

# Biostatistics HomeWork 1

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$$dist(i, j) = \sqrt{\sum_{k=1}^p (x_{ik} - x_{jk})^2}$$

where  $x_{ik}$  stands for the gene expression value of the  $i$ -th sample and the  $k$ -th gene, and  $p = 6,830$ . Which cell line and two samples have the smallest pairwise distance? Include the numerical value of the smallest distance with two sample ID number (1 ~ 64) and the name of the corresponding cancer cell line. Note that computation of distance between two samples is limited the same cancer cell line. . . . .

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## 0. Package and Data

```
library(ISLR)
data("NCI60")
unique(NCI60$labs)
```

```
## [1] "CNS"          "RENAL"        "BREAST"       "NSCLC"       "UNKNOWN"
## [6] "OVARIAN"      "MELANOMA"     "PROSTATE"     "LEUKEMIA"    "K562B-repro"
## [11] "K562A-repro" "COLON"        "MCF7A-repro"  "MCF7D-repro"
```

```
dim(NCI60$data) # row = cancer cell lines(samples), col = gene expression
```

```
## [1] 64 6830
```

```
str(NCI60)
```

```
## List of 2
## $ data: num [1:64, 1:6830] 0.3 0.68 0.94 0.28 0.485 ...
## ..- attr(*, "dimnames")=List of 2
## .. ..$ : chr [1:64] "V1" "V2" "V3" "V4" ...
## .. ..$ : chr [1:6830] "1" "2" "3" "4" ...
## $ labs: chr [1:64] "CNS" "CNS" "CNS" "RENAL" ...
```

```
NCI60$data[1:5, 1:10]
```

```
##           1           2           3           4           5           6           7
## V1 0.300000  1.180000  0.550000  1.140000 -0.265000 -7.000000e-02 0.350000
## V2 0.679961  1.289961  0.169961  0.379961  0.464961  5.799610e-01 0.699961
## V3 0.940000 -0.040000 -0.170000 -0.040000 -0.605000  0.000000e+00 0.090000
## V4 0.280000 -0.310000  0.680000 -0.810000  0.625000 -1.387779e-17 0.170000
## V5 0.485000 -0.465000  0.395000  0.905000  0.200000 -5.000000e-03 0.085000
##           8           9          10
## V1 -0.315000 -0.45000000 -0.65498050
## V2  0.724961 -0.04003899 -0.28501950
## V3  0.645000  0.43000000  0.47501950
## V4  0.245000  0.02000000  0.09501949
## V5  0.110000  0.23500000  1.49001949
```

```
sum(is.na(NCI60$data))
```

```
## [1] 0
```

1. For each cancer cell line, compute average gene expression values. Identify two cell lines that have the largest and the smallest mean values. Also, include the maximum and minimum mean values.

```

sol_1 = function(x = NCI60$data, cell_name = NCI60$labs){

  avg_gene_expr_cancer_cell = apply(x, 1, mean)

  max_idx = which.max(avg_gene_expr_cancer_cell)
  min_idx = which.min(avg_gene_expr_cancer_cell)

  max_cell_name = cell_name[max_idx]
  min_cell_name = cell_name[min_idx]

  max_value = avg_gene_expr_cancer_cell[max_idx]
  min_value = avg_gene_expr_cancer_cell[min_idx]

  return(
    list(
      avg_gene_expr_cancer_cell = avg_gene_expr_cancer_cell,
      max_cell_name = max_cell_name,
      max_value = max_value,
      min_cell_name = min_cell_name,
      min_value = min_value
    )
  )
}

sol_1()

```

```

## $avg_gene_expr_cancer_cell
##      V1      V2      V3      V4      V5      V6
## 0.065301161 0.050764025 0.072186913 0.093828598 0.148587415 0.051984464
##      V7      V8      V9     V10     V11     V12
## 0.045946454 0.034898165 0.030765650 0.071969531 0.082987492 0.097510887
##      V13     V14     V15     V16     V17     V18
## 0.043871076 0.080305578 0.086590327 0.068228701 0.036918312 0.005414269
##      V19     V20     V21     V22     V23     V24
## 0.044108654 -0.010810123 0.022486014 0.021204167 0.022557379 0.028589256
##      V25     V26     V27     V28     V29     V30
## 0.055356775 0.076016757 0.037696115 0.030543813 0.052745532 0.029498474
##      V31     V32     V33     V34     V35     V36
## 0.065867052 0.045337045 0.035683095 0.008683965 -0.025011443 -0.067179793
##      V37     V38     V39     V40     V41     V42
## -0.073247688 -0.059364277 -0.142086454 -0.112343414 -0.079673926 0.016840221
##      V43     V44     V45     V46     V47     V48
## -0.022744231 -0.045290706 0.013481493 0.008972460 0.009429658 0.005350211
##      V49     V50     V51     V52     V53     V54
## -0.070572553 -0.045211715 -0.015887593 0.014101316 0.050248954 -0.033281552
##      V55     V56     V57     V58     V59     V60
## -0.043874535 0.016277763 -0.004496054 -0.019257425 0.040631693 0.065602038
##      V61     V62     V63     V64
## 0.040684766 0.072229801 0.021697977 0.039845104
##
## $max_cell_name
## [1] "BREAST"

