

Statistics 452: Statistical Learning and Prediction

Chapter 10, part 3: Hierarchical Clustering

Brad McNeney

Hierarchical Clustering

- ▶ Instead of setting the number of clusters in advance, as in *K*-means/medoids, we create a tree drawing (dendrogram) that represents a hierarchy of nested partitions of the objects into clusters.
 - ▶ See the example on the next slide.
- ▶ We can create the hierarchy in a top-down or bottom-up fashion.
- ▶ Bottom-up, or agglomerative clustering is the most common and will be described.
 - ▶ Given a measure of dissimilarity between clusters, we successively fuse, or merge clusters, starting with n clusters of size one and ending with a single cluster of size n .

Example: Hierarchical Clustering of Irises

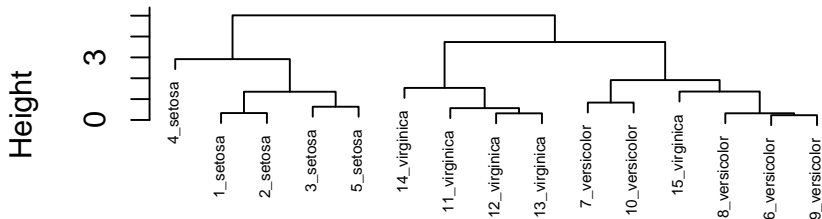
- ▶ First select a subsample of 5 irises from each species, then remove the species information.
- ▶ We use the function `hclust()` to generate the hierarchical clustering.

```
data(iris)
set.seed(1)
iris <- iris %>%
  group_by(Species) %>%
  sample_n(size=5) %>%
  ungroup()
irisX <- iris %>%
  select(-Species) %>%
  scale()
rownames(irisX) <- paste(rownames(iris),iris$Species,sep="_")
ic <- hclust(dist(irisX))
```

Plotting the Dendrogram

```
plot(ic,cex=.5)
```

Cluster Dendrogram



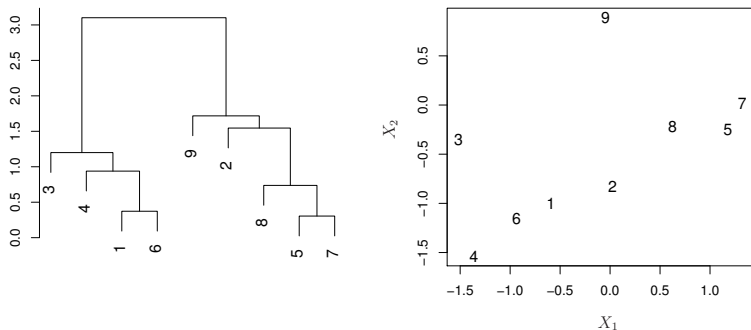
dist(irisX)
hclust (*, "complete")

Interpretation of the Dendrogram

- ▶ The height of a node reflects the dissimilarity of its two descendant clusters.
 - ▶ Branch lengths are not generally informative.
- ▶ The first node on the dendrogram partitions the data in to two clear clusters.
 - ▶ Knowing the species we can see this reflects the separation between the *setosa* and other species.
- ▶ The second node roughly separates the *versicolor* and *virginica* species, though there is one *virginica* in the *versicolor* cluster.
 - ▶ Note: The subtrees can be rotated without changing the structure of the dendrogram, so we should not interpret the horizontal placement of the leaves and/or branches.
 - ▶ Note: This clustering is for a *subset* of the iris data. Different subsets yield slightly different clusters.

Simulated Data Example

- Figure 10.10 from the text:



- The height of the node that merges $\{9\}$ with $\{2, 8, 5, 7\}$ reflects the dissimilarity. Branch lengths separating, say, 9 and 2 are not meaningful.

