## STAT347: Generalized Linear Models Lecture 13

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## Today's topics:

- GLMM: generalized linear mixed effect model
- Binomial response: logistic-normal models
- Poisson GLMM
- Marginal likelihood MLE for GLMM: Gauss-Hermite Quadrature
- Generalized estimating equations
- Example: modeling correlated survey responses


## LMM V.S. GLMM

For LMM, the form is

$$
y_{i s}=X_{i s}^{T} \beta+Z_{i s}^{T} u_{i}+\epsilon_{i s}
$$

with $u_{i}$ and $\epsilon_{i s}$ random. With the typical assumption that $E\left(u_{i}\right)=E\left(\epsilon_{i s}\right)=$ 0 , we would also have marginally

$$
E\left(y_{i s}\right)=X_{i s}^{T} \beta
$$

If we ignore the random effects but use a regular linear model

- We underestimate the uncertainty in $\hat{\beta}$
- Our estimates for $\beta$ will still be consistent


## LMM V.S. GLMM

However, for GLMM, the model is

$$
g\left[E\left(y_{i s} \mid u_{i}\right)\right]=X_{i s}^{T} \beta+Z_{i s}^{T} u_{i}
$$

when the link function $g$ is non-linear, marginally after integrating out the randomness in $\mu_{i}$ we would have

$$
g\left[E\left(y_{i s}\right)\right] \neq X_{i s}^{T} \beta
$$

If we ignore the random effects but use a regular GLM model

- Our estimates for $\beta$ will be biased
- The uncertainty in $\hat{\beta}$ will also be wrongly evaluated (likely under-estimated)


## GLMM for binary response:

 Latent variable threshold model with random effectsWe can view GLMM for binary responses as latent variable threshold model with random effects

We assume that

$$
P\left(y_{i s}=1 \mid u_{i}\right)=F\left(X_{i s}^{T} \beta+Z_{i s}^{T} u_{i}\right)
$$

we assume there is a latent $y_{i s}^{\star}$ where

$$
y_{i s}^{\star}=X_{i s}^{T} \beta+Z_{i s}^{T} u_{i}+\epsilon_{i s}
$$

where $\epsilon_{i s}$ are i.i.d. following some distribution (normal, logistic, ...) and we have

$$
y_{i s}= \begin{cases}1 & \text { if } y_{i s}^{\star}>=0 \\ 0 & \text { else }\end{cases}
$$

## Example: probit model with random intercept

- Latent continuous variable follow LMM:

$$
y_{i s}^{*}=X_{i s}^{T} \beta+u_{i}+\epsilon_{i s}, \quad \epsilon_{i s} \sim N(0,1), u_{i} \sim N\left(0, \sigma_{u}^{2}\right)
$$

- Conditional mean model for the observed $y_{i s}$

$$
P\left(y_{i s}=1 \mid u_{i}\right)=\Phi\left(X_{i s}^{T} \beta+u_{i}\right)
$$

- Marginal mean model for the observed $y_{i s}$

$$
P\left(y_{i s}=1\right)=P\left(u_{i}+\epsilon_{i s} \leq X_{i s}^{T} \beta\right)=\Phi\left(\frac{X_{i s}^{T} \beta}{\sqrt{1+\sigma_{u}^{2}}}\right)
$$

## Example: probit model with random intercept

$$
g\left(P\left(y_{i s}=1\right)\right)=\frac{X_{i s}^{T} \beta}{\sqrt{1+\sigma_{u}^{2}}}
$$

- This indicates that the marginal probabilities still follow a probit link, but with

$$
\beta^{\text {marginal }}=\frac{\beta}{\sqrt{1+\sigma_{u}^{2}}}
$$

- If we ignore the random effects but fit a probit GLM, our estimates for $\beta$ will be biased by $1 / \sqrt{1+\sigma_{u}^{2}}$
- We still underestimate the uncertainty in $\hat{\beta}^{\text {marginal }}$ (as we ignore the fact that samples are correlated)


## GLMM for binomial response

Logistic-normal model:

$$
\operatorname{logit}\left[P\left(y_{i s}=1 \mid u_{i}\right)\right]=X_{i s}^{T} \beta+Z_{i s}^{T} u_{i}
$$

where $u_{i} \sim N\left(0, \Sigma_{u}\right)$ and are independent

- Example: item-response models

Item response models: $y_{i j}$ the yes/no (correct/incorrect) response of subject $i$ on question $j$

$$
\operatorname{logit}\left[P\left(y_{i j} \mid u_{i}\right)\right]=\beta_{0}+\beta_{j}+u_{i}
$$

