Introduction to disease transmission models

Model assumption and stochastic processes

Dr. Gustavo Machado

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College of Veterinary Medicine
Lab website NCSU:https://machado-lab.github.io

NC STATE UNIVERSITY
COLLEGE OF VETERINARY MEDICINE

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Transmission and simulation in decision-making

1. Mathematical and simulation models are commonly used to inform policy by evaluating which control strategies will minimize the impact of the epidemic [1, 2].
2. Used by many countries before, during and after and epidemic [1, 2].
   1. Real-time epidemic modeling.
   2. Early in the infection, loads of uncertainty, do we need to wait for more data before calibrating a model for forwarding simulation?
   3. Late in the epidemic (can one wait)?
3. MHASpread FMD transmission models for Latin America.

Introduction to modelling

Why do we use models for infectious diseases?

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1. The dynamics of infectious diseases are complex.
2. Non-linearities.
   - Small changes in input can produce large changes in output.
3. Emergent properties.
   - More is different.

Basics definitions of models

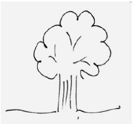
Models in science have two different roles: **understanding** what happens and **predict** will happen.

Models can be of two types:

1. Simple (minimal number of parameters)
2. Complex systems (more interactions and parameters).

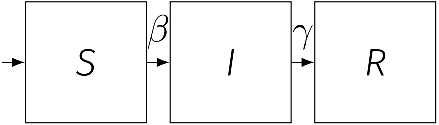
Simplicity ⟷ Realism

(understanding) (prediction)



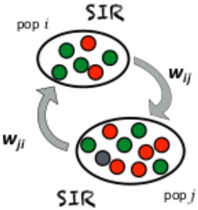
Simplicity (understanding):

1. Compartmental models

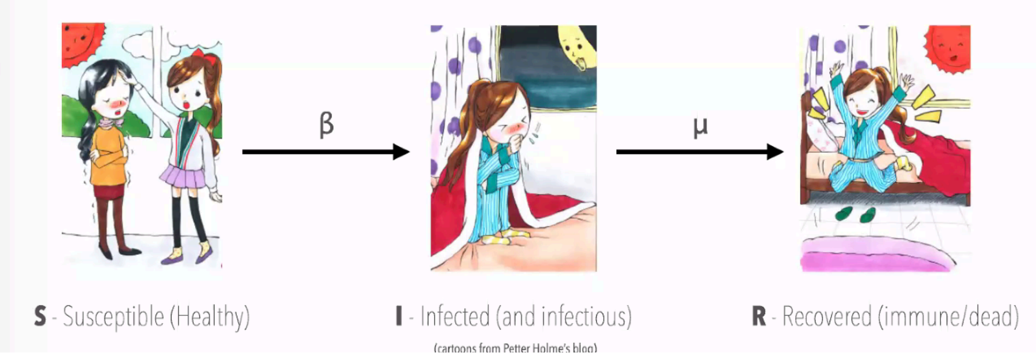


Realism (prediction):

1. Metapopulation
2. Individual-based
3. Network



Population divided into **categories defined by health or disease status.**



Basic models assumptions

Basic models

Basic models assume well-mixed populations (homogeneous mixing.)

In the well-mixed population assumptions:

- All individuals are **equivalent**, hence everyone has the same probability of being infected;

In practice, because the time-scale of simulation is so little that we may/want consider a **close population.**

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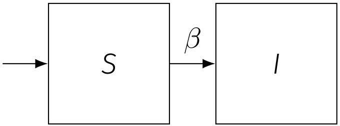
- All individuals are **equivalent**, hence everyone has the same probability of being infected;
- Every individual has the **same number of contacts on average**;
- **Closed population**. **(No births or deaths.)**

In practice, because the time-scale of simulation is so little that we may/want consider a **close population.**

The simplest model one can think of is the **SI** (**S***usceptible* **I***infected*).

No recovery from infection!!!

The **transition diagram** that describes this model is the following:



β is the *"effective contact rate" infection rate* and dictates the speed of dissemination. Of note, β accounts for the transmissibility of the disease.

1. β that drives the spreading 1.

