Pair-based likelihood approximations for stochastic epidemic models

Stockdale et al. (*Biostatistics, 2019*)

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Problem framing

- Epidemic models afford insight into the incidence, spread, and control of contagions that threaten human welfare
  - How do mitigation efforts affect disease spread?
  - How do diseases spread between subpopulations?
- Partially observed process
  - Removal[1] times $r_1, \ldots, r_n$ ✓
  - Infection times $i_1, \ldots, i_n$ ✗
- Analyses with partial data
  - Integrate over $i_1, \ldots, i_n$
  - Or, augment $i_1, \ldots, i_n$ in Bayesian framework
- Independence between pairs of individuals provides **likelihood approximations** as fast frequentist methods.

[1] Removal means an individual can no longer infect others.

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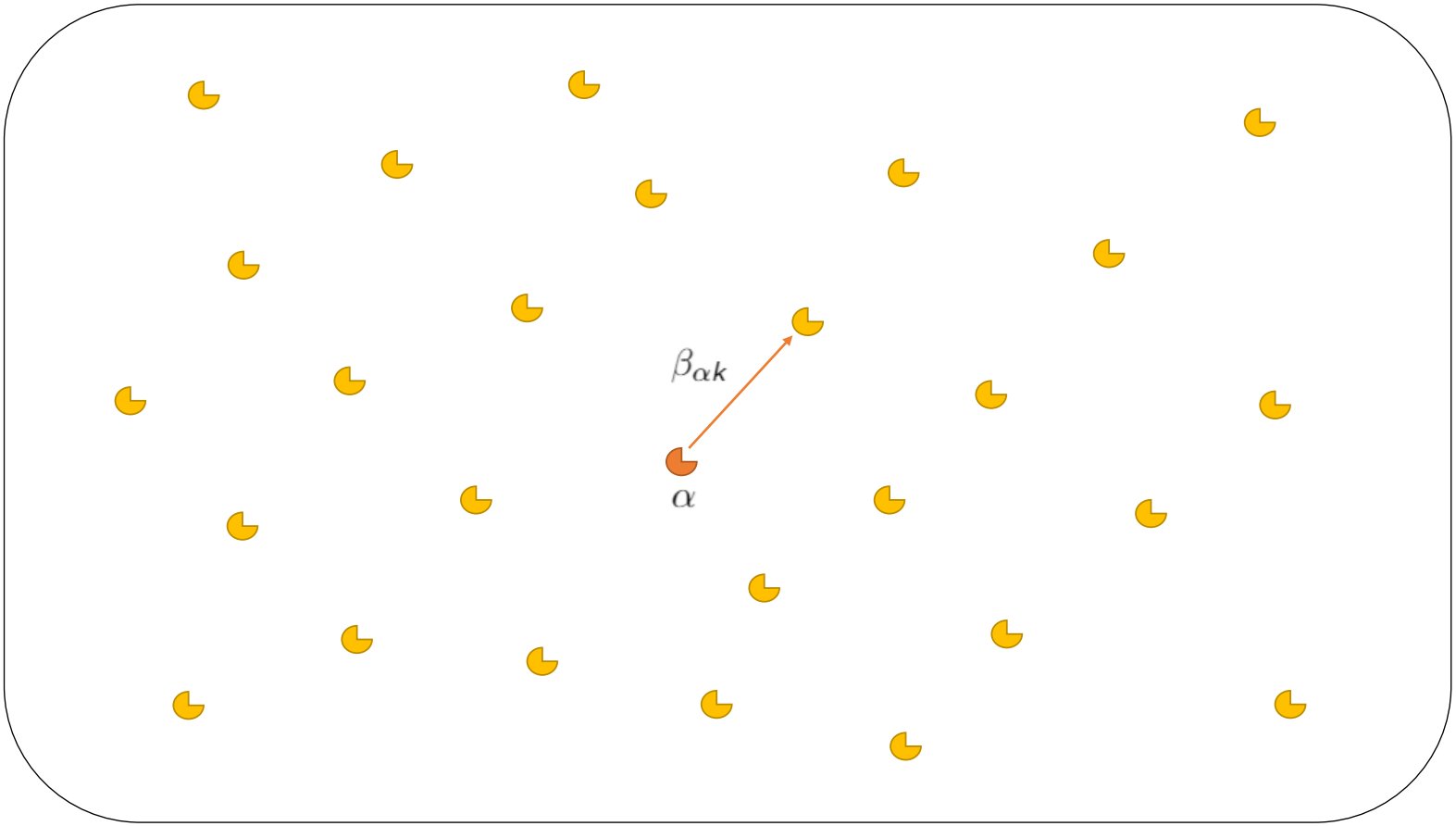
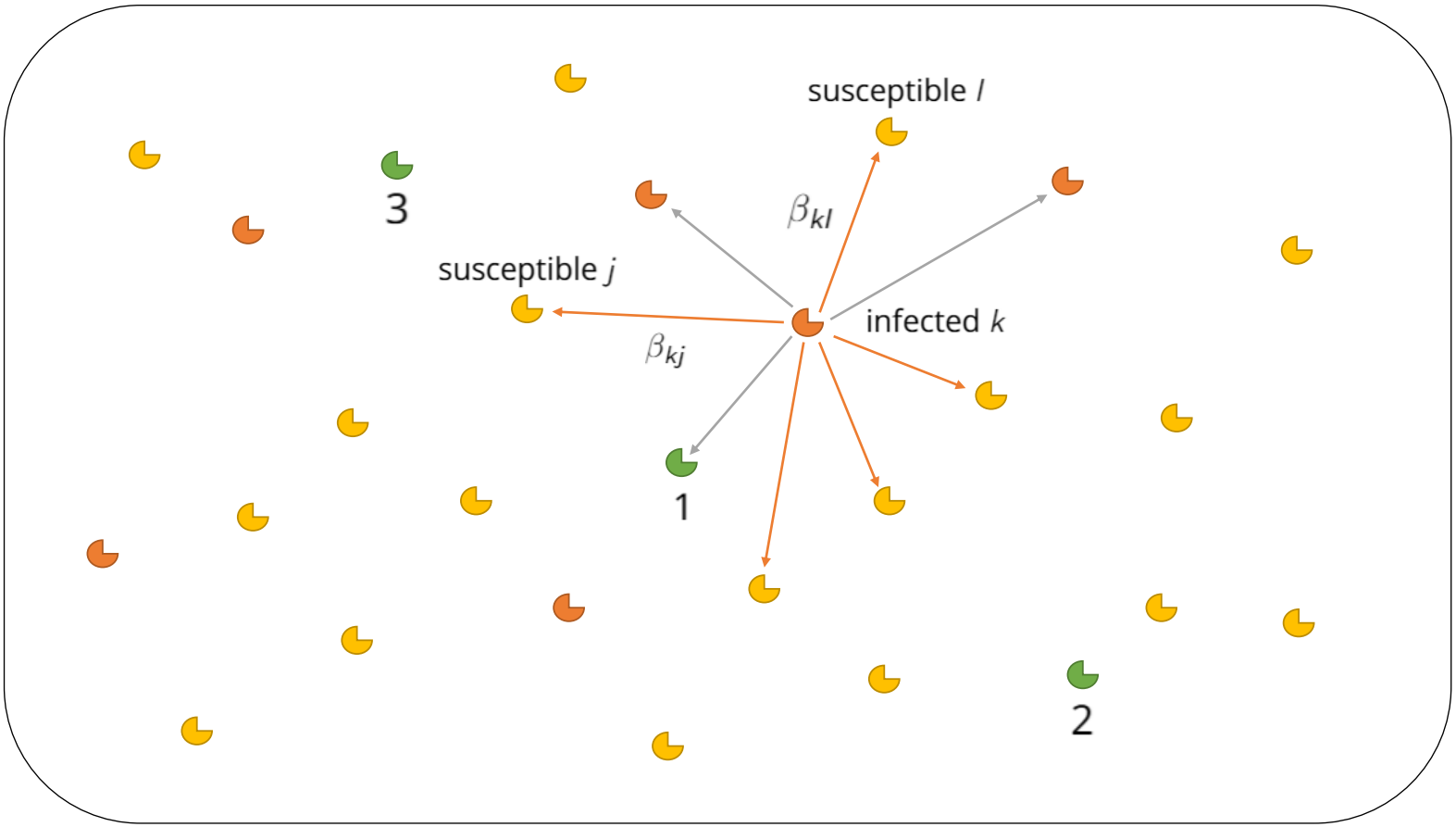
Stochastic epidemic

Infection rates β_{kj} and removals after $r_j - i_j \sim \text{Gamma}(m_j, \gamma_j)$



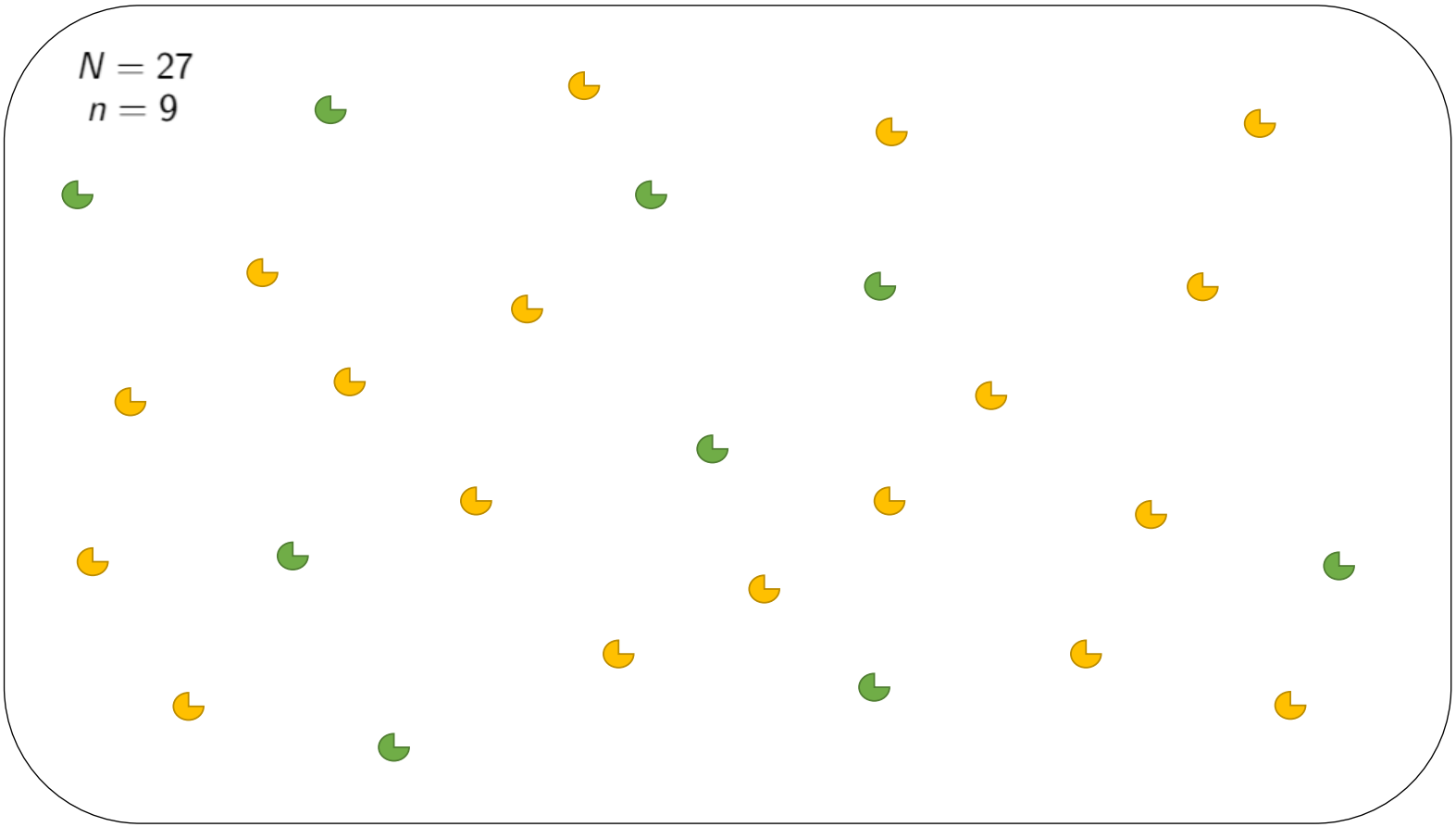
Stochastic epidemic

At time t, $S(t)$ susceptibles, $I(t)$ infecteds, and $R(t)$ removeds, with $N = S(t) + I(t) + R(t)$.



