Incorporating Mass Vaccination into Dynamical System Models

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Overview

- Differential equation models can have differences in scope.
  - **Epidemic** models are for short time periods.
  - **Endemic** models are for indefinitely long time periods.
- Investigations of **epidemic** models center on questions regarding the development of the outbreak and the final state of the population.
  - Methods are primarily numerical.
  - Long-term processes, such as birth and natural death, are usually omitted.
- Investigations of **endemic** models center on questions regarding equilibrium solutions and their stability.
  - Methods are primarily analytical.

Vaccination in Disease Models

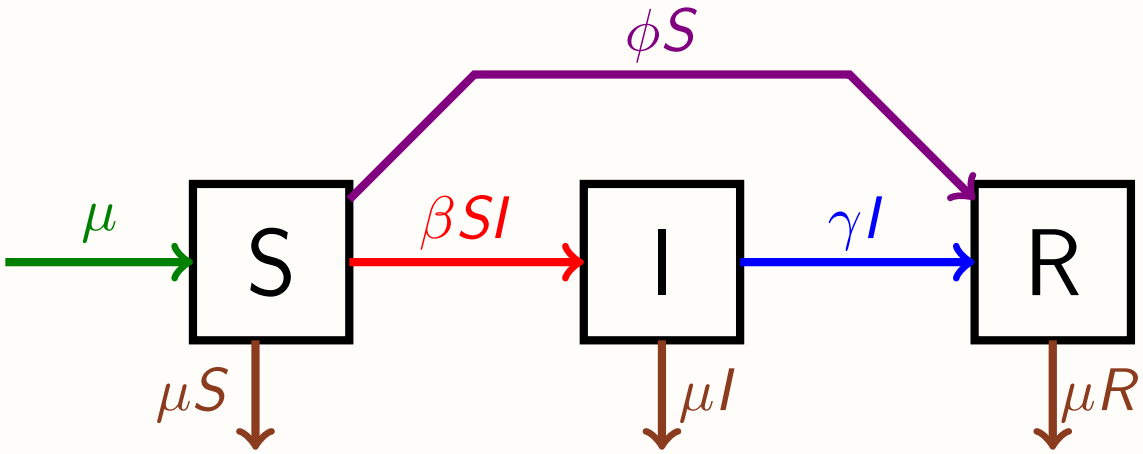
- The standard treatment of vaccination in disease models is too naive. This talk is about improved ways of incorporating vaccination into disease models.

1. We'll start with a simple **endemic** model.
2. Then we'll add features needed for a **epidemic** model.
3. We'll finish with new work on an **endemic** model that incorporates changing attitudes toward vaccination, with surprising results.

Part 1: Vaccination in a Simple **Endemic** Model

1. We add vaccination to the standard SIR model with fixed population size.
2. We see that full vaccine acceptance yields herd immunity, given an adequate booster program (we're assuming the vaccine is 100% effective to represent a best case).
3. We design a model to investigate the impact of vaccine non-acceptance (which is not considered in standard models).
4. The results show that non-acceptance can significantly reduce the impact of a vaccination program.

SIR Endemic Model with Vaccination



(S)usceptible, (I)nfectious, (R)emoved

transmission, recovery, vaccination, death, birth

The arrows indicate process rates; e.g.

$$\frac{dS}{dt} = -\beta SI - \phi S - \mu S + \mu$$

Primary Assumptions and Results

1. Vaccination and recovery are 100% effective against infection.
2. Vaccine acceptors update their vaccinations to prevent loss of immunity.
3. **Everyone** accepts vaccination.

- The disease disappears if the vaccine-reduced basic reproduction number

$$\mathcal{R}_v = \frac{\mathcal{R}_0}{v}$$

  is less than 1 (guaranteed for any reasonable vaccination rate).
- Otherwise, the equilibrium infectious population is

$$I^* = \epsilon \left(1 - \mathcal{R}_v^{-1}\right)$$

Research Question

Suppose we keep the assumptions of 100% effectiveness and regular updates by acceptors, but we allow for a significant number of non-acceptors. How does this change the results?

