

Final Project: First Draft

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Questions for Kan

- Why are there 7 treatment groups now?
-

Exploratory Data Analysis

Data preparation

```
## Response [https://raw.githubusercontent.com/luokan1227/537P1/master/Data.xlsx]
##   Date: 2020-10-22 05:47
##   Status: 200
##   Content-Type: application/octet-stream
##   Size: 341 kB
## <ON DISK>  C:\Users\shihn\AppData\Local\Temp\RtmpQ1uFXd\file108228a7b21.xlsx

## Response [https://raw.githubusercontent.com/luokan1227/537P1/master/MonkeyID.xlsx]
##   Date: 2020-10-22 05:47
##   Status: 200
##   Content-Type: application/octet-stream
##   Size: 50.1 kB
## <ON DISK>  C:\Users\shihn\AppData\Local\Temp\RtmpQ1uFXd\file10867bd2df3.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
```

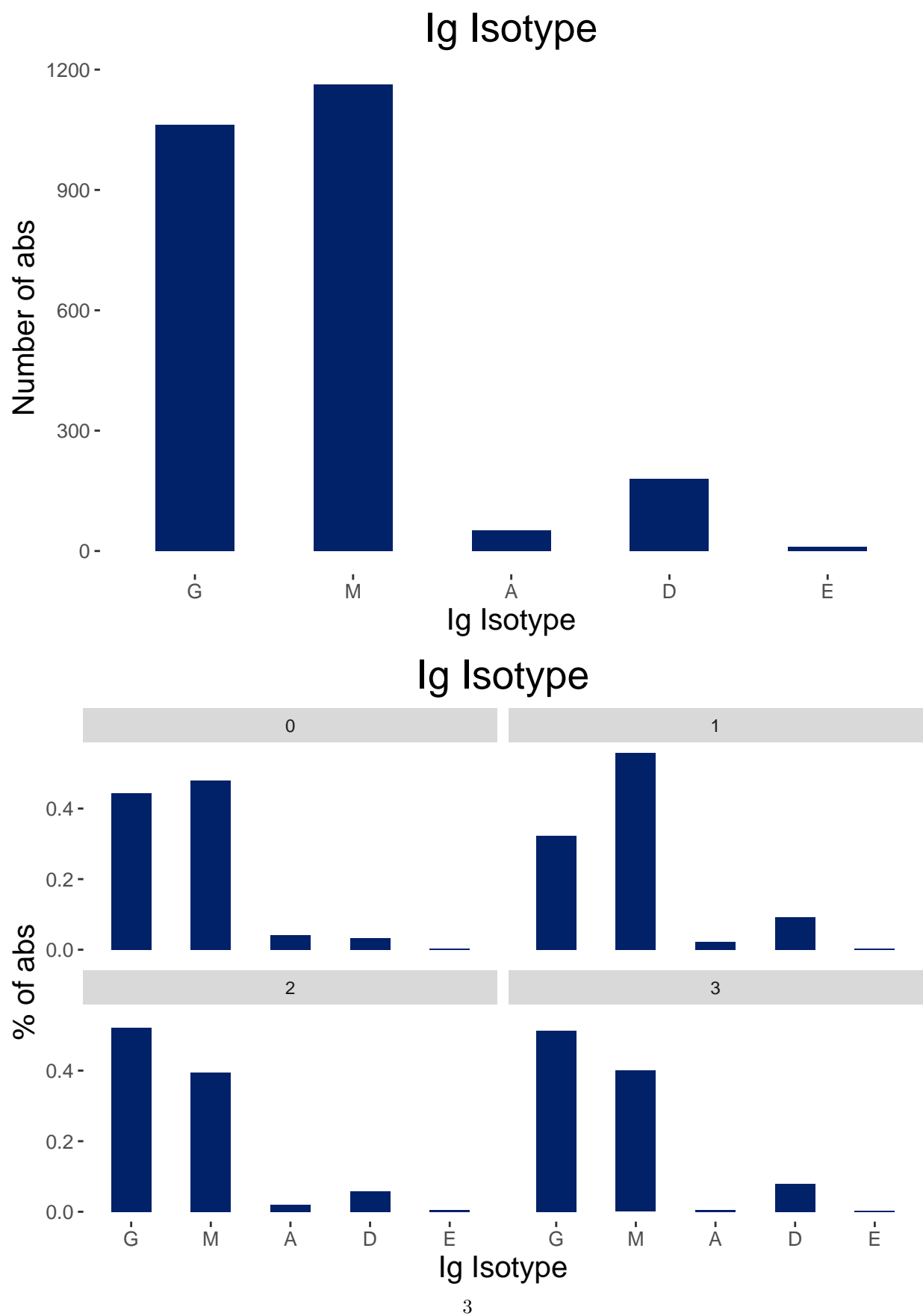
```
table(Data2$Treatment)
```

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

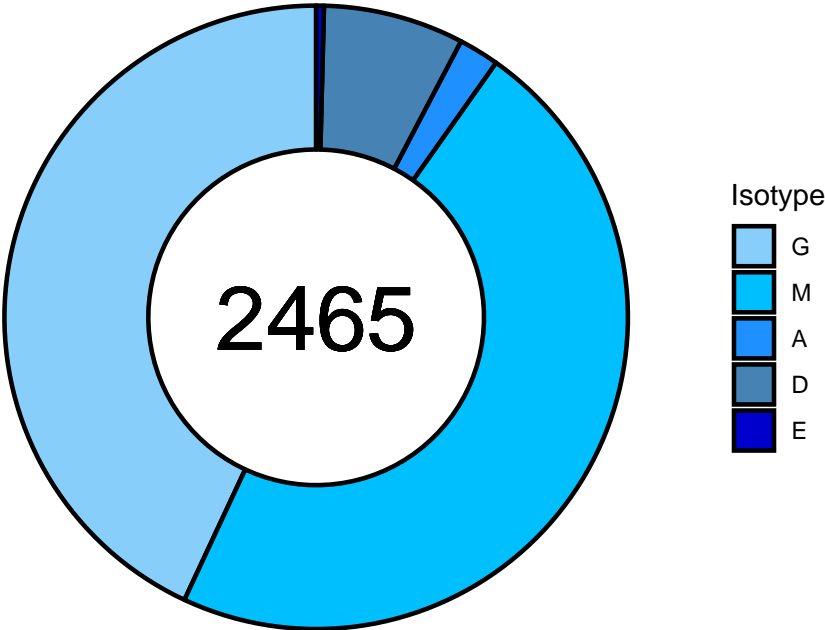
```
table(Data2$Time_Point, Data2$Treatment)
```

```
##
##      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
```

