## Perfect Epidemics

### Applied Probability Seminar Department of Statistics, University of Warwick

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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.

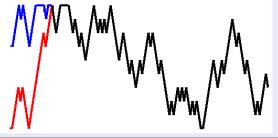
WSK acknowledges the support of UK EPSRC grant EP/R022100.

#### 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).

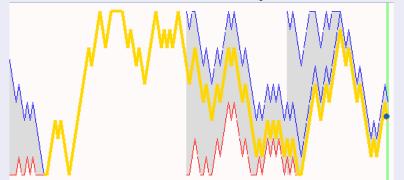
### Classic CFTP for a simple random walk (I)

- 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, 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 10<sup>6</sup> 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  $\alpha SI$ , Removal:  $I \rightarrow I-1$ ,  $R \rightarrow R+1$  at rate  $\beta I$ .

These 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,  $\alpha$ ,  $\beta$  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.
- Evolve whole S-I-R trajectory in algorithmic time (alter potential infections and removals using immigration-death in discrete algorithmic time).
- Sesult: trajectory-valued chain, unconditioned S-I-R as equilibrium.

### From incidents to unconditioned epidemic trajectories (1/3)

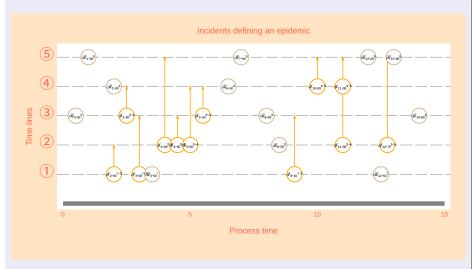


Figure 1: Light-orange circles denote potential infections (arrows point upwards to targets); light-brown circles denote potential removals.

### From incidents to unconditioned epidemic trajectories (2/3)

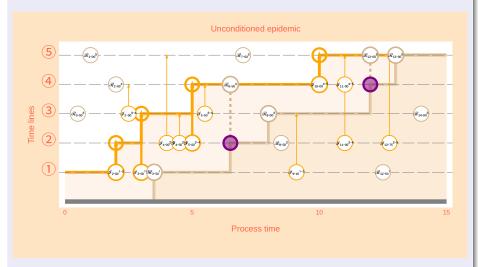


Figure 2: Activate *infection* if target on lowest uninfected timeline. *removal* if in infected region and remove lowest infected (purple disk if different timeline).

### From incidents to unconditioned epidemic trajectories (3/3)

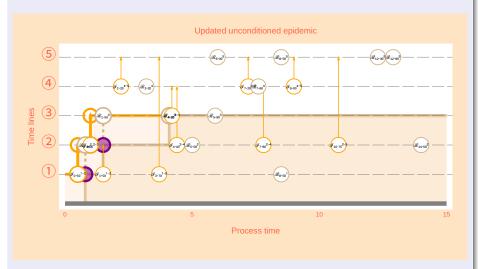


Figure 3: A step in algorithmic time for the unconditioned epidemic simply involves replacing the original incidents by a new set of incidents.

## Crucial technical point

- Updates in algorithmic time  $\tau$  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:
  - Replace removals (Rs);

  - 3 Replace infections (Is).
- Re-express using continuously varying  $\tau$ . 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)

