Mixed-Effects Models for Factorial Designs

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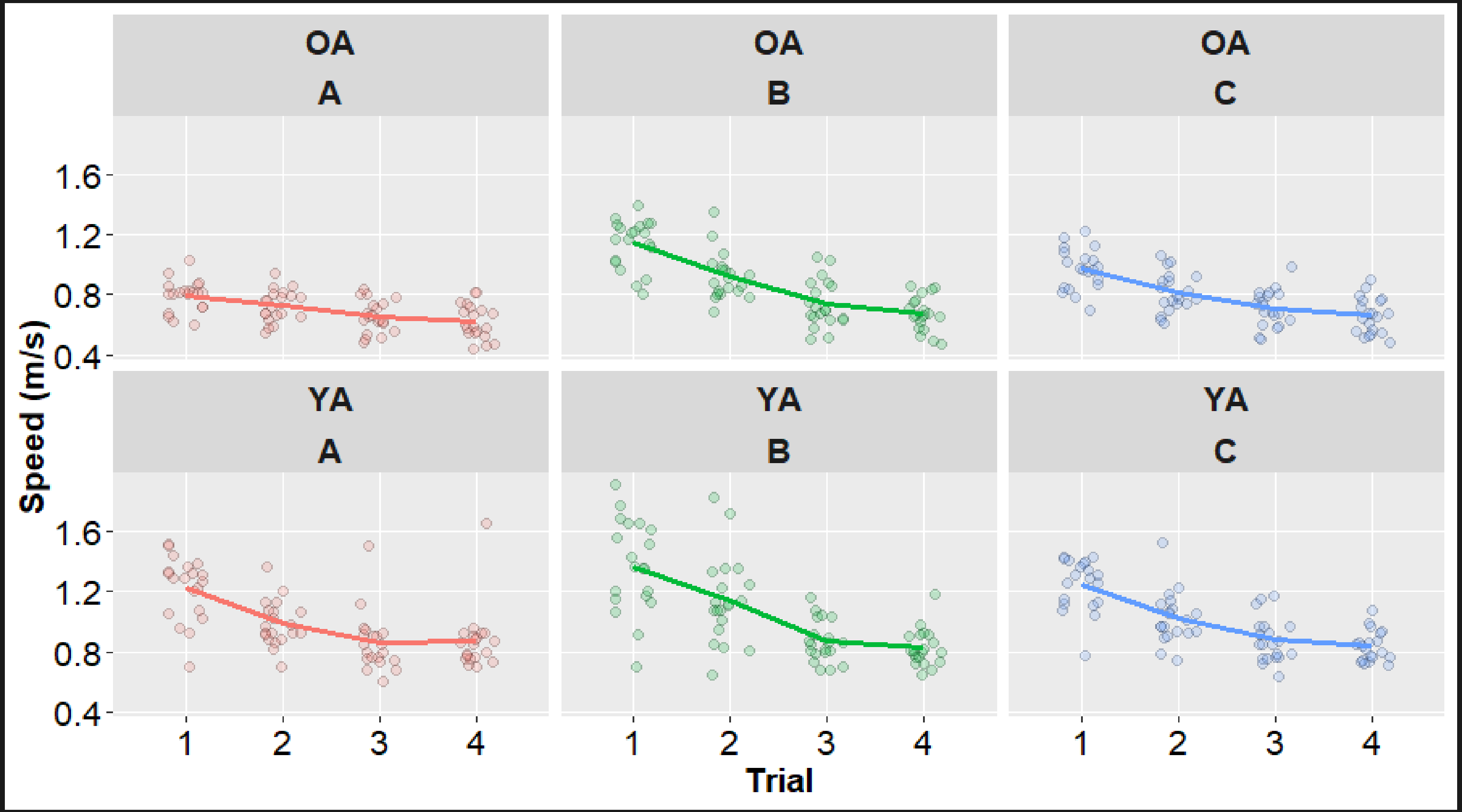
An Example Study Design