Isotype Plots and Table

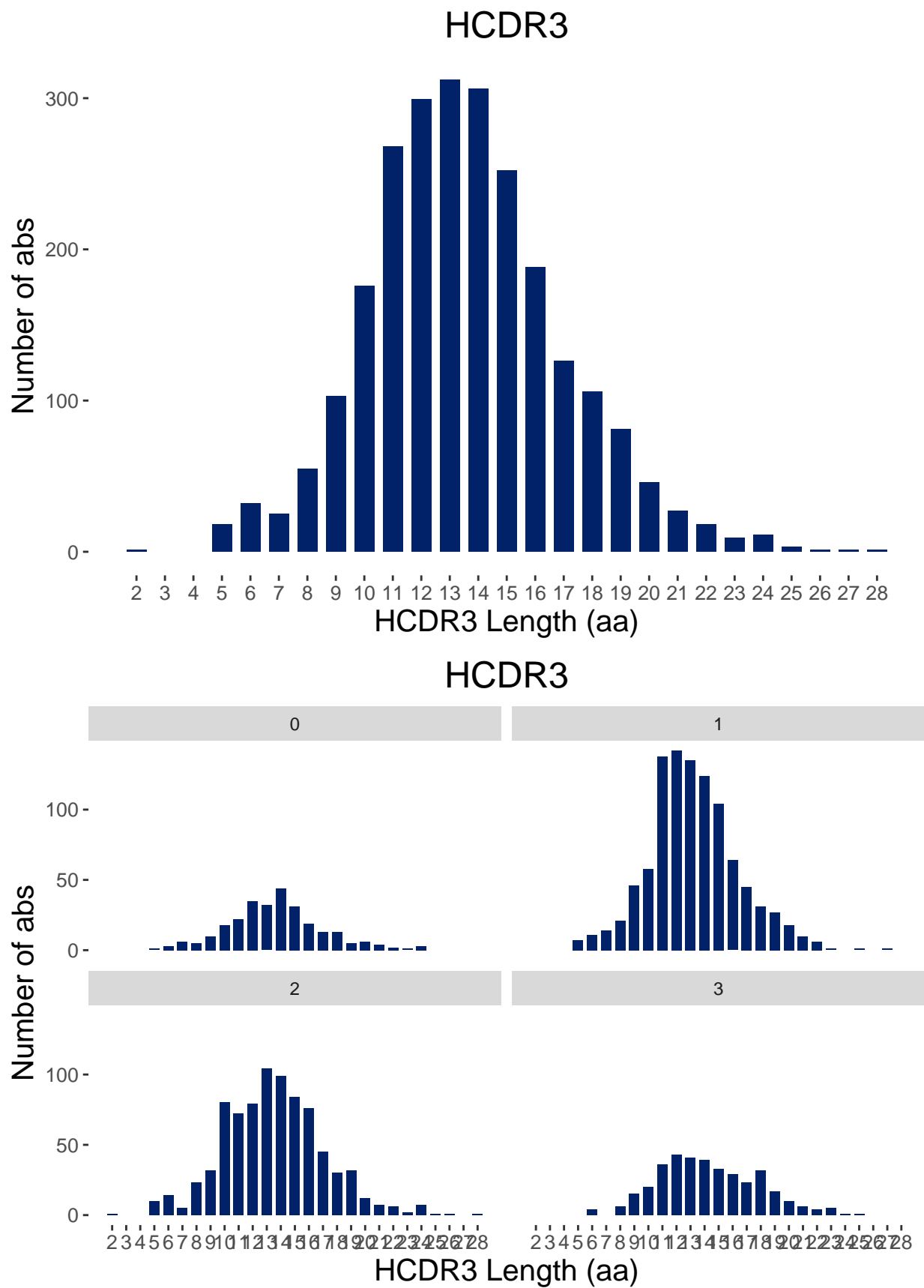


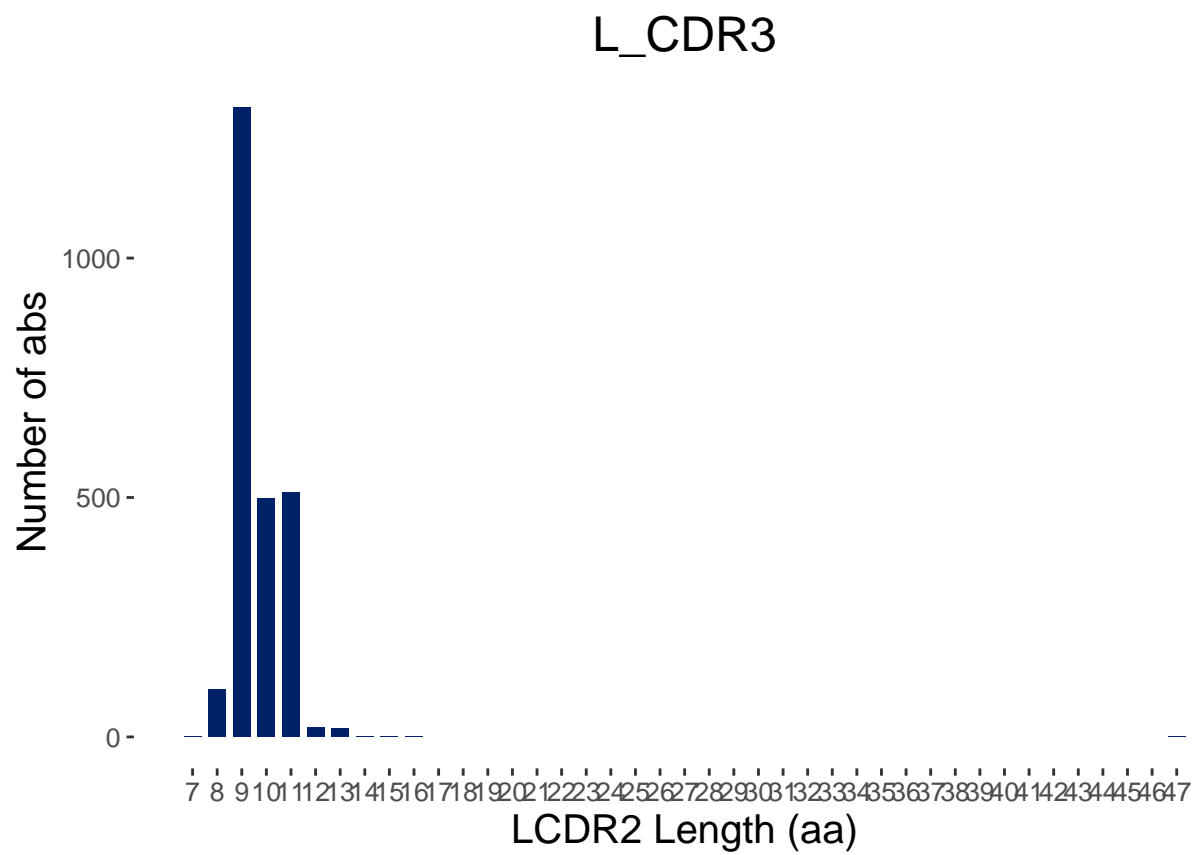
Ig Isotype

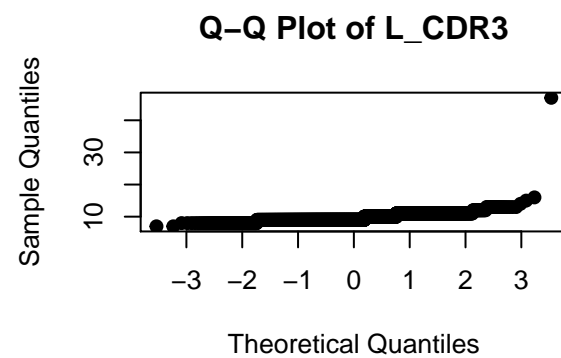
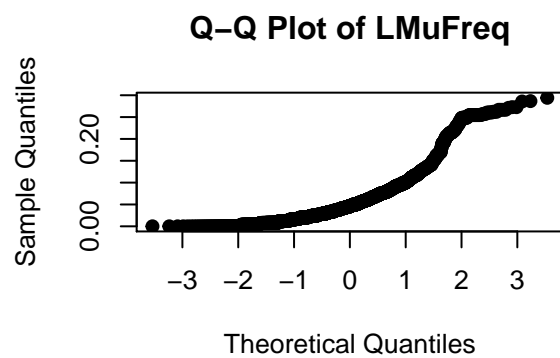
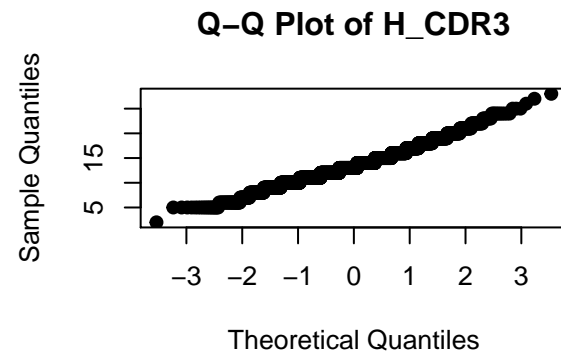
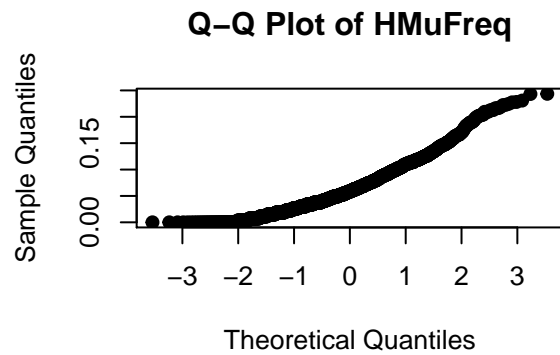


##	Isotype	Ab #	Ab %
## 1	A	51	2.1
## 2	D	179	7.3
## 3	E	10	0.4
## 4	G	1062	43.1
## 5	M	1163	47.2

CDR_3 Plots and tables







Outlier detection

[Need to add more]

Notice may have outlier in L_CDR3 variable:

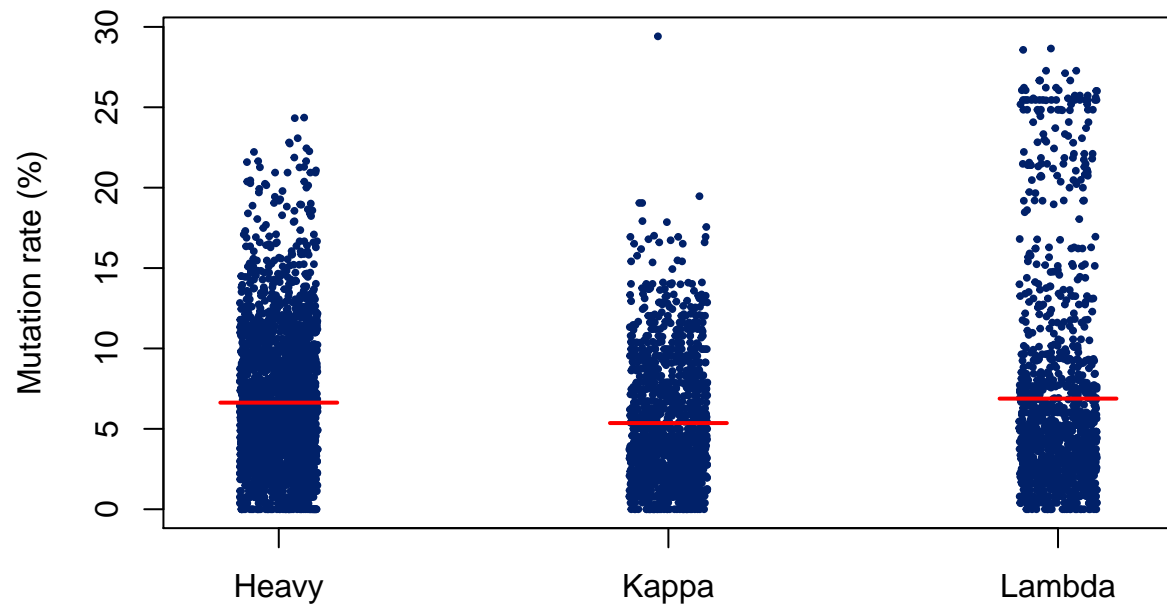
```
summary(Data$L_CDR3)
```

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

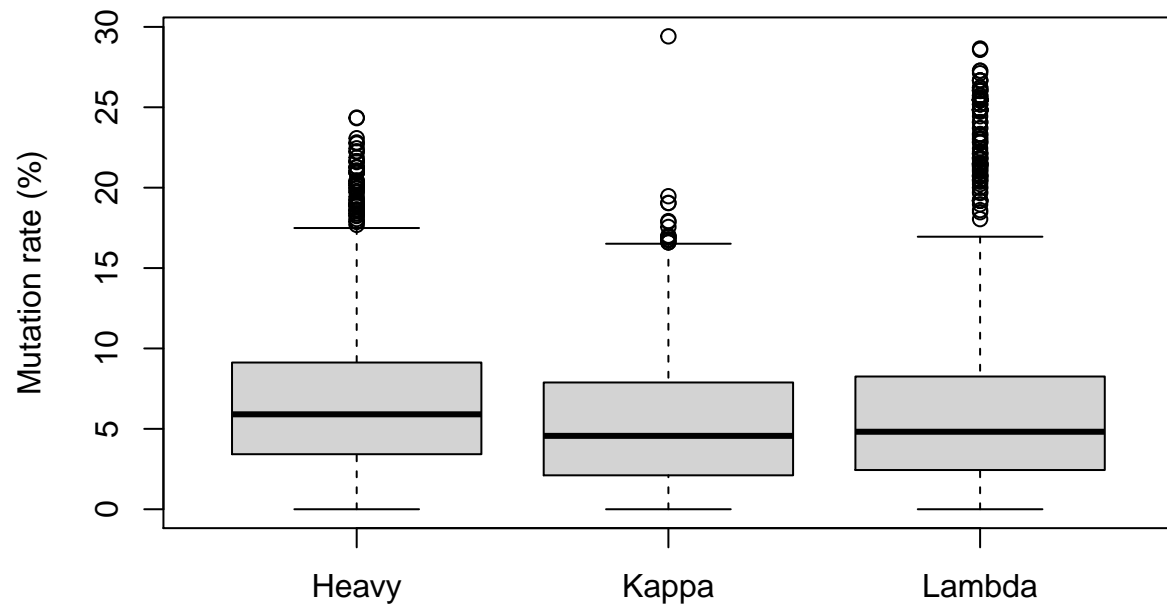
Mutation Rate

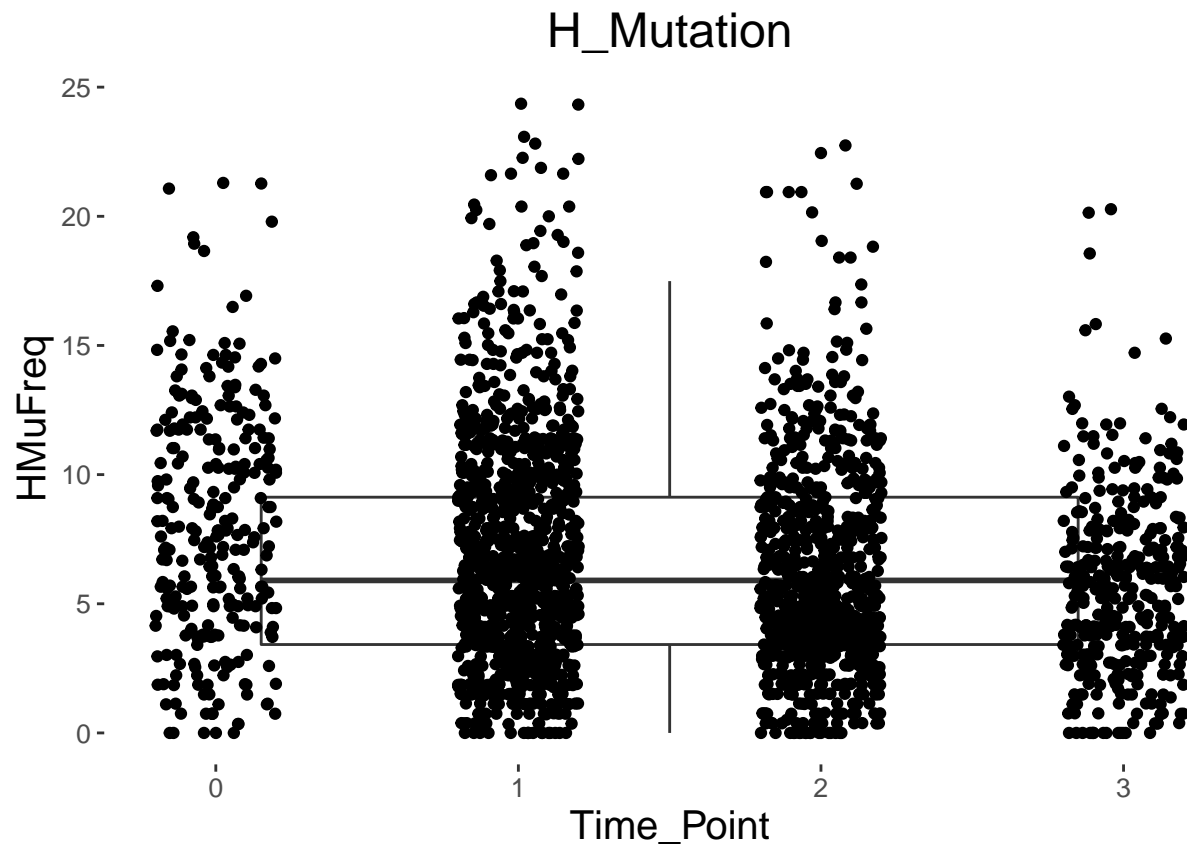
```
