Estimating β and $\boldsymbol{\theta}$

$$e^{\ell(\beta,\boldsymbol{\theta})} \propto |\mathbf{D}|^{-\frac{1}{2}} \int e^{\left\{\sum_{i=1}^{n} \ell_i(Y_i|\mathbf{b};\beta)-\frac{1}{2}\mathbf{b}^{\mathbf{T}}\mathbf{D}^{-\mathbf{1}}\mathbf{b}\right\}} d\mathbf{b}$$

So far, to estimate β and $\boldsymbol{\theta}$:

1. Conditional inference (condition on sufficient statistic)
2. Full MLE using numerical integration (Gaussian Quadrature)
3. Approximate Inference
   - Laplace Approximation
   - Solomon-Cox Approximation
   - PQL and CPQL
4. Expectation Maximization algorithm
5. Gibbs Sampling

What about estimating $\mathbf{b}_i$?

Estimating $\mathbf{b}_i$:

- In general: interest is usually in β and $\mathbf{D}$
- $\mathbf{b}_i$ reflect between subject variability
  - Subject specific trajectories
  - Identify outlier subjects
- Similar approach to estimation from LMMs

Estimating $\mathbf{b}_i$ for GLMMs via Empirical Bayes

Posterior density of $\mathbf{b}_i$:

$$f(\mathbf{b}_i|\mathbf{Y}_i, \beta, \mathbf{D}) = \frac{f_i(\mathbf{Y}_i|\mathbf{b}_i, \beta) f(\mathbf{b}_i|\mathbf{D})}{\int f_i(\mathbf{Y}_i|\mathbf{b}_i, \beta) f(\mathbf{b}_i|\mathbf{D}) d\mathbf{b}_i}$$

- $\widehat{\mathbf{b}}_i$ maximizes $f_i(\mathbf{b}_i|\mathbf{Y}_i, \beta, \mathbf{D})$
- Note: $\widehat{\mathbf{b}}_i$ is posterior mode rather than posterior mean (no longer normal)
- We plug in the MLEs for β and $\mathbf{D}$ $\rightarrow$ Empirical Bayes estimate

Statistical Inference

- β are MLE's so usual inferential methods hold
  - Wald
  - Score
  - LRT
- Variance component testing subject to similar concerns as in LMMs
- Note that β and $\boldsymbol{\theta}$ no longer orthogonal
- The computation and calculation can be a bit messier here
  - Recall the PQL fits a sequence of LMMs: can often use working linear (mixed) model at convergence

Indonesian infectious disease data

- 275 Indonesian children, each was followed for up to 6 consecutive quarters
- Outcome=respiratory infection (Y/N).
- Covariates=age, sex, xerophthalmia status, season, height
- Logistic mixed effects model:

$$
\begin{aligned}
logit(\mu_{ij}^{\mathbf{b}}) &= \mathbf{X}_{ij}^T\beta + b_i \\
&\textit{and} \\
b_i &\sim N(0, \theta)
\end{aligned}
$$

Indonesian infectious disease data (2)

```
> indon = read.table("indon1.dat", col.names =
    c("id", "season", "xero", "age", "sex", "height", "infect"))
> head(indon)
      id season xero age sex height infect
1 121013     -1    0  31   0     -3      0
2 121013      0    0  34   0     -3      0
3 121013      1    0  37   0     -2      0
4 121013      0    0  40   0     -2      0
5 121013     -1    0  43   0     -2      1
6 121013      0    0  46   0     -3      0
> library(lme4)
> mod = glmer(infect ~ season + xero + age + sex + height+(1|id),
          family = binomial, data = indon)
> summary(mod)
```

Indonesian infectious disease data (3)

```
Generalized linear mixed model fit by maximum likelihood (Laplace
  Approximation) [glmerMod]
 Family: binomial  ( logit )
Formula: infect ~ season + xero + age + sex + height + (1 | id)
   Data: indon

     AIC      BIC   logLik deviance df.resid
   683.0    718.6   -334.5    669.0     1193

Scaled residuals:
    Min      1Q  Median      3Q     Max
-0.8907 -0.2998 -0.2203 -0.1549  7.3498

Random effects:
 Groups Name        Variance Std.Dev.
 id     (Intercept) 0.8013   0.8951
Number of obs: 1200, groups:  id, 275
```

Indonesian infectious disease data (4)

```
Fixed effects:
             Estimate Std. Error z value Pr(>|z|)
(Intercept) -2.650928   0.215055 -12.327  < 2e-16 ***
season      -0.566753   0.168528  -3.363 0.000771 ***
xero         0.576959   0.486746   1.185 0.235883
age         -0.033278   0.007383  -4.507 6.56e-06 ***
sex         -0.443127   0.264479  -1.675 0.093841 .
height      -0.053845   0.022801  -2.361 0.018202 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
       (Intr) season xero   age    sex
season  0.350
xero   -0.157 -0.100
age     0.136  0.008 -0.099
sex    -0.399  0.008  0.084  0.037
height  0.038  0.006  0.037  0.395  0.046
```