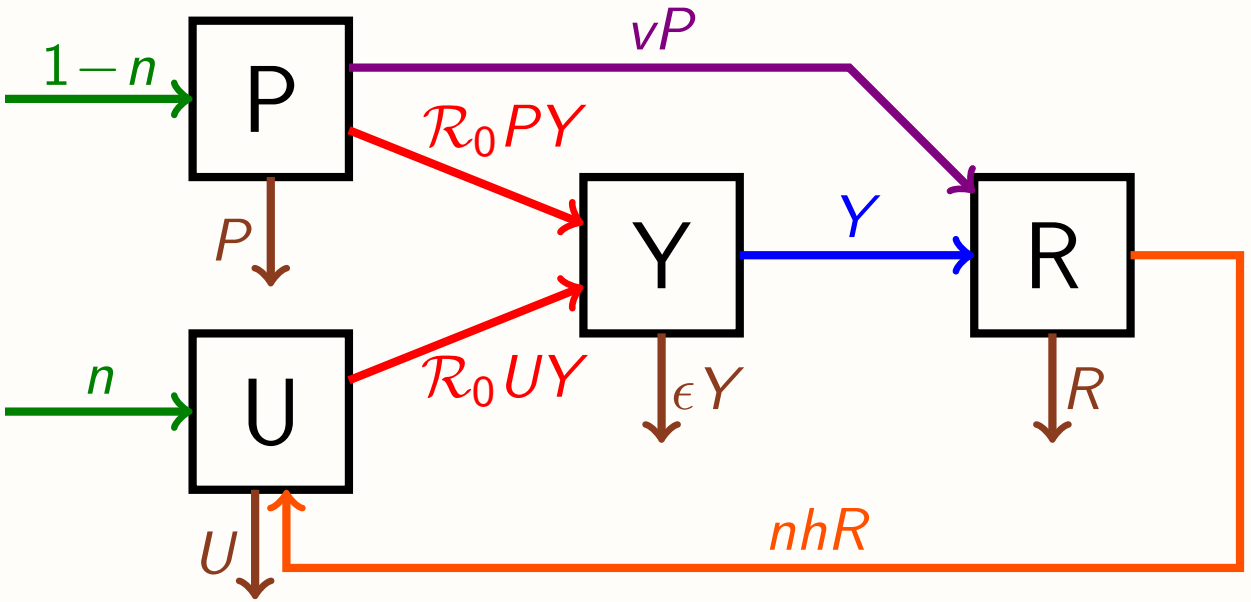
Investigating the Impact of Vaccine Non-Acceptance

- Requirements:
  1. Demographic processes of birth and natural death.
  2. Vaccination.
  3. Vaccine non-acceptance.
  4. Loss of immunity.

- Class Structure:
  - Start with SIR.
  - Partition S into (P)revaccinated and (U)nprotected subclasses.

- Principal Input Parameters:
  - $\mathcal{R}_0$ in the absence of vaccination.
  - Vaccination rate (v).
  - Loss of immunity rate (h).
  - Non-acceptance fraction (n).

The Endemic PUIRU Model (scaled)



transmission, recovery, vaccination, birth, death, loss of immunity

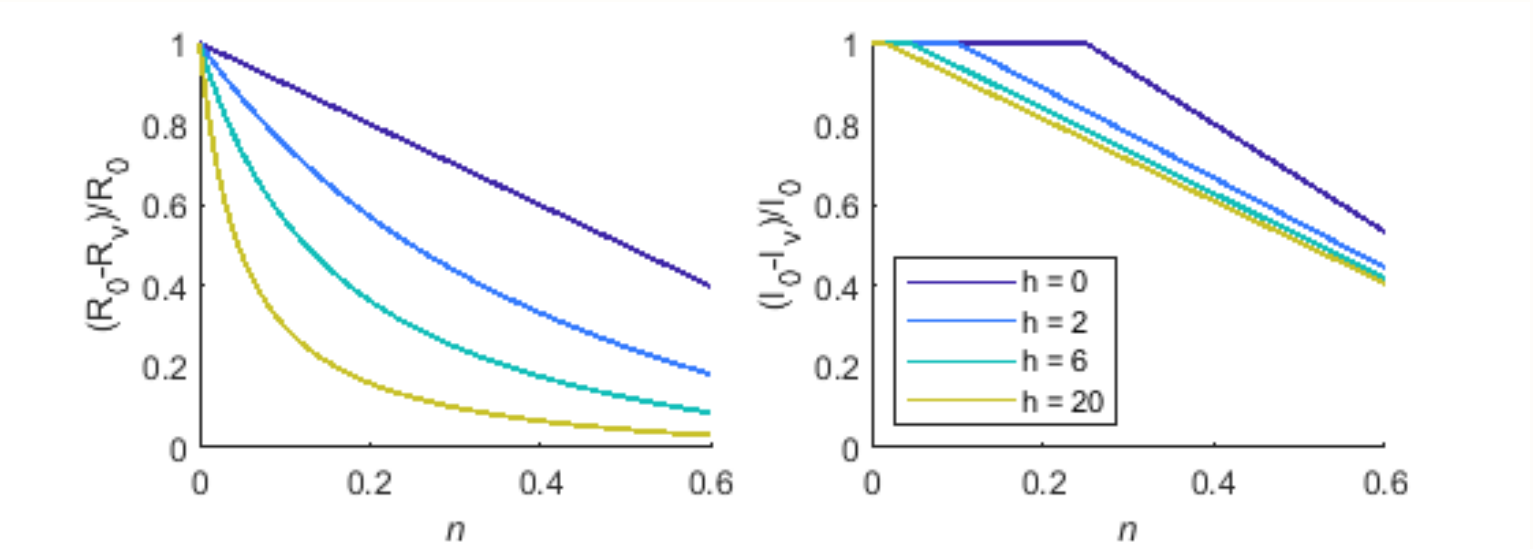
boosters prevent loss of immunity for protected people

