

Perfect Epidemics

Applied Probability Seminar

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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.

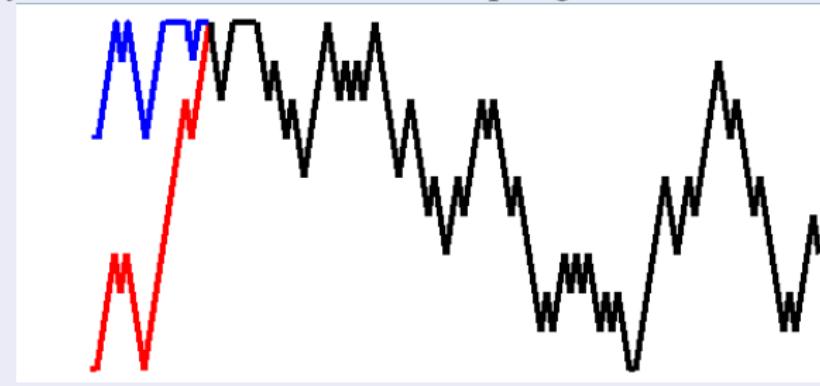
This is initial work on using perfect simulation (CFTP) for epidemics.
WSK acknowledges the support of UK EPSRC grant EP/R022100.

1. Introduction to Perfect Simulation

- Propp & Wilson (1996) invented exact simulation / Coupling from the Past (CFTP) / perfect simulation;
- The term “perfect simulation” (WSK, 1998) was chosen so as to make you suspicious: perfection is never achieved!
- 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).

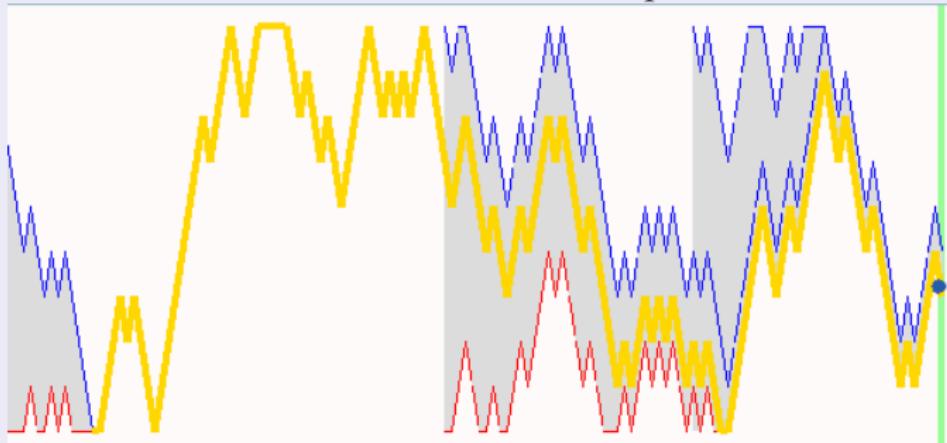
Classic CFTP for a simple random walk (I)

- Consider a simple random walk on $0:9 = \{0, 1, 2, 3, 4, 5, 6, 7, 8, 9\}$.
 - $\mathbb{P} [+1 \text{ jump}] = p \in (0, 1)$, while $\mathbb{P} [-1 \text{ jump}] = 1-p$, **except that**
 - at state 9 replace the +1 jump by “staying still”, **and**
 - at state 0 replace the -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)

- Start at top (9) and bottom (0) at negative time $-T$, run to time 0.
- If not coupled by time 0, then back-off to time $-2T$ and repeat.
NB re-use randomness!
- 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!



A little 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 (**SBC & WSK, 2007a**; *nb* corrigendum **SBC & 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**.)

2. 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: $S \rightarrow S - 1$, $I \rightarrow I + 1$ at rate $\alpha S I$,

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.



Inference on the R-number

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

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

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)

An important step on the way: generating an *unconditioned* epidemic.

- ➊ Thus n, α, β are known, removal times are 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 First step: 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.

From incidents to unconditioned epidemic trajectories (1/3)

Incidents defining an epidemic

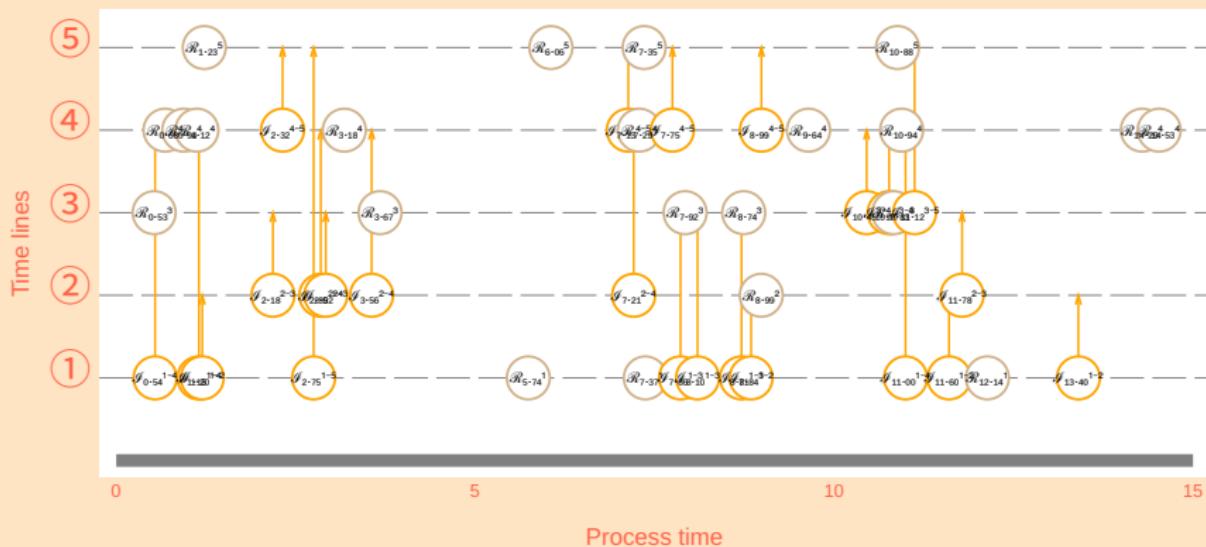


Figure 1: Light-orange circles denote potential infections (arrows point upwards to targets); light-brown circles denote potential removals.

From incidents to unconditioned epidemic trajectories (2/3)

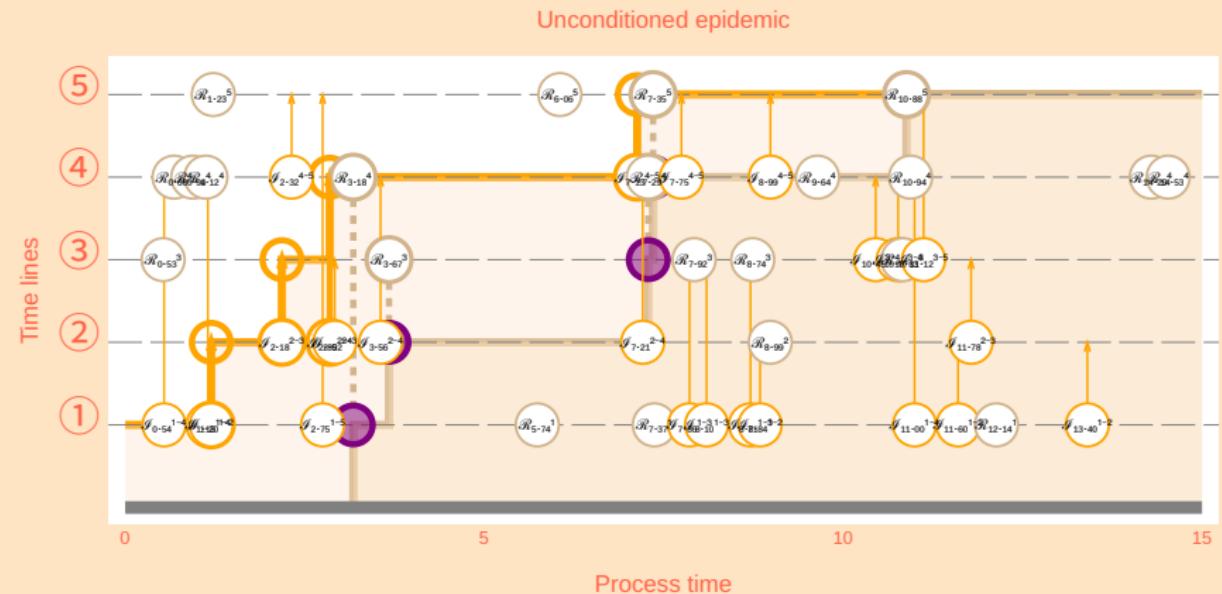


Figure 2: Activate (a) *infection* if target on lowest uninfected timeline; (b) *removal* if in infected region, then remove lowest infected (purple disk if different timeline).

