Using Covid-19 to Teach Statistics and Differential Equations

YING LIN

SANTA ROSA JUNIOR COLLEGE

Topics Covered in the Talk

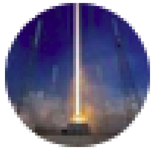
STATISTICS TOPICS:

- Conditional Probability
- Bayes Formula
- Expected Value
- Type I and Type II Errors

DIFF EQ / CALCULUS TOPICS

- System of ODEs
- Compartmental Models
- Stability Analysis

COVID Testing and Probability



Elon Musk
@elonmusk

Something extremely bogus is going on. Was tested for covid four times today. Two tests came back negative, two came back positive. Same machine, same test, same nurse. Rapid antigen test from BD.

9:47 PM · Nov 12, 2020 · Twitter for iPhone

126.5K Retweets **40.8K** Quote Tweets **481K** Likes

Conditional Probability: Specificity and Sensitivity

- Specificity: P(Test = - | Infected = no)
  - Low specificity: high false positives
- Sensitivity: P(Test = + | Infected = yes)
  - Low sensitivity: high false negatives

	Nasal swab + PCR	Chest CT
Specificity	90%	25%
Sensitivity	70%	97%

Source: Ai et al (2020)

Example: Bayes Formula

- Assume that the Nasal Swab/PCR test for COVID-19 has Specificity P(negative | no infection) = 0.9, and Sensitivity P(positive | infection) = 0.7
- Suppose you went to a party before taking this test, and 40% of the people at the party were infected. What is your chance of being infected after testing positive?

Bayes Formula with one positive test

- Writing P(I = yes | T= +) for P(infection | positive)

$$
\begin{aligned}
P(I = yes|T = +) &= \frac{P(I = yes, T = +)}{P(T = +)} \\
&= \frac{P(T = +|I = yes) \cdot P(I = yes)}{P(T = +|I = yes) \cdot P(I = yes) + P(T = +|I = no) \cdot P(I = no)} \\
&= \frac{0.7 \cdot 0.4}{0.7 \cdot 0.4 + (1 - 0.9) \cdot 0.6} \\
&= 0.824
\end{aligned}
$$

How likely was someone infected, Given mixed test results: (-, +, -, +) ?

Assume the prior probability P(Infected = yes) = 0.4

Specificity and Sensitivity estimate from the previous example.

Tests are conditionally independent given the infection status.

$$P(I = yes|\{T_i = t_i\})$$

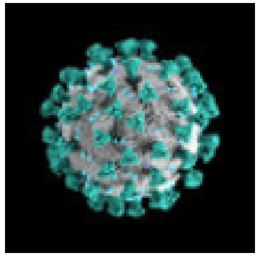
$$= \frac{P(I = yes, \{T_i = t_i\})}{P(\{T_i = t_i\})}$$

$$= \frac{P(\{T_i = t_i\}|I = yes) \cdot P(I = yes)}{P(\{T_i = t_i\}|I = yes) \cdot P(I = yes) + P(\{T_i = t_i\}|I = no) \cdot P(I = no)}$$

$$= \frac{\prod_{i=1}^{4} P(T_i = t_i|I = yes) \cdot P(I = yes)}{\prod_{i=1}^{4} P(T_i = t_i|I = yes) \cdot P(I = yes) + \prod_{i=1}^{4} P(T_i = t_i|I = no) \cdot P(I = no)}$$

$$= \frac{0.3^2 \cdot 0.7^2 \cdot \ 0.4}{0.3^2 \cdot 0.7^2 \cdot \ 0.4 + 0.9^2 \cdot 0.1^2 \cdot \ 0.6}$$

$$= 0.784$$



SPECIAL SERIES

The Coronavirus Crisis

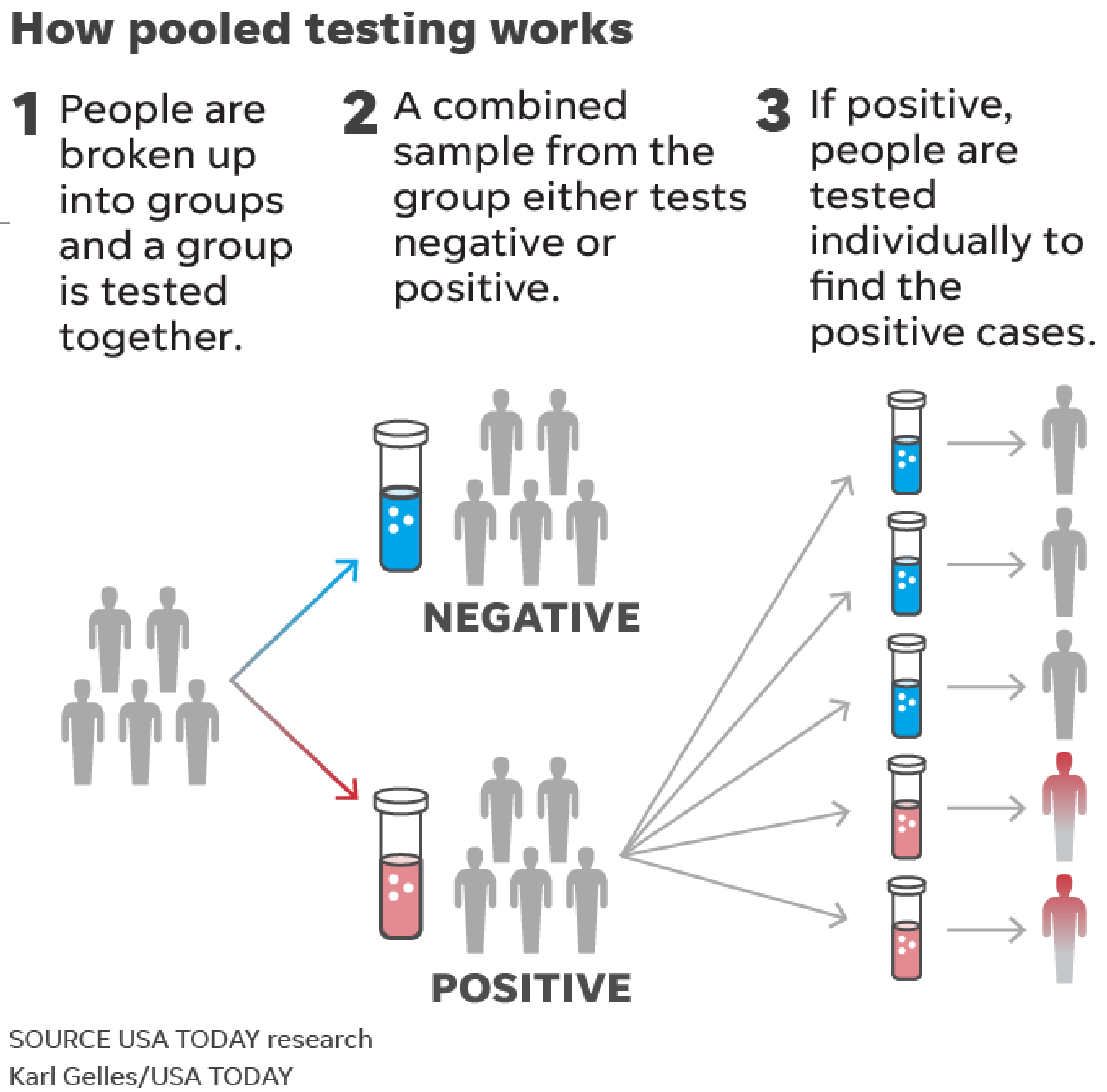
Colleges Turn To Wastewater Testing In An Effort To Flush Out The Coronavirus

October 26, 2020 · 5:01 AM ET

Heard on Morning Edition

Pooled Testing

- Does it reduce the average number of tests?
- How are false positive and false negative rates impacted?