Y is 'fast' (rate multiplied by $1/\epsilon$, where $\epsilon = \mu/(\gamma + \mu) \ll 1$)

Results for $\mathcal{R}_0 = 4$ (approximated for large v)

Fractional improvements compared to the no-vaccine control:

left is $\mathcal{R}_v$; right is equilibrium I

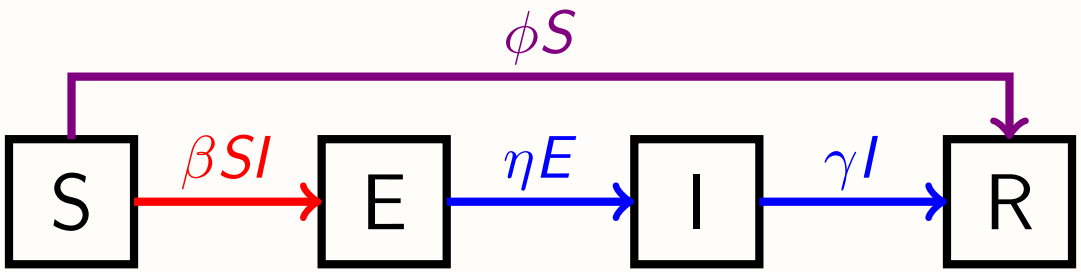


- Even a small non-acceptance rate makes a big difference to $\mathcal{R}_v$ for diseases with short-lived immunity.
- Non-acceptance decreases the reduction in case counts.
- This is a **best case** scenario!

Part 2: Vaccination in a Simple **Epidemic** Model for a Novel Disease

1. We start with a naive SEIR epidemic model with vaccination.
   - Vaccination has a large impact in this model.
2. We show the poor fit of the standard vaccination model to data and catalog its flawed assumptions.
3. We develop a vaccination model that corrects these flaws and fits US data.
4. We examine the impact of vaccination using the more realistic model.
   - Guess what happens!

Standard SEIR Epidemic Model with Vaccination



$$S' = -\beta SI - \phi S, \qquad S(0) = S_0;$$

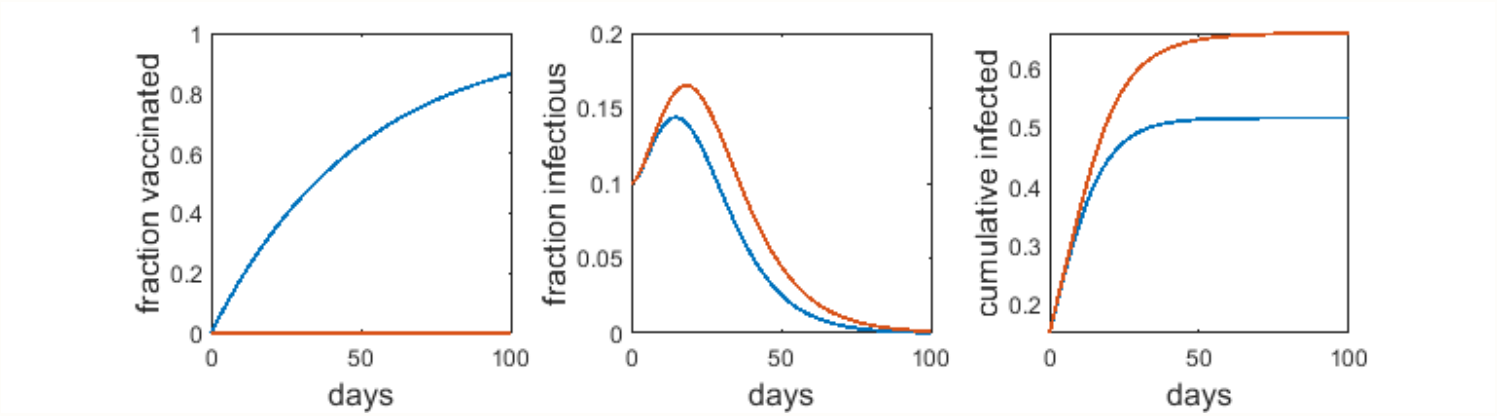
$$E' = \beta SI - \eta E, \qquad E(0) = E_0;$$

