### Correlated Data Overview

### FW8051 Statistics for Ecologists

Department of Fisheries, Wildlife and Conservation Biology



# Learning Objectives

 Be able to model correlated binary and correlated count data using generalized linear mixed effect models (GLMMs) and generalized estimating equations (GEEs)

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- Be able to interpret parameters in linear and generalized linear mixed effects models
- Be able to describe models and their assumptions using equations and text and match parameters in these equations to estimates in computer output.

# Correlated Data Methods in Ecology

### For data that are normally distributed:

- Linear mixed effects model
- Generalized Least Squares

### For count or binary data:

- Generalized linear mixed effects models (GLMMS)
- Generalized Estimating Equations (GEE)

# Correlated Data Methods in Ecology

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Fieberg, J., Rieger, R.H., Zicus, M. C., Schildcrout, J. S. 2009. Regression modelling of correlated data in ecology: subject specific and population averaged response patterns. Journal of Applied Ecology 46:1018-1025.

# Mallard Nesting structures



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# Mallard Nesting structures



**Research Questions**: which types of cylinders are best (single or double)? Where should they be placed?

### Mallard Data

- 110 nest structures placed in 104 wetlands
- Structure type (single versus double) was chosen randomly at each location
  - 53 single-cylinders, 57 double-cylinders
- Occupancy (0,1) and clutch sizes were recorded in 1997, 1998, 1999

Zicus, M.C., J. Fieberg and D. P. Rave. 2003. Does mallard clutch size vary with landscape composition: a different view. Wilson Bulletin 114:409-413.

Zicus, M. C., D. P. Rave, and J. Fieberg. 2006. Cost effectiveness of single-vs. double-cylinder over-water nest structures. Wildlife Society Bulletin 34:647-655.

Zicus, M. C., Rave, D. P., Das, A., Riggs, M. R., and Buitenwerf, M. L. (2006). Influence of land use on mallard nest-structure occupancy. The Journal of wildlife management, 70(5), 1325-1333.

# Example Clutch Size Data

 $Y_{ij}$  = clutch size for the  $i^{th}$  structure during year j

 ${\tt Init.Date}_{ij} = {\tt nest}$  initiation date (Julian day) for the  $i^{th}$  structure during year j

I (deply=2)  $_{i}$  = 0 if  $i^{th}$  structure is a single cylinder, 1 if double cylinder

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#### <u>Model</u>

$$\begin{split} Y_{ij} = (\beta_0 + b_{0i}) + \beta_1 \texttt{Init.Date}_{ij} + & \beta_2 \texttt{I(deply=2)}_i + \epsilon_{ij} \\ \epsilon_{ij} \sim & N(0, \sigma_\epsilon^2) \\ b_{0i} \sim & N(0, \sigma_{b_0}^2) \end{split}$$

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Assume  $\epsilon_{ij}$  and  $b_{0i}$  are independent.

Similar to including "structure" as a series of dummy variables with the added assumption that the parameters are drawn from a normal distribution

# Generalized Least Squares

For normally distributed response data, we can fit correlated data models without having to resort to random effects:

$$\begin{array}{c} \text{Clutch size}_{ij} = \beta_0 + \beta_1 \text{Init.Date}_{ij} + \beta_2 \text{I (deply=2)}_{i} + \epsilon_{ij} \\ \epsilon_{ij} \sim N(0,\Omega) \end{array}$$

 $\Omega$  = Var/Cov matrix for  $\epsilon$ . We no longer assume the errors,  $\epsilon_{ij}$ , are independent!

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Compound symmetric covariance matrix for within-cluster data:

$$\Omega = \begin{bmatrix} \Sigma_i & 0 & \cdots & 0 \\ 0 & \ddots & \ddots & \vdots \\ \vdots & \ddots & \ddots & 0 \\ 0 & \cdots & 0 & \Sigma_i \end{bmatrix} \text{ with } \Sigma_i = \begin{bmatrix} \sigma^2 & \rho\sigma^2 & \cdots & \rho\sigma^2 \\ \rho\sigma^2 & \ddots & \ddots & \vdots \\ \vdots & \ddots & \ddots & \rho\sigma^2 \\ \rho\sigma^2 & \cdots & \rho\sigma^2 & \sigma^2 \end{bmatrix}$$

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#### Correlation between:

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This model is equivalent to a linear mixed effects model with random intercepts for each structure! Note:  $\rho = \frac{\sigma_{b_0}^2}{\sigma_{b_0}^2 + \sigma_{\epsilon}^2}$  and  $\sigma^2 = \sigma_{b_0}^2 + \sigma_{\epsilon}^2$ .