Stochastic epidemic

Epidemic ends when $I(t) = 0$.



Stochastic epidemic

To simulate an epidemic, we exploit **Poisson processes (PPs)**. Define a ***race*** as the minimum of (exponential) rvs.

Algorithm (Epidemic Simulator)

1. $S(0) = N - 1, I(0) = 1$
2. Until $I(t) = 0$:
   - 2.1 **Race $S(t)I(t)$ PPs with rate β and $I(t)$ PPs with rate γ,** where t_1 is the winning race time.
   - 2.2 If a γ-PP wins, $I(t_1) = I(t) - 1$ and $R(t_1) = R(t) + 1$.
   - 2.3 If a β-PP wins, $S(t_1) = S(t) - 1$ and $I(t_1) = I(t) + 1$.
   - 2.4 Update $t = t_1$.

Stochastic epidemic model

$\{S(t), I(t)\}$ is a continuous-time Markov chain (CTMC) with "jumps" based on an underlying Poisson process.

- $\tau_{kj} := r_k \wedge i_j - i_k \wedge i_j$
  - Time k tries to infect j
- $\psi_j = \exp(-\sum_{k \neq j}^{n} \beta_{kj} \tau_{kj})$
  - Probability j not infected before i_j
  - $\psi_{kj} = \exp(-\beta_{kj} \tau_{kj})$ is marginal term
- $\chi_j = \sum_{k \neq j}^{n} \beta_{kj} 1_{\{i_k < i_j < r_k\}}$
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Stochastic epidemic model

With $i_1, \ldots, i_n$ known, the *augmented model likelihood* is

$$\pi(\mathsf{i}_{-1}, \mathsf{r} | \boldsymbol{\beta}, \boldsymbol{\theta}, i_1) = \left\{ \prod_{j=2}^{n} \psi_j \chi_j \phi_j f_j(r_j - i_j | \theta_j) \right\} \phi_1 f_1(r_1 - i_1 | \theta_1) \quad (1)$$

MLE is easy with complete data. For common (β, γ) and $m = 1$:

$$\hat{\beta} = \frac{N(n-1)}{\sum_{j=2}^{n} \sum_{k \neq j} \tau_{kj} + (N-n) \sum_{j=1}^{n} r_j - i_j}$$

$$\hat{\gamma} = \frac{1}{n} \sum_{j=1}^{n} r_j - i_j$$

[0] We can generalize to unknown patient zero, i.e. α unknown.

DAMCMC for SEM

Construct a Metropolis-within-Gibbs sampling routine.
Assume common β and $\theta = (m, \gamma)$ for infectious periods.

$$\beta \mid \gamma, \alpha, i_\alpha, \mathsf{i}_{-\alpha}, \mathsf{r} \sim \Gamma(m_\beta + n - 1, \nu_\beta + A_\mathsf{i})$$
$$\gamma \mid \beta, \alpha, i_\alpha, \mathsf{i}_{-\alpha}, \mathsf{r} \sim \Gamma(m_\gamma + n, \nu_\gamma + C_\mathsf{i})$$
$$A_\mathsf{i} = \sum_{j=1}^{n} \sum_{k=1}^{N} \tau_{jk}$$
$$C_\mathsf{i} = \sum_{j=1}^{n} r_j - i_j$$
$$i_1, \ldots, i_n \sim f(\cdot) \text{ (Metropolis-Hastings)}$$

Scheme suffers from **high posterior correlations**. Either fix this issue (Kypraios, 2007; Neal and Roberts, 2005), or evade it.

Pair-based likelihood approximations

First, Stockdale et al. (2019) derive *partial data likelihood*:

1. Integrate over $i_1, \ldots, i_n$
2. Change of variable $a(\theta_j, -B_j)g_j = \phi_j f_j$
   - Absorbs info on never-infecteds into density
   - Permanence of $g_j \sim \text{Gamma}(m_j, \delta_j)$
   - New rate $\delta_j = \gamma_j + B_j = \gamma_j + \sum_{k=n+1}^{N} \beta_{jk}$
   - $a(\theta_j, \cdot)$ is mgf of $r_j - i_j$

$$\pi(\mathrm{r}|\boldsymbol{\beta}, \boldsymbol{\theta}) = \int \pi(\mathrm{i}_{-1}, \mathrm{r}|\boldsymbol{\beta}, \boldsymbol{\theta}, i_1)\pi(i_1)\, d(i_1, \ldots, i_n)$$

$$= \left\{ \prod_{j=1}^{n} a(\theta_j, -B_j) \right\} \mathbb{E}_{\mathrm{g}}[\pi(i_1)] \underbrace{\mathbb{E}_{\mathrm{g}}\left[\left\{ \prod_{j=2}^{n} \psi_j \chi_j \right\} \right]}_{\text{approximate}} \qquad (2)$$

Pair-based likelihood approximations

Second, they approximate the expected product.

$$\mathbb{E}_g\left[\left\{\prod_{j=2}^{n}\psi_j\chi_j\right\}\right] \approx \prod_{j=2}^{n}\mathbb{E}_g[\psi_j]\cdot\mathbb{E}_g[\chi_j] \tag{3}$$

$$\begin{aligned}
\mathbb{E}_g\left[\left\{\prod_{j=2}^{n}\psi_j\chi_j\right\}\right] &\approx \left\{\prod_{j=2}^{n}\mathbb{E}_g[\chi_j]\right\}\left\{\mathbb{E}_g\left[\prod_{j=2}^{n}\psi_j\right]\right\} \\
&= \left\{\prod_{j=2}^{n}\mathbb{E}_g[\chi_j]\right\}\mathbb{E}_g\left[\exp\left(-\sum_{j=2}^{n}\sum_{k\neq j}^{n}\beta_{kj}\tau_{kj}\right)\right] \\
&= \left\{\prod_{j=2}^{n}\mathbb{E}_g[\chi_j]\right\}\underbrace{\mathbb{E}_g\left[\exp\left(-\frac{\beta}{N}\sum_{j=2}^{n}\sum_{k\neq j}^{n}\tau_{kj}\right)\right]}_{\text{mgf of } W \text{ at } -\beta/N}
\end{aligned} \tag{4}$$

[0] W is cumulative time that infecteds try to infect susceptibles.

Pair-based likelihood approximations

The *standard pair-based likelihood approximation (PBLA)* assumes **marginal pairwise independence**.

$$\begin{aligned}
\mathbb{E}_{\mathbf{g}}[\psi_j]\mathbb{E}_{\mathbf{g}}[\chi_j] &= \mathbb{E}_{\mathbf{g}}\left[\prod_{l\neq j}^{n}\psi_{lj}\right]\mathbb{E}_{\mathbf{g}}\left[\sum_{k\neq j}^{n}\beta_{kj}1_{\{i_k<i_j<r_k\}}\right] \\
&\approx \left\{\prod_{l\neq j}^{n}\mathbb{E}_{g_l,g_j}[\psi_{lj}]\right\}\left\{\sum_{k\neq j}^{n}\beta_{kj}\mathbb{E}_{g_k,g_j}\left[1_{\{i_k<i_j<r_k\}}\frac{\psi_{kj}}{\psi_{kj}}\right]\right\} \\
&\approx \left\{\prod_{l\neq j}^{n}\mathbb{E}[\psi_{lj}]\right\}\sum_{k\neq j}^{n}\beta_{kj}\mathbb{E}[\psi_{kj}1_{\{i_k<i_j<r_k\}}](\mathbb{E}[\psi_{kj}])^{-1}
\end{aligned} \tag{5}$$

* Two similarly derived PBLAs are proposed.

Pair-based expectations

Lemma (1)

Let $1 \leq j, k \leq n$ with $j \neq k$, and $\beta_{kj} > 0$. For each j, suppose $r_j - i_j \sim \text{Exponential}(\delta_j)$. Then,

$$\mathbb{E}[\psi_{kj}] = \mathbb{E}[\exp(-\beta_{kj}\tau_{kj})] \tag{6}$$
$$= \begin{cases} 1 - \frac{\beta_{kj}\delta_j}{(\delta_j+\delta_k)(\beta_{jk}+\delta_k)} \exp(-\delta_k(r_k - r_j)), & r_j < r_k \\ \frac{\delta_k}{\beta_{kj}+\delta_k} + \frac{\beta_{kj}\delta_k}{(\delta_j+\delta_k)(\beta_{kj}+\delta_k)} \exp(-\delta_j(r_j - r_k)), & r_j > r_k \end{cases}$$

$$\mathbb{E}[1_{\{i_k<i_j<r_k\}} \exp(-\beta_{kj}\tau_{kj})] \tag{7}$$
$$= \begin{cases} \frac{\delta_j\delta_k}{(\delta_j+\delta_k)(\beta_{kj}+\delta_k)} \exp(-\delta_k(r_k - r_j)), & r_j < r_k \\ \frac{\delta_j\delta_k}{(\delta_j+\delta_k)(\beta_{kj}+\delta_k)} \exp(-\delta_j(r_j - r_k)), & r_j > r_k \end{cases}$$

Pair-based expectations

Proof. Based on cases of τ_{kj}, partition $\mathbb{E} := \mathbb{E}_{g_k, g_j}$.

$$\tau_{kj} := r_k \wedge i_j - i_k \wedge i_j = \begin{cases} 0, & i_j < i_k \\ i_j - i_k, & i_k < i_j < r_k \\ r_k - i_k, & i_j > r_k \end{cases}$$

$$\begin{aligned} &\mathbb{E}[\exp(-\beta_{kj}\tau_{kj})] \\ &= \mathbb{E}[e^{-\beta_{kj}\tau_{kj}} 1_{\{i_j < i_k\}}] + \mathbb{E}[e^{-\beta_{kj}\tau_{kj}} 1_{\{i_j > r_k\}}] + \mathbb{E}[e^{-\beta_{kj}\tau_{kj}} 1_{\{i_k < i_j < r_k\}}] \\ &= \mathbb{E}[1_{\{i_j < i_k\}}] + \mathbb{E}[e^{-\beta_{kj}(r_k - i_k)} 1_{\{i_j > r_k\}}] + \mathbb{E}[e^{-\beta_{kj}(i_j - i_k)} 1_{\{i_k < i_j < r_k\}}] \end{aligned} \tag{8}$$

Evaluate terms in (8) separately. Direct integration is possible, but an argument using Poisson processes is more illuminating.

