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."

(The Long Earth, Pratchett & Baxter, 2012)





Handout is on the web: use the QR-code or visit wilfridskendall.github.io/talks/PerfectEpidemics.

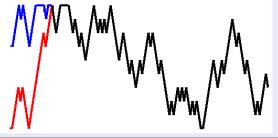
WSK acknowledges the support of UK EPSRC grant EP/R022100.

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).

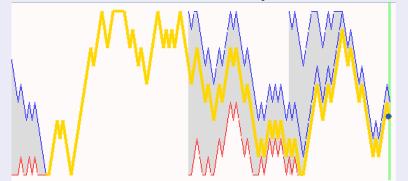
Classic CFTP for a simple random walk (I)

- Consider a simple random walk on $\{0, 1, 2, 3, 4, 5, 6, 7, 8, 9\}$.
 - $hild \mathbb{P}\left[+1 \text{ jump }
 ight] = p \in (0,1), \text{ while } \mathbb{P}\left[-1 \text{ jump }
 ight] = 1-p, \text{ except that }$
 - \triangleright at state 9 replace +1 jump by staying still, **and**
 - \triangleright at state 0 replace -1 jump by staying still.
- Conventional MCMC picks a starting point, then runs the simple random walk for long time till approximate equilibrium.
- How long? One way to *estimate* this is to run two (or several?) coupled copies till they meet. If probability of meeting by time T is high, then deviation of X_T from equilibrium is statistically small;
- Generally not true that location at coupling is a draw from equilibrium.



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 by time 0, than 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* we can show that
 - ► 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 Connor & WSK, 2007b).
- *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 10⁶ agents!, Fraser & Others, 2023):

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

$$\begin{array}{rcl} s' & = & -\alpha \; s \; i \, , \\[1mm] i' & = & (\alpha \; s - \beta \;) \; i \, , \\[1mm] r' & = & \beta \; i \, . \end{array}$$

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

Infection: $S \rightarrow S-1$, $I \rightarrow I+1$ at rate αSI , Removal: $I \rightarrow I-1$, $R \rightarrow R+1$ at rate βI .

Both models make an unrealistic assumption: 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:

- Modelling is tough. Either massive assumptions (homogeneous mixing)
 or very many parameters;
- ② Inference is really tough: hard to get information about infection times;
- 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);
- Markov chain Monte Carlo (MCMC) can be used (see next slide) but what about burn-in?
- On we use perfect simulation?

5: An easier question

An absurdly simple variant of contact tracing:

"When did the infections occur, supposing we only observe removals?" (Gibson & Renshaw, 1998; O'Neill & Roberts, 1999; Gibson & Renshaw, 2001)

- Thus n, α , β are known, removal times are observed, but unobserved infection times must be inferred.
- ② 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.
- Poisson point processes of appropriate rates yield an S-I-R epidemic.
- **1** First step: evolve whole S-I-R trajectory in *algorithmic time* (alter potential infections and removals using immigration-death in discrete algorithmic time).
- Result: trajectory-valued chain, unconditioned S-I-R as equilibrium.

From incidents to unconditioned epidemic trajectories (1/3)

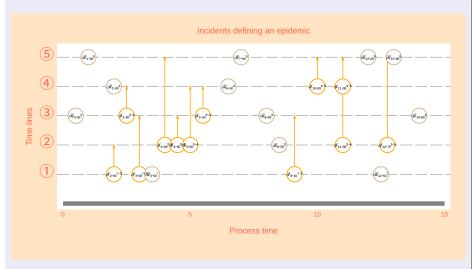


Figure 1: Light-orange circles denote potential infections (arrows point upwards to targets); light-brown circles denote potential removals.

From incidents to unconditioned epidemic trajectories (2/3)

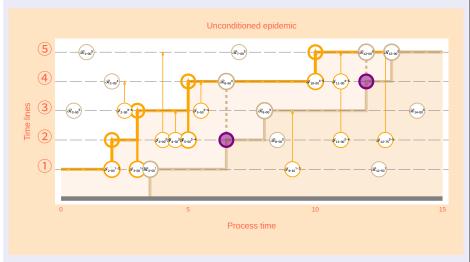


Figure 2: Activate (a) *infection* if target on lowest uninfected timeline; (b) *removal* if in infected region, then remove lowest infected (purple disk if different timeline).

From incidents to unconditioned epidemic trajectories (3/3)

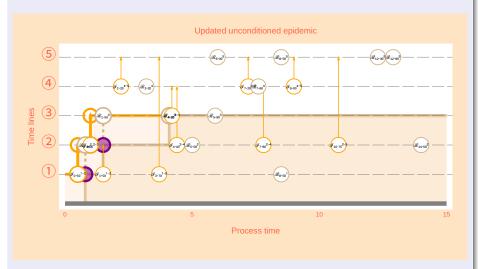


Figure 3: A step in algorithmic time for the unconditioned epidemic simply involves replacing the original incidents by a new set of incidents.

