



N-Mixture Models with Application to Disease Surveillance

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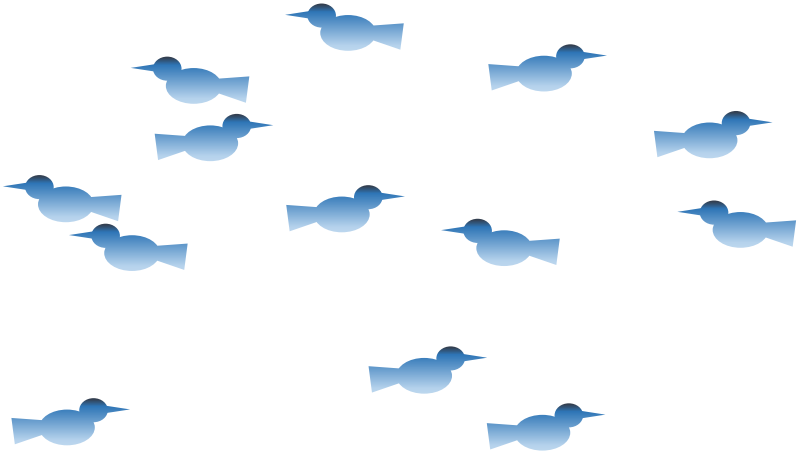
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April 8, 2022

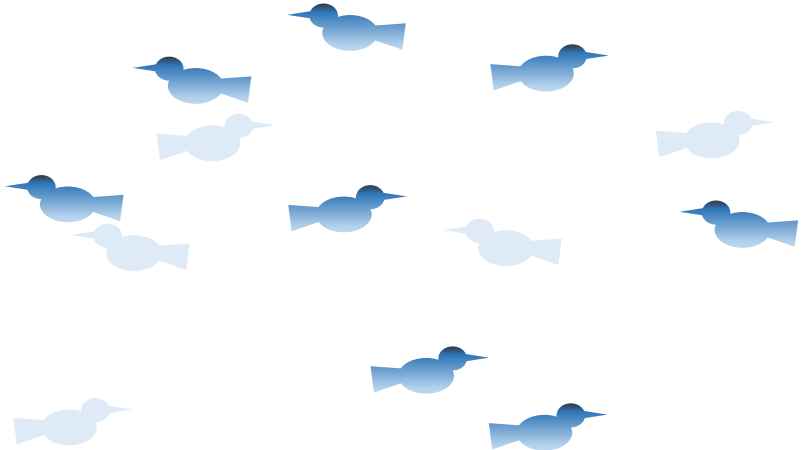


Estimating Population Size





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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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Spatial Model

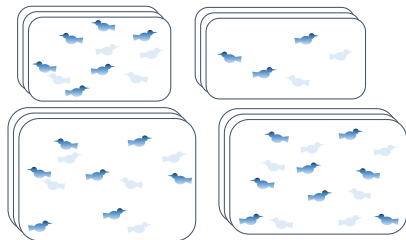
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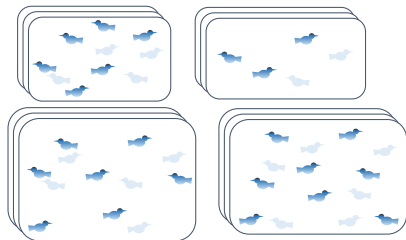
Royle (2004)



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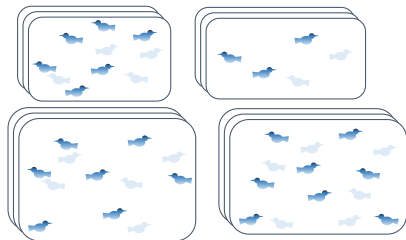
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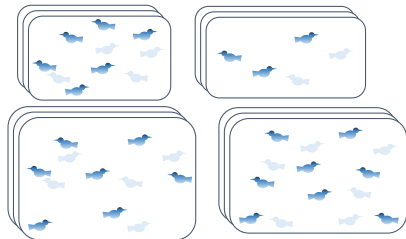
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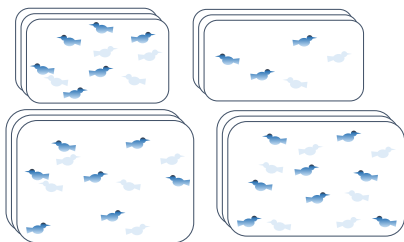


