

# N-Mixture Models with Application to Disease Surveillance

Lisa Madsen <sup>1</sup>   Ben Brintz <sup>2</sup>   Claudio Fuentes <sup>1</sup>

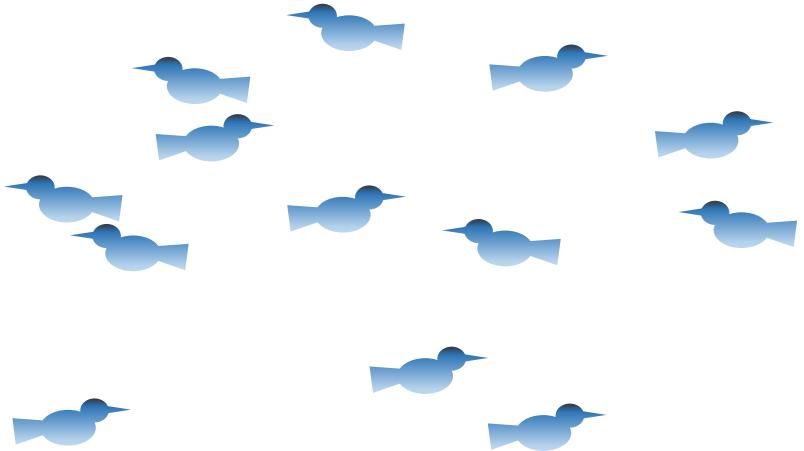
<sup>1</sup> Oregon State University

<sup>2</sup>University of Utah

August 27, 2020

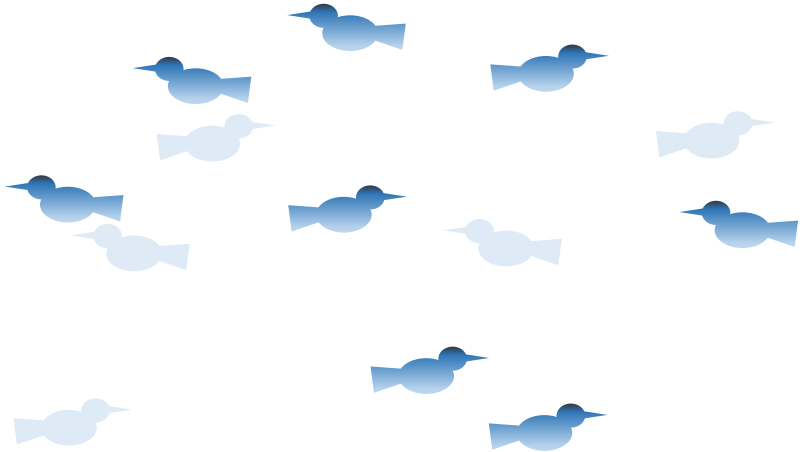


# Estimating Population Size





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# Outline

## N-Mixture Model History

- Royle's N-Mixture Model

- Generalized N-Mixture Model

- Asymptotic Approximation

## Spatial N-Mixture Model

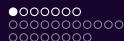
- Example

- Spatial Model

- Simulations

- Analysis of Chlamydia Data

## Summary



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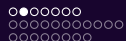
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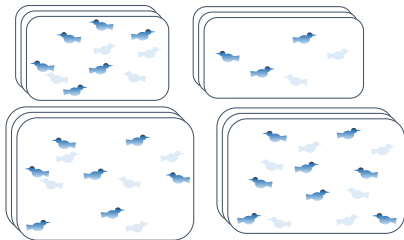
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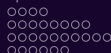
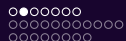
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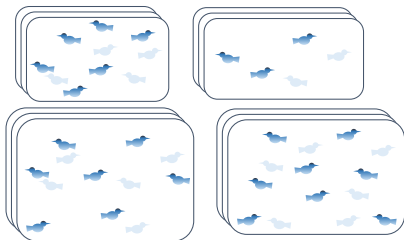
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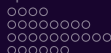
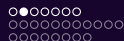
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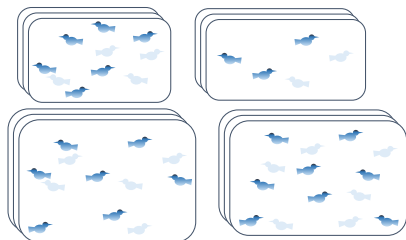
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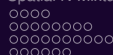
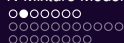


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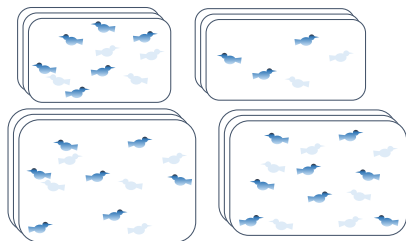


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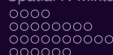
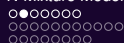


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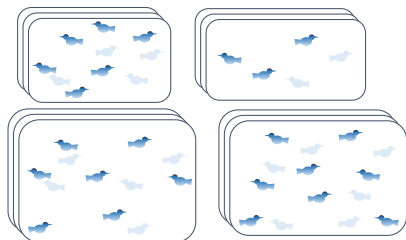


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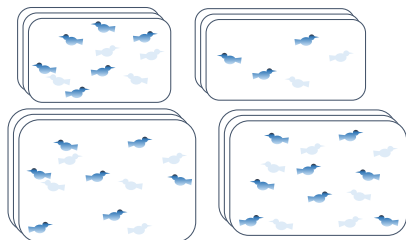


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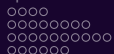
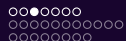
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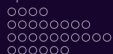
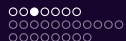
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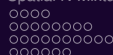
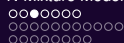
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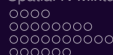
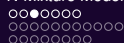
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$$p \sim \text{beta}(\alpha, \beta)$$

Form joint likelihood  $f(n_1, \dots, n_T | N, p) \cdot f(p | \alpha, \beta)$ , then integrate out  $p$  and maximize with respect to  $N$ ,  $\alpha$  and  $\beta$ .



