Today

- Bayesian analysis of logistic regression
- Generalized linear mixed models
- CD on fixed and random effects
- HW 2 due February 28
- Case Studies SSC 2014 Toronto
- March/April: Semi-parametric regression (§10.7), generalized additive models, penalized regression methods (ridge regression, lasso); proportional hazards models (§10.8)

not in office
Feb 20

Bayesian logistic regression

- $r_j \sim \text{Binom}(m_j, p_j)$
- $\log \dfrac{p_j}{1-p_j} = \alpha + \beta x_j$
- $L(\alpha, \beta; y) \propto \exp\{\alpha \Sigma y_j + \beta \Sigma (x_j y_j) - \Sigma m_j \log(1 + e^{\alpha + \beta x_j})\}$

$\hat\alpha, \hat\beta$ a. var$(\hat\alpha, \hat\beta) \doteq -\dfrac{\partial^2 \log L}{(\partial\alpha\partial\beta)^{\prime}}\Big|_{\hat\alpha, \hat\beta}$ $\partial\alpha\partial\beta$

$\hat\beta \pm 2 \cdot \hat{s.e}$ or LRT

- $\pi(\alpha, \beta \mid y) \propto L(\alpha, \beta; y)\pi(\alpha, \beta)$
- flat prior $\pi(\alpha, \beta) \propto 1$ popular for regression parameters
  proper posterior?
- implemented in the library `LearnBayes` via `logisticpost` Albert, 2009 *Bayesian Computation with R*
- bioassay data

log(dose)	deaths	sample size
-0.86	0	5
-0.30	1	5
-0.05	3	5
0.73	5	5

Bayesian logistic regression

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- $\log \dfrac{p_j}{1-p_j} = \alpha + \beta x_j$
- $L(\alpha, \beta; y) \propto \underline{\exp\{\alpha \Sigma y_j + \beta \Sigma (x_j y_j) - \Sigma m_j \log(1 + e^{\alpha + \beta x_j})\}}$
- $\pi(\alpha, \beta \mid y) \propto L(\alpha, \beta; y)\underline{\pi(\alpha, \beta)} \Big/ \int L(\alpha, \beta; y)\pi(\alpha, \beta)\,d\alpha\, d\beta$

joint dist^n of (α, β), given y

- flat prior $\pi(\alpha, \beta) \propto 1$ popular for regression parameters
  proper posterior?
- implemented in the library `LearnBayes` via `logisticpost` Albert, 2009 *Bayesian Computation with R*

$\hat\alpha, \hat\beta$ are f-n of y ← exact dist^n derives from Bin for y

- bioassay data

log(dose)	deaths	sample size
-0.86	0	5
-0.30	1	5
-0.05	3	5
0.73	5	5

Bayesian logistic regression

- $r_j \sim \text{Binom}(m_j, p_j)$
- $\log \dfrac{p_j}{1-p_j} = \alpha + \beta x_j$
- $L(\alpha, \beta; y) \propto \exp\{\alpha \Sigma y_j + \beta \Sigma (x_j y_j) - \Sigma m_j \log(1 + e^{\alpha + \beta x_j})\}$
- $\pi(\alpha, \beta \mid y) \propto L(\alpha, \beta; y)\pi(\alpha, \beta)$
- flat prior $\pi(\alpha, \beta) \propto 1$ popular for regression parameters
  proper posterior? ← need to $\int d\alpha\, d\beta = 1$
- implemented in the library `LearnBayes` via `logisticpost` Albert, 2009 *Bayesian Computation with R*
- bioassay data

log(dose)	deaths	sample size
-0.86	0	5
-0.30	1	5
-0.05	3	5
0.73	5	5

Bayesian logistic regression

- $r_j \sim \text{Binom}(m_j, p_j)$
- $\log \dfrac{p_j}{1-p_j} = \alpha + \beta x_j$
- $L(\alpha, \beta; y) \propto \exp\{\alpha \Sigma y_j + \beta \Sigma(x_j y_j) - \Sigma m_j \log(1 + e^{\alpha + \beta x_j})\}$
- $\pi(\alpha, \beta \mid y) \propto L(\alpha, \beta; y)\pi(\alpha, \beta)$
- flat prior $\pi(\alpha, \beta) \propto 1$ popular for regression parameters
  proper posterior?
- implemented in the library `LearnBayes` via `logisticpost` Albert, 2009 *Bayesian Computation with R*
- bioassay data

log(dose)	deaths	sample size	
-0.86	0	5	data
-0.30	1	5	
-0.05	3	5	
0.73	5	5	
prior: -0.70	1.12	4.68	
0.6	2.10	2.84	

