BIOST 546: Machine Learning for Biomedical Big Data

Ali Shojaie

Lecture 11: Clustering - Part I
Spring 2017

Recap

- Dimension reduction methods
  - PCA
  - MDS

Today's Class

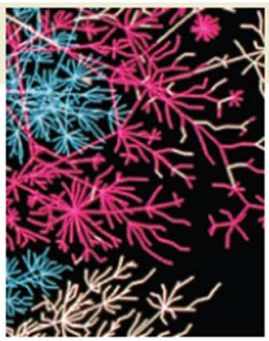
- Basics of clustering
- Hierarchical clustering

Dimension Reduction vs Cluster Analysis

- Dimension reduction methods find a low-dimensional representation of the observations that contain the good fraction of information in the original data
  - PCA tries to maximize the variance
  - MDS tries to preserve the distances among observations
- Clustering looks to find homogeneous subgroups among the observations

Cluster Analysis

Cluster analysis is one of the most-widely used techniques in analysis of omics data.



_computational BIOLOGY

PRIMER

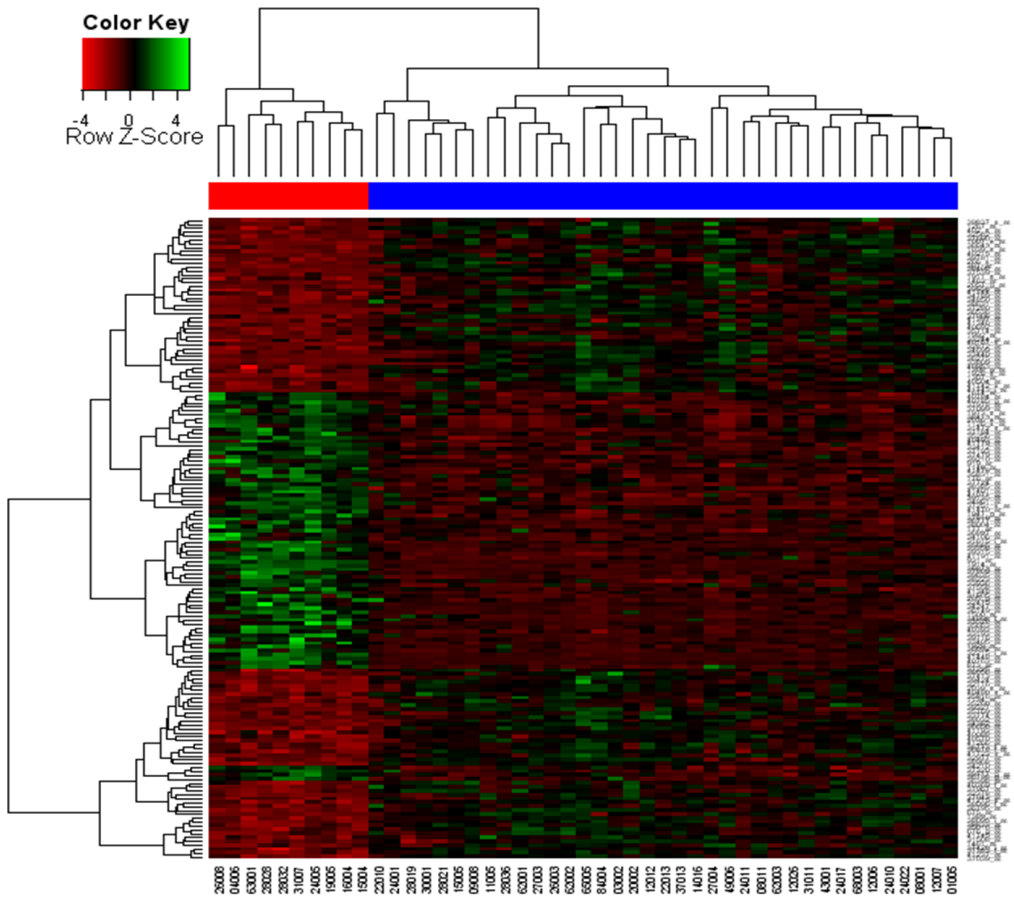
How does gene expression clustering work?

Patrik D'haeseleer

Clustering is often one of the first steps in gene expression analysis. How do clustering algorithms work, which ones should we use and what can we expect from them?

Cluster Analysis

Almost all papers on omics research, have a *heatmap*, which often includes a clustering of genes/samples.



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- Need to define what a “meaningful” cluster is
- Need to define what we mean by “similarity”
- Can cluster **observations** or **features**:
  - **observations**: clustering cancer samples to find cancer sub-types
  - **features**: clustering genes based on similar functions (pathways)
  - Clustering features is similar to clustering observations (work with the transpose of the data matrix)

Defining **meaningful** clusters

How many clusters?

How many clusters?

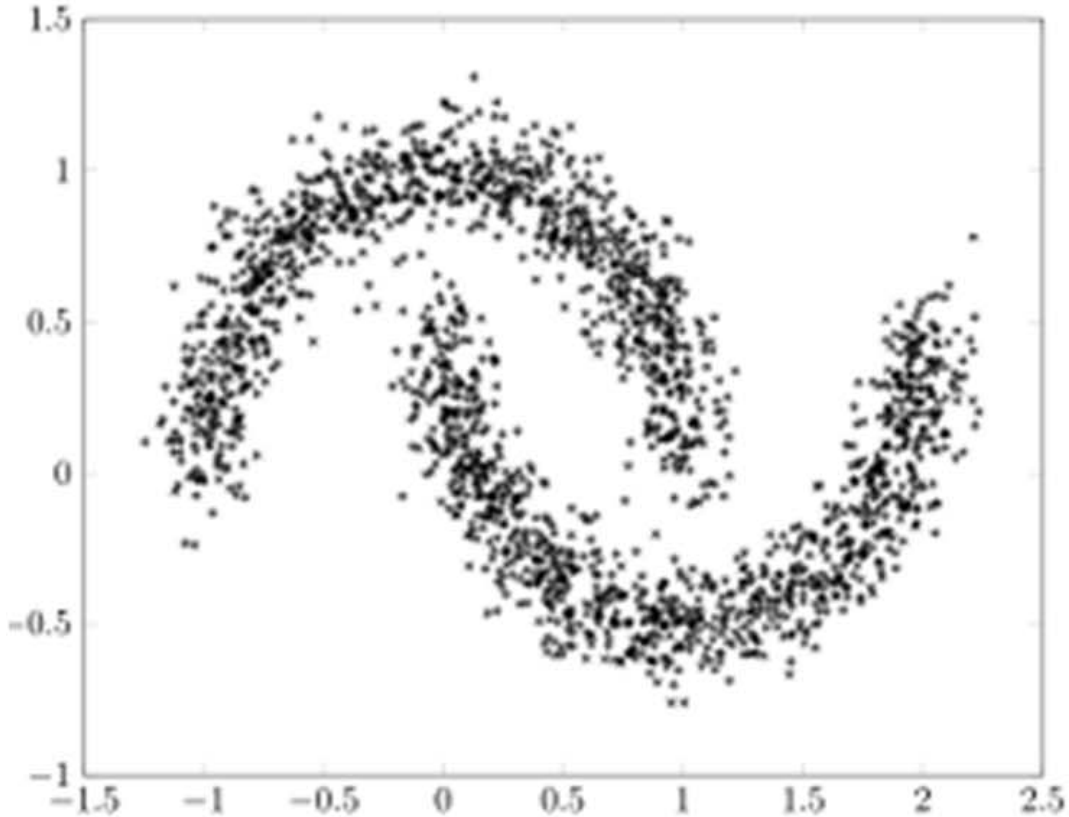
Six Clusters

Two Clusters

Four Clusters

Defining **meaningful** clusters

Which points are more similar?



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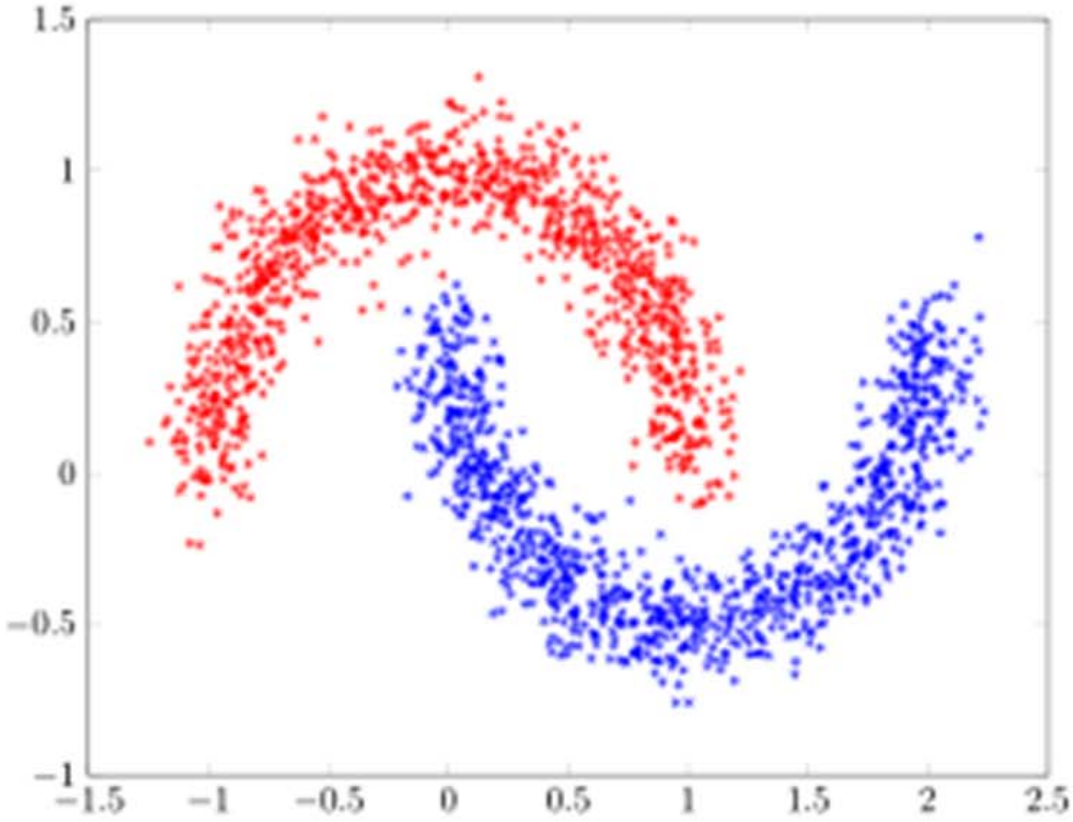

