Finding the Best Aqueous Solution that Dissolve Antihistamine

A 2^5 Factorial Design with 2 replicates

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Introduction and Background

We face various forms of drugs in our daily life. In most cases, we dose ourselves up with drugs orally. Taking oral drugs does not require a highly trained skill. We just need to follow the dosing instruction and take it with a cup of water. However, one of the defects of taking an oral drug is a slow medicinal effect. It takes some time until a drug is dissolved in our stomach and absorbed into our blood vessel. The antihistamine I usually have sought for more than a year is also one of the oral drugs. If I take the drug every, then there is a possibility that my body becomes tolerant of antihistamine.

For this reason, I do not take an antihistamine every day. I sought it whenever I undergo severe allergic symptoms. For this reason, the immediate medicinal effect is always expected every time I take the antihistamine. I assumed one of the steps to shorten the time is to take the drug with the aqueous solution that melts antihistamine fast.

In the experiment, I would like to identify the aqueous solutions that dissolve the antihistamine the most quickly. After the research, I want to apply what I find to my medication adherence; I need to find the affordable ingredients to make an aqueous solution. Based on these facts, I chose the factors; carbonation, salt, sugar, citrus acid, and the temperature of the water.

Experimental Procedure

Because I did not know how long it takes for the pills to dissolve completely, to avoid unnecessarily increase of the variance, the trial experiments had been done five times with a 473ml cup of water. I observed it took less than an hour for the pills to dissolve completely. The investigation did not take much labor; however, I must look at the cup for an hour, so it was quite a time-consuming experiment. I decided to run randomized within blocks 25 factorial design the experiment with 2 replicates over two different days to avoid spending more than two hours per day.

After I bought all ingredients from the market, I conducted the first experiment in the afternoon on Saturday, April 11, 2020. For the experiment, I kept eight bottles of carbonated water and eight bottles of plain water in the refrigerator for a day. The rest of eight bottles of carbonated water and eight bottles of plain water were kept in the room temperature. All the bottles were stored in a mint-condition to avoid missing carbonation from the carbonated water. During the experiment, I used thirty-two of 473ml size cups. I put the labels on each cup to prevent confusion. I poured the same amount of water and carbonated water into each cup. Also added 20ml of salt, 20ml of sugar, and 20ml of citric acid in conformity with the factor level. After that, I mixed the ingredients well and put the eight cups of a carbonated aqueous solution and the eight cups of aqueous solution back to the refrigerator. After a half-hour later, I took out all the cups and located them at the same spot on the floor. When I measured the temperature of refrigerated solutions, their temperatures were laid between the range of 5.8 and 6.1°C. On the other hand, the temperatures of room-temperature- kept-aqueous solutions were laid between the range of 22.3 and 22.6°C.

For the next step, I put a tablet of antihistamine in each cup. Watching all the cups, using the stopwatch, I measured the times until each of the pills dissolve completely in the different types of solutions. To prevent increasing the variance, I measured the time in minutes. The first experiment was run under the condition that room temperature was 22.2°C.

The second experiment was run on Wednesday, April 13, 2020. The trial had been done in the same procedure as the first. However, there were two differences, which are room temperature and the temperature of the room-temperature-kept-aqueous solution. The room temperature was

17.3°C and the temperatures of room-temperature-kept-solutions were laid between the range of 17.2 and 17.5°C. Other conditions were all the same or similar.

Table 1. Factor Level

Level	A	B	C	D	E
-	Plain Water	No Salt	No Sugar	No Citric Acid	Room Temperature of Water
+	Carbonated Water	20ml of Salt	20ml of Sugar	20ml of Citric Acid	Refrigerator Temperature of Water

Carbonation: I expected that carbonation is one of the factors that highly influence the experiment because of its acidity.

Salt: I choose the salt as a factor because it is readily available from any markets, and a variety of beverages contain salinity.

Sugar: Same as salt, I choose sugar as the factor since it is one of the materials at hand, and many kinds of beverages contain sugar.

Citric Acid: Compared to salt and sugar, it is not common material we can see at markets, but we can easily observe that it is in a variety of beverages. This is the reason why I choose citric acid as a factor.

The temperature of water: There were no explicitly assigned temperatures at both levels. Instead, I distinguished the temperatures as room temperature and refrigerator temperature.

Presentation of Data

I obtained the results as the following table:

Table 2. Experimental Data

Factors					Outcome (Minute)	
A	B	C	D	E	Block1	Block2
-	-	-	-	-	42	48
+	-	-	-	-	25	28
-	+	-	-	-	37	40
+	+	-	-	-	22	25
-	-	+	-	-	41	46
+	-	+	-	-	28	33
-	+	+	-	-	37	43
+	+	+	-	-	23	24
-	-	-	+	-	33	38
+	-	-	+	-	22	24
-	+	-	+	-	29	34
+	+	-	+	-	20	23
-	-	+	+	-	33	40
+	-	+	+	-	23	26
-	+	+	+	-	28	33
+	+	+	+	-	20	19
-	-	-	-	+	51	59
+	-	-	-	+	35	39
-	+	-	-	+	41	54
+	+	-	-	+	31	36
-	-	+	-	+	52	58
+	-	+	-	+	36	41
-	+	+	-	+	45	52
+	+	+	-	+	34	38
-	-	-	+	+	40	45
+	-	-	+	+	31	35
-	+	-	+	+	39	43
+	+	-	+	+	29	31
-	-	+	+	+	43	48
+	-	+	+	+	32	36
-	+	+	+	+	36	41
+	+	+	+	+	29	31

Note: There are two runs for the experiments, and those two runs had done on two different days.

Analysis of Data

I analyzed the data above with R. The all used codes for analysis will be provided in appendice. Since I expected a block effect, the model for the data analysis is the same as the following:

$$
\begin{aligned}
y &= \mu + \beta X + \delta_z + \epsilon \\
&= \mu + \left(\frac{A}{2}\right)x_1 + \left(\frac{B}{2}\right)x_2 + \left(\frac{C}{2}\right)x_3 + \left(\frac{D}{2}\right)x_4 + \left(\frac{E}{2}\right)x_5 + \left(\frac{AB}{2}\right)x_1x_2 + \left(\frac{AC}{2}\right)x_1x_3 + \left(\frac{AD}{2}\right)x_1x_4 \\
&+ \left(\frac{AE}{2}\right)x_1x_5 + \left(\frac{BC}{2}\right)x_2x_3 + \left(\frac{BD}{2}\right)x_2x_4 + \left(\frac{BE}{2}\right)x_2x_5 + \left(\frac{CD}{2}\right)x_3x_4 + \left(\frac{CE}{2}\right)x_3x_5 + \left(\frac{DE}{2}\right)x_4x_5 \\
&+ \left(\frac{ABC}{2}\right)x_1x_2x_3 + \left(\frac{ABD}{2}\right)x_1x_2x_4 + \left(\frac{ABE}{2}\right)x_1x_2x_5 + \left(\frac{ACD}{2}\right)x_1x_3x_4 + \left(\frac{ACE}{2}\right)x_1x_3x_5 \\
&+ \left(\frac{ADE}{2}\right)x_1x_4x_5 + \left(\frac{BCD}{2}\right)x_2x_3x_4 + \left(\frac{BCE}{2}\right)x_2x_3x_5 + \left(\frac{BDE}{2}\right)x_2x_4x_5 + \left(\frac{CDE}{2}\right)x_3x_4x_5 \\
&+ \left(\frac{ABCD}{2}\right)x_1x_2x_3x_4 + \left(\frac{ABCE}{2}\right)x_1x_2x_3x_5 + \left(\frac{ABDE}{2}\right)x_1x_2x_4x_5 + \left(\frac{ACDE}{2}\right)x_1x_3x_4x_5 \\
&+ \left(\frac{BCDE}{2}\right)x_2x_3x_4x_5 + \left(\frac{ABCDE}{2}\right)x_1x_2x_3x_4x_5 + \delta_z + \epsilon
\end{aligned}
$$

For the first step of the analysis, I need to check whether the data meet the assumptions or not. The assumptions for the analysis the same as follows:

1. Data should be normally distributed.

2. Data should have constant variance.

Figure 1.

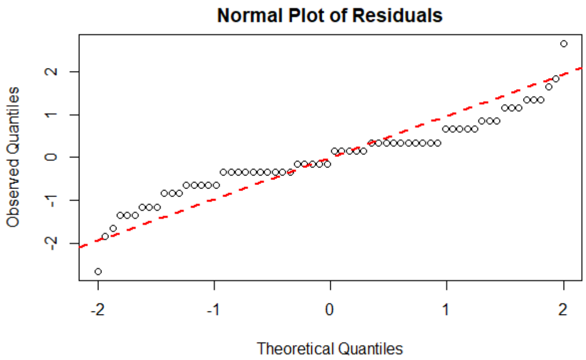
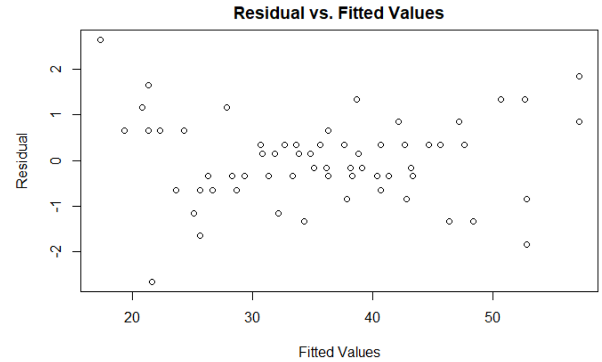


Figure 2.



By Figure 1., I notice that the data does not show the perfect but some degree of normality. However, in Figure 2., I observe that it does not satisfy the constant variance.

Hence, data transformation is required. I set the range of lambda between -2 and 2, and examine which value of lambda is the most proper for the data transformation.

Figure 3.