From incidents to unconditioned epidemic trajectories (3/3)

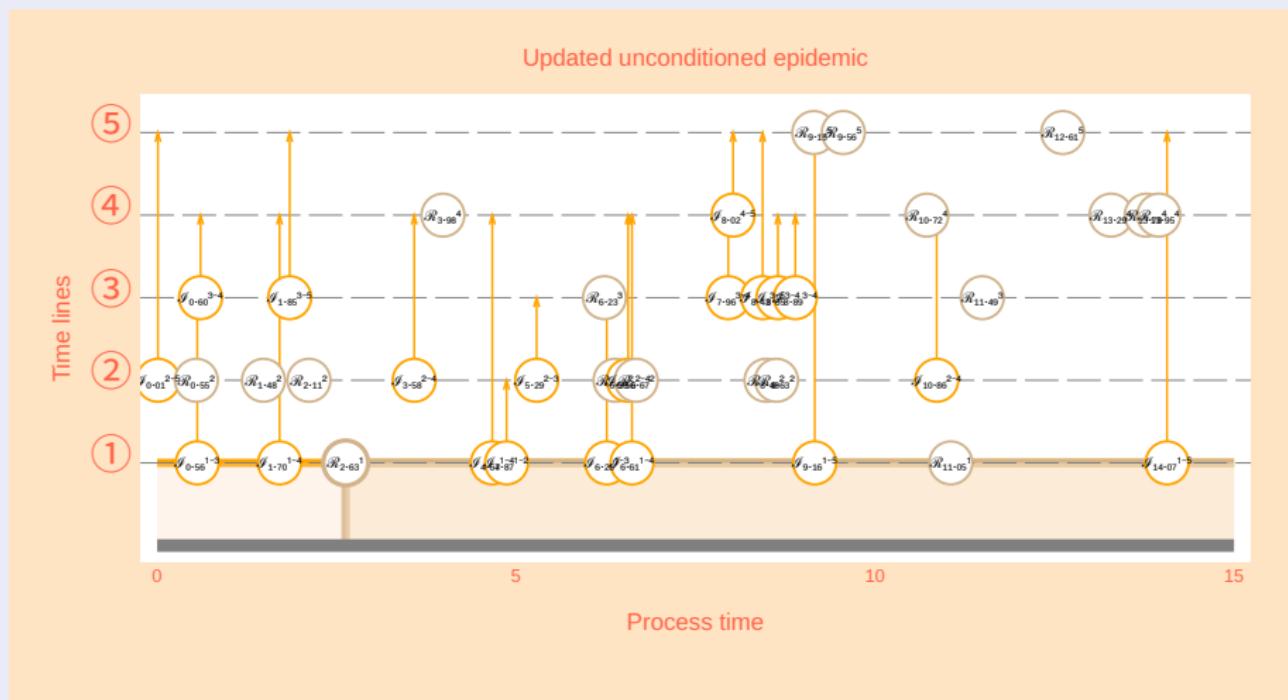


Figure 3: A step in algorithmic time for the unconditioned epidemic simply involves replacing the original incidents by a new set of incidents.

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:
 - ① Replace removals (Rs);
 - ② Re-sample timelines (though not times) of Rs ;
 - ③ Replace infections (Is).
- Re-express using continuously varying τ . Process time runs over $[0, T]$.
 - ① 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 ;
 - ③ For $(2n+1)T < \tau < (2n+2)T$, update old Is 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)

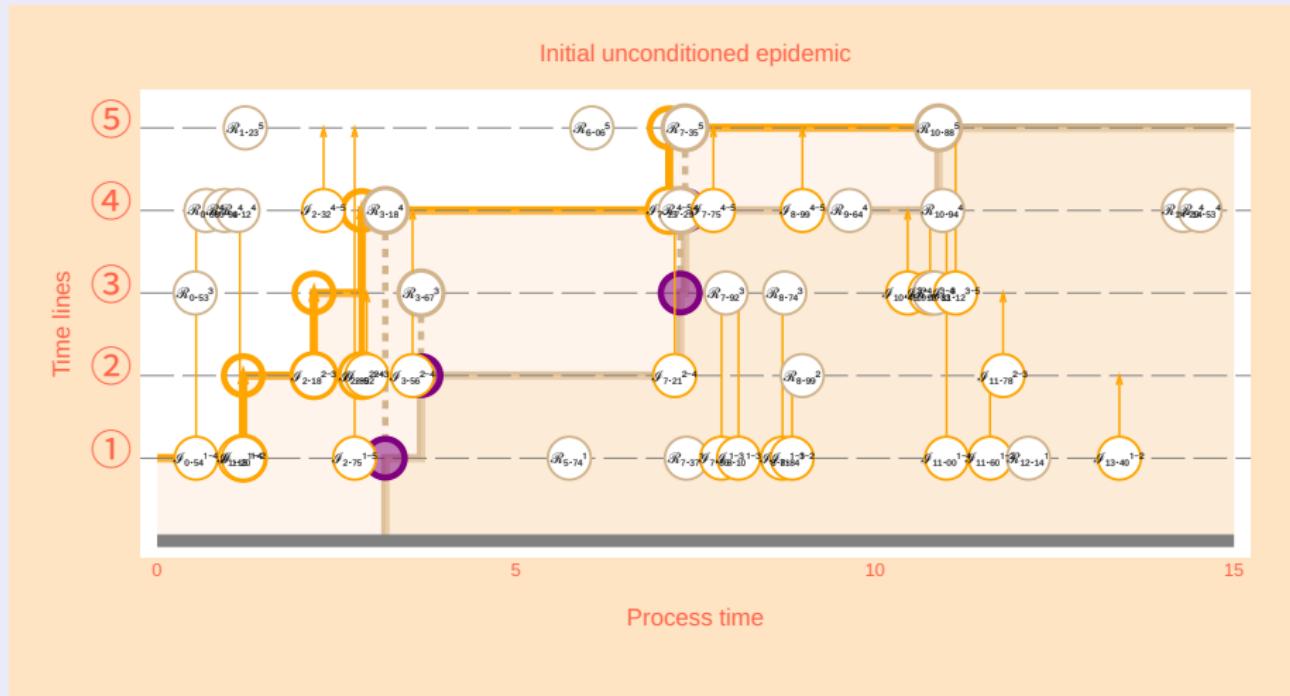


Figure 4: No change yet to removals or infections;

Illustration of technical point (2/8)

