

Introduction to disease transmission models

Model assumption and stochastic processes

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Table of content

1. Introduction to modelling
2. Basic models assumptions
3. SIS model
4. SIR model
5. Metapopulations
6. Transitions between health status
7. Control actions

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NC STATE UNIVERSITY



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Centro Panamericano de Fiebre Aftosa
y Salud Pública Veterinaria

Transmission and simulation in decision-making

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

Introduction to modelling

Why do we use models for infectious diseases?

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- ➌ 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:

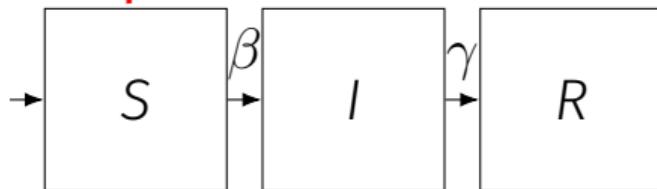
- ① Simple (minimal number of parameters)
- ② Complex systems (more interactions and parameters).

Simplicity
(understanding) ← → Realism
(prediction)



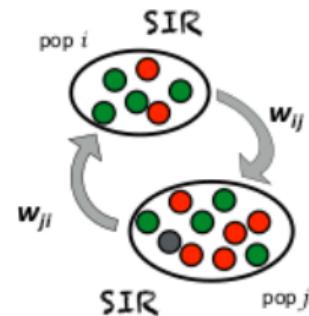
Simplicity (understanding):

① Compartmental models



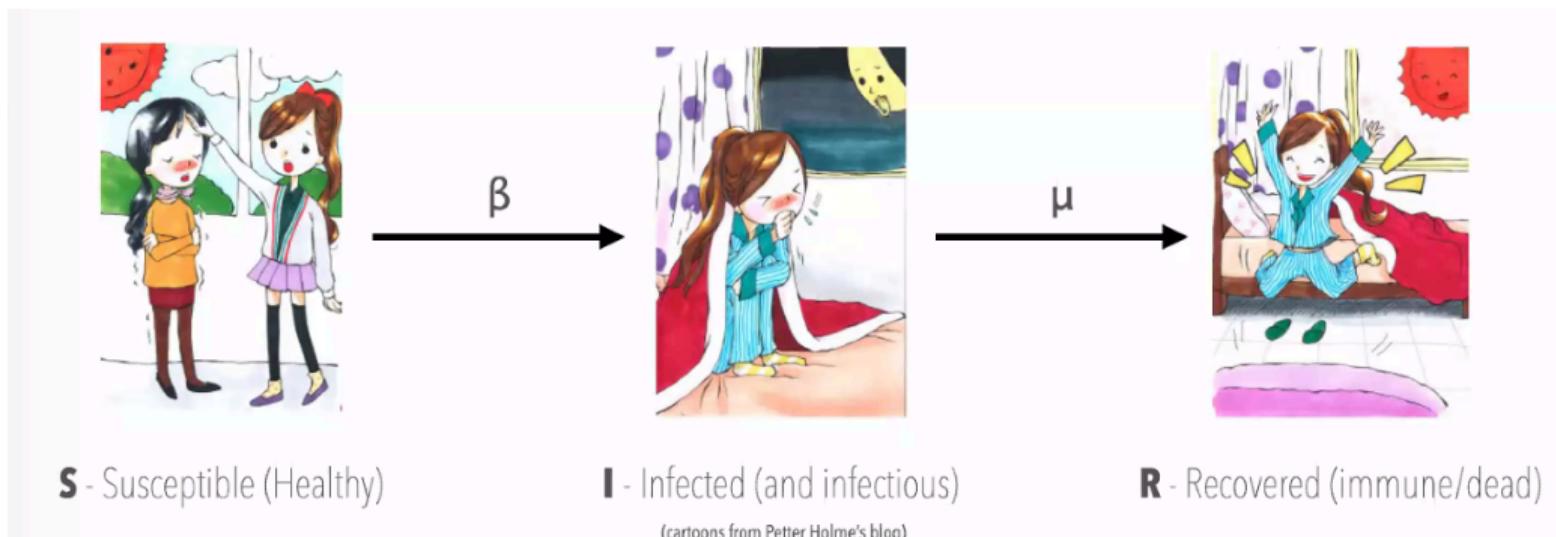
Realism (prediction):

- ① Metapopulation
- ② Individual-based
- ③ Network



Compartmental models

Population divided into categories defined by health or disease status.



Basic models assumptions

Basic models

Basic models assume well-mixed populations, or in other words **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 can 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.**

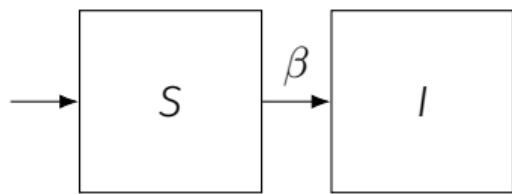
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Basic models SI

The simplest model one can think of is the **SI** (*Susceptible 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.

Basic models SI

- ➊ β that drives the spreading 1.

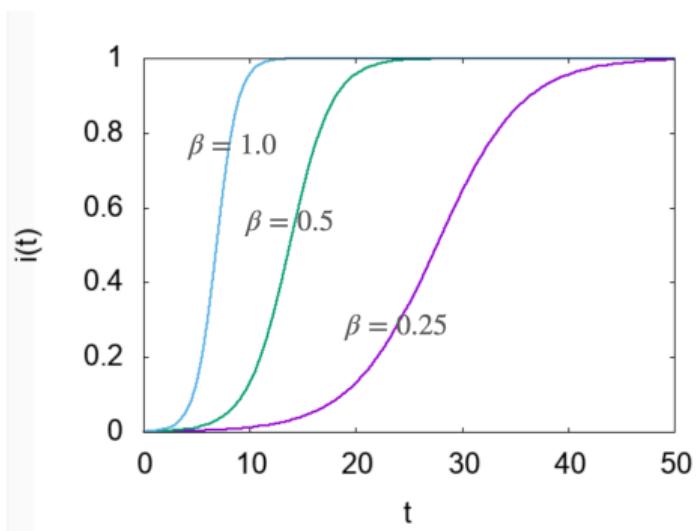


Figure 1: Plot of the solution of the SI model for different β .