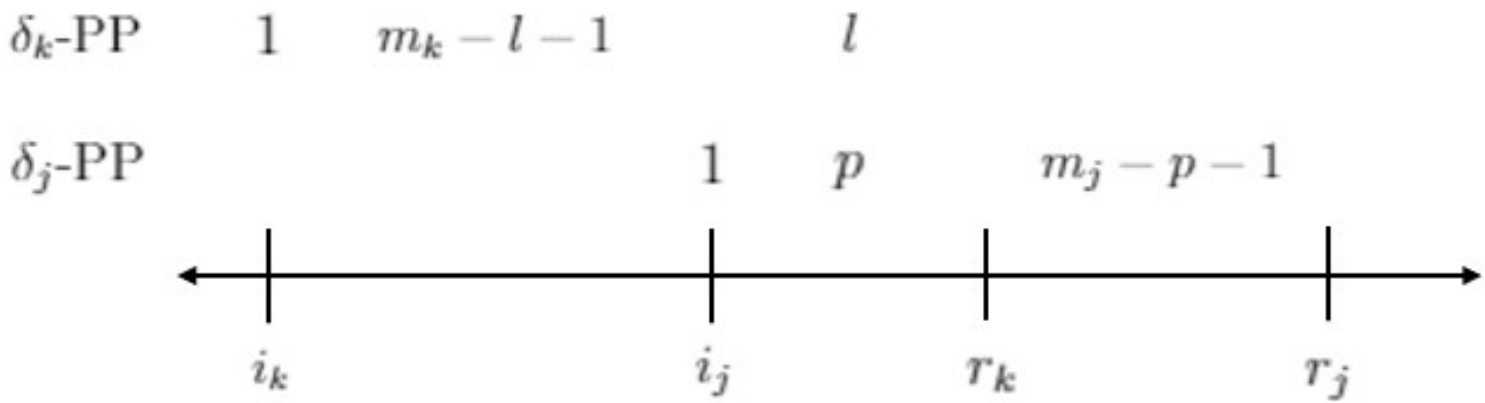
Pair-based expectations

1. Assume $r_k < r_j$
2. Traverse process backwards from r_j
3. δ_j-PP between (r_k, r_j)
   - 3.1 $\exp(-\delta_j(r_j - r_k))$ is probability of no renewal
   - 3.2 If renewed, renewal time is i_j
4. At r_k, δ_k-PP begins
   - 4.1 Compound $(\delta_j + \delta_k)$-PP if $i_j < r_k$.
   - 4.2 For $(\delta_j + \delta_k)$-PP, we have an **exponential race** with probabilities for renewals $\frac{\delta_j}{\delta_j+\delta_k}$, $\frac{\delta_k}{\delta_j+\delta_k}$

Races may also be set up with a β_{kj}-PP. With such probabilistic arguments, we derive expressions for terms in (8).

Pair-based expectations

Likewise, we can derive formulas for Erlang infectious periods. Draw line graphs to support combinatorial extension.



Product expectation

Lemma (2)

Let $\mathcal{K}$ be any subset of $\{1, \ldots, n\}$ with $K = |\mathcal{K}| \geq 2$. Suppose $\{r_k - i_k : k \in \mathcal{K}\} \overset{\text{iid}}{\sim} \text{Exponential}(\delta)$. Then

$$V = \sum_{\substack{j,k \in \mathcal{K} \\ j<k}} (\tau_{jk} + \tau_{kj}) = \sum_{\substack{j,k \in \mathcal{K} \\ j<k}} \omega_{jk} \sim \sum_{j=1}^{K-1} j \cdot Y_j$$

where $Y_1, \ldots, Y_{K-1} \sim \text{Exponential}(\delta)$.

Proof. Again, traverse process in reverse and make a convenient change of variable.

[0] If $\mathcal{K} = \{1, \ldots, n\}$, we have W.

[0] Recall W is cumulative time that infecteds try to infect susceptibles.

[0] We require its moment-generating function at $-\beta/N$.

Methods recap

Stockdale et al. (2019) propose 2 (6) PBLAs.

- MLE now possible despite partial observance
- Utilize properties of Poisson processes
- Expected product as product of expecteds
- Considering all pairs is $O(n^2)$

Simulation studies

I conducted additional[2] simulation studies[3] to ask:

- How fast are PBLAs?
- Behavior of PBLA-based MLEs
  - When is pairwise independence inappropriate?
  - Does PBLA inference offer consistent estimators?
- How does underreporting impact inference?
  - Undercounts result in lower R_0
  - Ad hoc adjustments assuming MCAR

[2] Stockdale et al. (2019) suggest that PBLAs can learn (β, γ) (Appendix B).
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Runtime comparisons

Table: Time in seconds to compute likelihood for standard, product, and weak PBLAs, and Eichner-Dietz approximation (2003).

n	N	Std	Prod	Weak	E+D
95	200	0.01	0.00*	0.00*	0.19
185	500	0.02	0.01	0.01	0.49
428	1,000	0.13	0.03	0.01	2.03
1,483	2,500	1.58	0.33	0.29	20.83
2,830	5,000	5.66	1.12	1.12	82.56
5,927	10,000	25.61	4.67	4.67	
11,819	20,000	106.81	19.81	21.24	
29,024	50,000	633.27	126.47	119.12	

* denotes very small, nonzero times.

Infected proportion

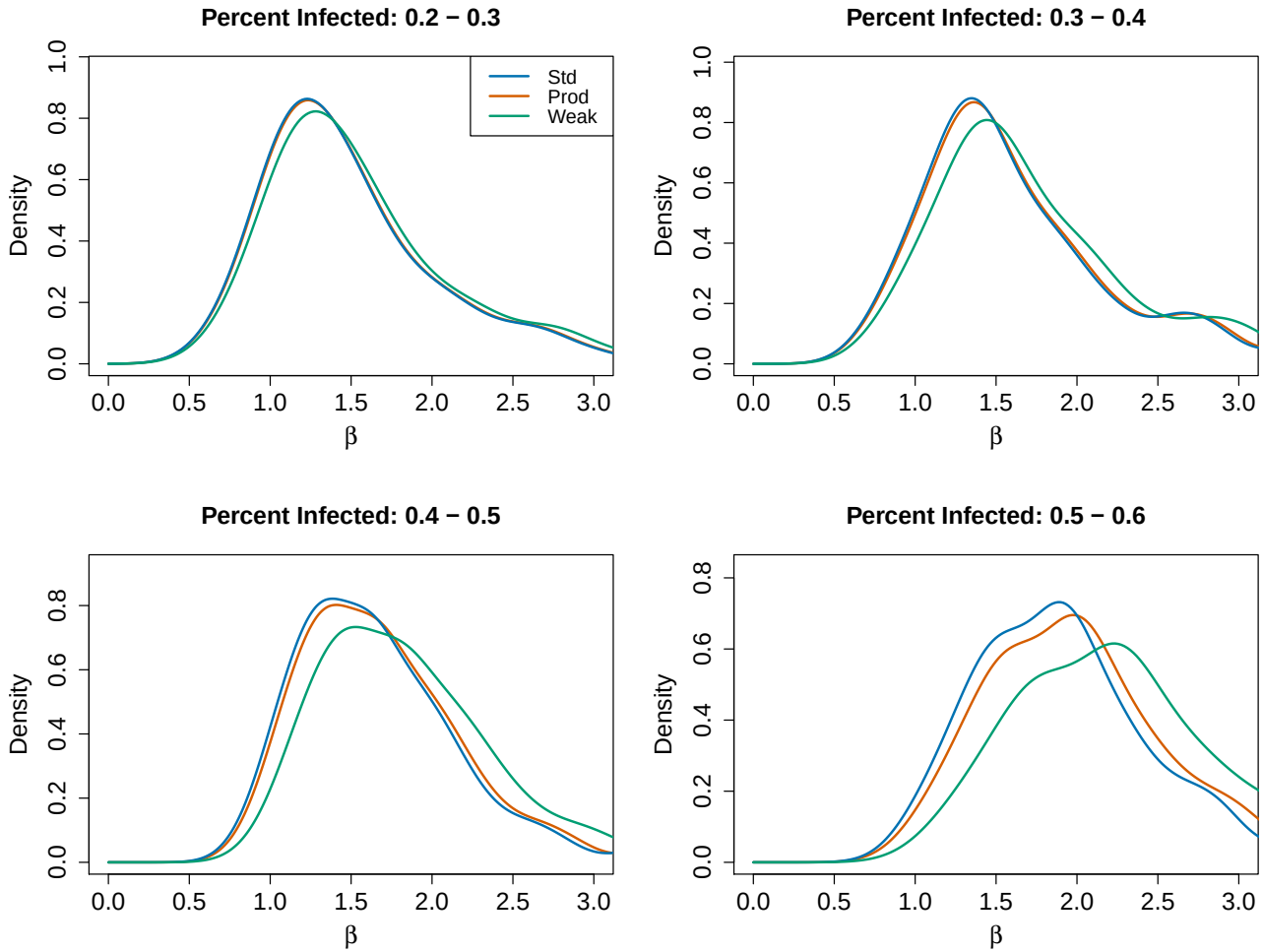

Figure: Inferences on (β, γ) for increasing infected proportion n/N. 2000 simulated epidemics with $(\beta, \gamma) = (1.5, 1)$. Plots for γ similar.