$$I' = \eta E - \gamma I, \qquad I(0) = I_0.$$

- No slow processes (natural death, birth, loss of immunity)
- Blue and violet processes are spontaneous transitions.
  - **Times are exponentially distributed.**

Vaccination Impact in the Standard Model

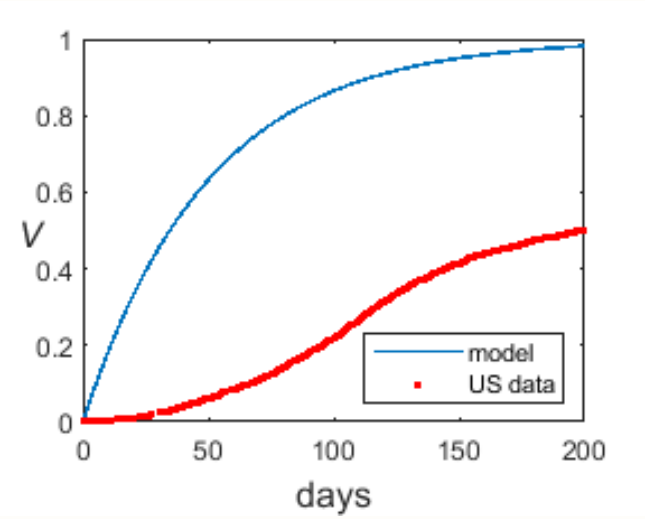
- $\phi = 0.02$ — mean time for vaccination is 50 days.
- Effective reproduction number 4.0, corresponding to delta variant of COVID-19 with some mitigation.



- Vaccination (blue vs red) makes a significant difference! But...

Reality Check

- The vaccination graph looks nothing like real data. (V is total vaccinations.)



- What is wrong with the spontaneous transition model?
  1. Everybody gets the vaccine.
  2. Supply is unlimited.
  3. Distribution is instantaneous.

A Short-Term Vaccination Model

- Partition the susceptible class into (P)revaccinated and (U)nprotected subclasses, with initial proportions $1-n$ and n.
- Vaccination is not reserved for susceptibles. If W is the population fraction waiting for vaccination, then a fraction P/W of vaccinations are administered to class P.

$$W'(t) = -\Phi(W,t)W, \quad W(0) = 1-n,$$

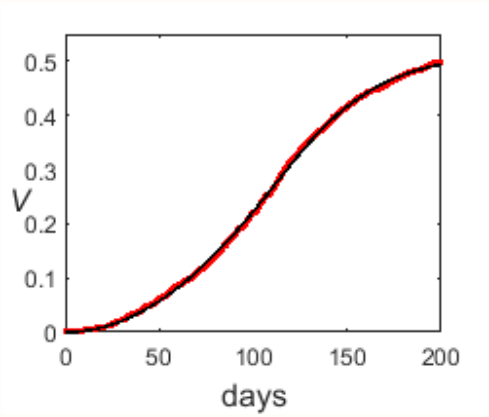
$$P'(t) = -\Phi(W,t)P - \beta PI, \quad P(0) = (1-n)S(0).$$

- $\Phi_t \geq 0$ because supply increases over time.
- $\Phi_W \leq 0$ because distribution is more difficult when there are few unvaccinated people.

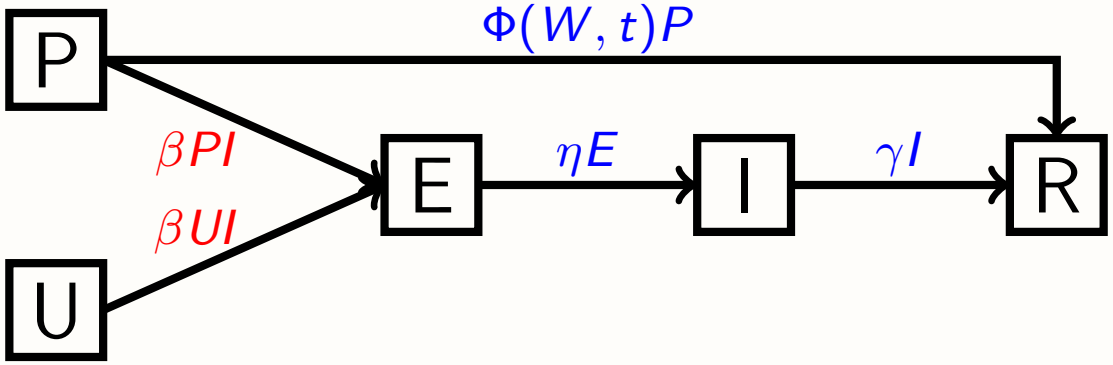
Accounting for Limited Distribution and Supply