Basic models SI

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

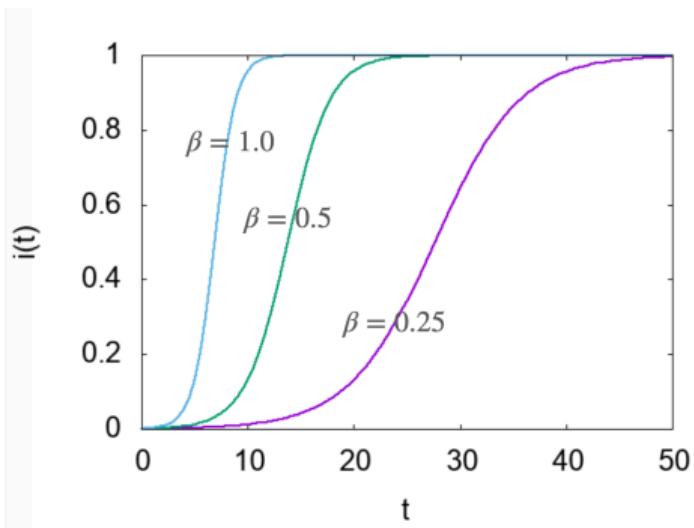
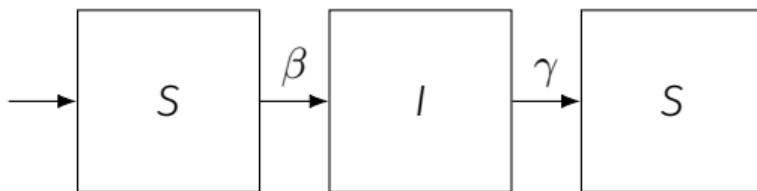


Figure 1: Plot of the solution of the SI model for different β .

SIS model

Basic models SIS

SIS model, where compartments are *Susceptible, Infected, Susceptible*. 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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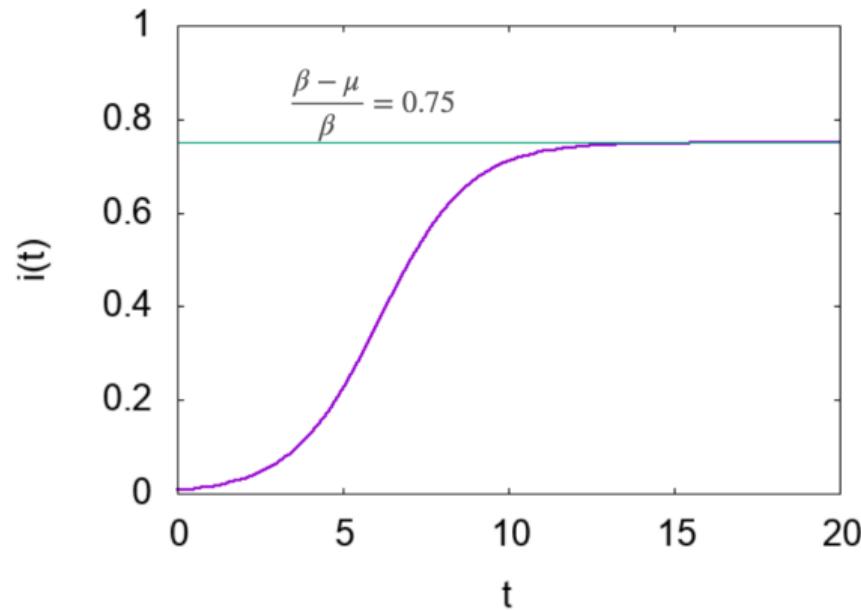
- This model is used for diseases that do not confer immunity.
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- Indeed, there are always **In contrast, S** individuals that can become infected and propagate disease,

Basic models SIS

- This model is used for diseases that do not confer immunity.
- "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 **In contrast, S** individuals that can become infected and propagate disease,
- While γ is the **recovery rate**.

Basic models SIS

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).



Basic models SIS

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).

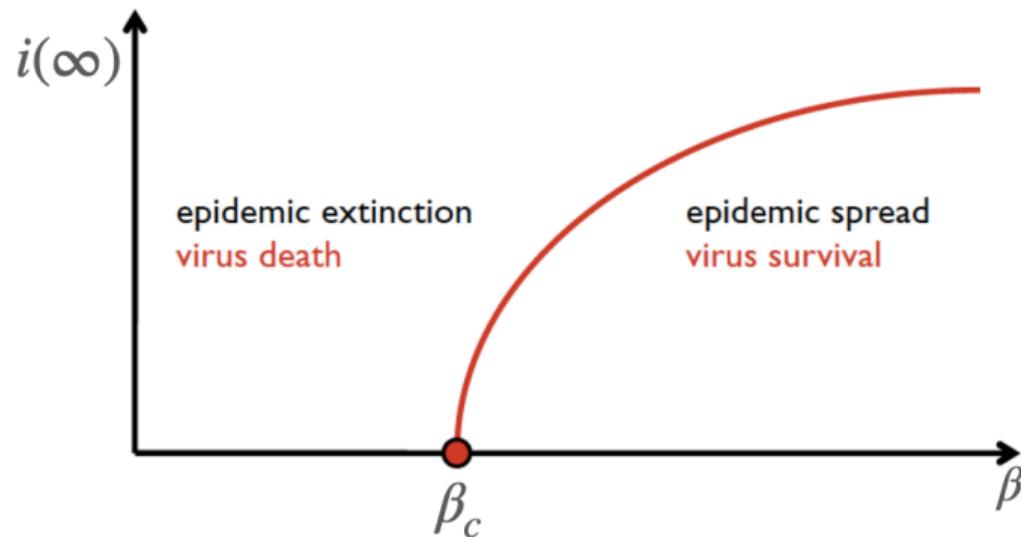


Figure 3: Epidemic diagram.