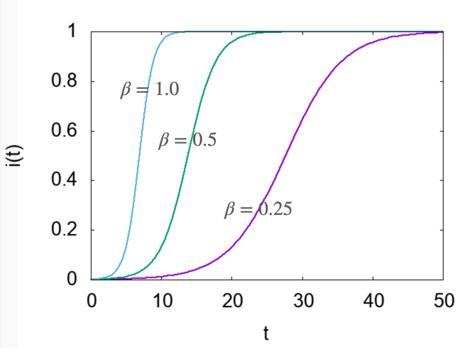


Figure 1: Plot of the solution of the **SI** model for different β.

Basic models SI

1. β that drives the spreading 1.
2. By increasing it, we obtain faster exponential growth.

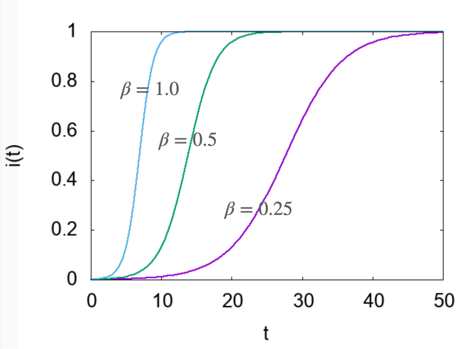
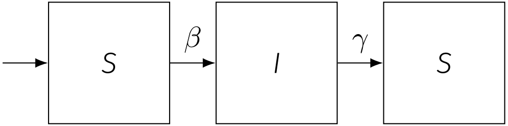


Figure 1: Plot of the solution of the **SI** model for different β.

SIS model

SIS model, where compartments are **S***usceptible*, **I***nfected*, **S***usceptible*. Now we have two transitions:



Where the first transition is mediated by I, that is to say, we need to encounter another infected individual to contract the disease, while the second event will occur **spontaneously** according to the rate γ.

Basic models SIS

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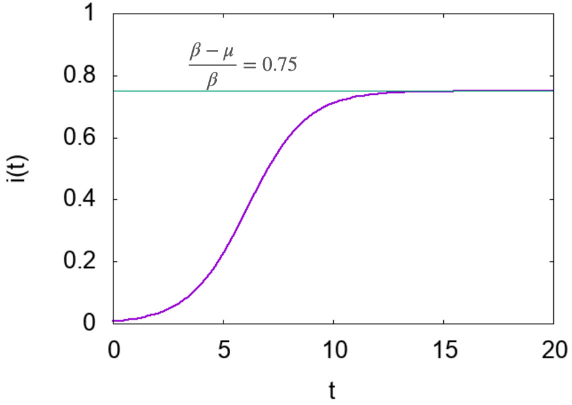
- **"Endemic state"** means that the disease keeps circulating in the population for **a very long time**.
- An individual may recover but does **not become immune**.
- Indeed, there are always individuals in S that can become infected and propagate disease,
- γ is the **recovery rate.**

Dynamical equilibrium: The density $i(t)$ will therefore fluctuate around this value $\frac{\beta-\gamma}{\beta}$ and, by enlarging γ, we can obtain larger fluctuations (Fig. 2).



The minimum value of the infection probability for which the disease survives.

This is what in physics is called a **second order phase transition** (Fig. 3).

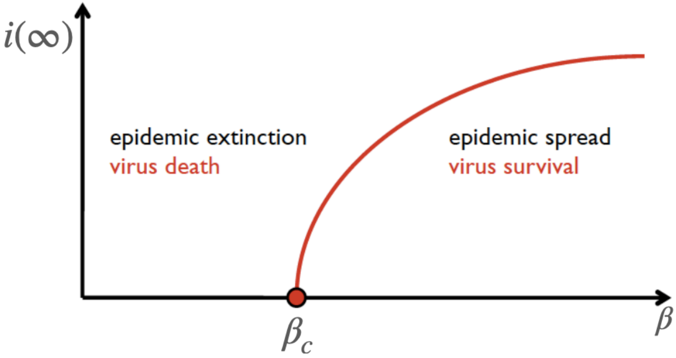


Figure 3: Epidemic diagram.

