Clustering (A)

Classical clustering methods.

Attempt to identify groups of observations that are similar with respect to a certain number of variables.

Similarity is "metric": proximity, given some distance, in a space where observations are points, and dimensions are the variables recorded on the observations.

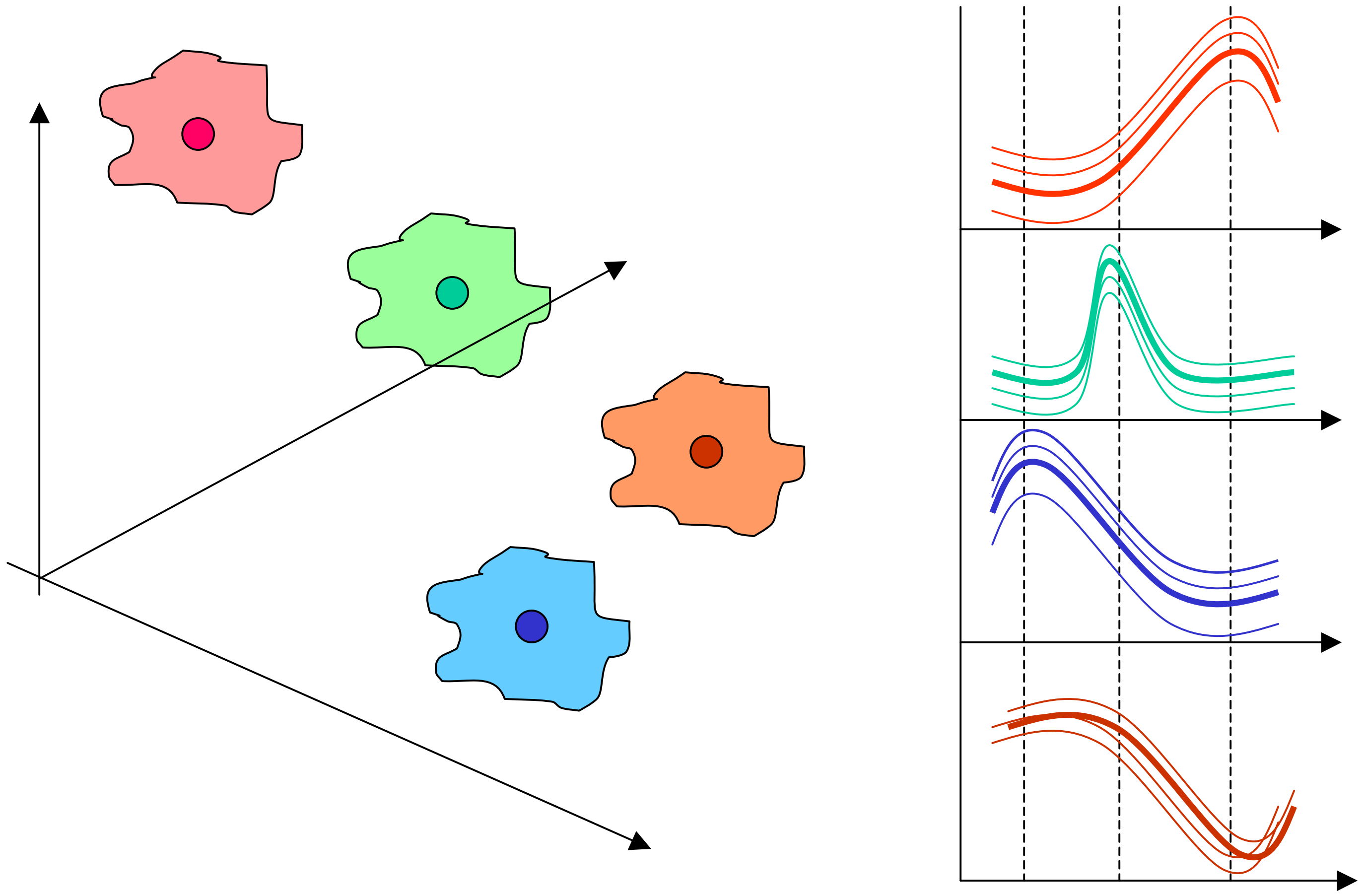
In microarray data analysis, it may be useful to cluster

- "Conditions", when they correspond to samples. In this case we have T observations and N variables (*T* points in an *N*-dimensional space). Unsupervised classification, or "class discovery" for the samples, based on gene expression.

