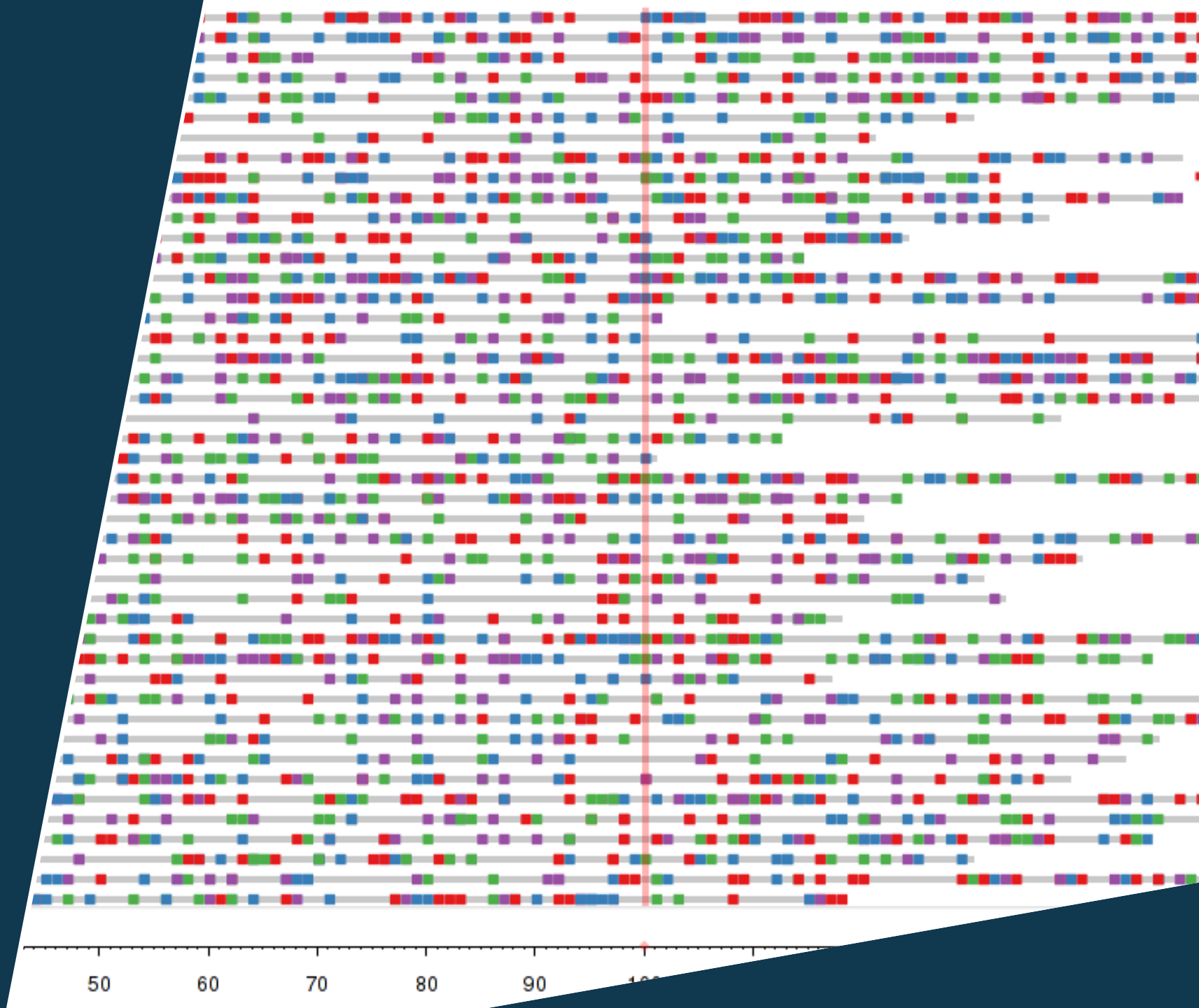
Seriation in

Megaplots



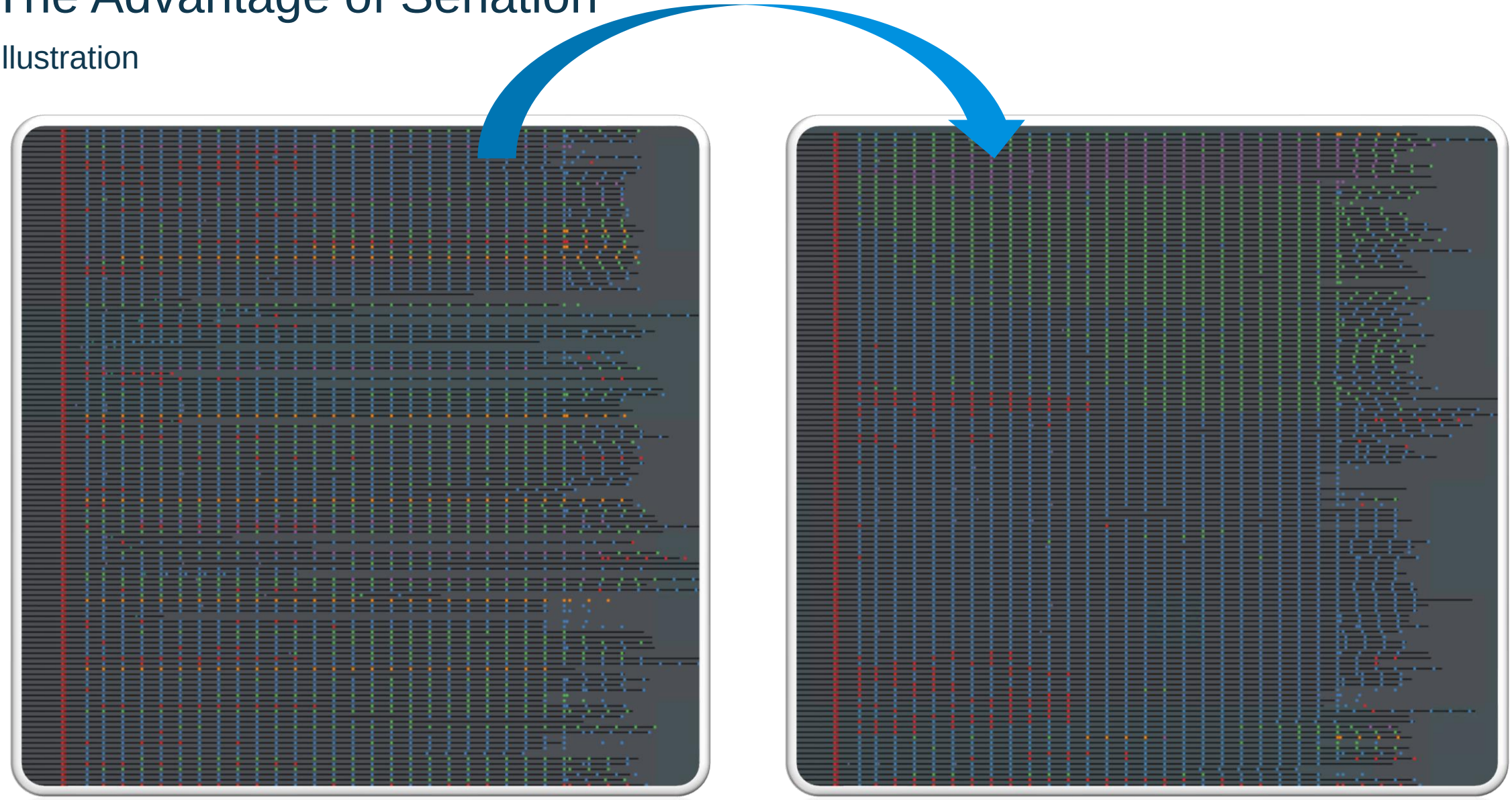
Why do we need Seriation?

