

Multivariate Analysis for the Behavioral Sciences,
Second Edition (Chapman and Hall/CRC, 2019)
Solutions to Exercises of Chapter 9:
Analysis of Longitudinal Data II: Linear
Mixed Effects Models for Normal Response
Variables

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19 November 2018

Exercises

Exercise 9.3

```
oestrogen <- read.table("data/oestrogen.txt", sep = "\t", header = TRUE)

str(oestrogen)

## 'data.frame':   366 obs. of  6 variables:
## $ subject   : int  1 1 1 1 1 1 2 2 2 2 ...
## $ treatment : Factor w/ 2 levels "oespatch","placebo": 2 2 2 2 2 2 2 2 2 2 ...
## $ BL1       : int  18 18 18 18 18 18 25 25 25 25 ...
## $ BL2       : int  18 18 18 18 18 18 27 27 27 27 ...
## $ time      : int  1 2 3 4 5 6 1 2 3 4 ...
## $ depression: num  17 26 17 14 12 19 13 26 26 9 ...

# the data are readily in the long form:
head(oestrogen, n = 10); tail(oestrogen, n = 10)

##   subject treatment BL1 BL2 time depression
## 1      1 placebo  18  18   1          17
## 2      1 placebo  18  18   2          26
## 3      1 placebo  18  18   3          17
## 4      1 placebo  18  18   4          14
## 5      1 placebo  18  18   5          12
## 6      1 placebo  18  18   6          19
## 7      2 placebo  25  27   1          13
## 8      2 placebo  25  27   2          26
## 9      2 placebo  25  27   3          26
## 10     2 placebo  25  27   4           9

##   subject treatment BL1 BL2 time depression
## 357     60 oespatch  18  22   3           1
## 358     60 oespatch  18  22   4          10
## 359     60 oespatch  18  22   5           5
## 360     60 oespatch  18  22   6           6
## 361     61 oespatch  23  26   1          NA
```

```
## 362      61 oespatch 23 26 2      3
## 363      61 oespatch 23 26 3      4
## 364      61 oespatch 23 26 4     NA
## 365      61 oespatch 23 26 5     NA
## 366      61 oespatch 23 26 6     NA
```

```
attach(oestrogen)
#independence model
oestrogen_reg <- lm(depression ~ treatment + BL1 + BL2 + time,
                    na.action = na.omit)
summary(oestrogen_reg)
```

```
##
## Call:
## lm(formula = depression ~ treatment + BL1 + BL2 + time, na.action = na.omit)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -13.0809  -4.3643  -0.3958   3.7219  15.4080
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    7.011455   2.591607   2.705  0.00723 **
## treatmentplacebo 4.700557   0.674300   6.971 2.14e-11 ***
## BL1            0.098669   0.123902   0.796  0.42648
## BL2            0.009731   0.105029   0.093  0.92625
## time          -0.113540   0.197977  -0.574  0.56675
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.77 on 289 degrees of freedom
## (72 observations deleted due to missingness)
## Multiple R-squared:  0.1472, Adjusted R-squared:  0.1354
## F-statistic: 12.48 on 4 and 289 DF, p-value: 2.248e-09
```

```
library("lme4")
```

```
## Loading required package: Matrix
```

```
#random intercept model
oestrogen_ref <- lmer(depression ~ treatment + BL1 + BL2 + time + (1 | subject),
                     na.action = na.omit)
summary(oestrogen_ref)
```

```
## Linear mixed model fit by REML ['lmerMod']
## Formula: depression ~ treatment + BL1 + BL2 + time + (1 | subject)
##
## REML criterion at convergence: 1863
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.28847 -0.70259 -0.04553  0.66328  2.66518
