Essentials of Aggregate System Dynamics Infectious Disease Models

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Comments on Mathematics & Dynamic Modeling

- Many accomplished & well-published dynamic modelers have very limited mathematical background
  - Can investigate pressing & important issues
  - Software tools are making this easier over time
- Can gain extra insight/flexibility if willing to push to learn some of the associated mathematics
- Achieving highest skill levels in dynamic modeling do require mathematical facility and sophistication
  - To do sophisticated work, often those lacking this background or inclination collaborate with someone with background

Applied Math & Dynamic Modeling

- Although you may not use it, the dynamic modeling presented rests on the tremendous deep & rich foundation of applied mathematics
  - Linear algebra
  - Calculus (Differentia/Integral, Uni& Multivariate)
  - Differential equations
  - Numerical analysis (including numerical integration, parameter estimation)
  - Control theory
  - Real & complex analysis
- For the mathematically inclined, the tools of these areas of applied math are available

Models in Mathematical Epidemiology of Infectious Disease

- Long & influential modeling tradition, beginning with Ross & Kermack-McKendrick (1920s)
- Models formulated for diverse situations (Cf. Anderson & May)
  - Latent & incubation period/Diversity in contact rates/Heterogeneity/Preferential mixing/Vaccinated groups/Zoonoses/Variations in clinical manifestations/Network structure
- Important tradition of closed-form analysis

Mathematical Models of Infectious Disease Link Together Diverse Factors

Typical Factors Included

- Infection
  - Mixing & Transmission
  - Development & loss of immunity – both individual and collective
  - Natural history (often multi-stage progression)
  - Recovery
- Birth & Migration
- Aging & Mortality
- Intervention impact

Sometimes Included

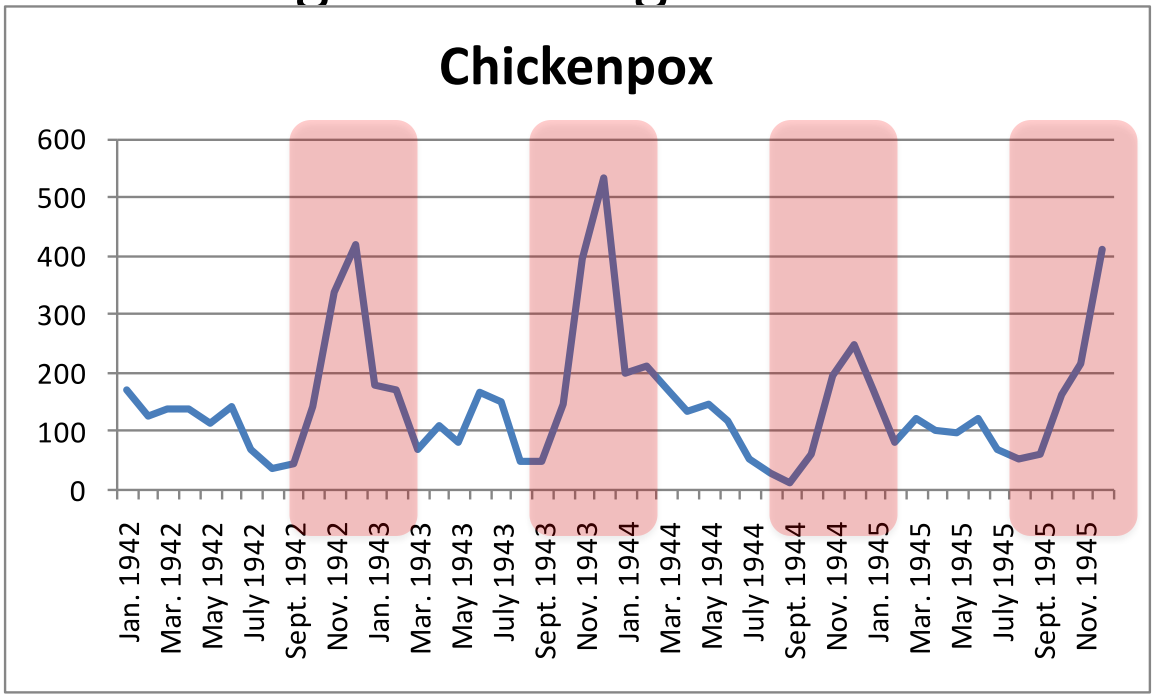
- Preferential mixing
- Variability in contacts
- Strain competition & cross-immunity
- Quality of life change
- Health services interaction
- Local perception
- Changes in behavior, attitude
- Immune response

Emergent Characteristics of Infectious Diseases Models

- Instability
- Nonlinearity
- Tipping points
- Oscillations
- Multiple fixed points/equilibria
  - "Endemic" equilibrium
  - Disease free equilibrium

Instability

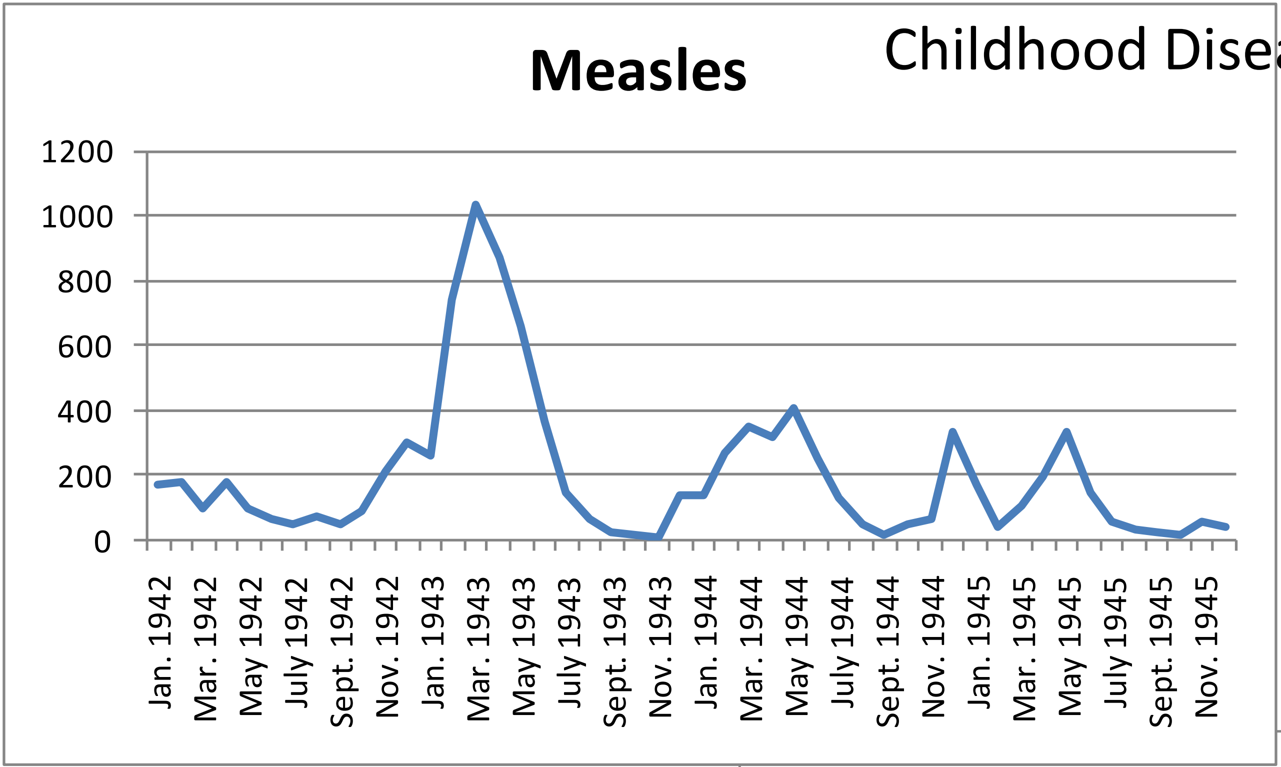
- Slight perturbation (e.g. arrival of infectious person on a plane) can cause big change in results
  - Contrast with "goal seeking" behaviour

