

Perfect Epidemics

Applied Probability Seminar

Department of Statistics, University of Warwick

W S Kendall S B Connor

Warwick, York

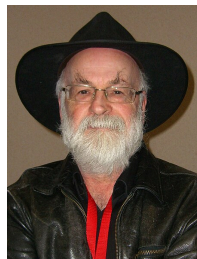
17 January 2025



Introduction

“Maybe the only significant difference between a really smart simulation and a human being was the noise they made when you punched them.”

(Terry Pratchett, [The Long Earth](#))



Handout available on the web: use the QR-code

or visit <https://wilfridskendall.github.io/talks/PerfectEpidemics/>.

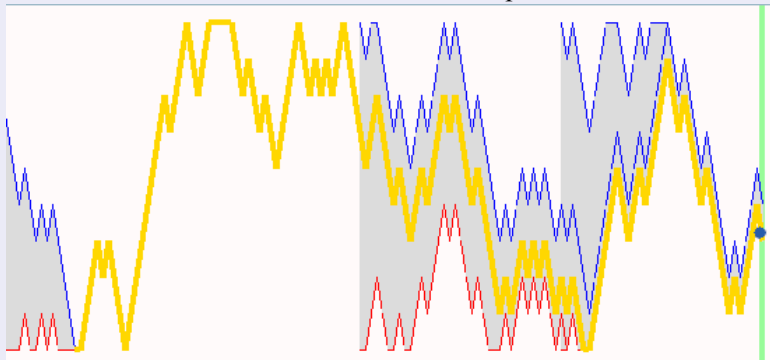
The author acknowledges support of UK EPSRC grant EP/R022100.

1: Introduction to Perfect Simulation

- Propp & Wilson (1996) invented exact simulation / Coupling from the Past (CFTP) / perfect simulation;
- The term “perfect simulation” (WSK, 1998) should make you suspicious: perfection is never achieved. This is why the term was chosen!
- Key ideas of “*classic CFTP*”:
 - ▶ extend simulation *backwards* through time not forwards;
 - ▶ exploit monotonicity (*couple* maximal and minimal processes);
 - ▶ seek coalescence.
- Simplest possible example: *random-walk-CFTP*
(can boost to use Ising model to do simple image reconstruction).

Classic CFTP for a simple random walk (I)

- So now start at top (9) and bottom (0) at negative time $-T$, run to time 0.
- If not coupled, then back-off to time $-2T$ and repeat.
- May need to iterate back-off doubling several times.
- When coupled, top and bottom yield a common value at time 0.
- The common value is an exact draw from equilibrium!



2: A short section on some theory about CFTP

- What about cases where monotonicity fails? or there isn't a sensible “maximal” process? Ideas (WSK, 1998):
 - ▶ cross-couple upper and lower envelope processes,
 - ▶ dominate by amenable “dominating process” (time-reversible, can draw from equilibrium, can couple target processes below dominating process);
- Theoretical limits: *in principle*
 - ▶ Classical CFTP equivalent to uniform ergodicity (Foss & Tweedie, 1998).
 - ▶ Dominated CFTP achievable under geometric ergodicity (WSK, 2004).
 - ▶ Dominated CFTP can work in some **non**-geometrically ergodicity cases (Connor & WSK, 2007a, *nb* corrigendum);
- Dominated CFTP can be used to carry out perfect simulation for stable point processes (WSK & Møller, 2000);
- Detailed expositions: WSK (2005), Huber (2015).
(Want to implement CFTP in R? see WSK, 2015.)

3: Perfect Epidemics: a challenge problem for CFTP

Many important inferential questions (Cori & Kucharski, 2024).

Simplest models (versus UK model with 10^6 agents!, Fraser & Others, 2023):

S-I-R deterministic epidemic: susceptibles s , infectives i , removals r (constant total population $s + i + r = n$):

$$\begin{aligned}s' &= -\alpha s i, \\ i' &= (\alpha s - \beta) i, \\ r' &= \beta i.\end{aligned}$$

S-I-R stochastic epidemic: a Markov chain (S, I, R) with transitions

Infection: $S \rightarrow S - 1, \quad I \rightarrow I + 1$ at rate $\alpha S I$,

Removal: $I \rightarrow I - 1, \quad R \rightarrow R + 1$ at rate βI .