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- Dissimilarity measure:
  - A numerical measure $d(i,j)$ that indicates how **different** two objects are (lower $d \equiv$ high similarity). Unlike similarity, the upper bound may vary
  - Properties: $d(i,j) \geq 0$ and $d(i,j) = d(j,i)$
  - Any **distance** naturally defines a dissimilarity measure

Common Dissimilarity Measures

- **Euclidean** distance: $d(i,j) = \sqrt{\sum_{k=1}^{p} (X_{ik} - X_{jk})^2}$
- **Manhattan** distance: $d(i,j) = \sum_{k=1}^{p} |X_{ik} - X_{jk}|$
- **Mahalanobis** distance: For p-dimensional vectors X_i and X_j,
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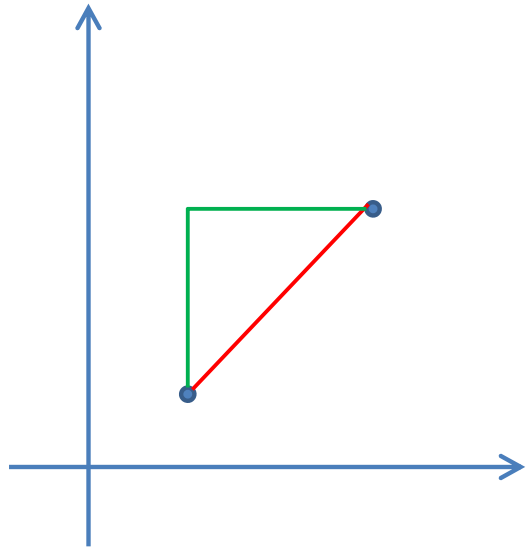

Common Similarity Measures

- **Correlation** coefficient
  - *Pearson* correlation (sample version):

$$r(X_i, X_j) = \frac{\sum_k (X_{ik} - \bar{X}_i)(X_{jk} - \bar{X}_j)}{\sqrt{\sum_k (X_{ik} - \bar{X}_i)^2 \sum_k (X_{jk} - \bar{X}_j)^2}}$$

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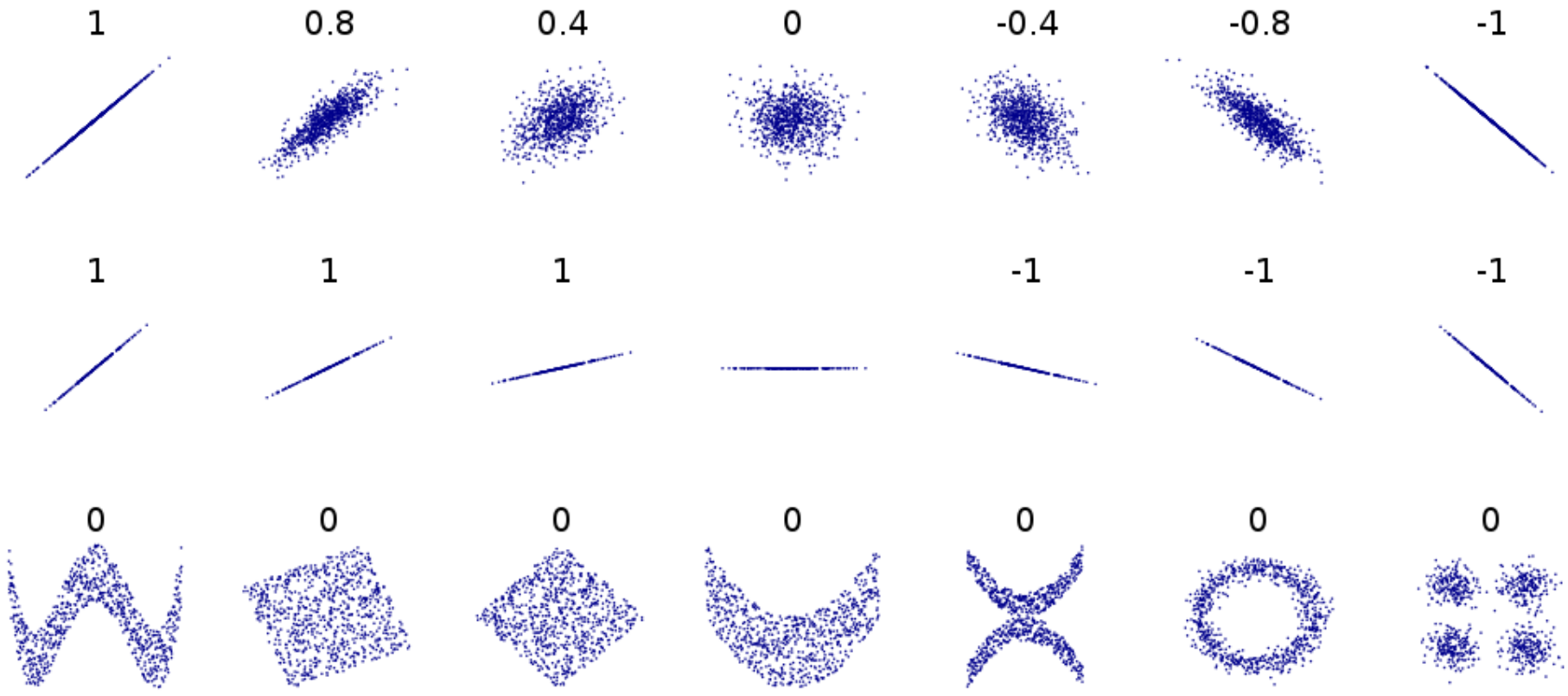
- **Cosine** measure: $\cos(X_i, X_j) = \frac{X_i \cdot X_j}{\|X_i\| \|X_j\|} = \frac{\sum_k X_{ik} X_{jk}}{\sqrt{\sum_k X_{ik}^2 \sum_k X_{jk}^2}}$ Measures the angle between two vectors, which determines how much they align.

Correlation Coefficient



Correlation Coefficient

Which data set has higher Pearson correlation?

