Teaching Modeling with Mosquito-Borne Disease Epidemics*

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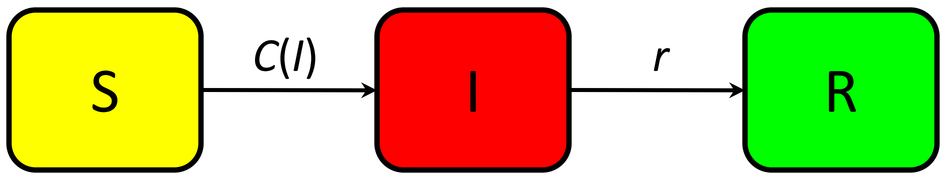
Overall Goals

- To create a *context* which fosters the symbiosis of biology, statistics, and mathematics
  - Multiple entry points for many different students
  - Multiple activities possible and available
- To create a *context* that can be used with (and become familiar to) a wide range of students
  - Freshman use it superficially; Seniors more depth
  - An “F=ma”-like alternative for the Life Sciences

SIR Epidemics

- A population of constant size N is partitioned into S = Susceptibles, I=Infecteds, R=Recovered



- $C(I)$ = Contact rate of infection (as a function of I)
- r = rate of recovery
- There are more sophisticated models
  - We stay simple for pedagogical purposes
  - Simple models are still highly applicable!

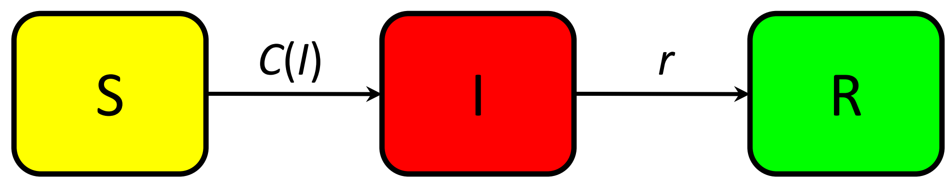
SIR Epidemic Model

- SIR models are either Systems of DE's or Systems of Difference Equations

$$\frac{dS}{dt} = -C(I)S$$

$$\frac{dI}{dt} = C(I)S - rI$$

$$\frac{dR}{dt} = rI$$



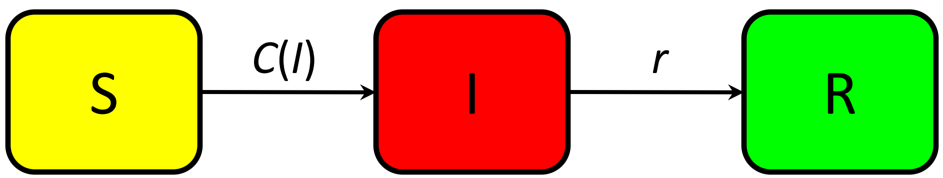
$$S_{t+1} = S_t \Delta t - C(I_t)S_t$$

$$I_{t+1} = I_t \Delta t + C(I_t)S_t - rI_t$$

$$R_{t+1} = R_t \Delta t + rI_t$$

Types of SIR Epidemics

- Epidemic type often defined by how the disease is spread (Human-Human contact, Insect-borne, water borne, airborne, etc)



- Human-Human Contact: $C(I) = b\,I$
- Mosquito-Human Contact: $C(I) =$ c

Assuming homogenous mixing of the populations

Which Epidemic is it??

