

Circadian Analysis

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Analysis for activity

```
wt <- read_xlsx("data/Activity_analysis_4_R.xlsx", sheet = 1)
mut <- read_xlsx("data/Activity_analysis_4_R.xlsx", sheet = 2)

wt <- wt %>%
  bind_cols(WT.M=rep("WT", nrow(wt)), time = decimal_date(ymd(wt$`Total_revolutions/day`)), .) %>%
  gather(mice, activity, -c(1:5)) %>%
  mutate(time = time-min(time)) %>%
  select(-`Total_revolutions/day`)

mut <- mut %>%
  bind_cols(WT.M=rep("M", nrow(mut)), time = decimal_date(ymd(mut$`Total_revolutions/day`)), .) %>%
  gather(mice, activity, -c(1:5)) %>%
  mutate(time = time-min(time)) %>%
  select(-`Total_revolutions/day`)

data <- wt %>% bind_rows(mut)

data <- data %>% filter(week>=3)

data$mice <- factor(data$mice, levels= unique(data$mice))
data$time_scaled <- scale(data$time, scale=FALSE)
data$period <- factor(data$period, levels= unique(data$period))
data$WT.M <-factor(data$WT.M, levels=c("WT", "M"))

mod <- lme(activity ~ time_scaled * WT.M, random=~1|mice, data = data)

cat("Estimates, errors and the significance")

## Estimates, errors and the significance
summary(mod)

## Linear mixed-effects model fit by REML
## Data: data
##      AIC      BIC    logLik
## 8681.339 8705.303 -4334.67
##
## Random effects:
## Formula: ~1 | mice
```

```
##          (Intercept) Residual
## StdDev:      14936.81 11161.46
##
## Fixed effects: activity ~ time_scaled * WT.M
##              Value Std.Error   DF   t-value p-value
## (Intercept)    38778.45   5335.29  388   7.268296  0.0000
## time_scaled    -20486.52  35588.68  388  -0.575647  0.5652
## WT.MM          -20324.26   7810.06   13  -2.602317  0.0219
## time_scaled:WT.MM -289880.69  52096.49  388  -5.564304  0.0000
## Correlation:
##              (Intr) tm_scl WT.MM
## time_scaled      0.000
## WT.MM           -0.683  0.000
## time_scaled:WT.MM 0.000 -0.683  0.000
##
## Standardized Within-Group Residuals:
##      Min      Q1      Med      Q3      Max
## -2.69133816 -0.63470177  0.03277689  0.63109234  3.19701990
##
## Number of Observations: 405
## Number of Groups: 15

cat("Bootstrap confidence intervals for the estimates")

## Bootstrap confidence intervals for the estimates
mod_lmer <- lmer(activity ~ time_scaled * WT.M + (1|mice), data = data)
confint.merMod(mod_lmer, method = "boot", nsim = 999)

## Computing bootstrap confidence intervals ...
##              2.5 %      97.5 %
## .sig01         8643.361   20403.180
## .sigma        10346.041   11960.872
## (Intercept)    28744.669   50179.240
## time_scaled    -93796.814   44322.642
## WT.MM          -36820.325   -5543.353
## time_scaled:WT.MM -390349.398 -187440.852

cat("ANOVA table")

## ANOVA table
anova.lme(mod, type = "marginal", adjustSigma = F)

##              numDF denDF   F-value p-value
## (Intercept)         1   388 52.82812 <.0001
## time_scaled         1   388  0.33137  0.5652
## WT.M                1    13  6.77206  0.0219
## time_scaled:WT.M     1   388 30.96148 <.0001
```