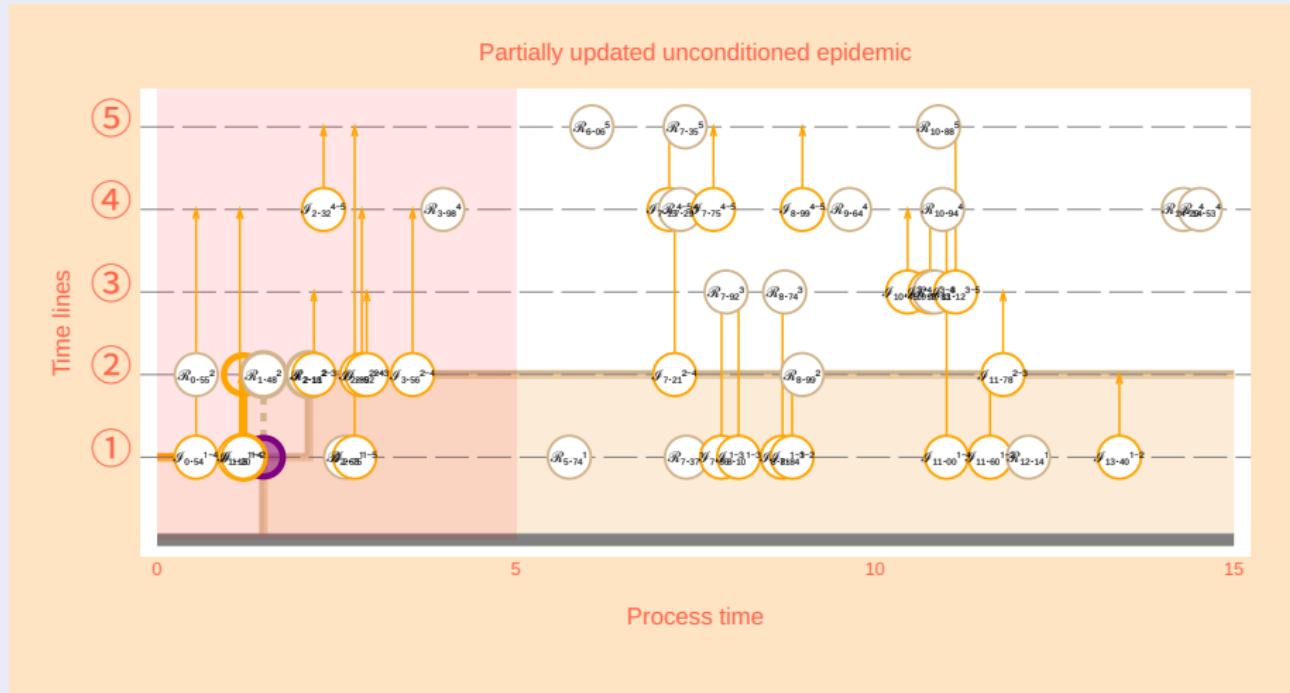


Figure 5: Replace first third of removals, infections unchanged;

Illustration of technical point (3/8)

Partially updated unconditioned epidemic

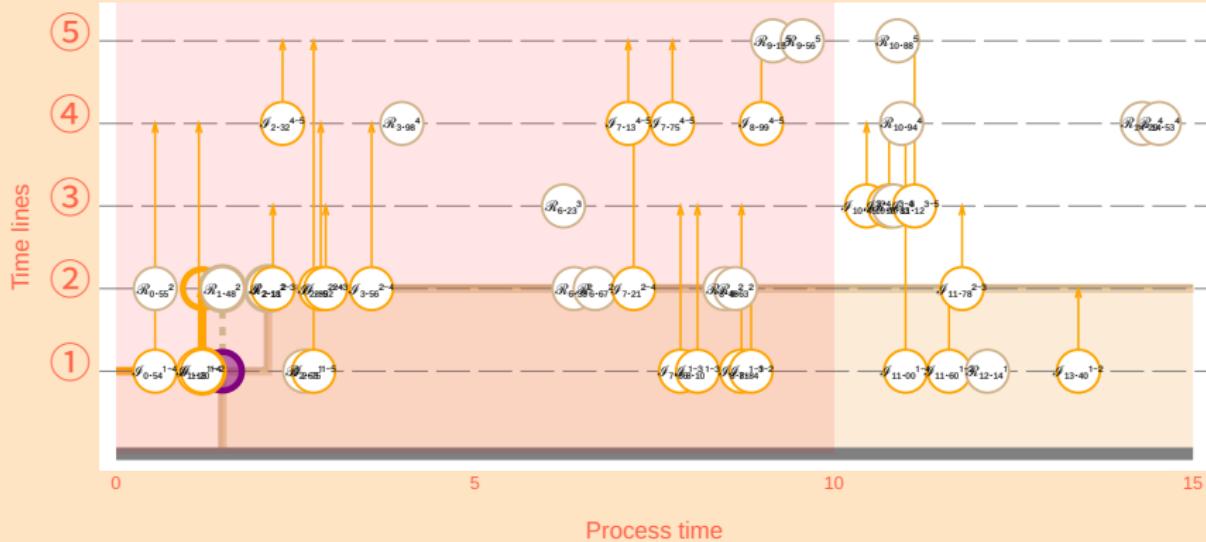


Figure 6: Replace first two-thirds of removals, infections unchanged;

Illustration of technical point (4/8)

Partially updated unconditioned epidemic

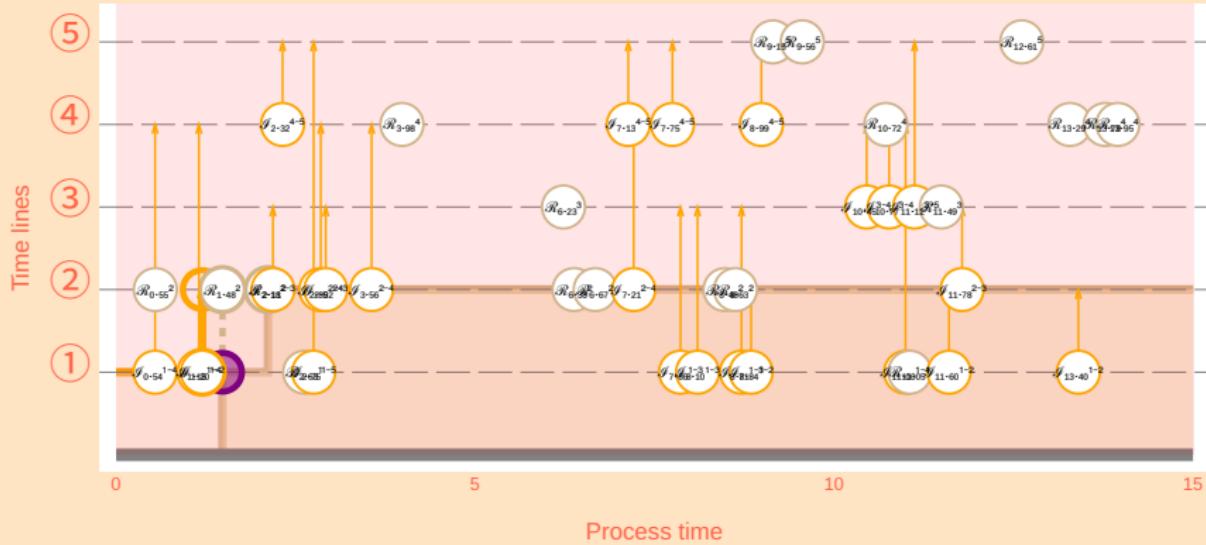


Figure 7: All removals resampled, infections as yet unchanged;

Illustration of technical point (5/8)

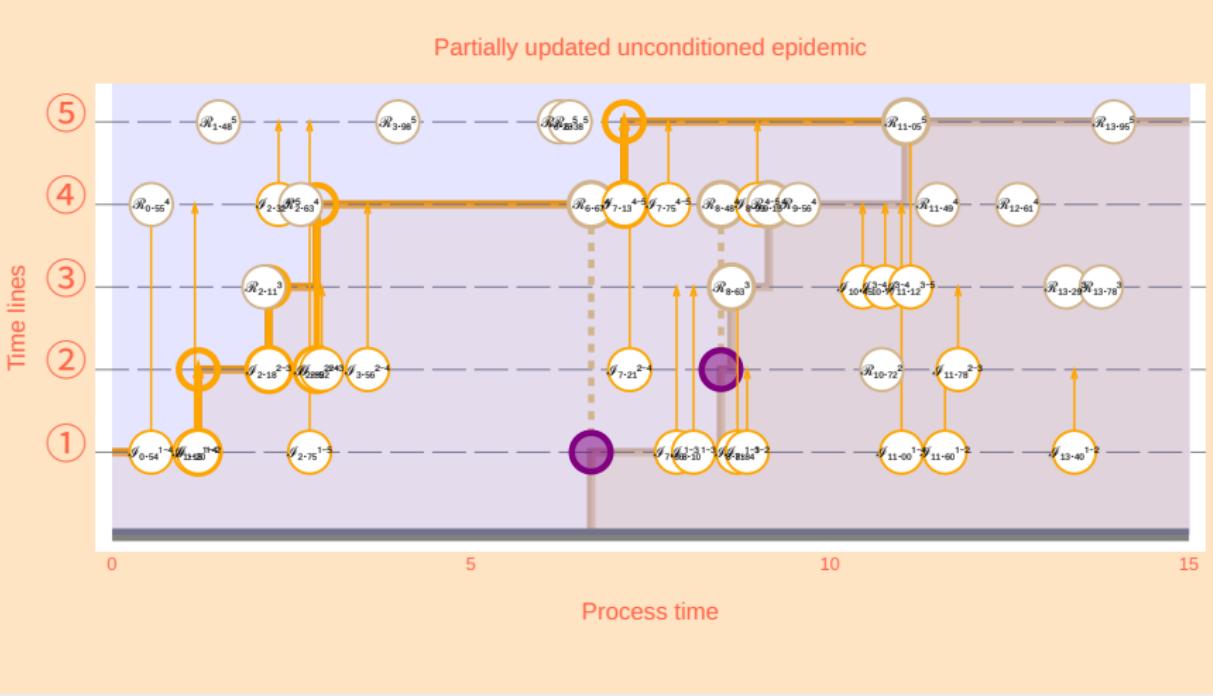


Figure 8: Re-sample all removal timelines, infections as yet unchanged;