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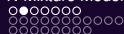
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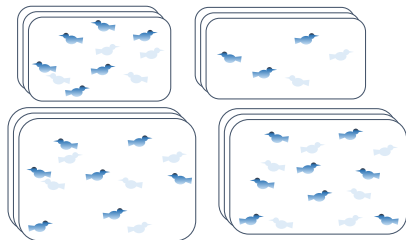
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Prehistory

Carroll and Lombard (1985):

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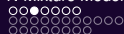
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Form joint likelihood $f(n_1, \dots, n_T | N, p) \cdot f(p | \alpha, \beta)$, then integrate out p and maximize with respect to N , α and β .



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



Model and Likelihood

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



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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:

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

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



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



Estimation

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

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



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$$E(N_i) = \lambda \quad \therefore \hat{N} = R \cdot \hat{\lambda}$$

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

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



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Open Populations

Site i

Visit 1



Visit 2



Visit 3

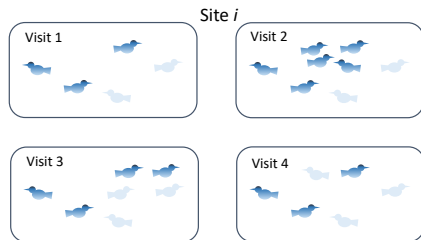


Visit 4





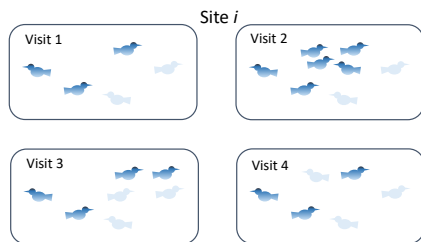
Generalized Setup



- R independent sites; T visits per site



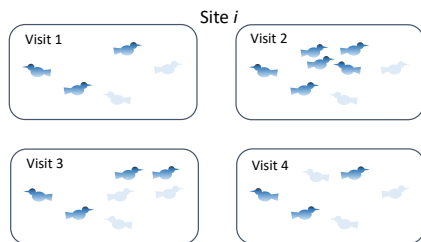
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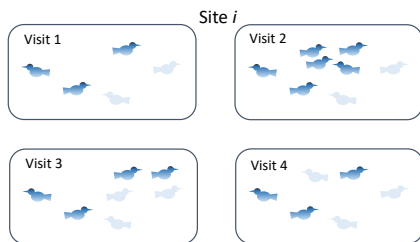
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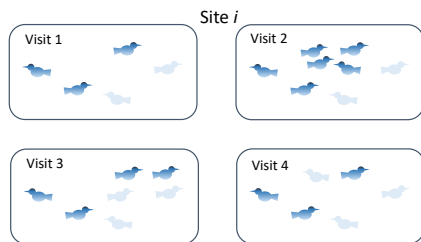


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Goal: Estimate abundance at time t : $N_{.t} \equiv \sum_{i=1}^R N_{it}$.



Model

Royle's model:

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

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



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



Generalized Model Population Dynamics

S_{it} = **survivors** at site i from time $t - 1$ to time t .



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survival rate ω and **recruitment rate** γ



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

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



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Royle's joint likelihood:

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Generalized Integrated Likelihood

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

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



Identifiability

Are the parameters of the generalized model identifiable?



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Can we distinguish

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



Identifiability

Are the parameters of the generalized model identifiable?

