Clustering

YOUR NAME

This was adapted from James, Witten, Hastie, and Ibshirani (2021) An Introduction to Statistical Learning.

K-Means Clustering

The function `kmeans()` performs K-means clustering in `R`. We begin with a simple simulated example in which there truly are two clusters in the data: the first 25 observations have a mean shift relative to the next 25 observations.

```r
set.seed(2)
x <- matrix(rnorm(50 * 2), ncol = 2)
x[1:25, 1] <- x[1:25, 1] + 3
x[1:25, 2] <- x[1:25, 2] - 4
```

We now perform K-means clustering with $K = 2$.

```r
km.out <- kmeans(x, 2, nstart = 20)
```

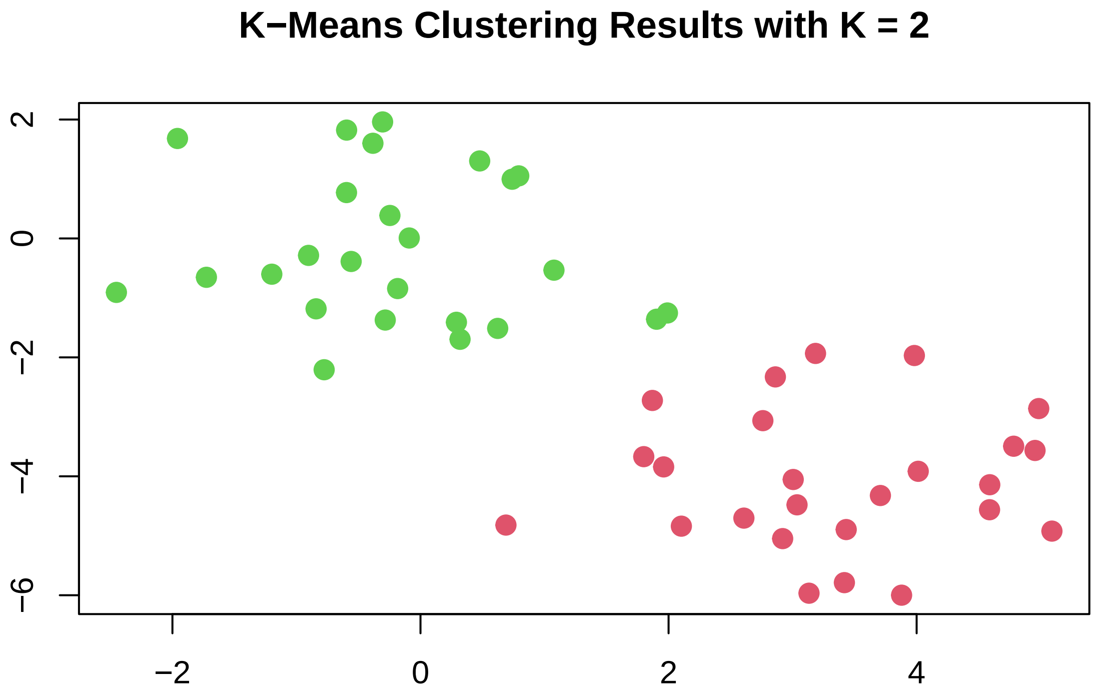
The cluster assignments of the 50 observations are contained in `km.out$cluster`.

```r
km.out$cluster
```

```
##  [1] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 2
## [39] 2 2 2 2 2 2 2 2 2 2 2 2
```

The K-means clustering perfectly separated the observations into two clusters even though we did not supply any group information to `kmeans()`. We can plot the data, with each observation colored according to its cluster assignment.

```r
#par(mfrow = c(1, 2))
plot(x, col = (km.out$cluster + 1),
    main = "K-Means Clustering Results with K = 2",
    xlab = "", ylab = "", pch = 20, cex = 2)
```



Here the observations can be easily plotted because they are two-dimensional. If there were more than two variables then we could instead perform PCA and plot the first two principal components score vectors.

