The Impact of Vaccine Resistance on Long-Term Epidemic Outcomes

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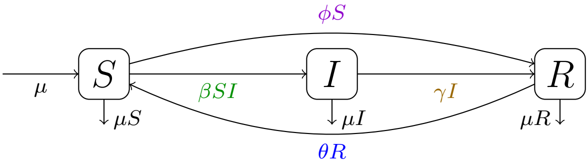
Overview

- Uniform vaccination can reduce the basic reproduction number of a disease from $\mathcal{R}_0 > 1$ to $\mathcal{R}_v$.
  - If $\mathcal{R}_v < 1$, the epidemic ends.
- A significant fraction of the population might be unwilling or unable to be vaccinated. This can help the disease become endemic.
- The unwilling fraction can change over time.
  - It should generally increase as the disease prevalence decreases.
- How does this influence epidemic outcomes?

Standard SIR with Vaccination and Loss of Immunity



- The rate constant ϕ can be reduced to reflect vaccine hesitancy.
  - But even if ϕ is small, everyone gets vaccinated eventually.

- If everyone gets boosters, the rate constant θ is reduced.

- Our experience with COVID-19 shows:
  - Many people never get vaccinated.
  - Most people stop getting boosters.

Outline

Model Formulation

General Results

When Vaccination Acceptance is Monotone Increasing

Vaccine Acceptance Peaks at $Y = Y_m$

Conclusions

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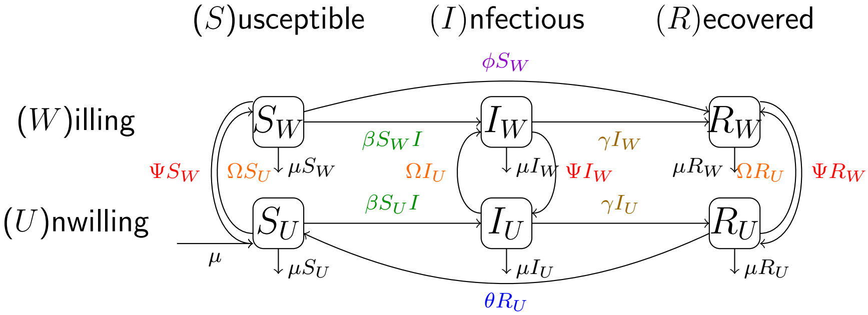
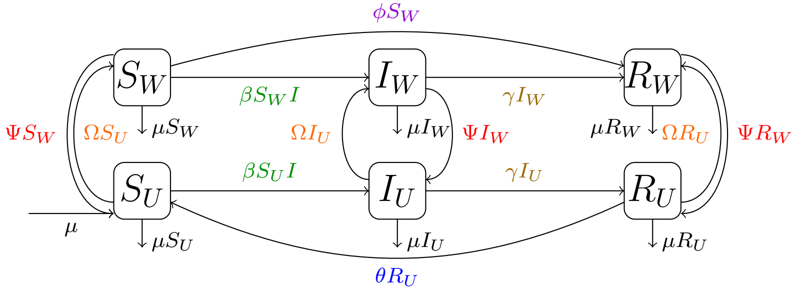
SIR-WU Model Assumptions



- Newborns are initially unable to be vaccinated.
- Willing Susceptibles are vaccinated at rate ϕS_W.
- Unwilling Recovereds lose immunity at rate θR_U.
- Unwilling become Willing with rate coefficient $\Omega(I)$.
- Willing become Unwilling with rate coefficient $\Psi(I)$.

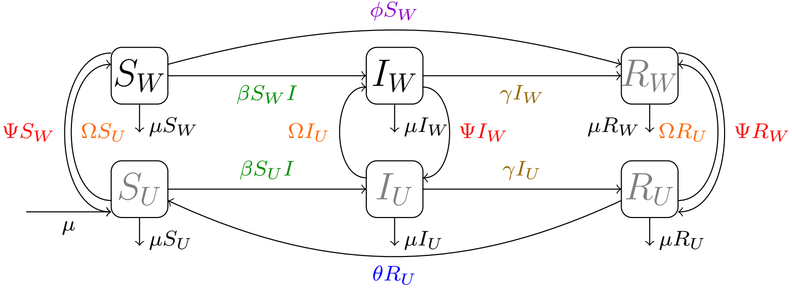
Simplifying Assumptions



1. No disease-induced mortality.
2. Infection confers total immunity for 100% of patients.
3. Willing Recovereds remain recovered through regular boosters.