Illustration of technical point (6/8)

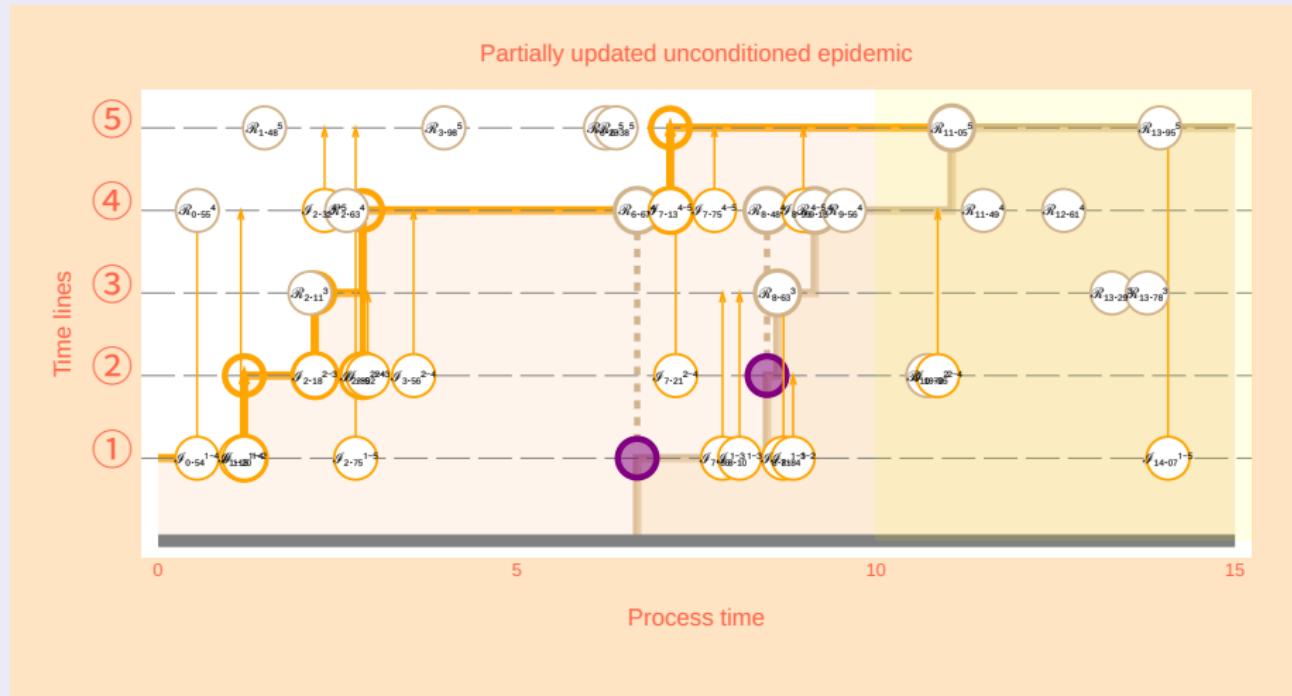


Figure 9: Re-sample last third of infections;

Illustration of technical point (7/8)

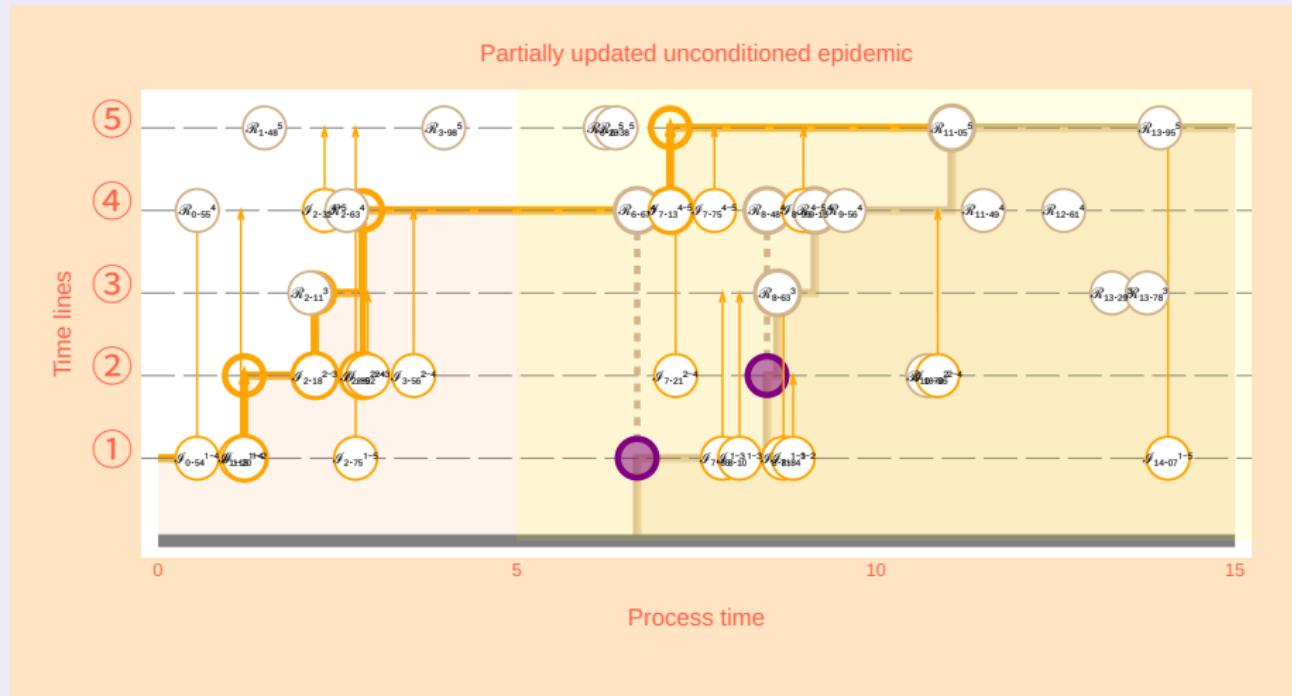


Figure 10: Re-sample last two-thirds of infections;

Illustration of technical point (8/8)

Fully updated unconditioned epidemic

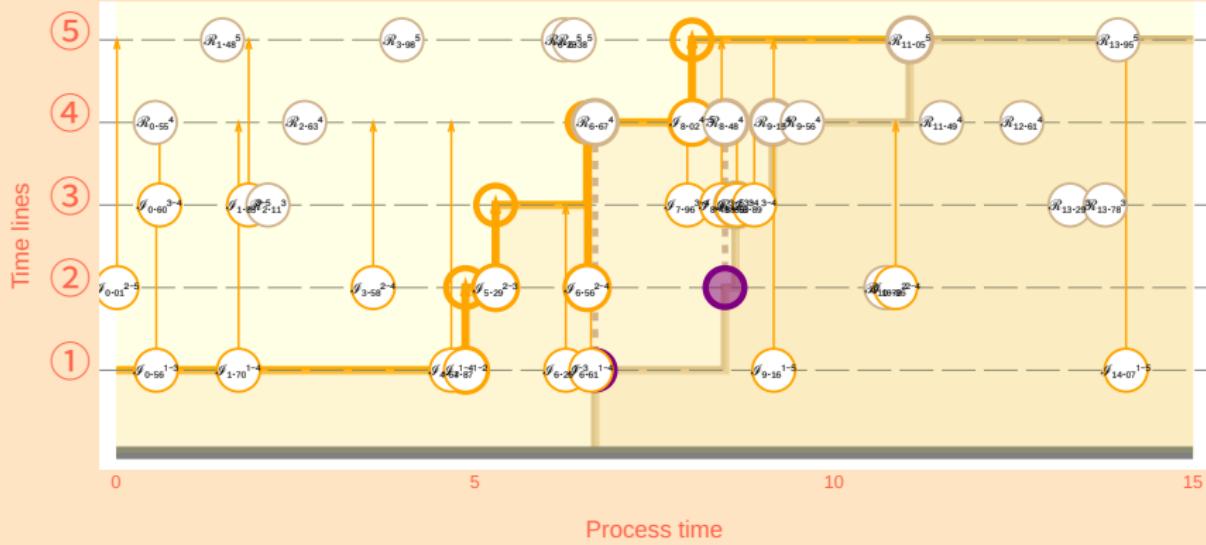


Figure 11: All infections now re-sampled.