## Marginal GLM for Logistic-normal model

- We have a similar approximation for the logistic-normal model if we only have random intercept

$$
g\left(P\left(y_{i s}=1\right)\right) \approx \frac{X_{i s}^{T} \beta}{\sqrt{1+\sigma_{u}^{2} / c^{2}}}
$$

where $c \approx 1.7$

## Marginal GLM for binary GLMM

- Why does the $\beta$ in the random effect model typically larger than the coefficient $\beta^{\text {marginal }}$ in the corresponding marginal GLM?


Figure 9.2 Logistic random-intercept GLMM, showing its subject-specific curves and the population-averaged marginal curve obtained at each $x$ by averaging the subject-specific probabilities.

## Some properties

- Conditional independence

$$
P\left(y_{i 1}=a_{1}, \cdots, y_{i d_{i}}=a_{d_{i}} \mid u_{i}=u_{\star}\right)=P\left(y_{i 1}=a_{1} \mid u_{i}=u_{\star}\right) \cdots P\left(y_{i d_{i}}=a_{d_{i}} \mid u_{i}=u_{\star}\right)
$$

- Latent class model
- Marginal correlation

$$
\begin{aligned}
\operatorname{cov}\left(y_{i s}, y_{i k}\right) & =E\left[\operatorname{cov}\left(y_{i s}, y_{i k} \mid u_{i}\right)\right]+\operatorname{cov}\left[E\left(y_{i s} \mid u_{i}\right), E\left(y_{i k} \mid u_{i}\right)\right] \\
& =0+\operatorname{cov}\left[F\left(X_{i s}^{T} \beta+Z_{i s}^{T} u_{i}\right), F\left(X_{i k}^{T} \beta+Z_{i k}^{T} u_{i}\right)\right]
\end{aligned}
$$

- For random intercept Binary GLMM, the correlation between two responses within the same group is still positive (same as LMM)

$$
\operatorname{cov}\left(y_{i s}, y_{i k}\right)>0
$$

## Poisson GLMM

$$
\log \left[E\left(y_{i s} \mid u_{i}\right)\right]=X_{i s}^{T} \beta+Z_{i s}^{T} u_{i}
$$

Equivalently,

$$
E\left[y_{i s} \mid u_{i}\right]=e^{Z_{i s}^{T} u_{i}} e^{X_{i s}^{T} \beta}
$$

For the random-intercept model where $Z_{i s}=1$ and $u_{i} \sim N\left(0, \sigma_{u}^{2}\right)$, we have

$$
E\left(y_{i s}\right)=e^{X_{i s}^{T} \beta+\sigma_{u}^{2} / 2}
$$

- For the marginal model, the link function is still log-linear
- The coefficient $\beta^{\text {marginal }}=\beta$ except for the intercept
- Marginal GLM is not longer a Poisson GLM $\rightarrow$ over-dispersion due to the random effect term (Agresti book Chapter 9.4.2)

$$
\operatorname{var}\left(y_{i s}\right)=E\left(y_{i s}\right)+\left(E\left(y_{i s}\right)\right)^{2}\left(e^{\sigma_{u}^{2}}-1\right)
$$

## Matrix form of the GLMM model

- Similar to LMM, denote the model for the whole dataset

$$
g(E[y \mid u])=X \beta+Z u
$$

$$
y=\left(\begin{array}{c}
y_{1} \\
\vdots \\
y_{n}
\end{array}\right), X=\left(\begin{array}{c}
X_{1} \\
\vdots \\
X_{n}
\end{array}\right), Z=\left(\begin{array}{cccc}
Z_{1} & 0 & \cdots & 0 \\
0 & Z_{2} & \cdots & 0 \\
0 & 0 & \ddots & 0 \\
0 & 0 & \cdots & Z_{n}
\end{array}\right), u=\left(\begin{array}{c}
u_{1} \\
\vdots \\
u_{n}
\end{array}\right), \epsilon=\left(\begin{array}{c}
\epsilon_{1} \\
\vdots \\
\epsilon_{n}
\end{array}\right)
$$