##      H_Mutation% K_Mutation% L_Mutation%
## Min.           0.00         0.00         0.00
## 1st Qu.        3.42         2.11         2.44
## Median         5.90         4.56         4.82
## Mean           6.63         5.36         6.88
## 3rd Qu.        9.13         7.88         8.25
## Max.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

H/K/L mutation rate



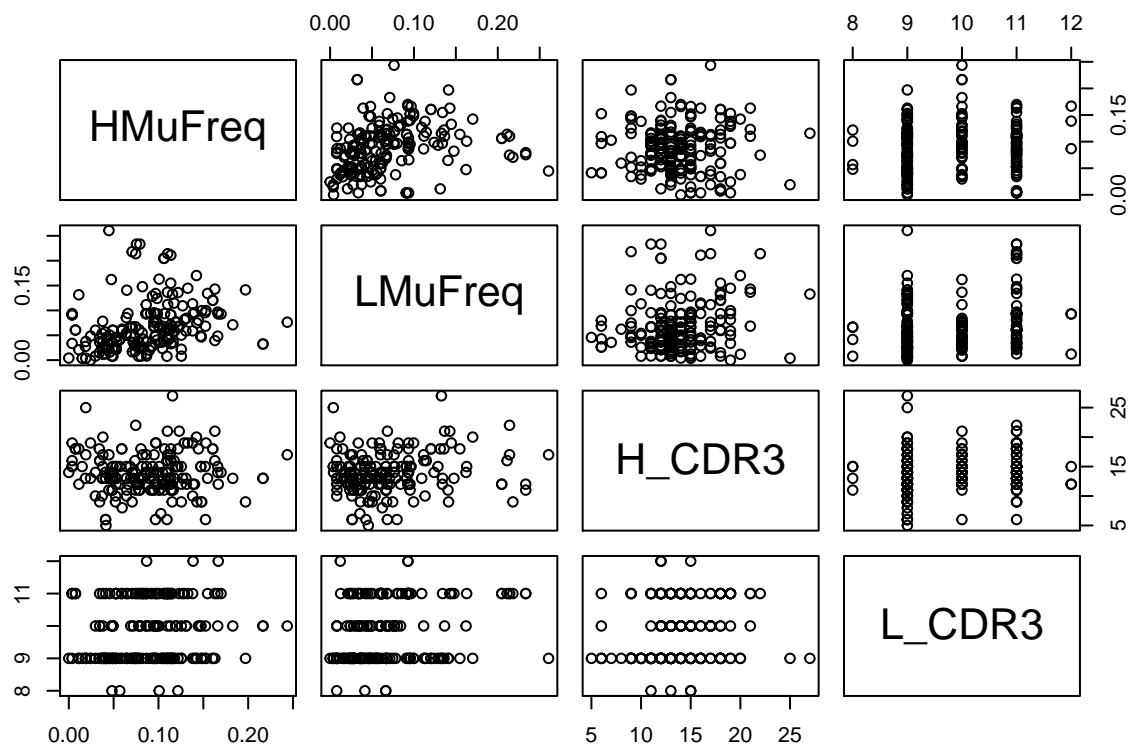
H/K/L mutation rate



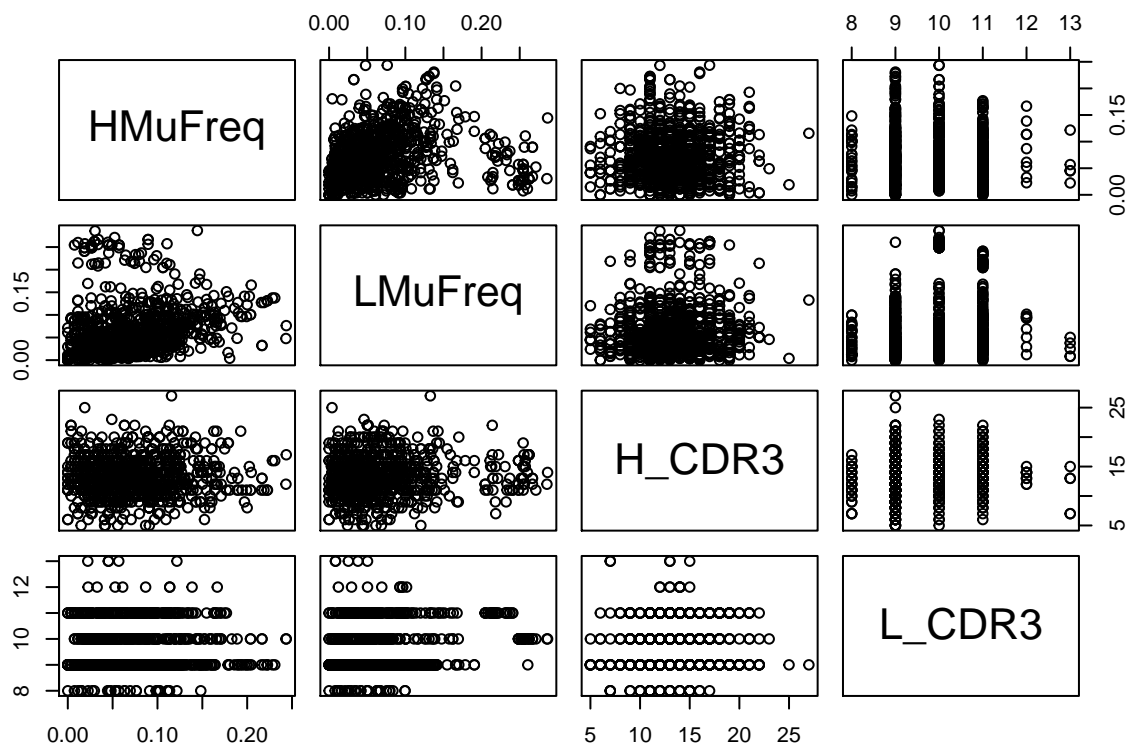


Test independence assumption