Basic models SIS

- ➊ Epidemic threshold is given by the condition under which we observe disease propagation.
- ➋ 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.
- ➌ Considering, for instance, the case of the SIS model, the β_c critical is such that it makes R_0 equal to 1:

$$\beta_c : \quad R_0 = \frac{\beta_c k}{\gamma} = 1 \quad (1)$$

Basic reproductive number, R_0

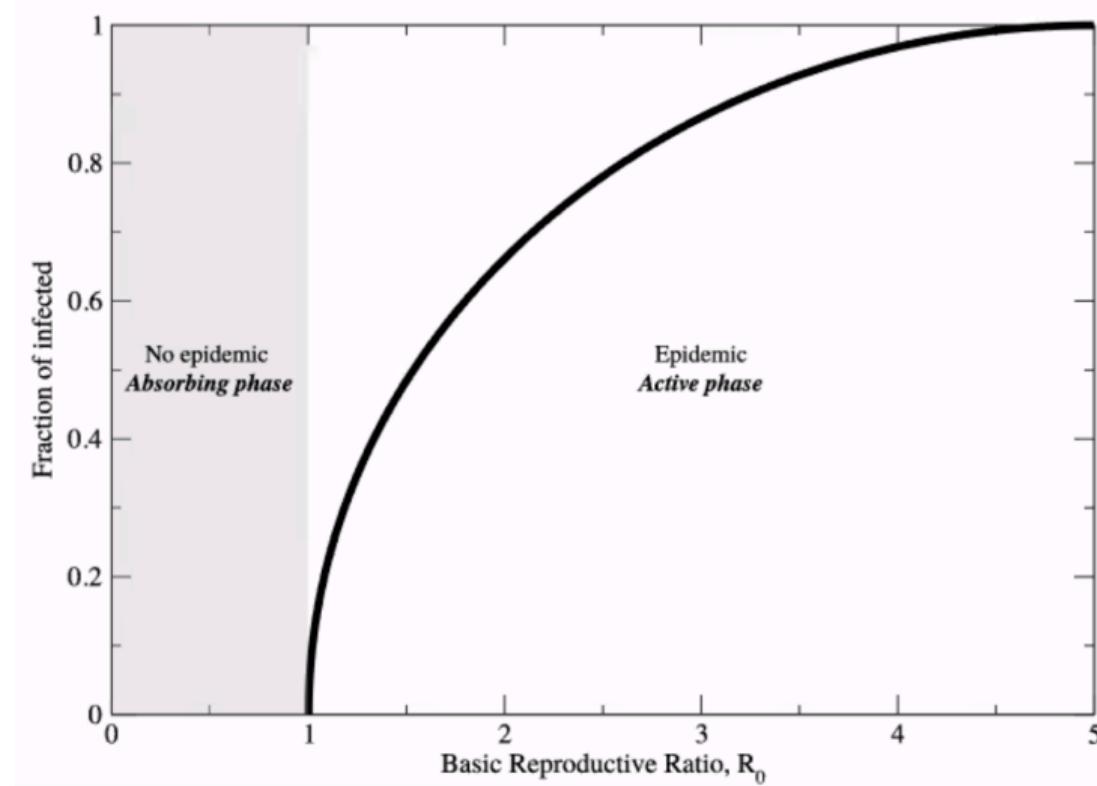
Expected number of secondary cases of disease produced directly by *an average* infectious individual entering an entirely susceptible population

$$R_0 > 1 \text{ Epidemic occurs} \quad (2)$$

$$R_0 = 1 \text{ Endemic} \quad (3)$$

$$R_0 < 1 \text{ No epidemic occurs} \quad (4)$$

Basic reproductive number



SIR model

Basic models SIR

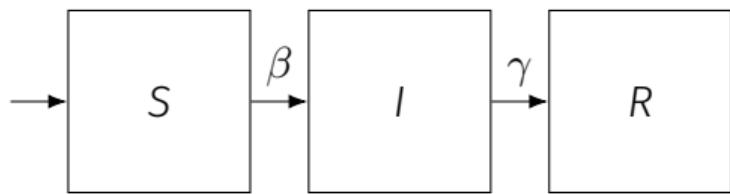
We now discuss the so called *SIR* model, whose compartments are *Susceptible*, *Infected* and *Recovered*.

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

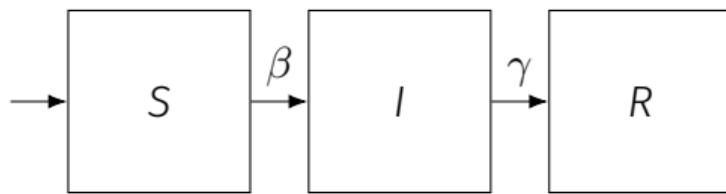
The transitions for this model are:



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

Basic models SIR

The transitions for this model are:



- Here we cannot have any endemic state, **why?**
- For a **large time**, all individuals will have been infected and recovered, so the disease will be spreading no more.