Basic models SIS

1. Epidemic threshold is given by the condition under which we observe disease propagation.
2. Mathematically, given a specific model, its critical version will return the values of the parameters for which $R_0 = 1$. If we are slightly above this threshold, **we only need a minimum of infected individuals**, and the disease will spread.

Basic models SIS and SIR

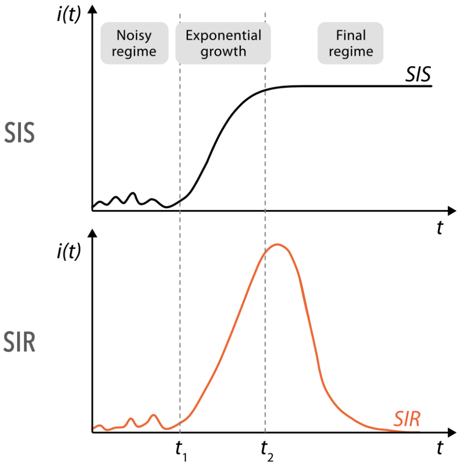


Figure 4: Epidemic regimes.

Basic reproductive number, R_0

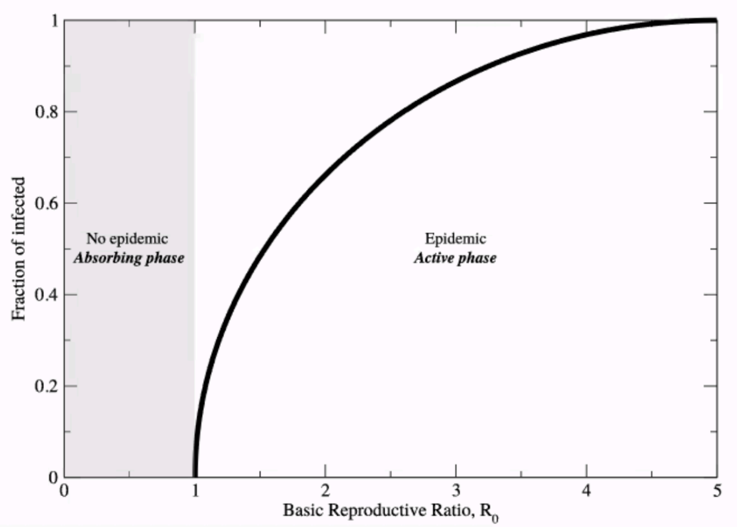
Expected number of secondary cases of disease produced directly by *an average* infectious individual entering an entirely susceptible population

$$R_0 > 1 \textit{ Epidemic occur} \tag{1}$$

$$R_0 = 1 \textit{ Endemic} \tag{2}$$

$$R_0 < 1 \textit{ No epidemic occurs} \tag{3}$$

Basic reproductive number



SIR model

Basic models SIR

We now discuss the so called *SIR* model, whose compartments are *Susceptible*, *Infected* *and Recovered*.

The idea behind is the same one of the SIS, but we are now adding a new state which accounts for long-lasting immunity (***Recovered***).

Hence, once an animal has got the disease and has recovered, thus, long

immunity.

Basic models SIR

The transitions for this model are:

$$\longrightarrow \boxed{S} \xrightarrow{\beta} \boxed{I} \xrightarrow{\gamma} \boxed{R}$$

- **Here we cannot have any endemic state,** why?

Basic models SIR

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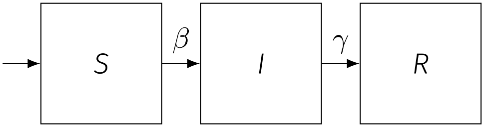

- **Here we cannot have any endemic state**, why?
- If take **several months in consideration**, all individuals will have been infected and recovered, so the disease will be spreading no more.

