Longitudinal Data Analysis

Case study of Trenal.XLS using Linear Mixed Effect Model

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Theory of Linear Mixed Effects Model(LMM)

Index description

Let us assume that a given input data set X has a dimension $N \times p$, with N observations and p predictors.

For each subject indexed with $i, i = 1, \cdots, I$, we can build a linear mixed effect model

$$\mathbf{Y_i} = \mathbf{X_i}\beta + \mathbf{Z_i b_i} + \epsilon_\mathbf{i}$$

The application of LMM

Linear Mixed Effects Model is used to analyse a data set, where the observations are not fully independent, while the top level clusters are assumed independent. Inside each cluster, the observations are correlated

Data set `Trenal.XLS` pre-analysis

The summary of the data set

Import data

```
library(readxl)
trenal <- read_excel("Trenal.XLS") # summary(trenal)
```

Data Preprocessing

```
trenal= trenal[,-18] #remove a noninformative column const
# Continuous or discrete variables
trenal$id = as.factor(trenal$id)
trenal$j = as.factor(trenal$j)
trenal$male = as.factor(trenal$male)
trenal$cardio = as.factor(trenal$cardio)
trenal$reject = as.factor(trenal$reject)

trenal.long = trenal[,13:20] # long table form
trenal.wide = trenal[,1:17] # wide table form

library(magrittr) # needs to be run every time you start R and want to use %>%
library(dplyr)
```

```
##
## Attaching package: 'dplyr'

## The following objects are masked from 'package:stats':
##
##     filter, lag

## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

```
data.long <- trenal.long %>% # reordered long table
  relocate(id) %>%
  relocate(j,.after=id)%>%
  relocate(time,.after = j)%>%
  relocate(respons,.after=time)
#summary(data.long)
sum(!is.na(data.long$respons))
```

```
## [1] 9558
```

```
data.long.noNA <- na.omit(data.long)# reordered long table without NAs
summary(data.long.noNA)
```

```
##        id              j             time           respons           age
##  3      :  12   2      :1159   Min.   : 0.000   Min.   :14.00   Min.   :15.00
##  5      :  12   1      :1158   1st Qu.: 1.000   1st Qu.:34.00   1st Qu.:35.00
##  6      :  12   3      :1158   Median : 3.000   Median :38.00   Median :46.00
##  8      :  12   4      :1072   Mean   : 3.432   Mean   :38.24   Mean   :45.27
##  9      :  12   5      : 954   3rd Qu.: 6.000   3rd Qu.:42.00   3rd Qu.:56.00
##  10     :  12   6      : 845   Max.   :10.000   Max.   :65.00   Max.   :76.00
##  (Other):9479   (Other):3205
##  male     cardio   reject
##  0:4213   0:7927   0:6314
##  1:5338   1:1624   1:3237
##
##
##
##
##
```

```
data.long.noNA$id[length(data.long.noNA$id)]
```

```
## [1] 1160
## 1160 Levels: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 ... 1160
```

Response variable and predictors

Response variable From the `summary(data.long.noNA)`, we can read that the response variable is a continuous variable `respons` HC level from $(15, 76)$ with Mean 38.24.

We have totally $I = 1160$ ids for subjects. Ideally each id would have 12 (start from $HC_0, HC_{0.5}, HC_1, HC_2, \cdots, HC_{10}$) HC level measurement, but in really not all subjects have all of the 12 measurements. We have totally $N = 9558 = \sum_{i=1}^{I} n_i$ missing values.

Predictors The explaining variables are

1. $X_1 = time$ in year as discrete values, only changes with j,$j = 1, \cdots, n_i$
2. $X_2 = age$ in year with 12 NAs; will only change with subject id i
3. $X_3 = male$ $0 =$ female, $1=$ male;will only change with subject id i
4. $X_4 = cardio$ $0 =$ no, $1=$ yes;will only change with subject id i
5. $X_5 = reject$ $0 =$ accept, $1=$ reject;will only change with subject id i
6. fixed intercept, continuous

In the data analysis part, we need to try out different variables accounting for fixed effects and random effects.

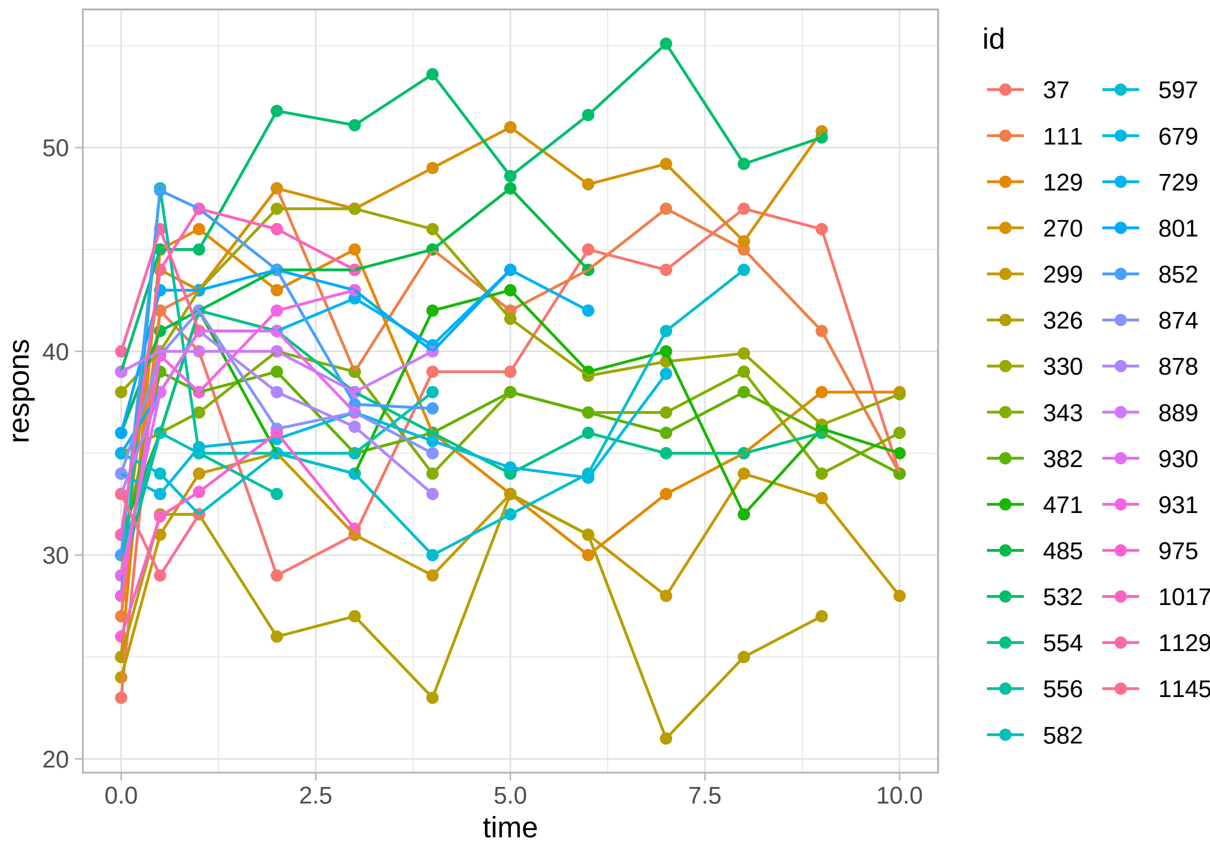
Data visualization and the information from the data

