Model fitting and inference for infectious disease dynamics

Centre for the Mathematical Modelling of Infectious Diseases
London School of Hygiene & Tropical Medicine

Outline

Introduction

Linking models to data

Bayesian inference

1. Introduction

Model fitting and inference for infectious disease dynamics

Model

A simplified description, especially a mathematical one, of a system or process, to assist calculations and predictions

Oxford English Dictionary

Mathematical model

Takes *parameters* and produces *output*
(using some set of rules / equations)

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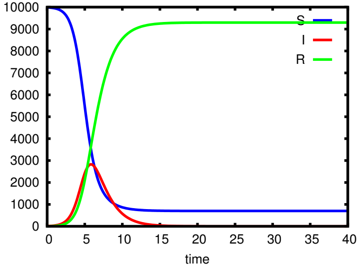
SIR-type models

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

$$\frac{dS}{dt} = -\beta I \frac{S}{N}$$
$$\frac{dI}{dt} = \beta I \frac{S}{N} - \gamma I$$
$$\frac{dR}{dt} = \gamma I$$



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SIR-type models

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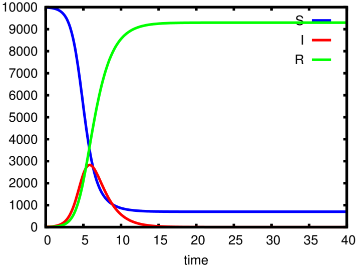

Mechanistic models

description vs mechanism

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Parameter estimation

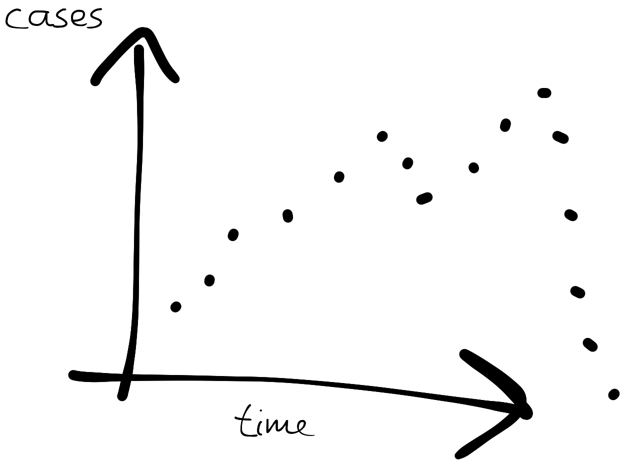
Given a model, what are the parameter combinations that best fit the data (in whichever way)

Why are we doing this?

- Learn something about the system
  - test a scientific hypothesis
    - e.g., why did the UK H1N1 epidemic wane in summer 2009? (Dureau et al., 2013)
  - estimate parameters
    - e.g. which fraction of infections with cholera in Bangladesh are asymptomatic? (King et al., 2008)
  - sometimes in real time
- Validate the model
  - especially: for prediction

Model fitting and inference for infectious disease dynamics

What do we mean by “best fit the data”?



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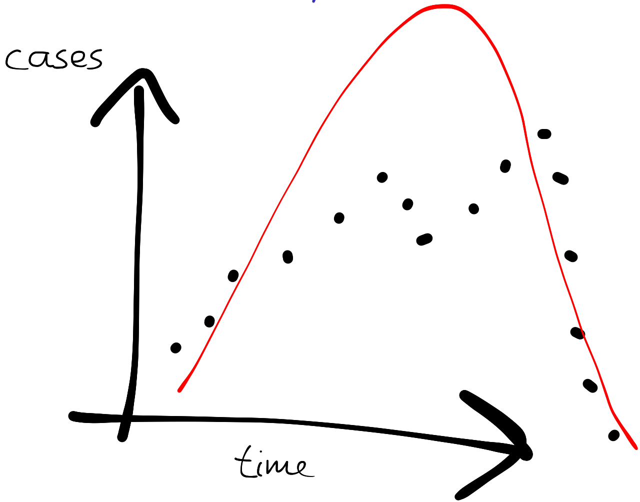

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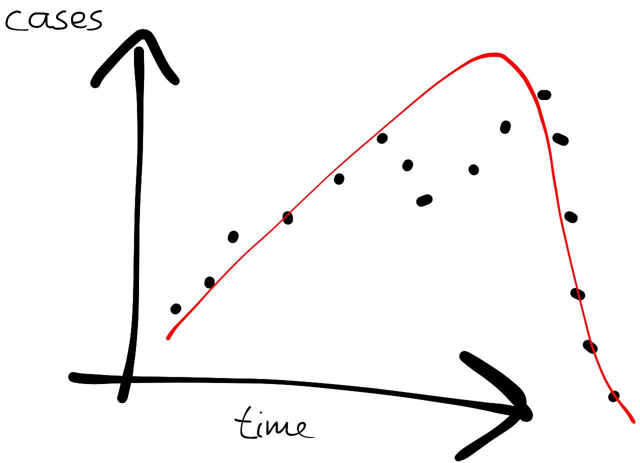

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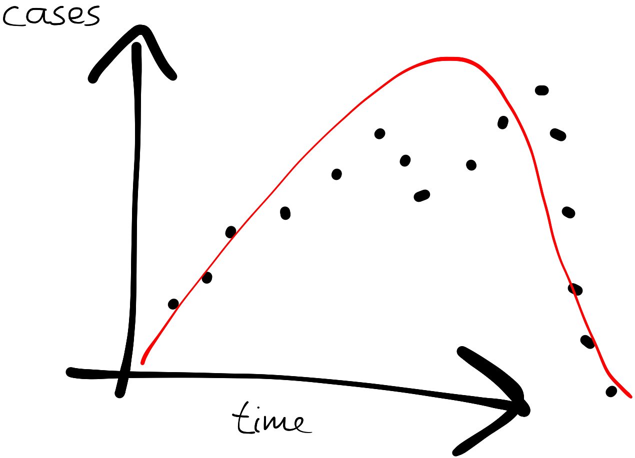

