TMA4268 Statistical Learning

Chapter 10: Unsupervised Learning

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Contents

Lab 3: NCI60 Data Example

The NCI60 data

The NCI60 cancer cell line microarray data consists of 6,830 gene expression measurements on 64 cancer cell lines.

```
library(ISLR)
nci.labs=NCI60$labs
nci.data=NCI60$data
```

The data has 64 rows and 6,830 columns.

```
dim(nci.data)
```

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

Each cell line is labeled with a cancer type. We begin by examining the cancer types for the cell lines.

```
nci.labs[1:4]
```

```
## [1] "CNS"   "CNS"   "CNS"   "RENAL"
```

```
table(nci.labs)
```

```
## nci.labs
##      BREAST         CNS       COLON K562A-repro K562B-repro    LEUKEMIA 
##           7           5           7           1           1           6 
## MCF7A-repro MCF7D-repro    MELANOMA       NSCLC     OVARIAN    PROSTATE 
##           1           1           8           9           6           2 
##       RENAL     UNKNOWN 
##           9           1
```

PCA on the NCI60 Data

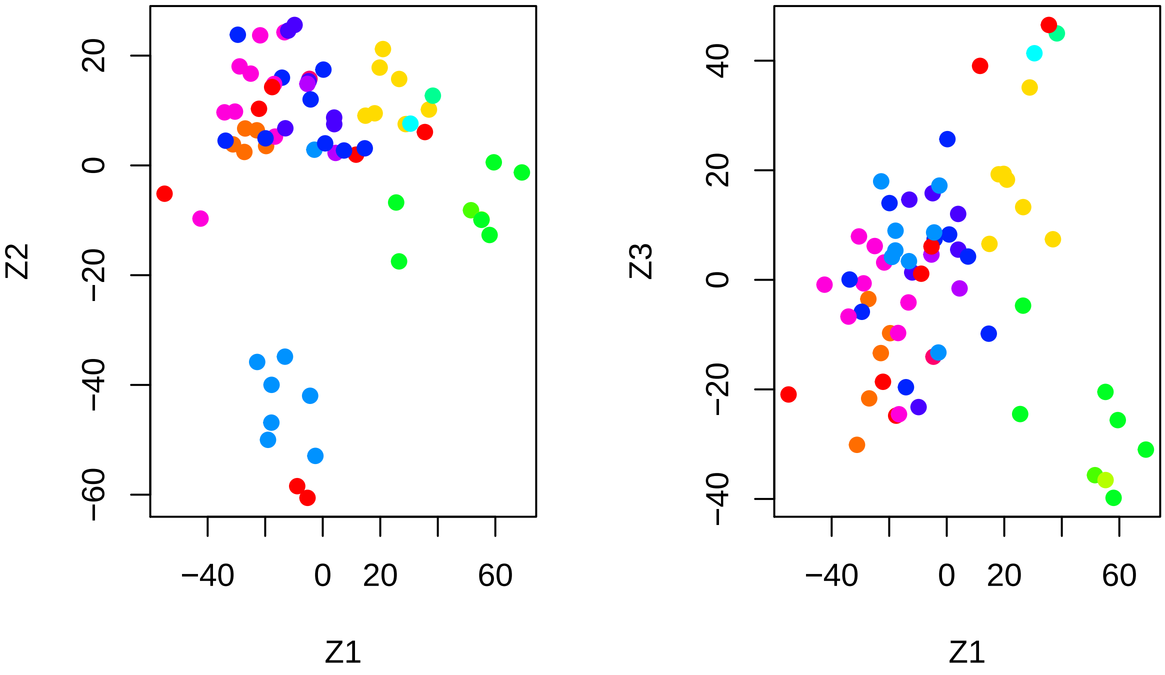
We first perform PCA on the data after scaling the variables (genes) to have standard deviation one, although one could reasonably argue that it is better not to scale the genes.

```r
pr.out=prcomp(nci.data, scale=TRUE)
```