```
library(ggplot2)
dim(data.long.noNA)
```

```
## [1] 9551    8
```

```
# since the data dimension is large 9551 x 8, we can select random 30 data to have a look
set.seed(1)
selected <- sample(1:length(unique(data.long.noNA$id)),30,replace=T) # random samples and permutations
#selected.vector = as.vector(selected)
data.selected = data.long.noNA[(data.long.noNA$id %in% c(selected)), ]
```

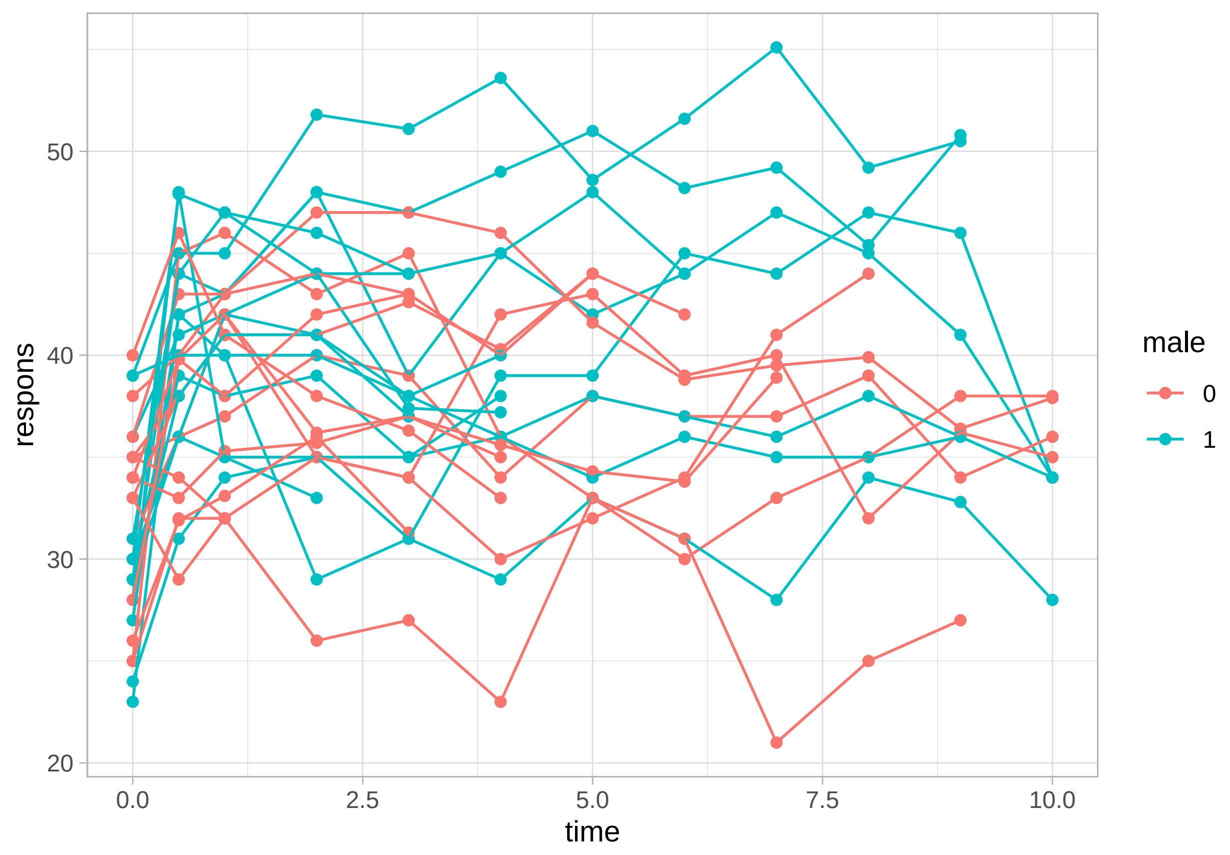
```
ggplot(data.selected,aes(x=time,y=respons,group=id,color=id))+geom_point()+ geom_line()+theme_light()
```



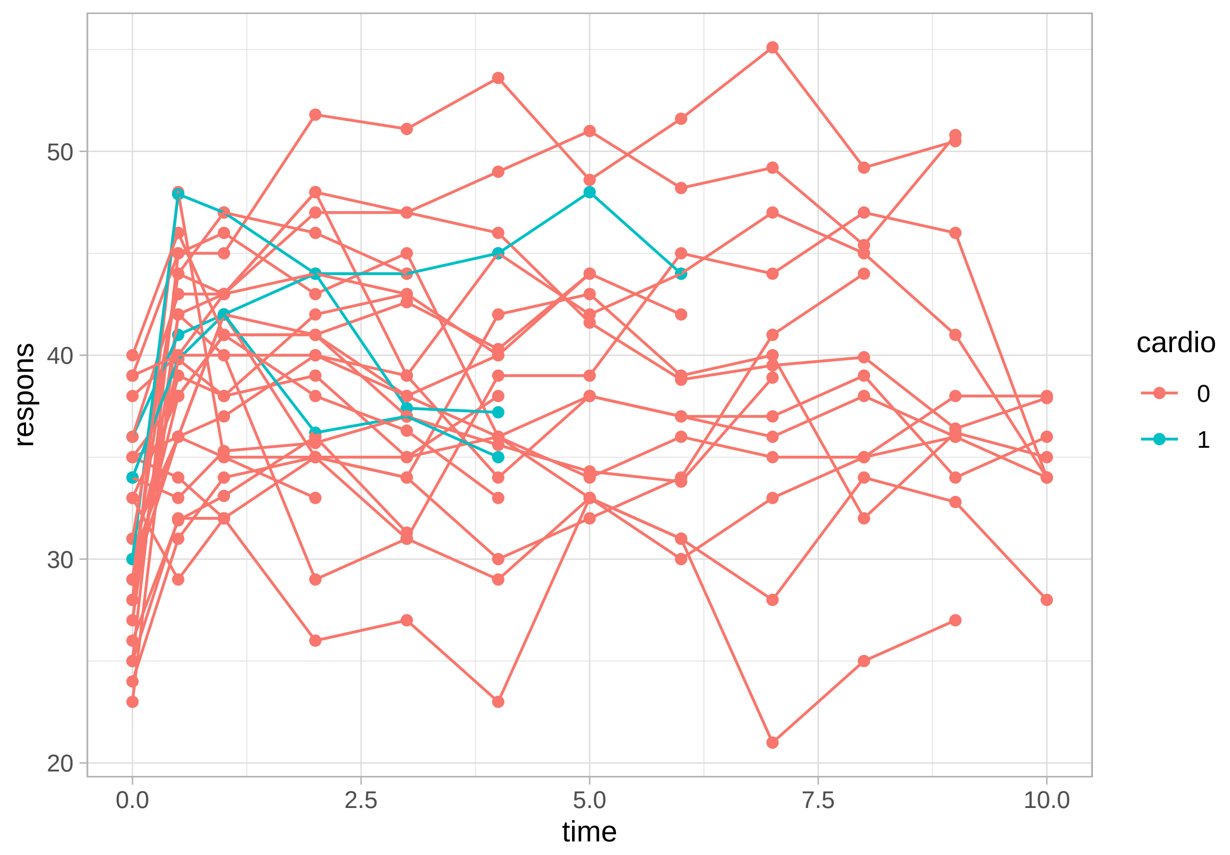
Spaghettic plot