Can we distinguish

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



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- Potential near non-identifiability



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- Potential near non-identifiability
- Approximating infinite sums



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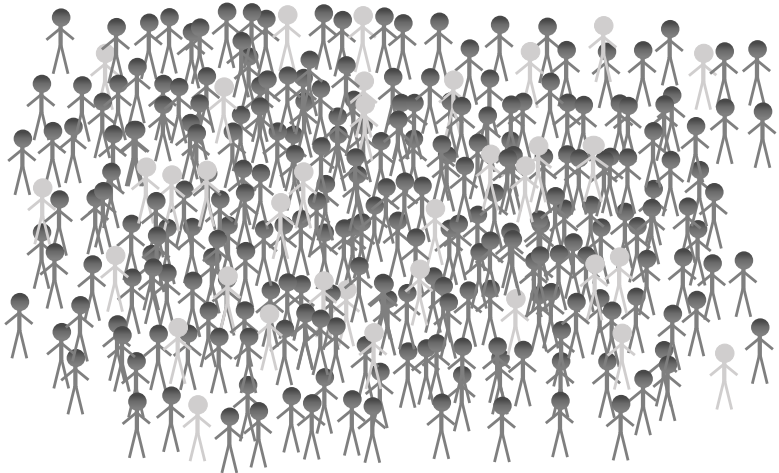
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Large Counts





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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

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

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

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

$$S_{it} | N_{it-1} \sim \text{Binomial}(N_{it-1}, \omega)$$

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Then

$$E(n_{it}) = \rho E(N_{it})$$

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Calculate elements of Σ similarly.



Estimation

Maximize log of approximate likelihood

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

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

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



Identifiability Diagnostic

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

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

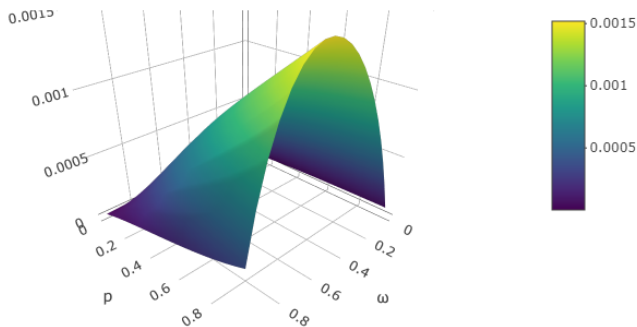
Use I to diagnose near-non-identifiability.



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

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Spatial N-Mixture Model

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Analysis of Chlamydia Data

Summary



Chlamydia in Oregon



Chlamydia in Oregon

Chlamydia is a common sexually-transmitted disease.

- Relatively easy to diagnose and cure



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



Example

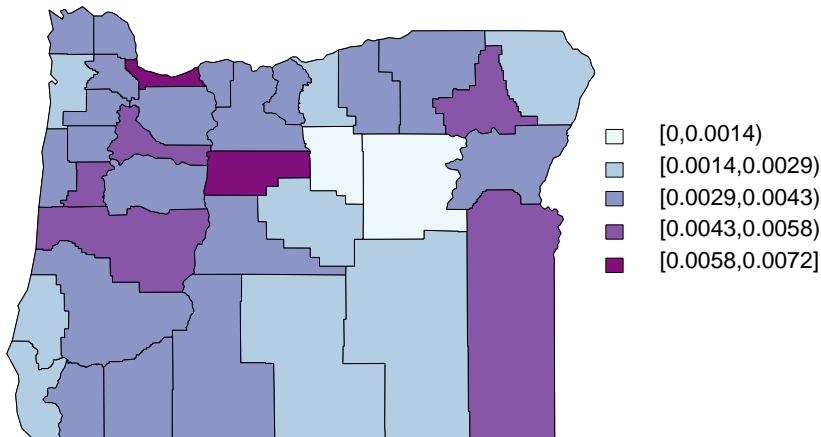
Oregon Population and Cases by County

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



Chlamydia in Oregon

Oregon Counties 2016 Reported Prevalence





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Notation and Terminology for Spatial Model



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

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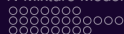
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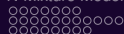
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$R \times R$ adjacency matrix:

$$A_{ij} = \begin{cases} 1, & \text{county } j \text{ borders county } i \text{ or } i = j \\ 0, & \text{otherwise} \end{cases}$$



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



Spatial Model

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



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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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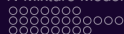
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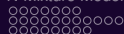
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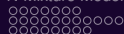
Estimation

As with the non-spatial normal-approximation model,

- Write MVN μ and Σ in terms of $\theta = (\rho, \beta, \omega, \gamma)$.
- Maximize log of approximate likelihood

$$L(\theta|\{n_{it}\}) = MVN(\{n_{it}\}; \mu, \Sigma)$$

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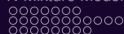
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Confidence Intervals

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

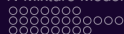
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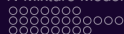
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Bootstrap sample $\hat{\theta}^{(1)}, \dots, \hat{\theta}^{(S)}$ represents the sampling distribution of $\hat{\theta}$.



