



# Bayesian Modelling of Epidemics

## Part IV: Analyzing Infectious Disease Data with the Epi-ILM R Package

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## 1. Inference for Discrete-time ILMs

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### 2.2 Spatial Model With Farm Size

### 2.3 Adding In the Sparks Term

### 2.4 Fitting SIR Models

## 3. Example 2: Network-based model

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# Likelihood function

For our class of discrete-time SI and SIR models, assuming we know when infection and removals occur,

the **likelihood** is given by:

$$L(D|\theta) = \prod_t \left[ \prod_{i \in S(t+1)} (1 - P(i, t)) \right] \left[ \prod_{i \in I(t+1)/I(t)} P(i, t) \right]$$

where:

$S(t + 1)$  is the set of all susceptible individuals at time  $t + 1$

$I(t + 1)/I(t)$  is the set of all newly infectious individuals at time  $t + 1$

# Statistical inference for ILMs

We will use Markov chain Monte Carlo (MCMC) techniques to sample from the posterior:

$$\pi(\boldsymbol{\theta} \mid \mathbf{D}) \propto L(\mathbf{D} \mid \boldsymbol{\theta}) Pr(\boldsymbol{\theta})$$

Programs like NIMBLE, JAGS or BUGS are not suited to these types of models

Basically, the likelihood is too computationally cumbersome

But we can use the EpiILM R package

(Uses FORTRAN code to calculate the likelihood function)

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## Example 1: Spatial Disease System

### Example:

Imagine we are modelling the spread of a transmissible disease through a series of farms.

We know the number of animals on each farm from a recent census

We know the spatial locations of the farms.

It seems reasonable to treat the farms themselves as individual level unit.

The extent of infection from outside the observed population of farms is unknown.

We have observed/estimated the times at which disease entered infected farms (infection times)

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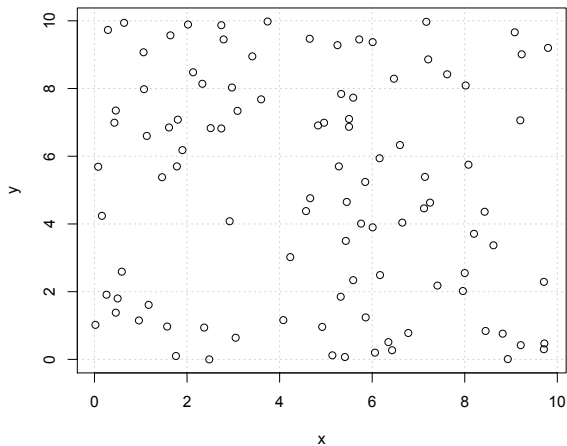


## Data set: "DATA/ISBA\_spatialepidemic.csv"

x	y	XA	inftime
3.11	4.92	141	2
1.07	0.61	47	2
1.54	0.93	23	2
6.21	8.53	576	4
4.16	9.94	11	5
6.61	8.37	231	5
8.45	6.6	10	5
0.52	5.08	16	4
5.68	3.36	140	4
0.49	5.21	23	4
0.29	8.05	54	5
5.34	0.14	10	5
5.96	1.51	36	4
3.91	5.92	176	3
5.35	5.89	164	4
3.09	1.92	139	2
6.24	9.7	93	5
1.9	4.39	211	3
6.49	4.28	53	4
3.14	5.57	262	3
1.72	2.85	52	2
9.4	0.81	30	5
1.03	8.24	77	5
9.12	1.48	2	6
4.21	7.16	157	3
. . .			