Plot Info: The intercept may vary according to each individual The slope is not very easy to see

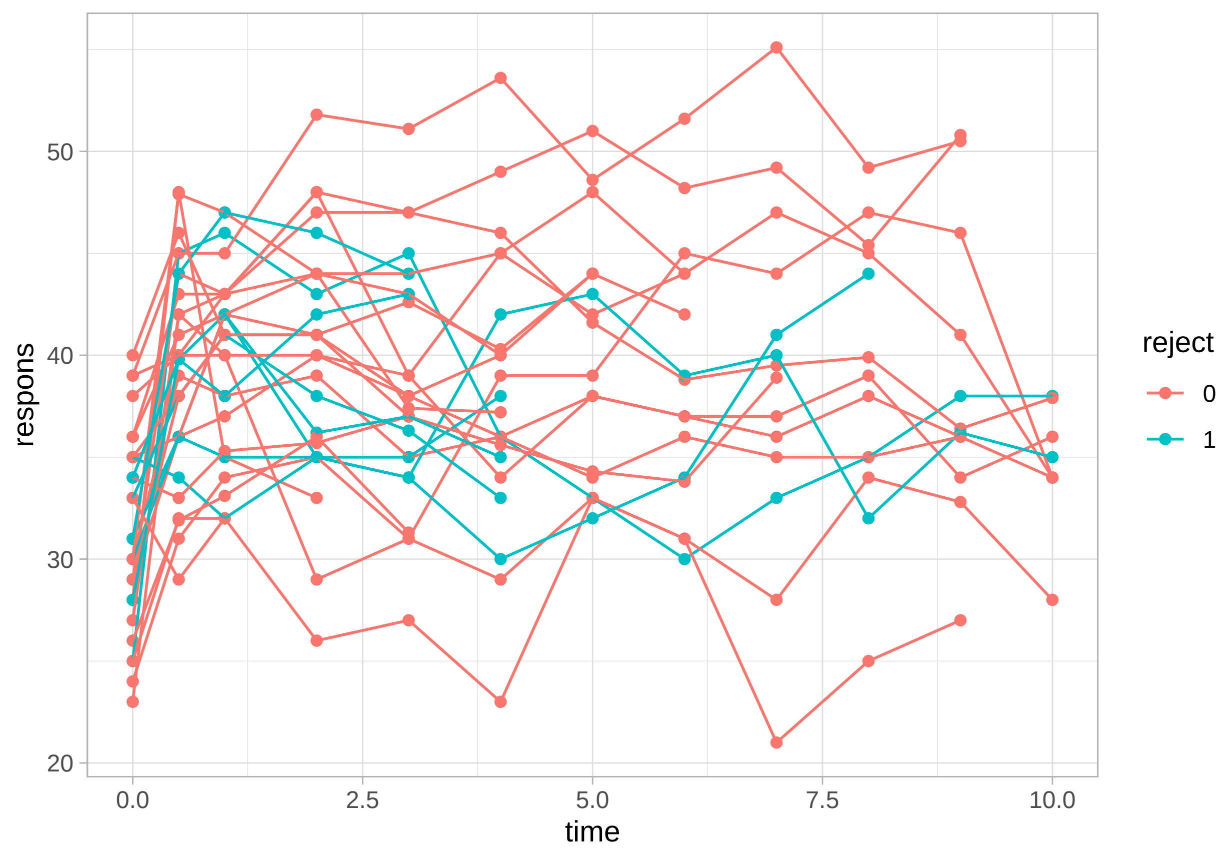
```
ggplot(data.selected,aes(x=time,y=respons,group=id,color=male)) +geom_point()+ geom_line()+theme_light(
```



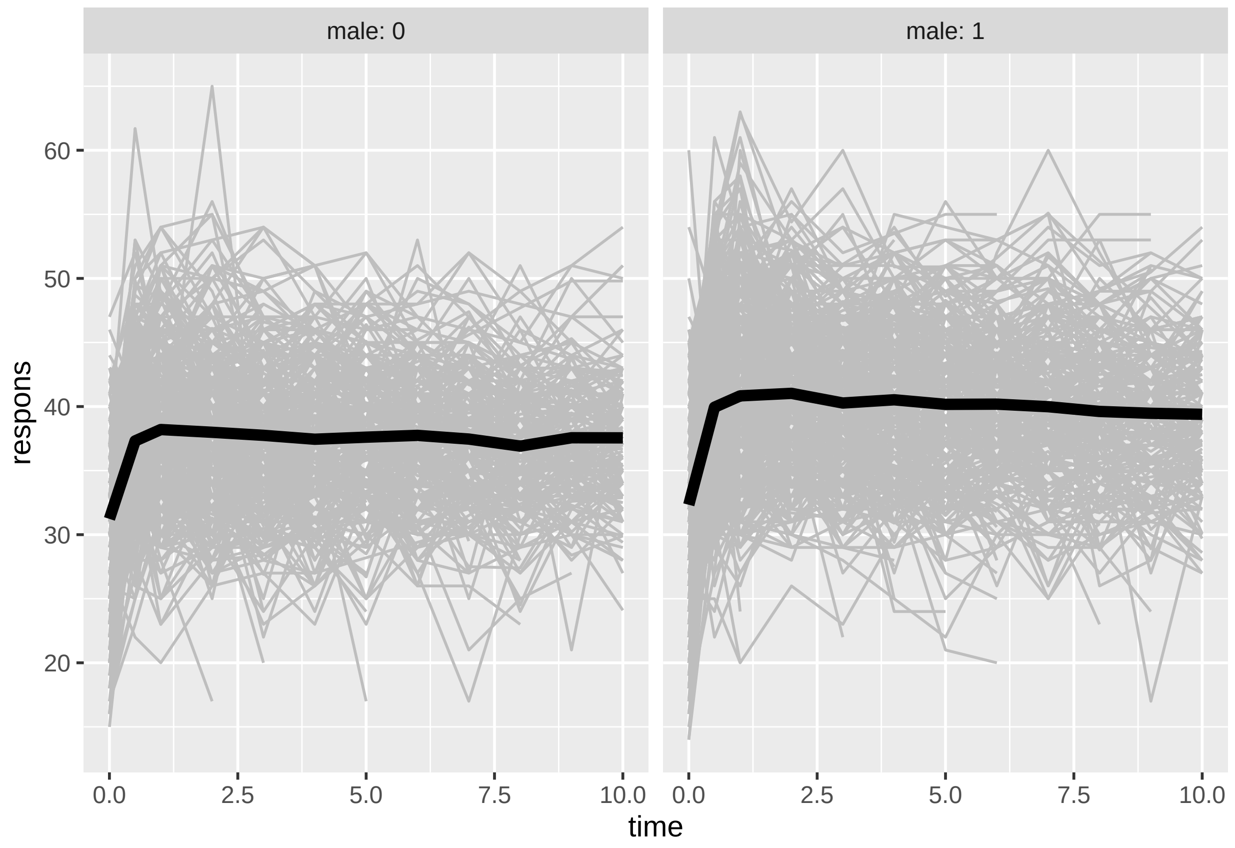
```
ggplot(data.selected,aes(x=time,y=respons,group=id,color=cardio)) +geom_point()+ geom_line()+theme_ligh
```



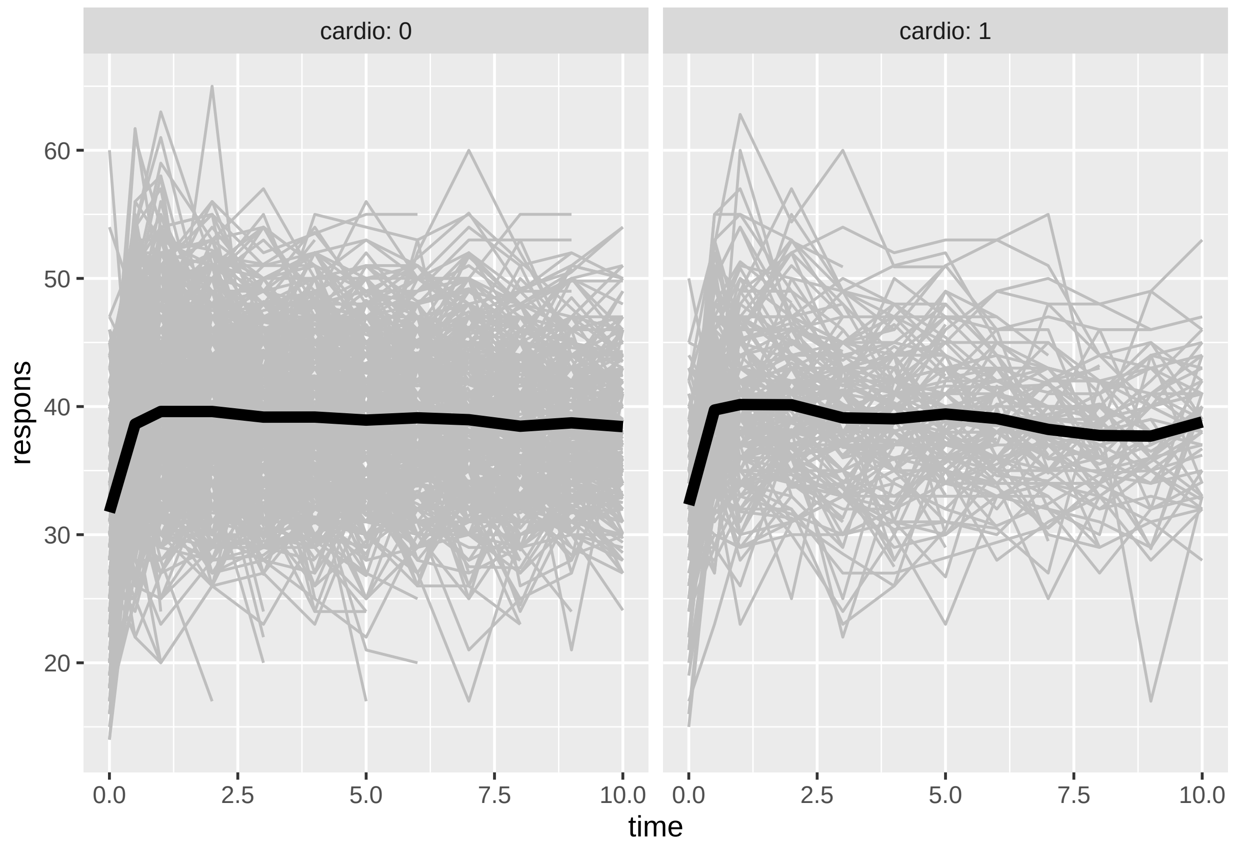
```
ggplot(data.selected,aes(x=time,y=respons,group=id,color=reject)) +geom_point()+ geom_line()+theme_ligh
```



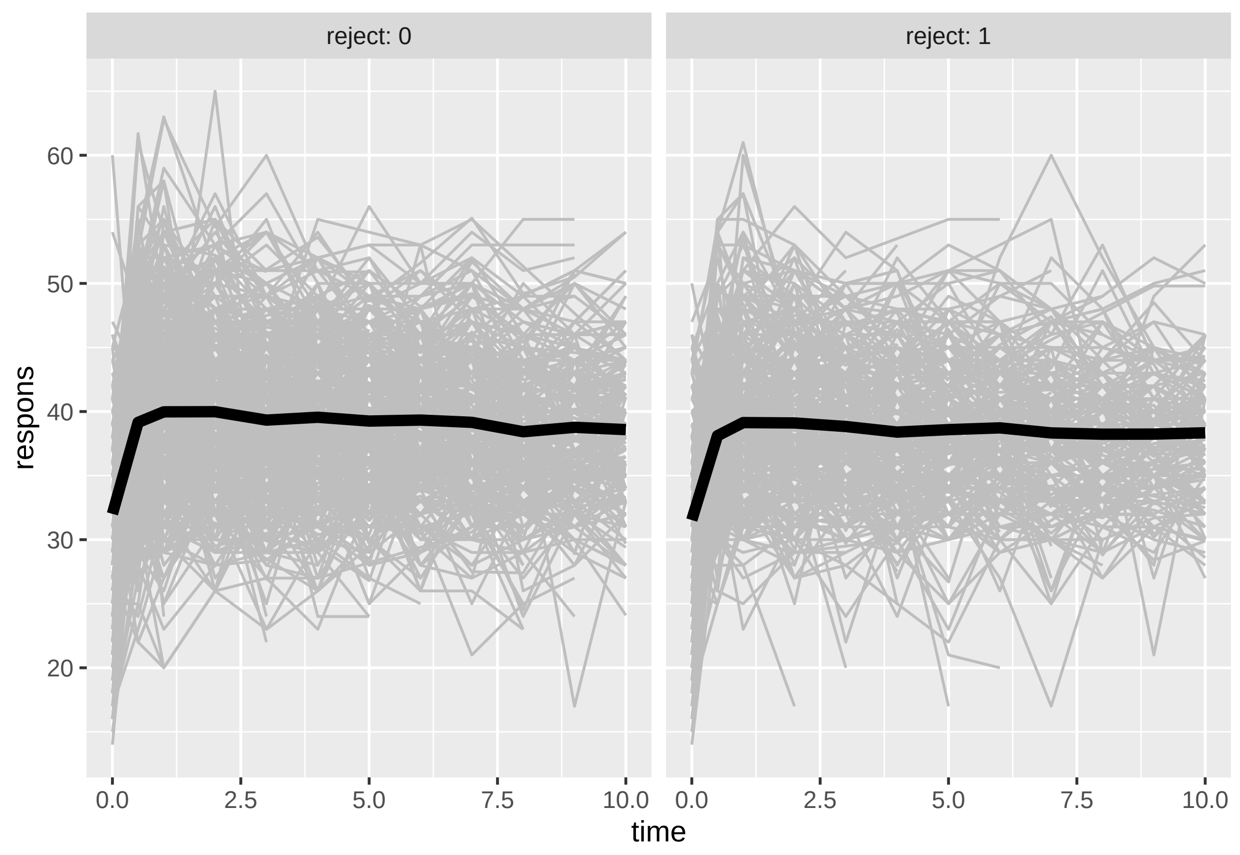