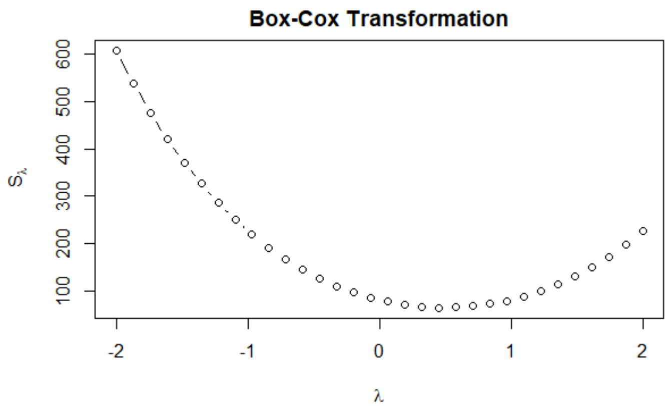


Table 3. Box-Cox Transformation Lambda & SSR

λ	SSR
-2.0000	607.45
-1.8710	538.57
-1.7419	476.64
-1.6129	421.02
-1.4839	371.12
-1.3548	326.41
-1.2258	286.44
-1.0968	250.80
-0.9677	219.13
-0.8387	191.10
-0.7097	166.44
-0.5806	144.92

-0.4516	126.29
-0.3226	110.40
-0.1935	97.09
-0.0645	86.23
0.0645	77.72
0.1935	71.47
0.3226	67.42
0.4516	65.55
0.5806	65.83
0.7097	68.26
0.8387	72.86
0.9677	79.69
1.0968	88.80
1.2258	100.27
1.3548	114.22
1.4839	130.76
1.6129	150.05
1.7419	172.26
1.8710	197.60
2.0000	226.29

Figure 4.

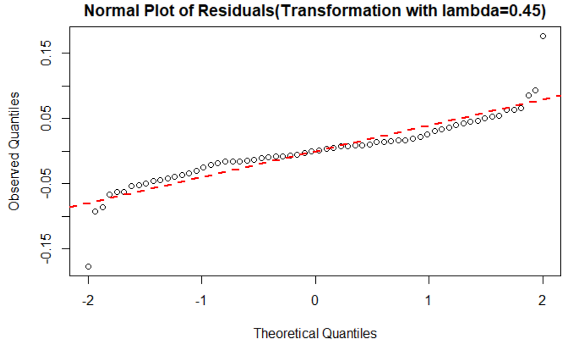
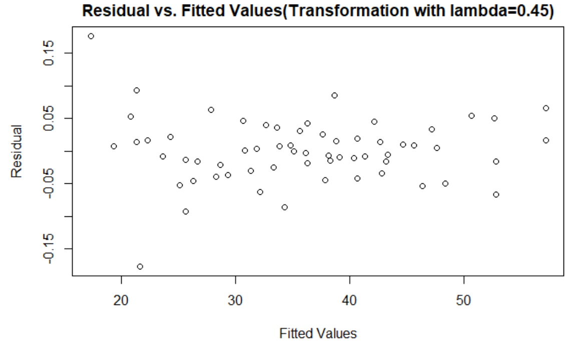


Figure 5.



From Figure 3. And Table 3. , I noticed the most proper lambda for the transformation is approximately 0.45. Since the value of lambda is an approximation, I performed two more transformations when the lambdas were 0.40 and 0.50. Those can be found in appendix C.

For the next step, I needed to check whether the block effect is negligible or not. I used the hypothesis test as following:

$$H_0: \mu + \beta X + \epsilon \qquad \text{vs.} \qquad H_a: \mu + \beta X + \delta_z + \epsilon$$

$RSS_0 = 1.288, V_0 = 32$ (refer the ANOVA table of m3 in appendix)

$RSS_1 = 0.163, V_1 = 31$ (refer the ANOVA table of m2 in appendix D)

$$\frac{(RSS_0 - RSS_1)/(V_0 - V_1)}{RSS_1/V_1} \sim F_{V_0 - V_1, V_1}$$

$F = 29.78882$

$P\text{-value} = 5.241005e\text{-}06$

The P-value for the F is 5.241005e-06, which is much smaller than 0.05. Hence, I rejected the null hypothesis at the significance level, 0.05. In other words, the block effect is not negligible.

I set the model for the rest of the analysis as the following: $y^{\lambda=0.45} = \mu + \beta X + \delta_z + \epsilon$

According to the model, the calculated coefficients of betas are the same as the following table:

Table 4. Beta Coefficients and RSE of the model

	coefficients	fitted.y1	fitted.y2
(Intercept)	4.8176	-	-
A	-0.4309	5.4099	5.6751
B	-0.1295	4.2355	4.5007
C	0.0138	5.036	5.3012
D	-0.1994	4.0051	4.2703
E	0.3207	5.3268	5.592
blk2	0.2652	-	-
A:B	0.0058	5.123	5.3882
A:C	0.0119	4.007	4.2722
B:C	-0.0214	4.8486	5.1138
A:D	0.0605	3.9664	4.2316
B:D	0.003	4.5869	4.8521
C:D	-0.0048	3.8424	4.1076
A:E	0.042	4.9086	5.1738
B:E	0.0183	4.0836	4.3488
C:E	0.0082	4.5187	4.7839
D:E	-0.0061	3.6735	3.9387
A:B:C	-0.0049	5.9331	6.1983
A:B:D	-0.0044	4.9435	5.2087
A:C:D	-0.0192	5.7048	5.97
B:C:D	-0.021	4.72	4.9852
A:B:E	-1.00E-04	5.9348	6.2

A:C:E	0.0058	5.0343	5.2995
B:C:E	0.0026	5.5994	5.8646
A:D:E	-3.00E-04	4.8812	5.1464
B:D:E	0.0034	5.2698	5.535
C:D:E	0.0082	4.6884	4.9536
A:B:C:D	0.0034	5.1839	5.4491
A:B:C:E	0.0244	4.4874	4.7526
A:B:D:E	-0.0133	5.4385	5.7037
A:C:D:E	-0.0076	4.7537	5.0189
B:C:D:E	0.0067	5.1537	5.4189
A:B:C:D:E	-0.0062	4.4874	4.7526
RSE	0.0725	-	-

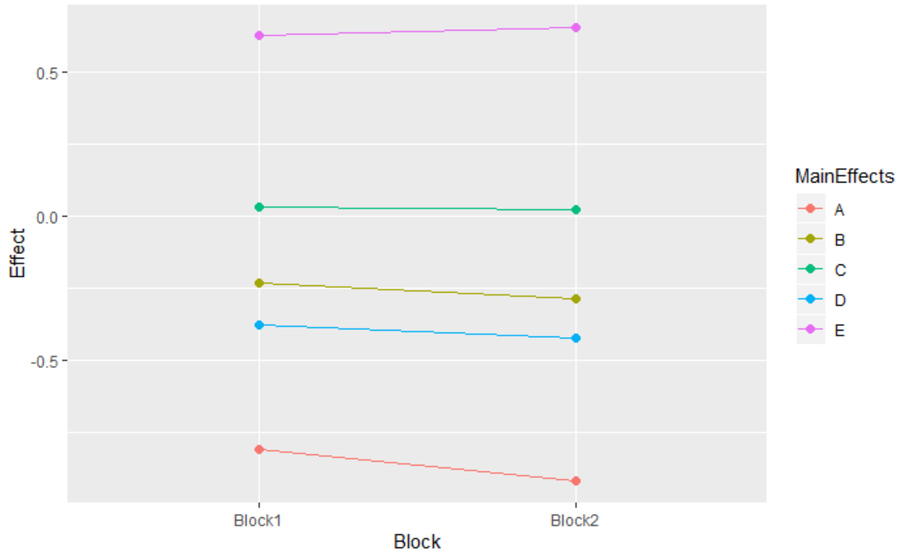
And the calculated factor effects are the same as following:

Table 5. Factor Effects

	Effects
A	-0.8618
B	-0.2590
C	0.0275
D	-0.3988
E	0.6415
AB	0.0115
AC	0.0238
AD	0.1211
AE	0.0841
BC	-0.0429
BD	0.0060
BE	0.0367
CD	-0.0096
CE	0.0165
DE	-0.0122
ABC	-0.0099
ABD	-0.0089
ABE	-0.0002
ACD	-0.0383
ACE	0.0116
ADE	-0.0006
BCD	-0.0419
BCE	0.0053
BDE	0.0068
CDE	0.0165
ABCD	0.0068

ABCE	0.0488
ABDE	-0.0266
ACDE	-0.0153
BCDE	0.0135
ABCDE	-0.0123

Figure 6. Interaction Plot between Main Effects and Block



I produced an interaction plot to see whether there is an interaction effect between the main effects and blocks. As I can see in Figure 6., There is no significant difference between the main effects in Block 1 and the main effects in Block 2, but A effect shows some difference.

To find out significant effects, I used interactions to estimate sigma square. In the first step, I assumed 5 factors interaction is negligible, and use it to estimate σ^2. I obtained no significant results from the first step. When I used 5 and 4 factors interactions to estimate σ^2, I observed A, B, D, E, AD, AE, ABCE are significant. When I used 5, 4, and 3 factors interactions to estimate σ^2, I observed A, B, C, D, E, AC, AD, AE, BC, BE, ACD, BCD, ABCE, ABDE are significant. Lastly, when I used 5, 4, 3, 2 factors interactions to estimate σ^2, I observed the same result from the very last one (Details of the calculation code can be found in appendix F).

I used improved Daniel's method (Loh's method) as well. I created all 32 possible plots, and among them, I chose a canonical plot. The chosen plot is the same as the following (the rest of the plots attached in the appendix G):

Figure 7. Canonical plot by improved Daniel's Method

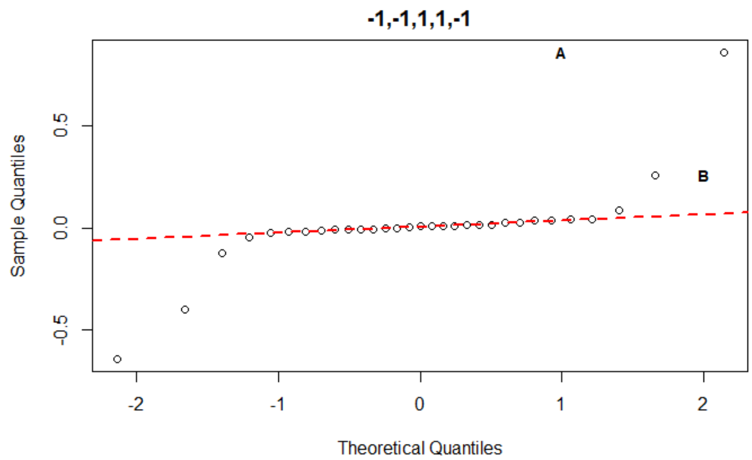


Table 6. Sorted ascending order of effect when i=-1, j=-1, k=1, l=1, m=-1

E	D	AD	ABCE	AC	CDE	CE	ACDE
-0.6415	0.3988	-0.1211	-0.0488	-0.0238	-0.0165	-0.0165	-0.0153
ABC	CD	ABD	BD	ADE	ABE	BCE	BDE
-0.0099	-0.0096	-0.0089	-0.0060	-0.0006	0.0002	0.0053	0.0068
ABCD	AB	ACE	DE	ABCDE	BCDE	ABDE	C
0.0068	0.0115	0.0116	-0.0122	0.0123	0.0135	0.0266	0.0275
BE	ACD	BCD	BC	AE	B	A	
0.0367	0.0383	0.0419	0.0429	0.0841	0.2590	0.8618	

From the *Figure 7*. and the *Table 6.*, I could identify effect A, B, D, E are significant.