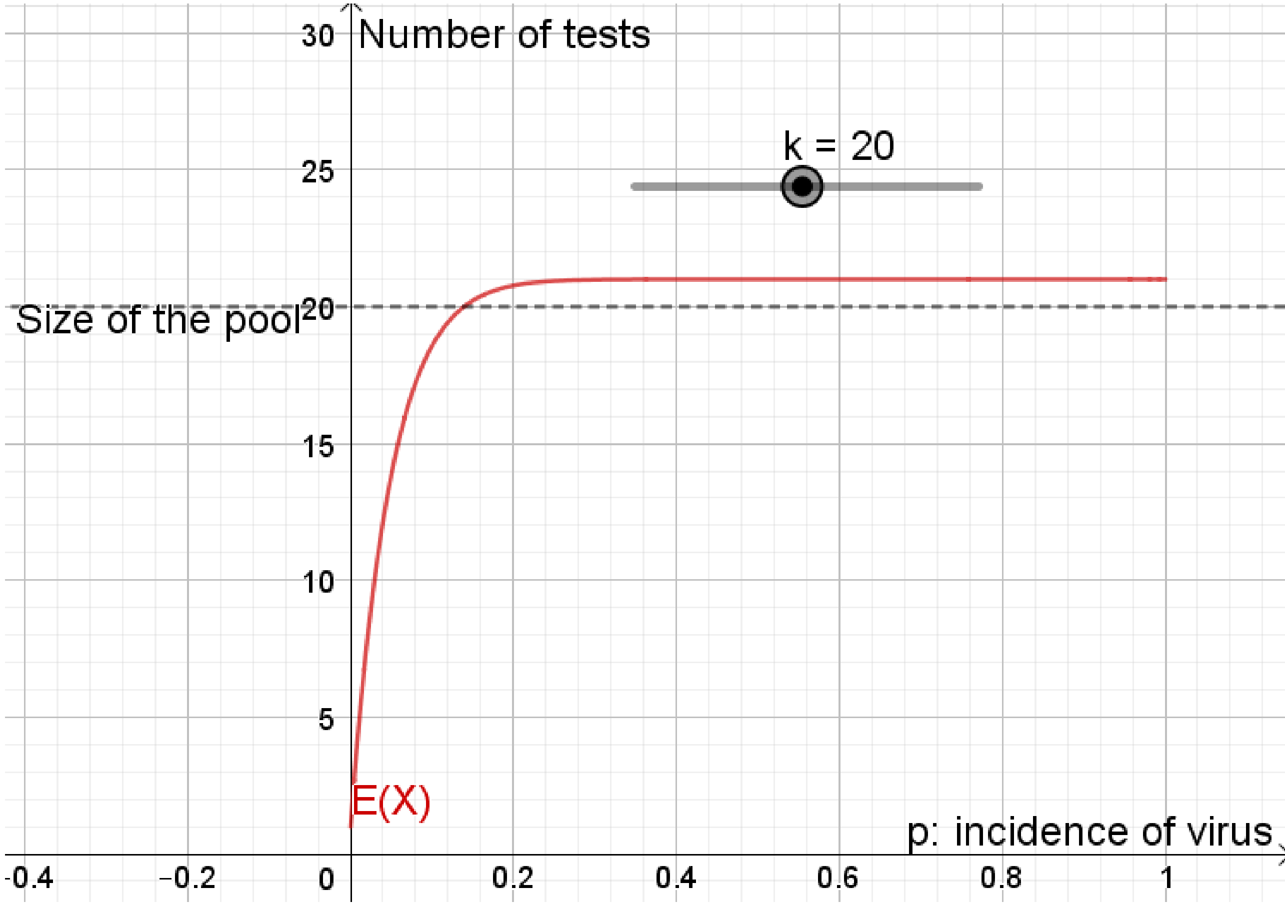
Expected Number of Tests in a Pooled Testing Regime

k: size of the pool, p: incidence of infection

Number of Tests (X)	Probability
1	$(1-p)^k$
k + 1	$1-(1-p)^k$

Expected Number of Tests:

$$E(X) = f(p) = (1-p)^k + (k+1)[1-(1-p)^k]$$



Type I, Type II Errors and Vaccine Trials

	Reject H_0	Do not reject H_0
H_0 true **Vaccinated group has the same infection rate as the placebo group**	TYPE I ERROR α	☺ $1 - \alpha$
H_0 false **Vaccinated group has a lower infection rate**	☺ Power of test = $1 - \beta$	TYPE II ERROR β

Recent news headlines about vaccines…

NEWS / Pfizer and BioNTech Conclude Phase 3 Study of COVID-19 Vaccine Candidate, Meeting All Primary Efficacy Endpoints

PFIZER AND BIONTECH CONCLUDE PHASE 3 STUDY OF COVID-19 VACCINE CANDIDATE, MEETING ALL PRIMARY EFFICACY ENDPOINTS

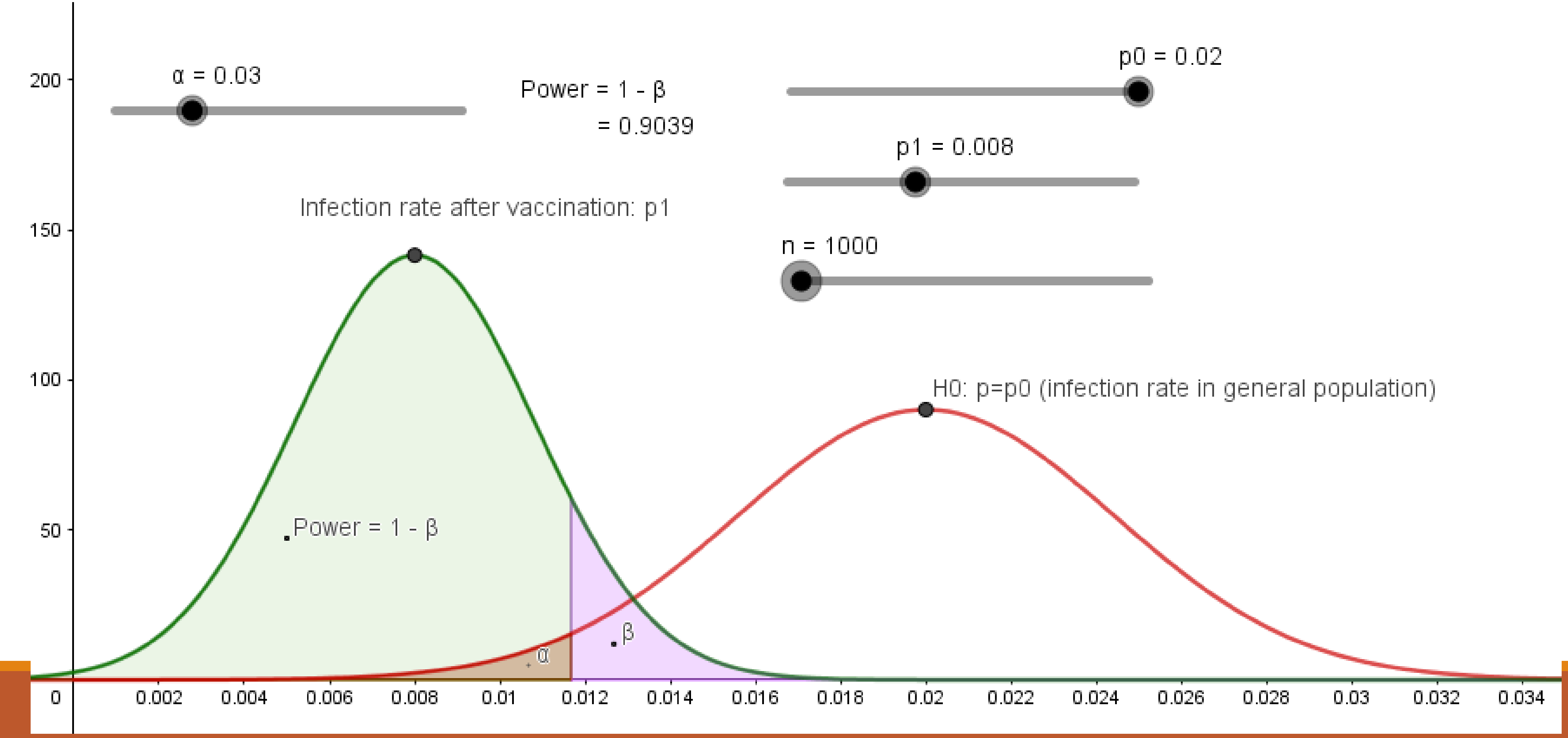
Wednesday, November 18, 2020 - 06:59am

Moderna Announces Primary Efficacy Analysis in Phase 3 COVE Study for Its COVID-19 Vaccine Candidate and Filing Today with U.S. FDA for Emergency Use Authorization

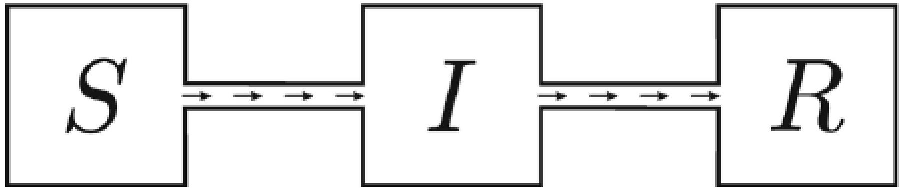
November 30, 2020 at 6:59 AM EST

Source: Pfizer and Moderna

Vaccine Trial Design: Determine Sample Size



The Susceptible-Infected-Resistant Model in Epidemiology



$$\frac{dS}{dt} = -\beta S I$$

$$\frac{dI}{dt} = \beta S I - \gamma I$$

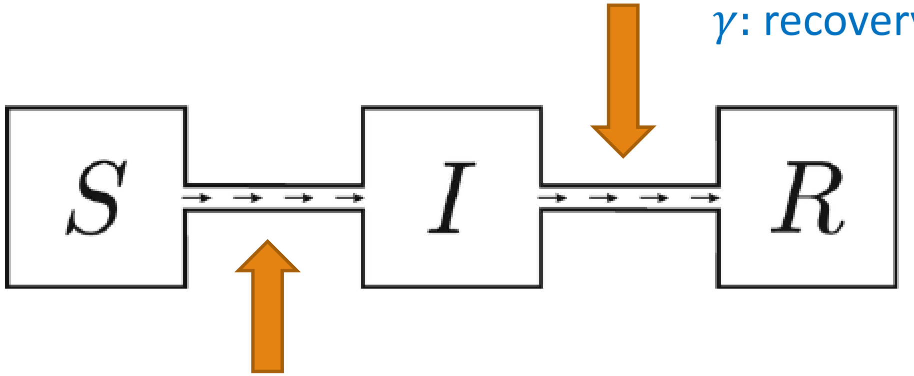
$$\frac{dR}{dt} = \gamma I$$

- Also known as “compartmental models”
- First proposed by Kermack and McKendrick (1927)
- Systems of non-linear, 1st order ordinary differential equations with time as independent variable
- Many variations (SIS, SIRS, SEIR, etc.)