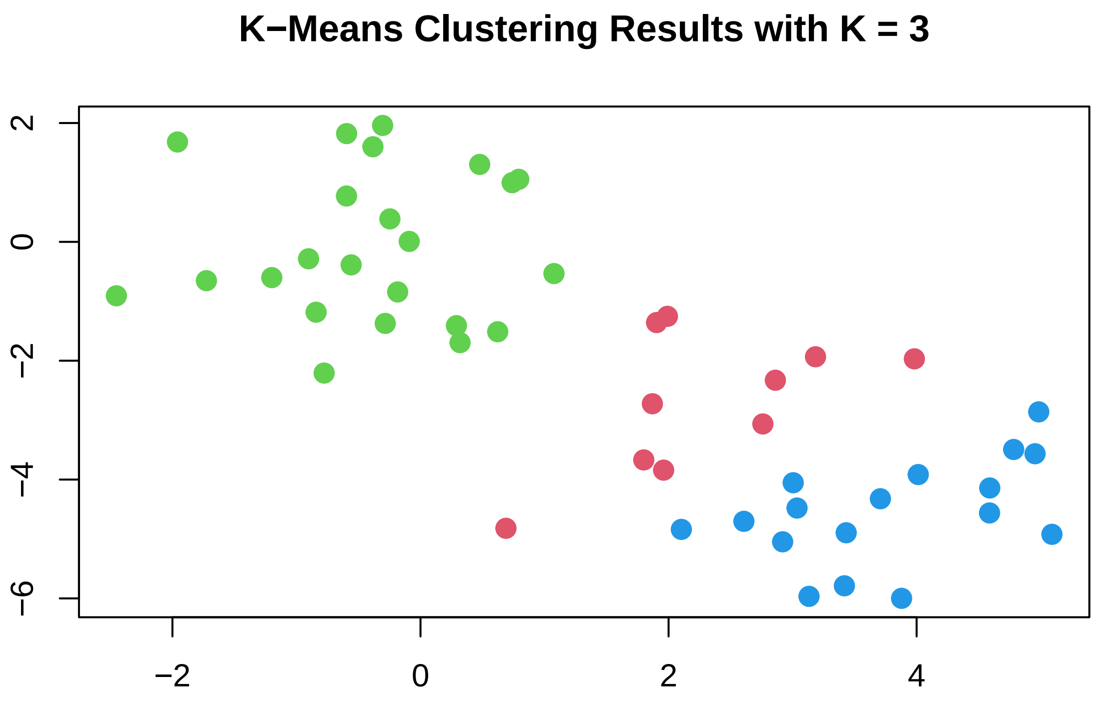
In this example, we knew that there really were two clusters because we generated the data. However, for real data, in general we do not know the true number of clusters. We could instead have performed K-means clustering on this example with $K = 3$.

```
set.seed(4)
km.out <- kmeans(x, 3, nstart = 20)
km.out
```

```
## K-means clustering with 3 clusters of sizes 10, 23, 17
##
## Cluster means:
##         [,1]        [,2]
## 1  2.3001545 -2.69622023
## 2 -0.3820397 -0.08740753
## 3  3.7789567 -4.56200798
##
## Clustering vector:
##  [1] 3 1 3 1 3 3 3 1 3 1 3 1 3 1 3 1 3 3 3 3 3 1 3 3 3 2 2 2 2 2 2 2 2 2 2 2 2
## [39] 2 2 2 2 2 1 2 1 2 2 2 2
##
## Within cluster sum of squares by cluster:
## [1] 19.56137 52.67700 25.74089
##  (between_SS / total_SS =  79.3 %)
##
```

```
## Available components:
##
## [1] "cluster"      "centers"      "totss"        "withinss"     "tot.withinss"
## [6] "betweenss"    "size"         "iter"         "ifault"
```

```
plot(x, col = (km.out$cluster + 1),
    main = "K-Means Clustering Results with K = 3",
    xlab = "", ylab = "", pch = 20, cex = 2)
```



When $K = 3$, K-means clustering splits up the two clusters.

To run the `kmeans()` function in `R` with multiple initial cluster assignments, we use the `nstart` argument. If a value of `nstart` greater than one is used, then K-means clustering will be performed using multiple random assignments in Step~1 of Algorithm 12.2, and the `kmeans()` function will report only the best results. Here we compare using `nstart = 1` to `nstart = 20`.

```
set.seed(4)
km.out <- kmeans(x, 3, nstart = 1)
km.out$tot.withinss
```

```
## [1] 104.3319
```

```
km.out <- kmeans(x, 3, nstart = 20)
km.out$tot.withinss
```

```
## [1] 97.97927
```

Note that `km.out$tot.withinss` is the total within-cluster sum of squares, which we seek to minimize by performing K-means clustering (Equation 12.17). The individual within-cluster sum-of-squares are contained in the vector `km.out$withinss`.

We *strongly* recommend always running K-means clustering with a large value of `nstart`, such as 20 or 50, since otherwise an undesirable local optimum may be obtained.

When performing K-means clustering, in addition to using multiple initial cluster assignments, it is also important to set a random seed using the `set.seed()` function. This way, the initial cluster assignments in Step~1 can be replicated, and the K-means output will be fully reproducible.

Hierarchical Clustering

The `hclust()` function implements hierarchical clustering in `R`. In the following example we use the data from the previous lab to plot the hierarchical clustering dendrogram using complete, single, and average linkage clustering, with Euclidean distance as the dissimilarity measure. We begin by clustering observations using complete linkage. The `dist()` function is used to compute the 50×50 inter-observation Euclidean distance matrix.

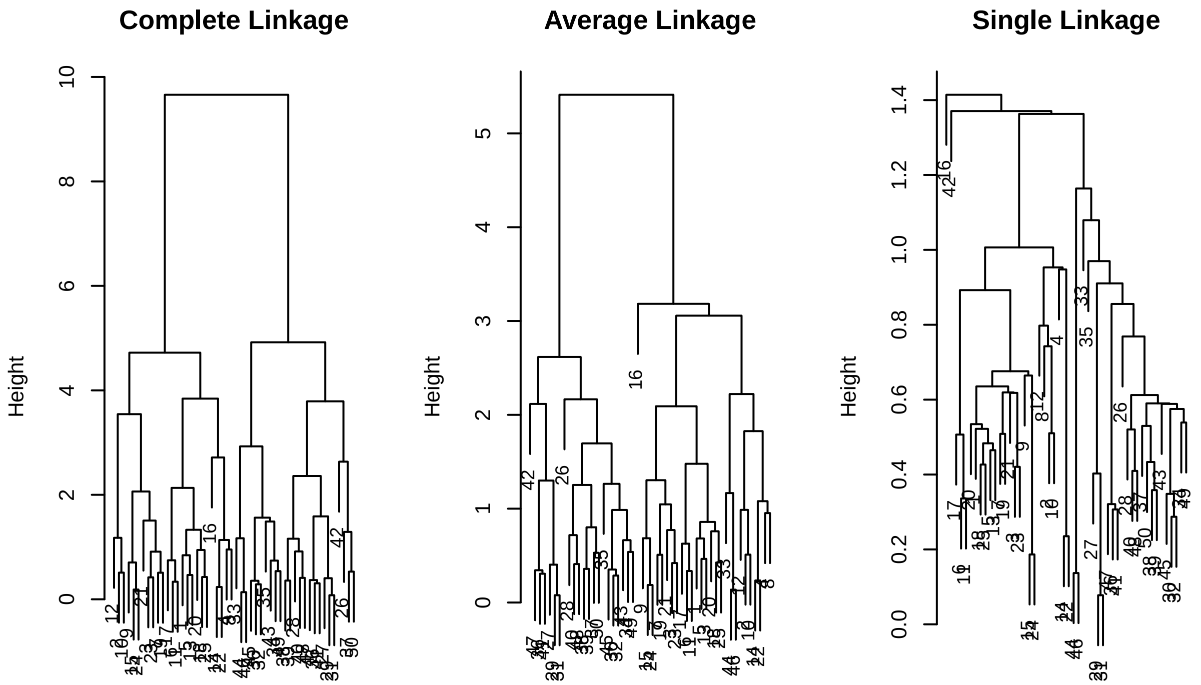
```r
hc.complete <- hclust(dist(x), method = "complete")
```