Analysis for alpha

```
wt <- read_xlsx("data/Alpha_Activity_analysis_4_R.xlsx", sheet = 1, na = "NA")
mut <- read_xlsx("data/Alpha_Activity_analysis_4_R.xlsx", sheet = 2, na = "NA")
```

```

wt <- wt %>%
  bind_cols(WT.M = rep("WT", nrow(wt)), time = decimal_date(ymd(wt$`Total_revolutions/day`)), .)%>%
  gather(mice, alpha, -c(1:5)) %>%
  mutate(time = time-min(time)) %>%
  select(-`Total_revolutions/day`)

mut <- mut %>%
  bind_cols(WT.M=rep("M", nrow(mut)), time = decimal_date(ymd(mut$`Total_revolutions/day`)), .)%>%
  gather(mice, alpha, -c(1:5)) %>%
  mutate(time = time-min(time)) %>%
  select(-`Total_revolutions/day`)

alpha_data <- wt %>% bind_rows(mut)

alpha_data <- alpha_data %>% filter(week>=3)
alpha_data<- na.omit(alpha_data)

alpha_data$mice <- factor(alpha_data$mice, levels= unique(alpha_data$mice))
alpha_data$time_scaled <- scale(alpha_data$time, scale=FALSE)
alpha_data$period <- factor(alpha_data$period, levels= unique(alpha_data$period))
alpha_data$WT.M <- factor(alpha_data$WT.M, levels=c("WT", "M"))
alpha_data$alpha <- as.numeric(alpha_data$alpha)

mod1 <- lme(alpha ~ time_scaled * WT.M, random=~1|mice, data = alpha_data, na.action = na.omit)

cat("Estimates, errors and the significance")

## Estimates, errors and the significance
summary(mod1)

## Linear mixed-effects model fit by REML
## Data: alpha_data
##      AIC      BIC    logLik
## 2068.243 2091.978 -1028.121
##
## Random effects:
## Formula: ~1 | mice
##      (Intercept) Residual
## StdDev:   0.6720236 3.405597
##
## Fixed effects: alpha ~ time_scaled * WT.M
##              Value Std.Error DF   t-value p-value
## (Intercept)  10.101010  0.334981 373 30.154013  0.0000
## time_scaled  -16.267322 11.031558 373 -1.474617  0.1412
## WT.MM        -0.714526  0.490361  13 -1.457142  0.1688
## time_scaled:WT.MM  2.360361 16.148547 373  0.146166  0.8839
## Correlation:
##              (Intr) tm_scl WT.MM
## time_scaled      0.000
## WT.MM           -0.683  0.000
## time_scaled:WT.MM 0.000 -0.683  0.000
##
## Standardized Within-Group Residuals:

```

```
##           Min           Q1           Med           Q3           Max
## -2.73631345 -0.48276146  0.06646042  0.49709145  3.94949030
##
## Number of Observations: 390
## Number of Groups: 15

cat("Bootstrap confidence intervals for the estimates")

## Bootstrap confidence intervals for the estimates
mod1_lmer <- lmer(alpha ~ time_scaled * WT.M + (1|mice), data = alpha_data)
confint.merMod(mod1_lmer, method = "boot", nsim = 999)

## Computing bootstrap confidence intervals ...
##
##           2.5 %       97.5 %
## .sig01       5.386829e-24  1.1201880
## .sigma       3.148692e+00  3.6392359
## (Intercept)   9.436860e+00 10.7416646
## time_scaled  -3.886561e+01  7.3806537
## WT.MM        -1.622018e+00  0.2386222
## time_scaled:WT.MM -3.048681e+01 34.6770024

cat("ANOVA table")

## ANOVA table
anova.lme(mod1, type = "marginal", adjustSigma = F)

##           numDF denDF  F-value p-value
## (Intercept)      1   373  909.2645 <.0001
## time_scaled      1   373   2.1745  0.1412
## WT.M             1    13   2.1233  0.1688
## time_scaled:WT.M  1   373   0.0214  0.8839
```