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- Start with generalized linear models (logistic or Poisson regression) and add random coefficients (intercepts, slopes)
- Use generalized estimating equations or cluster-level bootstrap (recognizing clusters serve as independent units)

### Option 1: Generalized linear mixed effects models

Option 2: Generalized Estimating equations

Systematic component: 
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- $f(y_i|x_i)$  is in the exponential family (includes normal, Poisson, binomial, gamma, inverse Gaussian)
- $f(y_i|x_i)$  that describes unmodeled variation about  $\mu_i = E[Y_i|X_i]$

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- $b_{0i}$  and  $b_{1i}$  allow intercepts and parameters to vary among groups.
- Usually assume:  $(b_{0i}, b_{1i}) \sim N(0, \Sigma)$

### Conditional models

#### Poisson-normal model:

- $Y_{ij}|b_i \sim \text{Poisson}(\lambda_{ij})$
- $log(\lambda_{ij}) = (\beta_0 + b_{0i}) + (\beta_1 + b_{1i})x_{ij}$
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Frequentist analysis: the b's are unobserved random variables... we do not estimate them! Rather, we estimate  $\beta_0, \beta_1, \Sigma$ .

# Non-linear models: Modeling Occupancy Probability

### Logistic-normal model:

$$\begin{aligned} Y_{ij}|b_i \sim \text{Bernoulli}(p_{ij})\\ \log[p_{ij}/(1-p_{ij})|b_i] &= \beta_0 + b_{0i} + \beta_1 VOM_{ij} + \beta_2 \text{I (deply=2)}_i\\ b_{0i} \sim N(0,\tau^2) \end{aligned}$$

Structures have different "propensities" of being occupied:

• Depending on visual obstruction (VOM), structure type, and other unmeasured characteristics ( $b_{0i}$ ) associated with the structure and the landscape in which it is placed.

### Parameter Estimation

To estimate parameters using Maximum Likelihood, we need to determine:

• the distribution of Y (not  $Y|b_i$ )

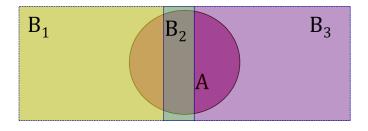
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Total law of Probability If events  $B_1, B_2, \dots, B_k$  are mutually exclusive and together make up all possibilities, then:

$$P(A) = \sum_{i} P(A|B_i)P(B)$$



### Unconditional Model and Likelihood

To determine the distribution of  $Y_{ij}$ , we integrate over the random effects:

$$L(Y_{ij}|\beta,\Sigma) = \int f(Y_{ij}|b_i)f(b_i)db_i$$

- $\beta$  = fixed effects parameters in  $f(Y_{ij}|b_i)$
- $\Sigma$  are variance parameters of the random effects distribution,  $f(b_i)$

# Normally Distributed Data: Linear Mixed Effects Models

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$$\mu_{ij} = X_{ij}\beta + Z_ib$$
  

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$$I = \begin{bmatrix} 1 & 0 & \cdots & 0 \\ 0 & \ddots & \ddots & \vdots \\ \vdots & \ddots & \ddots & 0 \\ 0 & \cdots & 0 & 1 \end{bmatrix}$$

$$(n \times n)$$

#### $Y \sim MVN(X\beta, \Omega)$

#### Random Intercept Model:

$$\Omega = \begin{bmatrix} \Sigma_i & 0 & \cdots & 0 \\ 0 & \ddots & \ddots & \vdots \\ \vdots & \ddots & \ddots & 0 \\ 0 & \cdots & 0 & \Sigma_i \end{bmatrix} \text{ with } \Sigma_i = \begin{bmatrix} \tau^2 + \sigma^2 & \tau^2 & \cdots & \tau^2 \\ \tau^2 & \ddots & \ddots & \vdots \\ \vdots & \ddots & \ddots & \tau^2 \\ \tau^2 & \cdots & \tau^2 & \tau^2 + \sigma^2 \end{bmatrix}$$