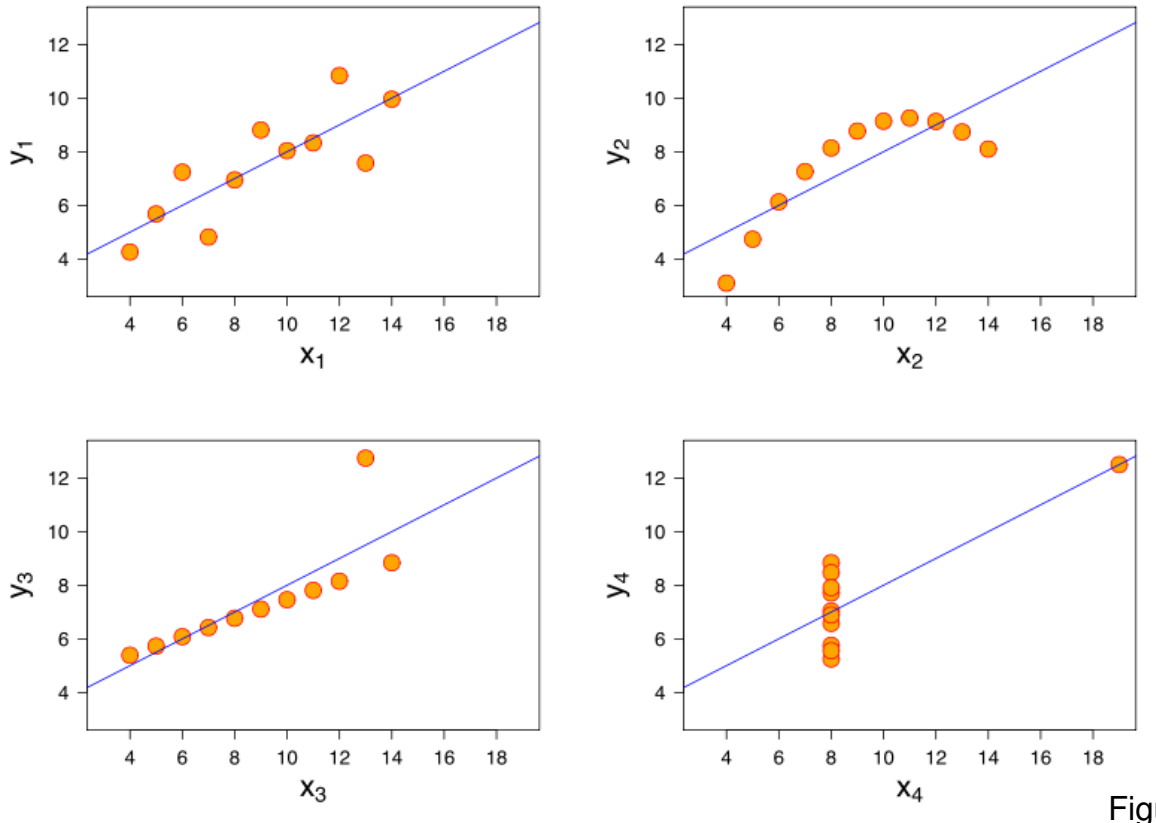


Figure courtesy of Wikipedia

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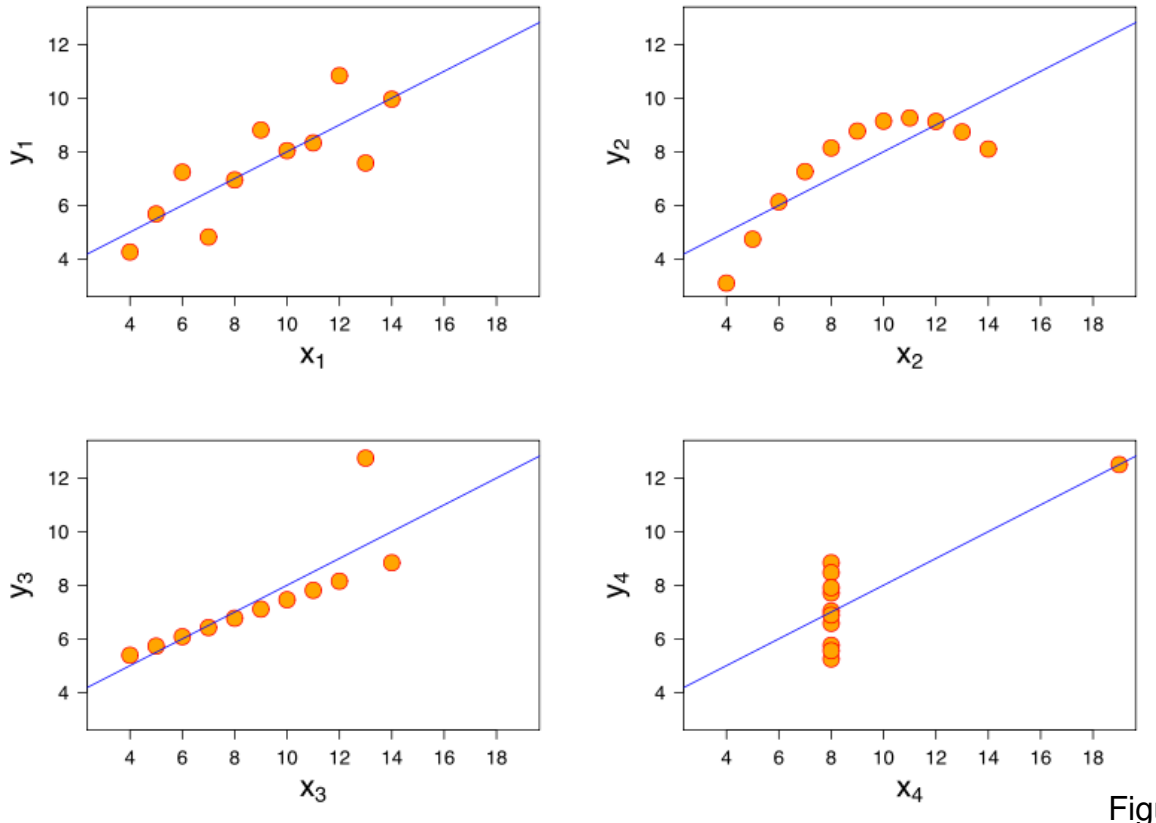

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In all of the above cases, $\mathbf{r = 0.816}$.

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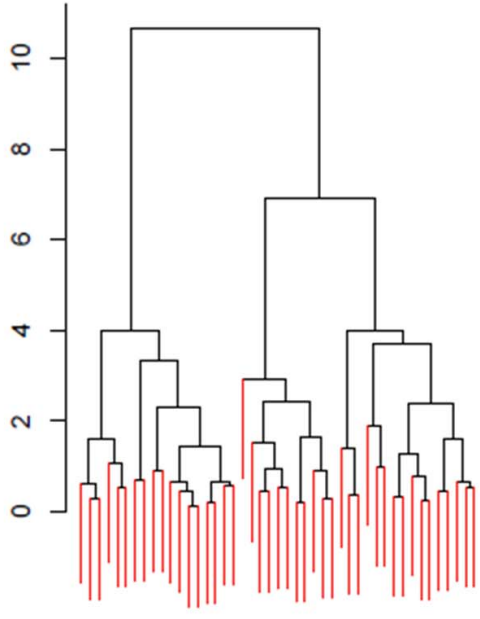
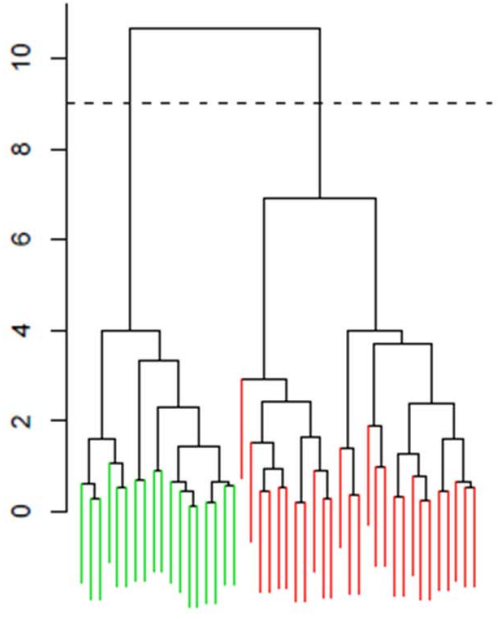
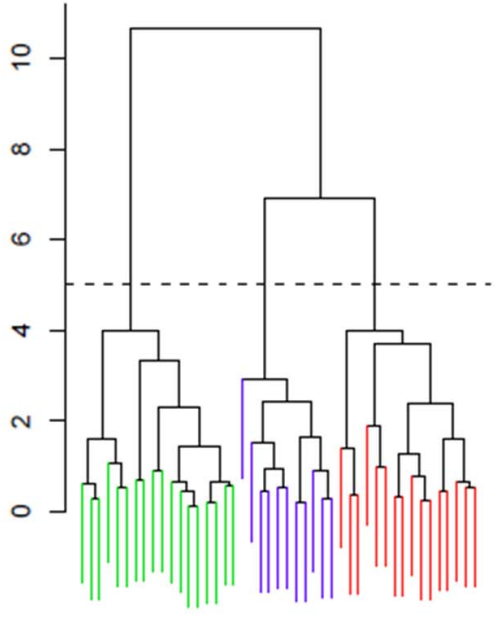
We will focus on Bottom-Up methods.

Interpreting the Dendrogram

How many clusters?

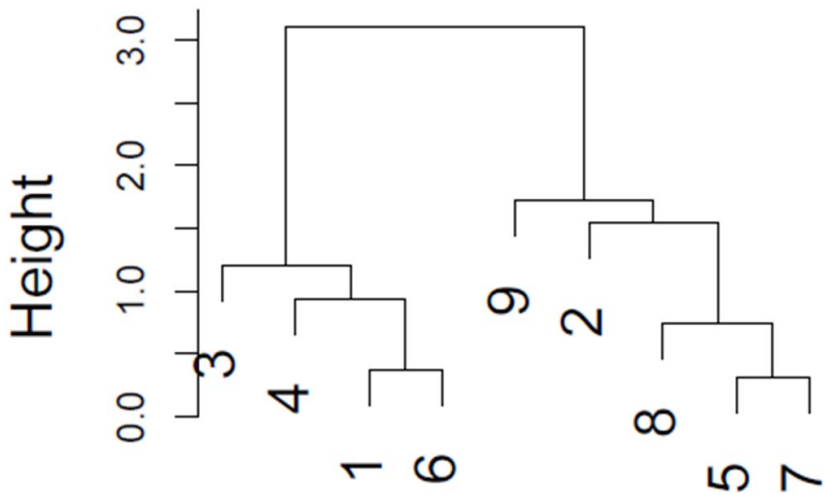






Interpreting the Dendrogram

Which points are clustered together?



How To Read The Dendrogram?