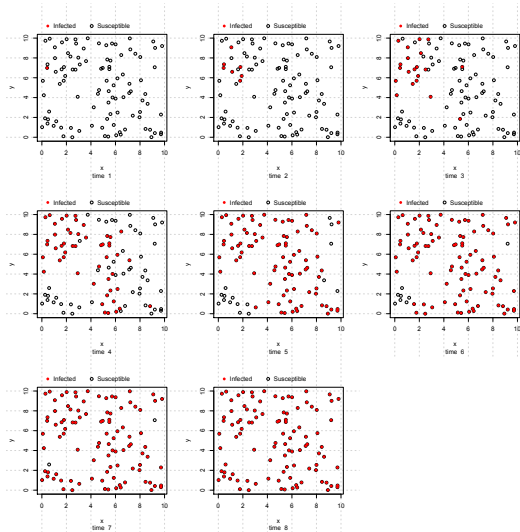


# Spatial plot



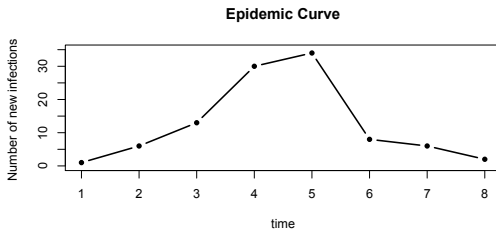
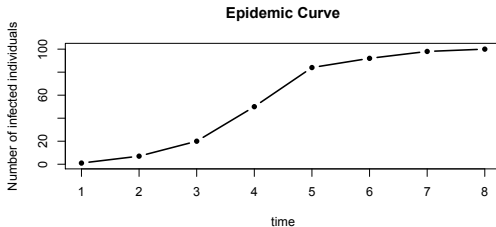
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# Spatial plot



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# Epidemic curves



# Simple Spatial Model

Initially, let us:

- assume an SI compartmental framework

- assume negligible infection from outside of the observed population  
(i.e.,  $\epsilon = 0$ )

- fit a purely spatial model, ignoring any number of animals effect

# Simple Spatial Model

For this model:

Susceptibility:	$\mathcal{S}(i)$	$=$	$\alpha$
Transmissibility:	$\mathcal{T}(j)$	$=$	$1$
Infection Kernel:	$\kappa(i, j)$	$=$	$d_{ij}^{-\beta}$
Sparks:	$\epsilon(i, t)$	$=$	$0$

So our model is:

$$P(i, t) = 1 - \exp \left( -\alpha \sum_{j \in I(t)} d_{ij}^{-\beta} \right)$$

where:

$d_{ij}$  is the spatial distance between individuals  $i$  and  $j$

$\alpha$  is an infectivity parameter

$\beta$  is a spatial parameter

# Priors

Here, we have two parameters:  $\theta = (\alpha, \beta)$

Let's assume we have no substantive prior knowledge about them we wish to include in our analysis.

We could do this using any of the three priors offered by EpiLM

- half normal
- gamma
- uniform

Here, we will put uniform priors on the parameters with a wide range:

$$\alpha \sim \text{Uniform}[0, 10000]$$

$$\beta \sim \text{Uniform}[0, 10000]$$

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# Spatial Model With Farm Size

We will now consider a model with farm size (number of animals) included as a susceptibility covariate

For this model:

$$\text{Susceptibility:} \quad S(i) = \alpha_0 + \alpha_1 X_A(i)$$

$$\text{Transmissibility:} \quad \mathcal{T}(j) = 1$$

$$\text{Infection Kernel:} \quad \kappa(i, j) = d_{ij}^{-\beta}$$

$$\text{Sparks:} \quad \epsilon(i, t) = 0$$

# Spatial Model With Farm Size

So our model is:

$$P(i, t) = 1 - \exp \left( -(\alpha_0 + \alpha_1 X_A(i)) \sum_{j \in I(t)} d_{ij}^{-\beta} \right)$$

where

$d_{ij}$  is the spatial distance between individuals  $i$  and  $j$

$\alpha_0$  is a baseline infectivity parameter

$\alpha_1$  is the farm size effect

$\beta$  is a spatial parameter

$X_A(i)$  is the number of animals on farm  $i$

# Priors

We now have 3 parameters to estimate:  $\theta = (\alpha_0, \alpha_1, \beta)$

Once again we will assume we have no substantive prior knowledge about the parameters we wish to include in our analysis.