An Example Study Design

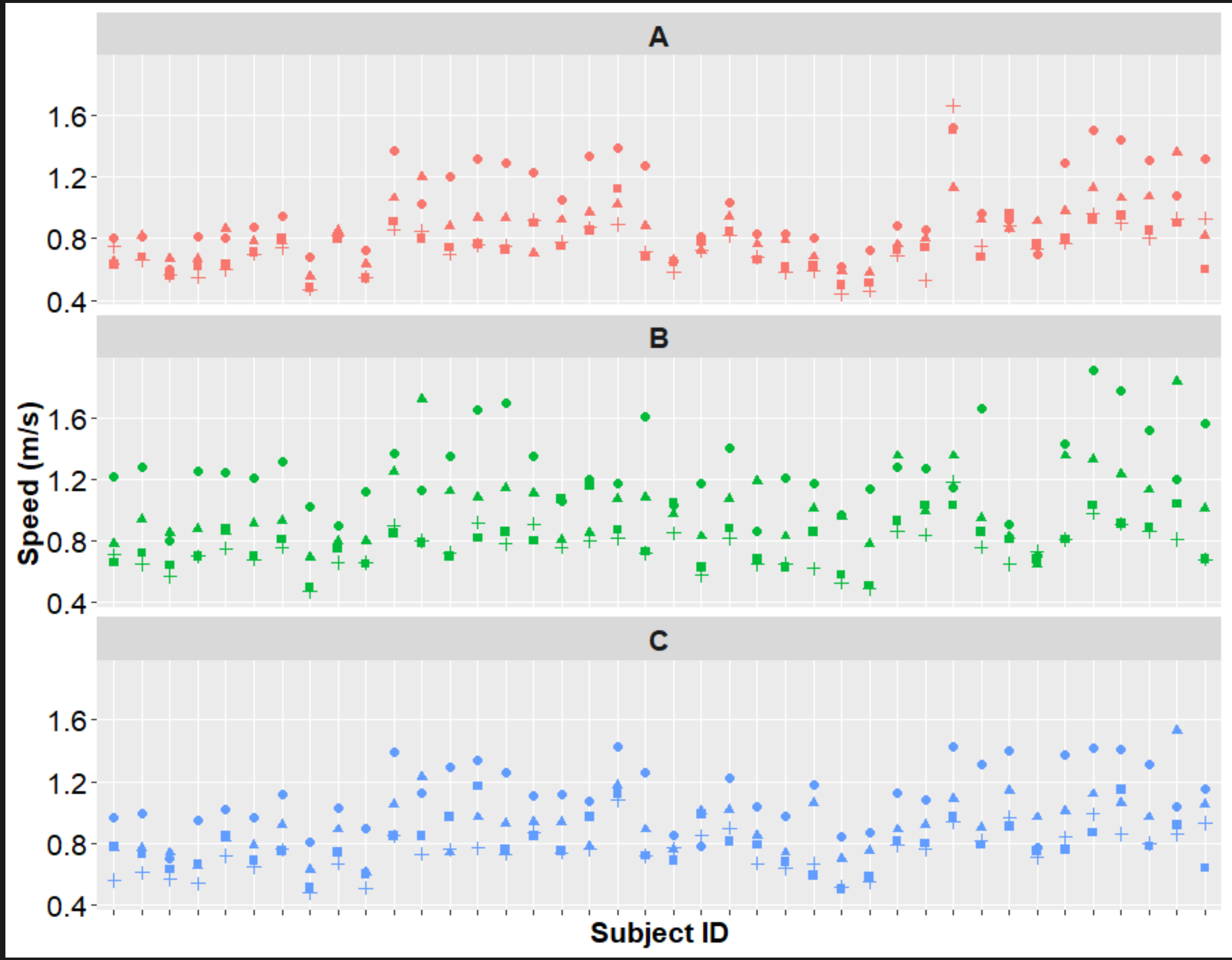
- We can think of this as a 2 (Group) x 3 (Condition) x 4 (Trial) mixed-factorial ANOVA.
  - Group is a **between-subjects** factor.
    - i.e., participants are **nested** withing groups.
  - Condition and Trial are **within-subject** factors.
    - i.e., condition and trial are **crossed** with the factor of subject.
    - Two factors are crossed when every category of one factor co-occurs in the design with every category of the other factor. In other words, there is at least one observation in every combination of categories for the two factors.

Subjects are Nested in Groups


```
> table(DATA$subID, DATA$age_group)

    OA YA
s01 12  0
s02 12  0
s03 12  0
s04 12  0
s05 12  0
s06 12  0
s07 12  0
s08 12  0
s09 12  0
s10 12  0
s11  0 12
s12  0 12
s13  0 12
s14  0 12
s15  0 12
s16  0 12
s17  0 12
s18  0 12
s19  0 12
s20  0 12
…
```