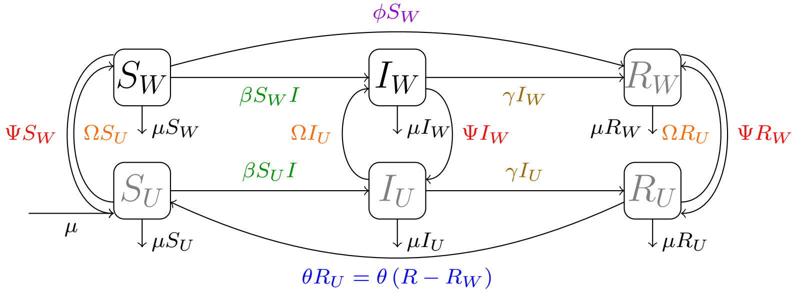
- These assumptions make disease eradication easier.
  - A more realistic model would add unnecessary complications.

Initial Formulation



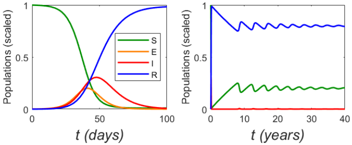
- Population total is constant ($N = 1$);
  we need 5 differential equations for the 6 variables.
- $S + I + R = 1$, so we can use S and I as dependent variables.
- $W + U = 1$, so we can use W as a dependent variable.
- We use S_W and I_W as the remaining dependent variables.

Initial Formulation



$$
\begin{aligned}
\frac{dI}{dt} &= -\mu I + \beta S I - \gamma I \\
\frac{dI_W}{dt} &= -\mu I_W + \beta S_W I - \gamma I_W + \Omega(I)(I - I_W) - \Psi(I) I_W \\
\frac{dS}{dt} &= \mu - \mu S - \beta S I - \phi S_W + \theta\,([1 - S - I] - R_W) \\
\frac{dS_W}{dt} &= -\mu S_W - \beta S_W I - \phi S_W + \Omega(I)(S - S_W) - \Psi(I) S_W \\
\frac{dW}{dt} &= -\mu W + \Omega(I)(1 - W) - \Psi(I) W
\end{aligned}
$$

Two Time Scales in Disease Models



- **The fast time scale (days) shows the epidemic phase.**
  - Infectious population fractions are significant.
  - Plots on the fast time scale show no clue to endemic behavior.
  - Demographic changes (birth, natural death, etc) are negligible.
- **The slow time scale (years) shows the long-term behavior.**
  - Infectious population fractions are very small.
  - On the slow scale, the epidemic behavior appears at $t = 0$.
  - Both demographic and disease processes are important.

Scaling for the Endemic Phase

- Time is referred to the demographic time scale $1/\mu$.
- Infectious populations are rescaled via $I = \epsilon Y$, $I_W = \epsilon Z$.
  - *This is necessary so that all variables are $O(1)$ as $t \to \infty$.*
- Slow process parameters are referred to a slow time scale.
  - Loss of immunity and behavior changes are slow.
  - $1/\mu$ is the principal slow time scale ($\approx$ 80 years).

$$h = \frac{\theta}{\mu}, \qquad \omega = \frac{\Omega}{\mu}, \qquad \Sigma = \frac{\Omega+\Psi}{\mu}.$$

- Fast process parameters are referred to a fast time scale.
  - Infection and vaccination are fast.
  - $1/(\gamma+\mu)$ is the principal fast time scale ($\approx$ 2 weeks).

$$\mathcal{R}_0 = \frac{\beta}{\gamma+\mu}, \qquad v = \frac{\phi}{\gamma+\mu}, \qquad \epsilon = \frac{\mu}{\gamma+\mu} \ll 1.$$

