An *SIRS* epidemic model with a rapidly decreasing probability for temporary immunity

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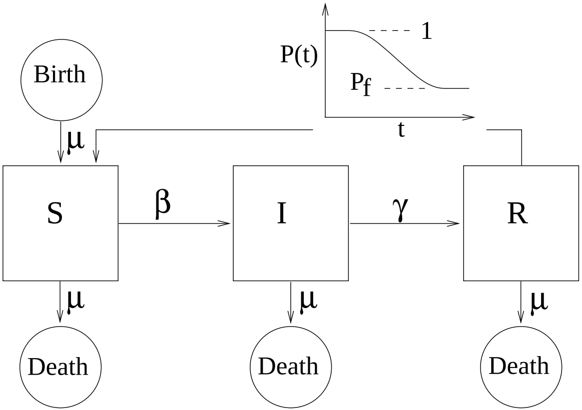
Abstract

We consider an SIRS model for disease dynamics that accounts for temporary immunity whereby recovered individuals return to the susceptible class. In particular, we allow for a general probability function of remaining immune for a given time after recovery such that the model is a system of integro-differential equations. We first show that by considering a rapidly decreasing probility function that the original model can be approximated by a system of delay-differential equations. Perturbation methods are then applied to the delay equations to determine how the amplititude of oscillations, which correspond to repeated epidemics, depends on the system parameters and, in particular, the zeroth, first, and second moments of the probability distribution.

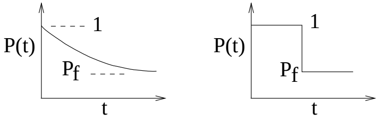
SIRS Disease Dynamics



Temporary immunity: influenza, cholera, pertussis, malaria,....

Diseases processes

- Probability for transmission, latency, recovery, maintaining immunity....
- Brauer, Castillo-Chavez, Cooke, Yorke, Hethcote, Tudor, Busenbert, Diekman, van den Driessche, Keeling, Grenfell, Feng, Lloyd, Camitz, Svensson, Arino, Blyss, Kyrychko, ...
- Some examples:
  - Keeling et al: measles data consistent with a distribution with small variation.
  - Hethcote et al./ Feng et al. /Arino et al./Blyss et al:
    R_0 depends on the mean of the infectious probability.
    Probability functions affect local and global stability properties.

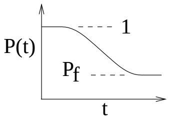


- Exponential: ODEs
- Step (delta distribution): DDEs
- Gamma distribution: Multistage classes of ODEs

Temporary Immunity in the (R)ecovered class

Recover from infection at $t = 0$.

$P(t)$: Probability for remaining immune a time t.



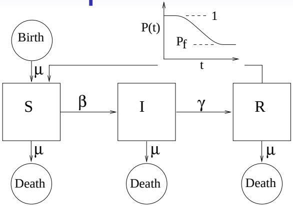
$$P(0) = 1, \quad \frac{dP}{dt} \leq 0, \quad \lim_{t \to \infty} = P_f.$$

$R(t)$: Fraction of population who are recovered/immune at time t.

$$R(t) = \int_{-\infty}^{t} \gamma I(r) e^{-\mu(t-r)} P(t-r) dr.$$

- The sum over all previously (I)nfectious individuals.
- Decremented by the probability of dying a natural death.
- Decremented by the probability an individual is still immune.

SIRS Epidemic Model



$$\frac{dS(t)}{dt} = \mu[1 - S(t)] - \beta S(t)I(t) - \int_0^\infty \gamma I(t-r)e^{-\mu r}\frac{dP(r)}{dr}dr,$$

$$\frac{dI(t)}{dt} = \beta S(t)I(t) - (\mu + \gamma)I(t),$$

$$\frac{dR(t)}{dt} = \gamma I(t) - \mu R(t) + \int_0^\infty \gamma I(t-r)e^{-\mu r}\frac{dP(r)}{dr}dr$$

- μ: Equal birth and death rates $\Rightarrow$ conserved population.
  $R = 1 - (S + I)$.
- β: Mass-action contact process for disease transmission.
- γ: Exponential probability for recovery.