Confidence Intervals

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

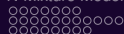


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$$\hat{N}_{i1}^{(s)} \sim \text{Poisson}(\hat{\beta}^{(s)} \text{pop}_{i1})$$



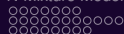
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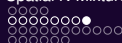
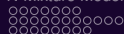
$$\begin{aligned} \hat{N}_{i1}^{(s)} &\sim \text{Poisson}(\hat{\beta}^{(s)} \text{pop}_{i1}) \\ \hat{N}_{it}^{(s)} | \hat{N}_{it-1}^{(s)} &= \mathbf{S}_{it}^{(s)} | \hat{N}_{it-1}^{(s)} + \mathbf{G}_{it}^{(s)} | \hat{N}_{it-1}^{(s)}, \quad t > 1 \\ \mathbf{S}_{it}^{(s)} | \hat{N}_{it-1}^{(s)} &\sim \text{Binomial}(\hat{N}_{it-1}^{(s)}, \hat{\omega}^{(s)}) \\ \mathbf{G}_{it}^{(s)} | \hat{N}_{\alpha,t-1}^{(s)} &\sim \text{Poisson}(\hat{\gamma}^{(s)} \cdot \hat{N}_{it-1}^{(s)}) \end{aligned}$$



Confidence Intervals

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

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

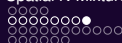
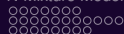


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Then calculate $\hat{N}_{\cdot t}^{(s)} = \sum_{i=1}^R \hat{N}_{it}^{(s)}$ to get $\hat{N}_{\cdot t}^{(1)}, \dots, \hat{N}_{\cdot t}^{(S)}$.

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



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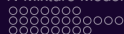
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Scenarios

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

	Parameter	Values
β	initial expected prevalence	0.005, 0.05
p	detection probability	0.4, 0.7, 0.9
ω	persistence rate	0.5, 0.8
γ	infection rate	0.3, 0.6



Procedure for k th Simulation

- Simulate $N_{it}^{(k)}$ for $t = 1, \dots, 9$, with Oregon's populations and map, and draw $n_{it}^{(k)} \sim \text{Bin}(N_{it}^{(k)}, p)$.



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$$\text{ARE}_{it}^{(k)} = \frac{|N_{it}^{(k)} - \widehat{N}_{it}^{(k)}|}{E(N_{it}^{(k)})}$$



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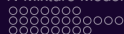
- Perform parametric bootstrap to simulate sampling distribution of \hat{N}_{i9} and calculate 90% interval estimate of $N_{i9}^{(k)}$.



Simulation Results

For each of the 24 simulation scenarios,

- Average parameters estimates $\hat{\rho}, \hat{\beta}, \hat{\omega}, \hat{\gamma}$ over the 1000 simulations.

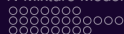


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$$\text{ARE} = \frac{1}{RT} \sum_{i=1}^R \sum_{t=1}^T \left[\frac{1}{1000} \sum_{k=1}^{1000} \frac{|N_{it}^{(k)} - \hat{N}_{it}^{(k)}|}{E(N_{it}^{(k)})} \right]$$



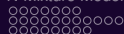
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- Average parameters estimates $\hat{\rho}, \hat{\beta}, \hat{\omega}, \hat{\gamma}$ over the 1000 simulations.
- Summarize absolute relative errors:

$$\text{ARE} = \frac{1}{RT} \sum_{i=1}^R \sum_{t=1}^T \left[\frac{1}{1000} \sum_{k=1}^{1000} \frac{|N_{it}^{(k)} - \hat{N}_{it}^{(k)}|}{E(N_{it}^{(k)})} \right]$$

- Calculate percentage of successful 90% interval estimates.