- Genes. In this case we have N observations *T* variables (*N* points in a T-dimensional space).
  Partition genes into classes presenting similar expression profiles over the conditions of interest. Rationale: genes with similar expression profiles may be involved in similar/related functions, and possibly be co-regulated. But the discussion on this is wide open…
  Also, ***extract "characteristic expression patterns"*** as cluster centroids.

(sometimes cluster both genes *and* samples …)

The basic geometric “cartoon”:



Pre-processing of the data matters a big deal:

Does it make sense to center and/or standardize by row? (then a typical Euclidean distance will score as similar profiles with similar shapes, regardless of their overall level or size).

Does it make sense to center and/or standardize by column? (then a typical Euclidean distance will be insensitive to original differences in variability scales and sizes for different "conditions")

In general, does it make sense to apply any left or right affine transformation to our data matrix $\boldsymbol{X}$? These questions may be posed equivalently in terms of choice of distance (other than Euclidean), and they matter.

The literature on clustering is huge (especially due to developments related to data mining), and our discussion will be far from a complete picture.

We consider only algorithms that create partitions of the data (**Exclusive**; overlapping clusters are not allowed; but algorithms allowing for overlapping do exist),

Also, we consider (here) only algorithms that do not use additional information on the possible groups (**Unsupervised**; intrinsic) – Supervised algorithms will go under "classification"; working with a response.

Hierarchical Clustering

Set of *N* data points in R^T

Define similarity/dissimilarity; choose a distance in the space, or give directly a *NxN* matrix of distances between pairs of points.

Proceeding in an agglomerative fashion (“bottom-up”), generate a sequence of nested partitions of the data – progressively less fine – starting with N clusters (each containing a single point), and ending with one cluster (containing *N* points).

- Choose a distance function for points, say $d(x_1,x_2)$. This could be simply the Euclidean distance, or a correlation distance, or any other more complicated distance. Sometimes the point distance is not defined explicitly as a function, but provided through an *NxN* matrix.
- Choose a distance function for clusters, say $D(C_1,C_2)$, which will be based on a summary of the distances among points, as measured by $d(x_1,x_2)$ (for clusters formed by just one points, *D* reduces to *d*).
- Start from *N* clusters, each containing one data point.
- At each iteration, proceed as follows:
  1. Using the current matrix of cluster distances, find the two closest clusters.
  2. Update the list of clusters by merging the two closest.
  3. Update the matrix of cluster distances accordingly
- Repeat until all data points are joined in one cluster.

The method is very sensitive to anomalous data points/outliers

Merging is un-revocable (cannot split a cluster after having created it); thus, a “bad” merging occurring early on will be carried all the way down, affecting the structure of the nested sequence.

If two pairs of clusters are equally (and maximally) close at a given iteration, we have to choose arbitrarily, the choice will affect the structure of the nested sequence.

Defining cluster distance: the linkage method.

Single Linkage (nearest neighbor): the distance between two clusters is defined as the minimum distance between points in them

$$D(C_1,C_2) = \min_{x_1 \in C_1, x_2 \in C_2} d(x_1, x_2)$$

Complete Linkage (farthest neighbor): the distance between two clusters is defined as the maximum distance between points in them

$$D(C_1,C_2) = \max_{x_1 \in C_1, x_2 \in C_2} d(x_1, x_2)$$

Average Linkage (… a compromise): the distance between two clusters is defined as the average distance between points in them

$$D(C_1,C_2) = \frac{1}{\#(C_1)\#(C_2)} \sum_{x_1 \in C_1, x_2 \in C_2} d(x_1, x_2)$$

Centroid Linkage: the distance between two clusters is defined as the distance between to centroids (the means, or else)

$$D(C_1,C_2) = d(\bar{x}_1, \bar{x}_2)$$

Single and complete linkages produce nested sequences that are invariant under monotone transformations of the distance d. This is not the case for the average linkage method. However, the latter is often preferred as a compromise because single linkage tends to produce “long” and “stringy” clusters, while complete linkage tends to produce “small”, “compact” clusters.

