The plague disease
Data
Modelling
Inference
Preliminary results
Final remarks
References

#### Bayesian analysis of plague in Kazakhstan

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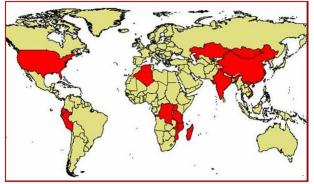
Smögen, August 16-20, 2010 Lise Heier, Hildegunn Viljugrein, Nils Chr Stenseth, Bård Ø. Kvaal



#### Outline

- The plague disease
- 2 Data
- Modelling
- Inference
- Preliminary results
- 6 Final remarks

## Human cases of Plague

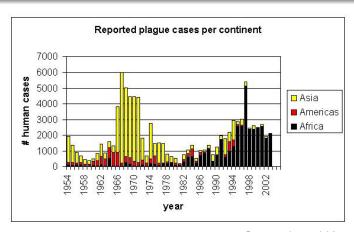


Kausrud [2009]

Stenseth and



# Cases per continent



Stenseth and Kausrud [2009]



## Plague is a highly variable disease

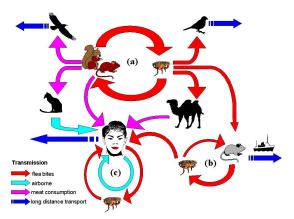
 Given rise to at least three pandemics, with smaller endemics in between.



- A variety of host species: Great Gerbils
- A variety of vector species (transmitting the bacteria (Yersinia pestis))
- Complex temporal patterns
- Complex spatial patterns



## Plague system



Stenseth and Kausrud [2009]



#### Questions of interest

- Biology: Understand the dynamics of plague
  - Why do plague "disappear" in periods?
  - How do population sizes influence occurence of plague
  - How do climatic variables influence plague and/or population sizes?
  - Are there spatial structure in where plague appear?
- Here: Mainly modelling absence/presence of plague



#### Kazakhstan data

Data collected within sectors (squares), spring and autumn



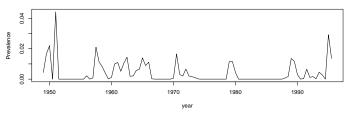


- Gerbils:
  - Observed ratio of occupied burrows,  $R_{t,i}$  ("density").
  - Number of tested  $N_{t,i}$  and positive  $Y_{t,i}$  animals
- Similar data for fleas.
- Much missing data

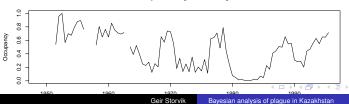


## Data aggregated over space

#### Observed prevalence of Plague, averaged over sites



#### Observed density of Great gerbils, averaged over sites



## Previous analyses

- Time series approach, Spatially aggregated/single sites [Davis et al., 2004, Park et al., 2006a,b]
- Bayesian analysis, only Gerbils [Frigessi et al., 2005]
- GLMM approach with spatial random effects [Heier, L. and Storvik, G. and Davis, S. A. and Viljugrein, H. and Ageyev, V, A and Klassovskaya, E. and Stenseth NC, 2010]
  - Can use standard software
  - Many missing variables of plague or gerbil density (multiple imputation possible)
  - Difficult to take into account measurement errors (both in responses and covariates)
- Main interest been in presence/absence of plague



#### Overall model structure

- Process models
  - Model for plague given host density
    - So far only considering presence/absence of plague
  - Model for host "density"
    - Density actually fraction of occupied collonies
    - Model needed because of missing observations
- Measurement models
  - Plaque data
  - Density data
- Bayesian approach
  - Prior models



## Model for plague

- $z_{t,i} = 1$  if plague in site i at time t
- Logistic type models with random effects for all cases.

$$logit(Pr(z_{t,i} = 1|past)) = \alpha_{t,i}(past) + \varepsilon_{t,i}$$

- $\{z_{t,i}, i = 1, ..., N\}$  independent given  $\{\alpha_{t,i}\}$  and  $\{\varepsilon_{t,i}\}$ .
- Spatial correlation through spatial correlation in  $\{\varepsilon_{t,i}\}$ .
- Temporal correlation through  $\alpha_{t,i}(past)$ .
- $\varepsilon_t \sim GCAR(\rho_{\varepsilon}, \tau_{\varepsilon})$ , independent in time.

