Sneaking non-Markovian Dynamics into Gillespie's Direct Method

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Abstract

Gillespie's direct method is a commonly-used Monte Carlo algorithm for simulating continuous-time Markov chain models of stochastic systems. In mathematical biology, it has been used to model systems at all levels, from collective cell behaviour to ecological models. We present an example from epidemiology, where we consider a contagion spreading on a bipartite network made up of individuals and infection contexts. In this situation, we find that some behaviours are poorly captured by the Markovian assumption and the resultant exponentially-distributed inter-event times.

To solve these issues, we introduce the rejection-based Gillespie Max method which allows the user to simulate non-exponentially distributed inter-event times, while still retaining the overall structure of Gillespie's direct method. By integrating thinning into the core simulation loop with delayed events, we model the complex interactions of non-pharmaceutical interventions on multiple outbreaks of Covid-19 in New Zealand.

Motivation

Non-Markovian dynamics are important!

Most events do not have exponentially distributed inter-event times.

But, they are difficult to simulate - requiring many expensive integral equations to be solved for each time an event fires.

Networks can have a LOT of events.

Because we track every individual in the network, and each individual can have potential for a large number of reactions, this can be computationally infeasible to track each potential reaction in memory.

Separation of Outcome and Hazard

Under the standard formulation, the probability of an outcome of multiple competing processes is intrinsically linked to the rates at which they occur.

If we want a event to fire with low probability but with a short inter-event time, then we must use thinning to achieve the correct probability of firing.

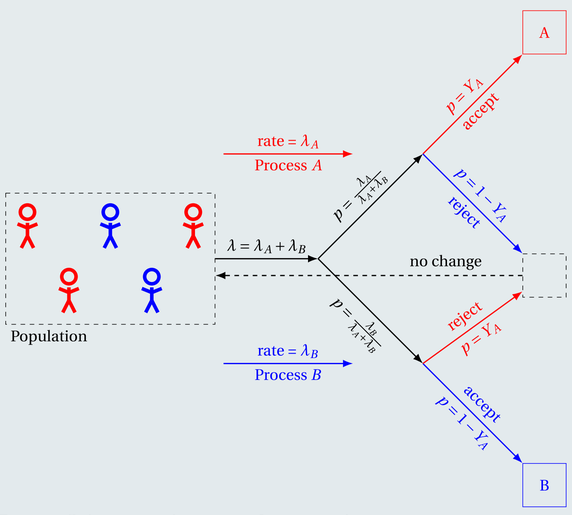

Figure: Schematic diagram of potential outcome process on two mutually exclusive processes A and B.

References

Anderson, D. F. (2007). A modified next reaction method for simulating chemical systems with time dependent propensities and delays. Journal of Chemical Physics, 127(21), 214107.

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Kiss, I. Z., Miller, J. C., & Simon, P. L. (2017). Mathematics of Epidemics on Networks (Vol. 46, Issue September 2005).

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The Gillespie Max Method

Correcting the Firing Probabilities

Lumped Events

Separate individuals into all potential reactions that can fire at the current time.

Thinning

Correct the probability of firing by using rejection.

Next Event to Fire

First Reaction Method Style Competing Processes

Delayed Effects

Reactions that initiate at time t do not complete until time $t + \tau$

τ does not need to be exponentially distributed!

Delayed effects stored in an ordered priority queue

Advantage: Flexible specification of reactions and effects.

But consumes a lot of memory.

Direct Method Loop

1. Draw time to next event

$$\Delta t \sim \mathrm{Exp}\left(\sum_i \lambda_i\right)$$

2. Draw the event to fire

$$p(i) = \lambda_i / \sum_j \lambda_j$$

Advantage: Memory-light!

Really important when the number of reactions is large.

But non-Markovian generalisation is expensive.

Thinning: Rejection-Based Correction

Core idea: Simulate at a 'maximum' rate, and correct the hazard by rejecting with probability $\lambda(t)/\lambda_{\max}$.

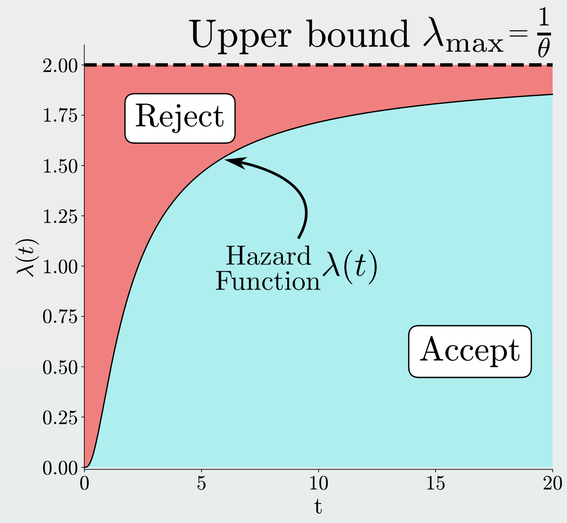

Figure: Hazard function correction for a gamma-distributed inter-event time, simulated with an exponential hazard upper bound.

This allows us to simulate any inter-event time distribution as if it were Markovian, as long as it is bounded above by some value.

We can also use this to correct for demographic heterogeneity, by rescaling the model parameters.

Finally, this is particularly useful for simulating the infection rate $\propto \frac{S}{N}$ by drawing from the neighbourhood and then performing a rejection step.