Crucial technical point

- Updates in algorithmic time τ are then (algorithmic-)time-reversible: so restriction to subset S of state-space (of 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:
 - Replace removals (Rs);

 - 3 Replace infections (Is).
- Re-express using continuously varying τ . Process time runs over [0, T].
 - For $2nT < \tau < (2n+1)T$, update old Rs with times in $(0, \tau 2nT)$;
 - ② For $\tau = (2n+1)T$, resample timelines (not times) of Rs;
 - $\textbf{ § For } (2n+1)T < \tau < (2n+2)T, \text{ update old } I\text{s in } ((2n+2)T-\tau,T).$
- 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)

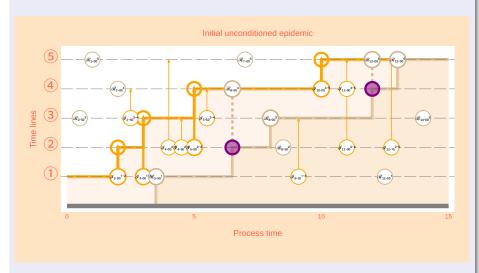


Figure 4: No change yet to removals or infections;

Illustration of technical point (2/8)

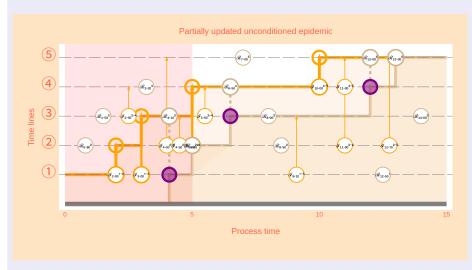


Figure 5: Replace first third of removals, infections unchanged;

Illustration of technical point (3/8)

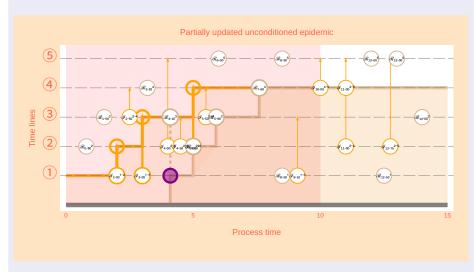


Figure 6: Replace first two-thirds of removals, infections unchanged;

Illustration of technical point (4/8)

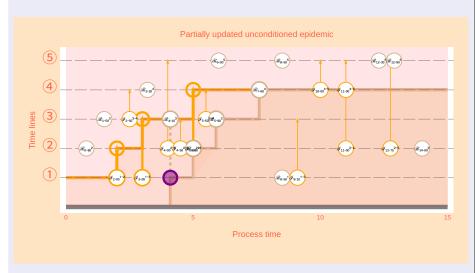


Figure 7: All removals resampled, infections as yet unchanged;

Illustration of technical point (5/8)

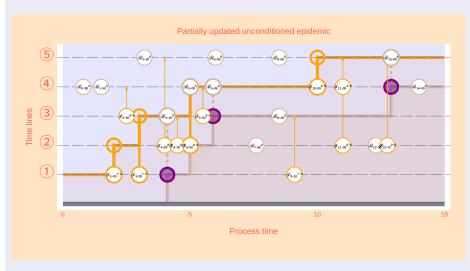


Figure 8: Re-sample all removal timelines, infections as yet unchanged;

Illustration of technical point (6/8)

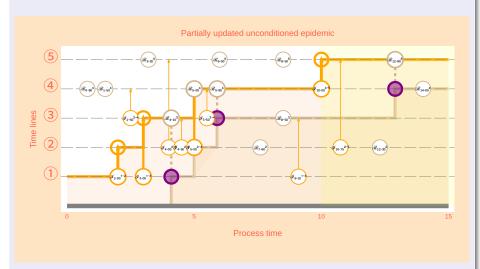


Figure 9: Re-sample last third of infections;

Illustration of technical point (7/8)

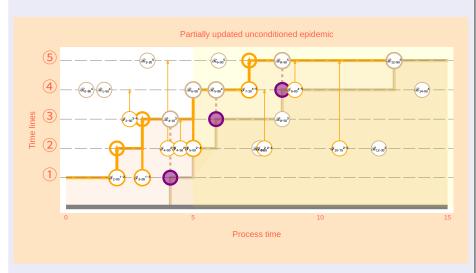


Figure 10: Re-sample last two-thirds of infections;

Illustration of technical point (8/8)

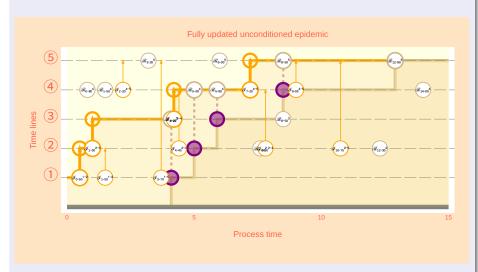


Figure 11: All infections now re-sampled.

