SOME STOCHASTIC MODELS IN EPIDEMICS

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INTRODUCTION

- stochastic models

  - the variables considered in the model are random and with a probability distribution

  - the distribution and model depend on some parameters

- Markov chain models (SIR)

  - model de evolution of the epidemics (number of Susceptible, Infected and Recovered individuals)

  - configuration of the population depends on present state only (given present the past and future history are independent)

  - also depend on some parameters (model assumed)

- Bayesian formulation and estimation

  - the parameters of the model are also considered random quantities with a probability distribution (density)

  - estimate the parameters using the so-called posterior distribution of the parameters

  - based on the relation among the posterior and prior distributions and the likelihood of the model, e.g.,

    * θ: vector of parameters of the model

    * $\mathbf{Y}$: observed data

    * $P(\theta \,|\, \mathbf{Y}) \propto L(\mathbf{Y} \,|\, \theta)\, P(\theta)$

- Markov chain Monte Carlo methods (MCMC me-thods)

  - posterior distribution does not have closed form

  - dimension of the vector of parameters is very large

  - use MCMC algorithms and the Law of Large Number

$$\int f(x)\, g(x)\, dx \sim \frac{1}{M} \sum_{i=1}^{M} f(X_i)$$

  - other quantities may also be estimated

    * density distribution

    * variance and standard deviation

– MCMC algorithms

* $\pi(\cdot)$: target distribution

$$\pi(x) = \frac{h(x)}{c}$$

* construct a Markov chain with $\pi(\cdot)$ as its stationary distribution

* allow the chain run for a suitable period and from that moment on the values simulated are drawn approximately from $\pi(\cdot)$

- Metropolis-Hastings algorithm

  * $X_n = x$ then generate a value y using a transition probability P_{xy}

  * calculate

  $$\alpha(x, y) = \min \left\{ 1, \frac{\pi(y) \, P_{yx}}{\pi(x) \, P_{xy}} \right\}$$

  * with probability $\alpha(x, y)$ accept the new value for the chain. i.e., $X_{n+1} = y$, otherwise no change occurs, i.e., $X_{n+1} = x$

– Gibbs sampling algorithm

  * $P(x_1, x_2, \ldots, x_d)$

  * $P(x'_i \mid x'_1, x'_2, \ldots, x'_{i-1}, x_{i+1}, x_d)$: easy to simulate value from it

  * successively simulate the corresponding values

  * Markov chain which under appropriate conditions is ergodic

EXAMPLE

- applied to influenza epidemics (theoretical part) - Cauchemez *et al.*, 2004

- Bayesian approach

- parameters of the models are estimated using Markov chain Monte Carlo methods

  - Metropolis-Hastings

- data from 334 households during winter 1999-2000

- absence/presence of influenza reported daily for 15 days

MATHEMATICAL DESCRIPTION OF THE PROBLEM

- k: number of households

- $N^{(k)}$: size of the kth household

- $N^{(f)}$: number of families

- $i \in \{1, 2, \ldots, N^{(k)}\}$: individual in family k

- $j \in \{0, 1, 2, \ldots, 14\}$: day at which individuals are observed

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Y_{ij}^{(k)} = \begin{cases} 1, & \text{clinical influenza was observed} \\ 0, & \text{otherwise} \end{cases}
$$

- $I^{(k)}$: individuals report at least one day with clinical influenza in family k

- $S^{(k)}$: remaining members of the k family

- $Z_i^{(k)}$: first day of influenza for individual $i \in I^{(k)}$

- $\nu_i^{(k)}$: start of infectious period for individual i in family k

- $\psi_i^{(k)}$: end of infectious period for individual i in family k

- $\nu = \{\nu_i^{(k)}, \, i = 1, 2, \ldots, N^{(k)}, \, k = 1, 2, \ldots, N^{(f)}\}$

- $\psi = \{\psi_i^{(k)}, \, i = 1, 2, \ldots, N^{(k)}, \, k = 1, 2, \ldots, N^{(f)}\}$

- I: set of individuals in the sample such that the starts of its infectious period fell between 1 and 3 days

- transmission level

  - s: susceptible individual just before time t

  - α_s: instantaneous risk of infection from the community (depends on characteristics of individuals s)

  - ϵ_s: susceptibility to infection of individual s

  - β_i: ability of infective individual i to infect others

  - n: size of a given household where individual s belongs to

- contribution of infective individual i in a household of size n

  - β_i / n

  - β_i / n^η

  where η is a parameter that also needs to be estimated

- $I^{(k)}(t) = \{i \in I^{(k)} : \nu_i^{(k)} < t \leq \psi_i^{(k)}\}$: group of infective just before time t

- $Y^{(k)} = \{Y_{ij}^{(k)}, i \in \{1, 2, \ldots, N^{(k)}\},$
  $j \in \{0, 1, 2, \ldots, 14\}\}$: all observations in family k

