

Continuous-time stochastic models

Modern Techniques in Modelling

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Introduction

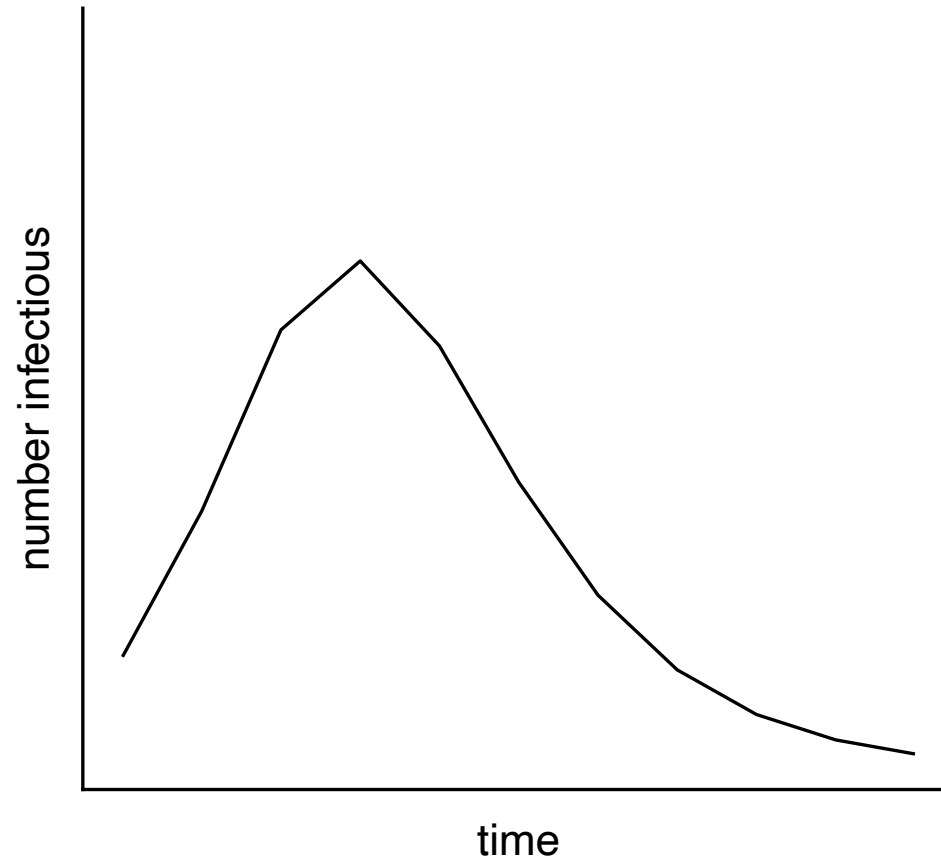
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- Introduce continuous-time stochastic models
- Implement Gillespie algorithm and analyse stochastic model output
- Implement a stochastic model with the `adaptivetau` package
- Discussion and concluding remarks