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GLS Model with compound-symmetric correlation structure:

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$$f(Y_{ij}|b_i) = p_{ij}^{Y_{ij}} (1 - p_{ij})^{1 - Y_{ij}}$$
  
•  $f(b_i) = \frac{1}{\sqrt{2\pi}\sigma_b} e^{\frac{(b_{0i} - 0)^2}{2\sigma_b^2}}$ 

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$$L(Y_{ij}|\beta,\Sigma) = \int f(Y_{ij}|b_i)f(b_i)db_i$$

$$\int \left[ \frac{exp(\beta_0 + b_{0i} + \beta_1 x_{ij})}{1 + exp(\beta_0 + b_{0i} + \beta_1 x_{ij})} \right]^{Y_{ij}} \left[ \frac{1}{1 + exp(\beta_0 + b_{0i} + \beta_1 x_{ij})} \right]^{1 - Y_{ij}} \frac{1}{\sqrt{2\pi}\sigma_b} e^{\frac{(b_{0i} - 0)^2}{2\sigma_b^2}} db_{0i}$$

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No closed-form solution!

How do we use maximum likelihood to estimate parameters?

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- Use numerical integration (can be slow, difficult, particularly with multiple random effects)
- Add priors, and use Bayesian techniques

### Numerical Integration: glmer

#### nAGQ

- specifies number of points per axis for evaluating the adaptive Gauss-Hermite approximation to the log-likelihood.
- default = 1 (Laplace approximation)
- values > 1 produce greater accuracy in the evaluation of the log-likelihood at the expense of speed.
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See also mixed\_model in the GLMMadaptive package.

#### Linear versus Generalized Linear Mixed Effects Models

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Parameters in generalized linear mixed effects models have a "subject-specific", but not "population-average" interpretation.

$$\begin{aligned} \text{Clutch size} &= (\beta_0 + b_{0i}) + \beta_1 \texttt{Init.Date}_{ij} + \beta_2 \texttt{I} \, (\texttt{deply=2})_{\,i} + \epsilon_{ij} \\ &\quad \epsilon_{ij} \sim N(0, \sigma^2) \\ &\quad b_{0i} \sim N(0, \sigma_{b_0}^2) \end{aligned}$$

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How does clutch size vary with nest initiation date and structure type for a "typical" structure (i.e., one with  $b_{0i} = 0$ )?

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Fixed effects parameters have both population-averaged and subject-specific interpretations!

$$\begin{aligned} Y_i|b_i \sim \text{Binomial}(1,p_i) \\ \log[p_{ij}/(1-p_{ij})|b_i] &= \beta_0 + b_{0i} + \beta_1 VOM_{ij} + \beta_2 \text{I (deply=2)}_{i} \\ b_{0i} \sim N(0,\sigma_{b_0}^2) \end{aligned}$$

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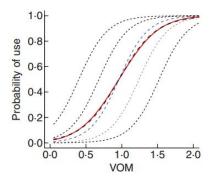
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- $exp(\beta_2)$  = change in the odds of occupancy if we were to change a particular structure from a single to double cylinder model (and hold VOM constant)

Note: a subject-specific interpretation may not be meaningful for predictors that are constant within a cluster.

## Interpretation of Parameters: GLMMS



 $E[Y_{ij}|X]$  (red curve) is no longer the same as  $E[Y_{ij}|X,b_{0i}=0]$  (blue curve)!

$$Y_{ij}|b_{0i}, b_{1i} \sim f(y_{ij}|b_{0i}, b_{1i})$$
  
 $(b_{0i}, b_{1i}) \sim N(0, \Sigma)$ , with

 $f(y_i|b_{0i},b_{1i})$  given by Poisson, binomial, negative binomial.

How can we quantify how E[Y|X] changes with X (as opposed to  $E[Y|X,b_{0i},b_{1i}]$  or  $E[Y|X,b_{0i}=b_{1i}=0]$ )?

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- mixed\_model + marginal\_coefs in GLMMadaptive package to estimate equivalent "marginal coefficients" (based on Hedeker et al. 2018).