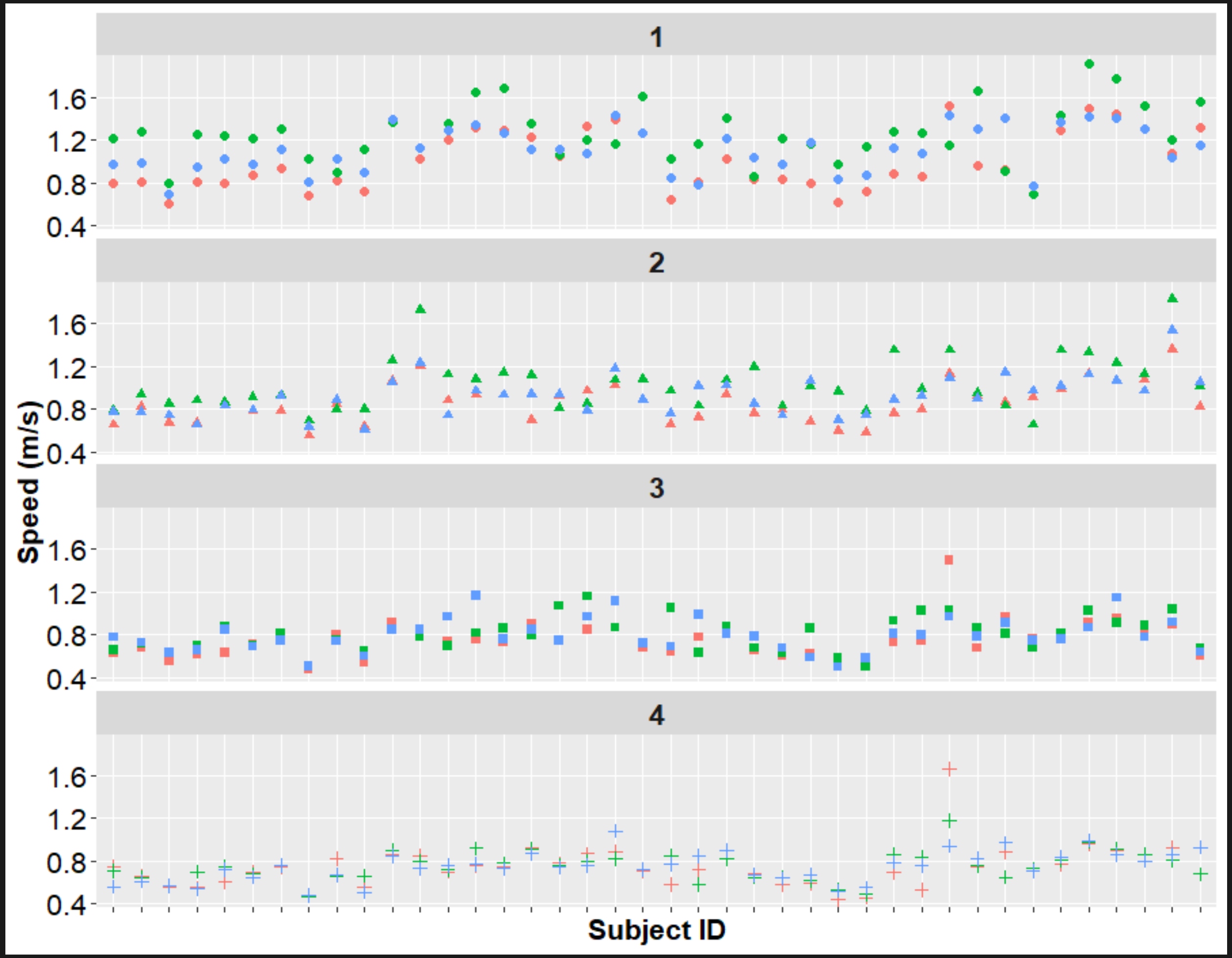
“Subject ID” is fully Crossed with *Condition*




```
> table(DATA$subID, DATA$condition)

    A B C
 s01 4 4 4
 s02 4 4 4
 s03 4 4 4
 s04 4 4 4
 s05 4 4 4
 s06 4 4 4
 s07 4 4 4
 s08 4 4 4
 s09 4 4 4
 s10 4 4 4
 …
```

“Subject ID” is fully Crossed with *Time*




```
> table(DATA$subID, DATA$time)

    1 2 3 4
s01 3 3 3 3
s02 3 3 3 3
s03 3 3 3 3
s04 3 3 3 3
s05 3 3 3 3
s06 3 3 3 3
s07 3 3 3 3
s08 3 3 3 3
s09 3 3 3 3
s10 3 3 3 3
…
```

How do we account for repeated measures?

- Clearly, we are going to face a problem as most of our analyses assume independence of residuals.

- When considering the effect of **age group**, how do we account for multiple observations from each condition and trial?
  - For the effect of **condition**, how do we account for the observations from different trials?
  - For the effect of **trial**, how do we account for the observations from different conditions?

How do we account for repeated measures?

- If we do this incorrectly, we will make very poor inferences.
  - We will artificially increase our degrees of freedom, making it seem like we have more data than we do.
  - We will also get the wrong standard error (often making it bigger), because many different sources of variation get lumped into the residuals.

How do we account for repeated measures?

- **Repeated Measures ANOVA**
  - Partitioning the Sum of Squared Errors in to different sources. Requires balanced data and assumes equal correlations among repeated measures.
  - Highly constrained, but simpler to implement.
- **Marginal Multi-Level Model**
  - In a marginal there is a single response and a single residual. However, unlike the linear model, the marginal model directly estimates the correlations among individual residuals (e.g., auto-regressive).
- **Mixed-Effects Model**
  - Rather than specify the correlation among repeated observations, we add one or more random effects to the model, depending on the experimental design.
  - Not at all constrained, so novice users often mis-specify models!