Final Formulation

$$\begin{aligned}
\epsilon Y' &= (\mathcal{R}_0 S - 1)\, Y, \\
S' &= \bar{h}(1-S) - P - hW - \mathcal{R}_0 SY + O(\epsilon), \\
\epsilon v^{-1} P' &= \omega(Y)S - P + O(\epsilon), \\
W' &= \omega(Y) - \bar{\Sigma}(Y)W,
\end{aligned}$$

$$P = vS_W, \qquad \bar{h} = h + 1, \qquad \bar{\Sigma} = \Sigma + 1.$$

Base Parameters and Values:

- $\mathcal{R}_0 = 4$: infectiousness is between influenza and Covid
- $v = 0.5$: vaccination takes a mean of one month
- $h = 10$: loss of immunity has a mean of 8 years
- $\Sigma = 8$: opinion change has a mean of 10 years
  (can be taken as constant)

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Disease-Free Equilibrium (DFE)

1. There is a unique disease-free equilibrium having susceptible fraction $S^0 < 1$.

2. There is a critical value $\omega_{cr} > 0$ such that the DFE is stable if and only if $\omega(0) > \omega_{cr}$.

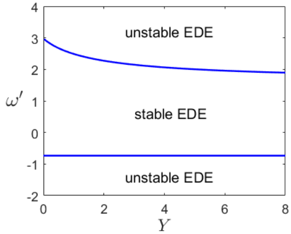
Interpretation

- If the infectious population drops to 0, very few Unwilling will become Willing.
  - Then $\omega(0) < \omega_{cr}$.

- **Optional vaccination means the disease will persist.**

Endemic Disease Equilibrium (EDE) ($\mathcal{R}_0 > 1$)

1. EDEs are solutions of $\omega(Y) = \omega_{cr}\left(1 - \frac{\mathcal{R}_0 Y}{(\mathcal{R}_0 - 1)\bar{h}}\right)$.
   - $\omega(0) < \omega_{cr}, \;\; \omega' > 0 \; (\forall\, Y)$: guarantees a unique EDE.
2. There exist functions $\Upsilon_1(Y) > 0$ and $\Upsilon_2(Y) > 0$ such that an EDE is stable if and only if $-\Upsilon_2(Y) < \omega' < \Upsilon_1(Y)$.



- **Extreme sensitivity of attitude to prevalence (large $|\omega'|$) is destabilizing.**

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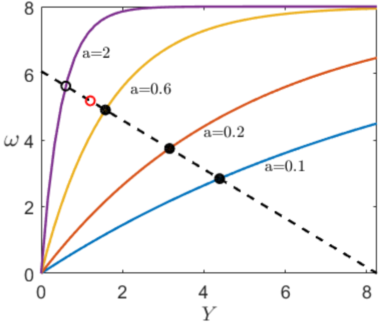
EDE for monotone ω (more disease $\to$ more vaccination)

- If $\omega(0) < \omega_{cr}$, then $\exists$ a unique EDE:

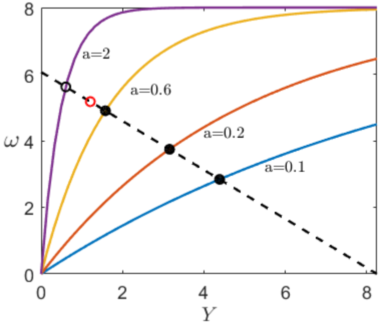
$$0 < Y^* < (\mathcal{R}_0 - 1)(h+1).$$

Example: $\omega = \Sigma\left(1 - e^{-aY}\right)$



EDE for monotone ω (more disease $\rightarrow$ more vaccination)

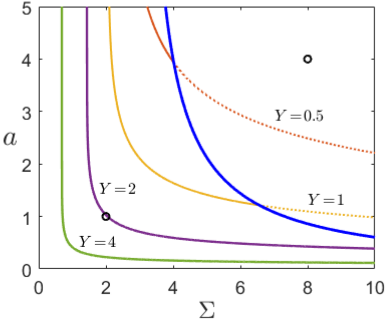
- The EDE is unstable if $\omega'(Y^*) > \Upsilon_1(Y^*)$.
  - $\omega = \Sigma\left(1 - e^{-aY}\right)$: Stable for smaller a.