Immunity Integral

$$\mathcal{I}(t) = \int_0^\infty \gamma I(t-r)e^{-\mu r}\frac{dP(r)}{dr}dr$$

Exponential probability

$$P(t) = e^{-\frac{t}{\tau}}$$

$$\mathcal{I} = -\frac{1}{\tau}I(t)$$

- IDEs $\Rightarrow$ ODEs
- Disease-free steady state
- Endemic steady state

Step probability

$$P(t) = \begin{cases} 1 & t < \tau \\ P_f & \tau \leq t \end{cases}$$

$$\mathcal{I} = -(1-P_f)e^{-\mu\tau}I(t-\tau)$$

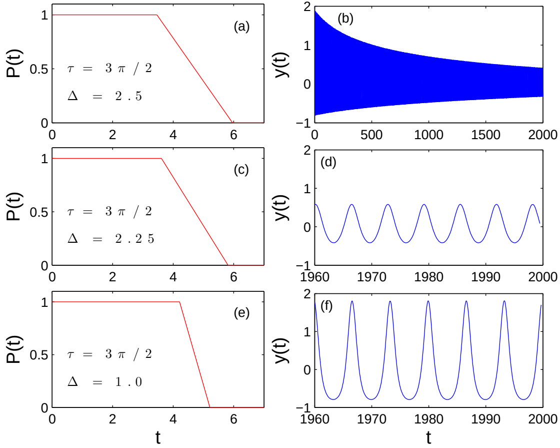
- IDEs $\Rightarrow$ DDEs
- Disease-free steady state
- Endemic steady state
- Epidemics $\Leftrightarrow$ oscillations

Slow - medium - rapid decreasing $P(t)$

$\frac{dP}{dt}$: Distribution $\tau =$ mean $\Delta =$ variance

Slow decrease
Exponential like
Decay

Rapid decrease
Step like
Oscillations



Questions

SIRS – IDE: Can they be analyzed?

- **For “rapidly” decreasing distributions – method of multiple scales.**

How dependent are observables on distribution differences?

- Test different distributions with matched and mismatched moments.

Asymptotic analysis of IDEs

Analysis of IDEs are most often:

- Special cases like exponential, step or gamma distributions.
  IDEs $\Rightarrow$ ODEs and DDEs.
- Existence, linear stabilty and global stability.

Our results:

- Constructive describing specific solution properties in terms of parameters.
- Can handle general probability functions.

Aysmptotic analysis of IDEs

- Assume a rapidly decreasing probability function.
  Approximate immunity integral by a series of delays.
  IDE $\Rightarrow$ DDE.
- Use linear stability, averaging and multiple scales.
- Describe amplitude of oscillations (recurrent epidemics) in terms of disease parameters and the properties of the probability function for temporary immunity.

Rapidly decreasing probability

Localized distribution at τ time in past

Immunity integral

$$\mathcal{I}(t) = \int_0^\infty f(t,r)\frac{dP(r)}{dr}dr, \text{ where } f(t,r) = \gamma I(t-r)e^{-\mu r}.$$

Expand $f(t,r)$ near $r = \tau$, τ to be determine.

$$f(t,r) = f(t,\tau) + f_r(t,\tau)[r-\tau] + \frac{1}{2}f_{rr}(t,\tau)[r-\tau]^2 + \dots,$$

Immunity integral

$$\begin{aligned}\mathcal{I}(t) &= f(t,\tau)\int_0^\infty \frac{dP(r)}{dr}dr + f_r(t,\tau)\int_0^\infty [r-\tau]\frac{dP(r)}{dr}dr \\ &\quad + \frac{1}{2}f_{rr}(t,\tau)\int_0^\infty [r-\tau]^2\frac{dP(r)}{dr}dr + \dots\end{aligned}$$

Rapidly decreasing probability

Localized distribution

0^{th} moment: P_s is the probability of becoming resusceptible.

$$\int_0^\infty \frac{dP(r)}{dr} dr = P(\infty) - P(0) = -P_s$$

1^{st} moment: τ is chosen as the mean, which eliminates the integral.

$$\int_0^\infty [r - \tau] \frac{dP(r)}{dr} dr = 0$$

2^{nd} moment: Rapidly decreasing implies small variance.