Basic models SIS and SIR

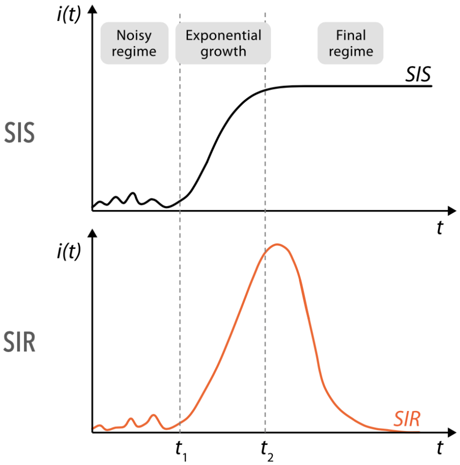

Figure 5: Epidemic regimes.

SIR: Compartment model as one example

- System of differential equations to simulate disease propagation

$$\frac{dS}{dt} = -\lambda \cdot S$$

$$\frac{dI}{dt} = \lambda \cdot S - \gamma \cdot I$$

$$\frac{dR}{dt} = \gamma \cdot I$$

$$\boldsymbol{\lambda} = \boldsymbol{\beta} \cdot \frac{\boldsymbol{I}}{\boldsymbol{N}}$$

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- System of differential equations to simulate disease propagation
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- Where γ describes the recovery rate
- Where λ describes infection rate (force of infection) defines a constant probability.

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SIR model (close population)

- Closed system/population: no births/deaths

$$\beta = \textbf{\textit{transmission parameter}} \frac{\textit{transmission probability parameter}}{\textit{contact} * \textit{contact rate}}$$

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- **Fixed population size (deaths=births)**

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SIR model (open population)

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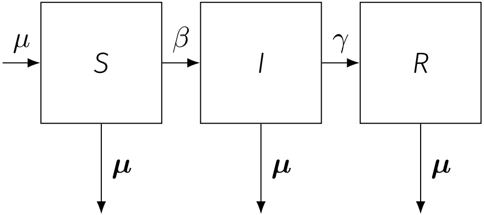

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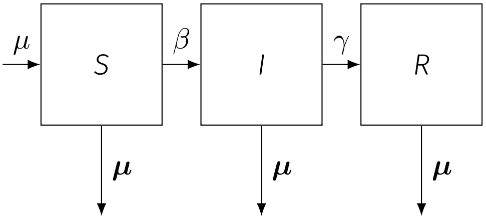

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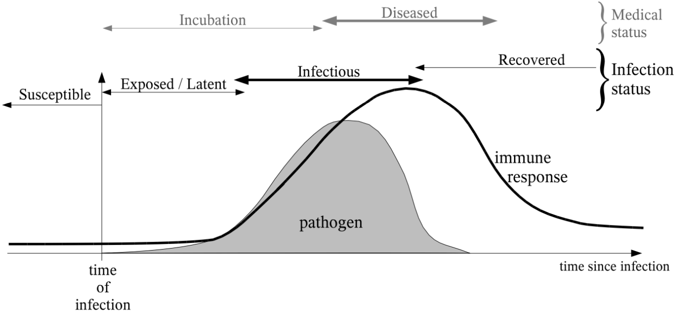
Other model structures

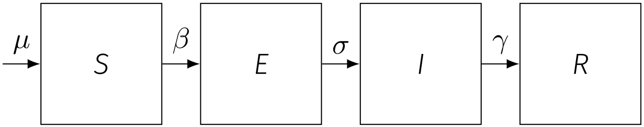
Different models vs type of the disease: for instance **SI, SIR, SIS, SEIR**, and so forth.

SEIR compartmental model, we have four main stages of the disease: starting from a healthy state (Susceptible), the individual can contract the disease (Exposed) and then, only after some time, becomes infectious (Infectious) until he recovers (Recovered)



SEIR model

1. In reality individuals do not become instantaneously infectious, but there is a **latent period** which is the time between infection and becoming infectious.