EDE Stability for monotone ω (more disease $\rightarrow$ more vaccination)

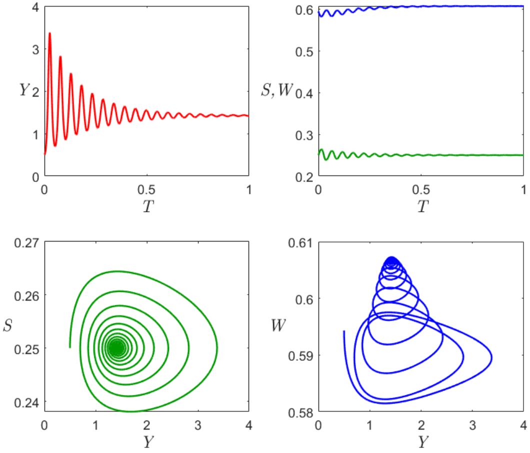
Example: $\omega = \Sigma\left(1 - e^{-aY}\right)$

- Σ is the mean number of opinion changes per lifetime.
- a is the sensitivity of the switch to vaccination.



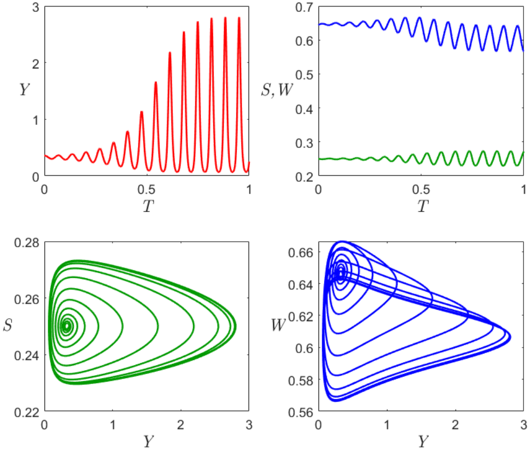
Numerical Solutions: Example 1, Stable Solution

$$R_0 = 4, \;\; h = 10, \;\; v = 0.5, \;\; \Sigma = 4, \;\; a = 1$$



Numerical Solutions: Example 2, Limit Cycle

$$R_0 = 4, \;\; h = 10, \;\; v = 0.5, \;\; \Sigma = 8, \;\; a = 2$$



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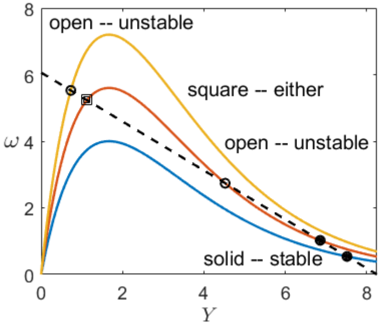
Non-monotone ω (high disease $\rightarrow$ waning confidence)

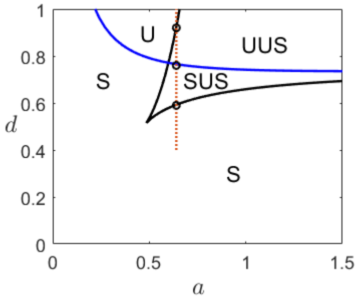
Example: $\omega = \Sigma d a Y e^{-aY}$



- Small d: large stable solution
- Moderate d: small maybe, middle unstable, large stable
- Large d: small unstable solution

Non-monotone ω (high disease $\to$ waning confidence)

Example: $\omega = \Sigma da Y e^{-aY}$



- Above/right of black curve: three solutions.
  - Middle unstable, largest stable.
- Above blue curve: smallest Y is unstable.
  - There is a stable limit cycle.

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- We proposed a disease spread model that includes flexible ideology on vaccination, where the transition of the opinion is a function of the disease spread.
- There is a unique endemic disease equilibrium for monotone increasing willingness, with a result that may be stable or unstable.
- By tuning the parameters carefully, we were able to observe limit cycles in the phase plane, that is, oscillatory endemic states.
- Multiple equilibria are possible with a willingness function that increases to a peak and then decreases.
  - There is a large Y stable equilibrium and either a small Y stable equilibrium or a small Y limit cycle.

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