Basic models SIS and SIR

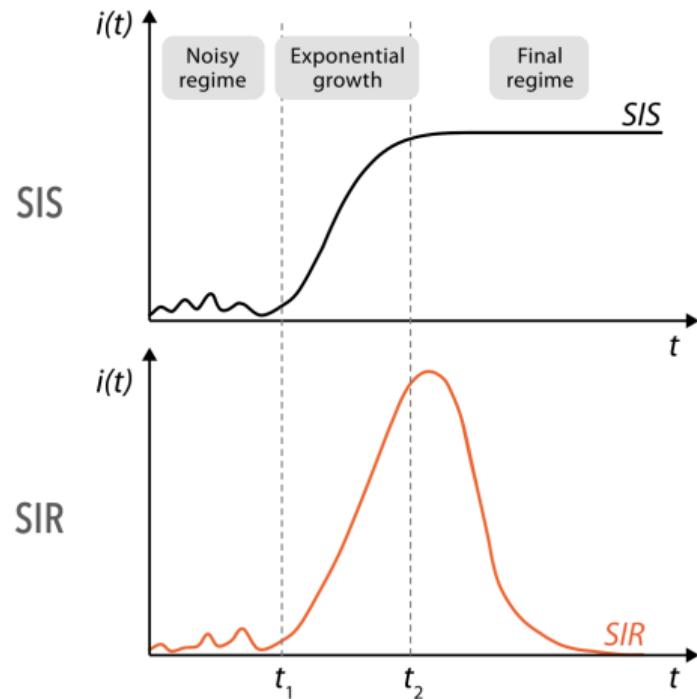


Figure 4: Epidemic regimes.

SIR: Compartment model as one example

- System of differential equations to simulate disease propagation

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

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

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

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

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- Where β represent the disease transmission rate
- Where γ describes the recovery rate
- Where λ describes infection rate defines a constant probability.

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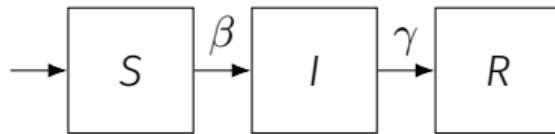
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SIR model (close population)

- Closed system/population: no births/deaths

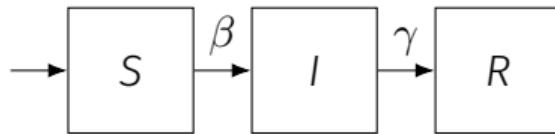
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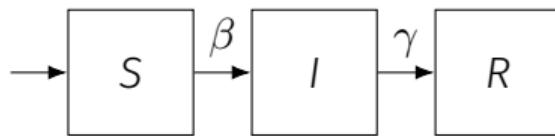
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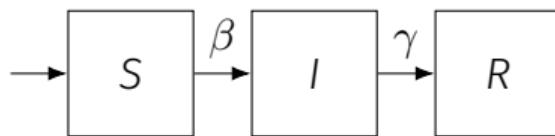


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- Fixed population size (deaths=births)

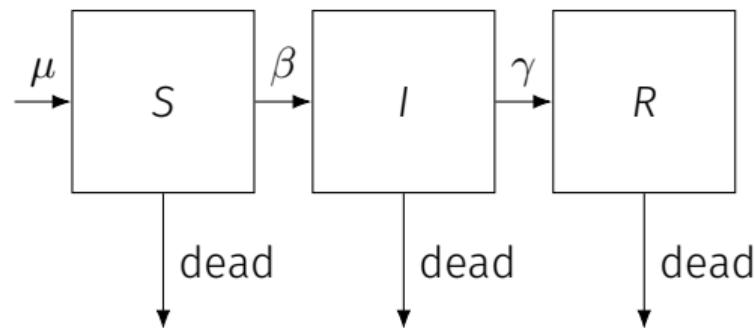
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SIR model (open population)

① Open population size (births)



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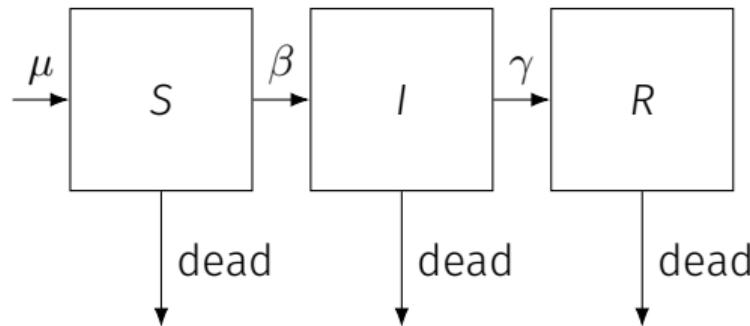
γ = *recovery rate*

μ = mortality or fertility 1/life expectancy

SIR model (open population)

① Open population size (births)

② Open population size (deaths)



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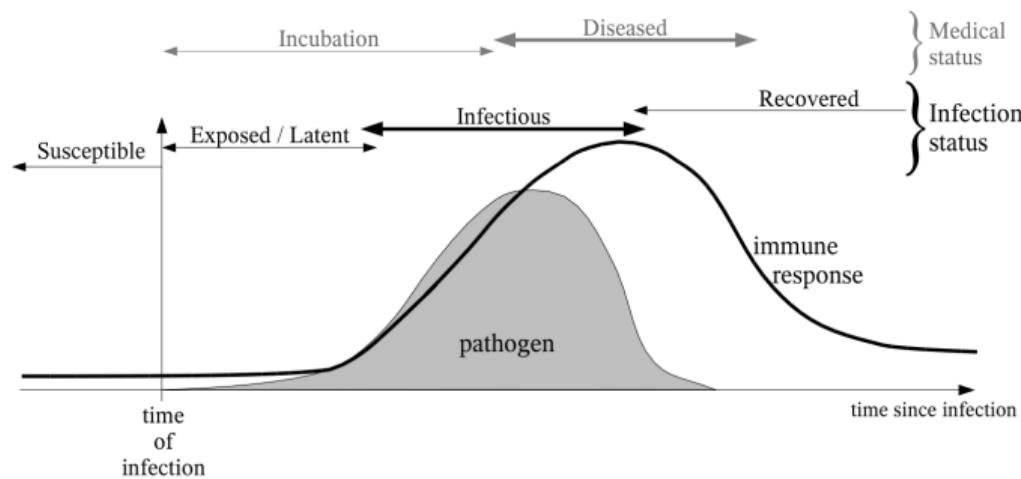
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Other model structures