#### Model for $\alpha$ 's

• Three "cases" of plague, depending on past:



Persistence: 
$$z_{t-1,i} = 1$$

Spread:
$$z_{t-1,i} = 0, \sum_{j \sim i} z_{t-1,j} > 0$$



Invasion:
$$z_{t-1,i} = 0, \sum_{j \sim i} z_{t-1,j} = 0$$

## Models for $\alpha$ 's (cont)

- $\phi_{t,i}$  is occupancy of gerbils at logit-scale.
- Persistence

$$\alpha_{t,i} = b_{p,P} \phi_{t,i} + c_{p,P} \sum_{j \in \delta_i} z_{t-1,j} + \mathbf{x}_{t,i}^{\mathsf{T}} \alpha_P$$

Spread

$$lpha_{t,i} = b_{p,S}\phi_{t,i} + c_{p,S}\sum_{j\in\delta_i}z_{t-1,j} + \mathbf{x}_{t,i}^{\mathsf{T}}lpha_{\mathcal{S}}$$

Invasion

$$\alpha_{t,i} = b_{p,l}\phi_{t,i} + \mathbf{x}_{t,i}^{\mathsf{T}}\alpha_l + s_{l,i}$$

•  $\{s_{l,i}\}$  spatial process  $\sim GCAR(\rho_S, \tau_S)$ .



## Measurement model

- Observed  $(N_{t,i}, Y_{t,i})$ .
- Assume no error in test
- Assume  $Y_{i,t} \sim \text{Binom}(N_{t,i}, p_{t,i}), p_{t,i}$  prevalence of plague
- $Z_{t,i} = 1$  iff  $p_{t,i} > 0$
- If  $Y_{t,i} > 0$ , then  $Z_{t,i} = 1$
- If  $Y_{t,i} = 0$ , then  $Z_{t,i} = ?$
- Assume  $p_{t,i} \sim \text{Beta}(\alpha, \beta)$  if  $Z_{t,i} = 1$ .
- Gives

$$Pr(Y_{t,i} = 0 | Z_{t,i} = 0) = 1$$

$$Pr(Y_{t,i} = 0 | Z_{t,i} = 1) = \frac{\Gamma(\alpha + \beta)\Gamma(n + \beta)}{\Gamma(\beta)\Gamma(n + \alpha + \beta)}$$



# Model for occupancy

$$\phi_{t,i} = \mathbf{x}_{t,i}^T \boldsymbol{\beta} + \rho_t (\phi_{t-1,i} - \mathbf{x}_{t-1,i}^T \boldsymbol{\beta}) + u_{t,i}$$

•  $\mathbf{u}_t \sim GCAR(\rho_\phi, \tau_\phi)$ , independent in time.

## Spatial models

 $GCAR(\rho, \tau)$  Gaussian conditional autoregressive model

$$\begin{aligned} \mathbf{U} \sim & \mathsf{MVN}(\mathbf{0}, (\tau \mathbf{Q}(\rho))^{-1}) \\ \mathbf{Q}(\rho) = & \rho \mathbf{P} + (1 - \rho)\mathbf{I} \\ P_{ij} = \begin{cases} m_i & j = i \\ -1 & j \in \delta_i \\ 0 & \text{otherwise} \end{cases} \end{aligned}$$

MacNab [2003]: avoiding potential identifiability problems.

 $\rho =$  1 corresponds to the intrinsic autregression model

 $\rho = 0$  corresponds to an independence model.

Note: Q is sparse!



## "Direct" approach

- $\theta_a$  parameters for abundance model
- $\theta_p$  parameters for plague model

$$f(\phi, \mathbf{Z}|\theta_a, \theta_p) = \prod_t f(\phi_t|\phi_{t-1}; \theta_a) f(\mathbf{Z}_t|\mathbf{Z}_{t-1}, \phi_t; \theta_p)$$

$$= \prod_t f(\phi_t|\phi_{t-1}; \theta_a)$$

$$\prod_t f(\mathbf{Z}_t|\mathbf{Z}_{t-1}, \phi_t; \theta_p)$$

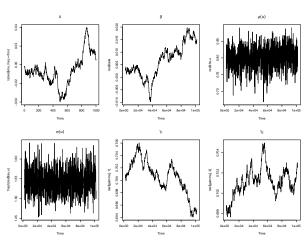
- Each part GLMM type
- Missing/incomplete data: Multiple imputation
- Works, but complicated, not utilizing data fully



## Bayesian analysis

- Denote  $\theta$  hyperparameters involved
  - Regression parameters
  - Precisions
  - Correlation parameters
- Prior  $\pi(\theta)$  mainly noninformative
- Bayesian inference:  $\pi(\theta, \phi, \mathbf{z}|\mathbf{y})$
- Computation through Markov Chain Monte Carlo
- Possible to use Winbugs/Jags?