Improved Lenth's method (Dong's Method) showed little bit different results (Specific calculation code is provided in appendix H). The median of the absolute value of effects was 0.016. Based upon the median the calculated S_0 was 0.025 and calculated S_1 and S_2 were the same as 0.023. As a result, factors A, B, D, E, AD and AE have the absolute values which are greater than $t_{25,0.002} \times S_2 = 0.073$

Lastly, I used studentized maximum modulus distribution to analyze the significance of effects. The $\hat{\sigma}$ for the analysis model $\mu + \beta X + \delta_z + \epsilon$, 0.0725 can be observed in the *Table 5.*, and it is the same as *0.0725.* The value of multiplier $M_{31,31}^{(0.1)}$, which is obtained from the table *Critical Values of Studentized Maximum Modulus Distribution* in appendix I, is 3.15. The value of $M_{31,31}^{(0.1)} \times \sqrt{4\hat{\sigma}\ /N}$ is 0.057 which is the same as the result that can be obtained from t-distribution ($t_{31,\frac{0.10}{2\times 31}} \times \sqrt{4\hat{\sigma}\ /N} = 0.057$) (specific calculation code is provided in appendix I). factors A, B, D, E, AD and AE have the absolute values which are greater than 0.057. It is the same result we obtained from the improved Lenth's method.

Conclusion and Lessons Learned

All the analysis methods commonly distinguished the factors A, B, D, and E as the significant factors. Interaction factors AD and AE are classified as the significant factors by the improved Lenth's method and analysis through studentized maximum modulus and t distribution.

When I used 5, 4 and 3 factors interactions to estimate σ^2, AD and AE are found as significant factors as well. Hence, according to the data analysis, the best model for analyzing the data is the same as the following:

$$y^{0.45} = \mu + \left(\frac{-0.8618}{2}\right)x_1 + \left(\frac{-0.2590}{2}\right)x_2 + \left(\frac{-0.3988}{2}\right)x_4 + \left(\frac{0.6415}{2}\right)x_5 + \left(\frac{0.1211}{2}\right)x_1x_4 + \left(\frac{0.0841}{2}\right)x_1x_5 +$$
$$+\epsilon \sim \mathrm{N}(0, \sigma^2)\ .$$

For more accurate analysis, Box-Cox transformation is needed for the given data set. The aqueous solution that was kept at room temperature for a day and contains carbonation, salt, citrus acid is the best aqueous solution for dissolving antihistamine pills.

As I expected highly influencing factor was A, the low level of A represent carbonation. The second most influential factor was factor, E which represents the temperature of the aqueous solution. Low level of factor E is the refrigerator temperature of an aqueous solution, and it increased times of the dissolution. High levels of factors B and D are salt and citrus acid, respectively. They also influenced the reduction of the time for the dissolution.

The block effect was also observed in the analysis. The two experiments had run in the two different room temperatures. During each experiment was going on, I put all the cups at room temperature. This might the cause of the block effect. An interesting fact is that Figure 6. showed some interaction effect between room temperature and carbonation. The room temperature was low in the second run, and the carbonation effect was increased. I do not see the significance of factor C, which represents whether sugar goes in or not. However, from the fact that interaction factor AE is significant, I observed an interesting phenomenon. As the temperature of the aqueous solution below or similar to refrigerator temperature, I figured out the carbonation effect was reduced.

From this fact, I could assume there would be a proper temperature range for the excellent performance of carbonation. From the significance of interaction effect AE, I figured out another interesting fact, that is stronger acid level (carbonation and citric acid are both acid) does not always guarantee the reduction of time to the dissolution of antihistamine.

I only used Zyrtec antihistamine for the experiment. However, in reality, there exists variety of antihistamine tablets. For the similar future study, I recommend using another type of antihistamine. Moreover, based upon what I found through my experiment and data analysis, it is worth conducting the experiments for finding the best pH and temperature range for dissolving antihistamine.

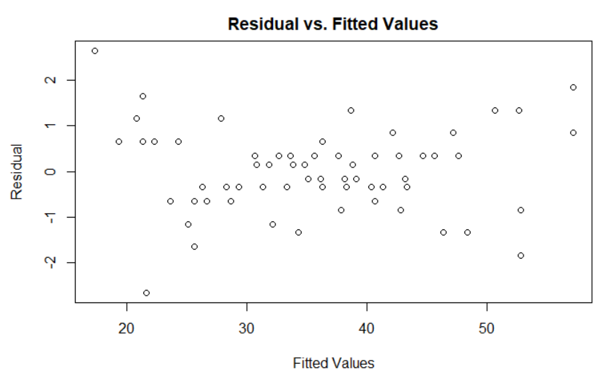
Appendices

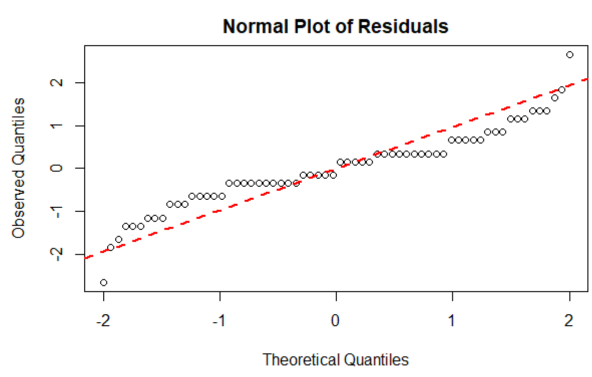
A. Data Preparation.

```
origin.dat <- read.table("project.data.csv", header=T, sep=",") #load the data
dat<- origin.dat[,-1] #excluding observation nubmer column
y<-vector()
for(i in 1:32){
  y<-rbind(y,dat$y1[i],dat$y2[i])
}
blk <-  c(rep(c("1","2"),32))
t.dat <- dat[rep(seq_len(nrow(dat)), each = 2),1:5] #making transfromed data
t.dat$blk <- blk
t.dat$y <- y
avg.y<-vector()
for(i in 1:32){
  avg.y[i] <- sum(y[2*i-1],y[2*i])/2
}
```

B. Normality and Constant Variance Checking.

```
m1 <- lm(y~A*B*C*D*E+blk,data= t.dat)
pred <- m1$fitted.values
r <- y-pred
plot(x=pred,y=r,xlab="Fitted Values",ylab = "Residual",main="Residual vs. Fitted Values")
theo.q <- seq(-2, 2, by=(4/(64-1)))
plot(x = theo.q,y=sort(r),xlab="Theoretical Quantiles",ylab="Observed Quantiles",
main="Normal Plot of Residuals")
qqline(sort(r),col = 2,lwd=2,lty=2)
```



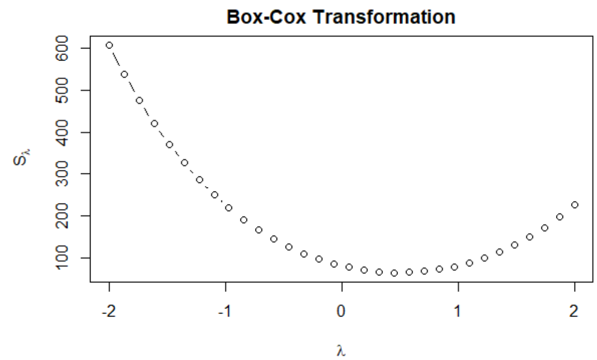


C. Box-Cox Transformation.

```
gm <- exp(mean(log(avg.y)))
x1 <- dat$A
x2 <- dat$B
```

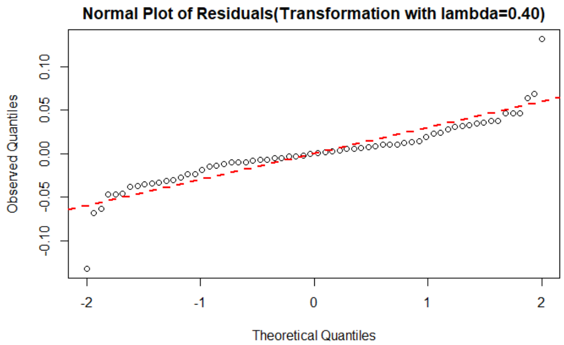
```
x3 <- dat$C
x4 <- dat$D
x5 <- dat$E
ssr <- NULL
lambda.seq<-seq(from=-2,to=2,length.out=32)
for(lambda in lambda.seq){
  if(lambda==0){
    y.0<-gm*log(avg.y)}
  else{
    y.0<-(avg.y^lambda-1)/(lambda*gm^{lambda-1})}
  fit<-lm(y.0~x1+x2+x3+x4+x5)
  ssr<-c(ssr,sum(fit$resid^2))
}
plot(lambda.seq,ssr,type="b",xlab=expression(lambda),
ylab=expression(S[lambda]),main="Box-Cox Transformation")
lambda.table <- cbind(lambda.seq,ssr)
lambda.table
lambda.table[which.min(ssr)]

lambd <- 0.40
m2.1 <- lm(y^(lambd)~A*B*C*D*E+blk,data= t.dat)
pred.1 <- m2.1$fitted.values
r.1 <- (t.dat$y)^(lambd)-pred.1
plot(x=pred,y=r.1,xlab="Fitted Values",ylab = "Residual",main="Residual vs. Fitted
Values(Transformation with lambda=0.40)")
theo.q <- seq(-2, 2, by=(4/(64-1)))
plot(x = theo.q,y=sort(r.1),xlab="Theoretical Quantiles",ylab="Observed Quantiles",
main="Normal Plot of Residuals(Transformation with lambda=0.40)")
qqline(sort(r.1),col = 2,lwd=2,lty=2)

lambd <- 0.45
m2.2 <- lm(y^(lambd)~A*B*C*D*E+blk,data= t.dat)
pred.1 <- m2.2$fitted.values
r.1 <- (t.dat$y)^(lambd)-pred.1
plot(x=pred,y=r.1,xlab="Fitted Values",ylab = "Residual",main="Residual vs. Fitted
Values(Transformation with lambda=0.45)")
theo.q <- seq(-2, 2, by=(4/(64-1)))
plot(x = theo.q,y=sort(r.1),xlab="Theoretical Quantiles",ylab="Observed Quantiles",
main="Normal Plot of Residuals(Transformation with lambda=0.45)")
qqline(sort(r.1),col = 2,lwd=2,lty=2)

lambd <- 0.50
m2.3 <- lm(y^(lambd)~A*B*C*D*E+blk,data= t.dat)
pred.1 <- m2.3$fitted.values
r.1 <- (t.dat$y)^(lambd)-pred.1
```