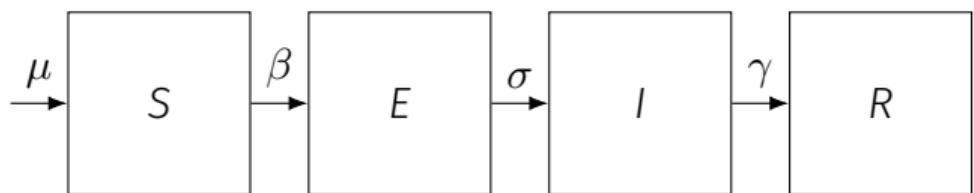
Different models vs type of the disease: for instance **SI**, **SIR**, **SIS**, **SEIR**, and so forth.

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**)



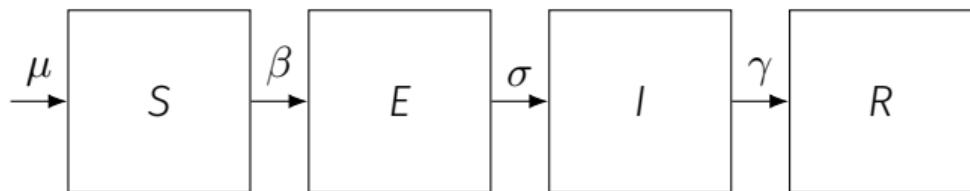
SEIR model

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



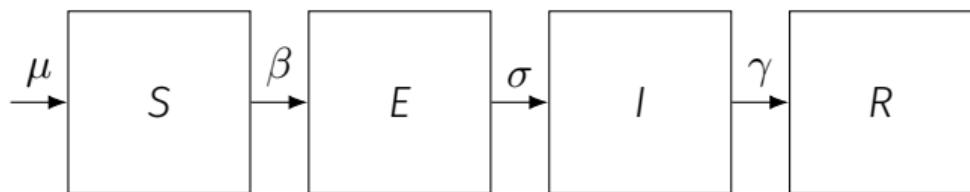
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SEIR model

- ➊ In reality individuals do not become instantaneously infectious, but there is a **latent period** which is the time between infection and becoming infectious.
- ➋ The pathogen replication takes time, i.e., viral load is too low to be able to transmit the infection.
- ➌ 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.



SEIR model

The SEIR can be the starting point for modeling realistic diseases: i.e. Covid-19 5

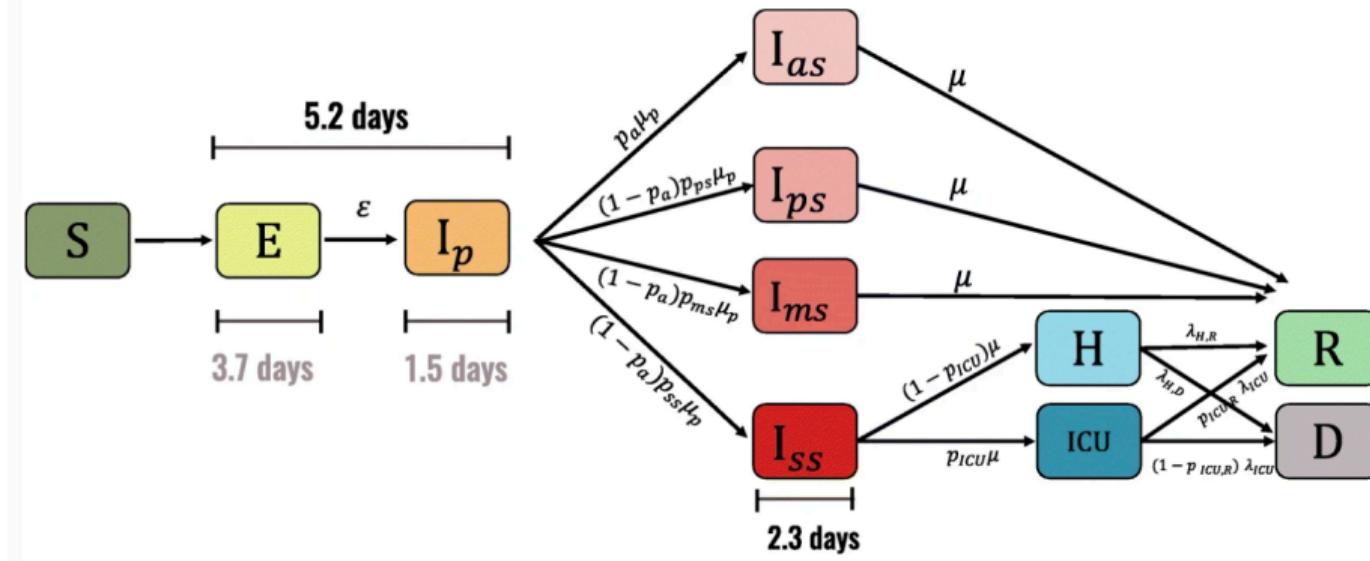
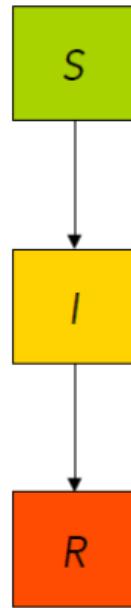
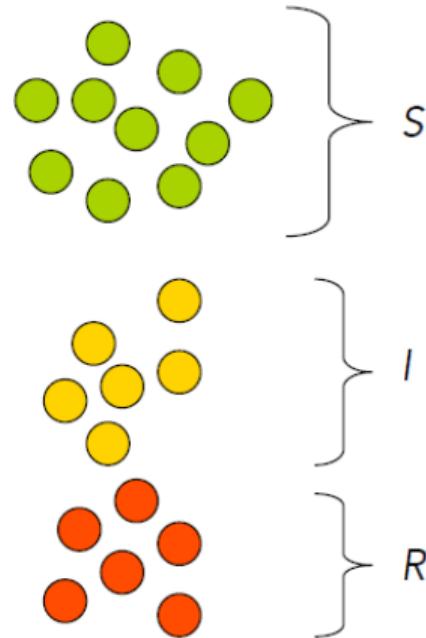


Figure 5: Model for Covid-19.

