

# Data augmentation in the general epidemic model

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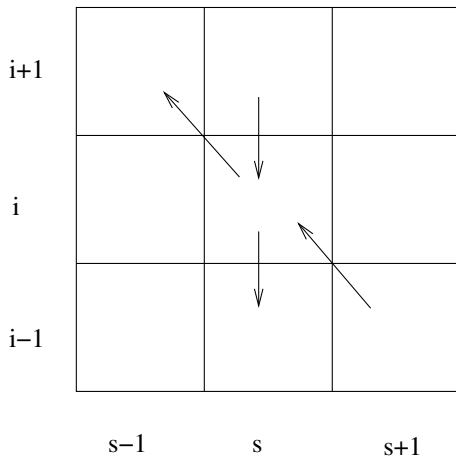
# Outline

- ▶ The general epidemic model
  - ▶ A simple Susceptible–Infected–Removed (SIR) model of an outbreak of infection in a closed population
- ▶ Likelihood function for the infection and removal rates
  - ▶ Complete data: both infection and removal times are observed
  - ▶ Under Gamma priors for the infection and removal rates, their full conditionals are also Gamma, so Gibbs updating steps can be used
- ▶ Incomplete data: only removal times are observed
  - ▶ Augment the unknown infection times
  - ▶ Additional Metropolis-Hastings steps for sampling infection times, requiring explicit computation of the complete data likelihood

# The SIR model

- ▶ Consider a closed population of  $M$  individuals
- ▶ One introductory case (infective) introduces the infection into a population of initially susceptible individuals, starting an outbreak
- ▶ Once the outbreak has started, the hazard of infection for a still susceptible individual depends on the number of infectives in the population:  $(\beta/M)I(t)$
- ▶ If an individual becomes infected, the hazard of clearing infection (and stopping being infective) is  $\gamma$ , i.e., he/she remains infective for an exponentially distributed period of time. He/she then becomes *removed* and does not contribute to the outbreak any more
- ▶ There is no latency

# Transitions in the state space



# The complete data

- ▶ Assume one introductory case whose infection takes place at time  $t = 0$  (this fixes the time origin)
- ▶ For  $M$  individuals followed from time 0 until the end of the outbreak at time  $T$  (after which time the number of infectives  $I(t) = 0$ ), the *complete data* record all event times
- ▶ This is equivalent to observing  $n - 1$  infection times and  $n$  removal times, and the fact the  $M - n$  individuals escaped infection throughout the outbreak

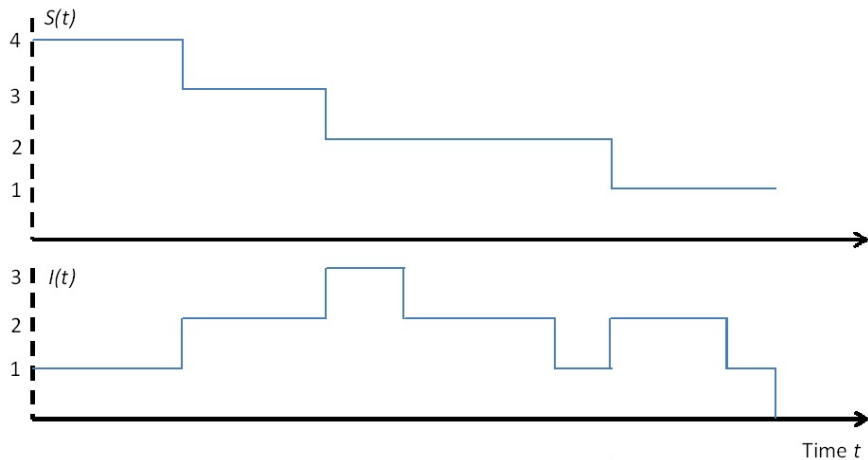
$$\overbrace{\{0 = i_1 < i_2 < \dots < i_n\}}^{\text{infection times}} \text{ and } \overbrace{\{r_1 < \dots < r_{n-1} < r_n = T\}}^{\text{removal times}}$$

- ▶ N.B. Here, the  $i_k$  and  $r_k$  do not correspond to the same individual (we will discuss this assumption later; see p. 19)