If $y \sim Bin(m, p)$

$\pi(p) \sim Beta(a, b)$

$\binom{m}{y} p^y (1-p)^{m-y} \cdot \sim \dfrac{p^{a-1}(1-p)^{b-1}}{B(a,b)}$ $0 < p < 1$

a, b to be spec'd

$\Rightarrow \pi(p \mid y) \sim Beta(y+a, m-y+b)$

in same class as prior

$p(x_L) \sim Be(a_1, b_1)$
$p(x_U) \sim Be(a_2, b_2)$
x_L, x_U chosen
$-.7$ $+.6$ $\approx$
adds 2 rows to data

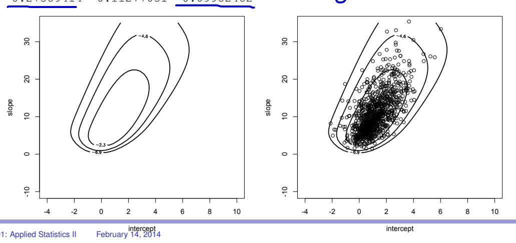
... Bayesian logistic regression

```
mycontour(logisticpost,c(-4,10,-10,35),bioassay)
## the limits were chosen using information in Gelman et al.,
## although they used 40 as the upper limit for beta, but I could not
> s <- simcontour(logisticpost, c(-4,10, -10, 35),m = 1000, data =bioassay)
> points(s) # just plotted 1000 points, otherwise plot is too black
> s <- simcontour(logisticpost, c(-4,10, -10, 35),m = 10000, data =bioassay)
# samples from posterior; more samples for getting quantiles
> quantile(s$x, c(0.025, 0.5, 0.975))
      2.5%        50%      97.5%
-0.6066507  1.2277272  3.7397231
> quantile(s$y, c(0.025, 0.5 0.975))
     2.5%       50%     97.5%
 3.463158 10.770726 24.980196
> quantile(-s$x/s$y,c(.025,.5,.975))
       2.5%         50%        97.5%
-0.27589414 -0.11277051  0.09982482
```

$\pi(-\frac{\alpha}{\beta} \mid y)$ $\log\frac{p}{1-p} = \alpha + \beta x$

$p < \frac{1}{2}$

log dose $\rightarrow x = -\frac{\alpha}{\beta}$



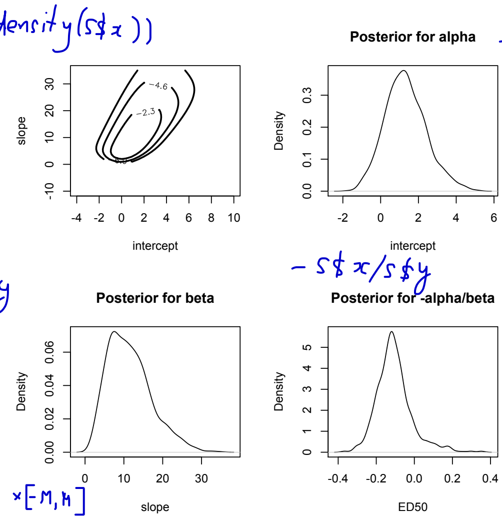
plot(density(s$x))

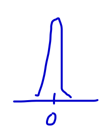
$\pi(\alpha, \beta)\, d\alpha\, d\beta = 1$

$\pi(-\frac{\alpha}{\beta})$ prior?

s$y

$-s\$x/s\$y$

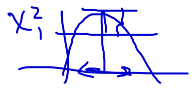




$[M, M] \times [-M, M]$

... Bayesian logistic regression

χ^2_1



GLM (usual)

		point estimate	lower 2.5% bound	upper 2.5% bound
α	Wald	0.8466 $\hat{\alpha}$	-1.1510	2.844
?	LRT		-0.8305	3.253
	Bayes		-0.5911	3.673
β	Wald	7.749 $\hat{\beta}$	-1.8020	17.30
	LRT		1.7060	18.01
	Bayes		3.4213	25.30
ED50	Wald	-0.1092 $-\hat{\alpha}/\hat{\beta}$	-0.2963	0.0778
	Bayes		-0.2783	0.1067