Hedeker, D., du Toit, S. H., Demirtas, H. and Gibbons, R. D. (2018), A note on marginalization of regression parameters from mixed models of binary outcomes. Biometrics 74, 354-361.

#### **GLMM** Resources on Canvas

#### Readings:

- Bolker et al. 2008. Generalized linear mixed models: a practical guide for ecology and evolution
- Bolker et al. 2013: Strategies for fitting nonlinear ecological models in R, AD Model Builder, and BUGS

#### Useful Links

- GLMM wiki
- GLMMS worked examples

Option 1: Generalized linear mixed effects models

Option 2: Generalized Estimating equations

## **Generalized Estimating Equations**

- Motivation (least squares, maximum likelihood...)
- Assumptions and implementation of GEE approach

### Least Squares and Maximum Likelihood

For Normally distributed data:

$$L(\mu, \sigma^2; y_1, y_2, \dots, y_n) = \prod_{i=1}^n \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{(y_i - \mu)^2}{2\sigma^2}\right)$$

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With linear regression, we assume  $Y_i \sim N(\beta_0 + x_i\beta_1, \sigma^2)$ , so...

$$L(\beta_0, \beta_1, \sigma; x) = \prod_{i=1}^n \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{(y_i - \beta_0 + x_i \beta_1)^2}{2\sigma^2}\right)$$
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$$= \frac{1}{(\sqrt{2\pi}\sigma)^n} \exp\left(-\sum_{i=1}^n \frac{(y_i - \beta_0 + x_i \beta_1)^2}{2\sigma^2}\right)$$
$$\Rightarrow log L = -nlog(\sigma) - \frac{n}{2}log(2\pi) - \sum_{i=1}^n \frac{(y_i - \beta_0 + x_i \beta_1)^2}{2\sigma^2}$$

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$$\begin{split} L(\beta_0,\beta_1,\sigma;x) &= \prod_{i=1}^n \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{(y_i-\beta_0+x_i\beta_1)^2}{2\sigma^2}\right) \\ &= \frac{1}{(\sqrt{2\pi}\sigma)^n} \exp\left(-\sum_{i=1}^n \frac{(y_i-\beta_0+x_i\beta_1)^2}{2\sigma^2}\right) \\ \Rightarrow logL &= -nlog(\sigma) - \frac{n}{2}log(2\pi) - \sum_{i=1}^n \frac{(y_i-\beta_0+x_i\beta_1)^2}{2\sigma^2} \\ \Rightarrow \text{maximizing logL} \Rightarrow \text{minimizing } \sum_{i=1}^n \frac{(y_i-\beta_0+x_i\beta_1)^2}{2\sigma^2} \\ \text{or, equivalently } \sum_{i=1}^n (y_i-\beta_0-x_i\beta_1)^2 \end{split}$$

## Least squares

$$\sum_{i=1}^{n} (y_i - E[Y_i|X_i])^2 = \sum_{i=1}^{n} (y_i - (\beta_0 + x_{1i}\beta_1 + \ldots))^2$$
 (1)

Least squares leads to the following set of equations for estimating parameters (take the derivative and set = 0):

$$2\sum_{i=1}^{n} \frac{\partial E[Y_i|X_i]}{\partial \beta} (Y_i - E[Y_i|X_i]) = 0$$
 (2)

Or, equivalently...

$$\sum_{i=1}^{n} X_i (Y_i - E[Y_i | X_i]) = 0$$
 (3)

## Generalized Linear Models

Maximum Likelihood estimators are found by solving:

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#### Poisson Regression:

- $E[Y_i|X_i] = exp(X_i\beta)$
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GEE: 
$$\hat{\beta}$$
 solves:  $\sum_{i=1}^{n} \frac{\partial \mu_i}{\partial \beta} V_i(\alpha)^{-1} (Y_i - E[Y_i|X_i]) = 0$ .

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 $R_i$  = working correlation model that describes within subject correlation.

 Examples include exchangeable (equal correlation among all observations), Ar(1) (time series), unstructured

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- Fit using geeglm in geepack library

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Uses "robust" (or "sandwich") standard errors, treating clusters as independent observational units

•  $\hat{\beta} \pm 1.96SE$  gives valid CIs (for large numbers of clusters)