## Using existing software - JAGS



#### Markov chain Monte Carlo

- Many variables to be updated
- Plague:  $\{z_{t,i}\}$ ,  $N \times T$ , binary
- Random effects plague:  $\{\varepsilon_{t,i}\}$ ,  $N \times T$ , Gaussian prior
- Invasion process:  $\{s_{l,i}\}$ , N, Gaussian prior
- Occupancy:  $\{\phi_{t,i}\}$ ,  $N \times T$ , Gaussian prior
- Regression parameters,  $b_{p,P/S/I}, c_{p,P/S}, \alpha_P, \alpha_S, \alpha_I, \beta$
- Precision parameters,  $\tau_{\varepsilon}, \tau_{\mathcal{S}}, \tau_{\phi}$
- Correlation parameters:  $\rho_{\varepsilon}$ ,  $\rho_{\mathcal{S}}$ ,  $\rho_{\phi}$ ,  $\rho_{t}$
- Fast convergence: Update (large) blocks simultaneously (GMRFLib)



## Block-updating continuous processes

- Knorr-Held and Rue [2002], Rue and Held [2005]
- Continuous processes of the form

$$\pi(\mathbf{x}|\mathbf{ heta},\mathbf{y}) \propto \exp\{-rac{1}{2}(\mathbf{x}-oldsymbol{\mu}(\mathbf{ heta}))^T\mathbf{Q}(\mathbf{ heta})(\mathbf{x}-oldsymbol{\mu}(\mathbf{ heta})) + \sum_i d_i \log g(x_i;y_i,oldsymbol{ heta})\}$$

- Regression parameters included in x.
- Metropolis Hastings:  $\theta^* \sim q_1(\cdot|\theta)$ ,  $\mathbf{x}^* \sim q_2(\cdot|\theta^*,\mathbf{x})$
- $q_2$  Gaussian approx. to  $\pi(\mathbf{x}|\boldsymbol{\theta}^*)$ , independent of  $\mathbf{x}$ !
- Acceptance ratio

$$R = \frac{\pi(\boldsymbol{\theta}^*)\pi(\mathbf{x}^*|\boldsymbol{\theta}^*)f(\mathbf{y}|\mathbf{x}^*,\boldsymbol{\theta}^*)}{\pi(\boldsymbol{\theta})\pi(\mathbf{x}|\boldsymbol{\theta}^*)f(\mathbf{y}|\mathbf{x},\boldsymbol{\theta})} \times \frac{q_1(\boldsymbol{\theta}|\boldsymbol{\theta}^*)q_2(\mathbf{x}|\boldsymbol{\theta},\mathbf{x}^*)}{q_1(\boldsymbol{\theta}^*|\boldsymbol{\theta})q_2(\mathbf{x}^*|\boldsymbol{\theta}^*,\mathbf{x})}$$



## Sparse matrix operations

- Q sparse, both in time and space.
- GMRFLib [Rue and Held, 2005], a C-library for automatic simulation from

$$\pi(\theta, \mathbf{x}|\mathbf{y}) \propto \pi(\theta) \exp\{-\frac{1}{2}(\mathbf{x} - \boldsymbol{\mu}(\theta))^T \mathbf{Q}(\theta)(\mathbf{x} - \boldsymbol{\mu}(\theta)) + \sum_i d_i \log g(x_i; y_i, \theta)\}$$

- Sparseness in time could have been handled through Kalman filter approximation.
- GMRFLib automatially handles spareness both in space and time.
- Example: Q 3480 × 3480, : Acceptance rate 0.29!



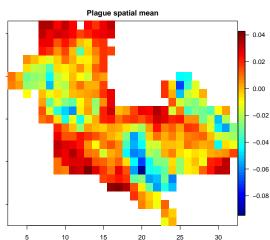
## Preliminary results

- Years 1986-1995
- Only gerbils data
- Only data from fall
- Covariate: Absolute minimum of air temperature in one month.
- MCMC: 1000 burnin, 50000 additional iterations

#### Results

- Density highly significant for plague
- Past presence of plague slightly significant
- Clear spatial structure both in density and in plague
- Absolute minimum of air temperature in one month slightly significant on density but not on plague
- Spatial structure in invasion but significant?

## Plague spatial mean (logit-scale)



Geir Storvik

Bayesian analysis of plague in Kazakhstan

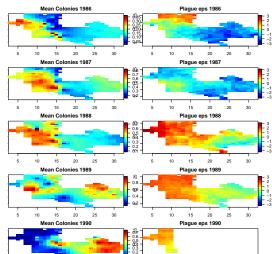
#### Residuals

#### Model

$$\phi_{t,i} = \rho_t \phi_{t-1,i} + \mathbf{x}_{t,i}^T \boldsymbol{\beta} + u_{t,i}$$
$$logit(Pr(z_{t,i} = 1|past)) = \alpha_{t,i}(past) + \varepsilon_{t,i}$$

Structure in  $\{\varepsilon_{t,i}\}$ ,  $\{u_{t,i}\}$ ?

#### Residuals



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#### Extensions

- Better observation models
- Including fleas data
- Nonlinear relation to gerbil density
- Better proposals in MCMC
- Model critisism/evaluation!

## Summary/Discussion

- Preliminary version of full Gerbil-plague analysis
- Seems to confirm previous analyses
- Efficient MCMC implementation
- Further improvements/extensions needed

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