We now plot the first few principal component score vectors, in order to visualize the data. The observations (cell lines) corresponding to a given cancer type will be plotted in the same color, so that we can see to what extent the observations within a cancer type are similar to each other.

```r
Cols=function(vec){
    cols=rainbow(length(unique(vec)))
    return(cols[as.numeric(as.factor(vec))])
}
```

```r
par(mfrow=c(1,2))
plot(pr.out$x[,1:2], col=Cols(nci.labs), pch=19,xlab="Z1",ylab="Z2")
plot(pr.out$x[,c(1,3)], col=Cols(nci.labs), pch=19,xlab="Z1",ylab="Z3")
```

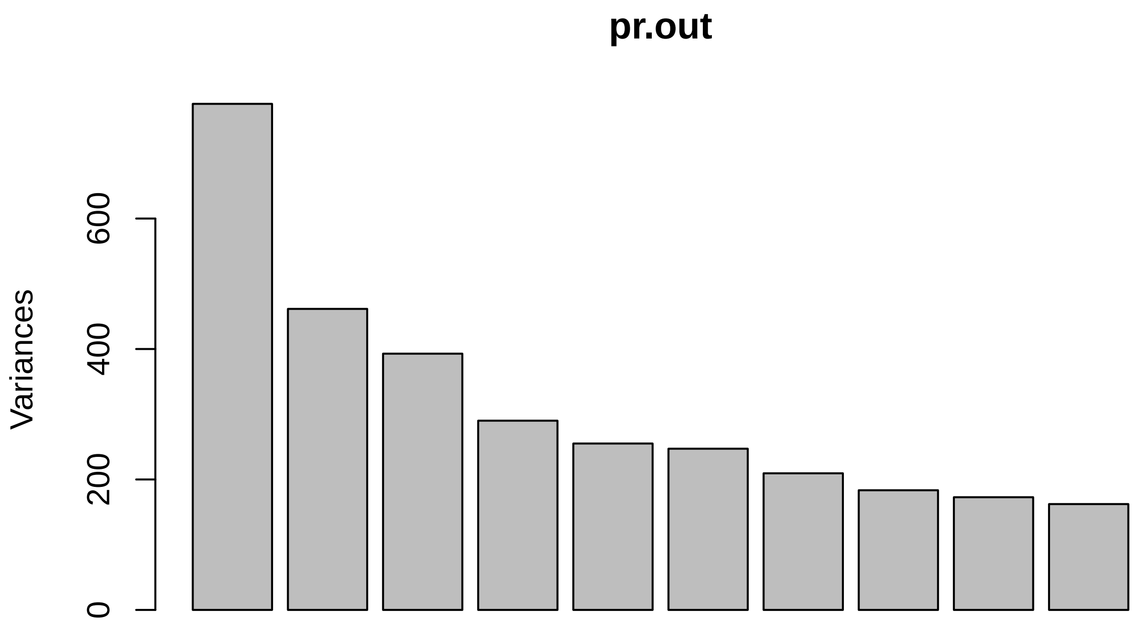


On the whole, cell lines corresponding to a single cancer type do tend to have similar values on the first few principal component score vectors. This indicates that cell lines from the same cancer type tend to have pretty similar gene expression levels.

```r
summary(pr.out)
```

