R Boot Camp Problem Set

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Establishing reliable biomarkers for assessing and validating clinical diagnosis at early stages of Parkinson's disease is crucial for developing therapies to slow or halt disease progression. This data set uses whole blood gene simulatedession profiling from over 500 individuals where we will attempt to find a gene signature. This repository contains the gene simulatedession profiles collected in the GENEPARK consortium. The main study sought a classifier for IPD. These data contain 233 healthy controls, 205 IPD patients, and 48 patients with other neurodegenerative diseases (NDD). Other samples are available in the data and can be used for additional analyses. The largest class of these additional samples are 22 samples from genetic unaffected controls and 41 genetic PD patients.

Note: the original study which uploaded this data to NIH Geo is not yet published.

Data Wrangling

Let's start by loading in our data sets. Download these from the canvas site, and make a new folder for R bootcamp. We'll switch to this directory here.

The tinyTex package will allow you to actually knit .pdf documentats from RMarkdown:

Note that we have both a phenotype file, as well as a file which includes the normalized and log transformed simulatedession values. We can use the read.csv function to load in these files.

```
# load data in here
pheno = read.csv("parkPheno.csv")
simulated = read.csv('simulatedData.csv')
```

We should start by summarizing both these files. Try the following functions: head(), and View(). Note that while the dimensions on our phenotype file are reasonable, we have 552 columns in our simulatedession file. Just summarize the first 10 columns of this file.

```
# your code here
#View(pheno)
#View(simulated)
```

Try summarizing the phenotype data:

```
# your code here
library(dplyr)

## Warning: package 'dplyr' was built under R version 4.2.1

##

## 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
summarize(pheno)
## data frame with 0 columns and 1 row
summarize(simulated)
```

data frame with 0 columns and 1 row

We make the following observations.

- 1. We have some unnecessary data in this file. We aren't interested in the submission and last update date. We can reduce the dimensions of this file so it handles nicer from now on.
- 2. We have a LOT of missing data. You'll learn how to handle this in some of your biostats classes! For now, we'll run what analyses we can given the data we have.
- 3. Some of our scores have been read in as character values (and they should be numbers). If you investigate this further, you'll find that some values have been recorded as "ND", which we'll assume means "no data". We will need to record these as NA values in R.

Our next step is to address item one. We will reduce the dimensions of our pheno data frame to include only that information that we're interested in modelling. We can exclude the dates, type (as it's all RNA), tissue (all whole blood), organism (all homo sapiens), and subject ID (we will be using geo_accession as our unique indicator). As well, we will exclude mutated_pd_genes, as we indend to define our own gene signature later this week.

Subset your pheno data frame to include columns 1,8,9,11:20.

```
# your code here
pheno = pheno[,c(1,8,9,11:20)]
head(pheno)
```

```
##
     geo_accession disease_label
                                         sex age_at_exam age_at_symptoms updrs
## 1
         GSM2631171
                       ATYPICAL PD
                                        Male
                                                        NΑ
## 2
                       ATYPICAL PD
                                                                          64
                                                                                  0
         GSM2631309
                                        Male
                                                        NA
                       ATYPICAL_PD
                                                                          NA
                                                                                  0
## 3
         GSM2631219
                                        Male
                                                        NΑ
                                                                          60
                                                                                  0
## 4
         GSM2630775
                                CBD
                                      Female
                                                        NA
## 5
         GSM2631147
                                CBD
                                      Female
                                                        NA
                                                                          66
                                                                                  0
                                                                                  0
## 6
         GSM2630853
                            CONTROL
                                        Male
                                                        NA
                                                                          41
##
     updrs_ii updrs_iii_score_on updrs_iii_score_off
                                                           updrs_iv hoehn_yahr_on
## 1
                                 19
             4
                                                         0
                                                                   0
                                                                                   2
## 2
             0
                                  0
                                                         0
                                                                   0
                                                                                   9
## 3
             0
                                  0
                                                         0
                                                                   0
                                                                                   0
## 4
             0
                                  0
                                                         0
                                                                   0
                                                                                   9
## 5
             0
                                 30
                                                         0
                                                                   0
                                                                                   9
## 6
             0
                                                         0
                                                                   0
                                                                                   8
                                   1
##
     hoehn yahr off moca score
## 1
                    0
                               21
## 2
                    0
                                0
## 3
                    0
                                0
## 4
                    0
                                0
                                0
## 5
                    0
## 6
                    0
                               30
```

Next we need to correct the columns which contain "ND". You can use the "which" function to find the index of of the matrices which are "ND", and then set these to NA. Set columns 8,9,11,12,13 to numeric values

using the "as.numeric" function inside a "sapply" loop. Run a summary of the data frame again.

```
#your code here
ix = which(pheno$disease_label == "ND", arr.ind = T)
pheno[ix] = NA

j = c(8,9,11,12,13)
pheno[,j] = sapply(unlist(pheno[,j]), as.numeric)
summary(pheno)
```

```
##
    geo_accession
                        disease_label
                                                                  age_at_exam
                                                 sex
##
    Length:550
                        Length: 550
                                             Length:550
                                                                         :30.00
                                                                 Min.
##
    Class : character
                        Class : character
                                             Class : character
                                                                  1st Qu.:54.75
    Mode :character
                        Mode :character
                                             Mode :character
                                                                 Median :61.00
##
                                                                         :60.56
                                                                 Mean
##
                                                                  3rd Qu.:68.25
##
                                                                         :82.00
                                                                 Max.
##
                                                                 NA's
                                                                         :266
##
    age_at_symptoms
                          updrs
                                           updrs ii
                                                          updrs iii score on
##
    Min.
            :10.00
                             : 0.000
                                               : 0.000
                                                          Min.
                                                                  : 0.0
                     Min.
                                       Min.
    1st Qu.:45.00
                     1st Qu.: 0.000
                                       1st Qu.: 0.000
                                                          1st Qu.: 0.0
##
##
    Median :55.00
                     Median : 0.000
                                       Median : 0.000
                                                          Median: 0.5
##
    Mean
            :53.61
                     Mean
                             : 1.171
                                       Mean
                                               : 4.593
                                                          Mean
                                                                  : 9.0
##
    3rd Qu.:64.00
                     3rd Qu.: 2.000
                                       3rd Qu.: 7.000
                                                          3rd Qu.:16.0
##
    Max.
            :78.00
                     Max.
                             :36.000
                                               :35.000
                                                          Max.
                                                                  :75.0
##
    NA's
            :325
                     NA's
                             :122
                                       NA's
                                               :123
                                                          NA's
                                                                  :154
##
    updrs_iii_score_off
                             updrs_iv
                                            hoehn_yahr_on
                                                             hoehn_yahr_off
##
    Min.
           : 0.000
                                 : 0.000
                                            Min.
                                                   :0.000
                                                             Min.
                                                                     :0.0000
                         Min.
##
    1st Qu.: 0.000
                          1st Qu.: 0.000
                                            1st Qu.:0.000
                                                             1st Qu.:0.0000
##
    Median : 0.000
                         Median : 0.000
                                            Median :1.000
                                                             Median :0.0000
           : 2.523
##
    Mean
                         Mean
                                 : 1.236
                                            Mean
                                                   :2.487
                                                             Mean
                                                                     :0.1961
##
    3rd Qu.: 0.000
                          3rd Qu.: 1.000
                                            3rd Qu.:3.000
                                                             3rd Qu.:0.0000
##
    Max.
            :64.000
                         Max.
                                 :14.000
                                            Max.
                                                   :9.000
                                                             Max.
                                                                     :5.0000
##
    NA's
            :110
                         NA's
                                 :118
                                            NA's
                                                    :158
                                                             NA's
                                                                     :109
##
      moca_score
##
    Min.
            : 0.00
##
    1st Qu.: 0.00
    Median :26.00
##
##
    Mean
            :17.62
##
    3rd Qu.:29.00
            :30.00
##
    Max.
##
    NA's
            :16
```

We have a LOT of missing values present in the data! As mentioned before, imputation of missing values is an entire field unto itself. While we won't be imputing data today, we are going to wrangle the above data to attempt to ameliorate some of these missing values.

To do this we will:

- 1. Combine our Age variables to be age_at_exam where known, but age_at_symptoms where that is observed without age at exam
- 2. Combine our updrs scores to be the average updrs
- 3. Combine our hoehn scores to be the average hoehn
- 4. Keep our moca score as is
- 5. Remove the old variables from our pheno dataset.

```
# your code here
#initializing AgeMaster with age_at_exam columns, and age_at_symptoms where age_at_exam values were NA.
pheno$AgeMaster = pheno$age_at_exam
pheno$AgeMaster[is.na(pheno$AgeMaster)] = pheno$age_at_symptoms[is.na(pheno$AgeMaster)]

updir_cols = c(6:10)
pheno$overallUPDRS = rowMeans(pheno[,updir_cols])

hoehn_cols = c(11,12)
pheno$overallHoehn = rowMeans(pheno[,hoehn_cols])

res = c(1,2,3,13,14,15,16)
pheno = pheno[,res]

#View(pheno)
```

As you can see, we have far fewer missing values to contend with!

Let's look at a summary of the first 10 columns of simulatedession data set.

summary(simulated[,1:10])

```
##
                      GeneName
                                          GSM2631171
                                                              GSM2631309
          X
##
   Min.
          :
                    Length: 20668
                                       Min.
                                               :-5.223788
                                                            Min.
                                                                    :-6.09018
                1
##
   1st Qu.: 5168
                    Class : character
                                       1st Qu.:-0.960423
                                                            1st Qu.:-0.92906
  Median :10334
                    Mode :character
                                       Median :-0.004842
                                                            Median: 0.01385
## Mean
           :10334
                                       Mean
                                               :-0.009648
                                                            Mean
                                                                   : 0.01249
   3rd Qu.:15501
                                        3rd Qu.: 0.953228
                                                            3rd Qu.: 0.95912
##
           :20668
##
  Max.
                                               : 5.766301
                                                            Max.
                                                                   : 5.66627
##
      GSM2631219
                         GSM2630775
                                              GSM2631147
                                                                 GSM2630853
## Min.
           :-6.39097
                       \mathtt{Min}.
                              :-5.206869
                                            Min.
                                                   :-5.27578
                                                               Min.
                                                                       :-6.115736
   1st Qu.:-0.97337
                                            1st Qu.:-0.96379
##
                       1st Qu.:-0.981831
                                                               1st Qu.:-0.944666
##
  Median :-0.01097
                       Median : 0.001772
                                            Median : 0.01906
                                                               Median :-0.007942
## Mean
           :-0.00354
                       Mean
                              :-0.000010
                                            Mean
                                                  : 0.00298
                                                               Mean
                                                                      :-0.009892
   3rd Qu.: 0.95324
                       3rd Qu.: 0.971013
                                            3rd Qu.: 0.98545
                                                               3rd Qu.: 0.945826
##
                                            Max.
## Max.
           : 6.56118
                              : 5.275719
                                                  : 5.18612
                                                               Max.
                                                                      : 5.570111
                       Max.
##
      GSM2630769
                          GSM2631196
## Min.
           :-5.608142
                        Min.
                                :-6.303044
##
  1st Qu.:-0.968002
                        1st Qu.:-0.970730
## Median :-0.001583
                        Median :-0.004689
## Mean
           : 0.014813
                        Mean
                               :-0.006484
  3rd Qu.: 0.987677
                        3rd Qu.: 0.977216
##
           : 5.591597
                        Max.
                               : 5.434250
```