Using the same idea as before, we will put uniform priors on the parameters with a wide range:

$$\alpha_0 \sim \text{Uniform}[0, 10000]$$

$$\alpha_1 \sim \text{Uniform}[0, 10000]$$

$$\beta \sim \text{Uniform}[0, 10000]$$

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# Spatial Model with Farm Size and Sparks term

Let us now add in a sparks term

This can be used to model infections coming in from outside the observed population

For this model:

Susceptibility:	$S(i)$	$=$	$\alpha_0 + \alpha_1 X_A(i)$
Transmissibility:	$\mathcal{T}(j)$	$=$	$1$
Infection Kernel:	$\kappa(i, j)$	$=$	$d_{ij}^{-\beta}$
Sparks:	$\epsilon(i, t)$	$=$	$\epsilon$

# Spatial Model with Farm Size and Sparks term

So our model is:

$$P(i, t) = 1 - \exp \left( - \left[ (\alpha_0 + \alpha_1 X_A(i)) \sum_{j \in I(t)} d_{ij}^{-\beta} + \epsilon \right] \right)$$

where

$d_{ij}$  is the spatial distance between individuals  $i$  and  $j$

$\alpha_0$  is a baseline infectivity parameter

$\alpha_1$  is the farm size effect

$\beta$  is a spatial parameter

$X_A(i)$  is the number of animals on farm  $i$

$\epsilon$  is a constant sparks parameter

# Priors

We now have 4 parameters to estimate:  $\theta = (\alpha_0, \beta, \alpha_1, \epsilon)$

Once again we will assume we have no substantive prior knowledge about the parameters we wish to include in our analysis.

Using the same idea as before, we will put uniform priors on the parameters with a wide range:

$$\alpha_0 \sim \text{Uniform}[0, 10000]$$

$$\alpha_1 \sim \text{Uniform}[0, 10000]$$

$$\beta \sim \text{Uniform}[0, 10000]$$

$$\epsilon \sim \text{Uniform}[0, 10000]$$

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# Fitting SIR Models

So far we have considered fitting only SI compartmental models, that assume infection and infectiousness continue until at least time  $t_{max}$

If we wish to fit an SIR model we can do.

However, EpiILM does not allow us to estimate the infectious period except in a fairly limited manner.

EpiILM-CT does in the context of continuous-time models (see later)

In EpiILM, with discrete-time models we have two broad options.

## Option 1: Known Removal Times

If we know the removal times for individuals, we can simply define these when carrying out our analysis.

For example, assume in our spatial disease system that we have recorded removal times.

Data set: "DATA / ISBA\_SIR\_fit.csv":

# SIR Simple Spatial Model

For this model:

Susceptibility:	$S(i)$	$=$	$\alpha$
Transmissibility:	$\mathcal{T}(j)$	$=$	$1$
Infection Kernel:	$\kappa(i, j)$	$=$	$d_{ij}^{-\beta}$
Sparks:	$\epsilon(i, t)$	$=$	$0$

So our model is:

$$P(i, t) = 1 - \exp \left( -\alpha \sum_{j \in I(t)} d_{ij}^{-\beta} \right)$$

where:

$d_{ij}$  is the spatial distance between individuals  $i$  and  $j$

$\alpha$  is an infectivity parameter

$\beta$  is a spatial parameter

# Priors

Once again, we have two parameters:  $\theta = (\alpha, \beta)$

Let's assume we have no substantive prior knowledge about them we wish to include in our analysis.

Once again, put uniform priors on the parameters with a wide range:

$$\alpha \sim \text{Uniform}[0, 10000]$$

$$\beta \sim \text{Uniform}[0, 10000]$$

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## Option 2: Unknown Constant Infectious Period

We can fit an SIR model in the situation that we do not know the removal times, but we assume the infectious period is the same for all individuals.

For example, say we want to test if the infectious period is 1, 3 or 5 time units long.

We can fit different models to the data in which varying assumptions are made about the infectious period, and then compare them (e.g., using the DIC)

Let us also assume that we don't know whether to include a Sparks term or not.

Then we have 6 models to fit

# Comparing Models

We can then compare these models using the DIC for each fitted model:

Infectious period	Without sparks term	With sparks term
1	NA	166.4
3	<b>154.7</b>	156.1
5	161.7	163.0

So, the model without the sparks term and an infectious period of 3 time units seems to fit the data best

Note: a model with an infectious period of 1 for all individuals is so inconsistent with the data that we get a likelihood of zero

# Using an SIR Model

Of course, in many situations we will not know the infection times and/or removal time with certainty

Further, we may not wish to assume that the infectious period is the same for all individuals.

In such cases, we can treat the infectious periods and/or infection times as unknown "nuisance"/latent variables

Then, a so-called Bayesian **data-augmented** analysis can be carried out (typically, using MCMC)

Unfortunately, EpiLM cannot currently carry out such analyses, but EpiLM-CT can...