Simulation Results

For each of the 24 simulation scenarios,

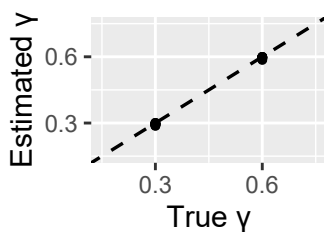
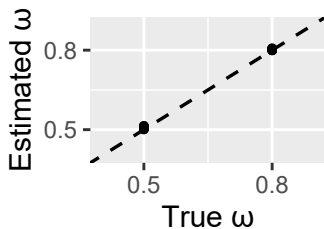
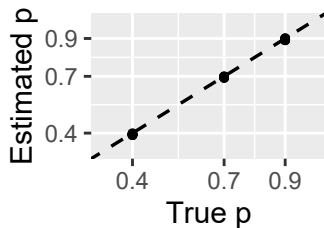
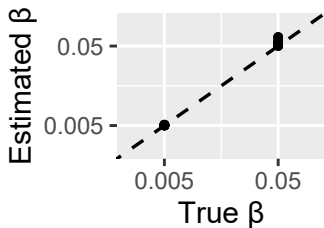
- Average parameters estimates $\hat{\rho}, \hat{\beta}, \hat{\omega}, \hat{\gamma}$ over the 1000 simulations.
- Summarize absolute relative errors:

$$\text{ARE} = \frac{1}{RT} \sum_{i=1}^R \sum_{t=1}^T \left[\frac{1}{1000} \sum_{k=1}^{1000} \frac{|N_{it}^{(k)} - \hat{N}_{it}^{(k)}|}{E(N_{it}^{(k)})} \right]$$

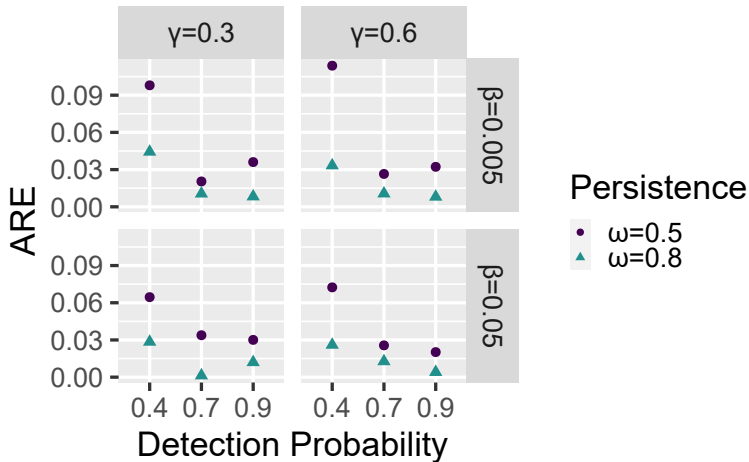
- Calculate percentage of successful 90% interval estimates.
- Calculate average width of 90% interval estimates.