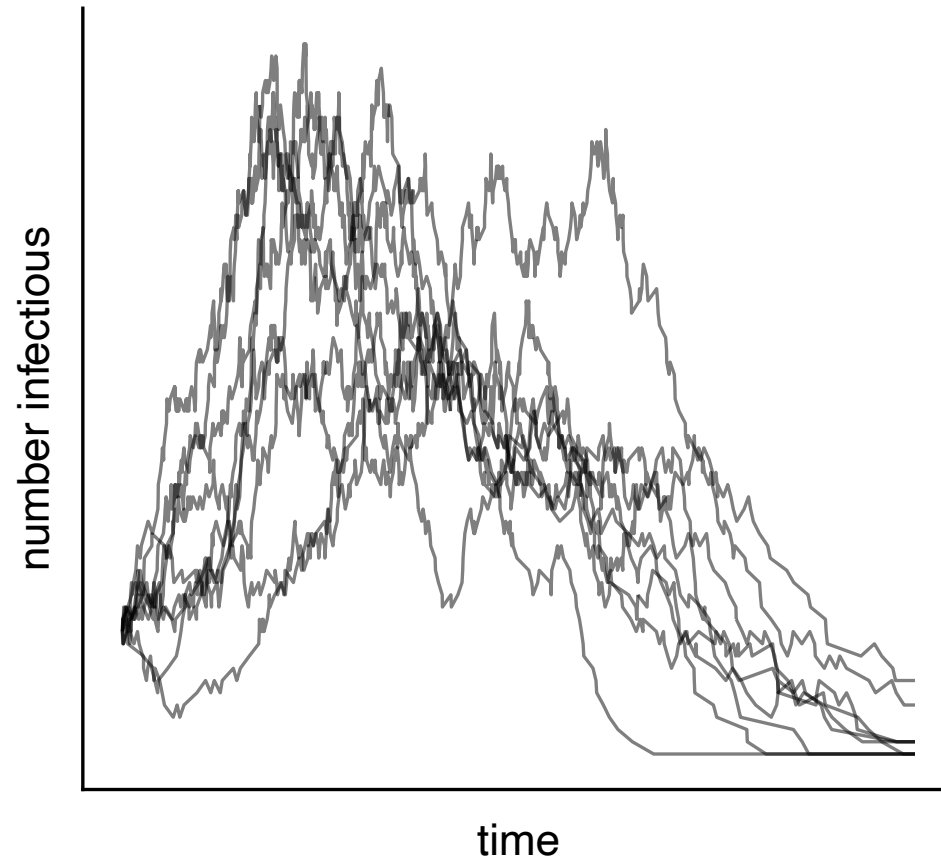
- Introduce continuous-time stochastic models
(~20 minutes)
- Implement Gillespie algorithm and analyse stochastic model output
(~60 minutes)
- Implement a stochastic model with the `adaptivetau` package
(~20 minutes)
- Discussion and concluding remarks
(~20 minutes)

Deterministic models



One set of parameters -> one trajectory

Stochastic models



One set of parameters \rightarrow many trajectories

Types of model

- discrete vs continuous *time*
- discrete vs continuous *compartments*
- deterministic vs stochastic *dynamics*

Example 1: difference equations

- discrete vs continuous *time*
- discrete vs continuous *compartments*
- deterministic vs stochastic *dynamics*

$$\begin{aligned}S(t + 1) &= S(t) - \beta S(t)I(t) \\I(t + 1) &= I(t) + \beta S(t)I(t) - \gamma I(t) \\R(t + 1) &= R(t) + \gamma I(t)\end{aligned}$$

Discrete-time deterministic models

- **discrete** vs continuous *time*
- discrete vs **continuous** *compartments*
- **deterministic** vs stochastic *dynamics*

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Example 2: ODEs

- discrete vs continuous *time*
- discrete vs continuous *compartments*
- deterministic vs stochastic *dynamics*

$$\begin{aligned}\frac{dS}{dt} &= -\beta SI/N \\ \frac{dI}{dt} &= \beta SI/N - \gamma I \\ \frac{dR}{dt} &= \gamma I\end{aligned}$$

Continuous-time deterministic models

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- discrete vs **continuous** *compartments*
- **deterministic** vs stochastic *dynamics*

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Example 3: individual-based model

- discrete vs continuous *time*
- discrete vs continuous *compartments*
- deterministic vs stochastic *dynamics*

```
For each ts from 1 to T {  
    lambda <- beta * I/N  
  
    For each i from 1 to N {  
        If individual i is susceptible:  
            with prob  $1 - \exp(-\lambda \cdot \Delta t)$  make infected.  
        Else-if individual i is infected:  
            with prob  $1 - \exp(-\gamma \cdot \Delta t)$  make susceptible.  
    }  
    Record population state  
}
```

Example 3: individual-based model

- **discrete** vs continuous *time*
- **discrete** vs continuous *compartments*
- deterministic vs **stochastic** *dynamics*

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Continuous-time stochastic models

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Continuous-time stochastic models

- discrete vs **continuous** *time*
- discrete vs continuous *compartments*
- deterministic vs **stochastic** *dynamics*

Stochastic differential equations (SDEs)

- discrete vs **continuous** *time*
- discrete vs **continuous** *compartments*
- deterministic vs **stochastic** *dynamics*

$$\begin{aligned}\frac{dS}{dt} &= -\beta SI/N - \sqrt{\beta SI/N} dW_1 \\ \frac{dI}{dt} &= \beta SI/N - \gamma I + \sqrt{\beta SI/N} dW_1 - \sqrt{\gamma I} dW_2 \\ \frac{dR}{dt} &= \gamma I + \sqrt{\gamma I} dW_2\end{aligned}$$

Can be solved with Euler method (see Session 7).