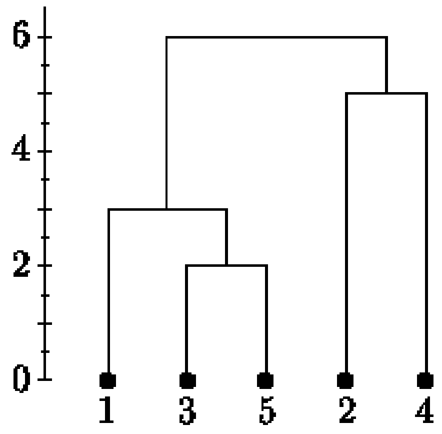
Example:
http://server3.winforms.phil.tubs.de/~treiners/diplom/node19.html

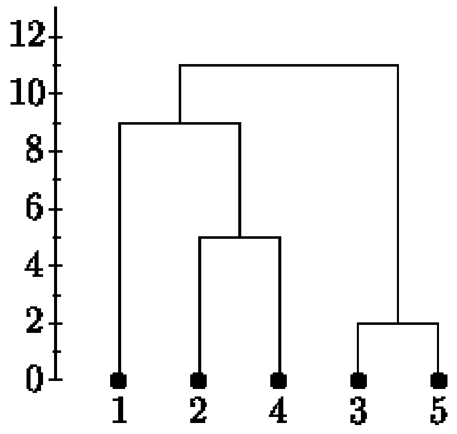
First step in constructing the nested sequence (first iteration): On the left is the matrix of distances among 5 data points. 3 and 5 are the closest, and are therefore merged in cluster "35". On the right is the new distance matrix computed with complete linkage

	1	2	3	4	5
1	0				
2	9	0			
3	3	7	0		
4	6	5	9	0	
5	11	10	$\boxed{2}$	8	0

	35	1	2	4
35	0			
1	11	0		
2	10	9	0	
4	9	6	5	0

Dendrogram representing the nested sequence produced by single linkage (left) and complete linkage (right). The ordinate shows the distance at which the merging occurred. The horizontal ordering of the data points is any order preventing intersections of dendrogram branches.





Hierarchical clustering, per se, does not dictate a partition, and a number of clusters. It provides a nested sequence of partitions, each containing one less cluster. This is more informative than just a partition.

To settle on one partition, we have to decide where to "cut" the dendrogram. We may do so based on

- A threshold distance (dissimilarity) level we are willing to "tolerate" within a cluster
- Looking for obvious "leaps" in distance as we move along the dendrogram
- Looking for an obvious "bend" in distance as we move along the dendrogram

In fact, if we are fairly confident that the selected linkage method is appropriate, and "accidents" along the merging sequence are minor, we could read the distance level associated to various numbers of clusters $\Delta(K,link,seq)=\Delta(K)$, from the top of the dendrogram (K=1 clusters) to the bottom ($K=N$), as a measure of "fit" of the partitioning in K groups. We will discuss choice of K later.

Hierarchical clustering of both "rows" (called observations) and "columns" (called variables), is easily performed in **Minitab**.

Various options for distance and linkage choice.

Can produce the dendrogram.

Can specify a number of clusters or a similarity level to settle on one partition along the nested sequence (possibly one cluster; will go all the way up). Corresponding **cluster memberships** *m(x)* are produced for each observation.

<u>Partitioning algorithms: K-means</u>.

Once again, one needs to select a distance functions for points. Here, we also need to fix the number of clusters we want in the output partition; *K* (<*N*).

Starting from given initial locations of the K cluster centroids, the algorithm uses the data points to iteratively relocate the centroids, and reallocate points to the closest centroid.

- Choose a distance function for points, say $d(x_1,x_2)$.
- Choose a *K*.
- Initialize the *K* centroids (e.g. *K* among the *N* data points, selected at random)

$$\bar{x}_1(0),\ldots\bar{x}_K(0)$$

- At each iteration, proceed as follows:
  1. Compute the distance of each data point from each current cluster centroid.

$$d(x,\bar{x}_k) \quad \forall x,\, k=1...K$$

  2. Update the current cluster membership of each data point, picking the cluster centroid to which the data point is closest.

$$m(x)=\arg\min_{k=1...K} d(x,\bar{x}_k) \quad \forall x$$

  3. Update the current cluster centroids, as averages of the new clusters formed in 2.

$$\bar{x}_k=\frac{1}{\#(x:m(x)=k)}\sum_{x:m(x)=k} x \quad k=1...K$$

- Repeat until cluster memberships, and thus cluster centroids, stop changing.