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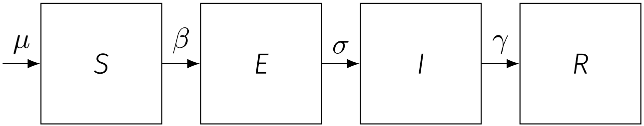


SEIR model

1. In reality individuals do not become instantaneously infectious, but there is a **latent period** which is the time between infection and becoming infectious.
2. The pathogen replication takes time, i.e., viral load is too low to be able to transmit the infection.
3. This argument leads us to introduce the **S**, **E**, **I**, **R** model, where the class **E** takes into account that an individual has already contracted the disease, hence is not susceptible anymore, but is not able to spread it yet.

$$\xrightarrow{\mu} \boxed{S} \xrightarrow{\beta} \boxed{E} \xrightarrow{\sigma} \boxed{I} \xrightarrow{\gamma} \boxed{R}$$

The SEIR can be the starting point for modeling realistic diseases: i.e. Covid-19 6

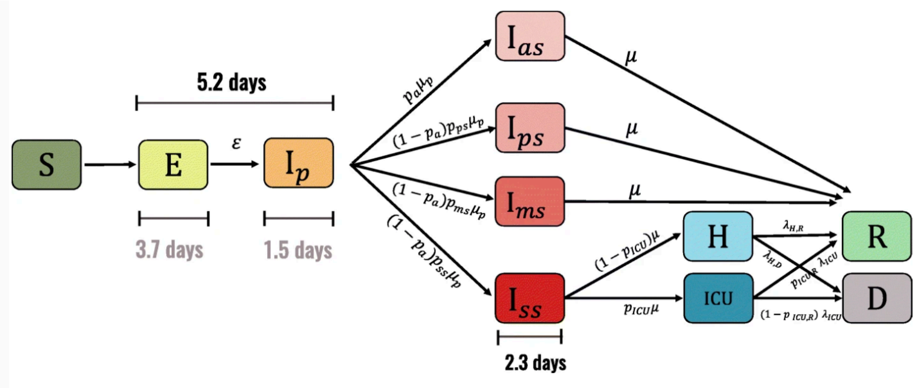
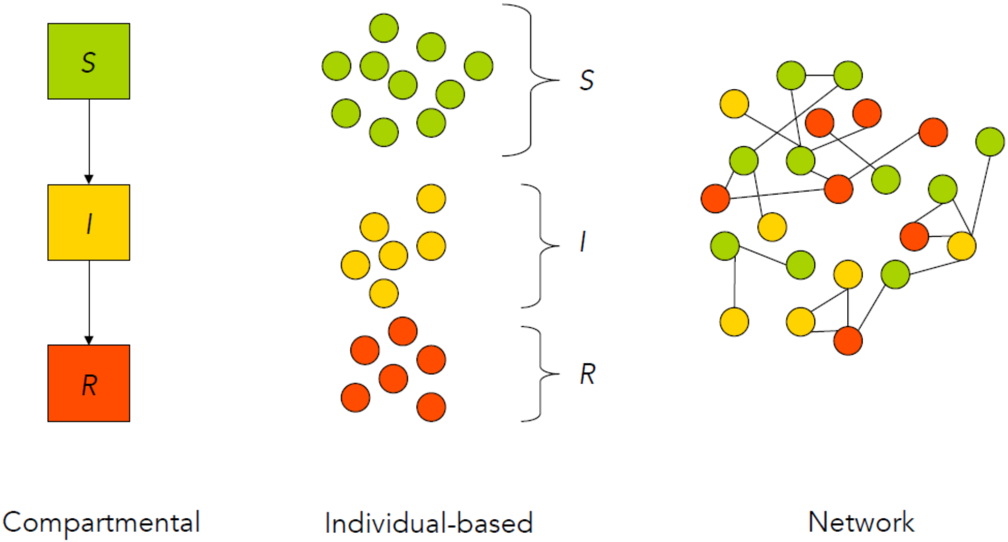


Figure 6: Model for Covid-19.

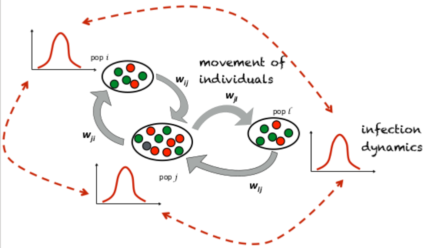
Can we include more realism?



Situations that often warrant other approaches

Ecology the concept of metapopulation models

1. The first models assumed that the **mixing between populations occurred homogeneously**.
2. We can or not keep track of every individual.



