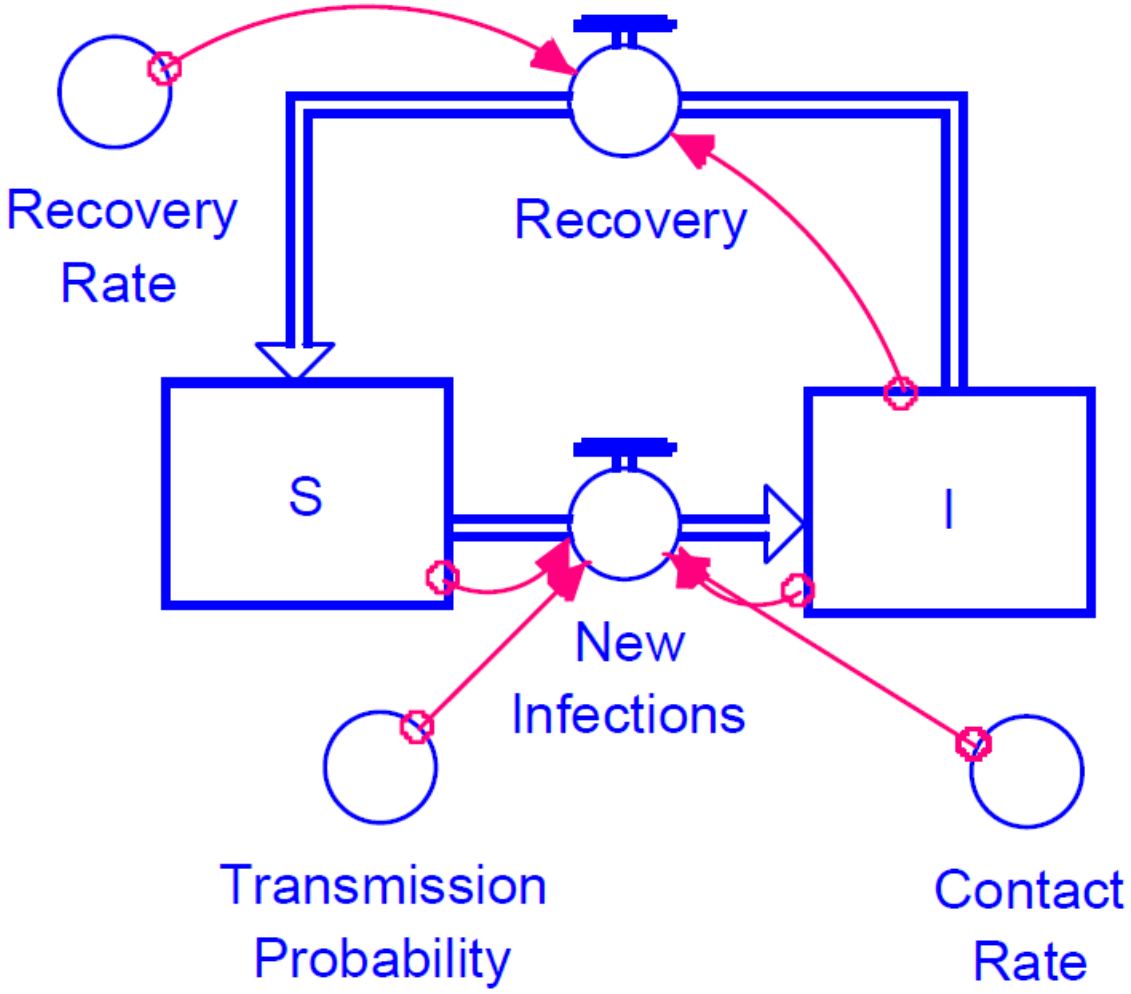
Average number of contacts per unit time

d: duration

Average duration of infectiousness

R_o is the average number of persons infected by one infected individual in an population where everyone is susceptible

Model #1: the SIS Model, R_o, and "Steady State"



Transmission probability (b)

- 0.10 (10%)

Contact rate (c)

- 5 per day

Recovery Rate (1/d)

- 1 per every 3 days

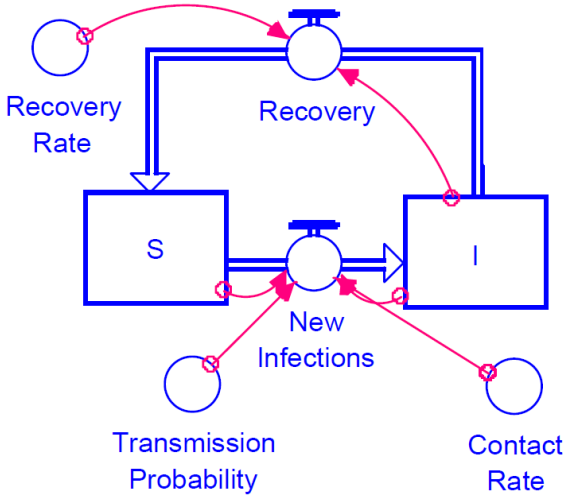
R_o = b*c*d
= 0.1 * 5 * 3
= 1.5

Steady State

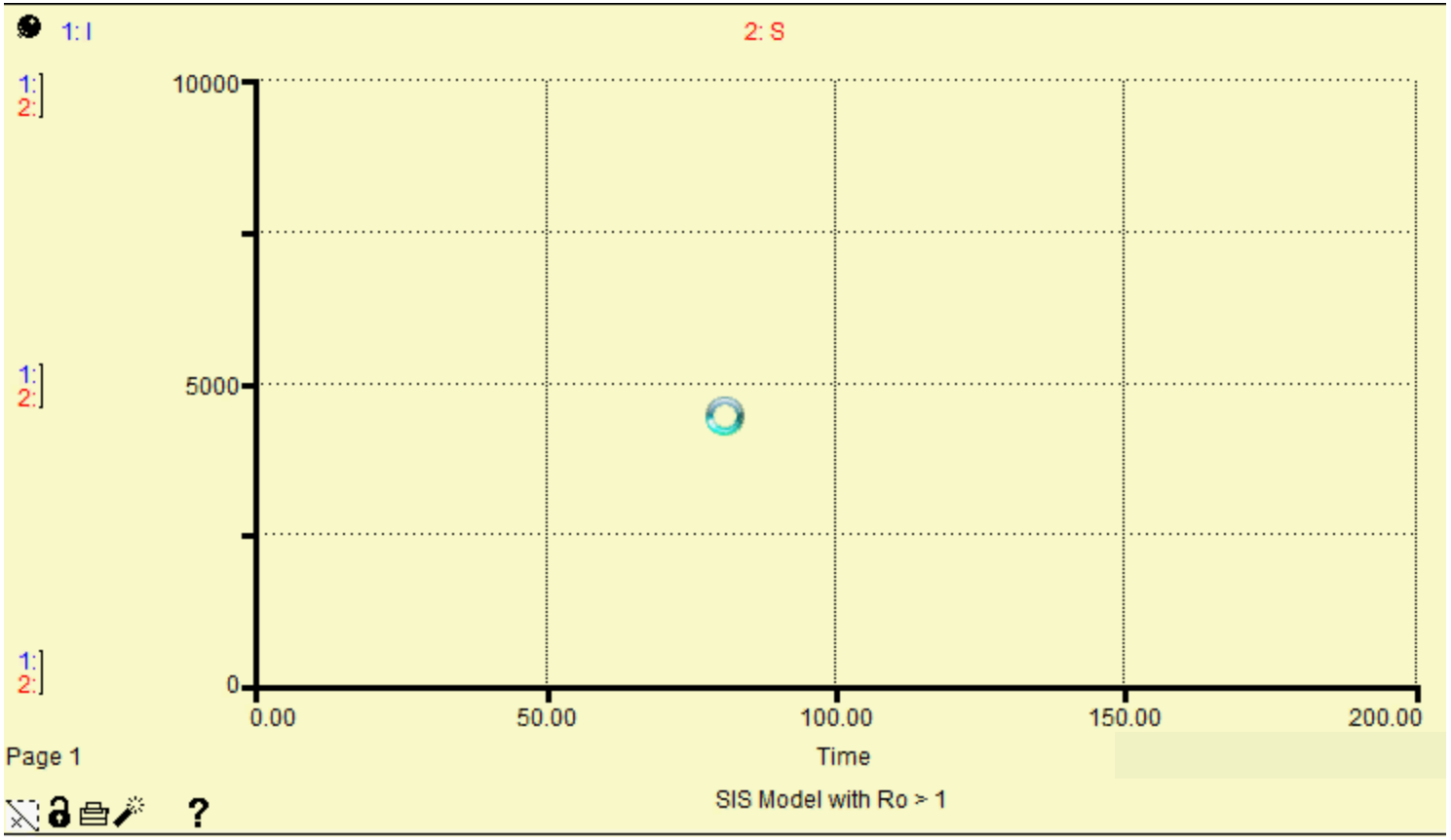
- Steady State: a population whose average distribution into compartments do not change over time
- For contagious disease modeling, steady state can occur in certain circumstances
  - In an SIS model, when the proportion moving from susceptible to infectious equals the proportion moving from infectious to susceptible

Incidence Rate in compartmental models

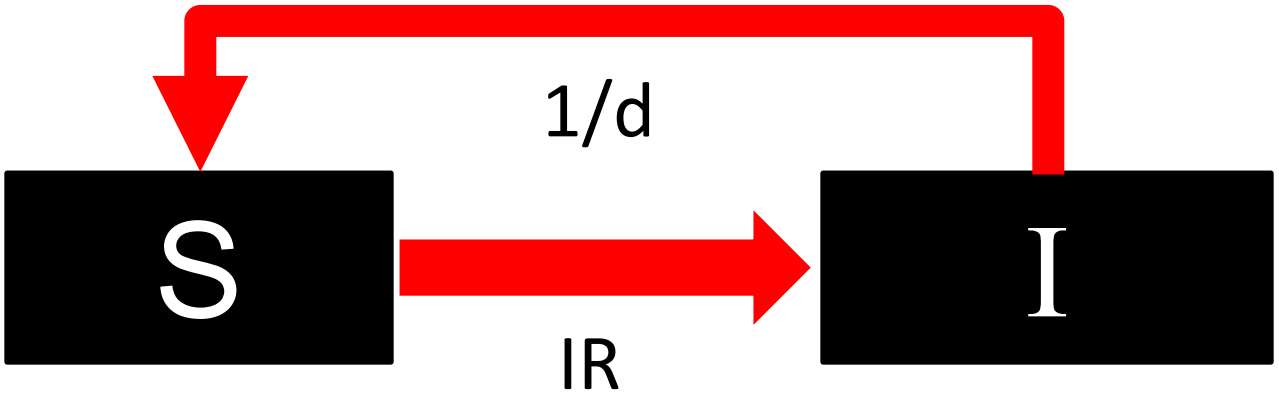
- Average Incidence Rate (Quant Foundations!)
  - number of new cases/person-time at risk
- When we are modeling a dynamic process, the "average" incidence rate is not sufficient
  - We want the incidence rate over increments of time
  - $incidence\ rate\ at\ time\ t = bc\frac{I(t)}{N}$



Compartmental models show us changes over time



Returning to things we glossed over in Quant



At Steady State, The number of Susceptibles and Infectives is staying the same, so the rate of change is zero.

$$\frac{dS}{dT} = \frac{I}{d} - bcI\frac{S}{N} = 0 \rightarrow \frac{I}{d} = bcI\frac{S}{N}$$

What is the relationship between incidence rate and prevalence at steady state?

