In this Chapter: Model selection as a result of choices for Σ

$\Sigma \uparrow Var(y)$

23. Repeated Measures

Repeated Measures Studies

- Measure the experimental unit multiple times
- Measurements often taken over time pay attention to time points being equally spaced vs. not
- Observations over time typically correlated
- Longitudinal versus crossover study designs
- Repeated measures analysis accounts for correlation

Repeated Measures Example

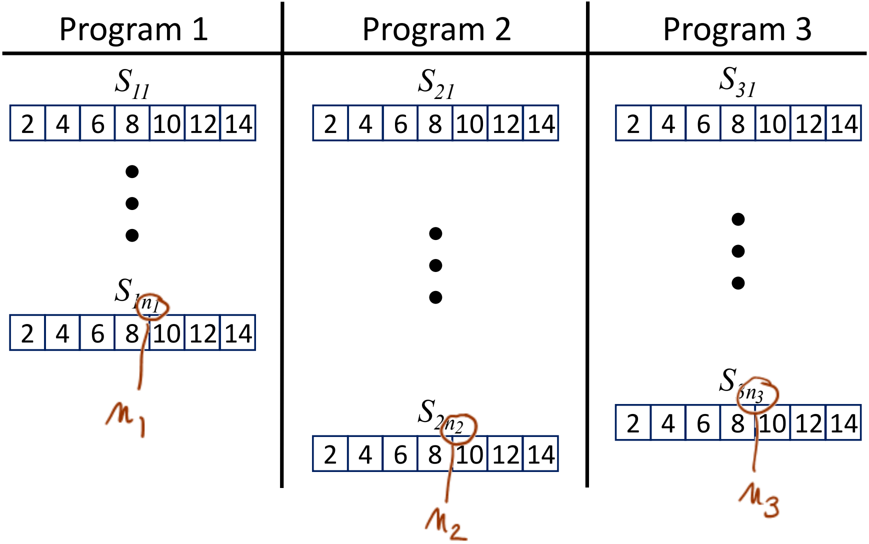
In an exercise therapy study, subjects were assigned to one of three weightlifting programs

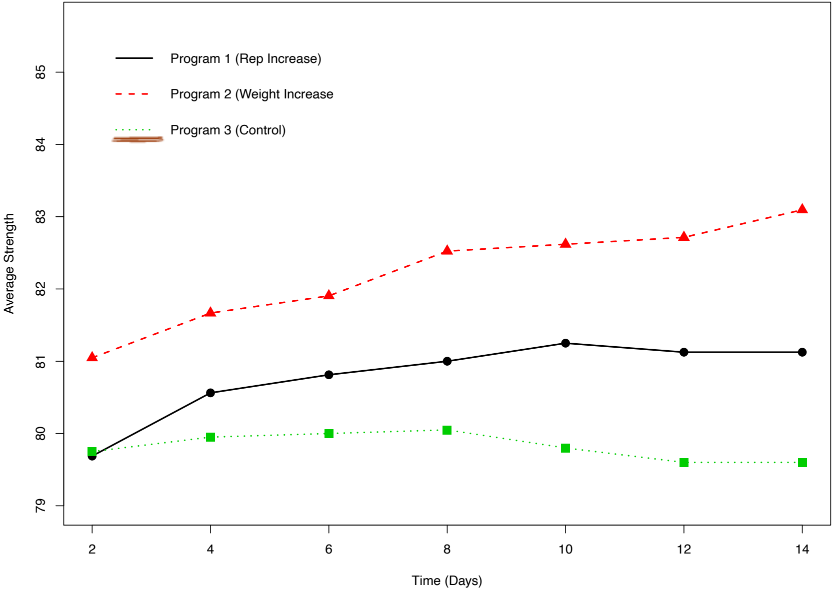
i=1: The number of repetitions of weightlifting was increased as subjects became stronger.

i=2: The amount of weight was increased as subjects became stronger.

i=3: Subjects did not participate in weightlifting.

- Measurements of strength (y) were taken on days 2, 4, 6, 8, 10, 12, and 14 for each subject.
- Source: Littel, Freund, and Spector (1991), SAS System for Linear Models.
- R code: RepeatedMeasures.R
- SAS code: RepeatedMeasures.sas


Program 1
Program 2
Program 3
S_{11}
S_{21}
S_{31}
2 4 6 8 10 12 14
S_{1n_1}
S_{2n_2}
S_{3n_3}
n_1
n_2
n_3


Program 1 (Rep Increase)
Program 2 (Weight Increase
Program 3 (Control)
Average Strength
79
80
81
82
83
84
85
2
4
6
8
10
12
14
Time (Days)

A Linear Mixed-Effects Model

Let y_{ijk} be the strength measurement for program i, subject j, and time point k. Suppose

random effects

$$y_{ijk} = \underline{\mu} + \underline{\alpha_i} + s_{ij} + \underline{\tau_k} + \underline{\gamma_{ik}} + e_{ijk},$$

fixed effects

where $\mu, \alpha_1, \alpha_2, \alpha_3, \tau_1, \ldots, \tau_7$, and $\gamma_{11}, \ldots, \gamma_{37}$ are unknown real-valued parameters, and

$$\boxed{s_{ij} \stackrel{iid}{\sim} \mathcal{N}(0, \sigma_s^2) \text{ independent of } e_{ijk} \stackrel{iid}{\sim} \mathcal{N}(0, \sigma_e^2).}$$

Note that this model is the same model we would use for a split-plot experiment in which the whole-plot part of the experiment has a completely randomized design.

