Final Project: First Draft

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Contents

Questions for Kan

- Why are there 7 treatment groups now?
  - Treatment 1-3: different doses for 1st drug
  - Treatment 4-6: different doses for 2nd drug
  - Treatment 7: control
- Next steps:
  - add outlier detection
  - create a new file to include only relevant sections

Exploratory Data Analysis

Data preparation

```
## Response [https://raw.githubusercontent.com/luokan1227/537P1/master/Data.xlsx]
##   Date: 2020-10-23 06:00
##   Status: 200
##   Content-Type: application/octet-stream
##   Size: 341 kB
## <ON DISK>  C:\Users\shihn\AppData\Local\Temp\RtmpuaeS8v\file1e2422cb15a0.xlsx
```

```
## Response [https://raw.githubusercontent.com/luokan1227/537P1/master/MonkeyID.xlsx]
##   Date: 2020-10-23 06:00
##   Status: 200
##   Content-Type: application/octet-stream
##   Size: 50.1 kB
## <ON DISK>  C:\Users\shihn\AppData\Local\Temp\RtmpuaeS8v\file1e2461681e67.xlsx
```

```
## 
##    1    2    3    4    5    6    7 
##  117  142 1045 1104   25   24    8
```

```
## 
##       1   2   3   4   5   6   7 
##   3 127 917 352 303 148 474 138
```

```
## 
##    1    2    3    4    5    6 
##  130   64   90 1368  468  345
```

```
## 
##   1  10  11   2   3   4   5   6   7   9 
## 890  43  15 800 450  39  84  47  93   4
```

```
## 
##    1    2    3    4    5    6 
##  674 1099  220  385    1   86
```

Two datasets for analysis:

- `Data`: Kan has been using this one.
- `Data2`: Shih-Ni created this subset, which removed some ID info that we won't use and added extracted information from antibodies.

Contingency Tables

```
table(Data2$MonkeyID)
```

```
## 
## 6104 6105 6107 6117 6118 6119 6125 6132 6160 6193 6199 6200 6201 6202 6203 6204 
##   35  228  239  243    7   55  216  251  183  117   48  191   73   78  238  156 
## 6205 6209 6210 6214 
##    5   46   50    6
```

```
table(Data2$Time_Point)
```

```
## 
##    0    1    2    3 
##  273 1004  823  365
```

```
table(Data2$Treatment)
```

```
## 
## group 1 group 2 group 3 group 4 group 5 group 6 group 7 
##     582     170      96     444     374     131     668
```

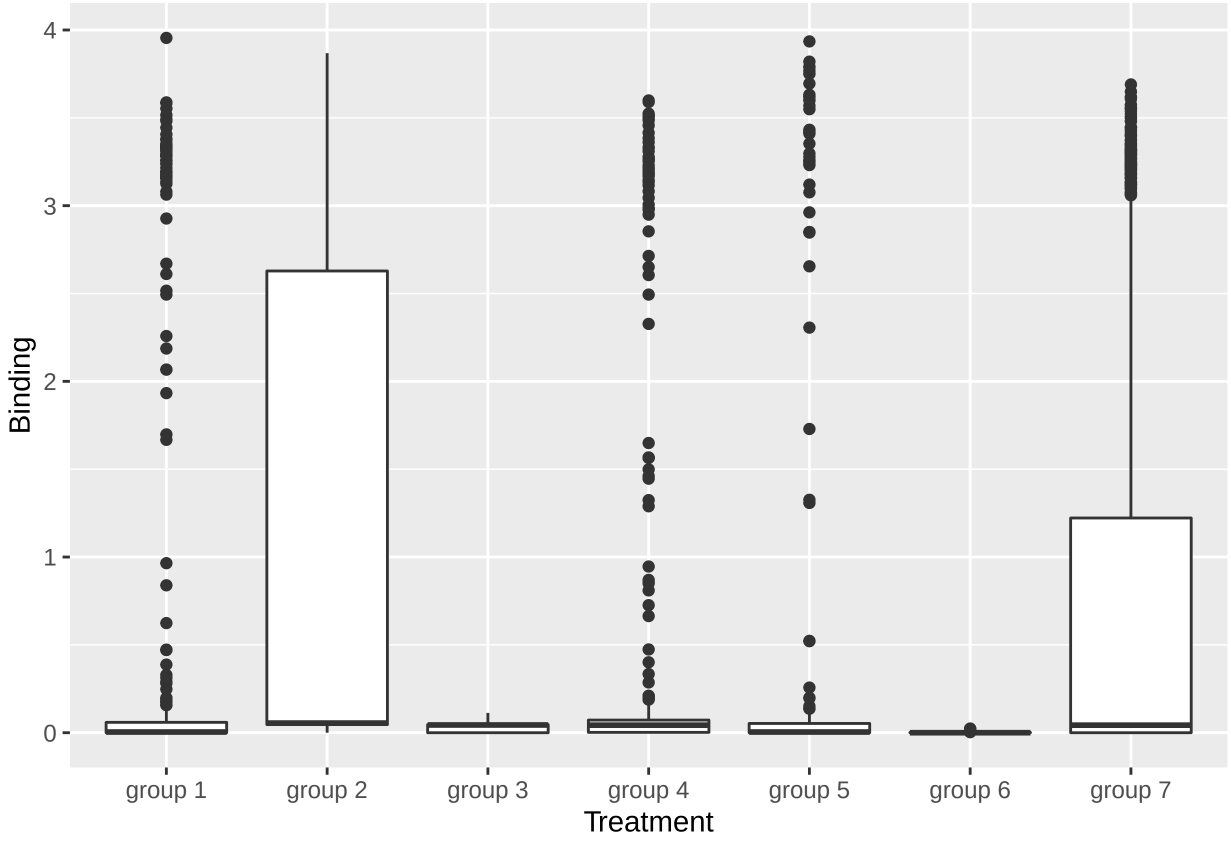
```
table(Data2$Time_Point, Data2$Treatment)
```

```
##    
##     group 1 group 2 group 3 group 4 group 5 group 6 group 7
##   0     129       0       0      90       0       0      54
##   1     190      60      96     105     297     131     125
##   2     141     110       0     148      77       0     347
##   3     122       0       0     101       0       0     142
```