##
## Random effects:
##  Groups   Name      Variance Std.Dev.
## subject (Intercept)  2.583    1.607
```

```

## Residual          30.863   5.555
## Number of obs: 294, groups:  subject, 60
##
## Fixed effects:
##              Estimate Std. Error t value
## (Intercept)   7.136838   2.955632   2.415
## treatmentplacebo 4.569782   0.776538   5.885
## BL1           0.099889   0.143330   0.697
## BL2           0.006227   0.122010   0.051
## time          -0.102538   0.191607  -0.535
##
## Correlation of Fixed Effects:
##              (Intr) trtmnt BL1    BL2
## tretmntplcb -0.148
## BL1         -0.599 -0.020
## BL2         -0.324  0.049 -0.522
## time        -0.192  0.008 -0.034  0.003

oestrogen1_ref <- lmer(depression ~ treatment + BL1 + BL2 + time + (time | subject),
                      na.action = na.omit)
summary(oestrogen1_ref)

## Linear mixed model fit by REML ['lmerMod']
## Formula: depression ~ treatment + BL1 + BL2 + time + (time | subject)
##
## REML criterion at convergence: 1860.6
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.49492 -0.72077 -0.03654  0.67304  2.55578
##
## Random effects:
##  Groups   Name                Variance Std.Dev. Corr
##  subject  (Intercept)  13.5526   3.6814
##           time           0.6203   0.7876  -0.90
## Residual                28.7638   5.3632
## Number of obs: 294, groups:  subject, 60
##
## Fixed effects:
##              Estimate Std. Error t value
## (Intercept)   6.747562   2.956933   2.282
## treatmentplacebo 4.659718   0.769400   6.056
## BL1           0.125359   0.141700   0.885
## BL2          -0.001861   0.120865  -0.015
## time          -0.115817   0.212987  -0.544
##
## Correlation of Fixed Effects:
##              (Intr) trtmnt BL1    BL2
## tretmntplcb -0.146
## BL1         -0.593 -0.018
## BL2         -0.324  0.049 -0.520
## time        -0.230 -0.001 -0.031  0.001

```

```

anova(oestrogen_ref, oestrogen1_ref)

## refitting model(s) with ML (instead of REML)
## Data: NULL
## Models:
## oestrogen_ref: depression ~ treatment + BL1 + BL2 + time + (1 | subject)
## oestrogen1_ref: depression ~ treatment + BL1 + BL2 + time + (time | subject)
##           Df      AIC      BIC logLik deviance Chisq Chi Df Pr(>Chisq)
## oestrogen_ref  7 1871.9 1897.7 -928.97  1857.9
## oestrogen1_ref  9 1873.6 1906.8 -927.81  1855.6 2.3199      2    0.3135
#random intercept model ok - CI for treatment effect:
treat_ci <- c(-4.57-2*0.78,-4.57+2*0.78)
treat_ci

## [1] -6.13 -3.01
detach(oestrogen)

```

Exercise 9.4

```
phosphate <- structure(list(

  group = structure(c(1L, 1L, 1L, 1L, 1L, 1L, 1L, 1L, 1L, 1L, 1L, 1L, 1L,
    1L, 1L, 1L, 1L, 1L, 1L, 2L, 2L, 2L, 2L, 2L, 2L, 2L, 2L,
    2L, 2L, 2L, 2L, 2L),
    .Label = c("control", "obese"), class = "factor"),

  t0 = c(4.3, 3.7, 4, 3.6, 4.1, 3.8, 3.8, 4.4, 5, 3.7, 3.7, 4.4, 4.7, 4.3, 5,
    4.6, 4.3, 3.1, 4.8, 3.7, 5.4, 3, 4.9, 4.8, 4.4, 4.9, 5.1, 4.8, 4.2,
    6.6, 3.6, 4.5, 4.6),

  t0.5 = c(3.3, 2.6, 4.1, 3, 3.8, 2.2, 3, 3.9, 4, 3.1, 2.6, 3.7, 3.1, 3.3, 4.9,
    4.4, 3.9, 3.1, 5, 3.1, 4.7, 2.5, 5, 4.3, 4.2, 4.3, 4.1, 4.6, 3.5, 6.1,
    3.4, 4, 4.4),

  t1 = c(3, 2.6, 3.1, 2.2, 2.1, 2, 2.4, 2.8, 3.4, 2.9, 2.6, 3.1, 3.2, 3, 4.1,
    3.9, 3.1, 3.3, 2.9, 3.3, 3.9, 2.3, 4.1, 4.7, 4.2, 4, 4.6, 4.6, 3.8,
    5.2, 3.1, 3.7, 3.8),

  t1.5 = c(2.6, 1.9, 2.3, 2.8, 3, 2.6, 2.5, 2.1, 3.4, 2.2, 2.3, 3.2, 3.3, 2.6,
    3.7, 3.9, 3.1, 2.6, 2.8, 2.8, 4.1, 2.2, 3.7, 4.6, 3.4, 4, 4.1, 4.4,
    3.6, 4.1, 2.8, 3.3, 3.8),

  t2 = c(2.2, 2.9, 2.9, 2.9, 3.6, 3.8, 3.1, 3.6, 3.3, 1.5, 2.9, 3.7, 3.2, 2.2,
    3.7, 3.7, 3.1, 2.6, 2.2, 2.9, 2.8, 2.1, 3.7, 4.7, 3.5, 3.3, 3.4, 4.1,
    3.3, 4.3, 2.1, 2.4, 3.8),

  t3 = c(2.5, 3.2, 3.1, 3.9, 3.4, 3.6, 3.4, 3.8, 3.6, 2.3, 2.2, 4.3, 4.2, 2.5,
    4.1, 4.2, 3.1, 1.9, 3.1, 3.6, 3.7, 2.6, 4.1, 3.7, 3.4, 4.1, 4.2, 4,
    3.1, 3.8, 2.4, 2.3, 3.6),

  t4 = c(3.4, 3.1, 3.9, 3.8, 3.6, 3, 3.5, 4, 4, 2.7, 3.1, 3.9, 3.7, 2.4, 4.7,
    4.8, 3.6, 2.3, 3.5, 4.3, 3.5, 3.2, 4.7, 3.6, 3.8, 4.2, 4.4, 3.8, 3.5,
    4.2, 2.5, 3.1, 3.8),

  t5 = c(4.4, 3.9, 4, 4, 3.7, 3.5, 3.7, 3.9, 4.3, 2.8, 3.9, 4.8, 4.3, 3.4, 4.9,
    5, 4, 2.7, 3.6, 4.4, 3.7, 3.5, 4.9, 3.9, 4, 4.3, 4.9, 3.8, 3.9, 4.8,
    3.5, 3.3, 3.8)),

.Names = c("group", "t0", "t0.5", "t1", "t1.5", "t2", "t3", "t4", "t5"),

row.names = c("1", "2", "3", "4", "5", "6", "7", "8", "9", "10", "11", "12",
  "13", "14", "15", "16", "17", "18", "19", "20", "21", "22", "23",
  "24", "25", "26", "27", "28", "29", "30", "31", "32", "33"),
class = "data.frame")
```

```
str(phosphate)
```