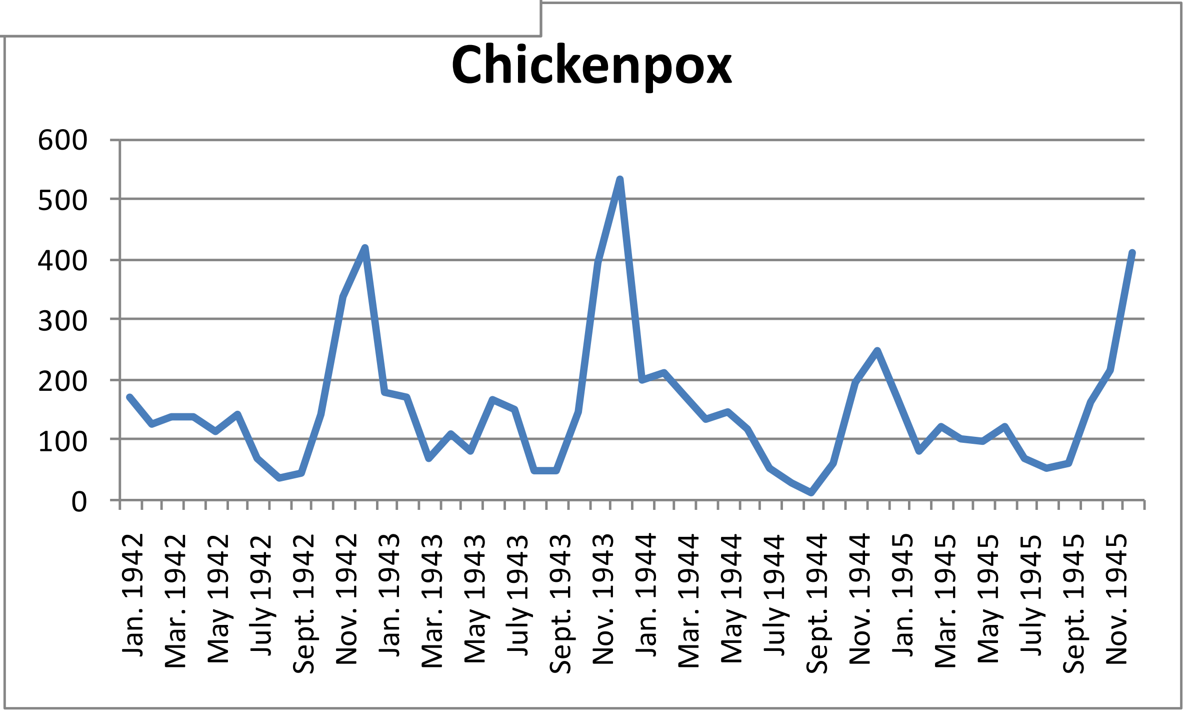


Oscillations & Delays

- The oscillations reflect negative feedback loops with delays
- These delays reflect “stock and flow” considerations and specific thresholds dictating whether net flow is positive or negative
  - Stock & Flow: Stock continues to deplete as long as outflow exceeds inflow, rise as inflow>outflow
    - The stock may stay reasonably high long after inflow is low!
  - Key threshold R*: When # of individuals being infected by a single infective = 1
    - This is the threshold at which outflows=inflows

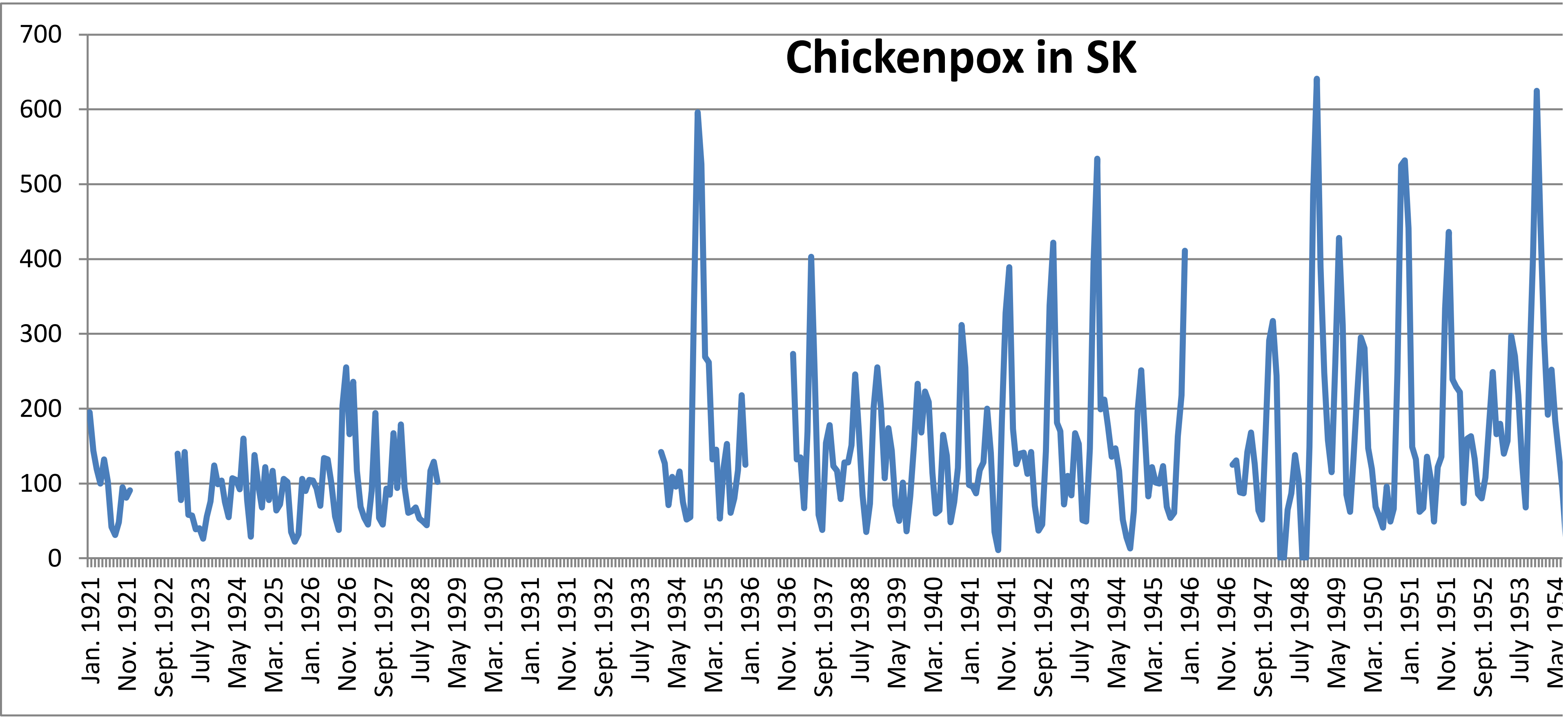
Childhood Diseases in Saskatchewan





Dynamic Complexity:

Tipping Points



Dynamic Complexity:

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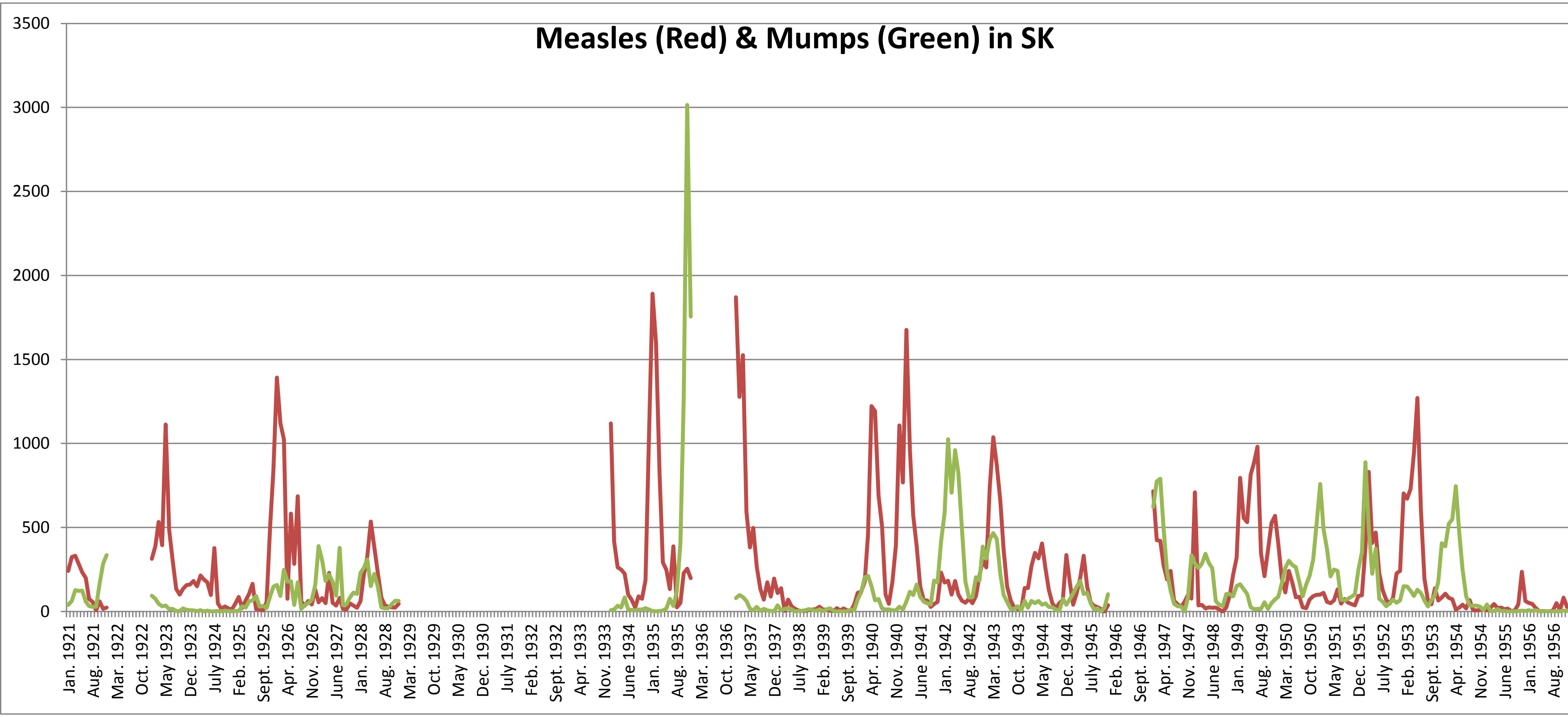