We could just as easily perform hierarchical clustering with average or single linkage instead:

```r
hc.average <- hclust(dist(x), method = "average")
hc.single <- hclust(dist(x), method = "single")
```

We can now plot the dendrograms obtained using the usual `plot()` function. The numbers at the bottom of the plot identify each observation.

```r
par(mfrow = c(1, 3))
plot(hc.complete, main = "Complete Linkage",
    xlab = "", sub = "", cex = .9)
plot(hc.average, main = "Average Linkage",
    xlab = "", sub = "", cex = .9)
plot(hc.single, main = "Single Linkage",
    xlab = "", sub = "", cex = .9)
```



To determine the cluster labels for each observation associated with a given cut of the dendrogram, we can use the `cutree()` function:

```
cutree(hc.complete, 2)
```

```
##  [1] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 2
## [39] 2 2 2 2 2 2 2 2 2 2 2 2
```

```
cutree(hc.average, 2)
```

```
##  [1] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 1 2 2 2 2 2
## [39] 2 2 2 2 2 1 2 1 2 2 2 2
```

```
cutree(hc.single, 2)
```

```
##  [1] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
## [39] 1 1 1 1 1 1 1 1 1 1 1 1
```

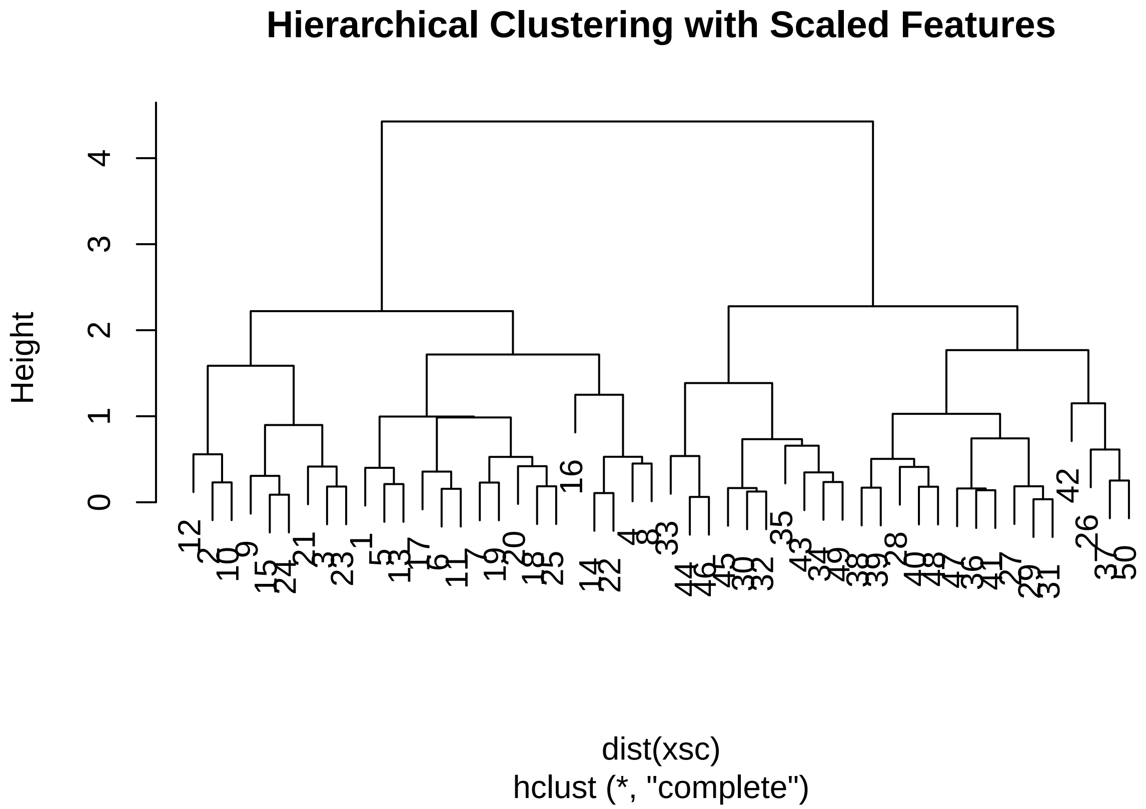
The second argument to `cutree()` is the number of clusters we wish to obtain. For this data, complete and average linkage generally separate the observations into their correct groups. However, single linkage identifies one point as belonging to its own cluster. A more sensible answer is obtained when four clusters are selected, although there are still two singletons.

```r
cutree(hc.single, 4)
```

```
##  [1] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 1 1 1 1 1 1 1 1 1 3 3 3 3 3 3 3 3 3 3 3 3 3
## [39] 3 3 3 4 3 3 3 3 3 3 3 3
```