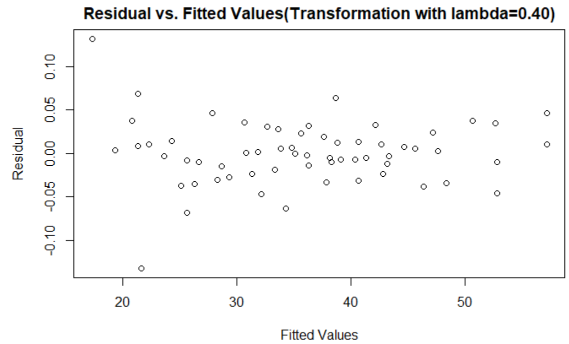
plot(x=pred,y=r.1,xlab="Fitted Values",ylab = "Residual",main="Residual vs. Fitted Values(Transformation with lambda=0.50)")
theo.q <- seq(-2, 2, by=(4/(64-1)))
plot(x = theo.q,y=sort(r.1),xlab="Theoretical Quantiles",ylab="Observed Quantiles", main="Normal Plot of Residuals(Transformation with lambda=0.50)")
qqline(sort(r.1),col = 2,lwd=2,lty=2)

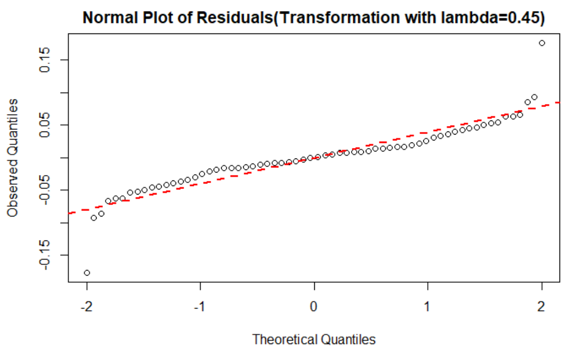


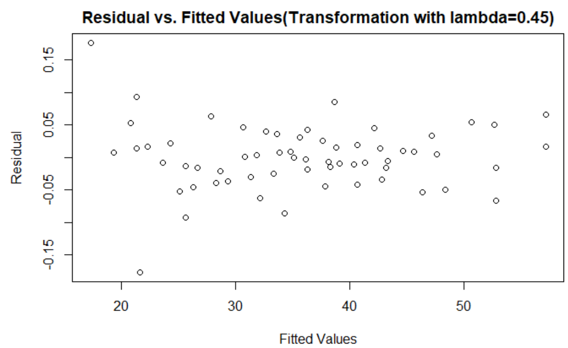
	lambda.seq	ssr
[1,]	-2.00000000	607.45161
[2,]	-1.87096774	538.56885
[3,]	-1.74193548	476.64416
[4,]	-1.61290323	421.02150
[5,]	-1.48387097	371.11680
[6,]	-1.35483871	326.41061
[7,]	-1.22580645	286.44163
[8,]	-1.09677419	250.80097
[9,]	-0.96774194	219.12710
[10,]	-0.83870968	191.10140
[11,]	-0.70967742	166.44422
[12,]	-0.58064516	144.91150
[13,]	-0.45161290	126.29173
[14,]	-0.32258065	110.40339
[15,]	-0.19354839	97.09270
[16,]	-0.06451613	86.23176
[17,]	0.06451613	77.71689
[18,]	0.19354839	71.46733
[19,]	0.32258065	67.42420
[20,]	0.45161290	65.54965
[21,]	0.58064516	65.82628
[22,]	0.70967742	68.25678
[23,]	0.83870968	72.86377
[24,]	0.96774194	79.68984
[25,]	1.09677419	88.79782
[26,]	1.22580645	100.27125
[27,]	1.35483871	114.21504
[28,]	1.48387097	130.75637
[29,]	1.61290323	150.04579
[30,]	1.74193548	172.25855
[31,]	1.87096774	197.59620
[32,]	2.00000000	226.28842

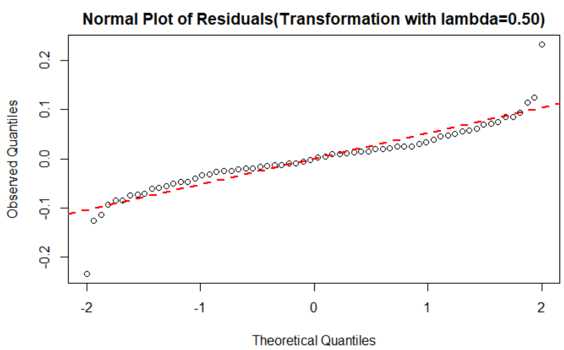
Box-Cox Transformation Lambda and SSR

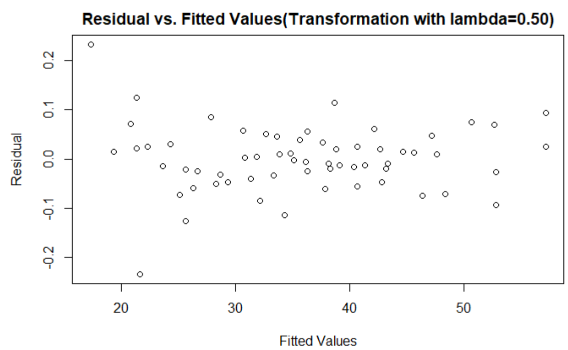












D. Checking whether the block effect is negligible or not.

```
m2 <- lm(y^(0.45)~A*B*C*D*E+blk,data= t.dat)
a.m2 <-aov(m2)
m3 <- lm(y^(0.45)~A*B*C*D*E,data= t.dat)
a.m3 <-aov(m3)
summary(a.m2)
summary(a.m3)
RSS.m2 <- 0.163
df.m2 <- 31
RSS.m3 <- 1.288
df.m3 <- 32
f.val <- ((RSS.m3-RSS.m2)/(df.m3-df.m2))/((RSS.m3)/(df.m3))
```

```
f.val
1-pf(f.val,df1=df.m3-df.m2, df2 = df.m3)
library(ggplot2)
A1 <- 1/16*(sum(dat[dat$A==1,]$y1^(0.45))-sum(dat[dat$A==-1,]$y1^(0.45)))
B1 <- 1/16*(sum(dat[dat$B==1,]$y1^(0.45))-sum(dat[dat$B==-1,]$y1^(0.45)))
C1 <- 1/16*(sum(dat[dat$C==1,]$y1^(0.45))-sum(dat[dat$C==-1,]$y1^(0.45)))
D1 <- 1/16*(sum(dat[dat$D==1,]$y1^(0.45))-sum(dat[dat$D==-1,]$y1^(0.45)))
E1 <- 1/16*(sum(dat[dat$E==1,]$y1^(0.45))-sum(dat[dat$E==-1,]$y1^(0.45)))
mean1 <- rbind(A1,B1,C1,D1,E1)

A2 <- 1/16*(sum(dat[dat$A==1,]$y2^(0.45))-sum(dat[dat$A==-1,]$y2^(0.45)))
B2 <- 1/16*(sum(dat[dat$B==1,]$y2^(0.45))-sum(dat[dat$B==-1,]$y2^(0.45)))
C2 <- 1/16*(sum(dat[dat$C==1,]$y2^(0.45))-sum(dat[dat$C==-1,]$y2^(0.45)))
D2 <- 1/16*(sum(dat[dat$D==1,]$y2^(0.45))-sum(dat[dat$D==-1,]$y2^(0.45)))
E2 <- 1/16*(sum(dat[dat$E==1,]$y2^(0.45))-sum(dat[dat$E==-1,]$y2^(0.45)))
mean2 <- rbind(A2,B2,C2,D2,E2)
Block <- c(rep("Block1",5),rep("Block2",5))
group <- rep(c("A","B","C","D","E"),2)

g.dat <- data.frame(MainEffects=group,Block=Block,Effect=c(mean1,mean2))

ggplot(data=g.dat,
aes(x=Block,y=Effect))+geom_line(aes(colour=MainEffects,group=MainEffects))+geo
m_point(aes(colour=MainEffects),size=2)
```