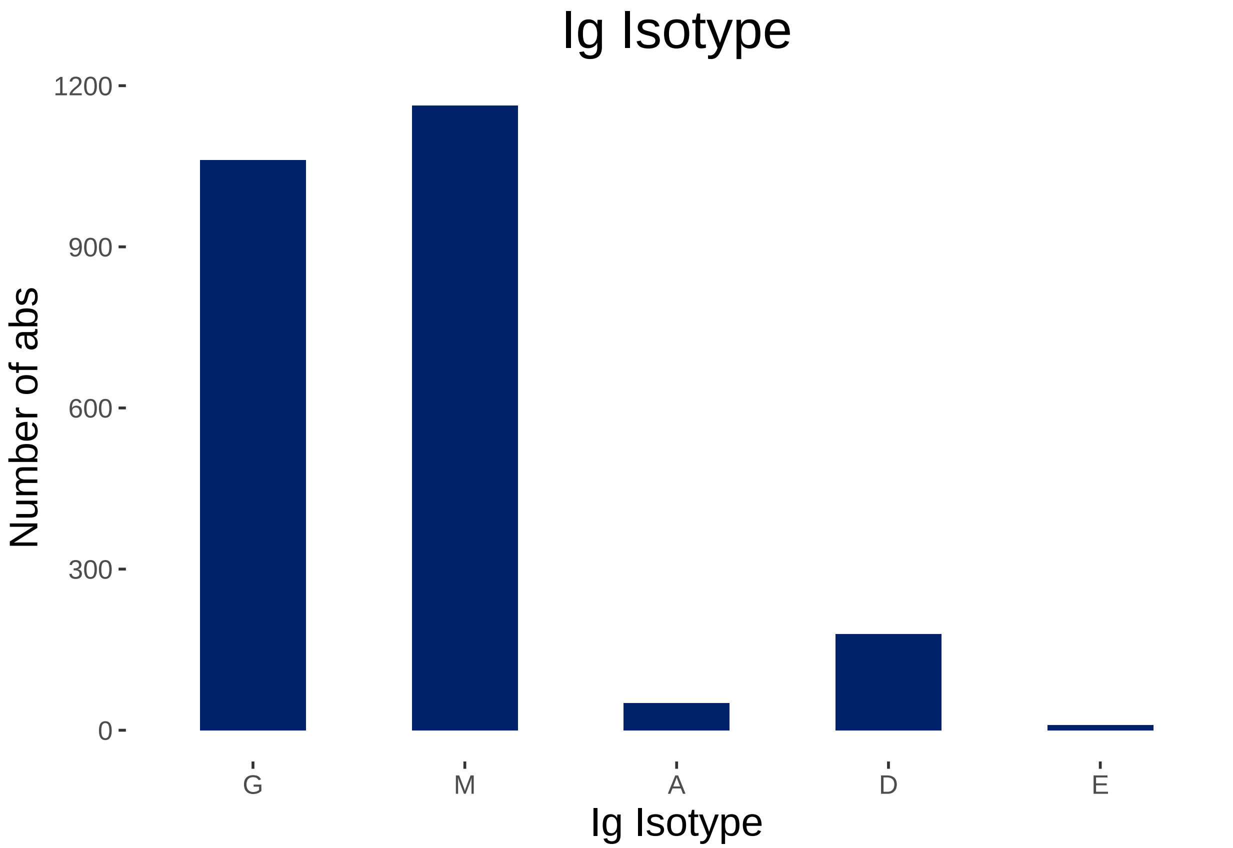
```r
table(Data2$MonkeyID, Data2$Treatment)
```

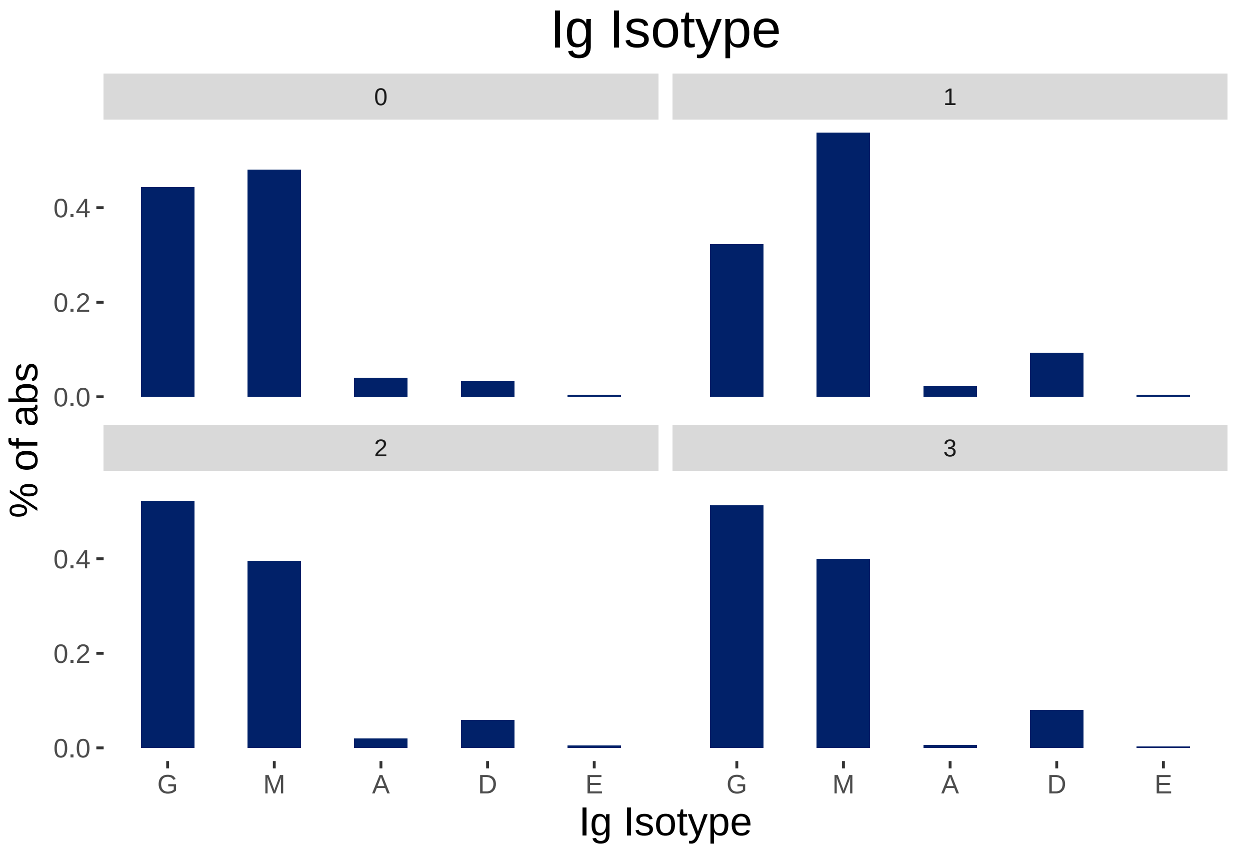
```
##
##        group 1 group 2 group 3 group 4 group 5 group 6 group 7
##   6104       0       0      35       0       0       0       0
##   6105       0       0       0     228       0       0       0
##   6107       0       0       0       0       0       0     239
##   6117     243       0       0       0       0       0       0
##   6118       0       7       0       0       0       0       0
##   6119       0       0      55       0       0       0       0
##   6125       0       0       0     216       0       0       0
##   6132       0       0       0       0     251       0       0
##   6160     183       0       0       0       0       0       0
##   6193       0     117       0       0       0       0       0
##   6199       0       0       0       0       0      48       0
##   6200       0       0       0       0       0       0     191
##   6201       0       0       0       0      73       0       0
##   6202       0       0       0       0       0      78       0
##   6203       0       0       0       0       0       0     238
##   6204     156       0       0       0       0       0       0
##   6205       0       0       0       0       0       5       0
##   6209       0      46       0       0       0       0       0
##   6210       0       0       0       0      50       0       0
##   6214       0       0       6       0       0       0       0
```