Properties of PBLA MLEs

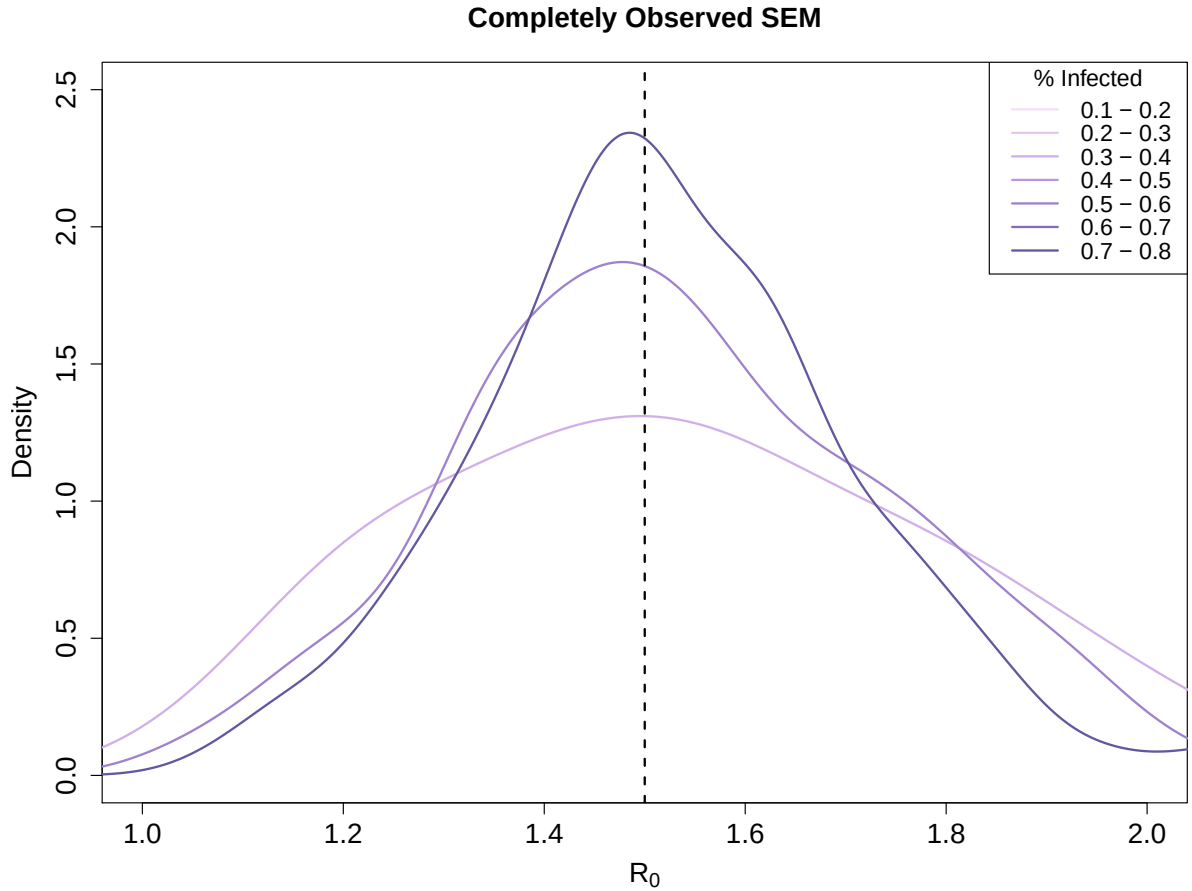

Figure: Inference on $R_0 := \beta/\gamma$ for increasing infected proportion. 2000 simulated epidemics with $(\beta, \gamma) = (1.5, 1)$.

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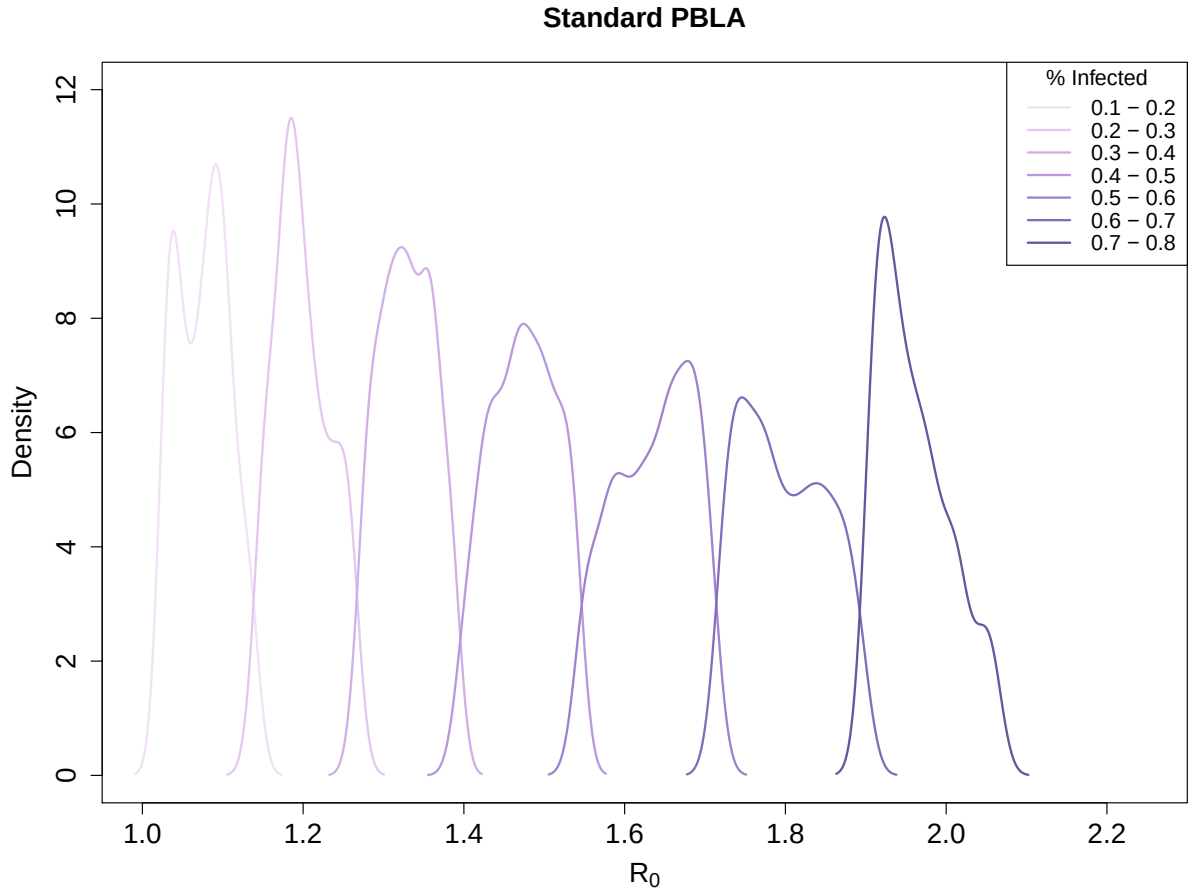

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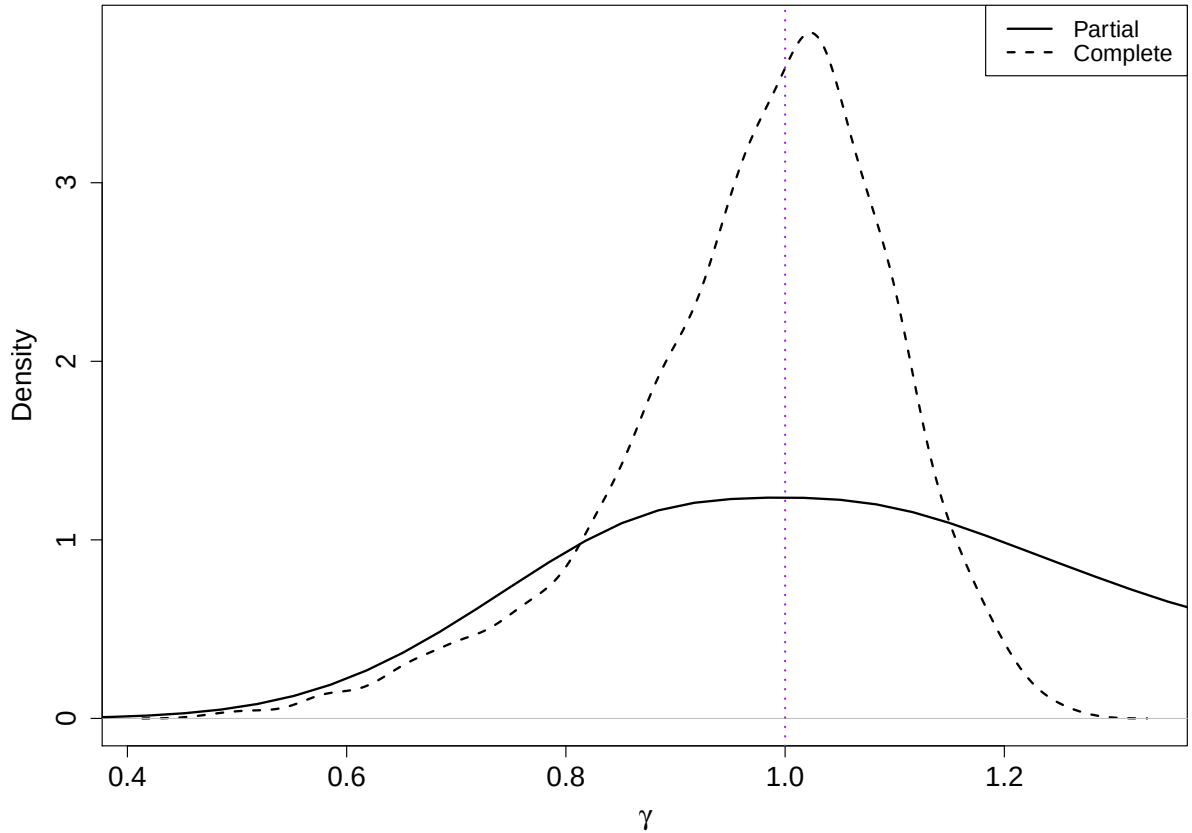

Figure: Inference on γ based on complete versus partial data. 2000 simulated epidemics with $(\beta, \gamma) = (1.5, 1)$.