```
# Spaghetti Ggplot separated by male =1
p <- ggplot(data=data.long.noNA,aes(x=time,y=respons,group=id))
p <- p + geom_line(col="grey")+stat_summary(aes(group=1),geom="line",fun=mean,linewidth=2)
p + facet_grid(~male,labeller=label_both)
```



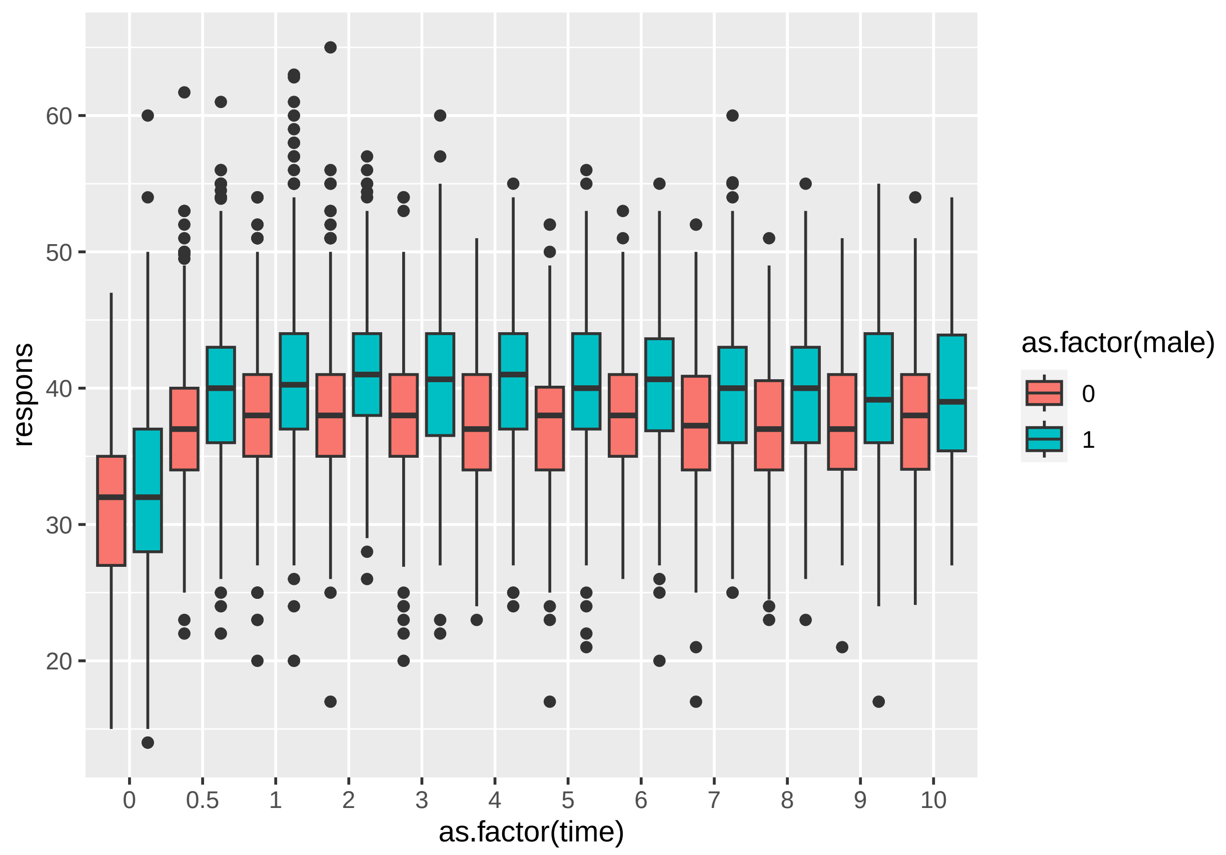
```r
# Spaghetti Ggplot separated by cardio
p <- ggplot(data=data.long.noNA,aes(x=time,y=respons,group=id))
p <- p + geom_line(col="grey")+stat_summary(aes(group=1),geom="line",fun=mean,linewidth=2)
cardio.labs <- c("Cardio = 0","Cardio = 1")
p + facet_grid(~cardio,labeller = label_both)
```