$$\sigma^2 = -\int_0^\infty [t - \tau]^2 \frac{dP(r)}{dr} dr \ll 1$$

$$\begin{aligned}
\frac{dS}{dt} &= \mu(1 - S) - \beta SI + \gamma \left[P_s e^{-\mu\tau} I(t - \tau) + \frac{\sigma^2}{2} \frac{d^2}{dr^2} \left(I(t - r) e^{-\mu r} \right) |_{r=\tau} + \ldots \right] \\
\frac{dI}{dt} &= \beta SI - (\mu + \gamma) I
\end{aligned}$$

Non-dimensionalized equations

$$S = S_c\left(1 + \sqrt{\frac{I_c}{S_c}}x\right), \quad I = I_c(1+y), \qquad s = \frac{1}{k}t, \; k = \frac{1}{\beta\sqrt{S_c I_c}},$$

- $(x, y) = (0, 0)$: Non-zero endemic steady state.
- $(x, y) \neq (0, 0)$: Deviations from endemic steady state.

$$\begin{aligned}\frac{dx}{ds} &= -y(s) - \epsilon x(s)[a + by] \\ &\quad + c\left[y(s-\tau_s) + \left(\frac{1}{2}\sigma_s^2\right)\left(\frac{e^{\epsilon d\tau_s}}{P_s}\right)\frac{d^2}{dr^2}\left(y(s-r)e^{-\epsilon dr}\right)|_{r=\tau_s}\right] \\ \frac{dy}{ds} &= (1+y)x\end{aligned}$$

$$\epsilon = \sqrt{\frac{\mu}{\beta}} \quad \epsilon a = k(\mu + \beta I_c) \quad \epsilon b = \sqrt{\frac{I_c}{S_c}} \quad c = \frac{P_s\gamma}{\mu+\gamma}e^{-\mu\tau} \quad \epsilon d = \mu k$$

- $\epsilon \ll 1$: Fast transmission relative to natural lifetime.
- $\frac{dP}{dt} = 0$: Weakly-damped conservative oscillator.
- $\frac{dP}{dt} \neq 0$: Need stimulus to excite oscillations/epidemics.

IDE $\Rightarrow$ DDE

Immunity integral

$$\mathcal{I} = f(t,\tau)(0^{th}\text{ moment}) + f_r(t,\tau)(0) + \frac{1}{2} f_{rr}(t,\tau)(2^{nd}\text{ moment}) + \ldots$$

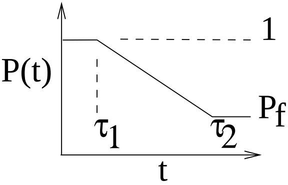
SIRS Equations

$$\begin{aligned} \frac{dx}{ds} &= -y - \epsilon[a + by] \\ &\quad + cy(s - \tau_s) + c\left(\frac{1}{2}\sigma_s^2\right)\left(\frac{e^{\epsilon d \tau_s}}{P_s}\right)\frac{d^2}{dr^2}\left(y(s-r)e^{-\epsilon dr}\right)\Big|_{r=\tau_s} \end{aligned}$$

Zeroth moment. First moment captured by τ. Second moment.

- Asymptotic analysis and bifurcations analyzed in Taylor & Carr (2009). Method of multiple scales applied to DDEs.
- Densities with equivalent moments approximated by same DDEs.
- Densities with equivalent moments generate equivalent dynamics.

Linear probability



$$c(\tau) = \frac{P_s\gamma}{\mu+\gamma}e^{-\mu\tau} \text{ : Fraction resusceptible}$$