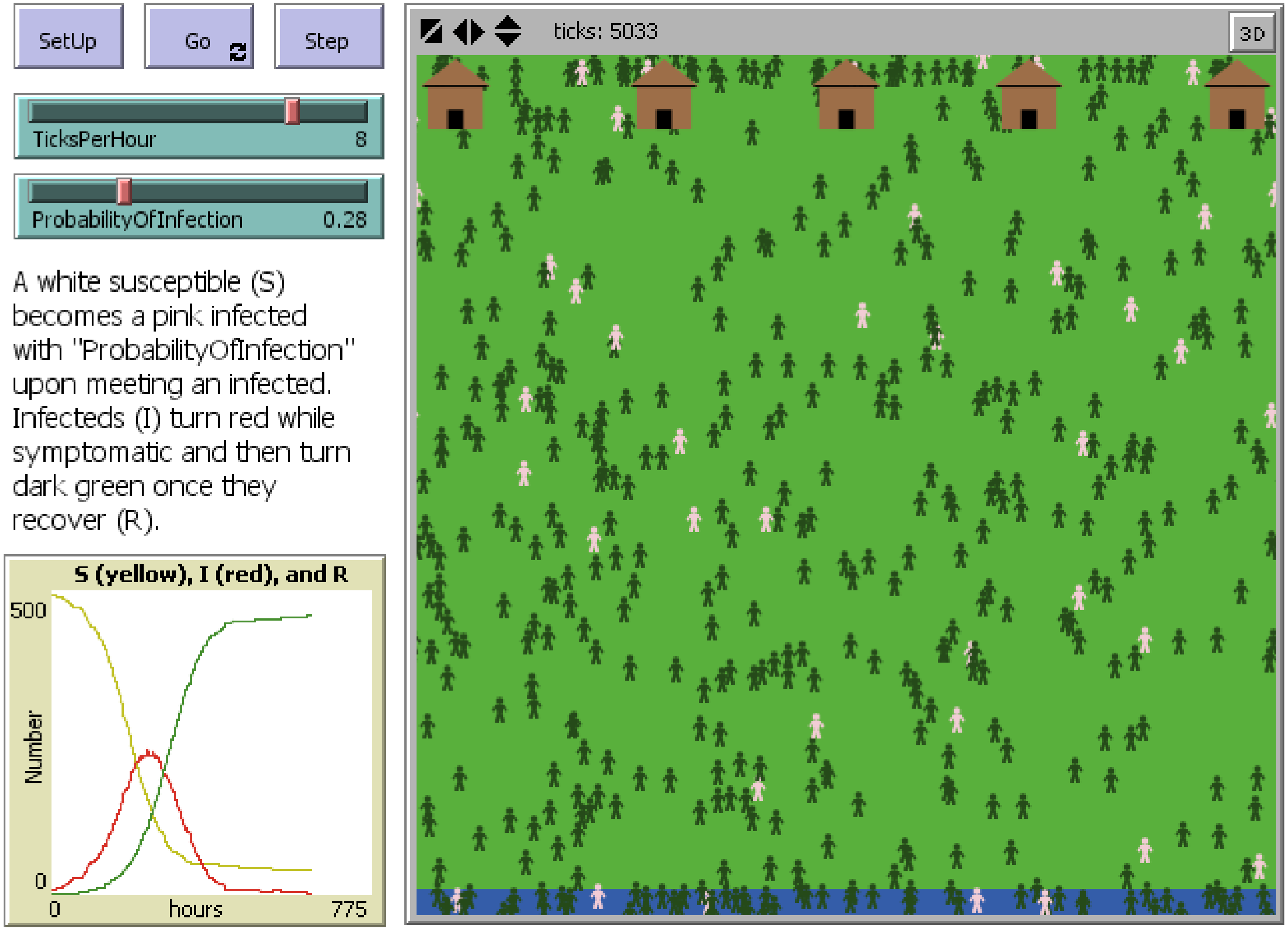
- There have been many instances where one epidemic type has been confused for another
  - Yellow fever is Mosquito-borne (Carlos Finlay, **1889**),
    - Proven to be Mosquito-borne in Cuba in **1900** (Maj. Walter Reed). Experiment cost Jesse Lazear his life.
    - Practically no cases of Yellow fever in Cuba since **1901**
  - Yellow fever officially remains a human-human transmitted disease (via poor sanitation) until **1905**.
    - Last Yellow Fever epidemic, **New Orleans, 1905**
    - Extensive outbreak in spite of elaborate sanitation efforts

Which Epidemic is it??

- This is still an Important Question – St. Louis Encephalitis, Dengue Fever, etc.
- And is a question we can explore
  - **Pedagogically:** Via Simulations (Netlogo) that generate data for each epidemic type (via models)
  - **Statistically:** Form Hypothesis, Analyze Data, Get *p*-value, Infer epidemic type
  - **Mathematically:** Why we should not be surprised that epidemic types are often confused?