$\operatorname{var}\{f(x,y)\} \doteq \sigma_x^2 \cdot \left(\frac{\partial f}{\partial x}\right)^2\Big|_{\mu_x,\mu_y} + \sigma_y^2 \left(\frac{\partial f}{\partial y}\right)^2\Big|_{\mu_x,\mu_y} + 2\sigma_{xy} \frac{\partial f}{\partial x}\frac{\partial f}{\partial y}\Big|_{\mu_x\mu_y}$

0	5
1	5
3	5
5	5

```
> library(MCMCpack)
> posterior <- MCMClogit(y˜x,data = databern)
> summary(posterior)
```

$f(x) \doteq f(\mu) + (x-\mu)f'(\mu)$

$y = \begin{cases} 1 \\ 0 \end{cases}$

... Bayesian logistic regression

```
> library(MCMCpack)
> posterior <- MCMClogit(y˜x,data = databern)
> summary(posterior)

Iterations = 1001:11000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

1. Empirical mean and standard deviation for each variable,
   plus standard error of the mean:
              Mean     SD Naive SE Time-series SE
(Intercept)  1.316 1.086  0.01086         0.03623
x           11.715 5.672  0.05672         0.20781

2. Quantiles for each variable:
          2.5%     25%     50%     75%   97.5%
(Intercept) -0.63 0.5706  1.235  1.984  3.623
x            3.42 7.4827 10.731 15.003 24.931
```


... Bayesian logistic regression

$p \sim e^{\alpha+\beta x}/(1+e^{\alpha+\beta x})$ $\log\left(\frac{p}{1-p}\right) = \alpha + \beta x$

		point estimate	lower 2.5% bound	upper 2.5% bound
α	Wald	0.8466	-1.1510	2.844
	LRT		-0.8305	3.253
	Bayes		-0.5911	3.673
			-0.6300	3.623
β	Wald	7.749	-1.8020	17.30
	LRT		1.7060	18.01
	Bayes		3.4213	25.30
			3.4200	24.93
ED50	Wald	-0.1092	-0.2963	0.0778
	Bayes		-0.2783	0.1067
			-0.2749	0.1049

```
> library(MCMCpack)
> posterior <- MCMClogit(y˜x,data = databern)
> summary(posterior)
```


Posterior mode

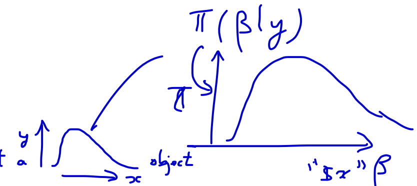
```
s # samples from the posterior
                  [,1]      [,2]
   [1,]  0.078564218  4.590313
   [2,] -0.130540858  6.144828
   [3,]  1.113368385 14.986545
   [4,] -0.567003218  6.761264
   [5,]  0.551048901  5.926414
   [6,]  1.563279919 14.031613
   [7,]  0.294370457  3.165679
   [8,]  1.869013672 14.637177
   [9,]  0.247018100 11.806818
  [10,]  2.018192523 16.877825
  [11,]  1.751898117 11.932195
  [12,]  3.013420092 20.085116

> post = density(s$y)
> which(post$y==max(post$y))
[1] 143
> post$x[143]
[1] 9.209531
> post2 = density(s$y, bw=1.5)
> which(post2$y == max(post2$y))
[1] 150
> post2$x[150]
[1] 8.867711
```

get a

mode of post for β

$\pi(\beta|y)$



Dependence through random effects

- Example: longitudinal data
- $Y_j = (Y_{j1}, \dots, Y_{jn_j})$ vector of observations on jth individual
- recall random effects model (normal theory):

known

$$Y_j = X_j\beta + Z_j b_j + \epsilon_j; \quad b_j \sim N(0, \sigma^2\Omega_b), \epsilon_j \sim N(0, \sigma^2\Omega_j)$$

'latent'

- marginal distribution:

$$Y_j \sim N(X_j\beta, \sigma^2\Upsilon_j^{-1}) = N(X_j\beta, \sigma^2(\underline{\Omega_j + Z_j\Omega_b Z_j^{\mathrm{T}}}))$$