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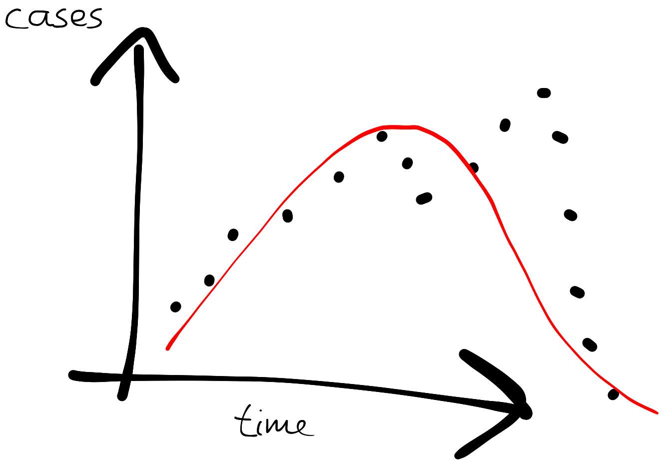
What do we mean by "best fit the data"?



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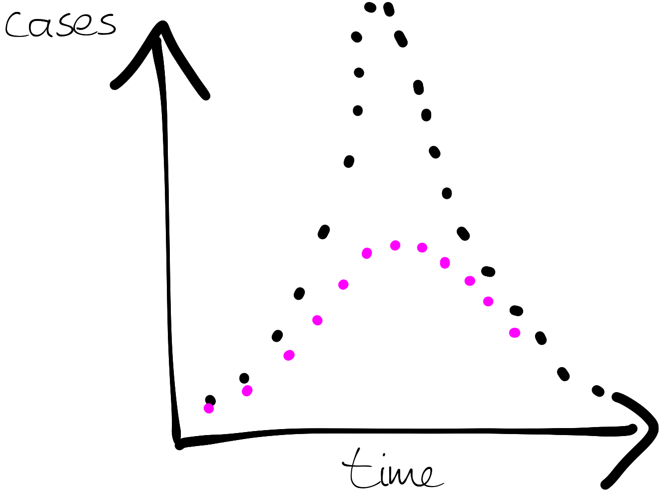
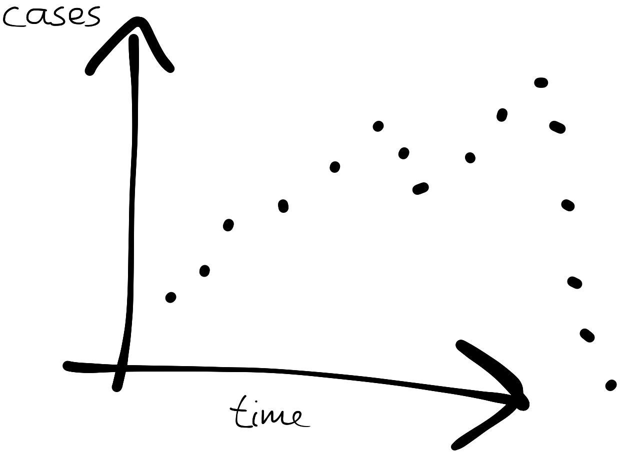
State estimation

Given what we observe, what is the state of the sytem?



Model selection

Given a set of potential models, how do we decide which is the right one?



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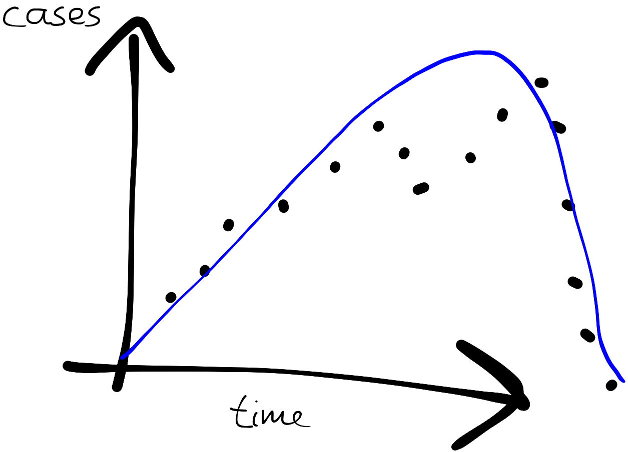

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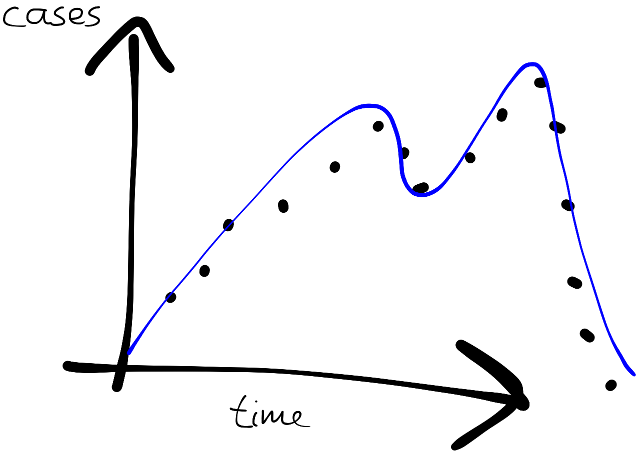