```
# Spaghetti Ggplot separated by reject =1
p <- ggplot(data=data.long.noNA,aes(x=time,y=respons,group=id))
p <- p + geom_line(col="grey")+stat_summary(aes(group=1),geom="line",fun=mean,linewidth=2)
p + facet_grid(~reject,labeller=label_both)
```

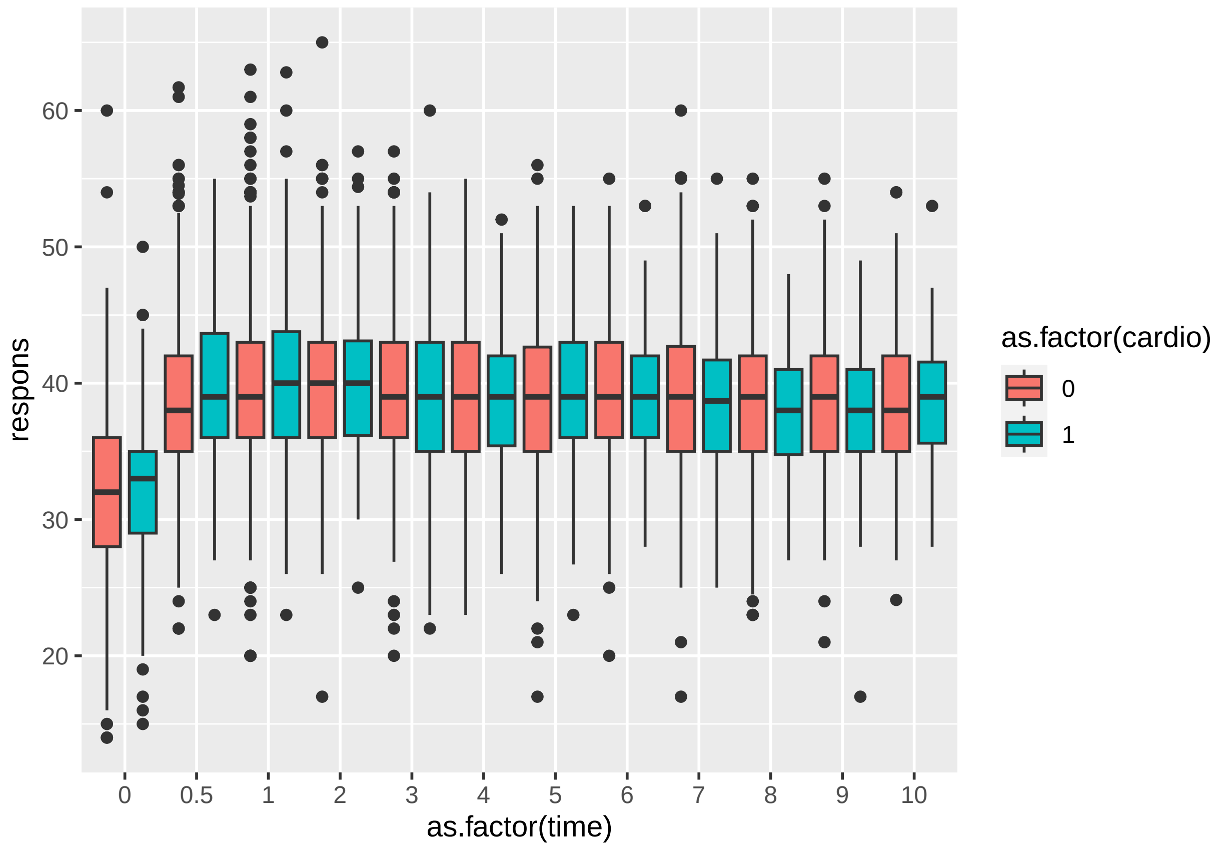