```

```
##
## $max_value
##      V5
## 0.1485874
##
## $min_cell_name
## [1] "LEUKEMIA"
##
## $min_value
##      V39
## -0.1420865
```

2. For each gene, compute average gene expression values of 64 cancer cell lines, including “UNKNOWN” label. Identify top 5 gene that have the largest mean expression values and top 5 genes that have smallest mean expression values. Also, include their mean values with gene ID number(1~6830).

```
sol_2 = function(x = NCI60$data){

  avg_gene_expr_gene = apply(x ,2, mean)

  top_5_max_idx = order(avg_gene_expr_gene, decreasing = TRUE)[1 : 5]
  top_5_min_idx = order(avg_gene_expr_gene)[1 : 5]

  top_5_max_gene = avg_gene_expr_gene[top_5_max_idx]
  top_5_min_gene = avg_gene_expr_gene[top_5_min_idx]

  return(
    list(
      top_5_max_gene = top_5_max_gene,
      top_5_min_gene = top_5_min_gene
    )
  )
}

sol_2()
```

```
## $top_5_max_gene
##      6393      256      257      4700      6391
## 1.1676457 1.1137491 1.0627335 0.9985928 0.9920303
##
## $top_5_min_gene
##      5869      5868      5984      3438      281
## -0.8621881 -0.7442193 -0.7360845 -0.7223447 -0.7109384
```

3. Suppose that group “A” contains “BREAST” and “NSCLC”, group “B” has “MELANOMA”, “OVARIAN” and “PROSTATE”, and group “C” has “LEUKEMIA”, “RENAL” and “UNKNOWN”. The other 6 cell lines belong to group “D”. For each cancer group, compute the mean expression values and the standard deviation of gene expression values.

```
cell_name = NCI60$labs

# grouping cells
A = c("BREAST", "NSCLC")
B = c("MELANOMA", "OVARIAN", "PROSTATE")
C = c("LEUKEMIA", "RENAL", "UNKNOWN")

cell_group = ifelse(cell_name %in% A, "A",
                    ifelse(cell_name %in% B, "B",
                          ifelse(cell_name %in% C, "C", "D")))
```

```
groups = c("A", "B", "C", "D")

sol_3 = function(x = NCI60$data, group = groups){

  group_mean = sapply(group,
                      function(g) {
                        mean(x[cell_group == g, ])
                      })

  group_sd = sapply(group,
                   function(g) {
                     sd(x[cell_group == g, ])
                   })

  list(
    group_mean = as.data.frame(group_mean),
    group_sd   = as.data.frame(group_sd)
  )
}

sol_3()
```

```
## $group_mean
##      group_mean
## A 0.025053741
## B 0.040698588
## C 0.008992817
## D 0.005848171
##
## $group_sd
##      group_sd
## A 0.8006589
## B 0.7368874
## C 0.8443378
## D 0.7924379
```