Properties of PBLA MLEs

- Infected proportion n/N calibrates $\hat{R}_{0,\text{PBLA}}$
  - Conditional on R_0, n/N is approximately normal (Andersson and Britton, 2012, Theorems 4.1-2)
- $(\hat{\beta}_{\text{PBLA}}, \hat{\gamma}_{\text{PBLA}})$ do not estimate true (β, γ)
  - In fact, even with fixed true β, γ, PBLA inference cannot consistently estimate the other
- **Partial data appears inadequate** for inferring adversarial dynamics of infection and removal processes

Real data analyses

- **Ebola virus in West Africa**
  - $n \in (2000, 5000)$
  - SEIR with fixed exposed period c
  - Time-varying infections
- Dog rabies in Central African Republic
  - Cases underreported
- Common cold on a remote island
  - $N = 254$, split into age groups
  - Accommodates multitype infections
- Foot-and-mouth disease in UK
  - Rich covariate set
  - β depend on distance

Ebola virus in West Africa

- Replace r_j with $r_j - c$ for fixed exposed period $c = 5.3$ days
- Fixed γ^{-1} = 5.61 days
- $\beta_{kj} = \beta_0 \exp(-k_0(T_{kj}))$ where T_{kj} is expected midpoint
- Compare Poisson model with deterministic SEIR fit (Althaus, 2014)

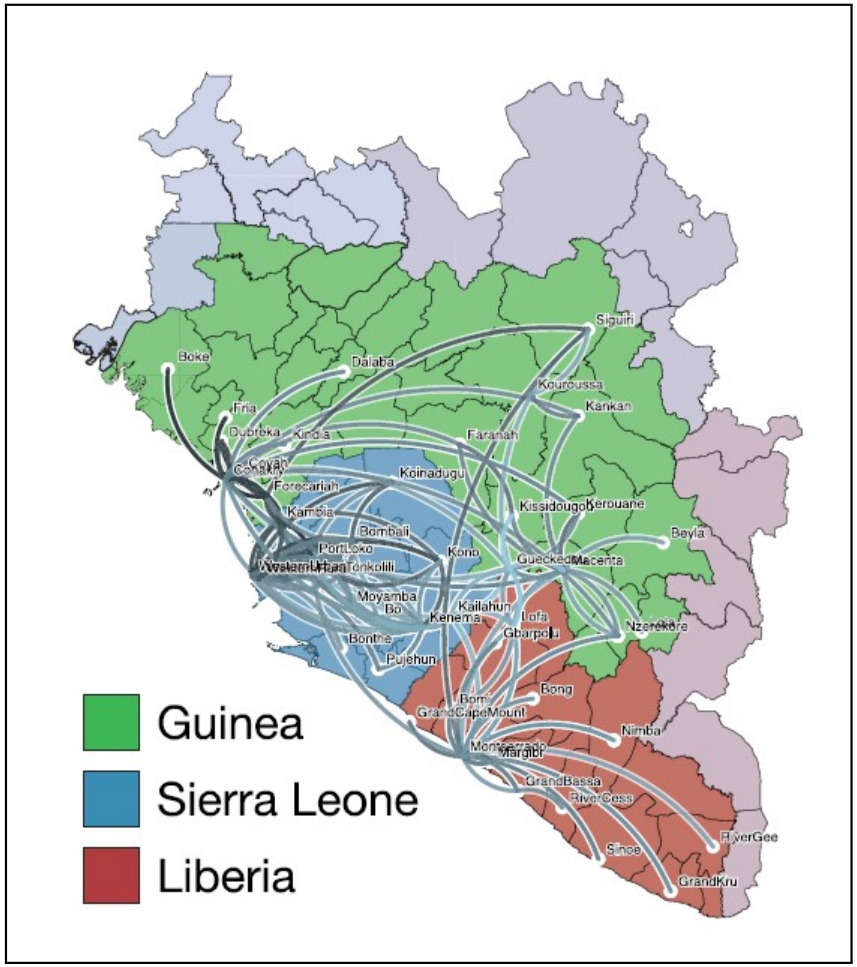

Figure: Suchard et al. (2018)

Ebola virus in West Africa: Estimates

Table: Parameter estimates from SEIR model of Ebola virus in West Africa. Temple and Stockdale et al. (2019) use PBLA whereas Althaus (2014) uses a deterministic model.

Country	Method	β_0	k_0	R_0
Guinea	PBLA	0.243	0.00105	1.36
	ODE	0.231	0.00071	1.30
Sierra Leone	PBLA	0.335	0.00289	1.88
	ODE	0.277	0.00180	1.55
Liberia	PBLA	0.266	0.00180	1.49
	ODE	0.303	0.00251	1.70

Stockdale et al. (2019) contributions

1. Propose likelihood approximations
   - MLE for partially observed epidemic
   - Faster than existing methods
2. Promote flexible framework for epidemiology
   - Specify formulas for β_{kj} and γ_j
   - Copious simulated and real examples
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2. Additional simulation studies
   - PBLA MLEs for (β, γ) are **not consistent**
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   - Underreporting biases estimation
3. Some corrections
   - Methods scale with n, not N
   - Ebola analysis takes longer than reported
   - Minor typos: $\pm$, constants

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   - Ebola analysis takes longer than reported
   - Minor typos: $\pm$, constants

My contributions

1. `R` package sdtemple/pblas
   - Highly scriptable; documented; no dependencies
   - Reproduces **all** simulation studies and data analyses
2. Additional simulation studies
   - PBLA MLEs for (β, γ) are **not consistent**
   - Pairwise independence fails for $n/N > 0.5$
   - Weak PBLA 
   - Underreporting biases estimation
3. Some corrections
   - Methods scale with n, not N
   - Ebola analysis takes longer than reported
   - Minor typos: $\pm$, constants

Future work

- **Consistency**
  - Are methods consistent with varying β_{kj}, γ_j ?
  - Can a partially observed SEM achieve consistency?
  - If so, develop consistent estimators.
- Compare to count-based models
  - Usually have aggregate counts
  - (Irons and Raftery, 2021; Fintzi et al., 2021)
- Relax various model assumptions
  - Set some $\beta_{kj} = 0$ (faster computations)
  - Adjust for underreporting
  - Study epidemics in progress (online inference)
  - Models with demography

References I

- J. Besag. Statistical analysis of non-lattice data. *Journal of the Royal Statistical Society: Series D (The Statistician)*, 24(3):179–195, 1975.
- D. T. Gillespie. Exact stochastic simulation of coupled chemical reactions. *The journal of physical chemistry*, 81(25):2340–2361, 1977.
- A. D. Barbour and G. Eagleson. Multiple comparisons and sums of dissociated random variables. *Advances in applied probability*:147–162, 1985.
- R. Durrett. *Essentials of stochastic processes*. Volume 1. Springer, 1999.

References II


M. Eichner and K. Dietz. Transmission potential of smallpox: estimates based on detailed data from an outbreak. *American Journal of epidemiology*, 158(2):110–117, 2003.


Y. Hayakawa, P. D. O'Neill, D. Upton, and P. S. Yip. Bayesian inference for a stochastic epidemic model with uncertain numbers of susceptibles of several types. *Australian & New Zealand Journal of Statistics*, 45(4):491–502, 2003.


P. J. Neal and G. O. Roberts. Statistical inference and model selection for the 1861 hagelloch measles epidemic. *Biostatistics*, 5(2):249–261, 2004.

References III


P. Neal and G. Roberts. A case study in non-centering for data augmentation: stochastic epidemics. *Statistics and Computing*, 15(4):315–327, 2005.


T. Kypraios. *Efficient Bayesian inference for partially observed stochastic epidemics and a new class of semi-parametric time series models*. PhD thesis, Lancaster University, 2007.


L. J. Allen. An introduction to stochastic epidemic models. In *Mathematical epidemiology*, pages 81–130. Springer, 2008.


C. Varin, N. Reid, and D. Firth. An overview of composite likelihood methods. *Statistica Sinica*:5–42, 2011.

References IV


H. Andersson and T. Britton. *Stochastic epidemic models and their statistical analysis*. Volume 151. Springer Science & Business Media, 2012.


C. L. Althaus. Estimating the reproduction number of ebola virus (ebov) during the 2014 outbreak in west africa. *PLoS currents*, 6, 2014.


M. A. Suchard, P. Lemey, G. Baele, D. L. Ayres, A. J. Drummond, and A. Rambaut. Bayesian phylogenetic and phylodynamic data integration using beast 1.10. *Virus evolution*, 4(1), 2018.


J. E. Stockdale. *Bayesian computational methods for stochastic epidemics*. PhD thesis, University of Nottingham, 2019.

References V


J. E. Stockdale, T. Kypraios, and P. D. O'Neill. Pair-based likelihood approximations for stochastic epidemic models. *Biostatistics*, 2019.


J. Fintzi, J. Wakefield, and V. N. Minin. A linear noise approximation for stochastic epidemic models fit to partially observed incidence counts. 2021. arXiv: 2001.05099.


N. J. Irons and A. E. Raftery. Estimating sars-cov-2 infections from deaths, confirmed cases, tests, and random surveys. *arXiv: 2102.10741*, 2021.

Color scheme

- Orange: times
- Violet: before infection probabilities
- Blue: infection rates
- Purple: removal rates

Glossary

- N total individuals and n infected individuals
- r_j and i_j are removal and infection times for j
- β_{kj} is infection rate k applies to j
- θ_j parameterizes infectious period $r_j - i_j \sim P_{\theta_j}$
  - $\theta_j = (m_j, \gamma_j)$ for Erlang periods
- τ_{kj} is time k applies pressure to j
  - $\omega_{jk} = \tau_{jk} + \tau_{kj}$ is joint time
- ψ_j is $P(j$ evades infection until time $i_j)$
  - ψ_{jk} is $P(j$ evades infection from k until time $i_j)$
- χ_j is infective pressure on j at i_j
- ϕ_j is $P(j$ fails to infect the $N - n$ never-infecteds)

Paper corrections

- Major
  - Methods scale with n, not N
  - Ebola virus epidemic analyses take 12, 31, and 51 minutes
    - Standard laptop with Intel i7 core
- Minor
  - $-\frac{3}{4}$ instead of $+\frac{3}{4}$ in $\mathbb{E}[T_{kj}]$ (Ebola virus epidemic)
    - Correct in code at jessicastockdale/PBLA
    - No impact on results
  - $(4n-5)$ instead of $(2n-1)$ (Lemma (3))
    - No impact on results
  - Subscript $_j$ instead of $_k$ for an Erlang case (Lemma (4))

Proof of Lemma (2)

1. Define infection and removal transitions in reverse time
   - $(S(t), I(t)) \to (S(t)+1, I(t)-1)$ with rate $\delta \cdot I(t)$
   - $(S(t), I(t)) \to (S(t), I(t)+1)$
2. Express $\int S(t)I(t)\,dt$ as a piecewise linear function
   - $T(i_1) = \sum_{k=2}^{2K} S(\tilde{t}_k) \cdot I(\tilde{t}_k) \cdot (\tilde{t}_k - \tilde{t}_{k-1})$
3. In each interval, make change of variable $t' = t \cdot I(t)^{-1}$
4. Consider weighted sum of renewal times
   - $T(i_1) = \sum_{k=2}^{K} S(\bar{t}_k)(\bar{t}_k - \bar{t}_{k-1})$
   - $Y_k := \bar{t}_k - \bar{t}_{k-1} \sim \text{Exponential}(\delta)$

A weak limit for multiple comparisons

Lemma (3)

Suppose $r_1 - i_1, \ldots, r_n - i_n \overset{\text{iid}}{\sim} \text{Exponential}(\delta)$. If $\{\omega_{jk} : j, k \in \{1, \ldots, n\}\}$ are ***dissociated***, then

$$W = \sum_{j=1}^{n} \sum_{k=j+1}^{n} \omega_{jk} \rightsquigarrow \text{Normal}\left(\frac{1}{\delta}\binom{n}{2}, \frac{4n-5}{3\delta^2}\binom{n}{2}\right)$$

- Central limit theorem for class of U-statistics
- Dissociation is independence assumption
- Appeal to Barbour and Eagleson (1985, Theorem 2.1)

---

[0] Recall W is cumulative time that infecteds try to infect susceptibles.

[0] We require its moment-generating function at $-\beta/N$.