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## Example:

Imagine we are modelling the spread of a disease through a series of farms in a region.

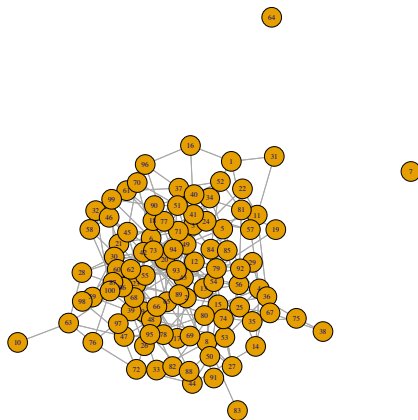
We have no individual-level covariates about the animals or farms, other than whether the farms share the same supply feed truck.

It seems reasonable to treat the farms themselves as individual level unit.

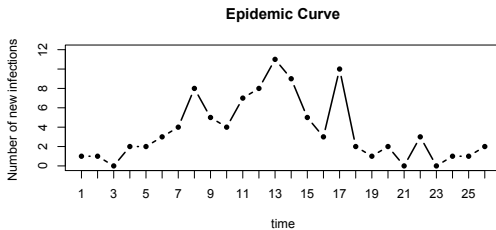
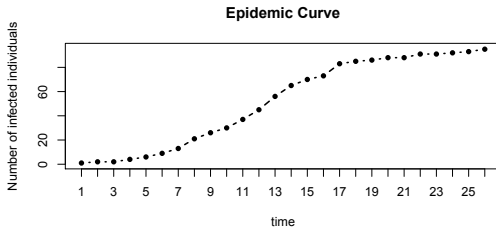
Further infection from outside the population of farms is expected to be negligible/non-existent.

Once infected, we assume infection remains on farm.

# Contact Network



# Epidemic curves



## Network-based model (Undirected)

We can fit the following model under SI framework

$$P(i, t) = 1 - \exp \left( -\alpha \sum_{j \in I(t)} c_{ij} \right)$$

where

$\alpha$  is an infectivity parameter

$$c_{ij} = c_{ji} = \begin{cases} 1 & \text{if } i \text{ and } j \text{ share a supplier} \\ 0 & \text{otherwise} \end{cases}$$

# MCMC Codes

Parameter to be estimated:  $\alpha$

Prior:  $\alpha \sim \text{Uniform}[0, 10000]$

Contact Matrix File: DATA/ISBA\_network\_fit.csv

Infection Times File: DATA/ISBA\_network\_inftime.csv

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# Posterior Predictive Forecasting

The posterior predictive distribution of new data  $\tilde{\mathbf{D}}$ , is the distribution of that data after accounting for parameter uncertainty via the posterior:

$$\pi(\tilde{\mathbf{D}} | \mathbf{D}) = \int_{\Theta} L(\tilde{\mathbf{D}} | \theta) \pi(\theta | \mathbf{D}) d\theta$$

Algorithmically we can produce realization of  $\tilde{\mathbf{D}}$  very simply:

1. Sample parameter(s)  $\tilde{\theta}$  from the posterior
2. Simulate data  $\tilde{\mathbf{D}}$  from model  $\mathcal{M}(\tilde{\theta})$
3. Repeat



# Posterior Predictive Forecasting

Imagine we have observed data from a partially unfolding epidemic

We can fit our model to data we have observed so far, and then use a posterior predictive approach to simulate the range of possible outcomes we expect to see

This gives us information as to what the most likely course of an epidemic is to be (under the posterior predictive mean)

And also gives us a plausible range of outcomes after accounting for our parameter uncertainty

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# Posterior Predictive Forecasting