# Counting infectives and susceptibles

- ▶ Denote the ordered event times  $i_1, \dots, i_n$  and  $r_1, \dots, r_n$  jointly as  $0 = u_1 < u_2 < \dots < u_{2n} = T$
- ▶ Denote the indicators of time  $u_k$  being an infection or removal time by  $D_k$  and  $R_k$ , respectively
- ▶ Denote the number of infectives at time  $t$  by  $I(t)$ 
  - ▶ it is a piecewise constant (left-continuous) function, assuming values in the set  $\{0, 1, \dots, M\}$
  - ▶ it jumps at times  $u_2 < \dots < u_{2n}$
- ▶ Denote the number of susceptibles at time  $t$  by  $S(t)$ 
  - ▶ it is a piecewise constant (left-continuous) function, jumping at times  $i_2 < \dots < i_n$
- ▶ Both  $I(t)$  and  $S(t)$  are determined by the complete data

## Example



$i_1 = 0$

$i_2$

$i_3$

$i_4$

$r_1$

$r_2$

$r_3$

$r_4 = T$

$u_1 = 0$

$u_2$

$u_3$

$u_4$

$u_5$

$u_6$

$u_7$

$u_8 = T$

$D_k$

0

1

1

0

0

1

0

0

$R_k$

0

0

0

1

1

0

1

1

# The process of infections

- ▶ The model of new infections is a non-homogeneous Poisson process with rate  $\beta I(t)S(t)/M$ 
  - ▶ the rate is a piecewise constant (left-continuous) function
  - ▶ it jumps at times  $u_2 < \dots < u_{2n}$ , with levels  $\beta I(u_2)S(u_2)/M, \beta I(u_3)S(u_3)/M, \dots, \beta I(u_{2n})S(u_{2n})/M$
- ▶ The probability density of the infection events is thus proportional to

$$\prod_{k=2}^{2n} \left[ ((\beta/M)I(u_k)S(u_k))^{D_k} e^{-\underbrace{(\beta/M)I(u_k)S(u_k)(u_k - u_{k-1})}_{\text{total time for "infectious pressure"}}} \right]$$
$$\propto \prod_{k=2}^{2n} (\beta I(u_k)S(u_k))^{D_k} \times e^{-\underbrace{(\beta/M) \sum_{k=2}^{2n} I(u_k)S(u_k)(u_k - u_{k-1})}_{\text{total time for "infectious pressure"}}$$



# The process of removals

- ▶ The model of removals is a non-homogeneous Poisson process with rate  $\gamma I(t)$ 
  - ▶ the rate is a piecewise constant (left-continuous) function
  - ▶ it jumps at times  $u_2 < \dots < u_{2n}$ , with levels  $\gamma I(u_2), \gamma I(u_3), \dots, \gamma I(u_{2n})$
- ▶ The probability density of the removal events is thus proportional to

$$\prod_{k=2}^{2n} \left[ (\gamma I(u_k))^{R_k} e^{-\gamma I(u_k)(u_k - u_{k-1})} \right]$$

total time spent infective

$$= \prod_{k=2}^{2n} (\gamma I(u_k))^{R_k} \times e^{-\gamma \sum_{k=2}^{2n} I(u_k)(u_k - u_{k-1})}$$

# Complete data likelihood

- The joint likelihood of parameters  $\beta$  and  $\gamma$ , based on the complete data:

$$\begin{aligned} \underbrace{f(\mathbf{i}, \mathbf{r} | \beta, \gamma)}_{L(\beta, \gamma; \mathbf{i}, \mathbf{r})} &= \prod_{k=2}^{2n} (\beta I(u_k) S(u_k))^{D_k} \prod_{k=2}^{2n} (\gamma I(u_k))^{R_k} \\ &\times e^{-\sum_{k=2}^{2n} ((\beta/M) I(u_k) S(u_k) + \gamma I(u_k)) (u_k - u_{k-1})} \\ &= \prod_{k=2}^n \{\beta I(i_k) S(i_k)\} \prod_{k=1}^n \{\gamma I(r_k)\} \\ &\times e^{-\sum_{k=2}^{2n} ((\beta/M) I(u_k) S(u_k) + \gamma I(u_k)) (u_k - u_{k-1})} \end{aligned}$$