- Finding recipients for a vaccinator is like finding prey for a predator—time is partitioned between searching and handling.
- Holling type 3 is slightly better than type 2.
  - It fits the data better.
  - Low patient density makes searching less efficient.
- Supply is limited by a bounded increasing function of time.

$$W' = -\frac{\phi g(t) W^2}{K^2 + W^2}, \qquad g(t) = \min\left(\frac{t}{\tau}, 1\right).$$



Limited Acceptance/Distribution/Supply Model



$$P' = -\beta PI - \Phi(W,t)P, \qquad P(0) = (1-n)S_0;$$

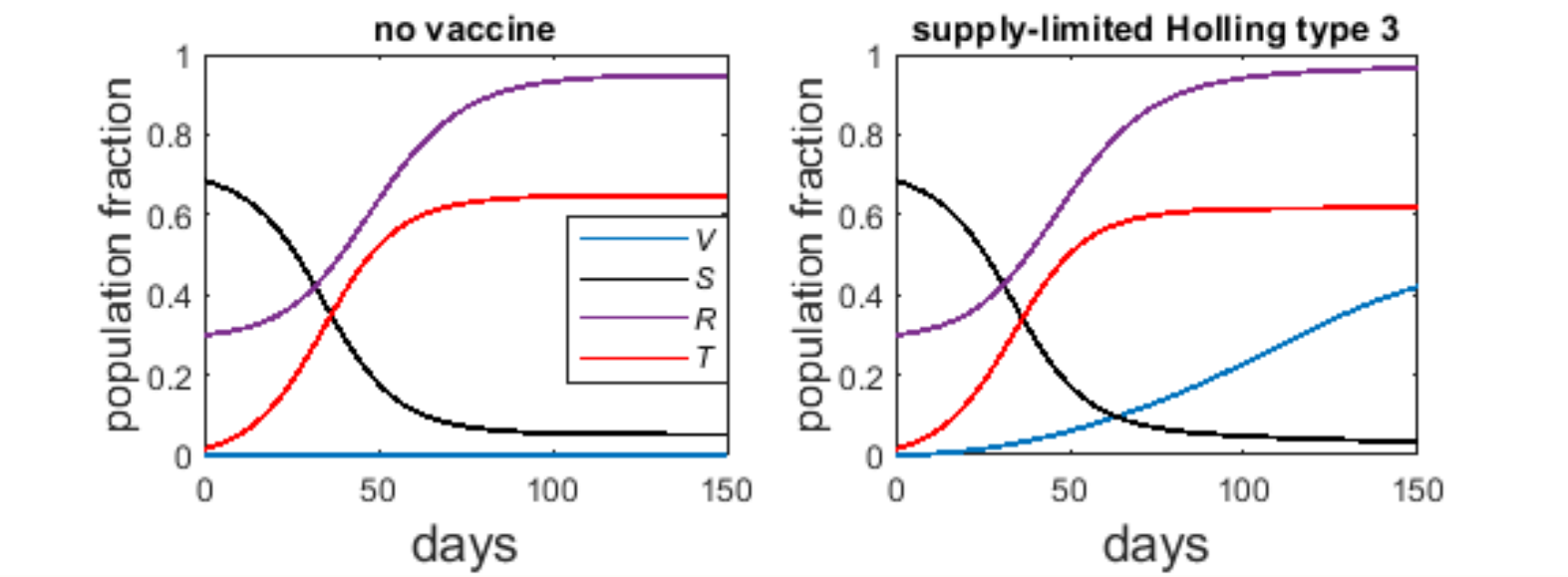
$$U' = -\beta UI, \qquad U(0) = nS_0;$$

$$E' = \beta(P+U)I - \eta E, \qquad E(0) = E_0;$$

$$I' = \eta E - \gamma I, \qquad I(0) = I_0;$$

$$W' = -\Phi(W)W, \qquad \Phi(W) = \frac{\phi g(t) W}{K^2 + W^2}, \qquad W(0) = 1-n.$$