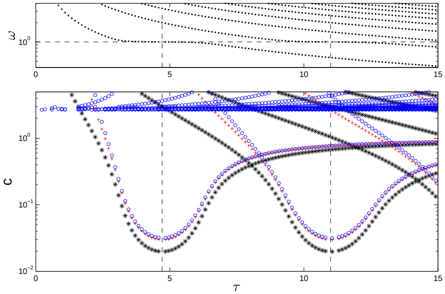
$$\tau = \frac{1}{2}(\tau_1+\tau_2) \text{ : mean}$$

$$\Delta = \tau_2 - \tau_1 \text{ : variance}$$

$$\frac{dx}{dt} = -y - \epsilon x[a+by] + c\left[y(t-\tau) + \left(\frac{\Delta^2}{24}\right)\frac{d^2}{dr^2}y(t-r)|_{r=\tau}\right]$$

$$\frac{dy}{dt} = [1+y]x$$

Linear stability



$$\lambda^2 + \epsilon a\lambda + 1 - c\frac{2}{\lambda\Delta}e^{-\lambda\tau}\sinh(\frac{\lambda\Delta}{2}) = 0.$$

$$(1-\omega^2)\tan(\omega\tau) + \epsilon a\omega = 0,$$

$$c_h^2 = \frac{(1-\omega^2)^2 + (\epsilon a\omega)^2}{\mathrm{sinc}^2(\frac{\omega\Delta}{2})},$$

- Black: $\Delta = 0$ and $\Delta = 1$ (difference imperceptible).
- Blue and Red: $\Delta = 3$ for IDEs and DDEs.
- Increasing $c \sim P_s$ leads to Hopf bifurcation.
- Increasing Δ postpones Hopf bifurcation.

Natural modes $\omega \approx 1$

Damping (ϵ) = Feedback (c) = 0.

$$\begin{aligned}\dot{x} &= -y \\ \dot{y} &= (1+y)x\end{aligned}$$

Conserved energy

$$E = \frac{1}{2}x^2 + y - \ln(1+y).$$

Slow evolution of energy with $\epsilon \neq 0$, $c \neq 0$.

$$\frac{dE(t)}{dt} = -\epsilon x(t)^2[a + by(t)] + cx[y(t-\tau) + \frac{\Delta^2}{24}y_{tt}(t-\tau)].$$

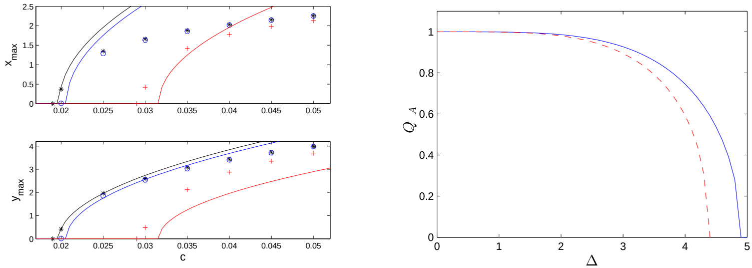
Averaging for periodic solutions.

$$-\epsilon a \int_0^\Phi x(t)^2 dt + c\int_0^\Phi x(t)\left[y(t-\tau) + \frac{\Delta^2}{24}y_{tt}(t-\tau)\right] dt = 0,$$

$$x_{max}^2 \sim y_{max}^2 \approx \frac{4}{c_{hn}\eta_n}(c - c_{hn})$$

$$c_{hn} = -\frac{\epsilon a}{\sin\tau(1 - \frac{\Delta^2}{24})} \text{ and } \eta_n = \frac{1}{6}\tau\cot\tau + \frac{5}{18} - \frac{4}{9}\cos\tau\left(\frac{1 - 4\frac{\Delta^2}{24}}{1 - \frac{\Delta^2}{24}}\right).$$

Amplitude of periodic solutions



- $\frac{1}{24}\Delta_{hn}^2 = 1 - \frac{1}{c}\frac{\epsilon a}{|\sin\tau|}$
  $\Delta > \Delta_{hn}$: Slow decrease / large variance / no oscillations
  $\Delta < \Delta_{hn}$: Rapid decrease / small variance / oscillations
- Amplitude $\Delta \neq 0$ vs. $\Delta = 0$.

$$Q_A = \sqrt{\frac{\left[\frac{4}{c_{hn}\eta_n}\right]}{\left[\frac{4}{c_{hn}\eta_n}\right]_{\Delta=0}}}$$