Also this method is very sensitive to anomalous data points/outliers.

Note that points can "move" from one cluster to another as the algorithm proceeds.

If two cluster centroids are equally (and maximally) close to an observation at a given iteration, we have to choose arbitrarily to what cluster to attribute the point (the problem here is not so serious because points can move…)

There are several "variants" of this algorithm. For example, only the centroid of the cluster getting a new observation may be updated. The iteration would then be described by:

- For each x :
  1. Compute the distances from the current centroids

$$d(x, \bar{x}_k) \quad k = 1...K$$

  2. Update the current cluster membership identifying the closes ("winning") centroid

$$m(x) = \arg\min_{k=1...K} d(x, \bar{x}_k)$$

  3. Update the winning centroid only

$$\bar{x}_k = \frac{1}{\#(x : m(x) = k)} \sum_{x:m(x)=k} x \quad k = 1...K$$

One may cycle through the observations several times before memberships and centroids "stabilize".

The *K*-means algorithm is guaranteed to converge to a local minimum of the function (total within-cluster square distance; if we use Euclidean distance, this is a total within cluster sum of squares)

$$\Delta(K, start) = \sum_{k=1}^{K} \sum_{x:m(x)=k} d^2(x, \bar{x}_k)$$

$$= \sum_{x} \min_{k=1\dots K} d^2(x, \bar{x}_k)$$

$$= \sum_{x} \sum_{k=1}^{K} Ind(m(x) = k) d^2(x, \bar{x}_k)$$

but not necessarily to a global one. The second form uses only the centroids as "optimization variables" (memberships can be derived from them), and helps us see how the final value of the objective function depends on the starting $\bar{x}_1(0), \dots \bar{x}_K(0)$. The third form is useful in comparison with SOM.

Other relevant remarks:

- A reasonable *K* may be unknown
- Initialization of the centroids may make a difference (determine in what local minimum we end up)
- Are cluster averages the most representative "prototypes" for clusters?
- Cluster boundaries tend to have the shape of a "ball" with respect to the chosen distance.

If we are fairly confident that initialization allows us to reach a "good" minimum, we could use *Δ(K,start)=Δ(K)* as a measure of "fit" of the partitioning in K groups and calculate it for several values of K. We could then fix a threshold, or look for "leaps" or "bends" in *Δ(K)*, to select a K.

K-means clustering of "rows" (observations) on the basis of "columns" (variables), is easily performed in **Minitab** (Euclidean distance only).

Can specify the final partition through a choice of *K*, or of an initial partition of the points. Corresponding **cluster memberships** are produced for each observation.

Some generalizations of partitioning algorithms:

- Self-Organizing Maps: add an underlying “topology” (neighboring structure on a lattice) that relates cluster centroids to one another.

- “Fuzzy” K-means: allow for a gradation of points between clusters; *soft partitions*.

Some remarks for both hierarchical and K-means clustering

Because methods are so sensitive to possibly “anomalous” positions of points, **stability analyses** are very important

- Perturb *adding noise* to the data, and repeat the clustering
-
- Perturb *deleting points* from the data
- (more generally, perturb *re-sampling* from the data)

Are the outcomes (dendrogram and chosen partition; partition in *K* groups and choice of *K*) stable? We will go into this for the choice of *K* (where to cut the dendrogram; how many groups to postulate).

How strong is the “association” of an observation x to the cluster to which it is attributed, say the *m(x)*-th ?

Cluster memberships do not provide this information, but we could compute

$$D(x,C_k) \quad \text{or} \quad d(x,\bar{x}_k)$$

for all clusters in the partition, to see if and by how much the distance from the *m(x)*-th cluster is smaller than the other ones.

Textbooks:

Hartigan, 1975, *Clustering Algorithms*, Wiley NY

Gnanadesikan; 2nd ed. 1997, *Methods for Statistical Data Analysis of Multivariate Observations*, Wiley NY

Seber, 1984, *Multivariate Observations*, Wiley NY

Kohonen, 2nd ed. 1997, *Self Organizing Maps*, Springer-Verlag