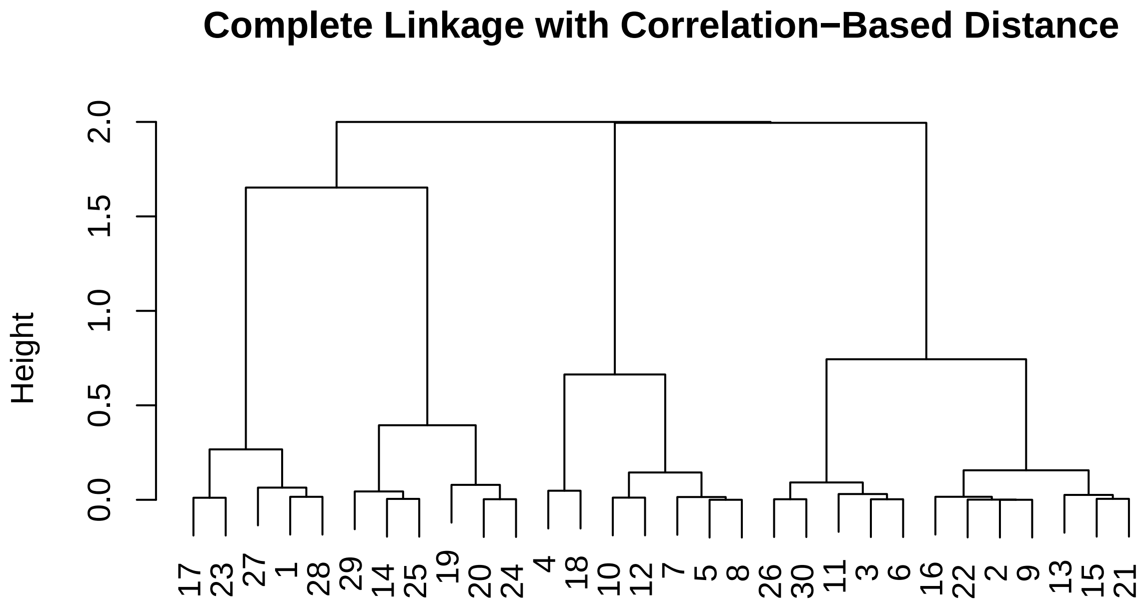
To scale the variables before performing hierarchical clustering of the observations, we use the `scale()` function:

```r
xsc <- scale(x)
plot(hclust(dist(xsc), method = "complete"),
    main = "Hierarchical Clustering with Scaled Features")
```



Correlation-based distance can be computed using the `as.dist()` function, which converts an arbitrary square symmetric matrix into a form that the `hclust()` function recognizes as a distance matrix. However, this only makes sense for data with at least three features since the absolute correlation between any two observations with measurements on two features is always 1. Hence, we will cluster a three-dimensional data set. This data set does not contain any true clusters.

```r
x <- matrix(rnorm(30 * 3), ncol = 3)
dd <- as.dist(1 - cor(t(x)))
plot(hclust(dd, method = "complete"),
    main = "Complete Linkage with Correlation-Based Distance",
    xlab = "", sub = "")
```



NCI60 Data Example

Unsupervised techniques are often used in the analysis of genomic data. In particular, PCA and hierarchical clustering are popular tools. We illustrate these techniques on the `NCI` cancer cell line microarray data, which consists of 6,830 gene expression measurements on 64 cancer cell lines.

```r
library(ISLR2)
nci.labs <- NCI60$labs
nci.data <- NCI60$data
```

Each cell line is labeled with a cancer type, given in `nci.labs`. We do not make use of the cancer types in performing PCA and clustering, as these are unsupervised techniques. But after performing PCA and clustering, we will check to see the extent to which these cancer types agree with the results of these unsupervised techniques.

The data has 64 rows and 6,830 columns.

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

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

We begin by examining the cancer types for the cell lines.

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

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

```r
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.

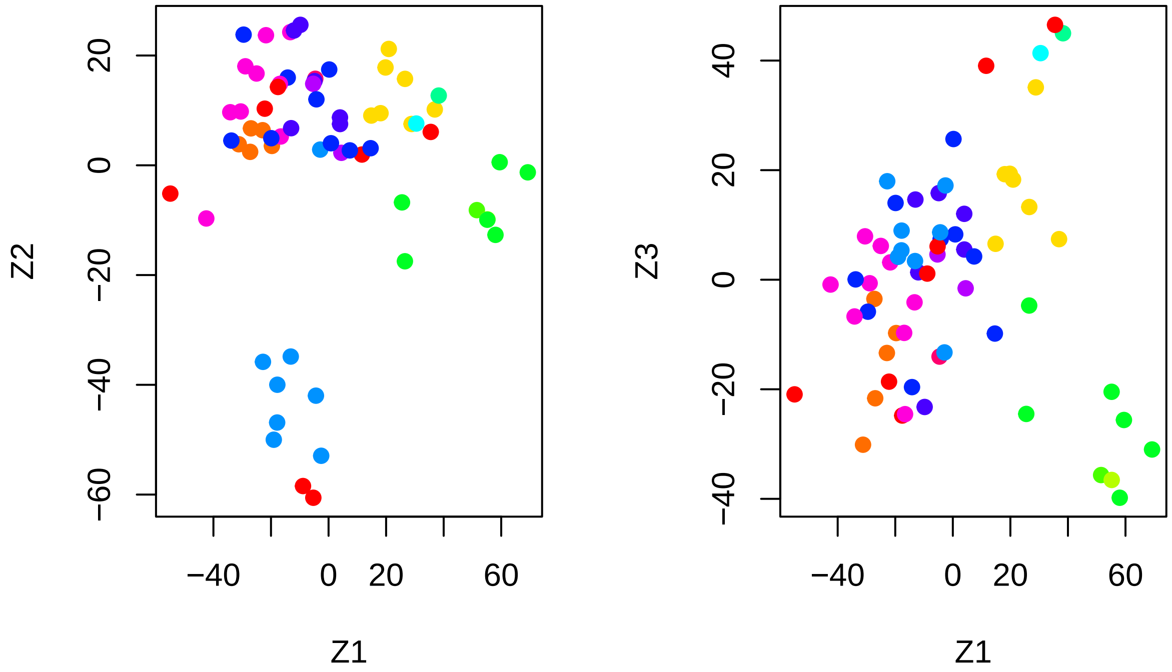
```r
pr.out <- prcomp(nci.data, scale = TRUE)
```

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. We first create a simple function that assigns a distinct color to each element of a numeric vector. The function will be used to assign a color to each of the 64 cell lines, based on the cancer type to which it corresponds.

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

Note that the `rainbow()` function takes as its argument a positive integer, and returns a vector containing that number of distinct colors. We now can plot the principal component score vectors.