Returning to things we glossed over in Quant

$$\frac{dS}{dT} = \frac{I}{d} - bcI\frac{S}{N} = 0 \rightarrow \frac{I}{d} = bcI\frac{S}{N}$$

What is the relationship between incidence rate and prevalence at steady state?

$$Prevalence = \frac{I}{N}$$

$$Prevalence\ ODDS = \frac{I/N}{S/N}$$

$$Incidence\ rate = bcI/N$$

So, let's do some substitution

$\frac{I}{d} = bcI\frac{S}{N}$ = IR*S ; move d to the right side and divide both sides by N

$\frac{I}{N} =$ IR*d$\frac{S}{N}$; now move S/N to the left side

Prevalence ODDS = incidence rate * disease duration

Relationship between R_o and steady-state prevalence

For a given R_o, what will the prevalence be at steady state?

$$\frac{I/N}{S/N} = Prevalence\ Odds = IR * d$$

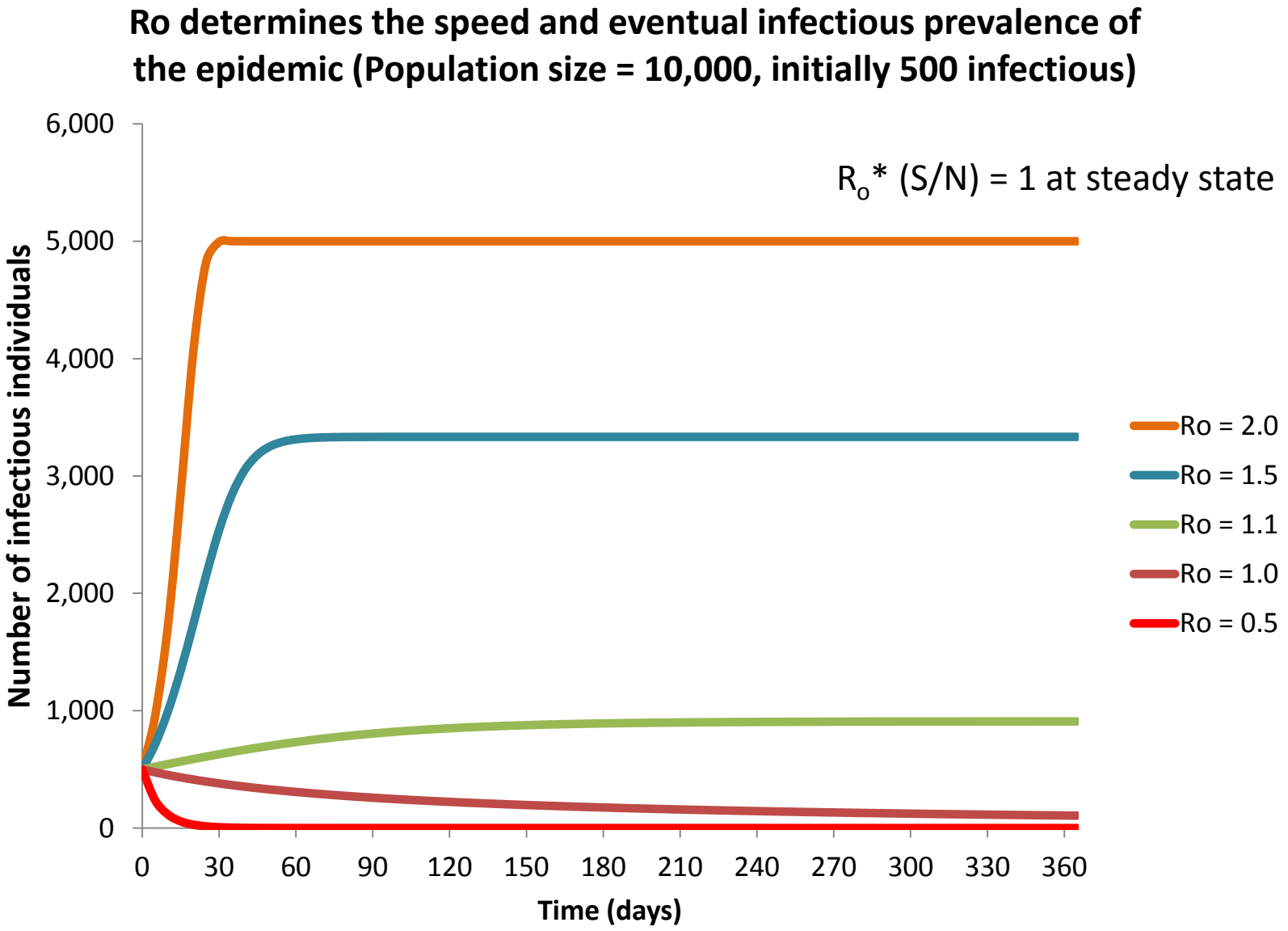
But IR = bc$\frac{I}{N}$; so Prevalence Odds = bc$d\frac{I}{N}$ = $R_o \frac{I}{N}$; now cancel out I/N

1/Proportion Susceptible = R_o → **Proportion Susceptible = $1/R_o$**

Since people are either S or I, we can get the proportion Infectious at steady state as a function of the basic reproductive number

Proportion infectious = $1-1/R_0$

Model #1: the SIS Model



The Reproductive number at time t (R(t))

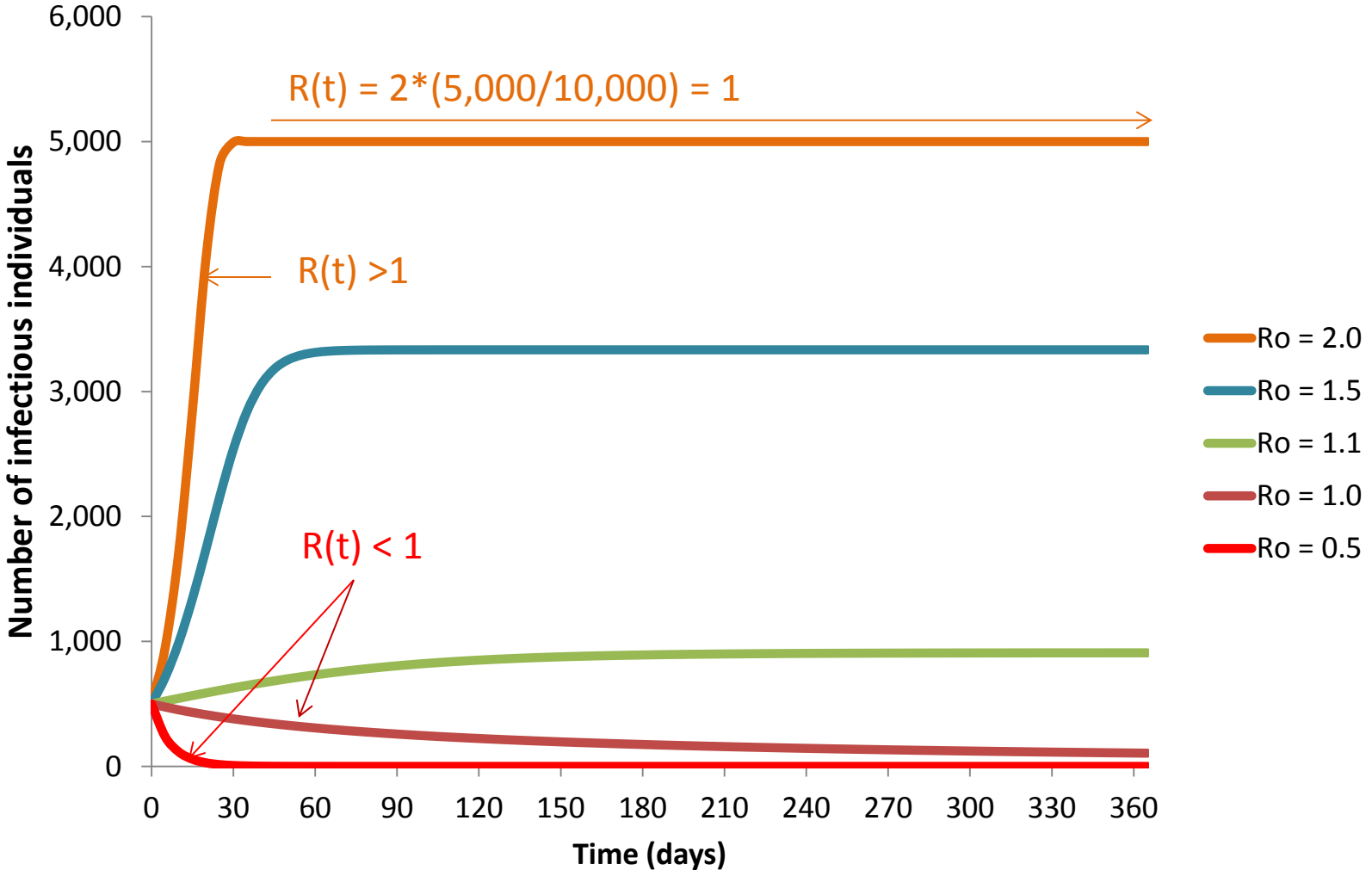
- $R(t) = R_o(S/N)$

- As an epidemic progresses, the proportion of the population (N) that are susceptible decreases, reducing R(t) and slowing the epidemic.

- R(t) = 1 implies steady state prevalence
- R(t) < 1 implies decreasing epidemic
- R(t) > 1 implies rising epidemic

Model #1: the SIS Model

Rt tells you whether the epidemic is currently increasing, decreasing, or at steady state



Which diseases can appropriately be modeled with SIS?

- Many bacterial diseases
  - Gonorrhea
  - Pneumococcal disease
- Very short latent period that we can ignore in most cases (3-7 days)
- Does not convey immunity

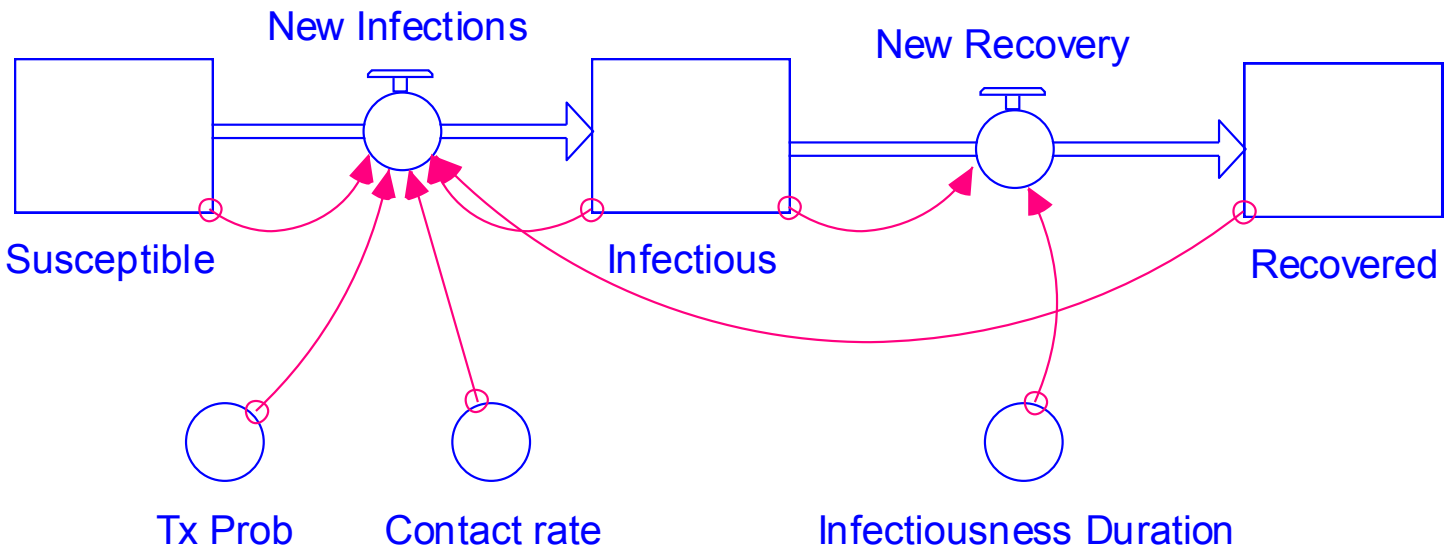
Let's get a bit fancier

- SIS models are unrealistic for many contagious diseases
  - For most, once you are infected, you acquire some level of immunity to future infection
- SIS models assume that you do not acquire any immunity