```
## 'data.frame': 33 obs. of 9 variables:
## $ group: Factor w/ 2 levels "control","obese": 1 1 1 1 1 1 1 1 1 1 ...
## $ t0 : num 4.3 3.7 4 3.6 4.1 3.8 3.8 4.4 5 3.7 ...
## $ t0.5 : num 3.3 2.6 4.1 3 3.8 2.2 3 3.9 4 3.1 ...
## $ t1 : num 3 2.6 3.1 2.2 2.1 2 2.4 2.8 3.4 2.9 ...
## $ t1.5 : num 2.6 1.9 2.3 2.8 3 2.6 2.5 2.1 3.4 2.2 ...
## $ t2 : num 2.2 2.9 2.9 2.9 3.6 3.8 3.1 3.6 3.3 1.5 ...
## $ t3 : num 2.5 3.2 3.1 3.9 3.4 3.6 3.4 3.8 3.6 2.3 ...
## $ t4 : num 3.4 3.1 3.9 3.8 3.6 3 3.5 4 4 2.7 ...
## $ t5 : num 4.4 3.9 4 4 3.7 3.5 3.7 3.9 4.3 2.8 ...
```

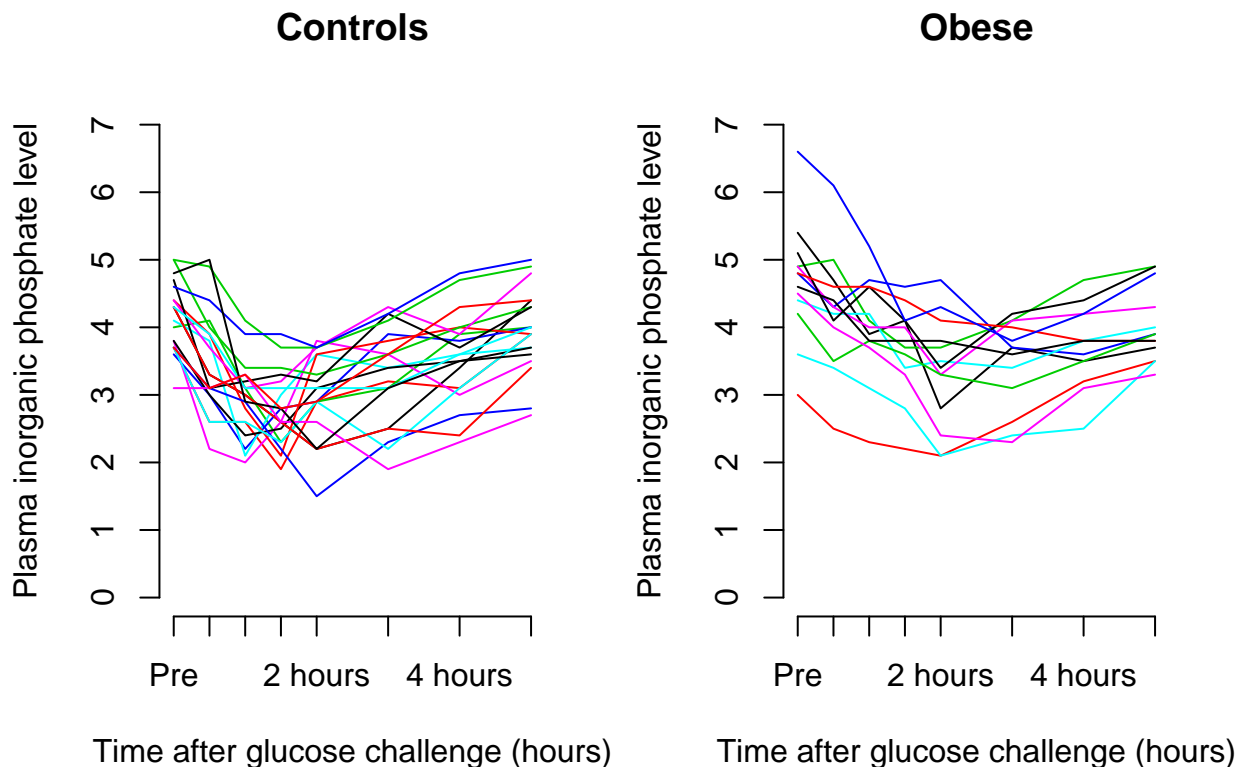
```
phosphate
```

```
##      group t0 t0.5 t1 t1.5 t2 t3 t4 t5
## 1 control 4.3 3.3 3.0 2.6 2.2 2.5 3.4 4.4
## 2 control 3.7 2.6 2.6 1.9 2.9 3.2 3.1 3.9
## 3 control 4.0 4.1 3.1 2.3 2.9 3.1 3.9 4.0
## 4 control 3.6 3.0 2.2 2.8 2.9 3.9 3.8 4.0
## 5 control 4.1 3.8 2.1 3.0 3.6 3.4 3.6 3.7
## 6 control 3.8 2.2 2.0 2.6 3.8 3.6 3.0 3.5
## 7 control 3.8 3.0 2.4 2.5 3.1 3.4 3.5 3.7
## 8 control 4.4 3.9 2.8 2.1 3.6 3.8 4.0 3.9
## 9 control 5.0 4.0 3.4 3.4 3.3 3.6 4.0 4.3
## 10 control 3.7 3.1 2.9 2.2 1.5 2.3 2.7 2.8
## 11 control 3.7 2.6 2.6 2.3 2.9 2.2 3.1 3.9
## 12 control 4.4 3.7 3.1 3.2 3.7 4.3 3.9 4.8
## 13 control 4.7 3.1 3.2 3.3 3.2 4.2 3.7 4.3
## 14 control 4.3 3.3 3.0 2.6 2.2 2.5 2.4 3.4
## 15 control 5.0 4.9 4.1 3.7 3.7 4.1 4.7 4.9
## 16 control 4.6 4.4 3.9 3.9 3.7 4.2 4.8 5.0
## 17 control 4.3 3.9 3.1 3.1 3.1 3.1 3.6 4.0
## 18 control 3.1 3.1 3.3 2.6 2.6 1.9 2.3 2.7
## 19 control 4.8 5.0 2.9 2.8 2.2 3.1 3.5 3.6
## 20 control 3.7 3.1 3.3 2.8 2.9 3.6 4.3 4.4
## 21 obese 5.4 4.7 3.9 4.1 2.8 3.7 3.5 3.7
## 22 obese 3.0 2.5 2.3 2.2 2.1 2.6 3.2 3.5
## 23 obese 4.9 5.0 4.1 3.7 3.7 4.1 4.7 4.9
## 24 obese 4.8 4.3 4.7 4.6 4.7 3.7 3.6 3.9
## 25 obese 4.4 4.2 4.2 3.4 3.5 3.4 3.8 4.0
## 26 obese 4.9 4.3 4.0 4.0 3.3 4.1 4.2 4.3
## 27 obese 5.1 4.1 4.6 4.1 3.4 4.2 4.4 4.9
## 28 obese 4.8 4.6 4.6 4.4 4.1 4.0 3.8 3.8
## 29 obese 4.2 3.5 3.8 3.6 3.3 3.1 3.5 3.9
## 30 obese 6.6 6.1 5.2 4.1 4.3 3.8 4.2 4.8
## 31 obese 3.6 3.4 3.1 2.8 2.1 2.4 2.5 3.5
## 32 obese 4.5 4.0 3.7 3.3 2.4 2.3 3.1 3.3
## 33 obese 4.6 4.4 3.8 3.8 3.8 3.6 3.8 3.8
```