```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.

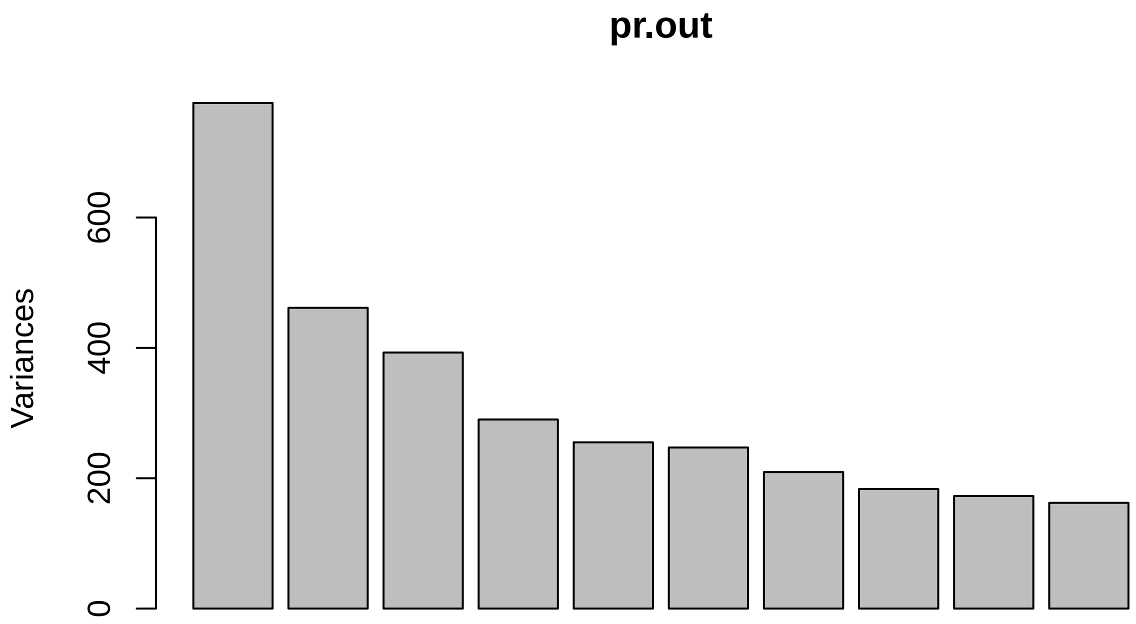
We can obtain a summary of the proportion of variance explained (PVE) of the first few principal components using the `summary()` method for a `prcomp` object (we have truncated the printout):

