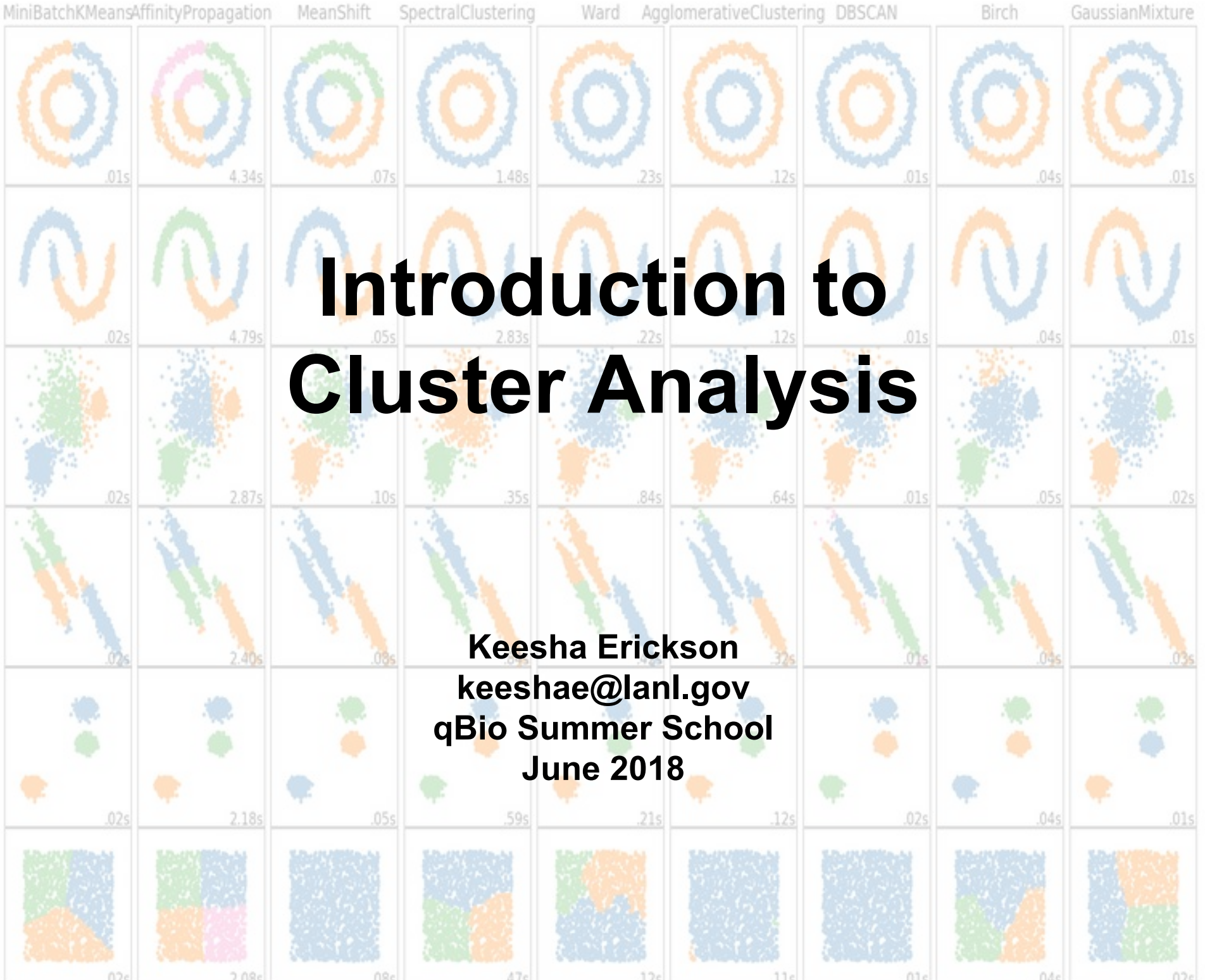

Introduction to Cluster Analysis

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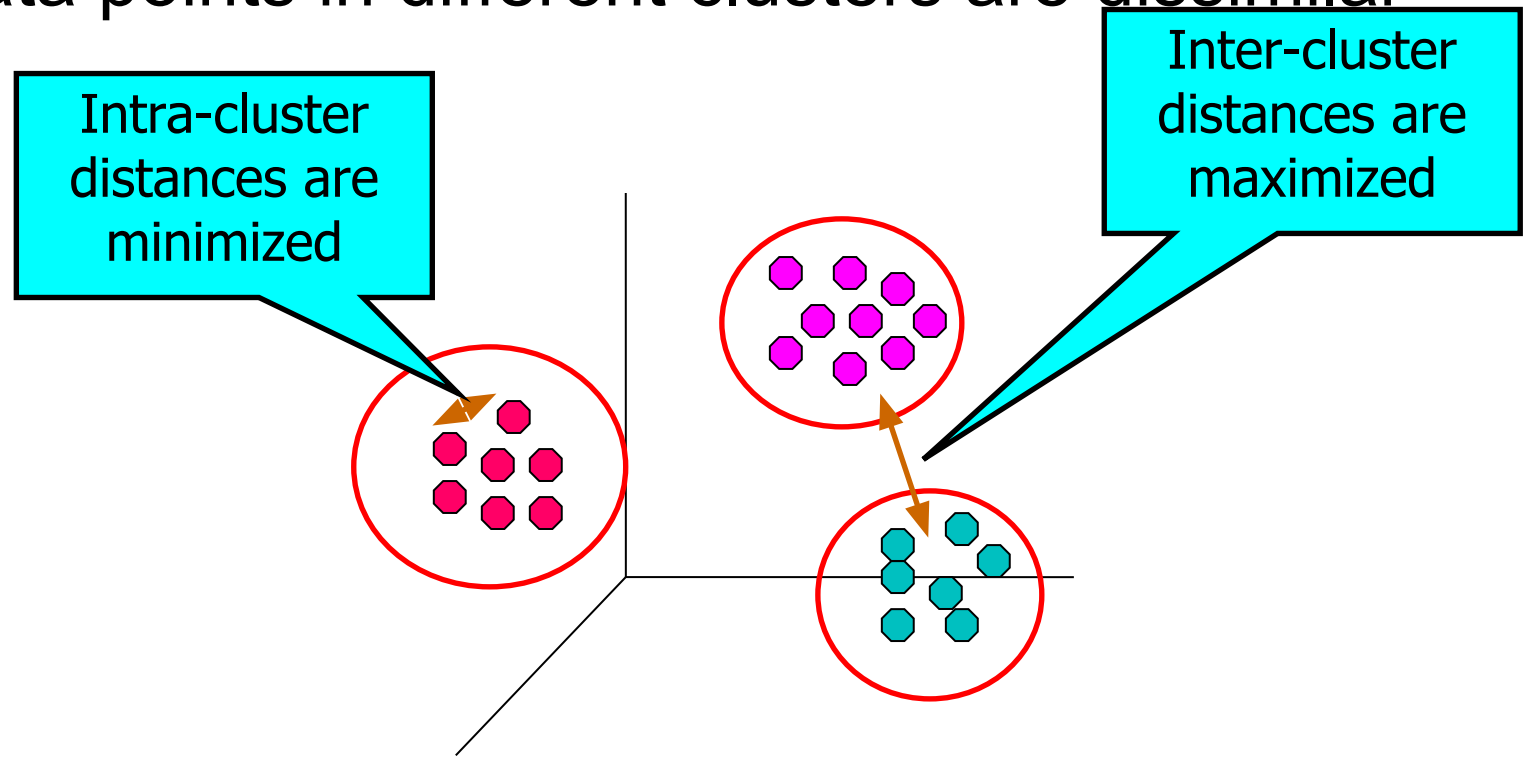
qBio Summer School
June 2018

Outline

- Background
  - Intro
  - Workflow
  - Similarity metrics
- Clustering algorithms
  - Hierarchical
  - K-means
  - Density-based
- Cluster evaluation
  - External
  - Internal

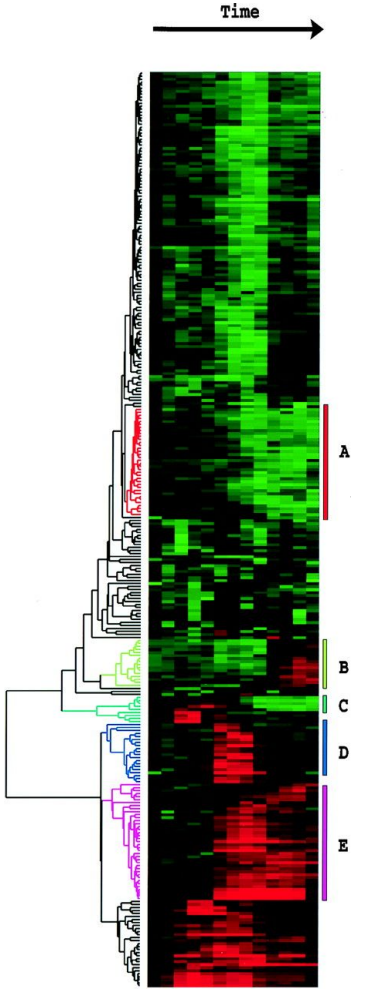
Cluster Analysis

- Data mining tool(s) for dividing a multivariate dataset into (meaningful, useful) groups
- Good clustering:
  - Data points in one cluster are highly similar
  - Data points in different clusters are dissimilar



Applications

- Gain understanding
  - Groups of genes/proteins with similar function (from nucleotide or amino acid sequence data)
  - Groups of cells with similar expression patterns (from RNAseq data)
- Summarize
  - Reduce the size of a large dataset



Clustering precipitation in Australia

Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.
Eisen, Brown, Botstein (1998) PNAS.

Cluster analysis is not...

Simple segmentation
i.e., Dividing students into different registration groups alphabetically, by last name
Although, some work in graph partitioning and more complex segmentation is related to clustering

The results of a query
Groupings are a result of an external specification

Supervised classification
Supervised classification has class label information
Clustering can be called **unsupervised** classification: labels derived from data

Association Analysis
Finding connections between items in datasets

Cluster evaluation has an element of subjectivity

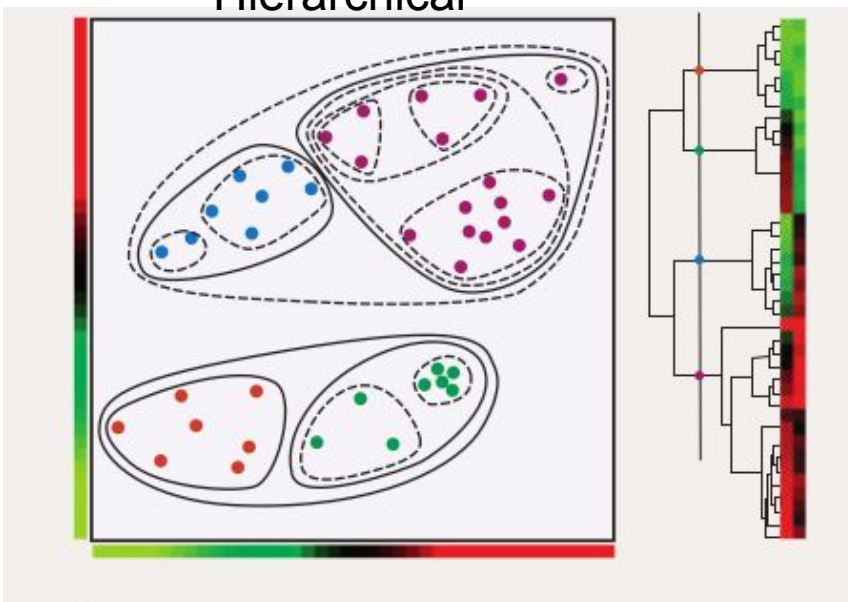
(a) Original points.

Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.

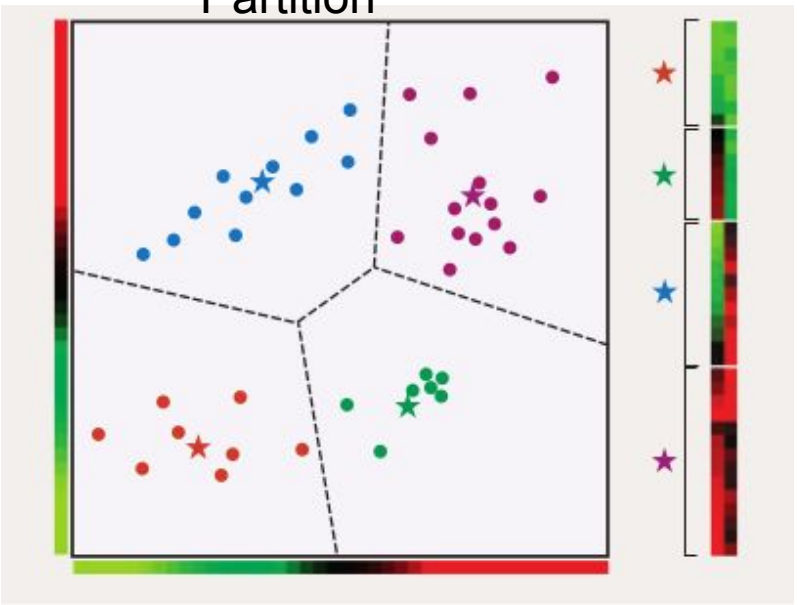
Traditional types of clusterings

- A clustering is a set of clusters
- Clusters can be:
  - **Hierarchical**: data are in nested clusters, organized in a hierarchical tree
  - **Partition**: data in non-overlapping subsets. One data object is in one subset.

Hierarchical



Partition



Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.
D'haeseleer (2005) Nature Biotech.

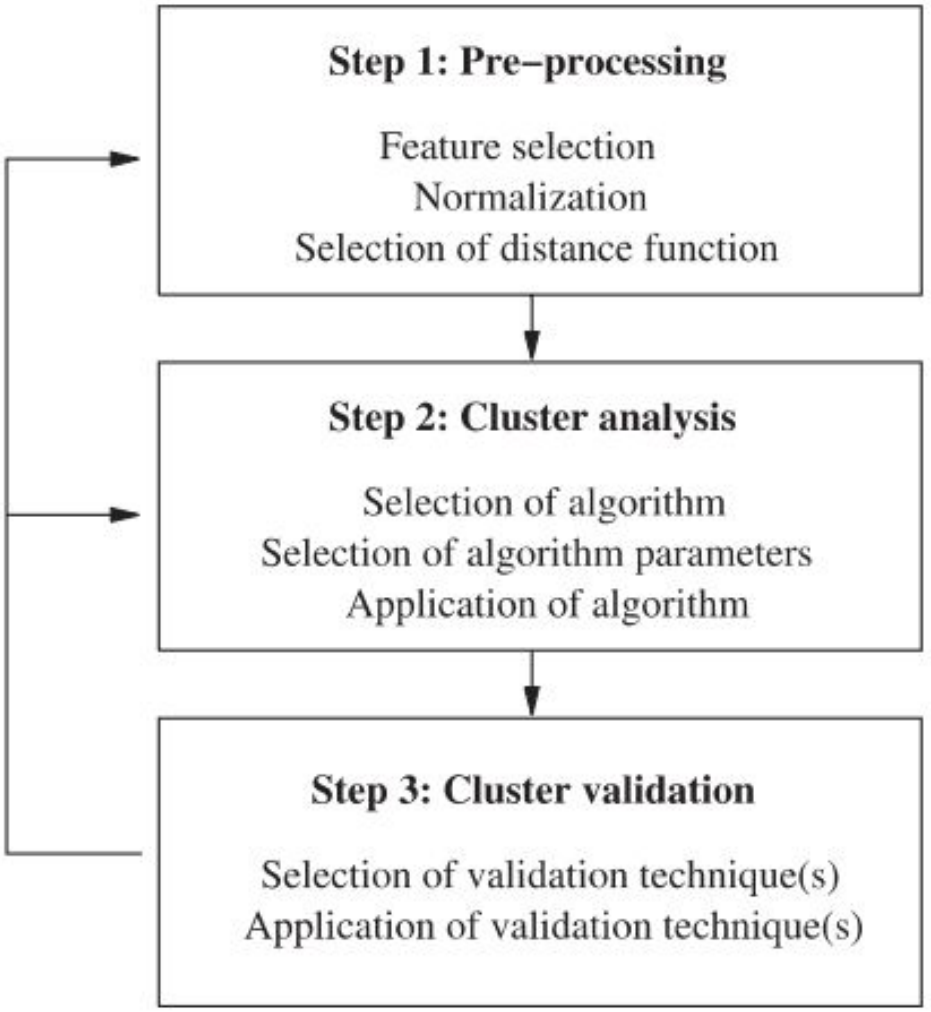
Other distinctions between clusters

- **Exclusive** vs **non-exclusive**
  - Exclusive: points belong to one cluster
  - Non-exclusive: points can belong to multiple
- **Fuzzy** vs **non-fuzzy**
  - In fuzzy clustering, a point belongs to every cluster with some weight (0 to 1)
  - Weights must sum to 1
  - Similar to probabilistic clustering
- **Partial** vs **complete**
  - Partial: only some of the data is clustered (can exclude outliers)
- **Heterogenous** vs **homogeneous**
  - Degree to which cluster size, shape, and density can vary

Why is cluster analysis hard?

- Clustering in two dimensions looks easy!
- Clustering small amounts of data looks easy
- In most cases, looks are **not** deceiving
- However, many applications involve more than 2 dimensions (i.e., human gene expression dataset has >10,000 dimensions)
- **High dimensional spaces look different**: Almost all pairs of points are at about the same distance

Typical workflow for cluster analysis



Handl, Knowles, Kell (2005) Bioinformatics.

Similarity (aka distance) metrics

Table 1 Gene expression similarity measures

Manhattan distance (city-block distance, L1 norm)	$d_{fg} = \sum_c \lvert e_{fc} - e_{gc} \rvert$
Euclidean distance (L2 norm)	$d_{fg} = \sqrt{\sum_c (e_{fc} - e_{gc})^2}$
Mahalanobis distance	$d_{fg} = (\mathrm{e}_f - \mathrm{e}_g)' \Sigma^{-1} (\mathrm{e}_f - \mathrm{e}_g)$, where $\boldsymbol{\Sigma}$ is the (full or within-cluster) covariance matrix of the data
Pearson correlation (centered correlation)	$d_{fg} = 1 - r_{fg}$, with $r_{fg} = \frac{\sum_c (e_{fc} - \bar{e}_f)(e_{gc} - \bar{e}_g)}{\sqrt{\sum_c (e_{fc} - \bar{e}_f)^2 \sum_c (e_{gc} - \bar{e}_g)^2}}$
Uncentered correlation (angular separation, cosine angle)	$d_{fg} = 1 - r_{fg}$, with $r_{fg} = \frac{\sum_c e_{fc} e_{gc}}{\sqrt{\sum_c e_{fc}^2 \sum_c e_{gc}^2}}$
Spellman rank correlation	As Pearson correlation, but replace $\boldsymbol{e_{gc}}$ with the rank of $\boldsymbol{e_{gc}}$ within the expression values of gene g across all conditions $\boldsymbol{c = 1 \ldots C}$
Absolute or squared correlation	$d_{fg} = 1 - \lvert r_{fg} \rvert$ or $d_{fg} = 1 - r_{fg}^2$

d_{fg}, distance between expression patterns for genes f and g. e_{gc}, expression level of gene g under condition c.

D'haeseleer (2005) Nature Biotech.

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- **Clustering algorithms**
  - Hierarchical
  - K-means
  - Density-based
- Cluster evaluation
  - External
  - Internal

Hierarchical clustering

Produces nested clusters

Can be visualized as a **dendrogram**

Can be either:

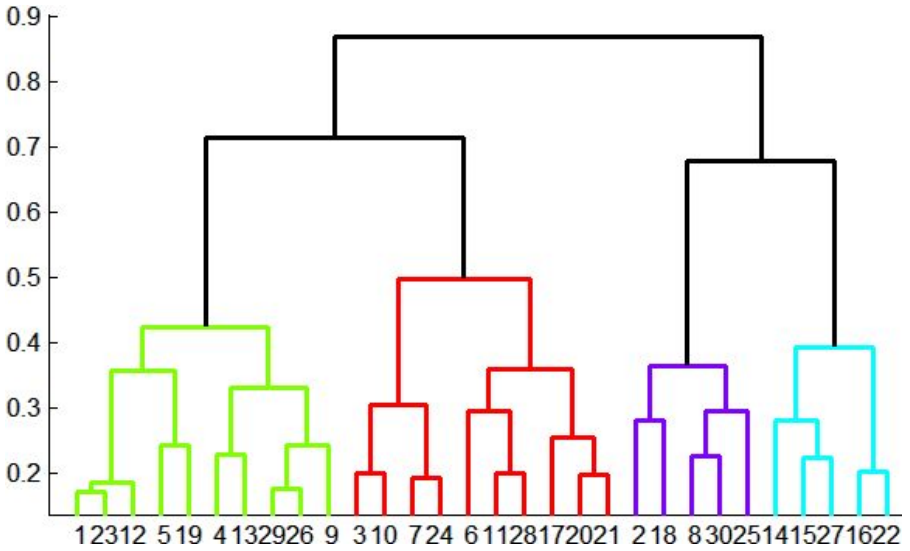
- Agglomerative (bottom up):

Initially, each point is a cluster

Repeatedly combine the two "nearest" clusters into one

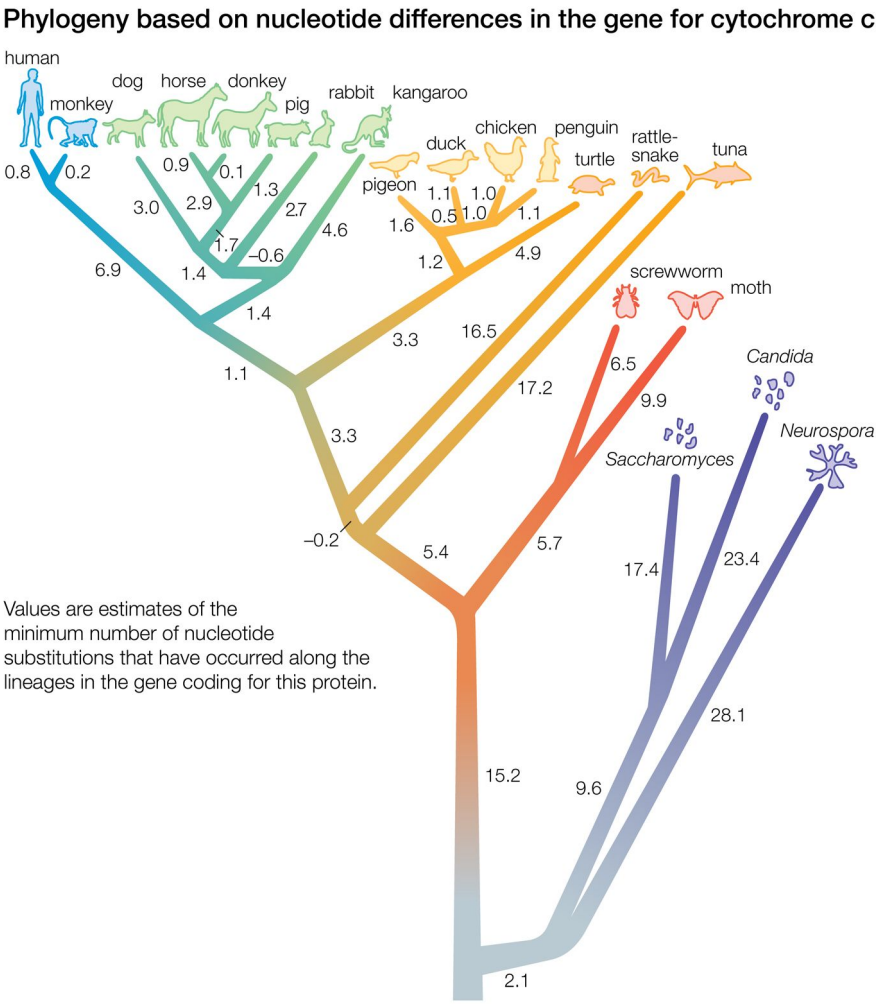
- Divisive (top down):