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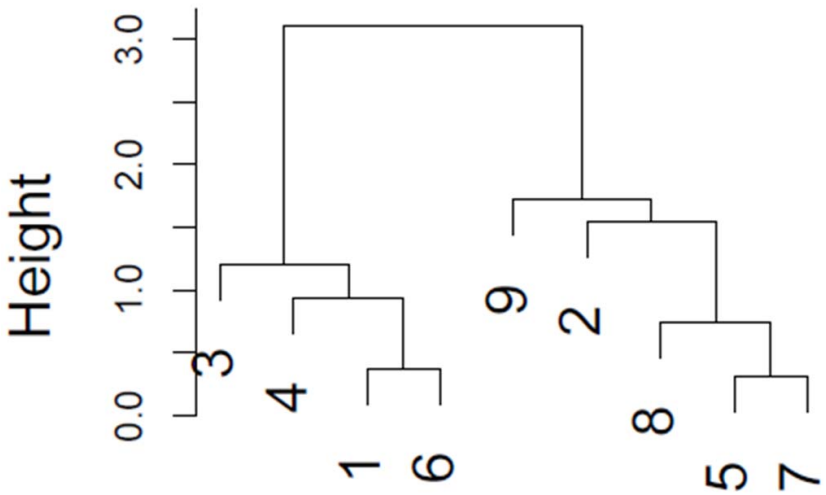

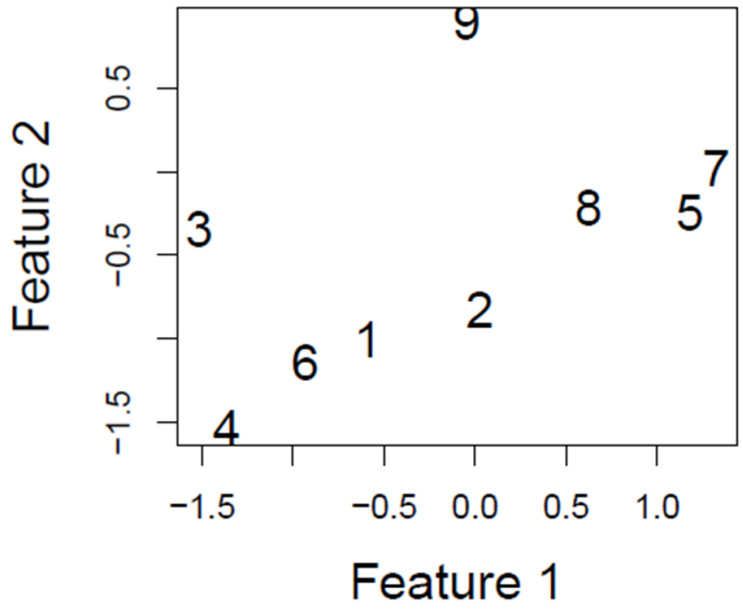

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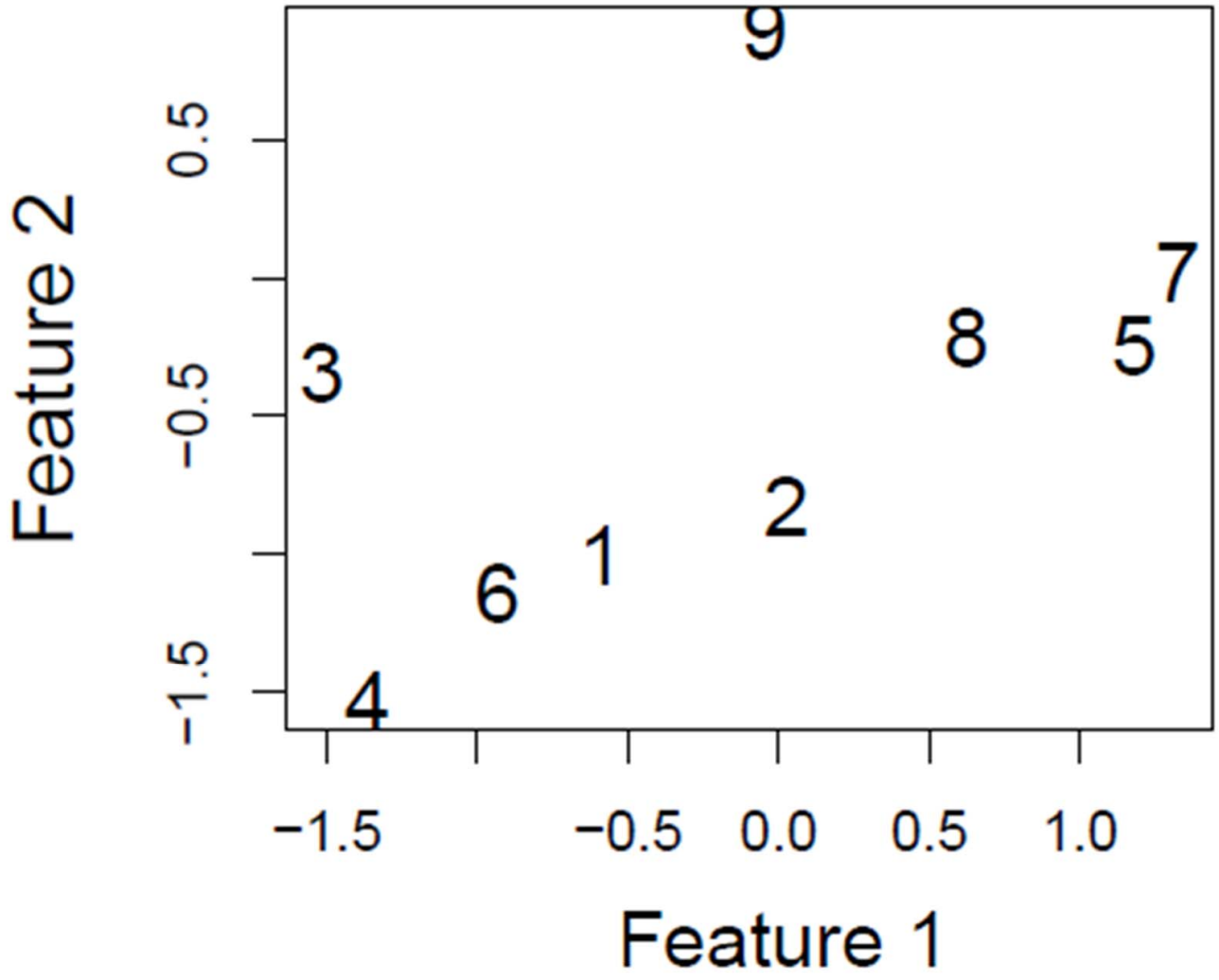

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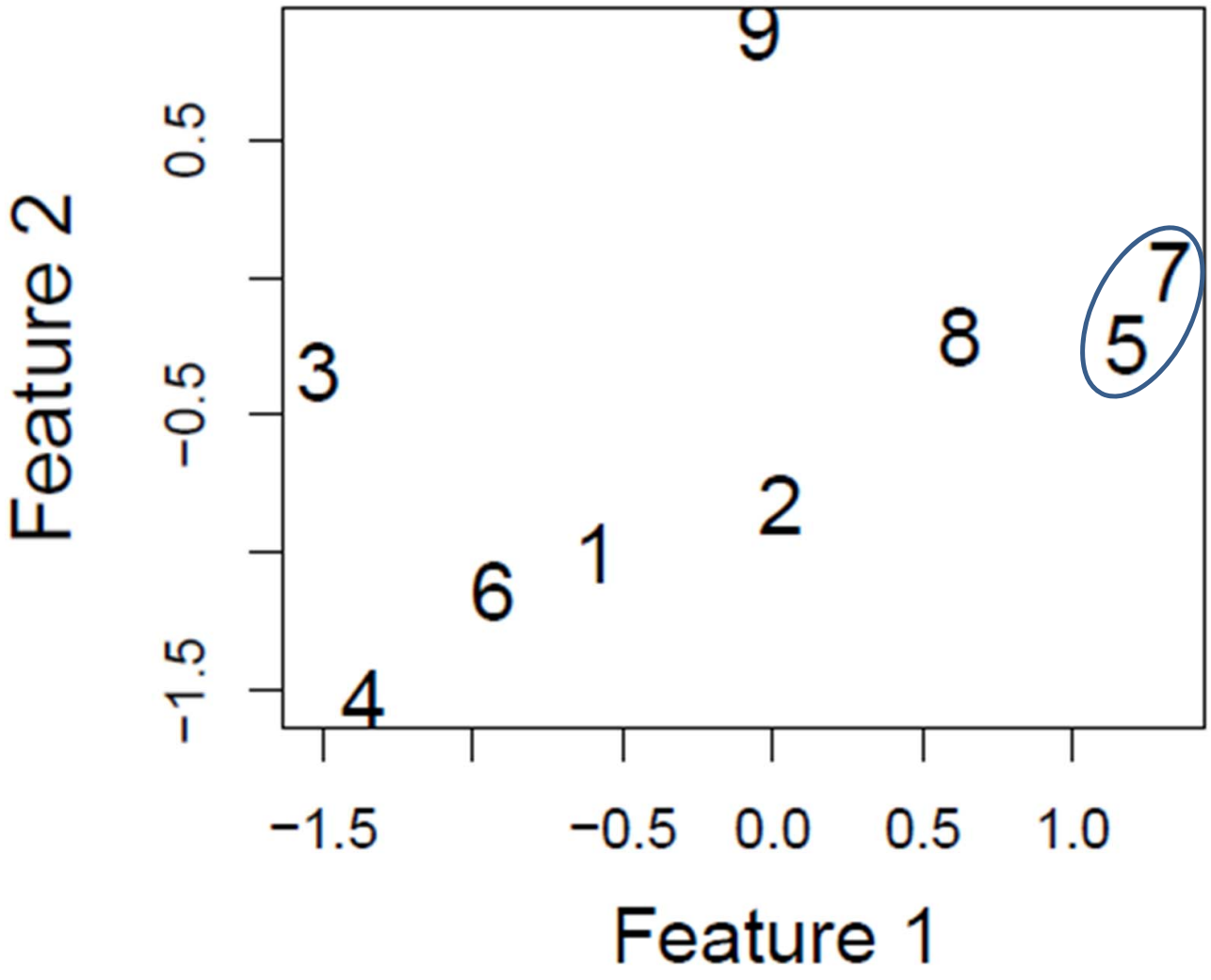