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Nonlinearity (in state variables)

- Effect of multiple policies non-additive
- Doubling investment does not yield doubling of results
- Leads to
  - Multiple basins of tracking (equilibrium)

Multiple Equilibria & Tipping Points

- Separate basins of attraction have qualitatively different behaviour
  - Oscillations
  - Endemic equilibrium
  - Disease-free equilibrium

Equilibria

- Disease free
  - No infectives in population
  - Entire population is susceptible
- Endemic
  - Steady-state equilibrium produced by spread of illness
  - Assumption is often that children get exposed when young

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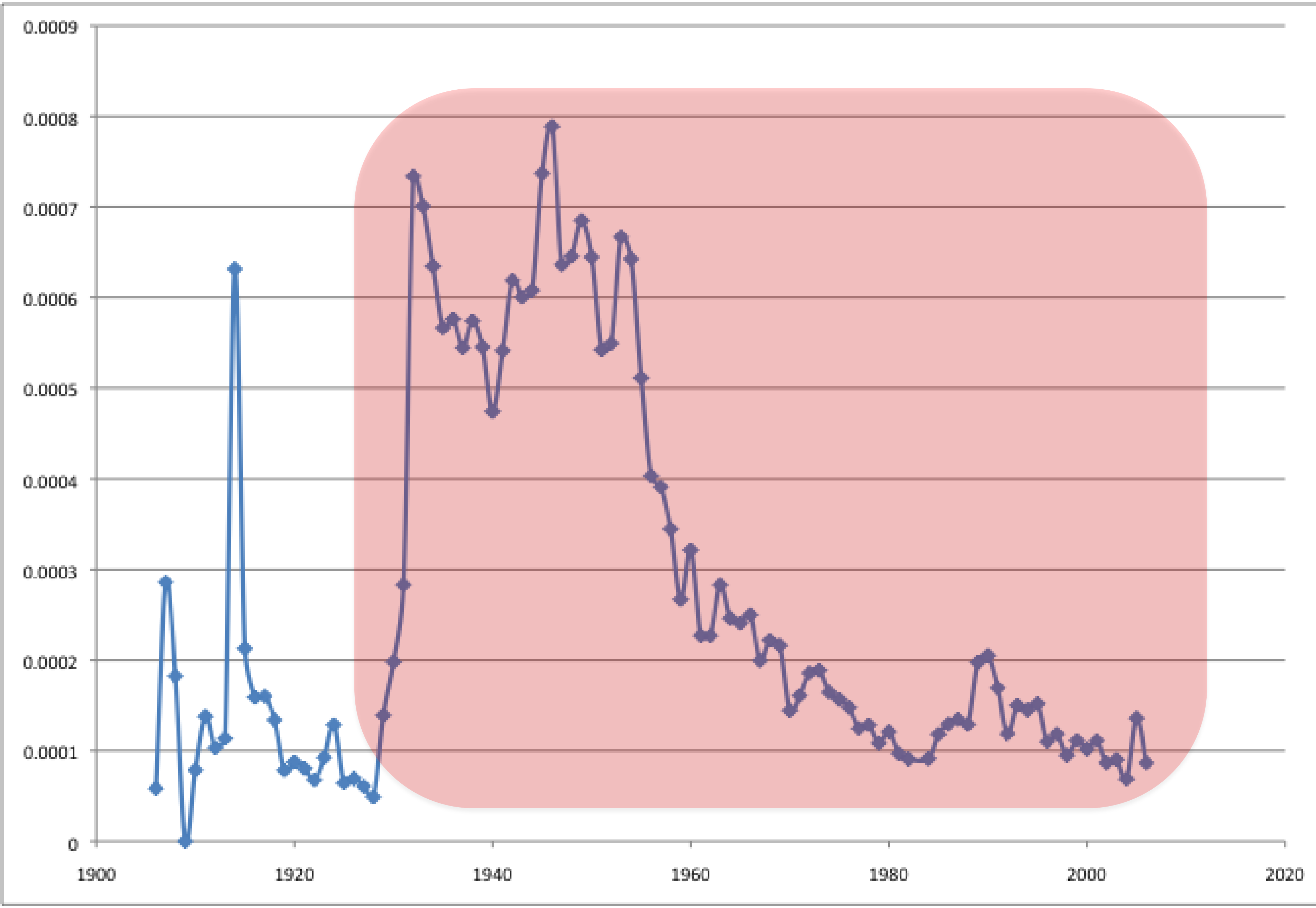
TB In SK