Massive assumption for these simple models: **homogeneous mixing**.

The first question asked about a new epidemic

“What is the R-number?”

The R-number is $\alpha s_0/\beta$: mean number of new infectives produced per infective at *start* of epidemic with initially s_0 susceptibles.

Whittle (1955)’s threshold theorem: R-number $\gg 1$ means positive chance of epidemic infecting significant proportion of the population.

Wikipedia: “The British-registered *Diamond Princess* was the first cruise ship to have a major [COVID-19] outbreak on board, with the ship quarantined at Yokohama from 4 February 2020 for about a month. Of 3711 passengers and crew, around 700 people became infected and 9 people died.”

Evidently $\alpha s_0/\beta \gg 1$ – as was sadly later confirmed, a sorrow for us all.



4: Inference on the R-number

Important, because the R-number controls severity of epidemic. However:

- 1 Modelling is **tough**. *Either* massive assumptions (homogeneous mixing) *or* very many parameters;
- 2 Inference is **really tough**: hard to get information about infection times;
- 3 It is all **especially tough** in early stages. Answers are most needed when hardly any information is available (a simplified example for a Warwick UG second-year statistics module shows how tough this can be);
- 4 Markov chain Monte Carlo (MCMC) can be used (see next slide) but what about burn-in?
- 5 Can we use **perfect simulation**?

5: An easier question

An absurdly simple variant on contact tracing:

“When did the infections occur. if we only observe removals?”

(Gibson & Renshaw, 1998; O'Neill & Roberts, 1999; Gibson & Renshaw, 2001)

- ➊ Thus n , α , β known, removal times observed, but unobserved infection times **must be inferred**.
- ➋ Visualize n timelines, along which incidents are scattered:
 - ▶ potential removals, activated if timeline is infected;
 - ▶ potential infections, activated if timeline is infected *and* if designated target timeline is lowest uninfected timeline.
- ➌ Poisson point processes of appropriate rates yield an S-I-R epidemic.
- ➍ Evolve whole S-I-R trajectory in *algorithmic time* (alter potential infections and removals using immigration-death in discrete algorithmic time).
- ➎ Result: *trajectory-valued chain*, unconditioned S-I-R as equilibrium.

Incidents defining an epidemic

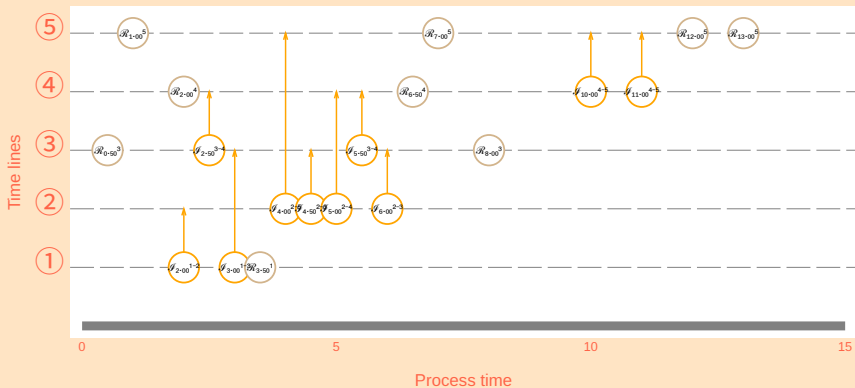


Figure 1: Light-orange circles denote potential infections (arrows point upwards to targets); light-brown circles denote potential removals.