Model #2: the SIR Model

- More realistic for infectious diseases that convey immunity after **recovery**
  - Recovered individuals no longer return to susceptible compartment, but instead go to a new compartment where they can no longer infect or be infected
  - Can be used to understand the impact of **vaccination** and **herd immunity**
    - **GET YOUR FLU SHOT!**

Model #2: the SIR Model

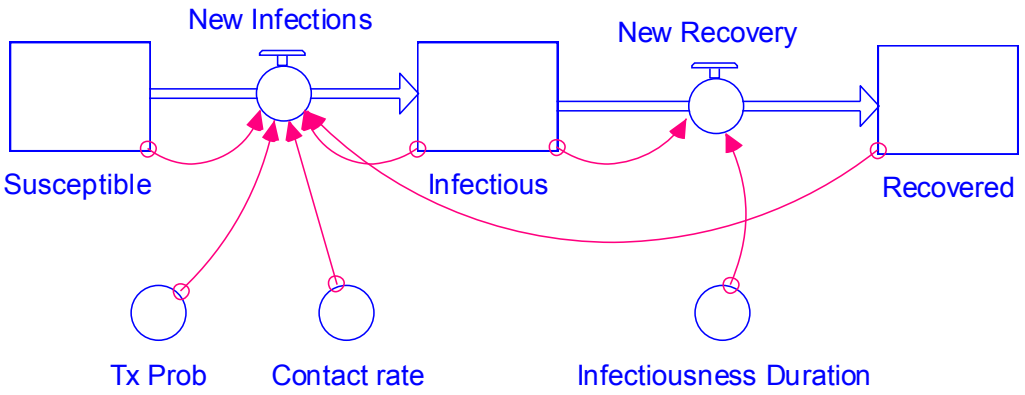


Model #2: the SIR Model: the math

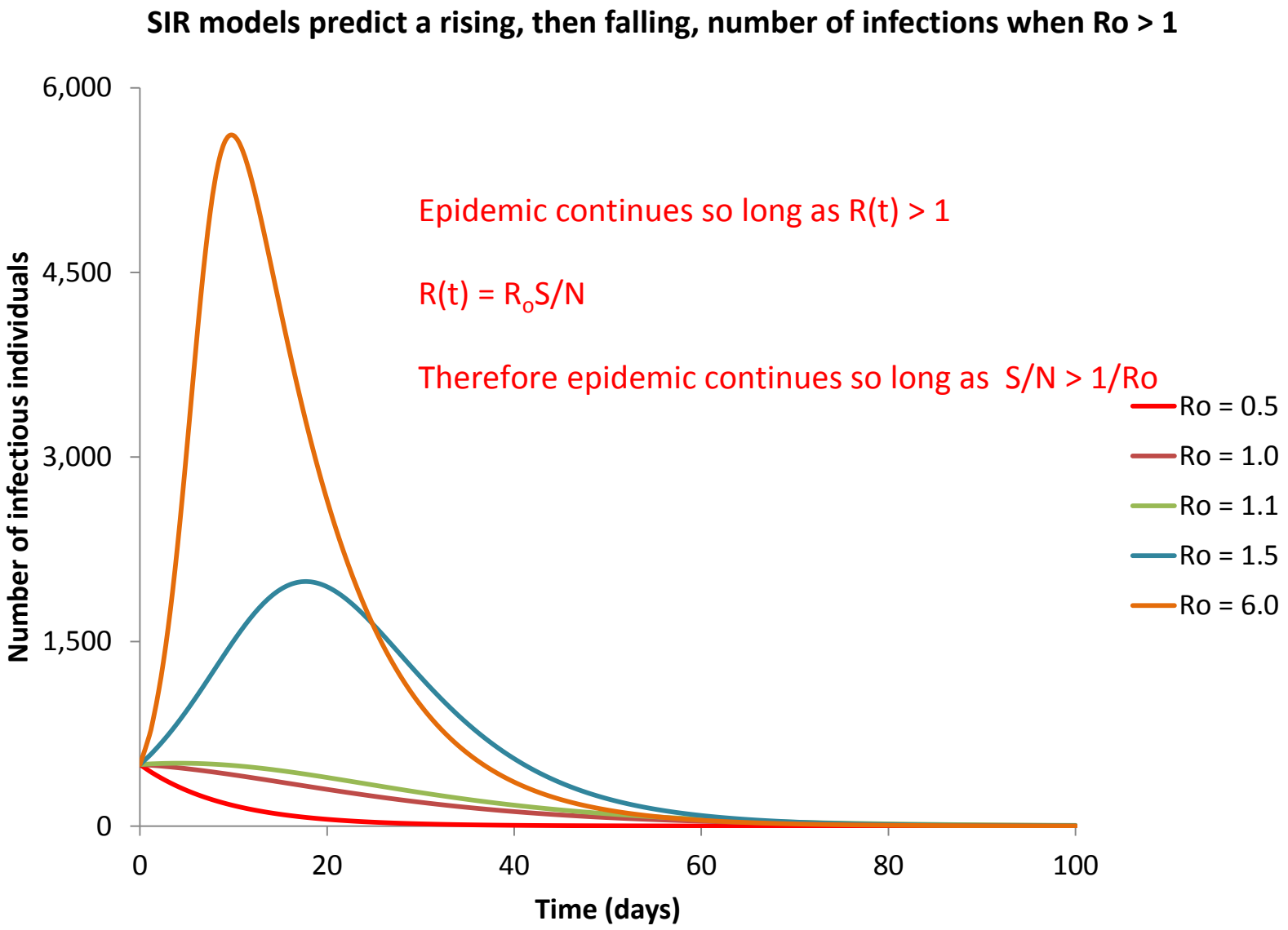
$$\frac{dS}{dT} = -bcI\frac{S}{N}$$

$$\frac{dI}{dT} = bcI\frac{S}{N} - \frac{I}{d}$$

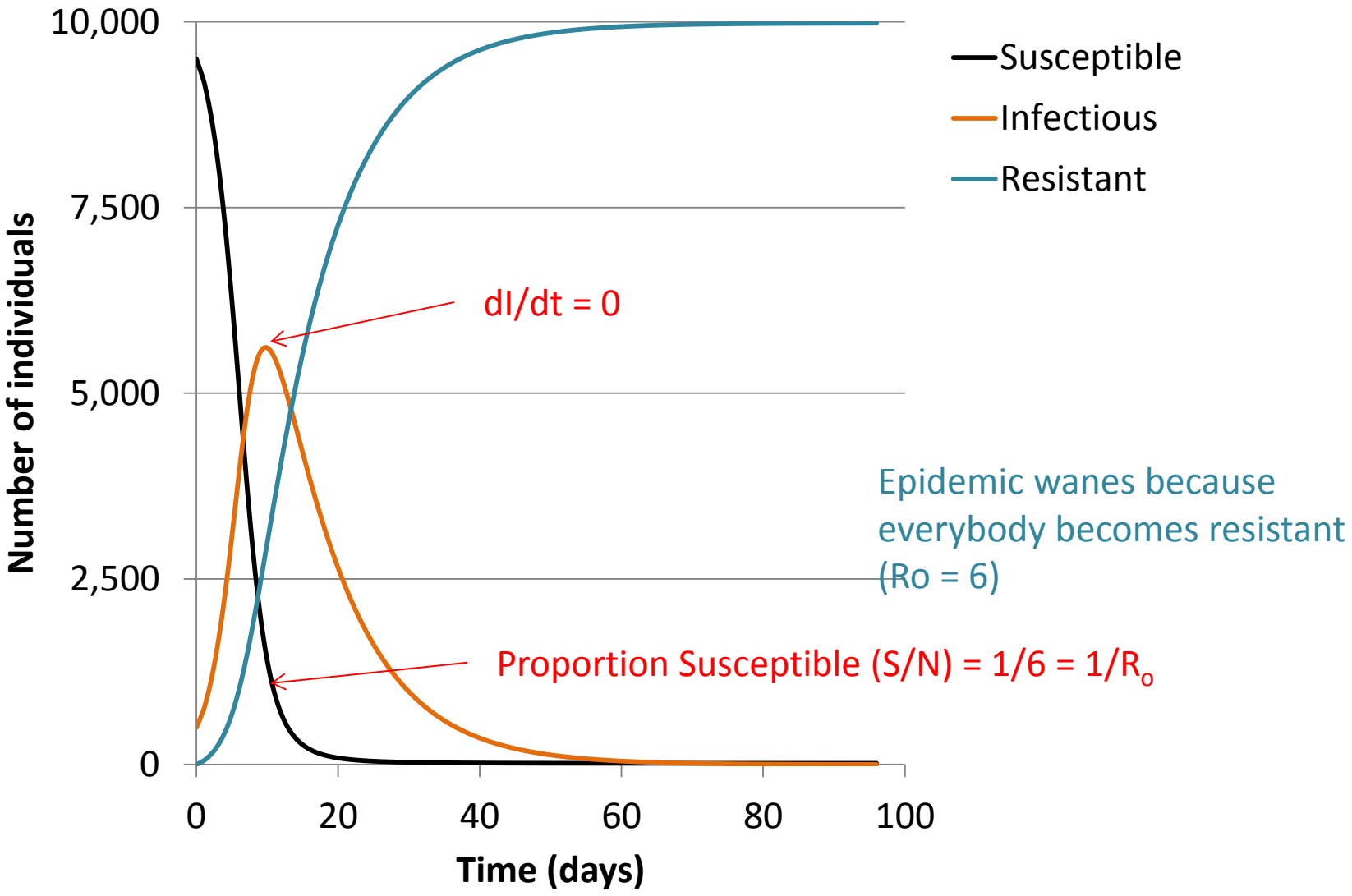
$$\frac{dR}{dT} = \frac{I}{d}$$



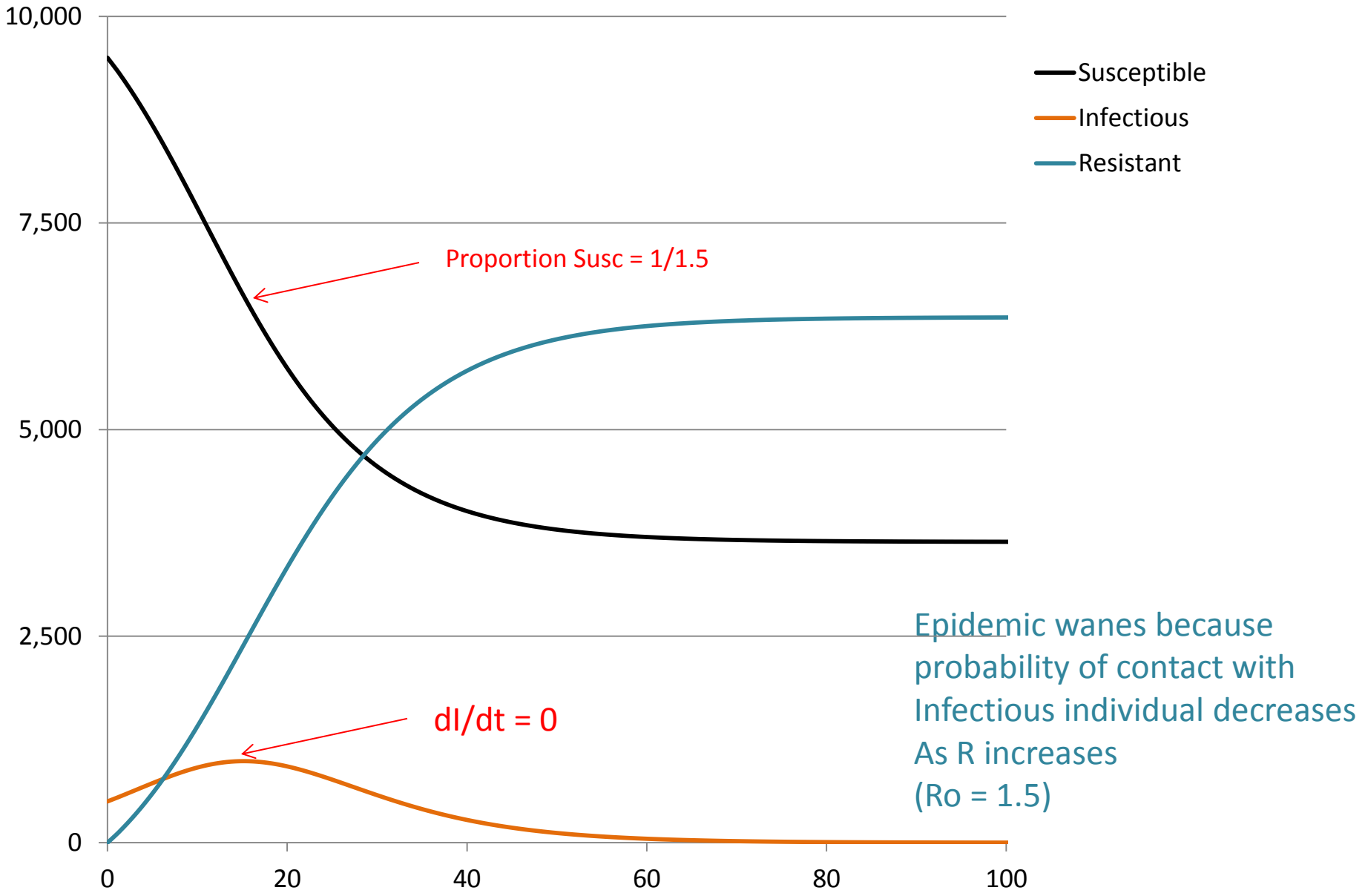
Model #2: the SIR Model



Model #2: the SIR Model (R_o = 6)



Model #2: the SIR Model (R_o= 1.5)



When do epidemics occur?

- R_0 is the Reproductive number assuming everyone is susceptible

- However, in many populations, not everyone is susceptible

- Epidemics occur when infections increase over time (when $dI/dT > 0$)