We don't need the X1 variable - this is just remaining row labels in the csv file. Let's remove this variable.

```
#your code here
simulated = simulated[,-1]
#head(simulated)
```

We don't see any evidence of missing values in our summary, but we should check all of the columns (excluding the GeneName). You can check this with the "anyNA"" function.

```
# your code here
anyNA(simulated)
```

[1] TRUE

your code here

Let's identify how big this problem is, and where it occurs.

```
na ix = which(is.na(simulated), arr.ind=T)
head(simulated)
    GeneName GSM2631171 GSM2631309 GSM2631219
                                                GSM2630775 GSM2631147
                                                                       GSM2630853
## 1
        A1BG -1.0366136 -0.27662929 -2.6292442
                                                1.52266682
                                                            0.3358301
                                                                       0.97332552
## 2 A1BG-AS1 -0.8753413 0.54284119 -1.4575540
                                                0.69927167
                                                            2.4918360 -1.30756851
## 3
              1.2650380
                         0.07009968 0.7666068
                                                0.02032404
        A1CF
                                                            2.5133798
                                                                      1.82584774
## 4
         A2M -1.1735898 -1.61353987
                                     0.3632498 -1.22731028
                                                            0.3997275
                                                                      0.86599329
## 5
              1.2247663 -0.93452615 0.4948203 0.75509020
     A2M-AS1
                                                            1.7236542 -0.22818120
## 6
       A2ML1 -0.4382954 0.51954673 0.2610932 -1.54324974
                                                            1.4411747
                                                                      0.01398596
                GSM2631196 GSM2631194 GSM2631197 GSM2631195
##
    GSM2630769
                                                             GSM2631198
## 1
     3.4533159
                1.81379834 -1.9211147
                                       0.7257764
                                                  0.6575387
                                                            -0.91583986
##
  2
     1.5772826
                4.00922478
                           0.4967702 -0.3360566 -1.5340809
                                                             1.05406203
               1.01145195
                            0.4692595 -0.3195250
     1.4629778
                                                 1.2800251
                                                             0.05179562
                            0.4852329 -1.8378022
     0.2364756 -0.87955380
                                                 1.2444026
                                                             0.99429936
## 5 -2.0413473 0.59855387
                            1.1834725 1.5956586 -1.8124371 -1.54911402
  6 -0.7479307 -0.07684364 -0.4987176 -0.1837047 -1.9271727
                                                             0.87524246
     GSM2631306 GSM2631162 GSM2631172 GSM2631241 GSM2631252
                                                             GSM2630927
## 1 -0.84655288
                 1.1791279 -3.9196878 0.4744313 -2.0468679
                                                             1.64638684
     1.26922525
                 1.4960082 -0.1600686 -0.5493613 -0.6329077
                                                             0.76567160
## 3 -0.61375284 -0.6789608 -0.6724768 1.0463665 -1.9405701
                                                             0.97085682
     0.03649272 -0.9076411 1.0203311 -0.7038708 -0.5943931 -0.01985207
     0.24188310 -0.9571613
                            0.7420052 -1.2601389  0.7727551 -1.60393326
## 5
## 6 -0.43301581 1.9297295 -0.7885334 0.6856696 -1.6556987 -0.21708071
    GSM2630928 GSM2631227 GSM2631231 GSM2631235 GSM2631236 GSM2631238
##
     2.3494621 -1.28747722 -0.1375166 -2.64930848 -0.5211835 2.3866101
## 1
     0.8918579
                2.20784667
                            0.2789515 -0.15288028 -1.0366904 -0.4633186
## 3 -0.7185732 0.02302333 -2.0125364 -1.64575408 0.8203788
                                                              2.4663765
     2.3943697 -0.27391520 3.0961026 -0.37190510 -0.5522156
## 5 -1.0772197 -0.61419330 -1.1996913 2.39657548 -1.6125899
                                                              0.1666942
     1.2236939 2.52062795
                            0.7489049 -0.06606603 -2.3478171 -0.6764611
##
    GSM2631239 GSM2631243 GSM2630771 GSM2630783 GSM2630830
                                                           GSM2630857
     1.4916053 -0.1782536
                           -1.659963 -0.7384035 0.9146473
                                                            1.38723172
               0.5192995
                          -1.277140
                                     0.4070137 -1.4913926
     0.6665841
                                                            0.31651129
## 3 -2.3290718
                0.8769891
                            0.296691
                                     0.0466384 -1.4333307
                            1.122082 -1.4973222 -1.1639669 0.31919656
    0.1494168 -1.6651591
                          -1.222706 -1.7475125 -1.2604841 -1.59258362
## 6 -1.4187163 -0.1474803
                            1.193786 2.7291049 -0.8678376 -0.07839134
##
       GSM2630868 GSM2630818 GSM2630907 GSM2630909 GSM2630916 GSM2630923
     2.0282589115 0.2867639
                              0.8765503 2.08729263 1.3751344 -1.0568484
## 2 -0.1954580107
                   2.6901454
                              0.1853255 -1.37467254 -1.5710871 -2.8557396
## 3 -2.2136408014 0.2940256
                              1.9085677 -2.50835849
                                                     0.7822219 -2.2953350
## 4 -1.5002781106 -0.2019019
                              1.3212764 -1.74592908 0.0169678 -2.5227859
    1.3021516710 -3.1433825
                              0.3361751 -0.85923943 -1.2375982 0.1887502
## 6 -0.0004901291 0.2447780
                              0.5887452 -0.03101765 0.3052142 -0.6726640
##
    GSM2630925 GSM2630929
                            GSM2630930
                                          GSM2630932
                                                       GSM2631221 GSM2631230
## 1 -0.2958283 -2.10300595 -0.04158138
                                        1.2354445734 0.945052270 -1.9297252
    1.3469523 -1.82135528 -0.38894496
                                        0.0071051808 -1.090033105 0.4064769
                                        2.1235227231 -1.135663786 -0.2278403
## 3 -3.8422052
               0.73112033
                            2.15930231
## 4 0.9195979 -0.33096684
                            0.62955475
                                        1.2427952651 0.004803398 -0.4513778
```

```
1.2995907 -0.01940292 0.73045524 -1.4692743866 -1.795355641 1.0710448
    1.1671110 0.48598974 2.22099957 0.0002136866 -1.077369034 0.1596775
    GSM2631232 GSM2631234 GSM2631237 GSM2631240 GSM2631242 GSM2631248
## 1 0.1310315 0.3029325 0.93292405 0.2450774 -2.2010466 0.07872818
## 2 -0.6413753 -1.8839945 0.97608066 0.4029095 -2.0829699 -1.47481732
    1.0109173 0.1761590 -0.09362843 -0.2220153 0.6564502 0.58223808
## 4 -0.2036200 -1.4464613 -2.10500710 1.4502341 0.9879688 -0.05621746
## 5 0.1302830 -2.6410427 -0.15299668 0.0286268 -0.6600126 1.15699441
## 6 -1.0913582 1.0965872 0.01632357 -1.4416563 2.6812462 -1.04320546
    GSM2630899 GSM2630905 GSM2630906 GSM2630917 GSM2630922 GSM2630924
## 1 -0.5619655 0.8303993 -0.24152334 -0.04881529 2.4694273 -0.2634438
## 2 -0.9276068 1.3494852 -0.52145494 0.65227447 2.6459861 0.5821107
    1.1728327 1.4226776 -1.05983269 0.52152354 2.5326991 -0.2391859