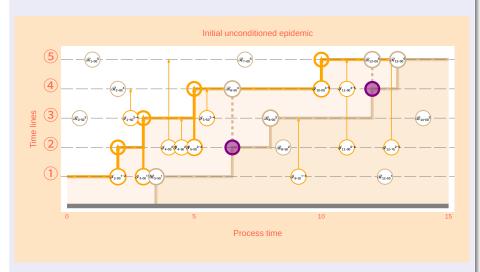


Figure 4: No change to removals or infections

## Illustration of technical point (2/8)

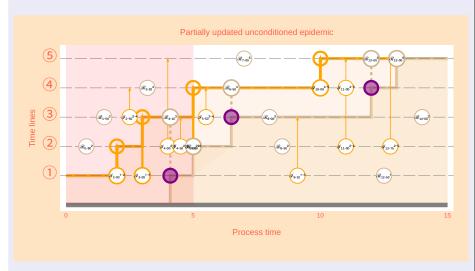


Figure 5: Replace first third of removals, infections unchanged

## Illustration of technical point (3/8)

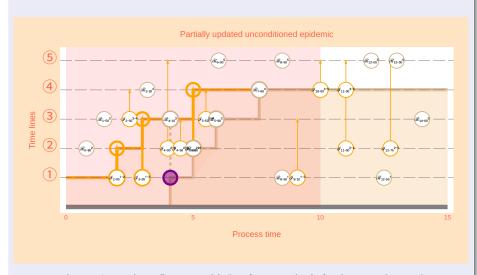


Figure 6: Replace first two-thirds of removals, infections unchanged

## Illustration of technical point (4/8)

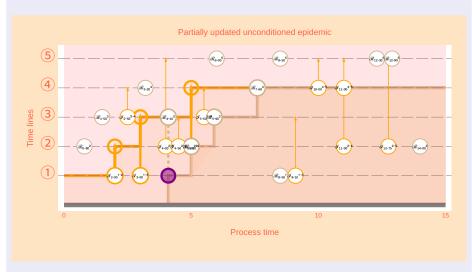


Figure 7: All removals resampled, infections unchanged

## Illustration of technical point (5/8)

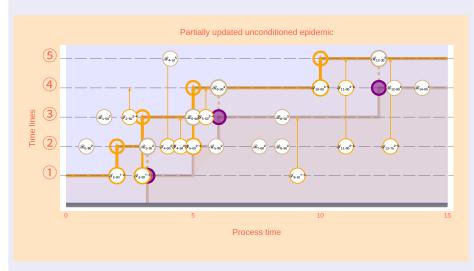


Figure 8: Re-sample all removal timelines, infections unchanged

## Illustration of technical point (6/8)

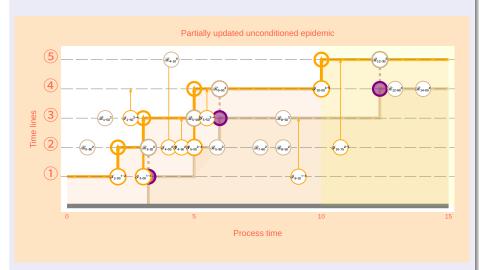


Figure 9: Re-sample last third of infections

## Illustration of technical point (7/8)

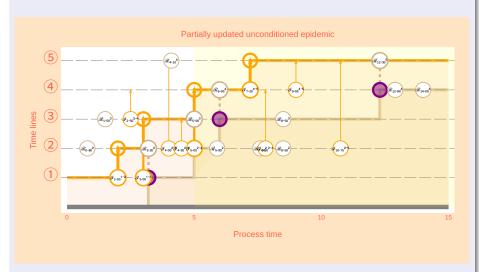


Figure 10: Re-sample last two-thirds of infections

## Illustration of technical point (8/8)

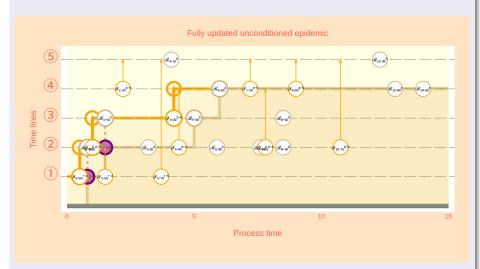


Figure 11: All infections now re-sampled.

## 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 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

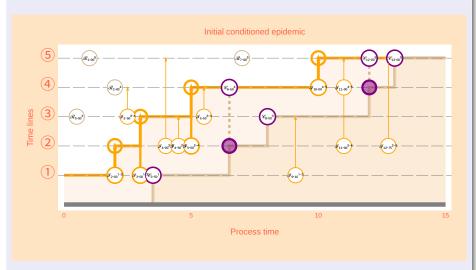


Figure 12: Initial epidemic with conditioned removals indicated using purple circles (and purple disks when different timelines are infected).