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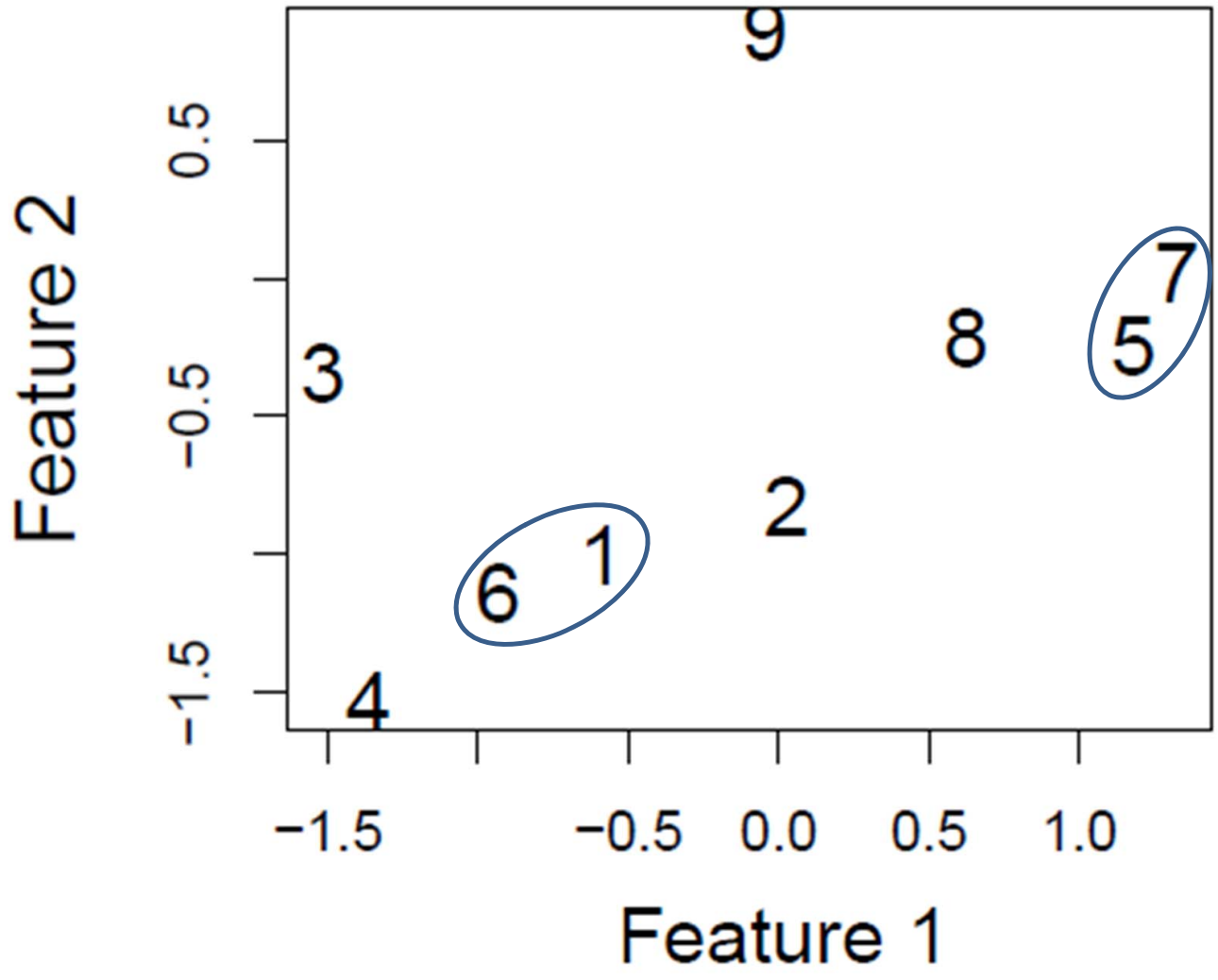

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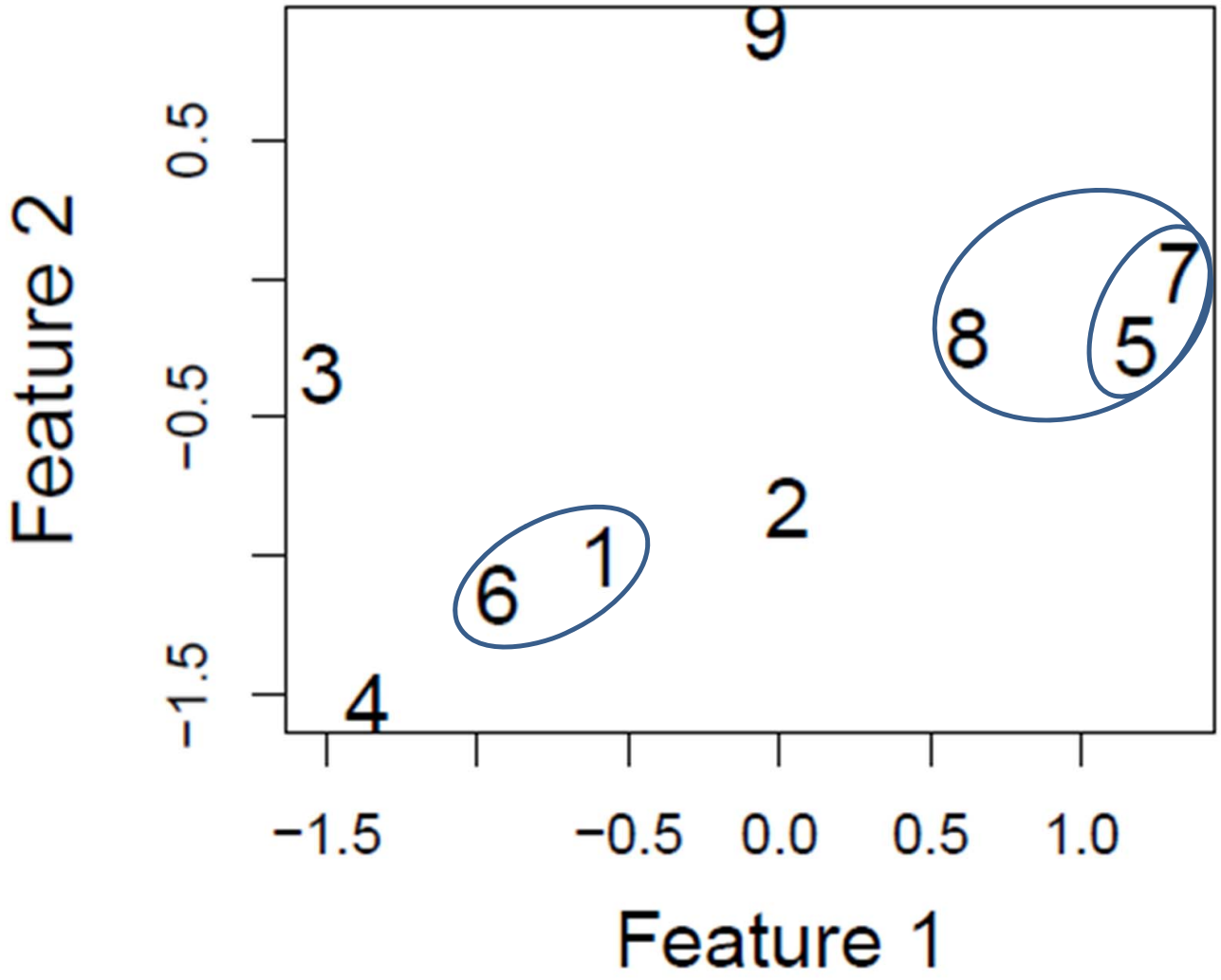

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- The height of the point in the tree where branches containing two observations are first fused, as measured on the *vertical axis*, indicates how different they are from each other
- However, we cannot draw conclusions about the similarity of two observations based on their proximity along the *horizontal axis*