The Susceptible-Infected-Resistant Model in Epidemiology

Rate of moving from I to R
= $\gamma \cdot I$

γ: recovery rate



Rate of moving from S to I
= $\beta \cdot S \cdot I$

β: contact rate

$$\frac{dS}{dt} = -\beta S I$$

$$\frac{dI}{dt} = \beta S I - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

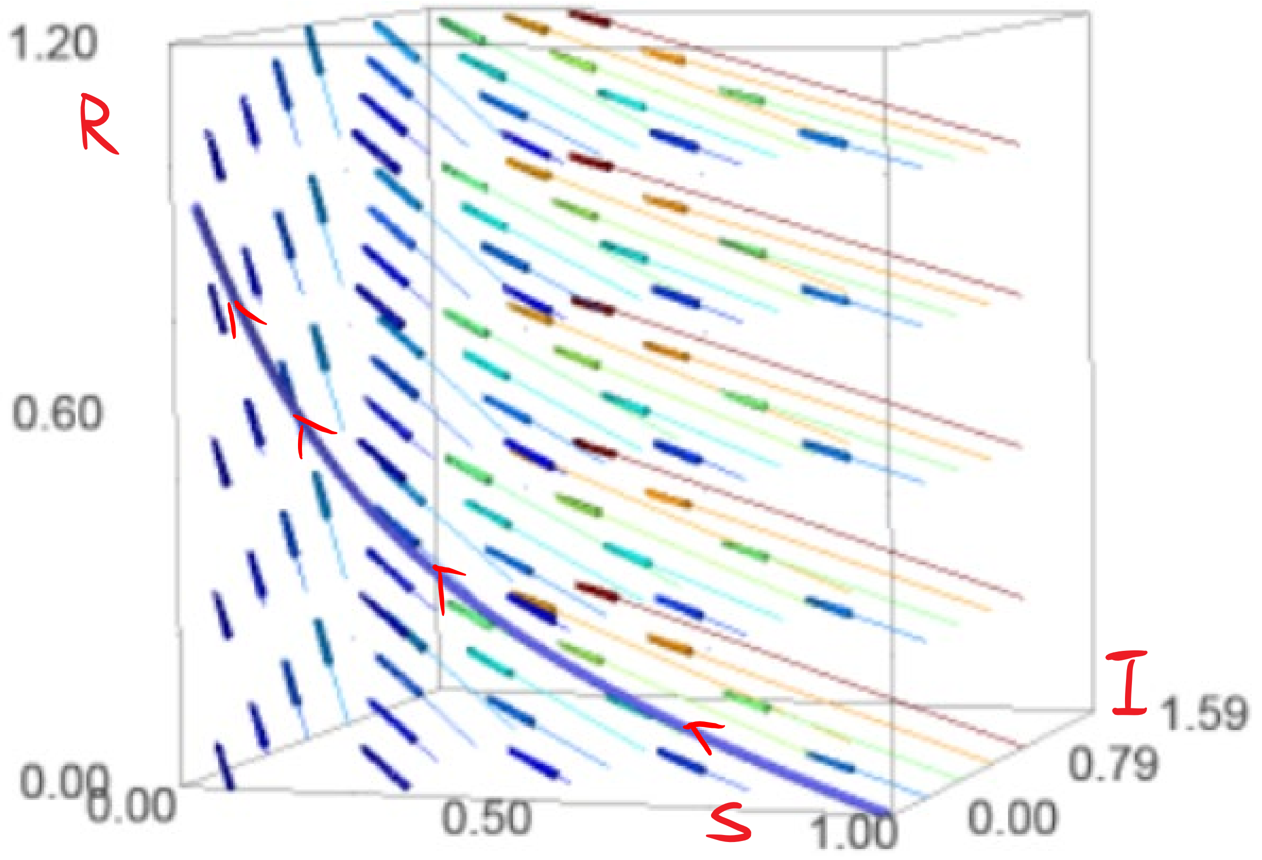
Additional constraint: S + I + R = 1
(No birth or death in the population.)

Initial condition: $(S(0), I(0), R(0))$

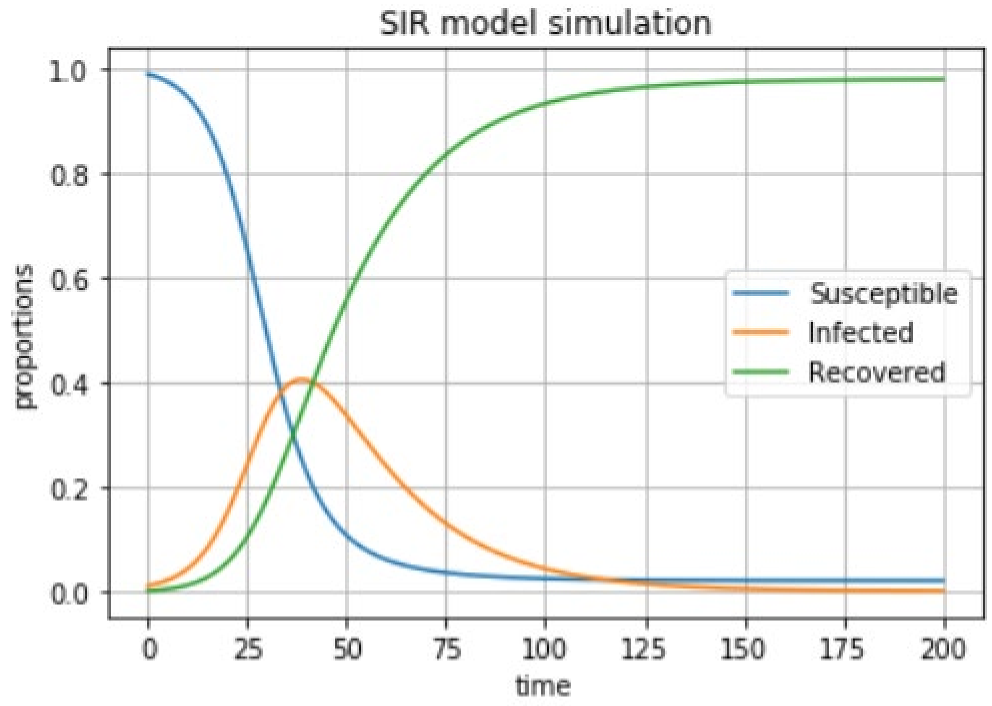
Can be solved using numerical ODE solver

Two Ways to Visualize Solutions

AS ORBITS IN PHASE SPACE



AS FUNCTIONS OF TIME



Stages of an Epidemic: Analyze Rates of Change

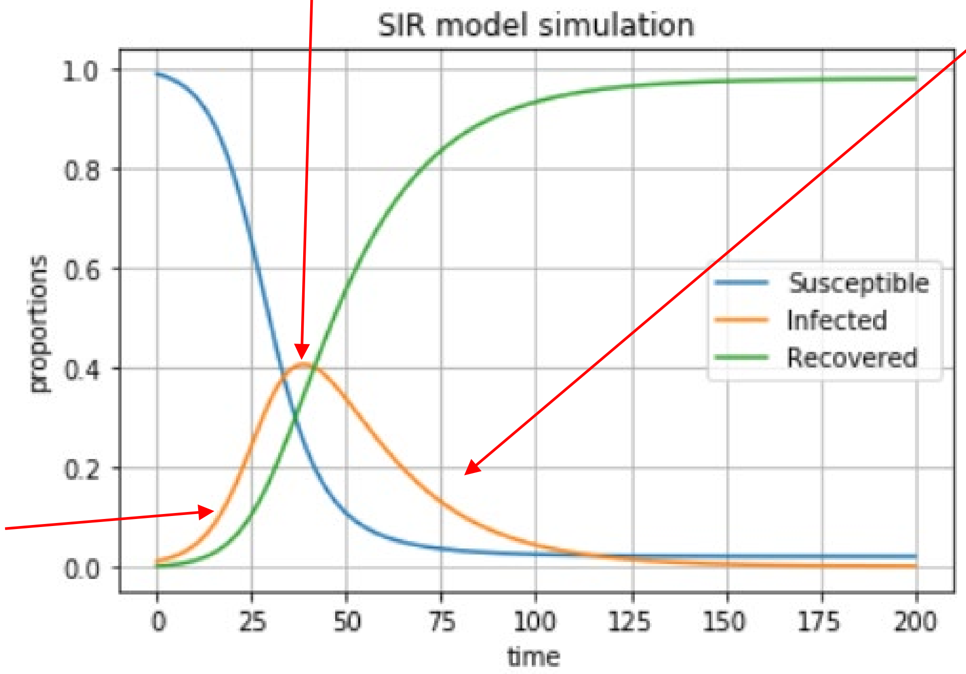
$$\frac{dI}{dt} = \beta SI - \gamma I$$

β: contact rate

γ: recovery rate

Susceptible is gradually depleted until $\beta S - \gamma = 0$. Infected reaches maximum.