[Hanski, I. & Gaggiotti, Elsevier, Academic Press, 2004]

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More complex and fine mechanisms

1. Spatial spread of disease.

Many of these issues can also be approximated using variations of compartmental models.

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3. Modeling complex interventions (e.g., targeting individuals via contact tracing).
4. Elimination of pathogens.
5. Emergence of new pathogens in populations.

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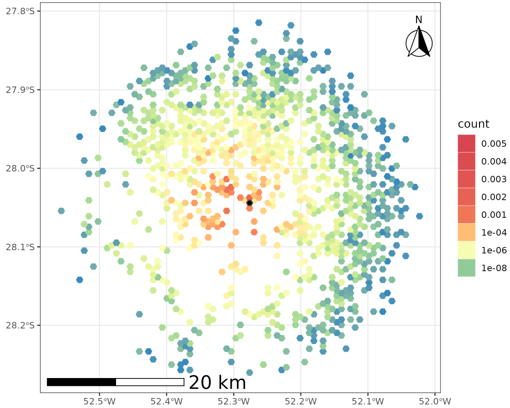
Spatial spread

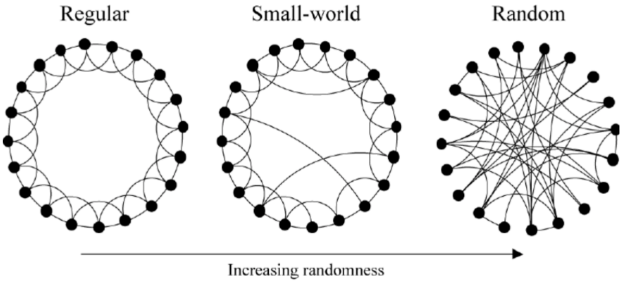


- **Distance (Km)**
- 1 km (prob. 0.012)
- 2 km (prob. 0.004)
- 3 km (prob. 0.002)
- ...40 km (prob. 4.56e-13)

Regular = Connected with its two nearest neighbors on both sides.

Small-word = Connected with its two nearest neighbors and some long jumps.

Random= Erdös and Rényi Model: random graphs, links between nodes are drawn at random.



Models to be used by policy makers

For policy-making, more complex models are sometimes required

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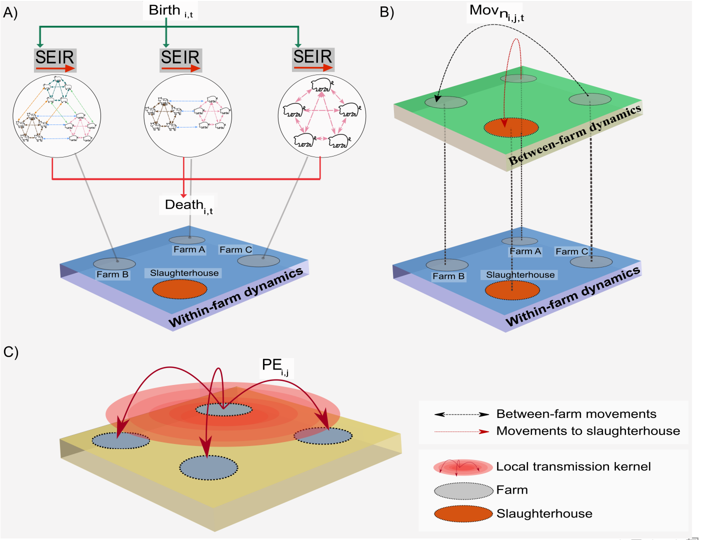
- “Predictive” models.
- Comparing the performance of alternative “realistic” interventions.
- Coupling with economic considerations to generate cost-effectiveness comparisons of different control strategies.

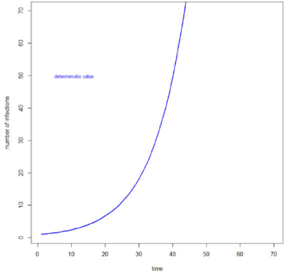
MHASpread: A multi-host Animal Spread Stochastic Multilevel Model



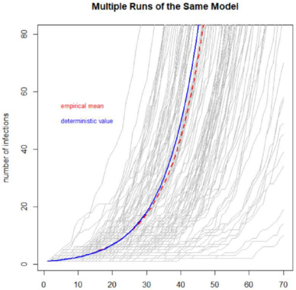
Transitions between health status

Deterministic vs stochastic

- Deterministic: fixed rate of transition between states.
    - Uses a population mean rate to govern flows.