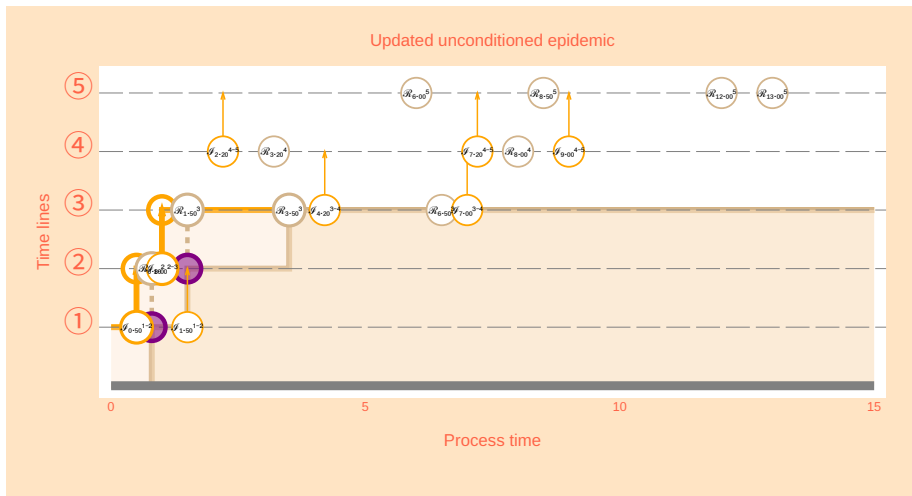


Figure 3: A step in algorithmic time for the unconditioned epidemic simply involves replacing all incidents by a new set of incidents.

Crucial technical point

- Updates in algorithmic time τ are then (algorithmic-)*time-reversible*: so restriction to subset S of state-space (in our case, *activated* removals occurring precisely at specified set of times) implies a new equilibrium which is the old equilibrium conditioned to lie in S .
- For later purposes it is convenient to stage the replacement as follows:
 - 1 Replace removals (R s);
 - 2 Re-sample timelines (though not times) of R s;
 - 3 Replace infections (I s).
- It is convenient to re-express this for continuously varying τ :
 - 1 For $2nT < \tau < (2n+1)T$, update old R s with times in $(0, \tau - 2nT)$;
 - 2 For $\tau = (2n+1)T$, resample timelines (not times) of R s;
 - 3 For $(2n+1)T < \tau < (2n+2)T$, update old I s in $((2n+2)T - \tau, T)$.
- Thus the original update is expressible as a (continuous) composition of updates, each of which satisfies detailed balance in equilibrium.
- The connection “restriction=conditioning” is thereby preserved.
- Crucially, step 2 ensures composition action is irreducible over S ! (So equilibrium under conditioning is unique.)

Illustration of technical point (1/8)

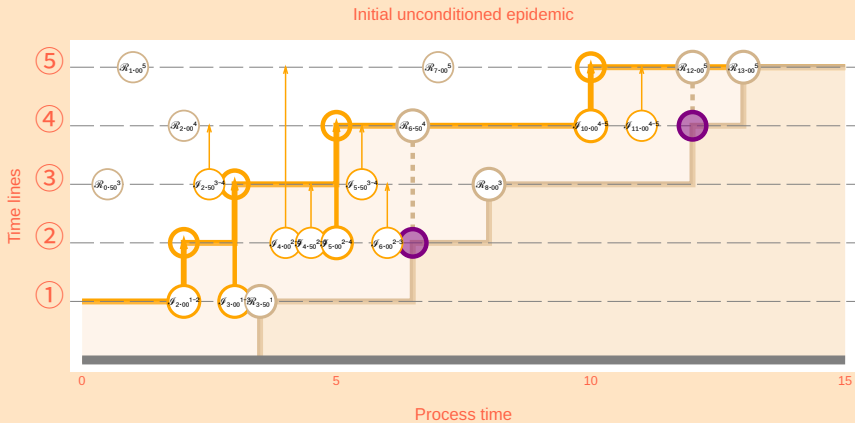


Figure 4: No change to removals or infections

Illustration of technical point (2/8)

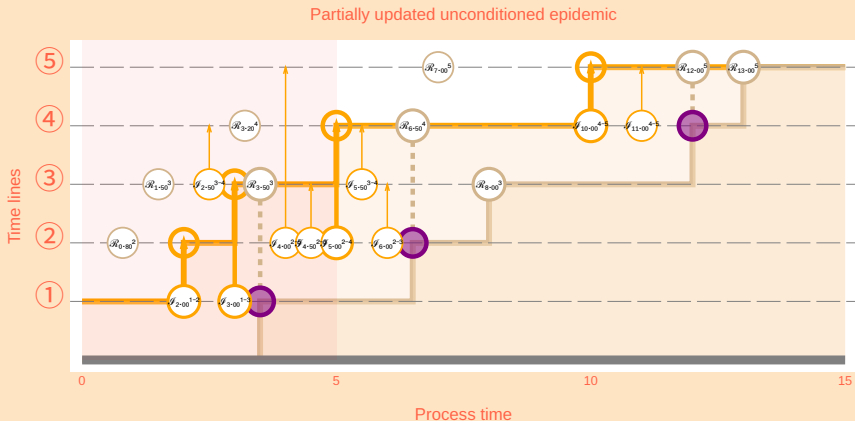


Figure 5: Replace first third of removals, infections unchanged

Illustration of technical point (3/8)