Continuous-time discrete stochastic models

- discrete vs **continuous** *time*
- **discrete** vs continuous *compartments*
- deterministic vs **stochastic** *dynamics*

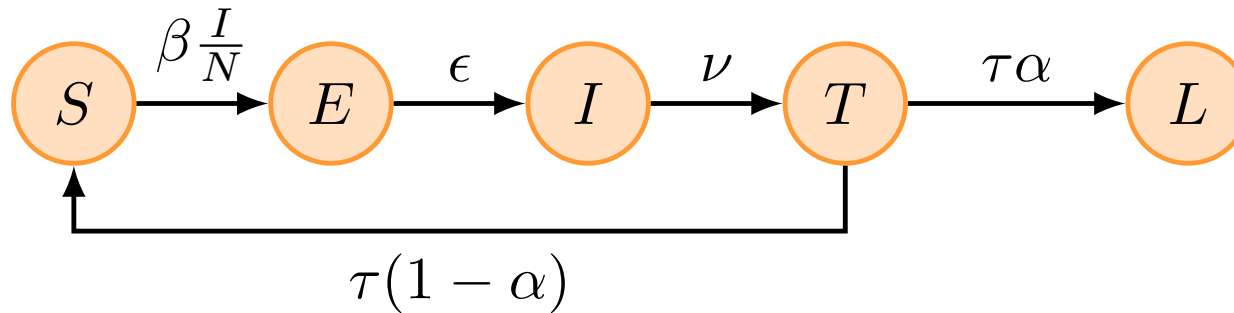
- discrete vs **continuous** *time*
- **discrete** vs continuous *compartments*
- deterministic vs **stochastic** *dynamics*

Event-based view:

- infection: $(S, I, R) \rightarrow (S - 1, I + 1, R)$ with rate $\beta SI/N$
- recovery: $(S, I, R) \rightarrow (S, I - 1, R + 1)$ with rate γI

We model these as a so-called **continuous-time Markov chain**.

Example: Influenza with short and long immunity



$$\begin{aligned}\frac{dS}{dt} &= -\beta S \frac{I}{N} + (1 - \alpha)\tau T \\ \frac{dE}{dt} &= \beta S \frac{I}{N} - \epsilon E \\ \frac{dI}{dt} &= \epsilon E - \nu I \\ \frac{dT}{dt} &= \nu I - \tau T \\ \frac{dL}{dt} &= \alpha \tau T\end{aligned}$$

QUESTION: Which events can happen, and at what rates?

DISCRETE

(session on individual-based models)

```
for (ts in 1:steps) { ... EVENTS ... }
```

CONTINUOUS

(here)

```
while (time < finaltime) { ...  
  time <- time + rexp(n = 1, rate = sum(rates))  
  if (time <= finaltime) { ... EVENTS ... }  
}
```

Waiting times between events in a Poisson process are exponentially distributed

Repeat until end time:

1. Calculate event rates

```
rates <- c()  
rates["infection"] <- beta * S * I / N  
rates["recovery"] <- gamma * I
```

2. Choose how long nothing happens

```
rexp(n = 1, rate = sum(rates))
```

3. Choose which event happens

```
sample(x = length(rates), size = 1, prob = rates)
```

and update system state according to event.



Now, put it in R!

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- Part 1: Stochastic simulation using the Gillespie algorithm
- Part 2: A faster alternative: the `adaptivetau` package

- Open the file

`10_StochasticContinuousractical/01_Gillespie.R`

and follow the instructions

- Objective: use the Gillespie algorithm to simulate the SIR model;
process outputs from stochastic models

Algorithm:

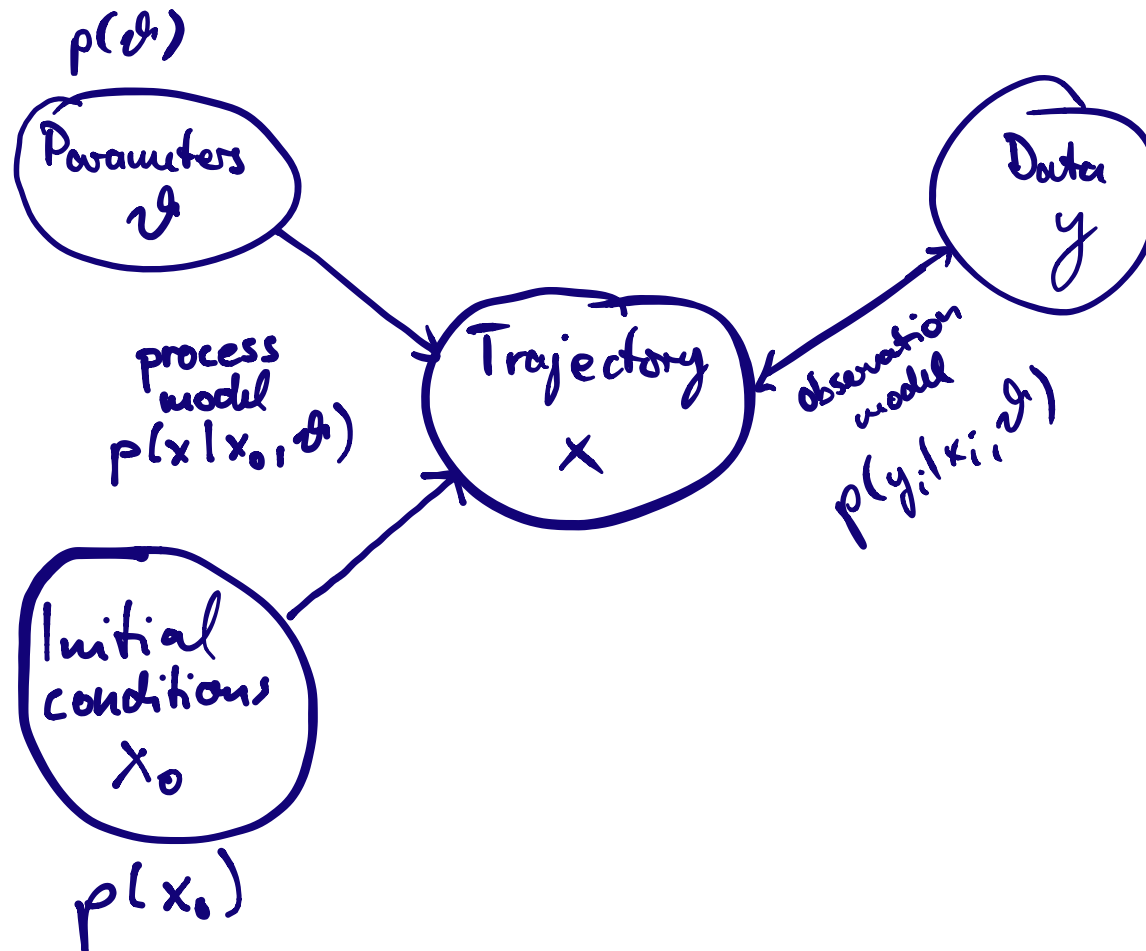
- Identifies periods during which all rates are not expected to change, and all variables are far from 0
- “Leaps” over these periods of time
- Adds the net effect of the Poisson-distributed number of transitions that should have occurred in that period

In R, the `ssa.adaptivetau` package implements this (and generates fast C code).