If $S \to 0$, $\frac{dI}{dt} \approx -\gamma I$
Resembles exponential decay

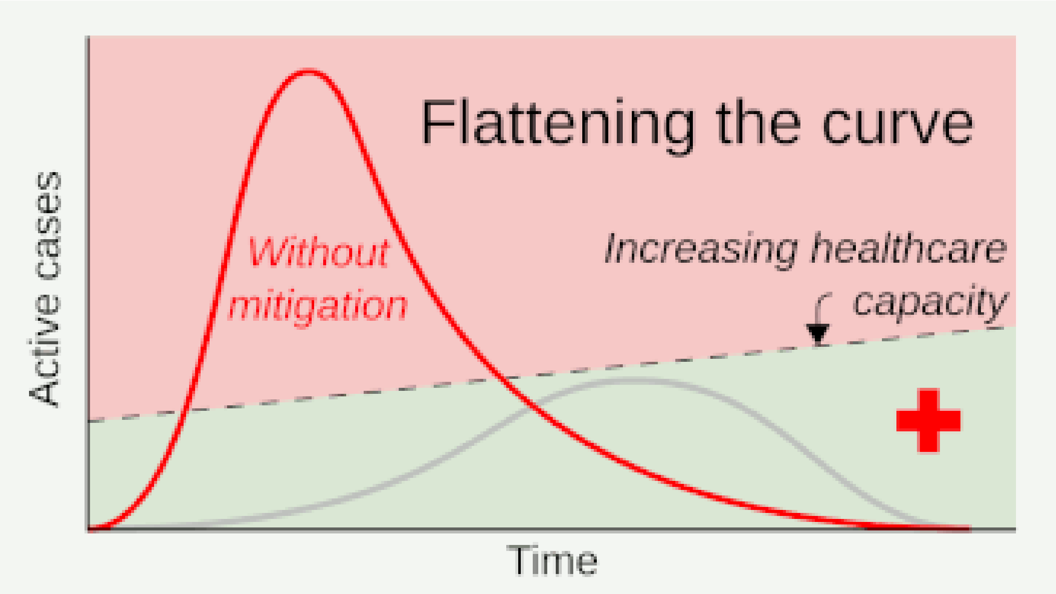


When Infected is small compared to Susceptible,

$$\frac{dI}{dt} \approx (\beta S(0) - \gamma)I$$

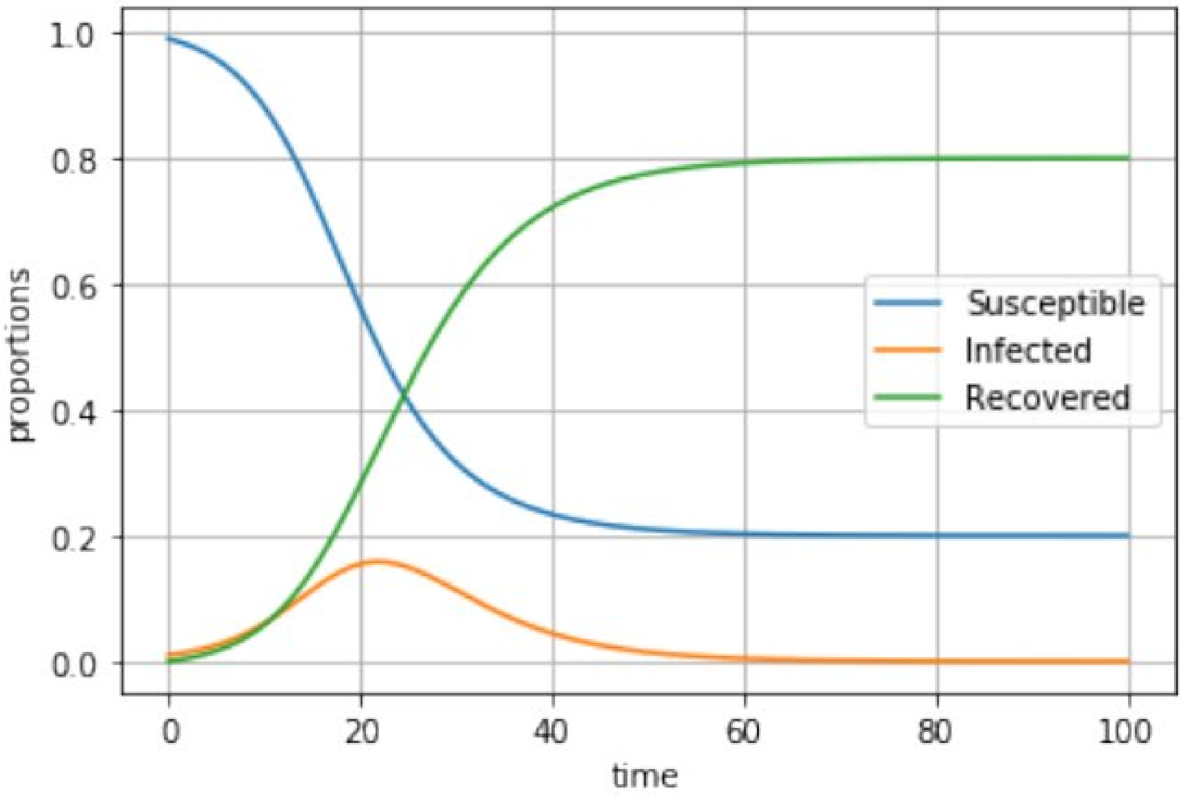
growth is approximately exponential

Flatten the Curve!

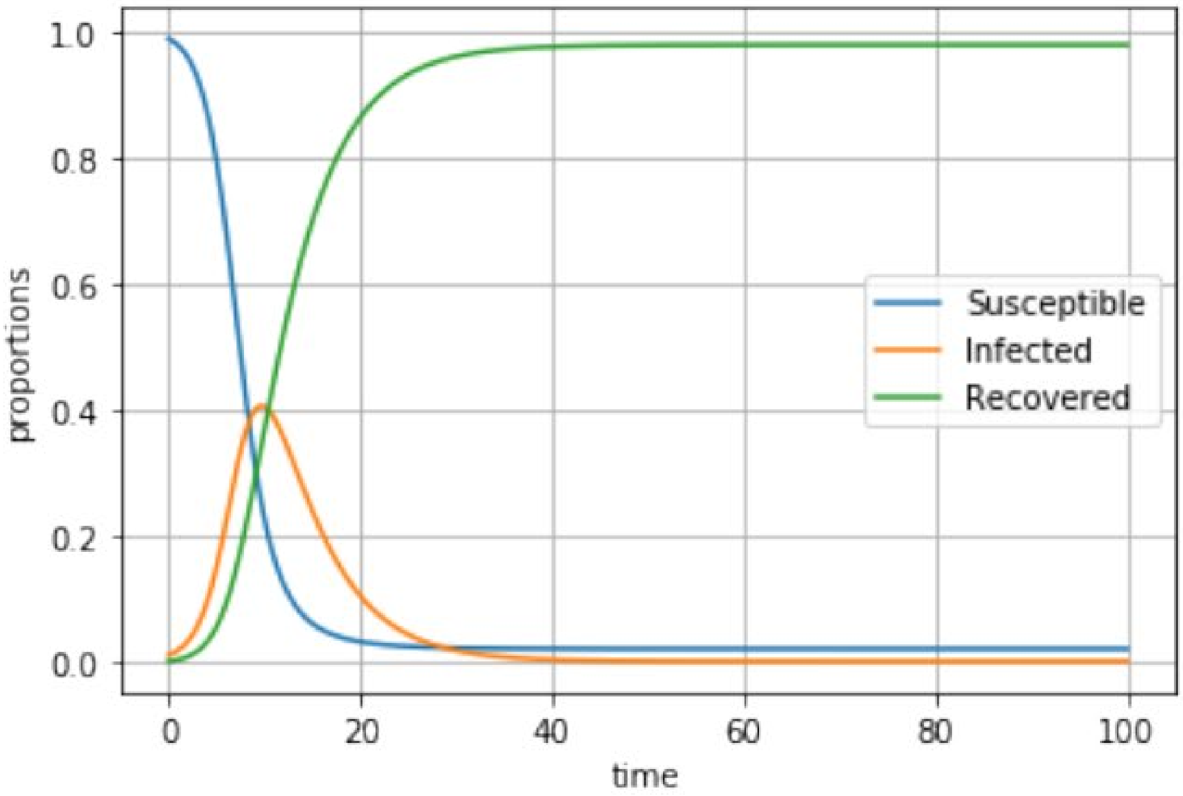


Flattening the Curve by lowering the contact rate parameter β

$$\frac{dS}{dt} = -\beta SI$$
$$\frac{dI}{dt} = \beta SI - \gamma I$$
$$\frac{dR}{dt} = \gamma I$$