R code to plot data and fit models that include a quadratic effect for time; this can be seen in the plots of the data:

```
Group <- phosphate[, 1]
#plot individual profiles separately for the two groups
par(mfrow = c(1,2))
matplot(c(0, 0.5, 1, 1.5, 2, 3, 4, 5), t(phosphate[Group == "control", 2:9]),
        type = "l", lty = 1, axes = F, xlab = "Time after glucose challenge (hours)",
        ylab = "Plasma inorganic phosphate level", ylim = c(0,7))
axis(1, at = c(0, 0.5, 1, 1.5, 2, 3, 4, 5),
     labels = c("Pre", "30 mins", "1 hour", "1.5 hours", "2 hours", "3 hours",
                "4 hours", "5 hours"))
axis(2)
title("Controls")

matplot(c(0, 0.5, 1, 1.5, 2, 3, 4, 5), t(phosphate[Group == "obese", 2:9]),
        type = "l", lty = 1, axes = F, xlab = "Time after glucose challenge (hours)",
        ylab = "Plasma inorganic phosphate level", ylim = c(0,7))
axis(1, at = c(0, 0.5, 1, 1.5, 2, 3, 4, 5),
     labels = c("Pre", "30 mins", "1 hour", "1.5 hours", "2 hours", "3 hours",
                "4 hours", "5 hours"))
axis(2)
title("Obese")
```



```
library("lme4")
#put data into long form for analysis
```

```

group <- rep(c(0, 1), c(104, 160))

time <- c(0.0, 0.5, 1.0, 1.5, 2.0, 3.0, 4.0, 5.0)
time <- rep(time, 33)

subject <- rep(1:33, rep(8, 33))
phosphatel <- cbind(subject, time, group, as.vector(t(phosphate[, 2:9])))
dimnames(phosphatel) <- list(NULL, c("Subject", "Time", "Group", "Plasma"))

phosphatel <- data.frame(phosphatel)
phosphatel$Group <- factor(phosphatel$Group, levels = c(0, 1), labels = c("Control", "Obese"))

str(phosphatel)

## 'data.frame': 264 obs. of 4 variables:
## $ Subject: num 1 1 1 1 1 1 1 1 2 2 ...
## $ Time : num 0 0.5 1 1.5 2 3 4 5 0 0.5 ...
## $ Group : Factor w/ 2 levels "Control","Obese": 1 1 1 1 1 1 1 1 1 1 ...
## $ Plasma : num 4.3 3.3 3 2.6 2.2 2.5 3.4 4.4 3.7 2.6 ...

head(phosphatel, n = 13)