Pedagogically: The Simulations

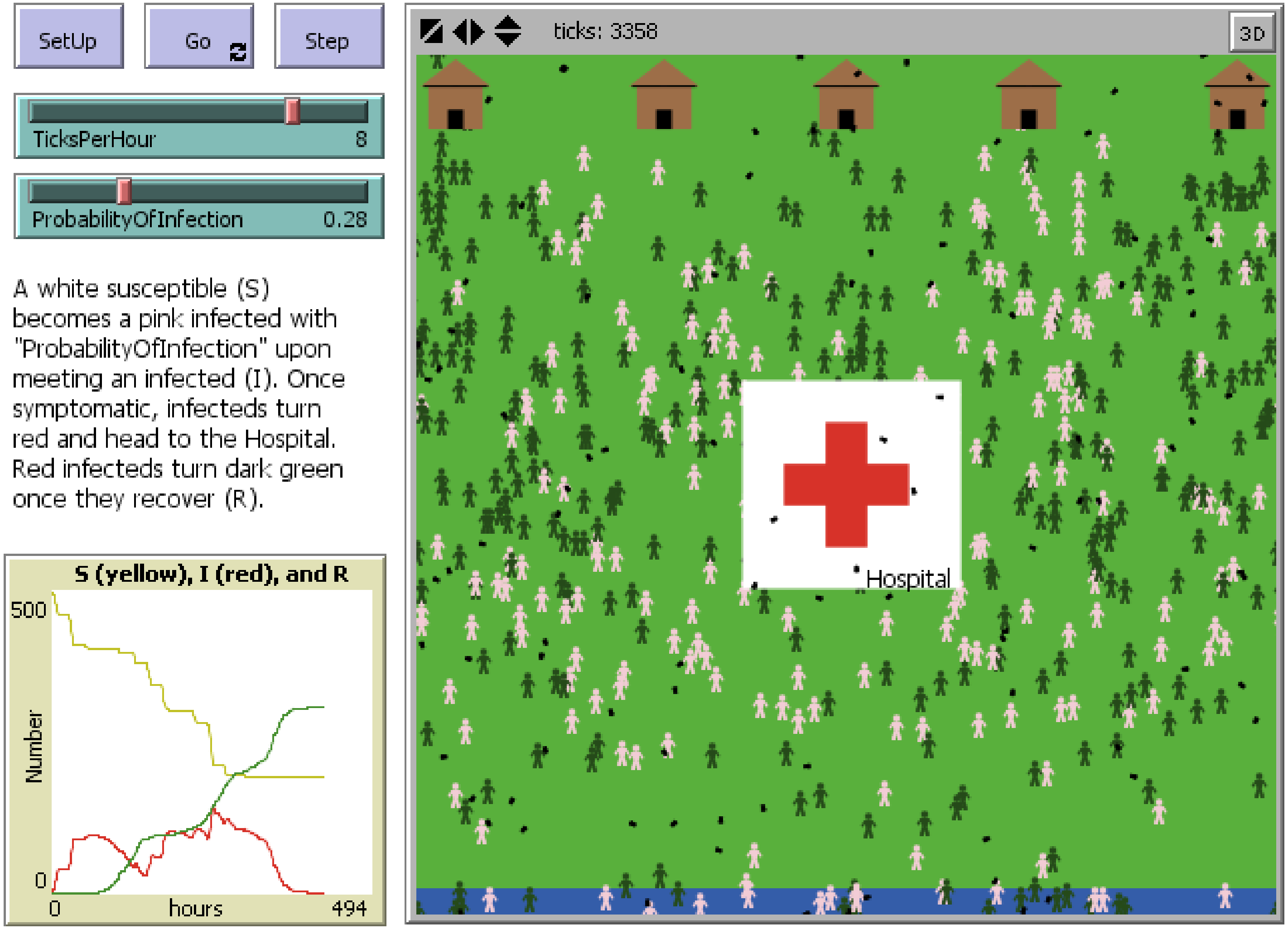
- Simple S-I-R interactions among N agents
  - All Simulations: Recovery with a fixed rate *r* depending on how long an individual is ill (on average)
  - Human-Human: Infections with a given probability when a Susceptible meets an Infected
  - Mosquito-Human: Infections with a given probability when a Susceptible meets a Mosquito (assuming all Mosquitoes are infected)
- We simulate a "village" near a river (N = 500)


SetUp
Go
Step
TicksPerHour 8
ProbabilityOfInfection 0.28
A white susceptible (S) becomes a pink infected with "ProbabilityOfInfection" upon meeting an infected. Infecteds (I) turn red while symptomatic and then turn dark green once they recover (R).
S (yellow), I (red), and R
500
0
Number
0
hours
775
ticks: 5033
3D