Seriation in MEGAPLOTS

- The idea behind Megaplots:
  - Visualizing clinical data by showing individual patient data during the course of the study
  - Detection of patterns in the data, e.g. time-dependent effects
- Arranging subjects helps detecting patterns
- Two Steps:
  - Choose a distance measure to calculate distances between study courses of subjects
  - Choose seriation algorithm to locate similar study courses close to each other

The Advantage of Seriation

Illustration



Distance Measures

Different Types of Distance Measures

- The choice of a suitable distance measure is very important, since it is the foundation of the seriation
- Distances calculated with R package TraMineR
- Treating the study course of each subject as a state sequence

- There are three different methods to calculate the distance between two sequences:
  I. Distances between the distributions of the sequences
  II. Distances based on the count of common attributes
  III. Edit distances

Gabadinho, A., Ritschard, G., Müller, N. S., & Studer, M. (2011). Analyzing and Visualizing State Sequences in R with TraMineR. Journal of Statistical Software,40(4), 1-37.

Distances between the distributions of sequences

Distance Measures: Method I

- Let $p_{j|x}$ be the proportion of time spent in state j in sequence x
- p_j is the overall proportion of time spent in state j
- Manhattan Distance:
  - $d_{MAN}(x,y) = \sum_{j=1}^{|E|} |p_{j|x} - p_{j|y}|$
- X²-Distance:
  - $d_{CHI2}(x,y) = \sum_{j=1}^{|E|} \frac{(p_{j|x} - p_{j|y})^2}{p_j}$

Example:

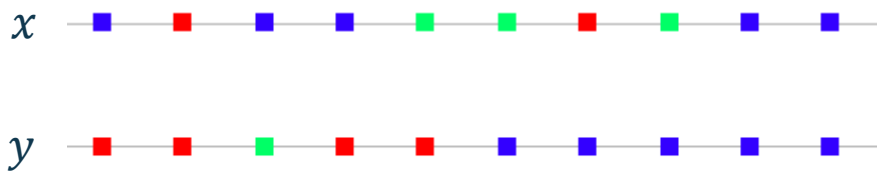
Distributions:
p_x = (0.2, 0.3, 0.5, 0)
p_y = (0.4, 0.1, 0.5, 0)
p = (0.3, 0.2, 0.5, 0)

Distances based on count of common attributes

Distance Measures: Method II

- Number of common attributes between sequence x and y: $A(x, y)$
- Distance: $d_A(x, y) = A(x, x) + A(y, y) - 2A(x, y)$
- Simple Hamming Distance
  - Only for Sequences of the same length
  - Counts the number of non-matching elements
- Longest Common Prefix
  - $A(x, y)$ is the number of successive common positions starting from the beginning of the sequences
- Longest Common Suffix
  - $A(x, y)$: number of common positions from the end
- Longest Common Subsequence
  - Number of Elements in one sequence that can be uniquely matched with elements occurring in the same order in the other sequence

Example:



Hamming Distance: $d_{HAM}(x, y) = 7$

Longest Common Prefix: $d_{LCP}(x, y) = 20$

Longest Common Suffix: $d_{RLCP}(x, y) = 16$

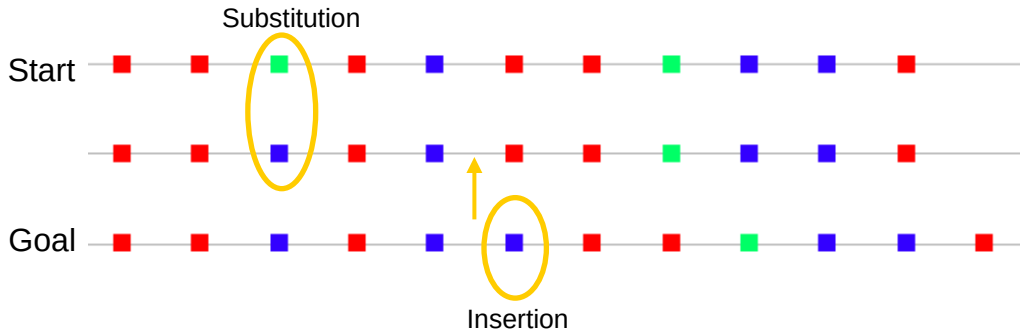
Longest Common Subsequence: $d_{LCS}(x, y) = 10$

Edit Distances - Overview

Distance Measures: Method III

Idea:

- Transform the one sequence into the other one
- For each transformation step, a cost is charged
- Distance: Minimal costs of transforming the one sequence into the other one



- Two types of possible operations/costs:
  - Substitution of state a by state b: $\gamma(a, b)$
  - Insertion or deletion (Indel) of state a: $c_{I(a)}$

Different types of edit distances:

- Optimal Matching $\mathbf{OM}$
  - Only substitution and indel possible
- Localized Optimal Matching $\mathbf{OMloc}$
- Spell-length-sensitive Optimal Matching $\mathbf{OMslen}$
- Optimal Matching of spell sequences $\mathbf{OMspell}$
- Optimal Matching of transition sequences $\mathbf{OMstran}$
- Dynamic Hamming Distance $\mathbf{DHD}$

Studer, M. & Ritschard, G. (2016). What matters in differences between life trajectories: A comparative review of sequence dissimilarity measures, Journal of the Royal Statistical Society, Series A, 179(2), 481-511. D

Edit Distances – Part 1

Distance Measures: Method III

Dynamic Hamming Distance DHD:

- No Insertion/Deletion → only for sequences of the same length
- Substitution cost depends on the position t in the sequence: calculate the cross-section of transition rates observed between position $t-1$ and t and between t and $t+1$
- Transition rates:
  - Higher cost for substituting between states when the transitions between them are rare; low cost when frequent transitions are observed
  - Transition rate between states a and b: probability $p(a|b)$ of switching from state a to state b between two successive positions

Localized Optimal Matching $OMloc$:

- Indel cost depends on the two adjacent states
  - Inserting/deleting a state similar to its neighbors would only change the length of the spell in that state → no effect on the sequencing
  - Insertion of a state different to its neighbors has more consequences → higher cost
  - Inserting state z between a and b:

$$c_I(z|a,b) = e\,\gamma_{max} + g\,\frac{\gamma(a,z)+\gamma(b,z)}{2}$$

  - γ_{max} maximal substitution cost
  - e cost of spell length transformation
  - g local insertion cost

Additional Parameters

Edit Distances – Part 2

Distance Measures: Method III

Spell-length-sensitive Optimal Matching **OMslen**:

- State a in a spell of length t will be denoted as a_t with a insertion/deletion cost defined as $\mathrm{c_I^H}(\mathrm{a}_t) = \frac{c_I(a_t)}{t^h}$
  - c_I basic insertion/deletion cost
  - h exponential weight of spell length
- Cost of substituting state a_{t_1} with b_{t_2}:

$$\gamma^H(a_{t_1}, b_{t_2}) = \gamma(a,b) \cdot link$$

  - $\gamma(a,b)$ basic substitution cost
  - $link$: function of $\frac{1}{\sqrt{t_1}}$ and $\frac{1}{\sqrt{t_2}}$
    - **mean** (default)
    - **gmean** (geometric mean)

Optimal Matching of spell sequences **OMspell**:

- Idea: consider for each different value of t a spell in state a during t units of time as a distinct element, denoted by a_t, of the alphabet
- Insertion/Deletion cost:

$$c_I^S(a_t) = c_I(a) + \delta \cdot (t-1)$$

- Substitution cost:

$$\gamma^S(a_{t_1}, b_{t_2}) = \begin{cases} \delta \cdot |t_1 - t_2| & if\ a = b \\ \gamma(a,b) + \delta \cdot (t_1 + t_2 - 2) & otherwise \end{cases}$$

  - $c_I(a)$ basic indel cost
  - $\gamma(a,b)$ basic substitution cost
  - δ cost of spell length transformation

Edit Distances – Part 3

Distance Measures: Method III

Optimal Matching of transition sequences **OMstran**:

- Idea: Instead of the states consider the transitions of the sequence
  - Example: Sequence: $a - a - b - b - c$
    Transitions: $aa - ab - bb - bc$
- Indel cost: $c_I^B(a \rightarrow b) = w\, c_I(a) + (1 - w)\, c_T(a \rightarrow b)$
- Substitution cost:

$$\gamma^B(a \rightarrow b, c \rightarrow d) = w\, \gamma(a, c) + (1 - w)\big(c_T(a \rightarrow b) + c_T(c \rightarrow d)\big)$$

- $c_I(a)$ indel cost of the origin state a
- $c_T(a \rightarrow b)$ transition type cost: **constant** (default), **subcost** (based on substitution cost), **prob** (based on transition probabilities)
- $\gamma(a, c)$ substitution cost between the origin states a and c
- $w \in [0,1]$ coefficient for controlling the trade-off between the cost related to the origin state and the cost related to the type of transition

Parameters for the Distance Measures – Part 1

Normalization

- d: distance between two sequences x and y
- $|x|, |y|$: length of the sequences x, resp. y
- m: maximal possible distance between two sequences of the length $|x|$ and $|y|$
- Possible values for the normalization parameter:
  - **none** (default)
  - **maxlength**: $\frac{d}{\max\{|x|,|y|\}}$
  - **gmean**: $1 - \frac{m-d}{\sqrt{|x| \cdot |y|}}$
  - **maxdist**: $\frac{d}{m}$
  - **YujianBo**: $2 \cdot \frac{d}{m+d}$
  - **auto**: **gmean** for distance measures **LCS, LCP, RCLP**, **maxlength** for distance measures **OM, HAM, DHD**, **YuhianBO** for distance measures **OMloc, OMslen, OMspell, OMstran**

Parameters for Distance Measures – Part 2

Insertion/Deletion Cost and Substitution Cost

- Insertion/Deletion Cost:
  - Possible values: **auto** (max(substitution cost) / 2), numeric value
- Substitution Cost:
  - **CONSTANT**: Same cost for all substitutions (default: 2)
  - **INDELS, INDELSLOG**: based on estimated indel cost
    - For each state a, derive state relative frequency f_a
    - **INDELS**: $indel_a = \frac{1}{f_a}$, **INDELSLOG**: $indel_a = \log\left[\frac{2}{1+f_a}\right]$
    - $\gamma(a,b) = indel_a + indel_b$
  - **TRATE**: derived from the observed transition rates
    - $P(a|b)$ probability of transition from state b to a
    - $\gamma(a,b) = 2 - P(a|b) - P(b|a)$
  - **ORDINAL:** states are considered ordinal, cost is proporional to distance of the two states

Overview of Distance Measures and their Parameters

Distance Measure	Parameters
OM	Substitution Cost, Insertion/Deletion Cost, Normalization
OMloc	Substitution Cost, Normalization, Cost of spell length transformation, Local Insertion Cost
OMslen	Substitution Cost, Insertion/Deletion Cost, Normalization, Substitution Cost Function, Exponential weight of spell length
OMspell	Substitution Cost, Insertion/Deletion Cost, Normalization, Cost of spell length transformation, Exponential weight of spell length
OMstran	Substitution Cost, Insertion/Deletion Cost, Normalization, Transition Indel Cost Method, Account for the transition from the previous state, Duplicate the last column, Origin-Transition Trade-Off weight
HAM, DHD	Substitution Cost, Normalization
CHI2	Normalization, Interval Length, Intervals Overlapping, Statedistribution as weights
EUCLID	Normalization, Interval Length, Intervals Overlapping
LCS, LCP, RLCP	Normalization

Seriation Algorithms

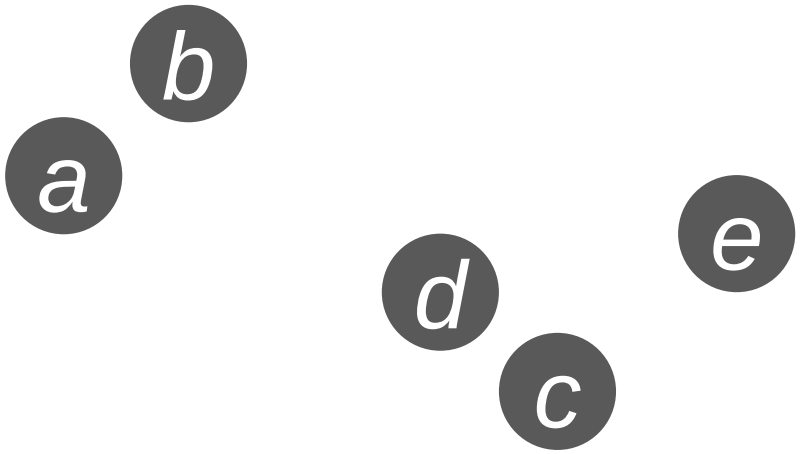
Seriation Algorithms

- Several seritation algorithms are available in Megaplots and can be selected by the user
- The implementation of these algorithms is based on the R package `seriation`
- Different Algorithms to arrange the subjects based on a matrix of pairwise distances:
  - Algorithms using hierarchical clustering and leaf ordering:
    - Hierarchical Clustering
    - Optimal-Leaf Ordering
    - Gruvaeus Wainer Heuristic
  - Algorithms minimizing the sum of distances
    - Visual Assessment of Tendency
    - Traveling Salesperson Problem

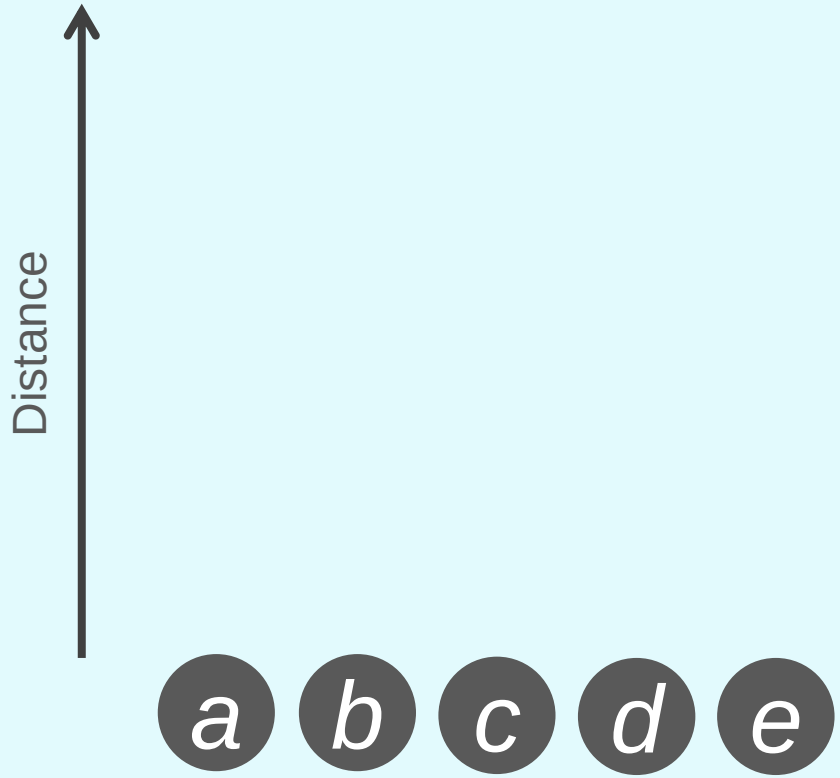
Hahsler M, Hornik K, Buchta C (2008). “Getting things in order: An introduction to the R package seriation.” Journal of Statistical Software, 25(3), 1–34. ISSN 1548-7660