(a) $\beta = 0.4, \gamma = 0.2$



(b) $\beta = 0.8, \gamma = 0.2$

The Basic Reproduction Number

$$R_0 = \frac{\beta \cdot S(0)}{\gamma}$$

- Interpretation: the number of secondary infections caused by an infected individual
- $R_0 > 1$ implies $\frac{dI}{dt}|_{t=0} > 0$: There is epidemic
- $R_0 < 1$ implies $\frac{dI}{dt}|_{t=0} < 0$: No epidemic

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

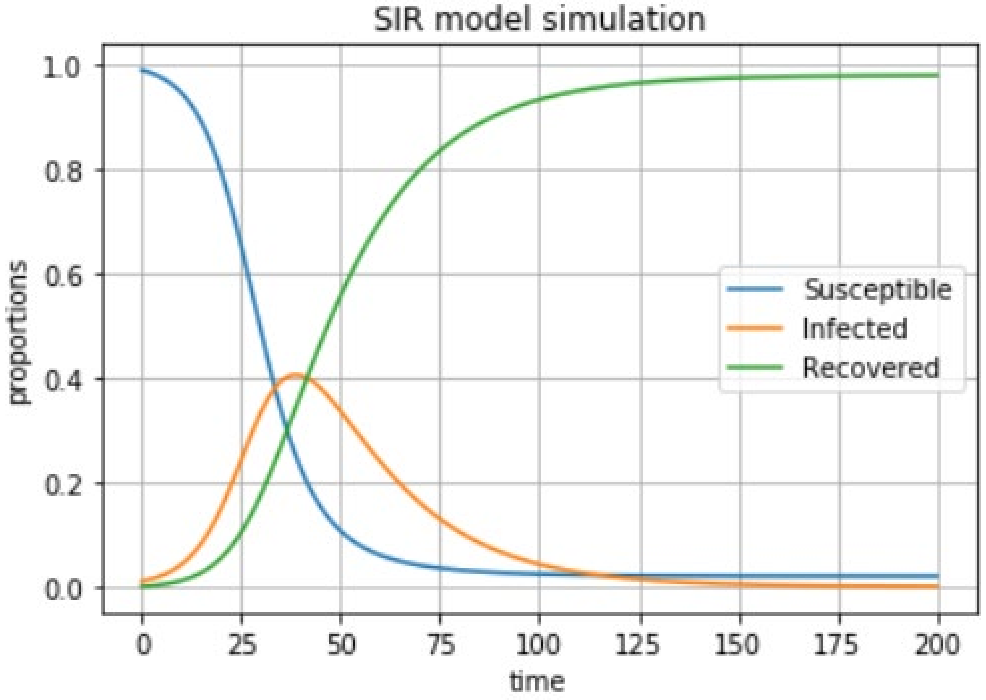
$$\frac{dR}{dt} = \gamma I$$

β: contact rate

γ: recovery rate

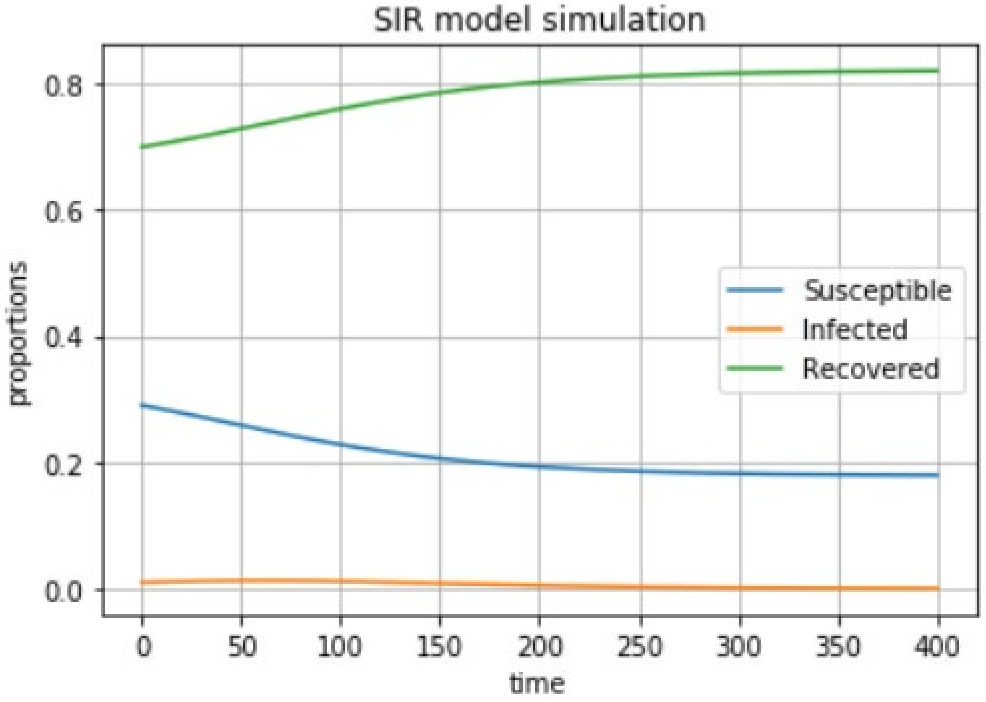
Effect of Mass Vaccination Initial Values

(S(0), I(0), R(0)) = (0.99, 0.01, 0)



$\beta = 0.20, \gamma = 0.05, R_0 = 3.96$

(S(0), I(0), R(0)) = (0.29, 0.01, 0.70)

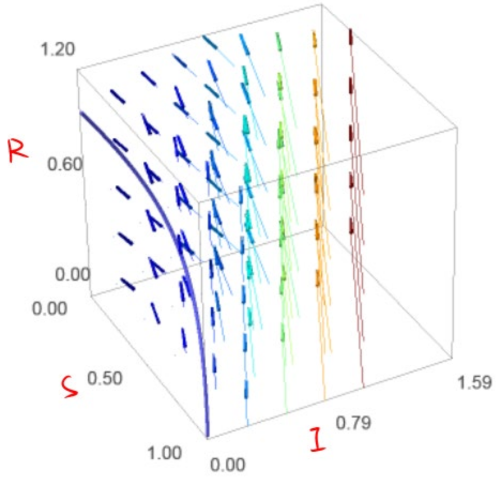


$\beta = 0.20, \gamma = 0.05, R_0 = 1.16$

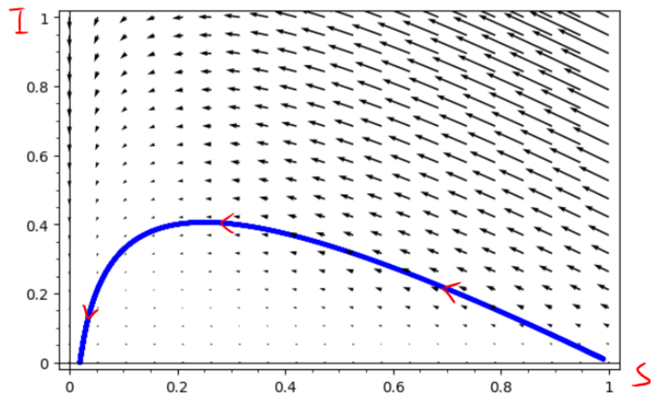
Further Analysis: Critical Points and Stability

$$\frac{dS}{dt} = -\beta SI$$
$$\frac{dI}{dt} = \beta SI - \gamma I$$
$$\frac{dR}{dt} = \gamma I$$

- Does the solution depend on initial values?
- Since S + I + R = 1, we can drop R and analyze the solution on the S-I plane.