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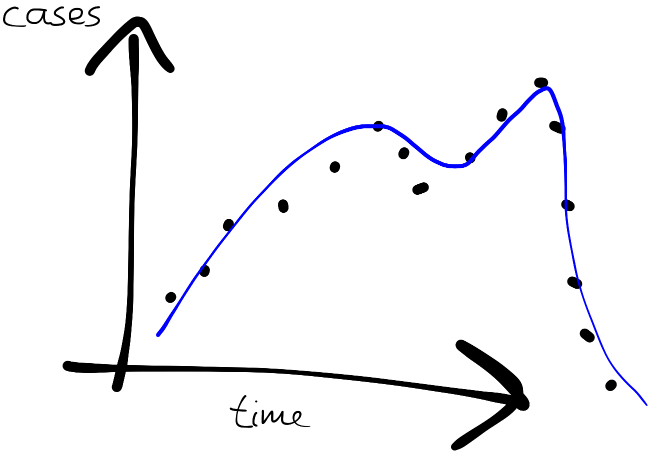

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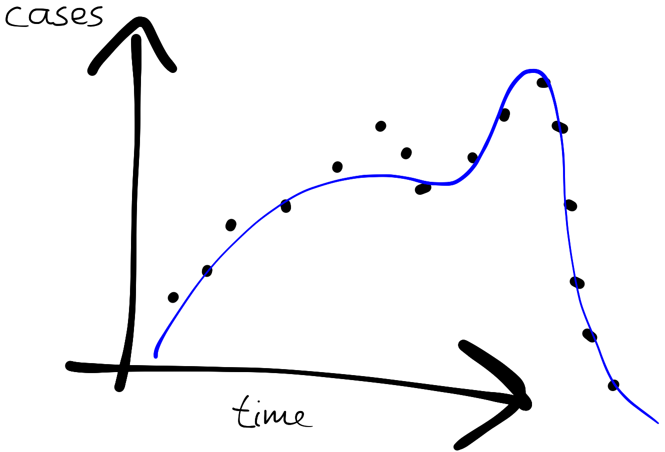
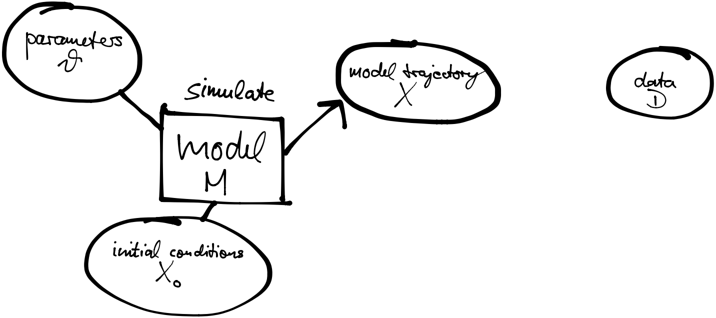
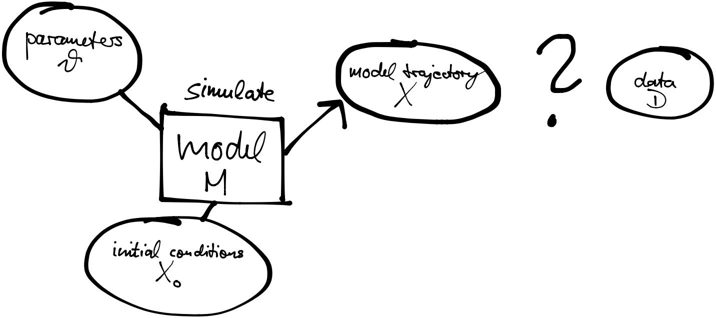


2. Linking models to data


model
M
data
D


parameters
ϑ
simulate
Model
M
model trajectory
X
data
D
initial conditions
X_0


parameters
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model trajectory
X
?
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D

Assessing the “closeness” of model output and data

- eyeballing
- absolute distance
- squared distance

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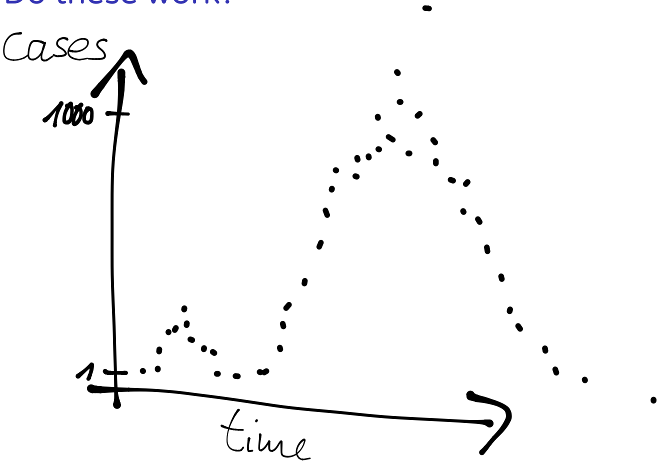
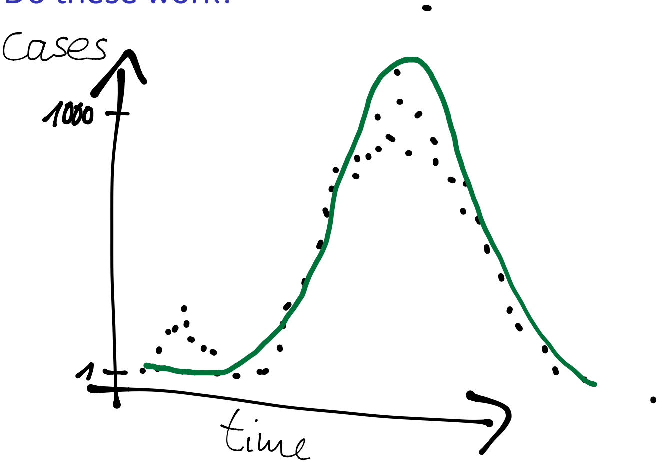
Do these work?