```
# Box plot by sex
ggplot(data.long.noNA,aes(x=as.factor(time),y=respons,fill=as.factor(male)))+
  geom_boxplot(position=position_dodge(1))
```

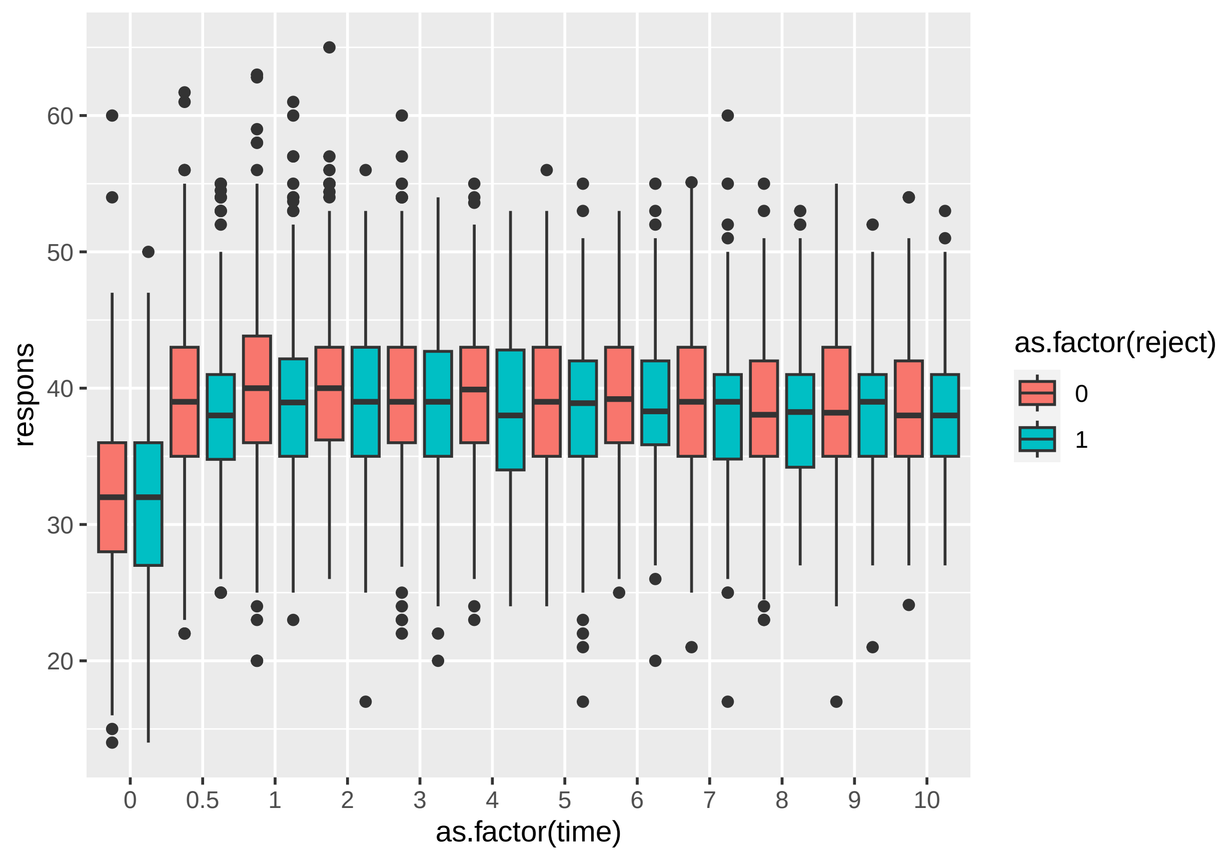


Boxplot