Υ_j^{-1}

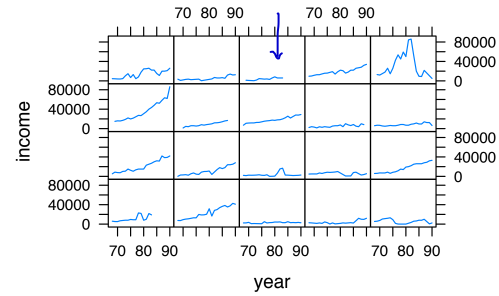
ind't

- sample of n ~~i.i.d.~~ such vectors leads to

$$Y \sim N(X\beta, \sigma^2\Upsilon^{-1}),$$

- $\Omega = \mathrm{diag}(\Omega_1, \dots, \Omega_m), \quad \tilde{\Omega}_b = \mathrm{diag}(\Omega_b, \dots, \Omega_b),$
- $Z = \mathrm{diag}(Z_1, \dots, Z_m), \quad \Upsilon^{-1} = \Omega + Z\tilde{\Omega}_b Z^{\mathrm{T}}$

Example: Panel Study of Income Dynamics Faraway, §9.1



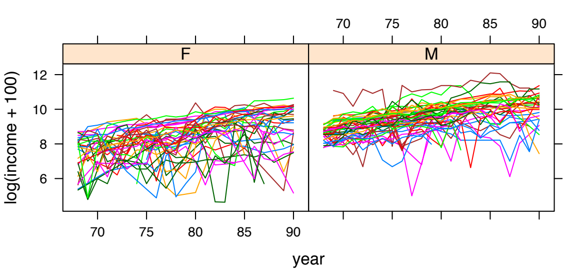
yr $ subj

$ vs yr.

$j = 1, \dots, 20$

```
library(lattice)
xyplot(income ~ year | person, data = psid,
type="l", subset = (person < 21), strip = F)
```


Example: Panel Study of Income Dynamics Faraway, §9.1




```
xyplot(log(income+100) ~ year | sex, data = psid,
type="l", groups=person)
```


... PSID

```
> data(psid)
> head(psid)
  age educ sex income year person
1  31   12   M   6000   68      1
2  31   12   M   5300   69      1
3  31   12   M   5200   70      1
4  31   12   M   6900   71      1
5  31   12   M   7500   72      1
6  31   12   M   8000   73      1
> dim(psid)
[1] 1661    6
> library(lme4)
> psid$cyear = psid$year - 78
> mmod = lmer(log(income) ~ cyear*sex + age + educ +
+ (cyear | person), data=psid)
```

lmer in this library

$$\begin{aligned}\log(\text{income})_{ij} &= \mu + \alpha\text{year}_i + \beta\text{sex}_j + (\alpha\beta)\text{year}_i \times \text{sex}_j \\ &+ \beta_2\text{educ}_j + \beta_3\text{age}_j + b_{0j} + b_{1j}\text{year}_i + \epsilon_{ij}, \\ &\epsilon_{ij} \sim N(0, \sigma^2), \quad b_j \sim N_2(0, \sigma^2\Omega_b)\end{aligned}$$

i year

j subject

... PSID

```
> mmod = lmer(log(income) ~ cyear*sex + age + educ +
+ (cyear | person), data=psid)
```

$$\begin{aligned}\log(\text{income})_{ij} &= \mu + \alpha\text{year}_i + \beta\text{sex}_j + (\alpha\beta)\text{year}_i \times \text{sex}_j \\ &\quad + \beta_2\text{educ}_j + \beta_3\text{age}_j + b_{0j} + b_{1j}\text{year}_i + \epsilon_{ij}, \\ &\quad \epsilon_{ij} \sim N(0, \sigma^2), \quad b_j \sim N_2(0, \sigma^2\Omega_b)\end{aligned}$$

- j indexes subjects, i indexes year
- variation in intercept between subjects b_{0j}; in increase per year between subjects b_{1j}
- year-to-year variation within subjects ϵ_{ij}