Theorem 2.1 of Barbour and Eagleson (1985)

Theorem

Let $D_n = \{(i,j) : 1 \leq i < j \leq n\}$, and consider $\{X_{ij} : (i,j) \in D_n\}$ to be a collection of mean-zero *dissociated* random variables such that $\mathbb{E}[|X_{ij}|^3] < \infty$ for all $(i,j) \in D_n$. Define $\sigma_n^2 := \sum_{(i,j),(k,l) \in D_n} \mathbb{E}[X_{ij} X_{kl}]$. Then

$$\sigma_n^{-3} \sum_{(i,j) \in D_n} (\mathbb{E}[|X_{ij}|^3])^{1/3} \left(\sum_{(k,l):|(i,j) \cap (k,l)|=0} (\mathbb{E}[|X_{kl}|^3])^{1/3} \right)^2 \to 0$$

implies $\sigma_n^{-1} \sum_{(i,j) \in D_n} X_{ij} = Z_n \rightsquigarrow N(0,1)$.

Pairwise comparisons are dependent if they share any indices.

Ebola virus in West Africa: Likelihood Surface

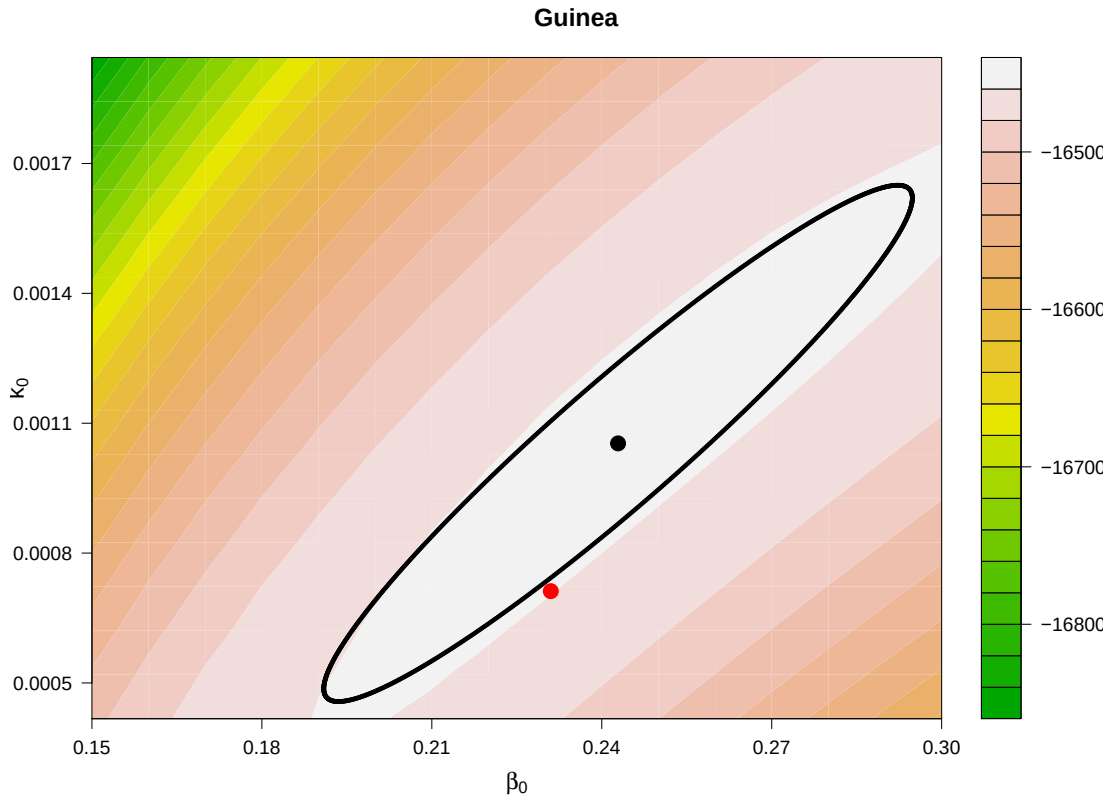

Figure: Log likelihood contours for Ebola virus epidemic in Guinea. Ellipses denote level set perimeter and dots denote MLEs. PBLA in black and Althaus (2014) in red.

Tristan da Cunha: A mutitype SEM

- $N = 254$ individuals split into three age groups
- 36% infants, 17% kids, and 13% adults
- $\beta_{kj} = \beta_{G(j)}$ depend on age group of susceptible
- Random walk MCMC vs. gold standard DAMCMC

Figure: Remote island community

[0] Compared against Hayakawa et al. (2003)

Tristan da Cunha: Trace plots

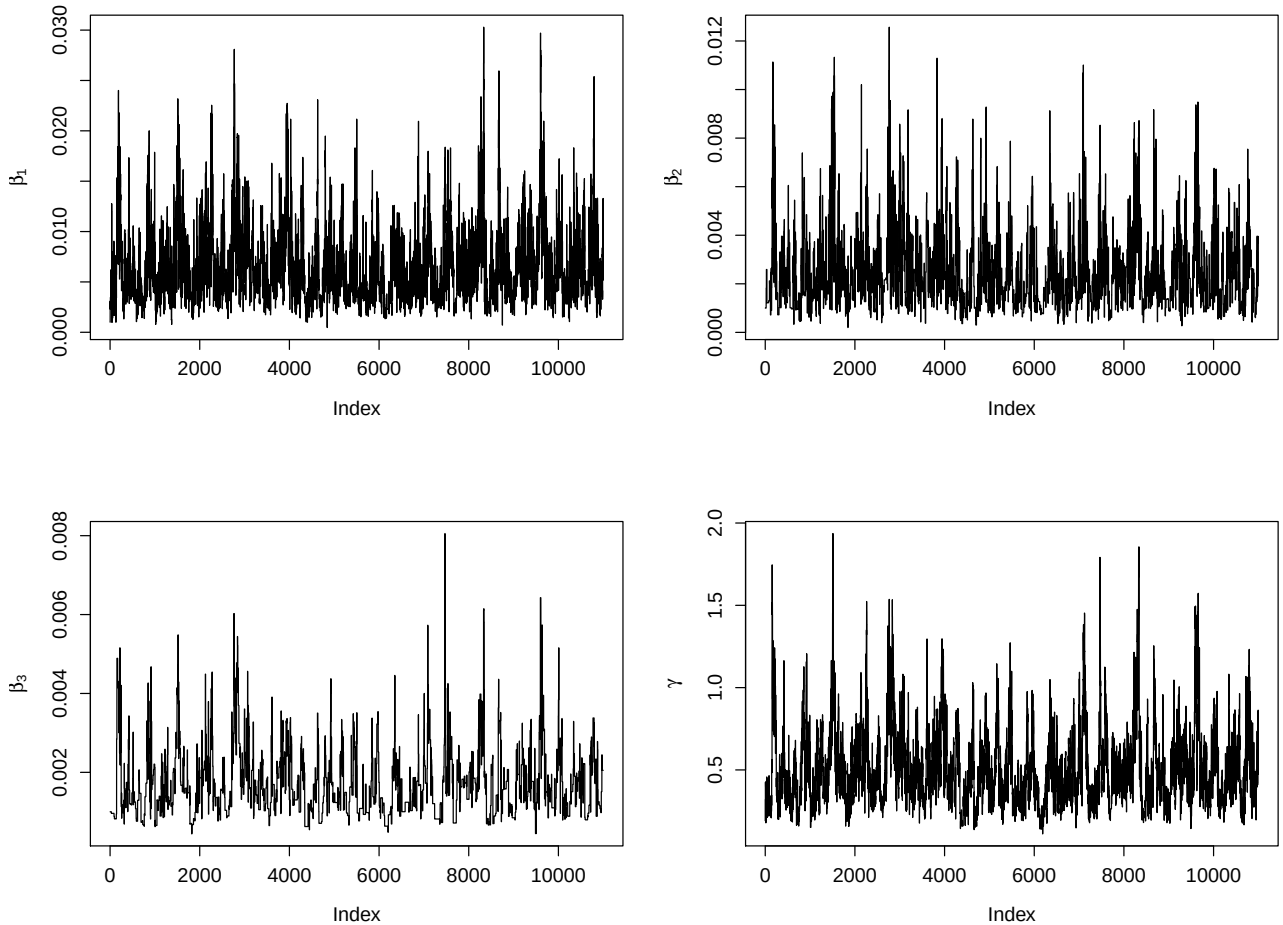

Figure: Trace plots of $(\beta_1, \beta_2, \beta_3, \gamma)$ for Tristan da Cunha common cold epidemic using PBLA MCMC.

Tristan da Cunha: Posterior Samples

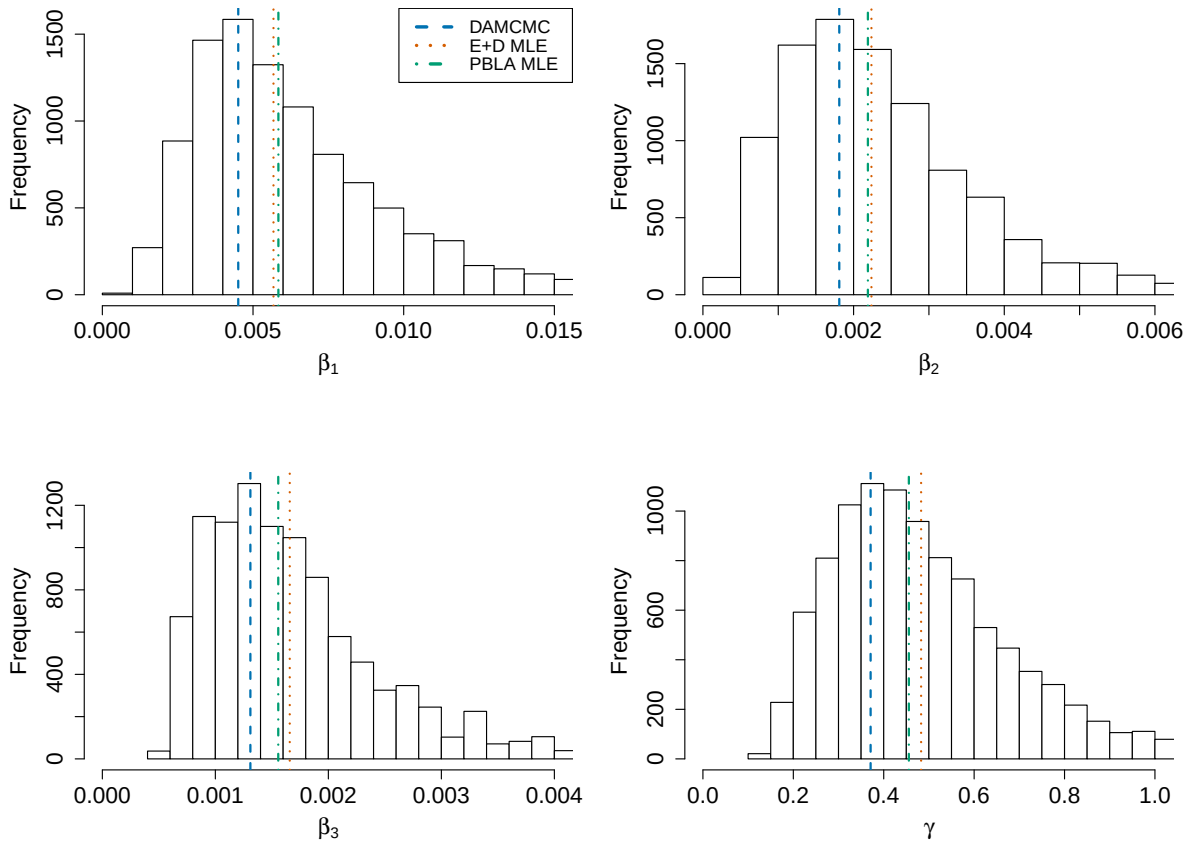

Figure: Histograms of $(\beta_1, \beta_2, \beta_3, \gamma)$ posterior samples for Tristan da Cunha common cold epidemic using PBLA MCMC. DAMCMC posterior mean (blue), E+D MLE (orange), and PBLA MLE (green).