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- **Repeated Measures ANOVA**
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- ~~**Marginal Multi-Level Model**~~
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- **Mixed-Effects Model**
  - Rather than specify the correlation among repeated observations, we add one or more random effects to the model, depending on the experimental design.
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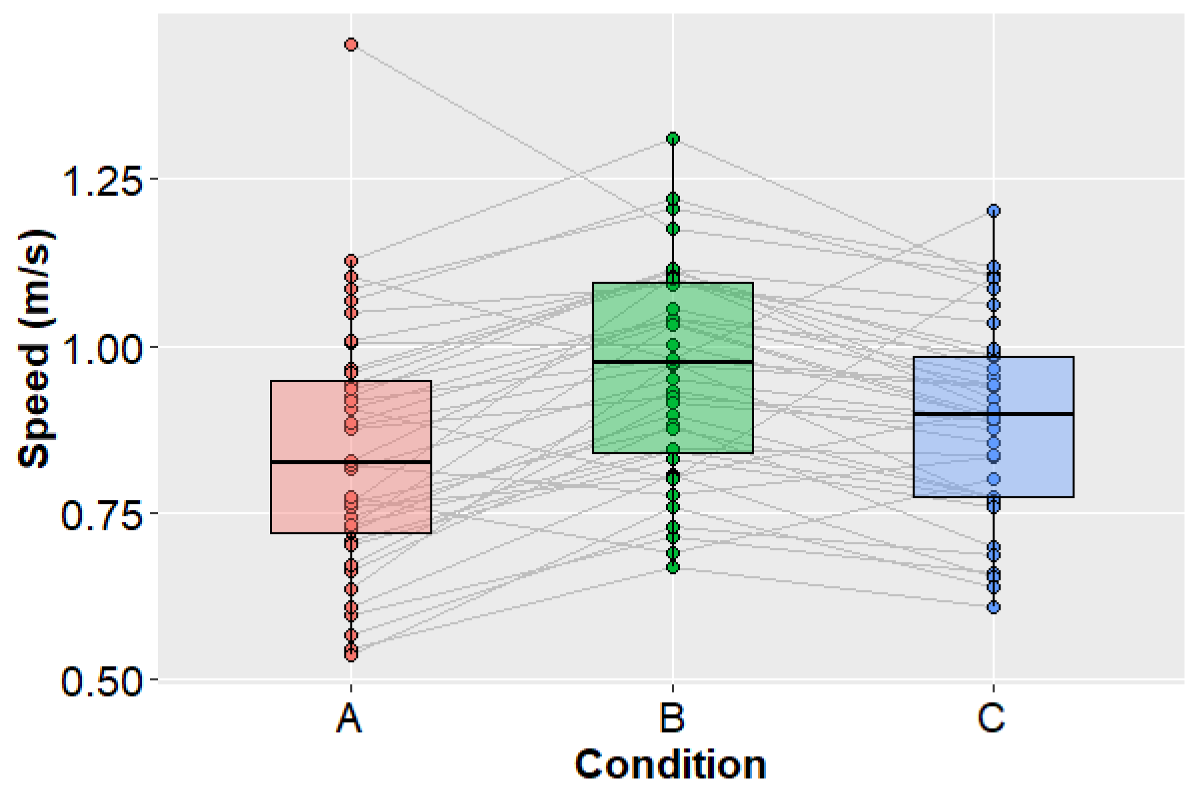
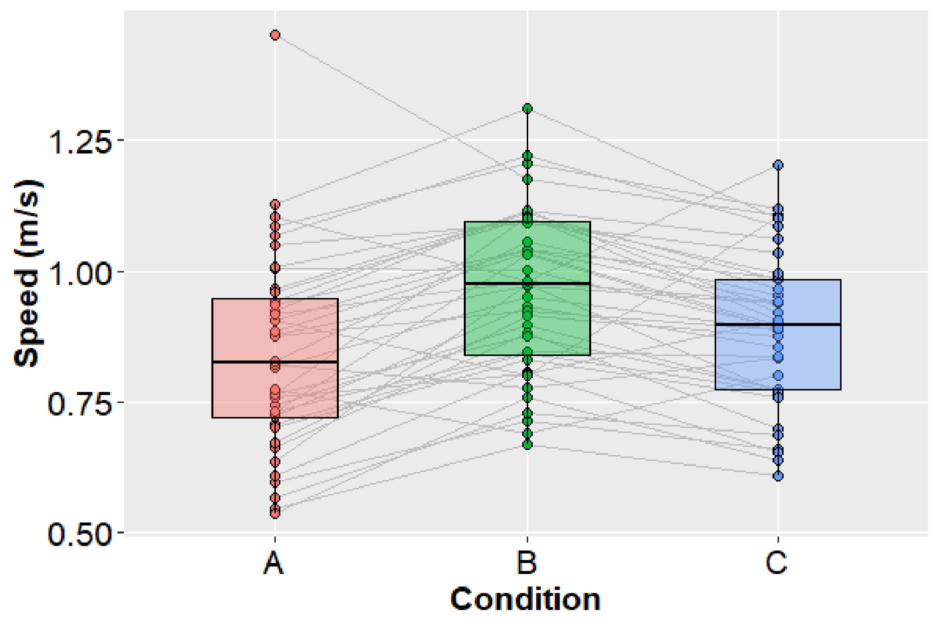
A Simpler Example: One-Way RM ANOVA

- Let’s average across trials to get a simpler design where we are only interested in the main-effect of Condition.