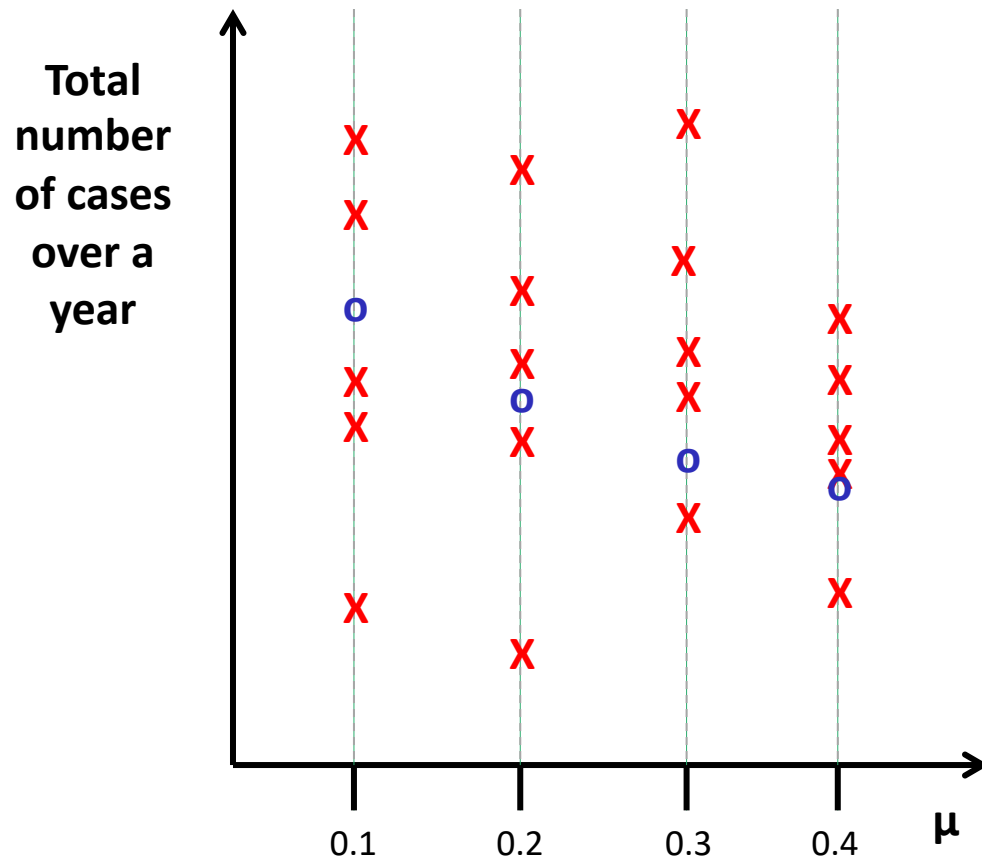
Practical part 2

- Open the file
`10_StochasticContinuousractical/02_AdaptiveTau.R` and follow the instructions
- Objective: use the `adaptivetau` packages to simulate the SIR and SEITL models

Representing uncertainty



Parameter variation

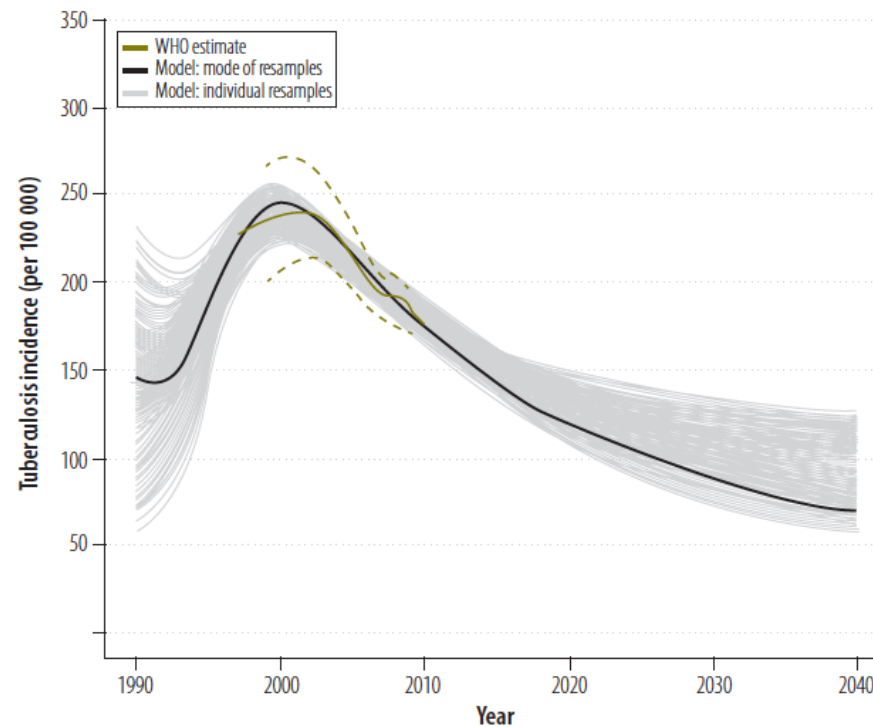


At each of 4 μ values,
5 runs of a model that is:

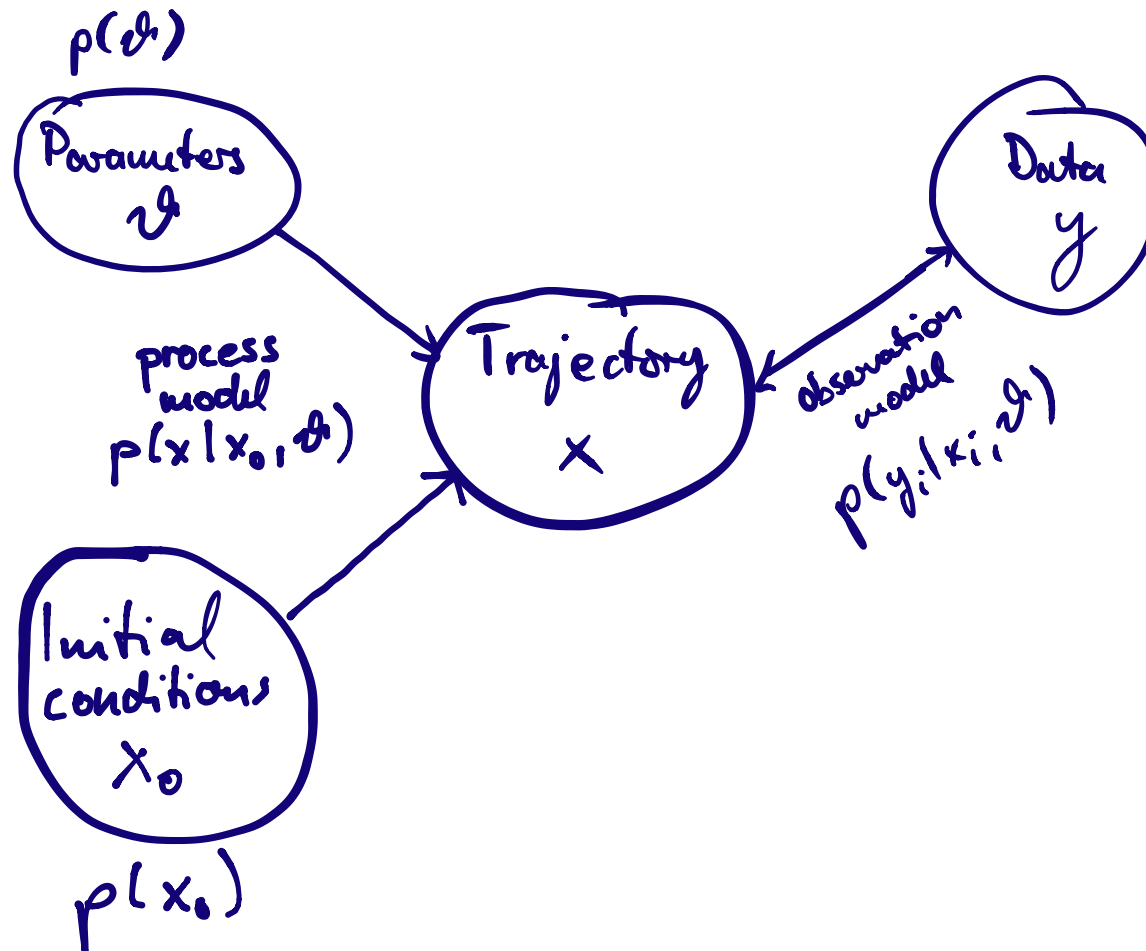
Stochastic = \circ / \times ?

Deterministic = \circ / \times ?

Fig. 2. **Incidence of tuberculosis (all forms) in the United Republic of Tanzania based on WHO estimates and projected incidence based on the calibrated epidemic model**



Representing uncertainty



- L.J.S. Allen (2017). A primer on stochastic epidemic models: Formulation, numerical simulation, and analysis. *Infectious Disease Modelling*, 2(2):128–142. <https://doi.org/10.1016/j.idm.2017.03.001>
- M.J. Keeling, P. Rohani (2017). *Modeling Infectious Diseases in Humans and Animals*. Princeton University Press.
- D.T. Gillespie (1976). A general method for numerically simulating the stochastic time evolution of coupled chemical reactions. *J Comput Phys*, 22(4):403–434, 1976. ISSN 0021-9991. [https://doi.org/10.1016/0021-9991\(76\)90041-3](https://doi.org/10.1016/0021-9991(76)90041-3)
- Y. Cao, D.T. Gillespie, and L.R. Petzold (2007). Adaptive explicit-implicit tau-leaping method with automatic tau selection. *J Chem Phys*, 126(22):224101 URL <https://doi.org/10.1063/1.2745299>
- A.A. King, M. Domenech de Cellès, F.M.G. Magpantay and Pejman Rohani (2015). Avoidable errors in the modelling of outbreaks of emerging pathogens, with special reference to Ebola. *Proc Roy Soc B* 282(1806). <https://doi.org/10.1098/rspb.2015.0347>