Smaller Δ / rapid decrease / step-like / larger amplitude

Delay modes $\omega \approx \frac{m\pi}{\tau}$

Method of multiple scales:

$$T = \epsilon t.$$

$$\frac{d}{dt} = \frac{\partial}{\partial t} + \epsilon \frac{\partial}{\partial T}$$

$$x(t) = \epsilon^{1/2} x_1(t, T) + \epsilon x_2(t, T) + \dots$$

$$c = c_0 + \epsilon c_1 + \dots$$

Apply to DDEs:

$$y(t - \tau) \to y(t - \tau, T - \epsilon\tau).$$

$$y(t - \tau) = y(t - \tau, T) - \epsilon\tau \frac{\partial}{\partial T} y(t - \tau, T) + \dots.$$

Delayed 2nd derivative due to IDE:

$$y_{tt}(t - \tau) = y_{tt}(t - \tau, T) + \epsilon[2y_{tT}(t - \tau, T) - \tau y_{ttT}(t - \tau, T)] + O(\epsilon^2)$$

Solvabilty condition

Solution to $O(\epsilon^{1/2})$ problem with slowly evolving amplitude:

$$x_1 \sim y_1 \sim A(T)\exp(i\omega t) + c.c.$$

$A(T)$ determined by solvability condition at $O(\epsilon^{3/2})$.

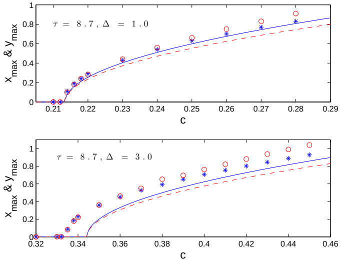
$$[i2\omega(1-\nu c_0\sigma^2) + \nu c_0 \tau D(\omega)]\frac{\partial A}{\partial T} = (-i\omega a + \nu c_1 D(\omega))A - \omega^2 \eta_d A|A|^2,$$

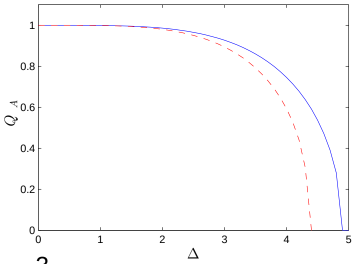
Steady-state solutions correspond to the amplitude of oscillations.

$$y_{max}^2 = \nu \frac{4D(\omega)}{\omega^2 \eta_d}(c - c_{hd}), \quad x_{max} = \omega y_{max},$$

$$c_{hd} = \nu \left[\frac{(1-\omega^2)}{D(\omega)} + \epsilon \frac{2\omega^2 a(1-\sigma^2)}{\tau(1-\omega^2)D(\omega)} \right].$$

Amplitude of periodic solutions





- Excellent fit for $\Delta = 1$, less so for $\Delta = 3$.
- Critical value for Δ.

$$\frac{1}{24}\Delta_h^2 = \frac{1}{\omega^2}\left(1 - \frac{\nu}{c}(1-\omega^2)\right), \quad \omega = \frac{m\pi}{\tau}$$

- Amplitude dependence on Δ

$$Q_A = \sqrt{D(\omega)}\sqrt{\frac{[\eta_d]_{\Delta=0}}{[\eta_d]}}$$

Questions

SIRS – IDE: Can they be analyzed?

- For “rapidly” decreasing distributions – method of multiple scales.

How dependent are observables on distribution differences?

- **Test different distributions with matched and mismatched moments.**

Numerical exploration of the effect of different densities

Nondimensionalize *SIR* equations... do not expand immunity integral.

$$\begin{aligned}\frac{dx(t)}{dt} &= -y(t) - \epsilon x(t)[a + by(t)] - \left(\frac{\gamma}{\mu+\gamma}\right)\int_0^\infty y(t-r)e^{-\mu k r}\frac{dP(r)}{dr}dr, \\ \frac{dy(t)}{dt} &= [1 + y(t)]x(t),\end{aligned}$$

- Considering different density functions $P(t)$.
- Observe the effect of matched or mismatched moments.
- Hoppensteadt et. al (2007): variable step-size Pouzet-Dormand-Prince RK pair of order 5 and 4.
- Individual simulations at each data point until convergence to limit cycle.
- $\mu = 0.01$: Average lifetime of 100 years. $\gamma = 100$: Recovery time of approximately 1 week. $\beta = 200$. $R_0 \approx \frac{\beta}{\gamma} \approx 2$ $\tau = 3\pi/2$: Immune time approximately 5 to 10 years.

