Linear Regression Models
P8111

Lecture 20

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Today’s Lecture

- Longitudinal data analysis

Focus on covariance

SLR, MLR, Non-line

Interactions

- We've extensively used OLS for the model

$$\boxed{\boldsymbol{y} = \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{\epsilon}}$$

  where $E(\boldsymbol{\epsilon}) = 0$ and $Var(\boldsymbol{\epsilon}) = \sigma^2 I$
- We are now more interested in the case of $Var(\boldsymbol{\epsilon}) = \sigma^2 V$
- WLS and GLS were useful in this setting, but required a known V matrix

W diag; $\frac{1}{w_i}$ Σ

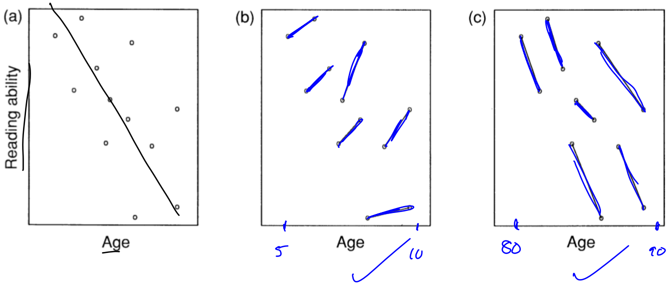
Longitudinal data

- Data is gathered at multiple time points for each study participant
- Repeated observations / responses
- Longitudinal data ~~regularly~~ always violates the "independent errors" assumption of OLS
- LDA allows the examination of changes over time (aging effects) and adjustment for individual differences (subject effects)

Some hypothetical data

OLS work?

- Ind hard to assess visually



Notation

- We observe data $\overset{\text{subj visit}}{y_{ij}}, \underline{x_{ij}}$ for subjects $\underline{i = 1, \ldots I}$ at visits $\underline{j = 1, \ldots, J_i}$ (J_i different over i ⇒ unbalanced) ($J_i = J$ ⇒ balanced)
- Vectors y_i and matrices X_i are subject-specific outcomes and design matrices
- Total number of visits is $\underline{n = \sum_{i=1}^{I} J_i}$
- For subjects i, let

$$\underline{y_i} = \underline{X_i}\beta + \underline{\epsilon_i}$$

where $\text{Var}(\epsilon_i) = \underline{\sigma^2 V_i}$

$$y_i = \begin{bmatrix} y_{i1} \\ \vdots \\ y_{iJ_i} \end{bmatrix} \qquad X_i = \begin{bmatrix} x_{i1} \\ \\ x_{iJ_i} \end{bmatrix}$$

Notation

- Overall, we pose the model

$$y = X\beta + \epsilon$$

$$\begin{bmatrix} y_{11} \\ \vdots \\ y_{ij_i} \\ \vdots \\ y_{Ij_i} \end{bmatrix} \quad \begin{bmatrix} X_1 \\ X_2 \\ \vdots \\ X_I \end{bmatrix} \quad \begin{bmatrix} \epsilon_1 \\ \vdots \\ \epsilon_I \end{bmatrix}$$

where $\text{Var}(\epsilon) = \sigma^2 V$ and

$$V = \begin{bmatrix} V_1 & 0 & \dots & 0 \\ 0 & V_2 & \dots & 0 \\ \vdots & \vdots & \ddots & \\ 0 & 0 & & V_I \end{bmatrix}$$

Covariates

The covariates $\boldsymbol{x}_{ij} = x_{ij1} \dots x_{ijp}$ can be

- Fixed at the subject level – for instance, sex, race, fixed treatment effects
- Time varying – age, BMI, smoking status, treatment in a cross-over design

Motivation

Why bother with LDA?

- Correct inference
- More efficient estimation of shared effects
- Estimation of subject-level effects / correlation
- The ability to "borrow strength" – use both subject- and population-level information