Pedagogically: The Simulations

- But there is more to the story
  - People work, eat, drink water during the day
  - People sleep at night (violates homogeneity assumptions)
  - When they are sick enough, they want medical attention (hospital)
- Given a randomly-generated epidemic, can a student determine what type of epidemic it is?
  - Our "real world" is not so pristine as the models
  - But features of the models do "survive"

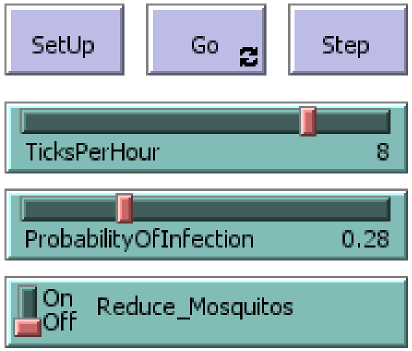
Human-Human Epidemic



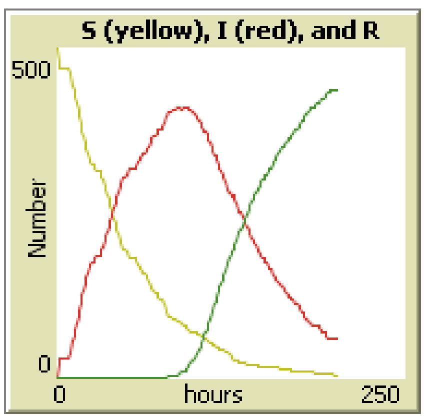
Statistically: The Data

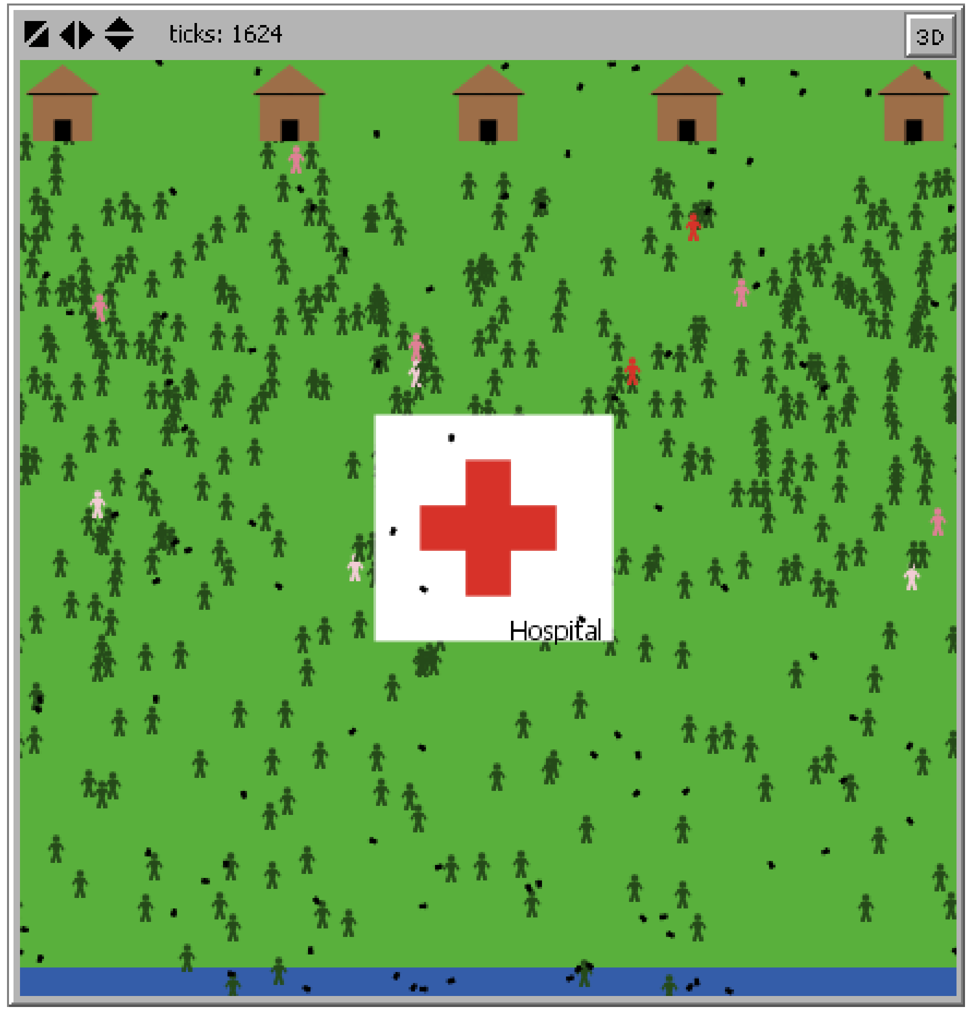
- Mosquito-Human epidemics are likewise set in "real world" circumstances
  - Model assumptions are violated
  - But same assumptions violated for all models!
- Although the models are developed mathematically, they are compared *statistically*
  - Especially given that assumptions are often violated
  - And that epidemics of different types tend to "look alike" (later)

