Data augmentation in the general epidemic model

SISMID/July 17–19, 2017

Instructors: Kari Auranen, Elizabeth Halloran, Vladimir Minin

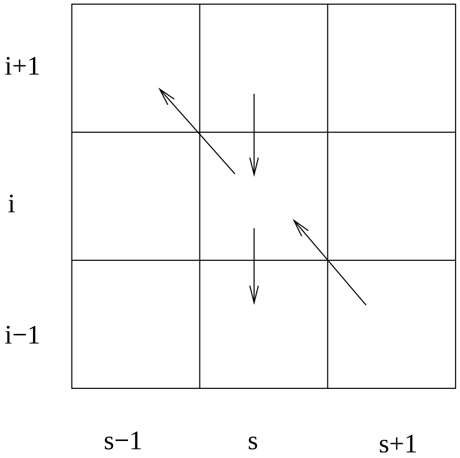
Outline

- The general epidemic model
  - A simple Susceptible–Infected–Removed (SIR) model of an outbreak of infection in a closed population
- Poisson likelihood for 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 γ, 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 $t = 0$ (i.e. 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

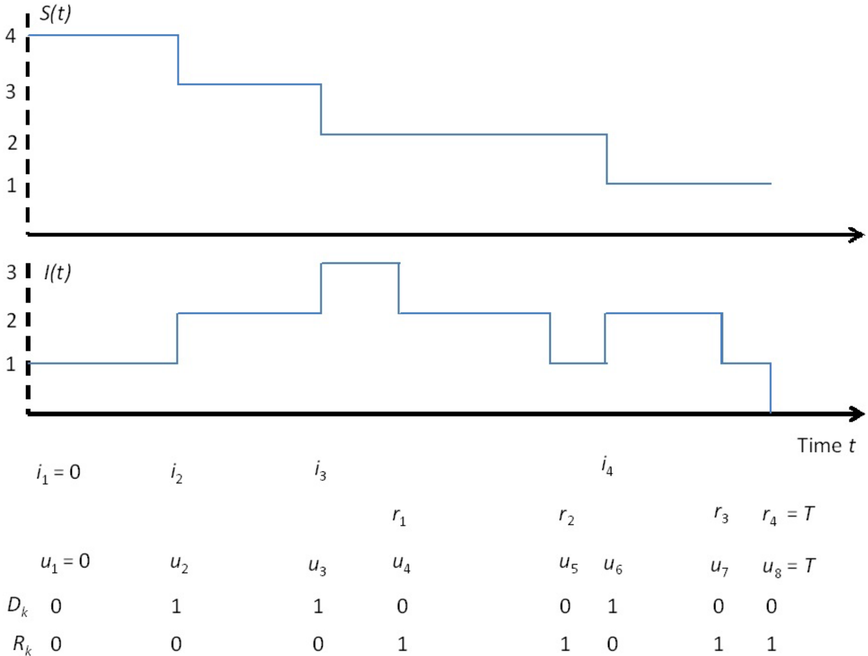
$$\overbrace{\{0 = i_1 < i_2 < \ldots < i_n\}}^{\text{infection times}} \text{ and } \overbrace{\{r_1 < \ldots < r_{n-1} < r_n = T\}}^{\text{removal times}}$$

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

Counting infectives and susceptibles

- Denote the ordered event times $i_1, \ldots, i_n$ and $r_1, \ldots, r_n$ jointly as $0 = u_1 < u_2 < \ldots < u_{2n} = T$
- 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 $\{0, 1, \ldots, M\}$
  - it jumps at times $u_2 < \ldots < u_{2n}$
- Denote the number of susceptibles at time t by $S(t)$
  - it is a piecewise constant (left-continuous) function, jumping at times $i_2 < \ldots < i_n$
- Both $I(t)$ and $S(t)$ are determined by the complete data

Example


S(t)
4
3
2
1
I(t)
3
2
1
Time t
i1 = 0
i2
i3
i4
r1
r2
r3
r4 = T
u1 = 0
u2
u3
u4
u5
u6
u7
u8 = T
Dk 0 1 1 0 0 1 0 0
Rk 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 $u_2 < \ldots < u_{2n}$, with levels $\beta I(u_2)S(u_2)/M, \beta I(u_3)S(u_3)/M, \ldots, \beta I(u_{2n})S(u_{2n})/M$
- The probability density of the infection events is thus proportional to

$$\prod_{k=2}^{2n} \left[((\beta/M) I(u_k) S(u_k))^{D_k} \exp^{-(\beta/M) I(u_k) S(u_k)(u_k - u_{k-1})} \right]$$

$$\propto \prod_{k=2}^{2n} (\beta I(u_k) S(u_k))^{D_k} \times \exp^{-(\beta/M) \overbrace{\sum_{k=2}^{2n} I(u_k) S(u_k)(u_k - u_{k-1})}^{\text{total time for ``infectious pressure''}}}$$

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 $u_2 < \ldots < u_{2n}$, with levels $\gamma I(u_2), \gamma I(u_3), \ldots, \gamma I(u_{2n})$
- The probability density of the removal events is thus proportional to

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

$$= \prod_{k=2}^{2n} (\gamma I(u_k))^{R_k} \times \exp^{-\gamma \overbrace{\sum_{k=2}^{2n} I(u_k)(u_k - u_{k-1})}^{\text{total time spent infective}}}$$

Complete data likelihood

- The joint likelihood of parameters β and γ, based on the complete data:

$$\overbrace{L(\beta, \gamma; \boldsymbol{i}, \boldsymbol{r})}^{f(\boldsymbol{i},\boldsymbol{r}|\beta,\gamma)} = \prod_{k=2}^{2n} (\beta I(u_k) S(u_k))^{D_k} \prod_{k=2}^{2n} (\gamma I(u_k))^{R_k}$$

$$\times \quad \exp^{-\sum_{k=2}^{2n}((\beta/M)I(u_k)S(u_k)+\gamma I(u_k))(u_k-u_{k-1})}$$

$$= \quad \prod_{k=2}^{n} \{\beta I(i_k) S(i_k)\} \prod_{k=1}^{n} \{\gamma I(r_k)\}$$

$$\times \quad \exp\ {-\sum_{k=2}^{2n}((\beta/M)I(u_k)S(u_k)+\gamma I(u_k))(u_k-u_{k-1})}$$

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 β and γ
- In particular, Gamma distributions can be used as conjugate priors for β and γ
- It follows that the full conditional distributions of β and γ are also Gamma and can be updated by Gibbs steps

Gamma prior distributions

- Rate parameters β and γ 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 β

- Parameter β can be updated through a Gibbs step

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

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

- This means that

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

The full conditional of γ

- Parameter γ can be updated through a Gibbs step:

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

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

- This means that

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

Computation of the integral terms

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

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

$$\overbrace{\int_0^T I(u)S(u)du}^{\text{total time for ``infectious pressure''}} = \sum_{k=1}^{n}\sum_{j=1}^{M}(\min(r_k, i_j) - \min(i_k, i_j))$$

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

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

Updating infection times

- The full conditional distributions of β and γ are as above
- The unknown infection times 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., $i_k^{(j+1)} := \tilde{i}$, with probability

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

- Here $\tilde{\boldsymbol{i}}$ is $\boldsymbol{i}$ except for the kth 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 $i_2, \ldots, i_n$ 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 $k = 1, \ldots, M$, the appropriate complete data likelihood is (cf. above)

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

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 β and γ from these outbreak; see the computer class exercise data

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.