# Simplifying the notation

- ▶ Note that  $\sum_k I(u_k)S(u_k)(u_k - u_{k-1}) = \int_0^T I(u)S(u)du$
- ▶ Similarly  $\sum_k I(u_k)(u_k - u_{k-1}) = \int_0^T I(u)du$
- ▶ The likelihood function can thus be written as

$$\prod_{k=2}^n \{\beta I(i_k)S(i_k)\} \prod_{k=1}^n \{\gamma I(r_k)\} \\ \times \exp \left( - \int_0^T \{(\beta/M)I(u)S(u) + \gamma I(u)\} du \right)$$

# Poisson likelihood and Gamma priors

- ▶ This above likelihood is the so called Poisson likelihood for parameters  $\beta$  and  $\gamma$
- ▶ In particular, Gamma distributions can be used as conjugate priors for  $\beta$  and  $\gamma$
- ▶ It follows that the full conditional distributions of  $\beta$  and  $\gamma$  are also Gamma and can be updated by Gibbs steps

# Gamma prior distributions

- ▶ Rate parameters  $\beta$  and  $\gamma$  are given independent Gamma priors

$$f(\beta) \propto \beta^{\nu_\beta - 1} \exp(-\lambda_\beta \beta)$$

$$f(\gamma) \propto \gamma^{\nu_\gamma - 1} \exp(-\lambda_\gamma \gamma)$$

- ▶ This allows easy updating of these parameters using Gibbs sampling (the next two pages)

# The full conditional of $\beta$

- ▶ Parameter  $\beta$  can be updated through a Gibbs step

$$\begin{aligned} f(\beta|\mathbf{i}, \mathbf{r}, \gamma) &\propto f(\beta, \gamma, \mathbf{i}, \mathbf{r}) \propto f(\mathbf{i}, \mathbf{r}|\beta, \gamma) f(\beta) \\ &\propto \beta^{n-1} \exp\left(-(\beta/M) \int_0^T I(u) S(u) du\right) \beta^{\nu_\beta-1} \exp(-\lambda_\beta \beta) \end{aligned}$$

- ▶ This means that

$$\beta|(\mathbf{i}, \mathbf{r}, \gamma) \sim \Gamma\left(n-1+\nu_\beta, (1/M) \int_0^T I(u) S(u) du + \lambda_\beta\right)$$

# The full conditional of $\gamma$

- ▶ Parameter  $\gamma$  can be updated through a Gibbs step:

$$f(\gamma|\mathbf{i}, \mathbf{r}, \beta) \propto f(\beta, \gamma, \mathbf{i}, \mathbf{r}) \propto f(\mathbf{i}, \mathbf{r}|\beta, \gamma)f(\gamma)$$

$$\propto \gamma^n \exp\left(-\gamma \int_0^T I(u)du\right) \gamma^{\nu_\gamma-1} \exp(-\lambda_\gamma \gamma)$$

- ▶ This means that

$$\gamma|(\mathbf{i}, \mathbf{r}, \beta) \sim \Gamma\left(n + \nu_\gamma, \int_0^T I(u)du + \lambda_\gamma\right)$$

# Computation of the integral terms

- In practice, the integral terms can be calculated as follows:

total time spent infective

$$\overbrace{\int_0^T I(u) du}^{\text{total time spent infective}} = \sum_{k=1}^n (r_k - i_k)$$

total time for "infectious pressure"

$$\overbrace{\int_0^T I(u) S(u) du}^{\text{total time for "infectious pressure"}} = \sum_{k=1}^n \sum_{j=1}^M (\min(r_k, i_j) - \min(i_k, i_j))$$

where  $i_j = \infty$  for  $j > n$ , i.e., for those never infected

- These expressions are invariant to choice of which  $r_k$  corresponds to which  $i_k$



# Incomplete data

- ▶ Assume that only the removal times  $\mathbf{r} = (r_1, \dots, r_n)$  have been observed
- ▶ Augment the set of unknowns ( $\beta$  and  $\gamma$ ) with infection times  $\mathbf{i} = (i_2, \dots, i_n)$
- ▶ The aim is to do statistical inference about rates  $\beta$  and  $\gamma$  (and times  $\mathbf{i}$ ), based on their posterior distribution  $f(\beta, \gamma, \mathbf{i} | \mathbf{r})$
- ▶ The posterior distribution is proportional to the joint distribution of all model quantities:

$$f(\beta, \gamma, \mathbf{i} | \mathbf{r}) \propto f(\beta, \gamma, \mathbf{i}, \mathbf{r}) = \overbrace{f(\mathbf{i}, \mathbf{r} | \beta, \gamma)}^{\text{complete data likelihood}} \overbrace{f(\beta)f(\gamma)}^{\text{prior}},$$