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

```
## Importance of components:
##                            PC1      PC2      PC3      PC4      PC5      PC6
## Standard deviation     27.8535 21.48136 19.82046 17.03256 15.97181 15.72108
## Proportion of Variance  0.1136  0.06756  0.05752  0.04248  0.03735  0.03619
## Cumulative Proportion   0.1136  0.18115  0.23867  0.28115  0.31850  0.35468
##                             PC7      PC8      PC9     PC10     PC11     PC12
## Standard deviation     14.47145 13.54427 13.14400 12.73860 12.68672 12.15769
## Proportion of Variance  0.03066  0.02686  0.02529  0.02376  0.02357  0.02164
## Cumulative Proportion   0.38534  0.41220  0.43750  0.46126  0.48482  0.50646
##                            PC13     PC14     PC15     PC16     PC17     PC18
## Standard deviation     11.83019 11.62554 11.43779 11.00051 10.65666 10.48880
## Proportion of Variance  0.02049  0.01979  0.01915  0.01772  0.01663  0.01611
## Cumulative Proportion   0.52695  0.54674  0.56590  0.58361  0.60024  0.61635
##                            PC19    PC20     PC21    PC22    PC23    PC24
## Standard deviation     10.43518 10.3219 10.14608 10.0544 9.90265 9.64766
## Proportion of Variance  0.01594  0.0156  0.01507  0.0148 0.01436 0.01363
## Cumulative Proportion   0.63229  0.6479  0.66296  0.6778 0.69212 0.70575
##                            PC25    PC26    PC27   PC28    PC29    PC30    PC31
## Standard deviation     9.50764 9.33253 9.27320 9.0900 8.98117 8.75003 8.59962
## Proportion of Variance 0.01324 0.01275 0.01259 0.0121 0.01181 0.01121 0.01083
## Cumulative Proportion  0.71899 0.73174 0.74433 0.7564 0.76824 0.77945 0.79027
##                            PC32    PC33    PC34    PC35    PC36    PC37    PC38
## Standard deviation     8.44738 8.37305 8.21579 8.15731 7.97465 7.90446 7.82127
## Proportion of Variance 0.01045 0.01026 0.00988 0.00974 0.00931 0.00915 0.00896
## Cumulative Proportion  0.80072 0.81099 0.82087 0.83061 0.83992 0.84907 0.85803
##                            PC39    PC40    PC41   PC42    PC43   PC44    PC45
## Standard deviation     7.72156 7.58603 7.45619 7.3444 7.10449 7.0131 6.95839
## Proportion of Variance 0.00873 0.00843 0.00814 0.0079 0.00739 0.0072 0.00709
## Cumulative Proportion  0.86676 0.87518 0.88332 0.8912 0.89861 0.9058 0.91290
##                           PC46    PC47    PC48    PC49    PC50    PC51    PC52
## Standard deviation     6.8663 6.80744 6.64763 6.61607 6.40793 6.21984 6.20326
## Proportion of Variance 0.0069 0.00678 0.00647 0.00641 0.00601 0.00566 0.00563
## Cumulative Proportion  0.9198 0.92659 0.93306 0.93947 0.94548 0.95114 0.95678
##                            PC53    PC54    PC55    PC56    PC57   PC58    PC59
## Standard deviation     6.06706 5.91805 5.91233 5.73539 5.47261 5.2921 5.02117
## Proportion of Variance 0.00539 0.00513 0.00512 0.00482 0.00438 0.0041 0.00369
## Cumulative Proportion  0.96216 0.96729 0.97241 0.97723 0.98161 0.9857 0.98940
##                            PC60    PC61    PC62    PC63      PC64
## Standard deviation     4.68398 4.17567 4.08212 4.04124 1.883e-14
## Proportion of Variance 0.00321 0.00255 0.00244 0.00239 0.000e+00
## Cumulative Proportion  0.99262 0.99517 0.99761 1.00000 1.000e+00
```

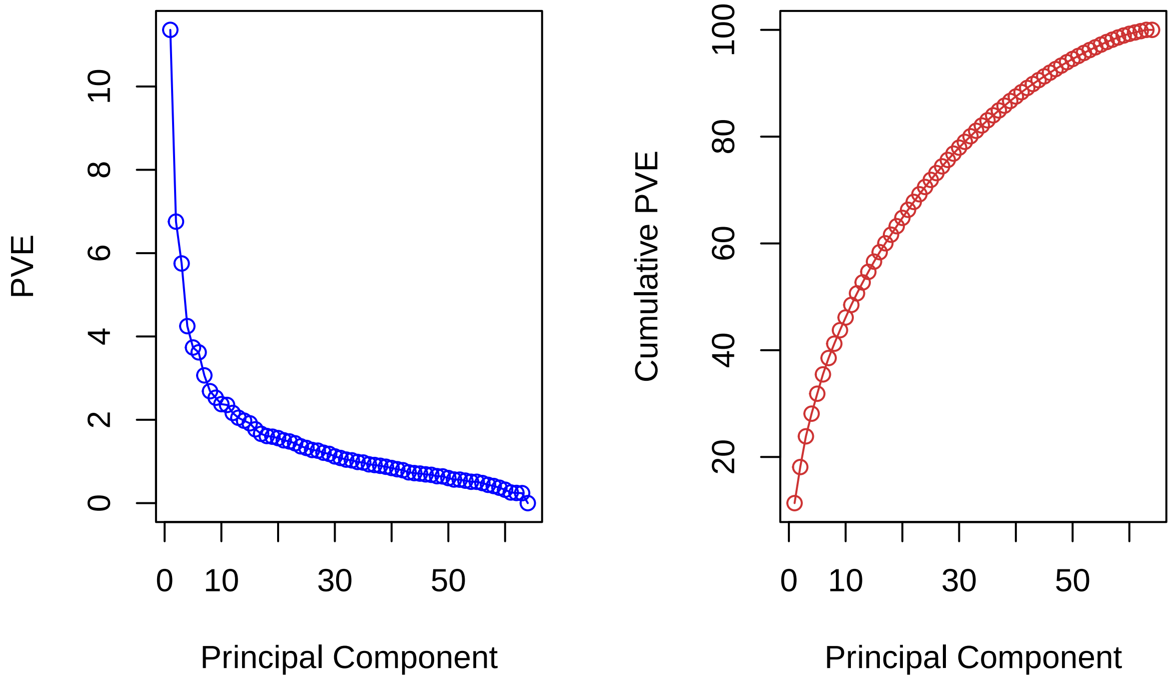
Using the `plot()` function, we can also plot the variance explained by the first few principal components.

```r
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.