## 4 1.0841522 1.2791545 0.09251289 0.35721429 -0.6689961 -0.5378807
## 5 -1.0304385 0.1649847 2.18569789 -0.52206253 -4.1137056 -1.2505132
## 6 -0.5379009  0.4572370  1.08616722 -0.92926893 -0.9148150  1.5600256
    GSM2631298 GSM2631300 GSM2631301 GSM2631304 GSM2631305 GSM2631310 GSM2631312
## 1 -2.4041004 0.4142408 2.3051650 1.2032466 0.3102905 1.7362371 -1.4367006
    1.2034354 0.6377265 1.4346190 2.6897943 -0.1815019 0.6370929 -0.4128298
     0.1616847  0.9017189  2.4009772  -2.0181330  1.0952450  1.6810226  1.5093923
## 4 -0.6081584 -2.3985431 -0.1928422 2.1144050 0.4915416 -2.0634988 1.1022631
    0.9835483 1.4162336 -3.5037736 1.2611128 -0.7937164 -0.7809311 2.0441711
## 6 1.2264029 0.7266947 3.9301177 0.5370959 1.5592591 1.1318930 -1.4997471
     GSM2631152 GSM2631153 GSM2631158 GSM2631159 GSM2631161 GSM2631163
## 1 -0.72592990 1.6656161 -1.2741775 0.5933994 2.69854110 -1.2529726
## 2 -2.29867241 -1.2727443 0.3678687 -1.2929641 1.80110090 -0.7875862
     2.07877411 -1.0814380 -0.7687855 -0.1583923 -0.21089494 4.0526096
     0.47757174 0.9726368 1.4798518 1.8658899 -2.30680656 -1.6684783
    2.39637960 1.0536109 1.4657355 -1.0820489 -0.07070203 -1.0199878
## 6 -0.09733715 0.4041567 1.0818082 0.7551520 -0.35814807 -1.0583512
    GSM2631165 GSM2631167 GSM2631175 GSM2631176 GSM2631177 GSM2630777 GSM2630788
## 1 -0.1222497 -1.0789216
                          1.566529 0.9987111 0.1889327 -2.57214026 2.3263281
## 2 -0.5373867 0.3892825 -2.082986 -2.1671795 -1.2980895 -1.20746737 1.8176666
## 3 -1.1355584 -0.9998817 1.055984 0.8628208 0.6923748 0.05547596 1.9799421
     0.3718242 -2.7818915
                           2.234714 1.0116093 -0.4044052 -0.25345266
## 5 0.2939756 0.5576378
                          0.880692 0.6894485 -1.7259526 -1.51679548 -0.8335691
## 6 -0.3863178 -1.5446292 -0.709811 2.0376934 -1.5553287 0.80176416 2.2422168
    GSM2631173 GSM2630908 GSM2630787 GSM2630790 GSM2630810 GSM2631138
    1.1433088 0.33480168 1.8895206 1.3762785 -0.74705084 2.5770894
## 2 -1.0086858 -2.13654681 -0.3511912 -0.4478314 -1.29001456 -1.7157469
## 3 -1.4209240 2.58002782 -2.1834945 -2.3061270 -0.30136830 -0.8003415
    0.4600274 1.13479164 -0.9740478 0.4491862 0.09954752 -1.4483073
    0.3648058 -0.07249906 -0.2107581 0.2913374 -1.03057215 1.9680884
## 6 -1.3754587 -1.66898638 3.2593801 1.1504076 -1.75377378 1.5024215
     GSM2631028 GSM2631287 GSM2631100
                                     GSM2631056 GSM2631118 GSM2631025
    0.52698585 -0.4075548
                           2.315731 0.008797516 0.9740736 -0.14549094
## 1
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## 1 -1.7351305 0.3808066 -1.5458882 -3.0564501 0.6290531 -0.59629003 -0.5823345
## 2 0.5947805 1.2028405 -0.6623765 1.5138483 3.3469296 -0.65688493 -0.5830482
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```
## 3 -2.5323911 -0.4115594 0.4554766 -0.5420236 1.8493693 -1.18571877 1.6540798
## 4 -1.8155050 0.1217753 1.3740148 -0.1332096 -0.1180980 -0.02744244 1.2625902
## 5 -1.7003155     0.6344448     0.9252425 -1.0453155     3.8906284 -2.30940390 -0.1582876
## 6 1.7512150 0.8523116 -0.1901621 -0.1564972 0.5843132 0.76503528 0.7188814
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## 2 0.07439874 -0.4595939 -0.4162442 0.3061578 2.0518596 -1.06527536
## 3 -0.48347565 1.2879970 0.3310463 0.2365571 -0.1488802 1.13474823
## 4 -2.33379235 -0.1357224 0.3258514 1.2145831 -2.3105343 -1.51628874
    0.28988425 -1.0916108 -0.8019365 -1.2614718 -0.7845362 -0.68313960
## 6 0.80314671 -1.4096304 1.8122266 1.1655381 -0.2559388 -0.34840860
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## 3 0.9797699 -2.5120573 0.76669521 -1.421151 -0.3183001 1.3330879 -2.1587893
## 4 -1.1977223 -0.6401546 -1.09335145
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## 3 -0.008372826  0.1633467 -1.5899370 -2.2073443  0.4280094 -2.2969203
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## 5 -0.335284994 2.5598942 -1.7941523 0.4791979 -2.2468236 0.7133927
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## 2 -0.812004639 -0.6701084 1.3709726 -2.6676896 1.2857053 0.6755781
## 3 0.287382440 0.2404943 0.4195041 0.8186180 1.8774089 -1.2489386
## 4 1.604406773 -0.9202510 -0.7035831 -1.1622770 -1.4313841 -1.6907005
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## 5 -2.5905611 0.34238483 -0.7013252 1.8971469 0.52884767 -1.6105446
## 6 -0.8236771 -0.09696512 0.2438323 2.1391033 0.77902942 0.9199876
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## 5 -2.7723251 1.5593833 -0.7030889 1.4760425 -0.69784088 -0.1664608 1.8601628
## 6 -0.5829344 0.8412565 -0.8365451 -0.4202488 -0.60715530 1.8582394 -0.9929007
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## 3 0.18512102 0.1622205 1.9511865 -1.6268437 0.379795128 0.03401872
## 4 -0.07084703 2.0315725 0.8087325 -0.5744978 -0.004533444 0.23779417
## 5 -3.15956761 1.4847417 -1.4685318 1.1553210 -1.472630009 -1.46899056
## 6 -1.88047059 1.2446217 0.5825393 -0.7047452 0.128044702 -0.12248576
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## 2 -2.6325459 0.9753336 -2.06325543 0.2677603 0.8322555 -0.1837639
## 3 -1.9535139 1.7832400 -2.52525359 -2.1364791 1.7778852 -0.1212560
## 4 1.8222826 2.5258067 -0.05292615 -2.7553230 1.0006457 -0.8630717
## 5 -2.6350817 -2.1917706 3.27001876 -1.3372618 1.9882784 1.6348581
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## 3 0.11774514 0.95298645 0.1331115 -0.08088916 -0.8476263 -2.05198372
## 4 -2.30145875 -1.35434587 1.2115518 0.61438292 1.3005096 -1.26011808
## 5 -0.22869657 0.08293144 -1.3751410 1.16766042 -1.3055796 -1.95834331
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     0.5947390 -2.1211387 -0.4001051 -1.4520147 0.5813996 0.1745257 -2.02068438
## 4 -0.8725275 1.5127311 1.8170247 0.6928014 0.3711322 0.3469125 1.05804235
    1.4441232 0.3009225 1.8997046 -3.2638935 -0.9294172 1.9492260 -0.41902617
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## 3 -2.8634790 0.5530108 0.3409070 -2.0879133 -0.1957375 -0.4510495 -0.5826275
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## 2 -0.03736602 0.5825417 -1.8838247 1.27382314 -2.15053713 -2.2294953
## 3 1.30731740 -0.4037840 0.5073351 0.68600903 -0.07151086 -1.1448278
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## 5 0.05869560 -1.4606700 -0.7883273 0.07768596 2.81996646 -1.6889511
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## 4 -1.19050468 0.004009321 1.0525064 -0.76345712 -1.4298399 1.5932022
## 5 0.19828946 1.226606156 -0.6484885 0.23352453 -1.8446979 -1.3383445
## 6 -0.03249254 -0.420138931 -0.9206416 1.00934982 1.4644204 -1.6721853
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## 4 0.3687222 2.3048555 2.4958387 0.31364276 -0.9460197 -0.008897561
## 5 -0.2289534 0.4649464 0.1510526 0.04284032 0.8720284 -4.312471140
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## 5 -1.3173954 1.16179577 1.0485654 -2.0757138
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## 3 -0.006553977 -0.07509473 -0.3930274 1.0986744
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## 5 -1.623538792 0.39021641 -1.9522432 2.1377246 1.6730906
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    0.588906510 -0.62497032 -2.4683918 -0.8707716 0.1429637
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## 2 -0.07732189 -0.9702949 1.18010654
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                                                          4 17293934
## 3 -1.05673436 0.6822056
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## 4 -0.75907847 0.5982004
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## 2 0.94214563
## 3 0.78668032 -1.900018 0.79750461 2.04656810 -0.8976752 -0.0147355
## 4 0.79246096
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## 5 0.94357695
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## 6 0.84446387
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## 2 -0.16429595 -0.8379603 1.5215375 -1.5221091 -1.6454411 0.8961529 0.2047758
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```