### Conditional epidemic update

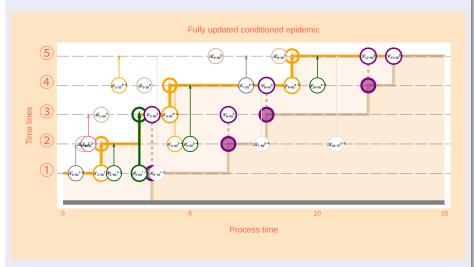


Figure 13: Epidemic updated under restriction: all conditioned removals remain activated, no new removals are activated. Green infections have been "perpetuated".

### Last feasible epidemic (LFE)

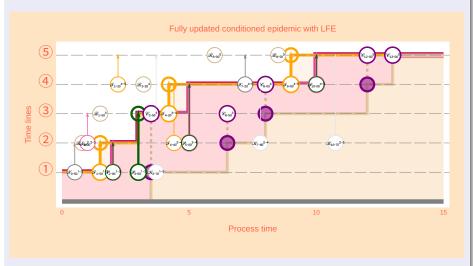


Figure 14: LFE computed recursively working right-to-left: the slowest sequence of infections deals with all infected timelines in order (includes perpetuated infections).

### No-fly zone (NFZ)

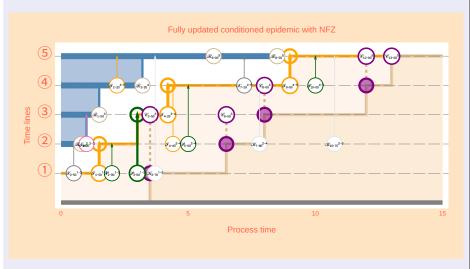


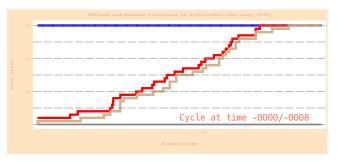
Figure 15: NFZ computed recursively working right-to-left: trace region of timelines that must not be infected if one is not to activate unobserved removals.

## Example

 Smallpox outbreak in a closed community of 120 individuals in Abakaliki, Nigeria (much studied! see 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 I<sub>0</sub> 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  $\alpha$  and  $\beta$ , when we need inference on R-number  $\alpha$   $n/\beta$  for *unknown*  $\alpha$  and  $\beta$ ?
- Good question. But a re-weighting argument allows us to get (unbiased) estimates based on *different*  $\alpha$  and  $\beta$ . 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  $\alpha$  and  $\beta$ ;
  - construct steepest ascent algorithm (in effect, variant of Robbins-Monro stochastic optimization) to find *maximum a posterior* estimates of  $\alpha$  and  $\beta$ ;
  - or even, with some computational effort, compute the entire posterior joint density for  $\alpha$  and  $\beta$ !
- 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?**



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## Image information

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



# A "near-maximal" configuration

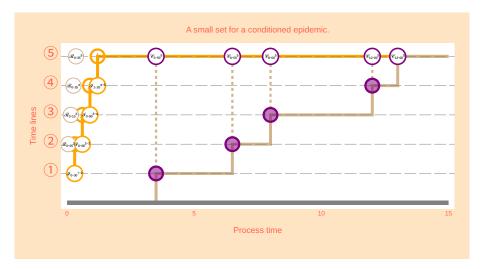


Figure 16: A conditional epidemic in which all activated infections occur before time 3.0, also before smallest observed removal time.

#### 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        | 2.2.585   | master | Wed Jan 15 16:27:48 2025 |

## Revision history

These notes were produced from PerfectEpidemics.qmd:

Author: Wilfrid Kendall W.S.Kendall@warwick.ac.uk

Date: Wed Jan 15 16:27:48 2025 +0000

Summary: Editing for style.

Added appendix on near-maximal configuration.