Recap of Central Results

- Longitudinal modeling of non-Gaussian outcomes is hard!
- Subject specific model $\rightarrow$ Random effects model $\rightarrow$ GLMMs
  - Conditional independence assumption
  - Note: LMM permits additional residual correlation
- GLMM vs. GEE
  - Underlying effects of covariates are the same (biology), but how we model them is different
    - Interpretations are model specific
    - Equal only in special cases
  - Subject specific vs. marginal interpretation
  - Challenging to interpret some parameters

Recap of Central Results (2)

- Inference and estimation
  - MLE from marginal model
  - Theoretical result follow from ML theory: consistency and asymptotic normality of $\widehat{\beta}$
  - Main challenge: computation
- Approaches to integration
  - Numerical integration via Adaptive Guassian Quadrature (or others)
  - Approximation: Laplace, Solomon-Cox, PQL and CPQL procedures
  - EM algorithm
  - Note that all of these can be problematic in different situations and slow!

Comments on Integration/Solving in R

- Tools in R:
  - `integrate()` and `cubature` package for integration
  - `nlm()` and `optim()` for optimization
  - `numDeriv()` for getting Hessians
- lme4 bundles a lot of this stuff for you
- SAS is (again) probably a little bit better
- **None of the R packages are perfect and need to look at the output carefully**
- GEE is a bit more stable (numerically)

GLMM Issues

- Assume: Mean model is correct
- Assume: Conditional independence: given b_i, Y_{ij}'s are independent
- Careful: causal statements on what happens if we change X by one unit

Advantages of GLMMs

- If we are interested in conditional inference
- If we want subject specific trajectories
- Major: dealing with missing data

Key References

- Breslow & Day (1989)
- Breslow & Clayton (1993)
- Zeger, Liang, Albert (1988)
- Neuhaus, Kalbfleish, Hauck (1991)
- Zeger & Liang (1992)
- Breslow & Lin (1995)
- Lin & Breslow (1996)
- Lin (1997)

Where we are in 571...

1. Introduction to Correlated Data
2. **Linear Mixed Models** (HW1)
3. Review of GLMs and Quasi-likelihood
4. **Generalized Estimating Equations** (HW2)
5. Final project description (HW 4)
6. **Generalized Linear Mixed Models** (HW3)
7. Missing Data
8. Classical and Modern Multivariate Analysis
9. Group Papers Due