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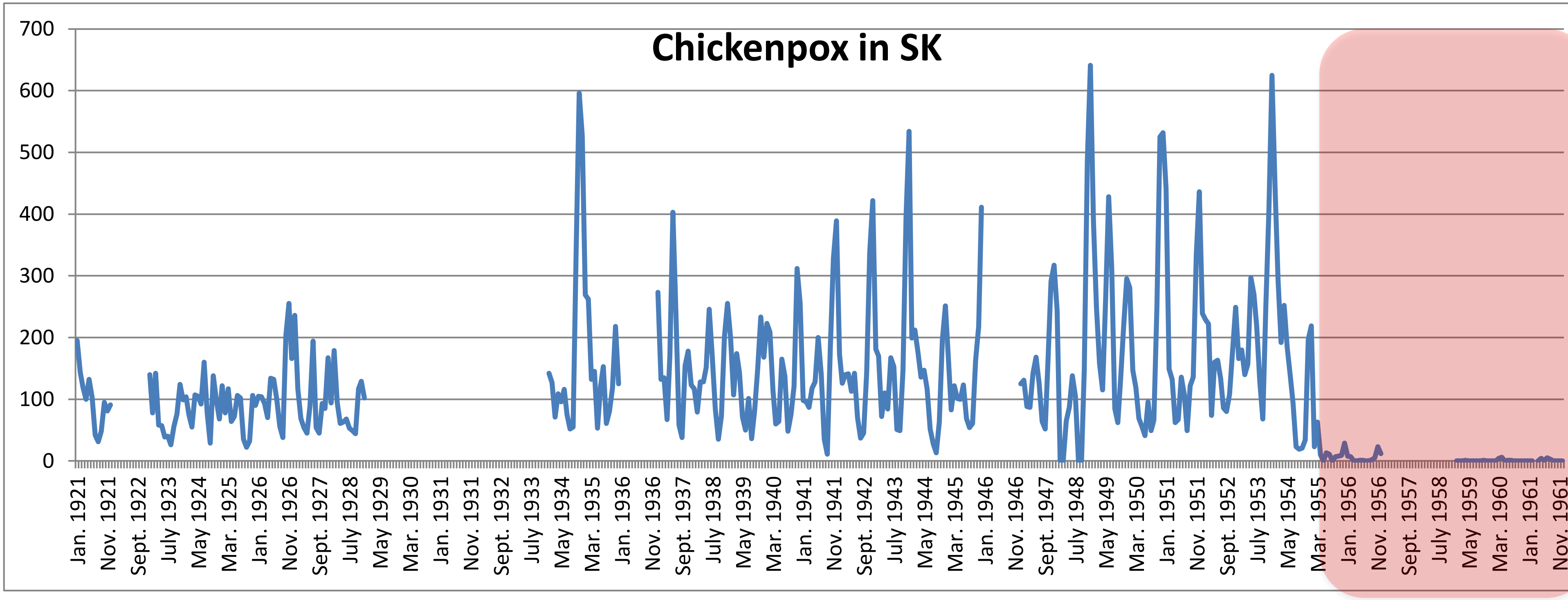
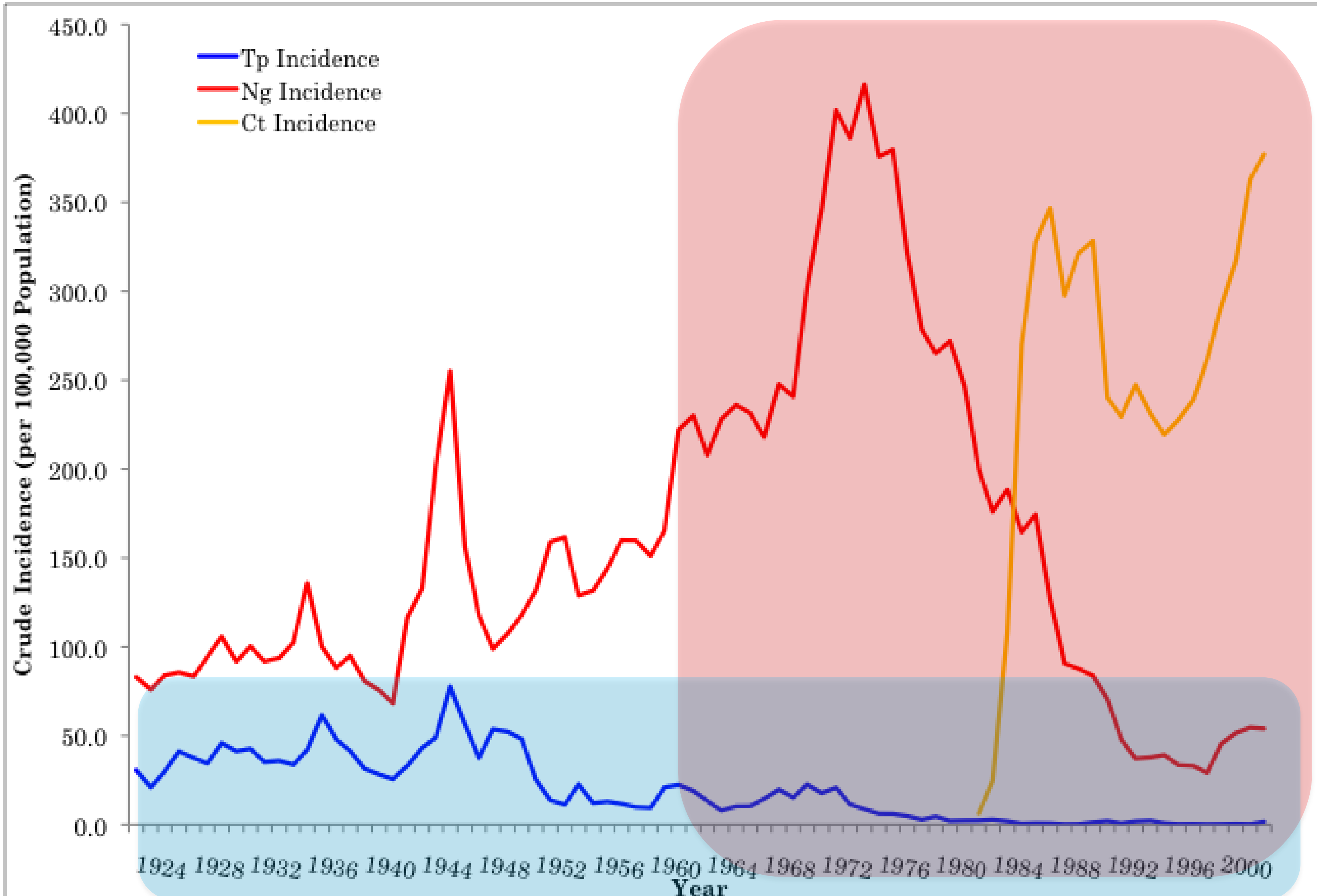
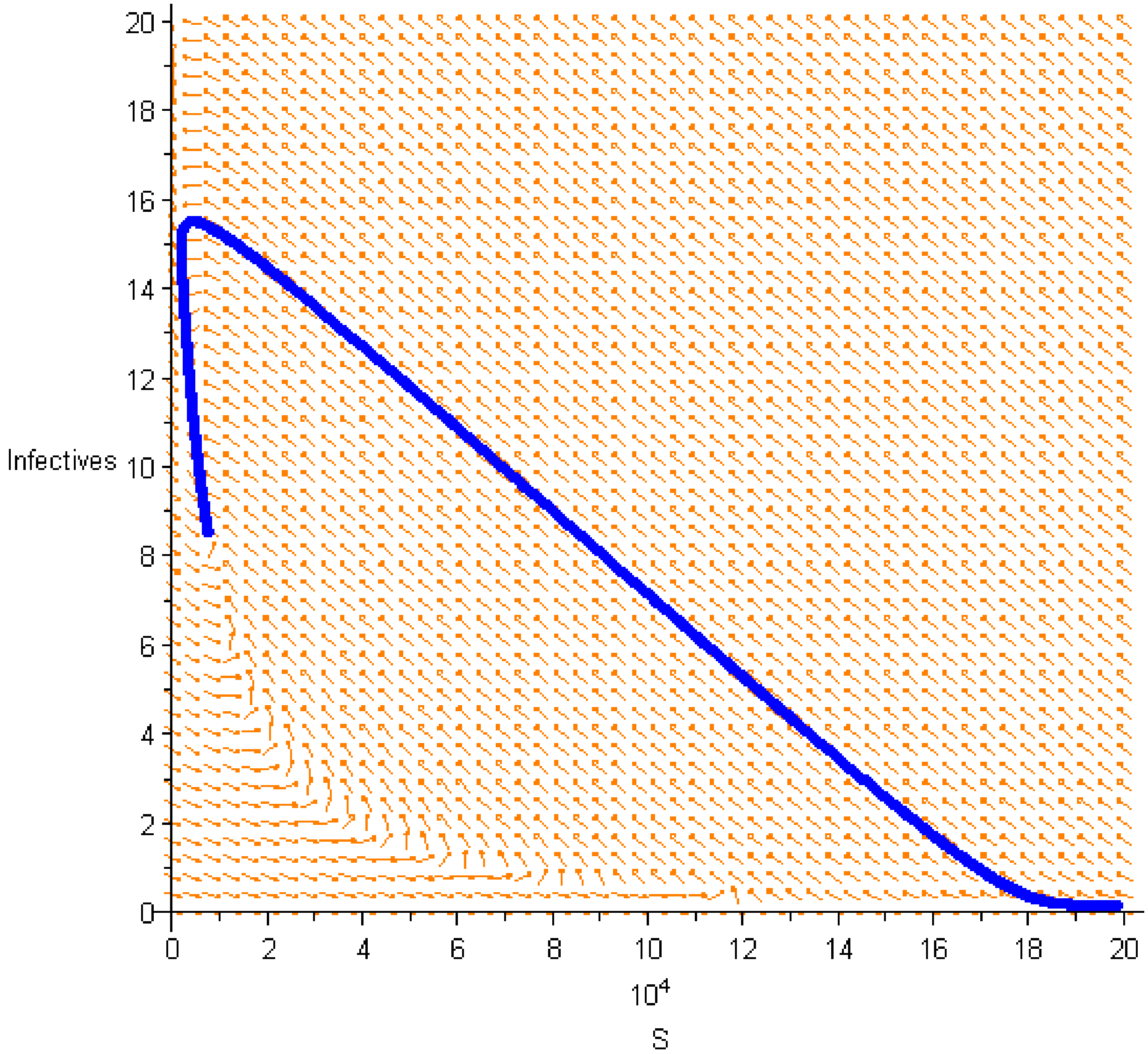
Dynamic Complexity:
Tipping Points



