CRN and the Epidemiology of Infectious Disease

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Infectious Disease Propagation and Chemical Reaction Networks

- Mathematical models are used to study, analyze, forecast epidemics and explore control strategies of infectious diseases.
- Different approaches- deterministic or stochastic models can be used
- Deterministic models Ê assume that known average rates of interaction have no random deviation in the populations they represent.
- Eg. A population has a 95% chance of surviving annually, then we can be reasonably certain that 95% of the total population will indeed survive.

Infectious Disease Propagation and Chemical Reaction Networks

- Stochastic models allow for random variations due either to uncertainties on the rates of transmission or to population sizes
- Eg A population having a probability 0.95 chance of surviving another year, random variations changes at the end of the year
- with probabilities of having zero survivors, one survivor, two survivors, and so on, up to the total number of survivors at the end of the year.

Chemical Reaction

- Chemical reaction describes a process in which reactants react chemically and convert into products by chemical transformation.
- It is made up of
  - A biochemical network is a system that consists of the species (S), which are the chemical components whose characteristic we wish to model
  - the complexes (C), which are non-negative integers that describe how the species interact, and
  - Reactions (R), which explain how the reactions can convert one complex to another.
- The biochemical reaction system consists of two parts: (i) a reaction network, and (ii) a choice of dynamics.

Reaction Networks Example

- A system with three species; A, B, and C where A and a B molecule merge to form a C molecule, can be described as
- $A + B \rightarrow C$
- This network model consists of species $S = A, B, C$, complexes $C = A + B, C$,and reactions $R = A + B \rightarrow C$.
- The interaction between species that allow transmission of a pathogen naturally define a network.
- The network defines potential transmission routes, an understanding of its structure can be used as part of disease control.
- the study of reaction networks, how they relate to the propagation of infectious diseases, and the underlying theory provides is a vital tool to inform infectious disease propagation and,
- therefore, potential for disease control

Approaches to Reaction Network and epidemiology

1. Define a network allow a complete description of spread of a infectious disease from the knowledge of individual species' behavior
2. Study the potential transmission routes of an infectious disease within a population; some are direct, others need thorough study to implement
3. Use behavioral networks, often generated from known interactions between individuals within a population
4. Use of movement networks, movement of individuals is another source of network information for infectious disease dynamics - meta-population model
5. Use of contact tracing Networks, identified cases are asked about their recent sexual partners, and these individuals are traced and tested;
6. if found to be infected, then contact tracing is repeated for these secondary cases.

The SIR model and its analogy with chemical kinetics

- The classic SIR epidemic model resembles a dynamic model of a batch reactor carrying out an autocatalytic reaction with catalyst deactivation
- Each member of the population is categorized based on their disease status -Susceptible, Infectious, or Recovered
- and possibly, their attributes and the treatment they received - into compartments
- model of theses dynamics is represented by differential equations - flow of individuals to and from the compartments as the population mixes
- The disease is spread/contracted, and infectees progress through the stages of the disease
- Differential equations are a natural choice -rates at which people are infected - progress through the stages of the disease

The SIR model formulation

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The SIR model formulation

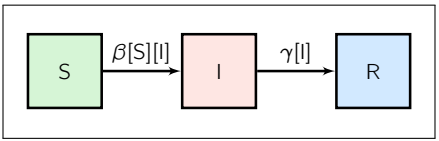

Figure: SIR Model

- Susceptibles can contract the disease if in contact with an infected.
- Once infected and infectious- to I compartment, ie. no delay
- This is like to an irreversible autocatalytic chemical reaction between a reactant, S, and catalyst, I:

$$S + I \rightarrow 2I \quad [1]$$

The SIR model formulation

- Infectious individuals can recover or die from the disease, -R compartment, cannot transmit or contract it again
- This is analogous to a reaction where the catalyst, I, irreversibly degrades or converts to a deactivated form, R:

$$I \rightarrow R \quad [2]$$

- We assume that recovery confers permanent immunity to reinfection,-no possibility of an $R \rightarrow S$ reaction.

The SIR model formulation

- An infectious individual (the catalyst, I)
  1. converts susceptibles (the reactant, S) into more infectious individuals (more catalyst I) and
  2. recovers (deactivates) with time.
- Note the absence of flow to/from external populations; as in a closed batch reactor
- we neglect immigration and emigration
- we take births and deaths (from causes other than the disease) to be negligible over the time scale of the epidemic

The Mathematics SIR model

- SIR model - a well-mixed, isothermal batch reactor carrying out the two homogeneous, elementary reactions. [1] and [2] above.
- Let $[S](t), [I](t)$, and $[R](t)$ be the fraction of the population that is susceptible, infectious, and recovered, respectively, at time t
- Considering a large population, we treat [S], [I], and [R] as continuous variables.
- The incidence rate. Assuming their spatial mixing is uniform, - law of mass action -model the rate at which susceptible and infectious individuals react via bimolecular, autocatalytic reaction[1]
- The recovery rate. - infectious individuals 'decay' (recover) via reaction [2] with first-order kinetics, i.e., with rate γ (per capita).
- The inverse of the first-order recovery rate constant $\gamma > 0$ is the average time period that an infected individual is infectious.