Results: Parameter Estimates

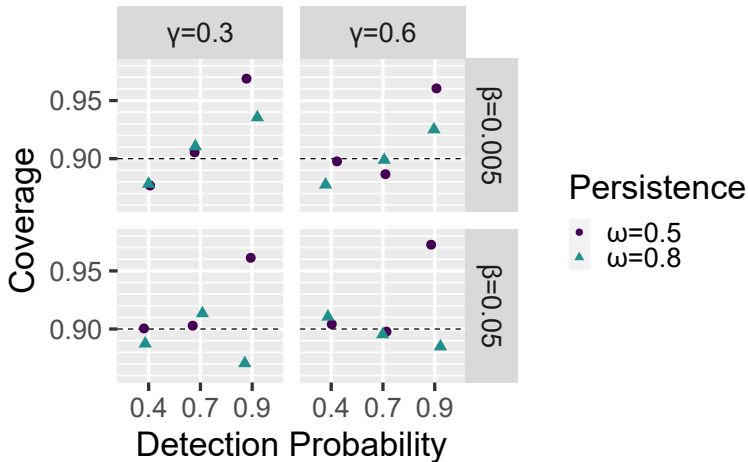


Results: Absolute Relative Error





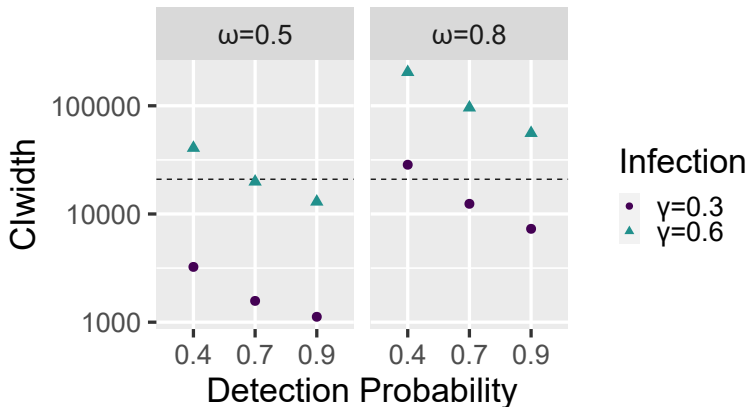
Results: Confidence Coverage





Results: Confidence Interval Width

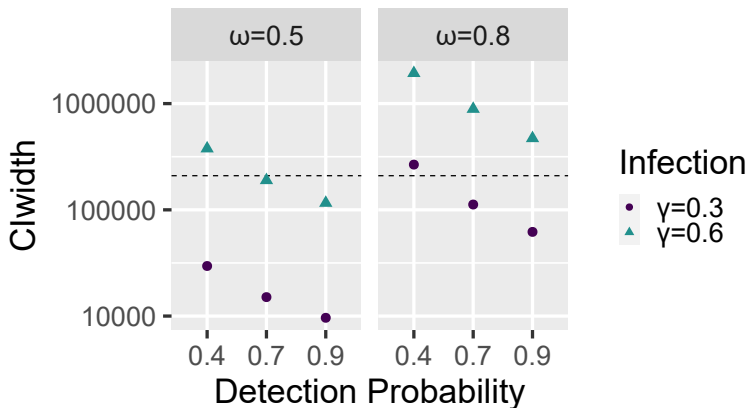
Initial Prevalence $\beta=0.005$





Results: Confidence Interval Width

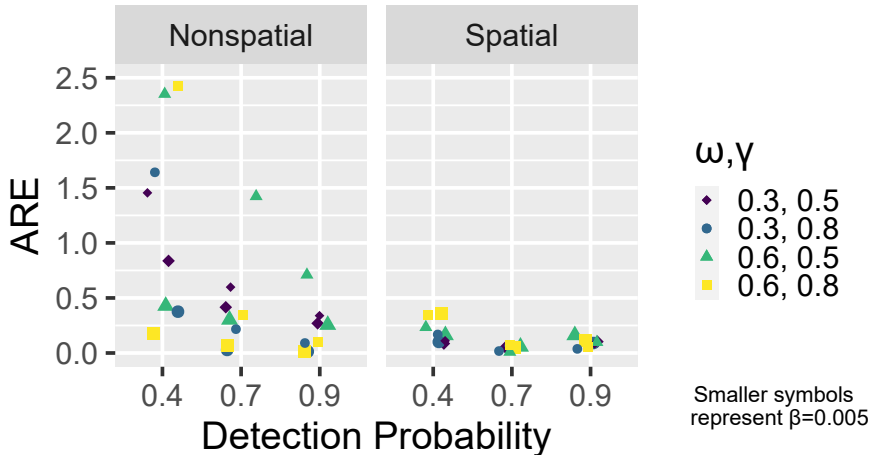
Initial Prevalence $\beta=0.05$





Robustness

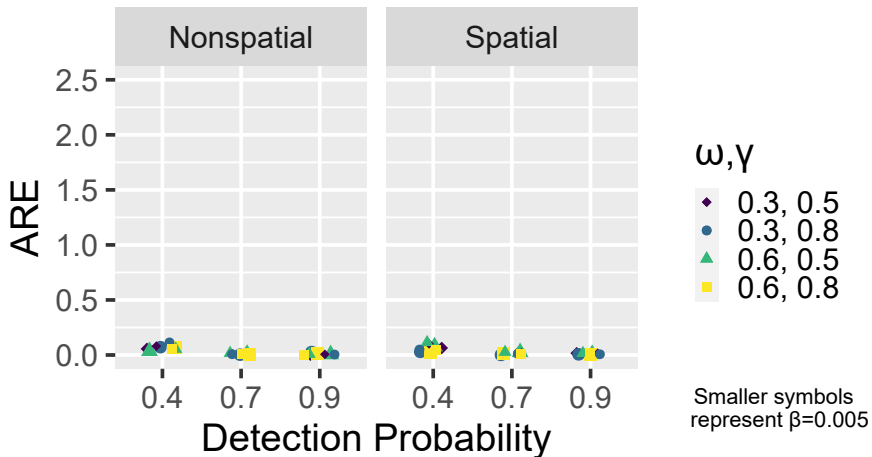
Misspecified Model Fit





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

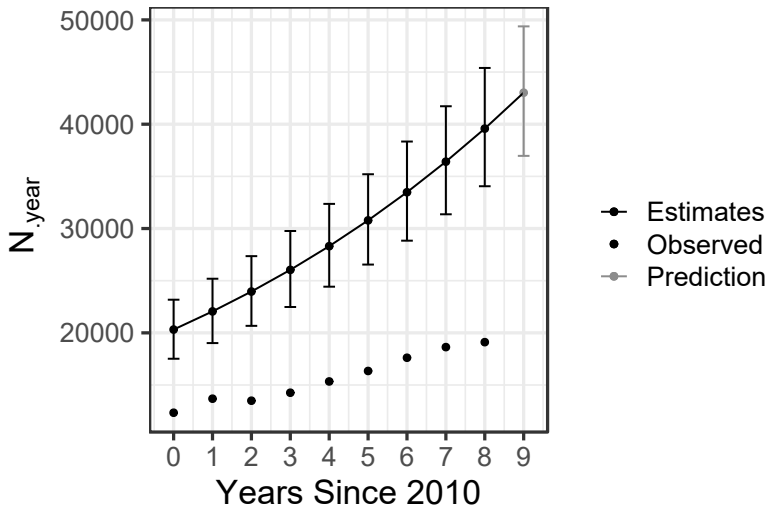


Parameter Estimates (SEs)

Initial expected prevalence	$\hat{\beta} = 0.0053 (0.000000014)$
Detection probability	$\hat{\rho} = 0.669 (0.047)$
Persistence rate	$\hat{\omega} = 0.917 (0.032)$
Infection rate	$\hat{\gamma} = 0.169 (0.032)$