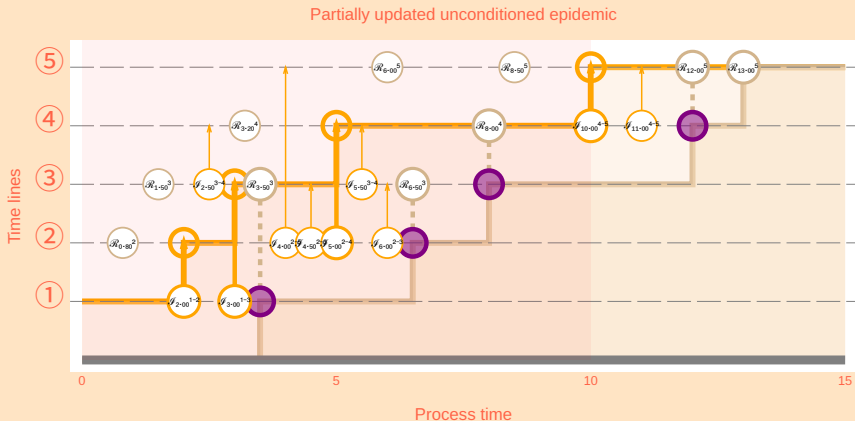


Figure 6: Replace first two-thirds of removals, infections unchanged

Illustration of technical point (4/8)

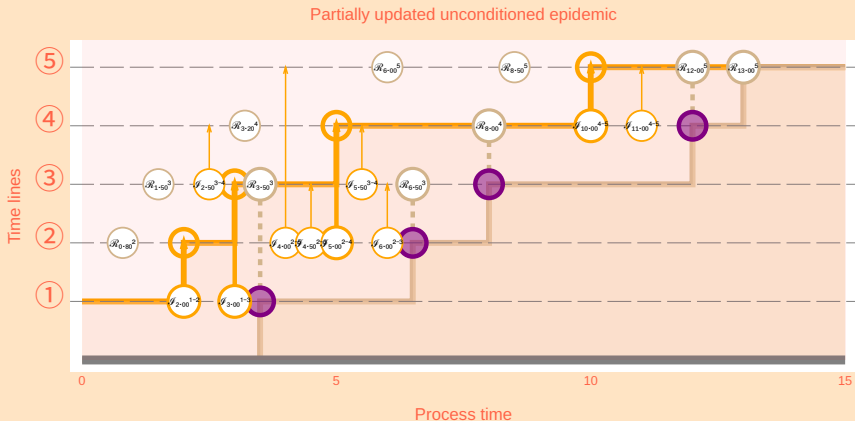


Figure 7: Replace all removals, infections unchanged

Illustration of technical point (5/8)

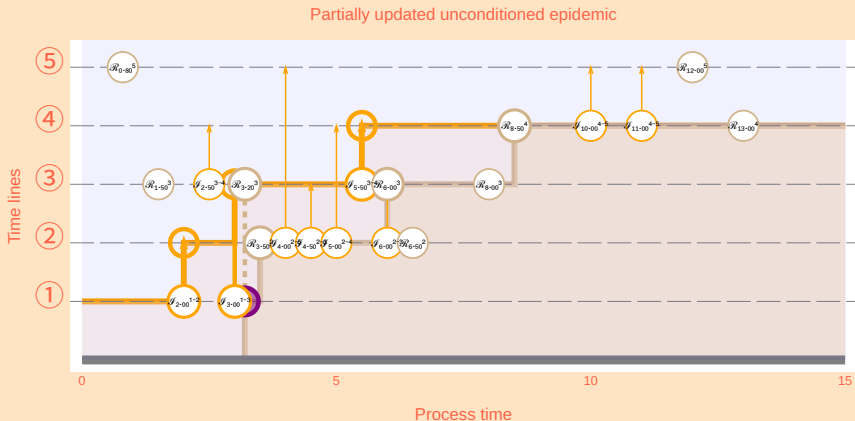


Figure 8: Re-sample all removal timelines, infections unchanged

Illustration of technical point (6/8)