One-Way RM ANOVA



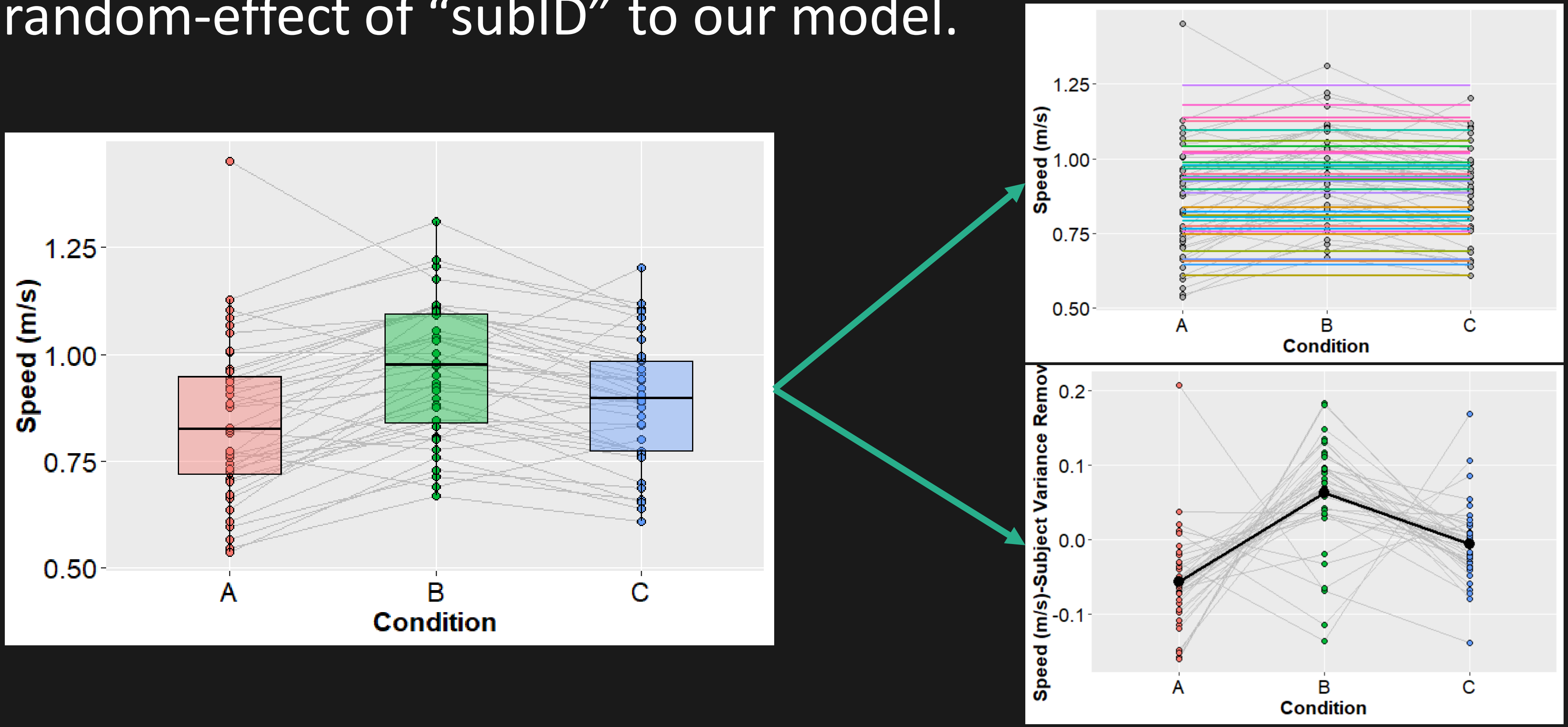
Source	SS	df	MS	F-Obs
Total Between Subjects	2.751	39	0.07054	
Total Within Subjects	0.7316	80		
-- Condition	0.282	2	0.14098	24.246
-- Error Within	0.4496	78	0.00576	
Total	3.4827	119		

N = 40, k=3, n=120 total observations

TOTAL df: n -1 = 120-1=119, the variation of each point around the grand mean.
BS df: N-1 = 40 – 1 = 39, 40 independent subject means vary around the population mean.
WS df: (N-1) * (k-1) = 39*2 = 78, each subject provides and estimate of the condition effect, which takes k-1 degrees of freedom to test, so we have (N-1)*(k-1) denominator degrees of freedom.

