Lab 2: Mixed-effects models

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Laws of probability

1. Axiom of conditional probability

$$\Pr(X, Y) = \Pr(Y|X)\Pr(X)$$

   - Often easier to specify conditional probabilities than joint probabilities

2. Law of total probability

$$\Pr(X) = \int \Pr(X, Y)\mathrm{d}Y$$

   - Used when justifying hierarchical models

Bayes rule

- By the Axiom of conditional probability

$$\Pr(\theta|y)\Pr(y) = \Pr(y,\theta) = \Pr(\mathrm{y}|\theta)\Pr(\theta)$$

- Therefore

$$\Pr(\theta|y) = \frac{\Pr(\mathrm{y}|\theta)\Pr(\theta)}{\Pr(y)}$$

- By the Law of total probability

$$\Pr(y) = \int \Pr(y,\theta)\mathrm{d}y = \int \Pr(\mathrm{y}|\theta)\Pr(\theta)\,\mathrm{d}y$$

- Therefore

$$\Pr(\theta|y) = \frac{\Pr(\mathrm{y}|\theta)\Pr(\theta)}{\int \Pr(\mathrm{y}|\theta)\Pr(\theta)\,\mathrm{d}y}$$

- MCMC gives you

$$\Pr(\theta|y) \propto \Pr(\mathrm{y}|\theta)\Pr(\theta)$$

Mixed-effects models

Empirical Bayes

- By the definition of a likelihood

$$L(\theta; y) = \Pr(y|\theta)$$

- By the Law of total probability

$$\Pr(y|\theta) = \int \Pr(\mathrm{y}, \varepsilon|\theta)\mathrm{d}\varepsilon$$

- By the Axiom of conditional probability

$$\Pr(\mathrm{y}, \varepsilon|\theta) = \Pr(\mathrm{y}\ |\varepsilon, \theta)\Pr(\varepsilon|\theta)$$

- Therefore

$$\Pr(y|\theta) = \int \Pr(\mathrm{y}\ |\varepsilon, \theta)\Pr(\varepsilon|\theta)\mathrm{d}\varepsilon$$

Mixed-effects models

Generalized linear mixed model

1. Specify distribution for response variable

$$c_i \sim Poisson(\lambda_i)$$

2. Specify function for expected value

$$g^{-1}(\lambda_i) = x_0 + \mathbf{x}_i^T \boldsymbol{\beta} + \mathbf{z}_i^T \boldsymbol{\varepsilon}$$

3. Specify a link function

$$g^{-1}(a) = \log(a) \quad \rightarrow \quad g(a) = \exp(a)$$

4. Specify distribution for random effects

$$\varepsilon \sim Normal(0, \sigma_\varepsilon^2)$$

= General linear model + mixed effect(s)

Mixed-effects models

How to estimate standard errors?

– Estimate the "Hessian" at the log-marginal likelihood

$$H(\boldsymbol{\theta};\mathbf{y}) = \begin{bmatrix} \dfrac{\partial^2 \ln L(\boldsymbol{\theta};\mathbf{y})}{\partial\theta_1^2} & \dfrac{\partial^2 \ln L(\boldsymbol{\theta};\mathbf{y})}{\partial\theta_1\partial\theta_2} \\ \dfrac{\partial^2 \ln L(\boldsymbol{\theta};\mathbf{y})}{\partial\theta_1\delta\theta_2} & \dfrac{\partial^2 \ln L(\boldsymbol{\theta};\mathbf{y})}{\partial\theta_2^2} \end{bmatrix}$$