3. 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** used to establish that monotonicity still works: *last feasible epidemic (LFE)* and *no-fly zone (NFZ)*.

Initial conditional epidemic

Initial conditioned epidemic

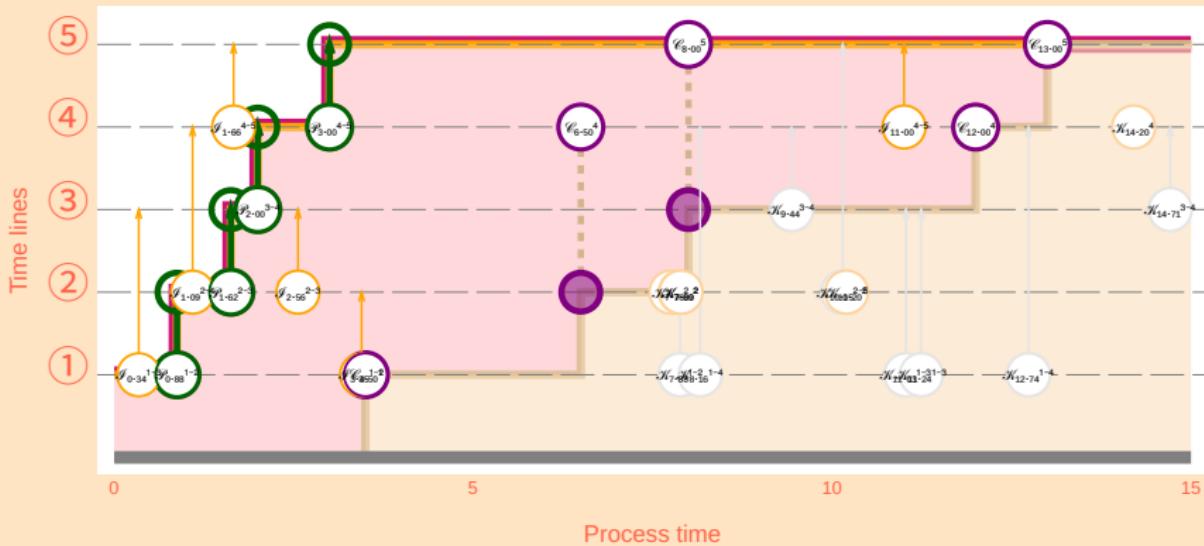


Figure 12: Initial epidemic with conditioned removals indicated using purple circles (and purple disks when different timelines are infected).

Conditional epidemic update

Fully updated conditioned epidemic

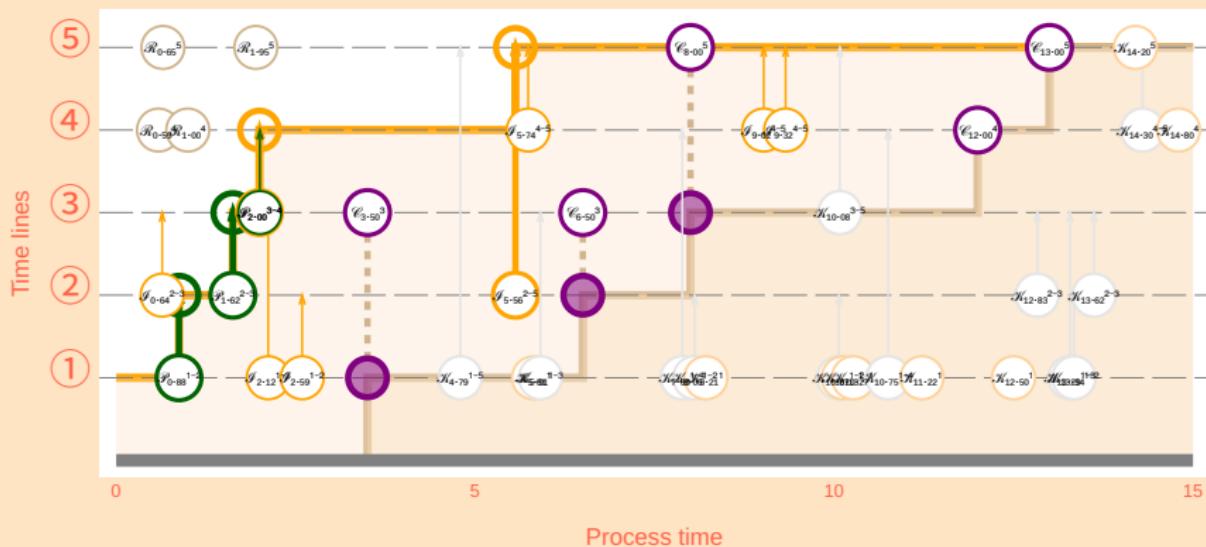


Figure 13: Epidemic updated under restriction: all conditioned removals remain activated, no new removals are activated. Green infections have been “perpetuated”.

Last feasible epidemic (LFE)

Fully updated conditioned epidemic with LFE

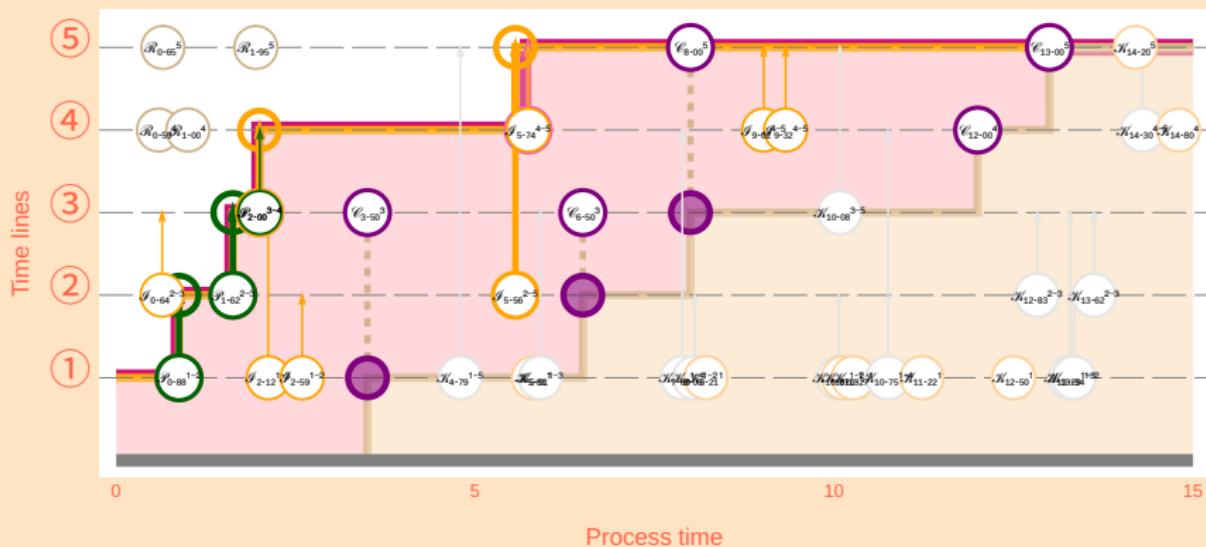


Figure 14: LFE computed recursively working right-to-left: the slowest sequence of infections deals with all infected timelines in order (includes perpetuated infections).

No-fly zone (NFZ)

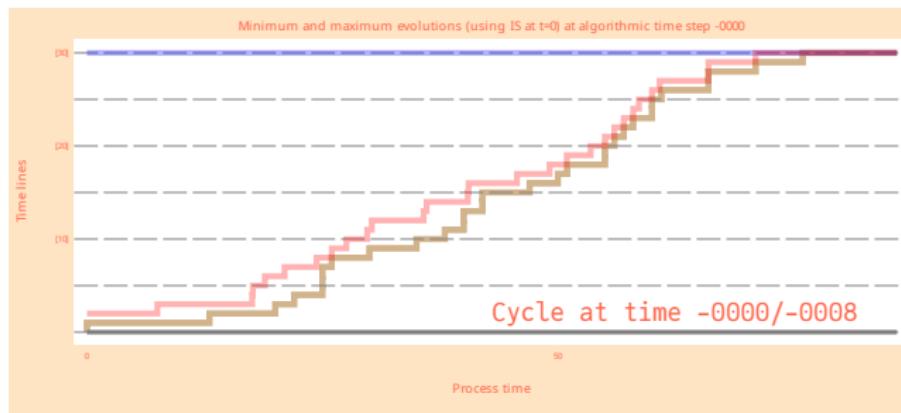
Fully updated conditioned epidemic with NFZ



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.