Example: STIs



$R_0 < 1$: 200 HC Workers, I_0=1425



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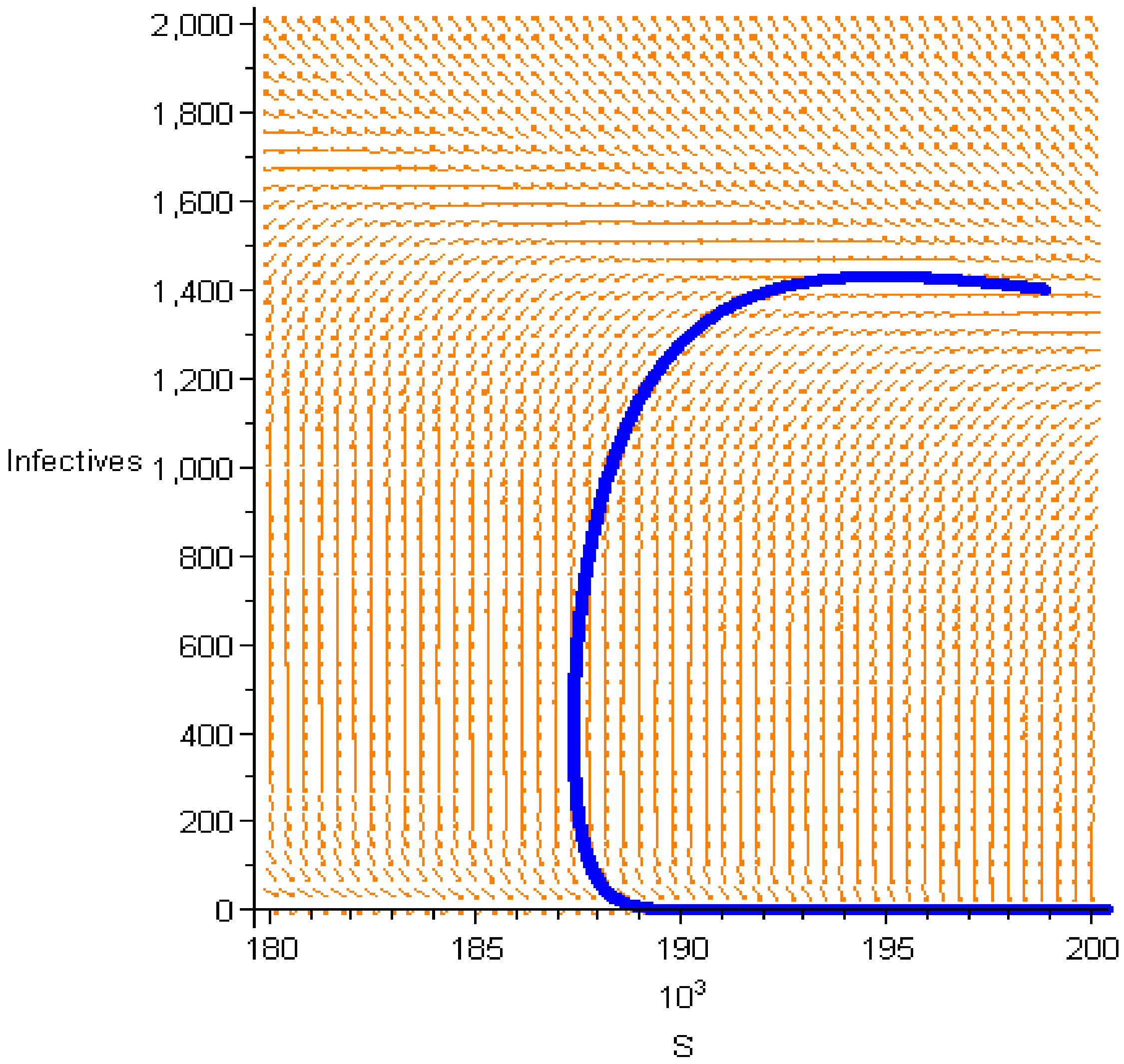

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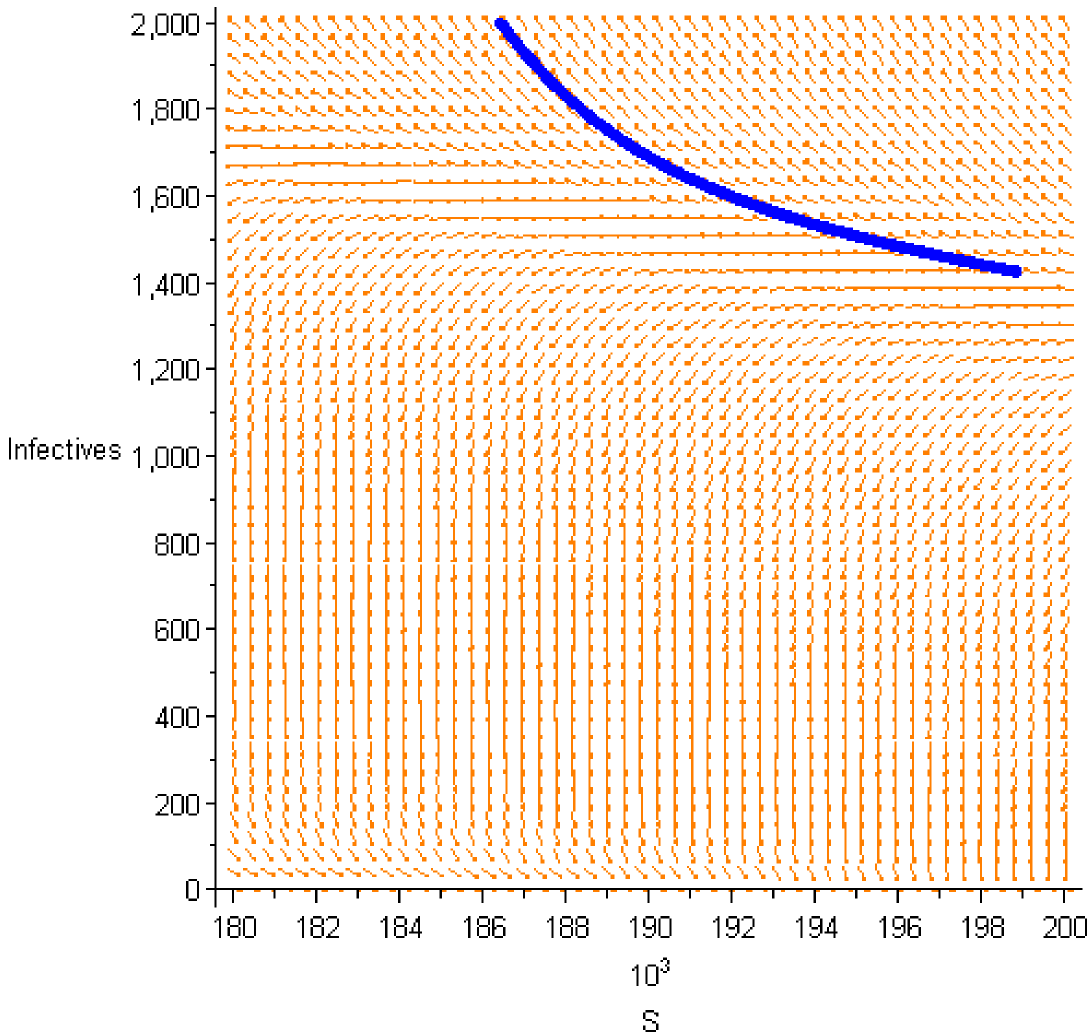
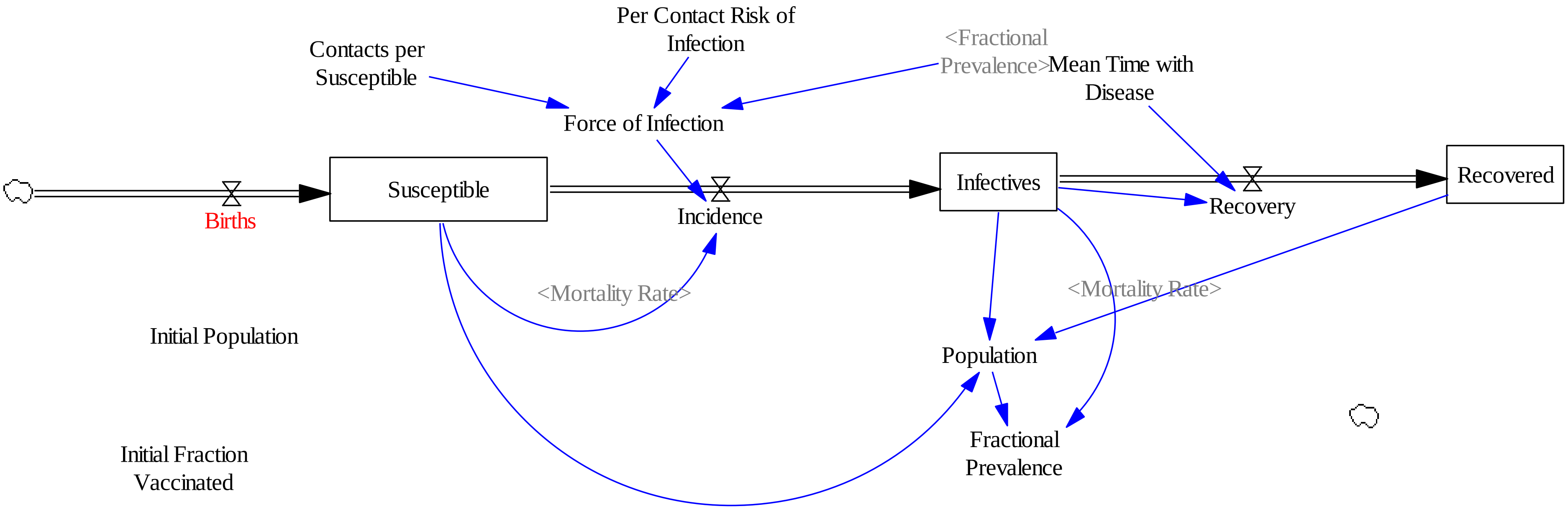