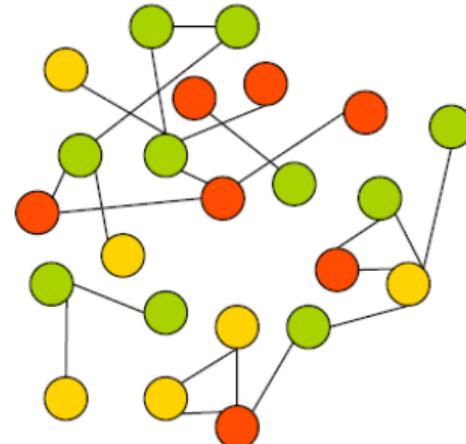
Can we include more realism?



Compartmental



Individual-based



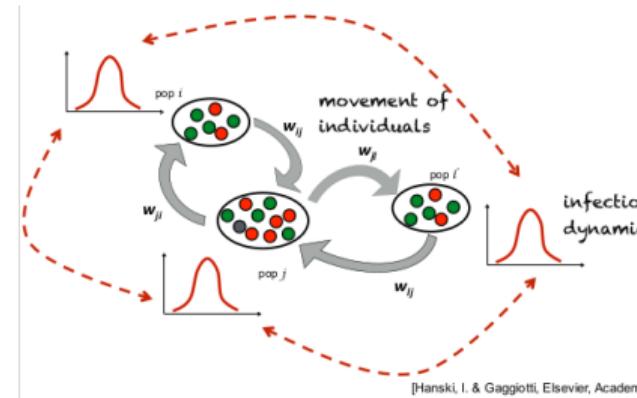
Network

Metapopulations

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]

Situations that often warrant other approaches

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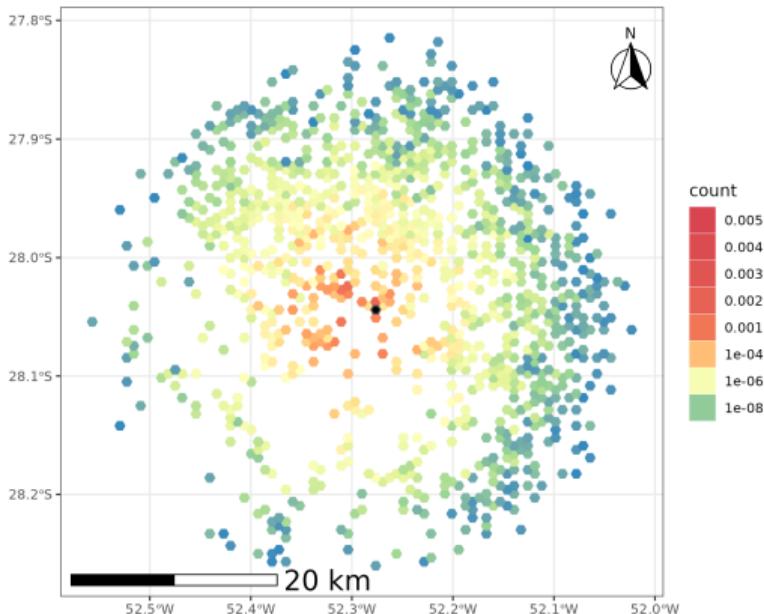
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- ③ Modeling complex interventions (e.g., targeting individuals via contact tracing).
- ④ Elimination of pathogens.
- ⑤ Emergence of new pathogens in populations.

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

Spatial spread



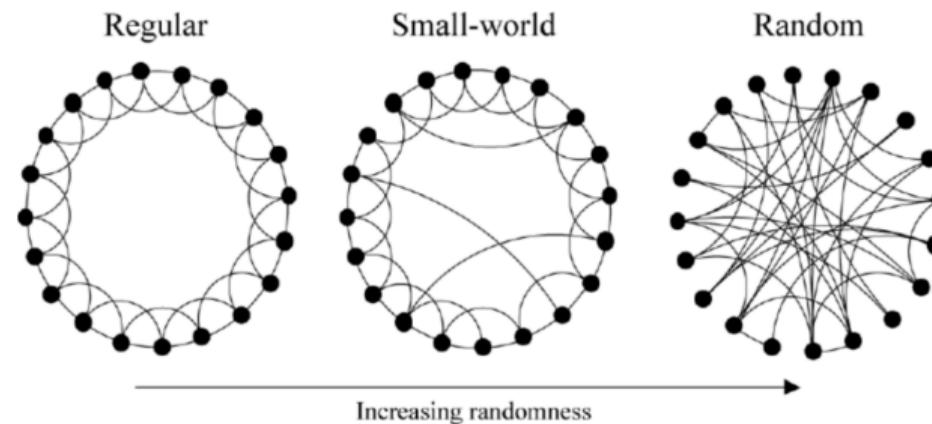
- Distance (Km)
- 1 km (prob. 0.012)
- 2 km (prob. 0.004)
- 3 km (prob. 0.002)
- ...40 km (prob. 4.56e-13)

Animal or vehicle movements== networks

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

Small-world = 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

- “Predictive” models.