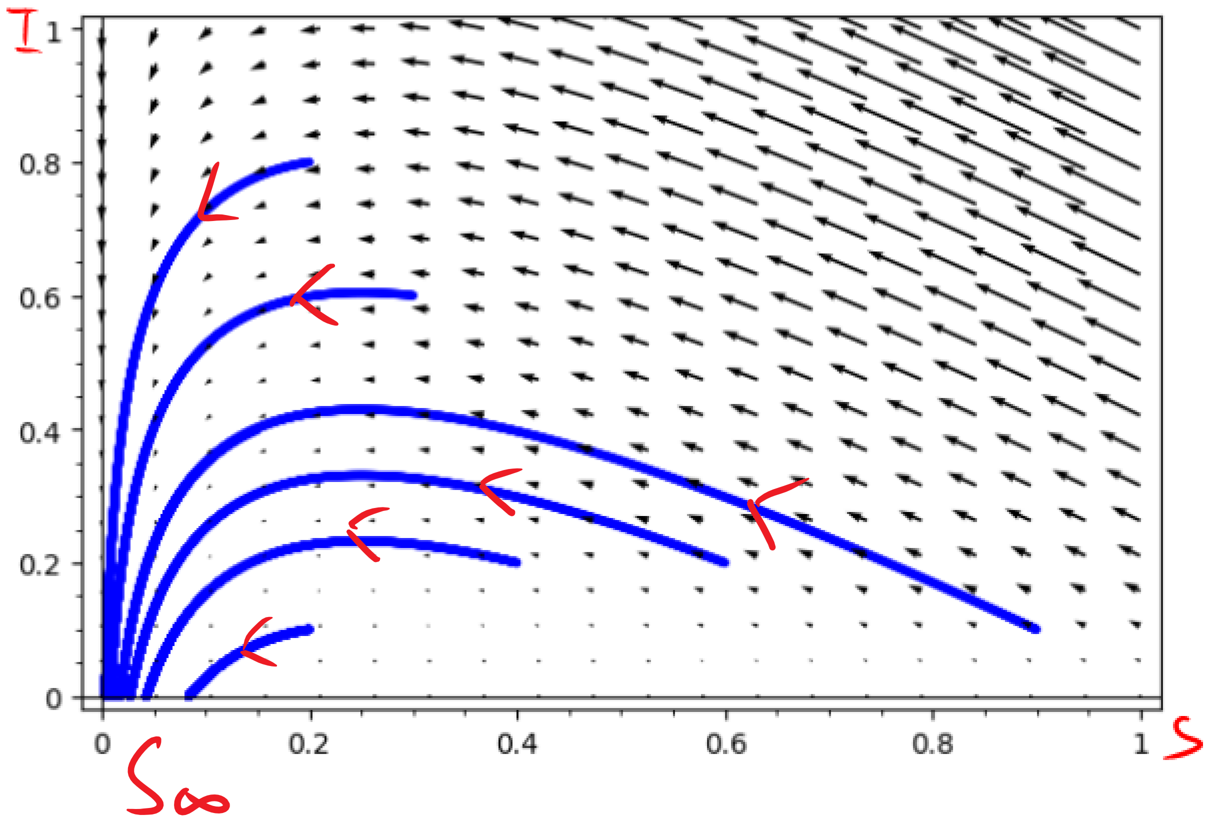
Project onto S-I plane



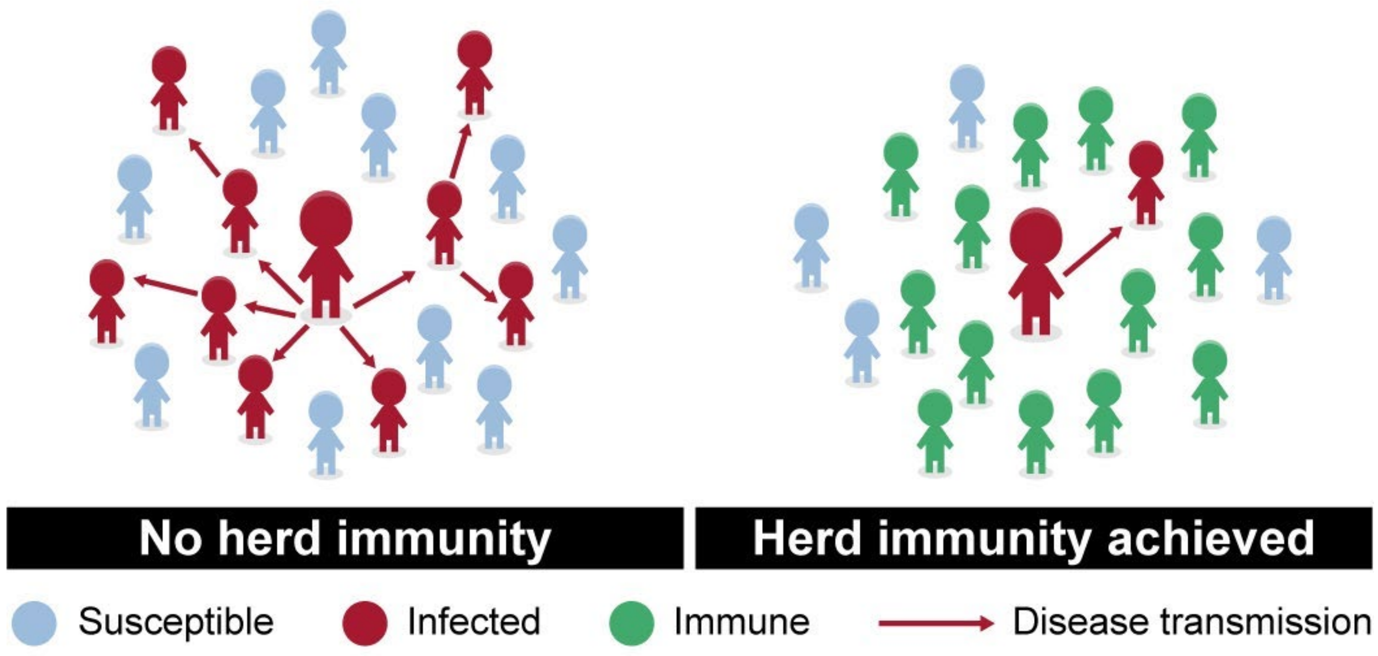
Orbits of Solutions in the S-I Plane

$$\frac{dS}{dt} = -\beta SI$$
$$\frac{dI}{dt} = \beta SI - \gamma I$$
$$\frac{dR}{dt} = \gamma I$$

- Equilibria all occur at $(S_\infty, 0)$, when the Infected disappears.
- Linearizing the system near $(S_\infty, 0)$ shows it's stable.
- Interpretation as "herd immunity"?



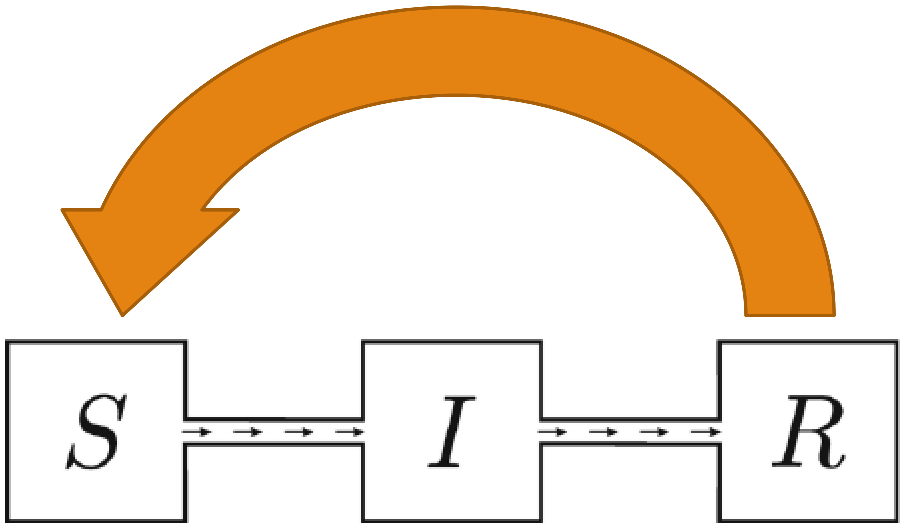
Does "herd immunity" just happen by itself without intervention?