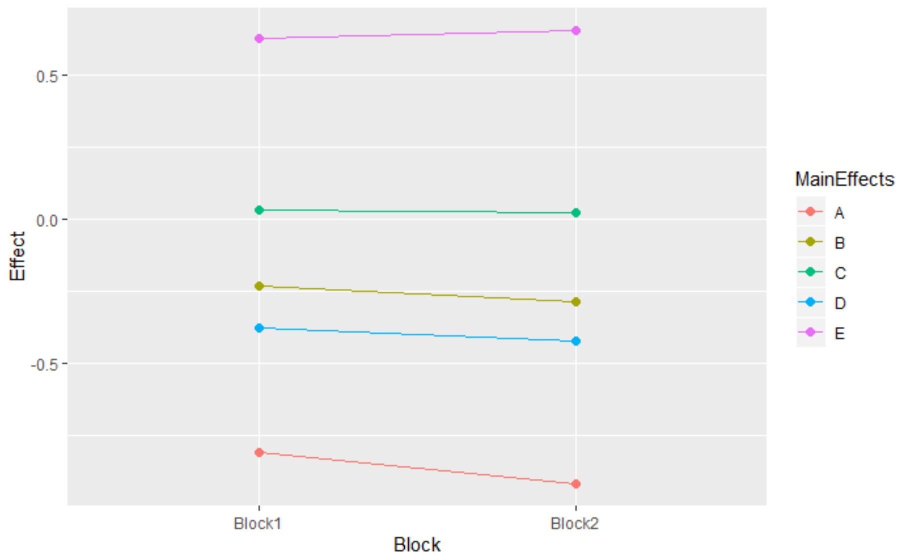
	Df	Sum Sq	Mean Sq	F value	Pr(>F)
A	1	11.883	11.883	2260.843	< 2e-16
B	1	1.073	1.073	204.132	3.49e-15
C	1	0.012	0.012	2.310	0.1386
D	1	2.545	2.545	484.182	< 2e-16
E	1	6.584	6.584	1252.588	< 2e-16
blk	1	1.125	1.125	214.097	1.83e-15
A:B	1	0.002	0.002	0.403	0.5303
A:C	1	0.009	0.009	1.718	0.1996
B:C	1	0.029	0.029	5.599	0.0244
A:D	1	0.234	0.234	44.610	1.81e-07
B:D	1	0.001	0.001	0.109	0.7430
C:D	1	0.001	0.001	0.278	0.6016
A:E	1	0.113	0.113	21.505	6.06e-05
B:E	1	0.022	0.022	4.093	0.0517
C:E	1	0.004	0.004	0.825	0.3706
D:E	1	0.002	0.002	0.454	0.5054
A:B:C	1	0.002	0.002	0.296	0.5905
A:B:D	1	0.001	0.001	0.239	0.6281
A:C:D	1	0.024	0.024	4.471	0.0426
B:C:D	1	0.028	0.028	5.354	0.0275
A:B:E	1	0.000	0.000	0.000	0.9923
A:C:E	1	0.002	0.002	0.408	0.5279
B:C:E	1	0.000	0.000	0.085	0.7732
A:D:E	1	0.000	0.000	0.001	0.9760
B:D:E	1	0.001	0.001	0.141	0.7102
C:D:E	1	0.004	0.004	0.829	0.3697
A:B:C:D	1	0.001	0.001	0.142	0.7093
A:B:C:E	1	0.038	0.038	7.240	0.0114
A:B:D:E	1	0.011	0.011	2.147	0.1529
A:C:D:E	1	0.004	0.004	0.712	0.4053
B:C:D:E	1	0.003	0.003	0.555	0.4621
A:B:C:D:E	1	0.002	0.002	0.464	0.5010
Residuals	31	0.163	0.005		

ANOVA table of m2

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
A	1	11.883	11.883	295.177	< 2e-16
B	1	1.073	1.073	26.652	1.24e-05
C	1	0.012	0.012	0.302	0.5867
D	1	2.545	2.545	63.215	4.48e-09
E	1	6.584	6.584	163.539	4.03e-14
A:B	1	0.002	0.002	0.053	0.8201
A:C	1	0.009	0.009	0.224	0.6390
B:C	1	0.029	0.029	0.731	0.3989
A:D	1	0.234	0.234	5.824	0.0217
B:D	1	0.001	0.001	0.014	0.9056
C:D	1	0.001	0.001	0.036	0.8500
A:E	1	0.113	0.113	2.808	0.1036
B:E	1	0.022	0.022	0.534	0.4701
C:E	1	0.004	0.004	0.108	0.7448
D:E	1	0.002	0.002	0.059	0.8092
A:B:C	1	0.002	0.002	0.039	0.8455
A:B:D	1	0.001	0.001	0.031	0.8608
A:C:D	1	0.024	0.024	0.584	0.4504
B:C:D	1	0.028	0.028	0.699	0.4093
A:B:E	1	0.000	0.000	0.000	0.9972
A:C:E	1	0.002	0.002	0.053	0.8190
B:C:E	1	0.000	0.000	0.011	0.9170
A:D:E	1	0.000	0.000	0.000	0.9913
B:D:E	1	0.001	0.001	0.018	0.8930
C:D:E	1	0.004	0.004	0.108	0.7444
A:B:C:D	1	0.001	0.001	0.018	0.8927
A:B:C:E	1	0.038	0.038	0.945	0.3382
A:B:D:E	1	0.011	0.011	0.280	0.6001
A:C:D:E	1	0.004	0.004	0.093	0.7624
B:C:D:E	1	0.003	0.003	0.072	0.7896
A:B:C:D:E	1	0.002	0.002	0.061	0.8072
Residuals	32	1.288	0.040		

ANOVA table of m3

Interaction Plot between Main Effects and Block



E. Calculating the effects of factors based upon model m2.

```
summary(m2)
coef <- round(m2$coefficients, digits = 4)
coef
fitted.y1 <- c()
fitted.y2 <- c()
for(i in 1:32){
  fitted.y1[i] <- a.m2$fitted.values[2*i-1]
  fitted.y2[i] <- a.m2$fitted.values[2*i]
}
fitted.y1 <- c("-",round(fitted.y1,digits=4))
fitted.y2 <- c("-",round(fitted.y2,digits=4))
fitted.dat <- data.frame(coefficients=coef,fitted.y1=fitted.y1,fitted.y2=fitted.y2)
RSE <- c(0.0725)
fitted.dat <- rbind(fitted.dat,RSE)
fitted.dat[7,2:3] <- c("-","-")
fitted.dat[34,2:3] <- c("-", "-")
row.names(fitted.dat)[34] <- "RSE"

e.A <- 2*(m2$coefficients[2])
e.B <- 2*(m2$coefficients[3])
e.C <- 2*(m2$coefficients[4])
e.D <- 2*(m2$coefficients[5])
e.E <- 2*(m2$coefficients[6])
e.AB <- 2*(m2$coefficients[8])
e.AC <- 2*(m2$coefficients[9])
e.AD <- 2*(m2$coefficients[11])
```

```
e.AE <- 2*(m2$coefficients[14])
e.BC <- 2*(m2$coefficients[10])
e.BD <- 2*(m2$coefficients[12])
e.BE <- 2*(m2$coefficients[15])
e.CD <- 2*(m2$coefficients[13])
e.CE <- 2*(m2$coefficients[16])
e.DE <- 2*(m2$coefficients[17])
e.ABC <- 2*(m2$coefficients[18])
e.ABD <- 2*(m2$coefficients[19])
e.ABE <- 2*(m2$coefficients[22])
e.ACD <- 2*(m2$coefficients[20])
e.ACE <- 2*(m2$coefficients[23])
e.ADE <- 2*(m2$coefficients[25])
e.BCD <- 2*(m2$coefficients[21])
e.BCE <- 2*(m2$coefficients[24])
e.BDE <- 2*(m2$coefficients[26])
e.CDE <- 2*(m2$coefficients[27])
e.ABCD <- 2*(m2$coefficients[28])
e.ABCE <- 2*(m2$coefficients[29])
e.ABDE <- 2*(m2$coefficients[30])
e.ACDE <- 2*(m2$coefficients[31])
e.BCDE <- 2*(m2$coefficients[32])
e.ABCDE <- 2*(m2$coefficients[33])

effects <- rbind(e.A,e.B,e.C,e.D,e.E,e.AB,e.AC, e.AD,e.AE, e.BC, e.BD, e.BE,e.CD,
e.CE,e.DE,e.ABC,e.ABD,e.ABE,e.ACD,e.ACE,e.ADE,e.BCD,e.BCE,e.BDE,e.CDE,e.ABC
D,e.ABCE, e.ABDE,e.ACDE,e.BCDE,e.ABCDE)
```

Coefficients and RSE of the model

```
Coefficients:
              Estimate Std. Error t value Pr(>|t|)    
(Intercept)  4.818e+00  1.282e-02 375.902  < 2e-16 ***
A           -4.309e-01  9.062e-03 -47.548  < 2e-16 ***
B           -1.295e-01  9.062e-03 -14.287 3.49e-15 ***
C            1.377e-02  9.062e-03   1.520   0.1386    
D           -1.994e-01  9.062e-03 -22.004  < 2e-16 ***
E            3.207e-01  9.062e-03  35.392  < 2e-16 ***
blk2         2.652e-01  1.812e-02  14.632 1.83e-15 ***
A:B          5.751e-03  9.062e-03   0.635   0.5303    
A:C          1.188e-02  9.062e-03   1.311   0.1996    
B:C         -2.144e-02  9.062e-03  -2.366   0.0244 *  
A:D          6.053e-02  9.062e-03   6.679 1.81e-07 ***
B:D          2.998e-03  9.062e-03   0.331   0.7430    
C:D         -4.781e-03  9.062e-03  -0.528   0.6016    
A:E          4.203e-02  9.062e-03   4.637 6.06e-05 ***
B:E          1.834e-02  9.062e-03   2.023   0.0517 .  
C:E          8.233e-03  9.062e-03   0.908   0.3706    
D:E         -6.107e-03  9.062e-03  -0.674   0.5054    
A:B:C       -4.927e-03  9.062e-03  -0.544   0.5905    
A:B:D       -4.433e-03  9.062e-03  -0.489   0.6281    
A:C:D       -1.916e-02  9.062e-03  -2.114   0.0426 *  
B:C:D       -2.097e-02  9.062e-03  -2.314   0.0275 *  
A:B:E       -8.845e-05  9.062e-03  -0.010   0.9923    
A:C:E        5.785e-03  9.062e-03   0.638   0.5279    
B:C:E        2.635e-03  9.062e-03   0.291   0.7732    
A:D:E       -2.753e-04  9.062e-03  -0.030   0.9760    
B:D:E        3.399e-03  9.062e-03   0.375   0.7102    
C:D:E        8.249e-03  9.062e-03   0.910   0.3697    
A:B:C:D      3.410e-03  9.062e-03   0.376   0.7093    
A:B:C:E      2.438e-02  9.062e-03   2.691   0.0114 *  
A:B:D:E     -1.328e-02  9.062e-03  -1.465   0.1529    
A:C:D:E     -7.646e-03  9.062e-03  -0.844   0.4053    
B:C:D:E      6.749e-03  9.062e-03   0.745   0.4621    
A:B:C:D:E   -6.170e-03  9.062e-03  -0.681   0.5010    
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.0725 on 31 degrees of freedom
Multiple R-squared:  0.9932,	Adjusted R-squared:  0.9862 
F-statistic: 141.3 on 32 and 31 DF,  p-value: < 2.2e-16
```

Factor Effects

```
e.A      -0.8618053189
e.B      -0.2589580374
e.C       0.0275494554
e.D      -0.3988212220
e.E       0.6414724764
e.AB      0.0115029918
e.AC      0.0237575522
e.AD      0.1210565436
e.AE      0.0840502570
e.BC     -0.0428879124
e.BD      0.0059951981
e.BE      0.0366703026
e.CD     -0.0095610338
e.CE      0.0164661898
e.DE     -0.0122142460
e.ABC    -0.0098543120
e.ABD    -0.0088665951
e.ABE    -0.0001768960
e.ACD    -0.0383247890
e.ACE     0.0115710057
e.ADE    -0.0005506685
e.BCD    -0.0419400646
e.BCE     0.0052702781
e.BDE     0.0067980692
e.CDE     0.0164988569
e.ABCD    0.0068200707
e.ABCE    0.0487692944
e.ABDE   -0.0265603581
e.ACDE   -0.0152922186
e.BCDE    0.0134978811
e.ABCDE  -0.0123402538
```