Analysis for period

```
wt <- read_xlsx("data/Period_analysis_4_R.xlsx", sheet = 1) %>% gather(mice, value, -1)
wt <- data.frame(WT.M=rep("WT", nrow(wt))) %>% bind_cols(wt)
mut <- read_xlsx("data/Period_analysis_4_R.xlsx", sheet = 2) %>% gather(mice, value, -1)
mut <- data.frame(WT.M=rep("M", nrow(mut))) %>% bind_cols(mut)

period_data <- wt %>% bind_rows(mut)
period_data$value <- as.numeric(period_data$value)

mod2 <- lme(value ~ week * WT.M, random = ~1|mice, data = period_data)

cat("Estimates, errors and the significance")

## Estimates, errors and the significance
summary(mod2)

## Linear mixed-effects model fit by REML
## Data: period_data
##           AIC      BIC    logLik
```

```
## 309.1875 328.7 -144.5938
##
## Random effects:
## Formula: ~1 | mice
## (Intercept) Residual
## StdDev: 0.7251103 3.268825
##
## Fixed effects: value ~ week * WT.M
## Value Std.Error DF t-value p-value
## (Intercept) 23.721429 1.265532 39 18.744234 0.0000
## weekDD_Week_2 -3.381429 1.747260 39 -1.935275 0.0602
## weekDD_Week_3 2.055714 1.747260 39 1.176536 0.2465
## weekLD_Week_3 0.208571 1.747260 39 0.119371 0.9056
## WT.MWT 0.137321 1.732901 13 0.079244 0.9380
## weekDD_Week_2:WT.MWT 3.251429 2.392535 39 1.358989 0.1820
## weekDD_Week_3:WT.MWT -2.426964 2.392535 39 -1.014390 0.3166
## weekLD_Week_3:WT.MWT -0.063571 2.392535 39 -0.026571 0.9789
## Correlation:
## (Intr) wkDD_W_2 wkDD_W_3 wkLD_W_3 WT.MWT wDD_W_2:
## weekDD_Week_2 -0.690
## weekDD_Week_3 -0.690 0.500
## weekLD_Week_3 -0.690 0.500 0.500
## WT.MWT -0.730 0.504 0.504 0.504
## weekDD_Week_2:WT.MWT 0.504 -0.730 -0.365 -0.365 -0.690
## weekDD_Week_3:WT.MWT 0.504 -0.365 -0.730 -0.365 -0.690 0.500
## weekLD_Week_3:WT.MWT 0.504 -0.365 -0.365 -0.730 -0.690 0.500
## wDD_W_3:
## weekDD_Week_2
## weekDD_Week_3
## weekLD_Week_3
## WT.MWT
## weekDD_Week_2:WT.MWT
## weekDD_Week_3:WT.MWT
## weekLD_Week_3:WT.MWT 0.500
##
## Standardized Within-Group Residuals:
## Min Q1 Med Q3 Max
## -5.938352181 -0.067963537 -0.001414478 0.093674882 1.778532447
##
## Number of Observations: 60
## Number of Groups: 15
```

```
cat("Bootstrap confidence intervals for the estimates")
```

```
## Bootstrap confidence intervals for the estimates
```

```
mod2_lmer <- lmer(value ~ week * WT.M + (1|mice), data = period_data)
confint.merMod(mod2_lmer, method = "boot", nsim = 999)
```

```
## Computing bootstrap confidence intervals ...
```

```
## 2.5 % 97.5 %
## .sig01 0.000000 2.08600463
## .sigma 2.457618 3.79672236
## (Intercept) 21.350624 26.08873235
## weekDD_Week_2 -6.829508 0.06209273
```

```
## weekDD_Week_3      -1.268164  5.44414614
## weekLD_Week_3      -3.239692  3.69206314
## WT.MWT             -3.194185  3.27042623
## weekDD_Week_2:WT.MWT -1.170840  7.92218587
## weekDD_Week_3:WT.MWT -6.937359  1.98217656
## weekLD_Week_3:WT.MWT -4.689009  4.59438116
```

```
cat("ANOVA table")
```

```
## ANOVA table
```

```
anova.lme(mod2, type = "marginal", adjustSigma = F)
```

```
##          numDF denDF  F-value p-value
## (Intercept)      1    39 351.3463  <.0001
## week            3    39   3.3611  0.0282
## WT.M            1    13   0.0063  0.9380
## week:WT.M       3    39   1.9008  0.1454
```