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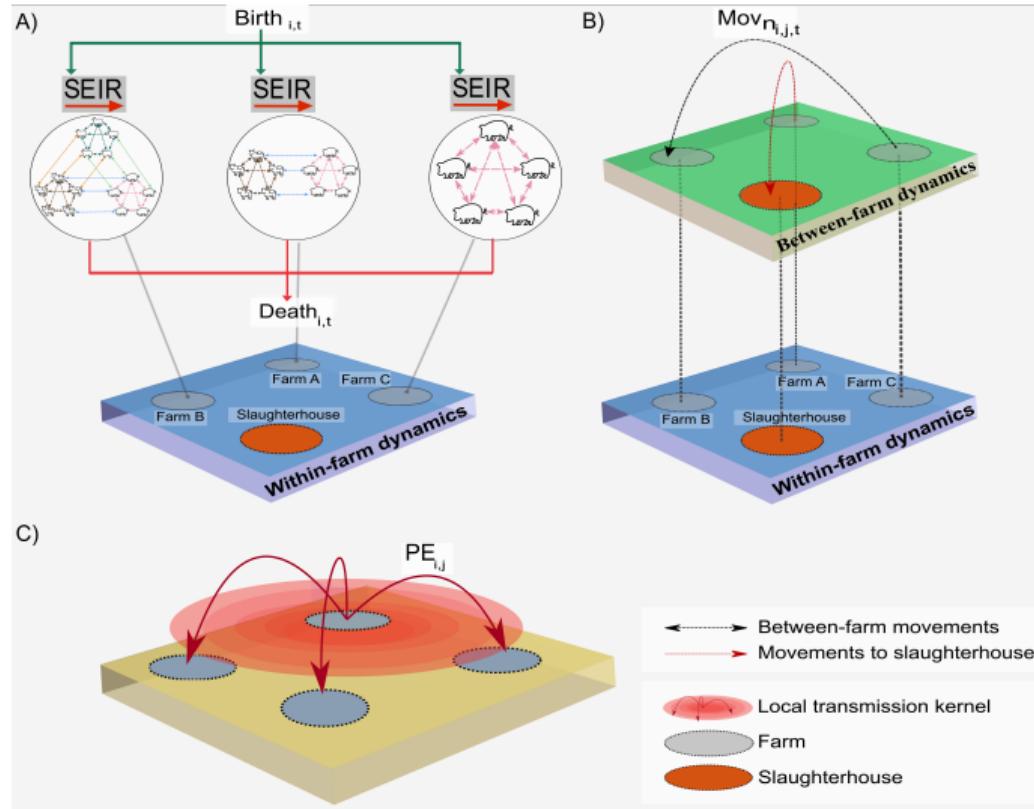
- “Predictive” models.
- Comparing the performance of alternative “realistic” interventions.

Models to be used by policy makers

For policy-making, more complex models are sometimes required

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

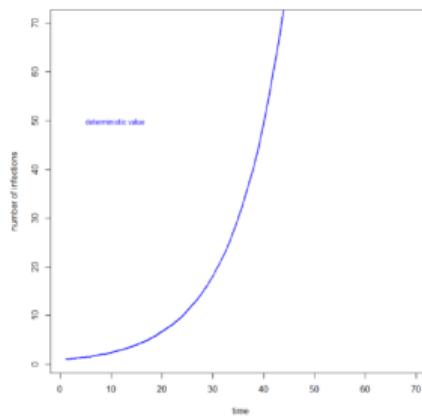
MHASpread: A multi-host Animal Spread Stochastic Multilevel Model



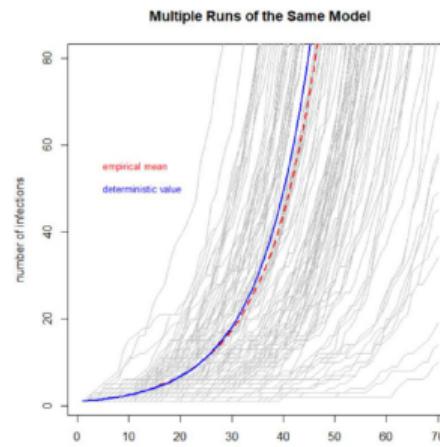
Transitions between health status

Deterministic vs stochastic

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



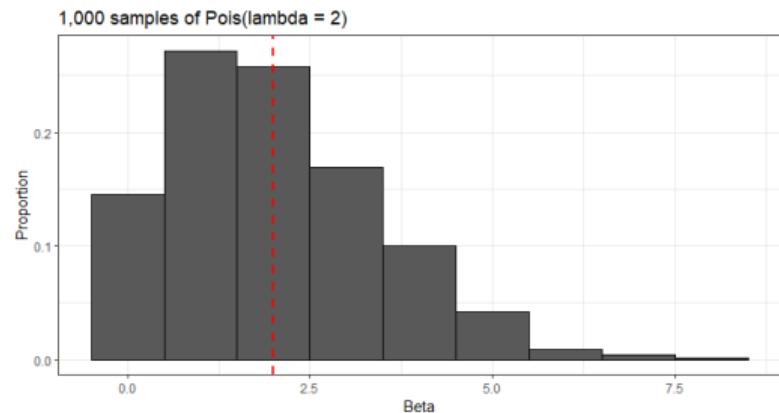
- Stochastic: probability that an element transitions between states.
 - Uses a draw from a probability distribution to govern flows.



What does stochastic mean?

In general: random, or variable

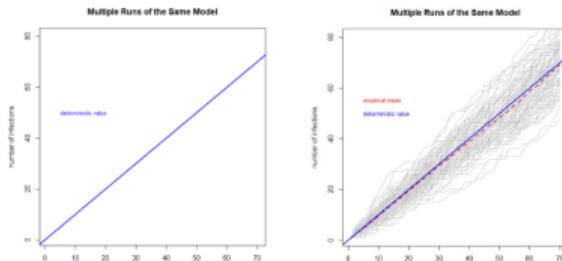
- In particular:
 - A random draw.
 - From the possible range of outcome values.
 - With a probability assigned to each value.
- Typically, the probabilities are summarized by:
 - A probability density function (PDF).
 - Defined by one or more parameters.
 - e.g., binomial, Poisson, normal, etc.