- Number of groups is $n$
- $y_{i}, X_{i}, Z_{i}, u_{i}$ are the response, covariates and random effects for group $i$
- Can also allow multiple grouping structures (hierarchical or not)


## Fitting GLMM

- Fitting GLMM is more challenging than fitting LMM as the marginal distributions of the responses $y_{i s}$ typically do not have closed forms
- Typical methods
- Full Bayes approach MCMC
- EM algorithm (not easy)
- Approximate the marginal likelihood numerically
- Generalized estimating equations (GEE): fitting the marginal model

The marginal likelihood

$$
l\left(\beta, \Sigma_{u} ; y\right)=f\left(y ; \beta, \Sigma_{u}\right)=\int f(y \mid u, \beta) f\left(u ; \Sigma_{u}\right) d u
$$

## Laplace approximation

Laplace approximation: the marginal density of our data has the form

$$
\int e^{l(u)} d u \approx \int e^{l\left(u_{0}\right)+\frac{1}{2} l^{\prime \prime}\left(u_{0}\right)\left(u-u_{0}\right)^{2}} d u=e^{l\left(u_{0}\right)} \sqrt{\frac{2 \pi}{\left|l^{\prime \prime}\left(u_{0}\right)\right|}}
$$

Here $u_{0}$ is the global maximum of $l(u)$ satisfying $l^{\prime}\left(u_{0}\right)=0$. Laplace approximation can be used when $u$ is multi-dimensional.

- $l(u)=\log [f(y \mid u, \beta)]+\log \left[f\left(u, \Sigma_{u}\right)\right]$ which is the log density of the joint likelihood of $y$ and $u$
- For canonical link, $i(u)=\frac{z^{T}(y-E[y \mid u])}{a(\phi)}-\Sigma_{u}^{-1} u$


## Gauss-Hermite Quadrature

Gauss-Hermite Quadrature methods: approximate the integral by a weighted sum

$$
\int h(u) \exp \left(-u^{2}\right) d u \approx \sum_{k=1}^{q} c_{k} h\left(s_{k}\right)
$$

- the tabulated weights $\left\{c_{k}\right\}$ and quadrature points $\left\{s_{k}\right\}$ are the roots of Hermite polynomials.
- The approximation is more more accurate with larger $q$. For more details, read chapter 9.5.2.
- The approximated likelihood is maximized with optimization algorithms such as Newton's method


## Generalized estimating equations (GEE)

- A way to estimate the marginal model under dependence across observations
- For group $i$, the response is $y_{i}=\left(y_{i 1}, \cdots, y_{i n_{i}}\right)$
- Denote the marginal means as $\mu_{i}=E\left(y_{i}\right)$, marginal GLM:

$$
g\left(\mu_{i s}\right)=X_{i s}^{T} \beta
$$

- Elements in $y_{i}$ are correlated due to shared random effects, we just model a working covariance matrix (may not be true):

$$
\operatorname{var}\left(y_{i}\right)=V_{i}(\alpha)=v\left(\mu_{i}\right)
$$

- Responses across groups are independent


## Generalized estimating equations (GEE)

- Generalized estimating equation for $\beta$

$$
\sum_{i=1}^{n}\left(\partial \mu_{i} / \partial \boldsymbol{\beta}\right)^{\mathrm{T}} v\left(\mu_{i}\right)^{-1}\left(y_{i}-\mu_{i}\right)=\mathbf{0}
$$

- Compare with estimating equation for $\beta$ for independent responses

$$
\varphi_{1 j}(\beta, \phi)=\frac{\partial L}{\partial \beta_{j}}=\sum_{i} \frac{\left(y_{i}-\mu_{i}\right) x_{i j}}{a\left(\mu_{i}, \phi\right)} \frac{1}{g^{\prime}\left(\mu_{i}\right)}=0
$$

- We also need a generalized estimating equation for scale parameters $\alpha$
- We can use moment equations as before

$$
\sum_{i=1}^{n}\left(y_{i}-\mu_{i}\right)^{T} V_{i}(\alpha)^{-1}\left(y_{i}-\mu_{i}\right)=N-p
$$

- Typically, we assume the correlation matrix is shared across groups
- Can use Sandwich estimator to robustly estimate the variance of $\hat{\beta}$


## Example: modeling correlated survey responses

- Check Example9 R notebook