Start with one cluster and recursively split



Advantages of Hierarchical Clustering

- Do not have to assume any particular number of clusters
  - Any desired number of clusters can be obtained by cutting the dendrogram at the proper level
- No random component (clusters will be the same from run to run)
- Clusters may correspond to meaningful taxonomies
  - Especially in biological sciences (e.g., phylogeny reconstruction)



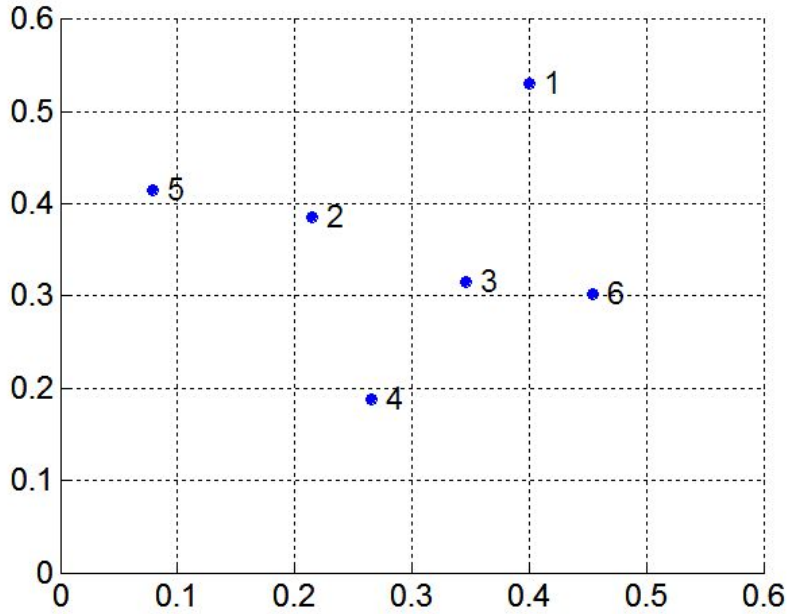
Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.
Image from Encyclopedia Britannica Online. Phylogeny entry. Web. 05 Jun 2018.

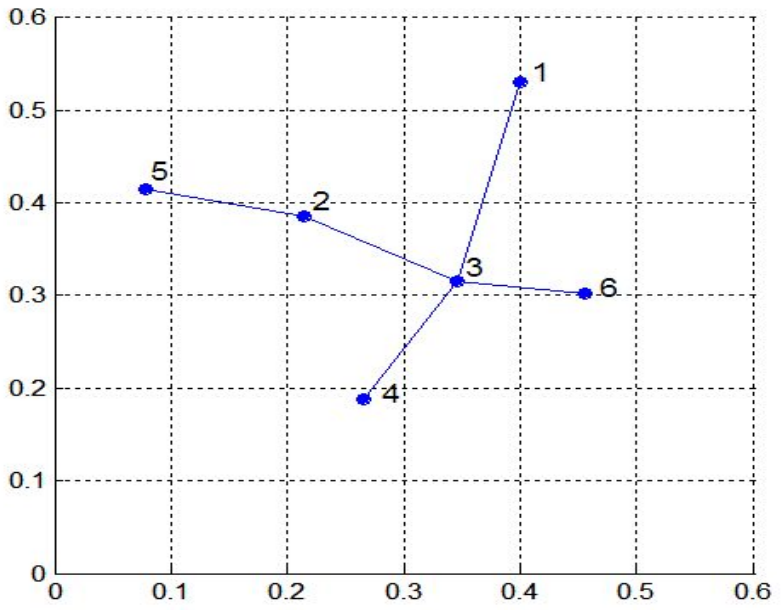
Agglomerative Clustering Algorithm

- Most popular hierarchical clustering technique
- Basic algorithm:
  1) Compute the proximity metric
  2) Let each data point be a cluster
  3) **Repeat**
  4) Merge the two closest clusters
  5) Update the proximity metric
  6) **Until** only a single cluster remains
- Key operation is the computation of the proximity between two clusters
  - Different approaches to defining this distance distinguish the different algorithms

Divisive Clustering Algorithm

- Minimum spanning tree (MST)
  - Start with one point
  - In successive steps, look for closest pair of points (**p**,**q**) such that **p** is in the tree but **q** is not.
  - Add **q** to the tree (add edge between **p** and **q**)



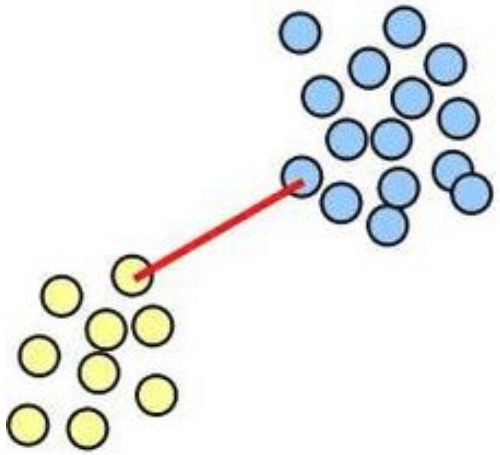


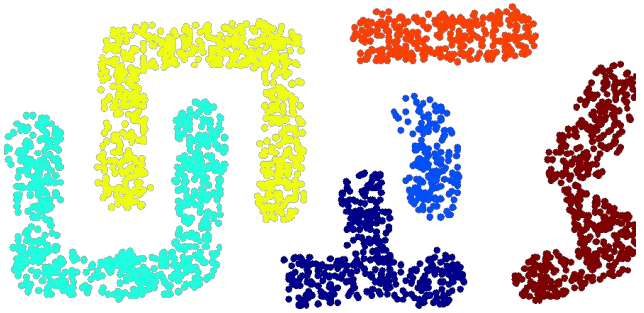
Linkages

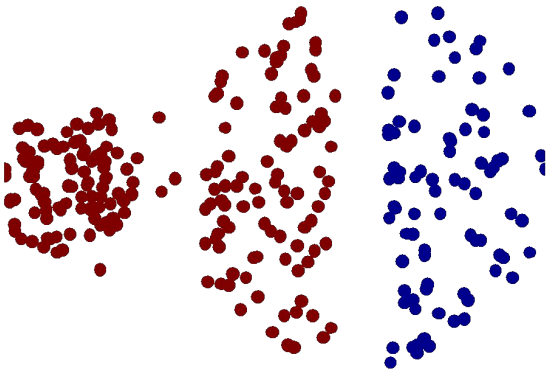
- Linkage: measure of dissimilarity between clusters
- Many methods:
  - Single linkage
  - Complete linkage
  - Average linkage
  - Centroids
  - Ward's method

Single linkage (aka nearest neighbor)

- Proximity of two clusters is based on the two closest points in the different cluster
- Proximity is determined by one pair of points (i.e., one link)
- Can handle non-elliptical shapes
- Sensitive to noise and outliers

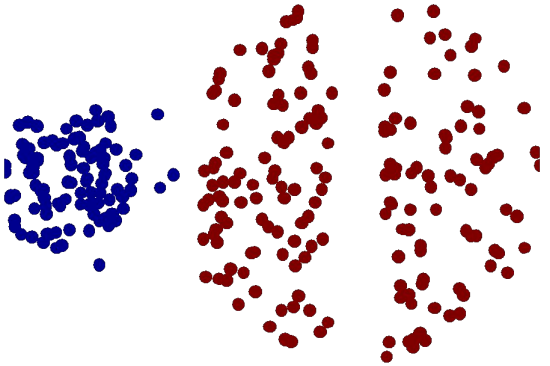


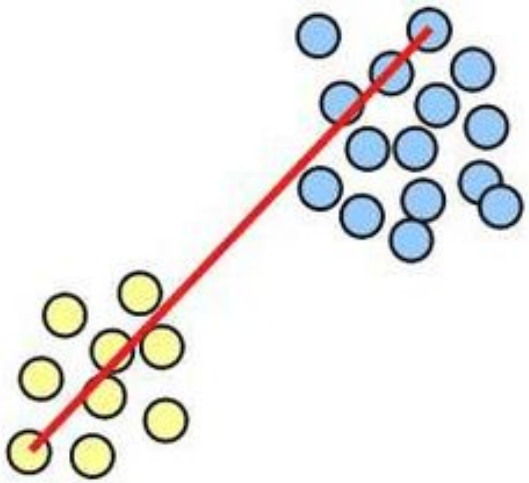


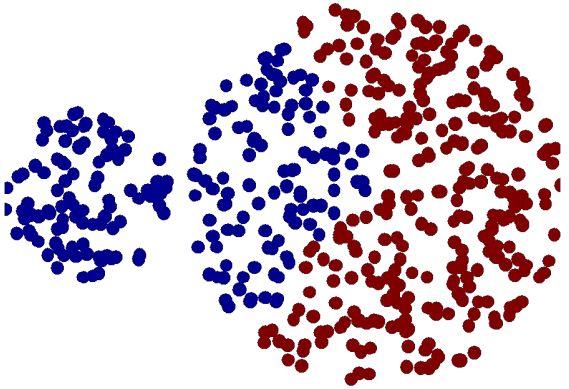


Complete linkage

- Proximity of two clusters is based on the two most distant points in the different clusters
- Less susceptible to noise and outliers
- May break large clusters
- Biased toward globular clusters