– Calculate its inverse

$$\widehat{\mathbb{V}}(\boldsymbol{\theta};\mathbf{y}) = \mathbf{H}^{-1}$$

– Extract element and take square root

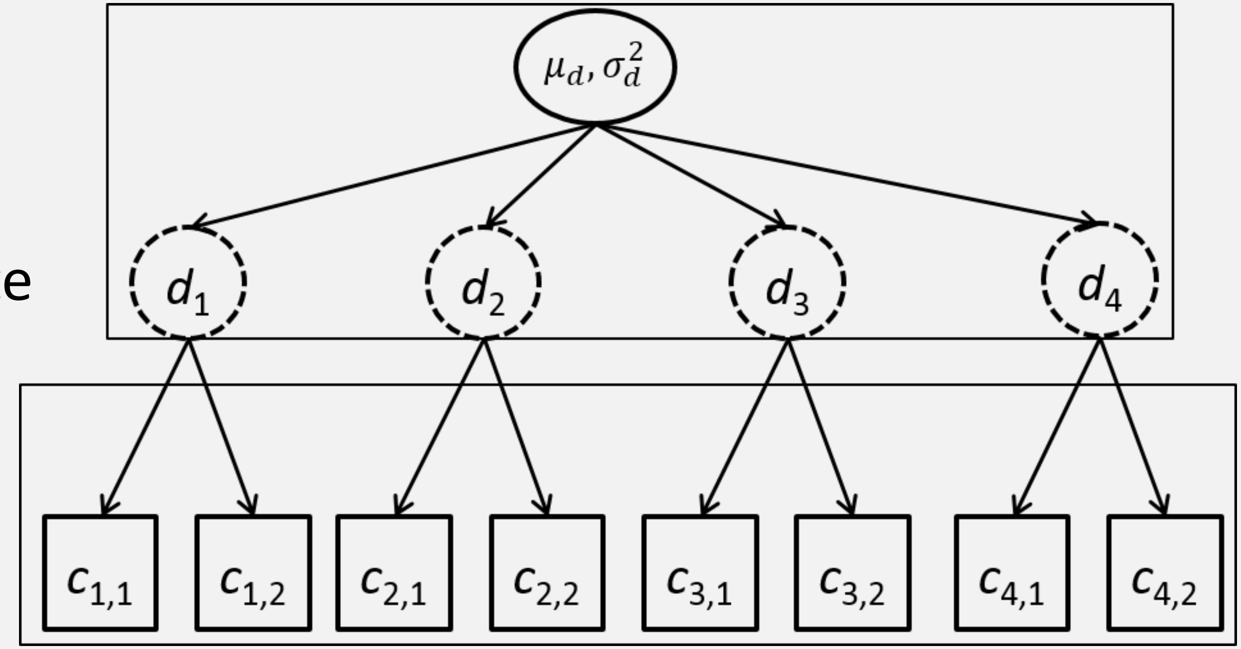
$$\widehat{\mathrm{SE}}(\theta_i;\mathbf{y}) = \sqrt{\widehat{\mathbb{V}}(\boldsymbol{\theta};\mathbf{y})_{i,i}}$$

Mixed-effects models

Example – Hierarchical count samples

$$\log(d_j) \sim Normal(\mu_d, \sigma_d^2)$$
$$c_{i,j} \sim Poisson(d_j)$$

- Counts
  - 4 sites
  - 2 observations/site
  - 3 fixed effects
  - 4 random effects



Mixed-effects models

- Simulating data
  - [See R code]

Mixed-effects models

Fit using R

- Using *lme4* package
- *formula*: way to specify model

1. Linear model – *lm(formula= …)*

- Count ~ 0 + factor(Site)
- "Count" – response variable
- "0" – Don't include intercept
- "factor(Site)" – Include a fixed effect for each site

2. Linear mixed model – *lm(formula = … | …)*

- Count ~ (1 | factor(Site))
- "(1 | factor(Site))" – Include a random effect for each site

Mixed-effects models

Fit using R

- **[See R code]**

Fit using TMB

Steps during optimization

1. Write joint log-likelihood $\Pr(y, \varepsilon|\theta)$ in CPP file

$$f(\theta, \varepsilon) = \log(\Pr(y|\theta_1, \varepsilon) \Pr(\varepsilon|\theta_2))$$

2. Choose initial values for fixed θ_0 and random ε_0
3. "Inner optimization" – Optimize random effects with $\theta_0$held constant

$$\hat{\varepsilon} = \text{argmax}_\varepsilon\big(f(\theta_0, \varepsilon)\big)$$

4. Calculate Laplace approx. for marginal likelihood of fixed effects

$$\ln L(\theta_0; y) \cong f(\theta_0, \hat{\varepsilon}) - \frac{1}{2}\log(|\mathbf{H}|)$$

   - TMB also provides the gradient of the penalized likelihood with respect to fixed effects

5. "Outer optimization" – Repeat steps 2-3
   - Outer optimization is done in R using the function value and gradient provided by TMB

Fit using TMB

[See R code]

Mixed-effects models

- Benefits of using linear mixed models
  - Separate estimate of measurement and between-site variability
  - Include covariates for either one
  - Improved precision
  - *“Shrinkage”*
- Draw-backs
  - Biased if random effects aren’t “exchangeable”

Mixed-effects models

Restricted maximum likelihood models (REML)

- Maximum likelihood (ML) estimates of variance parameters are biased
  - ML estimate $\hat{\sigma}_{ML}{}^2$

$$\hat{\sigma}_{ML}{}^2 = \frac{1}{n_i}\sum_{i=1}^{n_i}(y - \widehat{\mu_i})^2$$

  - Expectation

$$\hat{\sigma}_{unbiased}{}^2 = \frac{1}{n_i - 1}\sum_{i=1}^{n_i}(y - \widehat{\mu_i})^2$$

  - Same problem arises for variance estimates of random effects
- REML gives unbiased estimates of random-effect variances
  - Also sometimes helps convergence
  - Important when log-likelihood function is correlated with respect to random and fixed effects