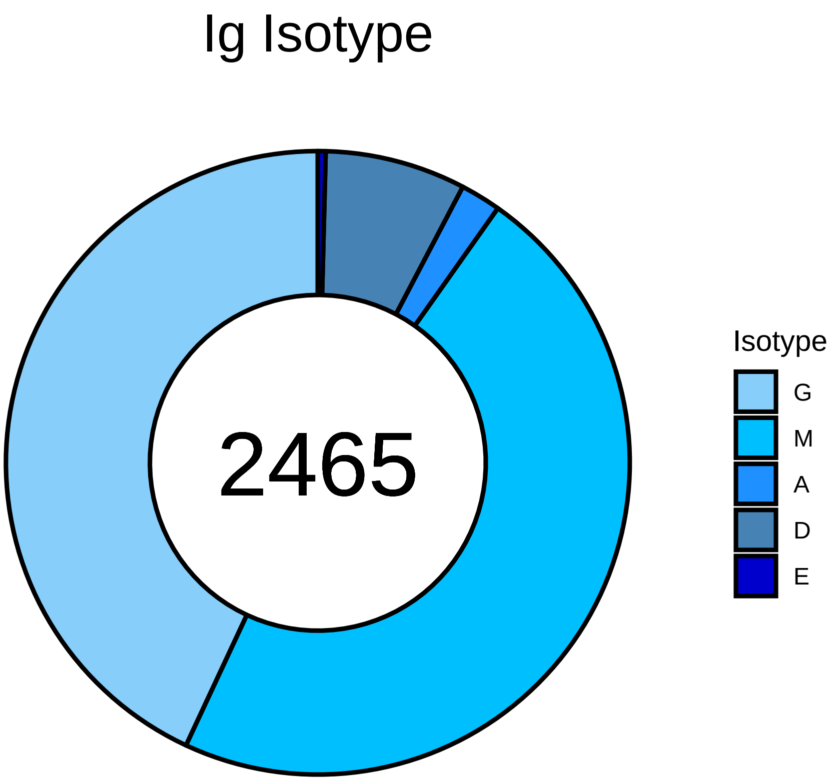
```r
ggplot(Data2, aes(x = Treatment, y = Binding)) + geom_boxplot()
```