```
## 4 -1.10750709 0.2068966 -2.9413087 -1.2214525 0.3450632 1.0765632 1.0693646
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## 2 -1.6429975
## 3 -1.0892822 -0.6486775 0.7668590 -0.82879079 1.1143742 -2.3096814
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    0.4330502
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## 1 -1.1957774 0.7416789 -1.3602342 -1.2033843 -1.1591597 -1.6338993 -1.2900632
## 2 -2.5780624 1.6053224 0.4777948 0.1404821 -3.2700809 -0.6436568 -1.3778382
## 3 -0.3753229 -0.3674893 0.4606674 -0.3981390 -0.4572879 -0.3462053 -0.5100098
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## 5 -1.6226672 2.2060799 -1.9641189 -0.7453575 -0.3718707 -0.8374466 -0.4228606
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## 1 -0.8571240 -1.232013640 -0.6049448 -0.3876590 -0.4828608 0.3324155
## 2 2.2085579 0.725556529 0.1797668 0.5050713 -0.5459387 -0.5667721
## 3 -0.1226983 0.316187786 -1.2629183 -0.8387031 -3.2483731 -1.0092337
     3.7153521 -0.170180663 -1.3881362 -2.3104037 0.5271802 0.1267025
## 5 -0.6905953 0.005194436 0.8770569 1.8385740 -0.9385243 -3.1400500
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## 1 -0.4391544 -1.0106745 -1.1083826 -2.6875508 -0.9173226 -0.76764428 -0.8589442
```

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## 2 -3.0193836 -1.6861420 0.7802439 -4.4755934 0.9281720 0.31830953 2.4942995
## 3 0.5970295 -0.7813371 3.0992954 -0.9053522 -0.8739992 -0.90370136 1.8898746
## 4 -0.4870853 -1.3489689 -3.7320674 1.9349311 -1.2551727 -0.25057233 -0.8521667
## 5 -2.2835696 -0.2769043 0.8979115 -1.9681822 1.7660997 1.49878465 -3.2712217
     1.5374995 1.0581987 0.4574137 0.9486238 -0.3122088 0.06904076 -0.3422267
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## 1 -0.4700442 -2.52265188 -1.8783165 0.93646900 -1.32825436 -0.9589495
## 2 1.1152344 0.02320227 -1.6913829 -0.06709222 -0.23105871 -0.4504241
## 3 -1.2218764 -0.93966881 -1.6289648 -0.78351058 0.03551342 -1.2130022
## 4 0.7468373 -1.30931469 -0.2513103 0.40717358 -1.55006601 0.6484371
0.6492021 0.03724693 0.5131735 -1.31520492 -0.33255513 -2.0283444
    GSM2630820 GSM2631251 GSM2630782 GSM2630858 GSM2630786 GSM2630846 GSM2631218
## 1 -1.8959157 0.2539446 -1.7701014 -1.4818171 -1.0376929 -2.5619360 0.08055711
## 2 1.7066288 -0.4483734 1.9770960 0.6629819 -0.3294843 -0.1178808 -1.09146696
## 3 -0.4437509 -0.9278382 0.3664970 -2.4278685 0.6942003 -0.4026135 -0.16974664
## 4 0.9282020 -1.3645759 -0.2582078 -0.6430071 0.2017015 1.7539388 0.73544571
## 5 -1.1668979 1.2727199 1.8558053 -1.2931958 0.5405148 1.0531320 1.06966646
## 6 -0.9555321 -0.1518477 -0.4512699 -1.9903513 -0.7549119 1.5572617 2.67699011
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## 1 -1.2181568 -1.2855767 0.92995150 -1.2365196 -0.9722010 -2.0256017 -1.0897619
## 2 -0.7596254 -0.9498746 0.01636692 1.9682346 -0.5961916 -1.0113355 -1.8086644
## 3 1.5056399 -0.8748691 2.66524010 0.9106952 -0.9686264 0.8700383
## 4 -0.2335612 0.5153979 -0.50887611 2.6749423 0.7417117 -1.3553926
## 5 -2.5806811 1.7096362 0.19639006 -1.7216788 -2.8700579 -0.3126360
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## 6 0.9556707 -0.2197358 0.75427414 2.0605258 -1.0293989 1.2667391 1.4940747
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## 1 2.9288311 -0.7742563 1.2388876 -1.2170413 1.3385194 0.6549759
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## 2 0.9589744 2.2363733 -2.3101121 1.5750327 -0.4707110 -0.6389563 1.8540541
## 3 -0.2020964 -0.8730254 0.2259918 1.7408934 -2.0846519 1.5631676 -0.1804550
## 4 -1.1731534 0.5171663 -1.9527740 -0.5002877 -1.0827927 0.1556494 1.3622466
## 5
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## 6 -0.7964007 0.2629671 -1.1877441 0.5021782 0.6324775 1.5852673 0.7140946
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## 2 -0.2372467 0.4551308 -2.4641422 -0.50471745 0.4733015 -0.1420464
## 3 0.2700906 -0.9205626 -2.1934623 0.08449291 -1.1618634 -0.6817765
     0.6638912 -1.0448715 -2.0489023 -1.34335866 -0.2717609 -2.0272399
     0.8982164 2.8042585 2.0540807 -4.11715053 0.6947429 -0.4162787
## 6 -1.0398024 -1.4181667 0.5853475 -0.25083227 -3.2123897 -2.3554965
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## 2 -0.02988436 1.5154031 -1.3837900 0.7246344 1.0325210 -0.07185176
## 3 0.12082333 -1.6965196 4.0709246 1.2591368 -2.2517170 0.83825625
## 4 0.58136244 -1.7869708 1.7508827 -1.7100305 1.3080645 0.74248755
## 5 -1.69977363 4.2856709 1.6404151 -5.1151786 -0.1930789 -1.18802939
    1.02770076 1.7117783 0.6760802 -1.6974102 2.3210766 -0.39852916
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## 1 -1.5495944 -1.692934 -2.84909581 -2.3715391 0.3339154 -0.7573349 -1.4593277
## 2 -0.3880660
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## 3 0.7654619 -0.530256 2.63938842 -0.7979930 1.1283544 -1.3002454 1.8970389
## 4 -1.7384800 -1.413566 -0.42840880 -2.0496676 2.3717067 -1.2088167 -0.8437321
## 5 3.1044464 -1.332465 -0.19948102 0.2150763 0.3693599 0.4762589 -2.7803432
## 6 -0.4084369 -1.163991 -0.50482302 0.1794318 -0.8588559 -0.8153944 -0.1315860
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    1.58544511 0.5375188 0.4849139 0.1851821 -0.8126650 1.5784185 -0.4324193
## 3 -0.81259552 -0.5304101 1.4112754 -2.7503869 0.2768437 -0.3669341 -0.7770545
     1.21889363 0.6393521 0.5247390 -1.0666782 0.4229489 1.6791770 -1.9217731
    1.42478006 -0.2924676 -0.0393988 0.1494384 0.7503645 -1.2916385 -2.6804973
## 6 -0.07425011 0.4636789 -1.3464223 -2.3465660 -0.4503549 1.6227011 0.6490980
    GSM2630806 GSM2630921 GSM2630972 GSM2630807 GSM2631108 GSM2630988 GSM2630992
## 1 -1.7610496 -1.992002 -1.5775681 -0.2813225 -2.03602760 -1.2907785 -0.4253443
    1.3646026 -1.099208 -1.0487502 -0.3115299 -2.32265723 2.6255155 -0.3318395
## 3 -1.8486124 -3.528570 2.1013188 1.3446661 0.03279319 -0.2083101 -0.1840665
     0.1547986 -1.376280 -0.3023897 2.5924390 0.44802348 -1.4146712 -0.1612782
## 5
     0.2857544
                2.531673 0.3394547 -0.3960770 -1.85661345 -1.1728334 -0.7997469
## 6 -2.1824287 -1.309204 -0.8410377 1.0544945 -0.20773138 0.2764553 -2.3564241
    GSM2631263 GSM2630823 GSM2631002 GSM2630949 GSM2631254 GSM2631050
## 1
     -0.510393 -1.2246214 -1.40324525 -2.4158496 -2.2235014 -0.76460953
     -2.085572 1.6518916 0.08143373 0.8454936 0.3612837 2.36792865
     -1.464422 0.6981699 -2.73991585 -0.7195946 -0.8606767 1.59327432
      2.168009 -0.7452748 -1.07063151 -1.4730156 -1.2451833 -1.95005075
     -0.491203 -1.0116534 1.56540344 0.3879424 -0.6131017 0.09477680
      2.074802 2.1189323 0.80792017 0.1068090 0.8428611 0.09846694
## 6
    GSM2631052 GSM2630835 GSM2631290 GSM2630994 GSM2630975 GSM2631021 GSM2630825
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     3.0024018 0.6702478 -1.7558121 -1.2562552 1.52141854 1.0846899 1.9321547
     0.5437075 -1.3103535 -3.1066575 -0.8986997 0.01229438 -0.2684751 -2.2043384
## 5 -0.3110372 1.2135375 0.9965829 -1.5967986 1.97630073 1.8143218 -0.8557193
    0.8761223 -1.9657801 -1.8767866 -0.8367942 0.45847003 0.8578002 -0.1522699
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## 1 -0.1622274 -1.1443590 -0.7532958 -1.5370875 1.82655665 0.7218192 -0.6612711
## 2 -0.7747135 -0.1513008 0.7612781 -0.3381853 0.42434275 0.2783784 -0.1561070
## 3 3.5773099 -0.8792346 -3.5246298 0.5523385 2.10679075 0.4791960 1.1697372
    0.8759624 0.1899872 0.6405843 1.4726698 0.68538181
                                                          0.2121191 1.2254250
## 5 -0.2486916 1.8689987 0.4489273 -4.0054246 0.01183867
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                                                           GSM2631120
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    1.5147531 -0.33091720 0.3136001 0.7050810 0.1423768 2.376800984
     1.9645479 1.29755515 -1.6743548 -0.5661822 0.4317530 2.010469875
     0.3114422 2.19449918 -0.8528134 0.3399771 -0.4818381 0.014261062
     0.4907612 -1.27699379 1.7048295 -0.3928432 0.8290455 -2.269813753
    1.5377082 -0.06833721 1.8263866 2.3763421 -4.4379861 -0.096749201
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## 2 -2.3326461 1.3236388 -0.4937494 0.68376772 0.9010151 2.20391920
## 3 1.6185871 -0.8923174 1.5692905 -0.65985416 -2.3261075 0.06090074
## 4 -1.5010816 1.0186319 -1.1515244 0.35782589 -2.2142404 -1.21951463
## 5 -0.6337451 -0.9952099 2.0115955 -0.03992841 1.6019707 -1.82031947
## 6 0.2654832 1.4005273 -2.3159228 -1.57183188 -1.5297614 0.99725330
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## 2 -0.4013985 0.76874921 0.7224752 -2.235160 -1.691606 -1.3247027 1.9265923
## 3 3.1137601 0.03180602 -0.3864629
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## 4 1.2743420 1.17901815 -0.2717955 -1.087226 -3.424833 -1.9517511 -1.5062462
```

```
## 5 -1.8709296 -1.11761266 -0.7103786
                                    2.908685
                                                1.119041 3.6344712 -0.1916060
## 6 2.4145872 -0.33861885 1.9648486 -2.138953 -1.629056 -1.9914970 -1.7496990
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## 2 -1.1271187 1.8546198 -1.4207905 1.71342996 -0.8398652 -0.3581936
## 3 0.4113337 3.2900138 0.3106350 -1.64283867 0.3420142 -0.5601045
## 4 -1.8495338 -0.3747986 2.6810301 1.10387333 -0.3624510 0.4016261
    0.1597748 -2.9652716 -1.4968257 1.39734056 2.3799516 -1.2756506
     0.2731774 1.0885919 0.2276535 0.84098376 -1.5762497 0.7889591
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## 2 -0.06077072 -1.1702743 0.3868574 -0.2615195 -1.12221062 0.4073223
## 3 -1.59082985 0.7738476 0.2946796 1.6032987 0.47635309 1.7139224
## 4 -1.34028180 -1.2094223 1.2500812 -3.3455574 0.05965252 0.9890002
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    1.3451030 -2.2579868 0.7256644 1.3620749 -3.2233097 -0.1106730 0.92723336
     0.7512489 0.9713404 0.1347048 1.6651827 -0.0859006 -0.6275822 -0.04111648
    0.5394397 2.8804621 0.2687693 1.8066045 2.4093135 1.6035381 1.68328145
## 6 -0.3179972 0.3105416 1.3394577 1.5870281 1.9586991 -0.5295211 -1.14438473
     GSM2631271 GSM2630956 GSM2631008 GSM2630951 GSM2630957 GSM2631006
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## 2 -0.94077657 -1.48994087 -0.7464725 0.5604905 0.6845381 -1.1838408
## 3 -0.28826751 -0.11495293 -1.1190199 1.8939693 -1.1075196 -0.3041053
## 4 -1.33804070 0.02946498 -0.3750879 2.3603219 -0.8275910 -0.1254125
## 5 0.09384828 -0.26772644 -0.5678378 1.5751923 1.0989572 0.2713802
## 6 -1.01532791 -0.21394266 0.6173899 1.8608349 0.2065982 0.6213892
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## 3 -2.5127760 0.7456361 -0.1806734 0.8862420 -1.265041451 -2.0604068