Unbounded events can be simulated by periodically updating the upper bound using delayed effects.

This method is computationally simpler than existing non-Markovian approaches (Boguñá et al 2014 and Masuda et al 2018) that attempt to generalise the direct method by evaluating partial integrals of the hazard function. This method is similar to Großmann et al.'s RED algorithm, but incorporates the direct method loop instead of being purely first-reaction based.

Application: COVID-19 in Aotearoa New Zealand

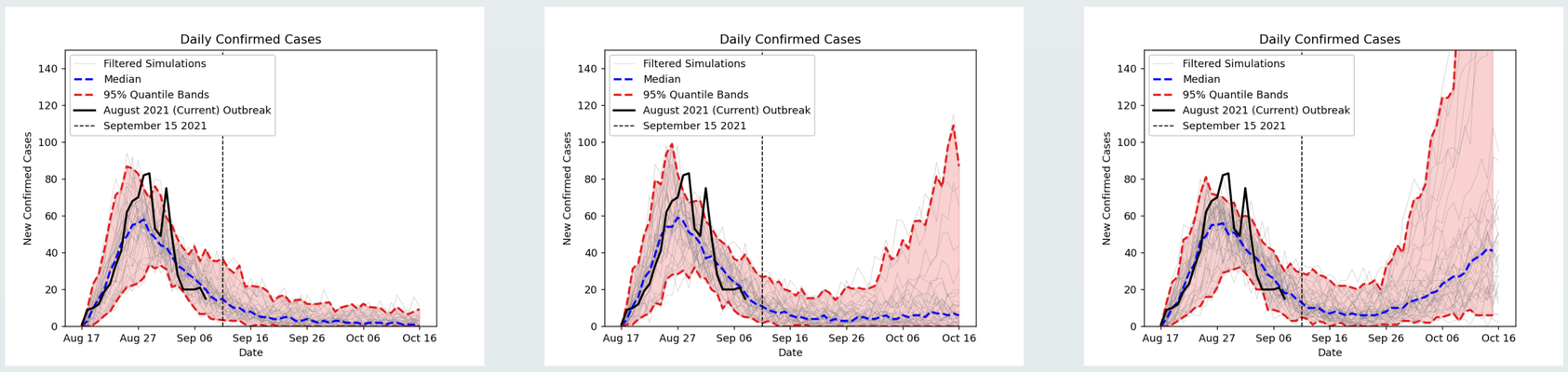

Figure: Realisations of simulations of (left) not relaxing or relaxing COVID-19 restrictions in an (centre) optimistic or (right) pessimistic scenario as the August 2021 Delta variant outbreak in New Zealand was trending downwards (data as of 9th September 2021). Simulations filtered using an ABC approach.

These methods were used to simulate a model of COVID-19 transmission and control in New Zealand on a 5 million-individual bipartite network. It modelled non-pharmaceutical interventions (testing, contact tracing, self-isolation, lockdowns) on top of transmission with latent and presymptomatic periods, as well as hospitalisation and mortality.

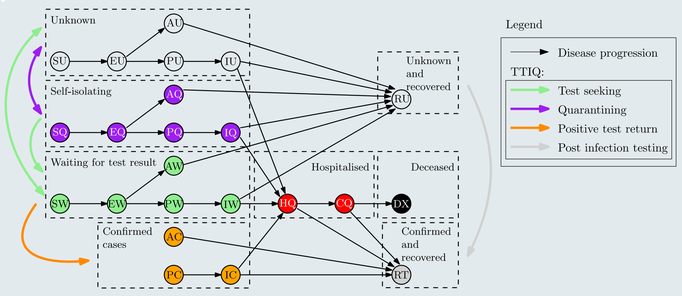

Figure: Transition diagram for states in the NZ COVID-19 network model

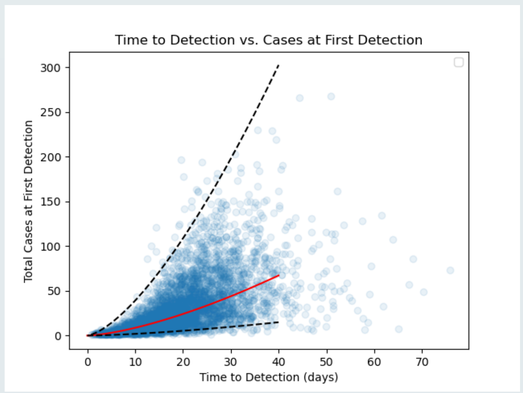

Figure: Distribution of time of first of first detection vs. total cases at first detection, calibrated to a small community outbreak in November 2020.

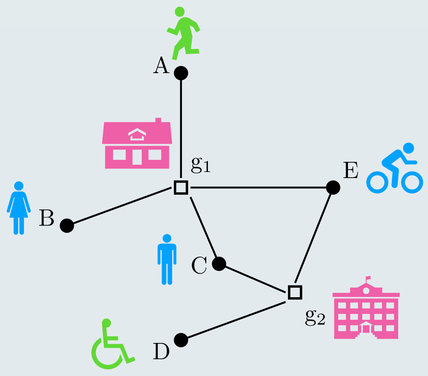

Figure: Diagrammatic example of a bipartite network, where the individuals are connected to group nodes.

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