Tristan da Cunha: Summary

Table: Posterior means from PBLA MCMC and DAMCMC methods, and MLEs using the E+D approximation and standard PBLA, for Tristan da Cunha common cold epidemic.

	PBLA MCMC	DAMCMC	E+D MLE	PBLA MLE
β_1	0.00648	0.00451	0.00568	0.00584
β_2	0.00244	0.00181	0.00224	0.00219
β_3	0.00171	0.00131	0.00166	0.00156
γ	0.50565	0.37100	0.48273	0.45562
R_0	1.17580	1.16102	1.12396	1.15301

Dog rabies in CAR

- $n = 123$ infecteds between 2006 and 2012
- N unknown
- Undercounts likely
- $\beta_{kj} = \beta_0 \exp(-\theta \cdot \rho(i,j))$ where ρ is distance
  - Vanishingly small θ

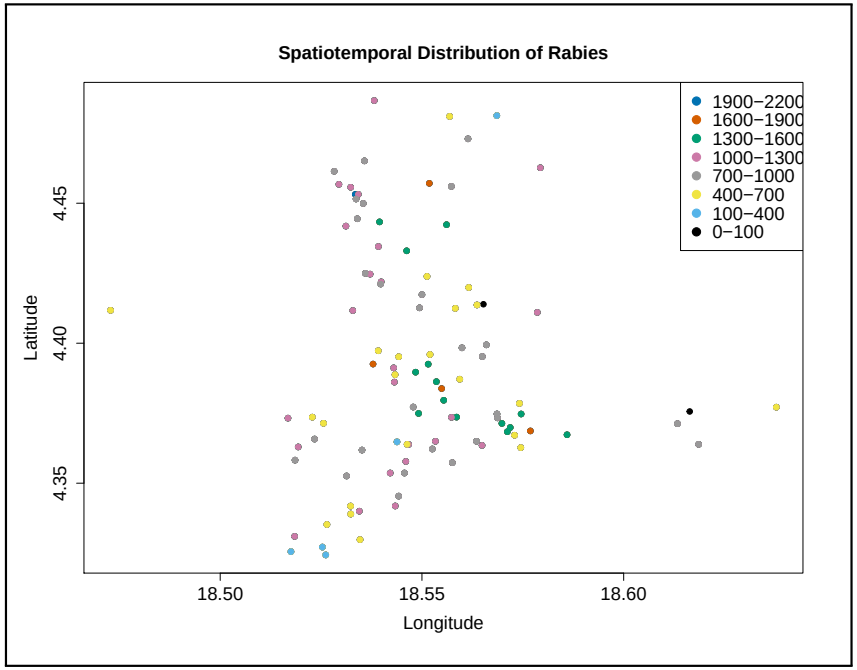

Figure: Spread of dog rabies

Dog rabies in CAR: Underreporting

Table: Inferences on (β, γ, R_0) using product PBLA, psuedo-removals adjustment, and total population size $N = 10,000$ for rabies epidemic in Bangui, Central African Republic.

η	β	γ	R_0	Interval R_0
1.000	0.172	0.172	1.001	(0.656, 1.527)
0.500	0.203	0.200	1.015	(0.752, 1.368)
0.200	0.294	0.281	1.045	(0.884, 1.235)
0.100	0.424	0.385	1.099	(0.974, 1.240)

Dog rabies in CAR: Sensitivity analysis for N

Table: Inferences on (β, γ, R_0) with increasing total population size N.

N	η	β	γ	R_0	Interval R_0
25,000	1.000	0.171	0.171	0.996	(0.652, 1.518)
	0.500	0.209	0.208	1.003	(0.747, 1.347)
	0.200	0.399	0.392	1.017	(0.766, 1.348)
	0.100	0.447	0.431	1.037	(0.916, 1.173)
50,000	1.000	0.170	0.171	0.994	(0.651, 1.516)
	0.500	0.312	0.312	1.000	(0.733, 1.363)
	0.200	0.263	0.261	1.007	(0.841, 1.207)
	0.100	0.384	0.377	1.017	(0.901 1.149)
100,000	1.000	0.170	0.171	0.993	(0.650, 1.514)
	0.500	0.189	0.189	0.998	(0.757, 1.315)
	0.200	0.263	0.262	1.003	(0.847, 1.187)
	0.100	0.331	0.329	1.008	(0.894, 1.136)

Underreporting

- Undercount of size n biases estimation of R_0
  - Theorems 4.1-2 (Andersson and Britton, 2000) say that n/N is asymptotically normally distributed conditional on R_0
- Given reporting rate η, I propose bias corrections:
  1. Draw pseudo-removal times from KDE
  2. Scale $N^* = N \cdot \eta$
- I suggest that η is not identifiable from removal times only.

Underreporting

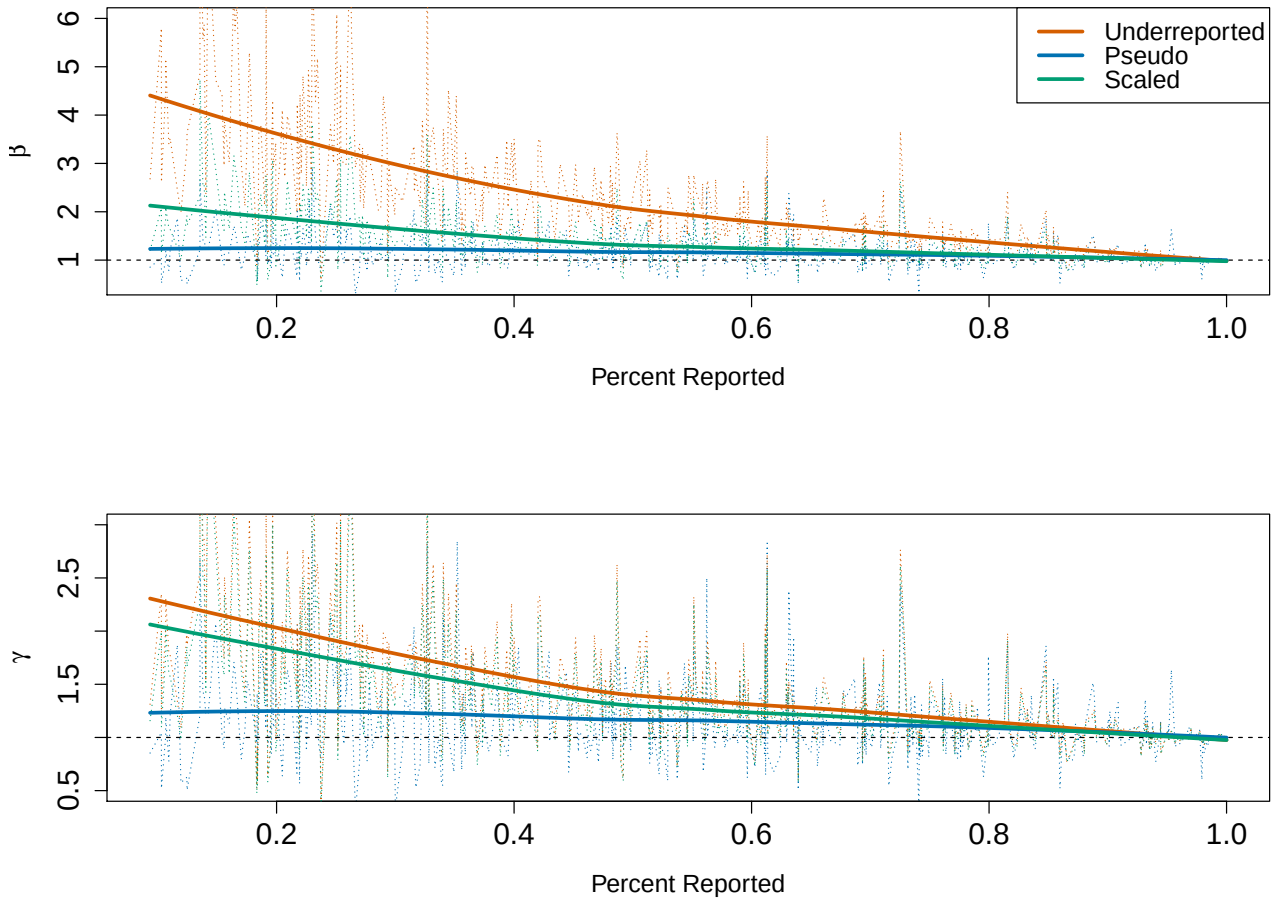

Figure: Scaled ratio of PBLA MLEs with full partial data versus underreported partial data. β (top) and γ (bottom).