Symmetric densities (dP/dt)

Linear

$$P(t) = \begin{cases} 1, & 0 \le t < T_1 \\ 1 - \frac{1}{2}(1-P_f)\left[1 + 2\left(\frac{t-\tau}{T_2-T_1}\right)\right], & T_1 \le t < T_2 \\ P_f, & T_2 \le t \end{cases}$$

Arctangent ($\Delta_a \approx 0.0131$)

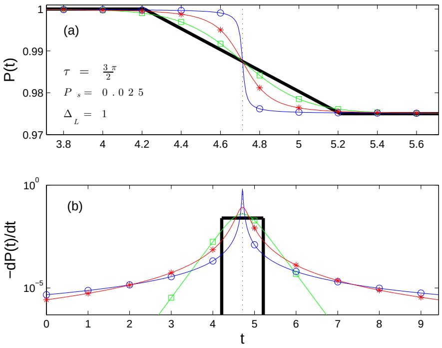
$$P(t) = 1 - \frac{1}{2}(1-P_f)\left[1 + \frac{2}{\pi}\arctan\left(\frac{t-\tau}{\Delta_t}\right)\right]$$

Algebraic ($\Delta_a \approx 0.1494$)

$$P(t) = 1 - \frac{1}{2}(1-P_f)\left(1 + \left(\frac{t-\tau}{\Delta_a}\right)\left[1 + \left(\frac{t-\tau}{\Delta_a}\right)^2\right]^{-1/2}\right)$$

Logistic ($\Delta_a \approx 0.1592$)

$$P(t) = \frac{P_f + \exp\left(-\frac{t-\tau}{\Delta_l}\right)}{1 + \exp\left(-\frac{t-\tau}{\Delta_l}\right)}$$



Asymmetric densities (dP/dt)

Linear

$$P(t) = \begin{cases} 1, & 0 \le t < T_1 \\ 1 - \frac{1}{2}(1 - P_f)\left[1 + 2\left(\frac{t-\tau}{T_2 - T_1}\right)\right], & T_1 \le t < T_2 \\ P_f, & T_2 \le t \end{cases}$$

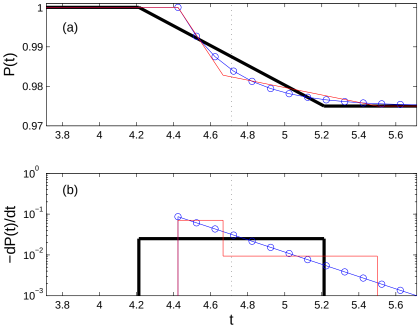
Exponential

$$P(t) = \begin{cases} 1, & 0 \le t < T_l \\ (1 - P_f)\exp(-\frac{t-T_l}{\Delta e}) + P_f, & T_l \le t \end{cases}$$

$$T_1 = \tau - \Delta_e, \quad \Delta_e = \frac{1}{2\sqrt{3}} \approx 0.2887.$$

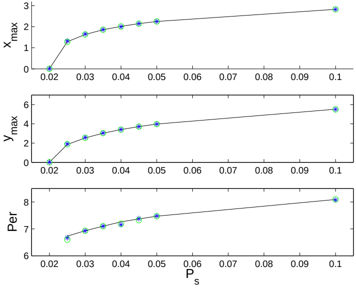
Piecewise linear

$$P(t) = \begin{cases} 1, & 0 \le t < T_l \\ 1 - \frac{1}{2}(1 - P_m)\left(\frac{t-T_l}{T_m - T_l}\right), & T_l \le t < T_m \\ P_m - \frac{1}{2}(P_m - P_f)\left(\frac{t-T_m}{T_u - T_m}\right), & T_m \le t < T_u \\ P_f, & T_u \le t \end{cases}$$