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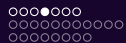
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Estimator doesn't perform well for small  $p$  or small  $N$ .



# Model and Likelihood

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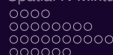
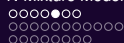
Joint likelihood:

$$L(\{N_i\}, p, \lambda | \{n_{it}\}) = \prod_{i=1}^R \left\{ \left( \prod_{t=1}^T \text{bin}(n_{it}; N_i, p) \right) \text{pois}(N_i; \lambda) \right\},$$

where

$$\text{bin}(n_{it}; N_i, p) = \binom{N_i}{n_{it}} p^{n_{it}} (1-p)^{N_i - n_{it}}$$

$$\text{pois}(N_i; \lambda) = \frac{e^{-\lambda} \lambda^{N_i}}{N_i!}$$

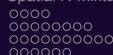
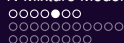


# Estimation

Integrated likelihood:

$$L(\boldsymbol{p}, \lambda | \{n_{it}\}) = \prod_{i=1}^R \left\{ \sum_{N_i=M_i}^{\infty} \left( \prod_{t=1}^T \text{bin}(n_{it}; N_i, \boldsymbol{p}) \right) \text{pois}(N_i; \lambda) \right\},$$

where  $M_i = \max_t \{n_{it}\}$ .



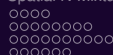
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Maximize  $\log(L)$  numerically with respect to  $p$  and  $\lambda$ .



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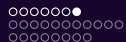
Integrated likelihood:

$$L(\boldsymbol{p}, \boldsymbol{\lambda} | \{n_{it}\}) = \prod_{i=1}^R \left\{ \sum_{N_i=M_i}^K \left( \prod_{t=1}^T \text{bin}(n_{it}; N_i, \boldsymbol{p}) \right) \text{pois}(N_i; \boldsymbol{\lambda}) \right\},$$

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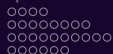
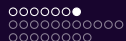
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$K \gg \max_{it} \{n_{it}\}$



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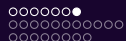
Estimating total abundance  $N = \sum_{i=1}^R N_i$ :



# Estimation

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$$E(N_i) = \lambda$$

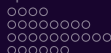
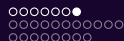


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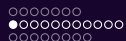
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$$\text{and } \text{SE}(\hat{N}) = R \cdot \text{SE}(\hat{\lambda})$$

where  $\text{SE}(\hat{\lambda})$  is from the inverse Hessian evaluated at the MLE.



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**Generalized N-Mixture Model**

Asymptotic Approximation

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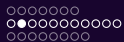
Example

Spatial Model

Simulations

Analysis of Chlamydia Data

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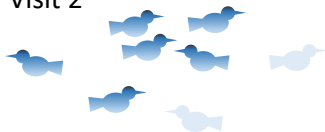
# Open Populations

Site  $i$

Visit 1



Visit 2

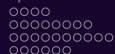
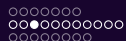


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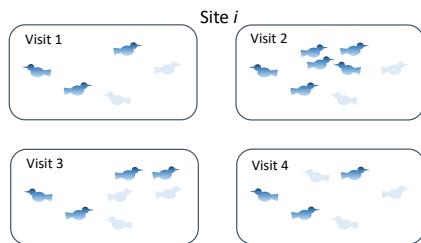


Visit 4

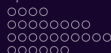
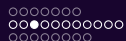




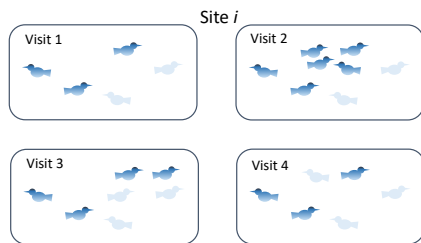
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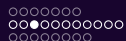
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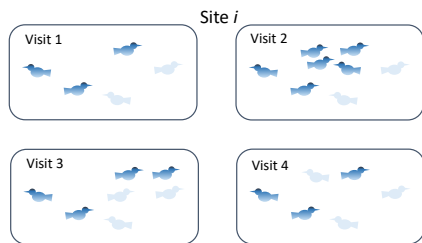
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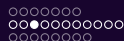
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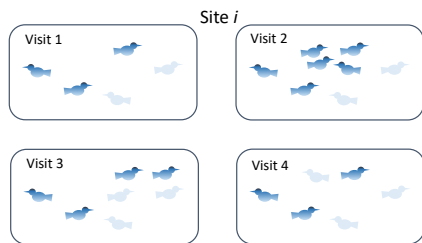
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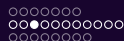


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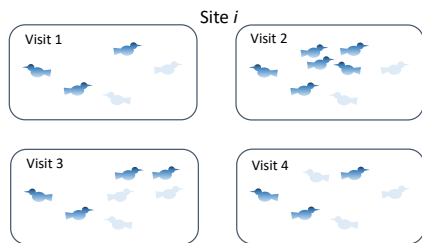


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Goal: Estimate abundance at time  $t$ :  $N_{.t} \equiv \sum_{i=1}^R N_{it}$ .