Nonlinear Coupled DE of the SIR model

$$\dot{S} = -\beta\,[S][I]$$

$$\dot{I} = -\beta\,[S][I] - \gamma\,[I] \tag{1}$$

$$\dot{R} = \gamma\,[I]$$

- The parameter γ could be estimated independently from studies on the duration of infectiousness
- The parameter β could be identified by fitting differential eqns 2 to epidemic time series data (case counts)
- Adding eqns. - confirms that the SIR model considers a closed system and neglects demography ; $[S] + [I] + [R] = 1$.
- As a consequence, eqns. and fully determine the SIR model dynamics, and [R](t) follows from $[R](t) = 1[S](t)[I](t)$.

The replacement and basic reproduction numbers

- The replacement number, $r = r(t)$, is the expected number of folks (directly) infected by a typical infectious individual, mixing in the population, over the course of their infectiousness
- Because the concentration of susceptible folks [S] = [S](t) in uences the frequency that a typical infectious individual contacts a susceptible individual, r changes over time
- In the SIR model, a typical infectious individual is expected to be infectious for a time period of γ^{-1}.
- During this time, the infectee will produce $\beta[S](t)$ new infections per unit time (incidence rate per infectious individual)
- The replacement number is therefore: $r = r(t) = \frac{\beta}{\gamma}[S](t)$

The replacement and basic reproduction numbers

- The basic reproduction number, R_0, is defined as the initial replacement number when one infectious individual is introduced into an all-susceptible population
- Because the entire population is susceptible, the replacement number becomes the $R_0 = \frac{\beta}{\gamma}$, $S \approx 1$
- R_0 is the expected number of infections directly caused by a single infectious individual introduced into an entirely susceptible population over the course of their infectiousness
- r, and basic reproduction number, R_0, are both dimensionless and are properties of both the disease and the population
- $r = r(t)$changes with time, R_0 is constant and defined only at the initial stage when one infectious individual is introduced to an all-susceptible population.
- The two numbers are related via $r(t) = R_0[S](t)$.

r and R_0 explained

- If the basic reproduction number R_0 is large , the infectious are infectious for a long period of time
- Then the disease is easily transmitted, and/or the mixing of susceptibles and infectious is vigorous
- If the basic reproduction number R_0 is small, the infectious are infectious for a short period of time
- Then the disease not easily transmitted, and/or the mixing of susceptibles and infectious not vigorous
- Under the analogy with chemical kinetics, since the activity and longevity of the catalyst, I, are embedded in β and γ , respectively:
- then R_0 is large (small) if the catalyst has a high (low) activity and/or remains active for a long (short) time.
- Because $r = R_0[S]$, these remarks hold for the replacement number, r, as well.

The initial Conditions

- What happens if we introduce a small number of infectious individuals into a large population of susceptible individuals?
- The corresponding initial conditions are:

$$S(0) = [S]_0,\ I(0) = [I]_0\ R(0) = 0] \tag{2}$$

- with $[S]0 + [I]0 = 1$, $[S]0, [I]0 > 0$, and $[I]0 \ll 1$.
- We consider$[R](0) = 0$ for the case - exposed to a novel pathogen without immunity.
- The replacement number $r(t)$ is key to understanding SIR model dynamics
- $[I](t)$ is increasing at time t if the replacement number $r(t) > 1$ and decreasing if $r(t) < 1$,
- so $r(t)$ determines the dynamic behaviour of $\dot{I}(t)$

Under CRN analogy, if $r0 < 1 (r0 > 1)$, the injected catalyst particles deactivate via reaction [1] faster (slower) than they catalyze reaction [2] to propagate autocatalytic reaction[1].

Analysis of the Endemic SIR Model

- Early in the epidemic, the number of infectious folks grows, approximately, exponentially with growth rate

$$\frac{dI}{dt} = (\beta[S][I] - \gamma[I] \quad \frac{dI}{dt} = \gamma(\frac{\beta}{\gamma}[S] - 1)I$$

- Integrating with respect tot t, is equivalent to

$$\frac{dI}{dt} = \gamma(r[S] - 1)I \quad \frac{dI}{dt} = \gamma(r-1)I, \; S = 1$$

- The solution gives

$$[I](t) = [I]_0 \, e^{r-1)\gamma t}$$

- valid only in the initial stage of the epidemic; as the disease spreads, [S] decreases and diminishes the replacement number

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