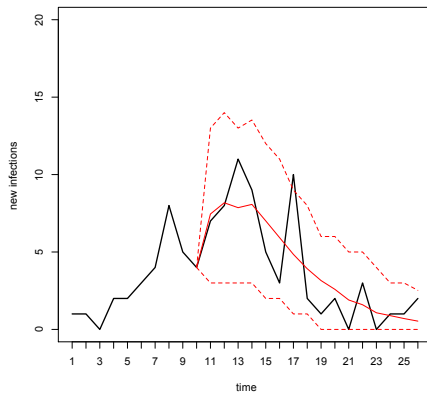
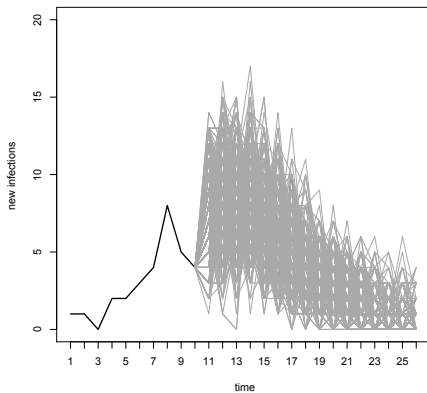
We have seen how we can fit our model to data we have observed so far, and then use a posterior predictive approach to simulate the range of possible outcomes we expect to see

We can also carry out such simulation while imposing various control strategies upon the unfolding epidemic, in order to ascertain their likely practical usefulness/costs

Here, we test the very simple (and unrealistic) strategy of imposing quarantine/culling on a random proportion of susceptible farms at a given point in time (here,  $t = 10$ ).

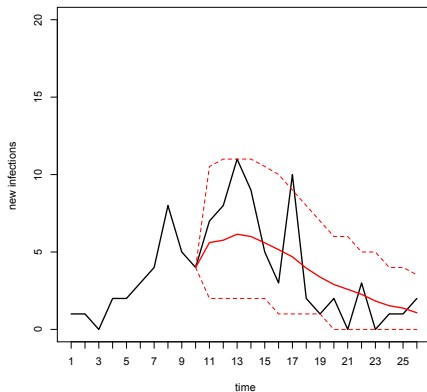
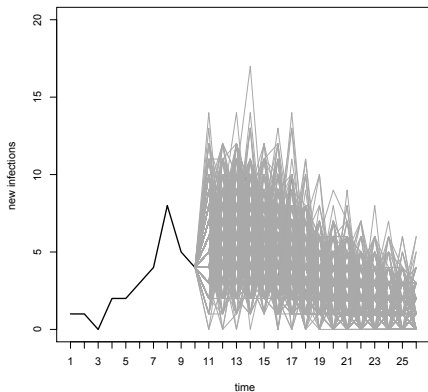
## Prediction from time point 10 (No Quarantine)

True (black) with 500 posterior predictions (gray)



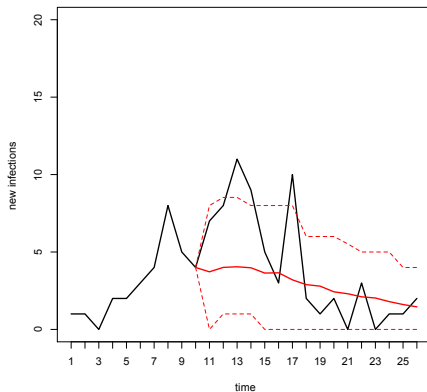
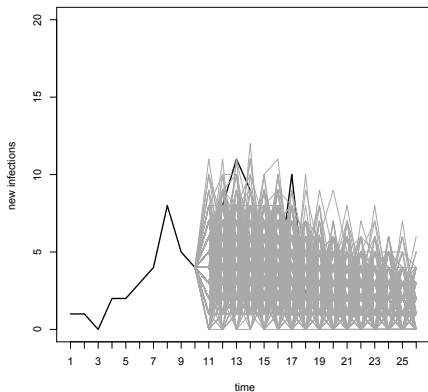
## Testing Control Policy from time point 10 (25% quarantined)

True (black) with 500 posterior predictions (gray)



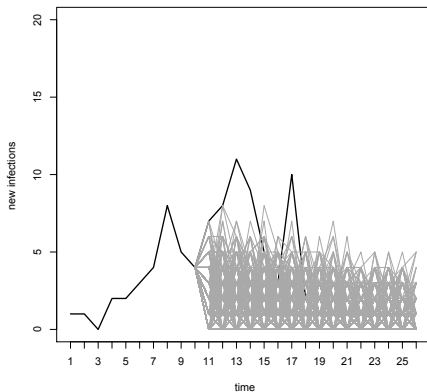
## Testing Control Policy from time point 10 (50% quarantined)

True (black) with 500 posterior predictions (gray)