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 action 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

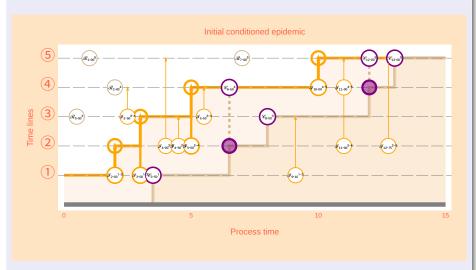


Figure 12: Initial epidemic with conditioned removals indicated using purple circles (and purple disks when different timelines are infected).

Conditional epidemic update

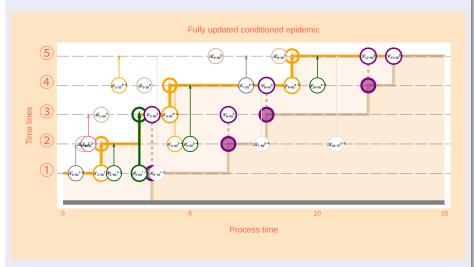


Figure 13: Epidemic updated under restriction: all conditioned removals remain activated, no new removals are activated. Green infections have been "perpetuated".

Last feasible epidemic (LFE)

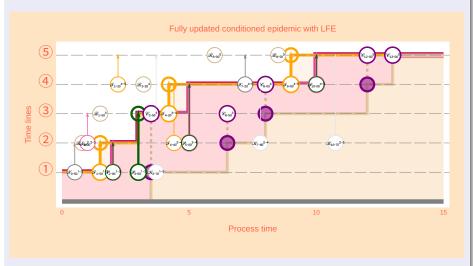


Figure 14: LFE computed recursively working right-to-left: the slowest sequence of infections deals with all infected timelines in order (includes perpetuated infections).

No-fly zone (NFZ)

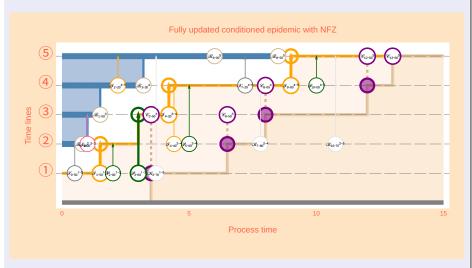


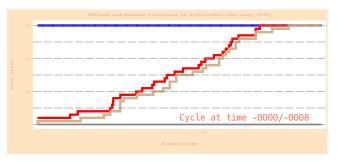
Figure 15: NFZ computed recursively working right-to-left: it traces the region of timelines that must not be infected if one is not to activate unobserved removals.

Example

 Smallpox outbreak in a closed community of 120 individuals in Abakaliki, Nigeria (much studied! see page 125 of 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 I₀ 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 α n/β 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 posterior* 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. (2020) Omnithermal Perfect Simulation for Multi-server Queues. ACM Transactions on Modeling and Computer Simulation, 30, 1–15.
- 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 (2015) Perfect simulation of M/G/c queues. Advances in Applied Probability, 47, 1039–1063.
- 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.



References II

- 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.
- 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.
- Pratchett, T. & Baxter, S. (2012) The Long Earth. Doubleday.
- 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

References III

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.



Image information

Image	Attribution	
Terry Pratchett Classic CFTP for a simple random walk	Luigi Novi Result of code written by WSK	CC BY 3.0
Diamond Princess Epidemic CFTP images and animation	Alpsdake Result of code written by WSK	CC BY-SA 4.0



A "near-maximal" configuration

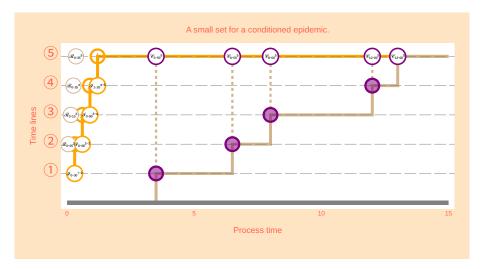


Figure 16: A conditional epidemic in which all activated infections occur before time 3.0, also before smallest observed removal time.

Other technical information

Software versions

Software used in computations:

Software	Version	Branch	Date of last commit
Quarto	1.6.39	_	
Running under julia	1.11.2	_	
Module EpidemicsCFTP	2.2.487	main	Fri Jan 10 20:17:28 2025
Module EpidemicsUtilities	0.1.2.154	main	Wed Jan 15 13:23:36 2025
This Quarto script	2.2.587	master	Thu Jan 16 17:01:55 2025

Revision history

These notes were produced from PerfectEpidemics.qmd:

Author: Wilfrid Kendall W.S.Kendall@warwick.ac.uk
Date: Thu Ian 16 17:01:55 2025 +0000

Summary: Final version for 17 January 2025.