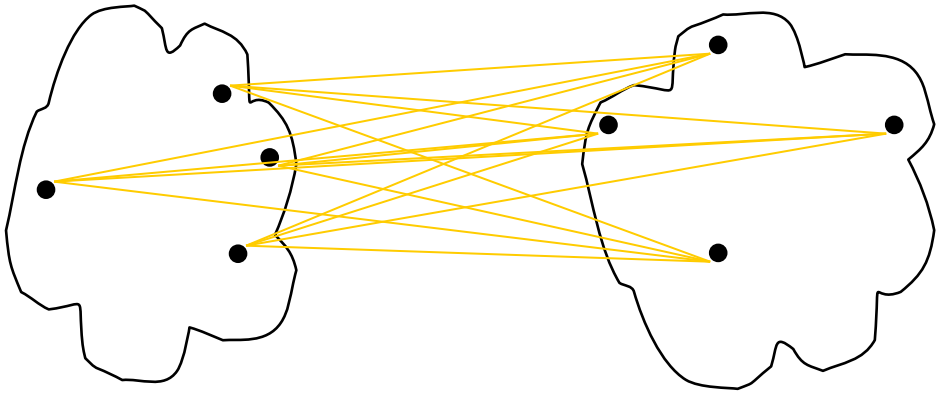






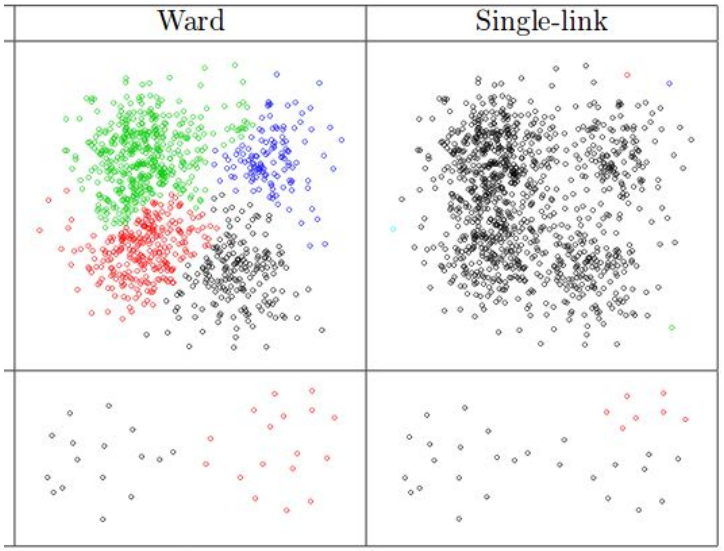
Average linkage

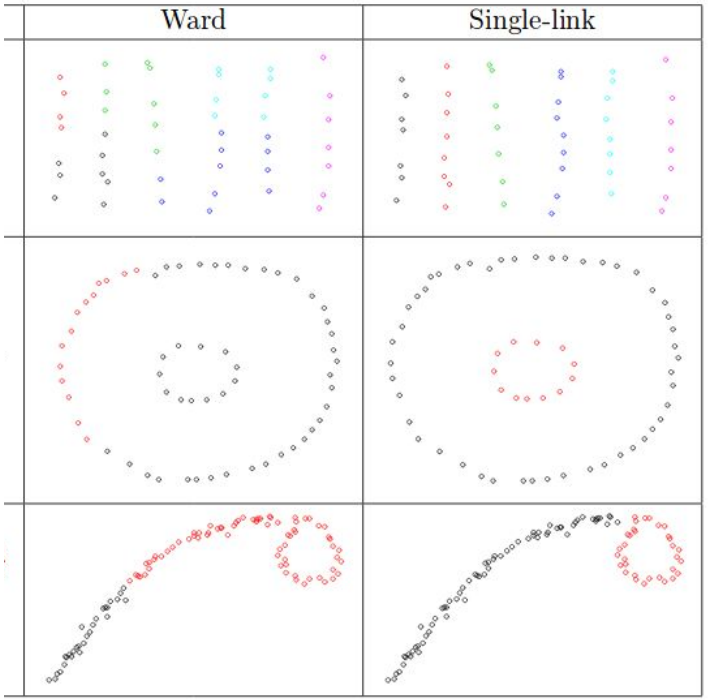
- Proximity of two clusters is the average of pairwise proximity between points in the clusters
- Less susceptible to noise and outliers
- Biased towards globular clusters



Ward's method

- Similiarity of two clusters is based on the increase in squared error when two clusters are merged
- Similar to group average if distance between points is distance squared
- Less susceptible to noise and outliers
- Biased towards globular clusters

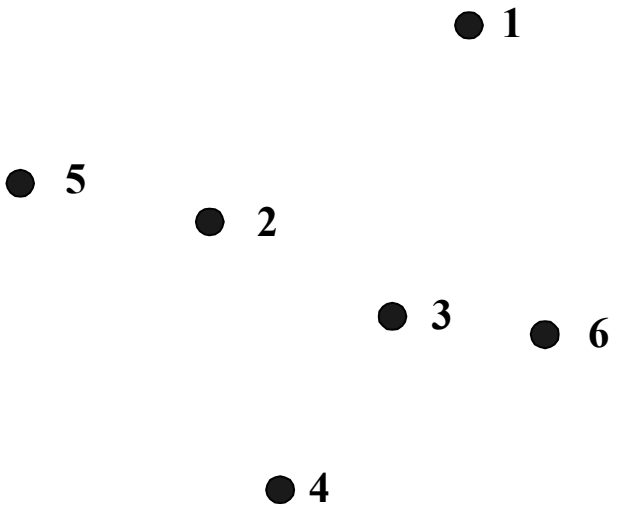


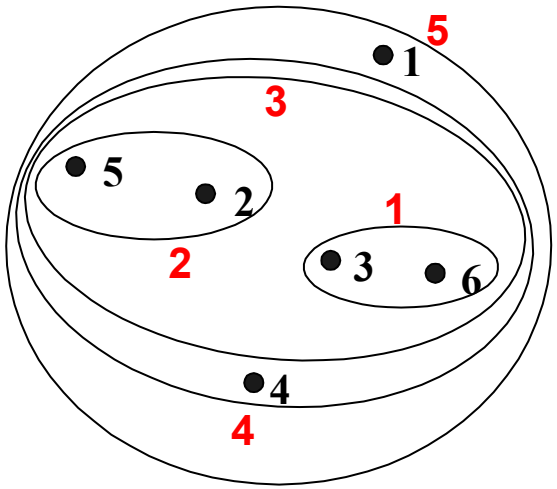


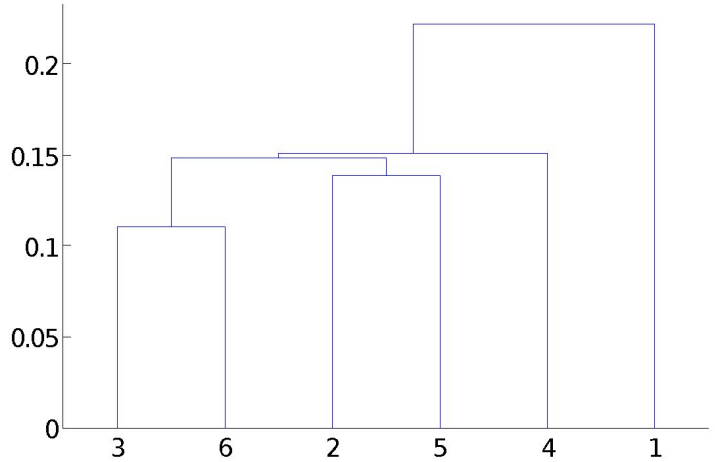
Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.
Lecture notes from C Shalizi, 36-350 Data Mining, Carnegie Mellon University.