Cutting Dendrograms to Obtain Clusters

- ▶ Cutting the dendrogram at a given dissimilarity value leads to clusters.
 - ▶ For example, on the iris dendrogram, cutting at about 4 gives two clusters (*setosa* vs others) and cutting at about 3 gives three clusters (*setosa* and roughly *versicolor* and *virginica*.)
- ▶ The `cutree()` function allows us to cut at either a height `h` or where there are `k` clusters.

```
cutree(ic,k=3)
```

```
##      1_setosa      2_setosa      3_setosa      4_setosa      5_setosa
##           1           1           1           1           1
## 6_versicolor 7_versicolor 8_versicolor 9_versicolor 10_versicolor
##           2           2           2           2           2
## 11_virginica 12_virginica 13_virginica 14_virginica 15_virginica
##           3           3           3           3           2
```

```
table(cutree(ic,k=3))
```

```
##
## 1 2 3
## 5 6 4
```

Hierarchical Clustering Algorithm

1. Begin with n observations and a measure of the $n(n - 1)/2$ pairwise dissimilarities. Treat each observation as its own cluster.
 2. For $i = n, n - 1, \dots, 2$:
 - (a) Identify the pair of clusters that are least dissimilar and merge them. The dissimilarity between merged clusters is the height of the new node on the dendrogram.
 - (b) Compute the pairwise inter-cluster dissimilarities among the $i - 1$ remaining clusters.
- To be determined: How do we measure dissimilarity between objects and between **clusters**?

Dissimilarity Between Objects

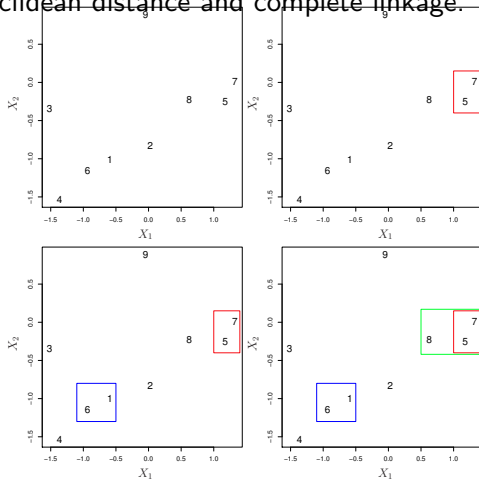
- ▶ Several possibilities:
 - ▶ Euclidean (ℓ_2) distance, $d(a, b) = \sqrt{\sum_{i=1}^p (a_i - b_i)^2}$.
 - ▶ Squared Euclidean (ℓ_2^2) distance, $d(a, b) = \sum_{i=1}^p (a_i - b_i)^2$.
 - ▶ Manhattan (ℓ_1) distance, $d(a, b) = \sum_{i=1}^p |a_i - b_i|$
 - ▶ Maximum (ℓ_∞) distance, $d(a, b) = \max_i |a_i - b_i|$.
- ▶ Euclidean, Manhattan and maximum distances are implemented in the `dist()` function in R, and squared Euclidean can be computed with `dist(x, method="euclidean")^2`.

Linkage: Dissimilarity Between Clusters

- ▶ The four most common linkages are:
 - ▶ Complete: $\max \{ d(a, b) : a \in A, b \in B \}$.
 - ▶ Average: $\frac{1}{|A||B|} \sum_{a \in A} \sum_{b \in B} d(a, b)$.
 - ▶ Centroid: $\|c_s - c_t\|$ where c_s and c_t are the centroids of clusters s and t , respectively.
 - ▶ Single: $\min \{ d(a, b) : a \in A, b \in B \}$.
- ▶ According to the text, average, complete and single linkage are the most popular among statisticians, and average and complete are preferred because they produce more balanced dendrograms than single.
- ▶ In `hclust()`, complete is the default, and the three others are options.

Example: Clustering of the Simulated Data Example

- Figure 10.11 from the text: The first three steps of clustering using Euclidean distance and complete linkage.



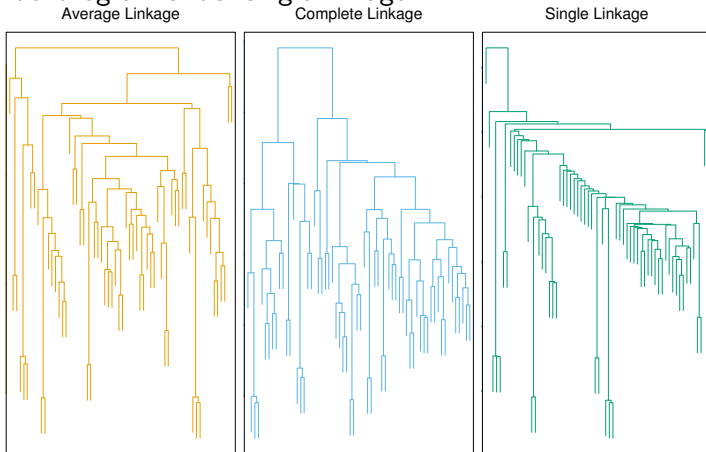
- Read top-left, top-right, bottom-left, bottom-right.