Subjects are the whole-plot experimental units, and measurement occasions within subject are treated like split-plot experimental units.

ANOVA Table

Source		DF
Program	trt fixed	$3-1$
Subject(Program)	ran	$\underbrace{(16-1)}_{n_1}+\underbrace{(21-1)}_{n_2}+\underbrace{(20-1)}_{n_3}$
Time	fixed	$7-1$
Program×Time	fixed	$(3-1)(7-1)$
Time×Subject(Program)	ran	$(7-1)(57-3)$
C. Total		$57\times 7-1$

The measurement occasions are not really split-plot experimental units because levels of the factor time (2, 4, . . ., 14) were not randomly assigned to measurement occasions.

Nonetheless, this split-plot model might be reasonable for some experiments where experimental units are measured repeatedly over time.

Average strength after $2k$ days on the ith program is

$$
\begin{aligned}
\mathrm{E}(\mathrm{y_{ijk}}) &= \mathrm{E}(\mu + \alpha_\mathrm{i} + \mathrm{s_{ij}} + \tau_\mathrm{k} + \gamma_\mathrm{ik} + \mathrm{e_{ijk}}) \\
&= \mu + \alpha_i + \underbrace{\mathrm{E}(\mathrm{s_{ij}})}_{=0} + \tau_\mathrm{k} + \gamma_\mathrm{ik} + \underbrace{\mathrm{E}(\mathrm{e_{ijk}})}_{=0} \\
&= \mu + \alpha_i + \tau_k + \gamma_{ik}
\end{aligned}
$$

for $i = 1, 2, 3$ and $k = 1, 2, \ldots, 7$. = Mean structure

The variance of any single observation is

$$
\begin{aligned}
\boxed{\mathrm{Var}(y_{ijk})} &= \mathrm{Var}(\cancel{\mu} + \cancel{\alpha_i} + s_{ij} + \cancel{\tau_k} + \cancel{\gamma_{ik}} + e_{ijk}) \\
&= \mathrm{Var}(s_{ij} + e_{ijk}) \\
&\overset{\text{indep.}}{=} \mathrm{Var}(s_{ij}) + \mathrm{Var}(e_{ijk}) \\
&= \underline{\sigma_s^2} + \underline{\sigma_e^2}.
\end{aligned}
$$

The covariance between any two different observations from the same subject is

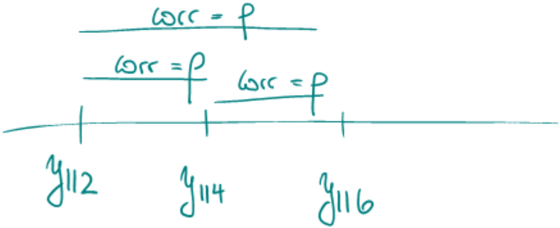
$$
\begin{aligned}
\mathrm{Cov}(y_{ijk}, y_{ij\ell}) &= \mathrm{Cov}(\mu + \alpha_i + s_{ij} + \tau_k + \gamma_{ik} + e_{ijk}, \\
&\qquad \mu + \alpha_i + s_{ij} + \tau_\ell + \gamma_{i\ell} + e_{ij\ell}) \\
&= \mathrm{Cov}(s_{ij} + e_{ijk}, s_{ij} + e_{ij\ell}) \\
&= \mathrm{Cov}(s_{ij}, s_{ij}) + \overset{=0}{\mathrm{Cov}(s_{ij}, e_{ij\ell})} \\
&\quad + \overset{=0}{\mathrm{Cov}(e_{ijk}, s_{ij})} + \underset{=0}{\mathrm{Cov}(e_{ijk}, e_{ij\ell})} \\
&= \mathrm{Var}(s_{ij}) = \sigma_s^2.
\end{aligned}
$$

The correlation between y_{ijk} and $y_{ij\ell}$ is

$$\frac{\sigma_s^2}{\sigma_s^2 + \sigma_e^2} \equiv \rho.$$

regardless of time point we assume the same correlation.