Model Results

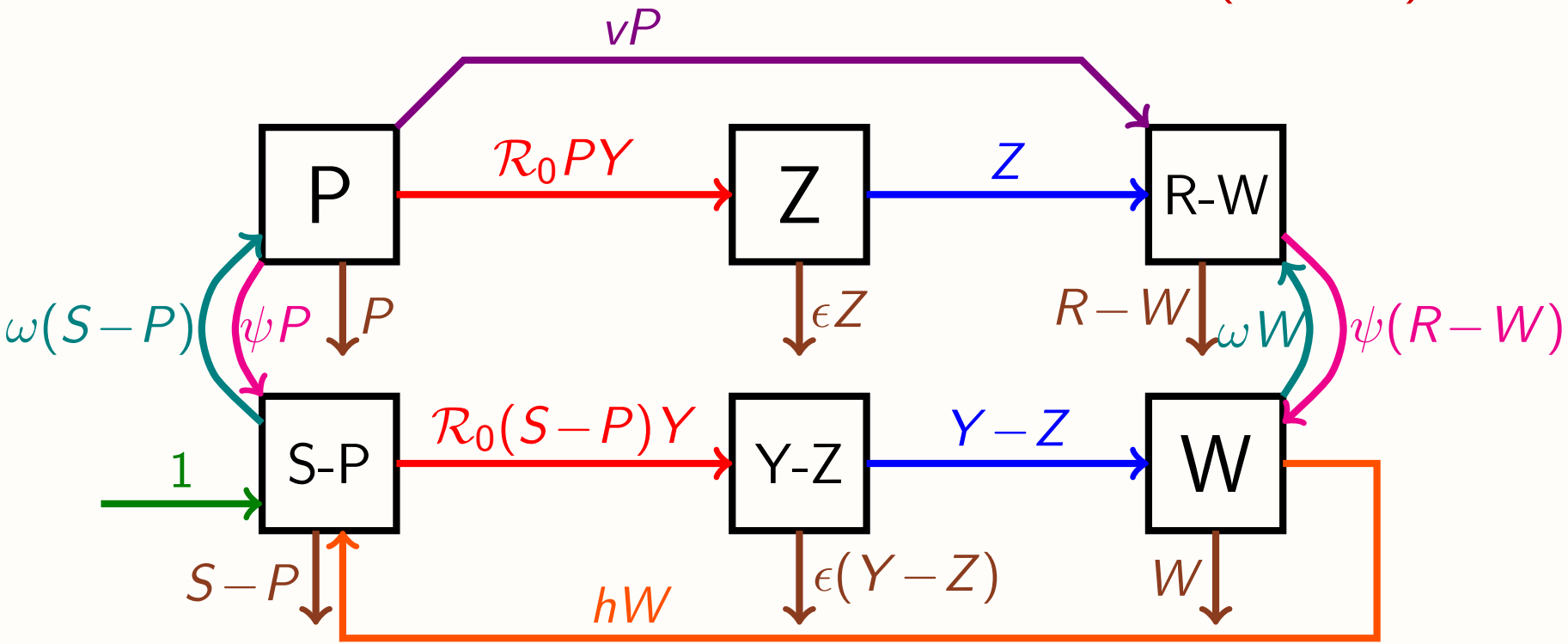


- V is total vaccinated, $S = P + U$, T is total infected.
- In this scenario, total infections are reduced by only 5% because vaccination takes too long.
- Non-acceptance doesn't matter because so little vaccine is available.

Part 3: An **Endemic** Model with Changing Attitudes Toward Vaccination

- We create a variant on PUIRU in which everyone is born unprotected, but there are mechanisms that cause people to change between being willing and unwilling to be vaccinated.
- We assume that higher infection counts encourage people to be vaccinated/boosted and lower counts encourage them not to.
- Conjecture: Having the total protected and unprotected populations depend on infection count could cause instability, which is rare in epidemiology models.

The Endemic 'Flexible Attitude' PUIRU Model (scaled)



Y and Z are 'fast'

We use total variables S, Y, R and component variables P, Z, W.