- Stochastic: probability that an element transitions between states.
- Uses a draw from a probability distribution to govern flows.



In general: random, or variable

- In particular:
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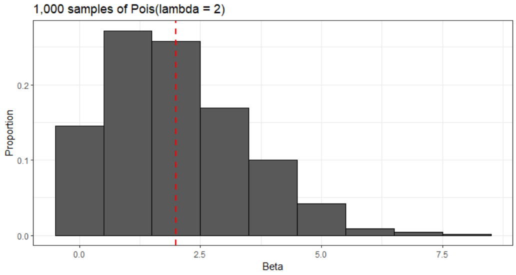

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What does stochastic mean?

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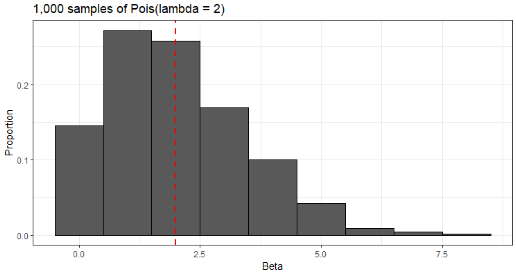

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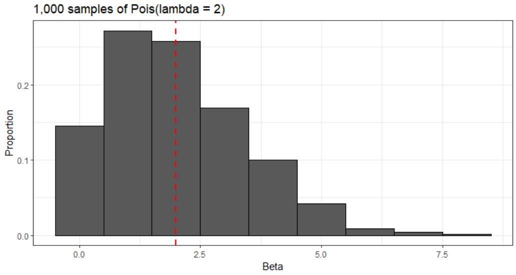

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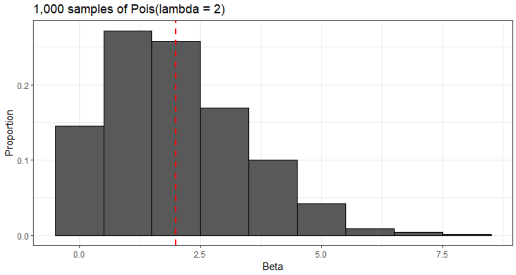

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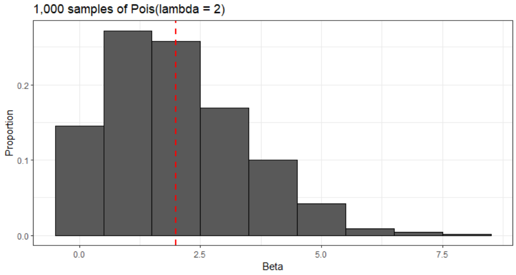
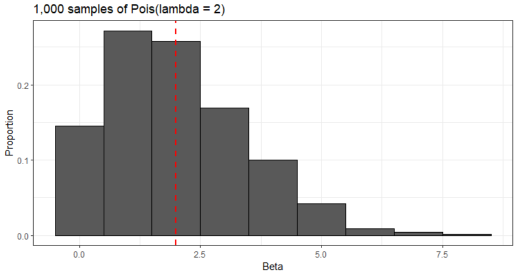
  - A probability density function (PDF).
  - Defined by one or more parameters.



What does stochastic mean?

In general: random, or variable

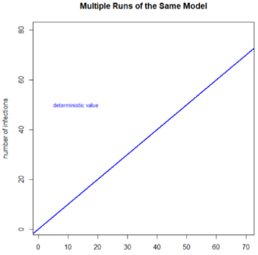
- In particular:
  - A random draw.
  - From the possible range of outcome values.
  - With a probability assigned to each value.
- Typically, the probabilities are summarized by:
  - A probability density function (PDF).
  - Defined by one or more parameters.
  - e.g., binomial, Poisson, normal, etc.