4. 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_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 obtain a perfect simulation **GIF** or **MP4** 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 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 SBC & 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?**



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Image information

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

Previous instances of this talk

<i>Date</i>	<i>Title</i>	<i>Location</i>
19/04/24	Perfect Epidemics	Short Research Talk (12min)
15/05/24	McMC and Perfect Simulation	Graduate Seminar, Aristotle Univ. (50min)
17/01/25	Perfect Epidemics	Applied Probability Seminar (50min)

Appendix A: A “near-maximal” configuration

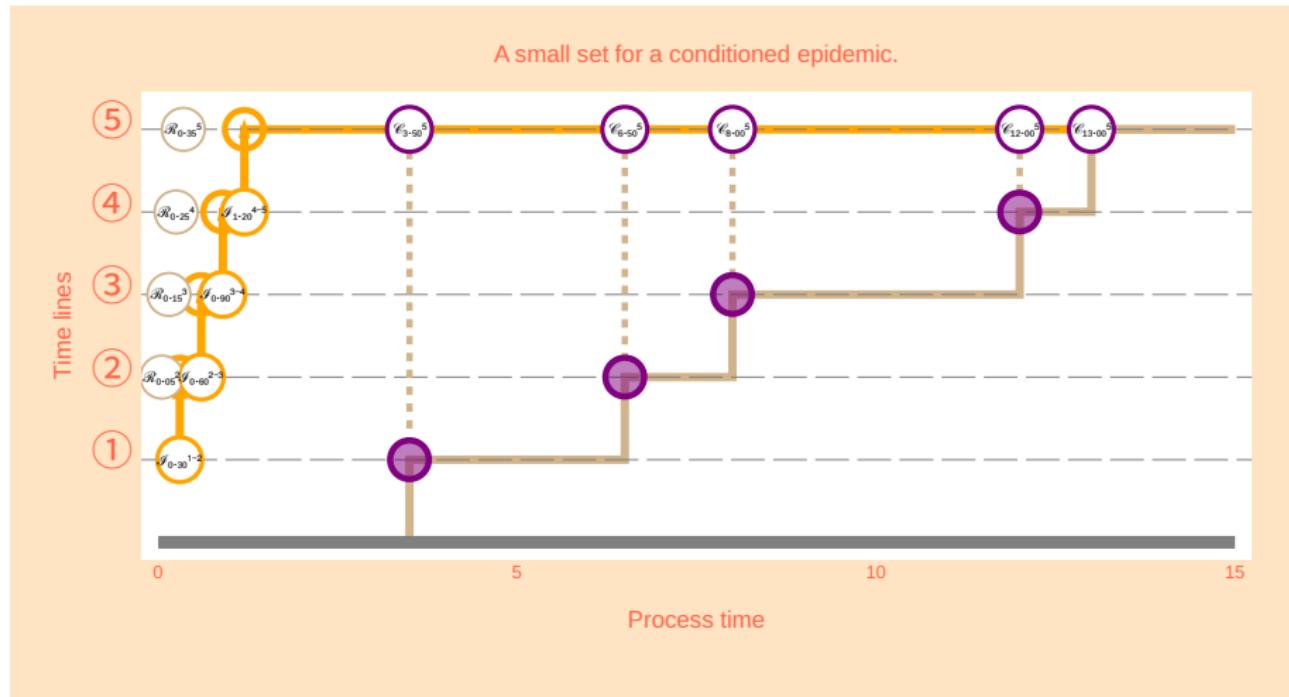


Figure 16: A conditional epidemic in which all activated infections occur before time 3.0, also before smallest observed removal time.

Appendix B: Updating a conditional epidemic INCOMPLETE

We now work through the update of the conditional epidemic in stages.

Initial conditional epidemic (1/8)

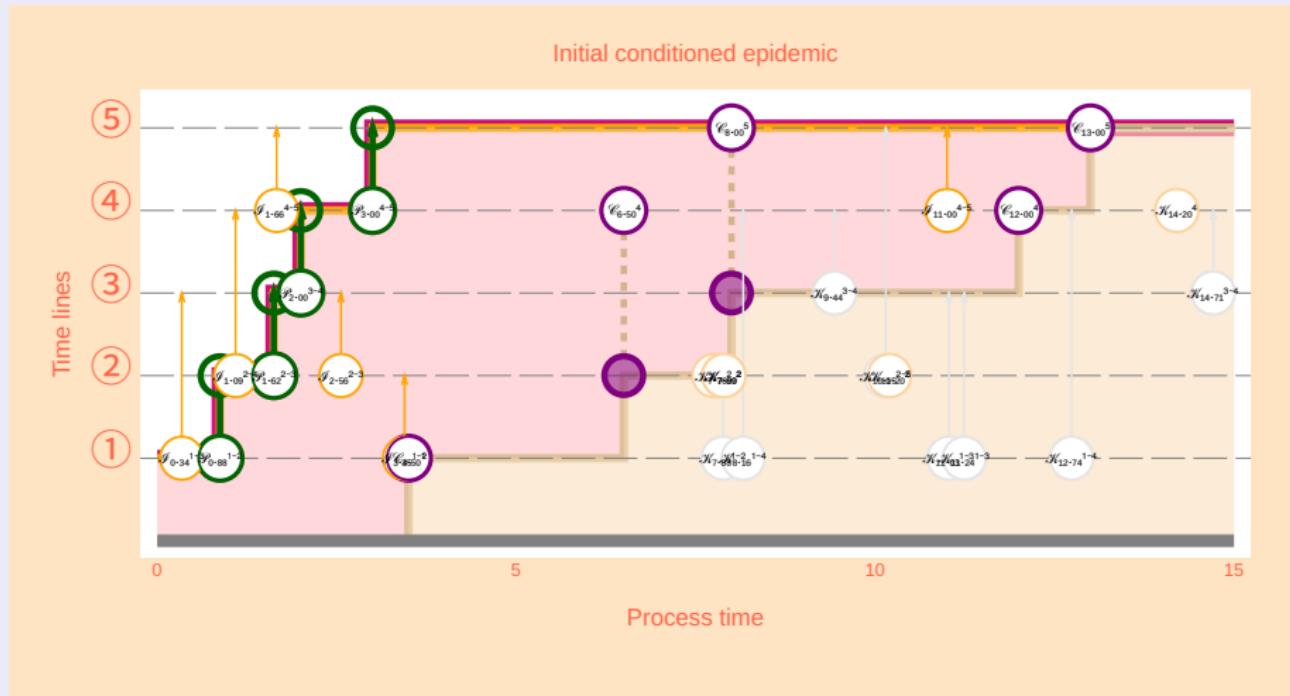


Figure 17: Initial epidemic with conditioned removals indicated by purple circles.