Agglomerative clustering exercise

- How do clusters change with different linkage methods?
- Single

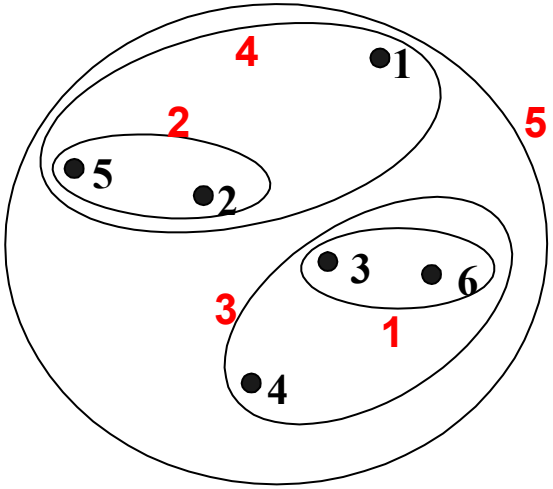


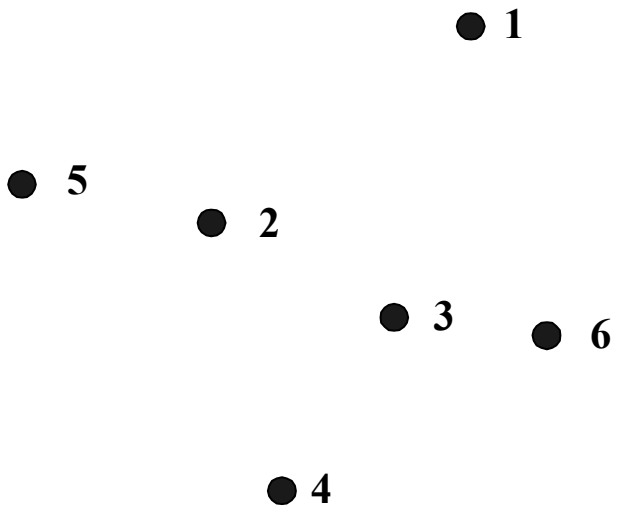


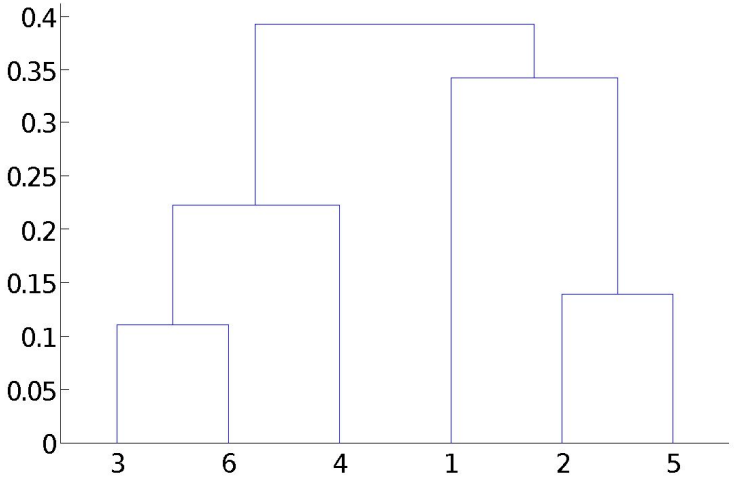


Agglomerative clustering exercise

- How do clusters change with different linkage methods?
- Complete

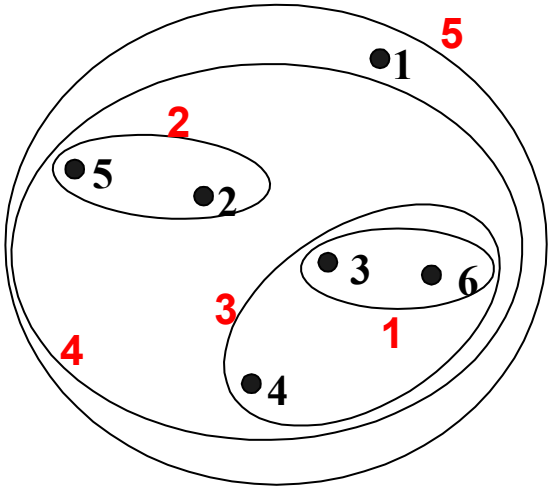


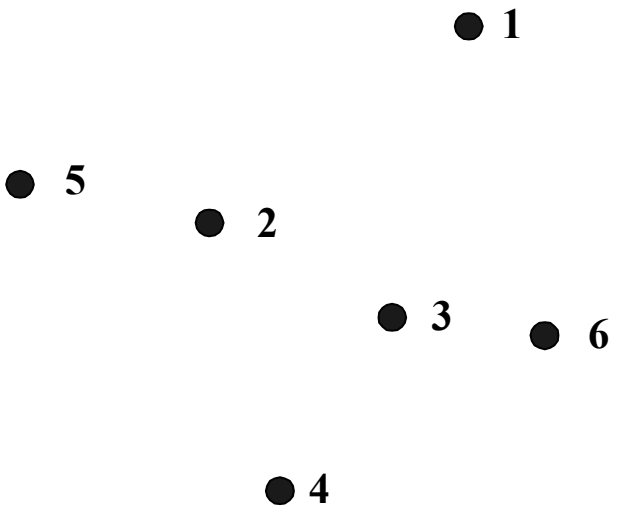


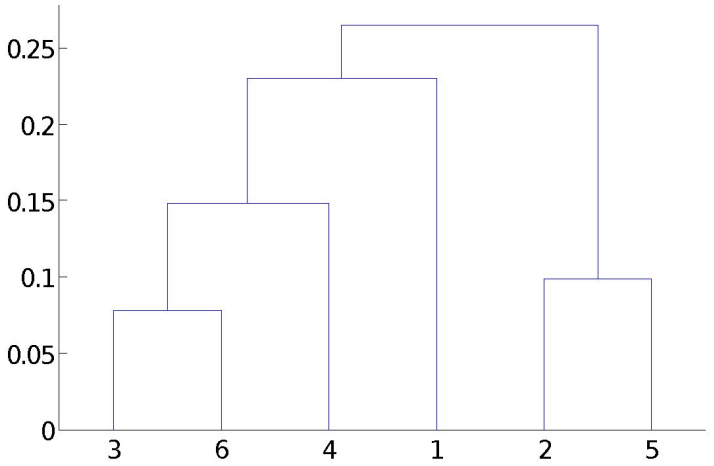


Agglomerative clustering exercise

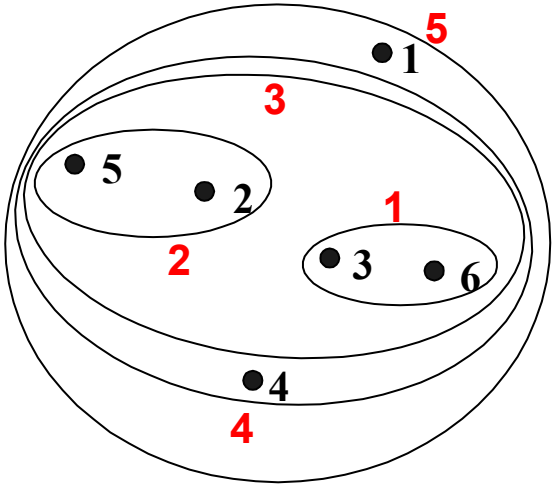
- How do clusters change with different linkage methods?
- Average





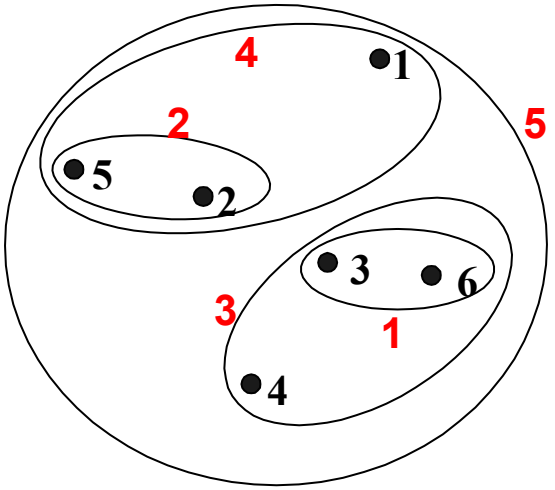


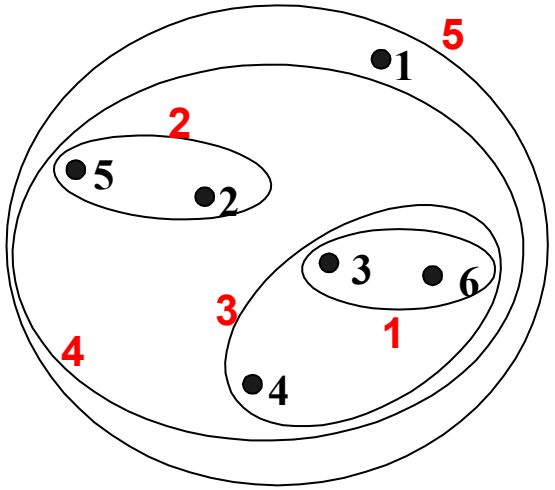
Linkage Comparison



Single

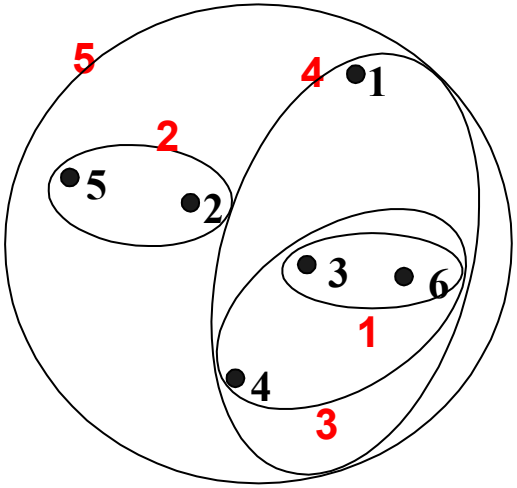
Complete





Average

Ward's Method

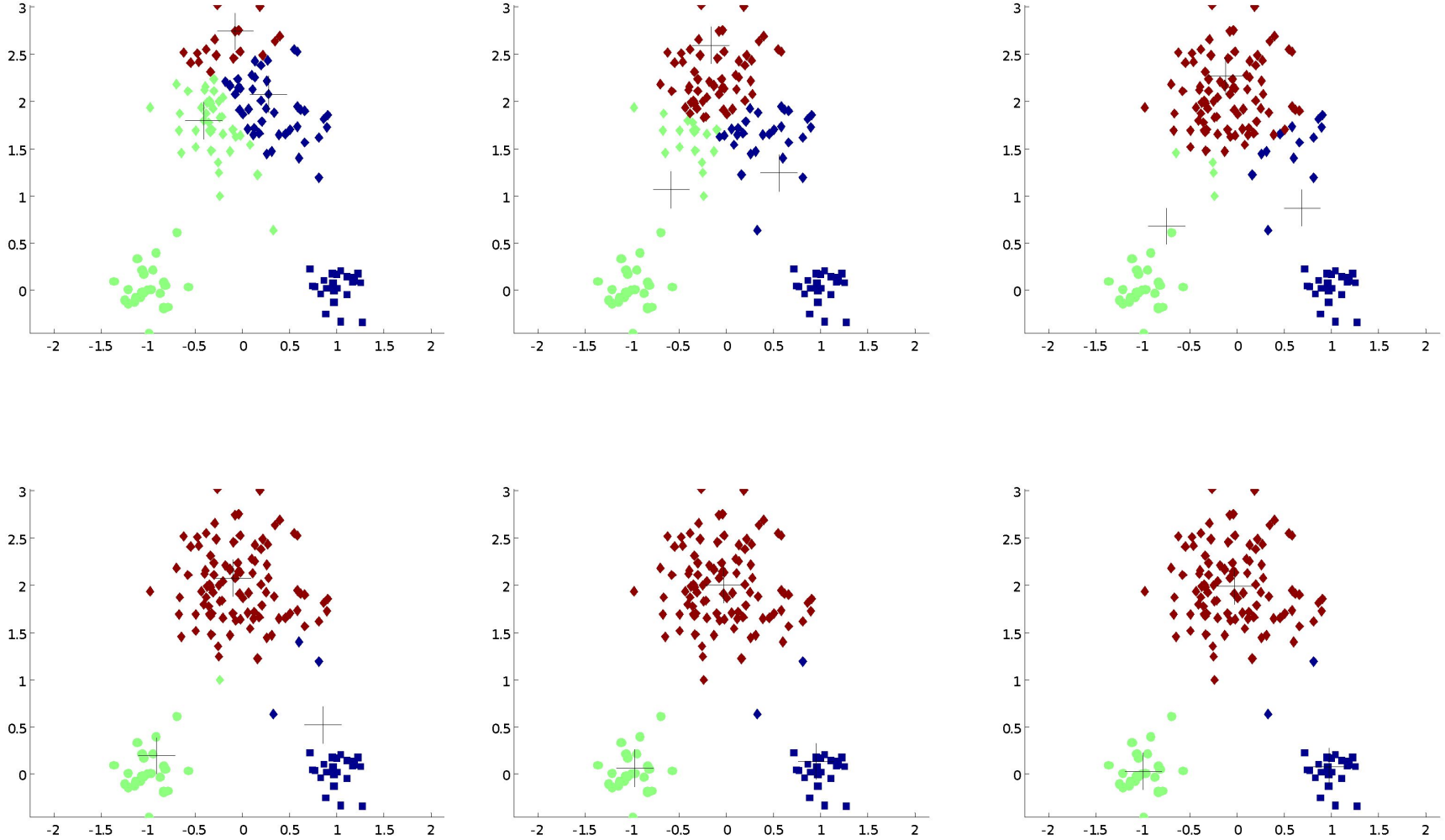


K-means clustering

- Partition clustering approach
- Number of clusters (*K*) must be specified
- Each cluster is associated with a centroid
- Each datapoint is assigned to the cluster with the closest centroid

1: Select K points as the initial centroids.
2: **repeat**
3: Form K clusters by assigning all points to the closest centroid.
4: Recompute the centroid of each cluster.
5: **until** The centroids don't change

Example of K-means clustering



Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.

More on K-means clustering

- Initial centroids often chosen randomly
  - Clusters will vary from one run to the next
- Centroid is typically the mean of the points in the cluster
- ‘Closeness’ is measured by similarity metric (e.g., Euclidean distance)
- Convergence usually happens within first few iterations

Evaluating K-means clusters

Most common measure is Sum of Squared Error (SSE)

- SSE is the sum of the squared distance between each member of the cluster and the cluster's centroid:

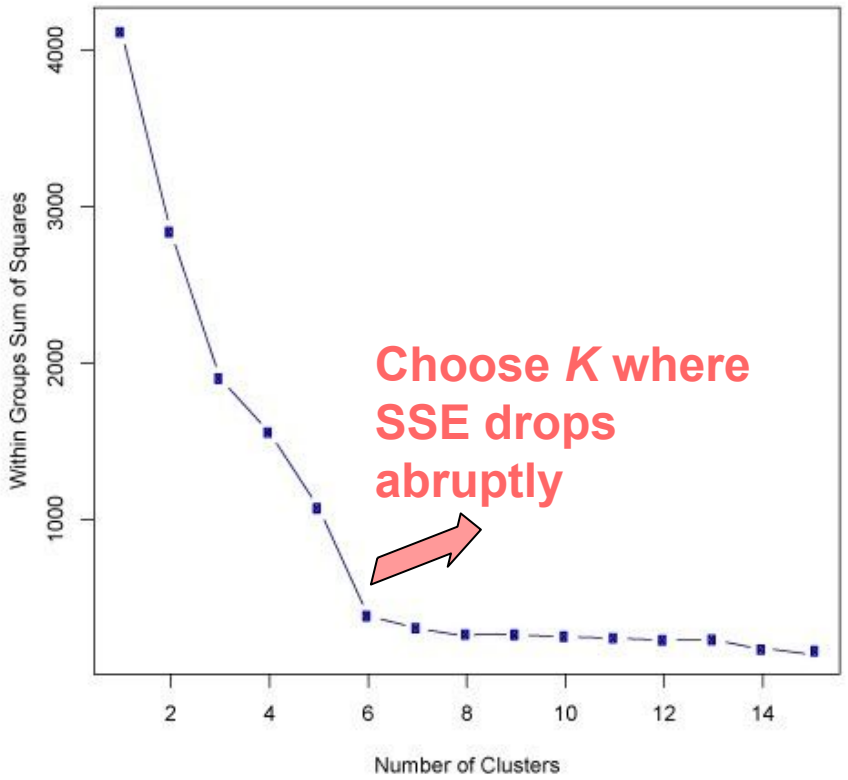
$$SSE = \sum_{i=1}^{K} \sum_{x \in C_i} dist^2(m_i, x)$$