Source: GAO adaptation of NIH graphic. | GAO-20-646SP

Loss of Resistance due to Mutation or Re-infection

- S-I-R model with feedback loop



$$\frac{dS}{dt} = -\beta SI + \alpha R$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I - \alpha R$$

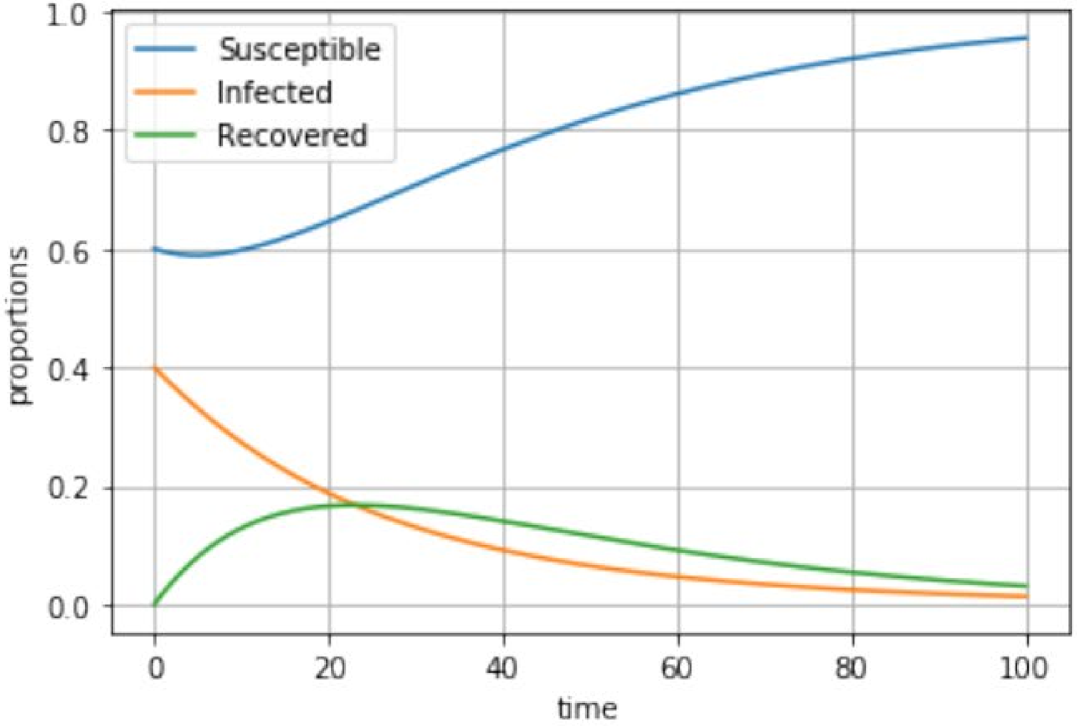
$S + I + R = 1$

$$\frac{dS}{dt} = -\beta SI + \alpha(1 - S - I)$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

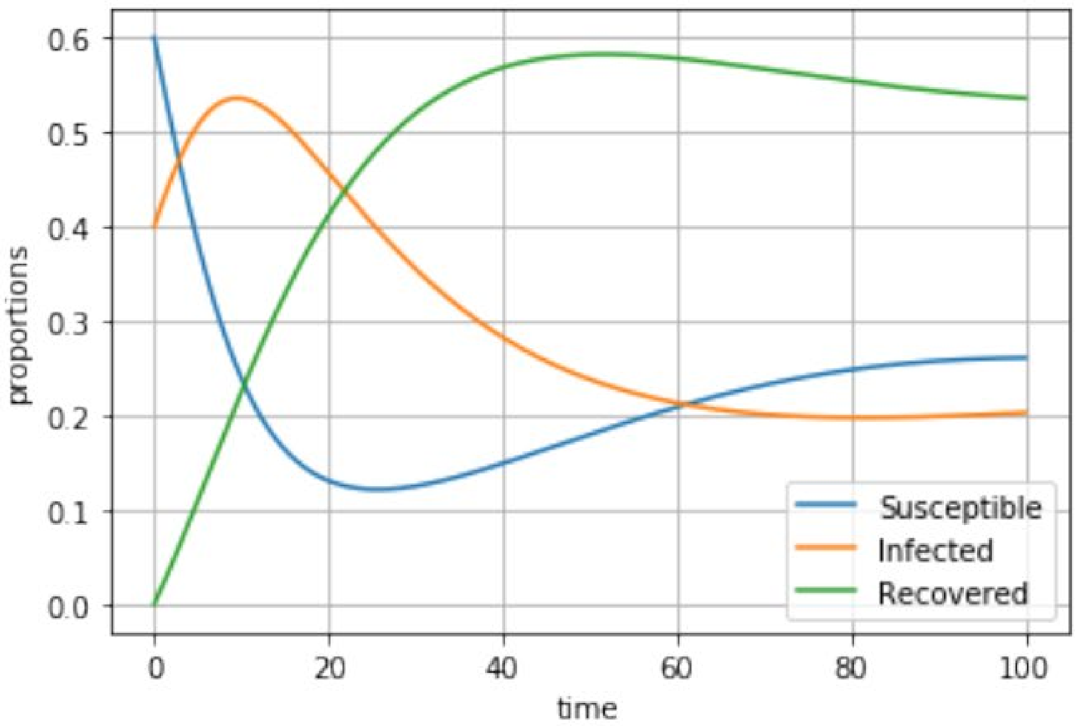
S-I-R with Loss of Resistance

Herd Immunity



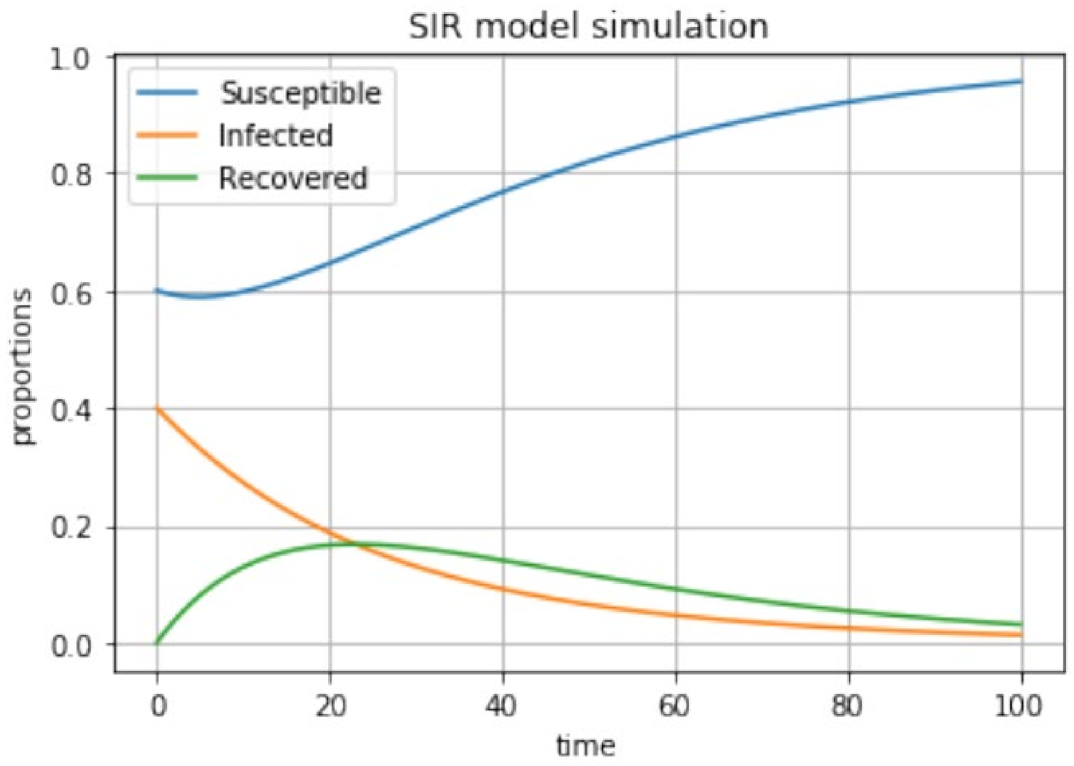
(a) $\alpha = 0.05, \beta = 0.02, \gamma = 0.05$