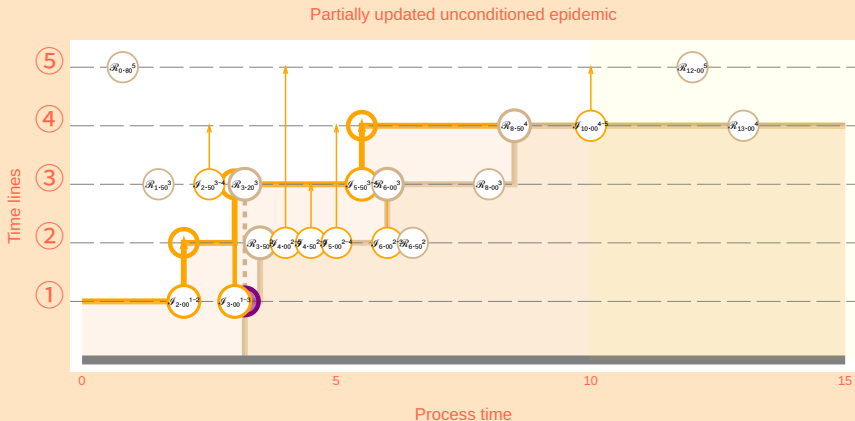


Figure 9: Re-sample last third of infections

Illustration of technical point (7/8)

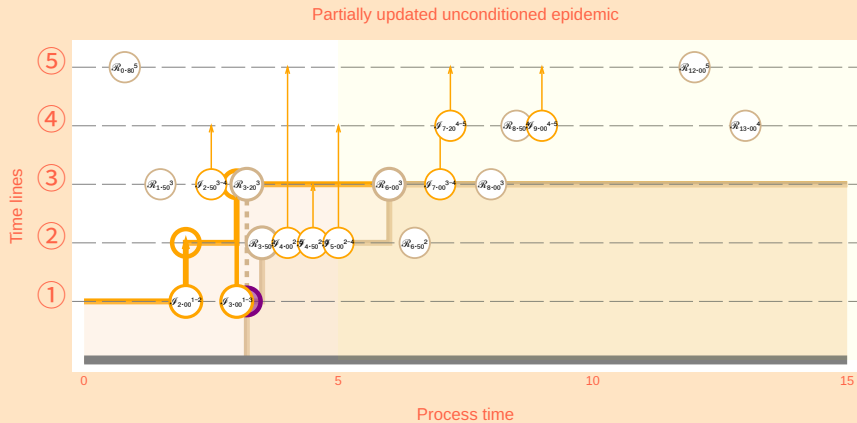


Figure 10: Re-sample last two-thirds of infections

Illustration of technical point (8/8)

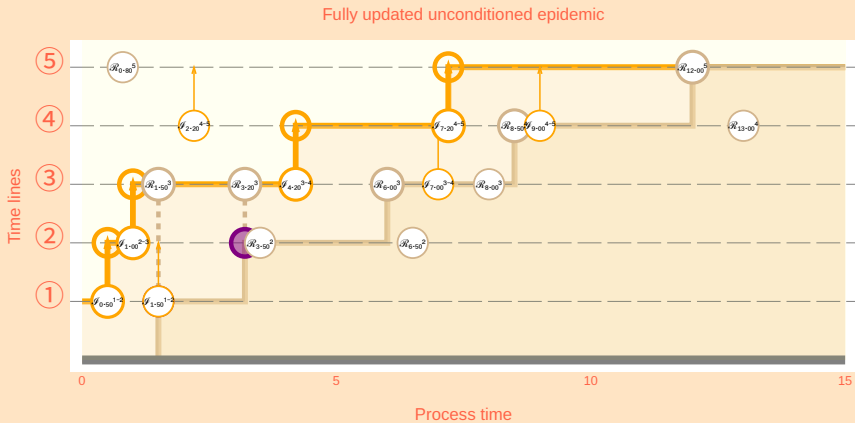


Figure 11: Re-sample all infections

Conditioning on observed removals

- The trajectory-valued chain is *dynamically reversible*, in *continuous algorithmic time*.
- Irreducibility is *vital* (otherwise equilibrium depends on starting point).
Consequently:
 - ▶ conditioned removals must be able to change timeline (but not time of occurrence);
- Forbidding removal of observed removals, and forbidding creation of new activated removals, yields a modified chain whose invariant probability measure conditions on observed pattern of removals.