m = centroid in cluster C_i
x = a data point in cluster C_i

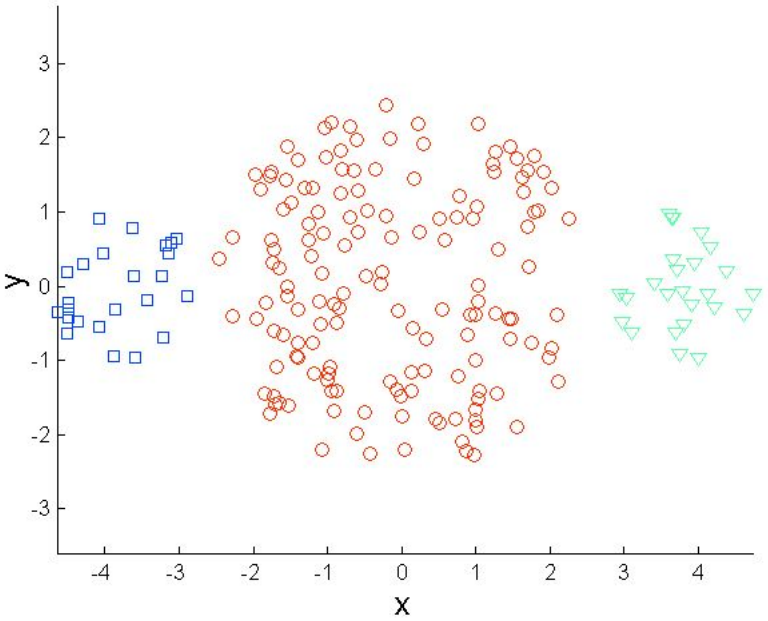
- Given two sets of clusters, we prefer the one with the smallest error
- One way to reduce SSE is to increase *K*
  - Although, a good clustering with small *K* can have a lower SSE than a poor clustering with high *K*

Choosing *K*

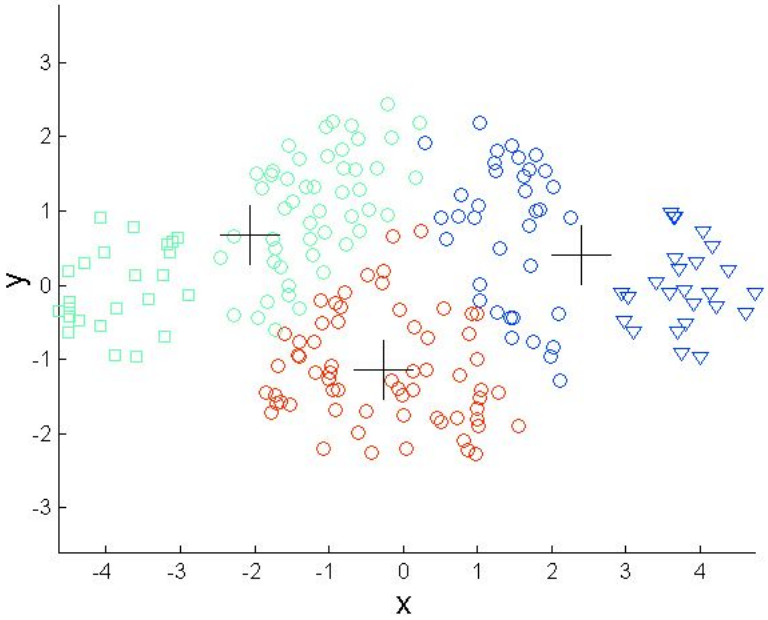
- Visual inspection
- "Elbow method"



Limitations of K-means: Different sizes

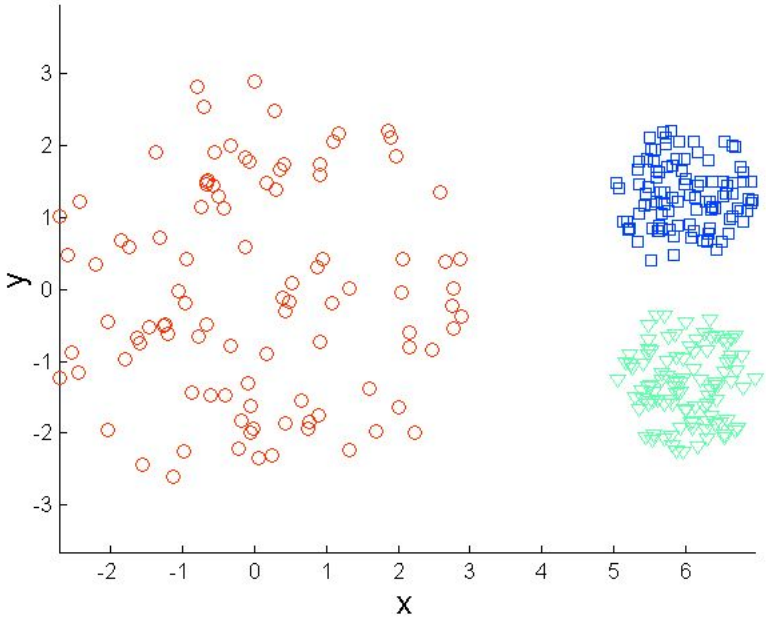


Original Points

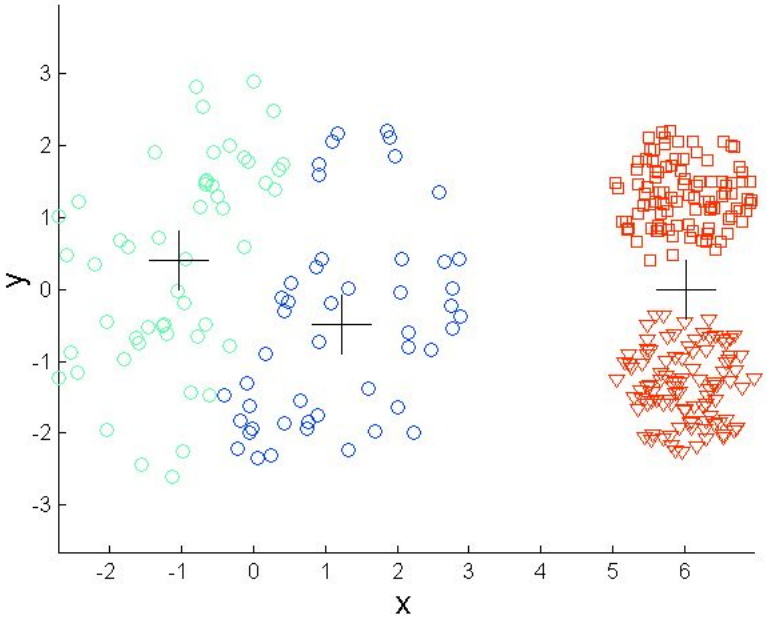


K-means (3 Clusters)

Limitations of K-means: Differing density

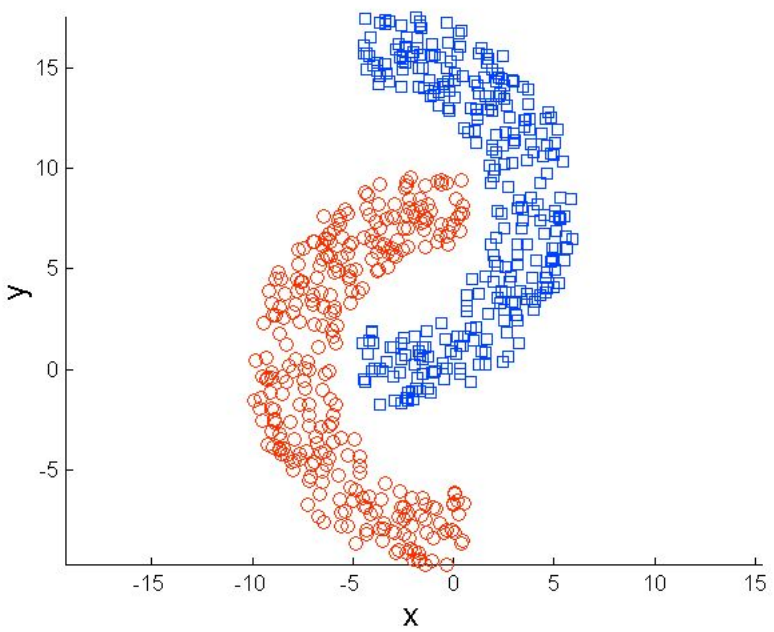


Original Points

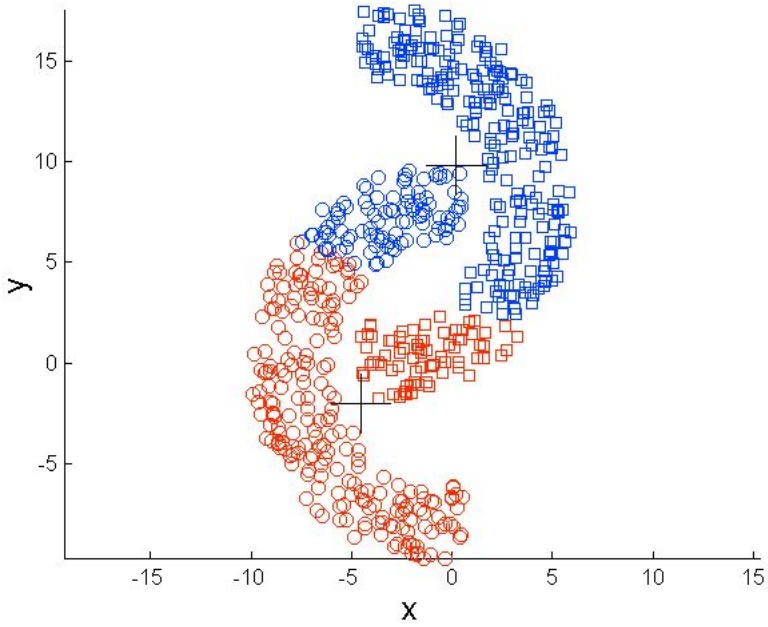


K-means (3 Clusters)