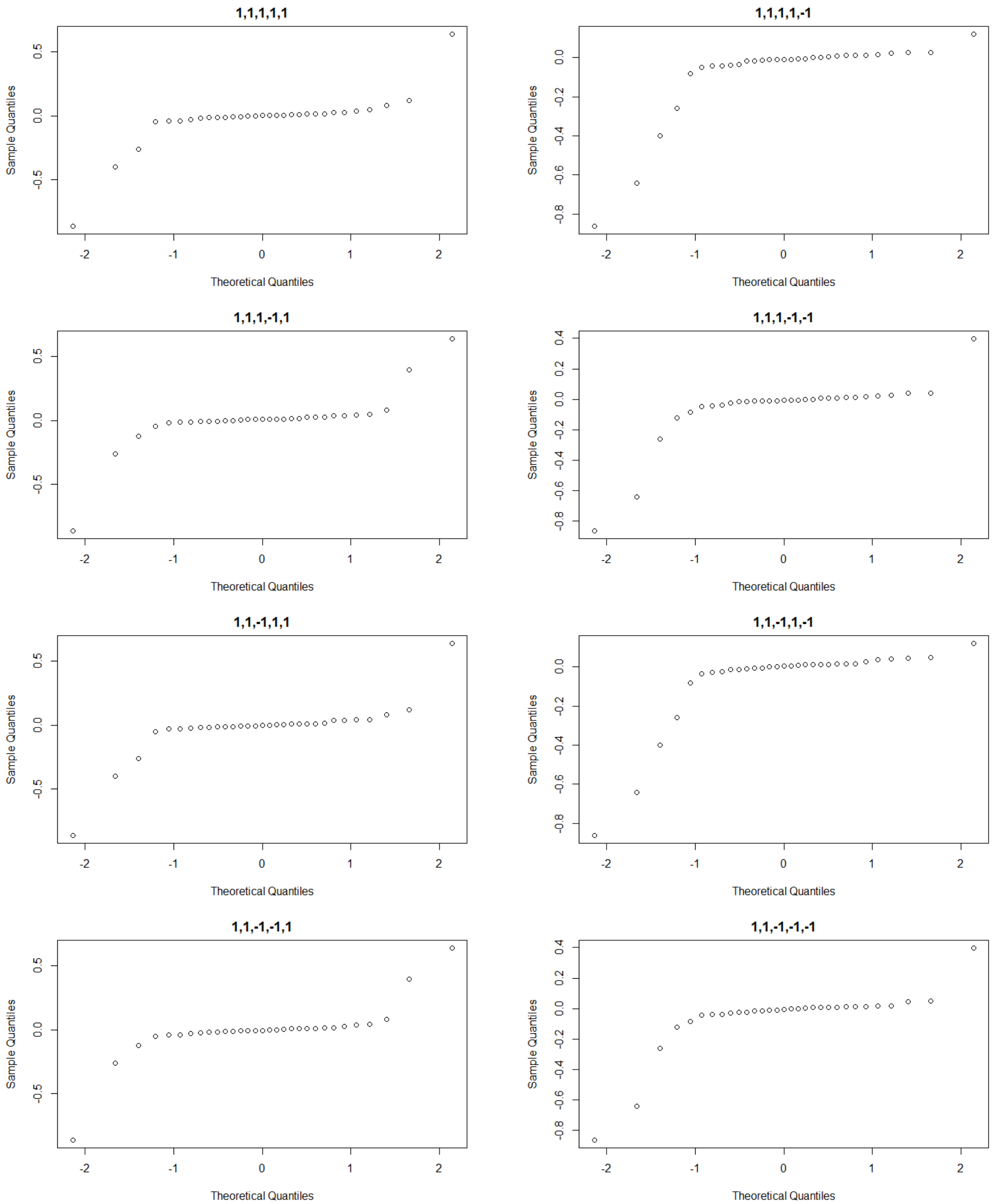
F. Using interactions to estimate sigma square

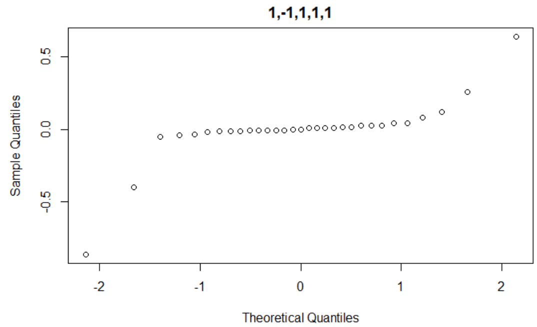
```
effectnames  <- names(effects)

sg1 <- sqrt(e.ABCDE^2) # If only 5 fi is assumed negligible
t1 <- qt(p=1-(0.10/2/30),df=1,lower.tail=T)
effectnames[which(abs(effects)>=sg1*t1)]

sg2  <-  sqrt(e.ABCD^2+e.ABCE^2+e.ABDE^2+e.ACDE^2+e.BCDE^2+e.ABCDE^2)/6# If 4 fi and 5 fi are assumed negligible
t2 <- qt(p=1-(0.10/2/25),df=6,lower.tail=T)
effectnames[which(abs(effects)>=sg2*t2)]

sg3 <- sqrt(e.ABC^2+e.ABD^2+e.ABE^2+e.ACD^2+e.ACE^2+e.ADE^2+e.BCD^2+e.BCE^2+e.BDE^2+e.CDE^2+e.ABCD^2+e.ABCE^2+e.ABDE^2+e.ACDE^2+e.BCDE^2+e.ABCDE^2)/16# If 3 fi, 4fi and 5fi are assumed negligible
t3 <- qt(p=1-(0.10/2/15),df=16,lower.tail=T)
effectnames[which(abs(effects)>=sg3*t3)]

sg4 <- sqrt(e.AB^2+e.AC^2+e.AD^2+e.AE^2+e.BC^2+e.BD^2+e.BE^2+e.CD^2+e.CE^2+e.DE^2+e.ABC^2+e.ABD^2+e.ABE^2+e.ACD^2+e.ACE^2+e.ADE^2+e.BCD^2+e.BCE^2+e.BDE^2+e.CDE^2+e.ABCD^2+e.ABCE^2+e.ABDE^2+e.ACDE^2+e.BCDE^2+e.ABCDE^2)/26# If 2fi, 3 fi, 4fi and 5fi are assumed negligible
t4 <- qt(p=1-(0.10/2/5),df=26,lower.tail=T)
effectnames[which(abs(effects)>=sg4*t4)]
```

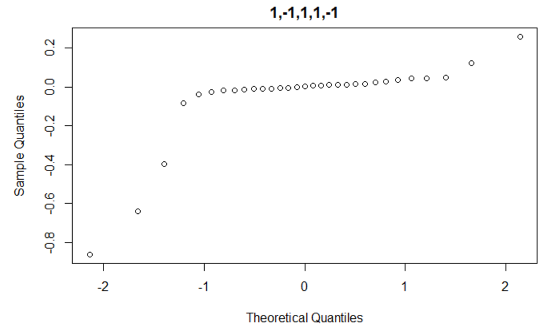
G. Improved Daniel's method (Loh's method)

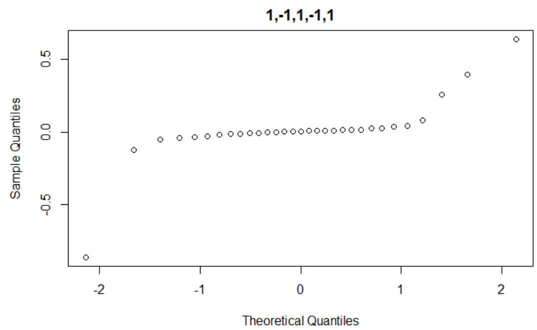
```
par(mfrow=c(8,4),pty="s", mar=rep(2,4))
i0<-0
j0<-0
k0<-0
r<-0
d<-Inf
effects<-NULL
for(i in c(1,-1)){
  for(j in c(1,-1)){
    for(k in c(1,-1)){
      for(l in c(1,-1)){
        for(m in c(1,-1)){
      new.effects<-
c(e.A*i,e.B*j,e.C*k,e.D*l,e.E*m,e.AB*i*j,e.AC*i*k,e.AD*i*l,e.AE*i*m,e.BC*j*k,e.BD*j
*l,e.BE*j*m,e.CD*k*l,e.CE*k*m,e.DE*l*m,e.ABC*i*j*k,e.ABD*i*j*l,e.ABE*i*j*m,e.AC
D*i*k*l,e.ACE*i*k*m,e.ADE*i*l*m,e.BCD*j*k*l,e.BCE*j*k*m,e.BDE*j*l*m,e.CDE*k*
l*m,e.ABCD*i*j*k*l,e.ABCE*i*j*k*m,e.ABDE*i*j*l*m,e.ACDE*i*k*l*m,e.BCDE*j*k*l
*m,e.ABCDE*i*j*k*l*m)
      qq<-qqnorm(new.effects,main=paste0(i,",",j,",",k,",",l,",",m))
      new.r<-cor(qq$x,qq$y)
      m<-median(new.effects)
      if(abs(m)<d|(abs(m)==d&new.r>r)){
        d<-abs(m)
        r<-new.r
        i0<-i
        j0<-j
        k0<-k
        effects<-new.effects } } } } } }
```

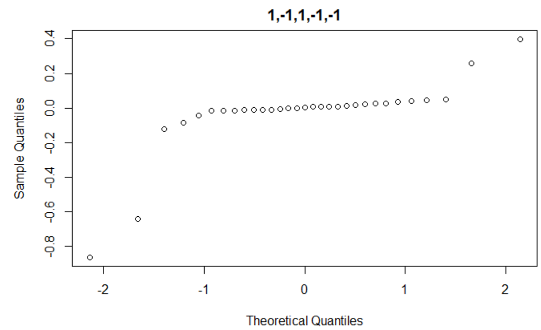
Plots for G. Improved Daniel's method (Loh's method)