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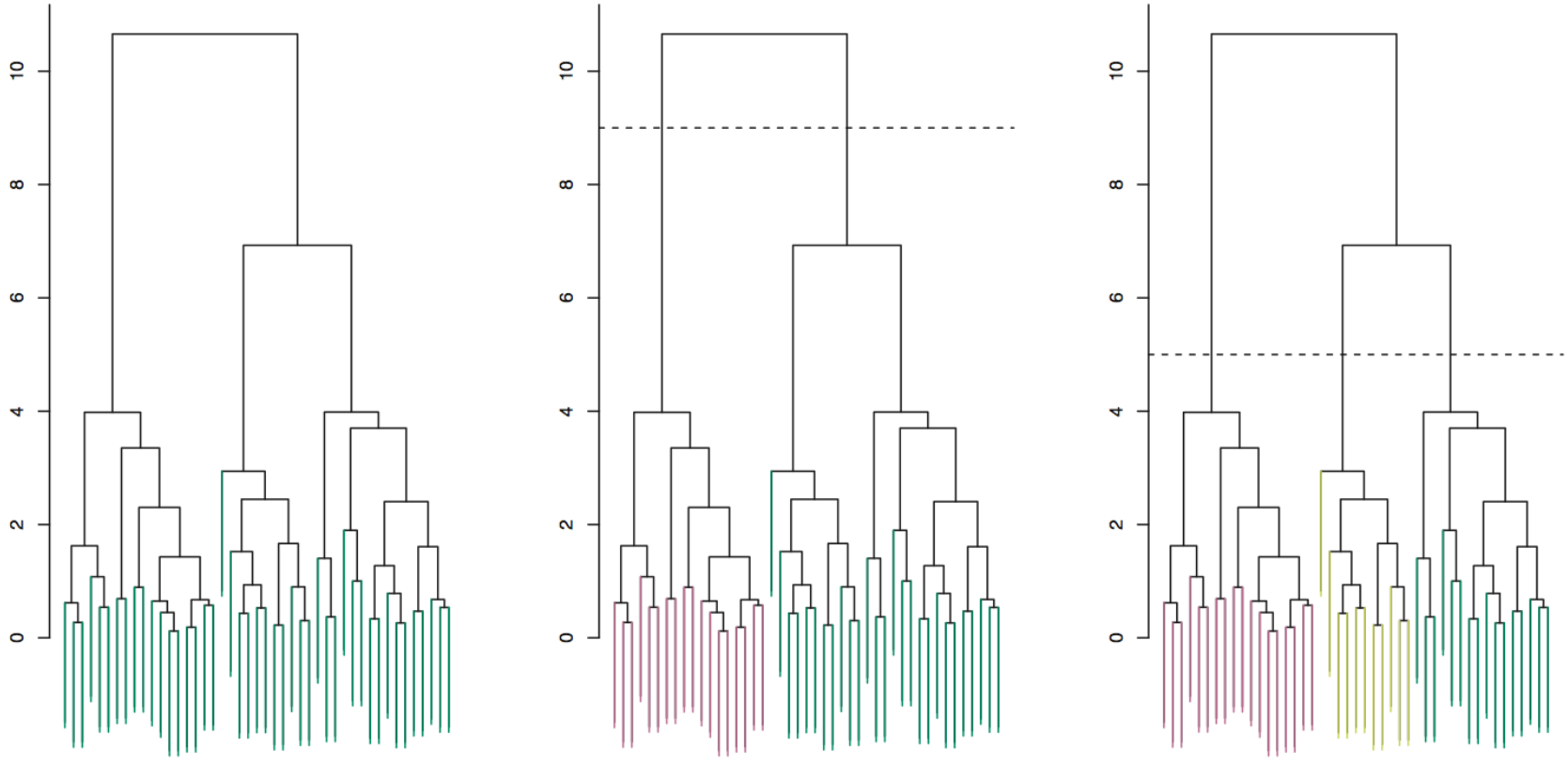

Measures of Inter-Cluster similarity

- Single linkage (min)
- Complete linkage (max)
- Average linkage
- Distance between centroids
- Ward's method

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- Can result in extended, trailing clusters in which observations are fused one-at-a-time

Complete Linkage

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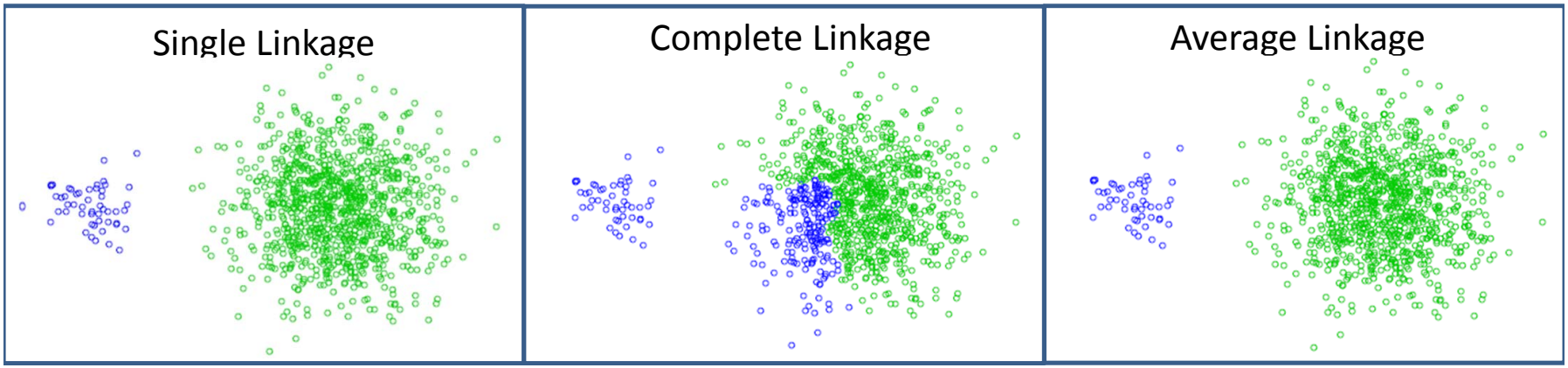
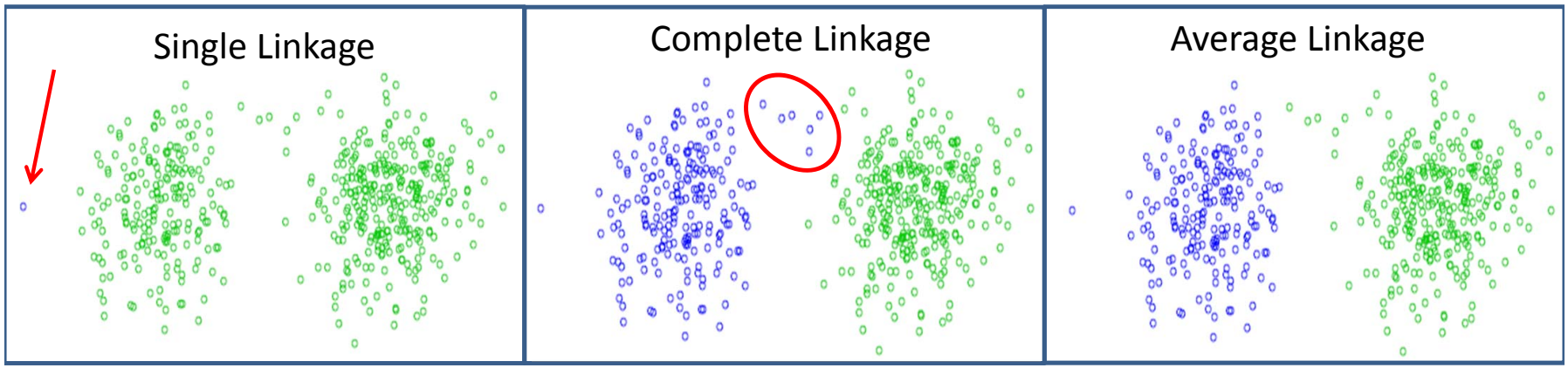
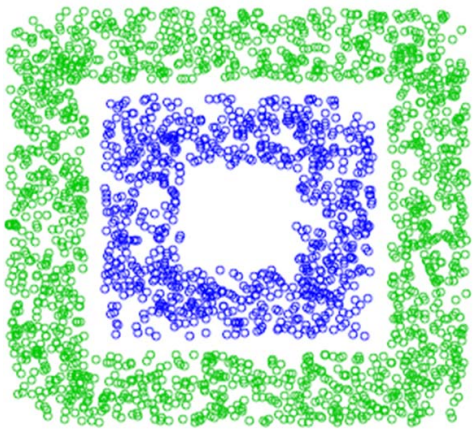
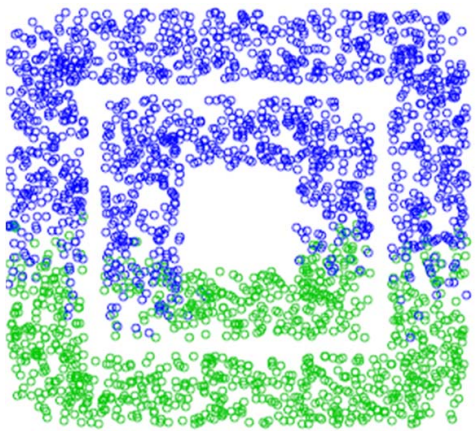
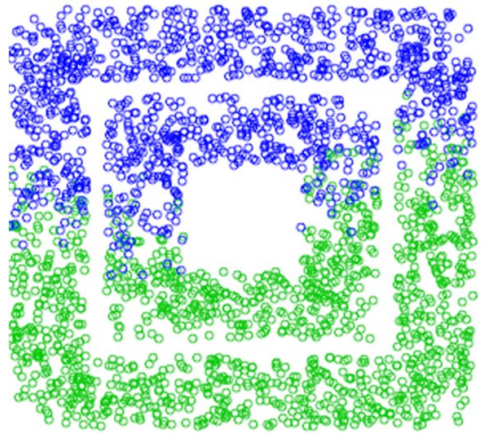
Unbalanced Clusters



Outliers



Non-Spherical Distributions

Single Linkage	Complete Linkage	Average Linkage
		

Example

- Clustering analysis on NCI60 data
- The dataset includes gene expression data for 6830 genes from 64 cancer samples
- Data can be downloaded form http://www-stat.stanford.edu/~tibs/ElemStatLearn/
- Missing values have been imputed
- Cluster the samples using different hierarchical clustering methods

Example, contd.