Limitations of K-means: Non-globular shapes

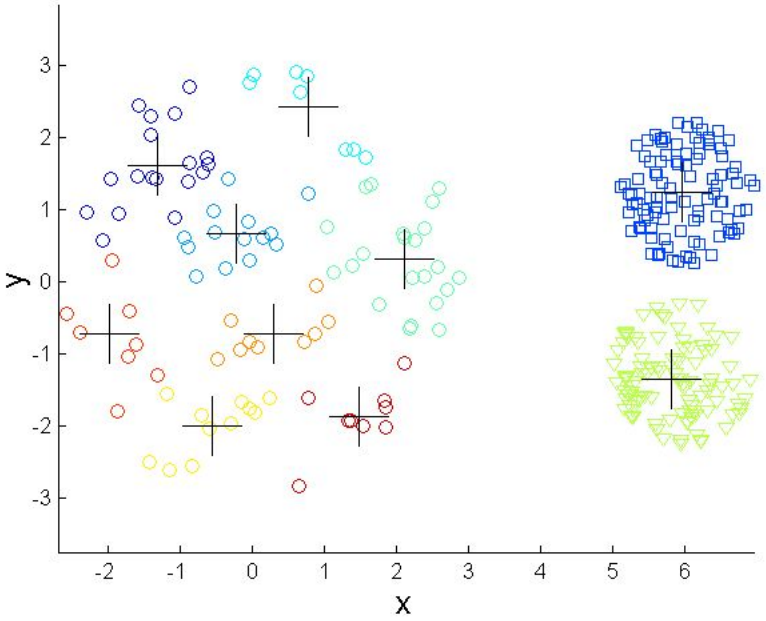


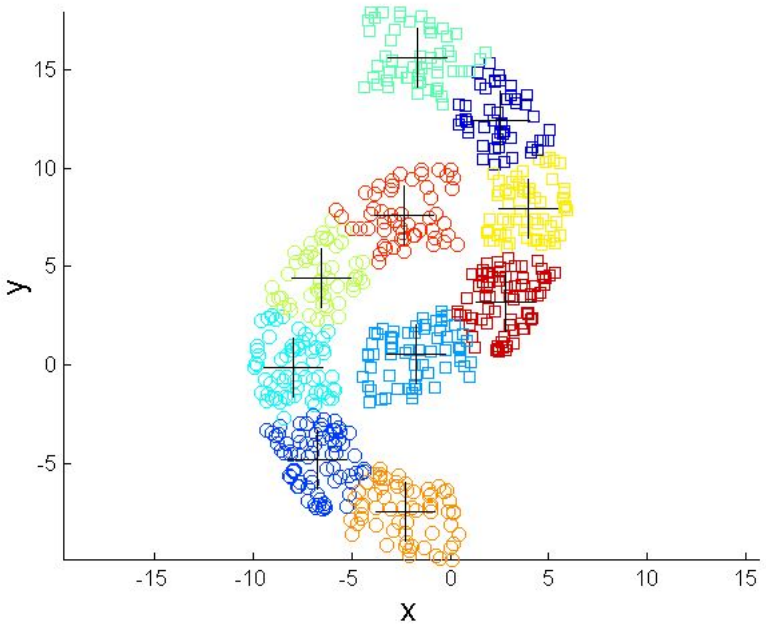
Original Points



K-means (2 Clusters)

Overcoming K-means Limitations





One solution is to use many clusters.
Find parts of desired clusters, but need to put together.

Concerns with selecting initial centroids

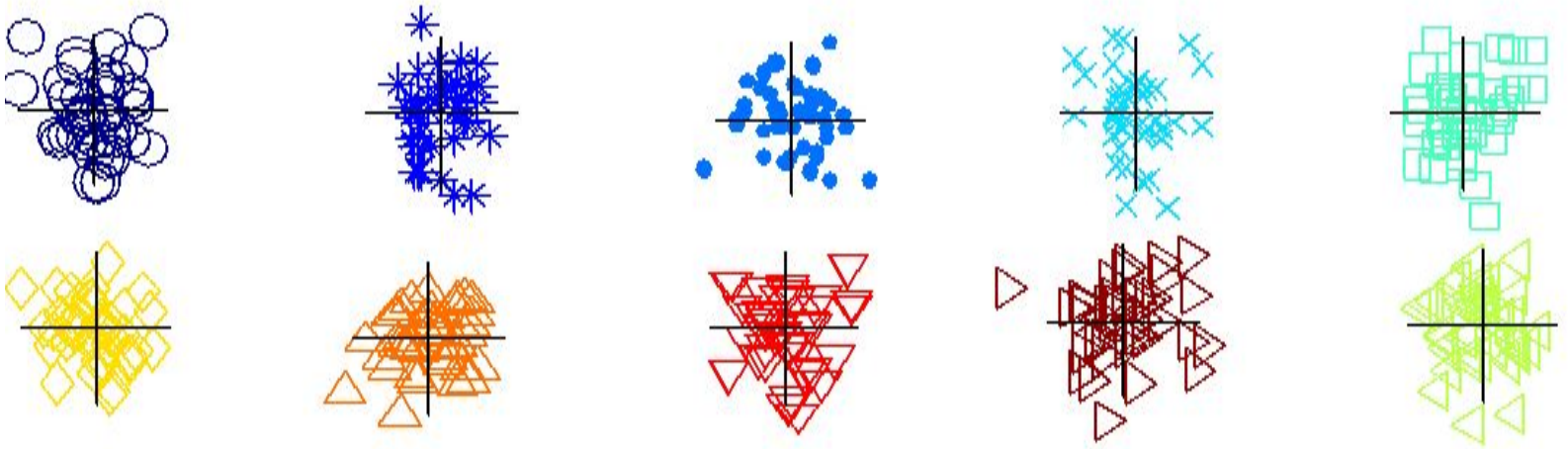
- If there are *K* "real" clusters, then the chance of initially selecting one centroid from each cluster is small

$$P = \frac{\text{number of ways to select one centroid from each cluster}}{\text{number of ways to select } K \text{ centroids}} = \frac{K!n^K}{(Kn)^K} = \frac{K!}{K^K}$$

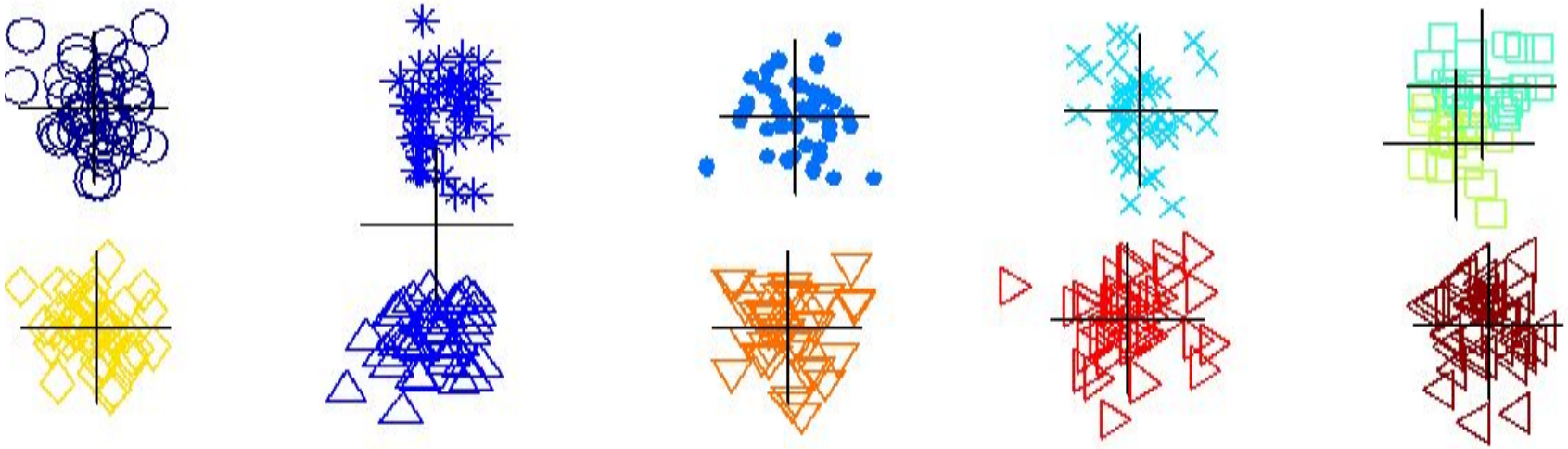
n = size of clusters (assuming relatively similar)

- If *K*=10, then *P* = 10!/10^{10} = 0.00036
- Consider an example of ten clusters….

"Real" clusters:



Clusters obtained with K=10, some "real" clusters without initial centroids:



Solving initial centroids issues

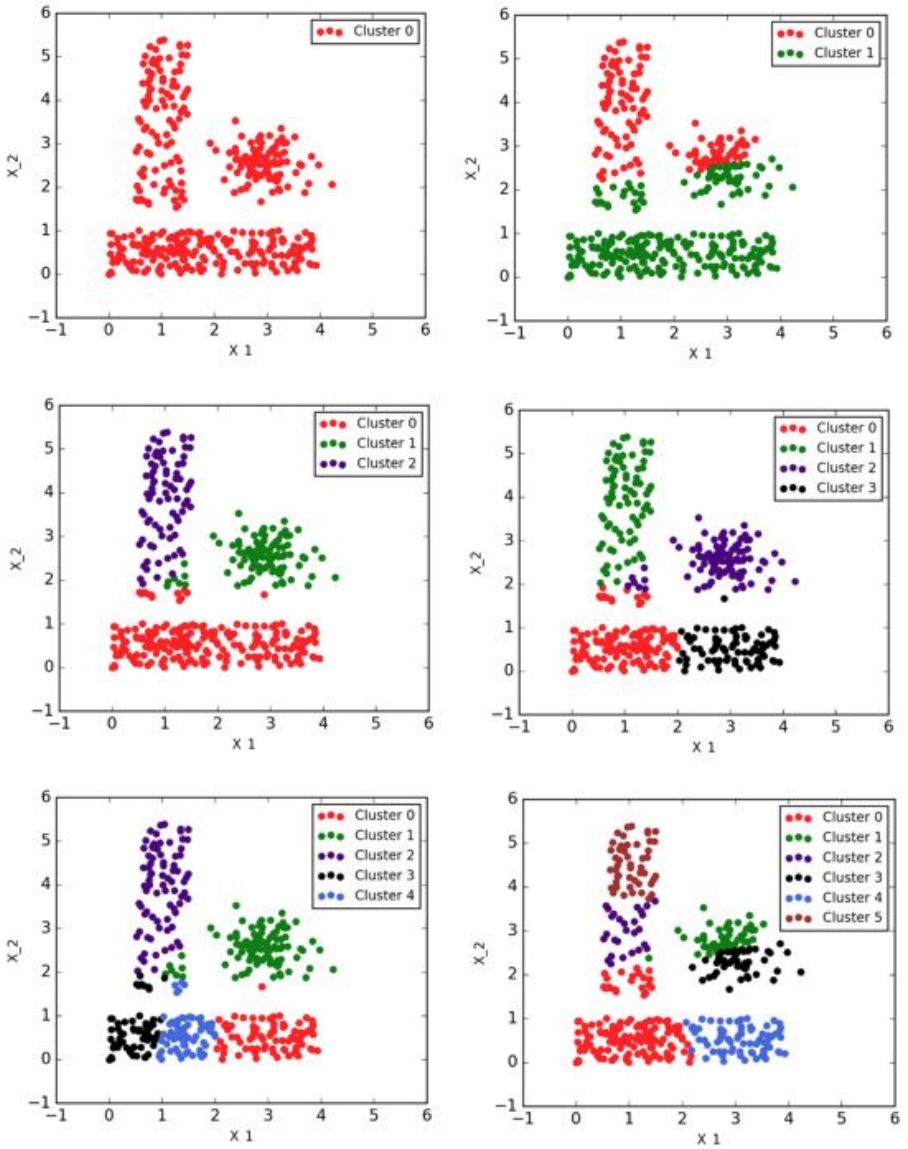
- Multiple runs
- Use hierarchical clustering to determine initial centroids
- Select more than *K* initial centroids, then subselect among these (select most widely separated)
- Post-processing
- Generate a larger number of clusters, then perform hierarchical clustering
- Use Bisecting K-means

Pre- and Post-processing

- Pre-processing
  - Normalize the data
  - Eliminate outliers
- Post-processing
  - Eliminate small clusters (may represent outliers)
  - Split ‘loose’ clusters (i.e., clusters w/ high SSE)
  - Merge clusters that are close (w/ low SSE)

