Generalized Linear Mixed Models

- Synthesize generalized linear models and linear mixed models
- Places random effects in the linear predictor of a glm
- Yields subject specific parameter interpretations
- Both non-linear optimization routines and numerical integration algorithms are required to fit these models
GLMM

• Notation
  – \( Y_{ij} \) response for observation \( j \) in cluster \( i \)
  – \( X_{ij} \) vector of explanatory variables
  – \( u_i \) vector of random effects
  – \( Z_{ij} \) vector of explanatory variables associated with the random effects
GLMM Model

- **Top level model**
  - $Y_{ij} | u_i$ is a glm with means $\mu_{ij}$
  - $g(\mu_{ij}) = X_{ij} \beta + Z_{ij} u_i$

- **Second level model**
  - $u_i$ is Normally distributed with mean 0 and variance matrix $\Sigma$

- **Natural extension of the conditionally specified linear mixed model**

- **Random effects are linear on the linear predictor scale, which makes a lot of sense if you consider them as representing variability due to unmeasured subject level covariates**
GLMM parameter interpretation

- Consider the instance where the are binary random variables and is the logit link

\[
\logit(\mu_{ij}) = \beta_0 + x_{1i} \beta_1 + x_{2ij} \beta_2 + u_i
\]

- where \(x_{1i}\) is a gender indicator and \(x_{2ij}\) is BMI for subject \(i\) and time \(j\)
- \(\beta_2\) is the increase in the log odds of success given a 1 unit increase in BMI for this subject
- \(\beta_1\) is the increase in the log odds of success comparing two people with different genders but with the same value of \(u_i\)
GLMMs (cont'd)

- Notice the subject specific interpretations of the coefficients, in contrast with the marginal interpretations given by GEE and the other marginal modeling approaches.

- Subject specific interpretations are a little harder for subject level (time invariant) covariates like gender.

- Random effect models imply a marginal model. Non-linear link functions often imply a complex relationship between subject specific effects and marginal effects (though see Tom's recent work on bridge distributions).
Example, binary matched pairs

First Survey

<table>
<thead>
<tr>
<th>Second</th>
<th>Approve</th>
<th>Disapprove</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approve</td>
<td>794</td>
<td>150</td>
</tr>
<tr>
<td>Disapprove</td>
<td>86</td>
<td>570</td>
</tr>
</tbody>
</table>

- Restructuring the data

<table>
<thead>
<tr>
<th>Time</th>
<th>Resp</th>
<th>Subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>“Approve”</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>“Approve”</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>“Approve”</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>“Approve”</td>
<td>2</td>
</tr>
</tbody>
</table>

- Notice that there really are only 4 kinds of subjects
GLMM model

- $Y_{ij}$ response for time $j$ for subject $i$

$$\text{logit}\{P(Y_{ij} = 1 \mid u_i)\} = \beta_0 + x_j \beta_1 + u_i$$

$$u_i \sim \text{Normal}(0, \sigma^2)$$

- Here $x_j$ is an indicator for time (1 for the second occasion).

- This model has a closed form estimate for $\beta_1$
  - If $\log(n_{11} n_{22} / n_{21} n_{22})$ is $\geq 0$ then it is $\log(n_{12} / n_{21})$
    the conditional ML estimate!
  - Otherwise it is $\log(n_{12} / n_{21})$
    the marginal ML estimate!
Prime minister approval data

- Estimate for $\beta_1$ was -.556, so that the odds of approval for the second survey were estimated to be $\exp(-.556) = .57$ those of the first survey for a given subject.

- The large variance component, $\sigma^2$, was estimated to be 5.16 (.35) suggest a high degree of correlation in the data (lots of observations down the diagonal).
GLMM fitting

- GLMM fitting maximizes the marginal model obtained by integrating out the random effects
  
  \[ \mathcal{L}(\beta, \Sigma) = \int f(y \mid u; \beta) f(u \mid \Sigma) du \]

- Which results in an integral without a closed form and a non-linear maximization problem

- When the response decompose into independent subjects then we have
  
  \[ \mathcal{L}(\beta, \Sigma) = \prod \int f(y_i \mid u_i; \beta) f(u_i \mid \Sigma) du_i \]
GLMMs fitting (cont'd)

- If the random effects are low dimensional, then fitting via numerical integration is reasonable
  - Be sure to verify that estimates have stabilized by refitting the model with more quadrature points

- Iteratively applied Laplace approximations (PQL) can work well, though can sometimes perform poorly such as in binary regression

- Another possibility is to put priors on $\beta$ and $\Sigma$ and use MCMC sampling
GLMM fitting software

- SAS – proc NLMIXED uses adaptive quadrature, see the course web site for some sample code
- SAS - %glimmix macro uses PQL
- R – glmmNQ uses quadrature
- R – GLMMGibbs uses Gibbs sampling
- R – glmmPQL uses PQL
  - There are some other packages for R