The Choice of Dissimilarity, Linkage and Scaling Affect the Dendrogram

- ▶ Each choice will influence the dendrogram.
- ▶ Illustrate sensitivity to linkage and scaling.

Sensitivity to Linkage

- Figure 10.12 from the text. Note the imbalance in the dendrogram under single linkage:



Sensitivity to Scaling

- ▶ Whether to scale or not is problem dependent.
- ▶ The amount of variation in a variable will determine how much it influences the dissimilarities, and therefore the linkages between clusters.
- ▶ Example: Decathlon data from the FactoMineR package.

```
library(FactoMineR) #install.packages("FactoMineR")
data(decathlon)
# Data processing strips off row names. Save for later.
rnames <- rownames(decathlon)
# Extract Olympics competition
rnames <- rnames[decathlon$Competition=="OlympicG"]
decathlon <- filter(decathlon,Competition=="OlympicG")
# Extract data on the 10 events.
decathlon <- decathlon[,1:10] # Extract data on the 10 events.
# In most events, a high score is good, but the opposite is true for running.
# Change the running to scores where high is good by subtracting the times from
# the maximum time
diffmax <- function(x) { max(x)-x }
decathlon <- mutate(decathlon,
  `100m` = diffmax(`100m`),
  `400m` = diffmax(`400m`),
  `110m.hurdle` = diffmax(`110m.hurdle`),
  `1500m` = diffmax(`1500m`))
rownames(decathlon) <- rnames
```

```
head(decathlon)
```

```
##      100m Long.jump Shot.put High.jump 400m 110m.hurdle Discus
## Sebrle 0.51      7.84    16.36      2.12 4.84      1.34 48.72
## Clay  0.92      7.96    15.23      2.06 4.01      1.26 50.11
## Karpov 0.86      7.81    15.93      2.09 6.39      1.42 51.65
## Macey  0.47      7.47    15.73      2.15 4.23      0.83 48.34
## Warners 0.74      7.74    14.48      1.97 5.23      1.38 43.73
## Zsivoczky 0.45      7.14    15.31      2.12 3.80      0.44 45.62
##      Pole.vault Javeline 1500m
## Sebrle      5.0     70.52 36.99
## Clay       4.9     69.71 35.00
## Karpov      4.6     55.54 38.89
## Macey       4.4     58.46 51.58
## Warners     4.9     55.39 38.95
## Zsivoczky   4.7     63.45 47.46
```

```
round(diag(var(decathlon)),3)
```

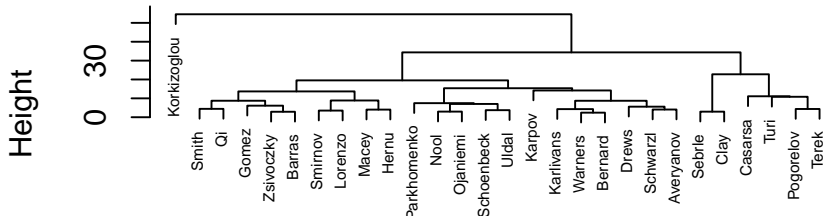
```
##      100m Long.jump Shot.put High.jump      400m 110m.hurdle
##      0.053      0.116      0.733      0.008      1.609      0.196
##      Discus Pole.vault Javeline      1500m
##      10.887      0.084      24.759      128.184
```

Clustering of the Decathlon Data Without Scaling

- Korkizoglou stands apart, because he beat the rest of the field by more than 20 seconds in the 1500m.

```
plot(hclust(dist(decathlon)),cex=.5)
```

Cluster Dendrogram



```
dist(decathlon)  
hclust (*, "complete")
```


Clustering of the Decathlon Data With Scaling

```
plot(hclust(dist(scale(decathlon))),cex=.5)
```