Bisecting K-means

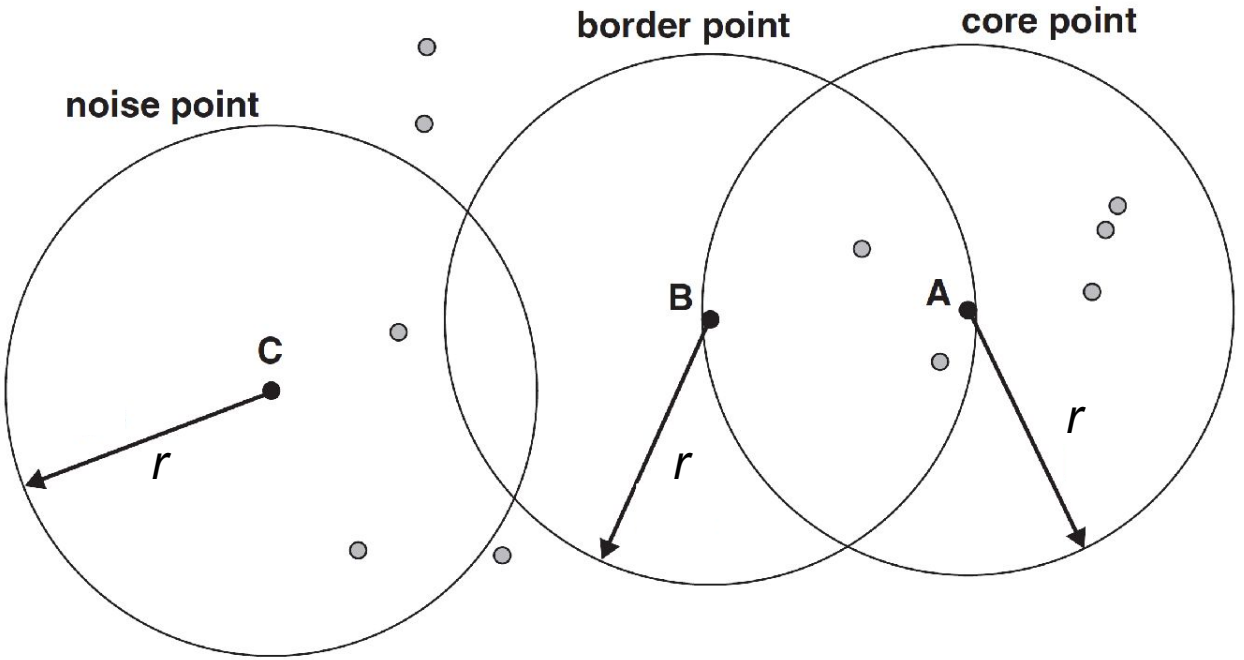
- Combines K-means and hierarchial clustering
- Clusters are iteratively split via regular K-means with *K*=2
- Stops when desired # of clusters is reached



Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.
Figure from Mo Velayati, hhttps://mvelayati.com

Density-based clustering

- Assumes clusters are areas of high density separated by areas of low density
- **Core points** are in areas of a certain density (at least *n* points in radius *r* from the core point)
- **Border points** aren't core points, but are w/in *r* of the core point
- **Noise points** are all other points



Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.

DBSCAN Algorithm

- Eliminate noise points
- Perform clustering on remaining points

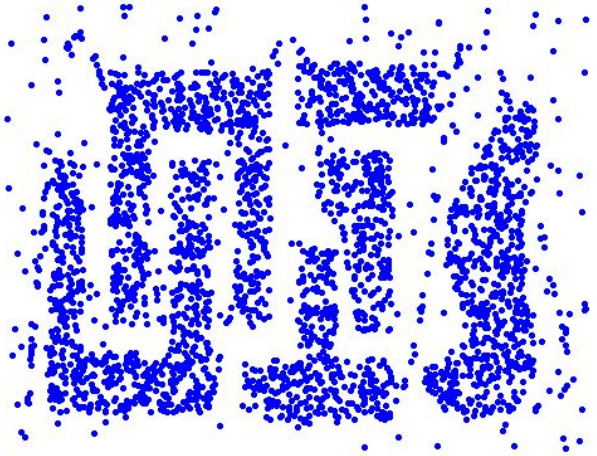
```
current_cluster_label ← 1
for all core points do
  if the core point has no cluster label then
    current_cluster_label ← current_cluster_label + 1
    Label the current core point with cluster label current_cluster_label
  end if
  for all points in the Eps-neighborhood, except i^th the point itself do
    if the point does not have a cluster label then
      Label the point with cluster label current_cluster_label
    end if
  end for
end for
```

Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.

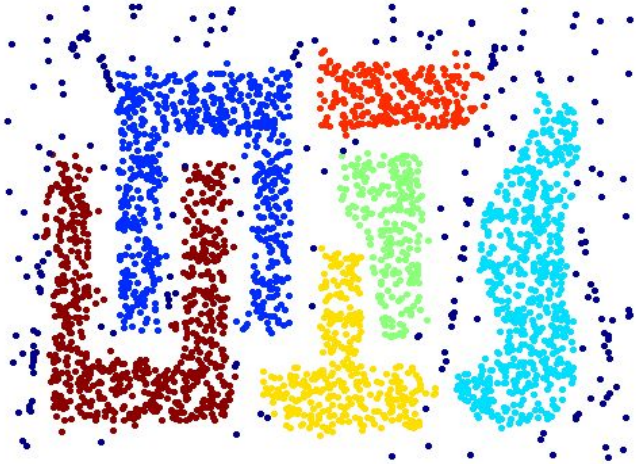
DBSCAN Advantages & Limitations

- **Advantages**:
- Resistant to noise
- Can handle clusters of different shapes and sizes
- Number of clusters is determined by the algorithm

Original data



Clustered



Limitations:

- Struggles to identify clusters with varying densities – clustering is often incomplete at points in low density regions are ignored
- Density can be difficult/expensive to compute in high-dimensional datasets

“Clusters are in the eye of the beholder”

But we might want to evaluate them anyway

Outline

- Background
  - Intro
  - Workflow
  - Similarity metrics
- Clustering algorithms
  - Hierarchical
  - K-means
  - Density-based
- **Cluster evaluation**
  - External
  - Internal

Cluster validation

1) Determining the **clustering tendency** of a set of data, i.e., distinguishing whether non-random structure actually exists in the data.
2) Comparing the results of a cluster analysis to externally known results, e.g., to externally given class labels.
3) Comparing the results of two different sets of cluster analyses to determine which is better.
4) Determining the 'correct' number of clusters.

For 2 and 3, we can further distinguish whether we want to evaluate the entire clustering or just individual clusters.

External measures of cluster validity

External Index: Extend to which cluster labels match externally supplied class labels

- e.g., gene functional groups, tissue of origin
- *F*-measure provides assessment of cluster **purity** and **completeness**
  - Purity: fraction of a cluster taken up by predominant class label
  - Completeness: fraction of items in the class grouped in the cluster at hand
- Rand index compares similarity between two clusterings, or known vs predicted labels

Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.
Handle, Knowles, Kell (2005) Bioinformatics.

Internal measures of cluster validity

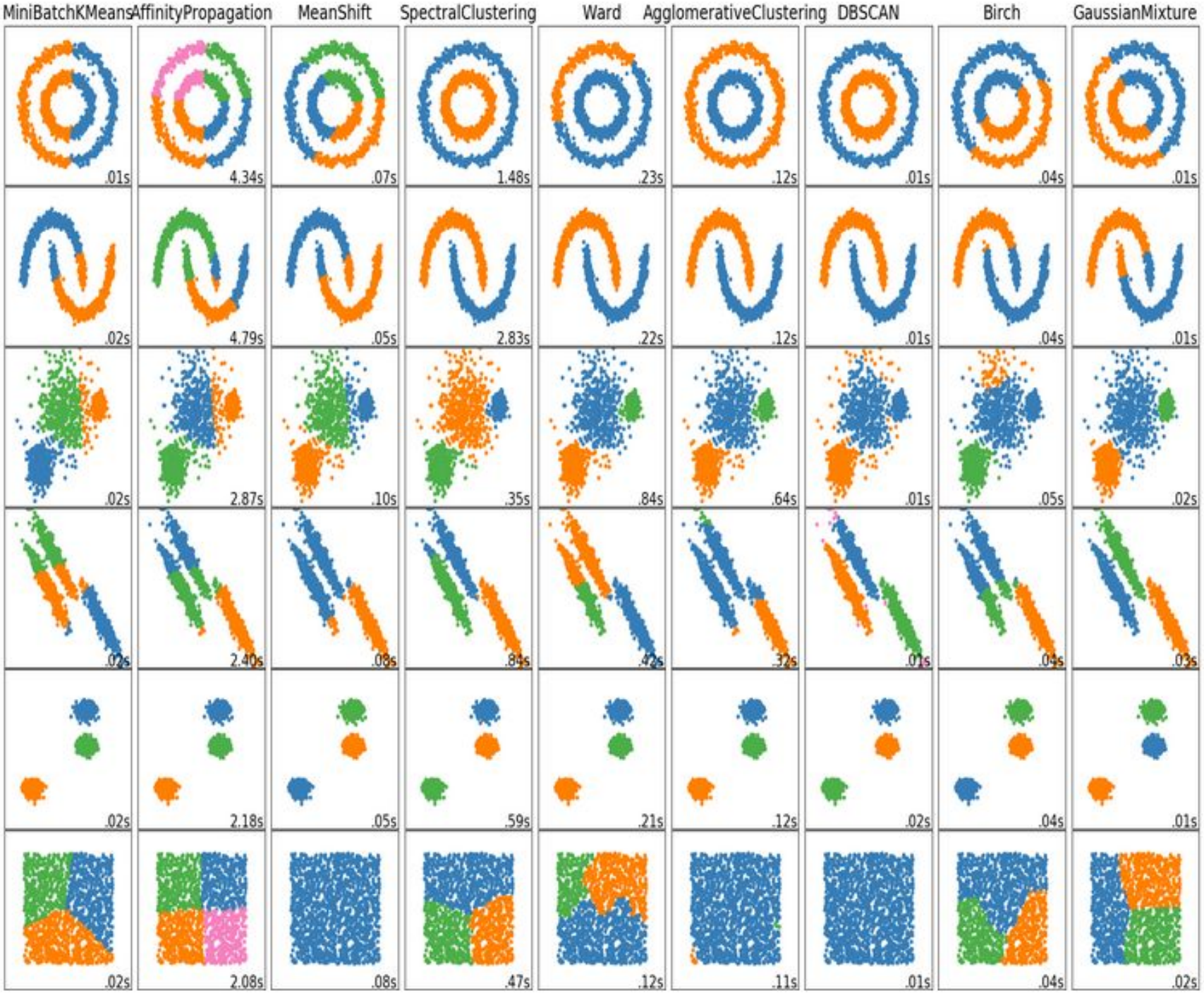
Internal Index: Measures goodness of clustering without respect to external info

- How compact are the clusters?
  - SSE
  - Average/maximum pairwise intra-cluster distances
- How well separated are the clusters?
  - Average inter-cluster distance
  - Minimum separation between individual clusters

Tan, Steinbach, Karpatne, Kumar. Introduction to Data Mining, 2nd Edition.
Handle, Knowles, Kell (2005) Bioinformatics.

“The validation of clustering structures is the most difficult and frustrating part of cluster analysis. Without a strong effort in this direction, cluster analysis will remain a black art accessible only to those true believers who have experience and great courage.”

Algorithms for Clustering Data, Jain and Dubes



http://scikit-learn.org/stable/modules/clustering.html