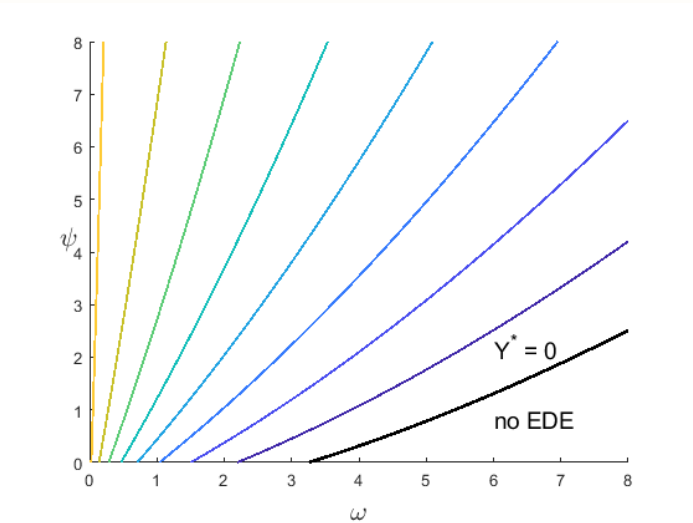
ω and ψ and are functions of Y. We expect $\omega' > 0$, $\psi' < 0$
(more disease means more vaccination acceptance)

Objectives for the Analysis

1. Obtain a simple numerical problem to connect ω and ψ to Y^* and use it to plot level curves Y^* =const in the $\omega\psi$ plane.
2. Assuming $\Sigma = \omega + \psi$ is constant, plot a curve of ω vs Y corresponding to solutions.
3. Identify approximate stability conditions to see if there might be scenarios with no stable equilibrium.
4. Propose a function family for $\omega(Y)$ and look for unstable regimes.
5. If an unstable regime can be found, examine the solution.

1. Relationship of ω^* and ψ^* to Y^*

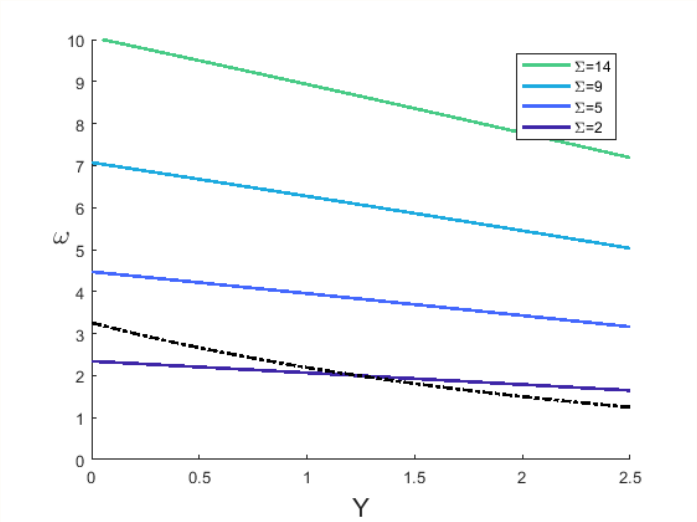
1. The equilibrium relations reduce to $\omega^* = f(Y^*, \Sigma^*)$.
2. Fix Y^* for a level curve. Using Σ^* as a parameter, calculate ω^* from f, and $\psi^* = \Sigma^* - \omega^*$.



- Larger ω is needed to compensate for larger ψ.
- Conversion from unprotected to protected is needed to obtain herd immunity (because everyone is born unprotected).

2. Required ω^* to get Y^* for given fixed Σ

1. Fix Σ^*. Calculate ω^* for a range of Y^*.



- If $\omega(0)$ is below the dashed line, the disease-free equilibrium is unstable.
- As ω increases with Y, it crosses the fixed Σ equilibrium line once with a value less than Σ.