## 4 -1.1569297 -2.5560028 -1.2356528 1.9492697 -0.003278473 1.0086813
## 5 -1.4449753 0.2492546 0.3432307 -0.5286115 -1.035860784 -0.5988114
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## 1 -1.2968154 0.22153774 -1.7380806 -0.5934177 -0.9629834 -0.1138853 -1.5898242
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## 3 -1.6356987 -1.5128747 -0.692826832 0.9829072 -2.033306 0.08873056
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## 4 -0.1552184  0.8863757  0.005652508 -0.2714030
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## 2 -0.2877108 -0.1810444 0.34667709 0.06280491 -1.7319095 -1.1627578
```

```
## 3 2.8949967 3.1345713 1.19697026 1.80316659 0.2212331 -0.4381697
## 4 0.1336727 -0.2269786 0.68194648 -0.16581476 0.3591209 1.2146119
## 5 -4.3992315 -0.6628863 0.73238797 -1.42973513 -0.4548546 -1.7927766
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    0.9519919 1.9416845 -0.008425992 -0.1088397 -2.0135913 1.1194101
## 4 -1.9585188 0.1666770 -0.442004812 -0.5209865 -2.5347666
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    1.0614899 -0.3866254 0.395022879 -1.5930349 0.8535663 -1.3680189
## 6 -0.3290498 1.0939036 0.099346939 -0.6914789 -1.1954855 4.4215435
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## 3 -1.6007191 2.39137770 0.2842064 -0.9194415 0.40088796 0.1044426
## 4 -1.9591825 -0.31676634 1.3168862 -1.1104305 0.70578663 0.1745603
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-1.930328
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## 5 -0.1510299 0.01744889 -0.9272385 -3.19901355 -1.32234578
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## 6 -2.0476375 -0.86173055 1.2566474 1.90342347 0.28276929
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## 3 -0.9975200 1.0420441 -1.1815935 0.8847078 0.78873469 1.02312460
## 4 -1.5579128 0.5954689 -1.5211193 1.1682399 -3.25535716 0.09272712
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## 6 -4.0821619 1.9401031 0.1563138 -1.0634005 -0.30759402 0.81010773
    GSM2631269 GSM2631129 GSM2631013 GSM2630968
                                           GSM2630893 GSM2630804
## 1 -1.4377106 -0.1690443 -2.0468439 0.5080472 -1.551709319 -2.0847908
## 2 -0.7957836 -1.6075090 -0.7125311 -0.4860767 -0.105184265 -0.5118204
    1.2394915 0.6369946 0.2236099 1.8891413 -2.273596535 -1.6314025
## 4 0.3978321 -0.6032546 -1.0590484 3.8411773 0.005706778 -1.7508346
## 5 -1.4730465 -1.4724794 -1.9039240 -1.1086202 -0.838587812 -1.5086458
    0.4062617 -0.1880743 -0.5164401 1.2926072 -2.325125187 1.9326107
    GSM2630995
               GSM2631099 GSM2631106 GSM2631146 GSM2631187 GSM2631261
## 1 -1.2917122 -0.011241915 -1.6440218 0.1035240 -0.9993951 -2.3166343
## 3 -0.7385566 -0.816077852 -0.1680688 0.2415535 -0.1269104 -0.1622849
    1.5285242 -0.450266476 1.5679011 1.5169937 -0.8112110 2.6269330
    ## 6 -0.1289923 -1.867645759 -0.4295978 1.6945018 0.2530582 -2.7495508
    GSM2630950 GSM2631128 GSM2631182 GSM2631078 GSM2631060 GSM2631189 GSM2630891
    0.8778112    0.4071387    -2.5472541    -0.8806653    0.2554293    -0.9725052    -0.2296447
## 1
    0.5140307
              1.1473247 0.9344183 -2.3892165 1.1715350 1.1034283 -2.3470833
    1.4708719 3.4444170 -0.8411303 2.4462454 -1.2068418 0.8252213 -0.5154171
    1.0298641 1.0138297 -0.9226196 -0.7691148 -2.5888016 0.9691800 -0.8953786
## 6 -0.3260145 0.0531847 0.2496307 -0.9531151 -0.9048991 -2.0074446 -2.7725265
    GSM2630976 GSM2630911 GSM2630856 GSM2630813 GSM2630827 GSM2631035 GSM2630841
```

```
## 1 -0.9915351 -1.8750664 -0.4646803 -2.5757948 0.5438591 -1.5434953 -1.3155691
## 2 -0.1011587 2.7102561 1.2333097 -0.8929845 1.8778427 -0.4226869 -1.7352509
    2.0353925 -0.8087983 3.1124356 0.5526647 -1.2078296 -0.8029114 -2.5366676
    2.4922071 -0.5692714 -1.0639654 1.2902401 0.9006928 -1.7780069 -0.7949673
     2.7523347 1.0825978 -0.6203469 -0.3998847 -0.3467247 -0.3430218 3.5007693
## 6 2.1888079 -0.7576955 1.5597356 0.7027909 -2.1996613 0.3258566 0.1920471
    GSM2630918 GSM2631249 GSM2630762 GSM2630817 GSM2630826 GSM2630895
## 1 -1.2986092 -2.42941895 -0.9350261 -0.37996662 -0.4584036 -0.69238779
     0.3465669 0.05149691 1.1108494 0.26030700 -2.2505916 0.89422510
## 3 0.8493634 -0.94044765 -1.2715152 0.81079661 0.1534913 -0.02163383
## 4 -1.5202480 -0.75500556 -0.7416564 0.05808131 -2.0597607 0.66738612
## 5 -1.7931431 -0.81336074 3.4432288 -0.36783057 -0.5720272 -2.78615588
## 6 -1.2726958 1.31302528 -1.0914065 0.06458691 2.0165737 0.41071473
    GSM2630915 GSM2630838 GSM2630900 GSM2631224 GSM2631244 GSM2631245 GSM2631246
## 1 -2.1617964 -2.9460590 -3.2483643 -1.0006847 -1.6309566 -2.0338106 -1.39393569
## 2 -1.1630619 -0.4383554 1.4244318 -2.1456871 -0.7838586 0.5408137 0.07039058
## 3 -0.1535229 -0.6301082 -2.8449701 -1.8251298 -0.8007756 0.2636484 -0.69858486
    1.7257607 0.4795585 0.3067929 -3.1554234 0.3294863 -1.4724555 -0.10892016
    0.5151349 -0.5017270 0.7477007 -0.8315515 1.1038200 0.1027122 2.11318780
## 6 0.3990196 -0.1669634 2.2484424 0.7162219 -0.2258110 0.8898958 0.25544186
    GSM2631247 GSM2630794 GSM2630870 GSM2630890 GSM2630901 GSM2630902
## 2 0.9822148 -0.2551122 0.83835754 -2.3165937 0.25015145 0.2488519
## 3 -1.4221877 0.6031899 -0.09603965 0.8903494 -1.04196712 1.4884015
## 4 -0.8548419 1.3079159 0.12845980 -1.6229459 -0.39361727 -0.9591289
    1.5416138 3.3182213 1.06532594 -1.4372410 -0.08971241 0.3287321
    GSM2630904 GSM2630764 GSM2630781 GSM2630791 GSM2630862 GSM2630898
## 1 0.1253636 0.6046803 -1.95391688 -0.6687297 -0.4248194 -0.08884345
    0.2945730 -1.2632990 -2.16164638 1.0633079 -1.4184357 2.10651825
    1.1114717 -0.9397692 0.94325478 -1.2234248 0.2227079 -0.06559287
    0.0718093 -2.0337492 -0.86594119 -0.8073664 -0.5313776 -0.10746751
## 5 -1.9445166 -0.3978018 0.07081287 -0.3135973 0.3379879 -1.43685363
GSM2630903 GSM2630931 GSM2631150 GSM2631151 GSM2631155 GSM2631156 GSM2631157
## 1 -0.9729093 -0.7205041 -1.8279255 -1.6272927 -1.02188472 -0.3030778 -0.5422523
## 2 2.1354871 3.2053897 0.3156530 0.9477126 -2.23292421 -0.2826414 -2.4505954
    2.1393422 1.3141604 -0.8578469 -1.7569774 1.25159885 1.3405230 -0.1525208
## 5 -0.9372988 -0.4733000 -0.5279991 0.4059818 -0.34102972 3.3732013 2.2906663
## 6 -0.2351801 0.8366783 -1.1768148 -2.0200991 -0.02430283 -1.1990947 -0.2696430
     GSM2631160 GSM2631169 GSM2631154 GSM2631164 GSM2631166 GSM2631168
## 1 0.04725979 -1.1099001 -1.0273597 -1.4456580 -1.7858547 -1.86787636
## 3 -0.33821937 0.1357660 -2.8707103 0.4180560 -1.2119563 -1.44836641
    1.96718555 1.3873547 -2.6130987 -0.6005612 0.2702867 -1.14206299
    ## 6 -1.22897043 -0.7205411 -0.4615426 2.5951893 1.2824862 -0.06497648
     GSM2631170
                 GSM2631178 GSM2631019 GSM2630886 GSM2630765 GSM2630831
## 1 -1.74967542 -1.1327505734 -3.008161 -0.9991245 -0.4969681 2.2484317
## 2 -0.82887470 -0.6814695654
                          -1.645220 1.8169026 2.3886774 1.4722638
## 3 -0.18454581 -1.4938808451
                           1.659018 -1.6057020 2.3485171 -0.9689060
## 4 -0.04992567 -1.4915257484 -3.531577 1.2048392 -0.9250487 1.3091459
## 5 0.15756681 0.9589022805 -1.191587 -1.1013387 -1.5079540 -0.8022214
```

```
2.41532699
                  0.0004061308
                                 3.065940 -3.4045271 1.8612625 -1.5007237
##
      GSM2631315 GSM2630814 GSM2630776
                                        GSM2631204 GSM2630943 GSM2631199
                                        1.76544755
## 1
     2.20927469
                  0.6651546
                             2.2135823
                                                    1.0995474
                                                               0.7946736
## 2 -1.47914201 -1.3190896 -0.5982497 -0.03760468
                                                    0.4629934
                                                               0.6515067
## 3 -1.11353700 -0.6498948
                             1.9491410 -2.13039273
                                                    0.8892568 -1.0151381
## 4 -0.37045225 -1.1137832 -1.6589510 -1.33587653 -0.7164474
                                                               0.8255911
## 5 -0.09040963
                  1.6516621
                             0.6565135
                                        1.89144254 -0.9794713 -0.6025549
## 6 -0.19918438
                  0.9448221
                             1.3535971
                                        1.49580444 -0.6143860
                                                               2.1925398
##
     GSM2631299 GSM2631223 GSM2631233 GSM2631313 GSM2630808 GSM2631314 GSM2630836
## 1
     2.3605210 -2.2012231 -0.02146046 -0.6326650
                                                   2.5049257 -2.3359606 -0.1942268
## 2 -1.7673217 -1.7258935 -0.25278472 -1.6125410 -2.3967102
                                                              0.5067168
                                                                         0.2582003
     0.8265741 -1.5204924 -0.51980557 -2.2917605
                                                   1.0289422 -0.4145393 -0.0167197
## 4 -0.8028693 -0.5615761 -2.08426765
                                        0.3029939 -0.3865245 -1.3629297 -1.0357384
     0.5505165  0.3204596  2.41206947  -0.7231661  -0.1578205
                                                              1.6636426 -1.0738555
     0.3544965 -0.9325789 -1.15736210 -1.7341359
                                                   3.7518119 -2.1687875 -0.2819072
## 6
##
      GSM2631216 GSM2630889 GSM2631174 GSM2630894 GSM2630792
## 1
     2.53162113 -1.1165815
                             1.4991129
                                        0.8804499
                                                   1.5075483
## 2 -0.08970246
                  0.9657226 -1.2643005
                                        0.1925006 -0.8114261
     1.75623085
                  0.3486122
                             0.2483123
                                        0.3231254
                                                   1.1785312
## 4 -0.73100763 -1.2232381
                             1.0063012
                                        0.2391760
                                                   1.8140335
## 5 0.42965378 -1.0862381
                             0.3670247
                                        0.5919914 -0.2519061
## 6 -0.72533283 -0.2918044 -0.4020399 -0.2462007 -0.4054978
```