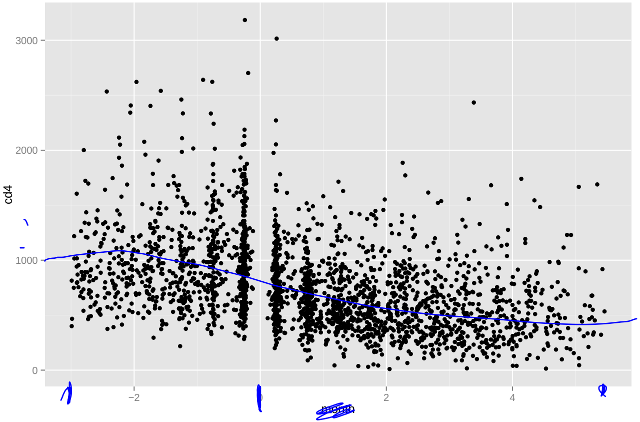
Example dataset

An example dataset comes from the Multicenter AIDS Cohort Study

- 366 HIV+ individuals
- Observation of CD4 cell count (a measure of disease progression)
- Between 1 and 11 observations per subject (1888 total observations)

unbalanced

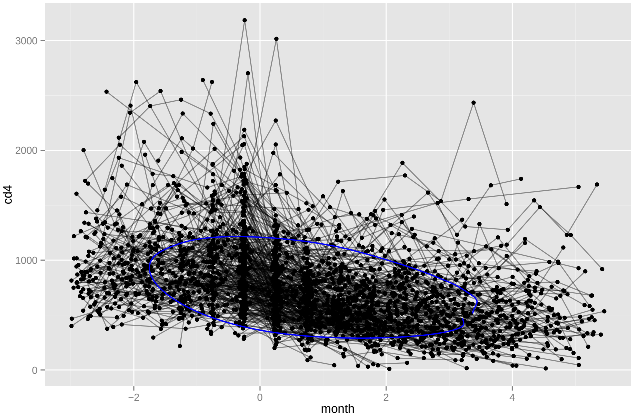
Example dataset



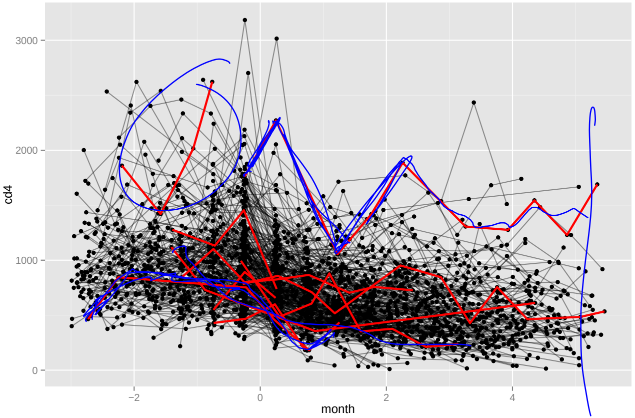
ye?

Example dataset

"Spaghetti" plot



Example dataset



Visualizing covariances

Suppose the data consists of three subjects with four data points each.

$$\mathrm{Var}(\epsilon) = \sigma^2 \begin{bmatrix} V_1 & 0 & 0 \\ 0 & V_2 & 0 \\ 0 & 0 & V_3 \end{bmatrix}$$

- In the model

$$\boldsymbol{y}_i = \boldsymbol{X}_i \boldsymbol{\beta} + \boldsymbol{\epsilon}_i$$

where $\mathrm{Var}(\boldsymbol{\epsilon}_i) = \sigma^2 V_i$, what are some forms for V_i?

Uniform / exchangeable

$$\begin{bmatrix} 1 & \rho & \rho & \rho \\ \rho & 1 & \rho & \\ \rho & \rho & 1 & \rho \\ \rho & \rho & \rho & 1 \end{bmatrix}$$

$V(\rho)$

exponential

$$\begin{bmatrix} 1 & \rho^1 & \rho^2 & \rho^3 \\ & 1 & \rho^1 & \rho^2 \\ & & 1 & \rho^1 \\ & & & 1 \end{bmatrix}$$

$V(\rho, \ldots)$

unstructured

$$\begin{bmatrix} 1 & \rho_1 & \rho_4 & \rho_6 \\ & 1 & \rho_2 & \rho_5 \\ & & 1 & \rho_3 \\ & & & 1 \end{bmatrix}$$

$U(\rho_1 \ldots \rho_6)$

Approaches to LDA

mixed models

We'll consider two main approaches to LDA

- Random effects models, which introduce random subject effects (i.e. effects coming from a distribution, rather than from a "true" parametric model)
- Marginal models, which focus on estimating the main effects and variance matrices but don't introduce subject effects

First problem: uniform correlation

$var(\epsilon_i) = \sigma^2 V_i$

Start with the model where

$$V_i = \begin{bmatrix} 1 & \rho & \dots & \rho \\ \rho & 1 & \dots & \rho \\ \vdots & \vdots & \ddots & \\ \rho & \rho & & 1 \end{bmatrix}$$