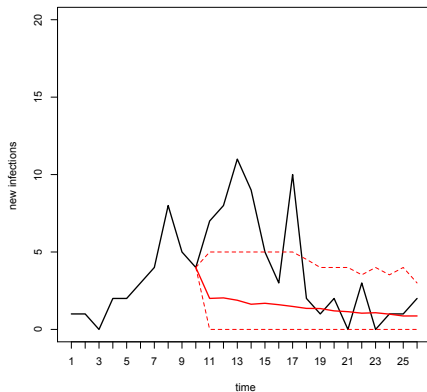


## Testing Control Policy from time point 10 (75% quarantined)

True (black) with 500 posterior predictions (gray)

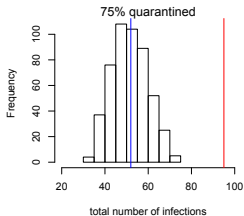
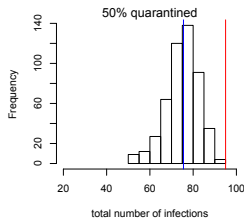
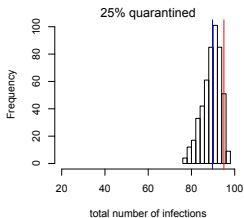


&



# Testing Control Policy from time point 10

red:true, blue:average





# Coding up quarantine/culling simulation

Coding is similar to that of the pure forecasting simulation.

Control policy can be coded as follows

For example:

We simulate an SIR rather than SI epidemic

By default, all individuals are given an infectious period greater than  $t_{max}$

However, before simulation, a certain proportion (e.g., 0.25, 0.5, 0.75) of infectious periods are set equal to zero, so those individuals will enter the removed state as soon as they are infected (i.e., never infectious)

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## Recall: General form of the individual level model (ILM)

The **probability of susceptible individual  $i$  being exposed/infected at time  $t$**  is given by:

$$P(i, t) = 1 - \exp \left( - \left[ \mathcal{S}(i) \left( \sum_{j \in I(t)} \mathcal{T}(j) \kappa(i, j) \right) + \epsilon(i, t) \right] \right) \quad (1)$$

where

$\mathcal{S}(i)$  is a susceptibility function for individual  $i$

$I(t)$  is the set of infectious individuals at time  $t$

$\mathcal{T}(j)$  is a transmissibility function for individual  $j$

$\kappa(i, j)$  is the infection kernel

$\epsilon(i, t)$  is the random sparks function

Additionally, it is assumed that  $\mathcal{S}(i)$ ,  $\mathcal{T}(j)$ ,  $\kappa(i, j)$  and  $\epsilon(i, t) \geq 0$  always

## Recall: General form of the individual level model (ILM)

The **probability of susceptible individual  $i$  being exposed/infected at time  $t$**  is given by:

$$P(i, t) = 1 - \exp \left( - \left[ S(i) \left( \sum_{j \in I(t)} \mathcal{T}(j) \kappa(i, j) \right) + \epsilon(i, t) \right] \right) \quad (2)$$

where

$S(i)$  is a susceptibility function for individual  $i$

$I(t)$  is the set of infectious individuals at time  $t$

$\mathcal{T}(j)$  is a transmissibility function for individual  $j$

$\kappa(i, j)$  is the infection kernel

$\epsilon(i, t)$  is the random sparks function

Additionally, it is assumed that  $S(i), \mathcal{T}(j), \kappa(i, j)$  and  $\epsilon(i, t) \geq 0$  always

# Positivity of Coefficients

Strictly, we have a mathematical requirement that:

$$\mathcal{S}(i) \left( \sum_{j \in I(t)} \mathcal{T}(j) \kappa(i, j) \right) + \epsilon(i, t) \geq 0$$

This requirement is necessary so that our  $P(i, t)$  are actually probabilities, bounded between zero and one.