Implications:

- ▶ a removal can be introduced only if it doesn't activate;
- ▶ a conditioned removal timeline can be altered only if it doesn't de-activate;
- ▶ an infection cannot be removed if that loses a conditioned removal;
- ▶ an infection can be introduced only if no new observed removals result.
- Does this produce a *feasible* and suitably monotonic algorithm?
- **Housekeeping details** required to establish that monotonicity still works.
Key notions: *last feasible epidemic* (LFE) and *no-fly zone* (NFZ).

Initial conditional epidemic

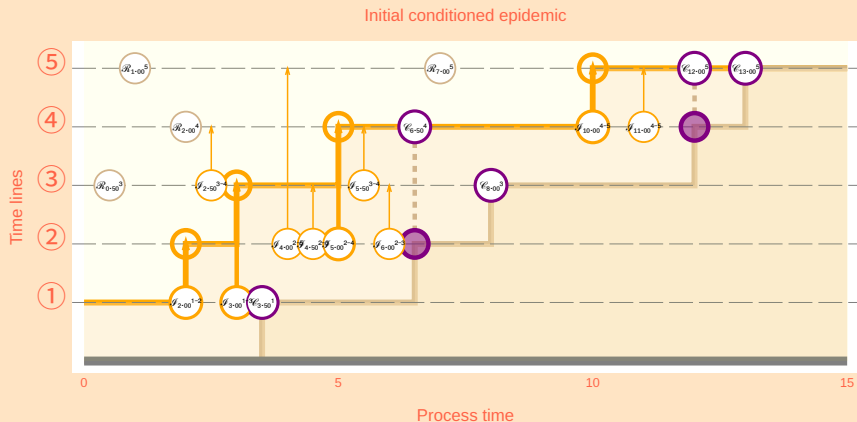


Figure 12: Initial epidemic with conditioned removals indicated using purple circles (and purple disks when different timelines are infected).

Conditional epidemic update

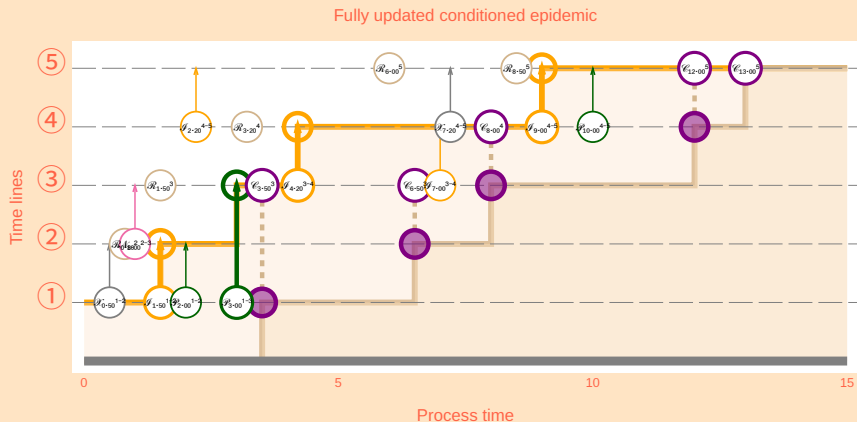


Figure 13: Epidemic updated under restriction: all conditioned removals remain activated, no new removals are activated. Green infections have been “perpetuated”.