State-wide Interval Estimates/Prediction





Analysis of Chlamydia Data

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)





Summary

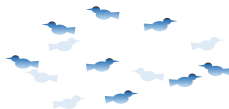
N-Mixture models provide estimates of N when $p < 1$.



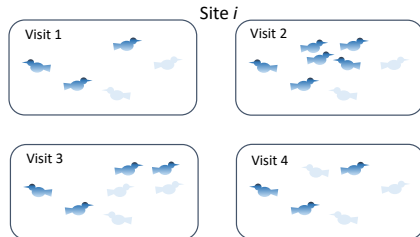


Summary

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



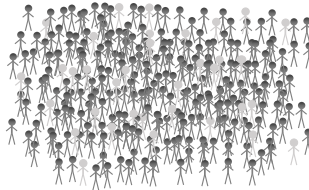
Generalized model allows open populations.





Summary

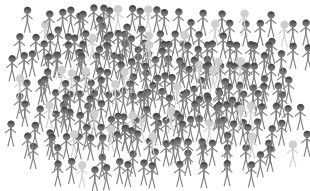
Asymptotic approximation allows large counts.



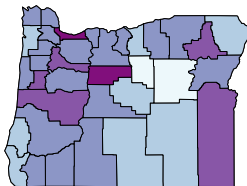


Summary

Asymptotic approximation allows large counts.



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.



Thanks to my coauthors, Ben and Claudio.

Thank you!



References

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