4. For each cancer group defined in Q3, compute the sample SD of gene expression values of individual genes. Find genes whose SD is less than 0.2 or greater than 2 for each cancer group, i.e.,  $SD < 0.2$  or  $SD > 2$ . How many genes are overlapped by 4 different cancer groups? How many genes are overlapped by exactly 3 different cancer groups? or exactly 2 different cancer groups? Also, how many genes are uniquely identified by only one cancer group? Summarize your answer, using the following table.

```
sol_4 = function(){
  group_sd = lapply(groups,
    function(grp) {
      apply(NCI60$data[cell_group == grp, ], 2, sd)
    })

  names(group_sd) = c("A", "B", "C", "D")

  filtered_genes = lapply(group_sd,
    function(sd_value){
      names(sd_value[sd_value < 0.2 | sd_value > 2])
    })

  unique_genes = unique(c(filtered_genes[["A"]],
    filtered_genes[["B"]],
    filtered_genes[["C"]],
    filtered_genes[["D"]]))

  num_overlapped = factor(apply(sapply(filtered_genes,
    function(g_list) {
      unique_genes %in% g_list
    }), 1, sum), levels = 1:4)

  sol_df = data.frame(
    x4 = length(num_overlapped[num_overlapped == "4"]),
    x3 = length(num_overlapped[num_overlapped == "3"]),
    x2 = length(num_overlapped[num_overlapped == "2"]),
    x1 = length(num_overlapped[num_overlapped == "1"])
  )

  rownames(sol_df) = "The number of genes"
  colnames(sol_df) = c("4 groups", "3 groups", "2 groups", "1 groups")

  return(
    list(
      filtered_genes = filtered_genes,
      sol_df = sol_df
    ))
}

sol_4()
```

```
## $filtered_genes
## $filtered_genes$A
```

```

## [1] "16" "111" "112" "113" "134" "196" "243" "245" "248" "251"
## [11] "252" "256" "257" "266" "267" "273" "281" "286" "472" "975"
## [21] "1106" "1215" "1258" "1865" "2068" "2504" "2838" "2875" "2914" "2927"
## [31] "3320" "3383" "3438" "3518" "3525" "3543" "3936" "3956" "3957" "4050"
## [41] "4154" "4280" "4288" "4344" "4353" "4354" "4699" "4700" "4701" "5036"
## [51] "5142" "5221" "5275" "5276" "5353" "5476" "5477" "5555" "5556" "5557"
## [61] "5586" "5587" "5661" "5692" "5705" "5706" "5707" "5723" "5732" "5760"
## [71] "5803" "5804" "5805" "5828" "5829" "5838" "5843" "5845" "5913" "5940"
## [81] "5942" "5943" "5948" "5980" "6128" "6148" "6149" "6150" "6151" "6152"
## [91] "6153" "6156" "6157" "6263" "6264" "6268" "6277" "6278" "6279" "6321"
## [101] "6328" "6356" "6391" "6392" "6393" "6415" "6416" "6419" "6429" "6430"
## [111] "6453" "6564" "6612" "6614" "6615" "6616" "6622" "6718"
##
## $filtered_genes$B
## [1] "124" "125" "128" "130" "133" "134" "196" "241" "242" "243"
## [11] "252" "256" "257" "286" "287" "408" "416" "561" "580" "581"
## [21] "592" "754" "755" "770" "1067" "1110" "1508" "1664" "1888" "1896"
## [31] "1897" "2100" "2216" "2239" "2551" "2678" "2680" "2891" "3234" "3706"
## [41] "3713" "3957" "4093" "4094" "4280" "4288" "4289" "4304" "4306" "4308"
## [51] "4320" "4327" "4344" "4353" "4354" "4375" "4383" "4387" "4388" "4425"
## [61] "4426" "4699" "4700" "4701" "4716" "4971" "5094" "5275" "5276" "5353"
## [71] "5555" "5556" "5557" "5586" "5804" "5948" "6149" "6150" "6322" "6356"
## [81] "6391" "6392" "6393" "6434" "6554" "6635" "6710"
##
## $filtered_genes$C
## [1] "16" "78" "133" "187" "196" "243" "252" "256" "281" "286"
## [11] "301" "415" "515" "707" "754" "755" "756" "806" "1199" "1229"
## [21] "1387" "1388" "1389" "1390" "1391" "2068" "2070" "2074" "2080" "2081"
## [31] "2082" "2083" "2102" "3234" "3248" "3282" "3372" "3373" "3490" "3491"
## [41] "3518" "3525" "3894" "4085" "4131" "4154" "4245" "4344" "4354" "4699"
## [51] "4700" "4701" "4716" "5127" "5221" "5270" "5301" "5336" "5392" "5481"
## [61] "5489" "5496" "5506" "5510" "5586" "5587" "5588" "5705" "5712" "5721"
## [71] "5729" "5732" "5758" "5760" "5774" "5796" "5803" "5804" "5805" "5867"
## [81] "5868" "5869" "5870" "5872" "5878" "5884" "5899" "5902" "5910" "5917"
## [91] "5921" "5927" "5928" "5937" "5940" "5941" "5942" "5943" "5946" "5948"
## [101] "5950" "5962" "5972" "5973" "5976" "5979" "5980" "5981" "5993" "6009"
## [111] "6010" "6017" "6018" "6035" "6039" "6046" "6084" "6085" "6086" "6087"
## [121] "6124" "6148" "6149" "6150" "6151" "6152" "6153" "6154" "6156" "6157"
## [131] "6169" "6243" "6272" "6274" "6277" "6278" "6279" "6288" "6289" "6382"
## [141] "6391" "6392" "6393" "6412" "6413" "6414" "6415" "6416" "6429" "6430"
## [151] "6592" "6596" "6635" "6644" "6646" "6688" "6689" "6710" "6717" "6817"
##
## $filtered_genes$D
## [1] "16" "112" "113" "161" "188" "224" "227" "228" "229" "243"
## [11] "248" "252" "256" "257" "267" "286" "301" "412" "582" "707"
## [21] "716" "754" "755" "770" "975" "1187" "1380" "1382" "1388" "1389"
## [31] "1390" "1391" "1393" "1396" "1613" "1716" "2080" "2081" "2096" "2104"
## [41] "2302" "3212" "3424" "3936" "3957" "4010" "4057" "4060" "4093" "4094"
## [51] "4119" "4154" "4231" "4344" "4472" "4612" "4644" "4699" "4700" "4701"
## [61] "4703" "4704" "4706" "4845" "4994" "5031" "5142" "5472" "5481" "5646"
## [71] "5680" "5691" "5692" "5696" "5705" "5706" "5707" "5732" "5804" "5805"
## [81] "5838" "5867" "5868" "5869" "5870" "5916" "5917" "5937" "5948" "5980"
## [91] "6068" "6149" "6274" "6391" "6392" "6393" "6415" "6416" "6612" "6635"
## [101] "6646" "6687" "6688" "6689"