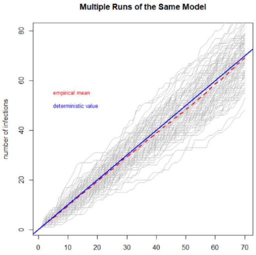


Impact of stochasticity on epidemic dynamics?

Using the Poisson distribution:

- A deterministic **lambda = 1** as expected new case per day.
- With the stochastic model, we set also **lambda = 1** the average number of new cases.
    - Variance in new cases each day is:

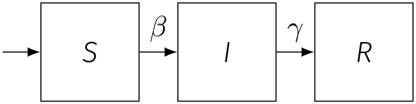


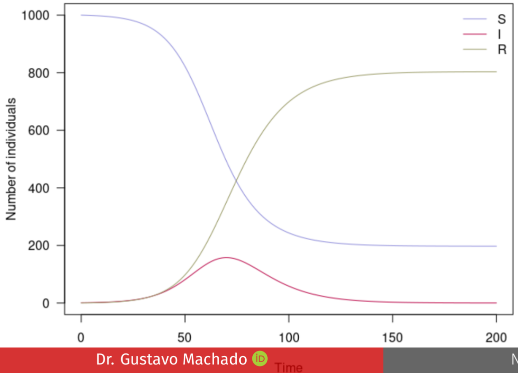


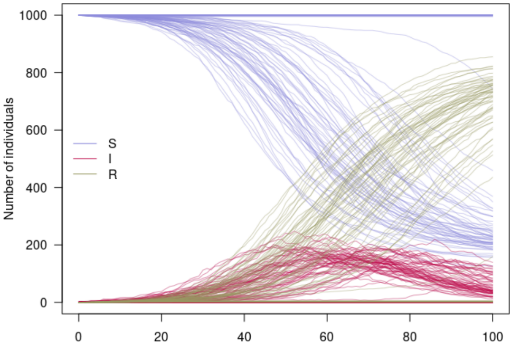
Key idea: Interpreting variability

- Stochastic variation can be large, particularly
  - At the beginning of an epidemic.
  - Small populations.

Key idea: Interpreting variability







Key idea: Interpreting variability

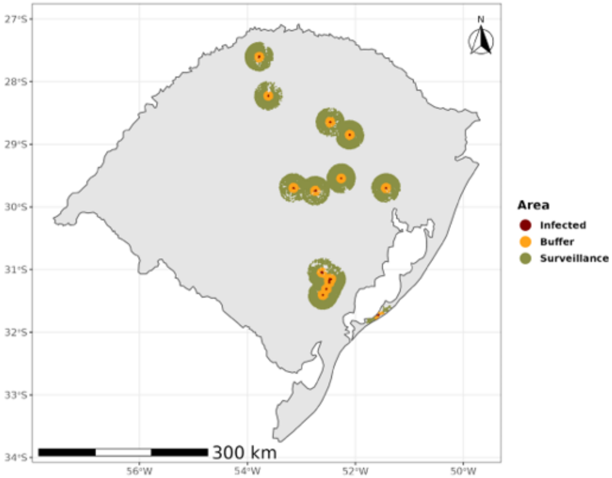
Be careful not to over-interpret!

Control actions

Control actions

1. Quarantine and depopulation.
2. Vaccination reactive and/or preventative.
3. Animal movement restrictions/standstill.
4. Contact tracing - direct and indirect.
5. Control zones.

Control actions



Summary

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- Models of infectious diseases may be of various forms.
- Comparing the performance of alternative “realistic” interventions.
- The structure and approach should be dictated by the research question and availability of data.
- Both simple and more complex models have proven to be useful tools for understanding disease dynamics, projecting disease trends, and informing control policy.

Thanks for listening

Questions?

References

[1] William JM Probert et al. “Real-time decision-making during emergency disease outbreaks”. In: *PLoS computational biology* 14.7 (2018), e1006202.

[2] SE Roche et al. “Evaluating vaccination strategies to control foot-and-mouth disease: a model comparison study”. In: *Epidemiology & Infection* 143.6 (2015), pp. 1256–1275.