Conditional epidemic (2/8)

Partially updated conditioned epidemic

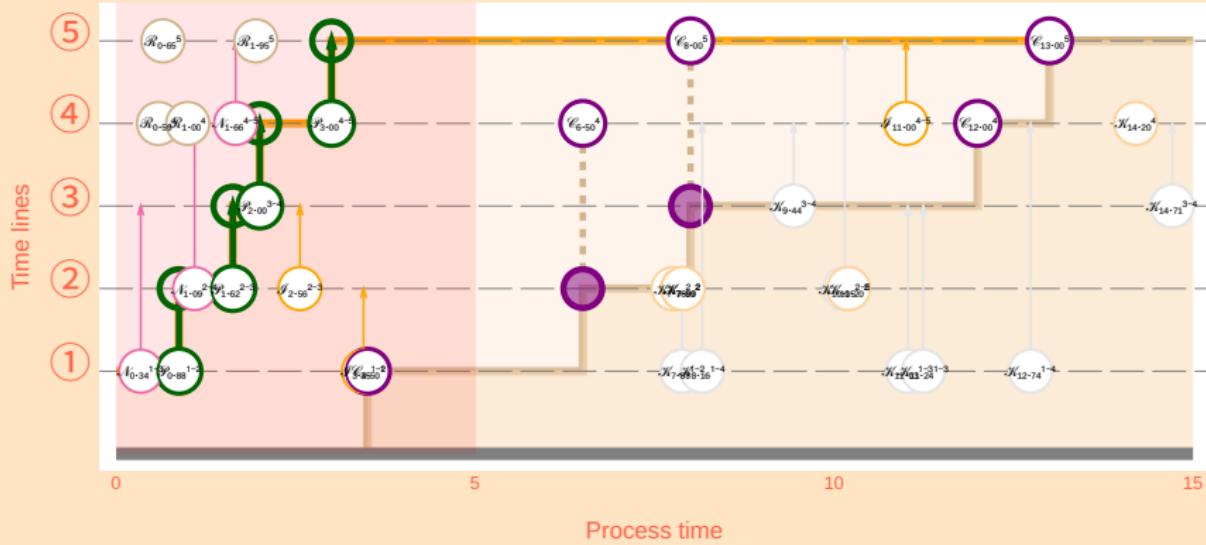


Figure 18: Replace first third of removals, infections unchanged;

Conditional epidemic (3/8)

Partially updated conditioned epidemic

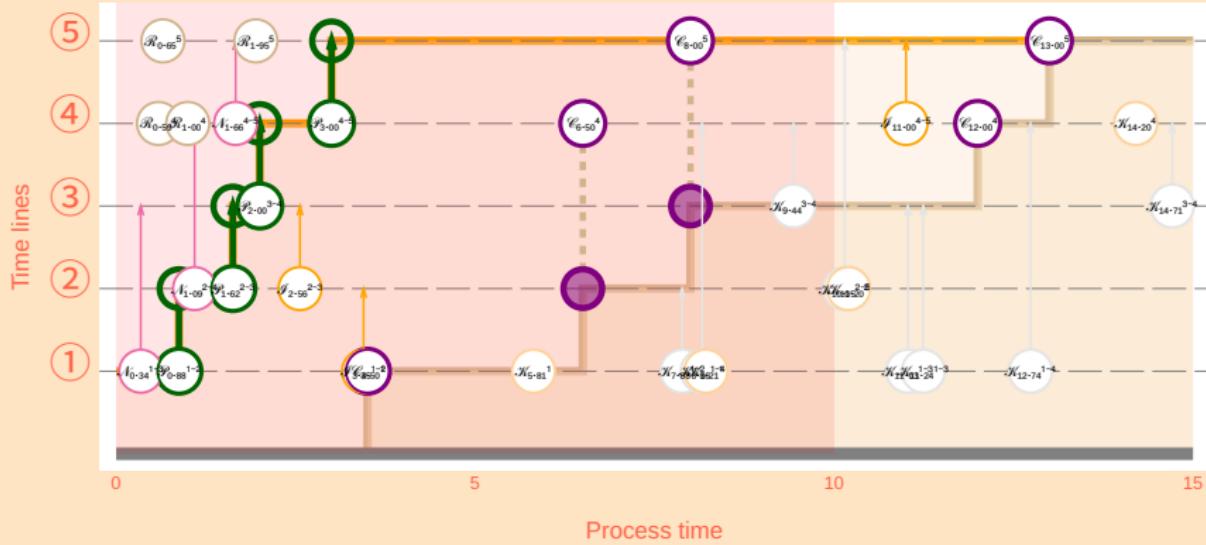


Figure 19: Replace second third of removals, infections unchanged;

Conditional epidemic (4/8)

Partially updated conditioned epidemic

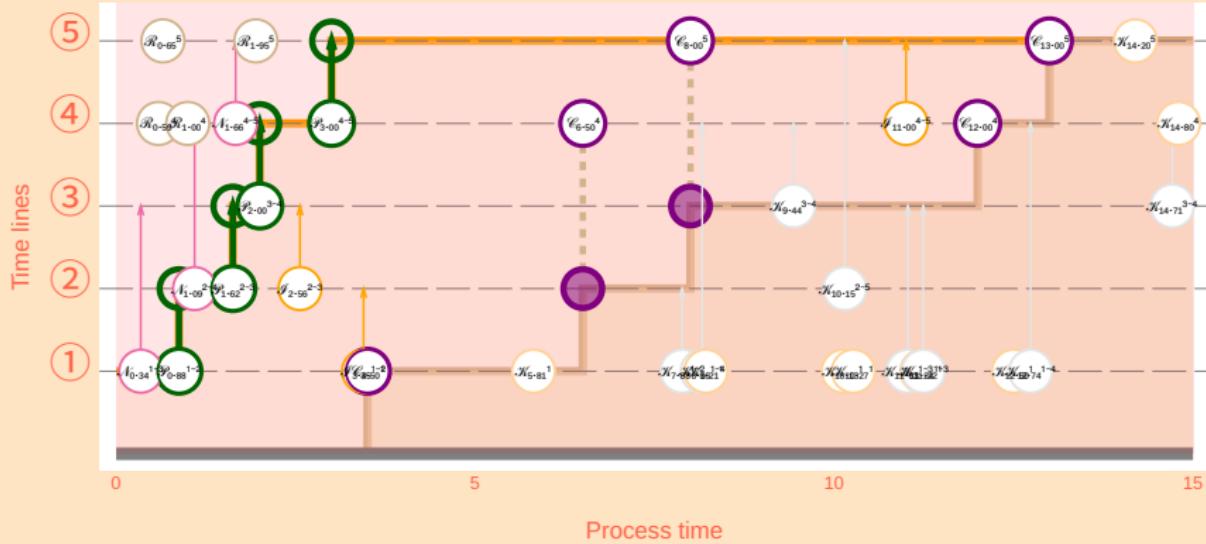


Figure 20: Replace remaining removals, infections unchanged;

Conditional epidemic (5/8)

Partially updated conditioned epidemic



Figure 21: Re-sample all removal timelines, infections as yet unchanged;

Eventual conditional epidemic after use of an innovation (6/8)

Still to be done: 1/3 of way through new infections, display current LFE and NFZ.

Eventual conditional epidemic after use of an innovation (7/8)

Still to be done: 2/3 of way through new infections, display current LFE and NFZ.

Eventual conditional epidemic after use of an innovation (8/8)

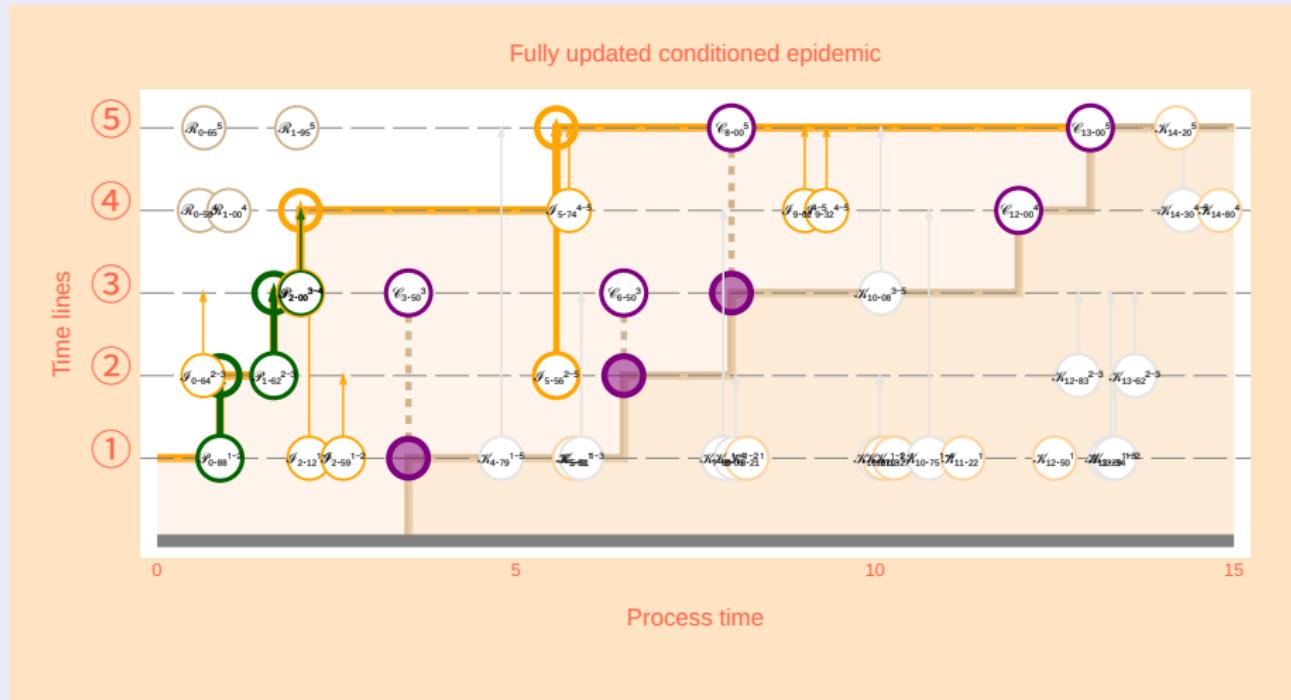


Figure 22: All infections now re-sampled. Green infections are “perpetuated”.