... PSID

$$\begin{aligned}\log(\text{income})_{ij} &= \mu + \alpha\text{year}_i + \beta\text{sex}_j + (\alpha\beta)\text{year}_i \times \text{sex}_j \\ &\quad + \beta_2\text{educ}_j + \beta_3\text{age}_j + b_{0j} + b_{1j}\text{year}_i + \epsilon_{ij}, \\ &\quad \underbrace{\epsilon_{ij} \sim N(0, \sigma^2)}_{\text{within}}, \quad \underbrace{b_j \sim N_2(0, \sigma^2\Omega_b)}_{\text{between}}\end{aligned}$$

```
> summary(mmod)
Linear mixed model fit by REML ['lmerMod']
Formula: log(income) ~ cyear * sex + age + educ + (cyear | person)
   Data: psid

REML criterion at convergence: 3819.776

Random effects:
 Groups   Name        Variance Std.Dev. Corr
 person   (Intercept) 0.2817   0.53071
          cyear       0.0024   0.04899  0.19
 Residual             0.4673   0.68357
Number of obs: 1661, groups: person, 85
Fixed effects:
            Estimate Std. Error t value
(Intercept)  6.67420    0.54332  12.284
cyear        0.08531    0.00900   9.480
sexM         1.15031    0.12129   9.484
age          0.01093    0.01352   0.808
educ         0.10421    0.02144   4.861
cyear:sexM  -0.02631    0.01224  -2.150
```

$\text{var}(\hat\beta_3) = ?$

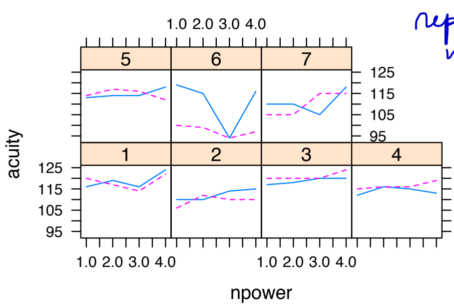
$\text{var}\,\varepsilon_{ij}$

$\Omega_b = \begin{bmatrix}\sigma^2_{b_0} & \sigma_{b_0b_1} \\ & \sigma^2_{b_1}\end{bmatrix} = \begin{bmatrix}.2817 & ? \\ & .0024\end{bmatrix}$

Example: Acuity of Vision

Faraway, §9.2

repeated measures




```
> xyplot(acuity ~ npower | subject, data=vision,
+ type="l", groups=eye, lty=1:2, layout = c(4,2))
```


... vision

```
> head(vision)
  acuity power   eye subject npower
1    116   6/6  left       1      1
2    119  6/18  left       1      2
3    116  6/36  left       1      3
4    124  6/60  left       1      4
5    120   6/6 right       1      1
6    117  6/18 right       1      2
> eyemod <- lmer(acuity ~ power + (1 | subject) +
+   (1 | subject:eye), data = vision)
```

s_i (over `(1 | subject)`), e_{ik} (under `(1 | subject:eye)`)

$$y_{ijk} = \mu + p_j + s_i + e_{ik} + \epsilon_{ijk}$$

$$s_i \sim N(0, \sigma_s^2), \quad e_{ik} \sim N(0, \sigma_e^2), \quad \epsilon_{ijk} \sim N(0, \sigma^2)$$

k eye 1, 2
i subj
j tst level (power)

... vision

```
> summary(eyemod)
Linear mixed model fit by REML ['lmerMod']
Formula: acuity ~ power + (1 | subject) + (1 | subject:eye)
   Data: vision

REML criterion at convergence: 328.7098

Random effects:
 Groups      Name        Variance Std.Dev.
 subject:eye (Intercept) 10.27    3.205
 subject     (Intercept) 21.53    4.640
 Residual                16.60    4.075
Number of obs: 56, groups: subject:eye, 14; subject, 7

Fixed effects:
            Estimate Std. Error t value
(Intercept) 112.6429     2.2349   50.40
power6/18     0.7857     1.5400    0.51
power6/36    -1.0000     1.5400   -0.65
power6/60     3.2857     1.5400    2.13
```


Generalized linear mixed models

$\text{logit}(p_{ij}) = \alpha + \beta x_i + b_{0i}$ — random effect for ith subj.