Impact of stochasticity on epidemic dynamics?

Using the Poisson distribution:

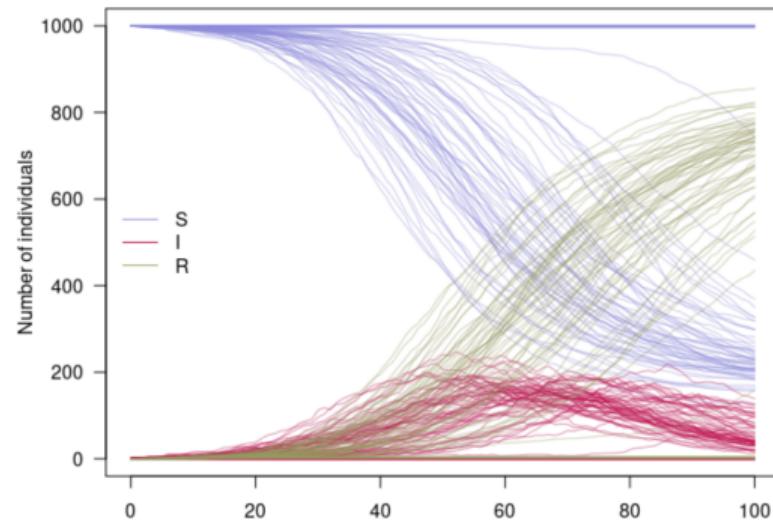
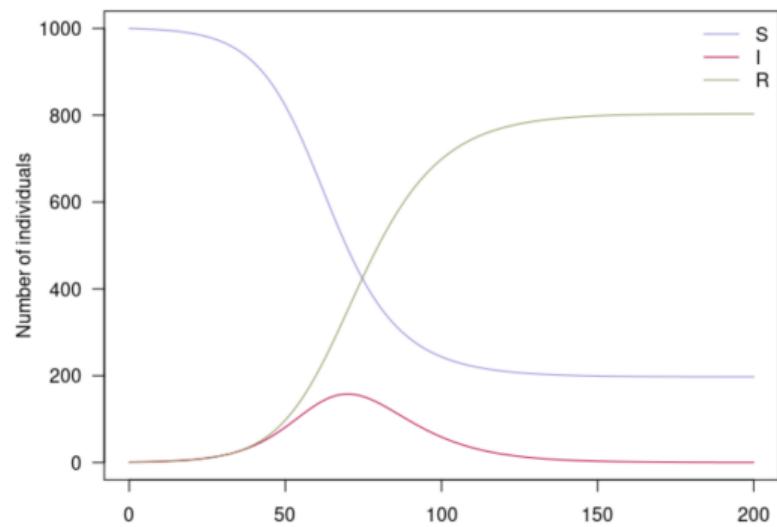
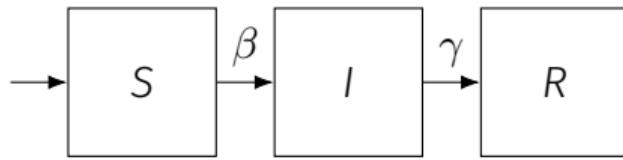
- A deterministic **lambda = 1** as expected new case per day.
- With the stochastic model, we set also **lambda = 1** the average number of new cases.
 - Variance in new cases each day is:
 - Standard deviation = $\sqrt{\text{lambda}}$



Key idea: Interpreting variability

- Stochastic variation can be large
 - At the beginning of an epidemic.
 - Or in small populations.

Key idea: Interpreting variability



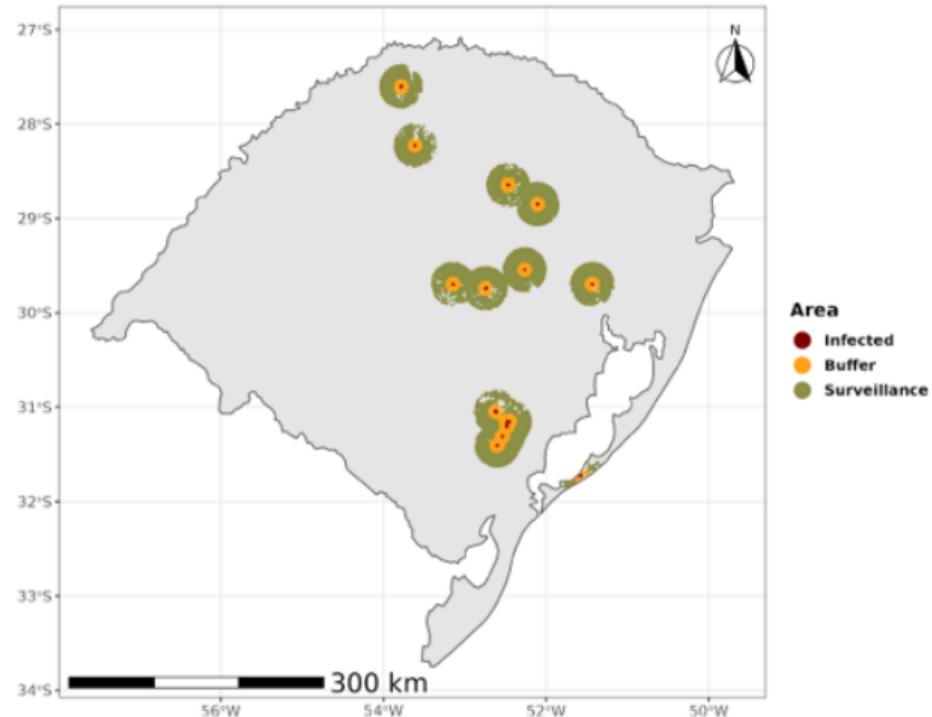
Be careful not to over-interpret!

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.

Summary

- 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.