One-Way RM ANOVA as a Mixed Model

- We can similarly partition the variance in our data by adding a random-effect of “subID” to our model.

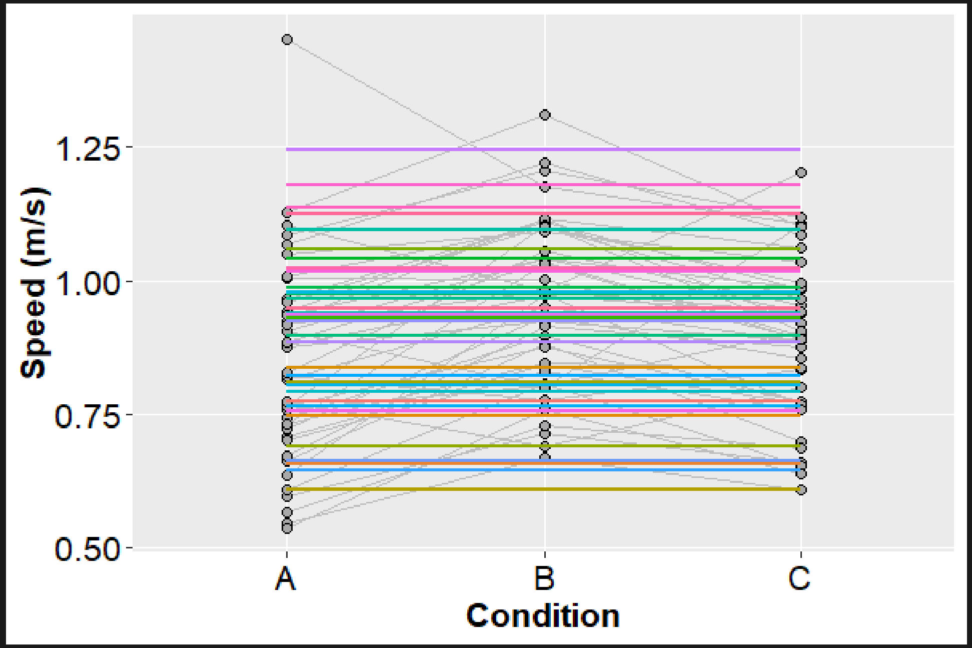


One-Way RM ANOVA as a Mixed Model

- We can similarly partition the variance in our data by adding a random-effect of “subID” to our model.

$$y_{ij} = \beta_0 + \beta_1(X1_{ij}) + \beta_2(X2_{ij}) + U_{0j} + \epsilon_{ij}$$

The **random-effect** of $subID$ estimates the mean for each person.



One-Way RM ANOVA as a Mixed Model

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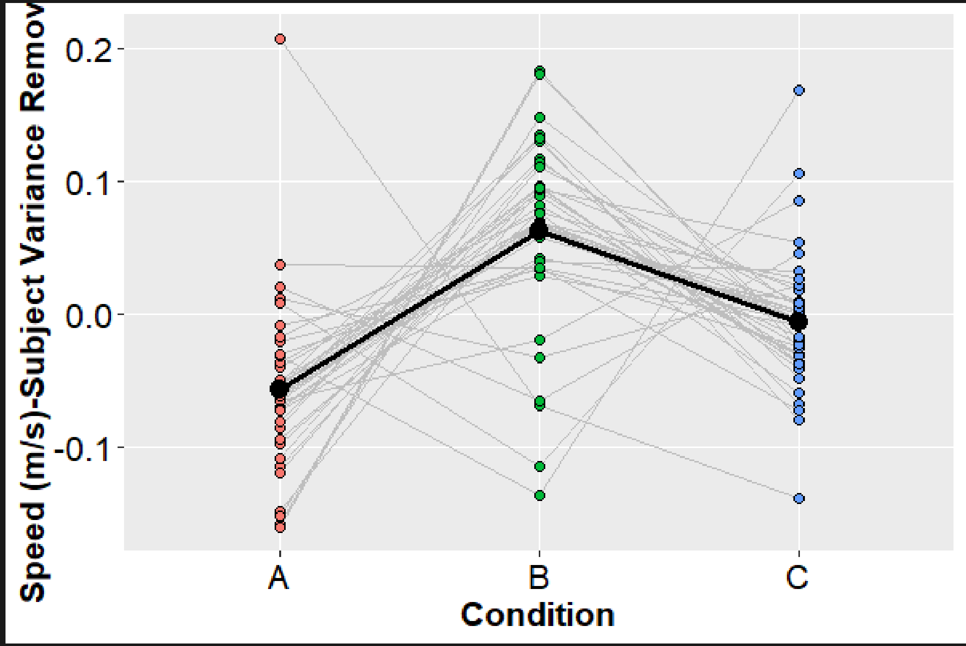
$$y_{ij} = \beta_0 + \beta_1(X1_{ij}) + \beta_2(X2_{ij}) + U_{0j} + \epsilon_{ij}$$

The **random-effect** of *subID* estimates the mean for each person.