Mosquito-Human Epidemic



Once bitten, a white susceptible (S) becomes a pink infected (I) with "ProbabilityOfInfection". Once symptomatic, infecteds turn red and head to the Hospital. Red infecteds turn dark green once they recover (R).

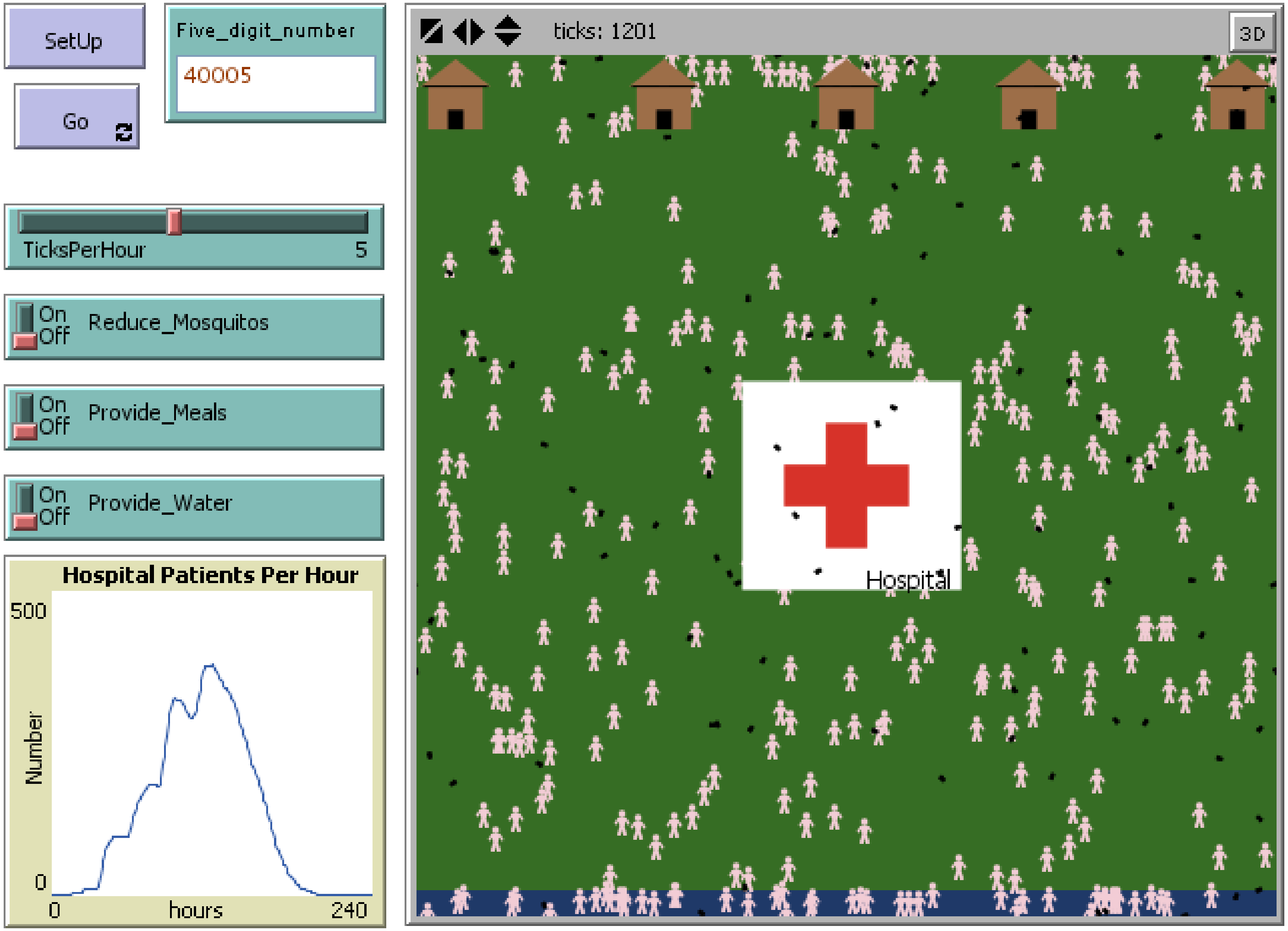




Statistically: Analyzing The Data

- EpidemicVector simulation randomly simulates one of 4 epidemic types (Human-Human, Mosquito-Human, Food Borne, Water Borne)
  - Based on a 5 digit number the student provides
  - They must determine which epidemic is generated
- Simulation mechanics:
  - People eat/drink during the day, sleep in huts at night
  - Once sufficiently ill, they go to the hospital