- $$f(y_j \mid \theta_j, \phi) = \exp\{\frac{y_j\theta_j - b(\theta_j)}{\phi a_j} + c(y_j; \phi a_j)\}$$
- $$b'(\theta_j) = \mu_j$$
- random effects
$$g(\mu_j) = x_j^{\mathrm{T}}\beta + z_j^{\mathrm{T}}b, \quad b \sim N(0, \Omega_b)$$
- likelihood
$$L(\beta, \phi; y) = \prod_{j=1}^{n} \int f(y_j \mid \beta, b, \phi) f(b; \Omega_b) db$$

Generalized linear mixed models

- $$f(y_j \mid \theta_j, \phi) = \exp\{\frac{y_j\theta_j - b(\theta_j)}{\phi a_j} + c(y_j; \phi a_j)\}$$
- $$b'(\theta_j) = \mu_j$$
- random effects
$$g(\mu_j) = x_j^{\mathrm{T}}\beta + z_j^{\mathrm{T}}b, \quad b \sim N(0, \Omega_b)$$
- likelihood
$$L(\beta, \phi; y) = \prod_{j=1}^{n} \int f(y_j \mid \beta, b, \phi) f(b; \Omega_b) db$$

... generalized linear mixed models

- likelihood
$$L(\beta, \phi; y) = \prod_{j=1}^{n} \int f(y_j \mid \beta, b, \phi) f(b; \Omega_b) db$$
- doesn't simplify unless $f(y_j \mid b)$ is normal
- solutions proposed include
  - numerical integration, e.g. by quadrature
  - integration by MCMC
  - Laplace approximation to the integral – penalized quasi-likelihood
- reference: `MASS` library and book (§10.4):
  `glmmNQ`, `GLMMGibbs`, `glmmPQL`, all in `library(MASS)`
  `glmer` in `library(lme4)`

Example: Balance experiment

Faraway, 10.1

- effects of surface and vision on balance; 2 levels of surface; 3 levels of vision
- surface: normal or foam
- vision: normal, eyes closed, domed
- 20 males and 20 females tested for balance, twice at each of 6 combinations of treatments
- auxiliary variables age, height, weight

Steele 1998, OzDASL

- linear predictor: `Sex + Age + Weight + Height + Surface + Vision + Subject(?)`
- response measured on a 4 point scale; converted by Faraway to binary (stable/not stable)
- analysed using linear models at OzDASL

Example: Balance experiment

Faraway, 10.1

- effects of surface and vision on balance; 2 levels of surface; 3 levels of vision
- surface: normal or foam
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Steele 1998, OzDASL

- linear predictor: `Sex + Age + Weight + Height + Surface + Vision + Subject(?)`
- response measured on a 4 point scale; converted by Faraway to binary (stable/not stable)
- analysed using linear models at OzDASL

STA 2201: Applied Statistics II   February 14, 2014   21/30

... balance

1, 0

```
> balance <- glmer(stable ~ Sex + Age + Height + Weight + Surface + Vision +
+ (1|Subject), family = binomial, data = ctsib)

# Subject effect is random

> summary(balance)
Generalized linear mixed model fit by maximum likelihood ['glmerMod']

 ...

Random effects:
 Groups  Name        Variance Std.Dev.
 Subject (Intercept) 8.197    2.863
Number of obs: 480, groups: Subject, 40

Fixed effects:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)  9.920750  13.358013   0.743    0.458
Sexmale      2.825305   1.762383   1.603    0.109
Age         -0.003644   0.080928  -0.045    0.964
Height      -0.151012   0.092174  -1.638    0.101
Weight       0.058927   0.061958   0.951    0.342
Surfacenorm  7.524423   0.888827   8.466  < 2e-16 ***
Visiondome   0.683931   0.530654   1.289    0.197
Visionopen   6.321098   0.839469   7.530 5.08e-14 ***
---
```

b_{0i} for subject i $\sim (0, \sigma_b^2)$

$\tilde{\sigma}_b^2 = 8.197$

		foam			norm		
	st.	O	C	D	O	C	D
F	0	35	40	40	11	37	30
F	1	5	0	0	29	3	10
M	0	35	40	40	4	26	28
M	1	5	0	0	36	14	12

... balance

```
> library(MASS)

> balance2 <- glmmPQL(stable ~ Sex + Age + Height + Weight + Surface + Vision,
+ random = ~1 | Subject, family = binomial, data = ctsib)
> summary(balance2)

Random effects:
 Formula: ~1 | Subject
        (Intercept)  Residual
StdDev:    3.060712 0.5906232

Variance function:
 Structure: fixed weights
 Formula: ~invwt

Fixed effects: stable ~ Sex + Age + Height + Weight + Surface + Vision
                Value Std.Error  DF   t-value p-value
(Intercept) 15.571494 13.498304 437  1.153589  0.2493
Sexmale      3.355340  1.752614  35  1.914478  0.0638
Age         -0.006638  0.081959  35 -0.080992  0.9359
Height      -0.190819  0.092023  35 -2.073601  0.0455
Weight       0.069467  0.062857  35  1.105155  0.2766
Surfacenorm  7.724078  0.573578 437 13.466492  0.0000
Visiondome   0.726464  0.325933 437  2.228873  0.0263
Visionopen   6.485257  0.543980 437 11.921876  0.0000
```

glmer + (1|Subject)

+ random ....