The **fixed-effect** of Condition can then be estimated with the between subject variance removed.



Comparing the Final Results

RM ANOVA

```
Error: subID:condition
          Df Sum Sq Mean Sq F value   Pr(>F)
condition  2 0.2820 0.14098   24.46 5.67e-09 ***
Residuals 78 0.4496 0.00576
```

CODE:

```
summary(aov(speed ~ condition + Error(subID/condition), data=data_COND))
```

MER with Subject Random Effect

```
Type III Analysis of Variance Table with Satterthwaite's method
           Sum Sq Mean Sq NumDF DenDF F value    Pr(>F)
condition 0.28196 0.14098     2    78   24.46 5.674e-09 ***
```

CODE:

```
mod1 <- lmer(speed ~ condition + (1|subID), data=data_COND, REML=TRUE)
```

What if I have multiple repeated measures?

- The same principle applies, but now we need to account for the different crossed factors.

- E.g., if we want a model equivalent to a 3 (Condition) x 4 (Time) RM ANOVA:

```
mod1 <- lmer(speed ~
        # Fixed Effects:
        condition*time +
        # Random Effects:
        (1|subID)+(1|condition:subID)+(1|time:subID),
        data=DATA, REML=TRUE)
```

Comparing the Final Results

RM ANOVA

```
Error: subID
          Df Sum Sq Mean Sq F value Pr(>F)
Residuals 39  11.01  0.2822

Error: subID:condition
          Df Sum Sq Mean Sq F value   Pr(>F)
condition  2  1.128  0.5639   24.46 5.67e-09 ***
Residuals 78  1.798  0.0231
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Error: subID:time
           Df Sum Sq Mean Sq F value Pr(>F)
time        3 10.618   3.539     106 <2e-16 ***
Residuals 117  3.909   0.033
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Error: subID:condition:time
                Df Sum Sq Mean Sq F value   Pr(>F)
condition:time   6 0.7851 0.13084   13.53 3.59e-13 ***
Residuals      234 2.2626 0.00967
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

CODE:

```
summary(aov(speed ~ condition*time +
Error(subID/(condition*time)), data=DATA))
```

MER with multiple Random Effects

```
Type III Analysis of Variance Table with Satterthwaite's method
                Sum Sq Mean Sq NumDF DenDF F value    Pr(>F)
condition      0.47304 0.23652     2    78  24.460 5.674e-09 ***
time           3.07345 1.02448     3   117 105.951 < 2.2e-16 ***
condition:time 0.78505 0.13084     6   234  13.531 3.588e-13 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

CODE:

```
mod1 <- lmer(speed ~
               # Fixed Effects:
               condition*time +
               # Random Effects
               (1|subID)+(1|condition:subID)+(1|time:subID),
              data=DATA, REML=TRUE)
```

Comparing the Final Results

RM ANOVA

```
Error: subID
          Df Sum Sq Mean Sq F value Pr(>F)
Residuals 39  11.01  0.2822

Error: subID:condition
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condition  2  1.128  0.5639   24.46 5.67e-09 ***
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condition:time   6 0.7851 0.13084   13.53 3.59e-13 ***
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Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

CODE:

```
summary(aov(speed ~ condition*time +
Error(subID/(condition*time)), data=DATA))
```

MER with multiple Random Effects

```
Type III Analysis of Variance Table with Satterthwaite's method
                Sum Sq Mean Sq NumDF DenDF F value    Pr(>F)
condition      0.47304 0.23652     2    78  24.460 5.674e-09 ***
time           3.07345 1.02448     3   117 105.951 < 2.2e-16 ***
condition:time 0.78505 0.13084     6   234  13.531 3.588e-13 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

CODE:

```
mod1 <- lmer(speed ~
             # Fixed Effects:
             condition*time +
             # Random Effects
             (1|subID)+(1|condition:subID)+(1|time:subID),
            data=DATA, REML=TRUE)
```

What if you mis-specify the model?

Correct* DF and F-Values

```
Type III Analysis of Variance Table with Satterthwaite's method
                Sum Sq Mean Sq NumDF DenDF F value    Pr(>F)    
condition      0.47304 0.23652     2    78  24.460 5.674e-09 ***
time           3.07345 1.02448     3   117 105.951 < 2.2e-16 ***
condition:time 0.78505 0.13084     6   234  13.531 3.588e-13 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
# Random Effects:

(1|subID)+(1|condition:subID)+(1|time:subID),
```

* Where correct = agrees with factorial ANOVA.