The Epidemic Threshold and "Herd Immunity"

For contagious diseases conveying immunity after infection, infectious disease principles tell us that we can prevent an outbreak by immunizing a fraction of the population!

$dI/dt = b*c*S*(I/N) - I/d > 0$

Implies

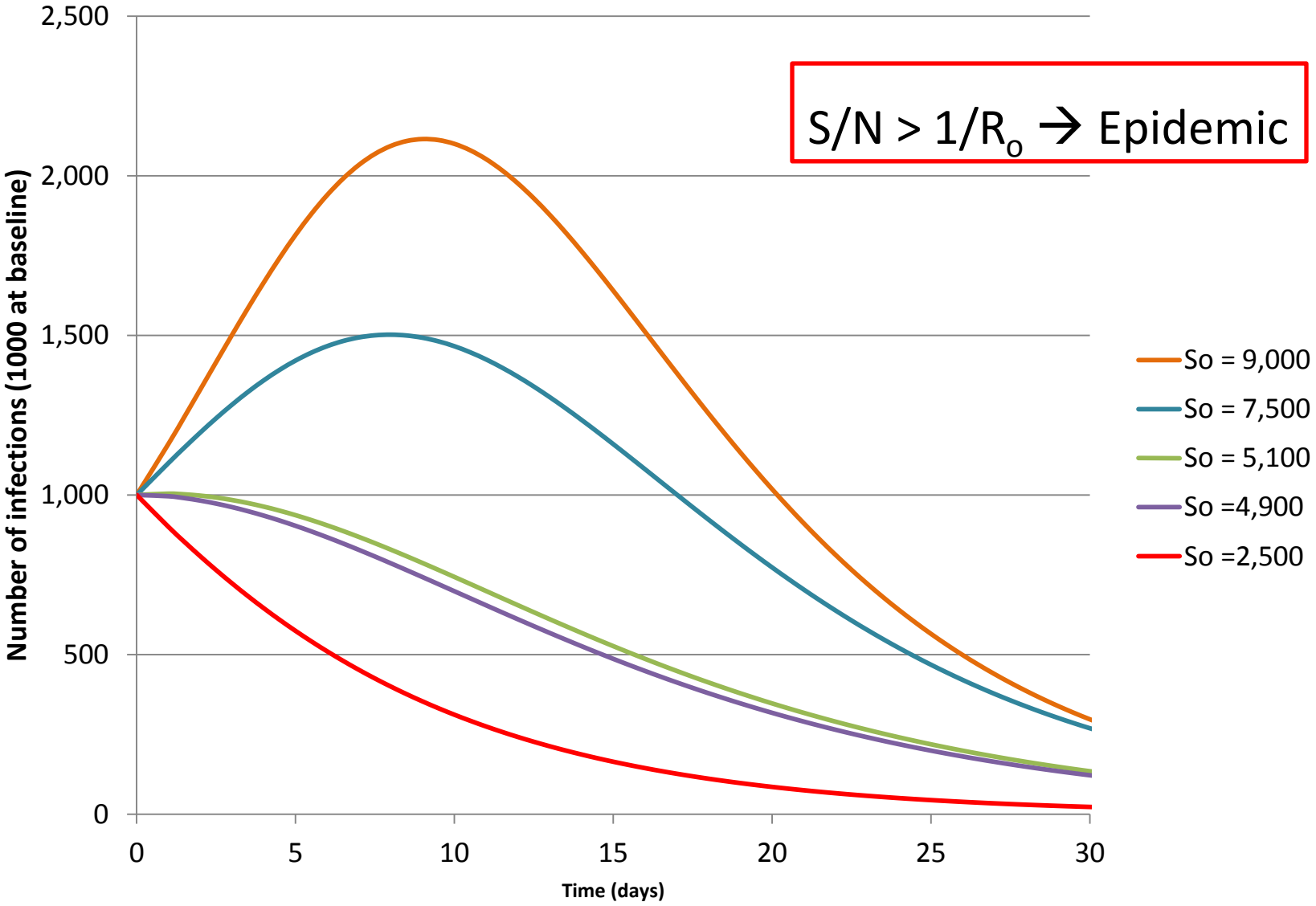
$b*c*(S/N) * \cancel{I} > \cancel{I}/d$; Substitute $R_o = bcd$

$S/N > 1/R_o$

Epidemic Threshold: When the proportion of Susceptibles in a Population is > 1/Ro, the infection will spread

If you get the proportion susceptible below $1/R_o$, no epidemic!!

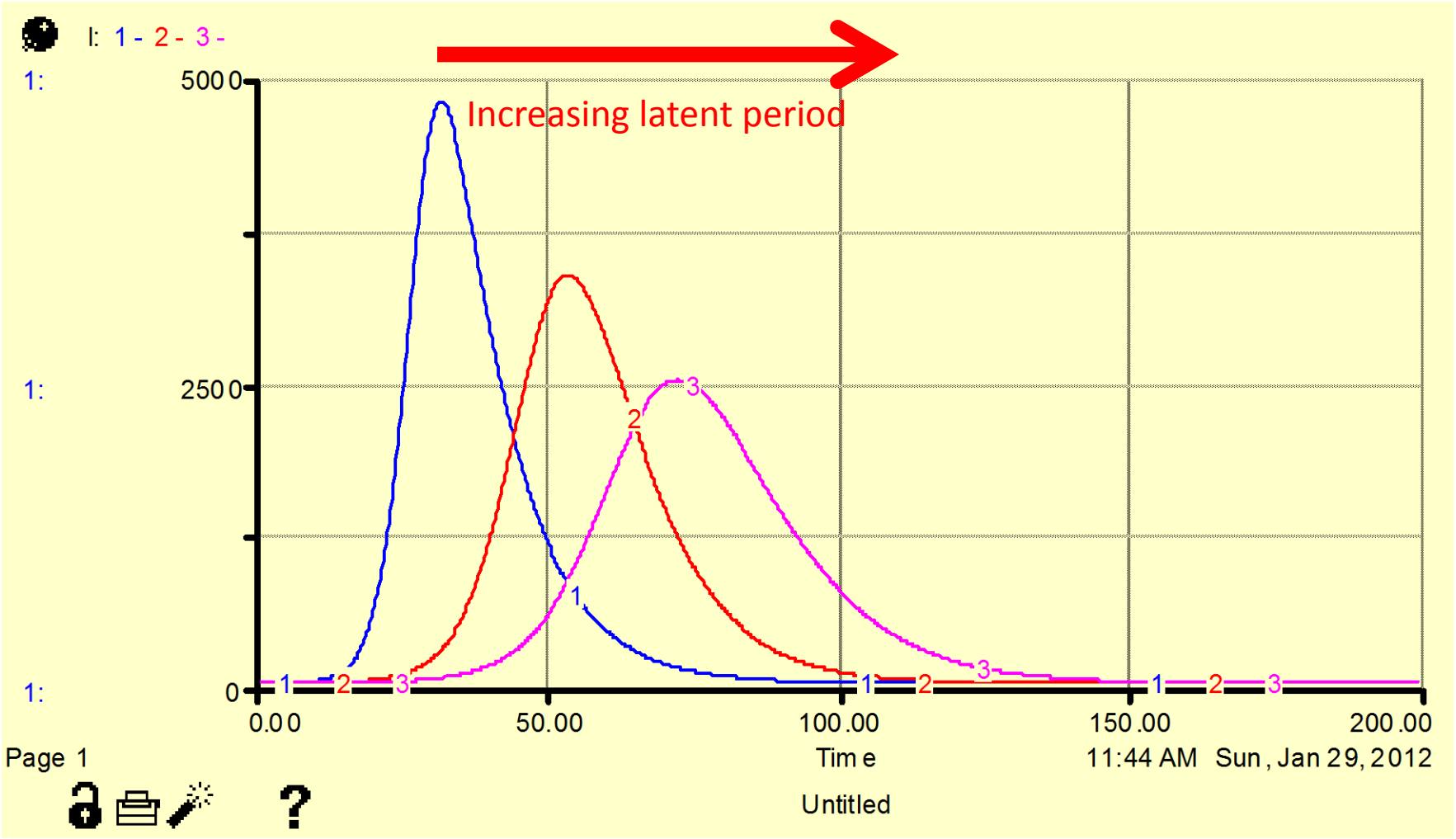
Impact of immunity on transmission (Ro = 2, N = 10,000)



Even fancier

- SLIR (or SEIR) models
  - Takes into account fact that for many infectious diseases, there is a lag time between becoming **infected** and becoming **infectious**
  - Biologically, infection needs to take hold and increase in concentration before it can be passed on
    - E.g., for Ebola, average incubation period of 8-10 days
  - Add a compartment between S and I