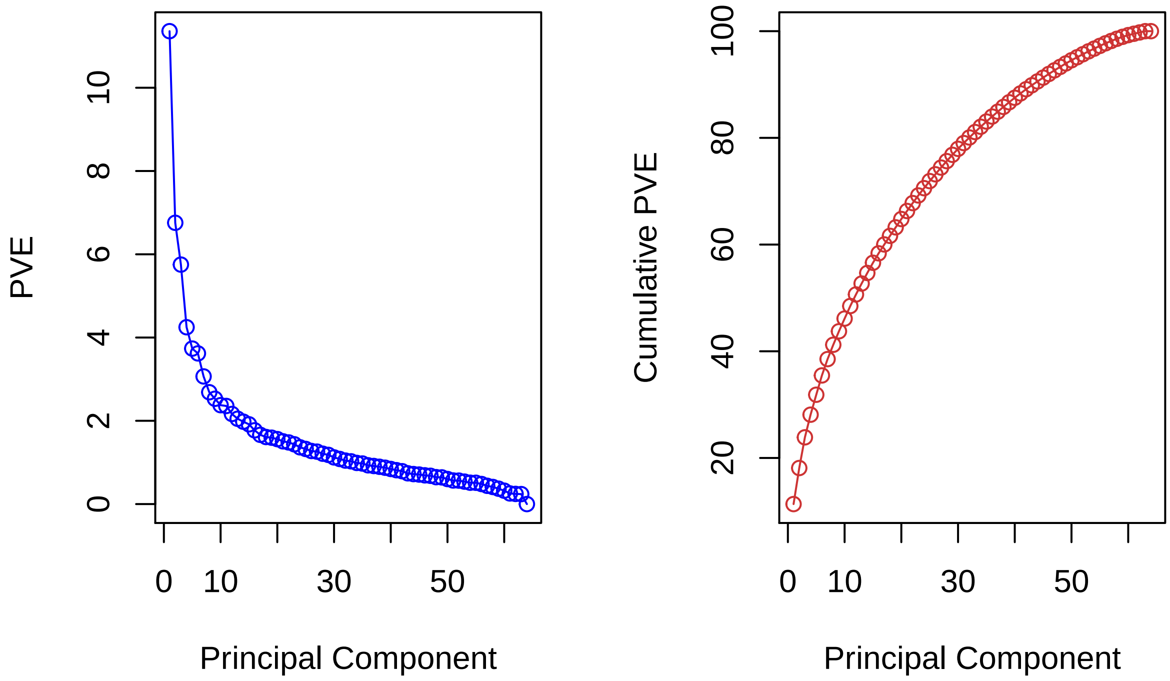
```
## Importance of components:
##                            PC1      PC2      PC3      PC4      PC5
## Standard deviation     27.8535 21.48136 19.82046 17.03256 15.97181
## Proportion of Variance  0.1136  0.06756  0.05752  0.04248  0.03735
## Cumulative Proportion   0.1136  0.18115  0.23867  0.28115  0.31850
##                             PC6      PC7      PC8      PC9     PC10
## Standard deviation     15.72108 14.47145 13.54427 13.14400 12.73860
## Proportion of Variance  0.03619  0.03066  0.02686  0.02529  0.02376
## Cumulative Proportion   0.35468  0.38534  0.41220  0.43750  0.46126
##                            PC11     PC12     PC13     PC14     PC15
## Standard deviation     12.68672 12.15769 11.83019 11.62554 11.43779
## Proportion of Variance  0.02357  0.02164  0.02049  0.01979  0.01915
## Cumulative Proportion   0.48482  0.50646  0.52695  0.54674  0.56590
##                            PC16     PC17     PC18     PC19    PC20
## Standard deviation     11.00051 10.65666 10.48880 10.43518 10.3219
## Proportion of Variance  0.01772  0.01663  0.01611  0.01594  0.0156
## Cumulative Proportion   0.58361  0.60024  0.61635  0.63229  0.6479
##                            PC21    PC22    PC23    PC24    PC25    PC26
## Standard deviation     10.14608 10.0544 9.90265 9.64766 9.50764 9.33253
## Proportion of Variance  0.01507  0.0148 0.01436 0.01363 0.01324 0.01275
## Cumulative Proportion   0.66296  0.6778 0.69212 0.70575 0.71899 0.73174
##                           PC27   PC28    PC29    PC30    PC31    PC32
## Standard deviation     9.27320 9.0900 8.98117 8.75003 8.59962 8.44738
## Proportion of Variance 0.01259 0.0121 0.01181 0.01121 0.01083 0.01045
## Cumulative