So one of our gene names is NA! This isn't useful, so let's remove this row.

```
# your code here
simulated_clean = simulated[-na_ix,]
#simulated_clean
anyNA(simulated_clean)
```

[1] FALSE

We should see if the unique identifiers in our two data sets match. Check for a perfect match using the "identical" function.

```
# your code here
identical(colnames(simulated_clean[,-1]),as.character(pheno[,1]))
```

[1] TRUE

So that we don't lose any work, let's clean up our workspace to include only our cleaned simulatedession and pheno data sets, which we can reload later.

Exploratory Data Analysis

In this section we are going to explore some of the data we have, and maybe develop a diagnostic signature for Parkinson's disease.

First, load in your data from yesterday.

Let's re-examine our pheno data set with the summary function again.

summary(pheno)

```
disease_label
    geo_accession
                                                sex
                                                                  moca_score
##
    Length:550
                        Length:550
                                            Length:550
                                                                Min.
                                                                        : 0.00
    Class : character
                        Class : character
                                            Class : character
                                                                1st Qu.: 0.00
                                                                Median :26.00
  Mode
          :character
                        Mode
                              :character
                                            Mode
                                                  :character
```

```
##
                                                                           :17.62
                                                                   Mean
                                                                   3rd Qu.:29.00
##
##
                                                                   Max.
                                                                           :30.00
##
                                                                   NA's
                                                                           :16
##
      AgeMaster
                       overallUPDRS
                                          overallHoehn
##
    Min.
            :10.00
                             : 0.000
                                        Min.
                                                :0.000
                      Min.
##
    1st Qu.:53.00
                      1st Qu.: 0.000
                                        1st Qu.:0.000
##
    Median :60.00
                      Median : 0.000
                                        Median :0.000
##
    Mean
            :59.37
                      Mean
                             : 1.525
                                        Mean
                                                 :1.364
##
    3rd Qu.:67.00
                      3rd Qu.: 0.600
                                        3rd Qu.:4.000
##
    Max.
            :82.00
                      Max.
                              :18.400
                                        Max.
                                                :4.500
    NA's
            :199
                      NA's
                                                :258
##
                              :264
                                        NA's
```

We need to further delve into our disease label in order to simplify some of this analysis. Attach your pheno data frame using the attach function, and then summarize the disease label vector.

```
attach(pheno)
summary(disease_label)
```

```
## Length Class Mode
## 550 character character
```

Here we have the counts of all the diseases in our data set. If you look at the actual excel file (not the csv), I've put in a dictionary for these acronyms if you're curious. Here, our controls and our genetic unaffected are both considered to be healthy controls. Any label which contains PD is some subset of Parkison's Disease, and the other labels represent other neurological disorders. We need to make a variable which records a 1 for our cases, and a 0 for our controls. Here, since we are interested in a signature that distinguishes PD from our other disease, the other diseases are technically part of the control set.

Try to set your case control vector using the grep function to find the indicies which contain "PD". At the end, sum your case vector to check that it worked. Make another variable of the words "case" and "control"

```
pdI = grep("PD", disease_label, value=F)
case = rep(0, length(disease_label))
case[pdI] = 1
sum(pdI)

## [1] 100799

##alternative
case = grep1("PD", disease_label)*1 #returns list of True and False
sum(case)
```

```
## [1] 251
caseName = ifelse(case ==1, "case", "control")
```

We need to find differentially simulatedessed genes. You'll learn more about this later. For now, feel free to use some of my code. Start by downloading the limma package

```
head(simulated_clean[,1])

## [1] "A1BG-AS1" "A1CF" "A2M" "A2M-AS1" "A2ML1" "A2MP1"

## If using Windows, first go to https://cran.rstudio.com/bin/windows/Rtools/ and install the appropria 
if (!requireNamespace("BiocManager", quietly = TRUE)) 
        install.packages("BiocManager")

#BiocManager::install("limma")
library(limma)
```

We will use the following code. Comment this code with your thoughts below.

```
#subset our data for a training and test set
set.seed(2) #seeding the dataset
prob = runif(ncol(simulated_clean)-2) #generating probability based on random uniformity of values in d
k = which(prob>=0.33333333) # selecting values with occurences more than 0.33
eset = simulated_clean[,2:ncol(simulated_clean)] #taking columns from GSM2631309.
eset = eset[,k] #updating the column vals with occurences of more than 33%.
rownames(eset) = simulated_clean[,1]
design = model.matrix(~0+as.factor(case[k]))
fit = eBayes(lmFit(eset,design)) #applying empirical bayesian statistical algorithm for differentiati
topTable(fit, coef=2) #table of top genes from linear model fit from second column.
##
                  logFC
                          AveExpr
                                                  P. Value
                                                              adj.P.Val
              3.142306 1.471867 29.50981 3.960809e-149 4.472996e-145 329.8665
## EXOC3L4
## FAM132A
              -3.159535 -1.461491 -29.50492 4.328845e-149 4.472996e-145 329.7780
## MDM2
              3.127701 1.426391 29.45016 1.171911e-148 8.072902e-145 328.7868
## CCR3
              -3.145072 -1.547047 -29.40990 2.436485e-148 1.258810e-144 328.0583
## MYO9A
              -3.172079 -1.571136 -29.27467 2.842523e-147 1.174872e-143 325.6132
## GADD45GIP1 -3.086818 -1.391784 -29.08998 8.109246e-146 2.793095e-142 322.2781
## ANXA2
             -3.106348 -1.517455 -29.04306 1.898445e-145 5.604751e-142 321.4315
## CCNJ
              -3.123721 -1.454289 -28.99762 4.324144e-145 1.117034e-141 320.6122
              3.070413 1.590585 28.97713 6.268035e-145 1.439280e-141 320.2427
## EMC6
## GEMIN4
              3.100428 1.427101 28.89015 3.027401e-144 6.256426e-141 318.6752
results = topTable(fit, coef=2, number=Inf) #number indicates maximum number of genes
```

Here, we have our gene names, our log fold change for simulatedession, average simulatedession, t statistic, pvalue, adjusted pvalue (for multiple testing!!), and the log odds of differential simulatedession.

Next, we select those genes that have adjusted p-values below 0.001. Comment the code with your thoughts about what its doing below.

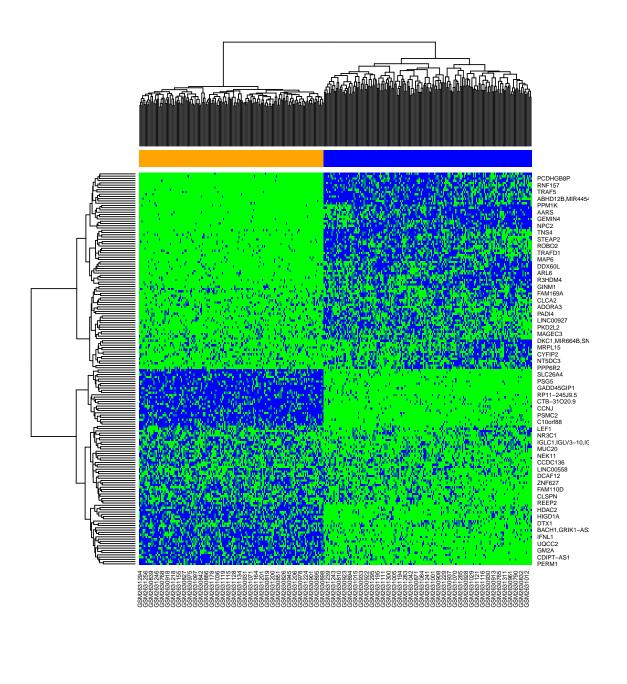
```
selected = row.names(results)[p.adjust(results$P.Value, method="fdr")<0.001] #selecting genes based on direction = sign(results$logFC) #using sign() function to get the sign of logFC scores for real numbers esetSel = eset[selected, ] #esetSel consists of rows of genes that were selected based on p values less nrow(esetSel)
```

[1] 174

Okay! So we're now looking at just 175 genes!

We are going to make a heat map here. I've provided the code, but **try changing colours, labels, etc. to** make it your own.

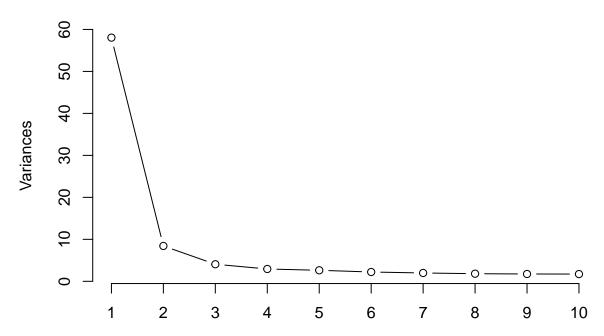
```
patientcolors = ifelse(case[k]==1,"orange","blue")
heatmap(as.matrix(esetSel), col=c("blue", "green"), ColSideColors=patientcolors, distfum = function(x)
```



Notice the annotation bar along the top. This indicates PD vs not PD samples. This heat map is an example of a 'non-supervised method' - where we didn't feed the labelled data to the algorithm. Instead, it is just clustering similar samples together. Because all of our PD samples cluster away from the non-PD samples, we are relatively certian we've picked good biomarkers! We should also check a PCA plot.

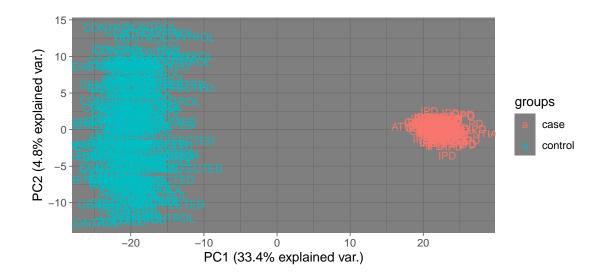
```
pc = prcomp(t(esetSel),center=T,scale=T) #reduce dimensionality to eigenvectors
plot(pc,type="l",main="Checking the number of Principle Components")
```

Checking the number of Principle Components



Again, I've provided code for you here. Change it to something you like better!

print(g)



We have separation! Notice the obvious differences between cases and controls.

Make a variable which only contains the differential gene names and call it diffGenes AND print out all of these gene names using one line of code.

```
#your code here
diffGenes = selected
```

To use these genes as a classifier, we will need to define a score function. Our score will be the sum of the average simulatedession for the upregulated (positive) genes and the average for the down regulated (negative) genes. Here, I've written you a function which will do this. Please enter it and **make comments to show you understand what its doing.**

```
PDscore = function(x,g,v,s){
  #x simulatedession values for a sample
  #q all the genes
  #v the diffGenes
  #s is the sign of the logFC
  i = which(g%in%v)
  x = x[i] #element in genes getting updated in a sample
  s = s[i] #logFC values of a element in genes, updated to s variable
  p = c() #initializing a vector
  n = c()
  for(i in 1:length(x)){ #looping in a sample and checking logFC scores > 0
   if(s[i]>0){
     p = append(p,(x[i])) # adding these values to a vector
   else if(s[i]<0){
     n = append(n,(x[i])) #negative logFC scores are updated here.
  }
  if(is.null(p)){p[1]=0} #replacing null values with 0
  if(is.null(n)){n[1]=0} #replacing null values with 0
  score = mean(p)-mean(n) #mean difference between vectors that have logFC positive and negative scores
  return(score)
}
```