Underreporting

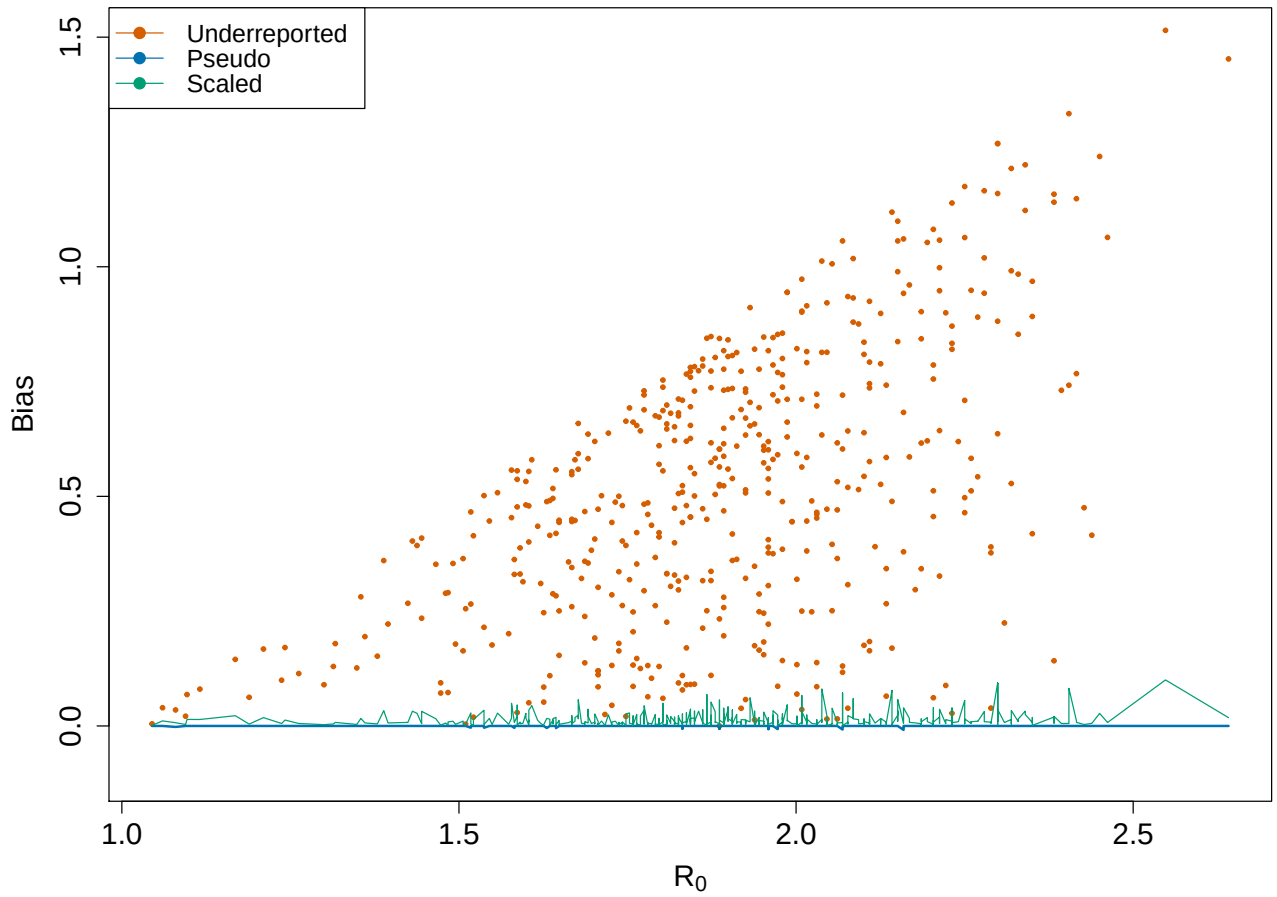

Figure: Difference in R_0 from PBLA MLEs with full partial data versus underreport partial data.

Varying (β, γ)

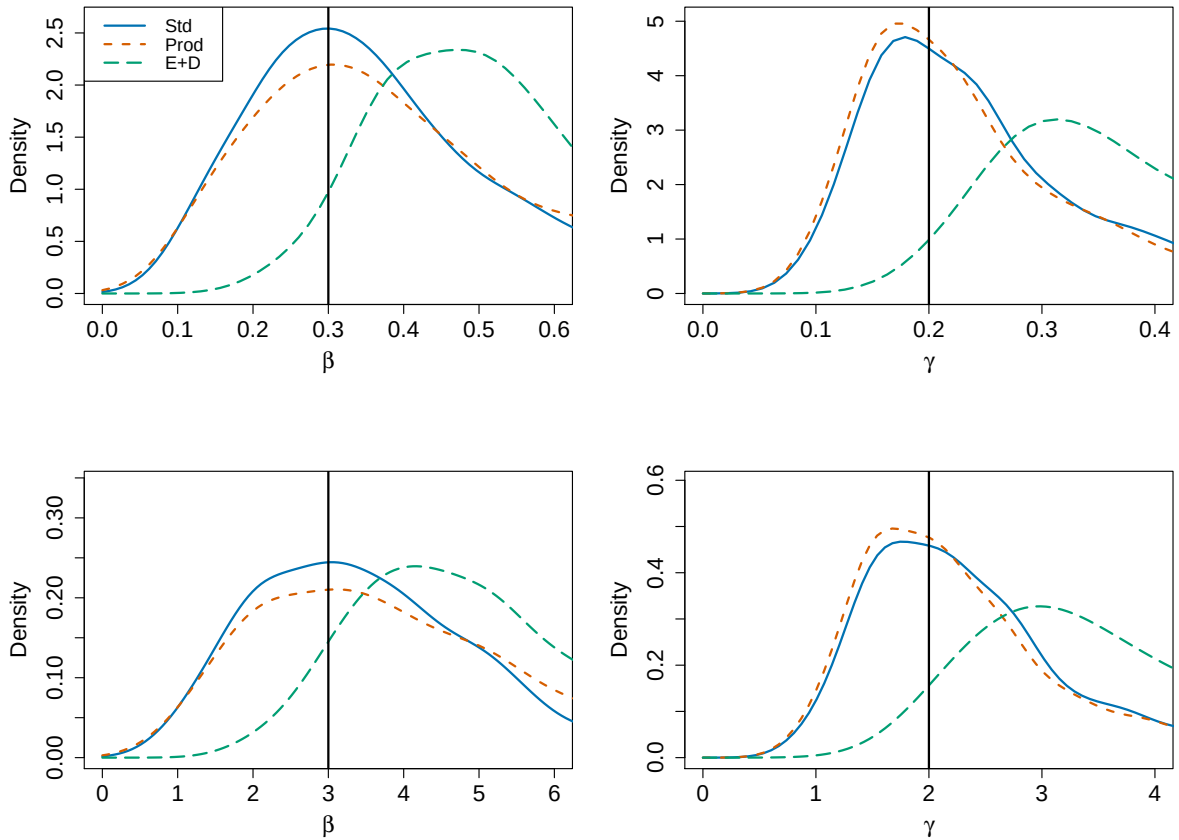

Figure: Varying parameters (β, γ): (0.3, 0.2) (top) and (3, 2) (bottom). MLEs from 1000 simulations with exponential infectious periods, $N = 100$, and $R_0 = \beta/\gamma = 1.5$.

PBLAs comparison

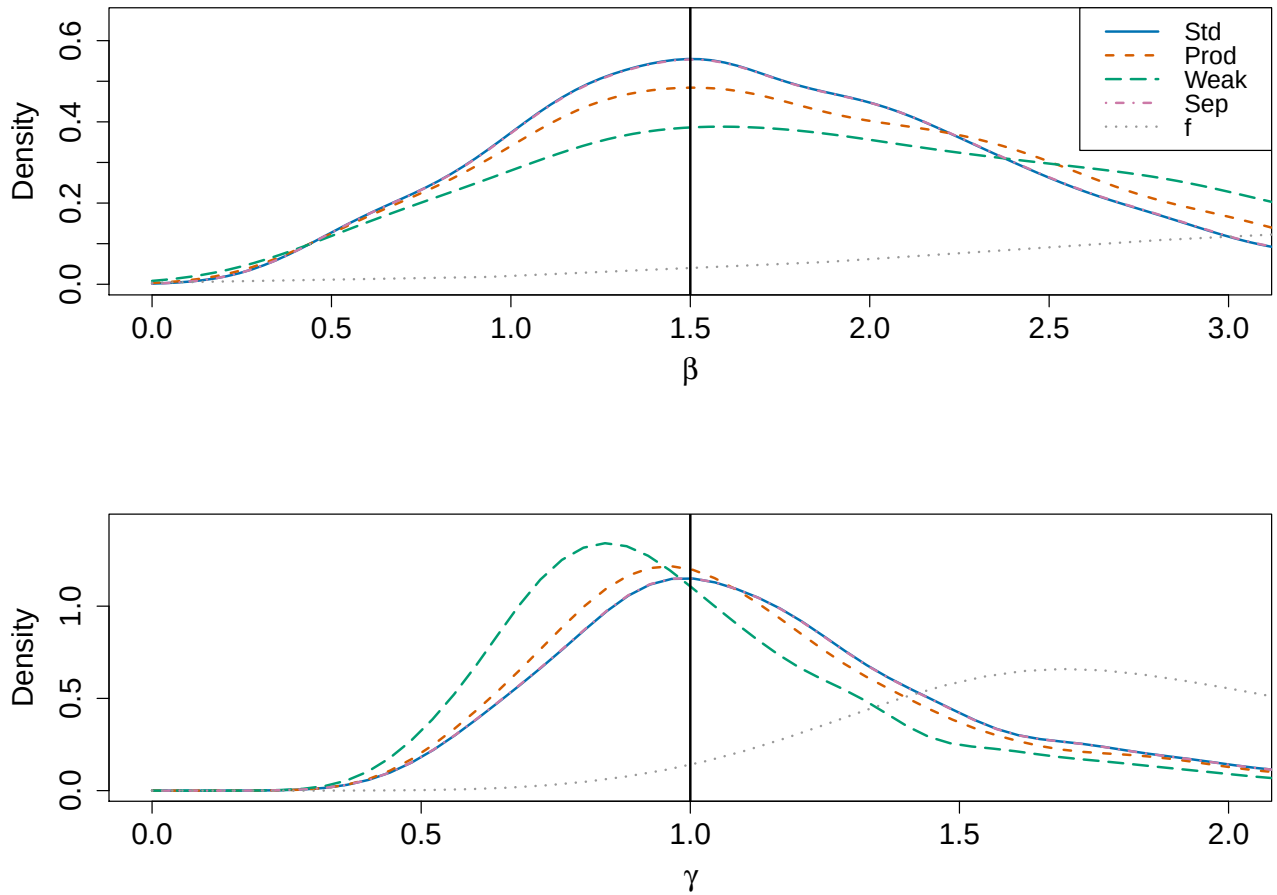

Figure: Comparison of pair-based likelihood approximations. MLEs from 1000 simulations with $(\beta, \gamma) = (1.5, 1)$, $N = 250$.

Partial data likelihood

$$
\begin{aligned}
\pi(\mathsf{r}|\boldsymbol{\beta},\boldsymbol{\theta}) &= \int \pi(\mathsf{i}_{-\alpha},\mathsf{r}|\boldsymbol{\beta},\boldsymbol{\theta},\alpha,i_\alpha)\pi(i_\alpha,\alpha)\, d\mathsf{i}_{-\alpha} d\, i_\alpha\, d\alpha \\
&= \sum_{j=1}^{n} \pi(\alpha) \int \left\{ \prod_{j\neq\alpha}^{n} \psi_j \chi_j \right\} \pi(i_\alpha|\alpha) \left\{ \prod_{j=1}^{n} \phi_j f_j(r_j - i_j|\theta_j) \right\} d\mathsf{i} \\
&= \left\{ \prod_{j=1}^{n} a(\theta_j, -B_j) \right\} \sum_{j=1}^{n} \pi(\alpha)\, \mathbb{E}_{\mathsf{g}} \left[\pi(i_\alpha|\alpha) \left\{ \prod_{j\neq\alpha}^{n} \psi_j \chi_j \right\} \right] \\
&\approx \left\{ \prod_{j=1}^{n} a(\theta_j, -B_j) \right\} \sum_{j=1}^{n} \pi(\alpha)\, \mathbb{E}_{\mathsf{g}}[\pi(i_\alpha|\alpha)]\, \mathbb{E}_{\mathsf{g}} \left[\left\{ \prod_{j\neq\alpha}^{n} \psi_j \chi_j \right\} \right]
\end{aligned}
\tag{9}
$$