  - Only the patient count per hour is available for analysis

Epidemic Simulations: 4 possible Methods of Transmission

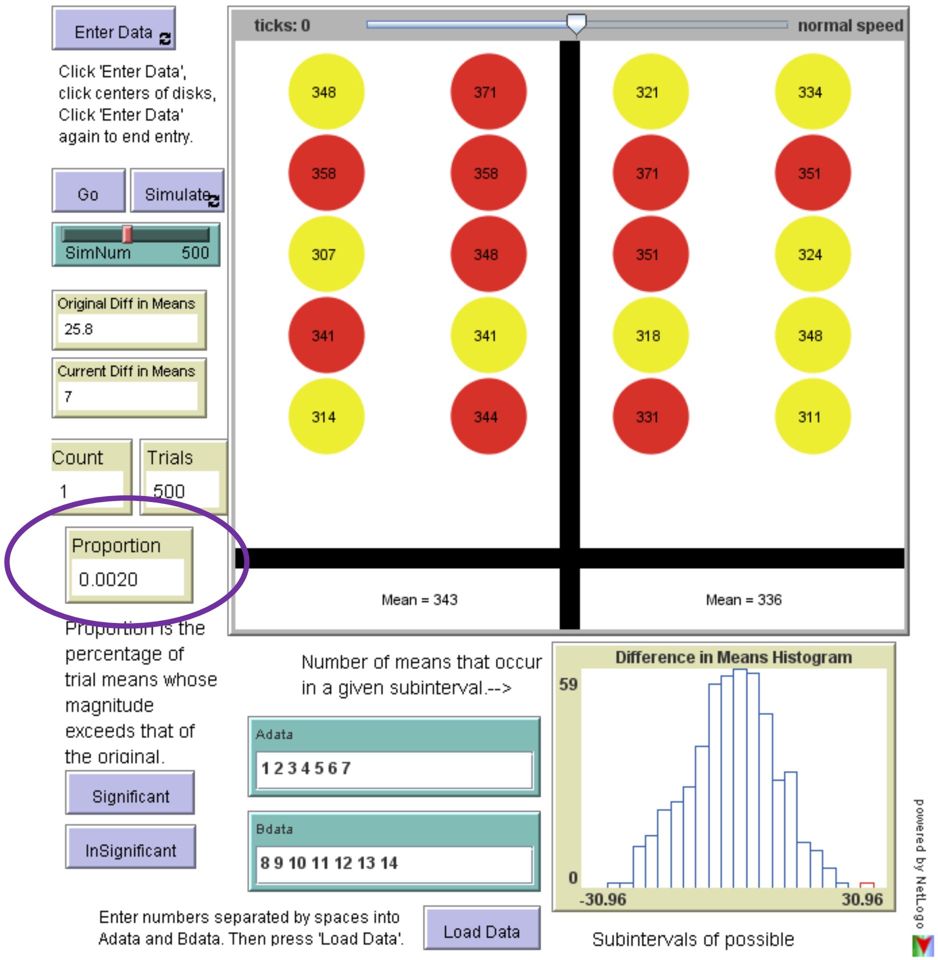


Statistically: Analyzing The Data

- Students can apply any of 3 interventions
  - Reduce the mosquito population
  - Provide untainted food to some of the population
  - Provide sterile water to some of the population
- Question: Which intervention reduces severity of the epidemic?
  - Simple approach: collect "max patient counts" in each simulation
  - Test for significance of difference between means of Experimental (with intervention) and Control
  - We have them do so with the randomization test