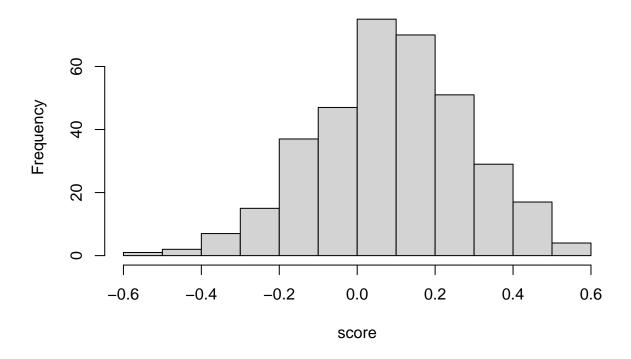
Now we can apply our function to our simulatedession set to define a score for each patient. **Comment** what this is doing and why each step is necessary!

```
score = c() #initializing empty vector

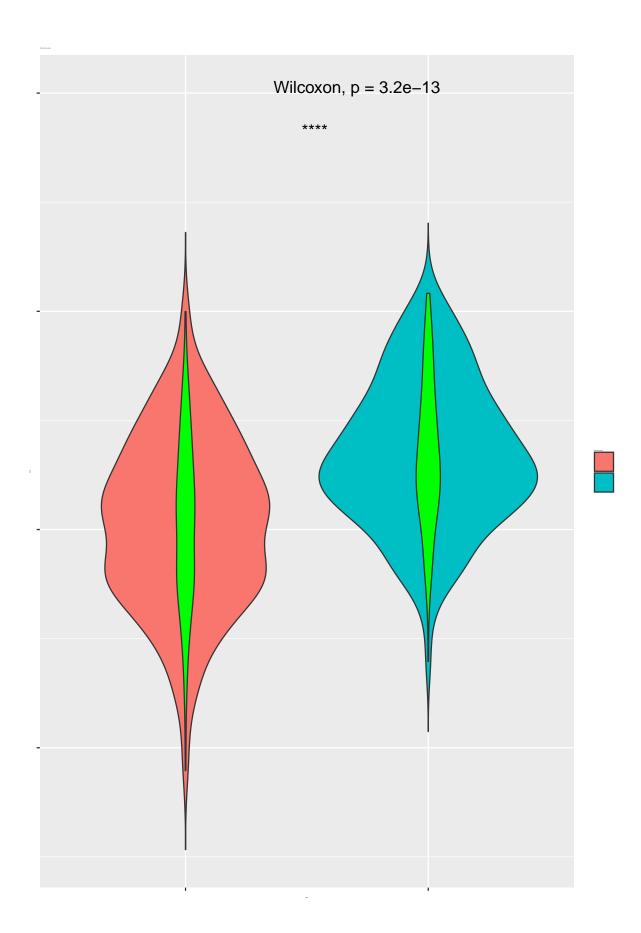
#char vals of results in simulated dataset.
allGenes = as.character(simulated[as.character(simulated$GeneName)%in%rownames(results),1])

#lopping in the subset and updating the score.
for(i in 1:ncol(eset)){
    score[i] = PDscore(eset[,i],allGenes,diffGenes,direction)
}
hist(score,main="Distribution of our PD Scores")
```

Distribution of our PD Scores



Now we'll use ggplot to make and interpret a violin plot of our score. I've provided some code to do this, but try to change labels, colours, etc. to make it your own.

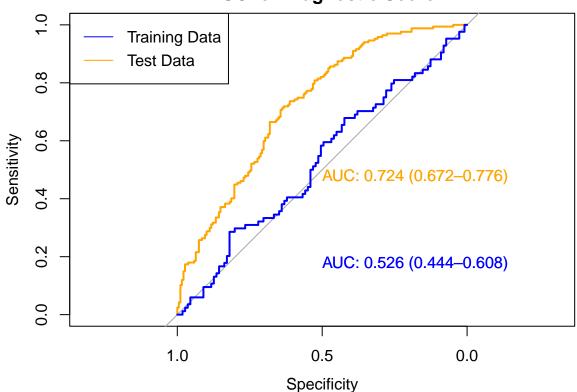


This shows not only the boxplot of our data, but also the distribution of our data points around the boxplot! As before, we can see that we DO have significant separation for our score, and we can see that the cases are trending to have a higher score. With more time and data cleaning we may be able to find something here!

Let's make a roc plot, first with our training data, and then with our test data. As before, **play with the plot options to make something you like!**

```
#install.packages("verification")
#install.packages("pROC")
library("pROC")
testEset = simulated[,2:ncol(simulated)]
testEset = testEset[,-k]
newScore = apply(testEset,2,FUN=PDscore,allGenes,diffGenes,direction)
plot.roc(case[k]~score, data=df,legacy.axes=F,print.auc=T, ci=T, main="AUC for Diagnostic Score",col="or plot.roc(case[-k]~newScore,data=data.frame(cbind(case[-k],newScore)),add=T,print.auc=T, ci=T, col="blue legend("topleft",c("Training Data","Test Data"),lty=c(1,1),col=c("blue","orange"))
```

AUC for Diagnostic Score



Notice that our score does better with our training data - this is expected! This is why we need to split our data, to avoid problems with over-fitting. These scores are better than random (the grey line), but we'd like to see an AUC as close to 1 as possible. Let's see if we can do better!

Statistics!

We can run a t-test to see if our score is significantly different between cases and controls. Try using the t.test function in R.

```
# your code here
allTscore = c(score, newScore)
mergeCase = c(case[k], case[-k])
t.test(allTscore[mergeCase == 0], allTscore[mergeCase == 1])
##
##
   Welch Two Sample t-test
##
## data: allTscore[mergeCase == 0] and allTscore[mergeCase == 1]
## t = -6.2832, df = 535.65, p-value = 6.875e-10
\#\# alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
## -0.14076017 -0.07370768
## sample estimates:
##
     mean of x
                 mean of y
## 0.009489271 0.116723192
```

The mean scores for our cases and controls are close, but they are significantly different with an extremely small p-value of 2.787e-13. This highlights a classical statistical fallacy - while small p-values are great, they are often meaningless without a large enough effect size. Here, we have achieved significance due to the large sample size of our study, hence our study is adequately powered.

We could also run a simple regression to examine the impact of the score on the log odds of being a case.

```
# your code here
logistic = glm(case[k]~score, family="binomial")
summary(logistic)
##
## Call:
  glm(formula = case[k] ~ score, family = "binomial")
##
## Deviance Residuals:
##
       Min
                 1Q
                      Median
                                   3Q
                                           Max
  -1.9915
           -1.0119 -0.5391
                               1.0851
                                        2.0686
##
## Coefficients:
##
               Estimate Std. Error z value Pr(>|z|)
## (Intercept) -0.5627
                            0.1343
                                    -4.191 2.78e-05 ***
                            0.6966
                                     6.892 5.51e-12 ***
## score
                 4.8012
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##
       Null deviance: 490.89
                              on 354
                                      degrees of freedom
## Residual deviance: 430.83
                              on 353
                                      degrees of freedom
## AIC: 434.83
##
```

Summarize this output!

Number of Fisher Scoring iterations: 3

Again, we conclude that the score is a statistically significant indicator of the odds of having PD. Let's build a larger model which examines other phenotype variables.

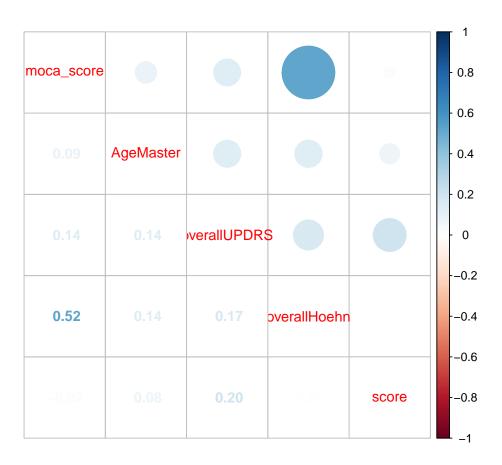
First, build a data frame which includes all the model data we're interested in. Start with the age variables in your pheno set, and then use the cbind() function to add on our scores and the binary case vector. Print a summary of the model data.

```
# your code here
modelData = cbind(pheno[k,3:7],score)
summary(modelData)
```

```
##
                          moca_score
                                           AgeMaster
                                                           overallUPDRS
        sex
##
    Length: 355
                        Min. : 0.00
                                         Min.
                                                :26.00
                                                                  : 0.000
                        1st Qu.: 0.00
                                         1st Qu.:53.50
                                                          1st Qu.: 0.000
##
    Class : character
##
    Mode :character
                        Median :25.00
                                         Median :62.00
                                                          Median : 0.000
##
                        Mean
                                :17.01
                                         Mean
                                                 :60.15
                                                          Mean
                                                                  : 1.489
##
                        3rd Qu.:29.00
                                         3rd Qu.:67.00
                                                          3rd Qu.: 0.600
                                :30.00
                                                 :82.00
                                                                  :15.800
##
                        Max.
                                         Max.
                                                          Max.
##
                        NA's
                                :12
                                         NA's
                                                 :132
                                                          NA's
                                                                  :167
##
     overallHoehn
                         score
##
    Min.
           :0.000
                     Min.
                            :-0.55225
##
    1st Qu.:0.000
                     1st Qu.:-0.05932
##
    Median :0.000
                     Median : 0.08870
##
   Mean
           :1.412
                            : 0.08669
                     Mean
##
    3rd Qu.:4.000
                     3rd Qu.: 0.21846
           :4.500
                            : 0.54121
##
    Max.
                     Max.
##
    NA's
           :161
```

We should examine the correlations in our data set. You can do this quickly by building a correlation plot matrix.

```
#install.packages("corrplot")
library(corrplot)
M = cor(modelData[,-1],use="pairwise.complete.obs") #for missing data
corrplot.mixed(M)
```



How would you interpret this output? **Answer below!**

4.98031

Number of Fisher Scoring iterations: 6

1Q

Median

0.2196

2.39979

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 68.752 on 55 degrees of freedom

Residual deviance: 41.104 on 49 degrees of freedom
(299 observations deleted due to missingness)

Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1

score

AIC: 55.104

modelData\$case = case[k]

Min

-2.8009 -0.3493

##

##

##

##

##

The blue color indicates the highest normalized correlation score between 0 and 1, from the plot it can be interpreted that not many variables are correlated with each other. The red color indicates no correlation exists between the variables.

Let's build our first model. Here, we consider the case as our dependent variable, and the others as our explanatory variables.

```
model1 = glm(case[k]~.,family=binomial,data=modelData)
summary(model1)
##
## Call:
## glm(formula = case[k] ~ ., family = binomial, data = modelData)
##
## Deviance Residuals:
##
       Min
                 10
                      Median
                                    30
                                             Max
##
  -2.8009
           -0.3493
                       0.2196
                                0.6385
                                          1.6723
##
## Coefficients:
##
                Estimate Std. Error z value Pr(>|z|)
## (Intercept)
                -4.90400
                             2.57394
                                      -1.905
                                                0.0567 .
## sex Male
                 0.66544
                             0.86314
                                       0.771
                                                0.4407
                                       2.330
## moca_score
                 0.11149
                             0.04786
                                                0.0198 *
## AgeMaster
                 0.04711
                             0.04002
                                       1.177
                                                0.2392
## overallUPDRS
                 0.28691
                             0.12524
                                       2.291
                                                0.0220
## overallHoehn 0.17082
                                       0.750
                                                0.4532
                             0.22774
```

2.075

0.0380 *

We will iteratively remove variables with the highest p-values, and then rerun the model until we have our optimal fit!. Try this on your own first.