INCORRECT* DF and F-Values

```
Type III Analysis of Variance Table with Satterthwaite's method
                Sum Sq Mean Sq NumDF DenDF  F value    Pr(>F)    
condition       1.1278  0.5639     2   429  30.3555 4.677e-13 ***
time           10.6185  3.5395     3   429 190.5324 < 2.2e-16 ***
condition:time  0.7851  0.1308     6   429   7.0433 3.646e-07 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
# Random Effects:
(1|subID)
```

If we only account for the mean of each subject, we ignore repeated measures from other sources.

This increase the denominator degrees of freedom and subsequently the F-values.

What if you mis-specify the model?

Correct* DF and F-Values

```
Type III Analysis of Variance Table with Satterthwaite's method
                Sum Sq Mean Sq NumDF DenDF F value    Pr(>F)    
condition      0.47304 0.23652     2    78  24.460 5.674e-09 ***
time           3.07345 1.02448     3   117 105.951 < 2.2e-16 ***
condition:time 0.78505 0.13084     6   234  13.531 3.588e-13 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

```
# Random Effects:
(1|subID)+(1|condition:subID)+(1|time:subID),
```

```
Random effects:
 Groups          Name        Variance Std.Dev.
 time:subID      (Intercept) 0.007912 0.08895 
 condition:subID (Intercept) 0.003346 0.05785 
 subID           (Intercept) 0.019616 0.14006 
 Residual                    0.009669 0.09833 
Number of obs: 480, groups:  time:subID, 160; condition:subID, 120; subID, 40
```

INCORRECT* DF and F-Values

```
Type III Analysis of Variance Table with Satterthwaite's method
                Sum Sq  Mean Sq NumDF DenDF F value    Pr(>F)    
condition      0.01995 0.009977     2   429  0.5371    0.5849    
time           0.06050 0.020166     3   429  1.0855    0.3549    
condition:time 0.78505 0.130842     6   429  7.0433 3.646e-07 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

```
# Random Effects:
(1|subID)+(1|condition)+(1|time)
```

```
Random effects:
 Groups    Name        Variance Std.Dev.
 subID     (Intercept) 0.021967 0.14821 
 time      (Intercept) 0.027017 0.16437 
 condition (Intercept) 0.006446 0.08029 
 Residual              0.018577 0.13630 
Number of obs: 480, groups:  subID, 40; time, 4; condition, 3
```

What if you mis-specify the model?

Correct* DF and F-Values

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               Sum Sq Mean Sq NumDF DenDF F value    Pr(>F)    
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condition:time 0.78505 0.13084     6   234  13.531 3.588e-13 ***
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# Random Effects:
(1|subID)+(1|condition:subID)+(1|time:subID),
```

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 subID           (Intercept) 0.019616 0.14006 
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                Sum Sq  Mean Sq NumDF DenDF F value    Pr(>F)    
condition      0.01995 0.009977     2   429  0.5371    0.5849    
time           0.06050 0.020166     3   429  1.0855    0.3549    
condition:time 0.78505 0.130842     6   429  7.0433 3.646e-07 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
# Random Effects:
(1|subID)+(1|condition)+(1|time)
```

This one is a little more difficult to see why it is wrong, but conceptually, we want to know how variable the time/condition effects are within each subject (e.g., time:subID), not remove the variability do to condition/time on average.

A Conceptual Approach to MER for Factorial Designs

- **Model Specification:** Identify crossed and nested factors in your design. Make sure they are coded correctly in the random-effects.

- For factorial ANOVAs, add subID:WS random-effects as needed:
  - DV ~ BS1+BS2+WS1+(1|subID)
  - DV ~ BS1+BS2+WS1+WS2+(1|subID)+(1|subID:WS1)+(1|subID:WS2)
  - DV ~ WS1+WS2+WS3+(1|subID)+(1|subID:WS1)+(1|subID:WS2) +(1|subID:WS3)
  - Etc…

A Conceptual Approach to MER for Factorial Designs

- **Model Specification:** Identify crossed and nested factors in your design. Make sure they are coded correctly in the random-effects.

- **Missing Data:** One of the advantages of MER over RM ANOVA is the ability to handle missing data.
  - However, data need to meet the assumptions of MCAR or MAR. DATA MNAR will bias model estimates.
  - “Handling” missing data is also not a panacea, you need to be worried about balanced designs.
  - But a few missing cases is okay and by using MER you can include a subject who otherwise would be dropped.

A Conceptual Approach to MER for Factorial Designs

- **Model Specification:** Identify crossed and nested factors in your design. Make sure they are coded correctly in the random-effects.

- **Missing Data:** One of the advantages of MER over RM ANOVA is the ability to handle missing data.

- **Model Convergence:** In a properly specified model with a (relatively) balanced factorial design, it should be pretty rare to get convergence warnings, but do not ignore these warnings when they arise.
  - Increase the number of iterations for ML estimation.
  - Consider changing the optimizer.
  - Inspect the variance/covariance matrix for the random-effects.