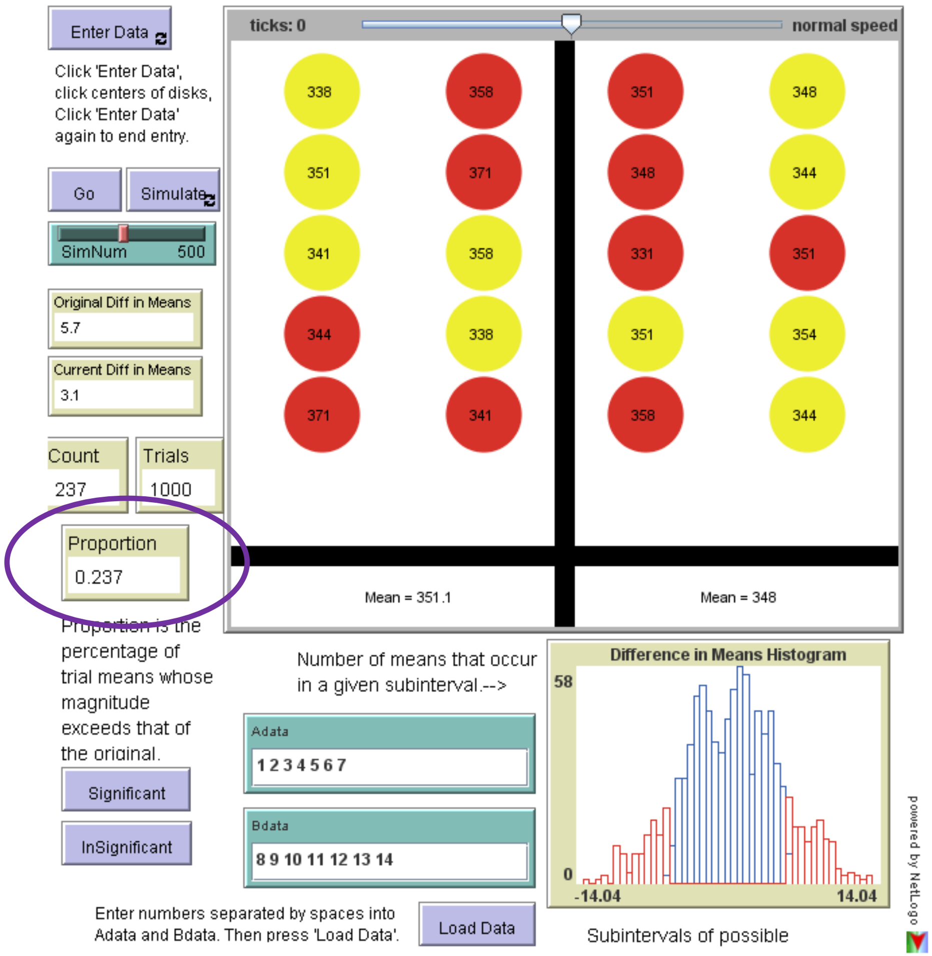
The Randomization Test

Result of Simulation with the data associated with the button **Significant**



The Randomization Test

Result of Simulation with the data associated with the button **InSignificant**



Mathematically: Linearization

- Mosquito-Human model is the *linearization* of the Human-Human model (in simple forms)

Human Human

$$\frac{dS}{dt} = -bIS$$

$$\frac{dI}{dt} = bIS - rI$$

$$\frac{dR}{dt} = rI$$

$$c = b\left(I_0 + S_0\right)$$

Mosquito Human

$$\frac{dS}{dt} = -cS$$

$$\frac{dI}{dt} = cS - rI$$

$$\frac{dR}{dt} = rI$$

Mathematically: Linearization

- Linearization is ‘valid’ as long as $R(t)$ is small
  - Thus, epidemic types often look “the same” for relatively long periods of time
  - Long term: Linearization (Mosquito) eventually infects everyone in the population (but may take “arbitarily long” to do so)
- Deep Mathematical Question: On what interval is a linearization a ‘valid’ approximation?

Goal: Contexts that become “familiar” and can be used in many situations

- Freshman, General Majors: Simulation generates data for statistical testing
- Sophomore, Math Majors: Linear difference equation as both (a) programming assignment and (b) excuse to study sequences and series
- Junior/Senior: Systems of DE’s, Linearization of DE’s, statistical modeling, time series analysis

Thank you!

Website: http://math.etsu.edu/Symbiosis/epidemics

- Data available from command line in Netlogo
- Netlogo interface with R can be used with Desktop Version of Netlogo (not enabled with applets)