Assessing the "closeness" of model output and data

- eyeballing
- absolute distance
- squared distance

Do these work?



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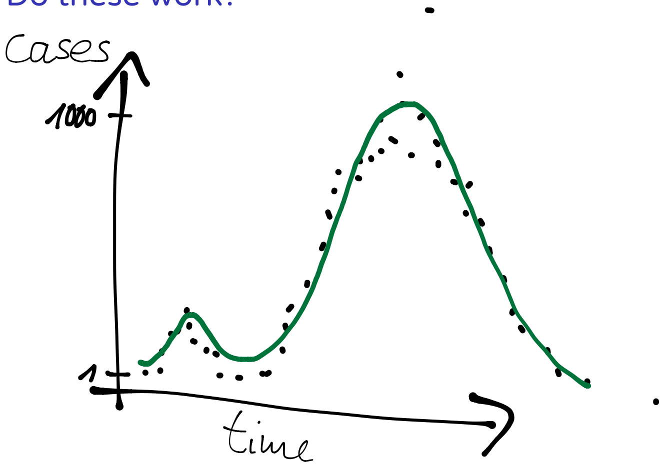


Probabilistic formulation

- Often we know something about how the data were taken $\rightarrow$ observations introduce uncertainty
- We can express the uncertainty in observing the process as a probability

$$p(\text{data}|\text{underlying process})$$

- By including this in our model, we get

$$p(\text{data}|\text{model output})$$

Interlude: probabilities I

Probability theory is nothing but common sense reduced to calculation.

Laplace, 1812

- If A is a random variable, we write

$$p(A = a)$$

for the probability that A takes value a.

- We often write

$$p(A = a) = p(a)$$

- Example: The probability that Andy Murray wins Wimbledon this year

$$p(\mathrm{T} = \mathrm{Andy}) = p(\mathrm{Andy})$$

- Normalisation

$$\sum_a p(a) = 1$$

Interlude: probabilities II

- If A and B are random variables, we write

$$p(A = a, B = b) = p(a, b)$$

  for the joint probability that A takes value a and B takes value b

- Example: The probability that Andy Murray wins Wimbledon and it is sunny final day

$$p(\mathrm{T} = \mathrm{Andy}, \mathrm{W} = \mathrm{sunny}) = p(\mathrm{Andy}, \mathrm{sunny})$$

- We can obtain a marginal probability from joint probabilities by summing

$$p(a) = \sum_b p(a, b)$$

Interlude: probabilities III

- The conditional probability of getting outcome a from random variable A, given that the outcome of random variable B was b, is written as

$$p(A = a|B = b) = p(a|b)$$

- Example: the probability that Andy Murray wins Wimbledon, given that it is sunny on final day

$$p(\,T = \text{Andy}|\,W = \text{sunny}) = p(\text{Andy}|\text{sunny})$$

- Conditional probabilities are related to joint probabilities as

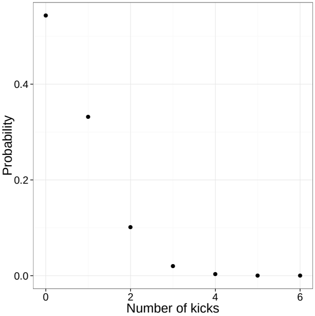
$$p(a|b) = \frac{p(a, b)}{p(b)}$$

- We can combine conditional probabilities in the chain rule

$$p(a, b, c) = p(a|b, c)p(b|c)p(c)$$

Probability distributions (discrete)

- E.g., how many people die of horse kicks if there are 0.61 kicks per year
- Described by the Poisson distribution



Two directions

1. Evaluate the probability
2. Randomly sample

Evaluating under the (Poisson) probability distribution

- E.g., how many people die of horse kicks if there are 0.61 kicks per year
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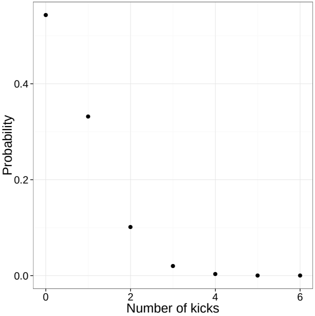


Evaluate

What is the probability of 2 deaths in a year?

```r
dpois(x = 2,
      lambda = 0.61)
```

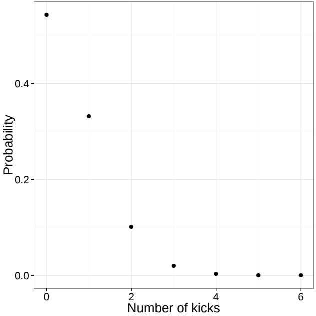
```
[1] 0.1010904
```

Two directions

1. Evaluate the probability
2. Randomly sample

Generating a random sample (Poisson distribution)

- E.g., how many people die of horse kicks if there are 0.61 kicks per year
- Described by the Poisson distribution