This implies

- $var(y_{ij}) = \sigma^2$
- $cov(y_{ij}, y_{ij'}) = \sigma^2 \rho$
- $cor(y_{ij}, y_{ij'}) = \rho$

Marginal model

If we assume a uniform correlation structure, the marginal model is

$$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{\epsilon}$$

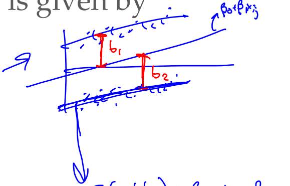
where

- $\text{Var}(\boldsymbol{\epsilon}) = \sigma^2 V$,
- $$V_i = \begin{bmatrix} 1 & \rho & \dots & \rho \\ \rho & 1 & \dots & \rho \\ \vdots & \vdots & \ddots & \\ \rho & \rho & & 1 \end{bmatrix}$$

Random effects model

A random intercept model with one covariate is given by

$$y_{ij} = \beta_0 + \boxed{b_i} + \beta_1 x_{ij} + \epsilon_{ij}$$



$E(y \mid b_i) = \beta_0 + b_i + \beta_1 x_{ij}$

$var(y_{ij} \mid b_i) = var(\epsilon_{ij}) = \sigma^2 I$

where

- $b_i \sim \mathrm{N}\left[0, \tau^2\right]$
- $\epsilon_{ij} \sim \mathrm{N}\left[0, \nu^2\right]$

Under this model

- $var(y_{ij}) =$ $var(\cancel{\beta_0} + b_i + \cancel{\beta_1 x_{ij}} + \epsilon_{ij}) = \tau^2 + \nu^2$
- $cov(y_{ij}, y_{ij'}) =$ $cov(b_i + \epsilon_{ij}, b_i + \epsilon_{ij'}) = \tau^2$
- $cor(y_{ij}, y_{ij'}) = \rho =$ $\dfrac{\tau^2}{\tau^2 + \nu^2}$

Relationship between marginal and RI models

The random intercept model implies a correlation structure equivalent to the mixed model, with

- $\sigma^2 = \tau^2 + \nu^2$
- $\rho = \frac{\tau^2}{\tau^2+\nu^2}$

$$\sigma^2 \begin{bmatrix} 1 & \rho \\ \rho & 1 \end{bmatrix} \qquad \begin{bmatrix} \tau^2+\nu^2 & \\ \frac{\tau^2}{\tau^2+\nu^2} & \ddots \end{bmatrix}$$

(This works with continuous responses, but be careful with generalized outcomes)

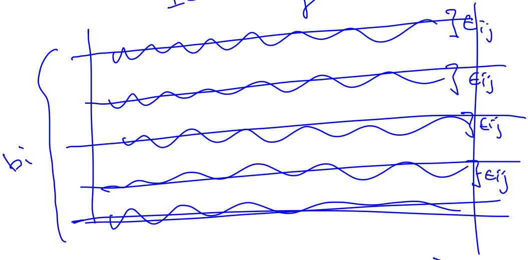
Partitioning variance

- Whether we look at random effects or marginal modeling, we have to partition total variability into subject-level variance and population-level variance
- In a random effects framework, we estimate between and within subject variance components
- In a marginal model framework, we estimate a within subject variance and a covariance matrix

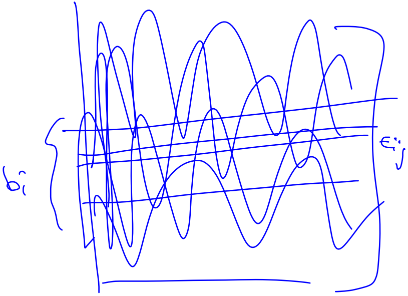
Interpretation of ICC

- The quantity $\boxed{\rho = \frac{\overset{a}{\tau^2}}{\tau^2+\nu^2}}$ is called the intraclass correlation
- It tells how strongly observations within a subject are correlated relative to the overall population variance
- Alternatively, the ICC tells what proportion of variability is within-subject variability