```

```
##
##
## $sol_df
##           4 groups 3 groups 2 groups 1 groups
## The number of genes      14      17      71      220
```

5. For each gene, compute the pairwise difference in mean expression values among 4 different cancer groups. Note that there are a total of 6 pairs among 4 cancer groups. Which gene and which cancer group pair have the largest difference in mean expression values? You should report the numerical value of the largest difference along with the gene ID number. Also, identify the corresponding cancer group pair that has the largest difference.

```
group_means = sapply(groups,
                      function(grp){
                        colMeans(NCI60$data[cell_group == grp, ])
                      })

pair = combn(1:4, 2) # col = # of pairs, row = combin of group

group_diffs = apply(pair, 2, # pair goes to arg of func ex. 1/(1, 2), 2/(1, 3)....
                    function(pair){
                      group_means[, pair[1]] - group_means[, pair[2]]
                    })

colnames(group_diffs)=c("A-B", "A-C", "A-D", "B-C", "B-D", "C-D")

ans = which(abs(group_diffs) == max(abs(group_diffs)), arr.ind = TRUE) # arr.ind !!!!

cat("The largest difference is", group_diffs[ans[1, 1], ans[1, 2]], "\n",
    "ID of Gene:", ans[1, 1], "\n",
    "Group Pair:", colnames(group_diffs)[ans[1, 2]], "\n")

## The largest difference is 2.915624
## ID of Gene: 6415
## Group Pair: A-B
```

6. Only 9 different cancer cell lines have at least 2 samples. For each of these 9 cell lines, compute the pairwise distance of expression values between two samples  $(i, j)$  s.t

$$dist(i, j) = \sqrt{\sum_{k=1}^p (x_{ik} - x_{jk})^2}$$



where  $x_{ik}$  stands for the gene expression value of the  $i$ -th sample and the  $k$ -th gene, and  $p = 6,830$ . Which cell line and two samples have the smallest pairwise distance? Include the numerical value of the smallest distance with two sample ID number (1 ~ 64) and the name of the corresponding cancer cell line. Note that computation of distance between two samples is limited the same cancer cell line.

```
filter_cell = names(table(NCI60$labs)[table(NCI60$labs) >= 2])

for(i in filter_cell){

  filter_cell_id = which(NCI60$labs == i)

  q6_data = NCI60$data[filter_cell_id, ]

}
```

```
filter_cell = names(table(NCI60$labs)[table(NCI60$labs) >= 2])

compr = Inf
ans_samples = NULL
ans_cell = NULL

for(cell in filter_cell){

  cell_id = which(NCI60$labs == cell)

  if(length(cell_id) >= 2){

    for(i in 1:(length(cell_id) - 1)){

      for(j in (i + 1):length(cell_id)){

        dist_cell = sqrt(sum((NCI60$data[cell_id[i], ] - NCI60$data[cell_id[j], ])^2))

        if(dist_cell < compr){

          compr = dist_cell

          ans_samples = c(cell_id[i], cell_id[j])

          ans_cell = cell
        }
      }
    }
  }
}

cat("Smallest dist:", compr, "\n",
    "Sample ID:", ans_samples, "\n",
    "Name of cancer cell line:", ans_cell)
```

```
## Smallest dist: 39.10562
## Sample ID: 57 58
## Name of cancer cell line: BREAST
```