Sample

Give me a random sample from the probability distribution

```
rpois(n = 1,
      lambda = 0.61)
```

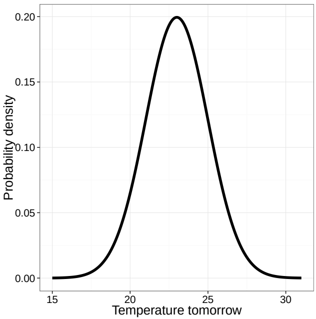
```
[1] 0
```

Two directions

1. Evaluate the probability
2. Randomly sample

Probability distributions (continuous)

- Extension of probabilities to continuous variables
- E.g., the temperature in London tomorrow



Normalisation:

$$\int p(a)\,da = 1$$

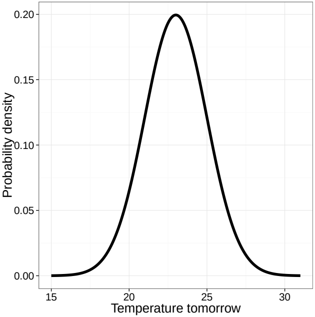
Marginal probabilities:

$$p(a) = \int p(a, b)\,db$$

Two directions

1. Evaluate the probability (density)
2. Randomly sample

Evaluating under the (normal) probability distribution



Evaluate

What is the probability density of $30^\circ C$ tomorrow?

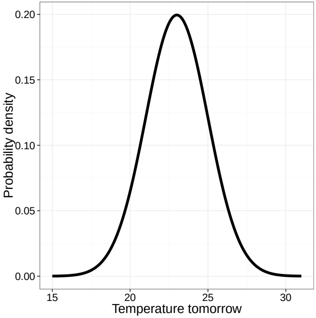
```
dnorm(x = 30,
      mean = 23,
      sd = 2)
```

```
[1] 0.0004363413
```

Two directions

1. Evaluate the probability (density)
2. Randomly sample

Generating a random sample (normal distribution)



Sample

Give me a random sample from the probability distribution

```
rnorm(n = 1,
      mean = 23,
      sd = 2)
```

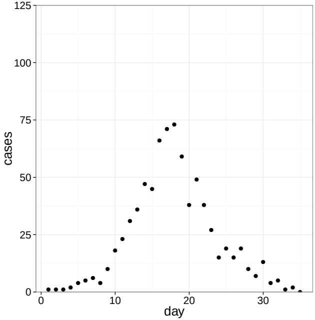
```
[1] 21.82921
```

Two directions

1. Evaluate the probability (density)
2. Randomly sample

Example: observation uncertainty

SIR model, assume that cases are detected with independent reporting probability $\rho = 0.5$.



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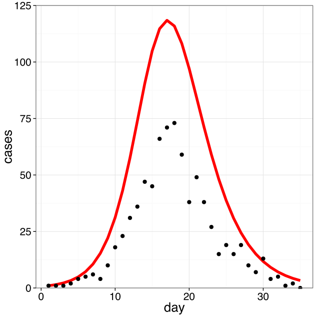

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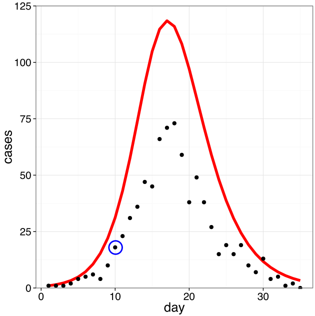

At time 10, 18 cases observed.

Example: observation uncertainty

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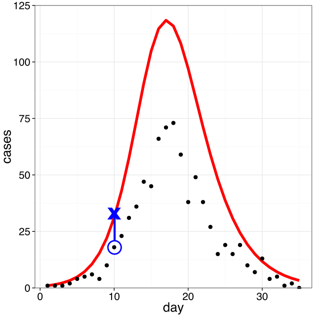

At time 10, 18 cases observed, 31.1 cases in the model.

Example: observation uncertainty

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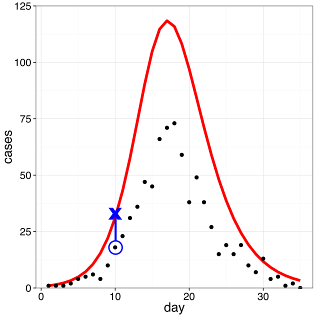

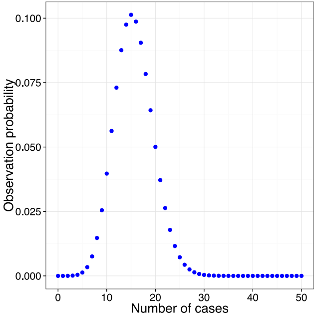

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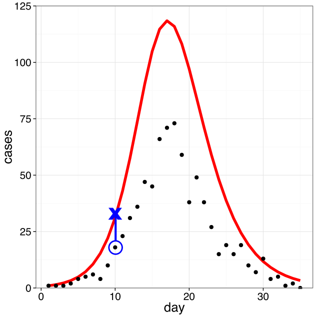