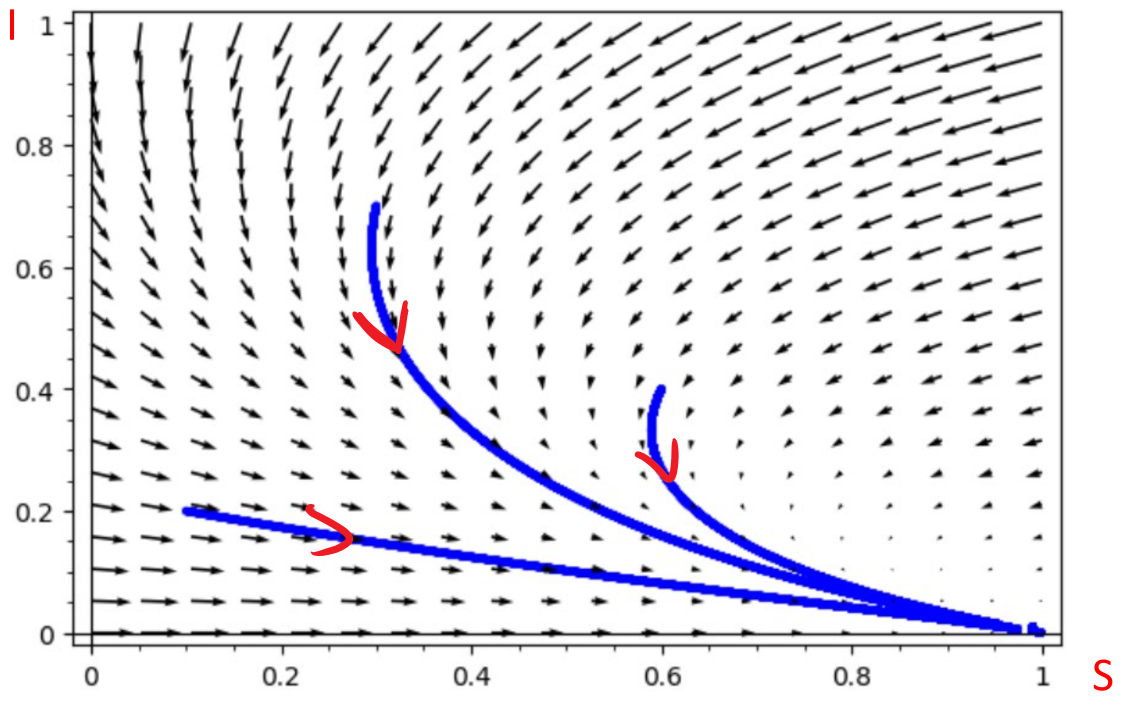
No Herd Immunity



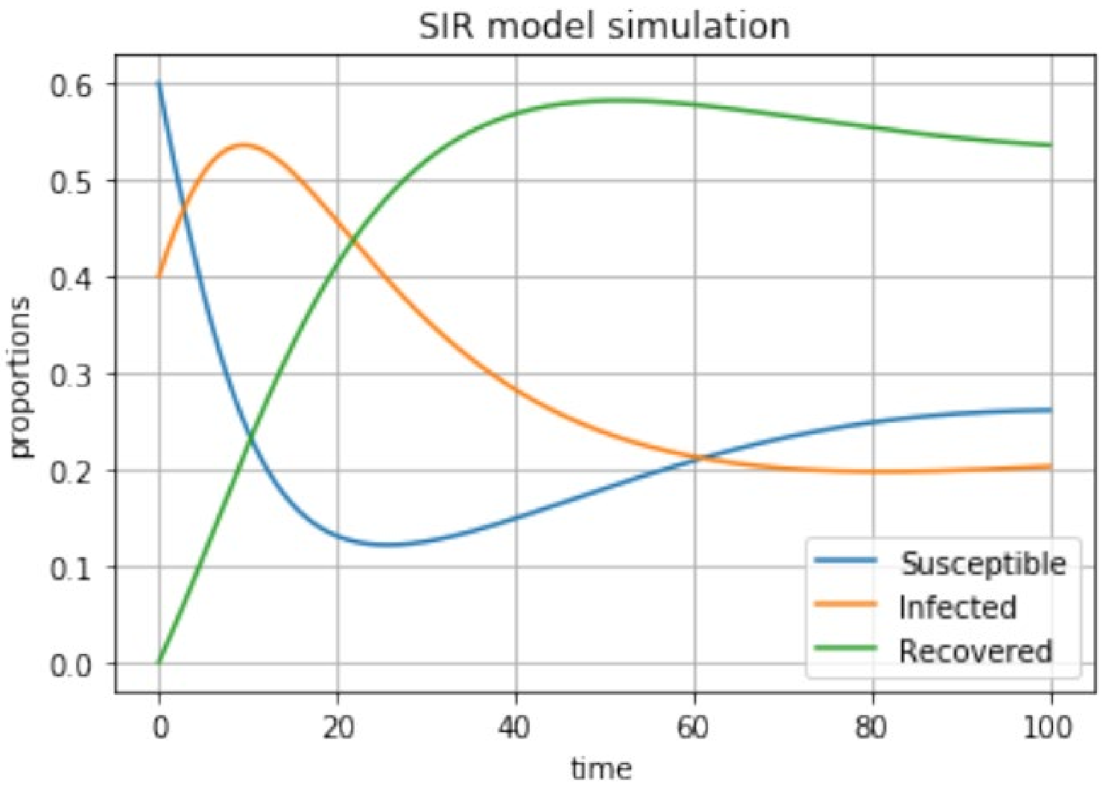
(b) $\alpha = 0.02, \beta = 0.20, \gamma = 0.05$

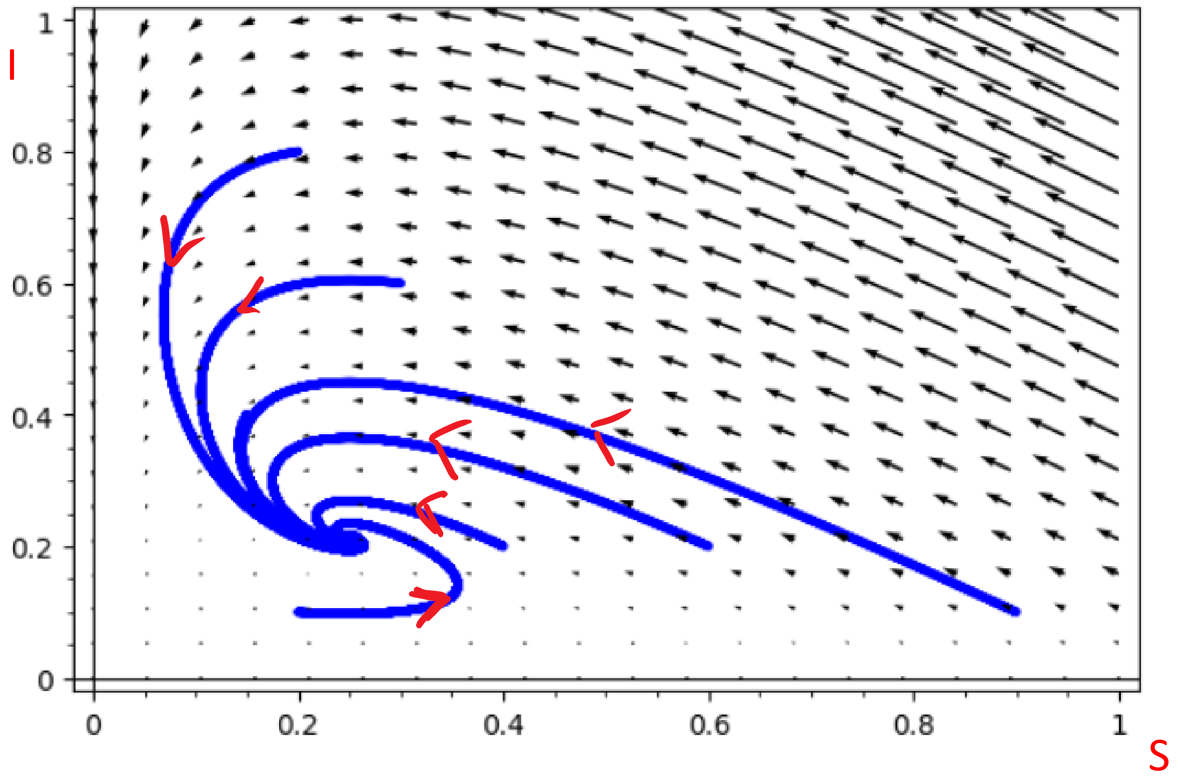
Herd Immunity is Stable only if $\beta < \gamma$ (Critical Point #1)





Herd Immunity Not Achievable: Critical Point #2 is stable under certain conditions

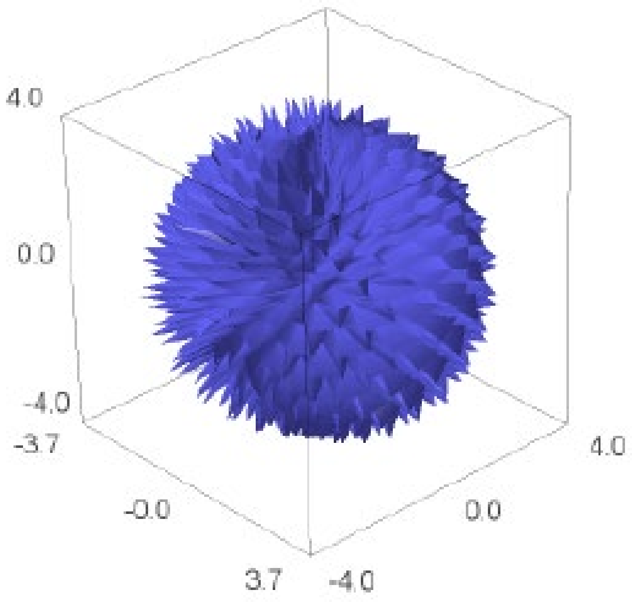




Resources

- Slides, references, the full report and source code are available on my webpage: https://srjcstaff.santarosa.edu/~ylin/

- Open source software:
  - https://www.sagemath.org/
  - https://www.geogebra.org/



Coronavirus-like surface in spherical coordinates:

$$\rho = r_0 + \sin(k \cdot (\phi + \theta))$$

Plotted with SageMath