Cluster Dendrogram



```
dist(scale(decathlon))  
hclust (*, "complete")
```

NCI60 data

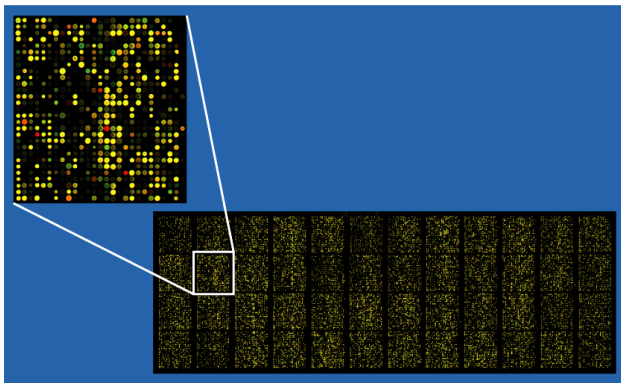
- ▶ We follow the lab on clustering of the NCI60 data set, which contains the results of a DNA microarray study of 64 cancer cells.
- ▶ Cancer cells are labelled by location of the cancer.
 - ▶ However, recent research suggests that classification based on location of the cancer may not be as useful as classification based on the cancer-causing mutation (e.g., a mutation in a gene responsible for DNA repair).

DNA Microarray Experiments

- ▶ See the Wikipedia page on microarrays (https://en.wikipedia.org/wiki/DNA_microarray) for a description.
- ▶ Briefly:
 - ▶ Genes in a cell are transcribed to produce messenger RNA, which is extracted and copied into DNA.
 - ▶ The DNA is fragmented, fluorescently labelled, and then exposed to an ordered array of complementary DNA molecules called probes that identify specific genes.
 - ▶ The array “lights up” where the labelled DNA has bound to the probes. The fluorescence intensity at each probe is a measure of how much of the corresponding gene was being expressed in the cell.

Microarray Picture

- ▶ Example micorarray with about 40,000 probes



Source: Wikimedia Commons

The NCI Data

- ▶ Rows are cancer cells, labelled by the type of cancer, and columns are the probes (genes).
- ▶ Entries of the data matrix are the fluorescence intensities after quality control has been applied.

```
library(ISLR)
data(NCI60)
nciX <- NCI60$data
dim(nciX)
```

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

```
cancer_types <- NCI60$labs
unique(cancer_types) # MCF7's are Breast and K562's are Leukemia
```

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

Collapse cancer types

```
ll <- (cancer_types=="MCF7A-repro") | (cancer_types=="MCF7D-repro")
cancer_types[ll] <- "LEUKEMIA"
bb <- (cancer_types=="K562A-repro") | (cancer_types=="K562B-repro")
cancer_types[bb] <- "BREAST"
rownames(nciX) <- cancer_types
nciX[1:5,1:5]
```

##		1	2	3	4	5
##	CNS	0.300000	1.180000	0.550000	1.140000	-0.265000
##	CNS	0.679961	1.289961	0.169961	0.379961	0.464961
##	CNS	0.940000	-0.040000	-0.170000	-0.040000	-0.605000
##	RENAL	0.280000	-0.310000	0.680000	-0.810000	0.625000
##	BREAST	0.485000	-0.465000	0.395000	0.905000	0.200000

PCA on the NCI60 Data

- ▶ One could argue that highly expressed genes **should** drive the PCs, but we scale.

```
nciX <- scale(nciX)
pcout <- prcomp(nciX)
summary(pcout)
```