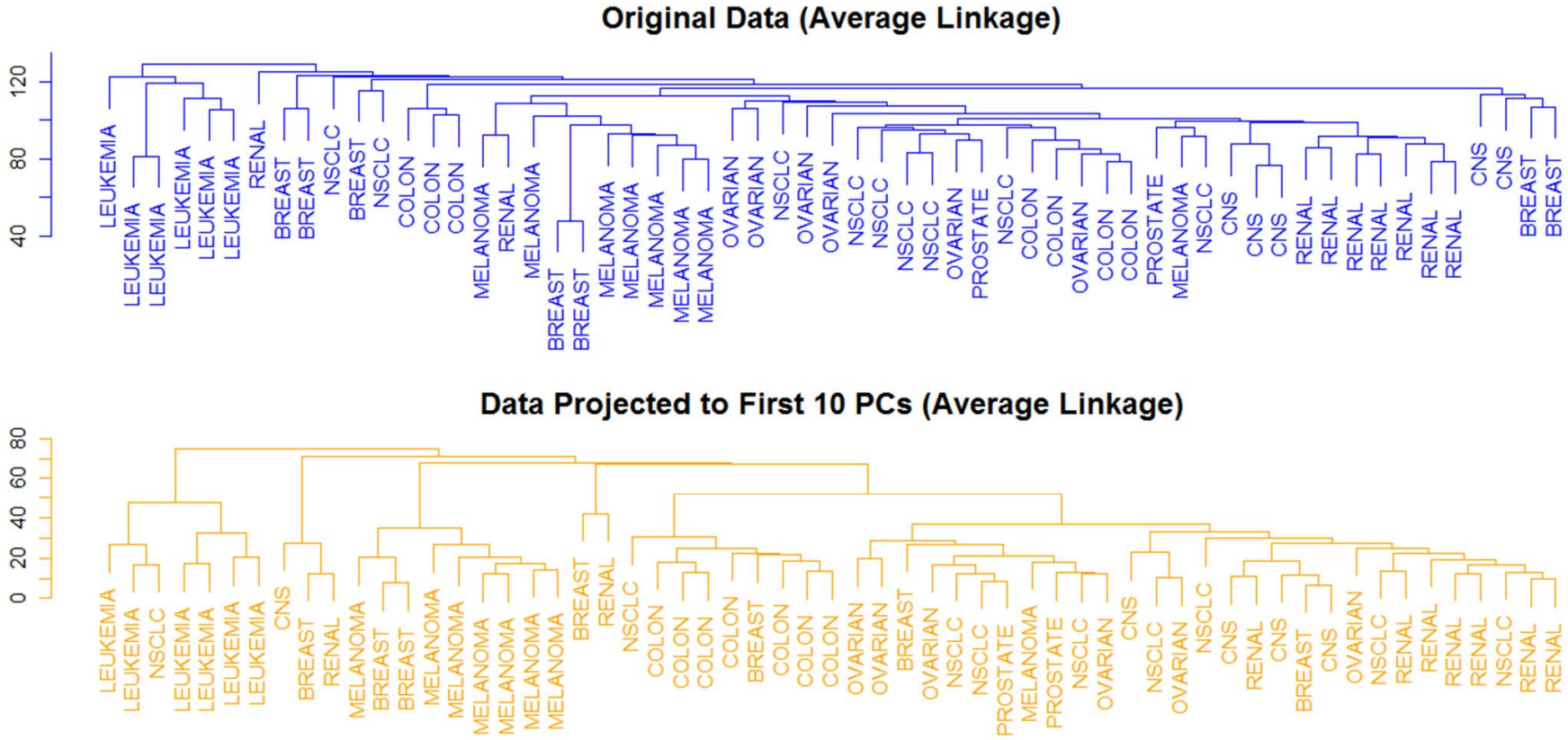
```
## Analysis NCI60 data
mydata <- read.table('nci.data')
dim(mydata)
mydata <- t(mydata)
mydata <- scale(mydata, center=F, scale=T)

labs <- read.table('nci.info', skip=14)
labs <- as.vector(as.matrix(labs))
table(labs)

## Define the distance
mydist <- dist(mydata)

## Plot the results
par(mfrow=c(1,3))
plot(hclust(mydist), labels=labs, col="green", main="Complete Linkage",
    hang=0.2, xlab="", sub="", ylab="", cex.main=1.5, cex.lab=0.6)
plot(hclust(mydist, method="average"), labels=labs, col="orange", hang=0.2
main="Average Linkage", xlab="", sub="", ylab="", cex.main=1.5, cex.lab=0.
plot(hclust(mydist, method="single"), labels=labs, col="blue", hang=0.2,
main="Single Linkage", xlab="", sub="", ylab="", cex.main=1.5, cex.lab=0.8
```

Hierarchical Clustering for NCI60 Data

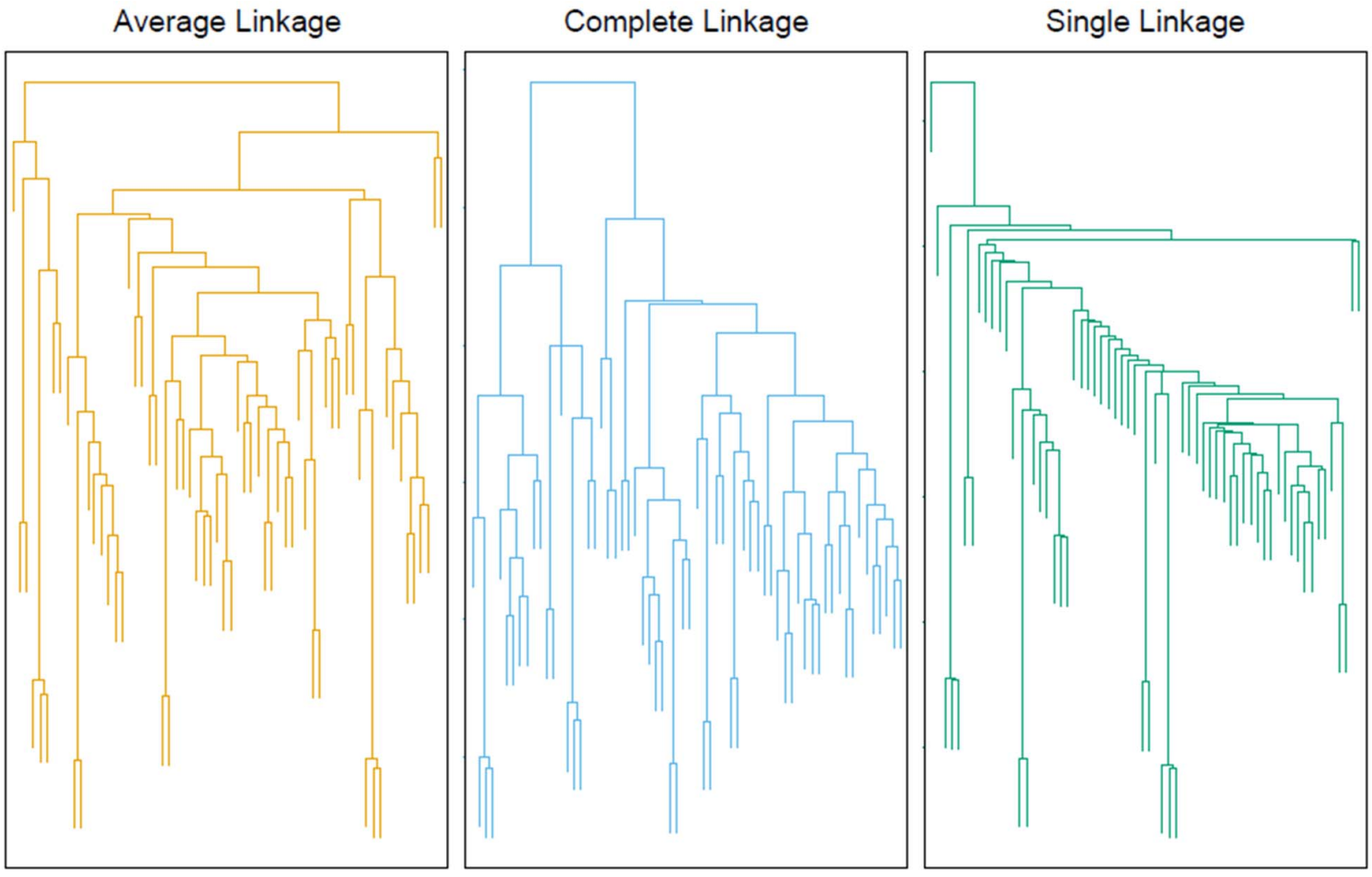


We will talk more about the second approach in the next lecture...