Isotype Plots and Table

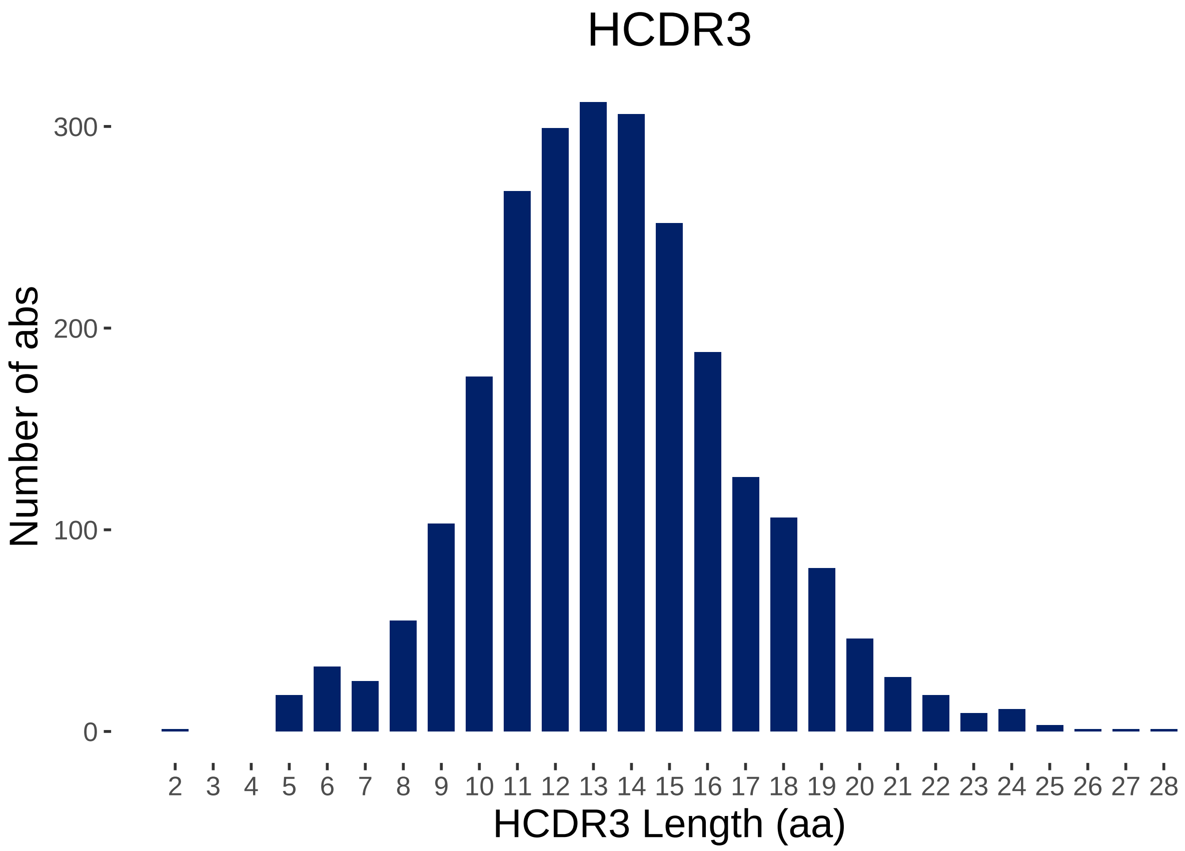


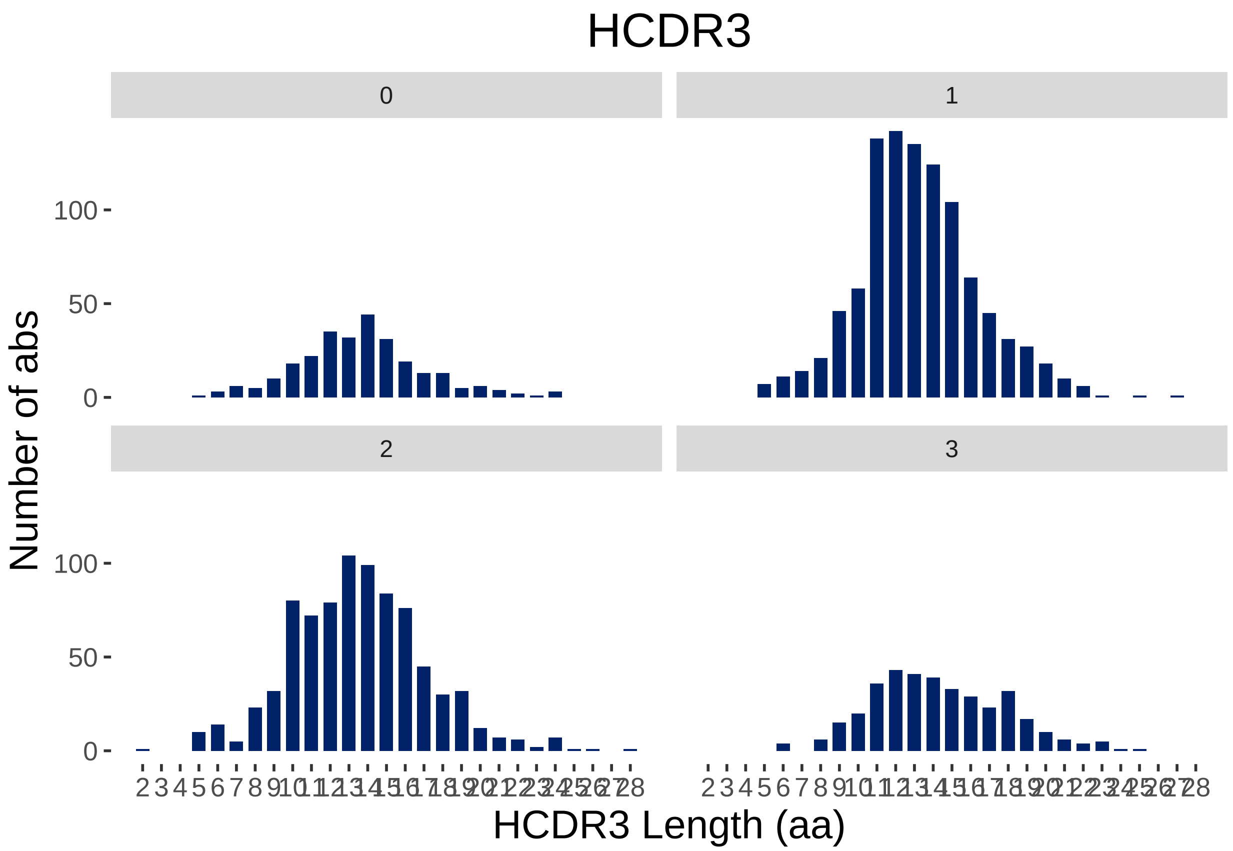


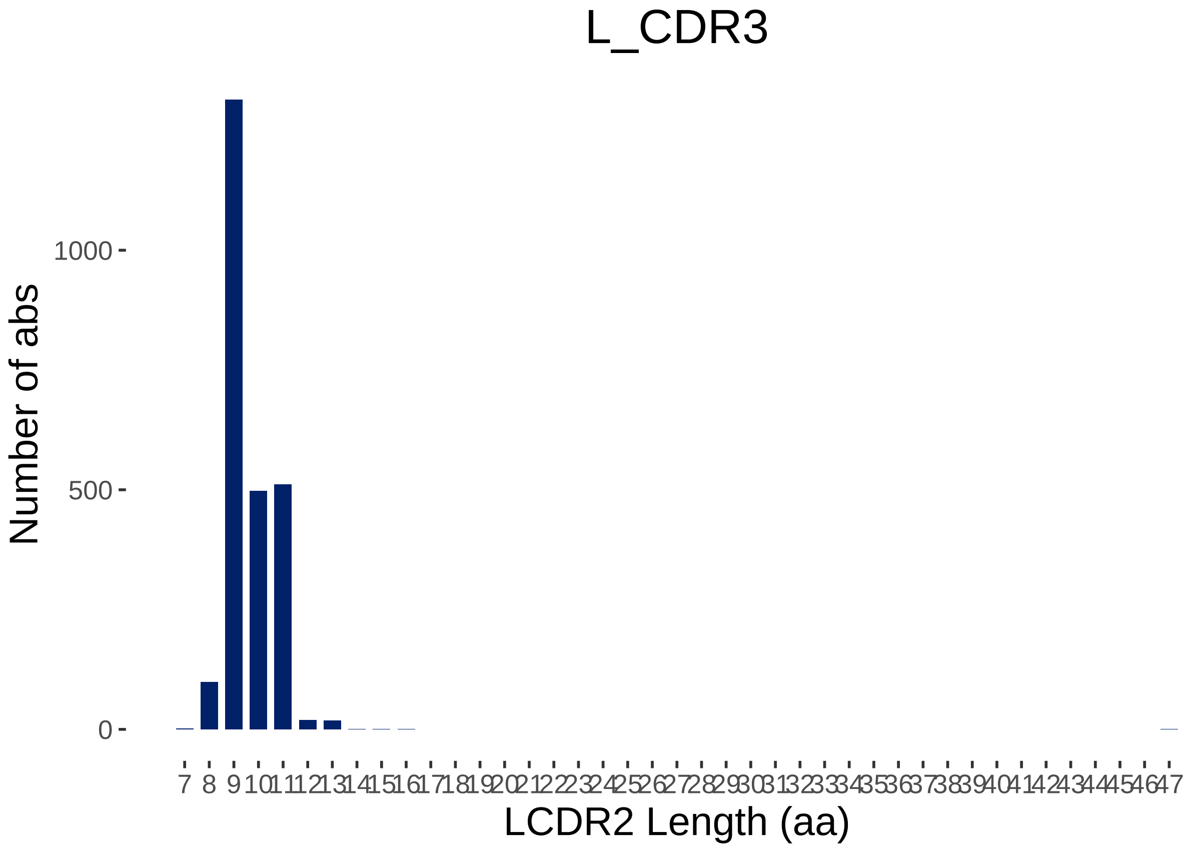


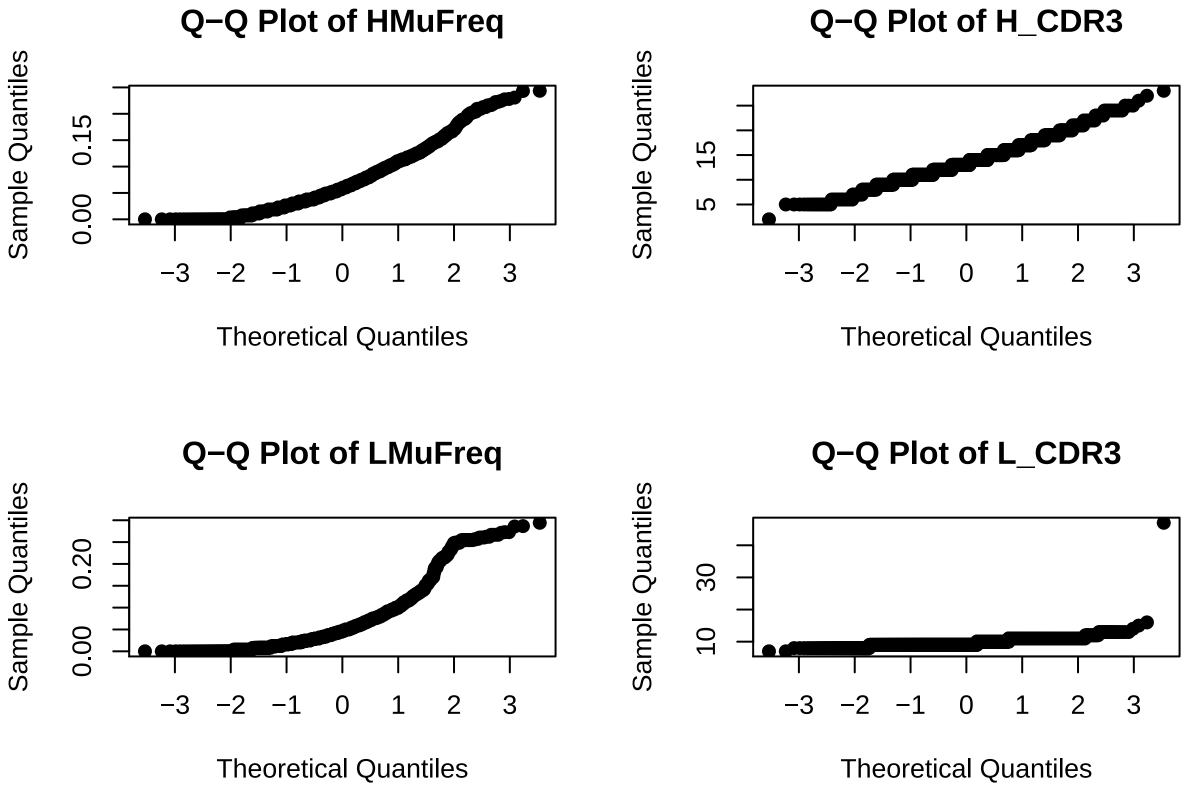
```
##   Isotype Ab # Ab %
## 1       A   51  2.1
## 2       D  179  7.3
## 3       E   10  0.4
## 4       G 1062 43.1
## 5       M 1163 47.2
```