Last feasible epidemic (LFE)

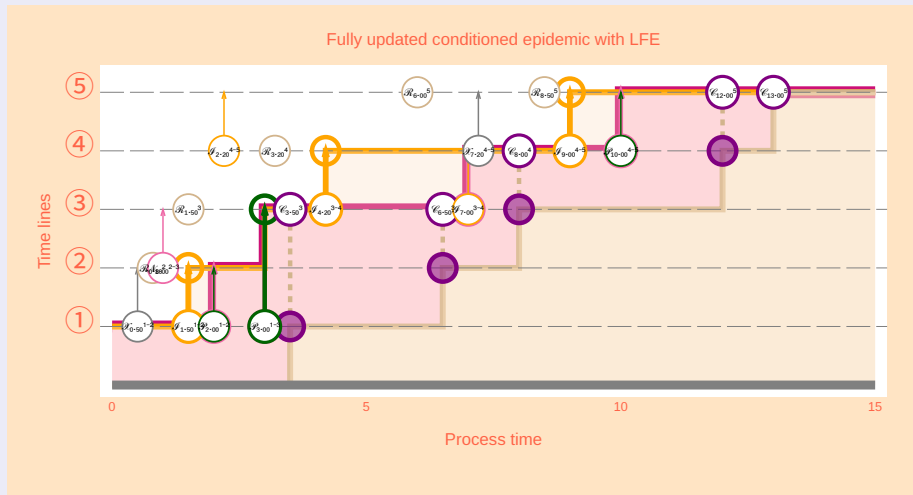


Figure 14: LFE computed recursively working right-to-left: the slowest sequence of infections deals with all infected timelines in order (includes perpetuated infections).

Fully updated conditioned epidemic with NFZ

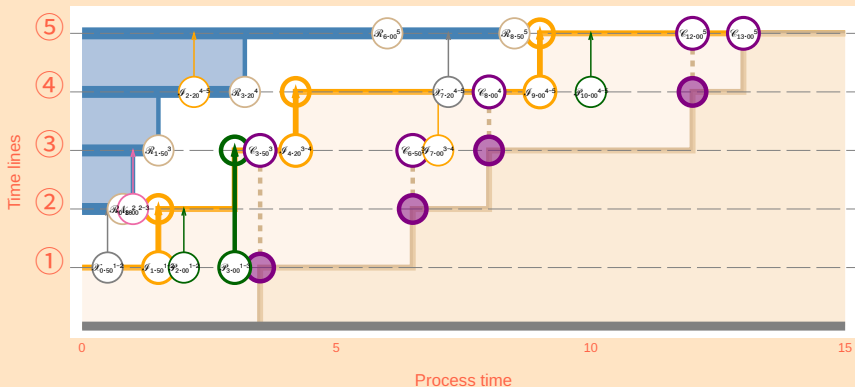
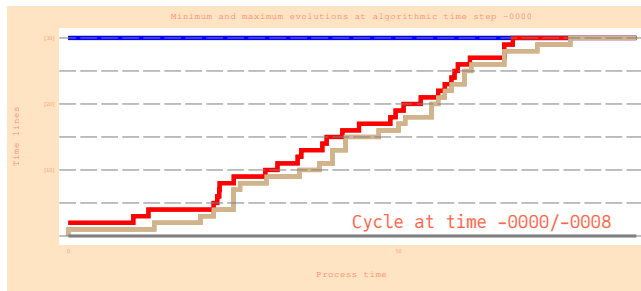


Figure 15: NFZ computed recursively working right-to-left: trace region of timelines that must not be infected if one is not to activate unobserved removals.

Example

- Smallpox outbreak in a closed community of 120 individuals in Abakaliki, Nigeria (much studied! see p. 125, [Bailey, 1975](#)).
- **Assume**
 - ▶ first observed removal is also the first removal: under a plausible improper prior we can then deduce what is the distribution of infectives I_0 at time 0;
 - ▶ *all* removals are recorded;
 - ▶ no further removals after last observed removal (makes life easier).
- Coding in *julia* ([Bezanson *et al.*, 2017](#)), we can construct a **perfect simulation GIF** yielding a draw from unobserved pattern of infections.



So what?

- why this emphasis on unobserved infections given fixed α and β , when we need inference on R-number $\alpha n/\beta$ for *unknown* α and β ?
- Good question. But a re-weighting argument allows us to get (unbiased) estimates based on *different* α and β . The perfect simulation provides exact simulation-based computation to integrate out pattern of unobserved infections.
- So (next steps after Connor & WSK, 2024)
 - ▶ estimate likelihood test statistic for specified α and β ;
 - ▶ construct steepest ascent algorithm (in effect, variant of Robbins-Monro stochastic optimization) to find *maximum a posteriori* estimates of α and β ;
 - ▶ or even, with some computational effort, compute the entire posterior joint density for α and β !
- Finally: generalize to other suitable compartment models?