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Royle's model:

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where  $\theta$  includes  $\lambda = E(N_{i1})$  and parameters describing population dynamics.



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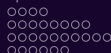
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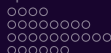


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$G_{it}$  = **gains** to site  $i$  from time  $t - 1$  to time  $t$ .

$$G_{it} | N_{it-1} \sim \text{Poisson}(\gamma)$$

Population dynamics parameters:

**survival rate**  $\omega$



## Generalized Model Population Dynamics

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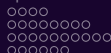
Population dynamics parameters:

**survival rate**  $\omega$  and **recruitment rate**  $\gamma$



# Joint Distribution of $N_{i1}, \dots, N_{iT}$

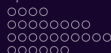
$$N_{i1} \sim \text{Poisson}(\lambda)$$



# Joint Distribution of $N_{i1}, \dots, N_{iT}$

$$N_{i1} \sim \text{Poisson}(\lambda)$$

$$N_{it}|N_{it-1} = S_{it}|N_{it-1} + G_{it}|N_{it-1}, t > 1$$



# Joint Distribution of $N_{i1}, \dots, N_{iT}$

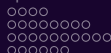
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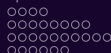
$S_{it}$  and  $G_{it}$  are conditionally independent given  $N_{it-1}$ .



# Likelihood

Royle's joint likelihood:

$$L(\{N_i\}, \boldsymbol{p}, \lambda | \{n_{it}\}) = \prod_{i=1}^R \left\{ \left( \prod_{t=1}^T \text{bin}(n_{it}; N_i, \boldsymbol{p}) \right) \text{pois}(N_i; \lambda) \right\},$$



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Generalized joint likelihood:

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## Likelihood

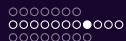
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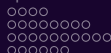
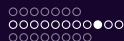
# Generalized Integrated Likelihood

$$L(\{N_{it}\}, \boldsymbol{p}, \boldsymbol{\theta} | \{n_{it}\}) = \prod_{i=1}^R \left\{ \sum_{N_{i1}=n_{i1}}^{\infty} \cdots \sum_{N_{iT}=n_{iT}}^{\infty} \left( \prod_{t=1}^T \text{bin}(n_{it}; N_{it}, \boldsymbol{p}) \right) f(\{N_{it}\}; \boldsymbol{\theta}) \right\}$$

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$$L(\{N_{it}\}, \boldsymbol{p}, \boldsymbol{\theta} | \{n_{it}\}) = \prod_{i=1}^R \left\{ \sum_{N_{i1}=n_{i1}}^K \cdots \sum_{N_{iT}=n_{iT}}^K \left( \prod_{t=1}^T \text{bin}(n_{it}; N_{it}, \boldsymbol{p}) \right) f(\{N_{it}\}; \boldsymbol{\theta}) \right\}$$

$$K \gg \max_{it} \{n_{it}\}$$

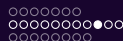


## Generalized Integrated Likelihood

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Maximize  $\log(L)$  numerically with respect to  $\boldsymbol{p}, \boldsymbol{\lambda}, \boldsymbol{\omega}, \boldsymbol{\gamma}$ ,



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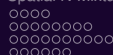
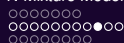
$$L(\{N_{it}\}, p, \theta | \{n_{it}\}) = \prod_{i=1}^R \left\{ \sum_{N_{i1}=n_{i1}}^K \cdots \sum_{N_{iT}=n_{iT}}^K \left( \prod_{t=1}^T \text{bin}(n_{it}; N_{it}, p) \right) f(\{N_{it}\}; \theta) \right\}$$

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$$\hat{N}_{\cdot 1} = R\hat{\lambda}$$

$$\hat{N}_{\cdot t} = \hat{\omega}\hat{N}_{\cdot t-1} + R\hat{\gamma}$$



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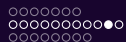
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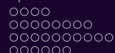
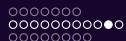
$$\hat{N}_{\cdot t} = \hat{\omega}\hat{N}_{\cdot t-1} + R\hat{\gamma}$$

SEs from inverse Hessian evaluated at MLE and multivariate delta method or parametric bootstrap.



# Identifiability

Are the parameters of the generalized model identifiable?

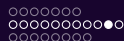


# Identifiability

Are the parameters of the generalized model identifiable?

Can we distinguish

High survival and low recruitment from low survival  
and high recruitment?



# Identifiability

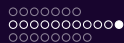
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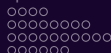
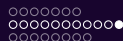
High survival and low recruitment from low survival and high recruitment?

Low detection probability and high abundance from high detection probability and low abundance?



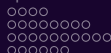
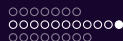


# Limitations of Generalized Model



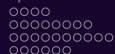
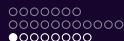
# Limitations of Generalized Model