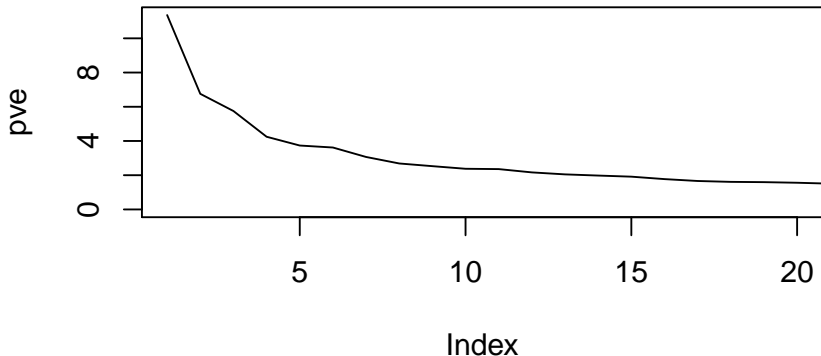
```
## Importance of components:
```

##	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

Scree Plot

- Express variances as percent total

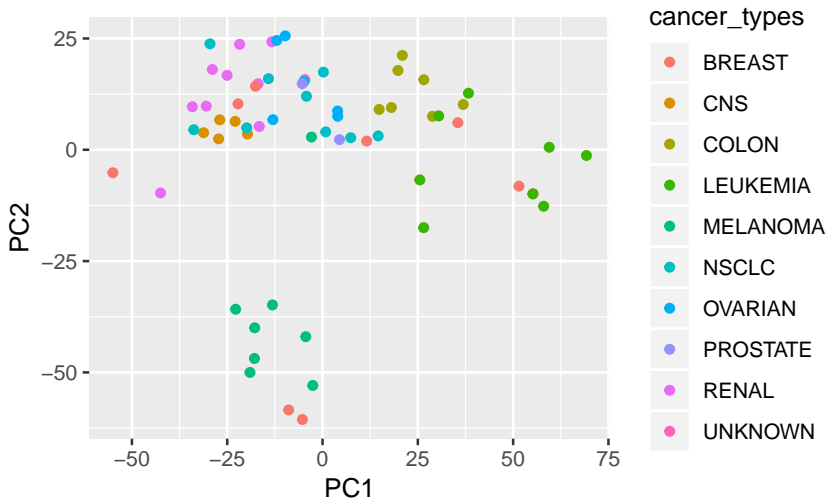
```
pve <- 100*pcout$sdev^2/sum(pcout$sdev^2)
plot(pve,xlim=c(1,20),type="l")
```



- Possible “elbow” at about 5 PCs

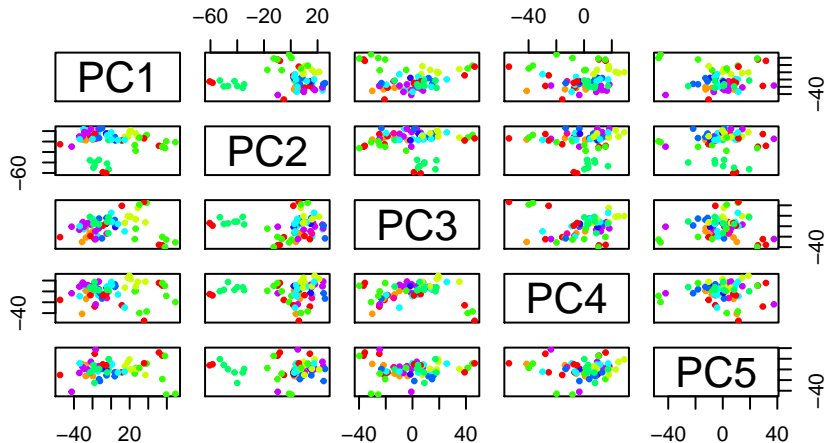
PC Plots

```
pcs <- as_tibble(pcout$x) %>% mutate(cancer_types = factor(cancer_types))  
ggplot(pcs, aes(x=PC1, y=PC2, color=cancer_types)) + geom_point()
```



Pairwise PC plots

```
rcols <- rainbow(length(unique(cancer_types)))  
ccols <- rcols[as.numeric(factor(cancer_types))]  
pairs(pcout$x[,1:5],col=ccols,pch=19,cex=.5)
```