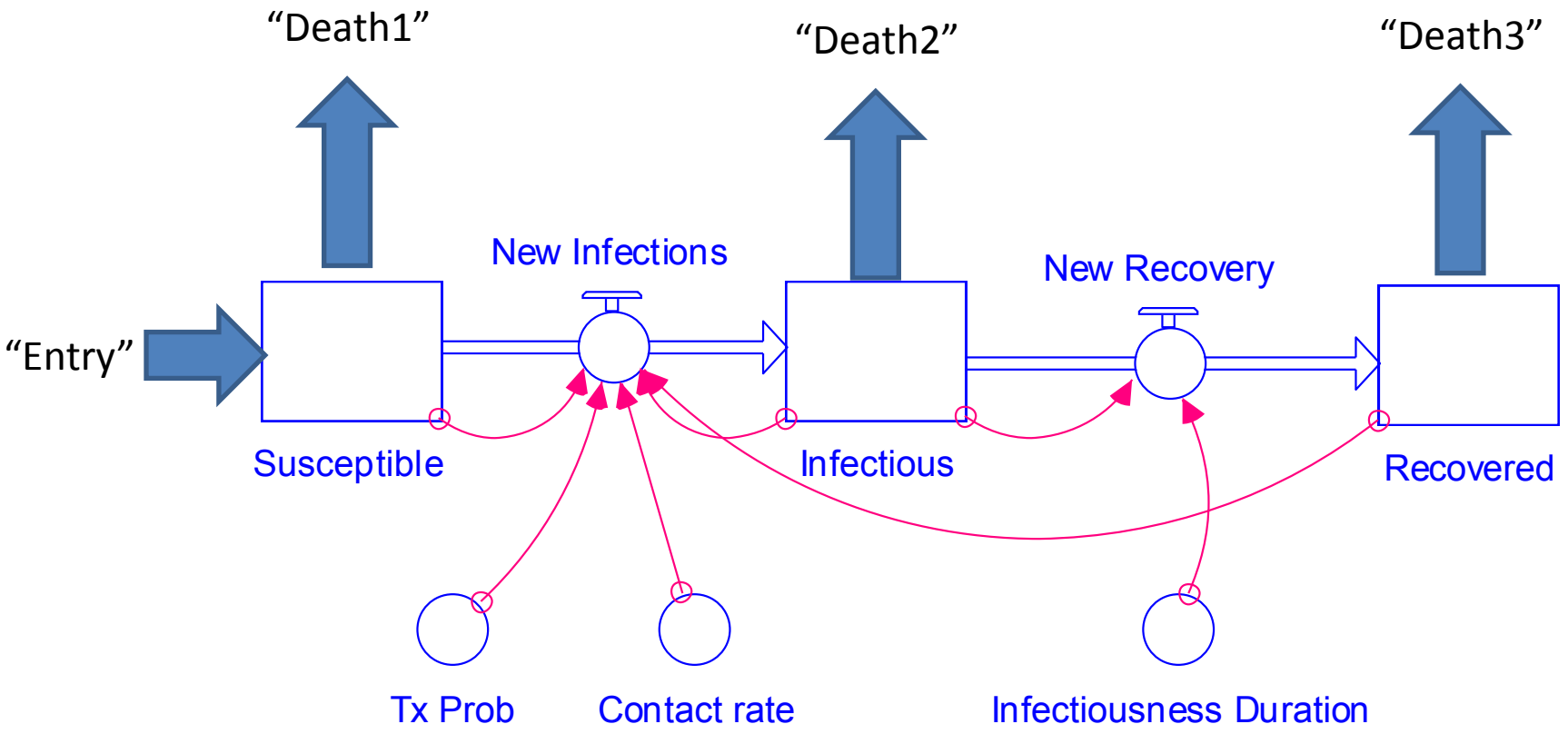
Model #3: the SLIR Model



Creating an open population

- So far, we've assumed nobody enters or leaves our population
- We can relax this assumption and model transmission dynamics with a simplifying assumption:
  - Model an open population at "steady state"
    - Total in = total out
- This lets us better model oscillating epidemics

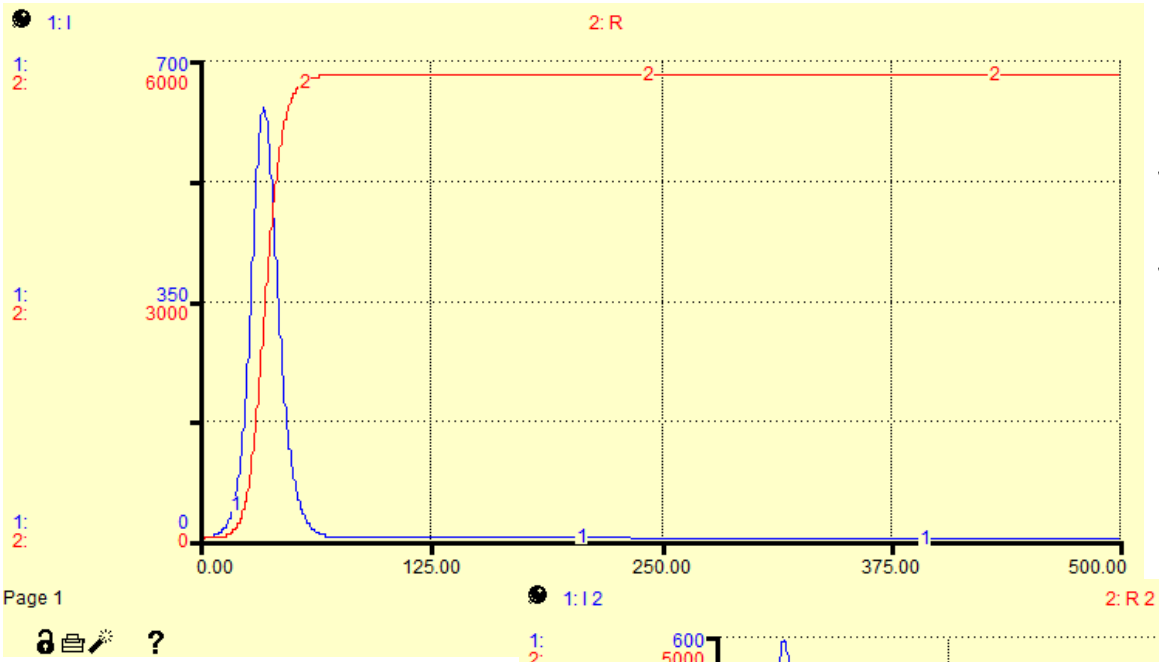
Model #2: the SIR Model: open population at steady state

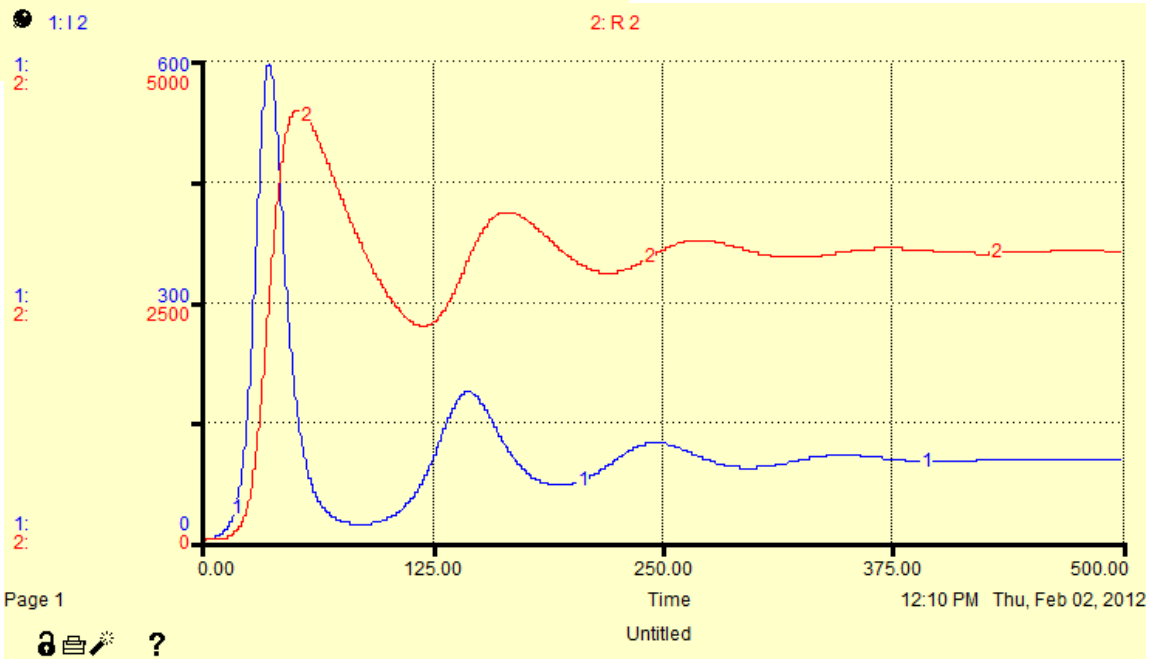


"Entry" Flow = Death flow1 + Death flow2 + Death flow3

We **assume** the number leaving our population is exactly balanced by the number entering

Model #3: the SIR: Open vs closed…

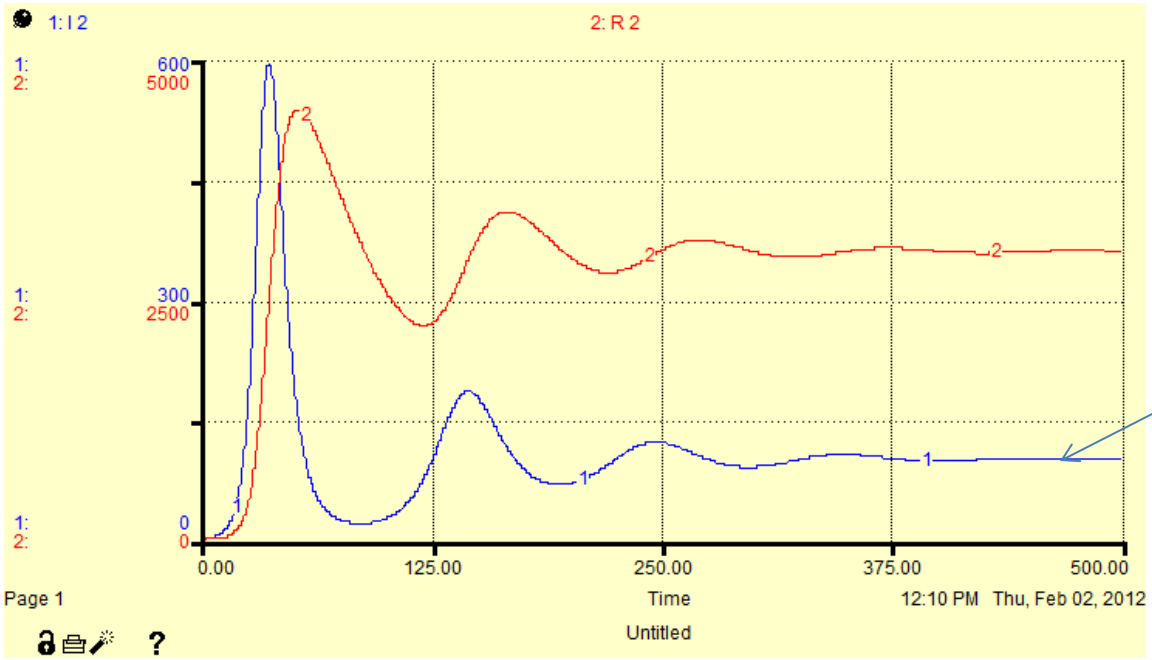




Which one is open,
Which closed?