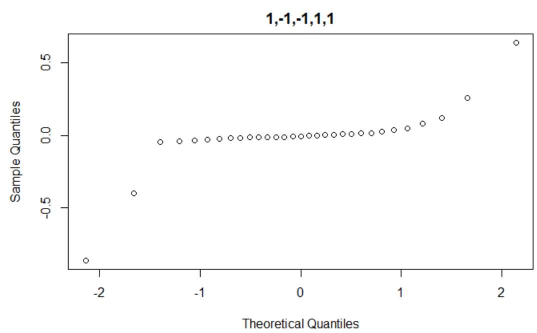

1,1,1,1,1
1,1,1,1,-1
1,1,1,-1,1
1,1,1,-1,-1
1,1,-1,1,1
1,1,-1,1,-1
1,1,-1,-1,1
1,1,-1,-1,-1
Sample Quantiles
Theoretical Quantiles

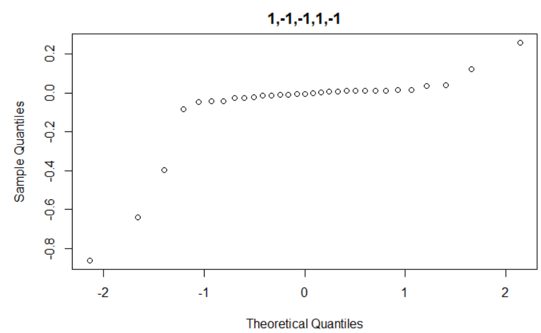

1,-1,1,1,1
Sample Quantiles
Theoretical Quantiles

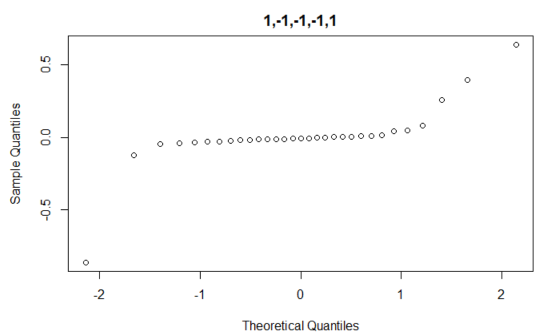

1,-1,1,1,-1
Sample Quantiles
Theoretical Quantiles

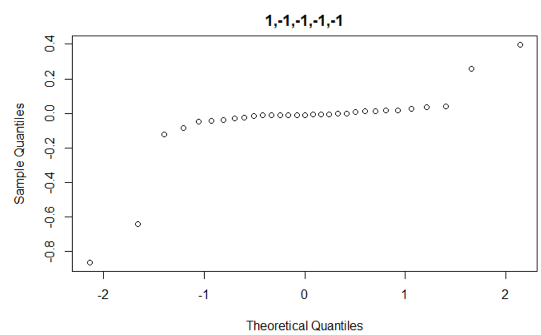

1,-1,1,-1,1
Sample Quantiles
Theoretical Quantiles

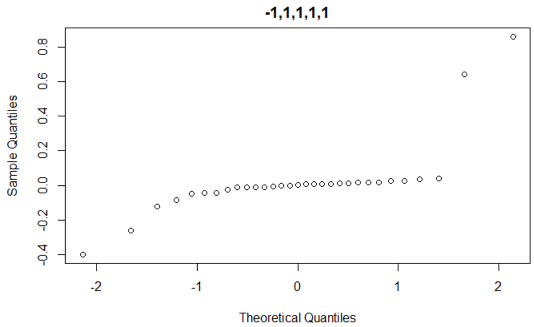

1,-1,1,-1,-1
Sample Quantiles
Theoretical Quantiles

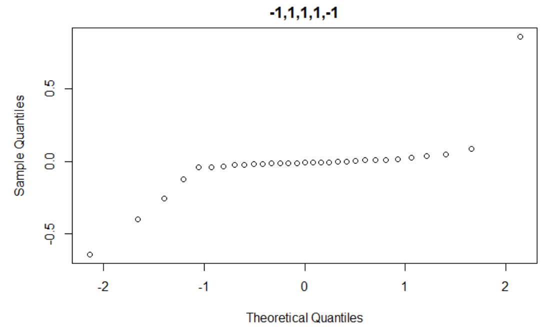

1,-1,-1,1,1
Sample Quantiles
Theoretical Quantiles

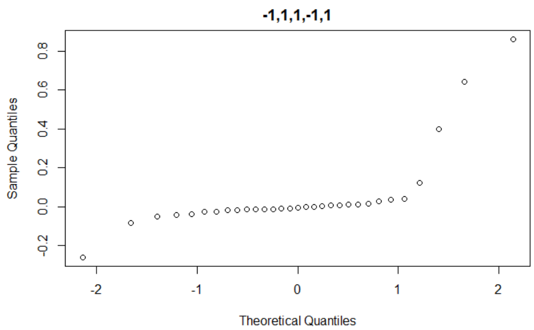

1,-1,-1,1,-1
Sample Quantiles
Theoretical Quantiles

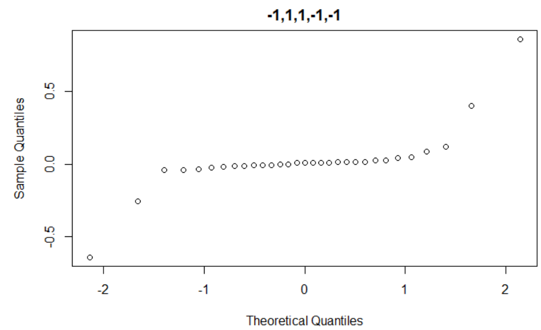

1,-1,-1,-1,1
Sample Quantiles
Theoretical Quantiles

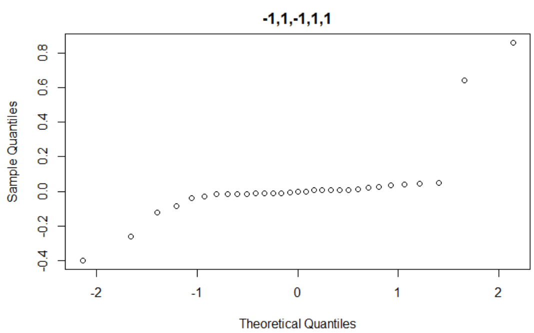

1,-1,-1,-1,-1
Sample Quantiles
Theoretical Quantiles

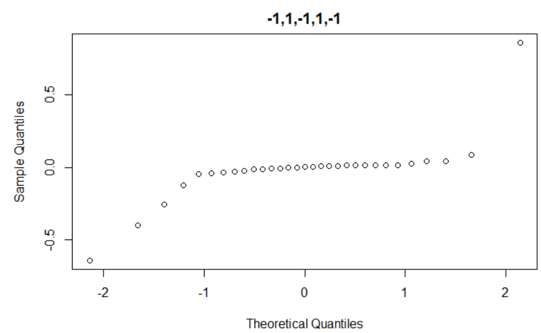

-1,1,1,1,1
Sample Quantiles
-0.4 -0.2 0.0 0.2 0.4 0.6 0.8
-2 -1 0 1 2
Theoretical Quantiles

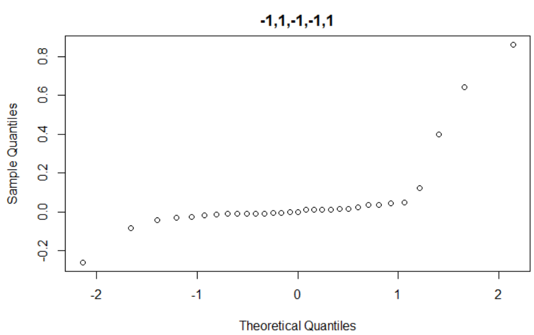

-1,1,1,1,-1
Sample Quantiles
-0.5 0.0 0.5
-2 -1 0 1 2
Theoretical Quantiles

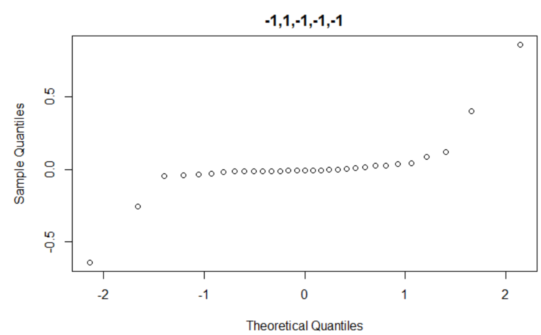

-1,1,1,-1,1
Sample Quantiles
-0.2 0.0 0.2 0.4 0.6 0.8
-2 -1 0 1 2
Theoretical Quantiles