Agglomerative Clustering

An introductory example

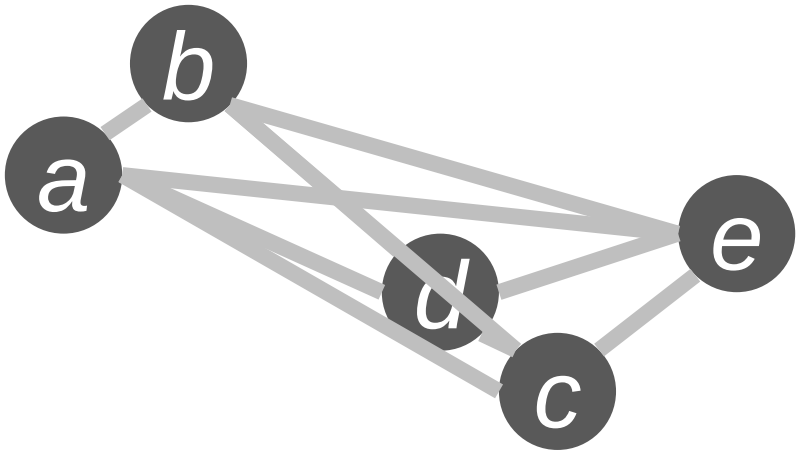


Each object forms an own cluster

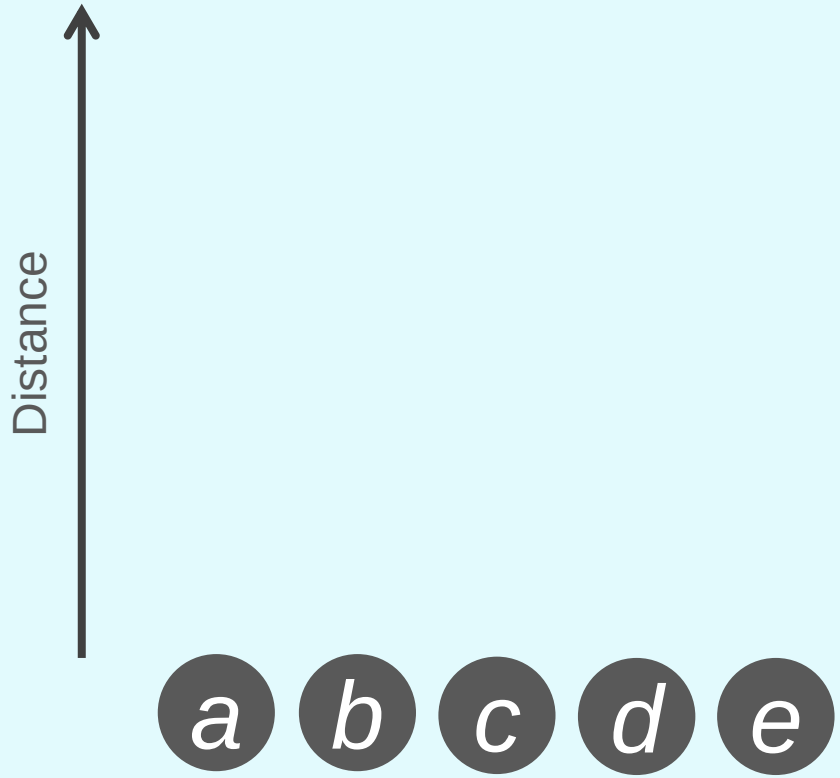


Agglomerative Clustering

An introductory example



Compute all pairwise distances



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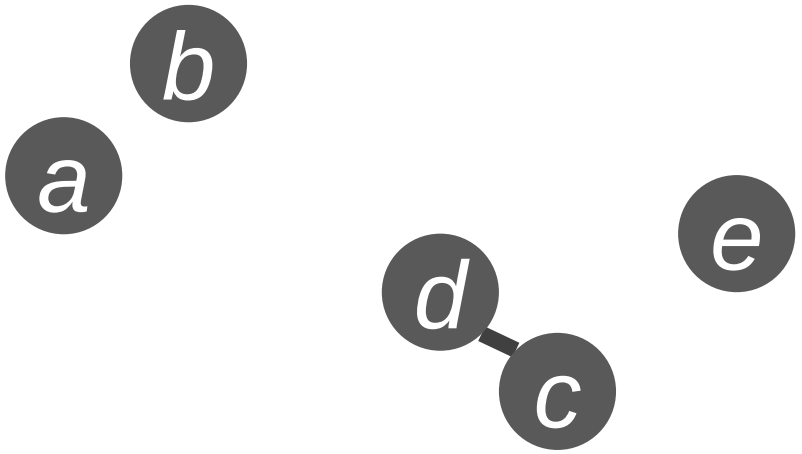
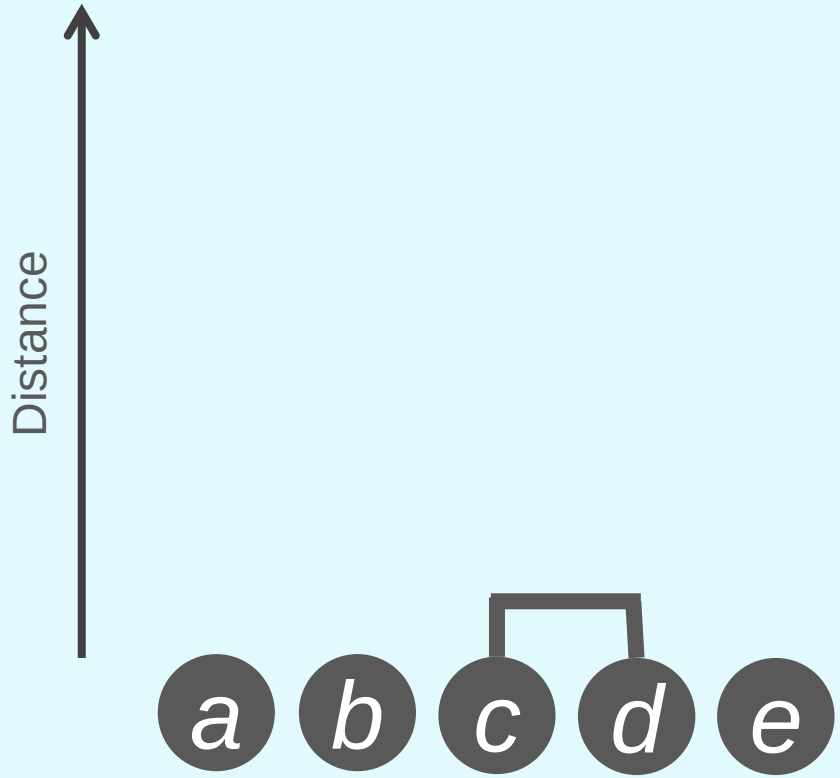
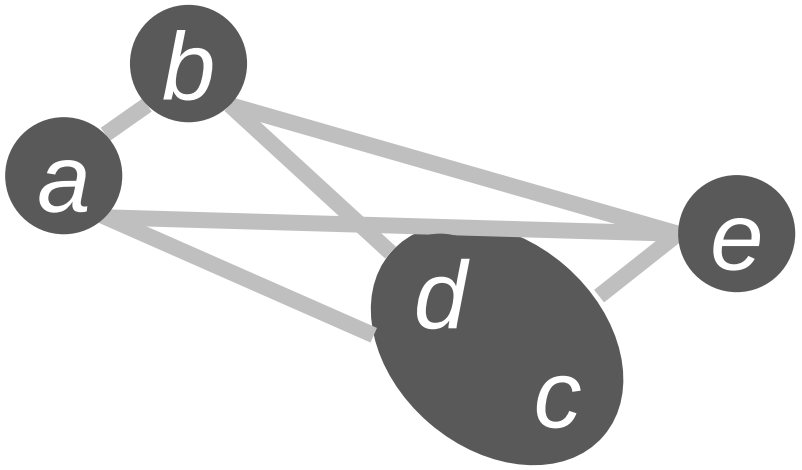




