Essentials of Aggregate System Dynamics
Infectious Disease Models

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CMPT 394

February 5, 2013
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
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

Measles

Chickenpox
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
Dynamic Complexity: Tipping Points

Chickenpox in SK
Example: STIs
$R_0 < 1 : 200$ HC Workers, $I_0 = 1425$
$R_0 < 1: 200$ HC Workers, $I_0 = 1400$
$R_0 < 1$: 200 HC Workers, $I_0 = 1425$
Kendrick-McKermack Model

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

\[
\begin{align*}
\dot{S} &= M - c \left( \frac{I}{N} \right) \beta S \\
\dot{I} &= c \left( \frac{I}{N} \right) \beta S - \frac{I}{\mu} \\
\dot{R} &= \frac{I}{\mu}
\end{align*}
\]
Our model: Set

- \( c = 10 \) (people/month)
- \( \beta = 0.04 \) (4% chance of transmission per S-I contact)
- \( \mu = 10 \)
- 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: $\beta$
  
  – 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

  \[ \text{# of Susceptibles} \times \text{"Likelihood" a given susceptible will be infected per unit time} = S \times \left( \text{"Force of Infection"} \right) \]
  \[ = S(c(I/N)\beta) \]

  – 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 = $S \times \left( \text{"Force of Infection"} \right) = S(\frac{c(I/N)}{\beta})$

• The above can also be phrased as the following: $S(\frac{c(I/N)}{\beta}) = I(\frac{c(S/N)}{\beta}) = I(c \times f \times \beta) = \# \text{ of Infectives} * \text{Mean # susceptibles infected per unit time by each infective}$

• This implies that as # of susceptibles falls=>$\# \text{ of susceptibles surrounding each infective falls}=>$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 is susceptible
Mathematical Notation

\[ S \] \hspace{1cm} \beta \hspace{1cm} c \hspace{1cm} I \hspace{1cm} \mu \hspace{1cm} R

\[ S \rightarrow I \text{ Incidence} \]
\[ I \rightarrow R \text{ Recovery} \]
\[ S \rightarrow \text{Immunization of Susceptibles} \]

N \hspace{1cm} \text{Fractional Prevalence}
Example Dynamics of SIR Model
(No Births or Deaths)

Susceptible Population $S$ : SIR example people
Infectious Population $I$ : SIR example people
Recovered Population $R$ : SIR example people
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

SIR Example

Susceptible Population S : SIR example people
Infectious Population I : SIR example people
Recovered Population R : SIR example people
Shifting Feedback Dominance

SIR Example

Susceptible Population $S$ : SIR example people
Infectious Population $I$ : SIR example people
Recovered Population $R$ : SIR example people

Time (days)

0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200