... balance

```
> balance4 <- glmer(stable ~ Sex + Age + Height + Weight + Surface + Vision +
+ (1|Subject), family = binomial, data = ctsib, nAGQ = 9)
> summary(balance4)

Random effects:
 Groups  Name        Variance Std.Dev.
 Subject (Intercept) 7.8      2.793
Number of obs: 480, groups: Subject, 40

Fixed effects:
             Estimate Std. Error z value Pr(>|z|)
(Intercept) 13.551847  13.067369   1.037   0.2997
Sexmale      3.109307   1.724797   1.803   0.0714 .
Age         -0.001804   0.079161  -0.023   0.9818
Height      -0.175061   0.090239  -1.940   0.0524 .
Weight       0.065742   0.060606   1.085   0.2780
Surfacenorm  7.428046   0.872416   8.514  < 2e-16 ***
Visiondome   0.682509   0.527836   1.293   0.1960
Visionopen   6.210825   0.822012   7.556 4.17e-14 ***
```

Gauss Quad

$-.001 \} \text{age}$

$-.003$

$-.006$

Non-specific effects

C&D §7.2

- example: a clinical trial involves several or many centres
- an agricultural field trial repeated at a number of different farms, and over a number of difference growing seasons
- a sociological study reposted in broadly similar form in a number of countries
- laboratory study uses different sets of analytical apparatus, imperfectly calibrated
- such factors are non-specific
- how do we account for them
  - on an appropriate scale, a parameter represents a shift in outcome
  - more complicated: the primary contrasts of concern vary across centres
  - i.e. treatment-center interaction

(no X^n)

$X^{\underline{n}}$ (

... non-specific effects

- suppose no treatment-center interaction
- example:

$$\text{logit}\{\Pr(Y_{ci} = 1)\} = \alpha_c + x_{ci}^T \beta$$

- should α_c be ?fixed? or ?random?
- effective use of a random-effects representation will require estimation of the variance component corresponding to the centre effects
- even under the most favourable conditions the precision achieved in that estimate will be at best that from estimating a single variance from a sample of a size equal to the number of centres
- very fragile unless there are at least, say, 10 centres and preferably considerably more

... non-specific effects

- if centres are chosen by an effectively random procedure from a large population of candidates, ... the random-effects representation has an attractive tangible interpretation. This would not apply, for example, to the countries of the EU in a social survey
- some general considerations in linear mixed models:
  - in balanced factorial designs, the analysis of treatment means is unchanged
  - in other cases, estimated effects will typically be 'shrunk', and precision improved
  - representation of the nonspecific effects as random effects involves independence assumptions which certainly need consideration and may need some empirical check

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√ shrinkage

§9.6(?)

$\boxed{\bar{y}_{i\cdot} - \bar{y}_{i\cdot}}$

- some general considerations in linear mixed models:
  - in balanced factorial designs, the analysis of treatment means is unchanged
  - in other cases, estimated effects will typically be 'shrunk', and precision improved   see SM Ch 9
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- in particular, if a more elaborate method gives an apparent improvement in precision, what are the assumptions on which that improvement is based, and are they reasonable?

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... non-specific effects

- if there is an interaction between an explanatory variable [e.g. treatment] and a nonspecific variable
- i.e. the effects of the explanatory variable change with different levels of the nonspecific factor
- the first step should be to explain this interaction, for example by transforming the scale on which the response variable is measure or by introducing a new explanatory variable
  - example: two medical treatments compared at a number of centres show different treatment effects, as measured by an ratio of event rates
  - possible explanation: the difference of the event rates might be stable across centres
  - possible explanation: the ratio depends on some characteristic of the patient population, e.g. socio-economic status
- an important special application of random-effect models for interactions is in connection with overviews, that is, assembling of information from different studies of