Join the two closest objects/clusters

Agglomerative Clustering

An introductory example



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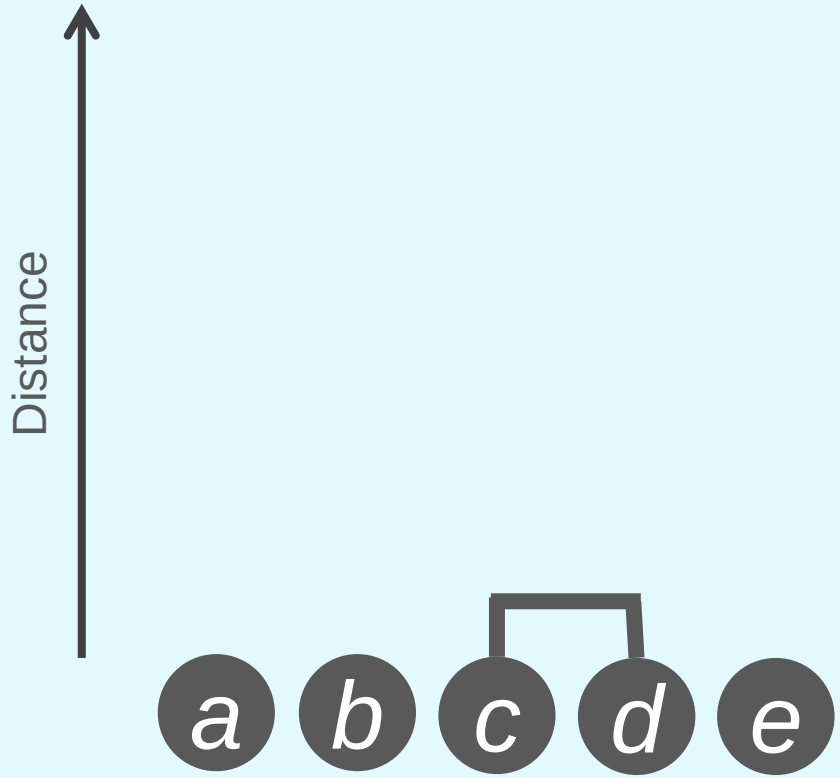

Agglomerative Clustering

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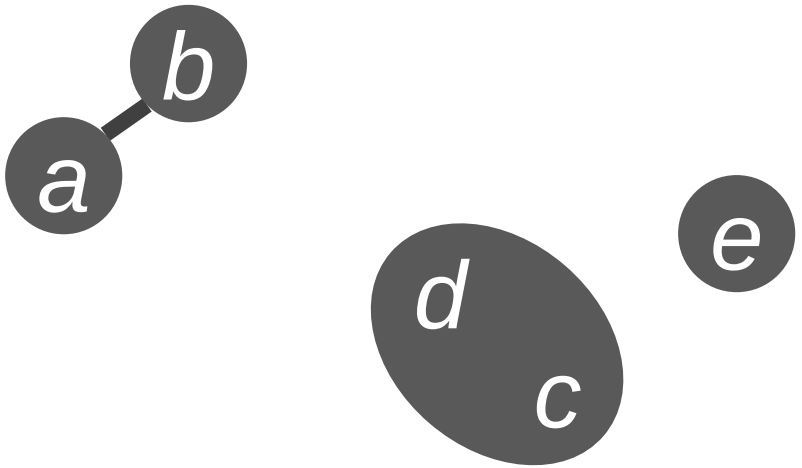
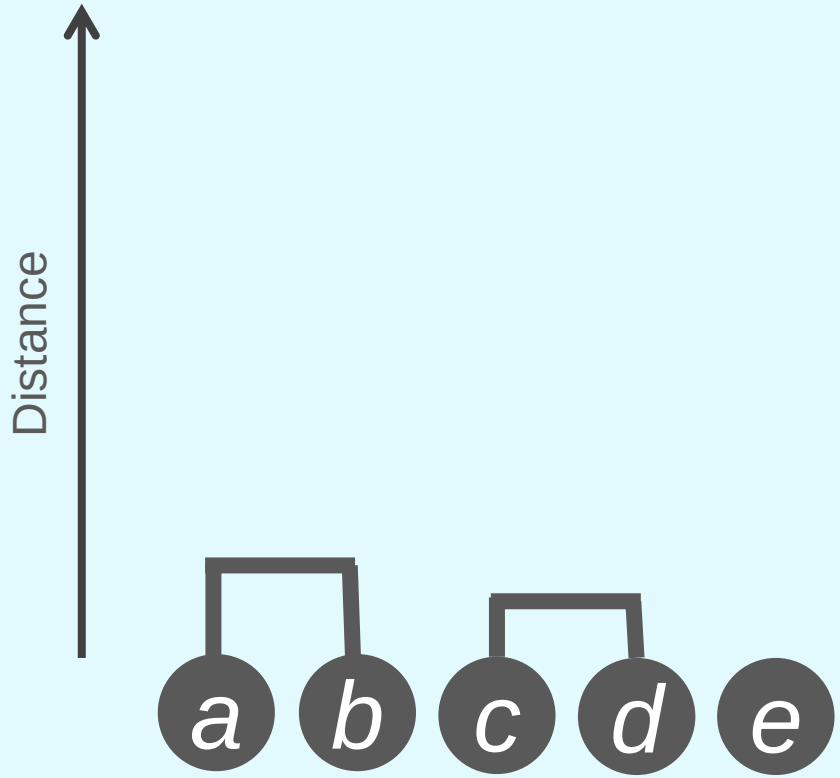


Join the two closest clusters



Agglomerative Clustering

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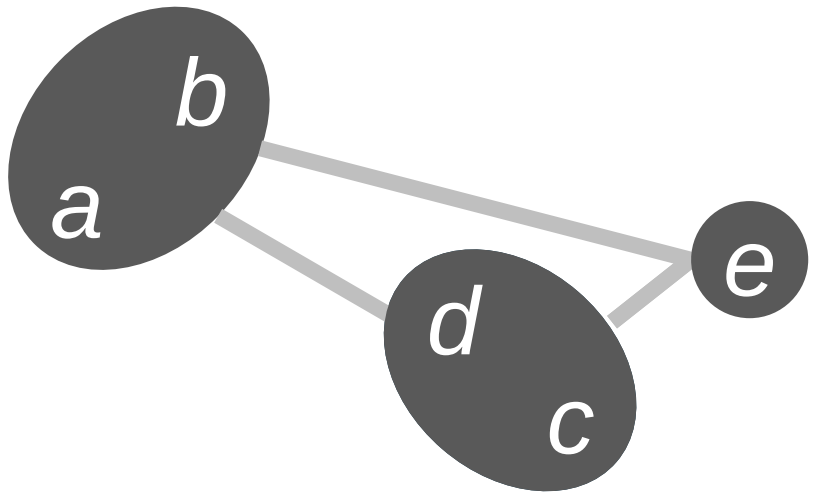

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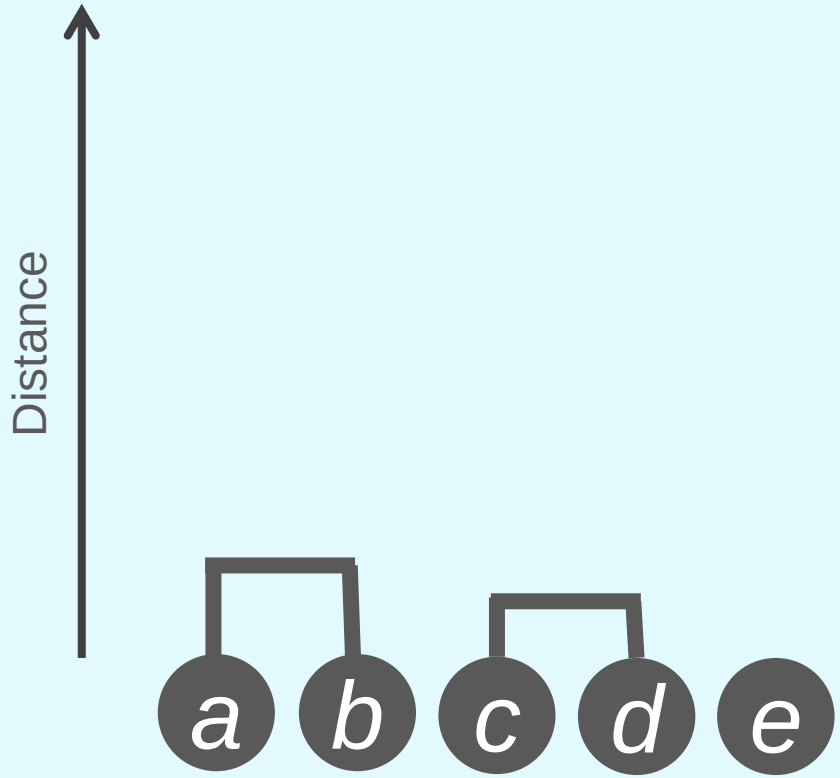