- Potential near non-identifiability



# Limitations of Generalized Model

- Potential near non-identifiability
- Approximating infinite sums



# Outline

## N-Mixture Model History

Royle's N-Mixture Model

Generalized N-Mixture Model

**Asymptotic Approximation**

## Spatial N-Mixture Model

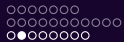
Example

Spatial Model

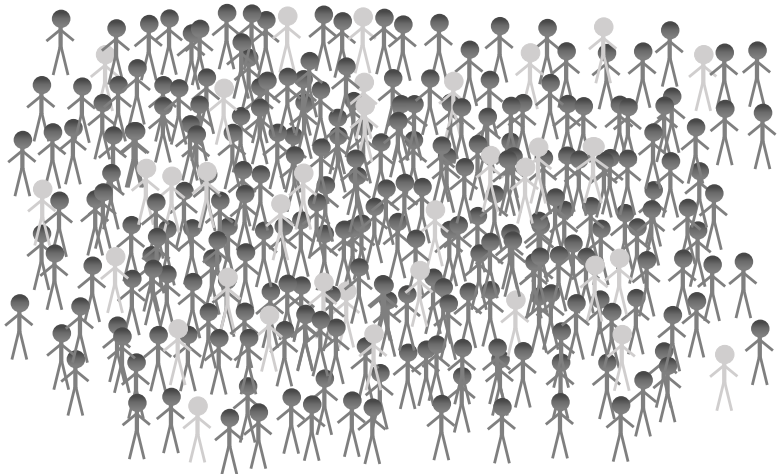
Simulations

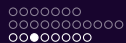
Analysis of Chlamydia Data

## Summary



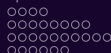
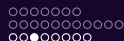
# Large Counts





# Large Counts

The generalized model was

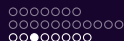


# Large Counts

The generalized model was

$$n_{it} | N_{it} \sim \text{Binomial}(N_{it}, p)$$

$$f(N_{i1}, \dots, N_{iT}; \theta) = f(N_{i1}; \theta) \prod_{t=2}^T f(N_{it} | N_{it-1}; \theta)$$



# Large Counts

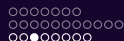
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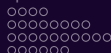
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If the  $n_{it}$  are large, then

$$n_{it} \overset{\text{approx}}{\sim} \text{Normal}(\mu_{it}, \sigma_{it}^2),$$

where  $\mu_{it} = E(n_{it})$  and  $\sigma_{it}^2 = \text{var}(n_{it})$ .



# Approximate Likelihood

Approximate the joint distribution as multivariate normal:

$$[n_{11} \quad n_{12} \quad \dots \quad n_{RT-1} \quad n_{RT}]' \overset{\text{approx}}{\sim} \text{MVN}(\boldsymbol{\mu}, \boldsymbol{\Sigma}),$$

where  $\boldsymbol{\mu}$  and  $\boldsymbol{\Sigma}$  are given by the generalized model.



## Calculating the Mean Vector

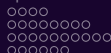
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$$N_{i1} \sim \text{Poisson}(\lambda)$$

$$N_{it} | N_{it-1} = S_{it} | N_{it-1} + G_{it} | N_{it-1}, \quad t > 1$$

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## Calculating the Mean Vector

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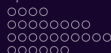
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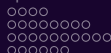
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Then

$$E(N_{i1}) = \lambda$$

$$E(N_{it}) = \omega E(N_{it-1}) + \gamma, \quad t > 1$$



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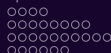
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Calculate elements of  $\Sigma$  similarly.



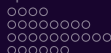
# Estimation

Maximize log of approximate likelihood

$$L(\rho, \lambda, \omega, \gamma | \{n_{it}\}) = MVN(\{n_{it}\}; \mu, \Sigma)$$

with respect to the parameters, then estimate  $N_t$  as before:





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# Identifiability Diagnostic

The  $MVN(\mu, \Sigma)$  model has a closed-form expression for  $jk$ th element of the Fisher Information  $I$ :



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$$I_{jk} = \frac{\partial \boldsymbol{\mu}'}{\partial \theta_j} \boldsymbol{\Sigma}^{-1} \frac{\partial \boldsymbol{\mu}}{\partial \theta_k} + \frac{1}{2} \text{tr} \left( \boldsymbol{\Sigma}^{-1} \frac{\partial \boldsymbol{\Sigma}}{\partial \theta_j} \boldsymbol{\Sigma}^{-1} \frac{\partial \boldsymbol{\Sigma}}{\partial \theta_k} \right)$$



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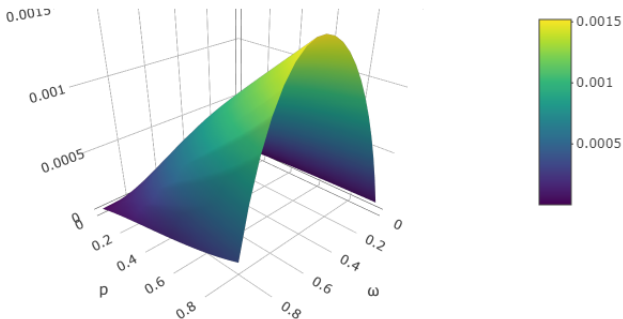
Use  $I$  to diagnose near-non-identifiability.

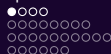
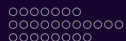


# Identifiability Diagnostic

Example:  $R = 1$ ,  $T = 2$ ,  $\lambda = 100$ , and  $\gamma = 90$

Minimum Eigenvalue of  $I$





# Outline

## N-Mixture Model History

Royle's N-Mixture Model

Generalized N-Mixture Model

Asymptotic Approximation

## Spatial N-Mixture Model

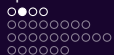
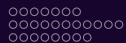
**Example**

Spatial Model

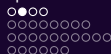
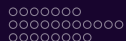
Simulations

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## Summary



# Chlamydia in Oregon

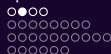
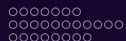


# Chlamydia in Oregon

**Chlamydia** is a common sexually-transmitted disease.

- Relatively easy to diagnose and cure

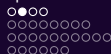
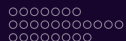




# Chlamydia in Oregon

**Chlamydia** is a common sexually-transmitted disease.

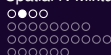
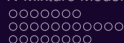
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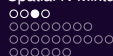
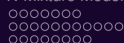


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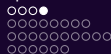
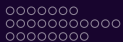
Goal: Use N-Mixture model to estimate chlamydia case counts.