Proportion  0.74433 0.7564 0.76824 0.77945 0.79027 0.80072
##                           PC33    PC34    PC35    PC36    PC37    PC38
## Standard deviation     8.37305 8.21579 8.15731 7.97465 7.90446 7.82127
## Proportion of Variance 0.01026 0.00988 0.00974 0.00931 0.00915 0.00896
## Cumulative Proportion  0.81099 0.82087 0.83061 0.83992 0.84907 0.85803
##                           PC39    PC40    PC41   PC42    PC43   PC44
## Standard deviation     7.72156 7.58603 7.45619 7.3444 7.10449 7.0131
## Proportion of Variance 0.00873 0.00843 0.00814 0.0079 0.00739 0.0072
## Cumulative Proportion  0.86676 0.87518 0.88332 0.8912 0.89861 0.9058
##                           PC45   PC46    PC47    PC48    PC49    PC50
## Standard deviation     6.95839 6.8663 6.80744 6.64763 6.61607 6.40793
## Proportion of Variance 0.00709 0.0069 0.00678 0.00647 0.00641 0.00601
## Cumulative Proportion  0.91290 0.9198 0.92659 0.93306 0.93947 0.94548
##                           PC51    PC52    PC53    PC54    PC55    PC56
## Standard deviation     6.21984 6.20326 6.06706 5.91805 5.91233 5.73539
## Proportion of Variance 0.00566 0.00563 0.00539 0.00513 0.00512 0.00482
## Cumulative Proportion  0.95114 0.95678 0.96216 0.96729 0.97241 0.97723
##                           PC57   PC58    PC59    PC60    PC61    PC62
## Standard deviation     5.47261 5.2921 5.02117 4.68398 4.17567 4.08212
## Proportion of Variance 0.00438 0.0041 0.00369 0.00321 0.00255 0.00244
## Cumulative Proportion  0.98161 0.9857 0.98940 0.99262 0.99517 0.99761
##                           PC63      PC64
## Standard deviation     4.04124 2.148e-14
## Proportion of Variance 0.00239 0.000e+00
## Cumulative Proportion  1.00000 1.000e+00
```

```
plot(pr.out)
```