Agglomerative Clustering

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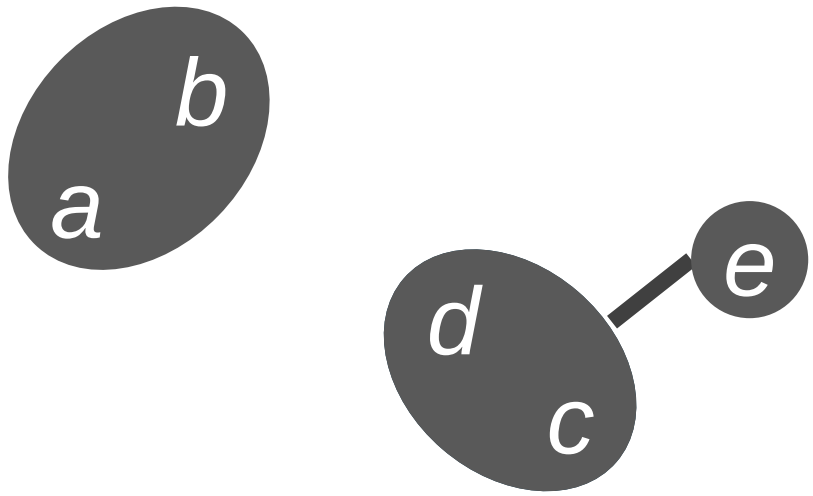

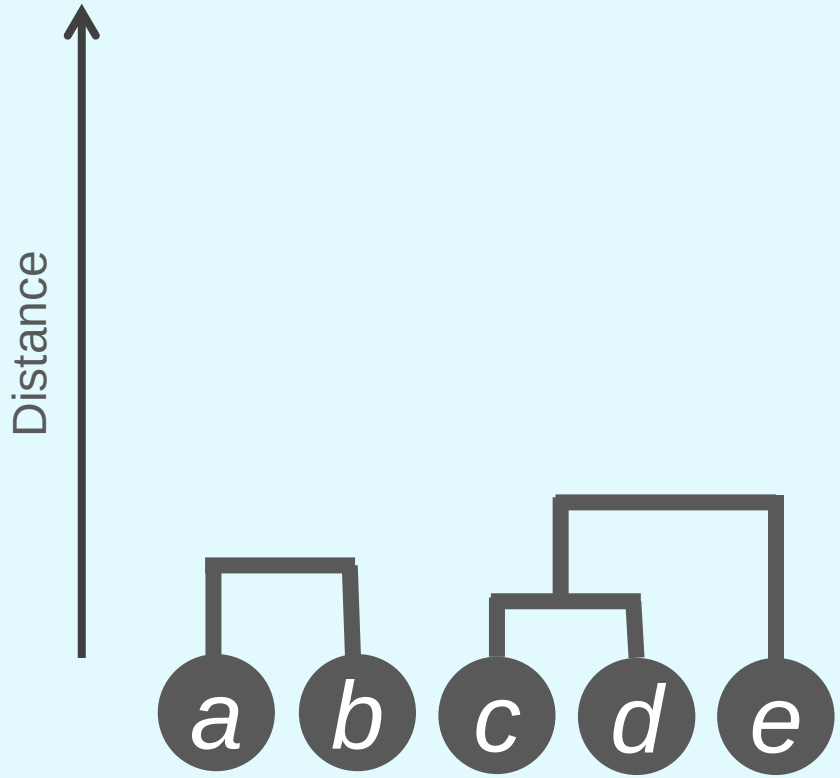

Join the two closest objects/clusters

Agglomerative Clustering

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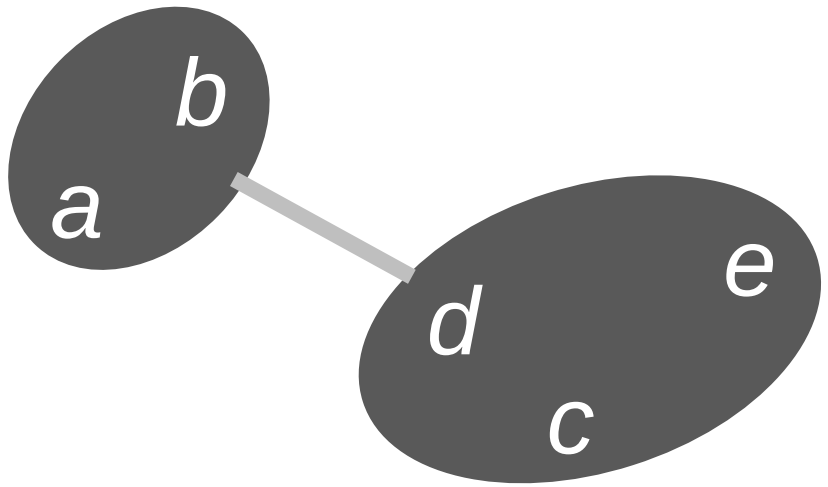

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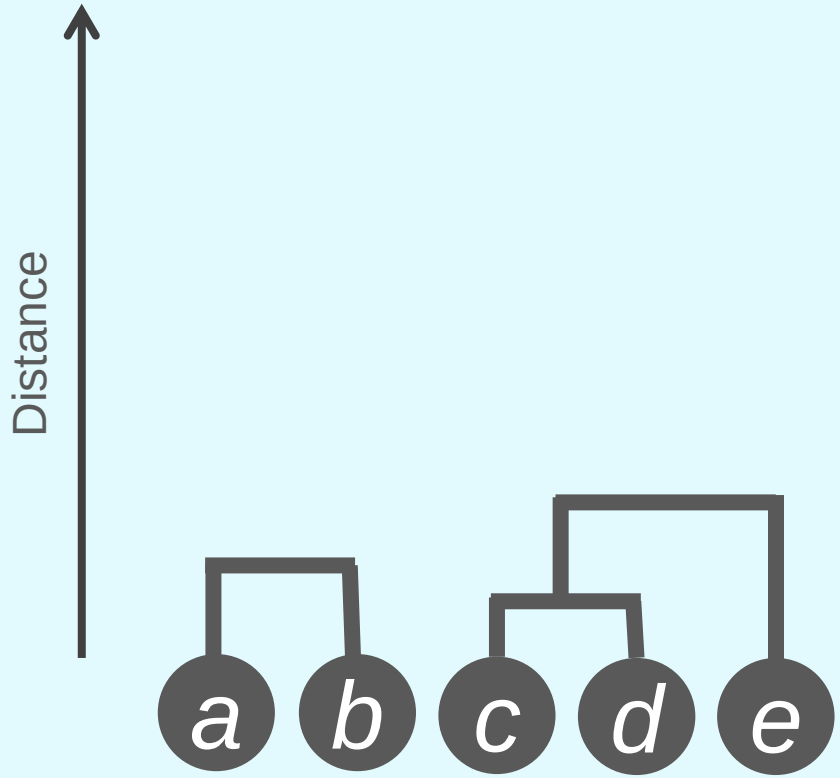