ICC large



ICC small

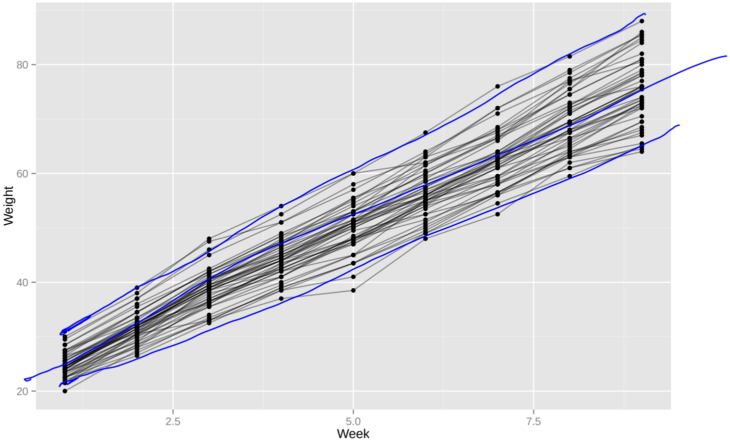


$Var(b_i)$ big v $Var(\epsilon_{ij})$

Pig weight data

- Weight on 48 pigs
- Nine measurements per pig

Pig weight data



Pig weight data

- Apparent linear relationship
- High variance across pigs compared to variance within pigs
- Each pig's "baseline" is very important for future observations

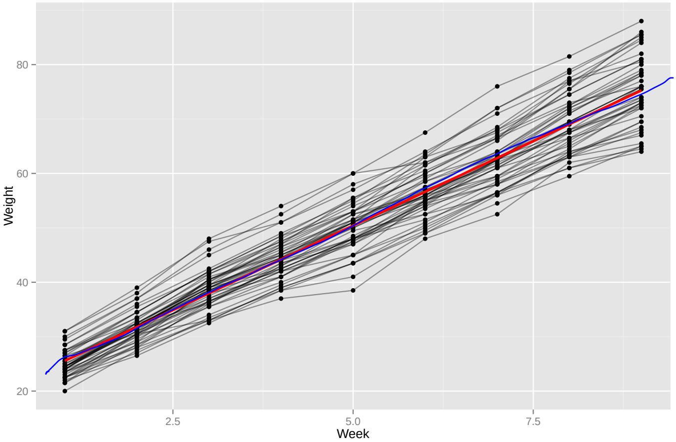
Pig weight data analysis

Using ordinary least squares, we find

```
Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept) 19.35561    0.46054   42.03   <2e-16 ***
num.weeks    6.20990    0.08184   75.88   <2e-16 ***

Residual standard error: 4.392 on 430 degrees of freedom
```

Pig weight data analysis



Pig weight data analysis

Using a random intercept model, we find

```
Random effects:
 Groups   Name        Variance Std.Dev.
 id.num   (Intercept) 15.1418  3.8913
 Residual              4.3947  2.0964
Number of obs: 432, groups: id.num, 48

Fixed effects:
            Estimate Std. Error t value
(Intercept) 19.35561    0.60311   32.09
num.weeks    6.20990    0.03906  158.97
```

b_i

ϵ_{ij}

τ^2 ν^2

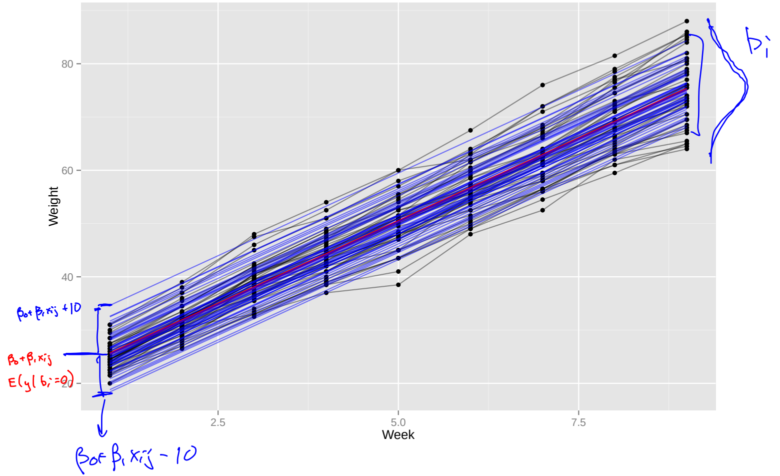
$$\frac{\tau^2}{\tau^2+\nu^2} \approx .75$$

balanced

on the same grid

b_i

Pig weight data analysis



Next time

- Why do we use random effects rather than creating subject-level indicator variables and estimating fixed effects?
- Next time we'll talk about estimation of random effect and marginal models

Today's big ideas

- Longitudinal data analysis
- Uniform correlation models