Note that the height of each bar in the bar plot is given by squaring the corresponding element of `pr.out$sdev`. However, it is more informative to plot the PVE of each principal component (i.e. a scree plot) and the cumulative PVE of each principal component. This can be done with just a little work. (Note that the elements of pve can also be computed directly from the summary, `summary(pr.out)$importance[2,]`, and the elements of `cumsum(pve)` are given by `summary(pr.out)$importance[3,]`.)

```
pve=100*pr.out$sdev^2/sum(pr.out$sdev^2)
par(mfrow=c(1,2))
plot(pve,  type="o", ylab="PVE", xlab="Principal Component", col="blue")
plot(cumsum(pve), type="o", ylab="Cumulative PVE", xlab="Principal Component", col="brown3")
```



We see that together, the first seven principal components explain around 40% of the variance in the data. This is not a huge amount of the variance. However, looking at the scree plot, we see that while each of the first seven principal components explain a substantial amount of variance, there is a marked decrease in the variance explained by further principal components. That is, there is an elbow in the plot after approximately the seventh principal component. This suggests that there may be little benefit to examining more than seven or so principal components (though even examining seven principal components may be difficult).

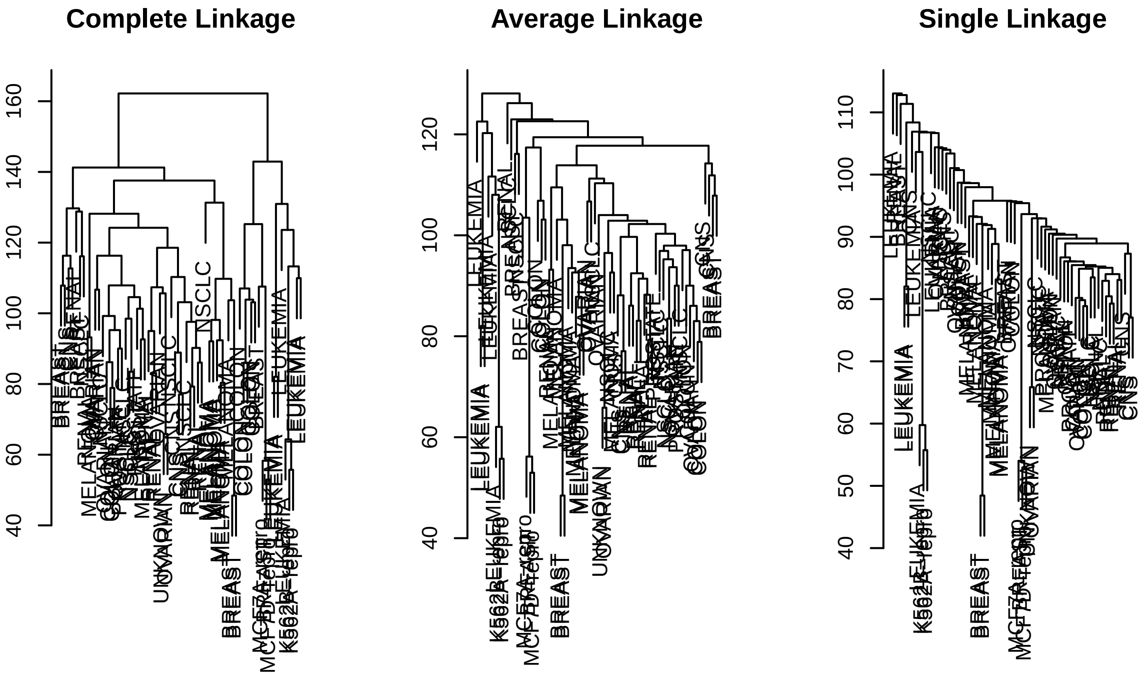
Clustering the Observations of the NCI60 Data

To begin, we standardize the variables to have mean zero and standard deviation one. As mentioned earlier, this step is optional and should be performed only if we want each gene to be on the same scale.

```
sd.data=scale(nci.data)
```

We now perform hierarchical clustering of the observations using complete, single, and average linkage. Euclidean distance is used as the dissimilarity measure.

```
par(mfrow=c(1,3))
data.dist=dist(sd.data)
plot(hclust(data.dist), labels=nci.labs, main="Complete Linkage", xlab="", sub="",ylab="")
plot(hclust(data.dist, method="average"), labels=nci.labs, main="Average Linkage", xlab="", sub="",ylab=
plot(hclust(data.dist, method="single"), labels=nci.labs,  main="Single Linkage", xlab="", sub="",ylab=
```



Typically, single linkage will tend to yield trailing clusters: very large clusters onto which individual observations attach one-by-one. On the other hand, complete and average linkage tend to yield more balanced, attractive clusters. We will use complete linkage hierarchical clustering for the analysis that follows.

We can cut the dendrogram at the height that will yield a particular number of clusters, say four:

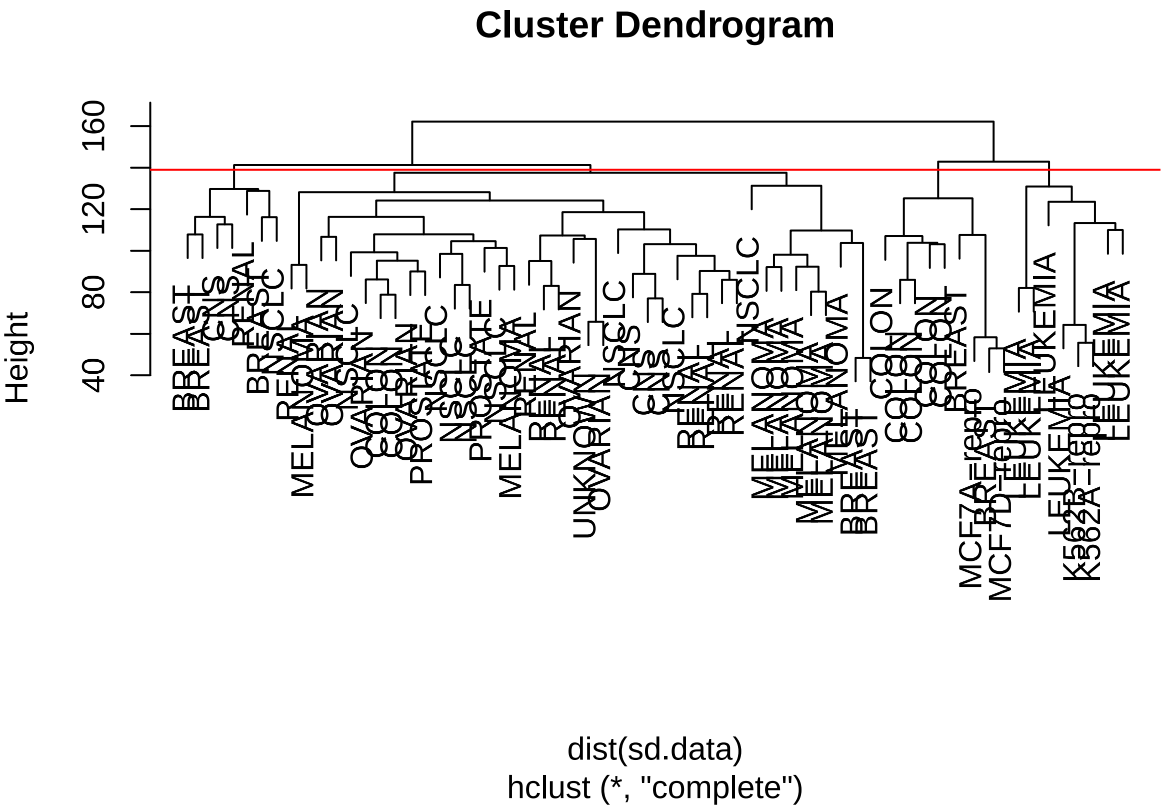
```
hc.out=hclust(dist(sd.data))
hc.clusters=cutree(hc.out,4)
table(hc.clusters,nci.labs)
```

```
##              nci.labs
## hc.clusters BREAST CNS COLON K562A-repro K562B-repro LEUKEMIA MCF7A-repro
##           1      2   3     2           0           0        0           0
##           2      3   2     0           0           0        0           0
##           3      0   0     0           1           1         6           0
##           4      2   0     5           0           0         0           1
##            nci.labs
## hc.clusters MCF7D-repro MELANOMA NSCLC OVARIAN PROSTATE RENAL UNKNOWN
##           1           0        8     8       6        2     8       1
##           2           0        0     1       0        0     1       0
##           3           0        0     0       0        0     0       0
##           4           1        0     0       0        0     0       0
```

There are some clear patterns. All the leukemia cell lines fall in cluster 3, while the breast cancer cell lines are spread out over three different clusters.

We can plot the cut on the dendrogram that produces these four clusters:

```
par(mfrow=c(1,1))
plot(hc.out, labels=nci.labs)
abline(h=139, col="red")
```



Printing the output of `hclust` gives a useful brief summary of the object:

```
hc.out
```

```
##
## Call:
## hclust(d = dist(sd.data))
##
## Cluster method   : complete
## Distance         : euclidean
## Number of objects: 64
```

We claimed earlier that K-means clustering and hierarchical clustering with the dendrogram cut to obtain the same number of clusters can yield very different results. How do these NCI60 hierarchical clustering results compare to what we get if we perform K-means clustering with K = 4?