## Example

## Oregon Population and Cases by County

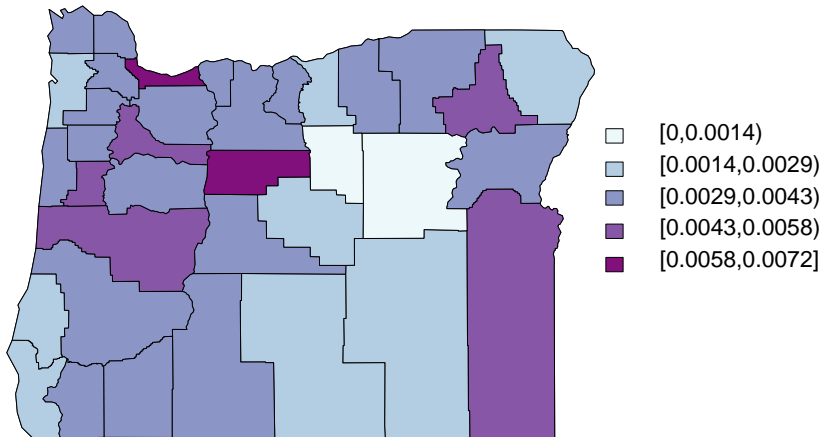
County	Population			Observed Cases		
	2010	...	2018	2010	...	2018
Multnomah	737,291	...	811,880	3296	...	5459
Washington	531,645	...	597,695	1390	...	2404
Clackamas	376,790	...	416,075	945	...	1394
Lane	351,923	...	379,611	1276	...	1844
Marion	315,951	...	346,868	1395	...	1887
⋮	⋮		⋮	⋮		⋮
Grant	7464	...	7176	14	...	24
Wallowa	7012	...	7081	9	...	9
Gilliam	1882	...	1894	3	...	3
Sherman	1779	...	1708	4	...	4
Wheeler	1447	...	1366	3	...	3

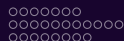


Example

# Chlamydia in Oregon

## Oregon Counties 2016 Reported Prevalence





# Outline

## N-Mixture Model History

Royle's N-Mixture Model

Generalized N-Mixture Model

Asymptotic Approximation

## Spatial N-Mixture Model

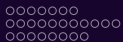
Example

**Spatial Model**

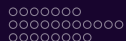
Simulations

Analysis of Chlamydia Data

## Summary



# Notation and Terminology for Spatial Model

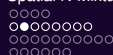
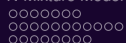


# Notation and Terminology for Spatial Model

$n_{it}$  = observed case count in county  $i$ , year  $t$

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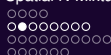
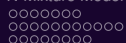


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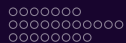
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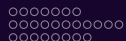
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Size of neighborhood of county  $i$ :  $A_{i\cdot} = \sum_{j=1}^R A_{ij}$ .



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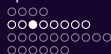
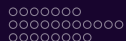
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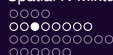
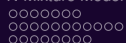
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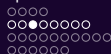
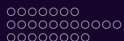
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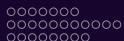
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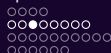
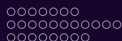
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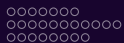
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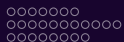
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$\tilde{N}_{it-1}$  is the population in county  $i$  at time  $t - 1$  times the average prevalence in its neighborhood.



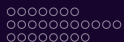
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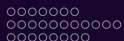
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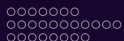


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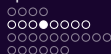
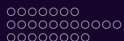


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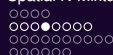
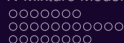


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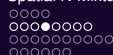
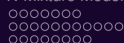
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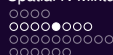
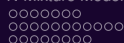
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As with the non-spatial normal-approximation model,

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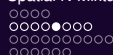
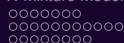
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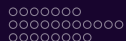
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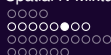
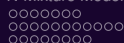


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Account for uncertainty in  $\hat{\theta}$  with a parametric bootstrap:

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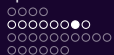
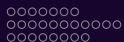
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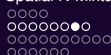
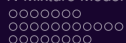
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Bootstrap sample  $\hat{\theta}^{(1)}, \dots, \hat{\theta}^{(S)}$  represents the sampling distribution of  $\hat{\theta}$ .



# Confidence Intervals

Similarly, account for the sampling variability in the  $N_{it}$ .

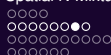
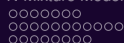


## Confidence Intervals

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Given  $\hat{\theta}^{(s)}$ , for each site  $i$ , generate  $\hat{N}_{i1}^{(s)}, \dots, \hat{N}_{iT}^{(s)}$  according to the model:

$$\hat{N}_{i1}^{(s)} \sim \text{Poisson}(\hat{\beta}^{(s)} \text{pop}_{i1})$$

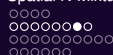
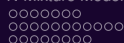


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# Confidence Intervals

For  $s = 1, \dots, S$  we have generated:

$$\begin{array}{ccc} \hat{N}_{11}^{(s)} & , \dots , & \hat{N}_{1T}^{(s)} \\ \vdots & & \vdots \\ \hat{N}_{R1}^{(s)} & , \dots , & \hat{N}_{RT}^{(s)} \end{array}$$

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Then calculate  $\hat{N}_{.t}^{(s)} = \sum_{i=1}^R \hat{N}_{it}^{(s)}$  to get  $\hat{N}_{.t}^{(1)}, \dots, \hat{N}_{.t}^{(S)}$ .