```
# Box plot by cardio
ggplot(data.long.noNA,aes(x=as.factor(time),y=respons,fill=as.factor(cardio)))+
  geom_boxplot(position=position_dodge(1))
```



```
# Box plot by reject
ggplot(data.long.noNA,aes(x=as.factor(time),y=respons,fill=as.factor(reject)))+
  geom_boxplot(position=position_dodge(1))
```



#### Correlation plot of Hc levels in different time

```
HcCorr = trenal.wide[,c(1:12)]
cor(HcCorr,use="complete.obs" ) # also COV for covariance
```

```
##             HC0      HC06       HC1       HC2       HC3       HC4       HC5
## HC0  1.00000000 0.2264123 0.1587116 0.1724777 0.2139805 0.1732267 0.1557624
## HC06 0.22641235 1.0000000 0.7562367 0.6233688 0.5520591 0.5278499 0.5143061
## HC1  0.15871158 0.7562367 1.0000000 0.7315995 0.6656006 0.6119867 0.5873331
## HC2  0.17247771 0.6233688 0.7315995 1.0000000 0.7284046 0.6382434 0.5996189
## HC3  0.21398049 0.5520591 0.6656006 0.7284046 1.0000000 0.7733522 0.7016965
## HC4  0.17322666 0.5278499 0.6119867 0.6382434 0.7733522 1.0000000 0.7888249
## HC5  0.15576243 0.5143061 0.5873331 0.5996189 0.7016965 0.7888249 1.0000000
## HC6  0.13620085 0.4569881 0.5004036 0.4869519 0.5786122 0.6814132 0.7592203
## HC7  0.10156045 0.3936597 0.4541699 0.4724703 0.5402798 0.6466212 0.7067887
## HC8  0.08419757 0.3687935 0.4454882 0.4244221 0.5030428 0.6040136 0.6080051
## HC9  0.08859254 0.3711560 0.4254622 0.3971477 0.4303661 0.5461579 0.5713338
## HC10 0.09718506 0.4210917 0.4301937 0.4647890 0.4972001 0.5629570 0.5800544
##            HC6       HC7        HC8        HC9       HC10
## HC0  0.1362008 0.1015604 0.08419757 0.08859254 0.09718506
## HC06 0.4569881 0.3936597 0.36879347 0.37115604 0.42109175
## HC1  0.5004036 0.4541699 0.44548815 0.42546216 0.43019368
## HC2  0.4869519 0.4724703 0.42442213 0.39714773 0.46478897
## HC3  0.5786122 0.5402798 0.50304282 0.43036614 0.49720006
## HC4  0.6814132 0.6466212 0.60401365 0.54615793 0.56295695
## HC5  0.7592203 0.7067887 0.60800514 0.57133378 0.58005440
## HC6  1.0000000 0.7414970 0.67347761 0.62938253 0.60329422
## HC7  0.7414970 1.0000000 0.71838142 0.63933448 0.65646214
## HC8  0.6734776 0.7183814 1.00000000 0.70316750 0.68501304
## HC9  0.6293825 0.6393345 0.70316750 1.00000000 0.74259683
## HC10 0.6032942 0.6564621 0.68501304 0.74259683 1.00000000
```

```
library("PerformanceAnalytics")
```

```
## Warning: package 'PerformanceAnalytics' was built under R version 4.2.3

## Loading required package: xts

## Loading required package: zoo

##
## Attaching package: 'zoo'

## The following objects are masked from 'package:base':
##
##     as.Date, as.Date.numeric

##
## ################################### WARNING ###################################
## # We noticed you have dplyr installed. The dplyr lag() function breaks how    #
## # base R's lag() function is supposed to work, which breaks lag(my_xts).      #
## #                                                                             #
## # Calls to lag(my_xts) that you enter or source() into this session won't     #
## # work correctly.                                                             #
## #                                                                             #
## # All package code is unaffected because it is protected by the R namespace   #
## # mechanism.                                                                  #
## #                                                                             #
## # Set `options(xts.warn_dplyr_breaks_lag = FALSE)` to suppress this warning.  #
## #                                                                             #
## # You can use stats::lag() to make sure you're not using dplyr::lag(), or you #
## # can add conflictRules('dplyr', exclude = 'lag') to your .Rprofile to stop   #
## # dplyr from breaking base R's lag() function.                                #
## ################################### WARNING ###################################