Kendrick-McKermack Model

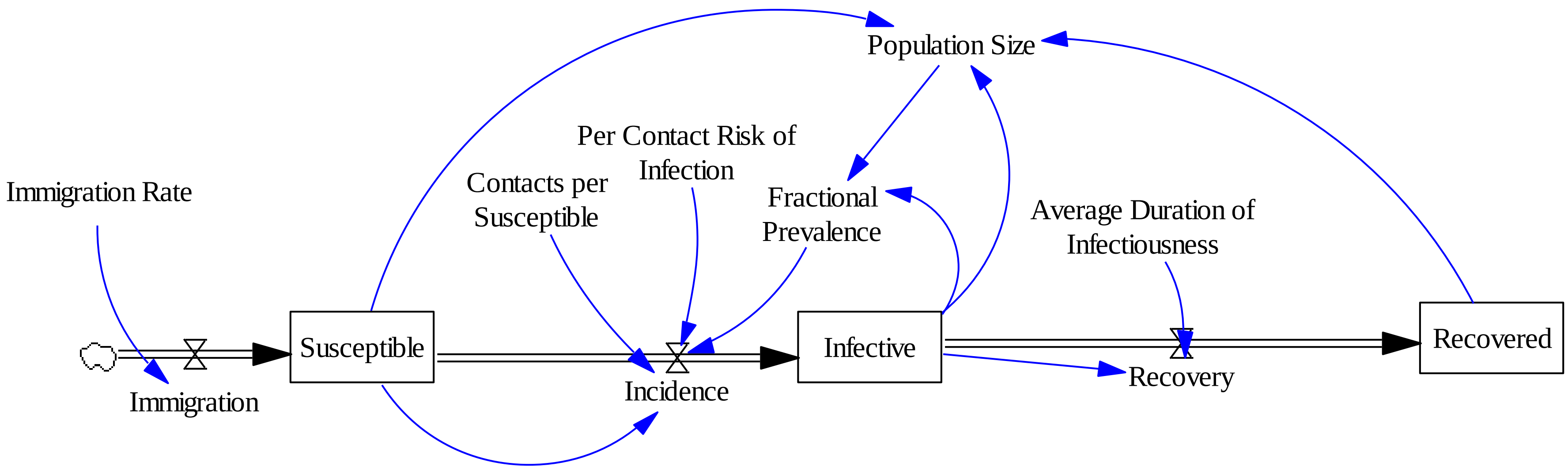
- Partitioning the population into 3 broad categories:
  - Susceptible (S)
  - Infectious (I)
  - Removed (R)


Per Contact Risk of Infection
Contacts per Susceptible
<Fractional Prevalence>
Mean Time with Disease
Force of Infection
Susceptible
Infectives
Recovered
Births
Incidence
Recovery
<Mortality Rate>
<Mortality Rate>
Initial Population
Population
Fractional Prevalence
Initial Fraction Vaccinated

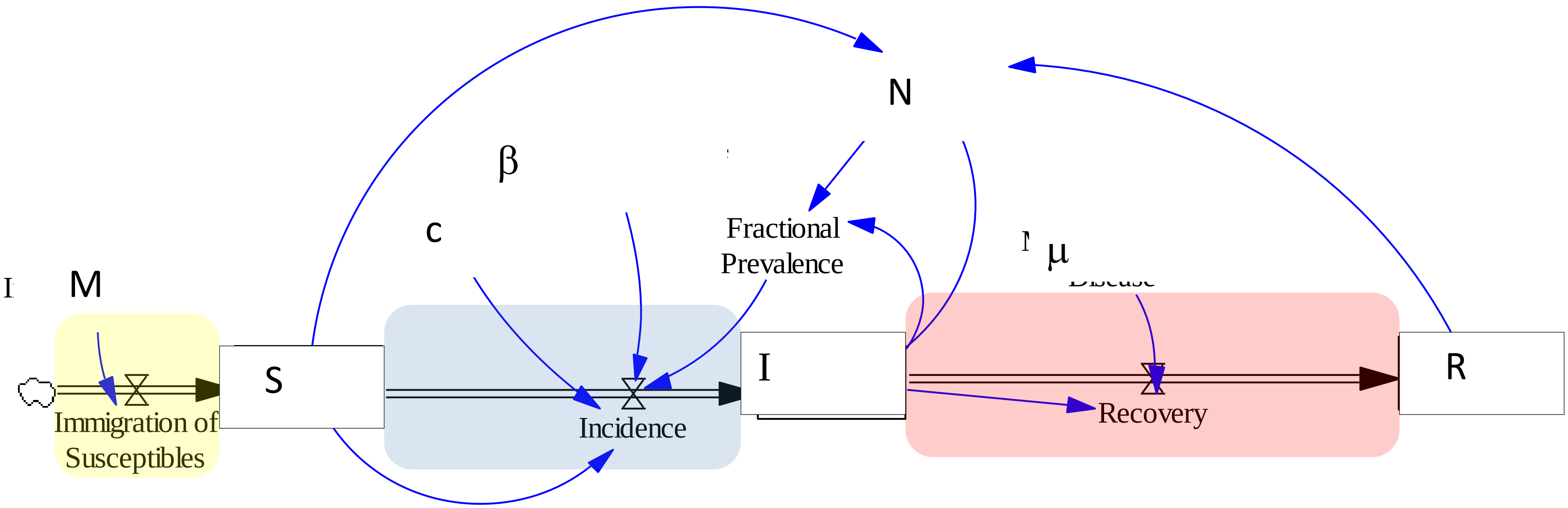
Shorthand for Key Quantities for Infectious Disease Models: Stocks

- *I* (or *Y*): Total number of infectives in population
  - This could be just one stock, or the sum of many stocks in the model (e.g. the sum of separate stocks for asymptomatic infectives and symptomatic infectives)
- N: Total size of population
  - This will typically be the sum of all the stocks of people
- S (or *X*): Number of susceptible individuals

Basic Model Structure



Mathematical Notation



Underlying Equations

$$\dot{S} = M - c\left(\frac{I}{N}\right)\beta S$$

$$\dot{I} = c\left(\frac{I}{N}\right)\beta S - \frac{I}{\mu}$$

$$\dot{R} = \frac{I}{\mu}$$

Our model : Set

- c=10 (people/month)
- β=0.04 (4% chance of transmission per S-I contact)
- μ=10
- Birth and death rate=0
- Initial infectives=1, other 999 susceptible

Key Quantities for Infectious Disease Models: Parameters

- Contacts per susceptible per unit time: c
  - e.g. 20 contacts per month
  - This is the number of contacts a given susceptible will have with *anyone*

- Per-infective-with-susceptible-contact transmission probability: β
  - This is the per-contact likelihood that the pathogen will be transmitted from an infective to a susceptible with whom they come into a single contact.

Intuition Behind Common Terms

- I/N: The Fraction of population members (or, by assumption, contacts!) that are infective
  - Important: Simplest models assume that this is also the fraction of a given susceptible's contacts that are infective! Many sophisticated models relax this assumption
- c(I/N): Average number of *infectives* that come into contact with a susceptible in a given unit time
- c(I/N)β: "Force of infection": *(Approx.) likelihood a given susceptible will be infected per unit time*
  - The idea is that if a given susceptible comes into contact with c(I/N) infectives per unit time, and if each such contact gives β likelihood of transmission of infection, then that susceptible has roughly a total likelihood of c(I/N) β of getting infected per unit time (e.g. month)

Key Term: Flow Rate of New Infections

- This is the key form of the equation in many infectious disease models
- Total # of susceptibles infected per unit time

  # of Susceptibles * "Likelihood" a given susceptible will be infected per unit time = S*("*Force of Infection*") $=S(c(I/N)\beta)$

  - Note that this is a term that multiplies both S and I !
    - This *non-linear* term is much different than the purely linear terms on which we have previously focused
  - "Likelihood" is actually a likelihood density (e.g. can be >1 – indicating that mean time to infection is <1)