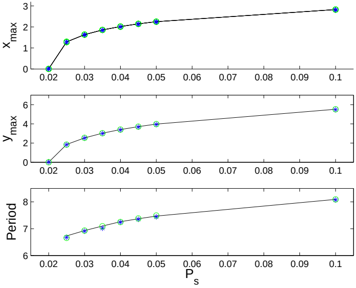
Bifurcation Diagrams

Symmetric densities



Linear
Arctan
Algebraic

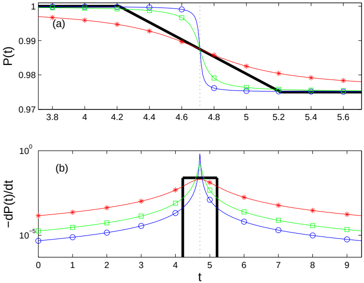
Asymmetric densities



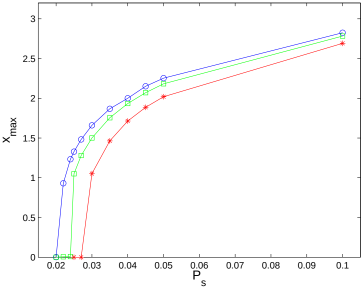
Linear
Exponential
Piecewise linear

Mis-matched moments

Probability distribution



Bifurcation diagram



Linear

Arctan $\Delta_t = 0.0131$ (optimal)

Arctan $\Delta_t = 0.05$

Arctan $\Delta_t = 0.12$

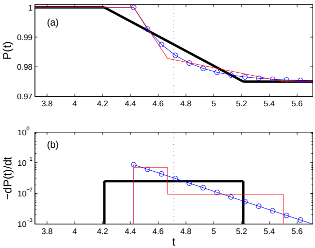
Arctan $\Delta_t = 0.0131$ (optimal)

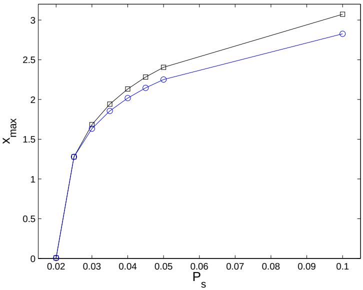
Arctan $\Delta_t = 0.05$

Arctan $\Delta_t = 0.12$

Piecewise linear: P_m depends on P_s

$$P(t) = \begin{cases} 1, & 0 \le t < T_l \\ 1 - \frac{1}{2}(1 - P_m)\left(\frac{t - T_l}{T_m - T_l}\right), & T_l \le t < T_m \\ P_m - \frac{1}{2}(P_m - P_f)\left(\frac{t - T_m}{T_u - T_m}\right), & T_m \le t < T_u \\ P_f, & T_u \le t \end{cases}$$





P_m optimized for each value of P_s.

$P_m = 0.9828$ ($P_s = 0.025$).

Summary

- We considered temporary immunity.
  - Could also generalize the recovery process and transmission process.
  - Not yet tested.

- IDE approximated by a DDE.
  Probability function characterized by:
  Feedback strength

$$\int_0^\infty \frac{dP(r)}{dr} dr = P(\infty) - P(0) = -P_s$$

  Delay time

$$\int_0^\infty [r - \tau] \frac{dP(r)}{dr} dr = 0$$

  Variance

$$\sigma^2 = -\int_0^\infty [t - \tau]^2 \frac{dP(r)}{dr} dr \ll 1$$

Summary

- Considered a linearly decreasing probability.
  - Any $P(t)$ with same P_f, τ and Δ should give equivalent results. Not yet tested.
- Good to excellent fit for even $\Delta = O(1)$.
- Crude generalization:
  - A more exponential like $P(t) \Rightarrow$ ODEs $\Rightarrow$ steady states.
  - A more step like $P(t) \Rightarrow$ DDEs $\Rightarrow$ oscillations.
- To decrease the severity of recurrent epidemics:
  - 0^{th} moment: Decrease P_s the fraction that become resusceptible.
  - 1^{st} moment: Detune τ from "resonance".
  - 2^{nd} moment: Increase the variance of probability for becoming resusceptible, i.e., increase the heterogeneity of the population.
- Tuning the moments...
  - Densities with equivalent first 3 moments generate equivalent epidemics.
  - Small mismatches lead to small differences.
  - Mismatch tolerances within experimental error?
- Caveats:
  - SIRS model with all its usual assumptions.
  - Examined temporary immunity.