# Updating infection times

- ▶ The full conditional distributions of  $\beta$  and  $\gamma$  are as above
- ▶ The unknown infection times  $\mathbf{t}$  require a Metropolis–Hastings step, including explicit evaluations of the Poisson likelihood
- ▶ If the current iterate of  $i_k$  is  $i_k^{(j)}$ , a new value  $\tilde{i}_k$  is first proposed (e.g.) from a uniform distribution on  $[0, T]$
- ▶ The proposal is then accepted, i.e.,  $i_k^{(j+1)} := \tilde{i}_k$ , with probability

$$\min\left\{1, \frac{f(\tilde{\mathbf{i}}, \mathbf{r} | \beta, \gamma)}{f(\mathbf{i}, \mathbf{r} | \beta, \gamma)}\right\}$$

- ▶ Here  $\tilde{\mathbf{i}}$  is  $\mathbf{i}$  except for the  $k$ th entry which is  $\tilde{i}_k$  (instead of  $i_k^{(j)}$ )

# Augmenting individual histories

- ▶ The likelihood above was constructed for the aggregate processes, i.e., to count the total numbers of susceptibles and infectives
- ▶ In such case, the corresponding augmentation model must not consider individuals
  - ▶ In particular, times  $i_2, \dots, i_n$  must not be tied to particular removal times, i.e., individual event histories must not be reconstructed
- ▶ If one considers individual event histories as pairs of times  $(i_k, r_k)$  for individuals  $k = 1, \dots, M$ , the appropriate complete data likelihood is

$$\gamma^n \prod_{k=2}^n \{\beta I(i_k)\} \exp \left( - \int_0^T (\gamma I(u) + (\beta/M) I(u) S(u)) du \right)$$

## Example: a smallpox outbreak

- ▶ The Abakaliki smallpox outbreak
  - ▶ A village of  $M = 120$  inhabitants
  - ▶ One introductory case
  - ▶ 29 subsequent cases; this means that  $n = 1 + 29 = 30$
- ▶ We will assume that the index case started being infectious on day 0 and that she/he entered the village starting the outbreak at the same day
- ▶ The observed data are the 30 removal times (in days) with respect to the time origin:

14, 27, 34, 36, 39, 39, 39, 40, 44, 49, 52, 54, 54, 56, 56,  
61, 64, 65, 69, 69, 70, 71, 72, 74, 74, 75, 80, 80, 85, 90

- ▶ The problem: to estimate rates  $\beta$  and  $\gamma$  from these data; see the computer lab data

## A useful reference

- ▶ The computer lab analysis of the Abakaliki data is not realistic as it omits
  - ▶ the relevant stages of infection (incubation time from exposure to infectiousness, possibly varying infectiousness during fever and the subsequent rash/symptoms)
  - ▶ the fact that isolation of cases at their symptomatic stage was only implemented at some point during the outbreak
  - ▶ community structure (compounds in the village and the larger community)
  - ▶ two more cases that occurred outside the particular group of faith with the 30 cases considered here
- ▶ For example, we assumed for simplicity that removal occurred at the time of symptoms although in reality removal only occurred at recovery/death or isolation, and only after some delay since symptom onset
- ▶ A proper analysis is given by Stockdale et al. (2017)

# References

- [1] O'Neill Ph. and Roberts G. Bayesian inference for partially observed stochastic processes. *Journal of the Royal Statistical Society, Series A*, 1999; 162: 121–129.
- [2] O'Neill Ph. A tutorial introduction to Bayesian inference for stochastic epidemic models using Markov chain Monte Carlo methods. *Mathematical Biosciences* 2002; 180:103–114.
- [3] Becker N. *Analysis of infectious disease data*. Chapman and Hall, New York 1989.
- [4] Andersen et al. *Statistical models based on counting processes*. Springer Verlag, New York, 1993.
- [5] Stockdale J, Kypraios Th., O'Neill Ph. Modelling and Bayesian analysis of the Abakaliki smallpox data. *Epidemics* 2017; 19:13–23.