CDR_3 Plots and tables






L_CDR3
Number of abs
1000
500
0
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 34 35 36 37 38 39 40 41 42 43 44 45 46 47
LCDR2 Length (aa)



Outlier detection

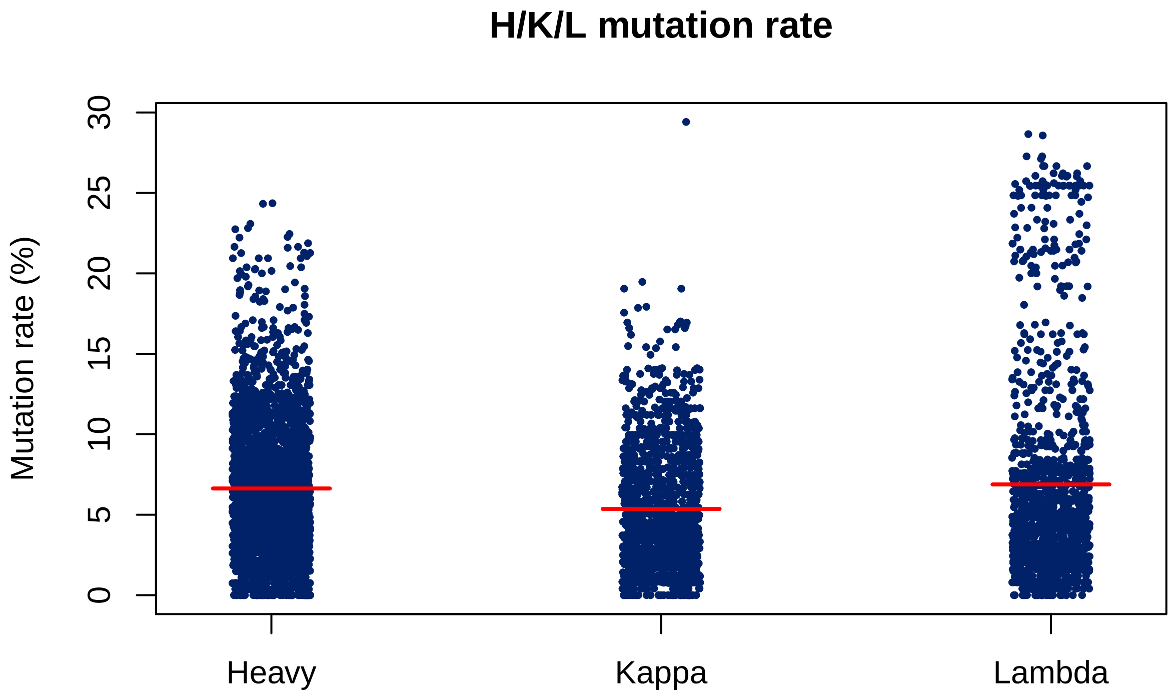
[Need to add more]
Notice may have outlier in LCDR3 variable:

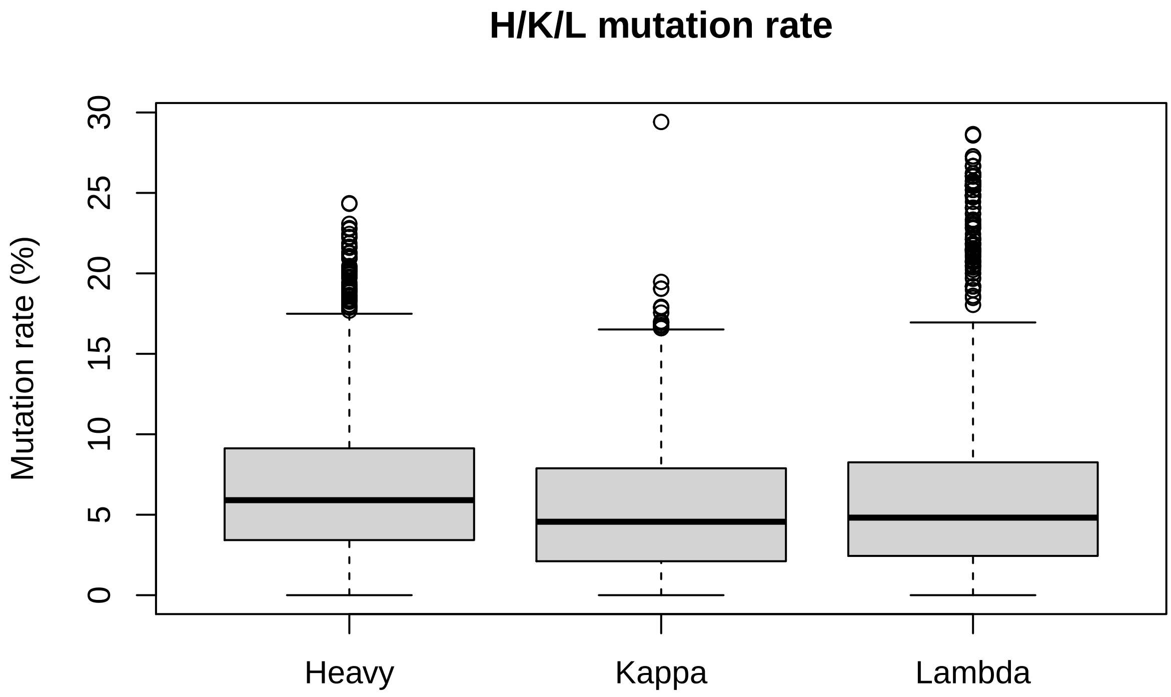
```
summary(Data$L_CDR3)
```

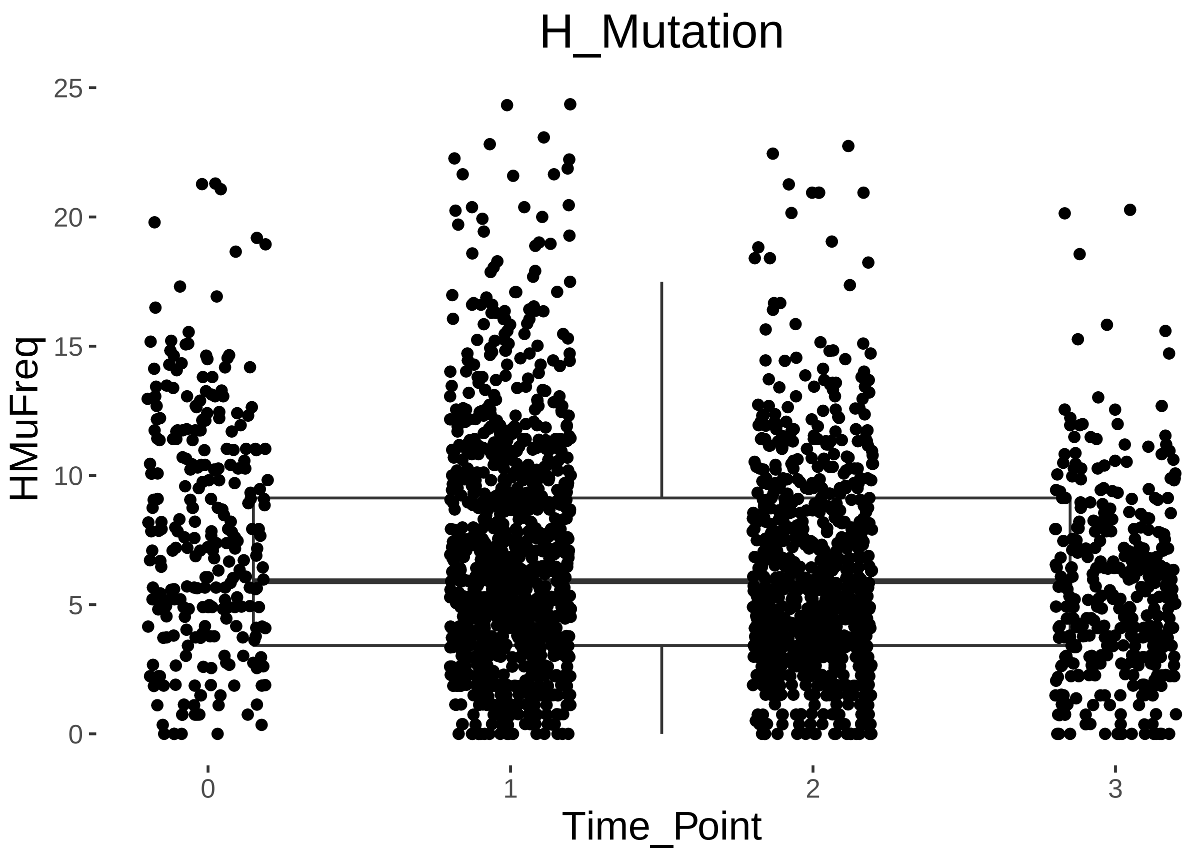
```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    7.00    9.00    9.00    9.65   10.00   47.00
```

Mutation Rate

```
##         H_Mutation% K_Mutation% L_Mutation%
## Min.           0.00        0.00        0.00
## 1st Qu.        3.42        2.11        2.44
## Median         5.90        4.56        4.82
## Mean           6.63        5.36        6.88
## 3rd Qu.        9.13        7.88        8.25
## Max.          24.36       29.41       28.65
```


H/K/L mutation rate
Mutation rate (%)
0
5
10
15
20
25
30
Heavy
Kappa
Lambda


H/K/L mutation rate
Mutation rate (%)
0
5
10
15
20
25
30
Heavy
Kappa
Lambda

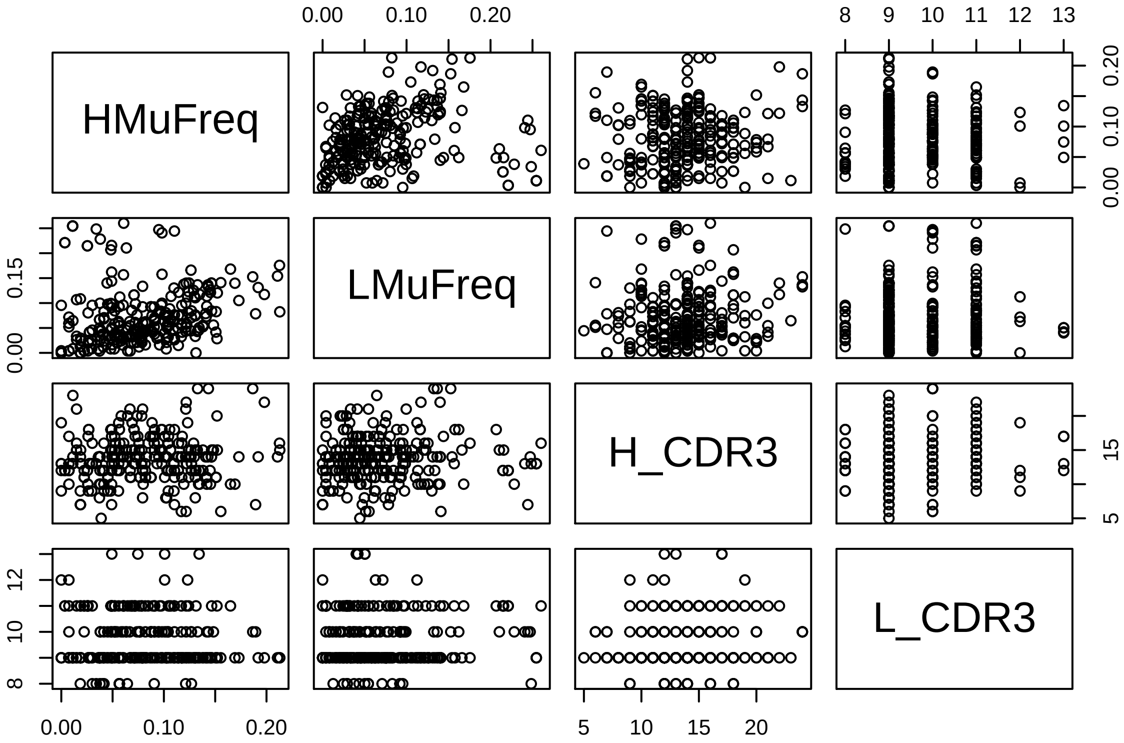


Test independence assumption

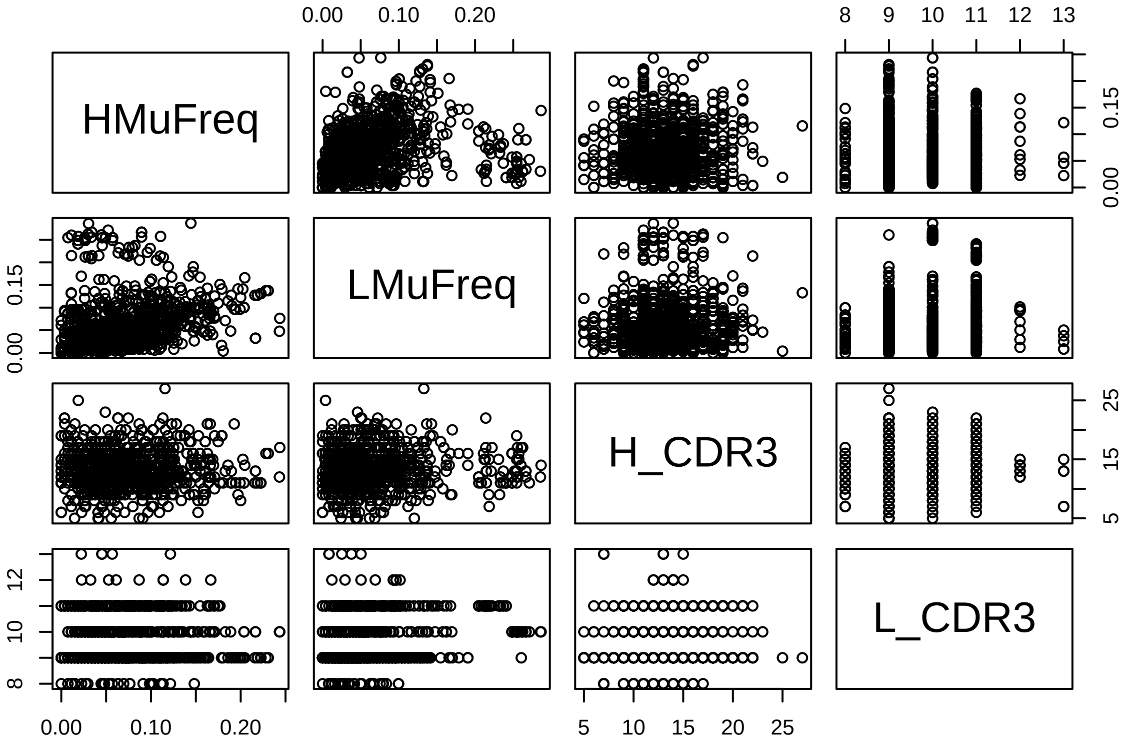
```
# combine all the extracted values; the most number of the same combination is 36
Data3 <- Data2 %>% unite("HID", c(HV_Extract:HJ_Extract, LV_Extract:LJ_Extract), remove = FALSE)
max(table(Data3$HID))
```

```
## [1] 36
```