It seems reasonable to achieve this by assuming:

$$\mathcal{S}(i) \geq 0$$

$$\mathcal{T}(j) \geq 0$$

$$\kappa(i, j) \geq 0$$

$$\epsilon(i, t) \geq 0$$

# Positivity of Coefficients

To help achieve this in EpiLM we require all individual model parameters/coefficients to be **positive**

So, for example, in the susceptibility function:

$$S(i) = \alpha_0 + \alpha_1 X_1(i) + \alpha_2 X_2(i) + \dots + \alpha_{n_S} X_{n_S}(i)$$

we require:

$$\alpha_0, \dots, \alpha_{n_S} \geq 0$$

So, if our covariate data are also positive ( $X_1, X_2, \dots \geq 0$ ) this ensures  $S(i) \geq 0$

# Positivity of Coefficients

Similarly:

For the spatial parameter in the spatial infection kernel:

$$\kappa(i, j) = d_{ij}^{-\beta}$$

we require:

$$\beta \geq 0$$



# Positivity of Coefficients

For the network parameters in a network-based infection kernel:

$$\kappa(i, j) = c_{ij}^{(0)} + \beta_1 c_{ij}^{(1)} + \beta_2 c_{ij}^{(2)} + \dots$$

we require:

$$\beta_1, \beta_2, \dots \geq 0$$

And finally, the sparks term:

$$\epsilon(i, t) = \epsilon$$

we require:

$$\epsilon \geq 0$$

## Positivity of Coefficients – Modelling Considerations

Example: Susceptibility

Consider an example in which we wanted to account for gender in the susceptibility function:

$$X_g(i) = \begin{cases} 0 & \text{if individual } i \text{ identifies as male} \\ 1 & \text{if individual } i \text{ identifies as female} \end{cases}$$

and let:

$$S(i) = \alpha_0 + \alpha_g X_g(i)$$

then  $\alpha_g$  is the gender effect associated with the risk of contracting this disease

## Positivity of Coefficients – Modelling Considerations

Since we require that  $\alpha_g \geq 0$ , we are assuming that  
female susceptibility cannot be lower than male susceptibility

If we wish to allow for higher male susceptibility, we need to re-code the gender indicator variable, using:

$$X_g(i) = \begin{cases} 1 & \text{if individual } i \text{ is male} \\ 0 & \text{if individual } i \text{ is female} \end{cases}$$

If we are fitting such a model to data, and do not know if male or female susceptibility would likely be higher, we can fit both models and compare

# Positivity of Coefficients – Modeling Considerations

## Example: Susceptibility

Consider an example in which we have a continuous covariate in our susceptibility function.

E.G., If  $X_A(i)$  is the number of animals on farm  $i$ , and we let:

$$S(i) = \alpha_0 + \alpha_1 X_A(i)$$

then  $\alpha_1$  denotes the effect of increasing  $X_A(i)$  by 1 animal on the risk of farm  $i$  contracting the disease

## Positivity of Coefficients – Modelling Considerations

However, we are inherently assuming a positive correlation between  $X_A$  and susceptibility

Might not be true – larger farms may tend to have better biosecurity measures.

How do we model this?

Answer: once again, recode our variable and use the recoded variable in our model

# Positivity of Coefficients – Modelling Considerations

There are a number of ways of recoding our variable

One possibility is to use:

$$X_A^*(i) = M - X_A(i)$$

where

$$M \geq \max \{X_A(i)\}$$

We then use a model with susceptibility function:

$$\mathcal{S}(i) = \alpha_0 + \alpha_1 X_A^*(i)$$

## Positivity of Coefficients – Modelling Considerations

Once again, if we are unsure as to whether increasing our covariate will increase or decrease susceptibility

... we can fit both versions of the model and then compare them.

Note: this means if we estimate a coefficient to be zero (e.g.,  $\alpha_1$ ) it may be our covariate has no effect upon susceptibility...

... or it could be a negatively correlated relationship exists, but our modelling constraints do not allow this

Note also: we can have similar issues with contact networks since their associated coefficients are also constrained to be positive

# Outline

## 1. Inference for Discrete-time ILMs

## 2. Example 1: Spatial Disease System

### 2.1 Simple Spatial Model

### 2.2 Spatial Model With Farm Size

### 2.3 Adding In the Sparks Term

### 2.4 Fitting SIR Models

## 3. Example 2: Network-based model

### 3.1 Data

### 3.2 Predicting the Future

### 3.3 Testing Control Policies By Simulation

## 4. Extras

### 4.1 EpiILM Coefficient Positivity

## 5. References and Research



# Selected Background References

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## Time-varying and behavioural change models

Work in progress...