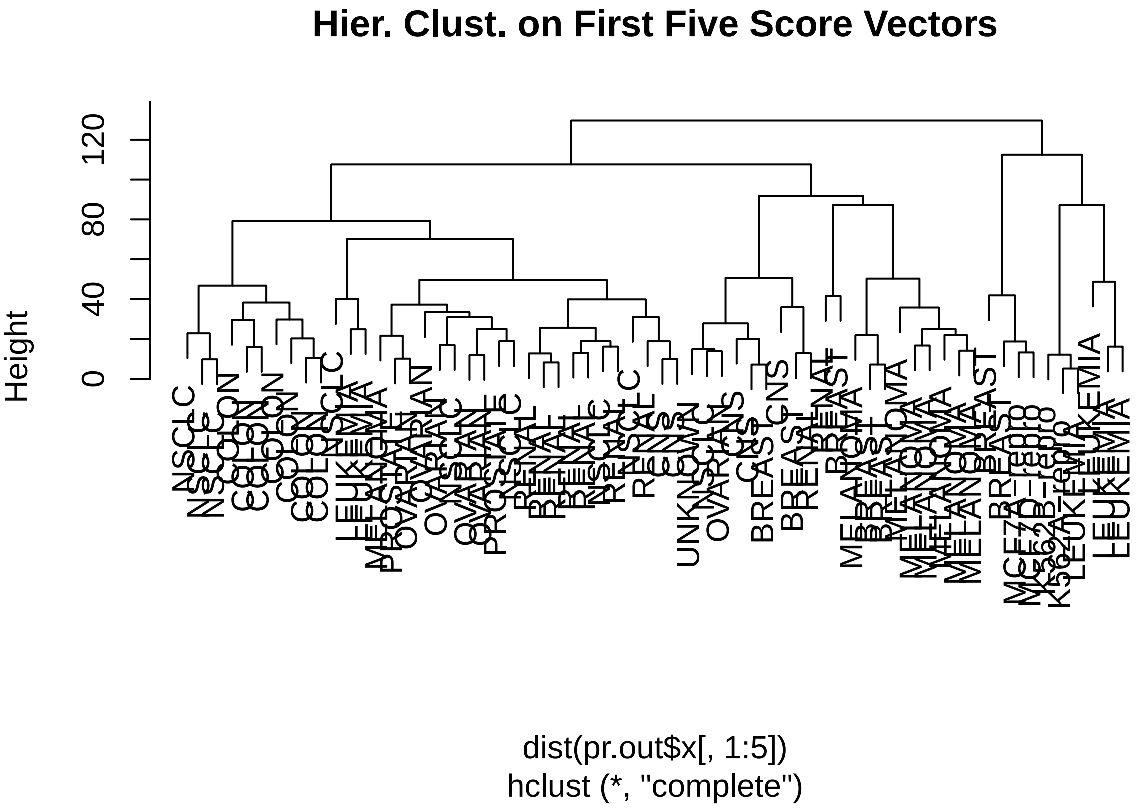
```
set.seed(2)
km.out=kmeans(sd.data, 4, nstart=20)
km.clusters=km.out$cluster
table(km.clusters,hc.clusters)
```

```
##             hc.clusters
## km.clusters  1  2  3  4
##           1 11  0  0  9
##           2 20  7  0  0
##           3  9  0  0  0
##           4  0  0  8  0
```

We see that the four clusters obtained using hierarchical clustering and Kmeans clustering are somewhat different.

Rather than performing hierarchical clustering on the entire data matrix, we can simply perform hierarchical clustering on the first few principal component score vectors, as follows:

```
hc.out=hclust(dist(pr.out$x[,1:5]))
plot(hc.out, labels=nci.labs, main="Hier. Clust. on First Five Score Vectors")
```



```
table(cutree(hc.out,4), nci.labs)
```

```
##    nci.labs
##     BREAST CNS COLON K562A-repro K562B-repro LEUKEMIA MCF7A-repro
##   1      0   2     7           0           0        2           0
##   2      5   3     0           0           0        0           0
##   3      0   0     0           1           1        4           0
##   4      2   0     0           0           0        0           1
##    nci.labs
##     MCF7D-repro MELANOMA NSCLC OVARIAN PROSTATE RENAL UNKNOWN
##   1           0        1     8       5        2     7       0
##   2           0        7     1       1        0     2       1
##   3           0        0     0       0        0     0       0
##   4           1        0     0       0        0     0       0
```

Not surprisingly, these results are different from the ones that we obtained when we performed hierarchical clustering on the full data set.

Sometimes performing clustering on the first few principal component score vectors can give better results than performing clustering on the full data. In this situation, we might view the principal component step as one of denoising the data.