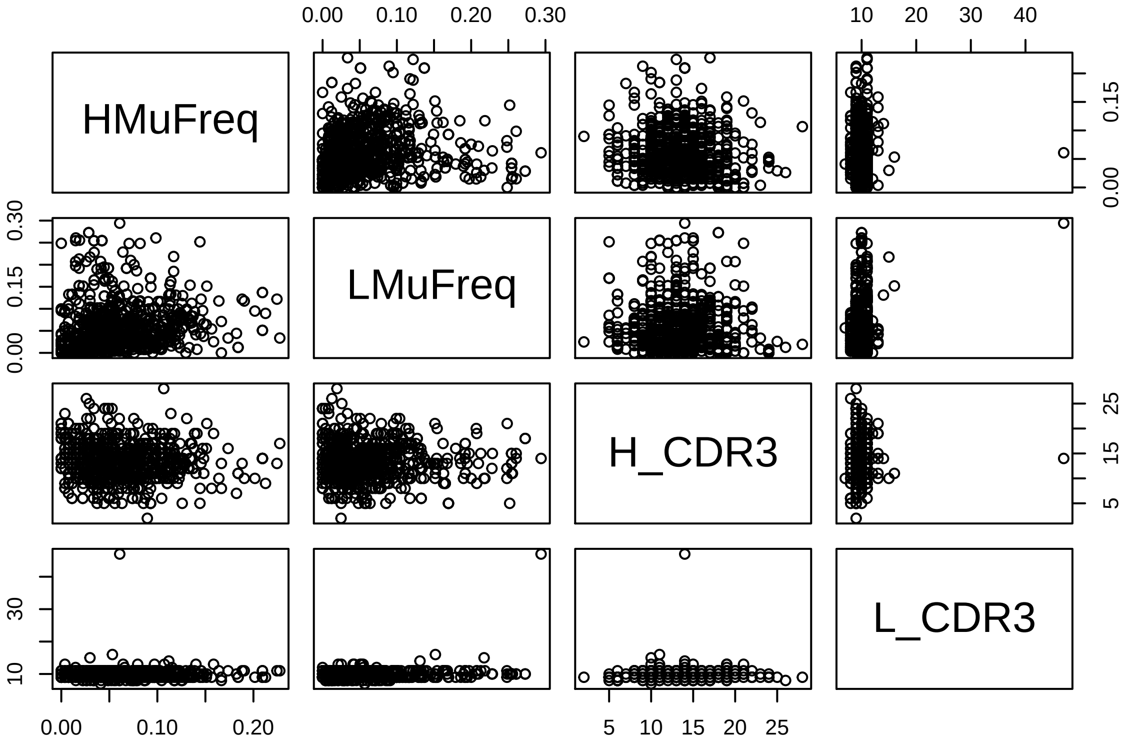
```
Data2 %>% filter(Time_Point == 0) %>% select(HMuFreq, LMuFreq, H_CDR3, L_CDR3) %>% pairs()
```



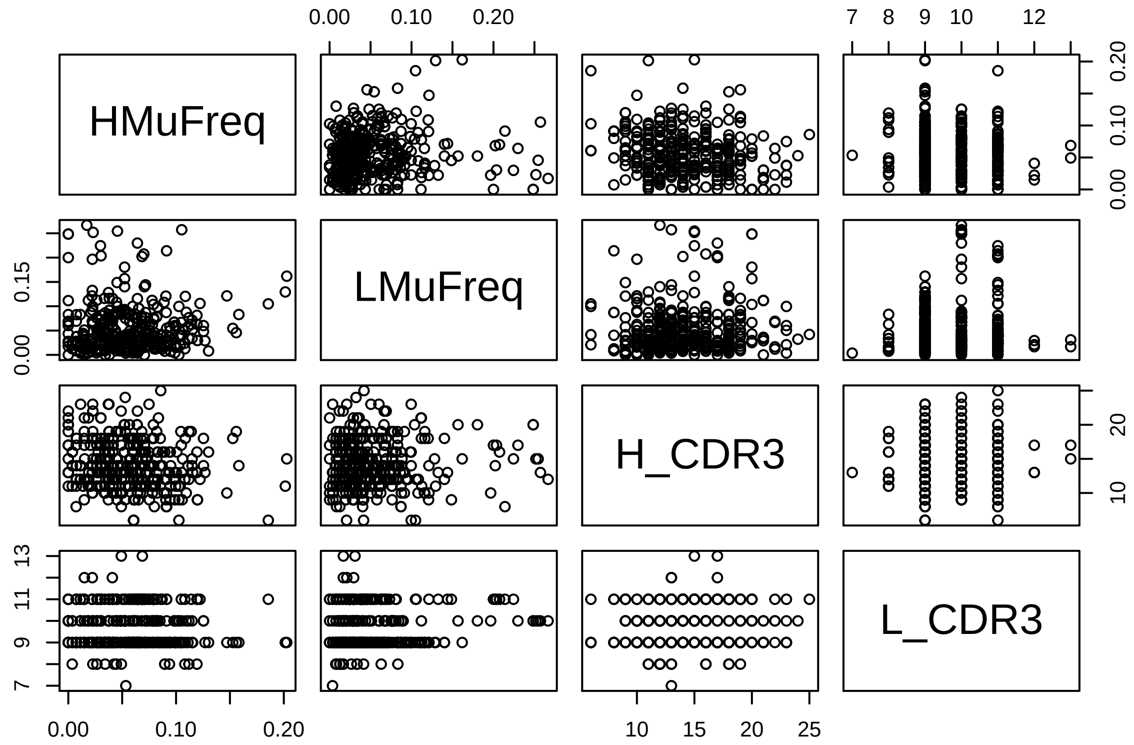
```
Data2 %>% filter(Time_Point == 1) %>% select(HMuFreq, LMuFreq, H_CDR3, L_CDR3) %>% pairs()
```



```
Data2 %>% filter(Time_Point == 2) %>% select(HMuFreq, LMuFreq, H_CDR3, L_CDR3) %>% pairs()
```



```
Data2 %>% filter(Time_Point == 3) %>% select(HMuFreq, LMuFreq, H_CDR3, L_CDR3) %>% pairs()
```