Agglomerative Clustering

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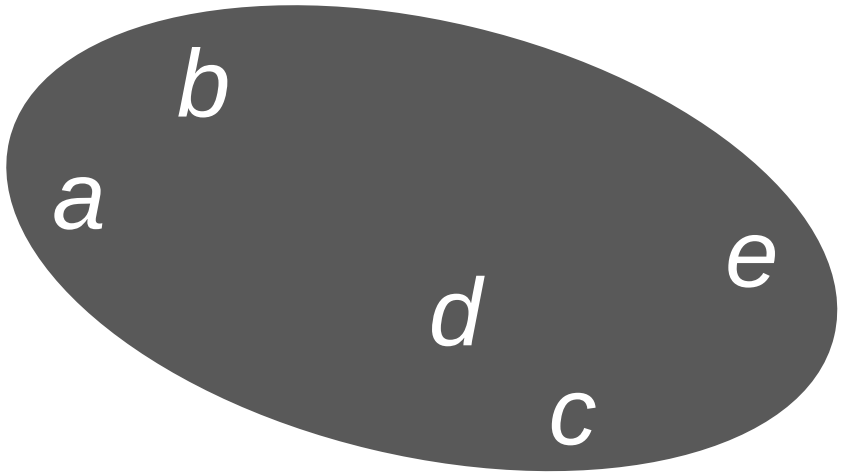
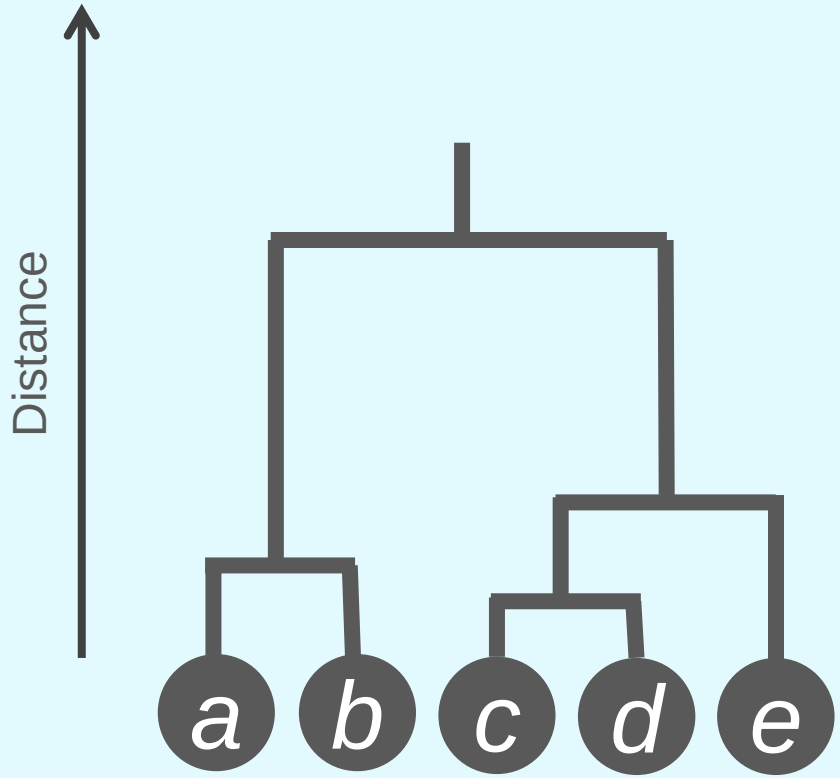


Join the two closest objects/clusters



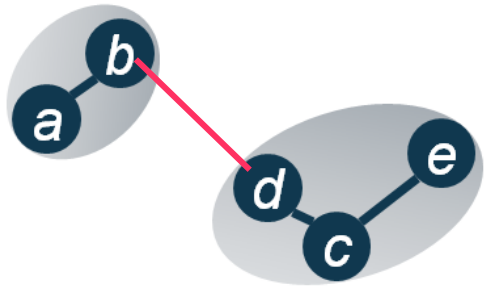
$a \rightarrow b \rightarrow c \rightarrow d \rightarrow e$

Distances between two clusters

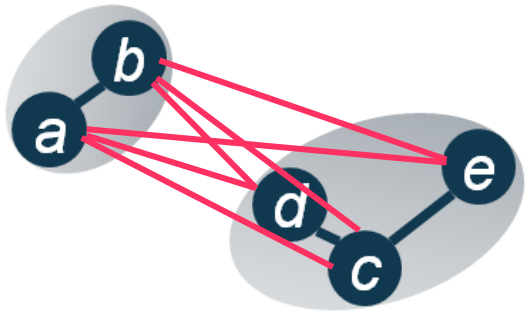
Linkage schemes

There are different methods to calculate the distance between two clusters containing multiple data points

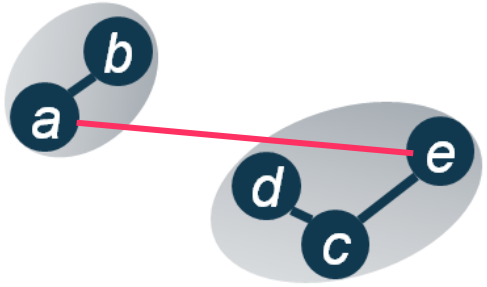
Single linkage



Average linkage



Complete linkage

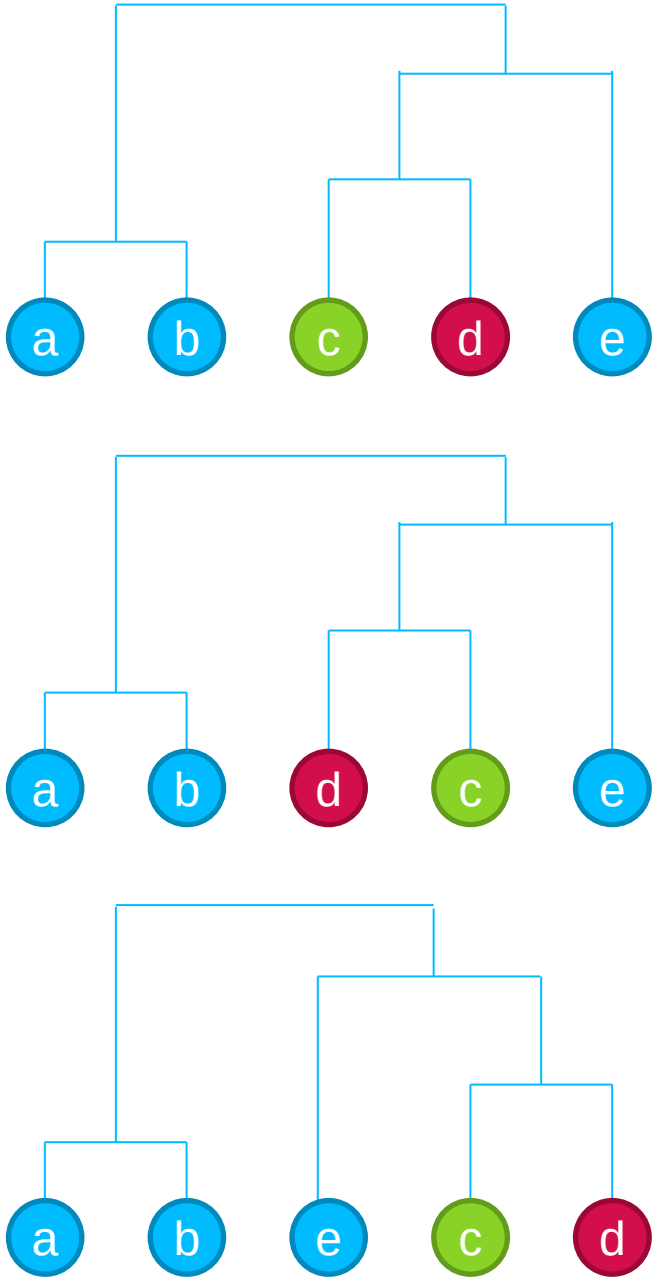


Ward linkage: $d(A,B) = \underbrace{\sum_{i \in A \cup B} d(x_i, m_{A \cup B})}_{\text{variance of the joint cluster A} \cup B} - \underbrace{\sum_{i \in A} d(x_i, m_A)}_{\text{variance of cluster } A} - \underbrace{\sum_{i \in B} d(x_i, m_B)}_{\text{variance of cluster } B}$

d : distance measure
m_j: center of cluster j

Dendrogram

- A dendrogram is a graphical tool to display the results of hierarchical clustering
- The order of leafs can be used for sorting the subjects in the Megaplots display
- BUT: a dendrogram is not unique!
  There are 2^{n-1} possible orderings consistent with the tree structure
- Rotation methods are used to sort leafs such that neighbored leafs are most similar