Open populations

- Introduce new susceptibles into the population
- This allows for serial epidemics to break out
- Eventually, we reach a steady-state determined by the rate of entry and exit from the model (due to entries and deaths)

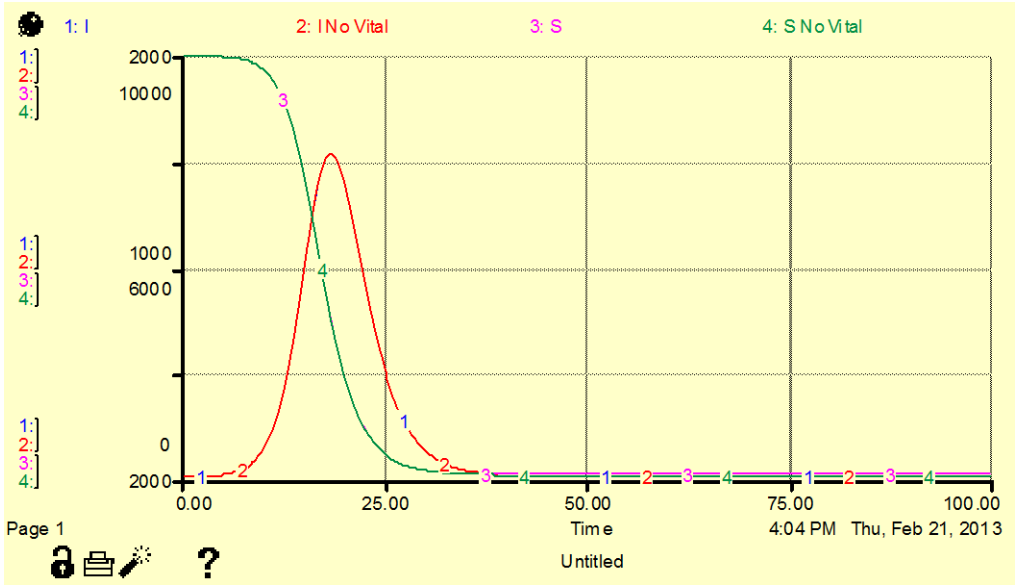


Steady state

Do we really need to do this?

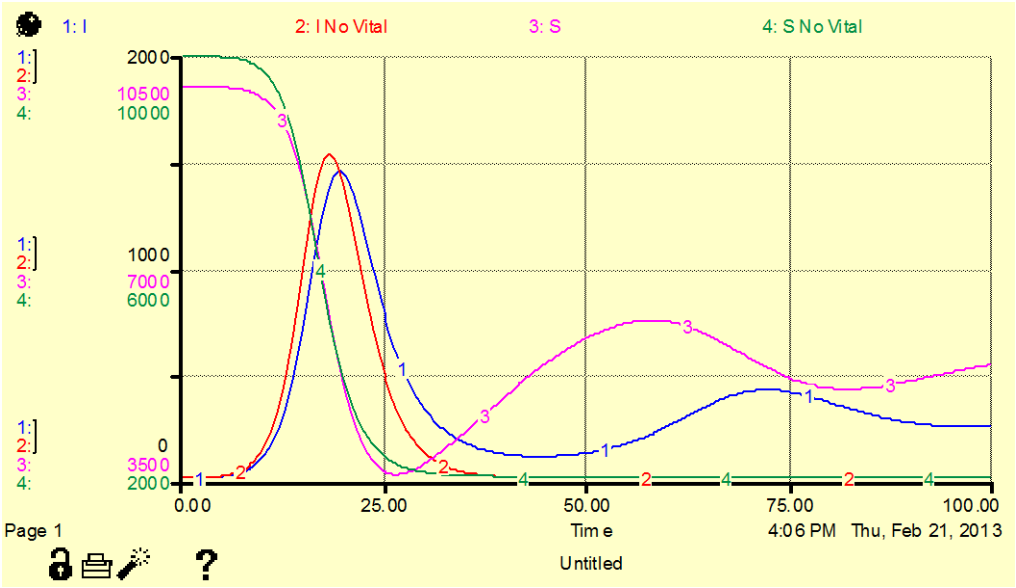
- Depends on how “static” our population is
  - If the average duration in the population is >> the average duration of infectiousness, the SIR model without vital dynamics is “good enough”
  - If we have a more transient population where the average duration in the population is ≈ the average duration of infectiousness, we need to take this into account

Do we really need to do this?



Average lifespan =
70 <u>years</u>

Avg duration of infectiousness =
2 days



Average lifespan =
30 <u>days</u>

Avg duration of infectiousness =
2 days

Standard Compartmental Epidemic Models: Refinements

- What if all susceptibles don't have the same infection probability?
  - Add more compartments (e.g., men & women, age)
- What if an infective's transmission probability depends on their stage of infection?
  - Add more compartments (e.g.,early, mid, late)
- What if transmission is determined by patient-level factors?
  - Stochastic models needed to account for patient-level differences

But, we can learn a lot from these simple models

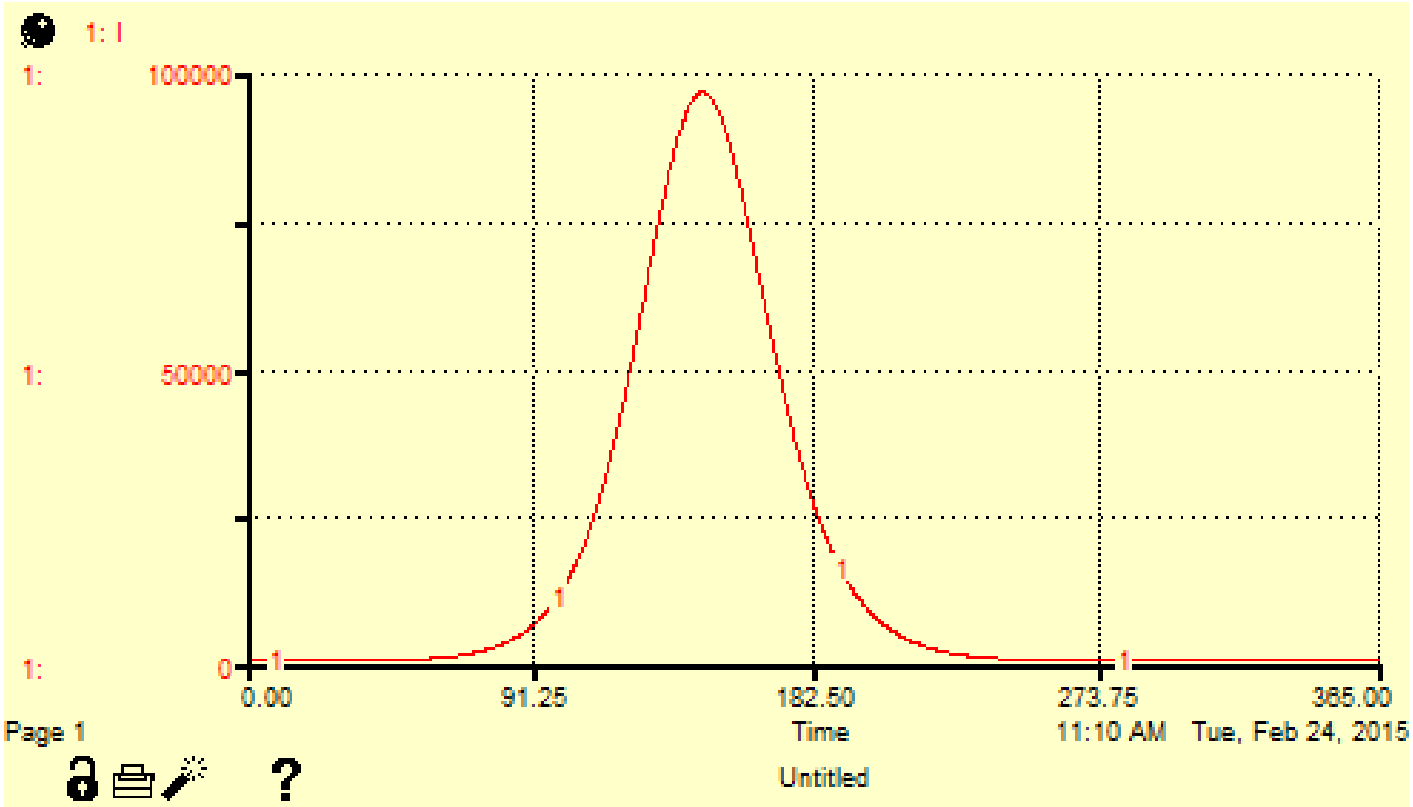
- Let's create a simple model of the Ebola epidemic[1]
  - Starting population: 1,000,000
    - R_o: 2.53
    - Transmission rate (per day) = 0.45*
    - Incubation period = 10 days
    - Infectiousness duration = 5.61 days
    - Case-fatality rate = 48%

*the per-contact transmission probability X the contact rate

1. Adapted from Althaus 2014, PLOS ONE.
Estimating the Reproduction Number of Ebola Virus (EBOV) During the 2014 Outbreak in West Africa