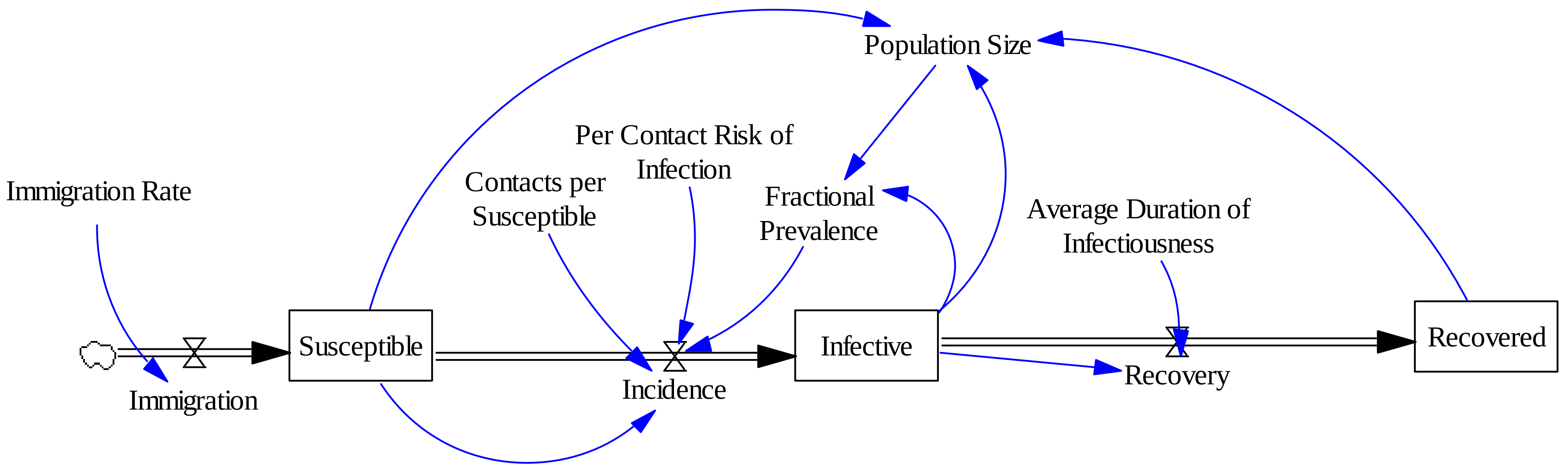
Another Useful View of this Flow

- Recall: Total # of susceptibles infected per unit time = # of Susceptibles * "Likelihood" a given susceptible will be infected per unit time = S*(*"Force of Infection"*) = $S(c(I/N)\beta)$
- The above can also be phrased as the following: $S(c(I/N)\beta)=I(c(S/N)\beta)=I(c*f*\beta)=$
  # of Infectives * Mean # susceptibles infected per unit time by each infective
- This implies that as # of susceptibles falls=># of susceptibles surrounding each infective falls=>the rate of new infections falls ("Less fuel for the fire" leads to a reduced burning rate)

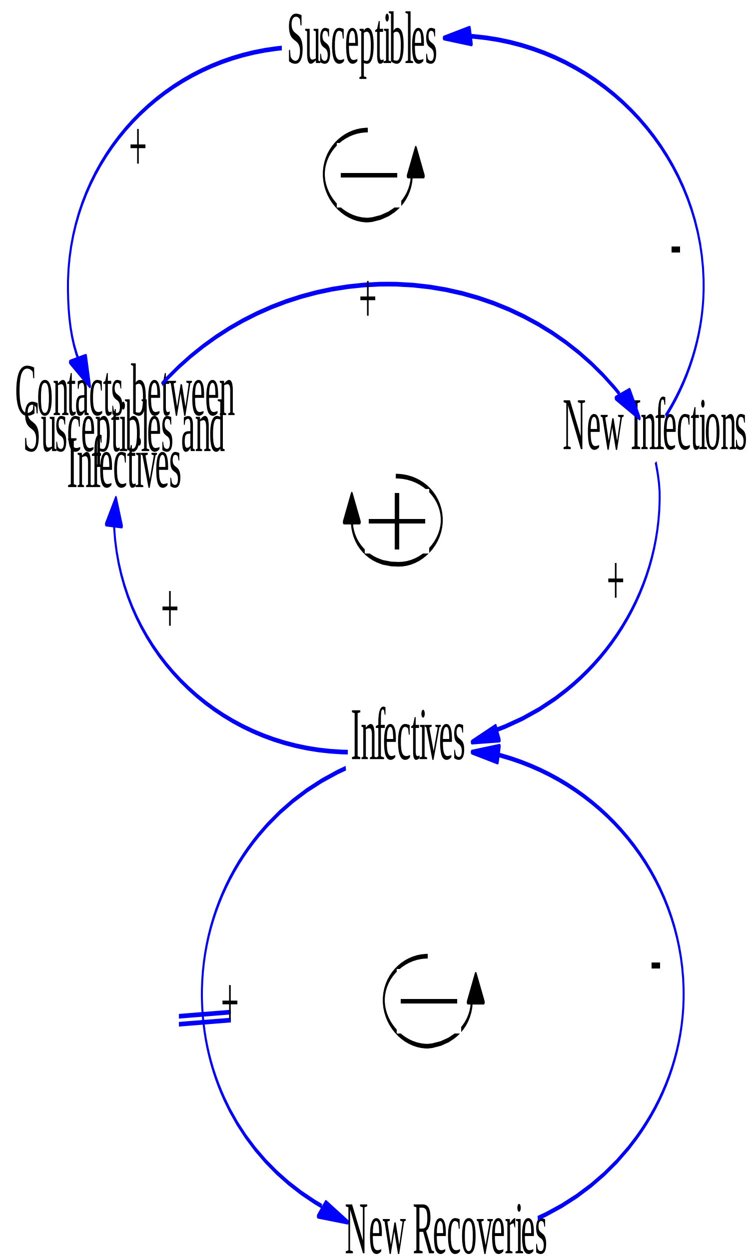
A Critical Throttle on Infection Spread: Fraction Susceptible (*f*)

- The fraction susceptible (here, S/N) is a key quantity limiting the spread of infection in a population
  - Recognizing its importance, we give this name *f* to the fraction of the population that issusceptible