Rotation Methods for Dendrograms

Optimal Leaf Ordering **OLO**:

- Idea: Maximize the sum of the similarity of adjacent elements
- Problem definition:
  - Tree T with $n-1$ internal leafs nodes, that can be flipped
  - Φ space of 2^{n-1} possible orderings
  - For $\phi \in \Phi$ define $D^{\phi}(T) = \sum_{i=1}^{n-1} S(z_{\phi_i}, z_{\phi_{i+1}})$
  - z_{ϕ_i} is the i^{th} leaf when T is ordered according to ϕ and S measures the similarity
  - → Maximize $D^{\phi}(T)$

Gravaeus Wainer Heuristic **GW**:

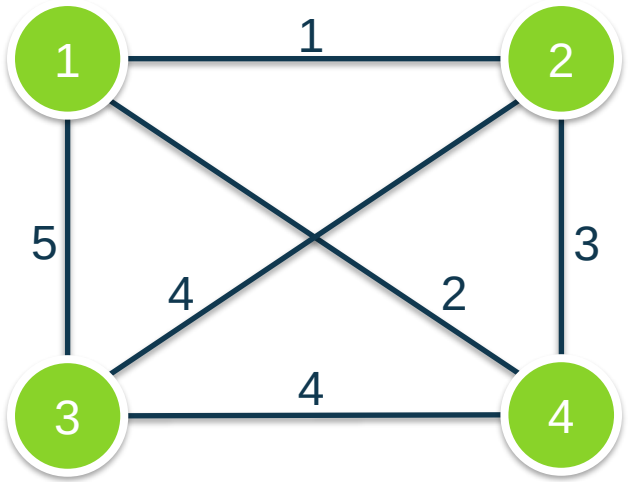
- Idea: Order the branches of the dendrogram in such way that the subjects at the edge of adjacent subtrees are most similar
- Minimizes hamiltonian path length
- Produces an unique order
- Faster than OLO but less optimal

Distance Matrix as a Graph

- With a chosen distance measure, we get pairwise distances between all subjects
- Let d_{ij} be the distance between subject i and subject j
- Distance matrix $D = (d_{ij})_{i,j=1,\dots,n}$

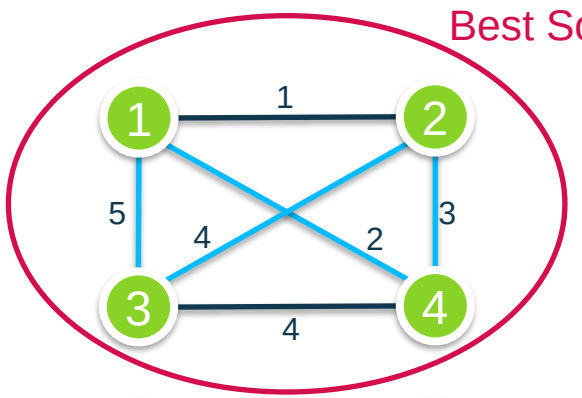
$$\mathrm{D} = \begin{pmatrix} 0 & 1 & 5 & 2 \\ 1 & 0 & 4 & 3 \\ 5 & 4 & 0 & 4 \\ 2 & 3 & 4 & 0 \end{pmatrix}$$

- Display distance matrix as undirected graph with subjects as vertices and distances as weights at the edges between the two vertices

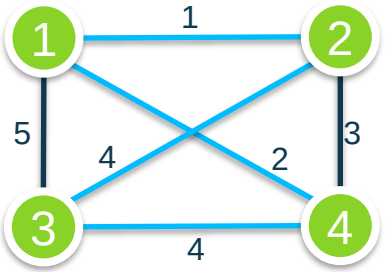


Traveling Salesperson Problem TSP

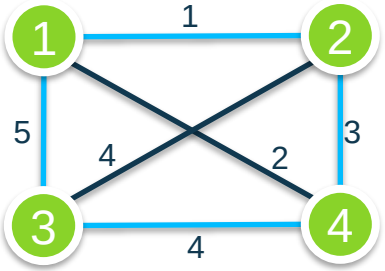
- Visit all subject-vertices once and get back to start subject
- For each edge traveled, sum up the weights → Minimize cost C
- Find the optimal route with the 2-opt technique:
  - Start with a random tour and iteratively swap out two edges represented by the distance matrix till no more improvements are possible
  - Repeat 10 times and choose best solution
- Since the output is a connected circle, find best cutting point: add dummy subject with equal distance to all other subjects and cut where the dummy city is located
- Arrange subjects in the order they where visited



C = 11



C = 14



C = 13

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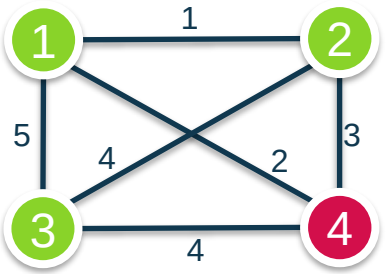
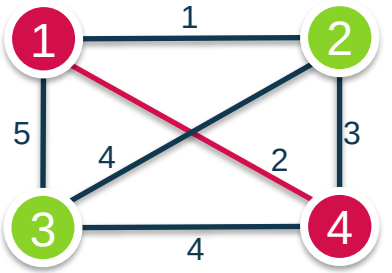
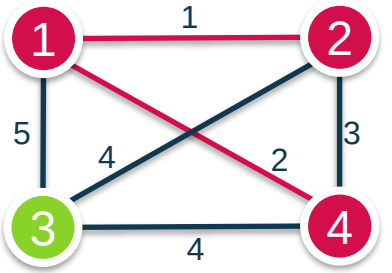
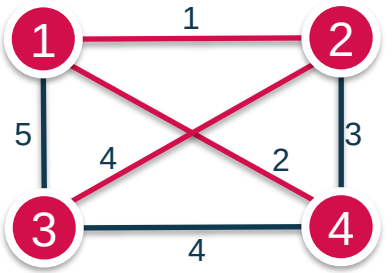
Visual Assessment of Tendency VAT

- Minimum Spanning Tree: Connects all vertices together, without any cycles and with the minimum possible total edge weight
- Prims‘s Algorithm:
  - Choose an arbitrary vertex
  - Grow the tree by one edge: find the edge that connects a new vertex to the tree with minimal edge weight and add it to the tree
  - Repeat until all vertices are part of the tree
- The order of the subjects is given by the order the subjects are added to the minimum spanning tree









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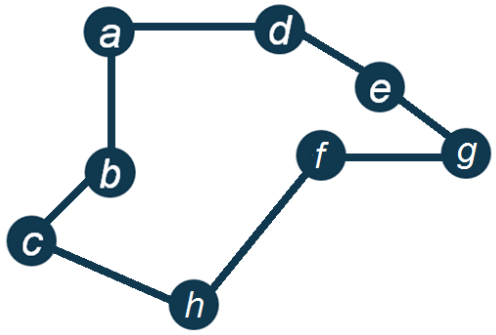
Anti-Robinson seriation by simulated annealing ARSA

- Idea:
  - For any possible seriation count the number of violations
  - Find the smallest number of violations from this concept → Choose corresponding seriation
  - In practice there are many possible seriations such that not all can be evaluated
  - → Use a partial enumeration method simulated annealing

- Number of violations
  - Get a seriation for all subjects
  - Check for each subject, if the order of the distances to the other subjects corresponds to the distance in the seriation
  - Example:
    - Seriation: $h - c - b - a - d - e - g - f$
    - e and f are more similar than f and g, but in the seriation g is between e and f
    - d and f are more similar than d and a



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