Appendix C: Naive approach to compartment models fails

- Consider a modification of this approach to the case of compartmentalized populations.
- Focus on the extreme case in which every individual j has infectivity (outgoing to individual k) $\alpha_{j,k}$ and removal parameter β_j .
- Suppose the conditioning on removals is specifically about named individuals j being removed at specified times r_j ; suppose also there are no “occult” (unobserved) removals for any other individuals.
- This would apply, for example, in the case of the *Diamond Princess* if α , β depended on age and location of cabin on the ship.

- ① Individuals no longer exchangeable, so S-I-R state space is unsuitable.
- ② Given population $N \in \mathbb{N}$, the ground space is a tuple of n timelines $(i, [0, T])$, one timeline per individual i , where T is the final time of observation of the epidemic.
- ③ Typical element of state-space: a locally-finite point pattern of
 - ▶ infections $\mathcal{I} = \mathcal{I}_{i,j}(t)$, marked by timelines i at various times t , each infection marked by a target timeline j other than its mark k ;
 - ▶ (inactivated) removals $\mathcal{R} = \mathcal{R}_i(t)$, marked by timelines i at times t ;
 - ▶ conditional removals $\mathcal{C} = \mathcal{C}_i(t)$, marked by timelines i at times t .
- ④ Initial stipulations:
 - ▶ the \mathcal{I} s, \mathcal{R} s and \mathcal{C} s all occur at different times;
 - ▶ there is at most one \mathcal{C} per timeline;
 - ▶ for convenience, no \mathcal{I} or \mathcal{R} occur after a \mathcal{C} on the same timeline;
- ⑤ Epidemic can be viewed as a union of intervals on different timelines;
 - ▶ intervals end at the \mathcal{C} in the timeline or at time T ;
 - ▶ intervals on initially infected timelines start at time 0;
 - ▶ intervals on eventually infected timelines start at the first time t an \mathcal{I} targets the timeline while marked by a timeline infected at t .

Process dynamics

Recall that infections and removals *after* a conditional removal have been censored out. A valid configuration must satisfy the following, derived from the process dynamics:

- ① initially infected timelines i possess no \mathcal{R}_i : if they possess a (single) $\mathcal{C}_i(t)$ then they contribute $(i, [0, t))$ to the epidemic, otherwise $(i, [0, T))$;
 - ② other timelines k only contribute if they possess $\mathcal{I}_{k,i}(s)$ such that timeline k is infected at time s , in which case the earliest s is chosen and the contribution is $(i, [s, t))$ when $\mathcal{C}_i(t)$ is the conditional removal of the timeline, otherwise $(i, [s, T))$;
 - ③ every inactivated removal $\mathcal{R}_i(t)$ satisfies $t < s$, where s is the time of first infection of the timeline i .
 - ④ every conditioned removal $\mathcal{C}_i(t)$ is at the right t of an infected interval.
- So each timeline is divided into a *susceptible interval* (empty if it is initially infected), an *infected interval* (empty if it is never infected), and a *removed interval* (empty if it has no conditioned removal).

Dynamics in algorithmic time

This closely corresponds to the evolution of the S-I-R epidemic above, but does not resample the mark i for each conditional removal \mathcal{C}_i ;

- ① Remove all \mathcal{R} s, and re-sample inactivated removals on the susceptible intervals of each timeline. Recompute **NFZ** as a union of $(i, [0, t_i))$ using the latest time $t_i = t$ of re-sampled $\mathcal{R}_i(t)$.
- ② List in *time-reverse order* original infections together with sampled *new* candidate $\tilde{\mathcal{I}}$ s in complements of the removed intervals.
- ③ Work iteratively through this list. Would discarding original $\mathcal{I}_{i,j}(t)$ result in failure to infect a conditional removal?. If so, **retain** $\mathcal{I}_{i,j}(t)$ as *perpetuated infection* $\mathcal{P}_{i,j}(t)$, otherwise **discard**.
- ④ Otherwise, at $\tilde{\mathcal{I}}_{a,b}(u)$, consider the latest update of **NFZ**.
 - ▶ If a infected at u and u is in b component of latest **NFZ**, **discard** $\tilde{\mathcal{I}}_{a,b}(u)$;
 - ▶ If a is not infected at u but u lies on b component of latest **NFZ**, **update** **NFZ** by adding/replacing interval of **NFZ** at a using $(a, [0, u))$;
 - ▶ Otherwise **retain** $\tilde{\mathcal{I}}_{a,b}(u)$ as $\mathcal{I}_{a,b}(u)$.

As in S-I-R case, the conditioned epidemic is the unique equilibrium.

Requirements for monotonicity

For CFTP we need to know that, for coupled iterations (using the same pattern of innovations of new \mathcal{I} s and \mathcal{R} s), if two variants are started so that the infected region of one contains the other, then this persists through development of the algorithmic time.

It would suffice to prove two technical results:

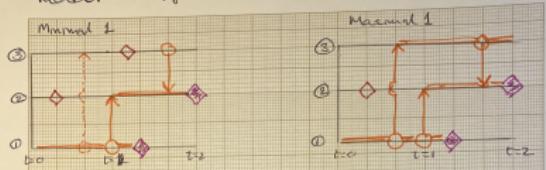
- ① If the old infected region of one contains the other, then the **NFZ** of the one is contained in the **NFZ** of the other;
- ② If the old infected region of one contains the other, and the **NFZ** of the one is contained in the **NFZ** of the other, then the new infected region of the one is contained in the other.

Then CFTP would make sense, and it would only be necessary to show that accessibility of a set of near-maximal configurations guarantees eventual coalescence.

Counterexample to monotonicity

"Observe" generalization to compartmental model can fail to be monotone!

1/2/25



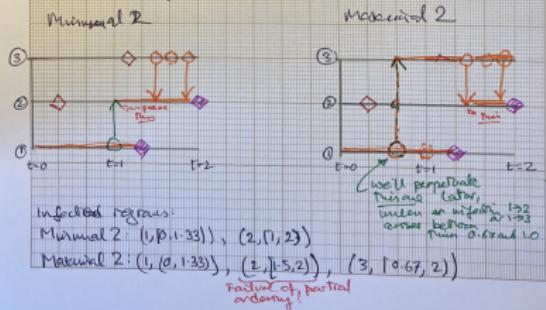
◆ Conditioned removal

◆ Infection

◆ Inactivated removal

This is after deleting all old inactivated removals and replacing by new inactivated removals.

Now work from right-to-left deleting all infections except where so doing would leave a conditioned removal uninfected. (and updating new ones)
At t=1 we get to:



Other technical information

Software used in computations

<i>Software</i>	<i>Version</i>	<i>Branch</i>	<i>Last commit</i>
quarto	1.6.39	—	
Running under julia	1.11.3	—	
EpidemicsCFTP	2.2.492	main	Thu Jan 23 20:50:07 2025
EpidemicsUtilities	0.1.2.156	main	Thu Jan 23 12:06:14 2025
This quarto script	2.2.619	Wilfrid-2025-01-30-compartment	Mon Feb 3 16:41:03 2025

Revision notes

These notes were produced from `PerfectEpidemics.qmd`:

Version:	2.2.620 [Wilfrid-2025-01-30-compartment]
Author:	Wilfrid Kendall <W.S.Kendall@warwick.ac.uk>
Date:	Mon Feb 3 17:54:28 2025 +0000
Summary:	Counterexample to naïve compartment model generalization. Stiffened up definition of evolution in algorithmic time. Added printing of <code>README.pdf</code> and <code>TODO.pdf</code> . Added <code>critic</code> filter using <code>_metadata.yml</code> .