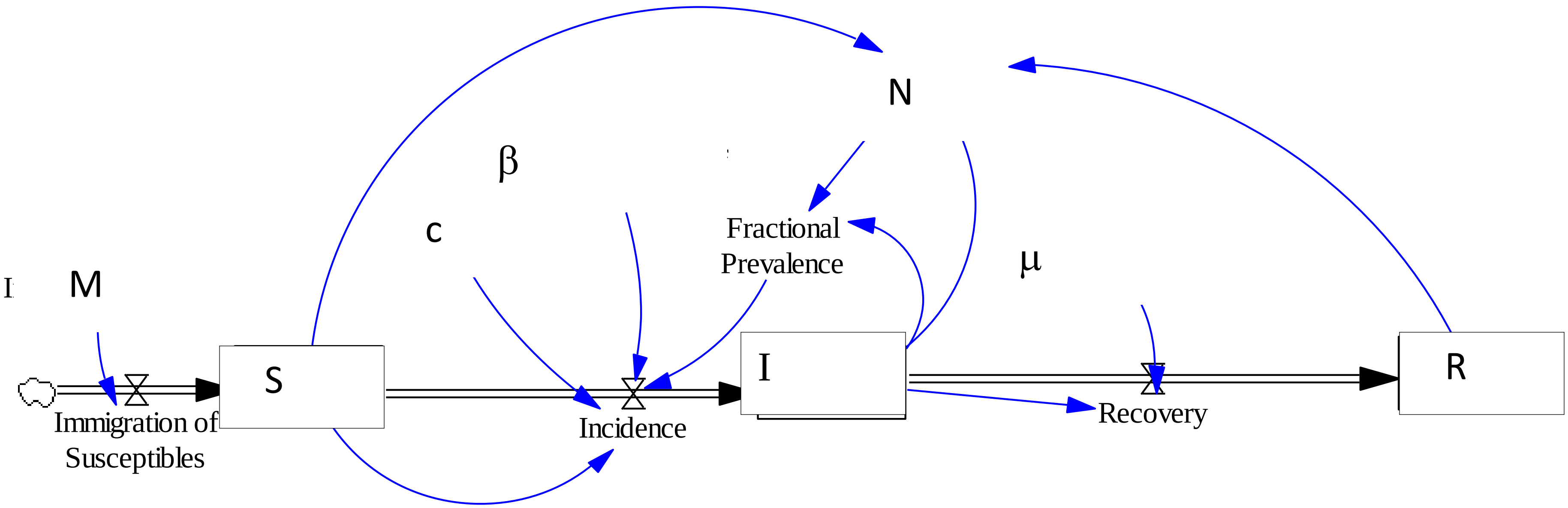
Basic Model Structure



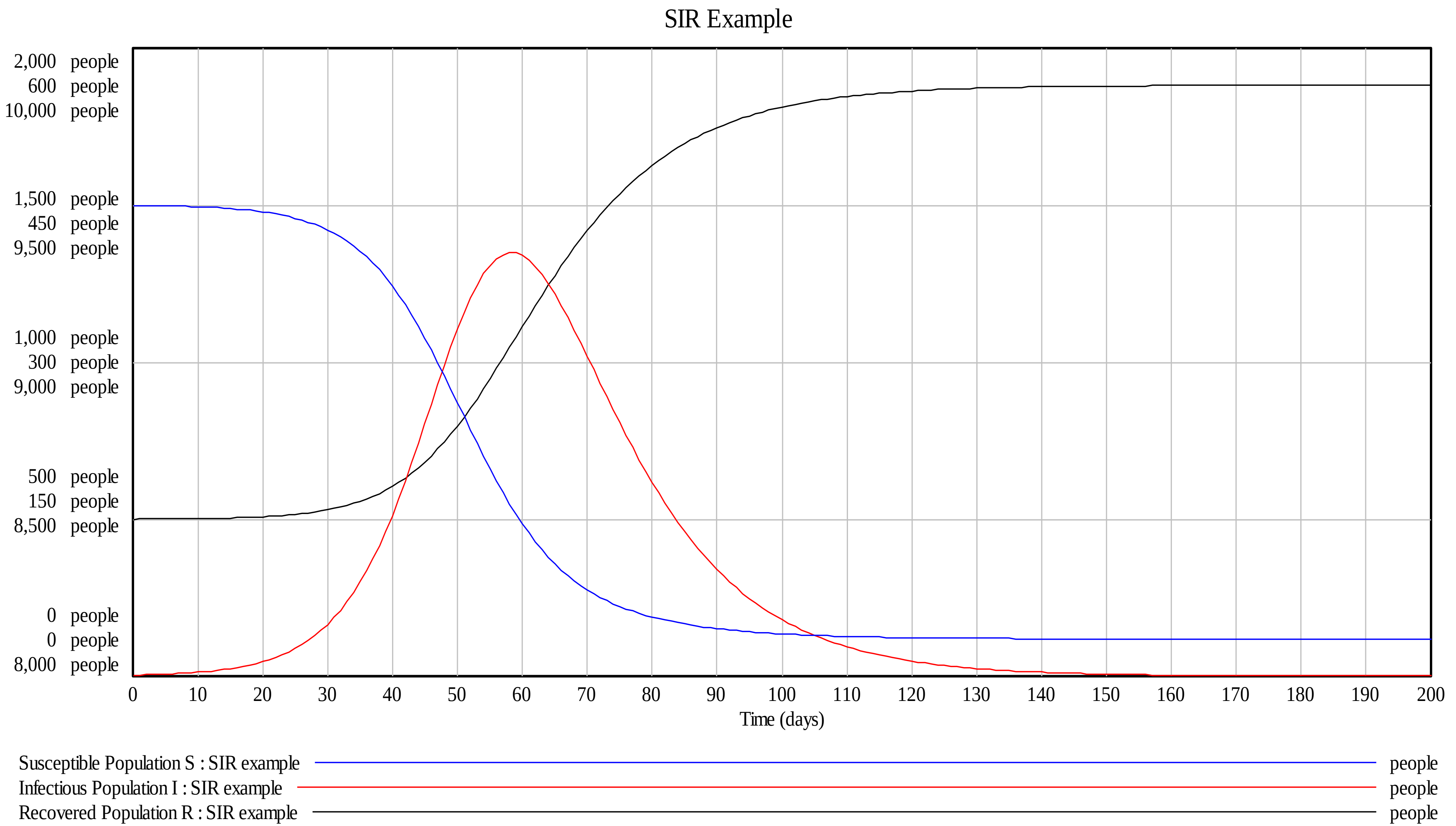
Associated Feedbacks



Mathematical Notation



Example Dynamics of SIR Model (No Births or Deaths)



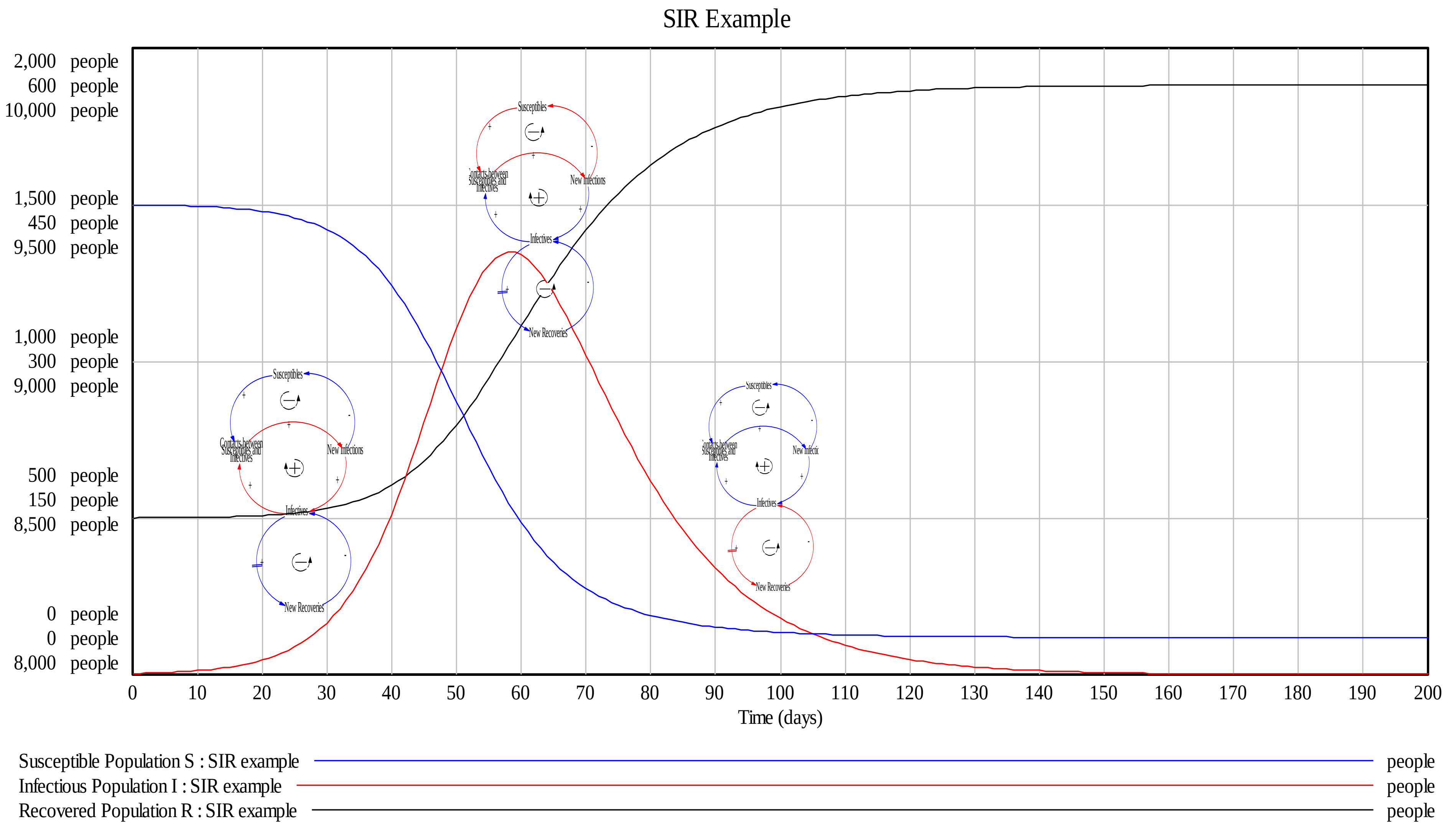
Explaining the Stock & Flow Dynamics: Infectives & Susceptibles

- Initially
  - Each infective infects $c(S/N)\beta \approx c\beta$ people on average for each time unit – the maximum possible rate
  - The rate of recoveries is 0
- In short term
  - # Infectives grows (quickly)=> rate of infection rises quickly
    - (Positive feedback!)
  - Susceptibles starts to decline, but still high enough that each infective is surrounded overwhelmingly by susceptibles, so efficient at transmitting
- Over time, more infectives, and fewer Susceptibles
  - Fewer S around each I =>Rate of infections per I declines
  - Many infectives start recovering => slower rise to I
- "Tipping point": # of infectives plateaus
  - Aggregate Level: Rate of infections = Rate of recoveries
  - Individual Level: Each infective infects exactly one "replacement" before recovering
- In longer term, declining # of infectives & susceptibles => Lower & lower rate of new infections!
- Change in I dominated by recoveries => goal seeking to 0 (negative feedback!)

Key Points

- Minimum value of stock of infectives occurs at different time than minimum of incidence!
  - # of Infectives continues to decrease even after incidence is rising, as long as the rate of recoveries is higher than rate of infection
- Maximum value of stock of infectives occurs at different time than maximum of incidence!
  - Maximum of incidence depends on both susceptible count and force of infection
  - Stock of infectives will keep rising as long as incidence is greater than the recovery rate

Case 1: Outbreak



Shifting Feedback Dominance