```r
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")
```



(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, ]`.) 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

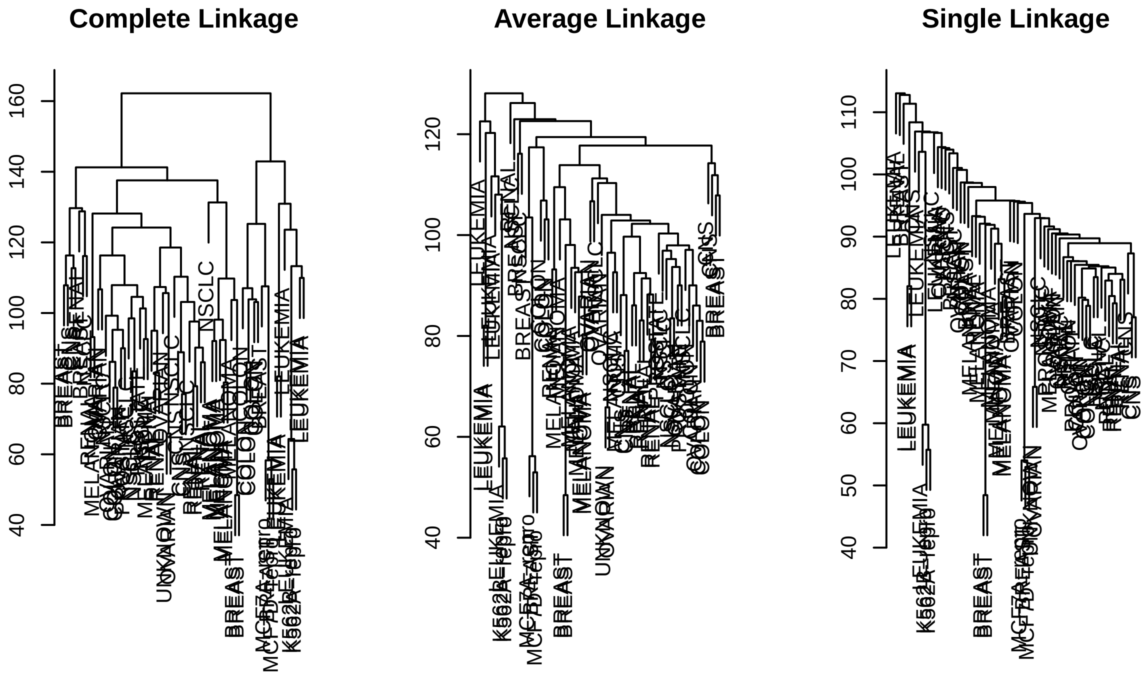
We now proceed to hierarchically cluster the cell lines in the `NCI` data, with the goal of finding out whether or not the observations cluster into distinct types of cancer. To begin, we standardize the variables to have mean zero and standard deviation one. As mentioned earlier, this step is optional 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), xlab = "", sub = "", ylab = "",
    labels = nci.labs, main = "Complete Linkage")
```

```
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 = "")
```


Complete Linkage

Average Linkage

Single Linkage

We see that the choice of linkage certainly does affect the results obtained. 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. For this reason, complete and average linkage are generally preferred to single linkage. Clearly cell lines within a single cancer type do tend to cluster together, although the clustering is not perfect. We will use complete linkage hierarchical clustering for the analysis that follows.

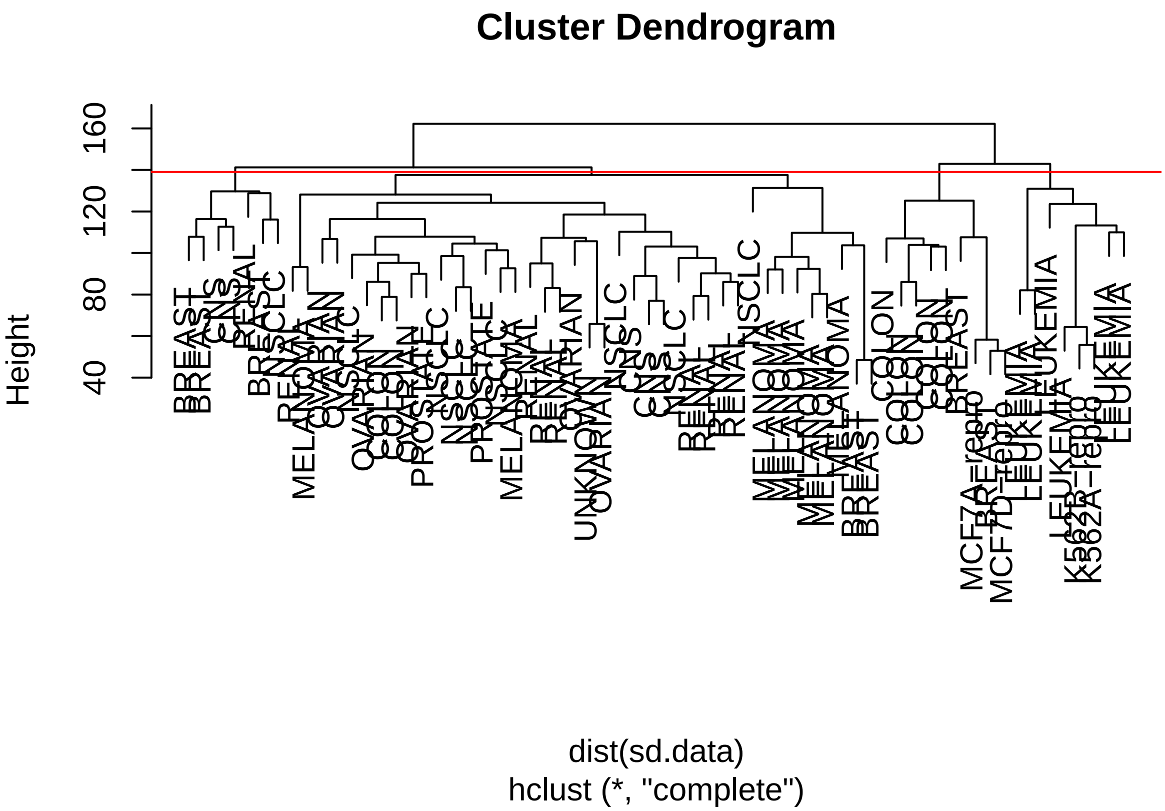
We can cut the dendrogram at the height that will yield a particular number of clusters, say four:

```
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.labels
## 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")
```



The `abline()` function draws a straight line on top of any existing plot in~R. The argument `h = 139` plots a horizontal line at height 139 on the dendrogram; this is the height that results in four distinct clusters. It is easy to verify that the resulting clusters are the same as the ones we obtained using `cutree(hc.out, 4)`.