##      Subject Time   Group Plasma
## 1         1  0.0 Control    4.3
## 2         1  0.5 Control    3.3
## 3         1  1.0 Control    3.0
## 4         1  1.5 Control    2.6
## 5         1  2.0 Control    2.2
## 6         1  3.0 Control    2.5
## 7         1  4.0 Control    3.4
## 8         1  5.0 Control    4.4
## 9         2  0.0 Control    3.7
## 10        2  0.5 Control    2.6
## 11        2  1.0 Control    2.6
## 12        2  1.5 Control    1.9
## 13        2  2.0 Control    2.9

tail(phosphatel, n = 13)

##      Subject Time   Group Plasma
## 252        32  1.5 Obese    3.3
## 253        32  2.0 Obese    2.4
## 254        32  3.0 Obese    2.3
## 255        32  4.0 Obese    3.1
## 256        32  5.0 Obese    3.3
## 257        33  0.0 Obese    4.6
## 258        33  0.5 Obese    4.4
## 259        33  1.0 Obese    3.8
## 260        33  1.5 Obese    3.8
## 261        33  2.0 Obese    3.8
## 262        33  3.0 Obese    3.6
## 263        33  4.0 Obese    3.8
## 264        33  5.0 Obese    3.8

```



```

#fit independence model allowing a quadratic effect for time
summary(lm(Plasma ~ Time + I(Time * Time) + Group, data = phosphatel))

##
## Call:
## lm(formula = Plasma ~ Time + I(Time * Time) + Group, data = phosphatel)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -1.60101 -0.50142  0.05601  0.49777  2.23351
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    3.90947    0.10785   36.248 < 2e-16 ***
## Time          -0.83115    0.09605   -8.654 5.29e-16 ***
## I(Time * Time)  0.16361    0.01859    8.803 < 2e-16 ***
## GroupObese     0.45702    0.08723    5.239 3.34e-07 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.6926 on 260 degrees of freedom
## Multiple R-squared:  0.2884, Adjusted R-squared:  0.2802
## F-statistic: 35.13 on 3 and 260 DF,  p-value: < 2.2e-16

#random intercept model
phosphate_lme1 <- lmer(Plasma ~ Time + I(Time * Time) + Group + (1 | Subject), data = phosphatel)
summary(phosphate_lme1)

## Linear mixed model fit by REML ['lmerMod']
## Formula: Plasma ~ Time + I(Time * Time) + Group + (1 | Subject)
## Data: phosphatel
##
## REML criterion at convergence: 444.8
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.59561 -0.68170 -0.00063  0.56488  2.68734