##
## Attaching package: 'xts'

## The following objects are masked from 'package:dplyr':
##
##     first, last

##
## Attaching package: 'PerformanceAnalytics'

## The following object is masked from 'package:graphics':
##
##     legend
```

```
chart.Correlation(HcCorr,historgram=TRUE)
```

```
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```
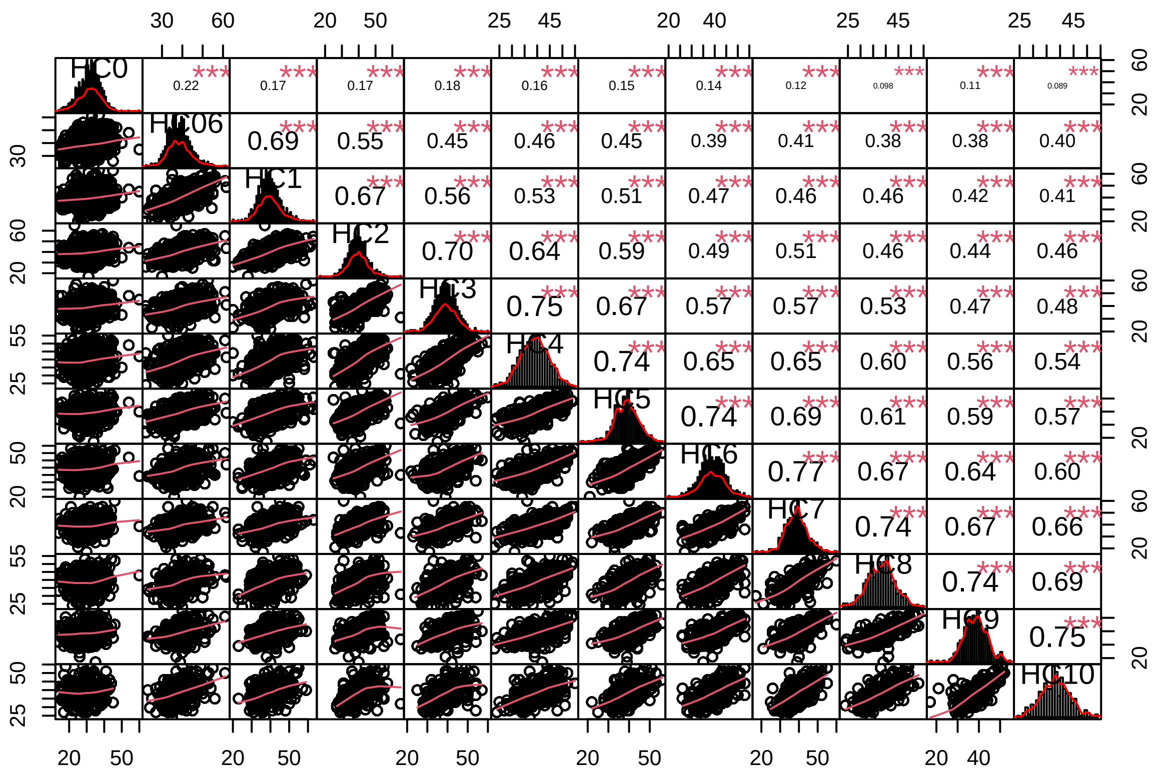



Hypothesis based on the plot 1.Age 2.Male 3.Cardio 4.Reject

Data set `Trenal.XLS` analysis with the linear mixed effects model

The chosen of fixed effects variable

We can choose all the predictors as the fixed effect variables, plus an intercept ## The chosen of random effects variable

This is an R Markdown document. Markdown is a simple formatting syntax for authoring HTML, PDF, and MS Word documents. For more details on using R Markdown see http://rmarkdown.rstudio.com.

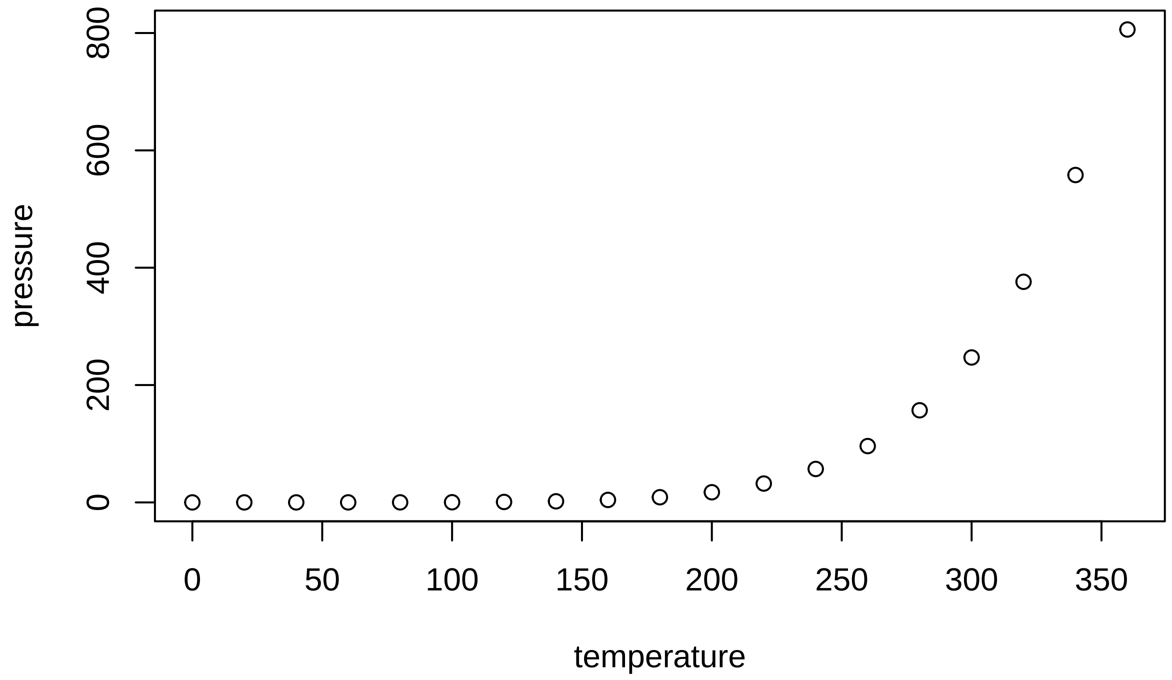
When you click the **Knit** button a document will be generated that includes both content as well as the output of any embedded R code chunks within the document. You can embed an R code chunk like this:

```
summary(cars)
```

```
##      speed           dist       
##  Min.   : 4.0   Min.   :  2.00  
##  1st Qu.:12.0   1st Qu.: 26.00  
##  Median :15.0   Median : 36.00  
##  Mean   :15.4   Mean   : 42.98  
##  3rd Qu.:19.0   3rd Qu.: 56.00  
##  Max.   :25.0   Max.   :120.00  
```

Including Plots

You can also embed plots, for example:



Note that the `echo = FALSE` parameter was added to the code chunk to prevent printing of the R code that generated the plot.