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 in Section 12.4.2 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 NCI hierarchical clustering results compare to what we get if we perform K-means clustering with $K = 4$?

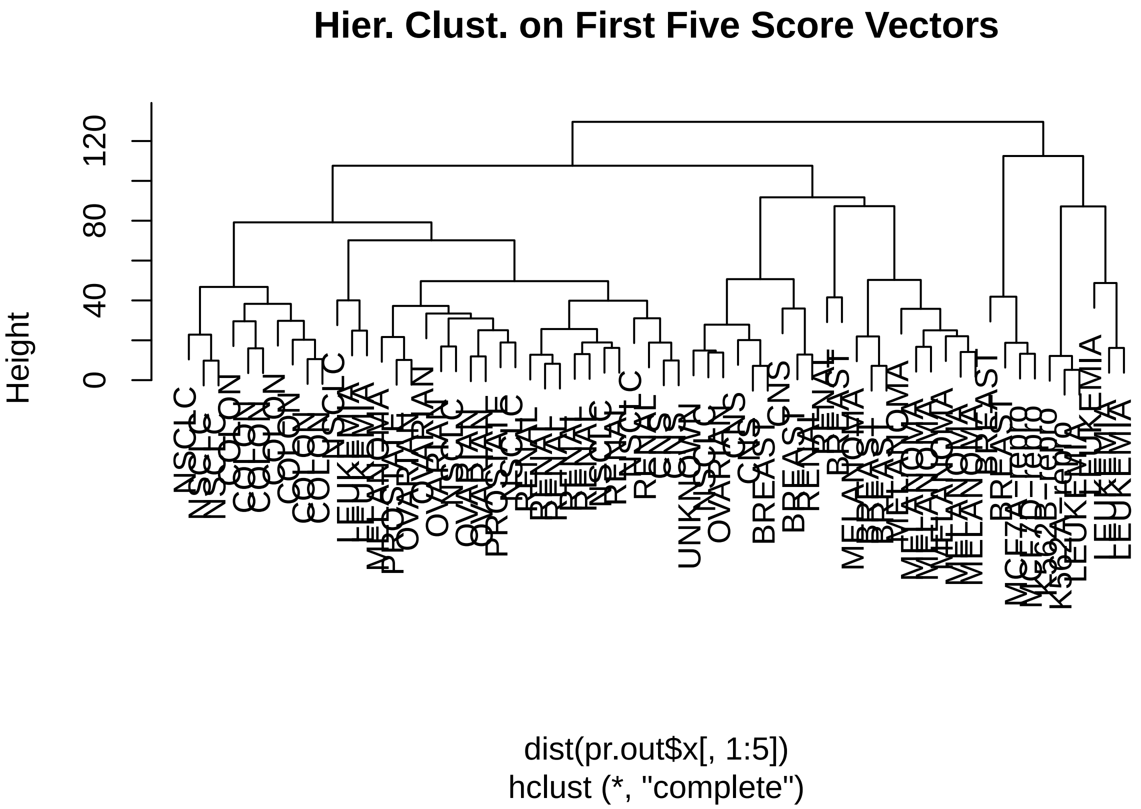
```
set.seed(2)
km.out <- kmeans(sd.data, 4, nstart = 20)
km.clusters <- km.out$cluster
table(km.clusters, hc.clusters)
```

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

We see that the four clusters obtained using hierarchical clustering and K-means clustering are somewhat different. Cluster 4 in K-means clustering is identical to cluster 3 in hierarchical clustering. However, the other clusters differ: for instance, cluster 2 in K-means clustering contains a portion of the observations assigned to cluster 1 by hierarchical clustering, as well as all of the observations assigned to cluster 2 by hierarchical clustering.

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")
```



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

```
##    nci.labs
##     BREAST CNS COLON K562A-repro K562B-repro LEUKEMIA MCF7A-repro MCF7D-repro
##   1      0   2     7           0           0        2           0           0
##   2      5   3     0           0           0        0           0           0
##   3      0   0     0           1           1        4           0           0
##   4      2   0     0           0           0        0           1           1
##    nci.labs
##     MELANOMA NSCLC OVARIAN PROSTATE RENAL UNKNOWN
##   1        1     8       5        2     7       0
##   2        7     1       1        0     2       1
##   3        0     0       0        0     0       0
##   4        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. We could also perform K-means clustering on the first few principal component score vectors rather than the full data set.

On Your Own

1. Consider the USArrests data. We will now perform hierarchical clustering on the states.

```
data("USArrests")
```

(a) Using hierarchical clustering with complete linkage and Euclidean distance, cluster the states.

(b) Cut the dendrogram at a height that results in three distinct clusters. Which states belong to which clusters?

(c) Hierarchically cluster the states using complete linkage and Euclidean distance, after scaling the variables to have standard deviation one.

(d) What effect does scaling the variables have on the hierarchical clustering obtained? In your opinion, should the variables be scaled before the inter-observation dissimilarities are computed? Provide a justification for your answer.