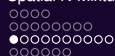
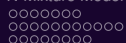
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$1 - \alpha$  confidence bounds for  $N_{.t}$  are the  $\alpha/2$  and  $1 - \alpha/2$  quantiles of the bootstrapped distribution of  $\widehat{N}_{.t}$ .



# Outline

## N-Mixture Model History

Royle's N-Mixture Model

Generalized N-Mixture Model

Asymptotic Approximation

## Spatial N-Mixture Model

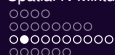
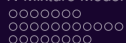
Example

Spatial Model

**Simulations**

Analysis of Chlamydia Data

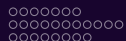
## Summary



## Scenarios

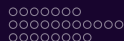
Using Oregon's populations and map, we ran 1000 simulations for each of 24 scenarios.

	Parameter	Values
$\beta$	initial expected prevalence	0.005, 0.05
$p$	detection probability	0.4, 0.7, 0.9
$\omega$	persistence rate	0.5, 0.8
$\gamma$	infection rate	0.3, 0.6



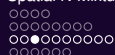
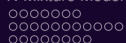
## Procedure

- Simulate data with  $R = 36$ ,  $T = 9$ , Oregon populations, and  $A$  from Oregon map.



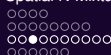
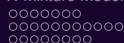
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## Procedure

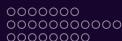
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- Record mean absolute relative error of  $\hat{N}_{.t}$ :

$$\text{MRE} = \frac{1}{9} \sum_{t=1}^9 |\hat{N}_{.t} - N_{.t}| / N_{.t}.$$



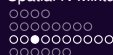
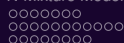
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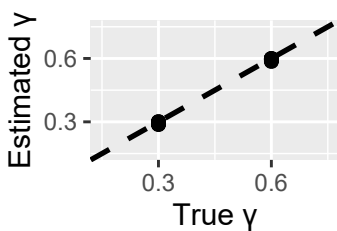
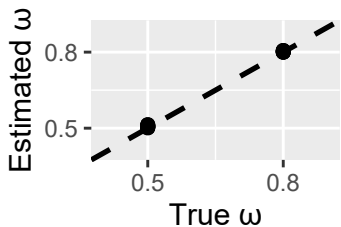
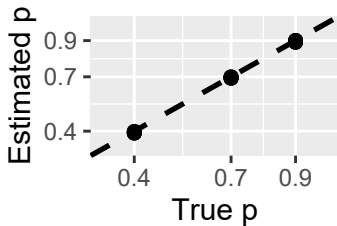
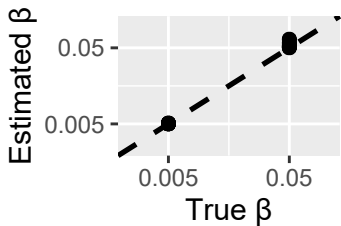
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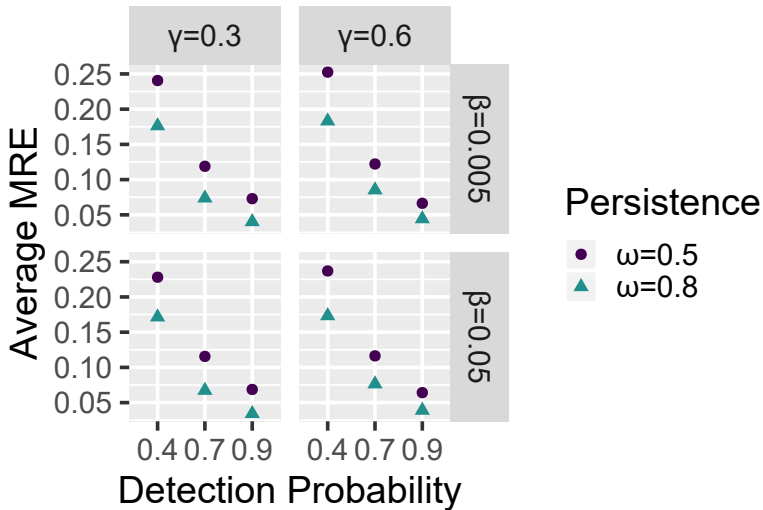
$$\text{MRE} = \frac{1}{9} \sum_{t=1}^9 |\hat{N}_{.t} - N_{.t}| / N_{.t}.$$

- Perform parametric bootstrap to simulate sampling distribution of  $\hat{N}_{.9}$ .
- Record success/failure of 90% interval estimate.
- Record interval width.