##
## Random effects:
## Groups Name Variance Std.Dev.
## Subject (Intercept) 0.2688  0.5185
## Residual          0.2233  0.4725
## Number of obs: 264, groups: Subject, 33
##
## Fixed effects:
##              Estimate Std. Error t value
## (Intercept)    3.90947    0.16153   24.203
## Time          -0.83115    0.06553  -12.684
## I(Time * Time)  0.16361    0.01268   12.903
## GroupObese     0.45702    0.19406    2.355
##
## Correlation of Fixed Effects:
##              (Intr) Time  I(T*T)
## Time          -0.319
## I(Tim*Time)    0.265 -0.962

```

```
## GroupObese -0.728 0.000 0.000
#random intercept and slope model
phosphate_lme2 <- lmer(Plasma ~ Time + Group + I(Time * Time) + (Time | Subject), data = phosphatel)
summary(phosphate_lme2)

## Linear mixed model fit by REML ['lmerMod']
## Formula: Plasma ~ Time + Group + I(Time * Time) + (Time | Subject)
## Data: phosphatel
##
## REML criterion at convergence: 424
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.84031 -0.54419 -0.04932  0.56562  2.74439
##
## Random effects:
## Groups Name Variance Std.Dev. Corr
## Subject (Intercept) 0.39433 0.6280
## Time 0.01592 0.1262 -0.56
## Residual 0.17569 0.4192
## Number of obs: 264, groups: Subject, 33
##
## Fixed effects:
## Estimate Std. Error t value
## (Intercept) 3.95456 0.16984 23.284
## Time -0.83115 0.06214 -13.375
## GroupObese 0.38262 0.19284 1.984
## I(Time * Time) 0.16361 0.01125 14.545
##
## Correlation of Fixed Effects:
## (Intr) Time GrpObs
## Time -0.380
## GroupObese -0.688 0.000
## I(Tim*Time) 0.224 -0.900 0.000
anova(phosphate_lme1, phosphate_lme2)

## refitting model(s) with ML (instead of REML)
## Data: phosphatel
## Models:
## phosphate_lme1: Plasma ~ Time + I(Time * Time) + Group + (1 | Subject)
## phosphate_lme2: Plasma ~ Time + Group + I(Time * Time) + (Time | Subject)
## Df AIC BIC logLik deviance Chisq Chi Df Pr(>Chisq)
## phosphate_lme1 6 439.28 460.74 -213.64 427.28
## phosphate_lme2 8 423.08 451.68 -203.54 407.08 20.209 2 4.089e-05
##
## phosphate_lme1
## phosphate_lme2 ***
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
#random intercept and slope model preferred
#plot fitted values
```

```

predictions <- matrix(fitted(phosphate_lme2), ncol = 8, byrow = T)
par(mfrow = c(1,2))
matplot(matrix(c(0.0, 0.5, 1, 1.5, 2, 3, 4, 5), ncol = 1),
        t(predictions[1:13, ]), type = "l", lty = 1, col = 1,
        xlab = "Time (hours after glucose challenge)",
        ylab="Plasma inorganic phosphate", ylim = c(0,7))
title("Fitted control")
matplot(matrix(c(0.0, 0.5, 1, 1.5, 2, 3, 4, 5), ncol = 1),
        t(predictions[14:33, ]), type = "l", lty = 1, col = 1,
        xlab = "Time (hours after glucose challenge)",
        ylab = "Plasma inorganic phosphate", ylim = c(0,7))
title("Fitted obese")

```