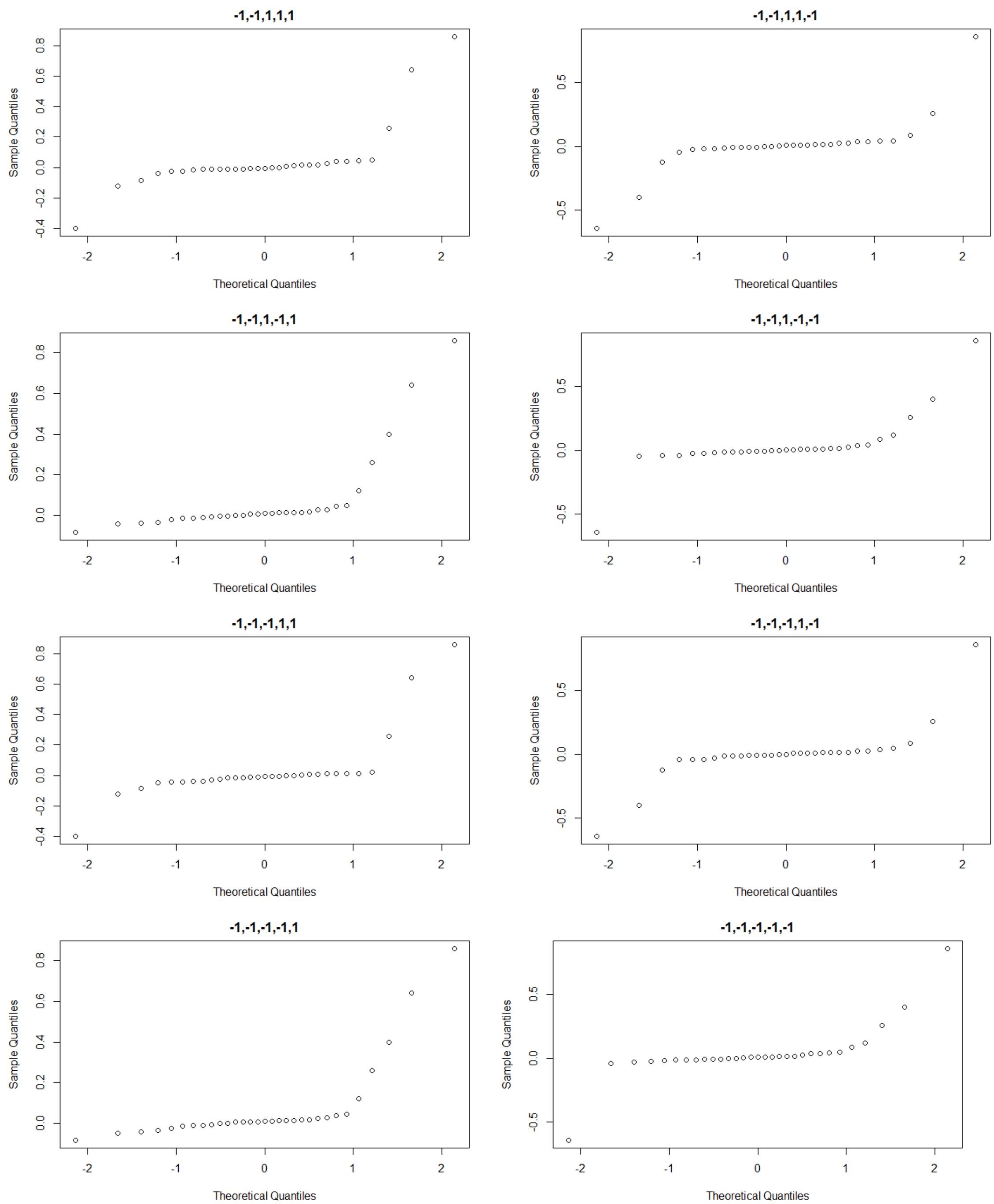

-1,1,1,-1,-1
Sample Quantiles
-0.5 0.0 0.5
-2 -1 0 1 2
Theoretical Quantiles


-1,1,-1,1,1
Sample Quantiles
-0.4 -0.2 0.0 0.2 0.4 0.6 0.8
-2 -1 0 1 2
Theoretical Quantiles


-1,1,-1,1,-1
Sample Quantiles
-0.5 0.0 0.5
-2 -1 0 1 2
Theoretical Quantiles


-1,1,-1,-1,1
Sample Quantiles
-0.2 0.0 0.2 0.4 0.6 0.8
-2 -1 0 1 2
Theoretical Quantiles


-1,1,-1,-1,-1
Sample Quantiles
-0.5 0.0 0.5
-2 -1 0 1 2
Theoretical Quantiles

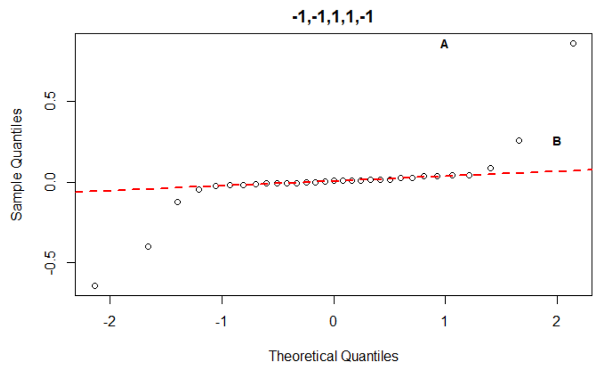


G-1. Chosen plot by improved Daniel's method

```
i<--1
j<--1
k<-1
l<-1
m<--1
d.effects<-
c(e.A*i,e.B*j,e.C*k,e.D*l,e.E*m,e.AB*i*j,e.AC*i*k,e.AD*i*l,e.AE*i*m,e.BC*j*k,e.BD*j
*l,e.BE*j*m,e.CD*k*l,e.CE*k*m,e.DE*l*m,e.ABC*i*j*k,e.ABD*i*j*l,e.ABE*i*j*m,e.AC
```

*D*i*k*l,e.ACE*i*k*m,e.ADE*i*l*m,e.BCD*j*k*l,e.BCE*j*k*m,e.BDE*j*l*m,e.CDE*k*l*m,e.ABCD*i*j*k*l,e.ABCE*i*j*k*m,e.ABDE*i*j*l*m,e.ACDE*i*k*l*m,e.BCDE*j*k*l*m,e.ABCDE*i*j*k*l*m)*

```
qqnorm(d.effects,main=paste0(i,",",j,",",k,",",l,",",m))
text(d.effects, labels = names(d.effects), cex=0.9, font=2)
qqline(d.effects,col = 2,lwd=2,lty=2)

sort(d.effects)
```



Sorted ascending order of effect when i=-1, j=-1, k=1, l=1, m=-1

```
            E             D           A:D       A:B:C:E           A:C         C:D:E           C:E       A:C:D:E         A:B:C           C:D         A:B:D
-0.6414724764 -0.3988212220 -0.1210565436 -0.0487692944 -0.0237575522 -0.0164988569 -0.0164661898 -0.0152922186 -0.0098543120 -0.0095610338 -0.0088665951
          B:D         A:D:E         A:B:E         B:C:E         B:D:E       A:B:C:D           A:B         A:C:E           D:E     A:B:C:D:E       B:C:D:E
-0.0059951981 -0.0005506685  0.0001768960  0.0052702781  0.0067980692  0.0068200707  0.0115029918  0.0115710057  0.0122142460  0.0123402538  0.0134978811
      A:B:D:E             C           B:E         A:C:D         B:C:D           B:C           A:E             B             A
 0.0265603581  0.0275494554  0.0366703026  0.0383247890  0.0419400646  0.0428879124  0.0840502570  0.2589580374  0.8618053189
```

H. Improved Lenth's method (Dong's method)

```
med <- median(abs(effects))
s0 <- 1.5*med
m.1 <- length(which(abs(effects)<=2.5*s0))
theta1 <- effects[which(abs(effects)<=2.5*s0)]
s1.sq <- sum(theta1^2)/m.1
s1 <- sqrt(s1.sq)

m.2 <- length(which(abs(effects)<=2.5*s1))
theta2 <- effects[which(abs(effects)<=2.5*s1)]
s2.sq <- sum(theta2^2)/m.2
s2 <- sqrt(s2.sq)

g.m <- 0.5*(1-(1-0.10)^(1/length(effects)))

t5 <- qt(p=1-g.m,df=m.2,lower.tail = T)
effectnames  <- names(effects)
effectnames[which(abs(effects)>=t5*s2)]
```

I. Studentized maximum modulus distribution

```
k <- 5
r <- 2
N <- 64
g <- 2^k -1
v <- (2^k-1)*(r-1)
sigma <- 0.0725
M <- 3.15
t6 <- qt(p=1-(0.10/2/g),df=v,lower.tail = T)

tres1 <- (2*sigma*M)/(sqrt(N))
effectnames[which(abs(effects)>=tres1)]

tres2 <- (2*sigma*t6)/(sqrt(N))
effectnames[which(abs(effects)>=tres2)]
```

Critical values of Studentized Maximum Modulus Distribution

$\alpha = 0.10$

	I																
ν	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
20	3.05	3.07	3.09	3.11	3.13	3.15	3.16	3.18	3.19	3.21	3.22	3.23	3.25	3.26	3.27	3.28	3.30
21	3.04	3.06	3.08	3.10	3.12	3.13	3.15	3.16	3.18	3.19	3.21	3.22	3.23	3.24	3.26	3.27	3.28
22	3.03	3.05	3.07	3.08	3.10	3.12	3.13	3.15	3.16	3.18	3.19	3.21	3.22	3.23	3.24	3.25	3.27
23	3.02	3.04	3.05	3.07	3.09	3.11	3.12	3.14	3.15	3.17	3.18	3.19	3.21	3.22	3.23	3.24	3.25
24	3.01	3.03	3.04	3.06	3.08	3.10	3.11	3.13	3.14	3.16	3.17	3.18	3.19	3.21	3.22	3.23	3.24
25	3.00	3.02	3.03	3.05	3.07	3.09	3.10	3.12	3.13	3.15	3.16	3.17	3.18	3.20	3.21	3.22	3.23
26	2.99	3.01	3.03	3.04	3.06	3.08	3.09	3.11	3.12	3.14	3.15	3.16	3.17	3.19	3.20	3.21	3.22
27	2.98	3.00	3.02	3.04	3.05	3.07	3.08	3.10	3.11	3.13	3.14	3.15	3.16	3.18	3.19	3.20	3.21
28	2.97	2.99	3.01	3.03	3.04	3.06	3.08	3.09	3.10	3.12	3.13	3.14	3.16	3.17	3.18	3.19	3.20
29	2.96	2.98	3.00	3.02	3.04	3.05	3.07	3.08	3.10	3.11	3.12	3.14	3.15	3.16	3.17	3.18	3.19
30	2.96	2.98	3.00	3.01	3.03	3.05	3.06	3.08	3.09	3.10	3.12	3.13	3.14	3.15	3.16	3.18	3.19
35	2.93	2.95	2.97	2.99	3.00	3.02	3.03	3.05	3.06	3.07	3.09	3.10	3.11	3.12	3.13	3.14	3.15
40	2.91	2.93	2.95	2.97	2.98	3.00	3.01	3.03	3.04	3.05	3.06	3.08	3.09	3.10	3.11	3.12	3.13
45	2.90	2.91	2.93	2.95	2.97	2.98	2.99	3.01	3.02	3.03	3.05	3.06	3.07	3.08	3.09	3.10	3.11
50	2.88	2.90	2.92	2.94	2.95	2.97	2.98	3.00	3.01	3.02	3.03	3.05	3.06	3.07	3.08	3.09	3.10
60	2.87	2.88	2.90	2.92	2.93	2.95	2.96	2.98	2.99	3.00	3.01	3.02	3.04	3.05	3.06	3.07	3.08
80	2.84	2.86	2.88	2.89	2.91	2.92	2.94	2.95	2.96	2.97	2.99	3.00	3.01	3.02	3.03	3.04	3.05
100	2.83	2.85	2.86	2.88	2.89	2.91	2.92	2.93	2.95	2.96	2.97	2.98	2.99	3.00	3.01	3.02	3.03
200	2.80	2.82	2.83	2.85	2.86	2.88	2.89	2.90	2.92	2.93	2.94	2.95	2.96	2.97	2.98	2.99	3.00
∞	2.77	2.79	2.81	2.82	2.84	2.85	2.86	2.87	2.89	2.90	2.91	2.92	2.93	2.94	2.95	2.96	2.97