Exercise

- The analysis here is performed using **Euclidean distance**. *Repeat the analysis using Spearman correlations, and compare the results*.
  Hint: A good starting point is: `as.dist(1-cor(t(x)))`

Which Linkage Function?



Properties of Hierarchical Clustering

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- Disadvantages: No optimization criterion; final solution chosen by the data analyst; different merging (splitting) criteria give different solutions

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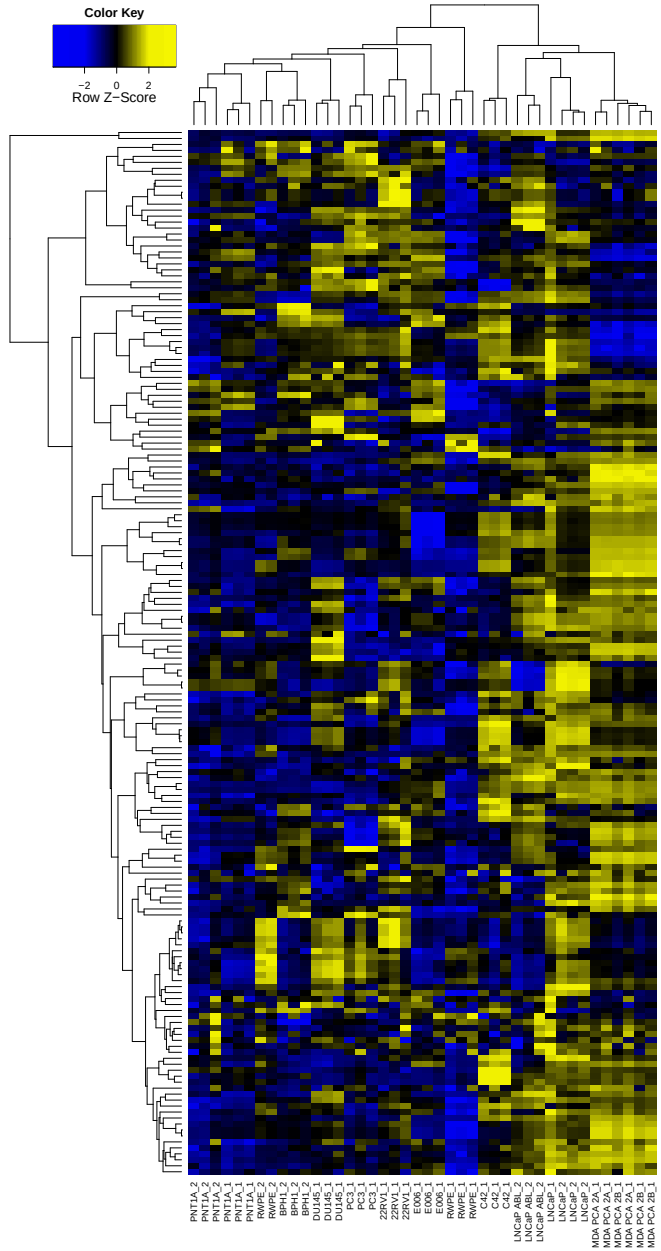
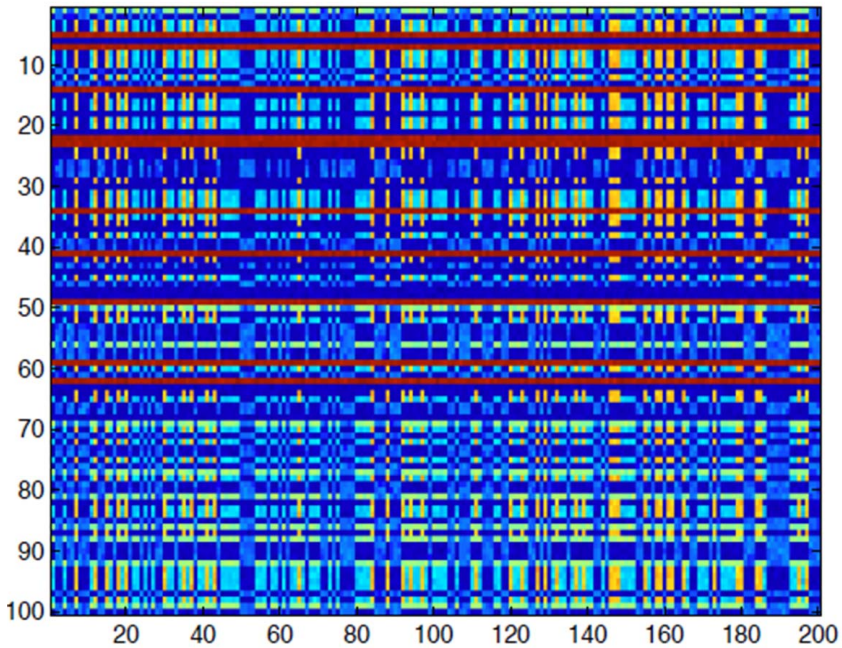


Bi-Clustering: Main Idea

Find a rearrangement of rows and columns that gives meaningful partitions



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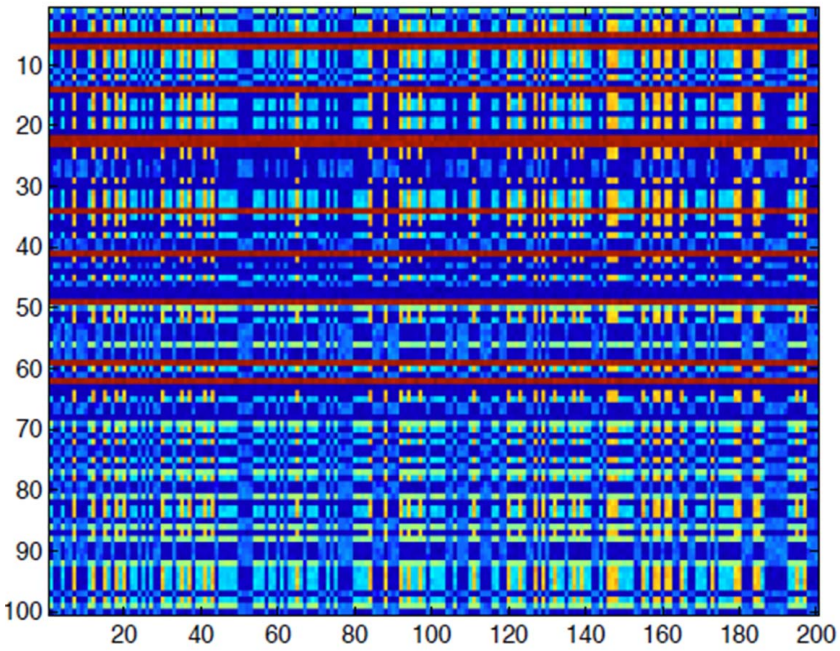

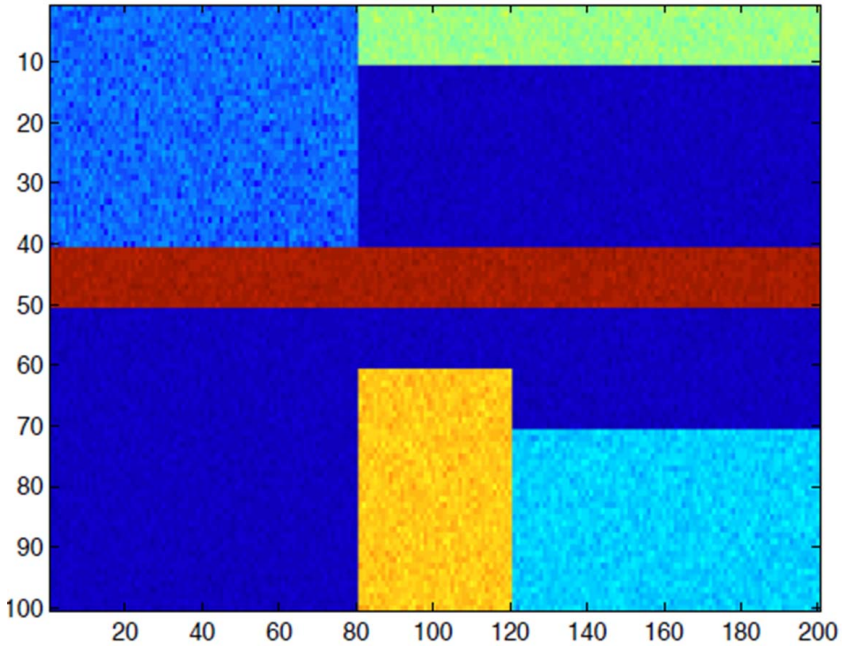

Next Time

- Other clustering methods
  - K-means clustering
  - Model-based clustering
  - Spectral clustering (briefly)