- $Y = \{Y^{(k)}, k = 1, 2, \ldots, N^{(f)}\}$: all observations

- $\lambda_s(t)$: instantaneous risk of infection at time t for the individual s

$$\lambda_s(t) = \alpha_s + \epsilon_s \sum_{i \in I(t)} \frac{\beta_i}{n}$$

BAYESIAN FORMULATION

- θ vector of parameter

- $P(\theta, \nu, \psi \,|\, Y) \propto L(Y \,|\, \nu, \psi)\, P(\nu, \psi \,|\, \theta)\, P(\theta)$

- Likelihood function of observed data

  - $L(Y \mid \nu, \psi) = \prod_{i=1}^{N^{(f)}} P(Y^{(k)} \mid \nu^{(k)}, \psi^{(k)})$

  - incubation period: $1 - 3$ days (augmented data were compatible with observations)

  - $\prod_{i \in I} I(Z_i - 3 < \nu_i < Z_i$ and $\nu_i < \psi_i)$

- Likelihood for augmented data

  - $P(\nu, \psi \,|\, \theta) = \prod_{i=1}^{N^{(f)}} P(\nu^{(k)} \,\psi^{(k)} \,|\, \theta)$

  - $\psi_i - \nu_i \stackrel{\mathcal{D}}{=}$ Gamma distribution with μ_i and standard deviation σ_i and density d_{μ_i, σ_i}

  - condition on ν'

$$P(\nu, \psi \,|\, \theta) = \left(\prod_{i \in I} d_{\mu_i, \sigma_i}(\psi_i - \nu_i) \right)$$

$$\left(\prod_{i \in I - \{1\}} \lambda_i(\nu_i) e^{\int_{\nu'}^{\nu_i} \lambda_i(t)\, dt} \right)$$

$$\left(\prod_{s \in S} e^{\int_{\nu'}^{15} \lambda_s(t)\, dt} \right)$$

where

* ν': start of the infectious period for the first infected individual (in the entire community)

* $I - \{1\}$: infective individuals without the first infective

* 15: number of observed days

- vector of parameters

  - $P(\theta)$: prior distribution of the vector of parameters

  - $\epsilon = (\epsilon_C, \epsilon_A)$

  - $\alpha = (\alpha_C, \alpha_A)$

  - $\theta = (\mu, \sigma, \alpha, \beta, \epsilon, \eta)$

- $CPI(i)$: probability for individual i to be infected from the community in the 15-day follow-up (Community Probability of Infection)

$$CPI(i) = 1 - e^{-15\,\alpha_i}$$

- $SAR(i \to s)$: (Secondary Attack Rate)

P(infective i infects susceptible s in household of size n)

$$SAR(i \to s) = 1 - \int_0^{\infty} e^{-\frac{\epsilon_s\,\beta_i}{n}t} \, d\mu_i,\sigma_i(t) \, dt$$

SIMULATION

- prior distributions used

  - $\mu, \sigma \overset{\mathcal{D}}{=}$ Gamma, mean 3 and SD 2

  - $\alpha, \beta \overset{\mathcal{D}}{=}$ Exp(0.001)

  - $\eta \overset{\mathcal{D}}{=} U[-3, 3]$

  - $\log(\epsilon_C) \overset{\mathcal{D}}{=}$ Logistic with scale parameter 1

  - adults were reference category $\rightarrow \epsilon_A = 1$

- initial values

  - $\nu_i^{(k)} \stackrel{\mathcal{D}}{=} U[Z_i^{(k)} - 3, Z_i^{(k)}]$

  - $\psi_i^{(k)} - \nu_i^{(k)} \stackrel{\mathcal{D}}{=} U[0, 20]$

  - $\alpha, \beta \stackrel{\mathcal{D}}{=} U[0, 1]$

  - $\mu, \sigma \stackrel{\mathcal{D}}{=} U[0, 10]$

  - $\epsilon_C, \eta \stackrel{\mathcal{D}}{=}$ respective prior distributions

COMMENTS

- several hypothesis were tested by the authors

- selection of the best hypothesis for the model fitting the data was made using Bayes Factor

- substantial evidence that children are more susceptible than adults $\epsilon_C > 1$

- substantial evidence that community risk is larger for children than adults $\alpha_C > \alpha_A$

- poor evidence against the hypothesis that on average children are infectious for a longer period than adults $\mu_C > \mu_A$

- strong evidence favoring that household risk is larger with infectious child than with infectious adult $\beta_C > \beta_A$

- decisive evidence that SAR is larger with infectious child that with infectious adult , i.e., for $n \in \{2, 3, 4, 5\}$, $SAR_C(n) > SAR_A(n)$

- modifications and further generalisations may be considered

- simplified by using the software Winbugs (Spiegelhalter *et al.*, 1999)

- http://www.mrc_bsu.cam.ac.uk/bug/winbugs/