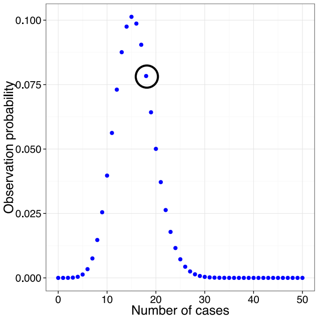

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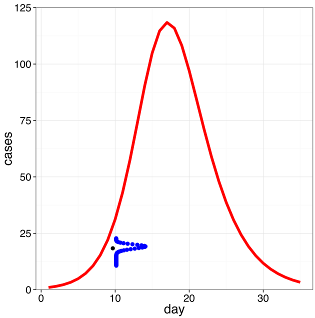
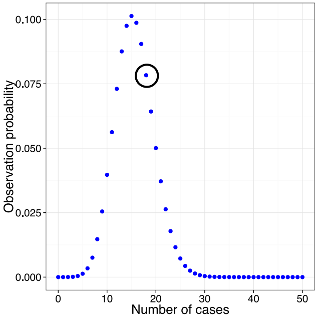


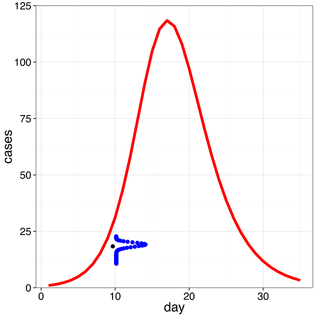


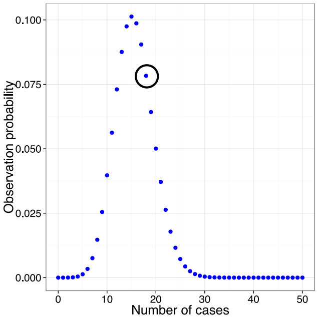
At time 10, 18 cases observed, 31.1 cases in the model.

$$p(\text{data point } 10|\theta) = 0.078$$

Example: observation uncertainty

SIR model, assume that cases are detected with independent reporting probability $\rho = 0.5$.





At time 10, 18 cases observed, 31.1 cases in the model.

$$p(\text{data point } 10|\theta) = 0.078$$

Multiply across the data to get the full trajectory likelihood.

$$p(\text{data}|\theta) = \prod_i p(\text{data point } i|\theta)$$

Example: observation uncertainty

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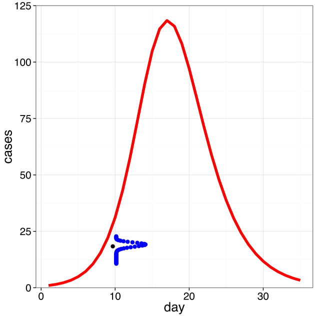
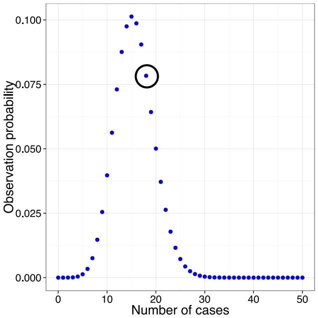


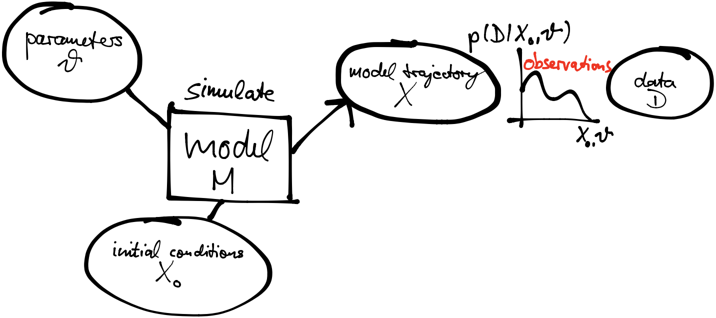


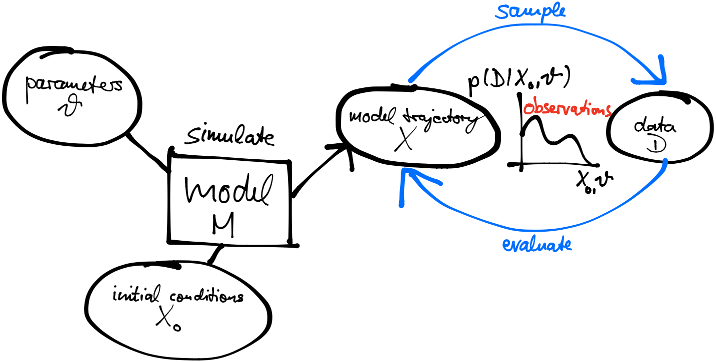
At time 10, 18 cases observed, 31.1 cases in the model.

$$p(\text{data point } 10|\theta) = 0.078$$

Sum across the data to get the full trajectory log-likelihood.

$$\log(p(\text{data}|\theta)) = \sum_i \log(p(\text{data point } i|\theta))$$


parameters
ϑ
simulate
model
M
initial conditions
X₀
model trajectory
X
p(D|X₀,ϑ)
observations
X₀,ϑ
data
D



parameters ϑ
simulate
Model M
initial conditions X_0
model trajectory X
sample
$p(D|X_0,\vartheta)$
observations
X_0,ϑ
data D
evaluate

The likelihood

- We have argued that it makes sense to write

$$p(\text{data}|\text{model output})$$

- For a given model the output depends on the parameters θ. So we can write

$$p(\text{data}|\theta)$$

  (note: θ encompasses all parameters; e.g., $\theta = \{\beta, \gamma\}$)
- This is called the likelihood of parameters θ
- likelihoods can span a wide range of orders of magnitude, which can lead to numerical problems

  Solution: take the logarithm to get the log-likelihood

$$\log p(\text{data}|\theta) = \sum_i \log p(\text{data point } i|\theta)$$

Frequentist vs Bayesian inference

Frequentist inference:

- there are ***true*** parameters in the world, the uncertainty comes from the data
- this is encoded in the likelihood: $p(\mathrm{data}|\theta)$
- in inference, I try to estimate these parameters
- probabilities express outcomes of repeated experiments

Frequentist vs Bayesian inference

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- there are ***true*** parameters in the world, the uncertainty comes from the data
- this is encoded in the likelihood: $p(\mathrm{data}|\theta)$
- in inference, I try to estimate these parameters
- probabilities express outcomes of repeated experiments

Bayesian inference

- there are no true parameters, the ***data*** are true; uncertainty is in parameters / hypotheses
- this is encoded in the posterior: $p(\theta|\mathrm{data})$
- probabilities express my belief in a given parameter
- the posterior is interpreted as the ***probability distribution*** of a ***random variable*** θ

3. Bayesian inference

Bayes' rule

- We said that in Bayesian inference, we need to calculate $p(\theta|\text{data})$. Applying the rule of conditional probabilities, we can write this as

$$p(\theta|\text{data}) = \frac{p(\text{data}|\theta)p(\theta)}{p(\text{data})}$$

- $p(\theta|\text{data})$ is the ***posterior***
- $p(\text{data}|\theta)$ is the ***likelihood***
- $p(\theta)$ is the ***prior***
- $p(\text{data})$ is a ***normalisation constant***
- In words,

$$(\text{posterior}) \propto (\text{normalised likelihood}) \times (\text{prior})$$

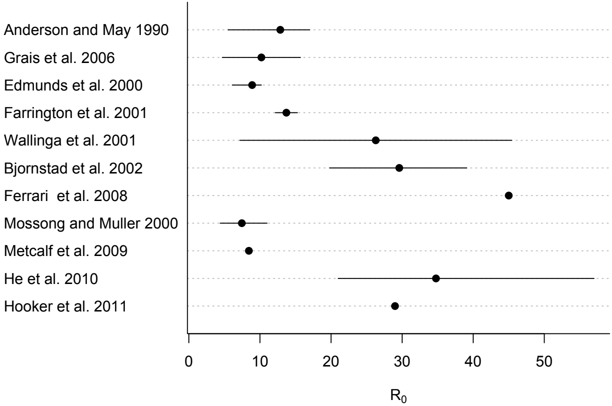
Prior probabilities

- $p(\theta)$ quantifies our degree of belief via a probability distribution before confronting the model with data:

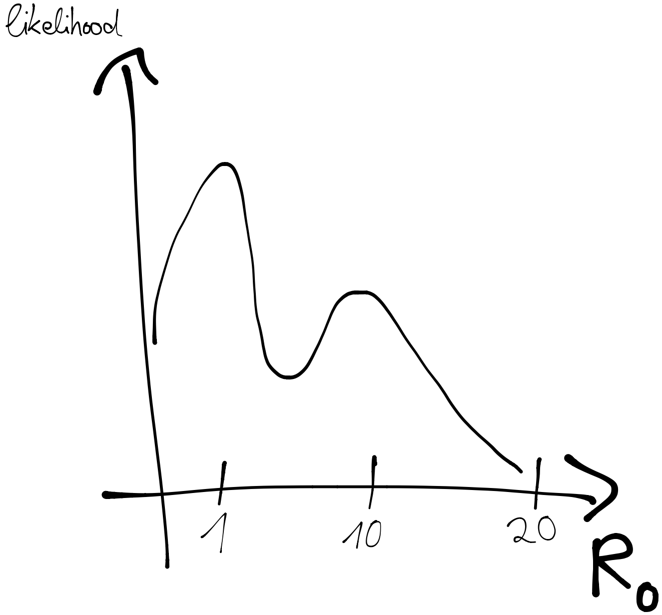
$$p(\theta)$$

  E.g., from previous measurements, literature, experts etc.