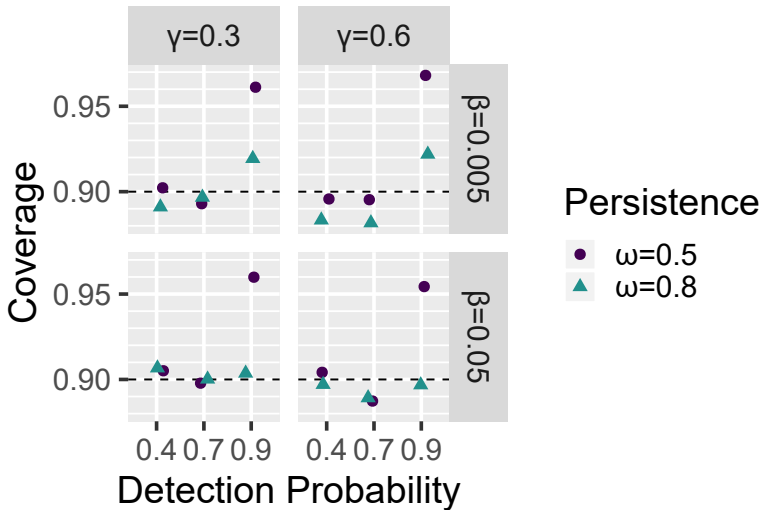
# Results



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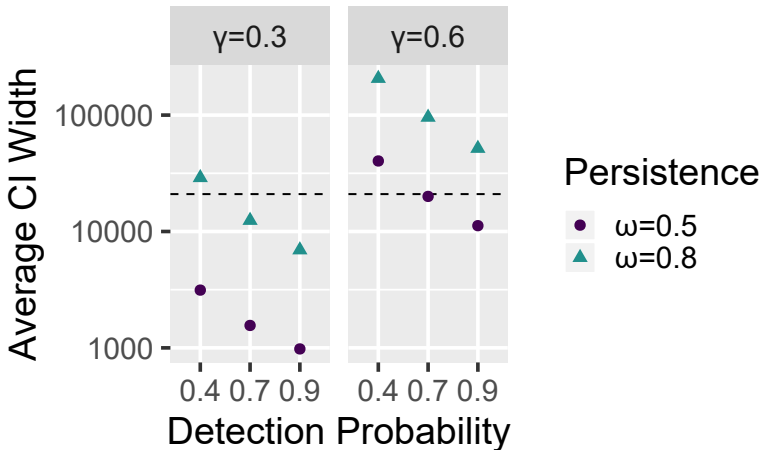


# Results



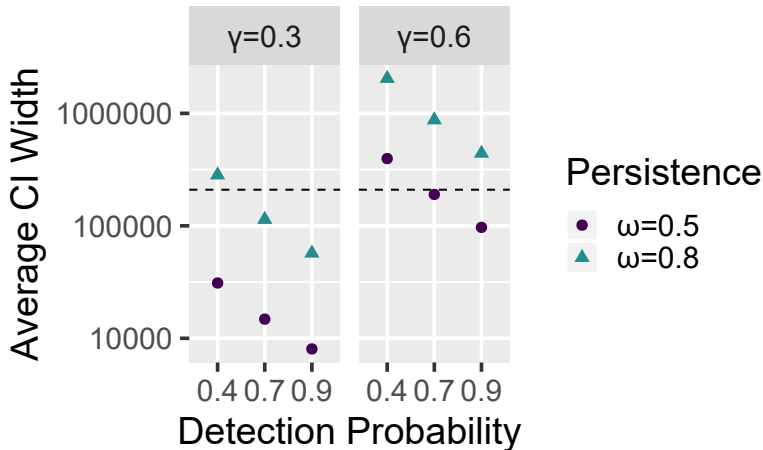
# Results

Initial Prevalence  $\beta=0.005$



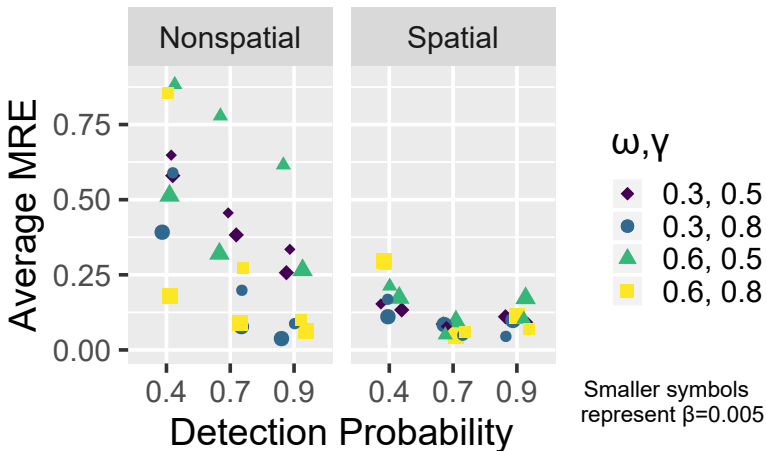
# Results

## Initial Prevalence $\beta=0.05$



# Robustness

## Misspecified Model Fit

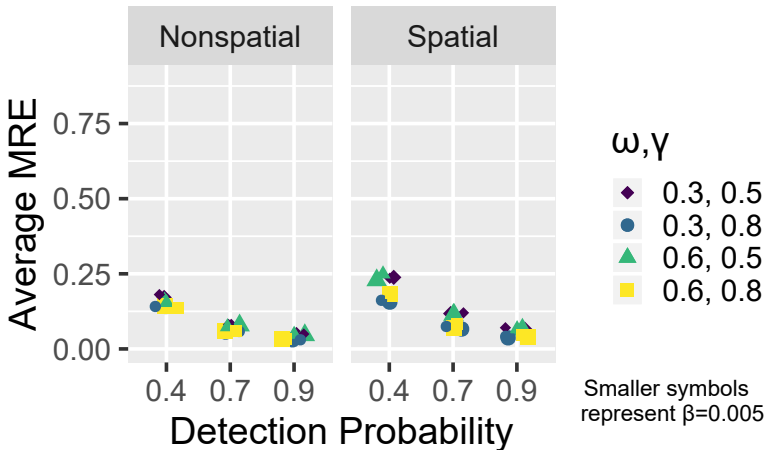


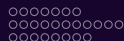
Smaller symbols  
represent  $\beta=0.005$