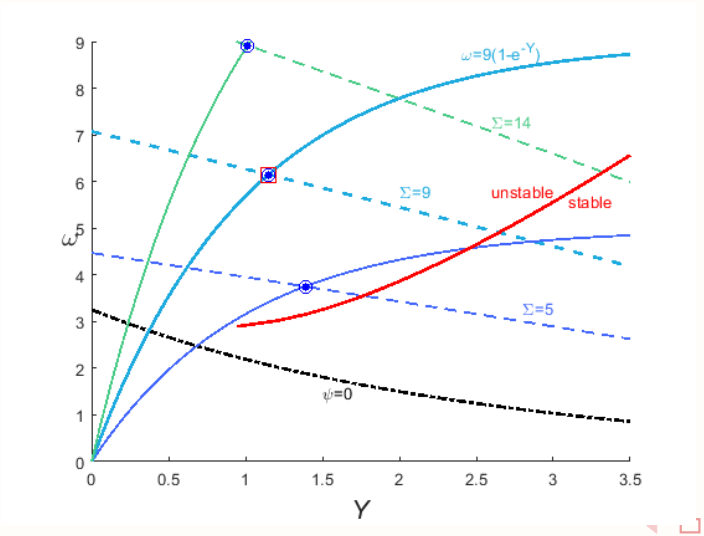
3. Instability Condition

1. Finding analytical formulas for eigenvalues of a 6×6 matrix is not feasible, but we don't need to do that.
2. We can find the characteristic polynomial and use asymptotics to calculate leading order coefficients as $\epsilon \to 0$.
3. We can use a Routh array to identify asymptotic Routh-Hurwitz conditions (inequalities in the parameter space).
4. All but one RH condition is automatically satisfied.
5. The remaining condition identifies a simple function g such that instability requires $\omega'(Y^*, \Sigma) > g(Y^*, \Sigma)$.

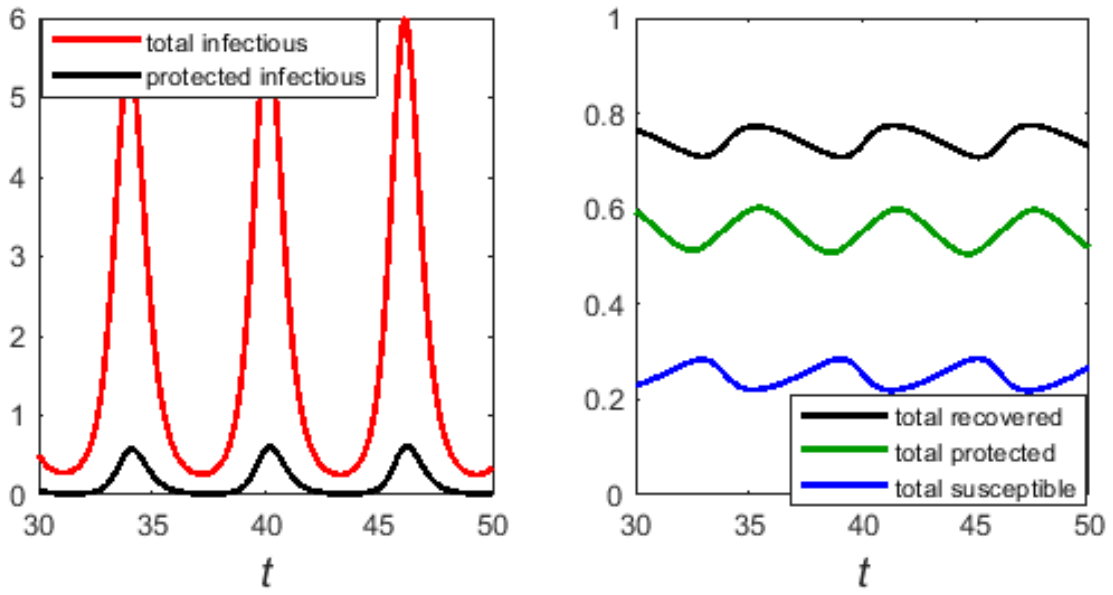
4. Instability for a Family of Decaying Exponential Functions

1. Assume
$$\omega(Y) = \Sigma\left(1 - e^{-aY}\right).$$

2. For given Σ and a, solve the stability bound equation for Y^*_{cr} and then find $\omega(Y^*_{cr})$.
3. $a = 1$ gives a large enough slope to see instability.



5. An Oscillatory Solution



- We obtain a cycle of about 6 years.
- The disease spikes when the total protected gets too low.

Thanks for your attention!

- **Shoot me an email to receive updates or offer feedback!**
  gledder@unl.edu

Resources

- For parts 1 and 2:

Ledder, Incorporating Mass Vaccination into Compartment Models for Infectious Diseases, *Math Biosci Eng*, 2022 Jun 28; 19(9):9457-9480. doi: 10.3934/mbe.2022440

- Part 3 is unpublished. It hasn't even been written up. Some of the results were obtained just this week!

Resources

- Ledder, Mathematical Modeling for Epidemiology and Ecology, 2ed, Springer, in press
  1. Modeling in Biology
  2. Empirical Modeling
  3. Mechanistic Modeling
     - 3.1 Transition processes (*includes vaccination*)
     - 3.2 Interaction processes
     - 3.3 Compartment analysis: The SEIR epidemic model
     - 3.4 SEIR model analysis
     - 3.5 Two scenarios from the COVID-19 pandemic
     - 3.9 Adding demographics to make an endemic disease model
  4. Dynamics of Single Populations
  5. Discrete Linear Systems
  6. Nonlinear Dynamical Systems