Observations taken on different subjects are uncorrelated.



matrix for 1 individual (out of the 57)

For the set of observations taken on a single subject, we have

$$\mathrm{Var}\left(\begin{bmatrix} y_{ij1} \\ y_{ij2} \\ \vdots \\ y_{ij7} \end{bmatrix}\right) = \begin{bmatrix} \sigma_e^2+\sigma_s^2 & \sigma_s^2 & \cdots & \sigma_s^2 \\ \sigma_s^2 & \sigma_e^2+\sigma_s^2 & \cdots & \sigma_s^2 \\ \vdots & \vdots & \ddots & \sigma_s^2 \\ \sigma_s^2 & \sigma_s^2 & \sigma_s^2 & \sigma_e^2+\sigma_s^2 \end{bmatrix}$$

$$= \sigma_e^2 \boldsymbol{I}_{7\times 7} + \sigma_s^2 \mathbf{1}\mathbf{1}_{7\times 7}^\top.$$

This is known as a *compound symmetric* covariance structure.

σ_e^2 & σ_s^2 requiring estimation

Using n_i to denote the number of subjects in the ith program, we can write this model in the form

$$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{Zu} + \boldsymbol{e}.$$

To make things slightly easier to write, let

$$\boldsymbol{y}_{ij} = [y_{ij1}, y_{ij2}, y_{ij3}, y_{ij4}, y_{ij5}, y_{ij6}, y_{ij7}]^\top$$

and

$$\boldsymbol{e}_{ij} = [e_{ij1}, e_{ij2}, e_{ij3}, e_{ij4}, e_{ij5}, e_{ij6}, e_{ij7}]^\top$$

for all $i = 1, 2, 3$ and all $j = 1, \ldots, n_i$.

$$
\begin{array}{cccc}
 & & \begin{array}{cccccccc} \mu & \alpha_1 & \alpha_2 & \alpha_3 & \text{time} \; \tilde{z}_1 \ldots \tilde{z}_7 & & & \end{array} & \beta \\
\begin{array}{c} n_1 \; \text{trt1} \\ \\ n_2 \; \text{trt2} \\ \\ n_3 \; \text{trt3} \; \text{control} \end{array}
\begin{bmatrix} \boldsymbol{y}_{11} \\ \boldsymbol{y}_{12} \\ \vdots \\ \boldsymbol{y}_{1n_1} \\ \boldsymbol{y}_{21} \\ \boldsymbol{y}_{22} \\ \vdots \\ \boldsymbol{y}_{2n_2} \\ \boldsymbol{y}_{31} \\ \boldsymbol{y}_{32} \\ \vdots \\ \boldsymbol{y}_{3n_3} \end{bmatrix}
& = &
\underbrace{\begin{bmatrix}
\boldsymbol{1}_{7\times 1} & \boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{I}_{7\times 7} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{0}_{7\times 7} \\
\boldsymbol{1}_{7\times 1} & \boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{I}_{7\times 7} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{0}_{7\times 7} \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\
\boldsymbol{1}_{7\times 1} & \boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{I}_{7\times 7} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{0}_{7\times 7} \\
\boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} \\
\boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\
\boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} \\
\boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{1}_{7\times 1} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{I}_{7\times 7} \\
\boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{1}_{7\times 1} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{I}_{7\times 7} \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\
\boldsymbol{1}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{0}_{7\times 1} & \boldsymbol{1}_{7\times 1} & \boldsymbol{I}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{0}_{7\times 7} & \boldsymbol{I}_{7\times 7}
\end{bmatrix}}_{X}
&
\begin{bmatrix} \mu \\ \alpha_1 \\ \alpha_2 \; \text{trt} \\ \alpha_3 \\ \tau_1 \\ \tau_2 \\ \tau_3 \\ \tau_4 \\ \tau_5 \\ \tau_6 \\ \tau_7 \\ \gamma_{11} \\ \gamma_{12} \\ \vdots \\ \gamma_{37} \end{bmatrix}
\begin{array}{l} \\ \\ \\ \\ \\ \text{time points} \\ \\ \\ \\ \\ \\ \\ \text{21 elements} \\ \\ \\ \end{array}
\end{array}
$$

interaction btw. trt 3 & time 7

end lecture 37 +1 = Lecture 38

04-30-25

$$\underbrace{\left[\boldsymbol{I}_{(n_1+n_2+n_3)\times(n_1+n_2+n_3)} \otimes \mathbf{1}_{7\times 1}\right]}_{\underset{\sim}{z}} \begin{bmatrix} s_{11} \\ s_{12} \\ \vdots \\ s_{1n_1} \\ s_{21} \\ s_{22} \\ \vdots \\ s_{2n_2} \\ s_{31} \\ s_{32} \\ \vdots \\ s_{3n_3} \end{bmatrix} + \begin{bmatrix} e_{11} \\ e_{12} \\ \vdots \\ e_{1n_1} \\ e_{21} \\ e_{22} \\ \vdots \\ e_{2n_2} \\ e_{31} \\ e_{32} \\ \vdots \\ e_{3n_3} \end{bmatrix}$$

$$= \underset{\sim}{u} \qquad \underset{\sim}{e}$$