# Robustness

## Correct Model Fit





# Outline

## N-Mixture Model History

Royle's N-Mixture Model

Generalized N-Mixture Model

Asymptotic Approximation

## Spatial N-Mixture Model

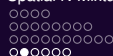
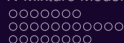
Example

Spatial Model

Simulations

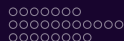
Analysis of Chlamydia Data

## Summary



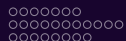
# Oregon Chlamydia Data 2010-2018

County	Population			Observed Cases		
	2010	...	2018	2010	...	2018
Multnomah	737,291	...	811,880	3296	...	5459
Washington	531,645	...	597,695	1390	...	2404
Clackamas	376,790	...	416,075	945	...	1394
Lane	351,923	...	379,611	1276	...	1844
Marion	315,951	...	346,868	1395	...	1887
⋮	⋮		⋮	⋮		⋮
Grant	7464	...	7176	14	...	24
Wallowa	7012	...	7081	9	...	9
Gilliam	1882	...	1894	3	...	3
Sherman	1779	...	1708	4	...	4
Wheeler	1447	...	1366	3	...	3

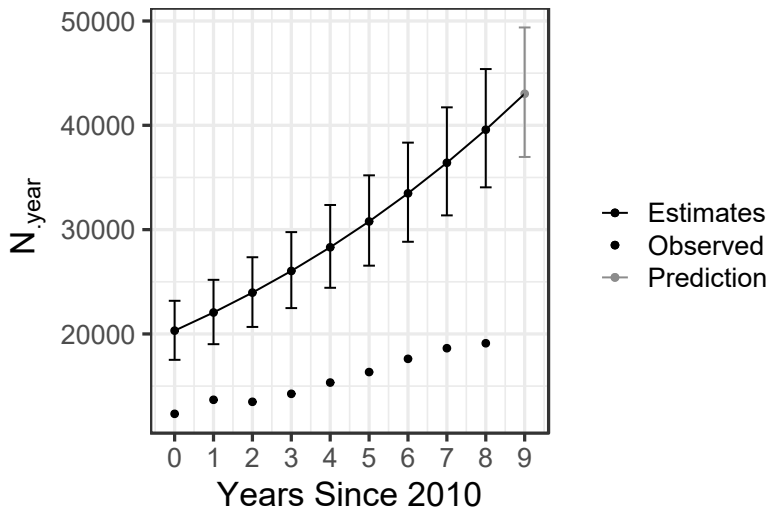


## Parameter Estimates (SEs)

Initial expected prevalence	$\hat{\beta} = 0.0053 (0.0001)$
Detection probability	$\hat{p} = 0.669 (0.047)$
Persistence rate	$\hat{\omega} = 0.917 (0.032)$
Infection rate	$\hat{\gamma} = 0.169 (0.032)$



# State-wide Interval Estimates/Prediction



County	2018 Population	Estimated Case Count	95% CL
Multnomah	811,880	7651	(6696, 8574)
Washington	597,695	5558	(4863, 6227)
Clackamas	416,075	3896	(3405, 4373)
Lane	379,611	3607	(3155, 4050)
Marion	346,868	3244	(2829, 3646)
⋮	⋮	⋮	⋮
Grant	7176	75	(56, 95)
Wallowa	7081	71	(52, 91)
Gilliam	1894	20	(11, 29)
Sherman	1708	18	(9, 28)
Wheeler	1366	14	(7, 22)

N-Mixture Model History

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○○○○○○○○○

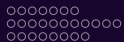
Spatial N-Mixture Model

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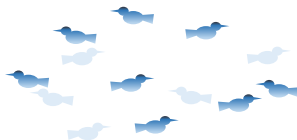
Summary

○○○○

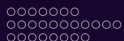
Analysis of Chlamydia Data



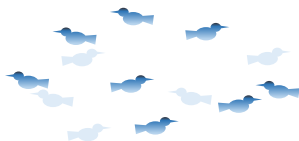
N-Mixture models provide estimates of  $N$  when  $p < 1$ .



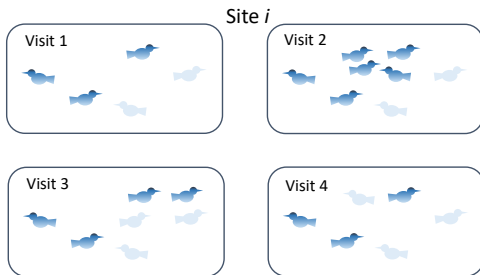




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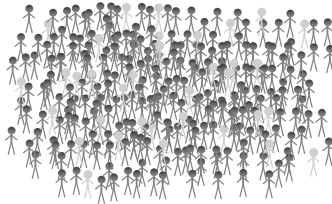


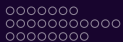
Generalized model allows open populations.



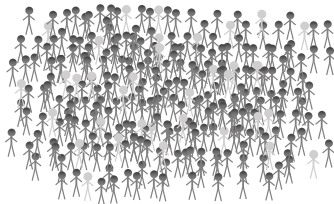


Asymptotic approximation allows large counts.

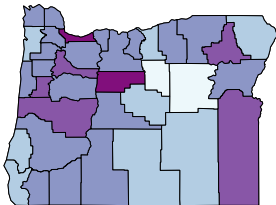


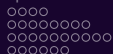
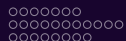


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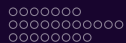
Spatial model accounts for spatial dependence.



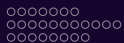


# Future Work

- Further model testing and refinement
- Develop identifiability diagnostic
- Adapt model for other diseases  
(susceptible/infected/recovered)



Thanks to my coauthors, Ben and Claudio.



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Thank you!