But, we can learn a lot from these simple models

Model 1: no control measures



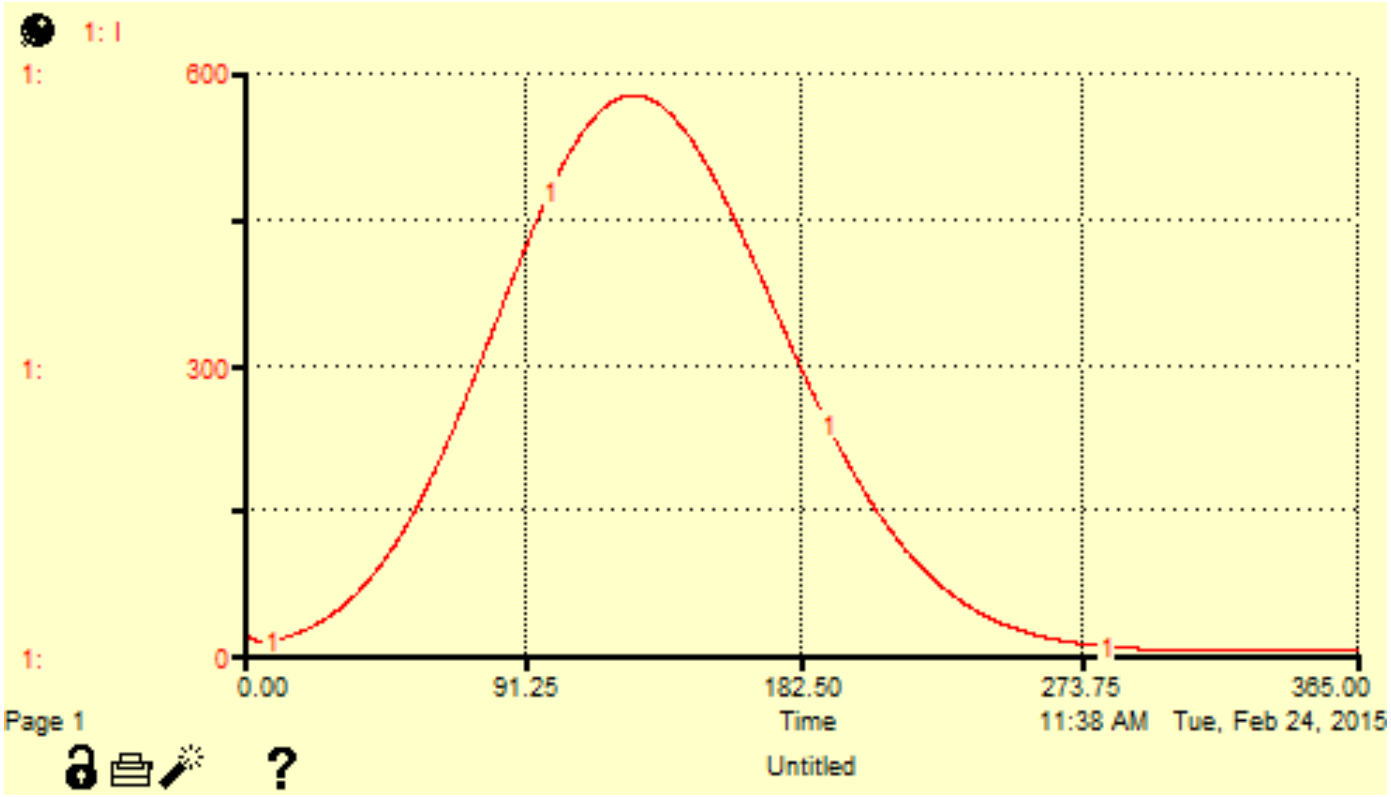
The New York Times

Ebola Cases Could Reach 1.4 Million Within Four Months, C.D.C. Estimates

By DENISE GRADYSEPT. 23, 2014

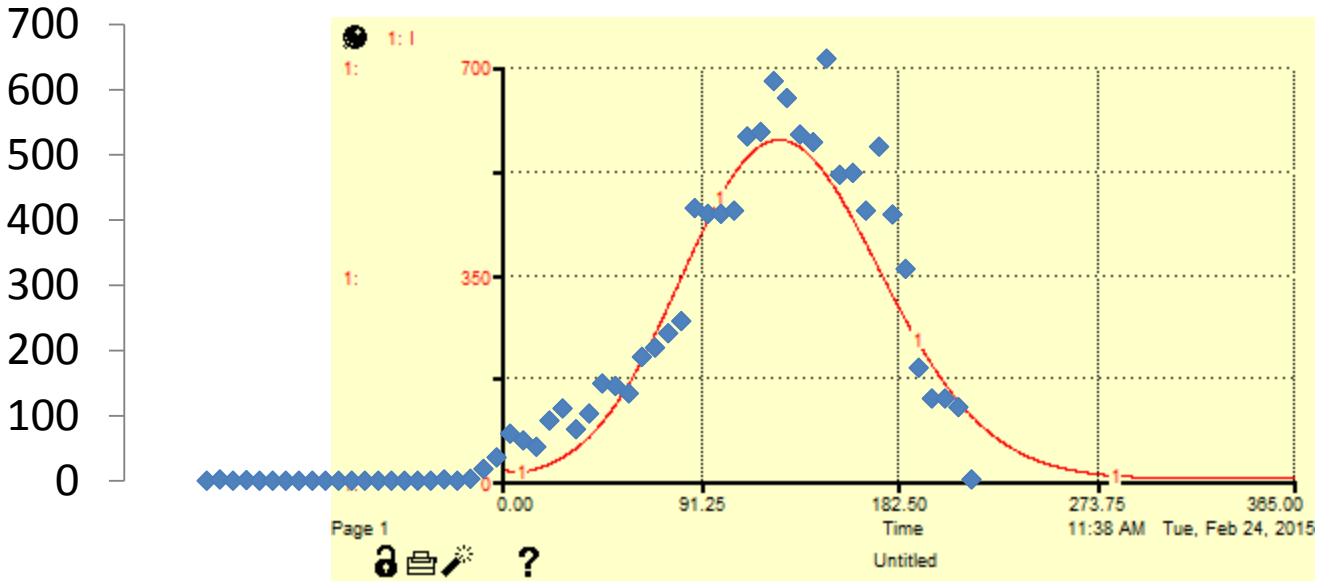
But, we can learn a lot from these simple models

Model 2: Assume increasingly effective control measures exponentially decreasing transmission probability.
Transmission probability decreases over time by exp(-0.0075*time)[1]



1. Adapted from Althaus 2014, PLOS ONE.
[Estimating the Reproduction Number of Ebola Virus (EBOV) During the 2014 Outbreak in West Africa]

Compare the model to the case count in Sierra Leone



1. Adapted from Althaus 2014, PLOS ONE.
[Estimating the Reproduction Number of Ebola Virus (EBOV) During the 2014 Outbreak in West Africa]

Questions?

On to the fun part!

Stella

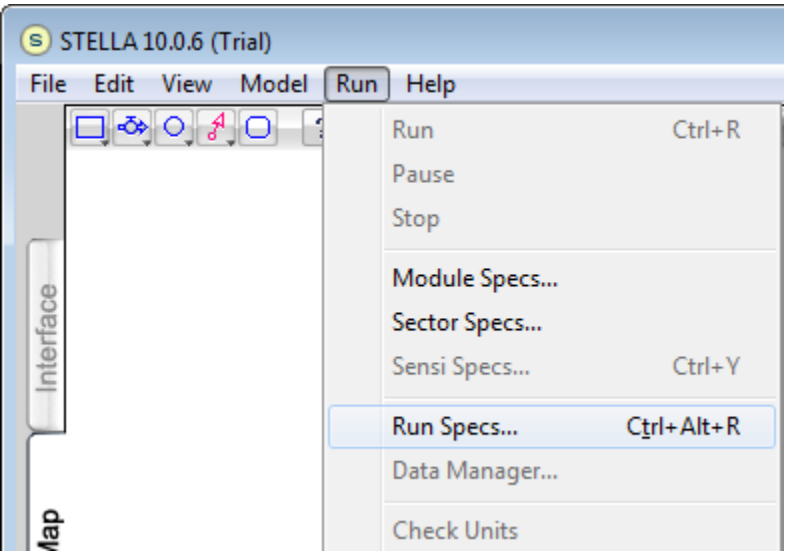
- Open program and go to “Model” Tab

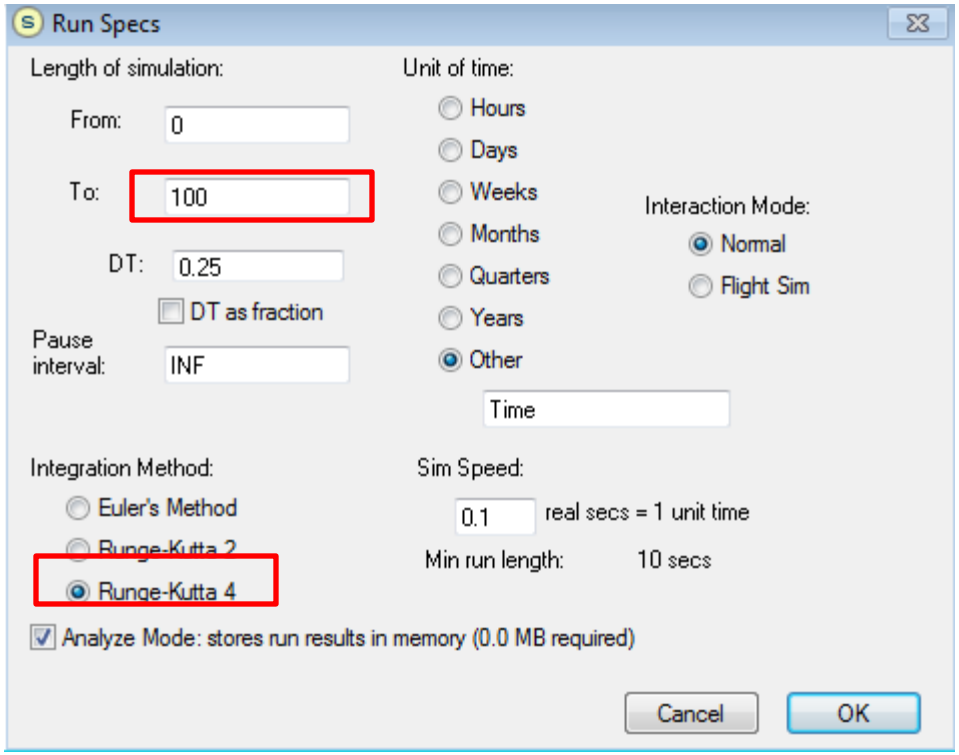
- Let’s construct a **closed SIR model**
- Initial values for compartments
  - S = 9999
  - I = 1
  - R = 0
- Values for R_0 components
  - b = 0.5
  - c = 2
  - d = 2

$R_0 = 0.5*2*2 = 2$

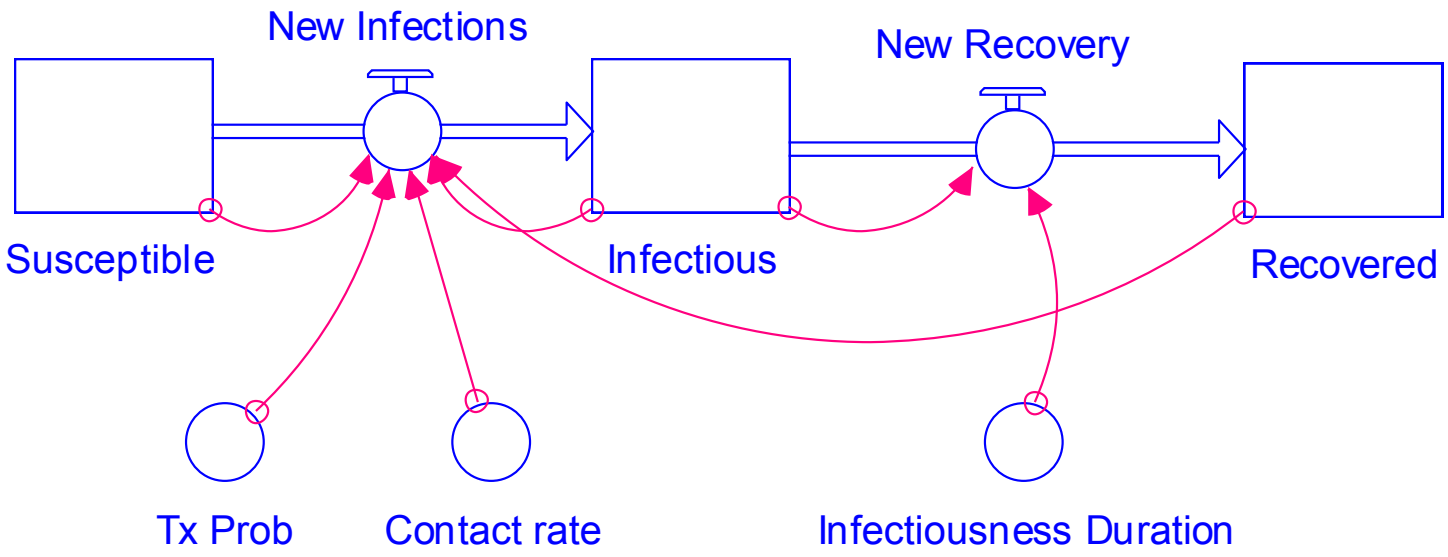
Stella

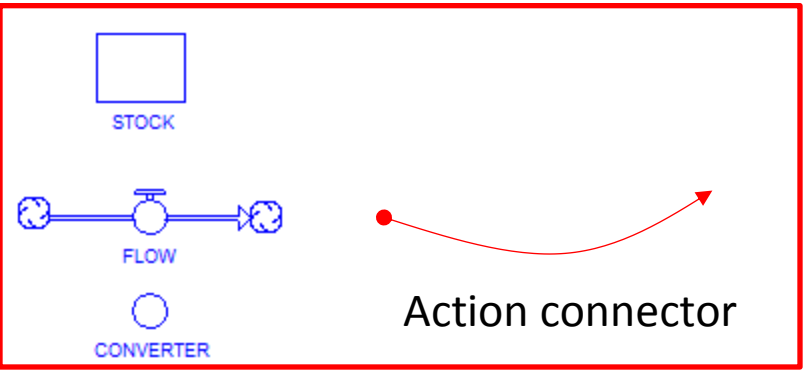
- But first, change these (trust me)





Model #2: the SIR Model





Stella

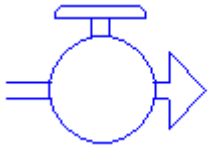
Let's write the flow equations.