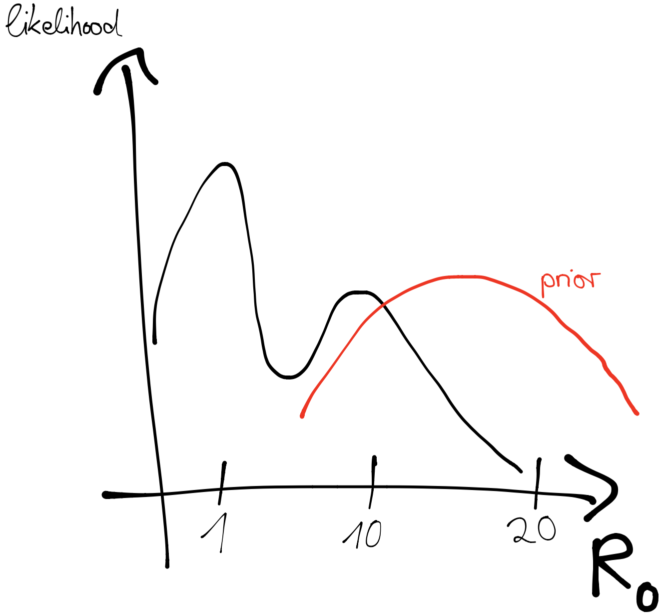
- Example: R_0 of measles



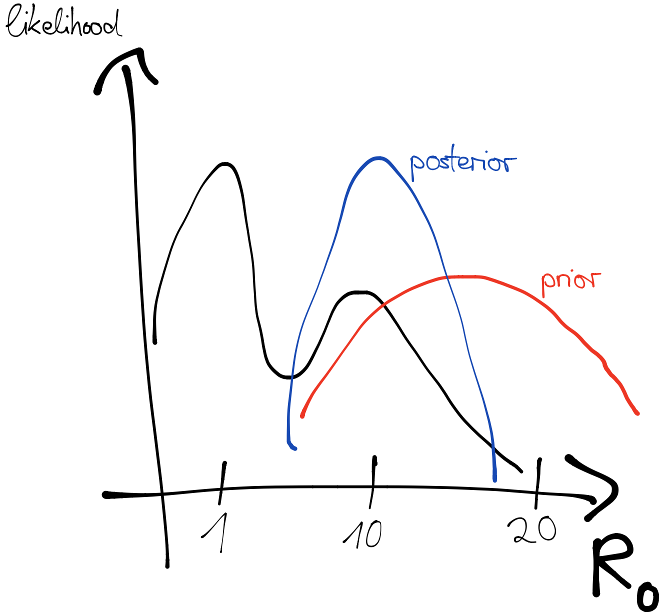
Example: estimating R_0 of measles



Example: prior for estimating R_0 of measles



Example: posterior for estimating R_0 of measles



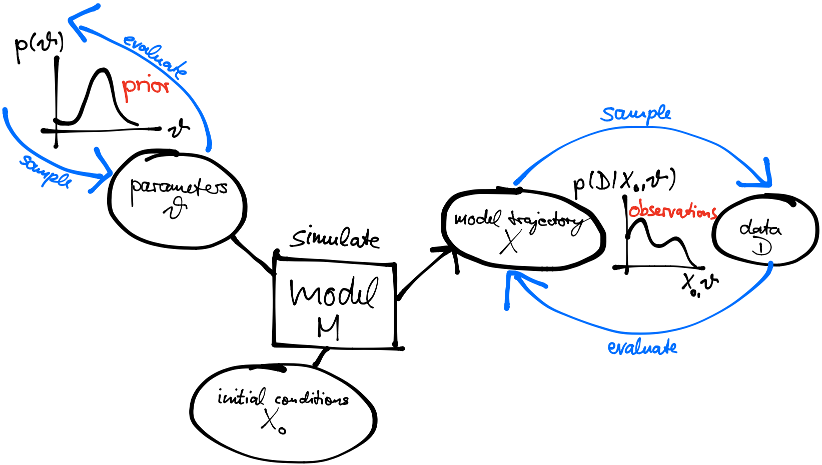
Sampling from the posterior

Bayesian statistics

Parameter(s) θ are interpreted as a ***random*** variable, distributed according to the posterior.

$$p(\theta|\mathrm{data}) \propto p(\mathrm{data}|\theta)p(\theta)$$

We want to generate samples of θ from this distribution.



p(ϑ)
prior
ϑ
evaluate
sample
parameters ϑ
simulate
Model M
initial conditions X0
model trajectory X
p(D|X0,ϑ)
observations
X0,ϑ
data D
sample
evaluate

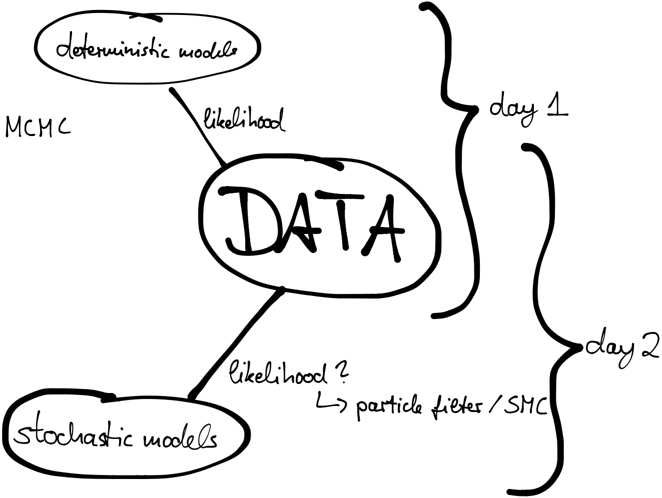
deterministic models

MCMC

likelihood

DATA

day 1


deterministic models
MCMC
likelihood
DATA
likelihood ?
↳ particle filter / SMC
stochastic models
day 1
day 2

deterministic models

likelihood

MCMC

DATA

day 1

day 2/3

MCMC

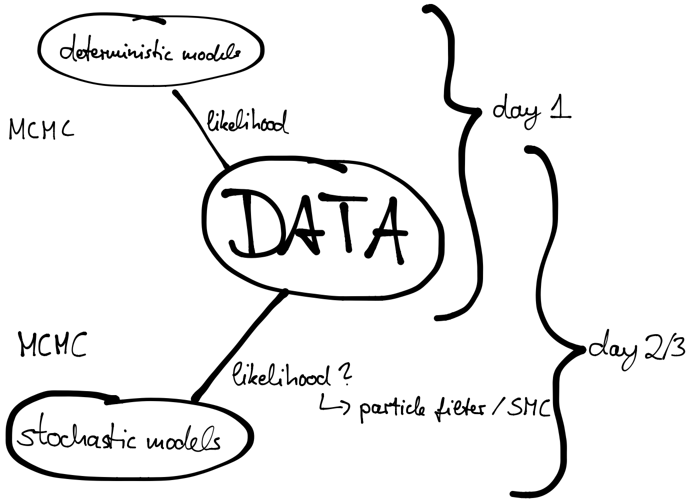
likelihood ?

↳ particle filter / SMC

stochastic models

day 3 (afternoon):

- discussion / open session



day 3 (afternoon):
- discussion / open session

day 4:
- other methods
- available software
- final discussion