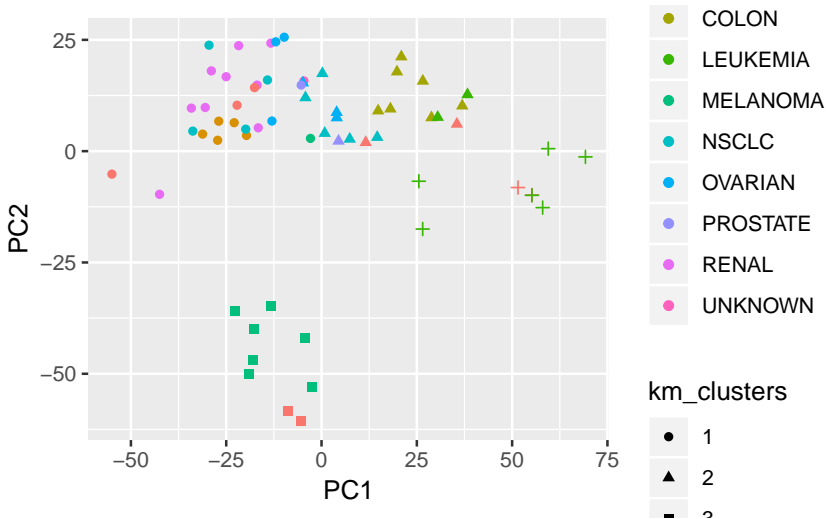
K-Means Clustering of NCI60 Data

- ▶ Remember that `nciX` has already been scaled.
- ▶ We know there are 16 different cancer types, but would not specify this many clusters in practice.
 - ▶ Try $K = 4$.

```
kout <- kmeans(nciX,centers=4)
table(kout$cluster,cancer_types)
```

```
##      cancer_types
##      BREAST  CNS  COLON  LEUKEMIA  MELANOMA  NSCLC  OVARIAN  PROSTATE  RENAL
##  1         3   5     0         0         1     4         3         1     9
##  2         2   0     7         2         0     5         3         1     0
##  3         2   0     0         0         7     0         0         0     0
##  4         2   0     0         6         0     0         0         0     0
##      cancer_types
##      UNKNOWN
##  1         1
##  2         0
##  3         0
##  4         0
```

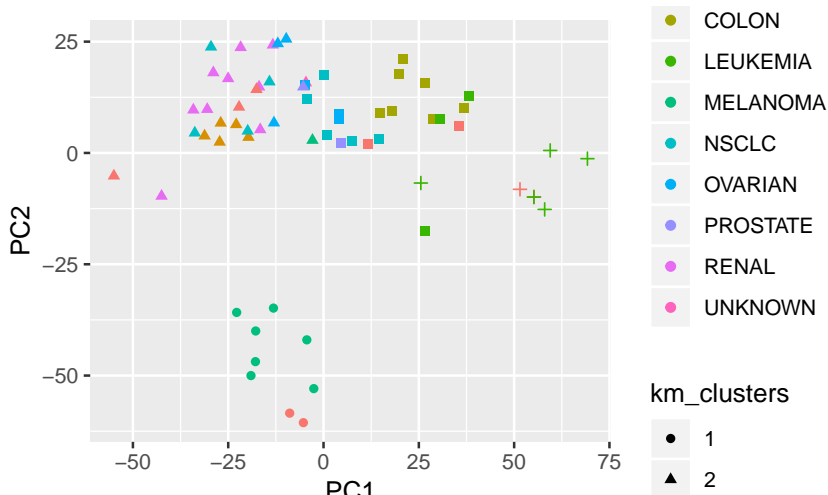
```
pcs <- mutate(pcs, km_clusters = factor(kout$cluster))
ggplot(pcs, aes(x=PC1, y=PC2, color=cancer_types, shape=km_clusters)) +
  geom_point()
```



Clustering on PCs

- Can also use the PCs as the data.

```
kout2 <- kmeans(pcout$x[,1:5],centers=4)
pcs <- mutate(pcs,km_clusters = factor(kout2$cluster))
ggplot(pcs,aes(x=PC1,y=PC2,color=cancer_types,shape=km_clusters)) +
  geom_point()
```

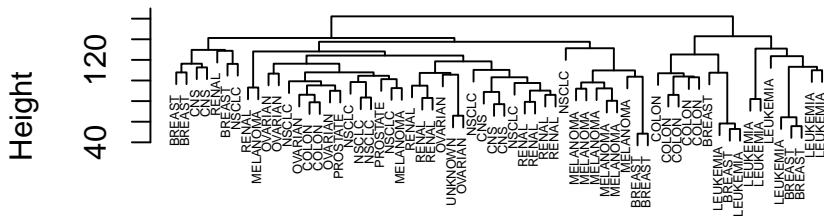


Hierarchical Clustering of NCI60 Data

- ▶ Use Euclidean distance and complete linkage
 - ▶ See the text for a comparison of complete, average and single linkage

```
hcout <- hclust(dist(nciX))  
plot(hcout,cex=.4)
```

Cluster Dendrogram



dist(nciX)

hclust (* "complete")

```
pcs <- mutate(pcs, h_clusters = factor(cutree(hcout, k=4)))
ggplot(pcs, aes(x=PC1, y=PC2, color=cancer_types, shape=h_clusters)) +
  geom_point()
```