Flow from S to I:

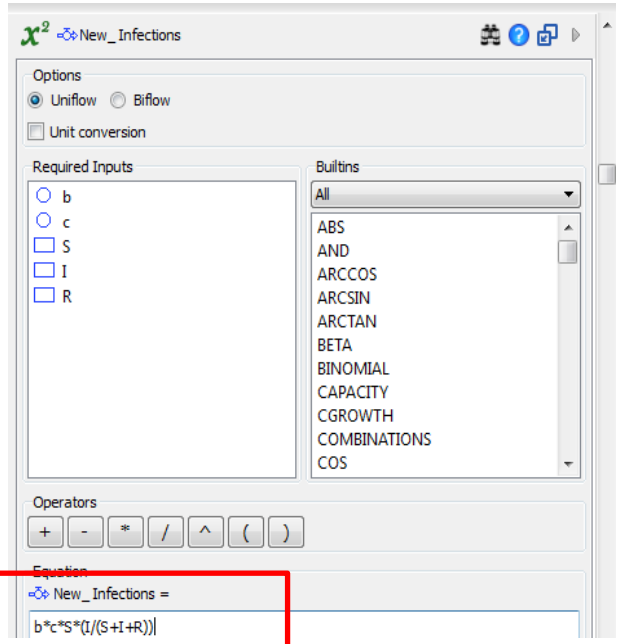
- IR *S*(I/(S+I+R))
- IR = b*c

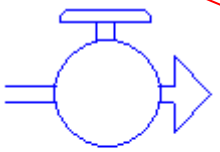
Flow from I to R:

- Recovery rate*I
- = I/d

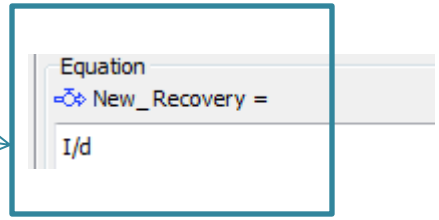


New Infections

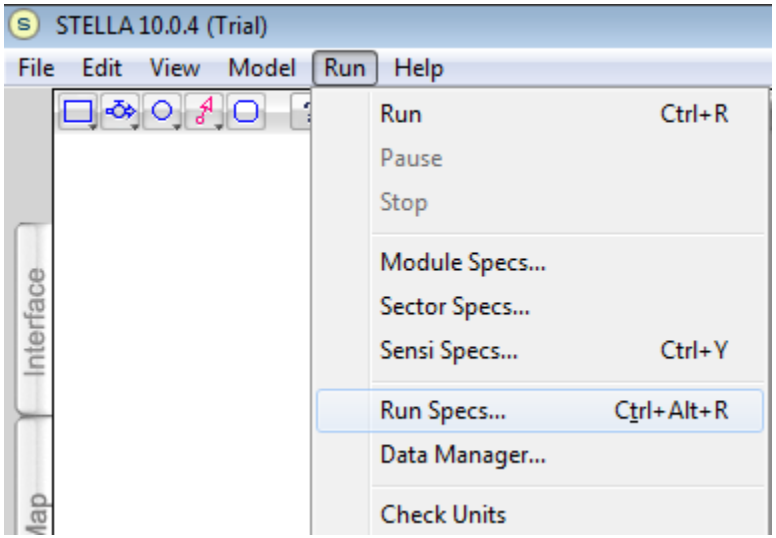


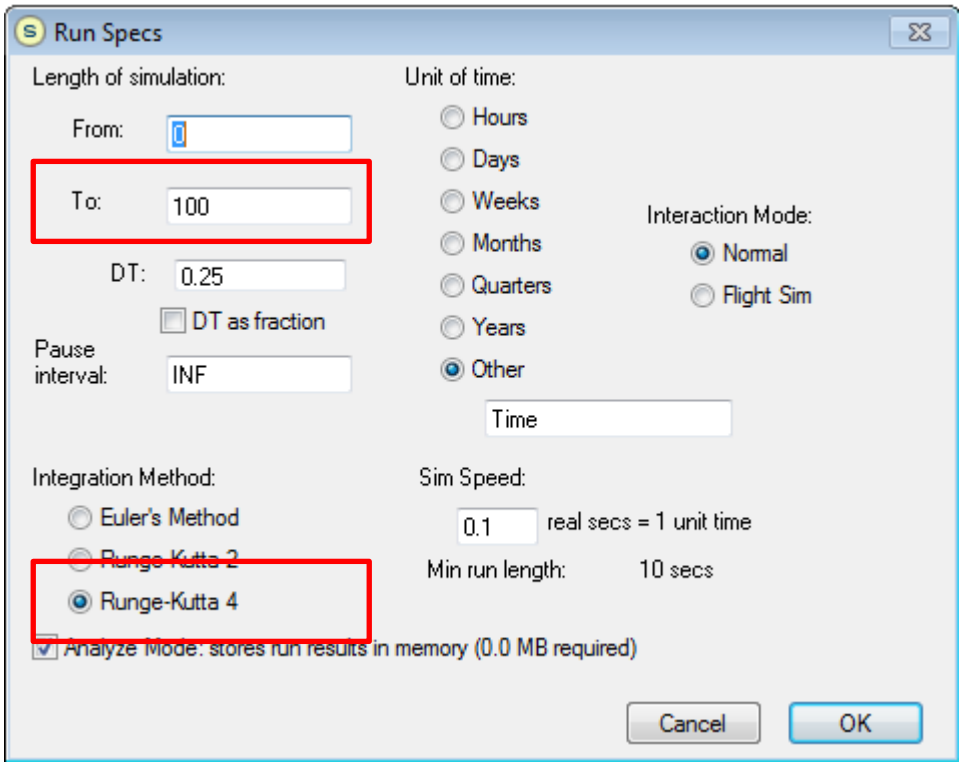


New Recovery

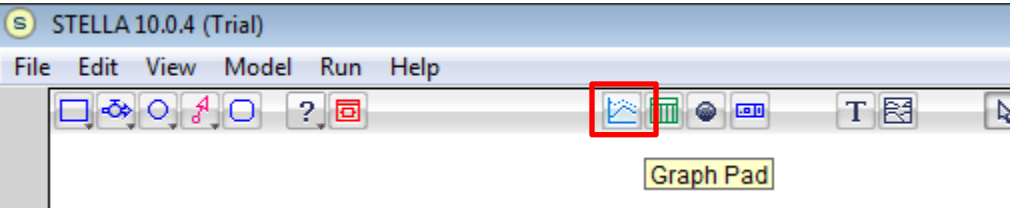


Let's set up the model to run

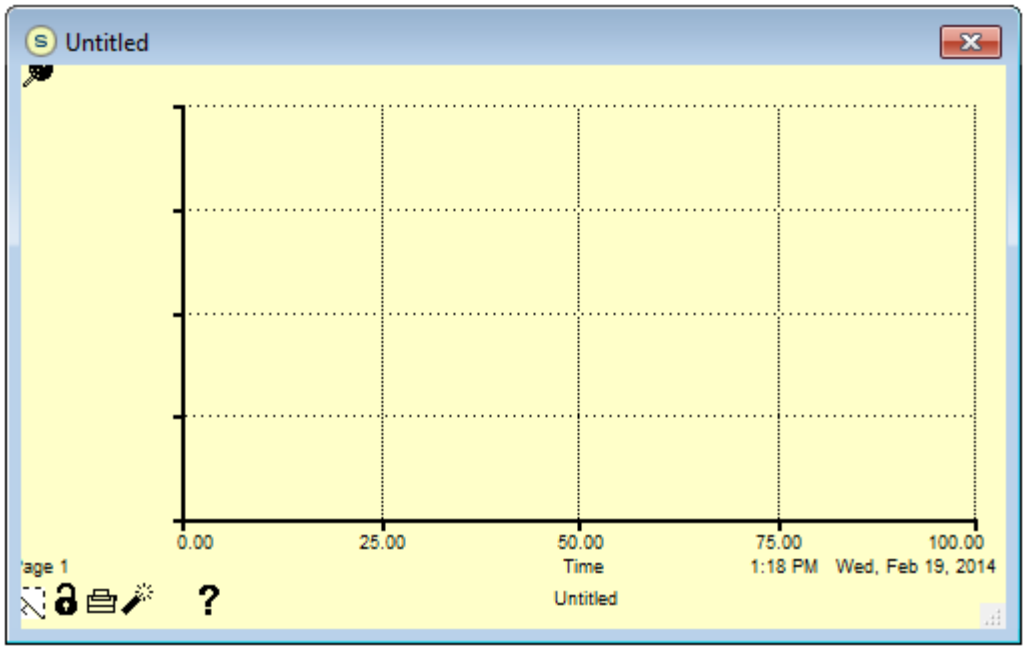




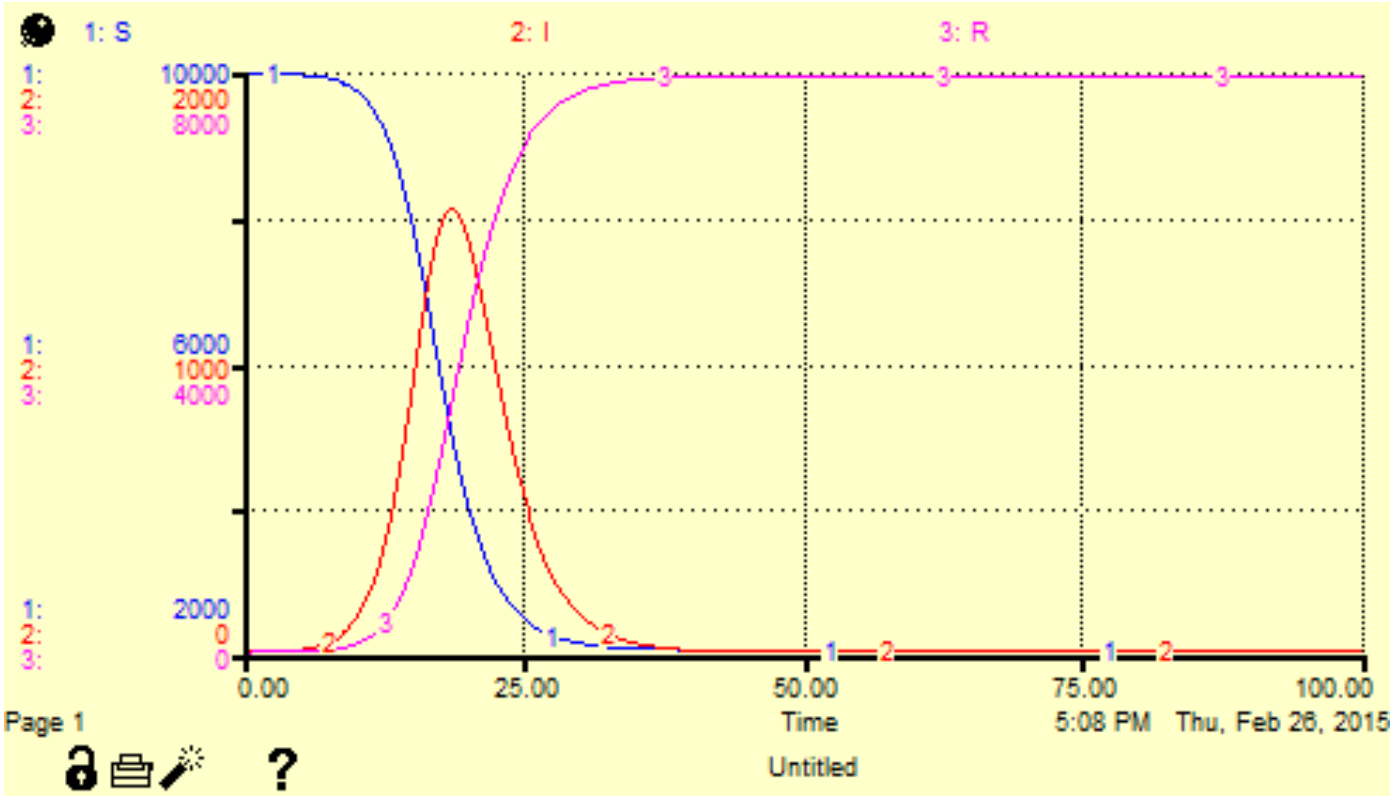
Now, let's add a graph



Then, click anywhere on your white space model sheet



Did you get something like this?



Exercise

1. What would happen if this was introduced into a population where, due to a new vaccination campaign, the initial proportion of Resistant increased (reducing S by increasing R)?
   - At what initial number of R does the epidemic not occur?
2. By how much would we have to decrease the contact rate in order to prevent the epidemic in the original population?
3. How would these answers differ in an open population at steady state?

Exercise: Open Population