Multivariate Data Analysis

```
ID <- as.factor(Data2$MonkeyID)
trt <- as.factor(Data2$Treatment)
tp <- as.factor(Data2$Time_Point)
it <- as.factor(Data2$Isotype)
# four-way manova
fit.manova4 <- manova(cbind(Data2$L_CDR3, Data2$LMuFreq, Data2$H_CDR3, Data2$HMuFreq) ~ trt + tp + it +
summary(fit.manova4)
```

```
##             Df   Pillai approx F num Df den Df    Pr(>F)
## trt          6 0.050662   5.2060     24   9740 1.659e-15 ***
## tp           3 0.043749   9.0050     12   7302 < 2.2e-16 ***
## it           4 0.104184  16.2795     16   9740 < 2.2e-16 ***
## ID          13 0.063121   3.0031     52   9740 3.175e-12 ***
## Residuals 2435
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Longitudinal Data Analysis

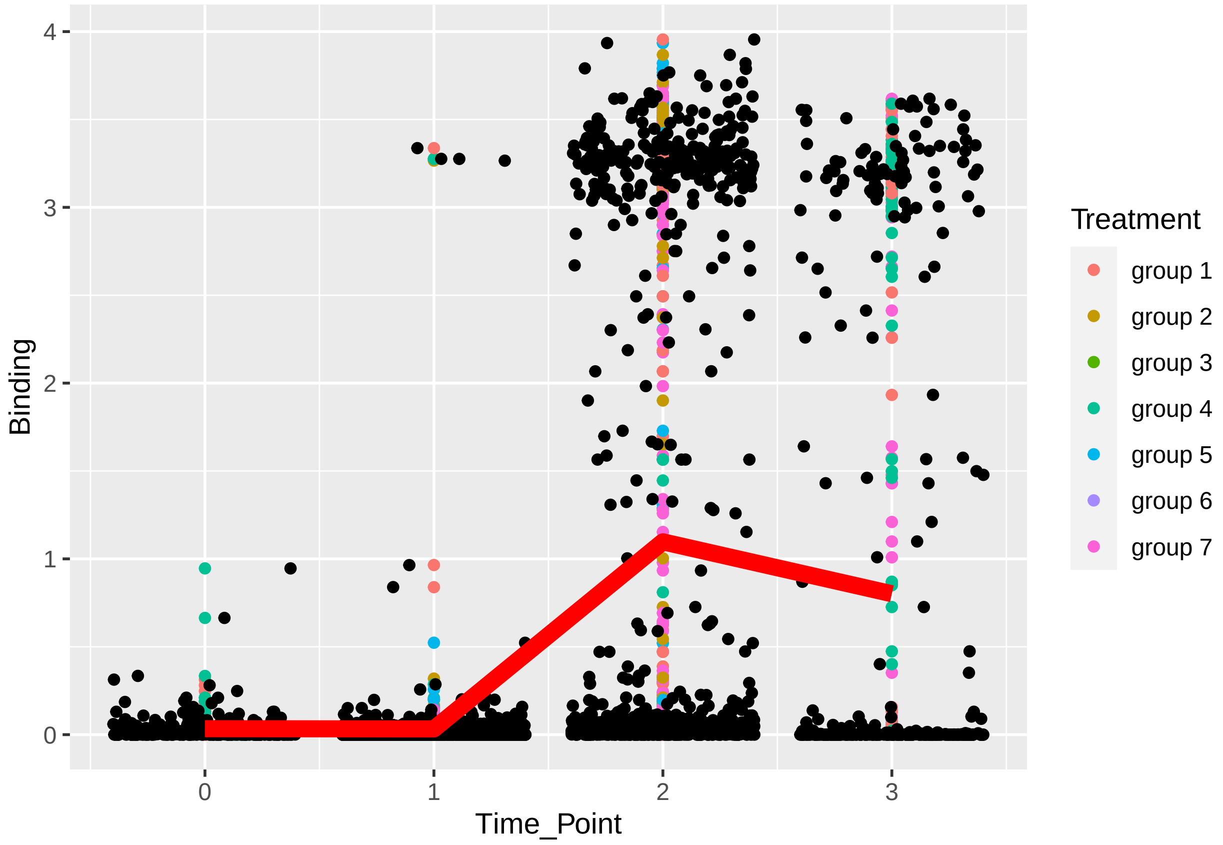
First we don't consider treatments but only plot the mean trend over time.

$$Y_{ij} = \beta_0 + \beta_1 Time_{ij} + e_{ij}$$

```
meanTrend <- lm(Data2$Binding ~ Data2$Time_Point)
summary(meanTrend)
```

```
##
## Call:
## lm(formula = Data2$Binding ~ Data2$Time_Point)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -1.1567 -0.6566 -0.2724  0.1697  3.2404
##
## Coefficients:
##                  Estimate Std. Error t value Pr(>|t|)
## (Intercept)      -0.16971    0.04233  -4.009 6.28e-05 ***
## Data2$Time_Point  0.44214    0.02414  18.316  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 1.05 on 2463 degrees of freedom
## Multiple R-squared:  0.1199, Adjusted R-squared:  0.1195
## F-statistic: 335.5 on 1 and 2463 DF,  p-value: < 2.2e-16
```

```
# simply connects the mean of each time point
ggplot(Data2, aes(x = Time_Point, y = Binding)) + geom_point(aes(color = Treatment)) + geom_jitter() +
```



Here we use Binding as the only response. Prdictors: `Treatment`.
Random effect for both intercept and slope.

$$Y_{ij} = \beta_0 + \beta_1 t_{ij} + b_{0i} + b_{1i} + e_{ij}$$

```r
lda <- lme(fixed = Binding ~ Time_Point + Treatment,
           random = ~ Time_Point | MonkeyID, data = Data2, method = "REML")
summary(lda)
```

```
## Linear mixed-effects model fit by REML
##  Data: Data2
##        AIC      BIC    logLik
##   6753.155 6822.836 -3364.578
##
## Random effects:
##  Formula: ~Time_Point | MonkeyID
##  Structure: General positive-definite, Log-Cholesky parametrization
##             StdDev    Corr
## (Intercept) 0.4643973 (Intr)
## Time_Point  0.5545189 -0.981
## Residual    0.9335139
##
## Fixed effects: Binding ~ Time_Point + Treatment
##                       Value Std.Error   DF   t-value p-value
## (Intercept)      -0.3652114 0.1578008 2444 -2.314383  0.0207
## Time_Point        0.6640931 0.1709633 2444  3.884418  0.0001
## Treatmentgroup 2 -0.1880652 0.1727988   13 -1.088348  0.2962
## Treatmentgroup 3 -0.2745892 0.1500821   13 -1.829593  0.0903
## Treatmentgroup 4 -0.0112400 0.1089163   13 -0.103199  0.9194
## Treatmentgroup 5 -0.3893418 0.1134100   13 -3.433045  0.0045
## Treatmentgroup 6 -0.2971236 0.1430497   13 -2.077066  0.0582
## Treatmentgroup 7 -0.0215799 0.1045159   13 -0.206475  0.8396
##  Correlation:
##                  (Intr) Tm_Pnt Trtmn2 Trtmn3 Trtmn4 Trtmn5 Trtmn6
## Time_Point       -0.899
## Treatmentgroup 2  0.002 -0.197
## Treatmentgroup 3 -0.027 -0.194  0.222
## Treatmentgroup 4 -0.277 -0.001  0.254  0.292
## Treatmentgroup 5 -0.169 -0.109  0.265  0.302  0.387
## Treatmentgroup 6 -0.029 -0.203  0.233  0.262  0.307  0.317
## Treatmentgroup 7 -0.272 -0.020  0.268  0.308  0.420  0.405  0.323
##
## Standardized Within-Group Residuals:
##         Min          Q1         Med          Q3         Max
## -3.52596967 -0.52101840 -0.10300523  0.03925278  3.58753831
##
## Number of Observations: 2465
## Number of Groups: 20
```