```
subset1 <- Data2 %>% filter(Time_Point == 1) %>% filter(MonkeyID == 6132) %>% select(HMuFreq, LMuFreq, I
```



```
subset1 <- Data2 %>% filter(Time_Point == 1) %>% 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)
fit.manova <- manova(cbind(Data2$L_CDR3, Data2$LMuFreq, Data2$H_CDR3, Data2$HMuFreq) ~ ID + trt + tp + it)
summary(fit.manova)
```

```
##           Df  Pillai approx F num Df den Df    Pr(>F)
## ID          19 0.126901   4.1991    76  9740 < 2.2e-16 ***
## tp           3 0.045931   9.4611    12  7302 < 2.2e-16 ***
## it           4 0.087622  13.6336    16  9740 < 2.2e-16 ***
## 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.

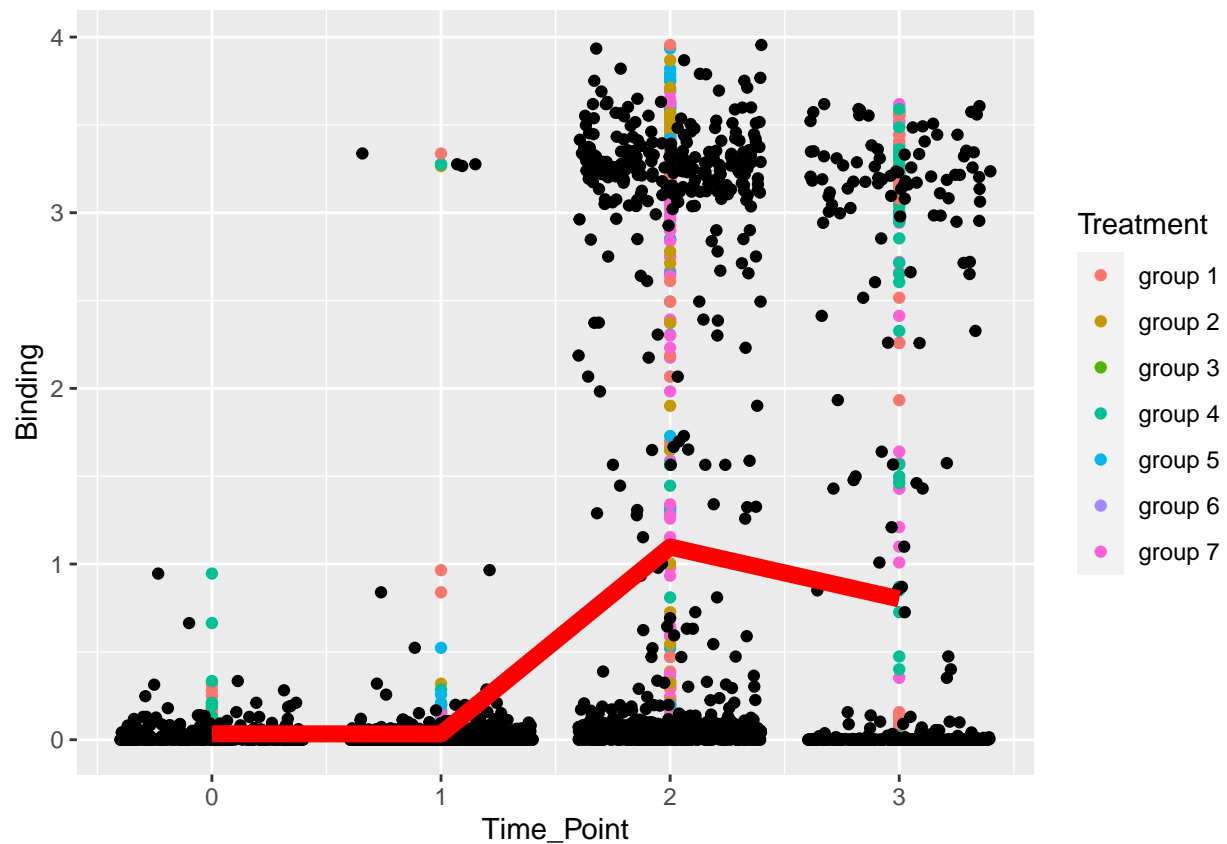
$$Y_{ij} = \beta_0 + \beta_1 Time_{ij} + e_{ij}$$

```
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. Predictors: Treatment.
Random effect for both intercept and slope.

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

```
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
```