Conclusion

- If MCMC burn-in is a concern, try to build a perfect simulation!
- CFTP works even for significantly complex and relevant models of real-life phenomena.
- *Of course* detailed models resist perfect simulation (but it will be helpful to compare with a simpler model using fewer parameters).
- Still to be done: statistical estimation of parameters, generalization to other compartment models.
- Thank you for your attention! **QUESTIONS?**



References I

- Bailey, N.T.J. (1975) *The mathematical theory of infectious diseases and its applications*, 2nd Ed. ed. Griffin.
- Bezanson, J., Edelman, A., Karpinski, S., & Shah, V.B. (2017) Julia: A Fresh Approach to Numerical Computing. *SIAM Review*, **59**, 65–98.
- Connor, S.B. & WSK (2007b) Perfect simulation for a class of positive recurrent Markov chains (corrigendum). *Annals of Applied Probability*, **17**, 1808–1810.
- Connor, S.B. & WSK (2007a) Perfect simulation for a class of positive recurrent Markov chains. *Annals of Applied Probability*, **17**, 781–808.
- Connor, S.B. & WSK (2024) Perfect Epidemics.
- Cori, A. & Kucharski, A. (2024) Inference of epidemic dynamics in the COVID-19 era and beyond. *Epidemics*, **48**, 100784.
- Foss, S.G. & Tweedie, R.L. (1998) Perfect simulation and backward coupling. *Stochastic Models*, **14**, 187–203.
- Fraser, C. & Others (2023) OpenABM-Covid19: Agent-based model for modelling the Covid-19 and Contact-Tracing.
- Gibson, G.J. & Renshaw, E. (1998) Estimating parameters in stochastic compartmental models using Markov chain methods. *Mathematical and Medical Biology*, **15**, 19–40.

References II

- Gibson, G.J. & Renshaw, E. (2001) Likelihood estimation for stochastic compartmental models using Markov chain methods. *Statistics and Computing*, **11**, 347–358.
- Huber, M.L. (2015) *Perfect Simulation*. Boca Raton: Chapman; Hall/CRC.
- O'Neill, P.D. & Roberts, G.O. (1999) Bayesian Inference for Partially Observed Stochastic Epidemics. *Journal of the Royal Statistical Society Series A: Statistics in Society*, **162**, 121–129.
- Propp, J.G. & Wilson, D.B. (1996) Exact sampling with coupled Markov chains and applications to statistical mechanics. *Random Structures and Algorithms*, **9**, 223–252.
- Whittle, P. (1955) The outcome of a stochastic epidemic—a note on Bailey's paper. *Biometrika*, **42**, 116–122.
- WSK (1998) Perfect Simulation for the Area-Interaction Point Process. *Probability towards 2000* (Accardi, L. & Heyde, C.C. eds). Springer-Verlag, pp. 218–234.
- WSK (2004) Geometric ergodicity and perfect simulation. *Electronic Communications in Probability*, **9**, 140–151.
- WSK (2005) Notes on Perfect Simulation. Singapore: World Scientific, pp. 93–146.
- WSK (2015) Introduction to CFTP using R. *Stochastic geometry, spatial statistics and random fields, Lecture notes in mathematics*. Springer, pp. 405–439.
- WSK & Møller, J. (2000) Perfect simulation using dominating processes on ordered spaces, with application to locally stable point processes. *Advances in Applied Probability*, **32**, 844–865.

Technical information

Image	Attribution	
<i>Terry Pratchett</i>	Luigi Novi	CC BY 3.0 https://creativecommons.org/licenses/by/3.0
Classic CFTP for a simple random walk <i>Diamond Princess</i>	Result of code written by WSK Alpsdake	<i>CC BY-SA 4.0</i>
Epidemic CFTP images and animation	Result of code written by WSK	

These notes were produced from `PerfectEpidemics.qmd`:

Author:	Wilfrid Kendall W.S.Kendall@warwick.ac.uk
Date:	Mon Jan 13 16:04:37 2025 +0000
Summary:	Added quote and picture. Checked URL links for handout and simulation.