Max

1.6723

3Q

0.6385

```
##
## Coefficients:
##
               Estimate Std. Error z value Pr(>|z|)
## (Intercept) -4.90400
                           2.57394 -1.905
                                             0.0567
## sex Male
                0.66544
                           0.86314
                                    0.771
                                             0.4407
## AgeMaster
                0.04711
                           0.04002
                                   1.177
                                             0.2392
                                   2.330
## moca score
                0.11149
                           0.04786
                                             0.0198 *
## overallUPDRS 0.28691
                           0.12524
                                    2.291
                                             0.0220 *
## overallHoehn 0.17082
                           0.22774
                                    0.750
                                             0.4532
## score
                4.98031
                           2.39979 2.075
                                             0.0380 *
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
## (Dispersion parameter for binomial family taken to be 1)
##
##
      Null deviance: 68.752 on 55 degrees of freedom
## Residual deviance: 41.104 on 49 degrees of freedom
## AIC: 55.104
## Number of Fisher Scoring iterations: 6
modelData2$sex = NULL #removing sex column since it threw error.
\#modelData2\$AgeMaster = NULL
model3 = glm(case~AgeMaster+moca_score+overal1UPDRS+overal1Hoehn+score, family=binomial, data=modelData2)
summary(model3)
##
## Call:
## glm(formula = case ~ AgeMaster + moca_score + overallUPDRS +
      overallHoehn + score, family = binomial, data = modelData2)
##
##
## Deviance Residuals:
                    Median
                                  3Q
      Min
                1Q
                                          Max
## -2.6673 -0.3431
                     0.2415
                              0.6291
                                       1.7149
##
## Coefficients:
               Estimate Std. Error z value Pr(>|z|)
##
## (Intercept) -4.86113
                           2.52803 -1.923
                                             0.0545 .
                                    1.368
                                             0.1712
## AgeMaster
                0.05279
                           0.03858
## moca_score
                0.11430
                           0.04795
                                    2.384
                                             0.0171 *
## overallUPDRS 0.25616
                           0.11283
                                    2.270
                                             0.0232 *
## overallHoehn 0.21284
                           0.22239
                                    0.957
                                             0.3385
## score
                4.83636
                           2.36102
                                     2.048
                                             0.0405 *
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
## (Dispersion parameter for binomial family taken to be 1)
##
      Null deviance: 68.752 on 55 degrees of freedom
## Residual deviance: 41.715 on 50 degrees of freedom
## AIC: 53.715
## Number of Fisher Scoring iterations: 6
```

This is our final model! Notice that our largest effect size is controlled by our genetic score. At a first glance, we might assume this means that the score has the largest effect on the model. However, if we recall how to interpret our coefficients, the estimated effect size is the change in log odds of being a case for a 1 unit increase in our score. Think about the score distribution: the range of our scores is fairly small. In contrast, the range of the updrs scores varies from 0 to 36. Keep in mind the scale of our data when interpreting these models!

Compare this to your outcome if you use a step function to reduce the model:

```
#your code here
stepModel = step(model3)
## Start: AIC=53.72
   case ~ AgeMaster + moca_score + overallUPDRS + overallHoehn +
##
       score
##
##
                  Df Deviance
                                  AIC
## - overallHoehn
                        42.680 52.680
## <none>
                        41.715 53.715
## - AgeMaster
                        43.863 53.863
                   1
                        46.543 56.543
## - score
## - overallUPDRS
                   1
                        47.771 57.771
                        50.233 60.233
## - moca_score
                   1
##
## Step: AIC=52.68
## case ~ AgeMaster + moca_score + overallUPDRS + score
##
##
                  Df Deviance
                                  AIC
## - AgeMaster
                        44.561 52.561
## <none>
                        42.680 52.680
## - score
                        47.094 55.094
                        49.515 57.515
## - overallUPDRS
                   1
## - moca_score
                   1
                        50.361 58.361
##
## Step: AIC=52.56
## case ~ moca_score + overallUPDRS + score
##
##
                  Df Deviance
                                  AIC
## <none>
                        44.561 52.561
## - score
                   1
                        49.481 55.481
                        50.543 56.543
## - moca score
                   1
## - overallUPDRS
                   1
                        54.169 60.169
summary(stepModel)
##
## glm(formula = case ~ moca_score + overallUPDRS + score, family = binomial,
##
       data = modelData2)
##
  Deviance Residuals:
##
##
       Min
                 1Q
                      Median
                                    3Q
                                            Max
                      0.2373
##
   -2.3970
           -0.5641
                                0.5741
                                          2.0603
##
## Coefficients:
                Estimate Std. Error z value Pr(>|z|)
##
```

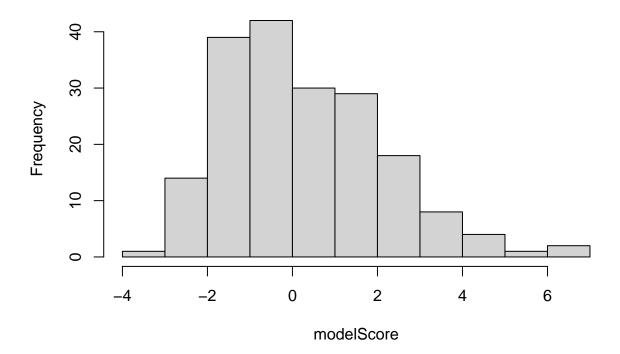
```
## (Intercept)
               -1.40257
                            0.64691
                                     -2.168 0.03015 *
                 0.08638
## moca_score
                            0.04217
                                      2.048
                                             0.04052 *
## overallUPDRS
                            0.11082
                0.30910
                                      2.789
                                             0.00529 **
                                      2.085
                                             0.03711 *
                 4.47227
                            2.14542
## score
##
                  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## Signif. codes:
## (Dispersion parameter for binomial family taken to be 1)
##
##
       Null deviance: 68.752 on 55
                                     degrees of freedom
## Residual deviance: 44.561
                              on 52
                                     degrees of freedom
  AIC: 52.561
##
##
## Number of Fisher Scoring iterations: 6
```

Let's predict the probability of having a case given our manually reduced model. Make a histogram of the score from this model.

```
# your code here

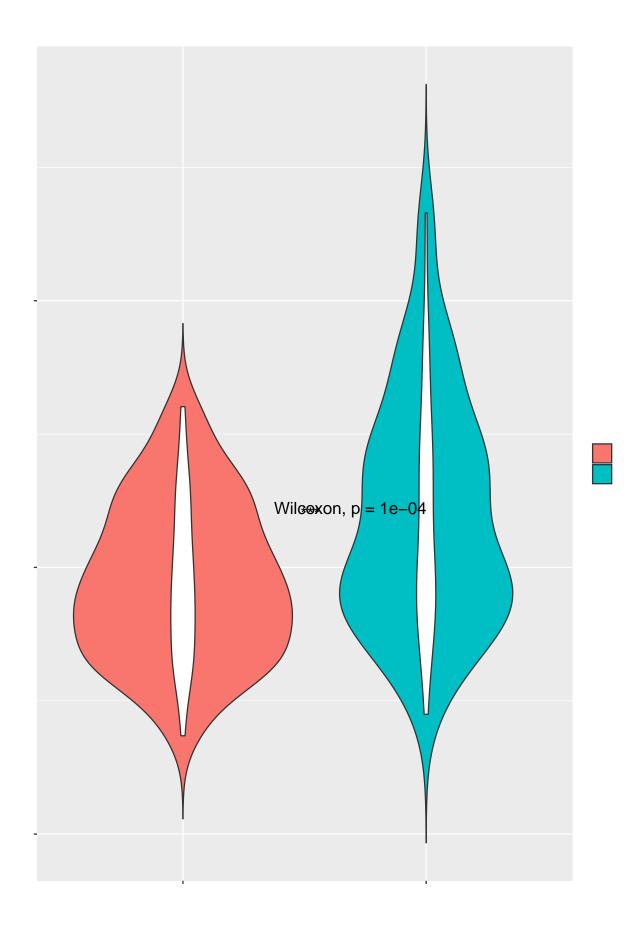
modelScore = predict(stepModel, newdata = modelData)
hist(modelScore, main="Histogram of Logistic Regression Model")
```

Histogram of Logistic Regression Model



Like before, we'll build a violin plot to compare the output of our regression model. See if you can adapt the violin plot code from before to do this now.

```
df = data.frame(cbind(case[k],modelScore))
dp = ggplot(df, aes(x=as.factor(case[k]), y=modelScore, fill=as.factor(case[k]))) +
```



Now we're starting to see a clearer separation of scores! It's clear that by including the established tests to pre-screen patients for PD and other neurological diseases we have improved overall performance. While this may be an obvious conclusion, it is worth noting that the context with which our diagnostic signature would be used would be on patients already exhibiting potential PD symptoms. Clearly this needs a little more work, but for a first pass at assessing raw data, it's not bad!

Again, we can examine ROC curves. I've done some of the set up to get the data in the right format. Use the ROC code above to then build your own plot!

```
library("pROC")
nd = cbind(pheno[-k,],newScore)
colnames(nd) = c(colnames(nd[1:ncol(nd)-1]),"score")
newMScore = predict(stepModel,newdata=nd)

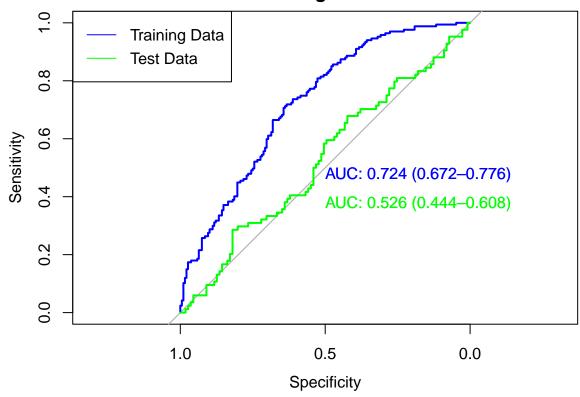
plot.roc(case[k]~score, data=df,legacy.axes=F,print.auc=T, ci=T, main="AUC for Diagnostic Score", col="
## Setting levels: control = 0, case = 1

## Setting direction: controls < cases
plot.roc(case[-k]~newScore,data=data.frame(cbind(case[-k],newScore)),add=T,print.auc=T, ci=T, col="gree"

## Setting levels: control = 0, case = 1

## Setting direction: controls < cases
legend("topleft",c("Training Data","Test Data"),lty=c(1,1),col=c("blue","green"))</pre>
```

AUC for Diagnostic Score



Here, we have a notable increase in AUC, particularly for our training data. Our test data shows an overal improvement as well, although with a large confidence interval. There are clearly some data points in here

which are abnormal - and perhaps worth investigating.

Congratulations, you have finished the R Bootcamp Assignment!